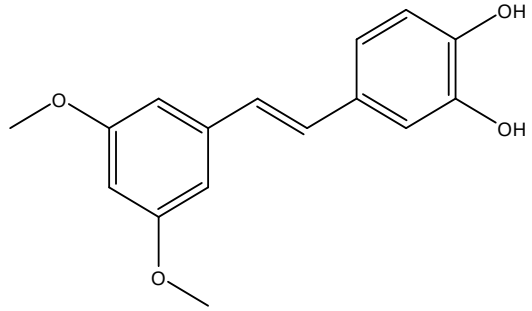
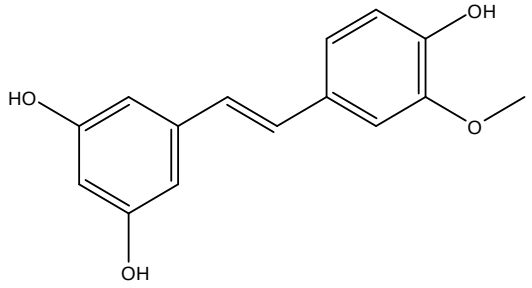
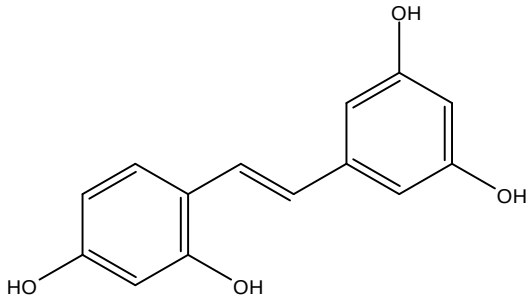
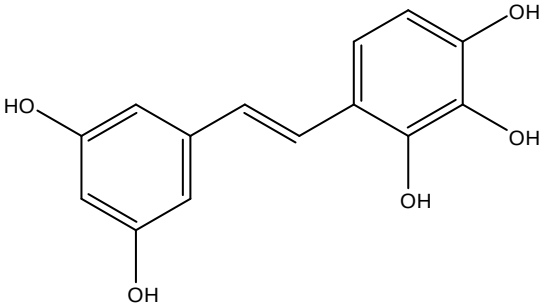
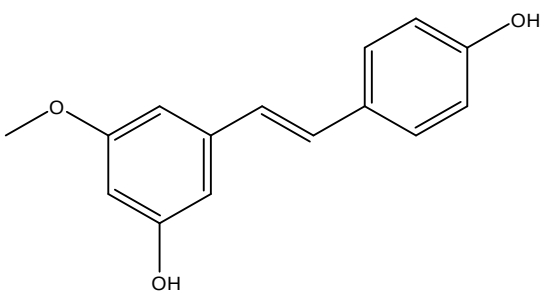
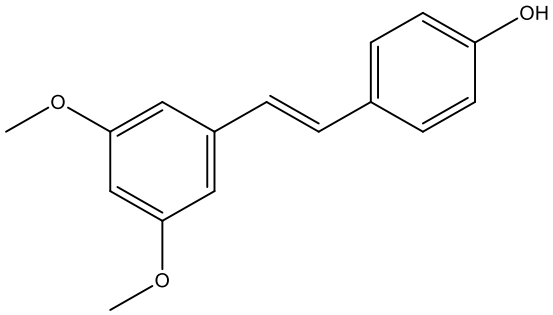
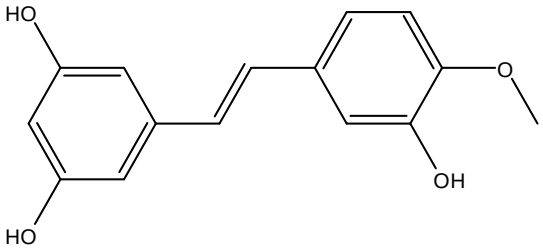
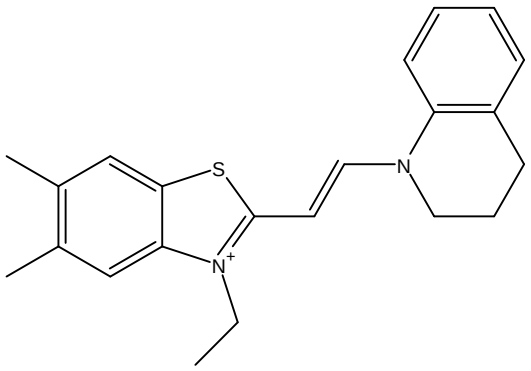
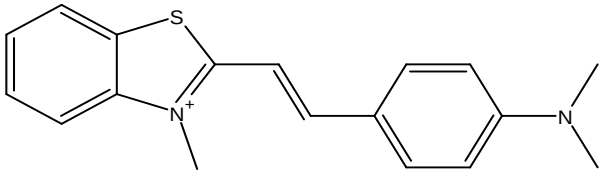
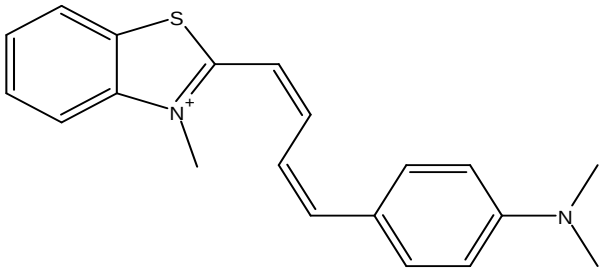
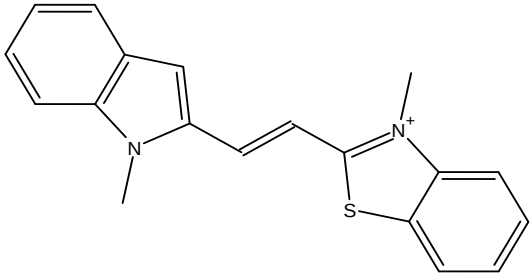
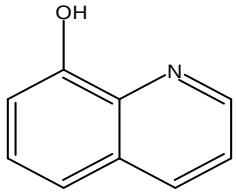
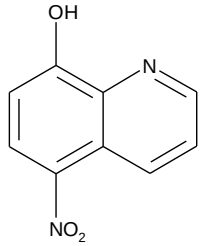
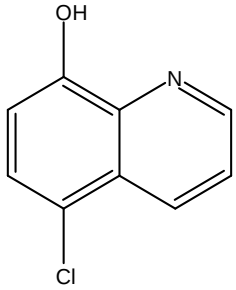
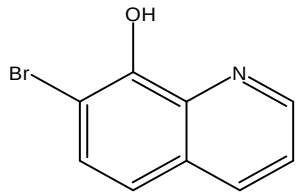
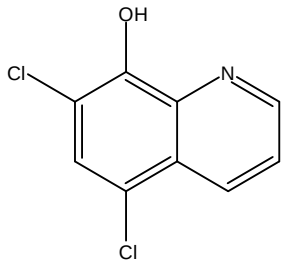
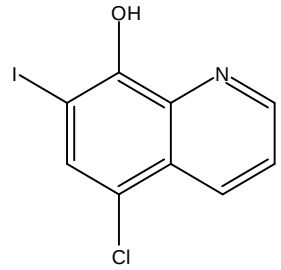
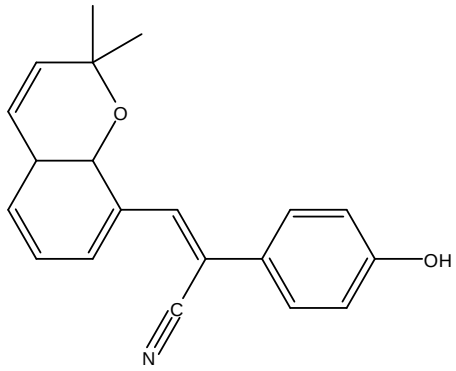
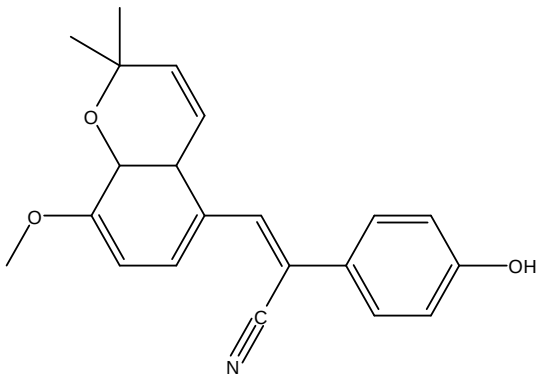
Supplementary Materials

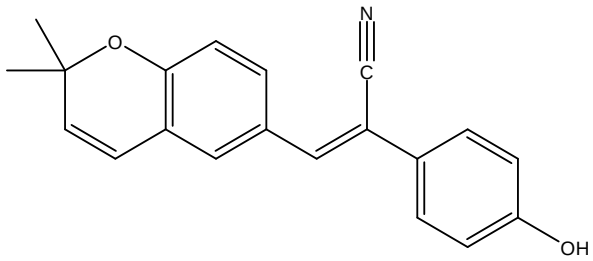
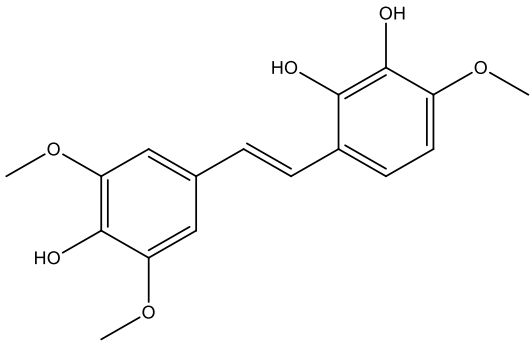
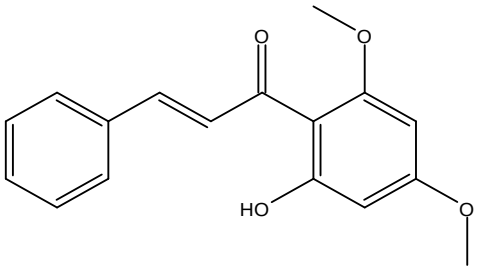
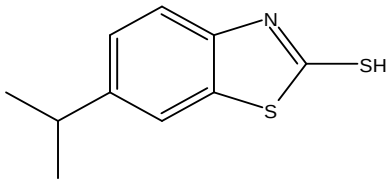
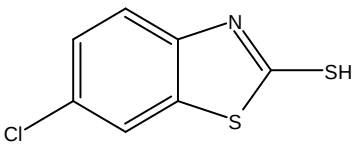
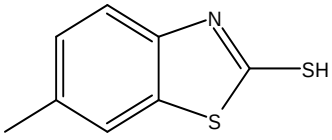
Table S1. Structures of the 40 compounds used to generate the QSARmodel in VolSurf+

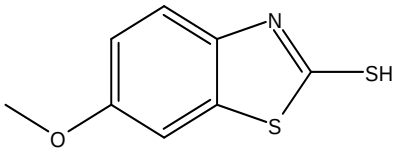
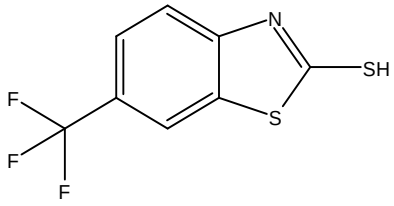
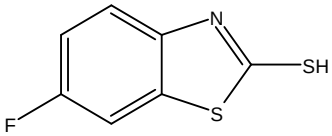
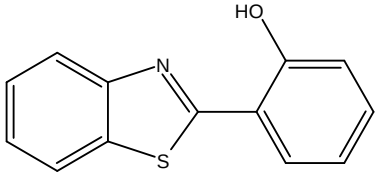
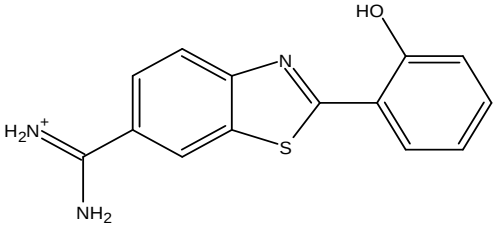
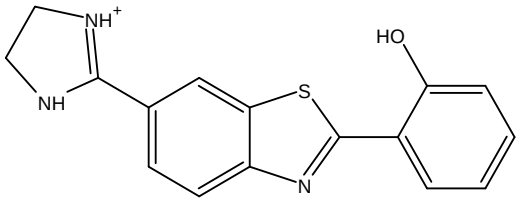
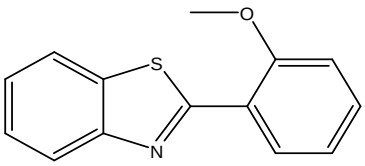
Molecular Structure **SMILE**	**ID VS+**	**MIC (μg/mL)**	**[Ref]**
 Oc1ccc(/C=C/c2cc(OC)cc(OC)c2)cc1O	[33]-1	128	[1]
 Oc1ccc(cc1OC)/C=C/c1cc(O)cc(O)c1	[33]-2	256	[1]
 Oc1cc(O)ccc1/C=C/c1cc(O)cc(O)c1	[33]-3	256	[1]
 Oc1ccc(/C=C/c2cc(O)cc(O)c2)c(O)c1O	[33]-4	64	[1]

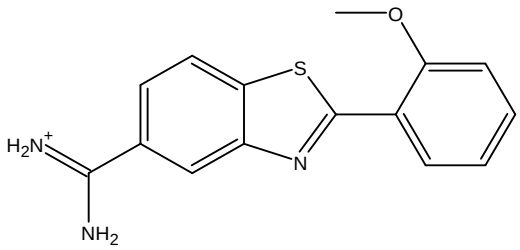
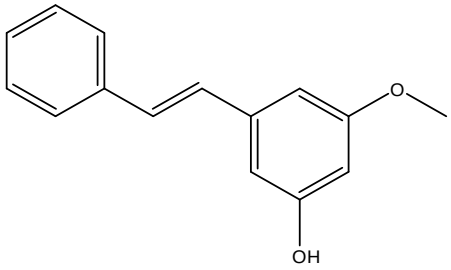
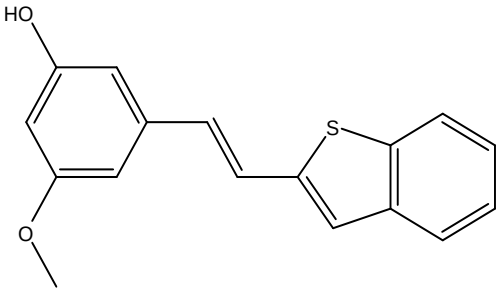
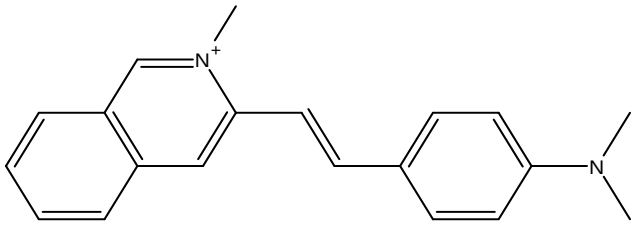
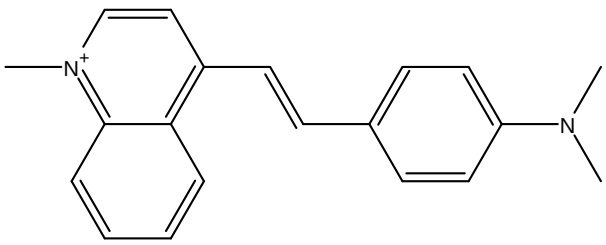
 Oc1cc(cc(OC)c1)/C=C/c1ccc(O)cc1	[33]-5	128	[1]
 COc1cc(OC)cc(\C=C\c2ccc(O)cc2)c1	[33]-6	32	[1]
 Oc1cc(cc(OC)c1)/C=C/c1ccc(O)cc1	[33]-8	256	[1]
 Cc1cc2c(cc1C)sc(/C=C/N1CCCc3ccccc31)[n+]2CC	[NE]-1	4	[2]
 CN(C)c1ccc(cc1)/C=C/c1sc2ccccc2[n+]1C	[BI]-1	8	[3]

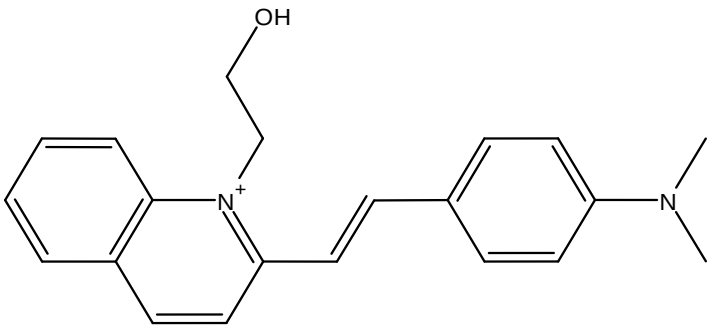
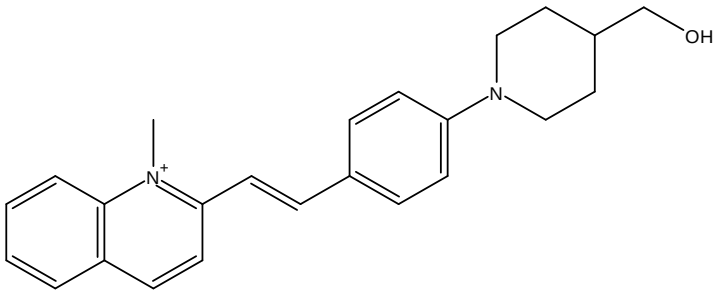
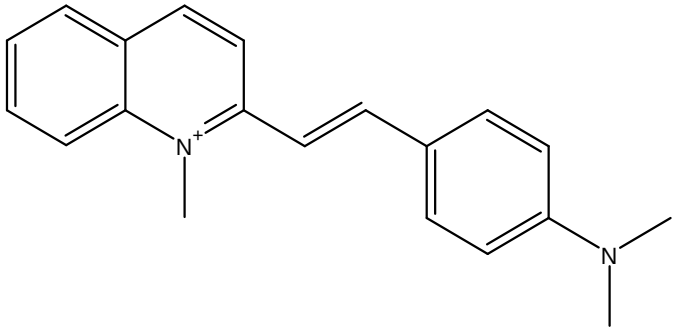
 CN(C)c1ccc(cc1)/C=C\C=C/c1sc2ccccc2[n+]1C	BI-2	4	[3]
 Cn1c2ccccc2cc1/C=C/c1sc2ccccc2[n+]1C	BI-3	4	[3]
 Oc1cccc2cccnc12	CH-1	6.89	[3]
 Oc1ccc(c2cccnc12)[N+](=O)[O-]	CH-2	42.07	[3]
 Oc1ccc(Cl)c2cccnc12	CH-3	89.1	[3]

 Oc1c(Br)ccc2cccnc12	CH-4	35.71	[3]
 Oc1c(Cl)cc(Cl)c2cccnc12	CH-5	37.37	[3]
 Oc1c(I)cc(Cl)c2cccnc12	CH-6	26.19	[3]
 Oc1ccc(cc1)C(\C#N)=C\C1=CC=CC2C=CC(C)(C)OC12	CN-1	3	[4]
 Oc1ccc(cc1)C(\C#N)=C\C1=CC=C(OC)C2OC(C)(C)C=CC12	CN-2	12	[4]

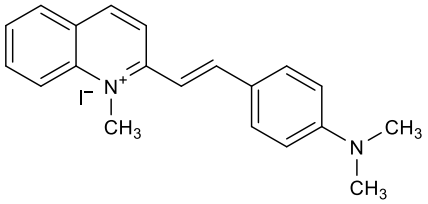
 Oc1ccc(cc1)C(\C#N)=C\c1ccc2OC(C)(C)C=Cc2c1	CN-3	25	[4]
	CW	16	[5]
 COc1cc(cc(O)c1C(=O)/C=C/c1ccccc1)OC	EL-1	40	[6]
 CC(C)c1ccc2nc(S)sc2c1	FR-2a	25	[7]
 Clc1ccc2nc(S)sc2c1	FR-2b	12.5	[7]
 Cc1ccc2nc(S)sc2c1	FR-2c	50	[7]

 COc1ccc2nc(S)sc2c1	FR-2d	50	[7]
 FC(F)(F)c1ccc2nc(S)sc2c1	FR-2e	3.12	[7]
 Fc1ccc2nc(S)sc2c1	FR-2f	25	[7]
 Oc1ccccc1c1nc2ccccc2s1	RL-5a	256	[8]
 [NH2+]=C(N)c1ccc2nc(sc2c1)c1ccccc1O	RL-5d	32	[8]
 Oc1ccccc1c1nc2ccc(cc2s1)C1=[NH+]CCN1	RL-5e	256	[8]
 COc1ccccc1c1nc2ccccc2s1	RL-6a	256	[8]

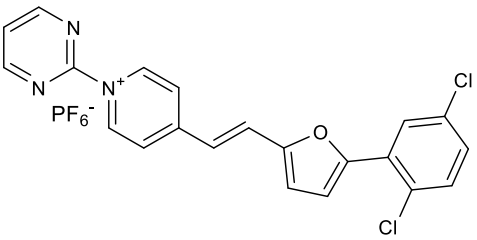
 [NH2+]=C(N)c1cc2nc(sc2cc1)c1ccccc1OC	RL-6d	128	[8]
 Oc1cc(cc(OC)c1)/C=C/c1ccccc1	SC-1	16	[9]
 Oc1cc(cc(OC)c1)/C=C/c1cc2ccccc2s1	SK-03-92	2	[10]
 CN(C)c1ccc(cc1)/C=C/c1cc2ccccc2c[n+]1C	Q-2	18.75	[11]
 CN(C)c1ccc(cc1)/C=C/c1cc[n+](C)c2ccccc21	Q-3	4.7	[11]

 CN(C)c1ccc(cc1)/C=C/c1ccc2ccccc2[n+]1CCO	Q-5	75	[11]
 C[n+]1c2ccccc2ccc1/C=C/c1ccc(cc1)N1CCC(CC1)CO	Q-7	75	[11]
 CN(C)c1ccc(cc1)/C=C/c1ccc2ccccc2[n+]1C	Q-11	4.7	[11]

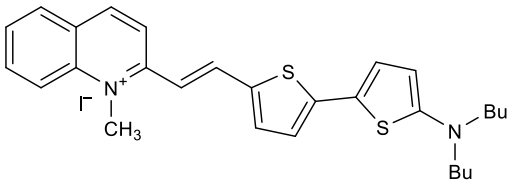
Scheme S1. Structures of the investigated PBn compounds.



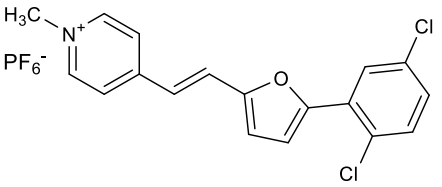
PB1



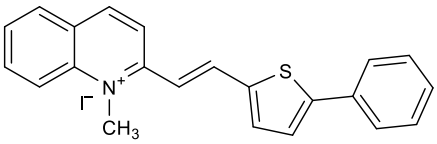
PB5



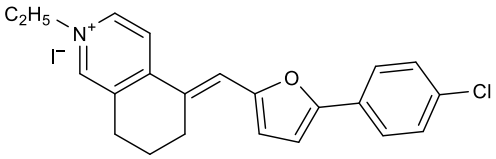
PB2



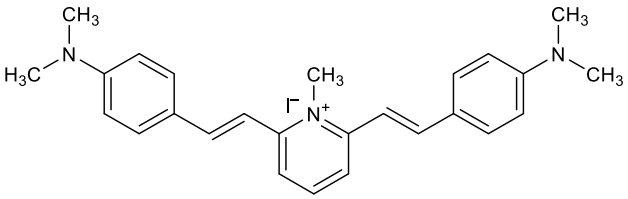
PB6



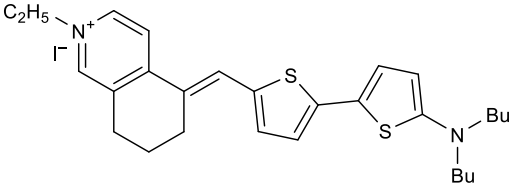
PB3



PB7



PB4

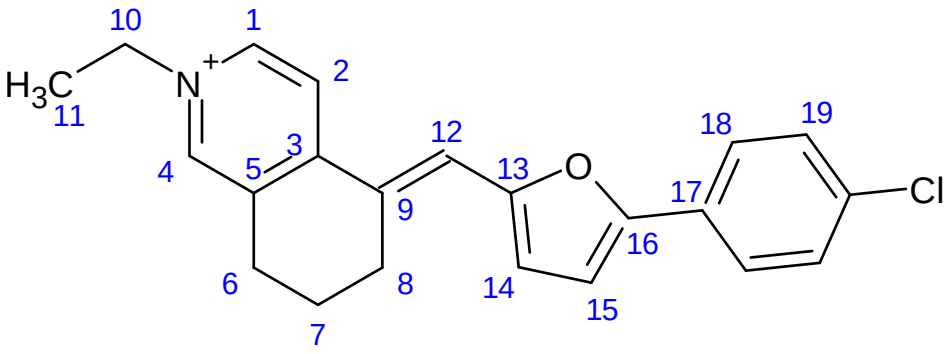


PB8

Synthesis of PB7

2-ethyl-5,6,7,8-tetrahydroisoquinolin-2-ium iodide (70.1 mg, 0.24 mmol) and 5-(3-chlorophenyl) furan-2-carbaldehyde (55.8 mg, 0.27 mmol) were mixed in 2 mL of ethanol and a minimum amount of dichloromethane to ensure solubilization of the aldehyde. A catalytic amount of Piperidine (20 μL) was added to the mixture and the reaction was carried out under reflux and vigorous stirring. The reaction was monitored through TLC and stopped after 17 hours.

The solvent was removed *in vacuo* and the solid purified through precipitation (dichloromethane / ethyl ether). The identity of the isolated product was confirmed by NMR spectroscopy. The yield of the synthesis and purification process is 42.2%.

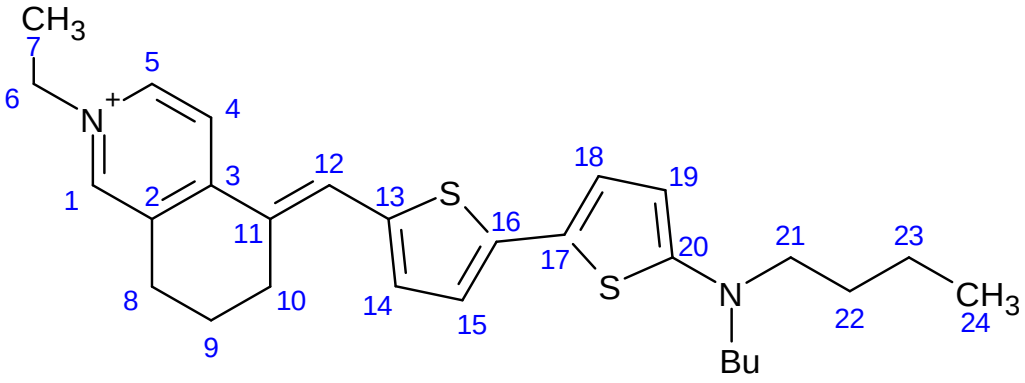


^{1}H-NMR (DMSO, 500 MHz, 300 K); δ(ppm): 8.82 (s; 1H; H4); 8.73 (d; 1H; J= 14 Hz; H1); 8.42 (d; 1H; J=14 Hz; H2); 7.83 (d; 2H; J= 18 Hz; H18); 7.69 (s; 1H; H12); 7.56 (d; 2H; J=18 Hz; H19); 7.3 (d; 1H; J=7 Hz; H14); 7.08 (d; 1H; J = 7 Hz; H15); 4.60 (q; 2H; J= 14 Hz; H10); 3.04 (t; 2H; J=12 Hz; H8); 2.88 (t; 2H; J=12 Hz; H6); 1.91 (q; 2H; J=12 Hz; H7); 1.52 (t; 3H; H= 14 HZ; H11).

^{13}C-NMR (DMSO, 125 MHz, 300 K); δ(ppm): 154.60, 152.45, 151.41, 143.44, 141.11, 136.95, 133.42, 129.69, 129.18, 128.61, 126.18, 121.69, 121.57, 119.76, 110.40, 55.39, 27.61, 27.10, 21.08, 16.59.

Synthesis of PB8

2-ethyl-5,6,7,8-tetrahydroisoquinolin-2-ium iodide (72.0 mg, 0.25 mmol) and 5′-(dibuthylamino)[2,2′-bithiophene]-5-carbaldehyde (88 mg, 0.27 mmol) were mixed in 2 mL of ethanol and a minimum amount of dichloromethane to ensure solubilization of the aldehyde. A catalytic amount of Piperidine (20 μL) was added to the mixture and the reaction was carried out under reflux and vigorous stirring. The reaction was monitored through TLC and stopped after 17 hours. The solvent was removed *in vacuo* and the oily product purified through chromatographic column (gradient elution, dichloromethane - dichloromethane: methanol = 90 : 10). The identity of the isolated product was confirmed by NMR spectroscopy. The yield of the synthesis and purification process is 47.3%.



^{1}H-NMR (DMSO, 500 MHz, 300 K); δ(ppm): 8.87 (s; 1H; H1); 8.77 (d; 1H; J=13.0 Hz; H4); 8.13 (d; 1H; J=14.0 Hz; H5); 7.73 (s; 1H; H12); 7.35 (d; 1H; H19); 7.03 (d; 1H; H18); 6.95 (d; 1H; H15); 5.75 (d; 1H; H14); 4.7 (d; 2H; H6); 3.27 (t; 3H; H7); 2.95 (t; 2H; H8); 2.87 (m; 2H; H9); 2.0 (d; 2H; J=11.0 Hz; H10); 1.63 (m; 12H; J=14.0 Hz; H21+H22+H23); 0.97 (t; 6H; J=14 Hz; H24).

^{13}C-NMR (DMSO, 125 MHz, 300 K); δ(ppm): 159.12, 152.84, 146.55, 141.59, 139.96, 136.32, 136.07, 134.40, 130.14, 126.37, 124.69, 120.57, 120.48, 118.02, 101.66, 55.39, 53.40, 29.19, 27.58, 27.40, 20.87, 20.25, 16.90, 13.90.

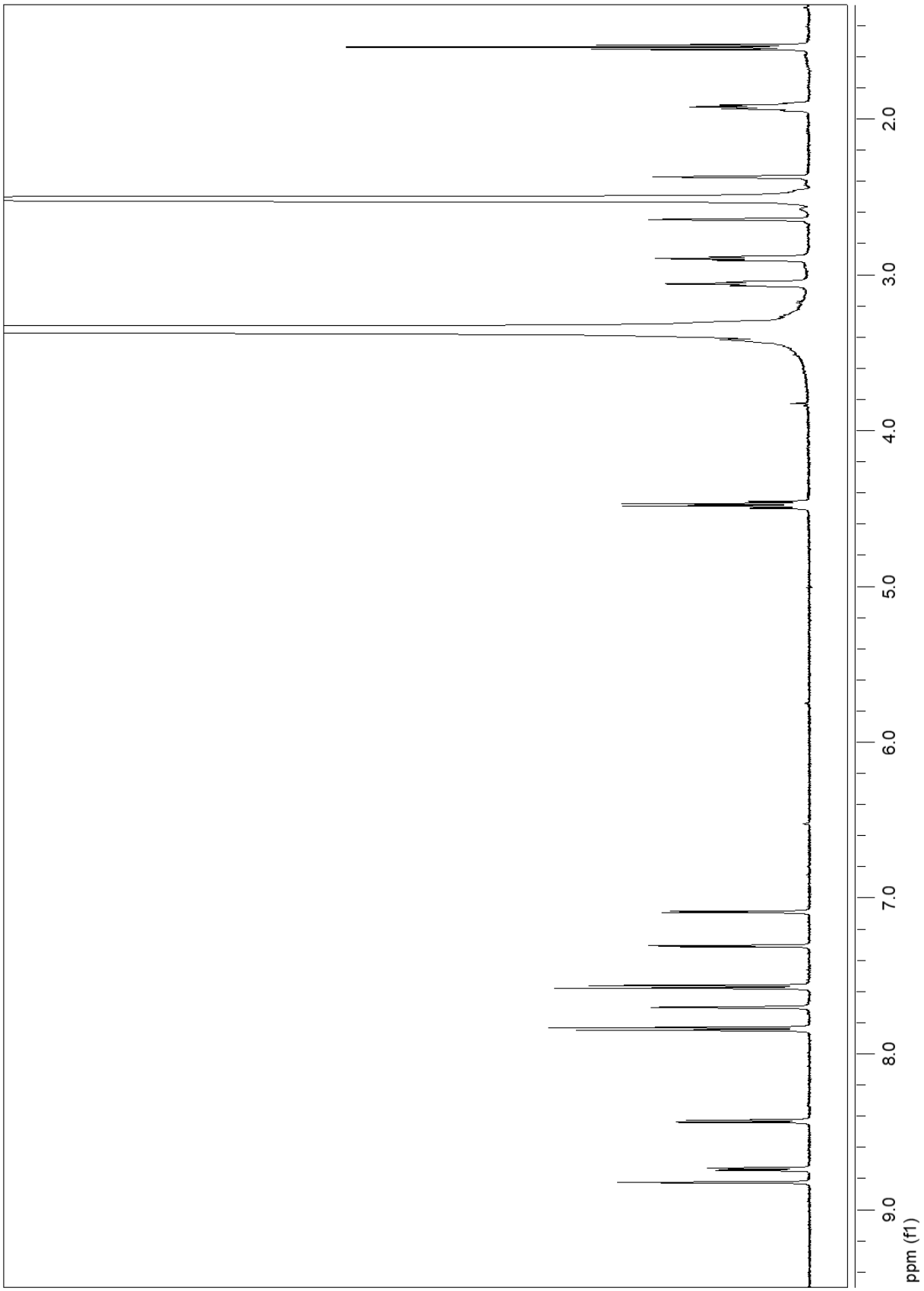


Figure S1. ^{1}H-NMR spectrum of **PB7** (500 MHz, 300 K, DMSO-D6).

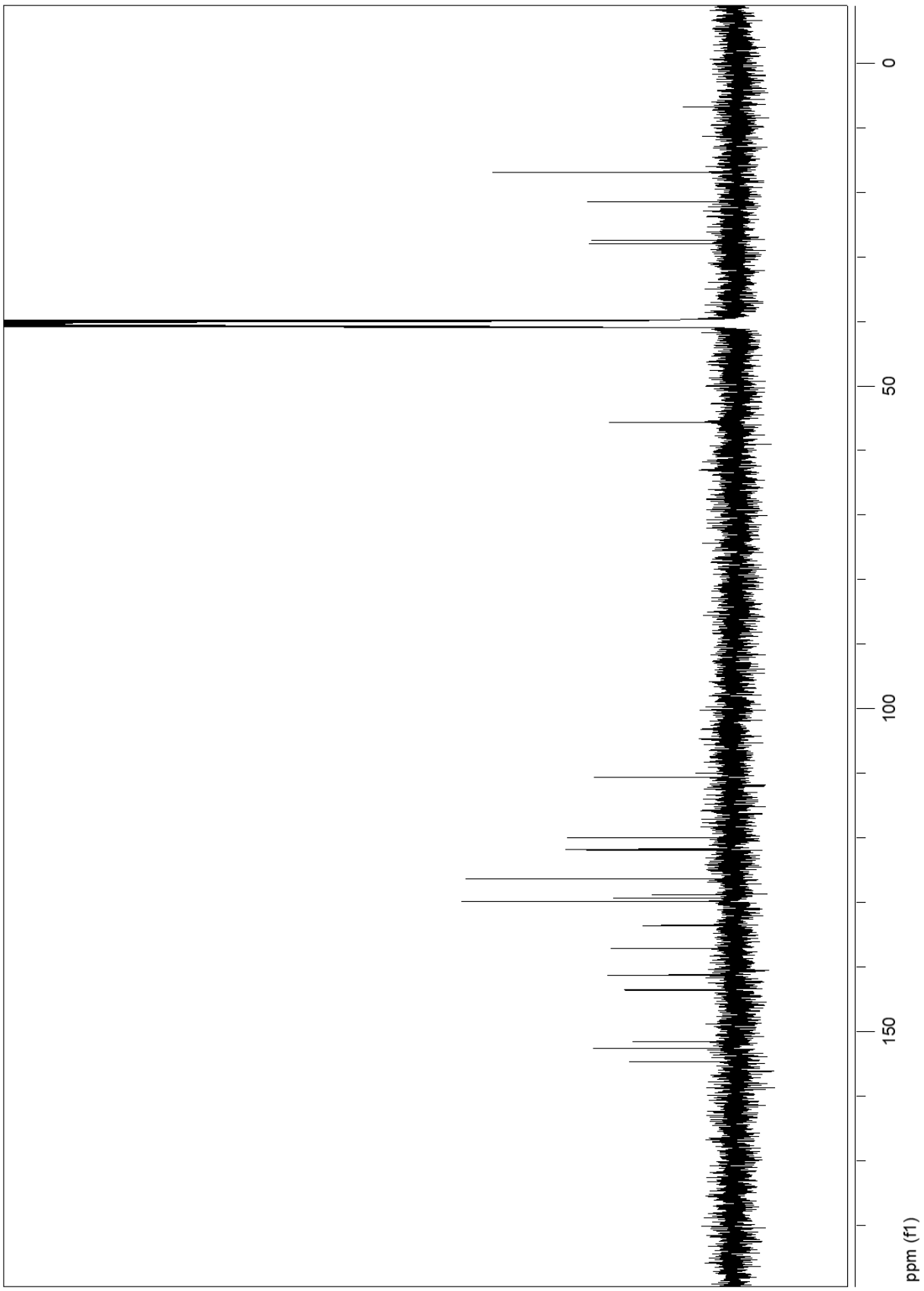


Figure S2. ^{13}C-NMR spectrum of **PB7** (125 MHz, 300 K, DMSO-D6).

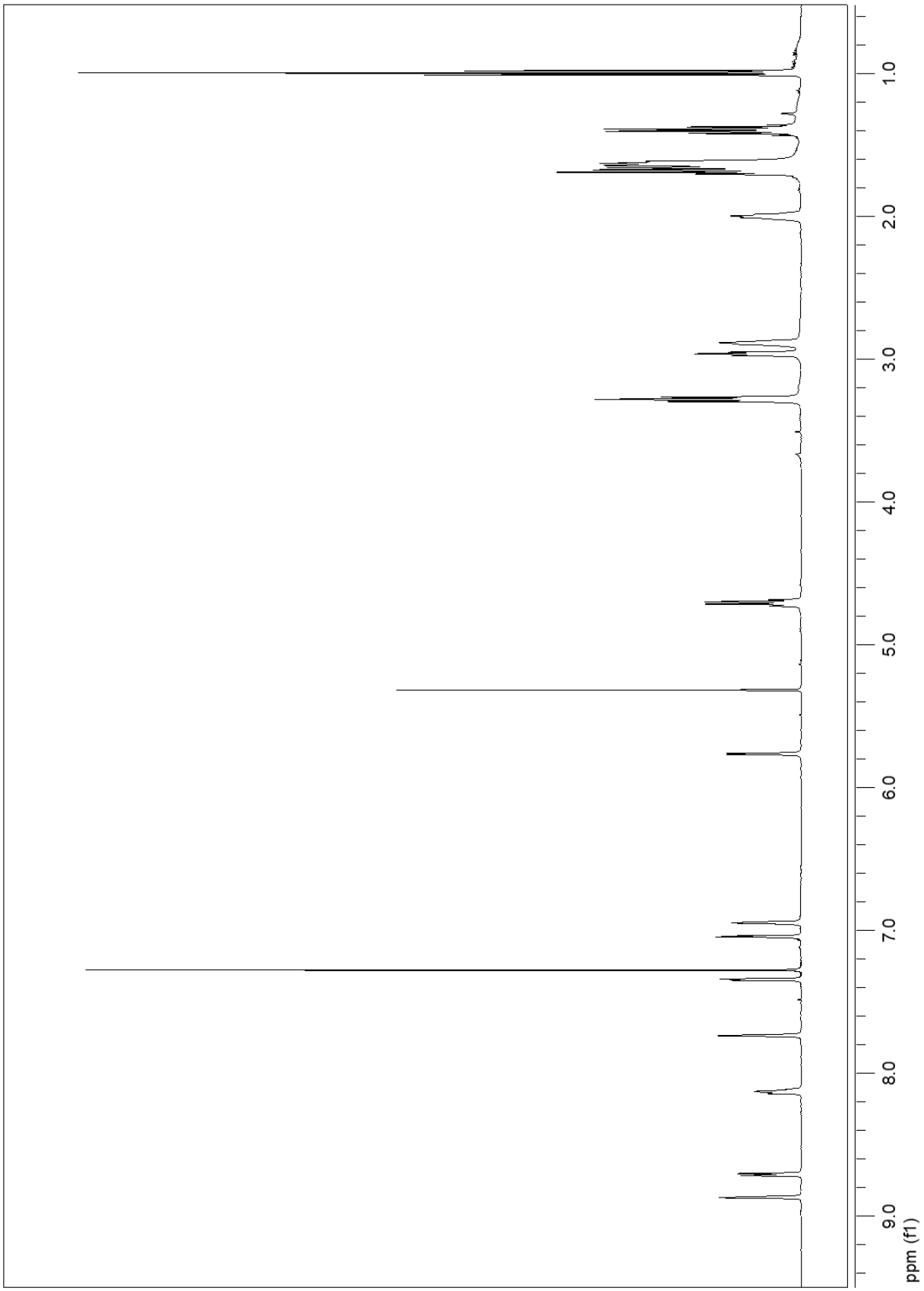


Figure S3. ^{1}H-NMR spectrum of **PB8** (500 MHz, 300 K, DMSO-D6).

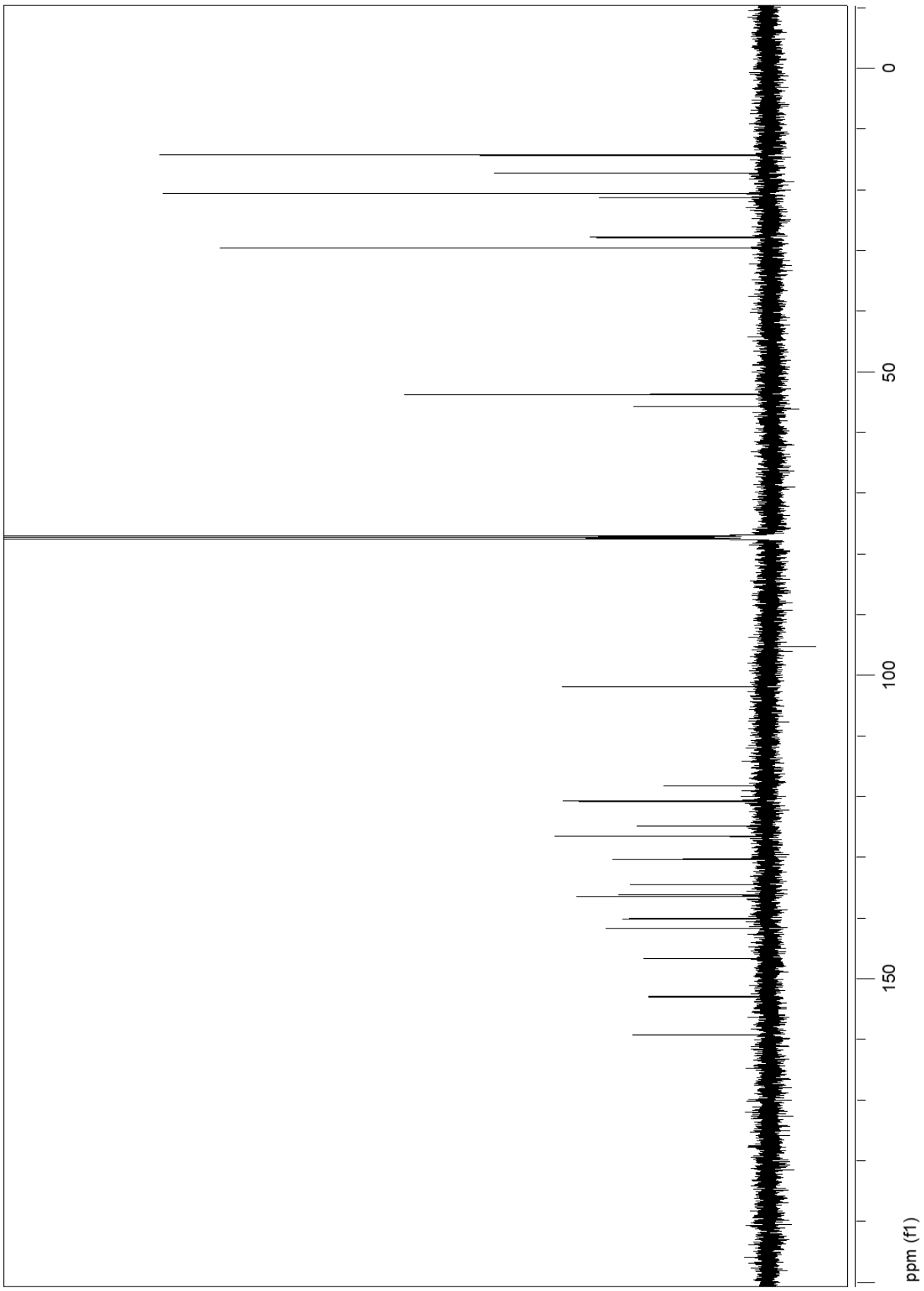


Figure S4. ^{13}C-NMR spectrum of **PB8** (125 MHz, 300 K, DMSO-D6).

Table S2. IC50 values obtained from the MTT assays after 24 hours of incubation relative to untreated controls.

Compounds	IC50 (μM)	95% confidence interval (μM)
PB1	1.202	0.6061 to 2.384
PB2	0.6025	0.2783 to 1.305
PB3	0.871	0.3319 to 2.286
PB4	0.3186	0.09087 to 1.117
PB5	3.901	1.566 to 9.717
PB6	6.788	1.849 to 24.92
PB7	1.362	0.5308 to 3.488
PB8	5.013	1.488 to 17.10
5-FU	27.361	10.96 to 87.70

Table S3. MIC values for ATCC12598 and ATCC51299 with different *inocula.*

		MIC (mg/L)			
		PB4	**PB5**	**PB7**	**PB8**
***S. aureus* ATCC12598**	1,00E+07	4	8	32	4
	1,00E+06	0,25	4	8	2
	1,00E+05	0,25	4	8	2
	1,00E+04	0,03	0,06	4	2
	1,00E+03	<0,015	0,03	4	2
	1,00E+02	<0,015	0,03	4	2
	1,00E+01	<0,015	0,03	2	0,5
***E. faecalis* ATCC51299**	1,00E+07	0,5	4	32	32
	1,00E+06	0,5	4	16	8
	1,00E+05	0,5	4	8	4
	1,00E+04	0,12	1	8	4
	1,00E+03	0,12	1	8	4
	1,00E+02	0,25	1	8	4
	1,00E+0	0,06	0,5	8	0,5

Table S4. PB4 MIC values for ATCC 17978 and ATCC25922 with different *inocula*

	MIC (mg/L)	
		PB4
***A. baumannii* ATCC 17978**	1,00E+07	1
	1,00E+06	0,25
	1,00E+05	0,25
	1,00E+04	0,25
	1,00E+03	<0,25
	1,00E+02	<0,25
	1,00E+01	<0,25
***E. coli* ATCC25922**	1,00E+07	2
	1,00E+06	1
	1,00E+05	1
	1,00E+04	0,5
	1,00E+03	0,5
	1,00E+02	0,5
	1,00E+0	0,5

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