Electronic Supplementary Information

Asymmetric total synthesis of (+)-propolisbenzofuran B

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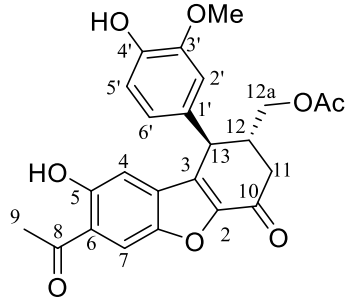
General Information: All the reactions were carried out using oven-dried glassware under an atmosphere of argon (Ar). All reagents were used as purchased from commercial suppliers without further purification. Solvents were dried and distilled following usual protocols. Heating reactions were performed in a silicon oil bath at the specified temperature. Flash column chromatography was performed in all cases using the indicated solvent system on purchased silica gel (230−400 mesh). Analytical thin-layer chromatography was performed using 60 F254 precoated silica gel plates (0.2 mm thickness), and compounds were visualized by irradiation of UV light. The ^{1}H NMR, and ^{13}C NMR spectra were measured with Bruker 400 (400 MHz) or 800 (800 MHz) using $CDCl_3$, DMSO-d_6 and Acetone-d_6. ^{1}H NMR chemicals shift are expressed in ppm(δ) relative to δ = 7.26 for $CDCl_3$, δ = 2.50 for DMSO-d_6 and δ = 2.05 for Acetone-d_6. ^{13}C NMR chemical shift are expressed in ppm(δ) relative to δ = 77.00 for $CDCl_3$, δ = 39.51 for DMSO-d_6 and δ = 29.8 for Acetone-d_6. Electrospray ionization (ESI) mass spectrometry (MS) experiments were performed on Agilent Technologies 6530 Accurate-Mass Q-TOF LC/MS. Enantiomeric excess (*ee*) was measured by HPLC analysis with chiral stationary phase. Infrared Spectra were recorded on a PerkinElmer FT-IR C91507. Organocatalysts and chiral auxiliaries were prepared according to literature procedures[3-5] and optical rotation was checked before use.

Table SI1. Comparison of ^{13}C (recorded in Acetone-d_6) and ^{1}H NMR (recorded in Acetone-d_6) Chemical Shifts and Coupling Constants of Natural & Synthetic Samples of Propolisbenzofuran B

		**propolisbenzofuran B (1)**		
C(n)	Isolated natural product (+)-**1** *(100 MHz)*	(±)-**1**; Thomson Group *(125 MHz)*	(±)-**1**; Ramana Group *(125 MHz)*	(+)-**1**, present study *(100 MHz)*
2	151.7	151.8	151.9	152.0
3	135.0	135.1	135.1	135.2

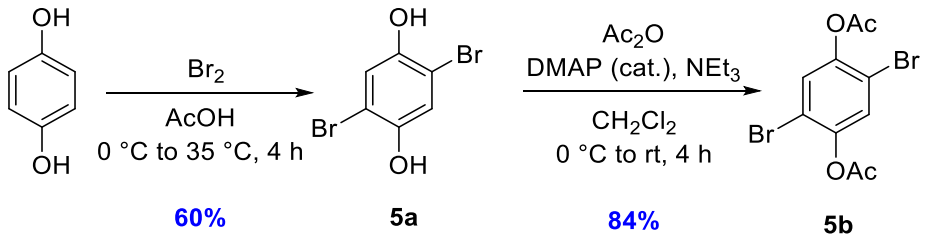
3a	134.0	134.1	134.2	134.3
4	110.0	110.0	110.1	110.2
5	158.2	158.2	158.3	158.4
6	120.5	120.6	120.6	120.7
7	115.5	115.6	115.6	115.7
7a	149.5	149.6	149.7	149.8
8	205.8	205.0	206.0	206.5
9	27.3	27.4	27.4	27.5
10	187.5	187.6	187.6	187.7
11	42.3	42.4	42.4	42.5
12	44.9	44.9	45.0	45.1
12a	65.2	65.2	65.3	65.4
13	43.1	43.1	43.2	43.3
1’	131.1	131.7	131.7	131.8
2’	112.9	112.9	113.0	113.1
3’	148.9	148.9	149.0	149.1
4’	147.2	147.2	147.3	147.4
5’	116.1	116.1	116.2	116.3
6’	122.5	122.5	122.6	122.7
OMe	56.3	56.3	56.4	56.5
OAc	20.6 170.8	20.7 (not given)	20.7 171.0	20.8 171.1
C(n)-H	Isolated natural product (+)-**1** *(100 MHz)*	(±)-**1**; Thomson Group *(125 MHz)*	(±)-**1**; Ramana Group *(125 MHz)*	(+)-**1**, present study *(100 MHz)*
4	6.13 s	6.14 (s)	6.14 (s, 1H)	6.17 (s, 1H)
7	8.21 s	8.24 (s, 1H)	8.21 (s, 1H)	8.23 (s, 1H)

9	2.75 s	2.76 (s, 3H)	2.76 (s, 3H)	2.77 (s, 3H)
11	2.86 (m, 2H)	2.81 (m, 2H)	2.82 (dd, *J* = 4.4, 16.3 Hz, 1H) 2.87 (dd, *J* = 11.9, 16.3 Hz, 1H)	2.88- 2.85 (m, 2H)
12	2.94 m	2.96 m	2.92–2.97 (m, 1H)	2.99–2.94 (m, 1H)
12a	4.05 (m, 2H)	4.05 (t, *J* = 4.5 Hz, 2H)	4.04 (dd, *J* = 5.7, 11.3 Hz, 1H) 4.07 (dd, *J* = 3.6, 11.3 Hz, 1H)	4.06 (dd, *J* = 5.4, 11.4 Hz, 1H) 4.10 (dd, *J* = 3.7, 11.2 Hz, 1H)
13	4.33 (d, *J* = 9.9 Hz)	4.35 (d, *J* = 9.9 Hz, 2H)	4.34 (d, *J* = 10.0 Hz, 1H)	4.37 (d, *J* = 9.8 Hz, 1H)
2’	7.02 (d, *J* = 2.0 Hz)	7.03 b s	7.03 (br. s, 1H)	7.04 (d, *J* = 1.6 Hz, 1H)
5’	6.89 (d, *J* = 8.0 Hz)	6.88 (d, *J* = 1.7 Hz, 2H)	6.89 (d, *J* = 8.1 Hz, 1H)	6.91 (d, *J* = 8.0 Hz, 1H)
6’	6.87 (dd, *J* = 8.0, 2.0 Hz)	6.88 (d, *J* = 1.7 Hz, 2H)	6.87 (dd, *J* = 1.6, 8.1 Hz, 1H)	6.88 (d, *J* = 8.0 Hz, 1H)
OMe	3.73 s	3.75 (s)	3.76 (s, 3H)	3.78 (s, 3H)
OAc	2.03 s	2.04 (s)	2.04 (s, 3H)	2.07 (s, 3H)
C(4’)–OH	8.01 b s	7.75 s	7.69 (s, 1H)	7.68 (s, 1H)
C(5)–OH	11.81 s	11.82 (s, 1H)	11.81 (s, 1H)	11.81 (s, 1H)

Table SI2: Optical rotation and melting point comparison chart of the synthesized Propolisbenzofuran B

Propolisbenzofuran B	Isolated natural product (+)-**1** *(100 MHz)*	(±)-**1**; Thomson Group *(125 MHz)*	(±)-**1**; Ramana Group *(125 MHz)*	(+)-**1**, present study *(100 MHz)*
Melting point (°C)	Not reported	Not reported	199-200	198-200
Optical rotation	+38.4 (c 0.08, $CHCl_3$)	Not applicable	Not applicable	+36.2 (c 0.36, $CHCl_3$)

Synthesis of 2,5-dibromo-1,4-hydroquinone (5a) and its *O*-acetyl derivative (5b)

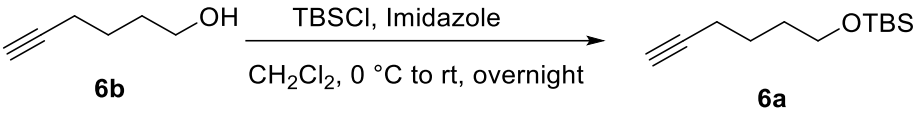


2,5-Dibromo-1,4-hydroquinone was synthesized according to a literature procedure.[1] In a 250 mL two-neck flask, hydroquinone (20 g, 182 mmol) was dissolved in 180 mL glacial acetic acid. Bromine (19.3 mL, 373 mmol) in 50 mL glacial acetic acid was then added dropwise at 0 °C. After stirring for 4 h at 35 °C. The suspension was filtered, and the solid was washed with cold glacial acetic acid. Recrystallization from glacial acetic acid gave 2,5-dibromohydroquinone **5a** as a white solid (29.2 g, 60% yield).

To a solution of **5a** (20 g, 74.63 mmol) in CH_2Cl_2 (400 mL) was added acetic anhydride (14.8 ml, 156.8 mmol), DMAP (1.82 g, 14.93 mmol) at 0 °C followed by triethylamine (26 mL, 186.6 mmol), then the mixture was stirred at room temperature. The reaction mixture was treated with aqueous ammonium chloride and extracted with CH_2Cl_2 (3

x 100 mL). The organic layer was washed with brine and dried (Na_2SO_4). The solvent was evaporated under reduced pressure. The crude product was washed with Et_2O (3×50 mL) to afford **5b** as a white solid (22 g, 84%). **MP:** 154-156 °C; $\mathbf{R_f}$ = 0.5 (PE: EA= 9:1); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.40 (s, 2H), 2.35 (s, 6H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 168.0, 146.4, 127.7, 115.2, 20.7; **IR (cm^{-1})** 1764, 1471, 1427, 1370, 1202, 1164, 1010; **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{10}H_8{}^{79}Br_2NaO_4^+$/ $C_{10}H_8{}^{79}Br^{81}BrNaO_4^+$/ $C_{10}H_8{}^{81}Br_2BrNaO_4^+$ 372.8682, 374.8661, and 376.8641; found 372.8681, 374.8663, and 376.8643 respectively.

Synthesis of 4-*tert*-butyldimethylsiloxyhex-5-yne (6a)



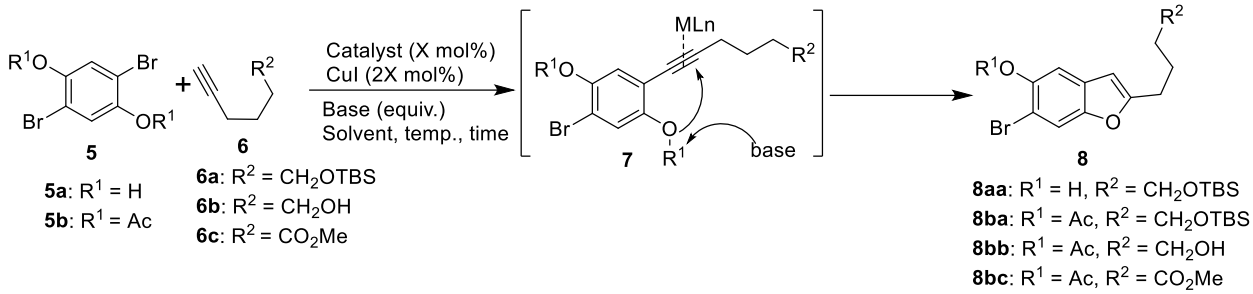
6b **6a**

Quantitative

To a solution of hex-5-yn-1-ol **6b** (20 g, 204.0 mmol, 1 equiv.) in CH_2Cl_2 (200 mL), was added imidazole (20.8 g, 306 mmol, 1.5 equiv.) followed by the addition of *tert*-butyldimethylsilyl chloride (36.9 g, 244.8 mmol, 1.2 equiv.) at 0 °C. The resulting mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched with a saturated aqueous NH_4Cl solution, and the aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude mixture was purified by silica gel column chromatography (PE/EA = 19:1) to afford **6a** (42.48 g, quantitative) as a colourless oil. The characterization data were identical to those previously reported.[6]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.63 (t, *J* = 6.0 Hz, 2H), 2.21 (td, *J* = 6.7, 2.6 Hz, 2H), 1.93 (t, *J* = 2.6 Hz, 1H), 1.67 – 1.54 (m, 4H), 0.89 (s, 9H), 0.04 (s, 6H).; **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 84.5, 68.2, 62.6, 31.8, 25.9, 24.9, 18.3, 18.2, -5.3; **IR (cm^{-1})** 3315, 2956, 2931, 2856, 1471, 1256, 1106.

Table SI3. Screening of reaction conditions for the deacetylative tandem Sonogashira-annulation reaction of 5 and 6



5

5a: R^1 = H
5b: R^1 = Ac

6

6a: R^2 = CH_2OTBS
6b: R^2 = CH_2OH
6c: R^2 = CO_2Me

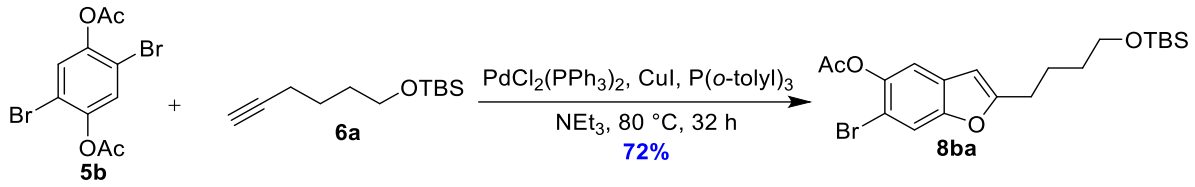
7

8

8aa: R^1 = H, R^2 = CH_2OTBS
8ba: R^1 = Ac, R^2 = CH_2OTBS
8bb: R^1 = Ac, R^2 = CH_2OH
8bc: R^1 = Ac, R^2 = CO_2Me

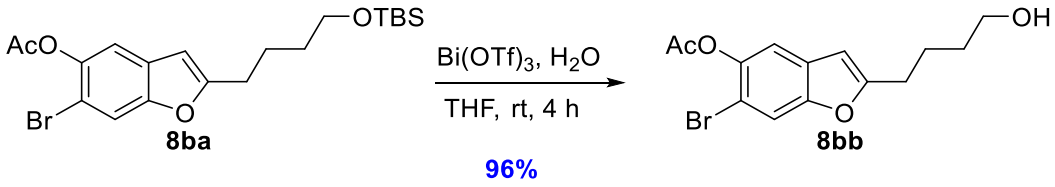
Entry	**5/6**	Catalyst (mol%)	Ligand	Base (equiv.)	Solvent	t (°C)	T (h)	Product	Yield (%)
1	**5a/6a**	$Pd(PPh_3)_4$/$Pd(OAc)_2$/ $PdCl_2(PPh_3)_2$/ (10)	--/ PPh_3 / P(*o*-tolyl)$_3$	Cs_2CO_3 /Et_3N /K_3PO_4	DMF/ THF /ACN	50-80	24 to 48	NDP	--
2	**5b/6a**	$Pd(PPh_3)_4$/ $Pd(OAc)_2$/ (10)	--/ PPh_3 / P(*o*-tolyl)$_3$	Cs_2CO_3 /Et_3N /K_3PO_4	DMF/ THF /ACN	50-80	24 to 48	NDP	--
3	**5b/6a**	$PdCl_2(PPh_3)_2$ (10)	--	Cs_2CO_3/ K_3PO_4/ DIPEA	DMF/ THF /ACN	50 to 80	24 to 48	**7ba/8ba**	Traces
4	**5b/6a**	$PdCl_2(PPh_3)_2$ (10)	--	Et_3N (4)	DMF	80	24	**8ba**	18
5	**5b/6a**	$PdCl_2(PPh_3)_2$ (10)	--	Et_3N	Et_3N:DMF (1:1)	80	24	**8ba**	36
6	**5b/6a**	$PdCl_2(PPh_3)_2$ (10)	--	Et_3N	Et_3N:THF (1:1)	80	24	**8ba**	22
7	**5b/6a**	$PdCl_2(PPh_3)_2$ (10)	--	Et_3N	Et_3N	80	30	**8ba**	65
8	**5b/6a**	$PdCl_2(PPh_3)_2$ (2)	--	Et_3N	Et_3N	80	30	**8ba**	65
9	**5b/6a**	$PdCl_2(PPh_3)_2$ (1)	--	Et_3N	Et_3N	80	30	**8ba**	52
10	**5b/6a**	$PdCl_2(PPh_3)_2$ (2)	PPh_3	Et_3N	Et_3N	80	24	**8ba**	72
11	**5b/6a**	$PdCl_2(PPh_3)_2$ (2)	P(*o*-tolyl)$_3$	Et_3N	Et_3N	80	24	**8ba**	78
12	**5b/6a**	$PdCl_2(PPh_3)_2$ (2)	$(CH_2)_4(PPh_2)_2$	Et_3N	Et_3N	80	24	**8ba**	44
13	**5b/6a**	$PdCl_2(PPh_3)_2$ (2)	PCy_3	Et_3N	Et_3N	80	24	**8ba**	76
14	**5b/6a**	$PdCl_2(PPh_3)_2$ (2)	P(*t*-Bu)$_3$	Et_3N	Et_3N	80	24	**8ba**	73
15	**5b/6a**	$PdCl_2(PPh_3)_2$ (2)	1,2-$(Ph_2P)_2C_6H_4$	Et_3N	Et_3N	80	24	**8ba**	12
16	**5b/6b**	$PdCl_2(PPh_3)_2$ (2)	P(*o*-tolyl)$_3$	Et_3N	Et_3N	80	48	**8bb**	32
17	**5b/6c**	$PdCl_2(PPh_3)_2$ (2)	P(*o*-tolyl)$_3$	Et_3N	Et_3N	80	24	**8bc**	40
18	**5b/6a** (2 g scale)	$PdCl_2(PPh_3)_2$ (2)	P(*o*-tolyl)$_3$	Et_3N	Et_3N	80	32	**8ba**	72

Synthesis of 6-bromo-2-(4-((*tert*-butyldimethylsilyl)oxy)butyl)benzofuran-5-yl acetate (8ba)



4-*tert*-Butyldimethylsiloxyhex-5-yne **6a** (3.14 g, 14.77 mmol) was added to the mixture of *O*-acetyl-2,5-dibromo-1,4-hydroquionone **5b** (4 g, 11.36 mmol), $PdCl_2(Ph_3P)_2$ (160 mg, 0.23 mmol), CuI (108 mg, 0.57 mmol), P(*o*-tolyl)$_3$ (174 mg, 0.57 mmol) and triethylamine (114 mL) at rt under N_2 atmosphere. The mixture was heated at 80 °C for 32 h under stirring. The resulting mixture was then cooled to rt and diluted with ethyl acetate (200 mL), filtered through a pad of 230-400 silica gel, filtrate part was washed with saturated aqueous NH_4Cl solution (2×100 mL) followed by water (2×50 mL) and brine. Then the resulting solution was dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel with petroleum-ethyl acetate (19:1) as the eluent to give compound **8ba** as a yellowish liquid. **Yield:** 3.61 g (72%). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.64 (d, *J* = 0.9 Hz, 1H), 7.21 (s, 1H), 6.35 (d, *J* = 0.9 Hz, 1H), 3.65 (t, *J* = 6.3 Hz, 2H), 2.76 (t, *J* = 7.6 Hz, 2H), 2.37 (s, 3H), 1.79 (p, *J* = 7.4 Hz, 2H), 1.60 (p, *J* = 6.1 Hz, 2H), 0.90 (s, 9H), 0.05 (s, 6H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 169.2, 161.7, 152.5, 143.5, 129.2, 115.1, 114.1, 110.4, 102.1, 62.7, 32.1, 28.2, 26.0, 24.0, 20.8, 18.4, -5.3; **IR (cm^{-1})** 2956, 2929, 2859, 1775, 1451, 1370, 1202, 1165, 1103. **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{20}H_{29}{}^{79}BrNaO_4Si^+$/ $C_{20}H_{29}{}^{81}BrNaO_4Si^+$ 463.0911, and 465.0890; found 463.0910, and 465.0898 respectively.

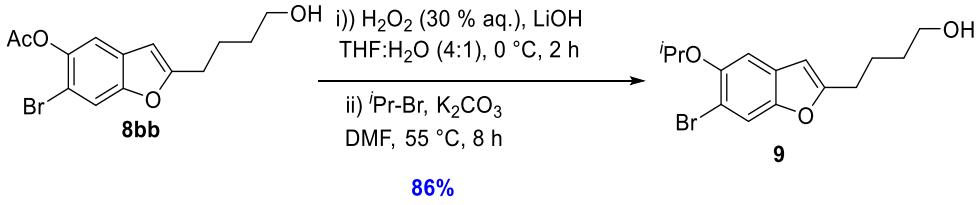
Synthesis of 6-bromo-2-(4-hydroxybutyl)benzofuran-5-yl acetate (8bb)



To a solution of **8ba** (3.5 g, 7.95 mmol) in THF (80 mL) were successively added distilled H_2O (72 µL, 5 equiv.) and Bi(OTf)$_3$ (525 mg, 0.8 mmol). Then the reaction mixture was vigorously stirred at rt for 4 h. Complete consumption of the starting material was monitored by TLC (40% EA in PE). THF was then evaporated out by using a rotary evaporator, resulting reaction

mixture was diluted with ethyl acetate (200 mL), washed with saturated aqueous NH_4Cl solution (2×50 mL) followed by water (2×50 mL) and brine. The resulting solution was dried over anhydrous Na_2SO_4. After the removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel with 40% ethyl acetate- hexanes as the eluent to give compound **8bb** as a gummy liquid (2.5 g, 96%). $\mathbf{R_f}$ = 0.3 (Hexanes/EtOAc, 3:2); **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 7.92 (d, *J* = 0.9 Hz, 1H), 7.45 (s, 1H), 6.63 (d, *J* = 1.0 Hz, 1H), 4.43 (t, *J* = 5.2 Hz, 1H), 3.42 (dd, *J* = 6.4 Hz, 2H), 2.77 (t, *J* = 7.5 Hz, 2H), 2.33 (s, 3H), 1.71 (p, *J* = 7.4 Hz, 2H), 1.48 (p, *J* = 6.4 Hz, 2H). **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 168.8, 161.8, 151.8, 143.2, 129.0, 114.8, 114.7, 110.1, 102.3, 60.3, 31.8, 27.5, 23.6, 20.6. **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{14}H_{15}{}^{79}BrNaO_4Si^+$/ $C_{14}H_{15}{}^{81}BrNaO_4Si^+$ 349.0046, and 351.0025; found 349.0049, and 351.0028 respectively.

Synthesis of 4-(6-bromo-5-isopropoxybenzofuran-2-yl)butan-1-ol (9)

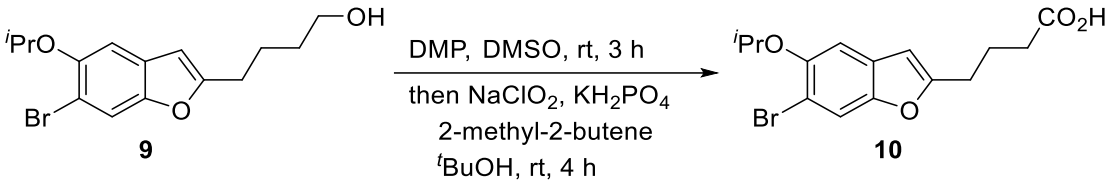


To a stirred solution of **8bb** (2.5 g, 7.65 mmol, 1.0 equiv.) in 40 mL of 4:1 THF-H_2O at 0 °C was added 8.7 mL (76.5 mmol) of 30% aqueous hydrogen peroxide followed by 459 mg (19.13 mmol) of lithium hydroxide in one portion. After stirring for 2 h at 0 °C, a solution of 9.65 g (76.5 mmol) of sodium sulphite in 20 mL of H_2O was added to quench excess hydrogen peroxide. The THF was removed *in vacuo*, and the resulting solution was extracted with CH_2Cl_2 (3×100 mL). The combined CH_2Cl_2 extract was dried over Na_2SO_4 and evaporated *in vacuo* to give a white solid. The crude product was pure enough to carry out the next stage.

A solution of the above crude product in DMF (40 mL) was treated K_2CO_3 (1.27 g, 9.18 mmol) at room temperature and stirred for 15 min. To this 2-bromopropane (1.5 mL, 15.3 mmol) was added and stirred at 55 °C for 8 h. After completion of reaction as indicated by TLC, the reaction was quenched with water and extracted using diethyl ether (3×100 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (30% ethyl acetate in petroleum ether) to afford **9** (2.2 g, 86% for two-steps) as a colourless oil. $\mathbf{R_f}$ = 0.2 (hexanes/EtOAc, 7:3); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.58 (d, *J* = 0.9 Hz, 1H), 7.02

(s, 1H), 6.29 (d, *J* = 1.0 Hz, 1H), 4.47 (hept, *J* = 6.1 Hz, 1H), 3.67 (t, *J* = 6.5 Hz, 2H), 2.75 (t, *J* = 7.4 Hz, 2H), 1.80 (p, *J* = 7.7 Hz, 2H), 1.64 (p, *J* = 8.5 Hz, 2H), 1.38 (d, *J* = 6.1 Hz, 6H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 160.5, 150.3, 149.7, 128.7, 115.1, 109.9, 107.9, 102.0, 73.5, 62.4, 32.0, 28.2, 23.8, 22.0; **IR (cm^{-1})** 3365, 2976, 2938, 2869, 1612, 1600, 1454, 1236,1185, 1109, 1000. **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{15}H_{19}{}^{79}BrNaO_3^+$/ $C_{15}H_{19}{}^{81}BrNaO_3^+$ 349.0410, and 351.0389; found 349.0411, and 351.0393 respectively.

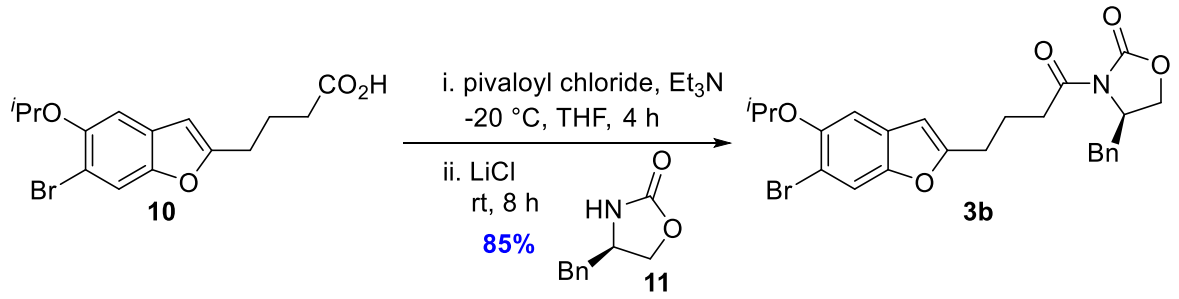
Synthesis of 4-(6-bromo-5-isopropoxybenzofuran-2-yl)butanoic acid (10)



To a stirred solution of **9** (2.15 g, 6.58 mmol) in DMSO (7 mL) at rt, Dess-Martin periodinane (DMP; 4.18 g, 9.86 mmol) was added. The combined reaction mixture stirred for 3 h. After full consumption of starting material, it was diluted with diethyl ether (200 mL). The organic layer was washed with saturated aqueous $Na_2S_2O_3$ solution, then successively with saturated bicarbonate solution and water. The combined aqueous part again extracted with diethyl ether (2×50 mL). Then combined ether solution was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was used for further oxidation reaction.

A freshly prepared solution of $NaClO_2$ (1.19 g, 13.16 mmol) and KH_2PO_4 (1.79 g, 13.16 mmol) in H_2O (4 mL) was added to a stirred solution of crude product obtained above and 2-methyl-2-butene (2.78 mL, 26.32 mmol) in ^{t}BuOH (7 mL) and the mixture was stirred vigorously at room temperature for 4 h. The mixture was extracted with ethyl acetate (3×50 mL). The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel 230-400 mesh, ethyl acetate/ petroleum ether 1/2 to 1/1) to afford **10** (1.97 g, 88%) as a white solid. **MP:** 92 - 94 °C; **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.60 (d, *J* = 1.0 Hz, 1H), 7.03 (s, 1H), 6.33 (d, *J* = 1.1 Hz, 1H), 4.48 (hept, *J* = 6.1 Hz, 1H), 2.80 (t, *J* = 7.3 Hz, 2H), 2.45 (t, *J* = 7.3 Hz, 2H), 2.06 (p, *J* = 7.3 Hz, 2H), 1.39 (s, 3H), 1.37 (s, 3H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 179.4, 159.2, 150.4, 149.8, 128.6, 115.2, 110.2, 107.9, 102.7, 73.5, 33.0, 27.6, 22.5, 22.0; **IR (cm^{-1})** 2976, 2926, 2856, 1710, 1611, 1455, 1424, 1308, 1235, 1185, 1112, 1001.

Synthesis of (*R*)-4-benzyl-3-(4-(6-bromo-5-isopropoxybenzofuran-2-yl)butanoyl)oxazolidin-2-one (3b)



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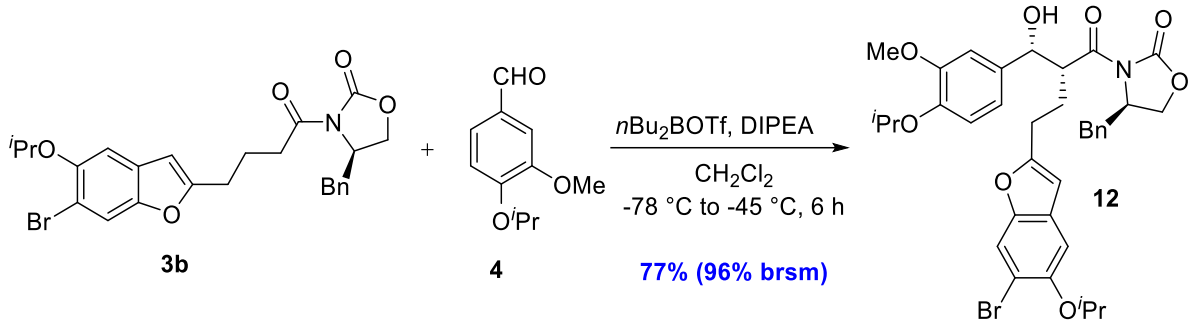
To a stirred solution of **10** (1.81 g, 5.32 mmol) in dry THF (6 mL) was added pivaloyl chloride (0.66 mL, 5.32 mmol, 1 equiv.) and Et_3N (2.3 mL, 15.96 mmol) at -20 °C and the mixture was stirred at the same temperature for 4 h. To this stirred suspension, chiral oxazolidinone **11** (1.04 g, 5.85 mmol) in dry THF (6 mL) was added dropwise followed by the addition of LiCl (23 mg, 5.32 mmol, 1 equiv.) after which it was stirred for an additional 15 min at -20 °C. The temperature was raised to at 25 °C and stirring continued for 8 h until the complete consumption of the starting materials (the progress of the reaction was monitored by TLC).

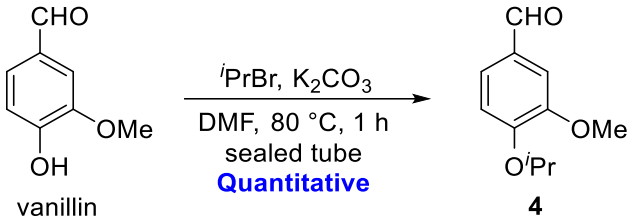
The product was then extracted with diethyl ether and the combined organic layer was washed with water, brine, and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure gave the crude product, which upon column chromatographic purification with petroleum ether/ ethyl acetate gave the desired product **3b** as a brownish oil (2.26 g, 4.52 mmol, 85%). $\mathbf{R_f}$ = 0.3 (EA/PE = 1:4); $\mathbf{[\alpha]_D^{25}}$**:** -32.67 (c = 0.9, $CHCl_3$) **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.60 (s, 1H), 7.35 – 7.23 (m, 3H), 7.18 (d, *J* = 7.0 Hz, 2H), 7.02 (s, 1H), 6.35 (s, 1H), 4.66 – 4.61 (m, 1H), 4.46 (hept, *J* = 6.0 Hz, 1H), 4.19 – 4.15 (m, 2H), 3.26 (dd, *J* = 13.4, 3.4 Hz, 1H), 3.10 – 2.96 (m, 2H), 2.84 (t, *J* = 7.4 Hz, 2H), 2.74 (dd, *J* = 13.4, 9.6 Hz, 1H), 2.13 (p, *J* = 7.2 Hz, 2H), 1.38 (s, 3H), 1.36 (s, 3H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 172.5, 159.5, 153.4, 150.4, 149.8, 135.1, 129.3, 128.9, 127.3, 115.2, 110.1, 107.8, 102.5, 73.4, 66.2, 55.1, 37.8, 34.7, 27.7, 22.0, 22.0; **IR (cm^{-1})** 3540, 2979, 2925, 1781, 1698, 1453, 1385, 1185, 1108; **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{25}H_{26}{}^{79}BrNNaO_5{}^+$/ $C_{25}H_{26}{}^{81}BrNNaO_5{}^+$ 522.0887 and 524.0866; found 522.0888 and 524.0871 respectively.

(*R*)-4-benzyl-3-((*R*)-4-(6-bromo-5-isopropoxybenzofuran-2-yl)-2-((*R*)-hydroxy(4-isopropoxy-3-methoxyphenyl)methyl)butanoyl)oxazolidin-2-one (12)



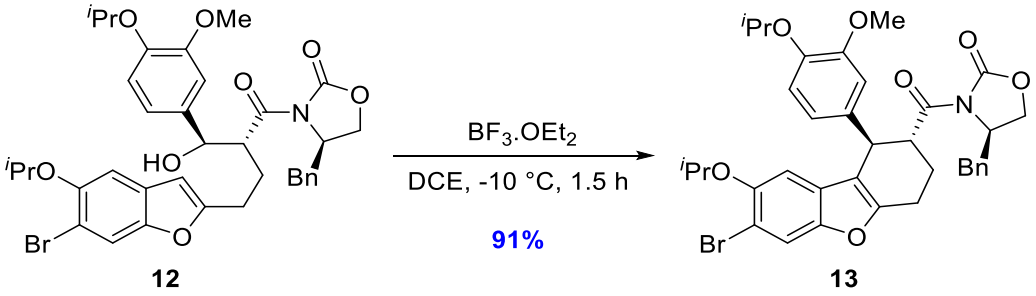
To a solution of compound **3b** (2.26 g, 4.52 mmol) in dry CH_2Cl_2 (25 mL) cooled at -78 °C was added a solution of *n*Bu_2BOTf (5.42 mL, 5.42 mmol) dropwise over 10 min. The resulting solution was allowed to stir at -78 °C for 30 min, and then i-Pr_2NEt (1.02 mL, 5.88 mmol) was slowly added. After stirring at -78 °C for 45 min, a solution of 4-isopropoxy-3-methoxybenzaldehyde **4** (2.63 g, 13.56 mmol) in dry CH_2Cl_2 (20 mL) was added dropwise over 10 min, then the resulting reaction mixture was allowed to stir at -45 °C for additional 6 h and quenched with saturated NH_4Cl solution. The cooling bath is replaced by an ice bath, stirred for 15 min, and then diluted with CH_2Cl_2 (200 mL) and H_2O (30 mL) added to it. The aqueous part was extracted with CH_2Cl_2 (2×50 mL). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel 230-400 mesh, ethyl acetate/ petroleum ether 1/9 → 1/2) to afford **12** as a gummy liquid (2.42 g, 77% isolated, 96% brsm, dr > 25:1 syn:anti). $\mathbf{R_f}$ = 0.2 (EA/PE = 1:2); $[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$**:** +48.49 (c = 1.46, $CHCl_3$); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.57 (s, 1H), 7.31 – 7.22 (m, 4H), 7.11 (d, *J* = 6.8 Hz, 2H),6.99 (s, 1H), 6.95 (d, *J* = 1.2 Hz, 1H), 6.85 (dd, J = 1.6 Hz, 8.3 Hz, 1H), 6.81 (d, *J* = 8.2 Hz, 1H), 6.27 (s, 1H), 4.86 (d, *J* = 6.4 Hz, 1H), 4.53 – 4.47 (m, 1H), 4.45 – 4.37 (m, 2H), 4.30 – 4.26 (m, 1H), 3.97 (dd, *J* = 1.9, 9.0 Hz, 1H), 3.83 (s, 3H), 3.72 (t, *J* = 8.3 Hz, 1H), 3.05 (dd, *J* = 3.1, 13.2 Hz, 1H), 2.76 (t, *J* = 7.6 Hz, 2H), 2.51 – 2.44 (m, 2H), 2.42 – 2.35 (m, 1H), 2.29 - 2021 (m, 1H), 1.34 (t, *J* = 6.4 Hz, 12H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 174.2, 159.6, 153.0, 150.4, 150.2, 149.7, 146.8, 135.0, 134.2, 129.2, 128.9, 128.6, 127.3, 118.4, 115.2, 110.0, 109.7, 107.7, 102.4, 75.1, 73.4, 71.4, 66.0, 55.8, 55.7, 50.0, 37.8, 26.6, 25.8, 22.0, 22.0, 21.9; **IR (cm^{-1})** 3496, 2976, 2926, 1778, 1690, 1605, 1454, 1386, 1264, 1232, 1185, 1138, 1109, 1033; **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{36}H_{40}{}^{79}BrNNaO_8{}^+$/ $C_{36}H_{40}{}^{81}BrNNaO_8{}^+$ 716.1830 and 718.1809; found 716.1822 and 718.1810 respectively.

Synthesis of 4-isopropoxy-3-methoxybenzaldehyde (4)



To a solution of vanillin (10 g, 65.72 mmol) in dry DMF were added successively 2-bromo propane (6.8 mL ,72.30 mmol) and potassium carbonate (13.6 g, 98.58 mmol) at rt. The mixture was then heated at 80 °C in a sealed tube for 1 h. After consumption of the vanillin, reaction mixture was diluted with diethyl ether followed by filtered through a pad of celite. The solution was washed with H_2O, brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The pure compound was obtained by chromatography on silica gel (hexanes/EtOAc, 5:1) to afford **4** as a colourless viscous liquid in quantitative yield (12.5 g). $\mathbf{R_f}$ = 0.4 (hexanes/EtOAc, 4:1); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 9.83 (s, 1H), 7.42 (dd, *J* = 10.0, 1.8 Hz, 2H), 6.97 (d, *J* = 8.1 Hz, 1H), 4.68 (hept, *J* = 6.1 Hz, 1H), 3.91 (s, 3H), 1.43 (s, 3H), 1.41 (s, 3H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 190.9, 153.1, 150.3, 129.7, 126.6, 112.8, 109.5, 71.3, 56.0, 21.8; **IR (cm^{-1})** 2979, 2935, 1685, 1591, 1506, 1466, 1425, 1267, 1132, 1030; **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{11}H_{14}NaO_3^+$ 217.0835, found: 217.0844.

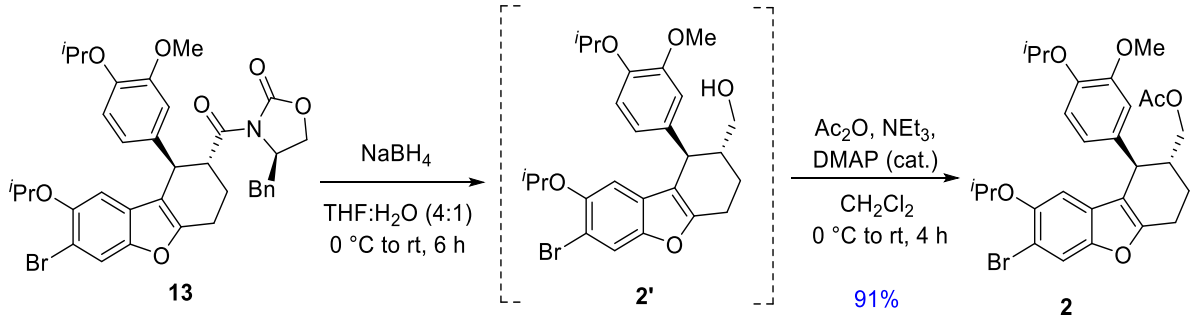
Synthesis of (*R*)-4-benzyl-3-((1*R*,2*R*)-7-bromo-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-carbonyl)oxazolidin-2-one (13)



To a stirred solution of aldol product **12** (2.42 g, 3.48 mmol) in 1,2- dichloroethane (DCE) (18 mL) at -10 °C freshly distilled $BF_3.OEt_2$ (0.86 mL, 6.96 mmol) was added dropwise. The reaction mixture was allowed to stir at the same temperature for 1.5 h. After completion of reaction as indicated by TLC, the reaction was quenched with saturated bicarbonate solution and diluted with ethyl acetate (300 mL). The organic layer was washed with H_2O, brine, dried

over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (15% ethyl acetate in petroleum ether) to afford **13** (2.15 g, 91%) as a gummy colourless liquid. $\mathbf{R_f}$ = 0.4 (EA/PE = 1:4); $[\alpha]_D^{25}$**:** +30.9 (c = 1, $CHCl_3$); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.55 (s, 1H), 7.33 – 7.24 (m, 3H), 7.18 (d, *J* = 7.0 Hz, 2H), 6.80 – 6.77 (m, 2H), 6.74 (s, 1H), 5.97 (s, 1H), 4.49 – 4.43 (m, 2H), 4.39 (d, *J* = 9.8 Hz, 1H), 4.23 (td, *J* = 2.0, 11.6 Hz, 1H), 4.07 – 3.99 (m, 2H), 3.89 (t, *J* = 8.2 Hz, 1H), 3.72 (s, 3H), 3.22 (dd, *J* = 3.4, 13.4 Hz, 1H), 3.14 – 3.03 (m, 1H), 2.90 (dd, *J* = 5.3, 17.2 Hz, 1H), 2.77 (dd, *J* = 9.5, 13.3 Hz, 1H), 2.41 – 2.36 (m, 1H), 2.15 (qd, *J* = 5.8, 11.9 Hz, 1H), 1.32 (dd, *J* = 1.8, 6.1 Hz, 6H), 1.18 (d, *J* = 6.1 Hz, 3H), 1.09 (d, *J* = 6.0 Hz, 3H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 174.2, 154.2, 152.9, 150.2, 149.7, 149.5, 146.3, 135.0, 133.6, 129.4, 128.9, 127.5, 127.3, 121.1, 115.4, 115.1, 114.8, 112.3, 109.4, 106.9, 72.7, 71.3, 66.0, 56.0, 55.2, 47.2, 42.3, 37.8, 26.5, 23.1, 22.0, 21.9, 21.8, 21.5; **IR (cm^{-1})** 2977, 2935, 1781, 1698, 1511, 1457, 1386, 1261, 1229, 1139, 1112; **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{36}H_{38}{}^{79}BrNNaO_7{}^+$/ $C_{36}H_{38}{}^{81}BrNNaO_7{}^+$ 698.1724 and 700.1703; found 698.1726 and 700.1708 respectively.

Synthesis of ((1*R*,2*R*)-7-bromo-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b,d*]furan-2-yl)methyl acetate (2)

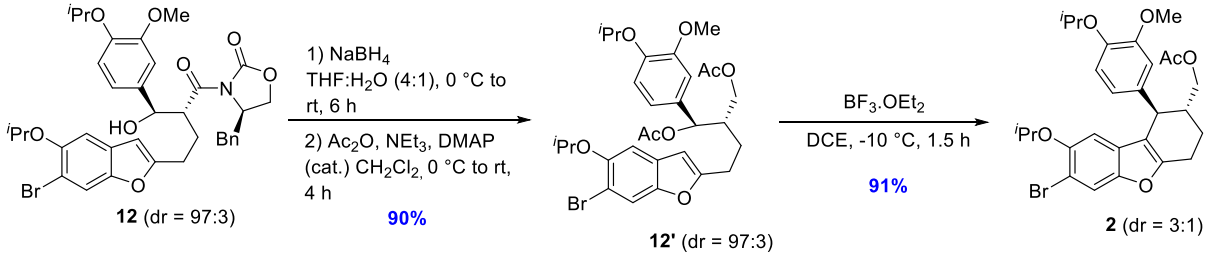


To a cooled (0 °C) solution of imide **13** (2.15 g, 3.10 mmol) in 15 ml THF: H_2O (4:1) was added $NaBH_4$ (470 mg, 12.40 mmol) in one portion. The mixture was stirred at rt for 6 h. The reaction was quenched by the addition of 30 mL saturated aqueous NH_4Cl and the mixture was extracted with EtOAc (3×100 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure to afford alcohol **2′** as a colourless viscous liquid, which was found to be sufficiently pure to move for the next step.

To a solution of crude **2′** (3.17 mmol) and DMAP (39 mg, 0.317 mmol) in CH_2Cl_2 (32 mL) at 0 °C was treated triethylamine (0.66 mL, 4.76 mmol) followed by Ac_2O (0.33 mL, 3.49 mmol).

The reaction mixture was warmed to room temperature and stirred for 4 h. After completion of the reaction as indicated by TLC, it was quenched by adding saturated NH_4Cl. The reaction mixture was diluted with CH_2Cl_2 (200 mL). The organic layer was washed with H_2O (2×50 mL), brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (15% ethyl acetate in petroleum ether) to afford **2** (1.54 g, 91%) as a colourless viscous liquid. $\mathbf{R_f}$ = 0.25 (EA/PE = 1:4) $[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{25}}$**:** +29.66 (c = 0.87, $CHCl_3$); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.54 (s, 1H), 6.82 (d, *J* = 8.1 Hz, 1H), 6.69 (dd, *J* = 2.0, 8.2 Hz, 1H), 6.65 (d, *J* = 2.1 Hz, 1H), 6.03 (s, 1H), 4.47 (hept, *J* = 6.1 Hz, 1H), 4.11 (dd, *J* = 4.1, 11.1 Hz, 1H), 4.08 – 4.00 (m, 2H), 3.76 (d, *J* = 2.5 Hz, 1H), 3.73 (s, 3H), 2.94 – 2.81 (m, 2H), 2.24 – 2.11 (m, 2H), 2.04 (s, 3H) 1.89 – 1.79 (m, 1H), 1.34 (dd, *J* = 2.0, 6.1 Hz, 6H), 1.19 (d, *J* = 6.1 Hz, 3H), 1.11 (d, *J* = 6.0 Hz, 3H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 171.1, 155.0, 150.5, 149.8, 149.5, 146.3, 134.5, 127.8, 120.9, 115.6, 115.1, 115.0, 112.2, 109.3, 106.9, 72.7, 71.4, 66.0, 56.1, 42.2, 42.0, 25.5, 22.7, 22.0, 22.0, 21.9, 21.6, 20.8; **IR (cm^{-1})** 2976, 2929, 1740, 1512, 1454, 1230, 1141, 1109, 1036; **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{28}H_{33}{}^{79}BrNaO_6{}^+$/ $C_{28}H_{33}{}^{81}BrNaO_6{}^+$ 567.1353 and 569.1332; found 567.1342 and 569.1332 respectively.

Friedel-Crafts cyclization of 12′ after reductive removal of chiral auxiliary 12



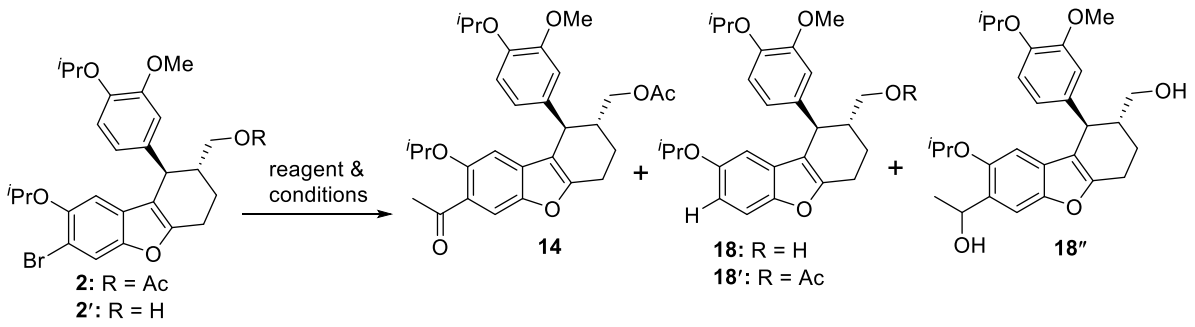
To a cooled (0 °C) solution of imide **12** (0.100 g, 0.14 mmol) in 2 ml THF: H_2O (4:1) was added $NaBH_4$ (21 mg, 0.56 mmol) in one portion. The mixture was stirred at rt for 6 h. The reaction was quenched by the addition of 5 mL saturated aqueous NH_4Cl and the mixture was extracted with EtOAc (3×100 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure to afford alcohol as a colourless viscous liquid, which was found to be sufficiently pure to move for the next step.

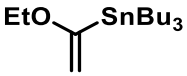
To a solution of alcohol product and DMAP (2 mg, 0.014 mmol) in CH_2Cl_2 (2 mL) at 0 °C was treated triethylamine (0.06 mL, 0.42 mmol) followed by Ac_2O (0.04 mL, 0.35 mmol). The reaction mixture was warmed to room temperature and stirred for 4 h. After completion of the

reaction as indicated by TLC, it was quenched by adding saturated NH_4Cl. The reaction mixture was diluted with CH_2Cl_2 (20 mL). The organic layer was washed with H_2O (2×5 mL), brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (20% ethyl acetate in petroleum ether) to afford **12'** (78 mg, 90%) without affecting the dr as a colourless viscous liquid. $\mathbf{R_f}$ = 0.30 (EA/PE = 1:4) **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.58 (s, 1H), 7.01 (s, 1H), 6.83 (d, *J* = 8.2 Hz, 1H), 6.78 (dd, *J* = 1.72, 8.4 Hz, 1H), 6.75 (d, *J* = 1.56 Hz), 6.22 (s, 1H), 5.81 (d, *J* = 6.9 Hz, 1H), 4.55 – 4.43 (m, 2H), 4.23 – 4.12 (m, 2H), 3.87 – 3.82 (m, 1H), 3.81 (s, 3H), 2.84 – 2.77 (m, 1H), 2.73 – 2.65 (m, 1H), 2.22 – 2.14 (m, 1H), 2.11 (s, 3H), 2.04 (s, 3H), 2.0 – 1.93 (m, 1H), 1.83 – 1.71 (m, 1H), 1.37 (dd, *J* = 9.3, 6.1 Hz, 12H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 170.9, 170.1, 159.7, 150.4, 150.2, 149.7, 147.1, 131.1, 128.6, 118.9, 115.2, 115.0, 110.3, 110.1, 107.8, 102.3, 75.5, 73.5, 71.3, 63.3, 56.0, 42.4, 26.1, 25.0, 22.1, 22.1, 21.2, 20.9; **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{30}H_{37}{}^{79}BrNaO_8{}^+$/ $C_{30}H_{37}{}^{81}BrNaO_8{}^+$ 627.1564 and 629.1544; found 627.1559 and 629.1545 respectively.

To a stirred solution of aldol product **12'** (78 mg, 0.13 mmol) in 1,2- dichloroethane (DCE) (3 mL) at -10 °C freshly distilled $BF_3.OEt_2$ (0.03 mL, 0.26 mmol) was added dropwise. The reaction mixture was allowed to stir at the same temperature for 1.5 h. After completion of reaction as indicated by TLC, the reaction was quenched with saturated bicarbonate solution and diluted with ethyl acetate (30 mL). The organic layer was washed with H_2O, brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (15% ethyl acetate in petroleum ether) to afford **2** (64 mg, 91%) as a gummy colourless liquid with dr of 3:1.

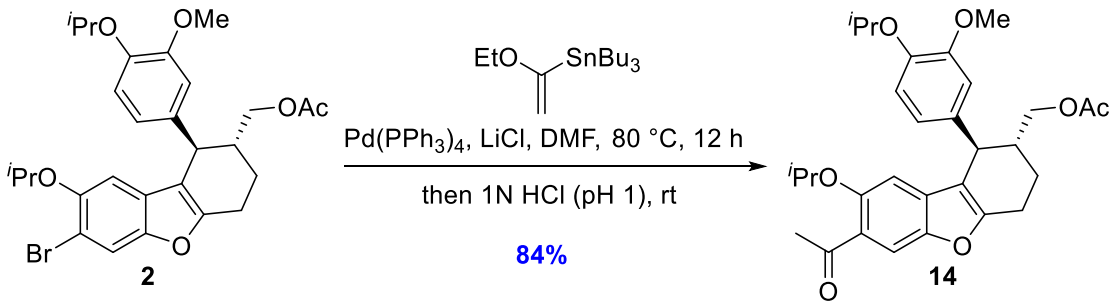
Table SI4. Screening of reaction conditions for the direct acetylation of bromo-compound 2/2′



entry	substrate	acetyl source	Reagent and reaction condition	Product/s	Yield (%)
1	2	AcTMS (2 equiv.)	$Pd(PPh_3)_4$ (5 mol%), CsF (4 equiv.), DMF (1 M), 80 °C, 24 h	**18′**	Traces
2	2	AcTMS (2 equiv.)	$Pd(PPh_3)_4$ (5 mol%), CsF (4 equiv.), DCE (1 M), 75 °C, 24 h	**18′**	Traces
3	2	AcTMS (2 equiv.)	$Pd_2(dba)_3$ (5 mol%), P(*o*-tolyl)$_3$, CsF (4 equiv.), DCE (1 M), 75 °C, 24 h	NDP	--
4	2′	Ac_2O	*n*-BuLi, THF, -78 °C to rt, 24 h	**18′**	91
5	2′	CH_3CHO	*n*-BuLi, THF, -78 °C to rt, 24 h	**18** (**18′**′ trace)	86
6	2′	$CH_3CON(OMe)Me$	*n*-BuLi, THF, -78 °C to rt, 24 h	18	90
7	2′	Ac_2O	^{i}PrMgCl.2LiCl, THF, -10 °C to rt, 24 h	NR	--
8	2′	$CH_3CON(OMe)Me$	^{i}PrMgCl.2LiCl, THF, -10 °C to rt, 24 h	NR	--
9	**2**		**$Pd(PPh_3)_4$ (10 mol%), LiCl (2 equiv.), DMF (0.1 M), 80 °C, 12 h then 1 N HCl, pH= 1, rt**	**14**	**84**

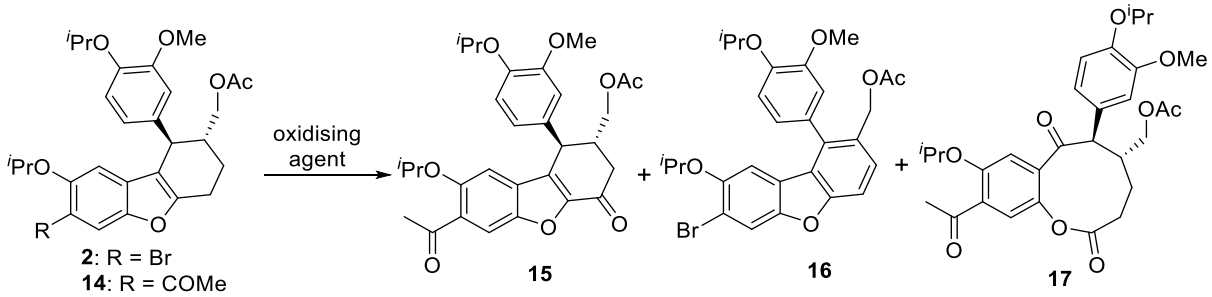
NDP: No desired product; NR: No reaction

Synthesis of ((1*R*,2*R*)-7-acetyl-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b,d*]furan-2-yl)methyl acetate (14)



Compound **2** (500 mg, 0.92 mmol) was taken in a two-neck RB flask in dry DMF (10 mL), and argon was flushed 10 times. $Pd(PPh_3)_4$ (106 mg, 0.092 mmol), LiCl (78 mg, 1.84 mmol), and tributyl(1-ethoxyvinyl)tin (0.62 mL, 1.84 mmol) were successively added to the reaction mixture. The reaction flask was again flushed with argon 6 times and heated to 80 °C in a preheated oil bath and continued for 12 h. After cooling to rt, the reaction mixture was acidified with 1M HCl to pH= 1. The mixture was diluted with diethyl ether (200 mL) and filtered through a short pad of celite. The residue part was again washed with diethyl ether (2×50 mL). The combined organic layer was successively washed with water (2×30 mL), and brine, dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (hexanes/ethyl acetate, 4:1) to get the title compound **14** as a colourless viscous liquid (393 mg, 84% over two-step). $\mathbf{R_f}$ = 0.6 (EA/PE = 1:1.5) $[\alpha]_D^{25}$**:** +31.04 (c = 2.4, $CHCl_3$); **^{1}H NMR (800 MHz, Chloroform-*d*)** δ 7.77 (s, 1H), 6.83 (d, *J* = 8.2 Hz, 1H), 6.72 (dd, *J* = 2.0, 8.2 Hz, 1H), 6.66 (d, *J* = 1.9 Hz, 1H), 5.95 (s, 1H), 4.48 (hept, *J* = 6.1 Hz, 1H), 4.17 – 4.12 (m, 1H), 4.11 (dd, *J* = 11.1, 4.0 Hz, 1H), 4.04 (dd, *J* = 6.9, 11.0 Hz, 1H), 3.76 (d, *J* = 6.8 Hz, 1H), 3.74 (s, 3H), 2.96- 2.92 (m, 1H), 2.90 – 2.87 (m, 1H), 2.57 (s, 3H), 2.24 – 2.21 (m, 1H), 2.19 – 2.14 (m, 1H), 2.04 (s, 3H), 1.88 – 1.82 (m, 1H), 1.35 (dd, *J* = 4.4, 6.1 Hz, 6H), 1.25 (d, *J* = 6.1 Hz, 3H), 1.06 (d, *J* = 6.0 Hz, 3H); **^{13}C NMR (200 MHz, Chloroform-*d*)** δ 199.7, 171.1, 158.0, 153.4, 150.5, 148.9, 146.4, 134.4, 132.6, 124.9, 120.9, 115.5, 115.2, 112.1, 112.0, 103.5, 71.3, 70.6, 66.0, 56.1, 42.1, 42.1, 32.2, 25.6, 23.0, 22.1, 22.0, 22.0, 21.3, 20.9; **IR (cm^{-1})** 2977, 2935, 1740, 1667, 1715, 1510, 1445, 1386, 1249, 1224, 1185, 1141, 1112, 1038; **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{30}H_{36}NaO_7^+$ 531.2353, found: 531.2365.

Table SI5. Benzylic oxidation of **2/23**

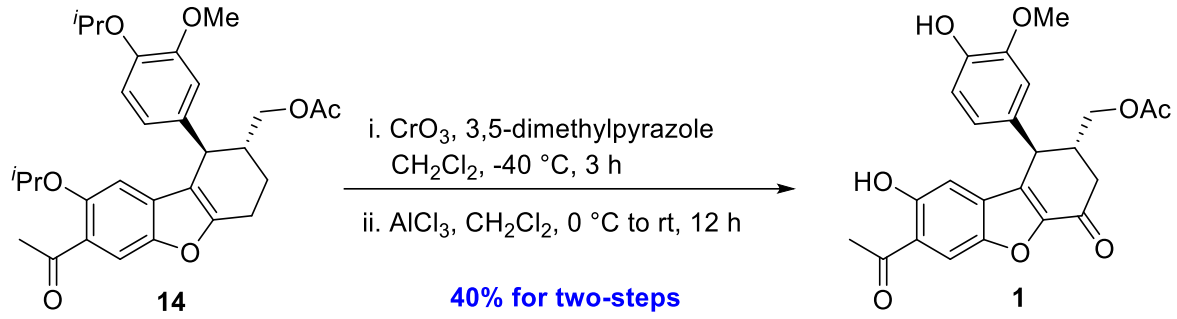


Entry	**2/14**	Oxidizing agent	Reaction conditions	Product[a]	Yield[b] (%)

1	**14**	IBX	Fluorobenzene/DMSO (2:1), 80 °C	NDP/MRP	--
2	**14**	$NaClO_2$, NHP (cat.)	ACN/H_2O (2:1), 50 °C	NDP/MRP	--
3	**2**	SeO_2	1,4-dioxane, 110 °C	**16**	70
4	**14**	CrO_3/ DMPyr	CH_2Cl_2, rt	**17**	64
5	**14**	CrO_3/ DMPyr	CH_2Cl_2, 0 °C	**15/17** (1:3)	57
6	**14**	CrO_3/ DMPyr	CH_2Cl_2, -20 °C	**15/17** (1:1)	62
7	**14**	CrO_3/ DMPyr	CH_2Cl_2, -40 °C	**15/17** (3:1)	61
8	**14**	CrO_3/ DMPyr	CH_2Cl_2, -50 °C	**15/17** (3:1)	60

[a] The value in the parenthesis referred to the isolated ratio of compounds **15** and **17**. [b] Combined isolated yield. NDP = No desired product; MRP = Messy reaction profile; NHP = *N*-hydroxyphthalimide; DMPyr = 3,5-dimethyl pyrazole; ACN = Acetonitrile.

Synthesis of (+)-propolisbenzofuran B (1)

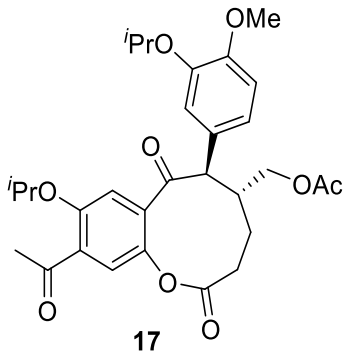


At –40 °C, to a stirred solution of CrO_3 (394 mg, 3.94 mmol) in dry CH_2Cl_2 (2 mL) and 3,5-dimethylpyrazole (378 mg, 3.94 mmol) was added a solution of **14** (100 mg, 0.197 mmol) in dry CH_2Cl_2 (2 mL) was added. The reaction mixture was continued at the same temperature for 3 h. The reaction mixture was pass through to a small pad of silica 230-400 mesh. The filtrate part was successively washed with 1N HCl (2×50 mL), water, and brine, concentrated under reduced pressure, and used in the next step without further purification.

At 0 °C, a solution of crude product in CH_2Cl_2 (4 mL) was treated with $AlCl_3$ (105 mg, 0.788 mmol) and stirred for 10 min. The reaction mixture was warmed to room temperature and stirred for 12 h. The reaction mixture was quenched with saturated NH_4Cl and partitioned between water (10 mL) and CH_2Cl_2 (50 mL). The organic layer was separated and the aqueous layer was extracted using CH_2Cl_2 (2×20 mL). The combined organic layer was washed using

brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by column chromatography (30→40% ethyl acetate in petroleum ether) to afford **1** (35 mg, 40% over two-steps) as yellow solid which matched the published spectral data (see Table SI1) $\mathbf{R_f}$ = 0.5 (EA/PE = 1:1.5); **MP:** 198- 200 °C; $[\alpha]_D^{25}$**:** +36.2 (c = 0.36, $CHCl_3$) [lit $[\alpha]_D^{25}$**:** +38.4 (c = 0.08, $CHCl_3$)][2] **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 11.83 (s, 1H), 7.93 (s, 1H), 6.92 (d, *J* = 8.1 Hz, 1H), 6.73 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.63 (d, *J* = 2.0 Hz, 1H), 6.26 (s, 1H), 5.65 (s, 1H), 4.18 (d, *J* = 9.7 Hz, 1H), 4.09 – 3.99 (m, 2H), 3.80 (s, 3H), 2.91 (d, *J* = 12.6 Hz, 1H), 2.82 – 2.74 (m, 2H), 2.69 (s, 3H), 2.08 (s, 3H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 204.0, 187.3, 170.6, 157.6, 150.7, 148.9, 147.1, 145.6, 134.3, 133.0, 130.2, 121.6, 120.0, 115.1, 114.0, 110.4, 110.1, 64.6, 56.0, 44.5, 42.6, 41.4, 27.0, 20.8; **^{1}H NMR (400 MHz, Acetone-d_6)** δ 11.81 (s, 1H), 8.23 (s, 1H), 7.68 (s, 1H), 7.04 (d, *J* = 1.7 Hz, 1H), 6.92-6.87 (dd, *J* = 2.1, 8 Hz, 2H), 6.17 (s, 1H), 4.37 (d, *J* = 9.8 Hz, 1H), 4.08 (t, *J* = 4.3 Hz, 2H), 3.78 (s, 3H), 3.02 – 2.93 (m, 1H), 2.89 – 2.84 (m, 2H), 2.77 (s, 4H), 2.07 (s, 3H); **^{13}C NMR (100 MHz, Acetone-d_6)** δ 206.5, 187.7, 171.1, 158.4, 152.0, 149.8, 149.1, 147.4, 135.2, 134.3, 131.8, 122.7, 120.7, 116.3, 115.7, 113.1, 110.2, 65.4, 56.5, 45.1, 43.3, 42.5, 27.5, 20.8; **IR (cm^{-1})** 3428, 2923, 1740, 1681, 1643, 1517, 1433, 1377, 1260, 1033. **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{24}H_{22}NaO_8^+$ 461.1207; found 461.1209.

((5*R*,6*R*)-10-acetyl-9-isopropoxy-6-(4-isopropoxy-3-methoxyphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydrobenzo[*b*]oxonin-5-yl)methyl acetate (17)



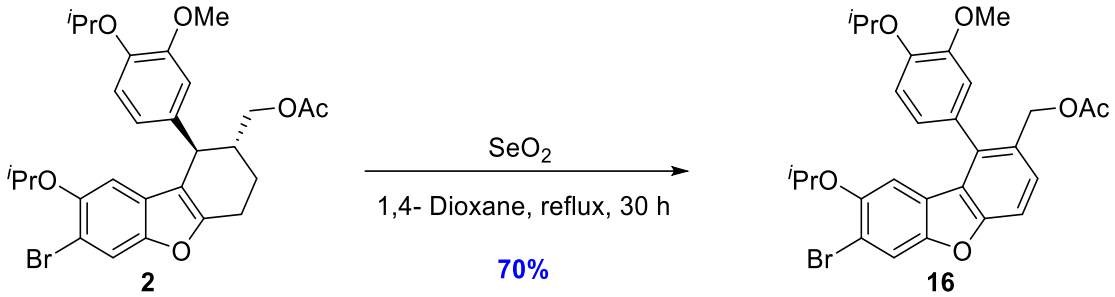
17

Physical Appearance: Yellowish gummy liquid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (s, 1H), 6.79 (d, *J* = 2.1 Hz, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 6.66 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.51 (s, 1H), 4.52 – 4.42 (m, 2H), 4.29 (d, *J* = 11.6 Hz, 1H), 3.92 – 3.84 (m, 2H), 3.81 (s, 3H), 3.00 – 2.93 (m, 1H), 2.76 – 2.63 (m, 2H), 2.59 (s, 3H), 2.40 – 2.31 (m, 1H), 2.17 – 2.10 (m, 1H), 2.01 (s, 3H), 1.34 (d, *J* = 2.7 Hz, 3H), 1.32 (d, *J* = 2.7 Hz, 3H), 1.30 (d, *J* = 6.0 Hz, 3H), 1.24 (d, *J* = 6.0 Hz, 3H); **^{13}C NMR (100 MHz,**

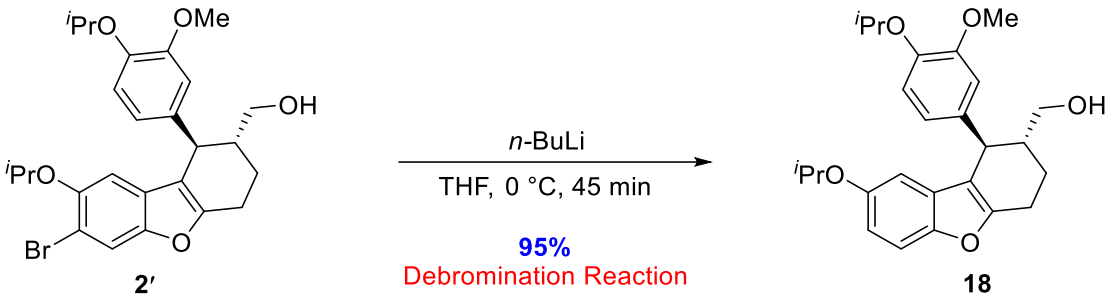
Chloroform-*d*) δ 203.0, 198.4, 174.3, 170.6, 155.1, 150.6, 147.2, 141.9, 138.7, 131.1, 127.4, 124.9, 121.6, 115.2, 112.3, 111.7, 71.4, 71.2, 64.5, 56.9, 56.0, 39.4, 31.9, 30.9, 26.5, 22.0, 22.0, 21.8, 21.7, 20.8; $[\alpha]_D^{25}$**:** +9 (c = 1, $CHCl_3$); **IR (cm^{-1})** 2977, 2935, 1766, 1740, 1681, 1511, 1477, 1401, 1235, 1176, 1141, 1106, 1036; **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{30}H_{36}NaO_9^+$ 563.2252; found 563.2255.

Synthesis of (7-bromo-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)dibenzo[*b,d*]furan-2-yl)methyl acetate (16)



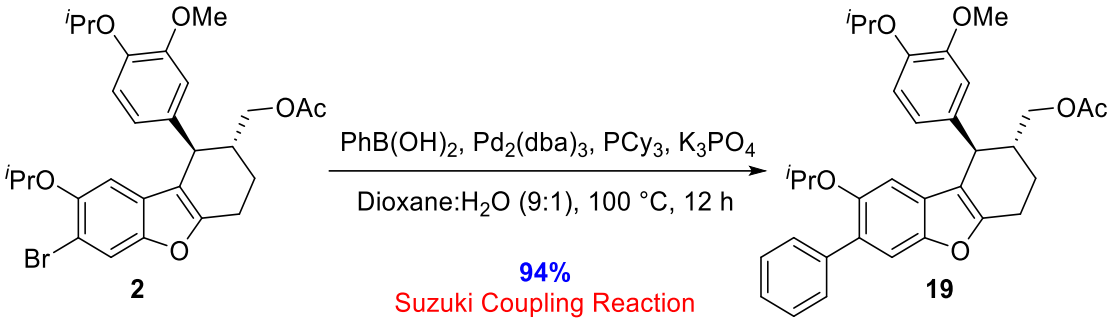
To a stirred solution of **2** (100 mg, 0.184 mmol) in anhydrous 1,4-dioxane (2 mL) was added SeO_2 (61 mg, 0.552 mmol) and the resulting mixture was heated under reflux for 30 h. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate (20 mL) and washed with water (30 mL). The aqueous layer was extracted with ethyl acetate (3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification was done by flash column chromatography (hexanes/ethyl acetate, 9:1) to get the title compound **16** as a white solid (70 mg, 70%). $\mathbf{R_f}$ = 0.5 (EA/PE = 1:4); **MP:** 130 – 132 °C; **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.72 (s, 1H), 7.58 (d, *J* = 8.6 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 6.95 – 6.90 (m, 2H), 6.34 (s, 1H), 5.08 (d, *J* = 3.2 Hz, 2H), 4.65 (hept, *J* = 6.1 Hz, 1H), 4.08 (p, *J* = 6.1 Hz, 1H), 3.82 (s, 3H), 2.05 (s, 3H), 1.46 (t, *J* = 6.4 Hz, 7H), 1.26 (t, *J* = 5.6 Hz, 6H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 170.6, 156.3, 151.0, 150.5, 150.2, 147.2, 137.2, 129.7, 128.9, 128.5, 123.8, 123.3, 121.3, 115.9, 115.4, 113.1, 112.9, 110.8, 108.4, 72.7, 71.5, 64.0, 56.0, 22.3, 21.9, 21.8, 21.7, 21.0; **IR (cm^{-1})** 2976, 2932, 1740, 1514, 1442, 1384, 1243, 1179, 1138, 1109, 1033; **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{28}H_{29}{}^{79}BrNaO_6^+$/ $C_{28}H_{29}{}^{81}BrNaO_6^+$ 563.1040 and 565.1019; found 563.1039 and 565.1024 respectively.

Synthesis of ((1*R*,2*R*)-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b,d*]furan-2-yl)methanol (18)



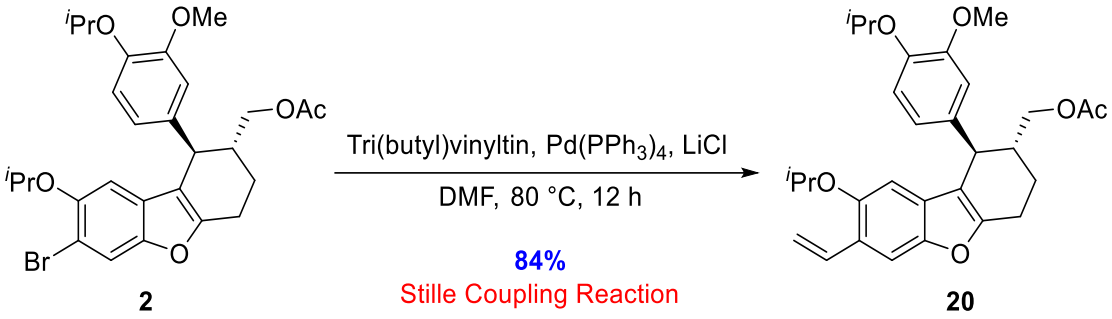
The compound **2′** (100 mg, 0.2 mol) was taken in a two neck RB flask in dry THF (2 mL), under an argon atmosphere at 0 °C. *n*BuLi (2.4 M in Hexanes) (0.21 mL, 0.500 mmol) was added dropwise and continued for 45 min. After the consumption of starting material, it was quenched with saturated NH_4Cl (10 mL) and diluted with EtOAc (50 mL). The organic layer was successively washed with water (2×20 mL), brine, dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (hexanes/ethyl acetate, 3:1) to get the title compound **18** as a white solid (81 mg, 95%). **R_f** = 0.3 (EA/PE = 1:1.5); **MP:** 112 – 114 °C; **$[\alpha]_D^{25}$:** +17.5 (c = 0.4, $CHCl_3$); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.24 (d, *J* = 8.8 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.74 – 6.68 (m, 3H), 6.07 (d, *J* = 2.6 Hz, 1H), 4.48 (hept, *J* = 6.1 Hz, 1H), 4.15 (hept, *J* = 6.1 Hz, 1H), 3.80 (d, *J* = 8.7 Hz, 1H), 3.75 (m, 1H), 3.74 (s, 3H), 3.58 (dd, *J* = 6.5, 10.6 Hz, 1H), 2.97 – 2.82 (m, 2H), 2.28 – 2.22 (m, 1H), 2.04 – 1.97 (m, 1H), 1.90 – 1.80 (m, 1H), 1.35 (dd, *J* = 1.7, 6.1 Hz, 6H), 1.19 (d, *J* = 6.1 Hz, 3H), 1.11 (d, *J* = 6.0 Hz, 3H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 154.8, 153.3, 150.5, 149.7, 146.1, 135.7, 128.7, 120.9, 115.9, 115.1, 113.4, 112.4, 110.9, 105.9, 71.5, 70.8, 64.8, 56.1, 45.5, 41.8, 25.2, 22.8, 22.1, 22.1, 22.0, 21.7; **IR (cm^{-1})** 3432, 2926, 1632, 1465, 1510, 1263; **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{26}H_{32}NaO_5^+$ 447.2142; found 447.2144.

Synthesis of ((1*R*,2*R*)-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-7-phenyl-1,2,3,4-tetrahydrodibenzo[*b,d*]furan-2-yl)methyl acetate (19)



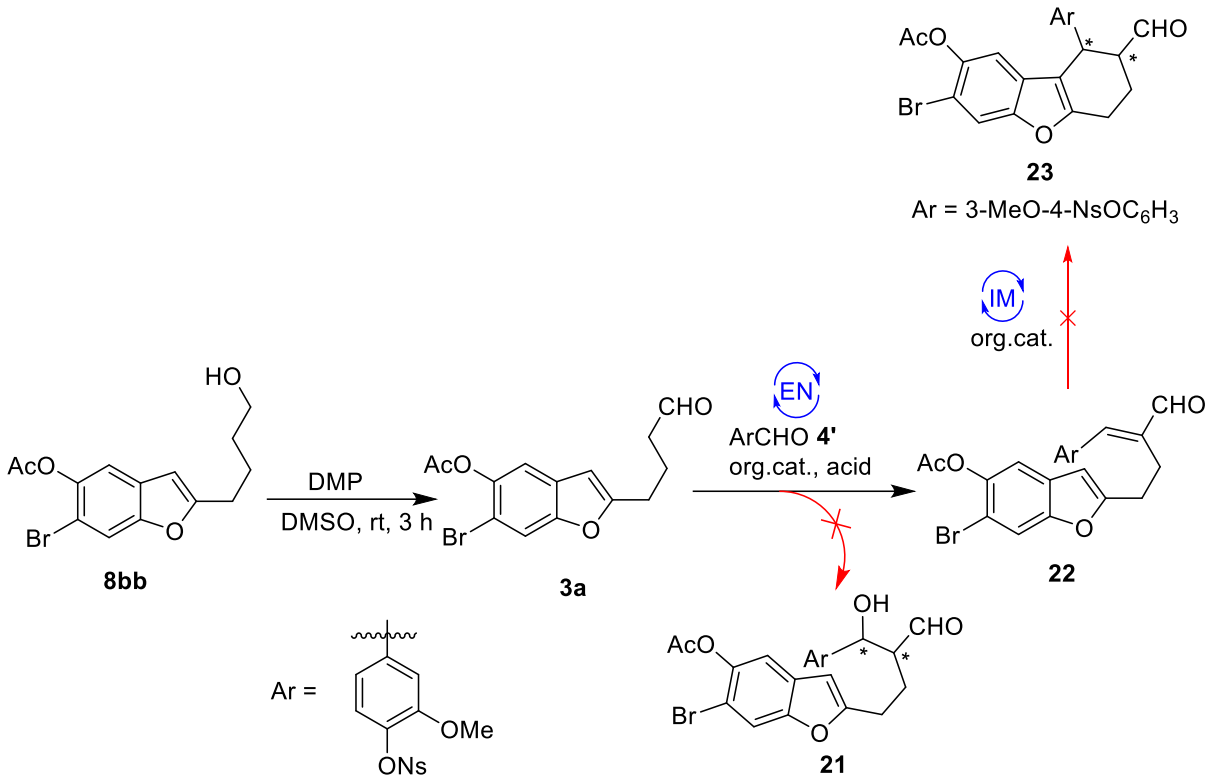
To a 5 mL oven-dried micro- reactor added compound **2** (100 mg, 0.184 mmol), Pd_2dba_3 (17 mg, 0.0184 mmol), K_3PO_4 (78 mg, 0.368 mmol), tricyclohexylphosphine (10 mg, 0.0368 mmol), phenylboronic acid (27 mg, 0.221 mmol) and degassed (purged with Ar for 30 min) 1,4-dioxane: H_2O (9:1) (2.0 mL) inside the glove box. It was then heated to 100 °C in a preheated oil bath for 20 h. Upon completion of the reaction, water (20 mL) was added and the organic mixture was extracted with EtOAc (3×50 mL). The combined organic extracts were successively washed with water (20 mL), brine, dried over Na_2SO_4, and concentrated *in vacuo*. The crude product obtained was purified by column chromatography to afford the title compound **19** (94 mg; 94%) as a gummy liquid. **R_f** 0.6 (Hexanes/EtOAc 1.5:1); **$[\alpha]_D^{25}$:** +16.51 (c = 1.06, $CHCl_3$); **^{1}H NMR (800 MHz, Chloroform-*d*)** δ 7.53 (d, *J* = 7.8 Hz, 2H), 7.36 (t, *J* = 7.7 Hz, 2H), 7.33 (s, 1H), 7.28 (t, *J* = 7.4 Hz, 1H), 6.85 (d, *J* = 8.2 Hz, 1H), 6.75 (dd, *J* = 1.9, 8.2 Hz, 1H), 6.73 (d, *J* = 1.9 Hz, 1H), 6.13 (s, 1H), 4.49 (hept, *J* = 6.2 Hz, 1H), 4.14 (dd, *J* = 4.1, 11.0 Hz, 1H), 4.07 (dd, *J* = 6.9, 11.0 Hz, 1H), 3.89 (hept, *J* = 6.0 Hz, 1H), 3.81 (d, *J* = 9.0 Hz, 1H), 3.78 (s, 3H), 2.97 – 2.93 (m, 1H), 2.91 – 2.88 (m, 1H), 2.24 – 2.18 (m, 2H), 2.06 (s, 3H), 1.89 – 1.84 (m, 1H), 1.35 (dd, *J* = 4.9, 6 Hz, 6H), 1.03 (d, *J* = 6.1 Hz, 3H), 0.96 (d, *J* = 6.1 Hz, 3H); **^{13}C NMR (200 MHz, Chloroform-*d*)** δ 171.1, 154.7, 150.4, 150.0, 146.3, 139.3, 134.8, 129.7, 128.5, 127.7, 127.5, 126.4, 120.9, 115.6, 114.9, 112.4, 112.3, 106.9, 71.7, 71.3, 66.1, 56.1, 42.2, 42.1, 25.6, 22.7, 22.1, 22.1, 21.8, 21.5, 20.9; **IR (cm^{-1})** 2976, 29929, 1740, 1509, 1468, 1427, 1383, 1369, 1232, 1183, 1165, 1138, 1112, 1036; **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{34}H_{38}NaO_6^+$ 565.2561; found 565.2562.

Synthesis of ((1*R*,2*R*)-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-7-vinyl-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methyl acetate (20)

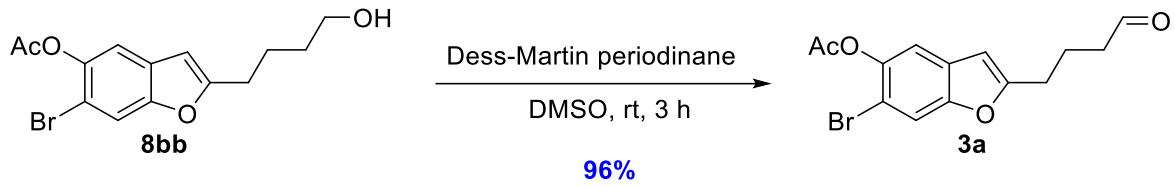


The compound **2** (100 mg, 0.184 mol) was taken in a two-neck RB flask in dry DMF (2 mL), argon was flushed for 10 times. $Pd(PPh_3)_4$ (21 mg, 0.0184 mmol), LiCl (15 mg, 0.368 mmol), and tributyl(vinyl)tin (0.06 mL, 0.202 mmol) were successively added to the reaction mixture. The reaction flask was again flushed with argon 6 times and heated to 80 °C in a preheated oil bath and continued for 12 h. After cooling to rt, the mixture was diluted with diethyl ether (50 mL) and filtered through a short pad of celite. The residue part was again washed with diethyl ether (2×20 mL). The combined organic layer was successively washed with water (2×20 mL), brine, dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (hexanes/ethyl acetate, 4:1) to get the title compound **20** as a light yellowish viscous liquid (75 mg, 84%). $\mathbf{R_f}$ = 0.3 (EA/PE = 1:1.5) $\mathbf{[\alpha]_D^{25}}$**:** +27.52 (c = 1.09, $CHCl_3$); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.47 (s, 1H), 7.05 (dd, *J* = 17.8, 6.6 Hz, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.71 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.68 (d, *J* = 2.0 Hz, 1H), 5.98 (s, 1H), 5.66 (dd, *J* = 17.7, 1.5 Hz, 1H), 5.16 (dd, *J* = 11.0, 1.5 Hz, 1H), 4.47 (hept, *J* = 6.1 Hz, 1H), 4.12 (dd, *J* = 11.1, 4.1 Hz, 1H), 4.07 – 3.99 (m, 2H), 3.77 – 3.76 (m, 1H), 3.74 (s, 3H), 2.96 – 2.83 (m, 2H), 2.23 – 2.1 (m, 2H), 2.04 (s, 3H), 1.89 – 1.79 (m, 1H), 1.35 (dd, *J* = 6.1, 2.4 Hz, 6H), 1.18 (d, *J* = 6.0 Hz, 3H), 1.07 (d, *J* = 6.0 Hz, 3H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 171.0, 154.9, 150.9, 150.5, 149.8, 146.2, 134.8, 132.4, 128.1, 124.23, 120.9, 115.8, 115.0, 112.6, 112.4, 107.3, 105.2, 71.4, 66.1, 56.0, 42.2, 42.1, 25.5, 22.8, 22.0, 22.0, 21.6, 20.8; **IR (cm^{-1})** 2976, 2933, 1740, 1620, 1512, 1445, 1229, 1112; **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{30}H_{36}NaO_6^+$ 515.2404; found 565.2418.

Synthesis of 4-(benzofuran-2-yl) butanal 3a and its organocatalytic reactions toward synthesis of 1-aryl-2,3-tetrahydrodibenzo[*b,d*]furan 23



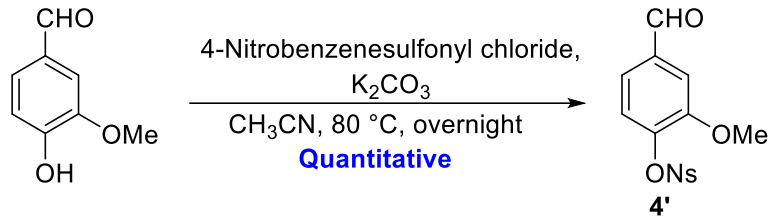
Synthesis of 6-bromo-2-(4-oxobutyl)benzofuran-5-yl acetate (3a)



To a stirred solution of **8bb** (2.5 g, 7.65 mmol, 1.0 equiv.) in DMSO (40 mL) at rt, Dess-Martin periodinane (4.87 g, 11.48 mmol) was added. The combined reaction mixture was stirred for 3 h. After full consumption of starting material, it was diluted with diethyl ether (200 mL). The organic layer was rapidly washed with saturated aqueous $Na_2S_2O_3$ solution, then successively with saturated bicarbonate solution and water. The combined aqueous part again extracted with diethyl ether (100 mL). Then combined ether solution was washed with brine and dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (hexanes/EtOAc, 3:1) to afford **3a** (2.39 g, 96%) as a viscous liquid. $\mathbf{R_f}$ = 0.2 (hexanes/EtOAc, 4:1); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 9.78 (s, 1H), 7.65 (s, 1H), 7.22 (s, 1H), 6.37 (s, 1H), 2.80 (t, *J* = 7.4 Hz, 2H), 2.53 (t, *J* = 7.2 Hz, 2H), 2.37 (s, 3H), 2.06 (p, *J* = 7.2 Hz, 2H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 201.4, 169.2, 160.2, 152.5, 143.6, 128.9, 115.1, 114.3, 110.7, 102.8, 42.8, 27.5, 20.8, 19.9. **HRMS(ESI-TOF) m/z** $[M+Na]^+$

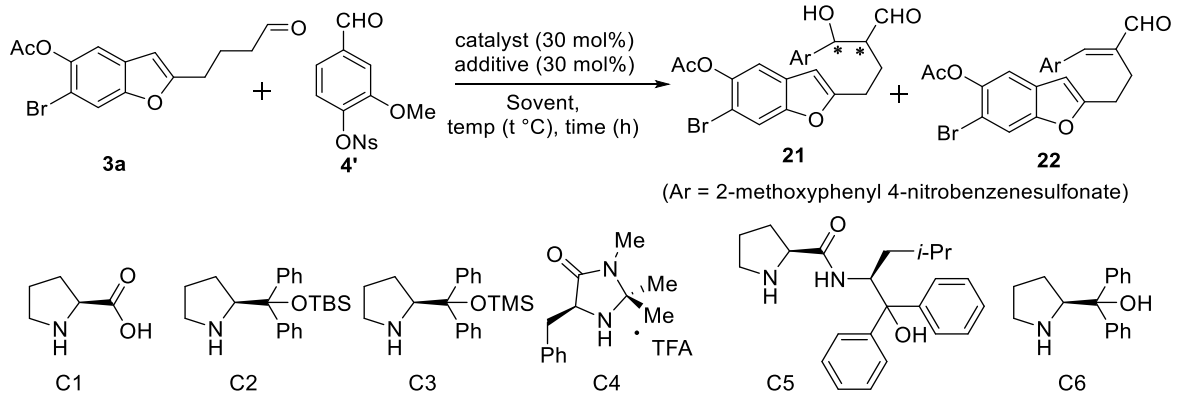
calcd for $C_{14}H_{13}{}^{79}BrNaO_4Si^+$/ $C_{14}H_{13}{}^{81}BrNaO_4Si^+$ 346.9889, and 348.9869; found 346.9892, and 348.9872 respectively.

Synthesis of 4-formyl-2-methoxyphenyl 4-nitrobenzenesulfonate (4')



To a solution of vanillin (10 g, 65.72 mmol) in dry acetonitrile were added successively 4-nitrobenzenesulfonyl chloride (17.5 g, 78.86 mmol) and potassium carbonate (13.96 g, 118.30 mmol) at rt. The mixture was then heated at 80 °C under inert atmosphere for overnight. The reaction was quenched by addition of NH_4Cl saturated and diluted with ethyl acetate. After extraction with ethyl acetate (3 times), the combined organic layers were washed successively with water and brine, dried over Na_2SO_4 and concentrated under reduced pressure. The pure compound was obtained by chromatography on silica gel (hexanes/EtOAc, 3:1) to afford nosyl-protected vanillin **4´** (21.73 g, quantitative). **R_f** = 0.25 (hexanes/EtOAc, 4:1); **^{1}H NMR (400 MHz, DMSO-*d*$_6$)** δ 9.95 (s, 1H), 8.45 (d, *J* = 8.8 Hz, 2H), 8.13 (d, *J* = 8.9 Hz, 2H), 7.57 (dd, *J* = 1.8 Hz, 8.2 Hz, 1H), 7.54 (s, 1H), 7.44 (d, *J* = 8.1 Hz, 1H), 3.58 (s, 3H); **^{13}C NMR (100 MHz, DMSO-*d*$_6$)** δ 192.0, 151.7, 151.1, 141.4, 140.2, 136.3, 130.0, 124.7, 124.6, 123.2, 112.9, 55.9; **IR (cm^{-1})** 1705, 1533, 1498, 133, 1350, 1273, 1199, 1147, 1115, 1089. **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{14}H_{11}NNaO_7S^+$ 360.0148; found 360.0144.

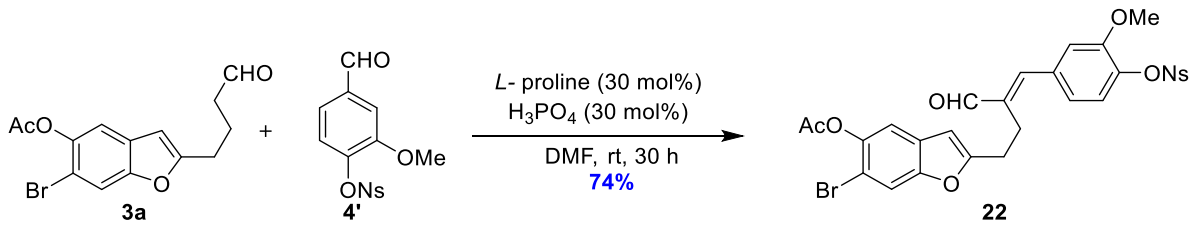
Table SI6. Unsuccessful trials of organocatalytic aldol reaction and optimization of aldol condensation reaction



entry	Catalyst	Additive	solvent	temp (^oC)	time (h)	Product	Yield (%)
1	C1	-	DMF	4	72	--	NR
2	C1	-	DMF	rt	48	**21**	traces
3	**C1**	**H_3PO_4**	**DMF**	**rt**	**30**	**22**	**74**
4	C1	4-nitro benzoic acid	DMF	rt	30	**22**	52
5	C1	rac- BPA	DMF	rt	48	**22**	58
6	C1	TFA	DMF	rt	48	**22**	43
7	C2-3	-	CH_2Cl_2	rt	24	--	NR
8	C2-3	-	Toluene	rt	24	--	NR
9	C2-3	H_3PO_4	DMF	rt	24	--	NR
10	C4	-	CH_2Cl_2	rt	12	--	NR
11	C4	-	DMF	rt	12	--	NR
12	C3	-	CH_2Cl_2	rt	24	--	NR
13	C3	-	DCE	rt	24	--	NR
14[b]	C6	-	THF/H_2O	20	48	--	NR
15[a]	C5	AcOH	DMSO	0-4 to rt	72	--	NR
16[a]	C5	AcOH	DMF	0-4 to rt	72	--	NR

All reactions were performed in 50 mg scale of the aldehyde **3a** using as a limiting reagent. Acceptor aldehyde **4′**was taken 5 equiv. [a]AcOH used 15 mol%, 5 mol% of C5 used, concentration 1M. [b] 3 mol% of C6 used. NR = No reaction.

Synthesis of (*E*)-6-bromo-2-(3-formyl-4-(3-methoxy-4-(((4-nitrophenyl)sulfonyl)oxy)phenyl)but-3-en-1-yl)benzofuran-5-yl acetate (22)

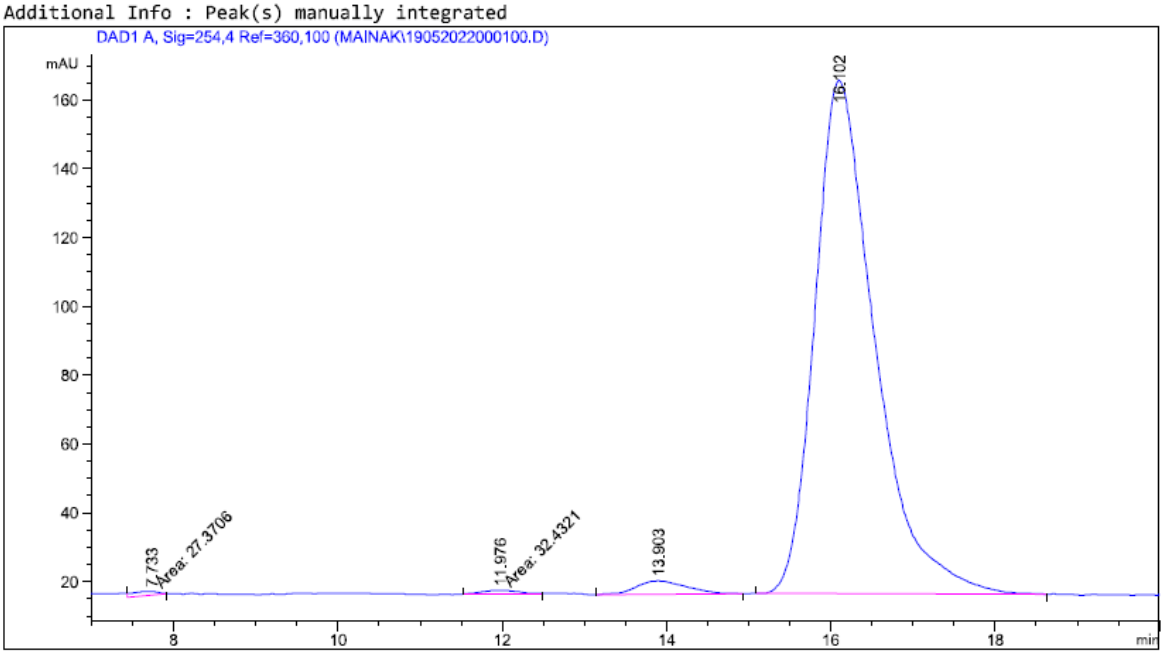


To a stirred solution of benzofuran aldehyde **3a** (500 mg, 1.54 mmol) and *L*-proline (53 mg, 0.46 mmol) in DMF (15.4 mL) at rt nosyl protected vanillin **4′**(2.6 g, 7.7 mmol) was added at a time and continued the reaction for 30 h at the same temperature. The reaction mixture was diluted with diethyl ether (200 mL) and water 50 mL. The aqueous part was again extracted with diethyl ether (2×50 mL). Next combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The pure compound was obtained by chromatography on silica gel (hexanes/EtOAc, 9:1 to 4:1) to afford **22** (733 mg) as a light green solid. **Yield:** 74%. $\mathbf{R_f}$ = 0.25 (hexanes/EtOAc, 3:1); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 9.60 (s, 1H), 8.42 (d, *J* = 8.4 Hz, 2H), 8.17 (d, *J* = 8.4 Hz, 2H), 7.54 (s, 1H), 7.29 (d, *J* = 10.0 Hz, 2H), 7.22 (s, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.84 (s, 1H), 6.35 (s, 1H), 3.55 (s, 3H), 2.98 (s, 4H), 2.40 (s, 3H); **^{13}C NMR (100 MHz, Chloroform-*d*)** δ 194.7, 169.1, 159.5, 152.4, 151.5, 150.9, 149.3, 143.7, 142.0, 141.9, 138.5, 134.9, 129.9, 128.8, 124.3, 124.0, 122.0, 115.0, 114.4, 113.2, 111.0, 103.2, 55.6, 26.7, 23.3, 20.8; **IR (cm^{-1})** 2976, 1764, 1681, 1532, 1500, 1450, 1404, 1377, 1348, 1205, 1185, 1160, 1120, 1090. **HRMS(ESI-TOF) m/z** $[M+Na]^+$ calcd for $C_{28}H_{22}{}^{79}BrNNaO_{10}S^+$/ $C_{28}H_{22}{}^{81}BrNNaO_{10}S^+$ 666.0040, and 668.0020; found 666.0046, and 668.0016 respectively.

HPLC chromatogram of aldol product 2

Sample Info : SAMPLE-342, PURE
MeOH/WATER- 80/20
FLOW RATE:..1.0mL/min
254nm
C18

Additional Info : Peak(s) manually integrated



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.733	MM	0.3141	27.37062	1.05599	0.3502
2	11.976	MM	0.5207	32.43206	1.03800	0.4150
3	13.903	BB	0.5181	172.42802	3.92818	2.2065
4	16.102	BB	0.7489	7582.45020	149.19926	97.0283
Totals :				7814.68089	155.22144	

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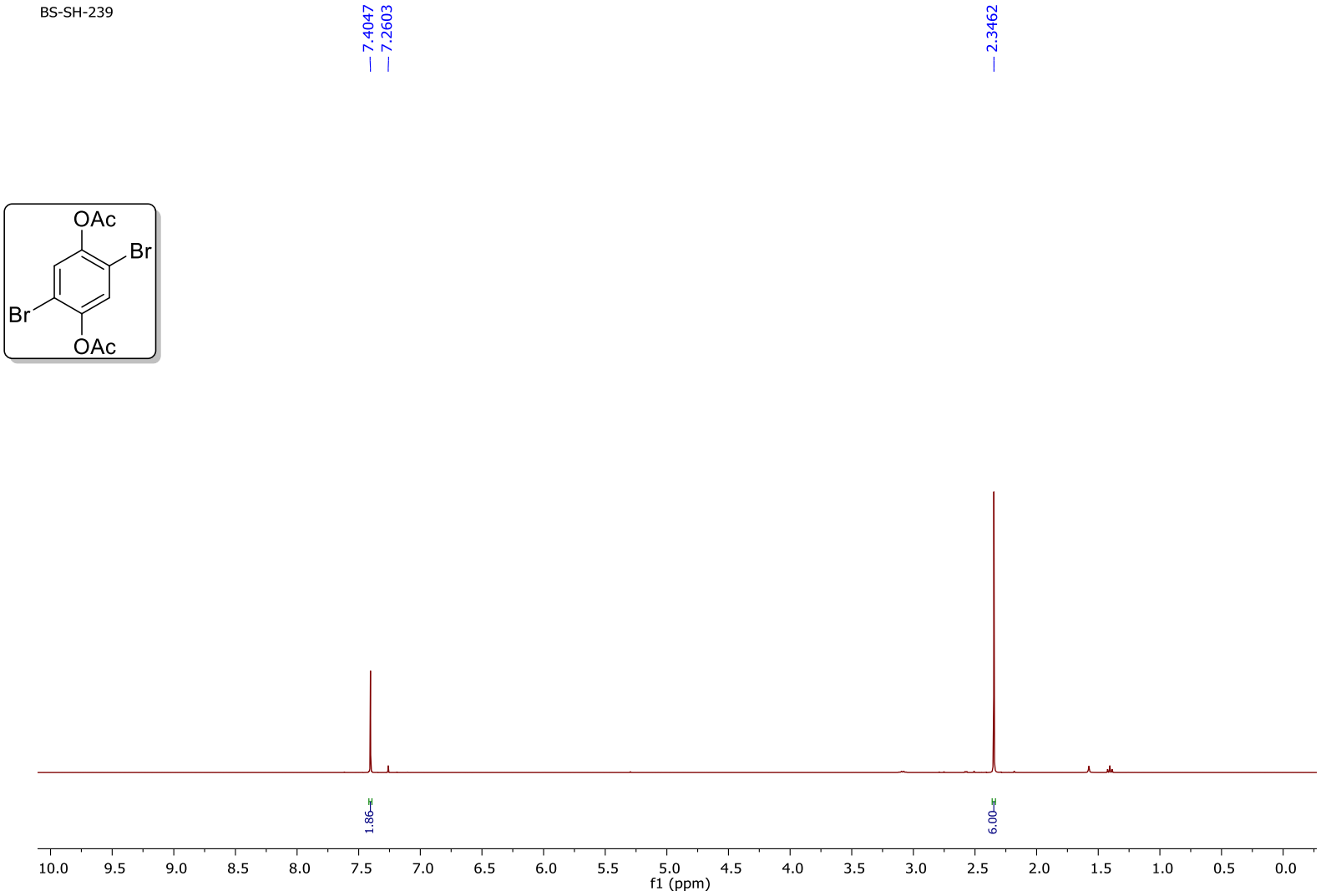
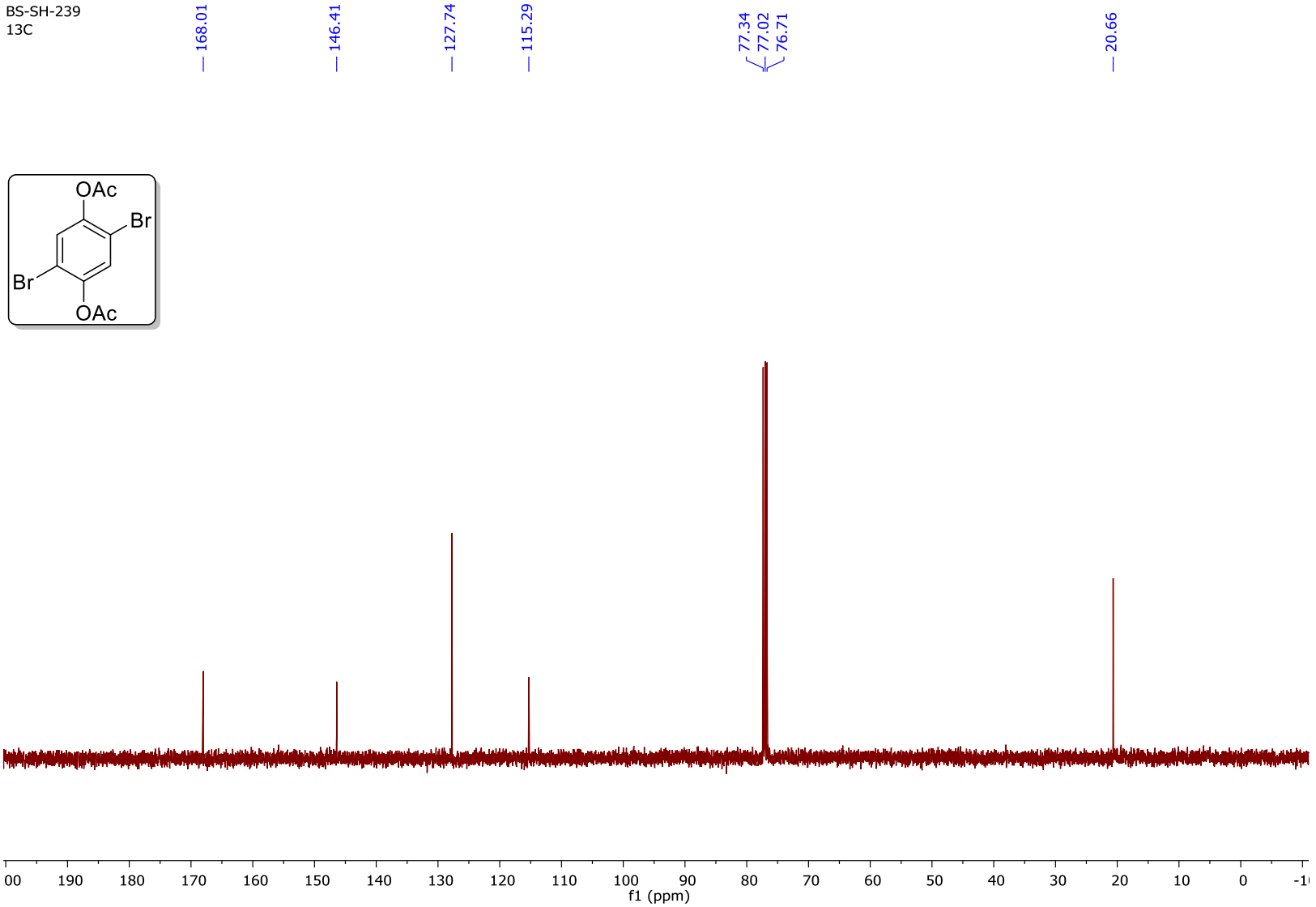
6) Guay, B.; Deslongchamps, P. *J. Org. Chem.* **2003**, *68*, 6140–6148.

SPECTRA

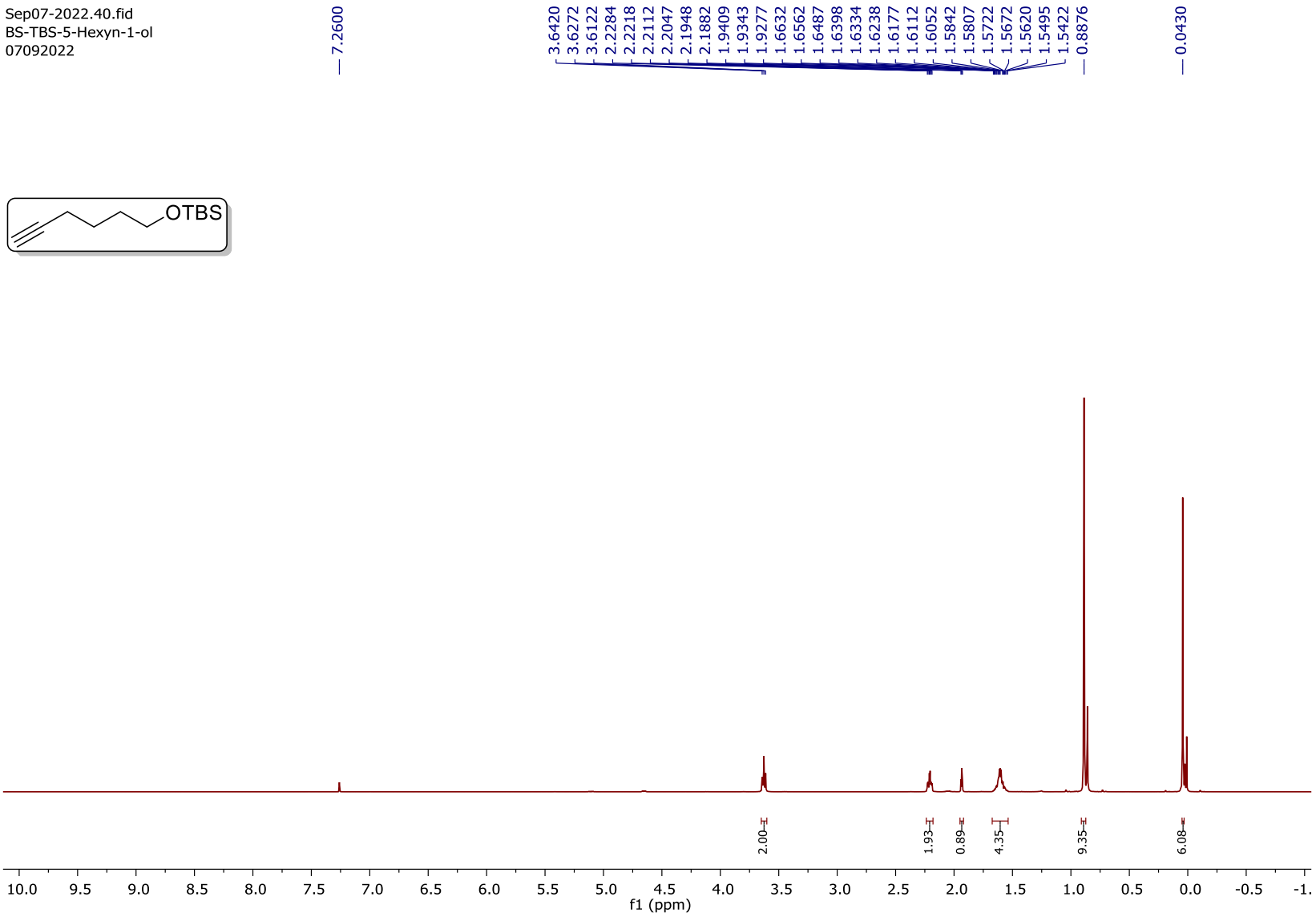
^{1}H NMR of 2,5-dibromo-1,4-phenylene diacetate (5b) (400 MHz, $CDCl_3$)



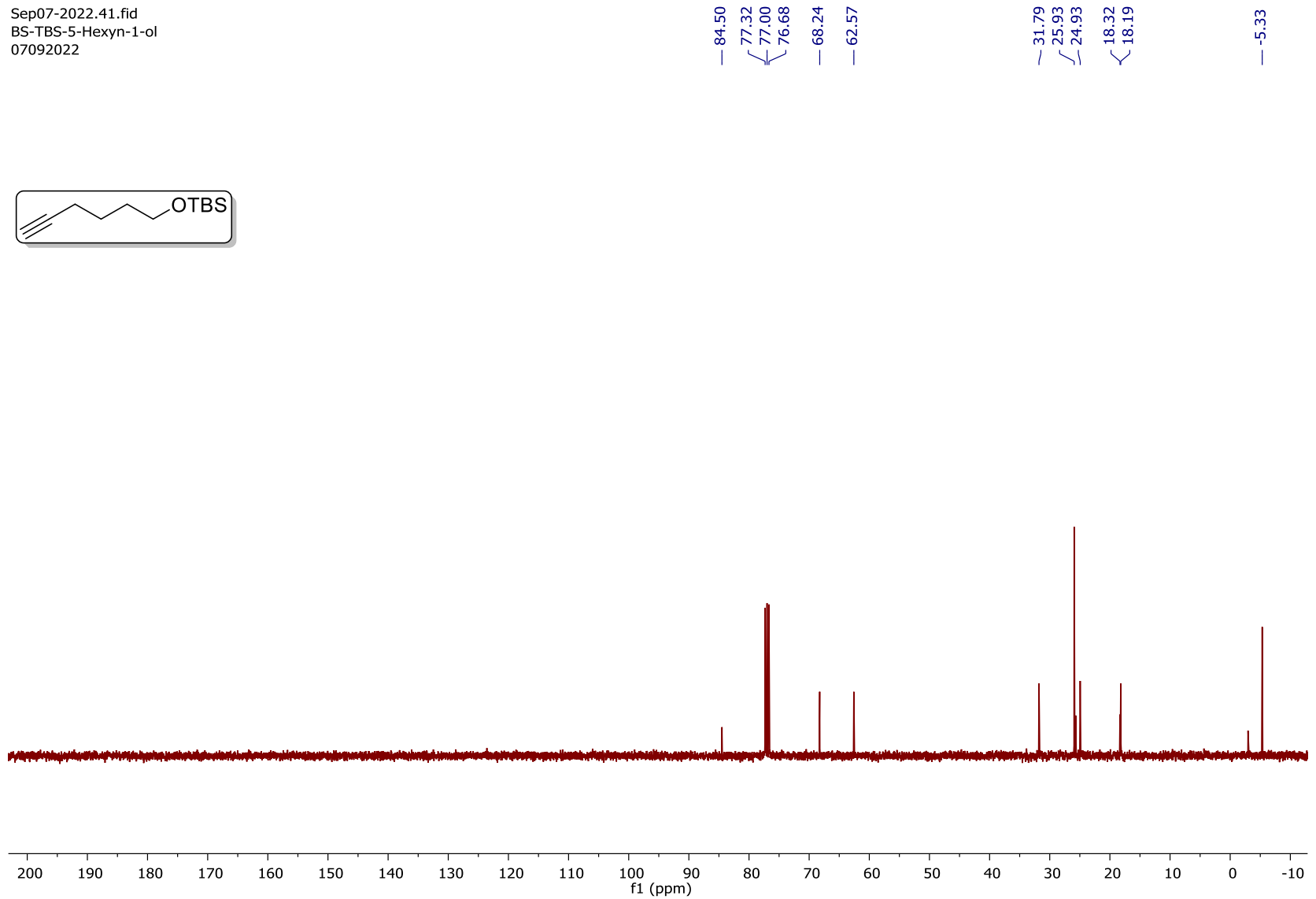
^{13}C NMR of 2,5-dibromo-1,4-phenylene diacetate (5b) (100 MHz, $CDCl_3$)



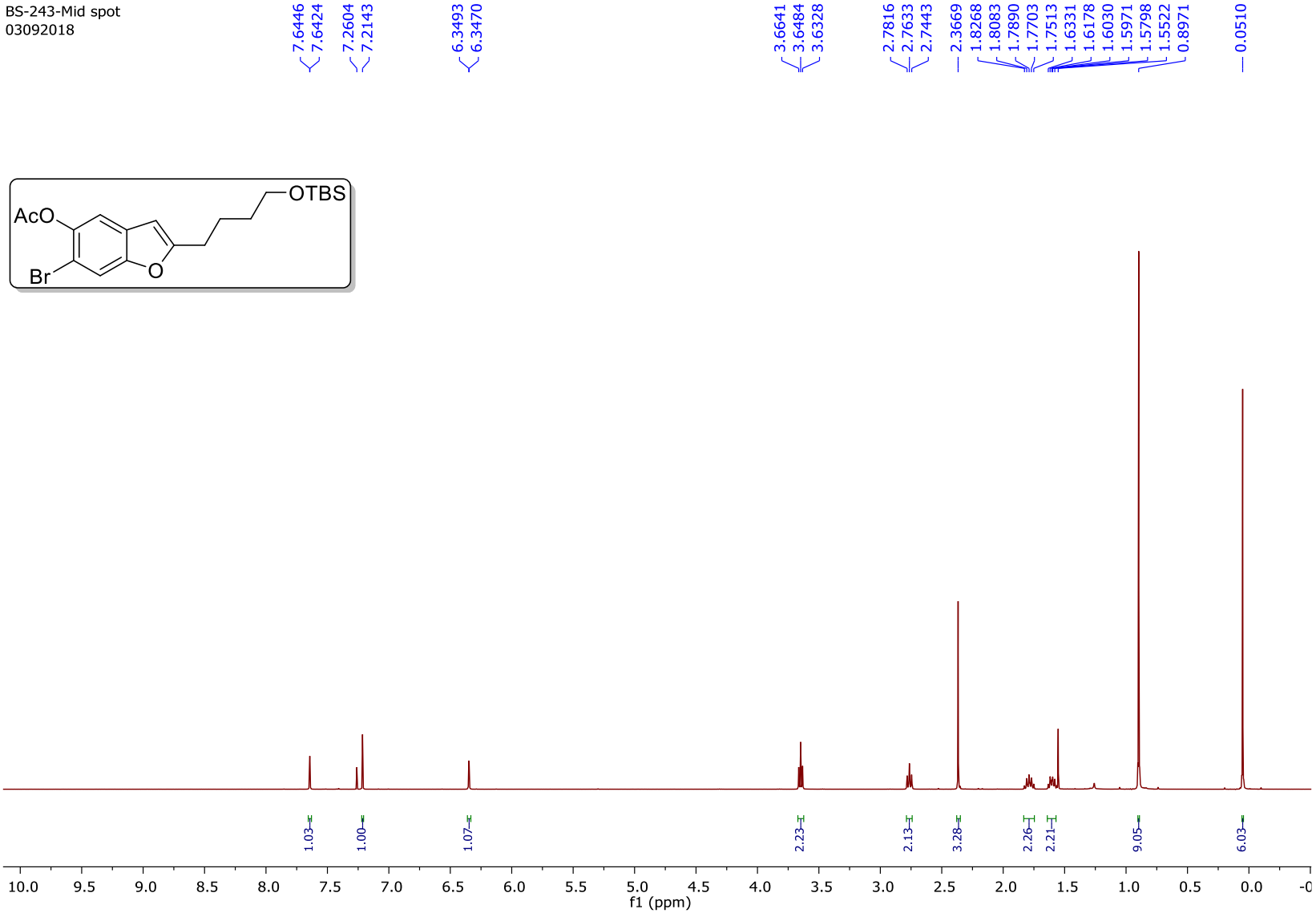
^{1}H NMR of *tert*-butyl(hex-5-yn-1-yloxy)dimethylsilane (6a) (400 MHz, $CDCl_3$)



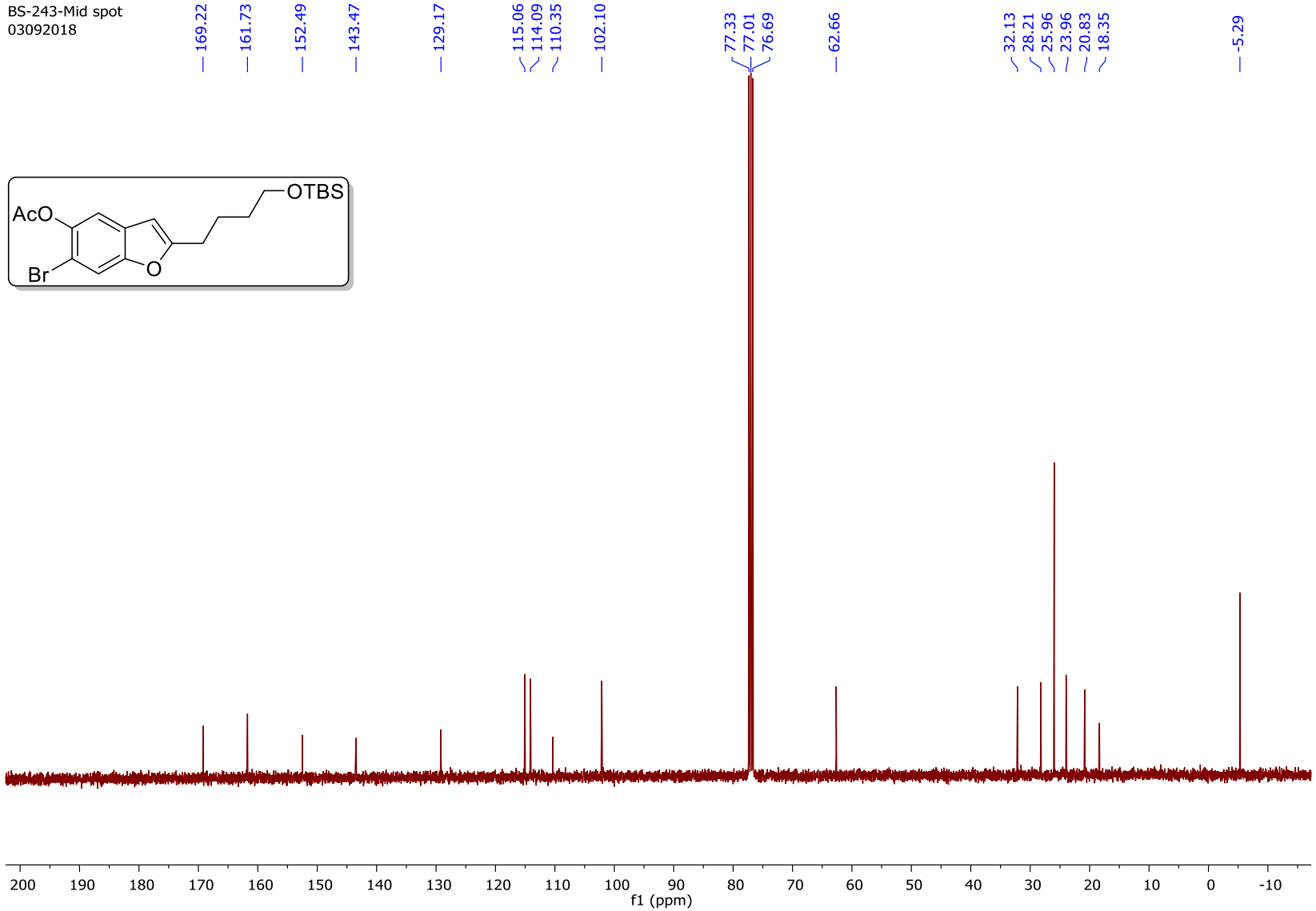
^{13}C NMR of *tert*-butyl(hex-5-yn-1-yloxy)dimethylsilane (6a) (100 MHz, $CDCl_3$)



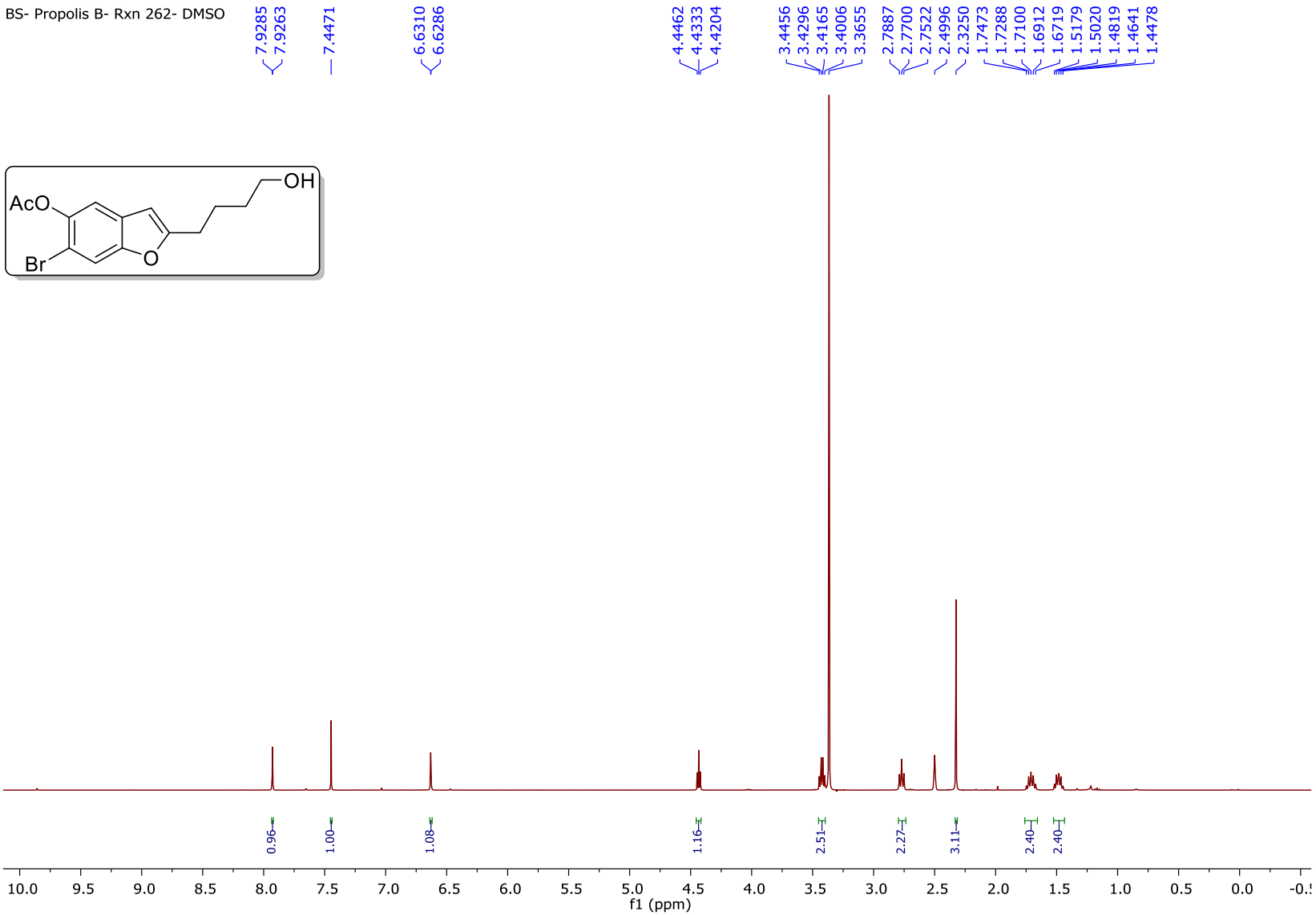
^{1}H NMR of 6-bromo-2-(4-((*tert*-butyldimethylsilyl)oxy)butyl)benzofuran-5-yl acetate (8ba) (400 MHz, $CDCl_3$)



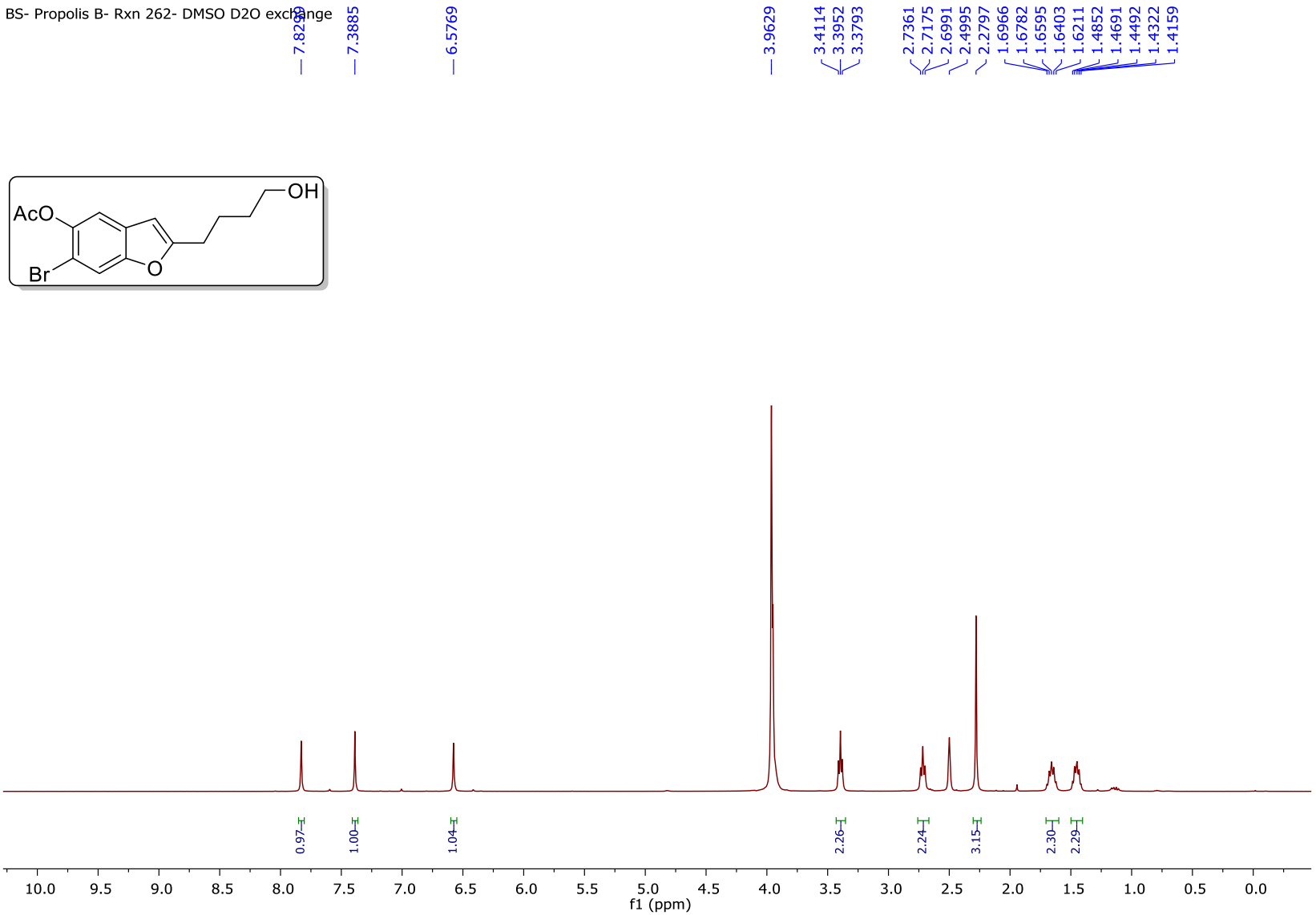
^{13}C NMR of 6-bromo-2-(4-((*tert*-butyldimethylsilyl)oxy)butyl)benzofuran-5-yl acetate (8ba) (100 MHz, $CDCl_3$)



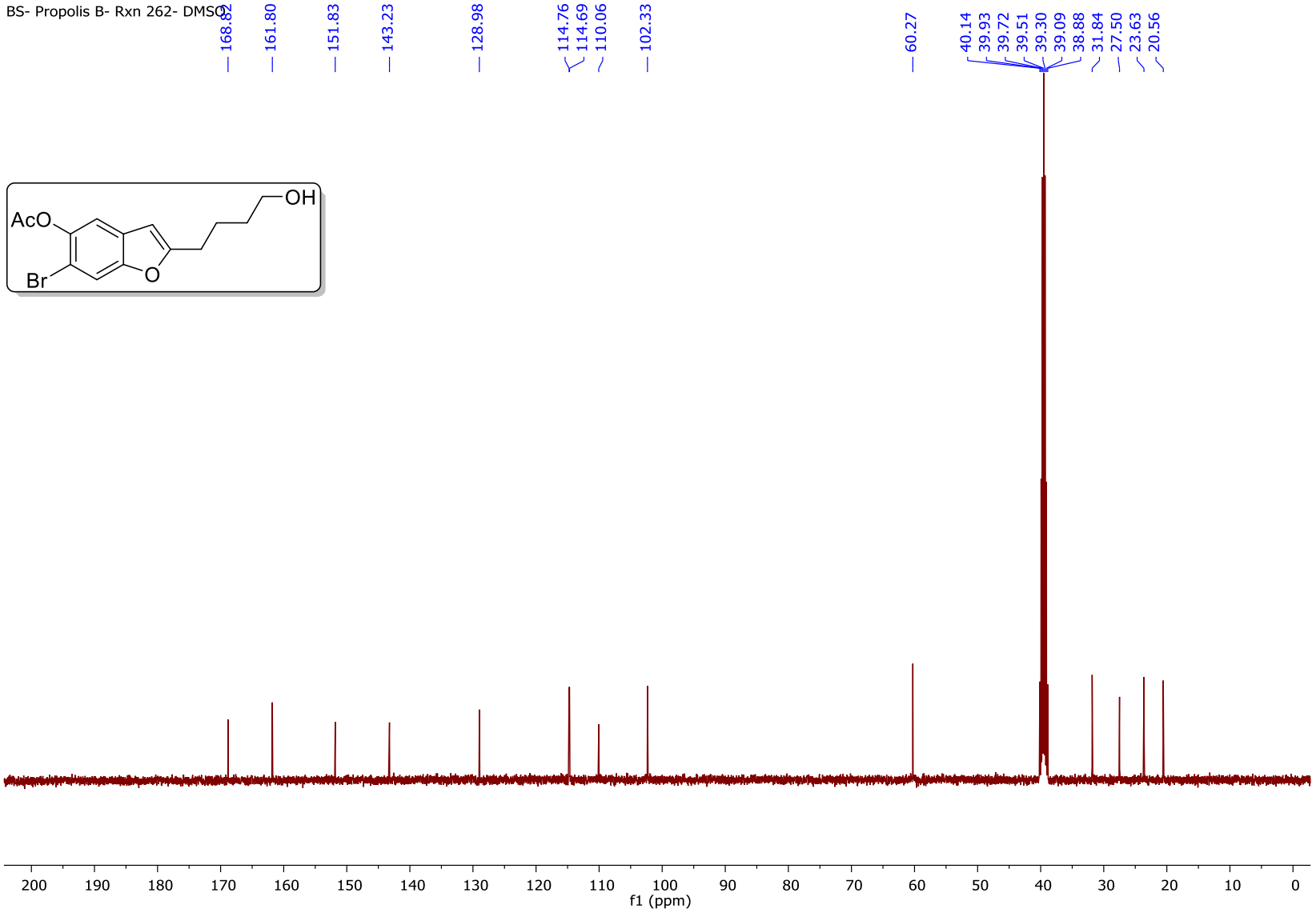
^{1}H NMR of 6-bromo-2-(4-hydroxybutyl)benzofuran-5-yl acetate (8bb) (400 MHz, DMSO-*d*$_6$)



D_2O exchanged ^1H NMR of 6-bromo-2-(4-hydroxybutyl)benzofuran-5-yl acetate (8bb) (400 MHz, DMSO-d_6)



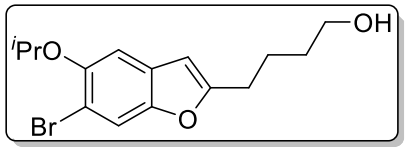
^{13}C NMR of 6-bromo-2-(4-hydroxybutyl)benzofuran-5-yl acetate (8bb) (100 MHz, DMSO-*d*$_6$)

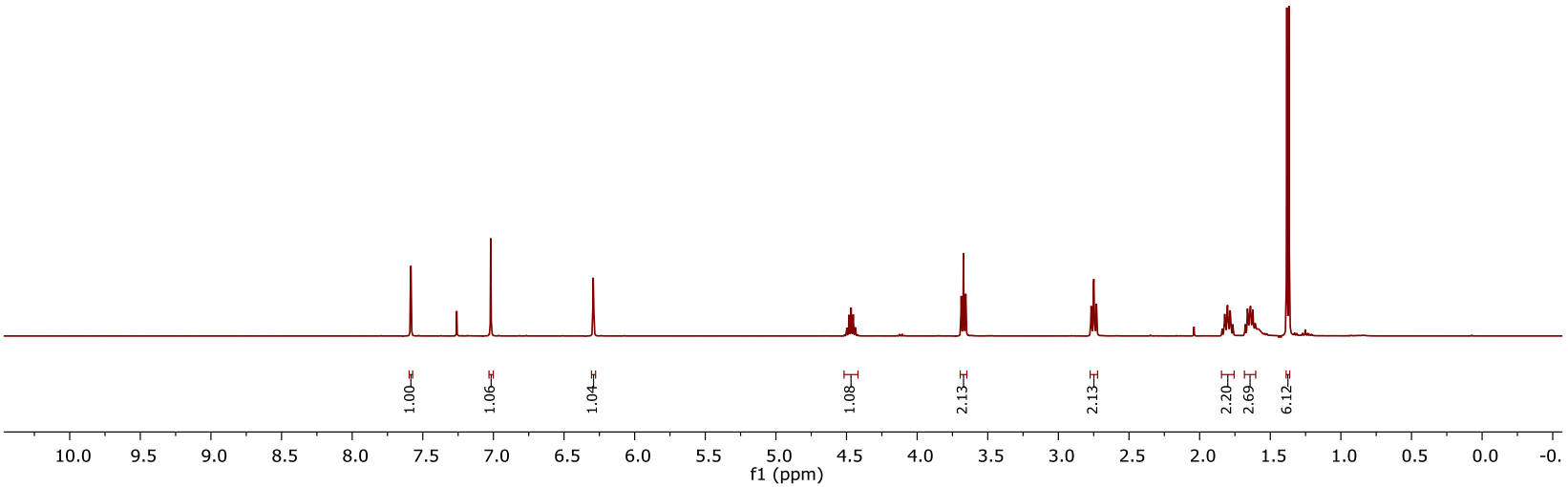


^{1}H NMR of 4-(6-bromo-5-isopropoxybenzofuran-2-yl)butan-1-ol (9) (400 MHz, $CDCl_3$)

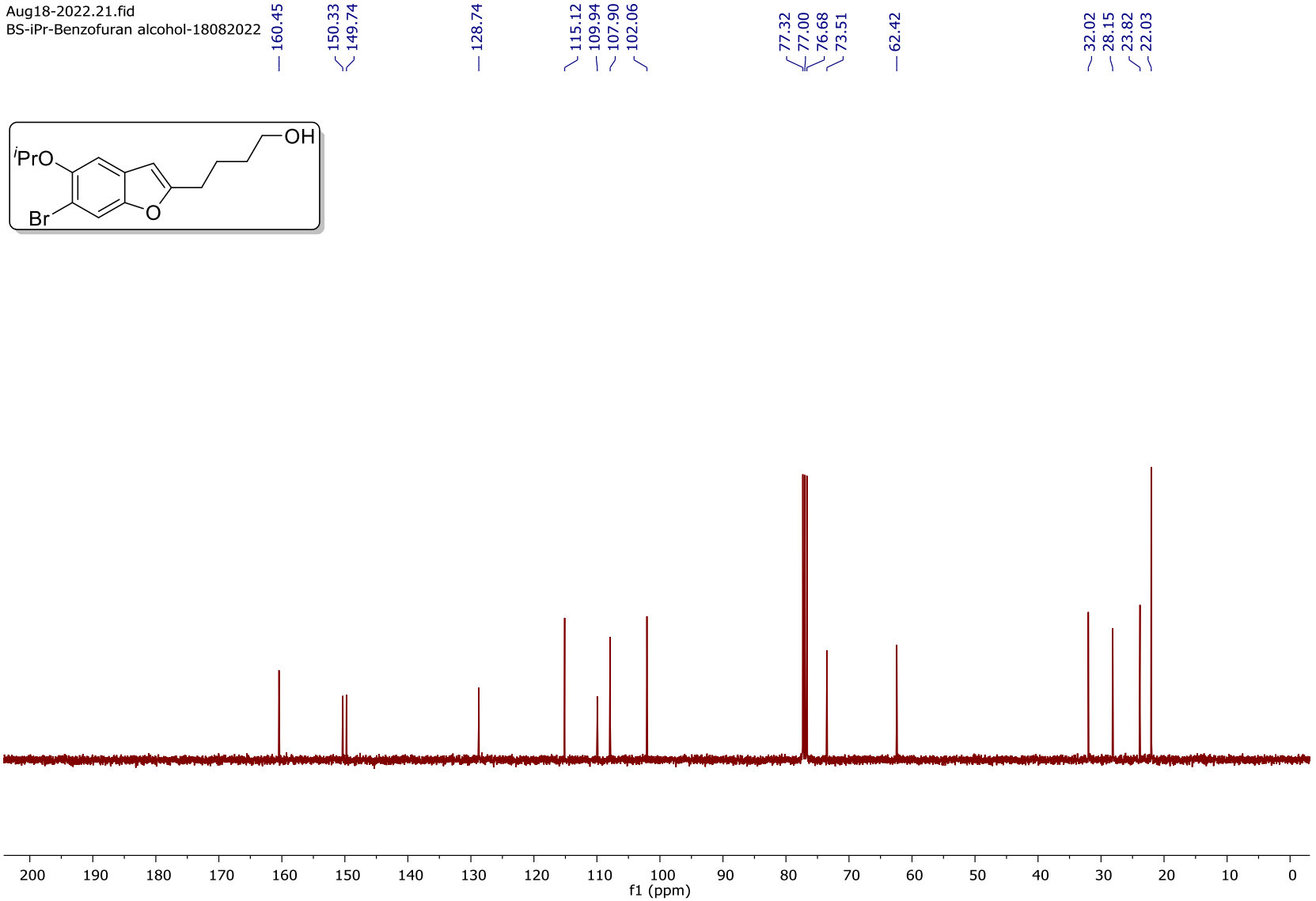
Aug18-2022.20.fid
BS-iPr-Benzofuran alcohol-18082022

7.5860 7.5837 7.2598 7.0192 6.2938 6.2914 4.5132 4.4980 4.4828 4.4676 4.4524 4.4371 4.4220 3.6880 3.6718 3.6559 2.7678 2.7494 2.7308 1.8404 1.8220 1.8026 1.7837 1.7648 1.6772 1.6612 1.6400 1.6234 1.6065 1.3829 1.3677

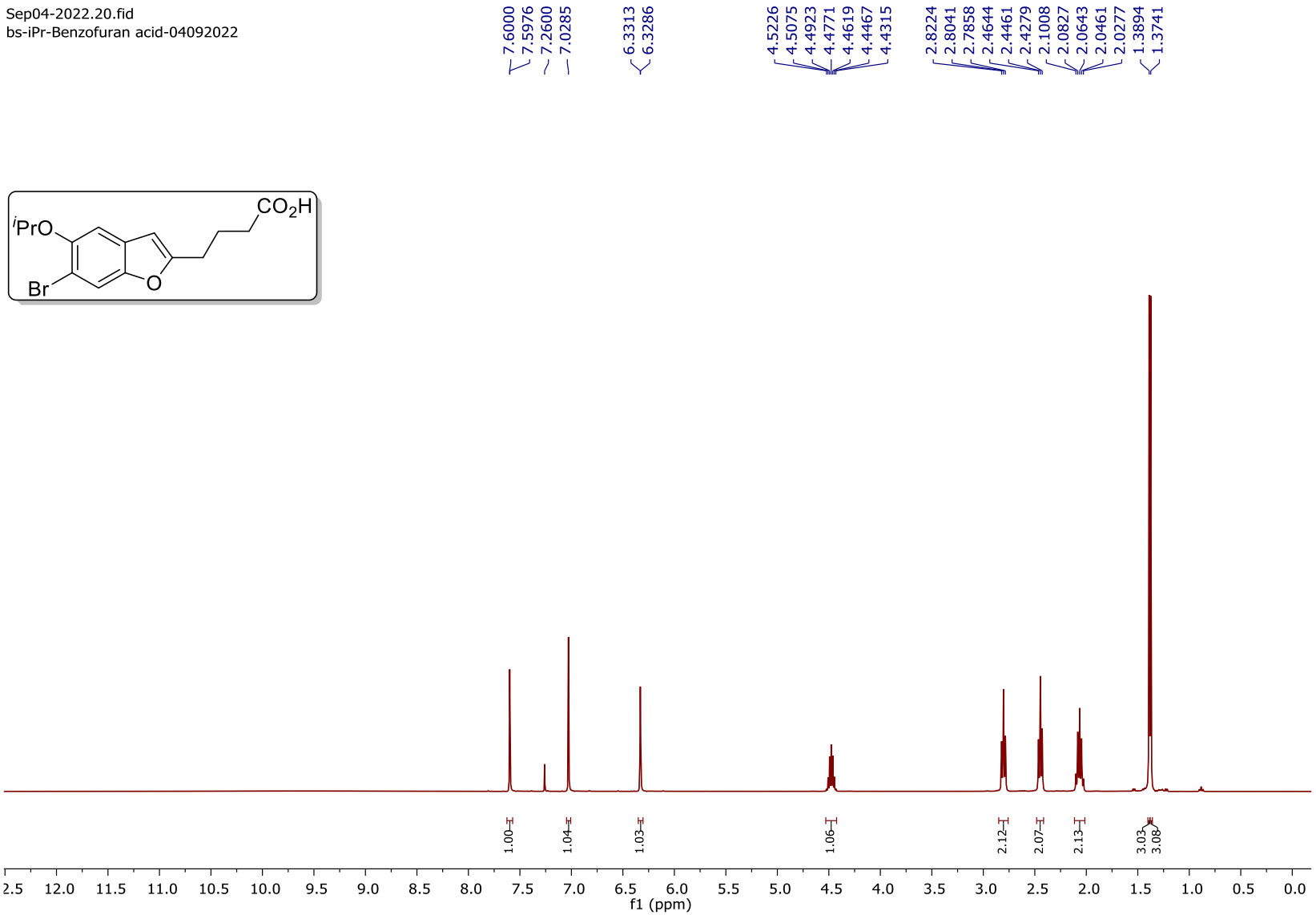




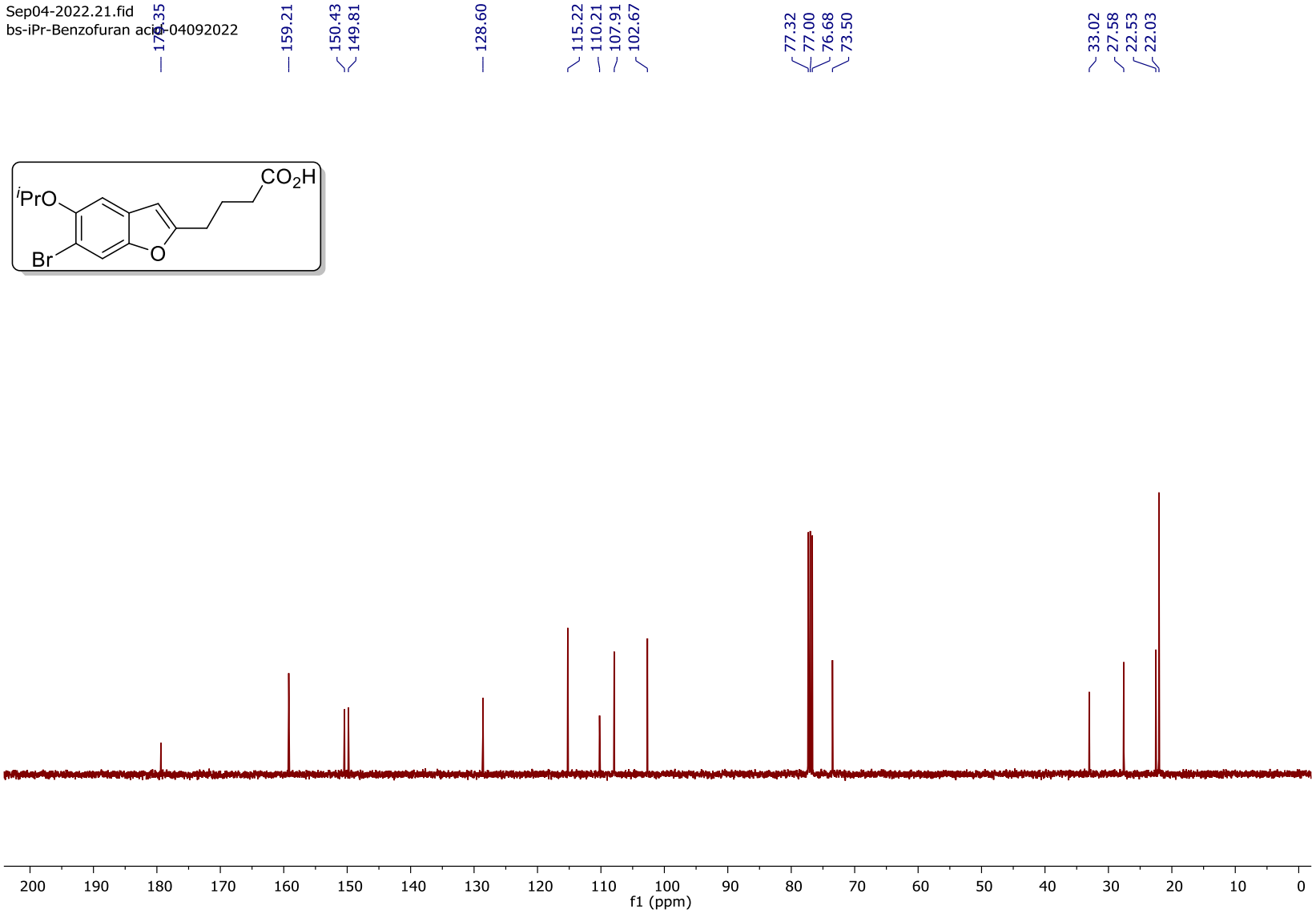
^{13}C NMR of 4-(6-bromo-5-isopropoxybenzofuran-2-yl)butan-1-ol (9) (100 MHz, $CDCl_3$)



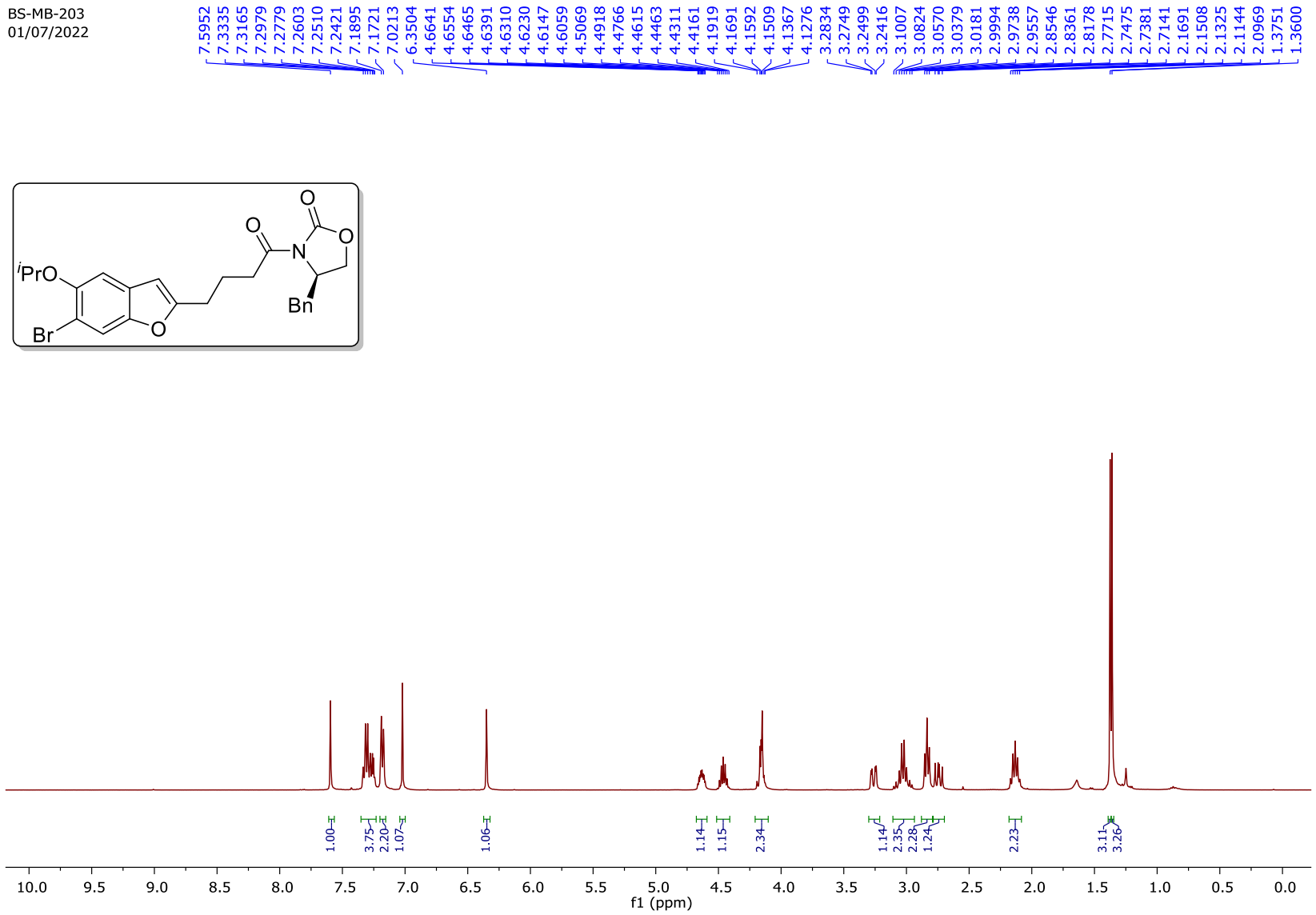
^{1}H NMR of 4-(6-bromo-5-isopropoxybenzofuran-2-yl)butanoic acid (10) (400 MHz, $CDCl_3$)



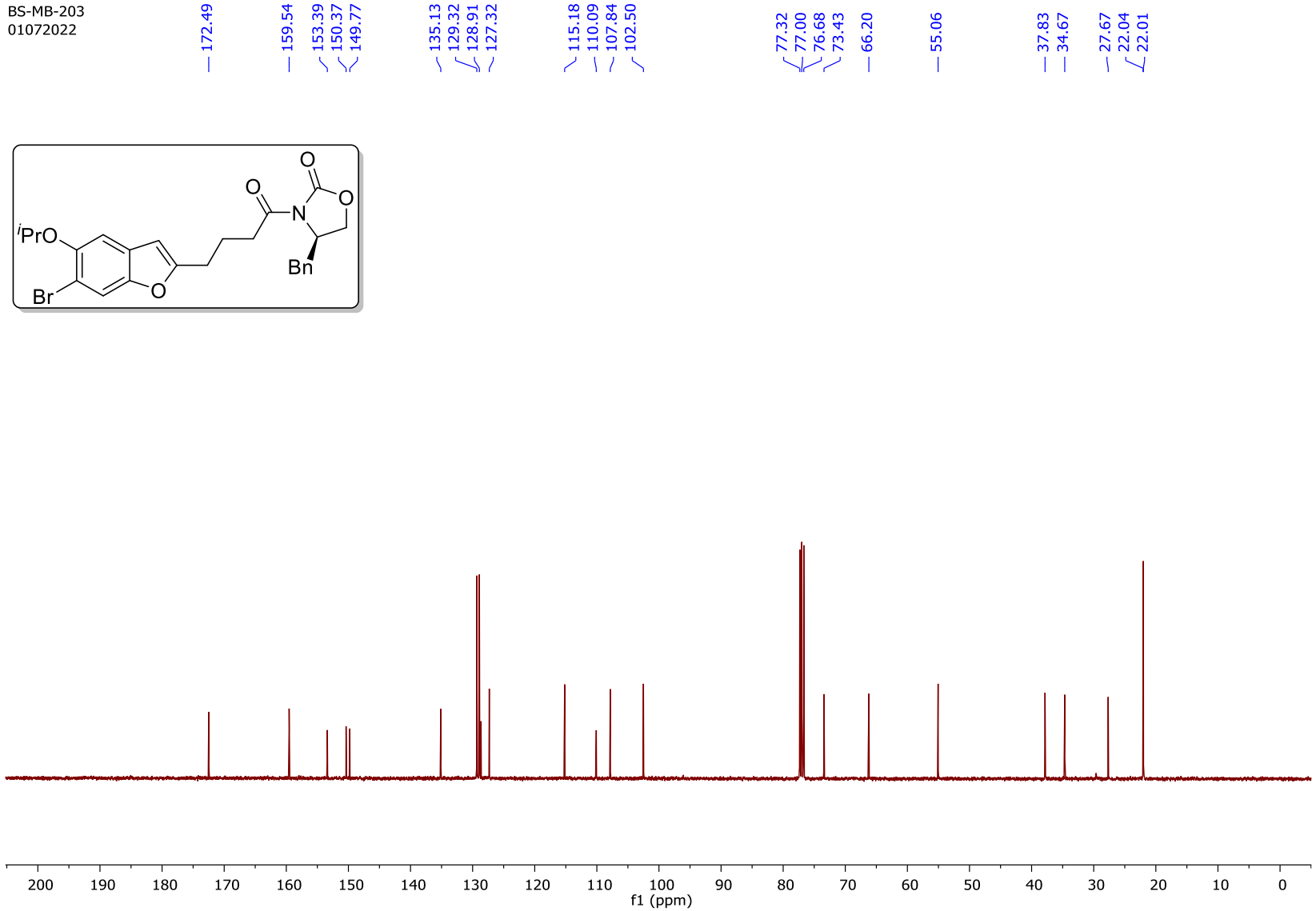
^{13}C NMR of 4-(6-bromo-5-isopropoxybenzofuran-2-yl)butanoic acid (10) (100 MHz, $CDCl_3$)



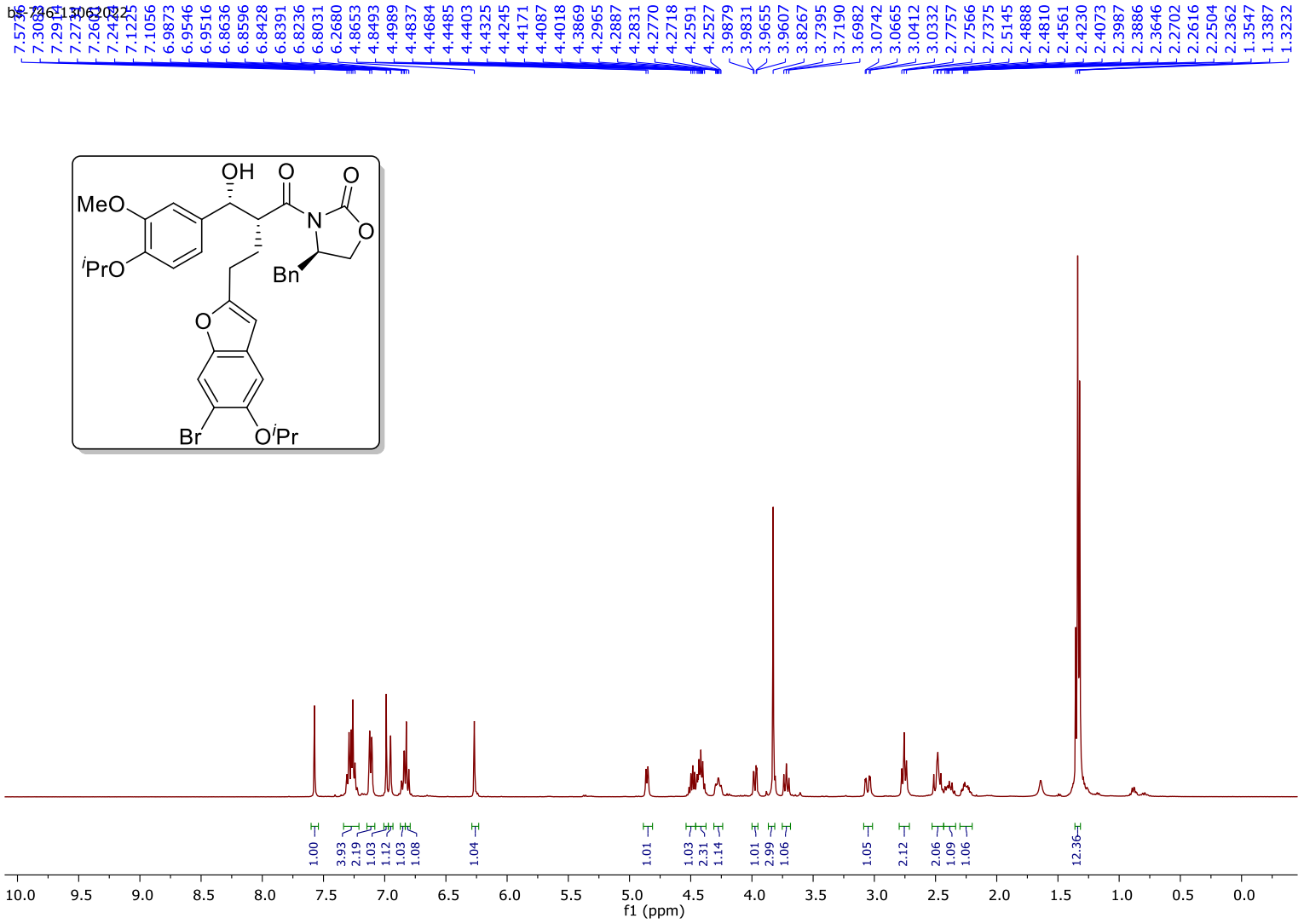
^{1}H NMR of (*R*)-4-benzyl-3-(4-(6-bromo-5-isopropoxybenzofuran-2-yl)butanoyl)oxazolidin-2-one (3b) (400 MHz, $CDCl_3$)



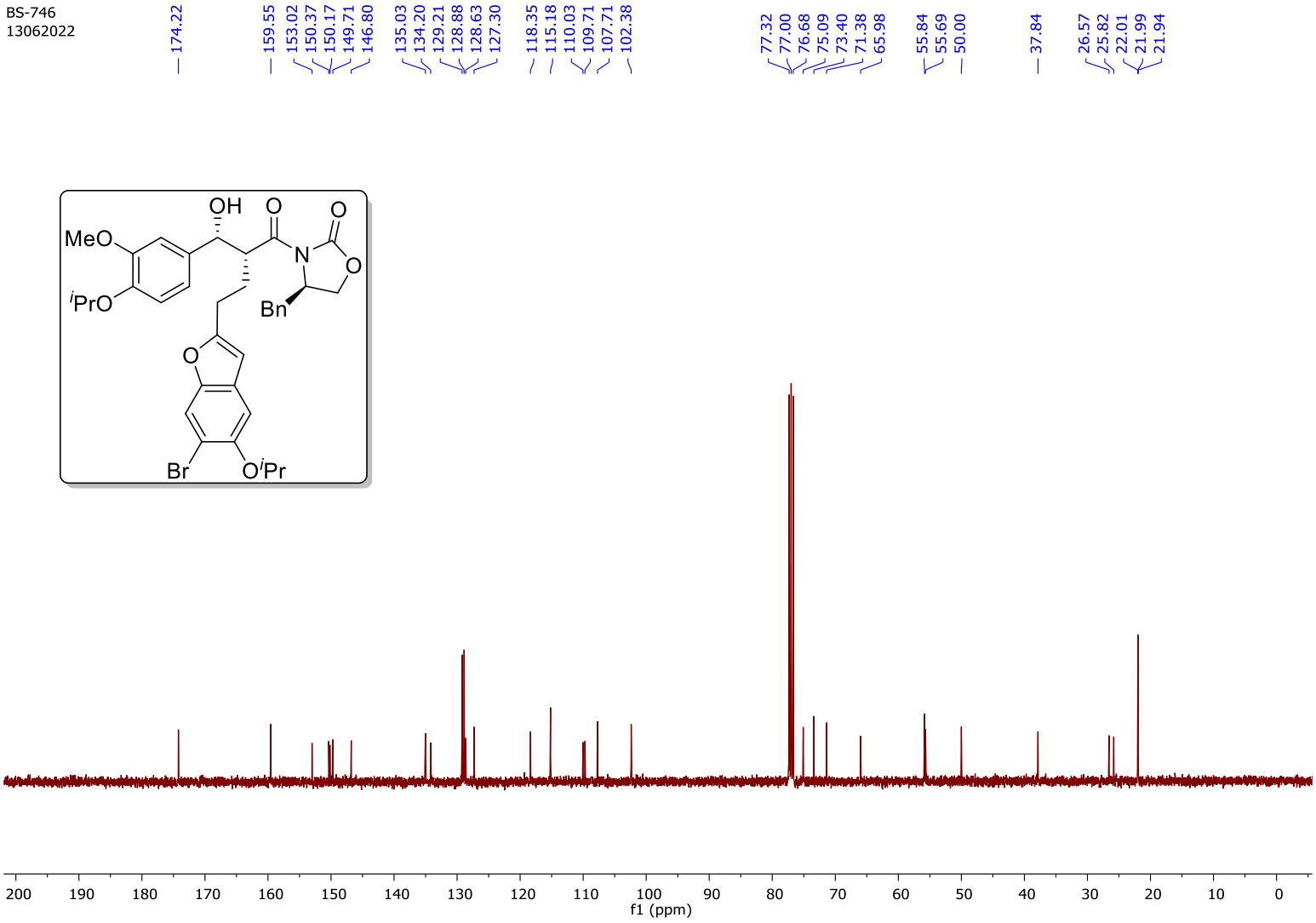
^{13}C NMR of (*R*)-4-benzyl-3-(4-(6-bromo-5-isopropoxybenzofuran-2-yl)butanoyl)oxazolidin-2-one (3b) (100 MHz, $CDCl_3$)



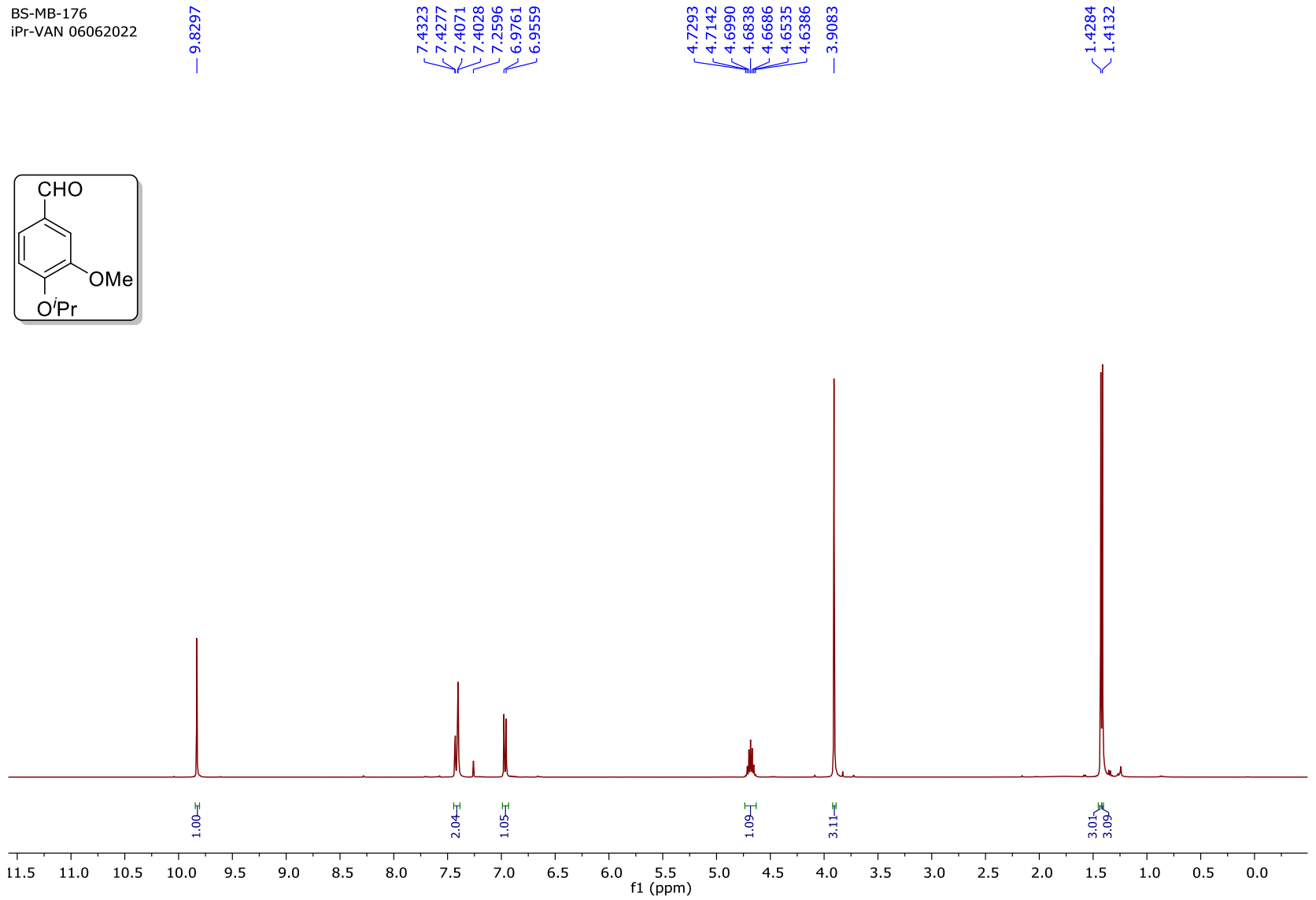
^{1}H NMR of (*R*)-4-benzyl-3-((*R*)-4-(6-bromo-5-isopropoxybenzofuran-2-yl)-2-((*R*)-hydroxy(4-isopropoxy-3-methoxyphenyl)methyl)butanoyl)oxazolidin-2-one (12) (400 MHz, $CDCl_3$)



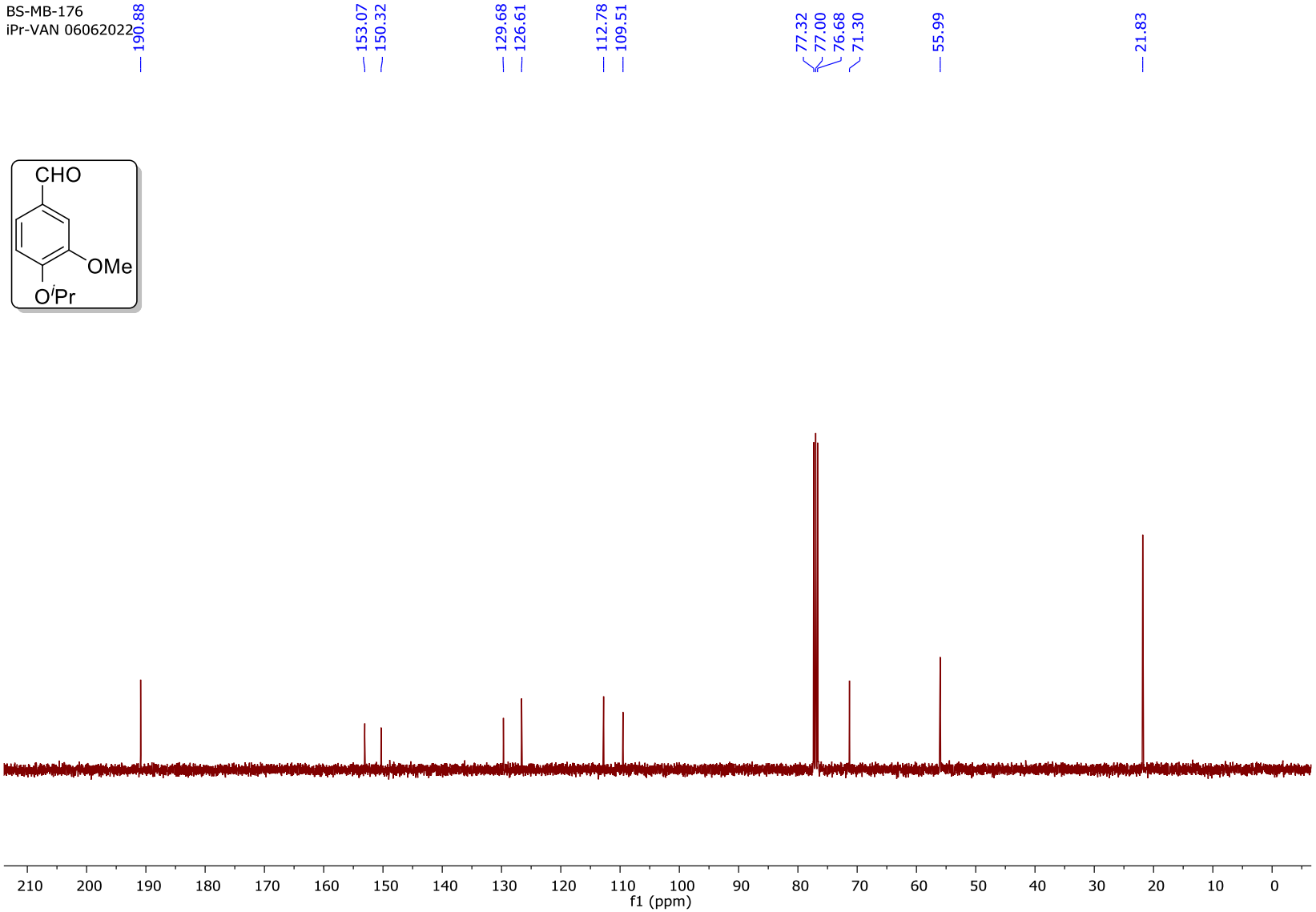
^{13}C NMR of (*R*)-4-benzyl-3-((*R*)-4-(6-bromo-5-isopropoxybenzofuran-2-yl)-2-((*R*)-hydroxy(4-isopropoxy-3-methoxyphenyl)methyl)butanoyl)oxazolidin-2-one (12) (100 MHz, $CDCl_3$)



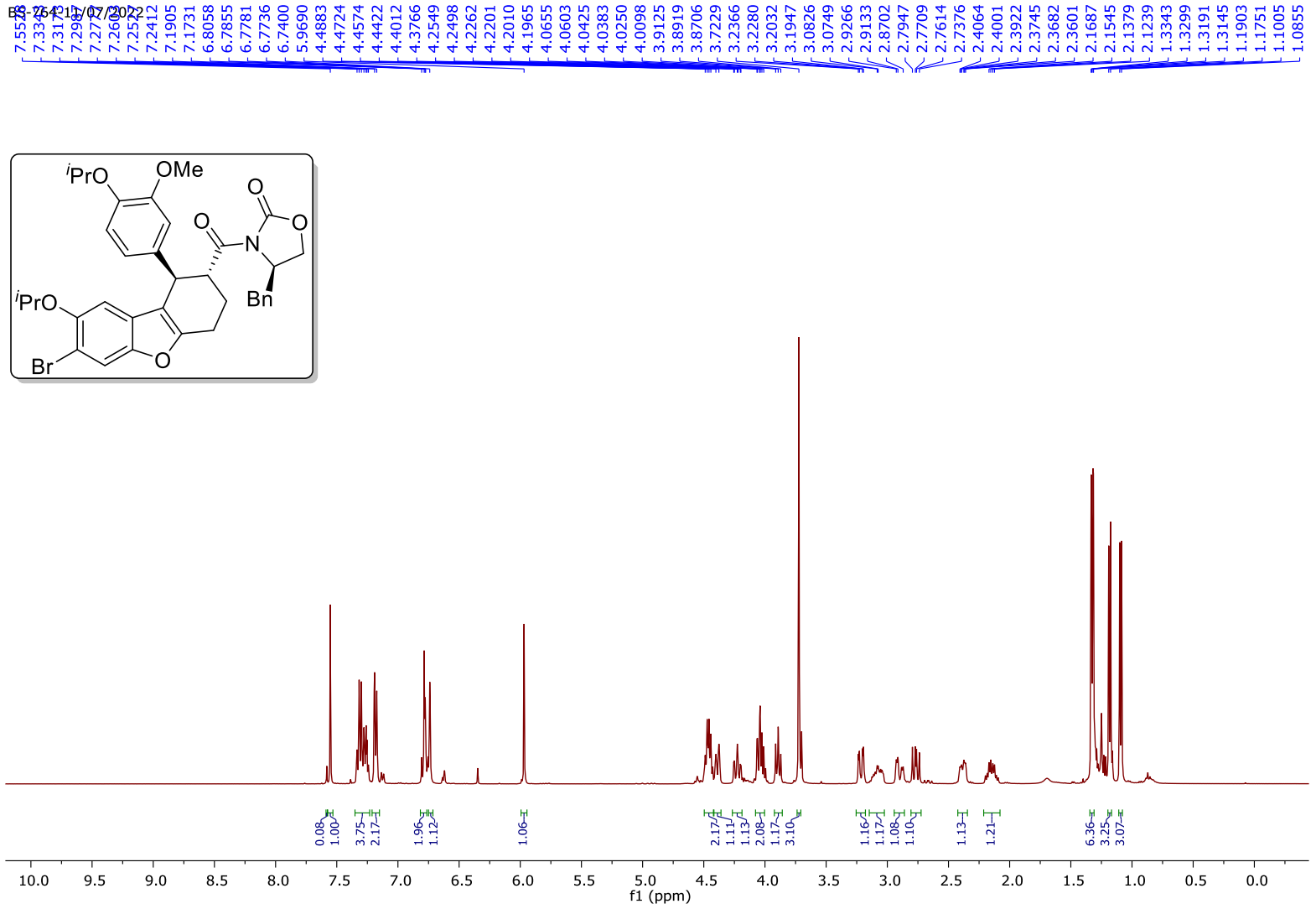
^{1}H NMR of 4-isopropoxy-3-methoxybenzaldehyde (4) (400 MHz, $CDCl_3$)



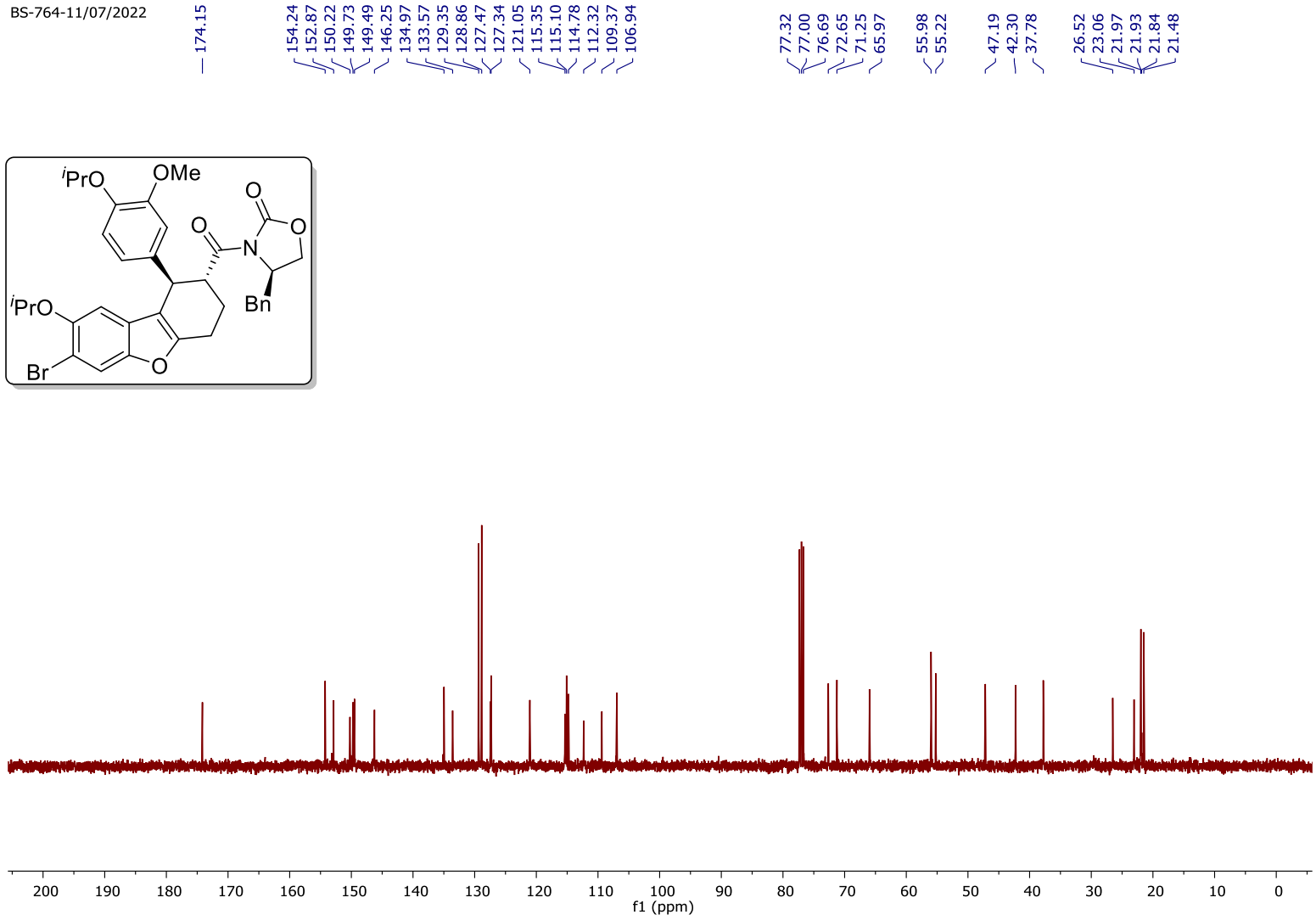
^{13}C NMR of 4-isopropoxy-3-methoxybenzaldehyde (4) (100 MHz, $CDCl_3$)



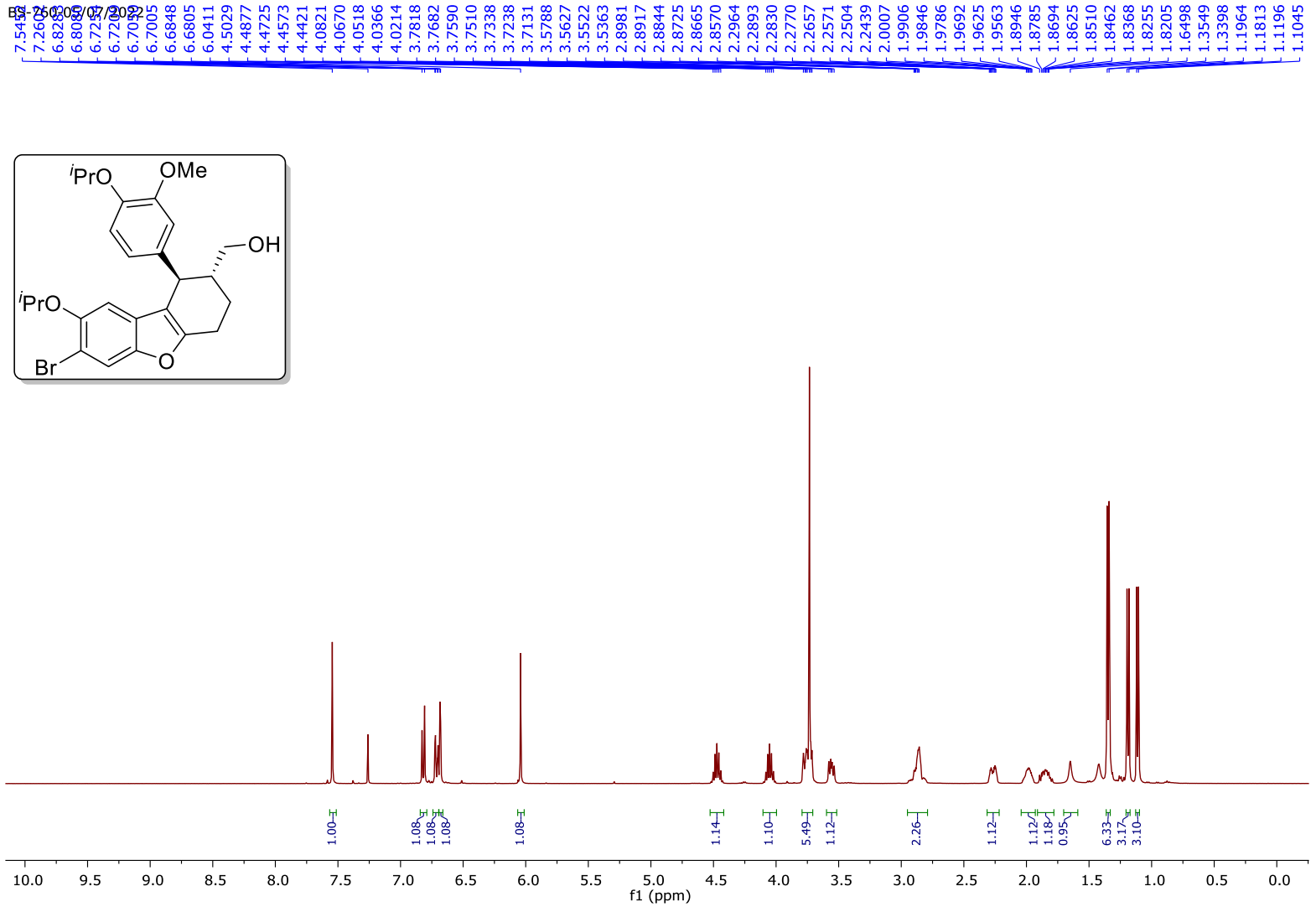
^{1}H NMR of (*R*)-4-benzyl-3-((1*R*,2*R*)-7-bromo-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-carbonyl)oxazolidin-2-one (13) (400 MHz, $CDCl_3$)



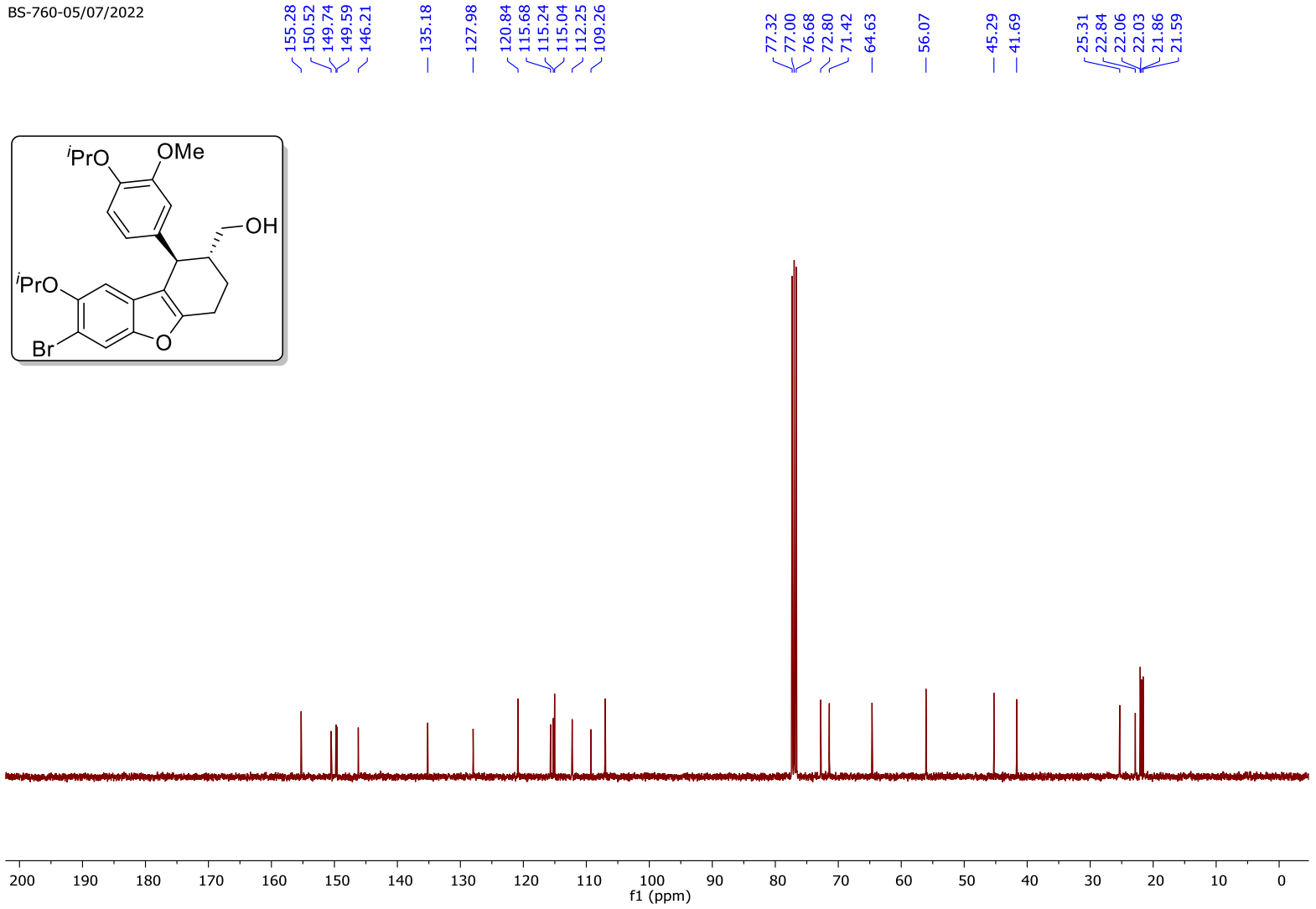
^{13}C NMR of (*R*)-4-benzyl-3-((1*R*,2*R*)-7-bromo-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-carbonyl)oxazolidin-2-one (13) (100 MHz, $CDCl_3$)



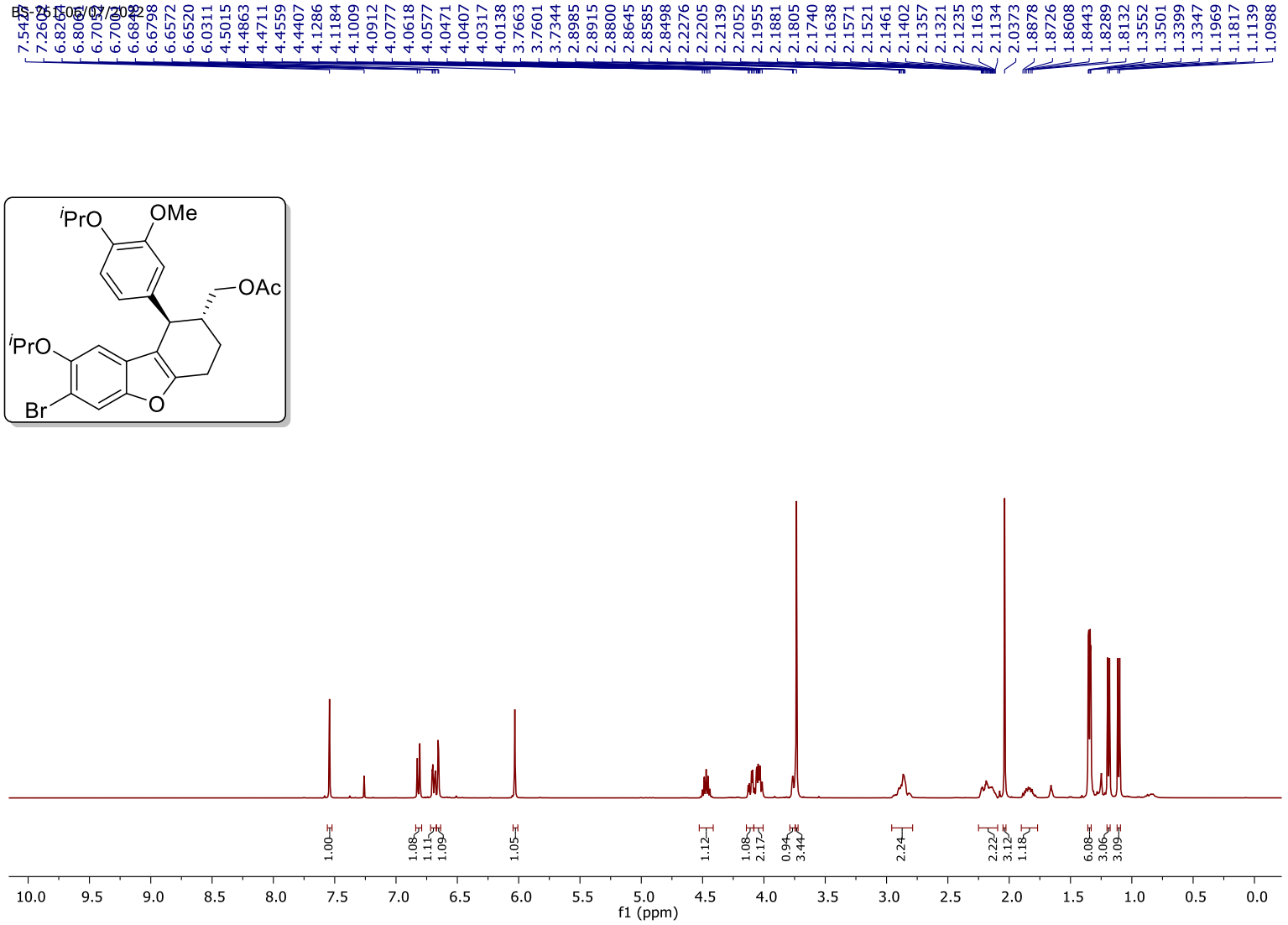
^{1}H NMR of ((1*R*,2*R*)-7-bromo-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methanol (2′) (400 MHz, $CDCl_3$)



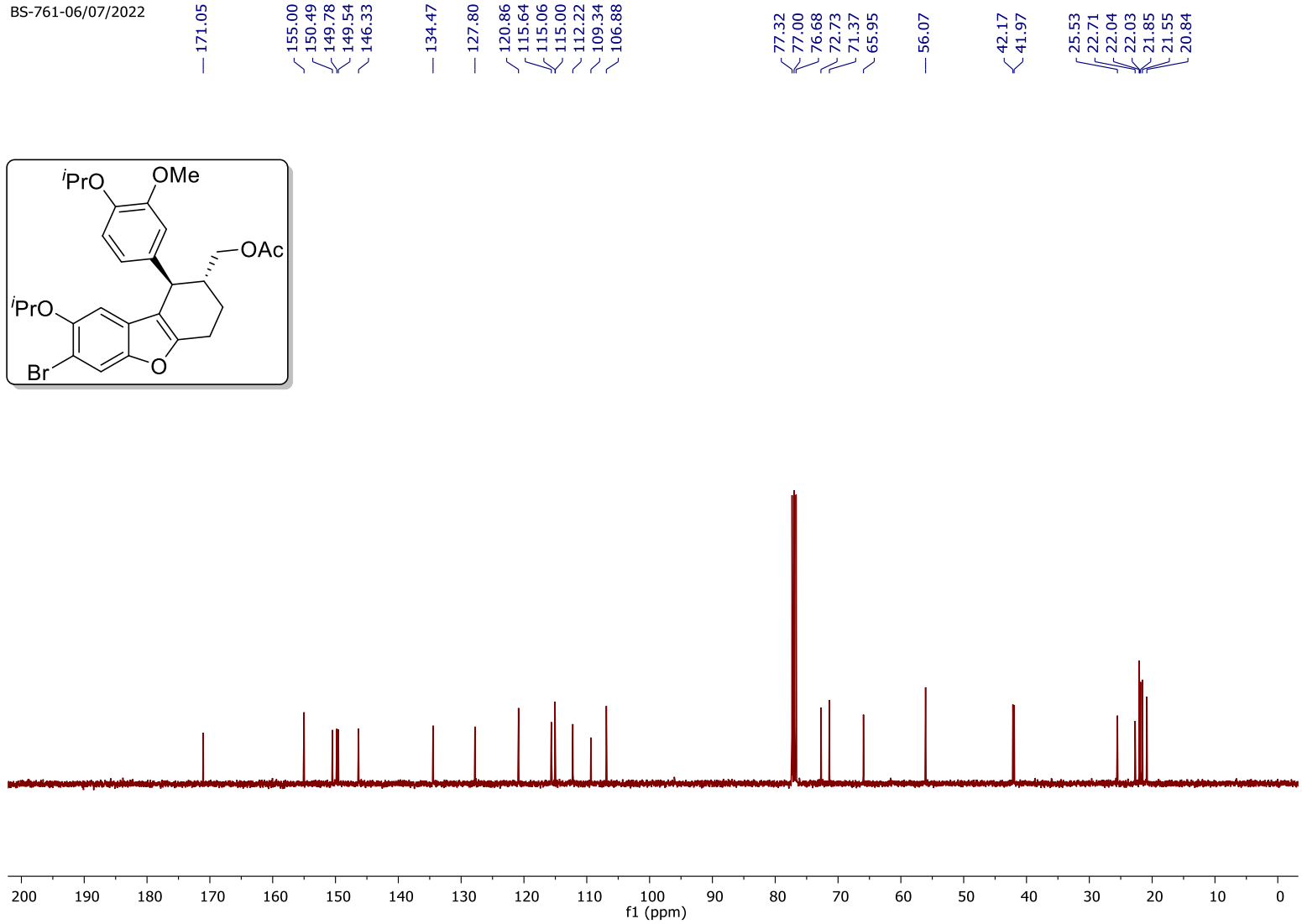
^{13}C NMR of ((1*R*,2*R*)-7-bromo-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methanol (2′) (100 MHz, $CDCl_3$)



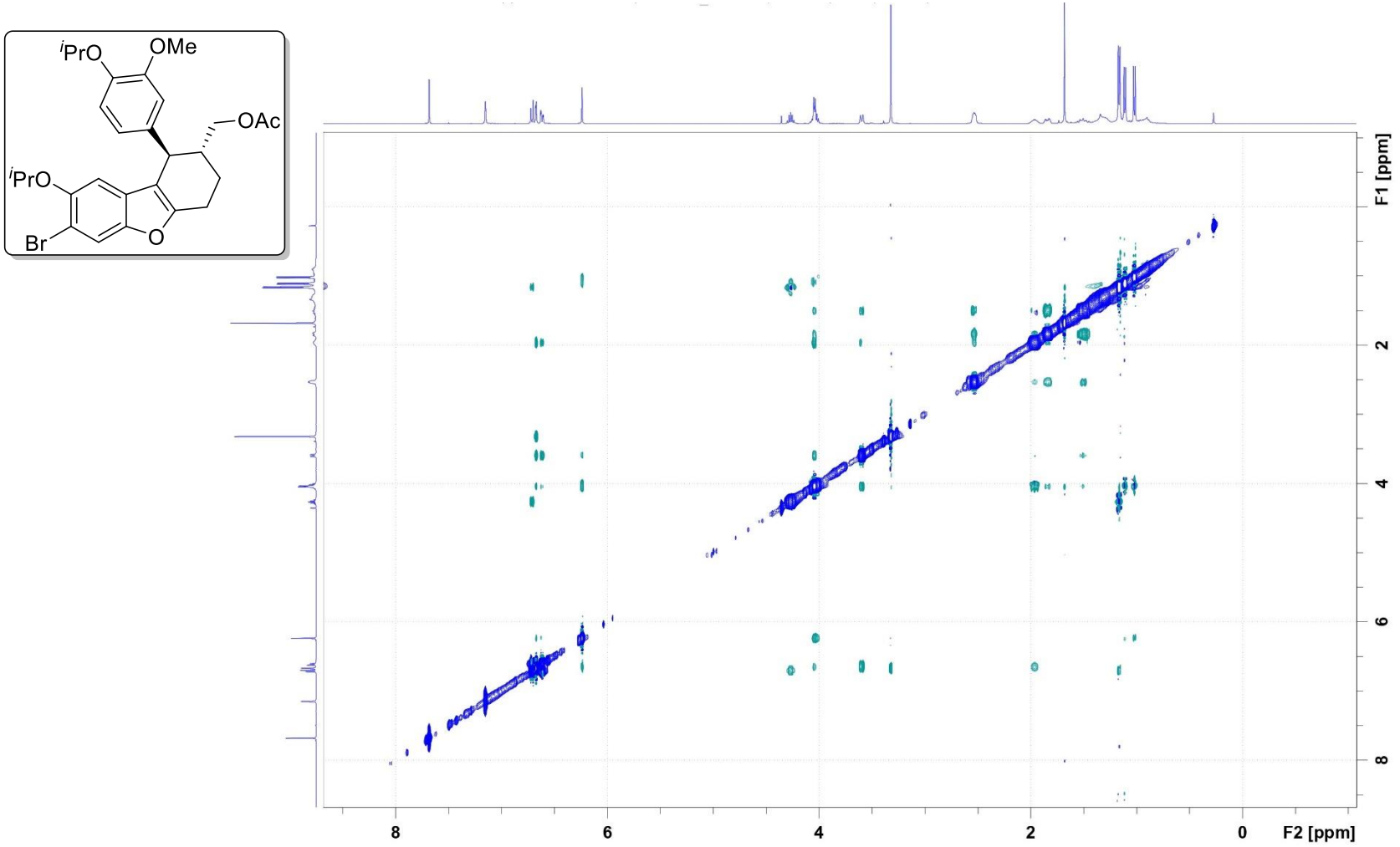
^{1}H NMR of ((1*R*,2*R*)-7-bromo-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methyl acetate (2) (400 MHz, $CDCl_3$)



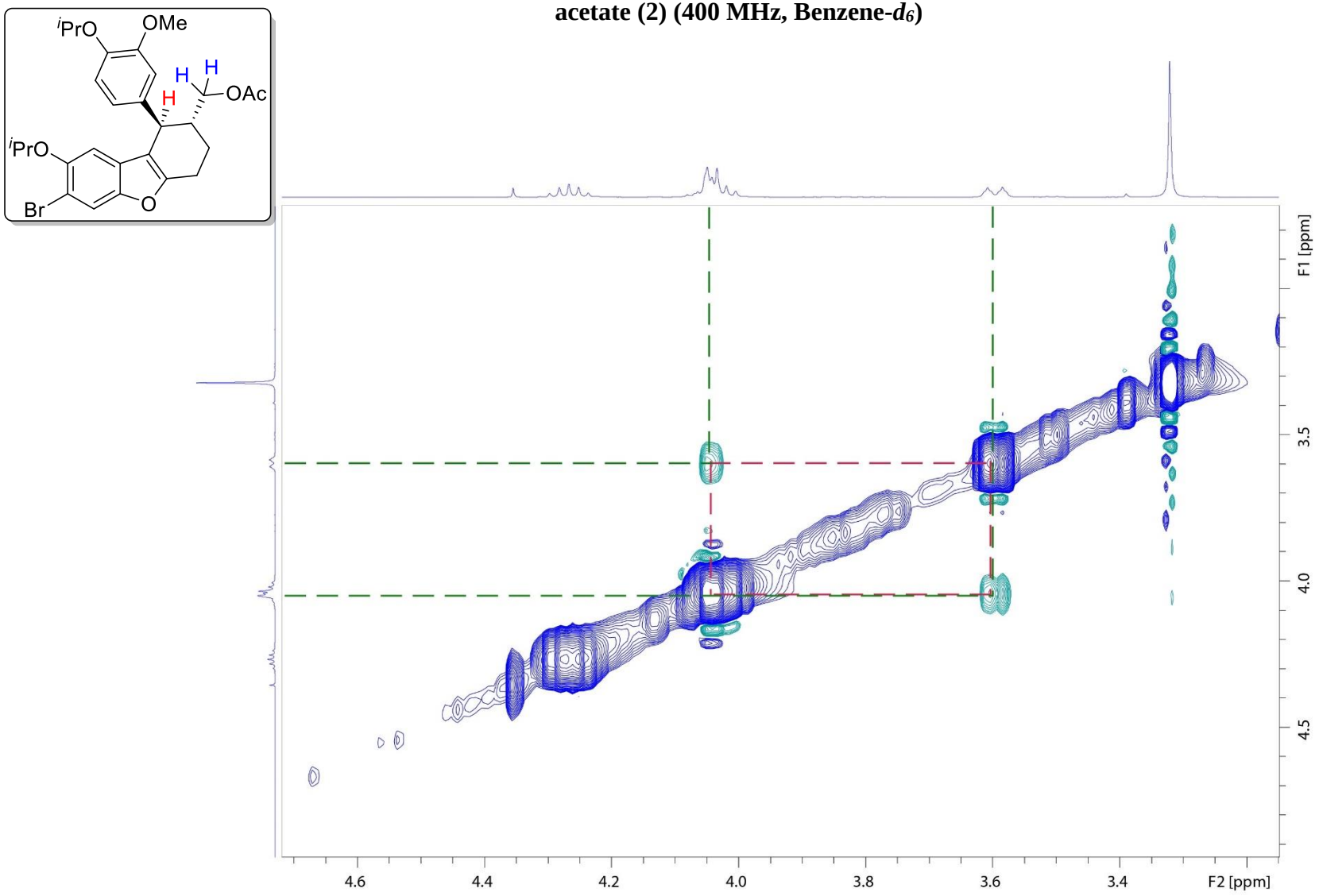
^{13}C NMR of ((1*R*,2*R*)-7-bromo-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methyl acetate (2) (100 MHz, $CDCl_3$)



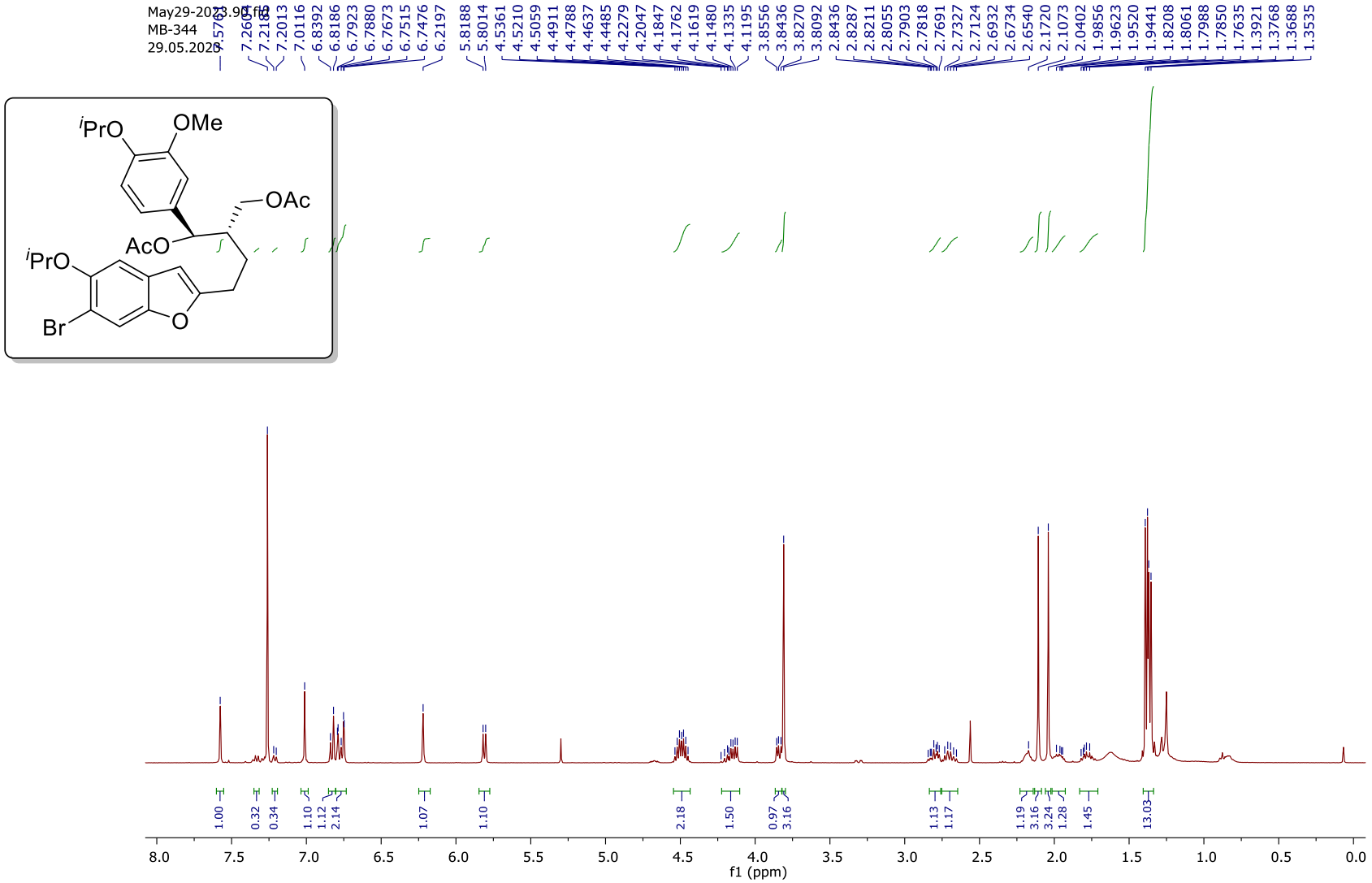
NOESY spectra of ((1*R*,2*R*)-7-bromo-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methyl acetate (2) (400 MHz, Benzene-d_6)



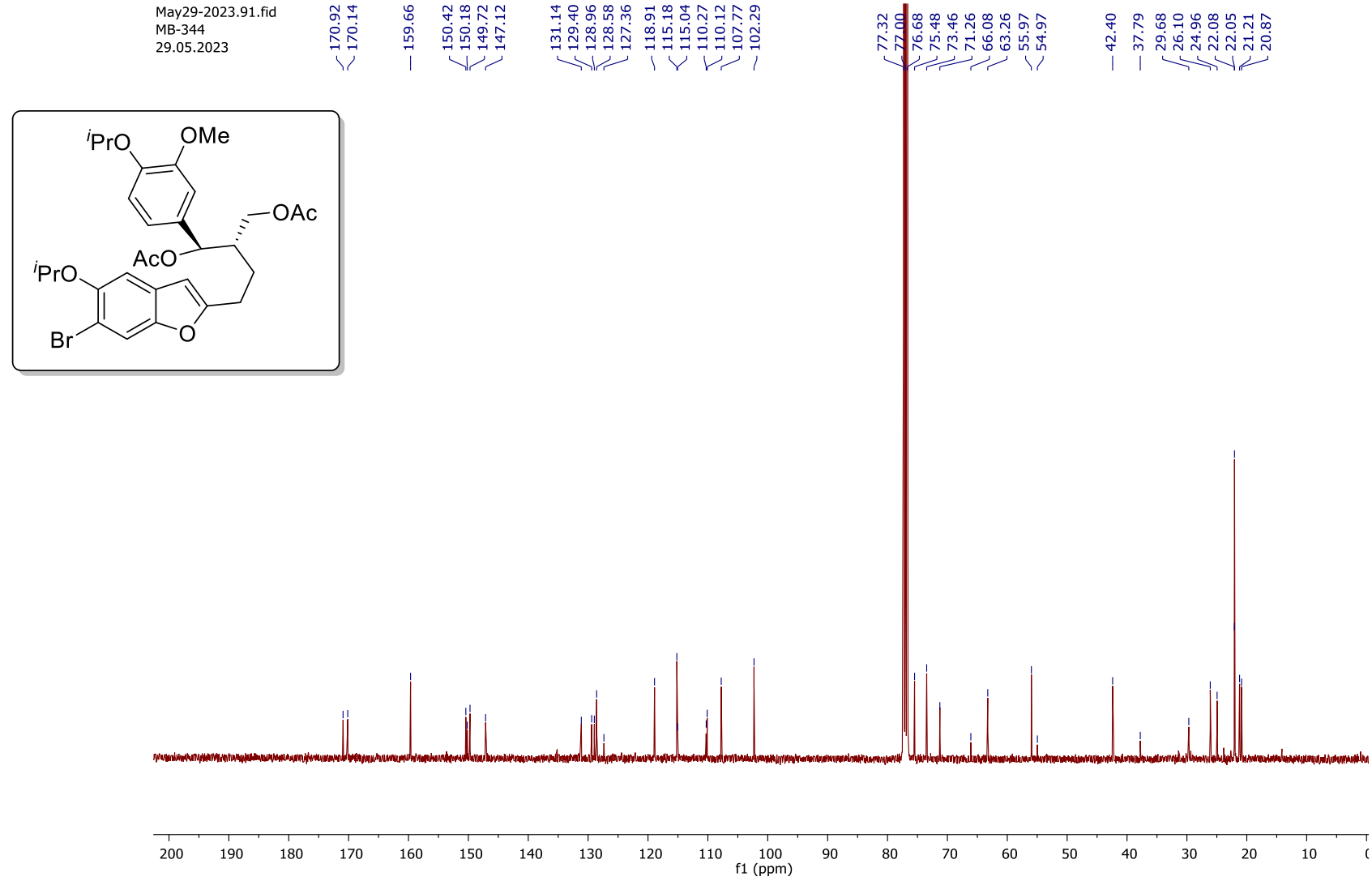
NOESY spectra of ((1*R*,2*R*)-7-bromo-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methyl acetate (2) (400 MHz, Benzene-d_6)



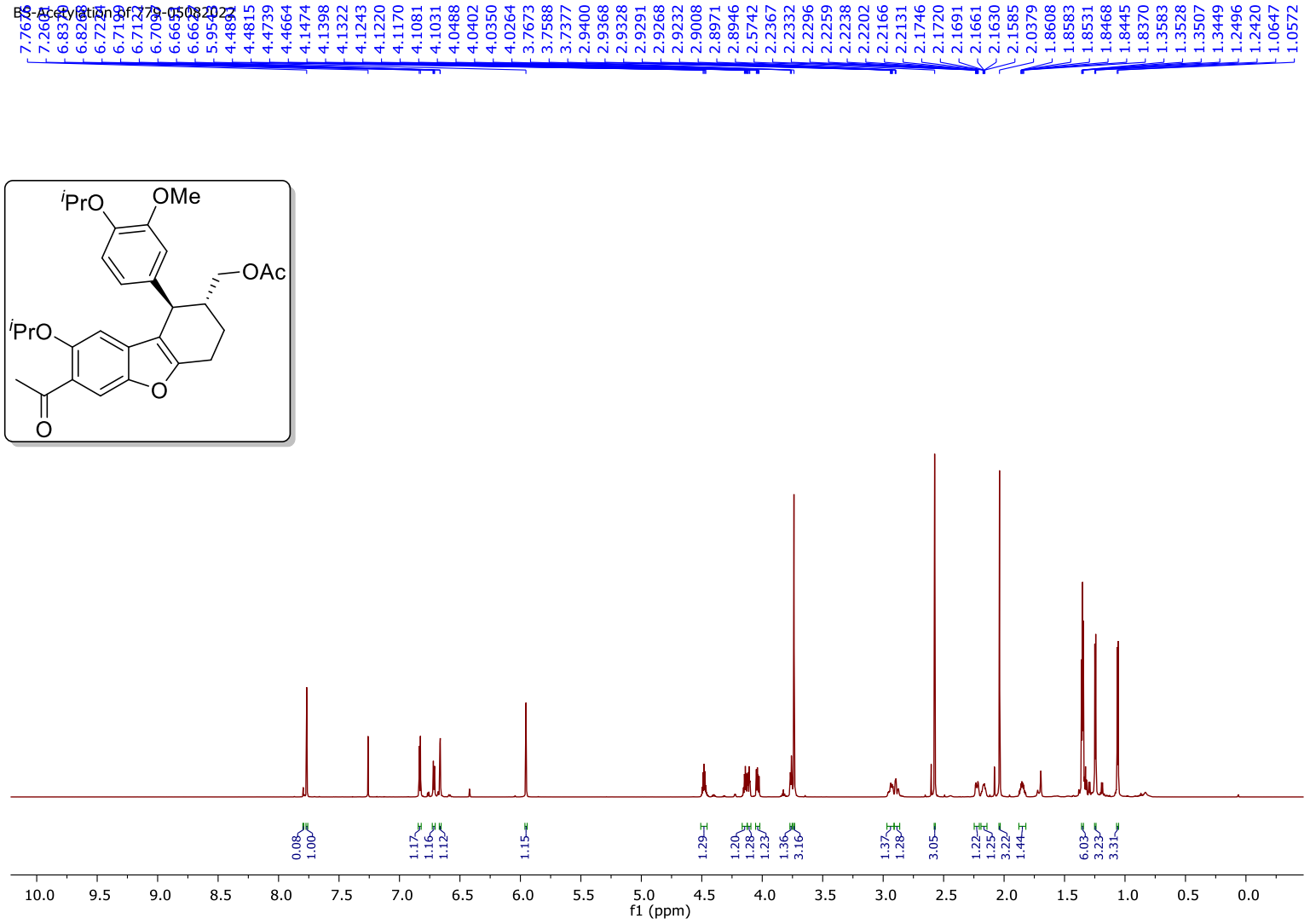
^{1}H NMR of (1*R*,2*S*)-2-(2-(6-bromo-5-isopropoxybenzofuran-2-yl)ethyl)-1-(4-isopropoxy-3-methoxyphenyl)propane-1,3-diyl diacetate (12') (400 MHz, $CDCl_3$)



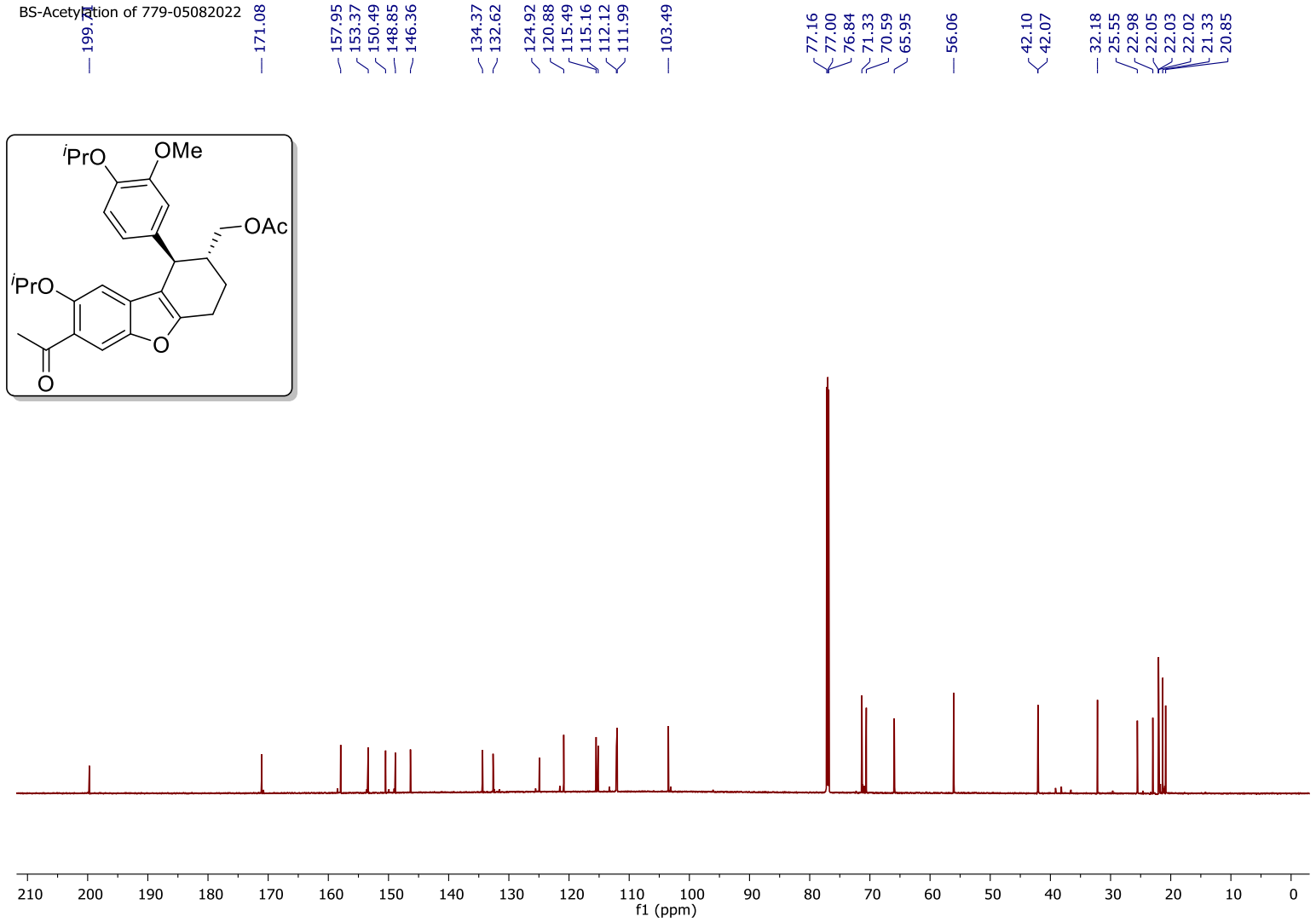
^{13}C NMR of (1*R*,2*S*)-2-(2-(6-bromo-5-isopropoxybenzofuran-2-yl)ethyl)-1-(4-isopropoxy-3-methoxyphenyl)propane-1,3-diyl diacetate (12') (100 MHz, $CDCl_3$)



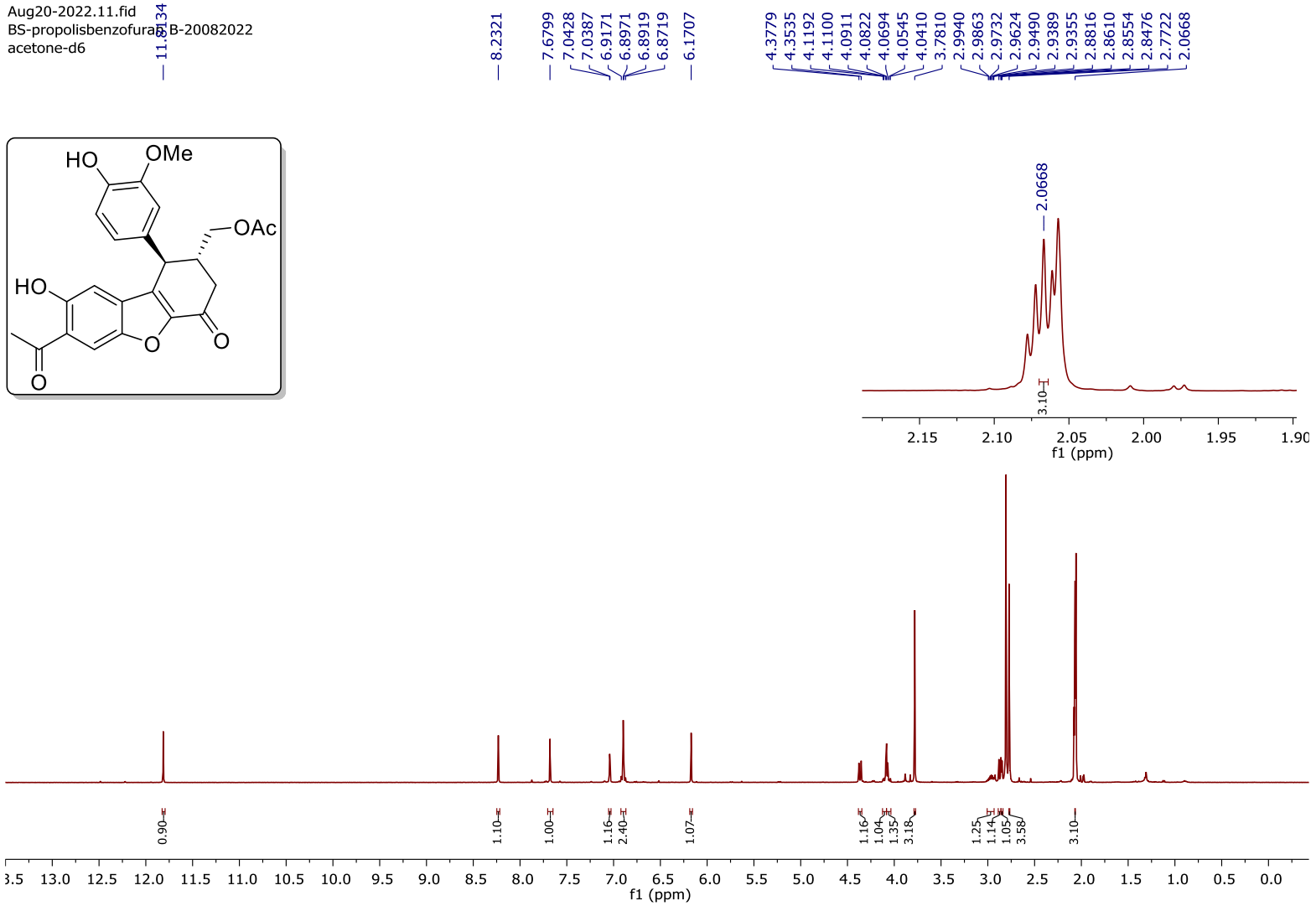
^{1}H NMR of ((1*R*,2*R*)-7-acetyl-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methyl acetate (14) (800 MHz, $CDCl_3$)



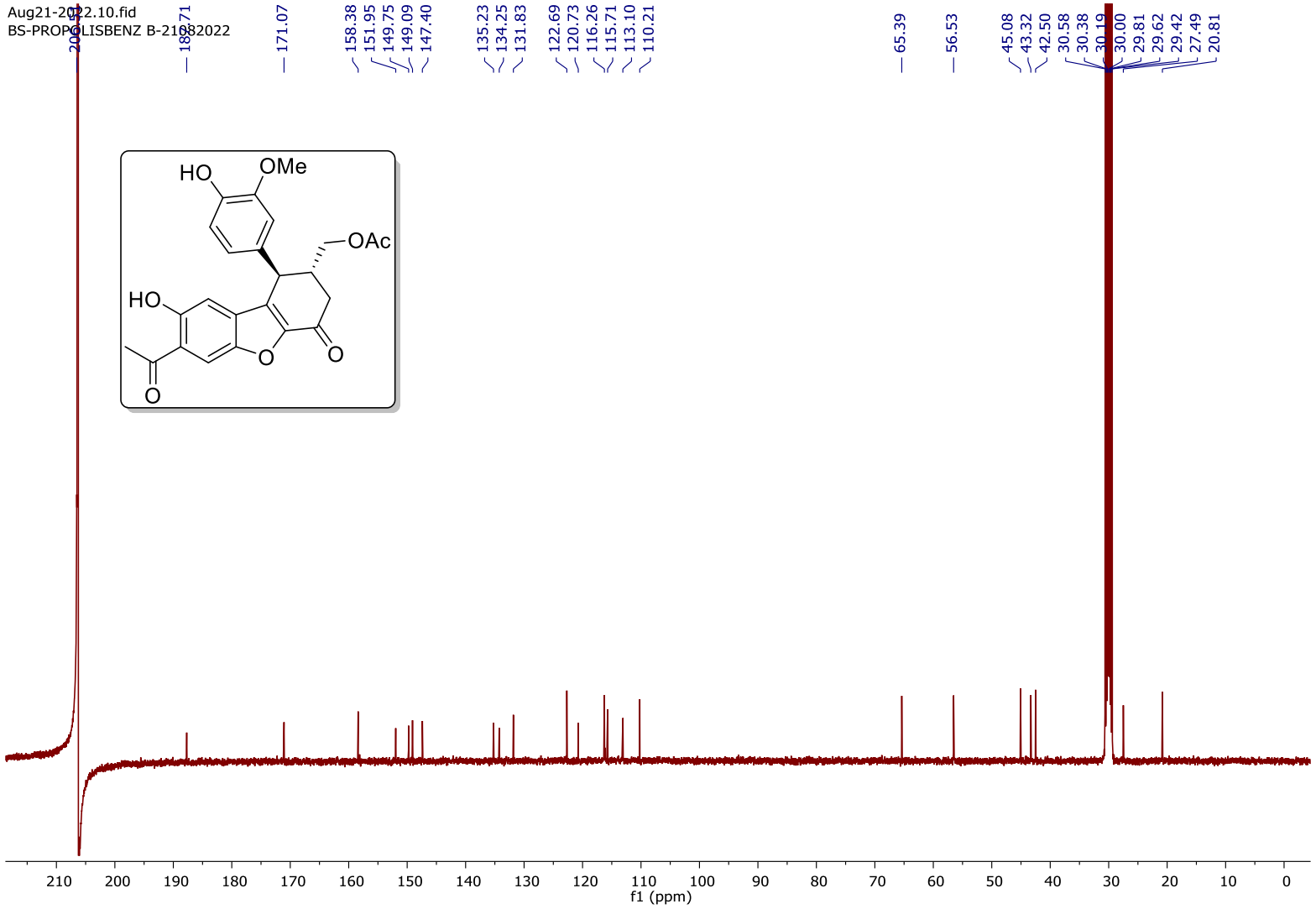
^{13}C NMR of ((1*R*,2*R*)-7-acetyl-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methyl acetate (14) (200 MHz, $CDCl_3$)



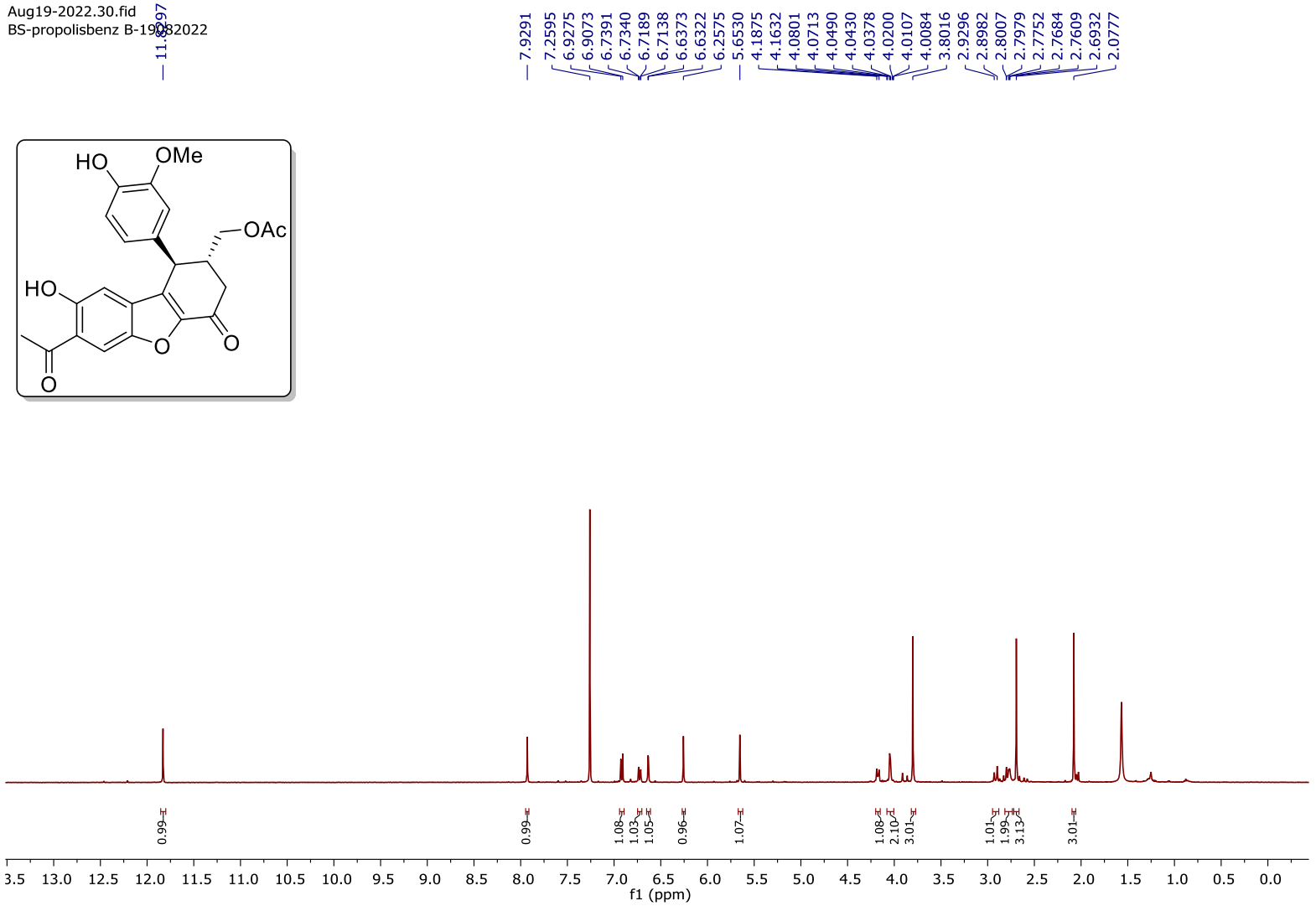
^{1}H NMR of (+)-propolisbenzofuran B (1) (400 MHz, Acetone-*d*$_6$)



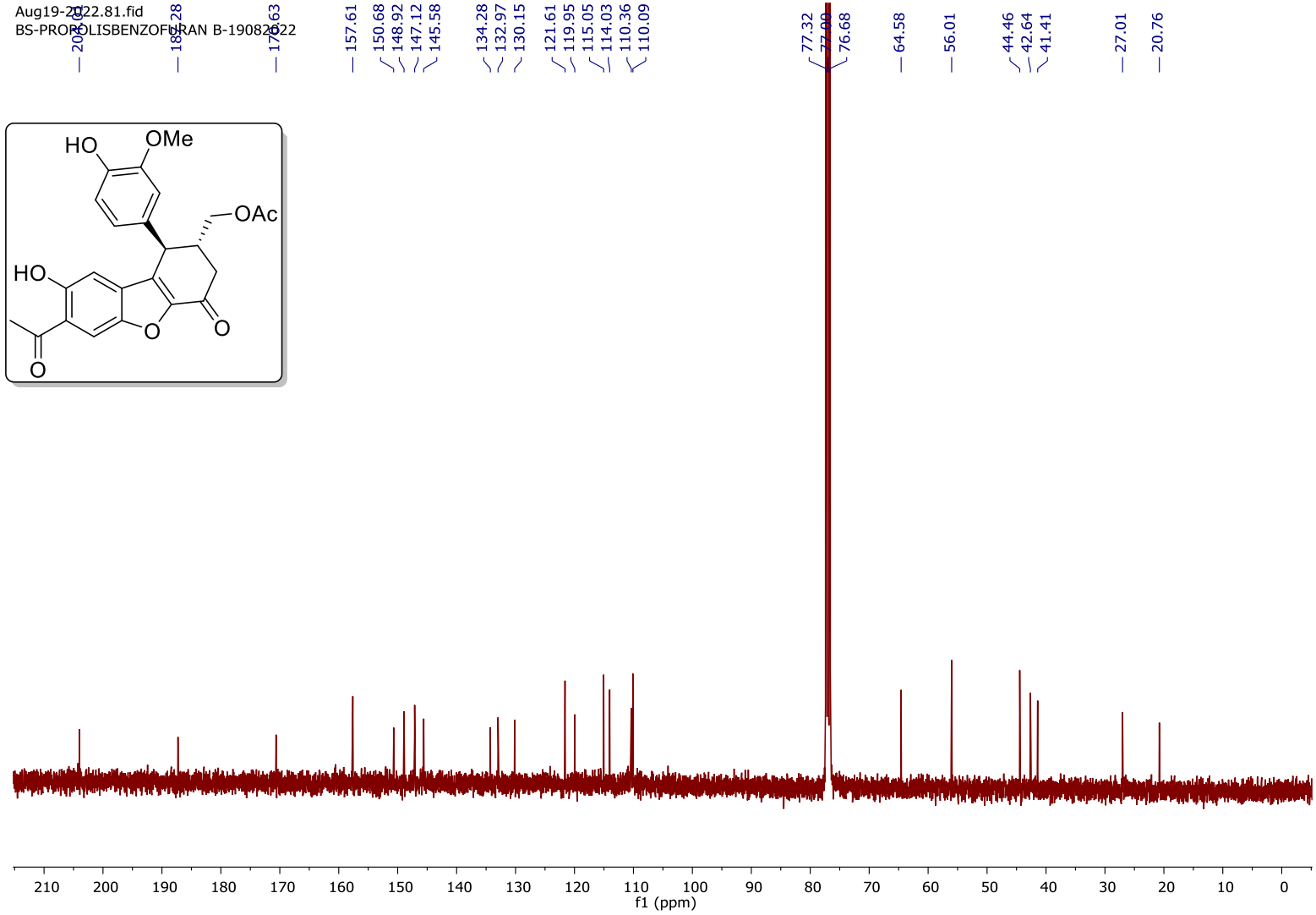
^{13}C NMR of (+)-propolisbenzofuran B (1) (100 MHz, Acetone-d_6)



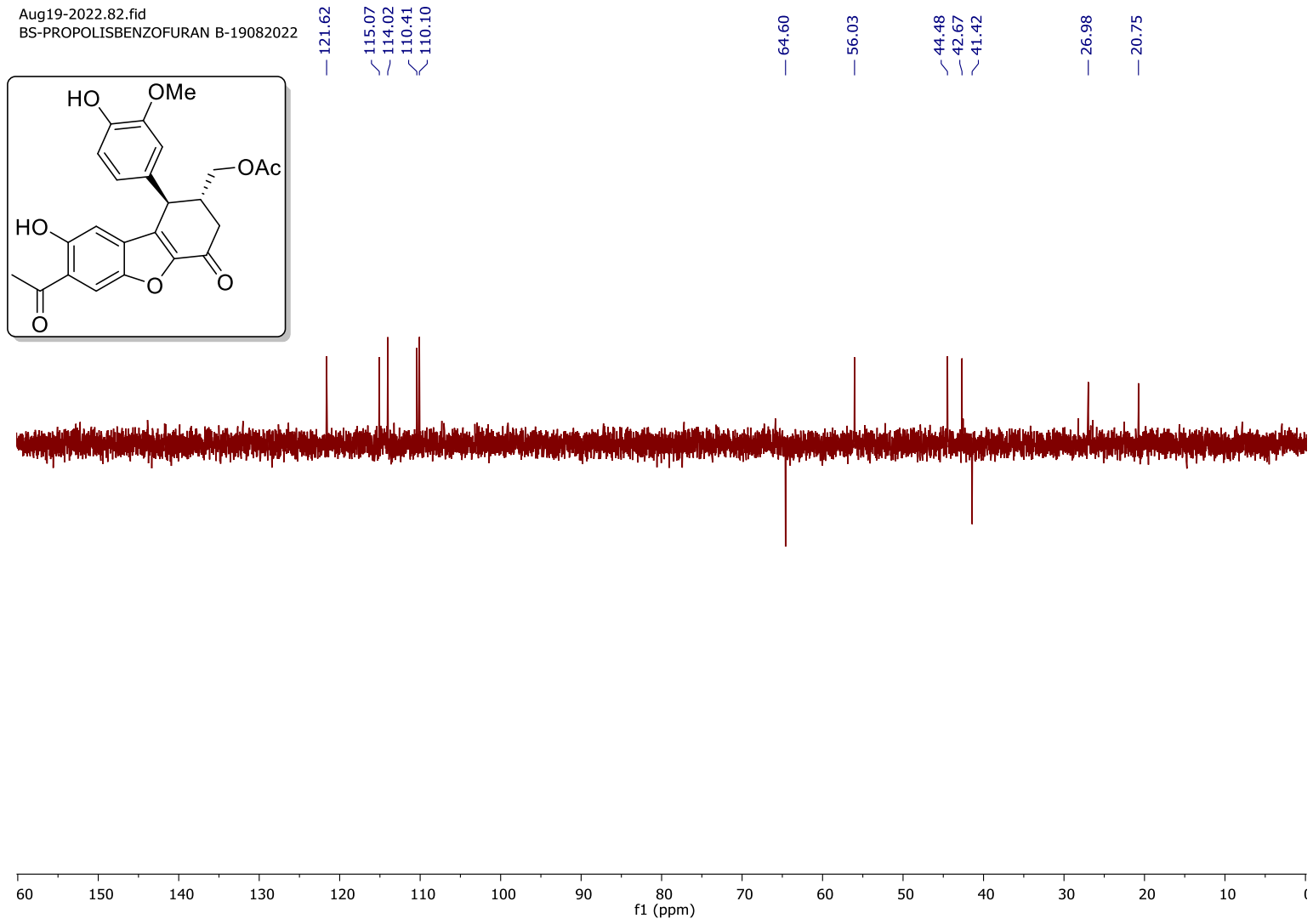
^{1}H NMR of (+)-propolisbenzofuran B (1) (400 MHz, $CDCl_3$)



^{13}C NMR of (+)-propolisbenzofuran B (1) (100 MHz, $CDCl_3$)



DEPT-135 NMR of (+)-propolisbenzofuran B (1) (100 MHz, $CDCl_3$)



^{1}H NMR of (7-bromo-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)dibenzo[*b*,*d*]furan-2-yl)methyl acetate (16) (400 MHz, $CDCl_3$)

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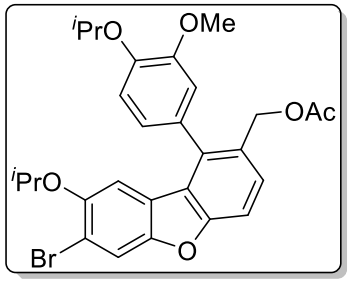
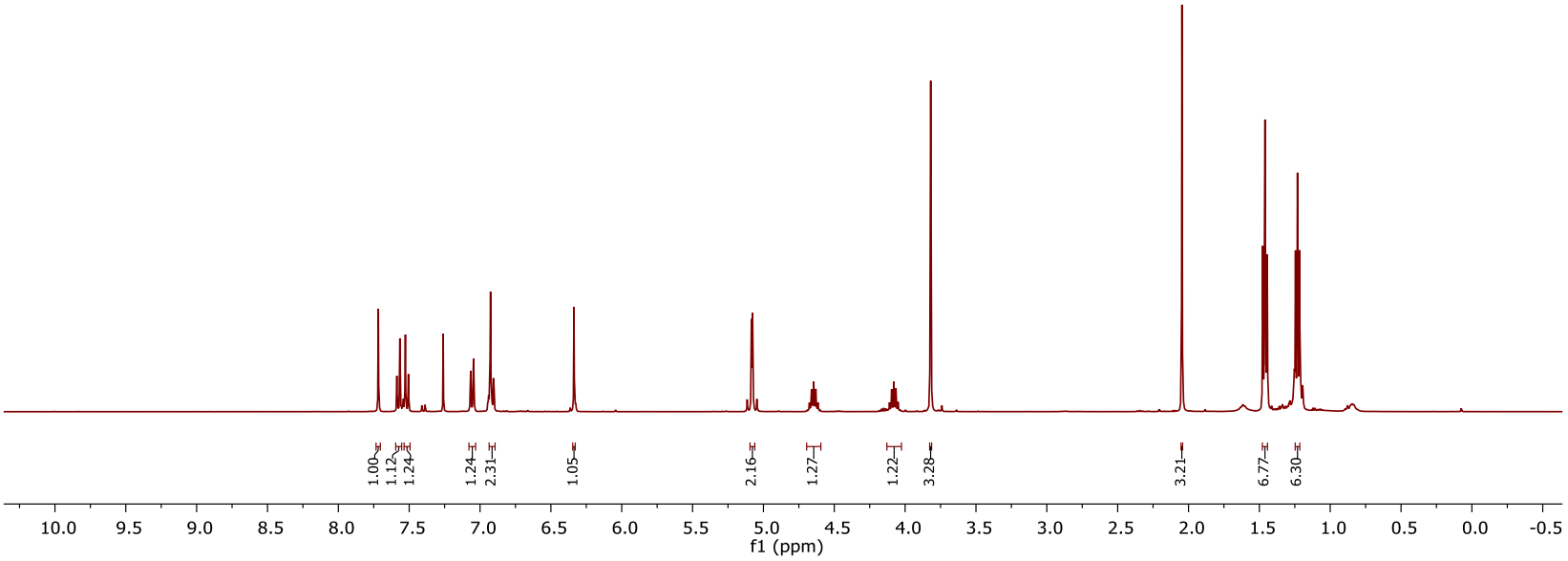
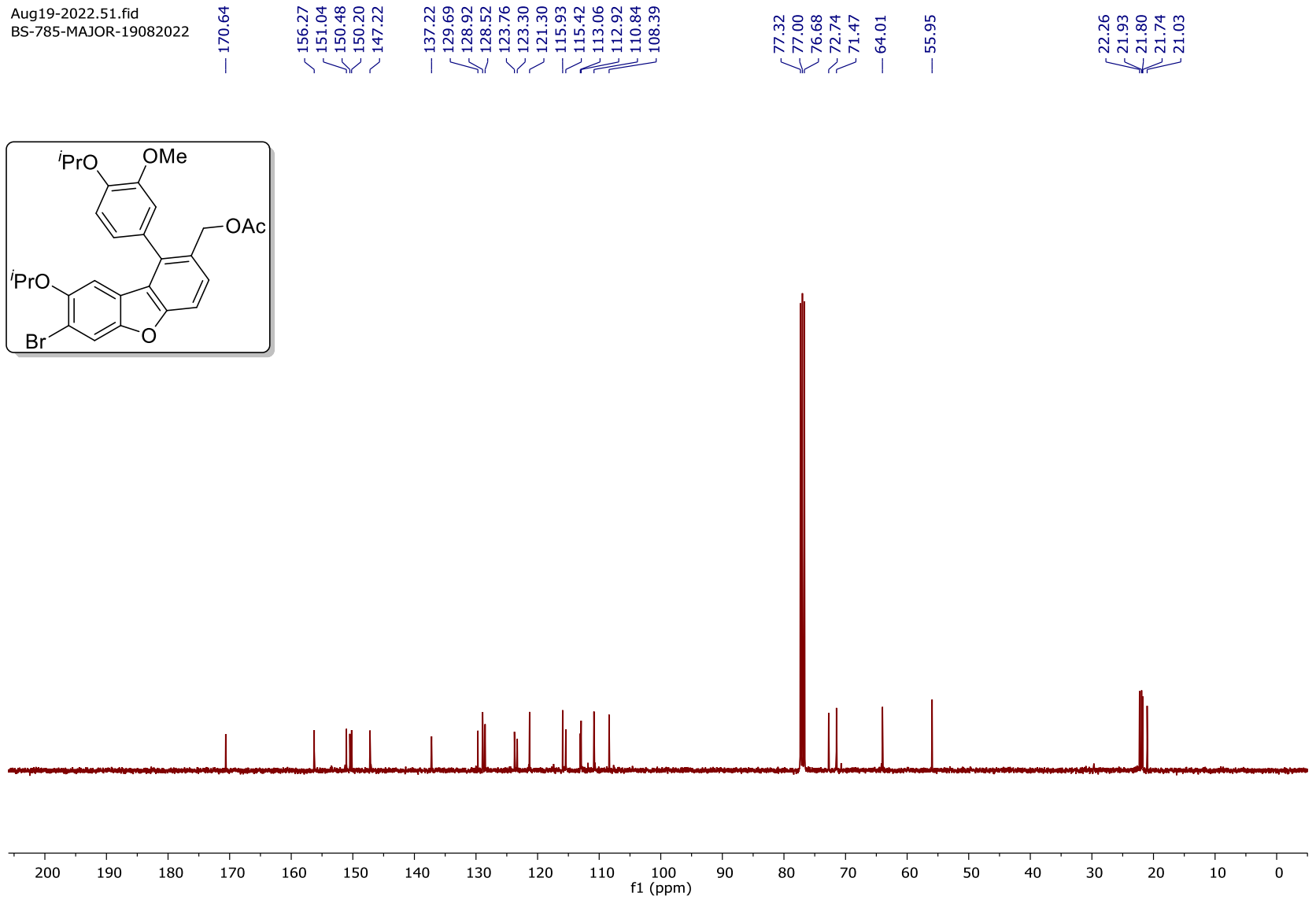
7.7178 7.5870 7.5656 7.5270 7.5057 7.2602 7.0657 7.0462 6.9455 6.9396 6.9261 6.9058 6.9008 6.3373
5.0846 5.0765 4.6906 4.6757 4.6605 4.6453 4.6301 4.6149 4.5998 4.1221 4.1104 4.0952 4.0800 4.0649 4.0497 4.0348 3.8195
2.0464
1.4762 1.4602 1.4444 1.2450 1.2309 1.2171

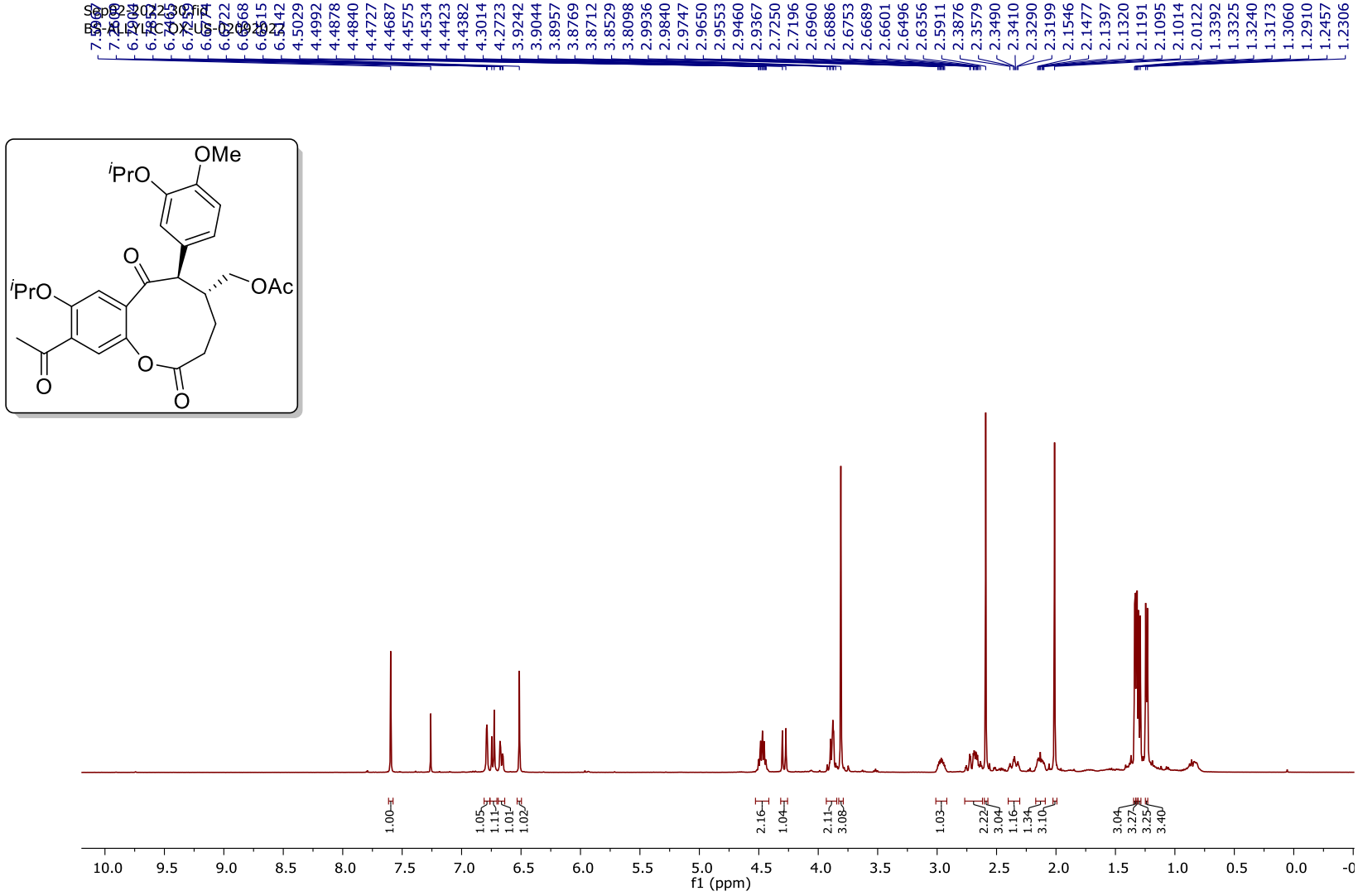




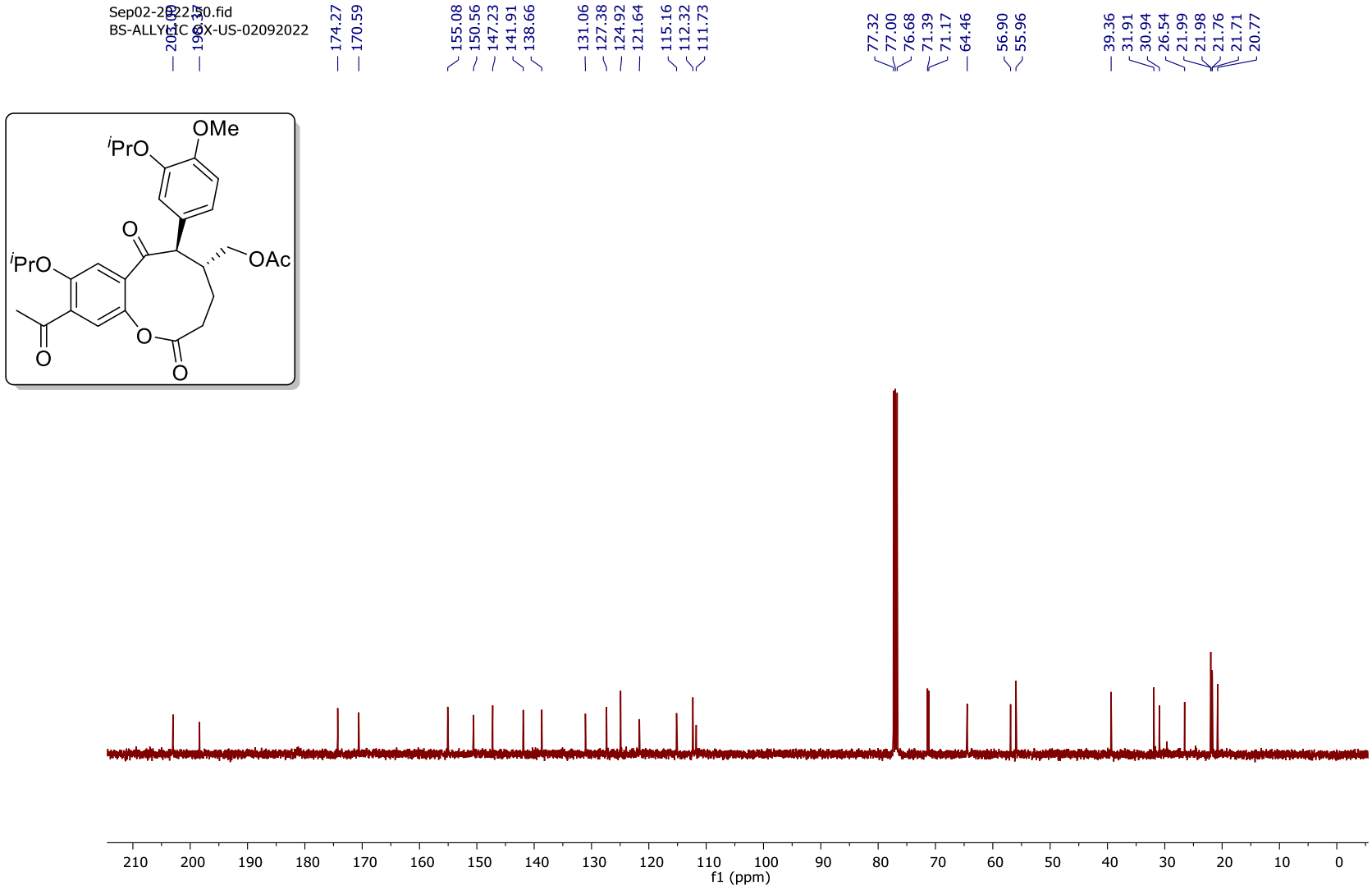
^{13}C NMR of (7-bromo-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)dibenzo[*b,d*]furan-2-yl)methyl acetate (16) (100 MHz, $CDCl_3$)



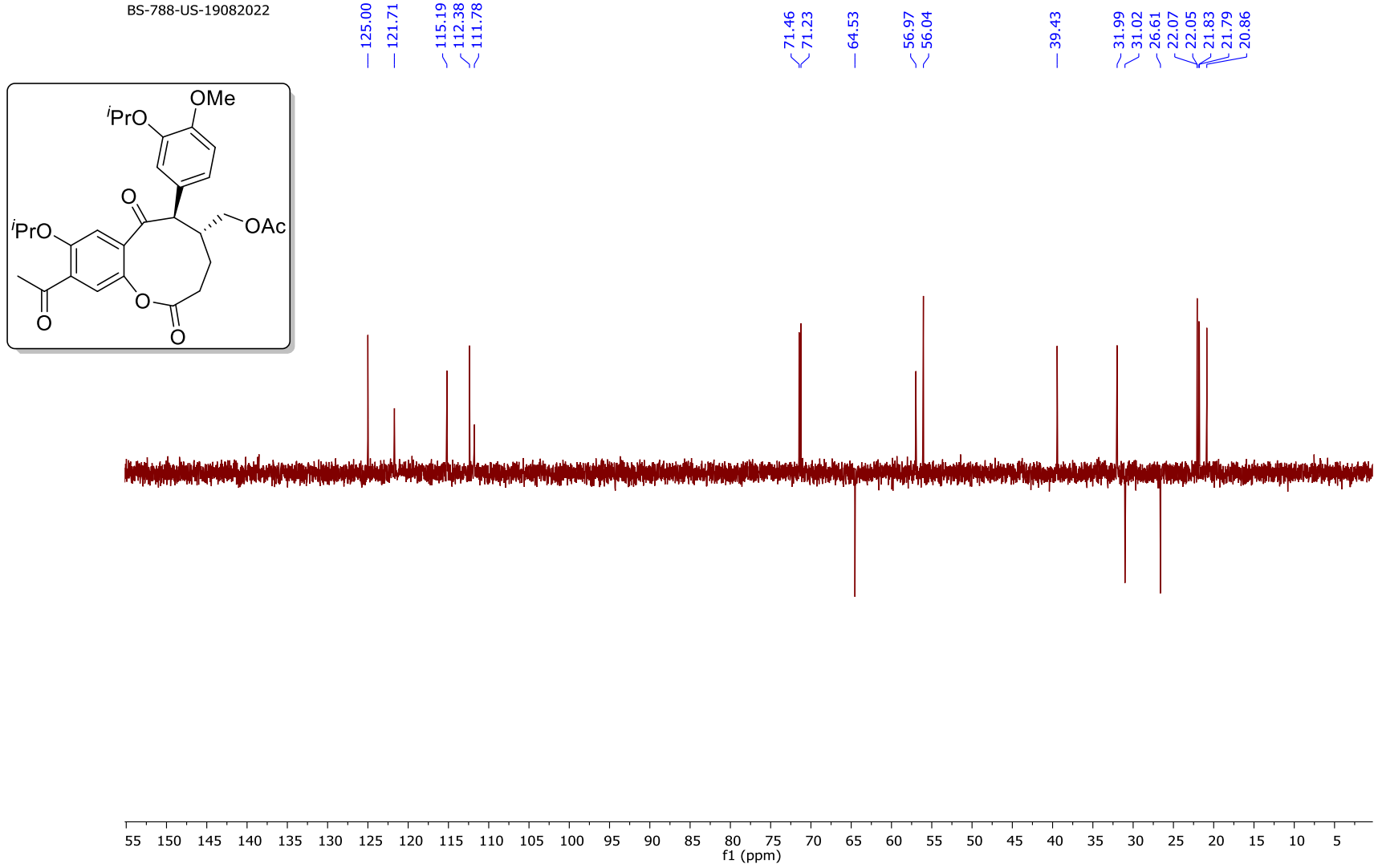
^{1}H NMR of ((5*R*,6*R*)-10-acetyl-9-isopropoxy-6-(4-isopropoxy-3-methoxyphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydrobenzo[*b*]oxonin-5-yl)methyl acetate (17) (400 MHz, $CDCl_3$)



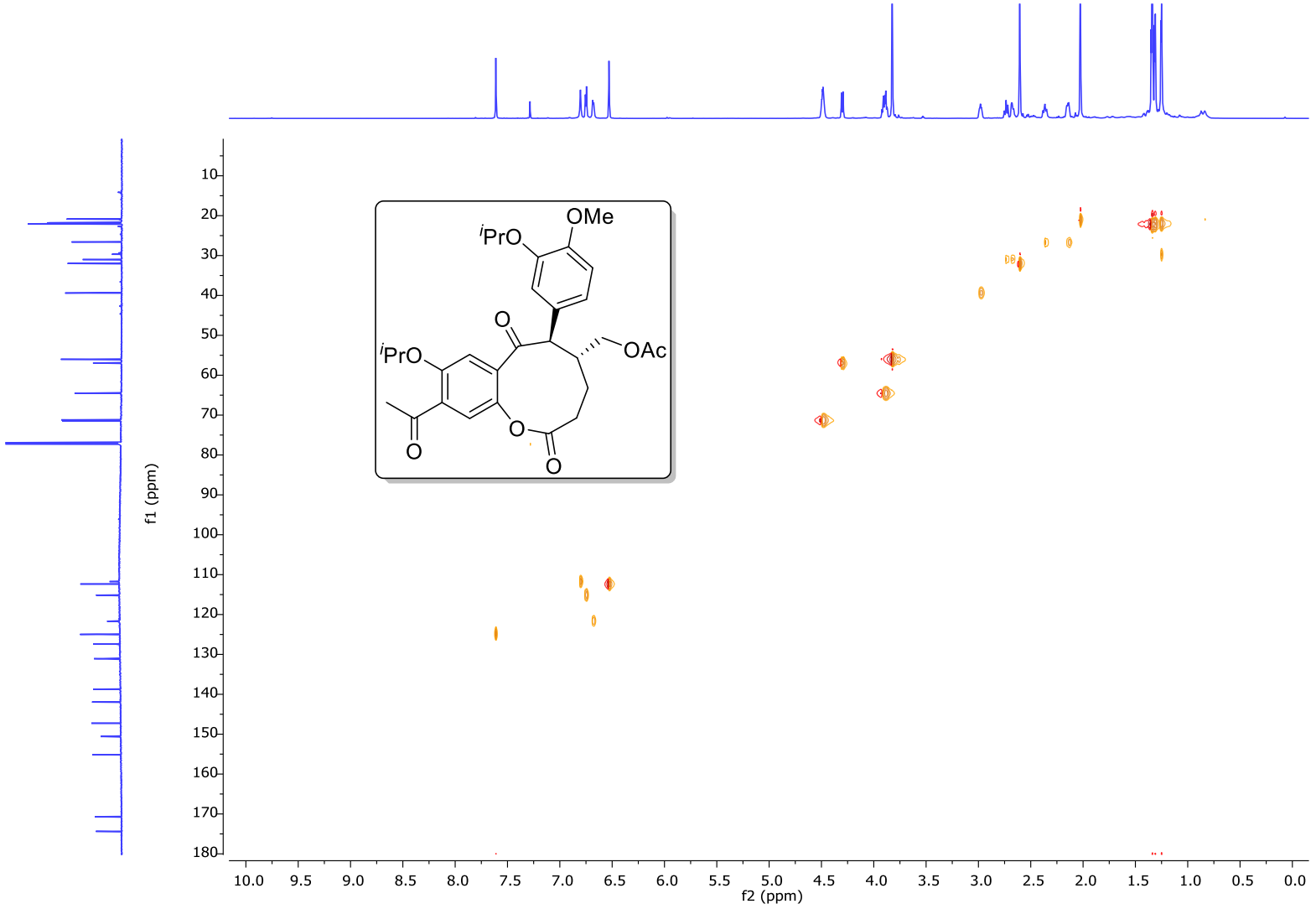
^{13}C NMR of ((5*R*,6*R*)-10-acetyl-9-isopropoxy-6-(4-isopropoxy-3-methoxyphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydrobenzo[*b*]oxonin-5-yl)methyl acetate (17) (100 MHz, $CDCl_3$)



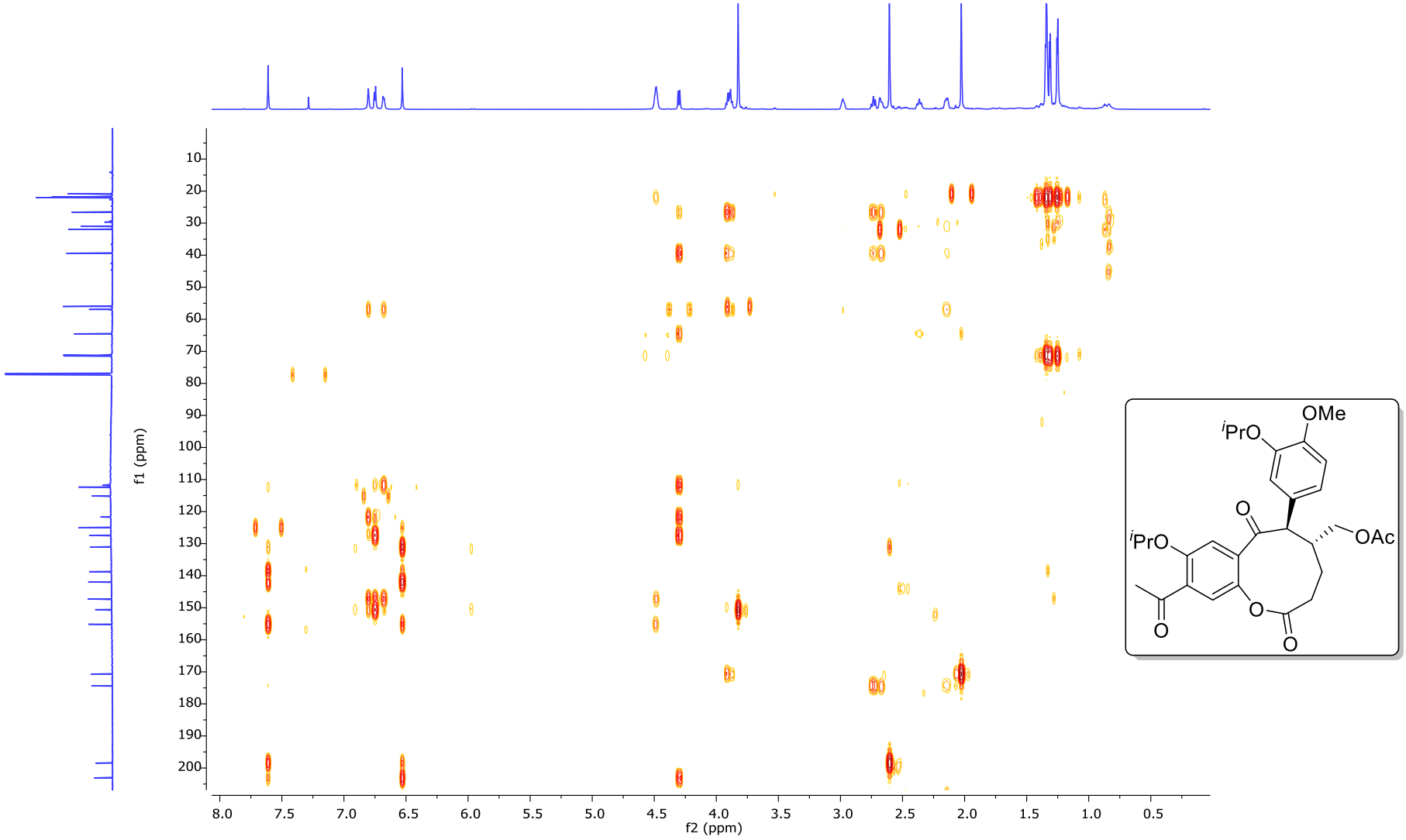
DEPT-135 NMR of ((5*R*,6*R*)-10-acetyl-9-isopropoxy-6-(4-isopropoxy-3-methoxyphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydrobenzo[*b*]oxonin-5-yl)methyl acetate (17) (100 MHz, $CDCl_3$)



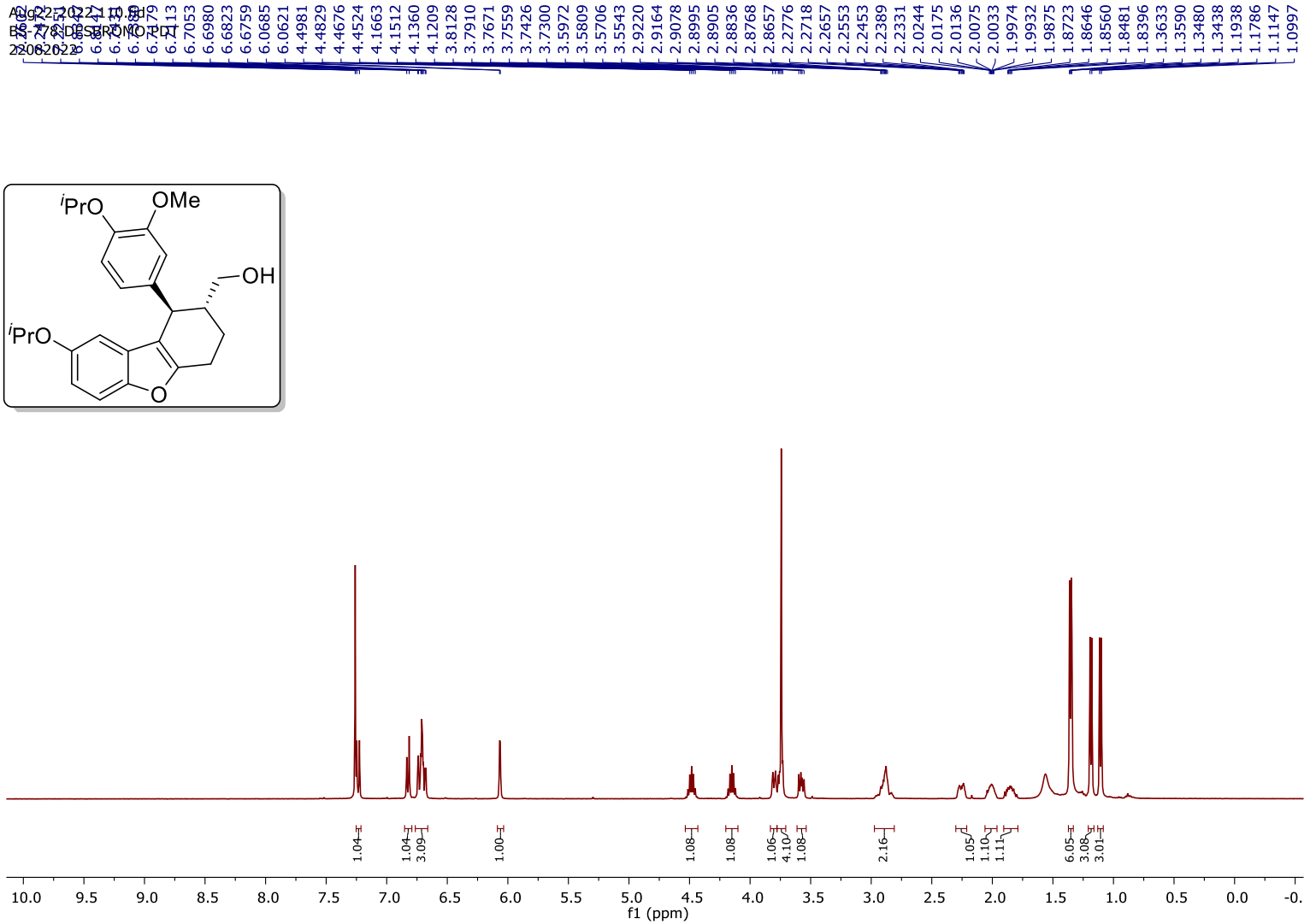
HSQC Spectra of ((5*R*,6*R*)-10-acetyl-9-isopropoxy-6-(4-isopropoxy-3-methoxyphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydrobenzo[*b*]oxonin-5-yl)methyl acetate (17) (200 MHz, $CDCl_3$)



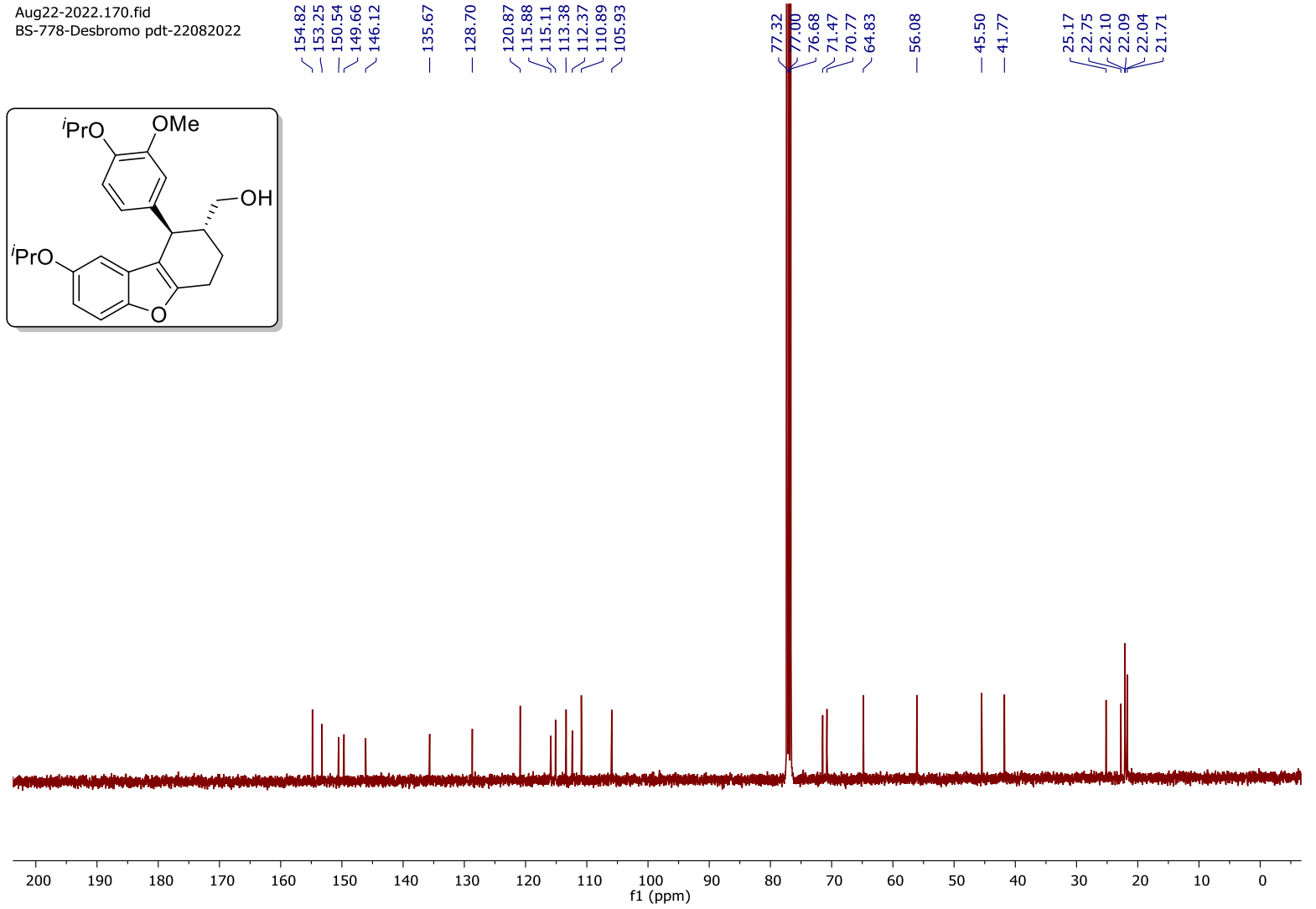
HMBC Spectra of ((5*R*,6*R*)-10-acetyl-9-isopropoxy-6-(4-isopropoxy-3-methoxyphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydrobenzo[*b*]oxonin-5-yl)methyl acetate (17) (200 MHz, $CDCl_3$)



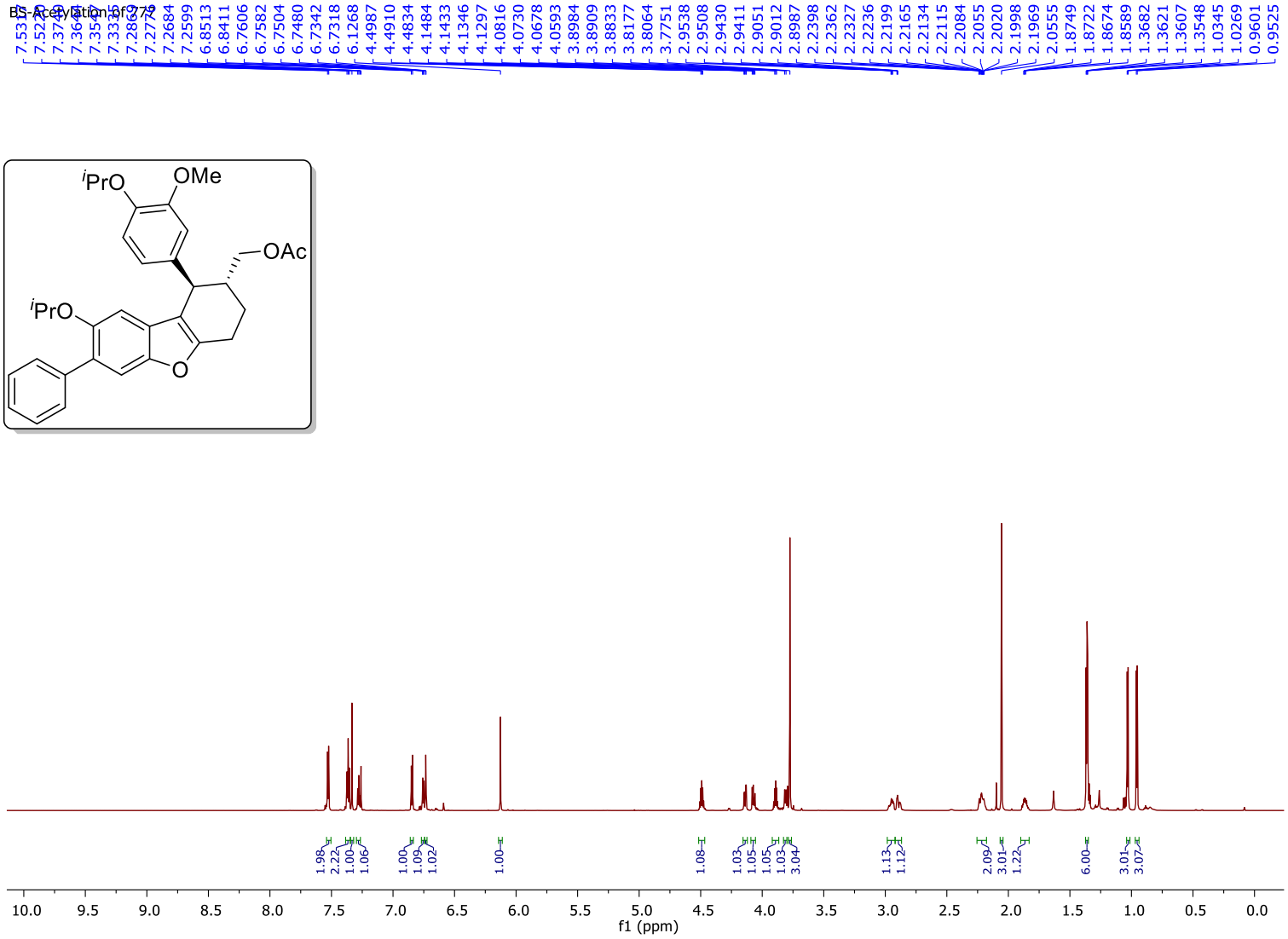
^{1}H NMR of ((1*R*,2*R*)-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methanol (18) (400 MHz, $CDCl_3$)



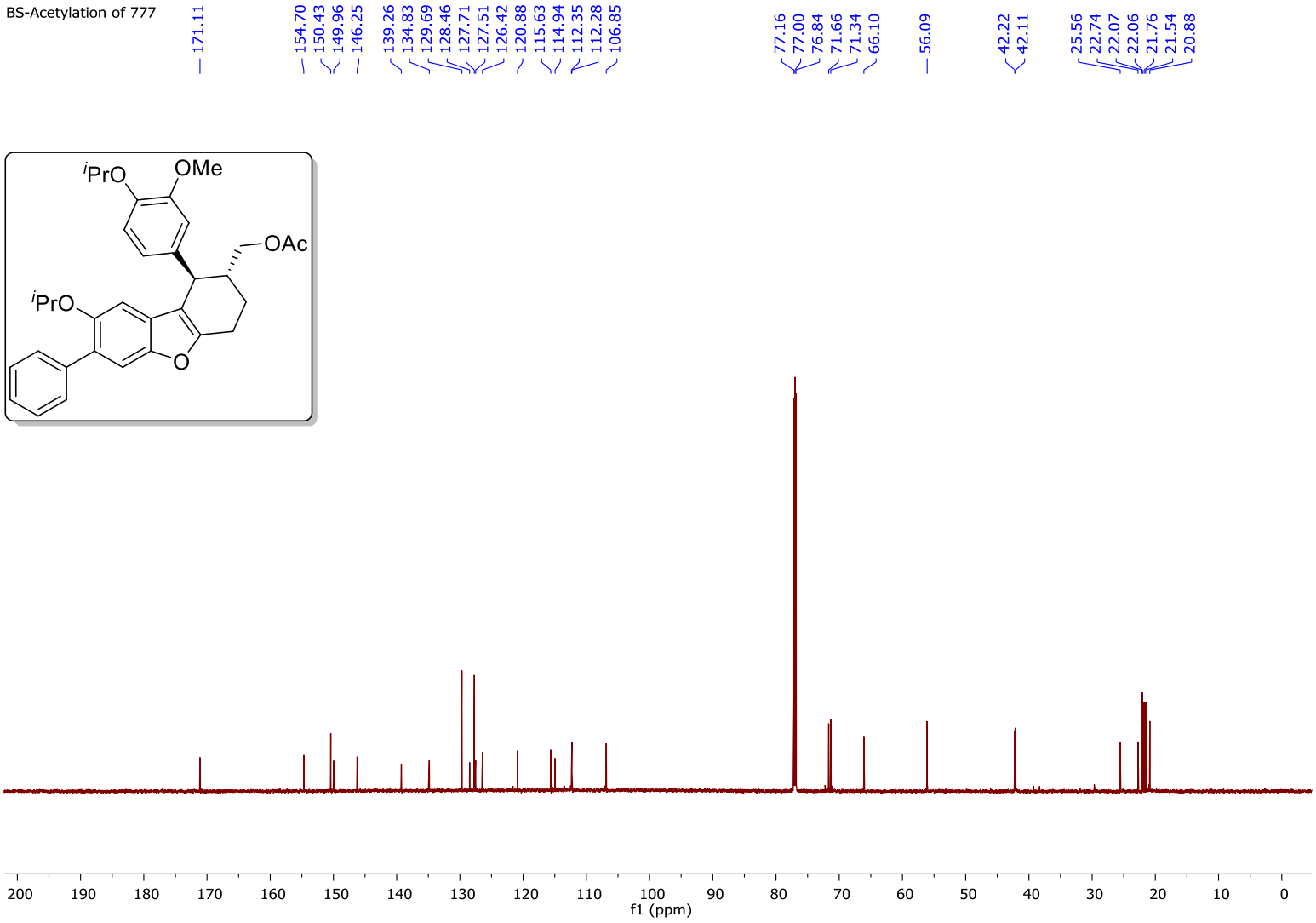
^{13}C NMR of ((1*R*,2*R*)-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methanol (18) (100 MHz, $CDCl_3$)



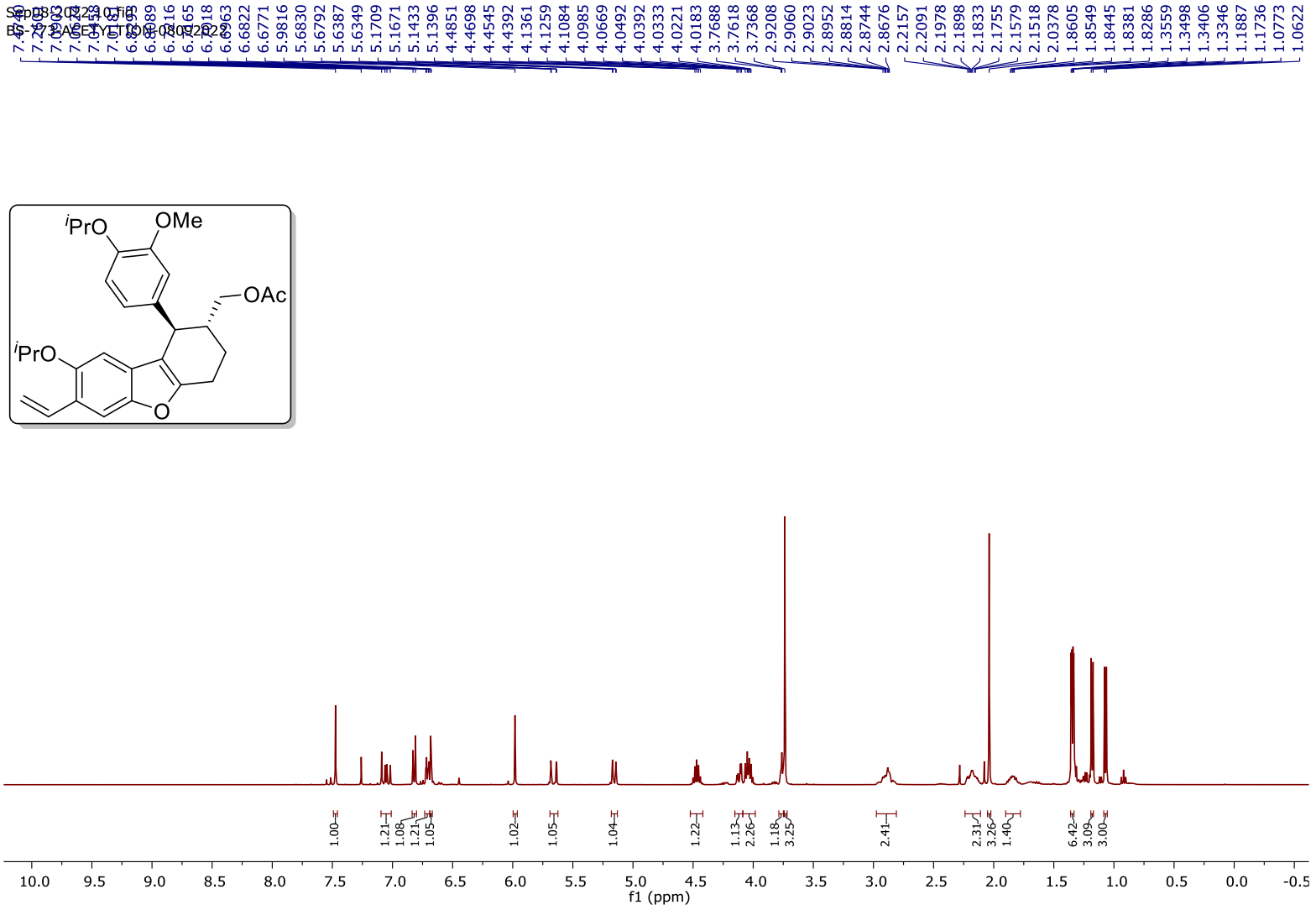
^{1}H NMR of ((1*R*,2*R*)-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-7-phenyl-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methyl acetate (19) (800 MHz, $CDCl_3$)



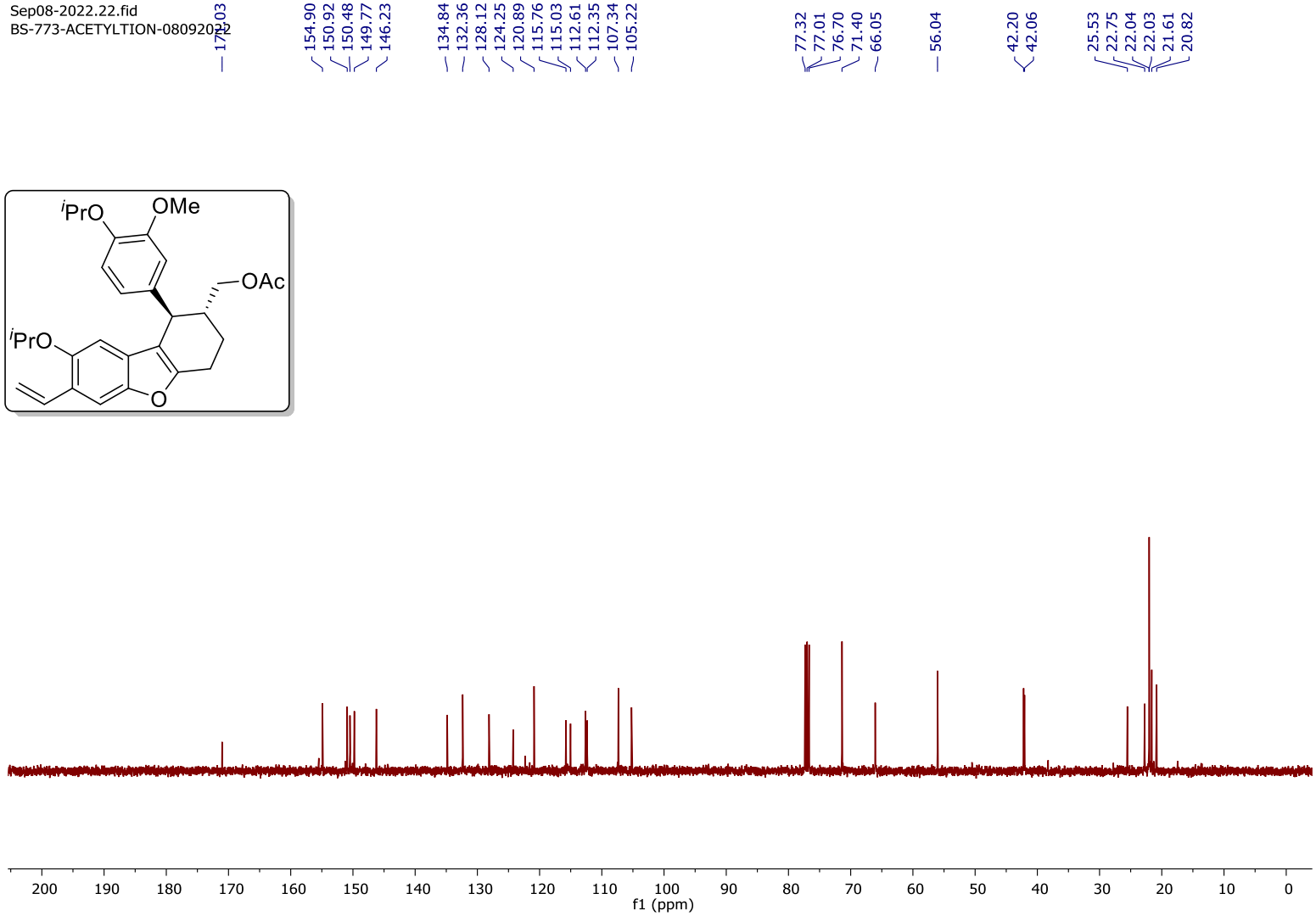
^{13}C NMR of ((1*R*,2*R*)-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-7-phenyl-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methyl acetate (19) (200 MHz, $CDCl_3$)



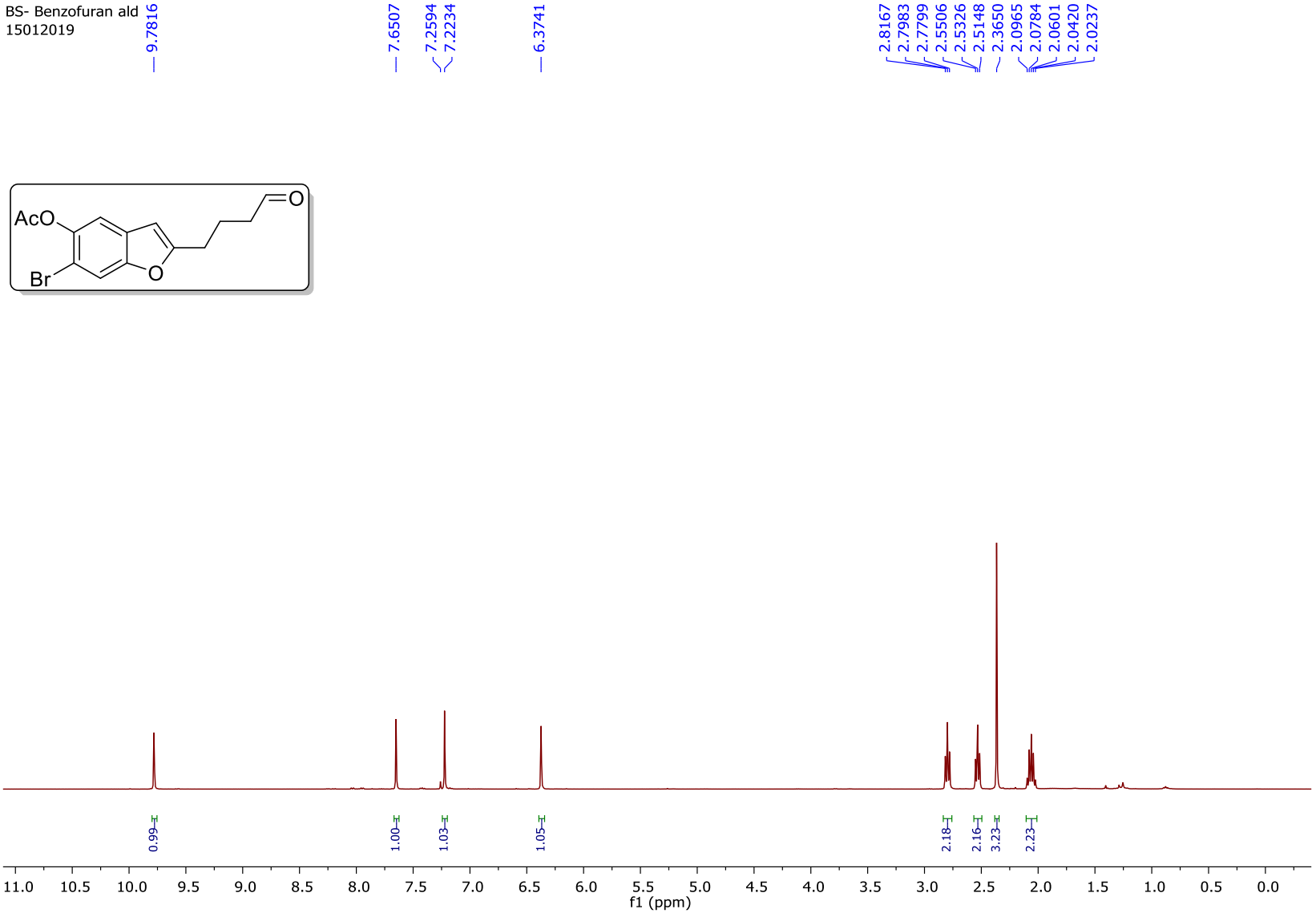
^{1}H NMR of ((1*R*,2*R*)-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-7-vinyl-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methyl acetate (20) (400 MHz, $CDCl_3$)



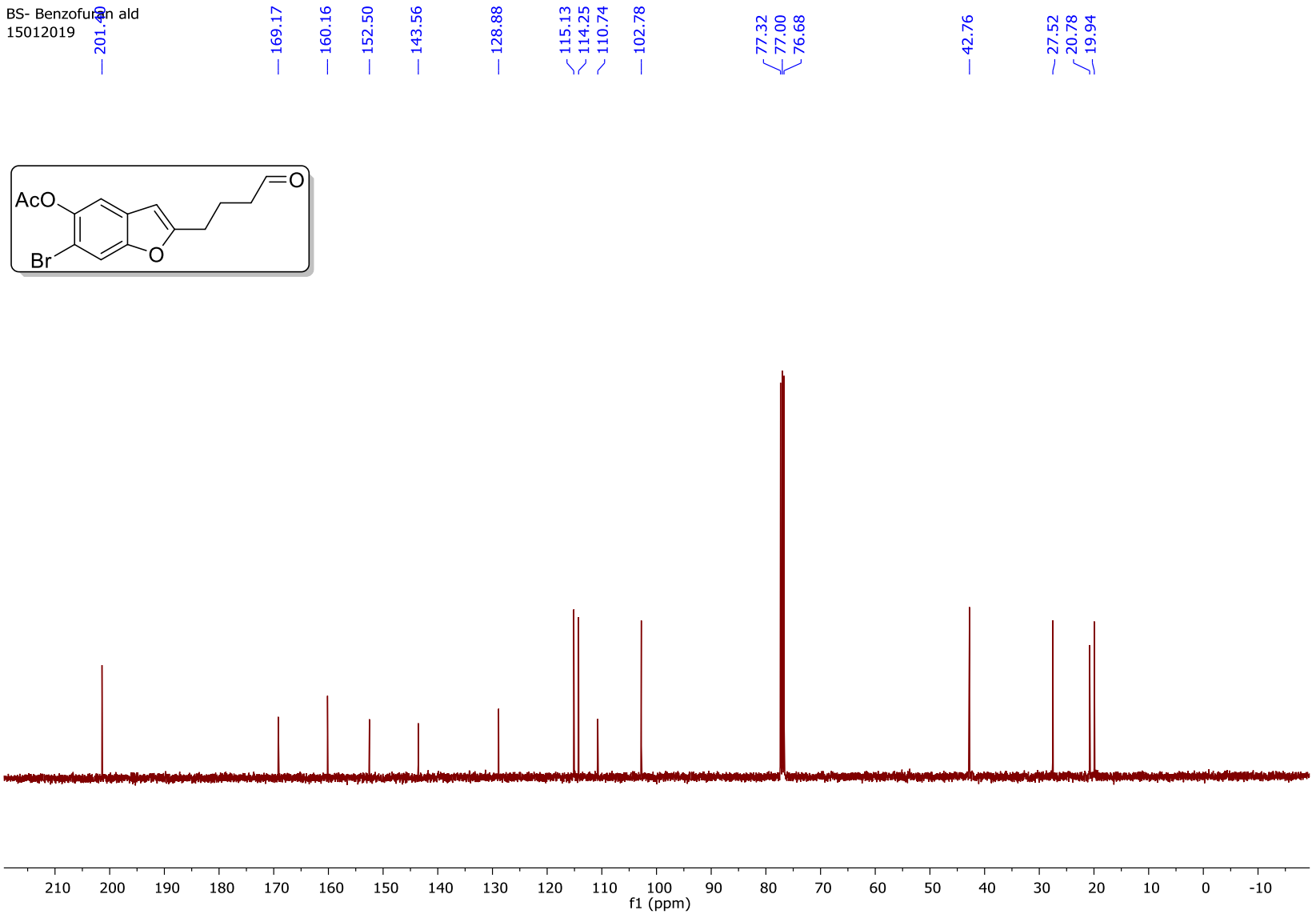
^{13}C NMR of ((1*R*,2*R*)-8-isopropoxy-1-(4-isopropoxy-3-methoxyphenyl)-7-vinyl-1,2,3,4-tetrahydrodibenzo[*b*,*d*]furan-2-yl)methyl acetate (20) (100 MHz, $CDCl_3$)



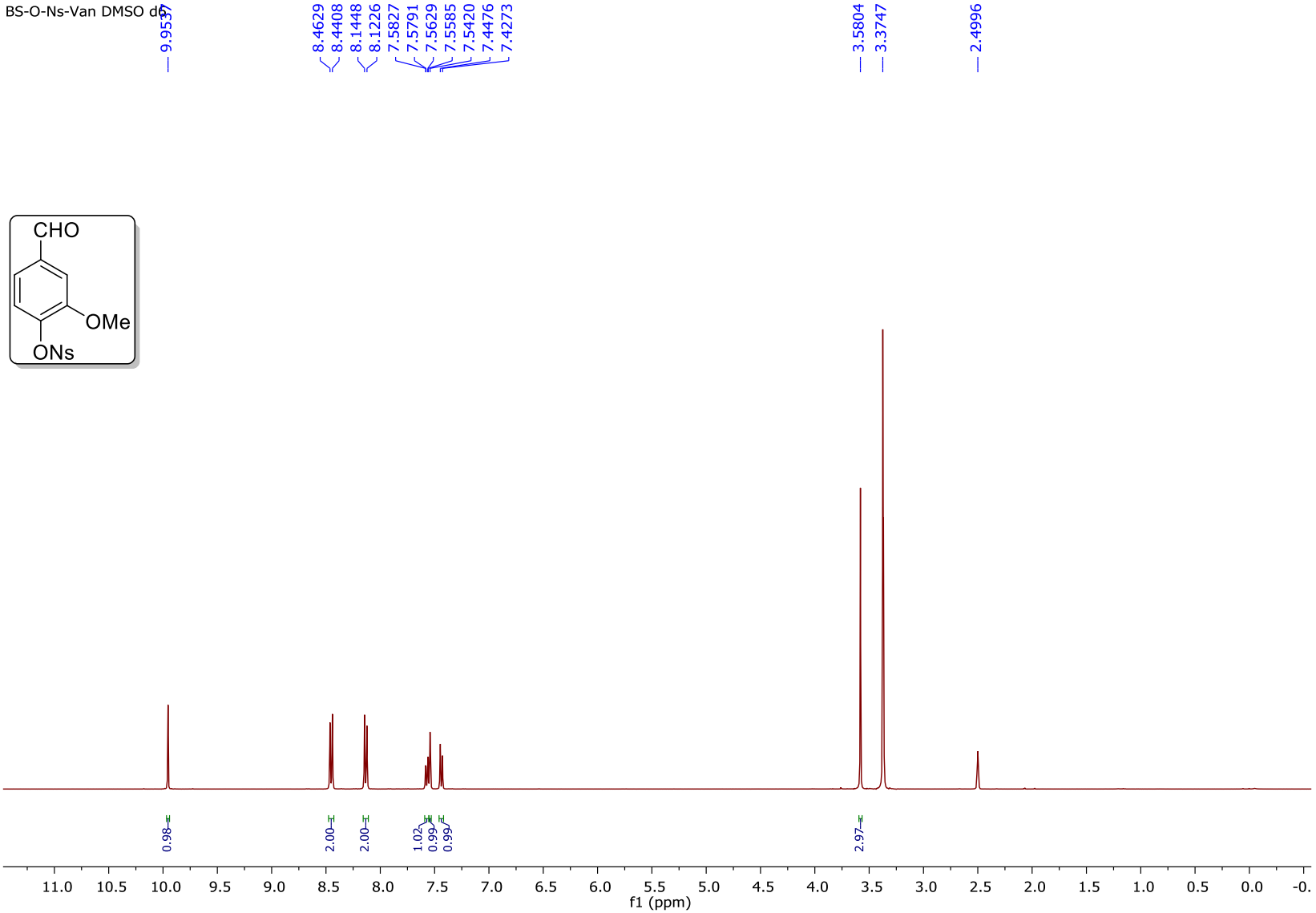
^{1}H NMR of 6-bromo-2-(4-oxobutyl)benzofuran-5-yl acetate (3a) (400 MHz, $CDCl_3$)



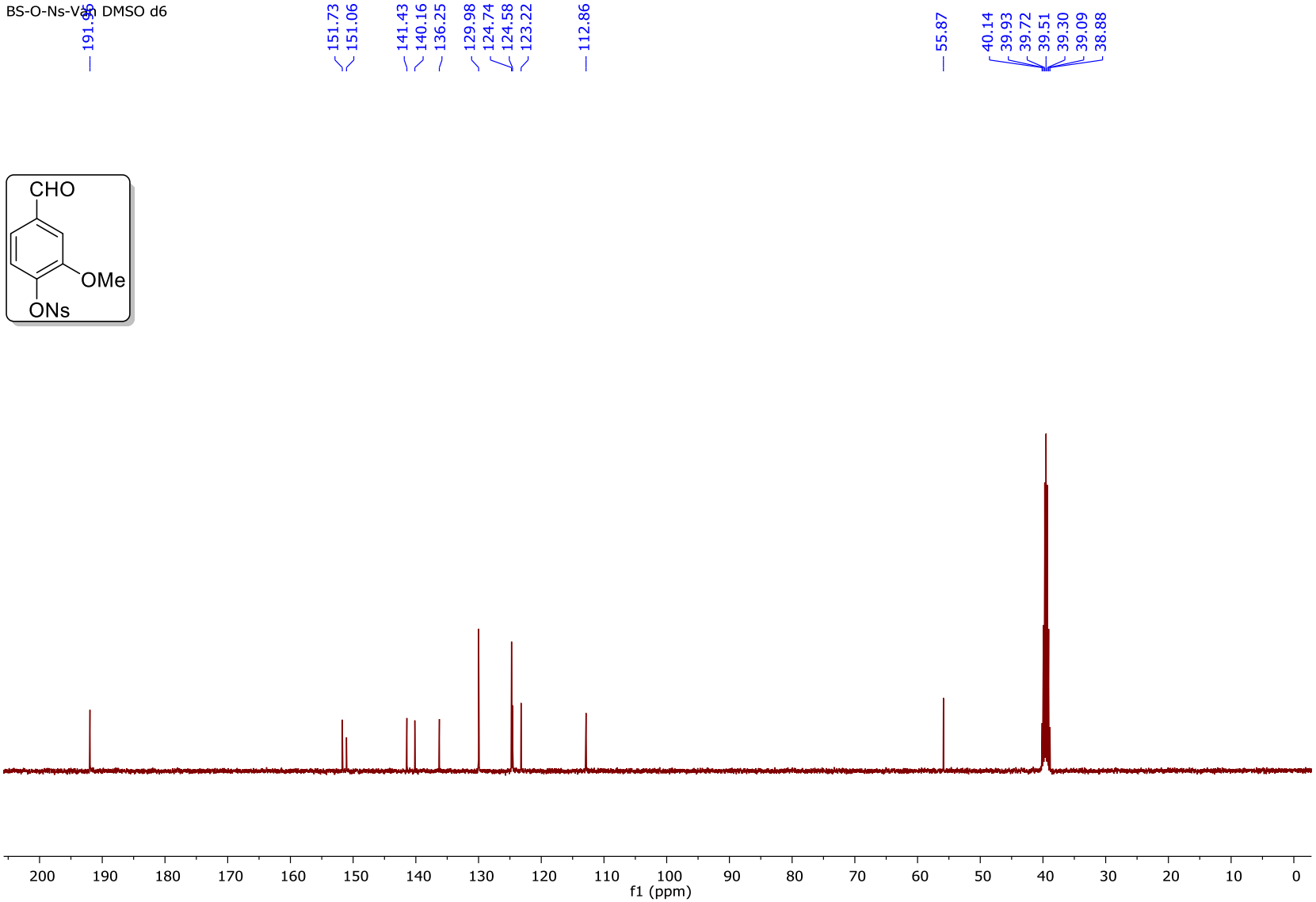
^{13}C NMR of 6-bromo-2-(4-oxobutyl)benzofuran-5-yl acetate (3a) (100 MHz, $CDCl_3$)



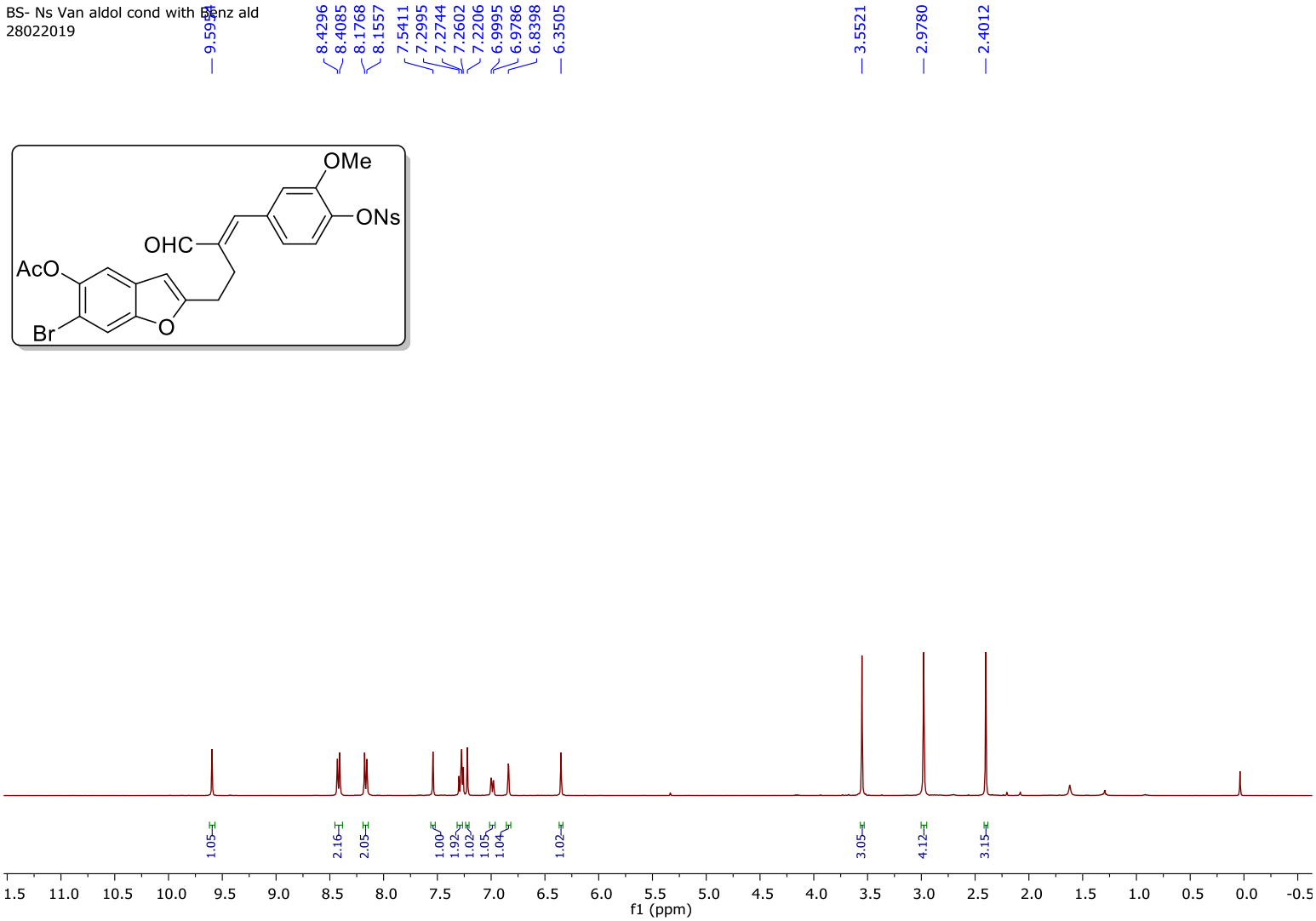
^{1}H NMR of 4-formyl-2-methoxyphenyl 4-nitrobenzenesulfonate (4) (400 MHz, DMSO-*d*$_6$)



^{13}C NMR of 4-formyl-2-methoxyphenyl 4-nitrobenzenesulfonate (4) (100 MHz, DMSO-d_6)



^{1}H NMR of (*E*)-6-bromo-2-(3-formyl-4-(3-methoxy-4-(((4-nitrophenyl)sulfonyl)oxy)phenyl)but-3-en-1-yl)benzofuran-5-yl acetate (22) (400 MHz, $CDCl_3$)



^{13}C NMR of (*E*)-6-bromo-2-(3-formyl-4-(3-methoxy-4-(((4-nitrophenyl)sulfonyl)oxy)phenyl)but-3-en-1-yl)benzofuran-5-yl acetate (22) (100 MHz, $CDCl_3$)