Supporting Information

Design and Synthesis of Aculeatin Oxo-Analogues and Aculeatin Natural Products Enabled by Oxo-Carbenium Ion Cyclization

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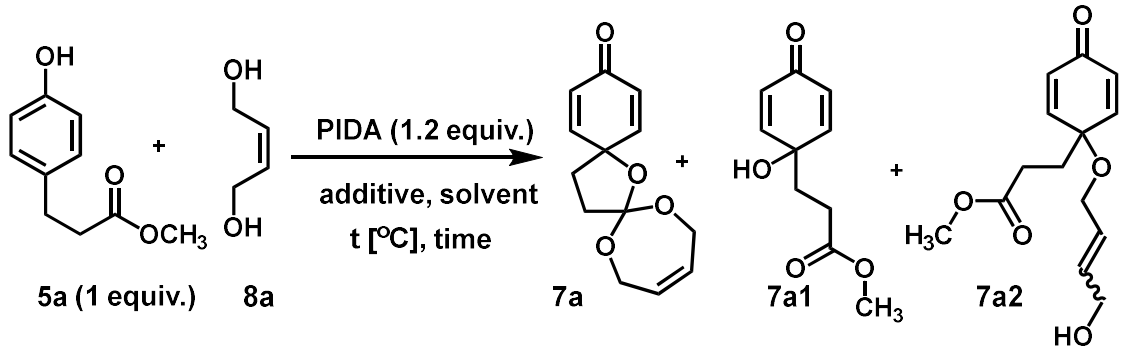
Content:

(I) General Information

All the chemicals were purchased commercially and used without further purification. All reactions were carried out in oven-dried glassware before use. Solvents were dried and distilled by standard laboratory purification techniques. Reactions were monitored by thin-layer chromatography (TLC) on 0.25 mm Merck silica gel plates (60F-254) using UV light as a visualizing agent and Phosphomolybdic acid ($H_3[Mo_{12}PO_{40}]\cdot 12H_2O$), $KMnO_4$, p-anisaldehyde, Iodine, and heat as developing agents. Flash column chromatography was performed using silica gel (size 100-200 and 230-400 mesh) and Alumina (basic). Yields refer to chromatographically pure material unless otherwise stated. ^1H and ^{13}C NMR spectra were recorded on Bruker Avance 500 and Bruker Avance 400 in Benzene-d6, DMSO-d6, and $CDCl_3$, with TMS (0.03%) as the internal standard. Mass spectrometric data were obtained using WATERS-Q-T and Agilent Premier-ESI-MS. Neat compounds were used to record all IR spectra. Melting points were obtained using a capillary melting point apparatus. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, ddd = doublet of doublet of doublet, m = multiplet. Structure drawings were prepared using ChemDraw 20.1.1.

(II) Detailed optimization



5a (1 equiv.) 8a 7a 7a1 7a2

S.No.	8a (equiv.)	Solvent	Additive (equiv.)	Temp. (°C)	Time	Isolated Yield (%) 7a	Isolated Yield (%) 7a1	Isolated Yield (%)7a2
1	12	-	-	0 to rt	24 h	30	-	31
2	12	CH_3CN (0.1 M)	-	rt	12 h	nr[a]	-	-
3	12	DCM (0.1 M)	-	rt	12 h	nr[a]	-	-
4	12	DCM (0.1 M)	-	0	12 h	nr[a]	-	-
5	12	DCM (0.1 M)	PTSA (0.5 eq.)	0	12 h	nr[a]	-	-
6	12	THF (0.1 M)	-	rt	12 h	nr[a]	-	-
7	12	Toluene (0.1 M)	-	rt	12 h	15	27	-
8	2.2	DMSO (0.1 M)	-	rt	12 h	23	24	-
9	2.2	HFIP (0.25 M)	-	rt	24 h	30	15	-
10	2.2	HFIP (0.25 M)	-	rt	1 min	71	14	-
11	2.2	HFIP (0.25 M)	-	rt	5 min	59	22	-
12	2.2	HFIP (2.5 M)	-	rt	5 min	52	19	-
13	2.2	HFIP (0.25 M)	-	rt	1 h	35	12	-
14	2.2	HFIP (0.25 M)	-	45	1 min	30	30	-
15	2.2	HFIP (0.25 M)		0	15 min	76	22	-
16	2.2	HFIP (0.25 M)	-	rt	30 min	15	52	-
17	2.2	HFIP (0.25 M)	Molecular sieves (10 mol %)	rt	10 min	41	19	-
18	2.2	HFIP (0.25 M)	Na_2SO_4 (3)	rt	1 min	11	20	-
19	2.2	HFIP (0.25 M)	Na_2CO_3 (2.2)	rt	15 min	39	15	-
20	2.2	HFIP (0.25 M)	$NaHCO_3$ (2.2)	rt	15 min	35	22	-
21	2.2	HFIP (0.25 M)	K_2CO_3 (2.2)	rt	15 min	55	30	-
22	2.2	HFIP (0.25 M)	DMAP (2.2)	rt	15 min	50	35	-
23	2.2	HFIP (0.25 M)	DABCO (2.2)	rt	15 min	45	38	-

24	2.2	HFIP (0.25 M)	2,6-lutidine (2.2)	rt	12 h	67	25	-
25	2.2	HFIP (0.25 M)	Et_3N (2.2)	rt	1 min	73		-
26	2.2	HFIP (0.25 M)	TEMPO (2.2)	rt	1 min	67	28	-
27	2.2	HFIP (0.25 M)	DBU (2.2)	rt	12 h	77	traces	-
28	2.2	HFIP (0.25 M)	DBU (5)	rt	12 h	72	7	-
29	2.2	HFIP (0.25 M)	DBU (1.2)	rt	12 h	56	16	-
30	2.2	HFIP: DCM (1:1) (0.25 M)	DBU (2.2)	rt	12 h	nr[a]	-	-
31	2.2	HFIP (0.25 M) CF_3CH_2OH (1:1)	-	rt	10 min	37	45	-
32	2.2	HFIP: THF (1:1) (0.25 M)	DBU (2.2)	rt	12 h	nr[a]	-	-
33	2.2	HFIP (0.25 M)	DBU (2.2)	0 to rt	12 h	83	traces	-
34	2.2	CF_3CH_2OH (0.25 M)	-	rt	12 h	22	17	-
35	PIFA (2.2)	HFIP (0.25 M)	-	rt	12 h	0	34	-
36	PhI (20 mol%) and *m*cpba (1.2 equiv.)	HFIP (0.25 M)	-	rt	12 h	-	-	-
37	2.2	HFIP (0.25 M)	DBU (2.2)	0 to rt	1 h	72	traces	-
38	2.2	HFIP (0.25 M)	DBU (2.2)	0 to rt	3 h	74	traces	-
39	2.2	HFIP (0.25 M)	DBU (2.2)	0 to rt	6 h	75	traces	-
40	2.2	HFIP (0.25 M)	DBU (2.2)	0 to rt	9 h	77	traces	-

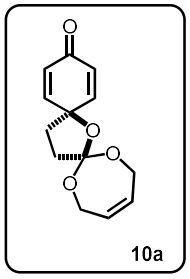
[a]complex mixture

(III) General procedure A

It involved adding $PhI(OAc)_2$ (PIDA, 1.2 equiv.) in a single portion to a stirred solution of HFIP (0.25 M) at 0 ºC under an N_2 atmosphere, followed by the addition of DBU (2.2 equiv.). The mixture was stirred at 0 ºC until PIDA dissolved completely. Afterward, a phenol derivative (1 equiv.) was added, and the diol was introduced upon observing a color change. The resulting mixture was allowed to warm to room temperature and stirred for 12 hours. Subsequently, the reaction mixture was diluted with ethyl acetate and evaporated under reduced pressure. The residue was purified using column chromatography to isolate the desired product.

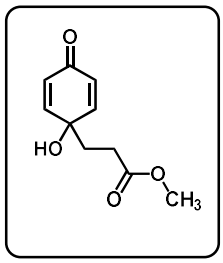
(IV) Experimental Data

7,9,14-trioxadispiro[5.1.68.26]hexadeca-1,4,11-trien-3-one (7a)



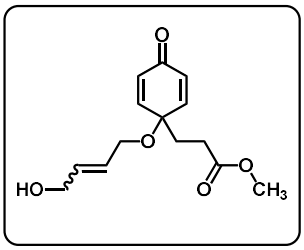
The general procedure **A** was followed using methyl 3-(4-hydroxyphenyl)propanoate (Cas No. 5597-50-2) (100 mg, 0.555 mmol, 1 equiv.) and (*Z*)-but-2-ene-1,4-diol (Cas No. 6117-80-2) (185.73 mg, 1.22 mmol, 2.2 equiv.) to obtain crude product **7a**. Purification by column chromatography (R_f = 0.5; *n*-hexane/ethyl acetate 50/50; UV-active; PMA-stain-active) yielded **7a** (107.8 mg, 83%) as a colorless white solid. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 6.92 (d, *J* = 10.0 Hz, 2H), 6.14 (d, *J* = 9.9 Hz, 2H), 5.70 (t, 2H), 4.49 (t, 2H), 4.20 (t, 2H), 2.34 (t, *J* = 7.6 Hz, 2H), 2.21 (t, *J* = 7.6 Hz, 2H). **^{13}C{^{1}H} NMR** (100 MHz, Chloroform-*d*) δ 185.1, 149.3, 128.5, 127.4, 125.1, 77.4, 62.8, 34.7, 33.1. **IR υ (cm-1)** 2921, 2853, 1725, 1668, 1628, 1438, 1381, 1315, 1209, 1167, 1074, 1046, 998, 961, 885, 913, 850, 804, 643, 612. **HRMS** (ESI-TOF) m/z: [M+H]- Calcd for $C_{13}H_{15}O_4$ 235.0970; Found 235.0965. **mp:** 91-93 °C.

Methyl-3-(1-((4-hydroxybut-2-en-1-yl)oxy)-4-oxocyclohexa-2,5-dien-1-yl)propanoate (7a1)



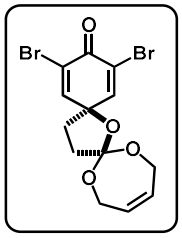
The general procedure **A** was followed using methyl 3-(4-hydroxyphenyl)propanoate (100 mg, 0.555 mmol, 1 equiv.) and (Z)-but-2-ene-1,4-diol (185.73 mg, 1.22 mmol, 2.2 equiv.) to obtain crude product **10a1**. Purification by column chromatography R_f (*n*-hexane/ethyl acetate 50/50, UV active, PMA stain active) = 0.2 yielded **7a1** (10.8 mg, 10%) as a yellow oil. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 6.81 (d, *J* = 10.4 Hz, 2H), 6.18 (d, *J* = 9.9 Hz, 2H), 3.66 (s, 3H), 2.73 (s, OH broad peak, 1H), 2.45 – 2.21 (m, 2H), 2.10 (t, *J* = 7.7 Hz, 2H). **^{13}C{^{1}H} NMR** (126 MHz, Chloroform-*d*) δ 185.3, 173.5, 150.4, 128.7, 69.3, 52.1, 34.6, 28.7.

Methyl-3-(1-((4-hydroxybut-2-en-1-yl)oxy)-4-oxocyclohexa-2,5-dien-1-yl)propanoate (7a2)



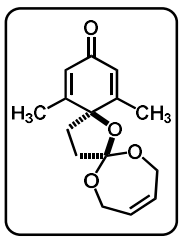
The general procedure **A** was followed using methyl 3-(4-hydroxyphenyl)propanoate (100 mg, 0.555 mmol, 1 equiv.) and (Z)-but-2-ene-1,4-diol (185.73 mg, 1.22 mmol, 2.2 equiv.) to obtain crude product **7a2**. Purification by column chromatography R_f (*n*-hexane/ethyl acetate 50/50, UV active, PMA stain active) = 0.5 yielded **7a2** (7.4 mg, 5%) as a yellow oil. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 6.72 (d, *J* = 10.4 Hz, 2H), 6.29 (d, *J* = 10.3 Hz, 2H), 5.74 – 5.62 (m, 1H), 5.54 (dddt, *J* = 11.2, 6.3, 3.0, 1.5 Hz, 1H), 4.10 – 4.02 (m, 2H), 3.90 – 3.82 (m, 2H), 3.57 (s, *J* = 1.5 Hz, 3H), 2.27 (qd, *J* = 7.6, 3.4 Hz, 2H), 2.11 – 1.94 (m, 2H). **^{13}C{^{1}H} NMR** (126 MHz, Chloroform-*d*) δ 185.1, 173.1, 150.2, 132.2, 131.5, 127.9, 74.9, 61.3, 58.5, 51.9, 34.2, 28.5. **IR υ (cm^{-1})** 3636, 3553, 3464, 2985, 2942, 2909, 2878, 1889, 1741, 1554, 1479, 1465, 1447, 1374, 1240, 1160, 1098, 1047. **HRMS (ESI):** m/z Calcd for [$C_{14}H_{18}O_5$, M+Na]: 289.1052.; Found: 289.1051.

2,4-dibromo-7,9,14-trioxadispiro[5.1.6^8.2^6]hexadeca-1,4,11-trien-3-one (7b)



The general procedure **A** was followed using methyl methyl 3-(3,5-dibromo-4-hydroxyphenyl)propanoate (*ACS Med. Chem. Lett*., 2017, **8**, 947–952.) (100 mg, 0.296 mmol, 1 equiv.) and (*Z*)-but-2-ene-1,4-diol (57.3 mg, 0.651 mmol, 2.2 equiv.) to obtain crude product **7b**. Purification by column chromatography R_f (*n*-hexane/ethyl acetate 75/25, UV active, PMA stain active) = 0.8 yielded **7b** (76.6 mg, 66%) as a colorless solid. **^{1}H NMR** (396 MHz, Chloroform-*d*) δ 6.98 (dd, *J* = 5.7, 2.5 Hz, 2H), 5.28 (q, *J* = 2.1 Hz, 2H), 4.19 (dq, *J* = 16.0, 2.3 Hz, 2H), 3.85 – 3.72 (m, 2H), 1.69 – 1.57 (m, 2H), 1.33 (dtd, *J* = 15.1, 7.5, 4.0 Hz, 2H). **^{13}C{^{1}H} NMR** (100 MHz, Chloroform-*d*) δ 171.5, 149.8, 128.7, 125.3, 121.5, 81.0, 63.0, 33.6, 32.2. **IR (neat) υ (cm^{-1})** 3040, 2957, 2922, 2870, 1956, 1737,1683, 1600, 1455, 1376, 1314, 1221, 1171,1073, 1036, 808, 696, 608, 559, 414. **HRMS** (ESI-TOF) m/z: [M+Na]- Calcd for $C_{13}H_{12}Br_2NaO_4$ 412.9000; Found 412.8991.

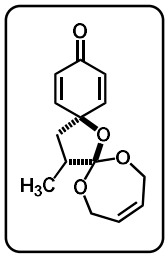
1,5-dimethyl-7,9,14-trioxadispiro[5.1.6^8.2^6]hexadeca-1,4,11-trien-3-one (7c)



The general procedure **A** was followed using methyl ethyl 3-(4-hydroxy-2,6-dimethylphenyl)propanoate (100 mg, 0.550 mmol, 1 equiv.) and (*Z*)-but-2-ene-1,4-diol (106.6 mg, 1.21 mmol, 2.2 equiv.) to obtain crude product **7c**. Purification by column chromatography R_f (*n*-hexane/ethyl acetate 50/50, UV active, PMA stain active) = 0.5 yielded **7c** (95.2 mg, 66%) as a colorless oil. **^{1}H NMR** (500 MHz, Benzene-d_6) δ 6.02 (s, 2H), 5.32 (s, 2H), 4.23 (d, *J* = 15.1 Hz, 2H), 3.81 (d, *J* = 14.5 Hz, 2H), 1.91 (dd, *J* = 9.5, 6.7 Hz, 2H), 1.81 (s, 6H), 1.66 (t, 2H). **^{13}C{^{1}H} NMR** (126 MHz,

Benzene-d_6) δ 184.6, 160.5, 128.9, 127.1, 126.3, 84.2, 62.7, 35.2, 34.5, 18.6. **IR (neat) υ (cm^{-1})** 2954, 2925, 1731, 1671, 1633, 1464, 1439,1384, 1316, 1236, 1193, 1090, 1045, 1070, 1030, 988, 875, 818, 610. **HRMS** (ESI-TOF) m/z: [M+H]- Calcd for $C_{15}H_{19}O_4$ 263.1283; Found 263.1290.

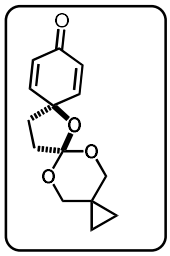
15-methyl-7,9,14-trioxadispiro[5.1.6^8.26]hexadeca-1,4,11-trien-3-one (7d)



The general procedure **A** was followed using methyl 3-(4-hydroxyphenyl)-2-methylpropanoate (100 mg, 0.514 mmol, 1 equiv.) and butane-1,4-diol (99.8 mg, 1.13 mmol, 2.2 equiv.) to obtain crude product **7d**. Purification by column chromatography R_f (*n*-hexane/ethyl acetate 70/30, UV active, PMA stain active) = 0.6 yielded **7d** (89 mg, 70%) as a colorless solid. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.94 (dd, J = 10.2, 2.9 Hz, 2H), 6.84 (dd, J = 9.8, 2.8 Hz, 2H), 6.25 – 6.05 (m, 4H), 5.68 (s, 4H), 4.55 – 4.33 (m, 4H), 4.33 – 4.17 (m, 4H), 2.64 (h, J = 7.1 Hz, 2H), 2.33 (dd, J = 13.3, 7.9 Hz, 2H), 1.93 (dd, J = 13.0, 7.3 Hz, 2H), 1.19 (d, J = 7.1 Hz, 6H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 185.4, 150.5, 150.2, 128.7, 128.6, 127.5, 127.0, 124.5, 75.4, 62.9, 62.7, 42.8, 40.1, 15.7. **IR (neat) υ (cm^{-1})** 2950, 2922, 1732, 1675, 1630, 1466, 1437,1382, 1315, 1238, 1196, 1091, 1041, 1078, 1031, 989, 878, 819. **HRMS** (ESI-TOF) m/z: [M+H]- Calcd for $C_{14}H_{17}O_4$ 249.1126; Found 249.1124.

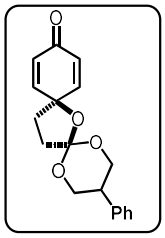
The interaction between the existing chiral center and the newly formed helical chirality (P and M) results in the formation of two diastereomers in a 1:1 ratio, which was confirmed by the doubling of specific peaks in the NMR.

5,7,16-trioxatrispiro[2.2.1.5$^{8.26.23}$]heptadeca-9,12-dien-11-one (7e)



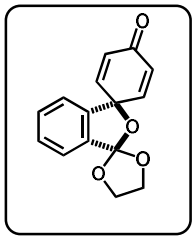
The general procedure **A** was followed using methyl 3-(4-hydroxyphenyl)propanoate (100 mg, 0.555 mmol, 1 equiv.) and cyclopropane-1,1-diyldimethanol (Cas No. 39590-81-3) (122.5 mg, 1.22 mmol, 2.2 equiv.) to obtain crude product **7e**. Purification by column chromatography R_f (*n*-hexane/ethyl acetate 70/30, UV active, PMA stain active) = 0.6 yielded **7e** (104.7 mg, 76%) as a colorless oil. **^{1}H NMR** (500 MHz, Benzene-d_6) 6.56 (d, *J* = 10.1 Hz, 2H), 6.12 (d, *J* = 10.1 Hz, 2H), 4.79 – 4.33 (m, 2H), 2.82 (d, *J* = 10.1 Hz, 2H), 2.18 (td, *J* = 7.8, 0.9 Hz, 2H), 1.83 – 1.66 (m, 2H), 0.59 – 0.49 (m, 2H), 0.11-0.06 (m, 2H). **^{13}C{^{1}H} NMR** (126 MHz, Benzene-d_6) δ 184.5, 149.2, 127.5, 121.2, 77.9, 68.0, 36.5, 34.3, 16.6, 13.8, 4.5. **IR (neat) υ (cm^{-1})** 3076, 2925, 2876, 1738, 1673, 1633, 1458, 1395, 1367, 1328, 1255, 1228, 1178, 1094, 1074, 1009, 983, 904, 872, 852, 766, 547, 461. **HRMS** (ESI-TOF) m/z: $[M+H]^+$ - Calcd for $C_{14}H_{17}O_4$ 249.1127; Found 249.1126.

3-phenyl-1,5,7-trioxadispiro[5.1.58.26]pentadeca-9,12-dien-11-one (7f)



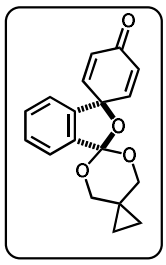
The general procedure **A** was followed using methyl 3-(4-hydroxyphenyl)propanoate (100 mg, 0.555 mmol, 1 equiv.) and 2-phenylpropane-1,3-diol (Cas No. 1570-95-2) (185.7 mg, 1.22 mmol, 2.2 equiv.) to obtain crude product **7f**. Purification by column chromatography R_f (*n*-hexane/ethyl acetate 70/30, UV active, PMA stain active) = 0.6 yielded **7f** (107.6 mg, 65%) as a colorless solid. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 7.36 – 7.29 (m, 2H), 7.29 – 7.22 (m, 3H), 7.04 (d, J = 10.1 Hz, 2H), 6.13 (d, J = 10.0 Hz, 2H), 4.14 (t, J = 11.6 Hz, 2H), 3.95 – 3.90 (m, 2H), 3.33 – 3.22 (m, 1H), 2.33 – 2.26 (m, 2H), 2.20 – 2.12 (m, 2H). **^{13}C{^{1}H} NMR** (101 MHz, DMSO-d_6) δ 184.6, 150.3, 137.5, 128.6, 127.6, 127.2, 126.6, 119.7, 77.4, 64.9, 39.1, 35.3, 33.4. **IR υ (cm^{-1})** 3030, 2987, 2952, 2919, , 2900, 1988, 1963, 1885, 1827, 1767, 1705, 1671, 1629, 1604, 1492, 1470, 1453, 1395, 1371, 1346, 1293, 1199, 1176, 1142, 1108, 1097, 1080, 1038, 1014, 999, 918, 895, 855, 762, 702, 629, 590. **HRMS** (ESI-TOF) m/z: $[M+H]^+$ - Calcd for $C_{18}H_{19}O_4$ 299.1283; Found 299.1273.

Dispiro[cyclohexane-1,1'-isobenzofuran-3',2''-[1,3]dioxolane]-2,5-dien-4-one (7h)



The general procedure **A** was followed using methyl 4'-hydroxy-[1,1'-biphenyl]-2-carboxylate (100 mg, 0.438 mmol, 1 equiv.) and ethane-1,2-diol (59.8 mg, 0.963 mmol, 2.2 equiv.) to obtain crude product **7h.** Purification by column chromatography R_f (*n*-hexane/ethyl acetate 70/30, UV active, PMA stain active) = 0.7 yielded **7h** (70.7 mg, 63%) as a colorless solid. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.36 – 7.20 (m, 3H), 6.94 – 6.79 (m, 1H), 6.58 (d, J = 10.1 Hz, 2H), 6.06 (d, J = 10.1 Hz, 2H), 4.26 – 4.14 (m, 2H), 4.12 – 4.04 (m, 2H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 185.4, 148.6, 139.5, 135.3, 131.2, 129.8, 129.0, 128.1, 123.8, 121.9, 80.5, 65.7. **IR υ (cm^{-1})** 2898, 1670, 1631, 1460, 1339, 1273, 1127, 1093, 1021, 930, 760580, 449. **HRMS** (ESI-TOF) m/z: [M+H]- Calcd for $C_{15}H_{13}O_4$ 257.0814; Found 257.0806. **p:** 115-118 °C.

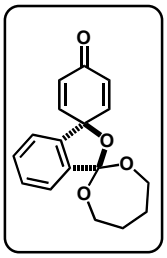
Trispiro[cyclohexane-1,1'-isobenzofuran-3',2''-[1,3]dioxane-5'',1'''-cyclopropane]-2,5-dien-4-one (10i)



The general procedure **A** was followed using methyl 4'-hydroxy-[1,1'-biphenyl]-2-carboxylate (100 mg, 0.438 mmol, 1 equiv.) and cyclopropane-1,1-diyldimethanol (98.4 mg, 0.963 mmol, 2.2 equiv.) to obtain crude product **7i**. Purification by column chromatography R_f (*n*-hexane/ethyl acetate 80/20, UV active, PMA stain active) = 0.6 yielded **7i** (64.9 mg, 50%) as a colorless solid. **^{1}H NMR** (500 MHz, DMSO-

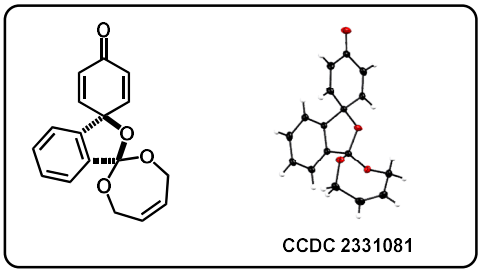
d_6) δ 7.55 – 7.50 (m, 1H), 7.51 – 7.44 (m, 2H), 7.28 – 7.07 (m, 1H), 6.97 – 6.72 (m, 2H), 6.27 (d, J = 10.0 Hz, 2H), 4.59 (d, J = 11.2 Hz, 2H), 3.25 (d, J = 11.8 Hz, 2H), 0.75 (t, 2H), 0.43 (t, 2H). **^{13}C{^{1}H} NMR** (126 MHz, DMSO-d_6) δ 184.5, 148.7, 138.3, 137.7, 130.9, 129.5, 127.6, 123.2, 121.8, 119.8, 80.9, 67.7, 16.4, 12.9, 4.4. **IR υ (cm^{-1})** 2957, 2873, 1671, 1638, 1460, 1350, 1301, 1272, 1200, 1129, 1098, 1045, 981, 925, 856, 762, 683, 592, 539. **HRMS** (ESI-TOF) m/z: [M+H]- Calcd for $C_{18}H_{17}O_4$ 297.1127; Found 297.1124. **mp:** 138-140 °C.

Dispiro[cyclohexane-1,1'-isobenzofuran-3',2''-[1,3]dioxepane]-2,5-dien-4-one (10j)



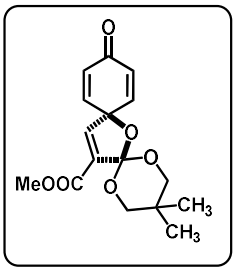
The general procedure **A** was followed using methyl 4'-hydroxy-[1,1'-biphenyl]-2-carboxylate (100 mg, 0.438 mmol, 1 equiv.) and butane-1,4-diol (88.8 mg, 0.963 mmol, 2.2 equiv.) to obtain crude product 7**j**. Purification by column chromatography R_f (*n*-hexane/ethyl acetate 70/30, UV active, PMA stain active) = 0.6 yielded **7j** (69.7 mg, 56%) as a colorless solid. **^{1}H NMR** (396 MHz, DMSO-d_6) δ 7.73 – 7.65 (m, 1H), 7.53 – 7.42 (m, 2H), 7.20 – 7.05 (m, 1H), 6.82 (d, J = 10.1 Hz, 2H), 6.24 (d, J = 9.9 Hz, 2H), 3.98 (d, J = 2.8 Hz, 4H), 1.73 (q, J = 4.4 Hz, 4H). **^{13}C{^{1}H} NMR** (101 MHz, DMSO-d_6) δ 184.6, 148.9, 138.7, 137.7, 130.3, 129.5, 127.5, 122.55, 122.52, 121.9, 80.1, 63.9, 28.7. **IR (neat) υ (cm^{-1})** 2957, 2920, 2852, 1772, 1674, 1633, 1562, 1465, 1376, 1288, 1239, 1164, 1106, 953, 926, 856, 748, 690, 612, 538. **HRMS** (ESI-TOF) m/z: [M+H]- Calcd for $C_{17}H_{17}O_4$ 285.1127; Found 285.1125.

4'',7''-dihydrodispiro[cyclohexane-1,1'-isobenzofuran-3',2''-[1,3]dioxepine]-2,5-dien-4-one (7k)



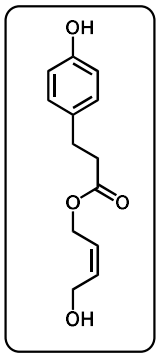
The general procedure **A** was followed using methyl 4'-hydroxy-[1,1'-biphenyl]-2-carboxylate (100 mg, 0.438 mmol, 1 equiv.) and (*Z*)-but-2-ene-1,4-diol (84.9 mg, 0.963 mmol, 2.2 equiv.) to obtain crude product **7k**. Purification by column chromatography R_f (*n*-hexane/ethyl acetate 60/40, UV active, PMA stain active) = 0.7 yielded **7k** (75.4 mg, 61%) as a colorless solid. **^{1}H NMR** (396 MHz, DMSO-d_6) δ 7.81 – 7.71 (m, 1H), 7.55 – 7.46 (m, 2H), 7.21 – 7.10 (m, 1H), 6.84 (d, J = 9.8 Hz, 2H), 6.26 (d, J = 10.2 Hz, 2H), 5.81 (s, 2H), 4.52 (s, 4H). **^{13}C{^{1}H} NMR** (101 MHz, DMSO-d_6) δ 184.3, 168.9, 146.4, 145.1, 135.5, 130.7, 129.5, 126.2, 125.4, 122.9, 80.4. **IR (neat) υ (cm^{-1})** 2956, 2921, 2851, 1771, 1673, 1632, 1561, 1464, 1379, 1284, 1237, 1163, 1104, 950, 929, 857, 747, 691, 618, 539. **HRMS** (ESI-TOF) m/z: [M+H]- Calcd for $C_{17}H_{15}O_4$ 283.0970; Found 283.0964. **Mp:** 120-123 °C.

methyl 3,3-dimethyl-11-oxo-1,5,7-trioxadispiro[5.1.58.26]pentadeca-9,12,14-triene-15-carboxylate (20)



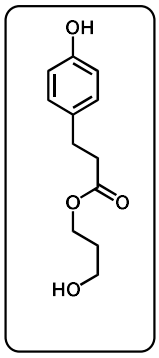
The general procedure **A** was followed using dimethyl 2-(4-hydroxybenzylidene)malonate (100 mg, 0.423 mmol, 1 equiv.) and 2,2-dimethylpropane-1,3-diol (97 mg, 0.931 mmol, 2.2 equiv.) to obtain crude product **20**. Purification by column chromatography R_f (*n*-hexane/ethyl acetate 60/40, UV active, $KMnO_4$ stain active) = 0.3 yielded **20** (13 mg, 10%) as a colorless liquid. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.13 (s, 1H), 6.72 (d, *J* = 10.2 Hz, 2H), 6.25 (d, *J* = 9.9 Hz, 2H), 3.88 (d, *J* = 10.6 Hz, 2H), 3.73 (s, 3H), 3.50 (d, *J* = 10.8 Hz, 2H), 1.25 (s, 3H), 0.76 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 184.0, 167.3, 148.0, 146.3, 144.5, 129.2, 80.6, 79.1, 70.7, 51.9, 29.1, 22.0, 21.2. **IR u (cm^{-1})** 3050, 2965, 2921, 2866, 1776, 1739, 1670, 1622, 1563, 1460, 1350, 1274, 1227, 1155, 1107, 1016, 810, 740, 699, 612, 593, 530, 456. **HRMS** (ESI-TOF) m/z: [M+Na]- Calcd for $C_{16}H_{19}NaO_6$ 306.1103; Found 306.1099.

(*Z*)-4-hydroxybut-2-en-1-yl 3-(4-hydroxyphenyl)propanoate (6a)



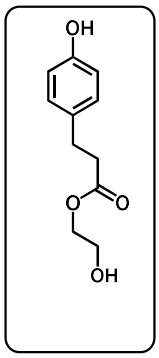
By following the known procedure, this compound was prepared. (H. Sharghi and M. H. Sarvari, *Tetrahedron*, 2003, **59**, 3627–3633.) **^{1}H NMR(500 MHz, Chloroform-*D*)** δ 7.05 (d, *J* = 8.5 Hz, 2H), 6.75 (d, *J* = 8.6 Hz, 2H), 5.84 (dt, *J* = 12.1, 6.5 Hz, 1H), 5.64 – 5.53 (m, 1H), 5.18 (s, 1H), 4.66 (d, *J* = 7.1 Hz, 2H), 4.24 (t, *J* = 6.0 Hz, 2H), 2.87 (t, *J* = 7.6 Hz, 2H), 2.60 (t, *J* = 7.6 Hz, 2H), 2.07 (t, *J* = 5.8 Hz, 1H). **^{13}C NMR (101 MHz, Chloroform-*D*)** δ 173.3, 154.3, 133.4, 132.5, 129.6, 125.8, 115.5, 60.2, 58.5, 36.4, 30.2. **IR *υ* (cm^{-1})** 3315, 1702 1620, 1516, 1422, 1392, 1316, 1263, 1208, 1151, 1102, 1065, 998, 902, 832. **HRMS** (ESI-TOF) m/z: [M+Na]- Calcd for $C_{13}H_{16}NaO_4$ 259.0946; Found 259.0944.

3-hydroxypropyl 3-(4-hydroxyphenyl)propanoate (6o)



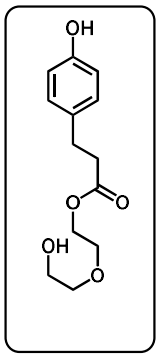
By following the known procedure, this compound was prepared. (H. Sharghi and M. H. Sarvari, *Tetrahedron*, 2003, **59**, 3627–3633.) **^{1}H NMR (396 MHz, Chloroform-*d*)** δ 7.02 (d, *J* = 8.4 Hz, 2H), 6.74 (d, *J* = 8.5 Hz, 2H), 4.19 (t, *J* = 6.2 Hz, 2H), 3.57 (t, *J* = 6.1 Hz, 2H), 2.85 (t, *J* = 7.5 Hz, 2H), 2.59 (t, *J* = 7.6 Hz, 2H), 1.80 (p, *J* = 6.1 Hz, 2H). **^{13}C NMR (101 MHz, Chloroform-*D*)** δ 174.0, 154.6, 132.1, 129.5, 115.5, 61.5, 59.2, 36.3, 31.6, 30.3. **IR *υ* (cm^{-1})** 3311, 1700, 1616, 1512, 1418, 1388, 1314, 1260, 1205, 1149, 1098, 1062, 996, 899, 830. **HRMS** (ESI-TOF) m/z: [M+Na]- Calcd for $C_{12}H_{16}NaO_4$ 247.0946; Found 247.0945.

2-hydroxyethyl 3-(4-hydroxyphenyl)propanoate (6p)



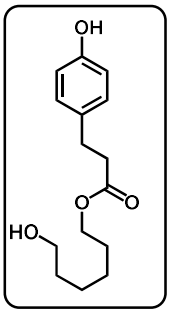
By following the known procedure, this compound was prepared. (H. Sharghi and M. H. Sarvari, *Tetrahedron*, 2003, **59**, 3627–3633.) **^{1}H NMR (396 MHz, Chloroform-*d*)** δ 7.07 (d, *J* = 8.5 Hz, 2H), 6.75 (d, *J* = 8.5 Hz, 2H), 4.55 – 4.12 (m, 2H), 3.75 (s, 1H), 3.69 – 3.57 (m, 2H), 2.90 (t, *J* = 7.7 Hz, 2H), 2.64 (dd, *J* = 8.2, 7.2 Hz, 2H). **^{13}C NMR (101 MHz, Chloroform-*D*)** δ 172.8, 154.2, 132.6, 129.6, 115.5, 64.1, 41.7, 36.1, 30.2. **IR *u* (cm^{-1})** 3312, 1698, 1617, 1513, 1419, 1389, 1312, 1259, 1204, 1147, 1099, 1061, 995, 898, 829. **HRMS** (ESI-TOF) m/z: [M+Na]- Calcd for $C_{11}H_{14}NaO_4$ 233.0790; Found 233.0787.

2-(2-hydroxyethoxy)ethyl 3-(4-hydroxyphenyl)propanoate (6q)



By following the known procedure, this compound was prepared. (H. Sharghi and M. H. Sarvari, *Tetrahedron*, 2003, **59**, 3627–3633.) **^{1}H NMR (396 MHz, Chloroform-*d*)** δ 7.04 – 6.96 (m, 2H), 6.73 (d, *J* = 8.4 Hz, 2H), 4.33 – 4.17 (m, 2H), 3.76 – 3.68 (m, 2H), 3.67 – 3.60 (m, 2H), 3.58 – 3.49 (m, 2H), 2.85 (t, *J* = 7.6 Hz, 2H), 2.60 (t, *J* = 7.5 Hz, 2H). **^{13}C NMR (101 MHz, Chloroform-*D*)** δ 173.4, 154.5, 132.2, 129.5, 115.5, 72.3, 69.3, 63.6, 61.8, 36.2, 30.2. **IR *u* (cm^{-1})** 3310, 1699, 1618, 1514, 1420, 1390, 1313, 1261, 1206, 1148, 1100, 1063, 994, 900, 831. **HRMS** (ESI-TOF) m/z: [M+Na]- Calcd for $C_{13}H_{18}NaO_5$ 277.1052; Found 277.1049.

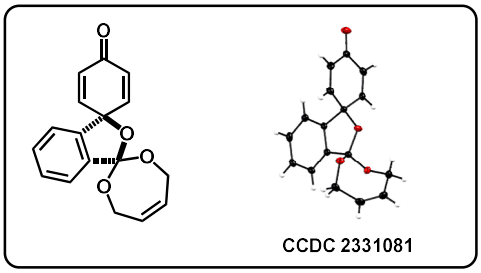
6-hydroxyhexyl 3-(4-hydroxyphenyl)propanoate (6r)



By following the known procedure, this compound was prepared. (H. Sharghi and M. H. Sarvari, *Tetrahedron*, 2003, **59**, 3627–3633.) **^{1}H NMR (396 MHz, Chloroform-*d*)** δ 7.04 (d, *J* = 8.5 Hz, 2H), 6.75 (d, *J* = 8.5 Hz, 2H), 6.40 (s, 1H), 4.03 (t, *J* = 6.4 Hz, 2H), 3.64 (t, *J* = 6.6 Hz, 2H), 2.87 (t, *J* = 7.4 Hz, 2H), 2.59 (t, *J* = 7.4 Hz, 2H), 2.02 (s, 1H), 1.53 (dtd, *J* = 14.9, 6.5, 1.8 Hz, 4H), 1.31 (dtd, *J* = 9.5, 7.2, 5.4 Hz, 2H), 1.25 – 1.16 (m, 2H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 173.6, 154.5, 132.3, 129.5, 115.6, 64.5, 63.0, 36.4, 32.5, 30.4, 28.8, 25.8, 25.5. **IR υ (cm^{-1})** 3310, 1699, 1618, 1514, 1420, 1390, 1313, 1261, 1206, 1148, 1100, 1063, 994, 900, 831. **HRMS** (ESI-TOF) m/z: [M+Na]- Calcd for $C_{15}H_{22}NaO_4$ 289.1416; Found 289.1413.

(VI) XRD Data

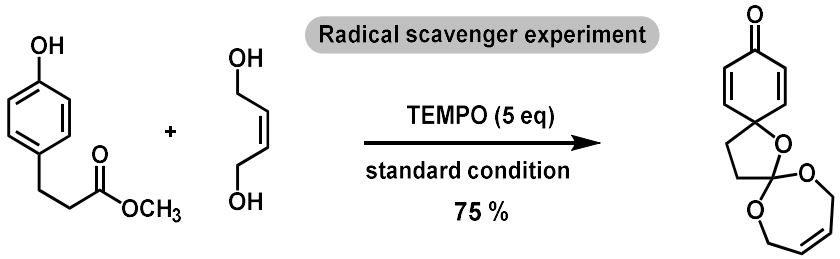
4'',7''-dihydrodispiro[cyclohexane-1,1'-isobenzofuran-3',2''-[1,3]dioxepine]-2,5-dien-4-one (7k)



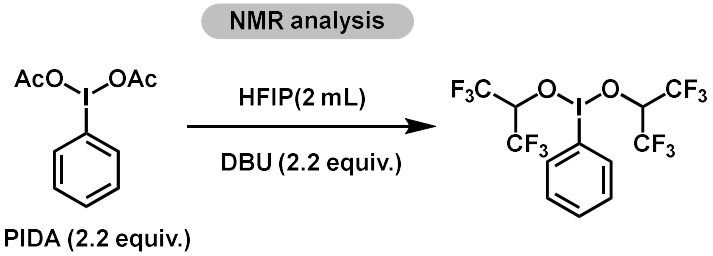
Structure of compound **7k** in the solid state. The anisotropic displacement parameters are drawn at the 50% probability displacement level. Red = Oxygen atom; Black = Carbon atom; White = Hydrogen atom. Crystal was grown in acetone (slow evaporation). X-Ray Crystal Structure Analysis of **7k**: Molecular formula = $C_{17}H_{14}O_4$, Mr. = 282.28 gmol^{-1}, colorless crystal, space group: $P2_1/n$, Hall group: -P 2yn, a = 10.9280(3) Å, b = 9.1501(2) Å, c = 13.8574(4) Å, α = 90°, β = 103.782(1)°, γ = 90°, Volume: 1345.74(6) Å^3, Temperature: 296 K, Z = 4, D_{calc} = 1.393 g cm^{-3}, D_{report} = 1.393 g cm^{-3}, λ = 0.71073 Å, m(Cu-Ka) = 0.099 mm^{-1}, empirical absorption correction(T_{min} = 0.680, T_{max} = 0.746), CCD Bruker SMART APEX diffractometer, structure was solved by direct methods and refined (SHELXL-97) by full matrix least squares based on F² to R(reflections)= 0.0391(2898) [I > 20(1)], wR_2 (reflections) = 0.0995(3351), S = 1.053.

(VII) Mechanistic Investigation:

(1) Radical scavenger experiment: The general procedure **A** was followed using methyl 3-(4-hydroxyphenyl)propanoate (100 mg, 0.555 mmol, 1 equiv.), (*Z*)-but-2-ene-1,4-diol (185.73 mg, 1.22 mmol, 2.2 equiv.) and TEMPO (86.7 mg, 2.77 mmol, 5 equiv) to obtain crude product **7a**. Purification by column chromatography R_f (*n*-hexane/ethyl acetate 50/50, UV active, PMA stain active) = 0.5 yielded **7a** (97.5 mg, 75%) as a colorless white solid.

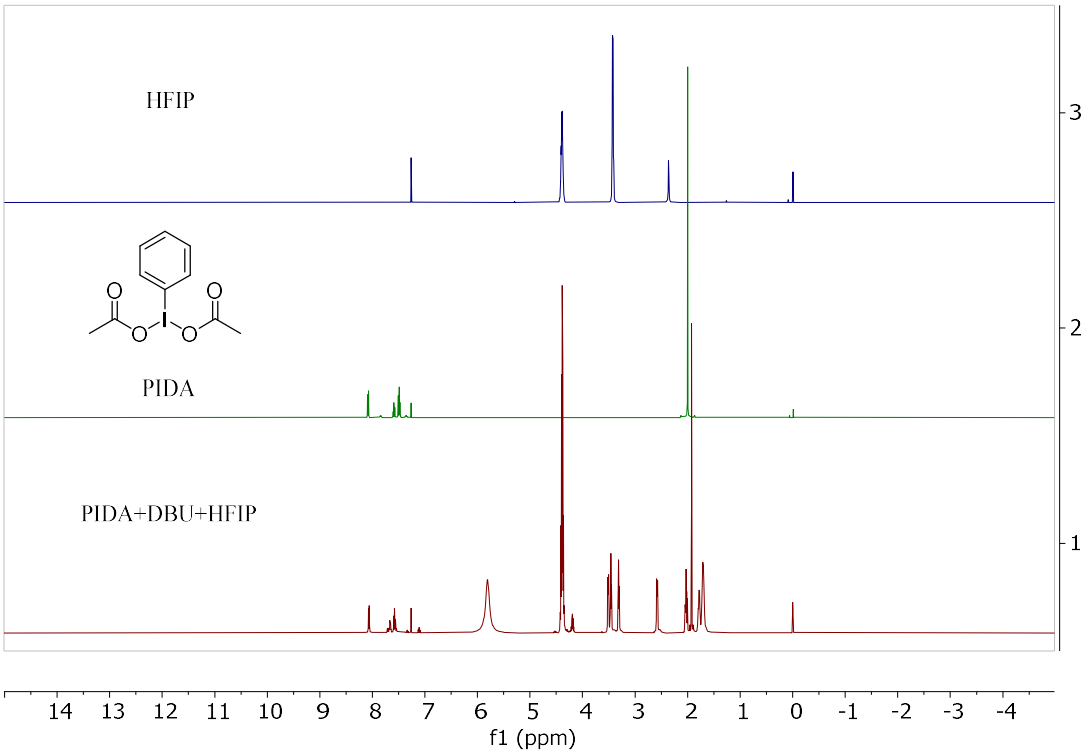


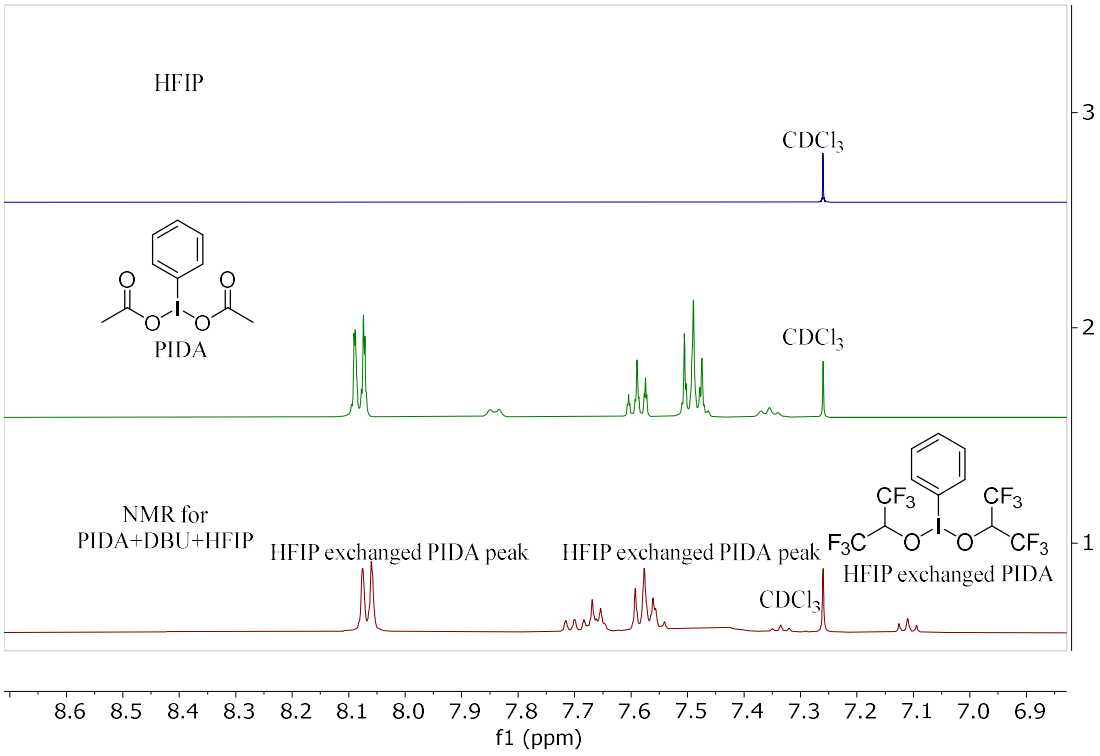
(2) NMR study for the exchange of HFIP with acetate (*in situ* generation of compound 13): To a stirred solution of HFIP (2 mL) was added DBU (2.2 equiv.) and PIDA (1.2 equiv.) at 0 °C, and it was stirred for 5 minutes, followed by the recording of NMR using 0.4 mL of $CDCl_3$. NMR data for compound **13** match those previously reported in *Angew. Chemie Int. Ed.,* 2019, **58**, 9811–9815.

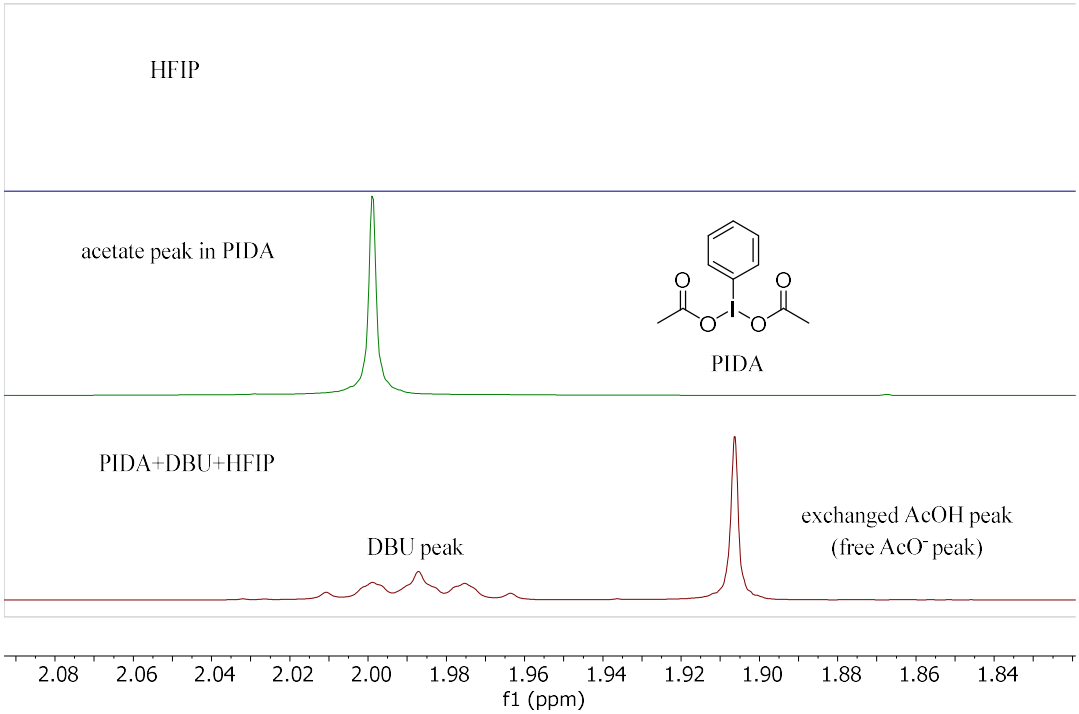


The NMR spectra shown here are for Hexafluoroisopropanol (HFIP), phenyliodine(III) diacetate (PIDA), and the mixture of PIDA, DBU, and HFIP (reaction mixture before adding the diol and phenolic ester starting materials) in $CDCl_3$. Once PIDA, DBU, and HFIP are mixed together, PIDA is consumed, and traces remain (after 5 min), as clearly visible in the NMR.

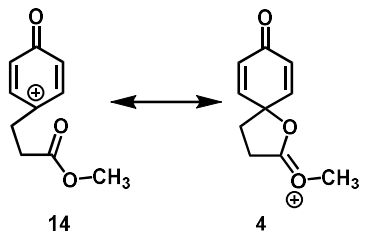
1) There is a slight shift in the acetate ion peak towards the shielding region, indicating the removal of acetate from Iodine (+3).





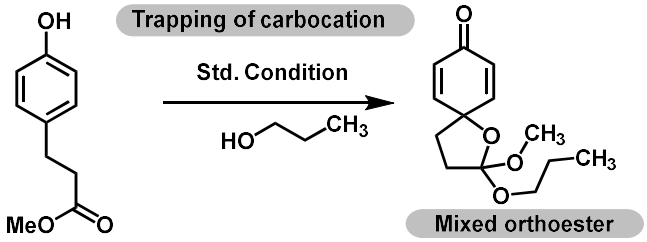


(3) HRMS (ESI-TOF) analysis for 14 or 4:



HRMS (ESI-TOF) m/z: [M+] Calcd for $C_{10}H_{11}O_3$ 179.0702; Found 179.0703.

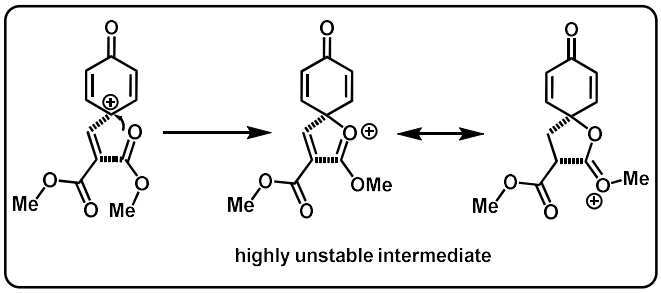
(4)Trapping of carbocation (2-methoxy-2-propoxy-1-oxaspiro[4.5]deca-6,9-dien-8-one (15))



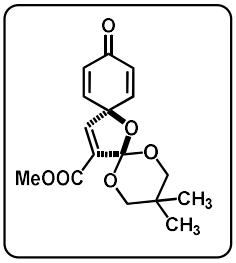
The general procedure **A** was followed using methyl 3-(4-hydroxyphenyl)propanoate (100 mg, 0.555 mmol, 1 equiv.) and 1-propanol (73.3 mg, 1.22 mmol, 2.2 equiv.) to obtain crude product **15**. Purification by column chromatography R_f(*n*-Hexane/ethyl acetate 80/20, UV active, PMA stain active) = 0.5 yielded **15** (60 mg, 45%) as a colorless liquid. **^{1}H NMR** (396 MHz, BENZENE-D_6) δ 6.17 – 5.98 (m, 4H), 3.30 (s, 3H), 2.91 (t, J = 6.4 Hz, 2H), 2.02 (dd, J = 8.9, 6.9 Hz, 2H), 1.85 (dd, J = 8.8, 6.9 Hz, 2H), 1.44 – 1.28 (m, 2H), 0.76 (t, J = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, Chloroform-*d*) δ 184.3, 172.6, 150.0, 131.5, 74.2, 66.8, 51.1, 34.7, 28.4, 23.8, 10.7. **IR υ (cm^{-1})** 3055, 2956, 2919, 2870, 2851, 1775, 1674, 1632, 1561, 1465, 1378, 1264, 1237, 1165, 1109, 1026, 80, 814, 747, 690, 618, 592, 538, 457. **HRMS** (ESI-TOF) m/z: [M+Na]- Calcd for $C_{13}H_{18}NaO_4$ 261.1103; Found 261.1099.

(5) Stability of carbocation (preparation of orthoester with electron-withdrawing group)

Further involvement of the carbocation was confirmed using a diester starting material, which gave only 10% of the Ortho ester due to destabilization of the tertiary carbocation by conjugation with the ester group through a pi bond (as shown below).

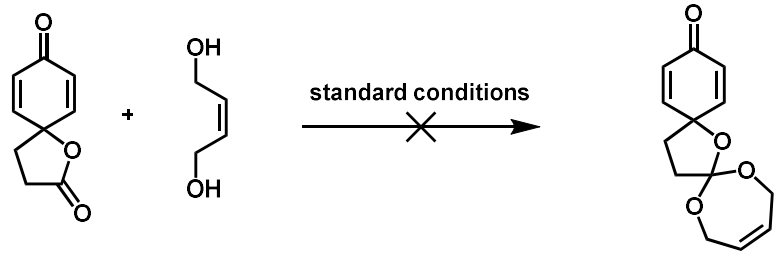


methyl 3,3-dimethyl-11-oxo-1,5,7-trioxadispiro[5.1.58.26]pentadeca-9,12,14-triene-15-carboxylate (20)



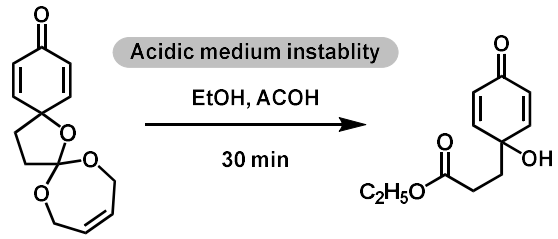
The general procedure **A** was followed using dimethyl 2-(4-hydroxybenzylidene)malonate (100 mg, 0.423 mmol, 1 equiv.) and 2,2-dimethylpropane-1,3-diol (97 mg, 0.931 mmol, 2.2 equiv.) to obtain crude product **20**. Purification by column chromatography R_f(*n*-Hexane/ethyl acetate 60/40, UV active, $KMnO_4$ stain active) = 0.3, yielded **20** (13 mg, 10%) as a colorless liquid. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.13 (s, 1H), 6.72 (d, J = 10.2 Hz, 2H), 6.25 (d, J = 9.9 Hz, 2H), 3.88 (d, J = 10.6 Hz, 2H), 3.73 (s, 3H), 3.50 (d, J = 10.8 Hz, 2H), 1.25 (s, 3H), 0.76 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 184.0, 167.3, 148.0, 146.3, 144.5, 129.2, 80.6, 79.1, 70.7, 51.9, 29.1, 22.0, 21.2. **IR υ (cm^{-1})** 3050, 2965, 2921, 2866, 1776, 1739, 1670, 1622, 1563, 1460, 1350, 1274, 1227, 1155, 1107, 1016, 810, 740, 699, 612, 593, 530, 456. **HRMS** (ESI-TOF) m/z: [M+Na]- Calcd for $C_{16}H_{19}NaO_6$ 306.1103; Found 306.1099.

(6) Checking another possible intermediate:



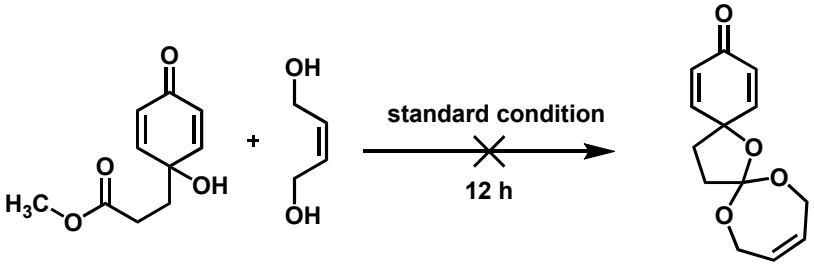
The general procedure **A** was followed using 1-oxaspiro[4.5]deca-6,9-diene-2,8-dione **24** (100 mg, 0.609 mmol, 1 equiv.) and (*Z*)-but-2-ene-1,4-diol (185.73 mg, 1.22 mmol, 2.2 equiv.). There was no product formation, indicating the reaction did not proceed *via* a neutral lactone.

(7) Decomposition study of compound 7a:



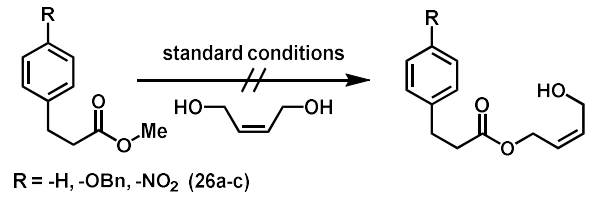
To a stirred solution of compound **7a (**50 mg, 0.213 mmol, 1 equiv.**)** in ethanol (2 mL) was added AcOH (0.5 equiv.) at room temperature under a nitrogen atmosphere. It was stirred for 30 minutes. The reaction progress was monitored by TLC. Upon completion of the reaction, it was concentrated *in vacuo* to remove ethanol, followed by column chromatography (R_f = 0.4; Hexane/EtOAc, 60:40) to provide **21** ethyl 3-(1-hydroxy-4-oxocyclohexa-2,5-dien-1-yl)propanoate (42.6 mg, 95%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (d, *J* = 10.2 Hz, 2H), 6.14 (d, *J* = 10.2 Hz, 2H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.25 (s, -OH peak, 1H), 2.31 (t, *J* = 7.7 Hz, 2H), 2.12 – 2.03 (t, *J* = 7.7 Hz, 2H), 1.22 (t, *J* = 7.2 Hz, 3H).

(8) Interconversion study of compound 7a1 to 7a:



General procedure **A** was followed using methyl 3-(1-hydroxy-4-oxocyclohexa-2,5-dien-1-yl)propanoate **(**50 mg, 0.254 mmol, 1 equiv.) and (*Z*)-but-2-ene-1,4-diol (185.73 mg, 1.22 mmol, 2.2 equiv.). There was no product formation indicating that compounds **7a1** and **7a** are not inconvertible.

(9) Transesterification experiment:



The general procedure **A** was followed using the known compound **22a-c** (100 mg, 1 equiv.) and (*Z*)-but-2-ene-1,4-diol (185.73 mg, 1.22 mmol, 2.2 equiv.). There was spiro-orthoester product formation,

and the starting material was isolated as such, indicating that the reaction does not proceed *via* the trans-esterification pathway.

(VI) DFT Calculations

Computational Methods.

Density functional theory (DFT) calculations were performed with Gaussian 16 rev. C.01.1[29] Geometry optimizations were initially performed using b3lyp/6-311G(2d,2p) basis set. The SMD implicit continuum solvation model[30] was used to account for the effect of hexafluoroisopropanol (HFIP) solvent on the computed Gibbs energy profile. Since HIFP solvent is not available in the list of default/pre-defined solvents in the Gaussian 16 software, it is herein parametrized using a set of seven parameters.[30] These include 1) the static dielectric constant of the solvent at 25ºC (Eps = 16.7);[31-34] 2) dynamic (optical) dielectric constant – the square of the refractive index value of 1.275 at 20ºC was used[35] (EpsInf = 1.625625); 3) hydrogen bond acidity (HBondAcidity = 0.77)[36] and 4) hydrogen bond basicity (H Bond Basicity = 0.10)14, which are Abraham's A and B values respectively; 5) the surface tension of the solvent at the interface (Surface Tension At Interface = 23.23)[37] this value is obtained from the conversion of the surface tension of HFIP at 16.14 mN/m at 25ºC[38] to cal mol^{-1} $Å^{-2}$ used in the SMD model by the conversion factor of 1 dyne/cm = 1 mN/m = 1.43932 cal mol-1 $Å^{-2}$ as outlined in the Truhlar's Minnesota Solvent Descriptor Database[39]; 6) carbon aromaticity the fraction of aromatic carbons (Carbon Aromaticity = 0.00) and 7) electronegative halogenicity the fraction of halogens (Electronegative Halogenicity = 0.60). These parameters were specified using the keyword "SCRF = (SMD, Solvent= Generic, Read)" in Gaussian 16. All Gibbs energy values in the text and figures are quoted in kJ mol^{-1}. All molecular structures were visualized using Gaussview6 software.

Cartesian coordinates for compound **4**

Total energy = -613.332470 Hartree

Temperature = 298.15 K

C	-3.20753	-0.08417	-0.53109
C	-2.47671	1.04698	-0.58073
C	-2.63072	-1.38046	-0.19687
C	-1.05043	1.00272	-0.3197
H	-2.89372	1.99496	-0.8906
C	-1.34505	-1.50589	0.14086
H	-3.27308	-2.24912	-0.23455
H	-0.89917	-2.4592	0.39162
C	-0.06657	-0.03057	1.77106
H	-0.08129	-0.96734	2.32225
H	-0.73703	0.67235	2.25559
C	1.3704	0.49736	1.64179
H	1.43433	1.58573	1.60962
H	2.05074	0.13988	2.41211
C	1.76981	-0.02498	0.31482
O	0.81631	-0.5321	-0.38282
O	2.95863	-0.00692	-0.11866
C	3.24881	-0.53049	-1.46517

H	2.65438	0.0221	-2.18613
H	4.30835	-0.3524	-1.59668
H	3.0146	-1.59041	-1.47974
C	-0.49014	-0.29852	0.29932
O	-0.2811	1.92701	-0.53204
H	-4.26009	-0.0525	-0.781

Cartesian coordinates for compound **4'**

Total energy = -613.332521 Hartree

Temperature = 298.15 K

O	-4.15073	-0.66865	-0.17563
C	-2.96266	-0.38101	-0.08826
C	-2.1528	-0.08994	-1.28558
C	-2.27719	-0.33768	1.21632
C	-0.86906	0.25024	-1.19168
H	-2.65456	-0.17106	-2.24036
C	-0.99241	-0.00331	1.31374
H	-2.86742	-0.59898	2.08434
H	-0.27297	0.45781	-2.07192
H	-0.48047	0.01782	2.26737
C	0.45494	1.83011	0.31105
H	0.40607	2.1206	1.35706
H	-0.07251	2.57147	-0.28072
C	1.91578	1.65603	-0.12613
H	2.09502	1.94887	-1.16364
H	2.64075	2.1774	0.49493
C	2.10606	0.19164	-0.03804
O	1.03236	-0.49374	0.10104
O	3.23999	-0.37072	-0.1103
C	3.32557	-1.84045	-0.05072
H	2.76562	-2.25373	-0.88387
H	4.38433	-2.04865	-0.1367
H	2.92704	-2.17136	0.90334
C	-0.18888	0.42682	0.13086

Cartesian coordinates for compound **10a**

Total energy = -804.885151 Hartree

Temperature = 298.15 K

O	-1.61339	-2.05443	-0.60817
C	-2.17416	-0.99406	-0.36132
C	-1.35246	0.20928	0.1425
C	-3.61437	-0.81962	-0.49431
C	-2.04908	1.52554	1.89E-4
C	-4.16012	0.41198	-0.44552
H	-4.1977	-1.7002	-0.72806
H	-1.43666	2.40521	0.15231
H	-5.22349	0.5341	-0.61073
C	-3.3639	1.60875	-0.22514
H	-3.85886	2.56955	-0.26337
C	-0.98454	-0.05754	1.63973
H	-1.76116	-0.61055	2.16239
H	-0.84016	0.89633	2.14399
C	0.33834	-0.80991	1.52036
H	0.96327	-0.69573	2.40192
H	0.18302	-1.86659	1.31781
C	0.97812	-0.17029	0.28879
O	-0.09452	0.23561	-0.54891
O	1.73109	-1.02142	-0.53
C	3.0633	-1.31756	-0.07885
H	3.0731	-1.50508	0.9991
H	3.31977	-2.25528	-0.57041
C	4.06029	-0.26024	-0.46516
H	5.06825	-0.61399	-0.65093
C	3.77736	1.02859	-0.61317
H	4.54985	1.71451	-0.9422
C	2.43873	1.64402	-0.3211
H	1.8193	1.71787	-1.21855
H	2.57406	2.65342	0.0657
O	1.72961	0.93558	0.71446

Cartesian coordinates for compound **7a**

Total energy = -804.883431 Hartree

Temperature = 298.15 K

O	4.81278	-1.01114	0.42096
C	3.65888	-0.62397	0.23938
C	2.97406	0.23388	1.21784
C	2.89584	-1.02026	-0.95432

C	1.73828	0.68479	0.99927
H	3.52038	0.46812	2.12239
C	1.65685	-0.57455	-1.16554
H	3.38748	-1.69833	-1.63975
C	0.97063	0.40336	-0.2619
H	1.23428	1.30144	1.73343
H	1.09327	-0.88103	-2.03819
C	0.62294	1.72095	-1.01095
H	0.47605	1.50366	-2.06805
H	1.41343	2.46087	-0.91502
C	-0.69336	2.13964	-0.36216
H	-0.53204	2.65851	0.58029
H	-1.31251	2.75803	-1.00636
C	-1.36624	0.80151	-0.07957
O	-0.32849	-0.14837	0.10736
O	-2.15508	0.90031	1.07162
C	-2.50689	-0.29685	1.7762
H	-1.61306	-0.71551	2.25145
H	-3.15814	0.05263	2.57722
C	-3.20139	-1.37628	1.00538
H	-3.73914	-2.06697	1.64793
C	-3.19948	-1.62546	-0.29981
H	-3.73616	-2.50456	-0.64367
C	-2.49936	-0.90628	-1.41109
H	-1.60416	-1.47282	-1.68977
H	-3.14421	-0.88126	-2.28955
O	-2.15296	0.46601	-1.19728

(X) References

(29) Reference Gaussian 16

Gaussian 16, Revision C.01,

M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2019.

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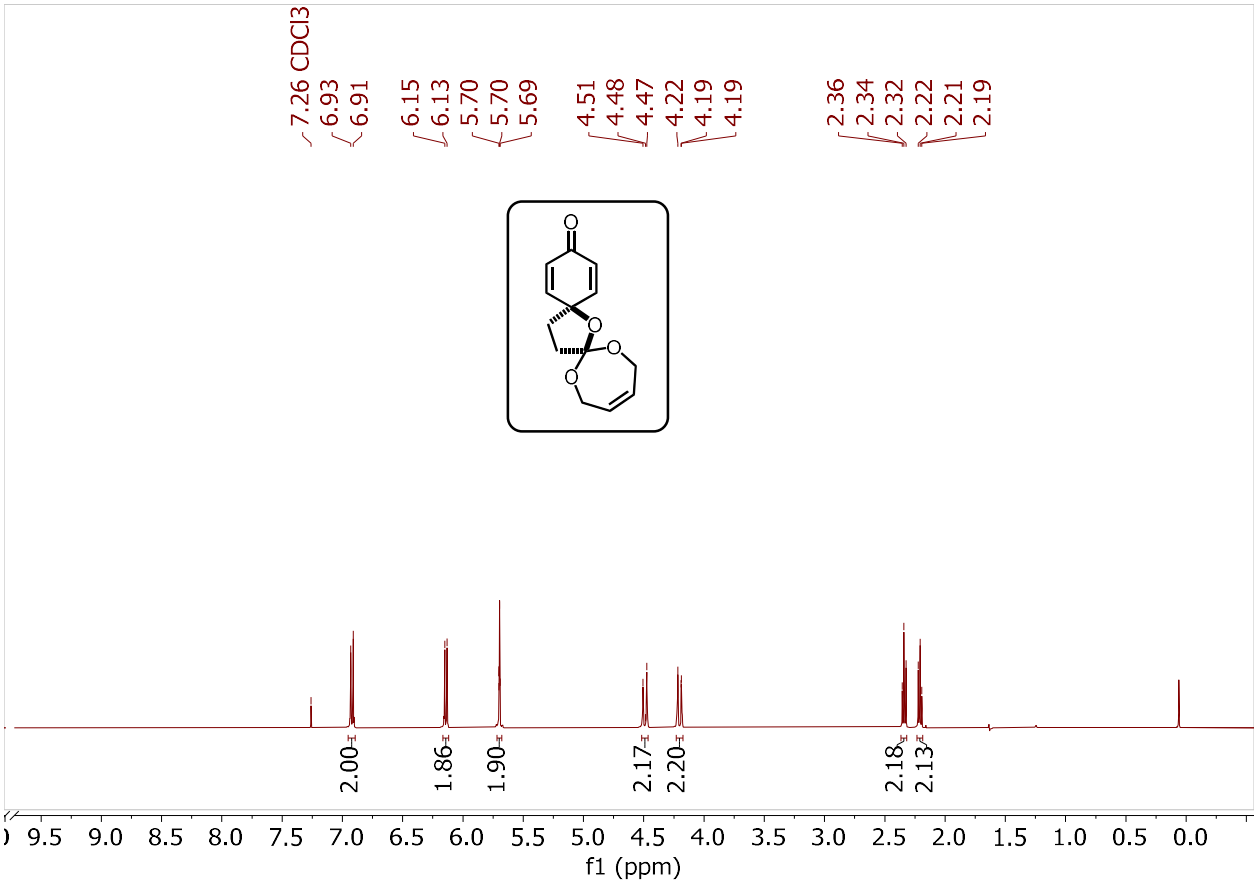
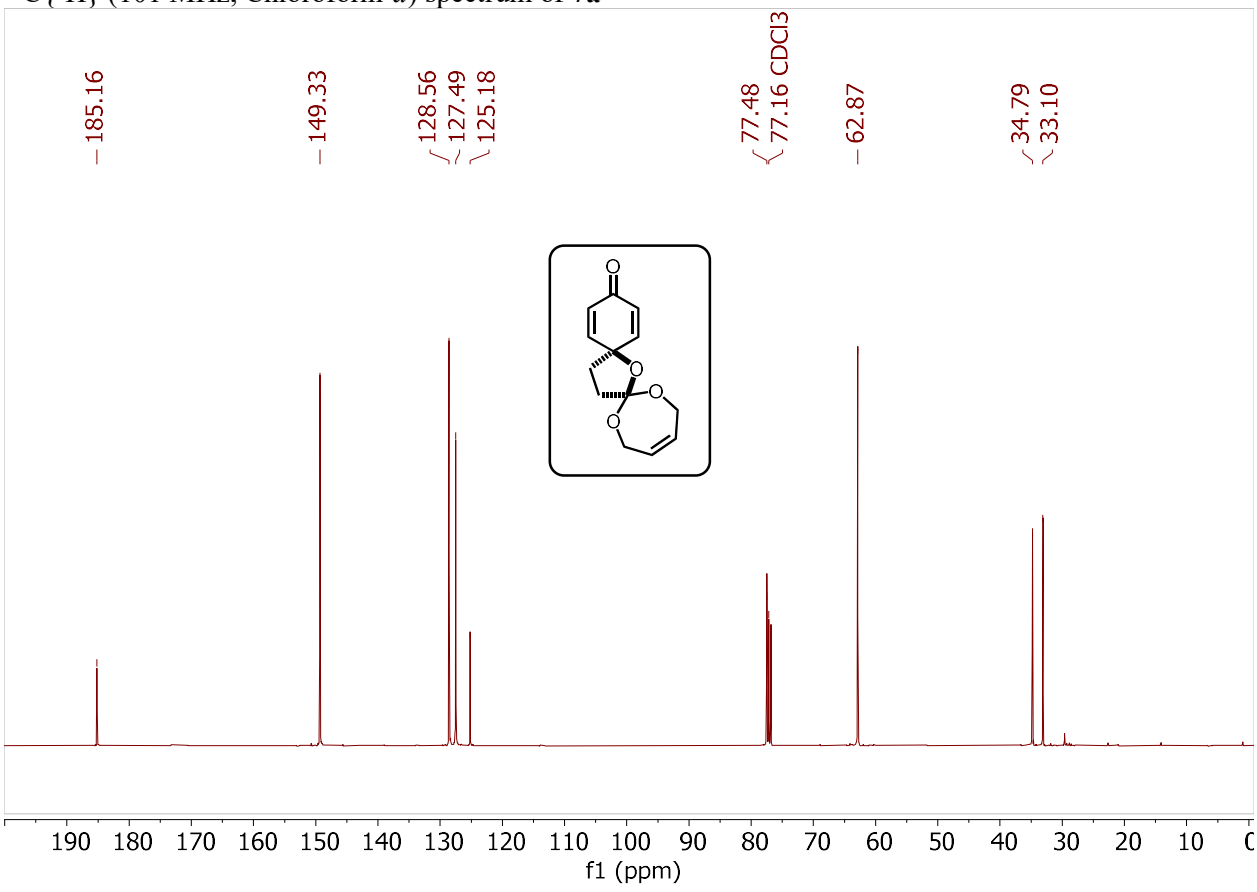
(XI) NMR spectra

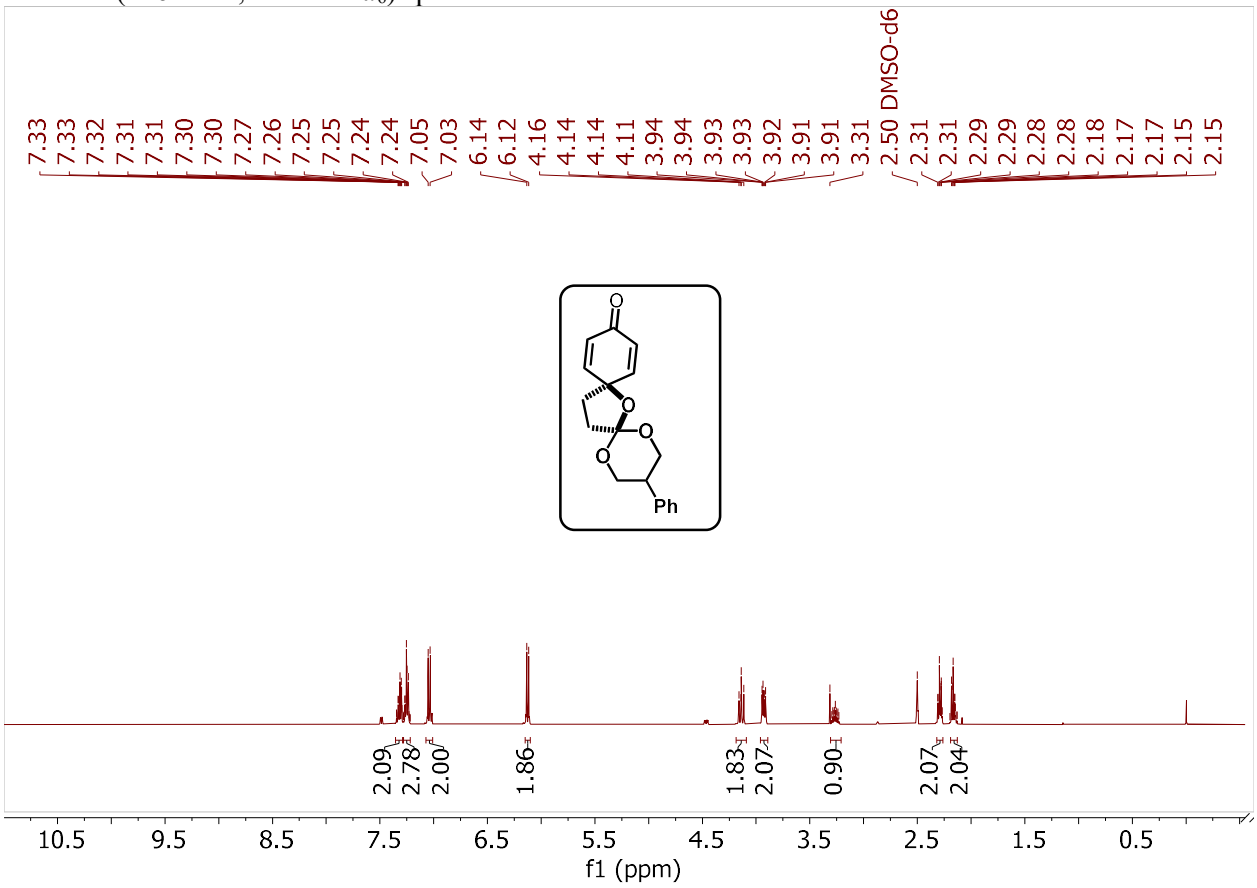
^{1}H NMR (500 MHz, Chloroform-*d*) spectrum of **7a**



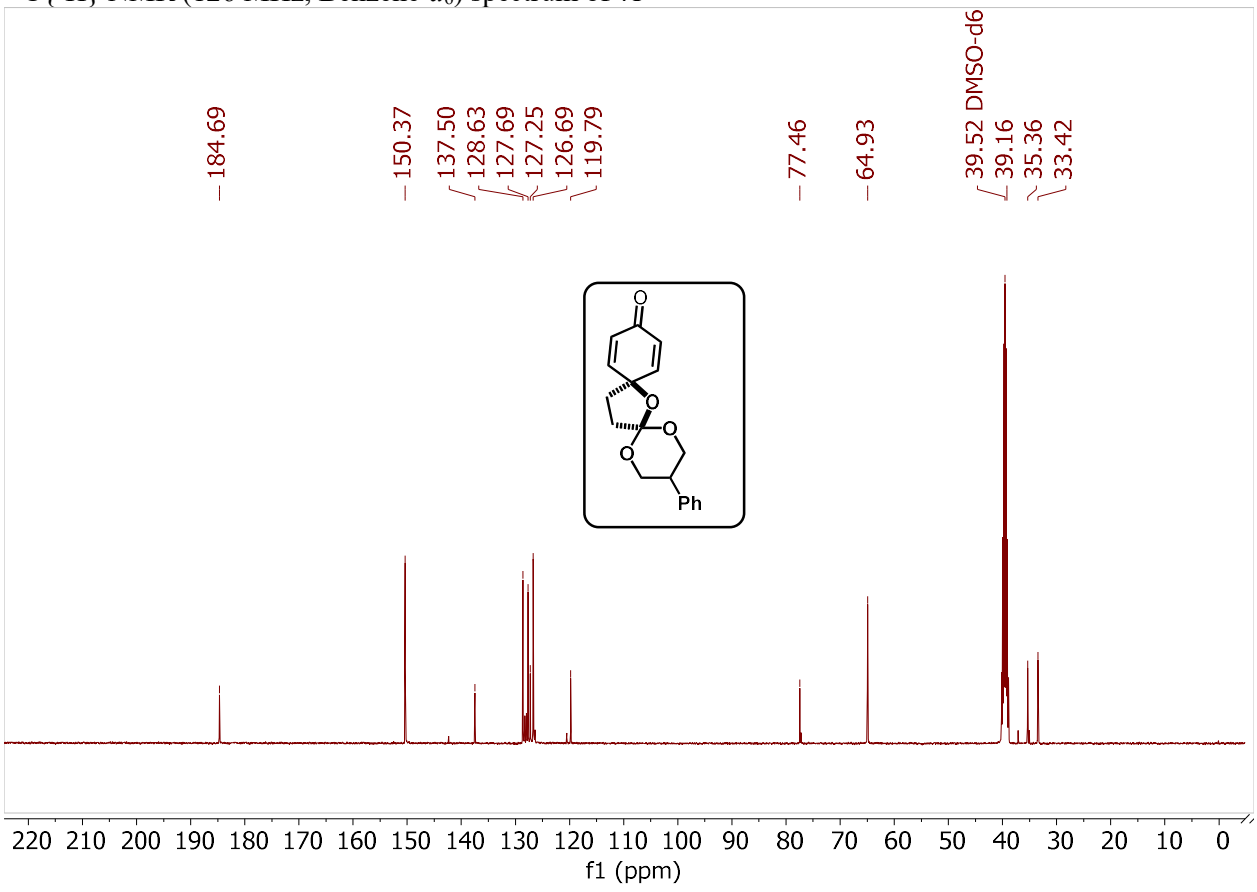
^{13}C{^{1}H} (101 MHz, Chloroform-*d*) spectrum of **7a**



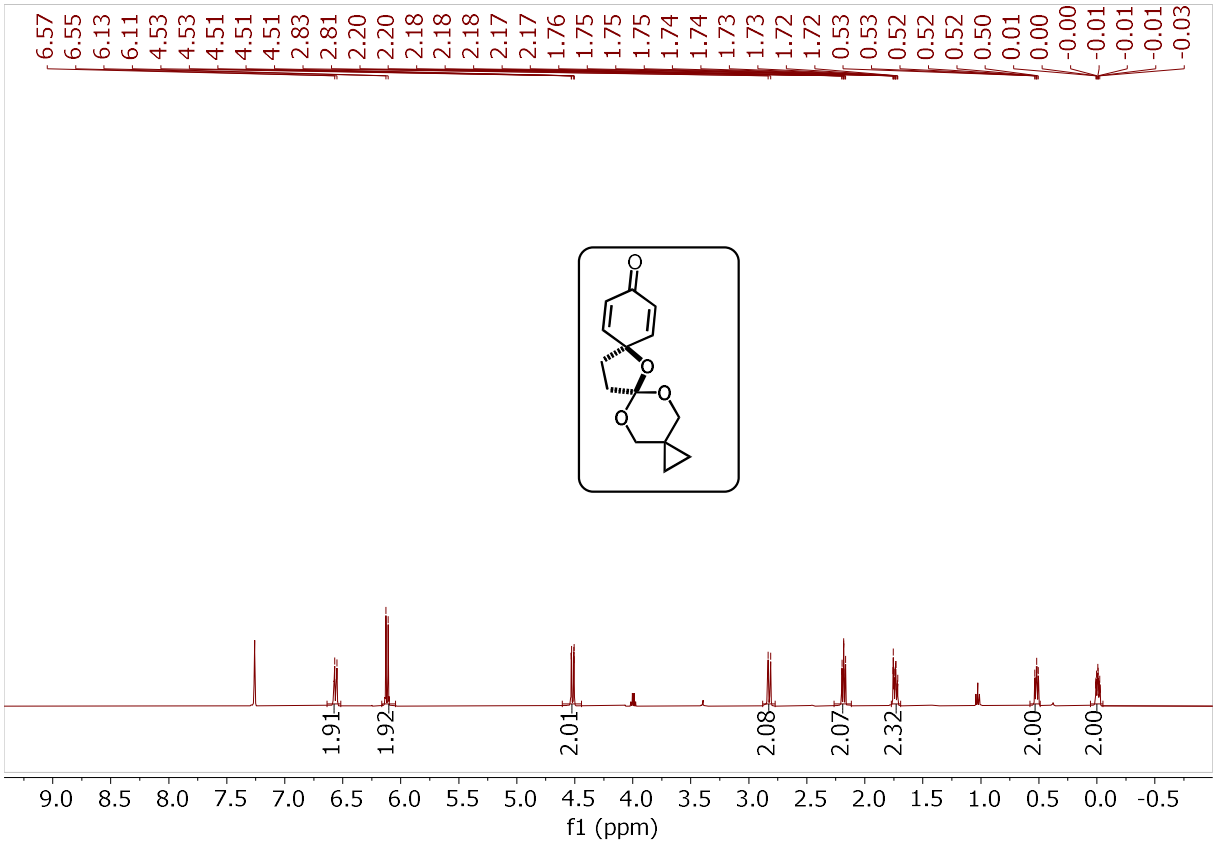
^{1}H NMR (126 MHz, Benzene-d_6) spectrum of **7f**



^{13}C{^{1}H} NMR (126 MHz, Benzene-d_6) spectrum of **7f**



^{1}H NMR (126 MHz, Benzene-d_6) spectrum of **7e**



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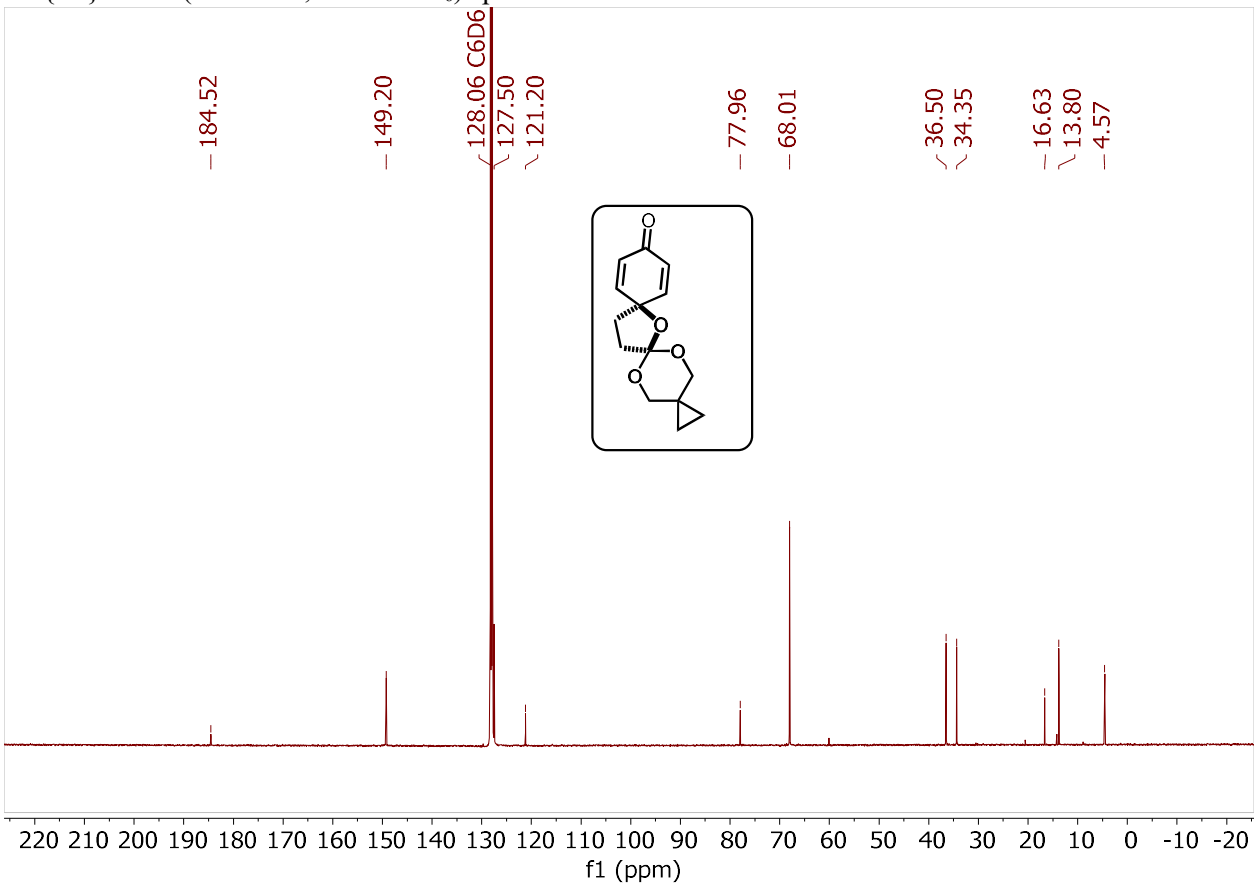
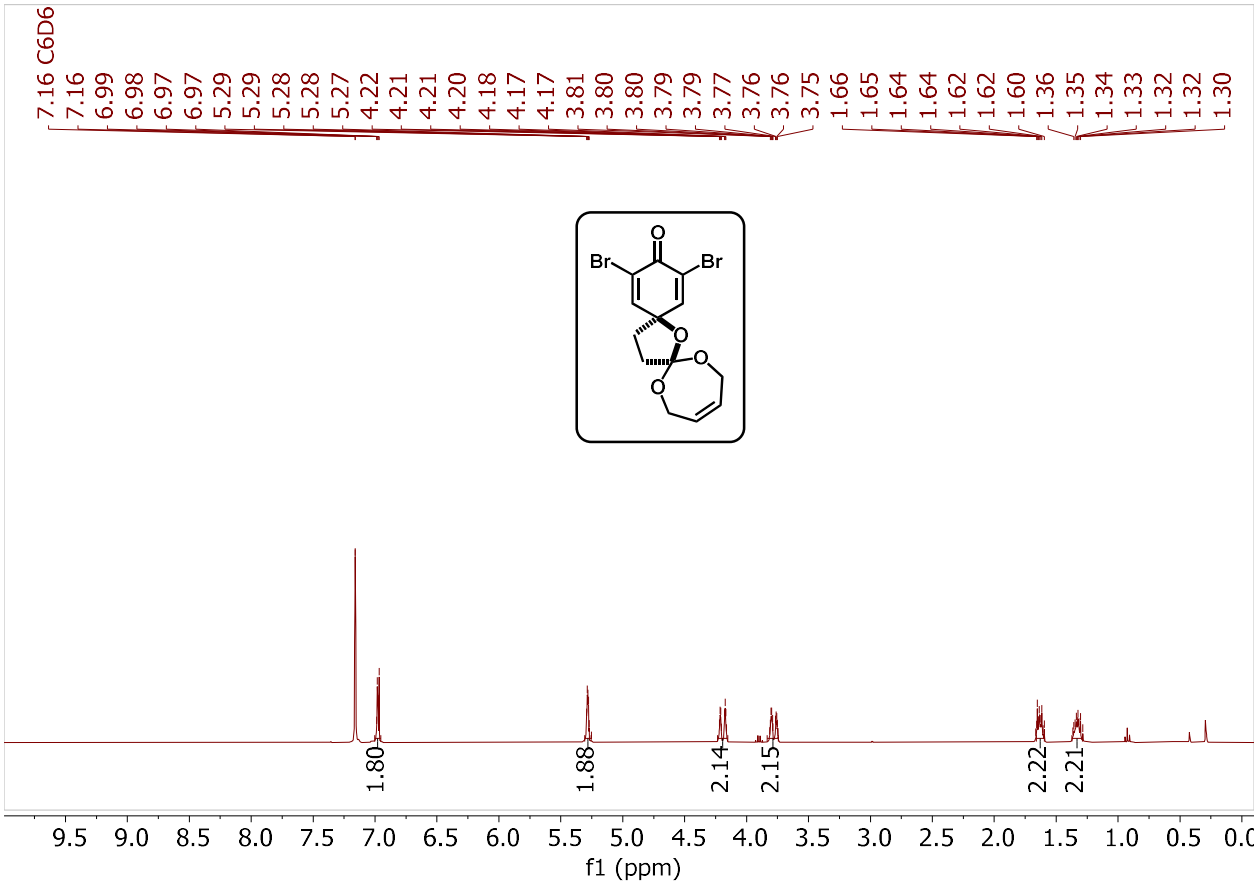
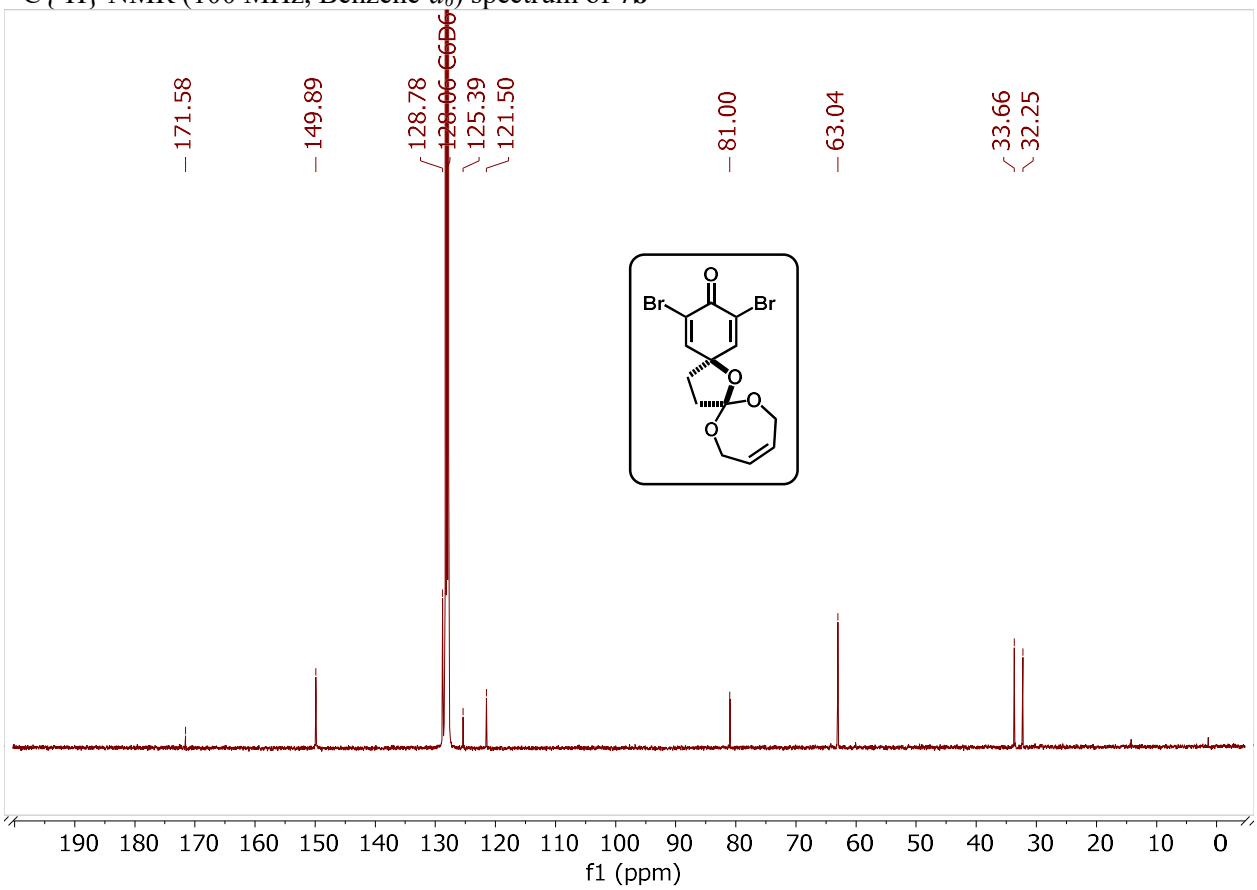


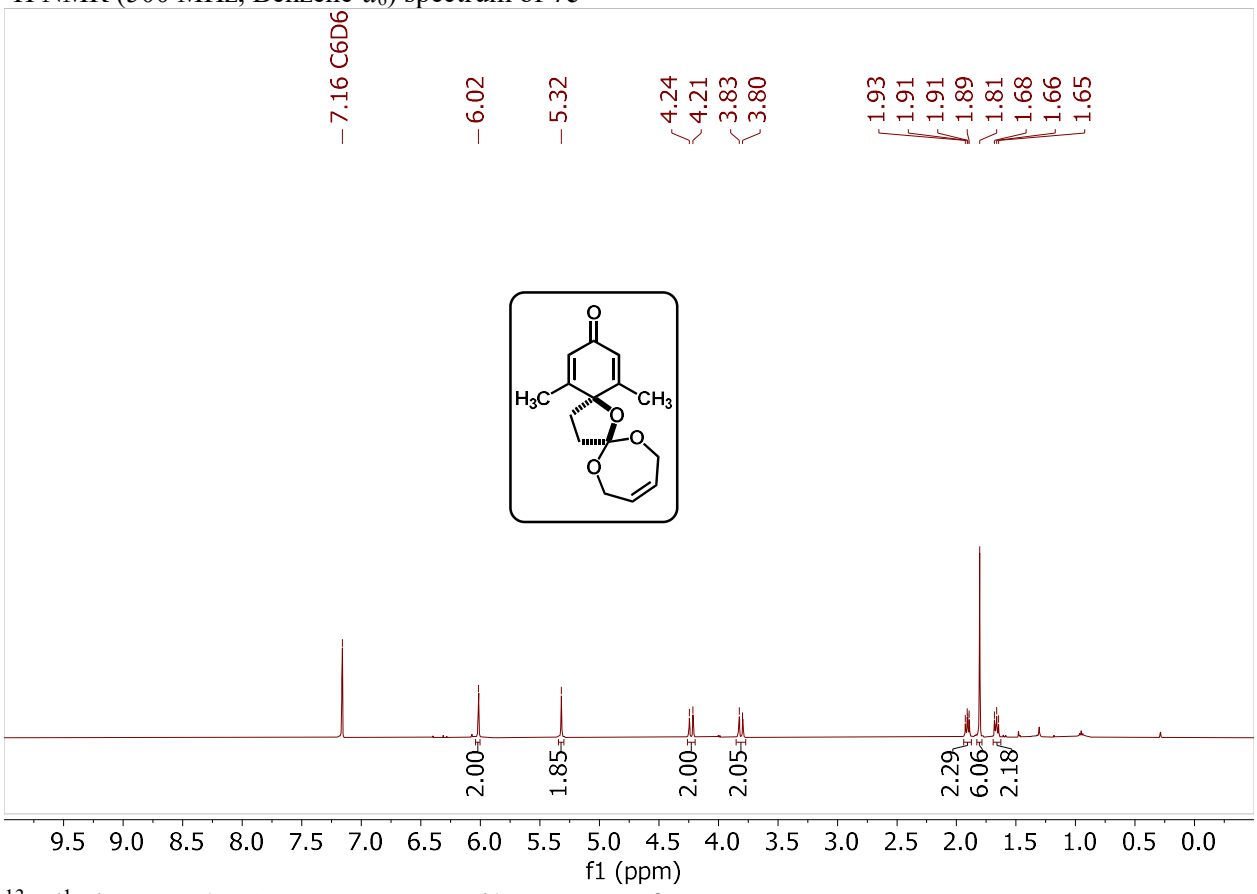
^{1}H NMR (396 MHz, Benzene-d_6) spectrum of **7b**



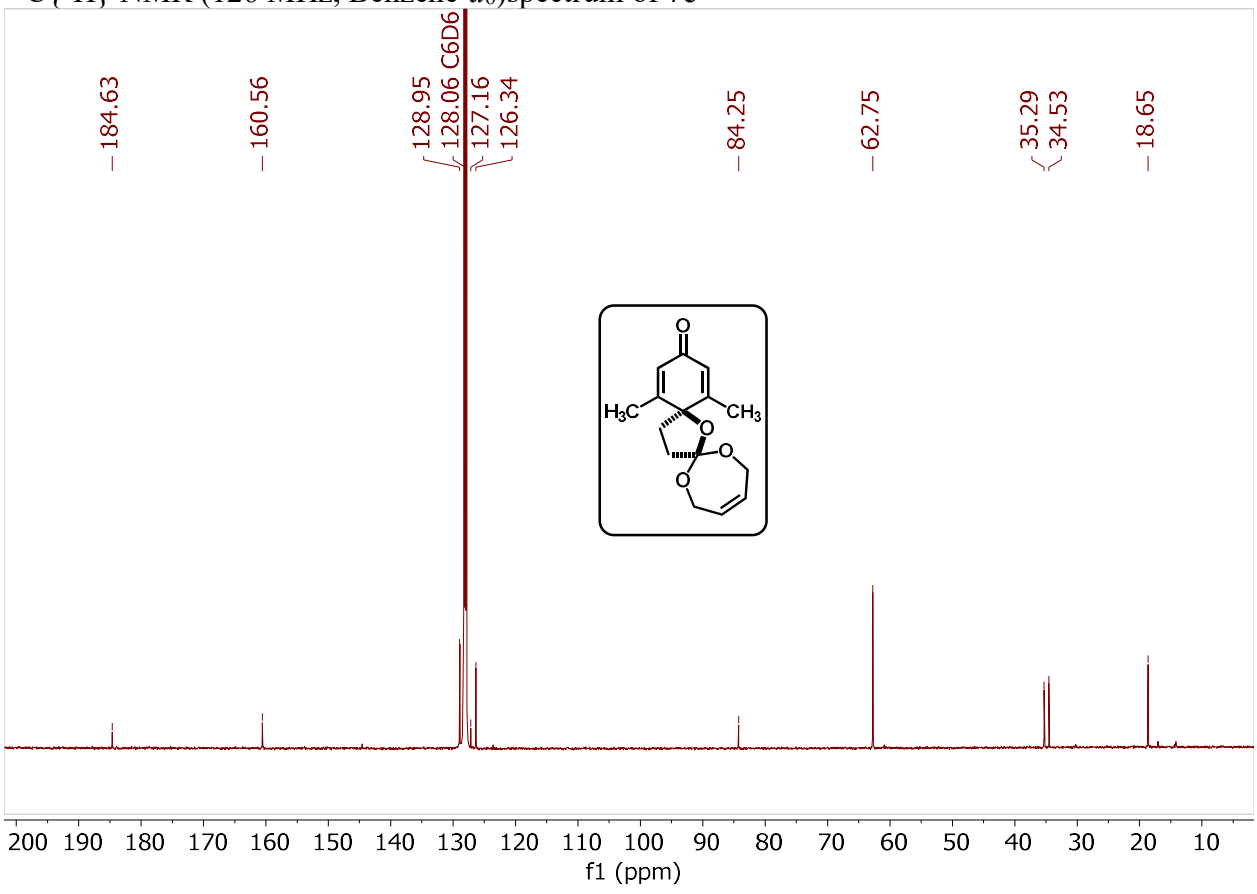
^{13}C{^{1}H} NMR (100 MHz, Benzene-d_6) spectrum of **7b**



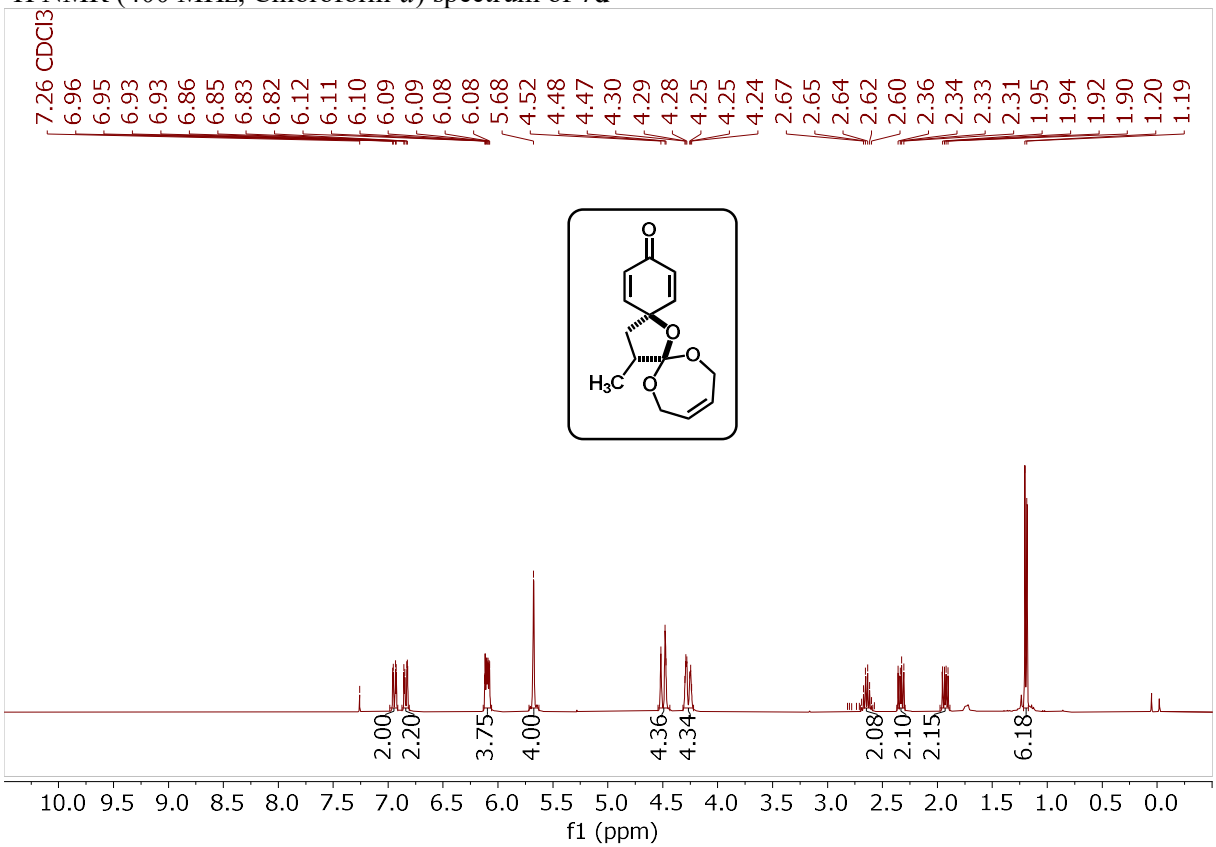
^{1}H NMR (500 MHz, Benzene-d_6) spectrum of **7c**



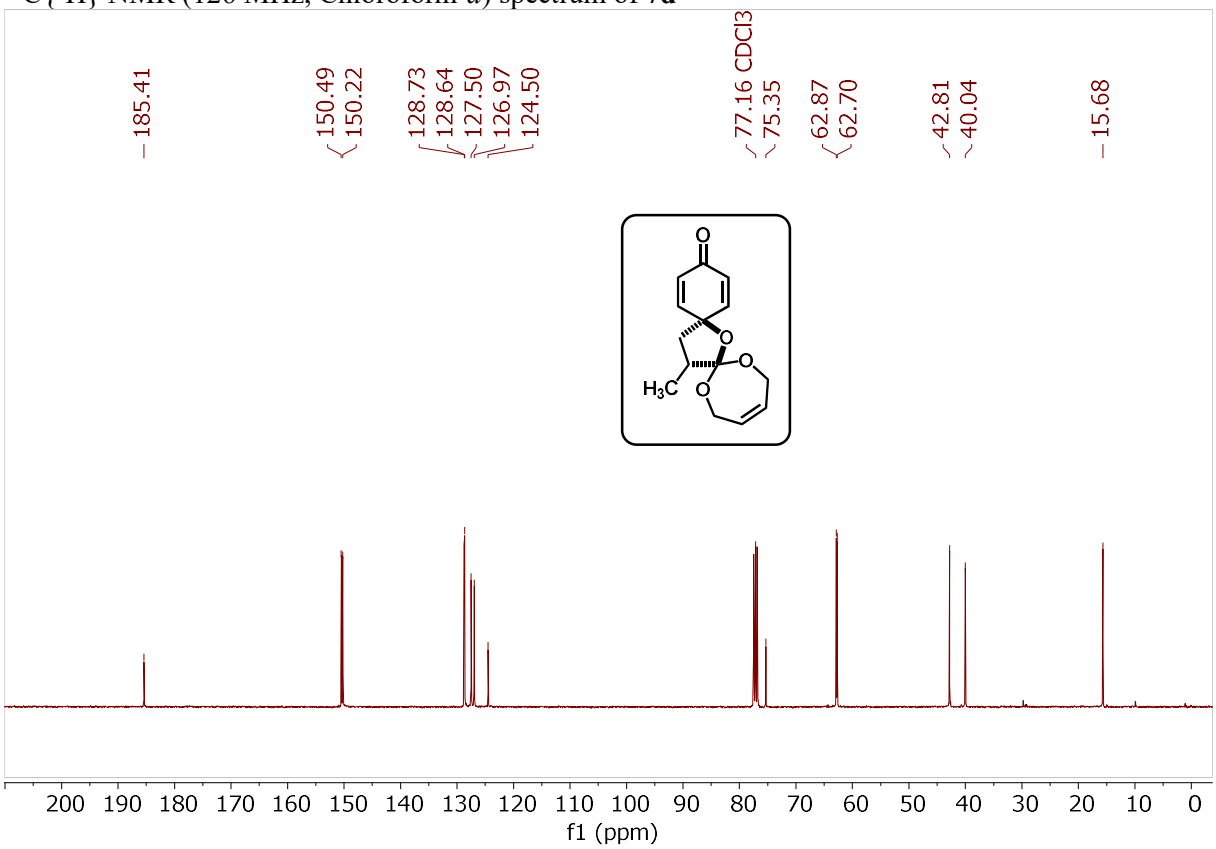
^{13}C{^{1}H} NMR (126 MHz, Benzene-d_6)spectrum of **7c**



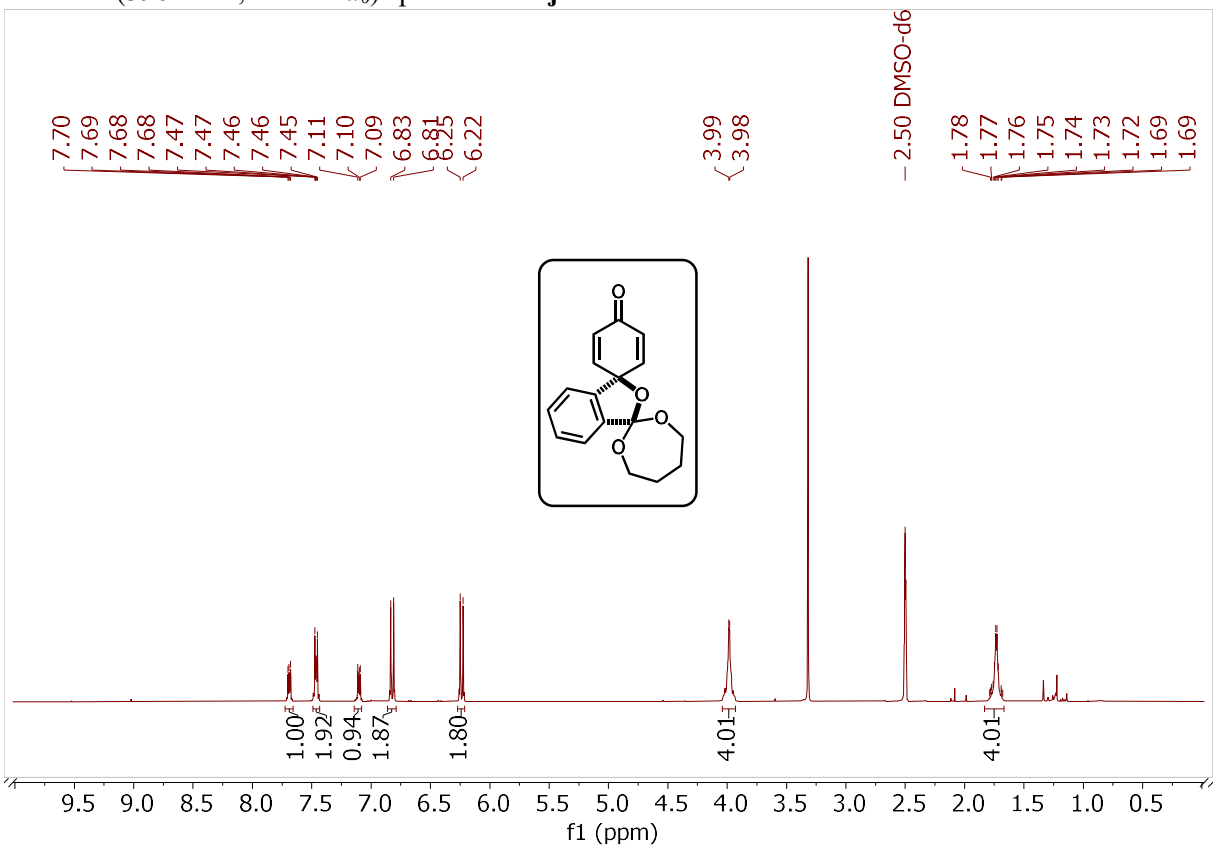
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of **7d**



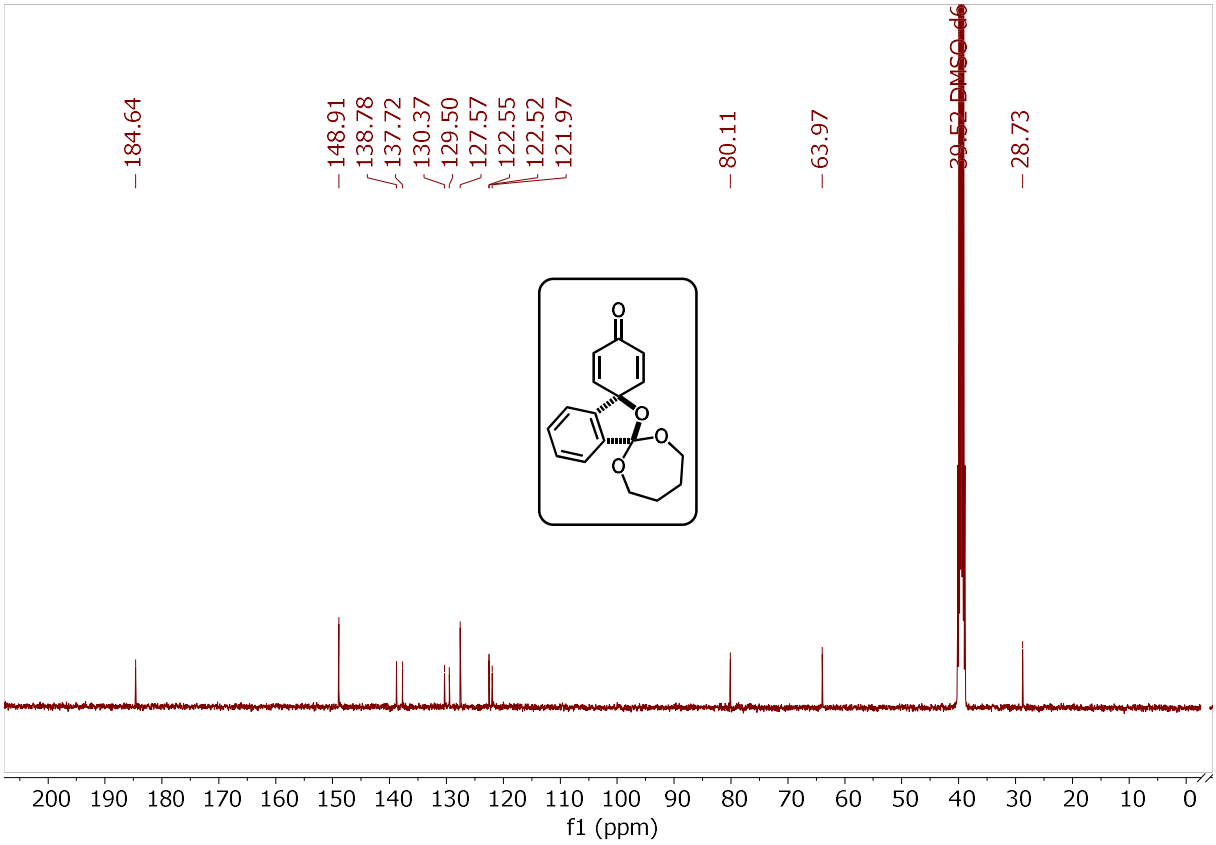
^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) spectrum of **7d**



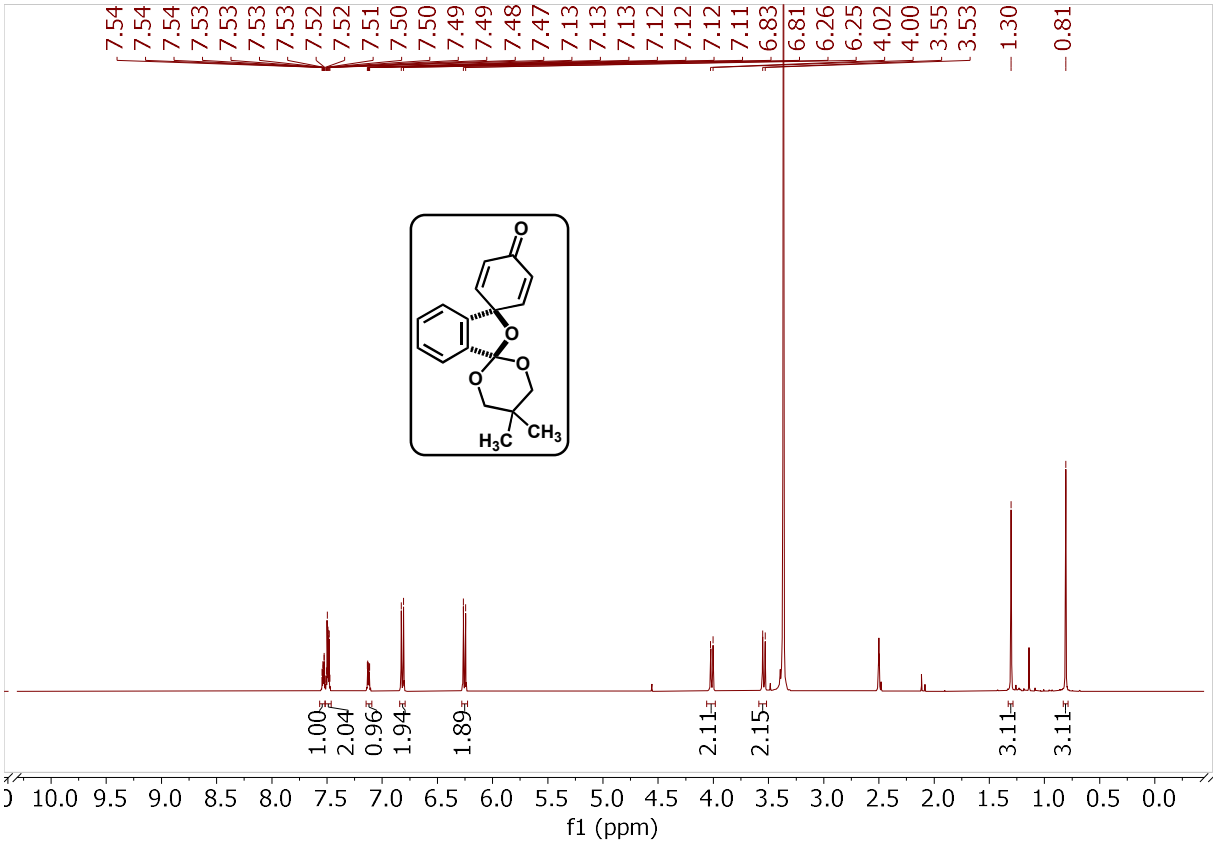
^{1}H NMR (396 MHz, DMSO-d_6) spectrum of **7j**



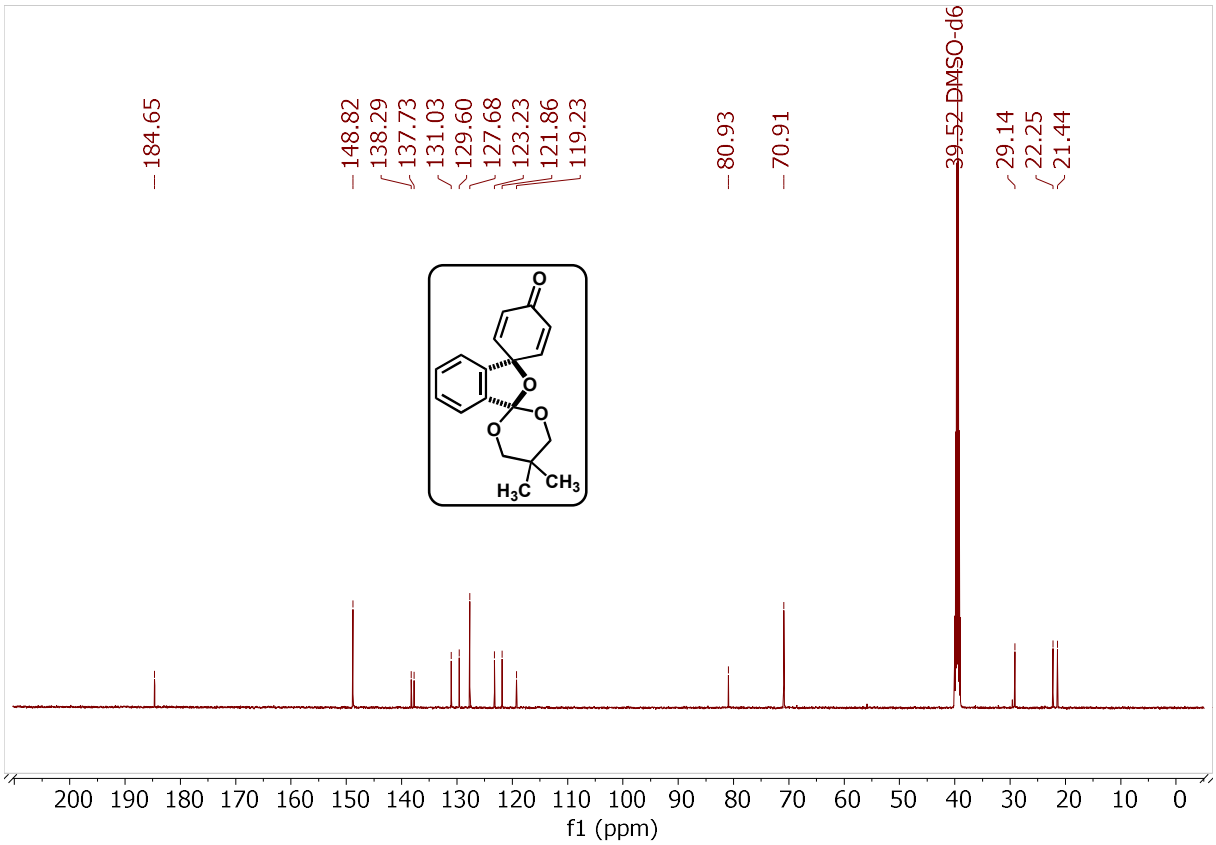
^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) spectrum of **7j**



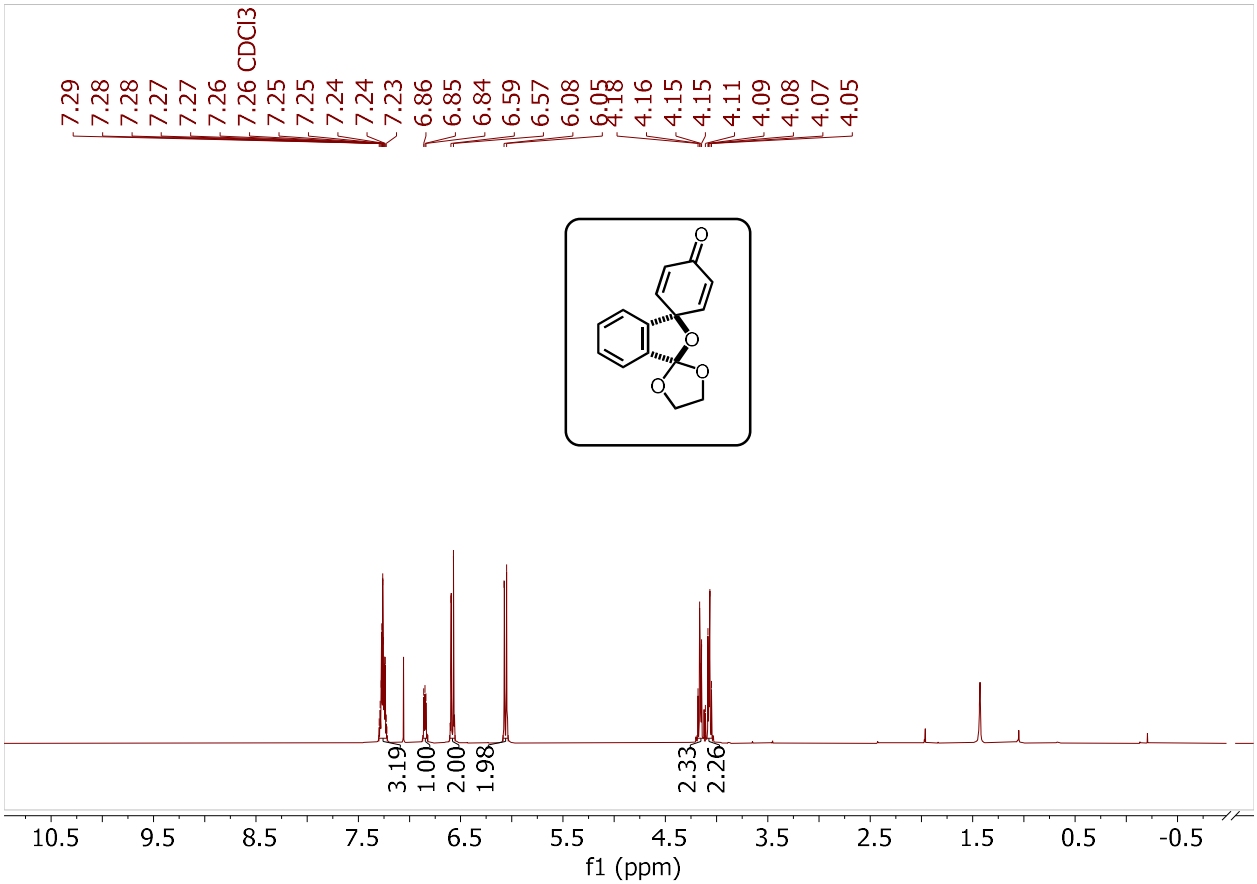
^{1}H NMR (500 MHz, Chloroform-*d*) spectrum of **7g**



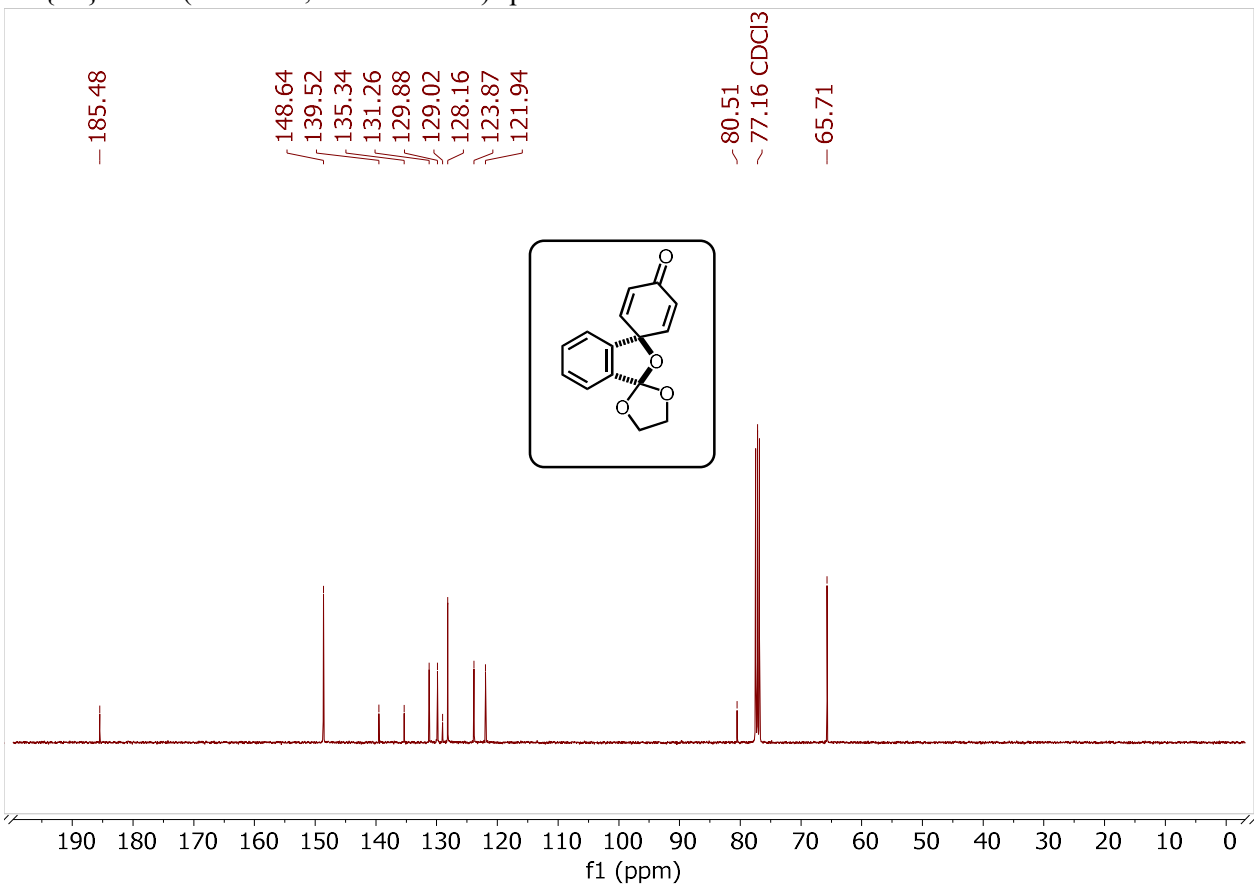
^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) spectrum of **7g**



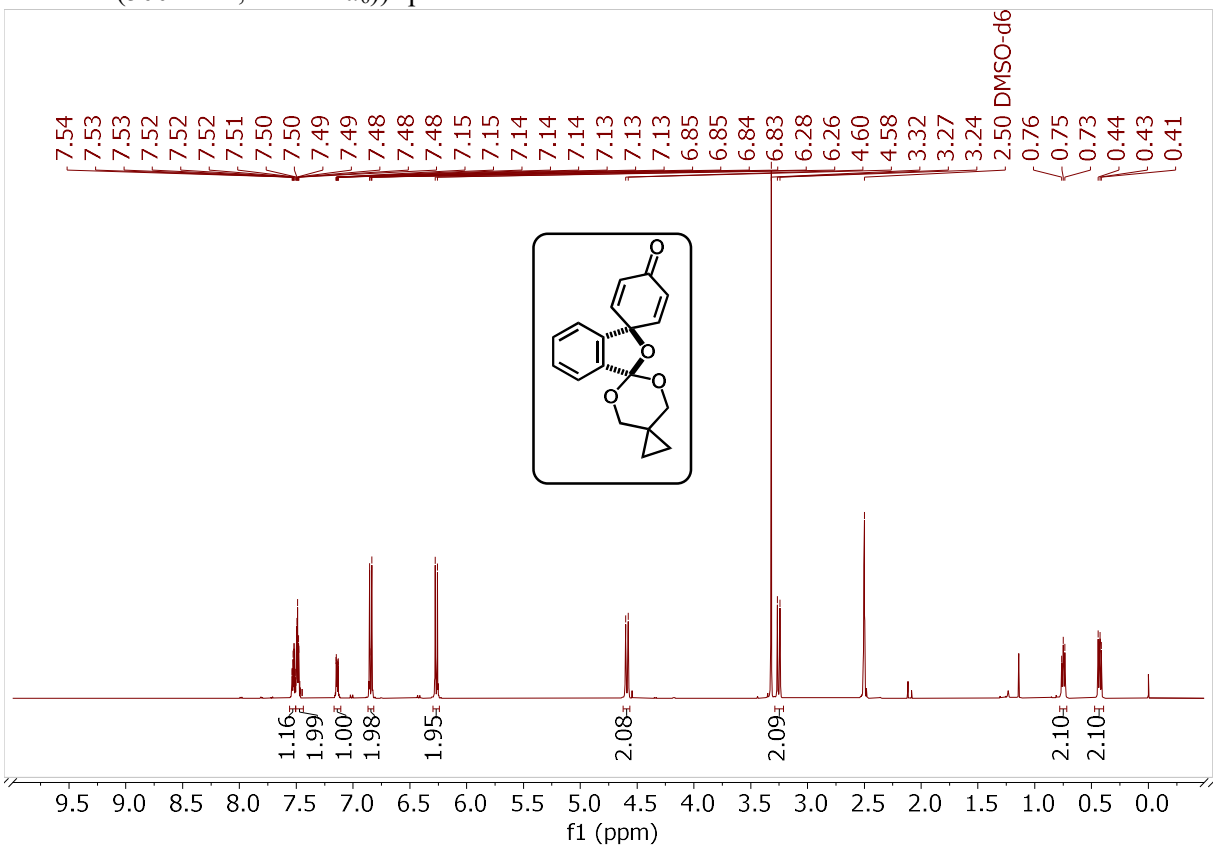
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of **7h**



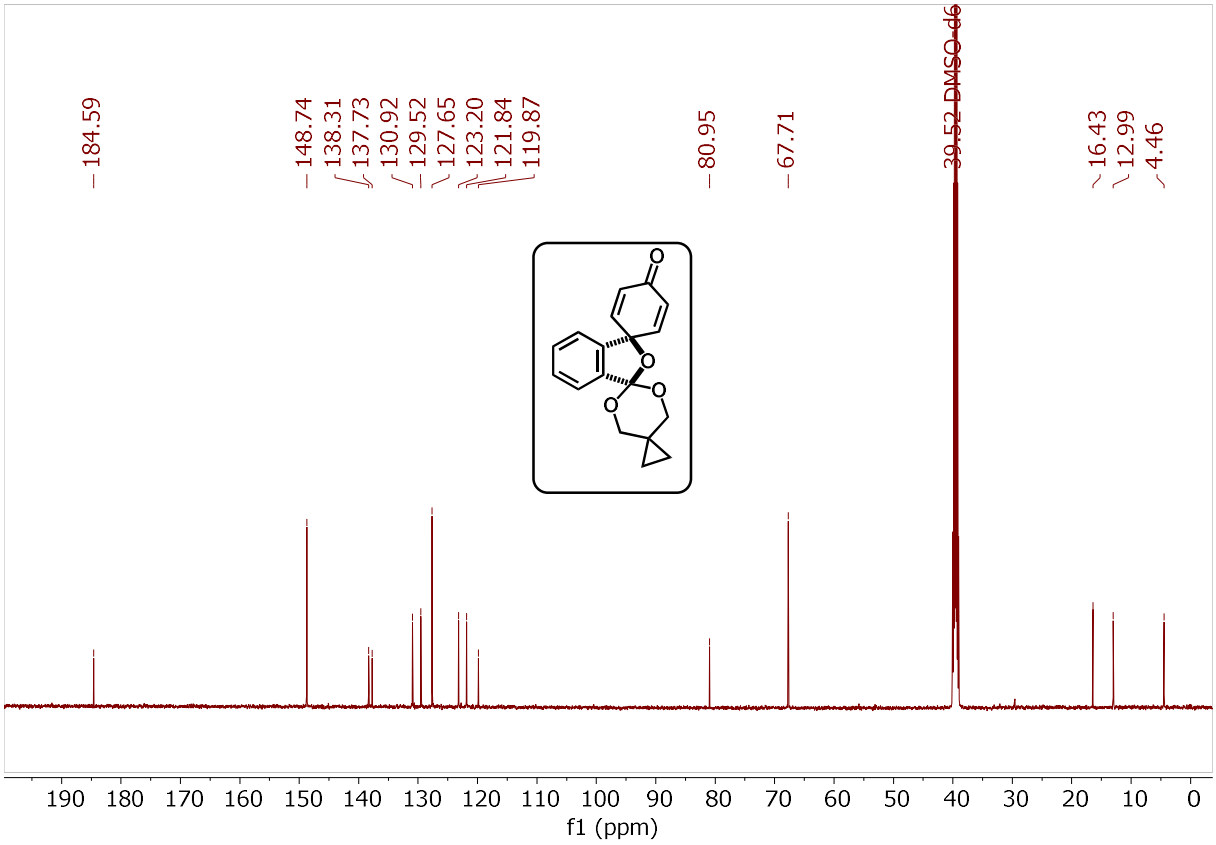
^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) spectrum of **7h**



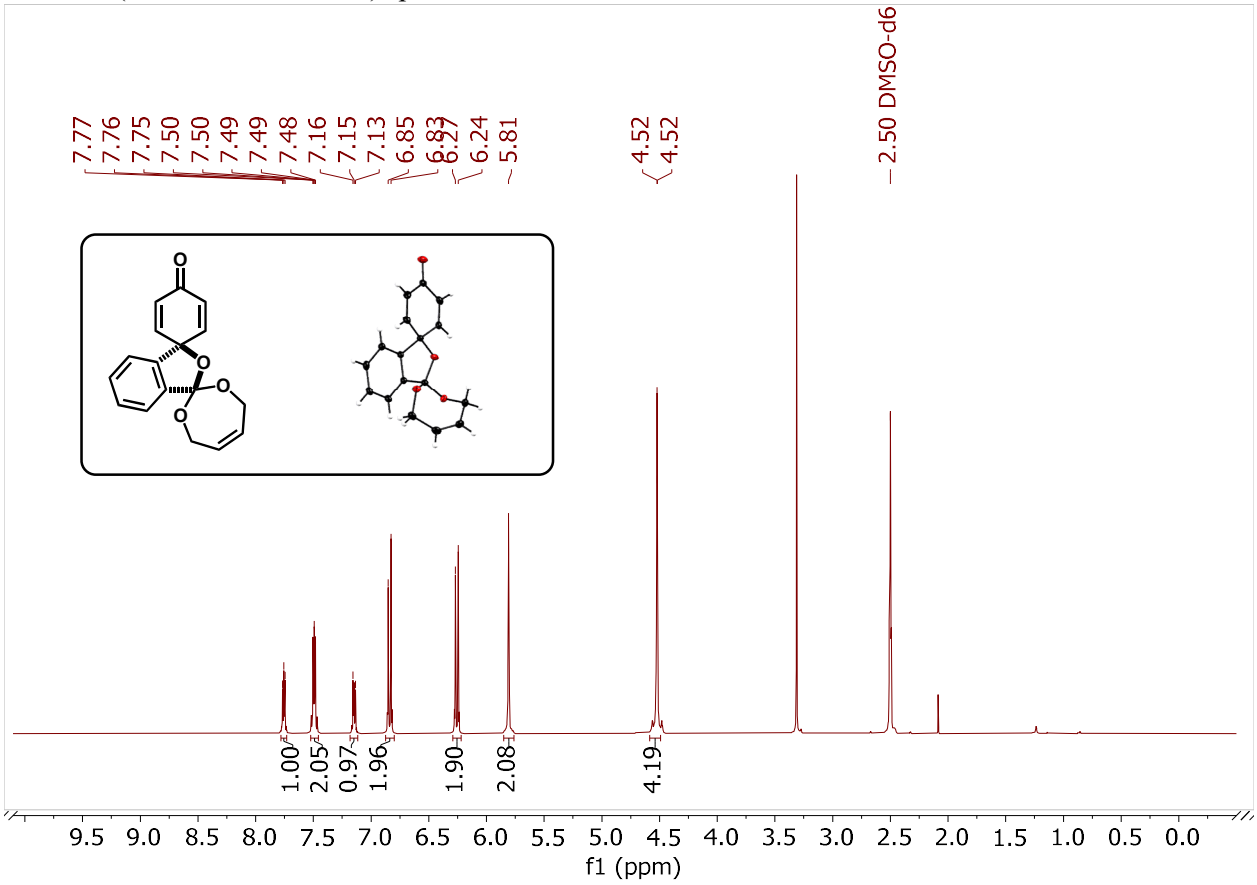
^{1}H NMR (500 MHz, DMSO-d_6)) spectrum of **7i**



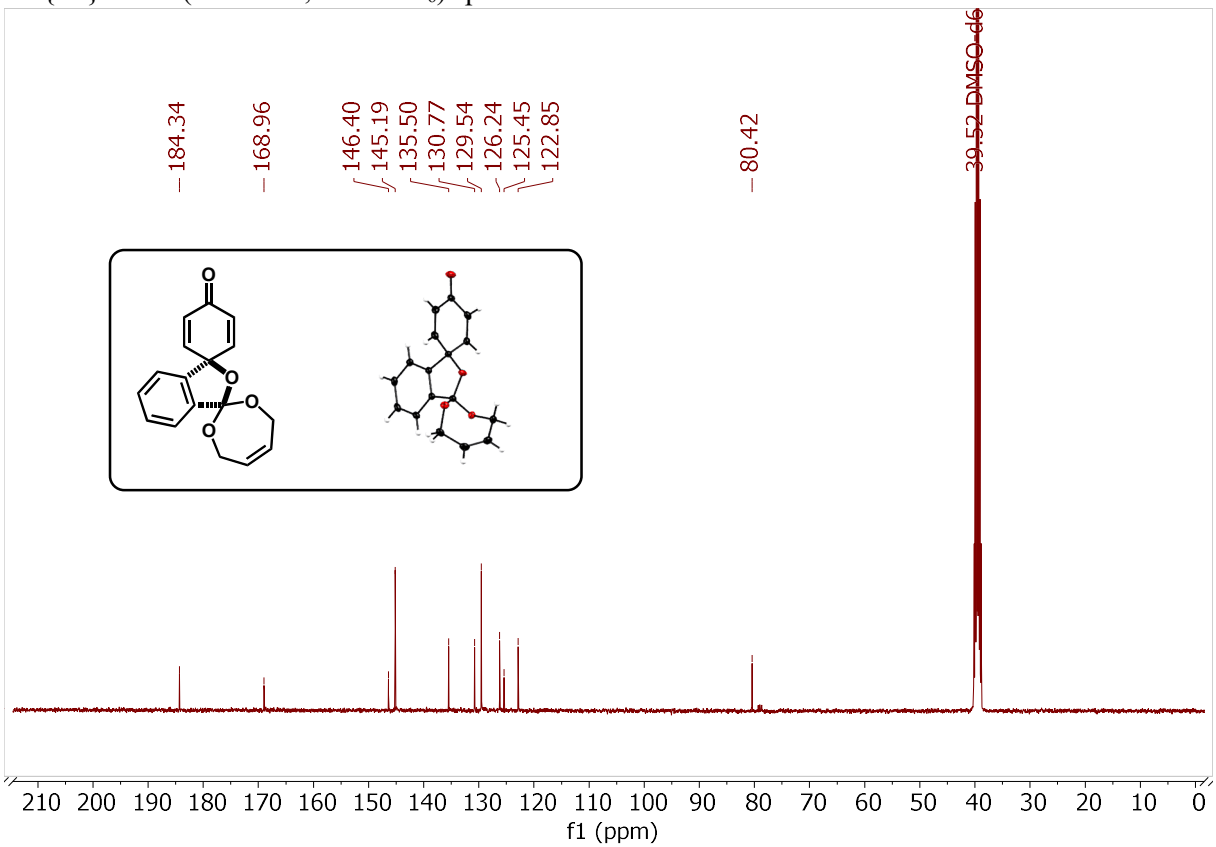
^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6)) spectrum of **7i**



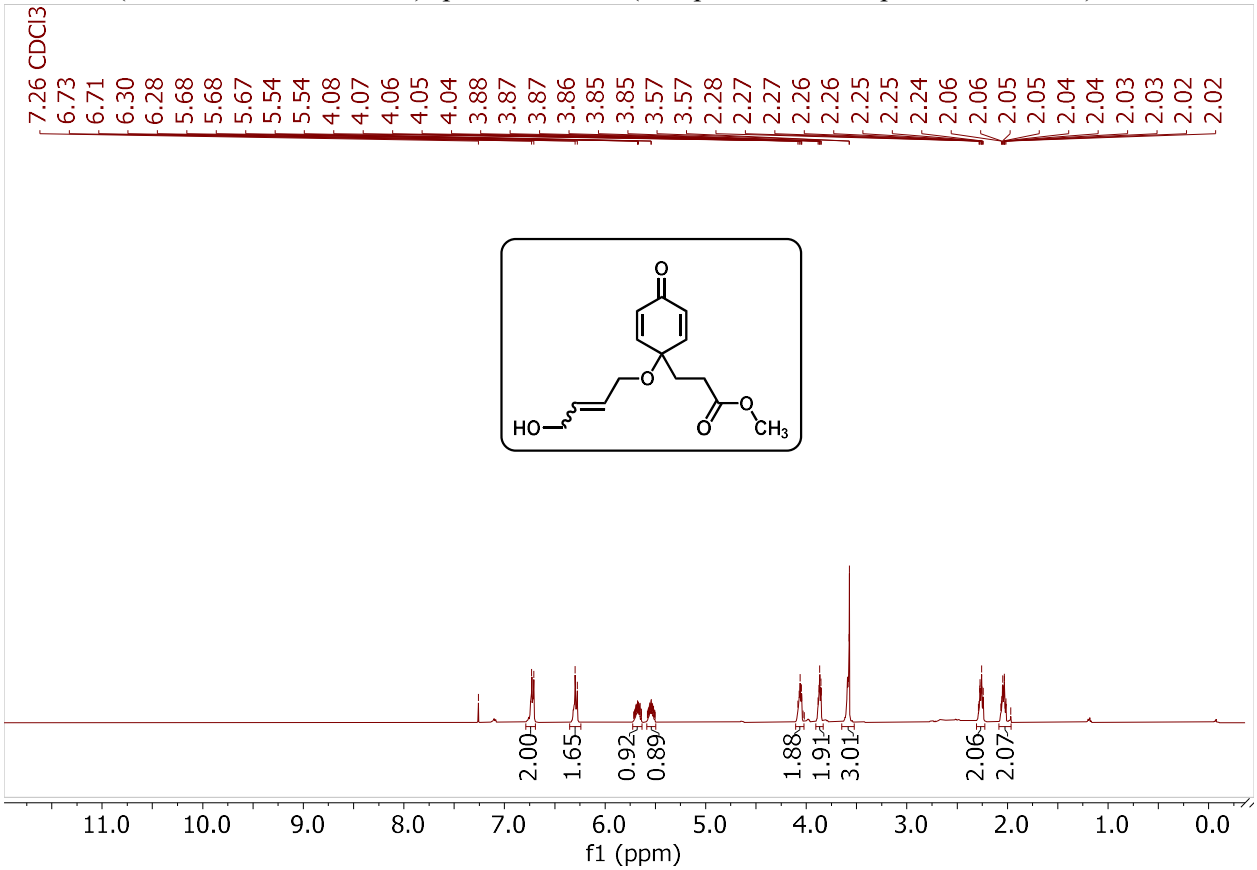
^{1}H NMR (396 MHz, DMSO-d_6) spectrum of **7k**



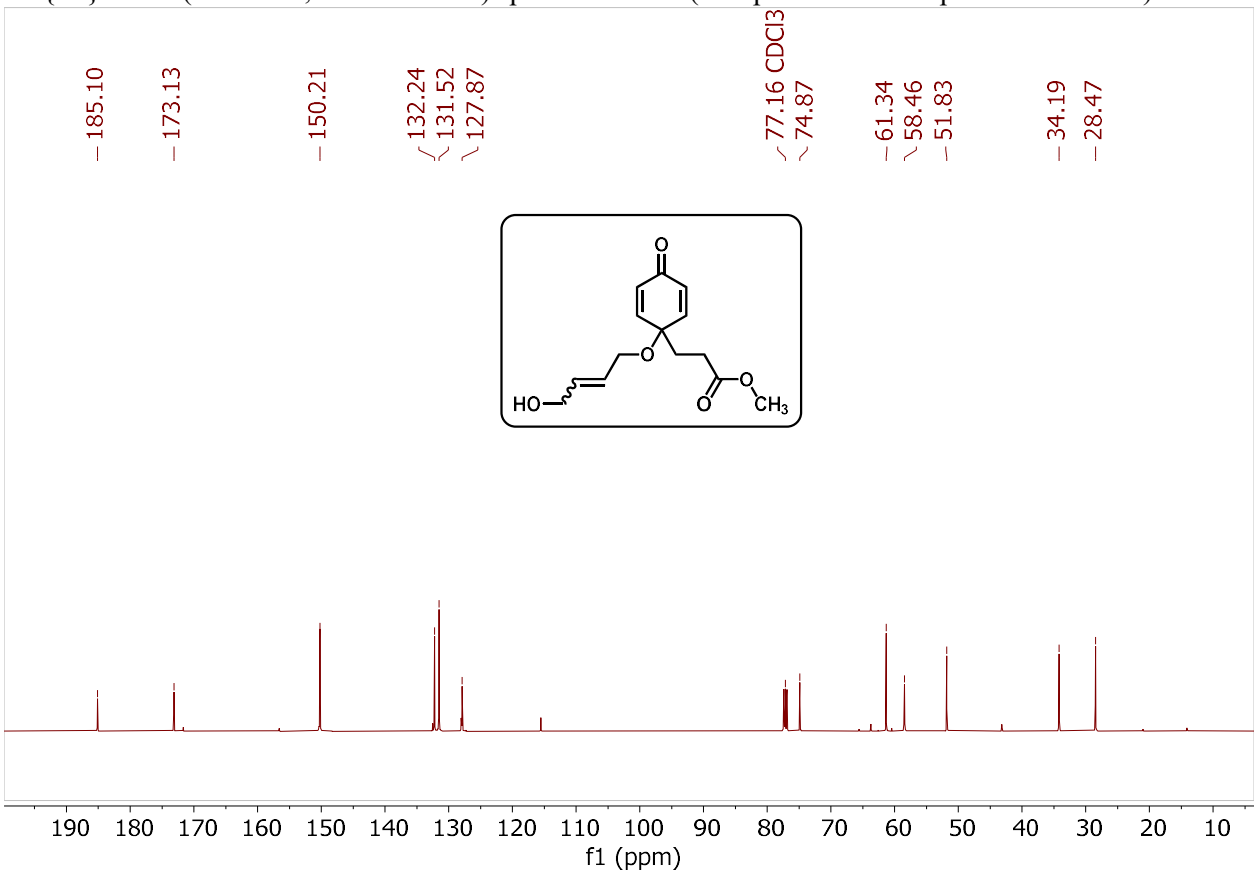
^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) spectrum of **7k**



^{1}H NMR (500 MHz, Chloroform-*d*) spectrum of **7a2** (side product of the optimized reaction)

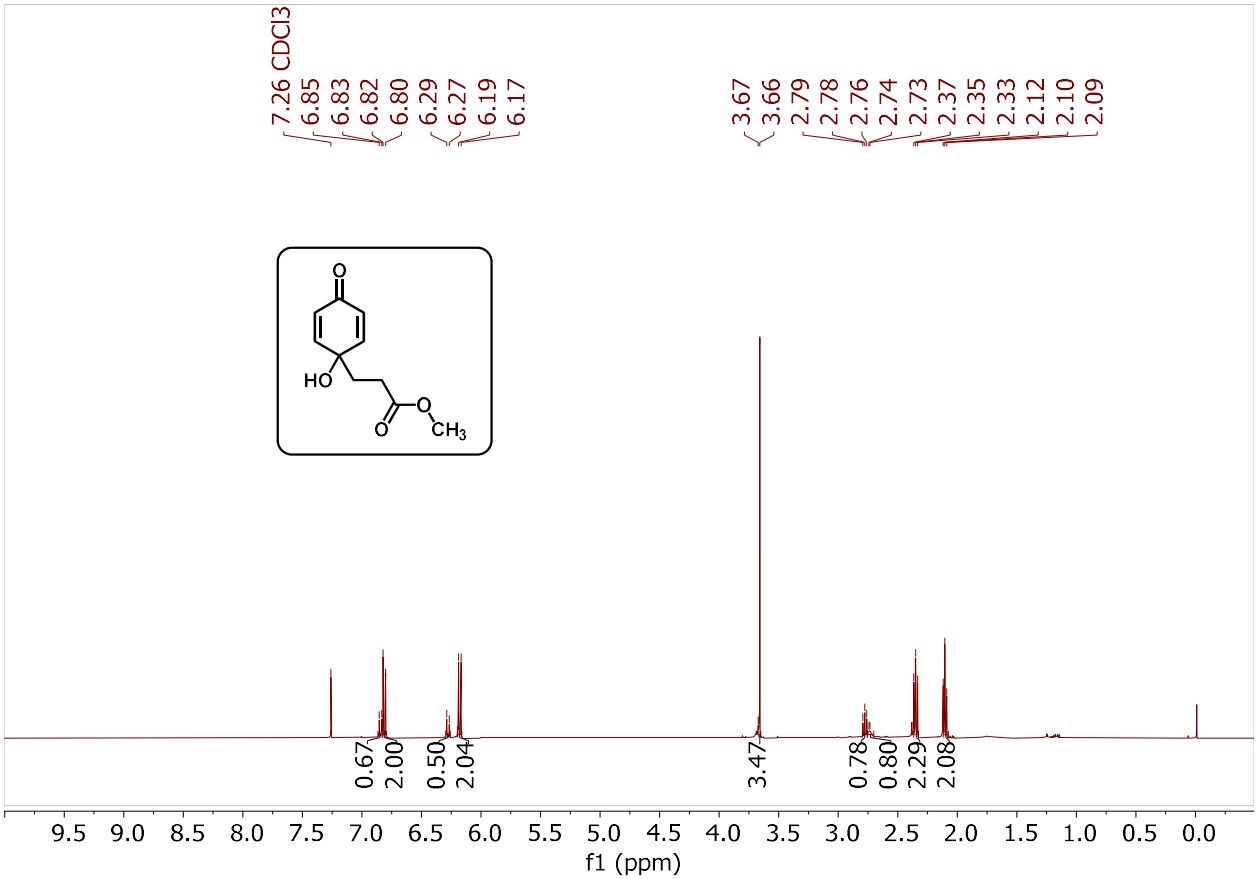


^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) spectrum of **7a2**(side product of the optimised reaction)

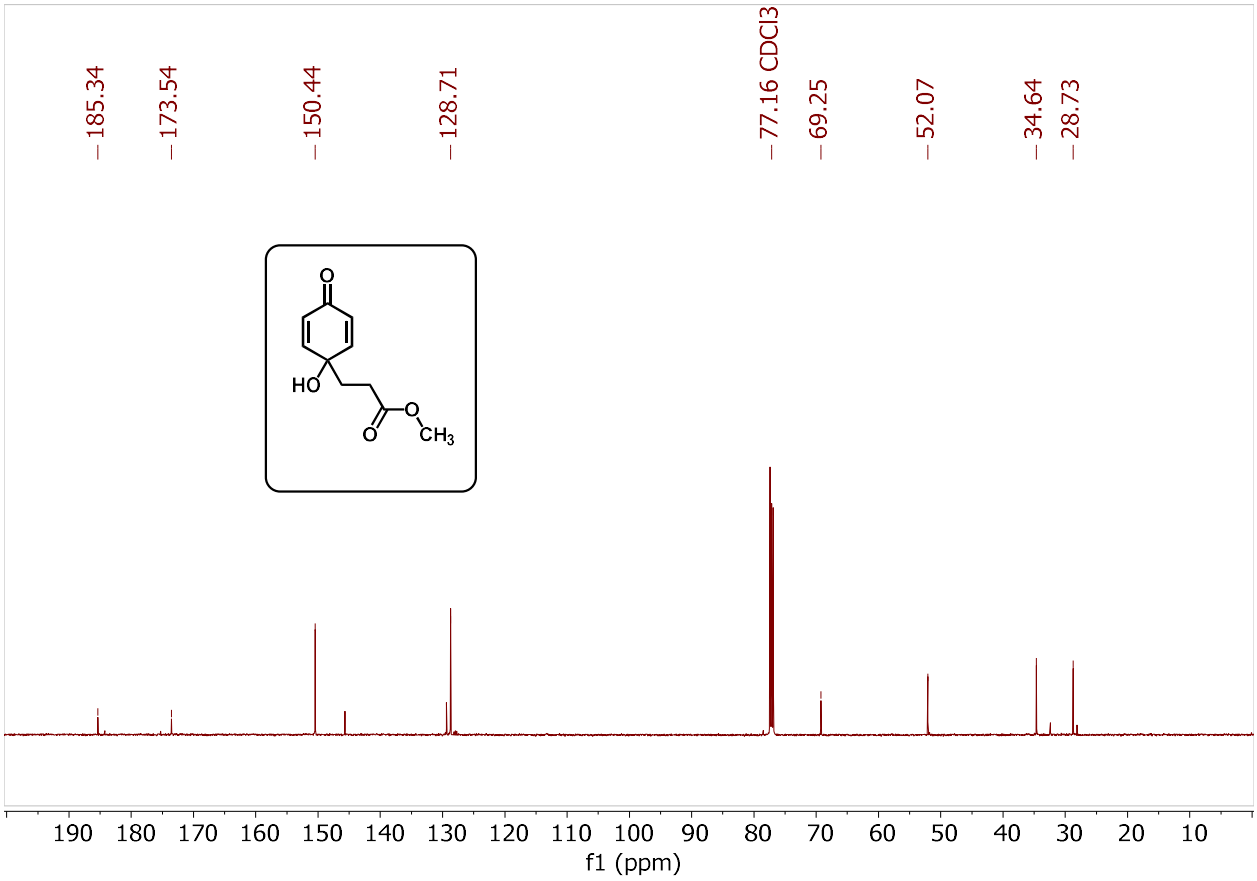


^{1}H NMR (500 MHz, Chloroform-*d*) spectrum of **7a1**

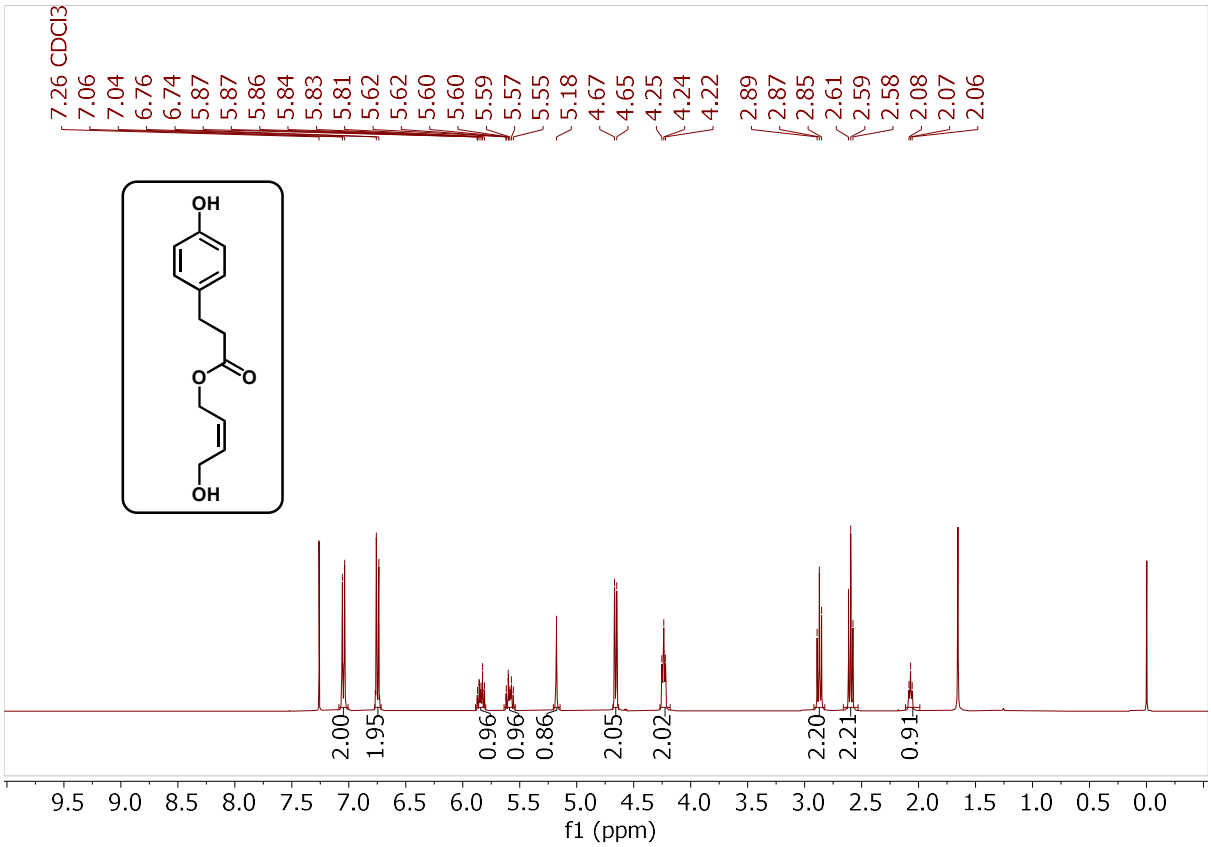
(side product of the optimized reaction)



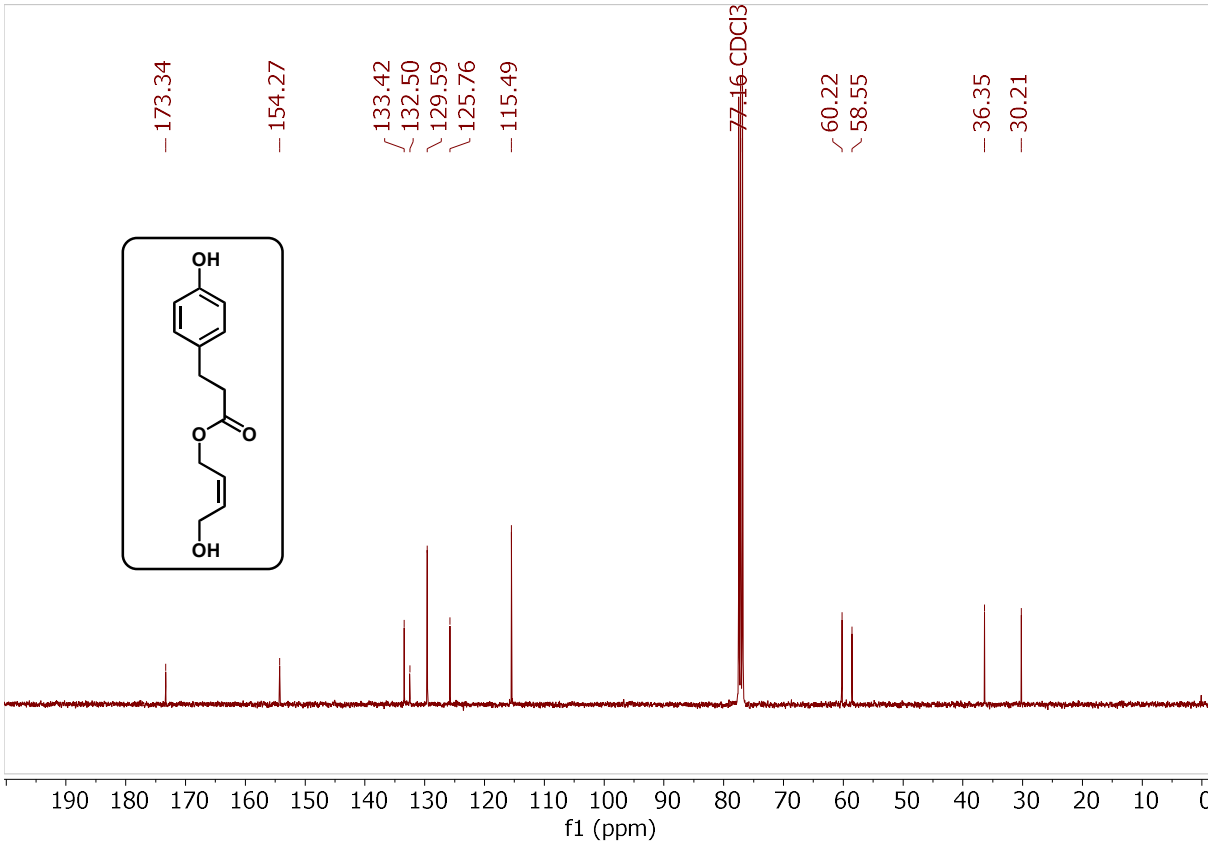
^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) spectrum of **7a1** (side product of the optimized reaction)



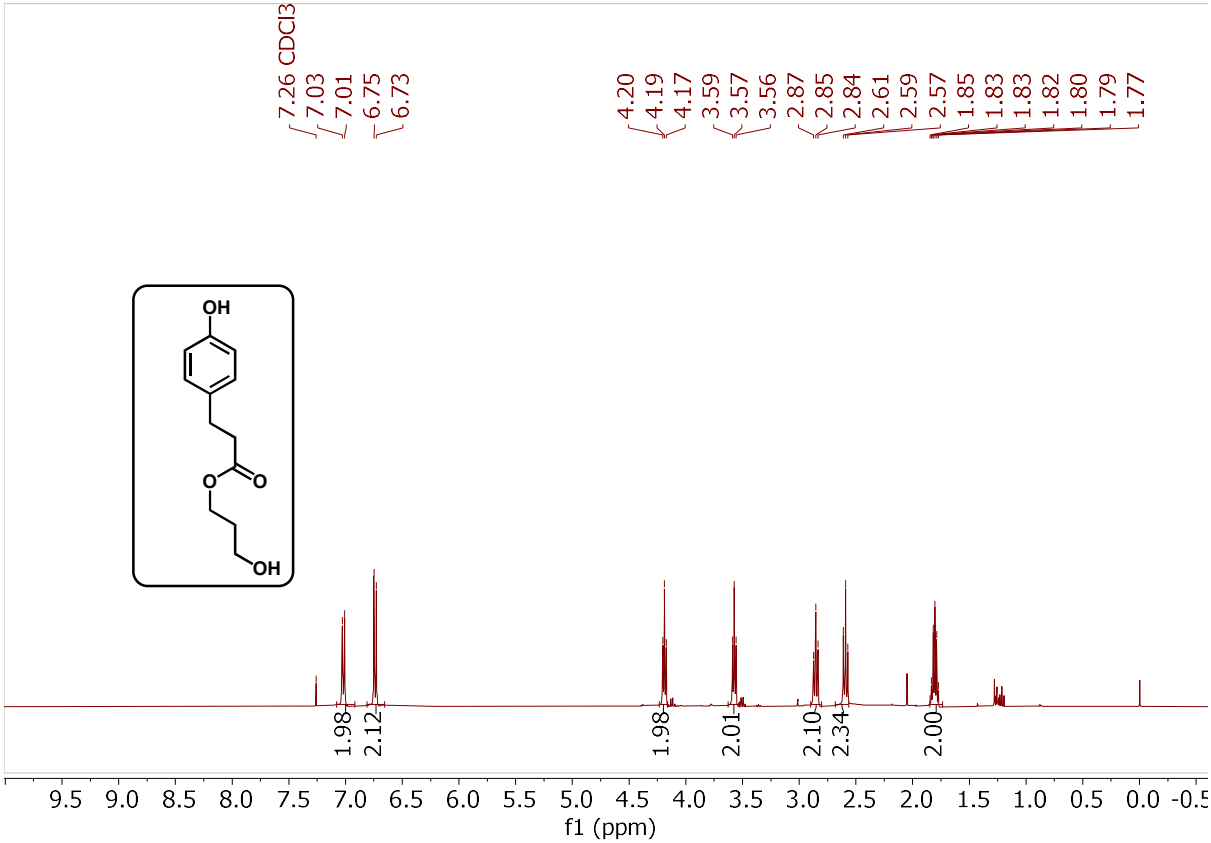
^{1}H NMR (500 MHz, Chloroform-*d*) spectrum of **6a**



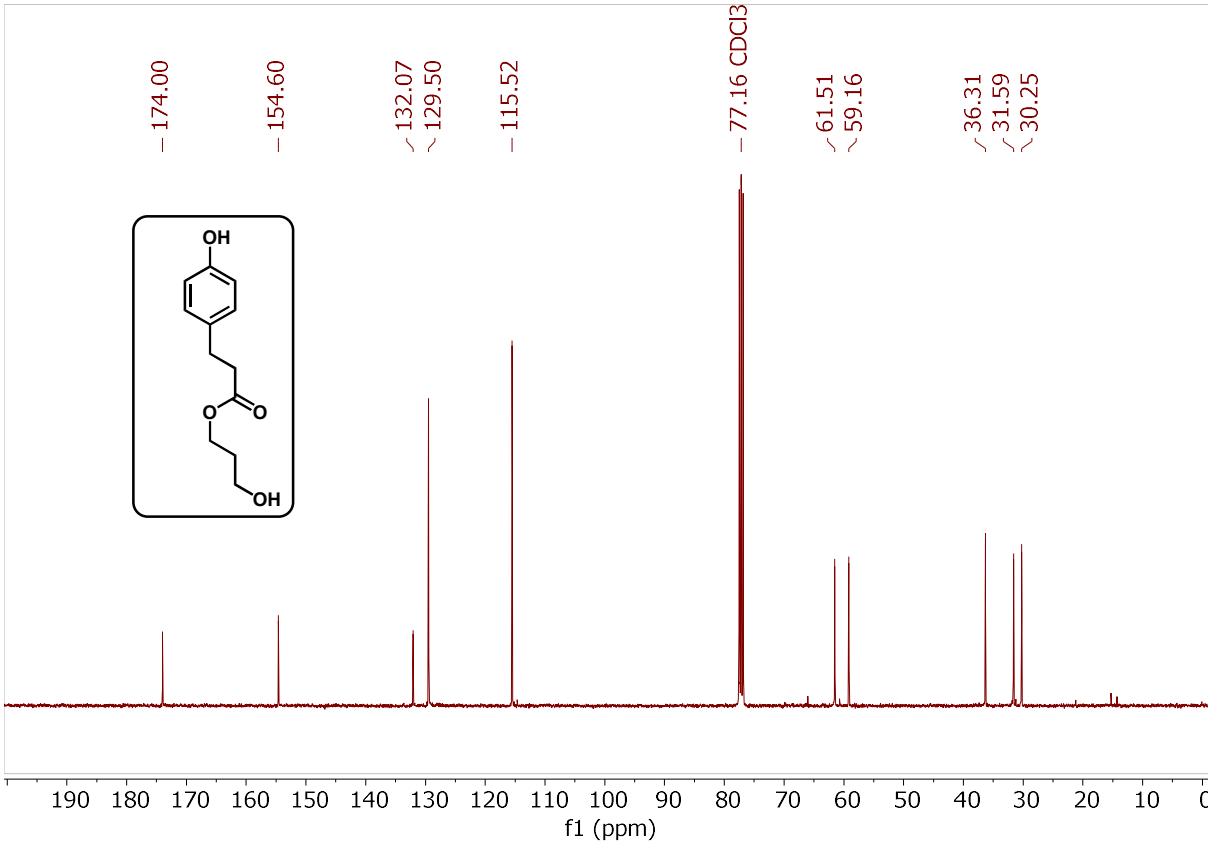
^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) spectrum of **6a**



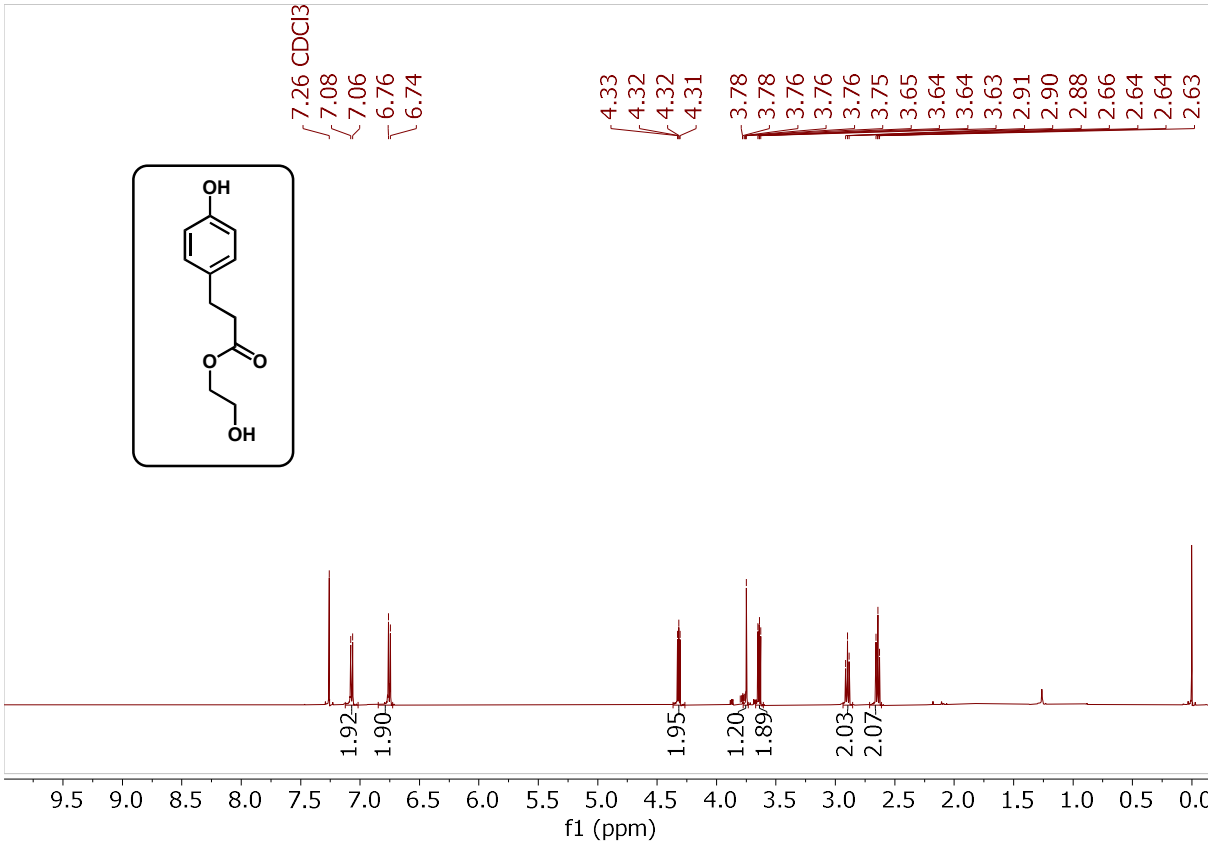
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of **6o**



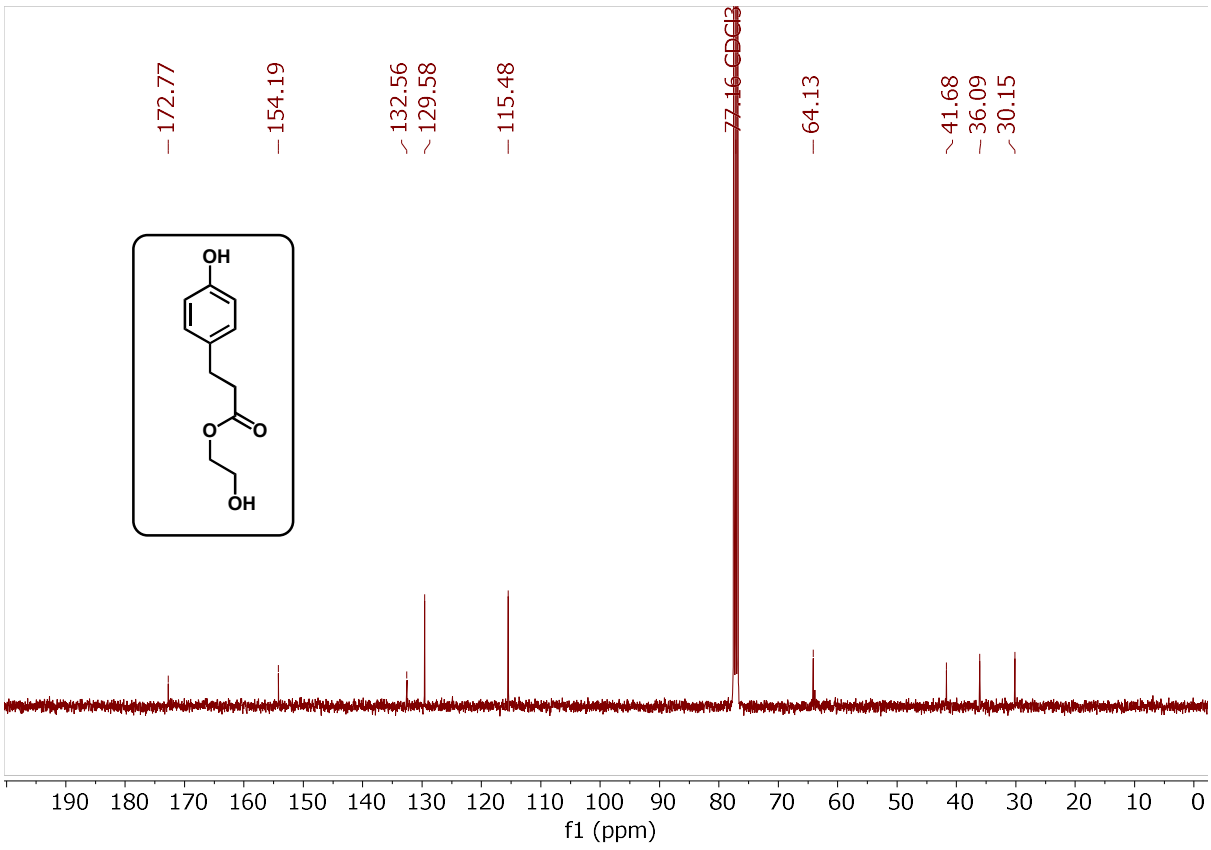
^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) spectrum of **6o**



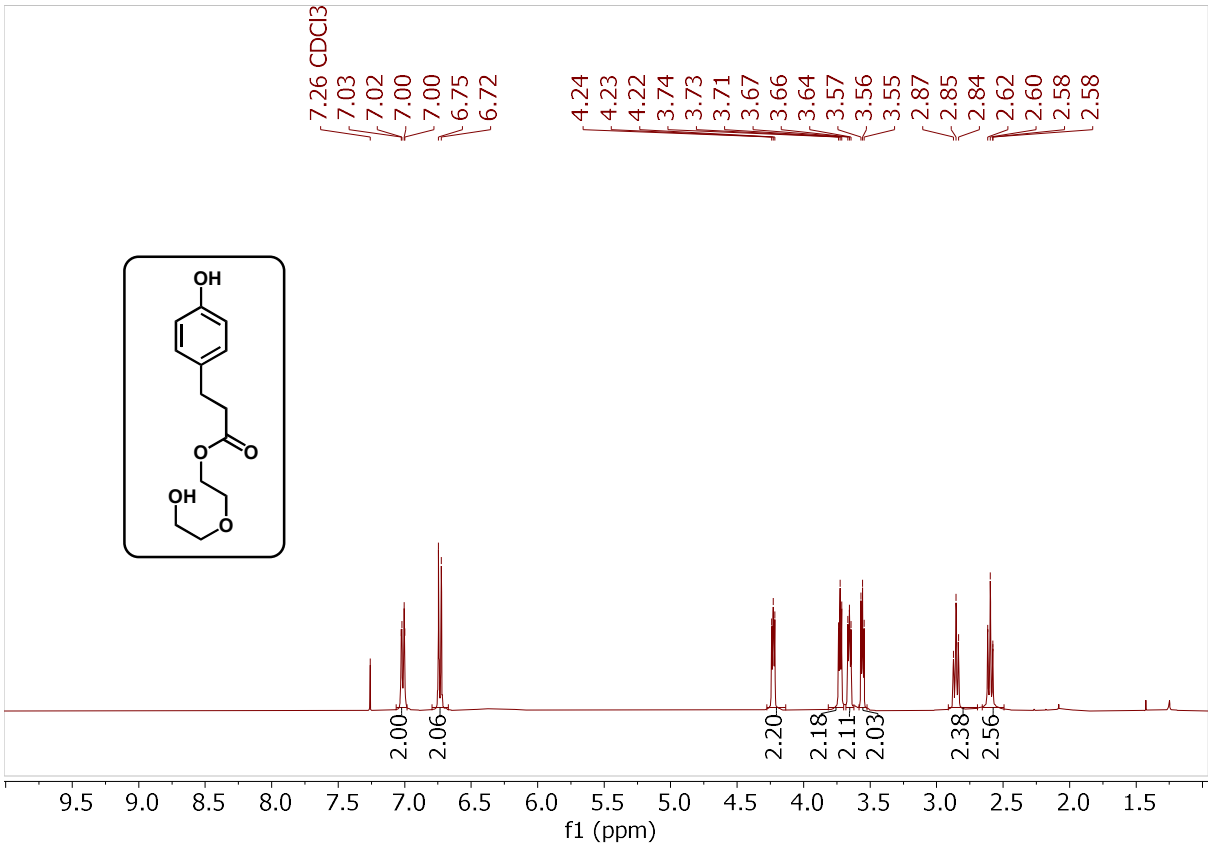
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of **6p**



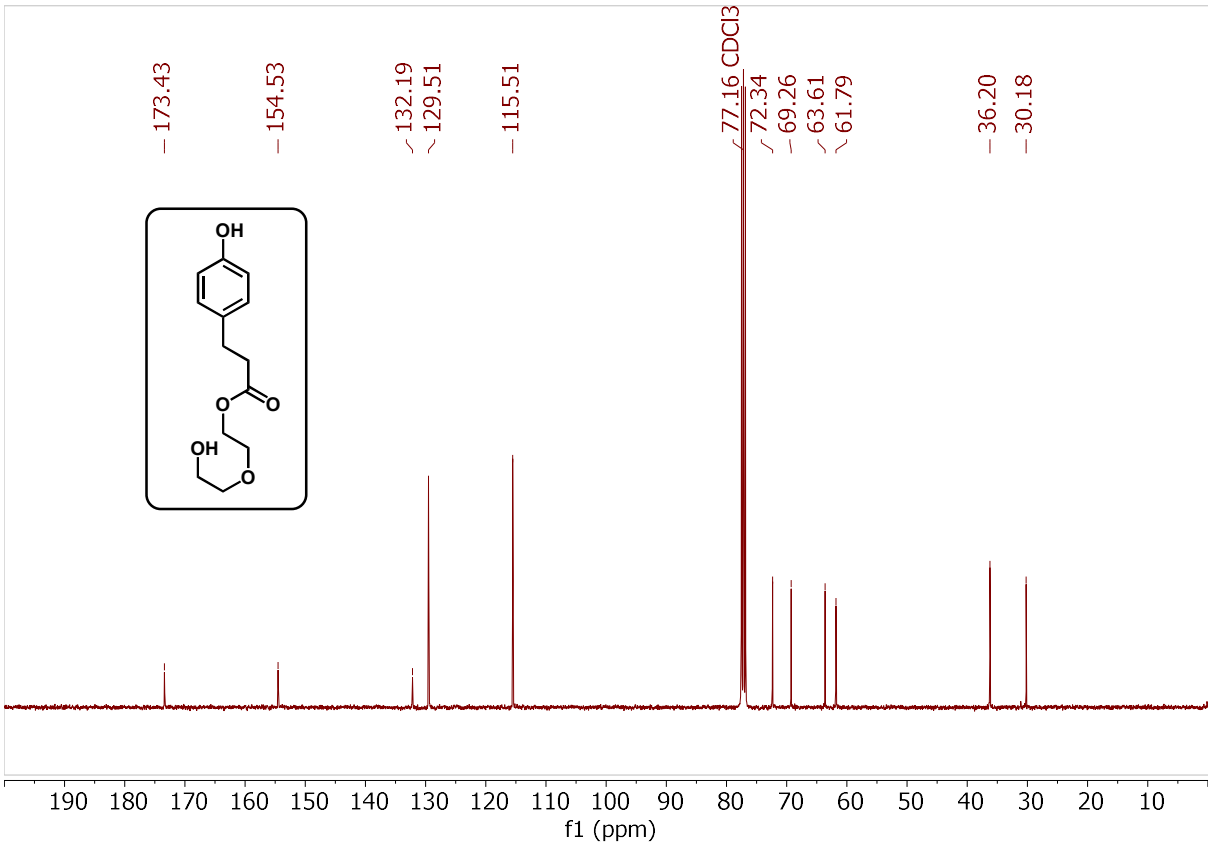
^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) spectrum of **6p**



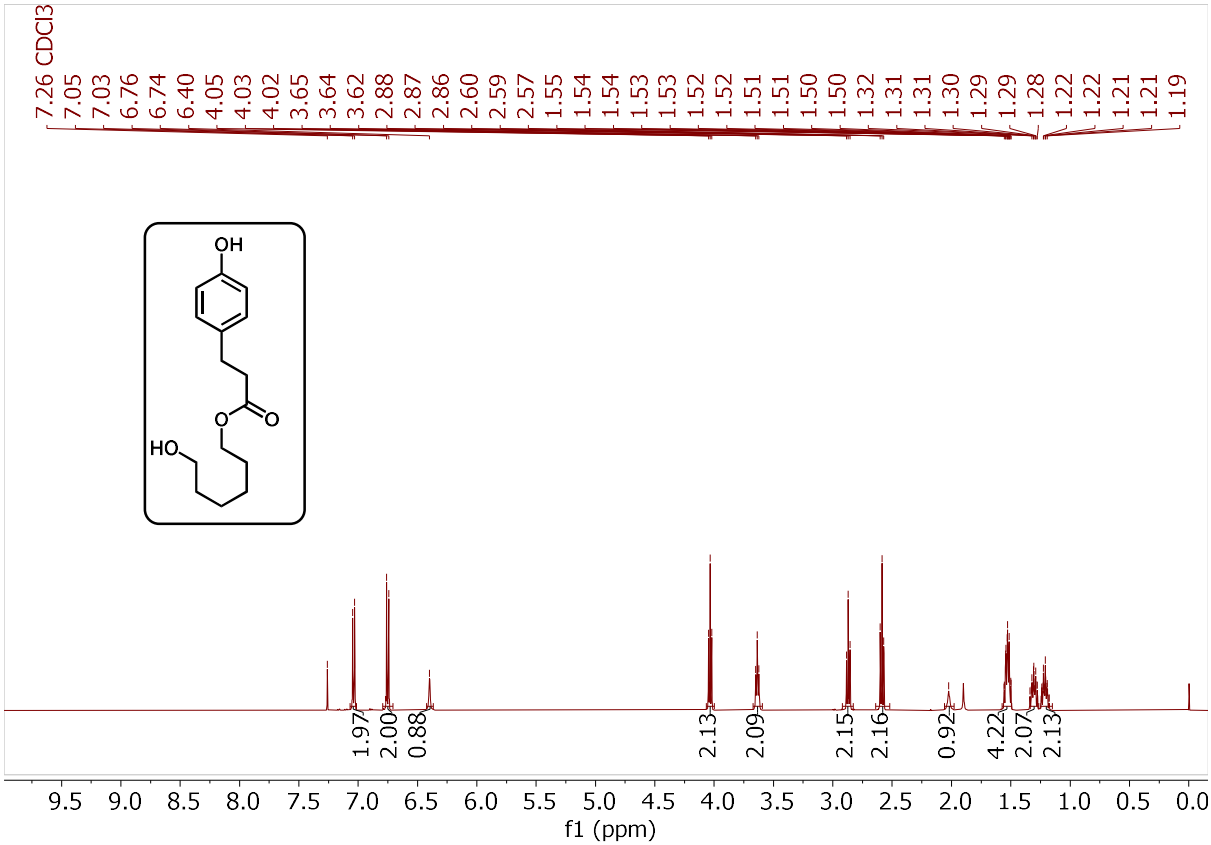
^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of **6q**



^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) spectrum of **6q**



^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of **6r**



^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) spectrum of **6r**