

## Supplementary:

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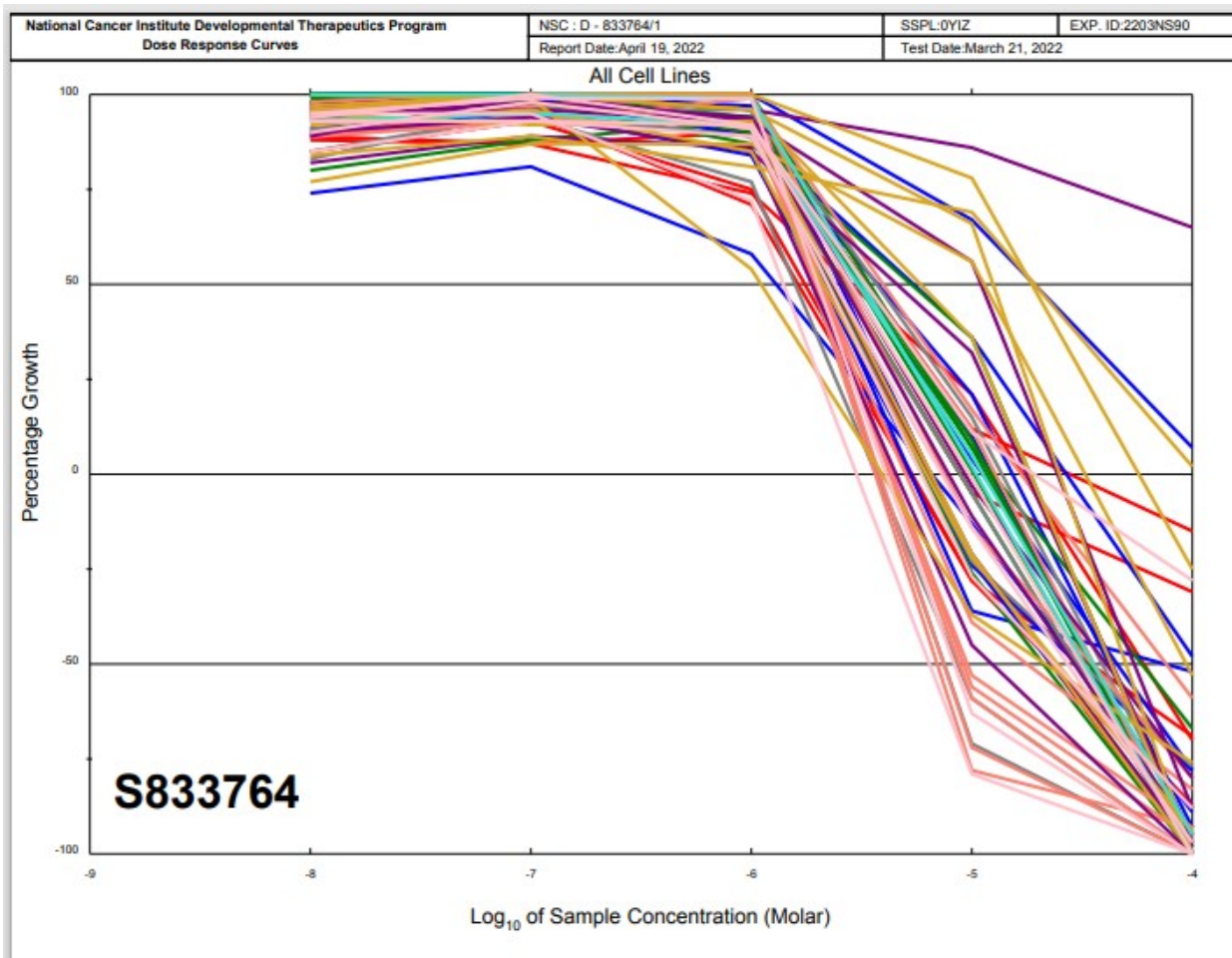
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S41: IR of compound **2a**  
S42: IR of compound **2b**  
S43: IR of compound **2e**  
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S46: Inhibition of CDK2/CyclinA2 by compounds **2a-g, 4, 7a-d, 8a-b, 9 &10** at 50  $\mu$ M.  
S47: The dose–response curves show the Inhibitory Concentration at 50% (IC<sub>50</sub>) curves of compounds **4, 7c, 7d, 8b and 9** in CDK2/Cyclin A2 protein kinase activity assay.  
S48: Flow cytometric analysis for cell cycle distribution. (A) Control HCT-116, (B) Compound **4**, and (C) graphical representation for cell cycle distribution analysis among differently treated cells.  
S49: Flow cytometric analysis of apoptosis among treated cells. (A) Control HCT-116, (B) Compound **4**, (C) Graphical illustration of apoptosis % among differently treated cells.  
S50: Cell cycle and apoptosis raw data  
S51: Western Blot assay for compounds **4, 9**  
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S55: Mass Results compound **9**  
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S1 Table of relative activity of the synthesized compounds

Sample no.	Relative activity
2a	51.4
2b	55.6
2c	59.3
2d	40.2
2e	56.6
2f	62.1
2g	59.5
4	24.7
7a	42.3
7b	70.7
7c	68.6
7d	11.5
8a	56.4
8b	27.1
9	14.5
10	49.9
DMSO	100

S2: Dose response curve of compound 4 at five dose assay against all cell lines at NCI

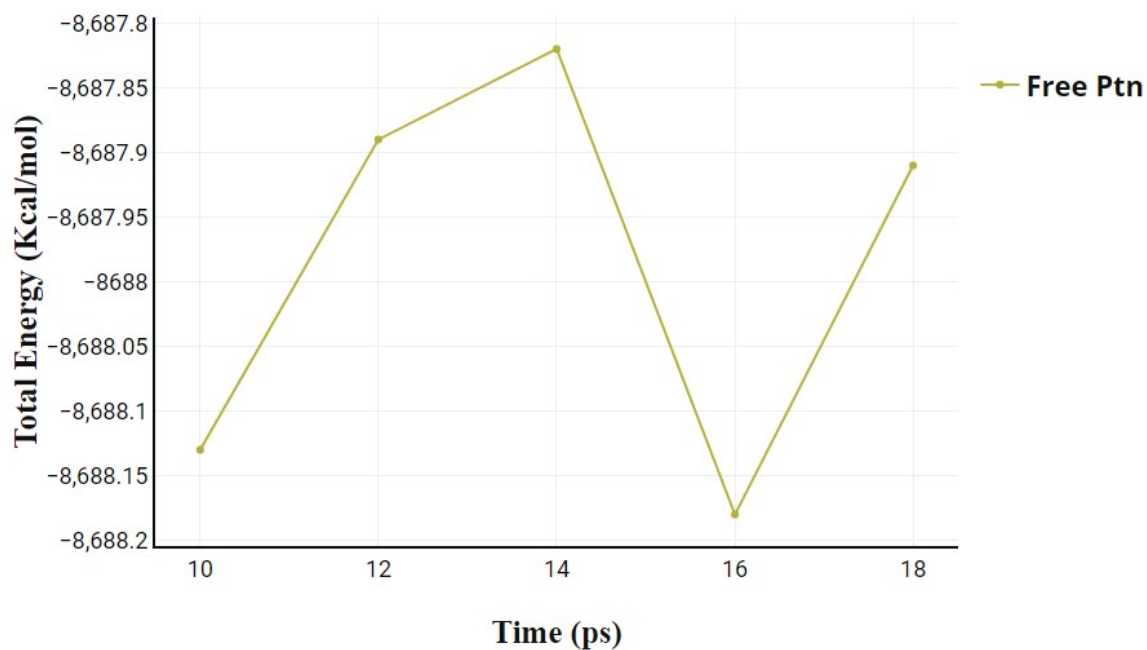


S3: Summary of five doses results of compound 4 from NCI

National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results															
NSC : D - 833764 / 1					Experiment ID : 2203NS90					Test Type : 08			Units : Molar		
Report Date : April 19, 2022					Test Date : March 21, 2022					QNS :			MC :		
COMI : h					Stain Reagent : SRB Dual-Pass Related					SSPL 0YIZ					
Log10 Concentration															
Panel/Cell Line	Time	Mean Optical Densities						Percent Growth					GI50	TGI	LC50
		Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0			
<b>Leukemia</b>															
CCRFB-CEM	1.043	3.064	3.018	3.061	2.854	0.994	0.716	98	100	90	-5	-31	2.63E-6	8.92E-6	> 1.00E-4
HL-60(TB)	0.485	1.427	1.326	1.309	1.185	0.684	0.146	89	87	74	21	-70	2.86E-6	1.71E-5	6.05E-5
K-562	0.270	1.741	1.571	1.548	1.599	0.211	-0.068	88	87	90	-22	-100	2.29E-6	6.37E-6	2.28E-5
MOLT-4	0.690	2.430	2.352	2.350	1.928	0.499	0.216	96	95	71	-28	-69	1.64E-6	5.24E-6	3.49E-5
RPMI-8226	0.822	2.690	2.705	2.714	2.537	1.053	0.698	101	101	92	12	-15	3.36E-6	2.82E-5	> 1.00E-4
SR	0.440	1.625	1.444	1.545	1.326	0.317	0.058	85	93	75	-28	-87	1.74E-6	5.33E-6	2.36E-5
<b>Non-Small Cell Lung Cancer</b>															
A549/ATCC	0.329	1.692	1.690	1.806	1.690	1.247	0.430	100	108	100	67	7	1.94E-5	> 1.00E-4	> 1.00E-4
EKVX	0.814	1.567	1.555	1.580	1.483	1.084	0.427	98	102	89	36	-48	5.39E-6	2.69E-5	> 1.00E-4
HOP-62	0.727	2.254	2.115	2.171	2.003	0.554	0.159	91	95	84	-24	-78	2.05E-6	6.00E-6	3.03E-5
HOP-92	1.287	1.716	1.603	1.632	1.537	1.118	0.143	74	81	58	-13	-89	1.30E-6	6.55E-6	3.07E-5
NCI-H226	0.741	2.104	2.044	2.135	2.013	0.878	-0.042	96	102	93	10	-100	3.31E-6	1.23E-5	3.51E-5
NCI-H23	0.509	1.650	1.702	1.708	1.644	0.394	0.011	105	105	99	-23	-98	2.54E-6	6.53E-6	2.31E-5
NCI-H322M	0.962	2.473	2.511	2.462	2.308	1.273	0.069	103	99	89	21	-93	3.72E-6	1.52E-5	4.19E-5
NCI-H460	0.248	2.503	2.543	2.568	2.445	0.334	0.054	102	103	97	4	-78	3.21E-6	1.11E-5	4.53E-5
NCI-H522	0.913	2.572	2.393	2.522	2.466	0.582	0.439	89	97	94	-36	-52	2.17E-6	5.25E-6	7.48E-5
<b>Colon Cancer</b>															
COLO 205	0.481	1.784	1.801	1.851	1.708	0.592	-0.049	101	105	94	9	-100	3.28E-6	1.20E-5	3.46E-5
HCC-2998	0.450	1.760	1.499	1.606	1.662	0.335	-0.232	80	88	93	-26	-100	2.29E-6	6.08E-6	2.13E-5
HCT-116	0.248	2.090	2.047	2.158	2.008	0.270	-0.019	98	104	96	1	-100	3.04E-6	1.03E-5	3.20E-5
HCT-15	0.159	0.999	0.993	0.979	0.888	0.461	-0.024	99	98	87	36	-100	5.29E-6	1.84E-5	4.29E-5
HT29	0.205	1.302	1.307	1.490	1.341	0.280	-0.071	100	117	104	7	-100	3.58E-6	1.16E-5	3.40E-5
KM12	0.483	2.454	2.409	2.477	2.261	0.461	-0.058	98	101	90	-5	-100	2.66E-6	8.95E-6	2.99E-5
SW-620	0.332	2.569	2.603	2.615	2.414	0.497	0.109	102	102	93	7	-67	3.18E-6	1.26E-5	5.88E-5
<b>CNS Cancer</b>															
SF-268	0.752	2.403	2.151	2.314	2.214	0.580	0.171	85	95	89	-23	-77	2.22E-6	6.23E-6	3.15E-5
SF-295	0.519	1.680	1.487	1.631	1.630	0.690	0.025	83	96	96	15	-95	3.67E-6	1.36E-5	3.87E-5
SF-539	0.682	2.085	1.925	2.008	1.764	0.278	-0.093	89	94	77	-59	-100	1.58E-6	3.68E-6	8.56E-6
SNB-19	0.825	2.472	2.329	2.369	2.293	0.780	-0.161	91	94	89	-5	-100	2.59E-6	8.76E-6	2.96E-5
U251	0.313	1.619	1.551	1.686	1.565	0.092	-0.072	95	105	96	-71	-100	1.88E-6	3.76E-6	7.51E-6
<b>Melanoma</b>															
LOX IMVI	0.298	2.411	2.369	2.446	2.479	0.123	-0.058	98	102	103	-59	-100	2.13E-6	4.33E-6	8.81E-6
MALME-3M	0.702	1.338	1.268	1.321	1.348	0.199	0.002	89	97	102	-72	-100	1.98E-6	3.86E-6	7.49E-6
M14	0.470	1.753	1.657	1.770	1.793	0.403	0.096	93	101	103	-14	-80	2.83E-6	7.55E-6	3.51E-5
MDA-MB-435	0.594	2.799	2.575	2.761	2.603	0.364	0.099	90	98	91	-39	-83	2.07E-6	5.03E-6	1.78E-5
SK-MEL-2	1.108	2.591	2.569	2.653	2.606	0.483	0.042	98	104	101	-56	-96	2.11E-6	4.38E-6	9.10E-6
SK-MEL-28	0.742	2.181	2.126	2.305	2.178	0.167	0.051	96	109	100	-78	-93	1.91E-6	3.65E-6	6.99E-6
SK-MEL-5	0.777	2.827	2.718	2.835	2.648	1.024	-0.162	95	100	91	12	-100	3.32E-6	1.28E-5	3.58E-5
UACC-257	1.043	2.587	2.423	2.486	2.574	1.306	0.425	89	93	99	17	-59	3.97E-6	1.67E-5	7.55E-5
UACC-62	0.696	2.421	2.238	2.293	2.290	0.330	0.051	89	93	92	-53	-93	1.96E-6	4.34E-6	9.60E-6
<b>Ovarian Cancer</b>															
IGROV1	0.550	2.438	2.257	2.327	2.149	1.146	0.018	90	94	85	32	-97	4.50E-6	1.76E-5	4.32E-5
OVCAR-3	0.365	1.636	1.410	1.491	1.452	0.202	-0.083	82	89	86	-45	-100	1.87E-6	4.54E-6	1.25E-5
OVCAR-4	0.612	1.772	1.699	1.753	1.704	0.592	0.123	94	98	94	-3	-80	2.84E-6	9.26E-6	4.07E-5
OVCAR-5	0.554	1.673	1.615	1.630	1.594	1.179	0.064	95	96	93	56	-88	1.10E-5	2.44E-5	5.42E-5
OVCAR-8	0.348	1.795	1.746	1.864	1.698	0.309	0.018	97	105	93	-11	-95	2.59E-6	7.81E-6	2.90E-5
NCI/ADR-RES	0.585	2.189	2.141	2.210	2.119	1.959	1.627	97	101	96	86	65	> 1.00E-4	> 1.00E-4	> 1.00E-4
SK-OV-3	0.924	1.958	1.847	1.979	1.872	0.727	0.022	89	102	92	-21	-98	2.34E-6	6.47E-6	2.37E-5
<b>Renal Cancer</b>															
786-0	0.653	2.376	2.239	2.305	2.126	0.511	0.041	92	96	85	-22	-94	2.14E-6	6.27E-6	2.47E-5
A498	1.761	2.578	2.391	2.475	2.475	2.218	0.836	77	87	87	56	-53	1.14E-5	3.28E-5	9.47E-5
ACHN	0.437	1.705	1.626	1.751	1.653	0.898	-0.127	94	104	96	36	-100	5.90E-6	1.85E-5	4.30E-5
CAKI-1	0.751	2.386	2.329	2.426	2.314	1.837	-0.026	96	102	96	66	-100	1.25E-5	2.51E-5	5.01E-5
RXF 393	1.039	1.583	1.598	1.580	1.331	0.650	0.247	103	99	54	-37	-76	1.10E-6	3.88E-6	2.11E-5
SN12C	0.440	1.727	1.658	1.630	1.631	0.350	-0.140	95	92	93	-21	-100	2.38E-6	6.58E-6	2.35E-5
TK-10	1.040	1.969	1.943	1.986	1.975	1.761	0.777	97	102	101	78	-25	1.86E-5	5.68E-5	> 1.00E-4
UO-31	0.717	2.277	2.028	2.103	1.986	1.800	0.747	84	89	81	69	2	1.94E-5	> 1.00E-4	> 1.00E-4
<b>Prostate Cancer</b>															
PC-3	0.592	2.296	2.178	2.220	2.162	0.684	0.033	93	95	92	5	-95	3.06E-6	1.13E-5	3.58E-5
DU-145	0.401	1.793	1.799	1.872	1.785	0.425	-0.215	100	106	99	2	-100	3.21E-6	1.04E-5	3.22E-5
<b>Breast Cancer</b>															
MCF7	0.656	2.780	2.634	2.639	2.547	0.566	0.022	93	93	89	-14	-97	2.40E-6	7.34E-6	2.74E-5
MDA-MB-231/ATCC	0.580	1.470	1.423	1.464	1.458	0.213	-0.198	95	99	99	-63	-100	2.00E-6	4.07E-6	8.28E-6
HS 578T	1.456	2.946	2.724	2.849	2.827	1.622	1.053	85	93	92	11	-28	3.31E-6	1.94E-5	> 1.00E-4
BT-549	1.070	1.879	1.829	1.921	1.818	1.055	-0.206	94	105	92	-1	-100	2.83E-6	9.66E-6	3.11E-5
T-47D	0.806	1.883	1.772	1.864	1.781	0.591	0.094	90	98	91	-27	-88	2.22E-6	5.92E-6	2.39E-5

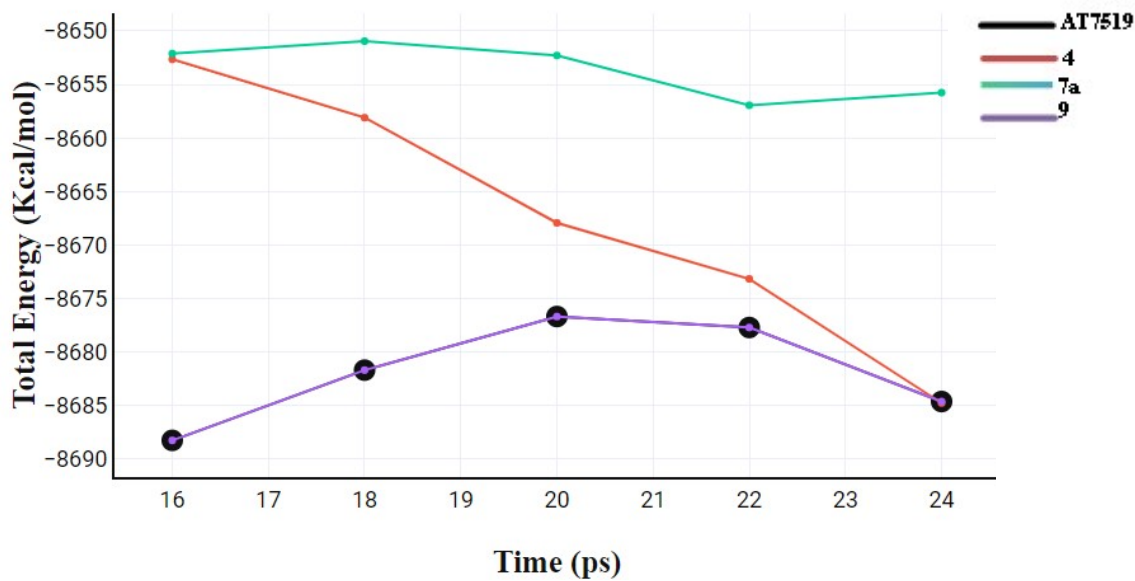
S4: Total energy versus time (production step) for the free protein

**Total Energy vs Time (Production step)**

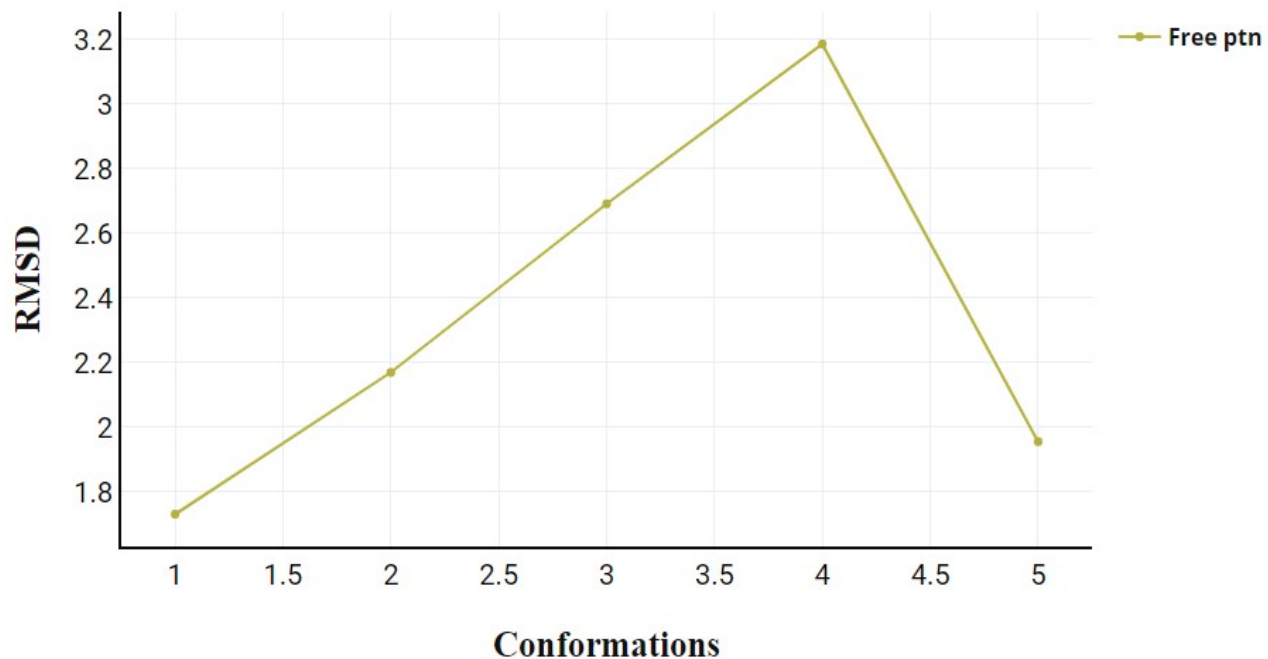


S5: Total energy versus time (production step) for compounds AT7519 (I), 4, 7a, and 9

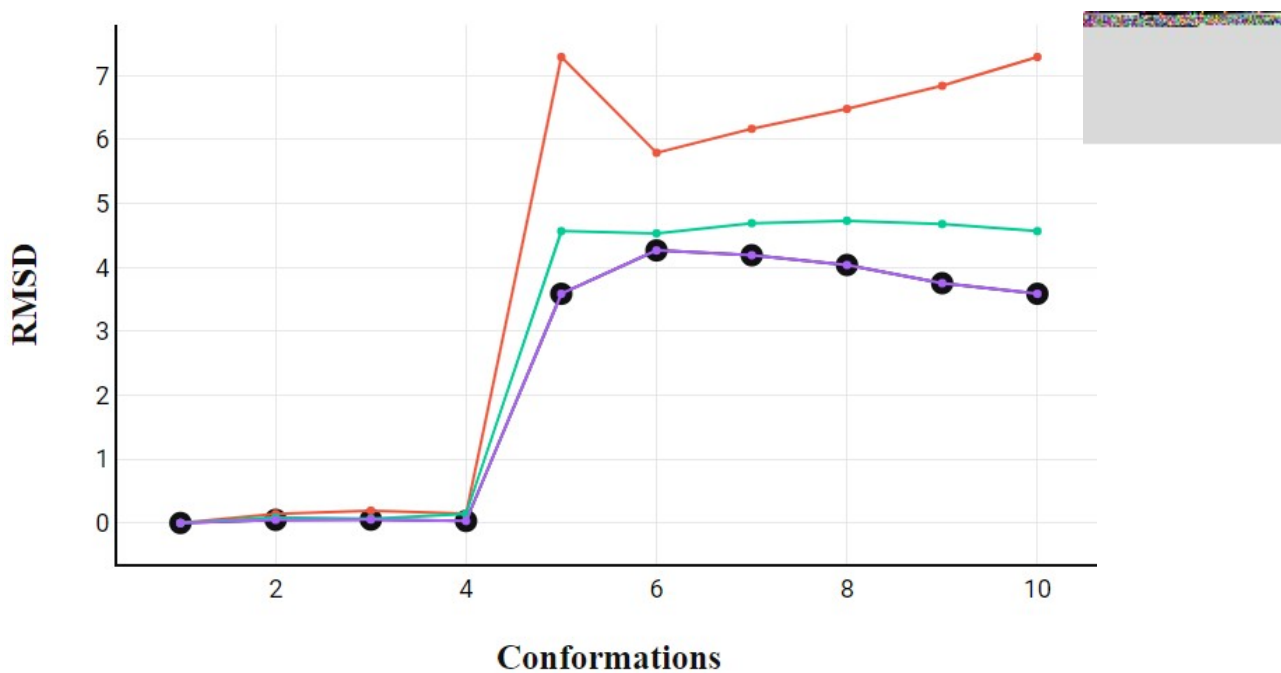
**Total Energy vs Time (Production step)**



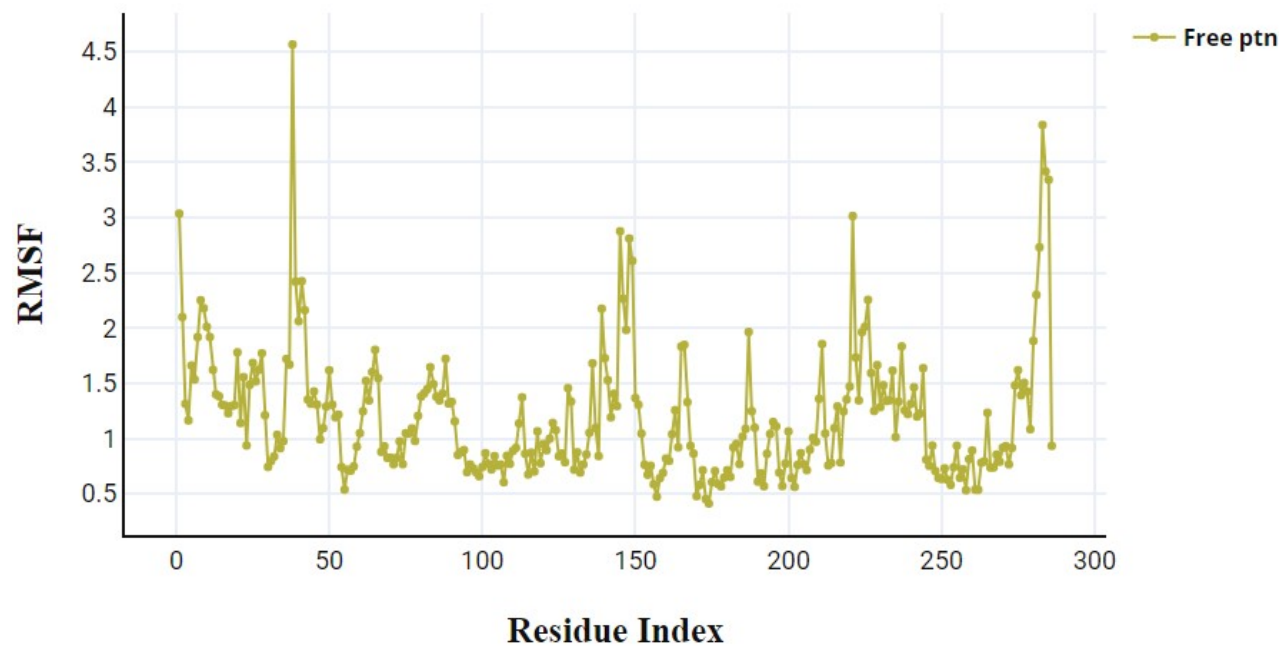
S6: RMSD free protein



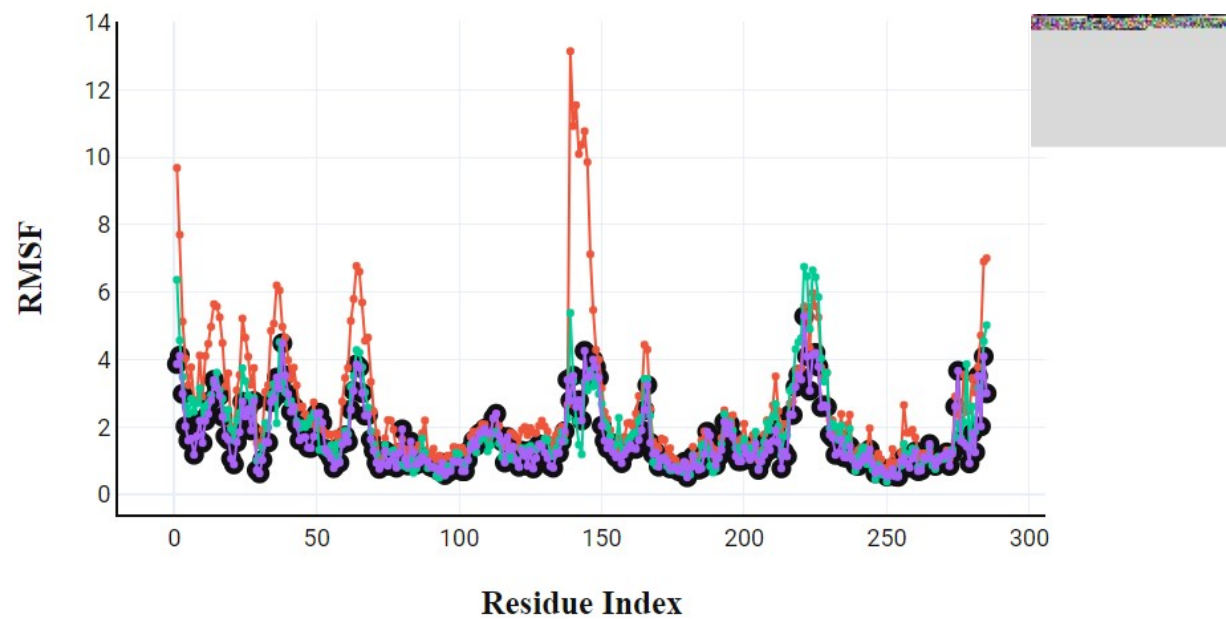
S7: RMSD compounds AT7519 (I), 4, 7a and 9



S8: RMSF free protein

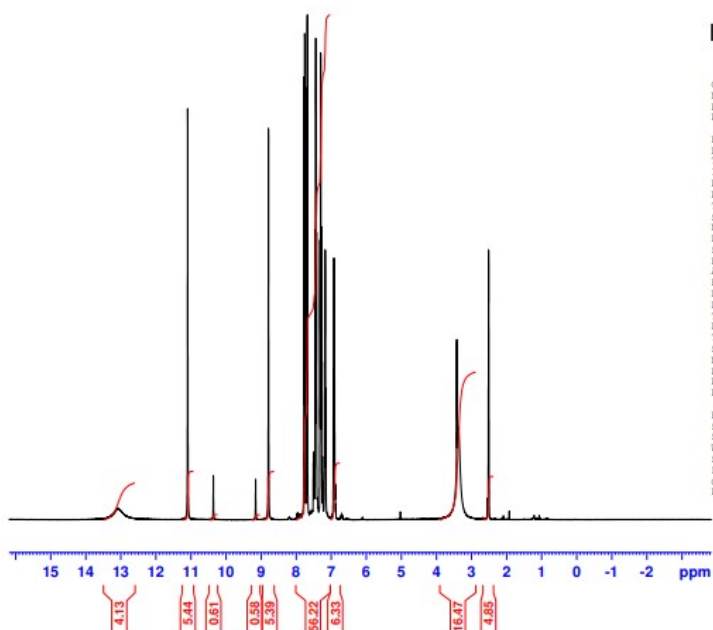
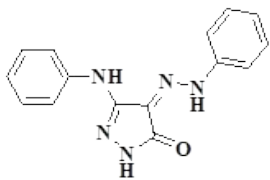


S9: RMSF compounds AT7519 (I), 4, 7a and 9





S10: <sup>1</sup>H-NMR of compound 2a



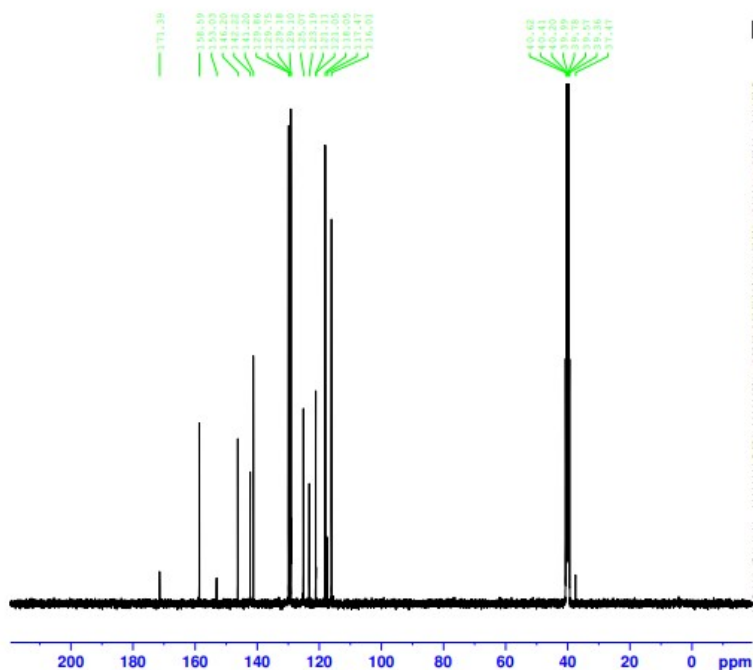
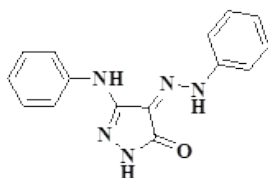
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Current Data Parameters
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EXPNO     10
PROCNO    1

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PROBHD    Z108618_0627 (
PULPROG   zg30
TD        65536
SOLVENT   DMSO
NS        16
DS        2
SWH       8012.820 Hz
FIDRES    0.244532 Hz
AQ        4.0894465 sec
RG        101
DW        62.400 usec
DE        16.92 usec
TE        298.2 K
D1        1.00000000 sec
TDO       1
SFO1      400.1324768 MHz
NUC1      1H
PQ        5.00 usec
P1        15.00 usec
PLM1     12.49199963 W

F2 - Processing parameters
SI        65536
SF        400.1300000 MHz
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SSB       0
LB        0.30 Hz
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PC        1.00
    
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S11: <sup>13</sup>C-NMR of compound 2a



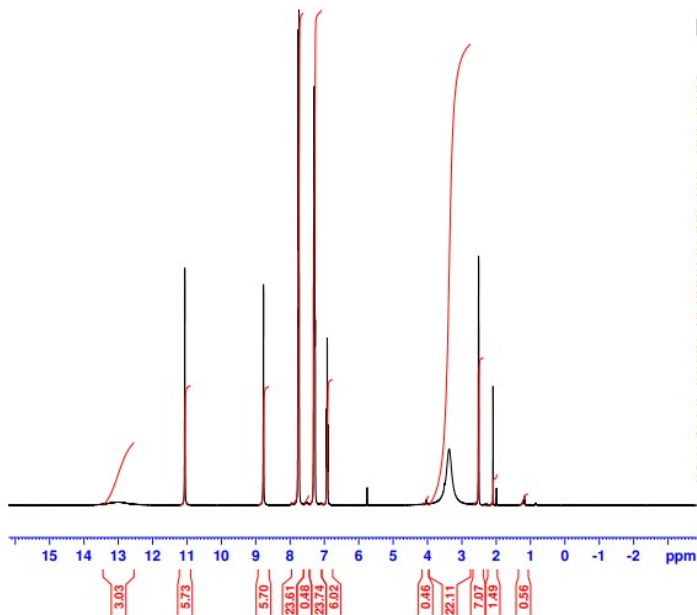
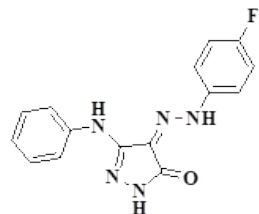
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EXPNO     11
PROCNO    1

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PROBHD    Z108618_0627 (
PULPROG   zgpg30
TD        65536
SOLVENT   DMSO
NS        1024
DS        4
SWH       24038.461 Hz
FIDRES    0.733596 Hz
AQ        1.3631488 sec
RG        203
DW        20.800 usec
DE        6.50 usec
TE        300.0 K
D1        2.00000000 sec
D11       0.03000000 sec
TDO       1
SFO1      100.6228298 MHz
NUC1      13C
PQ        3.33 usec
P1        10.00 usec
PLM1     54.08100128 W
SFO2      400.1316005 MHz
NUC2      1H
CPDPRG2   waltz165
PCPD2     90.00 usec
PLM2     12.49199963 W
PLM12    0.34698999 W
PLM13    0.17453000 W

F2 - Processing parameters
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S12: <sup>1</sup>H-NMR of compound **2b**



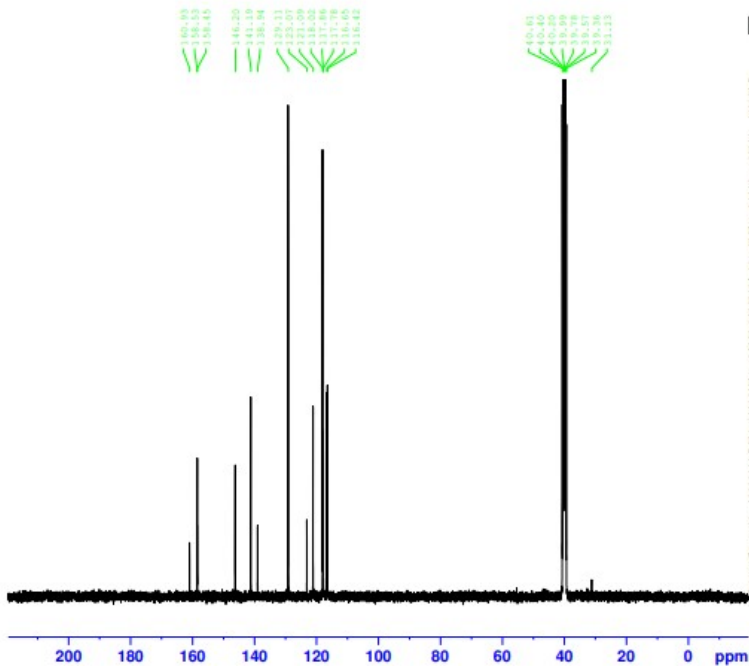
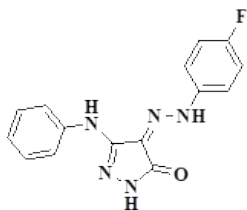
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Current Data Parameters
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EXPNO    10
PROCNO   1

F2 - Acquisition Parameters
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INSTRUM  spect
PROBHD   Z108618_0627 (
PULPROG  zg30
TD       65536
SOLVENT  DMSO
NS       16
DS       2
SWH      8012.820 Hz
FIDRES   0.244532 Hz
AQ       4.0894465 sec
RG       114
DM       62.400 usec
DE       16.92 usec
TE       298.9 K
D1       1.0000000 sec
TDO      1
SFO1     400.1324708 MHz
NUC1     1H
PQ       5.00 usec
P1       15.00 usec
PLW1     12.49199963 W

F2 - Processing parameters
SI       65536
SF       400.1300000 MHz
WDW      EM
SSB      0
LB       0.30 Hz
GB       0
PC       1.00
    
```

S13: <sup>13</sup>C-NMR of compound **2b**



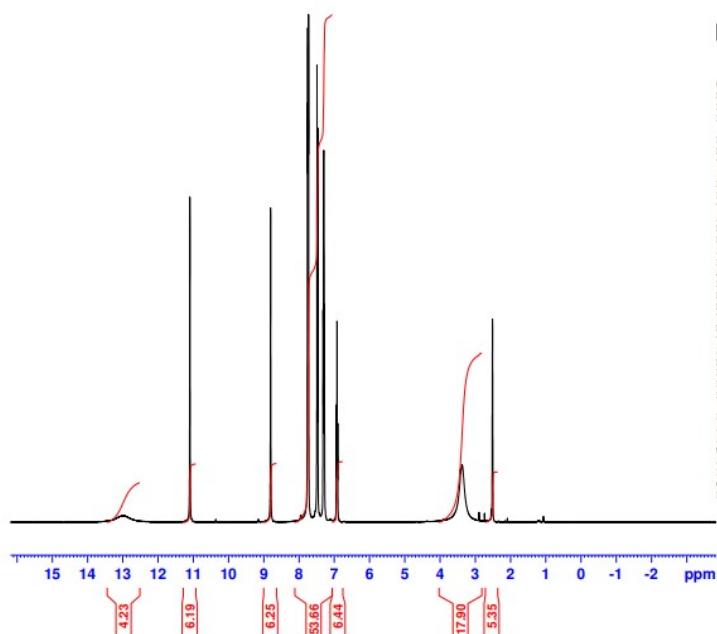
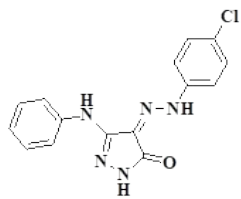
```

Current Data Parameters
NAME      5_ARM
EXPNO    11
PROCNO   1

F2 - Acquisition Parameters
Date_    20240216
Time     20.02 h
INSTRUM  spect
PROBHD   Z108618_0627 (
PULPROG  zgpg30
TD       65536
SOLVENT  DMSO
NS       1024
DS       4
SWH      24038.461 Hz
FIDRES   0.733596 Hz
AQ       1.3631488 sec
RG       203
DM       20.800 usec
DE       6.50 usec
TE       300.0 K
D1       2.0000000 sec
D11      0.0300000 sec
TDO      1
SFO1     100.6228298 MHz
NUC1     13C
PQ       3.33 usec
P1       10.00 usec
PLW1     54.08100128 W
SFO2     400.1316005 MHz
NUC2     1H
CPDPRG2  waltz65
PCPD2    90.00 usec
PLW2     12.49199963 W
PLW12    0.34698999 W
PLW13    0.17453000 W

F2 - Processing parameters
SI       32768
SF       100.6127690 MHz
WDW      EM
SSB      0
LB       1.00 Hz
GB       0
PC       1.40
    
```

S14: <sup>1</sup>H-NMR of compound 2c



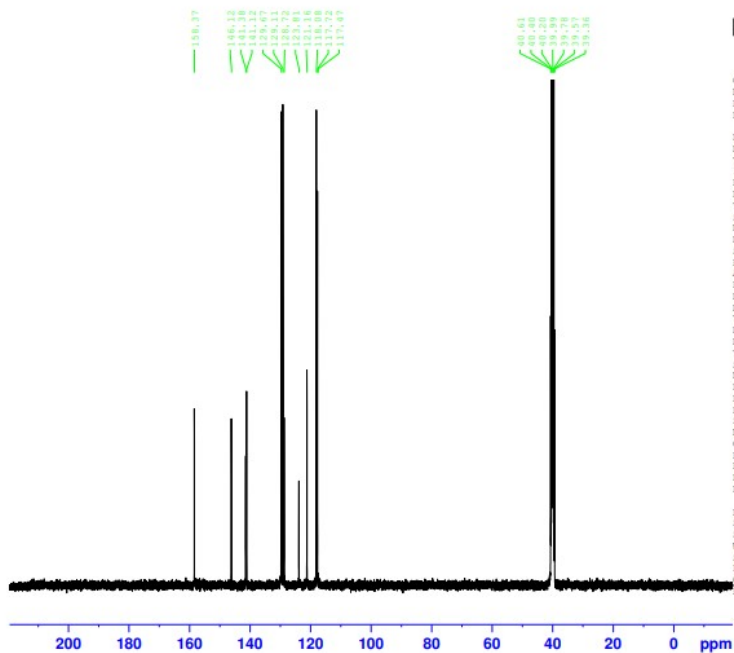
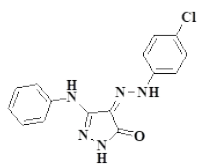
```

Current Data Parameters
NAME      1_ARM
EXPNO    10
PROCNO   1

F2 - Acquisition Parameters
Date_    20240216
Time     15.43 h
INSTRUM  spect
PROBHD   z108618_0627 (
PULPROG  zg30
TD        65536
SOLVENT  DMSO
NS        16
DS        2
SWH       8012.820 Hz
FIDRES    0.244532 Hz
AQ         4.0894465 sec
RG         101
DW         62.400 usec
DE         16.92 usec
TE         298.4 K
D1         1.00000000 sec
TDO        1
SFO1      400.1324708 MHz
NUC1       1H
FO         5.00 usec
P1         15.00 usec
PLW1      12.49199963 W

F2 - Processing parameters
SI         65536
SF         400.1300000 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
    
```

S15: <sup>13</sup>C-NMR of compound 2c



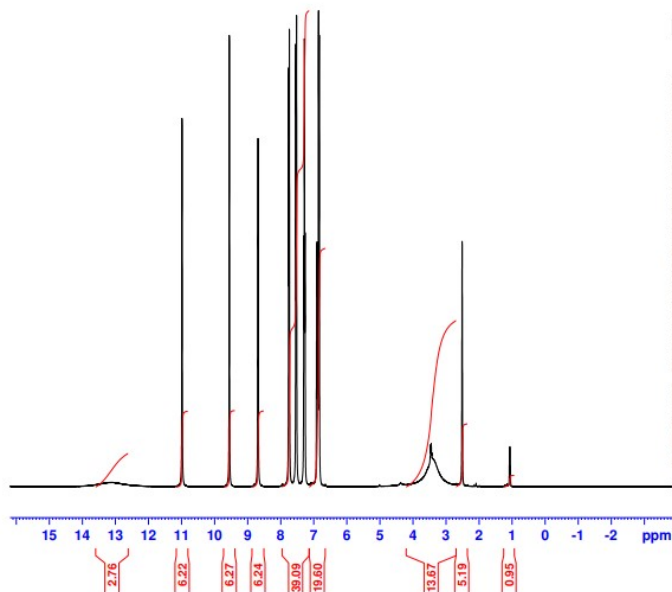
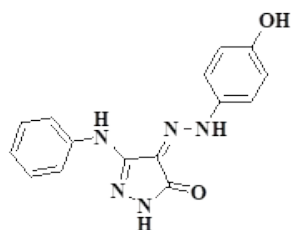
```

Current Data Parameters
NAME      1_ARM
EXPNO    11
PROCNO   1

F2 - Acquisition Parameters
Date_    20240216
Time     16.42 h
INSTRUM  spect
PROBHD   z108618_0627 (
PULPROG  zgpg30
TD        65536
SOLVENT  DMSO
NS        1024
DS        4
SWH       24038.461 Hz
FIDRES    0.733596 Hz
AQ         1.3631488 sec
RG         203
DW         20.800 usec
DE         6.50 usec
TE         300.2 K
D1         2.00000000 sec
D11        0.03000000 sec
TDO        1
SFO1      100.6228298 MHz
NUC1       13C
FO         3.33 usec
P1         10.00 usec
PLW1      54.08100128 W
SFO2      400.1316005 MHz
NUC2       1H
CPDPRG[2] waltz65
PCPD2     90.00 usec
PLW2      12.49199963 W
PLW12     0.34698999 W
PLW13     0.17453000 W

F2 - Processing parameters
SI         32768
SF         100.6127650 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.40
    
```

S16: <sup>1</sup>H-NMR of compound **2d**



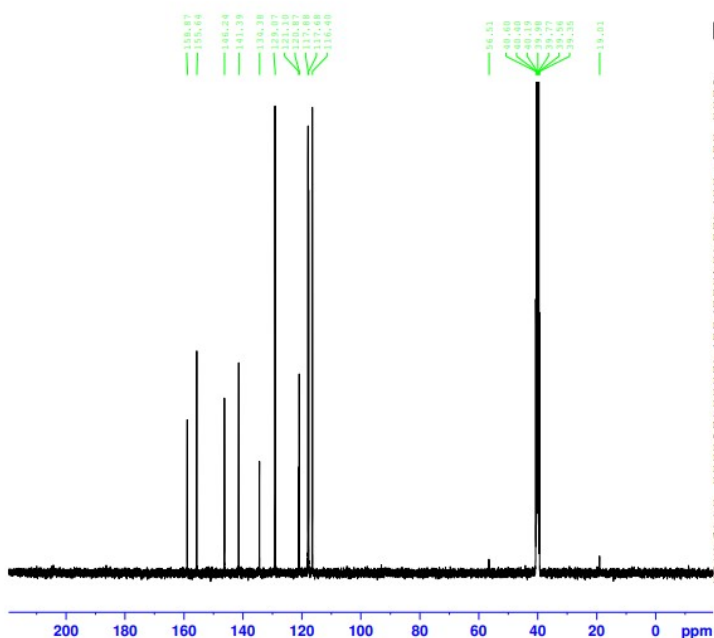
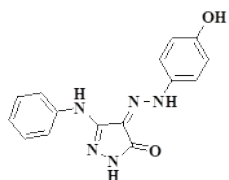
```

Current Data Parameters
NAME          2_AHM
EXPNO        10
PROCNO       1

F2 - Acquisition Parameters
Date_        20240216
Time         17.22 h
INSTRUM      spect
PROBHD       Z108618_0627 (
PULPROG      zg30
TD           65536
SOLVENT      DMSO
NS           16
DS           2
SWH          8012.820 Hz
FIDRES      0.244532 Hz
AQ          4.0894465 sec
RG           101
DW          62.400 usec
DE          16.92 usec
TE          298.9 K
D1          1.00000000 sec
TD0         1
SFO1        400.1324708 MHz
NUC1         1H
PO          5.00 usec
P1          15.00 usec
PLW1        12.49199963 W

F2 - Processing parameters
SI           65536
SF          400.1300000 MHz
WDW          EM
SSB          0
LB           0.30 Hz
GB           0
PC           1.00
    
```

S17: <sup>13</sup>C-NMR of compound **2d**



```

Current Data Parameters
NAME          2_AHM
EXPNO        11
PROCNO       1

F2 - Acquisition Parameters
Date_        20240216
Time         18.22 h
INSTRUM      spect
PROBHD       Z108618_0627 (
PULPROG      zgpg30
TD           65536
SOLVENT      DMSO
NS           1024
DS           4
SWH          24038.461 Hz
FIDRES      0.733596 Hz
AQ          1.3631488 sec
RG           203
DW          20.800 usec
DE          6.50 usec
TE          300.1 K
D1          2.00000000 sec
D11         0.03000000 sec
TD0         1
SFO1        100.6228298 MHz
NUC1         13C
PO          3.33 usec
P1          10.00 usec
PLW1        54.08100128 W
SFO2        400.1316005 MHz
NUC2         1H
CPDPRG[2]   waltz65
PCPD2       90.00 usec
PLW2        12.49199963 W
PLW12       0.34698999 W
PLW13       0.17453000 W

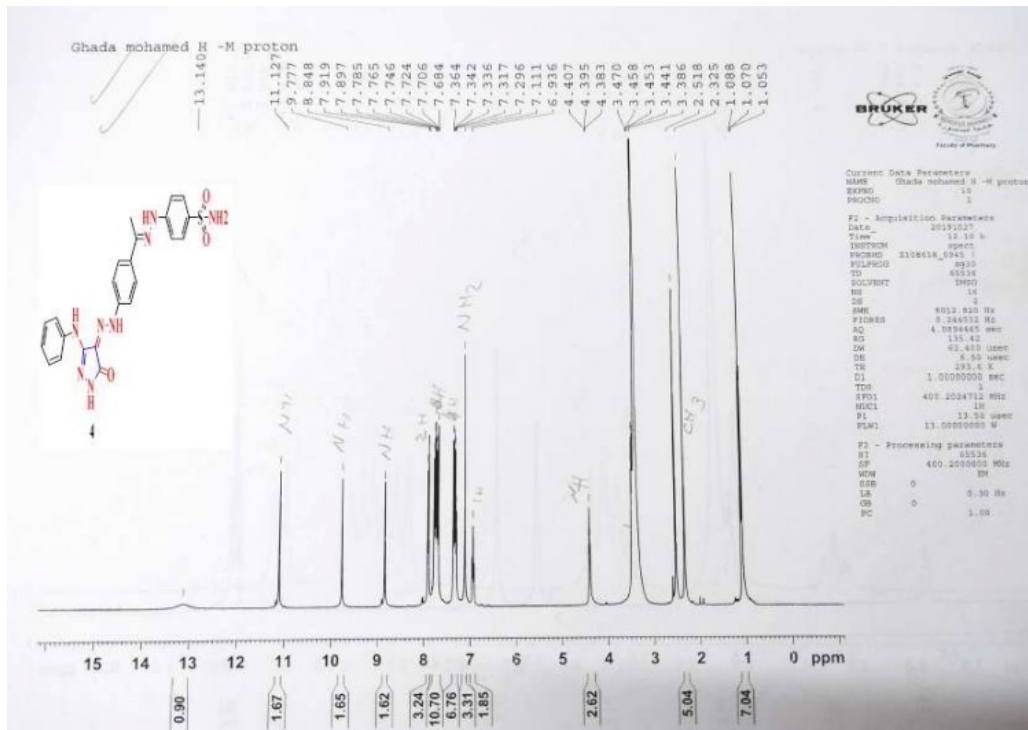
F2 - Processing parameters
SI           32768
SF          100.6127690 MHz
WDW          EM
SSB          0
LB           1.00 Hz
GB           0
PC           1.40
    
```



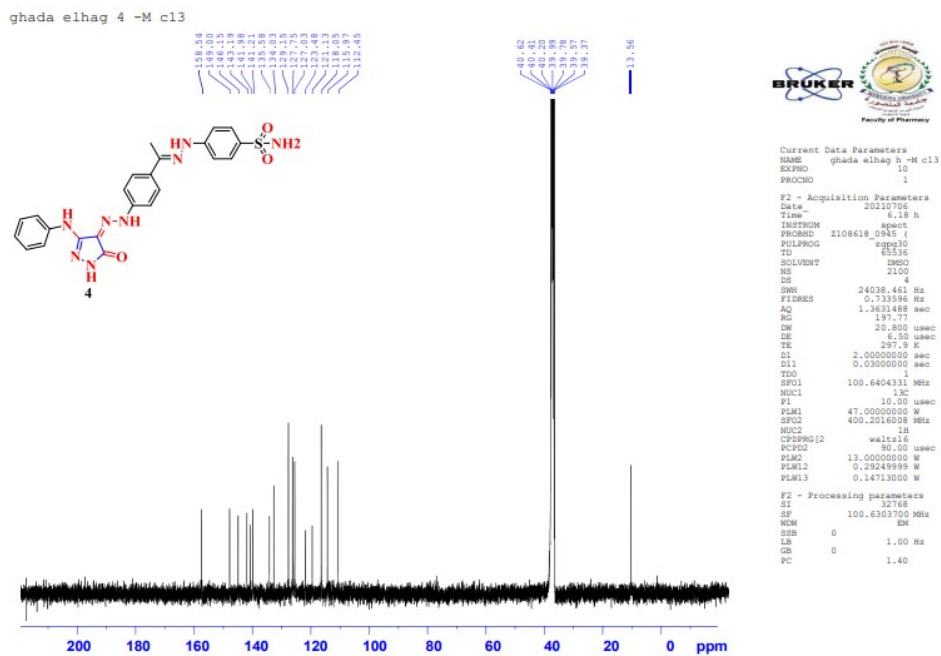




S24: <sup>1</sup>H-NMR of compound 4

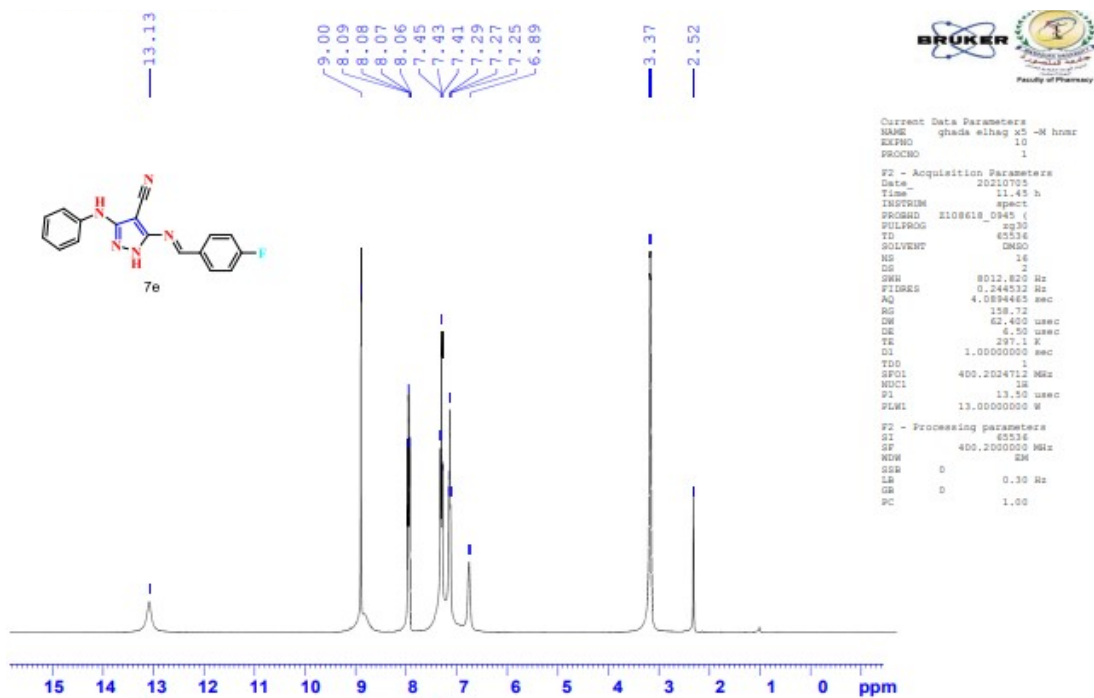


S25: <sup>13</sup>C-NMR of compound 4

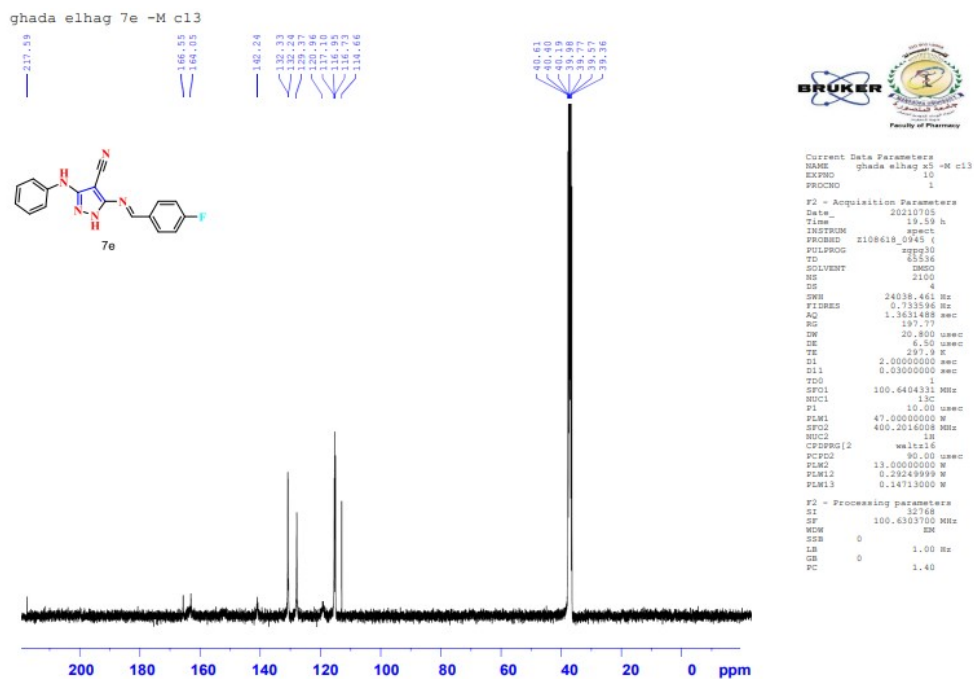




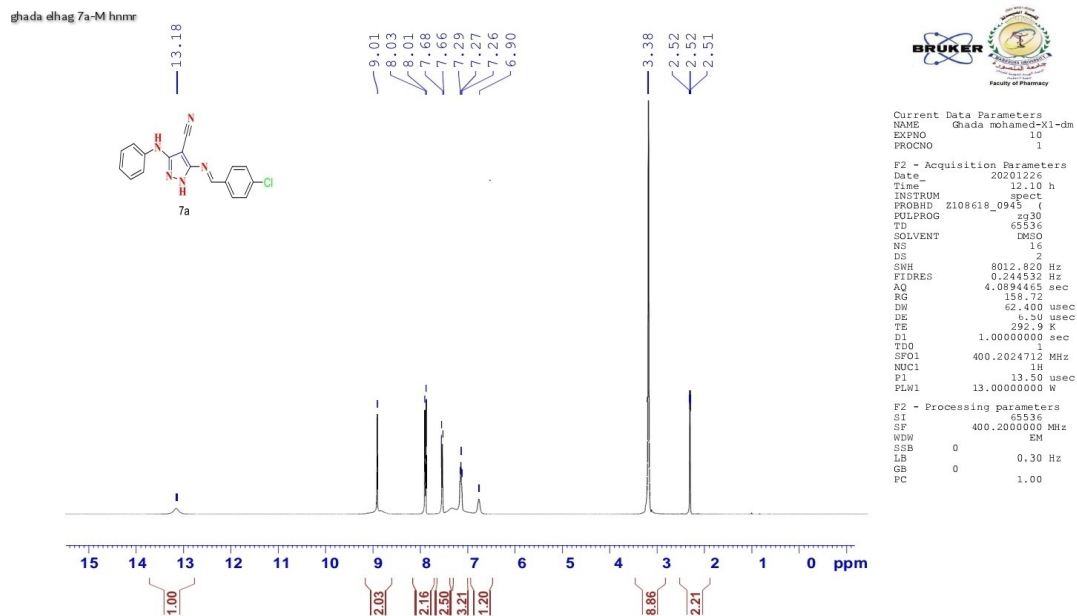
S26: <sup>1</sup>H-NMR of compound 7a



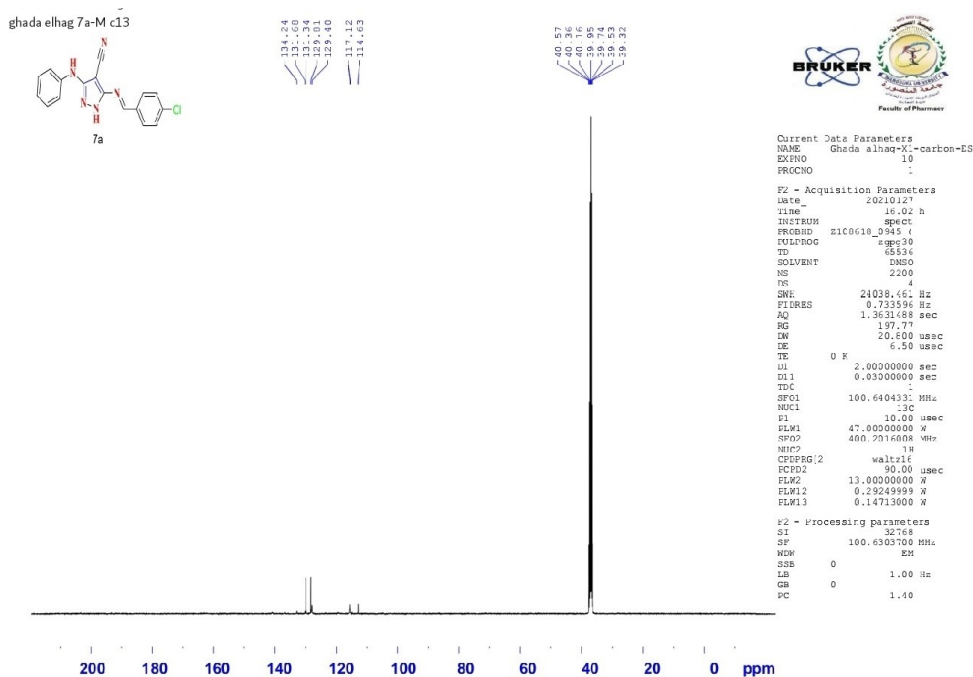
S27: <sup>13</sup>C-NMR of compound 7a



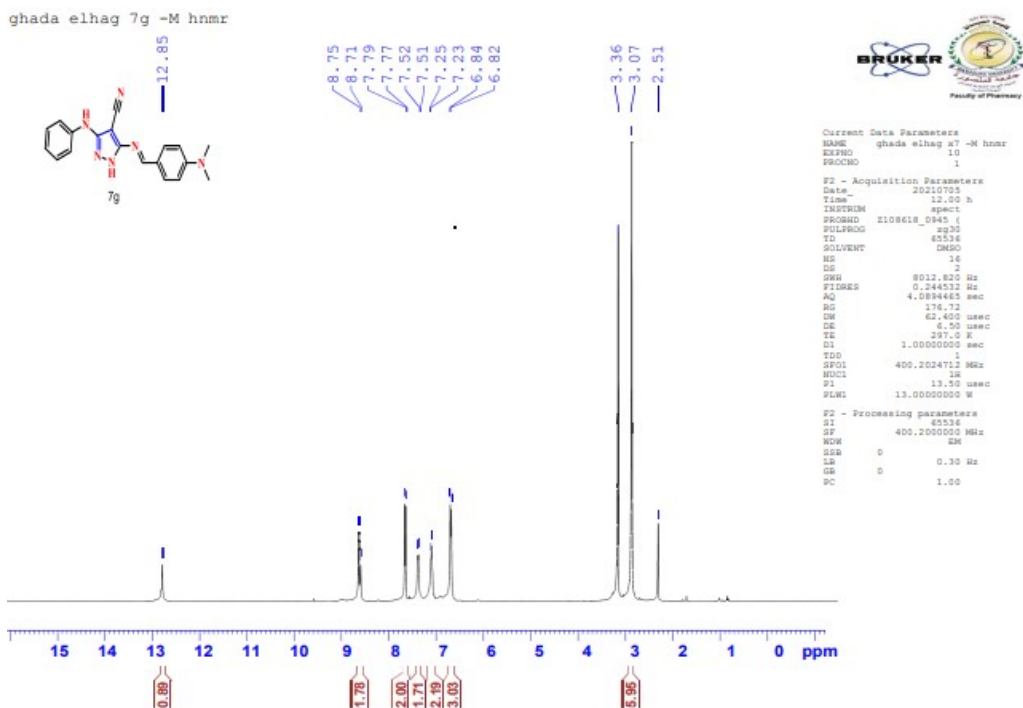
## S28: <sup>1</sup>H-NMR of compound 7b



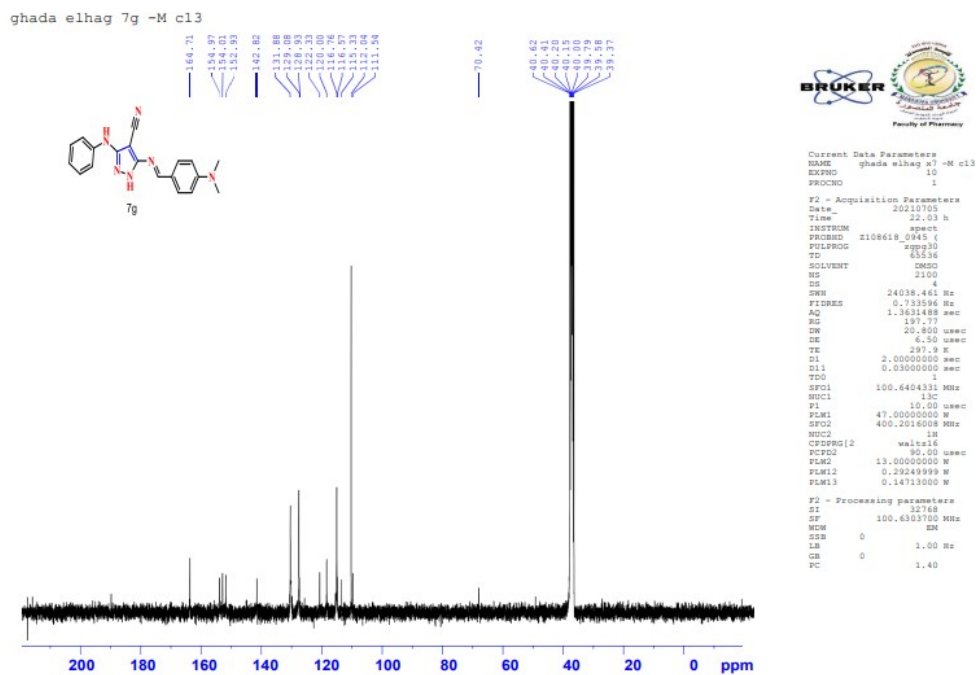
## S29: <sup>13</sup>C-NMR of compound 7b



### S30: <sup>1</sup>H-NMR of compound 7c

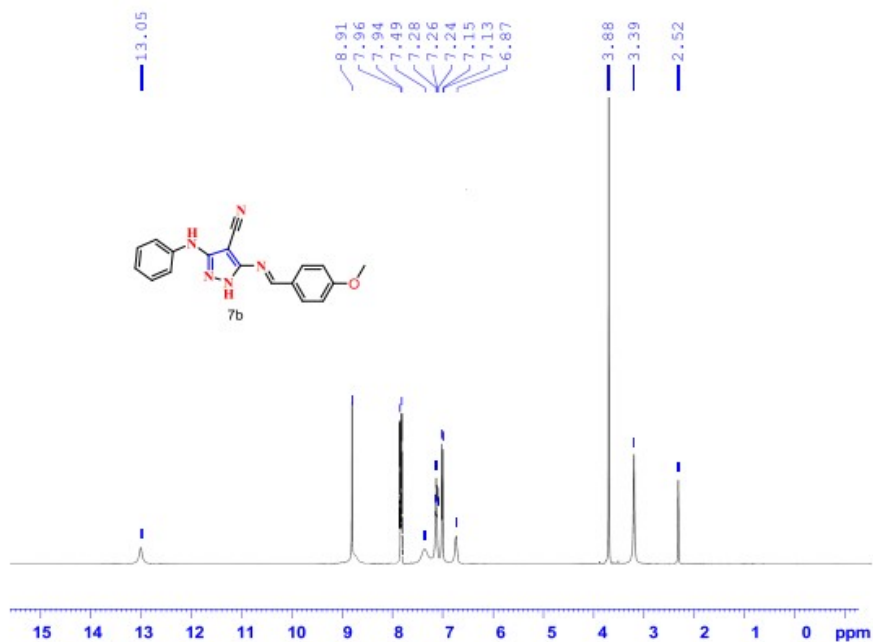


### S31: <sup>13</sup>C-NMR of compound 7c



### S32: <sup>1</sup>H-NMR of compound 7d

Ghada mohamed-7b-dmso-HNMR-OE



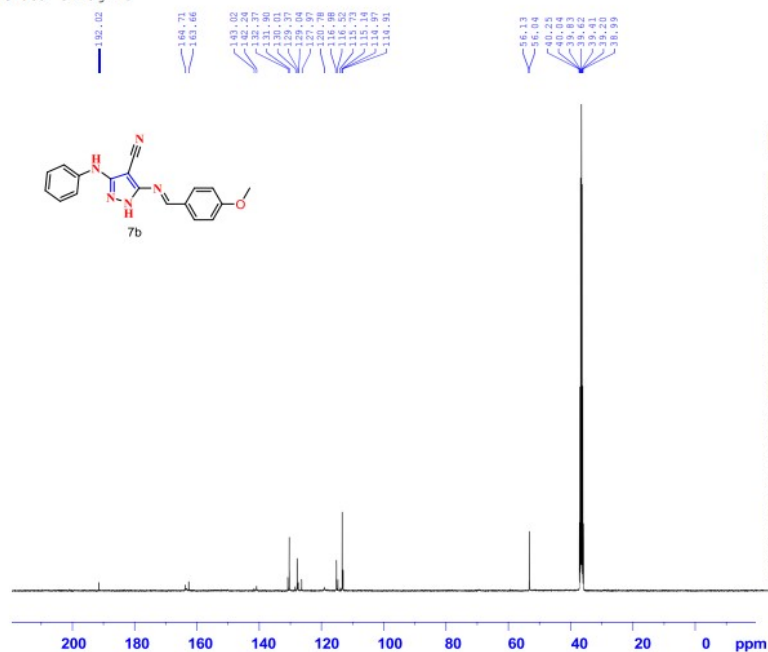
Current Data Parameters  
 NAME Ghada mohamed-X2-ds  
 EXPMO 10  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20201226  
 Time\_ 12.15 h  
 INSTRUM spect  
 PROBHD z108618\_0945 ( )  
 PULPROG zg30  
 TD 65536  
 SOLVENT DMSO  
 NS 16  
 DS 2  
 SWH 8012.820 Hz  
 FIDRES 0.244532 Hz  
 AQ 4.089465 sec  
 RG 120.93  
 DW 62.400 usec  
 DE 6.50 usec  
 TE 283.0 K  
 D1 1.00000000 sec  
 TDO 1  
 SFO1 400.202471 MHz  
 NUC1 1H  
 P1 13.50 usec  
 PLW1 13.00000000 W

F2 - Processing parameters  
 SI 65536  
 SF 400.2000000 MHz  
 WMW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00

### S33: <sup>13</sup>C-NMR of compound 7d

Ghada alhag-7b

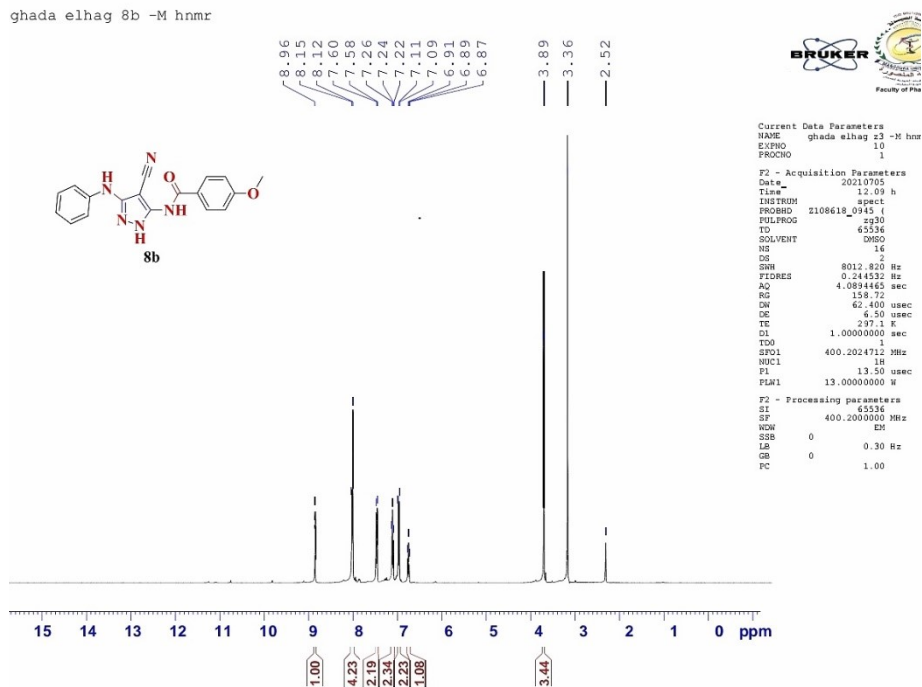


Current Data Parameters  
 NAME Ghada alhag-X2-carbon-ES  
 EXPMO 10  
 PROCNO 1

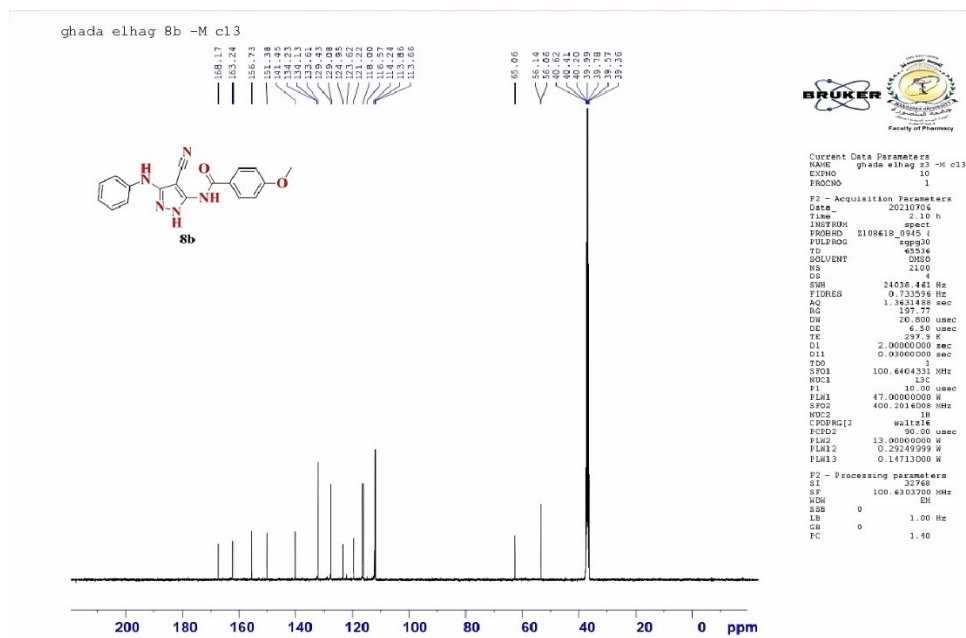
F2 - Acquisition Parameters  
 Date\_ 20210127  
 Time\_ 18.11 h  
 INSTRUM spect  
 PROBHD z108618\_0945 ( )  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT DMSO  
 NS 2200  
 DS 4  
 SWH 24038.461 Hz  
 FIDRES 0.733596 Hz  
 AQ 1.3631488 sec  
 RG 197.77  
 DW 20.800 usec  
 DE 6.50 usec  
 TE 0 K  
 D1 2.00000000 sec  
 D11 0.03000000 sec  
 TDO 1  
 SFO1 100.6404331 MHz  
 NUC1 13C  
 P1 10.00 usec  
 PLW1 47.00000000 W  
 SFO2 400.2016008 MHz  
 NSCC 16  
 CPOPG12 waitz16  
 PCPD2 90.00 usec  
 PLM2 13.00000000 W  
 PLM12 0.29249999 W  
 PLM13 0.14713000 W

F2 - Processing parameters  
 SI 32768  
 SF 100.6303700 MHz  
 WMW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40

### S34: <sup>1</sup>H-NMR of compound 8a

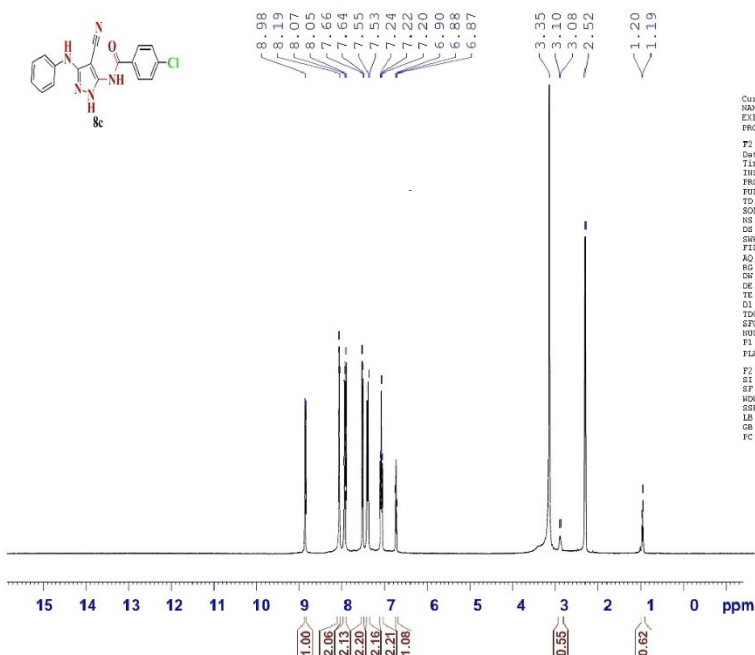
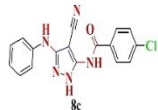


### S35: <sup>13</sup>C-NMR of compound 8a



### S36: <sup>1</sup>H-NMR of compound 8b

ghada elhag 8c -M hnmr



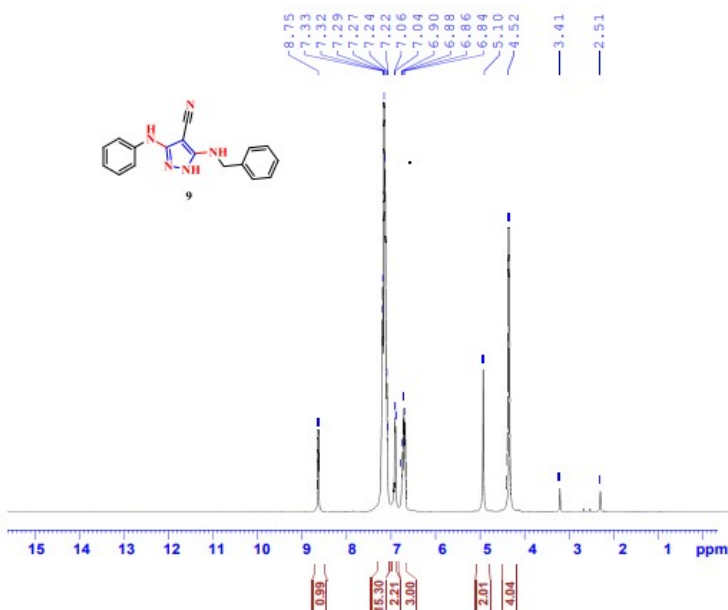
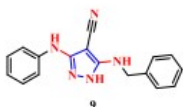
```
Current Data Parameters
NAME      ghada elhag 8c -M hnmr
EXPNO    10
PROCNO   1

F2 - Acquisition Parameters
Date_    20210705
Time     11.40 h
INSTRUM  spect
PROBHD   1108618_0945 1
PULPROG  zg30
TD       65536
SOLVENT  DMSO
NS       16
DS       2
SFO1     400.2024712 MHz
SF       400.2024712 MHz
NUC1     1H
PC       13.50 usec
PL1      13.00000000 W

F2 - Processing parameters
SI       65536
SF       400.2000000 MHz
WDW      EM
SSB      0
LB       0.30 Hz
GB       0
PC       1.00
```

### S37: <sup>1</sup>H-NMR of compound 9

Ghada elhag-9-DMSO-Hnmr-A



```
Current Data Parameters
NAME      Ghada elhag-9-DMSO-Hn
EXPNO    10
PROCNO   1

F2 - Acquisition Parameters
Date_    20210401
Time     11.51 h
INSTRUM  spect
PROBHD   1108618_0945 1
PULPROG  zg30
TD       65536
SOLVENT  DMSO
NS       16
DS       2
SFO1     400.2024712 MHz
SF       400.2024712 MHz
NUC1     1H
PC       13.50 usec
PL1      13.00000000 W

F2 - Processing parameters
SI       65536
SF       400.2000000 MHz
WDW      EM
SSB      0
LB       0.30 Hz
GB       0
PC       1.00
```

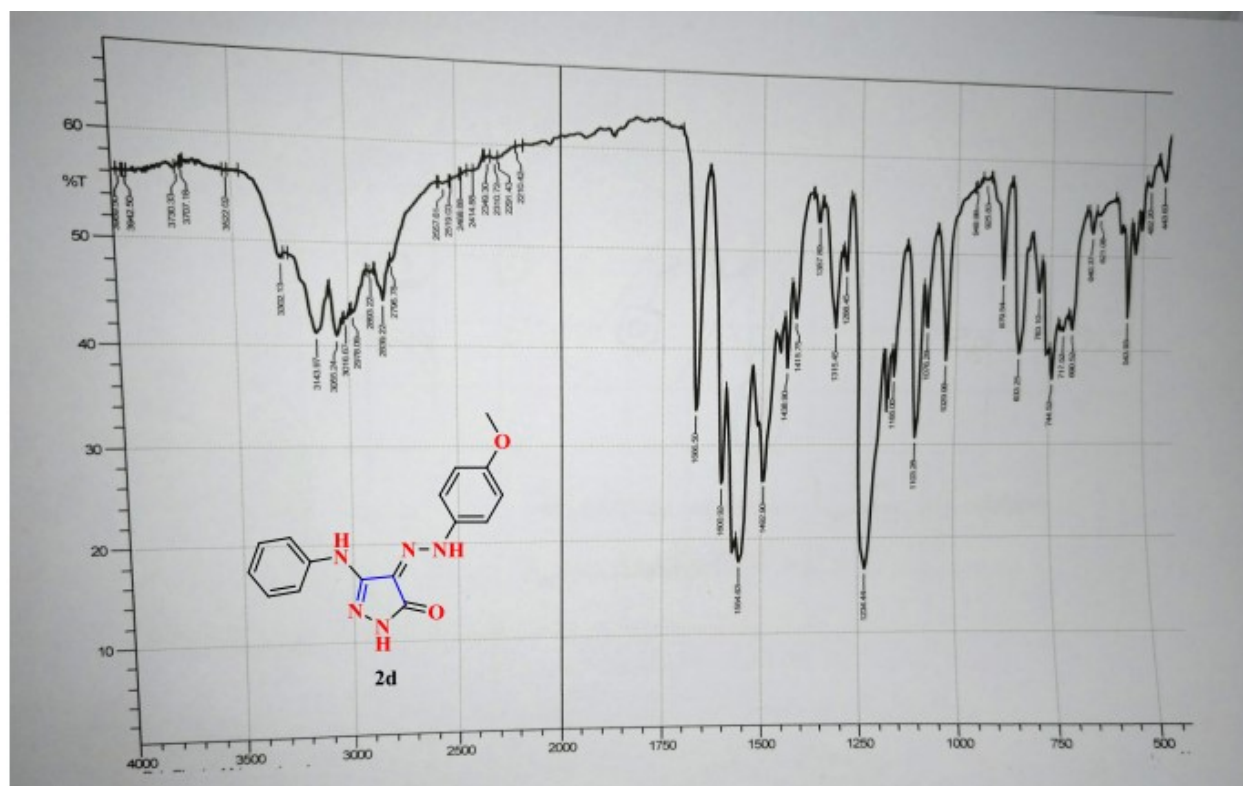




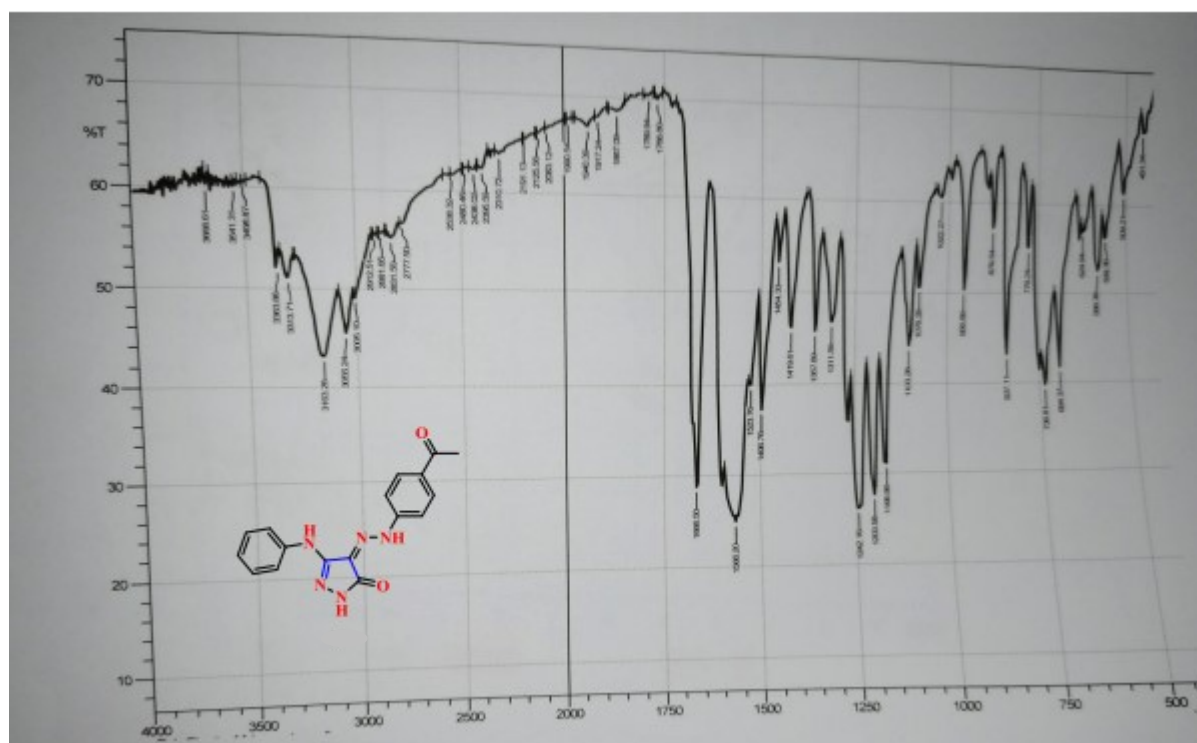




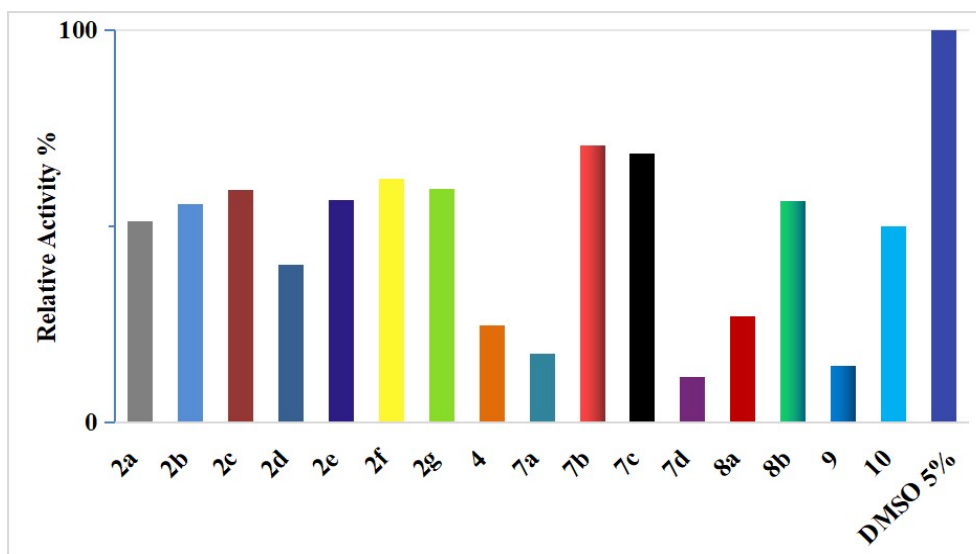
S44: IR of compound **2f**



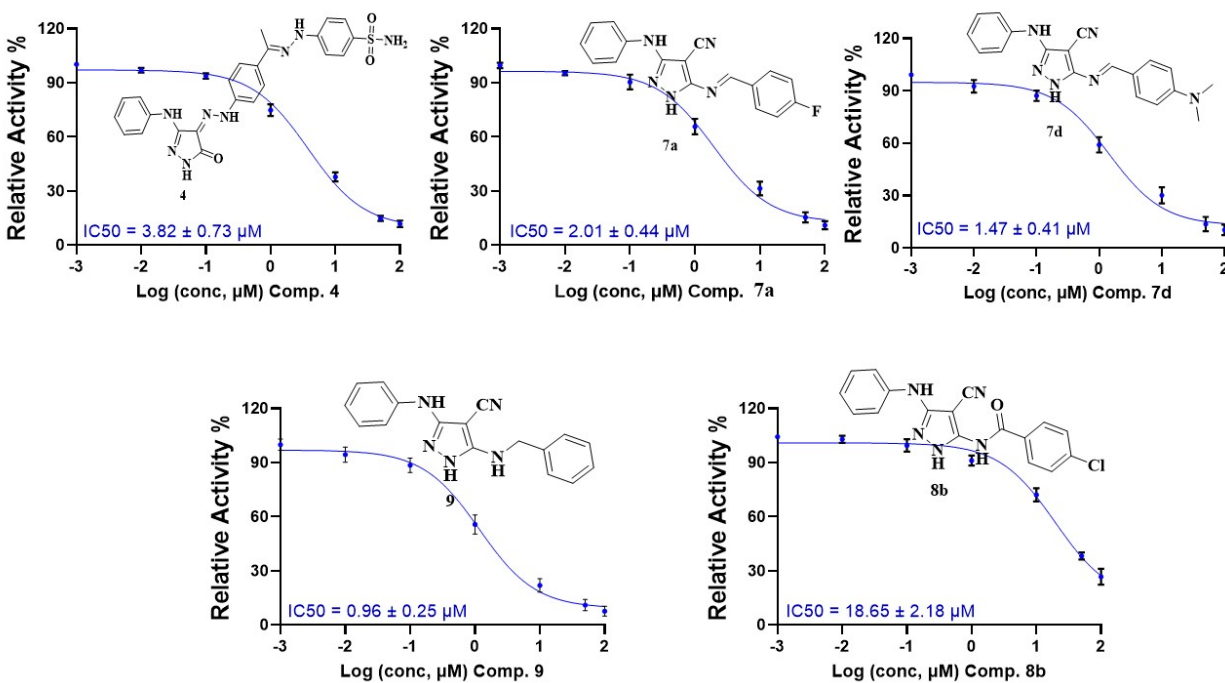
S45: IR of compound **2g**



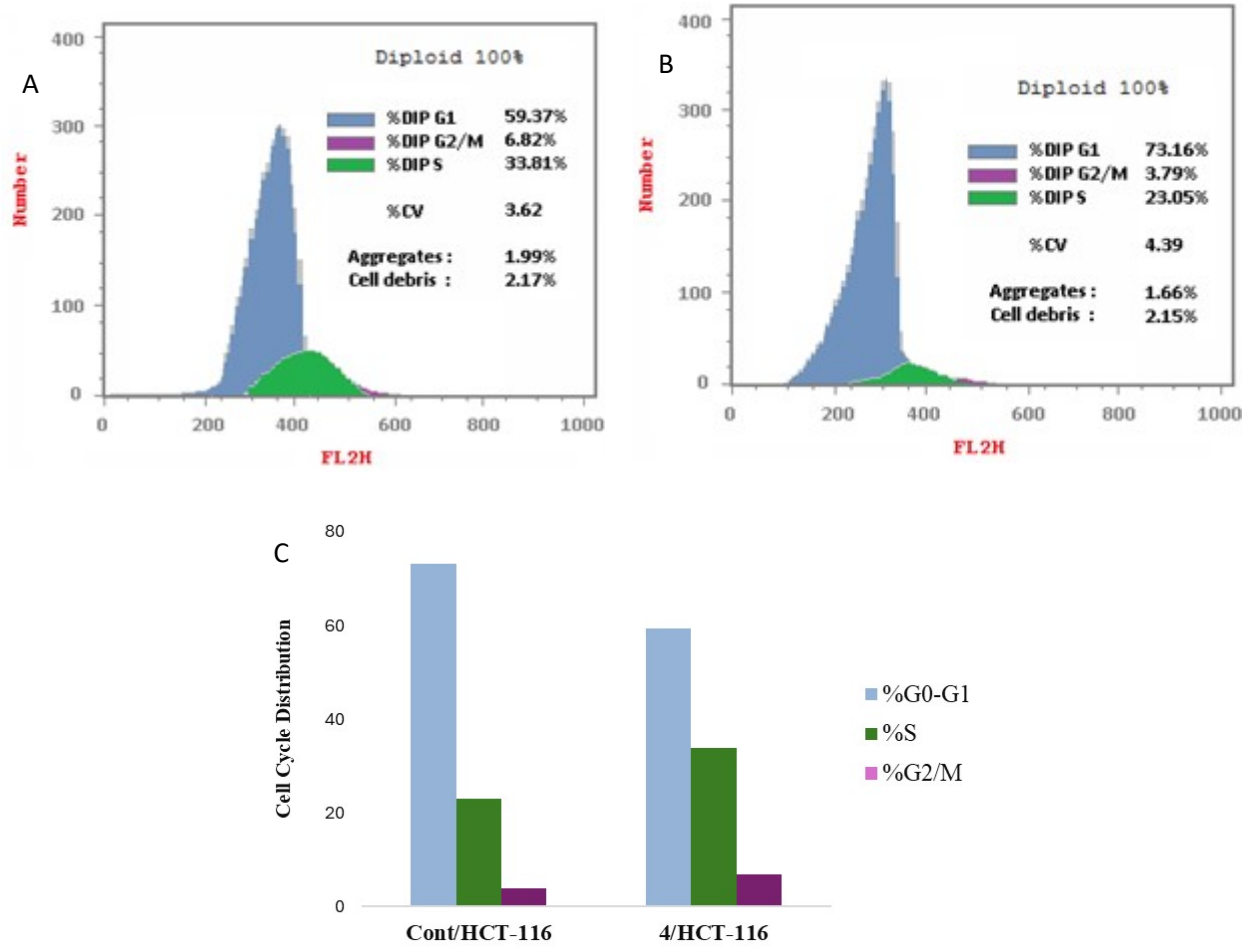
S46: Inhibition of CDK2/CyclinA2 by compounds **2a-g**, **4**, **7a-d**, **8a-b**, **9** & **10** at 50  $\mu$ M.



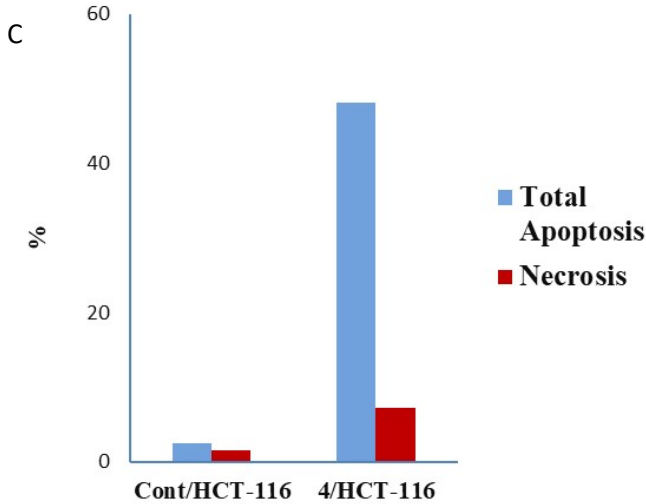
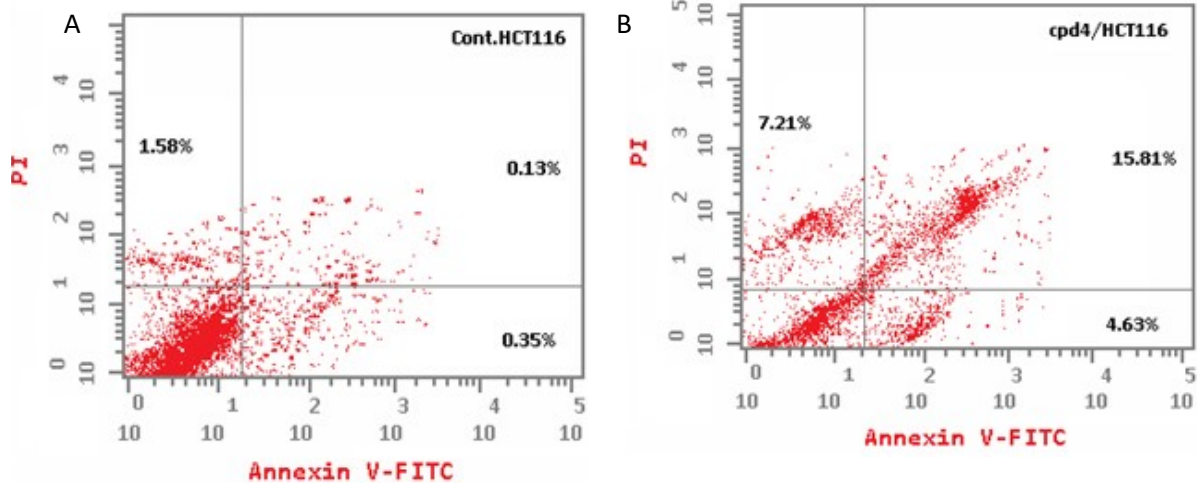
S47: The dose–response curves show the Inhibitory Concentration at 50% ( $IC_{50}$ ) curves of compounds **4**, **7c**, **7d**, **8b** and **9** in CDK2/Cyclin A2 protein kinase activity assay.



S48: Flow cytometric analysis for cell cycle distribution. (A) Control HCT-116, (B) Compound 4, and (C) graphical representation for cell cycle distribution analysis among differently treated cells.



S49: Flow cytometric analysis of apoptosis among treated cells. (A) Control HCT-116, (B) Compound 4, (C) Graphical illustration of apoptosis % among differently treated cells.



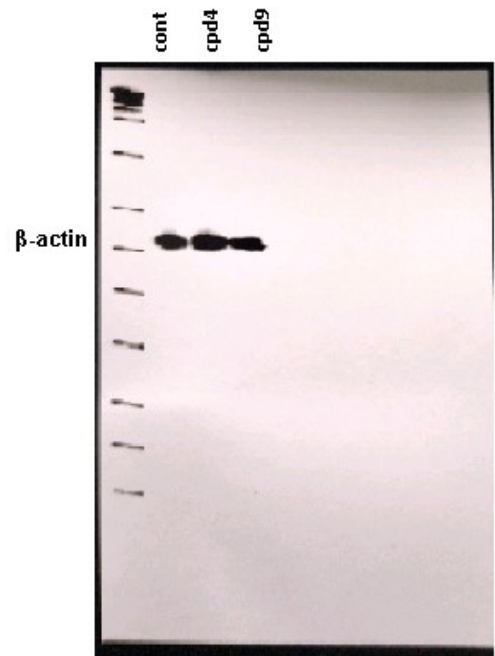
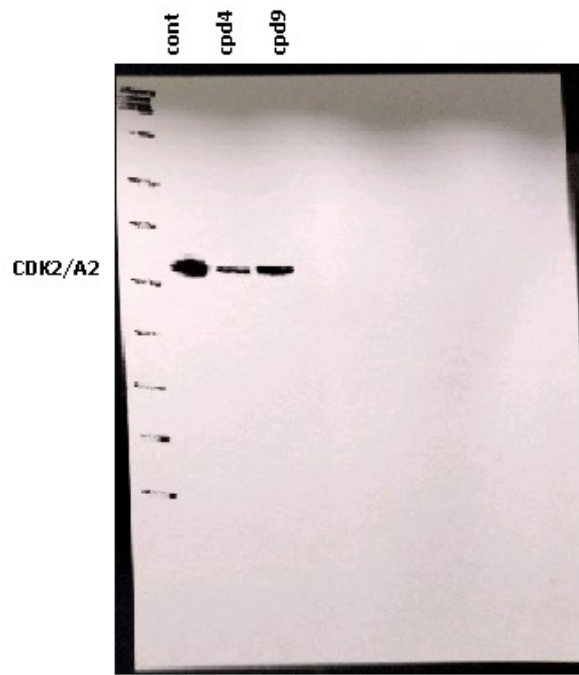
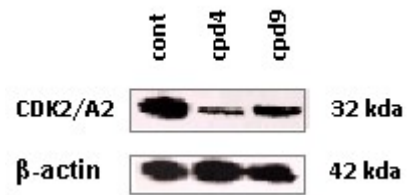
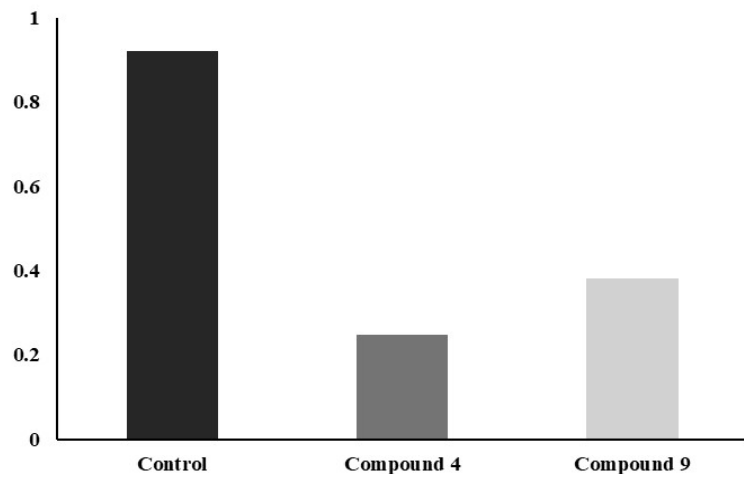
S50: Cell cycle and apoptosis raw data

Ser	Sample			Cytotoxicity	SD ±
	code	M.W g/mol	cells	IC50	
				uM	
1	cpd4	490.54	---	<b>1.806</b>	0.07
2	cpd9	289.33	---	<b>10.003</b>	0.39
3	Staurosporine	466.54	---	<b>7.022</b>	0.27

ser	Sample		DNA content			
	code	IC50 uM	%G0-G1	%S	%G2/M	Comment
1	cpd4/HCT116	---	73.16	23.05	3.79	cell growth arrest@ G1
2	Cont.HCT116	---	59.37	33.81	6.82	---

s	code	conc	Apoptosis			Necrosis
			Total	Early	Late	
1	cpd4/HCT116	---	<b>27.65</b>	<b>4.63</b>	<b>15.81</b>	<b>7.21</b>
2	Cont.HCT116	---	<b>2.06</b>	<b>0.35</b>	<b>0.13</b>	<b>1.58</b>

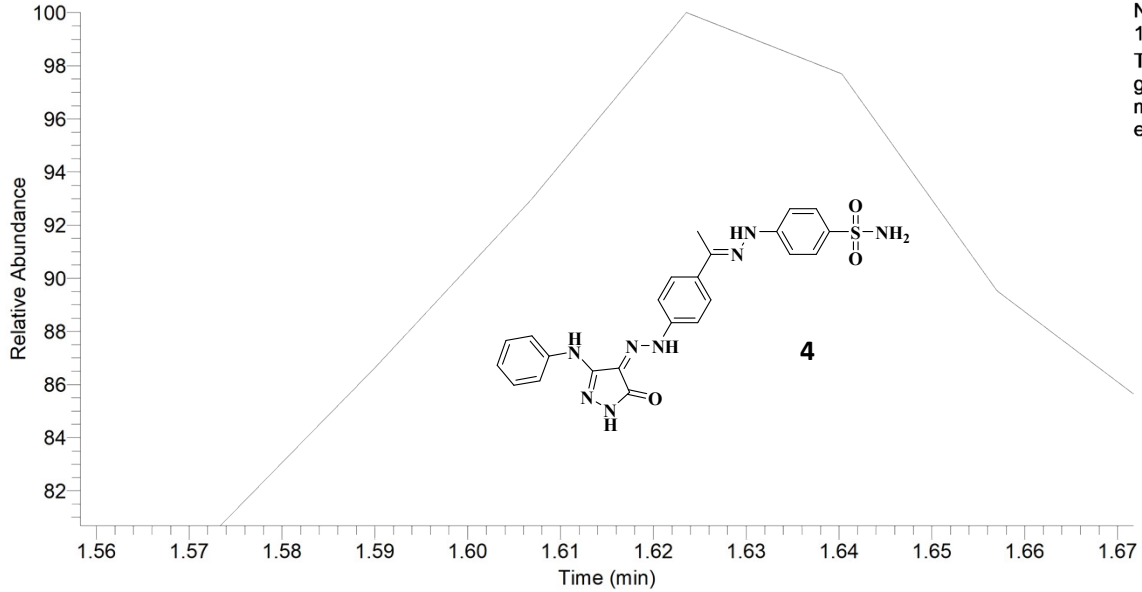
S51: Western Blot assay for compounds 4, 9



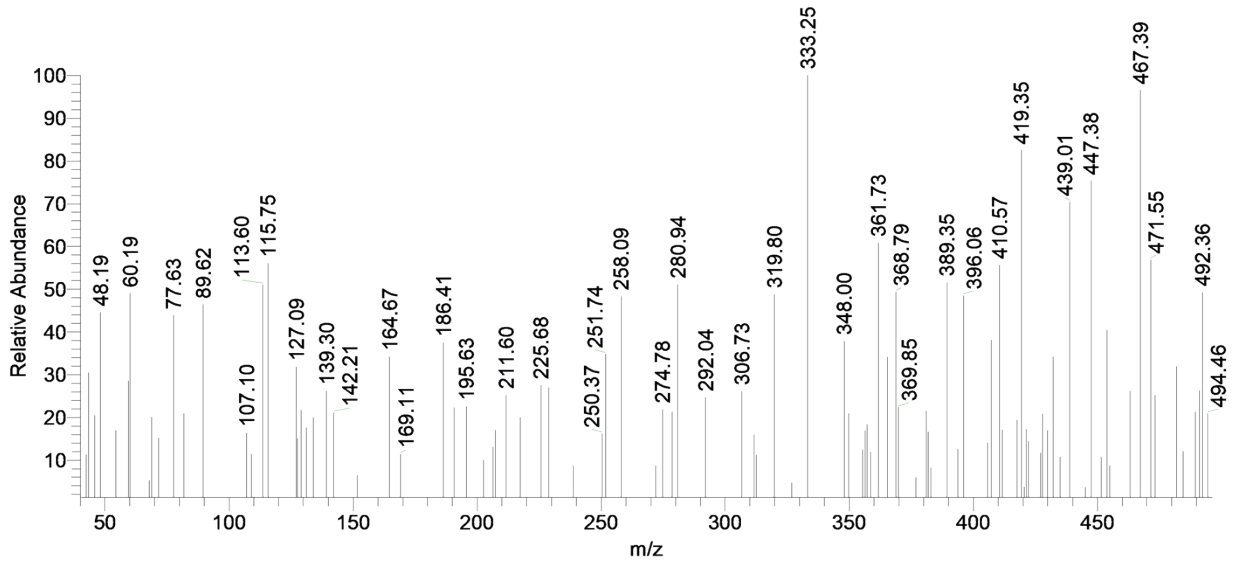
S52: Mass Results compound 4

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RT: 1.56 - 1.67 SM: 11B



ghada-mohamed-elhag-h #69-70 RT: 1.17-1.19 AV: 2 SB: 26 1.21-1.34, 0.87-1.14 NL: 1.90E2  
T: + c EI Full ms [40.00-1000.00]

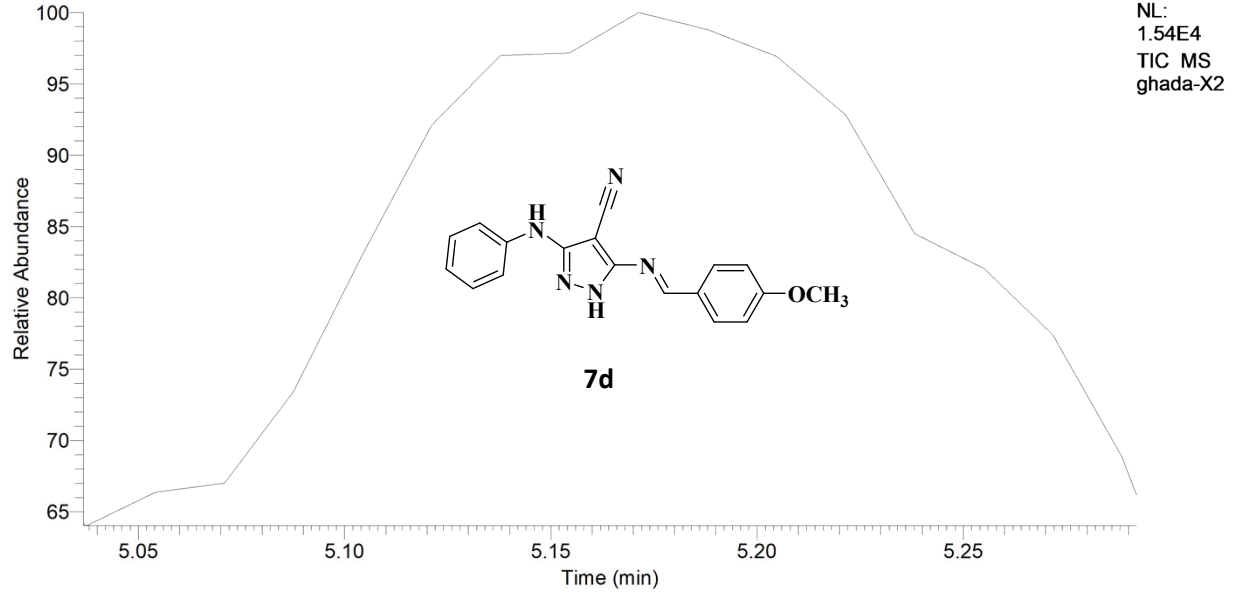




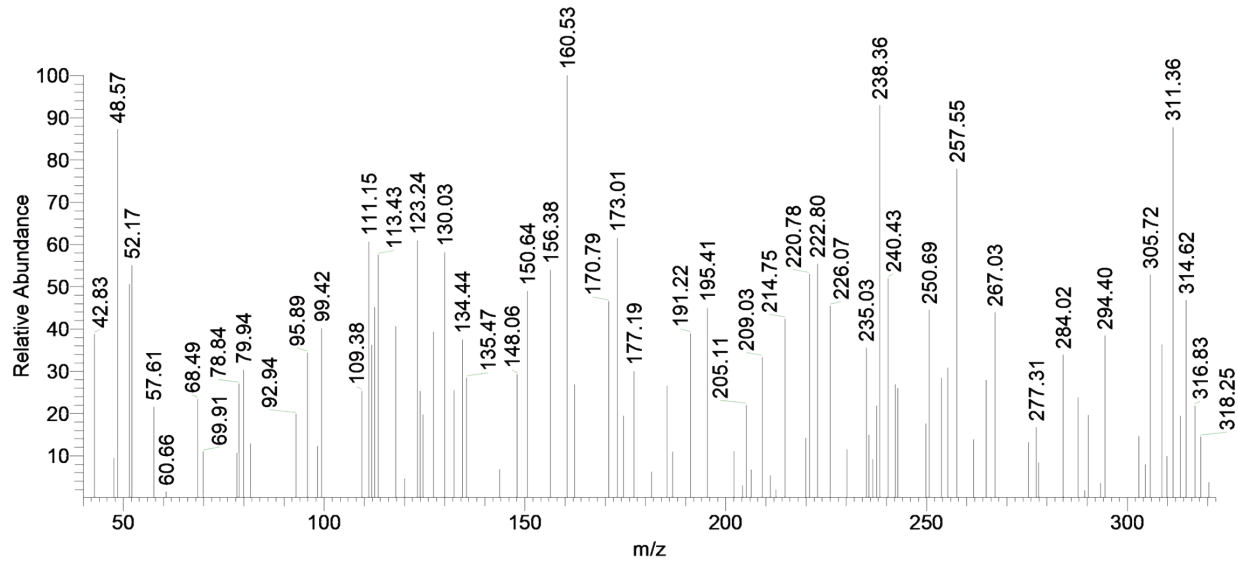
S53: Mass Results compound **7d**

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RCMB

RT: 5.04 - 5.29 SM: 11B



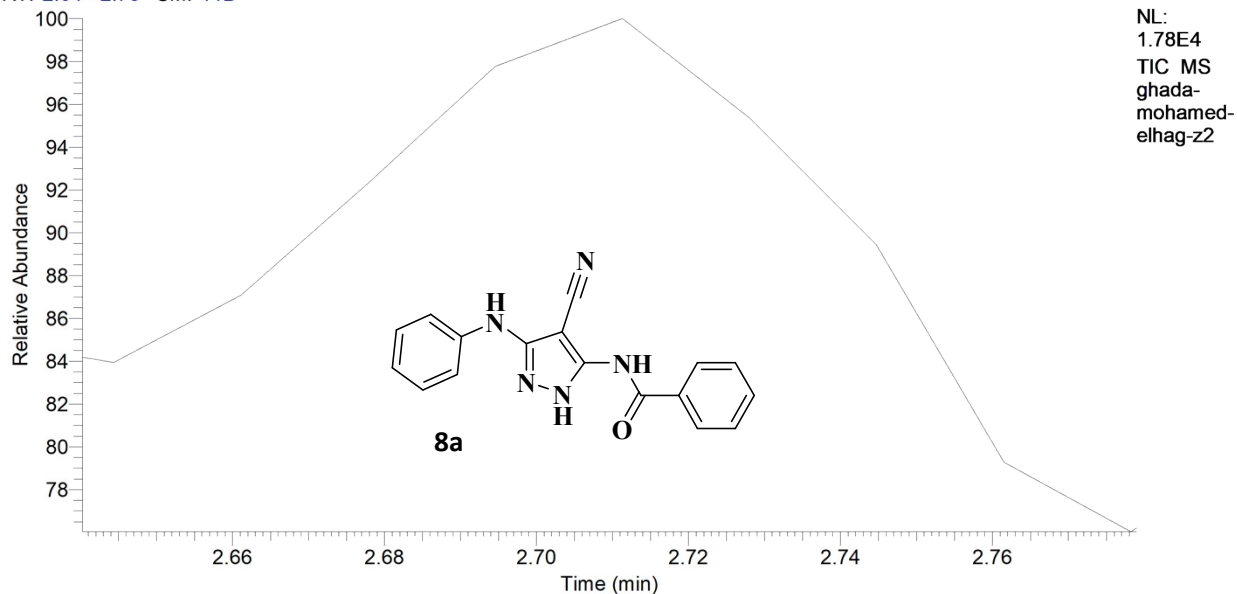
ghada-X2 #85-92 RT: 1.44-1.56 AV: 8 SB: 26 1.21-1.34, 0.87-1.14 NL: 5.14E1  
T: + c EI Full ms [40.00-1000.00]



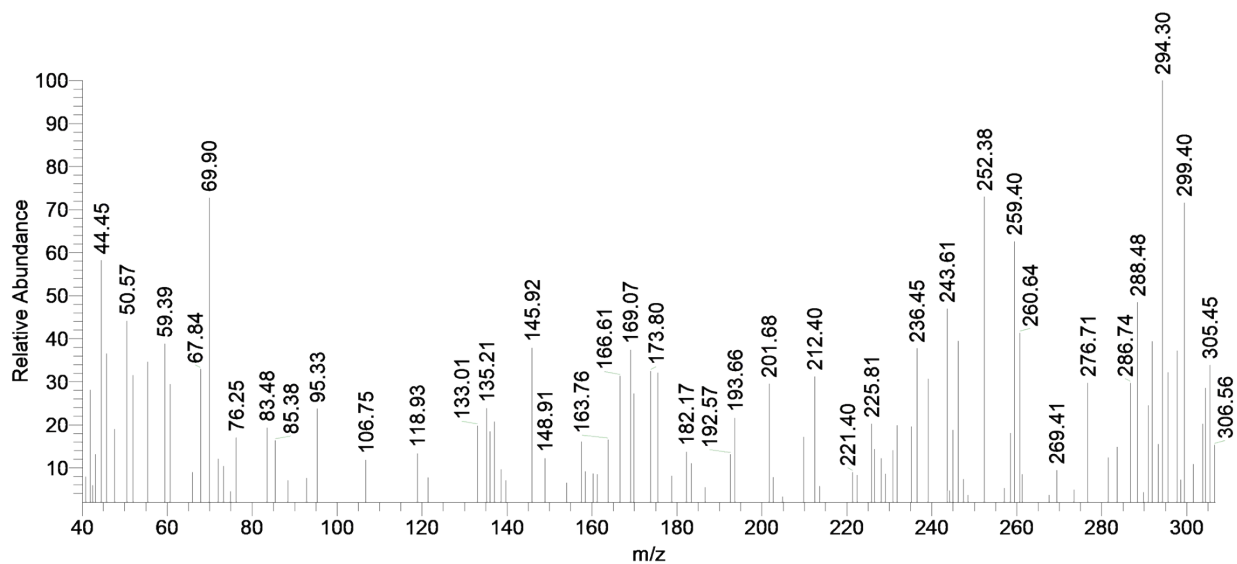
S54: Mass results compound **8a**

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RCMB

RT: 2.64 - 2.78 SM: 11B



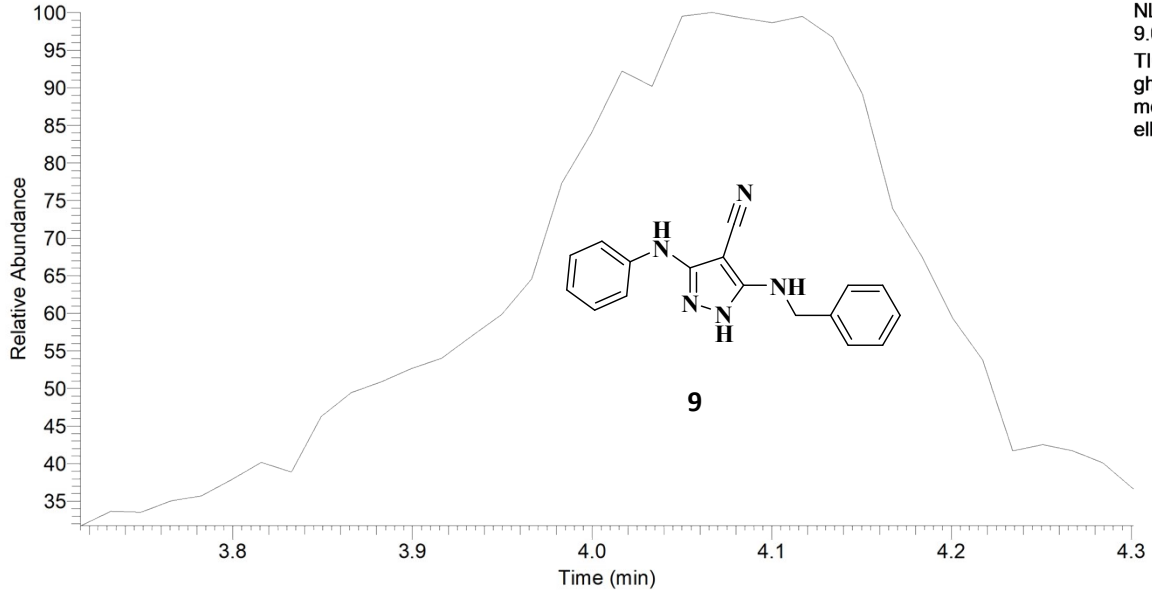
ghada-mohamed-elhag-z2 #216-220 RT: 3.63-3.70 AV: 5 SB: 26 1.21-1.34 , 0.87-1.14 NL: 1.45E2  
T: + c EI Full ms [40.00-1000.00]



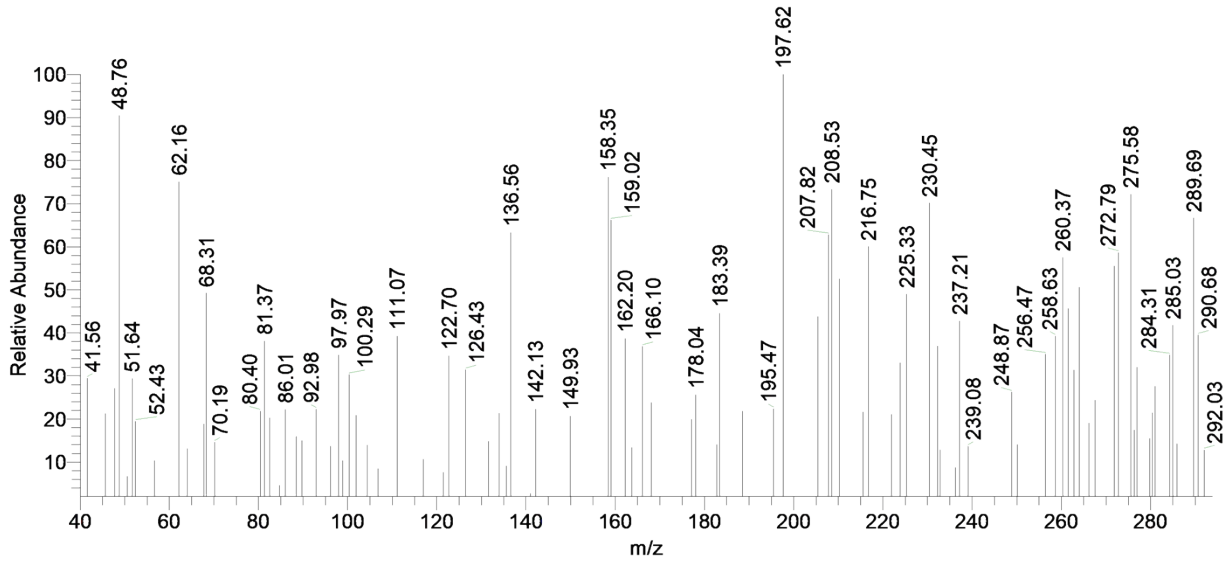
S55: Mass Results compound 9

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RT: 3.71 - 4.30 SM: 11B



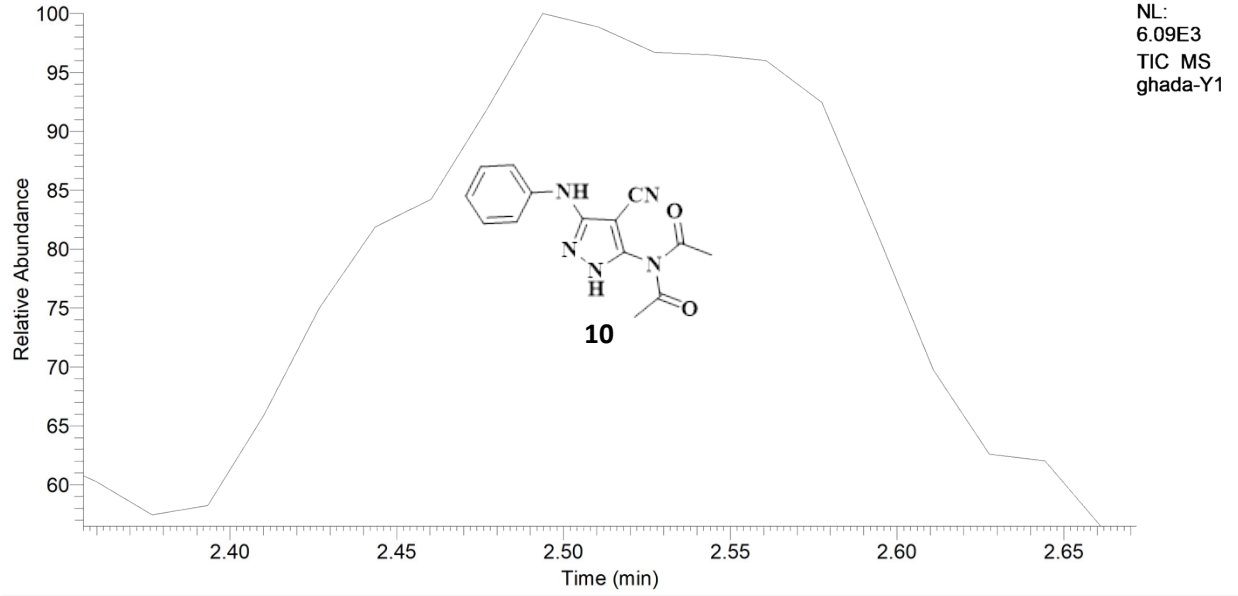
ghada-mohamed-elhag0-z1 #323-324 RT: 5.42-5.44 AV: 2 SB: 26 1.21-1.34 , 0.87-1.14 NL: 1.60E2  
T: + c EI Full ms [40.00-1000.00]



S56: Mass Results compound **10**

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RCMB

RT: 2.36 - 2.67 SM: 11B



ghada-Y1 #159-163 RT: 2.68-2.74 AV: 5 SB: 26 1.21-1.34 , 0.87-1.14 NL: 6.51E1  
T: + c EI Full ms [40.00-1000.00]

