Semisynthesis and Cytotoxic Evaluation of an Ether Analogue Library Based on a Polyhalogenated Diphenyl Ether Scaffold Isolated from a *Lamellodysidea* Sponge

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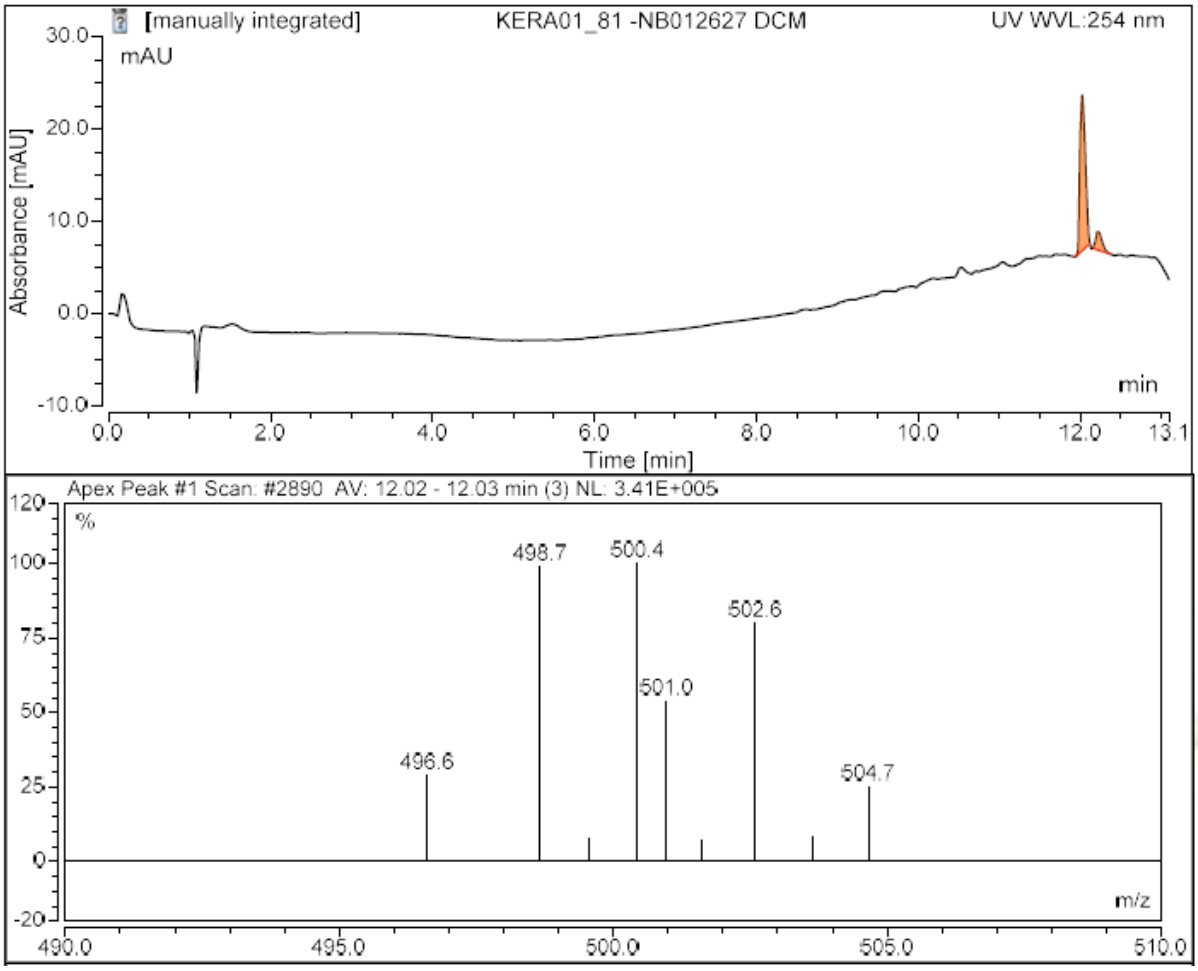
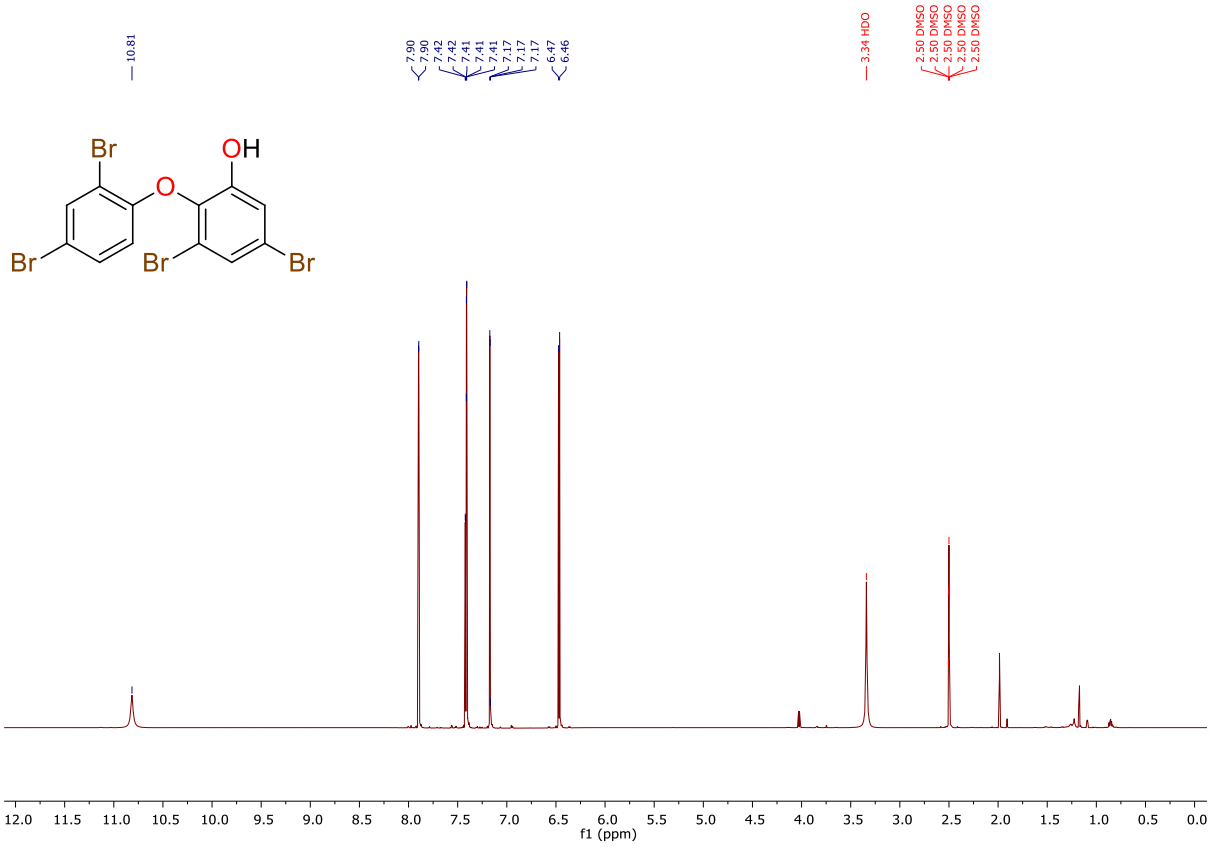
S1: UHPLC-MS Trace of *Lamellodysidea* sp. OTU 2054 CH_2Cl_2 Extract



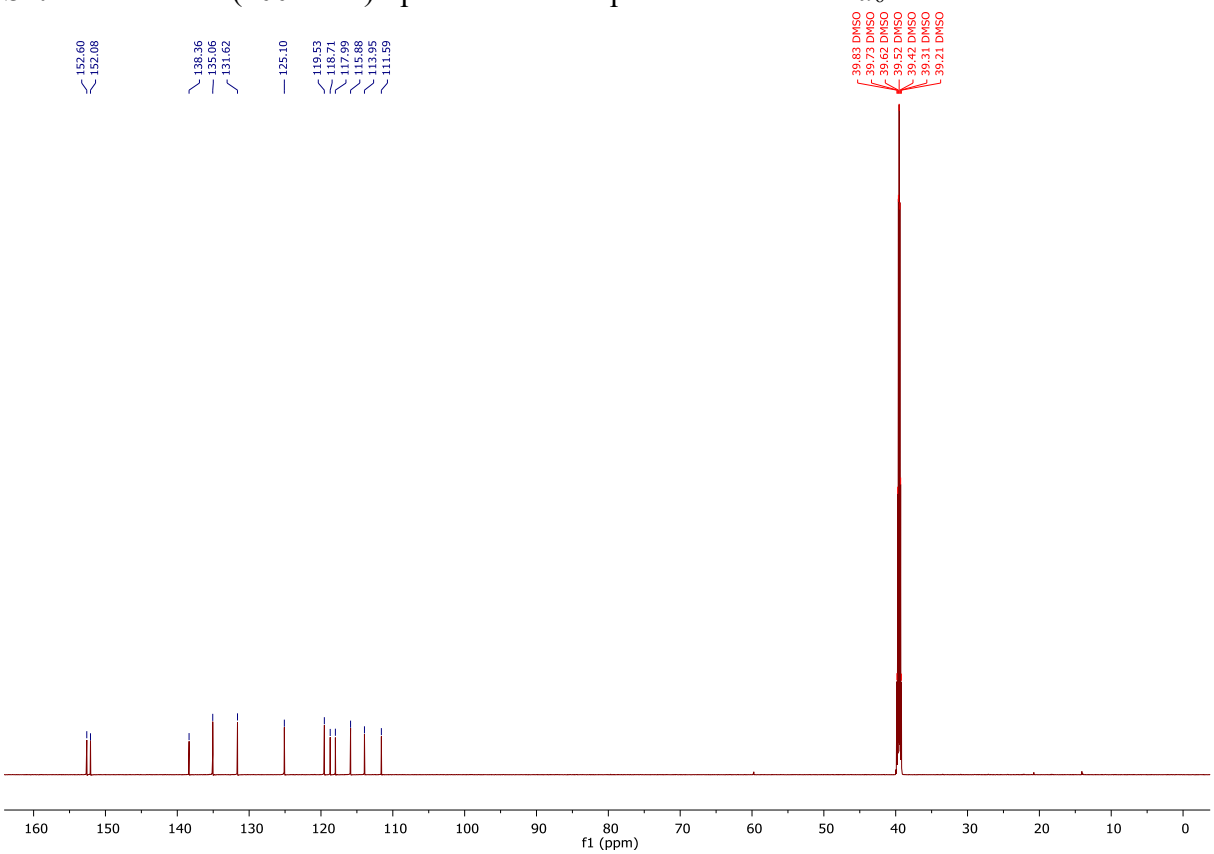
S2: Alkyl Halides (R-X) Used to Generate Compounds **2**–**13**.

Compound	**R-X**	**Yield**
2	methyl iodide	99%
3	allyl bromide	81%
4	bromoethanol	31%
5	cyclopentyl iodide	61%
6	benzyl bromide	62%
7	4-methylbenzyl bromide	88%
8	4-bromobenzyl bromide	61%
9	3-bromobenzyl bromide	81%
10	3-chlorobenzyl chloride	55%
11	3-nitrobenzyl bromide	99%
12	2,5-difluorobenzyl bromide	73%
13	2-phenylbenzyl bromide	17%

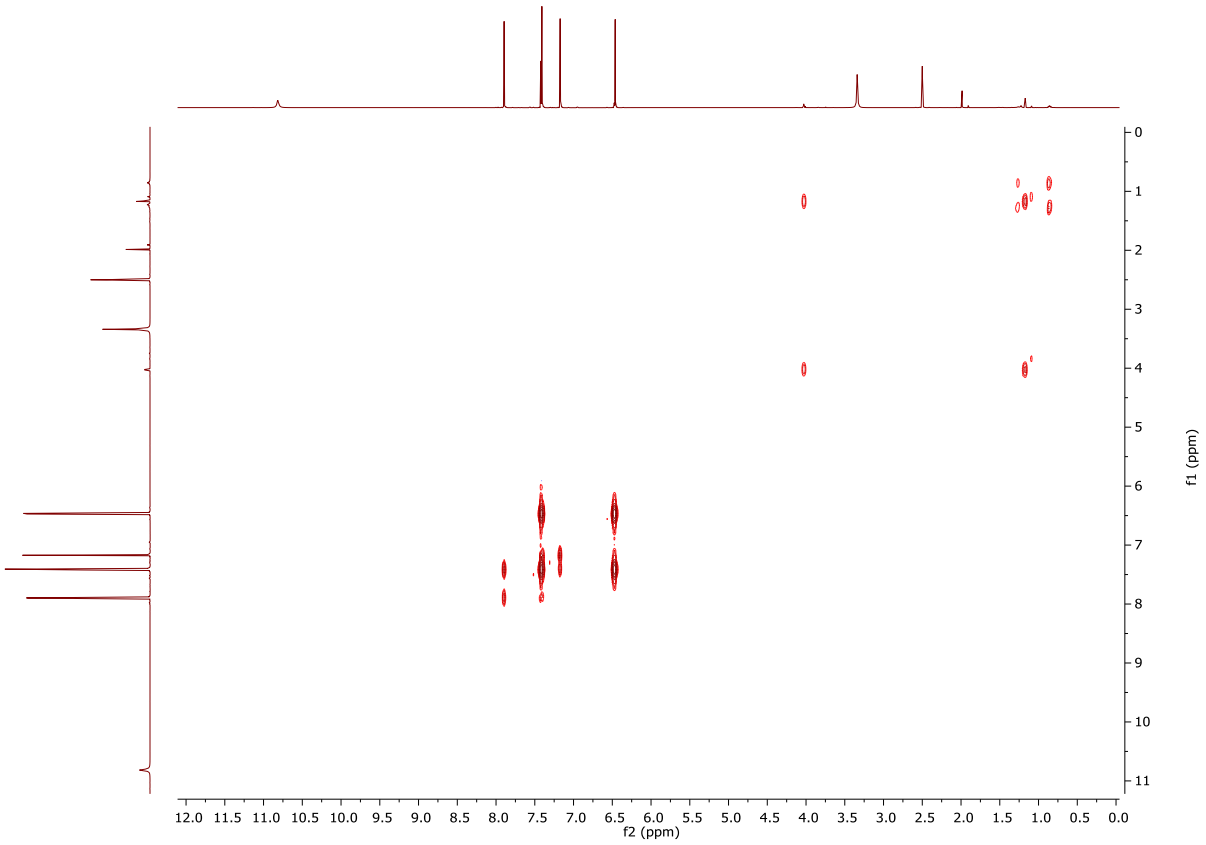
S3: ^{1}H NMR (800 MHz) Spectrum of Compound **1** in DMSO-d_6



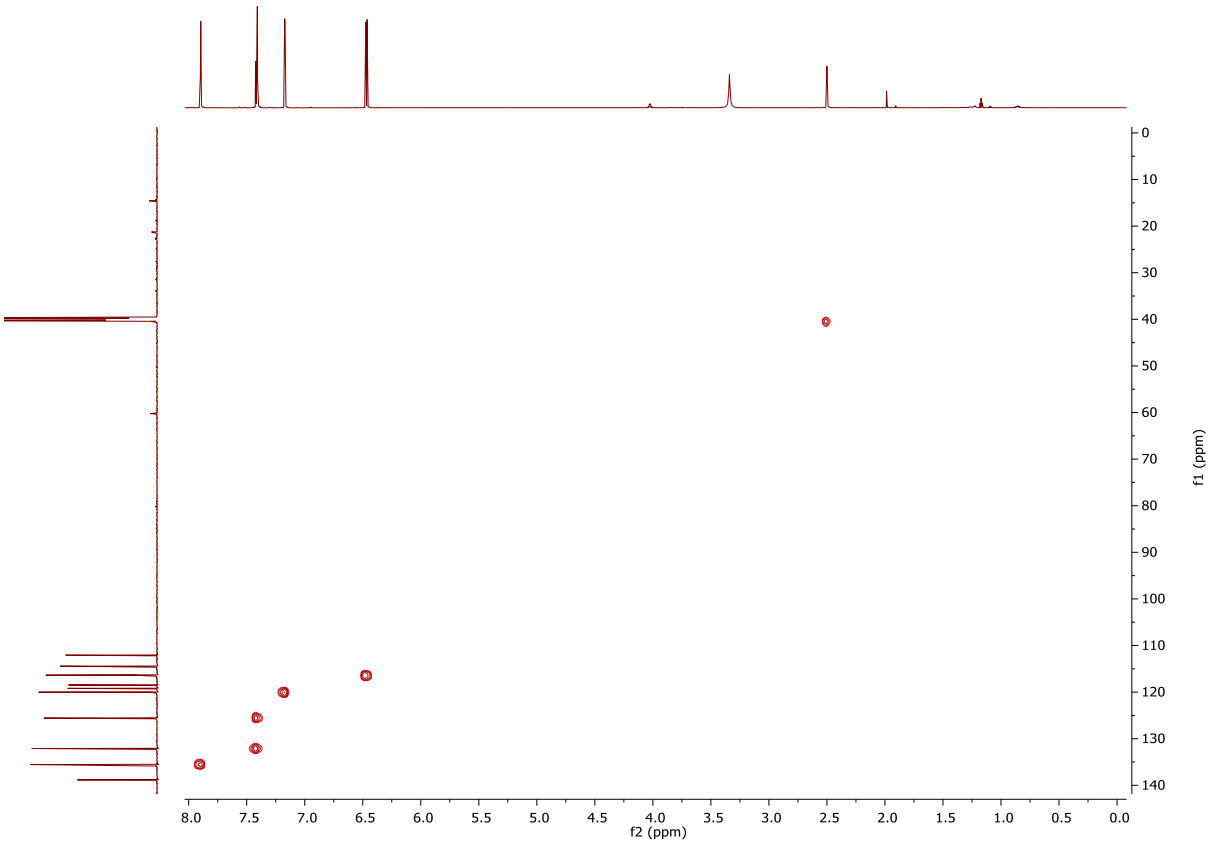
S4: ^{13}C NMR (200 MHz) Spectrum of Compound **1** in DMSO-d_6



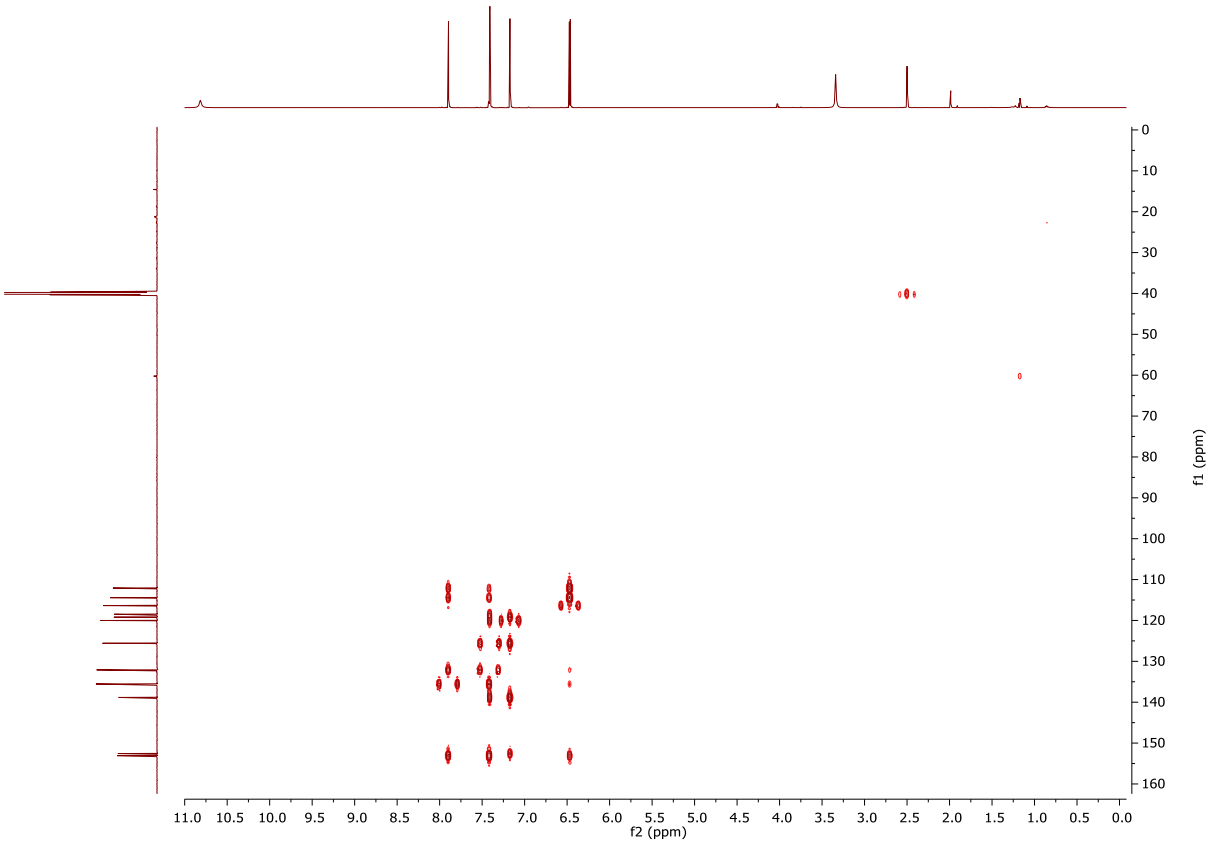
S5: COSY Spectrum of Compound **1** in DMSO-d_6



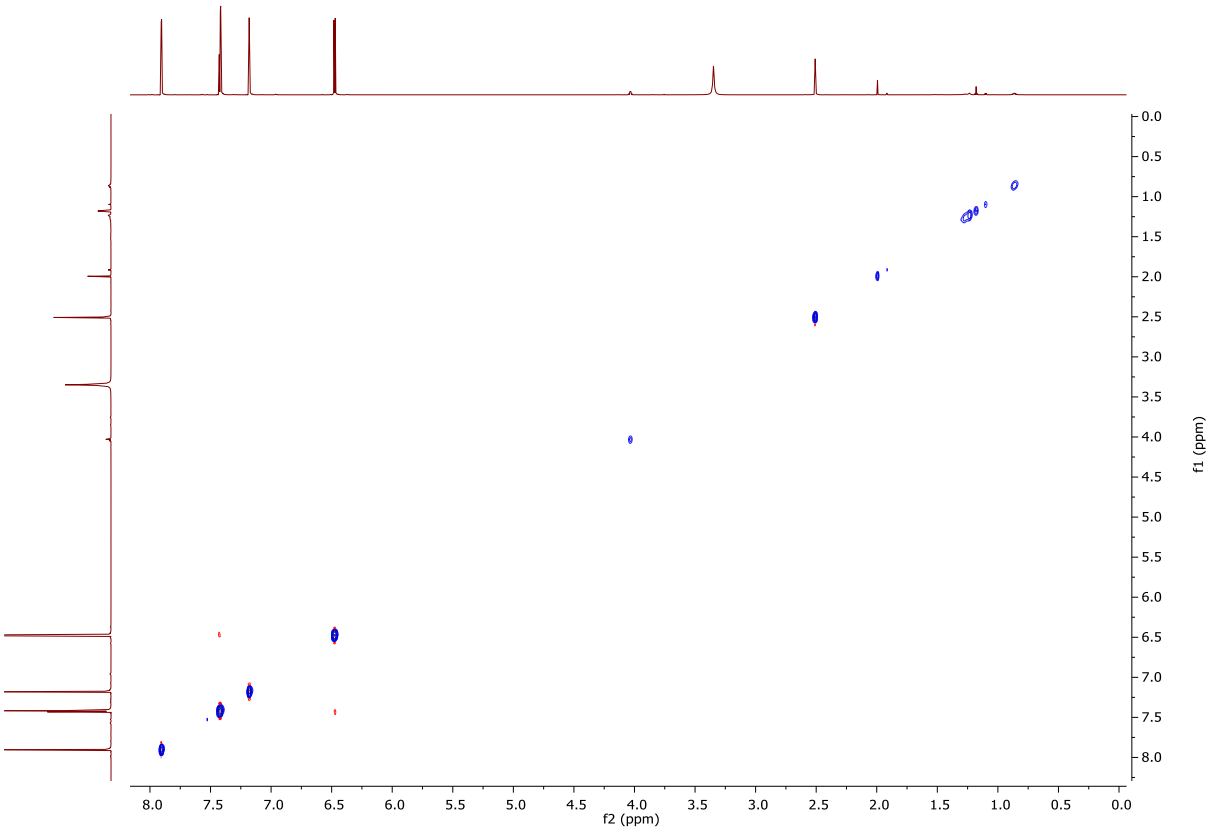
S6: HSQC Spectrum of Compound **1** in DMSO-d_6



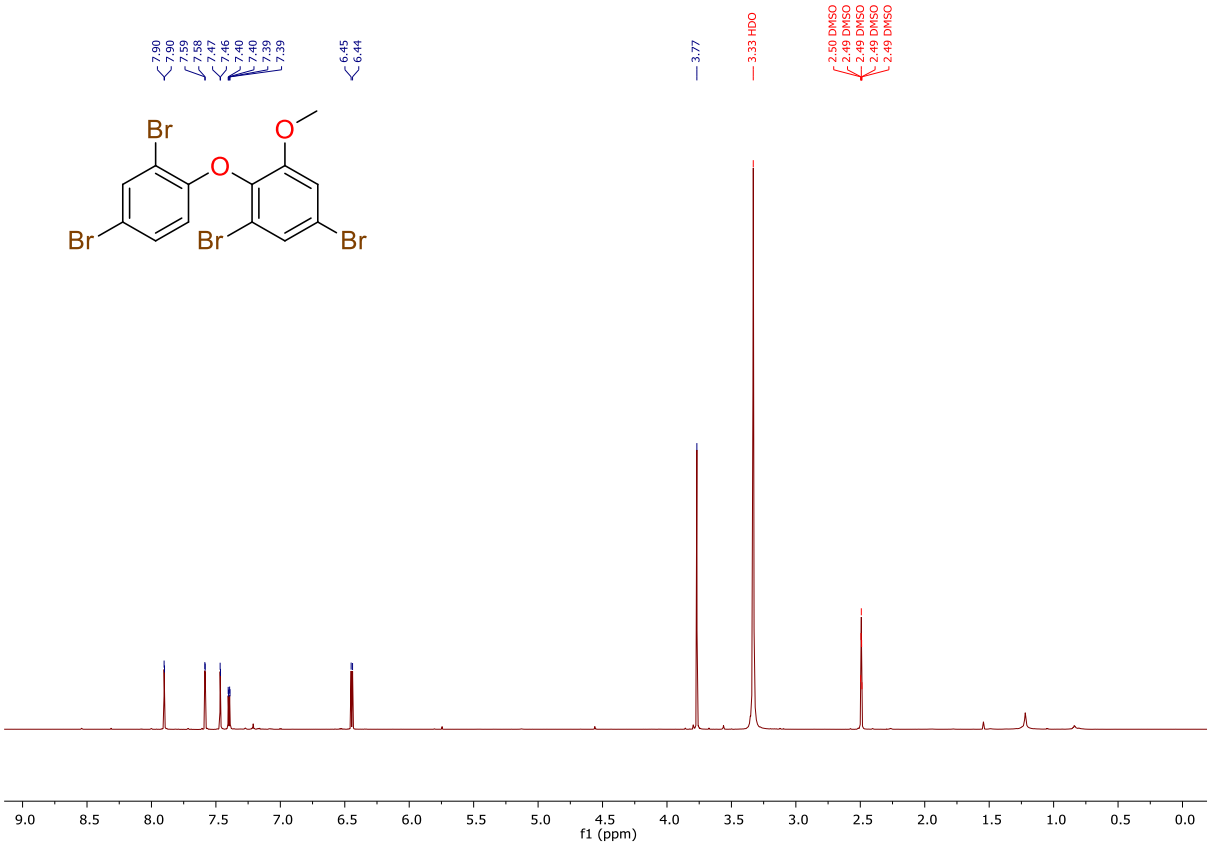
S7: HMBC Spectrum of Compound **1** in DMSO-d_6



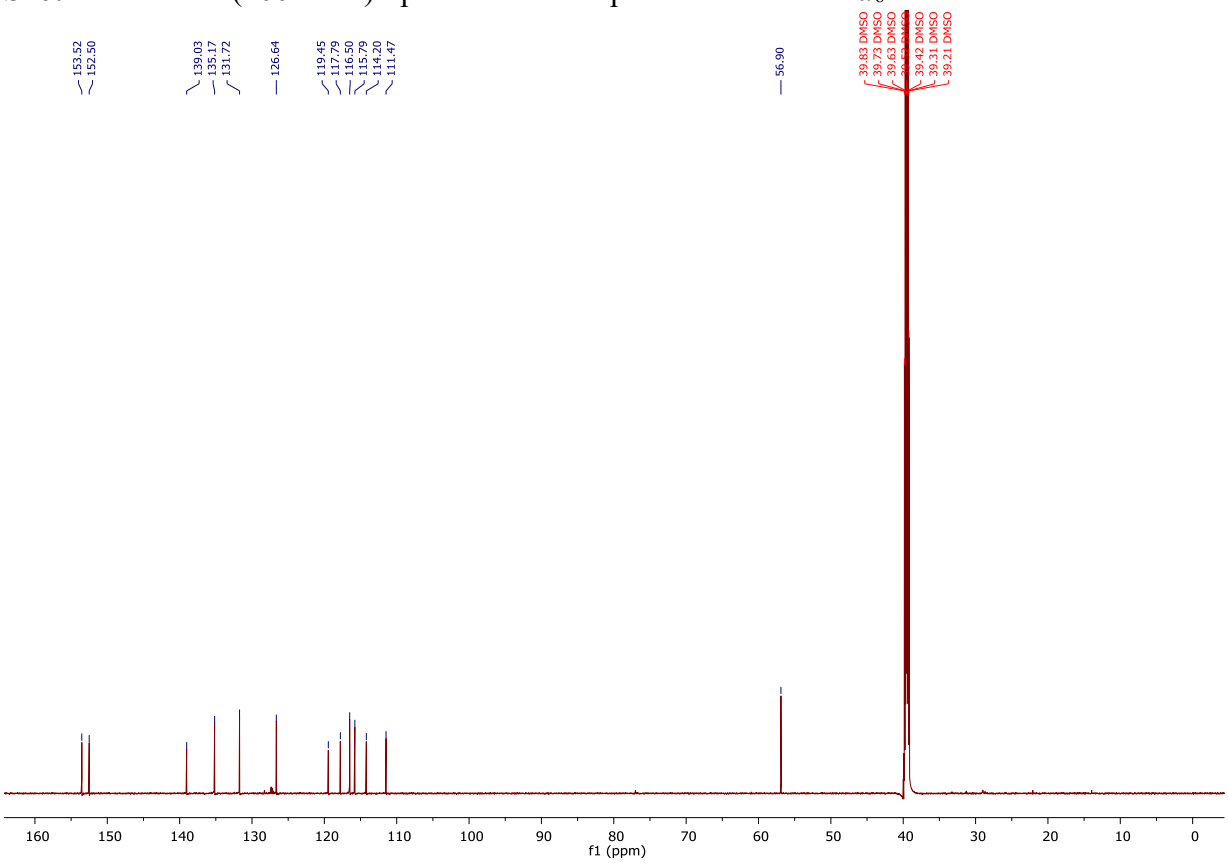
S8: ROESY Spectrum of Compound **1** in DMSO-d_6



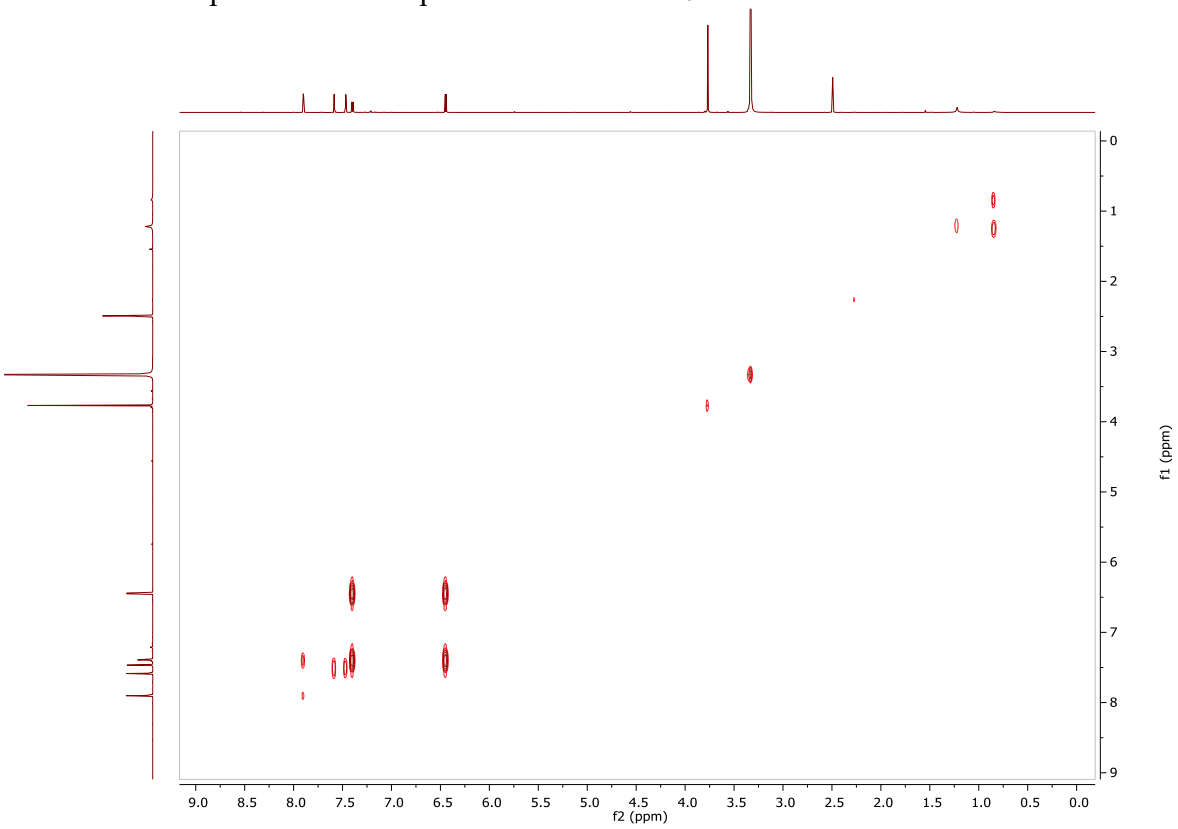
S9: ^{1}H NMR (800 MHz) Spectrum of Compound **2** in DMSO-d_6



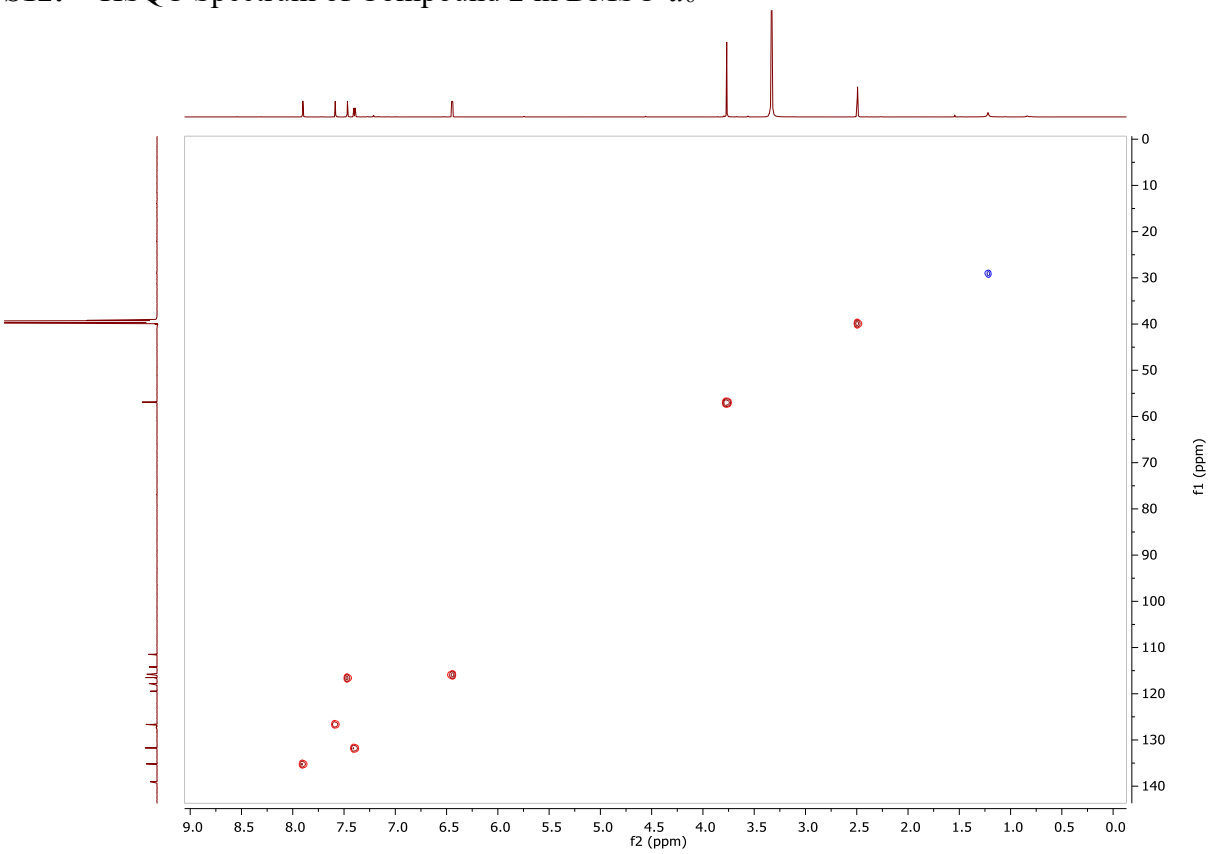
S10: ^{13}C NMR (200 MHz) Spectrum of Compound **2** in DMSO-d_6



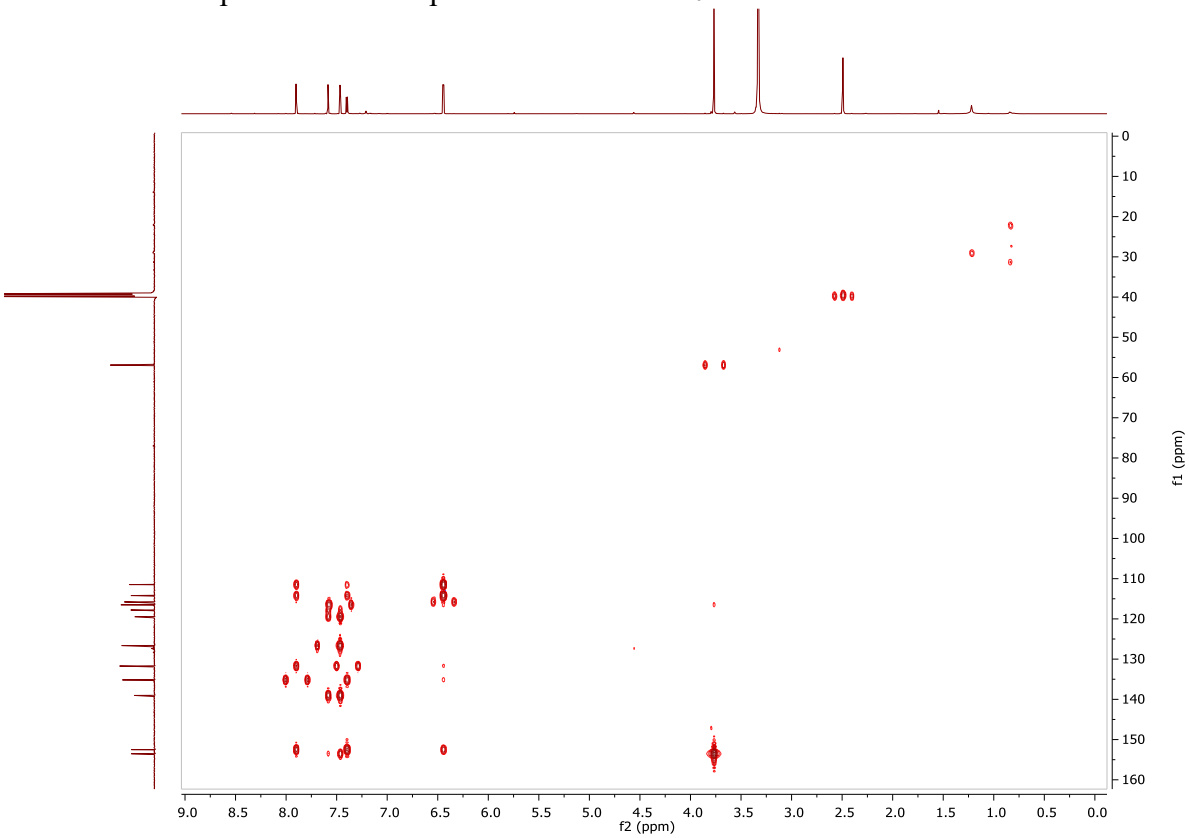
S11: COSY Spectrum of Compound **2** in DMSO-d_6



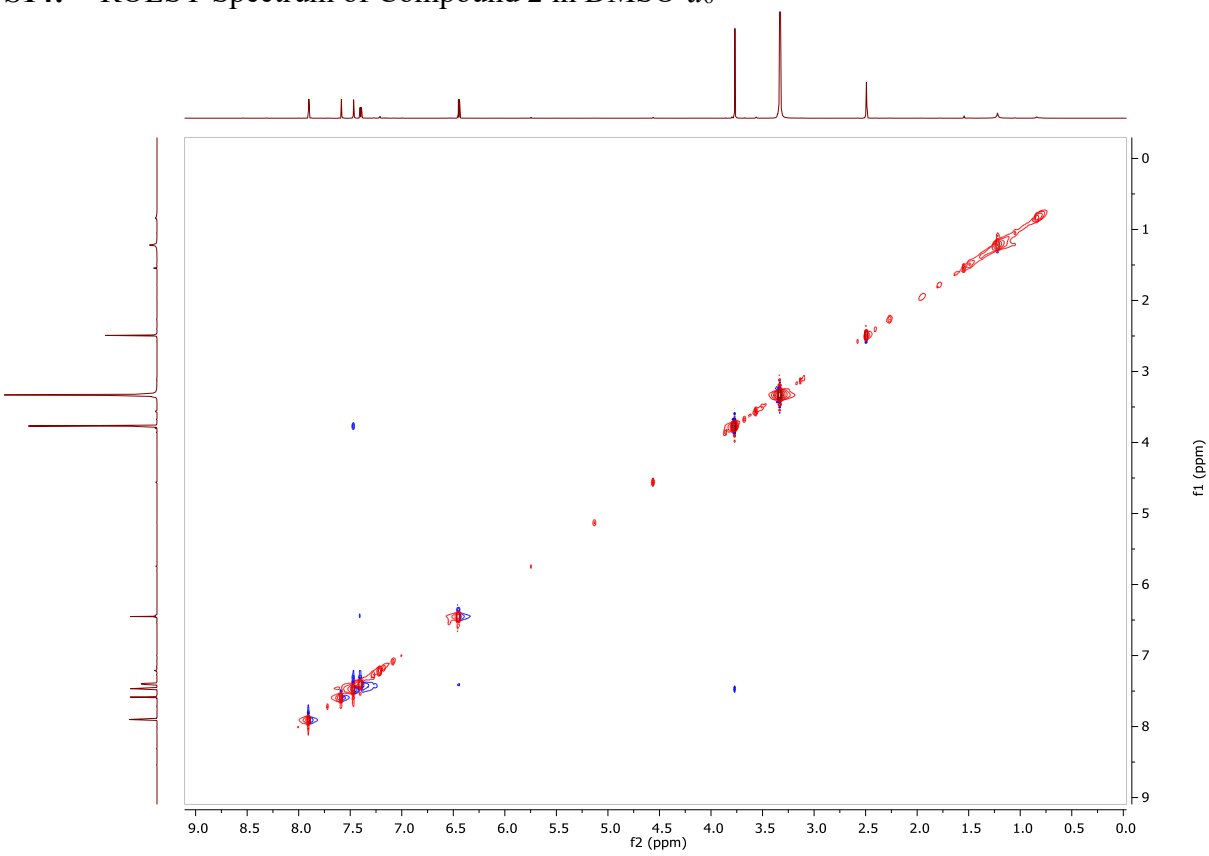
S12: HSQC Spectrum of Compound **2** in DMSO-d_6



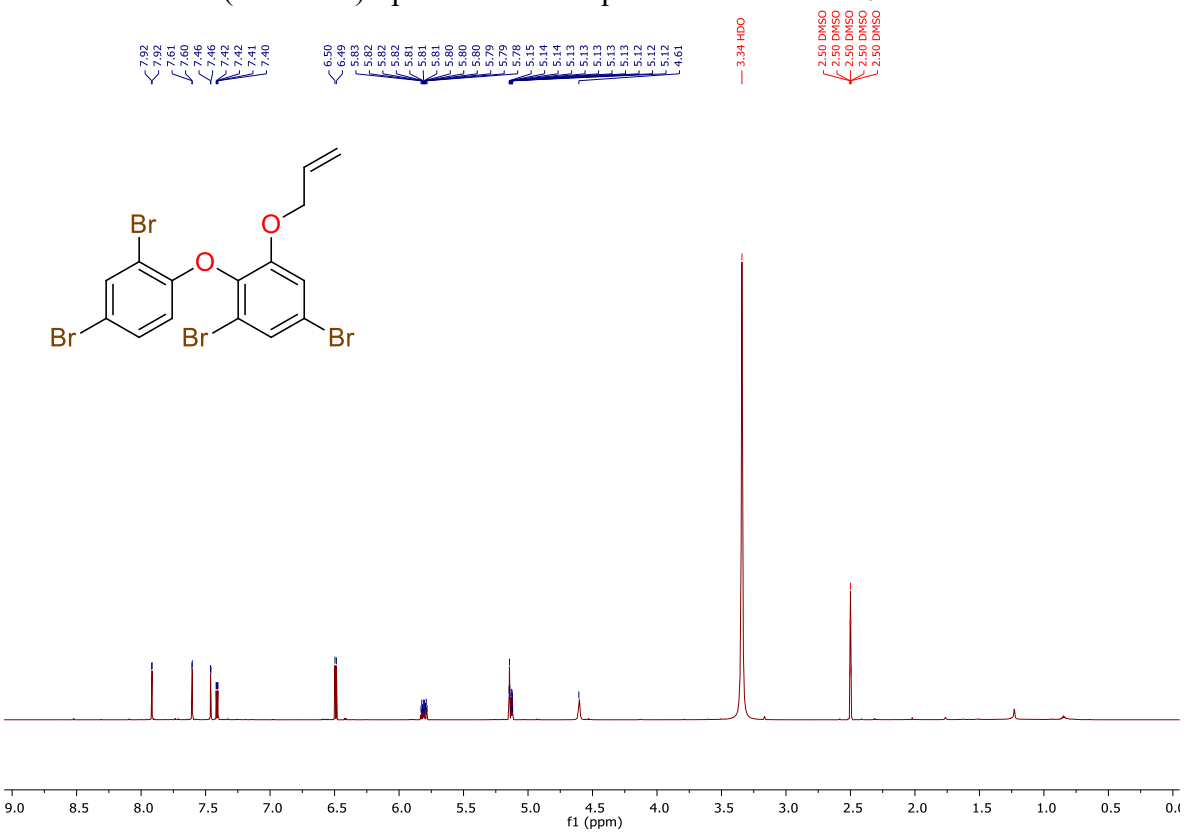
S13: HMBC Spectrum of Compound **2** in DMSO-d_6



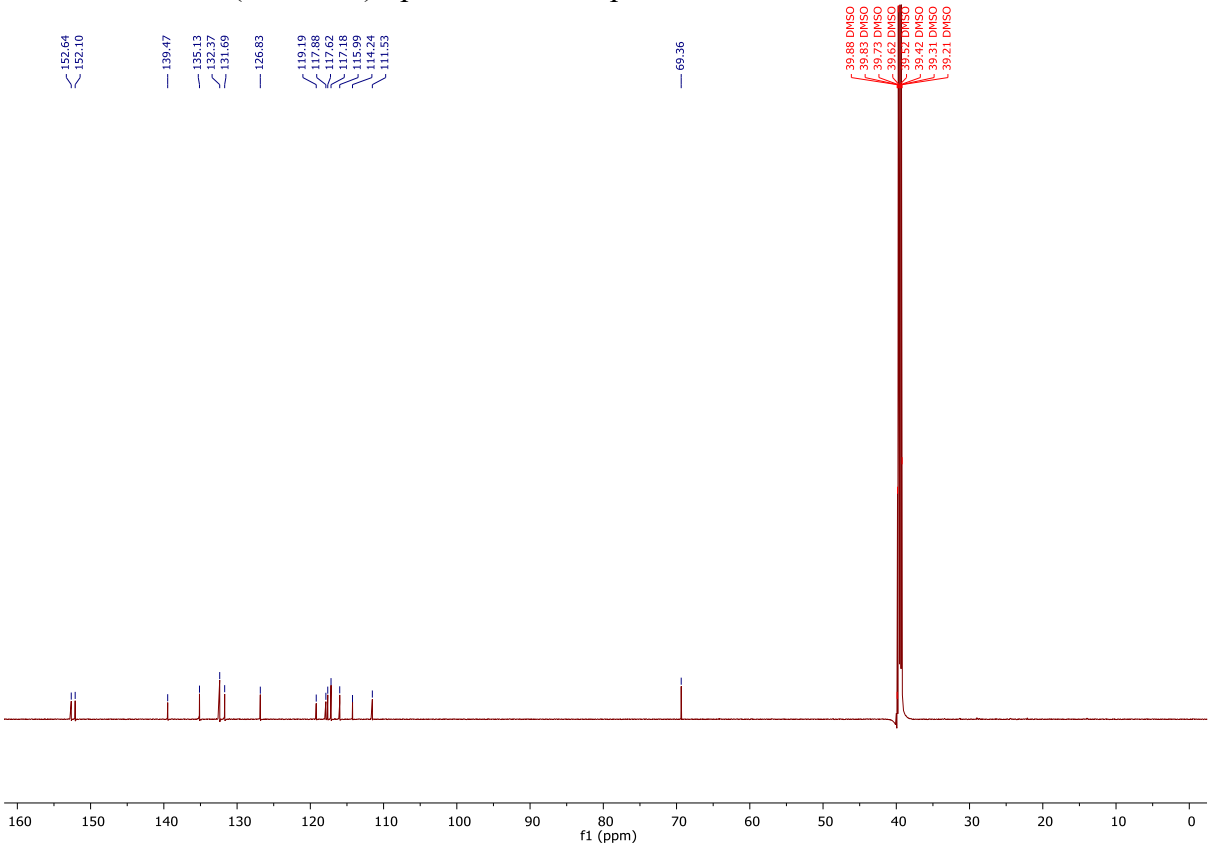
S14: ROESY Spectrum of Compound **2** in DMSO-d_6



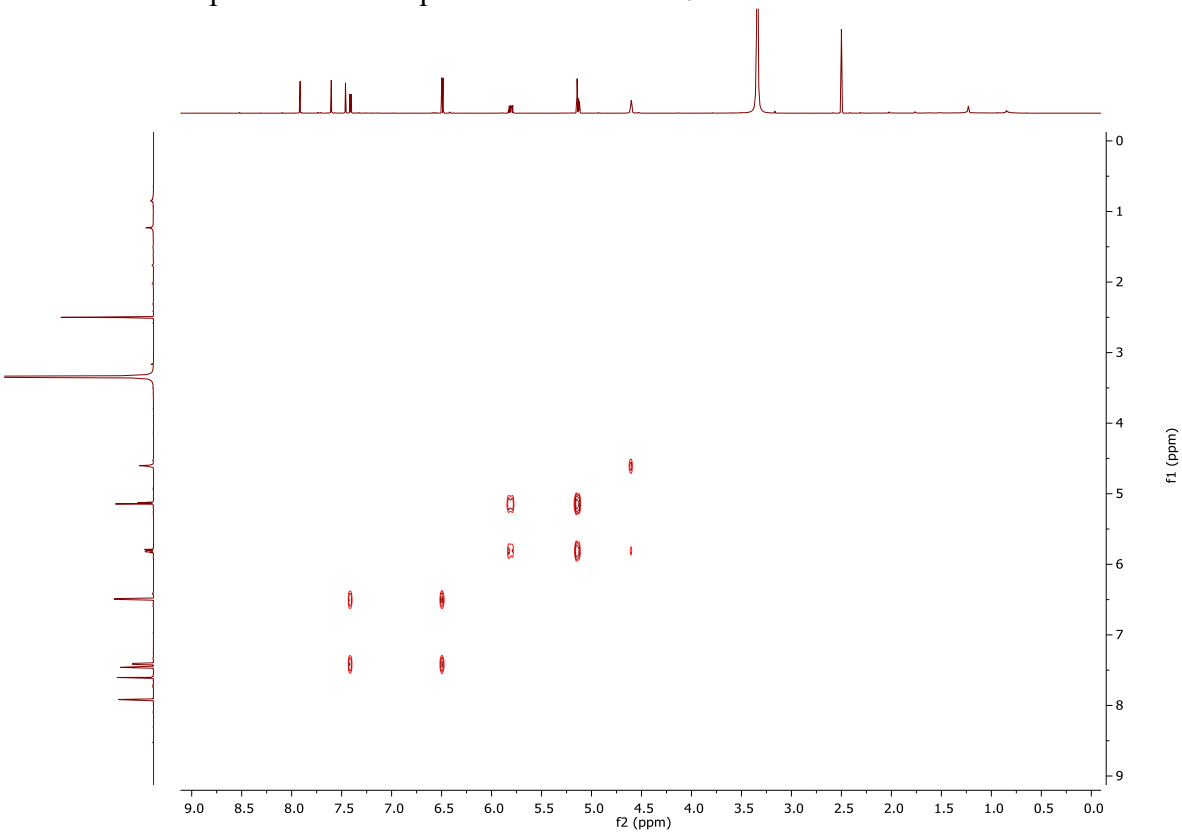
S15: ^{1}H NMR (800 MHz) Spectrum of Compound **3** in DMSO-d_6



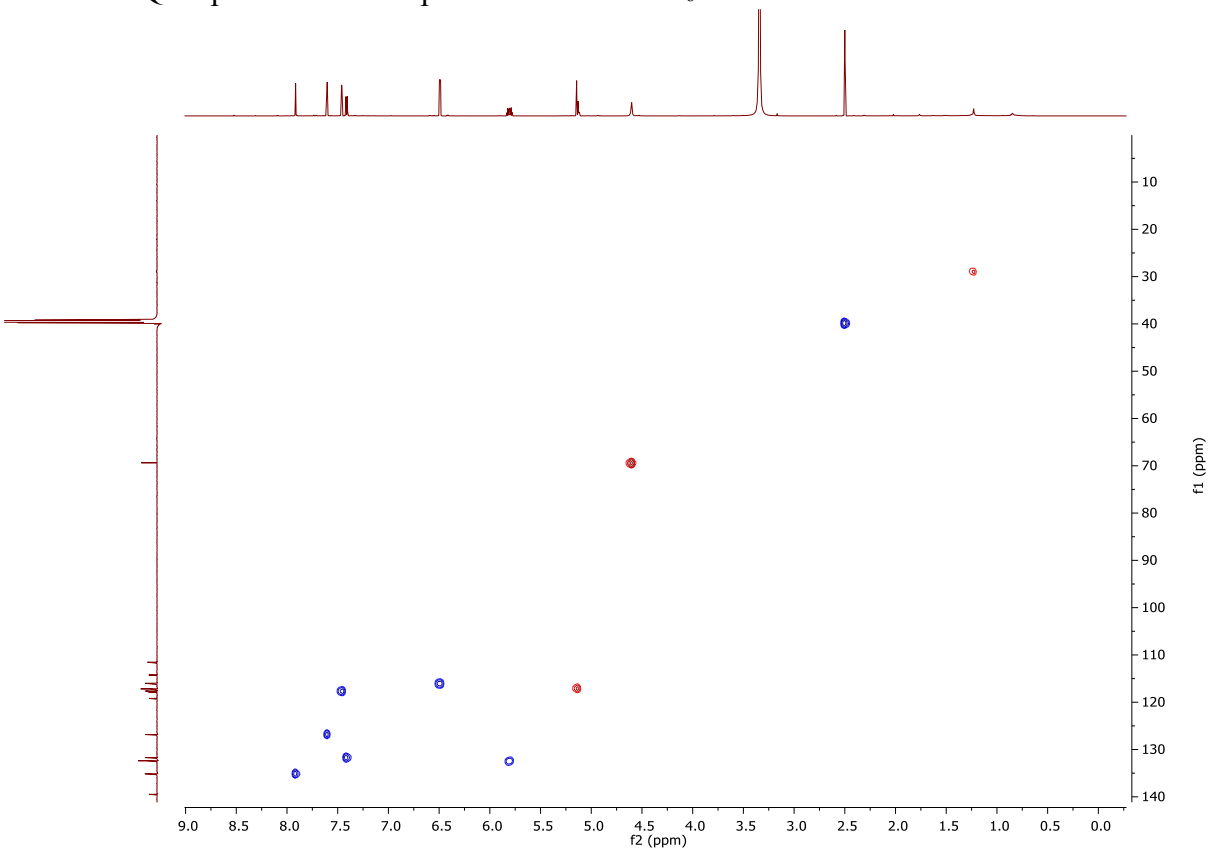
S16: ^{13}C NMR (200 MHz) Spectrum of Compound **3** in DMSO-d_6



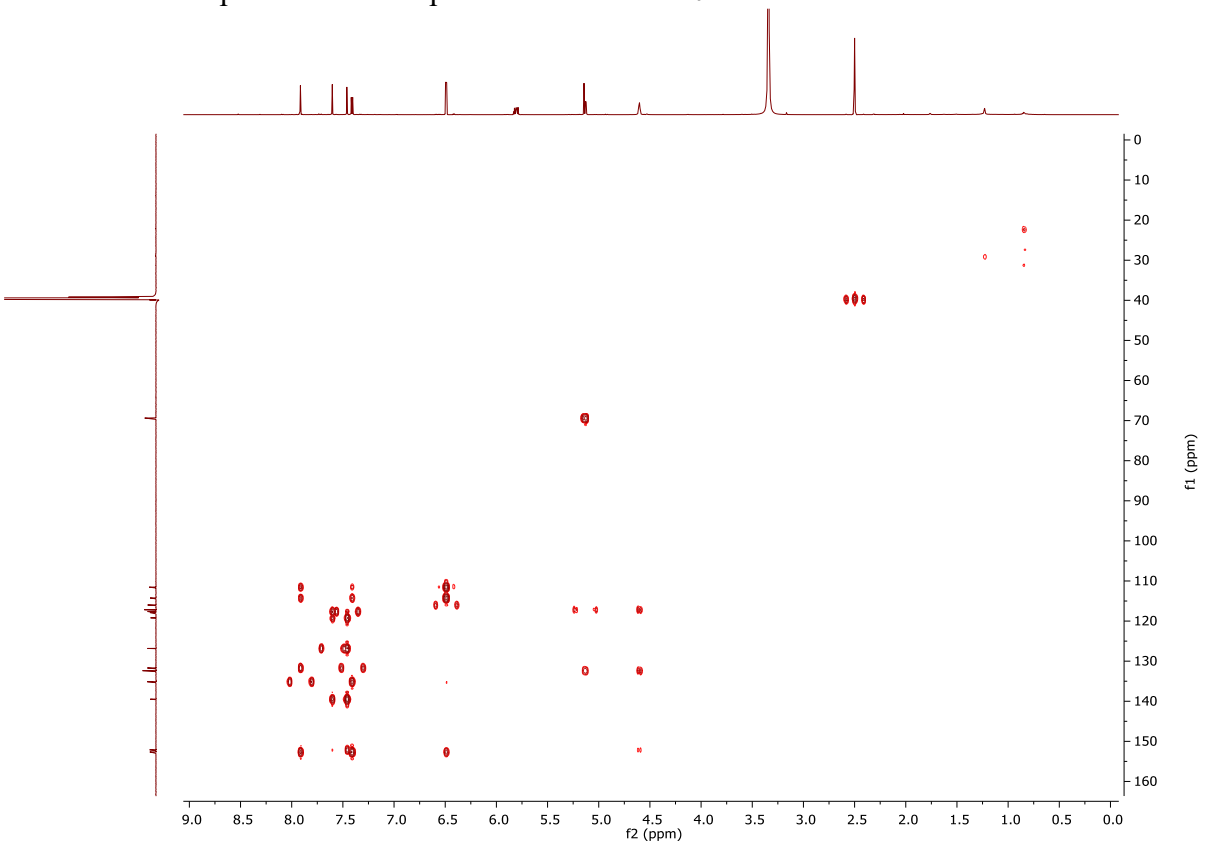
S17: COSY Spectrum of Compound **3** in DMSO-d_6



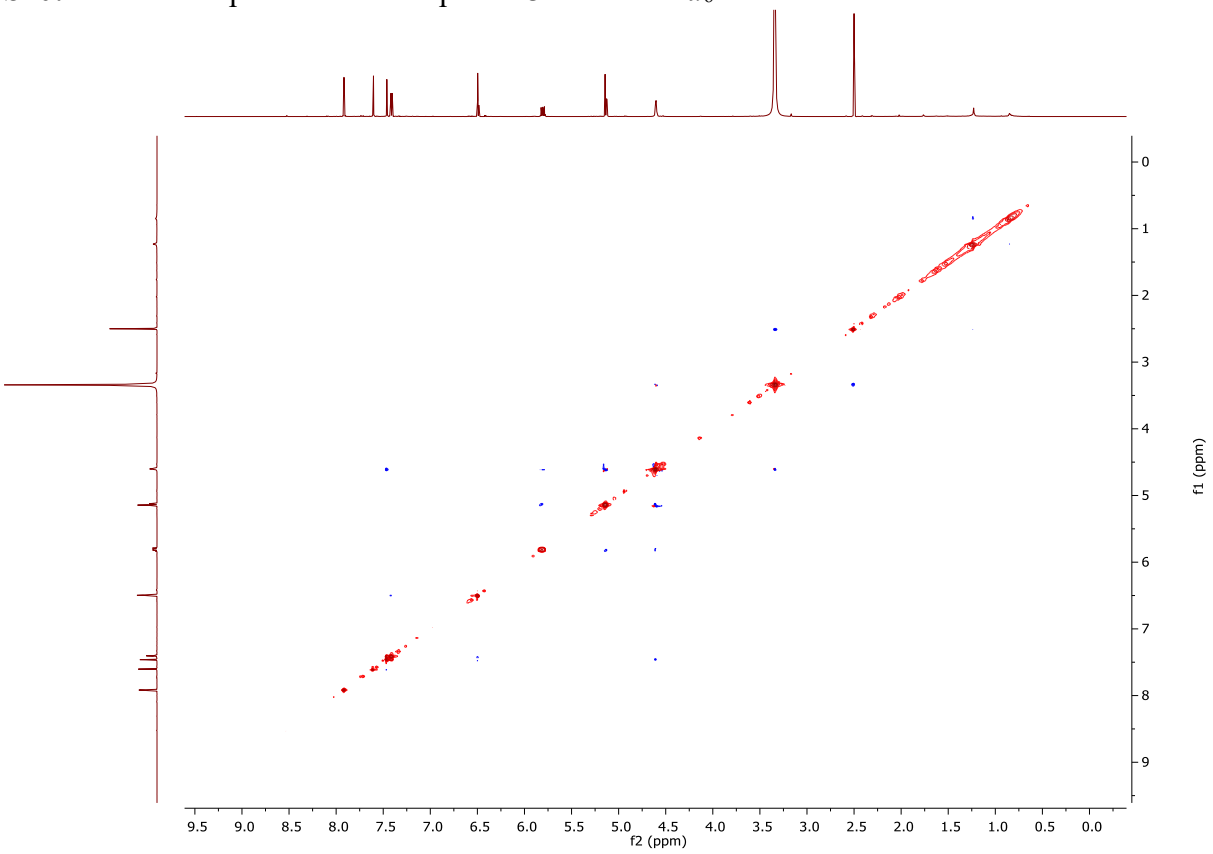
S18: HSQC Spectrum of Compound **3** in DMSO-d_6



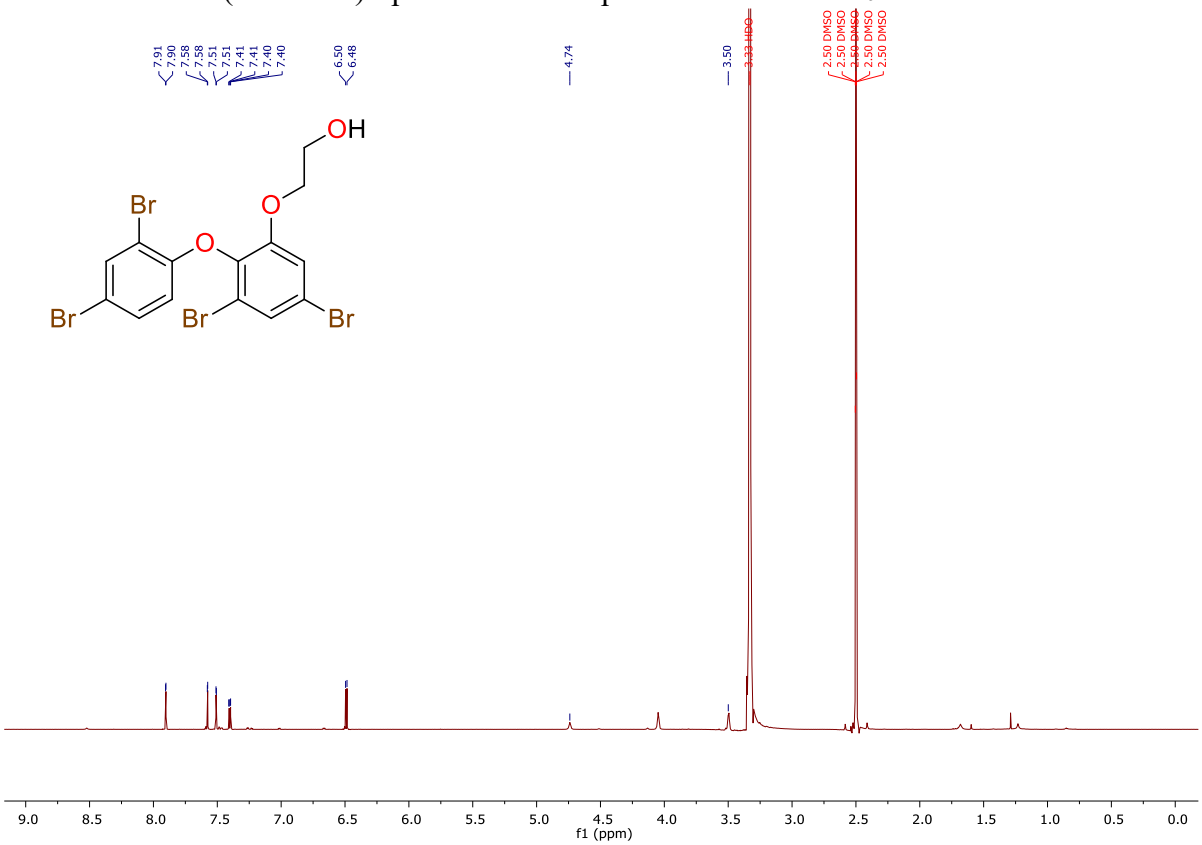
S19: HMBC Spectrum of Compound **3** in DMSO-d_6



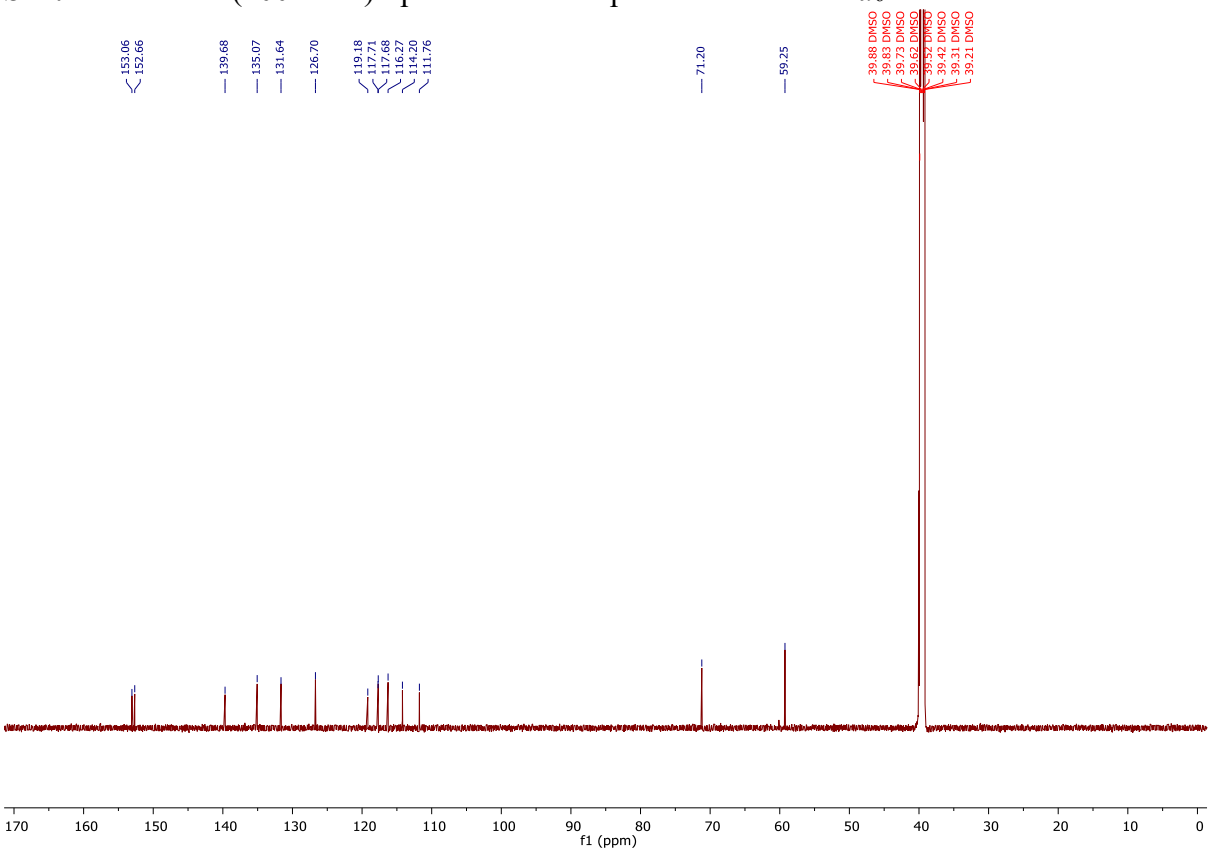
S20: ROESY Spectrum of Compound **3** in DMSO-d_6



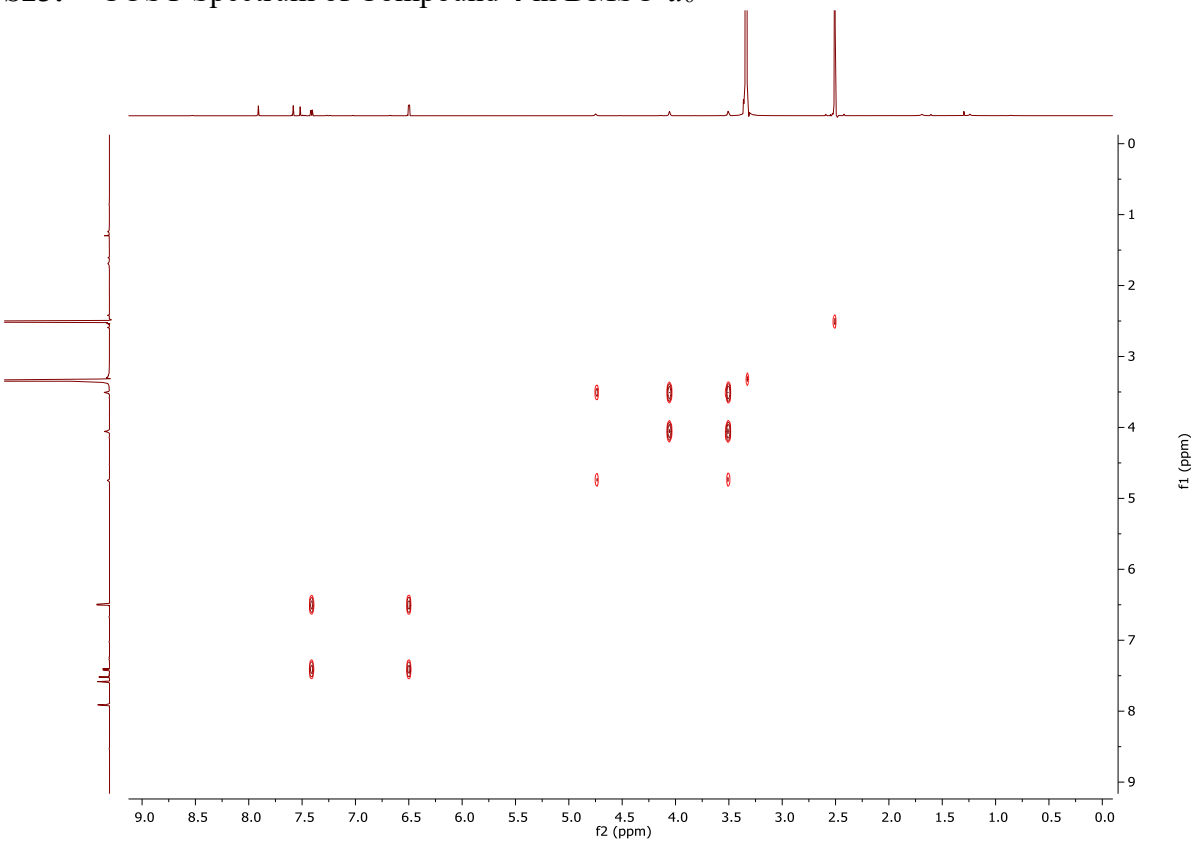
S21: ^{1}H NMR (800 MHz) Spectrum of Compound **4** in DMSO-*d*6



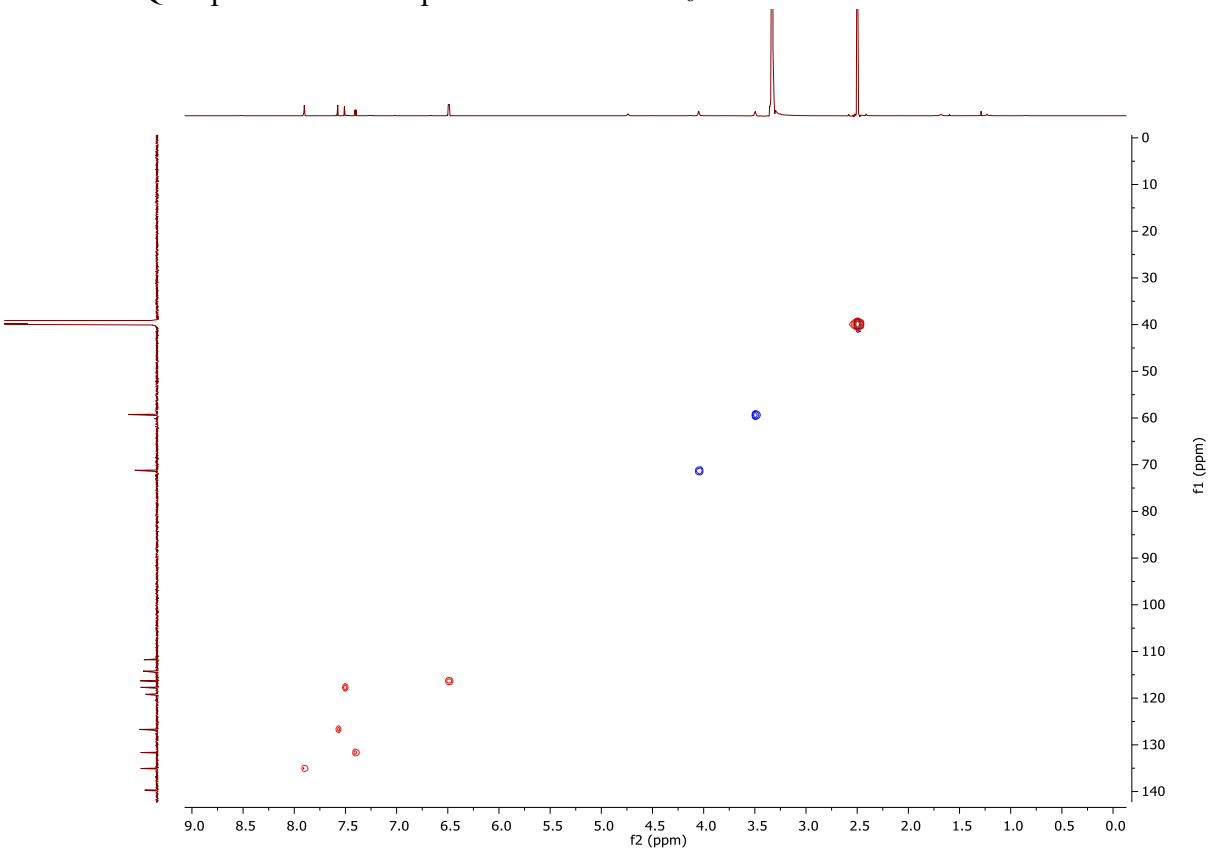
S22: ^{13}C NMR (200 MHz) Spectrum of Compound **4** in DMSO-*d*6



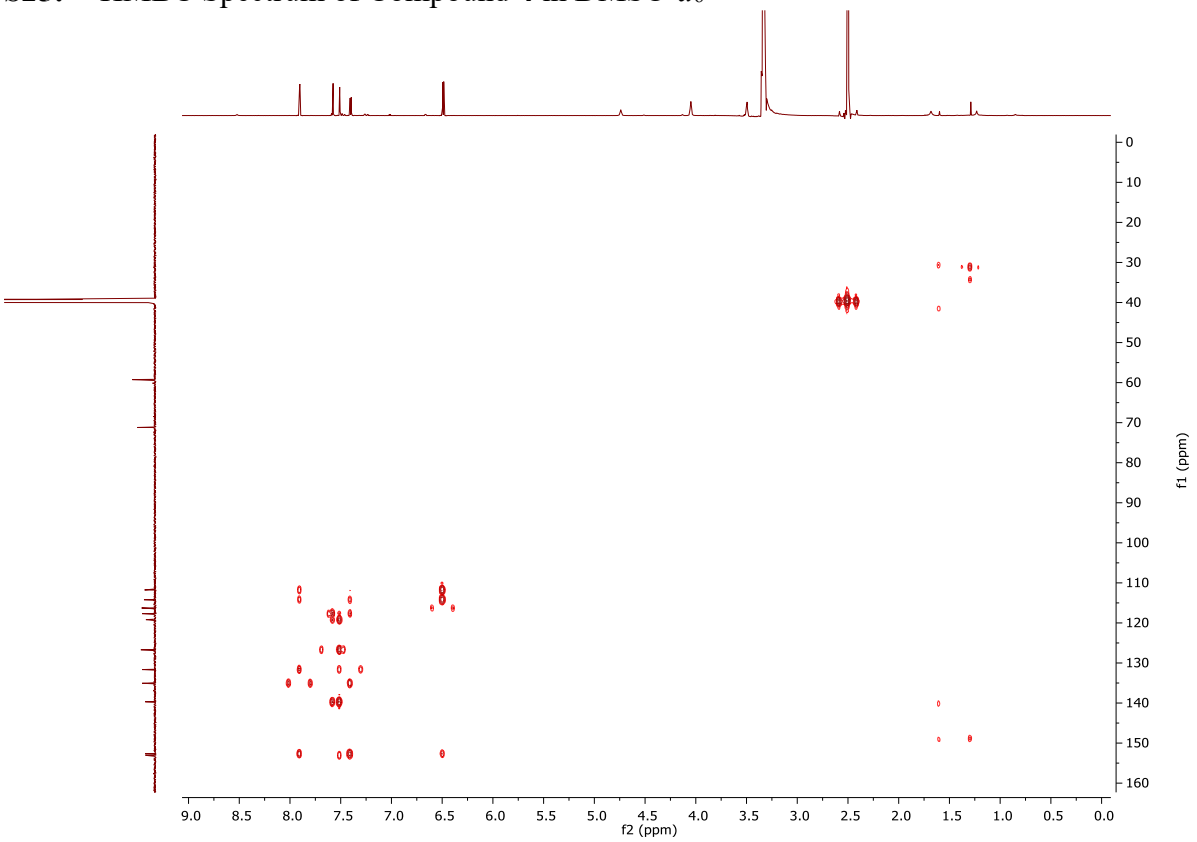
S23: COSY Spectrum of Compound **4** in DMSO-d_6



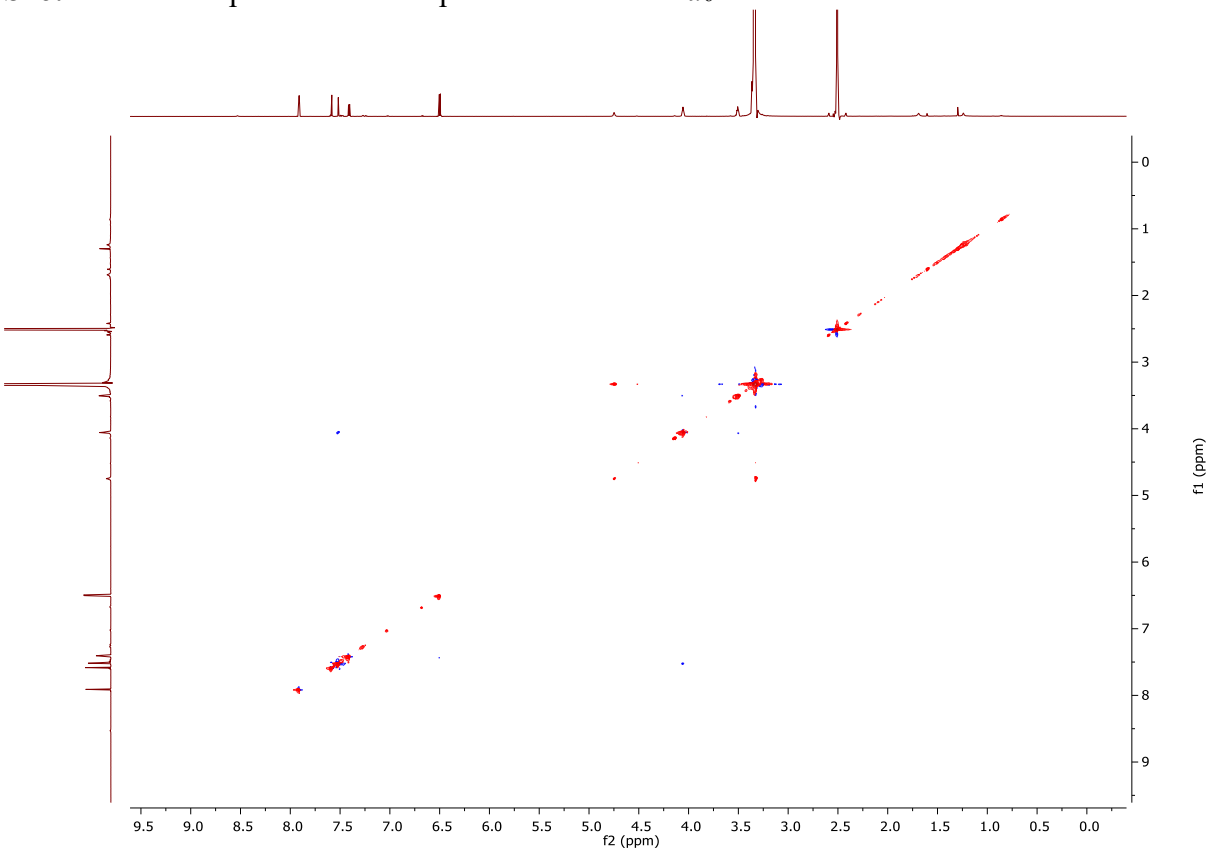
S24: HSQC Spectrum of Compound **4** in DMSO-d_6



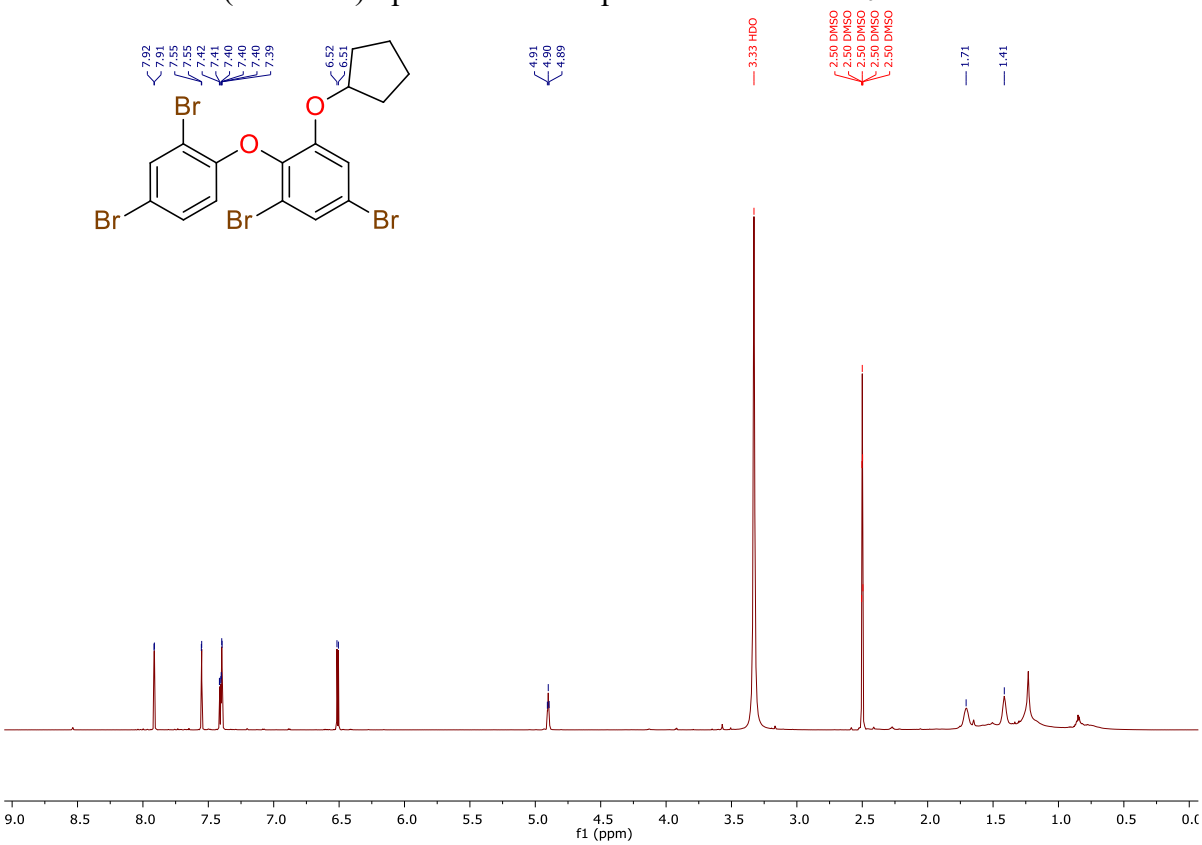
S25: HMBC Spectrum of Compound **4** in DMSO-d_6



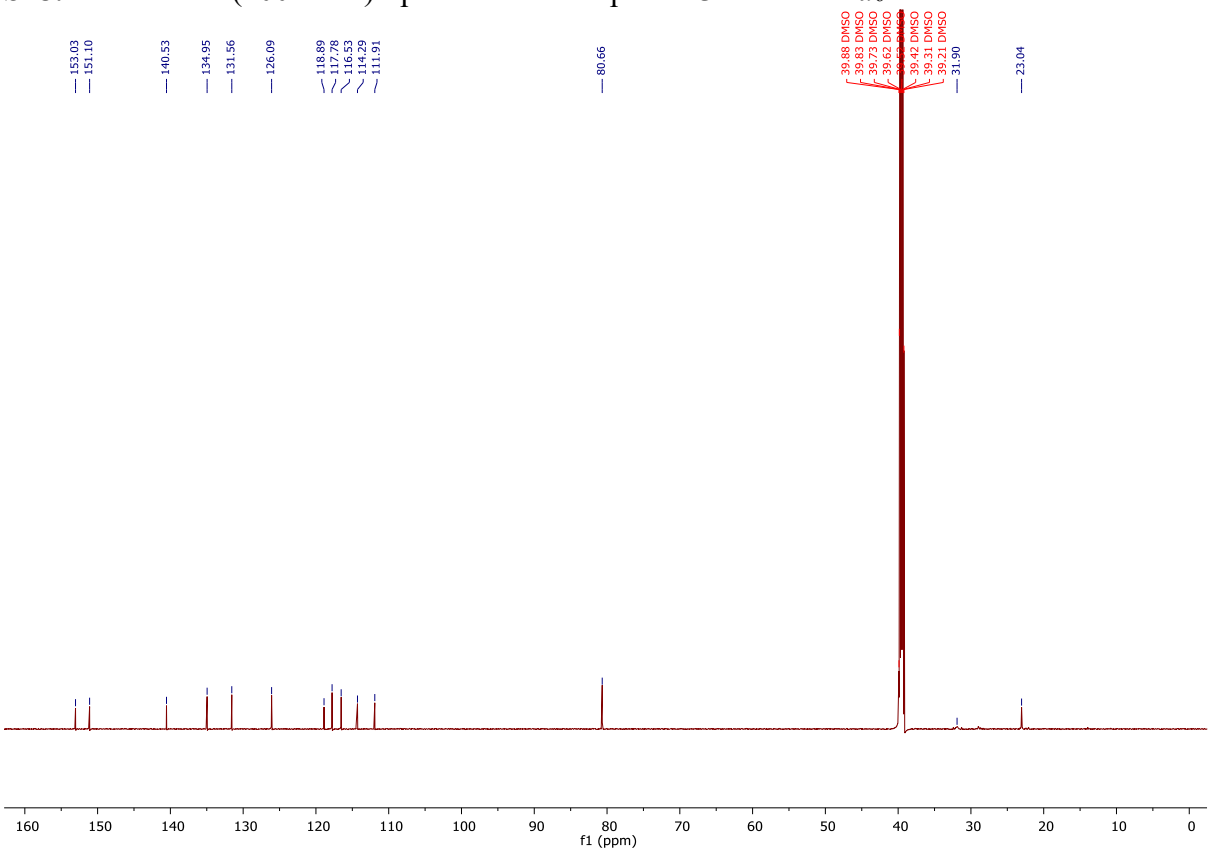
S26: ROESY Spectrum of Compound **4** in DMSO-d_6



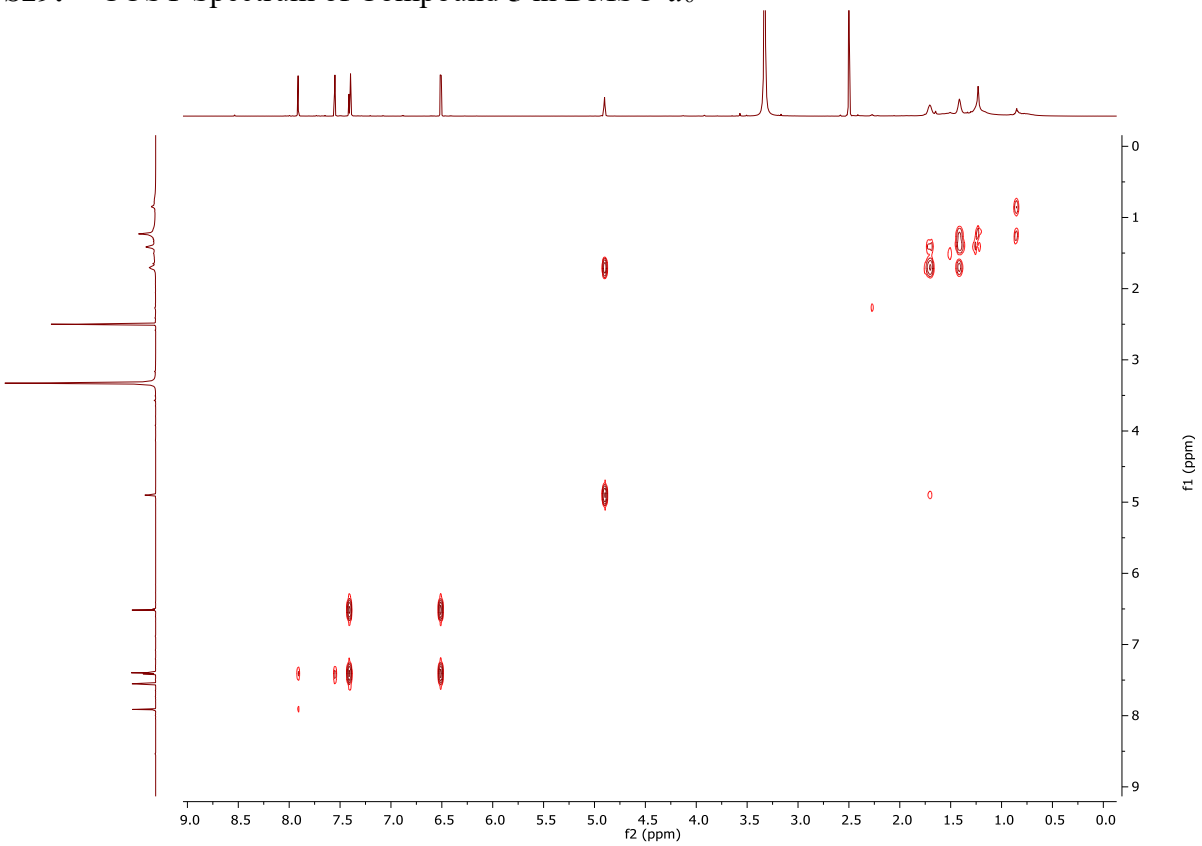
S27: ^{1}H NMR (800 MHz) Spectrum of Compound **5** in DMSO-*d*6



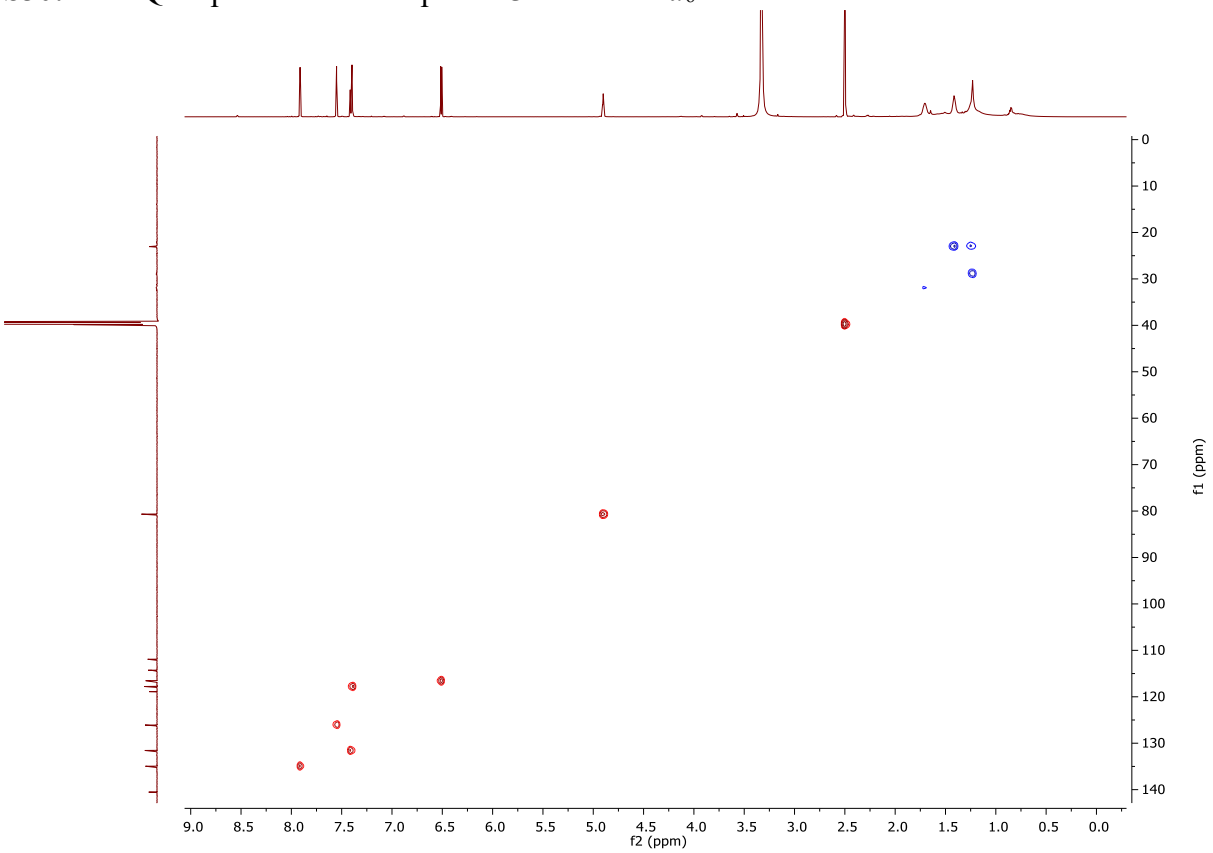
S28: ^{13}C NMR (200 MHz) Spectrum of Compound **5** in DMSO-*d*6



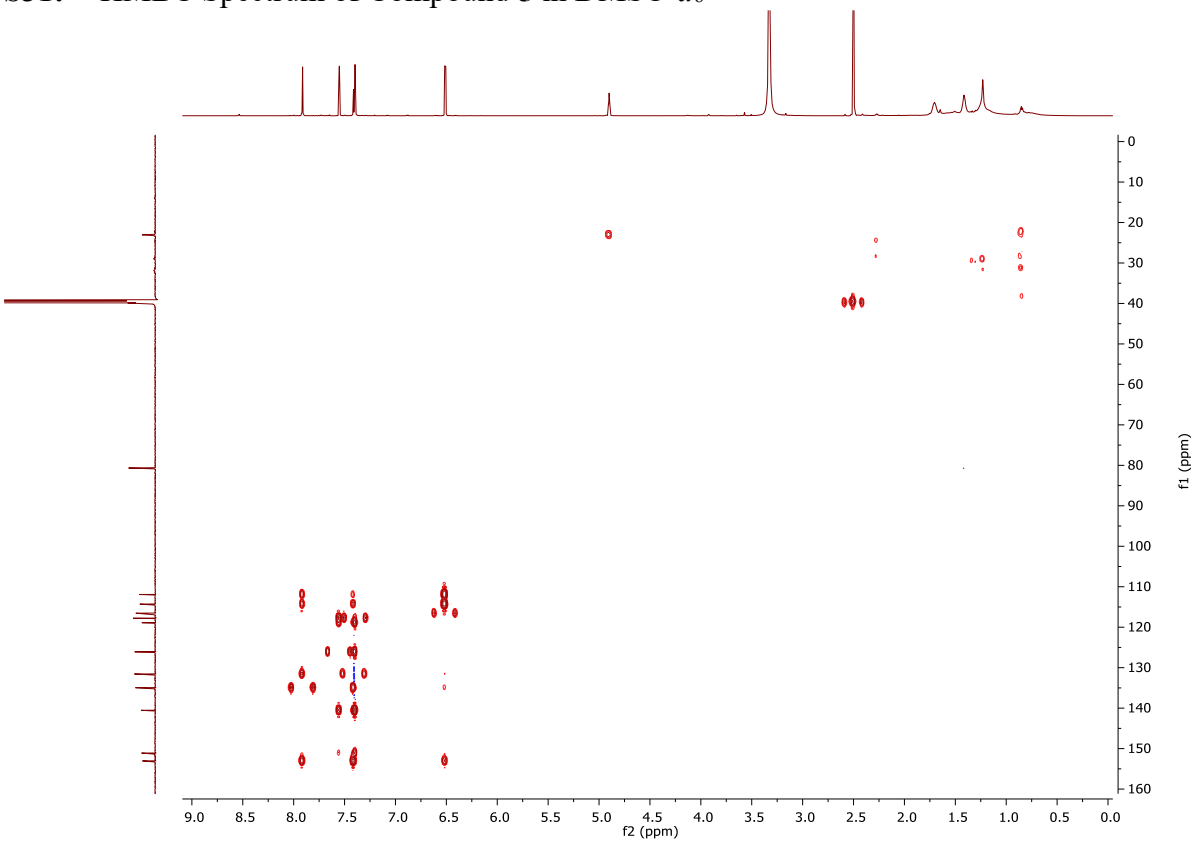
S29: COSY Spectrum of Compound **5** in DMSO-d_6



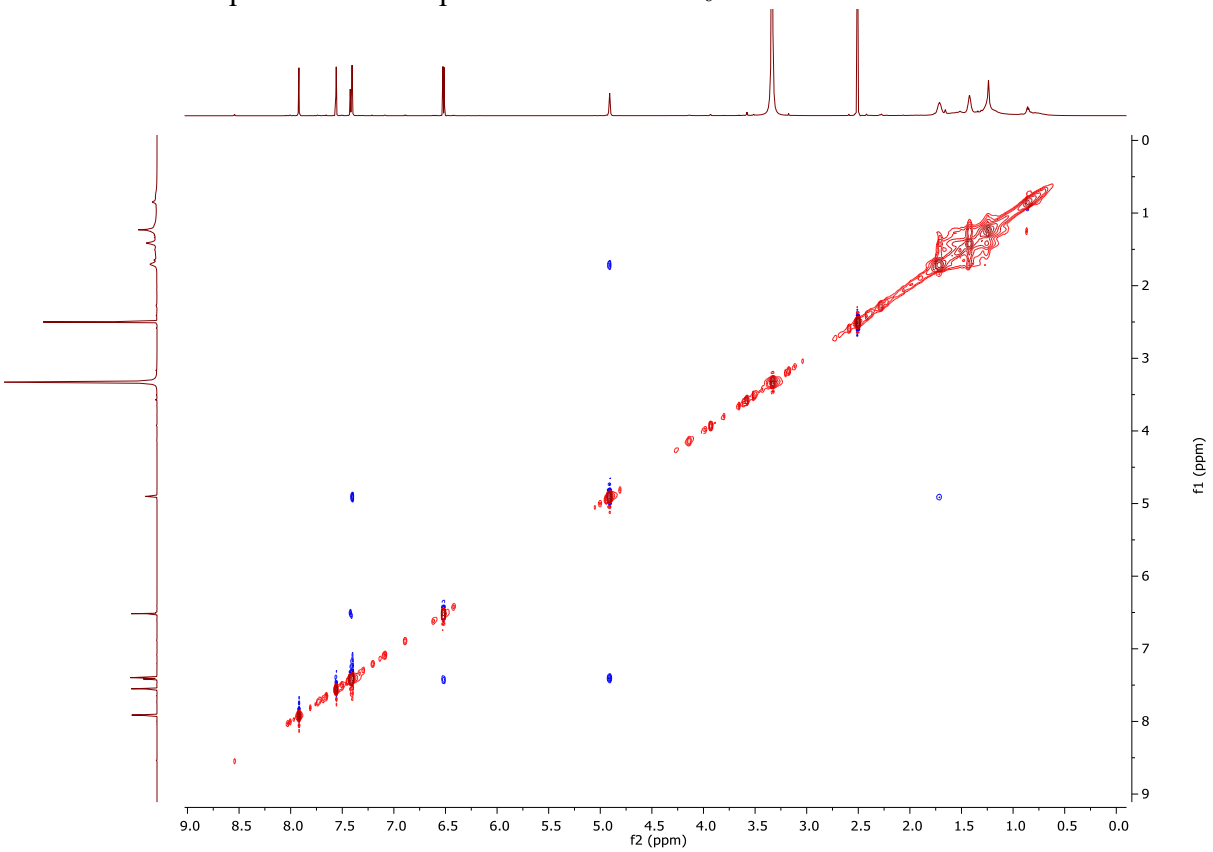
S30: HSQC Spectrum of Compound **5** in DMSO-d_6



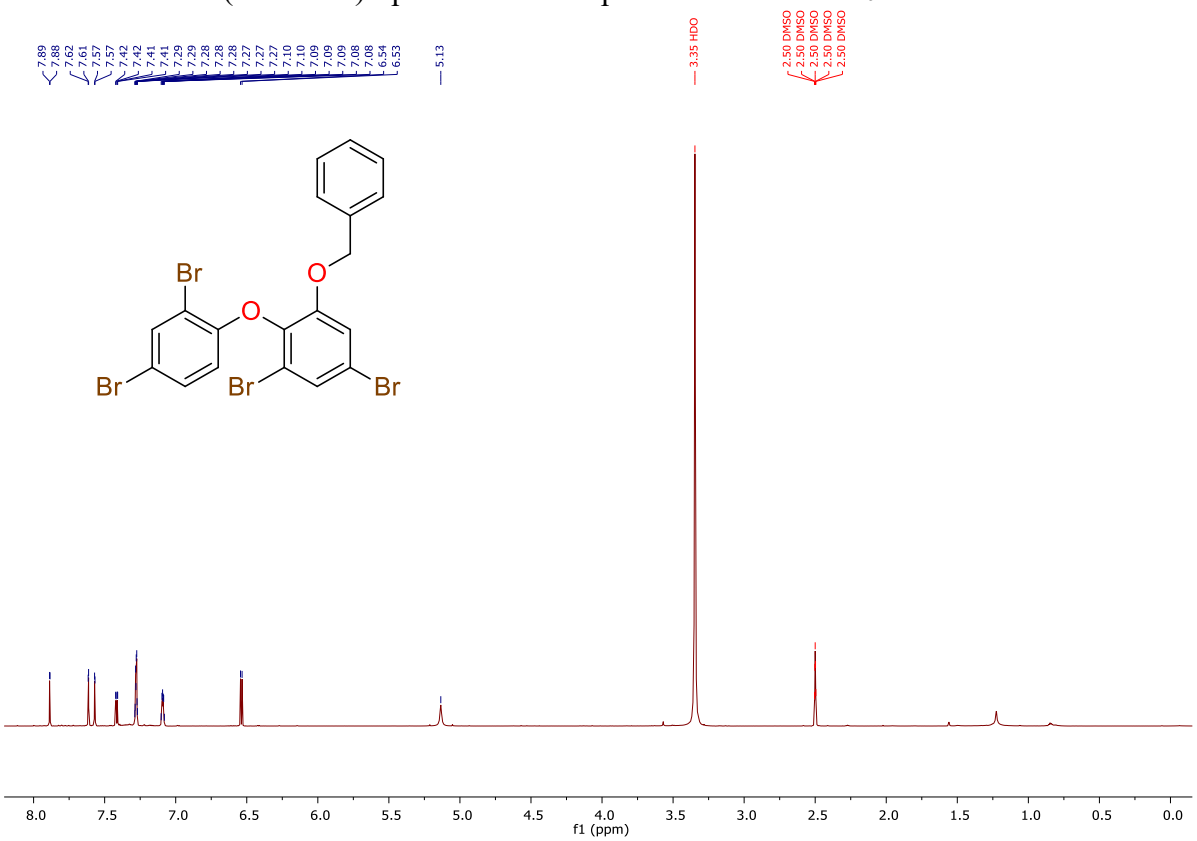
S31: HMBC Spectrum of Compound **5** in DMSO-d_6



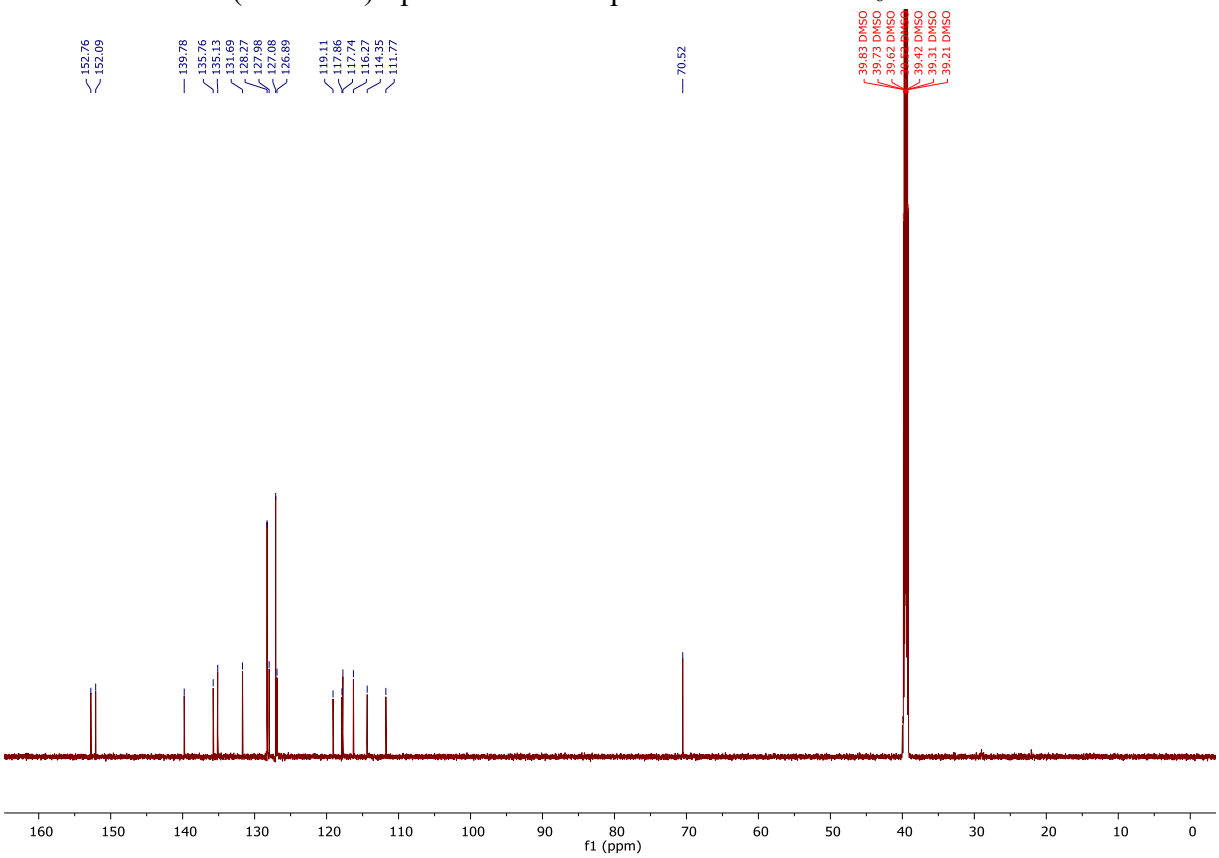
S32: ROESY Spectrum of Compound **5** in DMSO-d_6



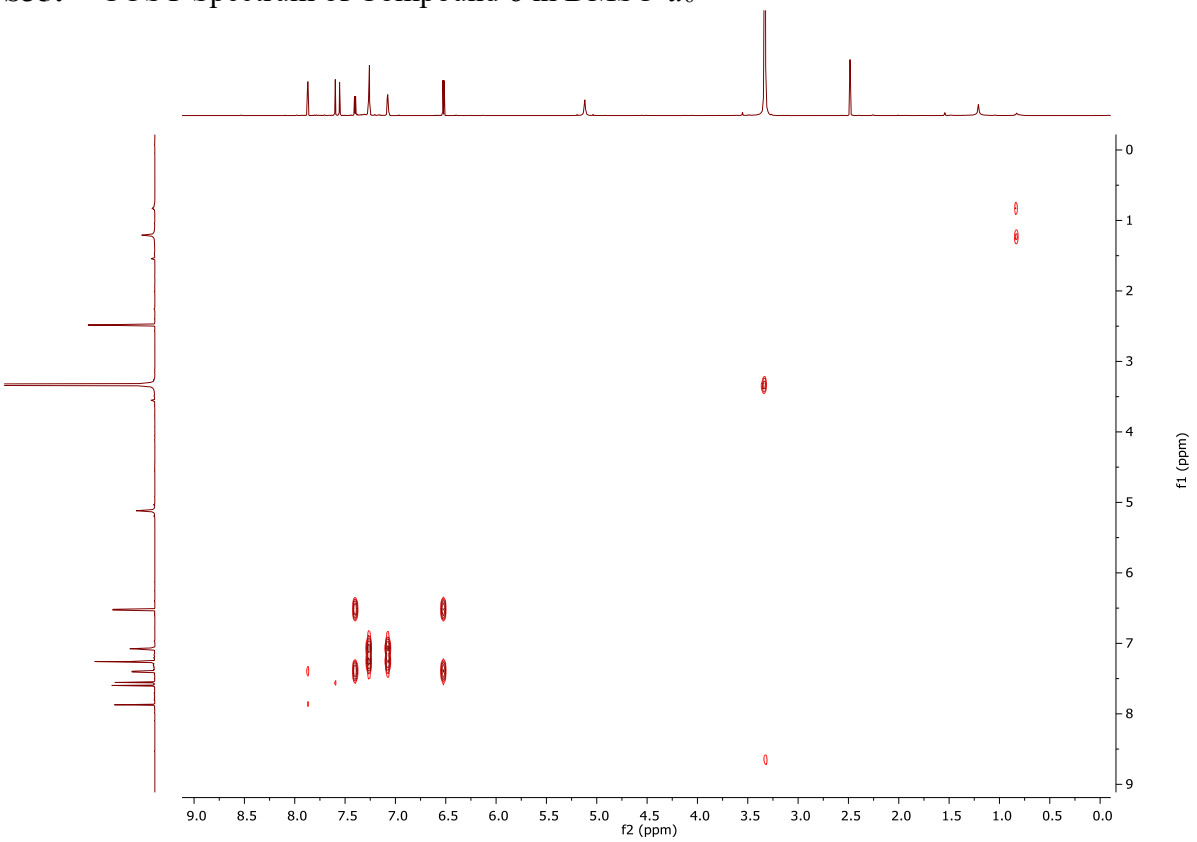
S33: ^{1}H NMR (800 MHz) Spectrum of Compound **6** in DMSO-d_6



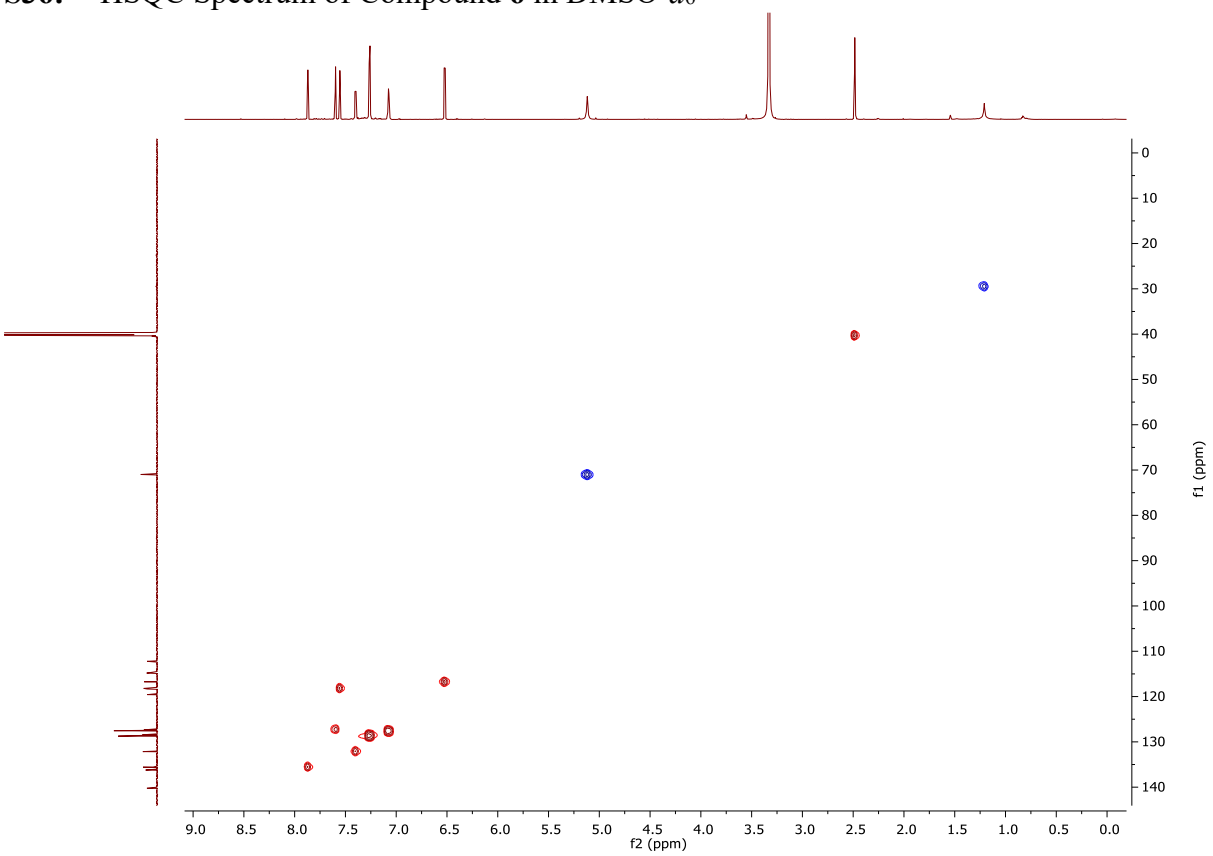
S34: ^{13}C NMR (200 MHz) Spectrum of Compound **6** in DMSO-d_6



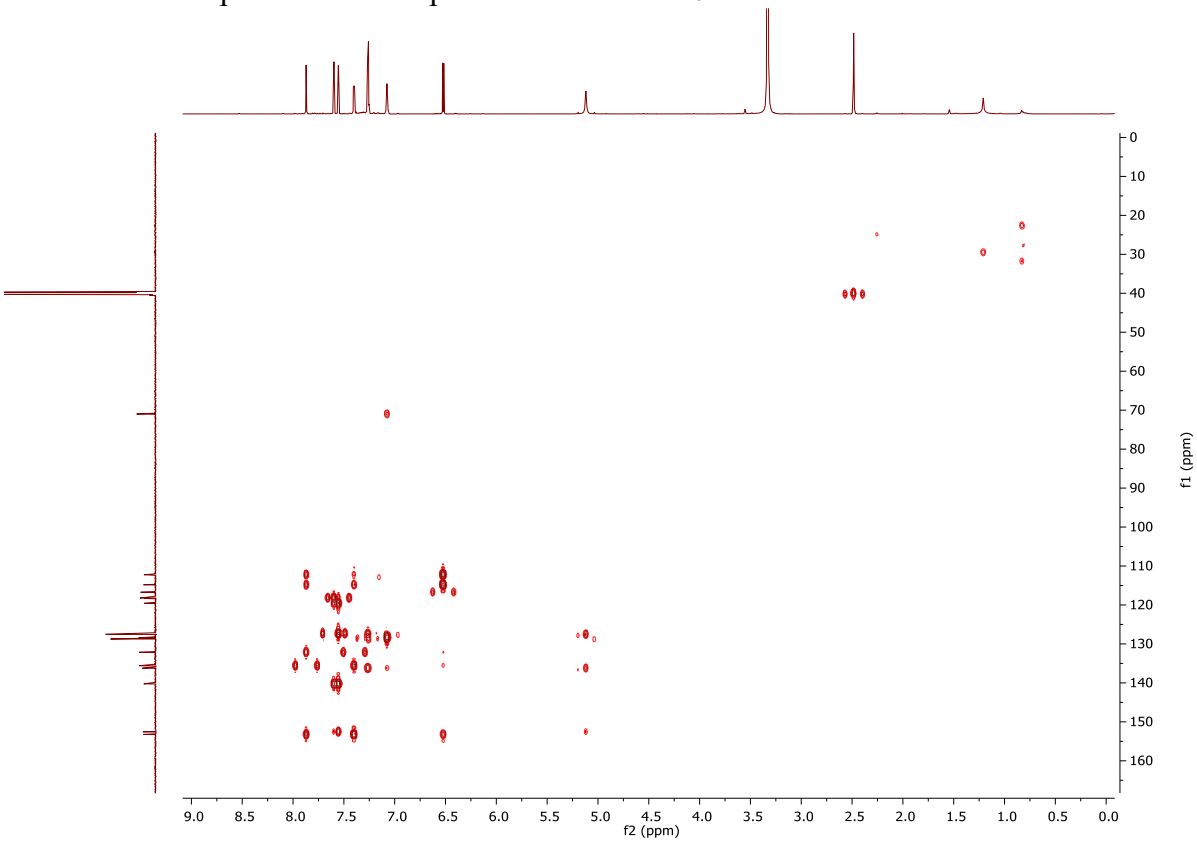
S35: COSY Spectrum of Compound **6** in DMSO-d_6



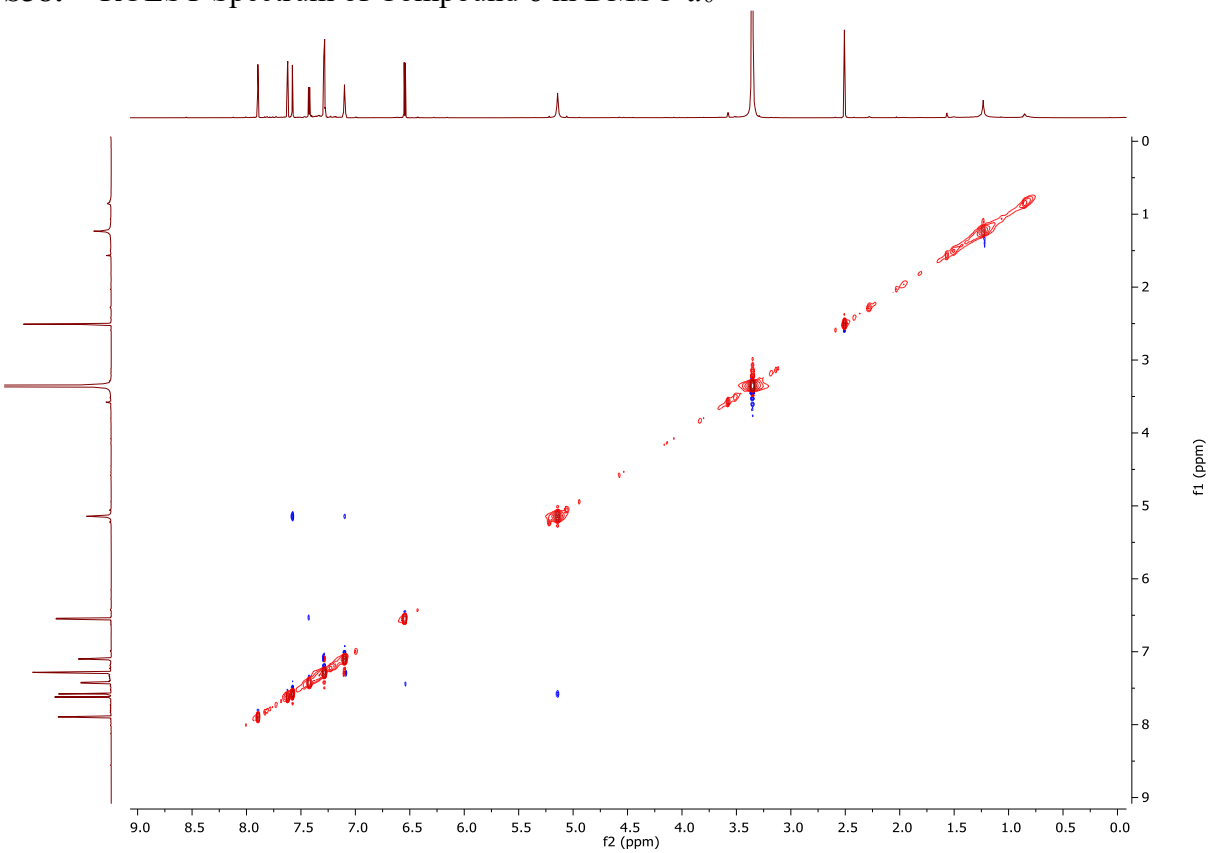
S36: HSQC Spectrum of Compound **6** in DMSO-d_6



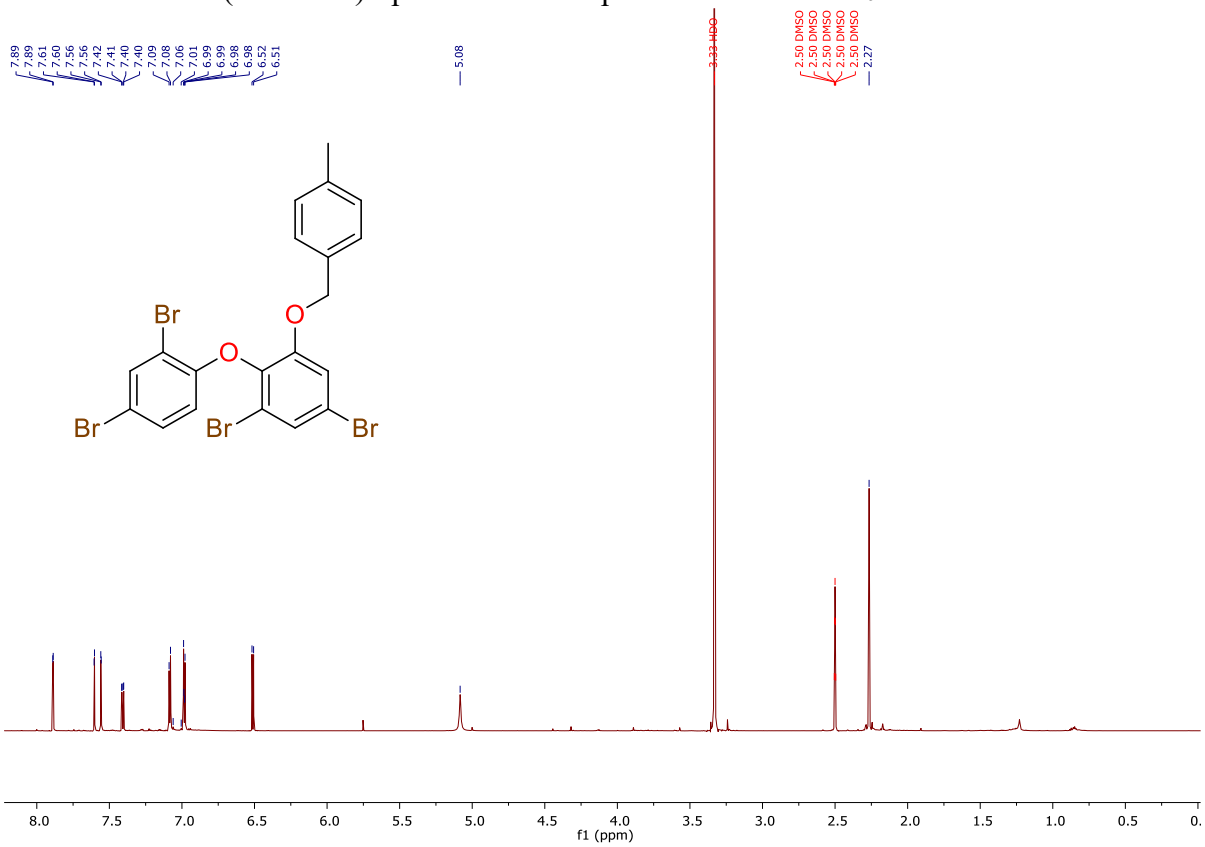
S37: HMBC Spectrum of Compound **6** in DMSO-d_6



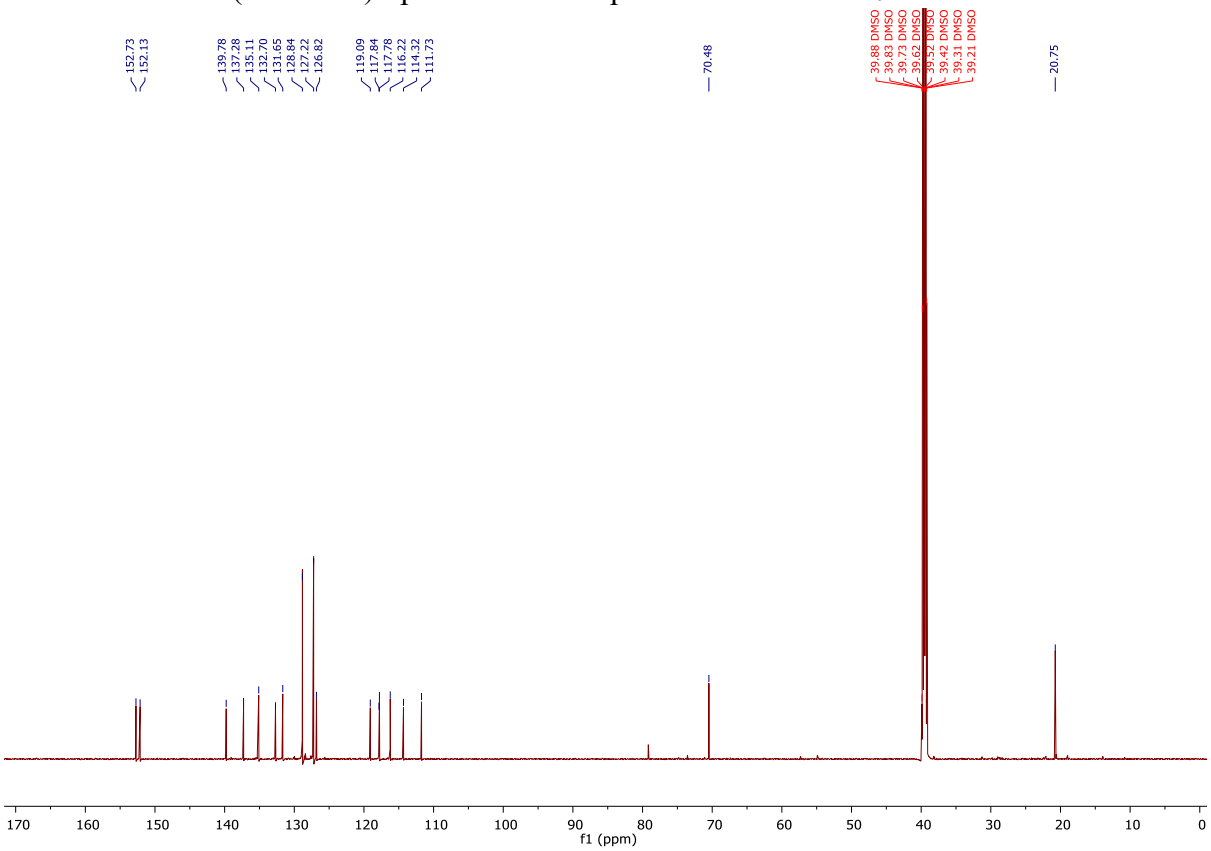
S38: ROESY Spectrum of Compound **6** in DMSO-d_6



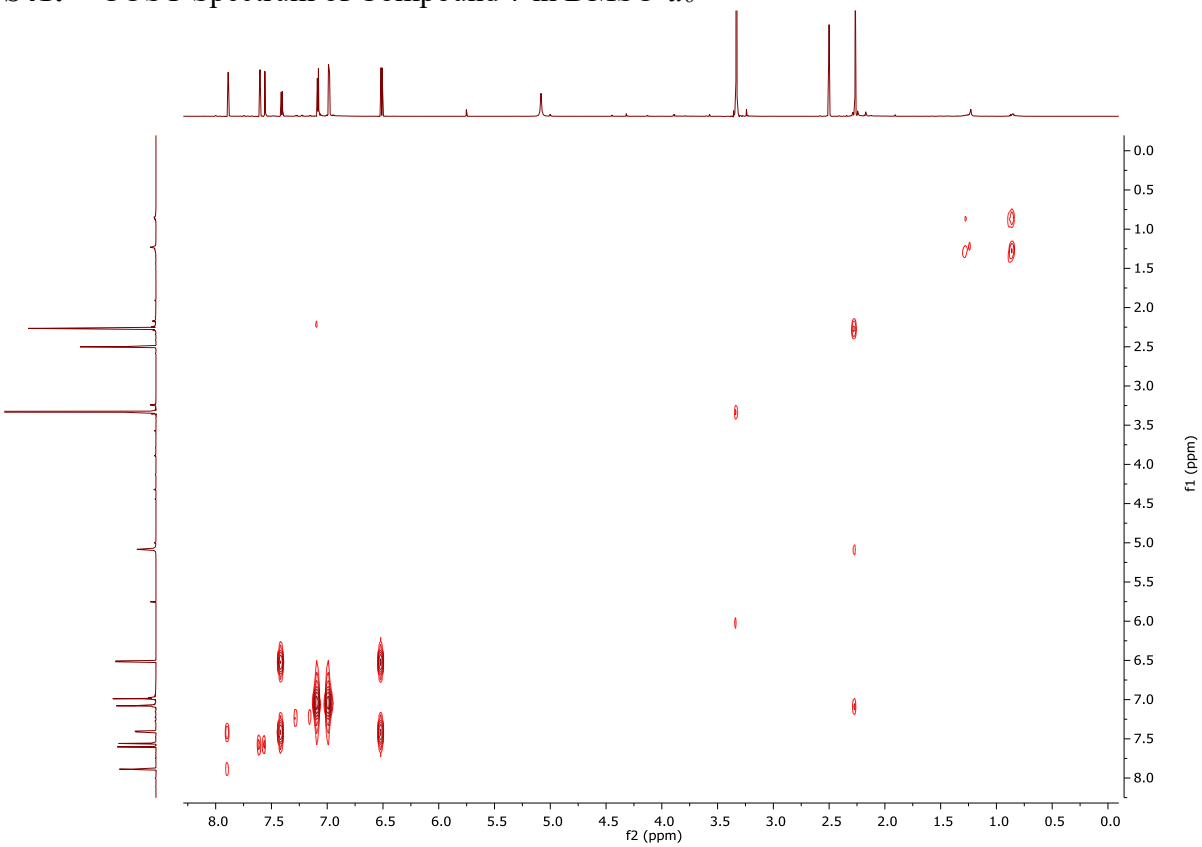
S39: ^{1}H NMR (800 MHz) Spectrum of Compound **7** in DMSO-d_6



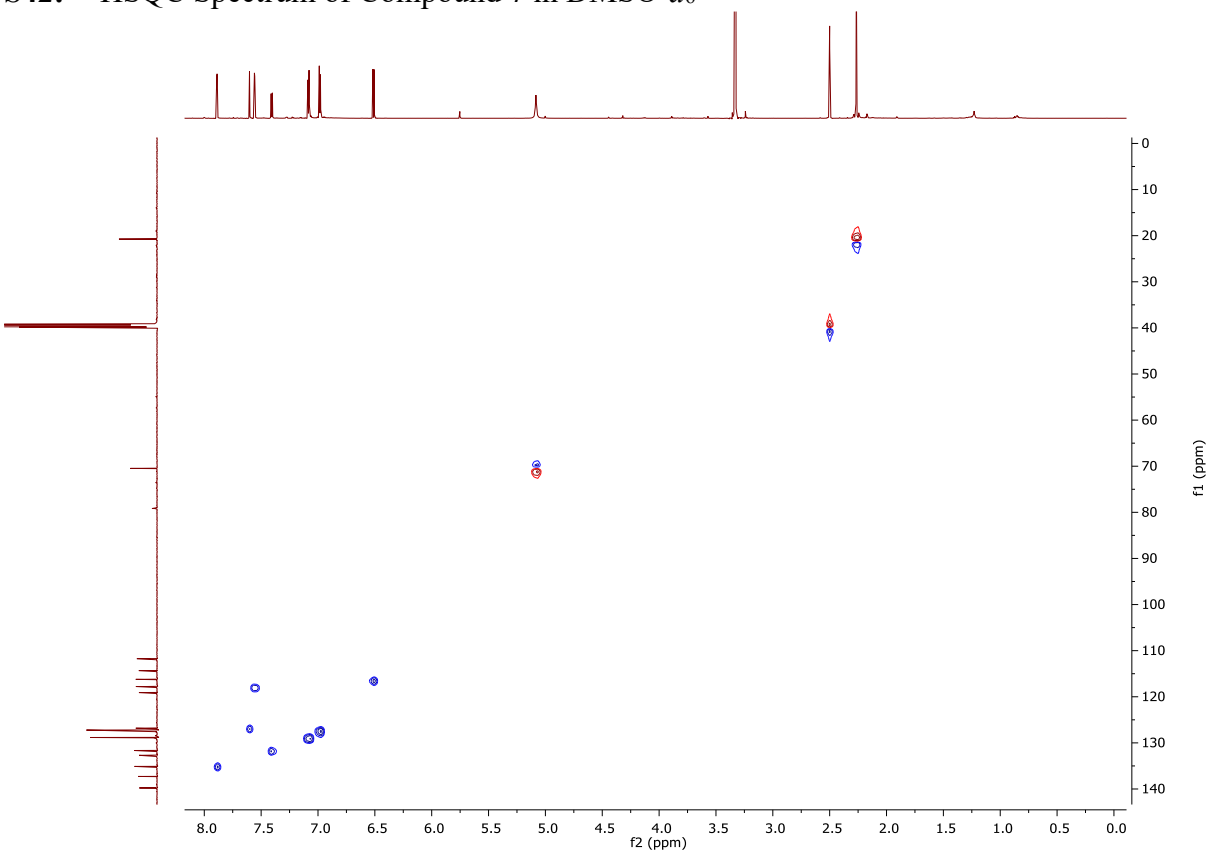
S40: ^{13}C NMR (200 MHz) Spectrum of Compound **7** in DMSO-d_6



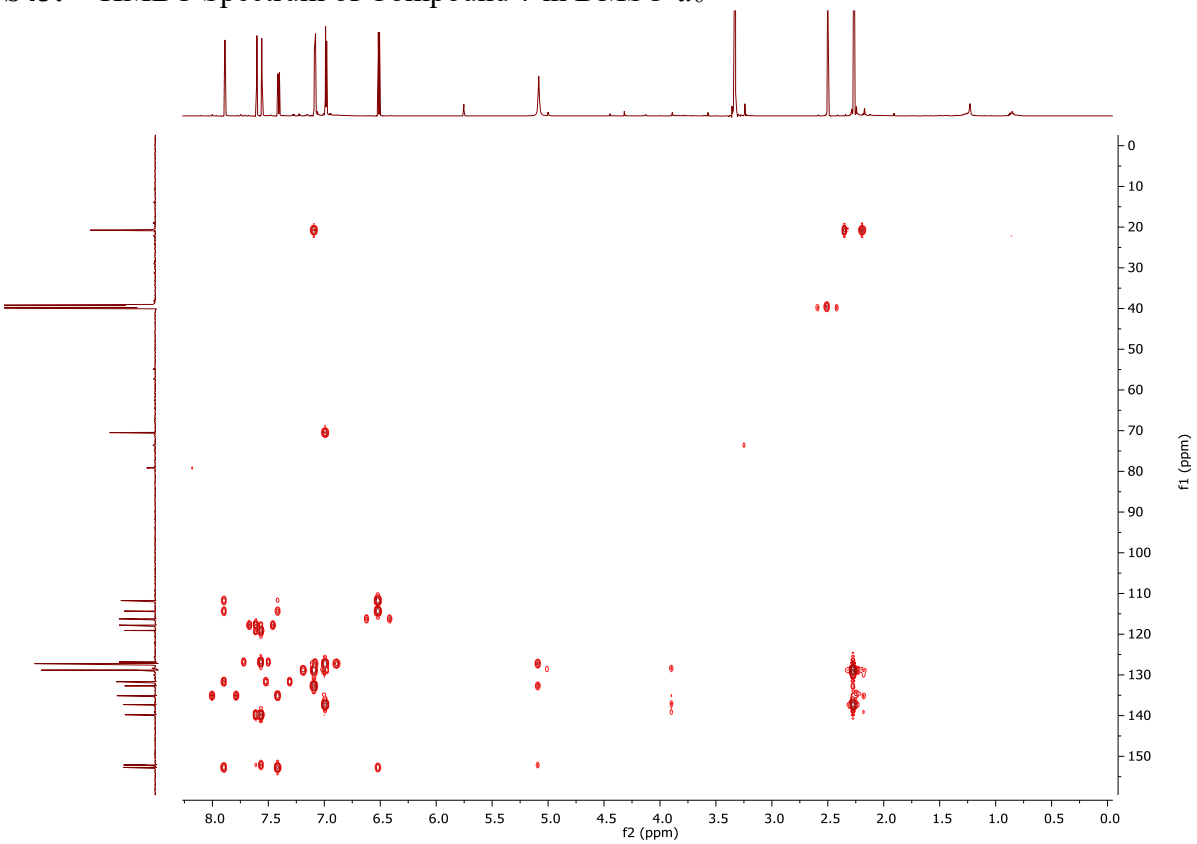
S41: COSY Spectrum of Compound **7** in DMSO-d_6



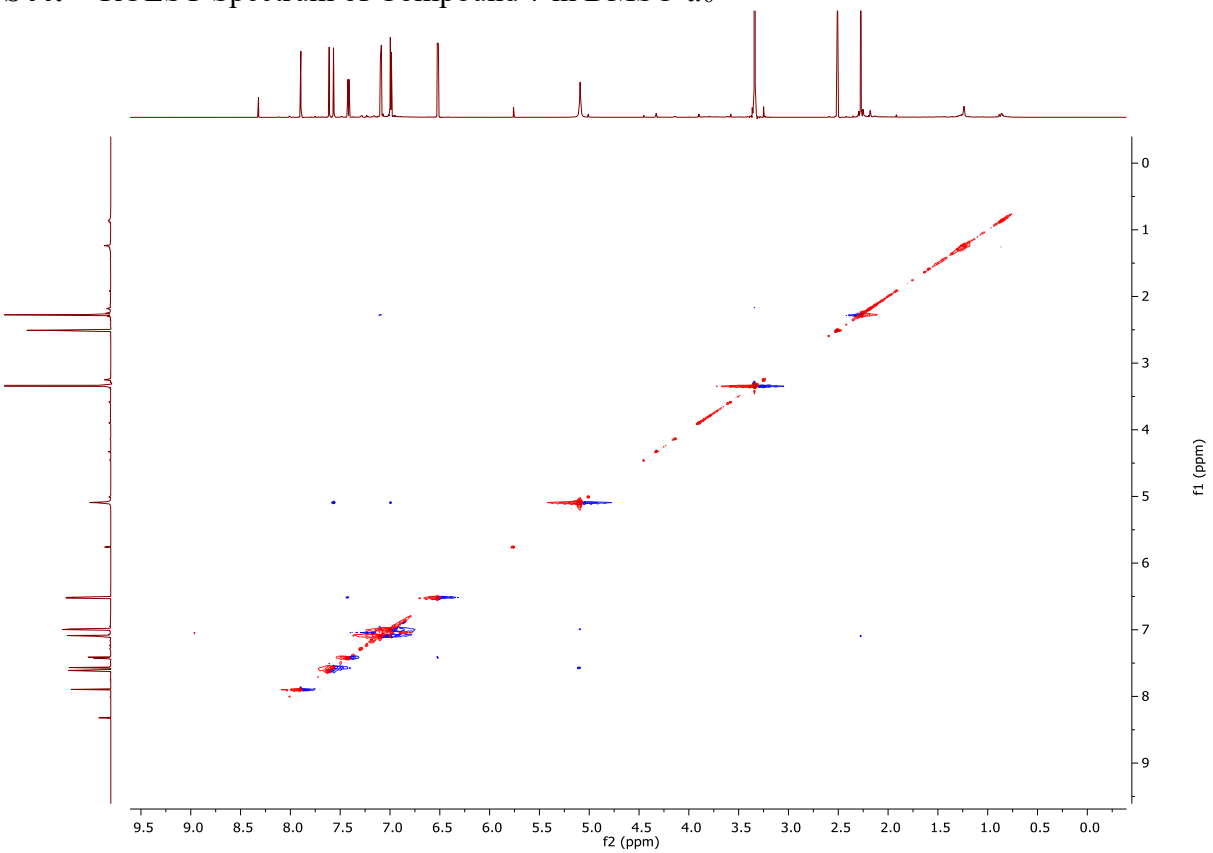
S42: HSQC Spectrum of Compound **7** in DMSO-d_6



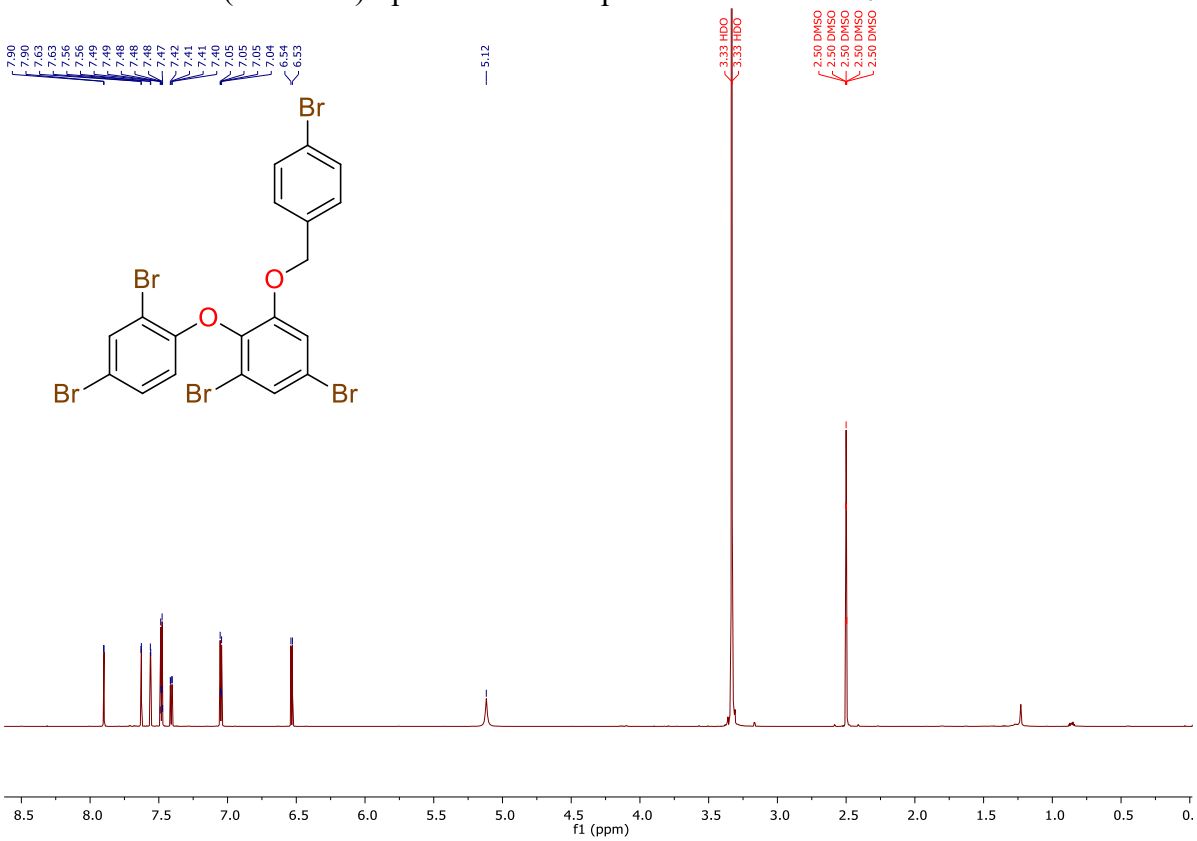
S43: HMBC Spectrum of Compound **7** in DMSO-d_6



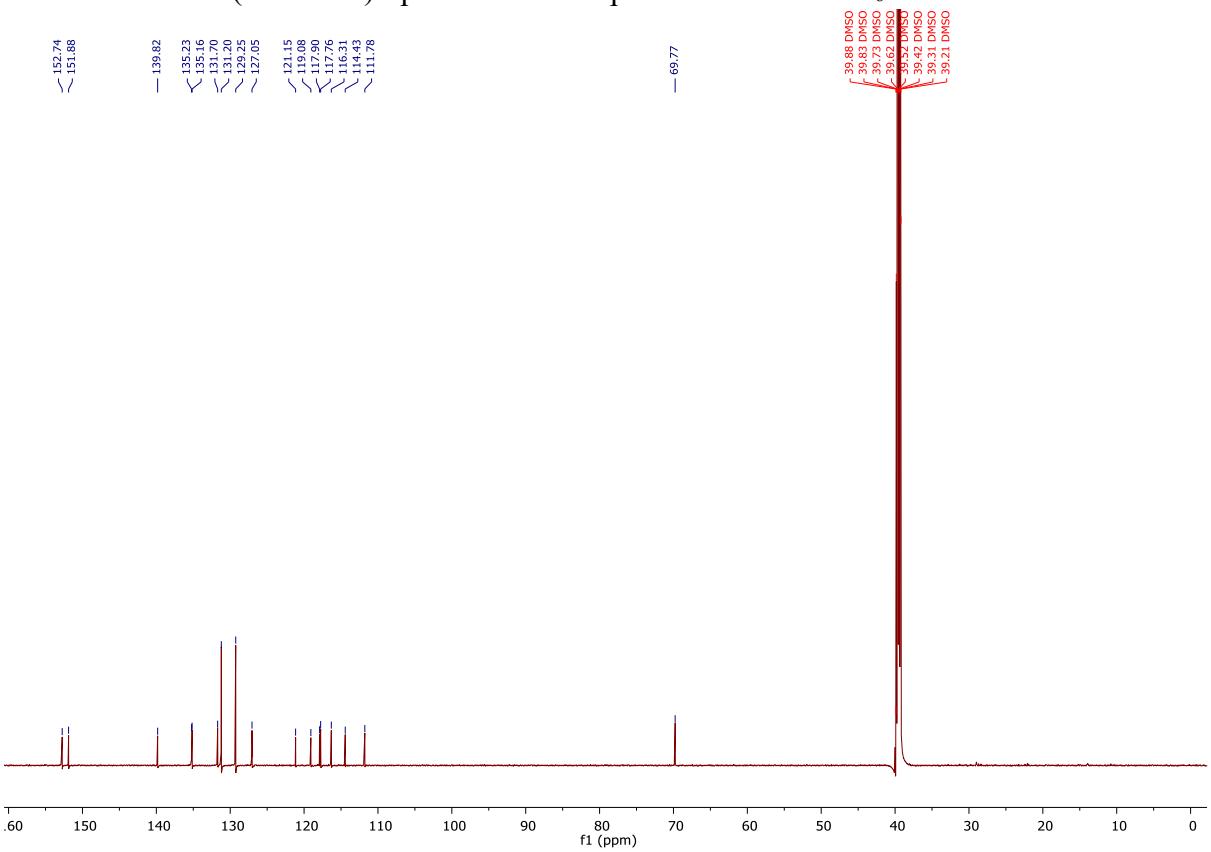
S44: ROESY Spectrum of Compound **7** in DMSO-d_6



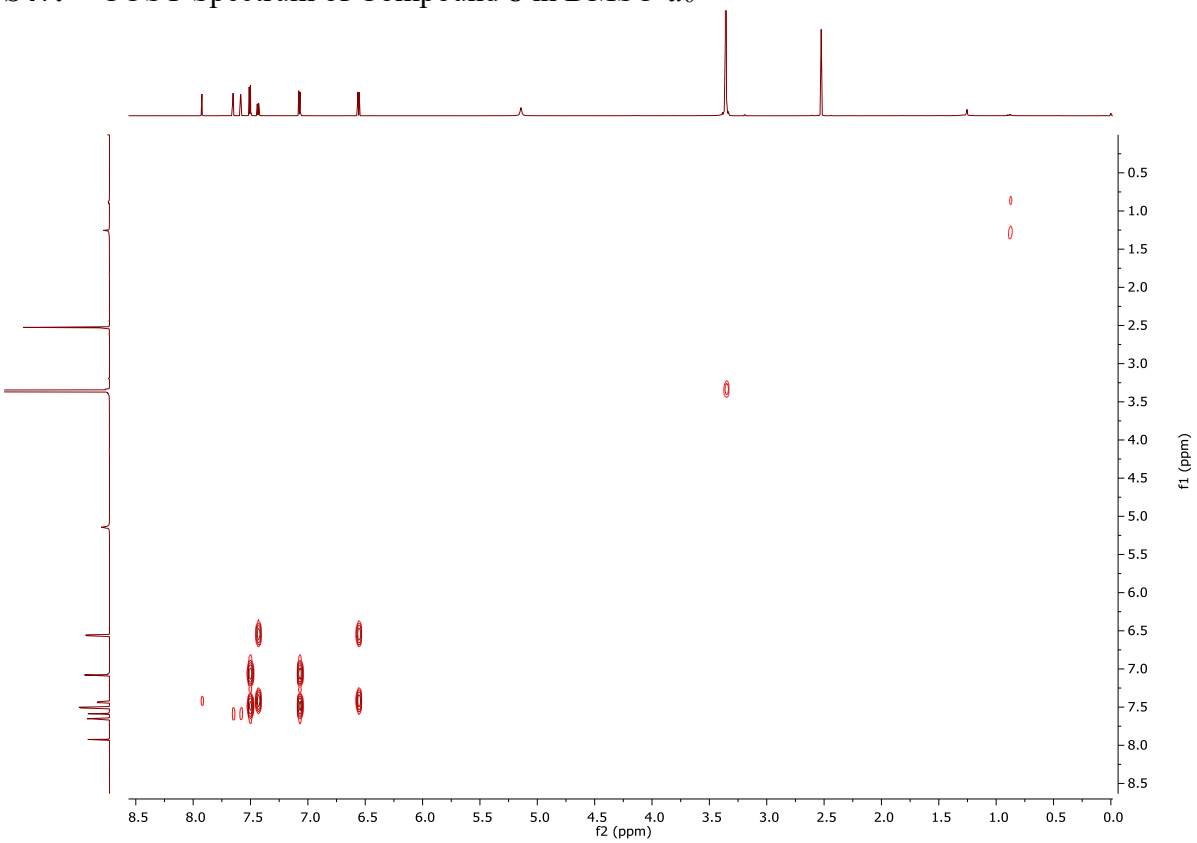
S45: ^{1}H NMR (800 MHz) Spectrum of Compound **8** in DMSO-d_6



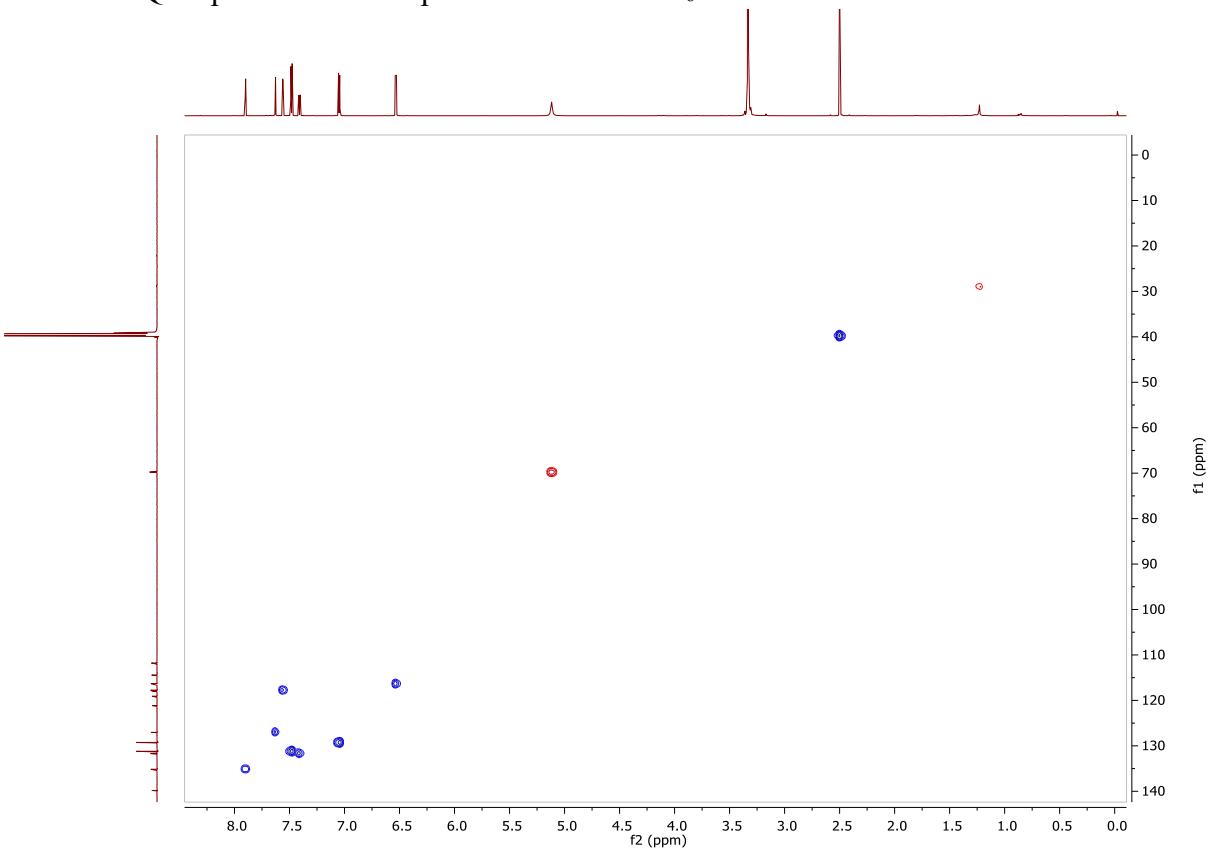
S46: ^{13}C NMR (200 MHz) Spectrum of Compound **8** in DMSO-d_6



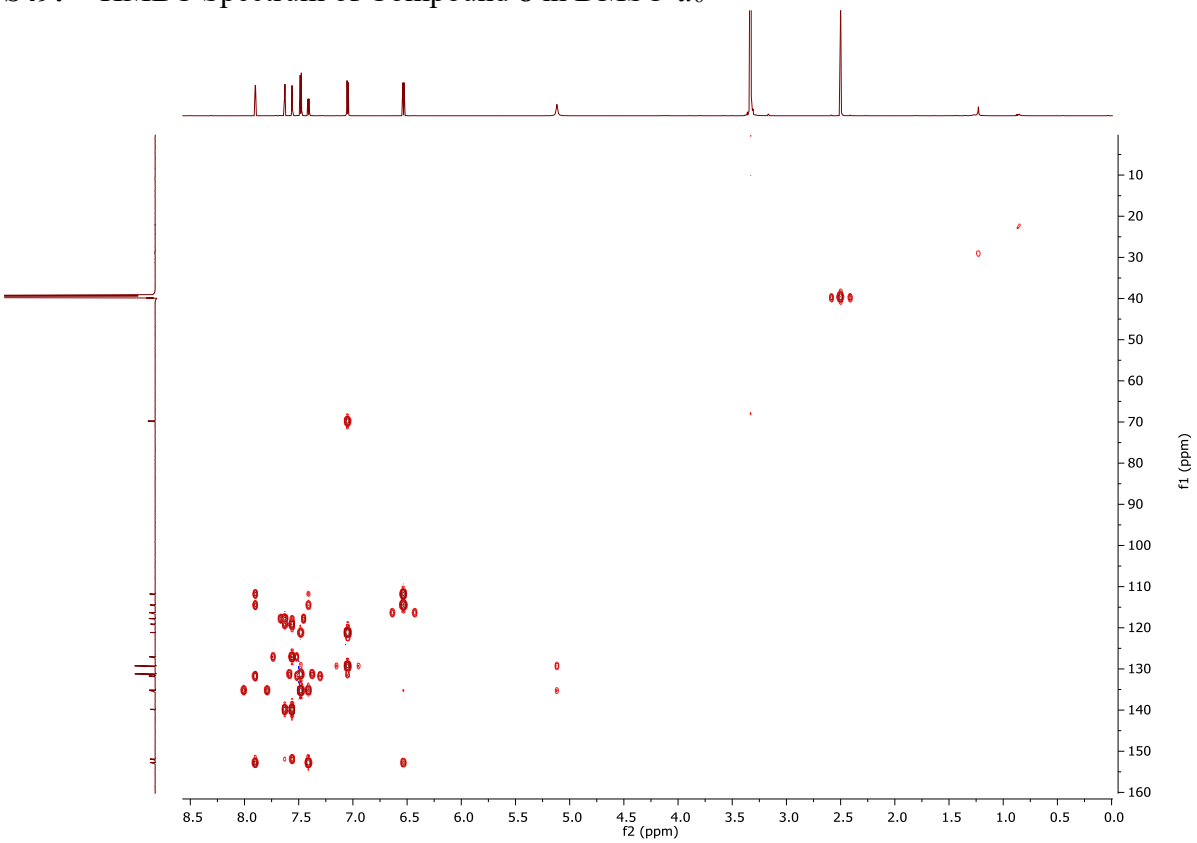
S47: COSY Spectrum of Compound **8** in DMSO-d_6



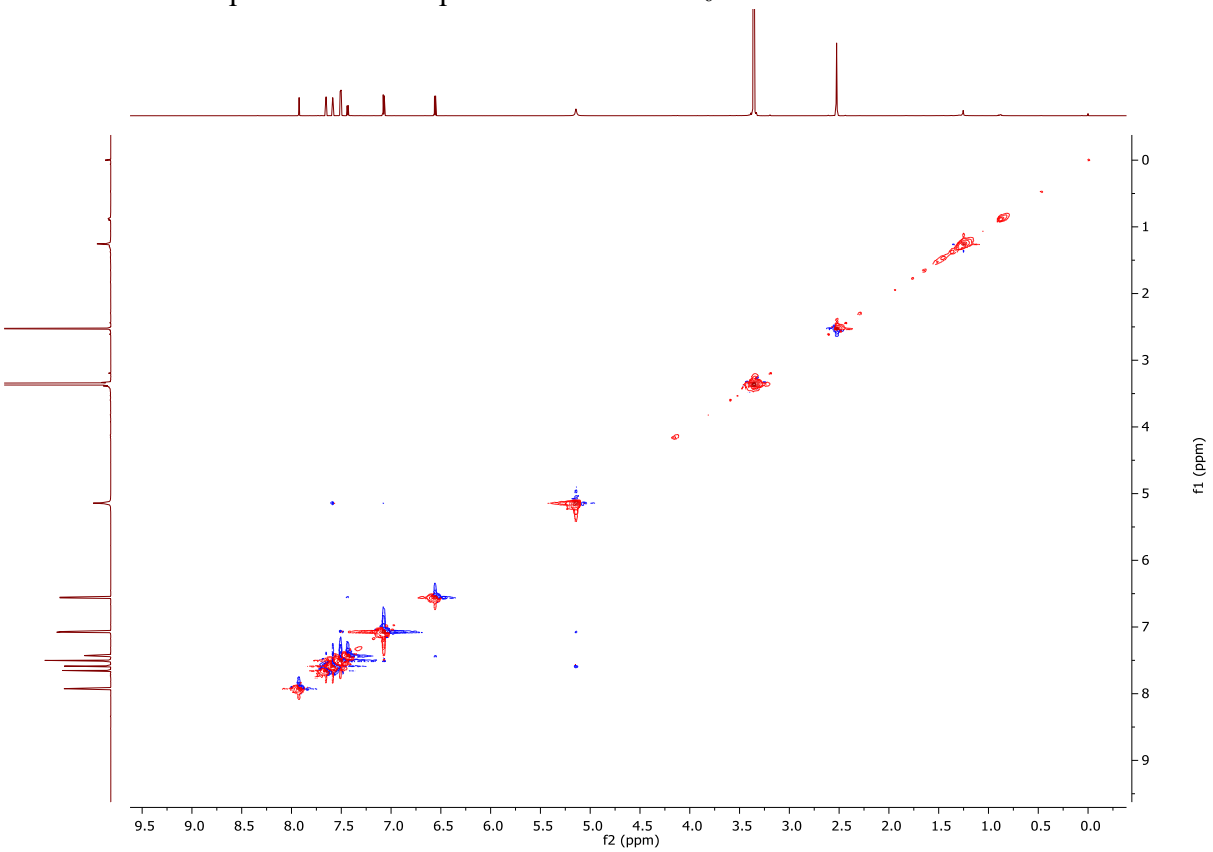
S48: HSQC Spectrum of Compound **8** in DMSO-d_6



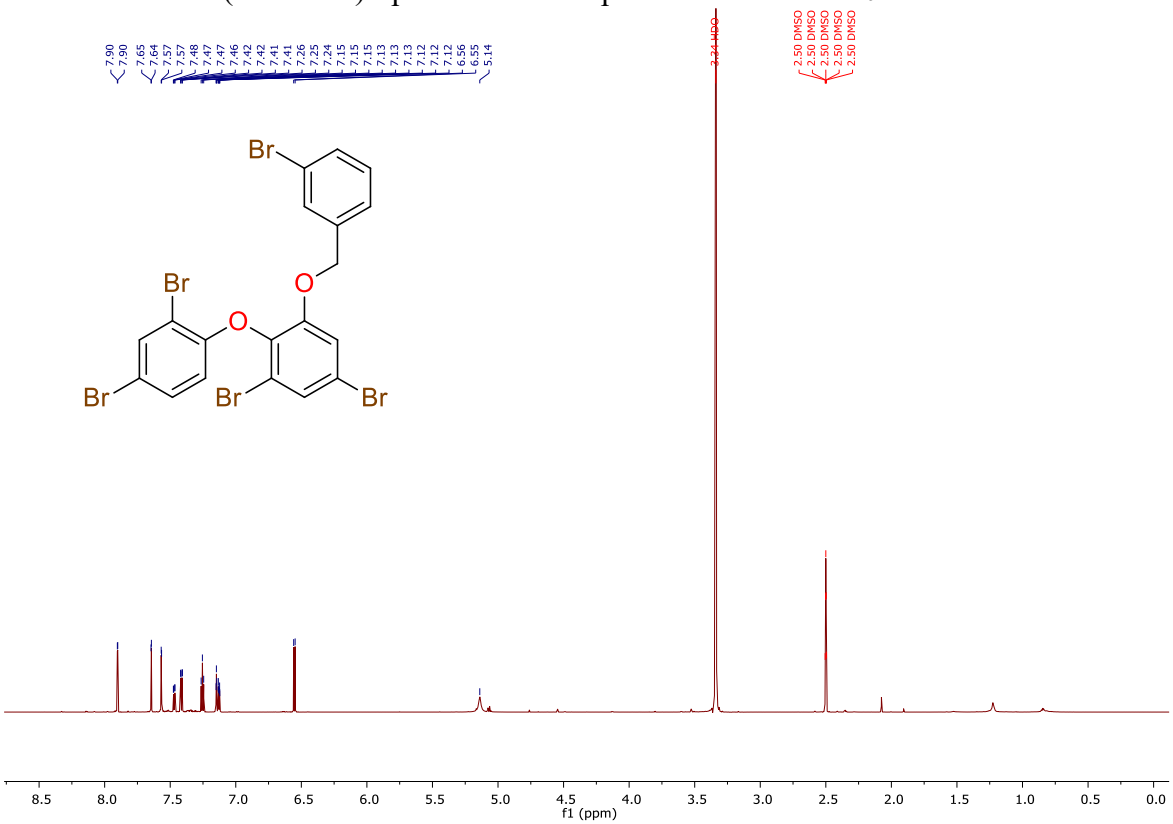
S49: HMBC Spectrum of Compound **8** in DMSO-d_6



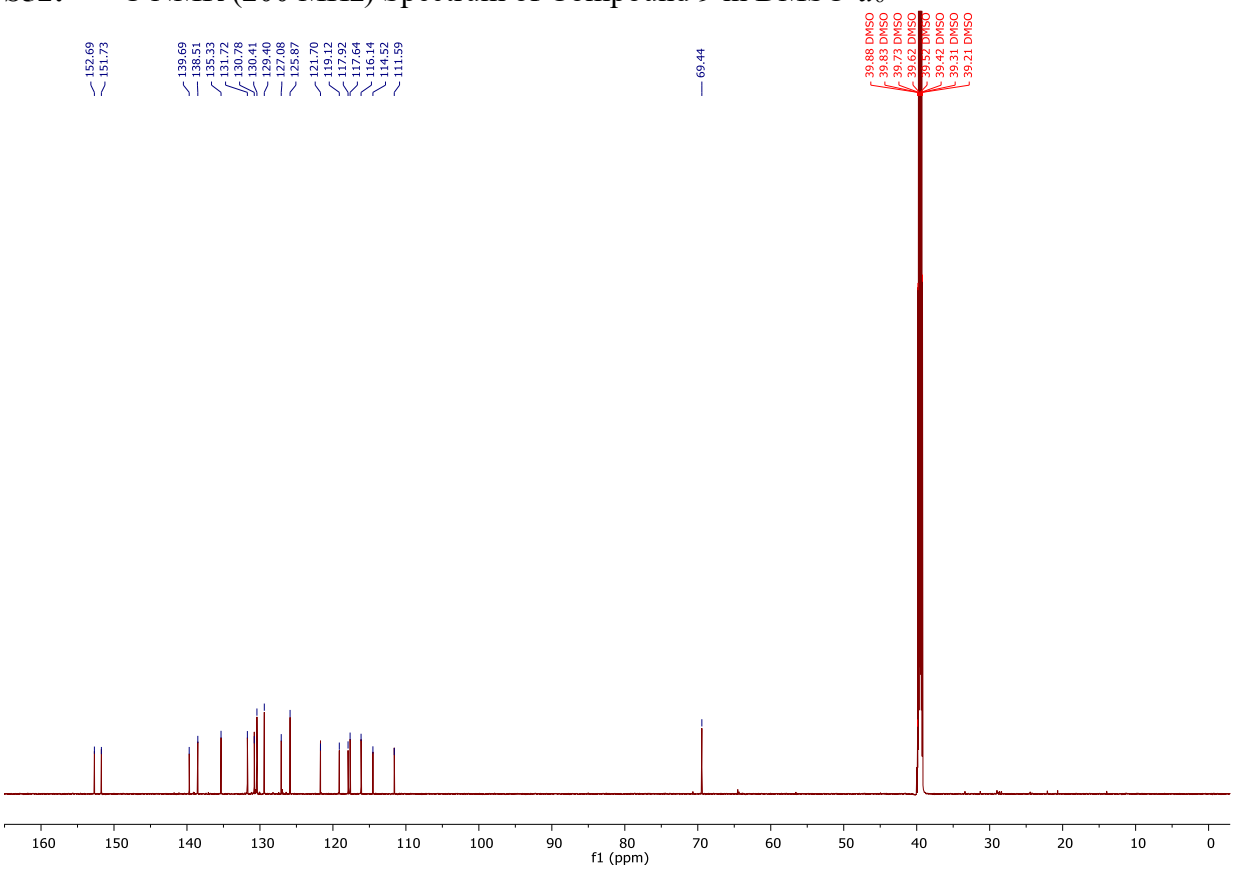
S50: ROESY Spectrum of Compound **8** in DMSO-d_6



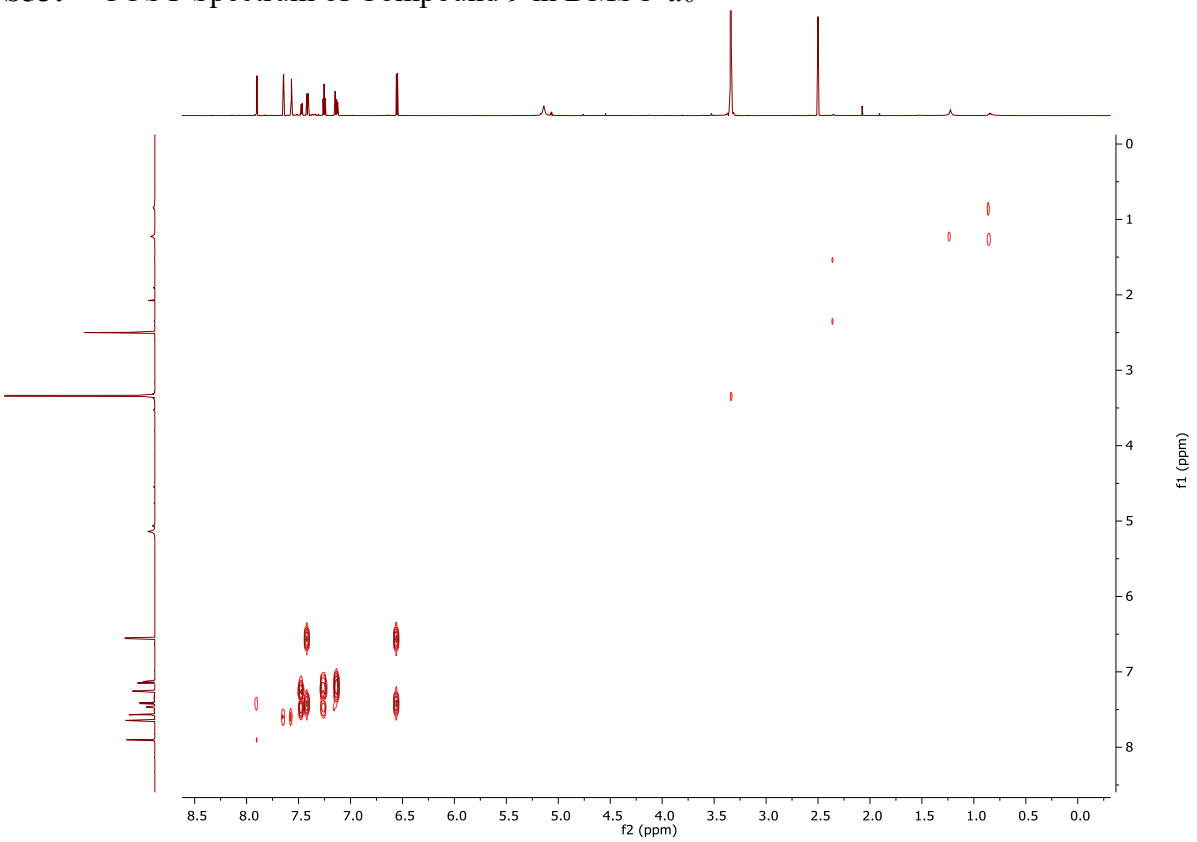
S51: ^{1}H NMR (800 MHz) Spectrum of Compound **9** in DMSO-d_6



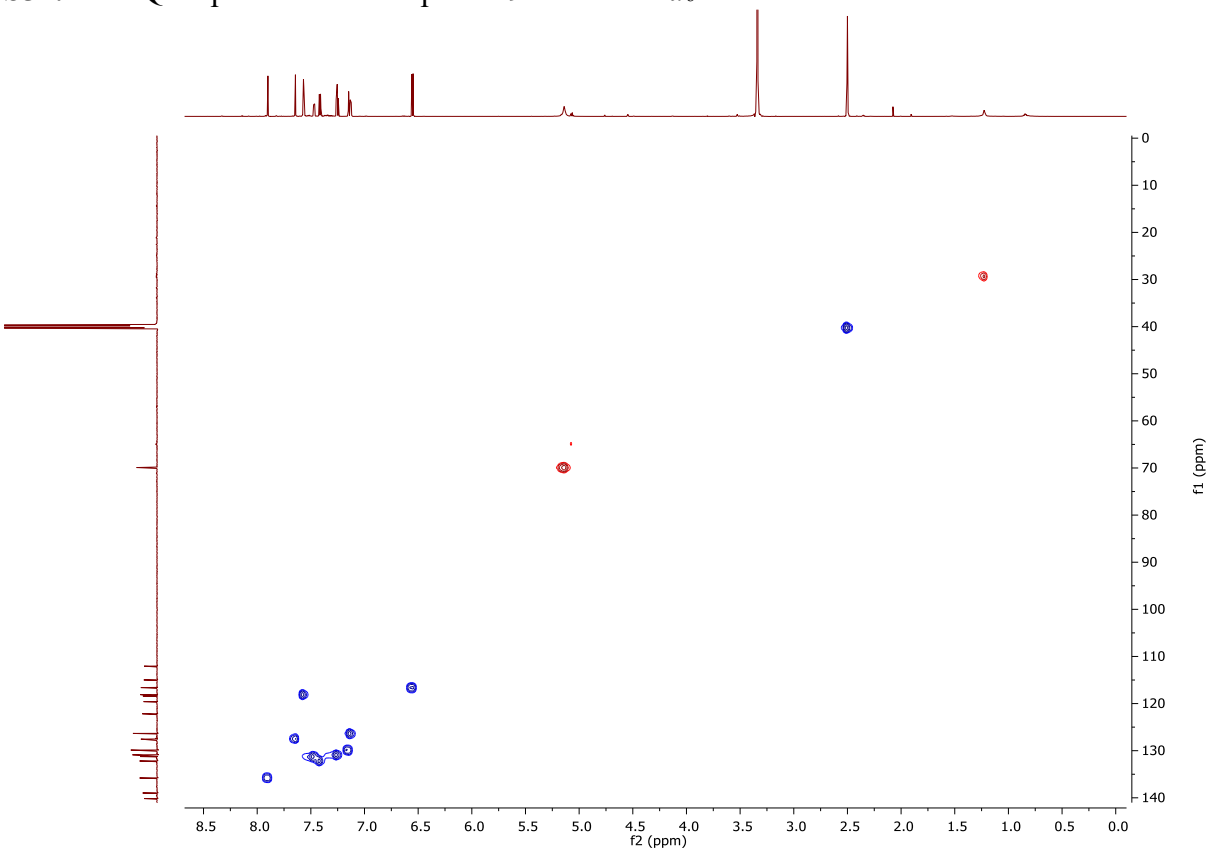
S52: ^{13}C NMR (200 MHz) Spectrum of Compound **9** in DMSO-d_6



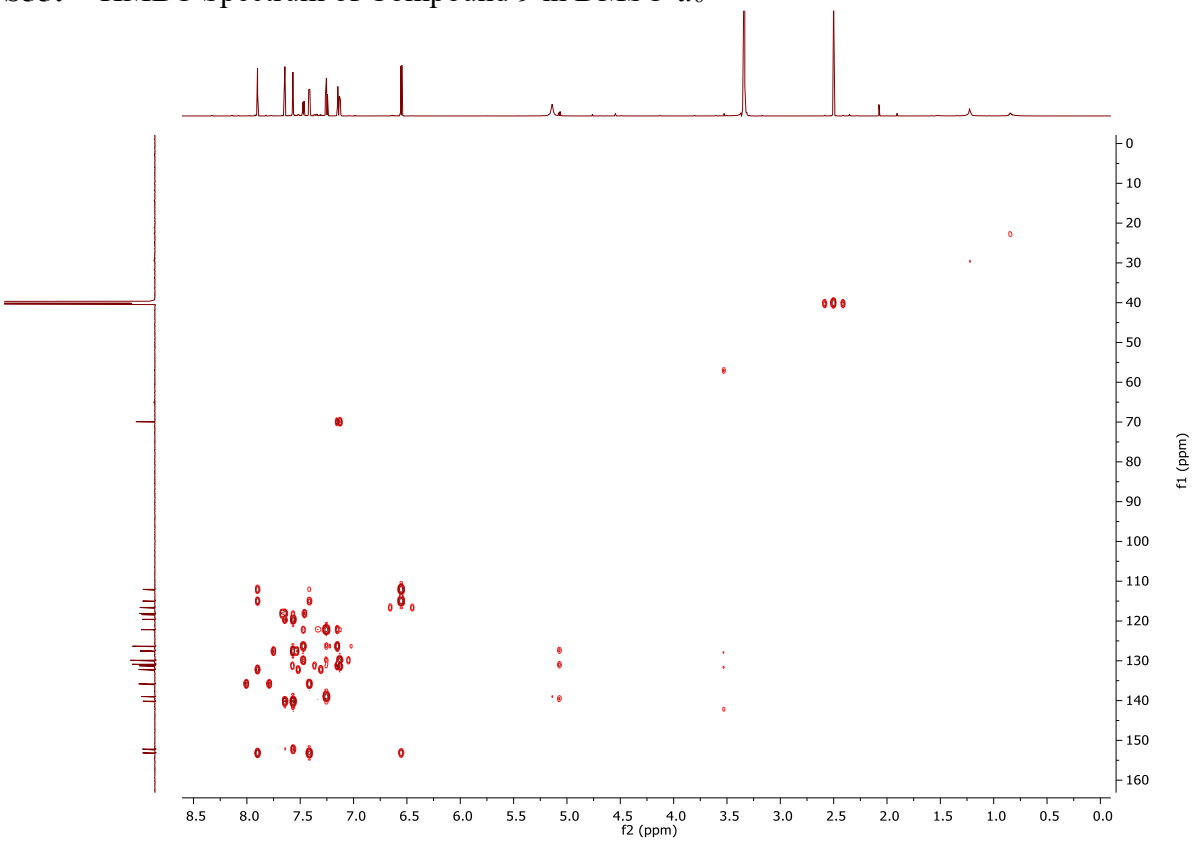
S53: COSY Spectrum of Compound **9** in DMSO-d_6



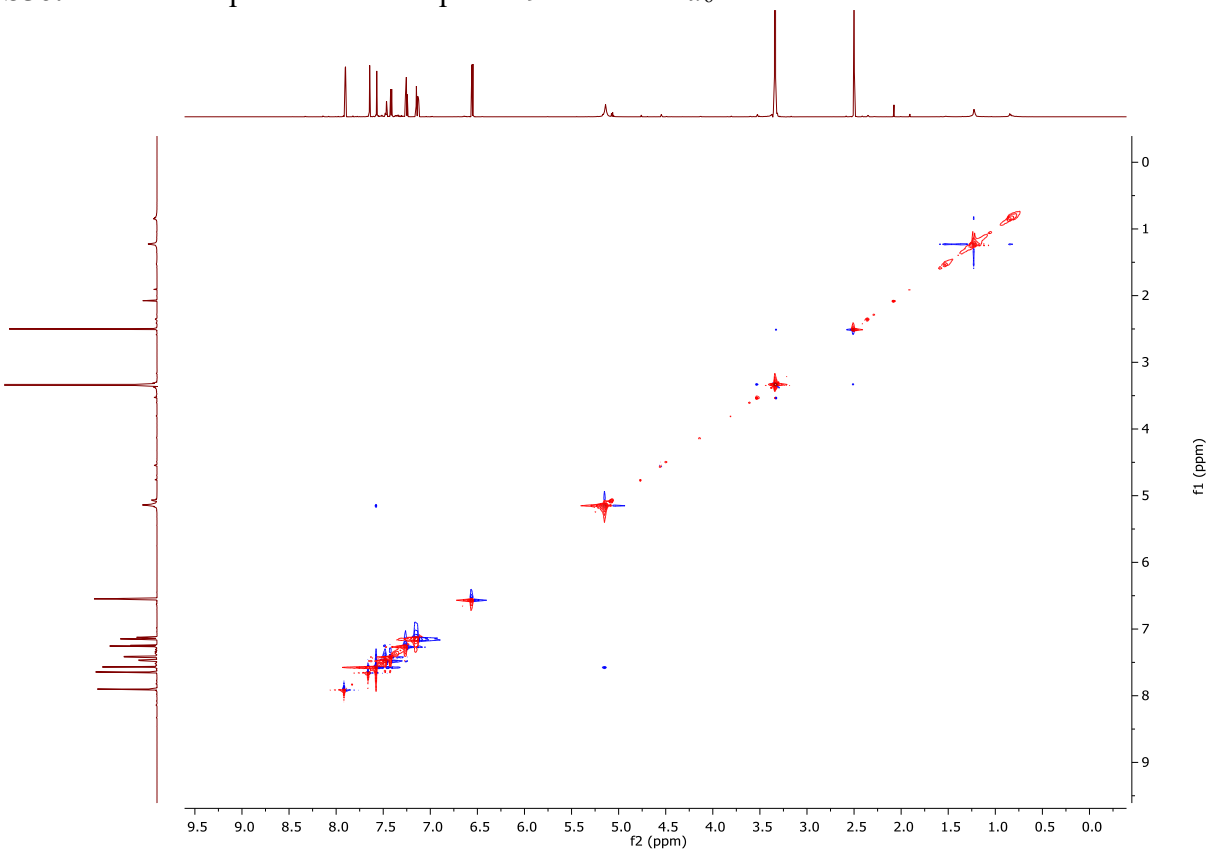
S54: HSQC Spectrum of Compound **9** in DMSO-d_6



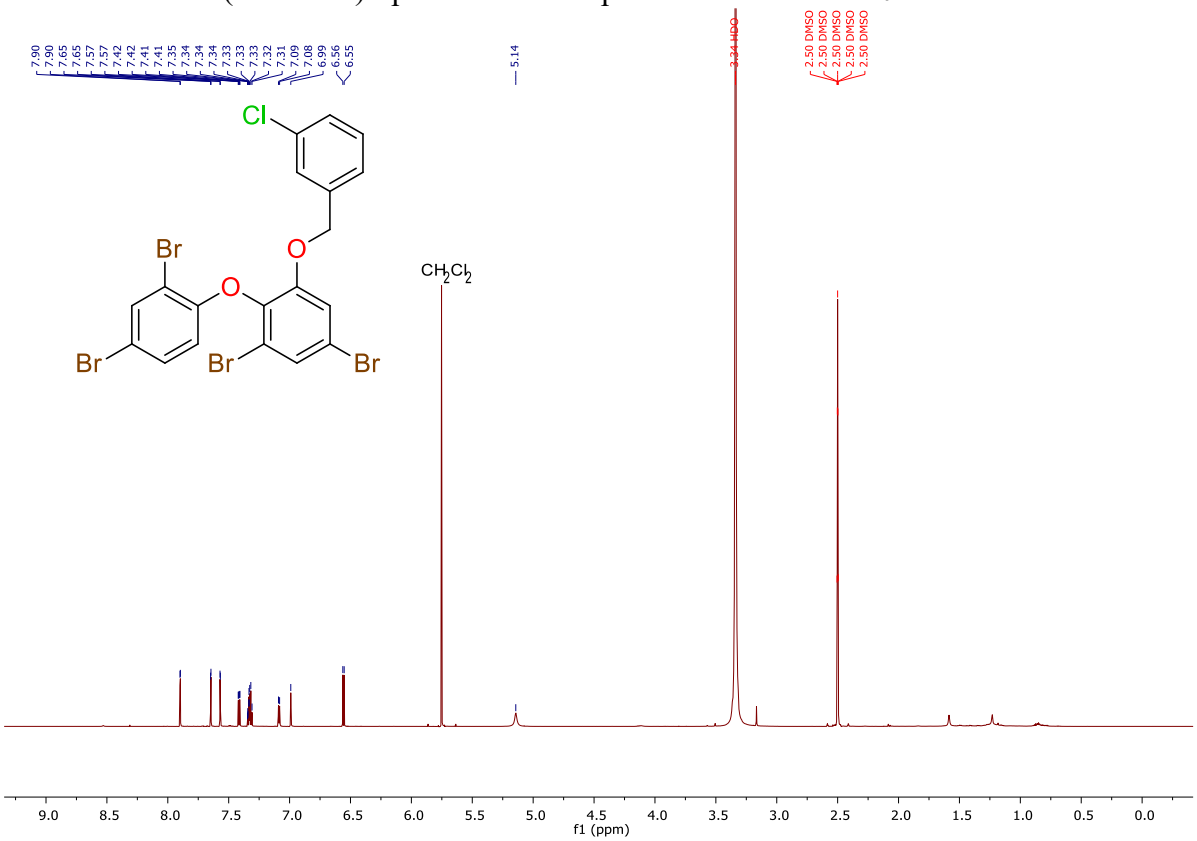
S55: HMBC Spectrum of Compound **9** in DMSO-d_6



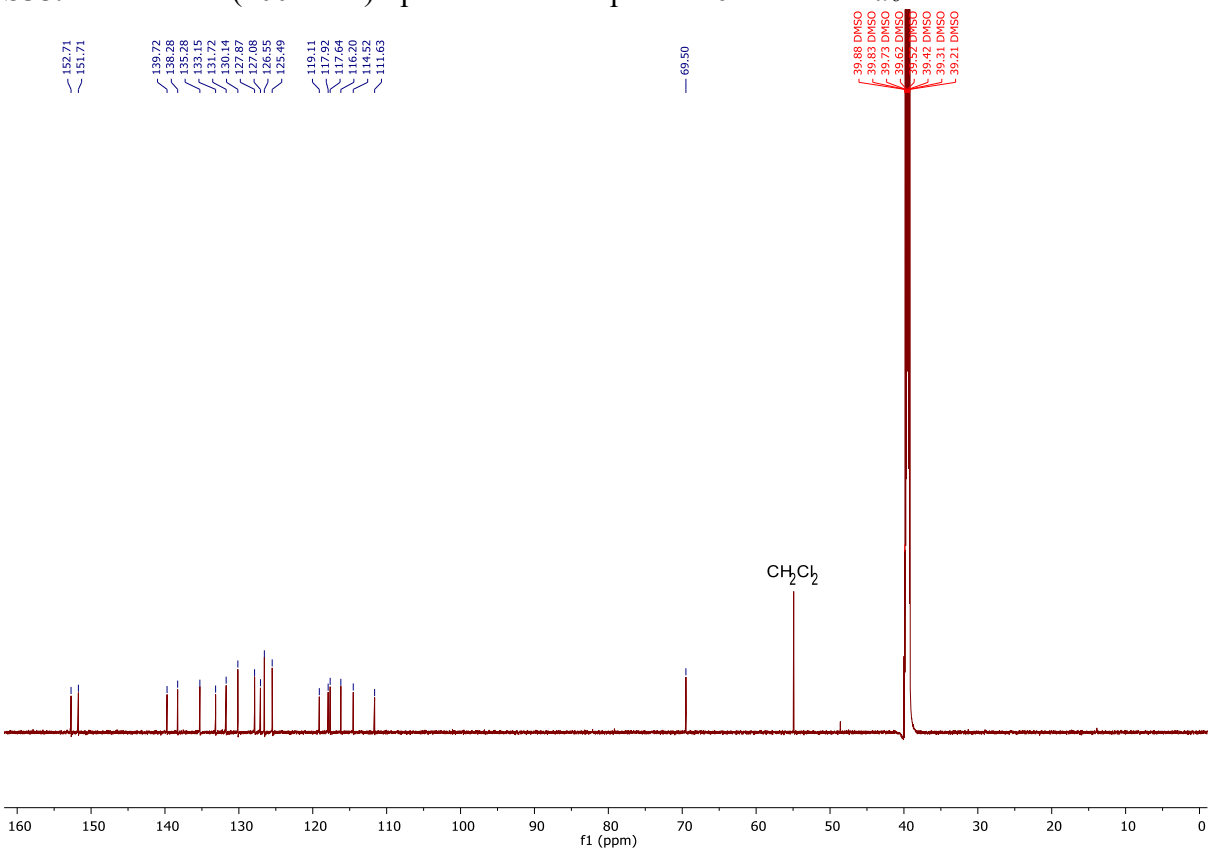
S56: ROESY Spectrum of Compound **9** in DMSO-d_6



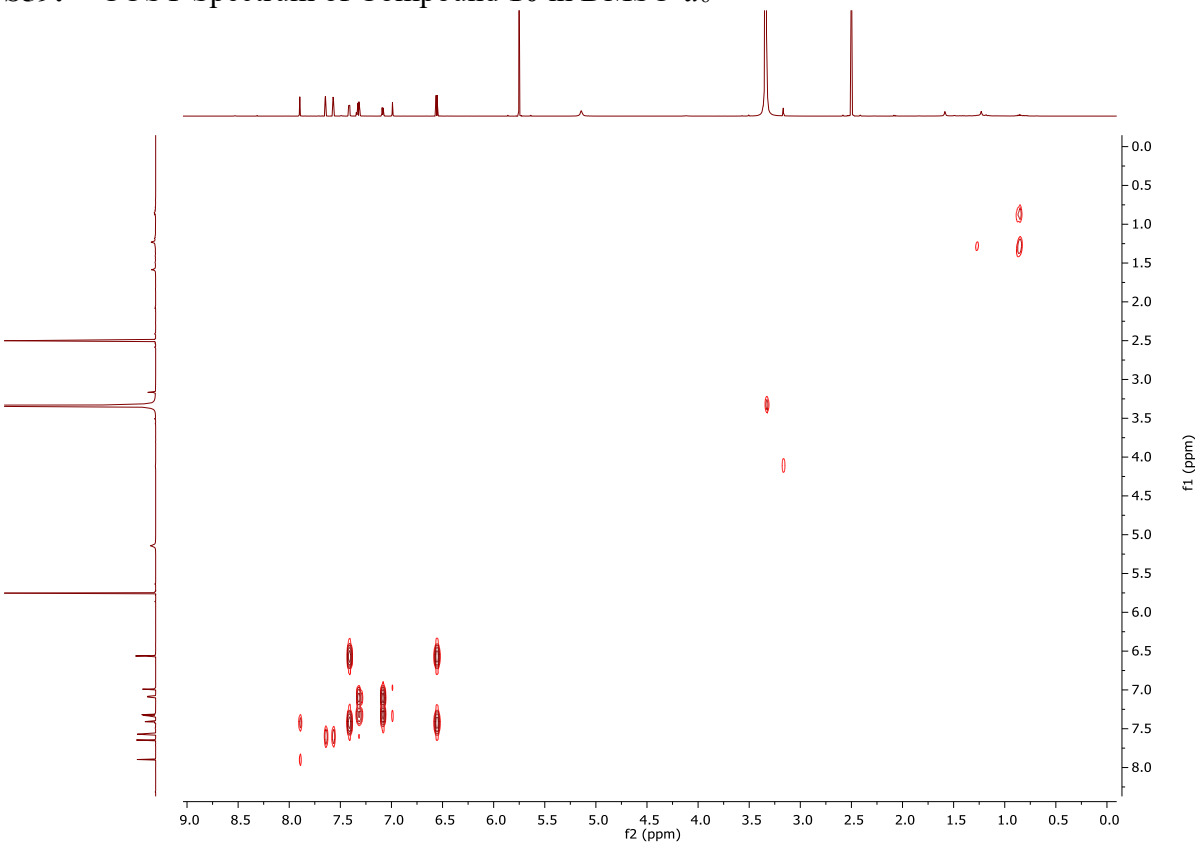
S57: ^{1}H NMR (800 MHz) Spectrum of Compound **10** in DMSO-d_6



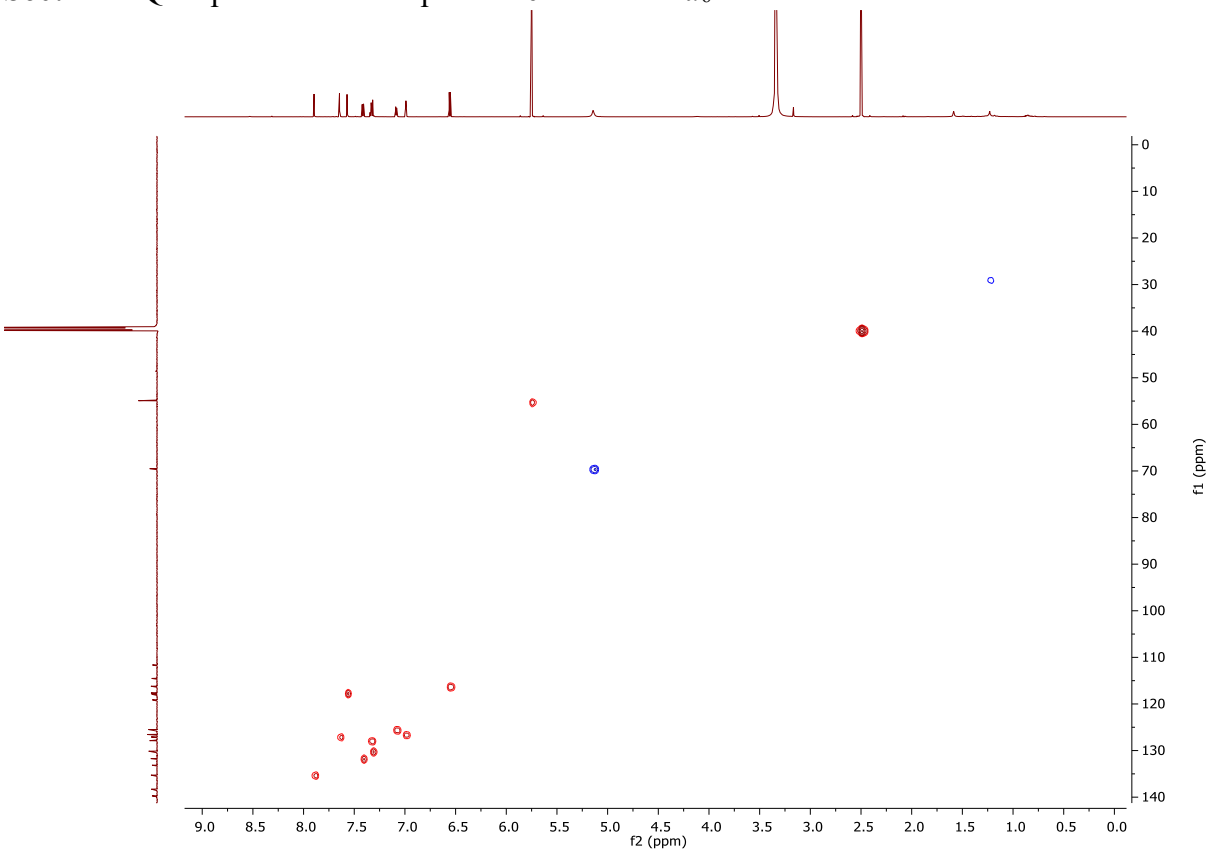
S58: ^{13}C NMR (200 MHz) Spectrum of Compound **10** in DMSO-d_6



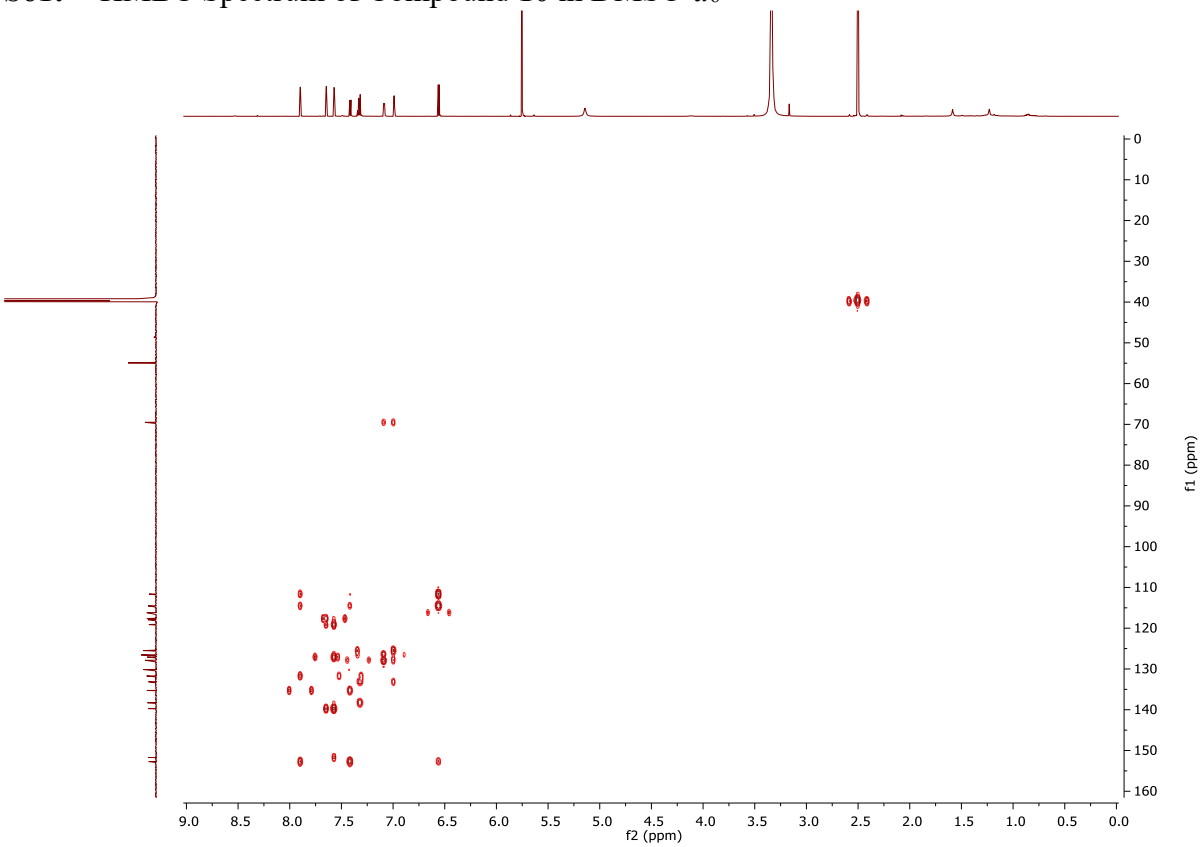
S59: COSY Spectrum of Compound **10** in DMSO-d_6



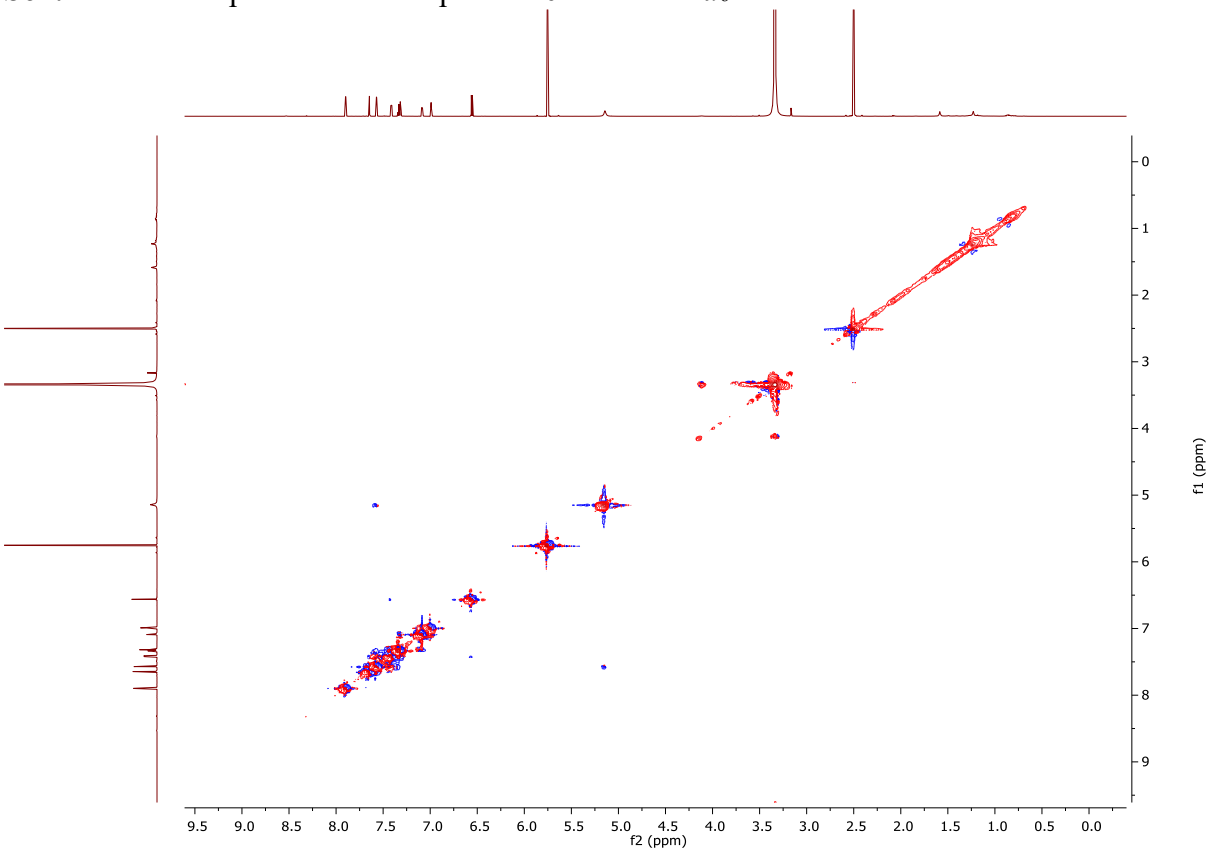
S60: HSQC Spectrum of Compound **10** in DMSO-d_6



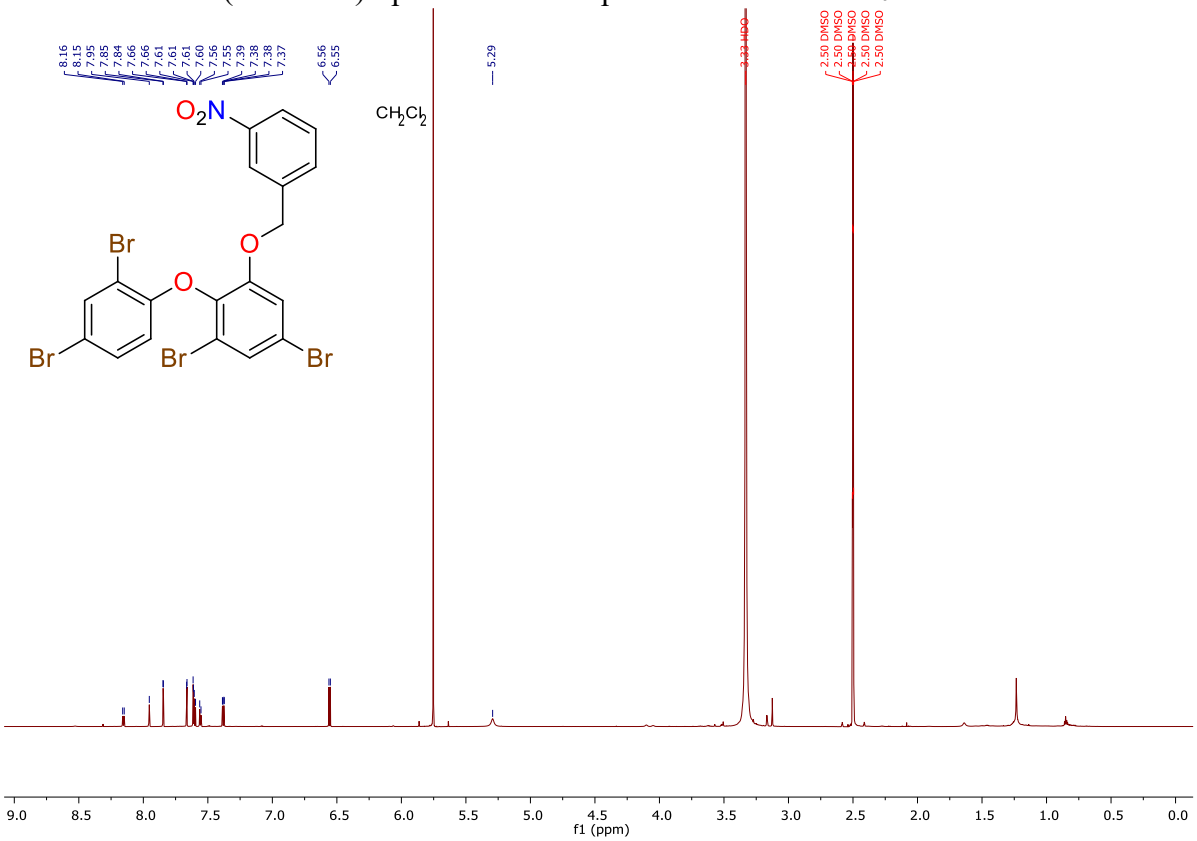
S61: HMBC Spectrum of Compound **10** in DMSO-d_6



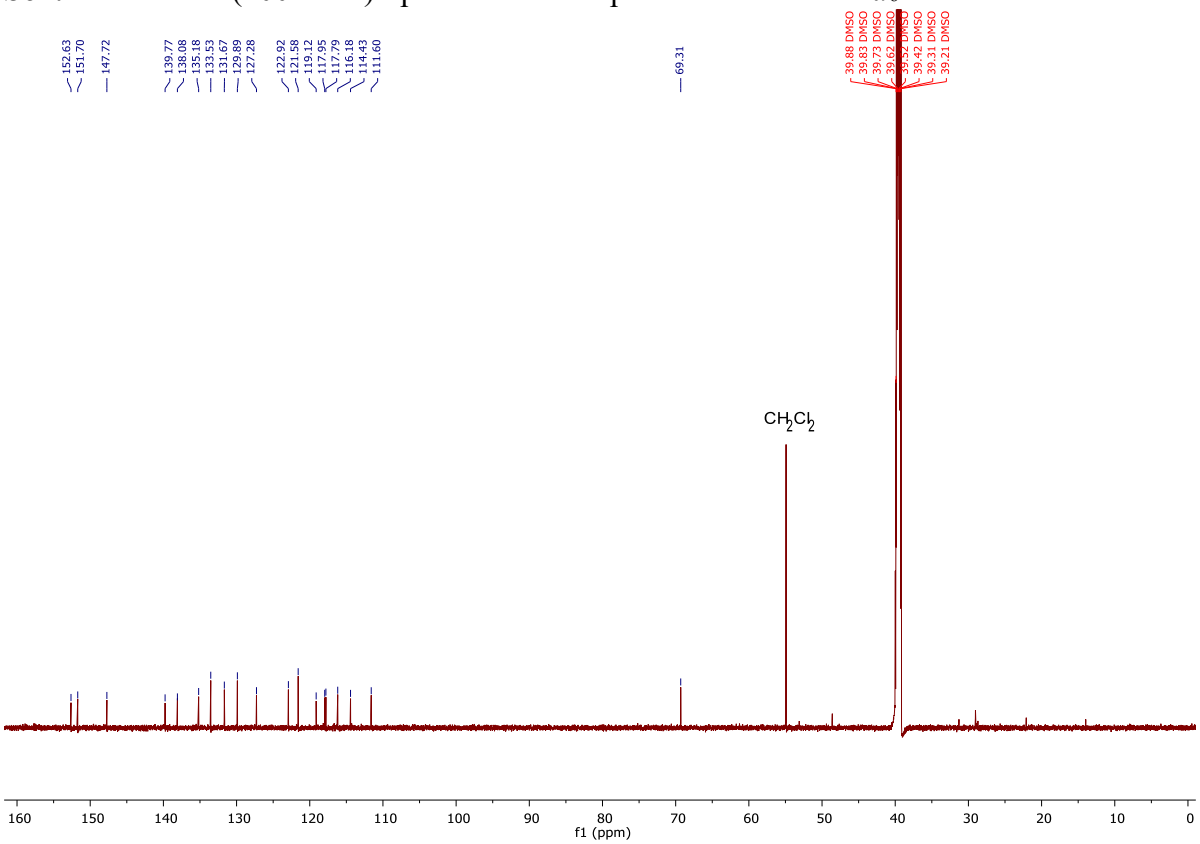
S62: ROESY Spectrum of Compound **10** in DMSO-d_6



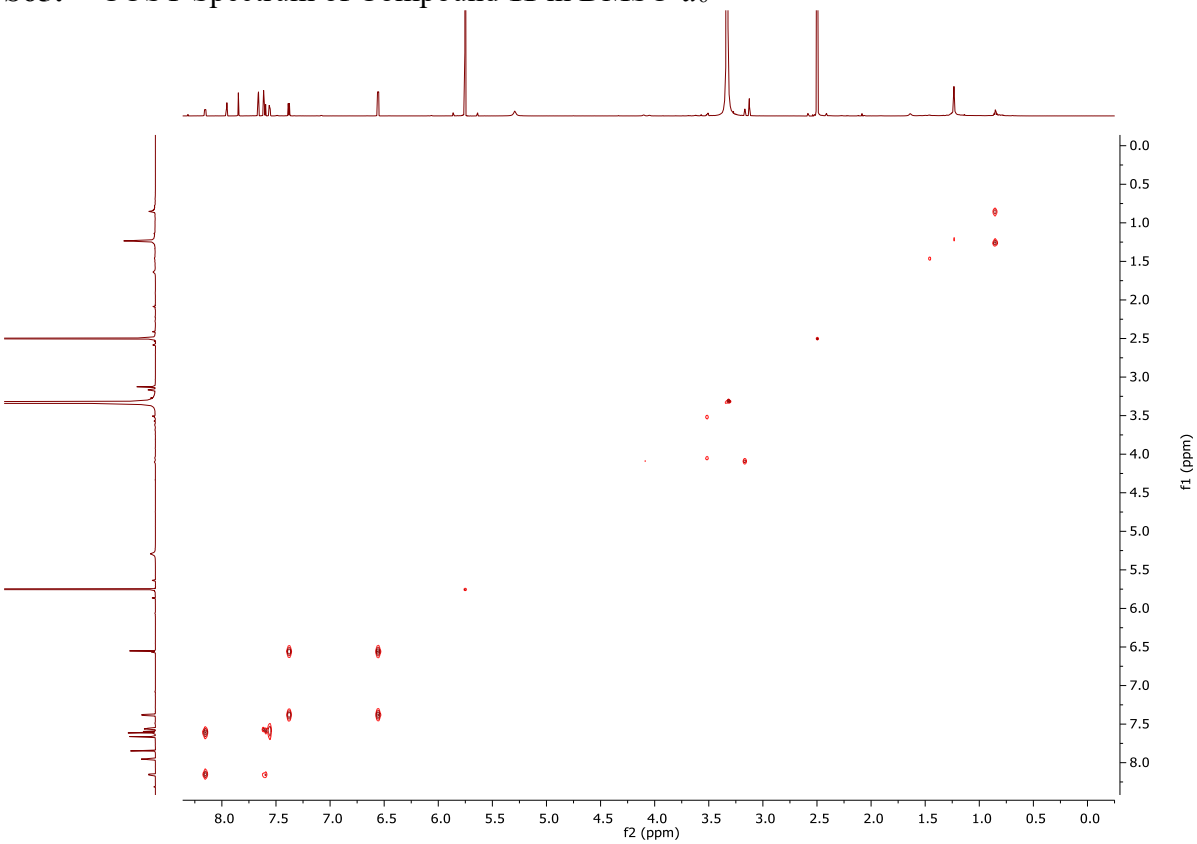
S63: ^{1}H NMR (800 MHz) Spectrum of Compound **11** in DMSO-d_6



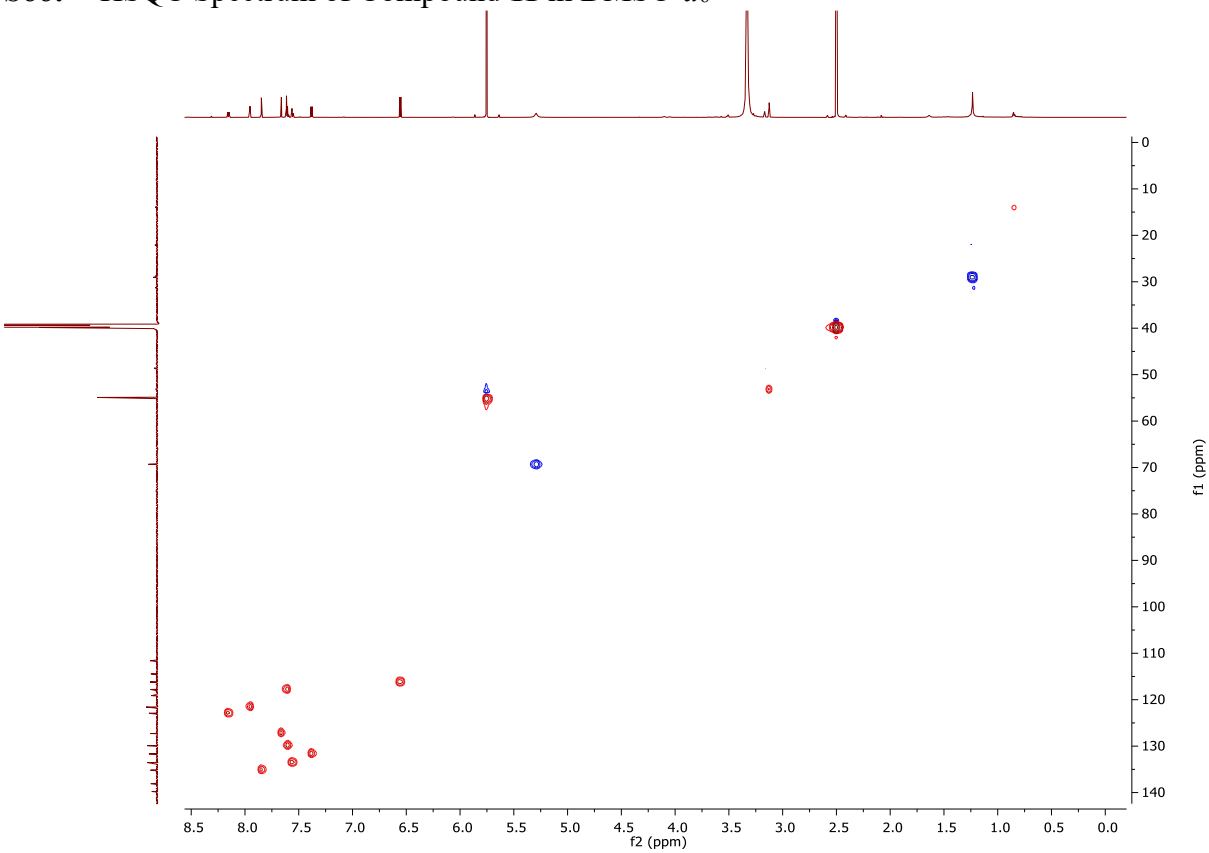
S64: ^{13}C NMR (200 MHz) Spectrum of Compound **11** in DMSO-d_6



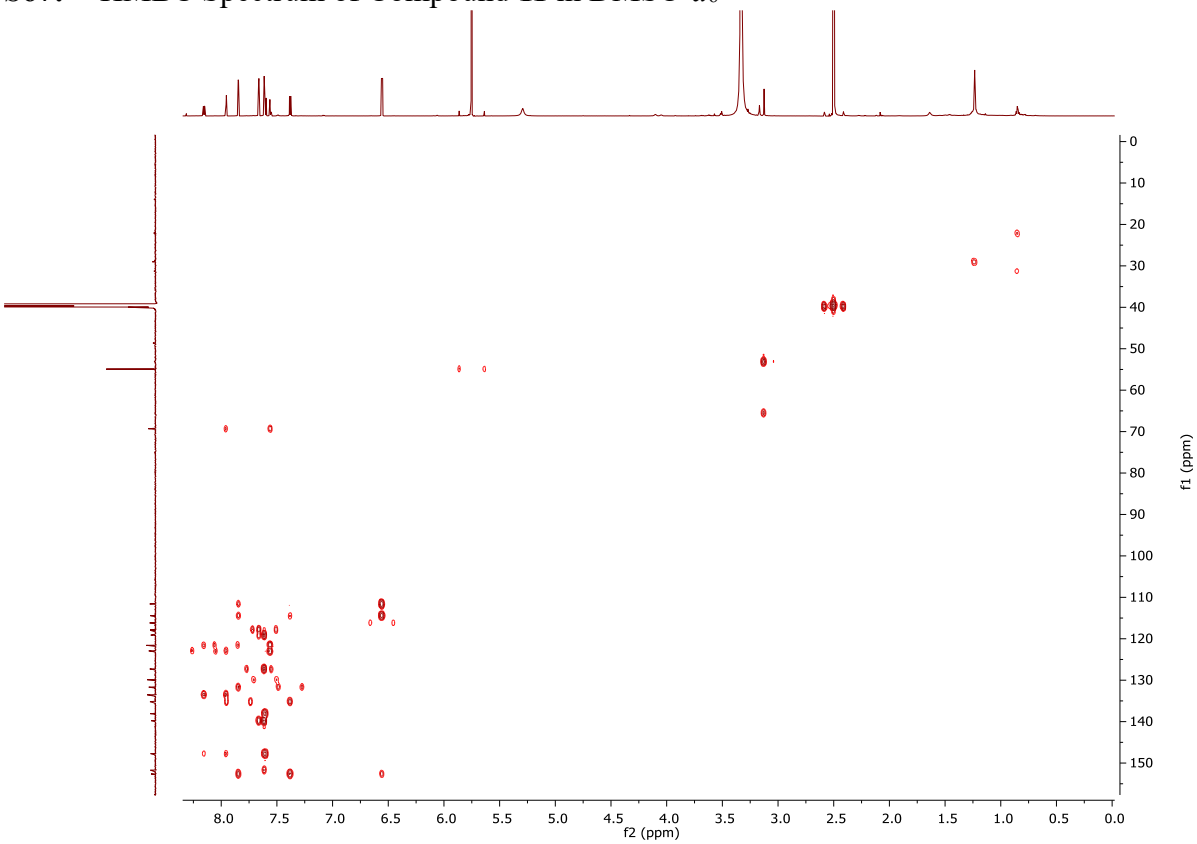
S65: COSY Spectrum of Compound **11** in DMSO-d_6



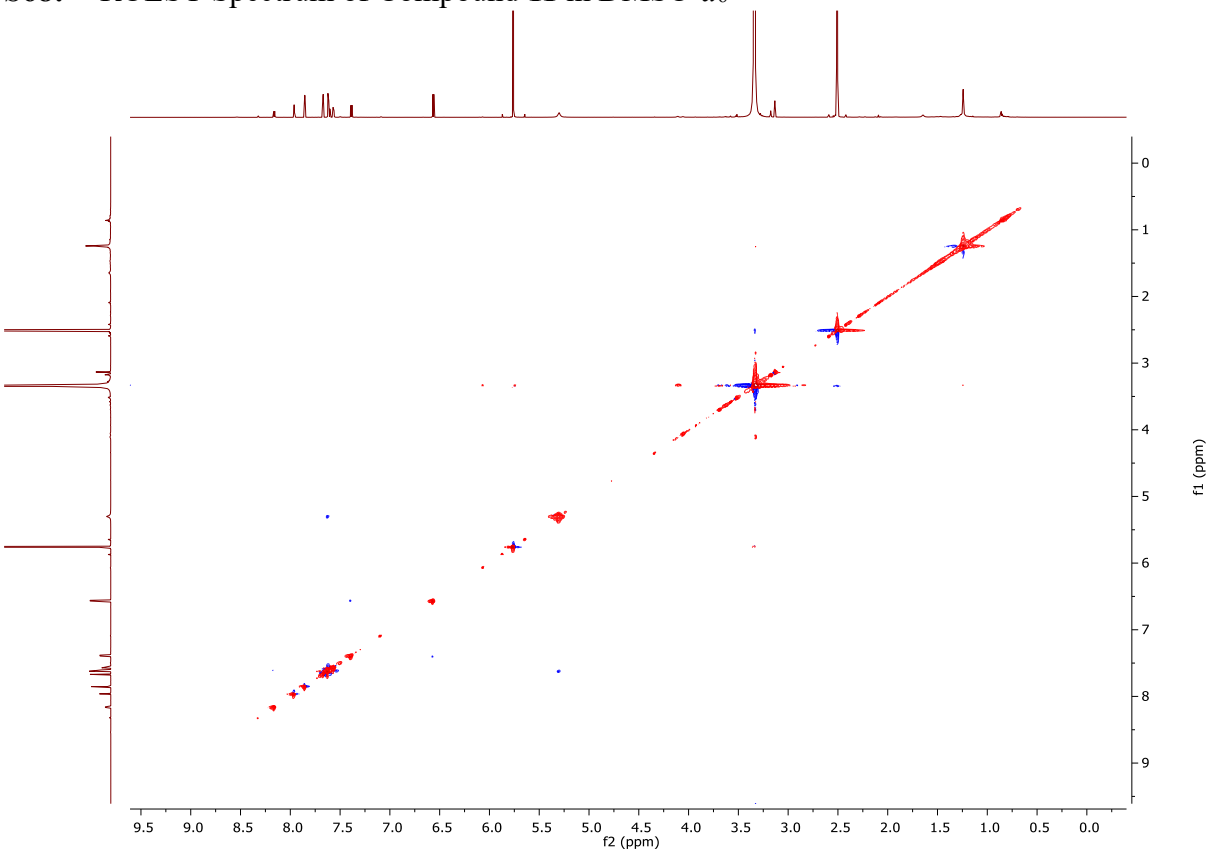
S66: HSQC Spectrum of Compound **11** in DMSO-d_6



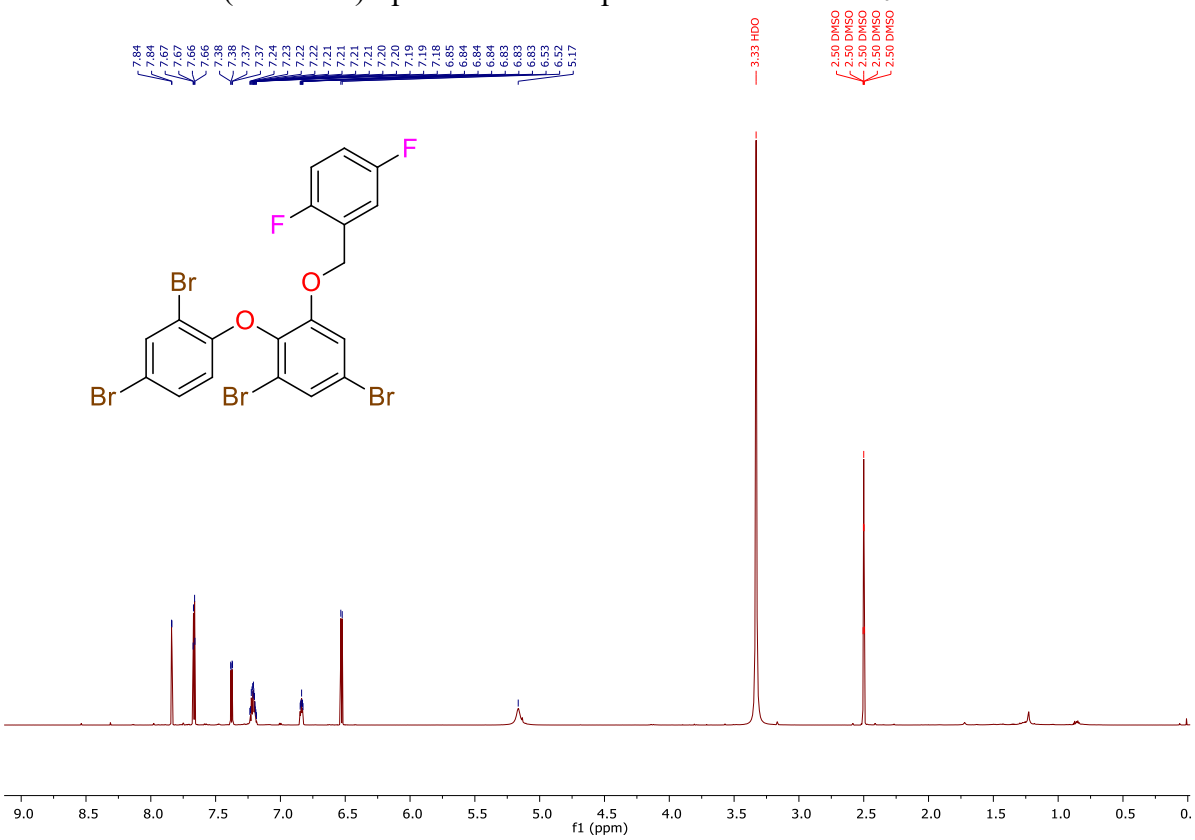
S67: HMBC Spectrum of Compound **11** in DMSO-d_6



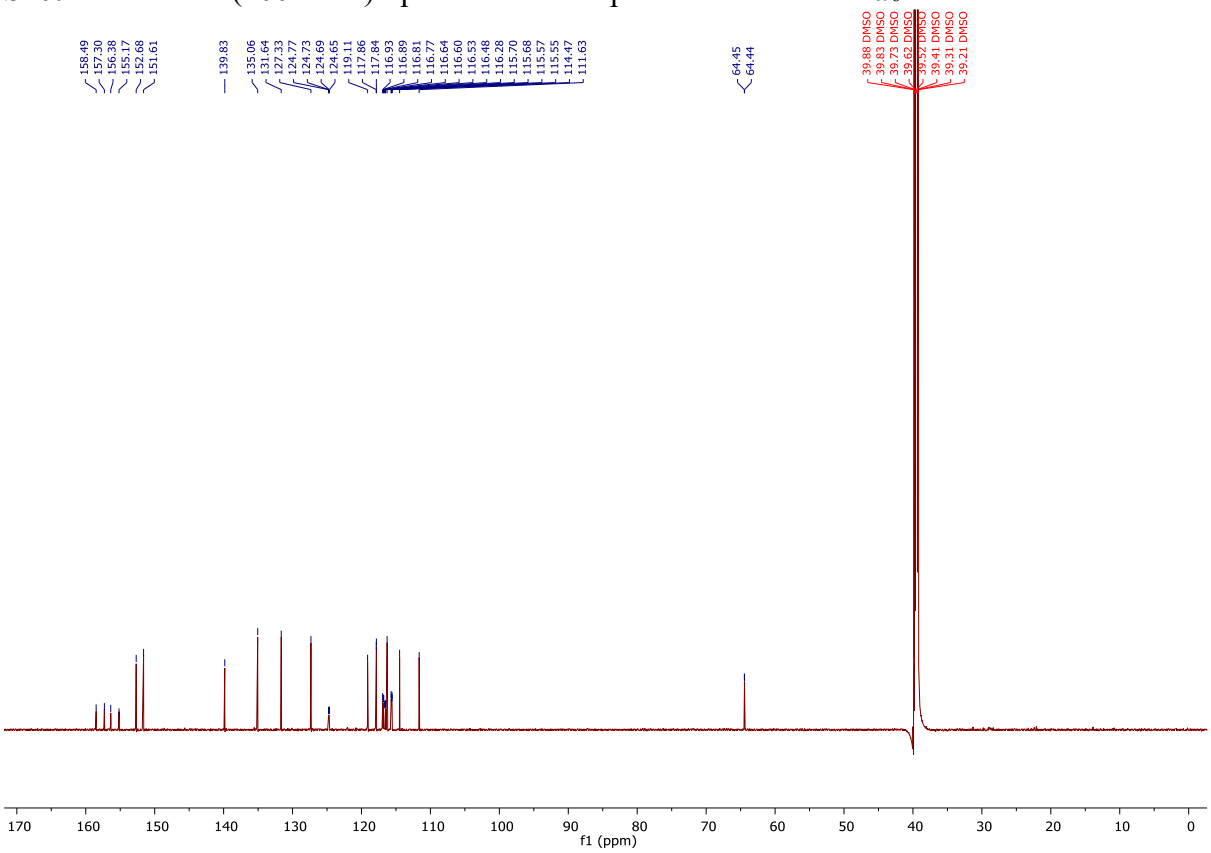
S68: ROESY Spectrum of Compound **11** in DMSO-d_6



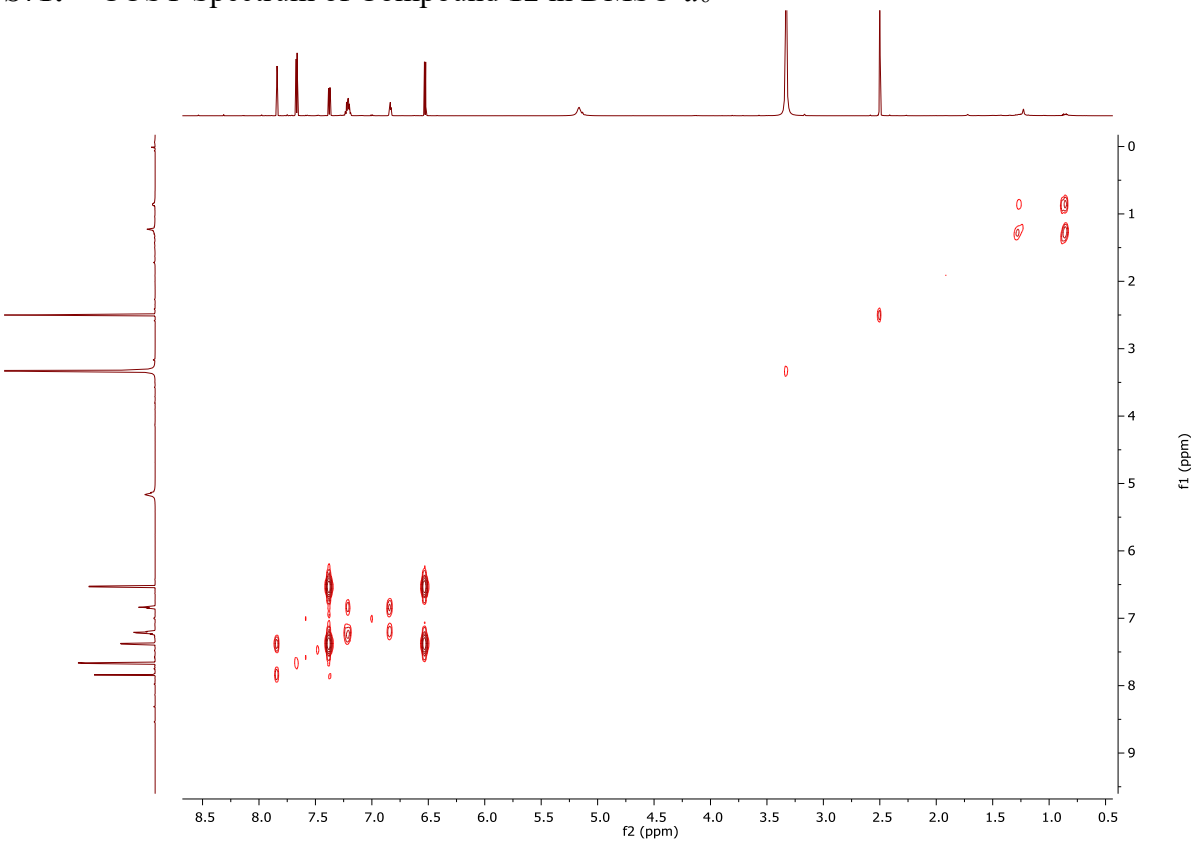
S69: ^{1}H NMR (800 MHz) Spectrum of Compound **12** in DMSO-d_6



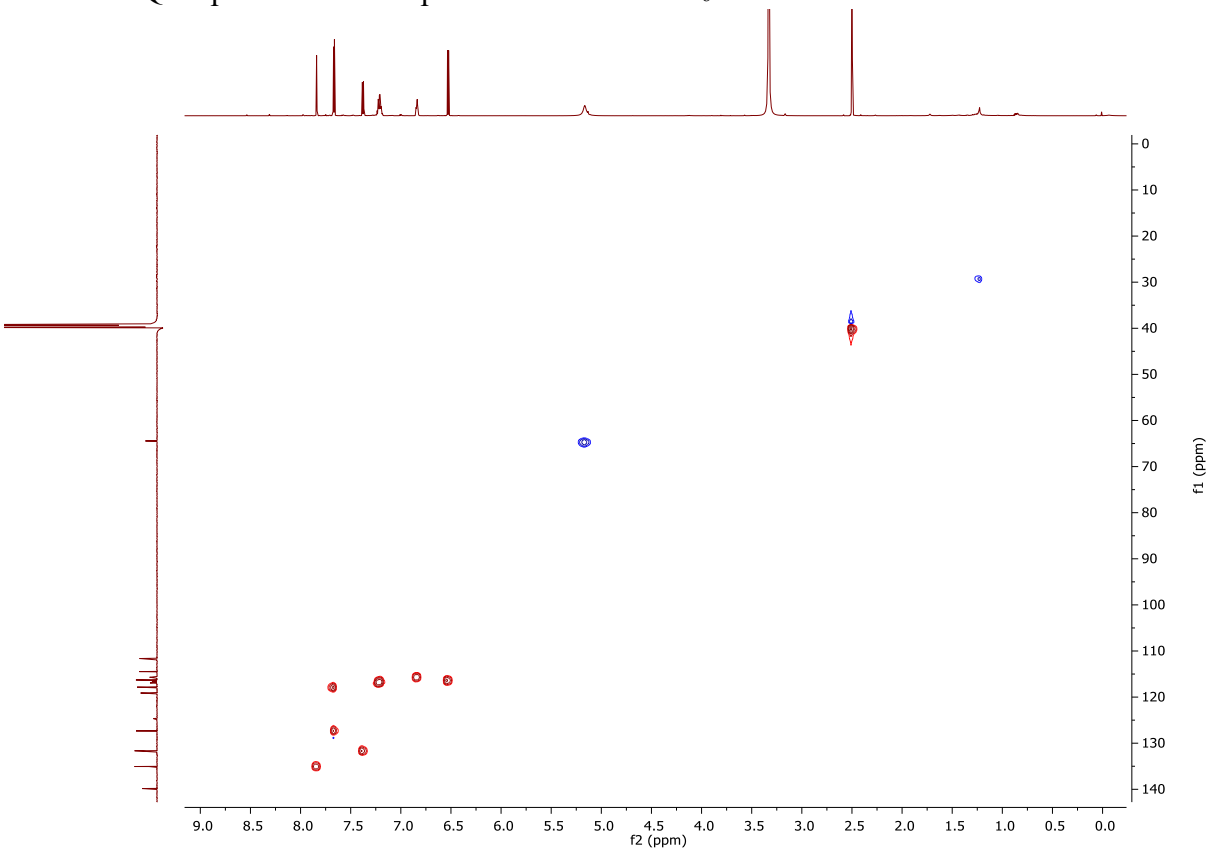
S70: ^{13}C NMR (200 MHz) Spectrum of Compound **12** in DMSO-d_6



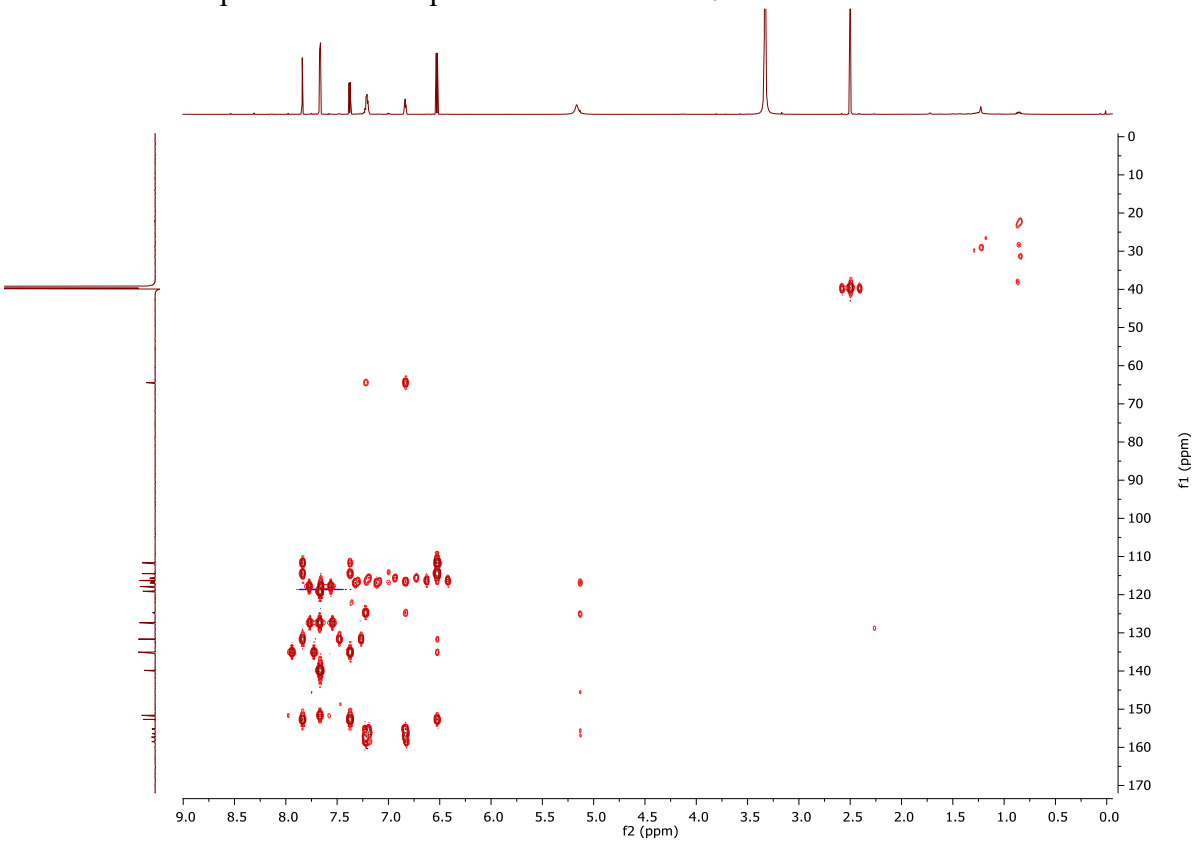
S71: COSY Spectrum of Compound **12** in DMSO-d_6



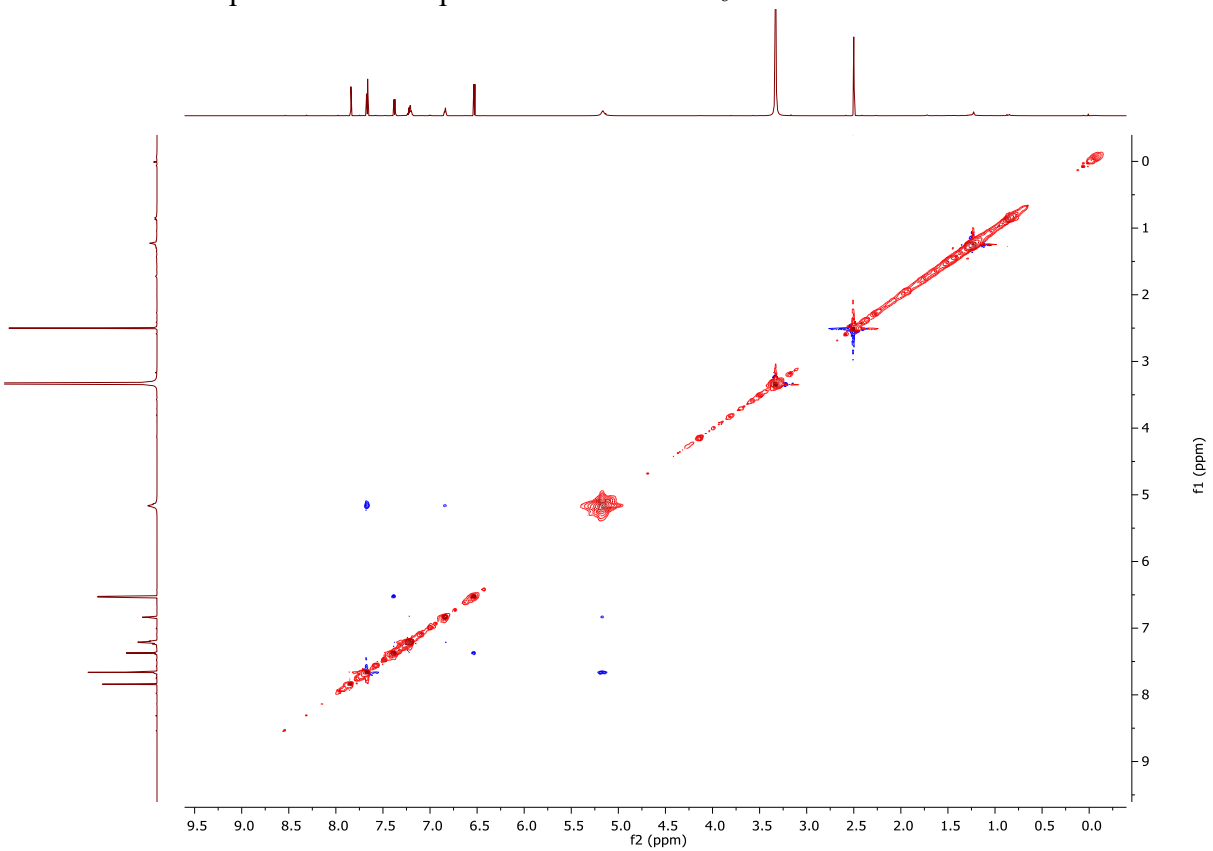
S72: HSQC Spectrum of Compound **12** in DMSO-d_6



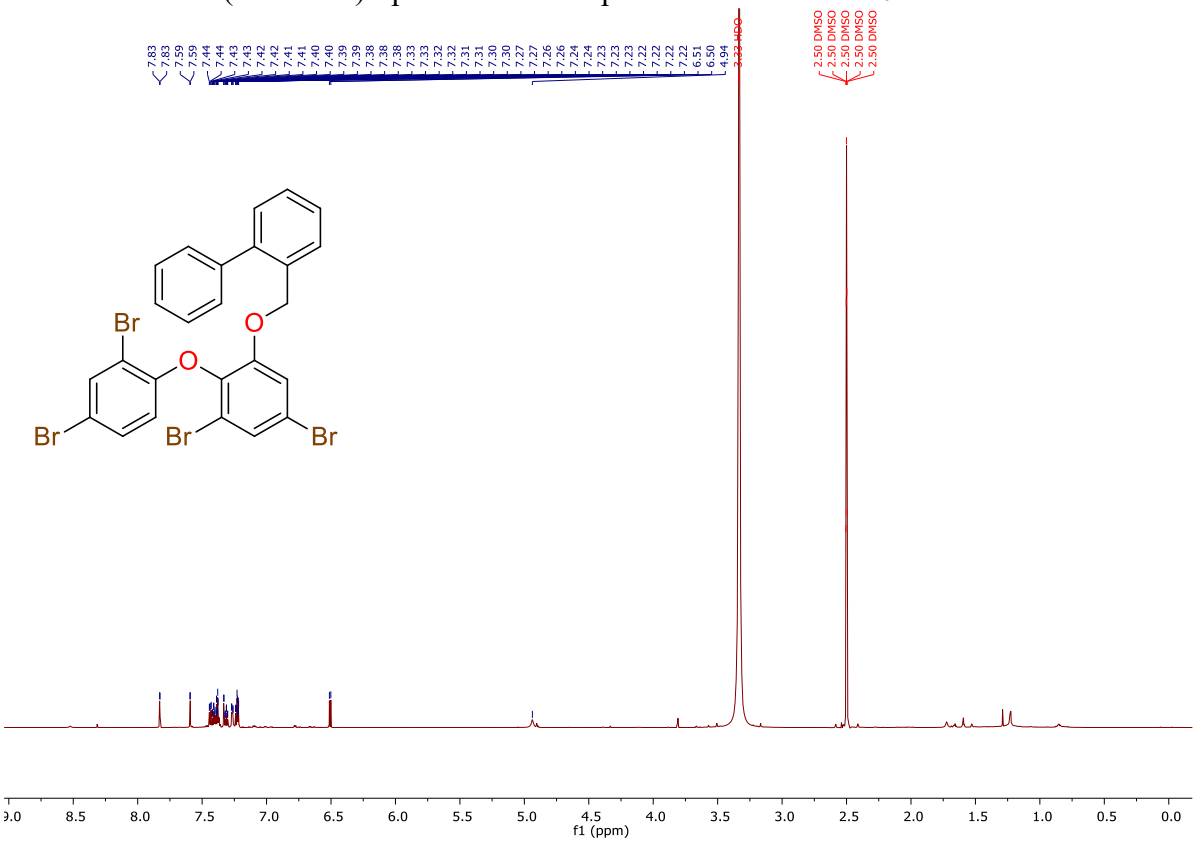
S73: HMBC Spectrum of Compound **12** in DMSO-d_6



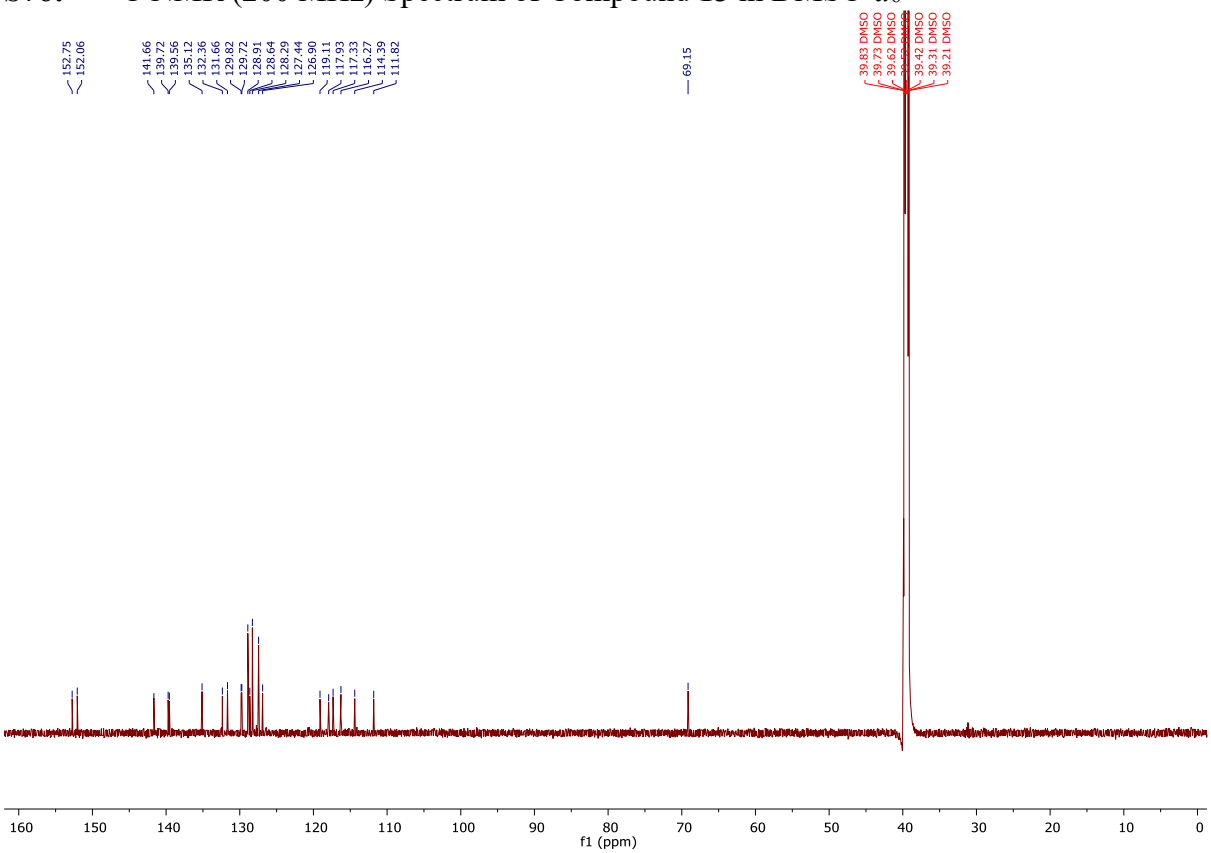
S74: ROESY Spectrum of Compound **12** in DMSO-d_6



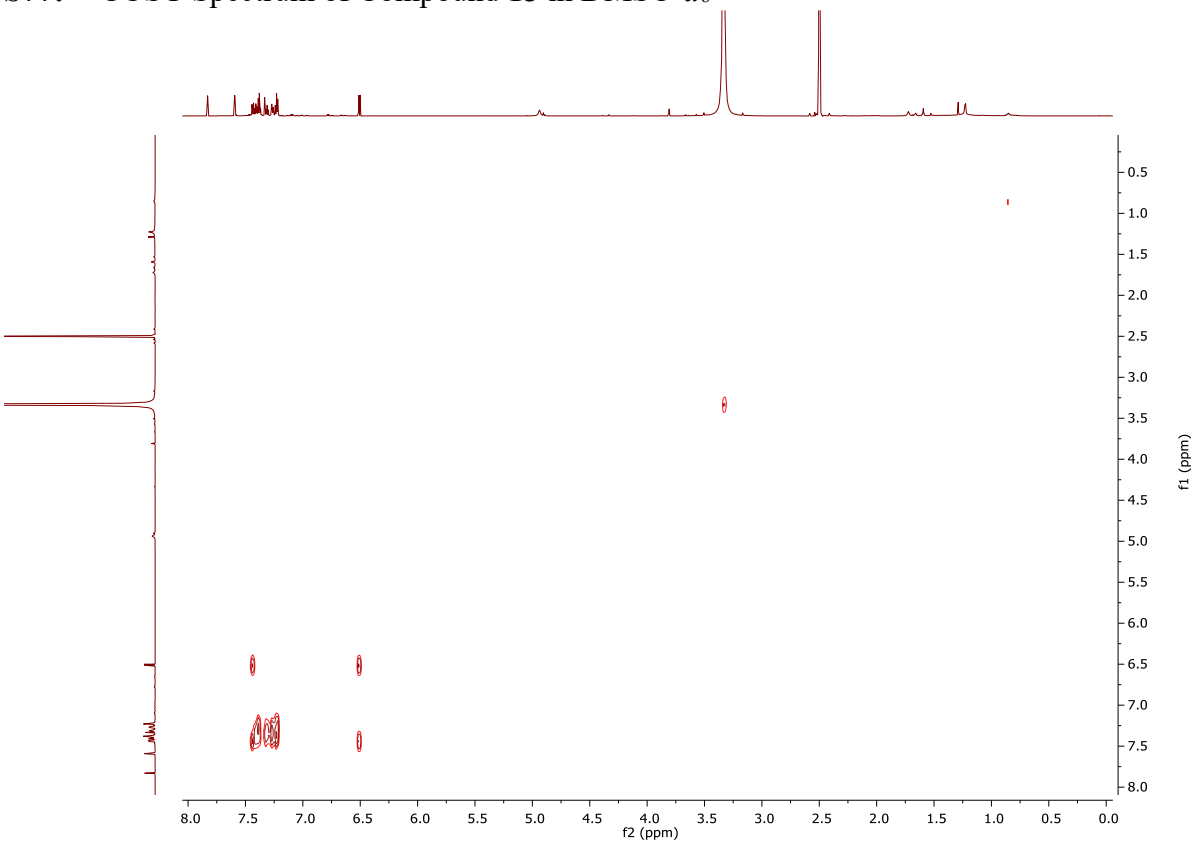
S75: ^{1}H NMR (800 MHz) Spectrum of Compound **13** in DMSO-*d*6



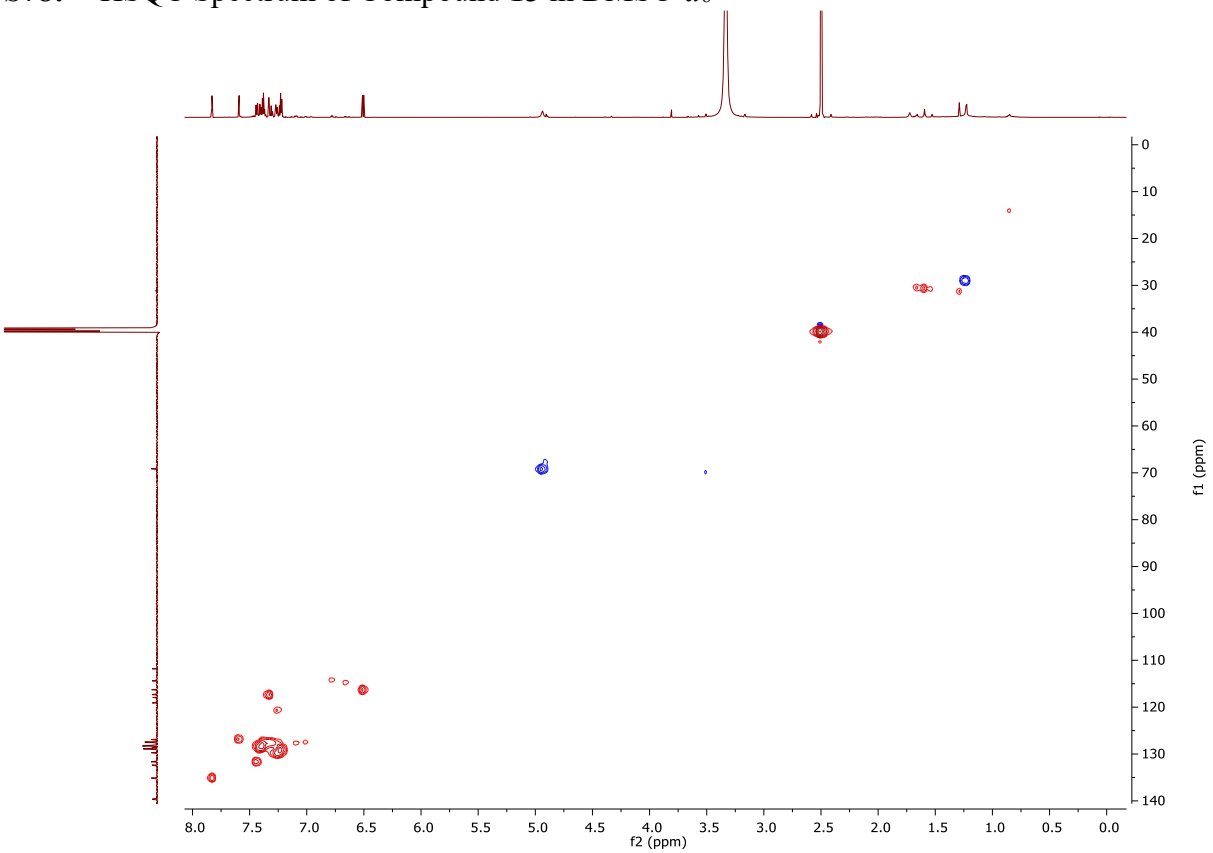
S76: ^{13}C NMR (200 MHz) Spectrum of Compound **13** in DMSO-*d*6



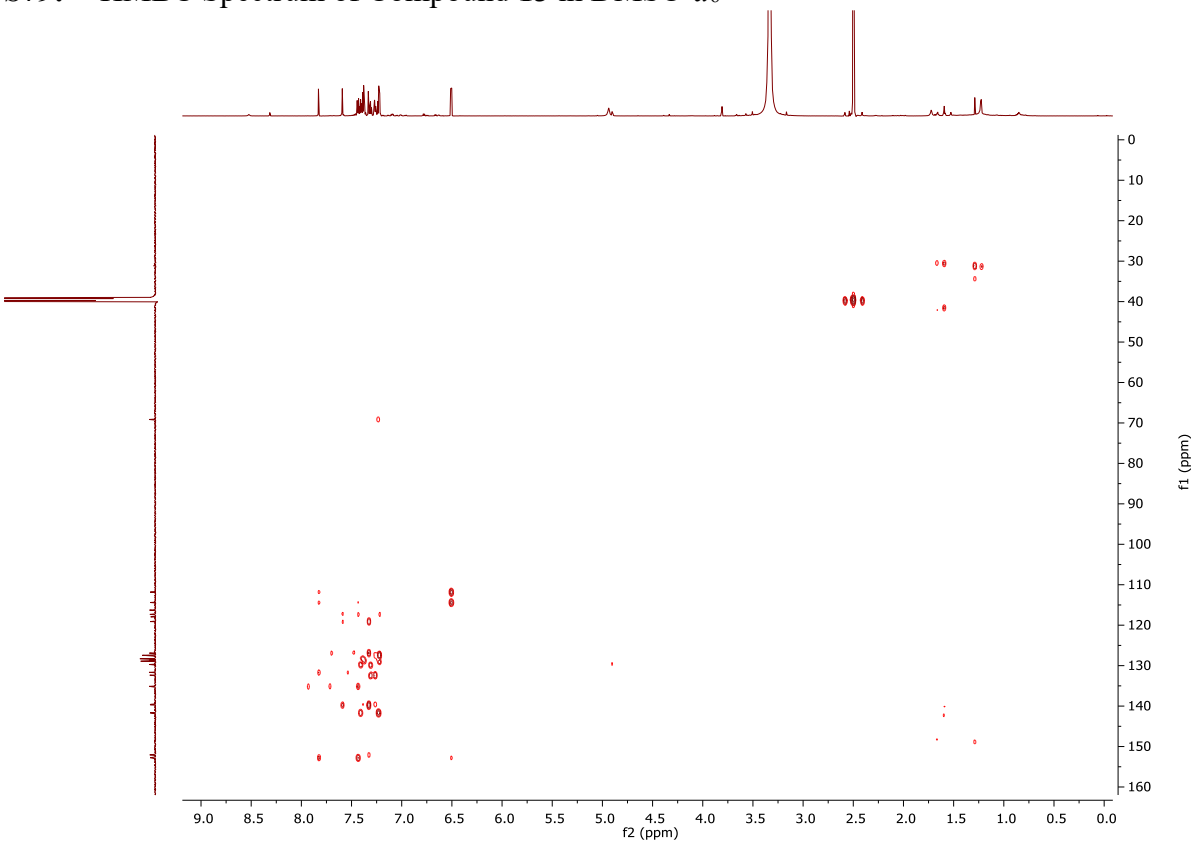
S77: COSY Spectrum of Compound **13** in DMSO-d_6



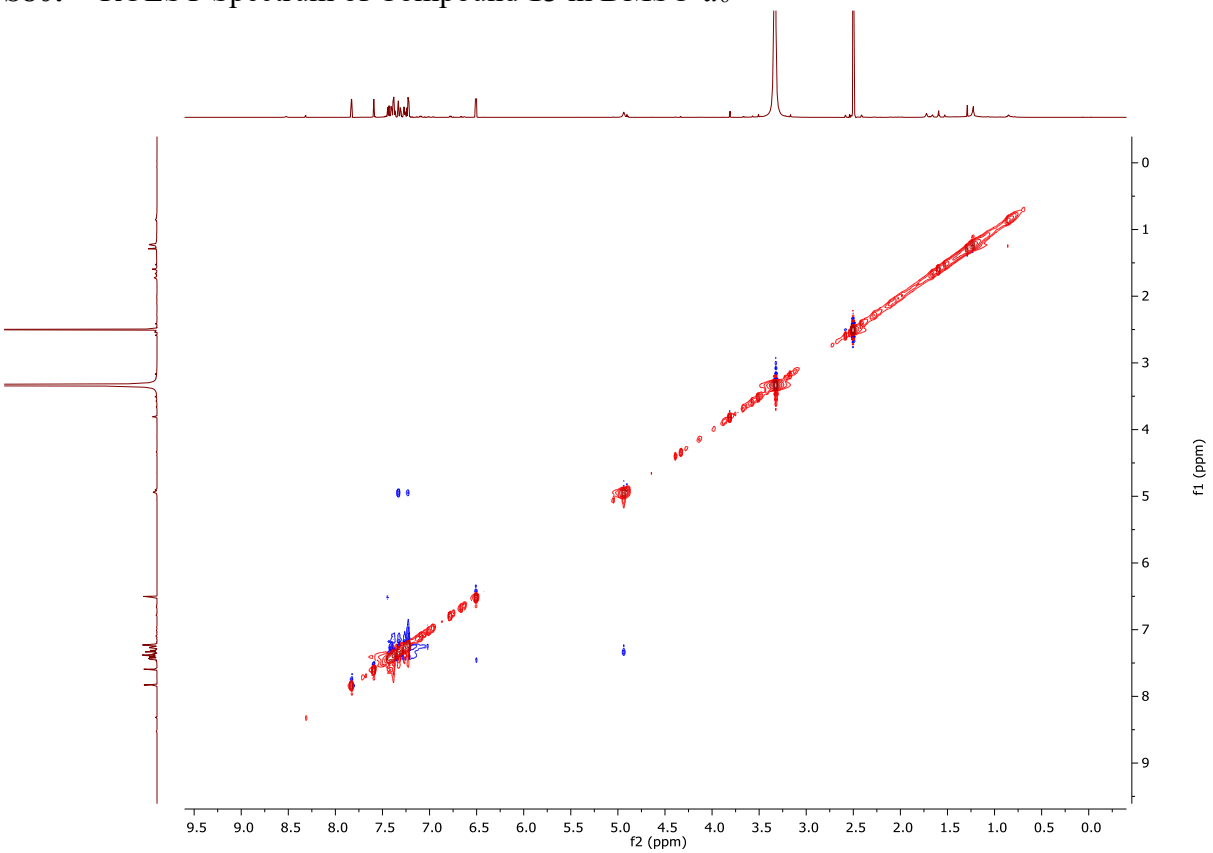
S78: HSQC Spectrum of Compound **13** in DMSO-d_6



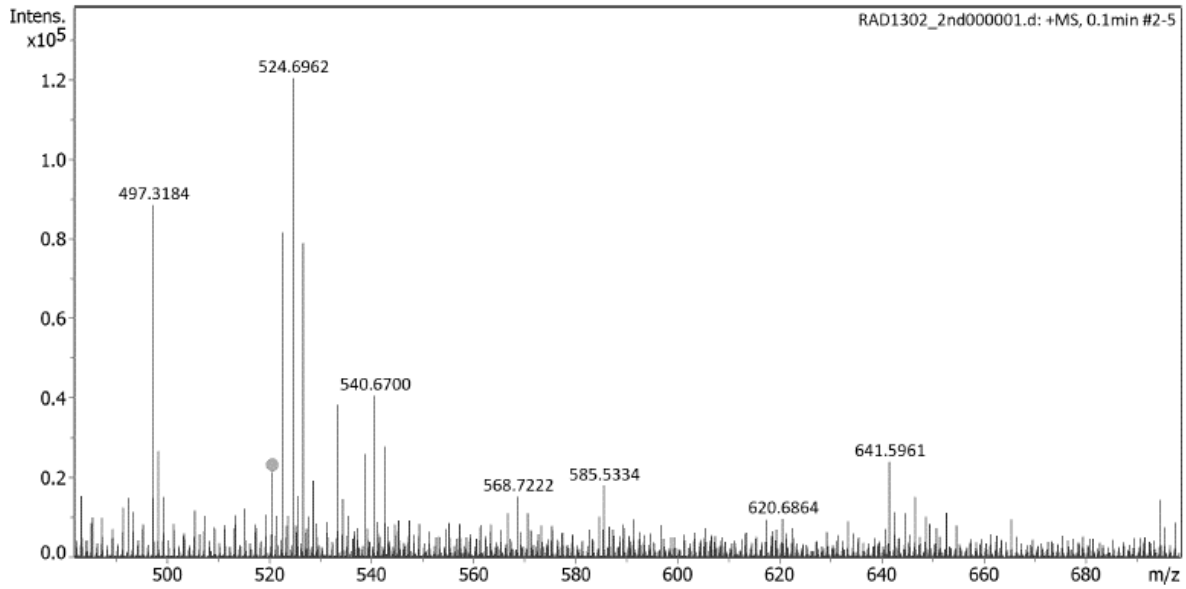
S79: HMBC Spectrum of Compound **13** in DMSO-d_6



S80: ROESY Spectrum of Compound **13** in DMSO-d_6

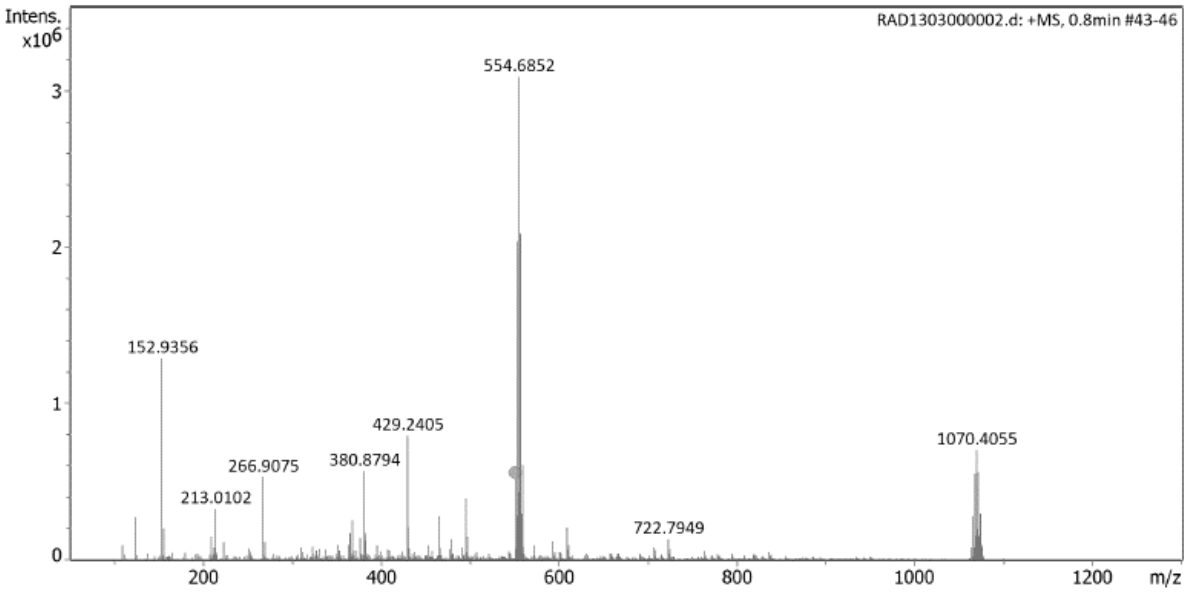


S81: HRESIMS Data of Compound **1**



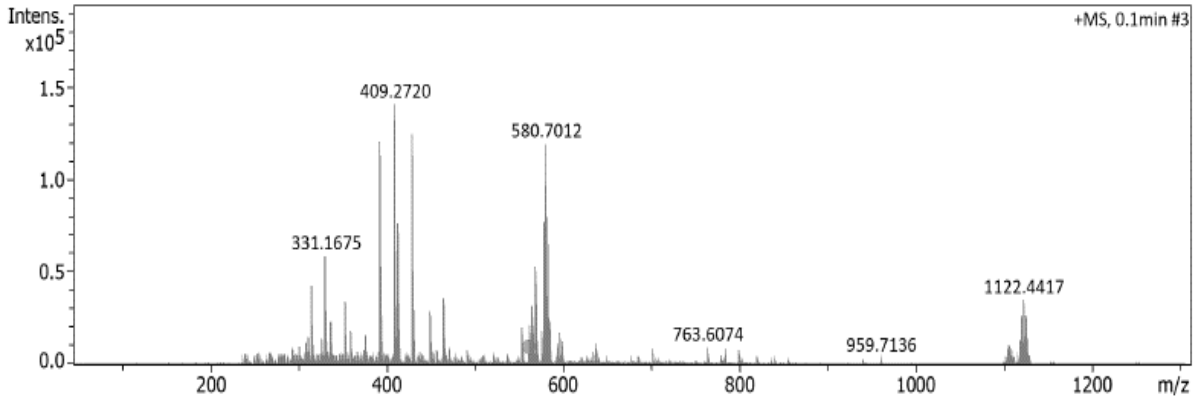
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
520.7002	1	C12H6Br4NaO2	520.6994	-1.7	3.1	1	100.00	16.0	even	ok

S82: HRESIMS Data of Compound **2**



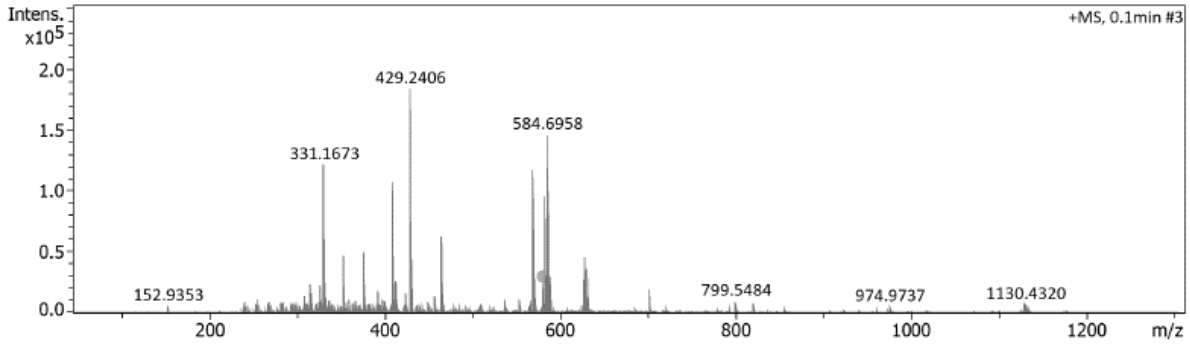
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
550.6893	1	C13H8Br4KO2	550.6889	-0.6	6.5	1	100.00	16.0	even	ok

S83: HRESIMS Data of Compound **3**



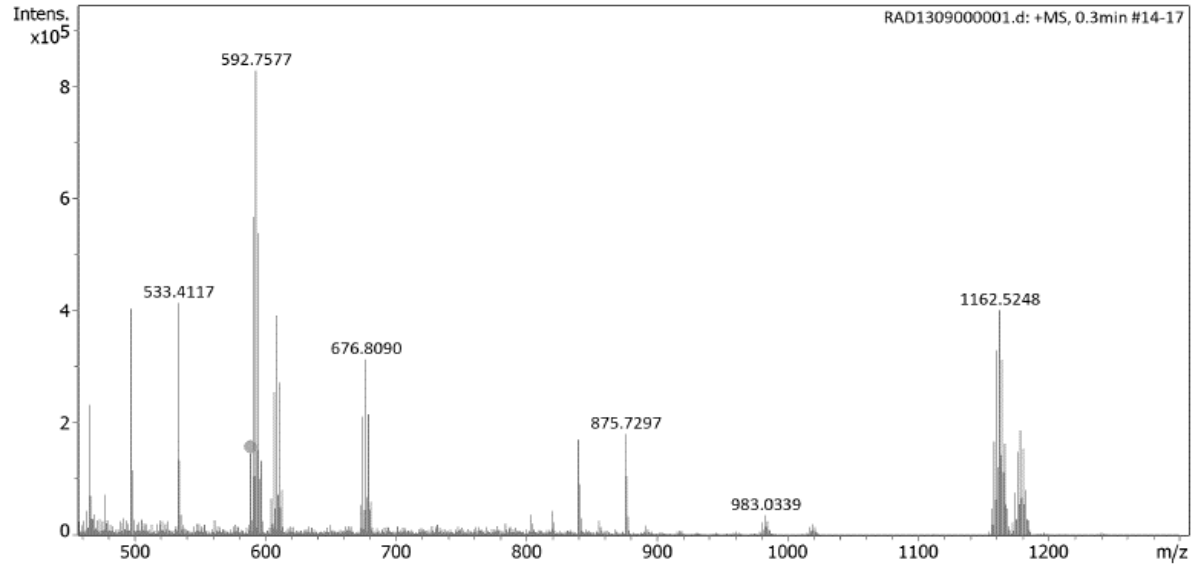
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
560.7306	1	C15H10Br4NaO2	560.7307	0.0	5.7	1	100.00	17.0	even	ok

S84: HRESIMS Data of Compound **4**



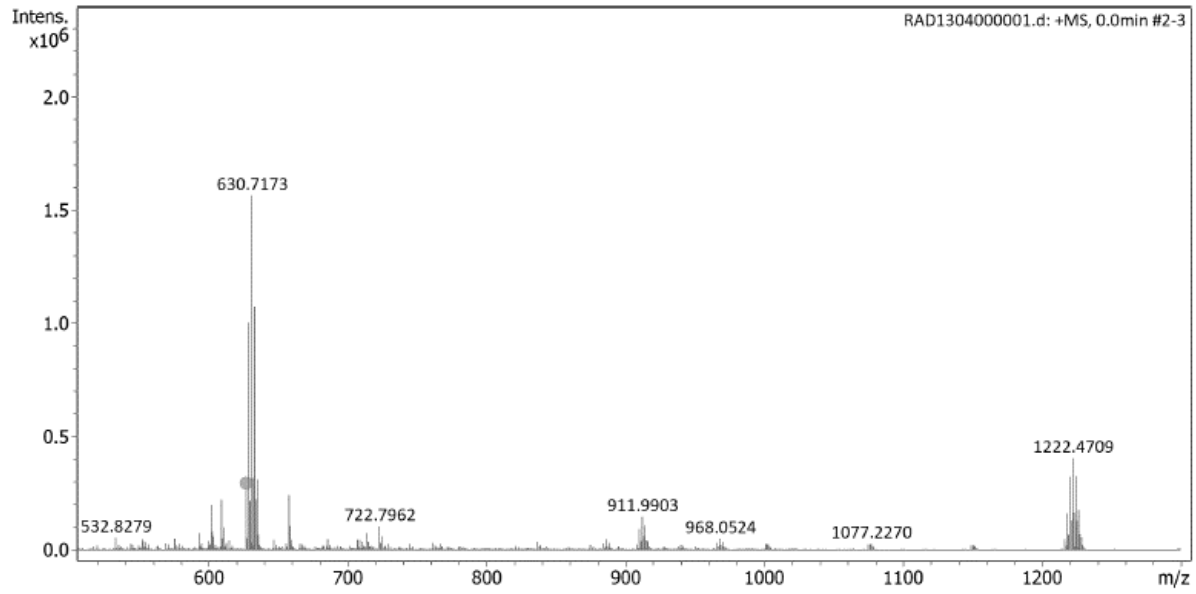
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
580.7000	1	C14H10Br4KO3	580.6995	-0.8	3.1	1	100.00	16.0	even	ok

S85: HRESIMS Data of Compound **5**



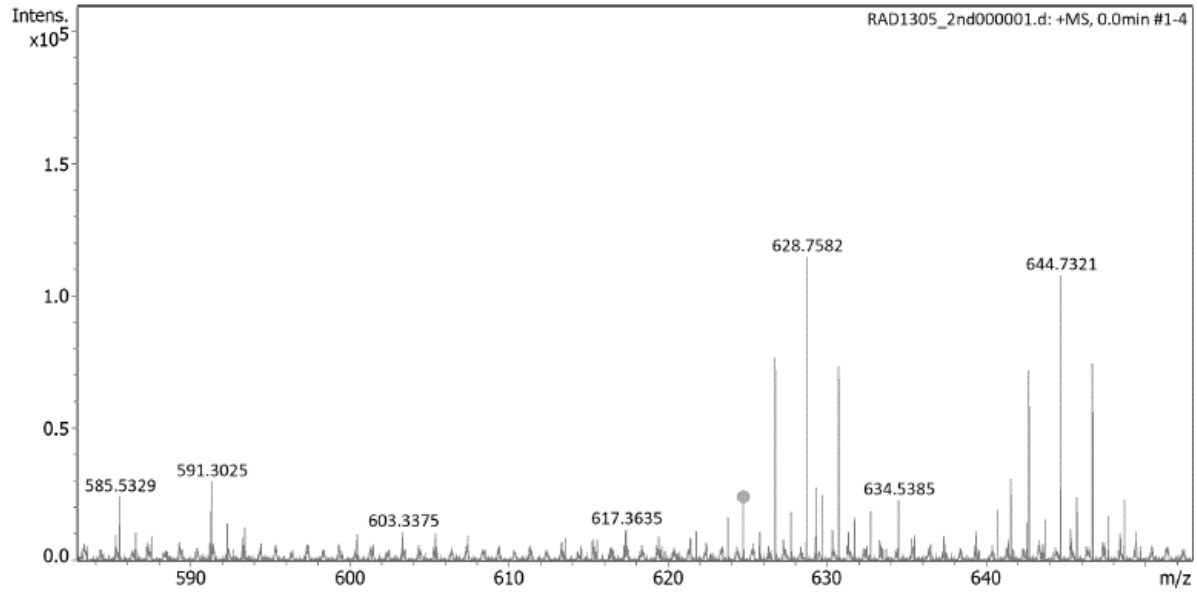
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
588.7618	1	C17H14Br4NaO2	588.7620	0.2	4.8	1	100.00	17.0	even	ok
	2	C13H10Br4N6Na	588.7593	-4.3	10.2	2	19.36	18.0	even	ok
	3	C12H14Br4N2NaO4	588.7579	-6.6	20.3	3	4.05	13.0	even	ok

S86: HRESIMS Data of Compound **6**



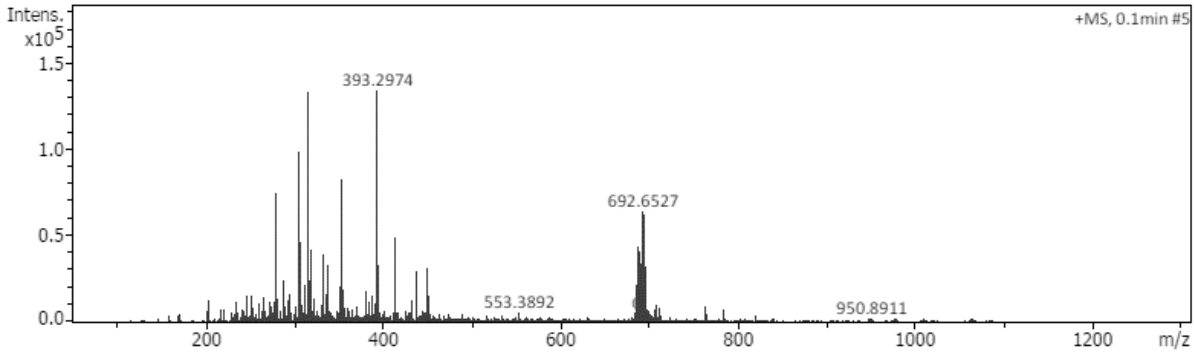
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
626.7214	1	C19H12Br4KO2	626.7202	-1.9	7.0	1	100.00	20.0	even	ok

S87: HRESIMS Data of Compound **7**



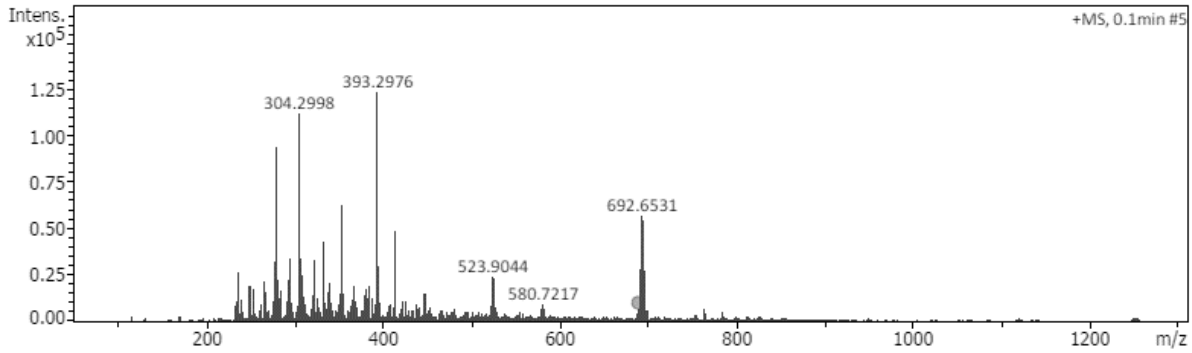
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
624.7621	1	C20H14Br4NaO2	624.7620	-0.2	10.9	1	100.00	20.0	even	ok

S88: HRESIMS Data of Compound **8**



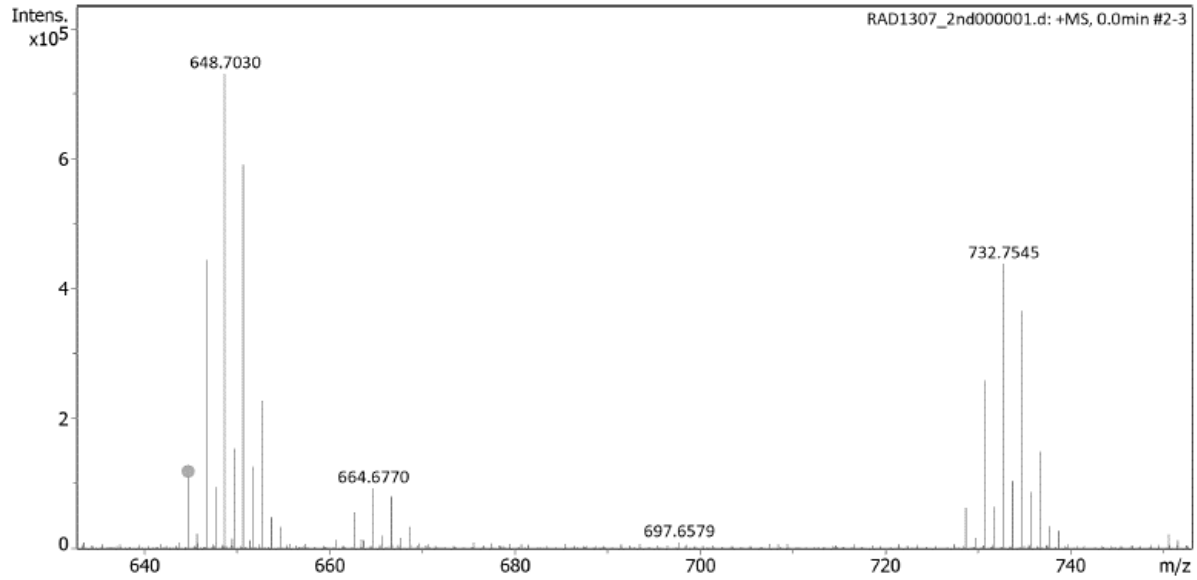
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
688.6566	1	C19H11Br5NaO2	688.6568	0.3	7.6	1	100.00	22.0	even	ok

S89: HRESIMS Data of Compound **9**



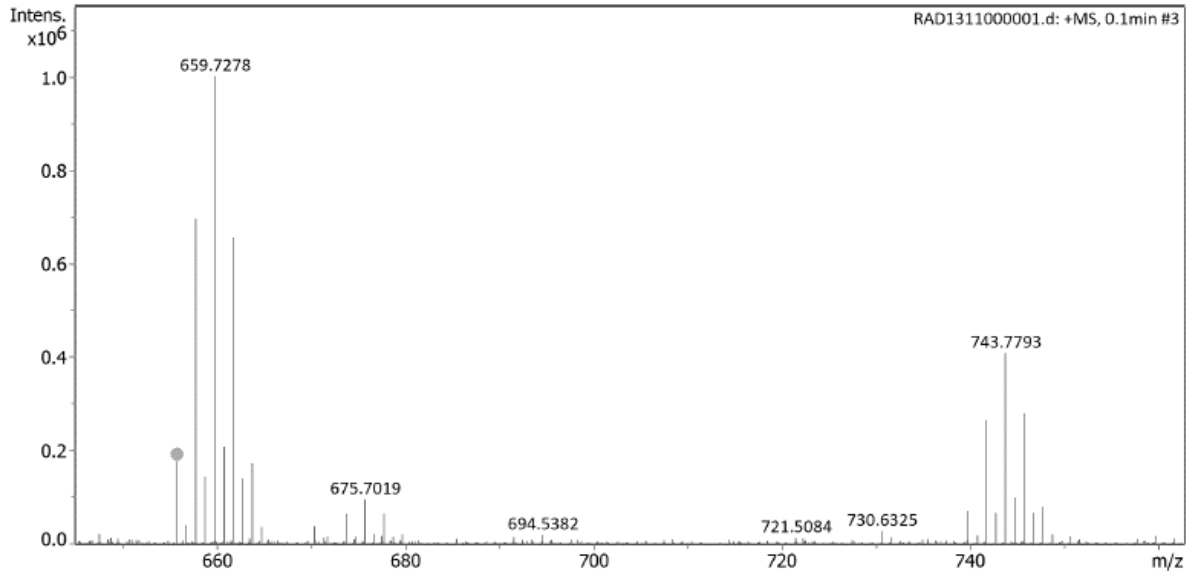
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
688.6569	1	C19H11Br5NaO2	688.6568	-0.1	11.5	1	100.00	22.0	even	ok

S90: HRESIMS Data of Compound **10**



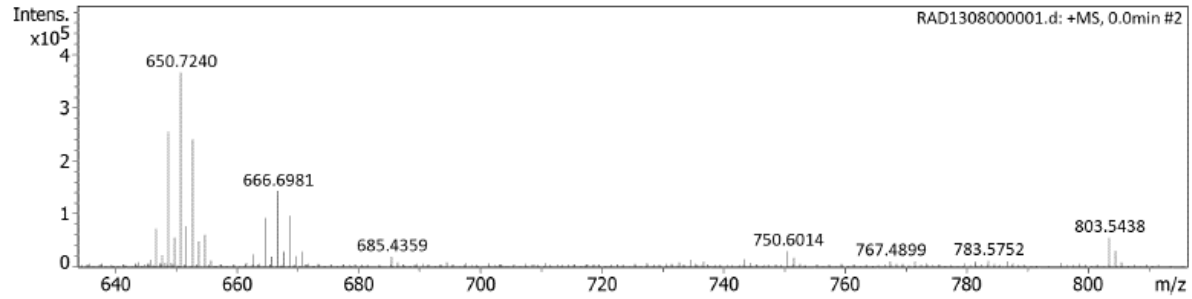
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
644.7073	1	C19H11Br4ClNaO2	644.7073	0.0	4.6	1	100.00	23.0	even	ok

S91: HRESIMS Data of Compound **11**



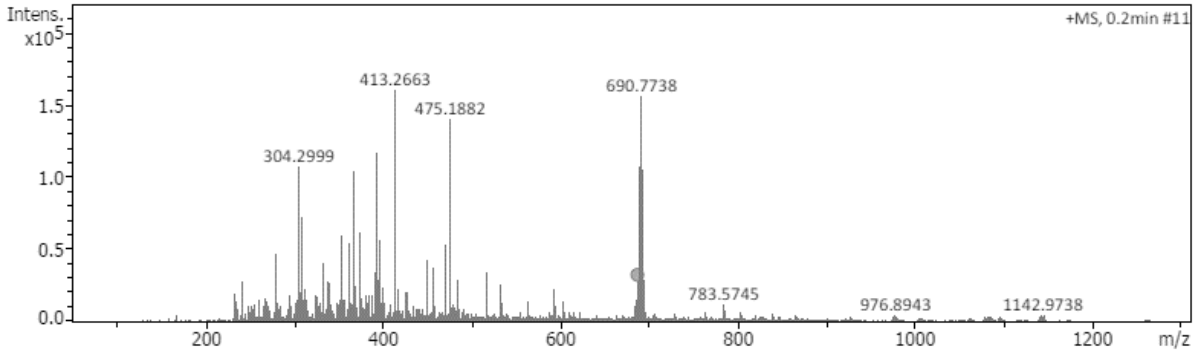
Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
655.7318	1	C19H11Br4NNaO4	655.7314	-0.7	6.9	1	100.00	21.0	even	ok

S92: HRESIMS Data of Compound **12**



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
646.7273	1	C19H10Br4F2NaO2	646.7275	0.3	15.5	1	100.00	20.0	even	ok

S93: HRESIMS Data of Compound **13**



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# mSigma	Score	rdb	e⁻ Conf	N-Rule
686.7777	1	C25H16Br4NaO2	686.7776	-0.1	5.3	1	100.00	24.0	even	ok
	2	C18H16Br4N6NaO2	686.7960	26.7	25.1	2	0.00	20.0	even	ok