

Design, synthesis, *in vitro*, and *in silico* studies on promising α -glucosidase inhibitors based on quinazolinone-thiophene scaffold

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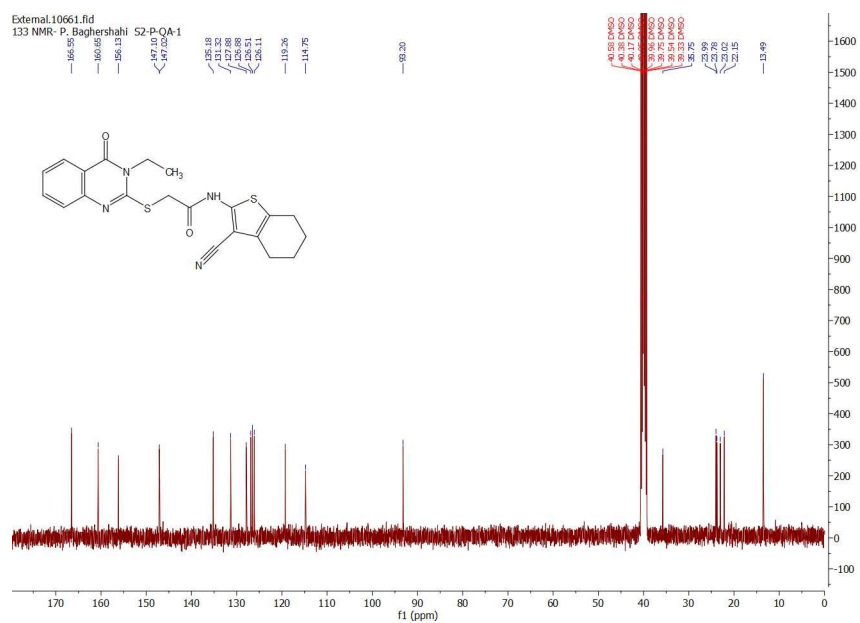
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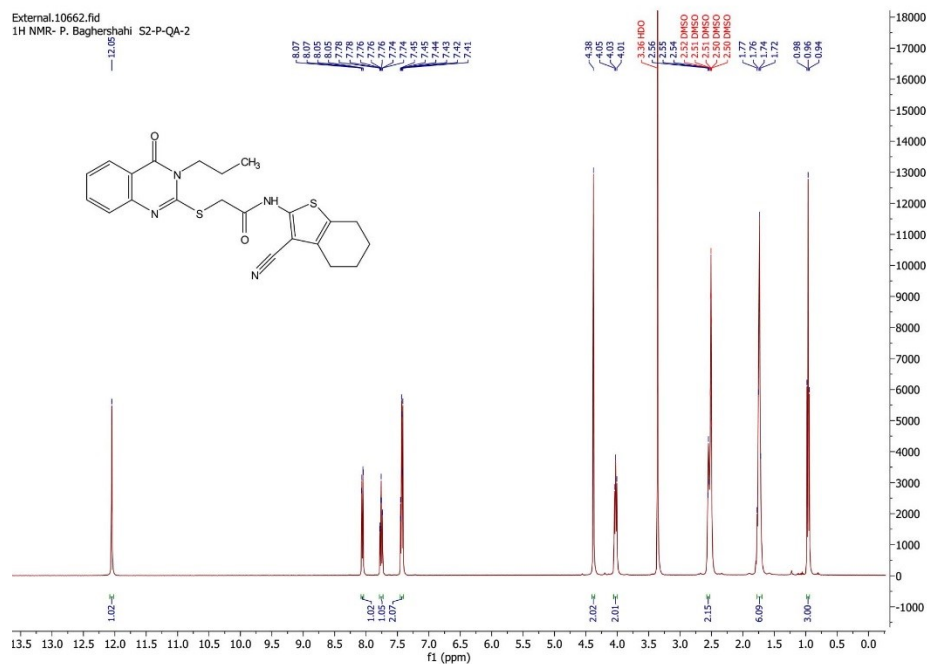
E-mail addresses: shjavan@iust.ac.ir (S. Javanshir), momahdavi@tums.ac.ir (M. Mahdavi).

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1H NMR- P. Baghershahi S2-P-QA-1

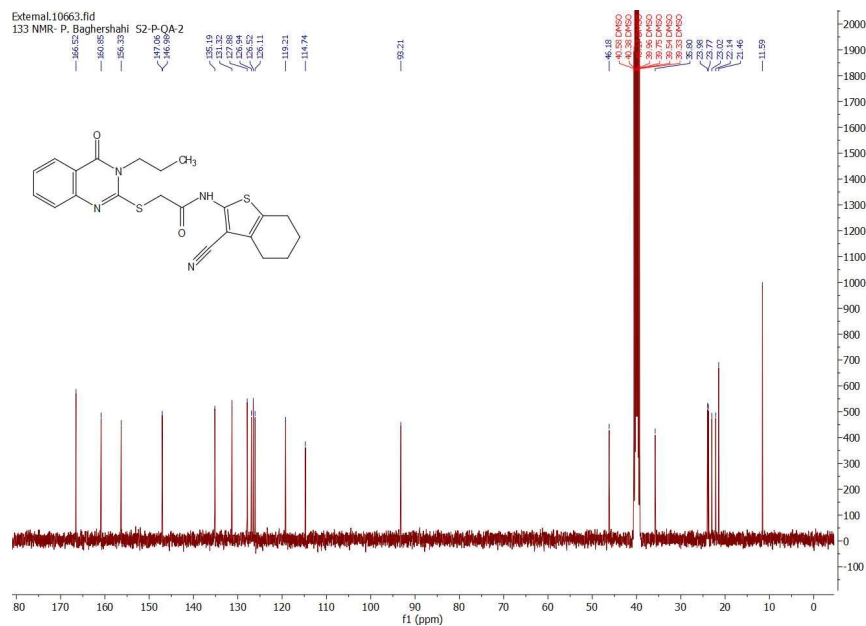


N-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophen-2-yl)-2-((4-oxo-3-propyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**14b**)

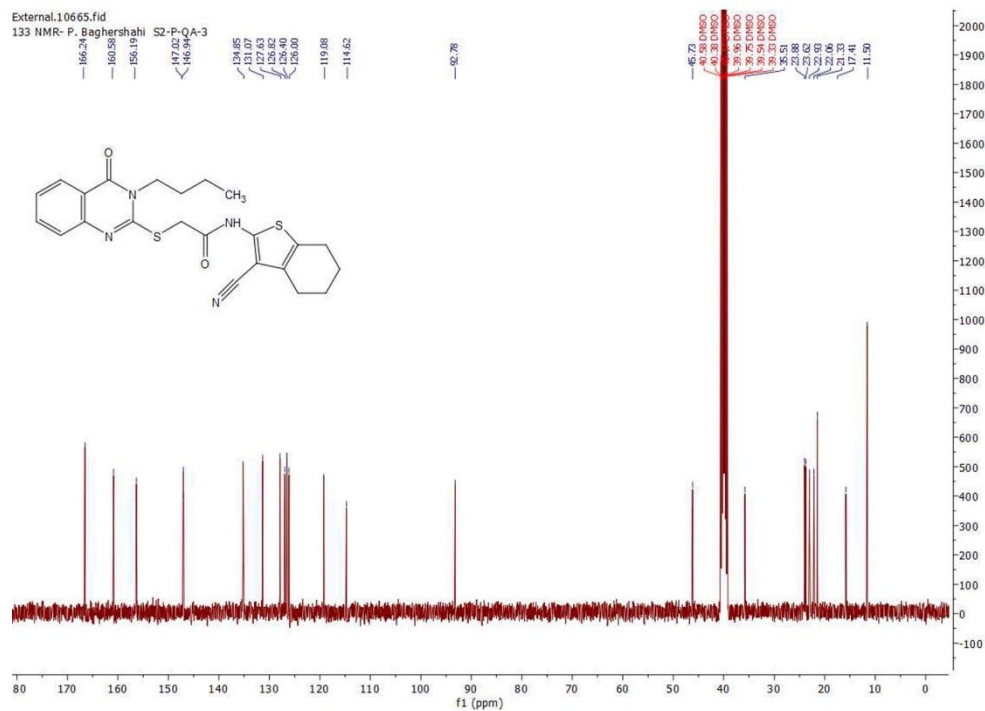
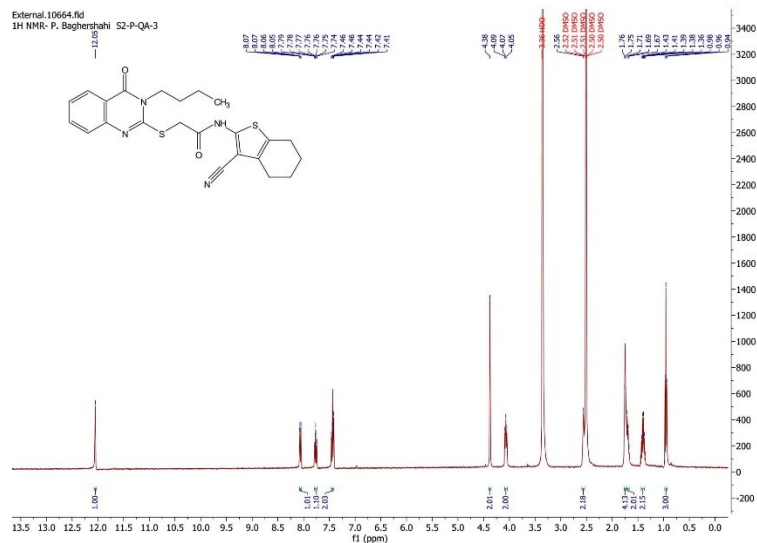
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1H NMR- P. Baghersahhi S2-P-QA-2



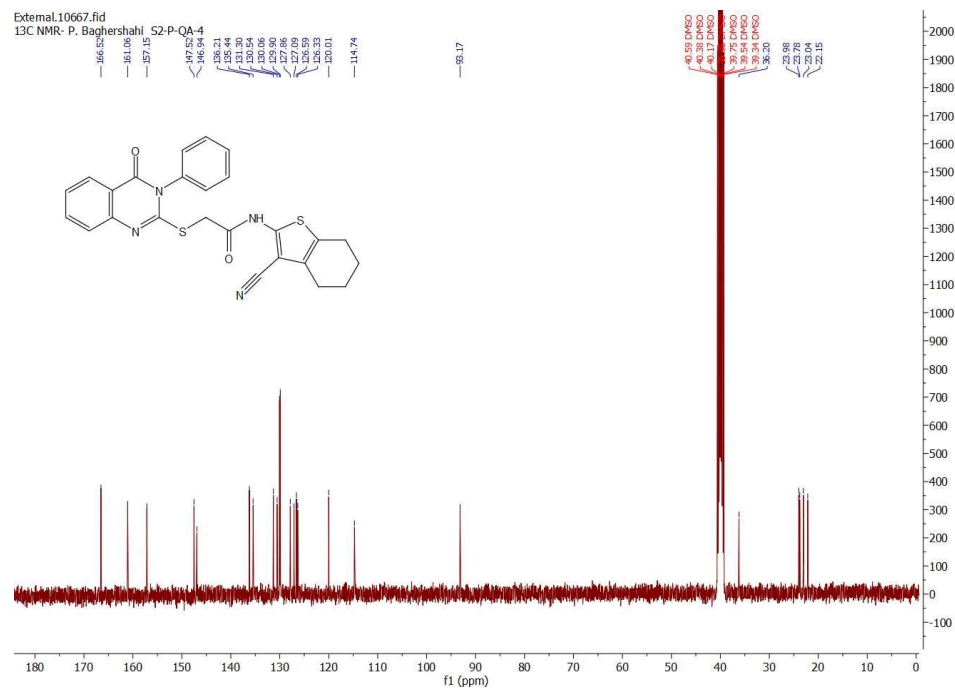
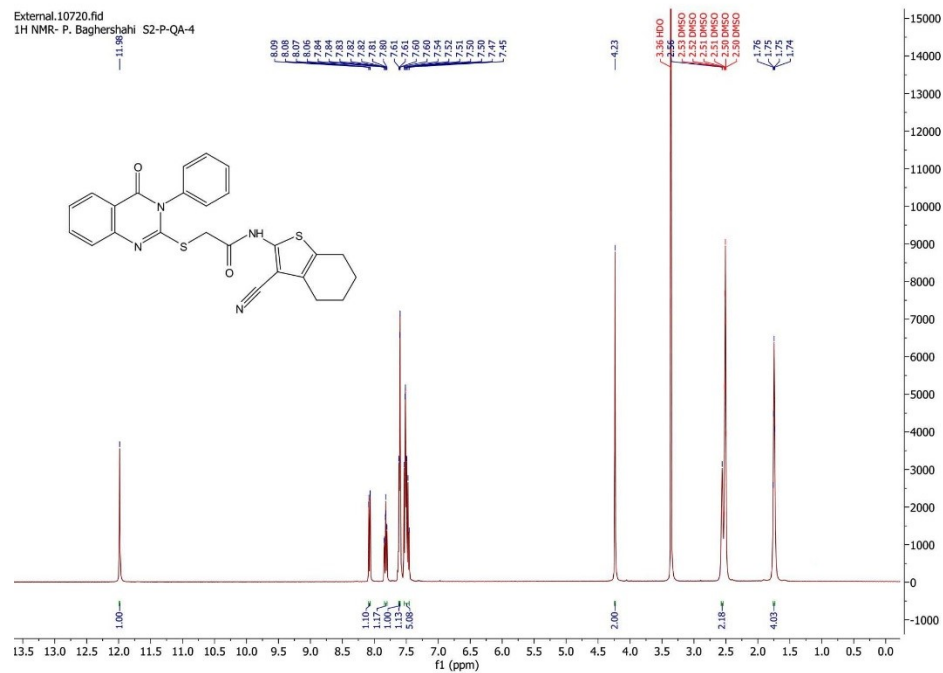
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13C NMR- P. Baghersahhi S2-P-QA-2



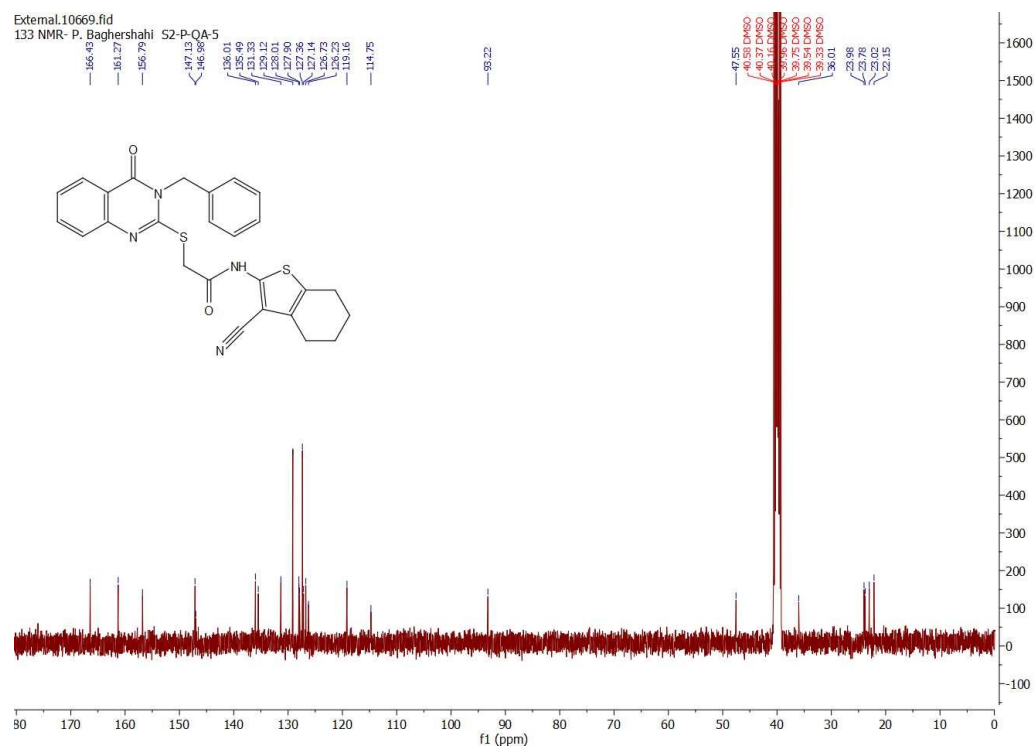
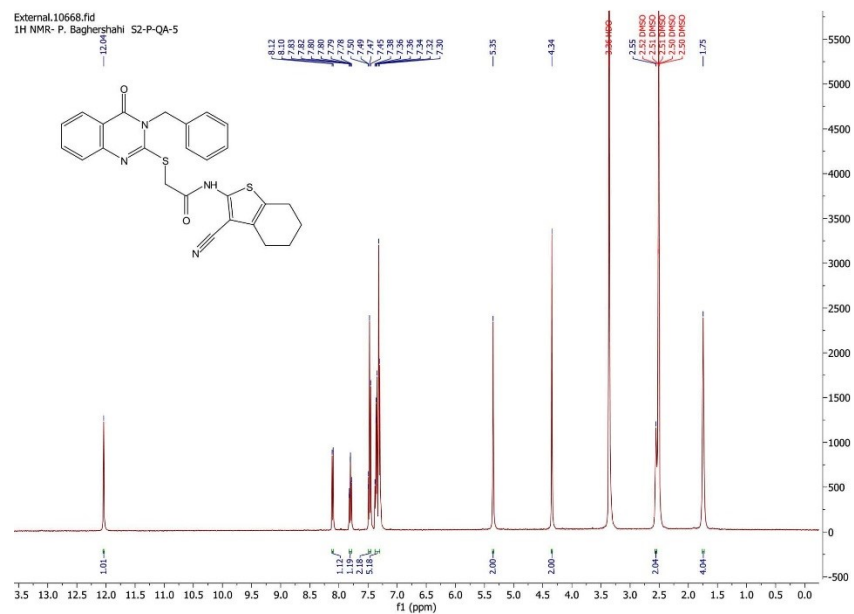
2-((3-butyl-4-oxo-3,4-dihydroquinazolin-2-yl)thio)-N-(3-cyano-4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl)acetamide (**14c**)

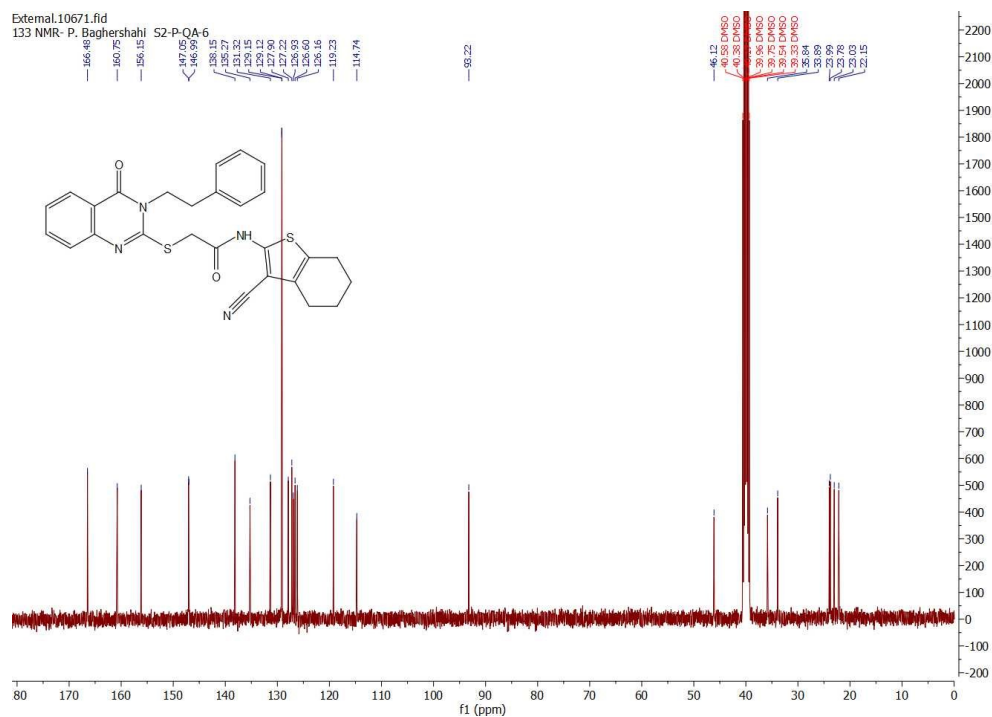


N-(3-cyano-4,5,6,7-tetrahydrobenzo[*b*]thiophen-2-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**14d**)

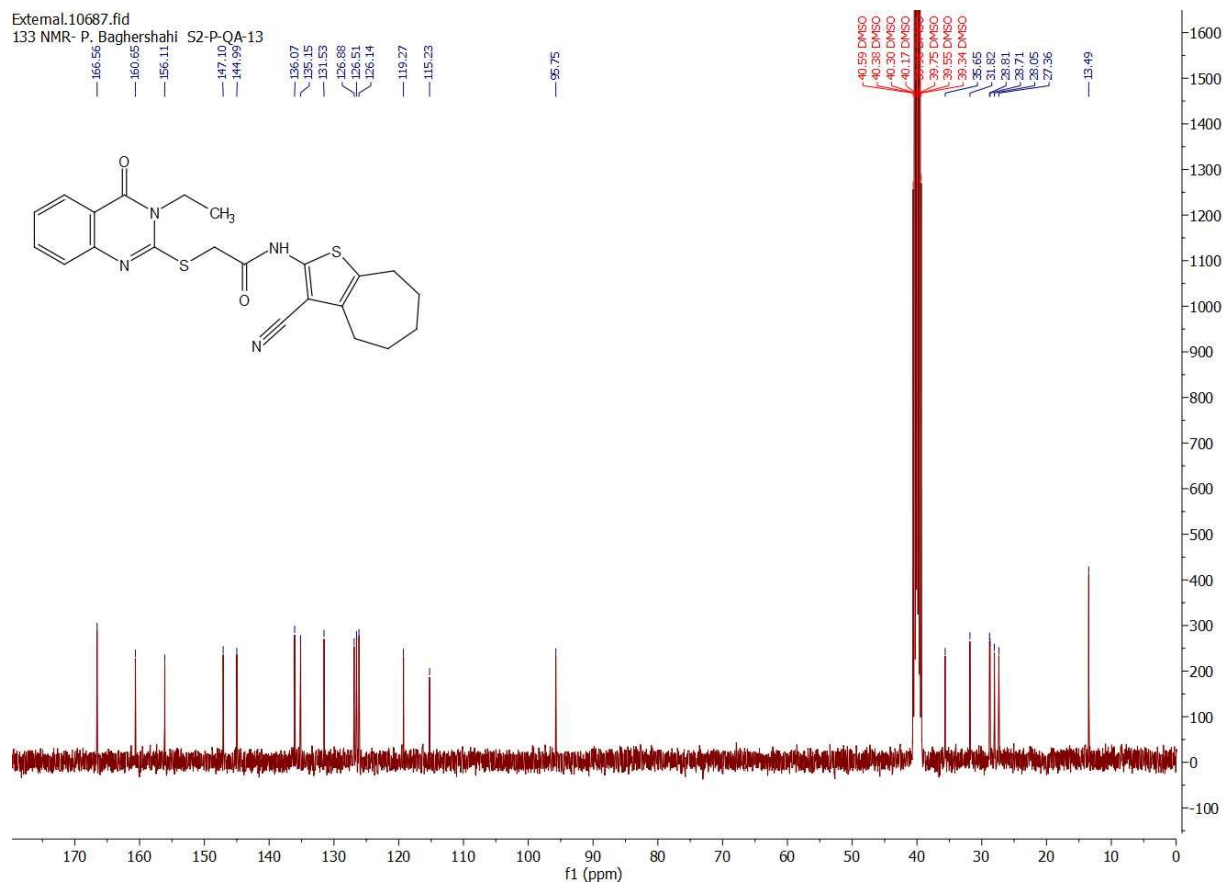
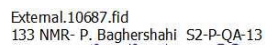


2-((3-benzyl-4-oxo-3,4-dihydroquinazolin-2-yl)thio)-N-(3-cyano-4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl)acetamide (**14e**)

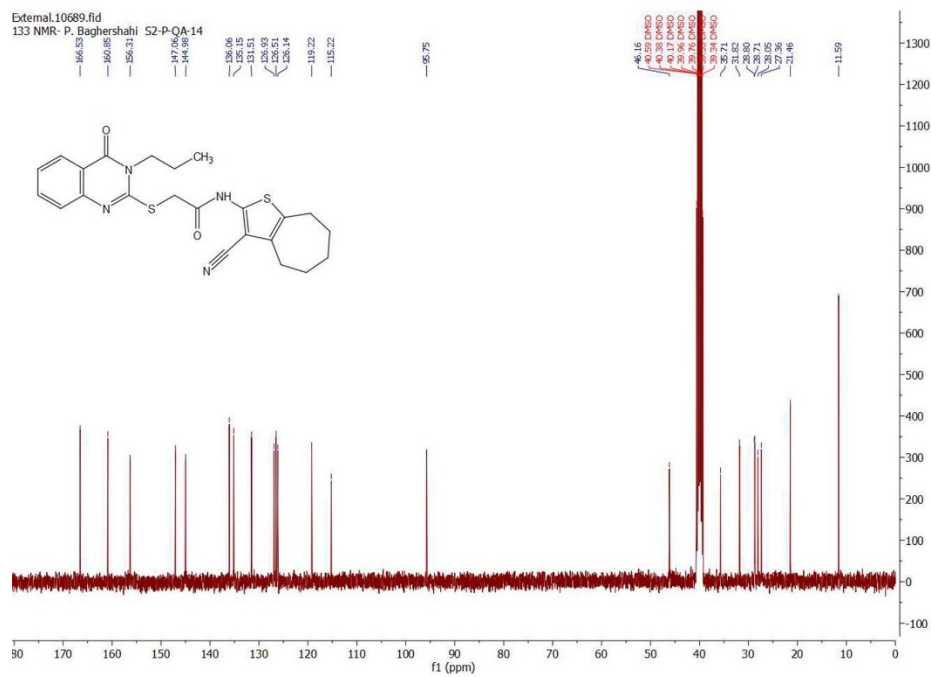
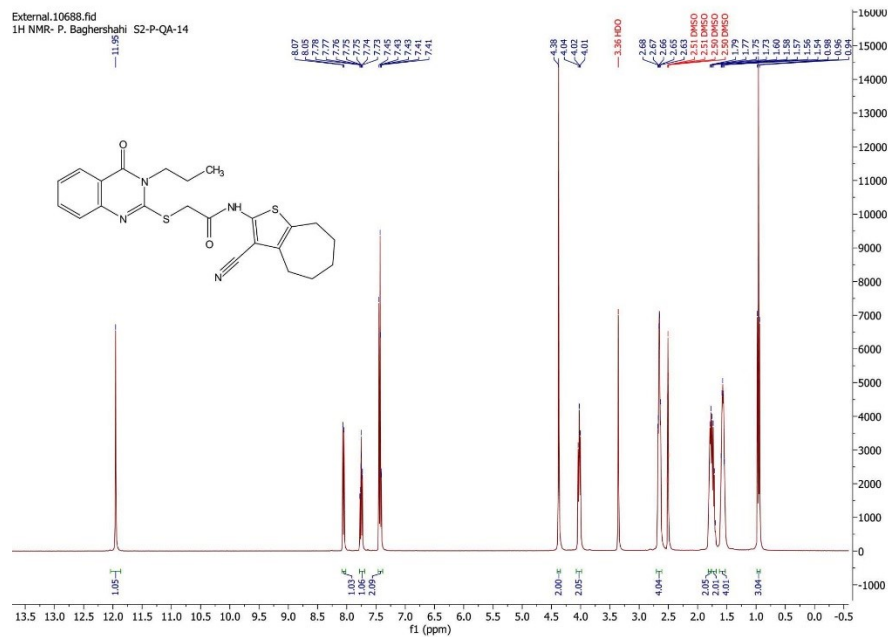


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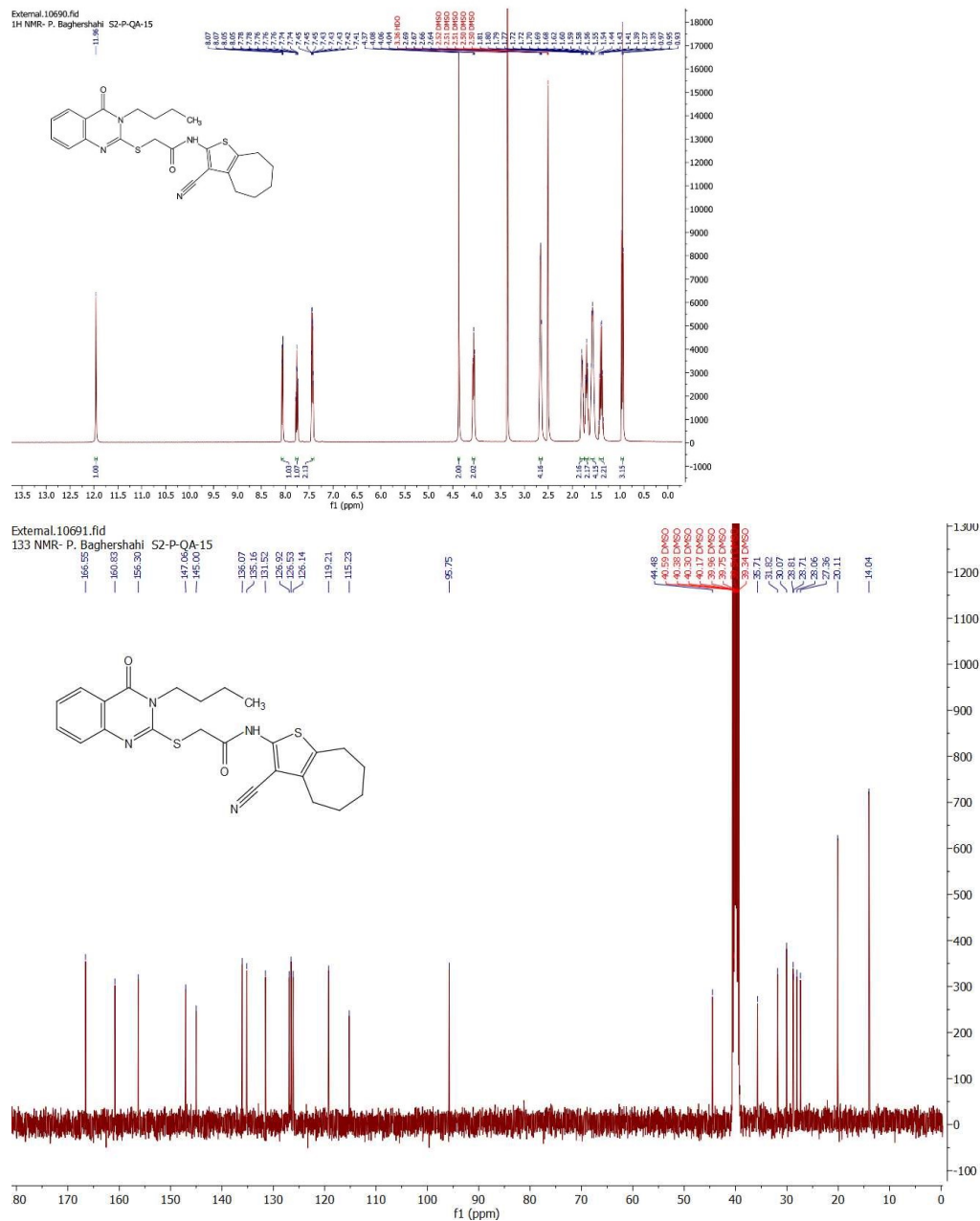
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1H NMR- P. Baghershahi S2-P-QA-13



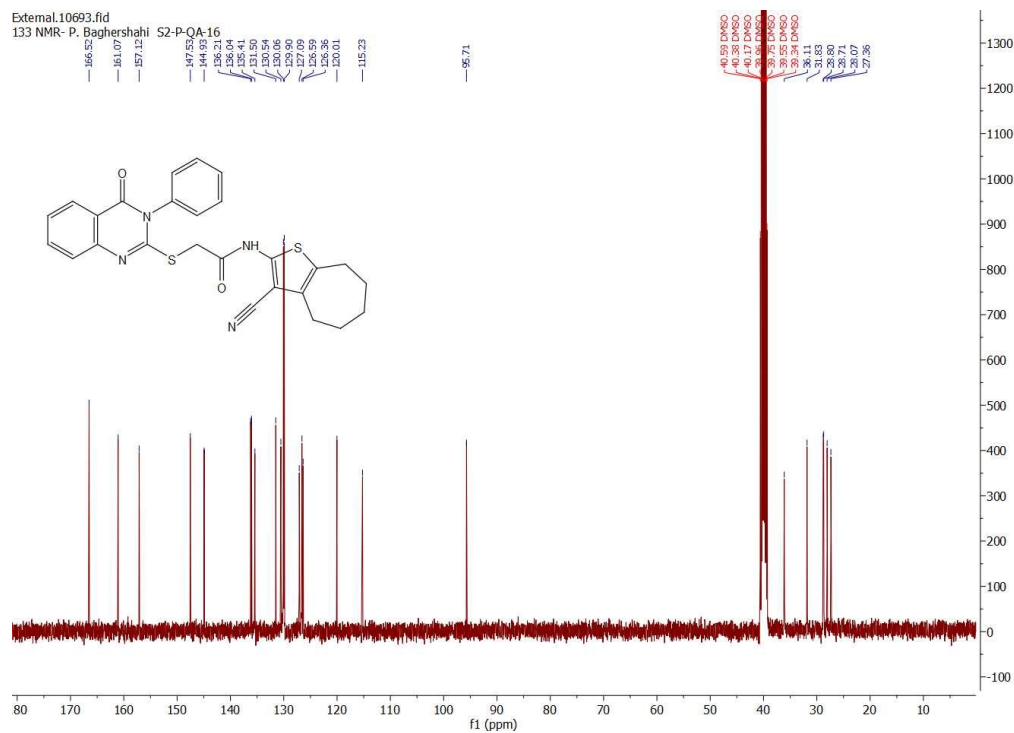
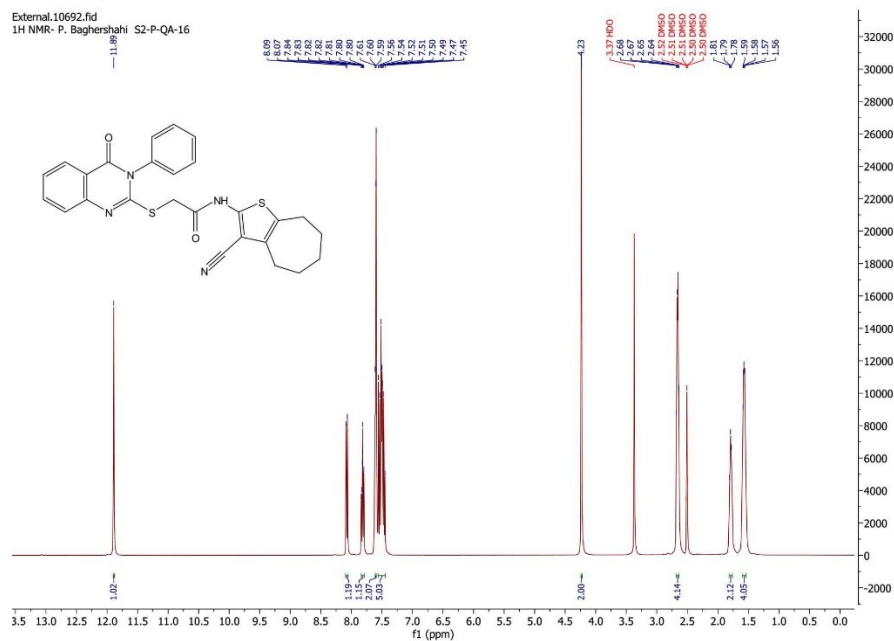
N-(3-cyano-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophen-2-yl)-2-((4-oxo-3-propyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**15b**)



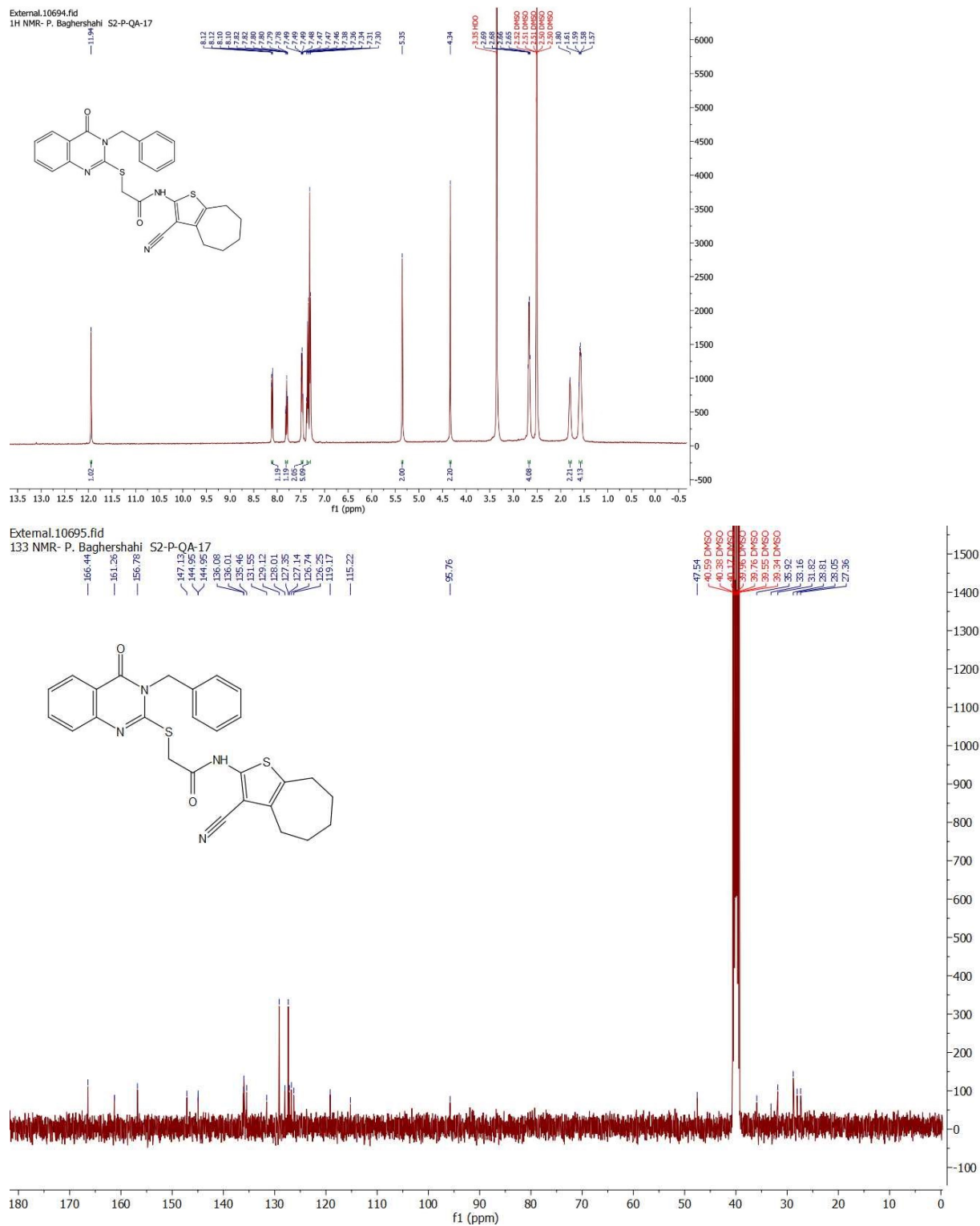
2-((3-butyl-4-oxo-3,4-dihydroquinazolin-2-yl)thio)-N-(3-cyano-5,6,7,8-tetrahydro-4H-cyclohepta[b]thiophen-2-yl)acetamide (**15c**)

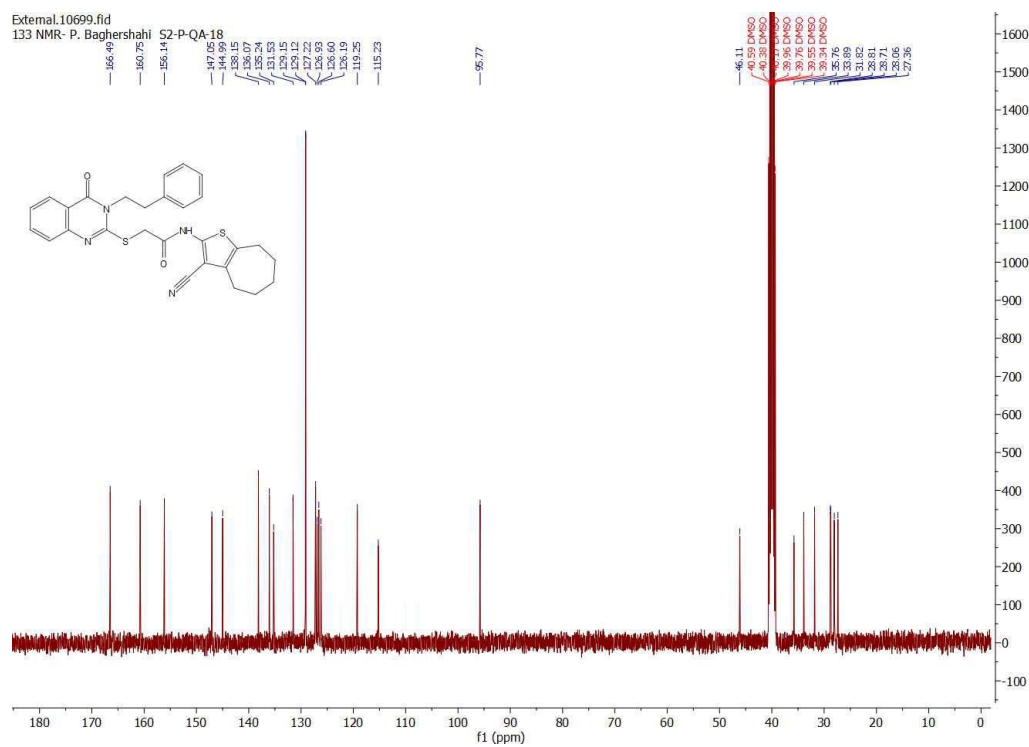


N-(3-cyano-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophen-2-yl)-2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamide (**15d**)



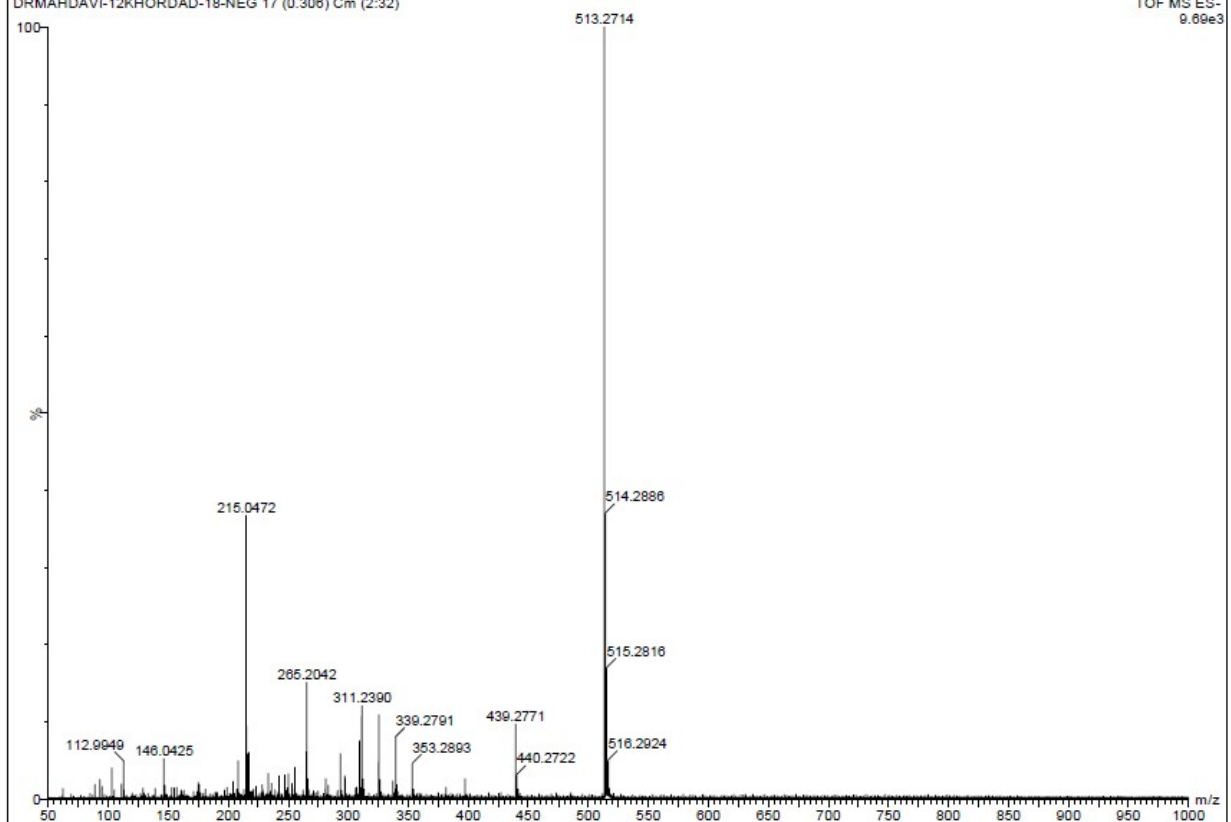
2-((3-benzyl-4-oxo-3,4-dihydroquinazolin-2-yl)thio)-N-(3-cyano-5,6,7,8-tetrahydro-4H-cyclohepta[b]thiophen-2-yl)acetamide (**15e**)



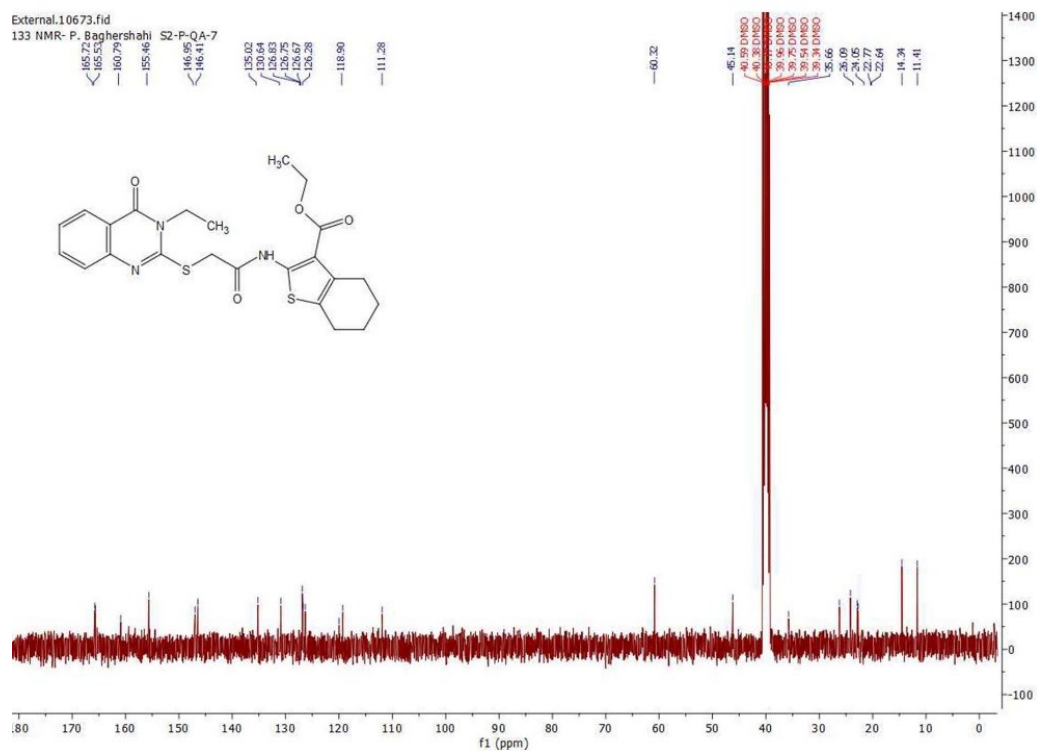
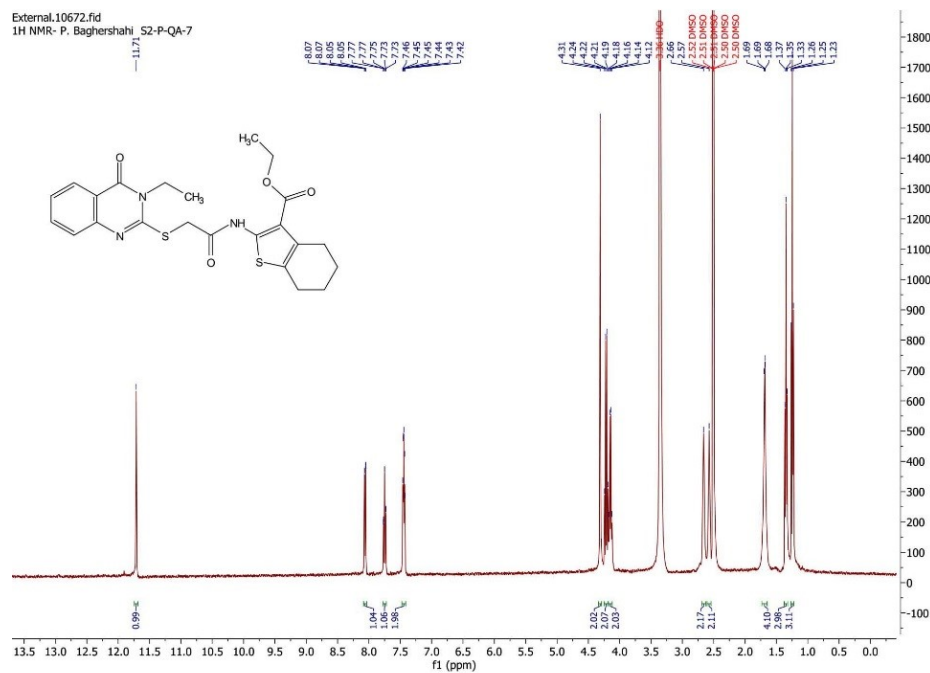
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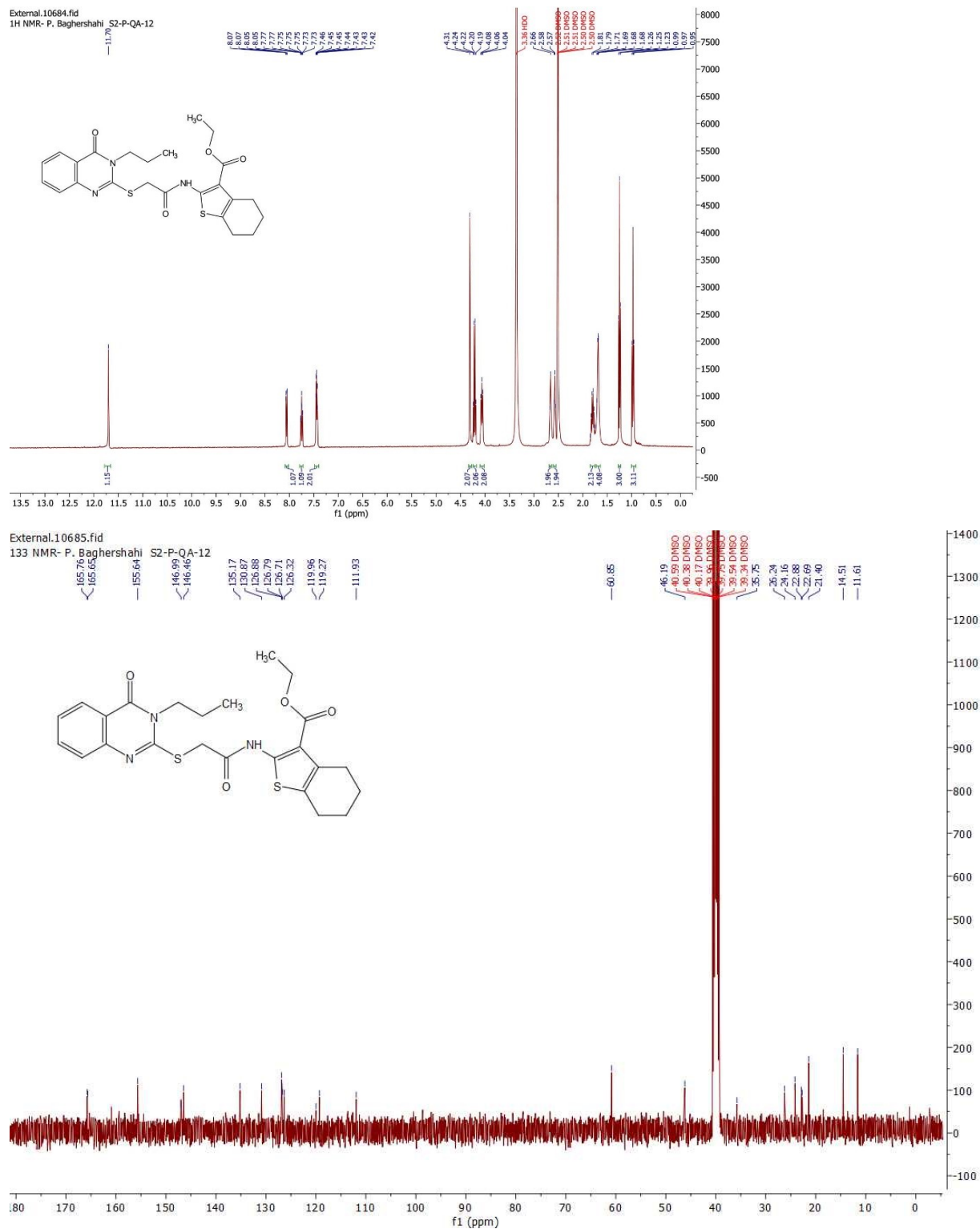
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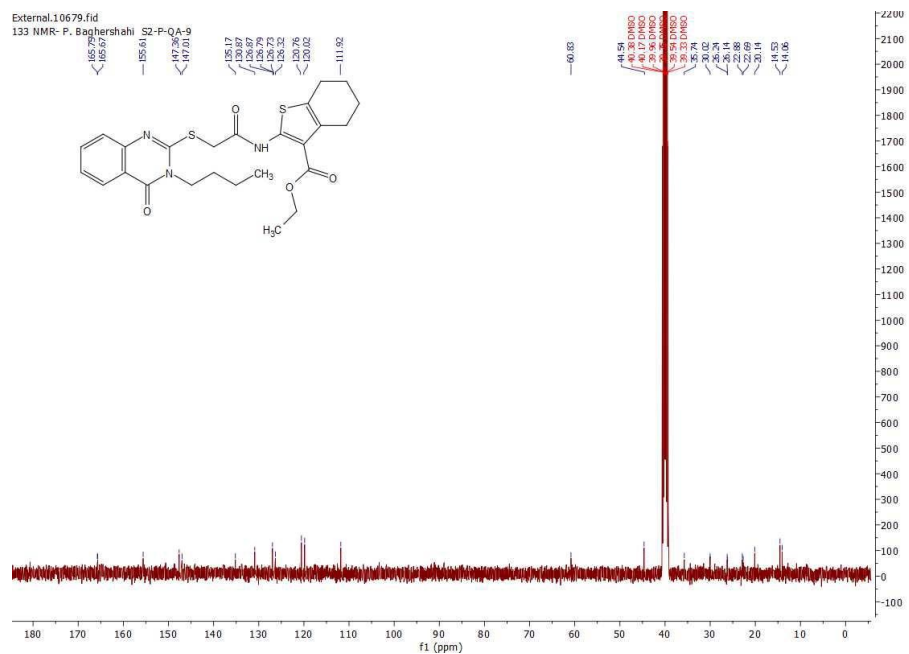
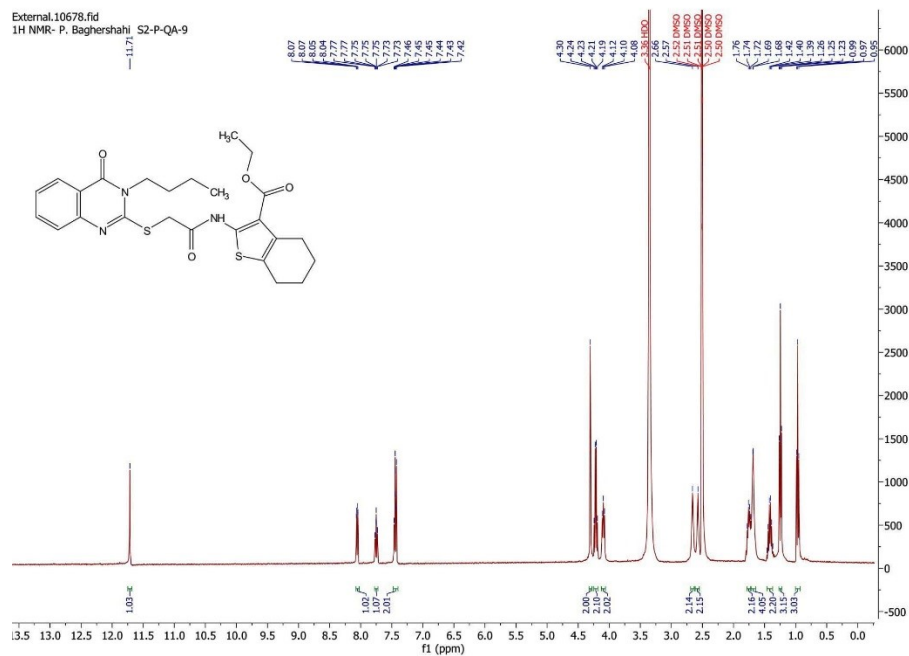
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1H NMR- P. Baghersshahi S2-P-QA-7



Ethyl 2-((4-oxo-3-propyl-3,4-dihydroquinazolin-2-yl)thio)acetamido)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (19b)

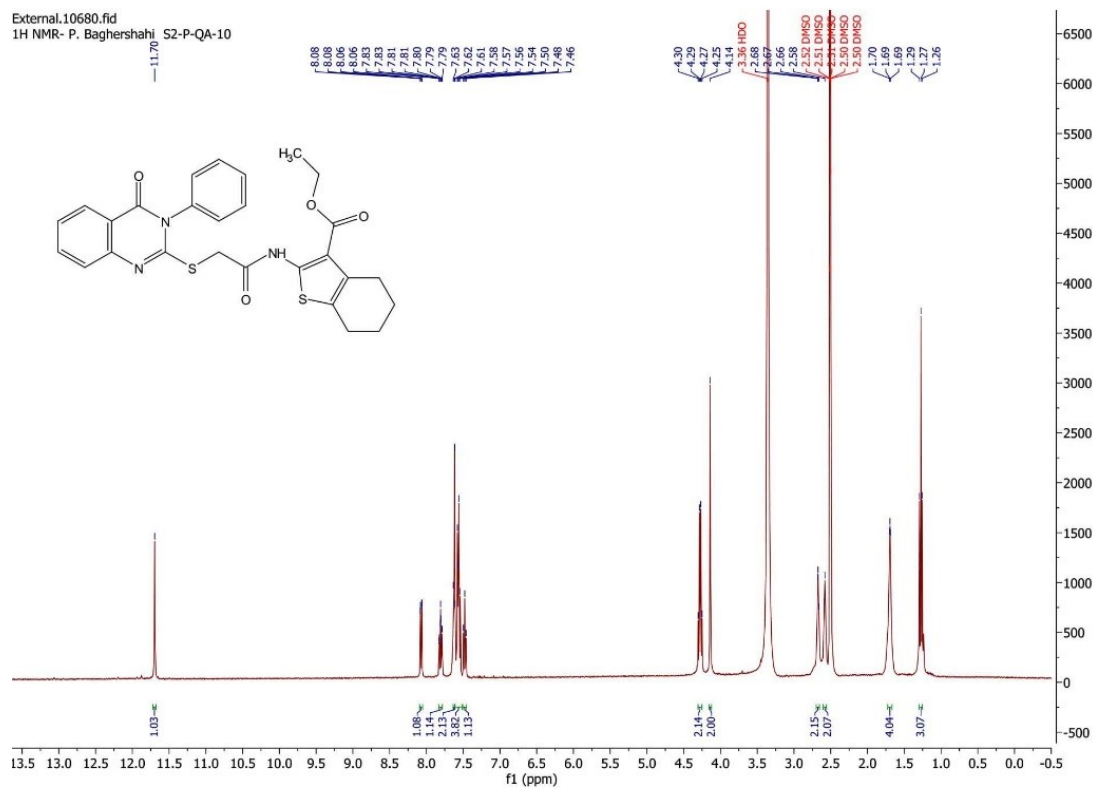


Ethyl 2-((3-butyl-4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetamido)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (19c)

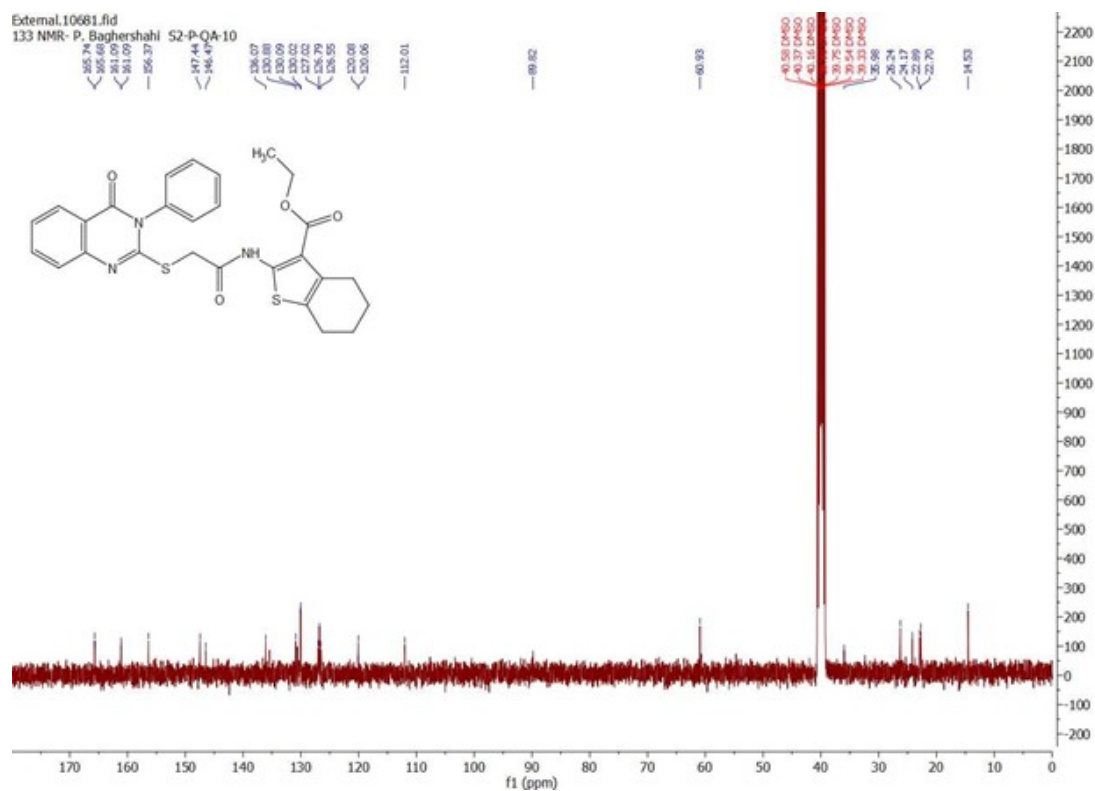


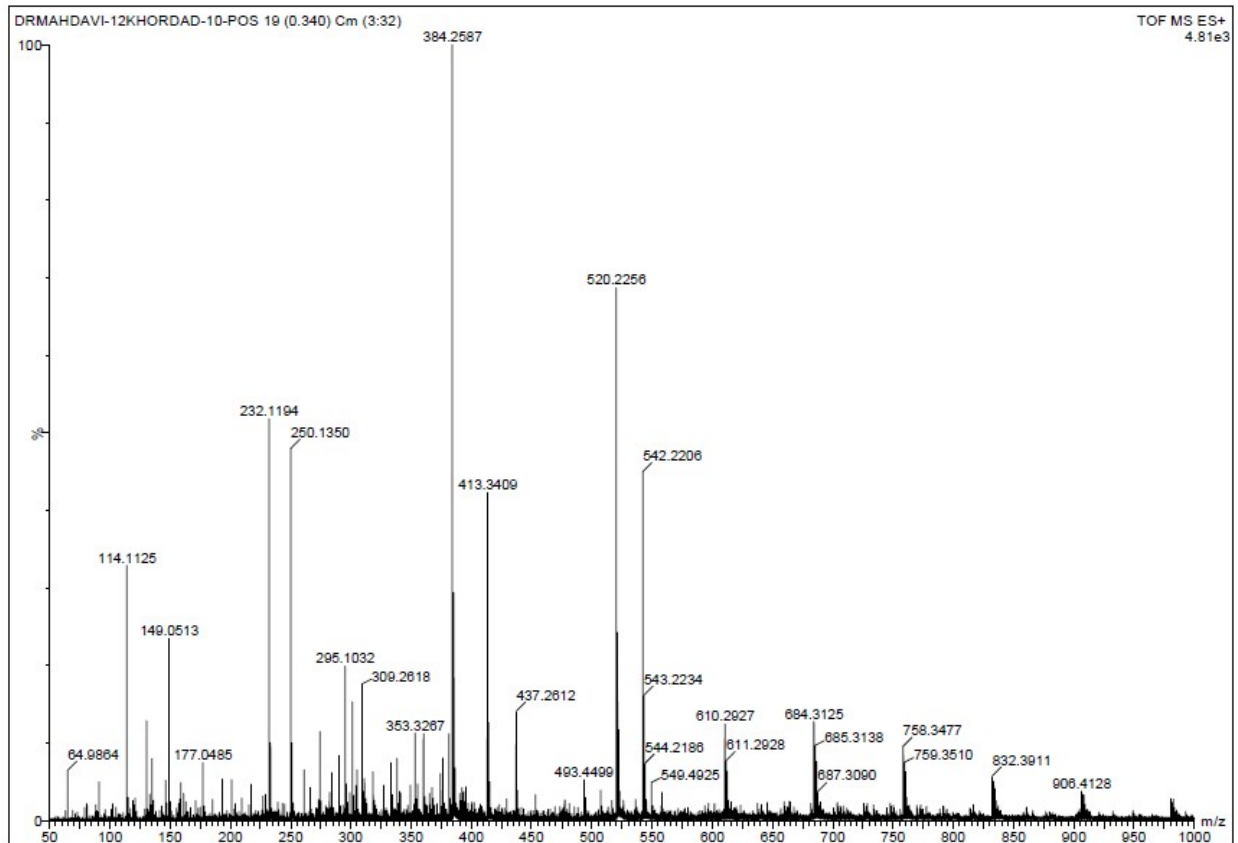
Ethyl 2-((4-oxo-3-phenyl-3,4-dihydroquinazolin-2-yl)thio)acetamido)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (19d)

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1H NMR- P. Baghershahi S2-P-QA-10

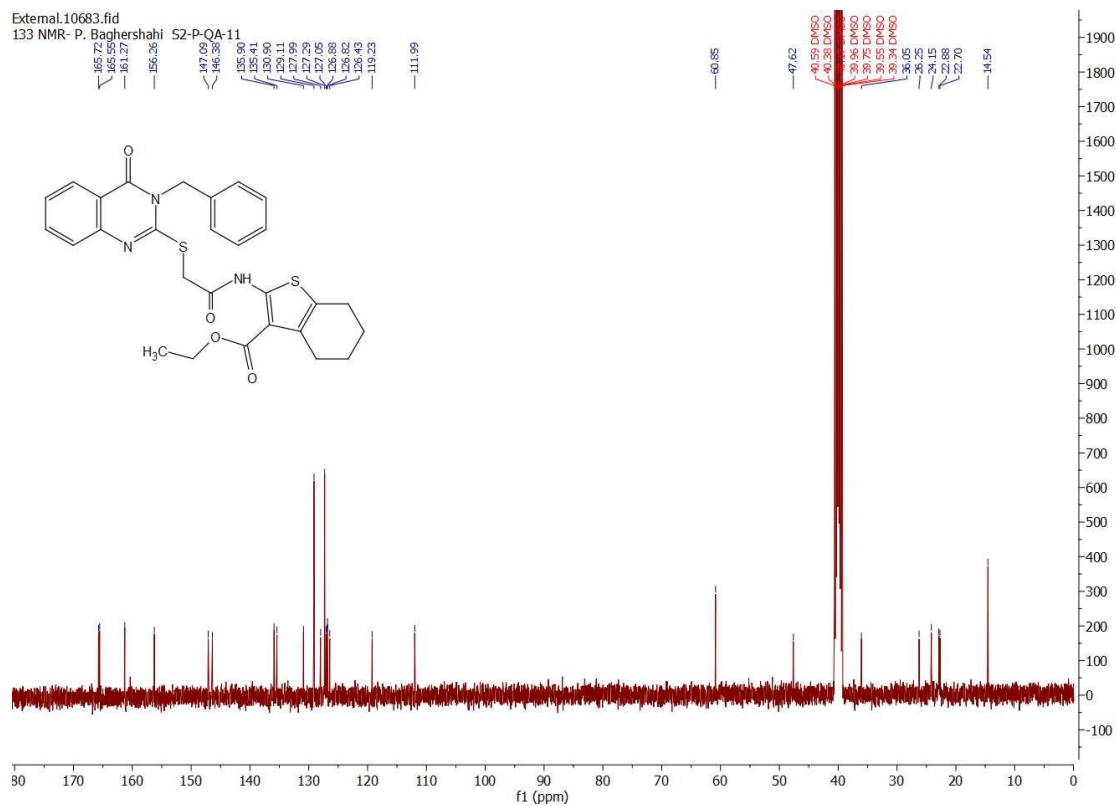
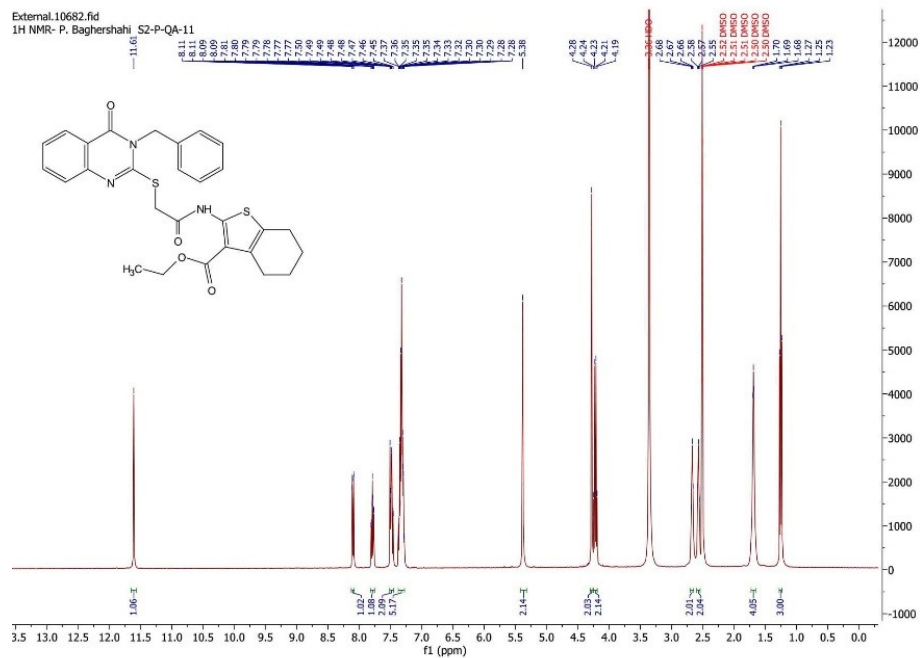


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133 NMR- P. Baghershahi S2-P-QA-10



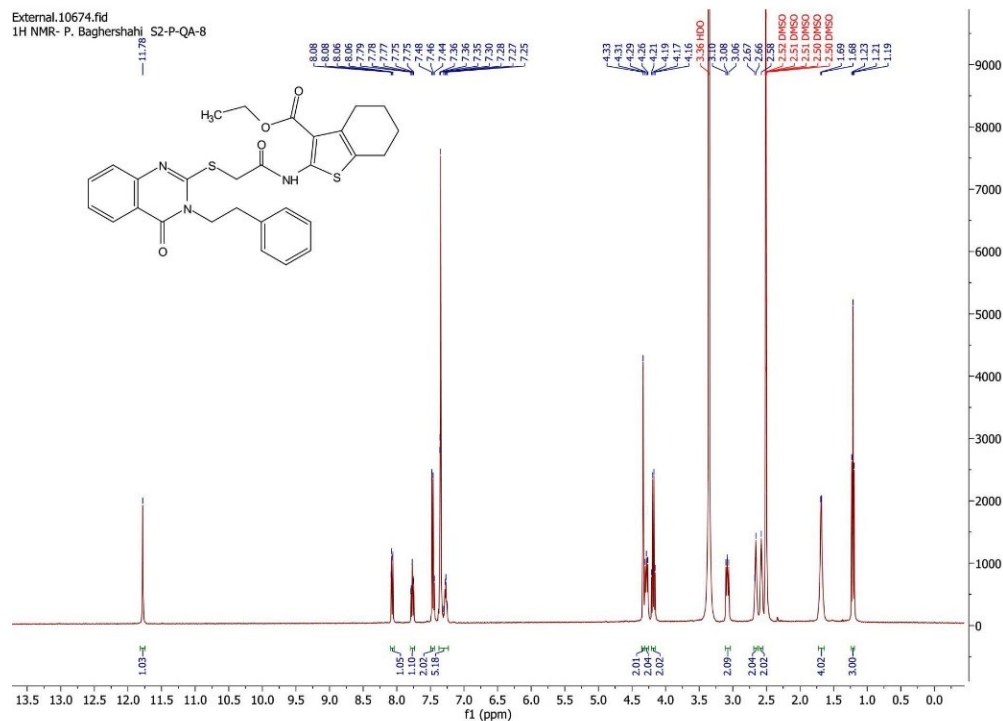


Ethyl 2-((3-benzyl-4-oxo-3,4-dihydroquinazolin-2-yl)thio)acetamido)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (19e)

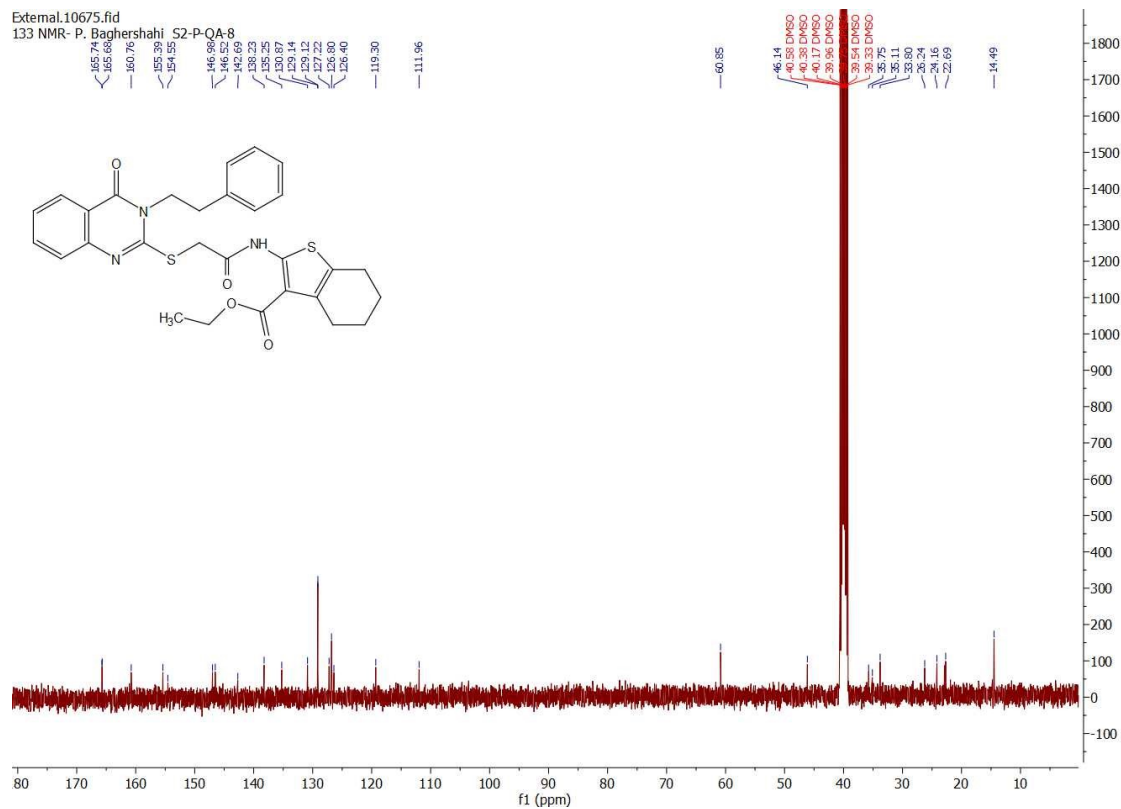


Ethyl 2-((4-oxo-3-phenethyl-3,4-dihydroquinazolin-2-yl)thio)acetamido)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (19f)

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1H NMR- P. Bagher Shahi S2-P-QA-8

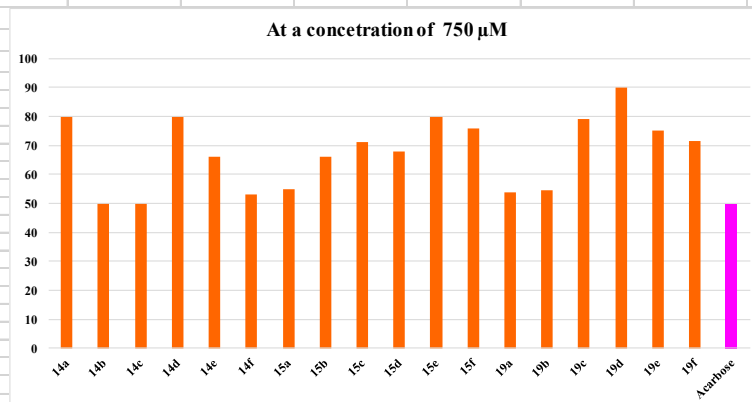


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133 NMR- P. Bagher Shahi S2-P-QA-8

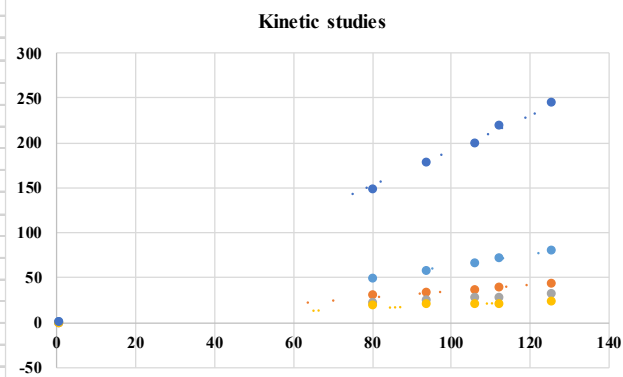


Biological data

Compound	Inhibition (%)
14a	80
14b	50
14c	50
14d	80
14e	66
14f	53
15a	55
15b	66
15c	71
15d	68
15e	80
15f	76
19a	54
19b	54.5
19c	79
19d	90
19e	75
19f	71.4
Acarbouse	50

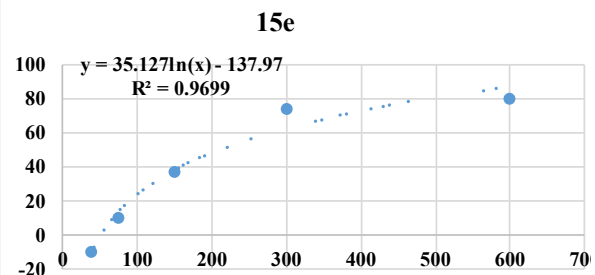


Conc.	1/V0	1/V1	1/V2	1/V3	1/V4
0.5	80.21	93.784	106.124	112.294	125.4
0.25	49.36	57.998	66.636	71.572	80.16064
0.125	30.85	33.318	35.786	39.1746	43.87556
0.083333	22.43636	24.68	27.148	28.382	31.78784
0.0625	19.90323	20.4844	20.361	20.978	23.49536
1	149	177.8	199.7	219.8	245.4



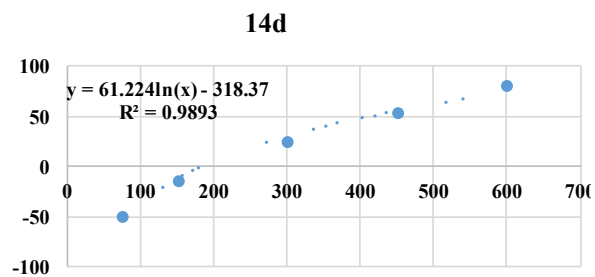
15e

Conc.	OD Blnak	OD Total	OD Final	In (%)
600	0.029	0.229	0.2	80
300	0.09	0.509	0.419	73.481013
150	0.06	1.06	1	36.708861
75	0.04	1.24	1.2	10
37.5	0.098	2.078	1.98	-10
IC50				210.81523



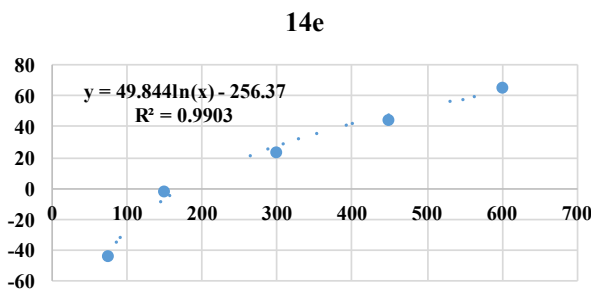
14d

Conc.	OD Blnak	OD Total	OD Final	In (%)
600	0.14	0.34	0.2	80
450	0.1	0.7	0.7	54
300	0.045	1.245	1.2	24.050633
150	0.078	1.878	1.8	-13.92405
75	0.012	2.012	2	-50
IC50				410.40778



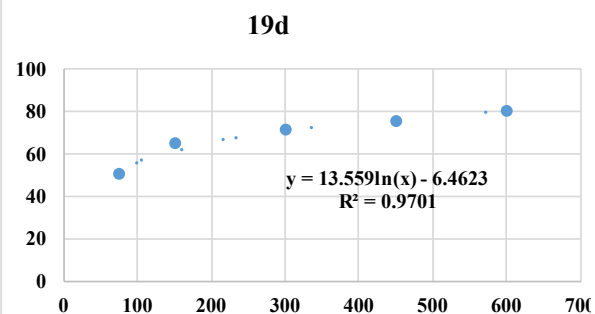
14e

Conc.	OD Blnak	OD Total	OD Final	In (%)
600	0.03	0.37	0.34	66
450	0.05	0.7	1	45
300	0.023	1.223	1.2	24.050633
150	0.012	1.612	1.6	-1.265823
75	0.05	2.05	2	-43
IC50				469.65953



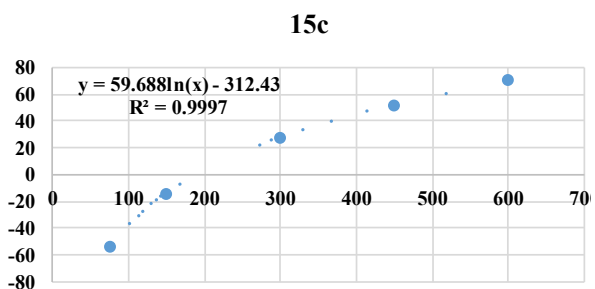
19d

Conc.	OD Blnak	OD Total	OD Final	In (%)
600	0.11	0.31	0.2	80
450	0.102	0.7	0.5	75
300	0.06	0.51	0.45	71.518987
150	0.045	0.605	0.56	64.556962
75	0.06	0.66	0.6	50
IC50				63.714474

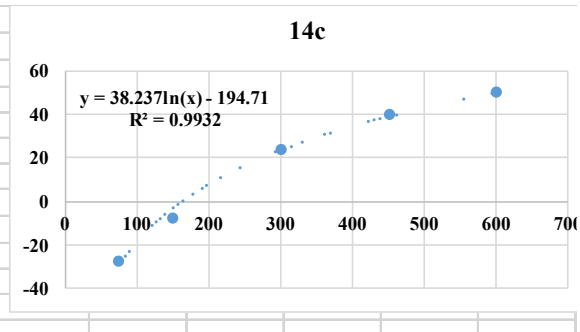


15c

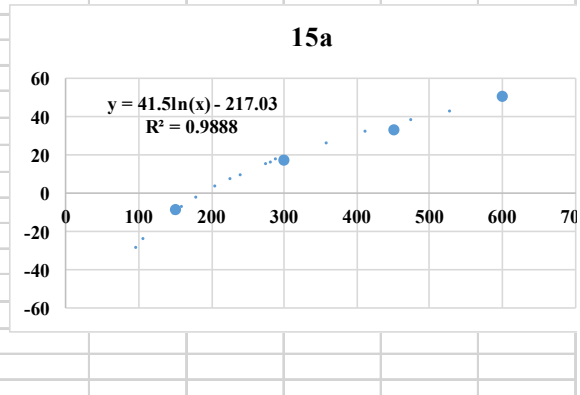
Conc.	OD Blnak	OD Total	OD Final	In (%)
600	0.056	0.352	0.296	70.4
450	0.098	0.7	0.7	52
300	0.043	1.195	1.152	27.088608
150	0.023	1.823	1.8	-13.92405
75	0.012	0.462	0.45	-54
IC50				433.93239



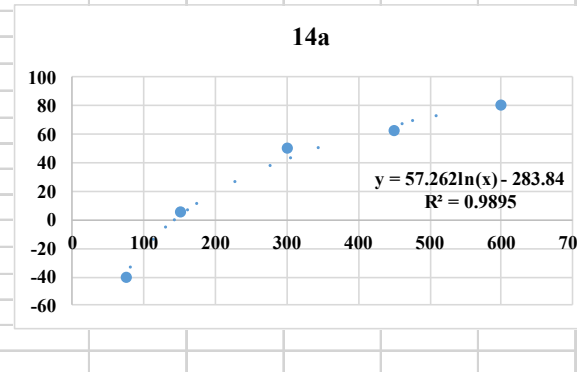
14c					
Conc.	OD Blnak	OD Total	OD Final	ln (%)	
600	0.029	0.529	0.5	0.5	50
450	0.056	0.7	0.68	0.68	40
300	0.027	1.227	1.2	24.050633	
150	0.058	1.758	1.7	-7.594937	
75	0.037	2.037	2	-27	
IC50				601.73802	



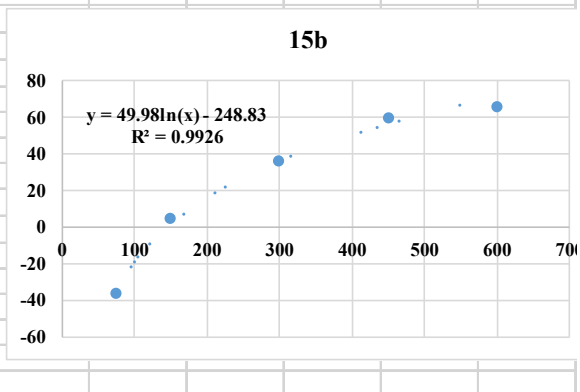
15a					
Conc.	OD Blnak	OD Total	OD Final	ln (%)	
600	0.034	0.52	0.486	51.4	
450	0.05	0.7	0.7	34	
300	0.03	1.33	1.3	17.721519	
150	0.05	1.75	1.7	-7.594937	
75	0.04	1.94	1.9		
IC50				622.49459	



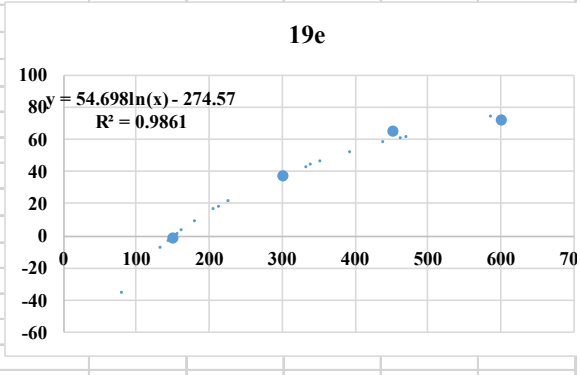
14a					
Conc.	OD Blnak	OD Total	OD Final	ln (%)	
600	0.04	0.24	0.2	80	
450	0.026	0.7	0.57	62	
300	0.032	0.812	0.78	50.632911	
150	0.049	1.549	1.5	5.0632911	
75	0.07	2.67	2.6	-40	
IC50				328.6907	



15b					
Conc.	OD Blnak	OD Total	OD Final	ln (%)	
600	0.078	0.414	0.336	66.4	
450	0.026	0.7	0.7	60	
300	0.049	1.049	1	36.708861	
150	0.028	1.528	1.5	5.0632911	
75	0.03	2.33	2.3	-36	
IC50				184.68361	

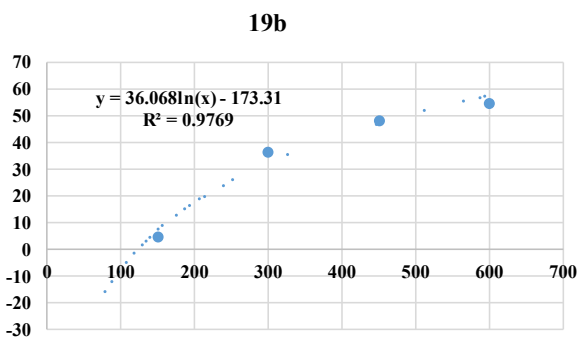


19e					
Conc.	OD Blnak	OD Total	OD Final	ln (%)	
600	0.09	0.376	0.286	71.4	
450	0.05	0.7	0.57	65	
300	0.012	1.012	1	36.708861	
150	0.034	1.634	1.6	-1.265823	
75	0.012	2.712	2.7		
IC50				377.52547	



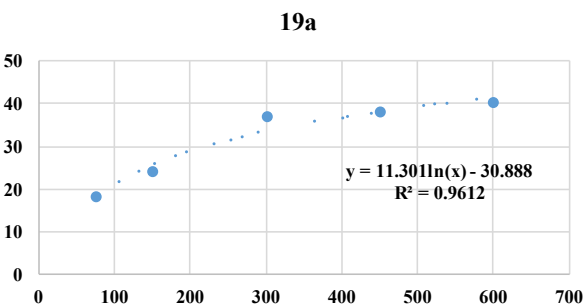
19b

Conc.	OD Blnak	OD Total	OD Final	In (%)
600	0.09	0.545	0.455	54.5
450	0.09	0.7	0.68	48
300	0.04	1.04	1	36.708861
150	0.04	1.54	1.5	5.0632911
75	0.032	3.032	3	
IC50				467.54706



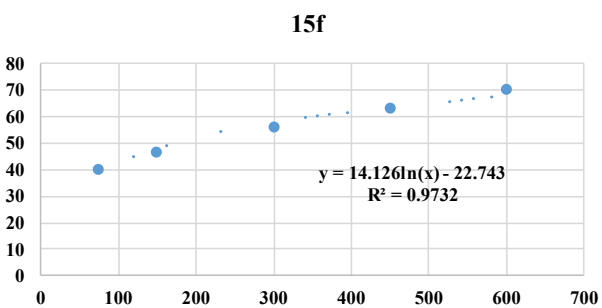
19a

Conc.	OD Blnak	OD Total	OD Final	In (%)
600	0.02	0.62	0.6	40
450	0.09	0.7	0.47	38
300	0.054	1.054	1	36.708861
150	0.043	1.243	1.2	24.050633
75	0.031	0.931	0.9	18
IC50				1274.6698



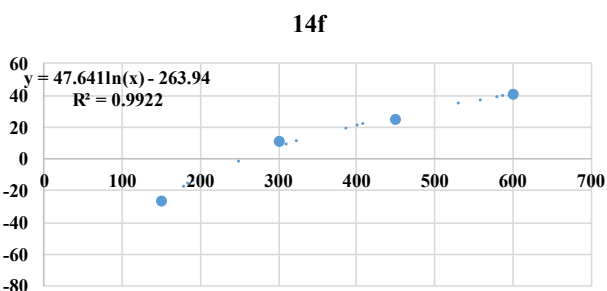
15f

Conc.	OD Blnak	OD Total	OD Final	In (%)
600	0.023	0.323	0.3	70
450	0.098	0.7	0.47	63
300	0.023	0.723	0.7	55.696203
150	0.04	0.884	0.844	46.582278
75	0.098	0.998	0.9	40
IC50				168.47048



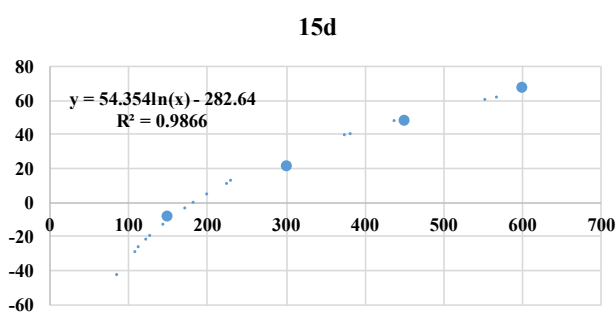
14f

Conc.	OD Blnak	OD Total	OD Final	In (%)
600	0.02	0.613	0.593	40.7
450	0.01	0.7	0.9	25
300	0.087	1.487	1.4	11.392405
150	0.064	2.064	2	-26.58228
75	0.07	2.77	2.7	
IC50				721.65801



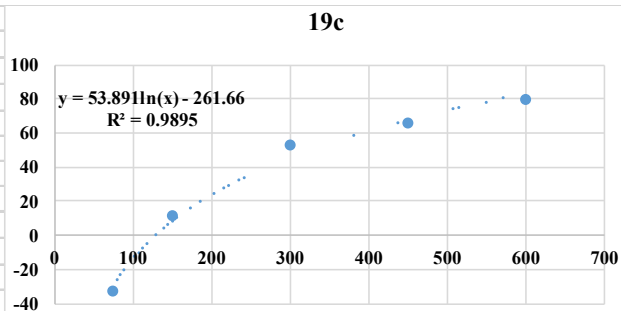
15d

Conc.	OD Blnak	OD Total	OD Final	In (%)
600	0.098	0.418	0.32	68
450	0.067	0.7	0.75	49
300	0.044	1.274	1.23	22.151899
150	0.027	1.727	1.7	-7.594937
75	0.08	2.88	2.8	
IC50				454.81047



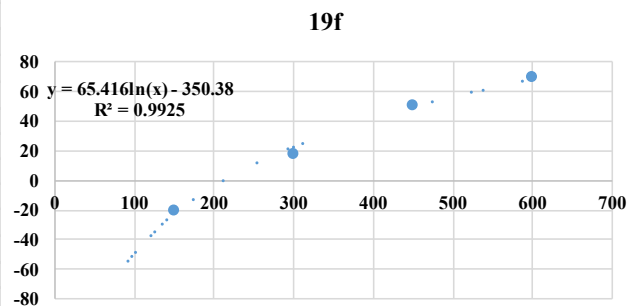
19c

Conc.	OD Blank	OD Total	OD Final	In (%)
600	0.098	0.78	0.682	79
450	0.07	0.7	0.7	66
300	0.05	0.803	0.753	52.341772
150	0.027	1.427	1.4	11.392405
75	0.067	2.867	2.8	-33
			IC50	324.81708



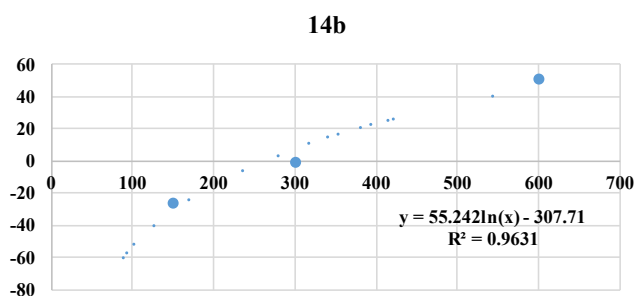
19f

Conc.	OD Blank	OD Total	OD Final	In (%)
600	0.06	0.36	0.3	70
450	0.013	0.7	0.9	50
300	0.067	1.367	1.3	17.721519
150	0.054	1.954	1.9	-20.25316
75	0.045	2.645	2.6	
			IC50	455.10173



14b

Conc.	OD Blank	OD Total	OD Final	In (%)
600	0.05	0.55	0.5	50
450	0.017	0.7	0.9	
300	0.037	1.637	1.6	-1.265823
150	0.034	2.034	2	-26.58228
75	0.056	2.656	2.6	
			IC50	648.93123



Aarbose

Conc.	OD Blank	OD Total	OD Final	In (%)
600	0.08	0.68	0.6	48
300	0.07	1	0.9	40
150	0.07	1.21	1.14	28
75	0.055	1.236	1.181	19
37.5	0.09	1.3	1.21	15.384615
			IC50	751.2518

