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Supporting Information

Total Synthesis, Structure Revision and Cytotoxic Activity of Sch 53825 and Its Derivatives

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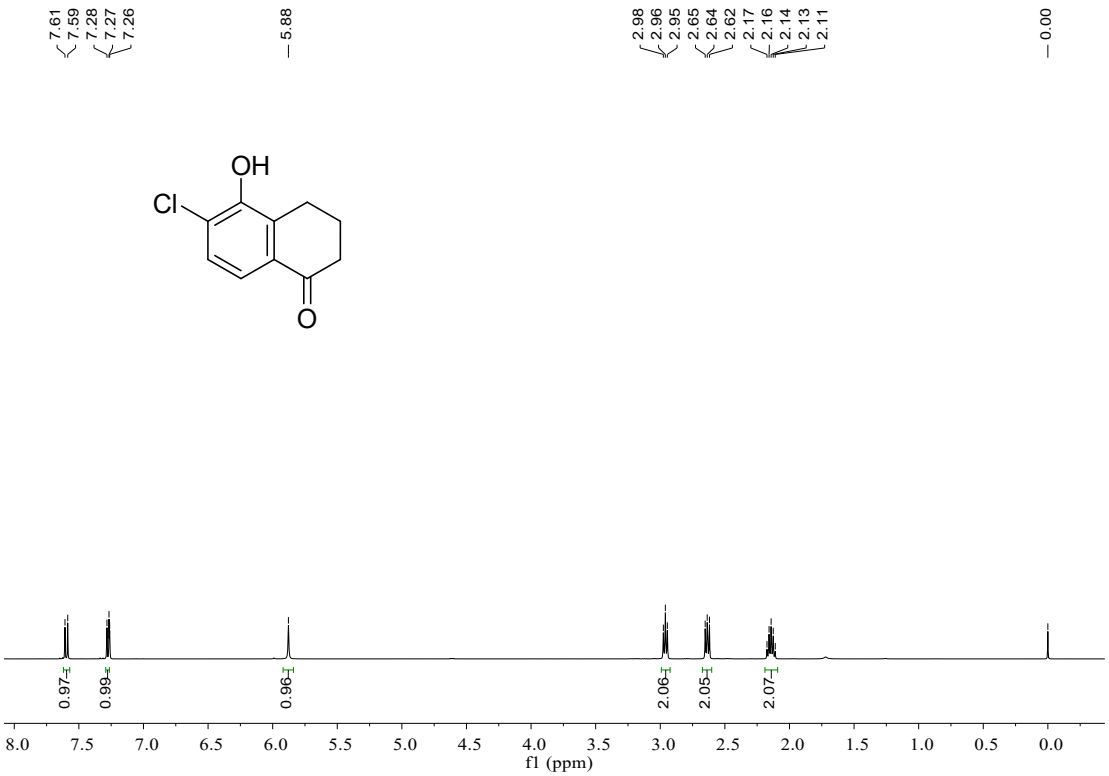


Figure S1 ^{1}H NMR of compound **6**

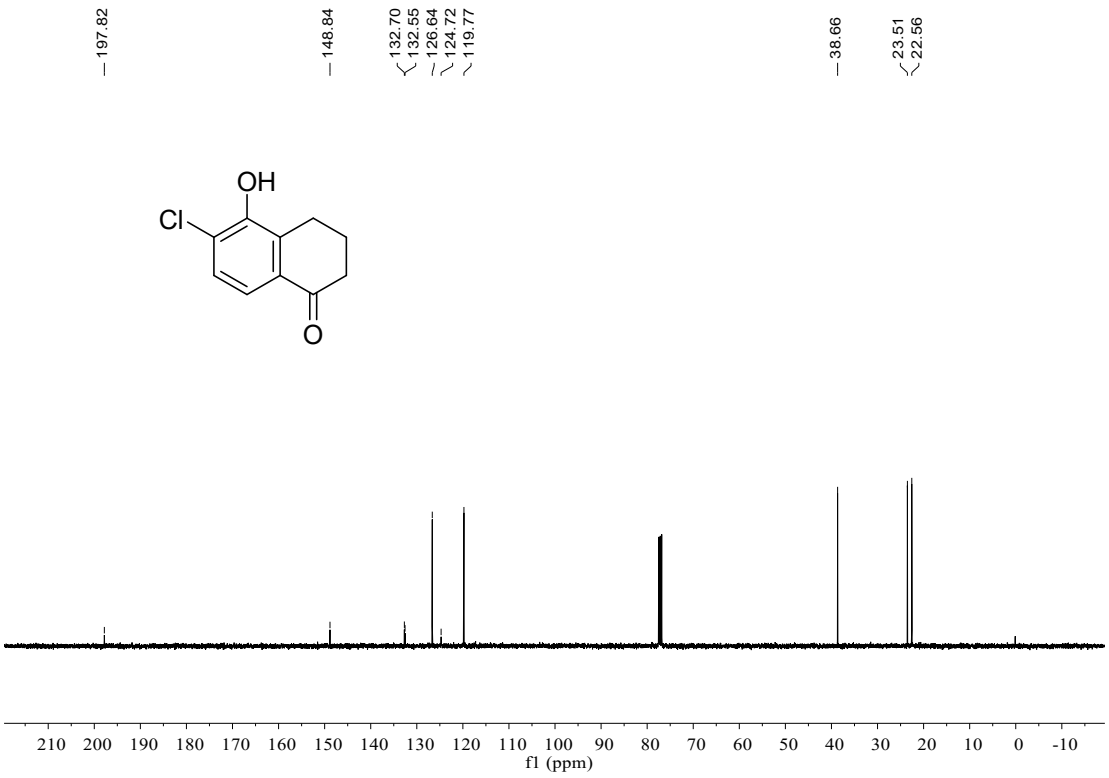


Figure S2 ^{13}C NMR of compound **6**

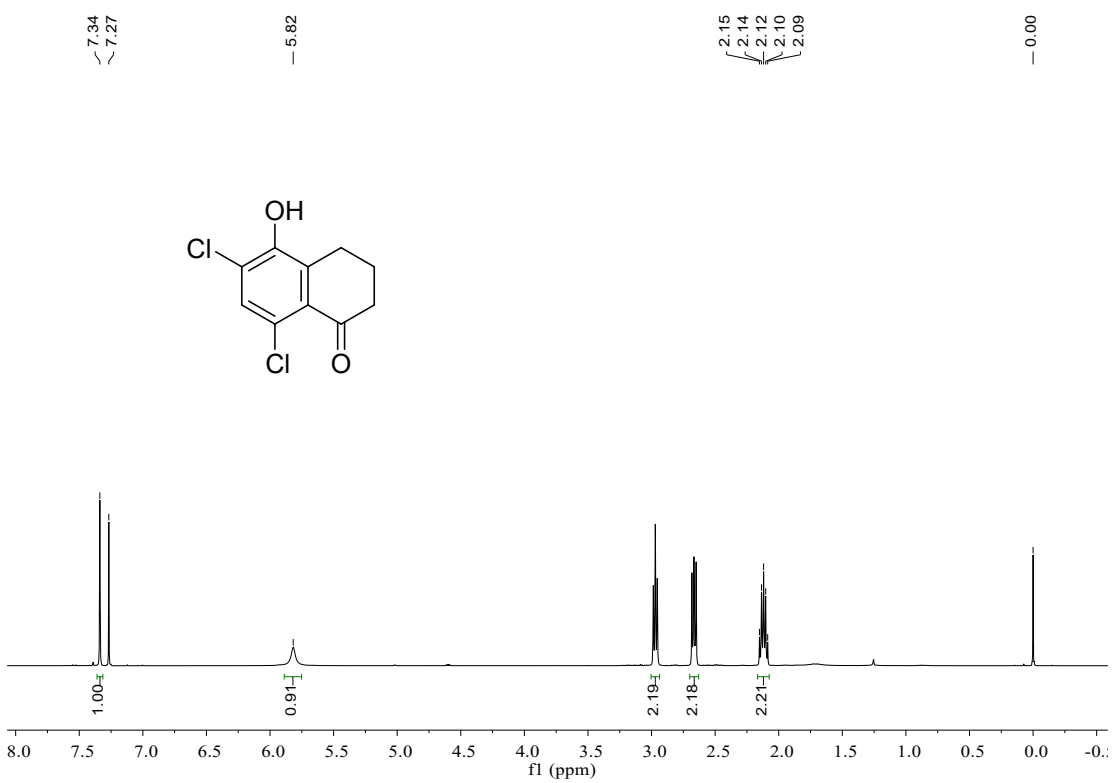


Figure S3 ^{1}H NMR of compound **5-hydroxy-6,8-dichlorotetralone**

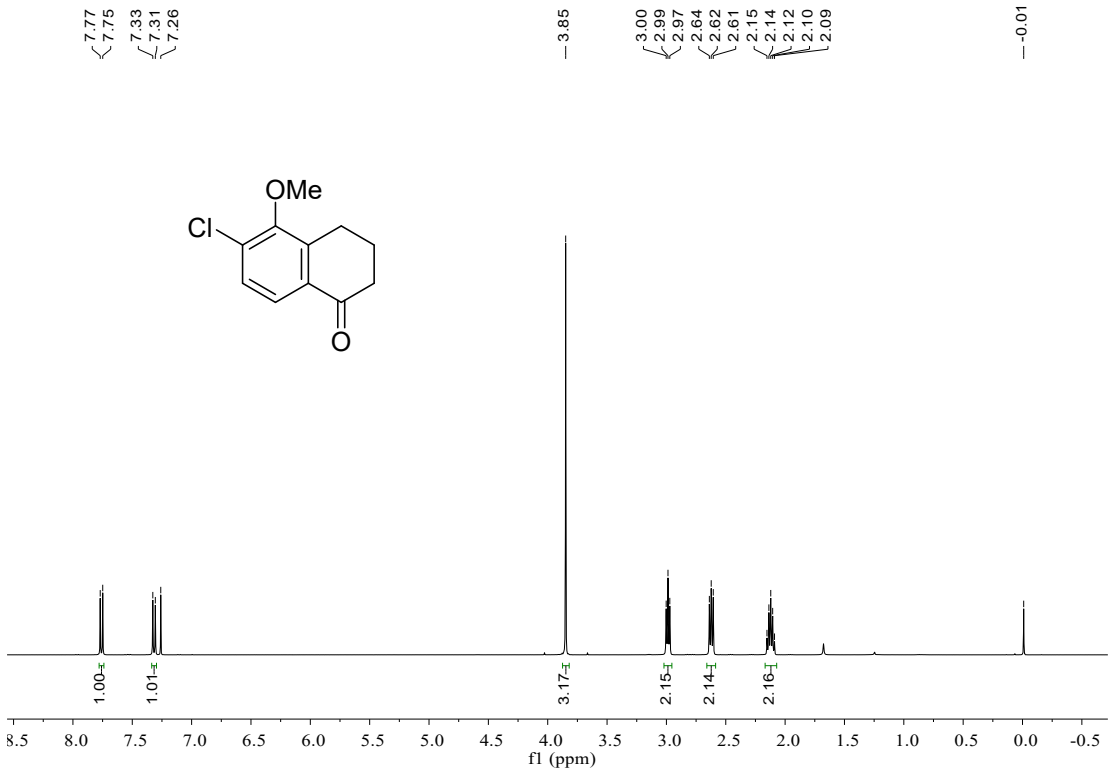


Figure S4 ^{1}H NMR Spectra of compound **7**

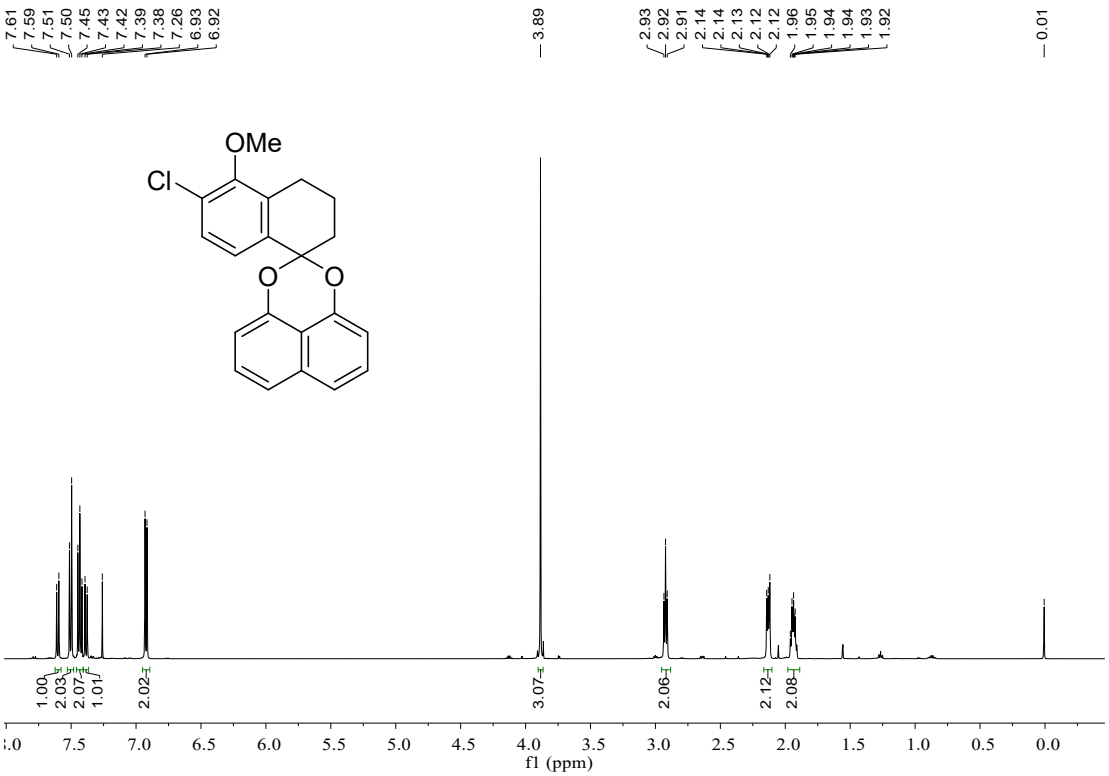


Figure S5 ^{1}H NMR Spectra of compound **9**

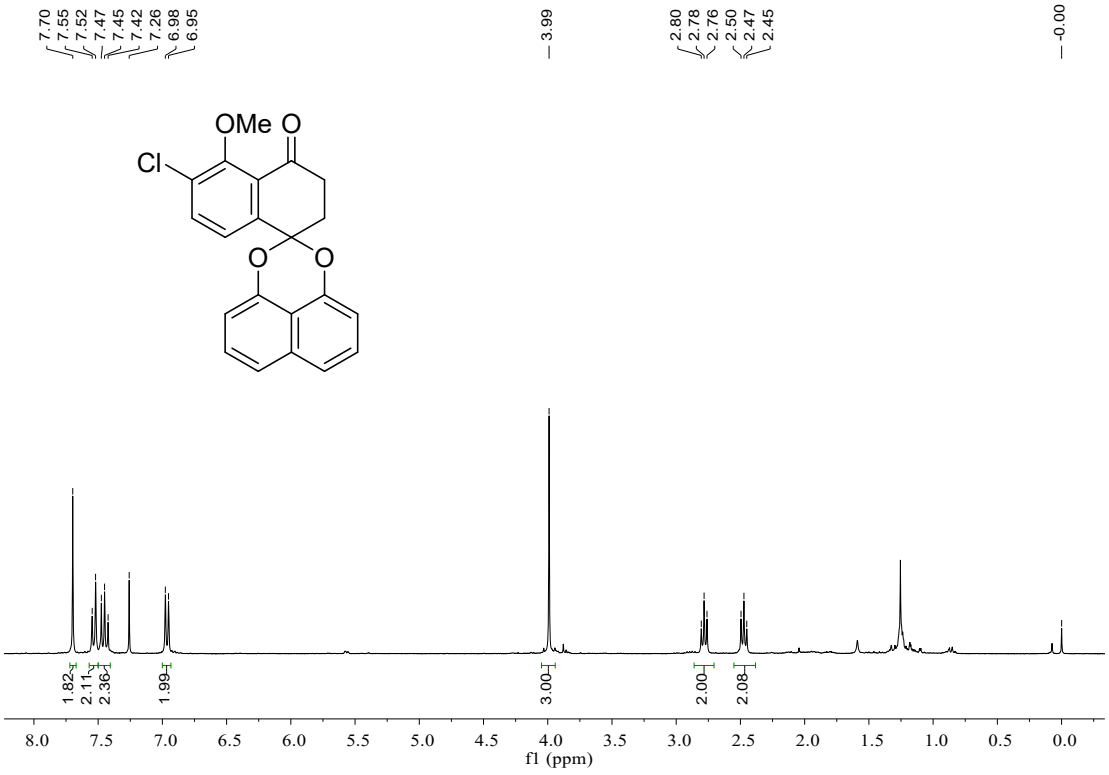


Figure S6 ^{1}H NMR Spectra of compound **10**

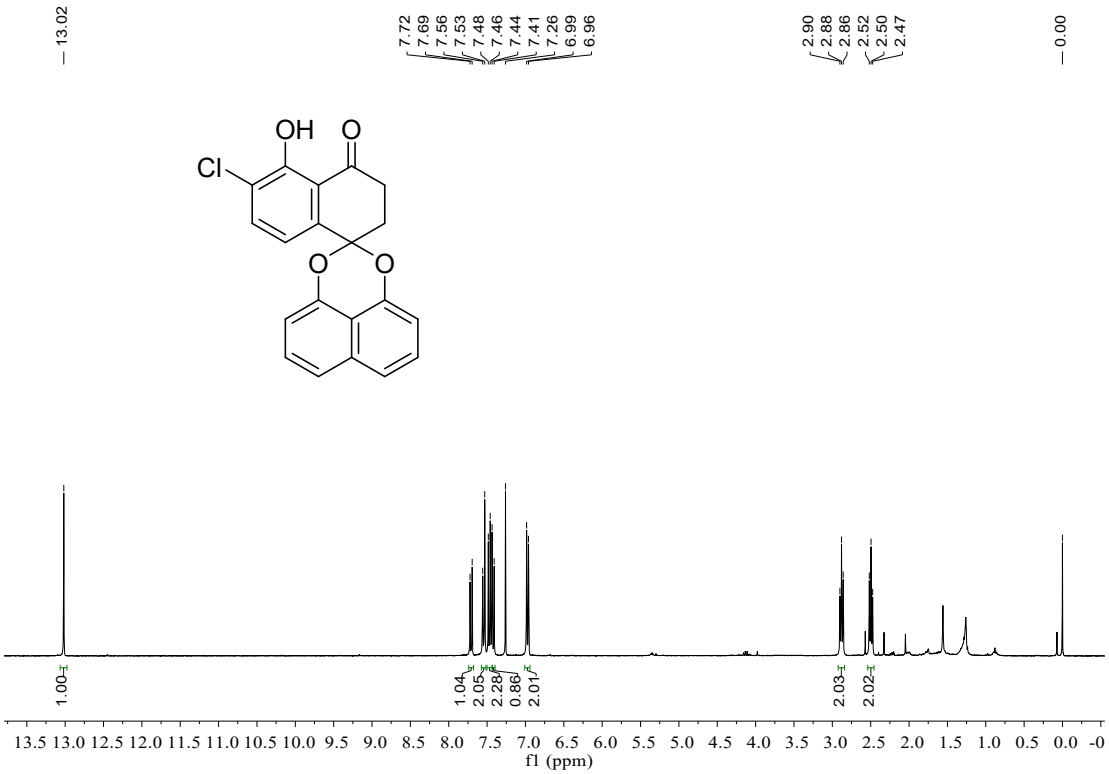


Figure S7 ^{1}H NMR Spectra of compound **2**

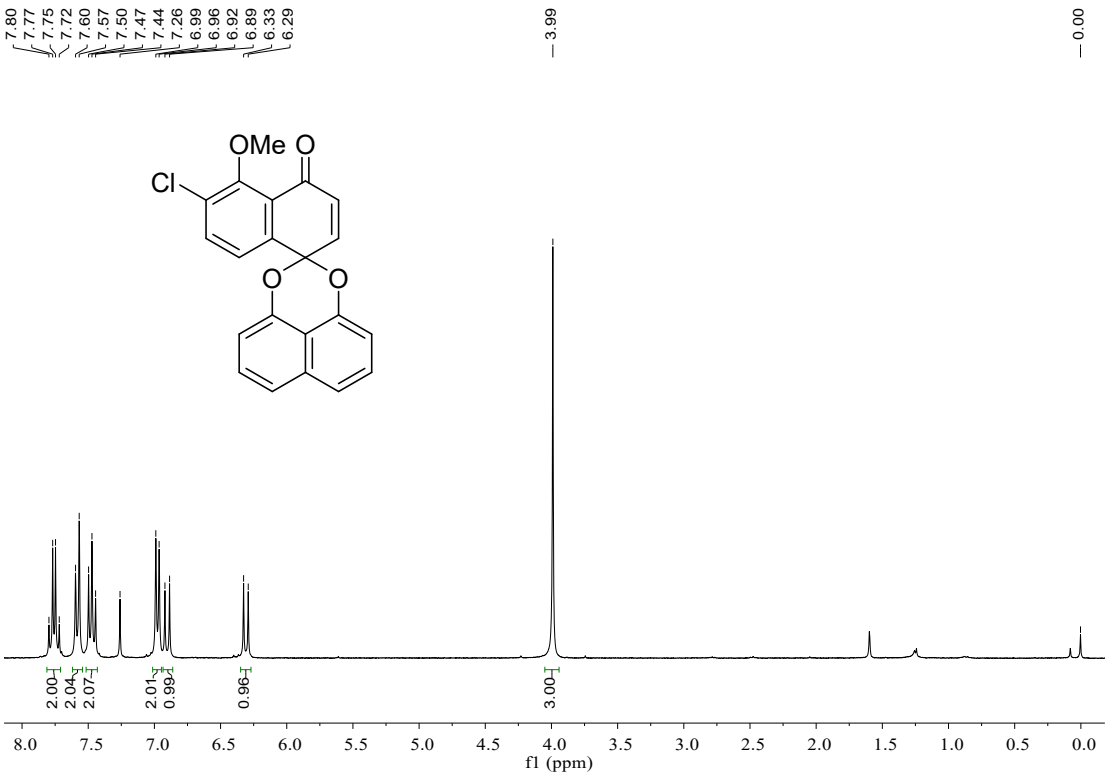


Figure S8 ^{1}H NMR Spectra of compound **11**

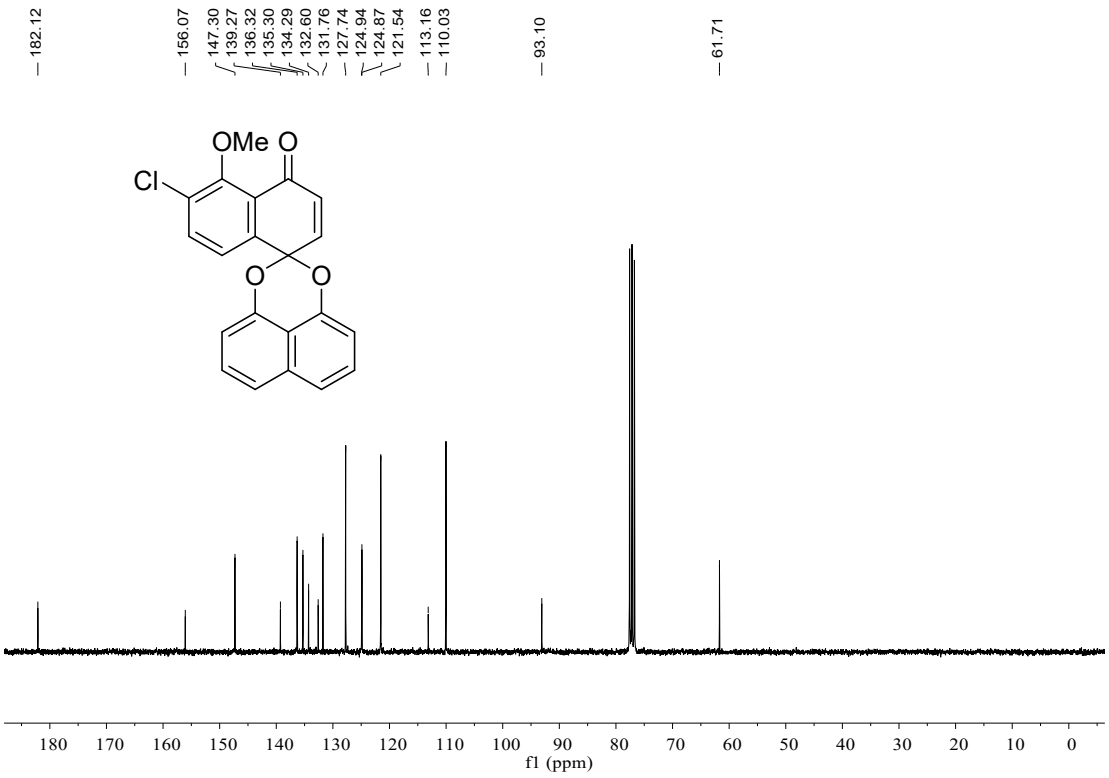
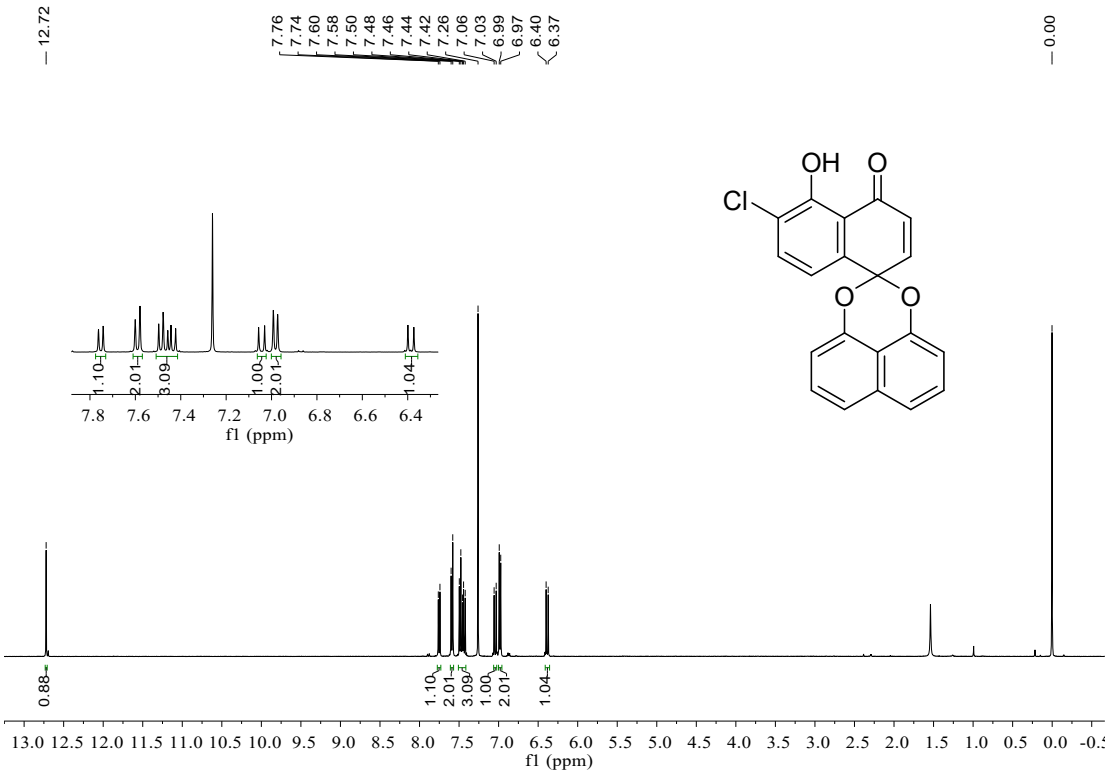


Figure S9 ^{13}C NMR Spectra of compound **11**



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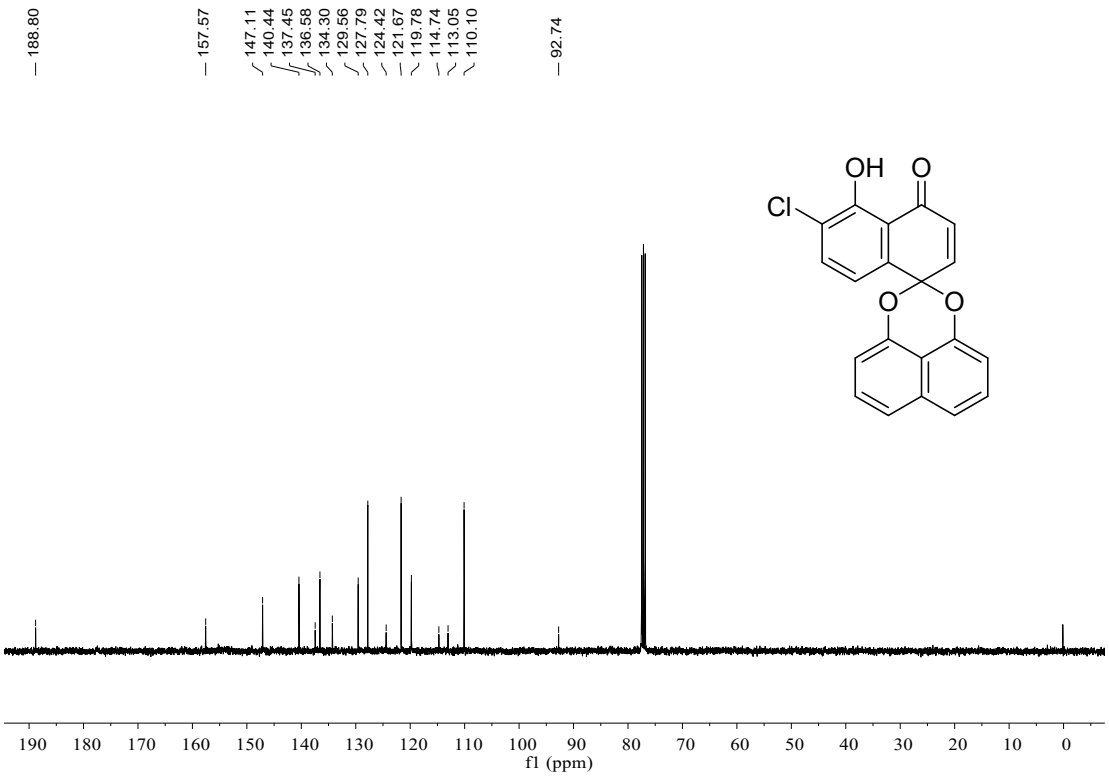

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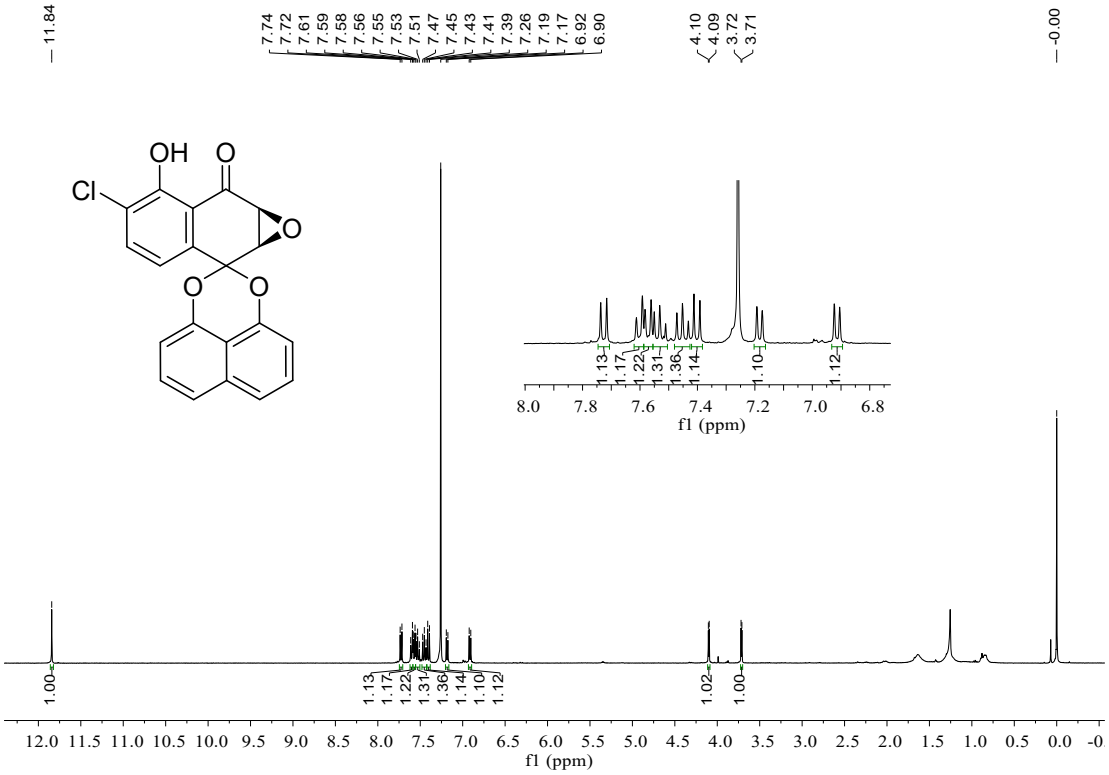

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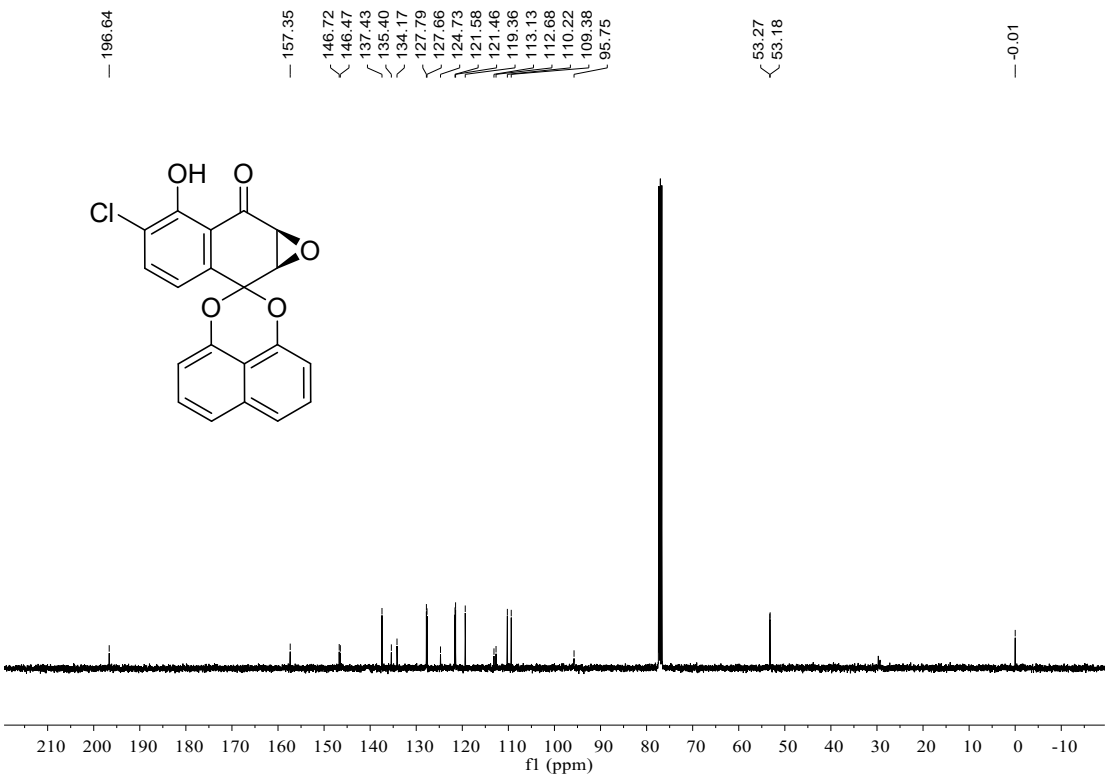

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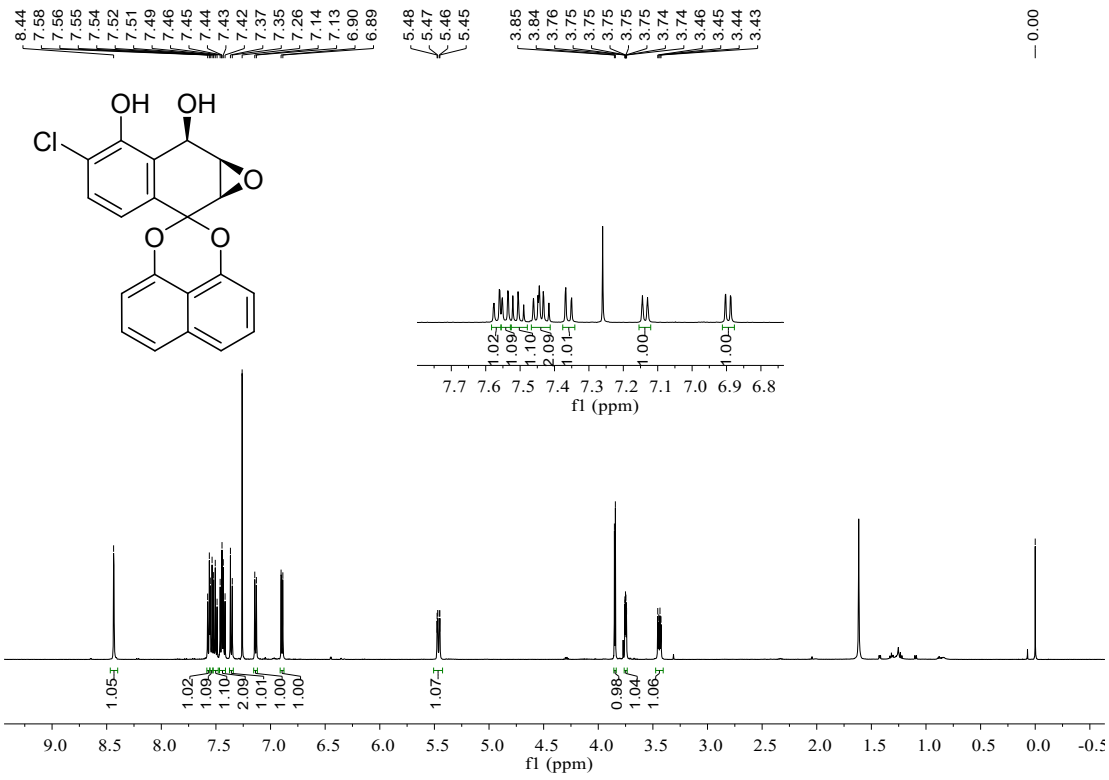

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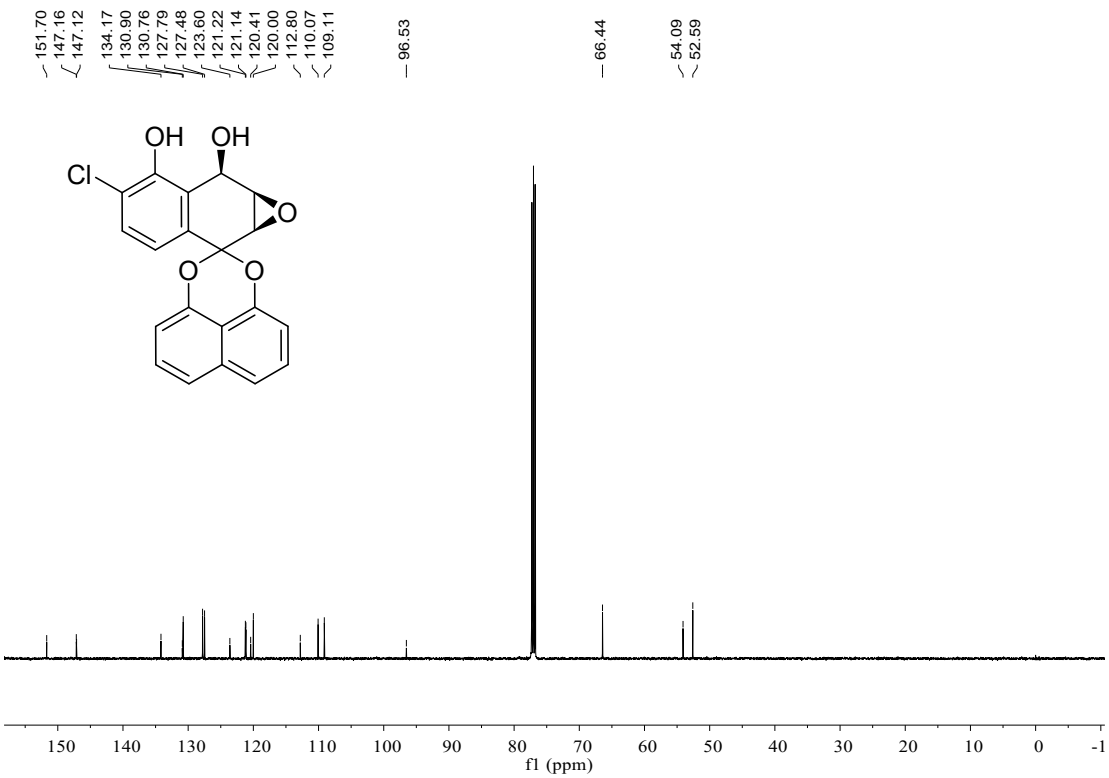

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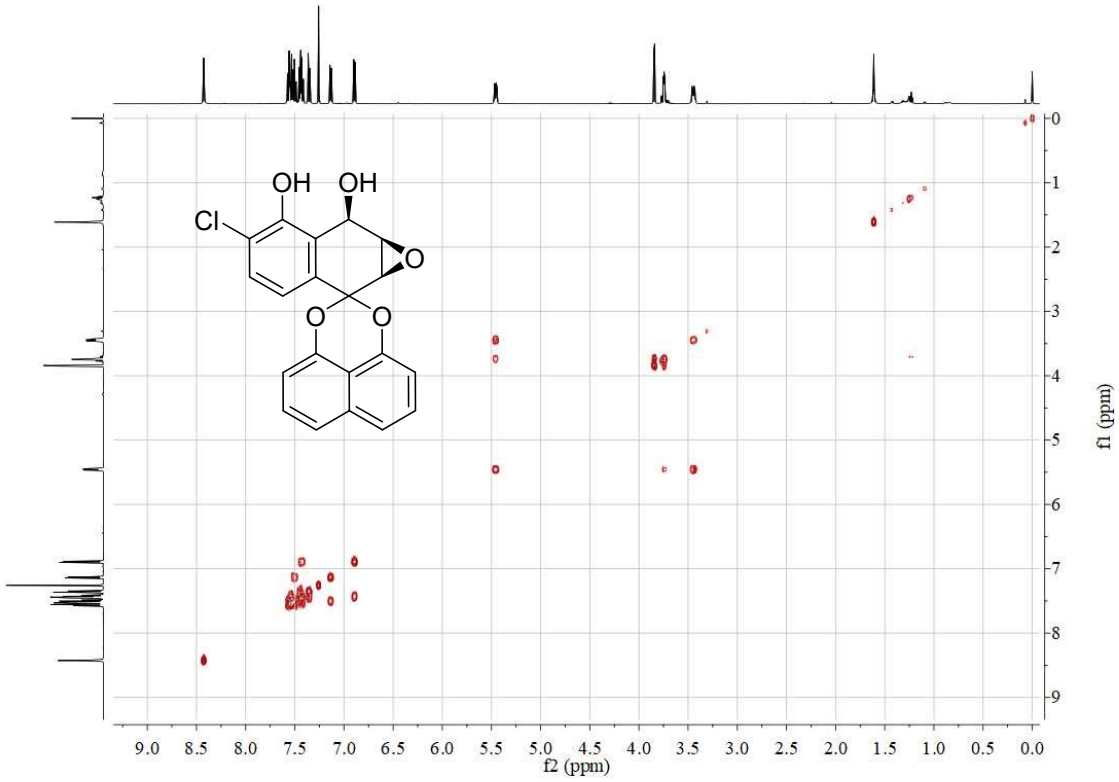

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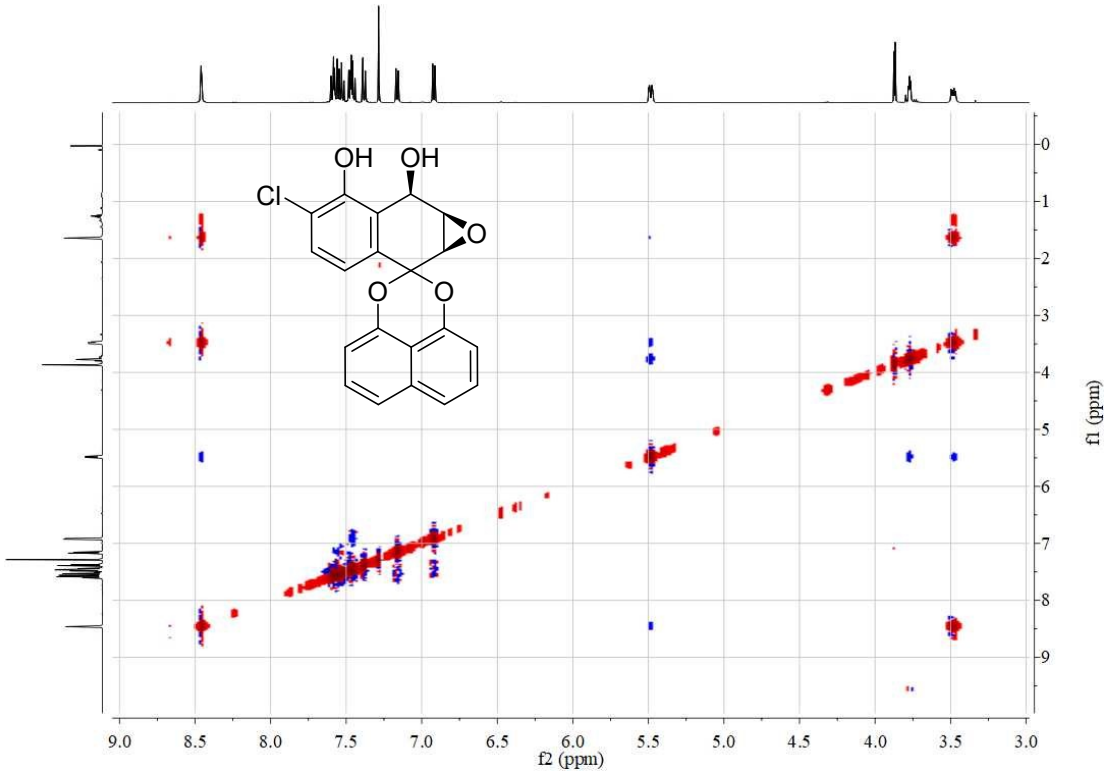
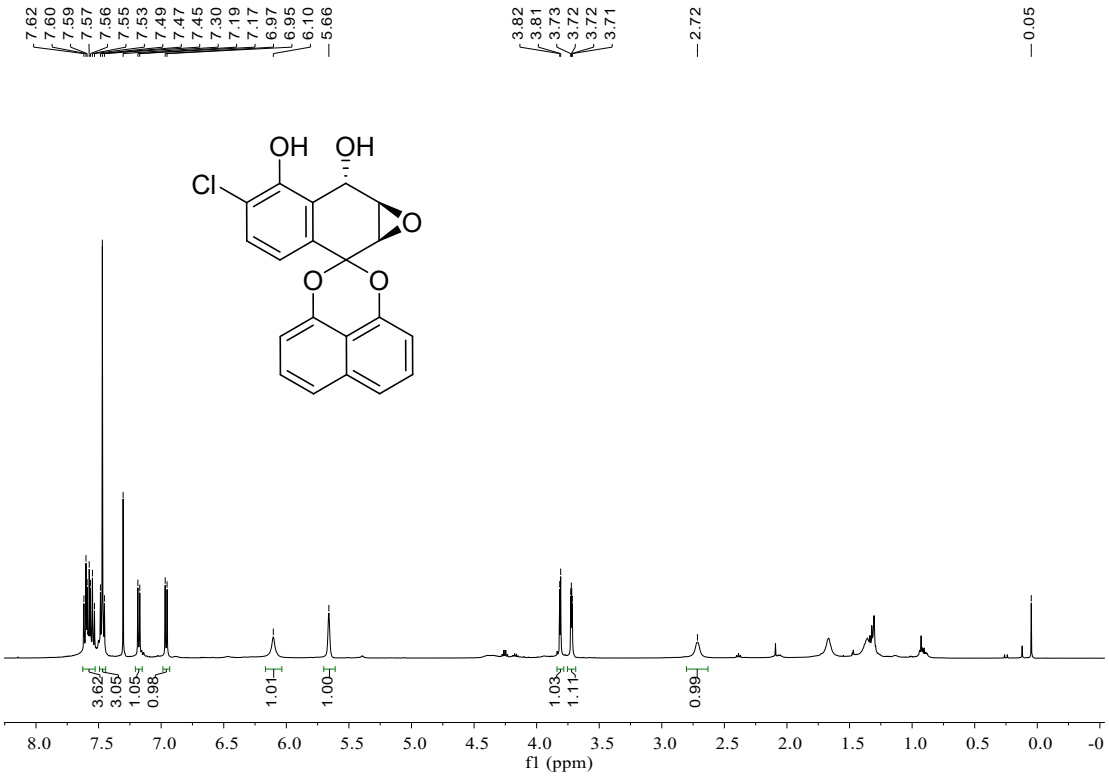


Figure S17 NOESY (500MHz, $CDCl_3$) Spectra of compound **1**



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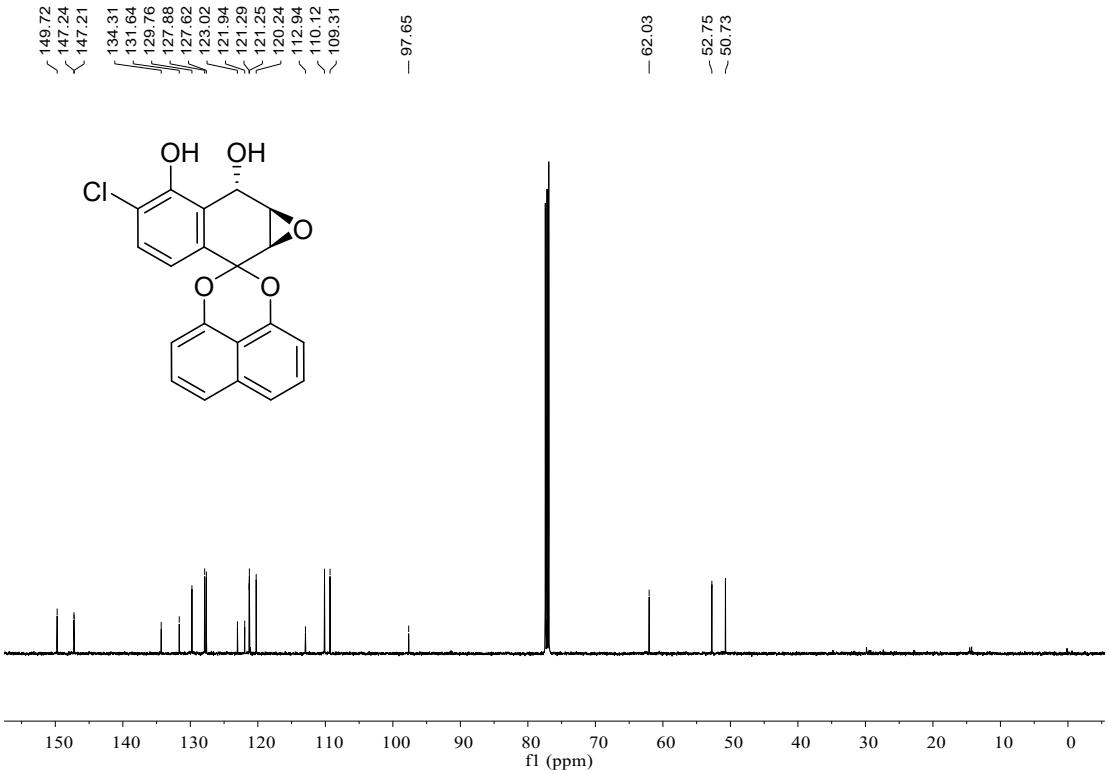

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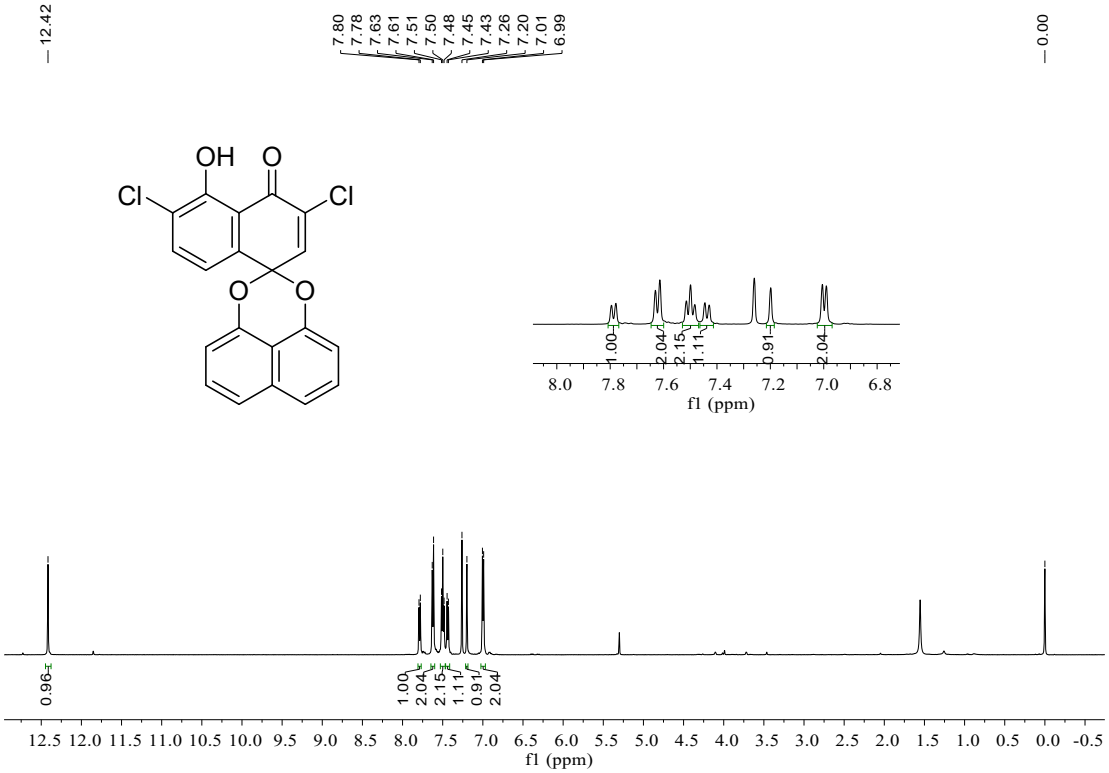

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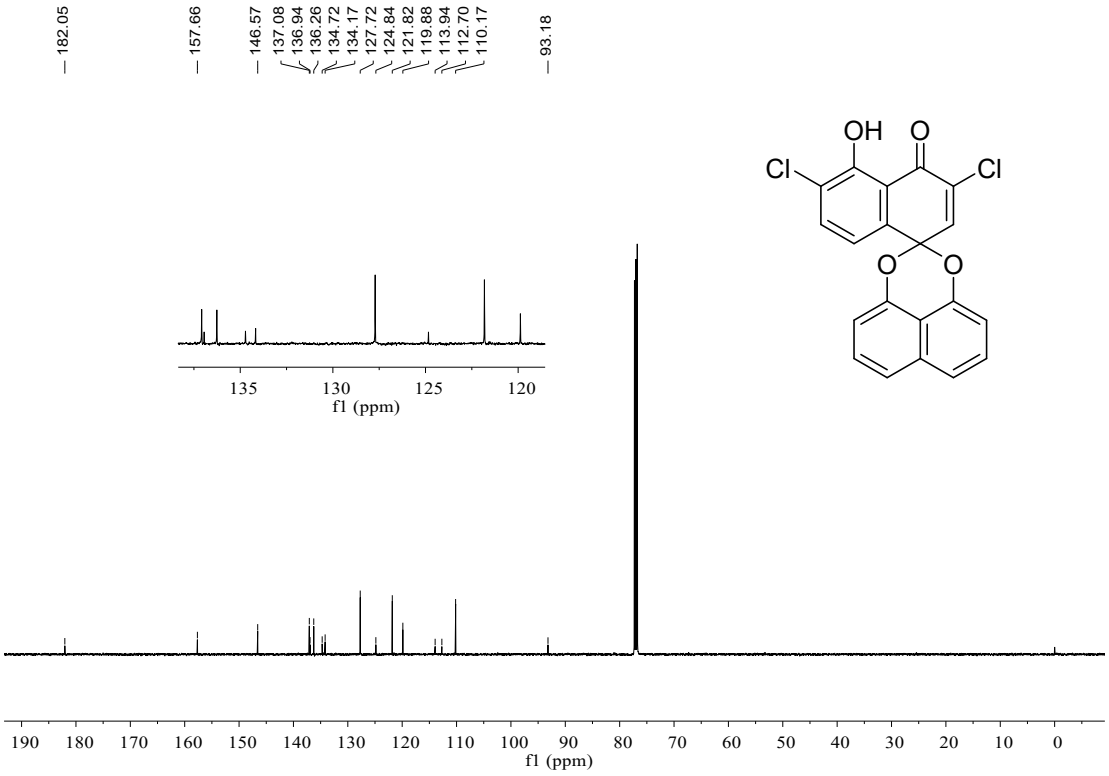

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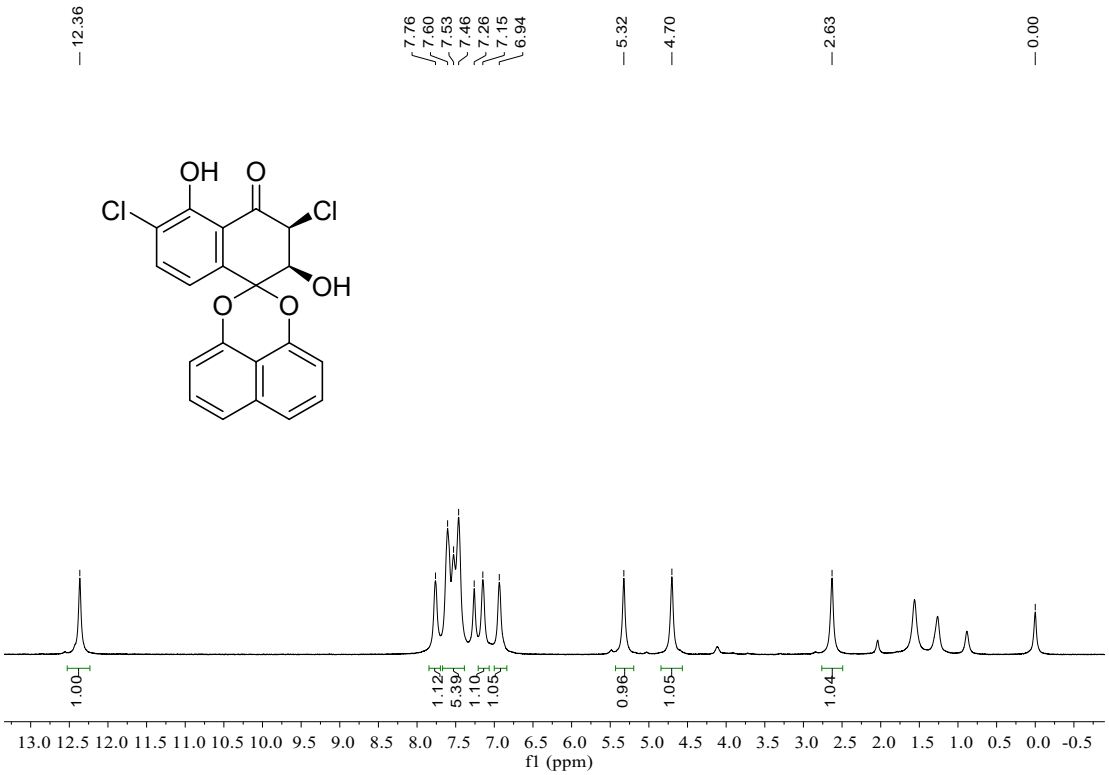


Figure S22 ^{1}H NMR Spectra of compound **15**

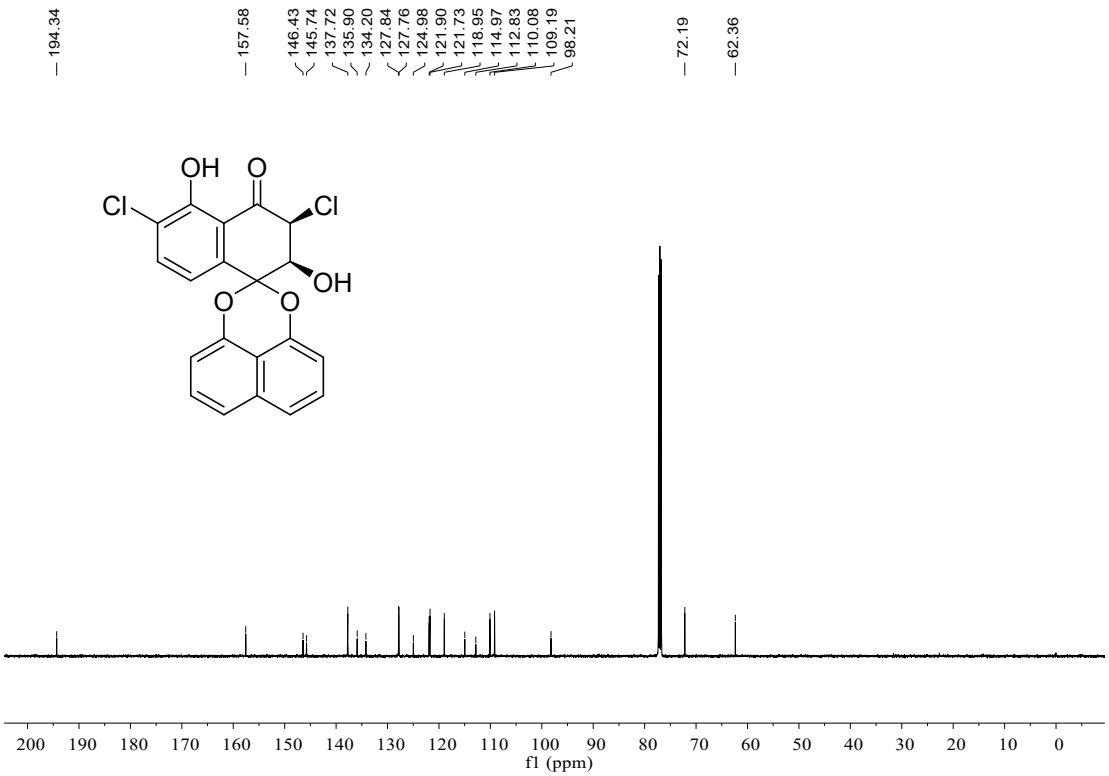
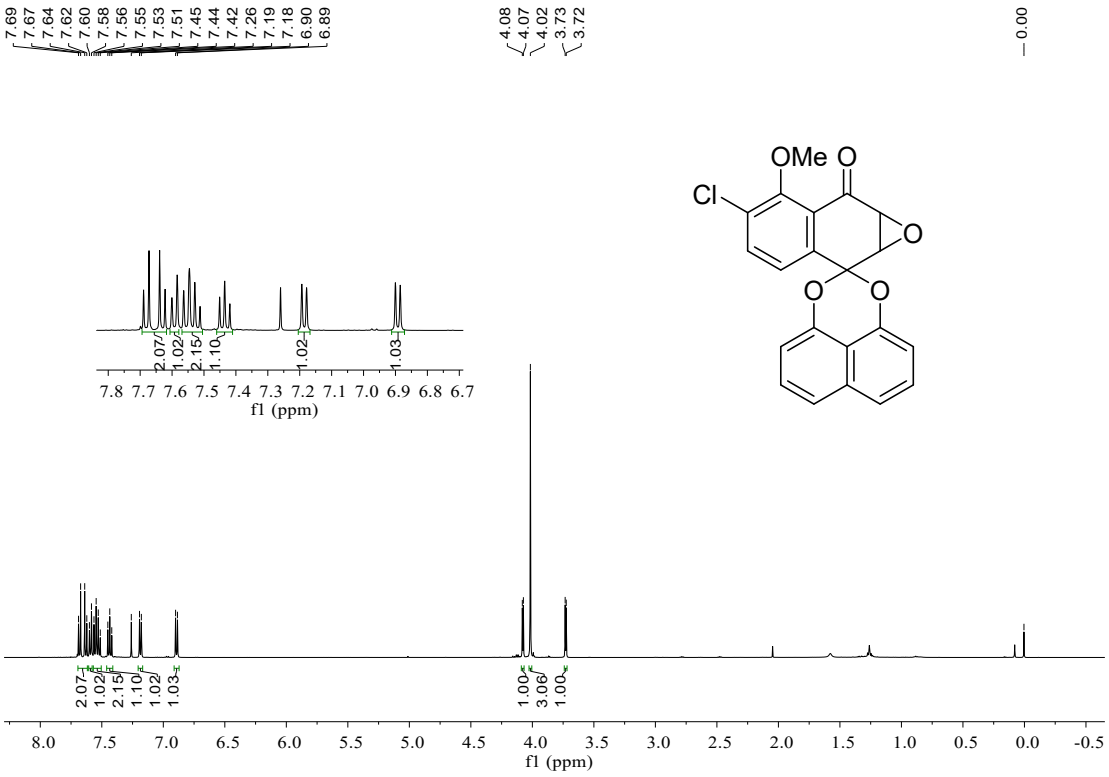


Figure S23 ^{13}C NMR Spectra of compound **15**



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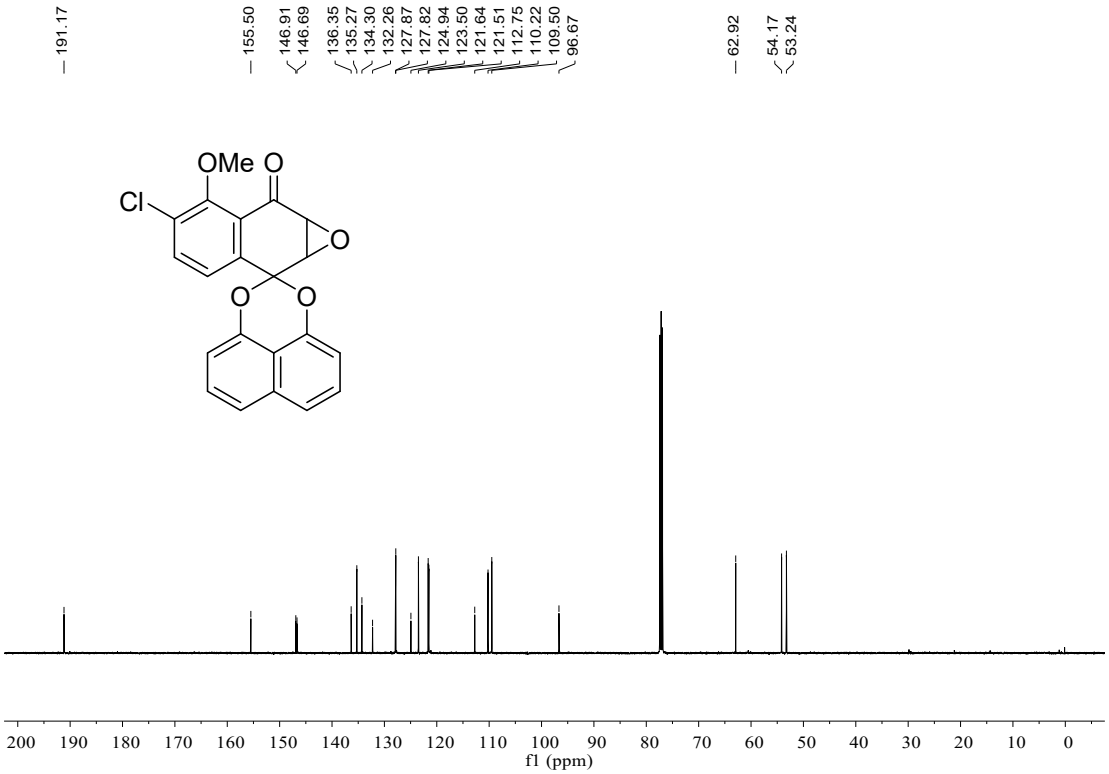


Figure S25 ^{13}C NMR Spectra of compound **16**

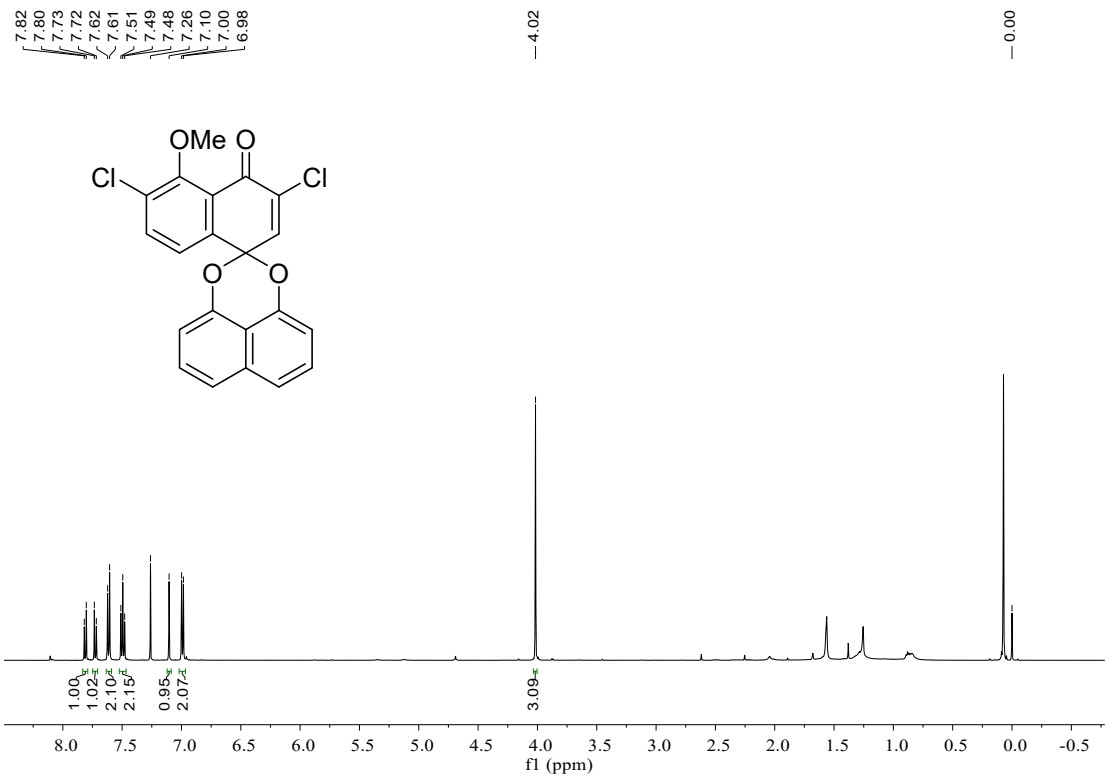


Figure S26 ^{1}H NMR Spectra of compound **17**

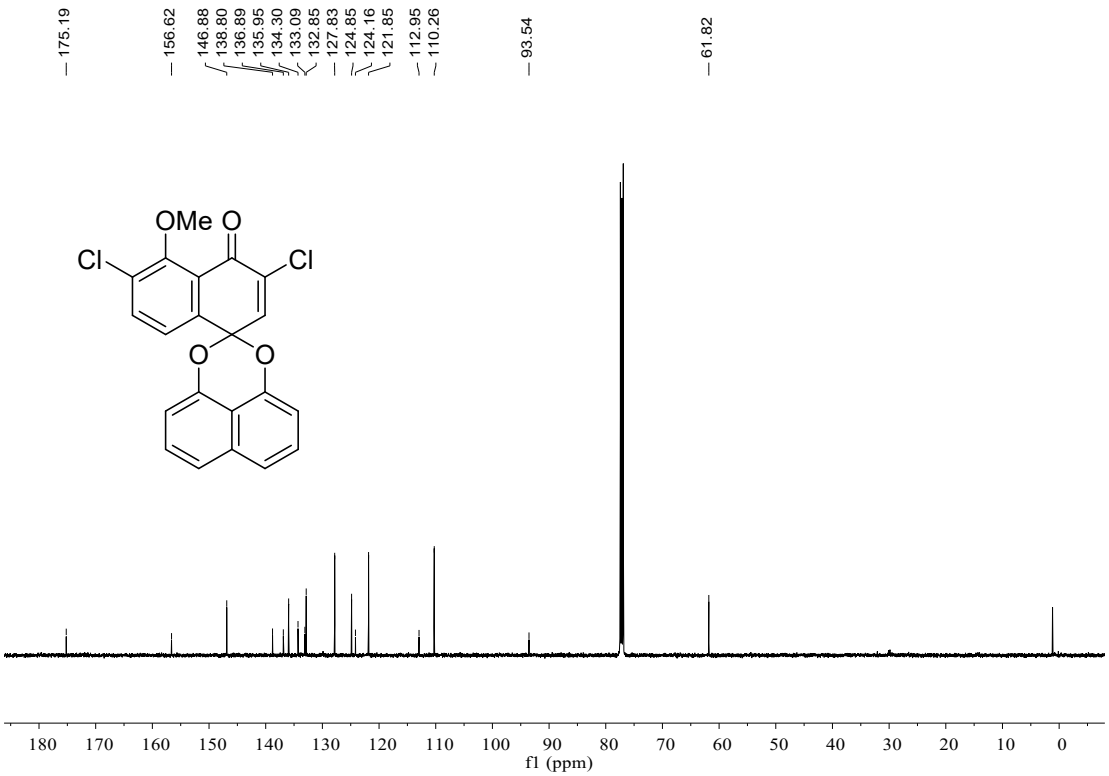


Figure S27 ^{13}C NMR Spectra of compound **17**

Table S1 The ^{1}H, ^{13}C NMR chemical shifts of compounds **1, 14** and **Sch 53825**

position	Sch 53825 ($CDCl_3$)		compound **1** ($CDCl_3$)		compound **14** ($CDCl_3$)	
	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)	δ_C
1	---	97.5	---	96.53	---	97.65
2	3.81 (d, 4.0)	50.5	3.74-3.76 (m)	52.59	3.81 (d, 3.9)	50.73
3	3.72 (dd, 2.3, 4.0)	52.9	3.42-3.45 (m)	54.09	3.72 (dd, 2.4, 3.9)	52.75
4	5.66 (brd, 2.3)	61.5	5.47 (dd, 2.5, 10)	66.44	5.66 (brs)	62.03
4a	---	122.3	---	121.22	---	121.94
5	---	150.2	---	151.70	---	149.72
6	---	123.4	---	123.60	---	123.02
7	7.44-7.48 (m)	130.0	7.42-7.46 (m)	130.76	7.45-7.49 (m)	129.76
8	7.44-7.48 (m)	120.1	7.42-7.46 (m)	120.00	7.45-7.49 (m)	120.24
8a	---	131.3	---	130.90	---	131.64
1′	---	147.3	---	147.12	---	147.21
2′	7.42-7.63 (m)	121.2	7.51 (d, 7.5)	121.14	7.45-7.49 (m)	121.29
3′	7.42-7.63 (m)	127.6	7.57 (d, 7.8)	127.48	7.53-7.62 (m)	127.62
4′	6.97 (d, 7.3)	109.2	6.90 (d, 8.0)	109.11	6.97 (d, 7.4)	109.31
4a′	---	134.3	---	134.17	---	134.31
5′	7.18 (d, 7.3)	110.0	7.14 (d, 7.4)	110.07	7.18 (d, 7.4)	110.12
6′	7.42-7.63 (m)	127.9	7.55 (d, 8.2)	127.79	7.53-7.62 (m)	127.88
7′	7.42-7.63 (m)	121.2	7.37 (d, 8.4)	120.41	7.53-7.62 (m)	121.25
8′	---	147.4	---	147.16	---	147.24
8a′	---	112.9	---	112.80	---	112.94

2. High Resolution Mass Spectro copies of Compounds 14 and 15

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
Compound 14	C_{20} H_{13} Cl O_5	C_{20} H_{13} Cl Na O_5	391.0341	391.0344	0.77

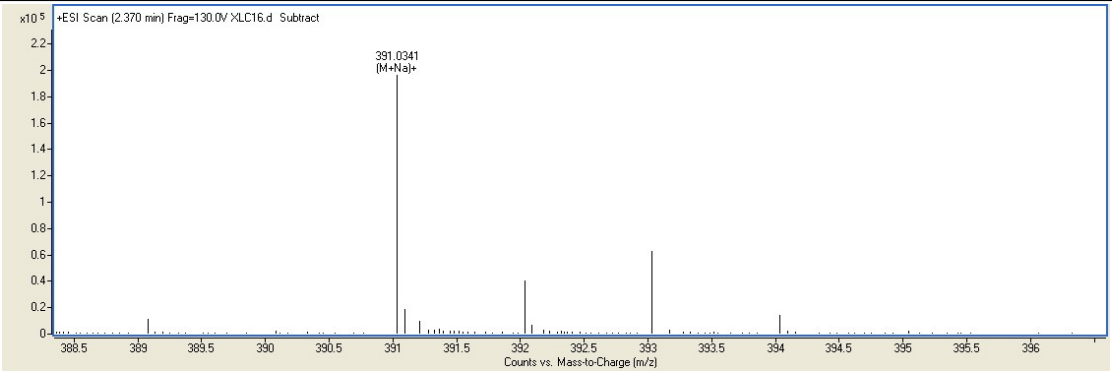


Figure S28 High resolution mass spectrometry report of compound **14**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
Compound 15	C_{20} H_{12} Cl_2 O_5	C_{20} H_{13} Cl_2 O_5	403.0134	403.0135	0.25

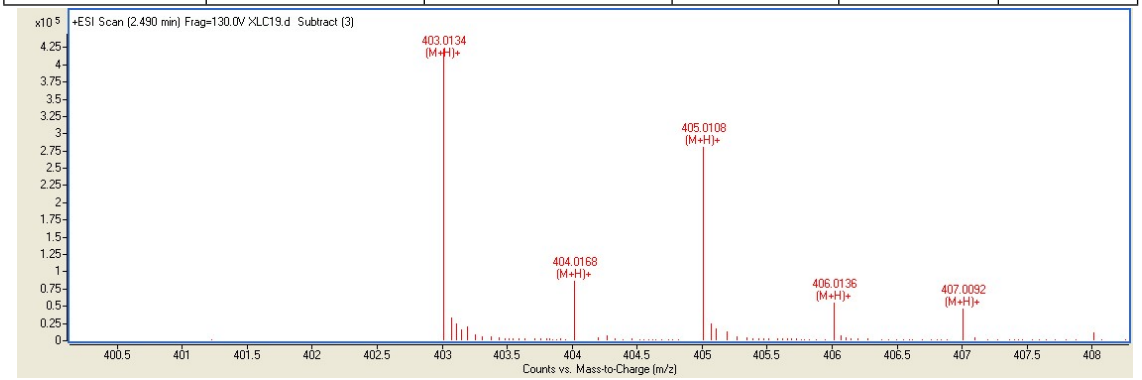
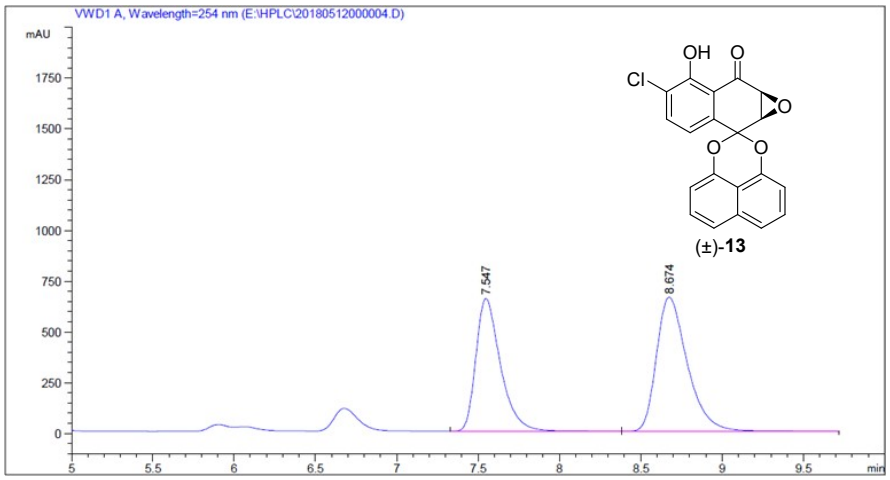
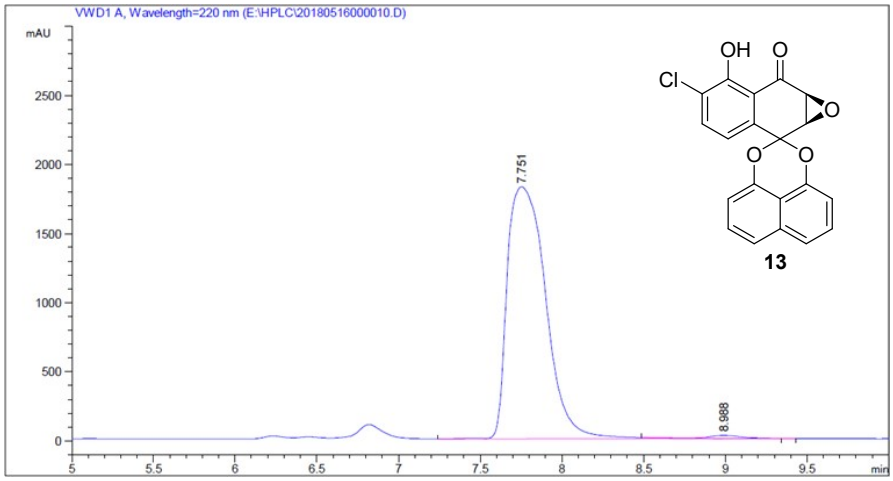


Figure S29 High reslution mass spectrometry report of compound **15**

3. HPLC profiles of compound (±)- and (+)-13



Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Conc. [%]
1	7.547	7875.209	652.997	47.542
2	8.674	8689.386	659.877	52.458
Total		16564.595		



Peak#	Ret. Time [min]	Area [mAU*s]	Height [mAU]	Conc. [%]
1	7.751	3.0038e4	1824.567	98.716
2	8.988	390.8433	22.421	1.284
Total		3.0428e4		

Figure S30 HPLC profiles of compound (±)- and (+)-**13**

4. The crystal structure parameters for compound 1

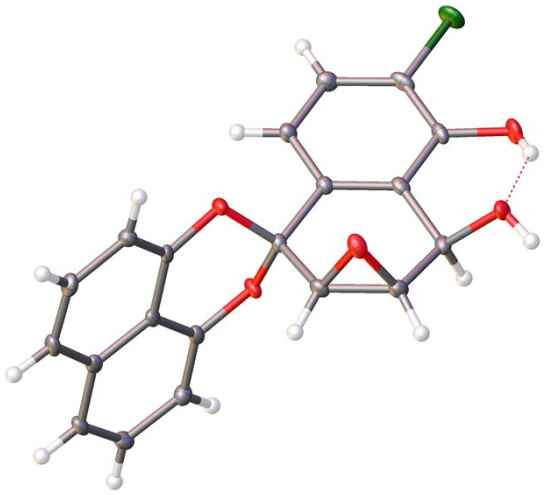


Table 1: Crystal data and structure refinement for exp_8018 (CCDC ID 2169161)

Identification code	exp_8018
Empirical formula	$C_{20}H_{13}ClO_5$
Formula weight	368.75
Temperature / K	117.65(10)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a / Å, b / Å, c / Å	5.15545(11), 11.6040(2), 25.9405(5)
α/°, β/°, γ/°	90.00, 90.00, 90.00
Volume / Å^3	1551.86(5)
Z	4
ρ_{calc} / mg mm^{-3}	1.578
μ / mm^{-1}	2.466
F(000)	760
Crystal size / mm^3	0.22 × 0.19 × 0.17
2Θ range for data collection	6.82 to 142.26°
Index ranges	$-6 \le h \le 6$, $-14 \le k \le 12$, $-31 \le l \le 17$
Reflections collected	5497
Independent reflections	2944[R(int) = 0.0330 (inf-0.9Å)]
Data/restraints/parameters	2944/0/237
Goodness-of-fit on F^2	1.030
Final R indexes [I>2σ (I) i.e. F_o>4σ (F_o)]	R_1 = 0.0369, wR_2 = 0.0942
Final R indexes [all data]	R_1 = 0.0386, wR_2 = 0.0962
Largest diff. peak/hole / e Å^{-3}	0.243/-0.292
Flack Parameters	0.002(15)
Completeness	0.9982

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for exp_8018. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
Cl1	8418.9(11)	6475.1(5)	702.32(19)	22.30(15)
O2	13372(3)	5652.6(12)	-1558.4(5)	13.0(3)
O5	12495(3)	4809.7(15)	561.7(6)	20.0(4)
C3	8297(4)	6328.7(17)	-336.8(8)	15.7(4)
O4	14130(3)	2999.8(14)	27.3(6)	15.5(3)
O1	12684(3)	2664.1(13)	-1076.7(6)	17.0(3)
C6	12268(4)	4674.8(18)	-373.2(8)	12.8(4)
O3	9748(3)	4406.9(13)	-1655.3(5)	13.5(3)
C16	12317(4)	4893.2(18)	-2396.5(8)	12.3(4)
C14	11199(5)	4086.2(19)	-3233.6(8)	16.1(4)
C2	9446(4)	5936.0(18)	113.3(8)	16.0(4)
C20	14772(4)	5536.6(18)	-3143.1(8)	15.4(4)
C4	9105(4)	5879.6(18)	-807.5(8)	14.0(4)
C9	13746(4)	3630.6(18)	-1348.6(8)	13.9(4)
C1	11422(4)	5121.5(18)	104.1(8)	14.1(4)
C12	8833(4)	3504.8(19)	-2464.5(8)	14.2(4)
C19	16245(4)	6223.1(18)	-2825.9(8)	15.8(4)
C5	11087(4)	5059.3(17)	-826.8(8)	12.0(4)
C11	10289(4)	4242.6(17)	-2173.7(7)	11.9(4)
C18	15815(4)	6267.6(18)	-2288.4(8)	14.8(4)
C7	14556(4)	3852.0(18)	-375.4(8)	13.3(4)
C15	12776(4)	4836.3(18)	-2935.8(8)	13.7(4)
C8	14964(4)	3235.9(18)	-877.0(8)	15.0(4)
C10	12005(4)	4679.3(17)	-1353.2(8)	11.7(4)
C17	13878(4)	5606.4(17)	-2083.6(7)	12.5(4)
C13	9315(4)	3441(2)	-3003.0(8)	16.0(4)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for exp_8018. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+...+2hka\times b\times U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Cl1	28.7(3)	25.5(3)	12.7(2)	-6.32(19)	7.6(2)	1.7(2)
O2	17.0(7)	14.8(7)	7.4(6)	0.0(5)	0.3(6)	-3.5(6)
O5	26.3(8)	26.0(8)	7.6(7)	-1.1(6)	-2.3(6)	1.8(7)
C3	17.4(10)	12.8(9)	16.8(10)	0.1(8)	2.7(9)	1.4(8)
O4	16.2(7)	18.2(7)	12.1(7)	6.2(6)	0.8(6)	2.7(6)
O1	25.2(8)	13.6(7)	12.1(7)	0.0(5)	-0.3(6)	-0.8(6)
C6	15.2(9)	12.6(9)	10.7(9)	1.1(7)	2.0(8)	-3.8(8)

O3	11.9(7)	20.2(7)	8.3(7)	0.5(5)	0.0(6)	-1.2(6)
C16	13.7(9)	12.9(9)	10.3(9)	3.1(7)	0.0(7)	4.4(7)
C14	20.0(11)	20.1(10)	8.1(9)	-0.4(8)	-0.9(8)	4.9(9)
C2	21.2(10)	15.4(10)	11.5(9)	-5.1(8)	5.7(9)	-5.0(8)
C20	18.6(10)	17.5(10)	9.9(9)	3.8(8)	3.3(8)	3.6(9)
C4	16.3(10)	14.2(9)	11.4(9)	1.8(8)	0.9(8)	2.2(8)
C9	16(1)	15.6(9)	10.2(9)	-1.4(8)	3.0(8)	0.5(8)
C1	18.1(9)	16.2(9)	7.9(9)	-0.5(7)	-0.7(8)	-5.4(8)
C12	13.2(9)	16.6(9)	12.8(9)	0.3(8)	1.3(8)	1.4(9)
C19	15(1)	14.8(9)	17.7(10)	7.6(8)	3.5(8)	1.2(7)
C5	13.3(10)	12.4(9)	10.4(9)	0.1(7)	0.0(8)	-1.3(7)
C11	13.0(9)	14.6(9)	8.0(9)	1.7(8)	-1.4(8)	4.0(8)
C18	15.7(10)	13.4(9)	15.2(10)	2.0(7)	-2.0(8)	0.5(7)
C7	13.4(10)	15.6(9)	10.8(9)	2.7(8)	-1.2(8)	-2.2(8)
C15	14.3(10)	15.2(9)	11.4(9)	0.8(7)	0.2(8)	5.9(8)
C8	14.8(9)	15.8(10)	14.4(10)	2.3(8)	2.6(8)	3.1(8)
C10	12.9(10)	12.6(9)	9.5(9)	1.4(7)	-1.5(8)	-0.5(7)
C17	15.1(10)	12.5(9)	9.8(9)	1.2(7)	0.4(8)	3.9(7)
C13	17.9(10)	17.3(10)	13.0(9)	-2.3(8)	-5.0(8)	1.1(9)

Table 4 Bond Lengths for exp_8018.

Atom	**Atom**	**Length/Å**	**Atom**	**Atom**	**Length/Å**
Cl1	C2	1.734(2)	C16	C17	1.411(3)
O2	C10	1.434(2)	C14	C15	1.420(3)
O2	C17	1.388(2)	C14	C13	1.364(3)
O5	C1	1.359(3)	C2	C1	1.390(3)
C3	C2	1.386(3)	C20	C19	1.374(3)
C3	C4	1.391(3)	C20	C15	1.417(3)
O4	C7	1.455(3)	C4	C5	1.397(3)
O1	C9	1.434(3)	C9	C8	1.449(3)
O1	C8	1.446(3)	C9	C10	1.512(3)
C6	C1	1.411(3)	C12	C11	1.366(3)
C6	C5	1.398(3)	C12	C13	1.421(3)
C6	C7	1.518(3)	C19	C18	1.413(3)
O3	C11	1.387(2)	C5	C10	1.511(3)
O3	C10	1.438(2)	C18	C17	1.366(3)
C16	C11	1.413(3)	C7	C8	1.500(3)
C16	C15	1.420(3)			

Table 5 Bond Angles for exp_8018.

Atom	**Atom**	**Atom**	**Angle/°**	**Atom**	**Atom**	**Atom**	**Angle/°**

C17	O2	C10	115.24(15)	C4	C5	C6	120.38(19)
C2	C3	C4	119.2(2)	C4	C5	C10	117.39(18)
C9	O1	C8	60.44(13)	O3	C11	C16	118.18(18)
C1	C6	C7	118.33(19)	C12	C11	O3	120.74(19)
C5	C6	C1	119.1(2)	C12	C11	C16	121.03(19)
C5	C6	C7	122.41(19)	C17	C18	C19	118.5(2)
C11	O3	C10	113.32(16)	O4	C7	C6	107.91(16)
C11	C16	C15	120.08(19)	O4	C7	C8	108.67(17)
C17	C16	C11	120.00(18)	C8	C7	C6	114.36(18)
C17	C16	C15	119.92(19)	C14	C15	C16	118.0(2)
C13	C14	C15	120.38(19)	C20	C15	C16	117.9(2)
C3	C2	Cl1	119.54(17)	C20	C15	C14	124.13(19)
C3	C2	C1	121.49(19)	O1	C8	C9	59.36(13)
C1	C2	Cl1	118.97(17)	O1	C8	C7	114.55(17)
C19	C20	C15	120.42(19)	C9	C8	C7	121.39(19)
C3	C4	C5	120.4(2)	O2	C10	O3	111.63(15)
O1	C9	C8	60.20(13)	O2	C10	C9	110.16(16)
O1	C9	C10	113.98(17)	O2	C10	C5	105.05(16)
C8	C9	C10	121.21(18)	O3	C10	C9	107.93(16)
O5	C1	C6	122.9(2)	O3	C10	C5	107.66(16)
O5	C1	C2	117.67(19)	C5	C10	C9	114.44(17)
C2	C1	C6	119.42(19)	O2	C17	C16	118.69(19)
C11	C12	C13	118.7(2)	C18	C17	O2	119.80(19)
C20	C19	C18	121.7(2)	C18	C17	C16	121.49(19)
C6	C5	C10	122.09(19)	C14	C13	C12	121.8(2)

Table 6 Torsion Angles for exp_8018.

A	**B**	**C**	**D**	**Angle/°**
Cl1	C2	C1	O5	-1.6(3)
Cl1	C2	C1	C6	179.81(16)
C3	C2	C1	O5	178.0(2)
C3	C2	C1	C6	-0.6(3)
C3	C4	C5	C6	0.5(3)
C3	C4	C5	C10	-175.34(18)
O4	C7	C8	O1	68.9(2)
O4	C7	C8	C9	136.7(2)
O1	C9	C8	C7	-101.8(2)
O1	C9	C10	O2	170.78(15)
O1	C9	C10	O3	-67.1(2)
O1	C9	C10	C5	52.7(2)
C6	C5	C10	O2	-105.0(2)

C6	C5	C10	O3	135.90(19)
C6	C5	C10	C9	15.9(3)
C6	C7	C8	O1	-51.7(2)
C6	C7	C8	C9	16.1(3)
C2	C3	C4	C5	-1.3(3)
C20	C19	C18	C17	0.0(3)
C4	C3	C2	Cl1	-179.04(16)
C4	C3	C2	C1	1.3(3)
C4	C5	C10	O2	70.7(2)
C4	C5	C10	O3	-48.4(2)
C4	C5	C10	C9	-168.33(18)
C9	O1	C8	C7	113.3(2)
C1	C6	C5	C4	0.3(3)
C1	C6	C5	C10	175.92(18)
C1	C6	C7	O4	46.9(2)
C1	C6	C7	C8	167.90(19)
C19	C20	C15	C16	1.6(3)
C19	C20	C15	C14	-178.7(2)
C19	C18	C17	O2	-178.54(18)
C19	C18	C17	C16	-0.2(3)
C5	C6	C1	O5	-178.81(19)
C5	C6	C1	C2	-0.3(3)
C5	C6	C7	O4	-137.33(19)
C5	C6	C7	C8	-16.3(3)
C11	O3	C10	O2	54.4(2)
C11	O3	C10	C9	-66.8(2)
C11	O3	C10	C5	169.21(16)
C11	C16	C15	C14	-1.9(3)
C11	C16	C15	C20	177.76(19)
C11	C16	C17	O2	-0.1(3)
C11	C16	C17	C18	-178.4(2)
C11	C12	C13	C14	0.6(3)
C7	C6	C1	O5	-2.9(3)
C7	C6	C1	C2	175.67(18)
C7	C6	C5	C4	-175.46(19)
C7	C6	C5	C10	0.1(3)
C15	C16	C11	O3	-173.91(18)
C15	C16	C11	C12	3.6(3)
C15	C16	C17	O2	179.48(18)
C15	C16	C17	C18	1.2(3)

C15	C14	C13	C12	1.0(3)
C15	C20	C19	C18	-0.7(3)
C8	O1	C9	C10	-113.5(2)
C8	C9	C10	O2	102.3(2)
C8	C9	C10	O3	-135.62(19)
C8	C9	C10	C5	-15.8(3)
C10	O2	C17	C16	22.4(3)
C10	O2	C17	C18	-159.22(18)
C10	O3	C11	C16	-32.9(2)
C10	O3	C11	C12	149.65(18)
C10	C9	C8	O1	101.6(2)
C10	C9	C8	C7	-0.2(3)
C17	O2	C10	O3	-49.3(2)
C17	O2	C10	C9	70.6(2)
C17	O2	C10	C5	-165.67(17)
C17	C16	C11	O3	5.7(3)
C17	C16	C11	C12	-176.85(19)
C17	C16	C15	C14	178.52(19)
C17	C16	C15	C20	-1.8(3)
C13	C14	C15	C16	-0.3(3)
C13	C14	C15	C20	-180.0(2)
C13	C12	C11	O3	174.53(18)
C13	C12	C11	C16	-2.9(3)

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for exp_8018.

Atom	***x***	***y***	***z***	**U(eq)**
H5	13240	4190	529	30
H3	7002	6886	-324	19
H4	15482	2647	81	23
H14	11451	4034	-3588	19
H20	15087	5532	-3496	18
H4A	8321	6127	-1111	17
H9	14666	3459	-1670	17
H12	7552	3053	-2313	17
H19	17559	6670	-2969	19
H18	16827	6737	-2079	18
H7	16131	4287	-293	16
H8	16611	2823	-916	18
H13	8319	2946	-3204	19