Appendix A – Hardware and Software

Table S1: Software used in the study

S.No.	Software	Study/Method
1	SWISS-MODEL [1]	Homology Modelling
4	UCSF DOCK6 [2]	Virtual Screening
5	UCSF Chimera [3], PyMOL [4] , VMD [5],	Molecular Visualisation
6	BIOVIA Discovery Studio [6], LigPlot [7], PLIP: Protein-Ligand Interaction Profiler [8]	Receptor-ligand interactions
7	Raccoon [9]	Splitting batch file of compounds library
8	OpenBabel [10]	Molecular file format conversion
9	Avogadro [11], HyperChem [12], ArgusLab [13], ChemDraw [14]	Molecular drawing and optimization
10	GROMACS 5.1.1 [15]	MD Simulations
11	MS Office 365, MS OneNote, Joplin	Drafting research

Table S2: Hardware specifications used in the study

S. No.	Virtual Machines	Processing	RAM	Hard Disk
1	VM-1	40 CPUs	64 GB	2.2 TB
2	VM-2	20 CPUs	32 GB	1.1 TB
3	VM-3	40 CPUs	64 GB	1.1 TB
4	VM-4	20 CPUs	64 GB	1.1 TB

Appendix B – Synthesis of Fragments of the Hit Compounds

Synthesis of N-(2,4,5-trichlorophenyl)methanesulfonamide (24MSC)

2,4,5-Tricholoroaniline (2 g) was taken in a round-bottomed flask (100 mL) and dissolved into 5% Sodium Carbonate (18 mL). The pH of the reaction mixture was maintained at 8-10. The residue was dissolved in 5% Sodium Carbonate, and methane sulfonyl chloride ($0.82\ cm^3$) was added and stirred at room temperature for 6 hours and 30 minutes. TLC (hexanes, acetate; 80:20) showed a single spot. The precipitates of products were filtered and dried.

Synthesis of N-(2-aminoethyl)-N-(2,4,5-trichlorophenyl)methanesulfonamide (M24D)

Bromoethylamine (0.18 g) was taken in a round-bottomed flask (150 mL) and dissolved into 5% DMF (15 mL). The residue was dissolved in DMF, and N-(2,4,5-trichlorophenyl)methanesulfonamide (0.4 g) was added and stirred at room temperature for 5 hours and 15 minutes. Lithium hydride (0.002 g) was also added as a catalyst. TLC (hexanes, acetate; 80:20) showed a single spot. The reaction mixture was quenched with the chilled water, the product got precipitated, filtered, and dried.

Synthesis of 1-(4-(bromomethyl)phenylsulfonyl)piperidine (BSPP)

Piperidine ($0.37\ cm^3$) was taken in a round-bottomed flask (100 mL) and dissolved into 5% Sodium Carbonate (18 mL). The pH of the reaction mixture was maintained at 8-10. Piperidine was dissolved in 5% Sodium Carbonate, and 4-(bromoethyl)benzene-1-sulfonyl chloride (1 g) was added and stirred at room temperature for 7 hours 50 minutes. TLC (hexanes, acetate; 80:20) showed a single spot. The precipitates of products were filtered and dried.

Synthesis of N-(2,4-dichlorophenyl)methanesulfonamide (ABR1)

2,4-dichloroaniline (2 g) was taken in a round-bottomed flask (100 mL) and dissolved into 5% Sodium Carbonate (18 mL). The pH of the reaction mixture was maintained at 8-10. Next, 2,4-dichloroaniline was dissolved in 5% Sodium Carbonate methane sulfonyl chloride (1.4136 g) was added into it and stirred at room temperature for 5 hours and 30 minutes. TLC (hexanes, acetate; 80:20) showed a single spot. Finally, the precipitates of products were filtered and dried.

Synthesis of N-(2-aminoethyl)-N-(2,4-dichlorophenyl)methanesulfonamide (ABR2)

N-(2,4-dichlorophenyl)methanesulfonamide (1 g) was taken in a round-bottomed flask (150 mL) and dissolved into 5% DMF (15 mL). The residue was dissolved in DMF, and Bromoethylamine (0.51 g) was added and stirred at room temperature for 5 hours. Lithium hydride (0.002 g) was also added as a catalyst. TLC (hexanes, acetate; 80:20) showed a single spot. The reaction mixture was quenched with chilled water, and the product precipitated, filtered, and dried.

Synthesis of 4-(4-(bromomethyl)phenylsulfonyl)morpholine (BBMP)

Morpholine (0.32 cm^3) was taken in the round-bottomed flask (100 mL) and dissolved into 5% Sodium Carbonate (18 mL). The pH of the reaction mixture was maintained at 8-10. Morpholine was dissolved in 5% Sodium Carbonate, and 4-(bromomethyl) benzene-1-sulfonyl chloride (1 g) was added to it and stirred at room temperature for 6 hours and 30 minutes. TLC (hexanes, acetate; 80:20) showed a single spot. The precipitates of products were filtered and dried.
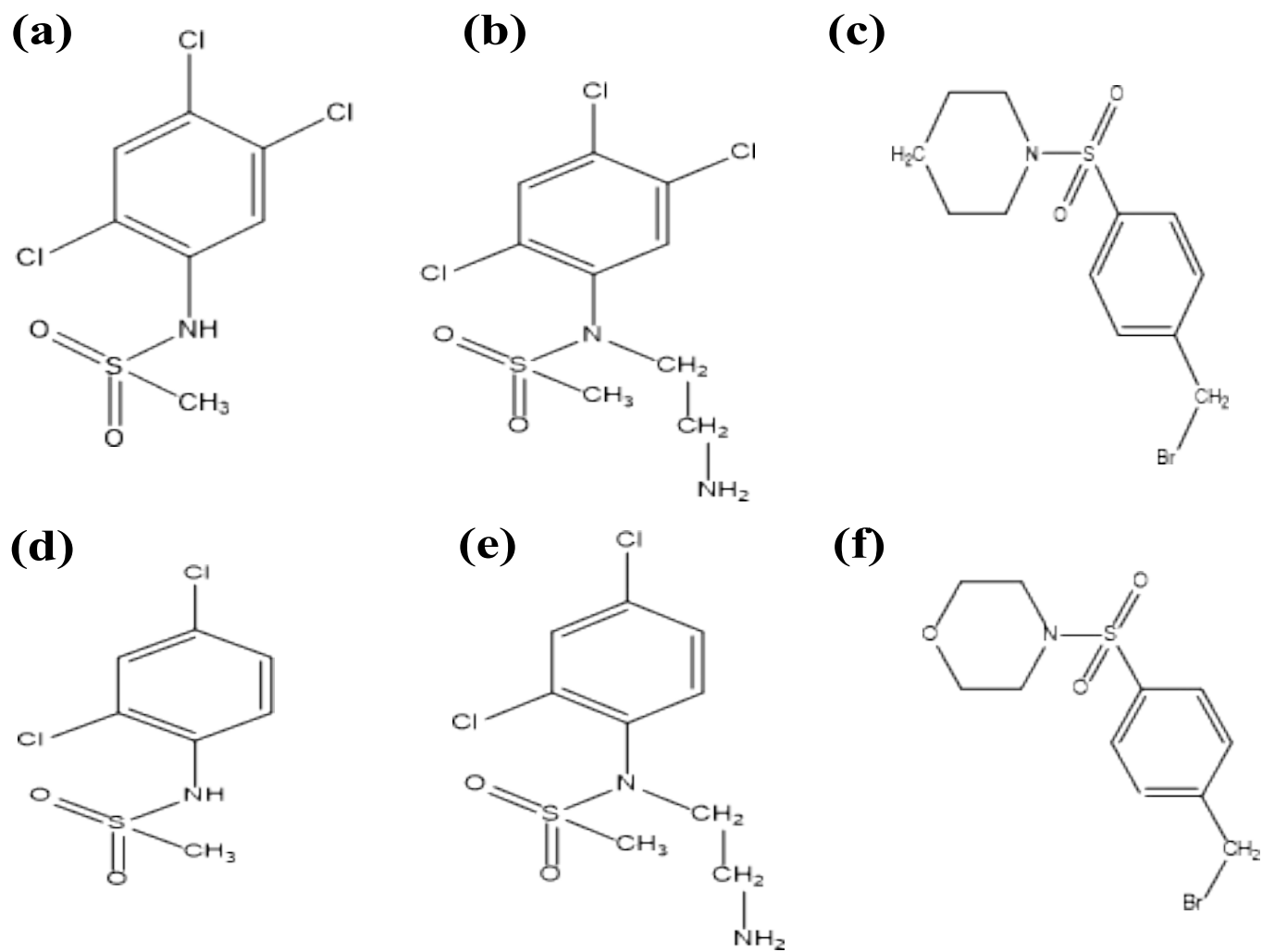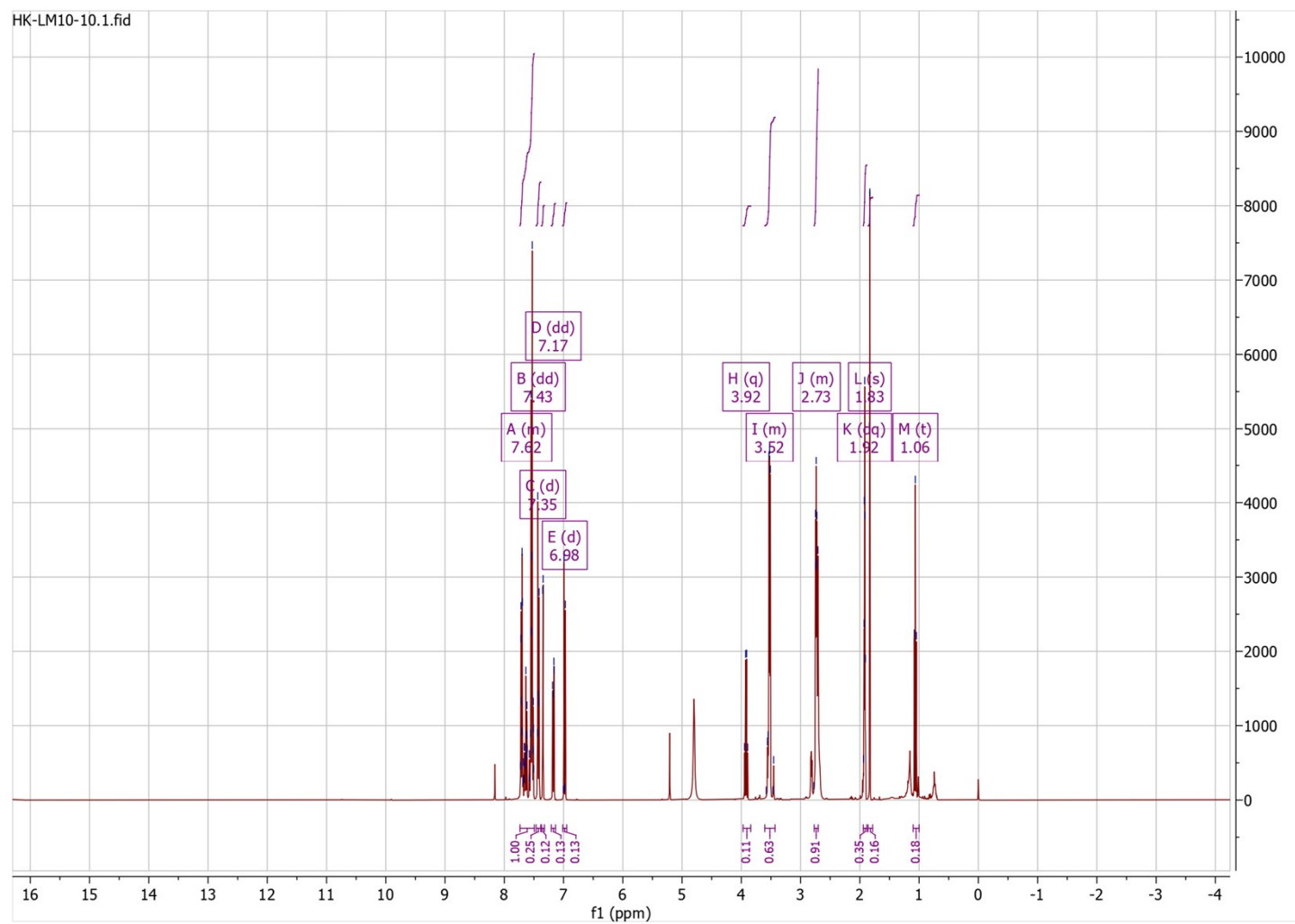
(a)

(b)

(c)

(d)

(e)

(f)

Figure S1: Structures of fragments of hit compounds TCM, TCP, DCP and DCM. The fragments are 24MSC (a), M24D (b), BSPP (c),ABR1 (d), ABR2 (e), BBMP (f)
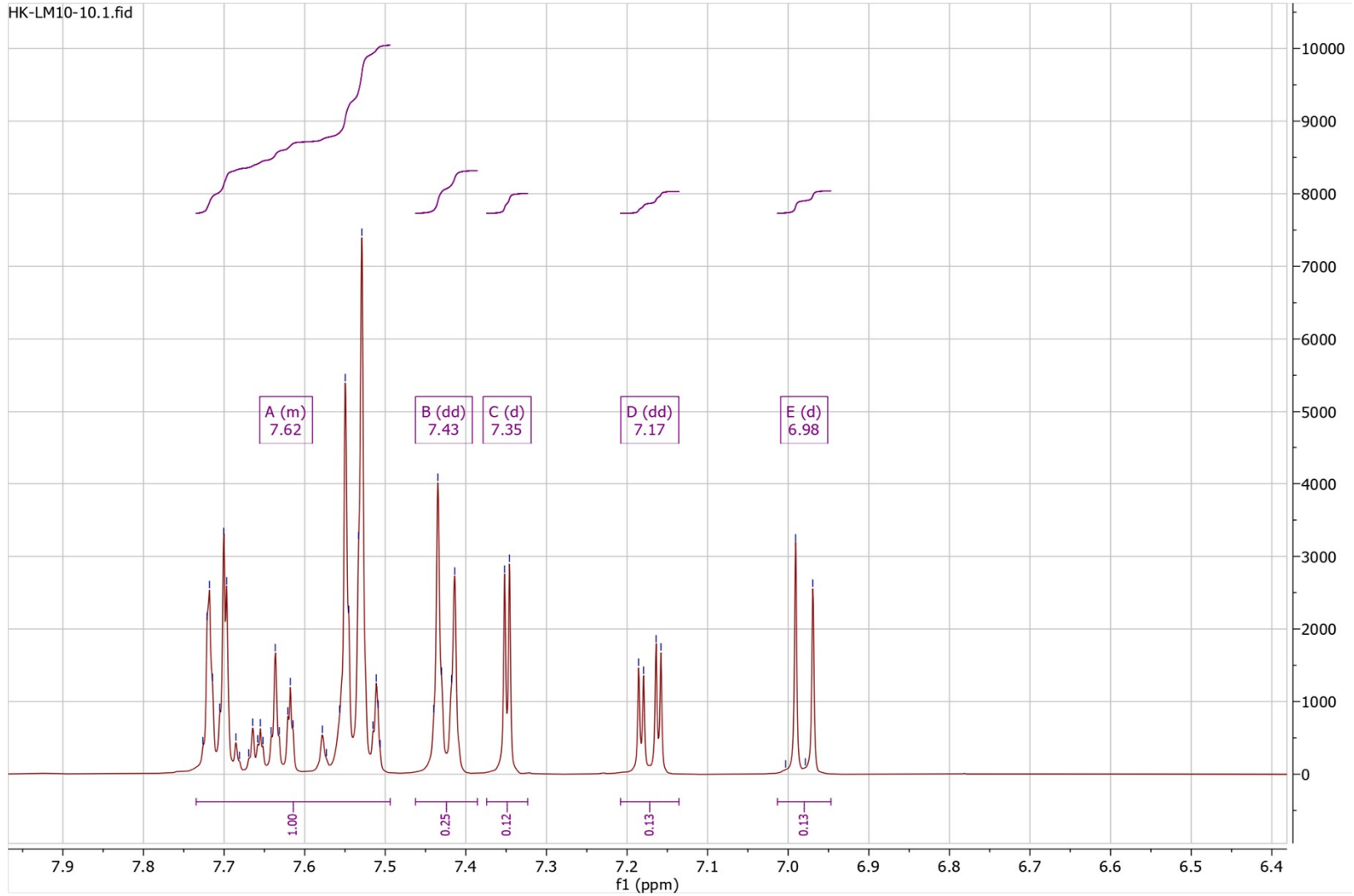
Table S1: Physical properties of fragments of the hit compounds TCM, TCP, DCP and DCM.
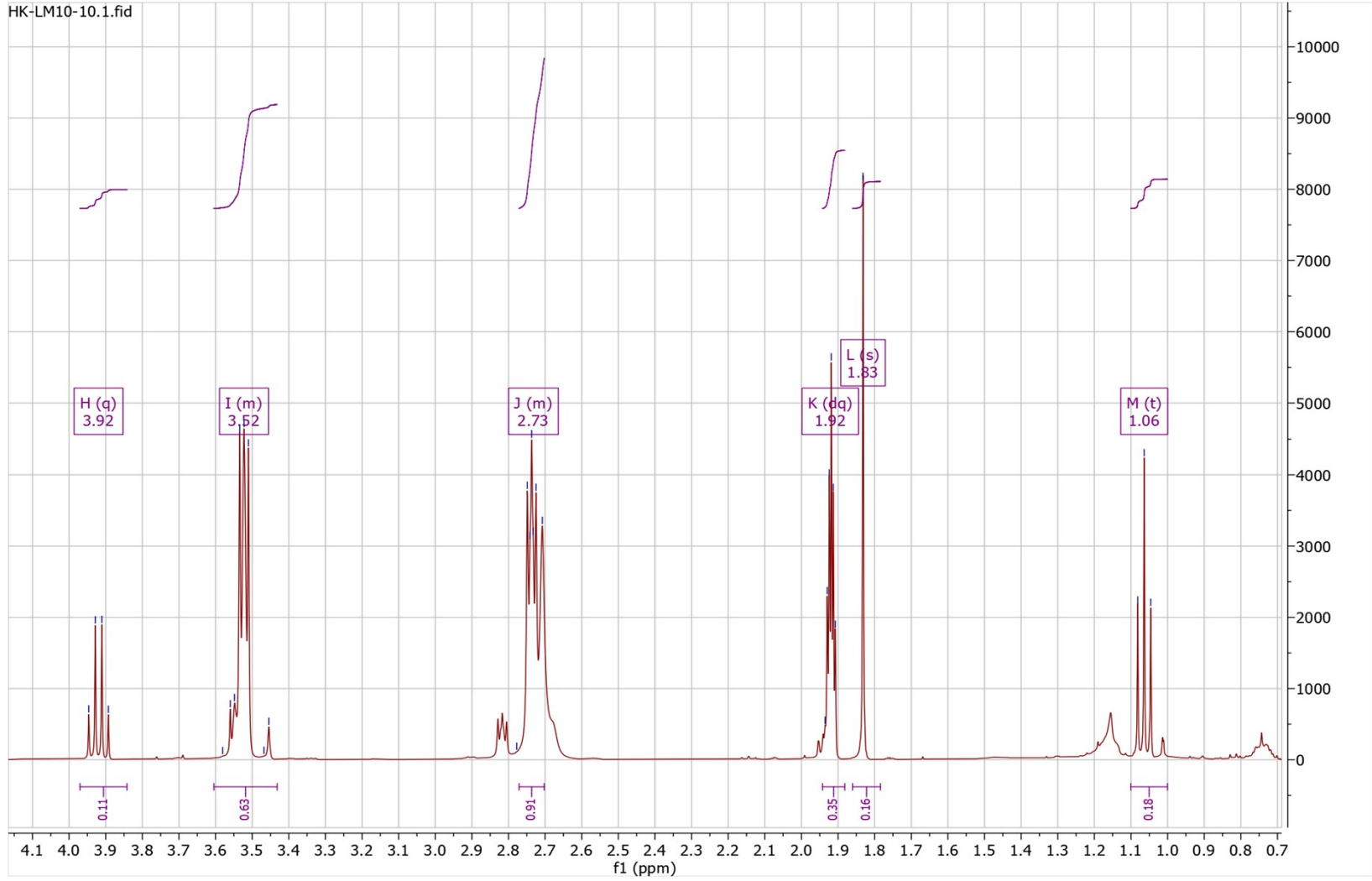
S. No.	Properties of Compounds	24MSC	M24D	BSPP	ABR1	ABR2	BBMP
1	**Physical appearance**	Solid	Solid	Solid	Solid	Solid	Solid
2	**Colour**	Beige	Vivid white	Cream	White	White	Pure white
3	**Chemical formula**	$C_7H_6Cl_3NO_2S$	$C_9H_{11}Cl_3N_2O_2S$	$C_{12}H_{16}BrNO_2S$	$C_7H_7Cl_2NO_2S$	$C_9H_{12}Cl_2N_2O_2S_2$	$C_{11}H_{14}BrNO_3S$
4	**Molecular weight**	274.55 g/mol	317.62 g/mol	320.20 g/mol	240.11.20 g/mol	283.17 g/mol	318.23 g/mol
5	**Solubility**	Chloroform DMSO	Chloroform DMSO	Chloroform DMSO	Chloroform DMSO	Chloroform DMSO	Chloroform DMSO
6	**Melting Point**	100 - 103 ℃	94 - 96 ℃	100 - 102 ℃	125 - 128 ℃	128 -130 ℃	150 -153 ℃

Appendix C – NMR spectra of the hit compounds

¹H NMR spectrum of DCM

HK-LM10-10.1.fid

D (dd) 7.17
B (dd) 7.43
A (m) 7.62
C (d) 7.35
E (d) 6.98
H (q) 3.92
I (m) 3.52
J (m) 2.73
L (s) 1.83
K (dq) 1.92
M (t) 1.06

1.00 0.25 0.12 0.13 0.13 0.11 0.63 0.91 0.35 0.16 0.18

HK-LM10-10.1.fid

| A (m)
7.62 | B (dd)
7.43 | C (d)
7.35 | D (dd)
7.17 | E (d)
6.98 |

1.00   0.25   0.12   0.13   0.13

f1 (ppm)

HK-LM10-10.1.fid

^{1}H NMR spectrum of TCM

HK-ASF2.1.fid

E (d)
6.62

B (dd)
7.27

F (dd)
6.22

A (dd)
7.60

D (t)
6.75

G (d)
5.28

H (s)
2.89

I (p)
2.06

C (dddd)
6.93

HK-ASF2.1.fid

A (dd)
7.60

B (dd)
7.27

C (dddd)
6.93

D (t)
6.75

E (d)
6.62

F (dd)
6.22

7.62
7.61
7.59
7.59

7.28
7.28
7.26
7.26

6.97
6.97
6.95
6.95
6.93
6.93
6.92
6.92
6.91
6.90
6.90
6.89
6.88

6.76
6.75
6.74
6.73

6.63
6.61

6.23
6.23
6.21
6.21

1.00   1.00   2.18   1.08   0.98   1.02

f1 (ppm)

^{1}H NMR spectrum of DCP

HK-BZ9-9.1.fid

A (m) 7.72
F (m) 7.64
B (m) 7.53
C (m) 7.40
D (dd) 7.17
E (d) 6.98

1.00   0.51   2.12   1.70   0.50   0.14   0.52

f1 (ppm)

13

^{1}H NMR spectrum of TCP

HK-BZ9-9.1.fid

A (s)	B (d)	C (m)	D (m)
3.46	2.72	1.90	1.09

1.00   18.90   18.37   10.77

f1 (ppm)

ASF1.1.fid

B (m)
7.57

A (dd)
7.71

C (m)
6.70

E (dt)
4.03

G (m)
3.13

D (d)
4.55

F (t)
3.62

H (q)
2.86

J (s)
2.09

K (d)
1.51

L (d)
1.35

I (p)
2.51

M (s)
1.24

15

ASF1.1.fid

A (dd)
7.71

B (m)
7.57

C (m)
6.70

7.73
7.71
7.71
7.69
7.69

7.60
7.58
7.57
7.55

6.72
6.71
6.70
6.70
6.68

2.00
1.00

1.59

0.92

8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 6.3 6.2
f1 (ppm)

Appendix D – pH Scouting

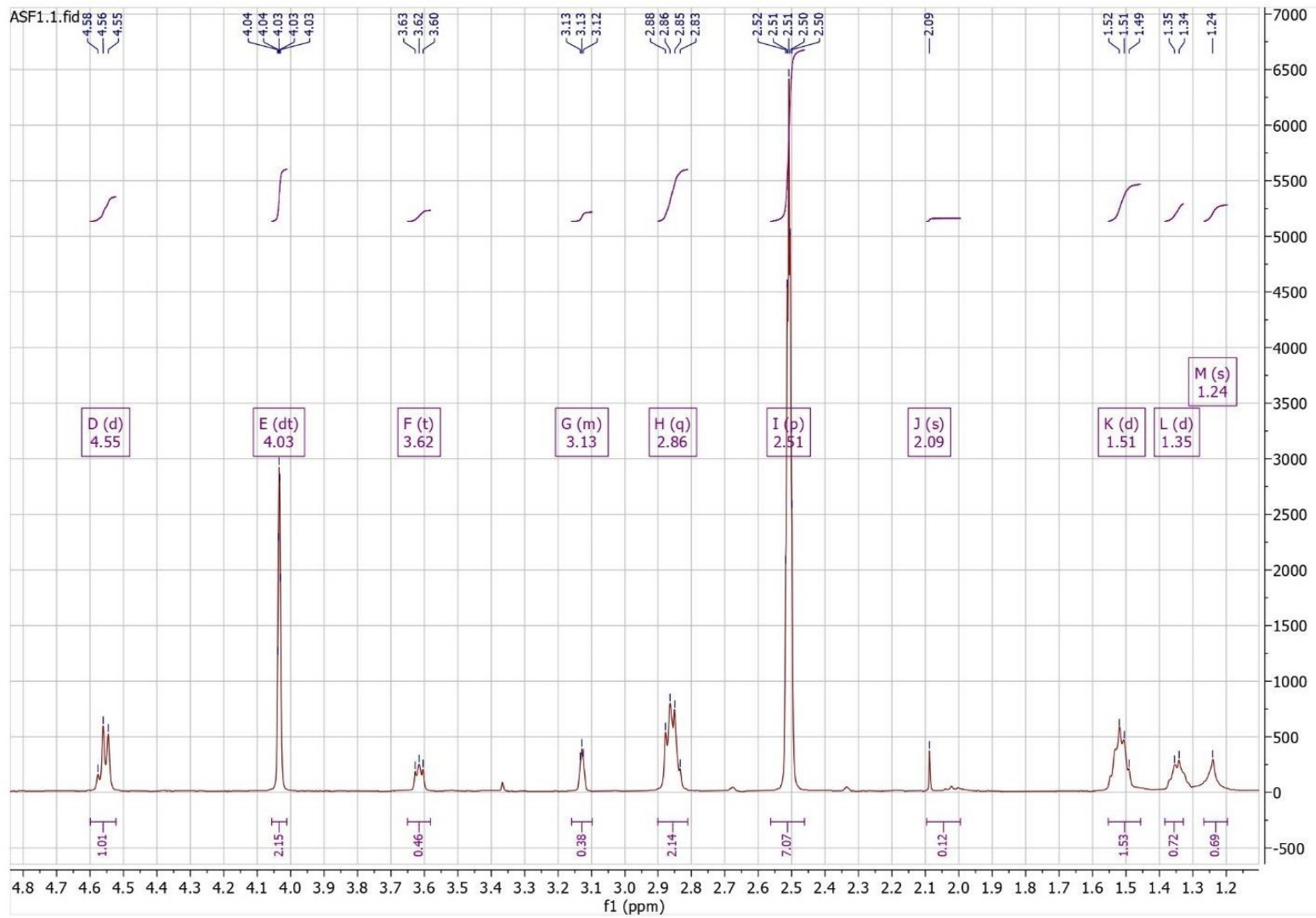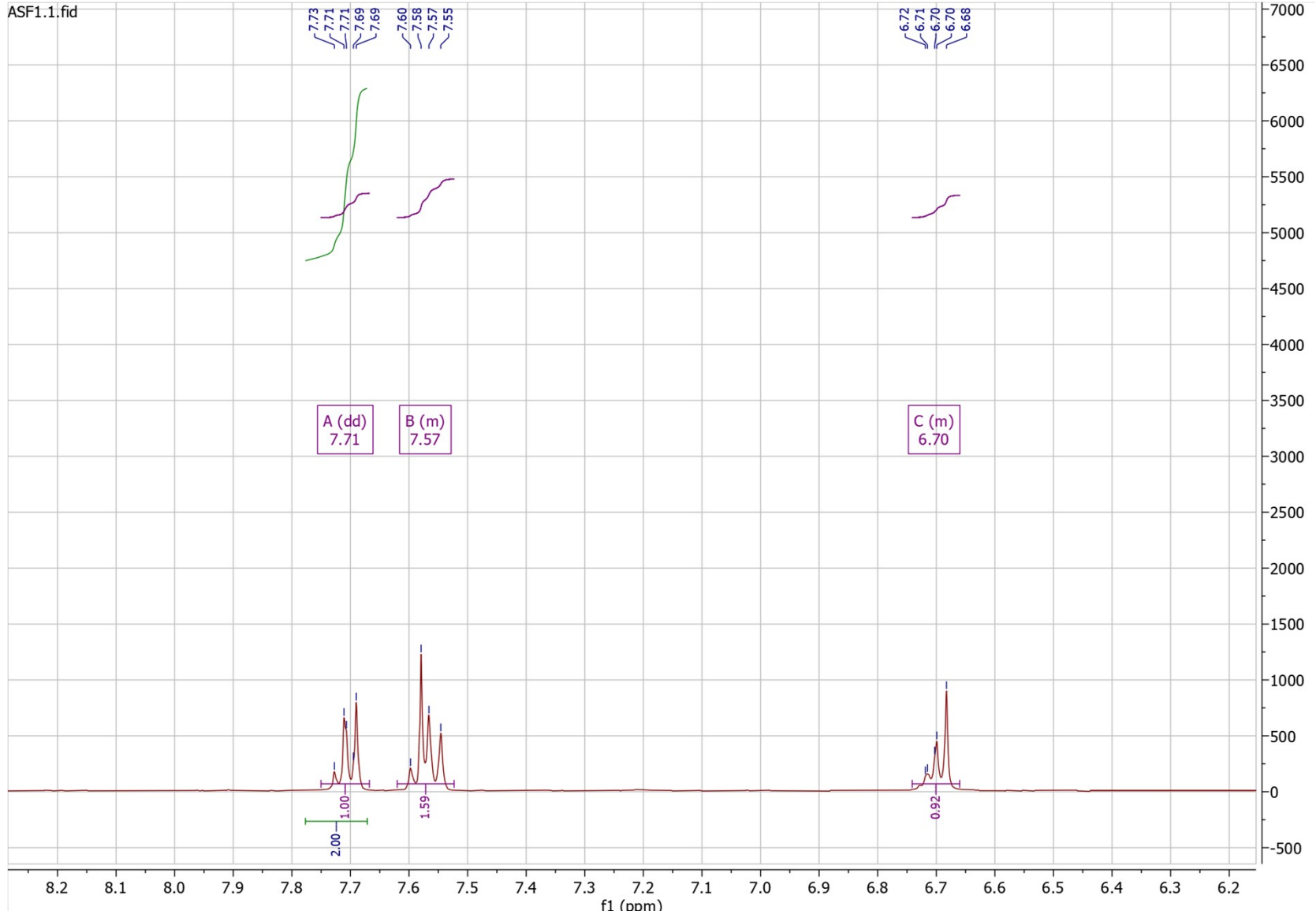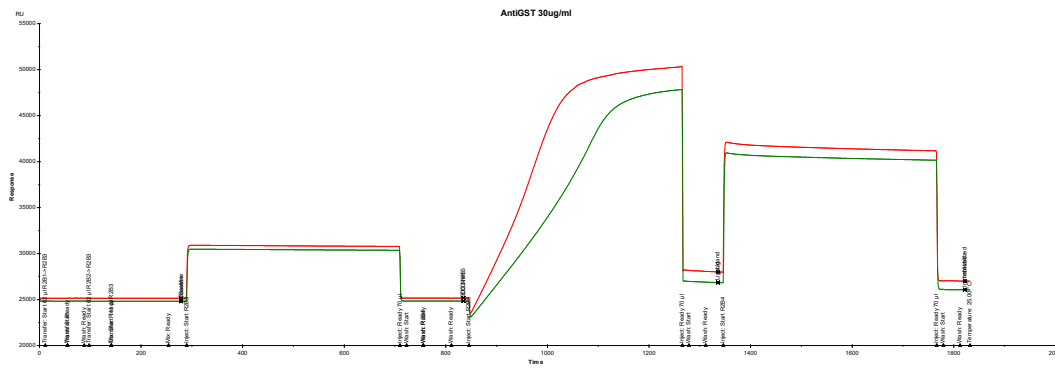**Figure S1:** pH Scouting graph

Figure S2: Graph showing Conditioning

Appendix E – SPR wizard parameters for single cell kinetics

<HtmlPreview>General settings

Temperature after run used   No

Sample compartment temperature   25°C

Sample compartment temperature varies   No

Data collection rate   10Hz

Concentration unit   nM

A   [No buffer name specified]

B   [No buffer name specified]

C   [No buffer name specified]

D   [No buffer name specified]

Detection   Multi

Flow path   2-1,4-3

Cycle Types

GST kinetics

GST conditioning

Commands in cycle type GST kinetics

Capture 1

  Capture solution   GST

  Contact time (s)   180

  Flow rate (μl/min)   5

  Flow path   1

Capture 2

  Capture solution   GST-CDK2

  Contact time (s)   180

Flow rate (μl/min)   5

Flow path   2

Stabilization period (s)   180

Capture 3

  Capture solution   GST

  Contact time (s)   60

  Flow rate (μl/min)   10

  Flow path   3

Capture 4

  Capture solution   GST-hcv

  Contact time (s)   60

  Flow rate (μl/min)   10

  Flow path   4

  Stabilization period (s)   180

Sample 1

  Type   Single Cycle Kinetics

  Sample solution   Is Variable

  Contact time (s)   120

  Dissociation time (s)   600

  Flow rate (μl/min)   30

  Flow path   1,2,3,4

  Extra wash solution   50% DMSO

  MW   Is variable

  Conc (1)   Is variable

  Conc (2)   Is variable

  Conc (3)   Is variable

  Conc (4)   Is variable

  Conc (5)   Is variable

Regeneration 1

Regeneration solution		Reg solution
Contact time (s)		120
Flow rate (µl/min)		30
Flow path	1,2,3,4	
High viscosity	No	

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