Supplementary Information

Rh(I)-Catalyzed Stereoselective Desymmetrization of Prochiral Cyclohexadienones via Highly *exo*-Selective Huisgen-Type [3+2] Cycloaddition

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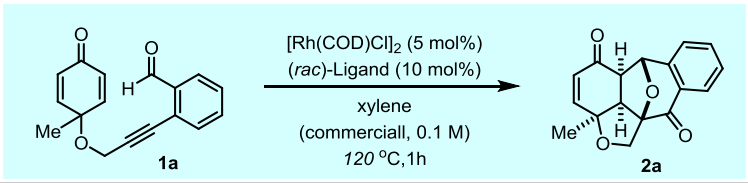
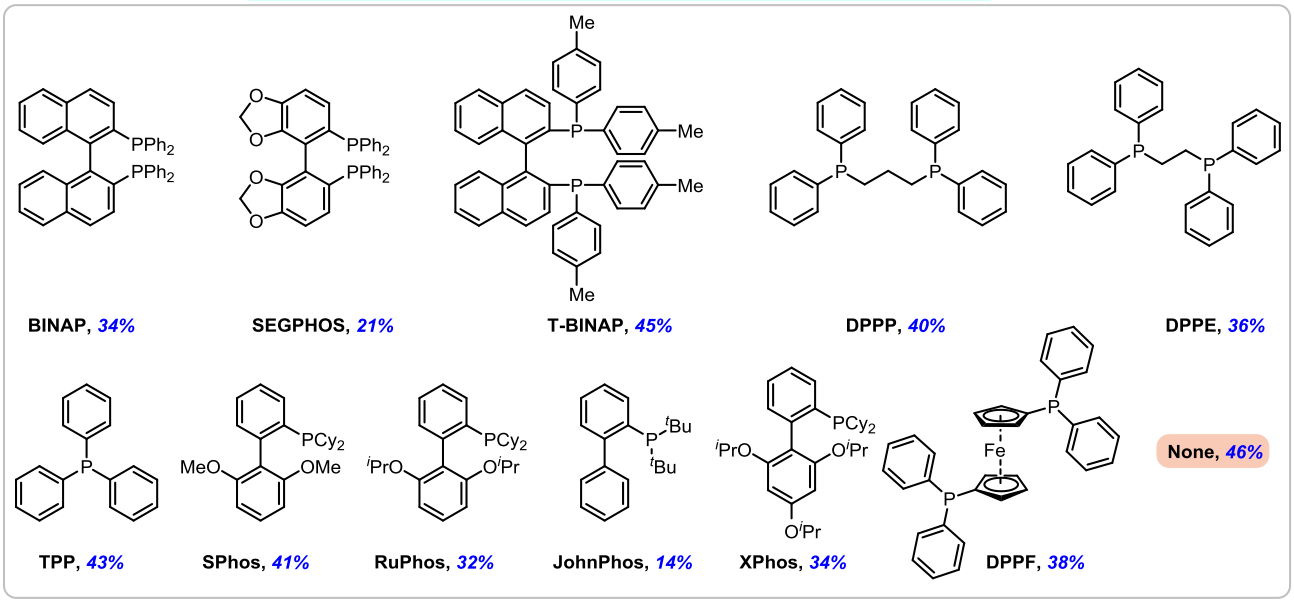
I. Complete Screening and Optimization of [3+2] cycloaddition:

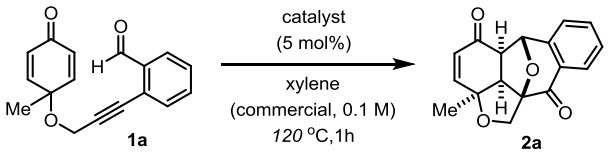
Table S1. Ligands screening for diastereoselective [3+2] cycloaddition[a]





[a]Isolated yield

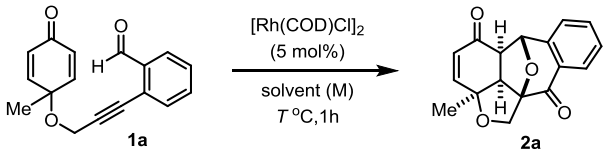
Table S2: Catalyst screening



entry	catalyst	yield [%][a]
1	$[Rh(COD)Cl]_2$	39
2	$[Ir(COD)Cl]_2$//DPPP	34
3	$Rh(COD)_2OTf$	16
4	$Rh(COD)_2SbF_6$	25
5	$[Ir(COD)Cl]_2$	21
6	$[Ru(p\text{-cymene})Cl_2]_2$	12
7	AgOTf	-[b]
8	$AgNTf_2$	-[b]
9	none	-[c]

a. Isolated yield; b. Starting meterial consumed and no product observed;
c. Starting material recovered

Table S3: Concentration, temperature and solvent screening[a,b]



entry	solvent	concentration	T °C	yield [%][c]
1	xylene	0.1 M	120	46
2	CH_2Cl_2	0.1M	50	<10
3	DCE	0.1 M	90	18
4	CH_3CN	0.1 M	80	21
5	THF	0.1M	70	32
6	dioxane	0.1 M	100	25
7	*t*-BuOH	0.1 M	85	31
8	5 % aq. xylene	0.1M	120	56
9	**H_2O**	**0.1 M**	**100**	**75**
10	H_2O	0.1 M	80	48
11	H_2O	0.2 M	100	62
12	H_2O	0.4 M	100	45
13	H_2O	0.05M	100	39
14	5 % aq. CH_2Cl_2	0.1 M	50	32
15	5 % aq. THF	0.1 M	70	38
16	5 % aq. TFT[d]	0.1 M	100	23
17	5 % aq. CH_3CN	0.1 M	100	29
18	dioxane/H_2O (5:1)	0.1 M	100	59
19	THF/H_2O (5:1)	0.1 M	100	53

a. Degassed commercial solvents used in the reaction; b. Distilled water used as a solvent; c. Isolated yields; d. α,α,α-Trifluorotoluene (TFT)

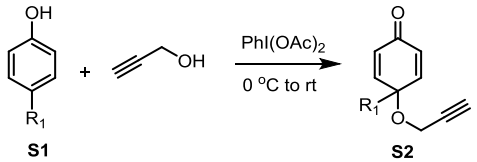
II. General details

***General information*:** Unless otherwise noted, all reagents and solvents were used as received from commercial suppliers. All catalysts and commercial ligands were purchased from Sigma-Aldrich, and used without further purification. All reactions were performed under inert atmosphere and in a flame-dried or oven-dried vessels and Teflon screw caps with magnetic stirring. Reactions were monitored using thin-layer chromatography (SiO_2). TLC plates were visualized with UV light (254 nm), iodine treatment or using *p*-anisaldehyde stain or *β*-napthol stain. Column chromatography was carried out using silica gel (100-200 mesh) packed in glass columns. NMR spectra were recorded at 300, 400, 500 MHz (H) and at 75, 100, 125, 176 MHz (C), respectively. Chemical shifts (δ) are reported in ppm, using the residual solvent peak in $CDCl_3$ (H: δ = 7.26 and C: δ = 77.16 ppm) as internal standard, and coupling constants (*J*) are given in Hz. HRMS were recorded using ESI-TOF techniques. Infrared (FT-IR) spectra were recorded on a Perkin Elmer Spectrum BX spectrophotometer, ν-max in cm^{-1}. Optical rotations were measured on JASCO P-2000 polarimeter at 20 °C using 50 mm cell of 1 mL capacity. HPLC analysis was performed on Shimadzu LC-20AD with UV detector.

III. Experimental procedures and analytical data

IIIA. Experimental procedures and analytical data of substrates

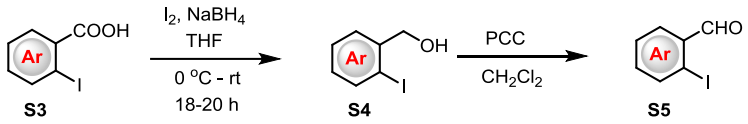
IIIAa. General procedure for the dearomatization of phenols:[1]



S1 **S2**

To a solution of the phenol **S1** (1.0 mmol) in 1 mL of propargyl alcohol was added phenyliodine(III) diacetate (1.5 mmol) in many portions at 0 °C. The resulting reaction mixture was stirred at room temperature for overnight. Then the reaction mixture was diluted with water (10 mL) and extracted with ethyl acetate (15 mL × 3). The combined organic solvent was washed with brine (15 mL), dried (Na_2SO_4), filtered, and concentrated *in vacuo*. The crude reaction mixture was purified by silica gel column chromatography (EtOAc/hexane) to give the desired product **S2**.

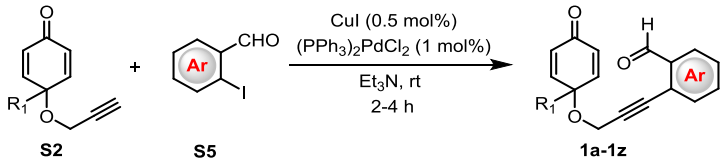
IIIAb. General Procedure for 2-iodobenzaldehydes



Following the reported procedure,[2] to a stirred solution of 2-iodobenzoic acid **S3** (15 mmol, 1 equiv) in dry THF (100 mL) was added $NaBH_4$ (60 mmol, 4 equiv) at 0 °C and a solution of iodine (15 mmol, 1 equiv) in dry THF (50 mL) was added dropwise. After that the stirring was continued for 16-24 h at room temperature and then the reaction was quenched with 1N HCl (200 mL), and the aqueous phase was extracted with Et_2O (3 x 100 mL). The combined organic phases were washed with brine and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure gave the crude product **S4** generally as a solid, which was used for next step without further purification.

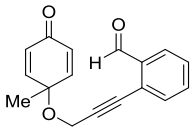
Following the reported procedure,[3] to a stirred solution of 2-iodobenzyl alcohol **S4** (15 mmol, 1.0 equiv) and SiO_2 (5.0 g) in dichloromethane was slowly added PCC (2.0 equiv) potion wise at 0 °C. The reaction mixture was stirred at room temperature for 2-3 hours. The solution was filtrated, evaporated and the residue was purified by silica gel chromatography to afford the required 2-iodobenzaldehyde **S5**. The spectral characteristics of all 2-iodobenzaldehyde derivatives were matched with the previously literature.

IIIAc. General procedure of Sonogashira coupling for the synthesis of *O*-tethered cyclohexadienones 1:[4]



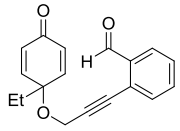
To a solution of *O*-tethered alkyne **S2** (3.0 mmol) in Et_3N (0.5 M, 6 mL) was added $Pd(PPh_3)_2Cl_2$ (21 mg, 1 mol%), CuI (2.8 mg, 0.5 mol%) and aryl iodide **S5** (3.6 mmol). The mixture was stirred at room temperature for 2-4 hours. The reaction was cooled to room temperature, water (15 mL) was added, and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic solvent was washed with 10% aqueous HCl (6 mL), dried (Na_2SO_4), filtered, and concentrated *in vacuo*. The mixture was purified by silica gel column chromatography (EtOAc/hexane) to give *O*-tethered cyclohexadienone **1a-1z** moderate to high yields.

2-(3-((1-Methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1a):



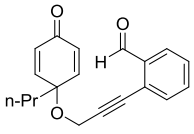
Prepared according to the general procedure as described above in 75% yield (0.59 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a white solid; mp = 81–83°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.45 (d, *J* = 0.7 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.45 – 7.41 (m, 1H), 6.87 (d, *J* = 10.2 Hz, 2H), 6.33 (d, *J* = 10.2 Hz, 2H), 4.27 (s, 2H), 1.49 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 184.9, 150.7, 136.2, 133.8, 133.5, 130.7, 129.1, 127.4, 125.8, 92.9, 82.4, 73.5, 54.4, 26.4; IR (neat): υ_{max} 3045, 2972, 2931, 2236, 1732, 1691, 1431, 1281, 954, 691 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{15}O_3$ $[M+H]^+$: 267.1021; found: 267.1021.

2-(3-((1-Ethyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1b):



Prepared according to the general procedure as described above in 82% yield (0.69 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a brown oil; ^{1}HNMR (500 MHz, $CDCl_3$) δ 10.44 (s, 1H), 7.87 (d, *J* = 7.5 Hz, 1H), 7.55 – 7.46 (m, 2H), 7.45 – 7.40 (m, 1H), 6.80 (d, *J* = 10.2 Hz, 2H), 6.38 (d, *J* = 10.2 Hz, 2H), 4.29 (s, 2H), 1.83 (q, *J* = 7.6 Hz, 2H), 0.84 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.4, 185.3, 149.9, 136.2, 133.8, 133.5, 131.9, 129.0, 127.3, 125.9, 93.1, 82.3, 77.2, 54.3, 32.3, 7.90; IR (neat): υ_{max} 3031, 2975, 2241,1722, 1671, 1423, 1059, 971, 693 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{17}O_3$ $[M+H]^+$: 281.1178; found: 281.1178.

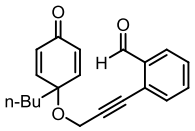
2-(3-((4-Oxo-1-propylcyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1c):



Prepared according to the general procedure as described above in 72% yield (0.63 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a yellow solid; mp = 74–76°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.40 (s, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.41 – 7.36 (m, 1H), 6.80 (d, *J* = 10.2 Hz, 2H), 6.33 (d, *J* = 10.2 Hz, 2H), 4.24 (s, 2H), 1.76 – 1.70 (m, 2H), 1.29 – 1.18 (m, 2H), 0.84 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.2, 185.1, 150.0, 136.1, 133.7, 133.3, 131.4, 128.9, 127.2, 125.8, 93.1, 82.1, 76.5, 54.1, 41.4, 16.8, 14.2.; IR (neat): υ_{max} 3049,

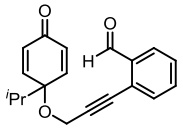
2982, 2245,1729, 1694, 1424, 1044, 964, 697 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}O_3$ $[M+H]^+$: 295.1334; found: 295.1339.

2-(3-((1-Butyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1d):



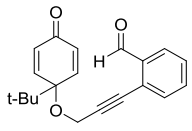
Prepared according to the general procedure as described above in 75% yield (0.69 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.43 (d, *J* = 12.3 Hz, 1H), 7.86 (dd, *J* = 13.2, 7.5 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.45 – 7.37 (m, 1H), 6.86 – 6.75 (m, 2H), 6.41 – 6.30 (m, 2H), 4.27 (d, *J* = 10.2 Hz, 2H), 1.82 – 1.71 (m, 2H), 1.34 – 1.11 (m, 4H), 0.88 – 0.78 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.4, 185.3, 150.2, 136.2, 133.8, 133.5, 131.6, 129.1, 127.4, 125.9, 93.1, 82.3, 76.7, 54.2, 39.2, 25.6, 22.9, 13.9; IR (neat): υ_{max} 3064, 2924, 2224, 1725,1691, 1457, 1057, 964, 693 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}O_3$ $[M+H]^+$: 309.1491; found: 309.1505.

2-(3-((1-Isopropyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1e):



Prepared according to the general procedure as described above in 84% yield (0.74 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a white solid; mp = 59–61°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.44 (d, *J* = 3.0 Hz, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.44 – 7.39 (m, 1H), 6.81 (d, *J* = 10.3 Hz, 2H), 6.41 (d, *J* = 10.3 Hz, 2H), 4.28 – 4.24 (m, 2H), 2.08 – 2.02 (m, 1H), 0.96 – 0.94 (m, 3H), 0.94 – 0.92 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.4, 185.4, 149.0, 136.1, 133.8, 133.4, 132.4, 129.0, 127.3, 125.9, 93.3, 82.1, 79.1, 54.2, 36.6, 17.1; IR (neat): υ_{max} 3091, 2931, 2237, 1734, 1694, 1444, 1259, 931, 751 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}O_3$ $[M+H]^+$: 295.1334; found: 295.1335.

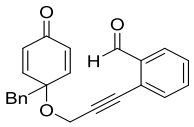
2-(3-((1-(*tert*-Butyl)-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1f):



Prepared according to the general procedure as described above in 65% yield (0.6 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a white solid; mp = 93–95°C; ^{1}H

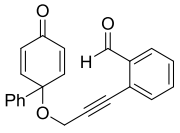
NMR (400 MHz, $CDCl_3$) δ 10.47 (d, *J* = 0.6 Hz, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.57 – 7.50 (m, 2H), 7.47 – 7.42 (m, 1H), 7.00 (d, *J* = 10.3 Hz, 2H), 6.43 (d, *J* = 10.3Hz, 2H), 4.27 (s, 2H), 1.05 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.6, 185.0, 149.5, 136.2, 133.9, 133.5, 132.5, 129.0, 127.4, 126.1, 93.7, 82.1, 80.6, 54.5, 39.7, 25.8; IR (neat): υ_{max} 3020, 2931, 2236, 1720, 1671, 1495, 1215, 940, 729, 654 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{20}O_3Na$ $[M+Na]^+$: 331.1310; found: 331.1317

2-(3-((1-Benzyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1g):



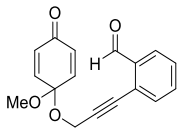
Prepared according to the general procedure as described above in 57% yield (0.58 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford as a reddish viscous oil; ^1H NMR (500 MHz, $CDCl_3$) δ 10.45 (s, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.57 – 7.50 (m, 2H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.29 – 7.23 (m, 3H), 7.20 – 7.17 (m, 2H), 6.85 (d, *J* = 10.2 Hz, 2H), 6.32 (d, *J* = 10.2 Hz, 2H), 4.30 (s, 2H), 3.09 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 184.9, 149.6, 136.2, 134.4, 133.8, 133.4, 131.5, 130.8, 129.0, 128.1, 127.4, 127.3, 125.9, 93.1, 82.4, 76.3, 54.4, 46.3; IR (neat): υ_{max} 3028, 2969, 2234, 1732, 1672, 1454, 1051, 959, 752, 693 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{19}O_3$ $[M+H]^+$: 343.1334; found: 343.1337.

2-(3-((4-Oxo-[1,1'-biphenyl]-1(4H)-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1h):



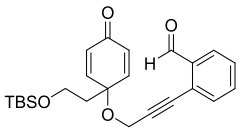
Prepared according to the general procedure as described above in 63% yield (0.62 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a white solid; mp = 117–119°C; ^1H NMR (500 MHz, $CDCl_3$) δ 10.50 (s, 1H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.58 – 7.54 (m, 2H), 7.52 – 7.45 (m, 3H), 7.40 – 7.36 (m, 2H), 7.35 – 7.31 (m, 1H), 6.94 (d, *J* = 10.3 Hz, 2H), 6.44 (d, *J* = 10.3 Hz, 2H), 4.54 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 185.4, 149.5, 137.6, 136.3, 133.9, 133.6, 130.2, 129.2, 129.0, 128.8, 127.5, 125.9, 93.0, 82.7, 77.2, 54.3; IR (neat): υ_{max} 3020, 2883, 2403,1725, 1681, 1452, 1215, 940, 769, 654 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{17}O_3$ $[M+H]^+$: 329.1178; found: 329.1182.

2-(3-((1-Methoxy-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1i):



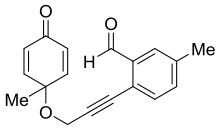
Prepared according to the general procedure as described above in 52% yield (0.44 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a yellow solid; mp = 90–92°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.45 (d, *J* = 0.7 Hz, 1H), 7.89 (d, *J* = 7.7 Hz, 1H), 7.56 – 7.50 (m, 2H), 7.47 – 7.41 (m, 1H), 6.90 (d, *J* = 10.4 Hz, 2H), 6.29 (d, *J* = 10.2 Hz, 2H), 4.58 (s, 2H), 3.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.3, 184.9, 142.5, 136.2, 133.8, 133.5, 130.0, 129.1, 127.5, 125.7, 93.0, 92.2, 82.2, 51.5, 50.9; IR (neat): υ_{max} 3031, 2874, 2403, 1721, 1675, 1449, 1058, 764, 657 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{15}O_4$ $[M+H]^+$: 283.0970; found: 283.0976.

2-(3-((1-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1j):



Prepared according to the general procedure as described above in 67% yield (0.82 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.44 (s, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.48 (m, 2H), 7.45 – 7.40 (m, 1H), 6.90 (d, *J* = 10.2 Hz, 2H), 6.33 (d, *J* = 10.2 Hz, 2H), 4.26 (s, 2H), 3.70 (t, *J* = 6.1 Hz, 2H), 2.01 (t, *J* = 6.1 Hz, 2H), 0.83 (s, 9H), -0.01 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.4, 185.3, 150.1, 136.2, 133.8, 133.5, 130.9, 129.0, 127.3, 125.9, 93.0, 82.3, 75.2, 57.9, 54.0, 42.9, 25.9, 18.2, -5.4; IR (neat): υ_{max} 3029, 2931, 2417, 1725, 1674, 1457, 1276, 1081, 764, 657 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{31}O_4Si$ $[M+H]^+$: 411.1992; found: 411.2027.

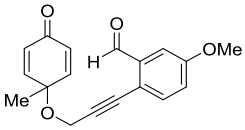
5-Methyl-2-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1k):



Prepared according to the general procedure as described above in 75% yield (0.63 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.35 (s, 1H), 7.62 (s, 1H), 7.35 (d, *J* = 7.9 Hz, 1H), 7.28 (dd, *J* = 7.9, 1.2 Hz, 1H), 6.82 (d, *J* = 10.2 Hz, 2H), 6.27 (d, *J* = 10.2 Hz, 2H), 4.21 (s, 2H), 2.31 (s, 3H), 1.44 (s, 3H); ^{13}C NMR

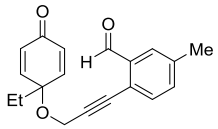
(101 MHz, $CDCl_3$) δ 191.3, 184.7, 150.6, 139.3, 135.9, 134.5, 133.2, 130.4, 127.5, 122.9, 92.0, 82.3, 73.2, 54.3, 26.2, 21.2; IR (neat): υ_{max} 3054, 2962, 2305,1724, 1671, 1442, 1265, 759, 691 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{17}O_3$ $[M+H]^+$: 281.1178; found: 281.1181.

5-Methoxy-2-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benz aldehyde (1m):



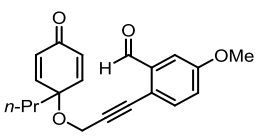
Prepared according to the general procedure as described above in 85% yield (0.75 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a white solid; mp = 96–98 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 10.41 (d, *J* = 1.9 Hz, 1H), 7.43 (d, *J* = 8.6 Hz, 1H), 7.36 (t, *J* = 3.8 Hz, 1H), 7.10 – 7.05 (m, 1H), 6.86 (d, *J* = 10.2 Hz, 2H), 6.32 (d, *J* = 10.2 Hz, 2H), 4.25 (s, 2H), 3.83 (s, 3H), 1.49 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.3, 185.0, 160.1, 150.8, 137.7, 134.9, 130.6, 121.6, 118.5, 110.1, 91.3, 82.3, 73.4, 55.7, 54.5, 26.4; IR (neat): υ_{max} 3022, 2952, 2403, 1724, 1694, 1459, 1254, 769, 654 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{17}O_4$ $[M+H]^+$: 297.1127; found: 297.1129.

2-(3-((1-Ethyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)-5-methylbenzaldehyde (1n):



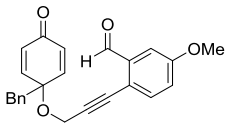
Prepared according to the general procedure as described above in 82% yield (0.71 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a light yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 10.41 (s, 1H), 7.68 (s, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 6.80 (d, *J* = 10.1 Hz, 2H), 6.38 (d, *J* = 10.1 Hz, 2H), 4.27 (s, 2H), 2.37 (s, 3H), 1.83 (q, *J* = 7.6 Hz, 2H), 0.83 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.6, 185.3, 150.0, 139.5, 136.1, 134.7, 133.4, 131.8, 127.7, 123.1, 92.2, 82.4, 77.2, 54.4, 32.3, 21.4, 7.9; IR (neat): υ_{max} 3045, 2945, 2405, 1722, 1693, 1447, 1254, 765, 694 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}O_3$ $[M+H]^+$: 295.1334; found: 295.1336.

5-Methoxy-2-(3-((4-oxo-1-propylcyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1o):



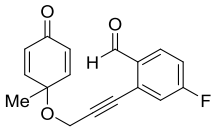
Prepared according to the general procedure as described above in 65% yield (0.63 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.43 (s, 1H), 7.45 (d, *J* = 8.6 Hz, 1H), 7.38 (d, *J* = 2.8 Hz, 1H), 7.10 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.84 (d, *J* = 10.2 Hz, 2H), 6.38 (d, *J* = 10.2 Hz, 2H), 4.28 (s, 2H), 3.86 (s, 3H), 1.81 – 1.76 (m, 2H), 1.33 – 1.28 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.5, 185.4, 160.2, 150.3, 137.8, 134.9, 131.6, 121.7, 118.7, 110.1, 91.6, 82.3, 76.7, 55.8, 54.4, 41.7, 17.0, 14.4; IR (neat): υ_{max} 3043, 2945, 2436, 1724, 1685, 1431, 1264, 1087, 761, 671 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}O_4$ $[M+H]^+$: 325.1440; found: 325.1440.

2-(3-((1-Benzyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)-5-methoxy benz aldehyde (1p):



Prepared according to the general procedure as described above in 71% yield (0.79 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a white solid; mp = 210–212°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.42 (s, 1H), 7.44 (d, *J* = 8.5 Hz, 1H), 7.39 (d, *J* = 2.8 Hz, 1H), 7.29 – 7.23 (m, 3H), 7.18 (dd, *J* = 7.7, 1.6 Hz, 2H), 7.10 (dd, *J* = 8.5, 2.8 Hz, 1H), 6.84 (d, *J* = 10.3 Hz, 2H), 6.31 (d, *J* = 10.3 Hz, 2H), 4.28 (s, 2H), 3.87 (s, 3H), 3.09 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 185.1, 160.2, 149.7, 137.8, 134.9, 134.5, 131.5, 130.9, 128.2, 127.4, 121.7, 118.7, 110.0, 91.5, 82.4, 76.4, 55.8, 54.6, 46.4; IR (neat): υ_{max} 3029, 2934, 2424,1721, 1671, 1459, 1274, 1075, 749, 654 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{21}O_4$ $[M+H]^+$: 373.1440; found: 373.1444.

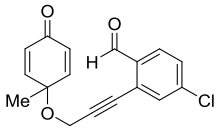
4-Fluoro-2-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benz aldehyde (1q):



Prepared according to the general procedure as described above in 52% yield (0.44 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a yellow solid; mp = 110–112°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.34 (s, 1H), 7.93 – 7.86 (m, 1H), 7.15 (dd, *J* = 19.3, 10.3 Hz, 2H), 6.84 (dd, *J* = 10.3, 2.2 Hz, 2H), 6.31 (dd, *J* = 10.2, 3.5 Hz, 2H), 4.24 (s, 2H), 1.49 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.7, 184.8, 165.6 (d, J_{CF} = 257.1 Hz), 150.4, 132.9 (d, J_{CF} = 1.9 Hz), 130.7, 130.2 (d, J_{CF} = 10.1 Hz), 128.3 (d, J_{CF} = 10.9 Hz), 120.0 (d, J_{CF} = 23.6 Hz), 117.0 (d, J_{CF} = 22.1 Hz), 94.0, 81.1 (d, J_{CF} = 2.2 Hz), 73.5, 54.2, 26.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -102.96 (s, 1F); IR (neat):

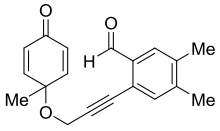
υ_{max} 3039, 2941, 2401, 1727, 1672, 1454, 1274, 764, 661 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{14}O_3F$ $[M+H]^+$: 285.0927; found: 285.0926.

4-Chloro-2-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benz aldehyde (1r):



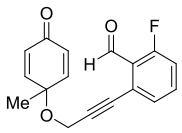
Prepared according to the general procedure as described above in 69% yield (0.62 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a white solid; mp = 90–92°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.38 (d, *J* = 0.8 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.51 (d, *J* = 2.0 Hz, 1H), 7.41 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.86 (d, *J* = 10.2 Hz, 2H), 6.34 (d, *J* = 10.2 Hz, 2H), 4.26 (s, 2H), 1.50 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.1, 184.9, 150.5, 140.3, 134.6, 133.2, 130.8, 129.7, 128.8, 127.3, 94.1, 81.1, 73.5, 54.3, 26.4; IR (neat): υ_{max} 3047, 2935, 2407, 1727, 1694, 1452, 1231, 707, 669 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{14}O_3Cl$ $[M+H]^+$: 301.0631; found: 301.0634.

4,5-Dimethyl-2-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1s):



Prepared according to the general procedure as described above in 72% yield (0.63 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a white solid; mp = 97–99°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.37 (d, 1H), 7.66 (s, 1H), 7.30 (s, 1H), 6.88 (d, *J* = 10.2 Hz, 2H), 6.34 (dd, *J* = 9.9, 1.2 Hz, 2H), 4.26 (s, 2H), 2.30 (s, 3H), 2.29 (s, 3H), 1.51 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.4, 185.0, 150.8, 143.9, 138.5, 134.4, 134.3, 130.7, 128.3, 123.4, 91.7, 82.7, 73.5, 54.6, 26.5, 20.1, 19.8; IR (neat): υ_{max} 3029, 2951, 2431, 1723, 1695, 1435, 1256, 779, 671 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}O_3$ $[M+H]^+$: 295.1334; found: 295.1335.

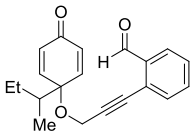
2-Fluoro-6-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1t):



Prepared according to the general procedure as described above in 65% yield (0.55 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.46 (s, 1H), 7.49 (td, *J* = 8.1, 5.4 Hz, 1H), 7.32 (d, *J* = 7.7 Hz, 1H), 7.13 (dd, *J* =

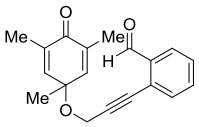
9.9, 8.6 Hz, 1H), 6.90 (d, *J* = 10.2 Hz, 2H), 6.33 (d, *J* = 10.2 Hz, 2H), 4.27 (s, 2H), 1.51 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.0, 185.1, 163.0 (d, J_{CF} = 262.3 Hz), 150.8, 135.0 (d, J_{CF} = 10.5 Hz), 130.8, 130.0 (d, J_{CF} = 3.2 Hz), 126.0 (d, J_{CF} = 2.7 Hz), 124.7 (d, J_{CF} = 8.2 Hz), 117.3 (d, J_{CF} = 21.4 Hz), 93.5, 82.7 (d, J_{CF} = 4.0 Hz), 73.6, 54.5, 26.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.42 (s, 1F); IR (neat): υ_{max} 3049, 2943, 2409, 1725,1694, 1431, 1254, 759, 694 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{14}O_3F[M+H]^+$: 285.0927; found: 285.0928.

2-(3-((1-(*sec*-Butyl)-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1u):



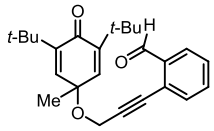
Prepared according to the general procedure as described above in 75% yield (0.69 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.44 (d, *J* = 1.9 Hz, 1H), 7.87 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.55 – 7.46 (m, 2H), 7.41 (t, *J* = 7.1 Hz, 1H), 6.79 (d, *J* = 10.1 Hz, 2H), 6.40 (dd, *J* = 9.8, 8.8 Hz, 2H), 4.26 (d, *J* = 2.1 Hz, 2H), 1.86 – 1.69 (m, 2H), 1.24 – 1.13 (m, 1H), 0.92 – 0.89 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 185.5, 149.4, 149.0, 136.2, 133.8, 133.4, 132.5, 132.1, 129.0, 127.3, 126.0, 93.4, 82.1, 79.3, 54.1, 43.5, 23.8, 13.4, 12.5; IR (neat): υ_{max} 3045, 2945, 2403, 1723, 1696, 1431, 1231, 765, 671 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}O_3$ $[M+H]^+$: 309.1491; found: 309.1492.

2-(3-((1,3,5-Trimethyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1v):



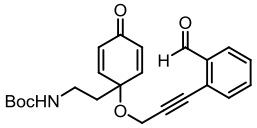
Prepared according to the general procedure as described above in 76% yield (0.67 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.4) to afford a white solid; mp = 73–75°C;^{1}H NMR (500 MHz, $CDCl_3$) δ 10.45 (s, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.58 – 7.47 (m, 2H), 7.45 – 7.38 (m, 1H), 6.58 (s, 2H), 4.21 (s, 2H), 1.89 (s, 6H), 1.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.5, 186.4, 145.7, 137.1, 136.2, 133.8, 133.5, 129.0, 127.3, 126.1, 93.6, 81.9, 73.4, 53.8, 26.6, 16.1; IR (neat): υ_{max} 3031, 2945, 2467, 1723, 1694, 1452, 1279, 765, 654 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}O_3$ $[M+H]^+$: 295.1334; found: 295.1339.

2-(3-((3,5-Di-*tert*-butyl-1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1w):



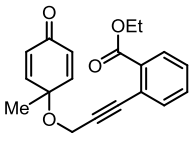
Prepared according to the general procedure as described above in 55% yield (0.62 g). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.5) to afford a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.51 (d, *J* = 0.8 Hz, 1H), 7.91 (d, *J* = 7.7 Hz, 1H), 7.55 (d, *J* = 3.9 Hz, 2H), 7.44 (dddd, *J* = 12.7,7.9, 3.9, 0.7 Hz, 1H), 6.52 (s, 2H), 4.18 (s, 2H), 1.45 (s, 3H), 1.23 (s, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.7, 185.8, 149.3, 141.6, 136.2, 133.9, 133.5, 129.0, 127.4, 126.2, 93.8, 81.7, 73.4, 53.5, 35.1, 29.7, 27.4; IR (neat): υ_{max} 3029, 2931, 2403, 1725, 1694, 1453, 1275, 794, 661 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{30}O_3Na$ $[M+Na]^+$: 401.2093 ; found: 401.2119.

***tert*-Butyl (2-(1-((3-(2-formylphenyl)prop-2-yn-1-yl)oxy)-4-oxocyclohexa-2,5-dien-1-yl)ethyl)carbamate (1x):**



Prepared according to the general procedure as described above in 62% yield (0.73 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a light yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.45 – 10.37 (m, 1H), 7.86 (t, *J* = 6.3 Hz, 1H), 7.56 – 7.38 (m, 3H), 6.88 (d, *J* = 9.7 Hz, 2H), 6.44 – 6.30 (m, 2H), 4.87 (br.s, 1H), 4.33 – 4.19 (m, 2H), 3.24 – 3.12 (m, 2H), 2.05 – 1.94 (m, 2H), 1.38 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 184.8, 155.8, 149.1, 136.2, 133.9, 133.5, 131.7, 129.1, 127.5, 125.7, 92.7, 82.6, 75.4, 54.2, 39.8, 36.0, 28.4; IR (neat): υ_{max} 3243, 2931, 2403, 1725, 1706, 1694, 1453, 1275, 794, 661 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{26}NO_5$ $[M+H]^+$: 396.1815; found: 396.1815.

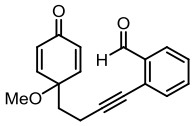
Ethyl 2-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzoate(1y):



Prepared according to the general procedure as described above in 84% yield (0.78 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.50 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.42 (td, *J* = 7.6, 1.4 Hz, 1H), 7.35 (td, *J* = 7.7, 1.3 Hz, 1H), 6.91 (d, *J* = 10.2 Hz, 2H), 6.30 (d, *J* = 10.2 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 4.26 (s, 2H), 1.48 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.2,

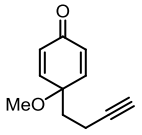
166.0, 151.2, 134.2, 132.2, 131.6, 130.4, 130.3, 128.3, 122.9, 90.9, 85.4, 73.4, 61.3, 54.8, 26.4, 14.3; IR (neat): υ_{max} 3029, 2931, 2403, 1725, 1694, 1453, 1275, 1094 794, 661 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}O_4$ $[M+H]^+$: 311.1283 ; found: 311.1286.

2-(4-(1-methyl-4-oxocyclohexa-2,5-dien-1-yl)but-1-yn-1-yl)benzaldehyde (1z):



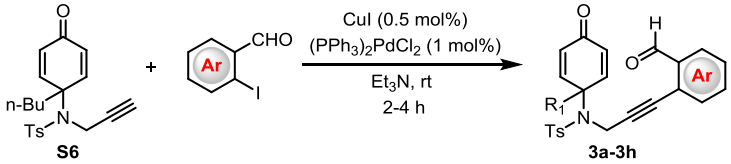
Prepared according to the general procedure as described above in 75% yield (0.59 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a reddish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.46 (s, 1H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.56 – 7.49 (m, 1H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 10.3 Hz, 2H), 6.41 (d, *J* = 10.2 Hz, 2H), 3.24 (s, 3H), 2.55 (t, *J* = 7.8 Hz, 2H), 2.09 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.0, 185.2, 150.2, 136.2, 133.9, 133.4, 132.1, 128.4, 127.3, 96.5, 75.0, 53.3, 38.6, 14.6; IR (neat): υ_{max} 3029, 2931, 2403, 1725, 1694, 1453,1093, 794, 661 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{17}O_3$[M+H]$^+$: 281.1178; found: 281.1186.

Note: Below *C*-tethered alkyne was prepared according to a previously reported procedure.[5]



C-tethered alkyne

IIIAd. General procedure of Sonogashira coupling for the synthesis of *N*-tethered cyclohexadienones 3:[4]



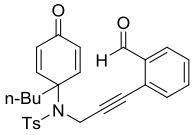
Modified procedure:

To a solution of *NTs*-tethered alkyne **S6**[6] (1.5 mmol) in degassed Et_3N (0.5 M, 3 mL) and DMSO (30µL) was added $Pd(PPh_3)_2Cl_2$(11 mg, 1 mol%), CuI (1.4 mg, 0.5 mol%), aryl iodide (1.8 mmol) and one drop of DMF. The mixture was stirred at room temperature for 2-4 hours. The reaction was cooled to room temperature, water (15 mL) was added, and the mixture was extracted with EtOAc (3 × 6 mL). The combined organic solvent was washed with 10% aqueous HCl (3 mL), dried (Na_2SO_4), filtered,

and concentrated *in vacuo*. The mixture was purified by silica gel column chromatography (EtOAc/hexane) to give *N*-tethered cyclohexadienone **3** moderate to high yields.

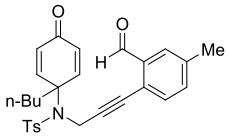
NBoc-Tethered Alkynes **S6′** was prepared according to a previously reported procedure.[7]

_N_-(1-Butyl-4-oxocyclohexa-2,5-dien-1-yl)-N-(3-(2-formylphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (3a):



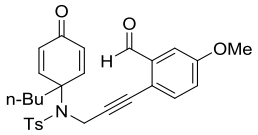
Prepared according to the general procedure as described above in 63% yield (0.43 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.29 (s, 1H), 7.91 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.81 (d, *J* = 8.3 Hz, 2H), 7.57 (td, *J* = 7.5, 1.4 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 10.2 Hz, 2H), 6.27 (d, *J* = 10.2 Hz, 2H), 4.56 (s, 2H), 2.39 (s, 3H), 2.07 – 2.00 (m, 2H), 1.25 – 1.18 (m, 2H), 1.13 – 1.06 (m, 2H), 0.79 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.0, 185.0, 149.5, 144.3, 138.8, 136.4, 133.9, 133.6, 129.8, 129.3, 128.1, 127.9, 125.4, 92.8, 81.3, 64.3, 37.1, 36.6, 26.3, 22.7, 21.7, 13.9; IR (neat): υ_{max} 3029, 2974, 2416, 1725, 1673, 1451, 1257, 754, 694 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{28}NO_4S$ $[M+H]^+$: 462.1739; found: 462.1742.

_N_-(1-Butyl-4-oxocyclohexa-2,5-dien-1-yl)-N-(3-(2-formyl-4-methylphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (3b):



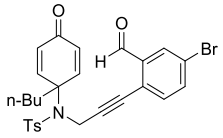
Prepared according to the general procedure as described above in 68% yield (0.48 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.25 (s, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.71 (s, 1H), 7.38 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 7.25 (d, *J* = 7.9 Hz, 2H), 6.99 (d, *J* = 10.3 Hz, 2H), 6.25 (d, *J* = 10.2 Hz, 2H), 4.55 (s, 2H), 2.42 (s, 3H), 2.39 (s, 3H), 2.07 – 2.00 (m, 2H), 1.24 – 1.18 (m, 2H), 1.12 – 1.07 (m, 2H), 0.79 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.2, 185.0, 149.6, 144.3, 139.8, 138.7, 136.3, 134.8, 133.5, 129.7, 129.6, 128.3, 127.9, 122.6, 91.9, 81.4, 64.2, 37.1, 36.6, 26.2, 22.7, 21.7, 21.5, 13.8; IR (neat): υ_{max} 3043, 2931, 2409, 1727, 1684, 1454, 765, 661 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{30}NO_4S$ $[M+H]^+$: 476.1896; found: 476.1902.

***N*-(1-Butyl-4-oxocyclohexa-2,5-dien-1-yl)-N-(3-(2-formyl-4-methoxyphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (3c):**



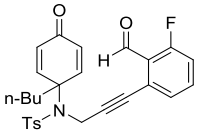
Prepared according to the general procedure as described above in 75% yield (0.55 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a light yellow solid; mp = 99–101°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 2.8 Hz, 1H), 7.36 (s, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.11 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.98 (d, *J* = 10.3 Hz, 2H), 6.25 (d, *J* = 10.3 Hz, 2H), 4.54 (s, 2H), 3.87 (s, 3H), 2.39 (s, 3H), 2.06 – 2.00 (m, 2H), 1.25 – 1.18 (m, 2H), 1.12 – 1.06 (m, 2H), 0.79 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.7, 184.7, 160.0, 149.4, 144.0, 138.4, 137.6, 134.7, 129.5, 129.3, 127.6, 121.2, 117.8, 110.4, 91.0, 80.9, 63.9, 55.6, 36.9, 36.4, 26.0, 22.5, 21.4, 13.6; IR (neat): υ_{max} 3043, 2942, 2416, 1728, 1694, 1459, 1054, 759, 697 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{30}NO_5S$ $[M+H]^+$: 492.1845; found: 492.1849.

***N*-(3-(4-Bromo-2-formylphenyl)prop-2-yn-1-yl)-N-(1-butyl-4-oxocyclohexa-2,5-dien-1-yl)-4-methylbenzenesulfonamide (3d):**



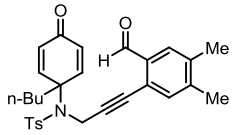
Prepared according to the general procedure as described above in 76% yield (0.61). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a colourless oil ;^{1}H NMR (400 MHz, $CDCl_3$) δ 10.21 (s, 1H), 8.03 (d, *J* = 2.1 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 2H), 7.68 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.31 (d, *J* = 8.2 Hz, 1H), 7.26 (d, *J* = 7.9 Hz, 2H), 6.96 (d, *J* = 10.3 Hz, 2H), 6.27 (d, *J* = 10.3 Hz, 2H), 4.52 (s, 2H), 2.40 (s, 3H), 2.06 – 1.99 (m, 2H), 1.27 – 1.15 (m, 2H), 1.12 – 1.05 (m, 2H), 0.78 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.6, 184.8, 149.3, 144.4, 138.8, 137.6, 136.8, 134.9, 131.0, 129.9, 129.8, 127.8, 124.1, 123.9, 94.0, 80.3, 64.4, 37.3, 36.5, 26.3, 22.7, 21.7, 13.8; IR (neat): υ_{max} 3045, 2951, 2423, 1724, 1694, 1451, 971, 759, 691 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{27}NO_4SBr$ $[M+H]^+$: 540.0844; found: 540.0848.

***N*-(1-Butyl-4-oxocyclohexa-2,5-dien-1-yl)-N-(3-(3-fluoro-2-formylphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (3e):**



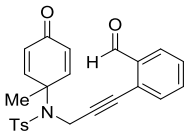
Prepared according to the general procedure as described above in 55% yield (0.39 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.38 (s, 1H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.51 (td, *J* = 8.1, 5.5 Hz, 1H), 7.24 (d, *J* = 8.3 Hz, 3H), 7.15 (dd, *J* = 10.2, 8.6 Hz, 1H), 7.05 (d, *J* = 10.2 Hz, 2H), 6.25 (d, *J* = 10.2 Hz, 2H), 4.54 (s, 2H), 2.38 (s, 3H), 2.06 – 2.00 (m, 2H), 1.28 – 1.16 (m, 2H), 1.11 – 1.04 (m, 2H), 0.77 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.0 (d, J_{CF} = 5.5 Hz), 185.1, 163.7 (d, J_{CF} = 261.3 Hz), 149.7, 144.1, 138.8, 135.0 (d, J_{CF} = 10.5 Hz), 130.2 (d, J_{CF} = 3.1 Hz), 129.7, 127.9, 124.8 (d, J_{CF} = 2.8 Hz), 124.67 (d, J_{CF} = 8.1 Hz), 117.2 (d, J_{CF} = 21.5 Hz), 92.9, 81.6 (d, J_{CF} = 4.1 Hz), 64.3, 37.0, 36.2, 26.2, 22.7, 21.6, 13.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.60 (s, 1F); IR (neat): υ_{max} 3043, 2872, 2409, 1721, 1694, 1457, 759, 693 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{27}NO_4FS$ $[M+H]^+$: 480.1645; found: 480.1645.

_N_-(1-Butyl-4-oxocyclohexa-2,5-dien-1-yl)-N-(3-(2-formyl-4,5-dimethylphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (3f):



Prepared according to the general procedure as described above in 85% yield (0.62 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.18 (s, 1H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.67 (s, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.19 (s, 1H), 7.00 (d, *J* = 10.3 Hz, 2H), 6.25 (d, *J* = 10.3 Hz, 2H), 4.55 (s, 2H), 2.39 (s, 3H), 2.32 (s, 3H), 2.31 (s, 3H), 2.05 – 1.99 (m, 2H), 1.22 (dd, *J* = 14.6, 7.3 Hz, 2H), 1.11 – 1.05 (m, 2H), 0.79 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.9, 185.0, 149.6, 144.2, 143.9, 138.7, 134.5, 134.4, 129.7, 129.6, 128.9, 127.9, 122.9, 91.4, 81.6, 64.2, 37.1, 36.6, 26.2, 22.7, 21.7, 20.2, 19.8, 13.9; IR (neat): υ_{max} 3054, 2942, 2236, 1722, 1676, 1454, 945, 752, 691 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{32}NO_4S$ $[M+H]^+$: 490.2052 ; found: 490.2061.

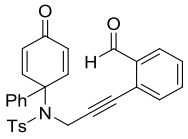
_N_-(3-(2-Formylphenyl)prop-2-yn-1-yl)-4-methyl-N-(1-methyl-4-oxocyclohexa-2,5-dien-1-yl)benzenesulfonamide (3g):



Prepared according to the general procedure as described above in 65% yield (0.48 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.29 (s, 1H), 7.91 (d, *J* = 7.7 Hz, 1H), 7.84 (d, *J* = 8.3 Hz, 2H), 7.58 (td, *J* = 7.6, 1.3

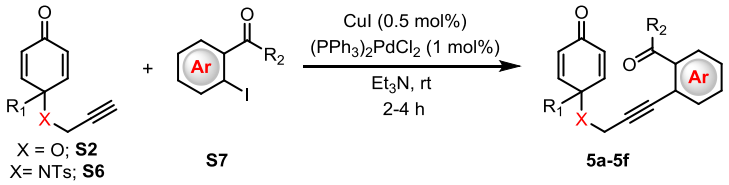
Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 7.7 Hz, 1H), 7.28 (d, *J* = 8.3 Hz, 2H), 7.08 (d, *J* = 10.2 Hz, 2H), 6.22 (d, *J* = 10.2 Hz, 2H), 4.54 (s, 2H), 2.40 (s, *J* = 7.2 Hz, 3H), 1.68 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.0, 184.4, 151.2, 144.3, 138.7, 136.4, 133.9, 133.6, 129.8, 129.3, 128.3, 128.1, 127.8, 125.3, 92.6, 81.4, 60.4, 37.4, 26.0, 21.7; IR (neat): υ_{max} 3028, 2872, 2409, 1725, 1675, 1437, 961, 754, 694 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{22}NO_4S$ $[M+H]^+$: 420.1270; found: 420.1275.

_N_-(3-(2-Formylphenyl)prop-2-yn-1-yl)-4-methyl-N-(4-oxo-[1,1'-biphenyl]-1(4*H*)-yl)benzenesulfonamide (3h):



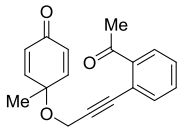
Prepared according to the general procedure as described above in 70% yield (0.5 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.18 (d, *J* = 0.6 Hz, 1H), 7.91 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.57 (td, *J* = 7.5, 1.5 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 1H),7.46 – 7.41 (m, 3H), 7.39 – 7.36 (m, 5H), 7.17 (d, *J* = 10.3 Hz, 2H), 6.20 (d, *J* = 10.3 Hz, 2H), 4.43 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.0, 184.7, 147.4, 144.5, 138.0, 137.1, 136.5, 133.9, 133.6, 129.6, 129.5, 129.3, 128.4, 128.0, 127.9, 126.8, 125.4, 92.4, 81.2, 65.4, 37.8, 21.7; IR (neat): υ_{max} 3045, 2934, 2403, 1721, 1674, 1453, 973, 765, 654 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{24}NO_4S$ $[M+H]^+$: 482.1426; found: 482.1428.

IIIAe. General procedure of Sonogashira coupling for the synthesis of Cyclohexadienone-tethered ketones 5:[4]



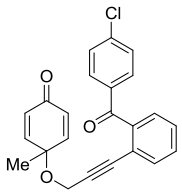
To a solution of *O*-tethered alkyne **S2** (1.5 mmol) or *N*-tethered alkyne **S6** in degassed Et_3N (0.5 M, 3 mL) was added $Pd(PPh_3)_2Cl_2$ (11 mg, 1 mol%), CuI (1.4 mg, 0.5 mol%) and aryl iodide (1.8 mmol). The mixture was stirred at room temperature for 2-4 hours. The reaction was cooled to room temperature, water (8 mL) was added, and the mixture was extracted with EtOAc (3 × 8 mL). The combined organic solvent was washed with 10% aqueous HCl (3 mL), dried (Na_2SO_4), filtered, and concentrated *in vacuo*. The mixture was purified by silica gel column chromatography (EtOAc/hexane) to give cyclohexadienone-tethered ketones **5a-5f** in moderate to high yields. [Note: For *N*-tethered alkyne **S6**, 30μL of DMSO and one drop of DMF was added to the reaction mixture and stirring continued for 12-14 hours]

4-((3-(2-Acetylphenyl)prop-2-yn-1-yl)oxy)-4-methylcyclohexa-2,5-dien-1-one (5a):



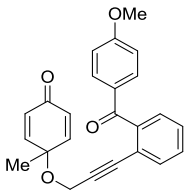
Prepared according to the general procedure as described above in 85% yield (0.36 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.7 Hz, 1H), 7.47 (d, *J* = 7.3 Hz, 1H), 7.42 – 7.32 (m, 2H), 6.88 (d, *J* = 10.2 Hz, 2H), 6.29 (d, *J* = 10.2 Hz, 2H), 4.22 (d, *J* = 1.3 Hz, 2H), 2.62 (d, *J*= 1.5 Hz, 3H), 1.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.9, 185.0, 151.0, 140.7, 134.1, 131.3, 130.4, 128.6, 128.5, 120.7, 91.3, 85.5, 73.3, 54.6, 29.7, 26.3; IR (neat): υ_{max} 3031, 2974, 2236, 2417, 1715, 1684, 1445, 974, 761, 654 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{17}O_3$ $[M+H]^+$: 281.1178; found: 281.1175.

4-((3-(2-(4-Chlorobenzoyl)phenyl)prop-2-yn-1-yl)oxy)-4-methylcyclohexa-2,5-dien-1-one (5b):



Prepared according to the general procedure as described above in 75% yield (0.42 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a light yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.5 Hz, 2H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.47 – 7.39 (m, 5H), 6.69 (d, *J* = 10.3 Hz, 2H), 6.21 (d, *J* = 10.3 Hz, 2H), 3.91 (s, 2H), 1.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 185.0, 150.8, 141.1, 139.6, 135.5, 133.1, 131.5, 130.5, 130.4, 128.7, 128.5, 128.4, 121.0, 91.6, 84.3, 73.2, 54.1, 26.2; IR (neat): υ_{max} 3045, 2932, 2403, 1713, 1692, 1452, 1057 972, 759, 691 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{18}O_3Cl$ $[M+H]^+$: 377.0944; found: 377.0946.

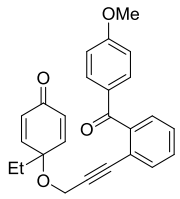
4-((3-(2-(4-Methoxybenzoyl)phenyl)prop-2-yn-1-yl)oxy)-4-methylcyclohexa-2,5-dien-1-one (5c):



Prepared according to the general procedure as described above in 72% yield (0.4 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford as a light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.9 Hz, 2H), 7.51 (dd, *J* = 6.4, 1.7 Hz, 1H), 7.45 – 7.37 (m, 3H), 6.92 (d, *J* = 8.9 Hz, 2H), 6.71 (d, *J* = 10.3 Hz, 2H), 6.20 (d, *J* = 10.3 Hz, 2H), 3.97 (s, 2H), 3.87 (s, 3H), 1.39

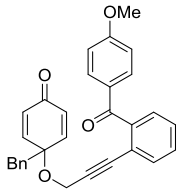
(s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.3, 185.2, 163.9, 151.0, 142.2, 133.0, 132.7, 130.3, 130.0, 129.9, 128.3, 128.1, 120.8, 113.8, 91.0, 84.5, 73.4, 55.6, 54.4, 26.3; IR (neat): υ_{max} 3045, 2975, 2406, 1711, 1679, 1454, 1254, 753, 697 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{21}O_4$ $[M+H]^+$: 373.1440; found: 373.1476.

4-Ethyl-4-((3-(2-(4-methoxybenzoyl)phenyl)prop-2-yn-1-yl)oxy)cyclohexa-2,5-dien-1-one (5d):



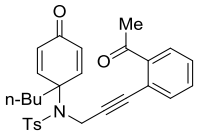
Prepared according to the general procedure as described above in 65% yield (0.38 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.9 Hz, 2H), 7.50 (dd, *J* = 6.8, 1.5 Hz, 1H), 7.45 – 7.36 (m, 3H), 6.92 (d, *J* = 8.9 Hz, 2H), 6.64 (d, *J* = 10.2 Hz, 2H), 6.26 (d, *J* = 10.2 Hz, 2H), 3.99 (s, 2H), 3.86 (s, 3H), 1.72 (q, *J* = 7.6 Hz, 2H), 0.77 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 185.6, 163.9, 150.2, 142.3, 133.0, 132.8, 131.6, 130.1, 129.8, 128.3, 128.0, 120.9, 113.8, 91.2, 84.5, 77.2, 55.6, 54.3, 32.3, 7.9; IR (neat): υ_{max} 3047, 2931, 2417, 1714, 1679, 1445, 1274, 759, 654 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{23}O_4$ $[M+H]^+$: 387.1596; found: 387.1663.

4-Benzyl-4-((3-(2-(4-methoxybenzoyl)phenyl)prop-2-yn-1-yl)oxy)cyclohexa-2,5-dien-1-one (5e):



Prepared according to the general procedure as described above in 75% yield (0.49 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.9 Hz, 2H), 7.51 (dd, *J* = 6.4, 1.8 Hz, 1H), 7.47 – 7.37 (m, 3H), 7.24 – 7.20 (m, 3H), 7.13 – 7.06 (m, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 6.66 (d, *J* = 10.2 Hz, 2H), 6.16 (d, *J* = 10.2 Hz, 2H), 3.99 (s, 2H), 3.87 (s, 3H), 2.96 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 185.2, 163.9, 149.8, 142.3, 134.6, 132.9, 132.8, 131.3, 130.8, 130.0, 129.8, 128.3, 128.1, 128.0, 127.2, 120.8, 113.8, 91.1, 84.6, 76.4, 55.6, 54.4, 46.3; IR (neat): υ_{max} 3029, 2945, 2406, 1713, 1691, 1457, 1253, 745, 654 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{25}O_4$ $[M+H]^+$: 449.1753; found: 449.1755.

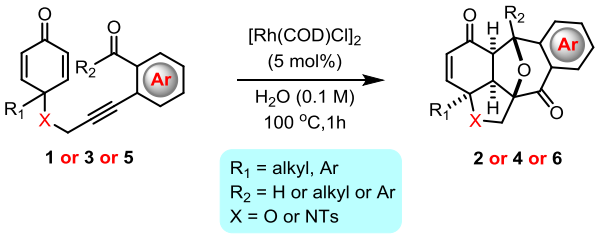
***N*-(3-(2-Acetylphenyl)prop-2-yn-1-yl)-*N*-(1-butyl-4-oxocyclohexa-2,5-dien-1-yl)-4-methylbenzenesulfonamide (5f):**



Prepared according to the general procedure as described above in 57% yield (0.41 g). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.4 Hz, 2H), 7.73 – 7.70 (m, 1H), 7.48 – 7.38 (m, 3H), 7.25 – 7.22 (m, 2H), 7.07 (d, *J* = 10.3 Hz, 2H), 6.24 (d, *J* = 10.3 Hz, 2H), 4.54 (s, 2H), 2.63 (s, 3H), 2.38 (s, 3H), 2.05 – 2.00 (m, 2H), 1.26 – 1.16 (m, 2H), 1.12 – 1.04 (m, 2H), 0.78 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.4, 185.2, 149.9, 144.0, 140.7, 138.9, 134.5, 131.4, 129.6, 129.5, 128.9, 128.7, 128.0, 120.7, 90.8, 84.1, 64.2, 37.1, 36.3, 29.5, 26.2, 22.7, 21.7, 13.9; IR (neat): υ_{max} 3047, 2956, 2413, 1715, 1671, 1437, 1245, 764, 651 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{30}NO_4S$ $[M+H]^+$: 476.1896; found: 476.1907.

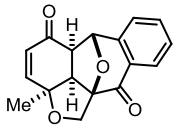
IIIB. Experimental procedures and analytical data of products

IIIBa: General procedure for Rh(I)-catalyzed Huisgen-type [3+2] cyclization:



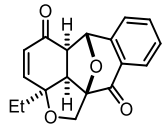
A dried screw-cap vial was charged with 2-alkynylbenaldehyes **1**(or) **3** (or) 2-alkynylphenyl ketones **5** (0.3 mmol, 1.0 equiv), and $[Rh(COD)Cl]_2$ (7.4 mg, 5.0 mol%) in distilled H_2O (1.5 mL, 0.1 M) under inert atmosphere, and the reaction mixture was stirred at 100 °C for 1 hour (monitored by TLC). Then, it was cooled to room temperature and diluted with EtOAc (8 mL). The mixture was extracted with EtOAc (3 x 8 mL) and combined organic solvent was concentrated under reduced pressure. The residue was purified by silica gel column chromatography on silica gel with a gradient eluent of petroleum ether and EtOAc to afford the desired [3+2] cyclization product **2** (or) **4** (or) **6**, respectively.

2a-Methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2a):



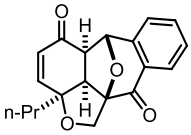
Prepared according to the general procedure as described above in 75% yield, (63 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford as a white solid; mp = 172–174°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 7.7, 0.6 Hz, 1H), 7.61 (td, *J* = 7.5, 1.3 Hz, 1H), 7.47 (td, *J* = 7.6, 1.1 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 6.84 (dd, *J* = 10.3, 0.7 Hz, 1H), 6.24 (d, *J* = 10.3 Hz, 1H), 5.66 (s, 1H), 4.83 (d, *J* = 10.3 Hz, 1H), 3.85 (d, *J* = 10.3 Hz, 1H), 3.00 (d, *J* = 8.8 Hz, 1H), 2.98 (d, *J* = 8.8 Hz, 1H), 1.49 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.4, 191.6, 153.1, 144.4, 134.7, 130.1, 129.0, 128.3, 127.6, 124.7, 99.7, 88.8, 77.8, 68.5, 54.2, 51.5, 27.9; IR (neat): υ_{max} 3029, 2925, 1705, 1674, 1447, 1274, 1054, 971, 759, 693 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{15}O_4$ $[M+H]^+$: 283.0970; found: 283.0976.

2a-Ethyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2b):



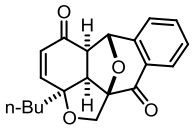
Prepared according to the general procedure as described above in 71%yield (63mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford as a white solid; mp = 124–126°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.8 Hz, 1H), 7.62 (td, *J* = 7.5, 1.3 Hz, 1H), 7.48 (td, *J* = 7.6, 1.1 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 6.76 (dd, *J* = 10.4, 1.0 Hz, 1H), 6.34 (d, *J* = 10.4 Hz, 1H), 5.64 (s, 1H), 4.84 (d, *J* = 10.3 Hz, 1H), 3.86 (d, *J* = 10.3 Hz, 1H), 2.97 (d, *J* = 8.8 Hz, 1H), 2.93 (d, *J* = 8.8 Hz, 1H), 1.82 – 1.76 (m, 2H), 0.85 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.7, 191.6, 152.1, 144.4, 134.6, 131.6, 129.0, 128.3, 127.6, 124.7, 99.4, 89.0, 81.4, 68.7, 52.5, 51.9, 33.2, 8.5; IR (neat): υ_{max} 3057, 2943,1706, 1694, 1453, 1274, 1049, 745, 675 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{17}O_4$ $[M+H]^+$: 297.1127; found: 297.1135.

2a-Propyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2c):



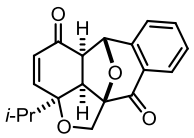
Prepared according to the general procedure as described above in 45% yield (41mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 7.1, 0.6 Hz, 1H), 7.62 (td, *J* = 7.5, 1.3 Hz, 1H), 7.48 (td, *J* = 7.6, 1.1 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 6.78 (dd, *J* = 10.4, 0.7 Hz, 1H), 6.31 (d, *J* = 10.4 Hz, 1H), 5.63 (s, 1H), 4.84 (d, *J* = 10.2 Hz, 1H), 3.84 (d, *J* = 10.3 Hz, 1H), 2.96 (d, *J* = 8.8 Hz, 1H), 2.94 (d, *J* = 8.8 Hz, 1H), 1.78 – 1.69 (m, 2H), 1.30 – 1.26 (m, 1H), 1.21 – 1.17 (m, 1H), 0.89 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.7, 191.6, 152.5, 144.4, 134.6, 131.3, 129.0, 128.3, 127.6, 124.7, 99.4, 89.0, 80.8, 68.6, 52.9, 51.8, 42.7, 17.7, 14.3; IR (neat): υ_{max} 3035, 2945, 1715, 1676, 1445, 1257, 1054, 757, 643 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}O_4$ $[M+H]^+$: 311.1283; found: 311.1292.

2a-Butyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2d):



Prepared according to the general procedure as described above in 42% yield (40mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.7 Hz, 1H), 7.62 (td, *J* = 7.5, 1.1 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 10.4 Hz, 1H), 6.32 (d, *J* = 10.4 Hz, 1H), 5.63 (s, 1H), 4.84 (d, *J* = 10.2 Hz, 1H), 3.84 (d, *J* = 10.2 Hz, 1H), 2.97 (d, *J*= 8.8 Hz, 1H), 2.94 (d, *J* = 8.8 Hz, 1H), 1.79 – 1.68 (m, 2H), 1.31 – 1.27 (m, 2H), 1.23 – 1.18 (m, 1H), 1.17 – 1.09 (m, 1H), 0.84 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.7, 191.6, 152.5, 144.4, 134.6, 131.3, 129.0, 128.3, 127.6, 124.7, 99.4, 89.1, 80.9, 68.6, 52.9, 51.8, 40.3, 26.4, 22.9, 14.0; IR (neat): υ_{max} 3029, 2945, 1716, 1686, 1452, 1279, 1054, 754, 645 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}O_4$$[M+H]^+$: 325.1440; found: 325.1437.

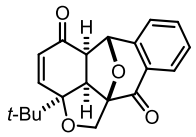
2a-Isopropyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzo furan 5,11 -dione (2e):



Prepared according to the general procedure as described above in 64% yield (59 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.62 (td, *J* = 7.5, 1.4 Hz, 1H), 7.48 (td, *J* = 7.6, 1.1 Hz, 1H), 7.40 (d, *J* = 7.5 Hz, 1H), 6.78 (dd, *J* = 10.5, 1.1 Hz, 1H), 6.39 (d, *J* = 10.5 Hz, 1H), 5.62 (s, 1H), 4.85 (d, *J* = 10.2 Hz, 1H), 3.83 (d, *J* = 10.2 Hz, 1H), 2.93 (d, *J* = 8.8 Hz, 1H), 2.90 (d, *J* = 8.8 Hz, 1H),

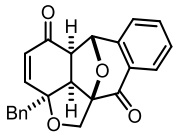
1.98 (dt, *J* = 13.8, 6.9 Hz, 1H), 0.94 (d, *J* = 6.9 Hz, 3H), 0.83 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.9, 191.6, 150.8, 144.4, 134.6, 132.4, 129.1, 127.7, 124.7, 99.3, 89.3, 83.8, 68.8, 52.2, 51.7, 37.5, 29.8, 17.4, 17.0; IR (neat): υ_{max} 3069, 2937, 1706, 1684, 1431, 1254, 1054, 795, 654 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}O_4$ $[M+H]^+$: 311.1283; found: 311.1278.

2a-(*tert*-Butyl)-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2f):



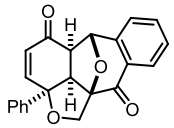
Prepared according to the general procedure as described above in 67% yield (54mg) It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08(dd, *J* = 7.7, 1.2 Hz, 1H), 7.62 (td, *J* = 7.5, 1.4 Hz, 1H), 7.49 (td, *J* = 7.6, 1.1 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 6.91 (dd, *J* = 10.6, 1.4 Hz, 1H), 6.40 (d, *J* = 10.6 Hz, 1H), 5.58 (s, 1H), 4.85 (d, *J* = 10.1 Hz, 1H), 3.81 (d, *J* = 10.1 Hz, 1H), 3.12 (dd, *J* = 8.5, 1.0 Hz, 1H), 2.89 (dd, *J* = 8.5, 0.5 Hz, 1H), 0.94 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.9, 191.5, 151.9, 144.5, 134.6, 132.1, 129.0, 128.2, 127.7, 124.7, 99.2, 89.4, 85.4, 69.2, 52.3, 49.0, 37.9, 25.0; IR (neat): υ_{max} 3043, 2942, 1706, 1676, 1454, 1267, 1060, 754, 675 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}O_4$ $[M+H]^+$: 325.1440; found: 325.1434 .

2a-Benzyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2g):



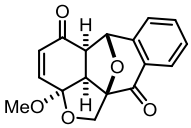
Prepared according to the general procedure as described above in 65% yield (70mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.6 Hz, 1H), 7.60 (td, *J* = 7.5, 1.3 Hz, 1H), 7.48 (td, *J* = 7.6, 0.9 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 1.9 Hz, 1H), 7.22 (d, *J* = 1.6 Hz, 2H), 7.11 (d, *J* = 2.7 Hz, 1H), 7.09 (d, *J* = 1.8 Hz, 1H), 6.74 (dd, *J* = 10.4, 0.9 Hz, 1H), 6.23 (d, *J* = 10.4 Hz, 1H), 5.51 (s, 1H), 4.90 (d, *J* = 10.3 Hz, 1H), 3.86 (d, *J* = 10.3 Hz, 1H), 3.12 (d, *J* = 13.5 Hz, 1H), 3.08 (d, *J* = 8.8 Hz, 1H), 2.98 (d, *J* = 13.5 Hz, 1H), 2.62 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.1, 191.5, 151.9, 144.4, 134.7, 134.7, 131.5, 130.5, 129.0, 128.5, 128.2, 127.7, 127.4, 124.7, 99.3, 89.0, 81.2, 68.8, 53.1, 51.6, 46.9; IR (neat): υ_{max} 3047, 2956, 1714, 1679, 1431, 1254, 1063, 745, 657 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{19}O_4$ $[M+H]^+$: 359.1283; found: 359.1278.

2a-Phenyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2h):



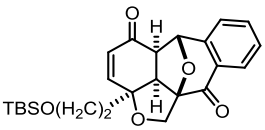
Prepared according to the general procedure as described above in 53% yield (58 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.60 (td, *J* = 7.5, 1.4 Hz, 1H), 7.46 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.44 – 7.41 (m, 1H), δ 7.36 – 7.31 (m, 4H).7.29 – 7.24 (m, 1H), 6.82 (dd, *J* = 10.3, 1.1 Hz, 1H), 6.40 (d, *J* = 10.3 Hz, 1H), 5.73 (s, 1H), 5.04 (d, *J* = 10.2 Hz, 1H), 4.07 (d, *J* = 10.2 Hz, 1H), 3.29 (d, *J* = 8.8 Hz, 1H), 3.12 (dd, *J* = 8.8, 0.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.7, 191.3, 151.5, 144.3, 142.2, 134.7, 130.2, 129.1, 129.0, 128.3, 127.6, 125.0, 124.7, 99.2, 89.1, 81.5, 68.9, 56.1, 51.5; IR (neat): υ_{max} 3049, 2945,1707, 1679, 1444, 1272, 1054, 749, 643 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{17}O_4$ $[M+H]^+$:345.1127 ; found: 345.1122.

2a-Methoxy-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2i):



Prepared according to the general procedure as described above in 51% yield (58 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.7 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.07 (d, *J* = 10.5 Hz, 1H), 6.26 (d, *J* = 10.5 Hz, 1H), 5.74 (s, 1H), 4.78 (d, *J* = 10.6 Hz, 1H), 4.17 (d, *J* = 10.6 Hz, 1H), 3.43 (s, 3H), 3.27 (d, *J* = 10.2 Hz, 1H), 3.08 (d, *J* = 10.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.6, 191.2, 144.9, 142.2, 134.9, 130.0, 128.9, 128.6, 127.3, 124.7, 101.9, 98.2, 83.9, 68.3, 54.9, 53.7, 49.6; IR (neat): υ_{max} 3047, 2928, 1713, 1672, 1431, 1262 1063, 971, 754, 657 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{15}O_5$ $[M+H]^+$: 299.0919; found: 299.0918.

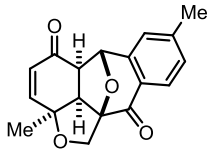
2a-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo [5,6] cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2j):



Prepared according to the general procedure as described above in 55% yield (69 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a light yellow oil; ^{1}H NMR (300

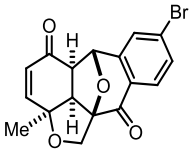
MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.2 Hz, 1H), 7.60 (td, *J* = 7.5, 1.3 Hz, 1H), 7.46 (td, *J* = 7.6, 1.1 Hz, 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 6.75 (dd, *J* = 10.4, 1.0 Hz, 1H), 6.32 (d, *J* = 10.4 Hz, 1H), 5.64 (s, 1H), 4.82 (d, *J* = 10.1 Hz, 1H), 3.79 (d, *J* = 10.1 Hz, 1H), 3.72 (dt, *J* = 10.7, 4.8 Hz, 1H), 3.58 (ddd, *J* = 11.0, 8.7, 4.2 Hz, 1H), 3.29 (d, *J* = 8.6 Hz, 1H), 2.97 (d, *J* = 8.6 Hz, 1H), 2.05 – 1.87 (m, 2H), 0.67 (s, 9H), -0.08 (s, 3H), -0.10 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.9, 191.8, 151.9, 144.5, 134.5, 131.5, 128.9, 128.3, 127.6, 124.6, 99.2, 89.1, 79.9, 68.1, 58.8, 53.1, 51.7, 42.6, 25.8, 18.1, -5.5, -5.6; IR (neat): υ_{max} 3045, 2979,1713, 1684, 1459,1249, 1054, 754, 691 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{31}O_5Si$ $[M+H]^+$: 427.1941; found: 427.1939.

2a,8-Dimethyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2k):



Prepared according to the general procedure as described above in 74% yield (81mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a white solid; mp = 180–182°C;^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.9 Hz, 1H), 7.27 (d, *J* = 8.1 Hz, 1H), 7.21 (s, 1H), 6.84 (d, *J* = 10.3 Hz, 1H), 6.24 (d, *J* = 10.3 Hz, 1H), 5.60 (s, 1H), 4.82 (d, *J* = 10.3 Hz, 1H), 3.85 (d, *J* = 10.3 Hz, 1H), 2.99 (d, *J* = 8.9 Hz, 1H), 2.96 (d, *J* = 8.9 Hz, 1H), 2.44 (s, 3H), 1.49 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.6, 191.5, 153.2, 146.0, 144.6, 130.0, 129.9, 127.6, 125.9, 125.2, 99.8, 88.8, 77.8, 68.5, 54.4, 51.7, 28.0, 22.1; IR (neat): υ_{max} 3059, 2939, 1704, 1674, 1447, 1263 1059, 757, 674 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{17}O_4$ $[M+H]^+$: 297.1127; found: 297.1120.

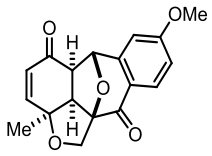
8-Bromo-2a-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2l):



Prepared according to the general procedure as described above in 85% yield (96mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a white solid; mp = 54–56°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.2 Hz, 1H), 7.63 – 7.59 (m, 2H), 6.84 (dd, *J* = 10.3, 0.8 Hz, 1H), 6.25 (d, *J* = 10.3 Hz, 1H), 5.61 (s, 1H), 4.80 (d, *J* = 10.4 Hz, 1H), 3.85 (d, *J* = 10.4 Hz, 1H), 3.01 (d, *J* = 8.9 Hz, 1H), 2.97 (d, *J* = 8.9 Hz, 1H), 1.50 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.8, 190.8, 153.0, 145.9, 132.5, 130.1, 129.9, 129.2, 127.9, 127.2, 99.7, 88.1, 77.7, 68.4, 54.2, 51.4, 27.9; IR

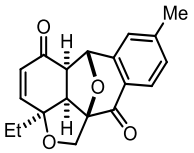
(neat): υ_{max} 3028, 2931,1708, 1674, 1449,1265, 1051, 749, 654 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{14}O_4Br$ $[M+H]^+$: 361.0075 ; found: 361.0078.

8-Methoxy-2a-methyl-2a,2a1,5a,6-tetrahydro-*1H*-6,11aepoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2m):



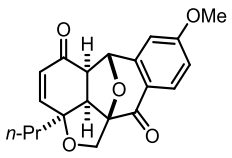
Prepared according to the general procedure as described above in 61% yield (58mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a white solid; mp = 172–174°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.7 Hz, 1H), 6.95 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.85 (d, *J* = 2.4 Hz, 1H), 6.84 (d, *J* = 10.3 Hz, 1H), 6.23 (d, *J* = 10.3 Hz, 1H), 5.58 (s, 1H), 4.82 (d, *J* = 10.3 Hz, 1H), 3.90 (s, 3H), 3.85 (d, *J* = 10.3 Hz, 1H), 3.00 (d, *J* = 8.9 Hz, 1H), 2.97 (d, *J* = 8.9 Hz, 1H), 1.49 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.6, 190.6, 164.6, 153.2, 147.0, 130.0, 121.5, 115.4, 108.8, 99.7, 88.7, 77.6, 68.5, 56.0, 54.6, 51.8, 28.0; IR (neat): υ_{max} 3054, 2981, 1719, 1674, 1427, 1254, 1053, 745, 661 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{17}O_5$ $[M+H]^+$: 313.1076; found: 313.1070

2a-Ethyl-8-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2n):



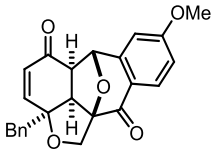
Prepared according to the general procedure as described above in 78% yield (73mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a white solid; mp = 124–126°C;^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.9 Hz, 1H), 7.27 (d, *J* = 8.1 Hz, 1H), 7.21 (s, 1H), 6.76 (dd, *J* = 10.4, 1.0 Hz, 1H), 6.33 (d, *J* = 10.4 Hz, 1H), 5.57 (s, 1H), 4.84 (d, *J* = 10.2 Hz, 1H), 3.85 (d, *J* = 10.2 Hz, 1H), 2.95 (d, *J* = 8.8 Hz, 1H), 2.91 (d, *J* = 8.8 Hz, 1H), 2.44 (s, 3H), 1.79 (dd, *J* = 7.6, 2.0 Hz, 1H), 1.76 (dd, *J* = 7.6, 2.0 Hz, 1H), 0.84 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.9, 191.5, 152.2, 146.0, 144.6, 131.5, 129.9, 127.7, 125.9, 125.2, 99.5, 89.0, 81.3, 68.7, 52.6, 52.0, 33.3, 22.1, 8.5; IR (neat): υ_{max} 3025, 2969, 1707, 1676, 1431, 1295, 1074, 754, 697 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}O_4$ $[M+H]^+$: 311.1283 ; found: 311.1288.

8-Methoxy-2a-propyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzo furan-5,11-dione (2o):



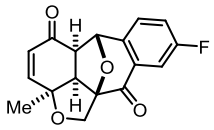
Prepared according to the general procedure as described above in 73% yield (73mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a light yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.7 Hz, 1H), 6.95 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.84 (d, *J* = 2.4 Hz, 1H), 6.78 (dd, *J* = 10.4, 0.8 Hz, 1H), 6.30 (d, *J* = 10.4 Hz, 1H), 5.55 (s, 1H), 4.82 (d, *J* = 10.2 Hz, 1H), 3.90 (s, 3H), 3.84 (d, *J* = 10.2 Hz, 1H), 2.96 (d, *J* = 8.8 Hz, 1H), 2.93 (d, *J* = 9.0 Hz, 1H), 1.77 – 1.65 (m, 2H), 1.31 – 1.26 (m, 1H), 1.21 – 1.15 (m, 1H), 0.89 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.9, 190.7, 164.6, 152.7, 147.0, 131.1, 130.0, 121.5, 115.4, 108.8, 99.5, 89.0, 80.7, 68.6, 56.0, 53.3, 52.1, 42.8, 17.7, 14.3; IR (neat): υ_{max} 3043, 2976, 2931, 1703, 1684, 1274, 1057, 753, 691 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}O_5$ $[M+H]^+$: 341.1389; found: 341.1394.

2a-Benzyl-8-methoxy-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-poxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2p):



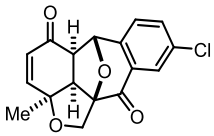
Prepared according to the general procedure as described above in 67% yield (52mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a white solid; mp = 120–122°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.7 Hz, 1H), 7.25 – 7.21 (m, 3H), 7.10 (dd, *J* = 7.3, 2.4 Hz, 2H), 6.95 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.78 (d, *J* = 2.4 Hz, 1H), 6.75 (dd, *J* = 10.4, 1.0 Hz, 1H), 6.22 (d, *J* = 10.4 Hz, 1H), 5.42 (s, 1H), 4.89 (d, *J* = 10.3 Hz, 1H), 3.88 (s, 3H), 3.86 (d, *J* = 10.3 Hz, 1H), 3.11 (d, *J* = 13.5 Hz, 1H), 3.07 (d, *J* = 8.7 Hz, 1H), 2.98 (d, *J* = 13.5 Hz, 1H), 2.62 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.4, 190.6, 164.6, 151.8, 147.0, 134.8, 131.3, 130.6, 130.1, 128.5, 127.4, 121.4, 115.5, 108.7, 99.4, 89.0, 81.2, 68.8, 55.9, 53.5, 51.9, 46.9; IR (neat): υ_{max} 3049, 2879, 1706, 1691, 1434,1247, 1081, 761, 692 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{21}O_5$ $[M+H]^+$: 389.1389; found: 389.1393.

9-Fluoro-2a-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzo furan-5,11-dione (2q):



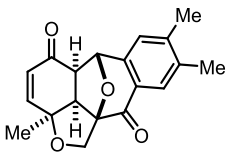
Prepared according to the general procedure as described above in 67% yield (60mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 8.3, 2.7 Hz, 1H), 7.41 (dd, *J* = 8.4, 4.8 Hz, 1H), 7.30 (td, *J* = 8.3, 2.7 Hz, 1H), 6.84 (d, *J* = 10.3 Hz, 1H), 6.24 (d, *J* = 10.3 Hz, 1H), 5.66 (s, 1H), 4.80 (d, *J* = 10.4 Hz, 1H), 3.84 (d, *J* = 10.4 Hz, 1H), 2.97 (s, 2H), 1.50 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.1, 190.6, 162.8 (d, J_{CF} = 250.2 Hz), 153.0, 140.4 (d, J_{CF} = 2.9 Hz), 130.4 (d, J_{CF} = 6.5 Hz), 130.1,126.9 (d, J_{CF} = 7.5 Hz), 121.8 (d, J_{CF} = 22.5 Hz), 113.9 (d, J_{CF} = 22.5 Hz), 99.3, 88.3, 77.8, 68.4, 54.1, 51.4, 27.9; ^{19}F NMR (377 MHz, $CDCl_3$) δ -110.64 (s, 1F); IR (neat): υ_{max} 3031, 2974, 1720, 1682, 1443, 1267, 1062, 757, 674 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{14}O_4F$ $[M+H]^+$: 301.0876; found: 301.0871.

9-Chloro-2a-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzo furan-5,11-dione (2r):



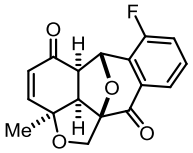
Prepared according to the general procedure as described above in 73% yield (46 mg). It was purified by flash chromatography (10% EtOAc/hexanes; R_f = 0.6) to afford a white solid; mp = 154–156°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 2.1 Hz, 1H), 7.57 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 6.84 (d, *J* = 10.3 Hz, 1H), 6.24 (d, *J* = 10.3 Hz, 1H), 5.65 (s, 1H), 4.80 (d, *J* = 10.4 Hz, 1H), 3.84 (d, *J* = 10.4 Hz, 1H), 2.96 (s, 2H), 1.49 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.9, 190.4, 153.0, 142.6, 135.3, 134.5, 130.1, 129.8, 127.4, 126.3, 99.5, 88.3, 77.8, 68.4, 54.1, 51.4, 27.9; IR (neat): υ_{max} 3031, 2945, 1706, 1679,, 1437, 1055, 1294, 761, 643 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{14}O_4Cl$ $[M+H]^+$: 317.0581; found: 317.0573.

2a,8,9-Trimethyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzo fura- -n-5,11-dione (2s):



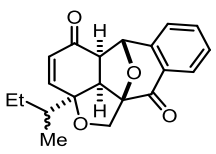
Prepared according to the general procedure as described above in 86% yield (82mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a white solid; mp = 100–102°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.16 (s, 1H), 6.82 (d, *J* = 10.3 Hz, 1H), 6.22 (d, *J* = 10.3 Hz, 1H), 5.57 (s, 1H), 4.81 (d, *J* = 10.3 Hz, 1H), 3.82 (d, *J* = 10.3 Hz, 1H), 2.95 (d, *J* = 8.9 Hz, 1H), 2.93 (d, *J* = 8.9 Hz, 1H), 2.33 (s, 3H), 2.30 (s, 3H), 1.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.7, 191.8, 153.1, 144.8, 142.2, 137.8, 130.1, 128.1, 126.0, 125.7, 99.6, 88.6, 77.7, 68.6, 54.4, 51.7, 27.9, 20.5, 19.7; IR (neat): υ_{max} 3049, 2931, 1715, 1691, 1435, 1279, 1081, 764, 657 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}O_4$ $[M+H]^+$: 311.1283; found: 311.1292.

7-Fluoro-2a-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzo furan-5,11-dione (2t):



Prepared according to the general procedure as described above in 38% yield (46mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford as a light yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.6 Hz, 1H), 7.47 (td, *J* = 8.0, 5.1 Hz, 1H), 7.34 (td, *J* = 8.6, 1.1 Hz, 1H), 6.83 (dd, *J* = 10.4, 0.8 Hz, 1H), 6.27 (d, *J* = 10.4 Hz, 1H), 5.99 (s, 1H), 4.81 (d, *J* = 10.4 Hz, 1H), 3.85 (d, *J* = 10.4 Hz, 1H), 3.04 (d, *J* = 8.9 Hz, 1H), 3.01 (d, *J* = 9.0 Hz, 1H), 1.50 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.5, 190.5, 157.4 (d, *J* = 250.0 Hz), 152.7, 131.2 (d, J_{CF} = 16.7 Hz), 130.3, 130.4 (d, J_{CF} = 6.9 Hz), 123.2 (d, J_{CF} = 3.0 Hz), 121.4 (d, J_{CF} = 20.5 Hz), 99.4, 83.3, 77.8, 68.4, 54.4, 50.6, 27.9; ^{19}F NMR (377 MHz, $CDCl_3$) δ -118.98 (s, 1F); IR (neat): υ_{max}3031, 2974, 1707, 1682, 1443, 1264, 1062, 781, 679 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{14}O_4F$ $[M+H]^+$: 301.0876; found: 301.0869.

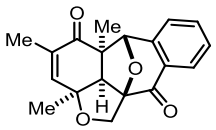
2a-(*sec*-Butyl)-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2u & 2u‘):



Prepared according to the general procedure as described above in 64% yield (64mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford in 1:1 ratio of inseparable diastereomers as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.7 Hz, 1H), 7.61 (td, *J* = 7.5, 1.3 Hz, 1H), 7.48 (td, *J* = 7.6, 1.1 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 6.84 – 6.70 (m, 1H), 6.38 (d, *J* = 10.5 Hz, 0.5H), 6.36 (d, *J* = 10.5 Hz, 0.5H), 5.62 (s, 0.5H), 5.62 (s, 0.5H), 4.84 (d, *J* = 10.2 Hz,

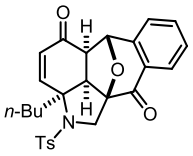
0.5H), 4.84 (d, *J* = 10.2 Hz, 0.5H), 3.82 (d, *J* = 10.2, Hz, 0.5H), 3.82 (d, *J* = 10.2, Hz, 0.5H), 2.94 (d, *J* = 8.6 Hz, 0.5H), 2.93 (d, *J* = 8.6 Hz, 0.5H), 2.90 (d, *J* = 8.8 Hz, 0.5H), 2.88 (d, *J* = 8.9 Hz, 0.5H), 1.85 – 1.57 (m, 3H), 0.94 (d, *J* = 6.9 Hz, 1.5H), 0.91 – 0.86 (m, 3H), 0.80 (d, *J* = 6.8 Hz, 1.5H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.9, 191.6, 151.2, 151.0, 144.4, 134.6, 132.4, 132.1, 129.0, 128.3, 127.7, 124.7, 99.2, 99.1, 89.3, 89.2, 84.0, 83.8, 68.7, 68.6, 52.3, 52.2, 52.1, 52.0, 44.9, 44.5, 24.2, 24.0, 13.9, 13.5, 12.3, 12.1; IR (neat): υ_{max} 3027, 2934, 1708, 1671, 1427, 1272, 1076, 764, 697 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}O_4$ $[M+H]^+$:325.1440 ; found: 325.1436.

2a,4,5a-Trimethyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione 2v):



Prepared according to the general procedure as described above in 34% yield (32mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a white solid; mp = 158–160°C;^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.6 Hz, 1H), 7.61 (td, *J* = 7.5, 1.1 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 7.5 Hz, 1H), 6.58 (s, 1H), 5.54 (s, 1H), 4.74 (d, *J* = 10.1 Hz, 1H), 3.74 (d, *J* = 10.1 Hz, 1H), 2.50 (s, 1H), 1.94 (d, *J* = 1.1 Hz, 3H), 1.46 (s, 3H), 0.99 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.9, 192.2, 147.3, 142.1, 136.7, 133.9, 129.1, 128.9, 127.7, 126.8, 99.3, 91.7, 77.4, 68.0, 61.7, 52.9, 28.2, 22.2, 16.9; IR (neat): υ_{max} 3049, 2972, 1706, 1671, 1434, 1294, 1084, 754, 695 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{19}O_4$ $[M+H]^+$: 311.1283; found: 311.1277.

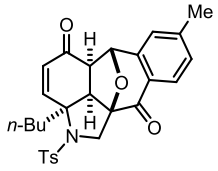
2a-Butyl-2-tosyl-1,2,2a,,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]indole-5,11-dione (4a):



Prepared according to the general procedure as described above in 61% yield (88mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.7) to afford a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 2H), 7.61 (td, *J* = 7.5, 1.3 Hz, 1H), 7.46 (td, *J* = 7.6, 1.1 Hz, 1H), 7.39 (dd, *J* = 7.6, 0.4 Hz, 1H), 7.34 – 7.29 (m, 3H), 6.29 (d, *J* = 10.5 Hz, 1H), 5.64 (s, 1H), 4.55 (d, *J* = 11.5 Hz, 1H), 3.58 (d, *J* = 11.5 Hz, 1H), 2.99 (d, *J* = 9.4 Hz, 1H), 2.93 (dd, *J* = 9.4, 0.6 Hz, 1H), 2.43 (s, 3H), 2.28 (td, *J* = 13.0, 4.3 Hz, 1H), 1.77 (td, *J* = 13.0, 4.6 Hz, 1H), 1.25 – 1.21 (m, 2H), 1.16 – 1.06 (m, 2H), 0.80 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ

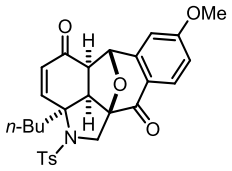
194.3, 191.3, 150.7, 144.5, 143.9, 138.4, 134.9, 130.0, 129.8, 129.1, 127.9, 127.7, 127.2, 124.7, 93.6, 85.6, 66.7, 53.3, 53.2, 50.8, 39.5, 26.9, 22.8, 21.7, 14.0; IR (neat): υ_{max} 3039, 2961, 1714, 1676, 1449, 1224, 1081, 794, 669 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{28}NO_5S$ $[M+H]^+$: 478.1688; found: 478.1695.

2a-Butyl-8-methyl-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta [1,2,3-cd] indole-5,11-dione (4b):



Prepared according to the general procedure as described above in 62% yield (61mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f= 0.6) to afford a white solid; mp = 158–160°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.9 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 2H), 7.34 – 7.31 (m, 2H), 7.30 (s, 1H), 7.27 – 7.24 (m, 2H), 7.19 (s, 1H), 6.28 (d, *J* = 10.5 Hz, 1H), 5.57 (s, 1H), 4.54 (d, *J* = 11.5 Hz, 1H), 2.97 (d, *J* = 9.4 Hz, 1H), 2.91 (d, *J* = 9.4 Hz, 1H), 2.43 (s, 3H), 2.42 (s, 3H), 2.28 (td, *J* = 13.0, 4.3 Hz, 1H), 1.77 (td, *J* = 13.0, 4.6 Hz, 1H), 1.24 – 1.20 (m, 2H), 1.16 – 1.05 (m, 2H), 0.79 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.5, 191.2, 150.8, 146.4, 144.6, 143.8, 138.4, 129.9, 129.9, 129.8, 127.8, 127.2, 125.4, 125.1, 93.6, 85.6, 66.7, 53.4, 53.3, 50.8, 39.6, 26.9, 22.8, 22.2, 21.7, 14.0; IR (neat): υ_{max} 3029, 2984, 1704, 1696, 1452, 1217, 1045,774, 645 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{30}NO_5S$ $[M+H]^+$: 492.1845; found: 492.1848.

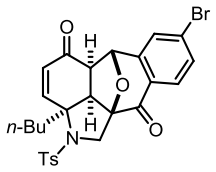
2a-Butyl-8-methoxy-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta [1,2,3-*cd*]indole-5,11-dione (4c):



Prepared according to the general procedure as described above in 67% yield (100mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.4) to afford a colourless oil;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.7 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 10.5 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 6.93 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.82 (d, *J* = 2.4 Hz, 1H), 6.28 (d, *J* = 10.5 Hz, 1H), 5.55 (s, 1H), 4.53 (d, *J* = 11.5 Hz, 1H), 3.89 (s, 3H), 3.57 (d, *J* = 11.5 Hz, 1H), 2.98 (d, *J* = 9.4 Hz, 1H), 2.93 (d, *J* = 9.8 Hz, 1H), 2.42 (s, 3H), 2.27 (td, *J* = 12.8, 4.3 Hz, 1H), 1.77 (td, *J* = 12.9, 4.7 Hz, 1H), 1.32 – 1.19 (m, 2H), 1.18 – 0.99 (m, 2H), 0.80 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.5, 190.3, 164.8, 150.9, 147.0, 143.8, 138.4, 130.1, 129.8, 127.2, 121.0, 115.4, 108.7, 93.6, 85.6,

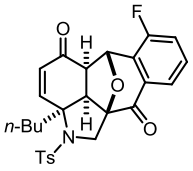
66.6, 56.0, 53.6, 53.5, 50.7, 39.6, 26.9, 22.8, 21.7, 14.0; IR (neat): υ_{max} 3084, 2954, 1706, 1694, 1443, 1216, 1071, 757, 694 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{30}NO_6S$ $[M+H]^+$: 508.I794; found: 508.1813.

8-Bromo-2a-butyl-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta [1,2,3-*cd*]indole-5,11-dione (4d):



Prepared according to the general procedure as described above in 38% yield (63mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.3 Hz, 1H), 7.76 (d, *J* = 8.3 Hz, 2H), 7.60 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.57 (d, *J* = 1.8 Hz, 1H), 7.33 (d, *J* = 10.7 Hz, 1H), 7.31 (d, *J* = 8.2 Hz, 2H), 6.29 (d, *J* = 10.5 Hz, 1H), 5.59 (s, 1H), 4.51 (d, *J* = 11.6 Hz, 1H), 3.56 (d, *J* = 11.6 Hz, 1H), 2.97 (d, *J* = 9.4 Hz, 1H), 2.93 (d, *J* = 9.4 Hz, 1H), 2.43 (s, 3H), 2.28 (td, *J* = 13.0, 4.2 Hz, 1H), 1.77 (td, *J* = 13.0, 4.6 Hz, 1H), 1.25 – 1.19 (m, 2H), 1.17 – 1.05 (m, 2H), 0.80 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.7, 190.5, 150.8, 145.9, 144.0, 138.3, 132.5, 130.2, 130.0, 129.8, 129.4, 127.9, 127.2, 126.7, 93.6, 84.9, 77.5, 66.6, 53.1, 50.6, 39.5, 26.9, 22.8, 21.7, 14.0; IR (neat): υ_{max} 3061, 2974, 1715, 1697, 1454,1213, 1062, 761, 657 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{27}NO_5SBr$ $[M+H]^+$: 556.0793; found: 556.0795.

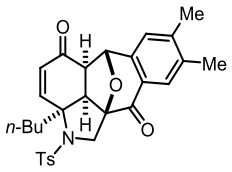
2a-Butyl-7-fluoro-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta [1,2,3-*cd*]indole-5,11-dione (4e):



Prepared according to the general procedure as described above in 32% yield (46mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.45 (td, *J* = 8.0, 5.0 Hz, 1H), 7.37 – 7.27 (m, 4H), 6.31 (d, *J* = 10.5 Hz, 1H), 5.99 (s, 1H), 4.54 (d, *J* = 11.6 Hz, 1H), 3.56 (d, *J* = 11.6 Hz, 1H), 2.98 (dd, *J* = 23.9, 9.4 Hz, 2H), 2.43 (s, 3H), 2.29 (td, *J* = 12.8, 4.3 Hz, 1H), 1.77 (td, *J* = 13.0, 4.6 Hz, 1H), 1.30 – 1.20 (m, 2H), 1.19 – 1.04 (m, 2H), 0.80 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.3, 190.3, 157.3 (d, J_{CF} = 250.3 Hz), 150.3, 143.9, 138.3, 131.1 (d, J_{CF} = 16.5 Hz), 130.3 (d, J_{CF} = 9.8 Hz), 130.3, 129.8, 127.5, 127.2, 123.4 (d, J_{CF} = 2.8 Hz), 121.6 (d, J_{CF} = 20.5 Hz), 93.2,

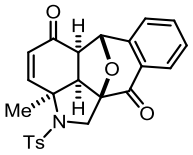
79.9, 66.5, 53.3, 52.3, 50.6, 39.4, 26.9, 22.8, 21.7, 14.0; IR (neat): υ_{max} 3069, 2964, 1713, 1694, 1454, 1215, 1072, 774, 659 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{27}NO_5SF$ $[M+H]^+$: 496.1594; found: 496.1595.

2a-Butyl-8,9-dimethyl-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohep ta [1,2,3-*cd*]indole-5,11-dione (4f):



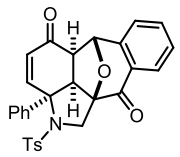
Prepared according to the general procedure as described above in 82% yield (127mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a white solid; mp = 212–214°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.75 (m, 3H), 7.33 – 7.29 (m, 3H), 7.15 (s, 1H), 6.27 (d, *J* = 10.5 Hz, 1H), 5.56 (s, 1H), 4.54 (d, *J* = 11.4 Hz, 1H), 3.56 (d, *J* = 11.5 Hz, 1H), 2.95 (d, *J* = 9.3 Hz, 1H), 2.88 (dd, *J* = 9.3, 0.4 Hz, 1H), 2.42 (s, 3H), 2.33 (s, 3H), 2.30 (s, 3H), 2.27 (td, *J* = 12.7, 4.1 Hz, 1H), 1.75 (td, *J* = 12.6, 4.7 Hz, 1H), 1.25 – 1.22 (m, 2H), 1.15 – 1.05 (m, 2H), 0.79 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.6, 191.5, 150.8, 145.2, 143.8, 142.3, 138.4, 137.9, 130.0, 129.8, 128.3, 127.2, 125.7, 125.6, 93.5, 85.5, 66.7, 53.5, 53.4, 50.8, 39.5, 26.9, 22.8, 21.7, 20.5, 19.7, 14.0; IR (neat): υ_{max} 3072, 2931, 1715, 1692, 1464, 1219, 1074, 754, 697 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{32}NO_5S$ $[M+H]^+$: 506.2001; found: 506.2044.

2a-Methyl-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]indole-5,11-dione (4g):



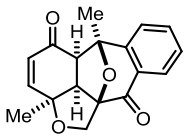
Prepared according to the general procedure as described above in 58% yield (75mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.2 Hz, 1H), 7.78 (d, *J* = 8.3 Hz, 2H), 7.61 (td, *J* = 7.5, 1.3 Hz, 1H), 7.46 (td, *J* = 7.6, 1.1 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 10.5 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 6.22 (d, *J* = 10.4 Hz, 1H), 5.67 (s, 1H), 4.56 (d, *J* = 11.5 Hz, 1H), 3.57 (d, *J* = 11.5 Hz, 1H), 2.98 (d, *J* = 9.5 Hz, 1H), 2.96 (d, *J* = 9.4 Hz, 1H), 2.43 (s, 3H), 1.65 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.0, 191.3, 151.9, 144.4, 143.9, 138.2, 134.9, 129.9, 129.1, 128.9, 127.9, 127.7, 127., 124.7, 93.4, 85.5, 62.7, 55.7, 52.4, 50.5, 28.0, 21.7; IR (neat): υ_{max} 3034, 2947, 1717, 1697, 1431, 1219, 1081, 797, 664 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{22}NO_5S$ $[M+H]^+$: 436.1219; found: 436.1221.

2a-Phenyl-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]indole-5,11-dione (4h):



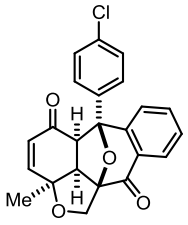
Prepared according to the general procedure as described above in 67% yield (103mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.7 Hz, 1H), 7.73 (dd, *J* = 10.6, 0.8 Hz, 1H), 7.59 – 7.55 (m, 3H), 7.42 (td, *J* = 7.6, 1.1 Hz, 1H), 7.36 (d, *J* = 7.7 Hz, 1H), 7.28 – 7.26 (m, 2H), 7.26 – 7.23 (m, 5H), 6.54 (d, *J* = 10.5 Hz, 1H), 5.67 (s, 1H), 4.73 (d, *J* = 11.4 Hz, 1H), 3.85 (d, *J* = 11.4 Hz, 1H), 3.34 (d, *J* = 9.3 Hz, 1H), 2.93 (d, *J* = 9.3 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.1, 191.1, 148.9, 144.1, 143.9, 143.0, 137.5, 134.9, 130.6, 129.6, 129.1, 129.0, 128.2, 127.8, 127.7, 127.4, 125.9, 124.7, 93.8, 85.9, 68.3, 59.4, 52.0, 51.4, 21.7; IR (neat): υ_{max} 3061, 2934, 1712, 1686, 1431, 1216, 1084, 797, 645 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{24}NO_5S$ $[M+H]^+$: 498.1375; found: 498.1376.

2a,6-Dimethyl-2a,2a1,5a,6-tetrahydro-1H-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (6a):



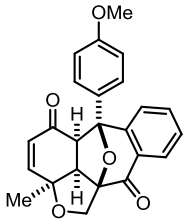
Prepared according to the general procedure as described above in 72% yield (65mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a white solid; mp = 120–122°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.63 (td, *J* = 7.7, 1.4 Hz, 1H), 7.46 (td, *J* = 7.6, 1.0 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 6.87 (dd, *J* = 10.3, 1.1 Hz, 1H), 6.21 (d, *J* = 10.3 Hz, 1H), 4.89 (d, *J* = 10.2 Hz, 1H), 3.87 (d, *J* = 10.2 Hz, 1H), 2.98 (dd, *J* = 8.8, 1.1 Hz, 1H), 2.93 (d, *J* = 8.8 Hz, 1H), 1.68 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.4, 191.8, 154.1, 149.4, 134.9, 130.2, 128.6, 128.0, 127.5, 123.4, 98.4, 91.3, 78.7, 69.4, 55.9, 54.7, 28.3, 21.7; IR (neat): υ_{max} 3081, 2945, 1714, 1697, 1454, 1279, 1072, 759, 694 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{17}O_4$ $[M+H]^+$: 297.1127; found: 297.1119.

6-(4-Chlorophenyl)-2a-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6] cycloh- -epta [1,2,3-*cd]* benzofuran-5,11-dione (6b):



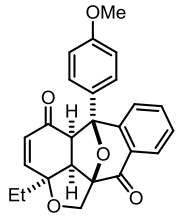
Prepared according to the general procedure as described above in 85% yield (112mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a white solid; mp = 214–216°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.57 – 7.53 (m, 2H), 7.49 (td, *J* = 7.6, 1.6 Hz, 1H), 7.44 (td, *J* = 7.5, 1.2 Hz, 1H), 7.40 – 7.36 (m, 2H), 7.24 (dd, *J* = 7.9, 0.8 Hz, 1H), 6.68 (dd, *J* = 10.3, 1.3 Hz, 1H), 5.77 (d, *J* = 10.3 Hz, 1H), 5.02 (d, *J* = 10.2 Hz, 1H), 4.03 (d, *J* = 10.2 Hz, 1H), 3.53 (d, *J* = 8.7 Hz, 1H), 3.13 (dd, *J* = 8.7, 1.3 Hz, 1H), 1.42 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.6, 191.4, 152.5, 147.4, 134.7, 134.7, 134.4, 130.4, 129.7, 128.9, 128.1, 128.0, 124.9, 98.6, 94.7, 79.3, 70.0, 56.9, 56.5, 28.3; IR (neat): υ_{max} 3084, 2931, 1712, 1694, 1495, 1297, 1094, 764, 681 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{18}O_4Cl$ $[M+H]^+$: 393.0894; found: 393.0887.

6-(4-Methoxyphenyl)-2a-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6] cyclohepta [1,2,3-*cd*]benzofuran-5,11-dione (6c):



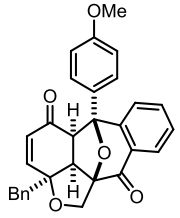
Prepared according to the general procedure as described above in 75% yield (87mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a white solid; mp = 152–154°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.51 (d, *J* = 8.9 Hz, 2H), 7.48 (td, *J* = 7.8, 1.4 Hz, 1H), 7.41 (td, *J* = 7.5, 1.1 Hz, 1H), 7.31 – 7.28 (m, 1H), 6.94 – 6.91 (m, 2H), 6.66 (dd, *J* = 10.3, 1.3 Hz, 1H), 5.76 (d, *J* = 10.3 Hz, 1H), 5.02 (d, *J* = 10.2 Hz, 1H), 4.03 (d, *J* = 10.2 Hz, 1H), 3.82 (s, 3H), 3.52 (d, *J* = 8.7 Hz, 1H), 3.11 (dd, *J* = 8.7, 1.3 Hz, 1H), 1.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.0, 191.8, 159.3, 152.1, 148.5, 134.6, 130.5, 129.5, 128.6, 128.4, 127.9, 127.7, 125.1, 113.2, 98.7, 94.9, 79.4, 70.1, 57.1, 56.8, 55.3, 28.3; IR (neat): υ_{max} 3071, 2945, 1717, 1693, 1297, 1084, 794, 675 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{21}O_5$ $[M+H]^+$: 389.1389; found: 389.1382.

2a-Ethyl-6-(4-methoxyphenyl)-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta [1,2,3-*cd*] benzofuran-5,11-dione (6d):



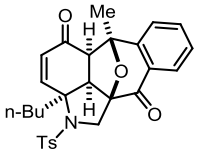
Prepared according to the general procedure as described above in 78% yield (93mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a light yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.52 (d, *J* = 9.0 Hz, 2H), 7.49 – 7.48 (td, *J* = 7.5, 1.6 Hz, 1H), 7.41 (td, *J* = 7.5, 1.2 Hz, 1H), 7.30 (dd, *J* = 7.9, 0.8 Hz, 1H), 6.93 (d, *J* = 9.0 Hz, 2H), 6.57 (dd, *J* = 10.4, 1.3 Hz, 1H), 5.86 (d, *J* = 10.4 Hz, 1H), 5.01 (d, *J* = 10.1 Hz, 1H), 4.06 (d, *J* = 10.1 Hz, 1H), 3.82 (s, 3H), 3.49 (d, *J* = 8.7 Hz, 1H), 3.08 (dd, *J* = 8.7, 1.3 Hz, 1H), 1.73 (qd, *J* = 7.5, 1.8 Hz, 2H), 0.81 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 196.2, 191.9, 159.2, 150.6, 148.5, 134.6, 131.5, 129.5, 128.6, 128.4, 128.0, 127.7, 125.1, 113.2, 98.2, 94.8, 82.6, 70.0, 57.3, 55.3, 55.0; 34.1, 8.4; IR (neat): υ_{max} 3072, 2932, 1716, 1697, 1475, 1296, 1094, 764, 685 cm^{-1}; calcd for $C_{25}H_{23}O_5$ $[M+H]^+$: 403.1545; found: 403.1541.

2a-Benzyl-6-(4-methoxyphenyl)-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6] cyclohepta [1,2,3-*cd*]benzofuran-5,11-dione (6e):



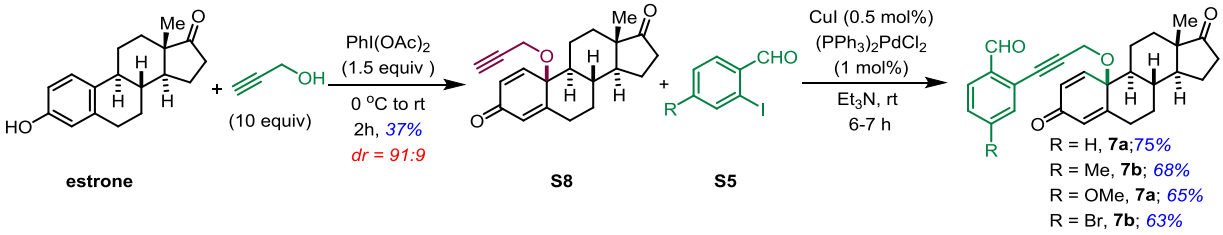
Prepared according to the general procedure as described above in 67% yield (118 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.46 (td, *J* = 7.6, 1.6 Hz, 1H), 7.44 – 7.39 (m, 3H), 7.26 – 7.17 (m, 4H), 7.09 – 7.02 (m, 2H), 6.89 – 6.84 (m, 2H), 6.49 (dd, *J* = 10.3, 1.3 Hz, 1H), 5.74 (d, *J* = 10.3 Hz, 1H), 5.05 (d, *J* = 10.1 Hz, 1H), 4.05 (d, *J* = 10.1 Hz, 1H), 3.79 (s, 3H), 3.22 (dd, *J* = 8.6, 1.3 Hz, 1H), 3.16 (d, *J* = 8.6 Hz, 1H), 3.02 (d, *J* = 13.4 Hz, 1H), 2.96 (d, *J* = 13.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.6, 191.9, 159.2, 149.8, 148.5, 134.6, 134.5, 131.9, 130.8, 129.5, 128.6, 128.5, 128.3, 127.9, 127.8, 127.3, 125.1, 113.1, 98.0, 94.8, 82.9, 70.1, 57.0, 55.5, 55.3, 47.1; IR (neat): υ_{max} 3087, 2945, 1716, 1686, 1475, 1297, 1081, 794, 661 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{25}O_5$ $[M+H]^+$: 465.1702; found: 465.1704.

2a-Butyl-6-methyl-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*] indole-5,11-dione (6f):



Prepared according to the general procedure as described above in 72% yield (105 mg). It was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.6) to afford a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.63 (td, *J* = 7.7, 1.4 Hz, 1H), 7.45 (td, *J* = 7.6, 1.0 Hz, 1H), 7.36 – 7.31 (m, 4H), 6.25 (d, *J* = 10.5 Hz, 1H), 4.60 (d, *J* = 11.4 Hz, 1H), 3.72 (d, *J* = 11.4 Hz, 1H), 2.97 (d, *J* = 9.4 Hz, 1H), 2.91 (d, *J* = 9.0 Hz, 1H), 2.43 (s, 3H), 2.23 (td, *J* = 13.0, 4.3 Hz, 1H), 1.70 (td, *J* = 13.0, 4.3 Hz, 1H), 1.64 (s, 3H), 1.22 – 1.18 (m, 2H), 1.11 – 1.00 (m, 1H), 1.00 – 0.88 (m, 1H), 0.76 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.7, 191.7, 150.8, 149.8, 143.8, 138.8, 135.2, 130.0, 129.8, 128.7, 127.7, 127.4, 127.2, 123.2, 92.5, 88.9, 67.8, 56.5, 55.0, 51.8, 39.9, 26.7, 22.7, 21.7, 21.4, 13.9; IR (neat): υ_{max} 3084, 2931, 1706, 1684, 1494, 1224, 1094, 745, 669 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{30}NO_5S[M+H]^+$:492.1845 ; found: 492.1847.

IIIBb: General Procedure for the synthesis of 2-enylbenzaldehyde-tethered estrone derivatives 8a-8d:



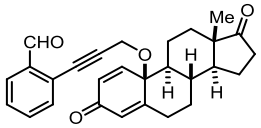
*Dearomatization procedure for the synthesis of **S8:**[8]*

Estrone (2 g, 7.4 mmol, 1 equiv) was dissolved in CH_2Cl_2 (5 mL), then propargyl alcohol (4.1 mL,10 equiv) was added diacetoxyiodobenzene (BAIB, 3.6 g, 1.5 equiv) in several portions at room temperature. The resulting mixture was stirred for 2 hours at room temperature. Then it was diluted with water (10 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phases were washed with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (EtOAc/hexane) to afford the desired product **S8** as a light yellow solid, yield 37% (0. 892 g) d.r.=91:9, (R_f = 0.5 in 30% EtOAc/hexanes).

General procedure for the synthesis of ***7:***[4]

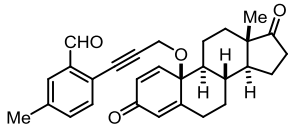
To a solution of alkyne -tethered estrone **S8** (0.5 mmol) in degassed Et_3N (0.25 M, 2 mL) was added $Pd(PPh_3)_2Cl_2$ (3.5 mg, 1 mol%), CuI (0.5 mg, 0.5 mol%) and aryl iodide **S5** (0.6 mmol). The mixture was stirred at room temperature for 6-7 hours. The reaction was diluted with water (5 mL) and extracted with EtOAc (3 × 5 mL). The combined organic solvent was washed with 10% aqueous HCl (2 mL), dried (Na_2SO_4), filtered, and concentrated *in vacuo*. The mixture was purified by column chromatography (EtOAc/hexane) to afford corresponding 2-enylbenzaldehyde-tethered estrone **7a-7d** in good yields.

2-(3-(((8S,9S,10S,13S,14S)-13-Methyl-3,17-dioxo-3,6,7,8,9,11,12,13,14,15,16,17-dodeca hydro-10H-cyclopenta[a]phenanthren-10-yl)oxy)prop-1-yn-1-yl)benzaldehyde (7a):



Prepared according to the general procedure as described above in 75% yield (160 mg). It was purified by flash chromatography (30% EtOAc/hexanes; R_f = 0.5) to afford **7a** (*dr* = 12:1) a colourless oil. $[\alpha]^{20}_D$ = -1.10° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.48 (d, *J* = 0.7 Hz, 1H), 7.92 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.55 (dtd, *J* = 8.8, 7.7, 1.3 Hz, 2H), 7.48 – 7.44 (m, 1H), 7.11 (d, *J* = 10.3 Hz, 1H), 6.40 (dd, *J* = 10.3, 2.0 Hz, 1H), 6.24 (t, *J* = 1.7 Hz, 1H), 4.17 (d, *J* = 0.8 Hz, 2H), 2.71 – 2.63 (m, 1H), 2.51 – 2.40 (m, 2H), 2.27 – 2.18 (m, 1H), 2.16 – 2.12 (m, 1H), 2.11 – 2.04 (m, 2H), 1.99 – 1.93 (m, 1H), 1.90 – 1.85 (m, 1H), 1.83 – 1.78 (m, 1H), 1.65 – 1.61 (m, 1H), 1.30 – 1.25 (m, 2H), 1.23 – 1.15 (m, 2H), 0.99 (s, 3H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 220.4, 191.6, 185.2, 163.4, 149.5, 136.3, 133.9, 133.5, 131.8, 129.2, 127.5, 126.8, 126.0, 92.9, 82.3, 76.7, 55.5, 53.6, 50.4, 48.0, 35.8, 34.8, 32.7, 32.4, 31.3, 22.4, 22.2, 14.0; IR (neat): υ_{max} 3087, 2931, 1731, 1714, 1684, 1473, 1275, 794, 673 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{29}O_4$ $[M+H]^+$: 429.2066; found: 429.2047.

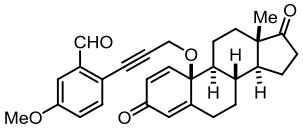
5-Methyl-2-(3-(((8S,9S,10S,13S,14S)-13-methyl-3,17-dioxo-3,6,7,8,9,11,12,13,14,15,16,17-dode cahydro-10*H*-cyclopenta[a]phenanthren-10-yl)oxy)prop-1-yn-1-yl)benzaldehyde (7b):



Prepared according to the general procedure as described above in 68% yield (150 mg). It was purified by flash chromatography (30% EtOAc/hexanes; R_f = 0.6) to afford **7b** (*dr* = 15:1) as a white solid; mp = 234-236°C; $[\alpha]^{20}_D$ = -35.94° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.43 (s, 1H), 7.71 (s,

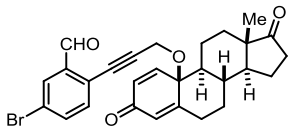
1H), 7.41 (d, *J* = 7.9 Hz, 1H), 7.36 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.10 (d, *J* = 10.3 Hz, 1H), 6.39 (dd, *J* = 10.3, 2.0 Hz, 1H), 6.22 (t, *J* = 1.5 Hz, 1H), 4.15 (s, 2H), 2.71 – 2.62 (m, 1H), 2.50 – 2.41 (m, 2H), 2.40 (s, 3H), 2.27 – 2.20 (m, 1H), 2.13 – 2.08 (m, 2H), 2.04 (d, *J* = 8.3 Hz, 1H), 1.98 – 1.92 (m, 1H), 1.90 – 1.84 (m, 1H), 1.82 – 1.77 (m, 1H), 1.65 – 1.57 (m, 1H), 1.29 – 1.26 (m, 1H), 1.22 – 1.19 (m, 2H), 1.17 – 1.13 (m, 1H), 0.97 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 220.4, 191.8, 185.2, 163.5, 149.5, 139.6, 136.2, 134.8, 133.4, 131.8, 127.8, 126.7, 123.2, 92.1, 82.4, 76.6, 55.5, 53.7, 50.4, 47.9, 35.8, 34.8, 32.7, 32.4, 31.3, 22.4, 22.1, 21.5, 14.0; IR (neat): υ_{max} 3084, 2947, 1732, 1715, 1684, 1475, 1297,794, 645 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{31}O_4$ $[M+H]^+$: 443.2222; found: 443.2223

5-Methoxy-2-(3-(((8S,9S,10S,13S,14S)-13-methyl-3,17-dioxo-3,6,7,8,9,11,12,13,14,15,16, 17 -dodecahydro-10*H*-cyclopenta[a]phenanthren-10-yl)oxy)prop-1-yn-1yl)benzaldehyde (7c):



Prepared according to the general procedure as described above in 65% yield (149 mg). It was purified by flash chromatography (30% EtOAc/hexanes; R_f = 0.4) to afford **7c** (*dr* = 9:1) a white solid; mp = 184–186°C;$[\alpha]^{20}_D$ = -30.26° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.42 (s, 1H), 7.43 (d, *J* = 8.5 Hz, 1H), 7.37 (d, *J* = 2.6 Hz, 1H), 7.12 – 7.08 (m, 2H), 6.38 (dd, *J* = 10.3, 1.6 Hz, 1H), 6.22 (s, 1H), 4.13 (s, 2H), 3.85 (s, 3H), 2.66 (td, *J* = 12.8, 4.5 Hz, 1H), 2.50 – 2.43 (m, 2H), 2.26 – 2.19 (m, 1H), 2.13 – 2.06 (m, 2H), 2.03 (d, *J* = 8.3 Hz, 1H), 1.97 – 1.93 (m, 1H), 1.89 – 1.83 (m, 1H), 1.81 – 1.76 (m, 1H), 1.64 – 1.57 (m, 1H), 1.27 (s, 1H), 1.22 – 1.16 (m, 2H), 1.14 – 1.10 (m, 1H), 0.97 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 220.4, 191.4, 185.2, 163.5, 160.2, 149.6, 137.8, 134.9, 131.7, 126.7, 121.7, 118.7, 110.1, 91.3, 82.2, 76.6, 55.8, 55.5, 53.7, 50.3, 47.9, 35.8, 34.8, 32.7, 32.4, 31.2, 22.3, 22.1, 14.0; IR (neat): υ_{max} 3087, 2946, 1725, 1713, 1694, 1454, 1275, 797, 674 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{31}O_5$ $[M+H]^+$: 459.2171; found: 459.2193.

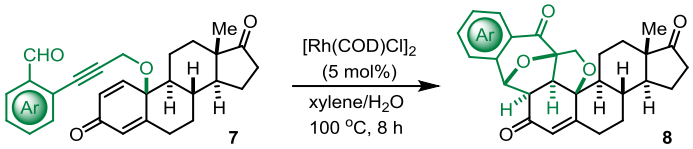
5-Bromo-2-(3-(((8S,9S,10S,13S,14S)-13-methyl-3,17-dioxo-3,6,7,8,9,11,12,13,14,15,16,17-dodecahydro-10H-cyclopenta[a]phenanthren-10-yl)oxy)prop-1-yn-1-yl)benzaldehyde (7d):



Prepared according to the general procedure as described above in 63% yield (159 mg). It was purified by flash chromatography (30% EtOAc/hexanes; R_f = 0.5) to afford **7d** (*dr* = 15:1) as a white solid; mp = 180–182°C; $[\alpha]^{20}_D$ = -29.70° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.38 (s, 1H), 8.02 (d, *J* = 2.1 Hz, 1H), 7.67 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 1H), 7.09 (d, *J* = 10.3 Hz, 1H), 6.39

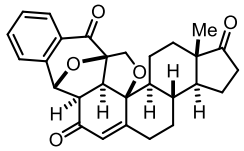
(dd, *J* = 10.3, 2.0 Hz, 1H), 6.22 (t, *J* = 1.6 Hz, 1H), 4.14 (d, *J* = 0.8 Hz, 2H), 2.68 – 2.61 (m, 1H), 2.50 – 2.45 (m, 1H), 2.43 – 2.40 (m, 1H), 2.25 – 2.19 (m, 1H), 2.12 – 2.09 (m, 2H), 2.06 – 2.03 (m, 1H), 1.97 – 1.93 (m, 1H), 1.89 – 1.85 (m, 1H), 1.82 – 1.78 (m, 1H), 1.64 – 1.58 (m, 1H), 1.28 (t, *J* = 3.0 Hz, 1H), 1.24 – 1.19 (m, 2H), 1.18 – 1.14 (m, 1H), 0.97 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 220.3, 190.1, 185.1, 163.2, 149.3, 137.4, 136.8, 134.8, 131.9, 130.5, 126.8, 124.7, 123.8, 94.0, 81.4, 76.7, 55.5, 53.6, 50.3, 47.9, 35.8, 34.8, 32.7, 32.4, 31.2, 22.3, 22.1, 14.0; IR (neat): υ_{max} 3074, 2934, 1729, 1715, 1686, 1475, 1281, 781, 674 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{28}O_4Br$ $[M+H]^+$: 507.1180; found: 507.1171.

IIIBc: General Procedure for the Rh(I)-catalyzed [3+2] cycloaddition of estrone derivatives:



A dried screw-cap vial was charged with 2-enylbenzaldehyde-tethered estrone **8** (0.2 mmol, 1 equiv) and $[Rh(COD)Cl]_2$ (4.9 mg, 5.0 mol%) in 5 % aqueous xylenes (1 mL, 0.2 M) under inert atmosphere, and the reaction mixture was stirred at 100 °C for 8 hour (monitored by TLC). Then, it was cooled to room temperature and concentrated under reduced pressure. The residue was directly subjected to silica gel column chromatography on silica gel with gradient eluent of petroleum ether and EtOAc to afford the desired product **8** with exclusive diastereoselectivity in moderate to good yield.

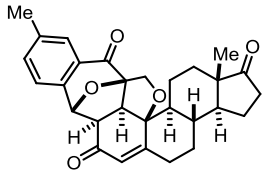
(3a*S*,3b*S*,7a*R*,7a^1*R*,8*R*,13a*R*,15a*R*,15b*S*,17a*S*)-17a-Methyl-2,3,3a,3b,4,5,7a,8,15b,16,17,17a-dodecahydro-14*H*-8,13a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]cyclopenta[5,6]naphtho[2,1-*h*]benzofuran-1,7,13(7a^1*H*)-trione (8a):



Prepared according to the general procedure as described above in 68% yield (64 mg). It was purified by flash chromatography (30% EtOAc/hexanes; R_f = 0.5) to afford a colourless oil; $[\alpha]^{20}_D$ = -62.20° (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.1 Hz, 1H), 7.61 (td, *J* = 7.5, 1.3 Hz, 1H), 7.47 (td, *J* = 7.6, 1.0 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 6.14 (d, *J* = 0.8 Hz, 1H), 5.71 (s, 1H), 4.82 (d, *J* = 10.1 Hz, 1H), 3.74 (d, *J* = 10.1 Hz, 1H), 3.30 (d, *J* = 8.9 Hz, 1H), 2.94 (d, *J* = 8.9 Hz, 1H), 2.82 (td, *J* = 12.6, 4.4 Hz, 1H), 2.47 (dd, *J* = 19.5, 8.6 Hz, 1H), 2.37 (ddd, *J* = 12.4, 3.8, 2.5 Hz, 1H), 2.12 – 2.04 (m, 3H), 1.96 – 1.89 (m, 1H), 1.86 – 1.81 (m, 1H),1.74 – 1.65 (m, 2H), 1.56 – 1.54 (m, 1H),

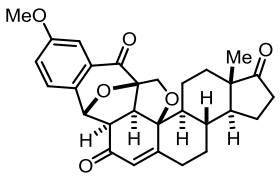
1.24 – 1.13 (m, 4H), 0.95 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 220.2, 194.7, 191.8, 167.2, 144.4, 134.6, 129.0, 128.2, 127.6, 126.3, 124.8, 99.3, 89.2, 82.0, 68.4, 53.0, 51.6, 50.8, 49.0, 48.0, 36.8, 35.9, 32.9, 32.1, 31.1, 21.8, 20.8, 14.0; IR (neat): υ_{max} 3081, 2942, 1716,1704, 1697, 1452, 1294,781, 694 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{29}O_5$ $[M+H]^+$: 445.2015; found: 445.2020.

(3a*S*,3b*S*,7a*R*,7a^1*R*,8*R*,13a*R*,15a*R*,15b*S*,17a*S*)-11,17a-Dimethyl-2,3,3a,3b,4,5,7a,8,15b, 16,17,17a-dodecahydro-14*H*-8,13a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]cyclopenta[5,6] naphtho[2,1-h]benzofuran-1,7,13(7a1*H*)-trione (8b):



Prepared according to the general procedure as described above in 54% yield (56mg). It was purified by flash chromatography (30% EtOAc/hexanes; R_f = 0.6) to afford a colourless oil; $[\alpha]^{20}_D$ =12.28° (c 1.0, $CHCl_3$);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.9 Hz, 1H), 7.28 – 7.27 (m, 1H), 7.22 (s, 1H), 6.13 (d, *J* = 0.8 Hz, 1H), 5.64 (s, 1H), 4.81 (d, *J* = 10.1 Hz, 1H), 3.74 (d, *J* = 10.1 Hz, 1H), 3.28 (d, *J* = 9.0 Hz, 1H), 2.92 (d, *J* = 9.0 Hz, 1H), 2.82 (ddd, *J* = 12.5, 5.0, 3.9 Hz, 1H), 2.48 (dd, *J* = 11.2, 8.2 Hz, 1H), 2.43 (s, 3H), 2.37 (ddd, *J* = 12.9, 3.9, 2.6 Hz, 1H), 2.11 – 2.05 (m, 3H), 1.96 – 1.89 (m, 1H), 1.86 – 1.80 (m, 1H), 1.75 – 1.63 (m, 2H), 1.75 – 1.63 (m, 2H), 1.23 – 1.14 (m, 3H), 0.94 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 220.3, 194.9, 191.6, 167.3, 146.0, 144.5, 129.8, 127.7, 126.2, 125.8, 125.2, 99.3, 89.2, 82.0, 68.5, 53.1, 51.8, 50.8, 49.2, 48.0, 36.8, 35.9, 32.9, 32.1, 31.1, 22.1, 21.8, 20.8, 14.0; IR (neat): υ_{max} 3064, 2952, 1715,1706, 1684, 1474, 1281,774, 667 cm^{-1}; HRMS(ESI) calcd $C_{29}H_{31}O_5$ $[M+H]^+$: 459.2171; found: 459.2179.

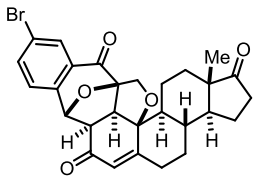
(3a*S*,3b*S*,7a*R*,7a^1*R*,8*R*,13a*R*,15a*R*,15b*S*,17a*S*)-11-Methoxy-17a-methyl-2,3,3a,3b,4,5, 7a, 8,15b,16,17,17a-dodecahydro-14*H*-8,13a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]cyclopenta [5,6]naphtho[2,1-h]benzofuran-1,7,13(7a^1*H*)-trione (8c):



Prepared according to the general procedure as described above in 57% yield (54mg). It was purified by flash chromatography (30% EtOAc/hexanes; R_f = 0.5) to afford a colourless oil; $[\alpha]^{20}_D$ = 33.52° (c 1.0, $CHCl_3$);^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.7 Hz, 1H), 6.95 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.86 (d, *J* = 2.4 Hz, 1H), 6.13 (d, *J* = 0.8 Hz, 1H), 5.62 (s, 1H), 4.81 (d, *J* = 10.1 Hz, 1H), 3.90 (s, 3H),

3.74 (d, *J* = 10.1 Hz, 1H), 3.29 (d, *J* = 9.0 Hz, 1H), 2.94 (d, *J* = 9.0 Hz, 1H), 2.82 (td, *J* = 12.5, 4.4 Hz, 1H), 2.47 (dd, *J* = 19.4, 8.4 Hz, 1H), 2.37 (ddd, *J* = 12.1, 3.6, 2.3 Hz, 1H),2.15 – 2.05 (m, 3H), 1.96 – 1.91 (m, 1H), 1.87 – 1.81 (m, 1H), 1.73 – 1.67 (m, 2H), 1.64 – 1.52 (m, 2H), 1.23 – 1.14 (m, 3H), 0.94 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 220.3, 195.0, 190.8, 167.5, 164.6, 146.9, 130.0, 126.1, 121.3, 115.5, 108.8, 99.3, 89.2, 81.9, 68.5, 56.0, 53.2, 51.9, 50.8, 49.5, 48.0, 36.8, 35.9, 32.9, 32.1, 31.1, 21.8, 20.8, 14.0; IR (neat): υ_{max} 3065, 2931, 1714,1705, 1684, 1464, 1297,745, 675 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{31}O_6$ $[M+H]^+$: 475.2121; found: 475.2121.

(3a*S*,3b*S*,7a*R*,7a^1*R*,8*R*,13a*R*,15a*R*,15b*S*,17a*S*)-11-bromo-17a-methyl-2,3,3a,3b,4,5,7a,8, 15b,16,17,17a-dodecahydro-14*H*-8,13a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]cyclo penta [5,6]naphtho[2,1-h]benzofuran-1,7,13(7a^1*H*)-trione (8d):



Prepared according to the general procedure as described above in 52% yield (54 mg). It was purified by flash chromatography (30% EtOAc/hexanes; R_f = 0.6) to afford a yellow oil; $[\alpha]^{20}_D$ = +43.96° (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.1 Hz, 1H), 7.62 – 7.59 (m, 2H), 6.14 (d, *J* = 0.8 Hz, 1H), 5.65 (s, 1H), 4.79 (d, *J* = 10.2 Hz, 1H), 3.73 (d, *J* = 10.2 Hz, 1H), 3.28 (d, *J* = 9.0 Hz, 1H), 2.94 (d, *J* = 9.0 Hz, 1H), 2.85 – 2.78 (m, 1H), 2.47 (dd, *J* = 19.5, 8.5 Hz, 1H), 2.37 (ddd, *J* = 10.5, 5.6, 3.5 Hz, 1H),2.12 – 2.05 (m, 3H), 1.95 – 1.91 (m, 1H), 1.85 – 1.81 (m, 1H), 1.76 – 1.52 (m, 4H), 1.33 – 1.15 (m, 3H), 0.94 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 220.1, 194.2, 190.9, 167.2, 145.8, 132.5, 129.8, 129.3, 128.0, 127.0, 126.2, 99.3, 88.6, 82.0, 68.3, 53.0, 51.4, 50.8, 49.0, 48.0, 36.8, 35.9, 32.9, 32.1, 31.0, 21.8, 20.8, 14.0; IR (neat): υ_{max} 3072, 2952, 1715,1712, 1694, 1475, 1264,769, 674 cm^{-1}; HRMS (ESI) calcd for $C_{28}H_{28}O_5Br$ $[M+H]^+$: 523.1120; found: 523.1132.

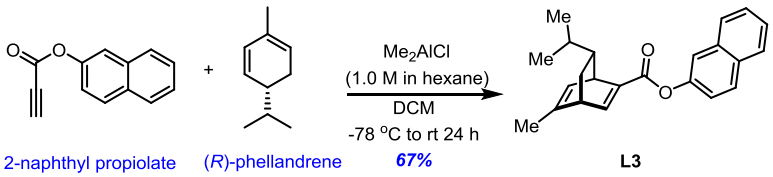
IV: Rh(I)-catalyzed enantioselective [3+2] cycloaddition

IVa. Preparation of Chiral Diene Ligands

Chiral dienes **L1**, **L2** and **L9** were commercial available and purchased from Sigma-Aldrich.

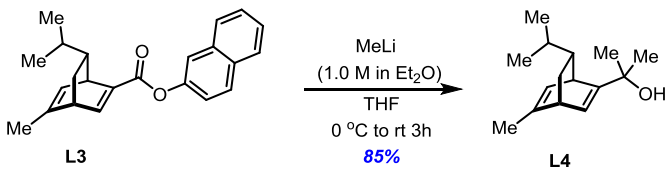
Chiral dienes **L3**, **L4**, **L5**, **L6**, and **L7** were prepared according to a previously reported procedure.[9-6]

Naphthalen-2-yl (1*R*,4*R*,7*R*)-7-isopropyl-5-methylbicyclo[2.2.2]octa-2,5-diene-2-carboxylate (L3):[9]



To a solution of 2-naphthyl propiolate (10.0 g, 51.0 mmol) and (*R*)-α-phellandrene (~70% purity, 10.8 g, 56.1 mmol) in CH_2Cl_2 (170 mL) was added Me_2AlCl (1.0 M in hexane, 52.4 mL, 56.1 mmol) slowly at -78 °C. While adding Me_2AlCl into reaction mixture color changes as colorless to orange liquid. After addition, reaction mixture was shifted to ice bath then slowly allowed to room temperature and stirring was continued for 24 h. The solution was carefully poured into a vigorously stirred, ice-cooled aqueous solution of 1N HCl (180 mL). The mixture was filtered and washed with 70 mL of CH_2Cl_2. The filtrate was then extracted with CH_2Cl_2 (3 × 70 mL). The combined organic layers were washed with brine (180 mL), dried (Na_2SO_4), filtered, and concentrated. The crude was applied on silica gel column chromatography (hexane/EtOAc = 20/1) to give 16.2 g of a mixture of **L3** & (*E*)-2-naphthyl 3-(5-isopropyl-2-methylenecyclohex-3-enyl)propenoate in a ratio of 20 to 1. The mixture was taken into the flask and diluted with 3.5 mL of CH_2Cl_2 and 50 mL of hexane and kept at room temperature for overnight. The precipitated crystals (white needles) were collected and then dried under vacuum to give 7.42 g of **L3** (43.9% yield) and its NMR spectra and rotation was matched with the reported data.[9]

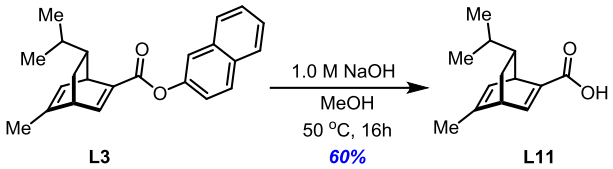
2-((1*R*,4*R*,7*R*)-7-Isopropyl-5-methylbicyclo[2.2.2]octa-2,5-dien-2-yl)propan-2-ol (L4):[10]



To a solution of **L3** (1.0 g, 3.0 mmol) in THF (10 mL) was added MeLi (1.0 M in Et_2O, 6.6 mL, 6.62 mmol) slowly at 0 °C and stirred at room temperature for 3 h. After completion of the reaction, the reaction mixture was poured into an ice-cooled solution of saturated aqueous NH_4Cl (10 mL). The aqueous layer was separated & extracted with EtOAc (3 × 10 mL). The combined organic layers were

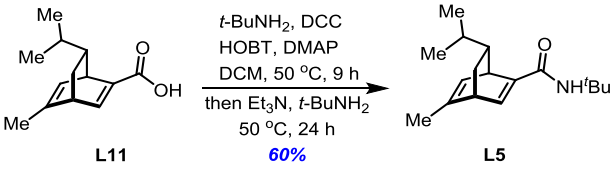
washed with brine (30 mL), dried (Na_2SO_4), filtered & concentrated. The residue was chromatographed on silica gel (hexane/EtOAc = 6/1) to give 0.562 g of **L4** (2.55 mmol, 85% yield) as pale yellow oil. Compound **L4** NMR spectra and rotation was matched with the reported data.[10]

(1*R*,4*R*,7*R*)-7-Isopropyl-5-methylbicyclo[2.2.2]octa-2,5-diene-2-carboxylic acid (L11):[11]



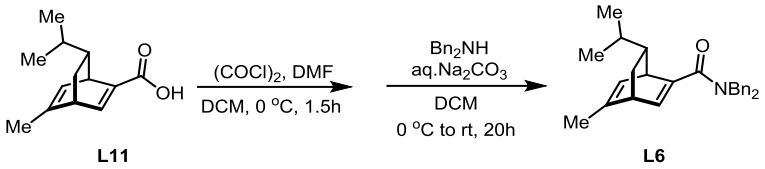
To a stirred solution of the ester **L3** (1.0 g, 3.0 mmol) in MeOH (15 mL) at room temperature was added 1 M aqueous NaOH solution (15 mL) slowly and the resulting mixture was heated to 50 °C for 16 h. The reaction was allowed to cool to room temperature and 1 M aqueous HCl solution (20 mL) was slowly added. The mixture was diluted with H_2O (20 mL) and extracted with Et_2O (4 x 30 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The crude compound was applied on silica gel column chromatography (hexane/EtOAc = 10/1) to give the carboxylic acid **L11** as a white solid (0.372 g, 60%). Compound **L11** NMR spectra and rotation was matched with the reported data. [11]

(1*R*,4*R*,7*R*)-N-(*tert*-Butyl)-7-isopropyl-5-methylbicyclo[2.2.2]octa-2,5-diene-2-carboxamide (L5):[12]



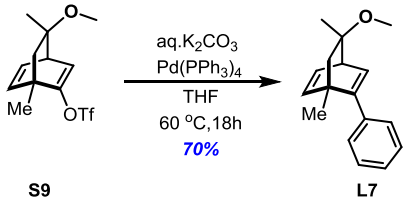
N,*N*'-diisopropylcarbodiimide (84 µL, 0.53 mmol) and *tert*-butylamine (51 µL, 0.48 mmol) in CH_2Cl_2 (1 mL) were added to a solution of acid **L11** (100 mg, 0.48 mmol), HOBT (65.5 mg, 0.48 mmol) and DMAP (3 mg, 0.025 mmol) in CH_2Cl_2 (1 mL) under nitrogen atmosphere. After stirring for 9 h at 50 ºC, Et_3N (135 µL, 0.97 mmol) and *tert*-butylamine (51 µL, 0.48 mmol) were added again to the reaction mixture. After stirring for 24 h at 50 ºC, 1N HCl (6 mL) was added. The precipitation was removed by filtration and the filtrate was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated. The crude was applied on silica gel column chromatography (hexane/EtOAc = 5/1) to obtain **L5** (47.6 mg, 60% yield) as a white solid. Compound **L5** NMR spectra and rotation was matched with the reported data. [12]

(1*R*,4*R*,7*R*)-*N*,*N*-Dibenzyl-7-isopropyl-5-methylbicyclo[2.2.2]octa-2,5-diene-2-carboxamide (L6):[13]



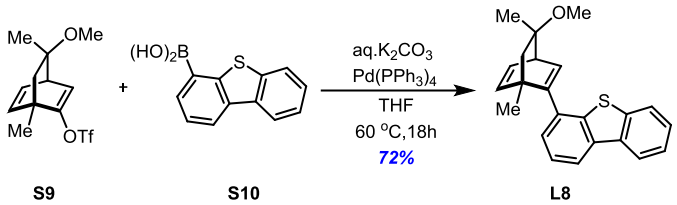
To a solution of carboxylic acid **L11** (100 mg, 0.48 mmol) and DMF (11 µL, 0.15 mmol) in CH_2Cl_2 (1 mL) at 0 °C was added oxalyl chloride (411 µL, 4.8 mmol) dropwise over 3 minutes. The mixture was stirred at 0 °C for 1.5 h to give a solution of the corresponding acid chloride. To a mixture of dibenzylamine (39 µL, 0.36 mmol) in CH_2Cl_2 (1 mL) and saturated aqueous Na_2CO_3 solution (1 mL) at 0 °C was added to the solution of the acid chloride dropwise *via* cannula. The mixture was then stirred at room temperature for 20 h. The mixture was partitioned between saturated aqueous $NaHCO_3$ solution (4 mL) & CH_2Cl_2 (4 mL). The aqueous layer was separated and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with 10% aqueous HCl solution (5 mL), dried (Na_2SO_4), filtered, and concentrated. The crude compound applied to silica gel column chromatography (3% EtOAc/hexane) to give the amide **L6** (167.4 mg, 90%) as a colorless liquid. Compound **L6** NMR spectra and rotation was matched with the reported data.[13]

(1*R*,4*R*,8*R*)-8-Methoxy-1,8-dimethyl-2-phenylbicyclo[2.2.2]octa-2,5-diene (L7):[14]



To a mixture of triflate **S9**[14] (100 mg, 0.32 mmol) and phenylboronic acid (58.6 mg, 0.48 mmol) in THF (6.0 ml) and K_2CO_3 (2.0 M in H_2O, 5.0 ml) was added $Pd(PPh_3)_4$ (7.4 mg, 0.0064 mmol) under nitrogen. The reaction mixture was stir at 60 °C for 18 h. After cooling to room temperature, THF was removed under reduced pressure. Ether was added to the mixture, and then the organic layer was washed with brine, and then dried (Na_2SO_4), and evaporated. The crude compound was purified by silica gel chromatography (10% EtOAc/hexane) to obtain compound **L7** (54 mg, 70%) as a colorless liquid. Compound **L7** NMR spectra and rotation was matched with the reported data. [14]

4-((1*R*,4*R*,8*R*)-8-Methoxy-1,8-dimethylbicyclo[2.2.2]octa-2,5-dien-2-yl)dibenzo[*b*,*d*]thiophene (L8):

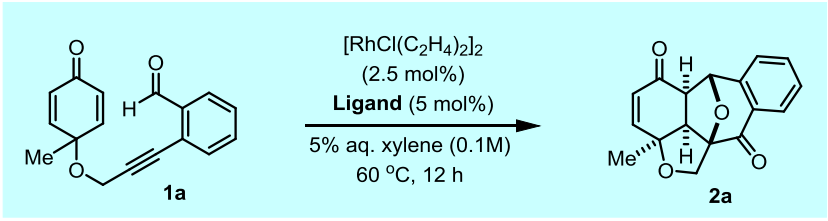


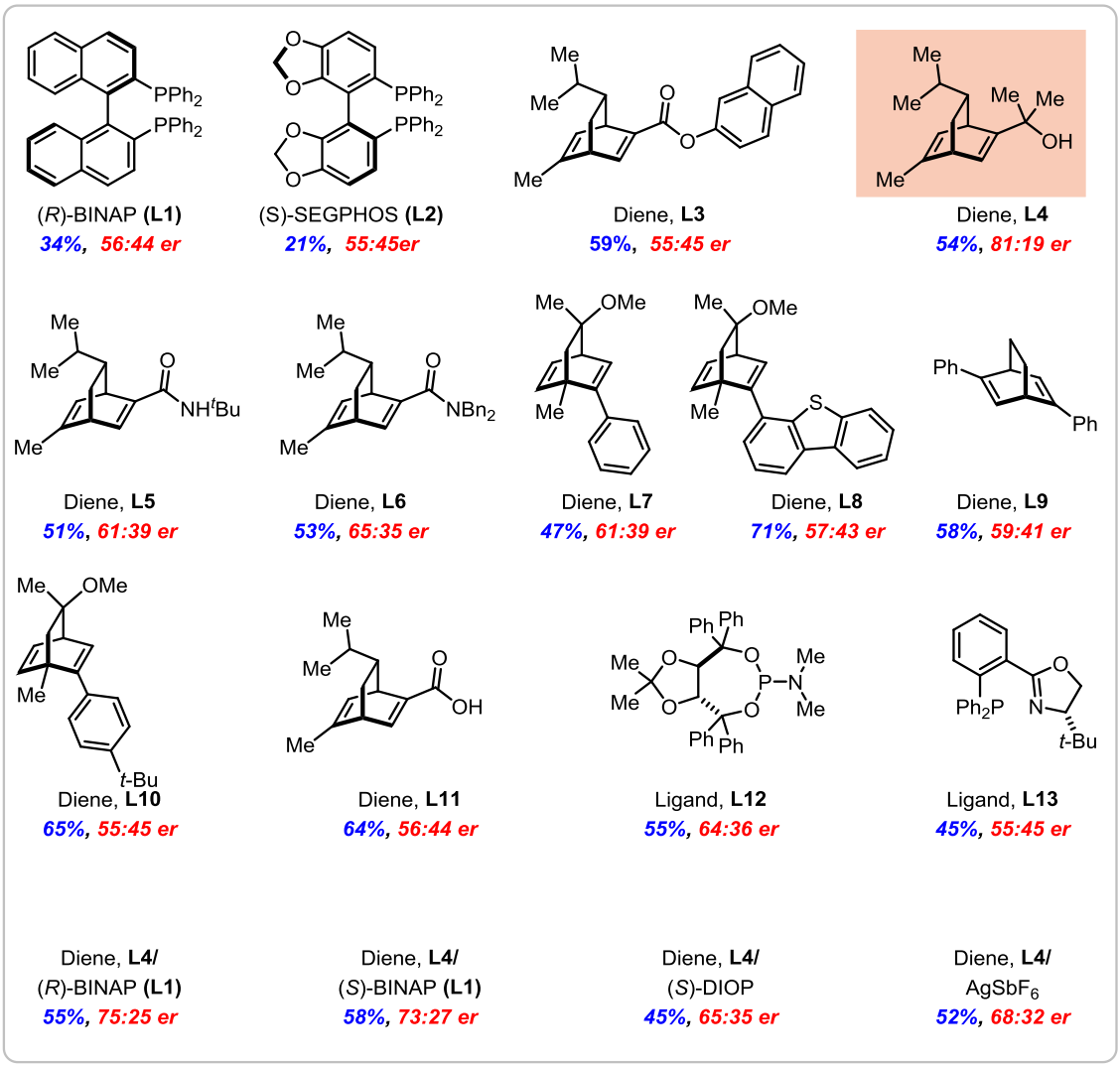
S9 **S10** **L8**

To a mixture of triflate **S9**[6] (100 mg, 0.32 mmol) and boronic acid **S10** (110 mg, 0.48 mmol) in THF (6.0 ml) and K_2CO_3 (2.0 M in H_2O, 5.0 ml) was added $Pd(PPh_3)_4$ (7.4 mg, 0.0064 mmol) under nitrogen atmosphere. The reaction mixture was stir at 60 °C for 18 h. After cooling to room temperature, solvent was removed by under vacuum, Et_2O (10 mL) was added to the crude residue. The organic layer was washed with brine, dried (Na_2SO_4) and then evaporated. The crude compound was purified by silica gel chromatography (10% EtOAc/hexane) to obtain compound **L8** (79.2 mg, 72%) as a colourless liquid. $[\alpha]^{20}_D$ = +2.70° (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 – 8.11 (m, 1H), 8.05 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.83 – 7.78 (m, 1H), 7.46 – 7.38 (m, 3H), 7.13 (dd, *J* = 7.3, 1.1 Hz, 1H), 6.48 – 6.44 (m, 2H), 6.26 (dd, *J* = 7.2, 1.2 Hz, 1H), 3.74 (td, *J* = 6.1, 1.2 Hz, 1H), 3.31 (s, 3H), 1.87 (d, *J* = 12.0 Hz, 1H), 1.37 (d, *J* = 12.0 Hz, 1H), 1.36 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.37, 141.74, 140.47, 139.93, 135.99, 135.29, 134.77, 133.94, 133.03, 126.59, 126.49, 124.14, 124.02, 122.68, 121.59, 119.80, 84.08, 50.52, 49.99, 47.85, 45.75, 24.90, 20.71; IR (neat): υ_{max} 3084, 2982, 2931,1464, 1252, 975, 781, 674 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{22}OKS$ $[M+K]^+$: 385.1023; found: 385.1041.

IVb. Complete screening for the Rh(I)-catalyzed enantioselective [3+2] cycloaddition

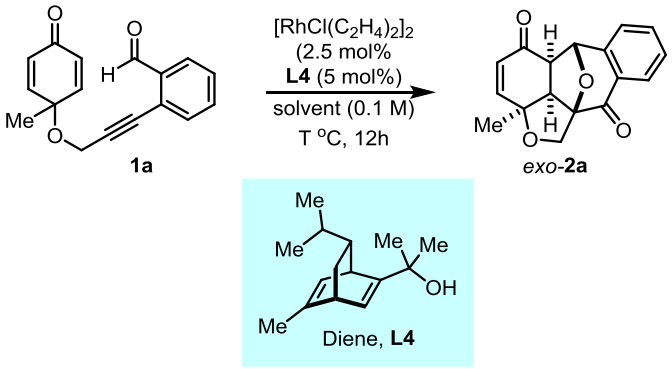
Table S4: Ligand screening[a,b]





[a] Isolated yields of exo-**2a**
[b] Er determined by HPLC analysis using a chiral stationary phase.

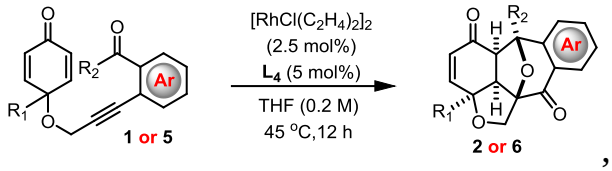
Table S5: Solvent and temperature screening



entry	sovent[a]	T °C	yield [%][b]	er[c]
1	5% aq. xylene	60	54	81:19
2	*t*-BuOH	60	70	88:12
3	THF	60	75	89:11
4	CH_3CN	60	55	81:19
5	DMF	60	32	78:22
6	DCE	60	47	76:24
7	*t*-BuOH	rt	67	89:11
8	THF	rt	68	90:10
9	THF	45	74	91:09
10	THF	0	25	86:14

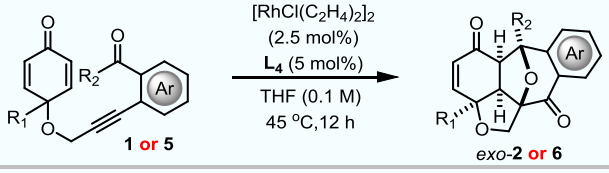
[a] Commertial solvents used in the reaction
[b] Isolated yields of *exo*-**2a**
[b] Er determined by HPLC analysis using a chiral stationary phase.

IVc. General Procedure for the Rh(I)-catalyzed enantioselective [3+2] cycloaddition



,

A dried screw-cap vial was charged with $[RhCl(C_2H_4)_2]_2$ (2.9 mg, 2.5 mol%) and diene ligand (5 mol%) in THF (1 mL) was stirred at room temperature for 10 minutes under inert atmosphere.Then, alkyne-tethered cyclohexadienone **1** (or) **5** (0.3 mmol, 1 equiv) in 2 mL of THF was added under argon atmosphere. Afterwards the resulting reaction mixture allowed to stir at 45 °C temperature for 12 h. Then the reaction mixture was diluted with water (5 mL) and extracted with ethyl acetate (10 mL × 3). The combined organic solvent was dried (Na_2SO_4), filtered, and concentrated *in vacuo*. The crude reaction mixture was purified by silica gel column chromatography (EtOAc/hexane) to give the desired products **2** (or) **6**.

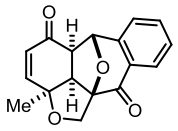


(+)-**2a**; *64%*; *91:09 er*	(+)-**2e**; *63%*; *83:17 er*	(+)-**2f**; *54%*; *89:11 er*
(+)-**2h**; *64%*; *83:17 er*	(+)-**2m**; *53%*; *92:08 er*	(+)-**2r**; *67%*; *91:09 er*
(+)-**2v**; *62%*; *82:18 er*	(+)-**6a**; *67%*; *74:26 er*	(+)-**6b**; *69%*; *78:22 er*

Table S6. Rh(I)-catalyzed enantioselective cyclization

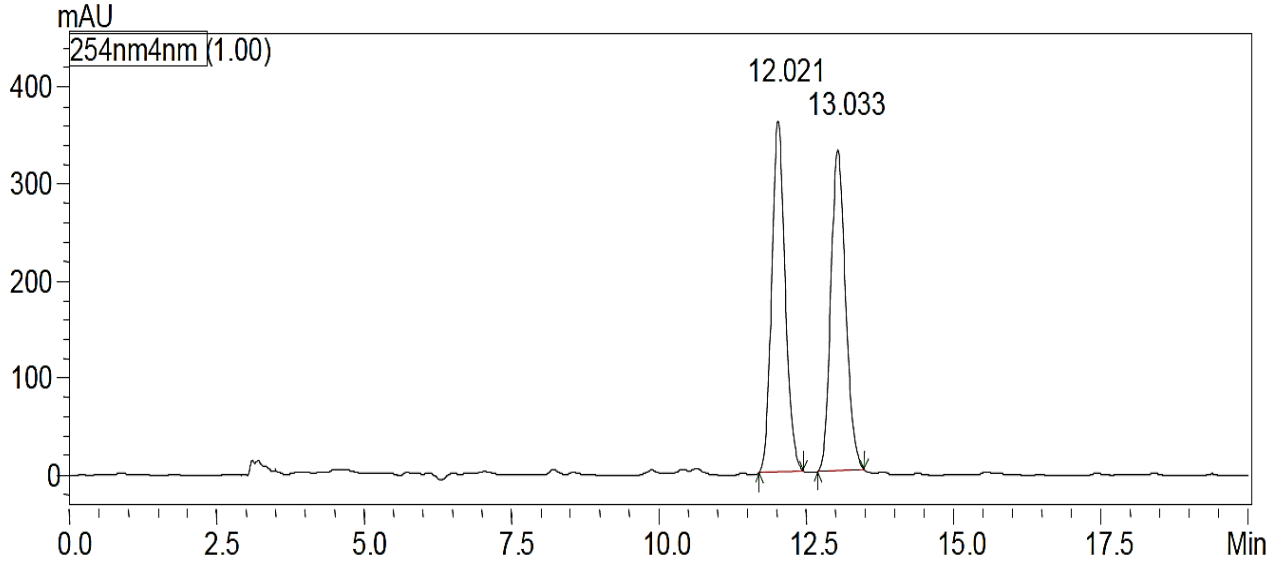
IVd. Chiral HPLC analysis of enantioselective [3+2] cycloaddition

(-)-2a-Methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2a):



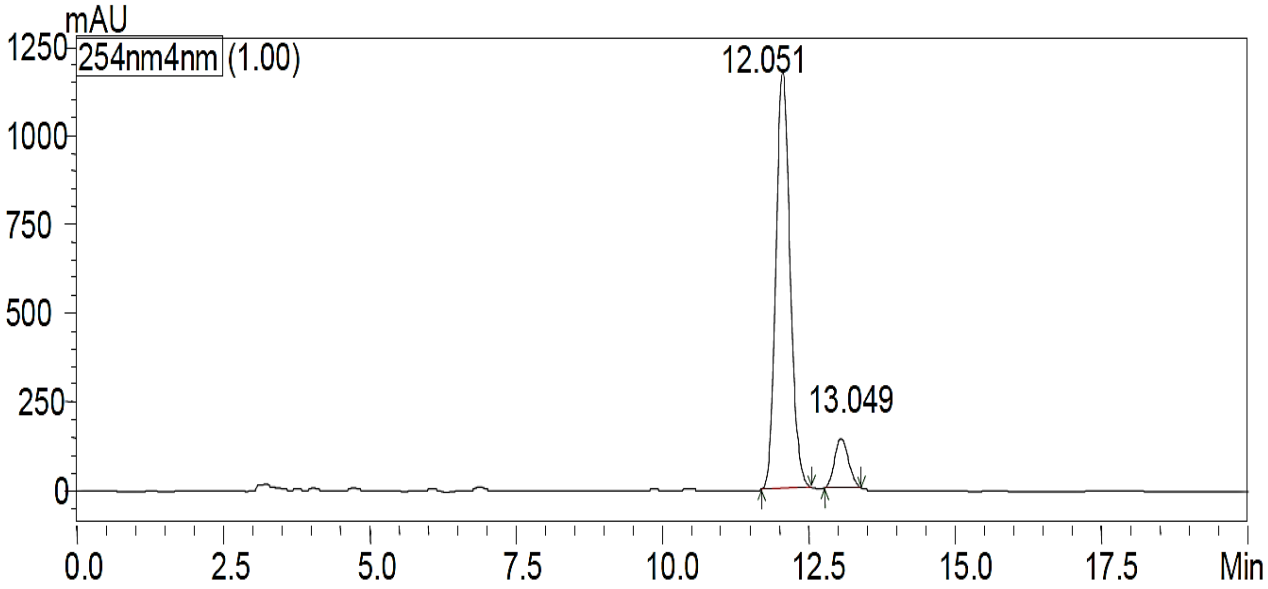
$[\alpha]^{20}_{D}$ = -15.50° (c 1.0, $CHCl_3$); 91:09 *er*

Chiral HPLC analysis of the product: Chiralpak IA 250 x 4.6 mm 5u column; hexane/2-propanol = 85/15, detected at 254 nm, Flow rate = 1 mL/min, Retention times: 12.05 min (major), 13.05 min (minor).



Peak table:

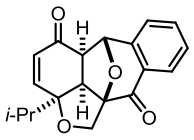
Peak	Ret. Time	Height	Height %	Area	Area%
1	12.021	360082	52.442	5706978	50.441
2	13.033	326551	47.558	5607203	49.559
Total		686633	100.000	11314181	100.000



Peak table:

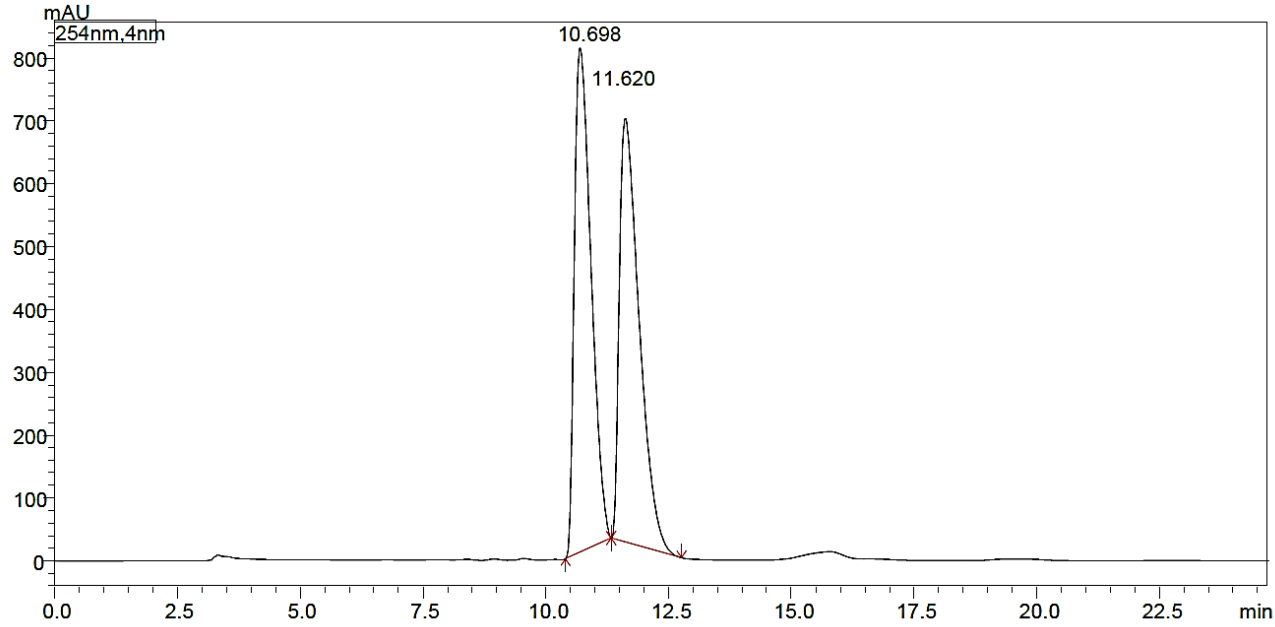
Peak	Ret. Time	Height	Height %	Area	Area%
1	12.051	1169538	89.846	19696177	90.581
2	13.049	132180	10.154	2048179	9.419
Total		1301718	100.000	21744355	100.000

(-)-2a-Isopropyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzo furan 5,11-dione (2e):



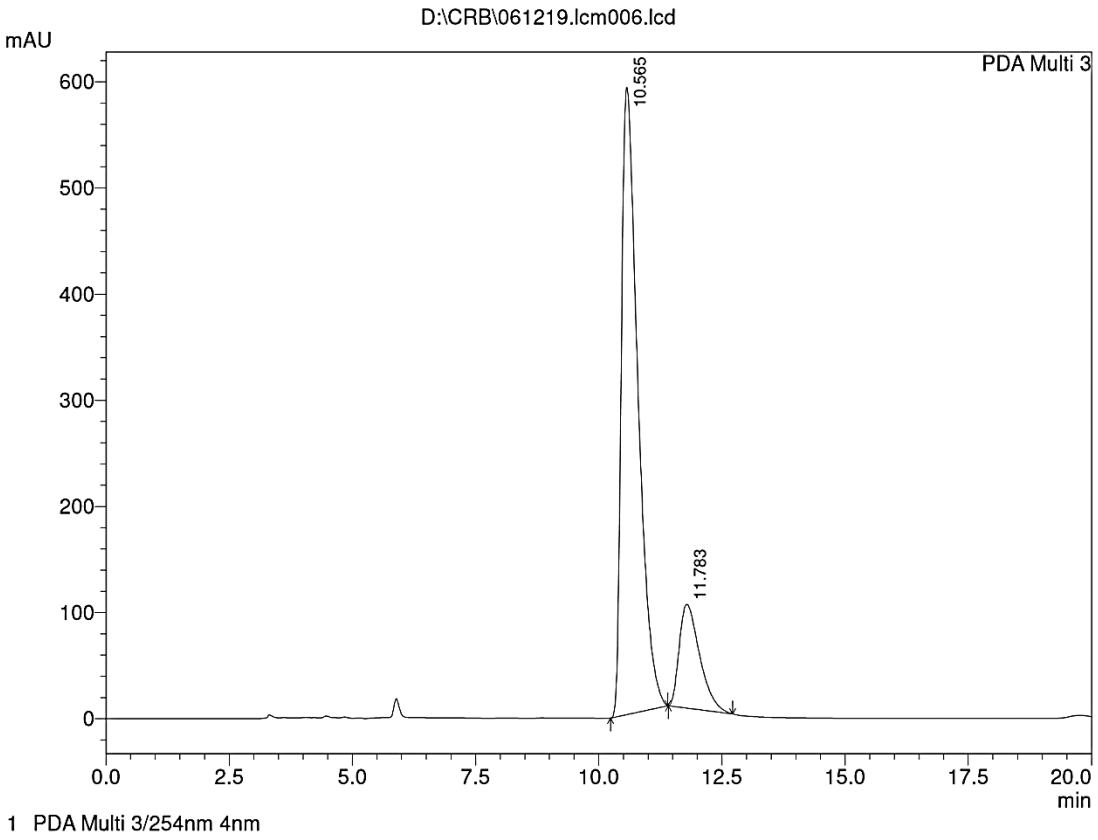
$[\alpha]^{20}_{D}$ = -57.32° (c 1.0, $CHCl_3$); 83:17*er*

Chiral HPLC analysis of the product: Chiralcel OJ-H 250 x 4.6 mm 5u column; hexane/2-propanol = 90/10, detected at 254 nm, Flow rate = 1 mL/min, Retention times: 10.56 min (major), 11.78 min (minor).



Peak Table

Peak	Ret.Time	Height	Height%	Area	Area%
1	10.698	796783	54.426	18698346	50.561
2	11.620	667204	45.574	18283379	49.439
Total		1463987	100.000	36981725	100.000

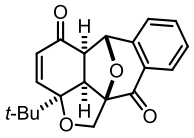


PeakTable

PDA Ch3 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.565	13808738	591031	83.034	85.798
2	11.783	2821408	97829	16.966	14.202
Total		16630147	688860	100.000	100.000

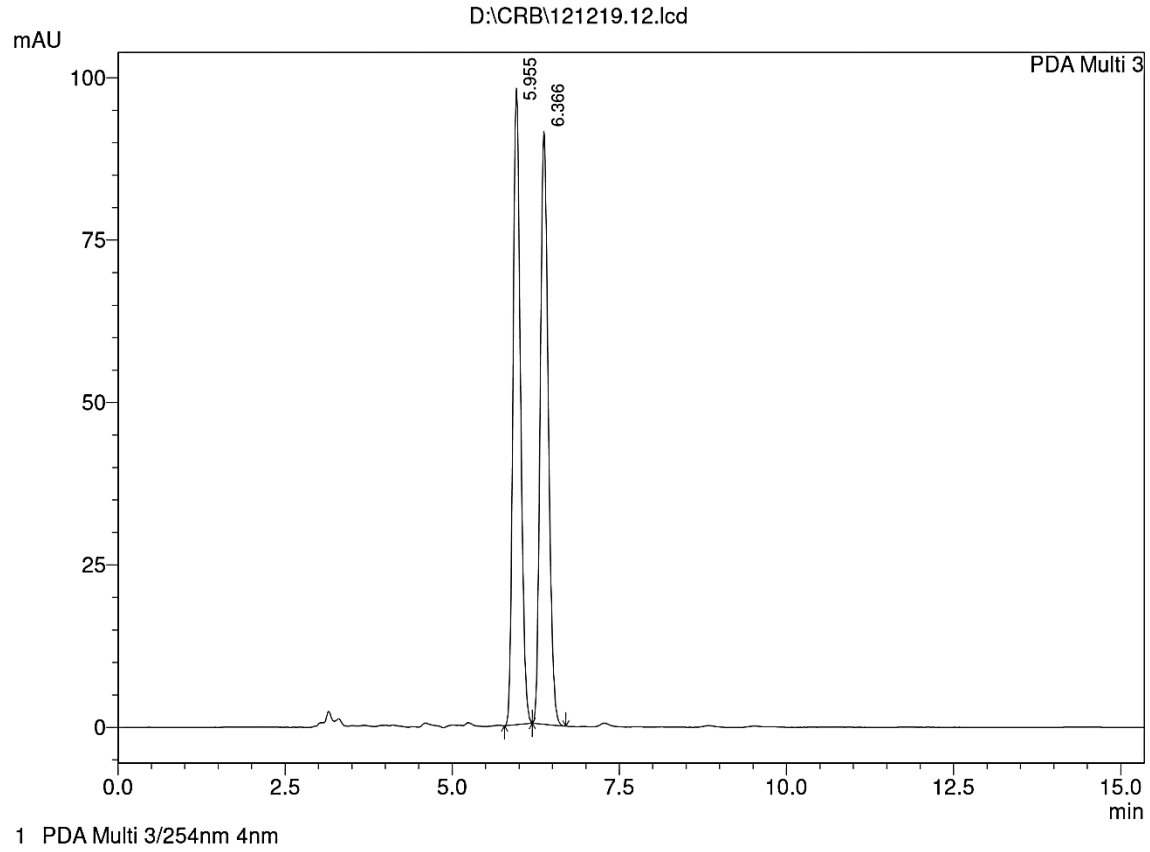
(+)-2a-(*tert*-Butyl)-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2f):



$[\alpha]^{20}_{D}$ = +3.10° (c 1.0, $CHCl_3$); 89:11*er*;

Chiral HPLC analysis of the product: Chiralpak AD-H 250 x 4.6 mm 5u column; hexane/2-propanol = 85/15, detected at 254 nm, Flow rate = 1 mL/min, Retention times: 5.96 min (major), 6.37 min (minor).

<Chromatogram>

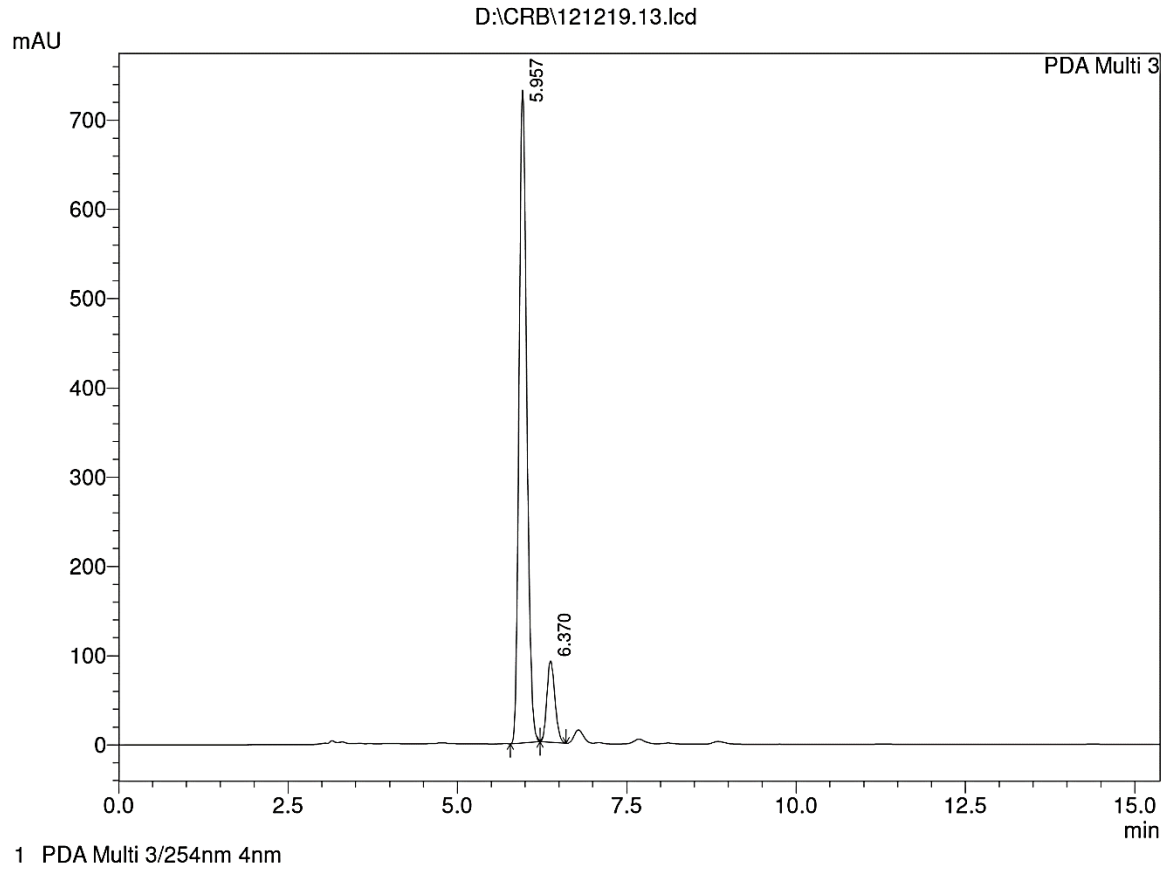


PeakTable

PDA Ch3 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.955	768101	97997	49.897	51.774
2	6.366	771287	91283	50.103	48.226
Total		1539387	189280	100.000	100.000

<Chromatogram>

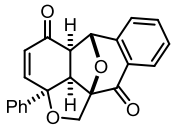


PeakTable

PDA Ch3 254nm 4nm

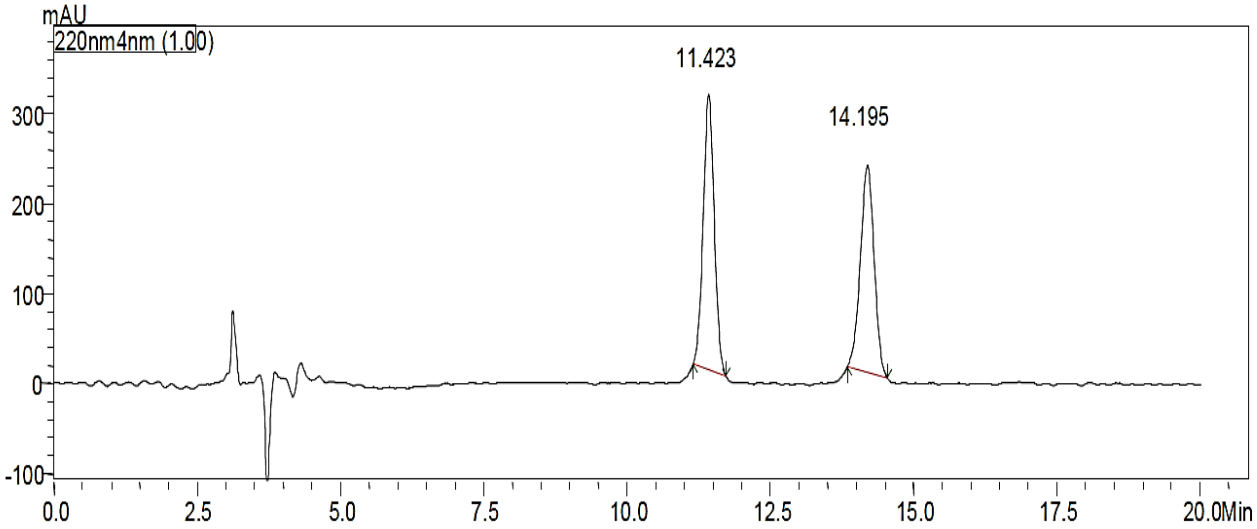
Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.957	5830714	731720	88.552	88.900
2	6.370	753790	91360	11.448	11.100
Total		6584505	823080	100.000	100.000

(+)-2a-Phenyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2h):



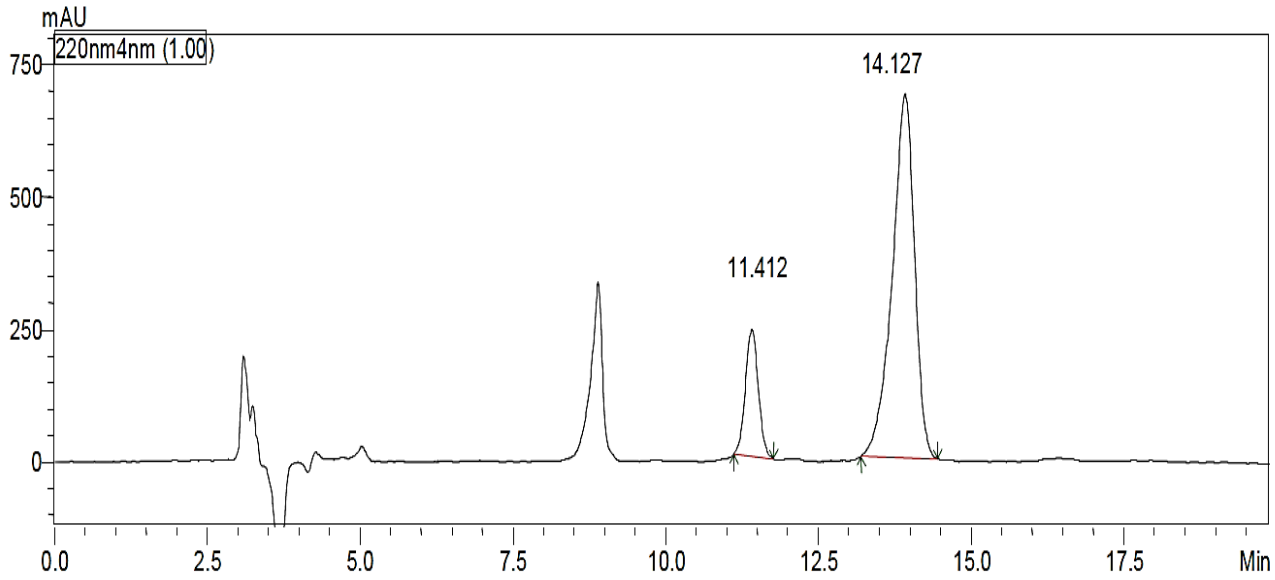
$[\alpha]^{20}_{D}$ = +23.60° (c 1.0, $CHCl_3$); 83:17*er*

Chiral HPLC analysis of the product: Chiralpak-IA 250 x 4.6 mm 5u column; hexane/2-propanol = 92/08, detected at 220 nm, Flow rate = 1 mL/min, Retention times: 11.41 min (minor), 14.13 min (major).



Peak table:

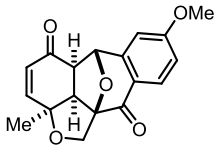
Peak	Ret. Time	Height	Height %	Area	Area%
1	11.423	305913	56.995	4082336	50.836
2	14.195	230826	43.005	3948147	49.164
Total		536739	100.000	8030483	100.000



Peak table:

Peak	Ret. Time	Height	Height %	Area	Area%
1	11.412	240077	25.886	3523223	16.824
2	14.127	687362	74.114	17418589	83.176
Total		927439	100.000	20941812	100.000

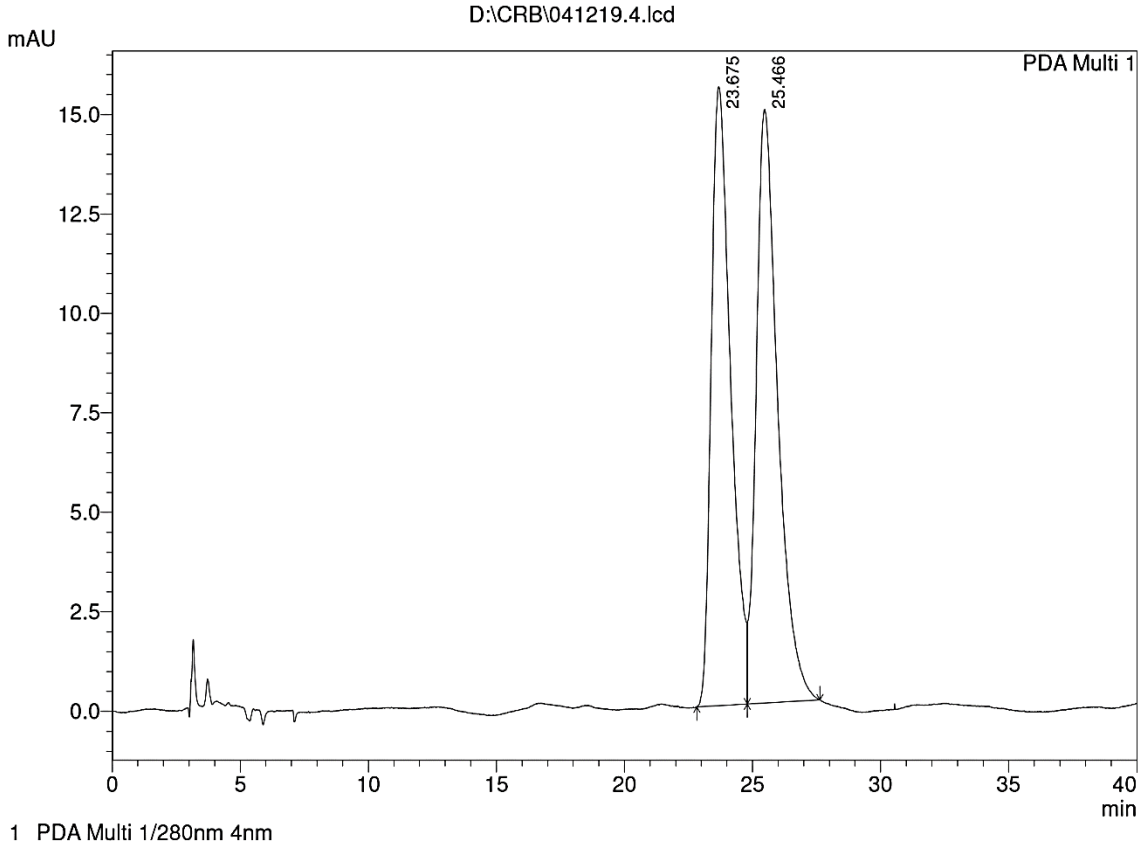
(+)-8-Methoxy-2a-methyl-2a,2a1,5a,6-tetrahydro-*1H*-6,11aepoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2m):



$[\alpha]^{20}_{D}$ = +1.86° (c 1.0, $CHCl_3$); 92:08*er*

Chiral HPLC analysis of the product: Eurocel 01 250 x 4.6 mm 5u column; hexane/2-propanol = 95/5, detected at 280 nm, Flow rate = 1 mL/min, Retention times: 23.33 min (major), 25.40 min (minor).

<Chromatogram>



PeakTable

PDA Ch1 280nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
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Total		1696081	30472	100.000	100.000

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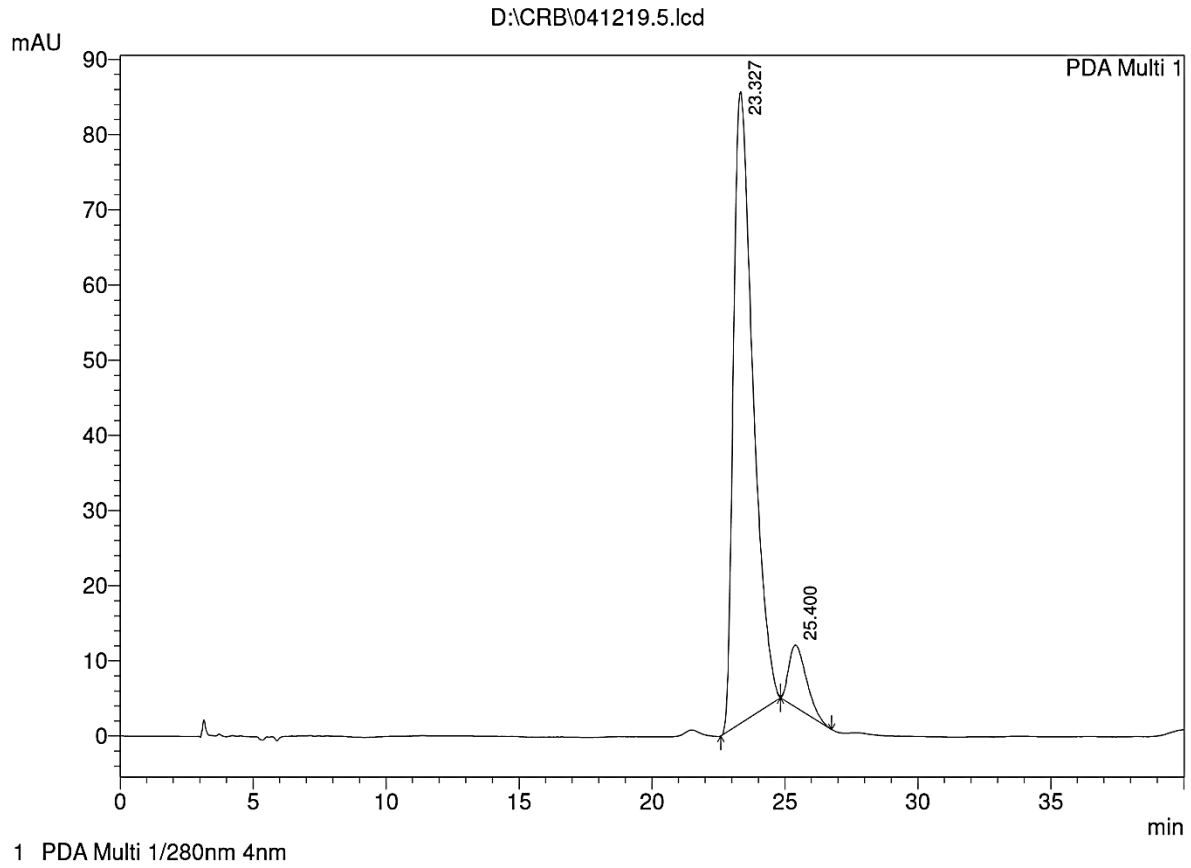
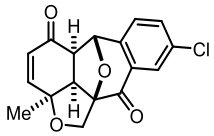


PeakTable

PDA Ch1 280nm 4nm

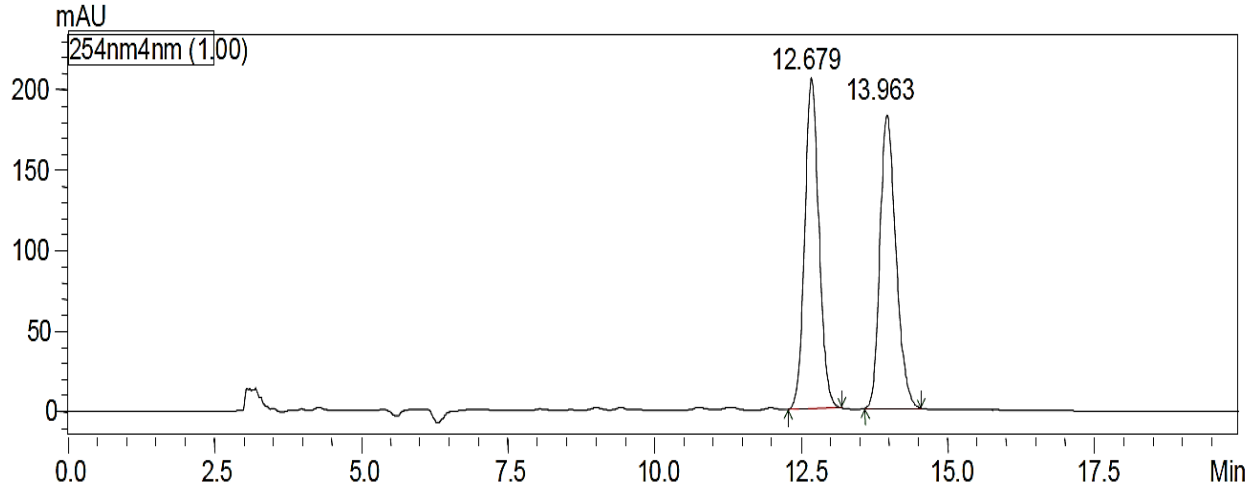
Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.327	4302098	84050	91.823	91.059
2	25.400	383099	8252	8.177	8.941
Total		4685197	92302	100.000	100.000

(-)-9-Chloro-2a-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzo furan-5,11-dione (2r):



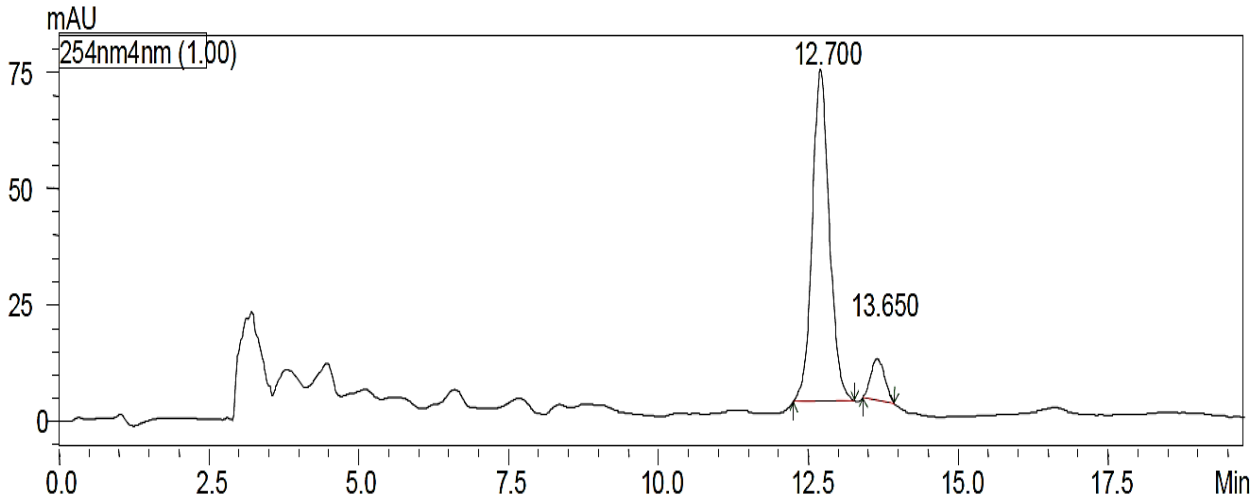
$[\alpha]^{20}_{D}$ = -12.40° (c 1.0, $CHCl_3$); 91:09*er*

Chiral HPLC analysis of the product: Chiralpak-IA 250 x 4.6 mm 5u column; hexane/2-propanol = 85/15, detected at 254 nm, Flow rate = 1 mL/min, Retention times: 12.70 min (major), 13.65 min (minor).



Peak table:

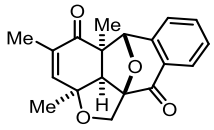
Peak	Ret. Time	Height	Height %	Area	Area%
1	12.679	205624	53.084	3476567	50.222
2	13.963	181733	46.916	3445878	49.778
Total		387356	100.000	6922444	100.000



Peak table:

Peak	Ret. Time	Height	Height %	Area	Area%
1	12.700	71295	89.028	1417620	90.876
2	13.650	8786	10.972	142329	9.124
Total		80081	100.000	1559949	100.000

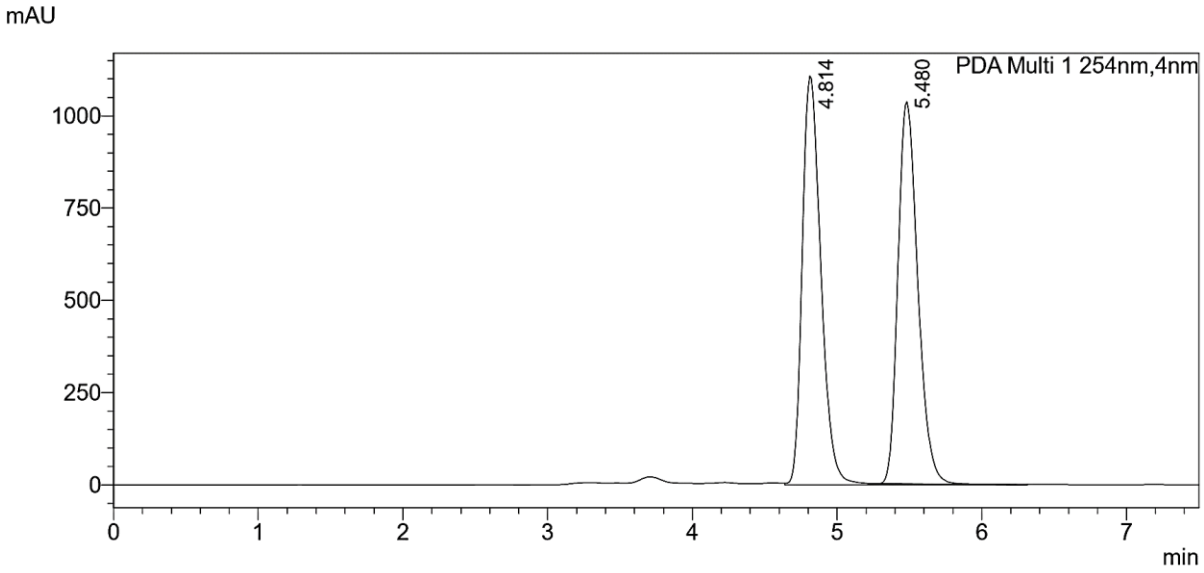
(-)-2a,4,5a-Trimethyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2v):



$[\alpha]^{20}_{D}$ = -1.64° (c 1.0, $CHCl_3$); 82:18*er*

Chiral HPLC analysis of the product: Chiralpack IA 250 x 4.6 mm 5u column; hexane/2-propanol = 70/30, detected at 254 nm, Flow rate = 1 mL/min, Retention times: 4.82 min (minor), 5.48 min (major).

<Chromatogram>

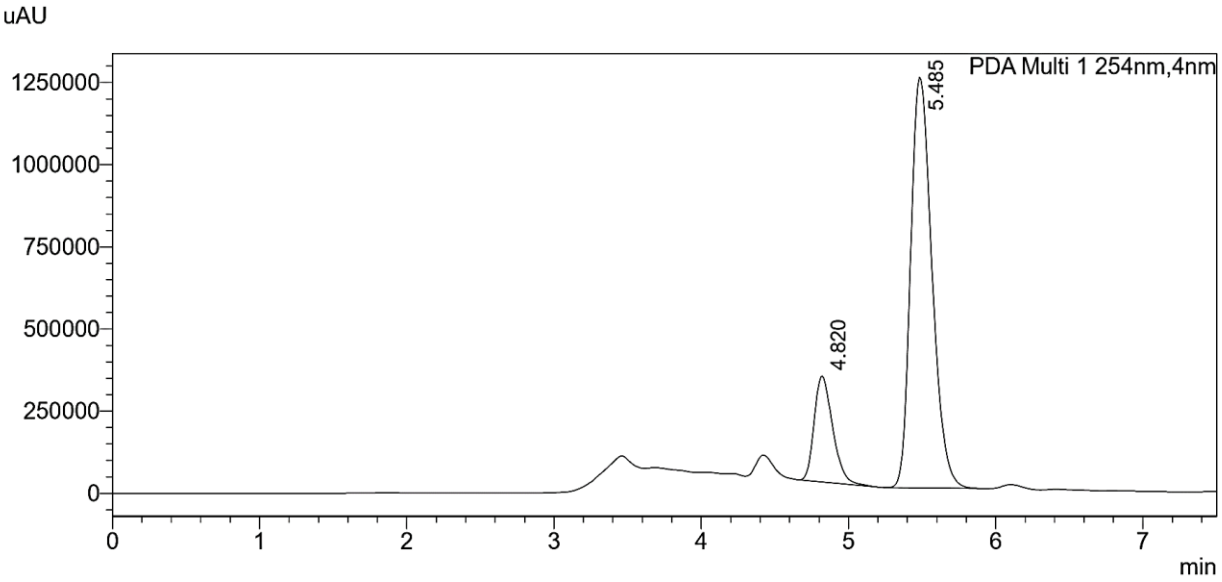


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	4.814	1108093	51.689	10025585	50.284
2	5.480	1035672	48.311	9912437	49.716
Total		2143765	100.000	19938022	100.000

<Chromatogram>

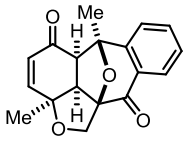


<Peak Table>

PDA Ch1 254nm

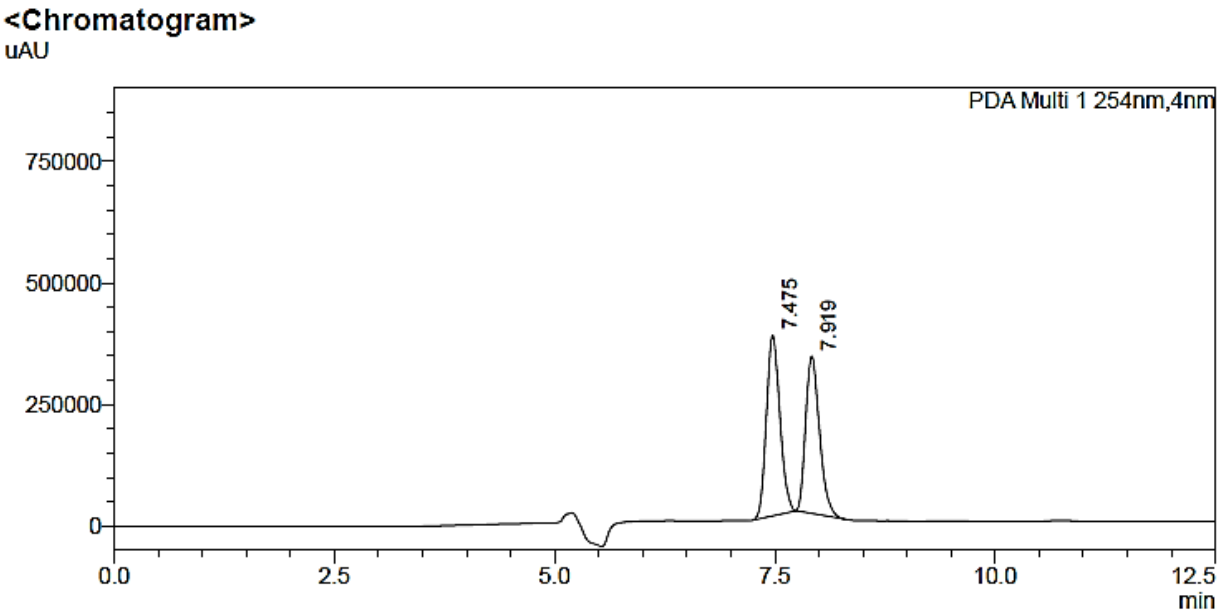
Peak#	Ret. Time	Height	Height%	Area	Area%
1	4.820	322683	20.517	2808944	18.226
2	5.485	1250092	79.483	12602894	81.774
Total		1572775	100.000	15411839	100.000

(-)-2a,6-Dimethyl-2a,2a1,5a,6-tetrahydro-1H-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (6a):



$[\alpha]^{20}_{D}$ = -27.28° (c 1.0, $CHCl_3$); 74:26 *er*

Chiral HPLC analysis of the product: Chiralpack IA 250 x 4.6 mm 5u column; hexane/2-propanol = 23/77, detected at 254 nm, Flow rate = 1 mL/min, Retention times: 7.43 min (minor), 7.87 min (major).

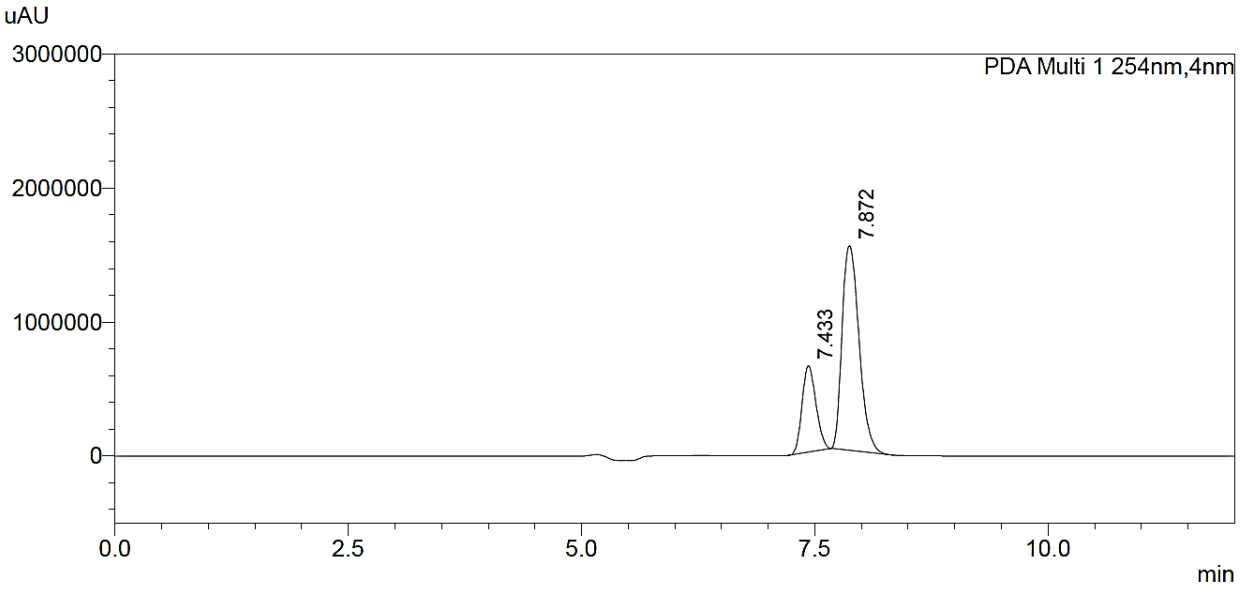


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	7.475	371555	53.462	3962594	52.772
2	7.919	323431	46.538	3546279	47.228
Total		694986	100.000	7508873	100.000

<Chromatogram>

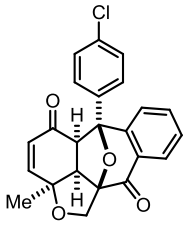


<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Height	Height%	Area	Area%
1	7.433	644220	29.675	6681837	25.736
2	7.872	1526694	70.325	19281600	74.264
Total		2170914	100.000	25963438	100.000

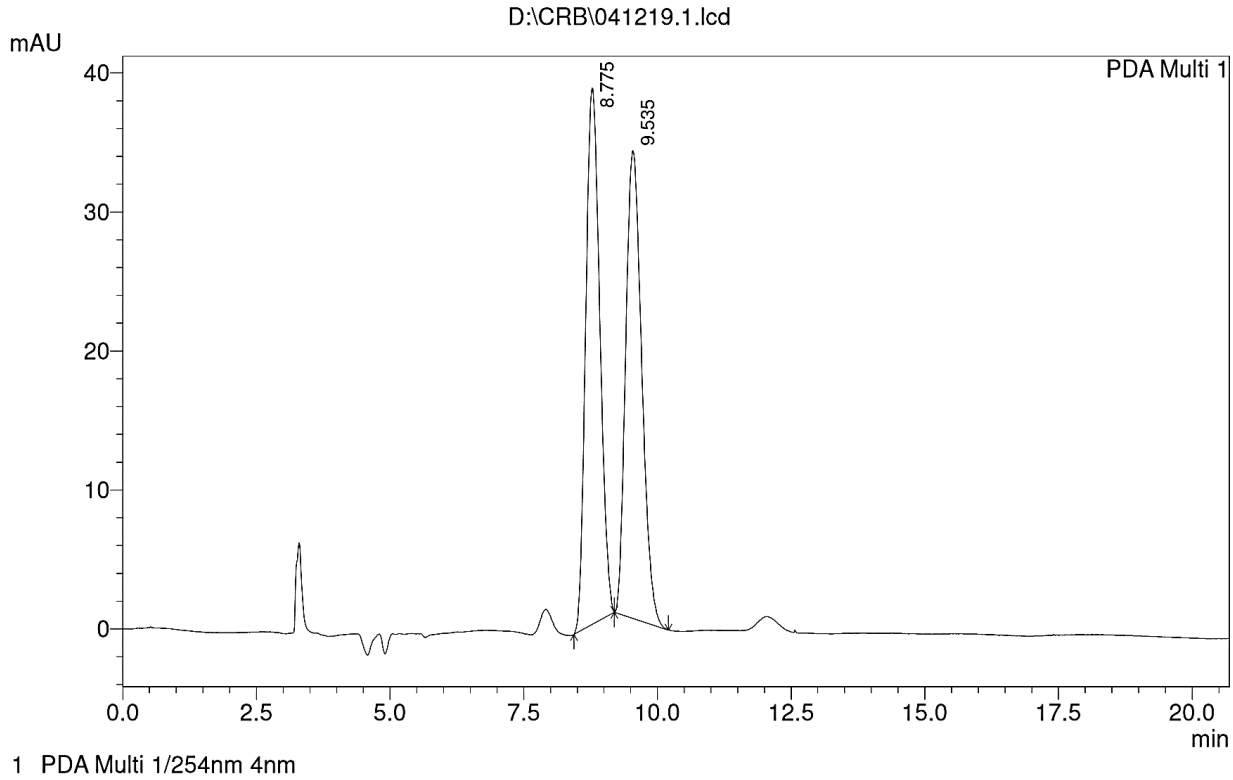
(-)-6-(4-Chlorophenyl)-2a-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6] cyclohepta [1,2,3-*cd]* benzofuran-5,11-dione (6b):



$[\alpha]^{20}_{D}$ = -5.42° (c 1.0, $CHCl_3$); 78:22*er*

Chiral HPLC analysis of the product: Chiralcel OD-H 250 x 4.6 mm 5u column; hexane/2-propanol = 70/30, detected at 254 nm, Flow rate = 1 mL/min, Retention times: 8.67 min (major), 9.42 min (minor).

<Chromatogram>

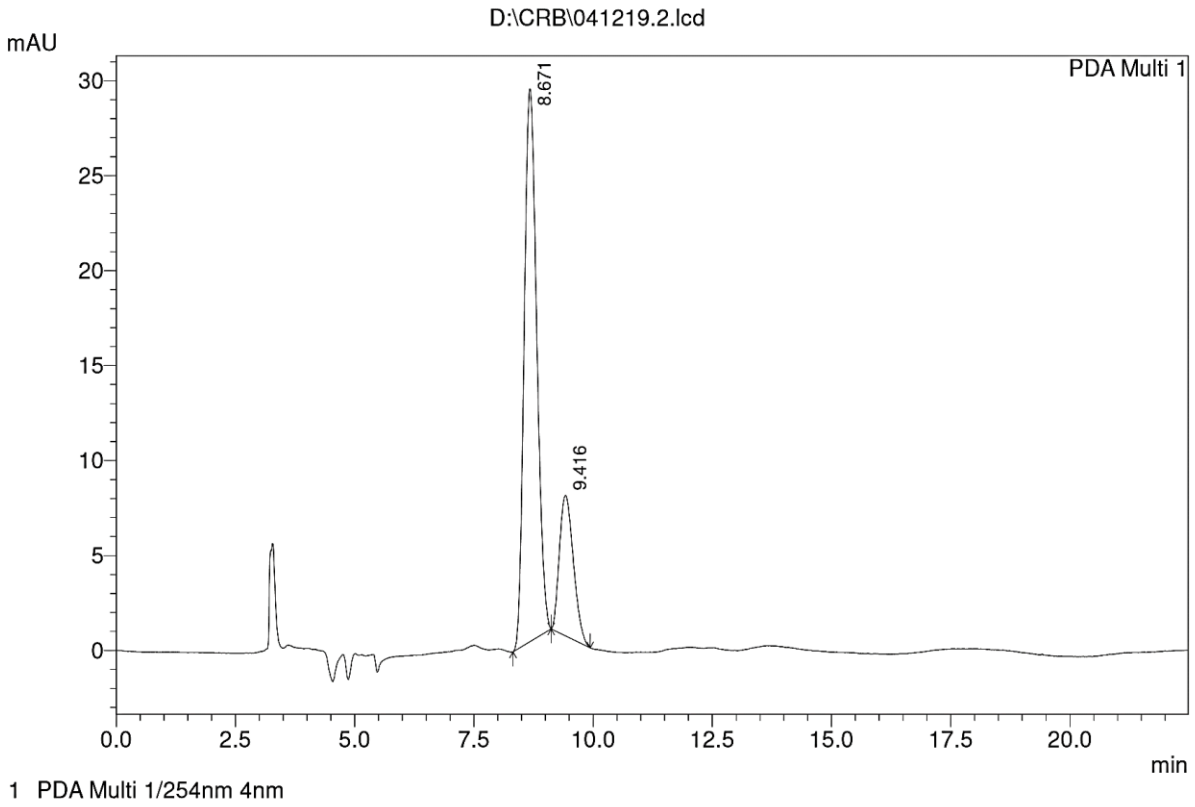


PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.775	709570	38602	50.303	53.443
2	9.535	701015	33629	49.697	46.557
Total		1410586	72231	100.000	100.000

<Chromatogram>



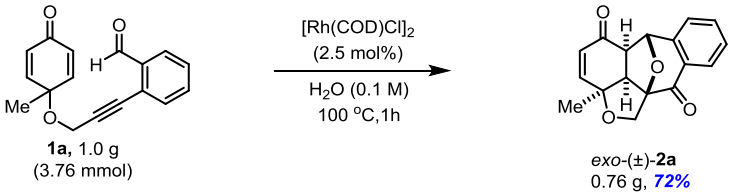
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.671	531582	29108	77.906	79.758
2	9.416	150752	7387	22.094	20.242
Total		682334	36495	100.000	100.000

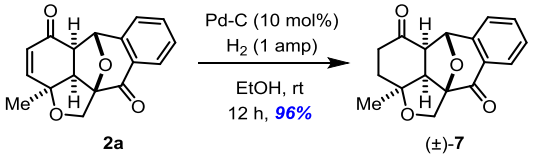
V: Gram scale reaction and subsequent transformations of the cycloaddition products

Va. Gram scale reaction:



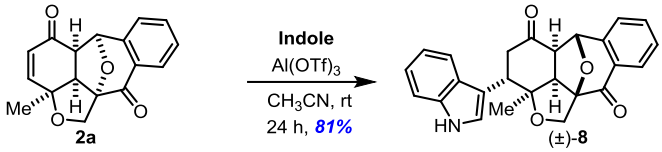
A dried screw-cap vial was charged with 2-alkynylbenaldehyes **1a** (1 g, 3.76 mmol), and $[Rh(COD)Cl]_2$ (46 mg, 2.5 mol%) in H_2O (37 mL) under inert atmosphere, and the reaction mixture was stirred at 100 ^oC for 1 hour (monitored by TLC). Then, it was cooled to room temperature and diluted with EtOAc (50 mL). The mixture was extracted with EtOAc (3 x 35 mL) and combined organic solvent was concentrated under reduced pressure. The residue was purified by silica gel column chromatography on silica gel with a gradient eluent of petroleum ether and EtOAc to afford the desired [3+2] cyclization product *exo*-(±)-**2a** in 72% yield (0.76 g).

Vb. Hydrogenation of compound 2a:



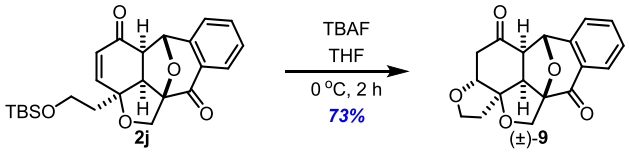
Olefin **2a** (50 mg, 0.17 mmol) was dissolved in 2 mL of EtOH and 10% Pd/C (5 mg, 10 wt% of **2a**) was added. The reaction flask was purged with hydrogen and it was stirred under 1 atmosphere of hydrogen pressure (balloon) at room temperature. The reaction was monitored by TLC until completion of starting material (12 h). The reaction mixture was filtered through a Celite pad and the solvent was removed under reduced pressure. The crude residue was purified by flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford (±)-**7** (46 mg, 96% yield) as a yellow solid; mp = 172–174°C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 7.7, 0.6 Hz, 1H), 7.57 (td, *J* = 7.5, 1.3 Hz, 1H), 7.44 (td, *J* = 7.6, 1.1 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 5.62 (s, 1H), 4.70 (d, *J* = 11.2 Hz, 1H), 4.09 (d, *J* = 11.2 Hz, 1H), 2.88 – 2.73 (m, 3H), 2.39 (ddd, *J* = 16.9, 3.5, 2.8 Hz, 1H), 2.24 (ddd, *J* = 14.5, 4.8, 3.6 Hz, 1H), 1.86 (td, *J* = 14.3, 3.7 Hz, 1H), 1.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.9, 192.4, 144.2, 134.4, 128.8, 127.0, 124.8, 99.0, 85.8, 79.8, 67.1, 55.6, 54.4, 35.5, 33.0, 26.7; IR (neat): υ_{max}2937, 1704, 1694, 1474, 1294, 1074, 971, 745, 697 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{17}O_4$ $[M+H]^+$: 285.1127; found: 285.1126.

Vc. Friedel-Crafts alkylation of compound 2a:[15]



A dried screw-cap vial was charged with enone **2a** (50 mg, 1.7 mmol, 1 equiv), indole (25 mg, 2.12 mmol, 1.2 equiv) and $Al(OTf)_3$ (21mg, 30 mol%) in CH_3CN (2.1mL, 0.1 M) under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 24h. Then, solvent was removed under reduced pressure. The residue was directly subjected to silica gel flash column chromatography on silica gel (20% EtOAc/hexanes; R_f = 0.5) to afford the desired product **(±)-8** with 81% yield (57 mg) as an orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 8.04 (d, *J* = 7.7 Hz, 1H), 7.61 (ddd, *J* = 8.7, 5.9, 2.1 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 6.72 (d, *J* = 2.1 Hz, 1H), 5.67 (s, 1H), 4.80 (d, *J* = 11.1 Hz, 1H), 4.23 (d, *J* = 11.1 Hz, 1H), 3.96 (t, *J* = 4.5 Hz, 1H), 3.33 (dd, *J* = 16.3, 5.0 Hz, 1H), 3.06 (d, *J* = 9.3 Hz, 1H), 2.90 (d, *J* = 9.2 Hz, 1H), 2.72 (dd, *J* = 16.2, 3.9 Hz, 1H), 1.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.3, 192.3, 144.5, 135.9, 134.5, 128.9, 128.8, 127.8, 127.2, 124.8, 122.8, 120.5, 120.0, 119.1, 115.3, 111.3, 99.5, 86.1, 84.0, 67.1, 55.3, 54.9, 43.2, 39.6, 24.5; HRMS (ESI) calcd for $C_{25}H_{22}NO_4$ $[M+H]^+$: 400.1549; found: 400.1546.

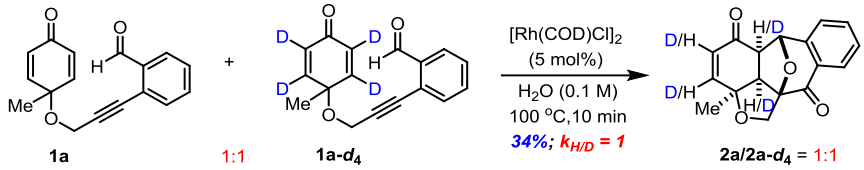
Vd. Desilylation of compound 2j:



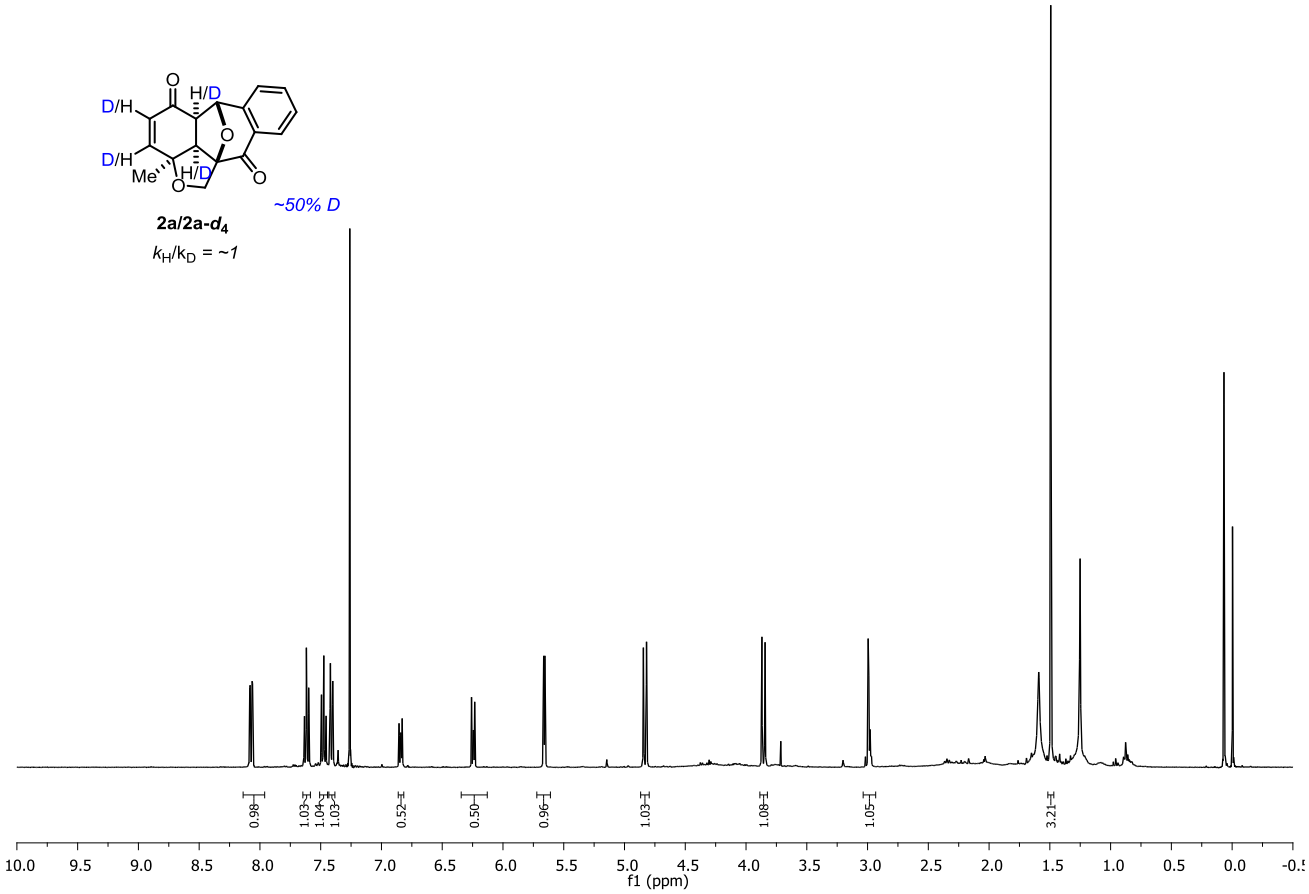
To a stirred solution of TBS ether **2j** (50 mg, 0.11 mmol) in THF (1.5 mL) was treated with TBAF (0.23 mL, 1.0 M in THF, 0.23 mmol) at 0 °C and stirred for 2 hours at room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was directly concentrated in *vacuo*, and then the crude reaction mixture was purified by silica gel flash column chromatography (30% EtOAc/hexane) to give the desired products **(±)-9** (27 mg, 73% yield) as a colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.7 Hz, 1H), 7.60 (td, *J* = 7.5, 1.3 Hz, 1H), 7.46 (td, *J* = 7.6, 1.0 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 5.67 (s, 1H), 4.69 (d, *J* = 11.0 Hz, 1H), 4.19 (d, *J* = 11.0 Hz, 1H), 4.18 (dd, *J* = 6.3, 4.9 Hz, 1H), 4.02 – 3.90 (m, 2H), 3.09 (d, *J* = 9.7 Hz, 1H), 2.99 (d, *J* = 9.7 Hz, 1H), 2.87 (dd, *J* = 14.6, 4.3 Hz, 1H), 2.61 (ddd, *J* = 14.6, 6.9, 0.8 Hz, 1H), 2.35 (ddd, *J* = 12.8, 7.7, 6.0 Hz, 1H)2.07 (dt, *J* = 12.6, 7.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.7, 191.9, 144.9, 134.9, 128.9, 128.4, 127.3, 124.6, 98.8, 87.1, 83.9, 80.5, 68.9, 66.4, 55.9, 55.1, 42.1, 39.4; IR (neat): υ_{max} 3047, 2954, 1715,1703, 1475, 1294, 1275, 1081, 769, 675 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{17}O_5$ $[M+H]^+$:313.1076; found: 313.1070.

VI. Labeling Experiments.

VIa. Intermolecular competition experiment between compound 1a and 1a-d_4:

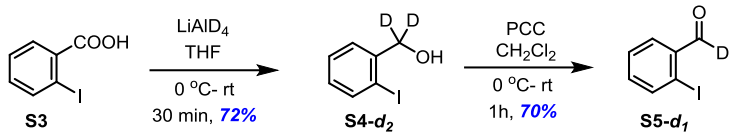


A dried screw-cap vial was charged with 2-alkynylbenaldehyes **1a** (35 mg, 0.13 mmol, 50 mol %), **1a-*d*$_4$** (35 mg, 0.13 mmol, 50 mol %), and $[Rh(COD)Cl]_2$ (6.4 mg, 5.0 mol%) in H_2O (2.6 mL, 0.1 M) under inert atmosphere, and the reaction mixture was stirred at 100 °C in preheated oil-bath for 10 minutes. Then, it was cooled to room temperature and diluted with EtOAc (10 mL). The mixture was extracted with EtOAc (3 x 8 mL) and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with a gradient eluent of petroleum ether and EtOAc to afford the desired product **2a/2a-*d*$_4$** with 34 % yield (25 mg) as a light orange oil with ≈50 % deuterium incorporation.The kinetic isotopic effect of this reaction was thus determined to be $k_H/k_D \approx 1.0$ utilizing ^{1}H NMR spectroscopy.



VIb. Intermolecular competition experiment between compound 1a and 1a-*d*$_1$:

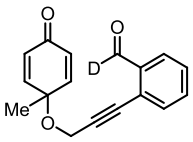
Procedure for deuterated 2-iodobenzaldehyde S5-*d*$_1$:



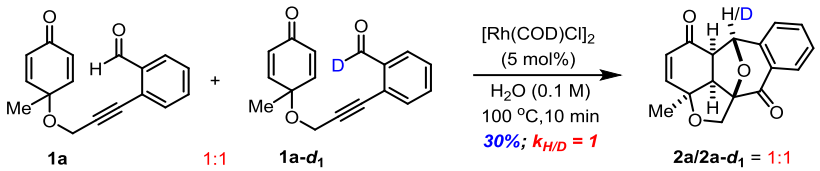
To a stirred solution of $LiAlD_4$ (68 mg, 1.61 mmol) in THF (3 mL) at 0°C was added slowly 2-iodobenzoic acid **S3** (400 mg 1.61 mmol) in dry THF (3 ml) under inert atmosphere. After that reaction was continued for 30 minute at room temperature, the reaction quenched with H_2O (10 mL) and then EtOAc (15 mL) was added to the reaction mixture. Two layers were separated and the water layer further extracted with EtOAc (3 x 15 mL). Then combined organic layers were washed with saturated aqueous $NaHCO_3$ (20 mL), dried over Na_2SO_4, felted and concentrated under reduced pressure to give 2-iodo benzyl alcohol **S4-*d*$_2$** (273 mg, 72%) as a white solid. The crude alcohol was used for next step with our purification.

To a solution of benzyl alcohol **S4-*d*$_2$** (250mg 1.06 mmol, 1.0 equiv.) in CH_2Cl_2 at 0°C was added PCC (274 mg 1.27 mmol, 1.2 equiv.) portion wise at 0^{o}C. The reaction mixture was allowed to stir at room temperature for 1h. Afterwards reaction quenched with $NaHCO_3$ saturated solution and then extracted in to CH_2Cl_2 (2 x 15 mL)). The combined organic layers were dried over (Na_2SO_4), filtered, and concentrated. The crude compound was purified by silica gel column chromatography on silica gel (hexane/EtOAc = 95/5) to afford deuterated 2-iodobenzaldehyde **S5-*d*$_1$** (172 mg, 70%) as a white solid. Compound **S5-*d*$_1$** NMR spectra data was matched with literature.[16]

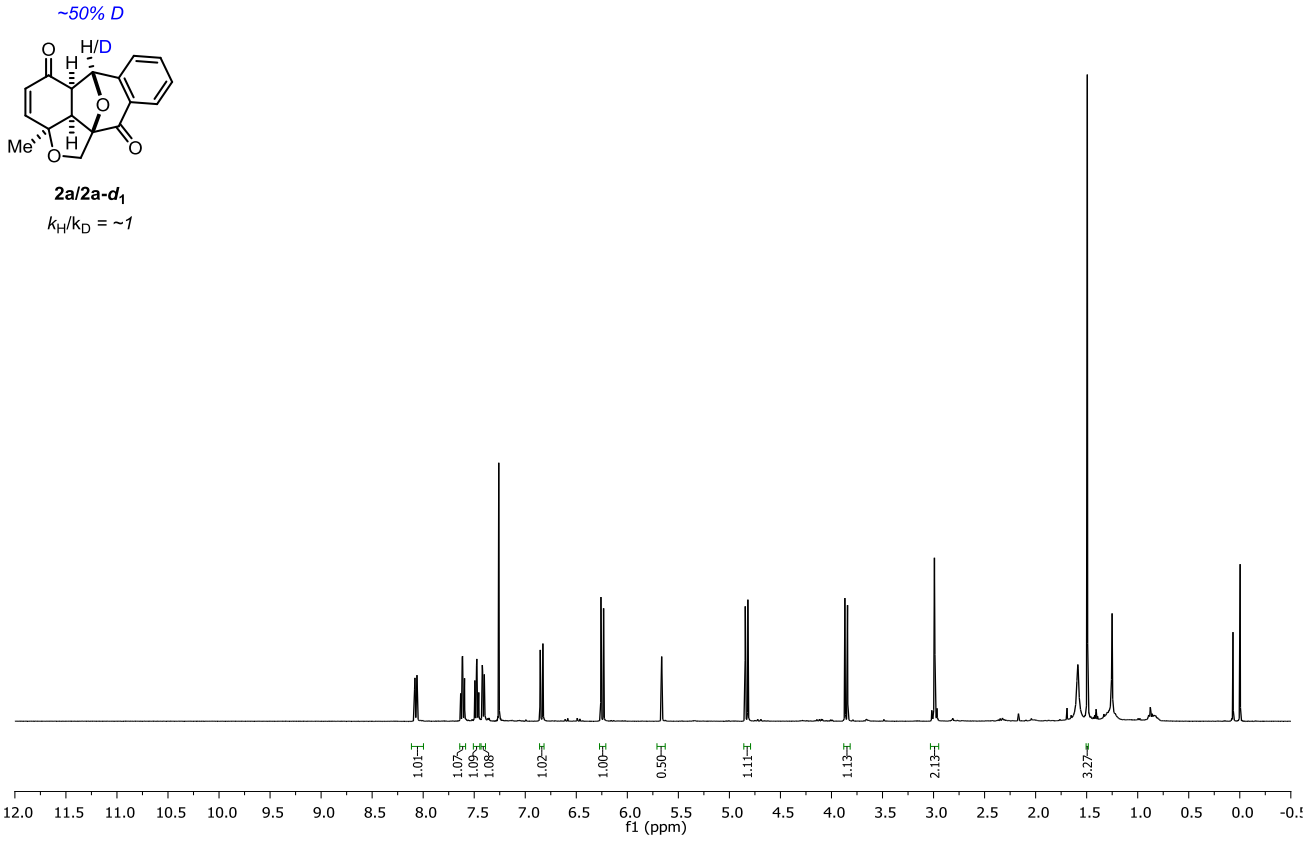
2-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde-*d*$_1$ (1a-*d*$_1$):



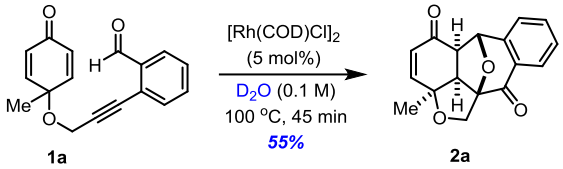
Prepared according to the general procedure as described above in 85% yield (0.2 mmol, 45mg). It was purified by silica gel flash chromatography (20% EtOAc/hexanes; R_f = 0.5) to afford a white solid; mp = 84–86°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.90 (m, 1H), 7.58 – 7.52 (m, 2H), 7.48 – 7.43 (m, 1H), 6.88 (d, *J* = 10.2 Hz, 2H), 6.35 (d, *J* = 10.2 Hz, 2H), 4.28 (s, 2H), 1.52 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.2 (t, *J* = 27.1 Hz), 185.0, 150.7, 136.2 (t, *J* = 3.0 Hz), 133.9, 133.6, 130.8, 129.4, 127.5, 125.9, 92.9, 82.5, 73.5, 54.5, 26.5; IR (neat): υ_{max} 3047, 2974, 2243, 1706, 1684, 1475, 1279, 759, 693 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{14}DO_3$ $[M+H]^+$: 268.1084; found: 268.1086.



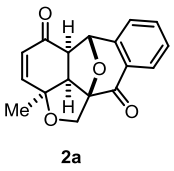
A dried screw-cap vial was charged with 2-alkynylbenaldehyes **1a** (35 mg, 0.13 mmol, 50 mol %), **1a-*d*$_1$** (35 mg, 0.13 mmol, 50 mol %), and [Rh(COD)Cl]$_2$ (6.4 mg, 5.0 mol%) in H_2O (2.6 mL,0.1 M) under inert atmosphere, and the reaction mixture was stirred at 100 ^oC in preheated oil-bath for 10 minutes. Then, it was cooled to room temperature and diluted with EtOAc(10 mL). The mixture was extracted with EtOAc(3 x 8 mL) and concentrated under reduced pressure. The residue was purified by silica gel column chromatography on silica gel with a gradient eluent of petroleum ether and EtOAc to afford the desired product **2a/2a-*d*$_1$** with 30% yield (22 mg) as an orange oil with ≈50 % deuterium incorporation.The kinetic isotopic effect of this reaction was thus determined to be $k_H/k_D \approx 1.0$ utilizing ^{1}H NMR spectroscopy.

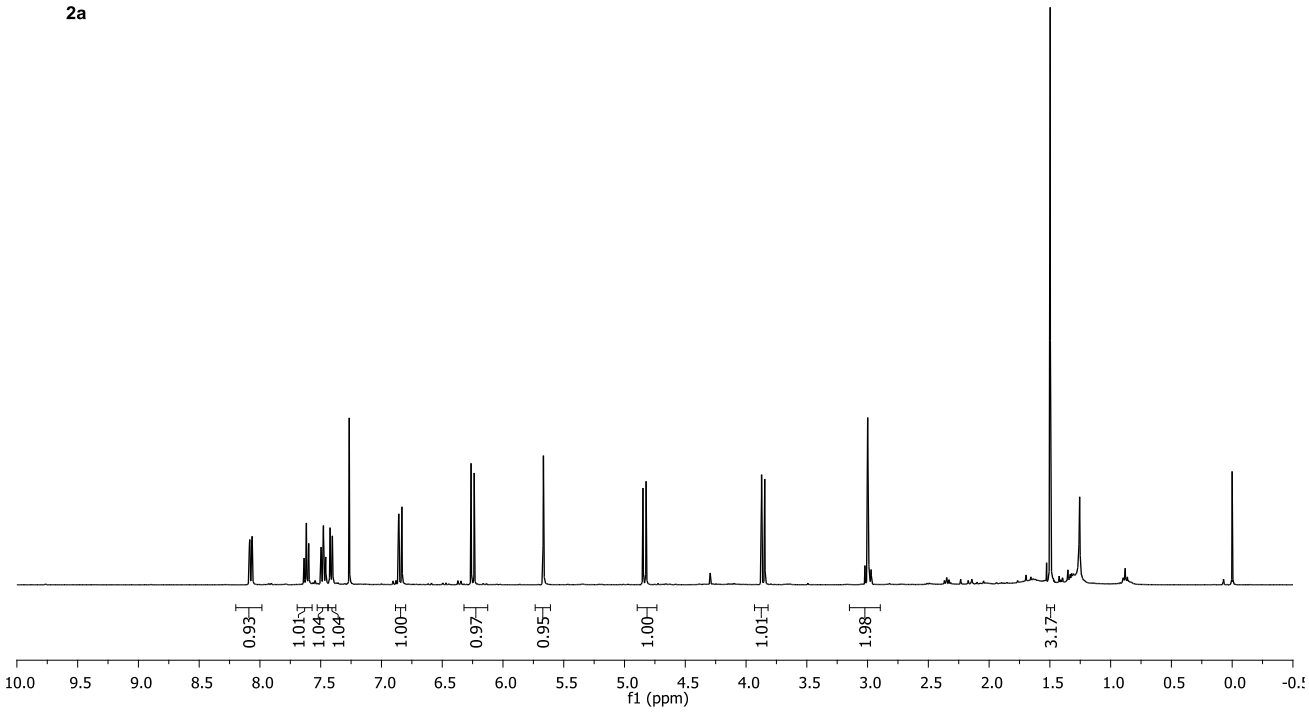


VIc. [3+2]-Cycloaddition reaction in D2O solvent:

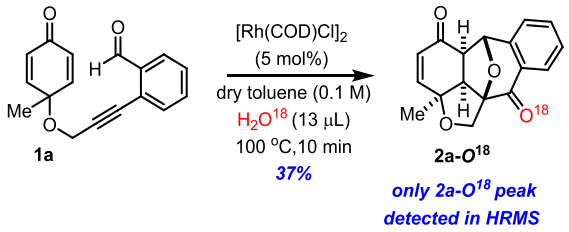


A dried screw-cap vial was charged with 2-alkynylbenaldehyes **1a** (53 mg, 0.2 mmol) and $[Rh(COD)Cl]_2$ (5 mg, 5.0 mol%) in D_2O (2 mL, 0.1 M) under inert atmosphere, and the reaction mixture was stirred at 100 ^oC in preheated oil-bath for 10 minutes. Then, it was cooled to room temperature and diluted with EtOAc (10 mL). The mixture was extracted with EtOAc (3 x 8 mL) and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with a gradient eluent of petroleum ether and EtOAc to afford the desired product **2a** with 55 % yield (31 mg) as a light orange oil. We did not observed any deuterium incorporation on product which is analysed by ^1H NMR spectroscopy.

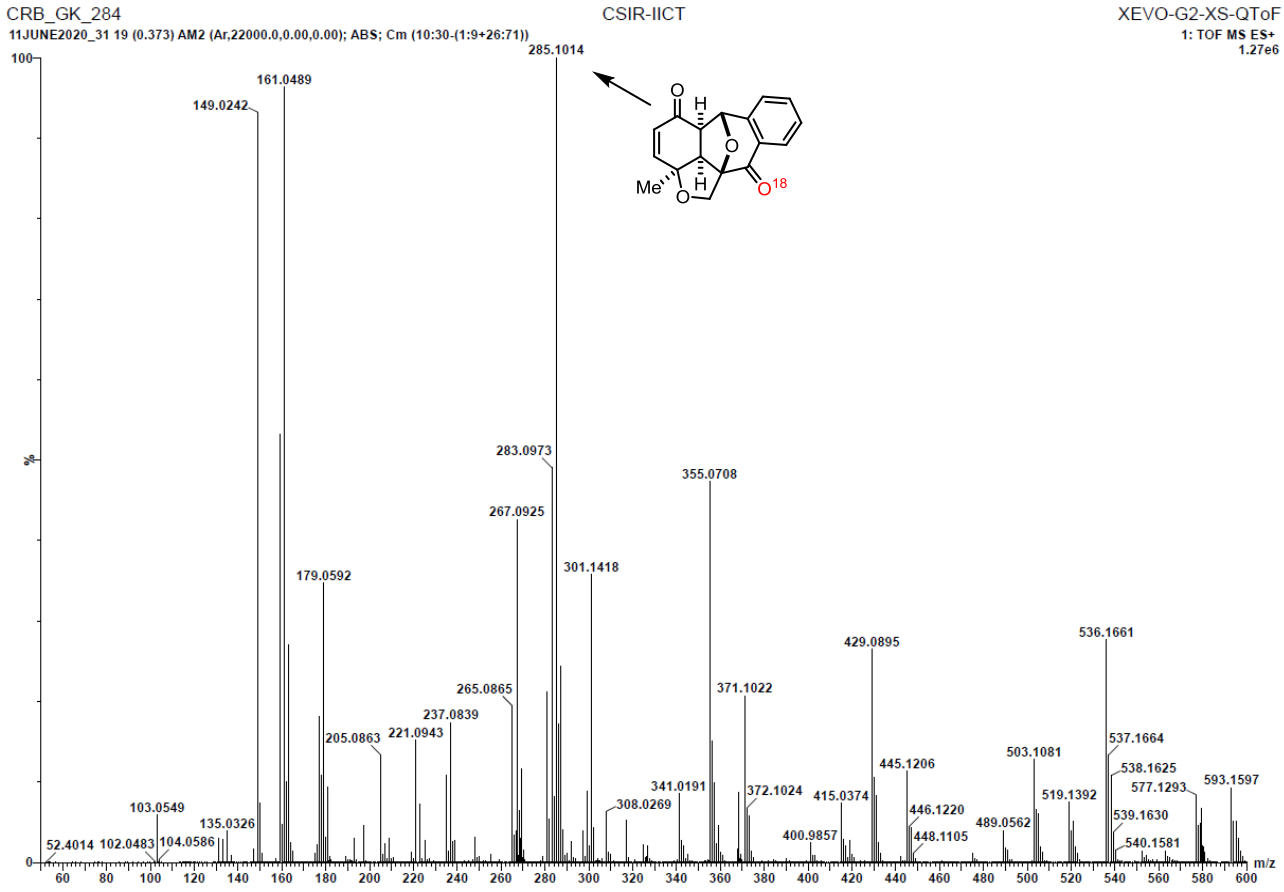




VId. Study of the ^{18}O isotope effect on oxidative cyclopropanation:



A dried screw-cap vial was charged with 2-alkynylbenaldehyes **1a** (35 mg, 0.13 mmol, 50 mol %), and $[Rh(COD)Cl]_2$ (3.2 mg, 5.0 mol%) in anhydrous THF(1.3 mL,0.1 M) and H_2O (13 µL) under inert atmosphere, and the reaction mixture was stirred at 100 ^oC in preheated oil-bath for 10 minutes. Then, it was cooled to room temperature and diluted with EtOAc (5 mL). The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography on silica gel with a gradient eluent of petroleum ether and EtOAc to afford the desired product **2a-^{18}O** with 37% yield (14 mg). Only **2a-^{18}O** $[M+H]^+$ ion was detected in HRMS analysis. HRMS (ESI) calcd for $C_{16}H_{15}{}^{18}O_3$ $[M+H]^+$285.1013; found: 285.1014.



VII. References

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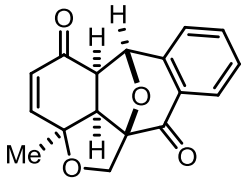
VIII. X-Ray crystallographic data:

X-ray crystallographic data for compound 2a:



compound **2a**

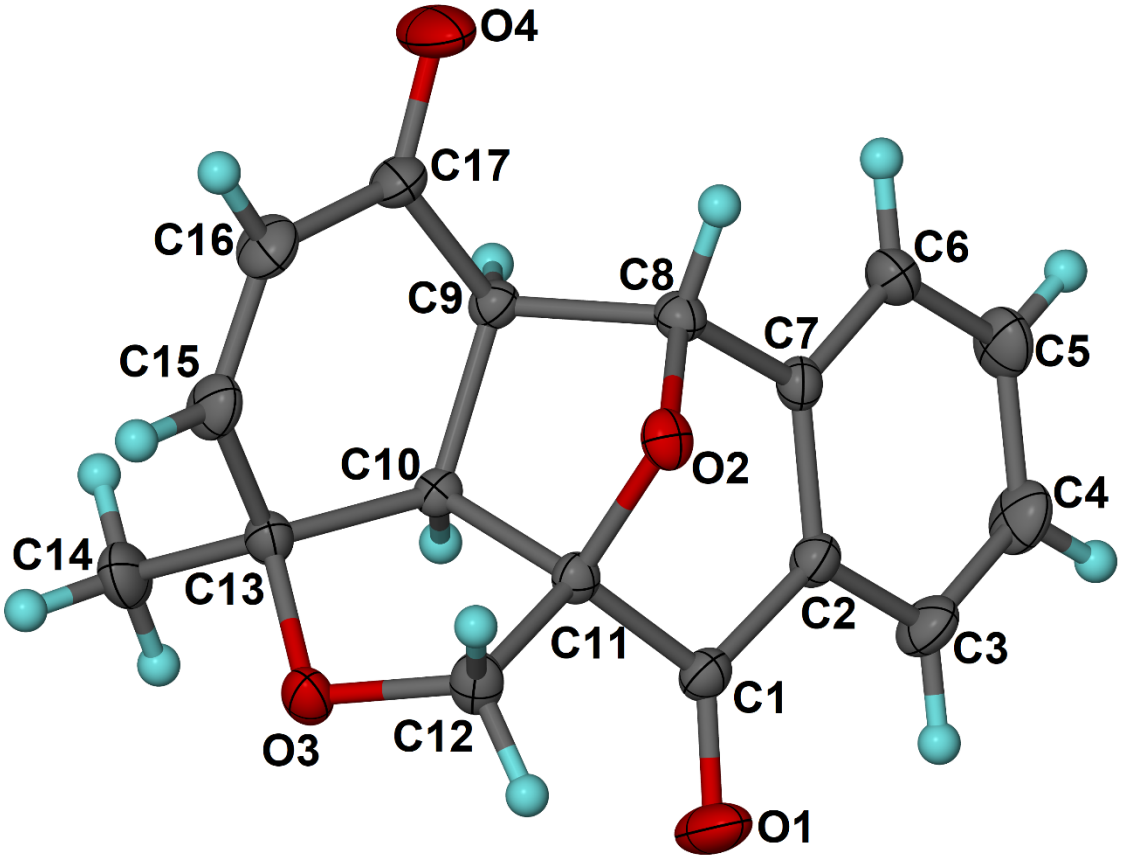


Figure caption: ORTEP diagram of compound **2a** (KA579) compound with the atom-numbering. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small spheres of arbitrary radius. CCDC 2008483 contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

Table S7. Crystallographic details of compound 2a (KA579) compound.

Datablock: KA579_0m

Bond precision: C-C = 0.0027 A Wavelength=0.71073

Cell: a=8.047(6) b=11.508(7) c=14.430(9)
alpha=90 beta=90.23(4) gamma=90
Temperature: 293 K

	Calculated	Reported
Volume	1336.3(15)	1336.3(15)
Space group	P 21/n	P 21/n
Hall group	-P 2yn	-P 2yn
Moiety formula	C17 H14 O4	C17 H14 O4
Sum formula	C17 H14 O4	C17 H14 O4
Mr	282.28	282.28
Dx,g cm-3	1.403	1.403
Z	4	4
Mu (mm-1)	0.100	0.100
F000	592.0	592.0
F000'	592.33	
h,k,lmax	10,14,18	10,14,18
Nref	3067	3063
Tmin,Tmax	0.975,0.984	0.715,0.746
Tmin'	0.974	

Correction method= # Reported T Limits: Tmin=0.715 Tmax=0.746
AbsCorr = MULTI-SCAN

Data completeness= 0.999 Theta(max)= 27.498

R(reflections)= 0.0484(2331) wR2(reflections)= 0.1241(3063)

S = 1.052 Npar= 191

Data collection and Structure solution details: Single crystal X-ray data for compound **2a** (KA579) compound were collected at room temperature on a Bruker D8 QUEST equipped with a four-circle kappa diffractometer and Photon 100 detector. An Iμs microfocus Mo source (λ=0.71073Å) supplied the multi-mirror monochromated incident beam. A combination of Phi and Omega scans were used to collect the necessary data and unit cell dimensions were determined using 9961 reflections for compound **2a** (KA579) data. Integration and scaling of intensity data were accomplished using SAINT program.[1] The structures were solved by Direct Methods using SHELXS97[2] and refinement was carried out by full-matrix least-squares technique using SHELXL-2014/7.[2-3] Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H distances of 0.93--0.97 Å, and with U_{iso}(H) = 1.2U_{eq} (C) or 1.5U_{eq} for methyl atoms. Structure with CCDC deposition number 2008483 contain the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

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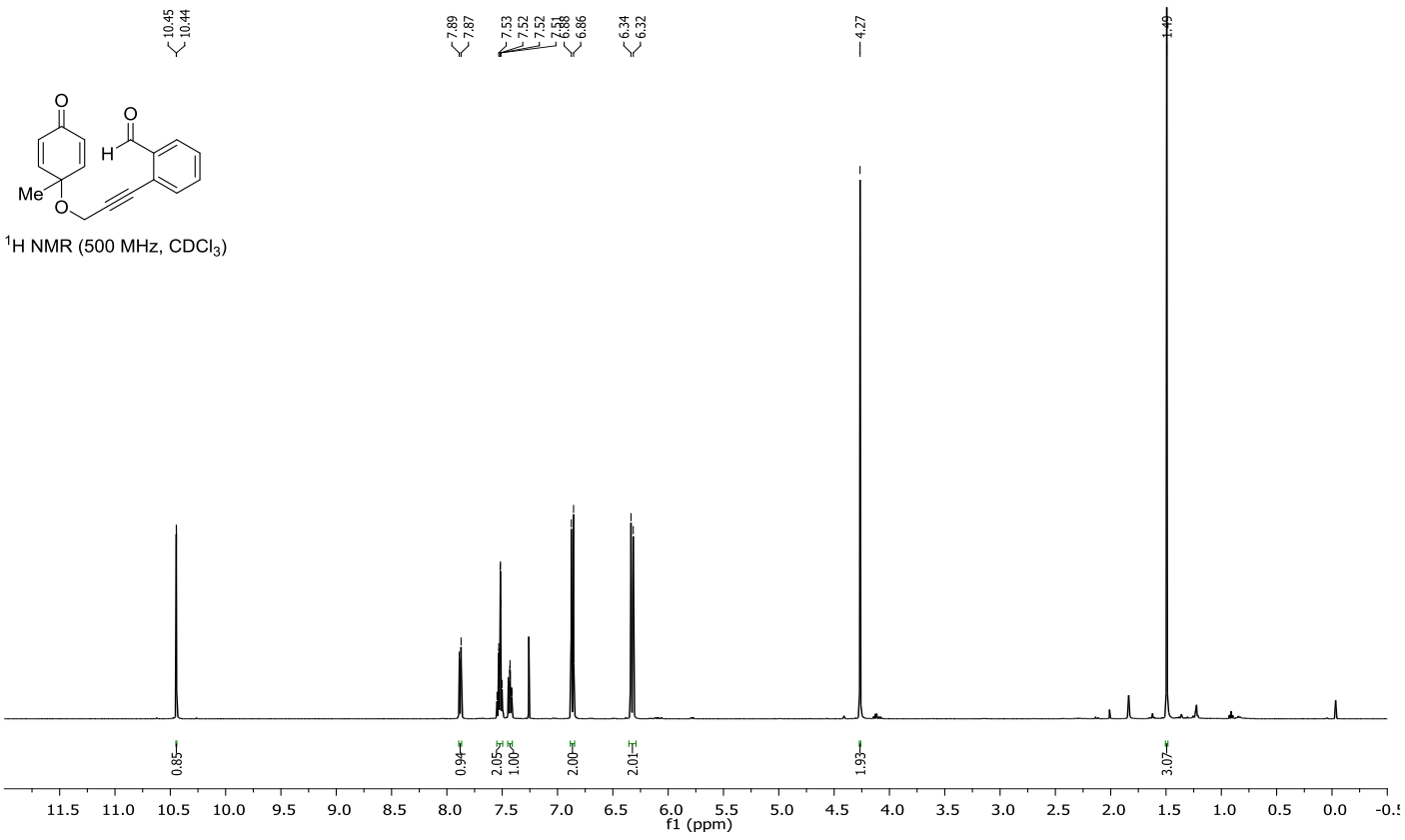
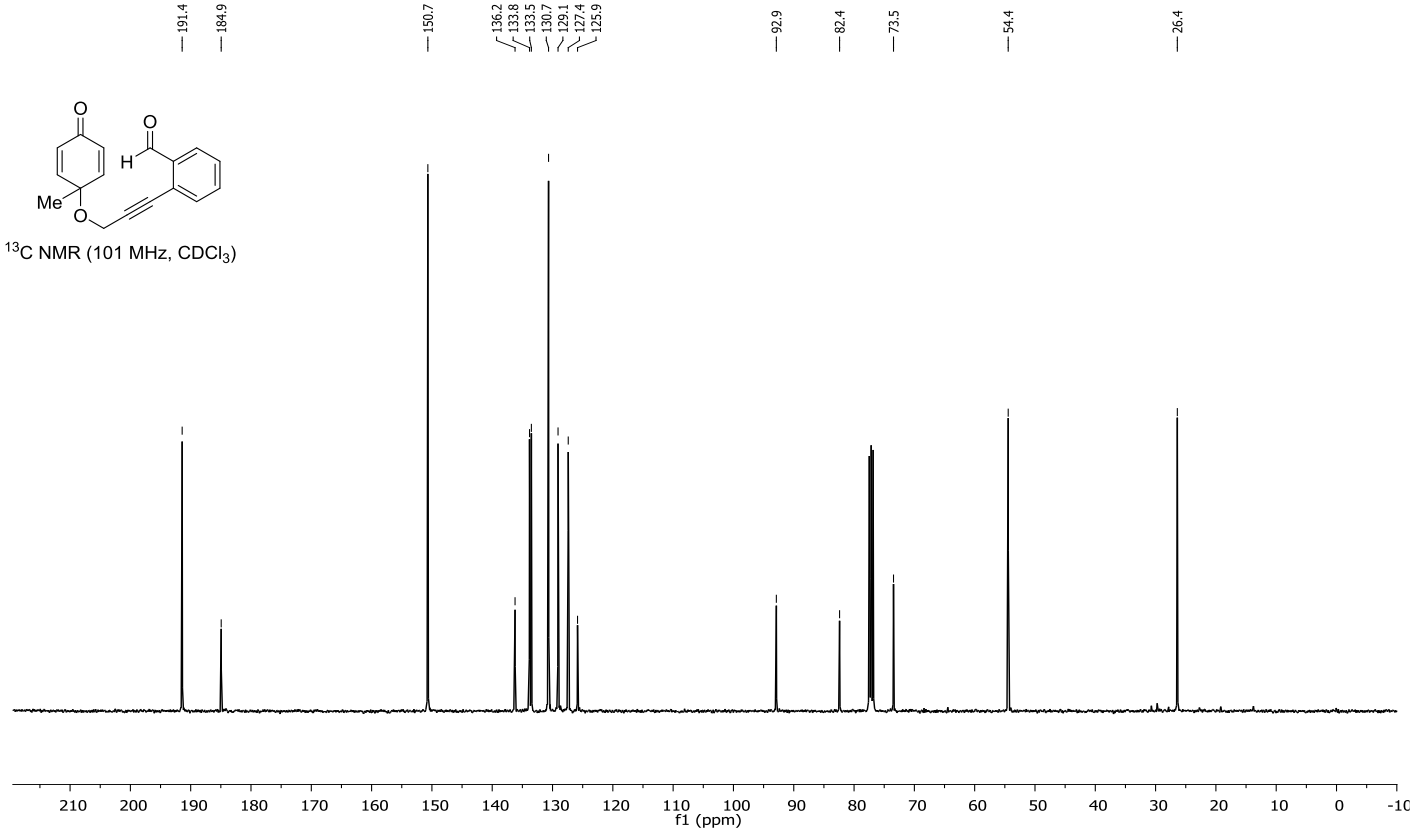
IX. ^{1}H &^{13}C Spectra

2-(3-((1-Methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1a):

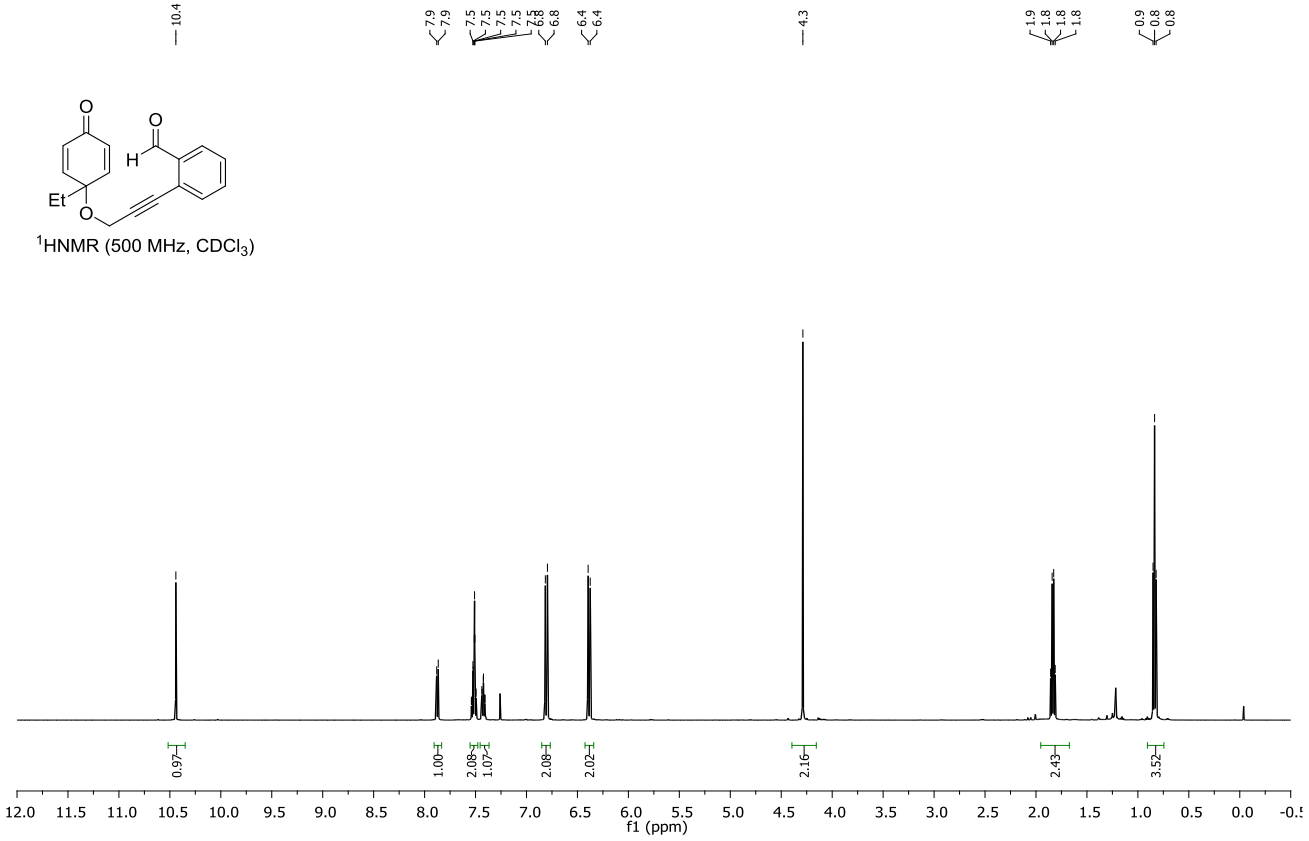


^{1}H NMR (500 MHz, $CDCl_3$)

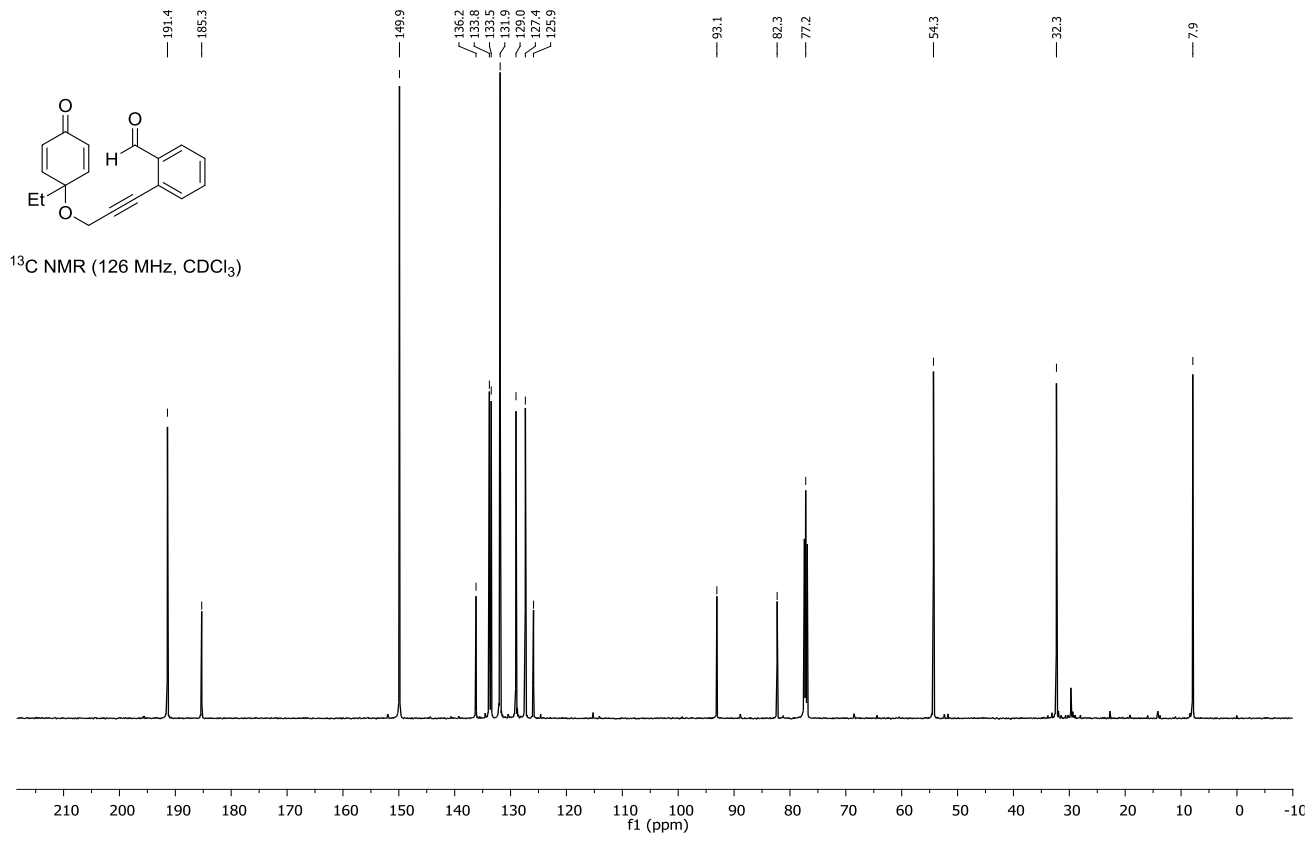


^{13}C NMR (101 MHz, $CDCl_3$)

2-(3-((1-Ethyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1b):

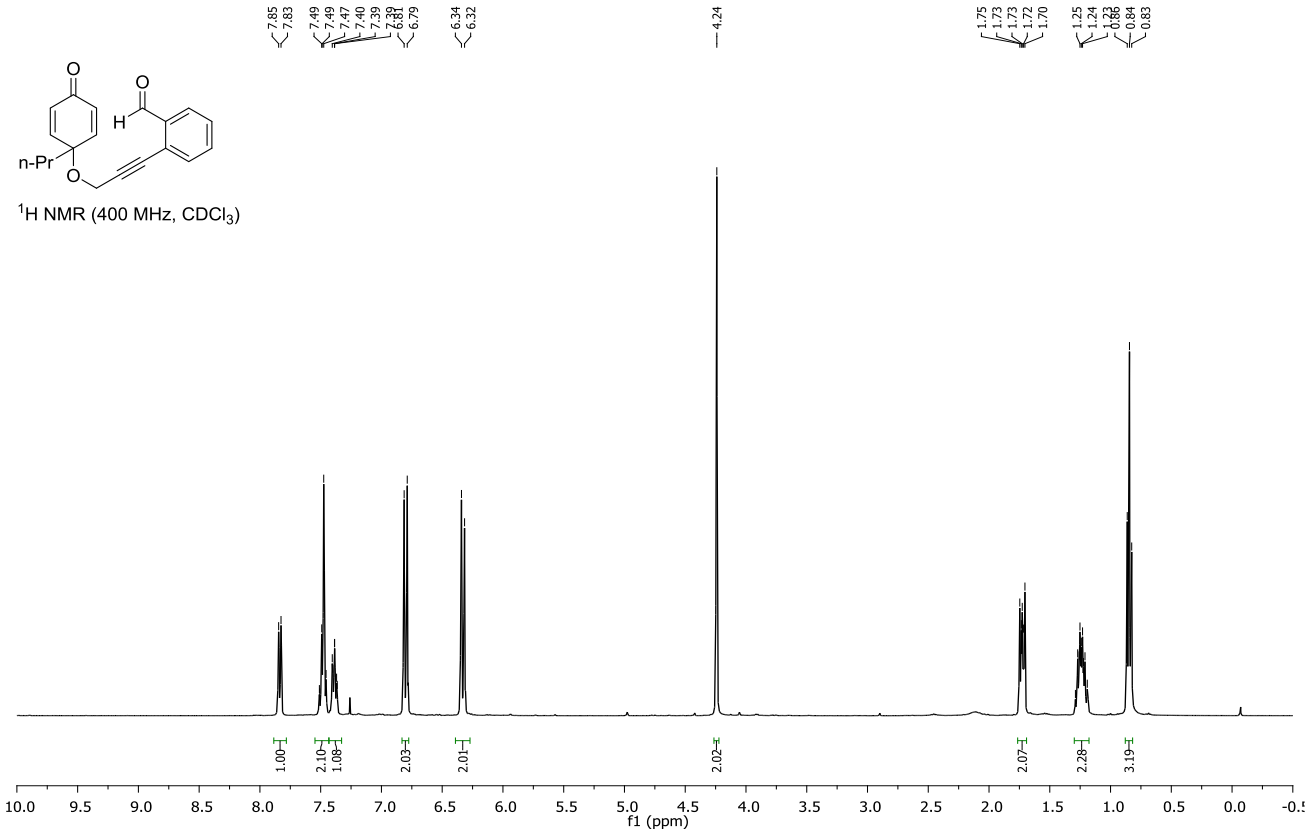


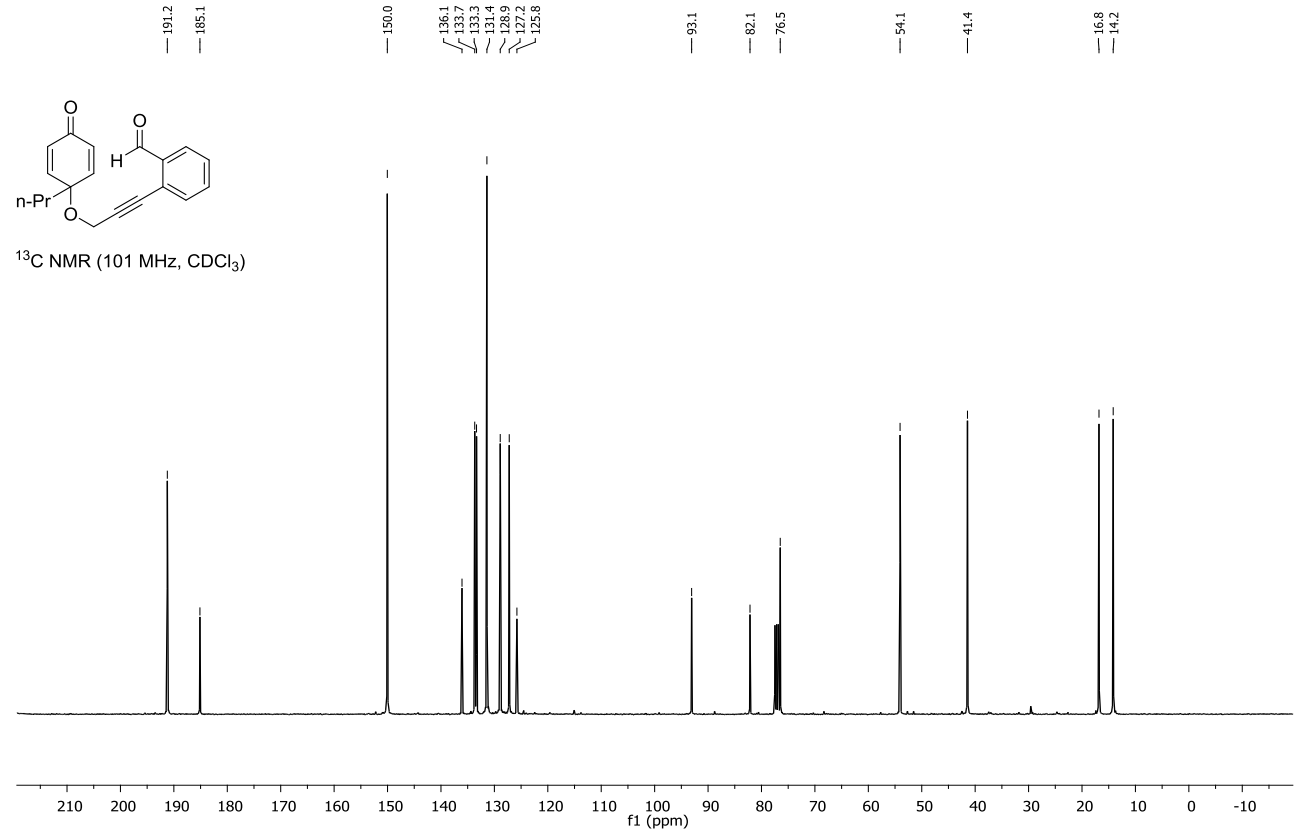
^{1}HNMR (500 MHz, $CDCl_3$)



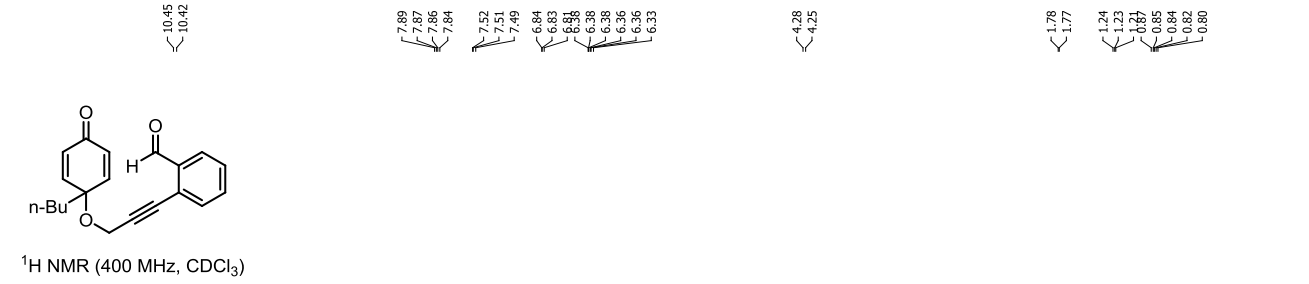
^{13}C NMR (126 MHz, $CDCl_3$)

2-(3-((4-Oxo-1-propylcyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1c):

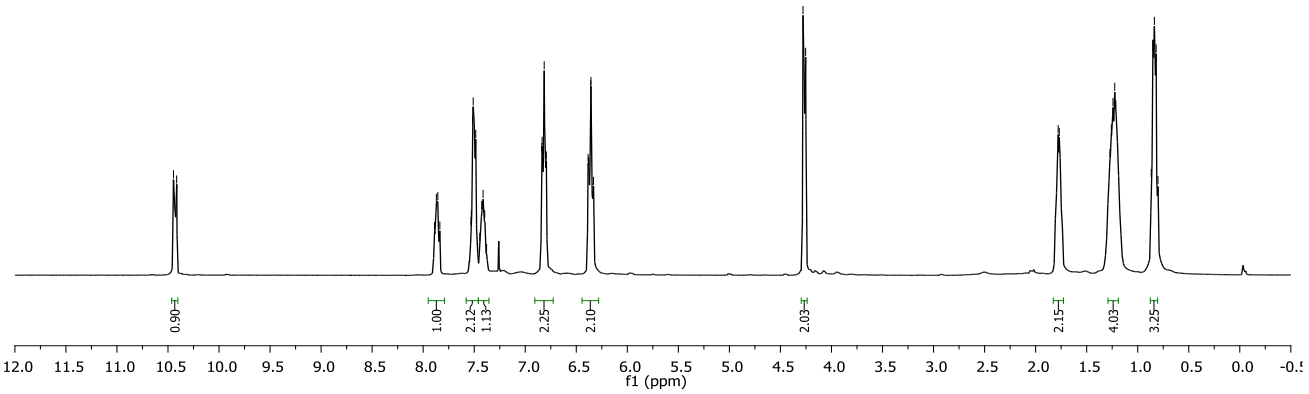


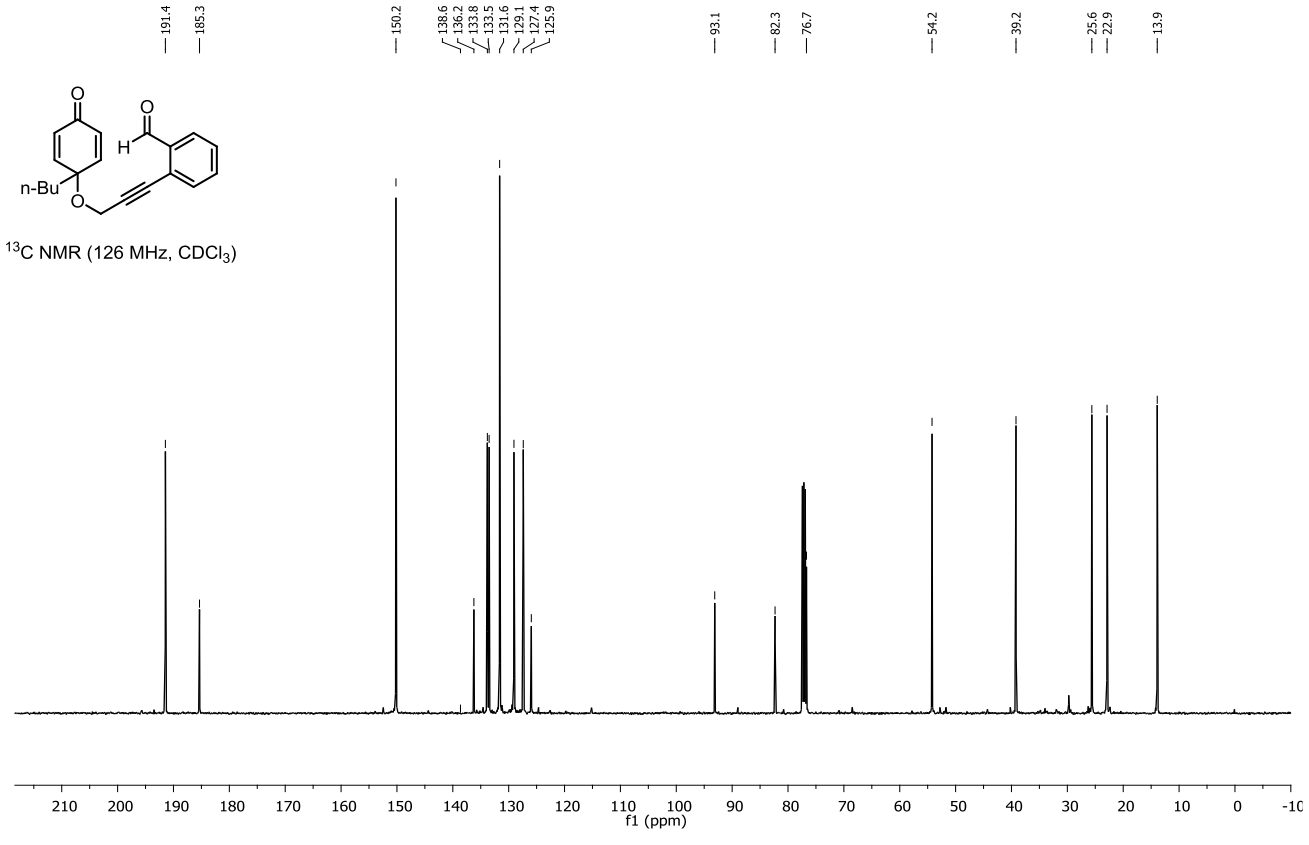


2-(3-((1-Butyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1d):



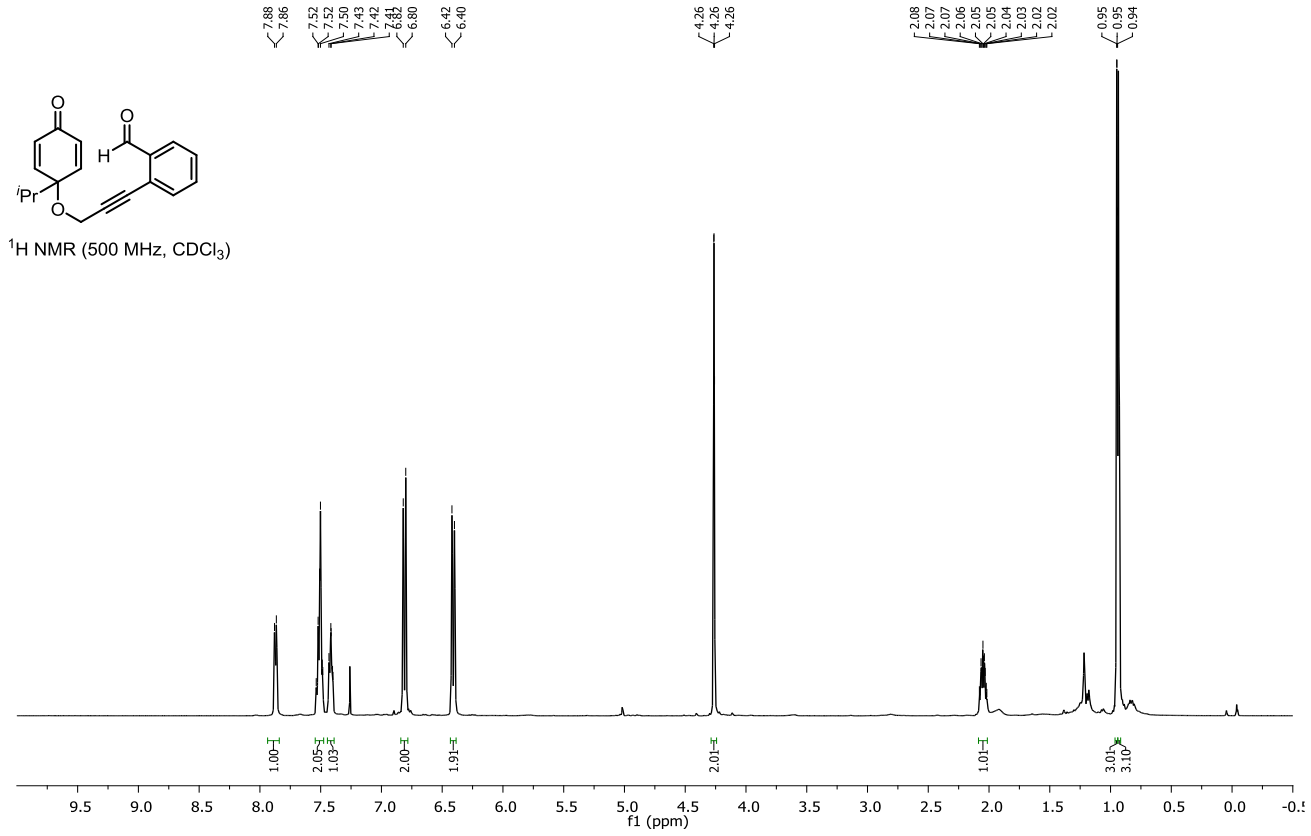
^{1}H NMR (400 MHz, $CDCl_3$)

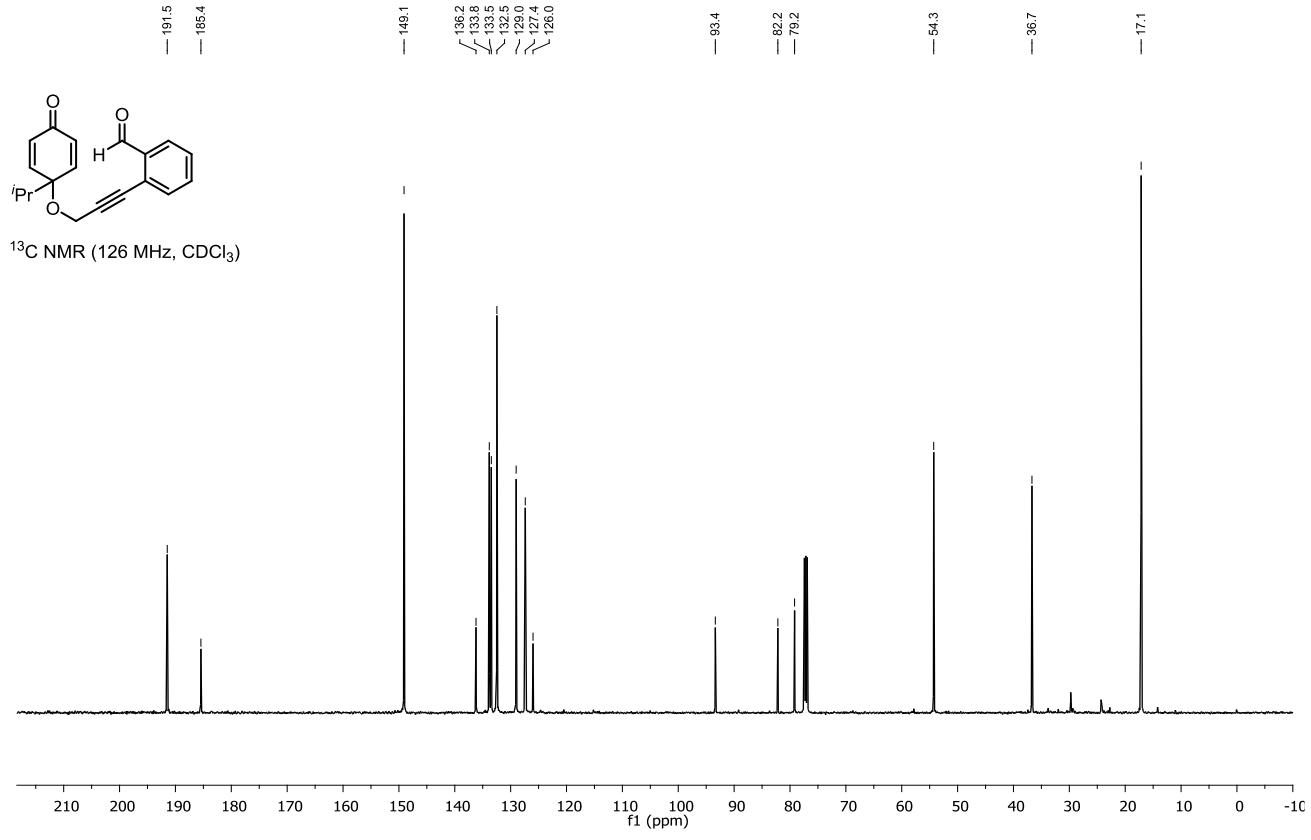




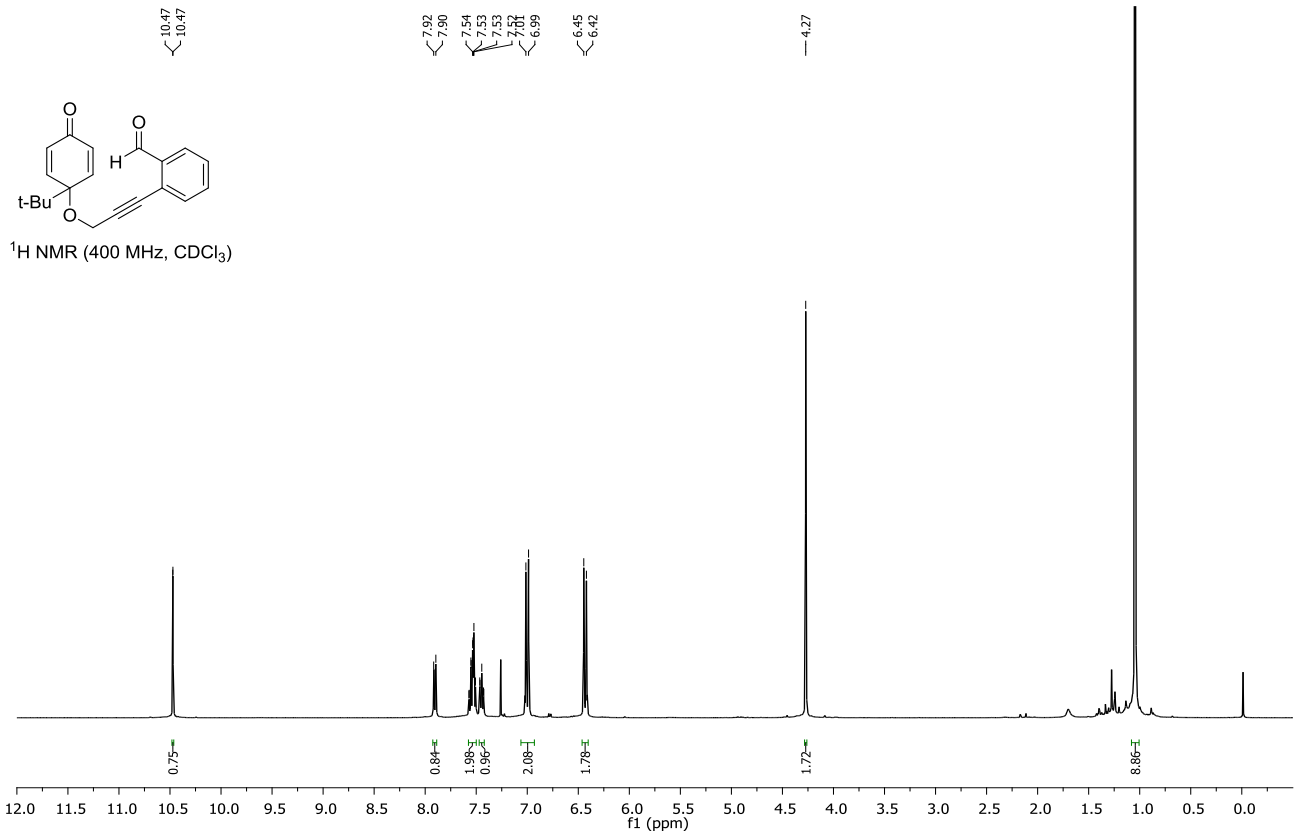
^{13}C NMR (126 MHz, $CDCl_3$)

2-(3-((1-Isopropyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1e):

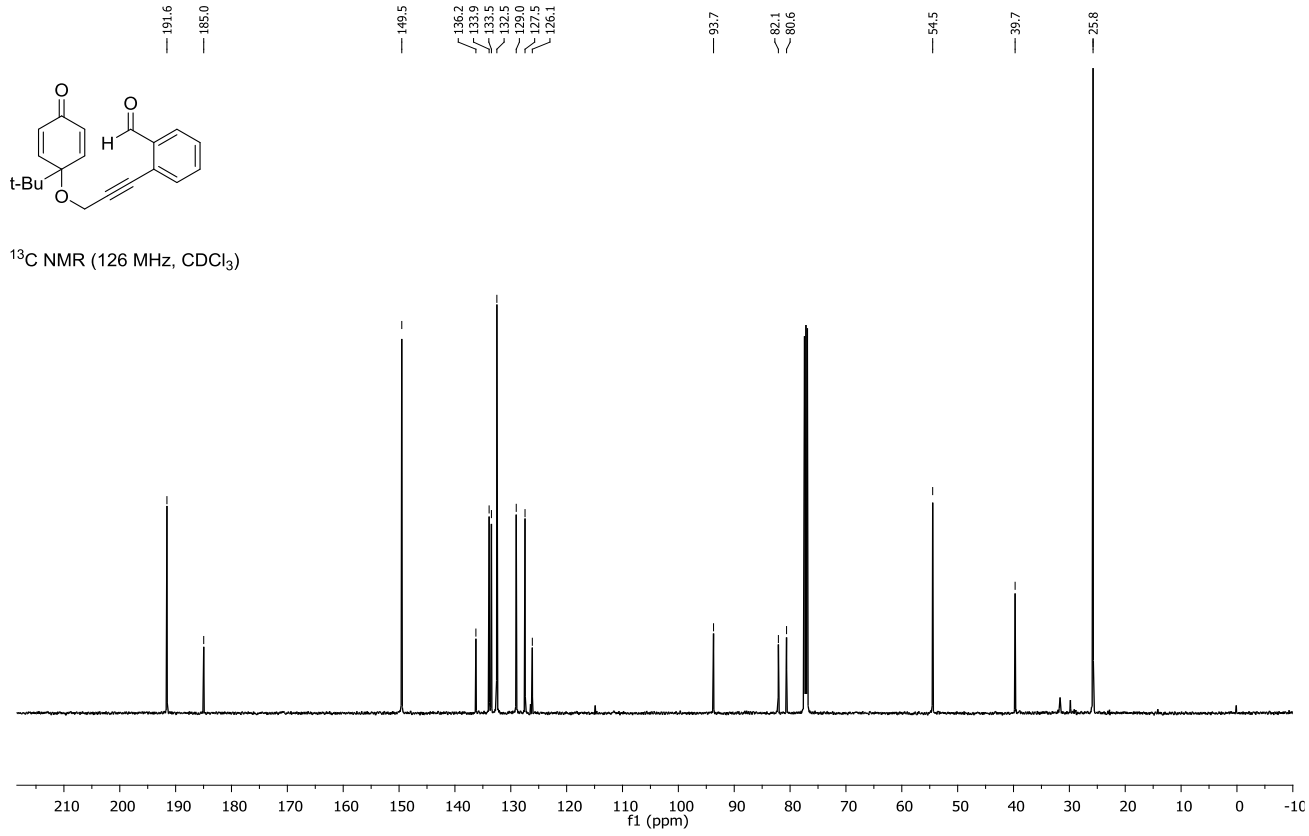




2-(3-((1-(*tert*-Butyl)-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1f):

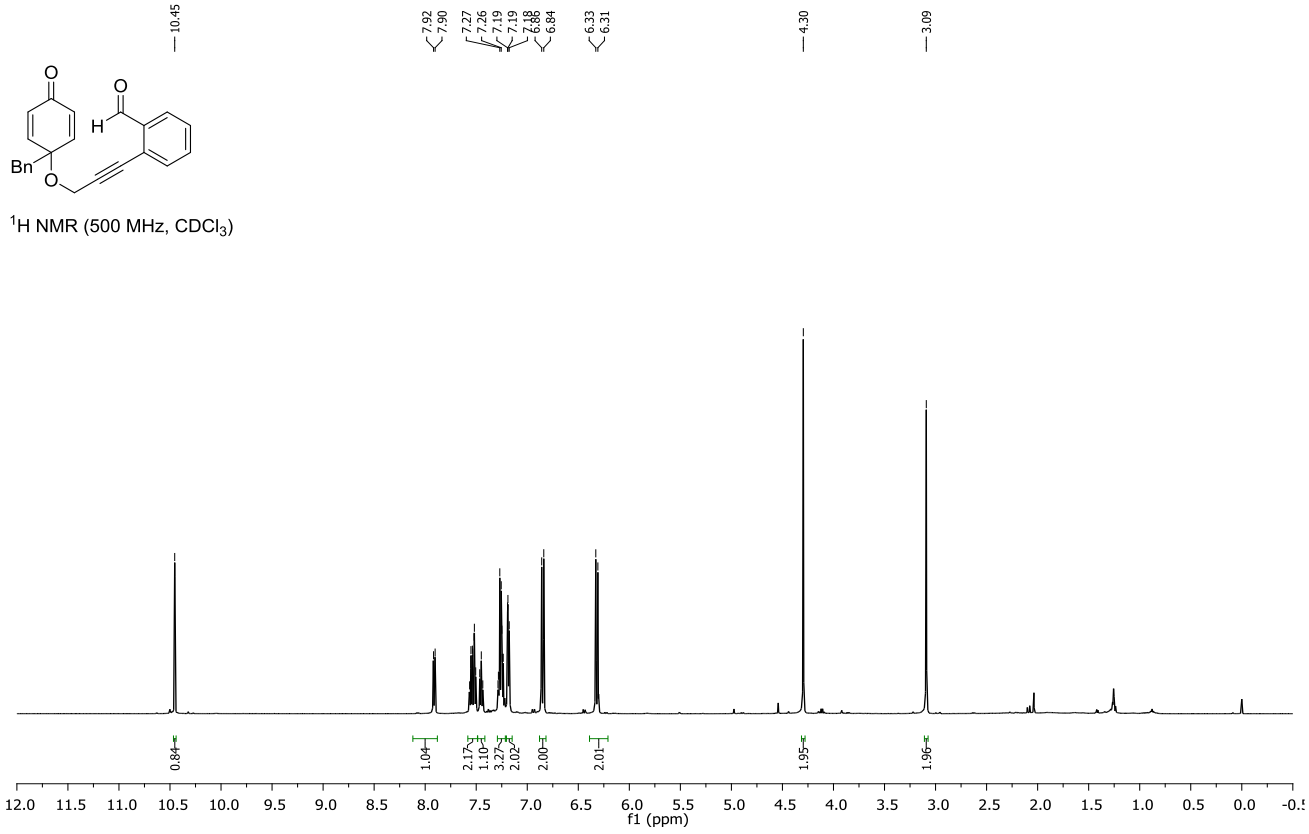


^{1}H NMR (400 MHz, $CDCl_3$)

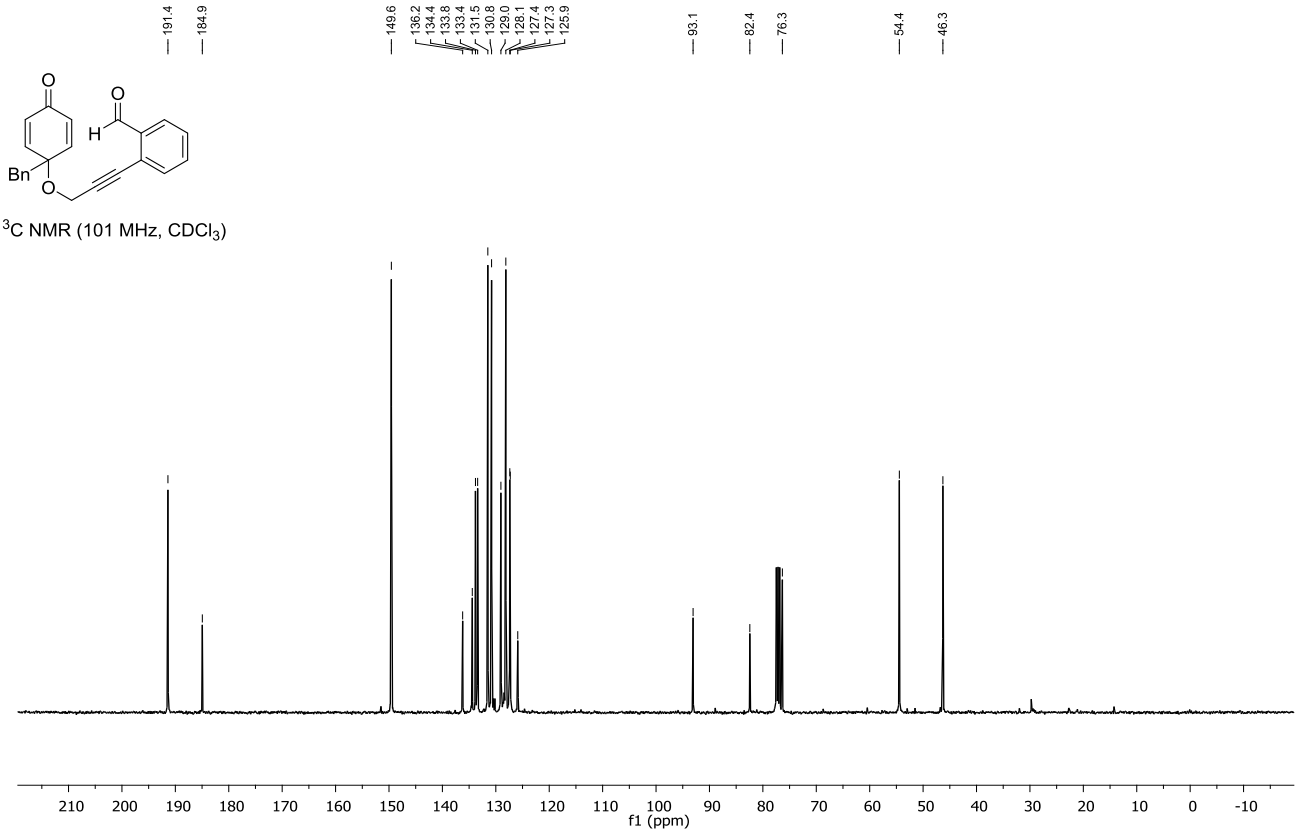


^{13}C NMR (126 MHz, $CDCl_3$)

2-(3-((1-Benzyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1g):

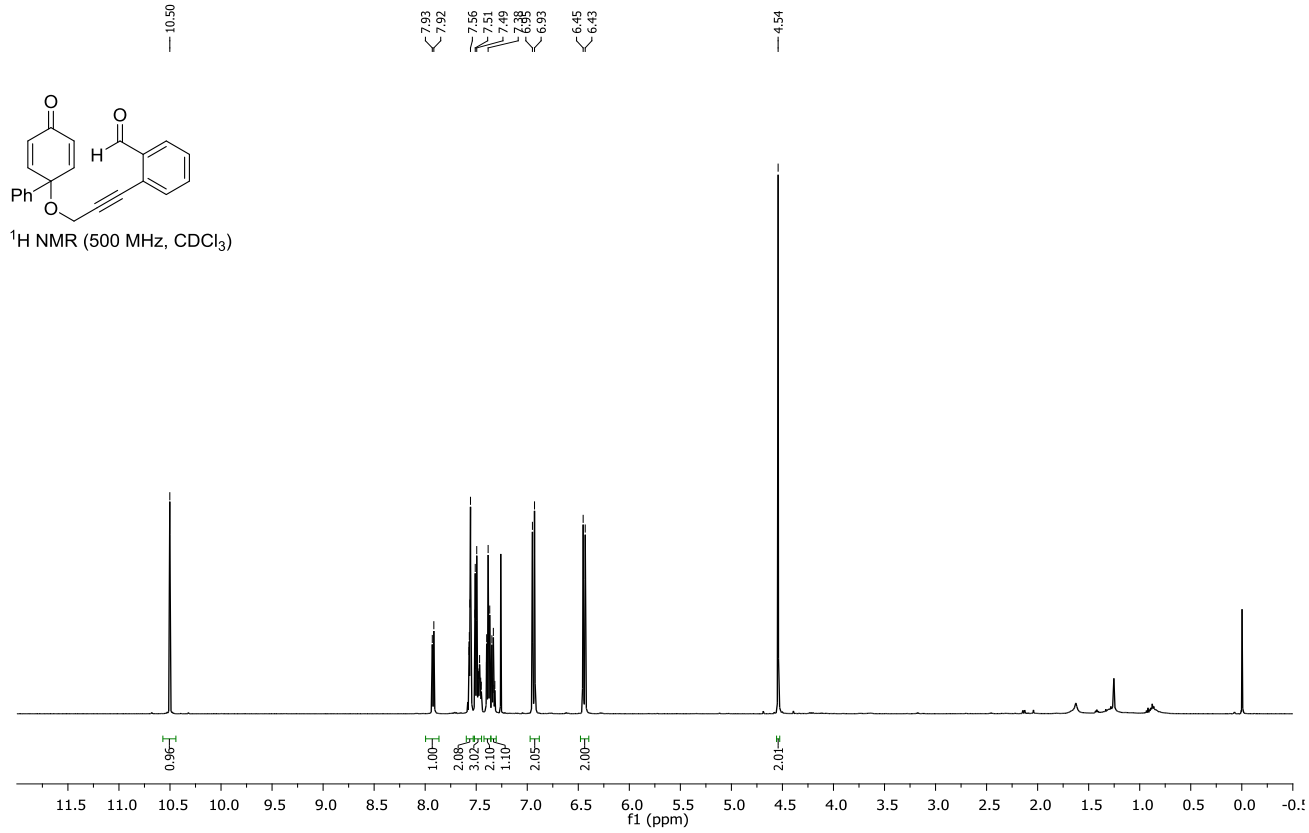


^{1}H NMR (500 MHz, $CDCl_3$)

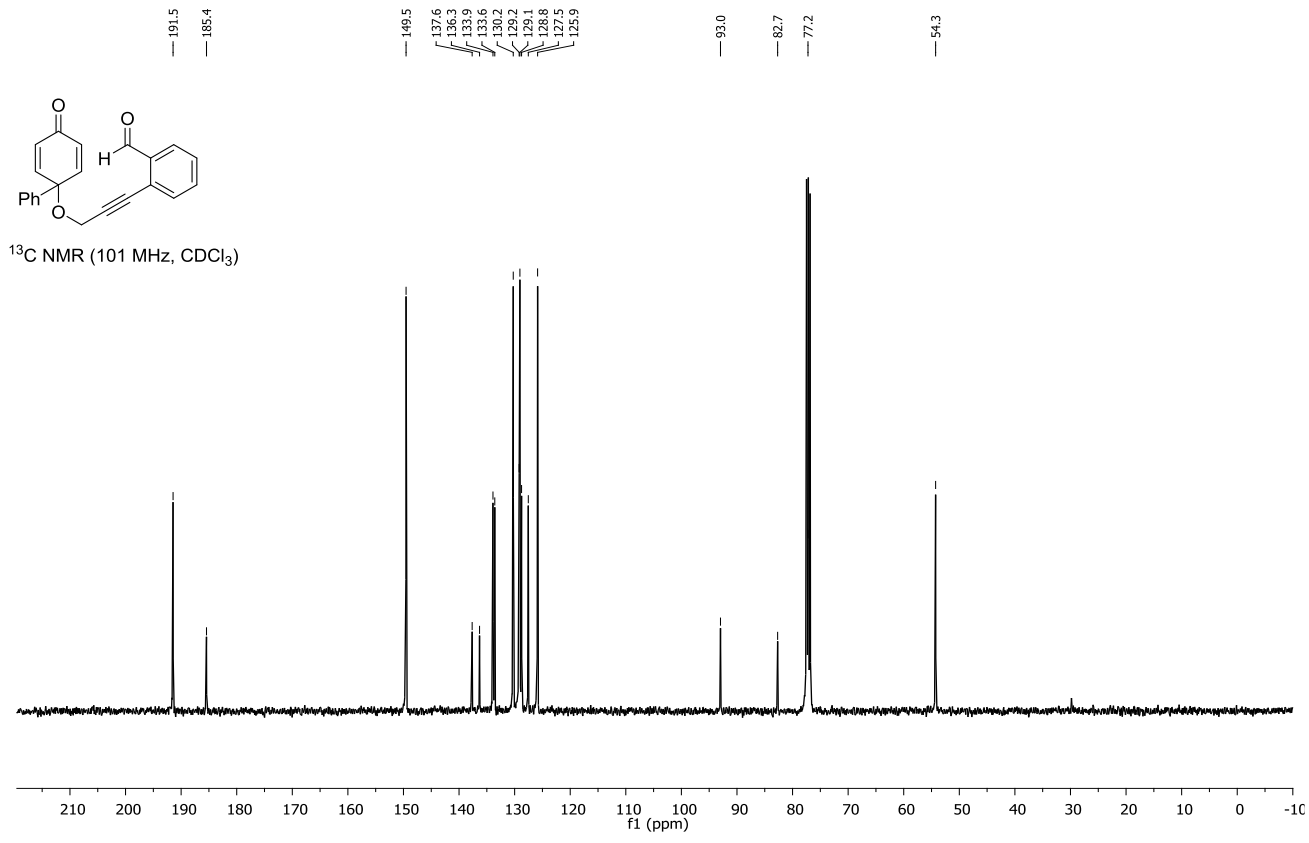


^{13}C NMR (101 MHz, $CDCl_3$)

2-(3-((4-Oxo-[1,1'-biphenyl]-1(4H)-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1h):

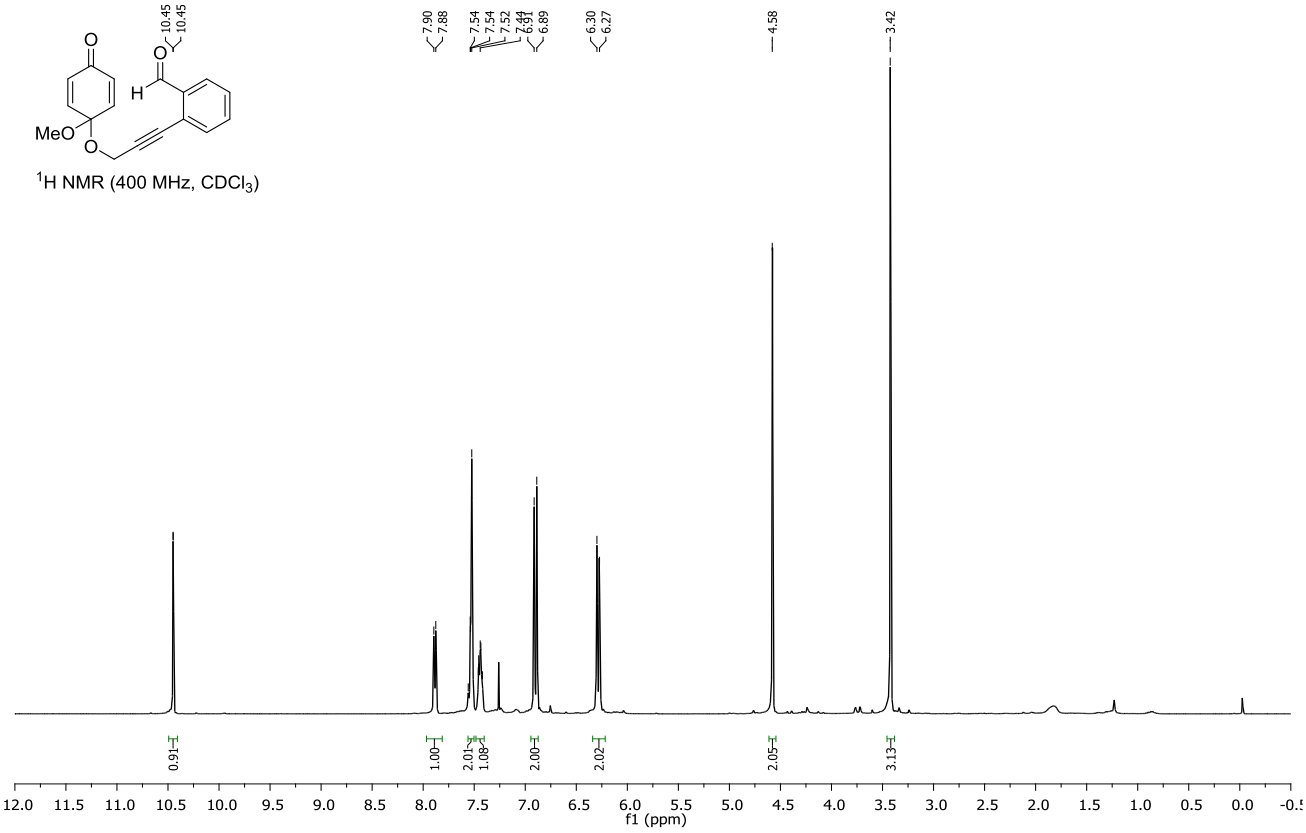


^{1}H NMR (500 MHz, $CDCl_3$)

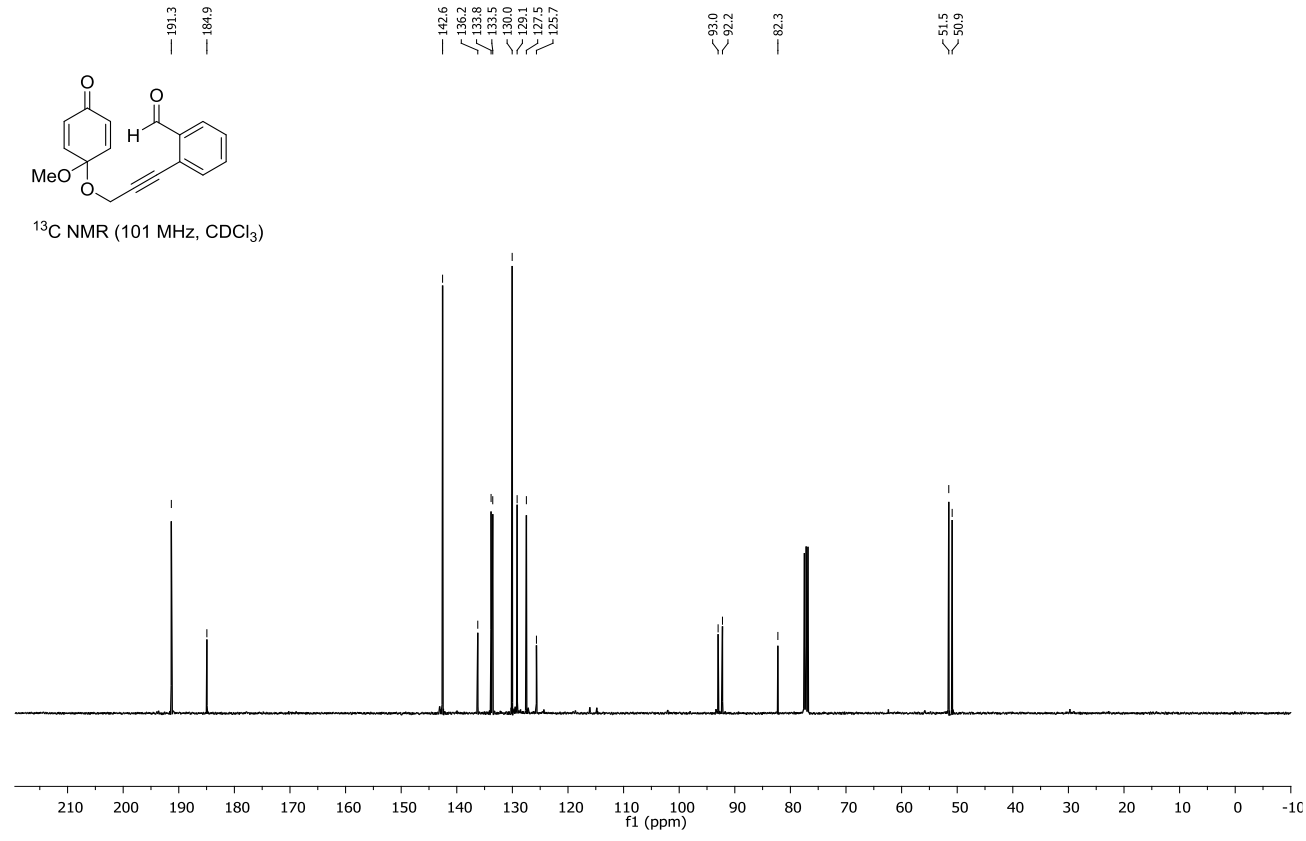


^{13}C NMR (101 MHz, $CDCl_3$)

2-(3-((1-Methoxy-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1i):

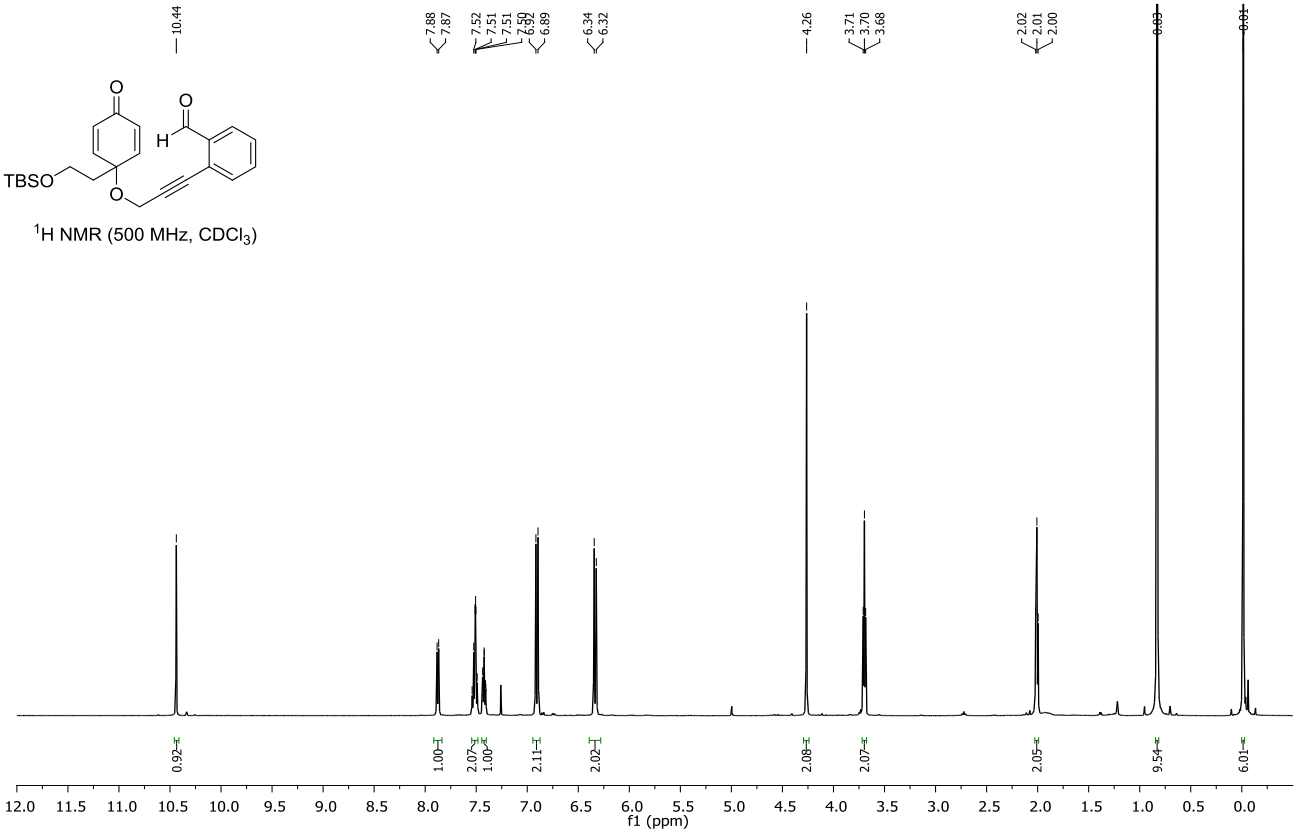


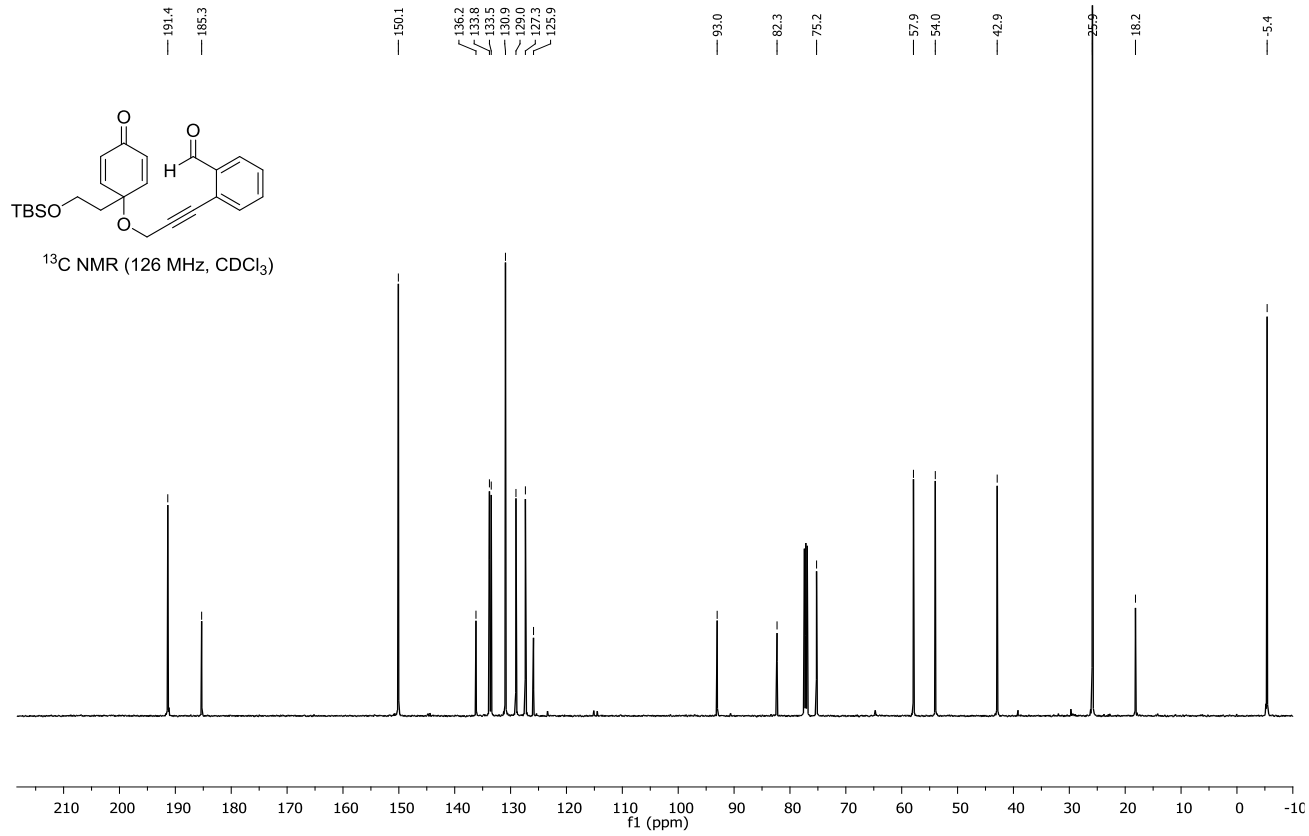
^{1}H NMR (400 MHz, $CDCl_3$)



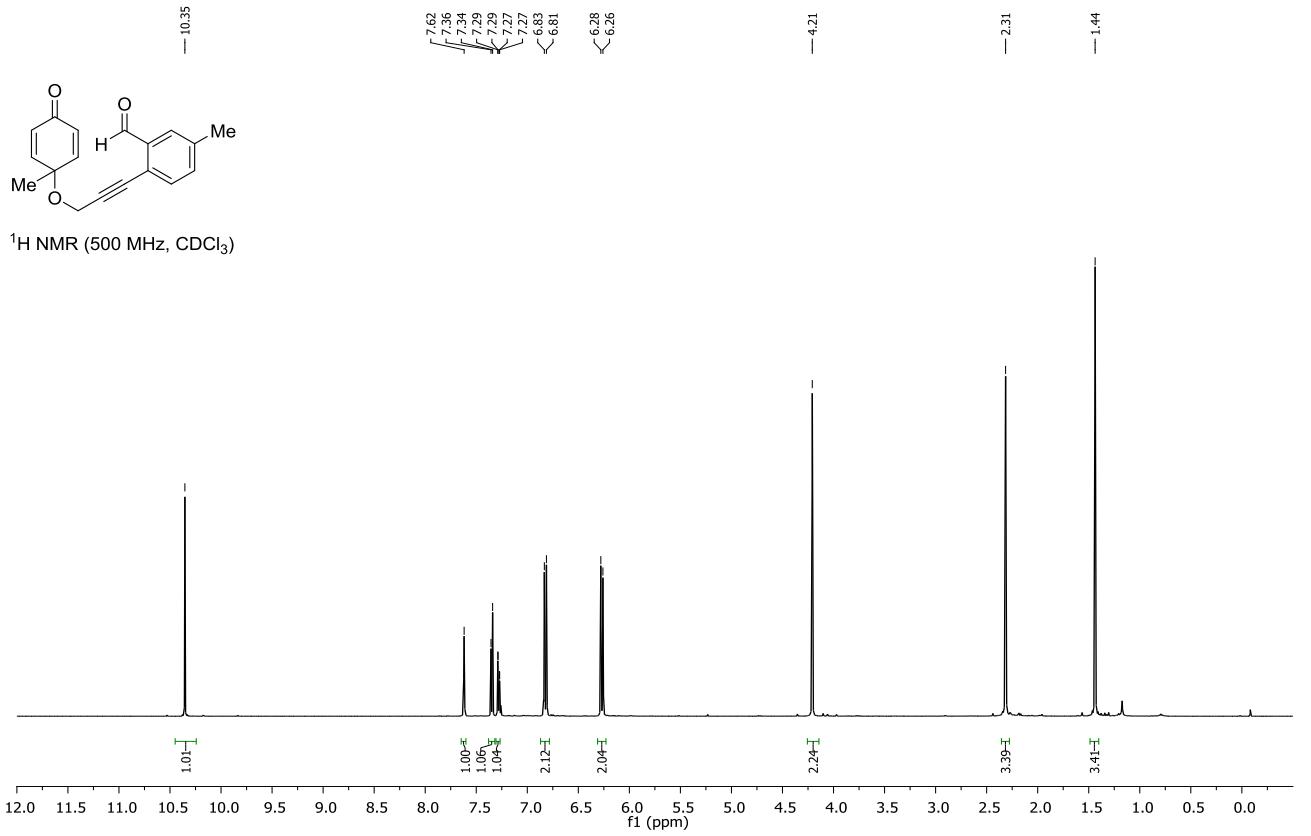
^{13}C NMR (101 MHz, $CDCl_3$)

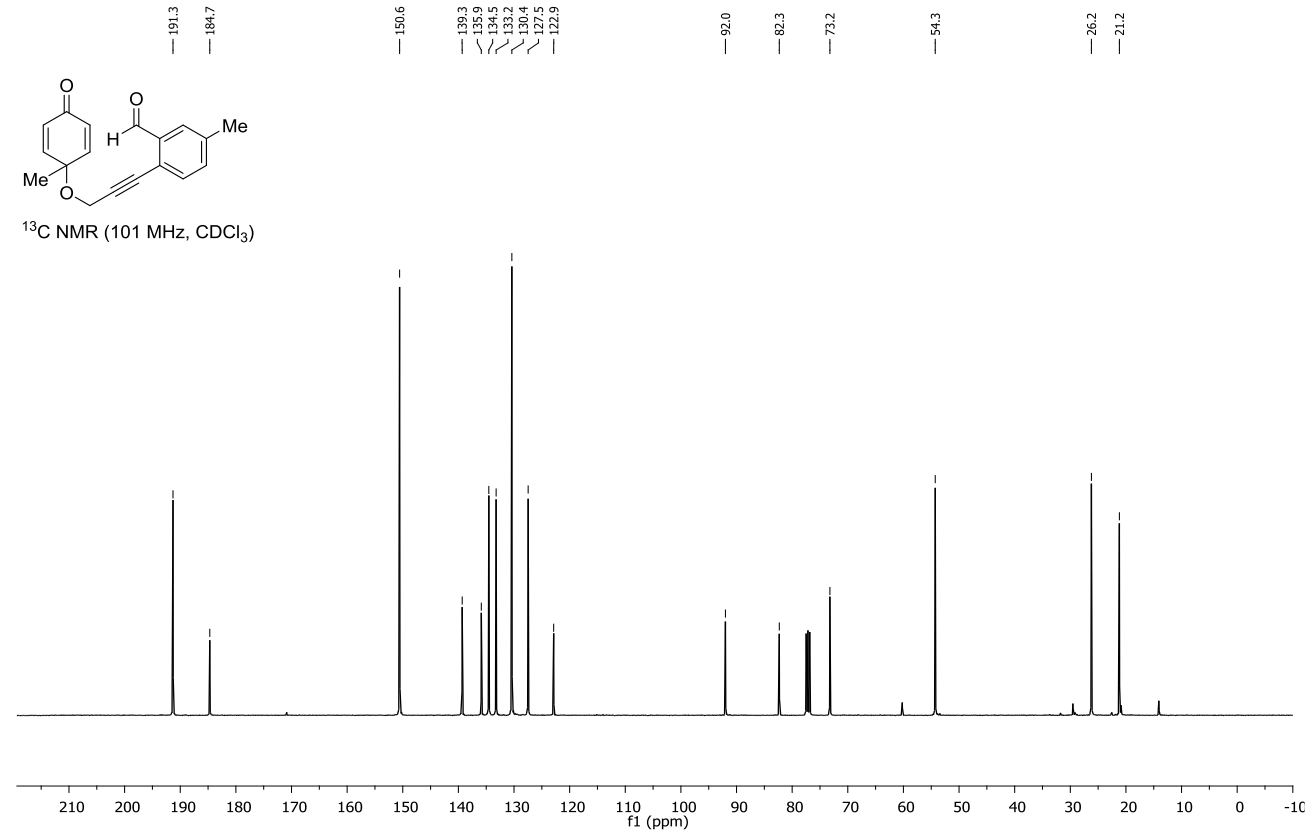
2-(3-((1-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1j):



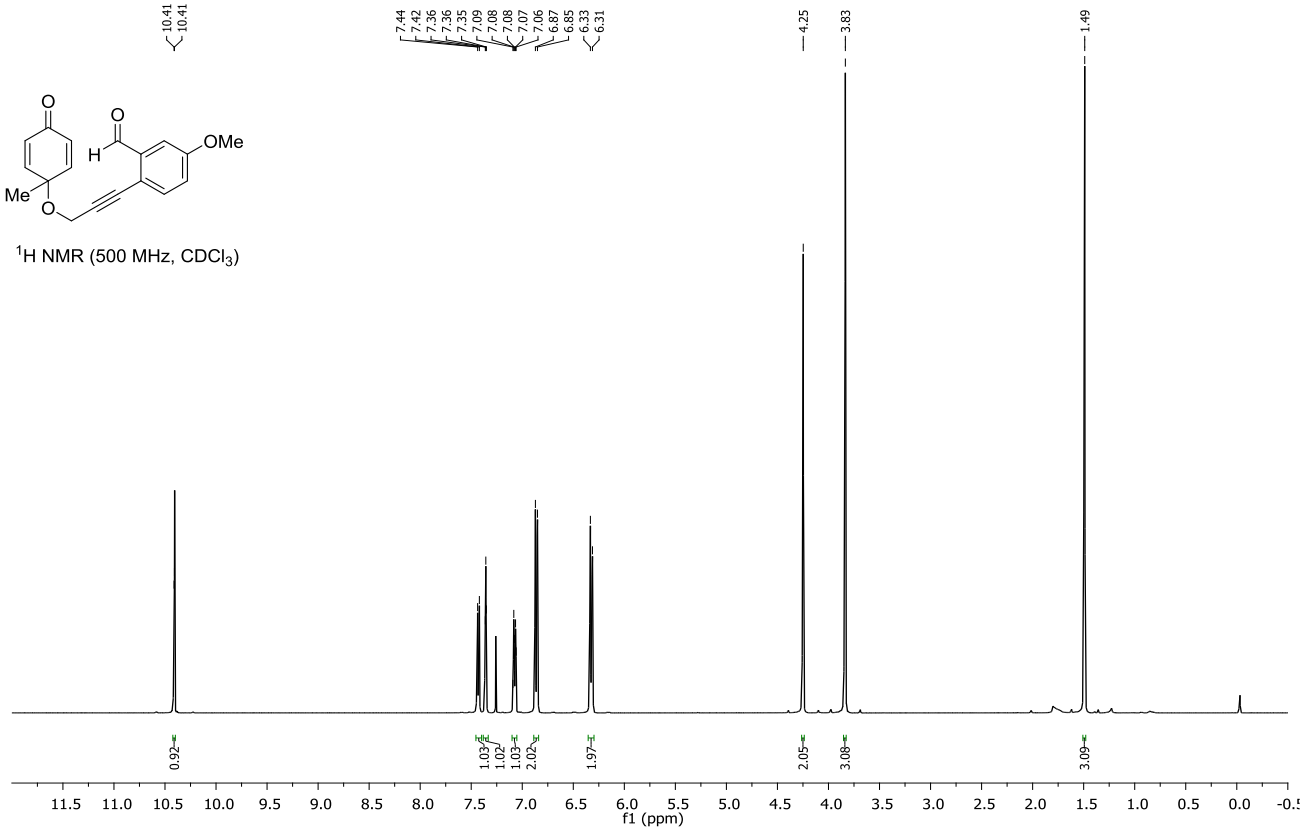


5-Methyl-2-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1k):

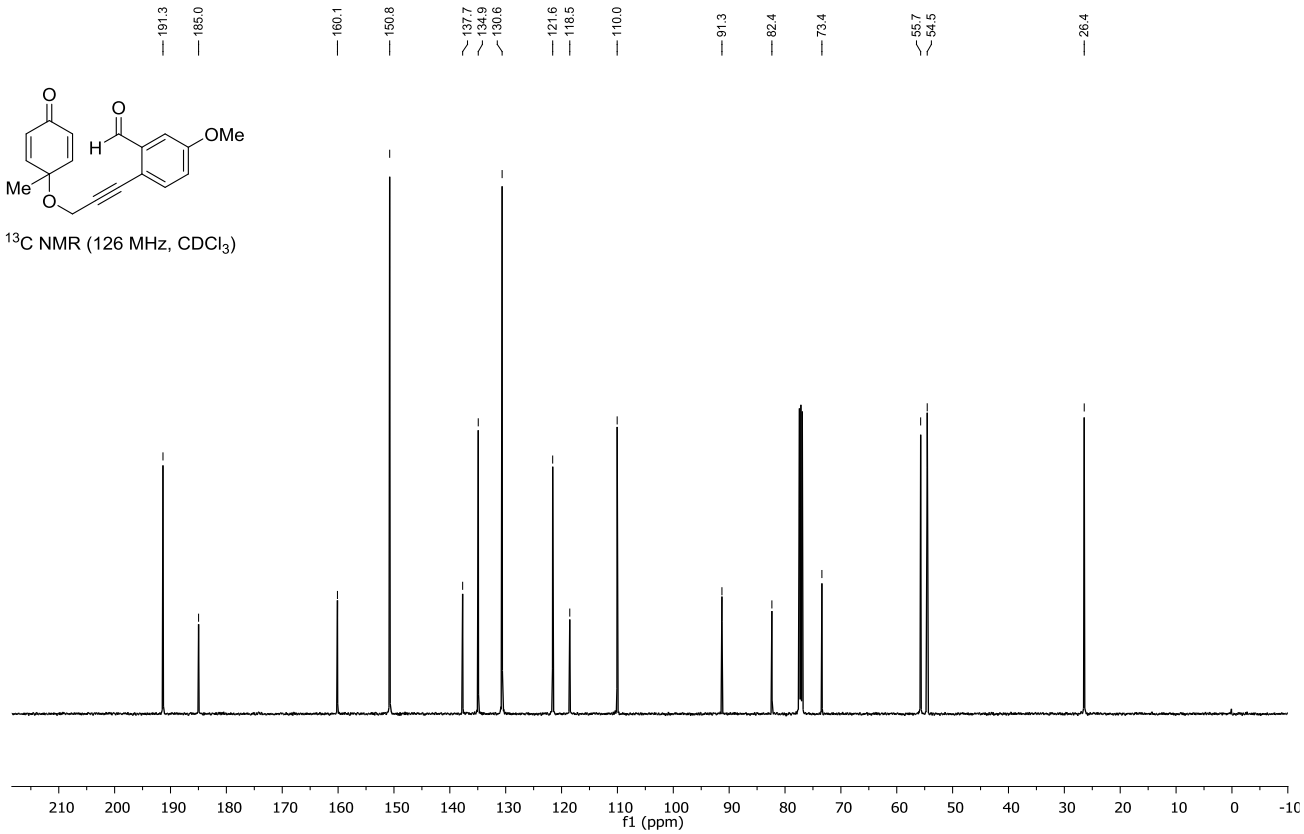




5-Methoxy-2-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benz aldehyde (1m):

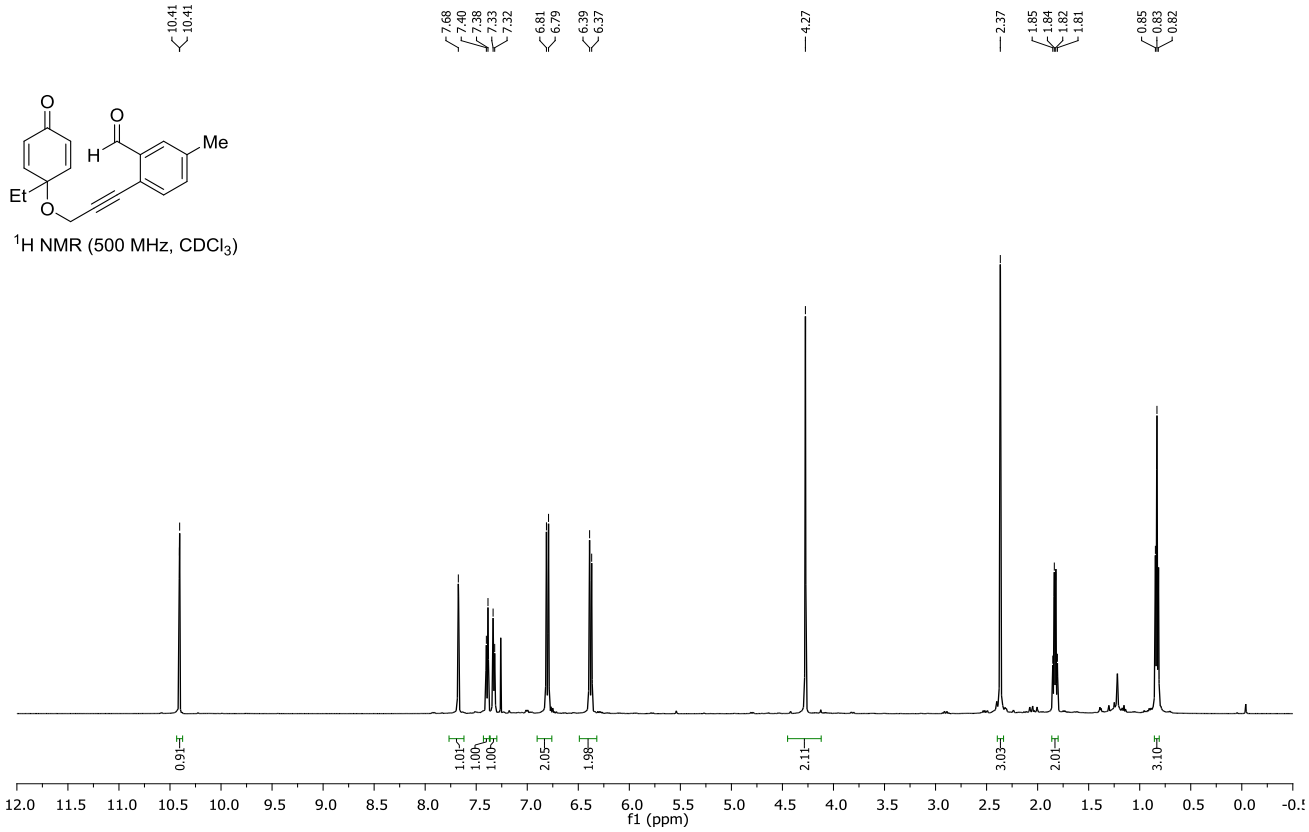


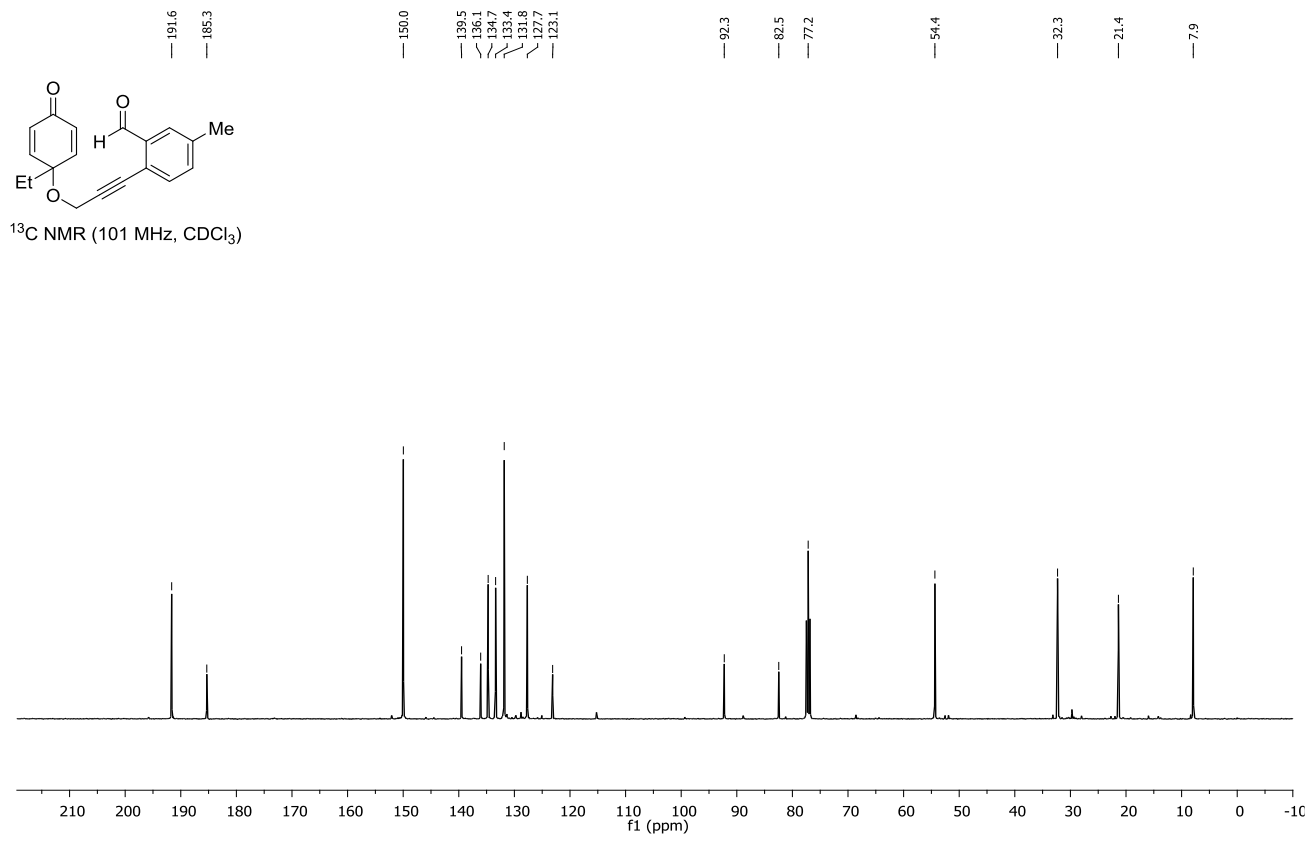
^{1}H NMR (500 MHz, $CDCl_3$)



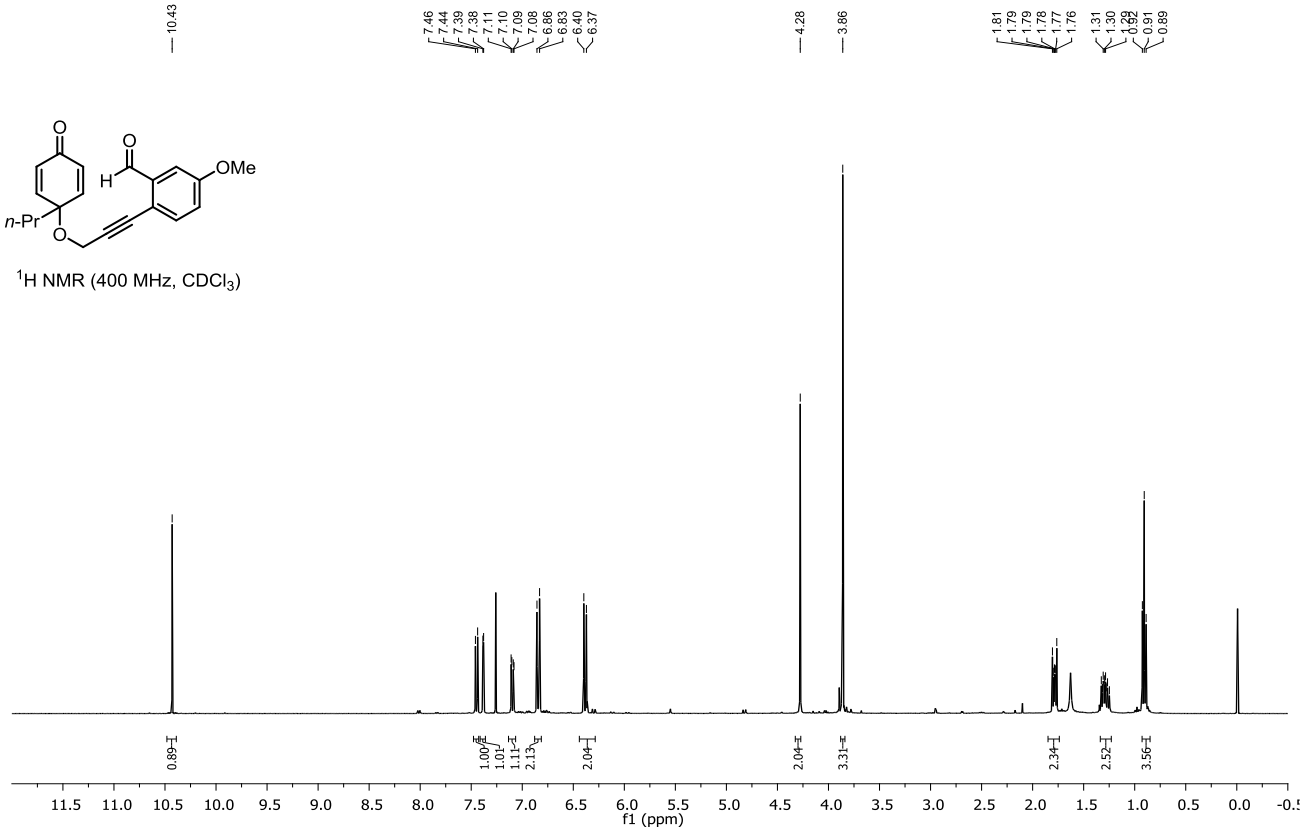
^{13}C NMR (126 MHz, $CDCl_3$)

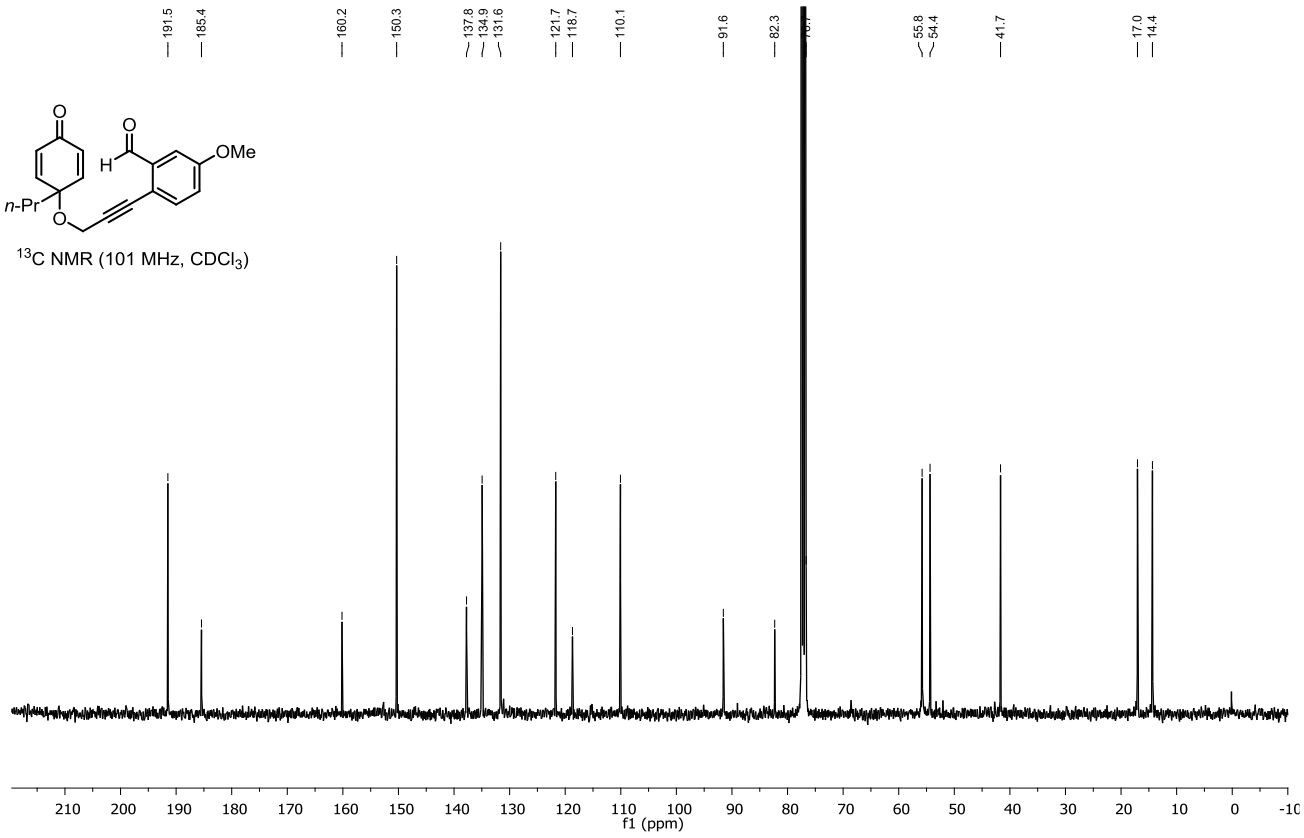
2-(3-((1-Ethyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)-5-methylbenzaldehyde (1n):



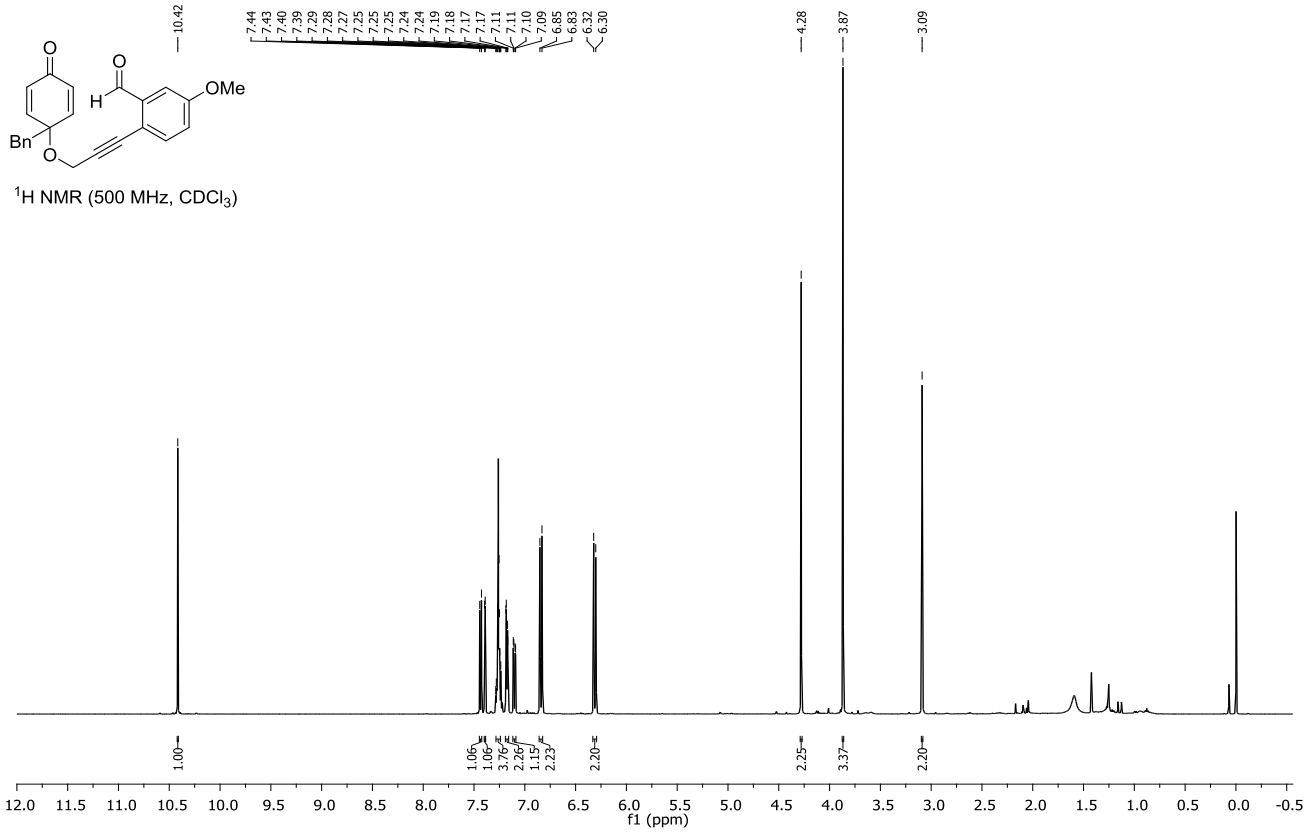


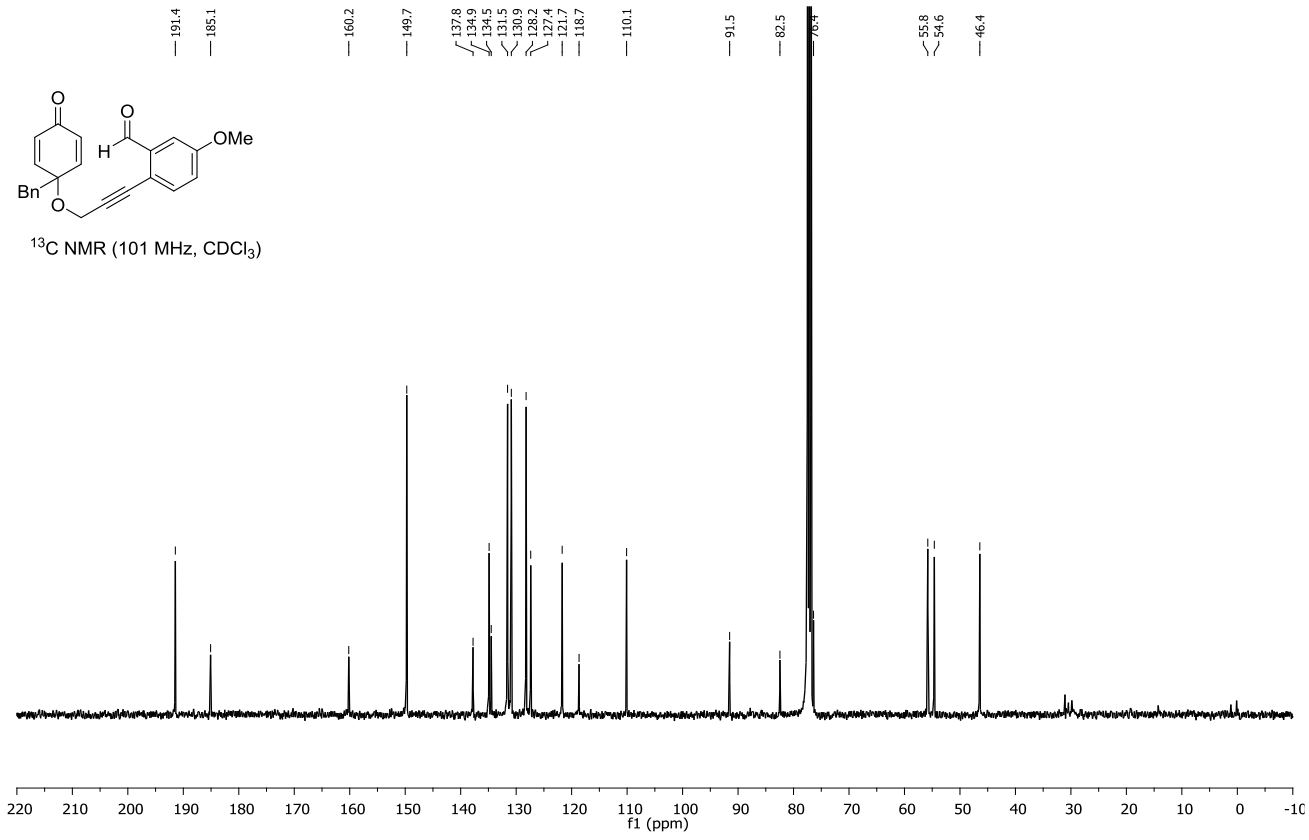
5-Methoxy-2-(3-((4-oxo-1-propylcyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1o):



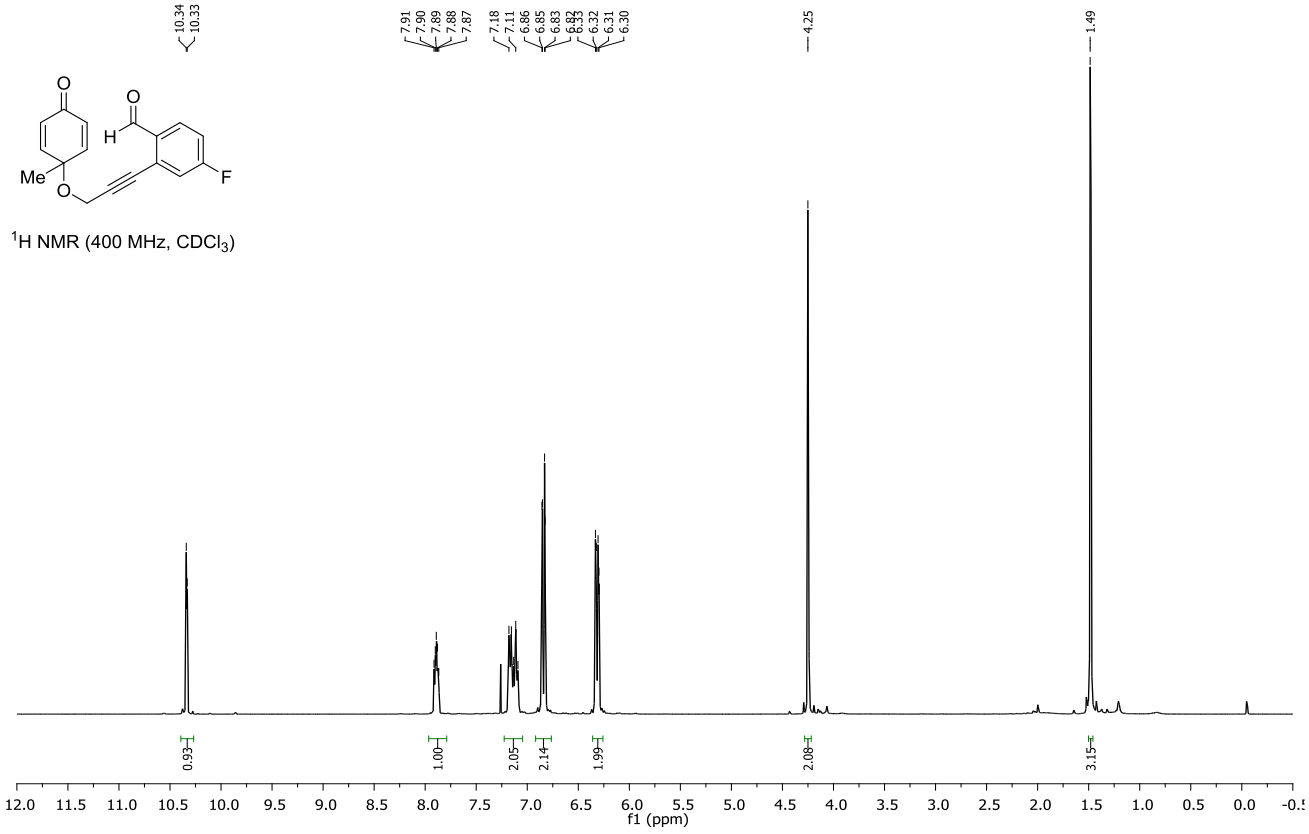


2-(3-((1-Benzyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)-5-methoxy benz aldehyde (1p):

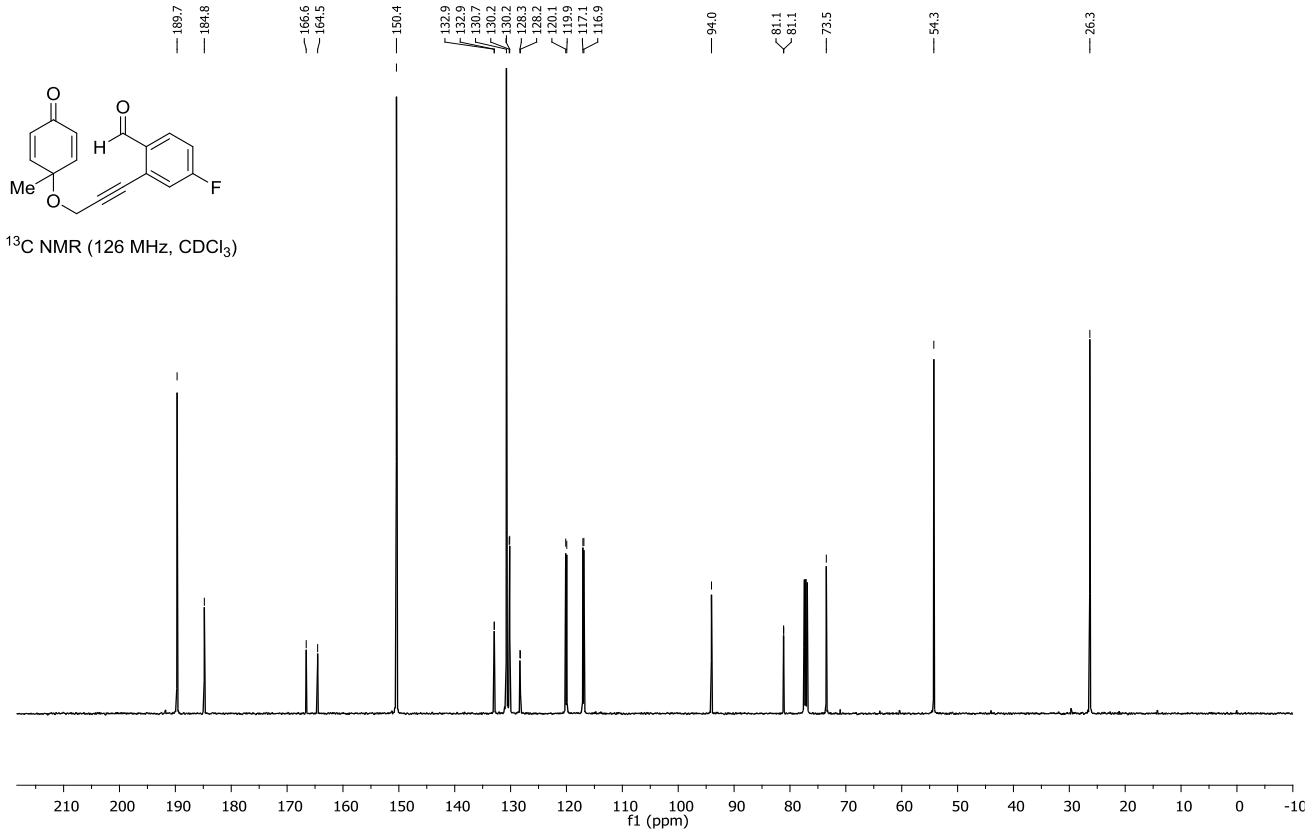




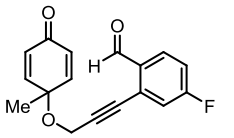
4-Fluoro-2-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benz aldehyde (1q):



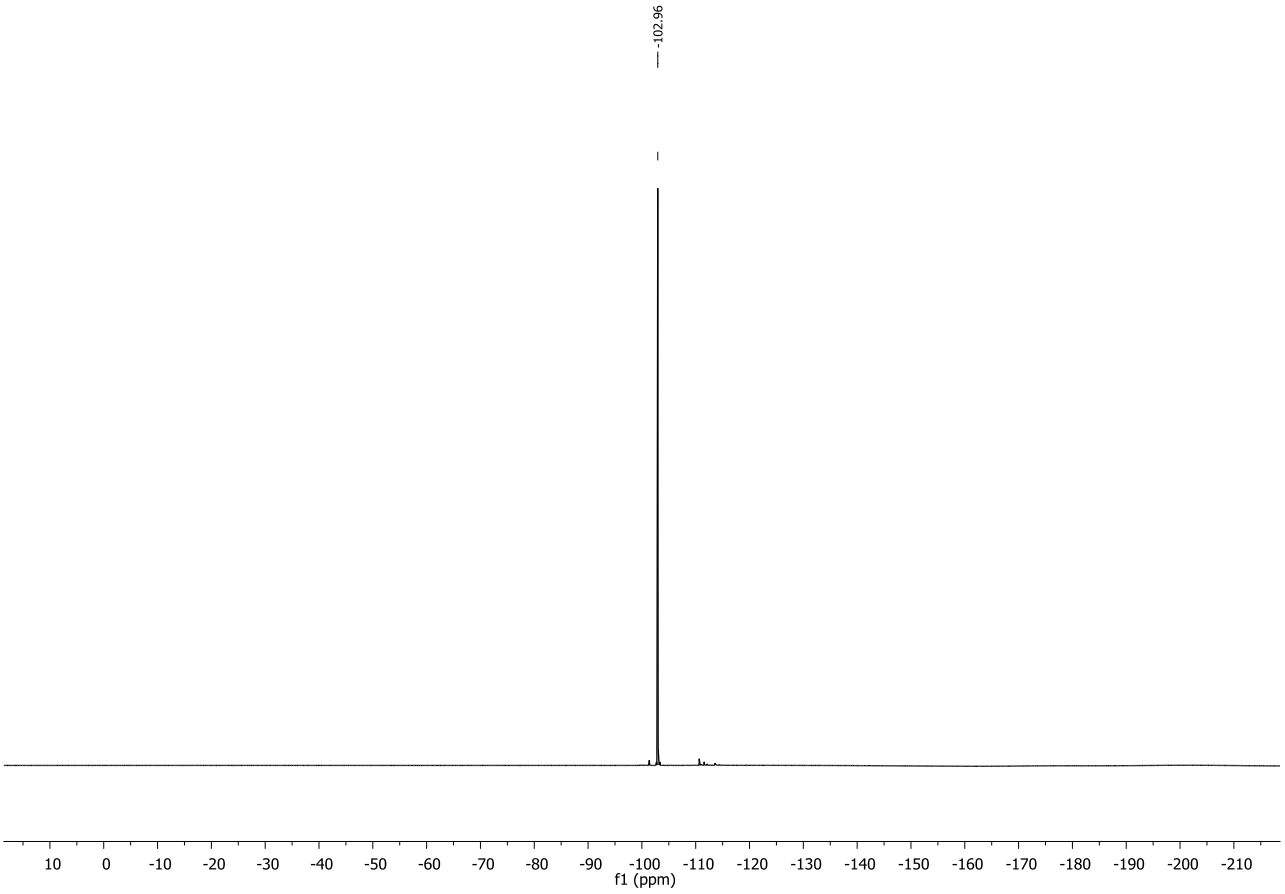
^{1}H NMR (400 MHz, $CDCl_3$)



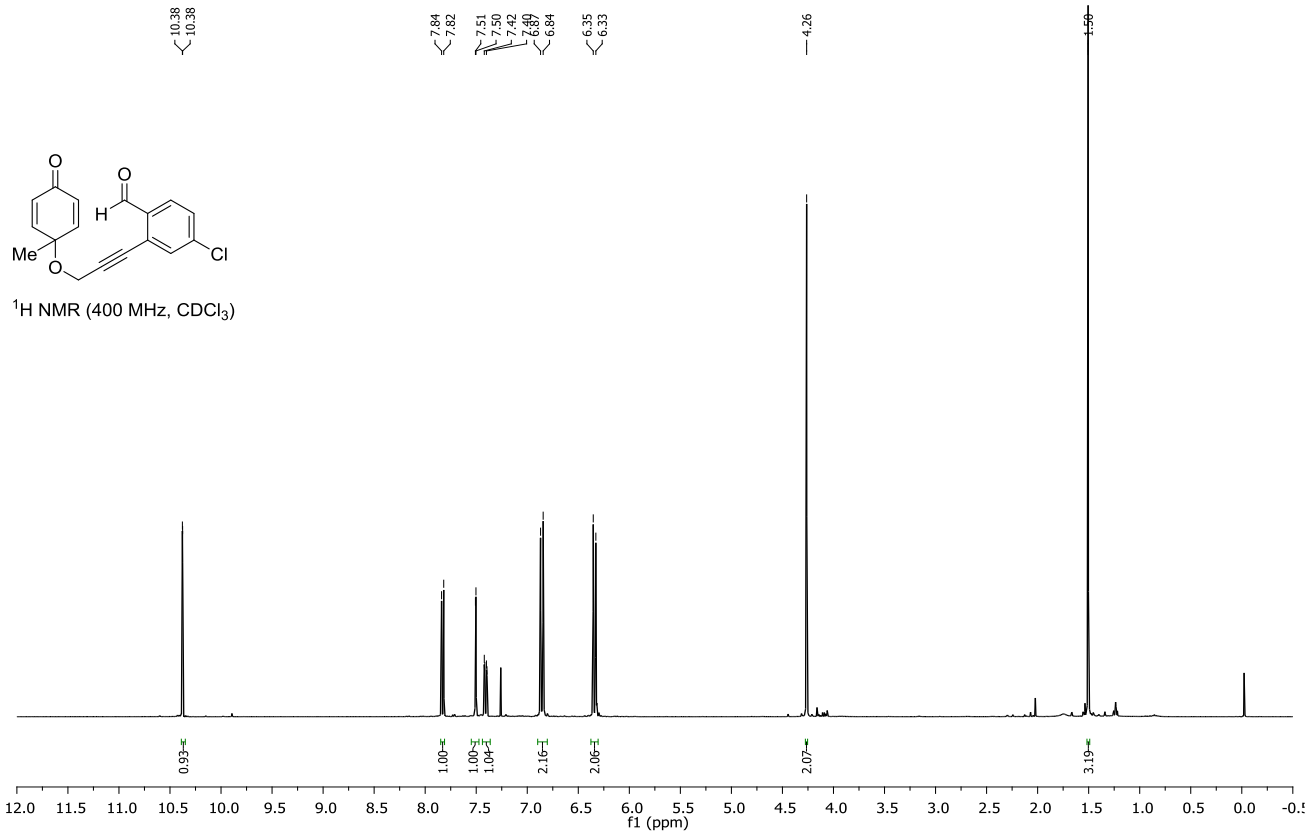
^{13}C NMR (126 MHz, $CDCl_3$)



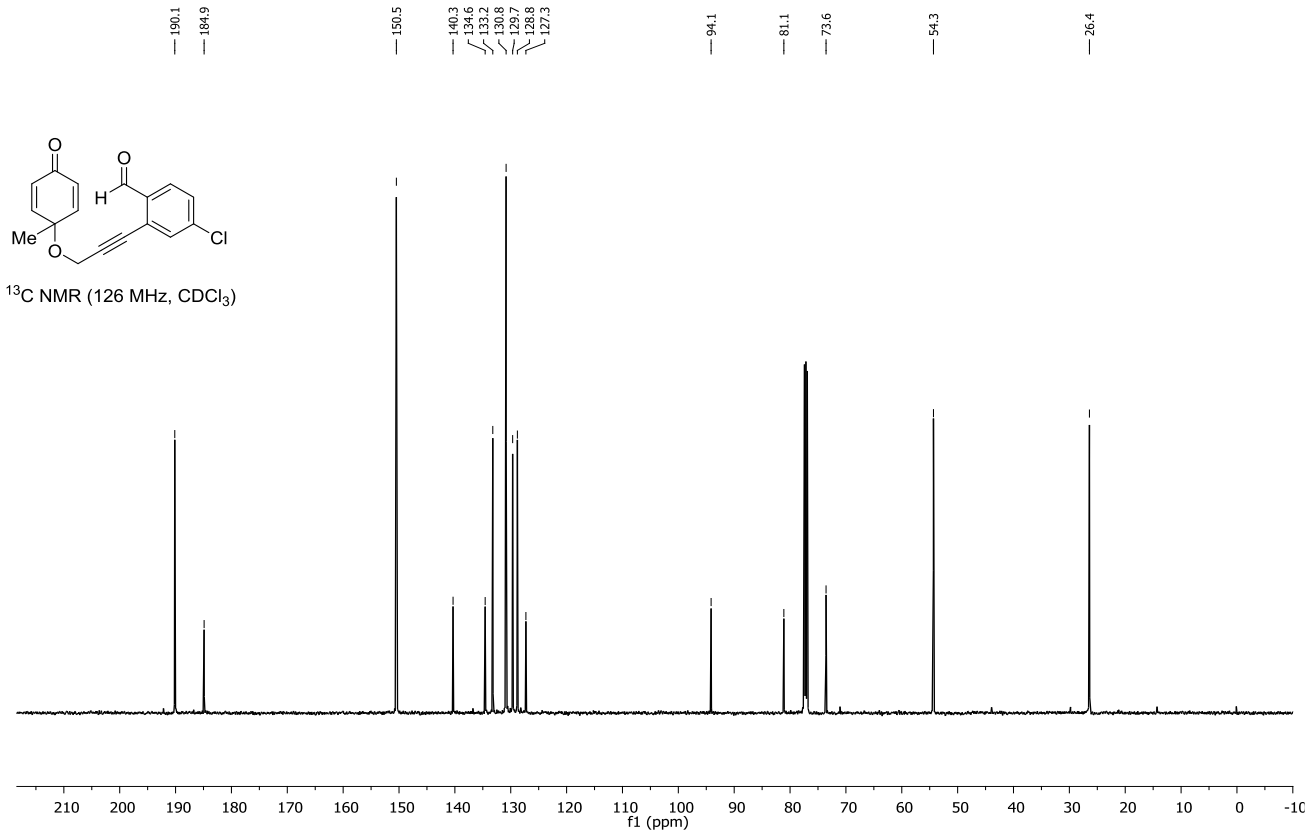
^{19}F NMR (377 MHz, $CDCl_3$)



4-Chloro-2-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benz aldehyde (1r):

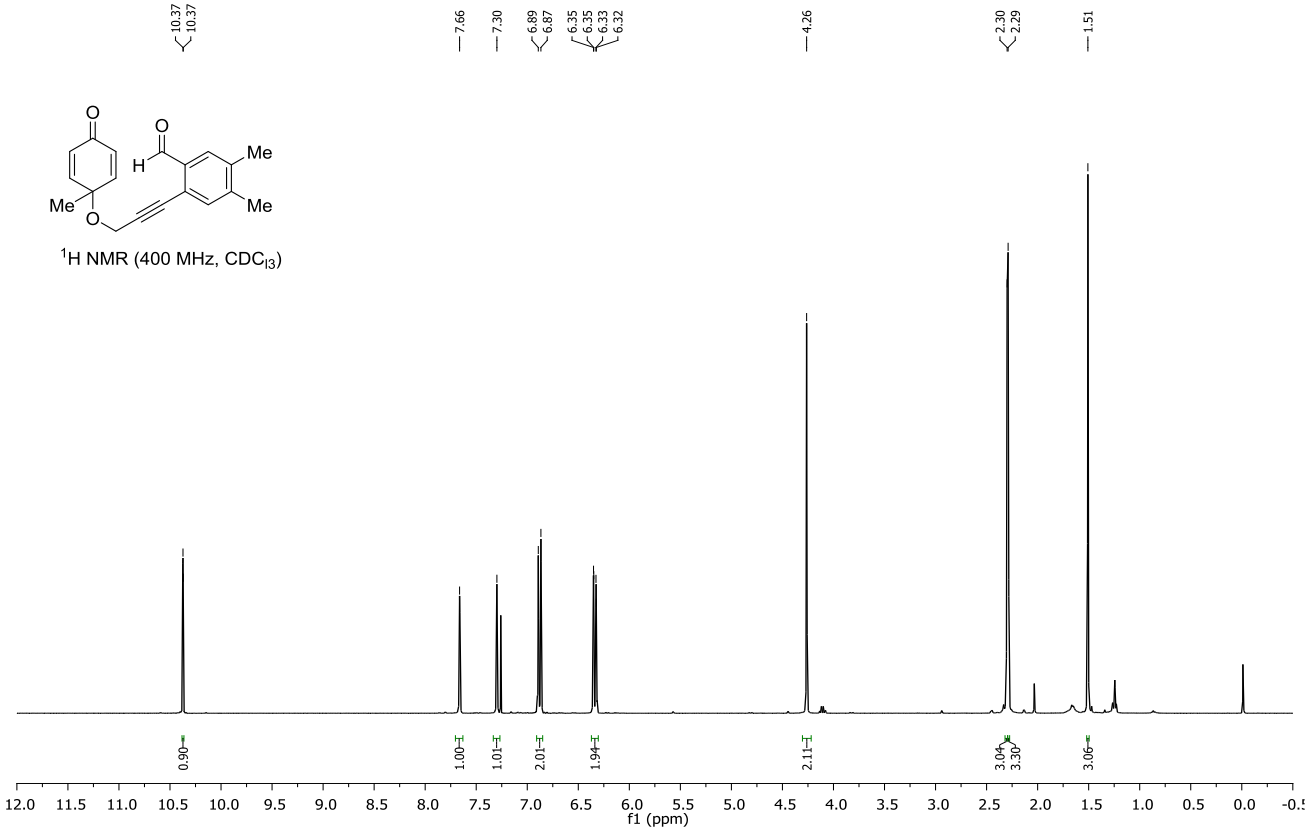


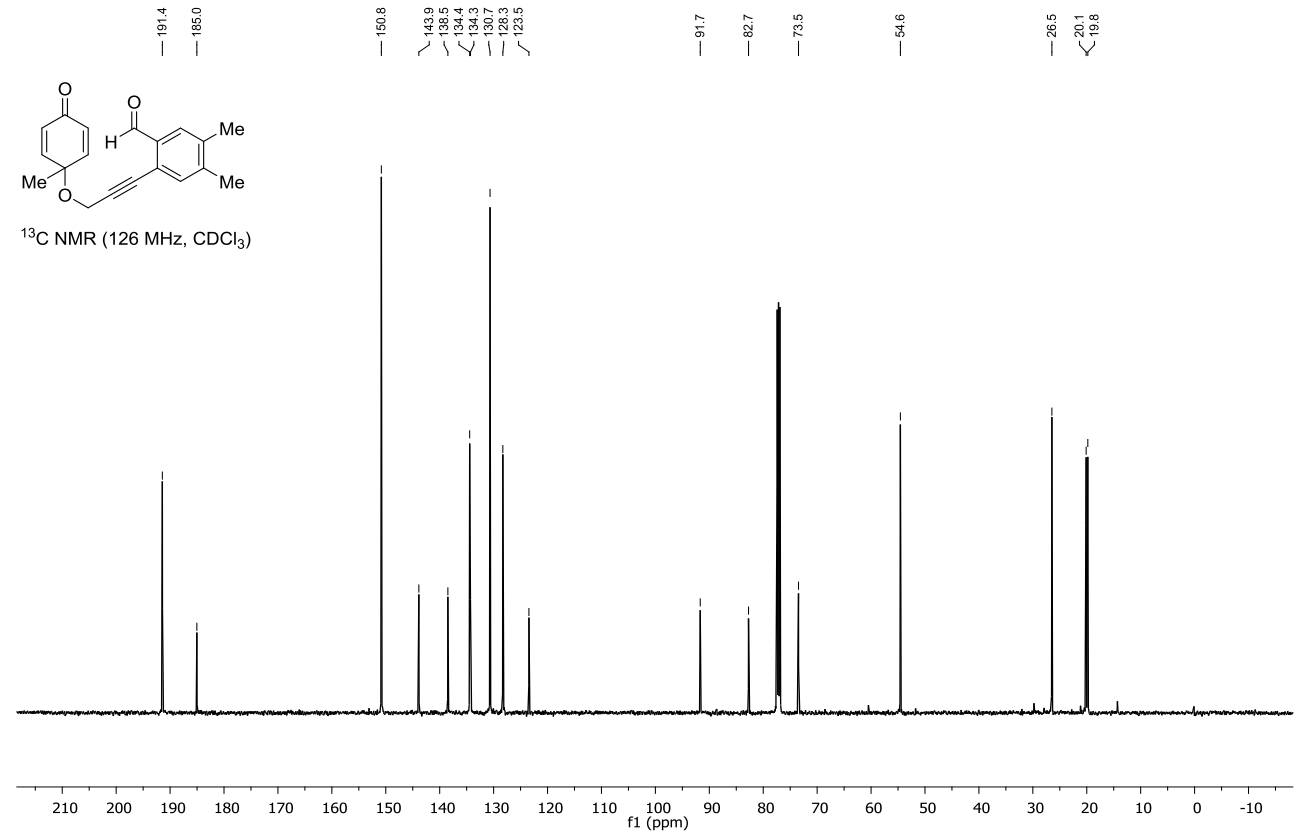
^{1}H NMR (400 MHz, $CDCl_3$)



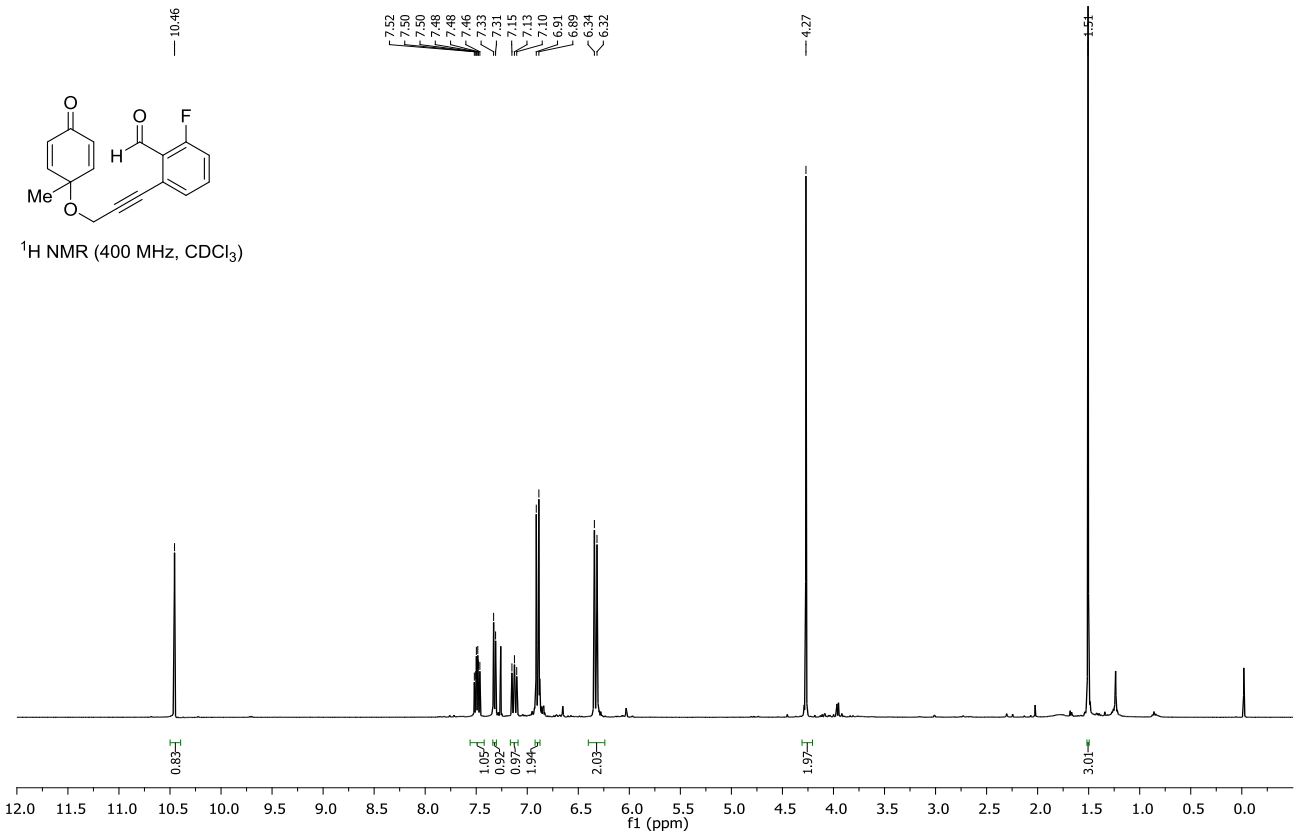
^{13}C NMR (126 MHz, $CDCl_3$)

4,5-Dimethyl-2-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1s):

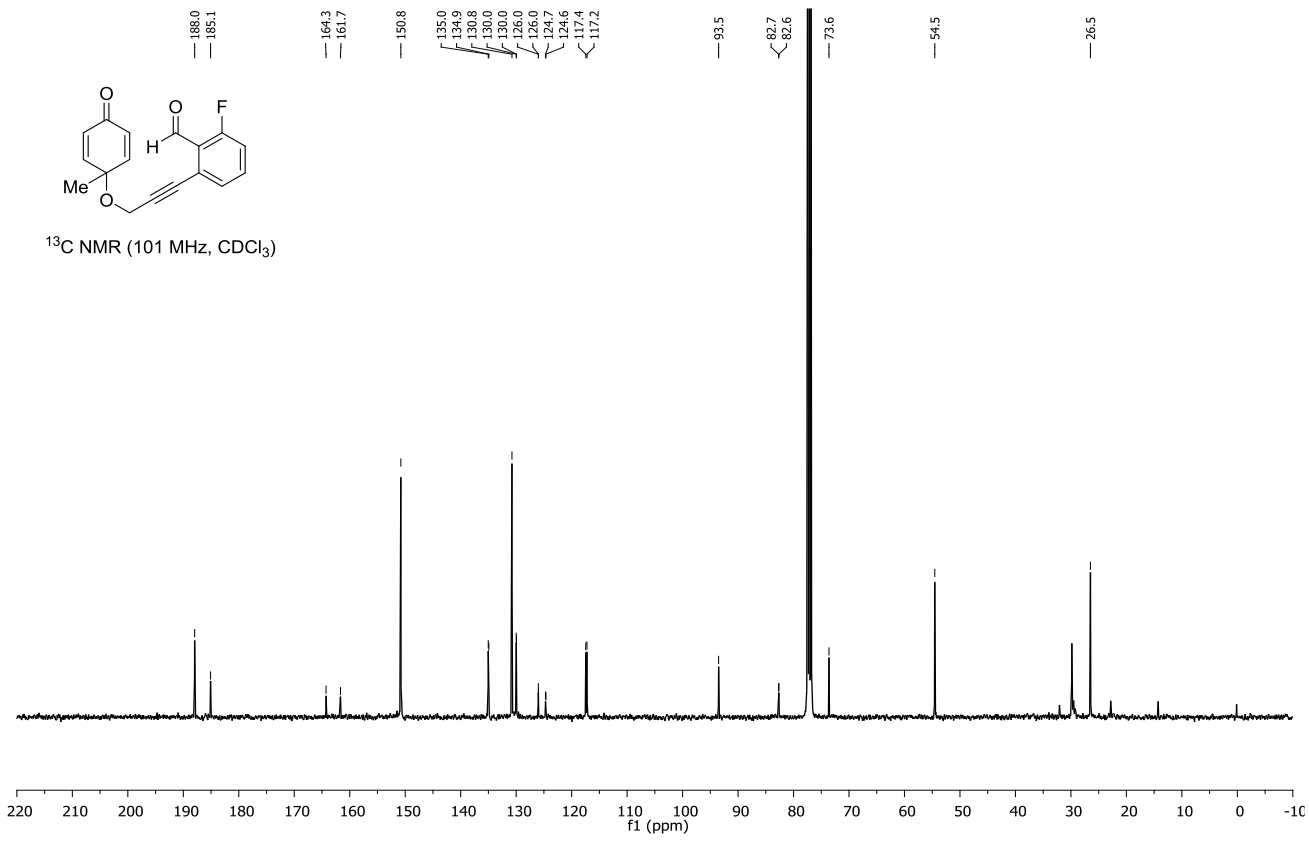




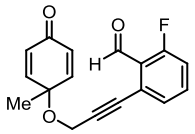
2-Fluoro-6-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1t):



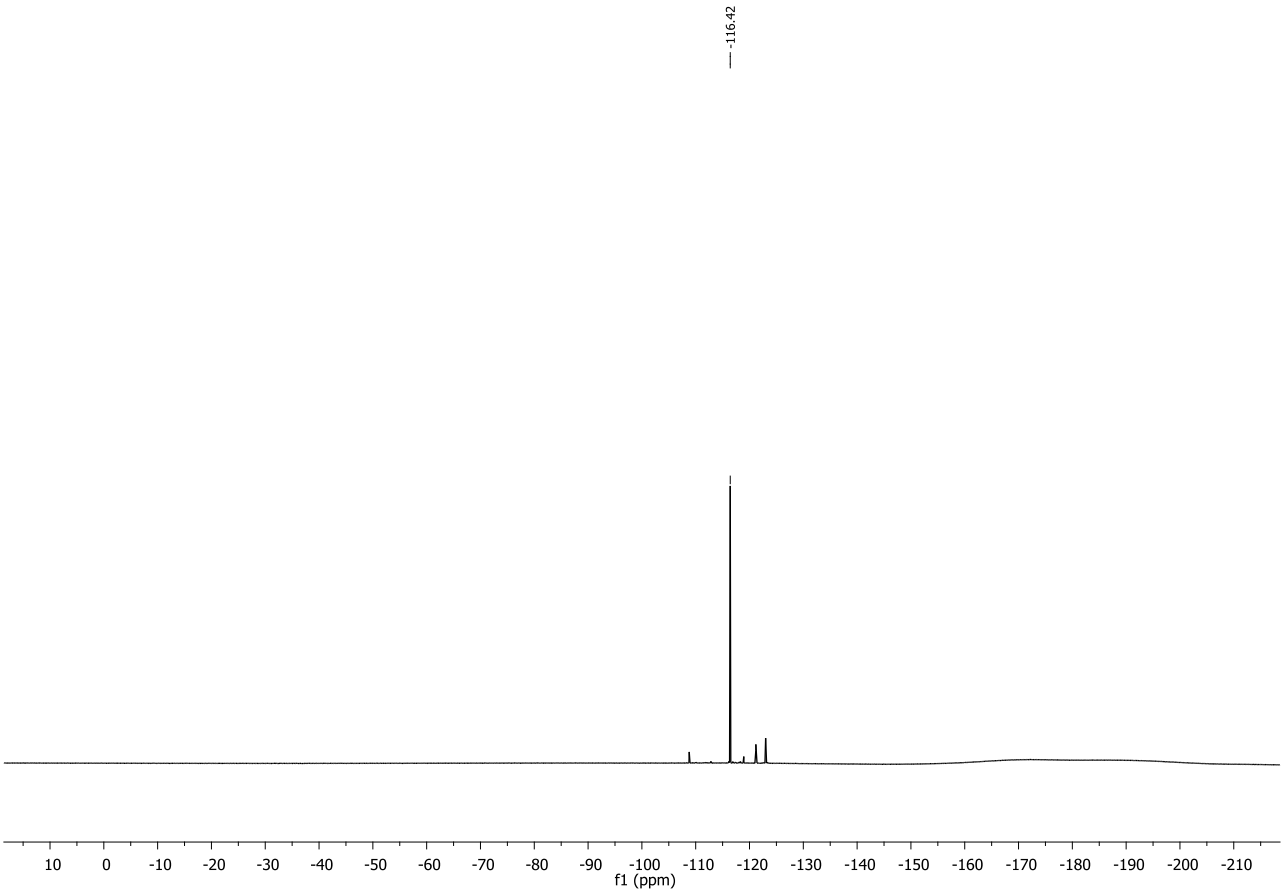
^{1}H NMR (400 MHz, $CDCl_3$)



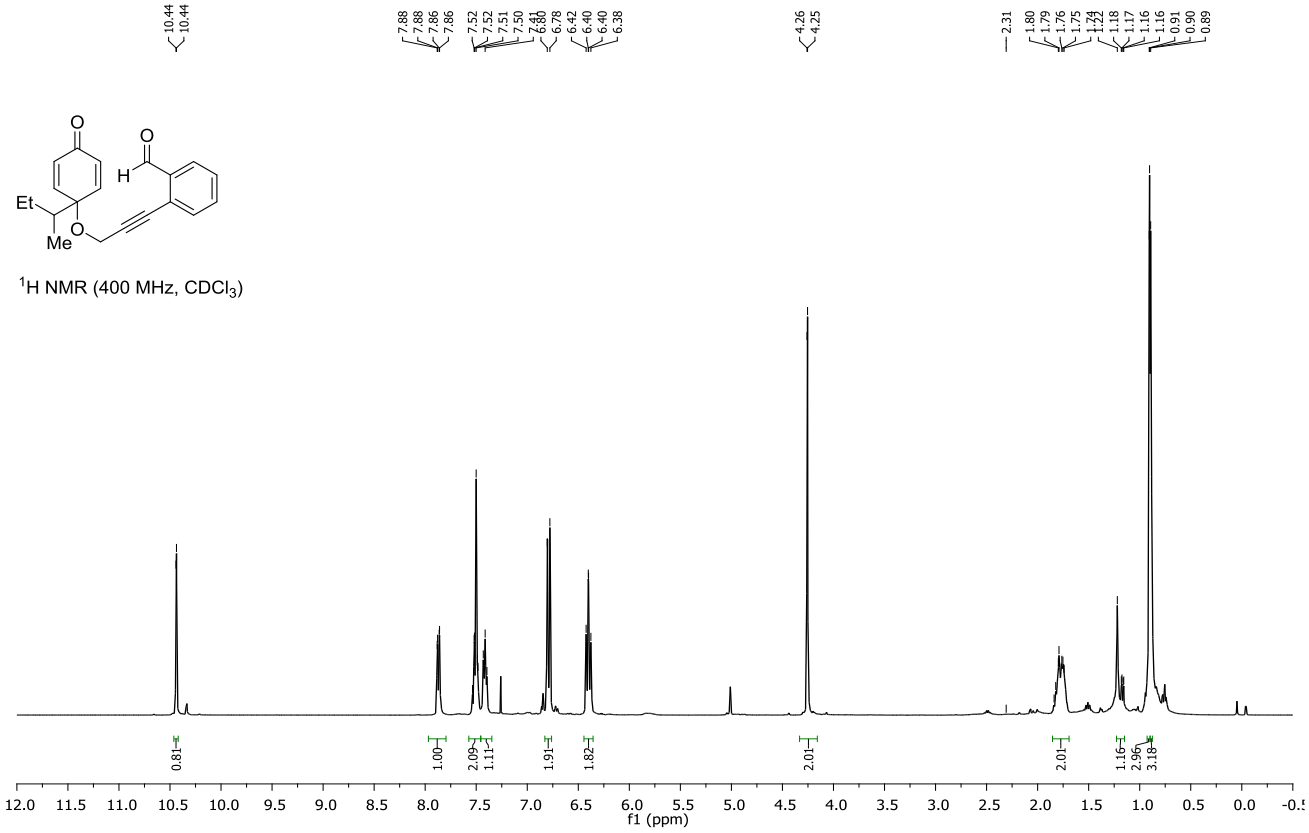
^{13}C NMR (101 MHz, $CDCl_3$)



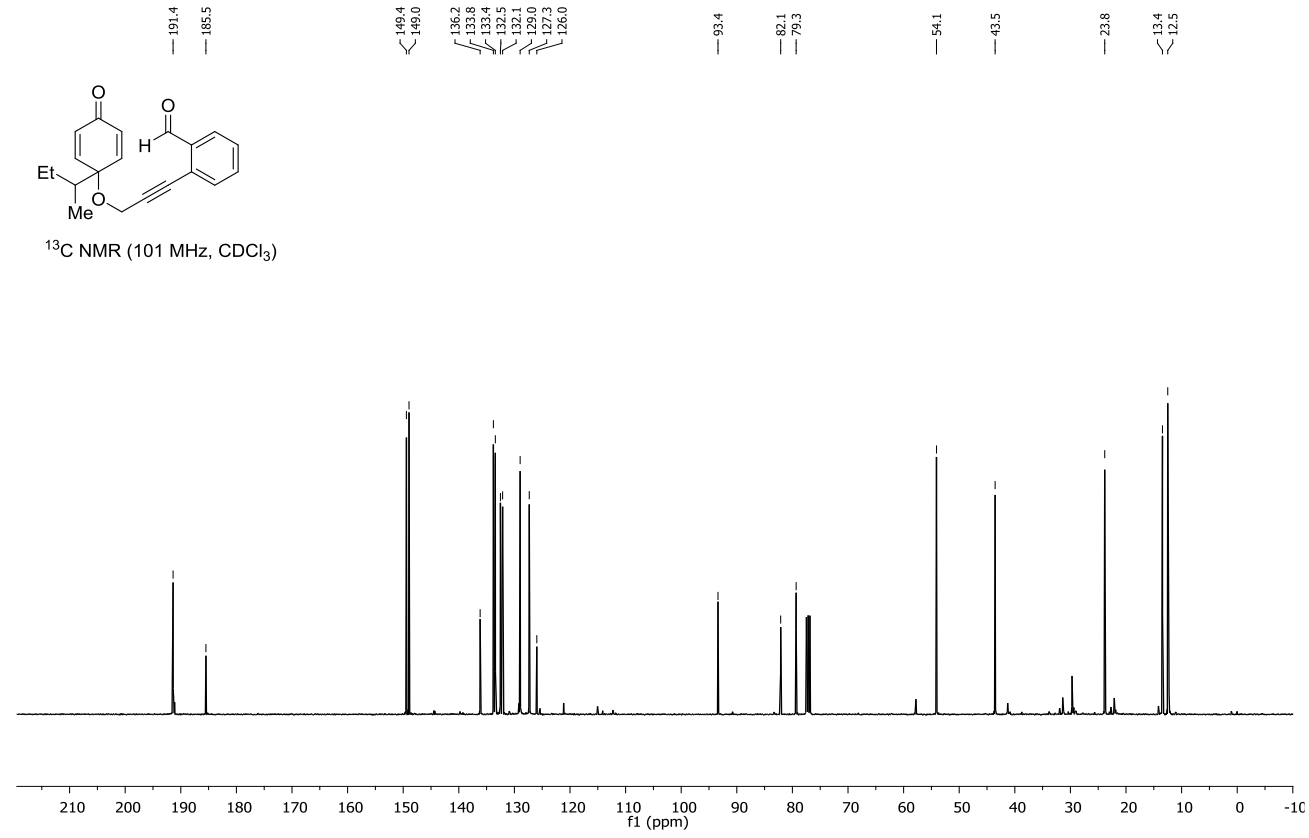
^{19}F NMR (376 MHz, $CDCl_3$)



2-(3-((1-(*sec*-Butyl)-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1u):

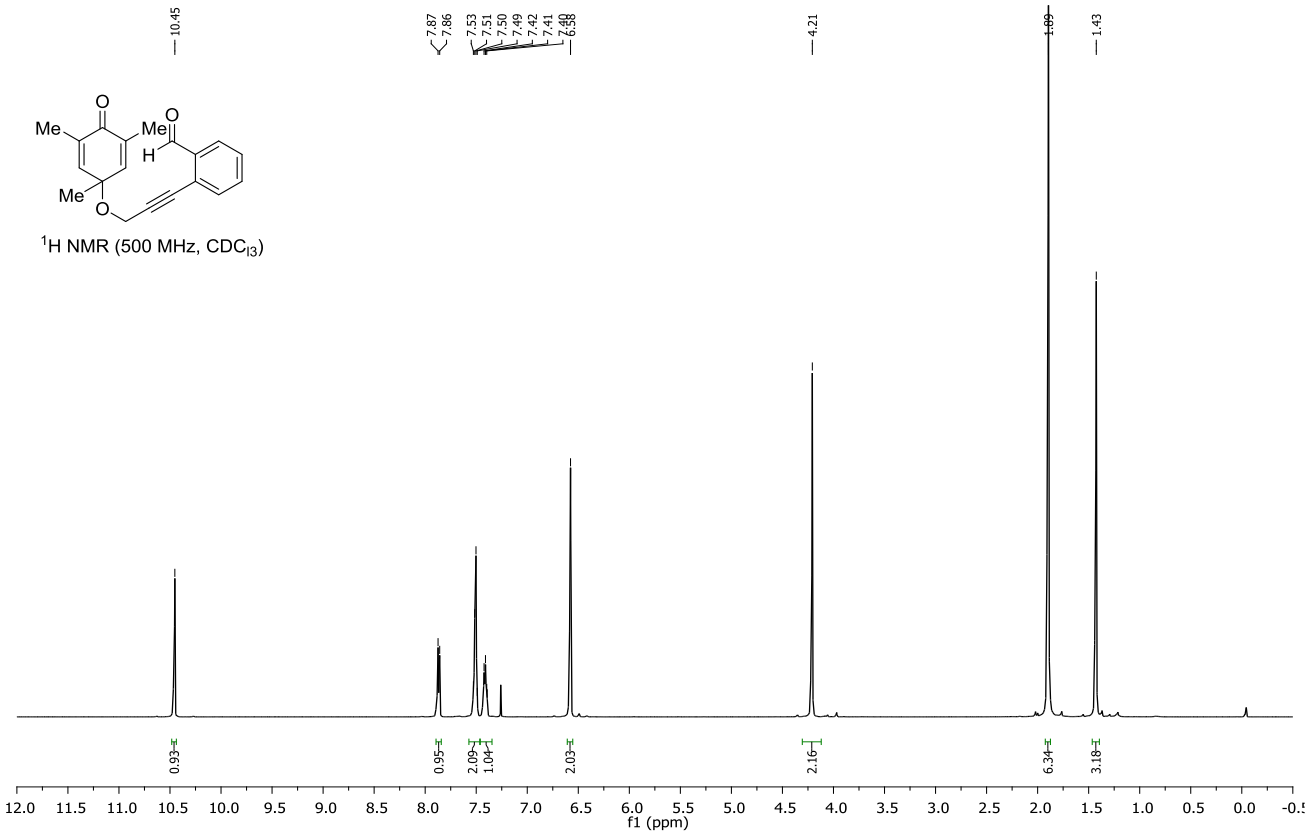


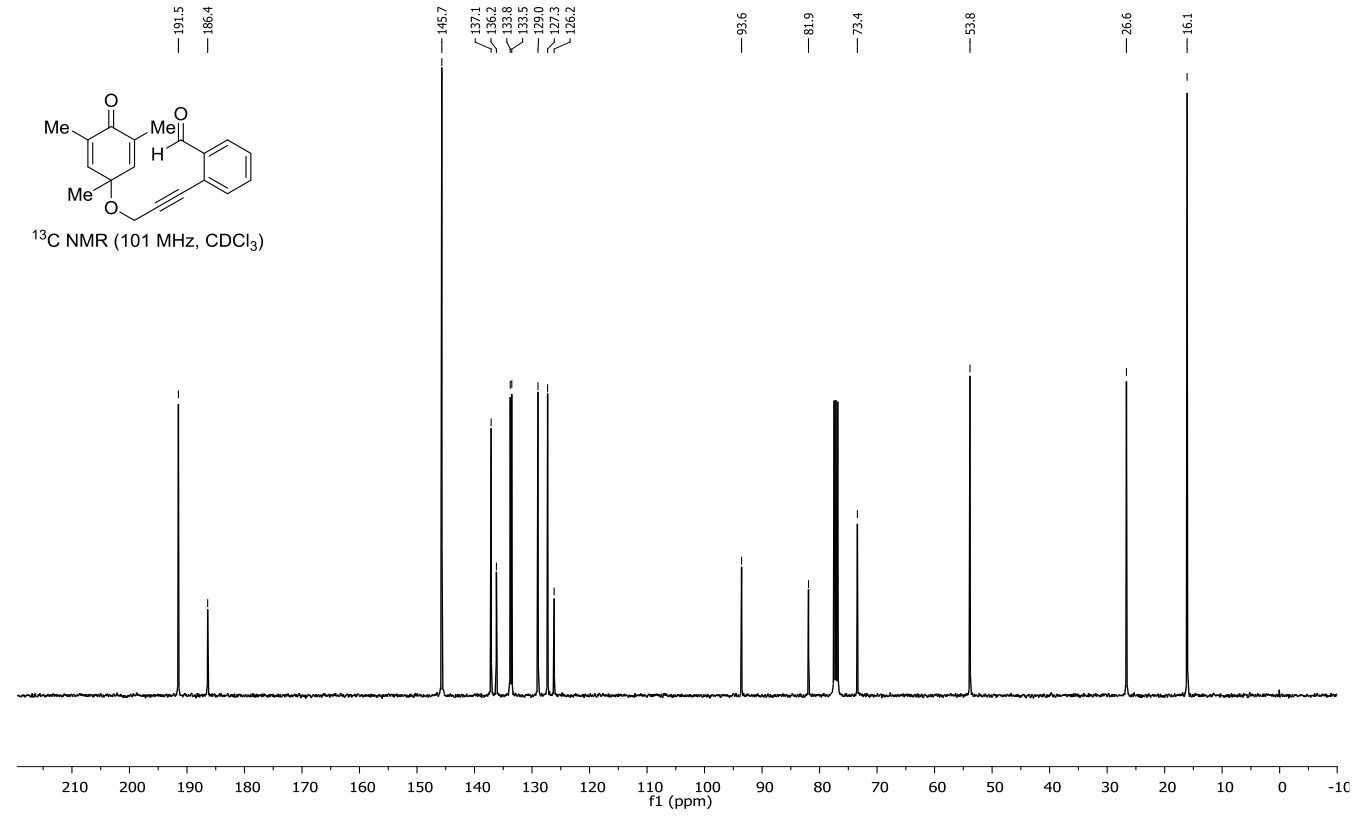
^{1}H NMR (400 MHz, $CDCl_3$)



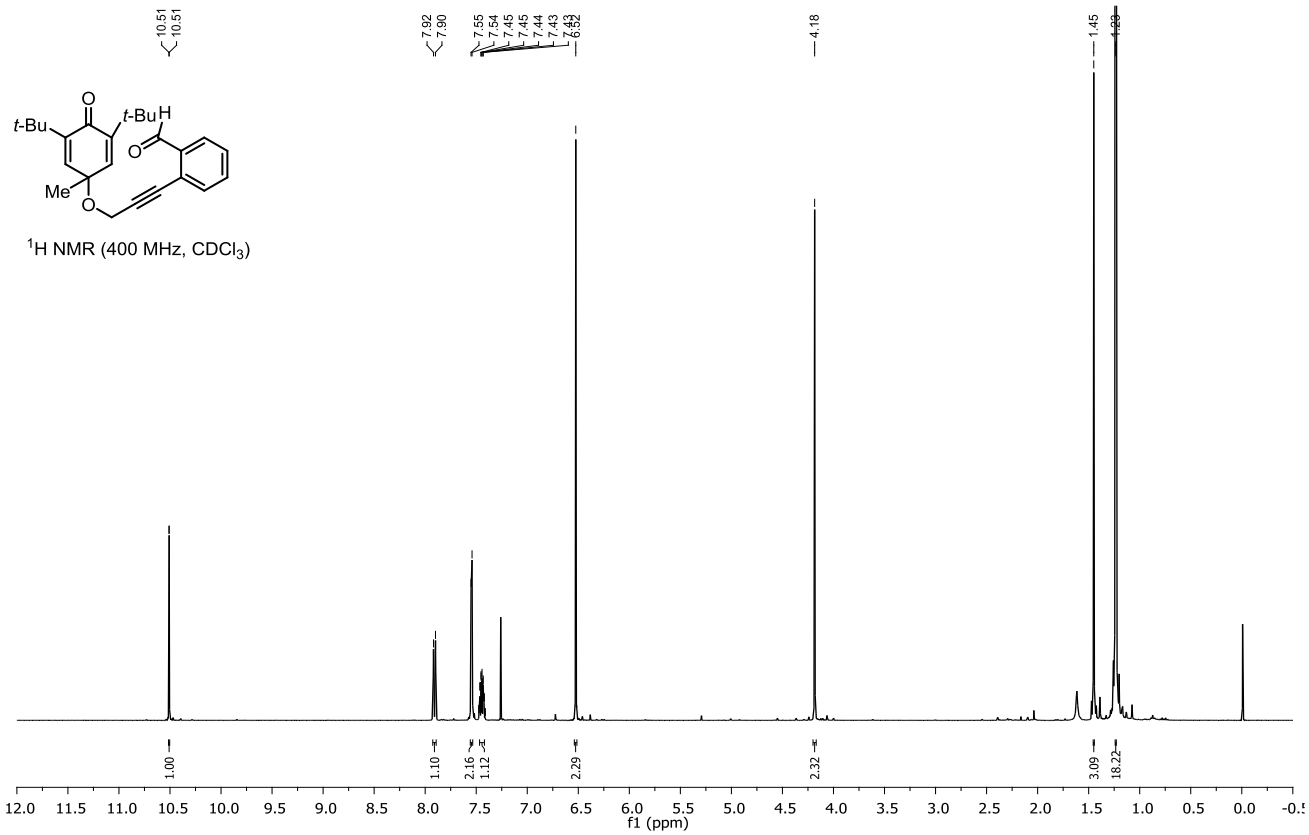
^{13}C NMR (101 MHz, $CDCl_3$)

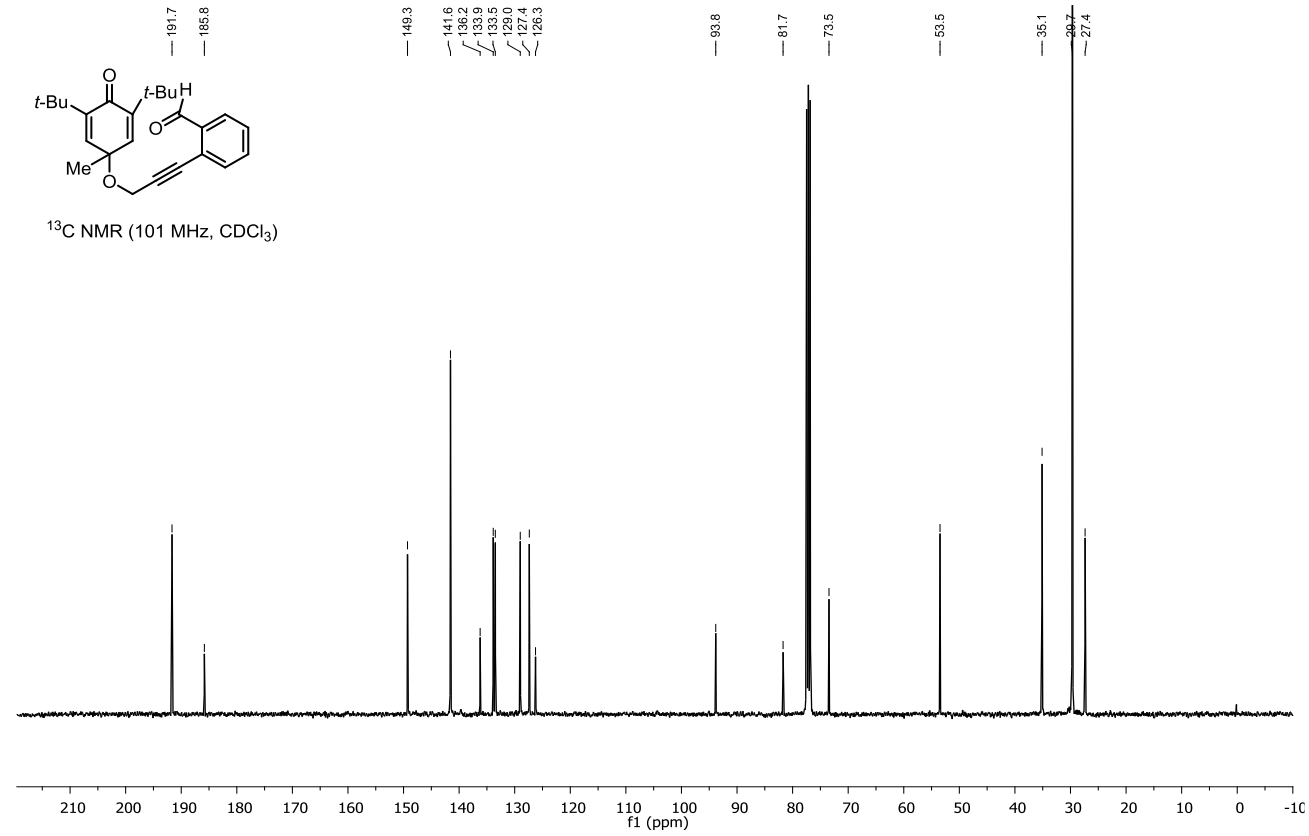
2-(3-((1,3,5-Trimethyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1v)



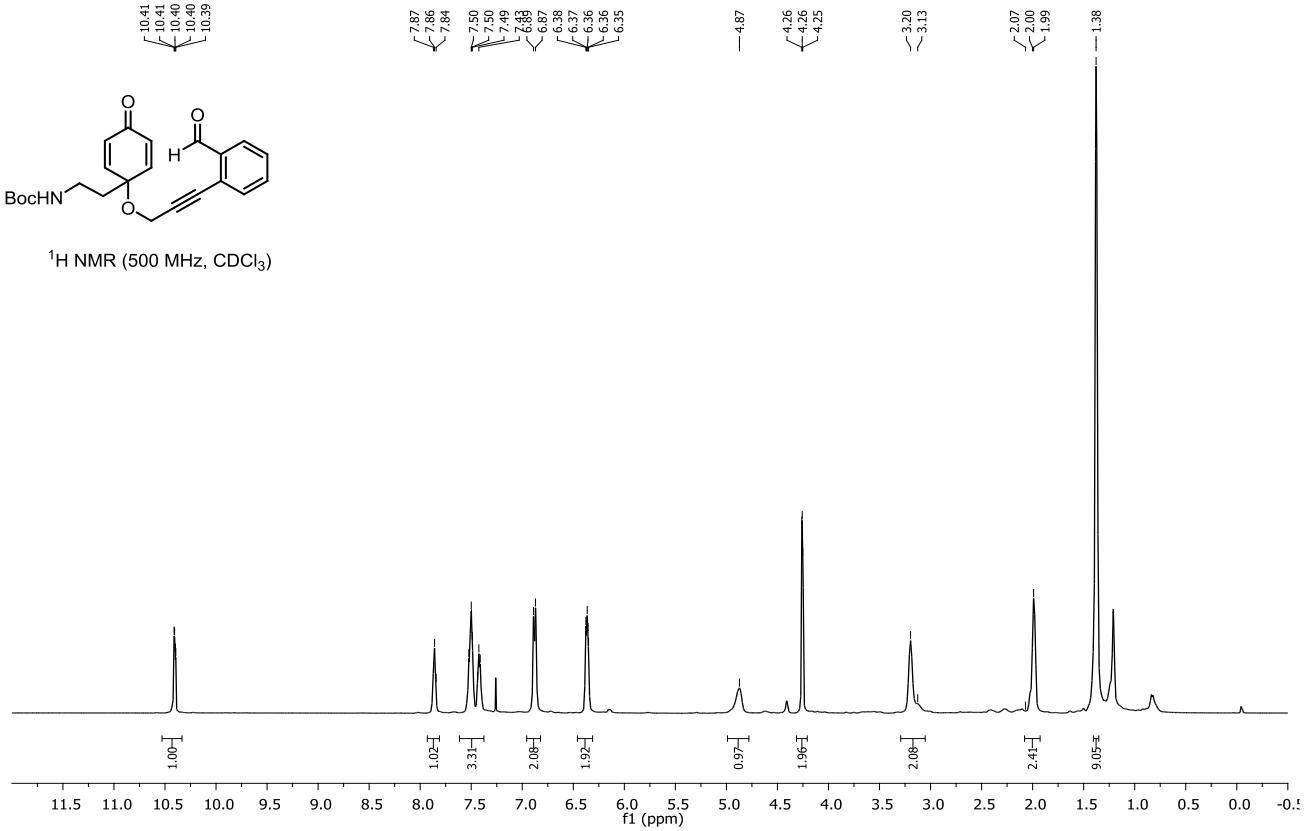


2-(3-((3,5-Di-*tert*-butyl-1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde (1w):

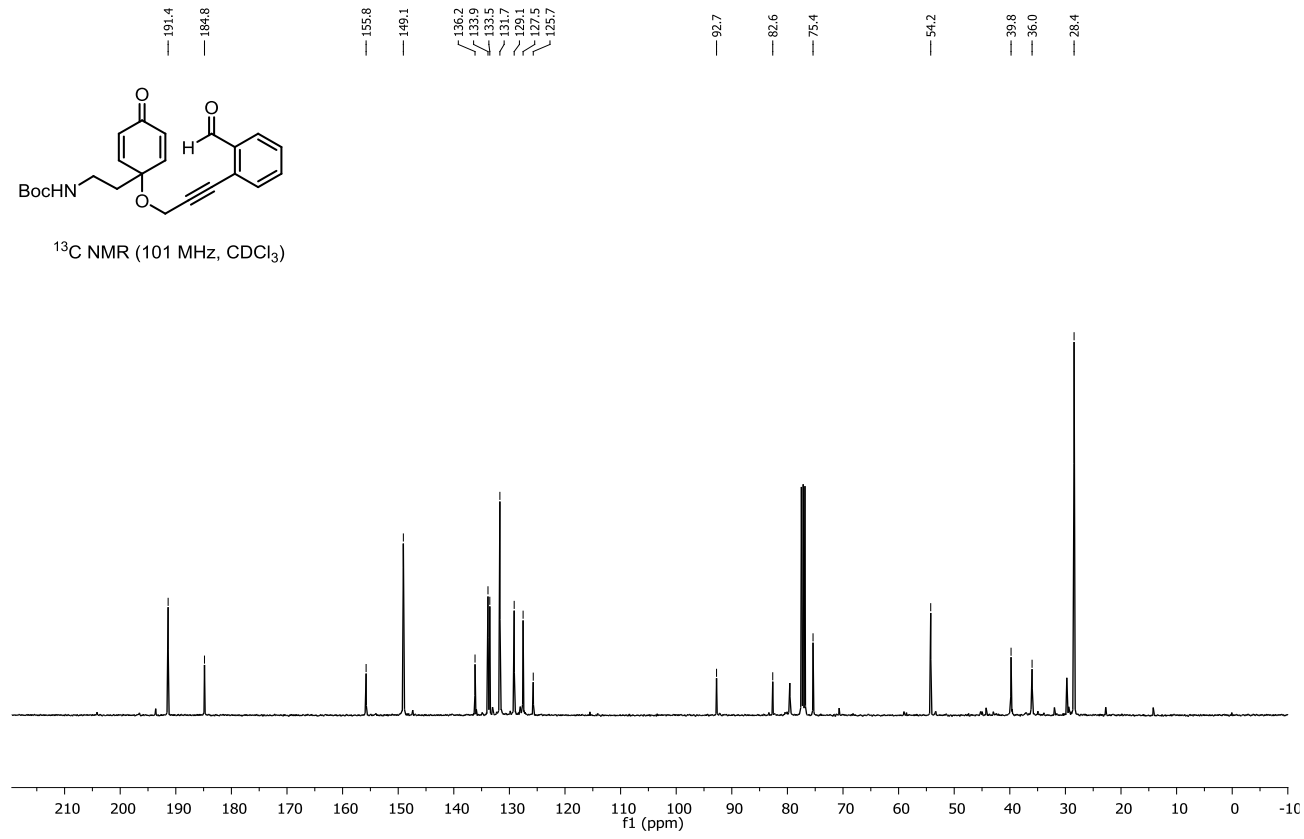




***tert*-Butyl(2-(1-((3-(2-formylphenyl)prop-2-yn-1-yl)oxy)-4-oxocyclohexa-2,5-dien-1-yl)ethyl)carbamate (1x):**

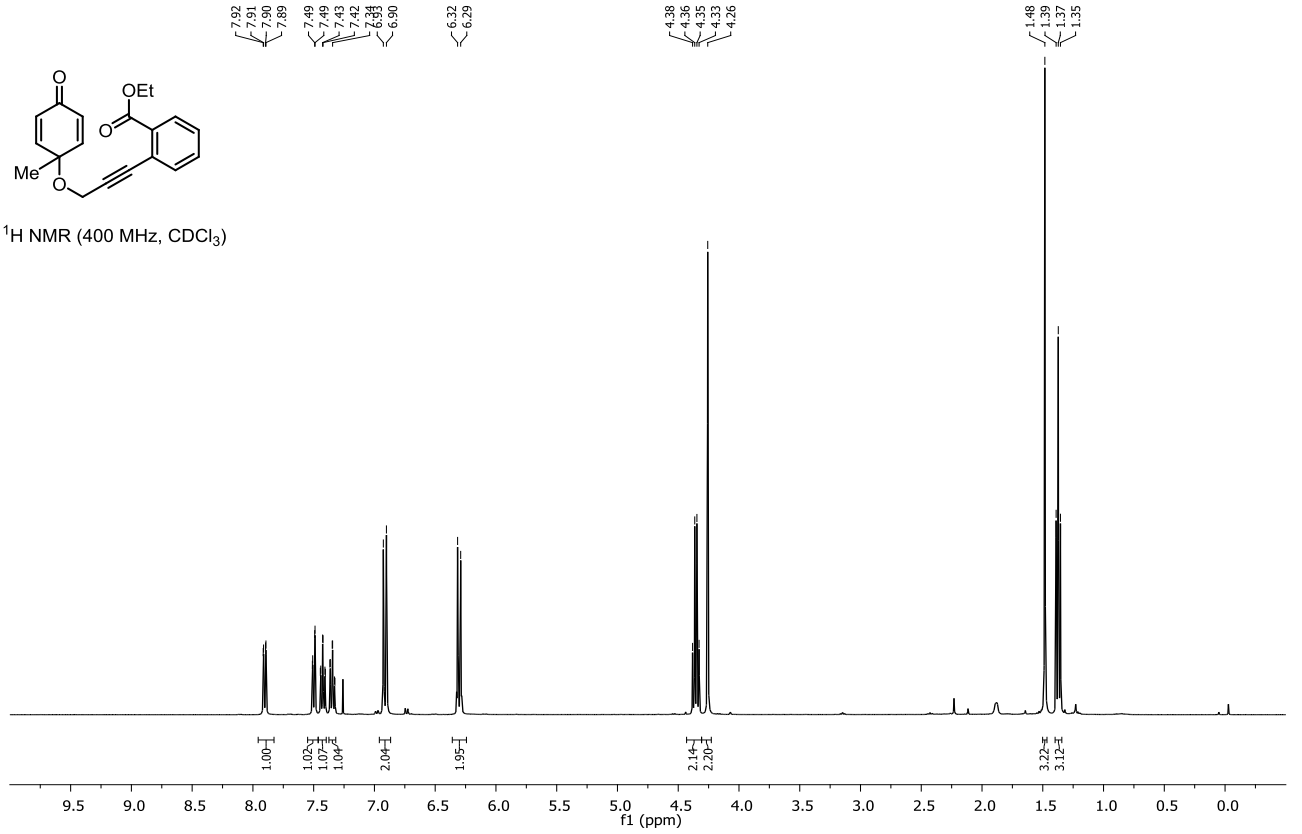


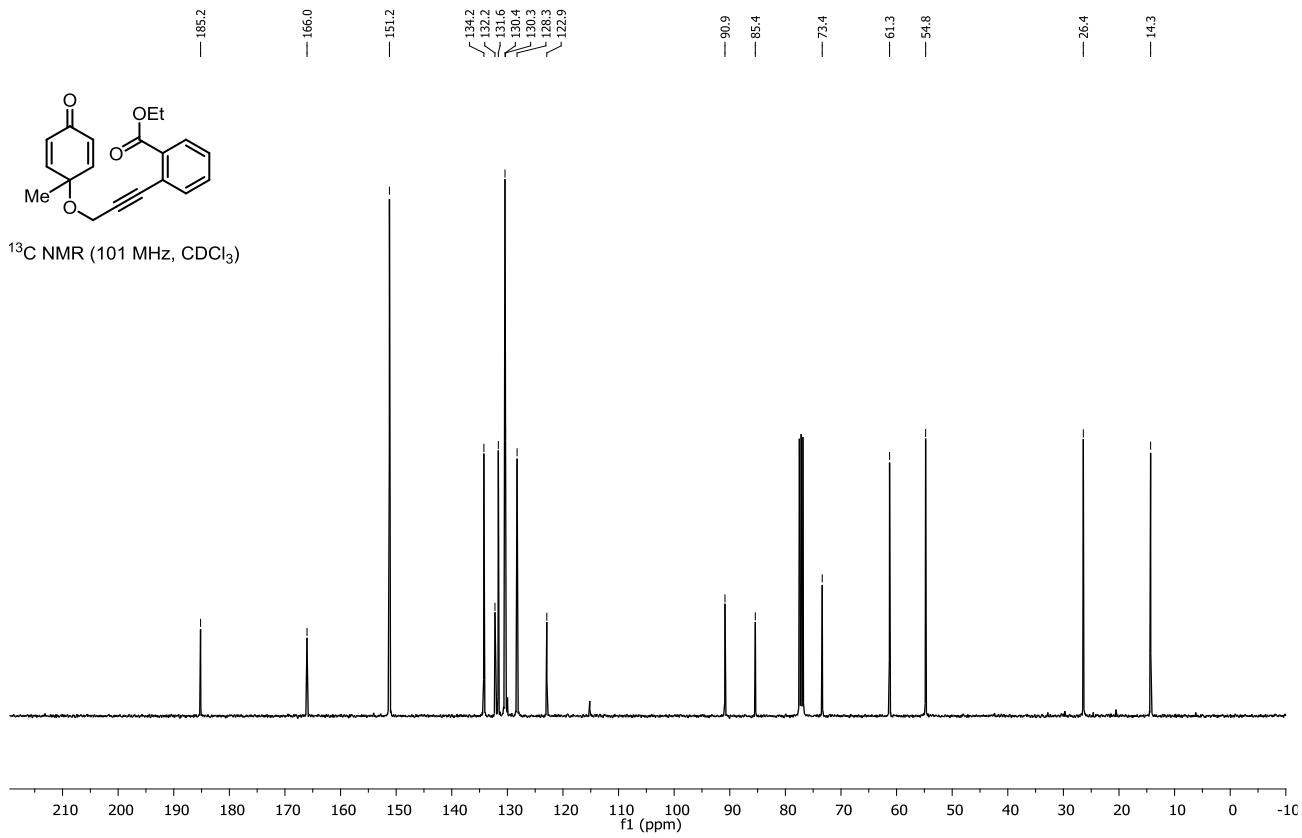
^{1}H NMR (500 MHz, $CDCl_3$)



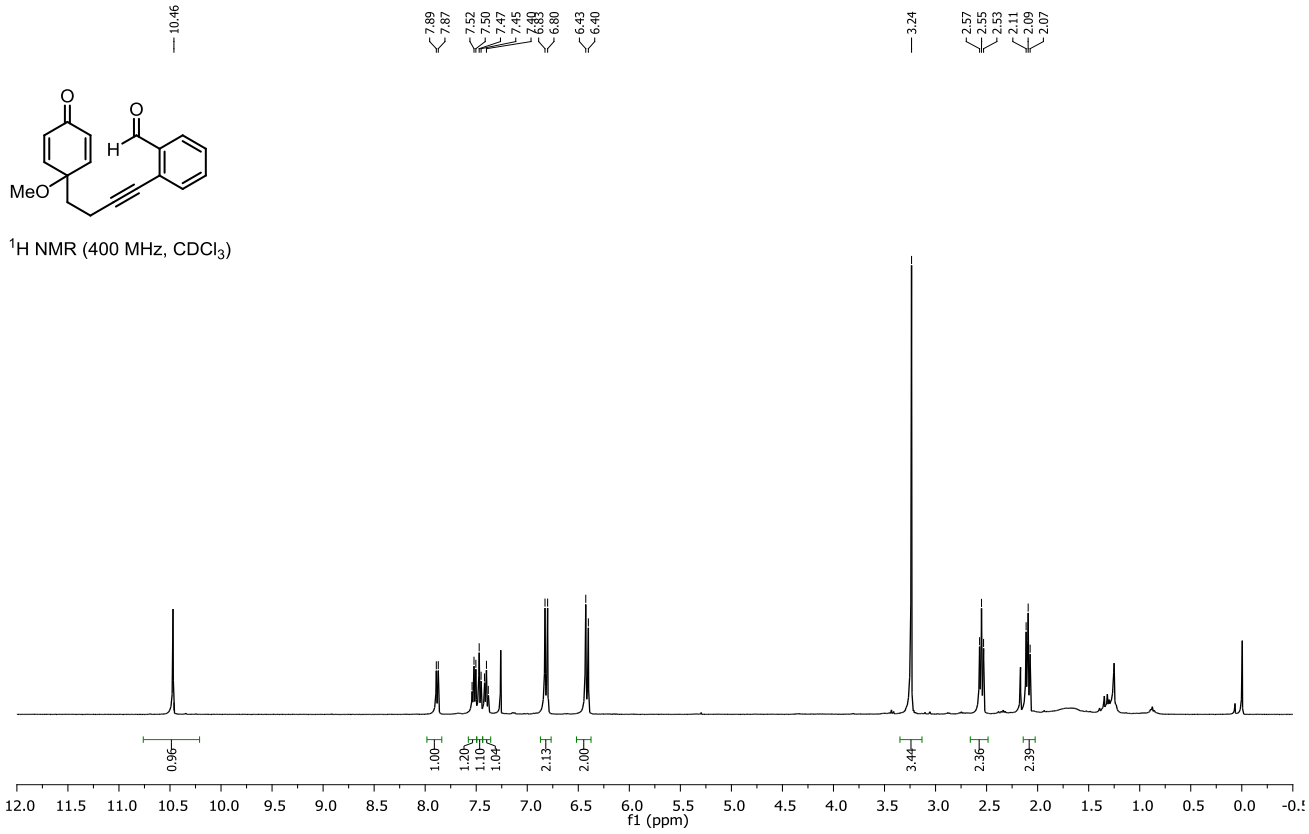
^{13}C NMR (101 MHz, $CDCl_3$)

Ethyl 2-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzoate (1y):

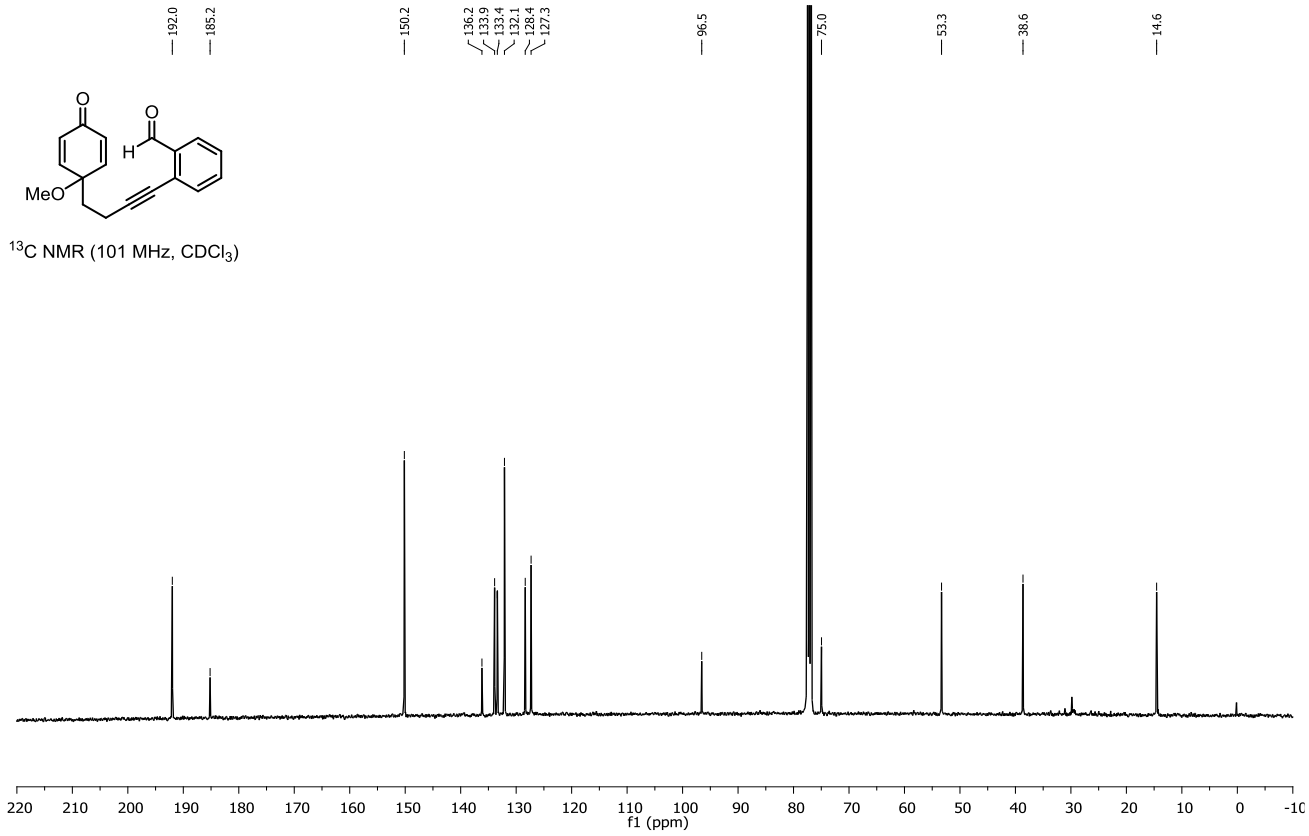




2-(4-(1-Methyl-4-oxocyclohexa-2,5-dien-1-yl)but-1-yn-1-yl)benzaldehyde (1z):

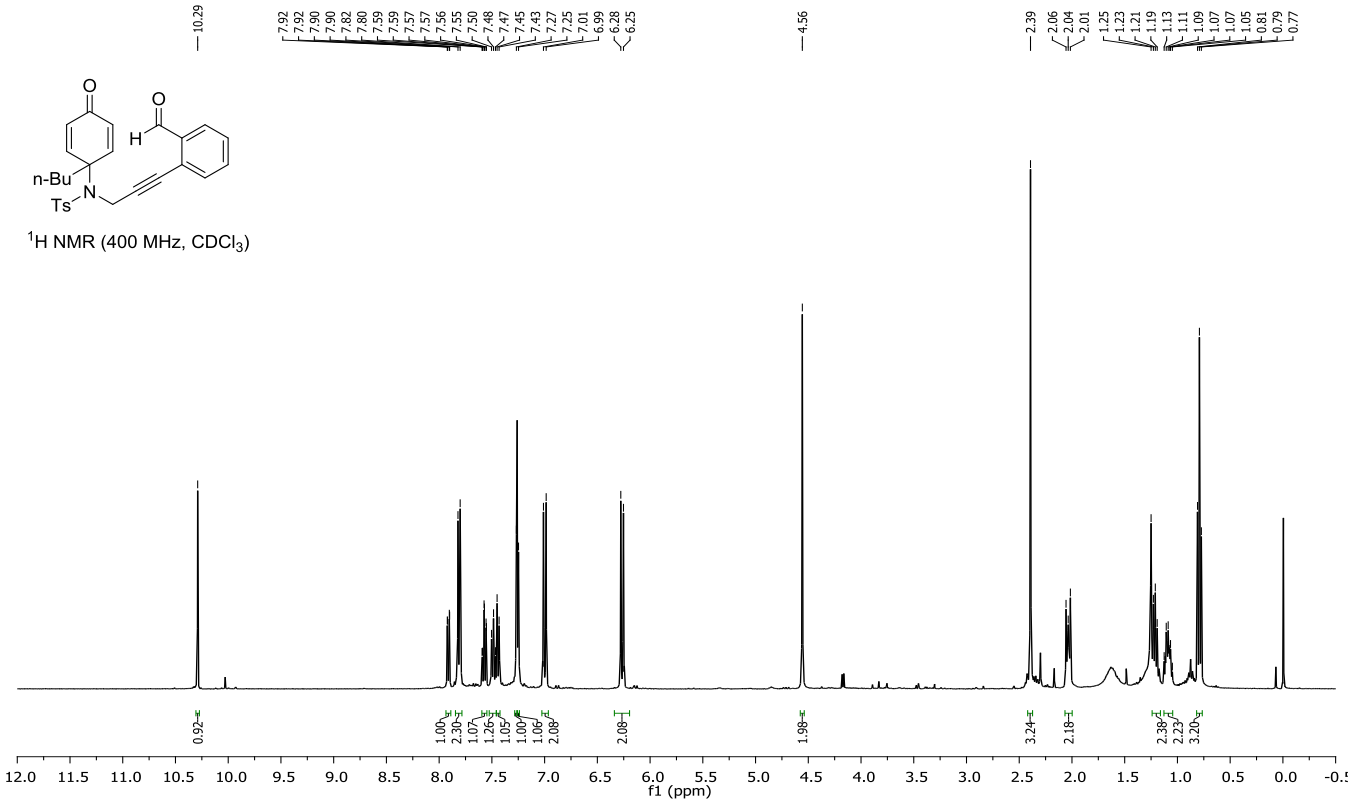


^{1}H NMR (400 MHz, $CDCl_3$)

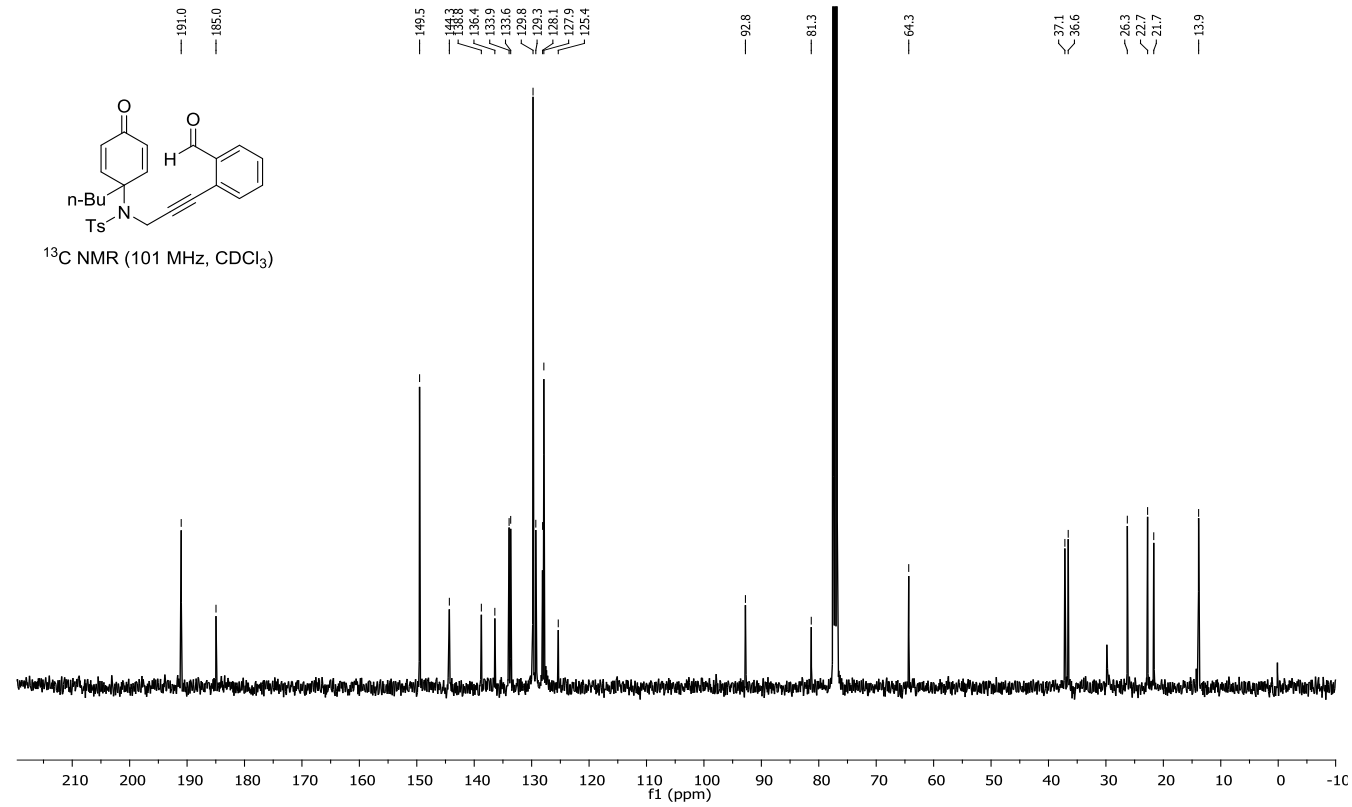


^{13}C NMR (101 MHz, $CDCl_3$)

_N_-(1-Butyl-4-oxocyclohexa-2,5-dien-1-yl)-N-(3-(2-formylphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (3a):

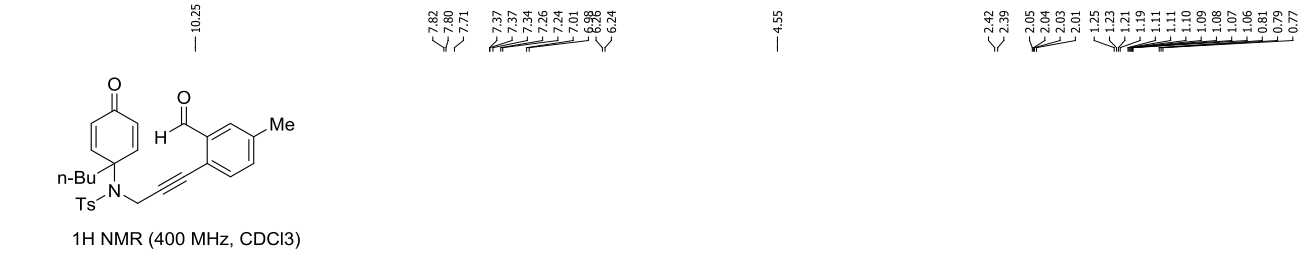


^{1}H NMR (400 MHz, $CDCl_3$)

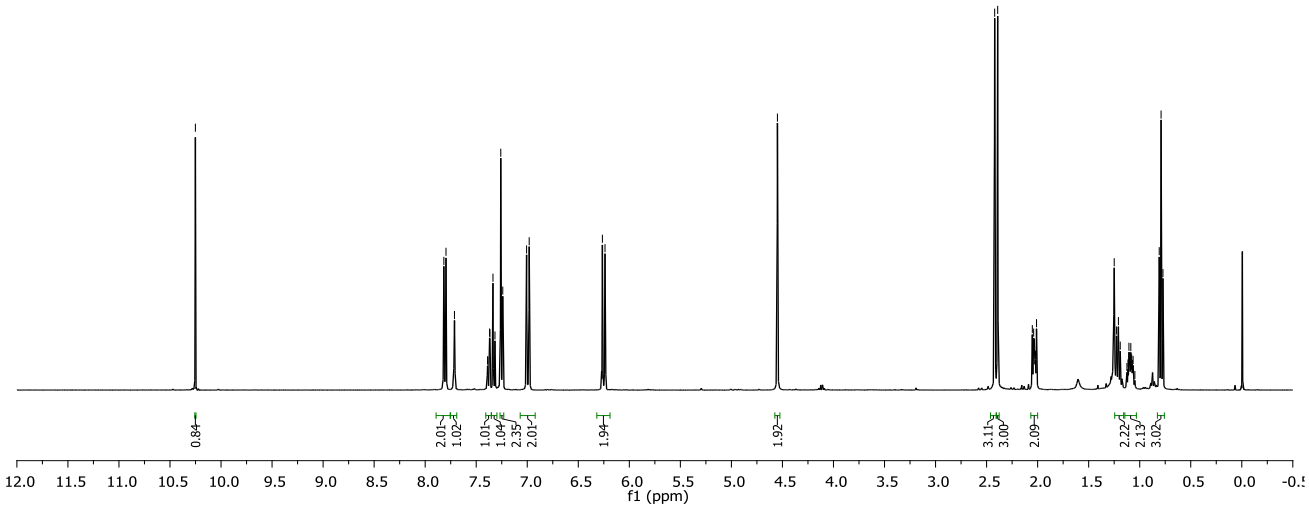


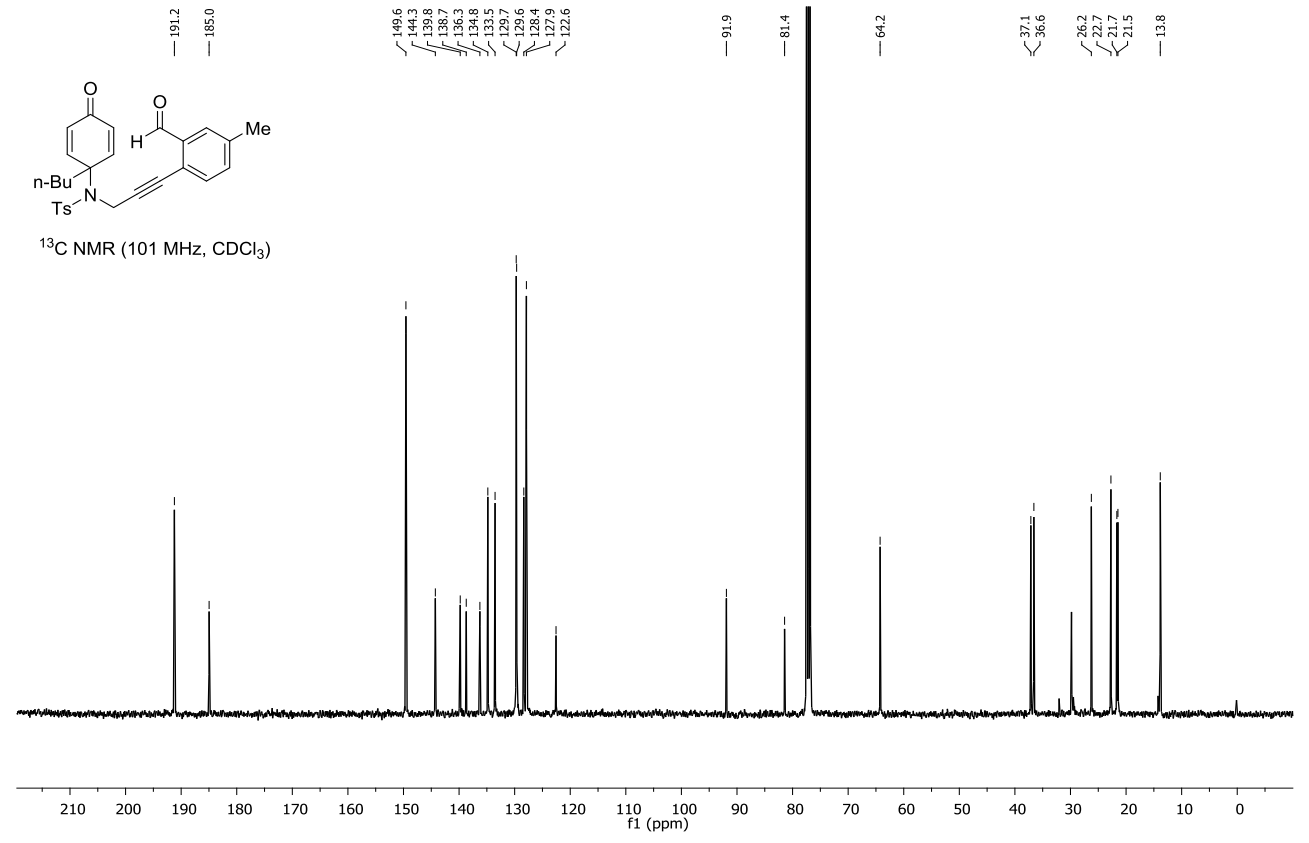
^{13}C NMR (101 MHz, $CDCl_3$)

_N_-(1-Butyl-4-oxocyclohexa-2,5-dien-1-yl)-N-(3-(2-formyl-4-methylphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (3b):



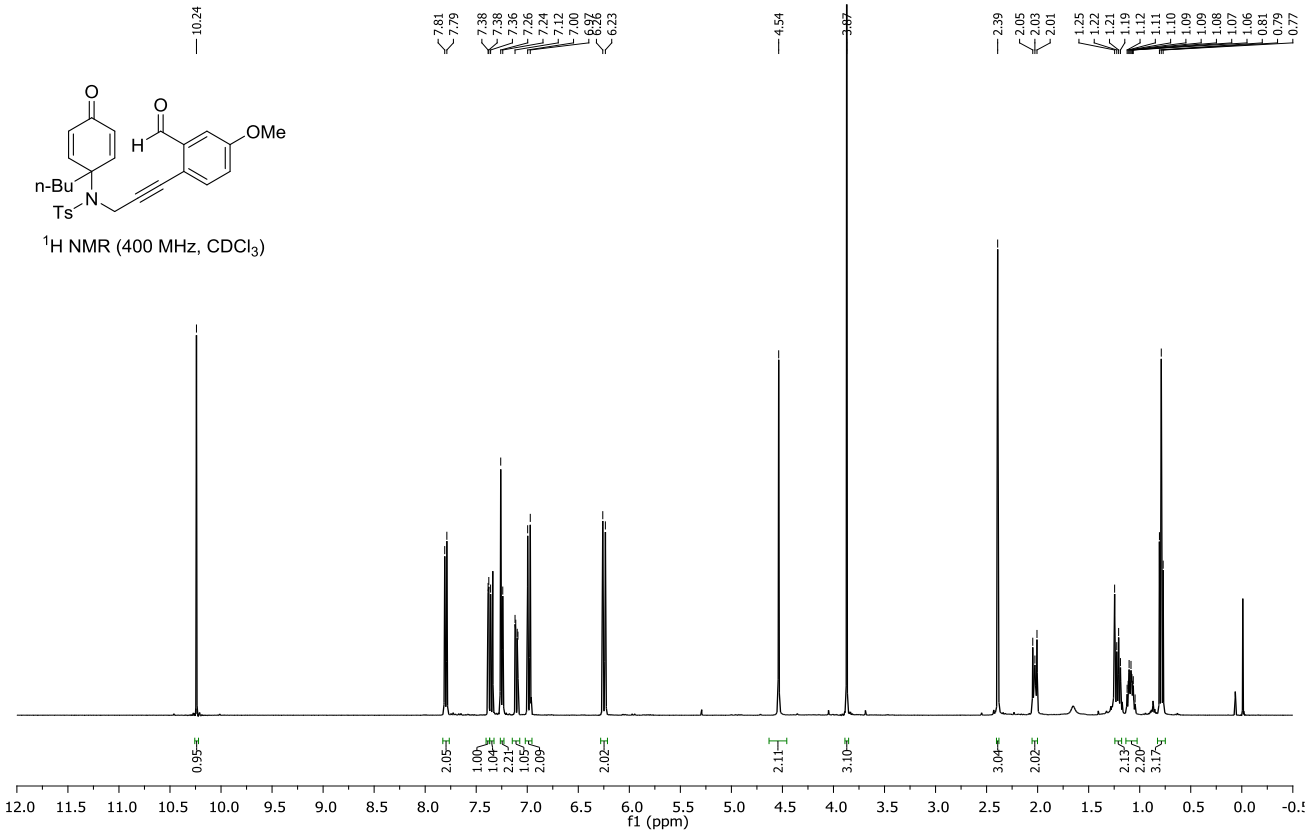
1H NMR (400 MHz, CDCl3)

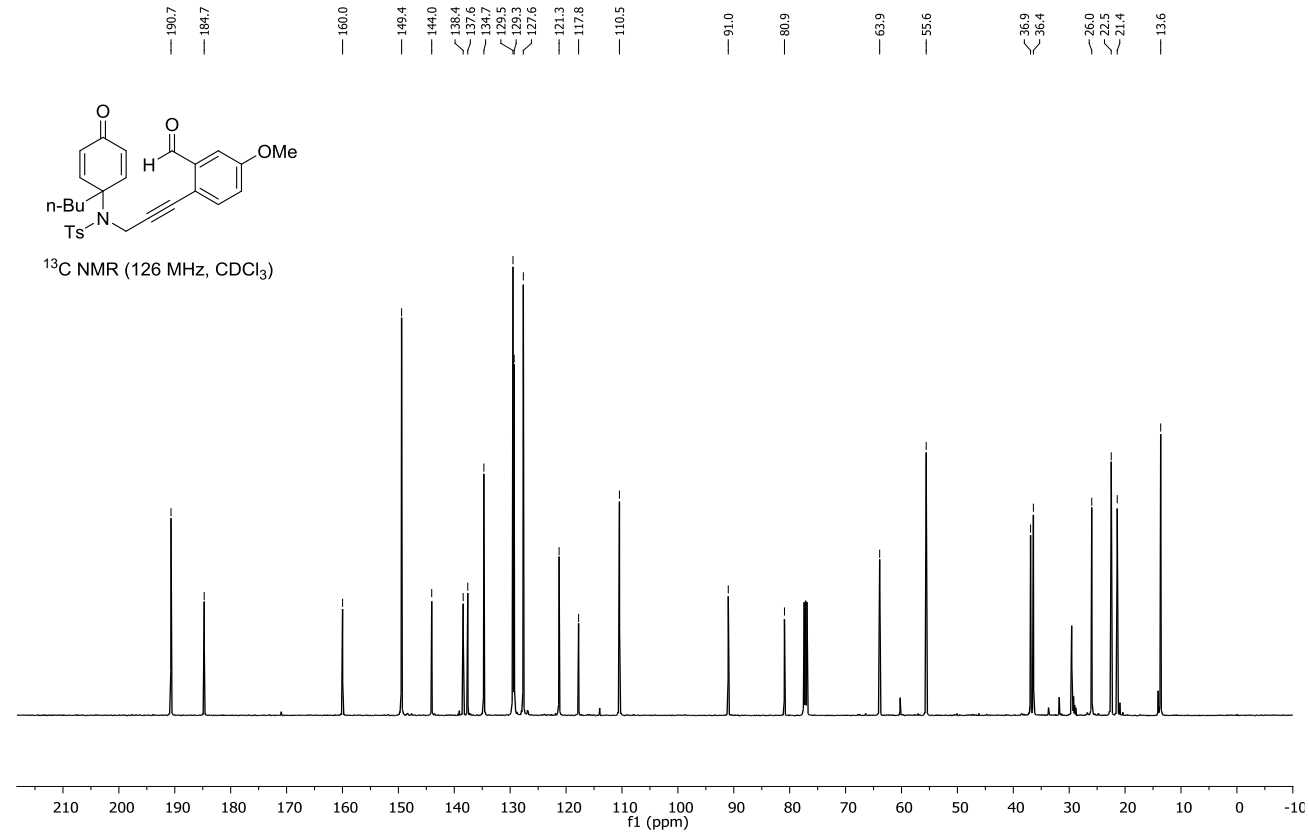




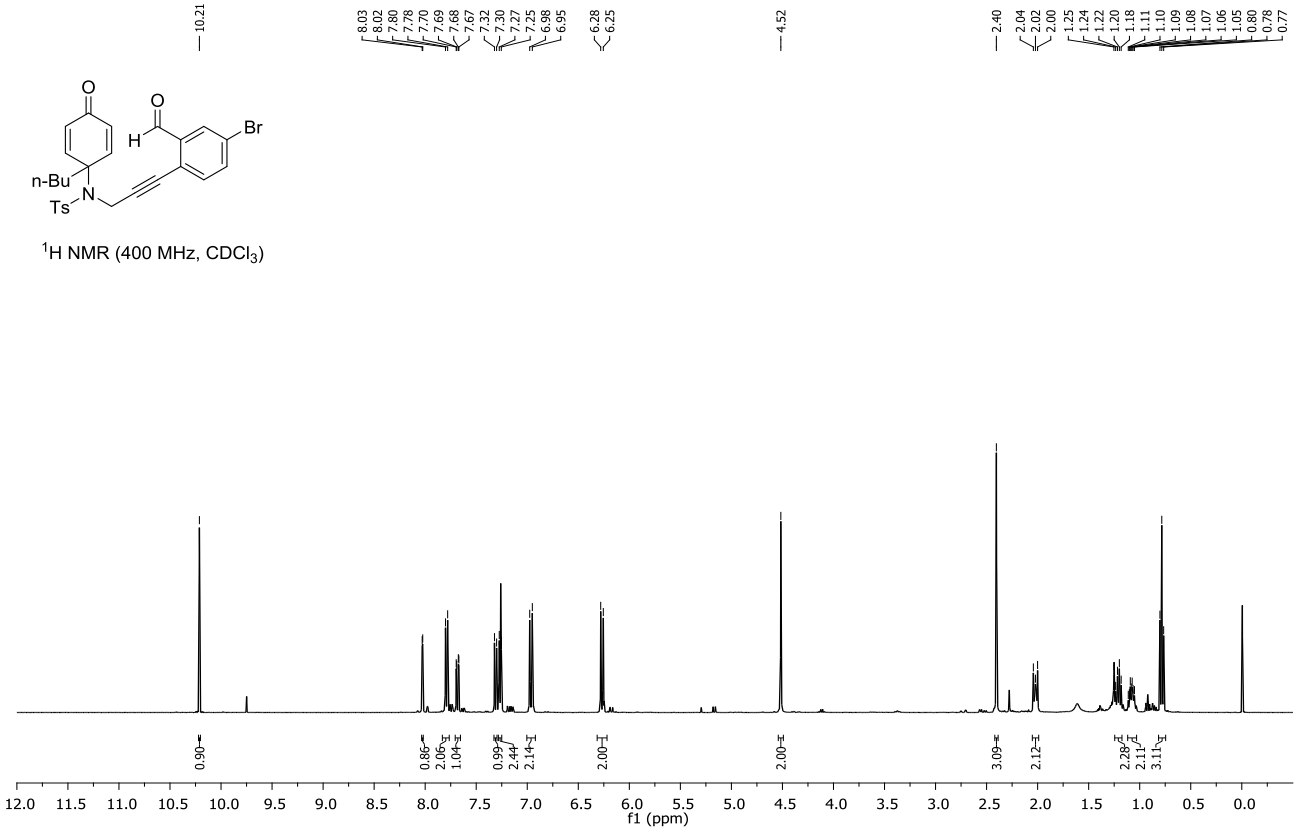
^{13}C NMR (101 MHz, $CDCl_3$)

***N*-(1-Butyl-4-oxocyclohexa-2,5-dien-1-yl)-N-(3-(2-formyl-4-methoxyphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (3c):**

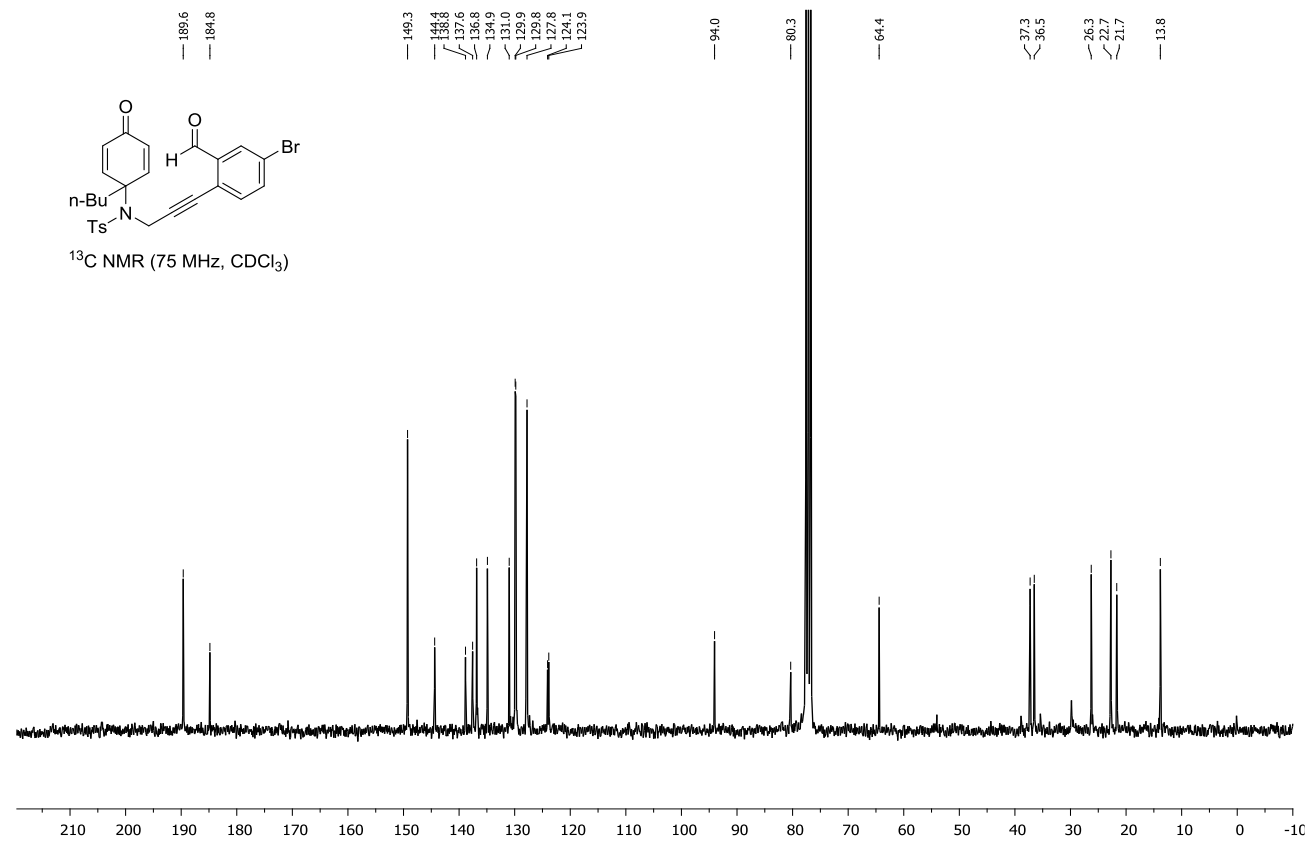




_N_-(3-(4-Bromo-2-formylphenyl)prop-2-yn-1-yl)-N-(1-butyl-4-oxocyclohexa-2,5-dien-1-yl)-4-methylbenzenesulfonamide (3d):

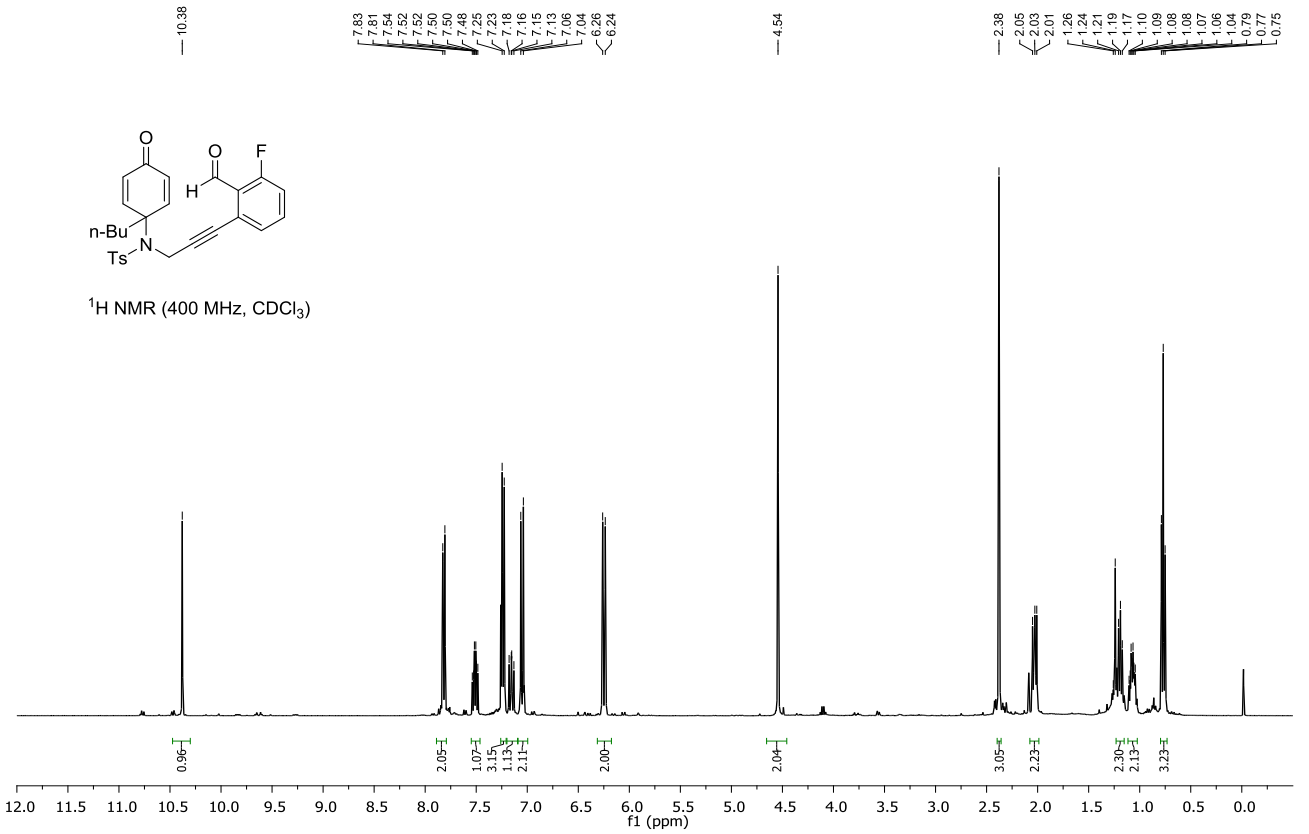


^{1}H NMR (400 MHz, $CDCl_3$)

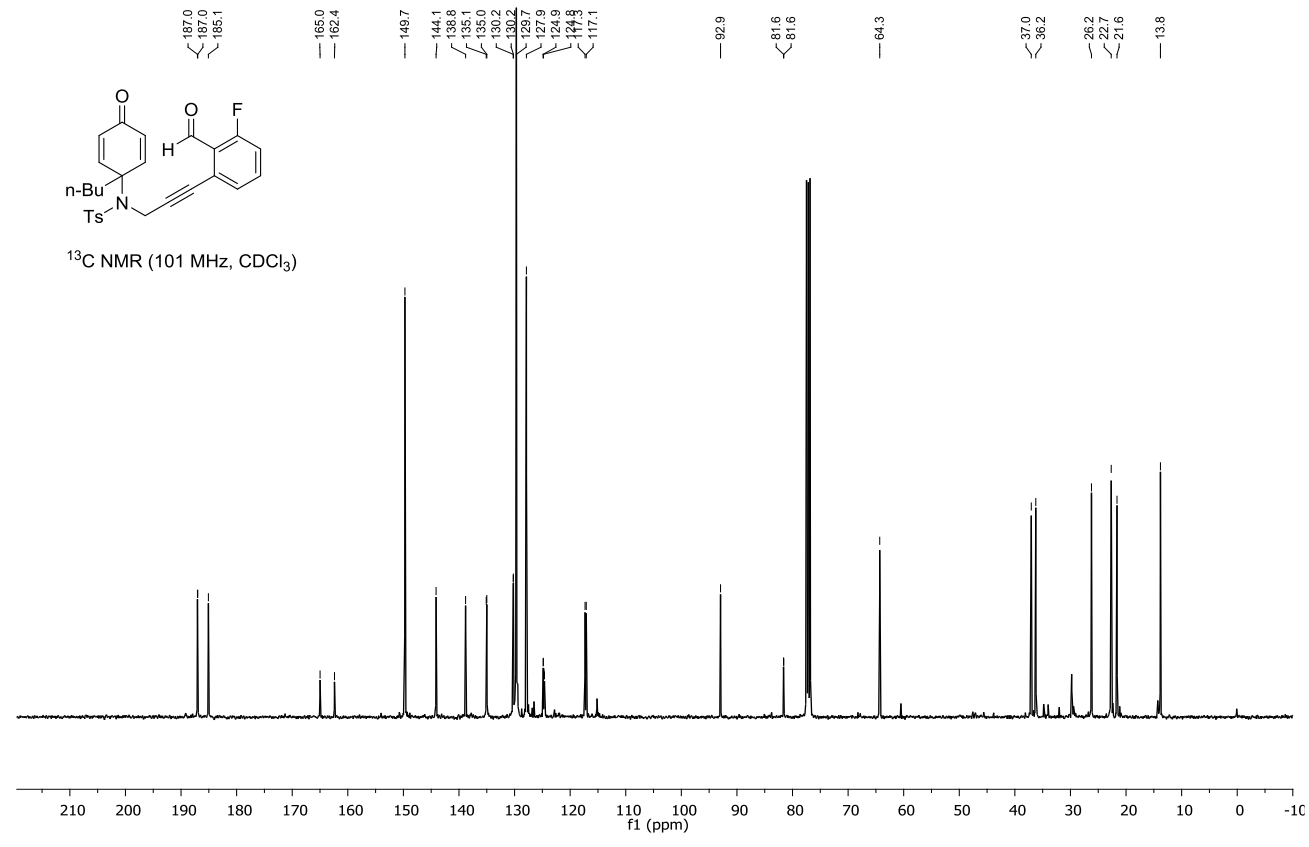


^{13}C NMR (75 MHz, $CDCl_3$)

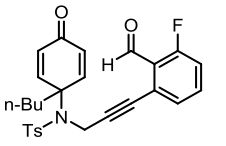
***N*-(1-Butyl-4-oxocyclohexa-2,5-dien-1-yl)-N-(3-(3-fluoro-2-formylphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (3e):**



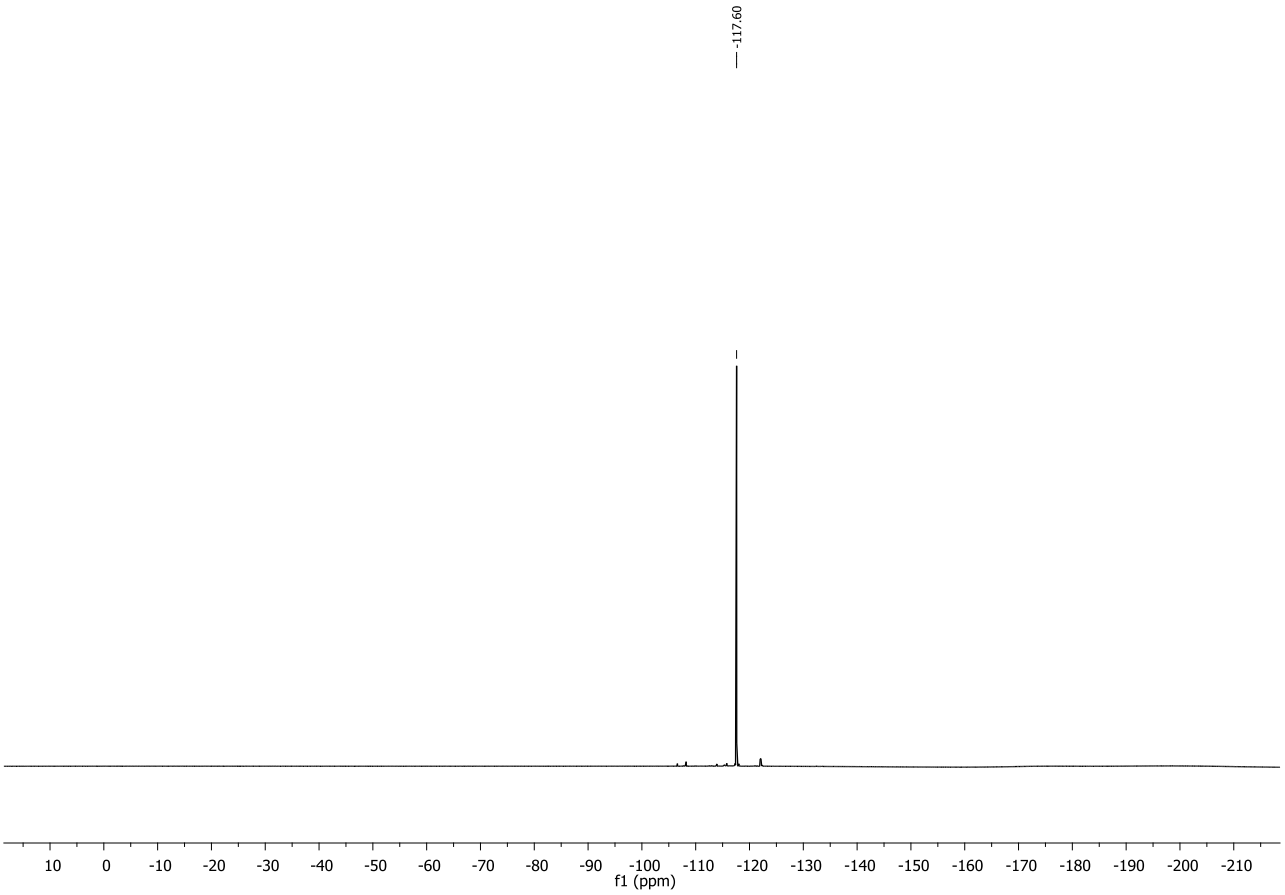
^{1}H NMR (400 MHz, $CDCl_3$)



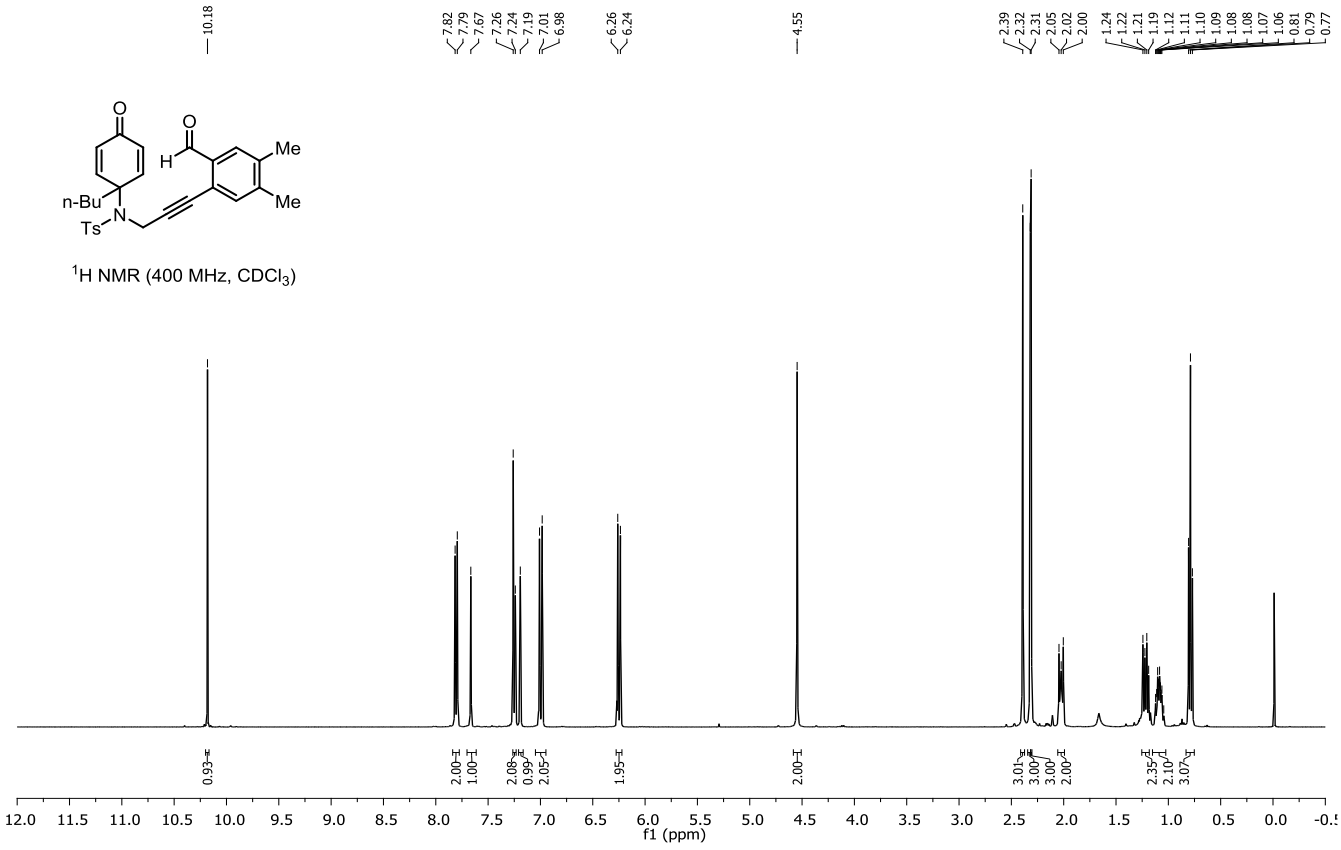
^{13}C NMR (101 MHz, $CDCl_3$)

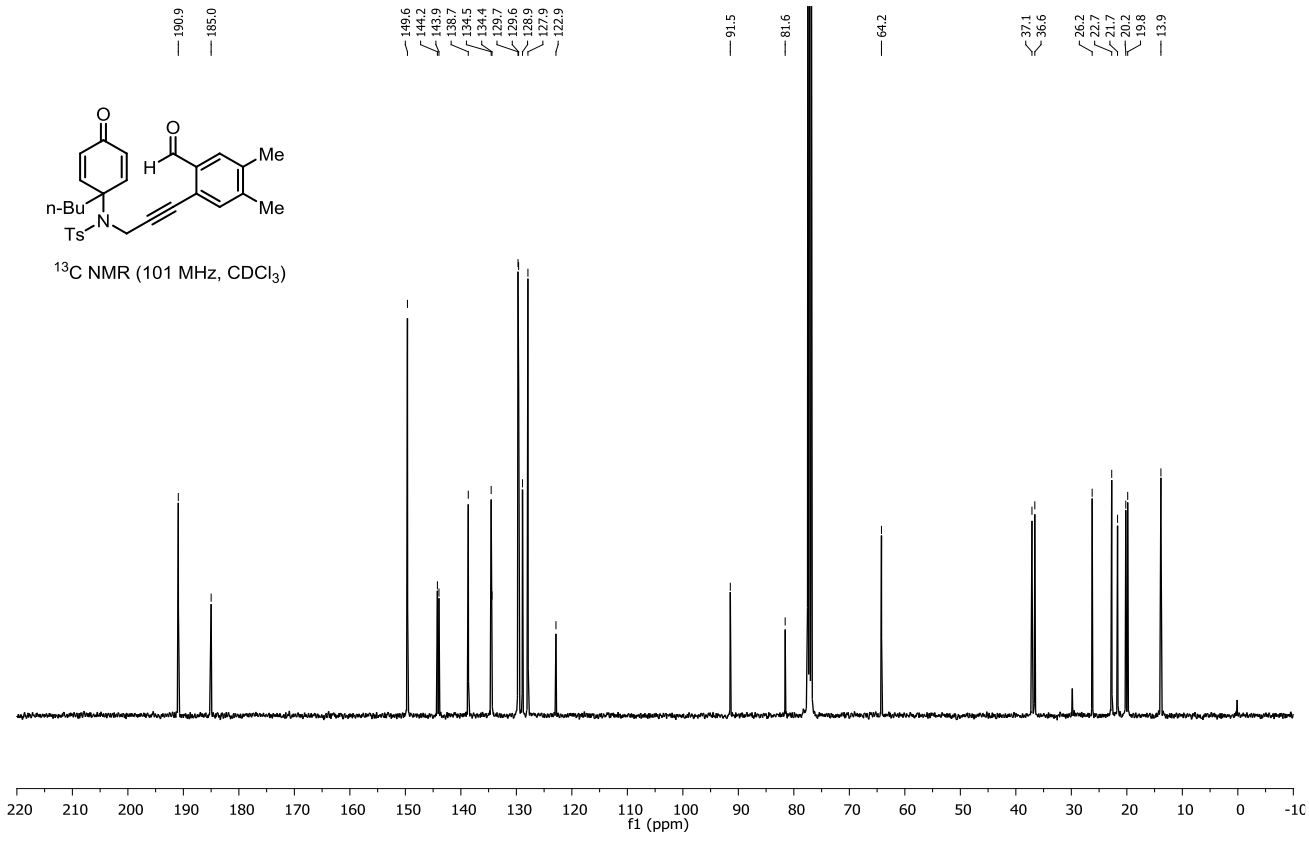


^{19}F NMR (376 MHz, $CDCl_3$)

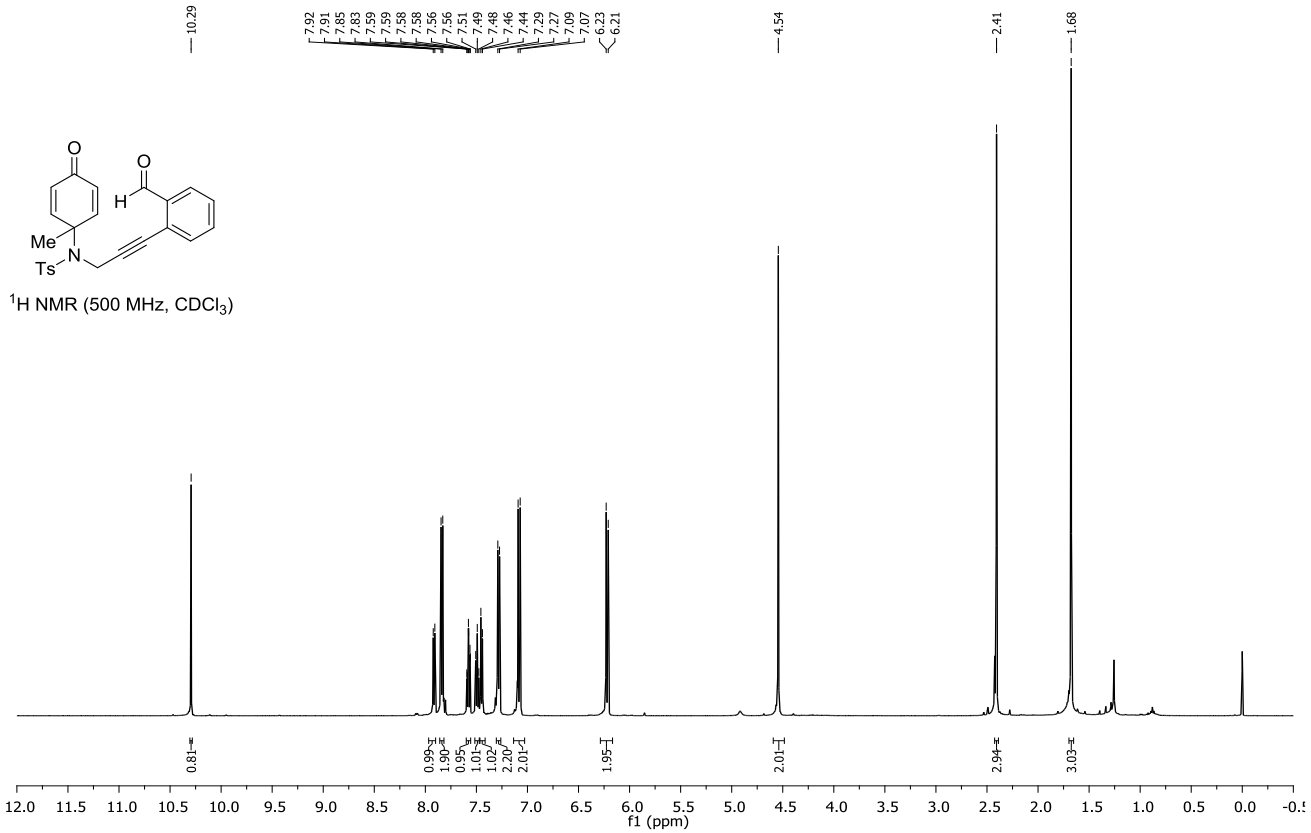


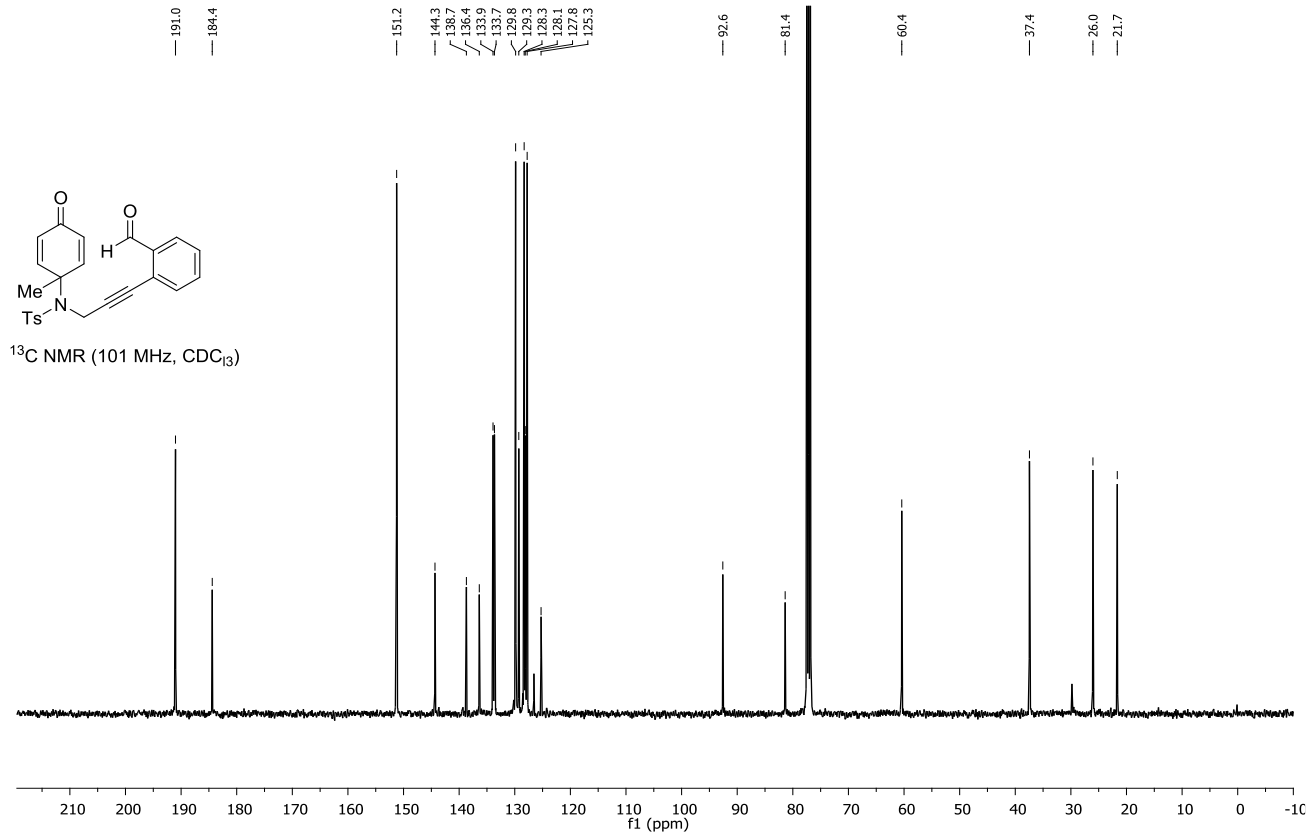
_N_-(1-Butyl-4-oxocyclohexa-2,5-dien-1-yl)-N-(3-(2-formyl-4,5-dimethylphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (3f):



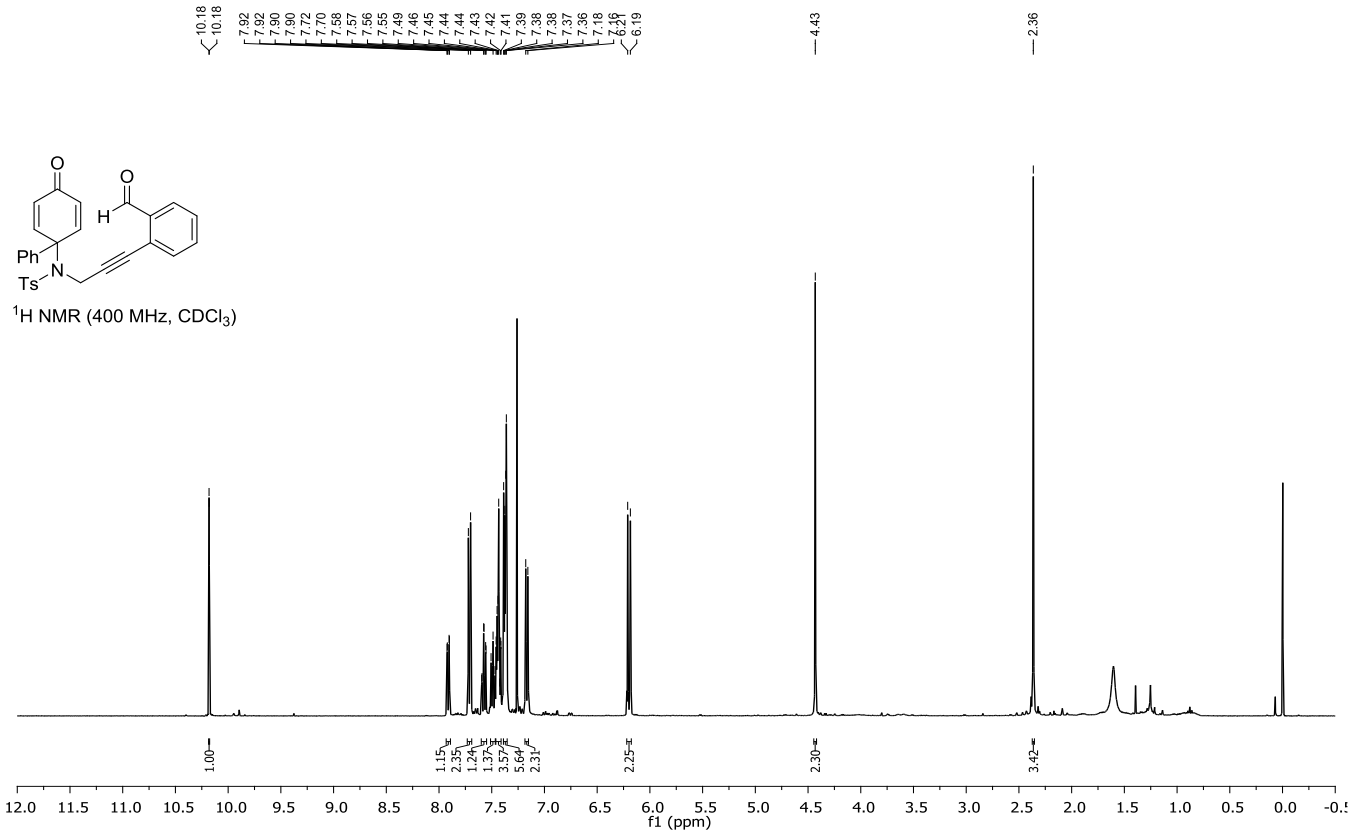


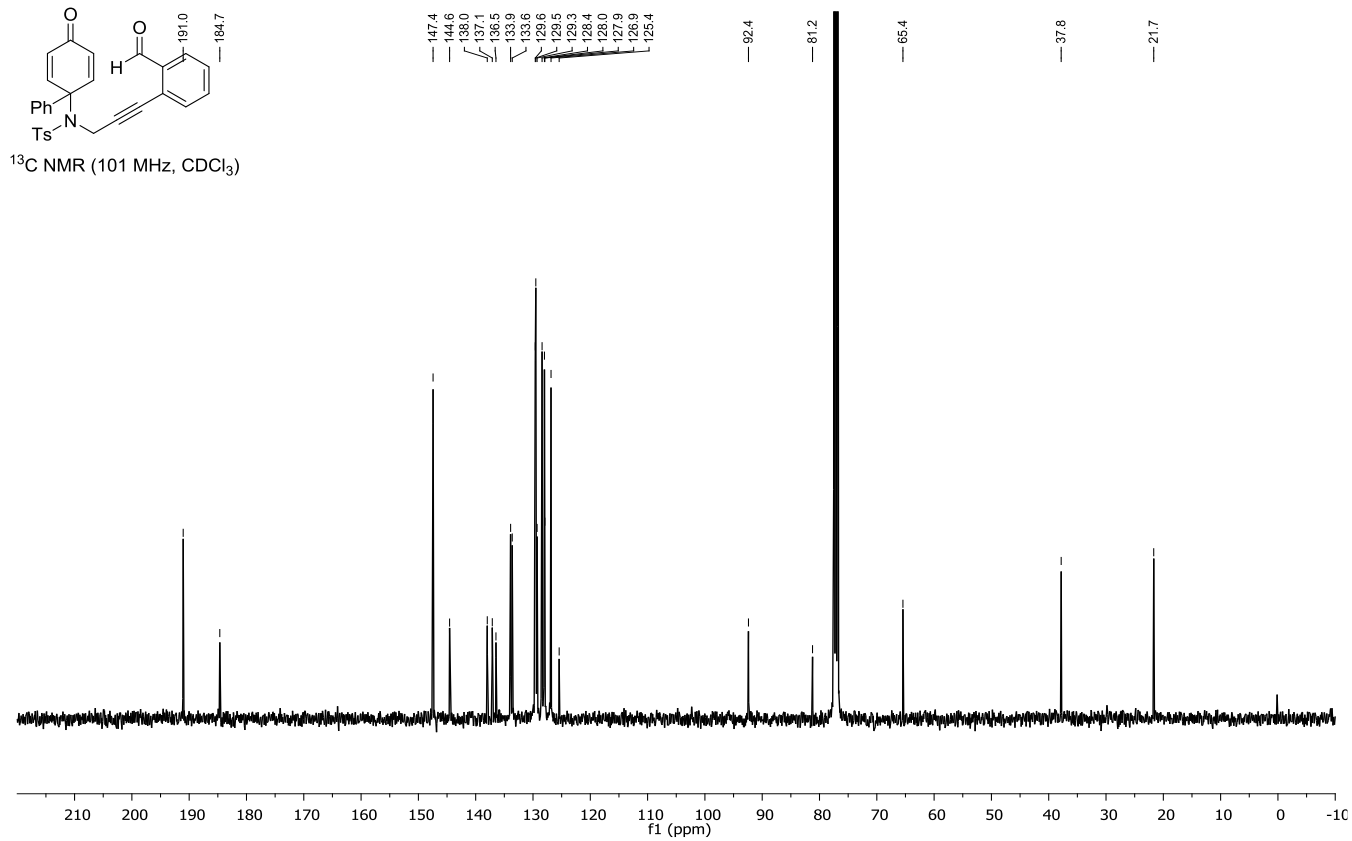
_N_-(3-(2-Formylphenyl)prop-2-yn-1-yl)-4-methyl-N-(1-methyl-4-oxocyclohexa-2,5-dien-1-yl)benzenesulfonamide (3g):



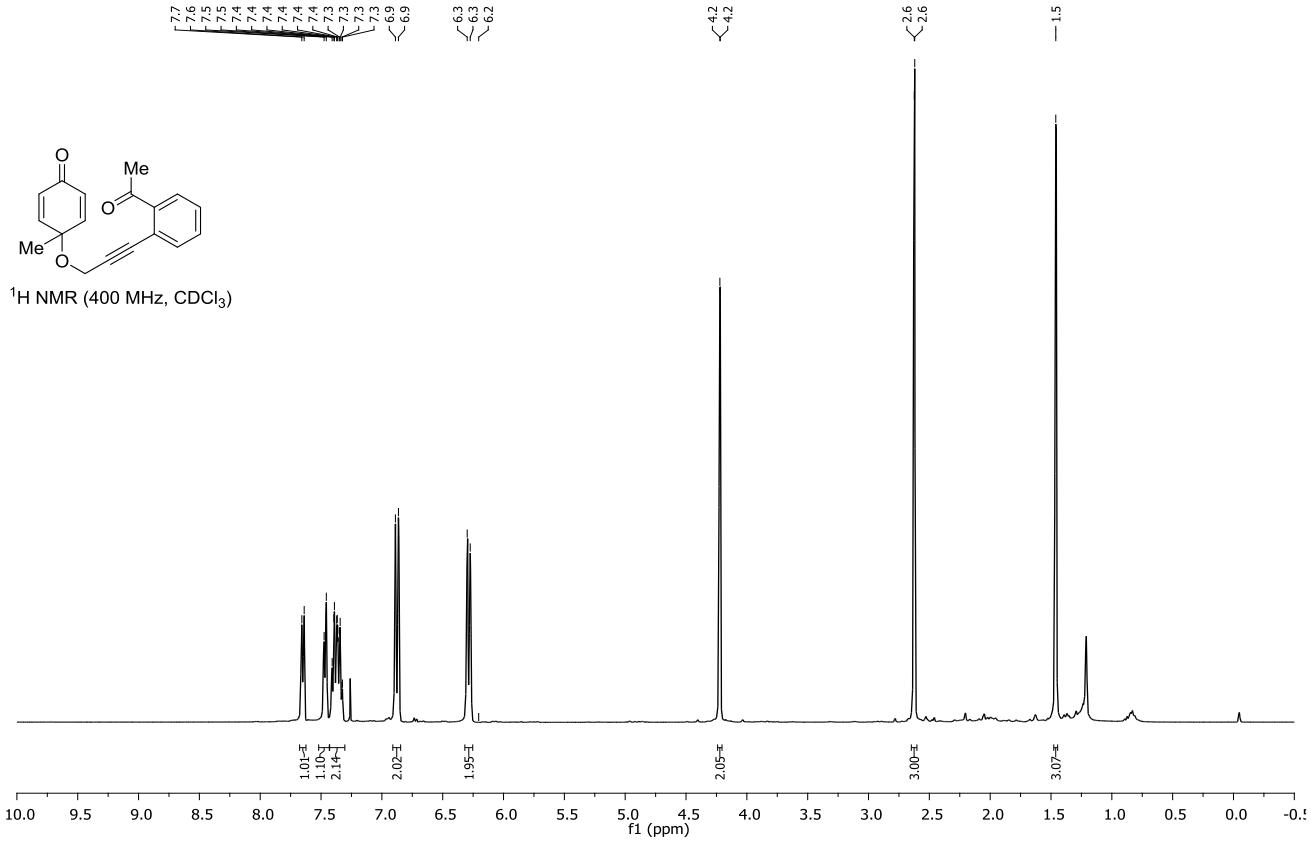


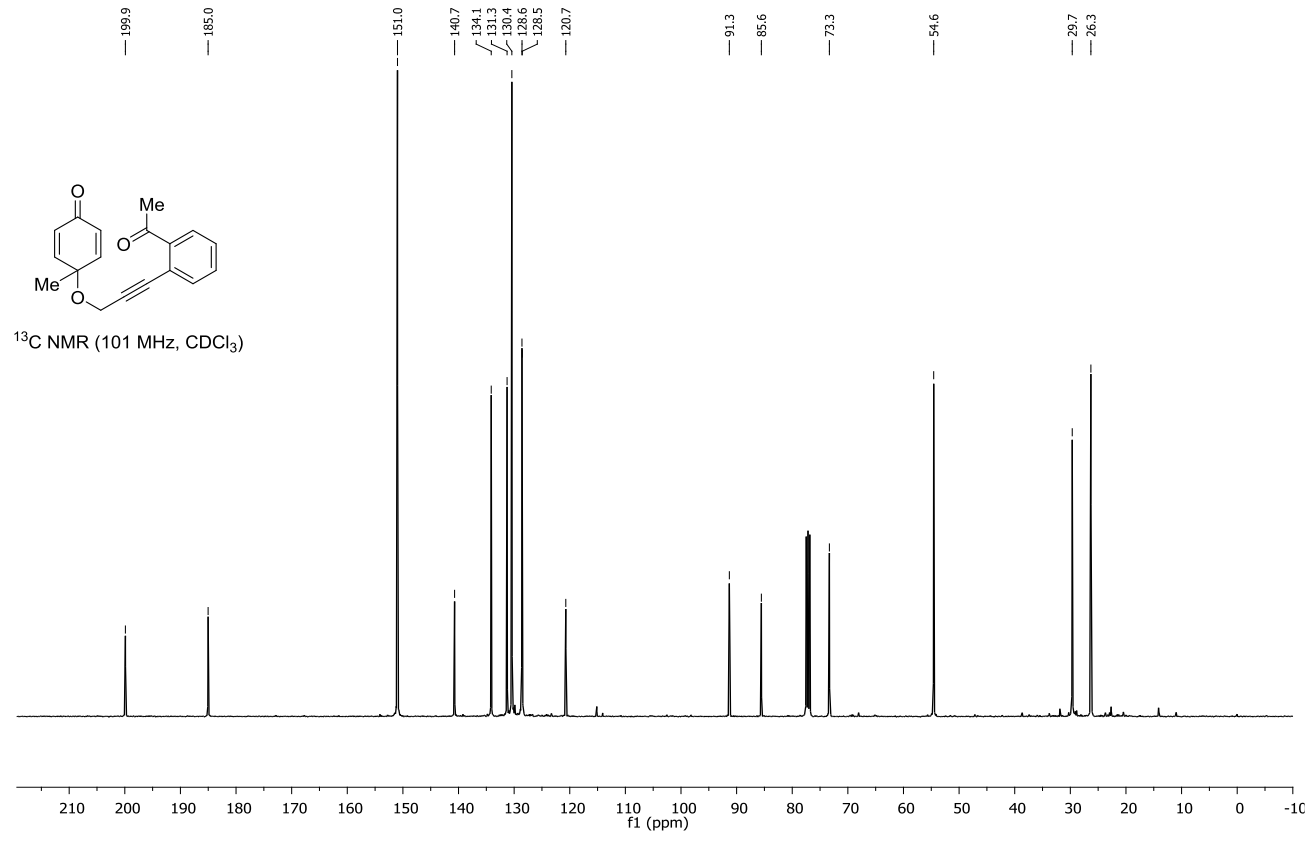
_N_-(3-(2-Formylphenyl)prop-2-yn-1-yl)-4-methyl-N-(4-oxo-[1,1'-biphenyl]-1(4_H_)-yl)benzenesulfonamide (3h):



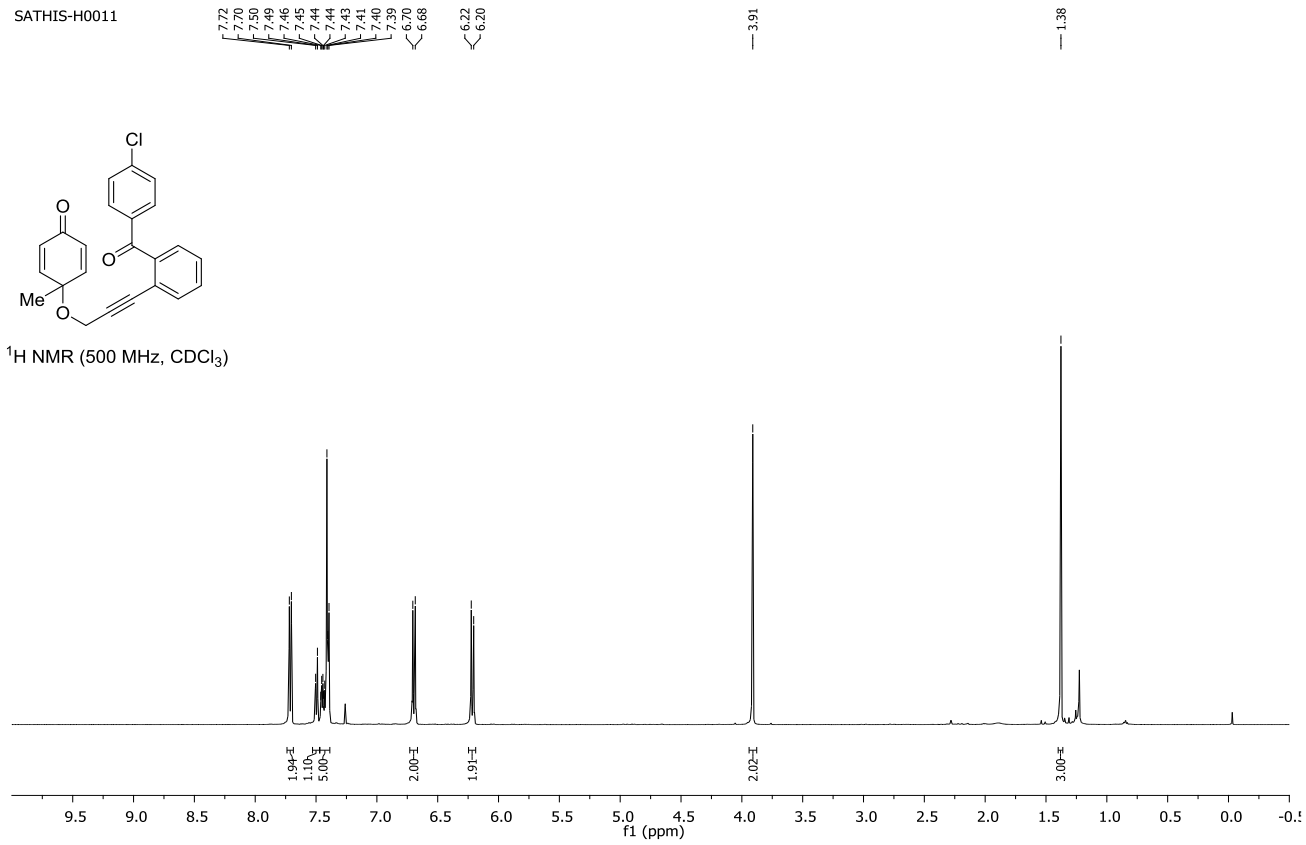


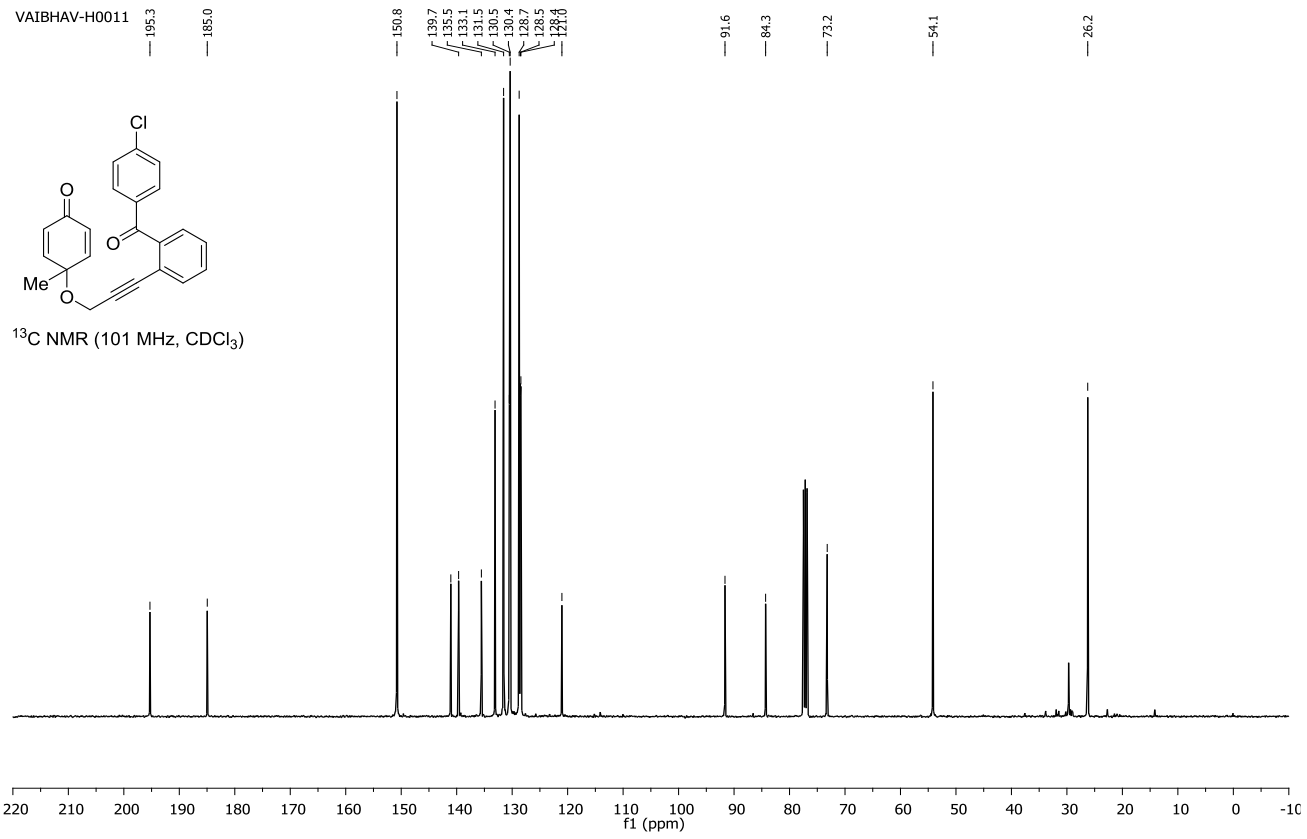
4-((3-(2-Acetylphenyl)prop-2-yn-1-yl)oxy)-4-methylcyclohexa-2,5-dien-1-one (5a):



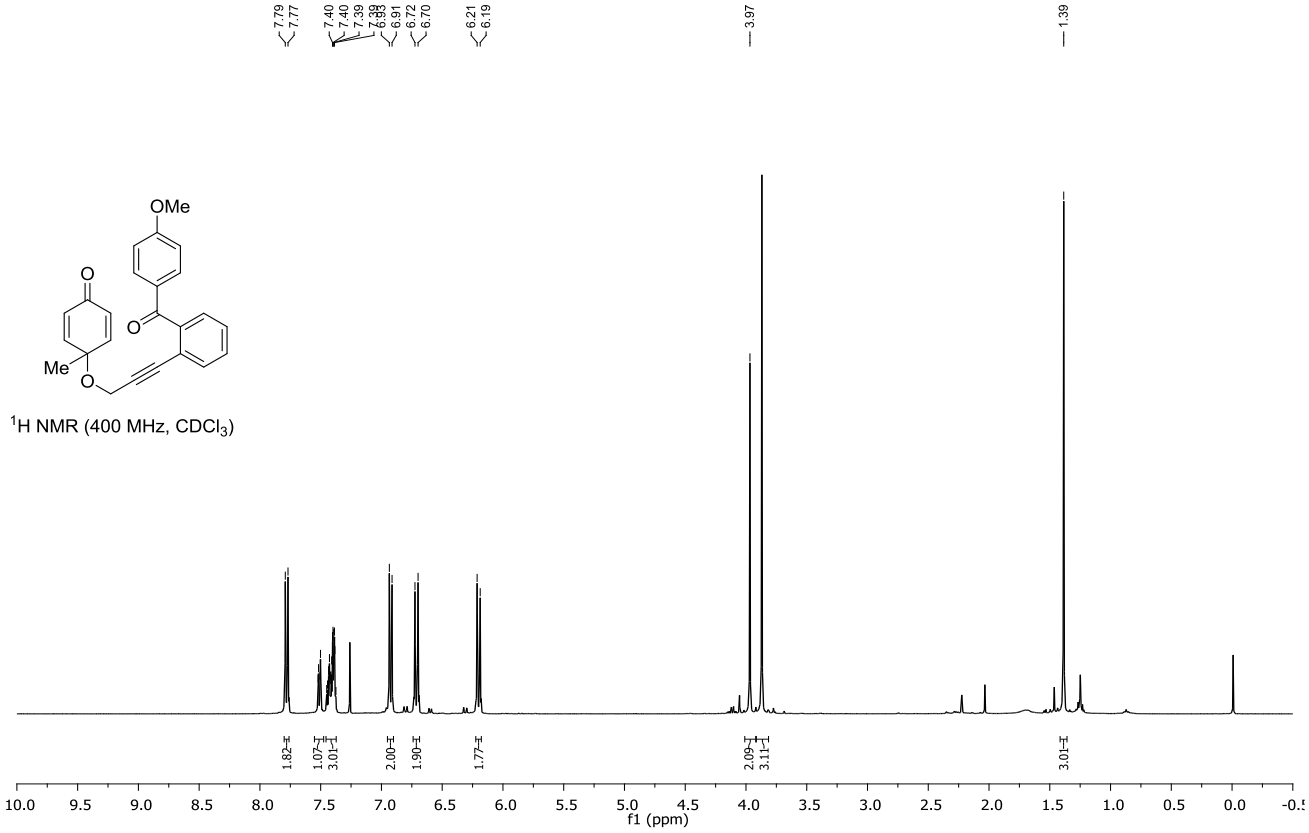


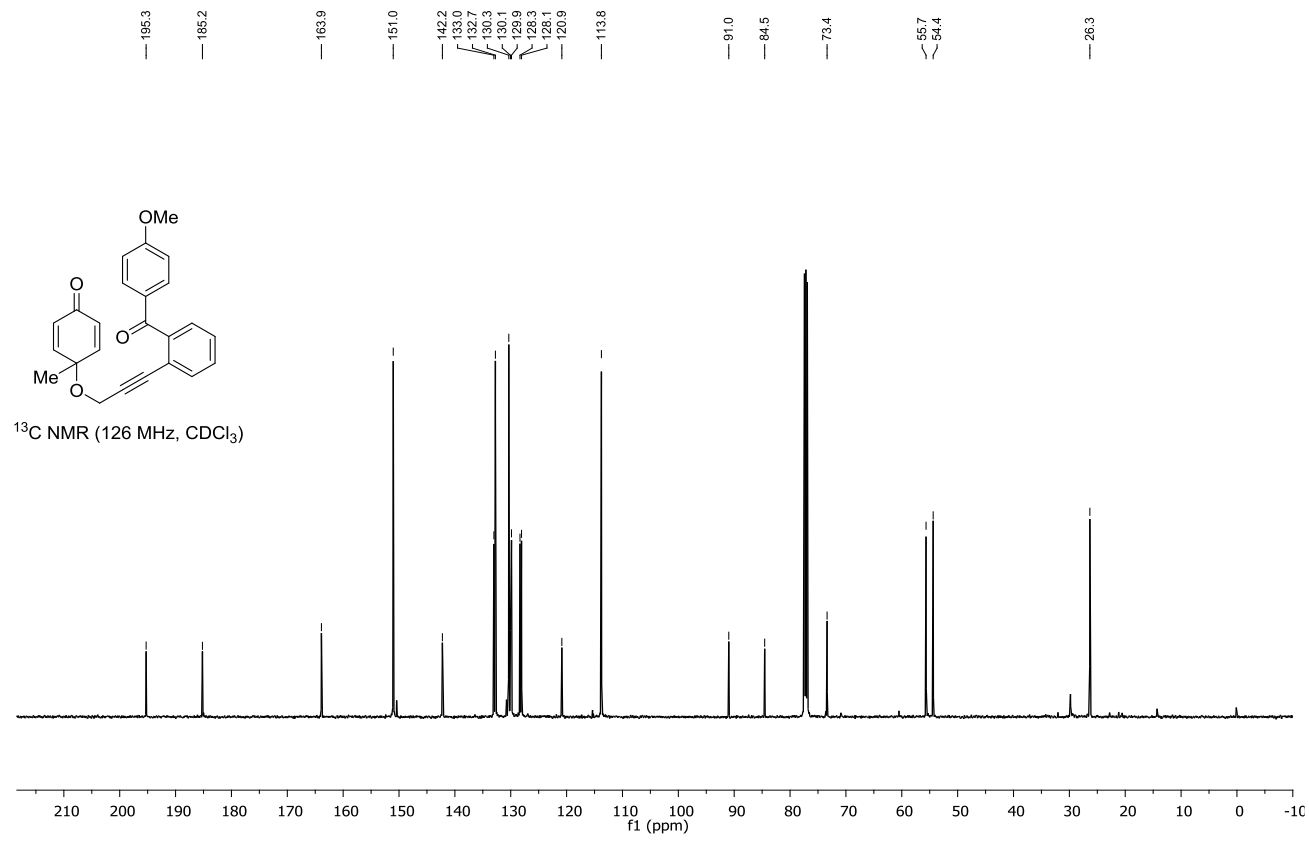
4-((3-(2-(4-Chlorobenzoyl)phenyl)prop-2-yn-1-yl)oxy)-4-methylcyclohexa-2,5-dien-1-one (5b):



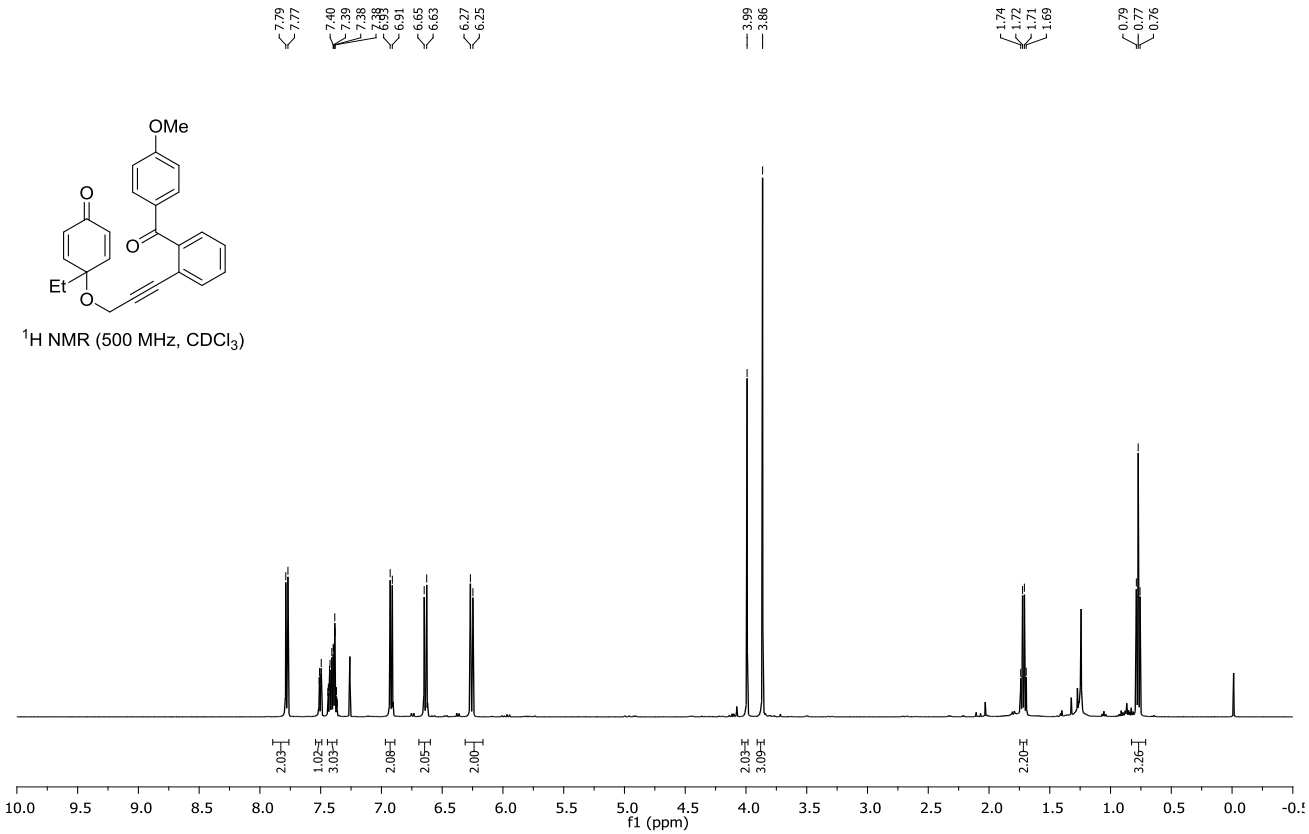


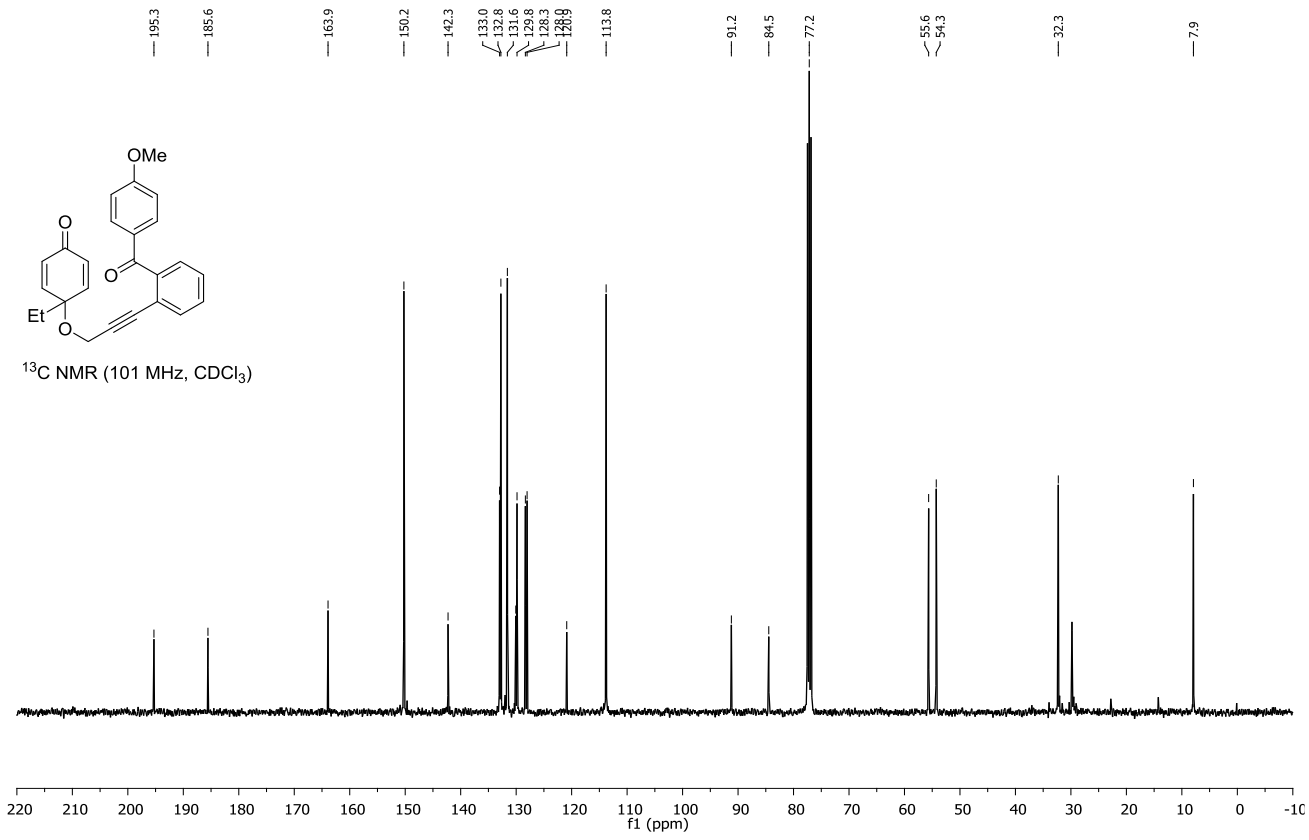
4-((3-(2-(4-Methoxybenzoyl)phenyl)prop-2-yn-1-yl)oxy)-4-methylcyclohexa-2,5-dien-1-one (5c):



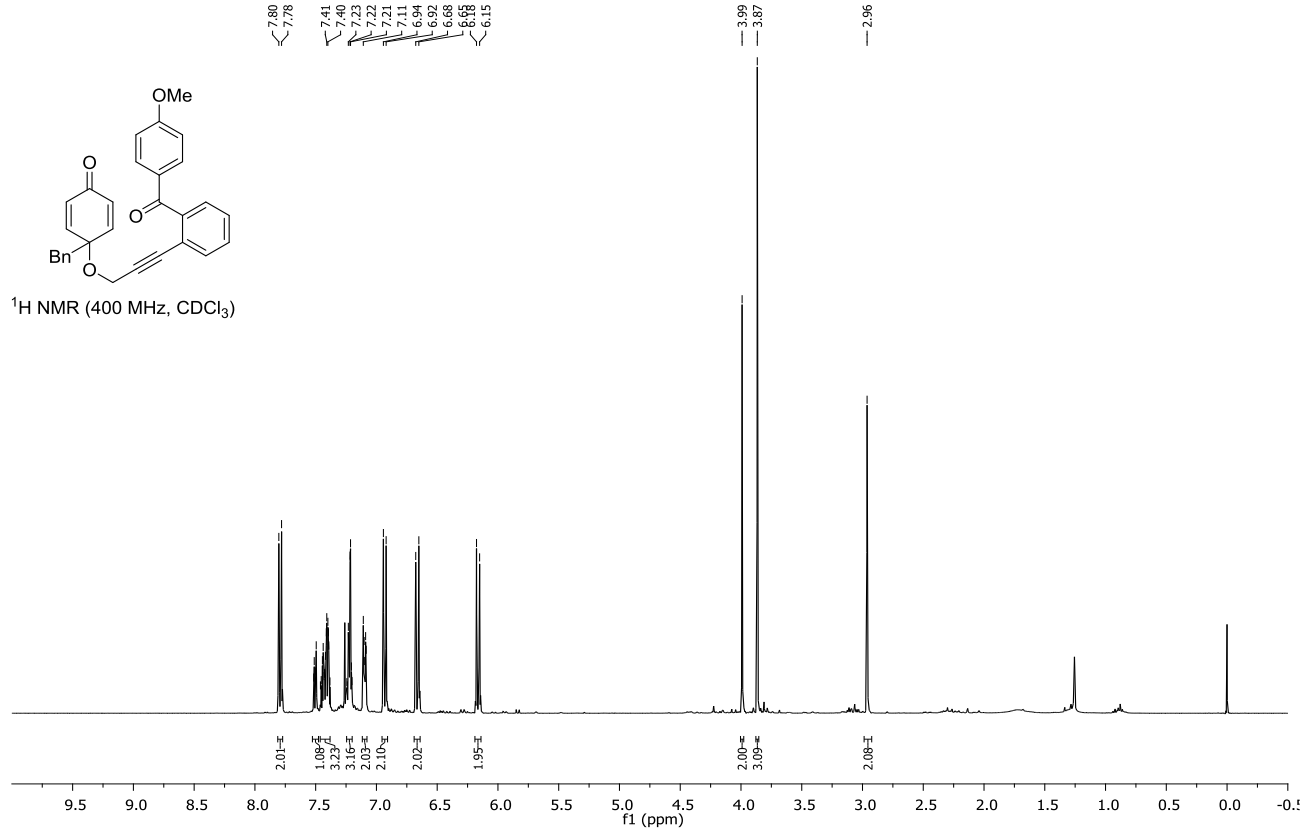


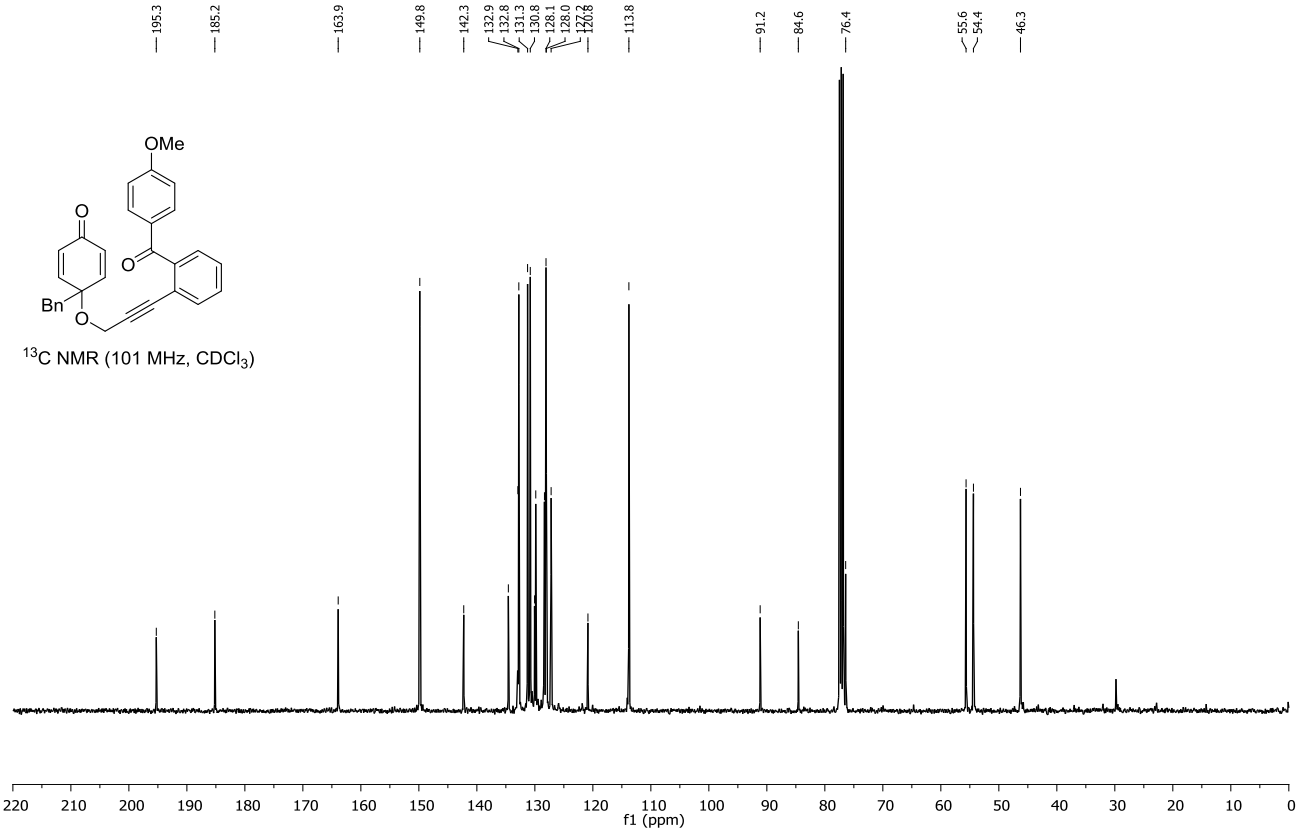
4-Ethyl-4-((3-(2-(4-methoxybenzoyl)phenyl)prop-2-yn-1-yl)oxy)cyclohexa-2,5-dien-1-one (5d):



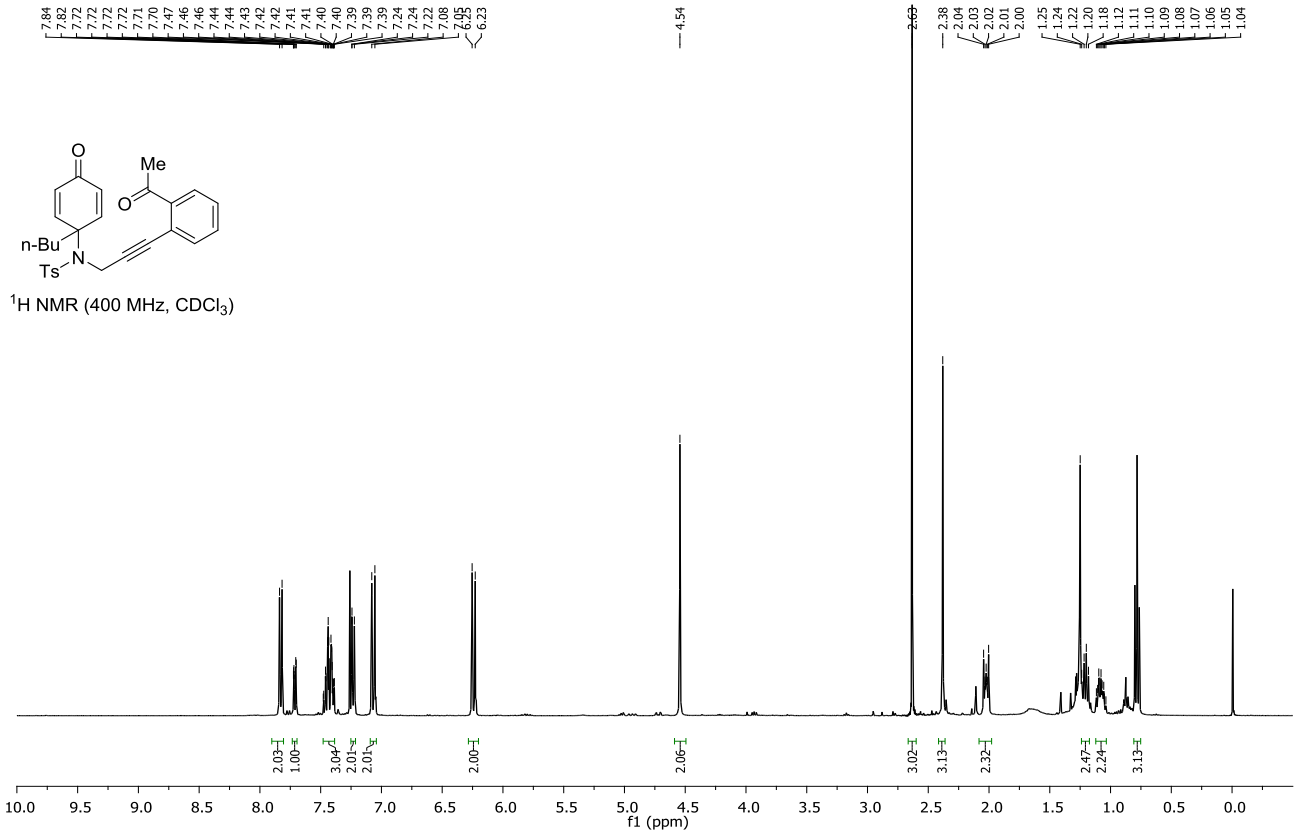


4-Benzyl-4-((3-(2-(4-methoxybenzoyl)phenyl)prop-2-yn-1-yl)oxy)cyclohexa-2,5-dien-1-one (5e):

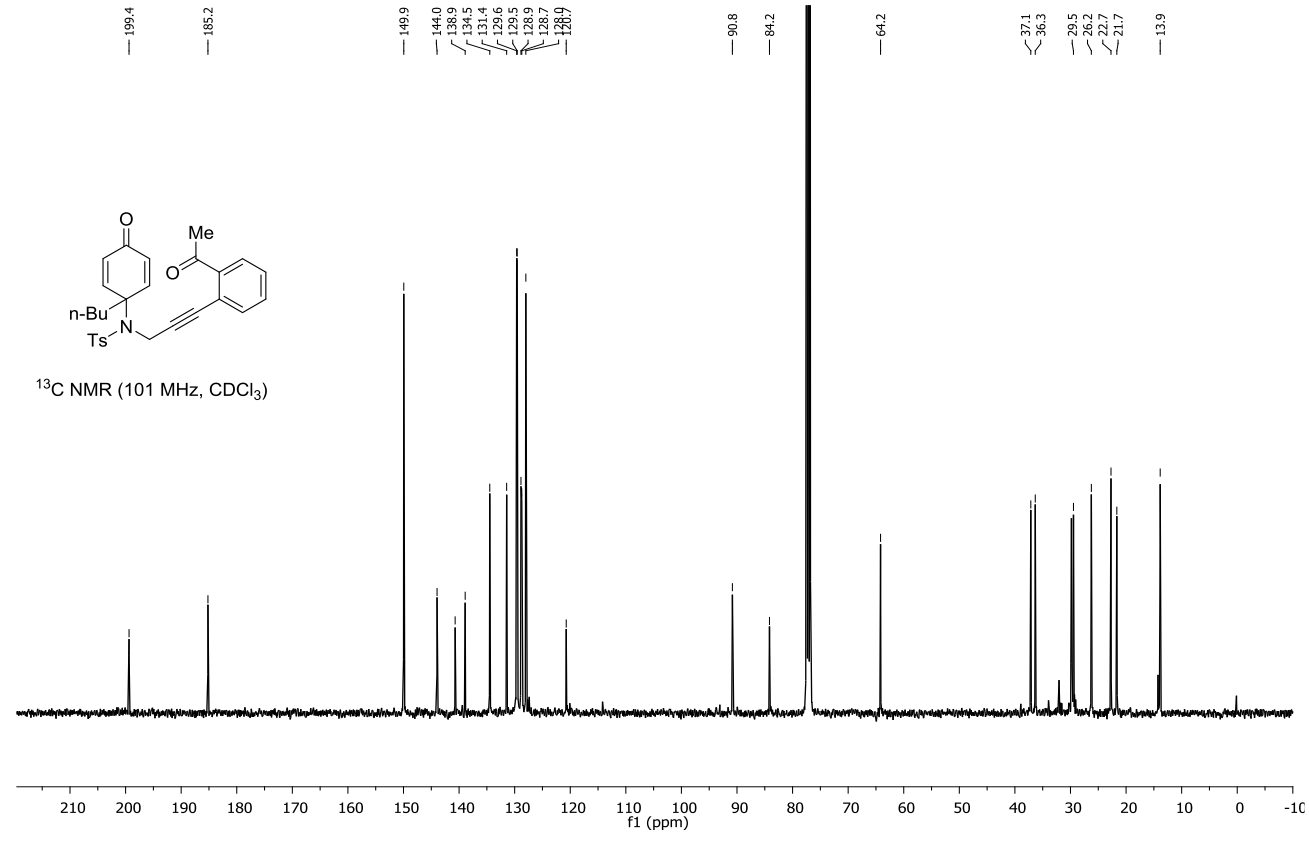




_N_-(3-(2-Acetylphenyl)prop-2-yn-1-yl)-N-(1-butyl-4-oxocyclohexa-2,5-dien-1-yl)-4-methylbenzenesulfonamide (5f):

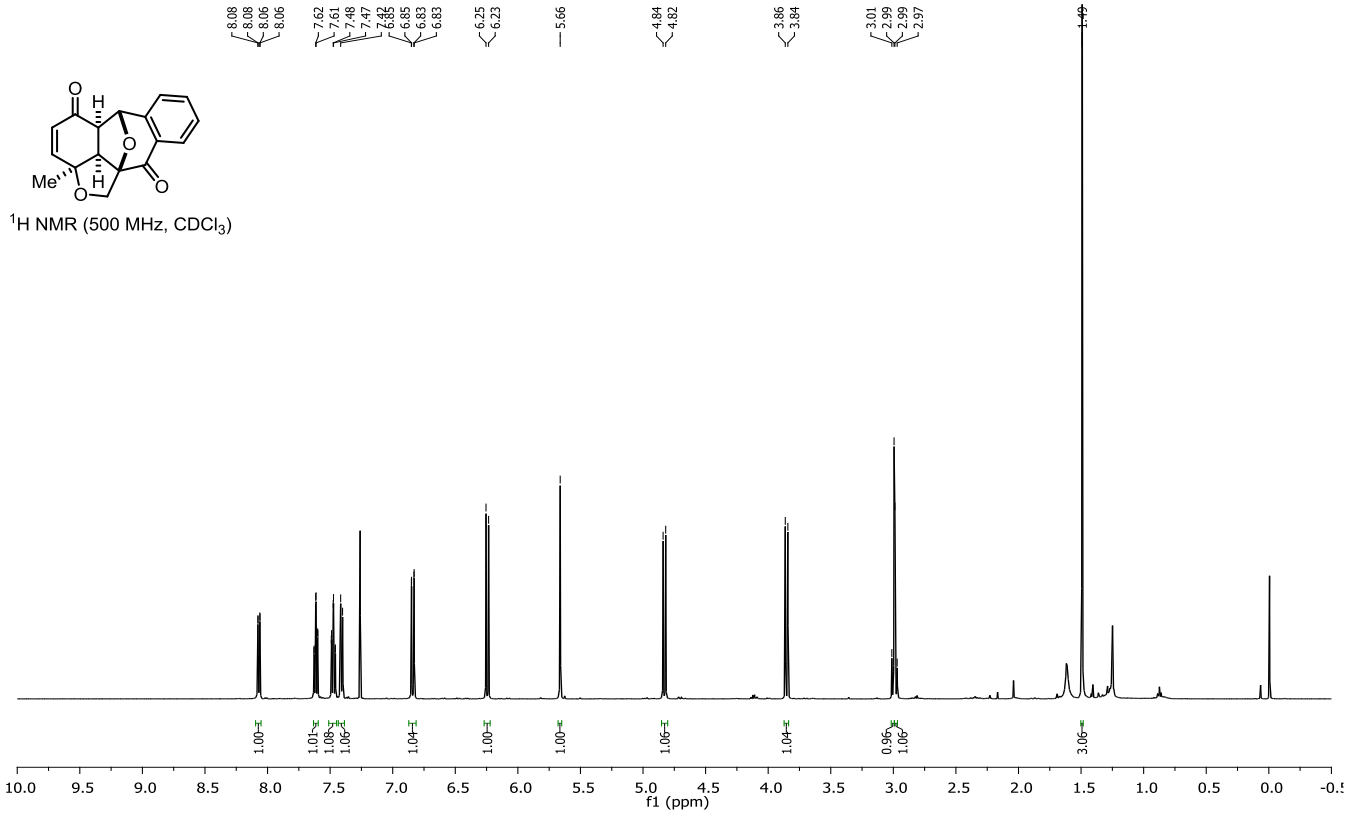


^{1}H NMR (400 MHz, $CDCl_3$)

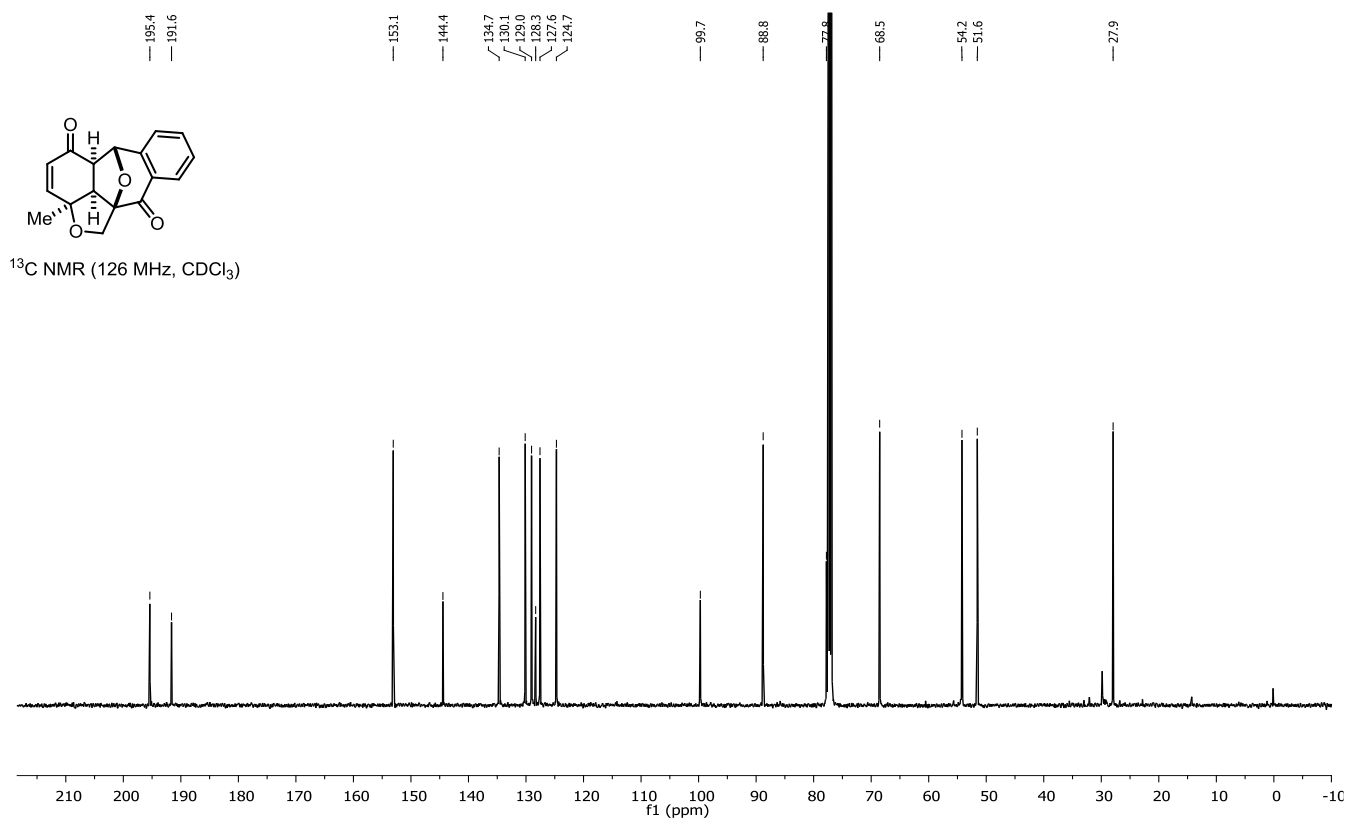


^{13}C NMR (101 MHz, $CDCl_3$)

2a-Methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2a):

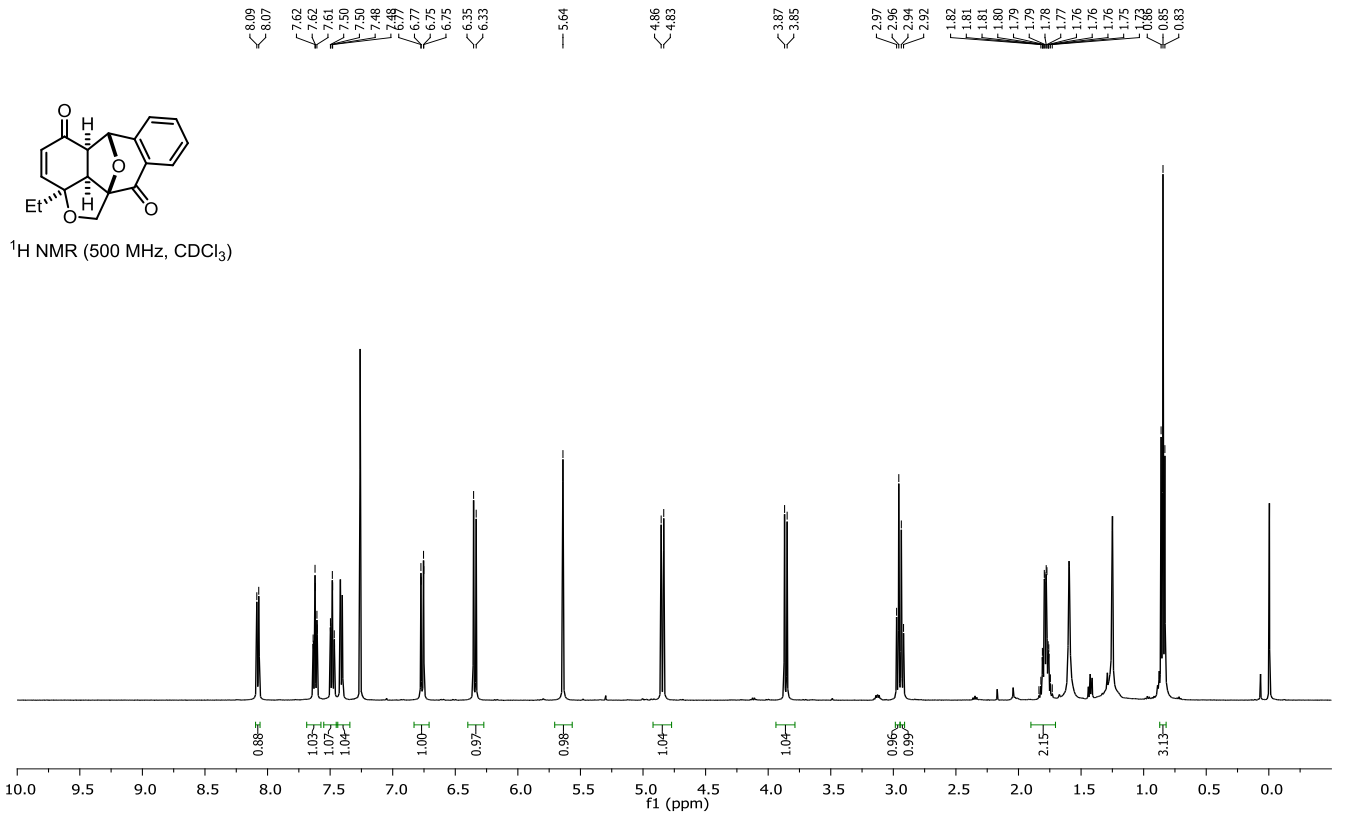


^{1}H NMR (500 MHz, $CDCl_3$)

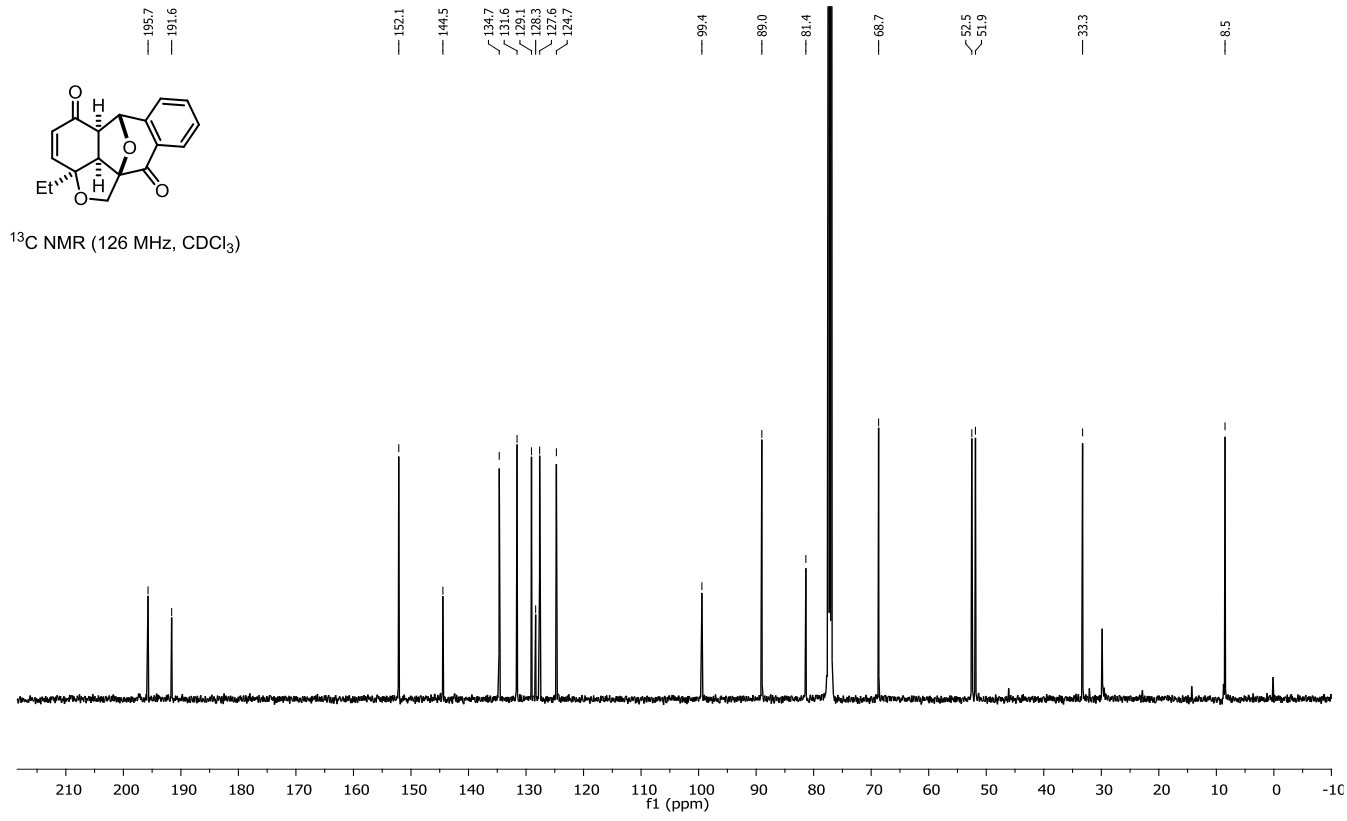


^{13}C NMR (126 MHz, $CDCl_3$)

2a-Ethyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2b):

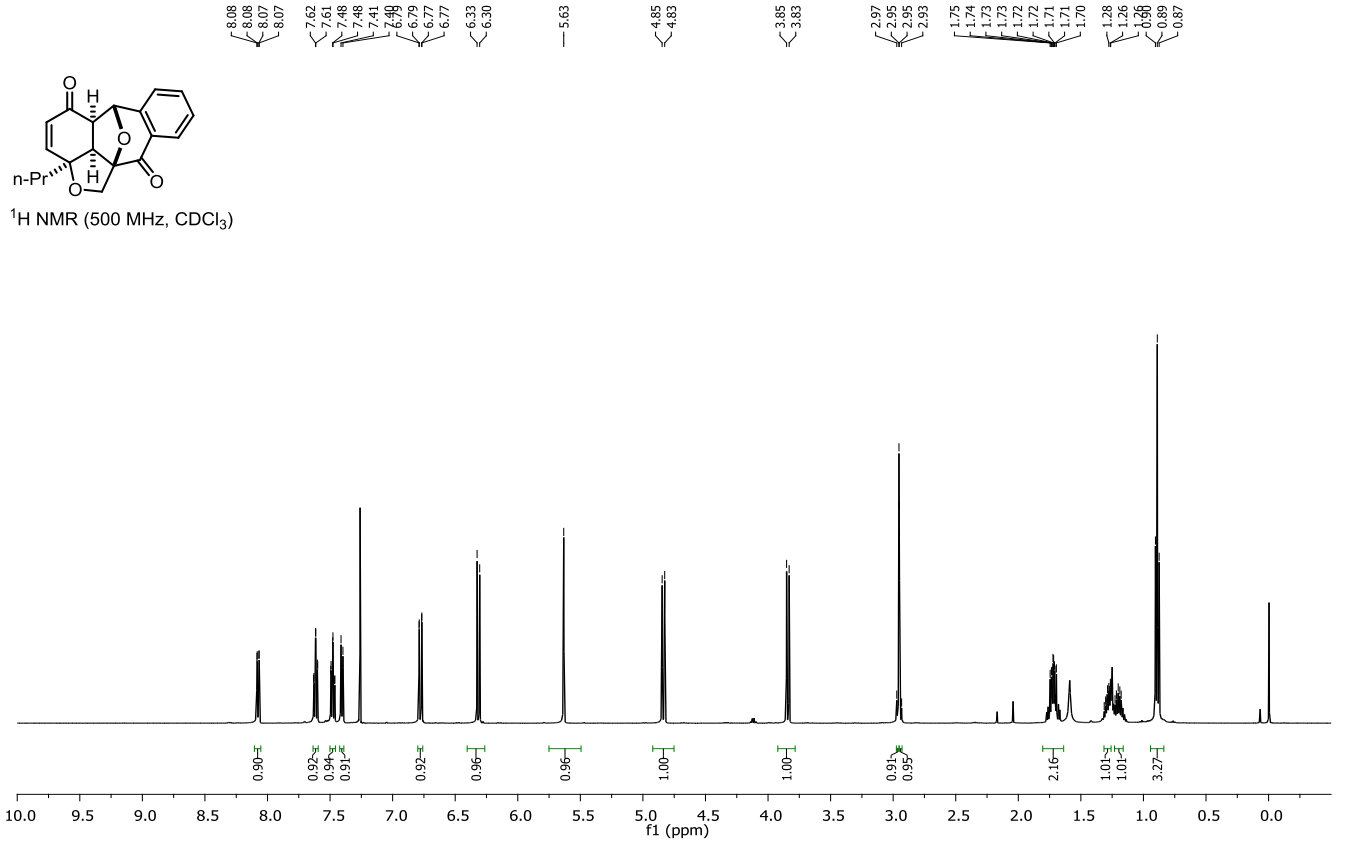


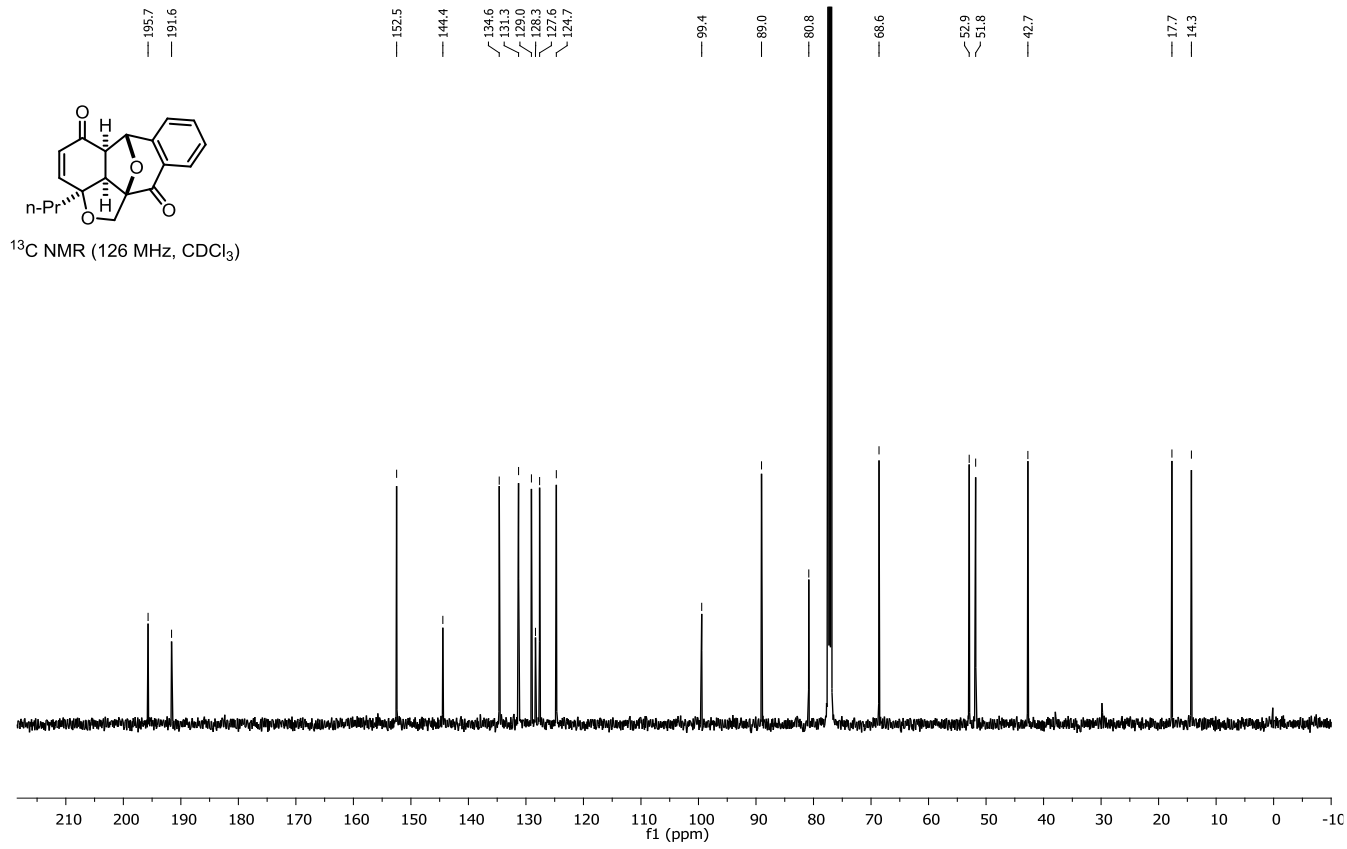
^{1}H NMR (500 MHz, $CDCl_3$)



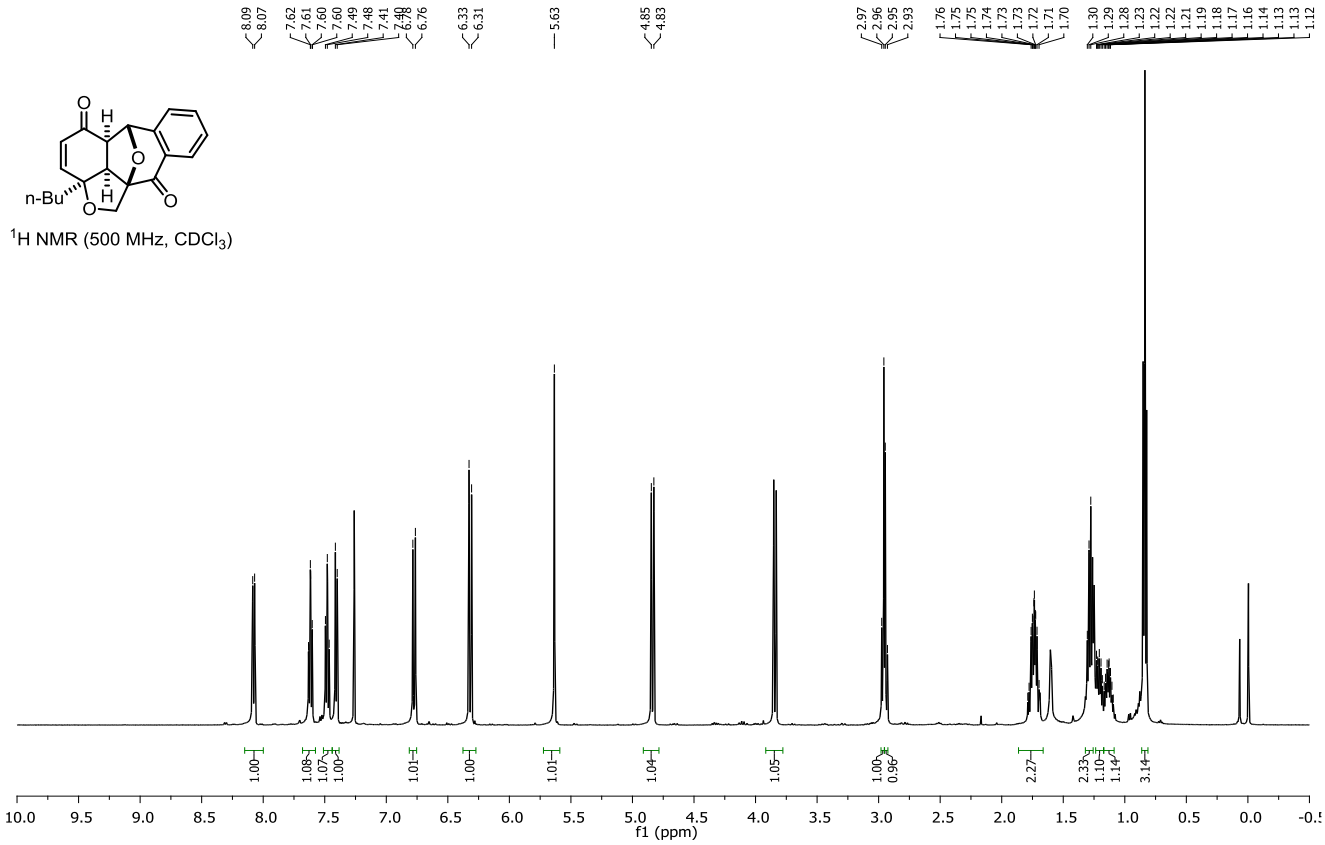
^{13}C NMR (126 MHz, $CDCl_3$)

2a-Propyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2c):

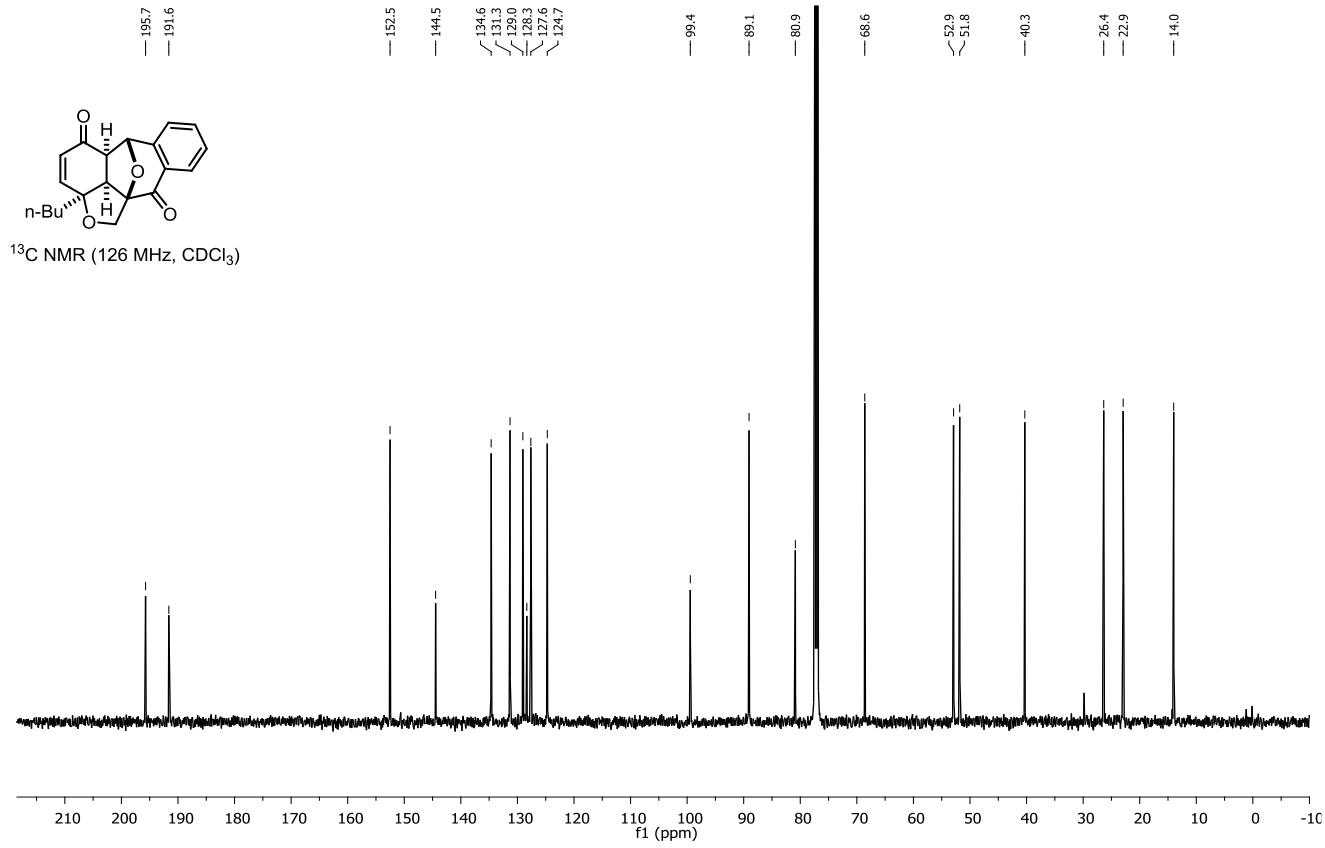




2a-Butyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2d):

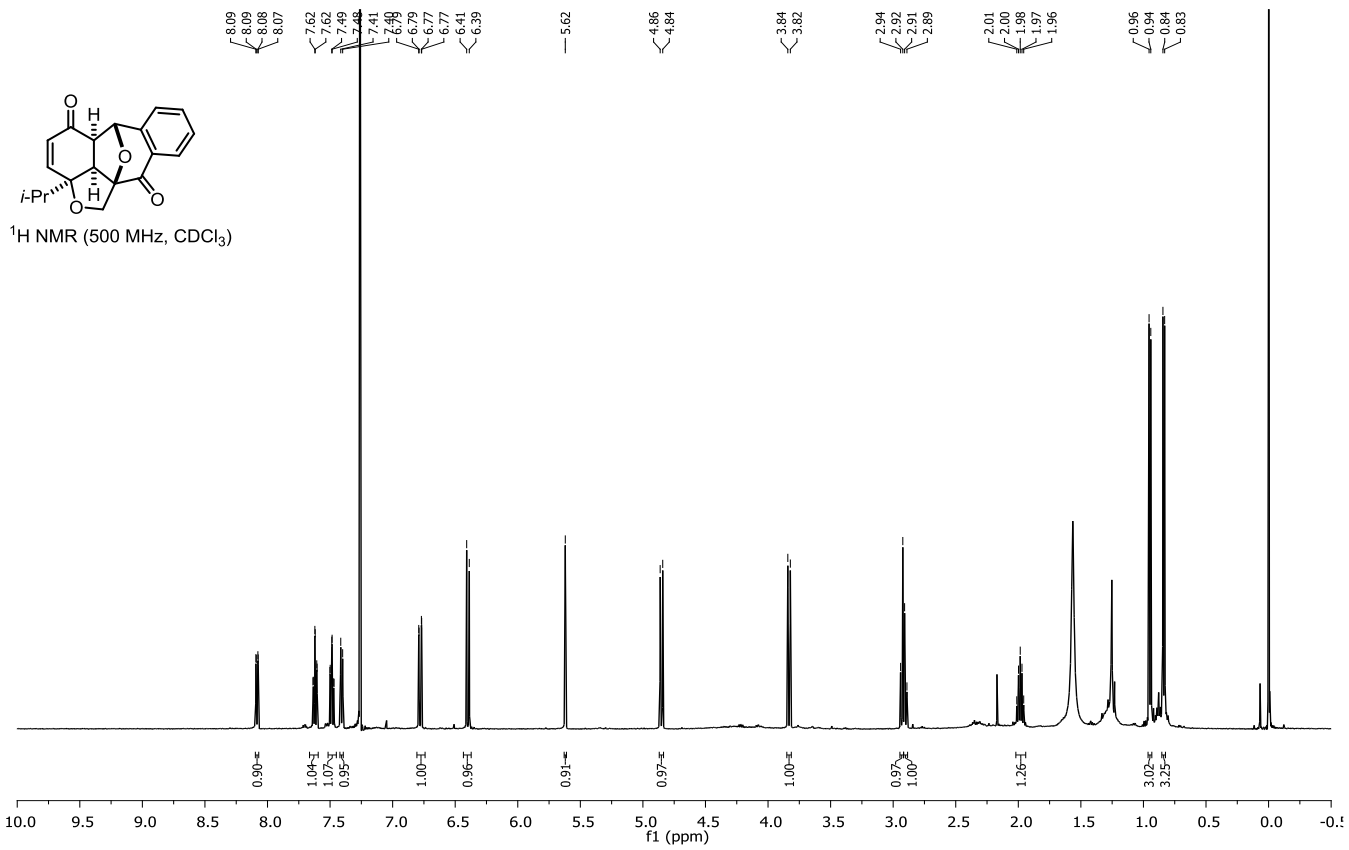


^{1}H NMR (500 MHz, $CDCl_3$)

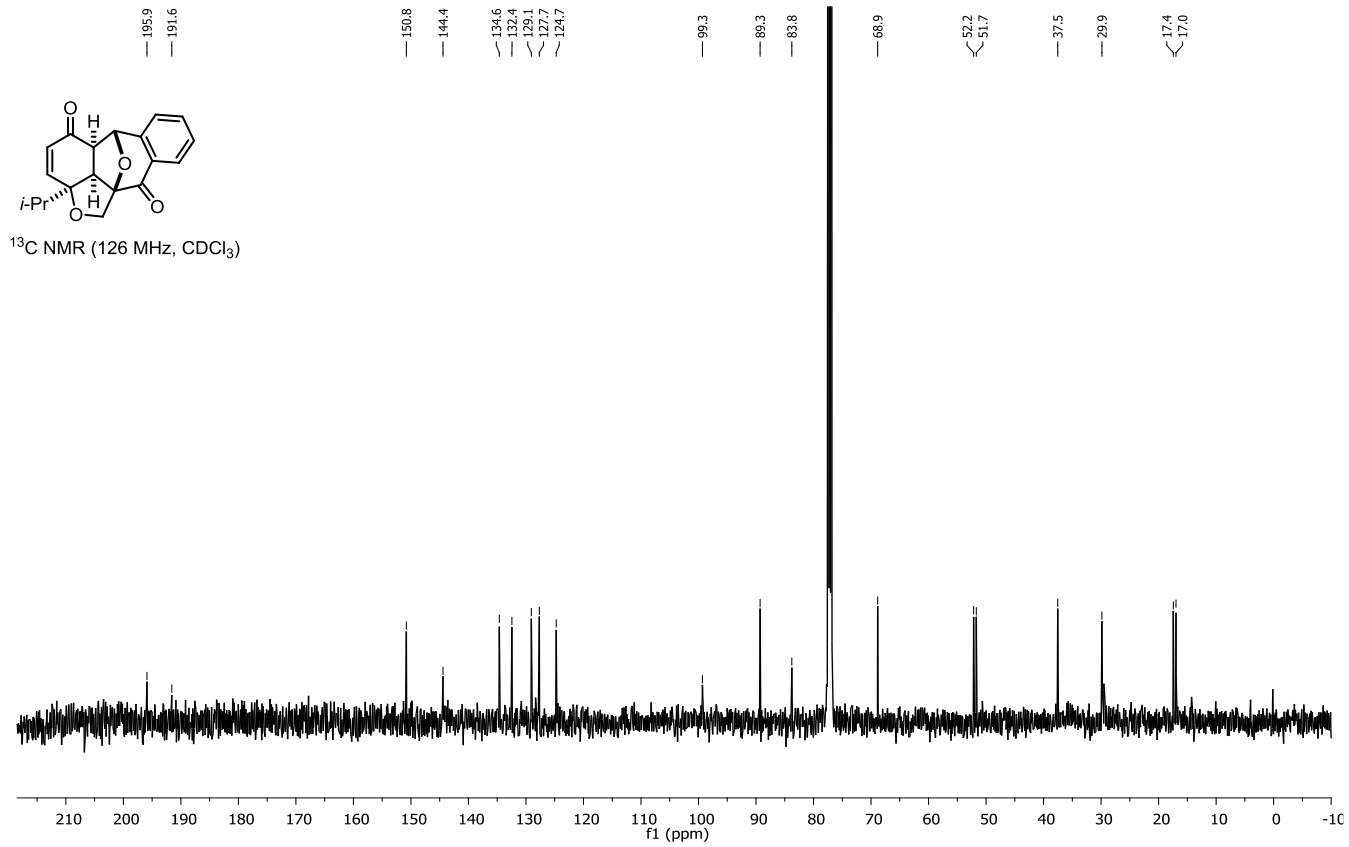


^{13}C NMR (126 MHz, $CDCl_3$)

2a-Isopropyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzo furan 5,11-dione (2e):

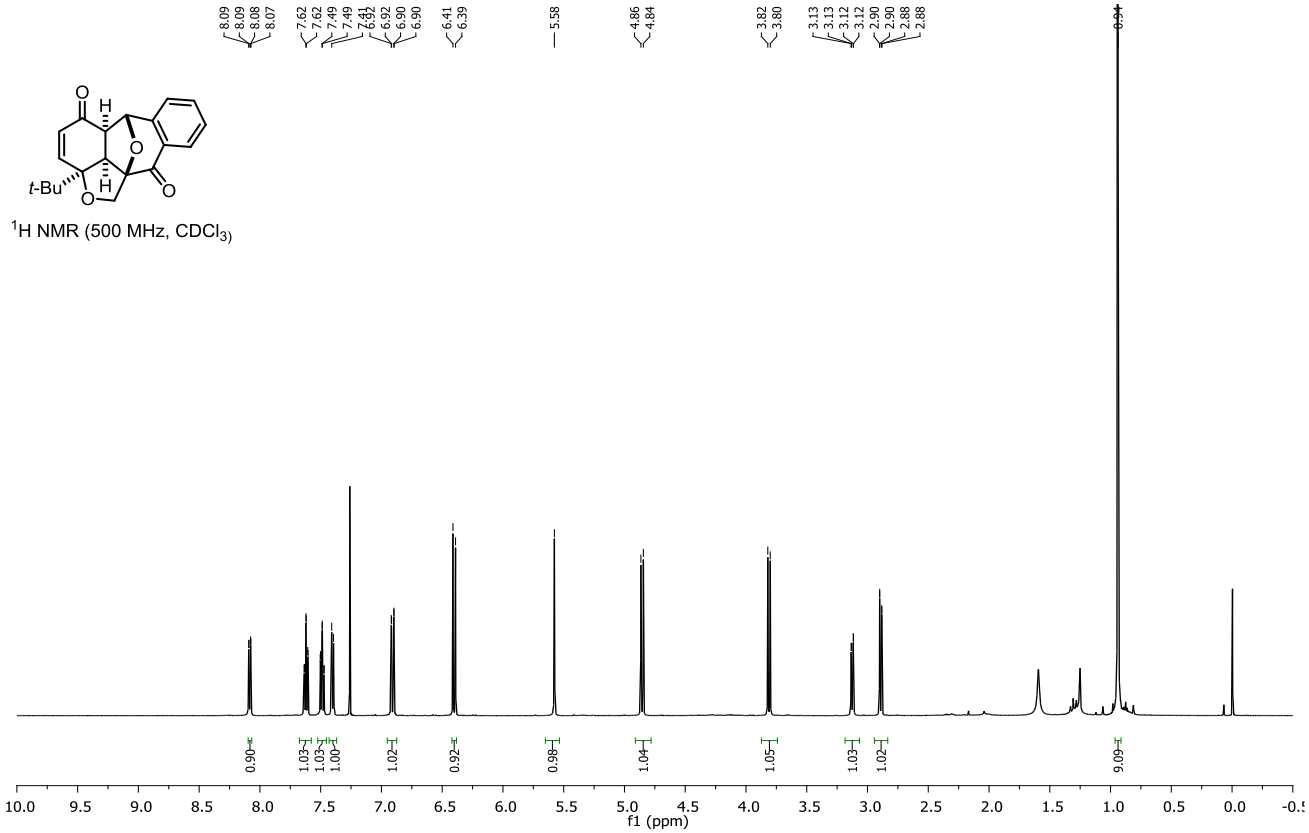


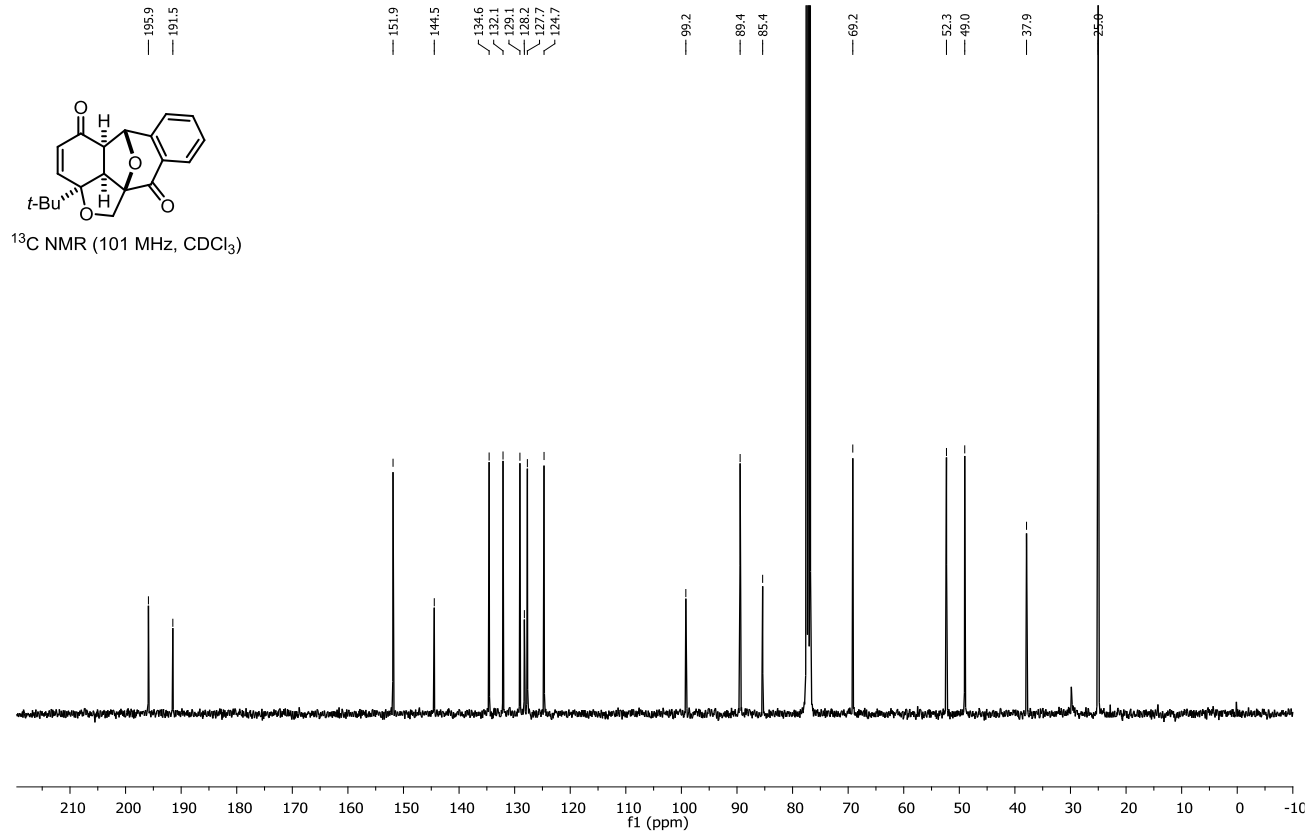
^{1}H NMR (500 MHz, $CDCl_3$)



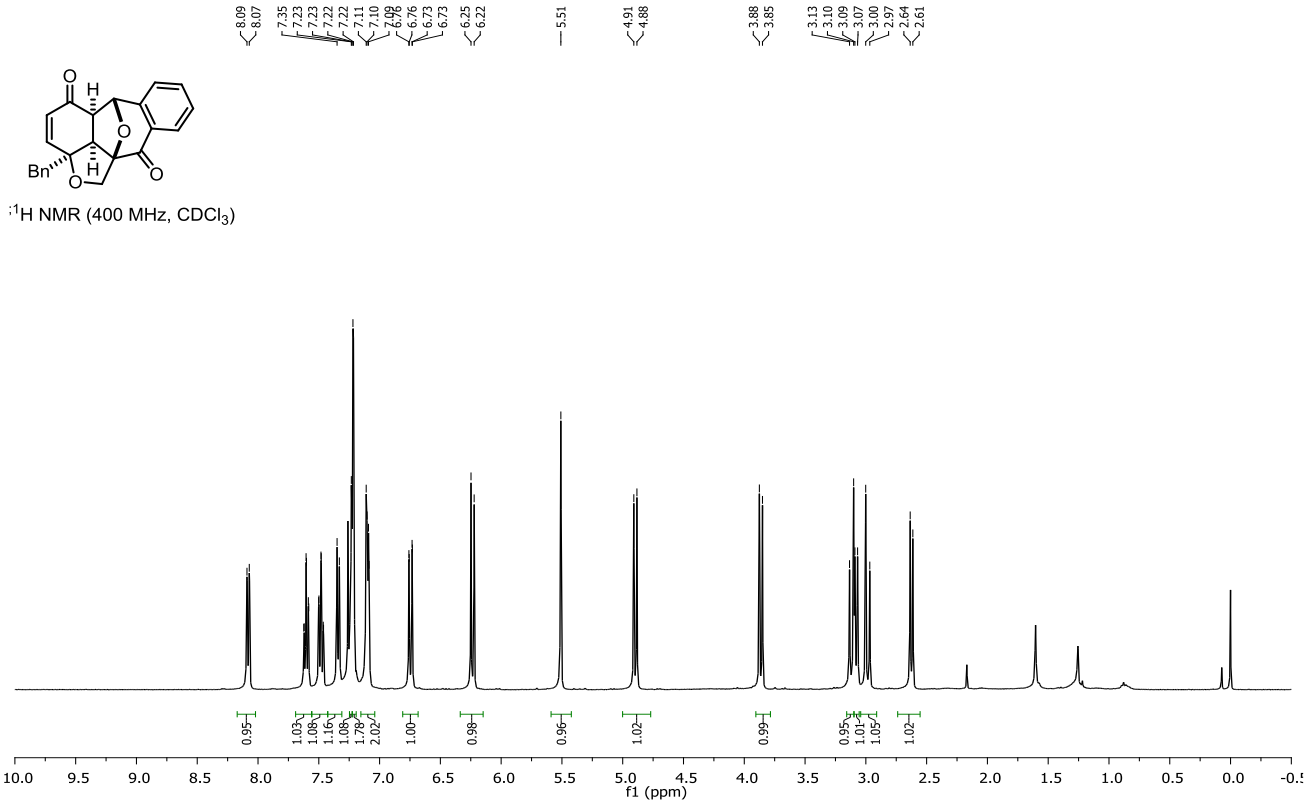
^{13}C NMR (126 MHz, $CDCl_3$)

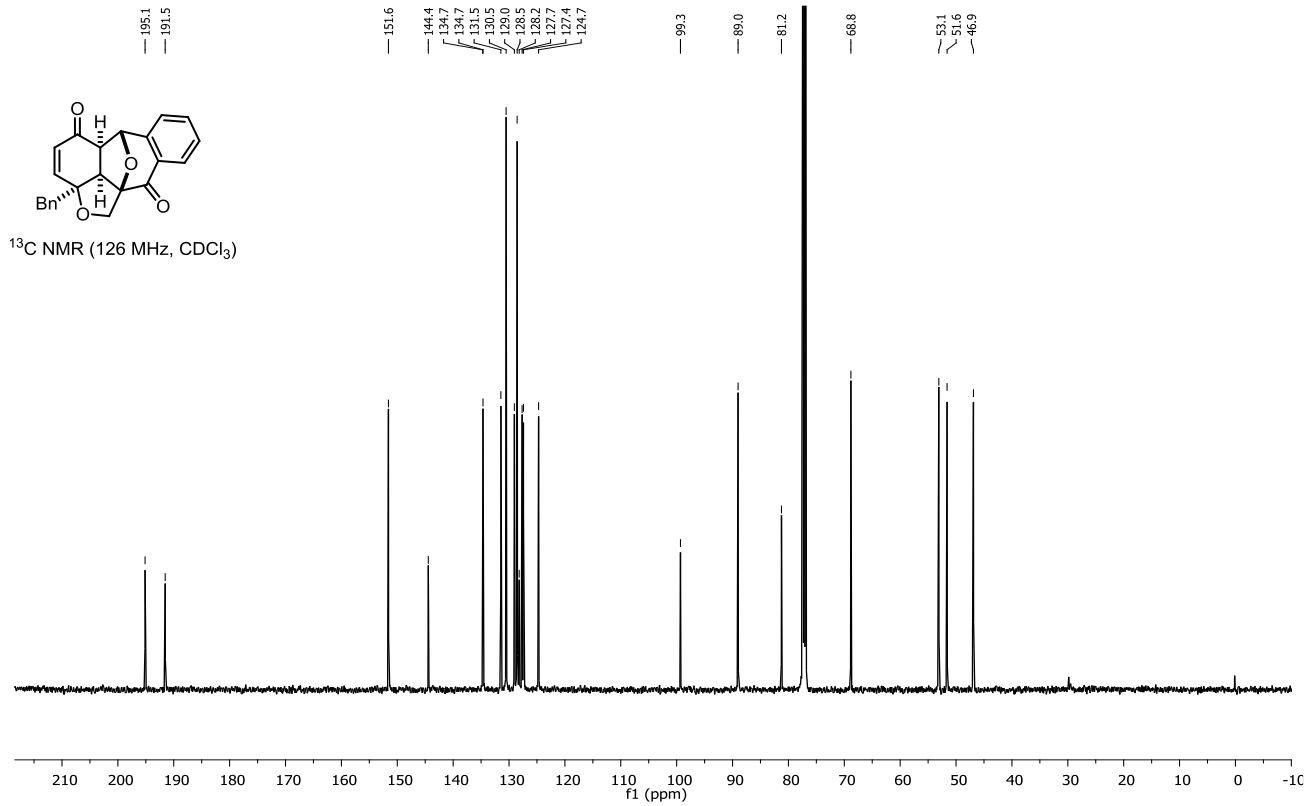
2a-(*tert*-Butyl)-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2f):



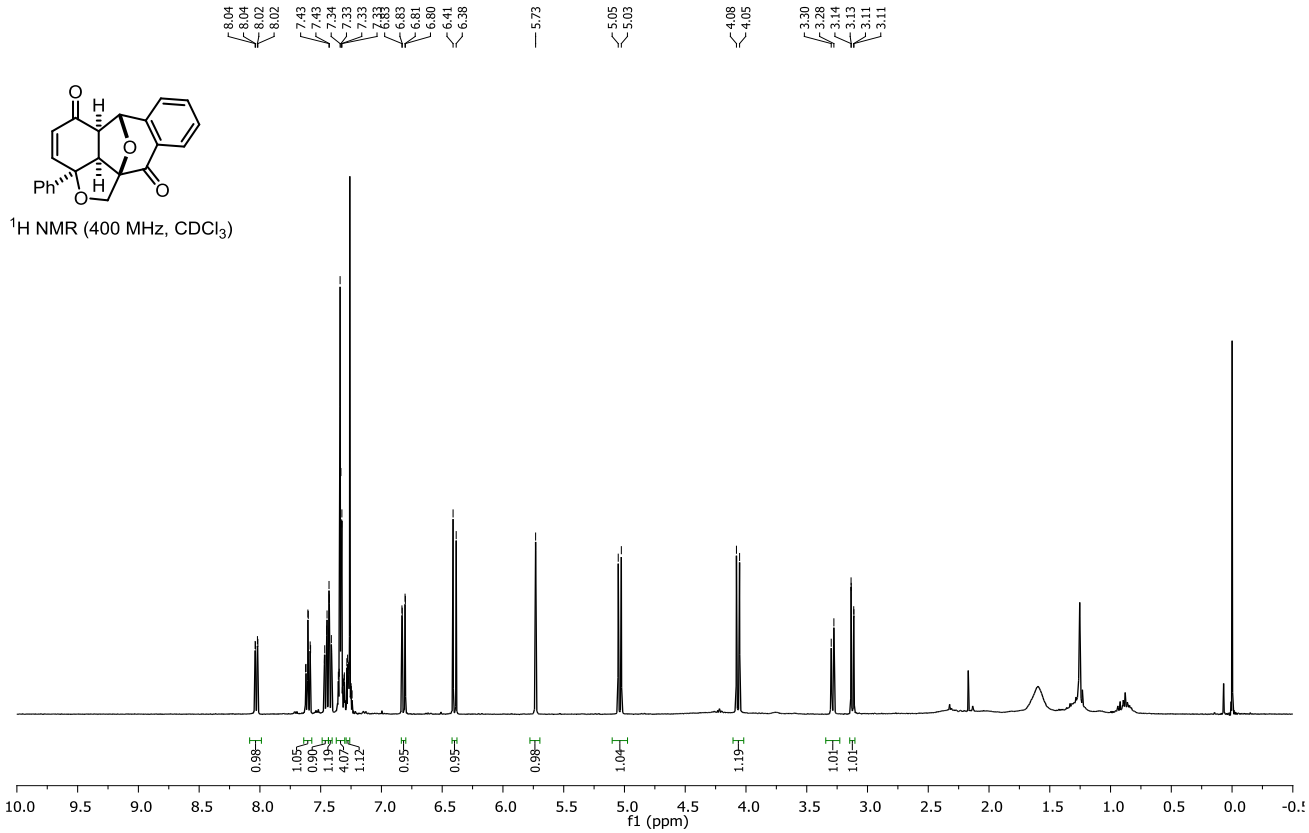


2a-Benzyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2g):

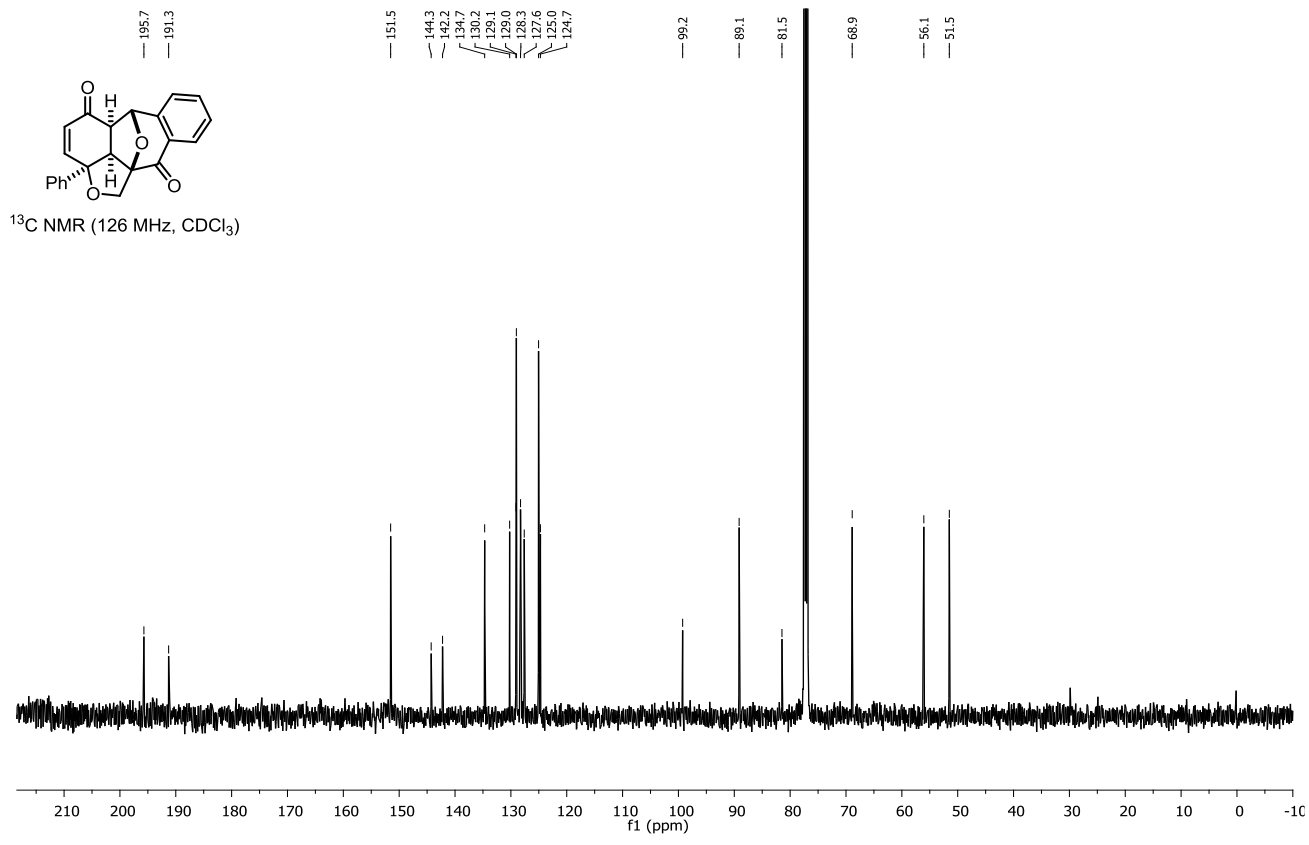




2a-Phenyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2h):

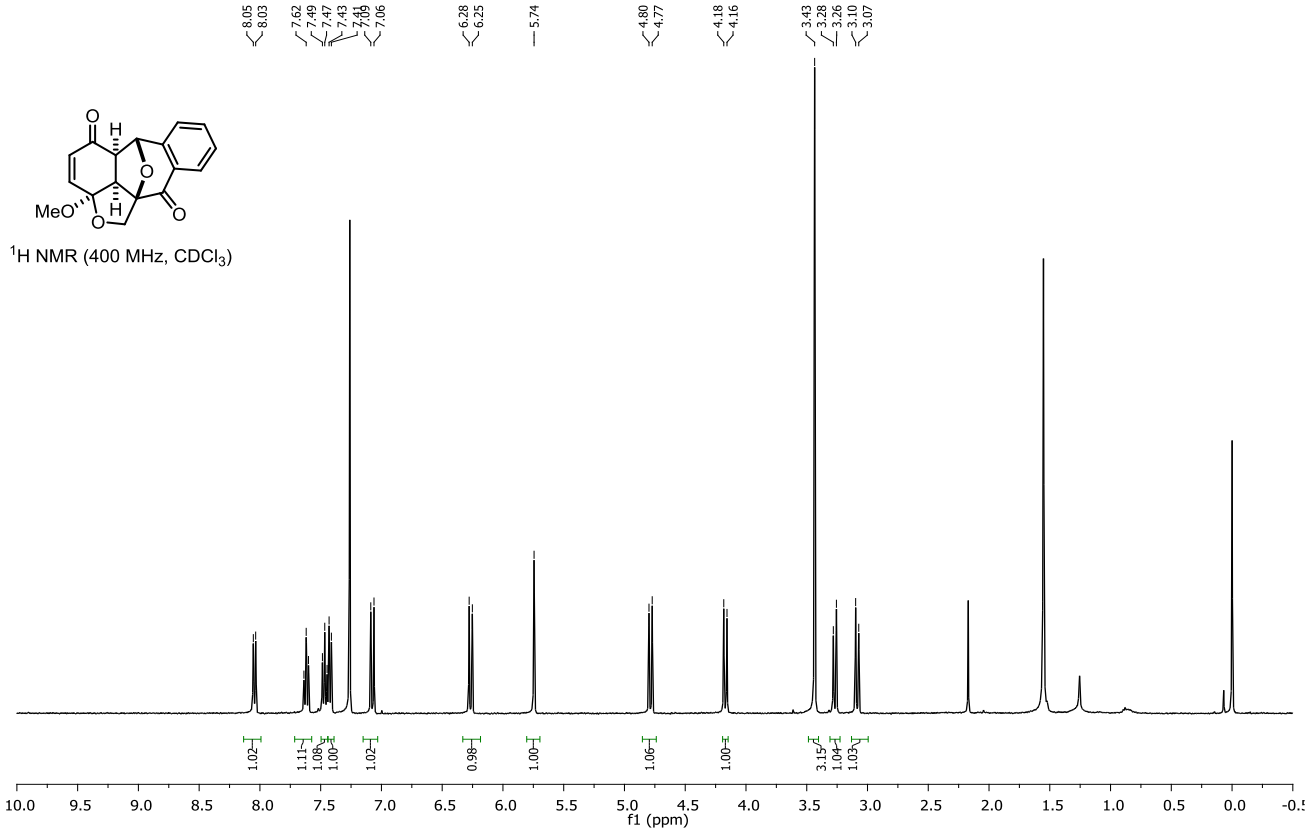


^{1}H NMR (400 MHz, $CDCl_3$)

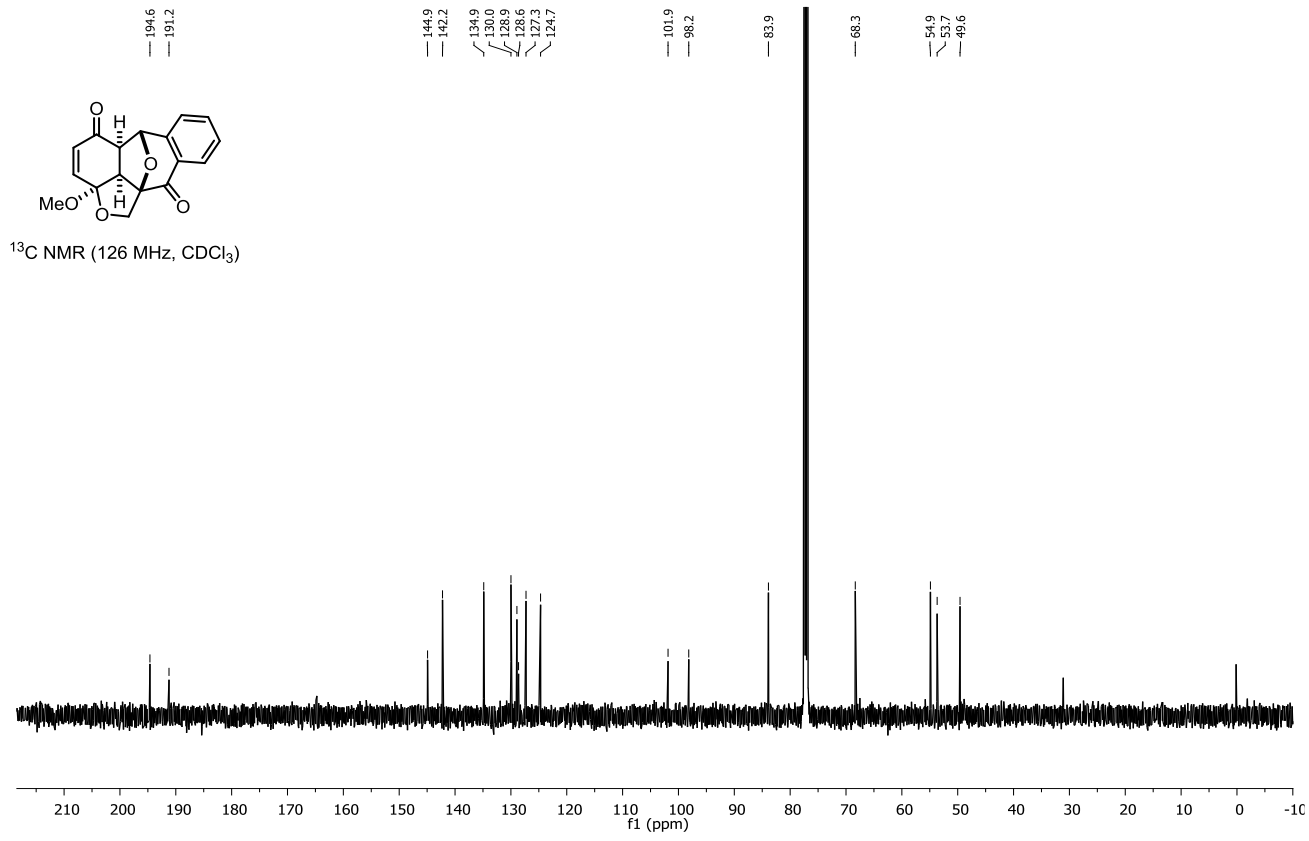


^{13}C NMR (126 MHz, $CDCl_3$)

2a-Methoxy-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2i):

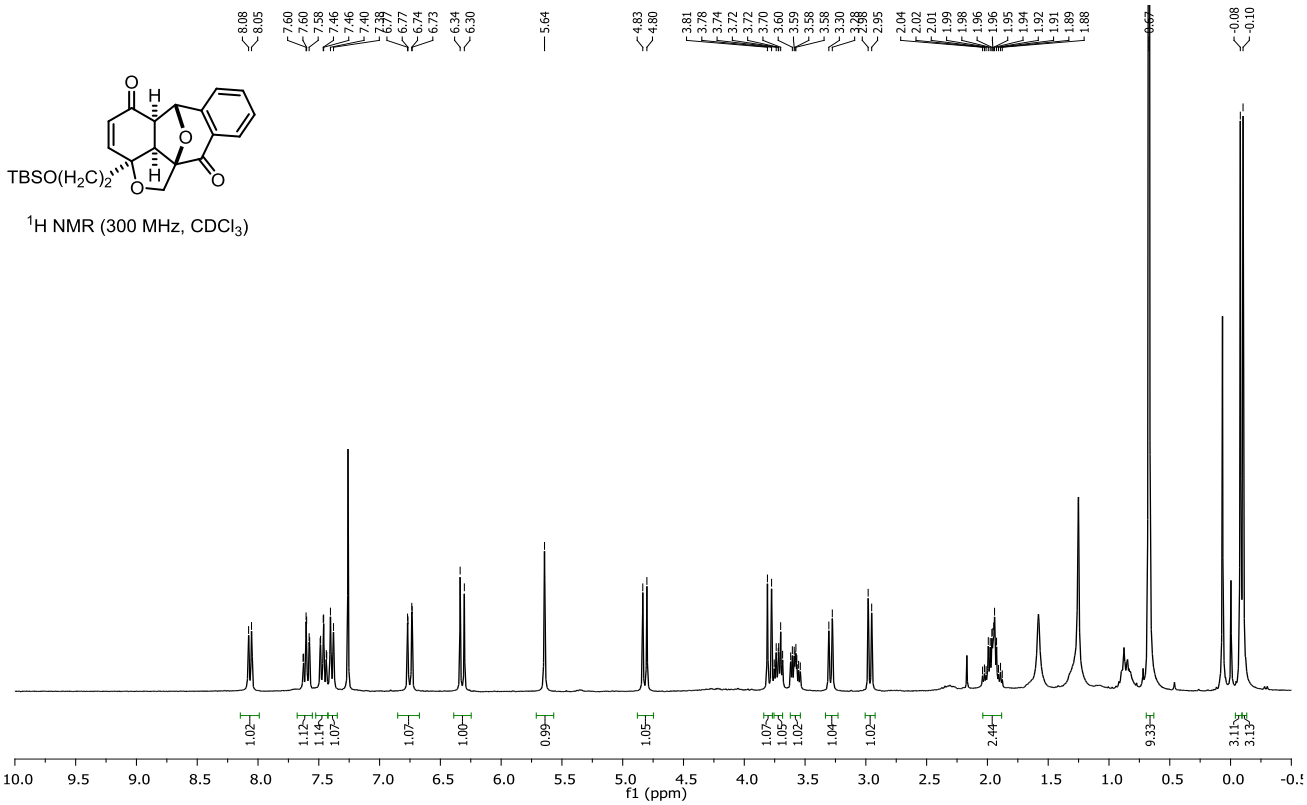


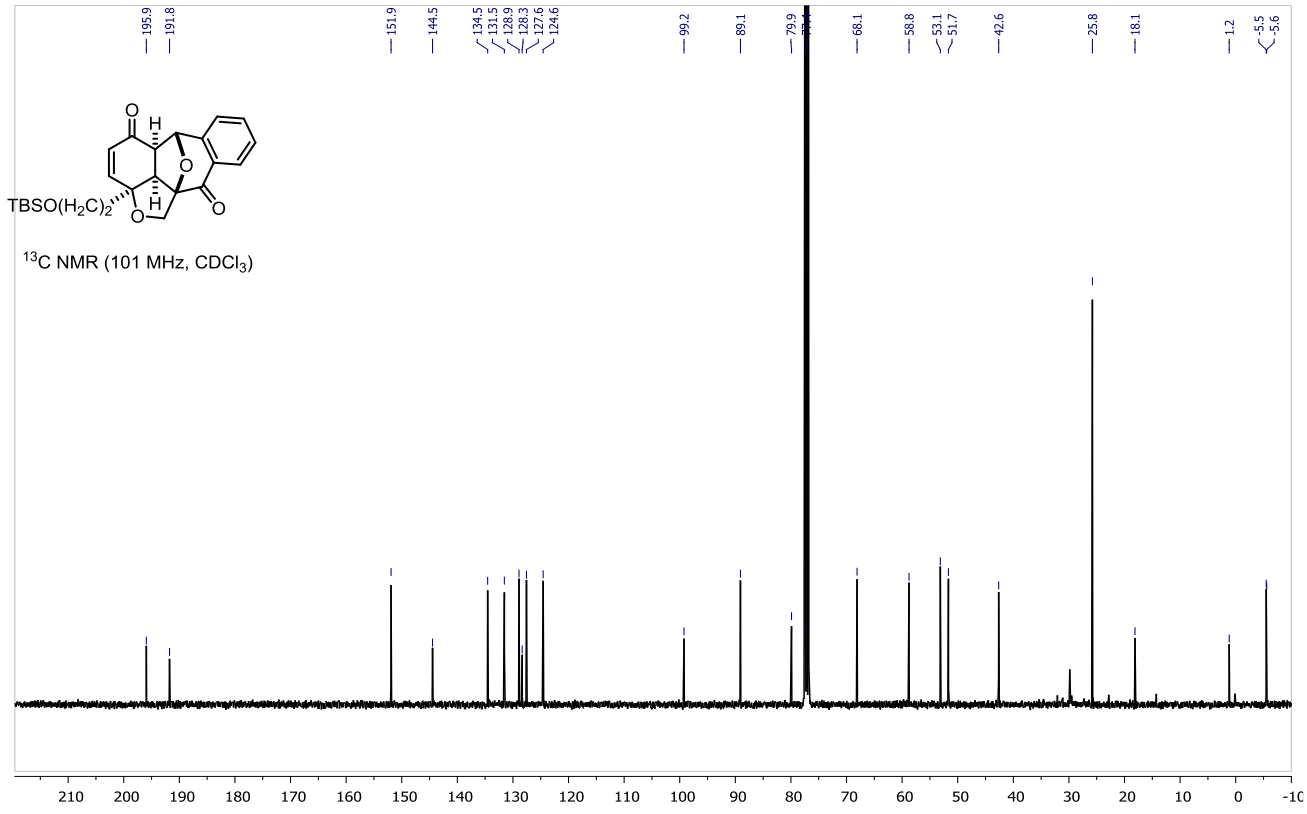
^{1}H NMR (400 MHz, $CDCl_3$)



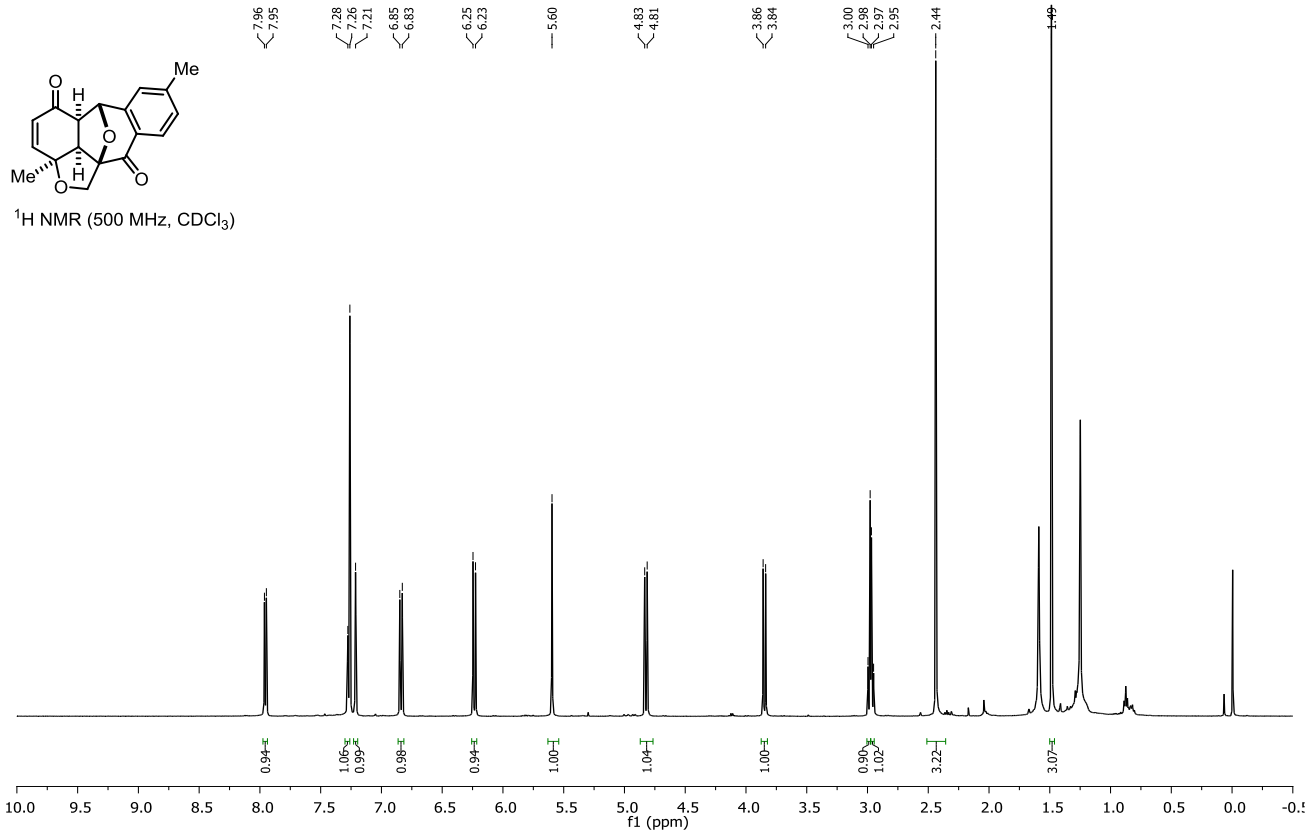
^{13}C NMR (126 MHz, $CDCl_3$)

2a-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo [5,6] cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2j):

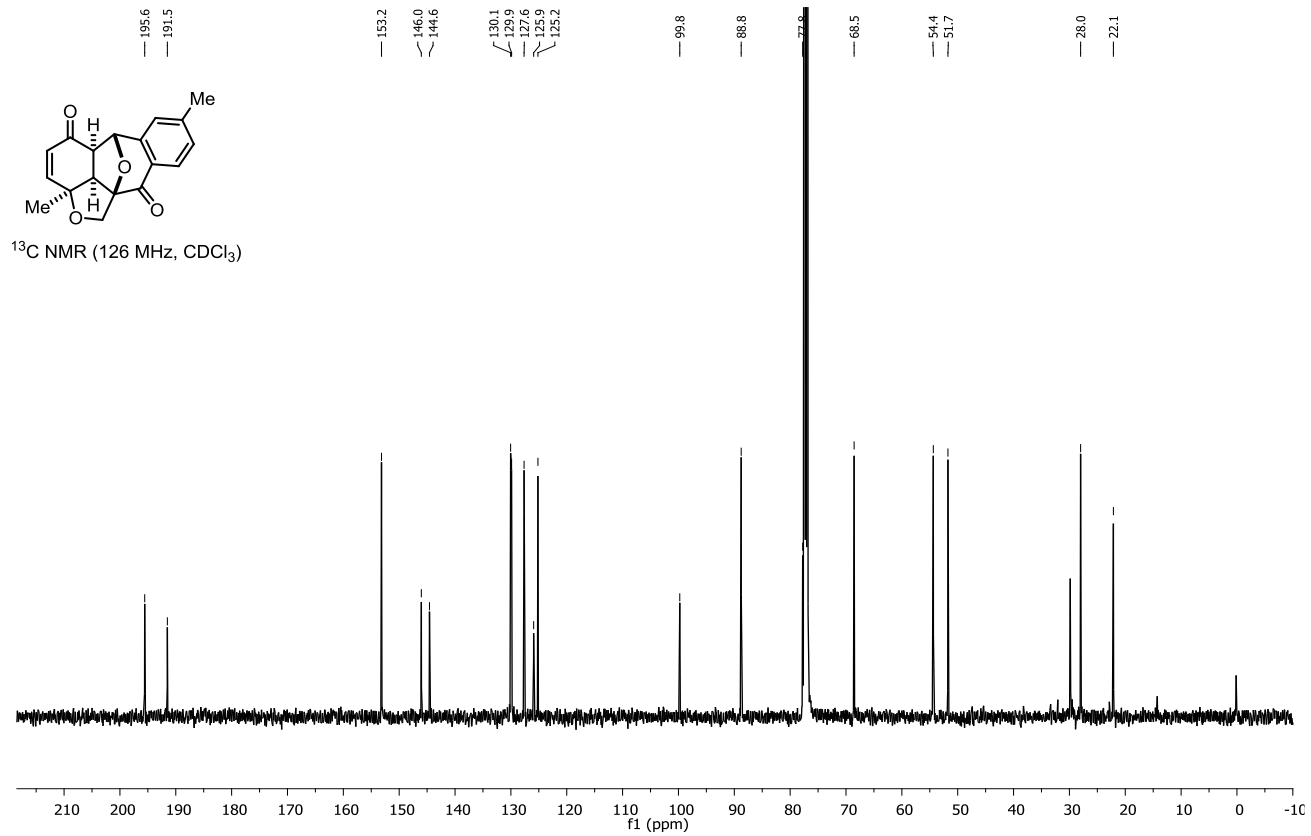




2a,8-Dimethyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2k):

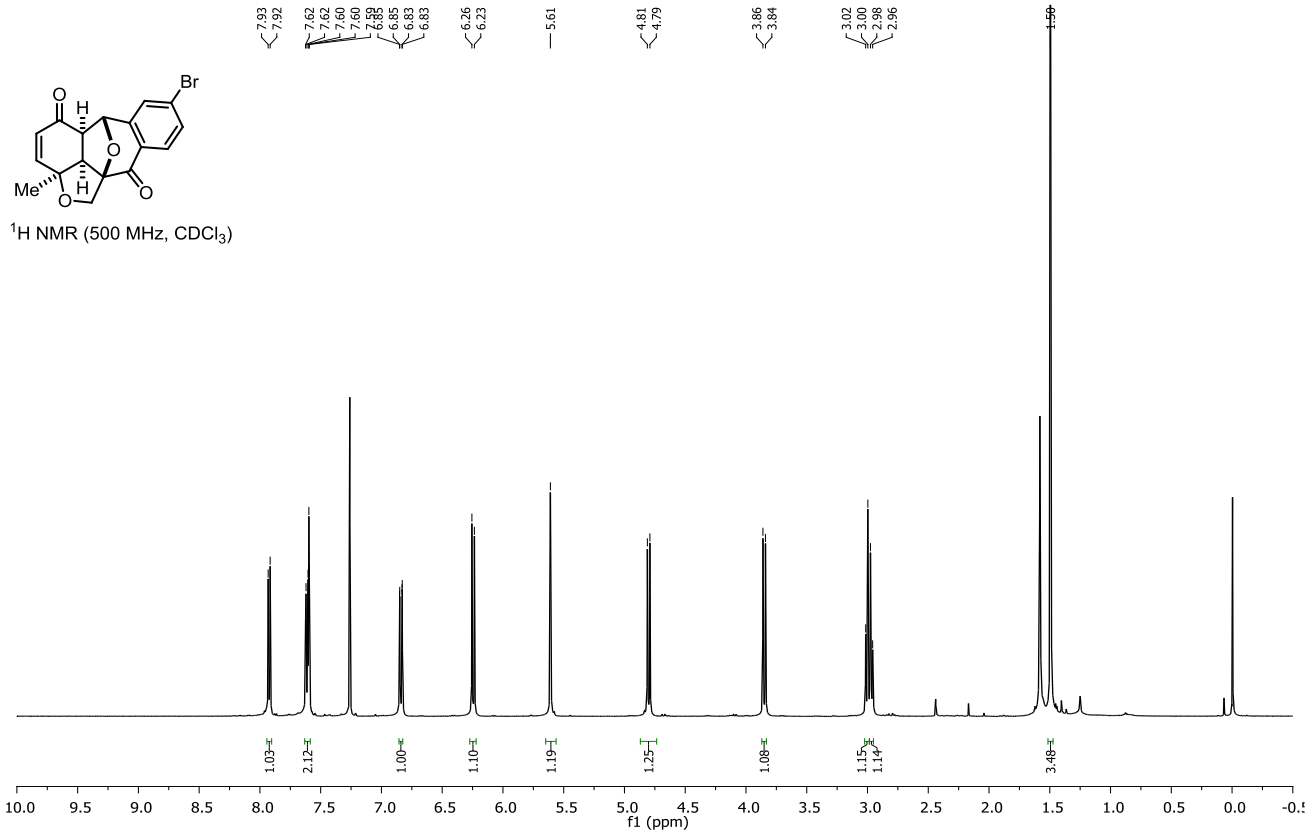


^{1}H NMR (500 MHz, $CDCl_3$)

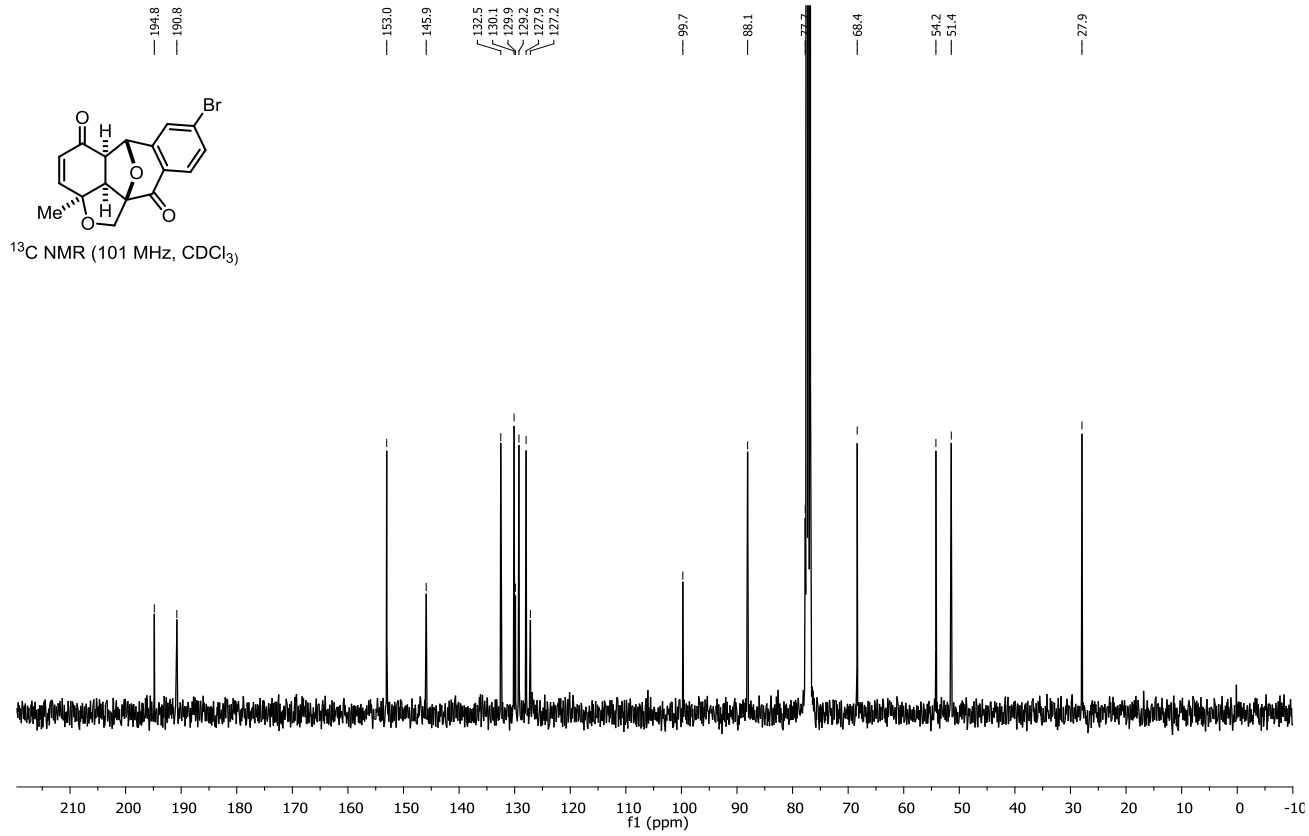


^{13}C NMR (126 MHz, $CDCl_3$)

8-Bromo-2a-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2l):

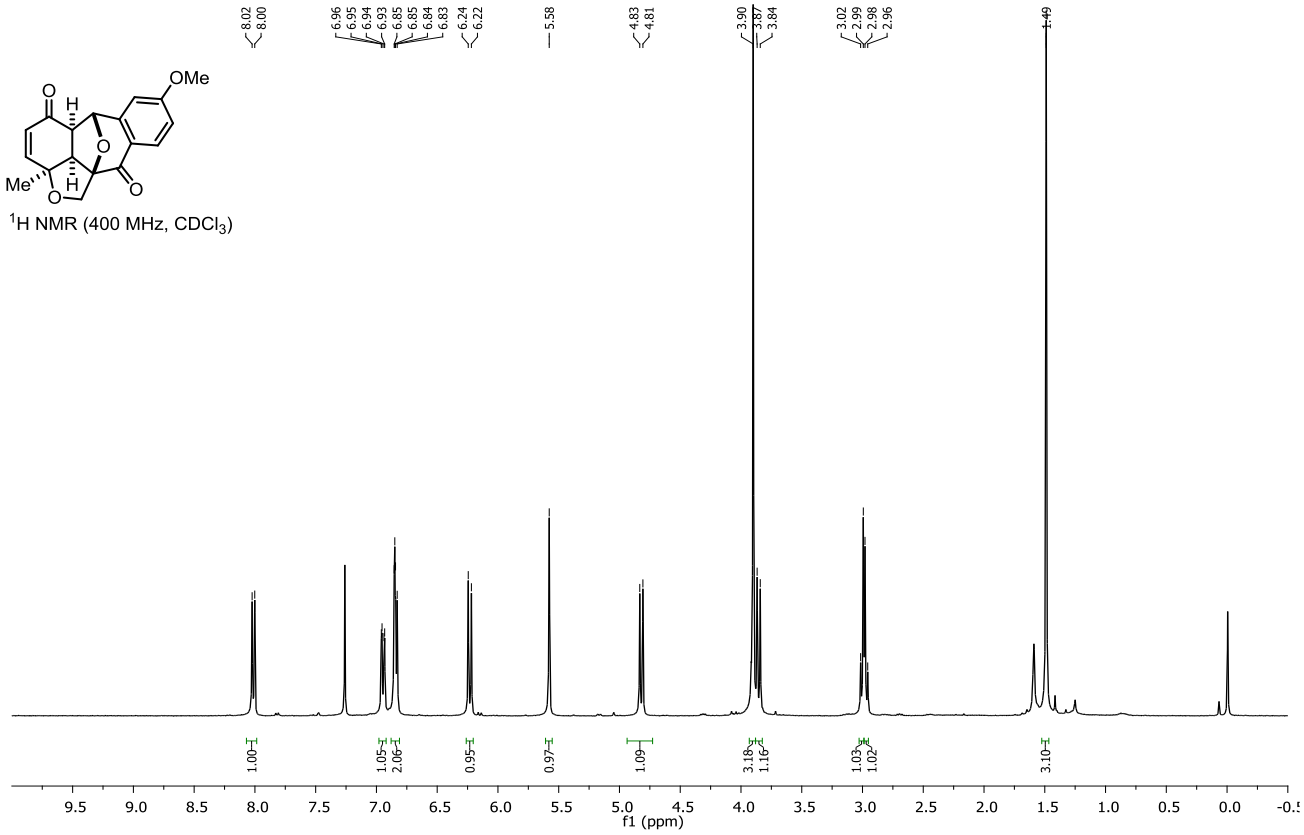


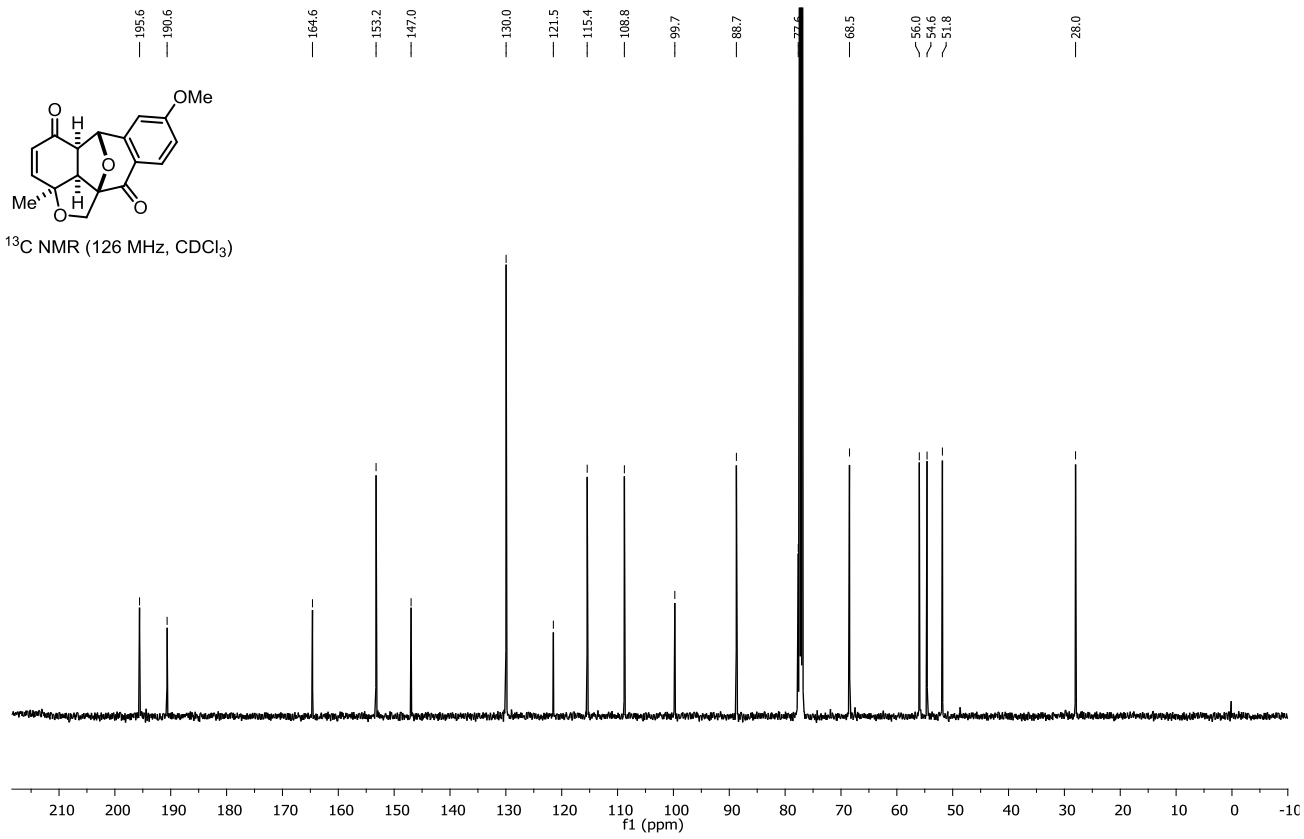
^{1}H NMR (500 MHz, $CDCl_3$)



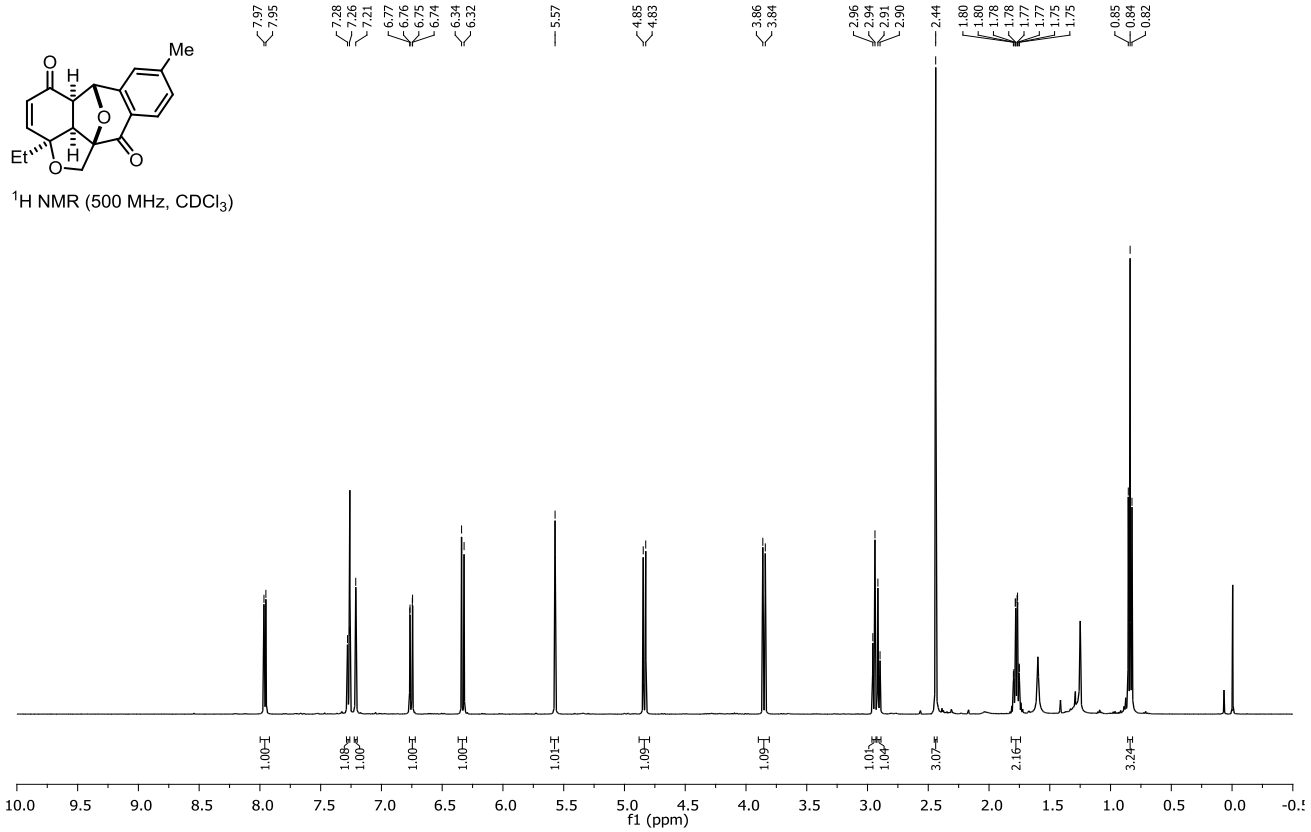
^{13}C NMR (101 MHz, $CDCl_3$)

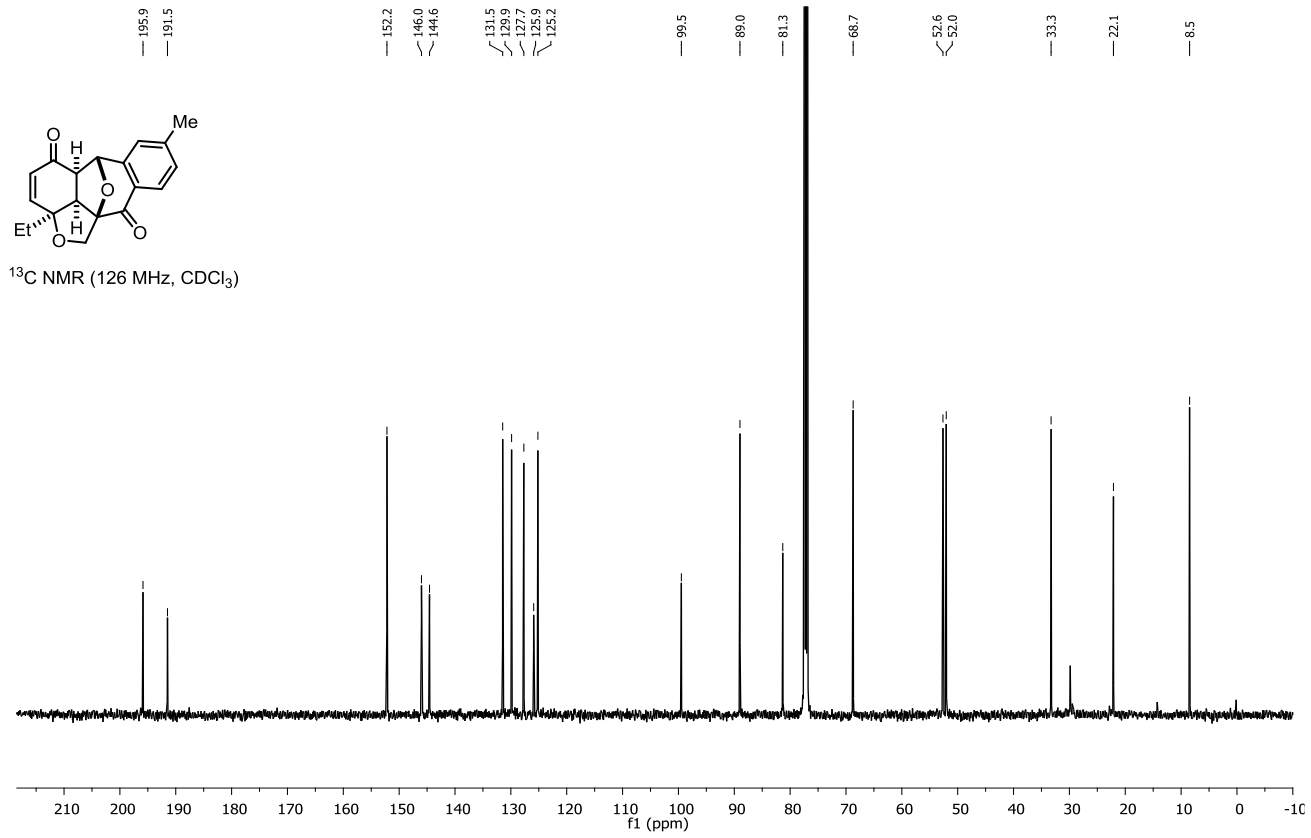
8-Methoxy-2a-methyl-2a,2a1,5a,6-tetrahydro-*1H*-6,11aepoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2m):



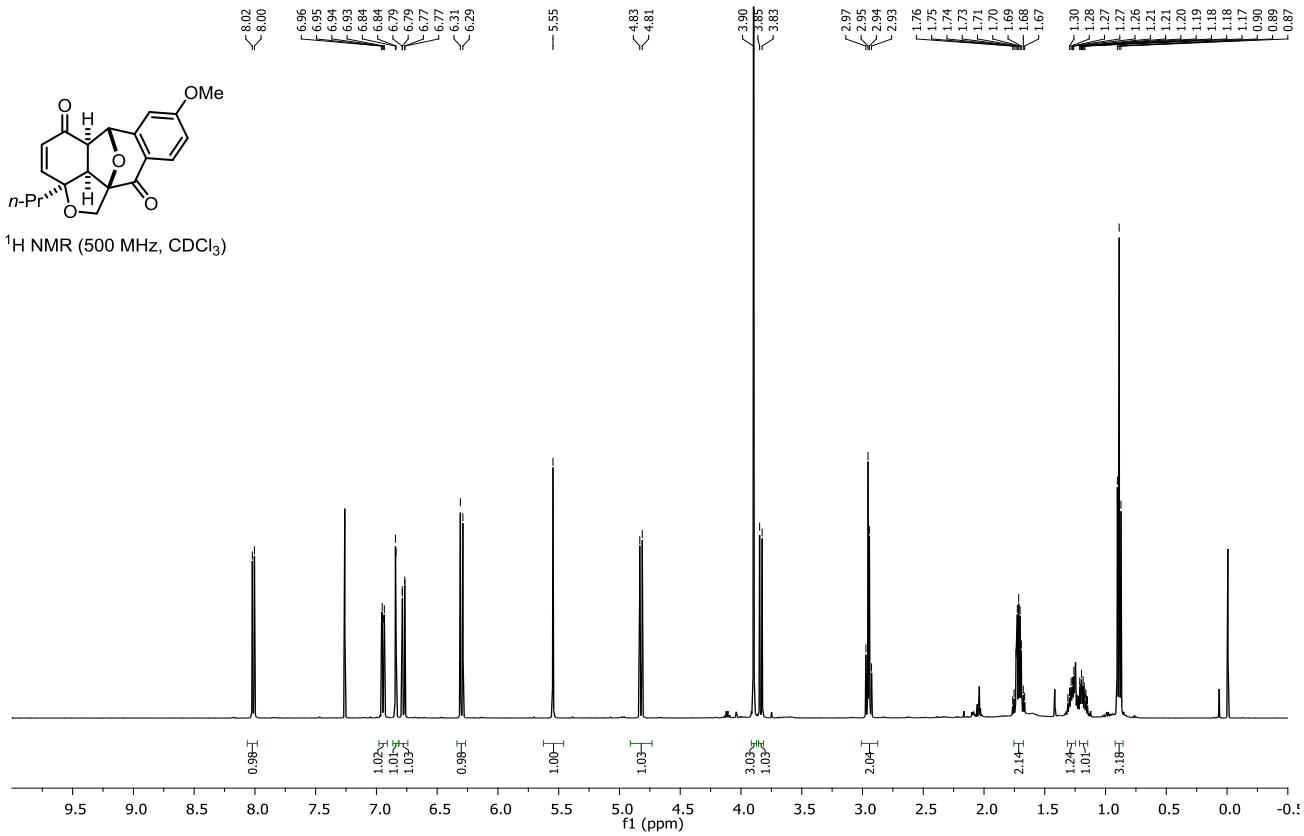


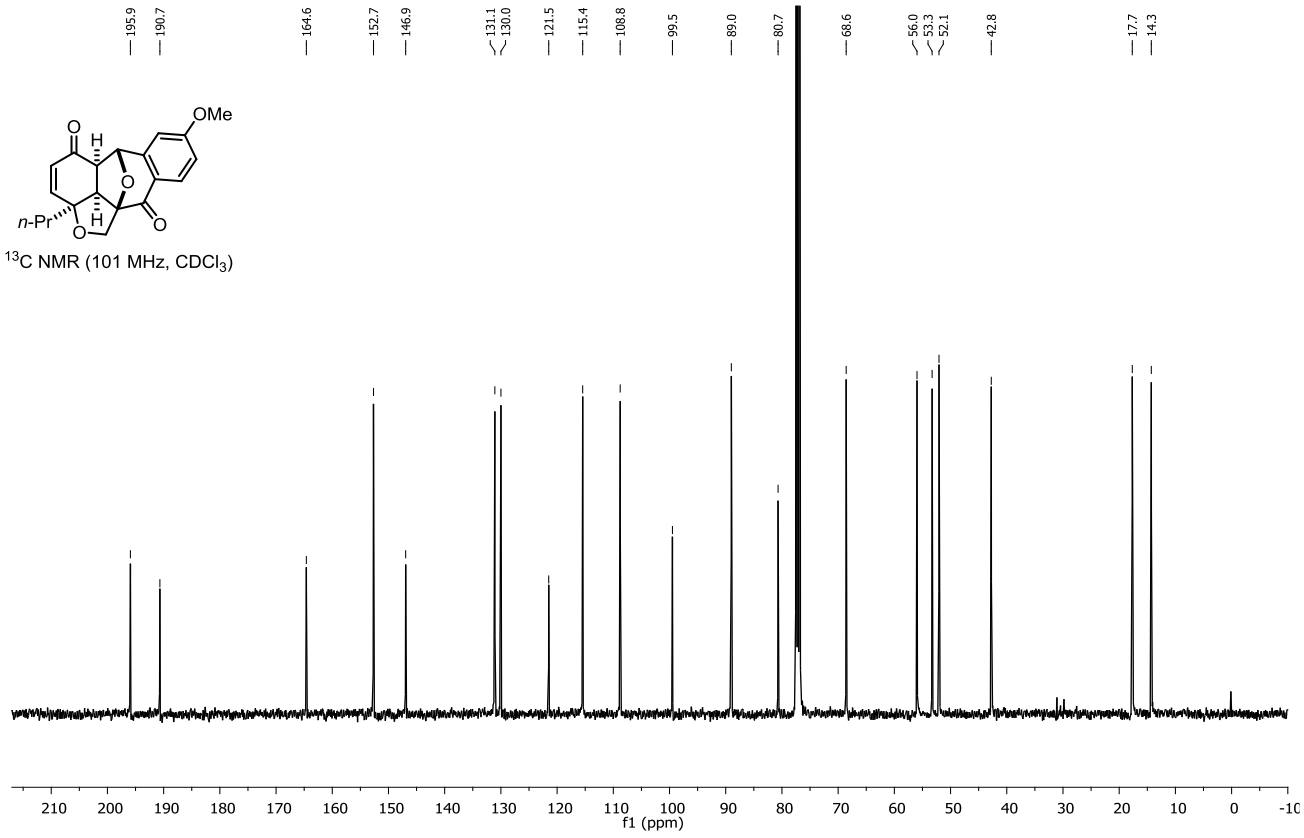
2a-Ethyl-8-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2n):



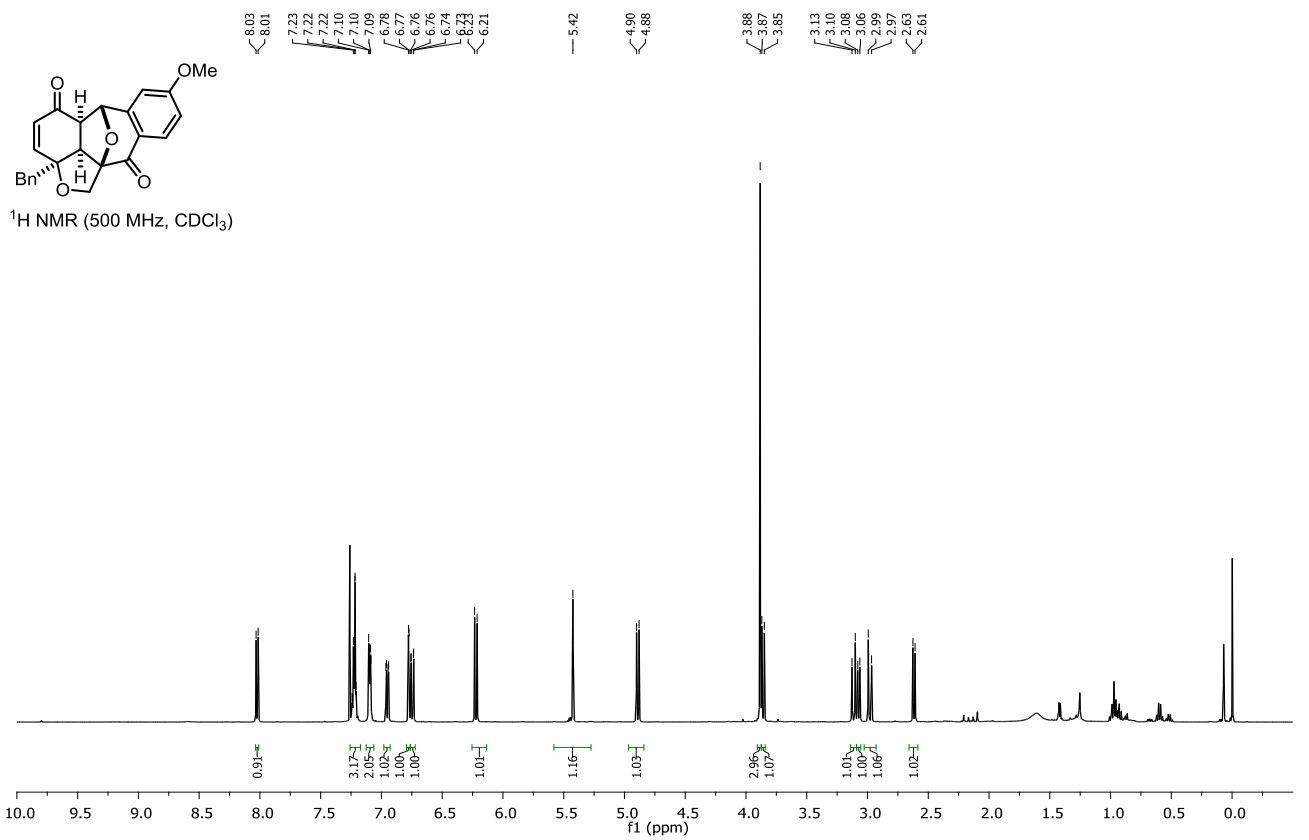


8-Methoxy-2a-propyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzo furan-5,11-dione (2o):

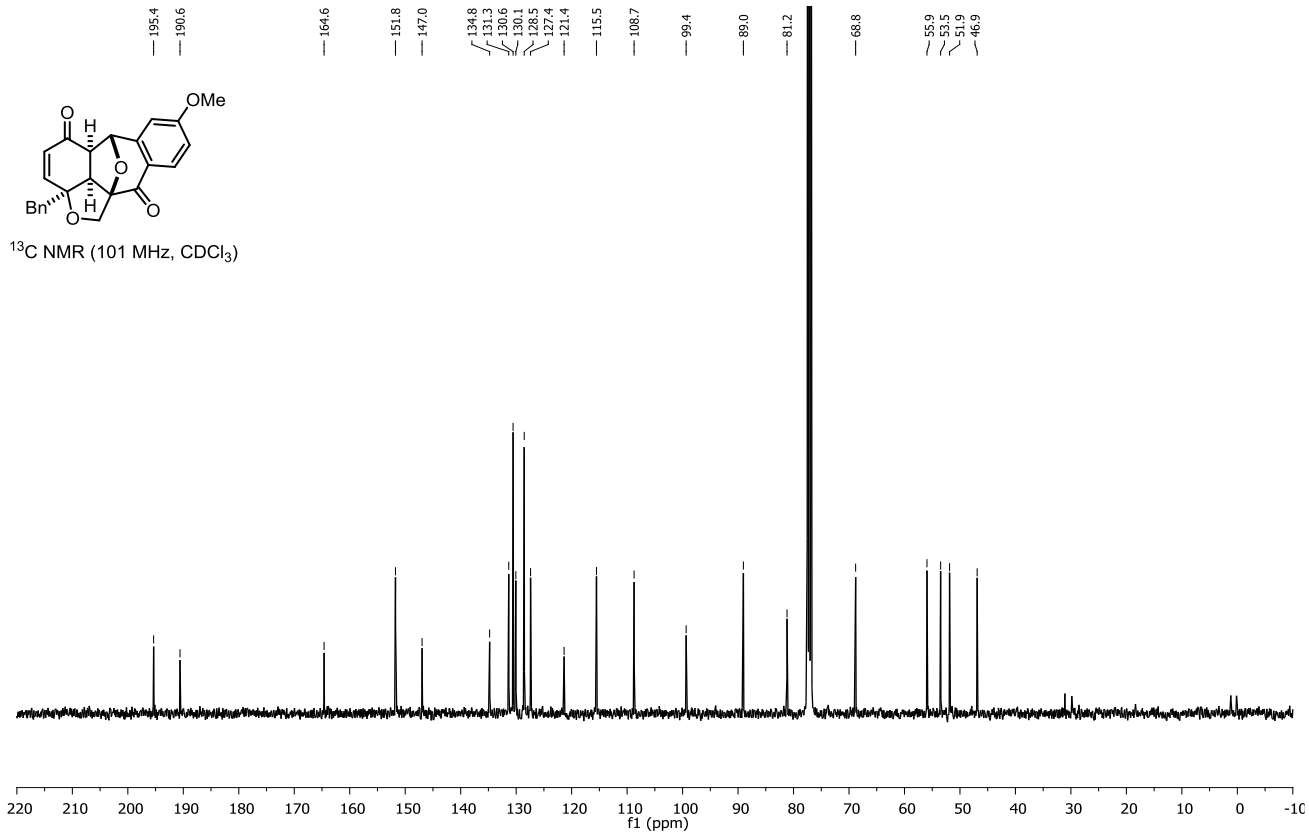




2a-Benzyl-8-methoxy-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-poxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2p):

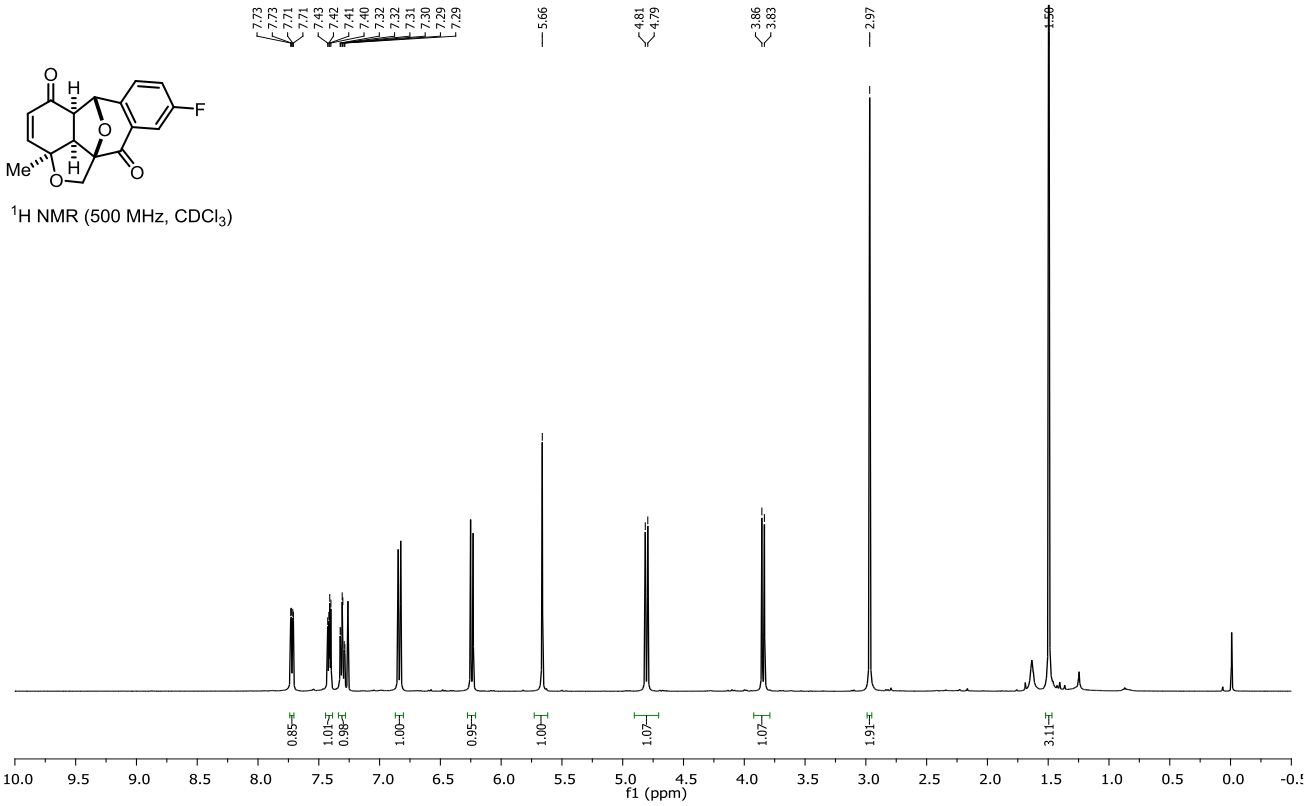


^{1}H NMR (500 MHz, $CDCl_3$)

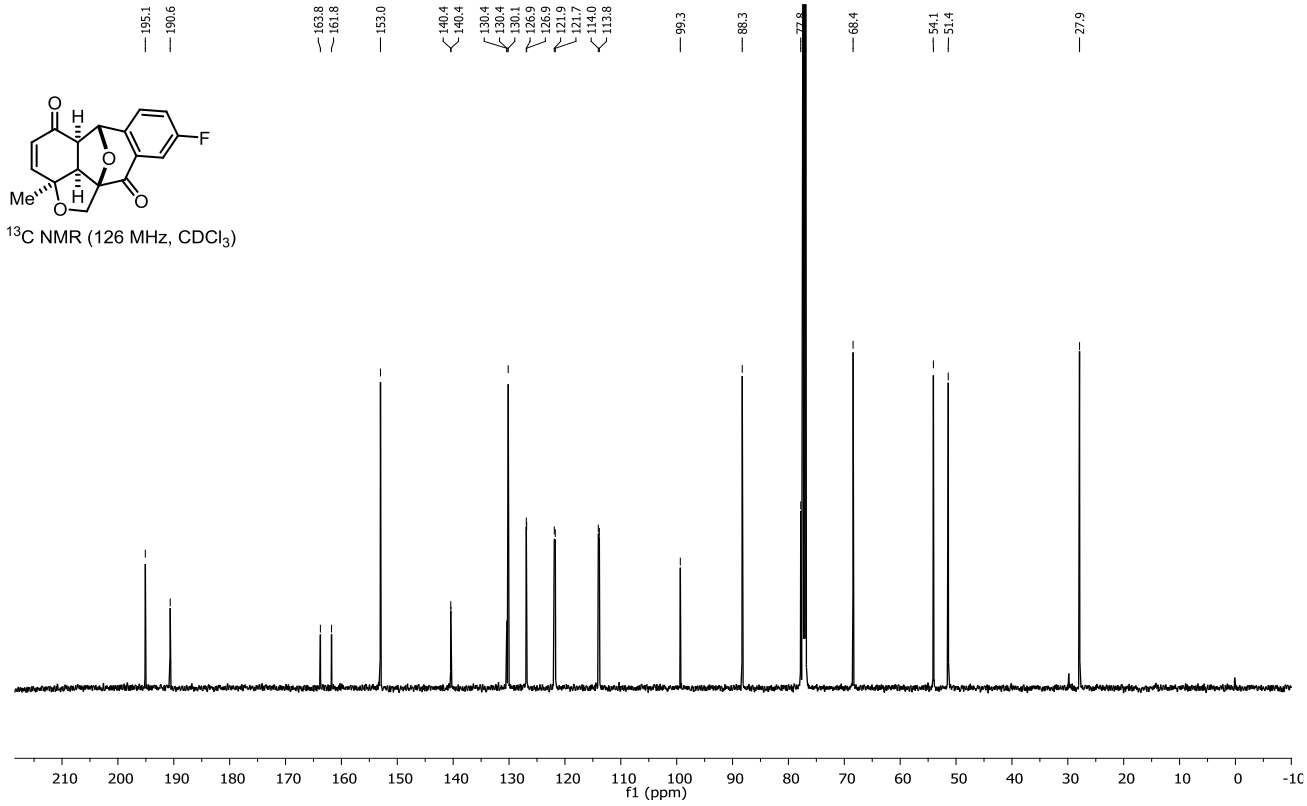


^{13}C NMR (101 MHz, $CDCl_3$)

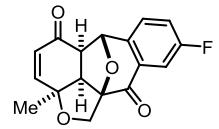
9-Fluoro-2a-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzo furan-5,11-dione (2q):



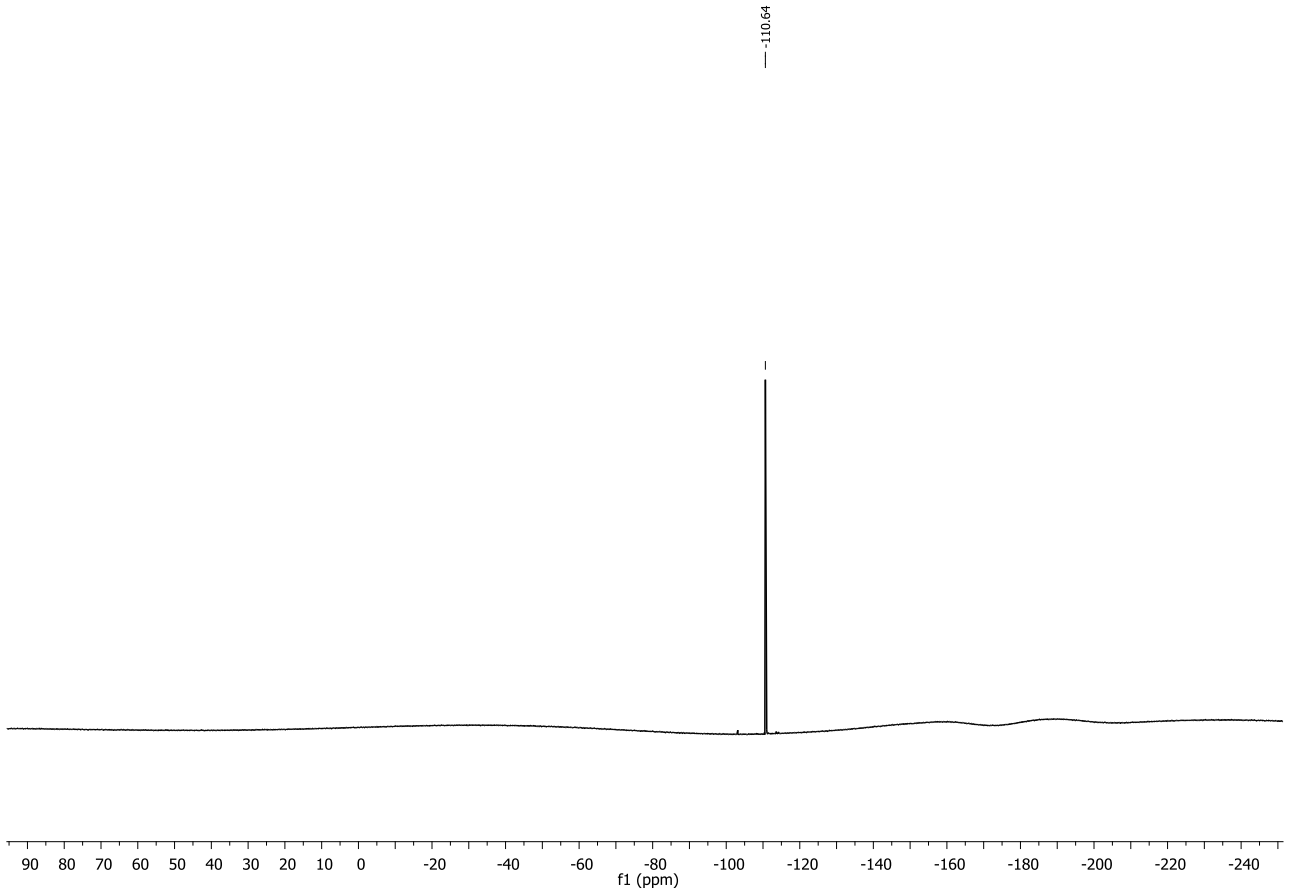
^{1}H NMR (500 MHz, $CDCl_3$)



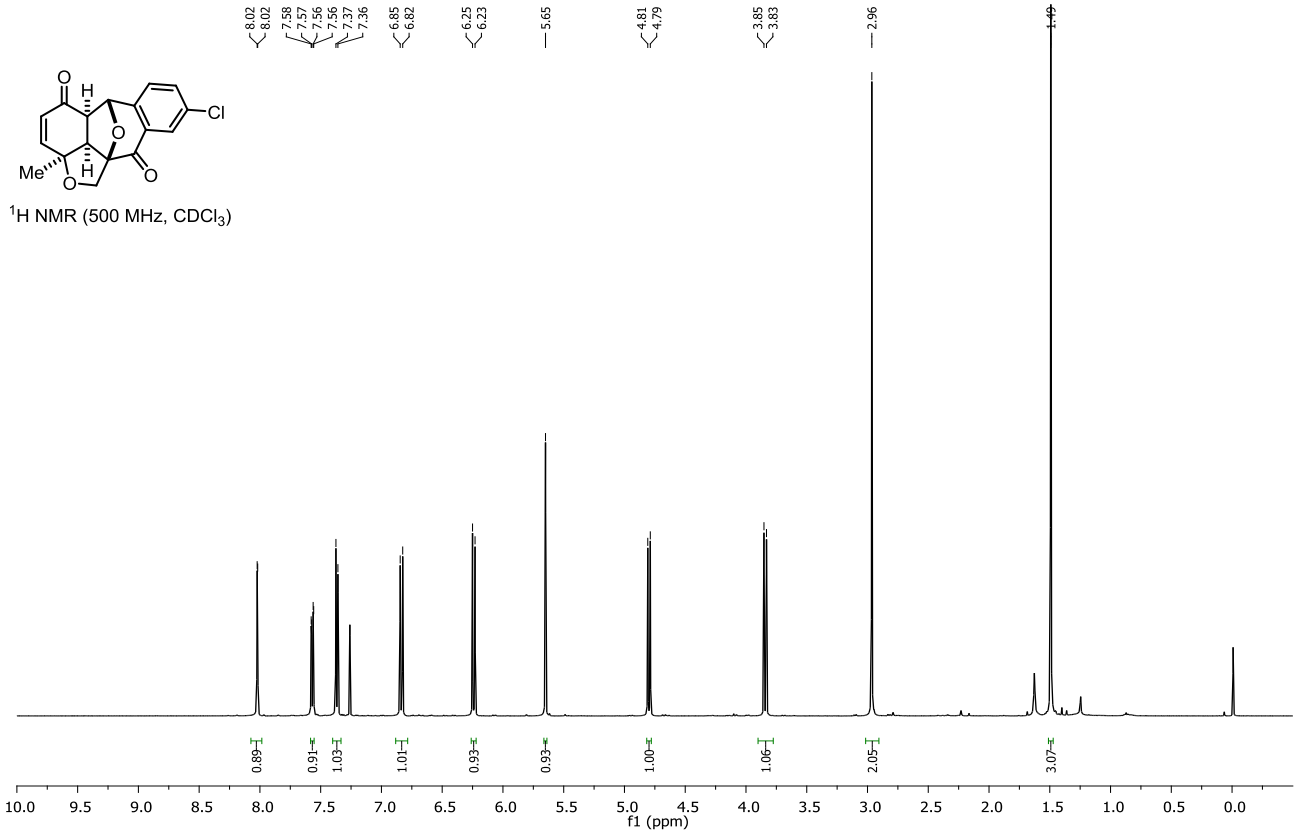
^{13}C NMR (126 MHz, $CDCl_3$)

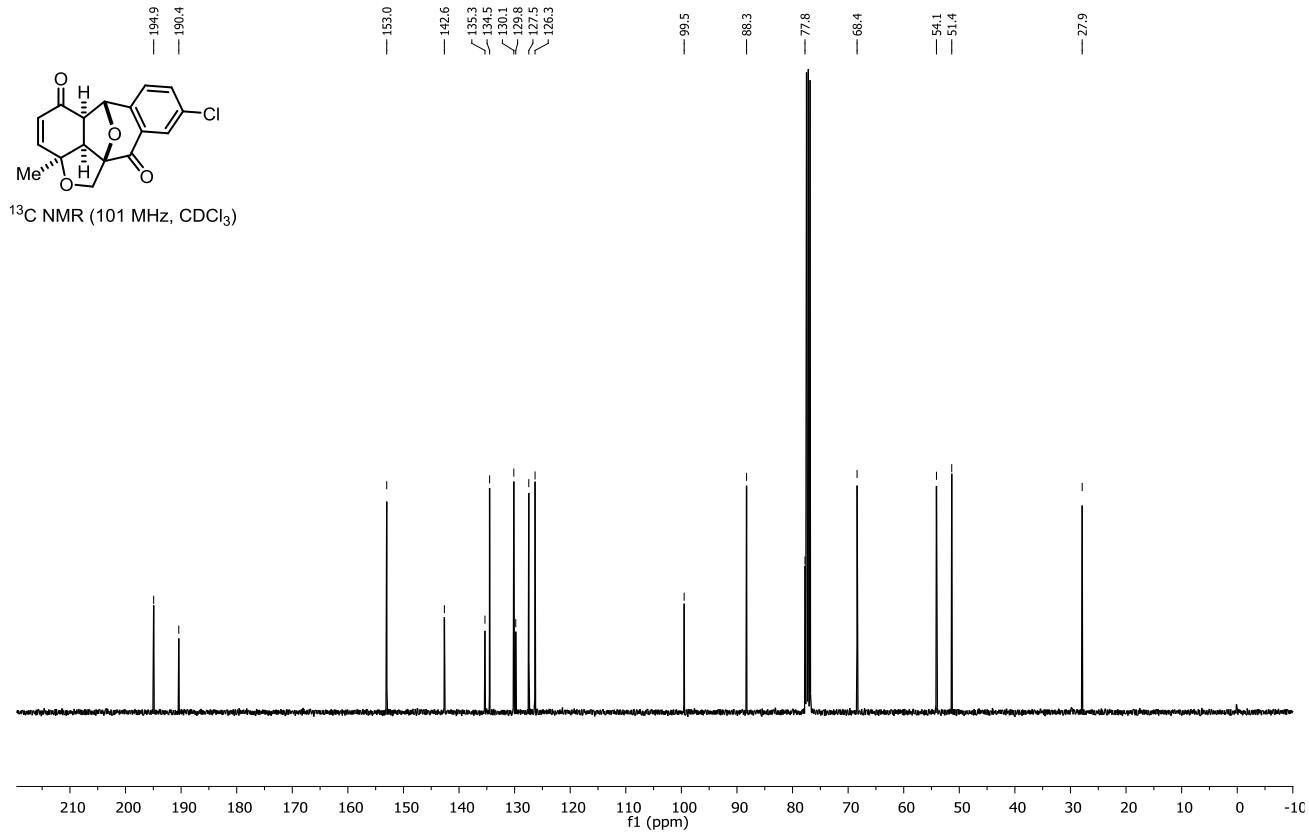


^{19}F NMR (377 MHz, $CDCl_3$)

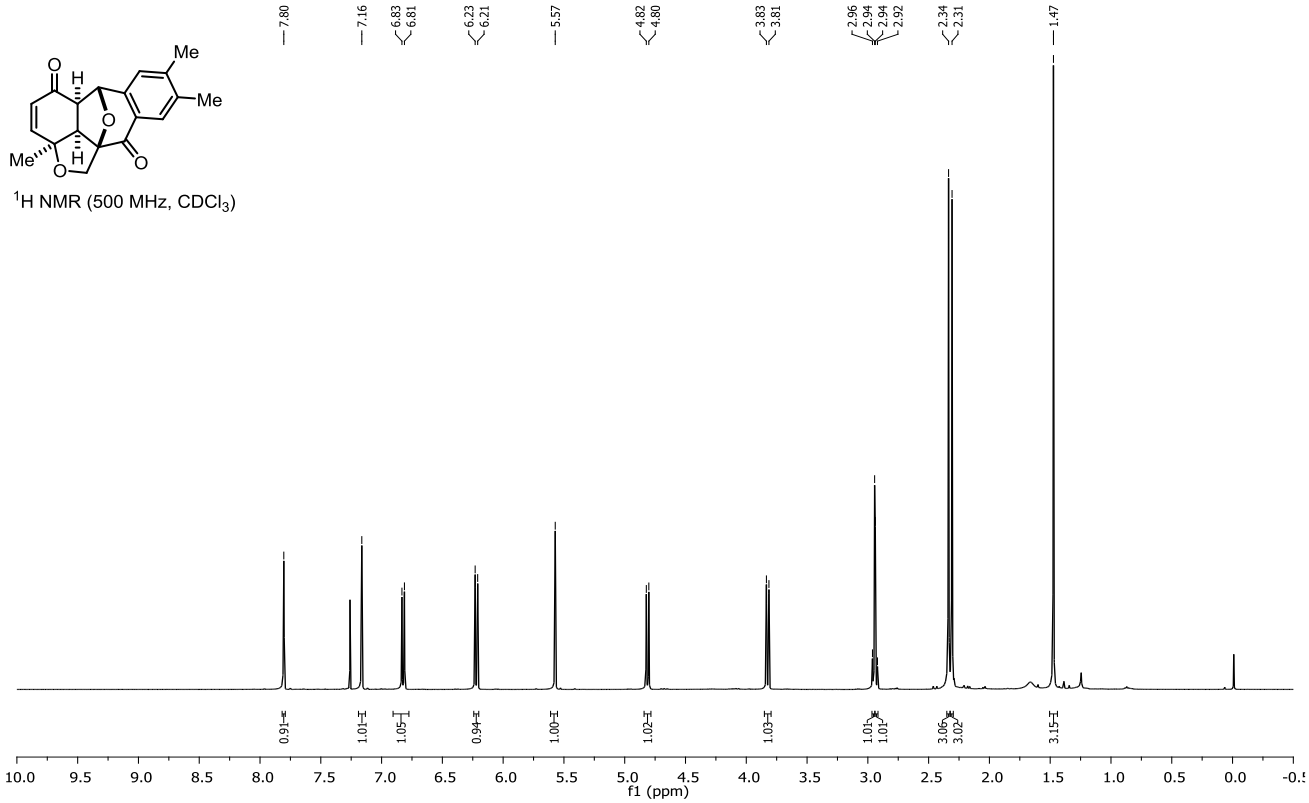


9-Chloro-2a-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzo furan-5,11-dione (2r):

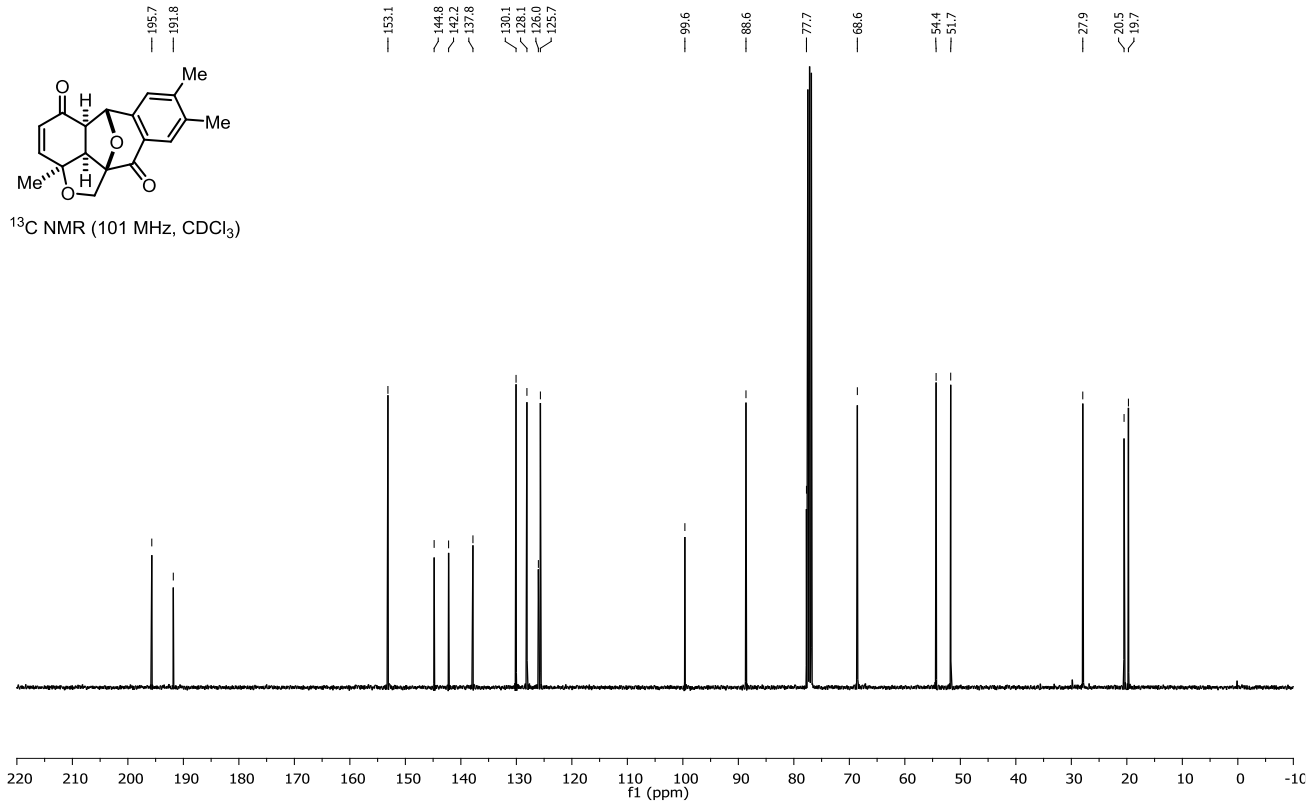




2a,8,9-Trimethyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2s):

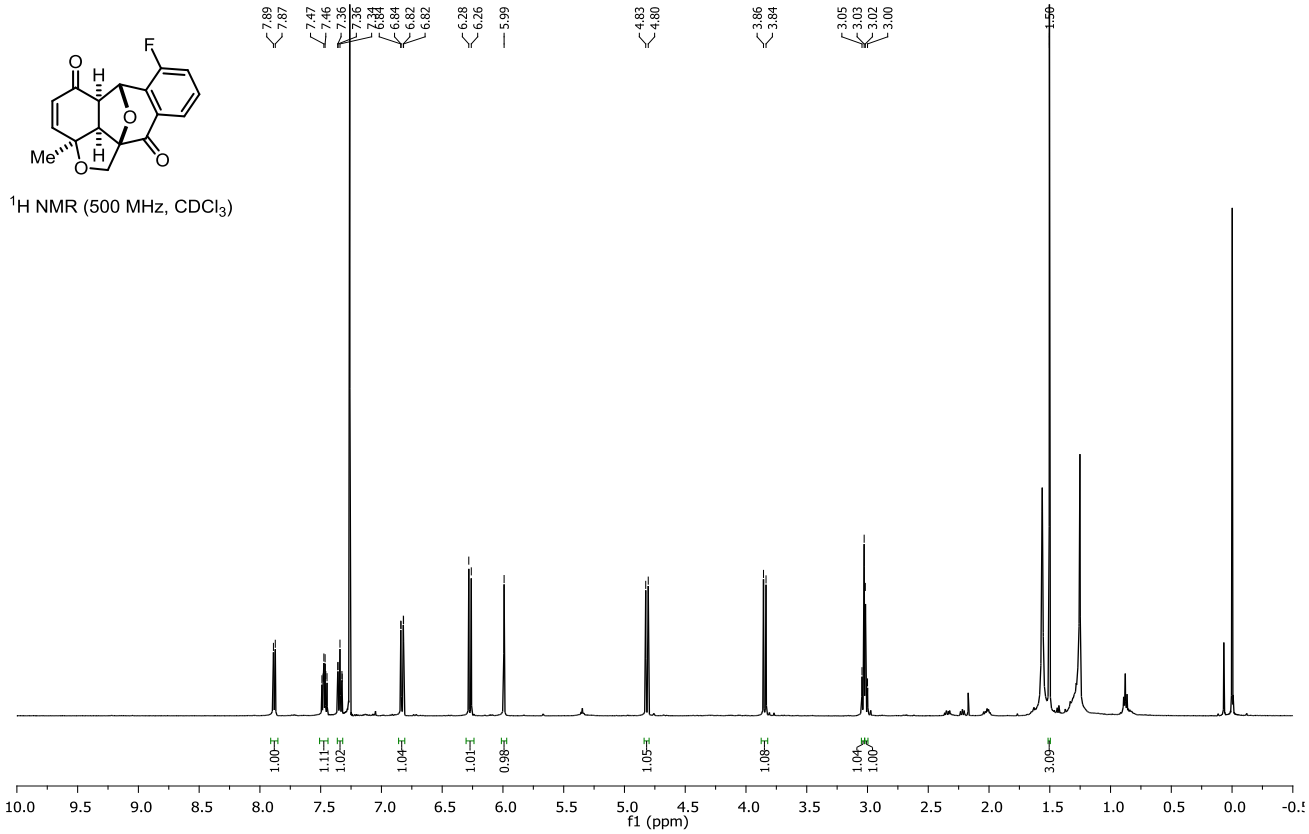


^{1}H NMR (500 MHz, $CDCl_3$)

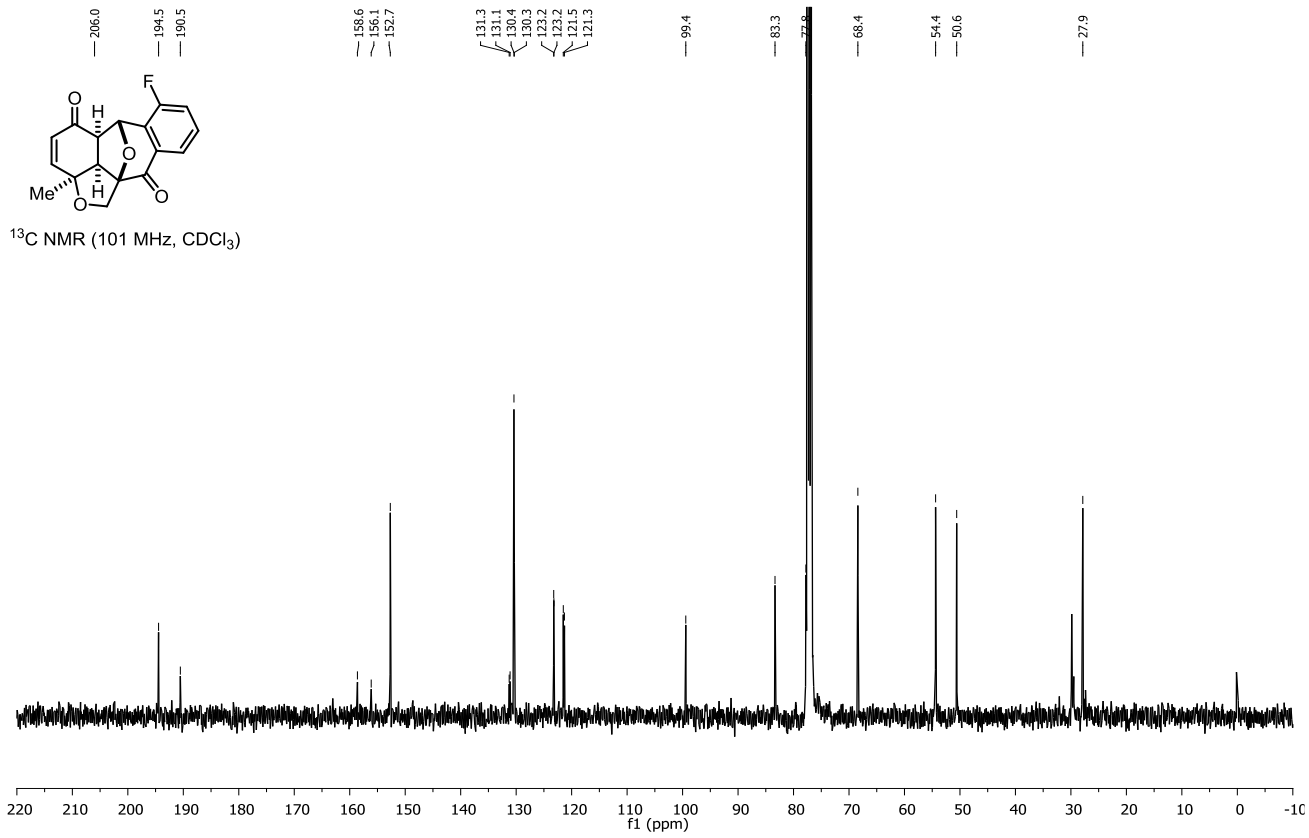


^{13}C NMR (101 MHz, $CDCl_3$)

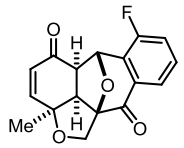
7-Fluoro-2a-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzo furan-5,11-dione (2t):



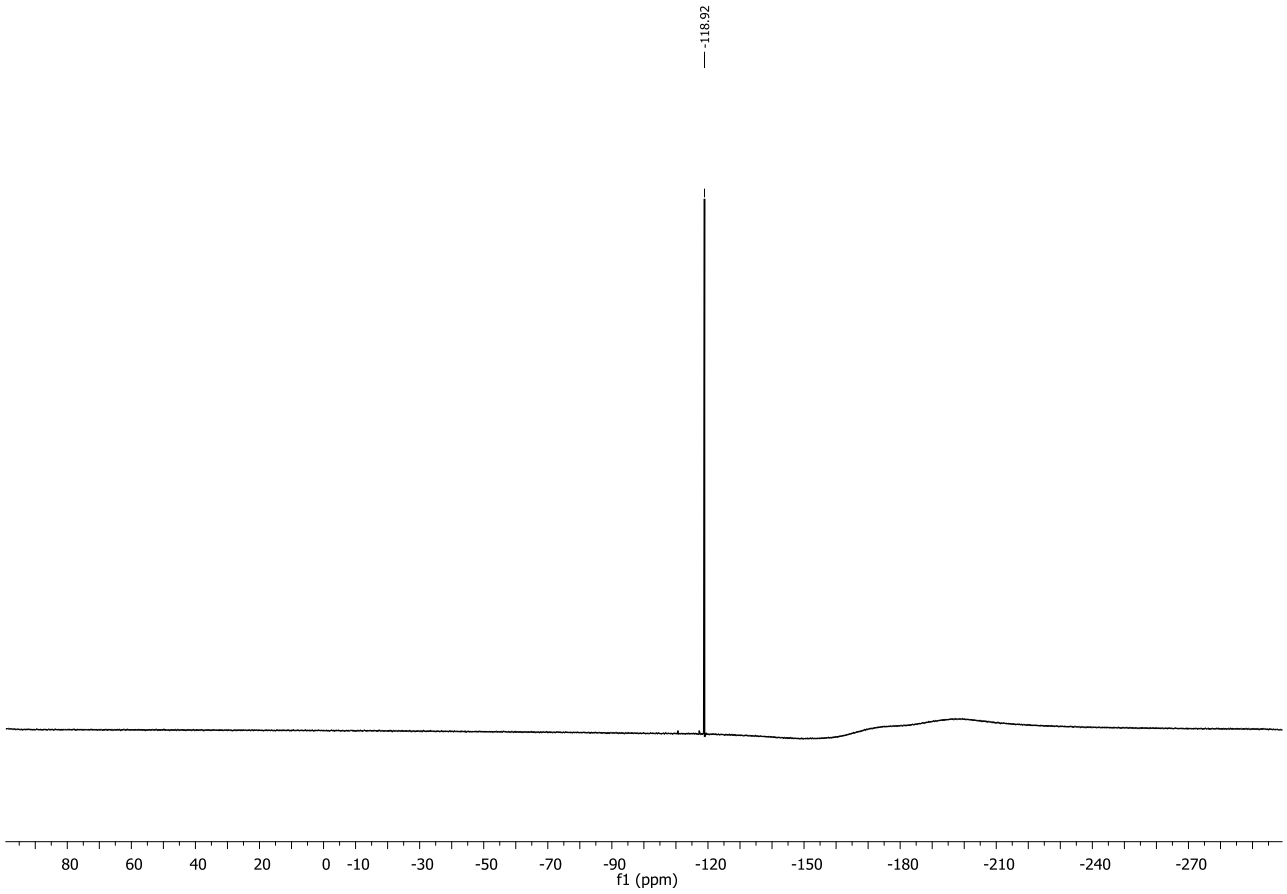
^{1}H NMR (500 MHz, $CDCl_3$)



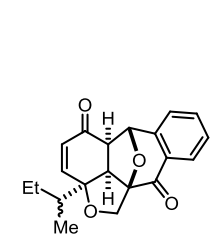
^{13}C NMR (101 MHz, $CDCl_3$)



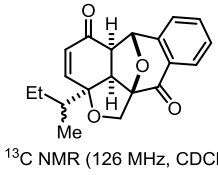
^{19}F NMR (377 MHz, $CDCl_3$)



2a-(*sec*-Butyl)-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (2u & 2u‘):

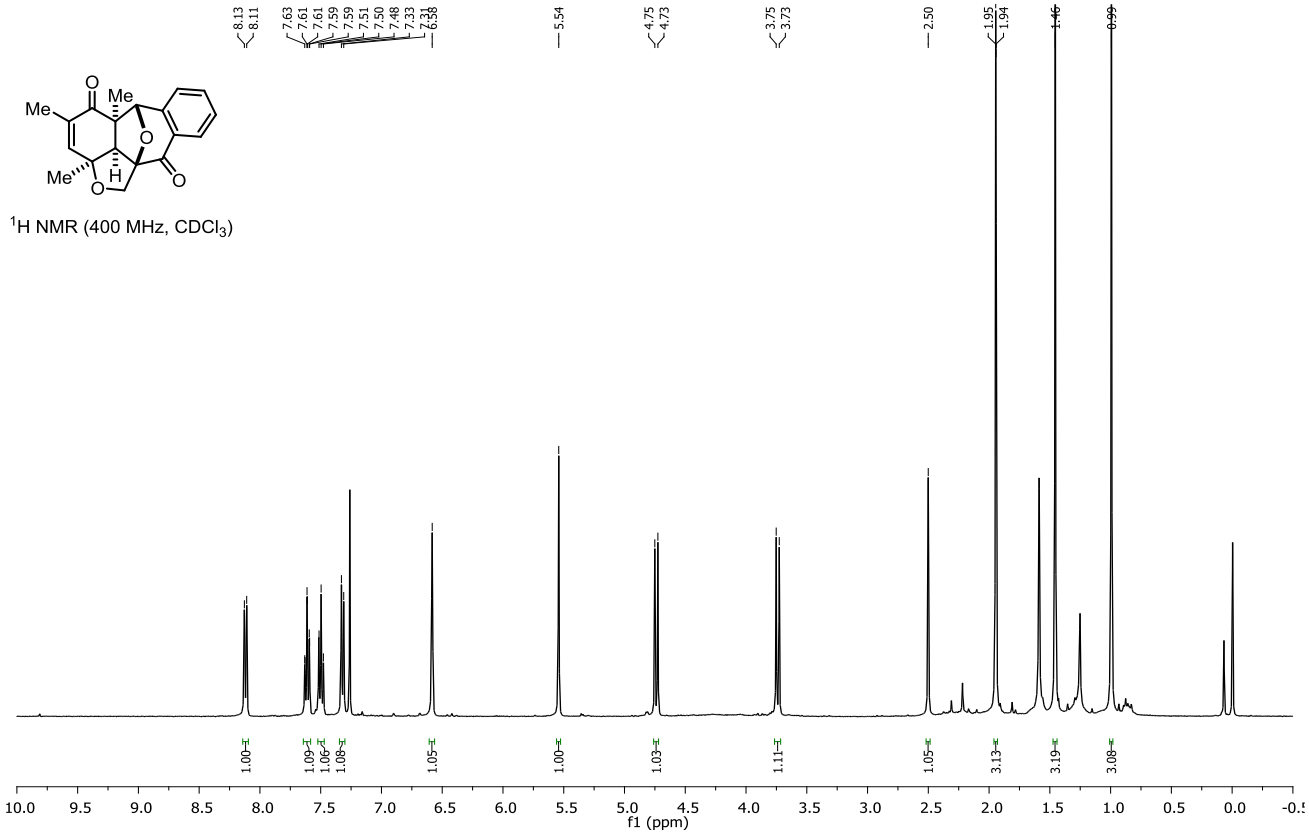


^{1}H NMR (400 MHz, $CDCl_3$)

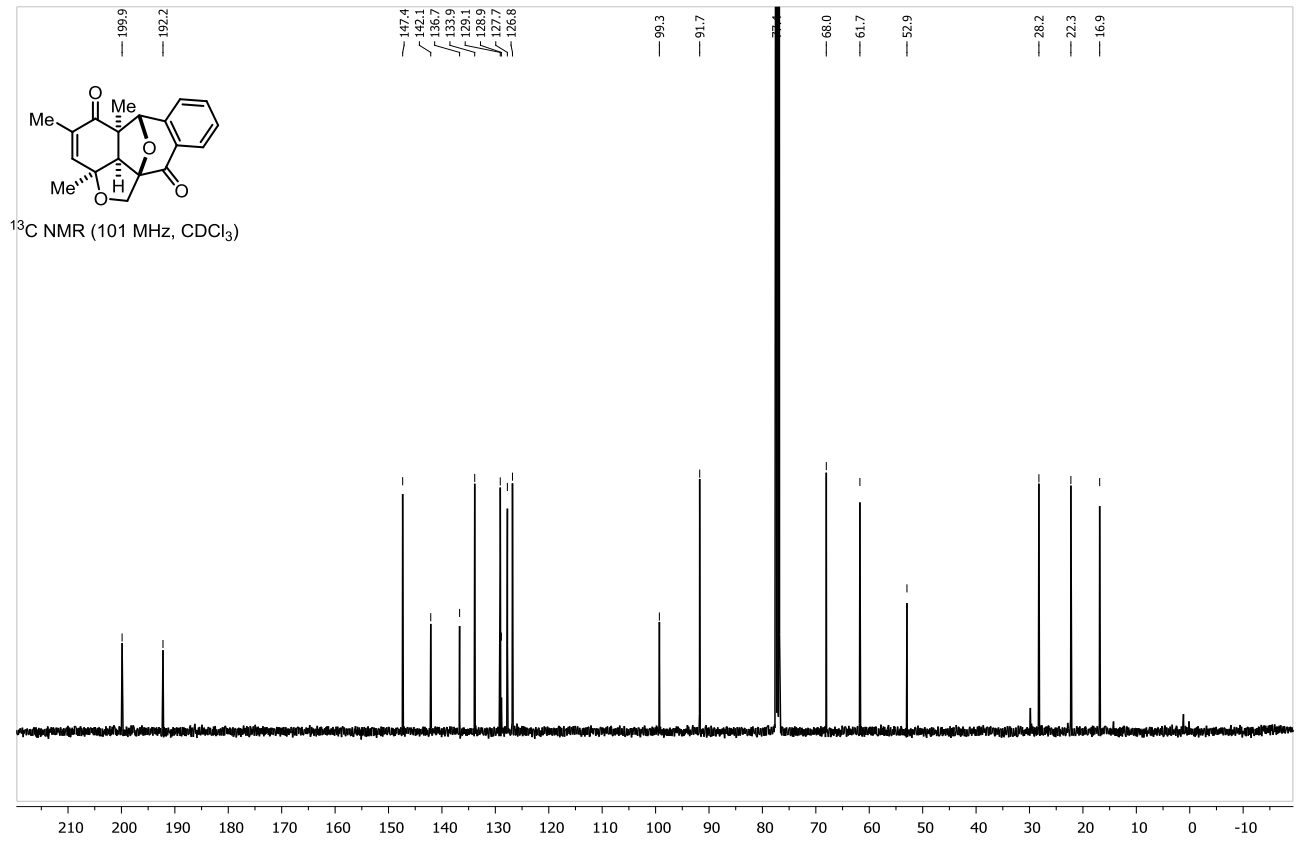


^{13}C NMR (126 MHz, $CDCl_3$)

2a,4,5a-Trimethyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione 2v):

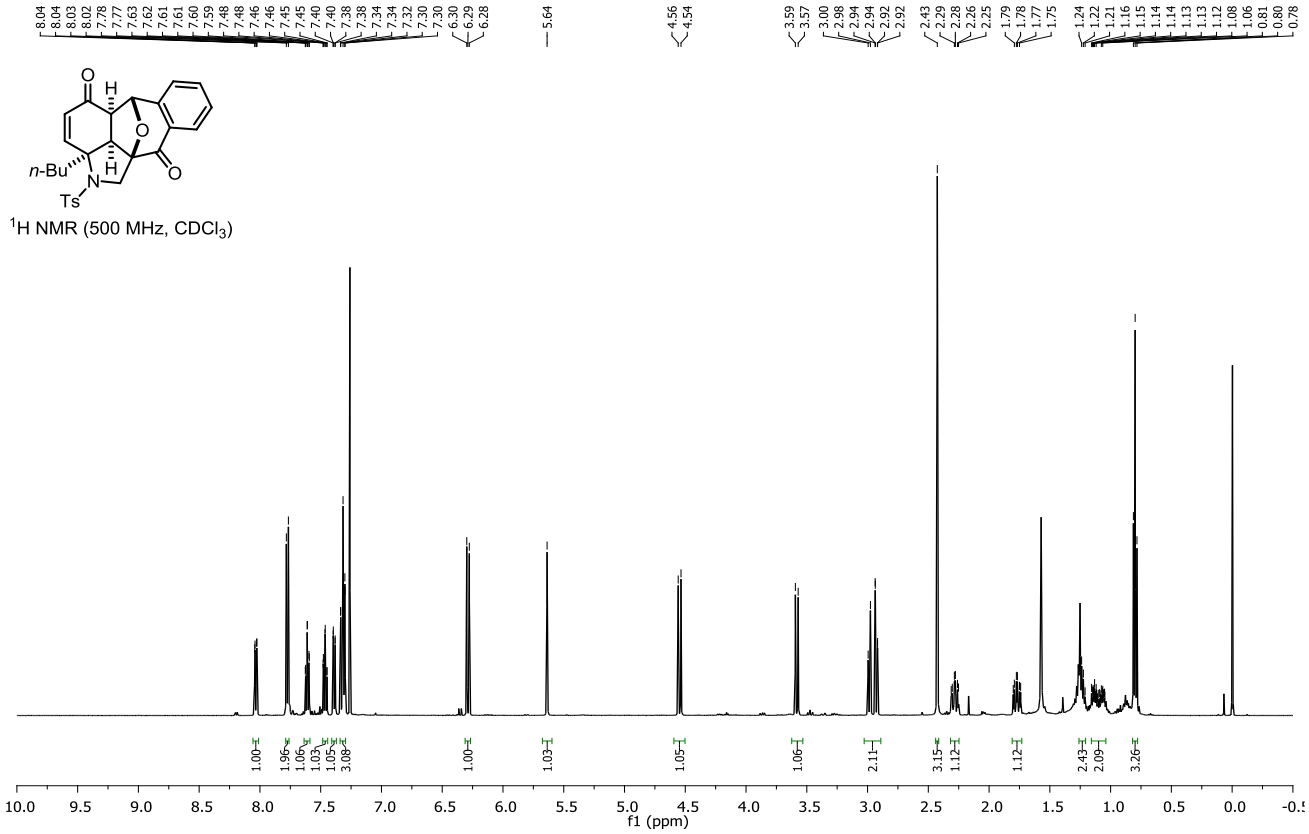


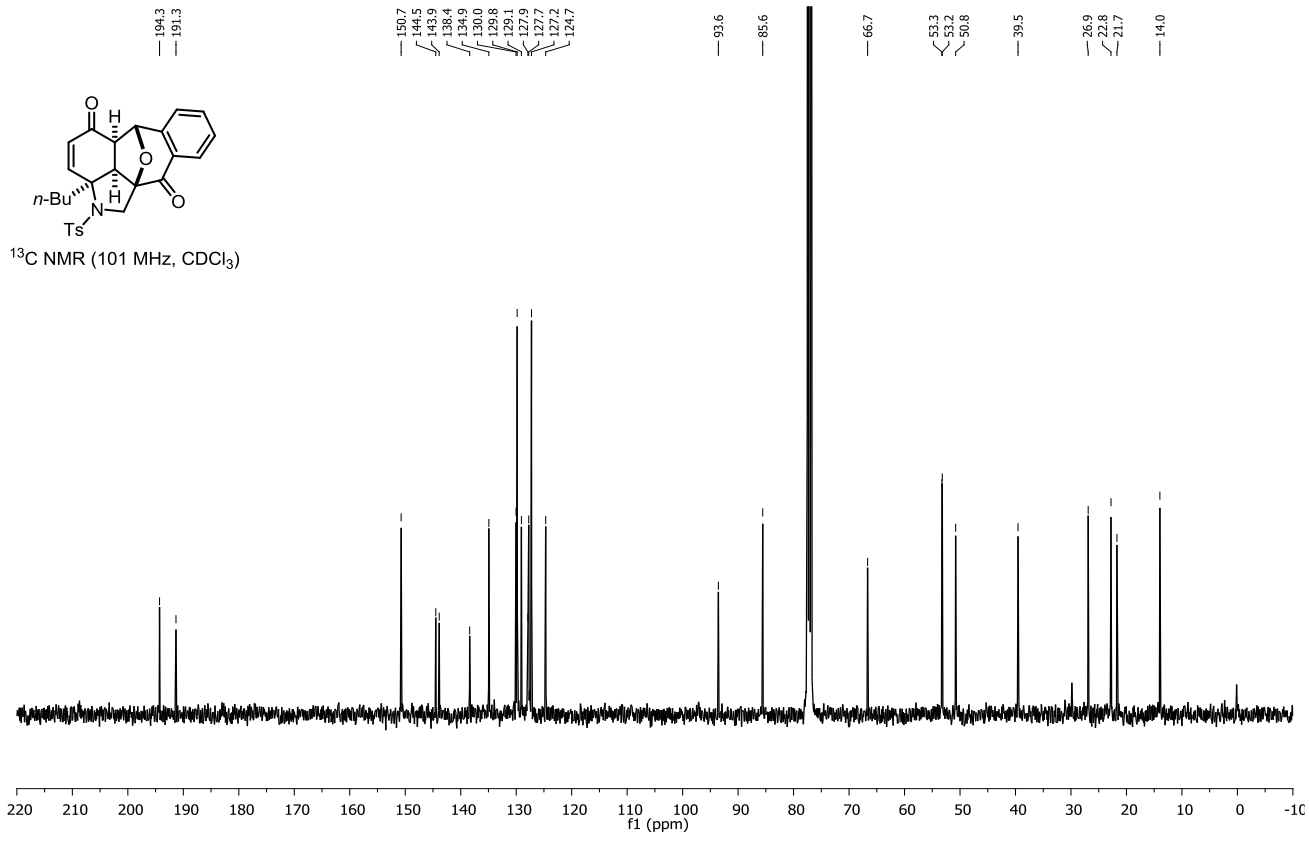
^{1}H NMR (400 MHz, $CDCl_3$)



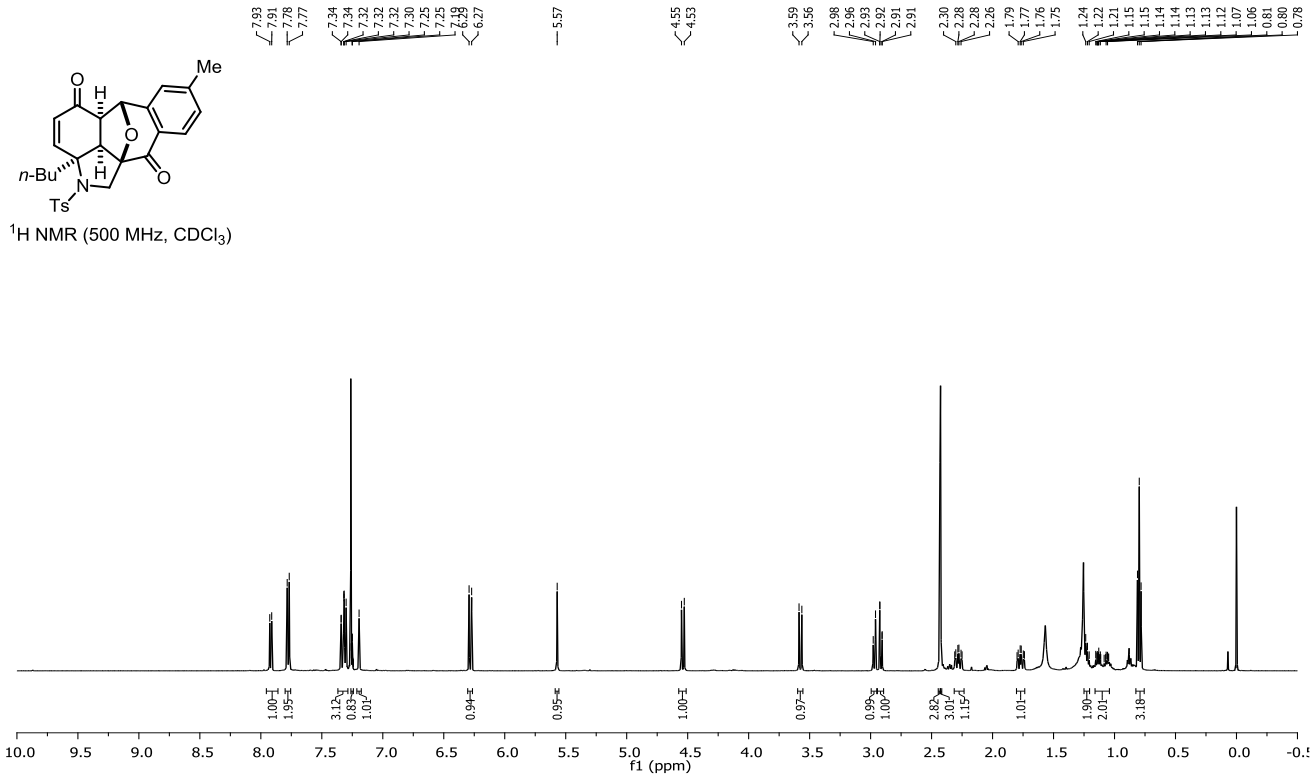
^{13}C NMR (101 MHz, $CDCl_3$)

2a-Butyl-2-tosyl-1,2,2a,,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]indole-5,11-dione (4a):

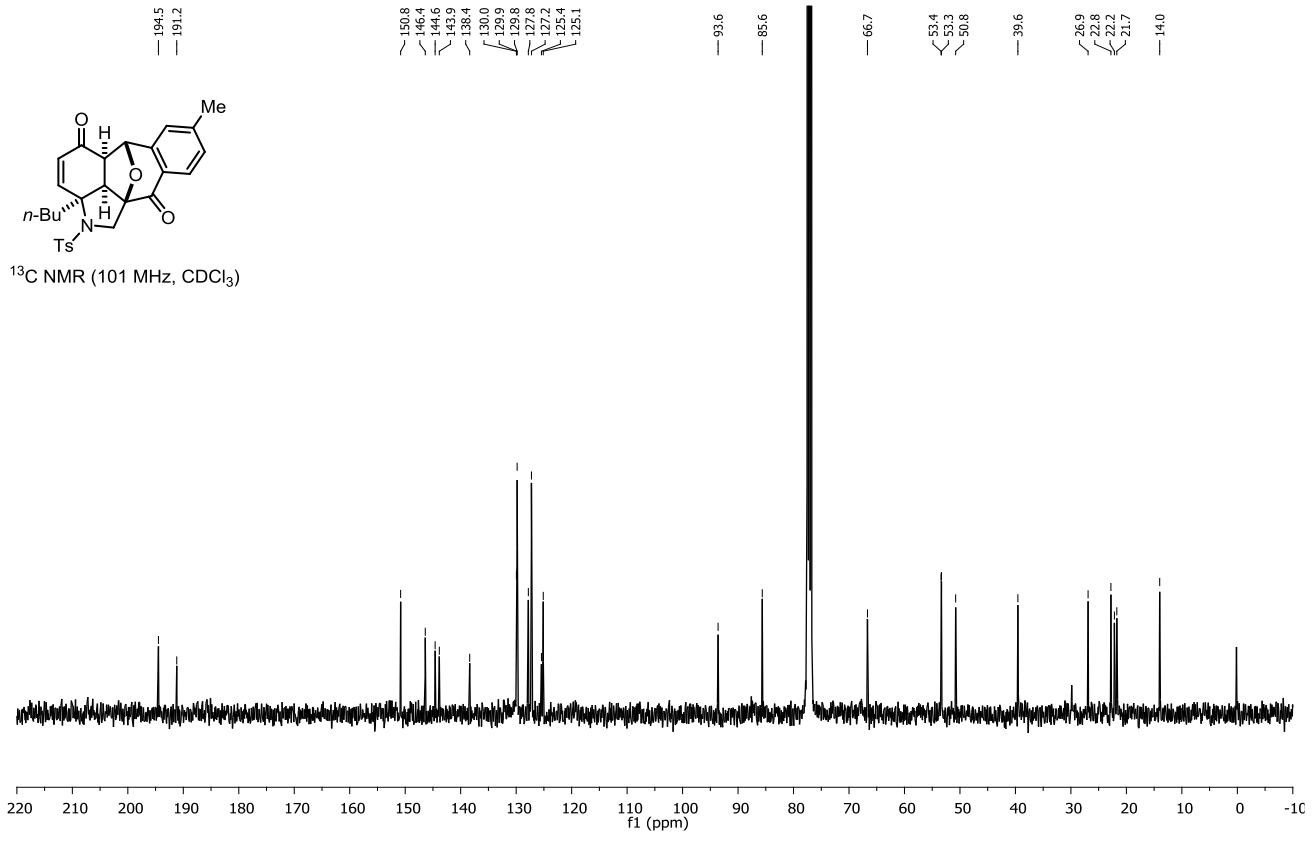




2a-Butyl-8-methyl-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta [1,2,3-cd] indole-5,11-dione (4b):

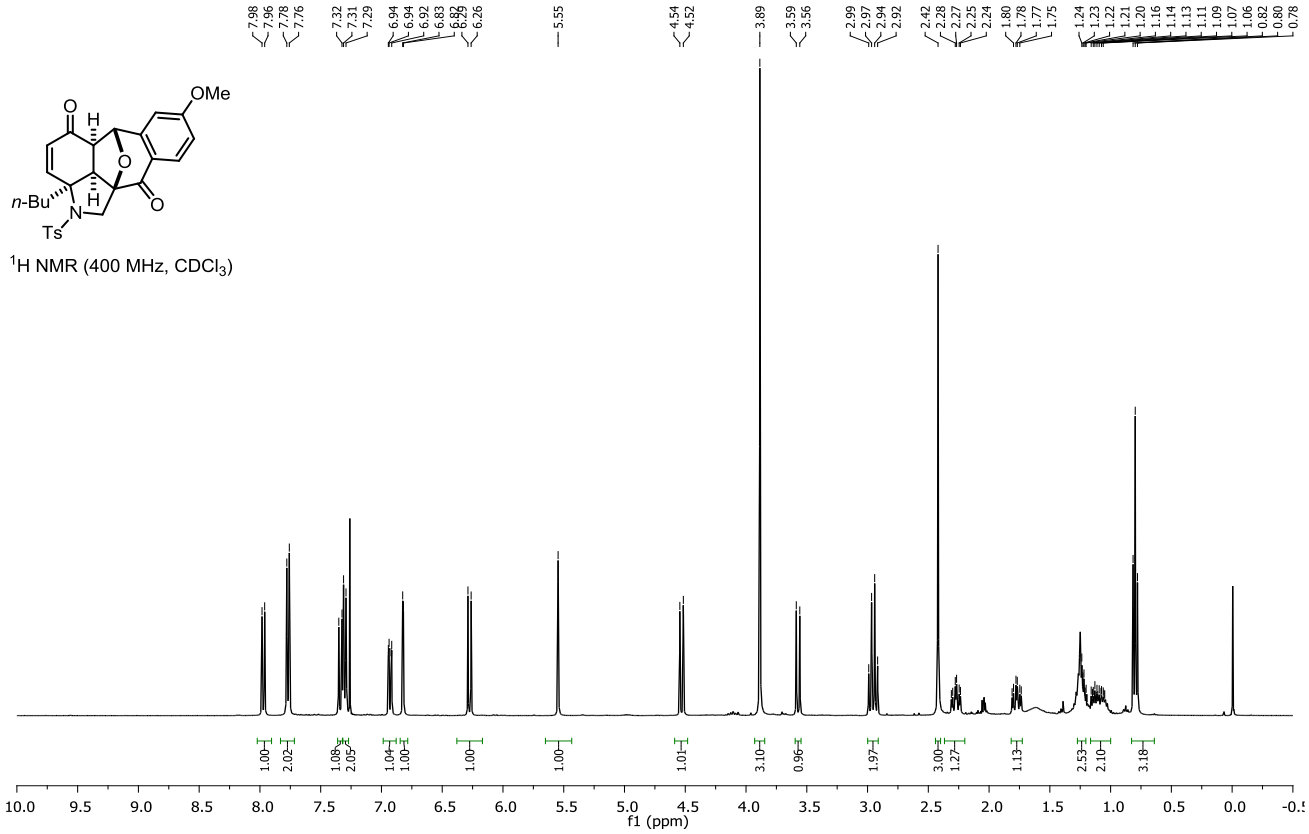


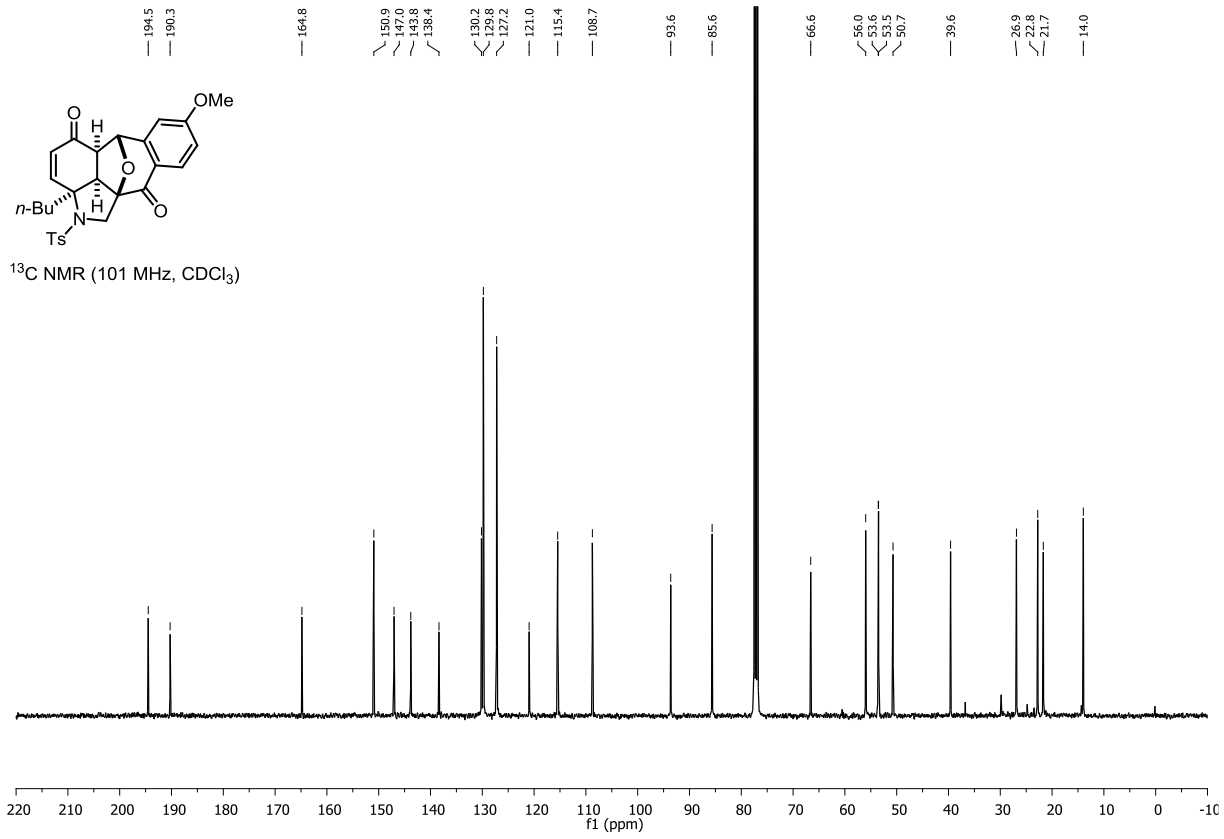
^{1}H NMR (500 MHz, $CDCl_3$)



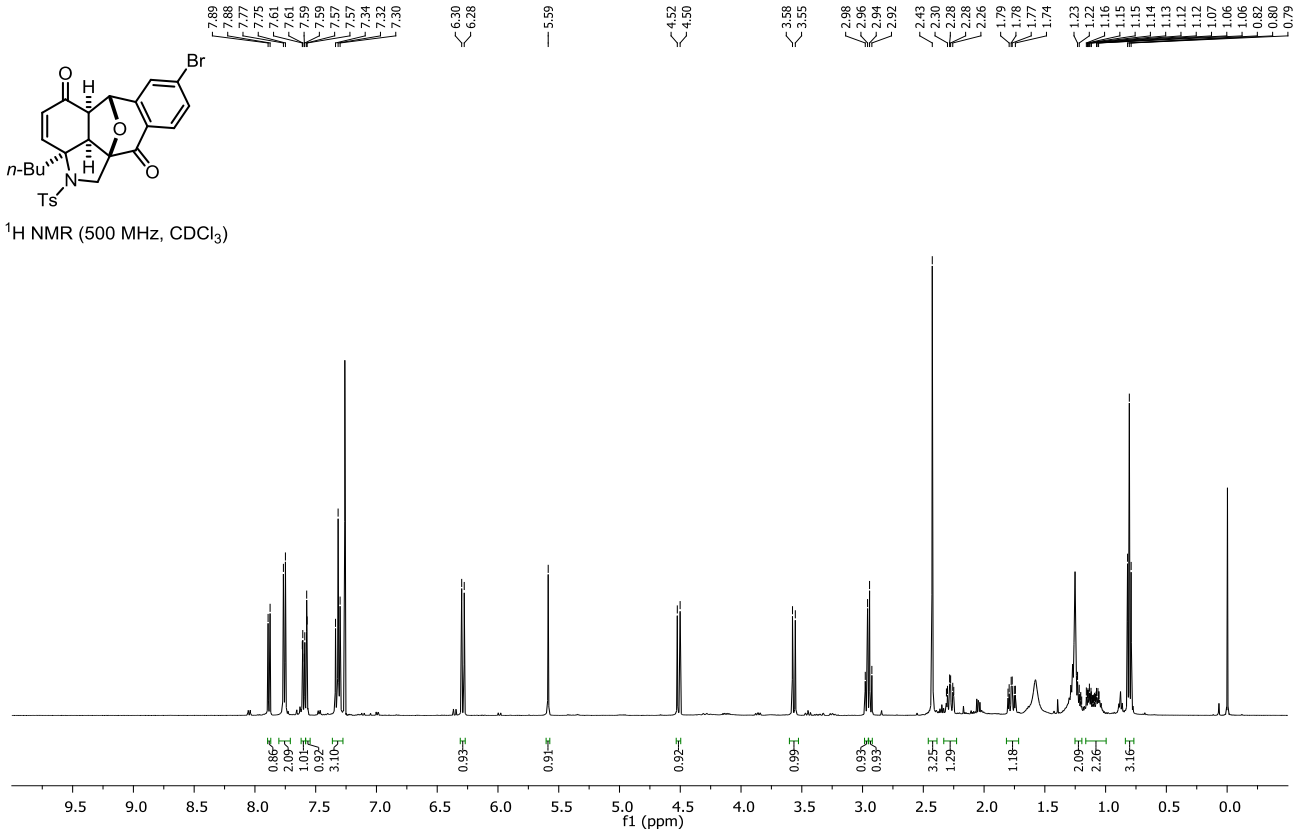
^{13}C NMR (101 MHz, $CDCl_3$)

2a-Butyl-8-methoxy-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta [1,2,3-*cd*]indole-5,11-dione (4c):

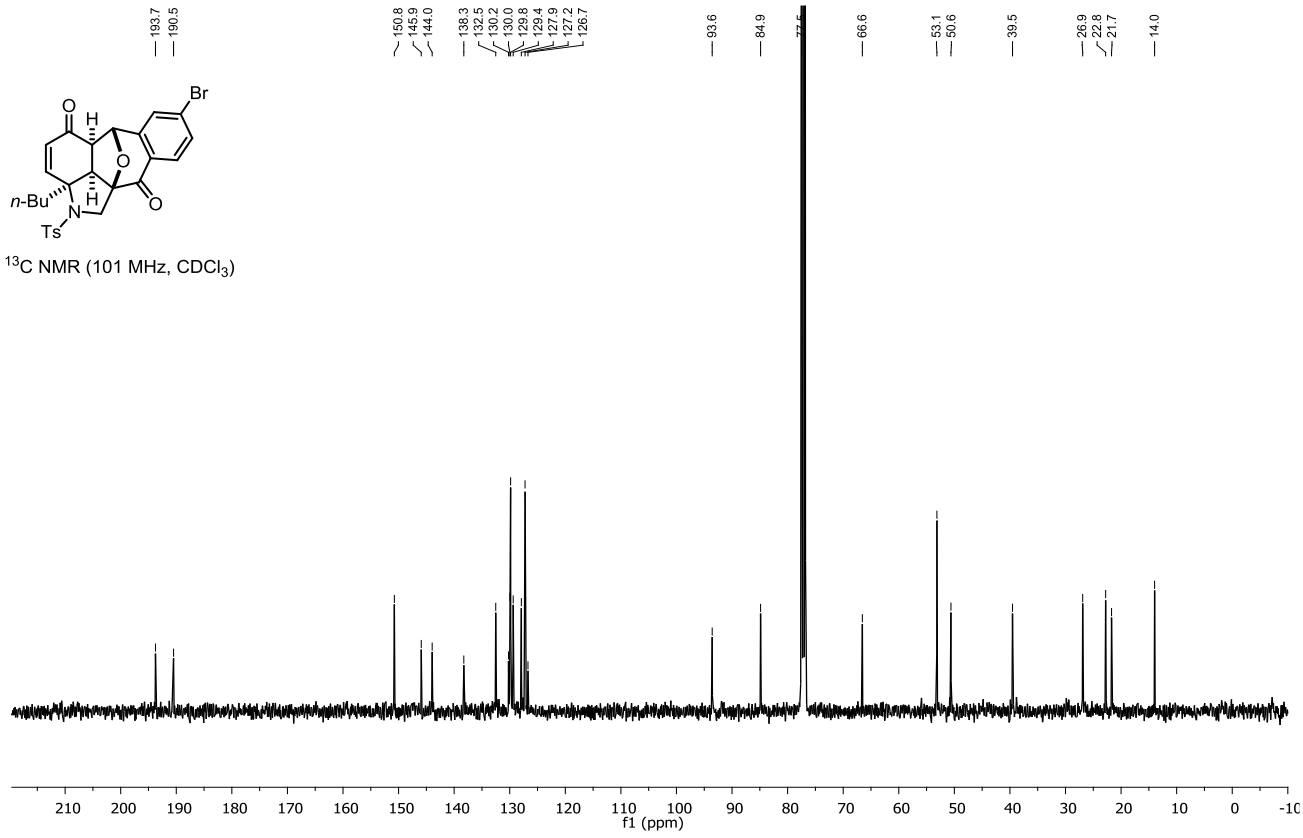




8-Bromo-2a-butyl-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta [1,2,3-*cd*]indole-5,11-dione (4d):

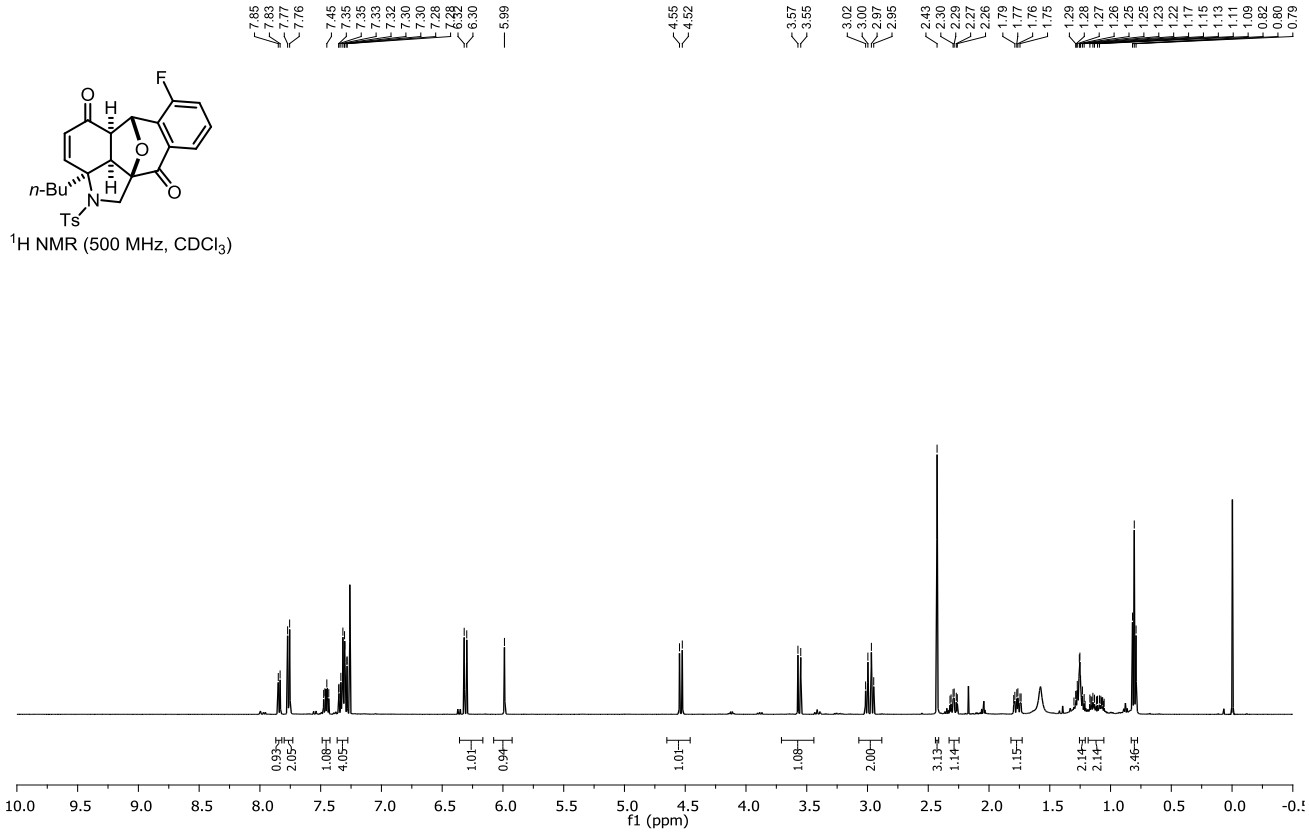


^{1}H NMR (500 MHz, $CDCl_3$)

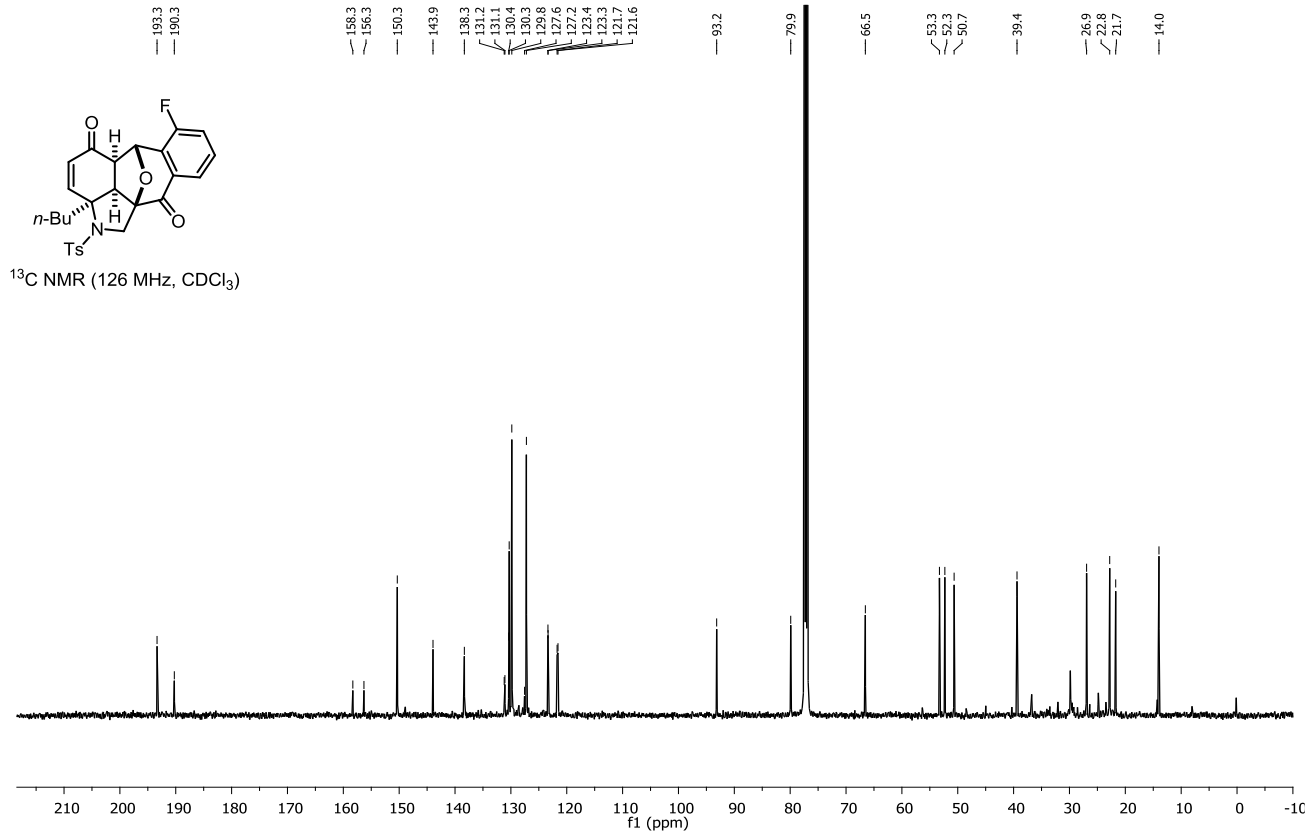


^{13}C NMR (101 MHz, $CDCl_3$)

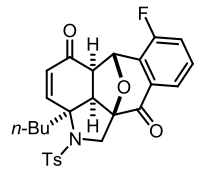
2a-Butyl-7-fluoro-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta [1,2,3-*cd*]indole-5,11-dione (4e):



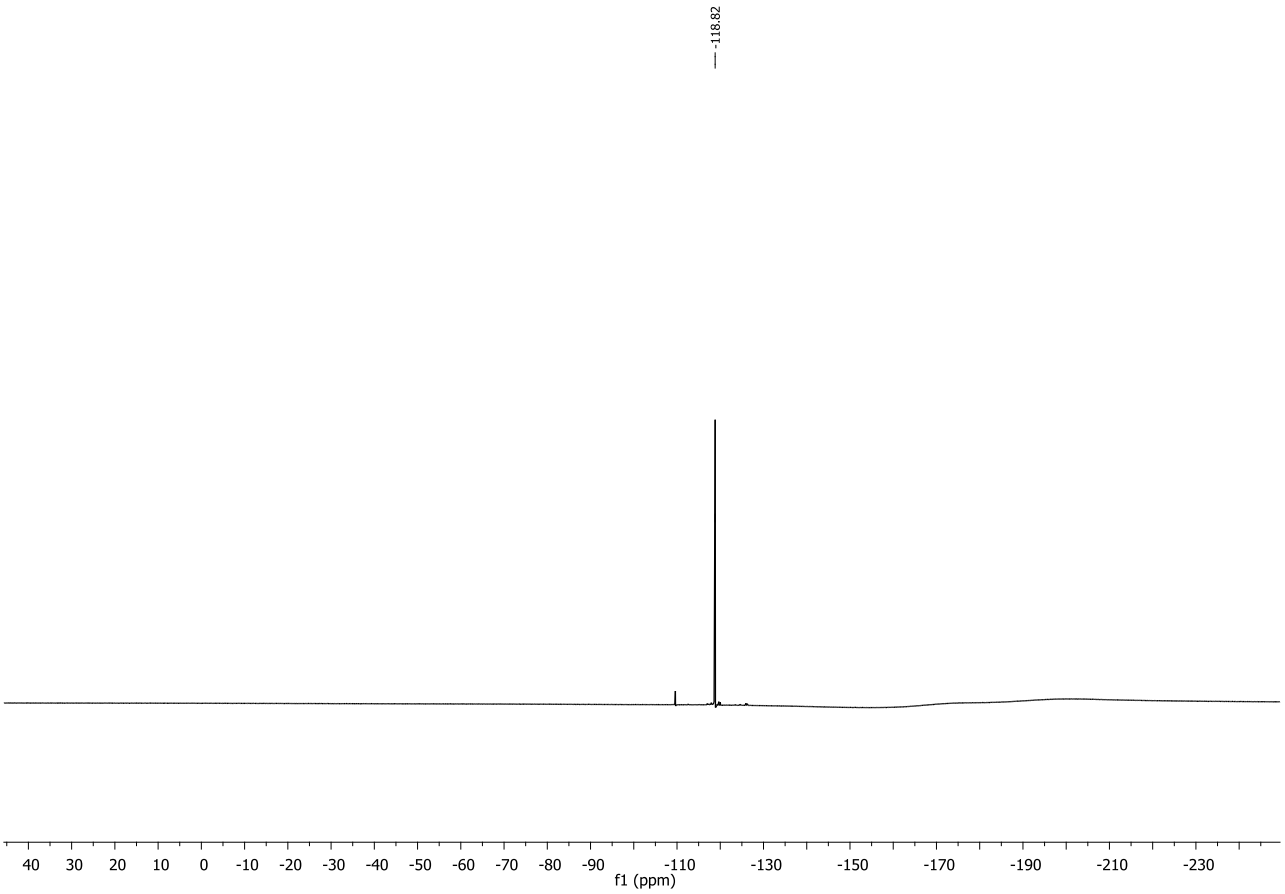
^{1}H NMR (500 MHz, $CDCl_3$)



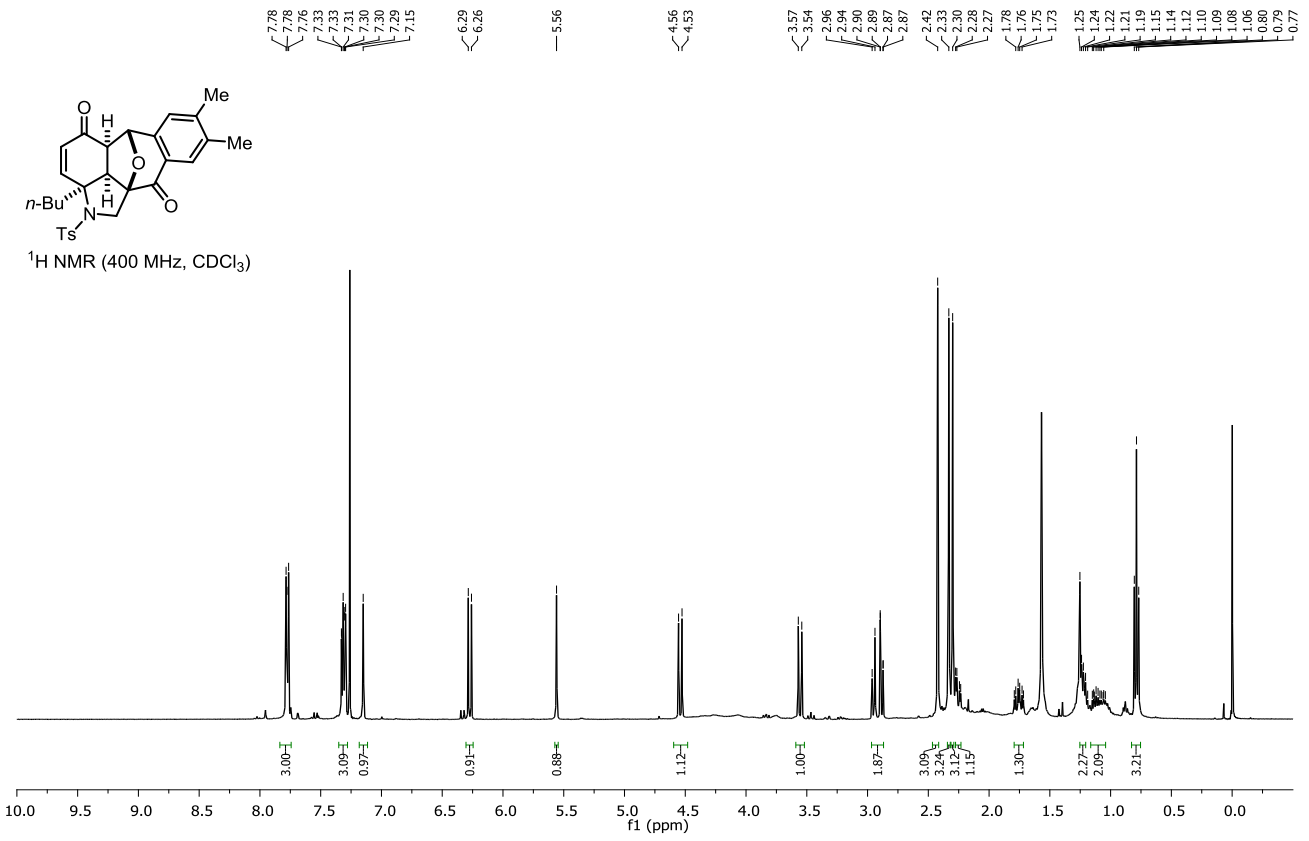
^{13}C NMR (126 MHz, $CDCl_3$)

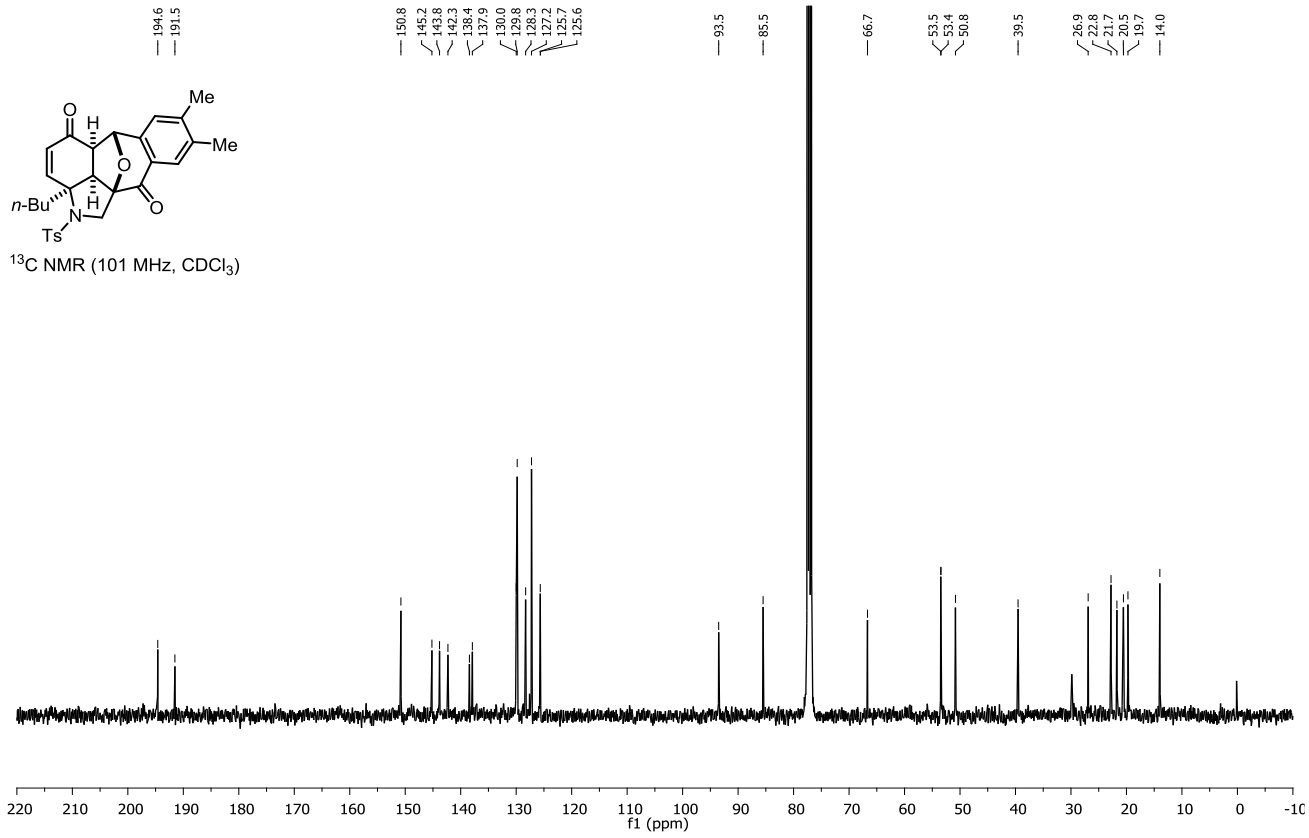


^{19}F NMR (377 MHz, $CDCl_3$)

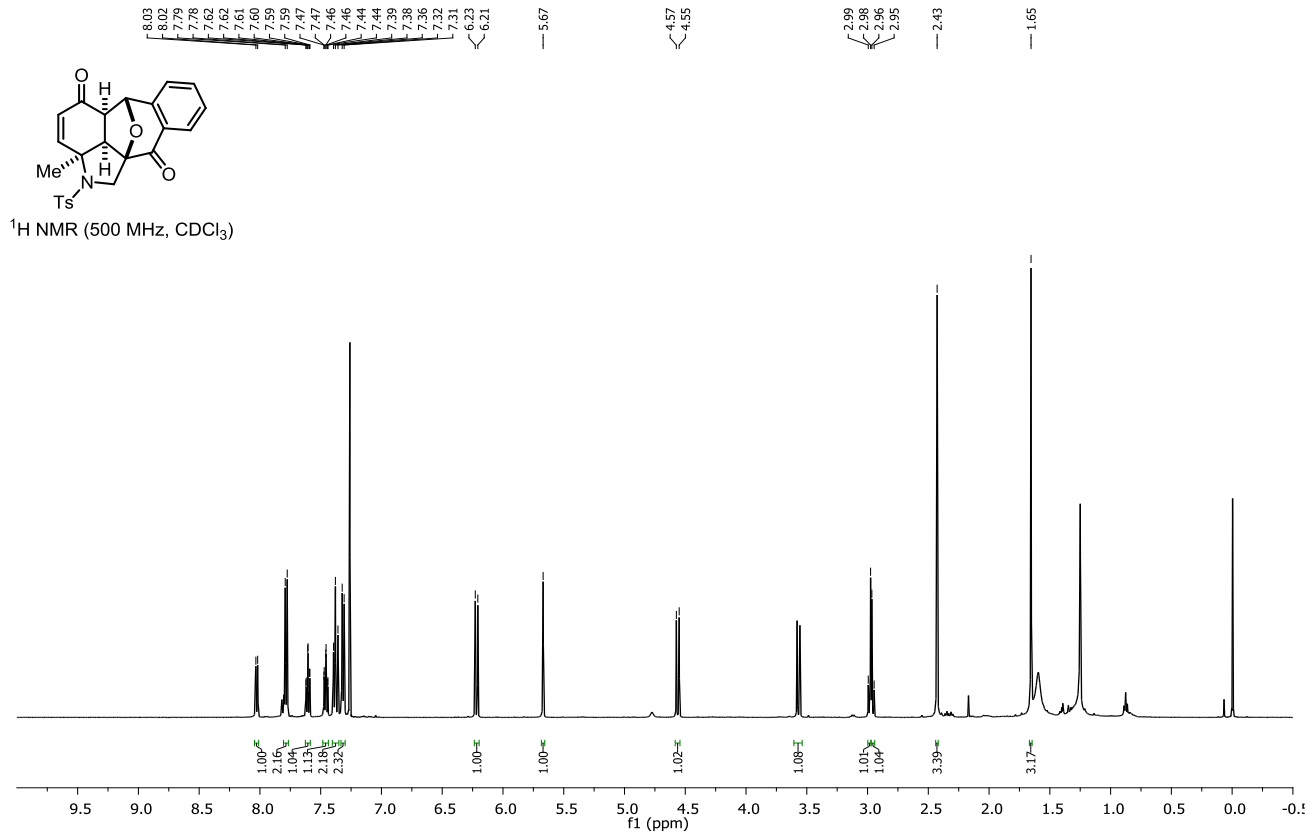


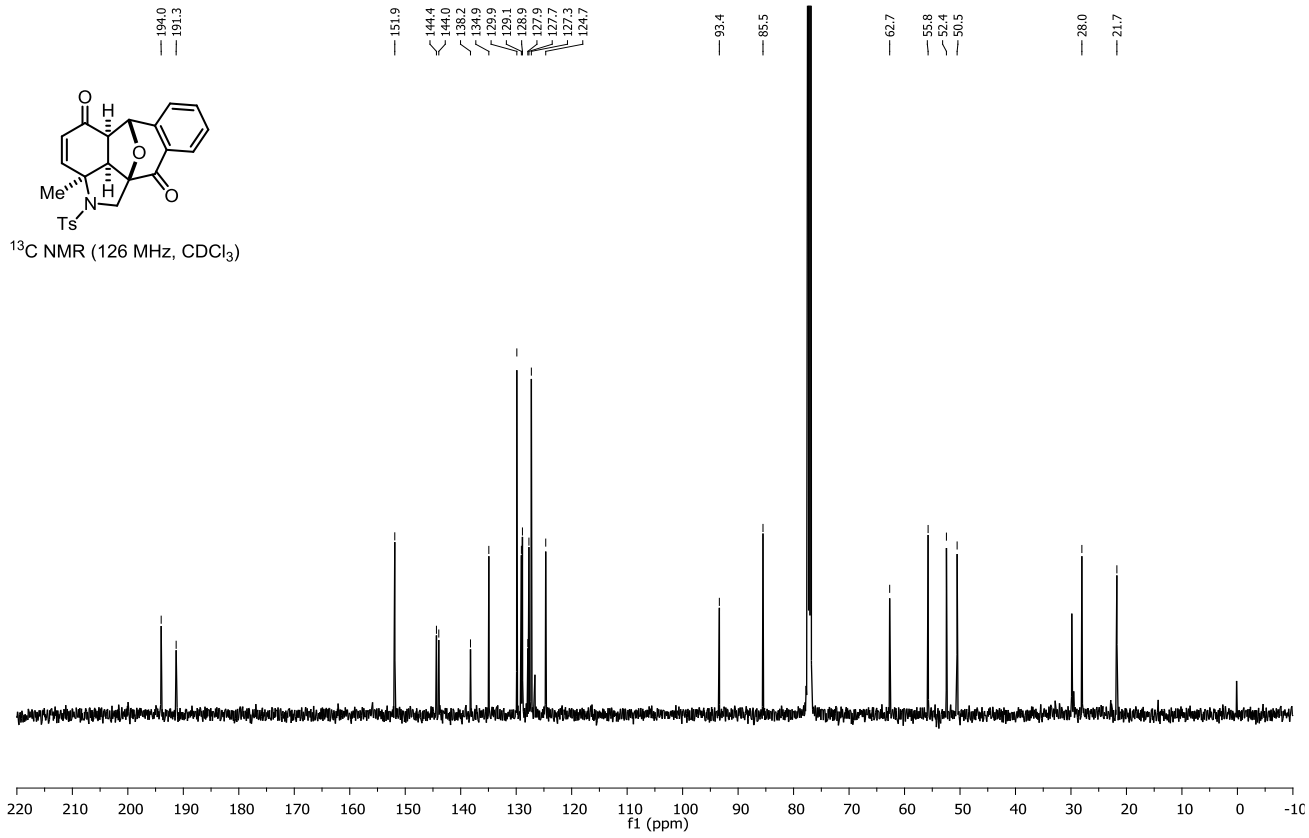
2a-Butyl-8,9-dimethyl-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohep ta [1,2,3-*cd*]indole-5,11-dione (4f):



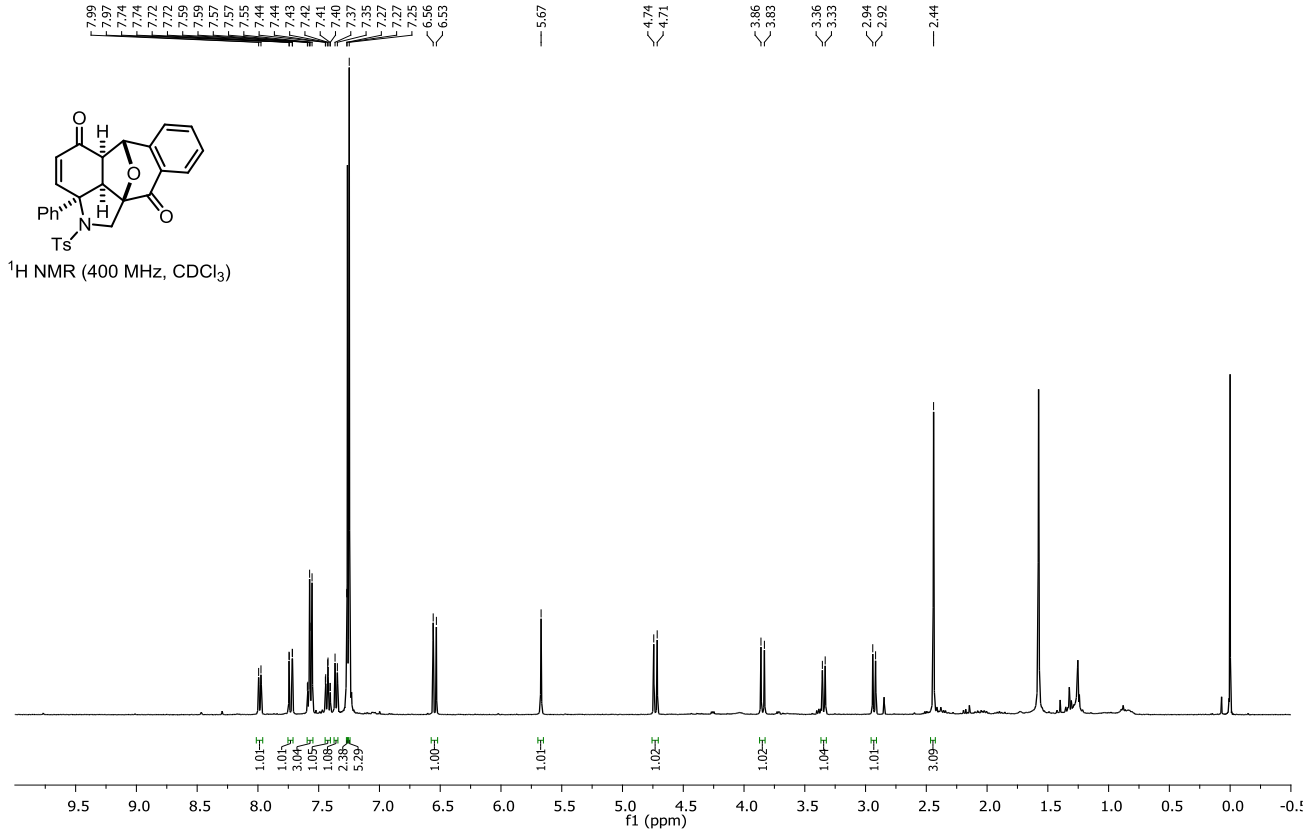


2a-Methyl-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]indole-5,11-dione (4g):

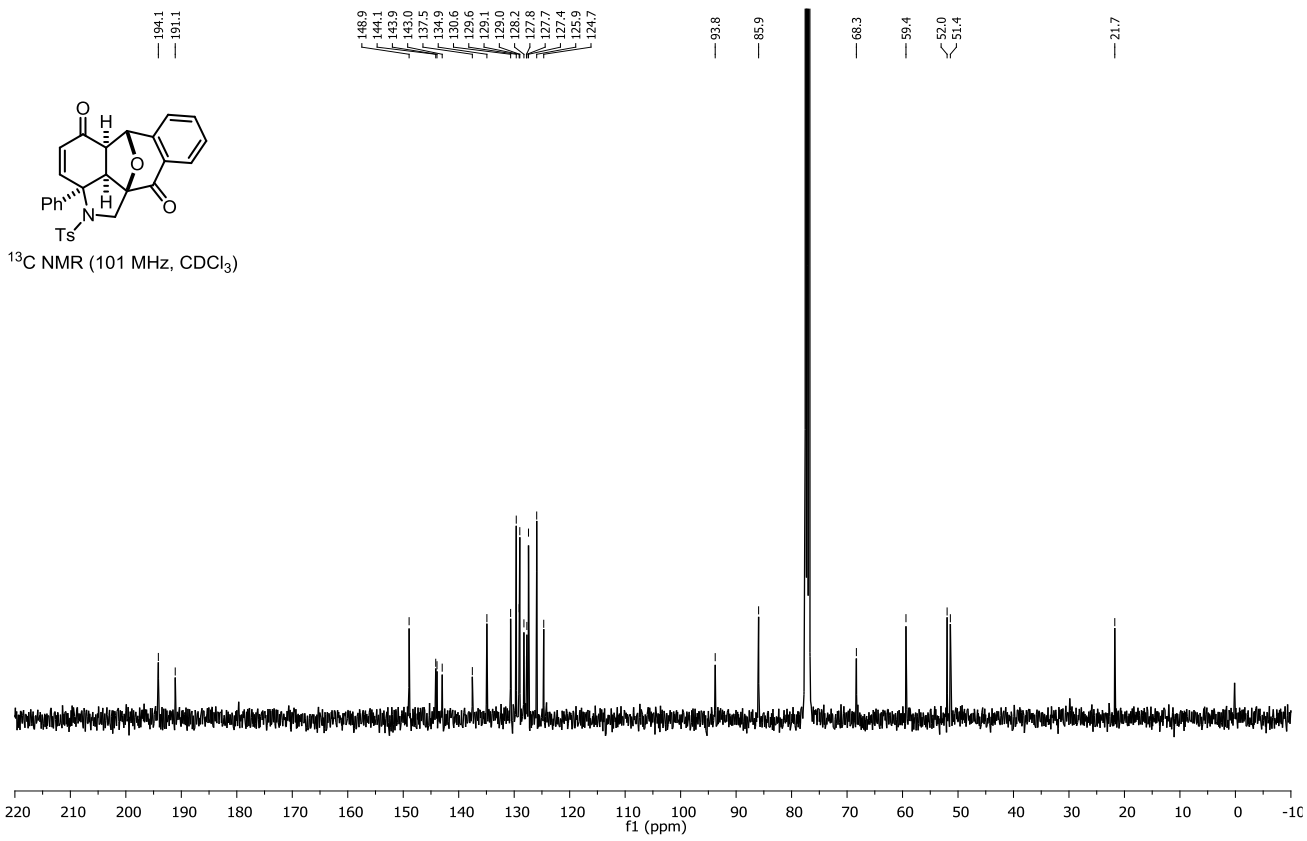




2a-Phenyl-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]indole-5,11-dione (4h):

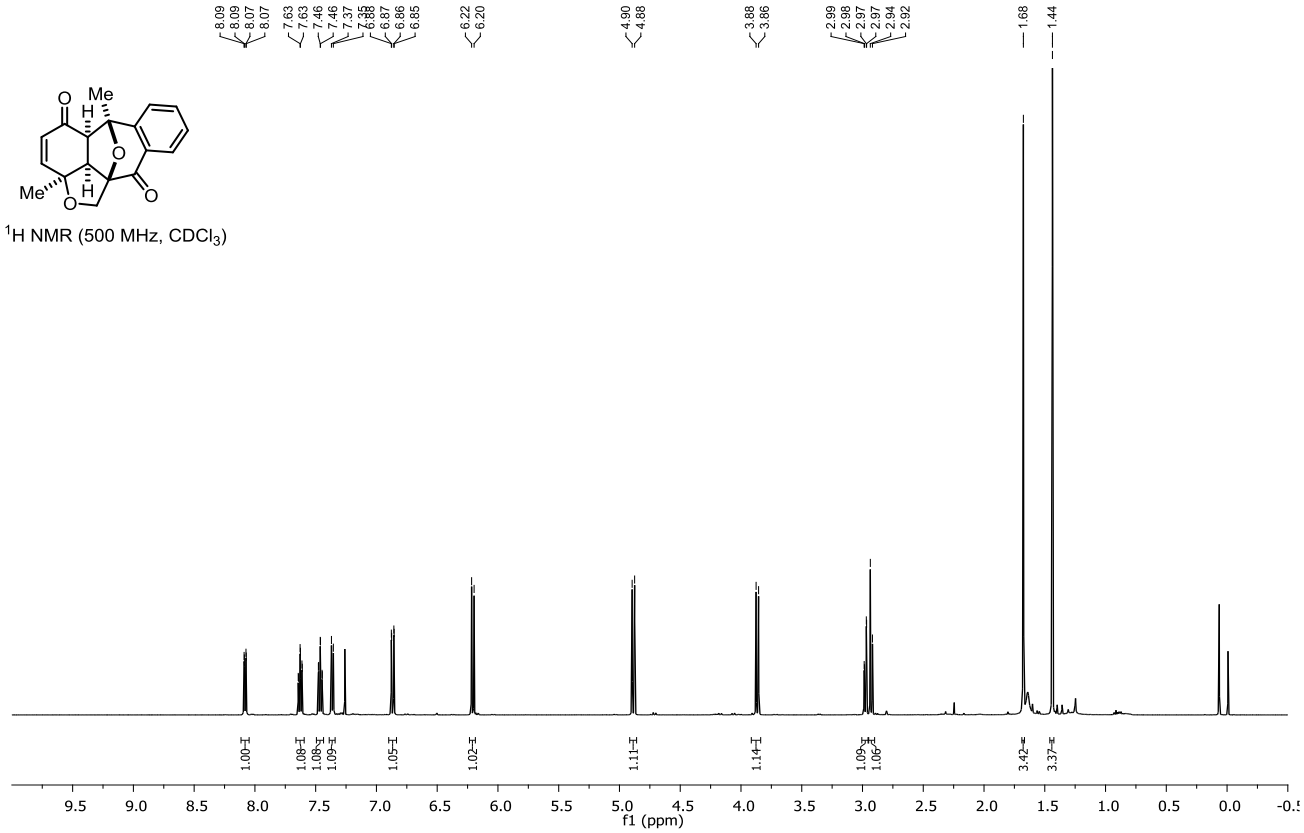


^{1}H NMR (400 MHz, $CDCl_3$)

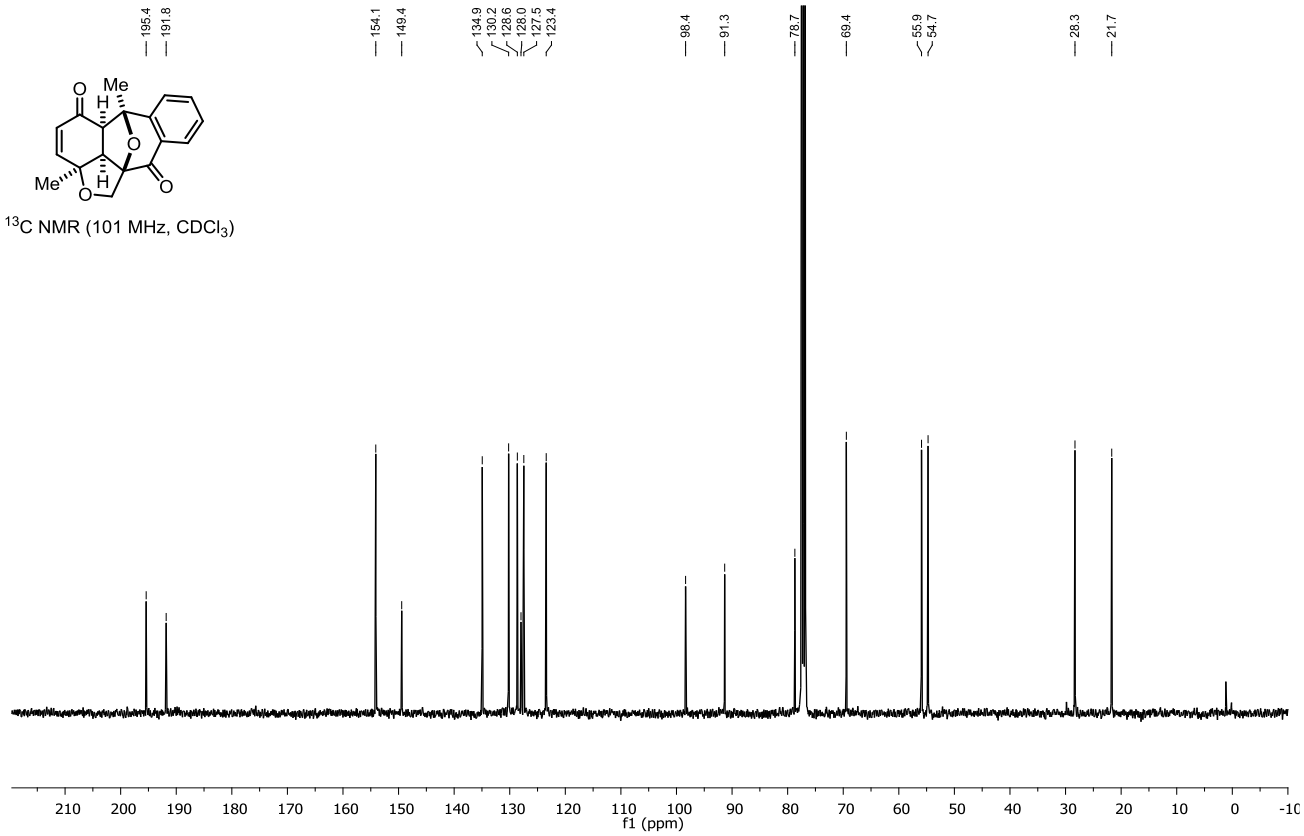


^{13}C NMR (101 MHz, $CDCl_3$)

2a,6-Dimethyl-2a,2a1,5a,6-tetrahydro-1H-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (6a):

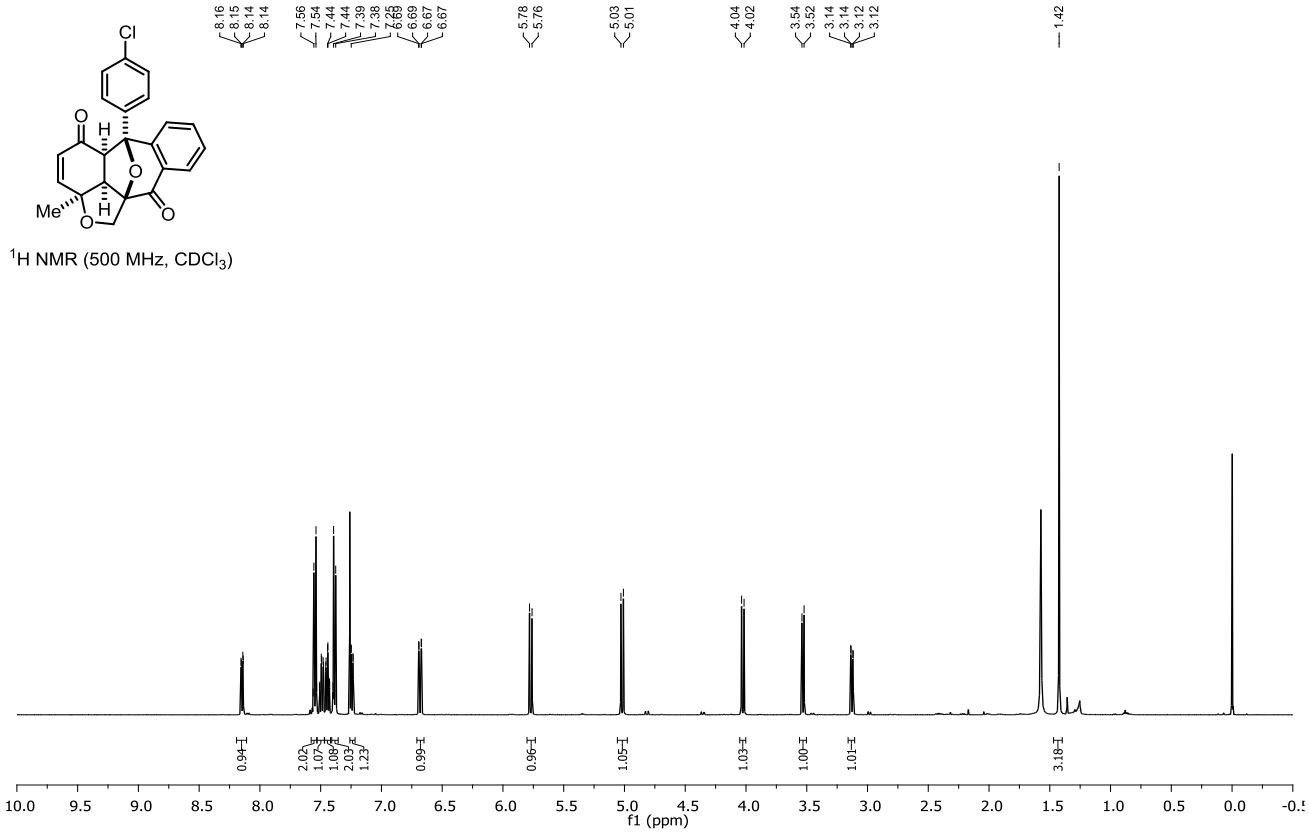


^{1}H NMR (500 MHz, $CDCl_3$)

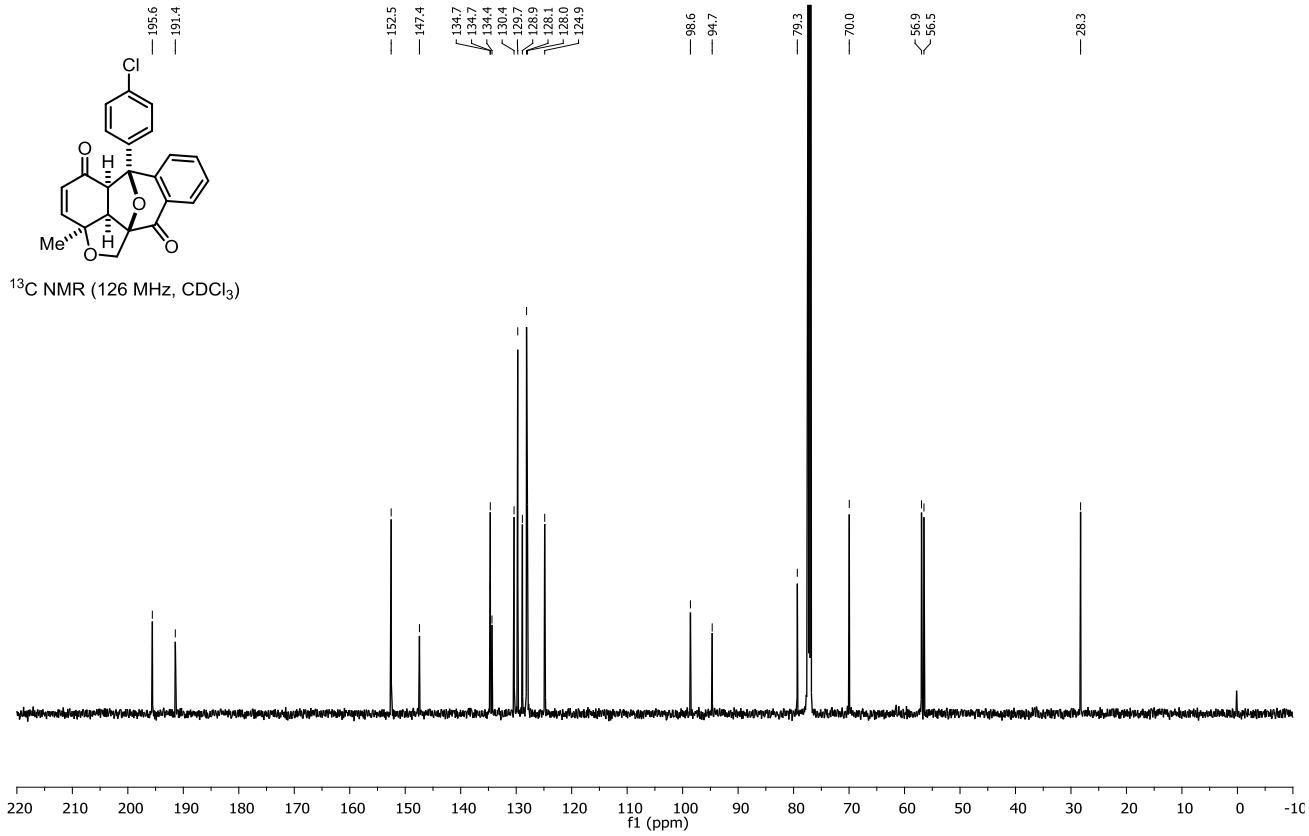


^{13}C NMR (101 MHz, $CDCl_3$)

6-(4-Chlorophenyl)-2a-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6] cyclohepta [1,2,3-*cd]* benzofuran-5,11-dione (6b):

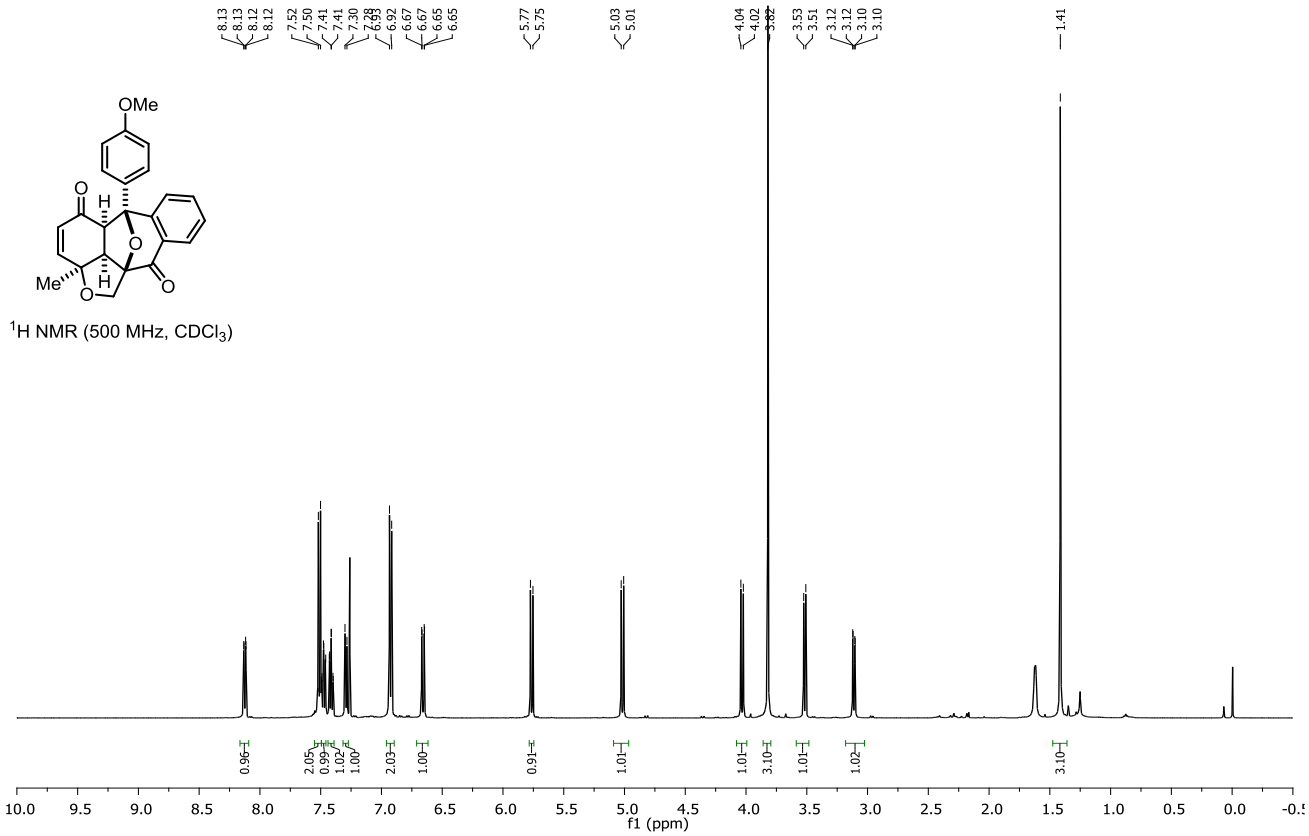


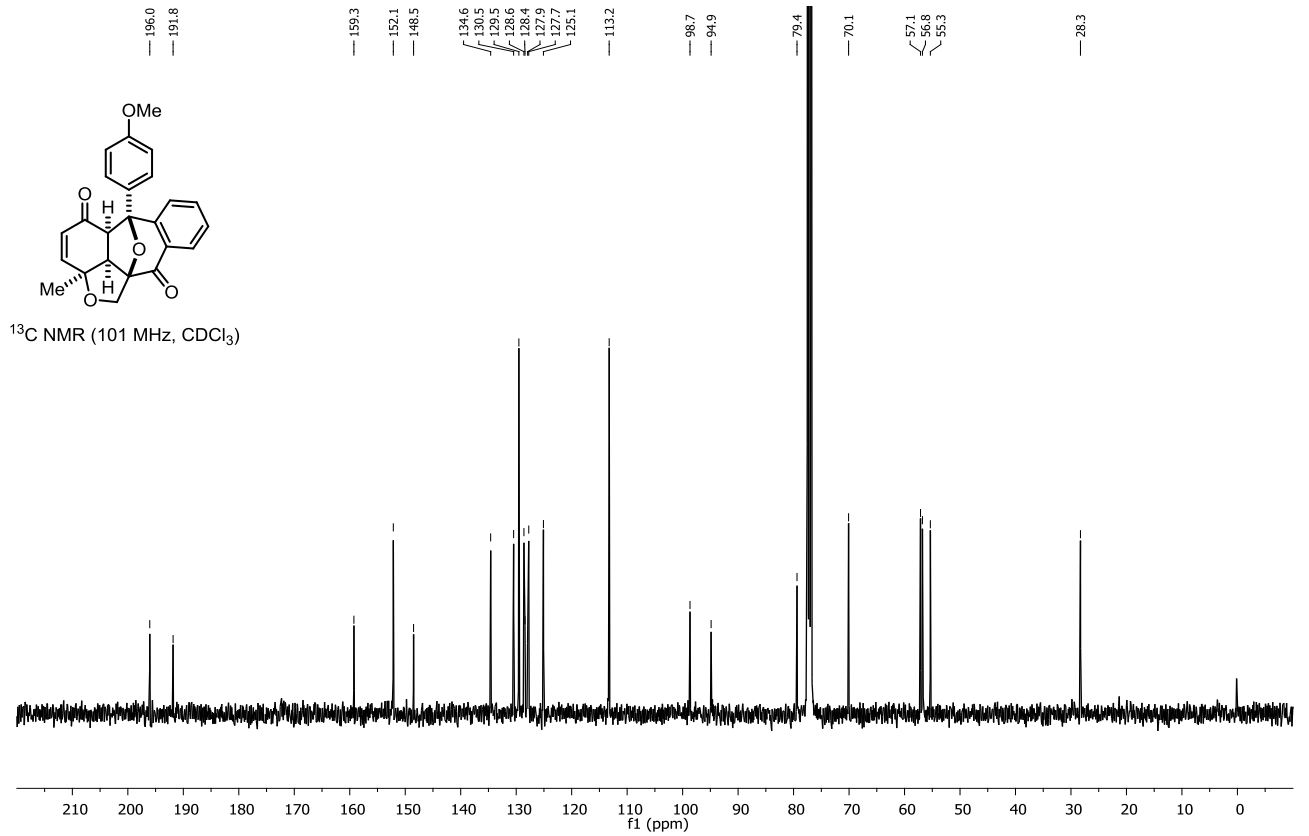
^{1}H NMR (500 MHz, $CDCl_3$)



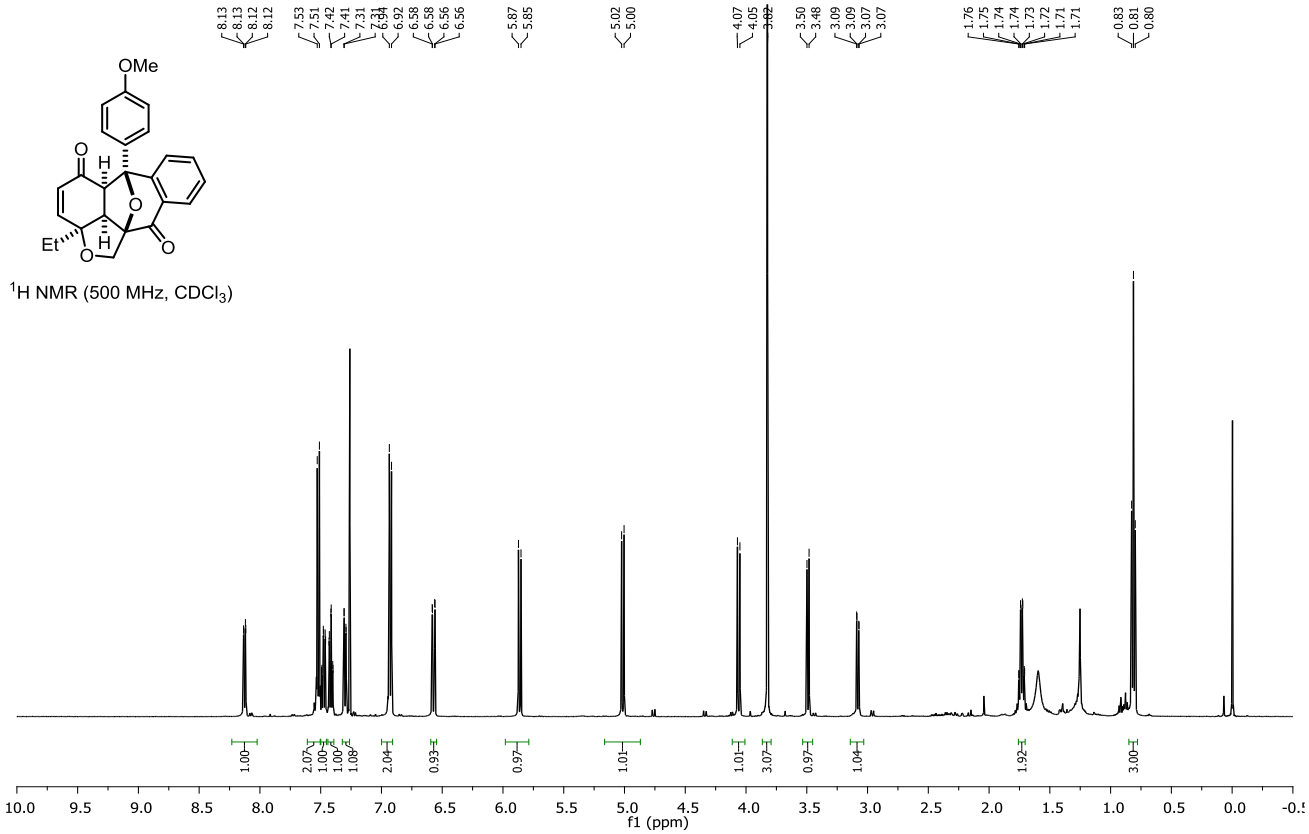
^{13}C NMR (126 MHz, $CDCl_3$)

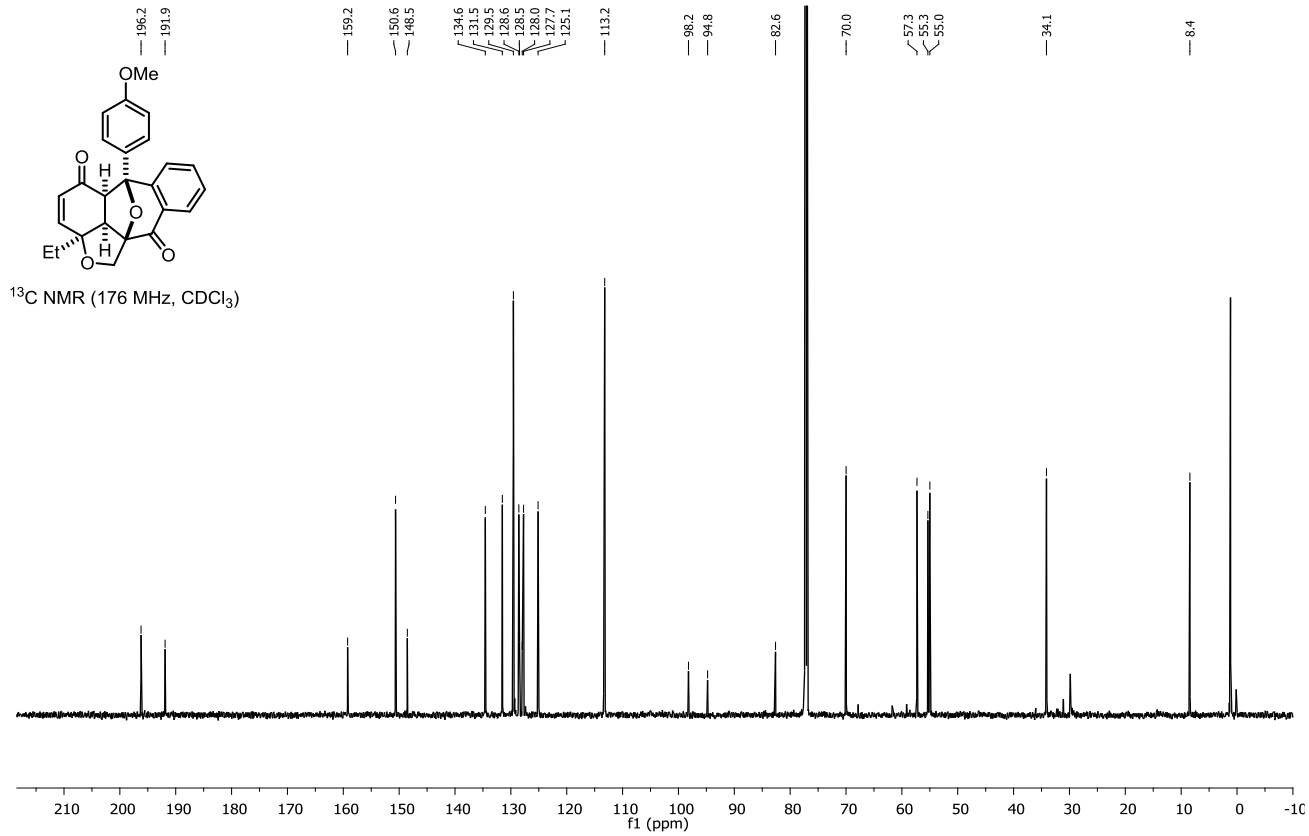
6-(4-Methoxyphenyl)-2a-methyl-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6] cyclohepta [1,2,3-*cd*]benzofuran-5,11-dione (6c):



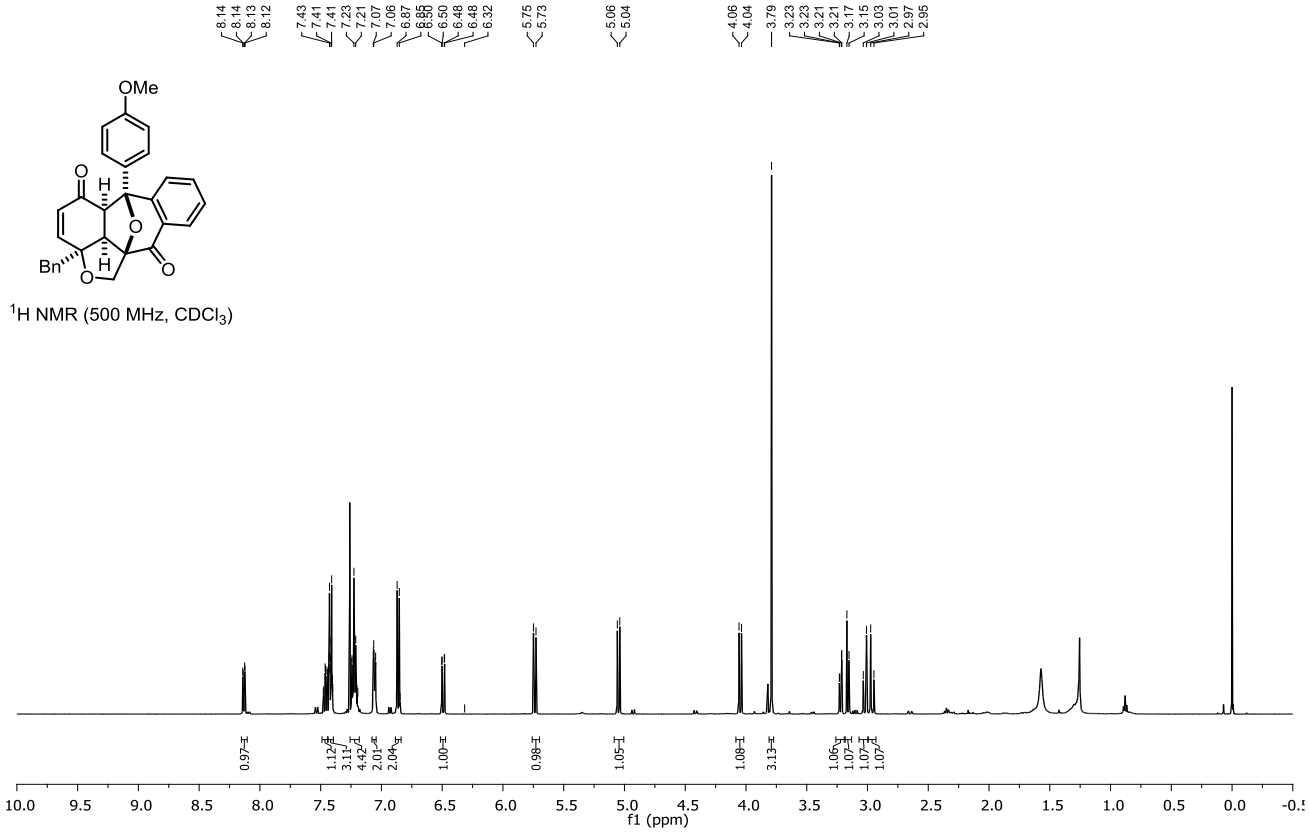


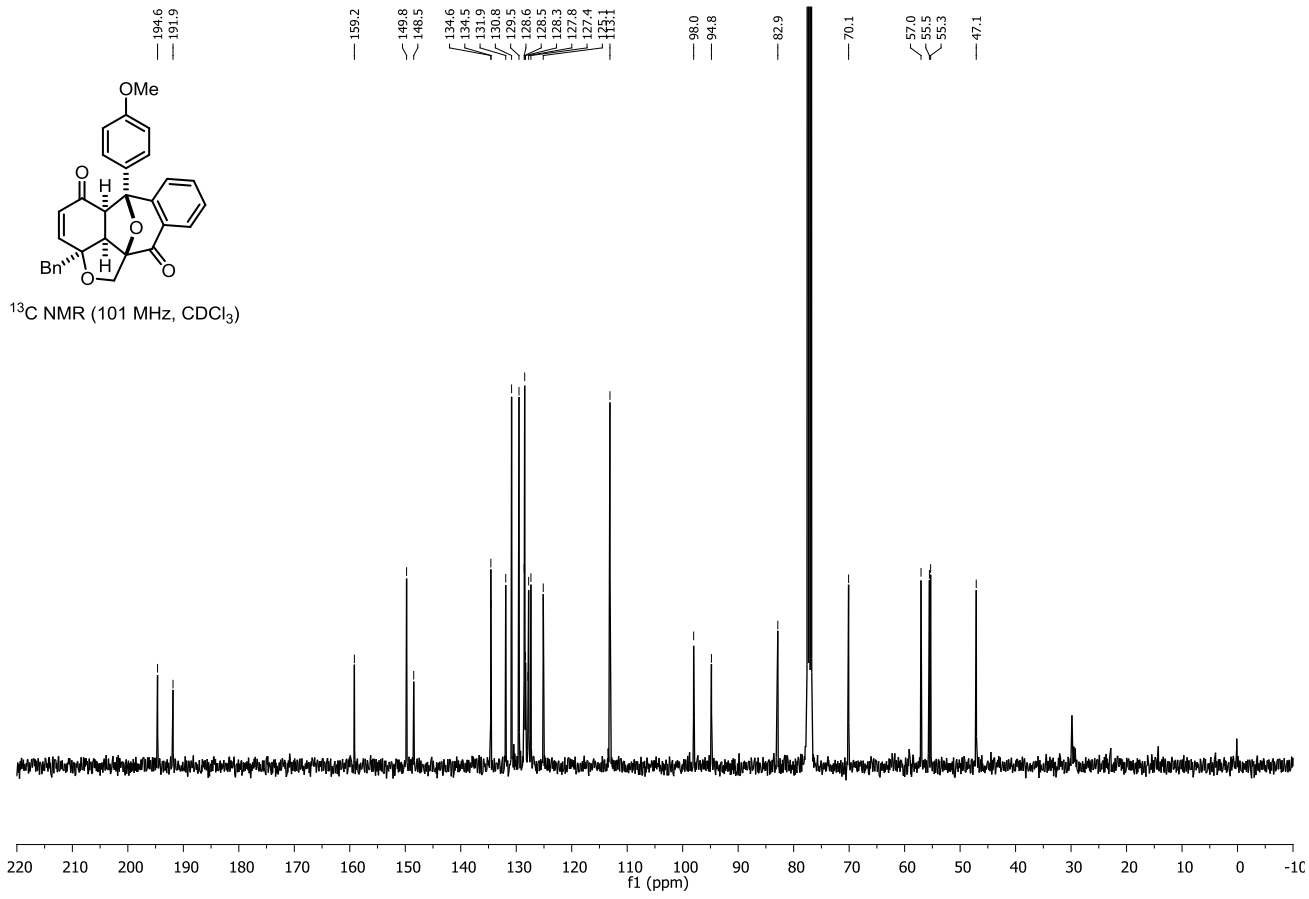
2a-Ethyl-6-(4-methoxyphenyl)-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta [1,2,3-*cd*] benzofuran-5,11-dione (6d):



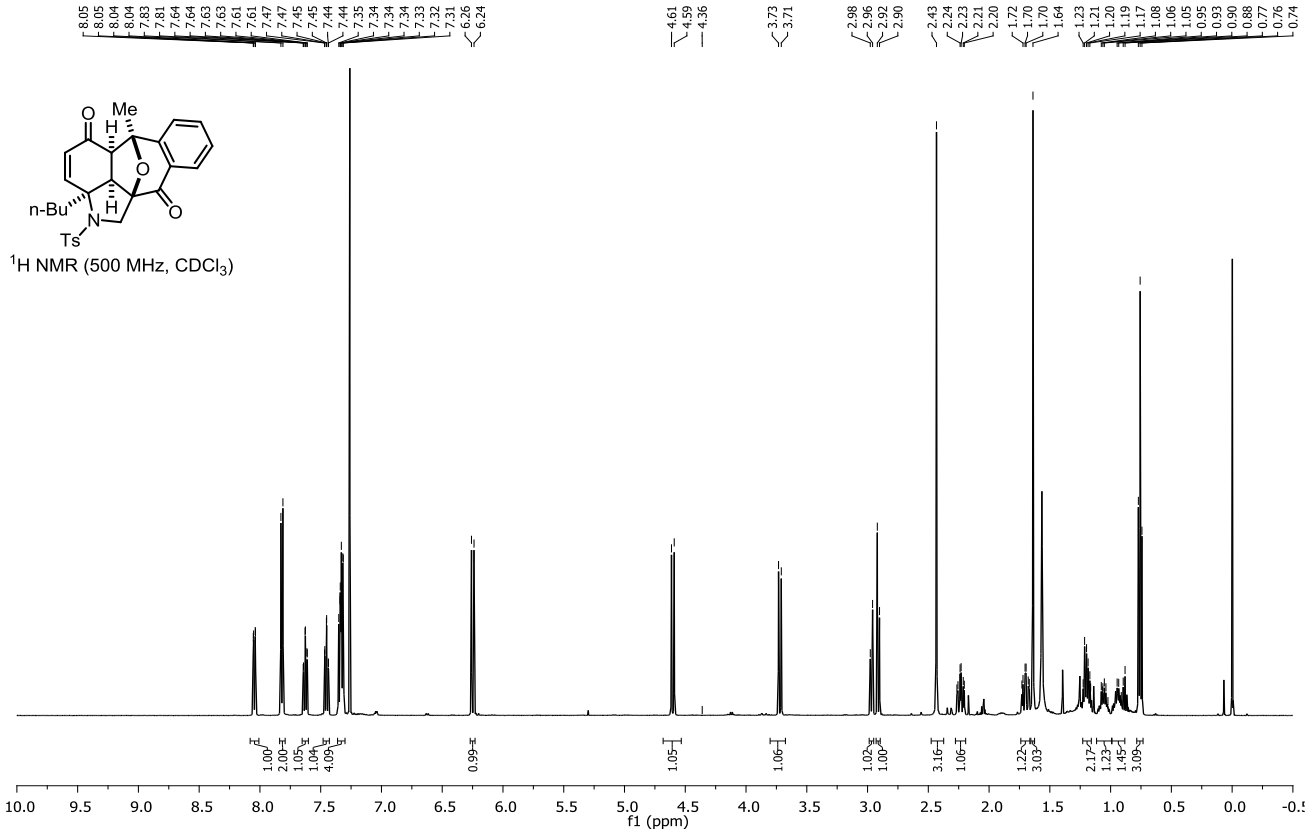


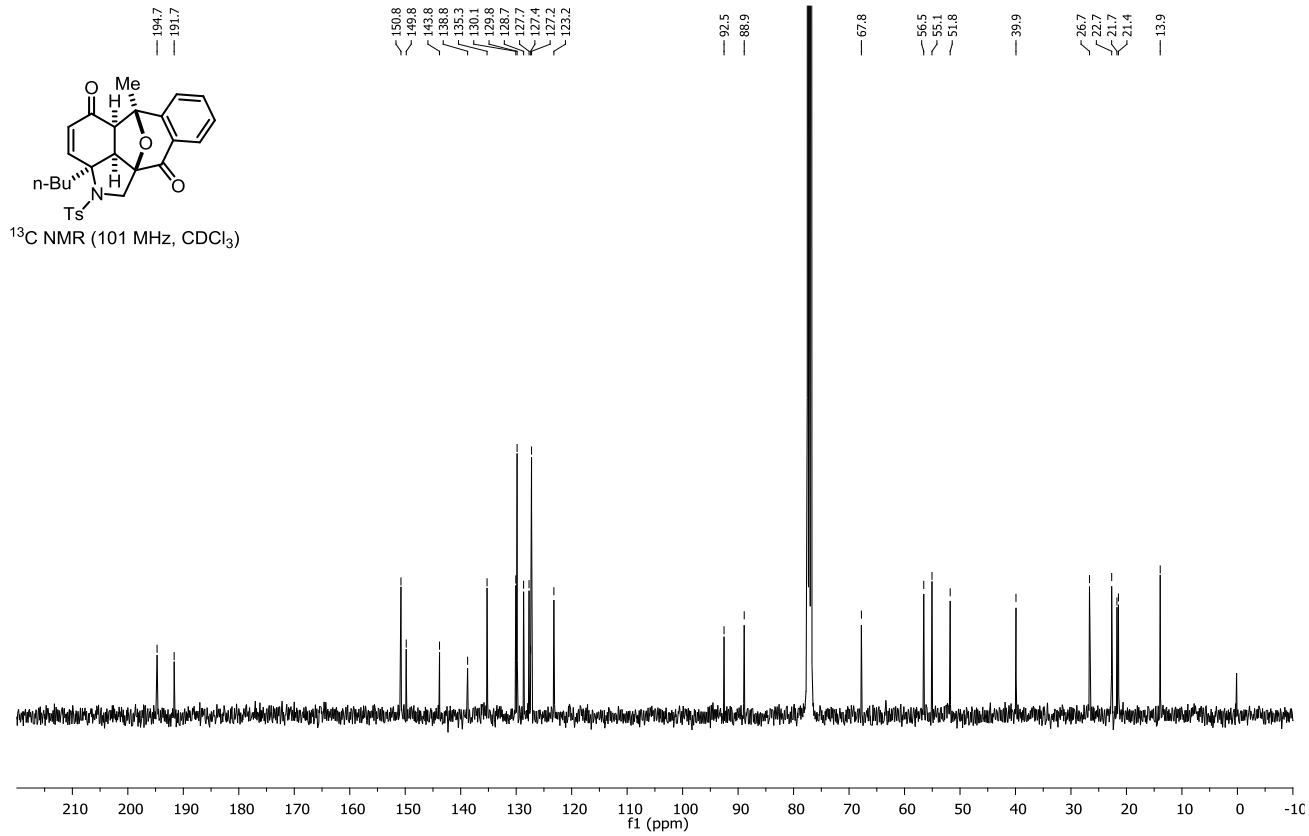
2a-Benzyl-6-(4-methoxyphenyl)-2a,2a1,5a,6-tetrahydro-1*H*-6,11a-epoxybenzo[5,6] cyclohepta [1,2,3-*cd*]benzofuran-5,11-dione (6e):



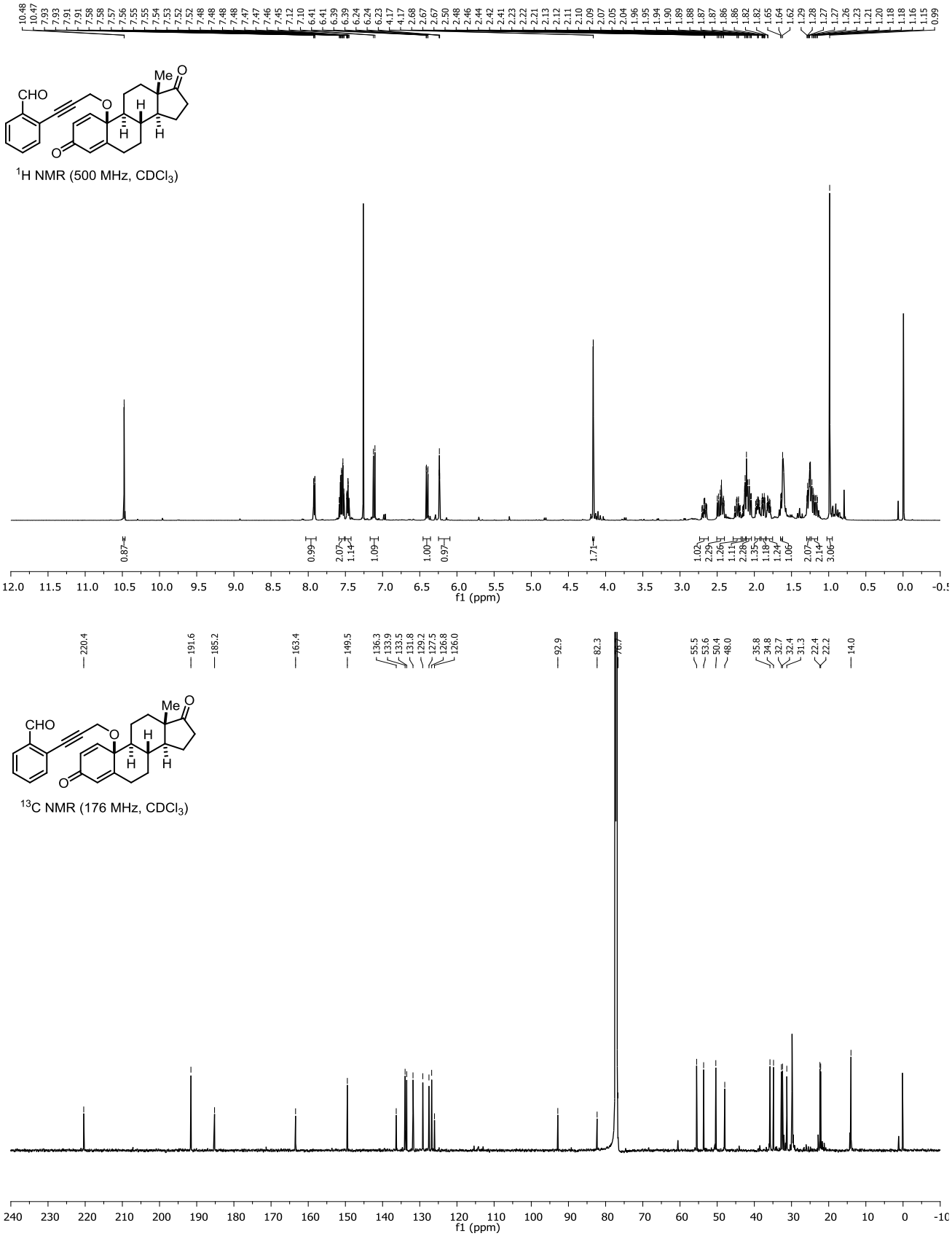


2a-Butyl-6-methyl-2-tosyl-1,2,2a,2a1,5a,6-hexahydro-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*] indole-5,11-dione (6f):

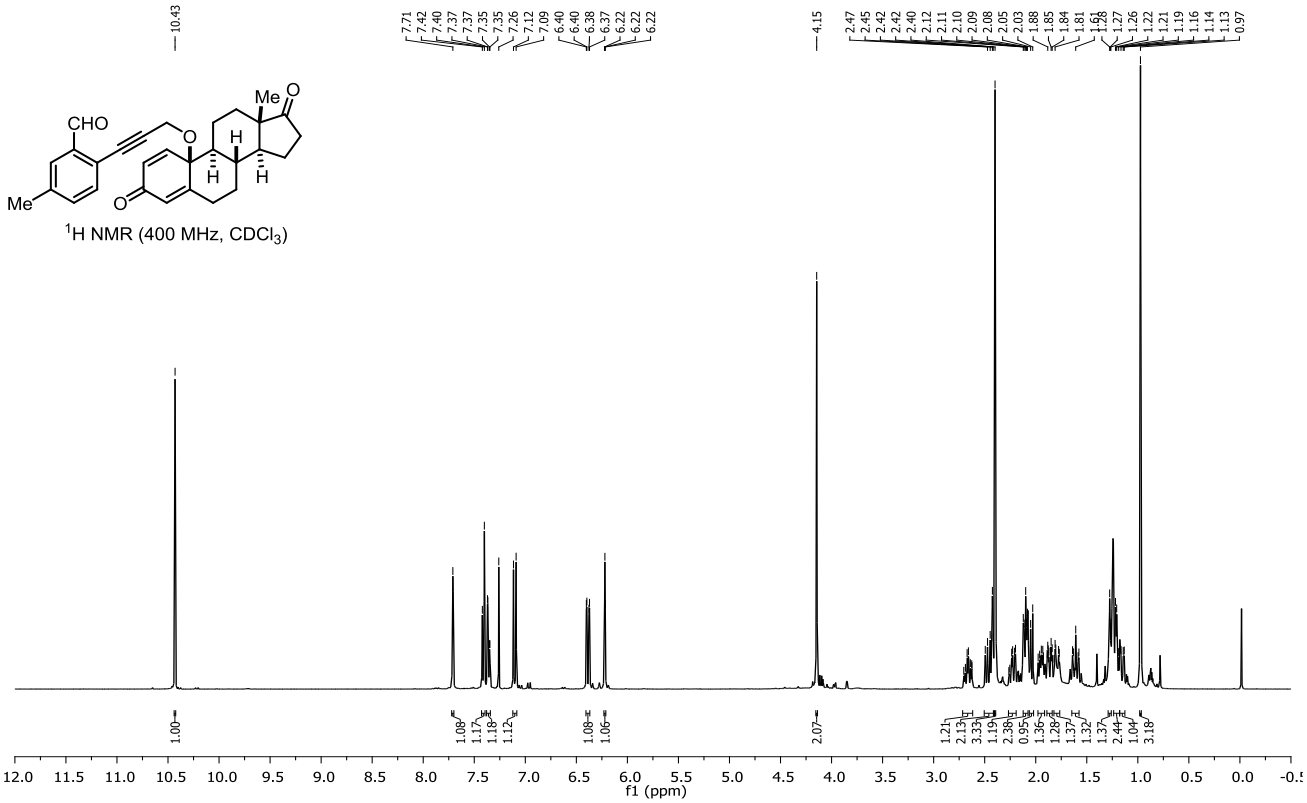


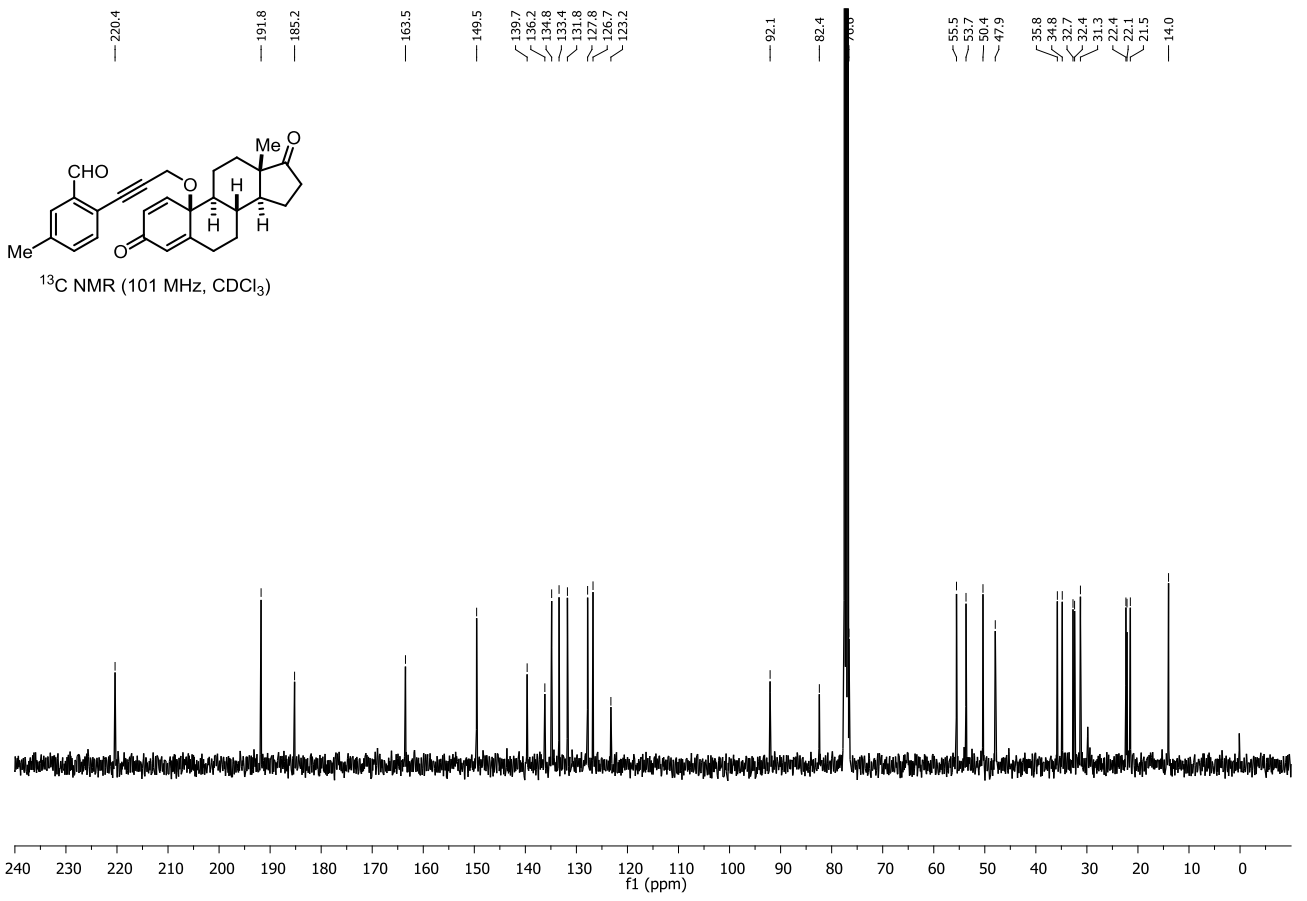


2-(3-(((8S,9S,10S,13S,14S)-13-Methyl-3,17-dioxo-3,6,7,8,9,11,12,13,14,15,16,17-dodeca hydro-10H-cyclopenta[a]phenanthren-10-yl)oxy)prop-1-yn-1-yl)benzaldehyde (7a):

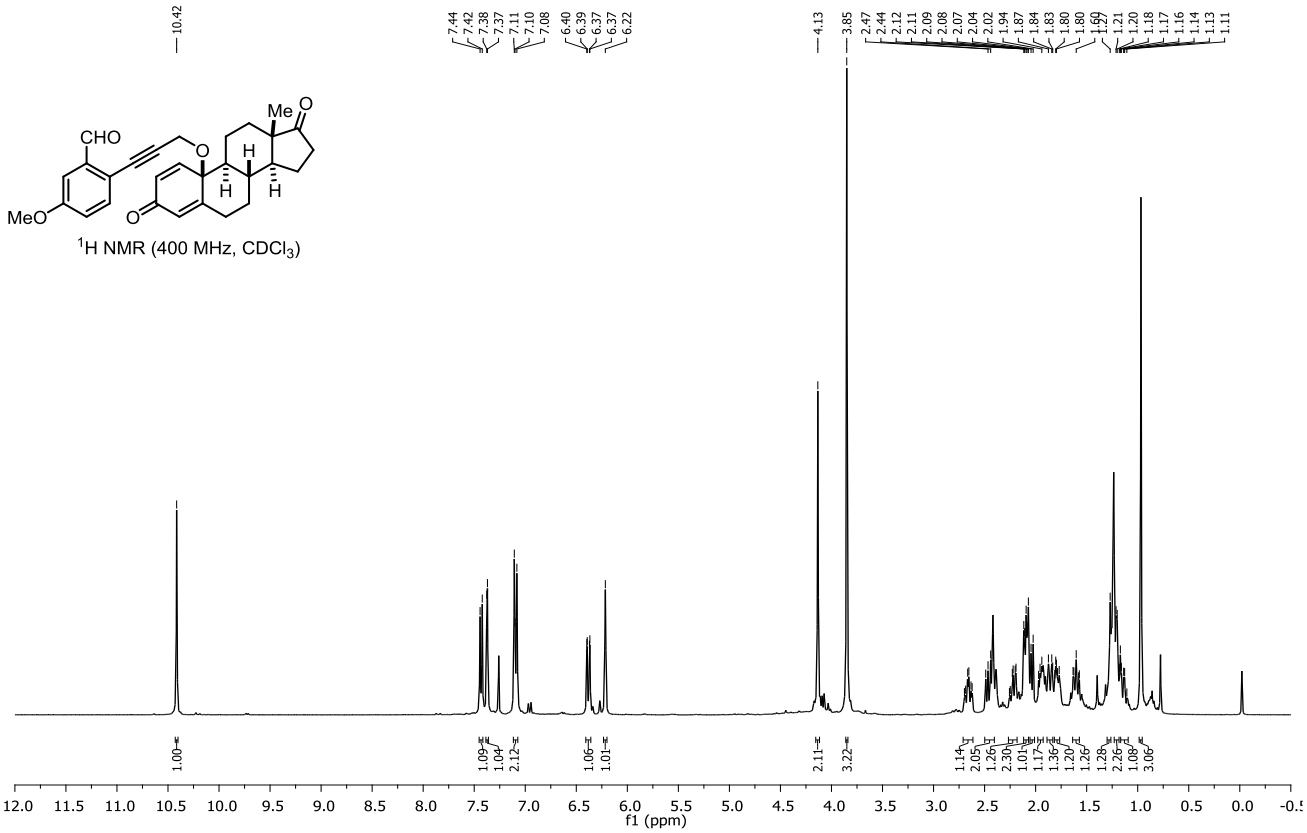


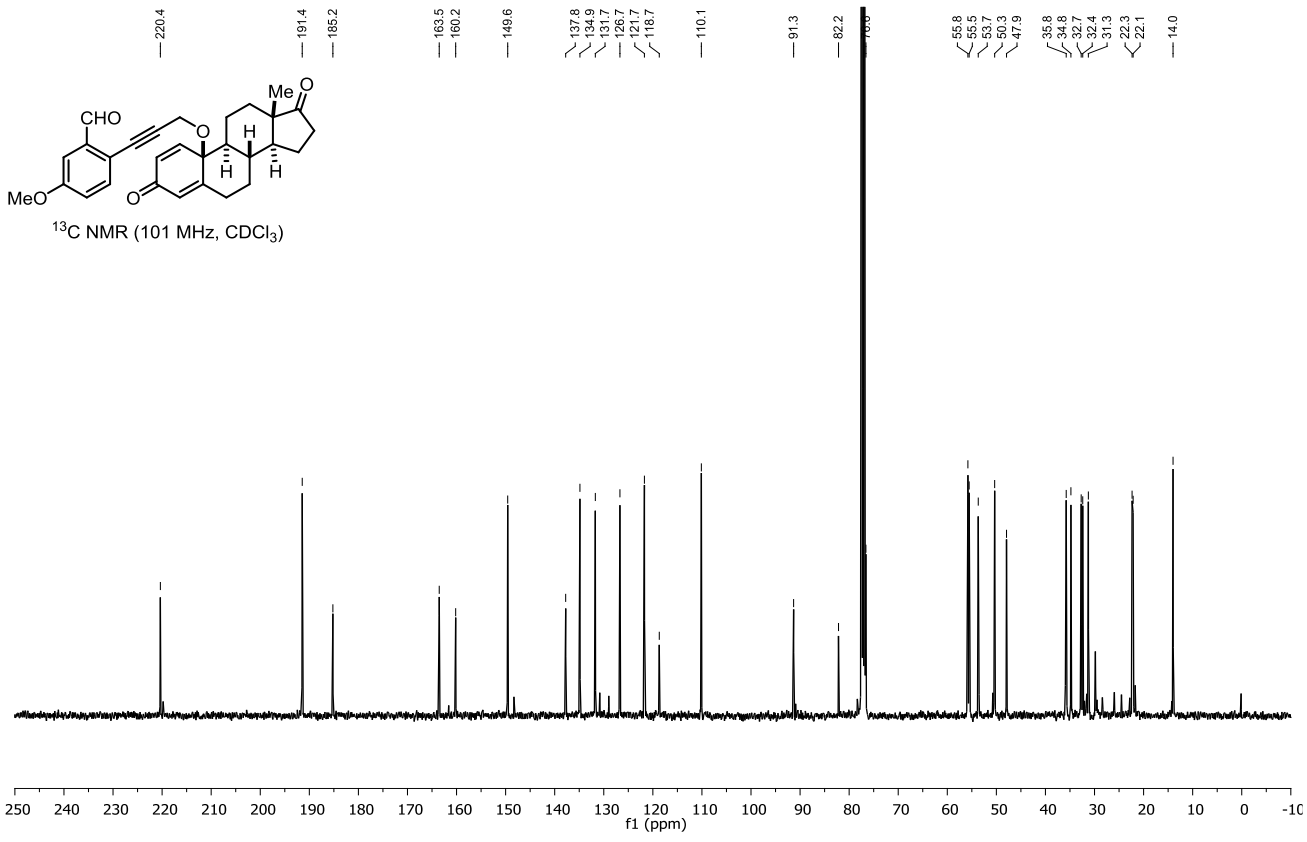
5-Methyl-2-(3-(((8S,9S,10S,13S,14S)-13-methyl-3,17-dioxo-3,6,7,8,9,11,12,13,14,15,16,17-dodecahydro-10*H*-cyclopenta[a]phenanthren-10-yl)oxy)prop-1-yn-1-yl)benzaldehyde (7b):



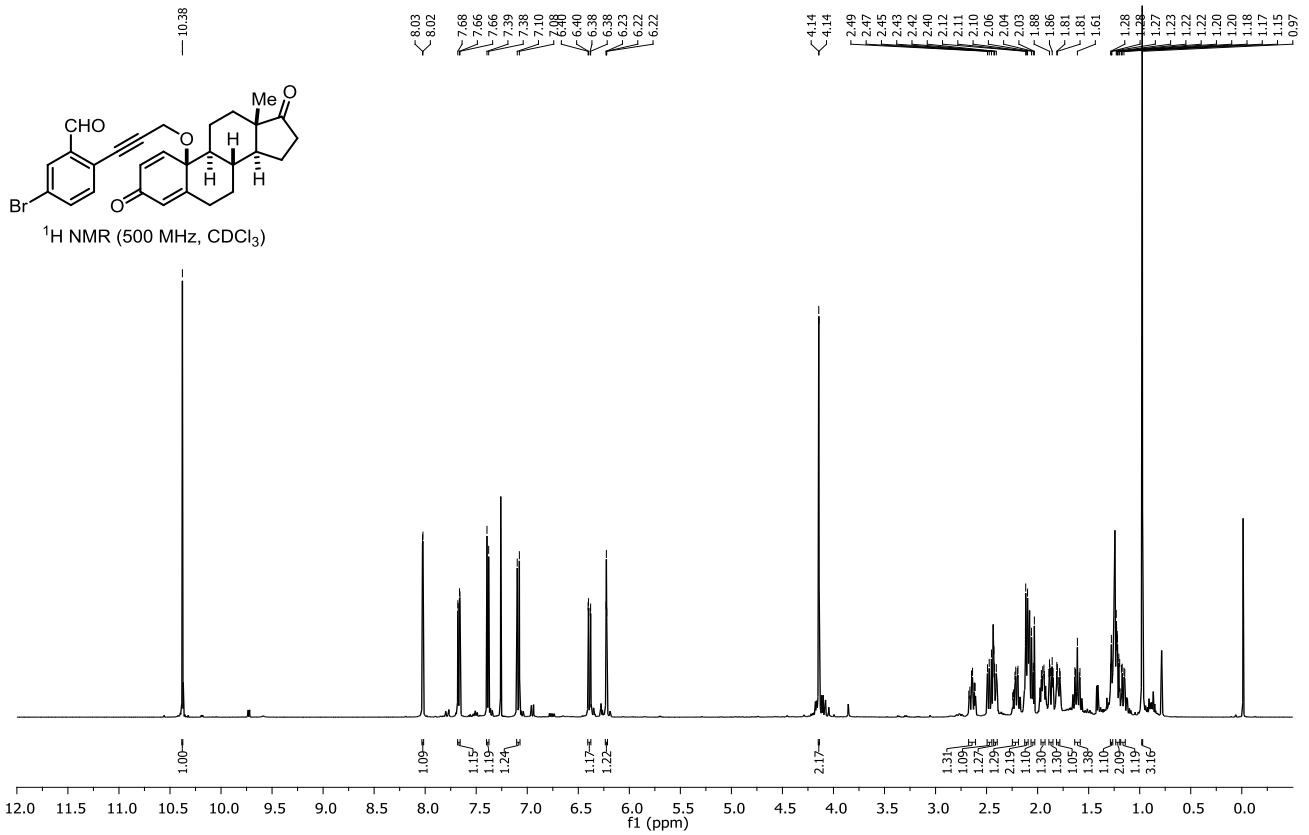


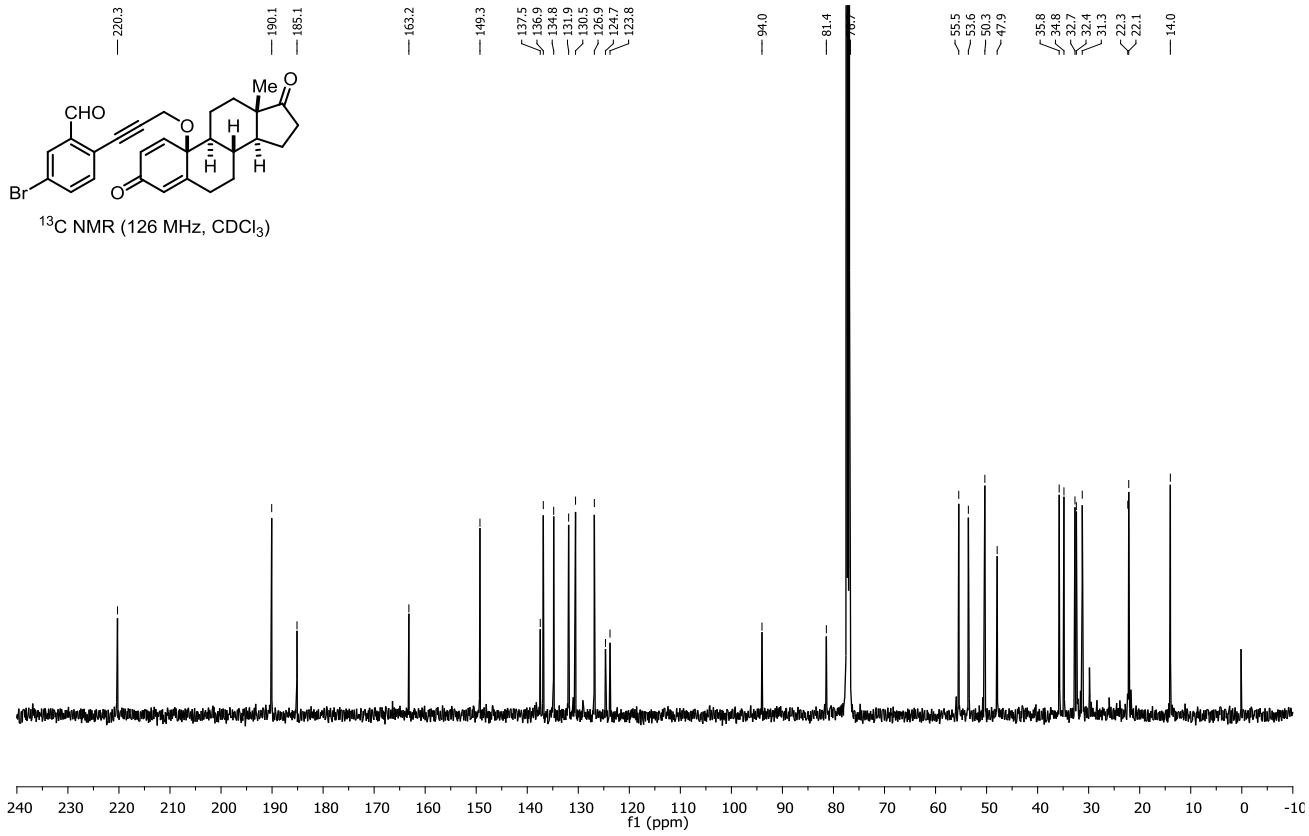
5-Methoxy-2-(3-(((8S,9S,10S,13S,14S)-13-methyl-3,17-dioxo-3,6,7,8,9,11,12,13,14,15,16, 17 -dodecahydro-10*H*-cyclopenta[a]phenanthren-10-yl)oxy)prop-1-yn-1yl)benzaldehyde (7c):



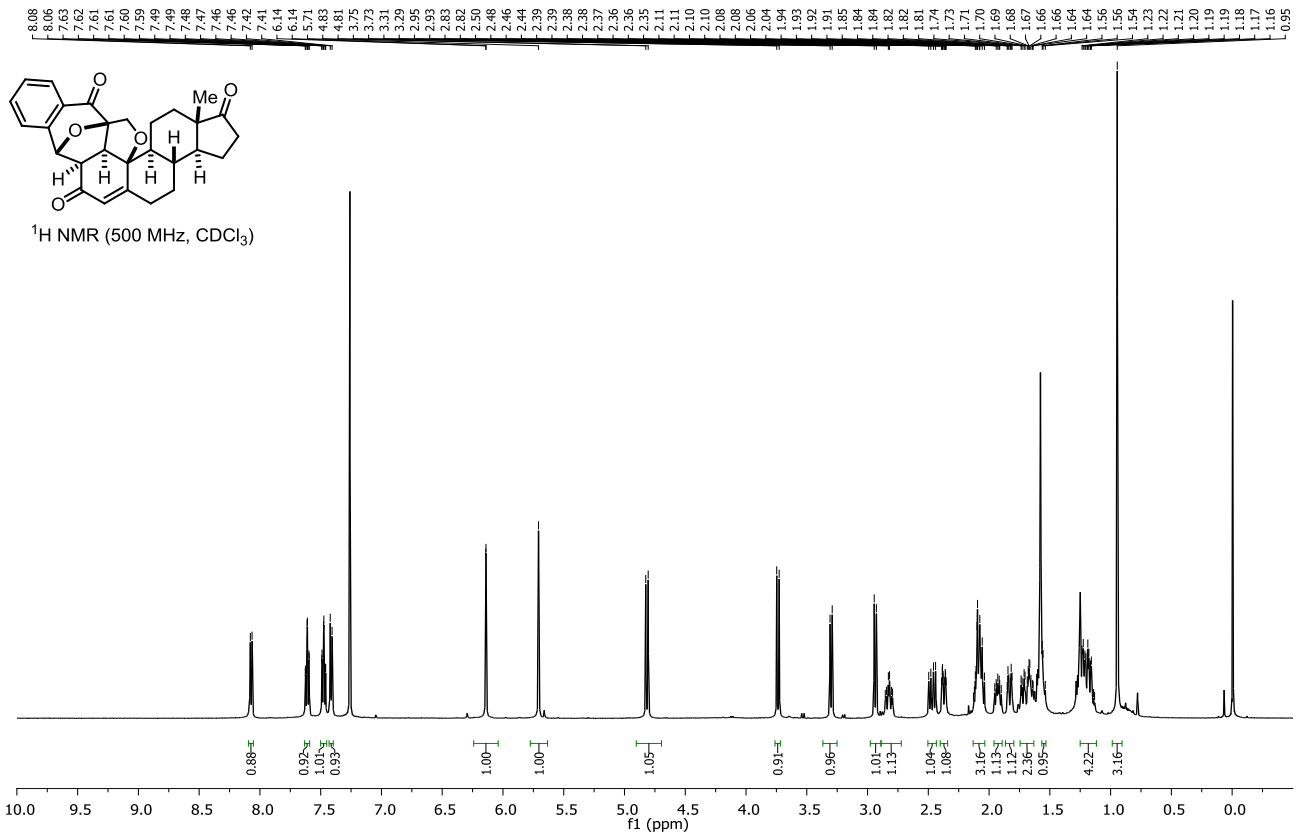


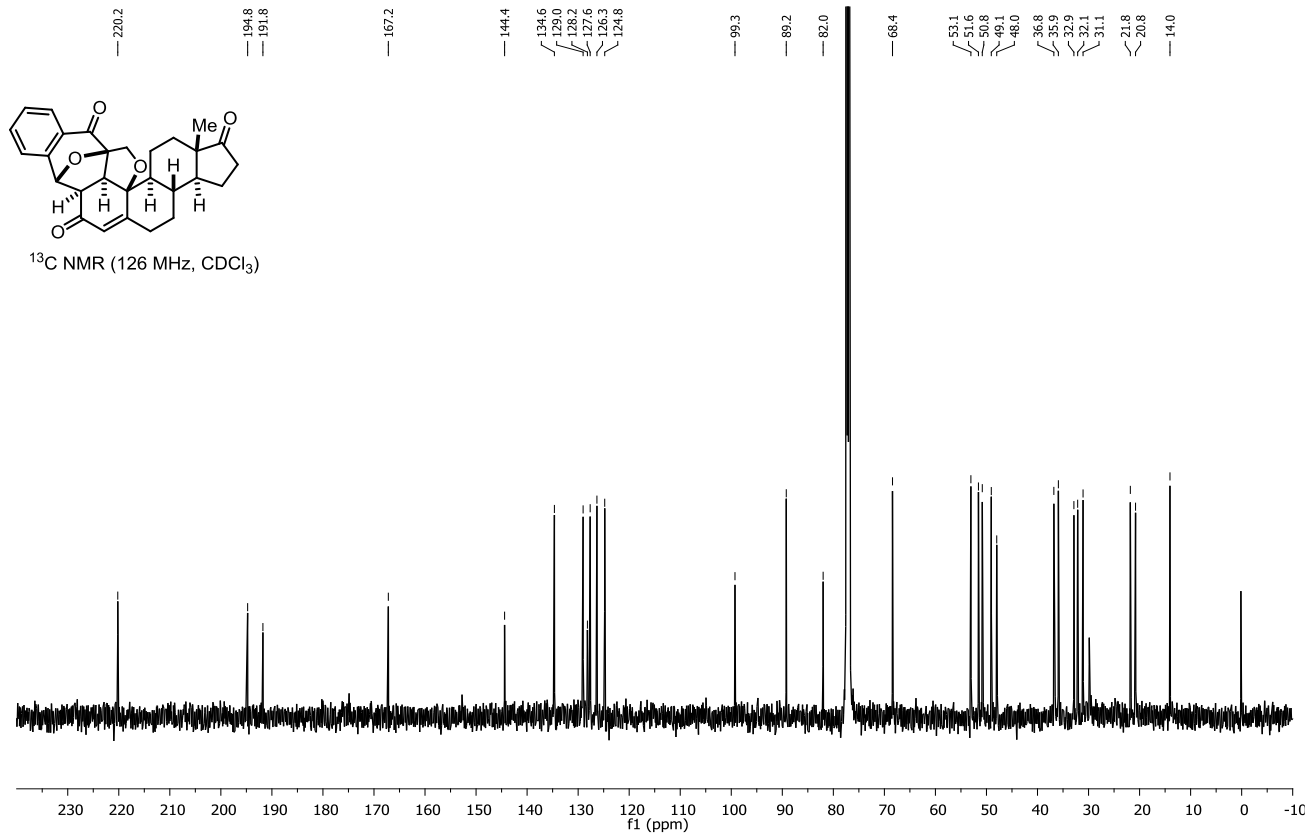
5-Bromo-2-(3-(((8S,9S,10S,13S,14S)-13-methyl-3,17-dioxo-3,6,7,8,9,11,12,13,14,15,16,17-dodecahydro-10H-cyclopenta[a]phenanthren-10-yl)oxy)prop-1-yn-1-yl)benzaldehyde (7d):



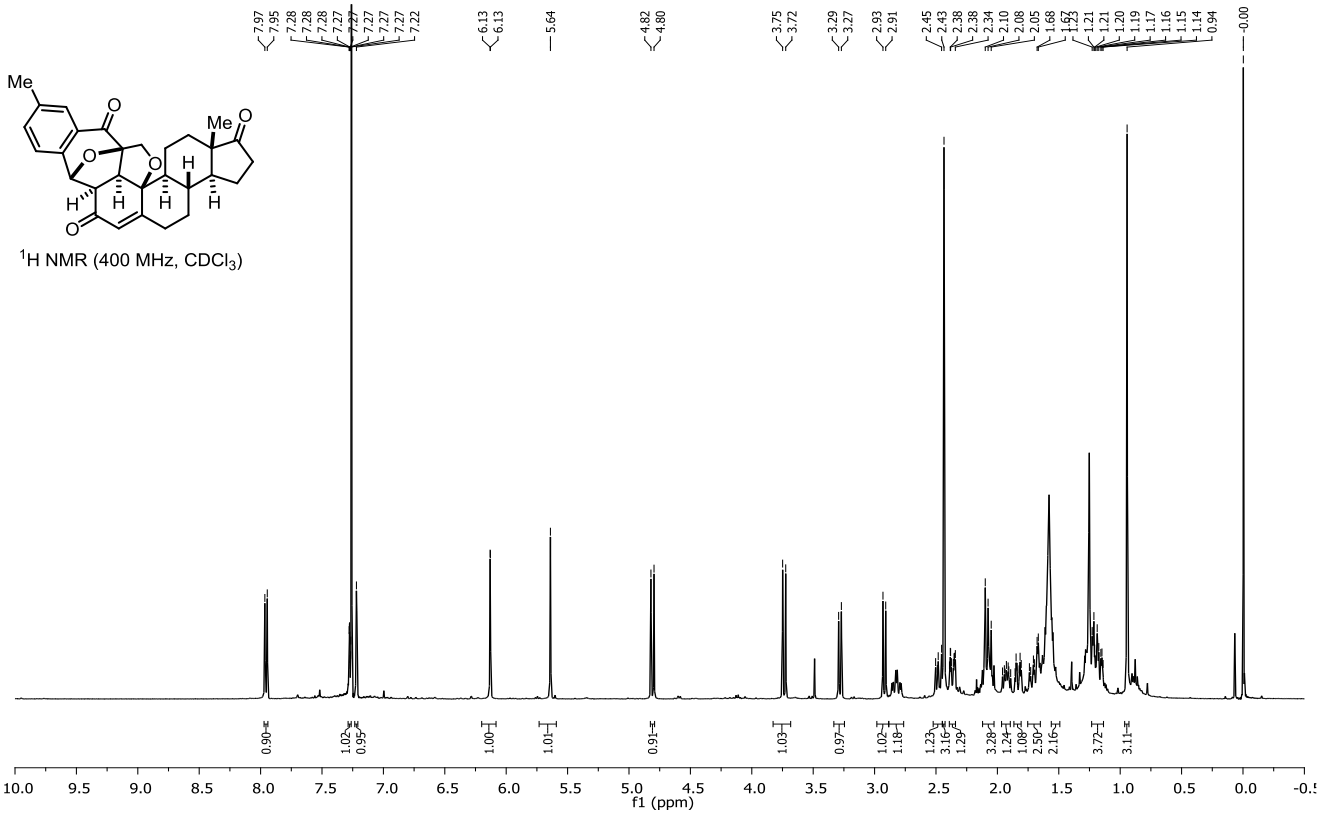


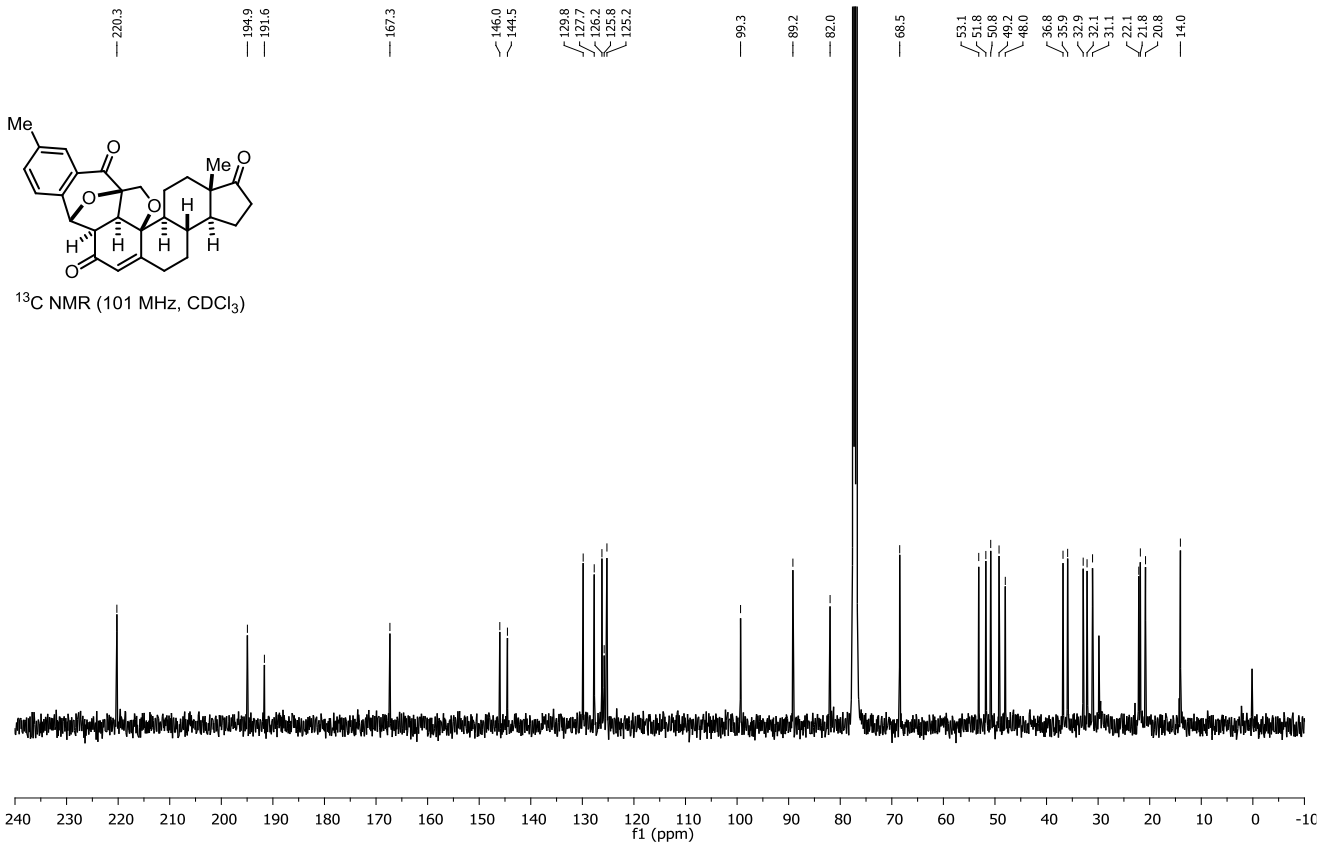
(3a*S*,3b*S*,7a*R*,7a^1*R*,8*R*,13a*R*,15a*R*,15b*S*,17a*S*)-17a-Methyl-2,3,3a,3b,4,5,7a,8,15b,16,17,17a-dodecahydro-14*H*-8,13a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]cyclopenta[5,6]naphtho[2,1-*h*]benzofuran-1,7,13(7a^1*H*)-trione (8a):



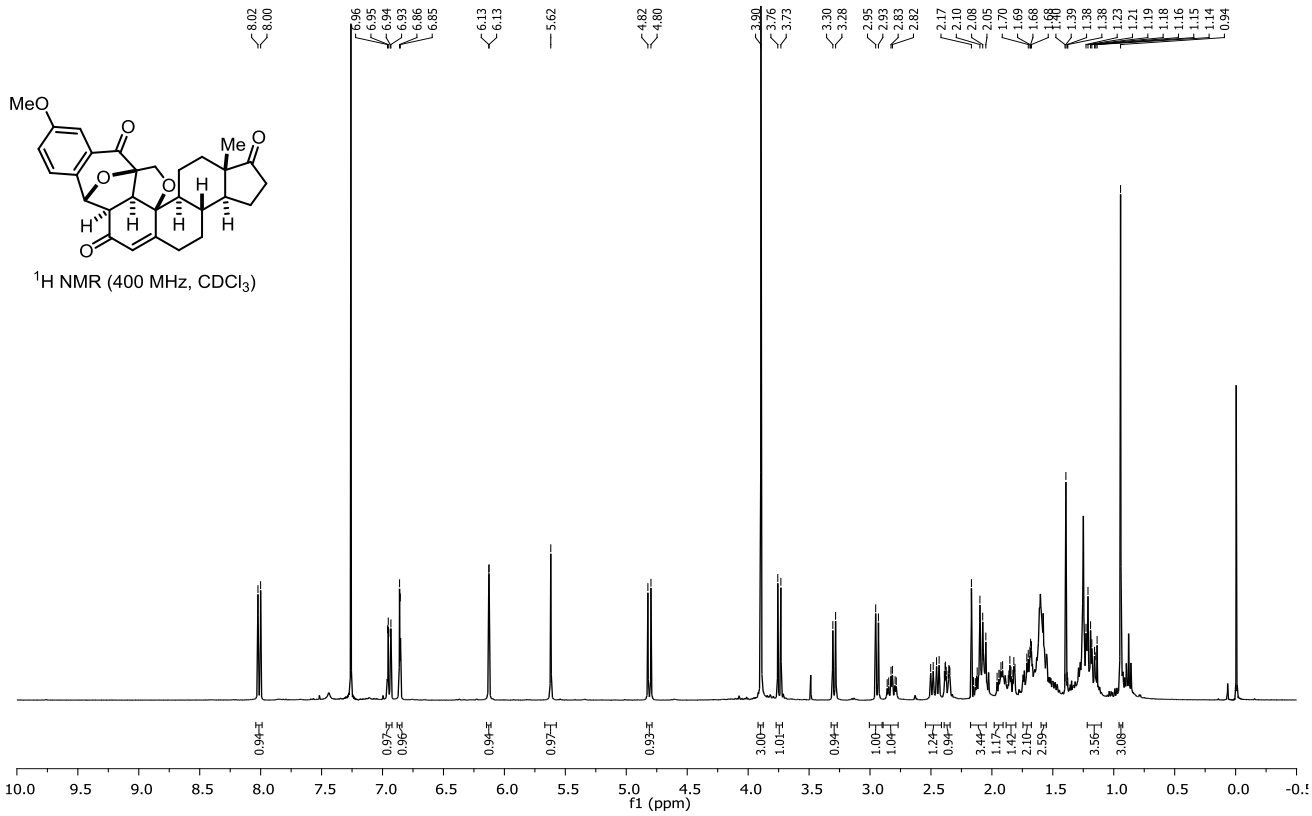


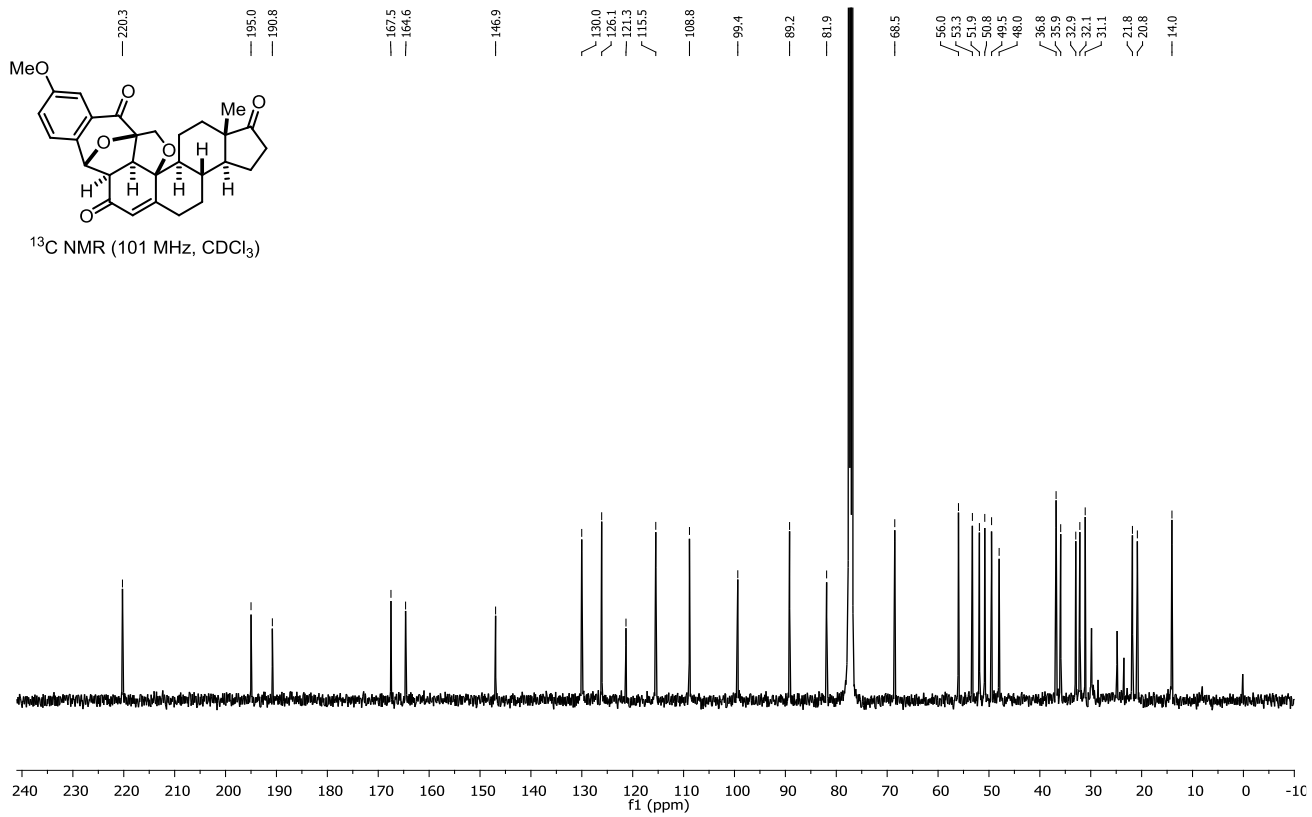
(3a*S*,3b*S*,7a*R*,7a[1]*R*,8*R*,13a*R*,15a*R*,15b*S*,17a*S*)-11,17a-Dimethyl-2,3,3a,3b,4,5,7a,8,15b, 16,17,17a-dodecahydro-14*H*-8,13a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]cyclopenta[5,6] naphtho[2,1-h]benzofuran-1,7,13(7a1*H*)-trione (8b):



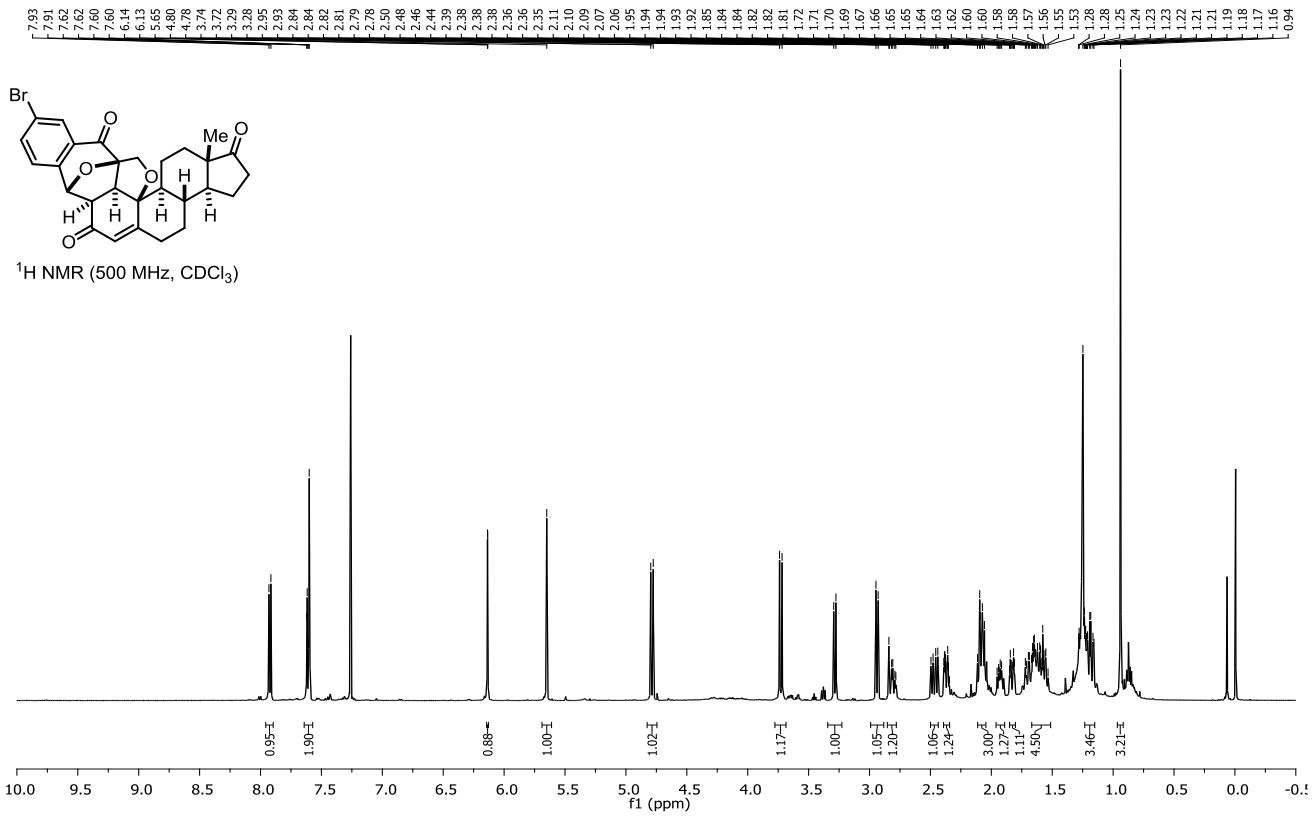


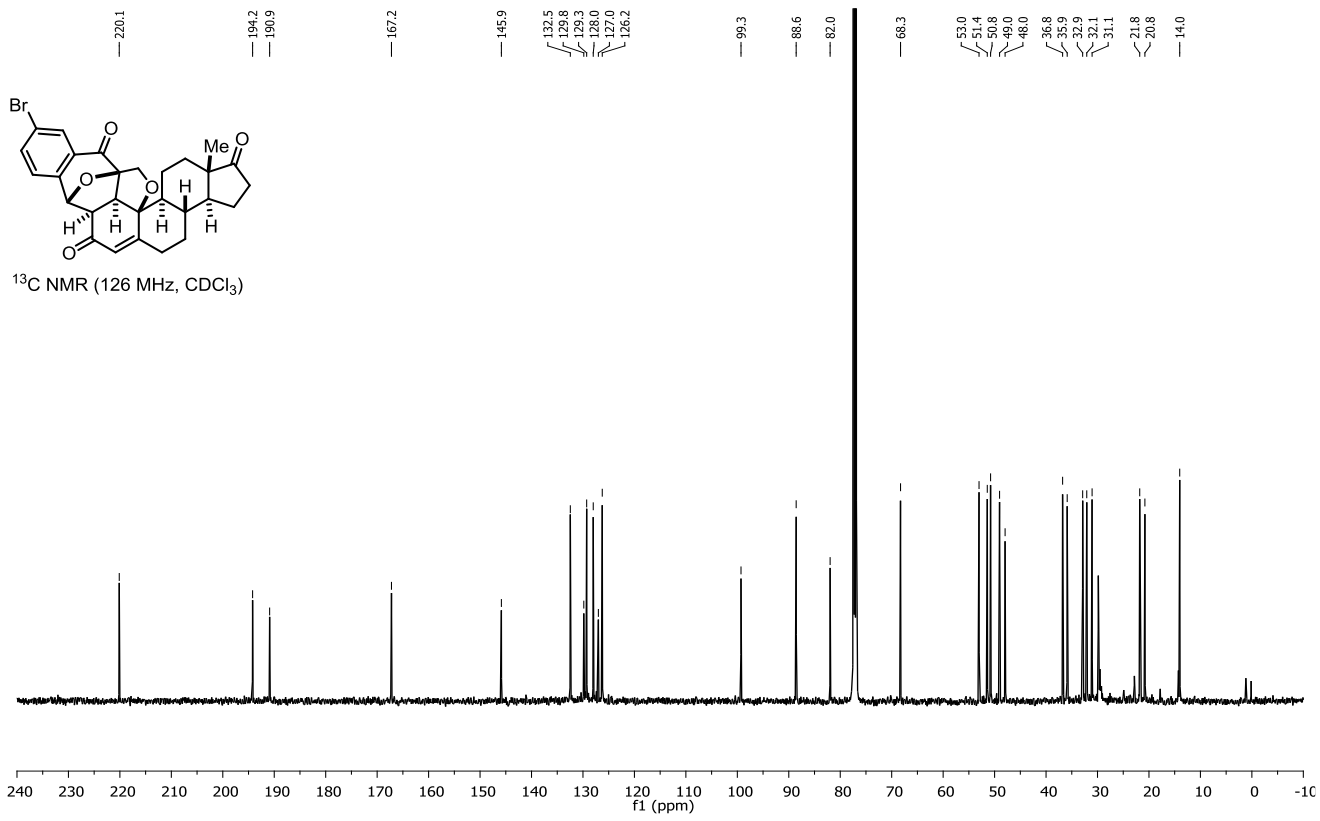
(3a*S*,3b*S*,7a*R*,7a^1*R*,8*R*,13a*R*,15a*R*,15b*S*,17a*S*)-11-Methoxy-17a-methyl-2,3,3a,3b,4,5, 7a, 8,15b,16,17,17a-dodecahydro-14*H*-8,13a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]cyclopenta [5,6]naphtho[2,1-h]benzofuran-1,7,13(7a^1*H*)-trione (8c):



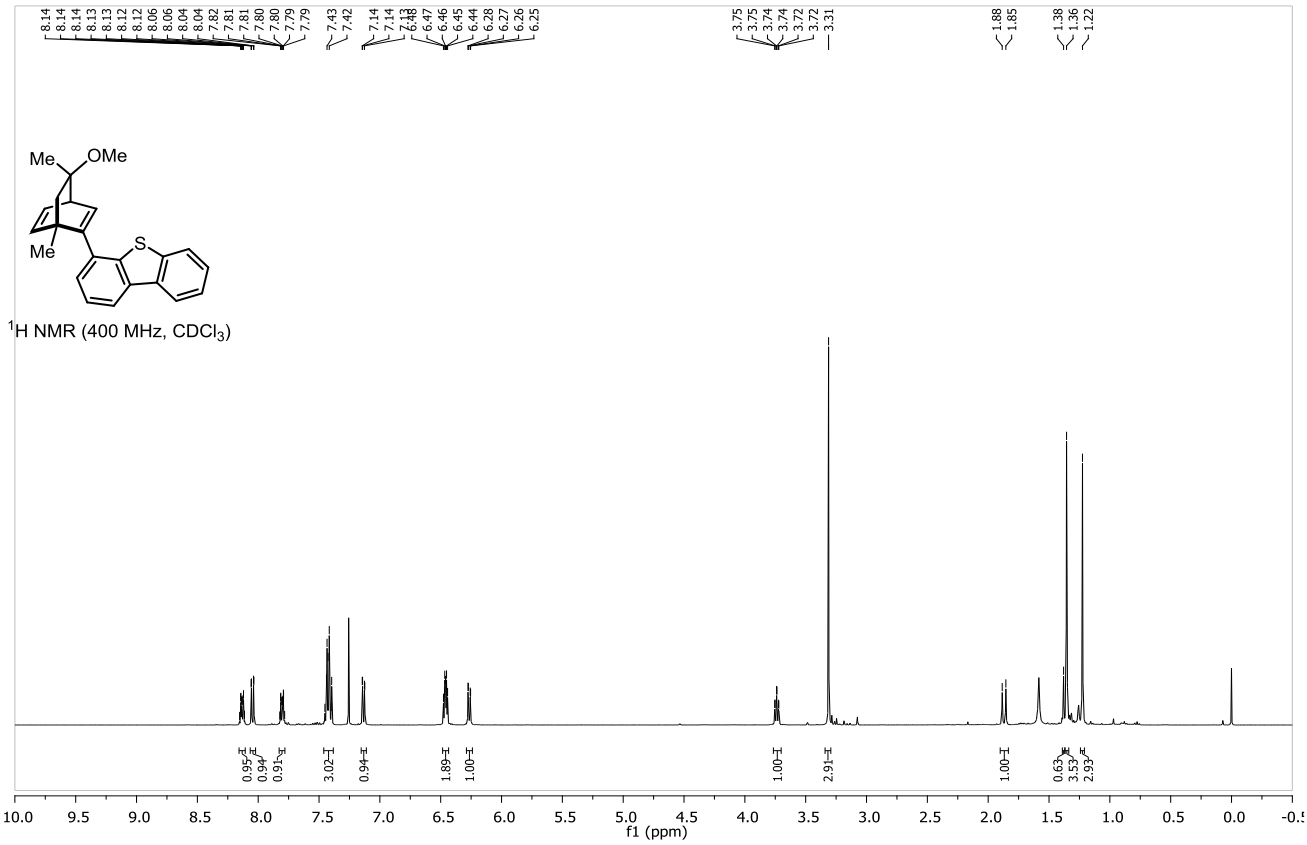


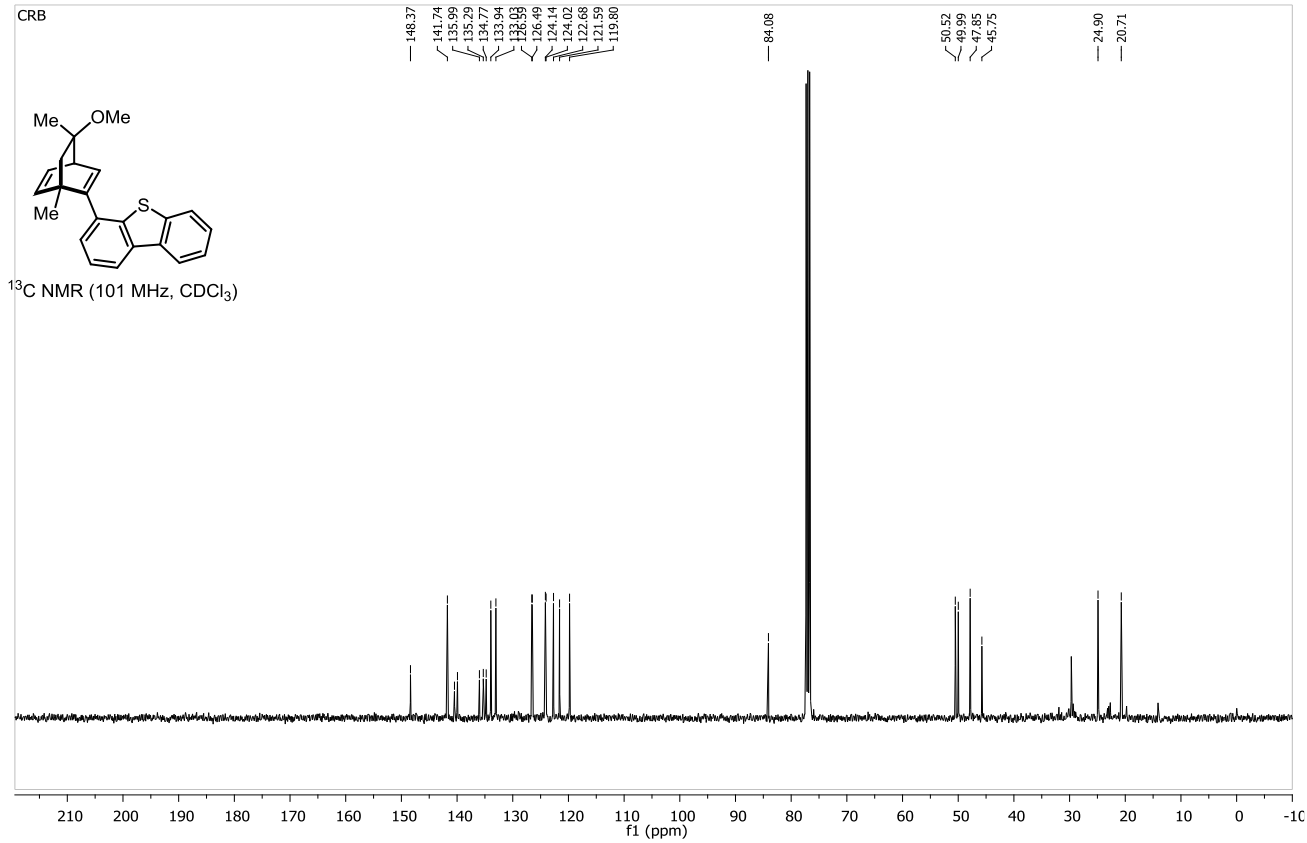
(3a*S*,3b*S*,7a*R*,7a^1*R*,8*R*,13a*R*,15a*R*,15b*S*,17a*S*)-11-bromo-17a-methyl-2,3,3a,3b,4,5,7a,8, 15b,16,17,17a-dodecahydro-14*H*-8,13a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]cyclo penta [5,6]naphtho[2,1-h]benzofuran-1,7,13(7a^1*H*)-trione (8d):



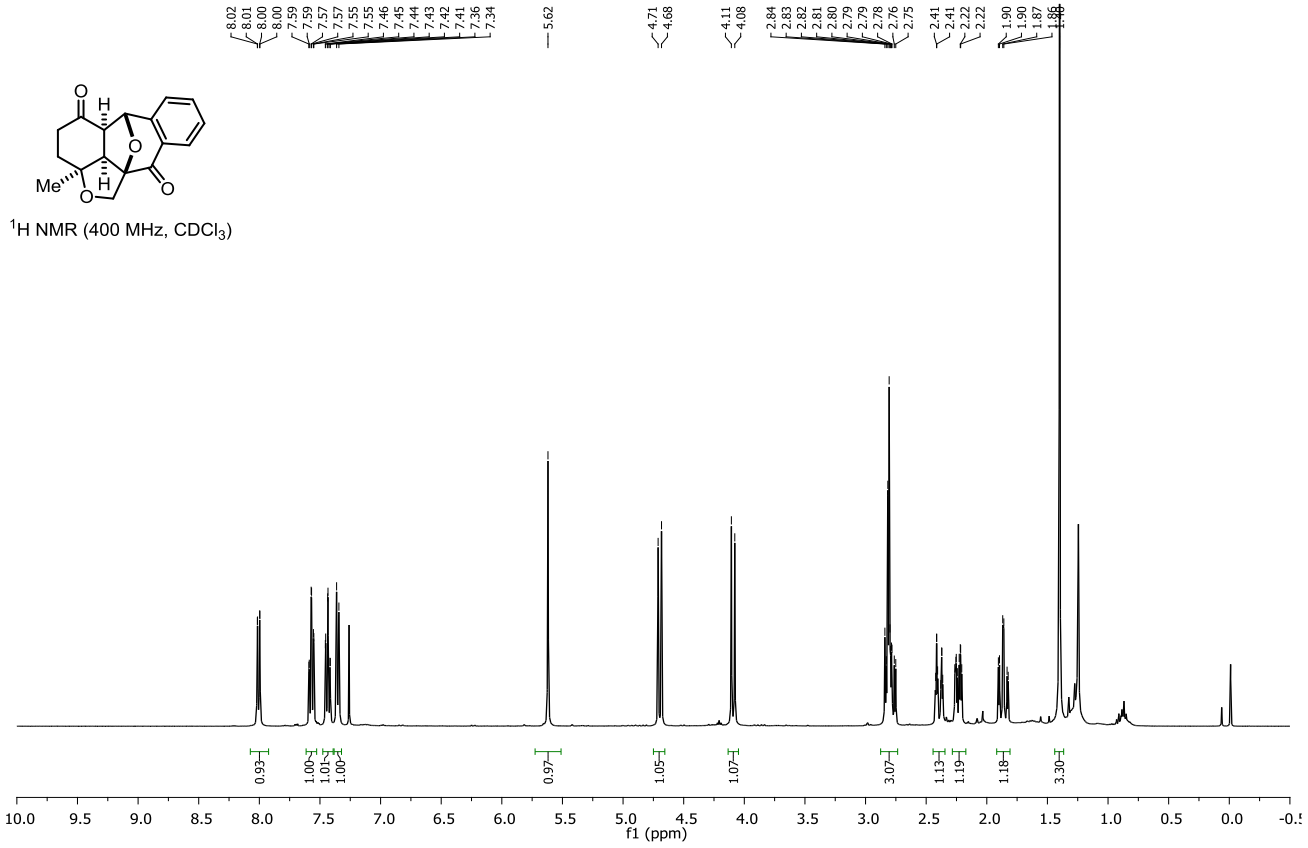


4-((1*R*,4*R*,8*R*)-8-methoxy-1,8-dimethylbicyclo[2.2.2]octa-2,5-dien-2-yl)dibenzo[*b*,*d*]thiophene (L8):

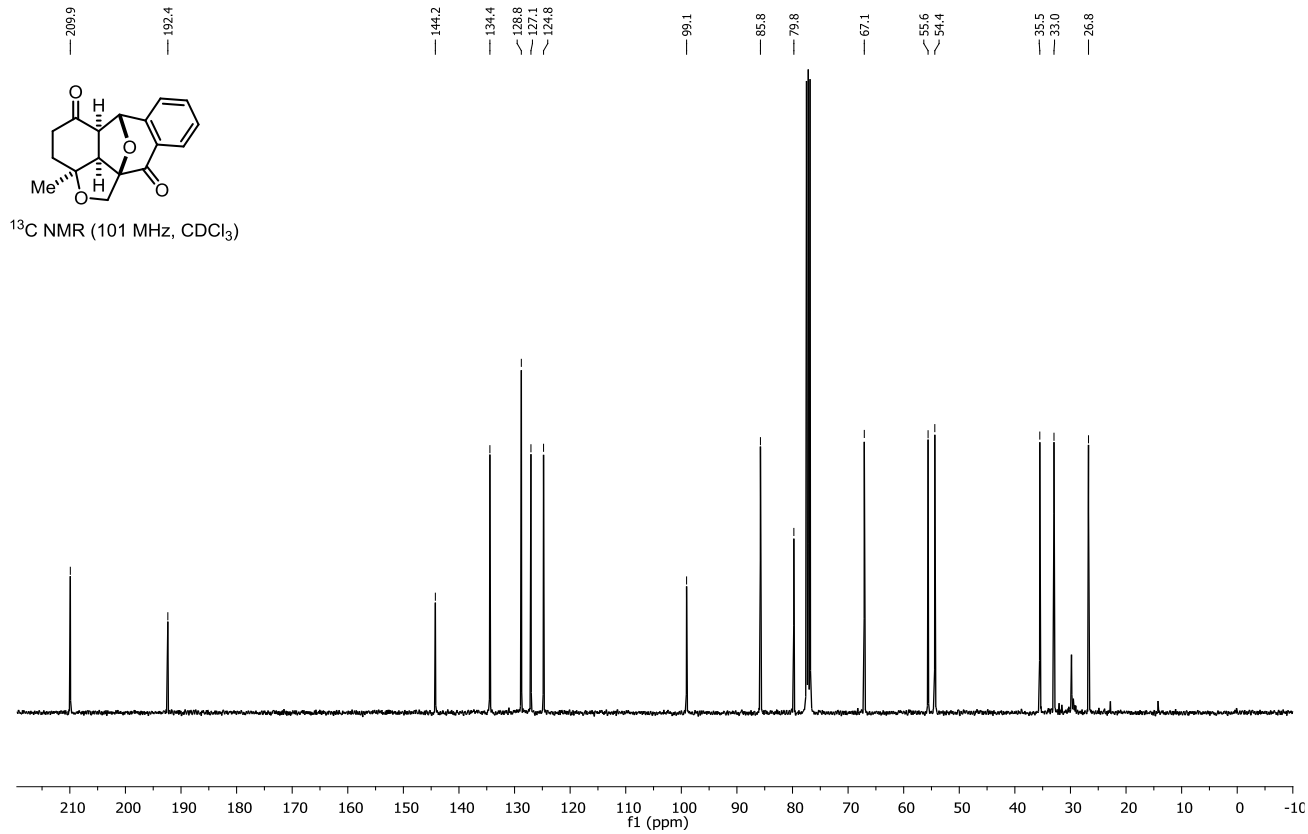




(±)-2a-methyl-2a,2a1,3,4,5a,6-hexahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (7):

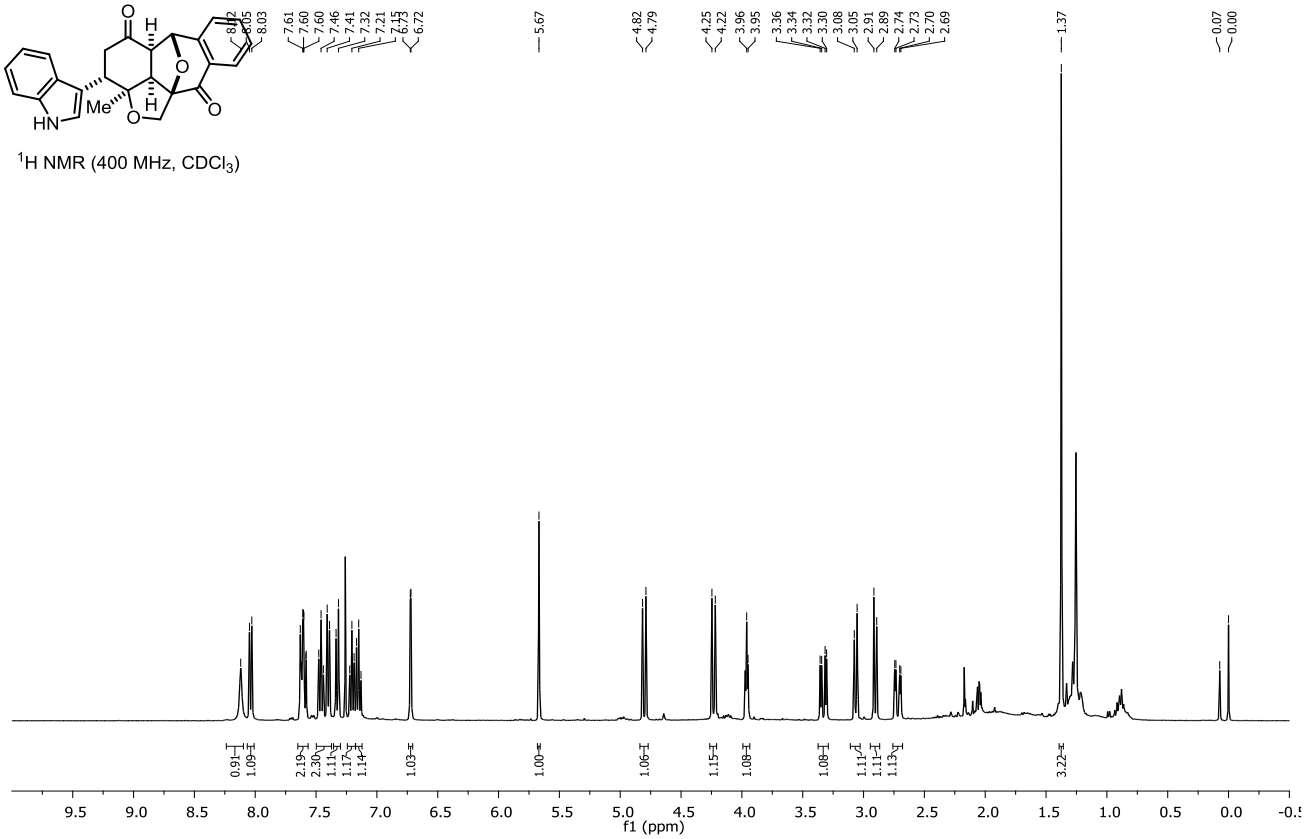


^{1}H NMR (400 MHz, $CDCl_3$)

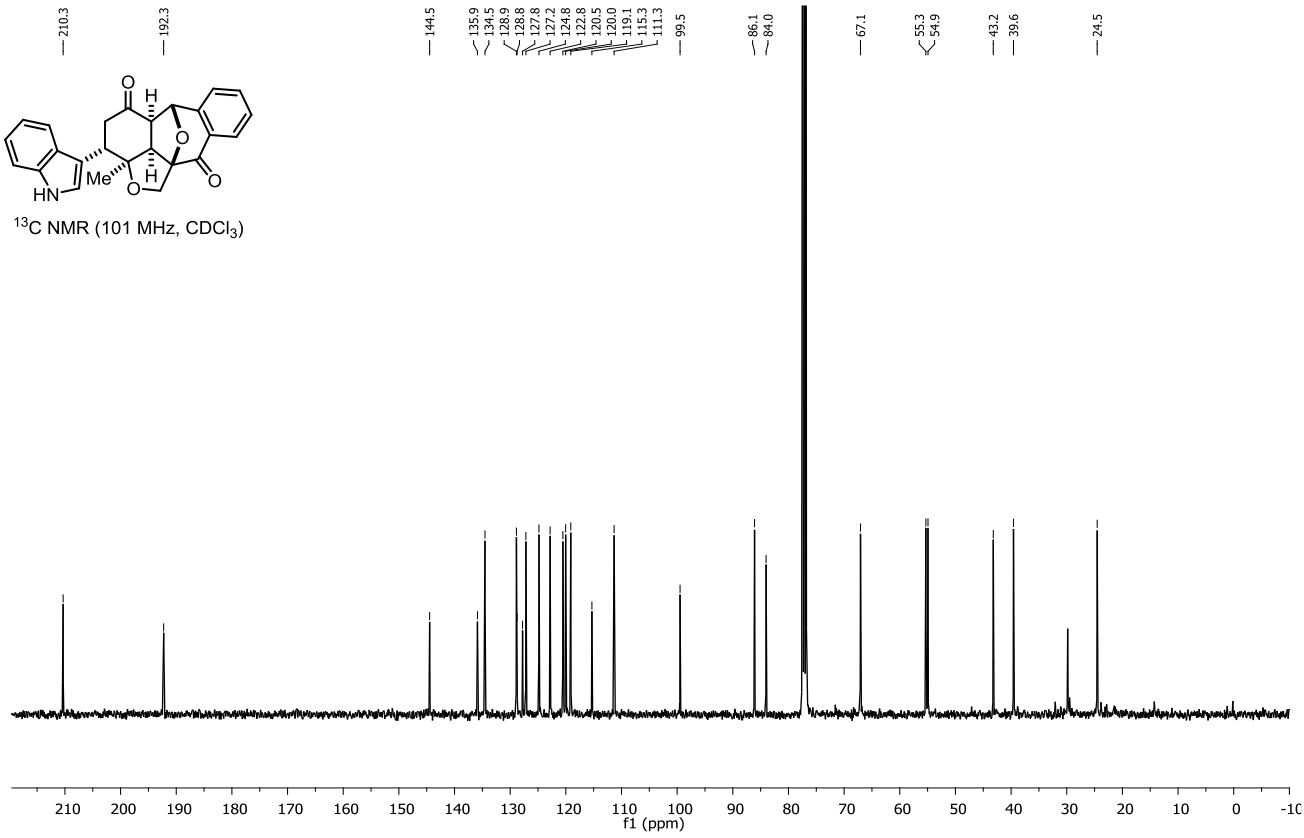


^{13}C NMR (101 MHz, $CDCl_3$)

(±)-3-(1*H*-Indol-3-yl)-2a-methyl-2a,2a1,3,4,5a,6-hexahydro-1*H*-6,11a-epoxybenzo[5,6]cyclohepta[1,2,3-*cd*]benzofuran-5,11-dione (8):

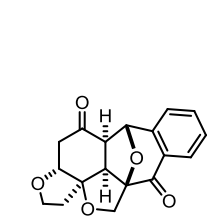


^{1}H NMR (400 MHz, $CDCl_3$)

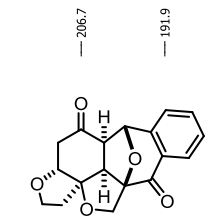


^{13}C NMR (101 MHz, $CDCl_3$)

Compound (±)-9:

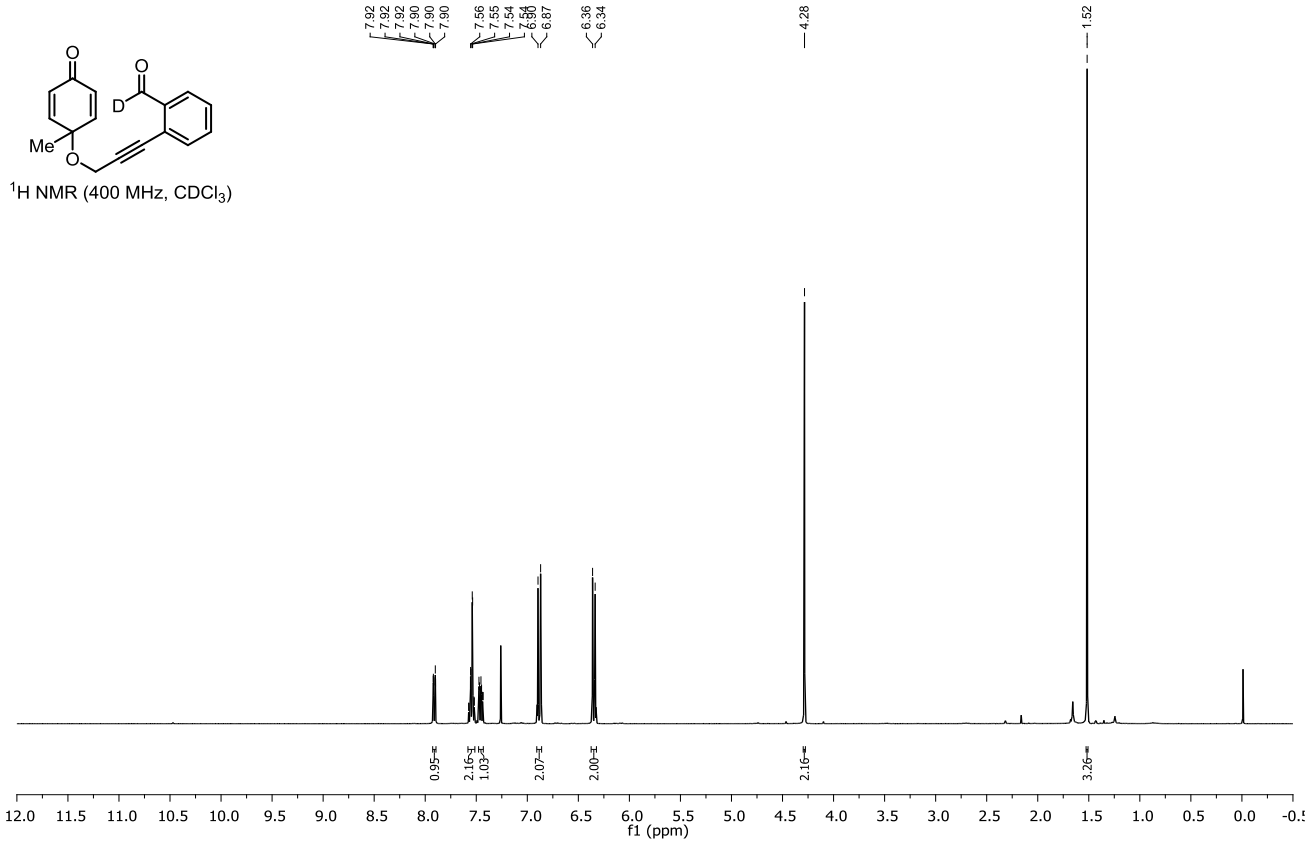


^{1}H NMR (400 MHz, $CDCl_3$)

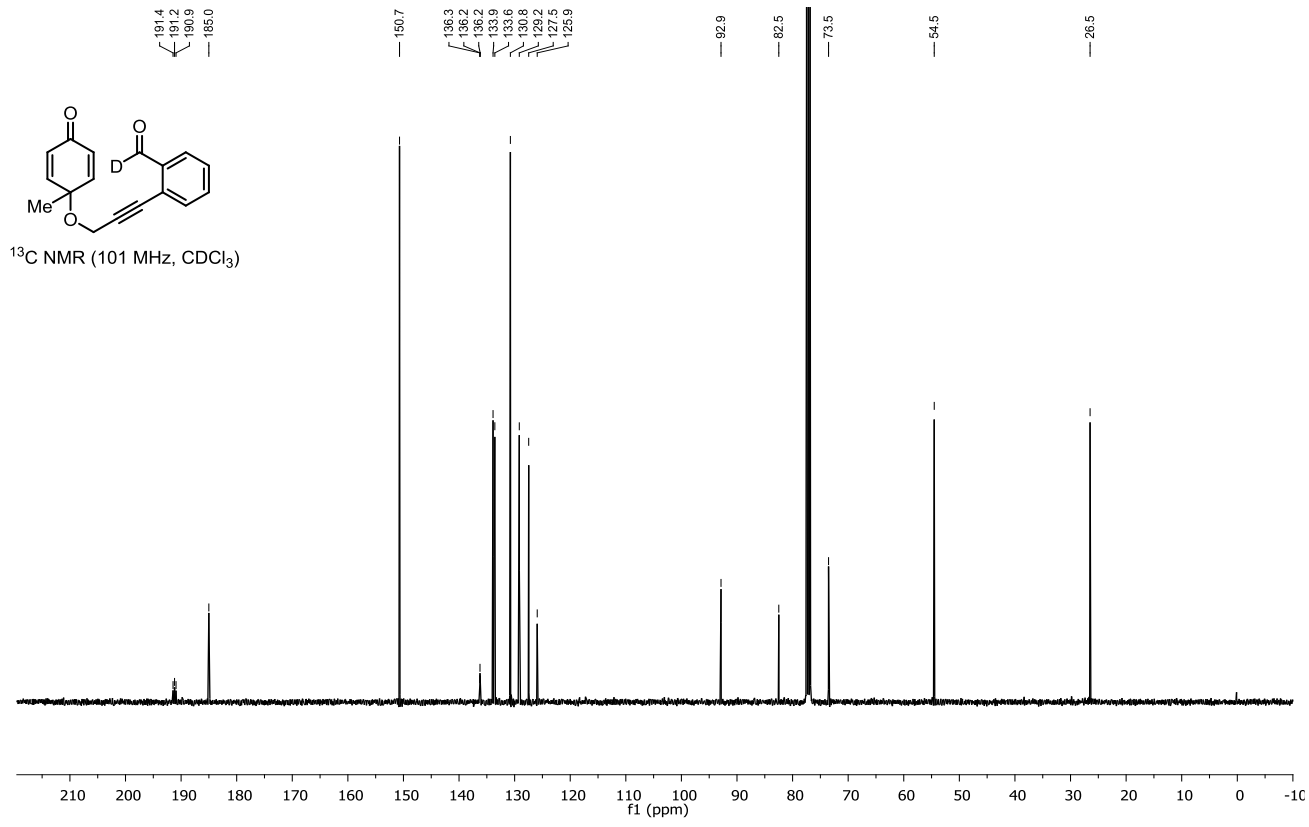


^{13}C NMR (126 MHz, $CDCl_3$)

2-(3-((1-methyl-4-oxocyclohexa-2,5-dien-1-yl)oxy)prop-1-yn-1-yl)benzaldehyde-d_1 (1a-d_1):



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



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