Electronic Supplementary Material (ESI) for RSC Advances.

Anticancer activity of new pyrimidodiazepines based on 2-chloro-4-anilinoquinazoline: synthesis, DNA binding and molecular docking

Viviana Cuartas [a,b], Alberto Aragón-Muriel [c], Yamil Liscano [d], Dorian Polo-Cerón [c], Maria del Pilar Crespo-Ortiz [e], Jairo Quiroga [a], Rodrigo Abonia [a], Braulio Insuasty [a,b*]

[a] Grupo de Investigación de Compuestos Heterocíclicos, Departamento de Química, Universidad del Valle, A. A. 25360 Cali, Colombia. [b] Centre for Bioinformatics and Photonics-CIBioFI, Calle 13 No. 100-00, Edificio E20, No. 1069, Cali, Colombia. [c] Laboratorio de Investigación en Catálisis y Procesos (LICAP), Departamento de Química, Universidad del Valle, 760001 Cali, Colombia. [d] Grupo de Investigación en Química y Biotecnología (QUIBIO), Universidad Santiago de Cali, 760031 Cali, Colombia. [e] Grupo de Biotecnología e Infecciones bacterianas, Departamento de Microbiología, Universidad del Valle, Cali 760043, Colombia. *Correspondence: braulio.insuasty@correounivalle.edu.co; Tel.: +57-315-484-6665; Fax: +57-2339-3248.

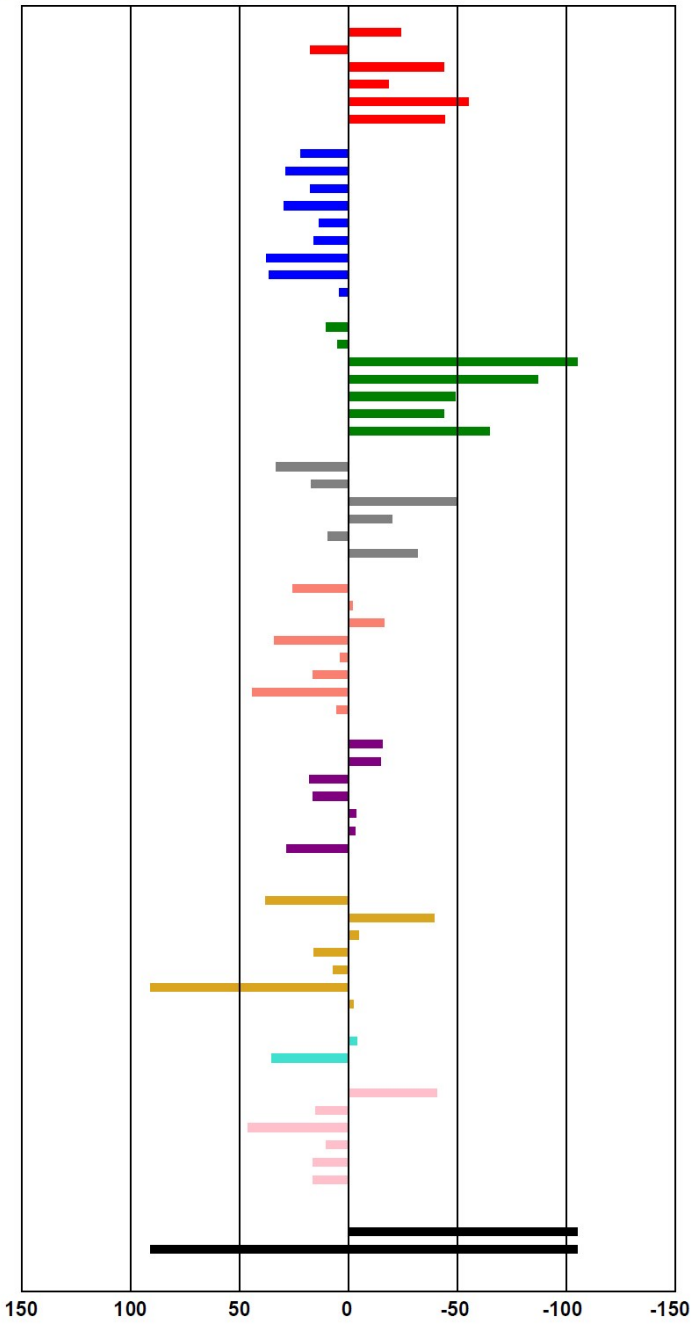
SUPPORTING INFORMATION

NCI 60 Cell One-Dose Screen - Compound 14g (NSC: 822723)

Developmental Therapeutics Program One Dose Mean Graph	NSC: D-822723 / 1	Conc: 1.00E-5 Molar	Test Date: Mar 23, 2020
	Experiment ID: 2003OS27		Report Date: Jul 21, 2020

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	28.88
HL-60(TB)	70.14
K-562	9.16
MOLT-4	34.55
RPMI-8226	-2.13
SR	8.85
Non-Small Cell Lung Cancer	
A549/ATCC	74.51
EKVX	81.51
HOP-62	70.08
HOP-92	82.21
NCI-H226	66.14
NCI-H23	68.58
NCI-H322M	90.26
NCI-H460	88.96
NCI-H522	56.92
Colon Cancer	
COLO 205	62.90
HCC-2998	57.44
HCT-116	-52.14
HCT-15	-34.08
HT29	4.17
KM12	9.13
SW-620	-11.91
CNS Cancer	
SF-268	85.90
SF-295	69.47
SF-539	2.74
SNB-19	32.93
SNB-75	62.12
U251	21.41
Melanoma	
MALME-3M	78.04
M14	51.19
MDA-MB-435	36.50
SK-MEL-2	86.75
SK-MEL-28	56.42
SK-MEL-5	68.77
UACC-257	96.46
UACC-62	57.79
Ovarian Cancer	
IGROV1	37.28
OVCAR-3	38.20
OVCAR-4	70.61
OVCAR-5	68.87
OVCAR-8	49.61
NCI/ADR-RES	49.89
SK-OV-3	81.07
Renal Cancer	
786-0	52.68
A498	90.61
ACHN	13.69
CAKI-1	48.42
RXF 393	68.35
SN12C	59.51
TK-10	143.45
UO-31	50.78
Prostate Cancer	
PC-3	49.22
DU-145	87.71
Breast Cancer	
MCF7	12.27
MDA-MB-231/ATCC	67.62
HS 578T	98.47
BT-549	62.91
T-47D	68.84
MDA-MB-468	68.87
Mean	52.70
Delta	104.84
Range	195.59

Mean Growth Percent - Growth Percent

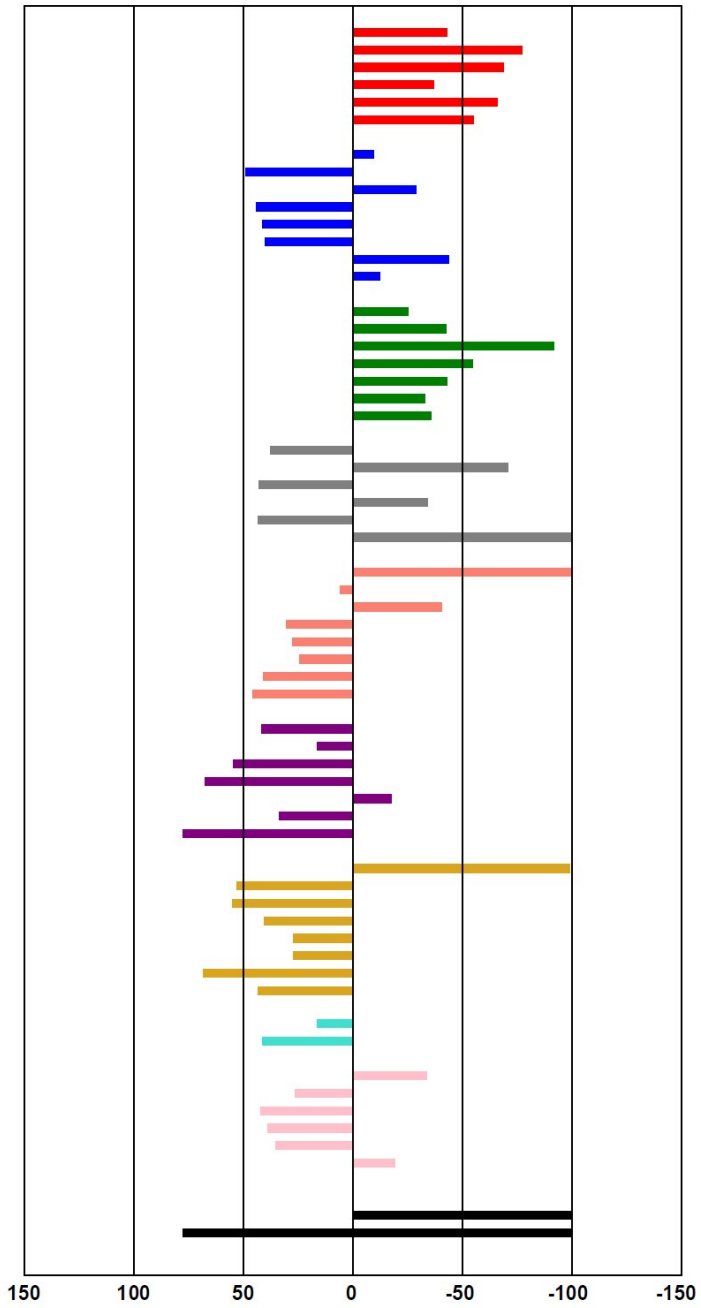


NCI 60 Cell One-Dose Screen - Compound 16a (NSC: 826382)

Developmental Therapeutics Program
One Dose Mean Graph

NSC: D-826382 / 1	**Conc:** 1.00E-5 Molar	**Test Date:** Oct 19, 2020
Experiment ID: 2010OS56		**Report Date:** Mar 07, 2021

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	3.94
HL-60(TB)	-30.26
K-562	-22.02
MOLT-4	10.02
RPMI-8226	-18.92
SR	-8.05
Non-Small Cell Lung Cancer	
A549/ATCC	37.22
EKVX	95.25
HOP-62	17.98
NCI-H226	90.42
NCI-H23	87.85
NCI-H322M	86.33
NCI-H460	2.91
NCI-H522	34.61
Colon Cancer	
COLO 205	21.53
HCC-2998	4.35
HCT-116	-44.82
HCT-15	-7.82
HT29	3.99
KM12	14.10
SW-620	11.17
CNS Cancer	
SF-268	84.22
SF-295	-23.90
SF-539	89.27
SNB-19	12.81
SNB-75	89.86
U251	-52.44
Melanoma	
LOX IMVI	-52.35
M14	52.18
MDA-MB-435	6.34
SK-MEL-2	76.90
SK-MEL-28	73.85
SK-MEL-5	70.64
UACC-257	87.33
UACC-62	92.04
Ovarian Cancer	
IGROV1	87.89
OVCAR-3	62.62
OVCAR-4	100.94
OVCAR-5	113.80
OVCAR-8	29.15
NCI/ADR-RES	80.09
SK-OV-3	123.82
Renal Cancer	
786-0	-52.06
A498	99.36
ACHN	101.55
CAKI-1	86.83
RXF 393	73.55
SN12C	73.66
TK-10	114.67
UO-31	89.87
Prostate Cancer	
PC-3	62.76
DU-145	87.66
Breast Cancer	
MCF7	12.96
MDA-MB-231/ATCC	72.86
HS 578T	88.62
BT-549	85.16
T-47D	81.68
MDA-MB-468	27.50
Mean	46.58
Delta	99.02
Range	176.26



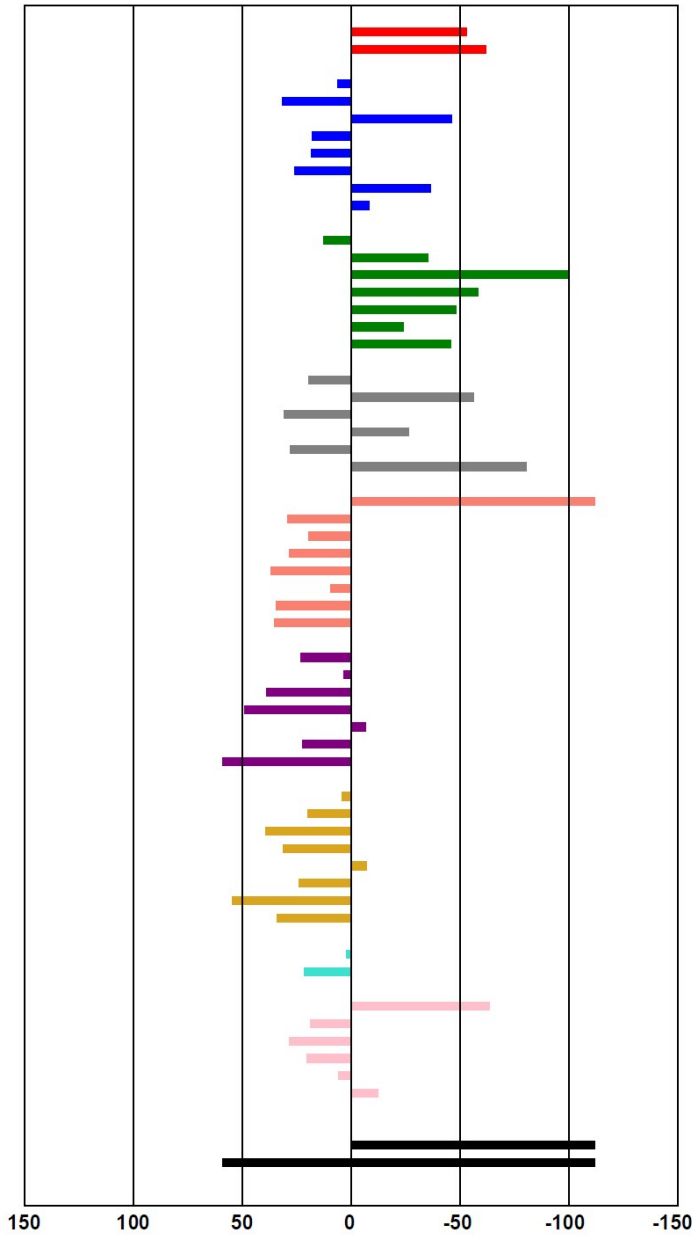
NCI 60 Cell One-Dose Screen - Compound 16c (NSC: 826384)

Developmental Therapeutics Program

One Dose Mean Graph

NSC: D-826384 / 1	Conc: 1.00E-5 Molar	Test Date: Oct 19, 2020
Experiment ID: 2010OS56		Report Date: Mar 07, 2021

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	5.40
RPMI-8226	-3.60
Non-Small Cell Lung Cancer	
A549/ATCC	64.22
EKVX	89.59
HOP-62	12.17
NCI-H226	75.75
NCI-H23	75.94
NCI-H322M	83.80
NCI-H460	21.72
NCI-H522	49.95
Colon Cancer	
COLO 205	70.66
HCC-2998	22.93
HCT-116	-41.74
HCT-15	0.16
HT29	9.87
KM12	34.12
SW-620	12.66
CNS Cancer	
SF-268	77.44
SF-295	2.02
SF-539	88.60
SNB-19	31.72
SNB-75	85.86
U251	-22.02
Melanoma	
LOX IMVI	-53.62
M14	86.82
MDA-MB-435	77.20
SK-MEL-2	86.03
SK-MEL-28	94.57
SK-MEL-5	67.09
UACC-257	92.06
UACC-62	92.97
Ovarian Cancer	
IGROV1	80.79
OVCAR-3	61.03
OVCAR-4	96.57
OVCAR-5	106.66
OVCAR-8	51.63
NCI/ADR-RES	79.98
SK-OV-3	116.71
Renal Cancer	
786-0	62.14
A498	77.92
ACHN	97.26
CAKI-1	88.83
RXF 393	51.07
SN12C	81.91
TK-10	112.49
UO-31	91.79
Prostate Cancer	
PC-3	59.87
DU-145	79.37
Breast Cancer	
MCF7	-5.06
MDA-MB-231/ATCC	76.39
HS 578T	86.10
BT-549	78.13
T-47D	63.72
MDA-MB-468	45.82
Mean	57.99
Delta	111.61
Range	170.33



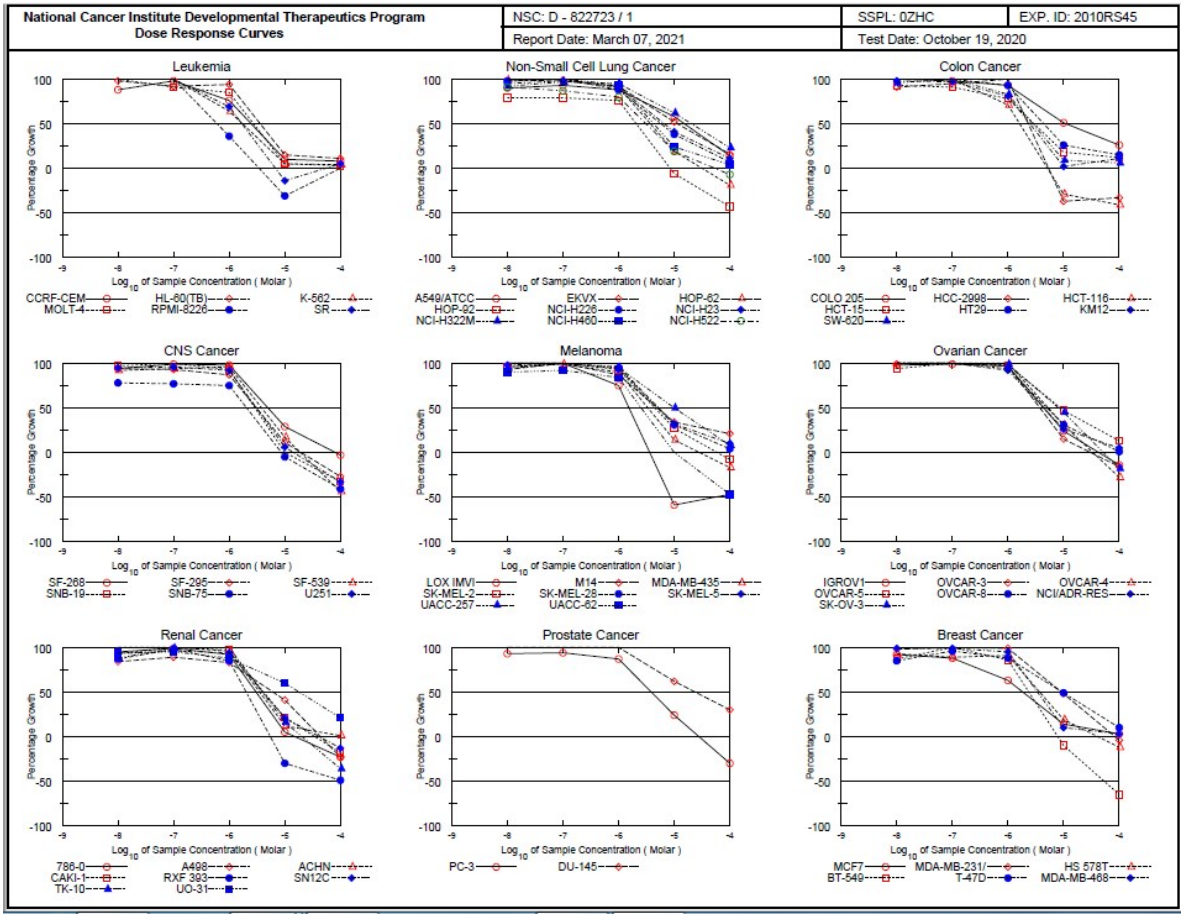
NCI 60 Cell Five-Dose Screen - Compound 14g (NSC: 822723)

National Cancer Institute Developmental Therapeutics Program
In-Vitro Testing Results

NSC : D - 822723 / 1	Experiment ID : 2010RS45	Test Type : 08	Units : Molar
Report Date : March 07, 2021	Test Date : October 19, 2020	QNS :	MC :
COMI : VCG-8Q	Stain Reagent : SRB Dual-Pass Related	SSPL : 0ZHC	

			Log10 Concentration												
	Time		Mean Optical Densities					Percent Growth							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
Leukemia															
CCRF-CEM	0.402	2.184	1.968	2.152	1.753	0.572	0.545	88	98	76	10	8	2.45E-6	> 1.00E-4	> 1.00E-4
HL-60(TB)	0.647	2.973	2.925	2.779	2.828	1.002	0.904	98	92	94	15	11	3.61E-6	> 1.00E-4	> 1.00E-4
K-562	0.151	1.581	1.612	1.590	1.068	0.226	0.210	102	101	64	5	4	1.74E-6	> 1.00E-4	> 1.00E-4
MOLT-4	0.450	2.642	2.797	2.446	2.321	0.568	0.523	107	91	85	5	3	2.77E-6	> 1.00E-4	> 1.00E-4
RPMI-8226	0.514	2.048	2.114	2.102	1.068	0.357	0.512	104	104	36	-31	.	6.22E-7	3.48E-6	> 1.00E-4
SR	0.264	0.782	0.868	0.861	0.622	0.227	0.288	117	115	69	-14	5	1.70E-6	.	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.451	2.437	2.234	2.299	2.205	1.598	0.720	90	93	88	58	14	1.50E-5	> 1.00E-4	> 1.00E-4
EKVX	0.641	1.886	1.861	1.878	1.790	1.289	0.837	98	99	92	52	16	1.14E-5	> 1.00E-4	> 1.00E-4
HOP-62	0.482	1.404	1.392	1.475	1.324	0.655	0.392	99	108	91	19	-19	3.71E-6	3.17E-5	> 1.00E-4
HOP-92	1.320	1.715	1.632	1.632	1.621	1.245	0.749	79	79	76	-6	-43	2.09E-6	8.51E-6	> 1.00E-4
NCI-H226	0.632	1.602	1.581	1.600	1.486	1.003	0.702	98	100	88	38	7	5.81E-6	> 1.00E-4	> 1.00E-4
NCI-H23	0.783	2.696	2.598	2.664	2.521	1.569	0.993	95	98	91	41	11	6.62E-6	> 1.00E-4	> 1.00E-4
NCI-H322M	0.915	2.297	2.189	2.250	2.225	1.771	1.240	92	97	95	62	23	2.04E-5	> 1.00E-4	> 1.00E-4
NCI-H460	0.235	2.441	2.551	2.556	2.301	0.757	0.321	105	105	94	24	4	4.20E-6	> 1.00E-4	> 1.00E-4
NCI-H522	1.057	2.668	2.523	2.465	2.344	1.361	0.980	91	87	80	19	-7	3.09E-6	5.26E-5	> 1.00E-4
Colon Cancer															
COLO 205	0.590	2.202	2.198	2.166	2.082	1.419	1.010	100	98	93	51	26	1.14E-5	> 1.00E-4	> 1.00E-4
HCC-2998	0.473	1.861	1.735	1.797	1.991	0.296	0.318	91	95	109	-37	-33	2.54E-6	5.56E-6	> 1.00E-4
HCT-116	0.333	2.744	2.769	2.762	2.046	0.238	0.197	101	101	71	-29	-41	1.62E-6	5.16E-6	> 1.00E-4
HCT-15	0.342	2.350	2.220	2.166	1.901	0.695	0.587	93	91	78	18	12	2.88E-6	> 1.00E-4	> 1.00E-4
HT29	0.583	2.833	2.842	2.863	2.686	1.164	0.912	100	101	93	26	15	4.39E-6	> 1.00E-4	> 1.00E-4
KM12	0.552	2.836	2.788	2.769	2.399	0.588	0.795	98	97	81	2	11	2.45E-6	> 1.00E-4	> 1.00E-4
SW-620	0.278	2.149	2.079	2.142	1.834	0.444	0.392	96	100	83	9	6	2.79E-6	> 1.00E-4	> 1.00E-4
CNS Cancer															
SF-268	1.070	2.627	2.540	2.605	2.590	1.529	1.039	94	99	98	29	-3	4.99E-6	8.14E-5	> 1.00E-4
SF-295	0.453	2.236	2.130	2.112	2.007	0.651	0.331	94	93	87	11	-27	3.08E-6	1.96E-5	> 1.00E-4
SF-539	1.082	3.026	2.865	2.911	2.943	1.417	0.609	92	94	96	17	-44	3.82E-6	1.92E-5	> 1.00E-4
SNB-19	0.533	2.013	1.967	2.018	1.905	0.536	0.358	97	100	93	.	-33	2.89E-6	1.01E-5	> 1.00E-4
SNB-75	1.401	2.384	2.170	2.153	2.140	1.328	0.821	78	77	75	-5	-41	2.06E-6	8.61E-6	> 1.00E-4
U251	0.420	2.127	2.044	2.065	1.996	0.529	0.282	95	96	92	6	-33	3.11E-6	1.45E-5	> 1.00E-4
Melanoma															
LOX IMVI	0.373	2.374	2.367	2.427	1.876	0.153	0.198	100	103	75	-59	-47	1.54E-6	3.63E-6	.
M14	0.589	2.308	2.195	2.318	2.082	1.176	0.946	93	101	87	34	21	5.01E-6	> 1.00E-4	> 1.00E-4
MDA-MB-435	0.617	2.723	2.642	2.697	2.523	0.918	0.514	96	99	90	14	-17	3.40E-6	2.89E-5	> 1.00E-4
SK-MEL-2	1.161	2.390	2.339	2.401	2.298	1.488	1.064	96	101	93	27	-8	4.42E-6	5.77E-5	> 1.00E-4
SK-MEL-28	0.662	2.132	2.138	2.205	2.045	1.121	0.725	100	105	94	31	4	5.03E-6	> 1.00E-4	> 1.00E-4
SK-MEL-5	0.845	3.290	3.246	3.292	3.192	1.619	1.096	98	100	96	32	10	5.18E-6	> 1.00E-4	> 1.00E-4
UACC-257	0.943	2.448	2.363	2.478	2.371	1.688	1.058	94	102	95	50	8	9.75E-6	> 1.00E-4	> 1.00E-4
UACC-62	0.669	2.667	2.467	2.515	2.352	0.672	0.356	90	92	84	.	-47	2.55E-6	1.01E-5	> 1.00E-4
Ovarian Cancer															
IGROV1	0.783	2.462	2.434	2.448	2.418	1.192	0.673	98	99	97	24	-14	4.45E-6	4.29E-5	> 1.00E-4
OVCAR-3	0.566	1.910	1.896	1.960	1.866	0.772	0.478	99	104	97	15	-16	3.75E-6	3.13E-5	> 1.00E-4
OVCAR-4	0.824	1.640	1.646	1.696	1.672	1.078	0.590	101	107	104	31	-28	5.50E-6	3.33E-5	> 1.00E-4
OVCAR-5	0.546	1.653	1.590	1.695	1.632	1.068	0.690	94	104	98	47	13	8.79E-6	> 1.00E-4	> 1.00E-4
OVCAR-8	0.748	2.938	2.940	2.970	2.816	1.422	0.780	100	101	94	31	1	4.99E-6	> 1.00E-4	> 1.00E-4
NCI/ADR-RES	0.583	2.192	2.230	2.228	2.056	0.994	0.668	102	102	92	26	5	4.26E-6	> 1.00E-4	> 1.00E-4
SK-OV-3	1.046	2.232	2.243	2.248	2.214	1.576	0.859	101	101	99	45	-18	7.96E-6	5.17E-5	> 1.00E-4
Renal Cancer															
786-0	0.692	2.711	2.612	2.700	2.558	0.790	0.536	95	99	92	5	-23	3.05E-6	1.50E-5	> 1.00E-4
A498	1.488	2.265	2.142	2.179	2.133	1.810	1.150	84	89	83	41	-23	6.23E-6	4.43E-5	> 1.00E-4
ACHN	0.395	1.800	1.822	1.867	1.738	0.564	0.414	102	105	96	12	1	3.51E-6	> 1.00E-4	> 1.00E-4
CAKI-1	0.828	2.810	2.670	2.815	2.749	1.250	0.683	93	100	97	21	-18	4.17E-6	3.54E-5	> 1.00E-4
RXF 393	1.169	1.851	1.762	1.839	1.751	0.814	0.601	87	98	85	-30	-49	2.02E-6	5.46E-6	> 1.00E-4
SN12C	0.639	2.347	2.229	2.281	2.237	0.997	0.555	93	96	94	21	-13	3.98E-6	4.11E-5	> 1.00E-4
TK-10	0.933	1.868	1.758	1.854	1.931	1.078	0.598	88	99	107	16	-36	4.19E-6	2.00E-5	> 1.00E-4
UO-31	1.469	3.076	2.972	3.003	2.883	2.427	1.809	94	95	88	60	21	1.78E-5	> 1.00E-4	> 1.00E-4
Prostate Cancer															
PC-3	0.618	2.249	2.128	2.152	2.030	1.013	0.431	93	94	87	24	-30	3.86E-6	2.78E-5	> 1.00E-4
DU-145	0.548	2.330	2.396	2.461	2.357	1.652	1.088	104	107	102	62	30	2.38E-5	> 1.00E-4	> 1.00E-4
Breast Cancer															
MCF7	0.484	2.526	2.361	2.291	1.762	0.763	0.548	92	88	63	14	3	1.81E-6	> 1.00E-4	> 1.00E-4
MDA-MB-231/ATCC	0.861	1.807	1.786	1.872	1.799	1.315	0.831	98	107	99	48	-4	9.14E-6	8.54E-5	> 1.00E-4
HS 578T	1.407	2.366	2.302	2.261	2.278	1.591	1.238	93	89	91	19	-12	3.71E-6	4.11E-5	> 1.00E-4
BT-549	1.122	2.409	2.238	2.407	2.227	1.008	0.395	87	100	86	-10	-65	2.36E-6	7.83E-6	5.36E-5
T-47D	1.067	2.397	2.197	2.340	2.240	1.712	1.200	85	96	88	49	10	9.17E-6	> 1.00E-4	> 1.00E-4
MDA-MB-468	0.969	2.112	2.104	2.102	2.052	1.088	1.008	99	99	95	10	3	3.39E-6	> 1.00E-4	> 1.00E-4

National Cancer Institute Developmental Therapeutics Program
Dose Response Curves - Compound 14g (NSC: 822723)



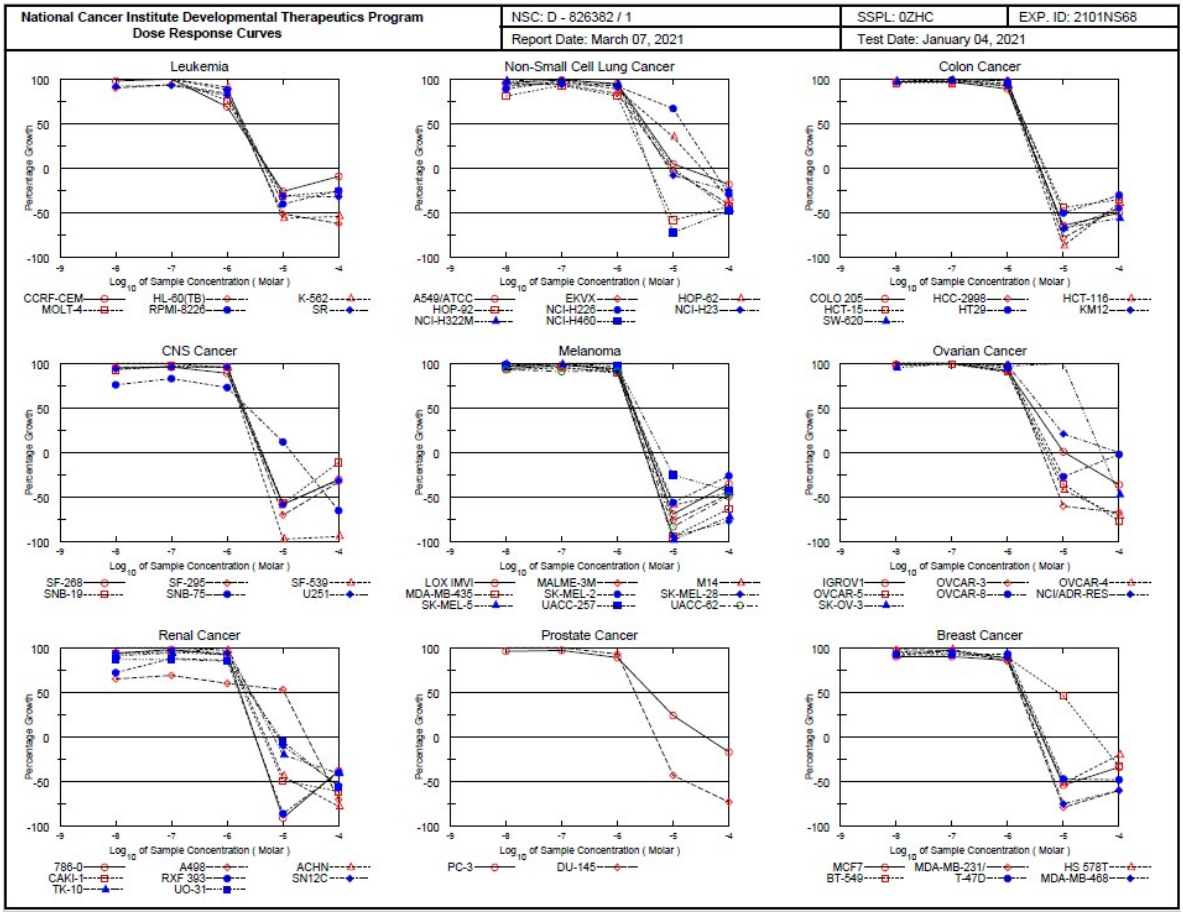
NCI 60 Cell Five-Dose Screen - Compound 16a (NSC: 826382)

National Cancer Institute Developmental Therapeutics Program
In-Vitro Testing Results

NSC : D - 826382 / 1	Experiment ID : 2101NS68	Test Type : 08	Units : Molar
Report Date : March 07, 2021	Test Date : January 04, 2021	QNS :	MC :
COMI : VCG-10Q	Stain Reagent : SRB Dual-Pass Related	SSPL : 0ZHC	

			Log10 Concentration												
	Time		Mean Optical Densities					Percent Growth							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
Leukemia															
CCRF-CEM	0.488	1.717	1.696	1.722	1.341	0.359	0.443	98	100	69	-26	-9	1.59E-6	5.30E-6	> 1.00E-4
HL-60(TB)	0.693	2.401	2.238	2.294	2.130	0.337	0.264	90	94	84	-51	-62	1.79E-6	4.18E-6	9.77E-6
K-562	0.282	2.307	2.299	2.400	2.133	0.124	0.129	100	105	91	-56	-54	1.91E-6	4.16E-6	9.08E-6
MOLT-4	0.721	2.579	2.571	2.640	2.134	0.494	0.531	100	103	76	-31	-26	1.75E-6	5.10E-6	> 1.00E-4
RPMI-8226	1.118	2.291	2.353	2.397	2.146	0.668	0.839	105	109	88	-40	-25	1.97E-6	4.84E-6	> 1.00E-4
SR	0.683	2.788	2.619	2.634	2.403	0.474	0.465	92	93	82	-31	-32	1.91E-6	5.33E-6	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.420	2.346	2.271	2.329	2.245	0.509	0.346	96	99	95	5	-18	3.14E-6	1.61E-5	> 1.00E-4
EKVX	0.568	1.618	1.555	1.557	1.448	0.550	0.341	94	94	84	-3	-40	2.44E-6	9.17E-6	> 1.00E-4
HOP-62	0.895	2.633	2.500	2.588	2.450	1.497	0.600	92	97	89	35	-33	5.24E-6	3.25E-5	> 1.00E-4
HOP-92	1.491	2.094	1.977	2.054	1.982	0.619	0.852	81	93	81	-58	-43	1.68E-6	3.82E-6	.
NCI-H226	1.047	2.314	2.171	2.292	2.218	1.890	0.749	89	98	92	67	-29	1.49E-5	5.01E-5	> 1.00E-4
NCI-H23	0.661	1.937	1.883	1.861	1.853	0.611	0.495	96	94	93	-8	-25	2.69E-6	8.40E-6	> 1.00E-4
NCI-H322M	0.767	2.138	2.104	2.135	2.060	0.764	0.414	98	100	94	.	-46	2.93E-6	9.91E-6	> 1.00E-4
NCI-H460	0.296	2.688	2.730	2.845	2.764	0.082	0.153	102	107	103	-72	-48	2.01E-6	3.87E-6	.
Colon Cancer															
COLO 205	0.637	2.766	2.710	2.708	2.534	0.228	0.319	97	97	89	-64	-50	1.80E-6	3.81E-6	.
HCC-2998	0.633	2.065	2.029	2.021	2.050	0.141	0.352	97	97	99	-78	-44	1.89E-6	3.63E-6	.
HCT-116	0.335	2.724	2.682	2.690	2.521	0.043	0.204	98	99	92	-87	-39	1.71E-6	3.25E-6	.
HCT-15	0.296	2.049	1.987	1.970	1.928	0.167	0.192	96	96	93	-44	-35	2.07E-6	4.80E-6	> 1.00E-4
HT29	0.442	2.711	2.770	2.692	2.604	0.221	0.310	103	99	95	-50	-30	2.05E-6	4.53E-6	> 1.00E-4
KM12	0.854	3.334	3.332	3.339	3.274	0.273	0.469	100	100	98	-68	-45	1.94E-6	3.88E-6	.
SW-620	0.321	1.993	1.948	1.990	1.872	0.105	0.142	97	100	93	-67	-56	1.85E-6	3.79E-6	7.78E-6
CNS Cancer															
SF-268	0.964	2.619	2.542	2.547	2.439	0.410	0.672	95	96	89	-58	-30	1.85E-6	4.05E-6	.
SF-295	0.980	3.240	3.143	3.154	3.152	0.293	0.656	96	96	96	-70	-33	1.89E-6	3.78E-6	.
SF-539	1.014	2.787	2.806	2.835	2.701	0.034	0.060	101	103	95	-97	-94	1.72E-6	3.13E-6	5.71E-6
SNB-19	0.546	1.918	1.826	1.878	1.862	0.233	0.485	93	97	96	-57	-11	1.99E-6	4.22E-6	.
SNB-75	1.164	2.103	1.877	1.943	1.852	1.275	0.409	76	83	73	12	-65	2.39E-6	1.43E-5	6.39E-5
U251	0.429	1.998	1.907	1.937	1.938	0.180	0.294	94	96	96	-58	-31	1.99E-6	4.20E-6	.
CNS Cancer															
SF-268	0.964	2.619	2.542	2.547	2.439	0.410	0.672	95	96	89	-58	-30	1.85E-6	4.05E-6	.
SF-295	0.980	3.240	3.143	3.154	3.152	0.293	0.656	96	96	96	-70	-33	1.89E-6	3.78E-6	.
SF-539	1.014	2.787	2.806	2.835	2.701	0.034	0.060	101	103	95	-97	-94	1.72E-6	3.13E-6	5.71E-6
SNB-19	0.546	1.918	1.826	1.878	1.862	0.233	0.485	93	97	96	-57	-11	1.99E-6	4.22E-6	.
SNB-75	1.164	2.103	1.877	1.943	1.852	1.275	0.409	76	83	73	12	-65	2.39E-6	1.43E-5	6.39E-5
U251	0.429	1.998	1.907	1.937	1.938	0.180	0.294	94	96	96	-58	-31	1.99E-6	4.20E-6	.
Melanoma															
LOX IMVI	0.305	2.007	1.897	1.978	1.909	0.096	0.197	94	98	94	-69	-35	1.87E-6	3.79E-6	.
MALME-3M	0.832	2.240	2.188	2.268	2.244	0.200	0.437	96	102	100	-76	-47	1.93E-6	3.71E-6	.
M14	0.545	2.031	1.922	1.962	1.894	0.224	0.302	93	95	91	-59	-45	1.87E-6	4.04E-6	.
MDA-MB-435	0.575	2.657	2.595	2.579	2.432	0.037	0.211	97	96	89	-94	-63	1.64E-6	3.07E-6	5.77E-6
SK-MEL-2	1.298	2.522	2.506	2.557	2.444	0.567	0.957	99	103	94	-56	-26	1.95E-6	4.21E-6	.
SK-MEL-28	0.553	1.684	1.658	1.737	1.581	0.033	0.127	98	105	91	-94	-77	1.66E-6	3.10E-6	5.78E-6
SK-MEL-5	1.089	3.249	3.237	3.233	3.101	0.025	0.301	99	99	93	-98	-72	1.68E-6	3.08E-6	5.62E-6
UACC-257	1.013	2.421	2.374	2.488	2.385	0.757	0.573	97	105	97	-25	-43	2.43E-6	6.22E-6	> 1.00E-4
UACC-62	0.918	2.624	2.502	2.474	2.463	0.153	0.471	93	91	91	-83	-49	1.71E-6	3.32E-6	.
Ovarian Cancer															
IGROV1	0.342	1.867	1.850	1.876	1.741	0.365	0.219	99	101	92	1	-36	2.90E-6	1.09E-5	> 1.00E-4
OVCAR-3	0.626	1.986	1.977	2.080	1.979	0.249	0.207	99	107	99	-60	-67	2.04E-6	4.20E-6	8.63E-6
OVCAR-4	0.761	2.093	2.089	2.095	1.955	0.444	0.223	100	100	90	-42	-71	2.00E-6	4.81E-6	1.93E-5
OVCAR-5	0.491	1.373	1.360	1.368	1.297	0.317	0.113	98	99	91	-35	-77	2.12E-6	5.25E-6	2.24E-5
OVCAR-8	0.738	2.827	2.822	2.878	2.732	0.536	0.725	100	102	95	-27	-2	2.35E-6	5.99E-6	> 1.00E-4
NCI/ADR-RES	0.514	1.797	1.813	1.858	1.766	0.780	0.510	101	105	98	21		4.16E-6	9.20E-5	> 1.00E-4
SK-OV-3	1.344	2.620	2.550	2.668	2.578	2.614	0.719	95	104	97	100	-47	2.18E-5	4.80E-5	> 1.00E-4
Renal Cancer															
786-0	0.678	2.643	2.527	2.613	2.485	0.061	0.424	94	98	92	-91	-38	1.70E-6	3.18E-6	.
A498	1.770	2.536	2.271	2.302	2.232	2.173	0.539	65	69	60	53	-70	1.05E-5	2.69E-5	6.92E-5
ACHN	0.474	1.909	1.935	1.982	1.862	0.266	0.107	102	105	97	-44	-78	2.15E-6	4.87E-6	1.52E-5
CAKI-1	0.918	2.989	2.846	2.884	2.832	0.466	0.356	93	95	92	-49	-61	1.99E-6	4.49E-6	1.15E-5
RXF 393	1.070	1.561	1.425	1.503	1.491	0.145	0.646	72	88	86	-86	-40	1.61E-6	3.14E-6	.
SN12C	1.323	3.330	3.213	3.264	3.220	1.197	0.609	94	97	94	-10	-54	2.68E-6	8.10E-6	8.14E-5
TK-10	1.107	2.052	1.968	1.992	2.053	0.891	0.653	91	94	100	-20	-41	2.62E-6	6.87E-6	> 1.00E-4
UO-31	0.716	2.305	2.104	2.098	2.074	0.683	0.315	87	87	85	-5	-56	2.48E-6	8.89E-6	7.64E-5
Prostate Cancer															
PC-3	0.835	2.442	2.381	2.397	2.269	1.216	0.691	96	97	89	24	-17	3.97E-6	3.79E-5	> 1.00E-4
DU-145	0.453	1.788	1.802	1.811	1.690	0.260	0.125	101	102	93	-43	-73	2.07E-6	4.84E-6	1.76E-5
Breast Cancer															
MCF7	0.480	2.427	2.237	2.224	2.146	0.222	0.316	90	90	86	-54	-34	1.80E-6	4.11E-6	.
MDA-MB-231/ATCC	0.685	1.553	1.537	1.531	1.421	0.143	0.277	98	97	85	-79	-60	1.63E-6	3.29E-6	6.64E-6
HS 578T	0.817	1.835	1.744	1.810	1.717	0.396	0.652	91	98	88	-52	-20	1.88E-6	4.28E-6	.
BT-549	1.257	2.331	2.285	2.253	2.218	1.747	0.842	96	93	89	46	-33	7.93E-6	3.80E-5	> 1.00E-4
T-47D	1.008	2.495	2.376	2.378	2.390	0.533	0.526	92	92	93	-47	-48	2.02E-6	4.61E-6	> 1.00E-4
MDA-MB-468	0.703	1.933	1.855	1.881	1.796	0.177	0.284	94	96	89	-75	-60	1.73E-6	3.49E-6	7.05E-6

National Cancer Institute Developmental Therapeutics Program
Dose Response Curves - Compound 16a (NSC: 826382)



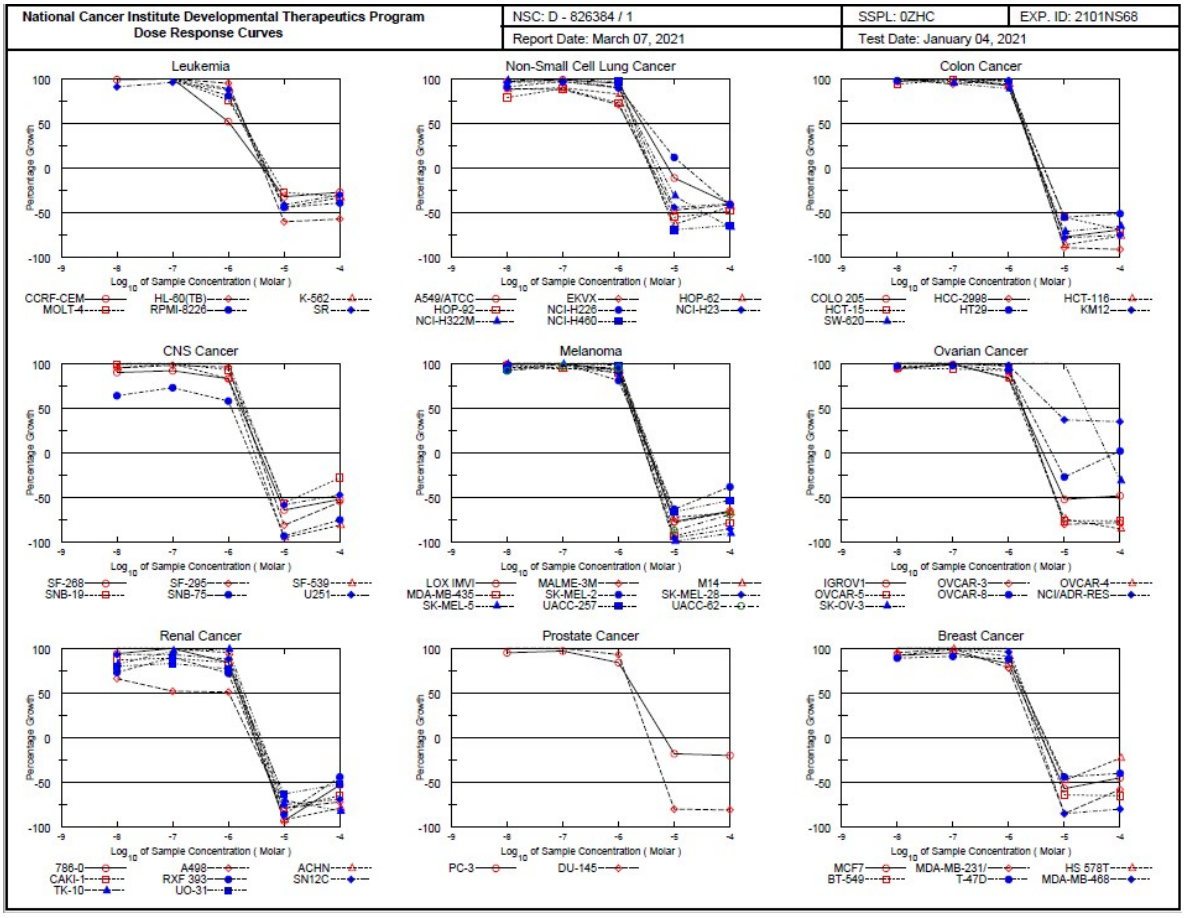
NCI 60 Cell Five-Dose Screen - Compound 16c (NSC: 826384)

National Cancer Institute Developmental Therapeutics Program
In-Vitro Testing Results

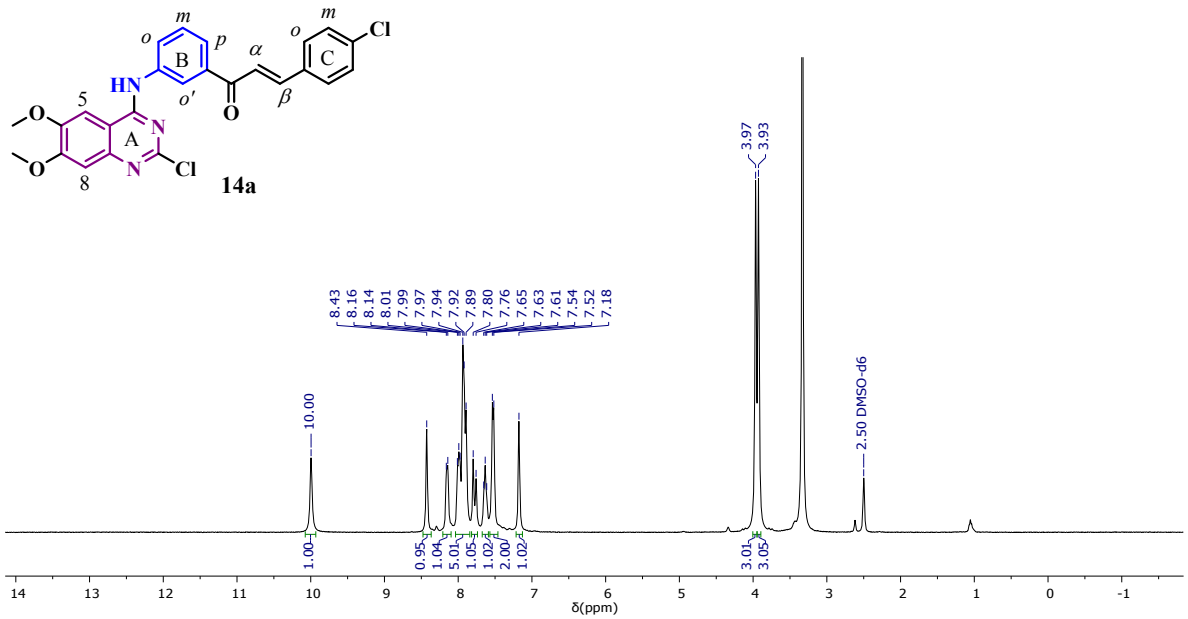
NSC : D - 826384 / 1	Experiment ID : 2101NS68	Test Type : 08	Units : Molar
Report Date : March 07, 2021	Test Date : January 04, 2021	QNS :	MC :
COMI : VCG-12Q	Stain Reagent : SRB Dual-Pass Related	SSPL : 0ZHC	

			Log10 Concentration												
	Time		Mean Optical Densities					Percent Growth							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
Leukemia															
CCRF-CEM	0.488	1.741	1.723	1.838	1.136	0.331	0.355	99	108	52	-32	-27	1.05E-6	4.14E-6	> 1.00E-4
HL-60(TB)	0.693	2.530	2.549	2.610	2.435	0.276	0.301	101	104	95	-60	-57	1.95E-6	4.09E-6	8.60E-6
K-562	0.282	2.429	2.461	2.550	2.189	0.159	0.190	101	106	89	-44	-33	1.96E-6	4.69E-6	> 1.00E-4
MOLT-4	0.721	2.642	2.652	2.679	2.171	0.526	0.493	101	102	76	-27	-32	1.77E-6	5.45E-6	> 1.00E-4
RPMI-8226	1.118	2.319	2.354	2.437	2.091	0.622	0.686	103	110	81	-44	-39	1.77E-6	4.42E-6	> 1.00E-4
SR	0.683	2.768	2.589	2.683	2.508	0.403	0.480	91	96	88	-41	-30	1.96E-6	4.80E-6	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.420	2.214	2.152	2.202	2.117	0.373	0.254	97	99	95	-11	-40	2.64E-6	7.82E-6	> 1.00E-4
EKVX	0.568	1.603	1.488	1.478	1.301	0.301	0.333	89	88	71	-47	-41	1.50E-6	3.99E-6	> 1.00E-4
HOP-62	0.895	2.576	2.375	2.414	2.287	0.329	0.507	88	90	83	-63	-43	1.68E-6	3.69E-6	.
HOP-92	1.491	2.135	2.000	2.064	1.958	0.677	0.776	79	89	73	-55	-48	1.50E-6	3.72E-6	.
NCI-H226	1.047	2.215	2.112	2.182	2.093	1.184	0.617	91	97	90	12	-41	3.22E-6	1.66E-5	> 1.00E-4
NCI-H23	0.661	1.894	1.850	1.851	1.776	0.373	0.399	96	97	90	-44	-40	2.00E-6	4.73E-6	> 1.00E-4
NCI-H322M	0.767	2.030	2.002	2.032	1.902	0.532	0.258	98	100	90	-31	-66	2.14E-6	5.57E-6	3.48E-5
NCI-H460	0.296	2.746	2.836	2.739	2.663	0.091	0.106	104	100	97	-69	-64	1.91E-6	3.82E-6	7.64E-6
Colon Cancer															
COLO 205	0.637	2.645	2.577	2.644	2.484	0.148	0.199	97	100	92	-77	-69	1.77E-6	3.51E-6	6.94E-6
HCC-2998	0.633	2.084	2.108	2.000	2.155	0.072	0.054	102	94	105	-89	-91	1.92E-6	3.48E-6	6.32E-6
HCT-116	0.335	2.626	2.652	2.547	2.496	0.048	0.082	101	97	94	-86	-76	1.76E-6	3.34E-6	6.33E-6
HCT-15	0.296	1.995	1.890	1.980	1.885	0.134	0.093	94	99	94	-55	-69	1.96E-6	4.27E-6	9.27E-6
HT29	0.442	2.650	2.601	2.690	2.592	0.201	0.218	98	102	97	-55	-51	2.05E-6	4.38E-6	9.34E-6
KM12	0.854	3.316	3.308	3.317	3.270	0.188	0.215	100	100	98	-78	-75	1.88E-6	3.61E-6	6.94E-6
SW-620	0.321	1.983	1.991	1.901	1.804	0.093	0.111	100	95	89	-71	-65	1.76E-6	3.60E-6	7.39E-6
CNS Cancer															
SF-268	0.964	2.557	2.395	2.431	2.288	0.350	0.464	90	92	83	-64	-52	1.68E-6	3.68E-6	8.07E-6
SF-295	0.980	3.214	3.106	3.165	3.128	0.191	0.445	95	98	96	-81	-55	1.82E-6	3.50E-6	6.72E-6
SF-539	1.014	2.861	2.762	2.856	2.546	0.054	0.188	95	100	83	-95	-81	1.53E-6	2.93E-6	5.60E-6
SNB-19	0.546	1.838	1.821	1.854	1.745	0.242	0.394	99	101	93	-56	-28	1.94E-6	4.22E-6	.
SNB-75	1.164	2.054	1.731	1.818	1.683	0.080	0.292	64	73	58	-93	-75	1.13E-6	2.42E-6	5.19E-6
U251	0.429	1.863	1.902	1.940	1.899	0.180	0.227	103	105	103	-58	-47	2.12E-6	4.35E-6	.
Melanoma															
LOX IMVI	0.305	1.939	1.929	2.008	1.818	0.070	0.108	99	104	93	-77	-65	1.78E-6	3.51E-6	6.93E-6
MALME-3M	0.832	2.088	2.096	2.187	2.163	0.181	0.284	101	108	106	-78	-66	2.01E-6	3.76E-6	7.03E-6
M14	0.545	1.964	1.911	1.873	1.899	0.151	0.179	96	94	95	-72	-67	1.86E-6	3.70E-6	7.36E-6
MDA-MB-435	0.575	2.652	2.603	2.558	2.444	0.043	0.125	98	95	90	-93	-78	1.66E-6	3.11E-6	5.84E-6
SK-MEL-2	1.298	2.444	2.355	2.478	2.231	0.486	0.811	92	103	81	-63	-38	1.65E-6	3.68E-6	.
SK-MEL-28	0.553	1.653	1.661	1.669	1.527	0.028	0.085	101	101	89	-95	-85	1.62E-6	3.04E-6	5.69E-6
SK-MEL-5	1.089	3.212	3.187	3.183	3.035	0.006	0.111	99	99	92	-99	-90	1.65E-6	3.02E-6	5.51E-6
UACC-257	1.013	2.311	2.237	2.308	2.284	0.340	0.478	94	100	98	-66	-53	1.96E-6	3.94E-6	7.94E-6
UACC-62	0.918	2.602	2.469	2.545	2.513	0.115	0.281	92	97	95	-87	-69	1.76E-6	3.31E-6	6.23E-6
Ovarian Cancer															
IGROV1	0.342	1.708	1.625	1.689	1.489	0.165	0.178	94	99	84	-52	-48	1.78E-6	4.16E-6	.
OVCAR-3	0.626	1.920	1.949	2.010	1.887	0.127	0.139	102	107	97	-80	-78	1.85E-6	3.55E-6	6.79E-6
OVCAR-4	0.761	1.968	1.908	1.974	1.766	0.197	0.115	95	100	83	-74	-85	1.63E-6	3.38E-6	7.03E-6
OVCAR-5	0.491	1.327	1.282	1.278	1.263	0.120	0.120	95	94	92	-76	-76	1.79E-6	3.55E-6	7.04E-6
OVCAR-8	0.738	2.697	2.637	2.653	2.570	0.539	0.781	97	98	93	-27	2	2.30E-6	.	> 1.00E-4
NCI/ADR-RES	0.514	1.776	1.811	1.824	1.752	0.977	0.951	103	104	98	37	35	6.07E-6	> 1.00E-4	> 1.00E-4
SK-OV-3	1.344	2.448	2.506	2.527	2.504	2.520	0.923	105	107	105	106	-31	2.57E-5	5.92E-5	> 1.00E-4
Renal Cancer															
786-0	0.678	2.525	2.416	2.533	2.238	0.046	0.322	94	100	84	-93	-53	1.56E-6	2.99E-6	5.71E-6
A498	1.770	2.477	2.239	2.138	2.129	0.376	0.492	66	52	51	-79	-72	1.01E-6	2.47E-6	6.00E-6
ACHN	0.474	1.955	1.964	1.994	1.882	0.039	0.101	101	103	95	-92	-79	1.74E-6	3.22E-6	5.97E-6
CAKI-1	0.918	2.896	2.632	2.686	2.575	0.193	0.318	87	89	84	-79	-65	1.61E-6	3.27E-6	6.64E-6
RXF 393	1.070	1.526	1.403	1.481	1.398	0.150	0.601	73	90	72	-86	-44	1.38E-6	2.85E-6	.
SN12C	1.323	3.254	3.128	3.116	3.028	0.334	0.410	93	93	88	-75	-69	1.72E-6	3.48E-6	7.05E-6
TK-10	1.107	1.938	1.789	1.916	1.929	0.335	0.197	82	97	99	-70	-82	1.95E-6	3.86E-6	7.63E-6
UO-31	0.716	2.186	1.899	1.939	1.841	0.265	0.347	80	83	77	-63	-52	1.55E-6	3.54E-6	8.07E-6
Prostate Cancer															
PC-3	0.835	2.451	2.363	2.398	2.200	0.685	0.664	95	97	84	-18	-20	2.17E-6	6.68E-6	> 1.00E-4
DU-145	0.453	1.773	1.777	1.792	1.681	0.089	0.087	100	101	93	-80	-81	1.77E-6	3.44E-6	6.67E-6
Breast Cancer															
MCF7	0.480	2.425	2.272	2.332	2.100	0.207	0.263	92	95	83	-57	-45	1.73E-6	3.92E-6	.
MDA-MB-231/ATCC	0.685	1.455	1.420	1.454	1.289	0.106	0.287	95	100	78	-85	-58	1.49E-6	3.03E-6	6.14E-6
HS 578T	0.817	1.779	1.702	1.771	1.696	0.426	0.628	92	99	91	-48	-23	1.98E-6	4.53E-6	> 1.00E-4
BT-549	1.257	2.180	2.237	2.180	2.309	0.451	0.436	106	100	114	-64	-65	2.29E-6	4.36E-6	8.33E-6
T-47D	1.008	2.472	2.318	2.346	2.290	0.567	0.602	89	91	88	-44	-40	1.93E-6	4.64E-6	> 1.00E-4
MDA-MB-468	0.703	1.891	1.899	1.947	1.842	0.107	0.140	101	105	96	-85	-80	1.79E-6	3.39E-6	6.42E-6

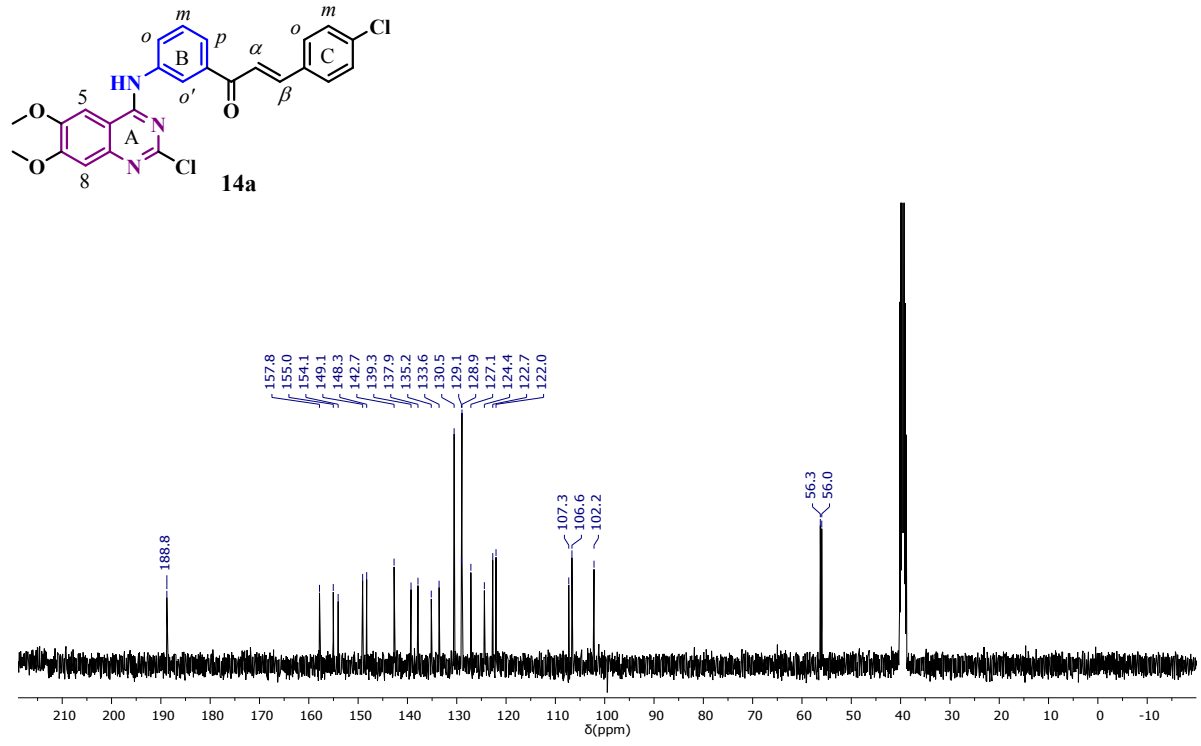
National Cancer Institute Developmental Therapeutics Program
Dose Response Curves - Compound 16c (NSC: 826384)



Compound 14a

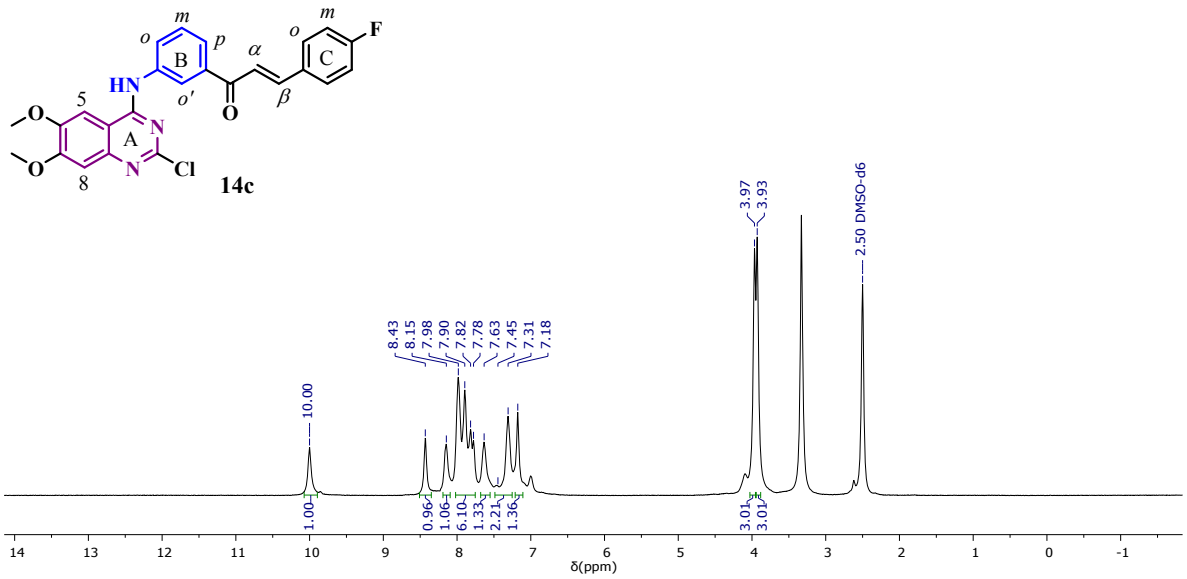


^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **14a**.

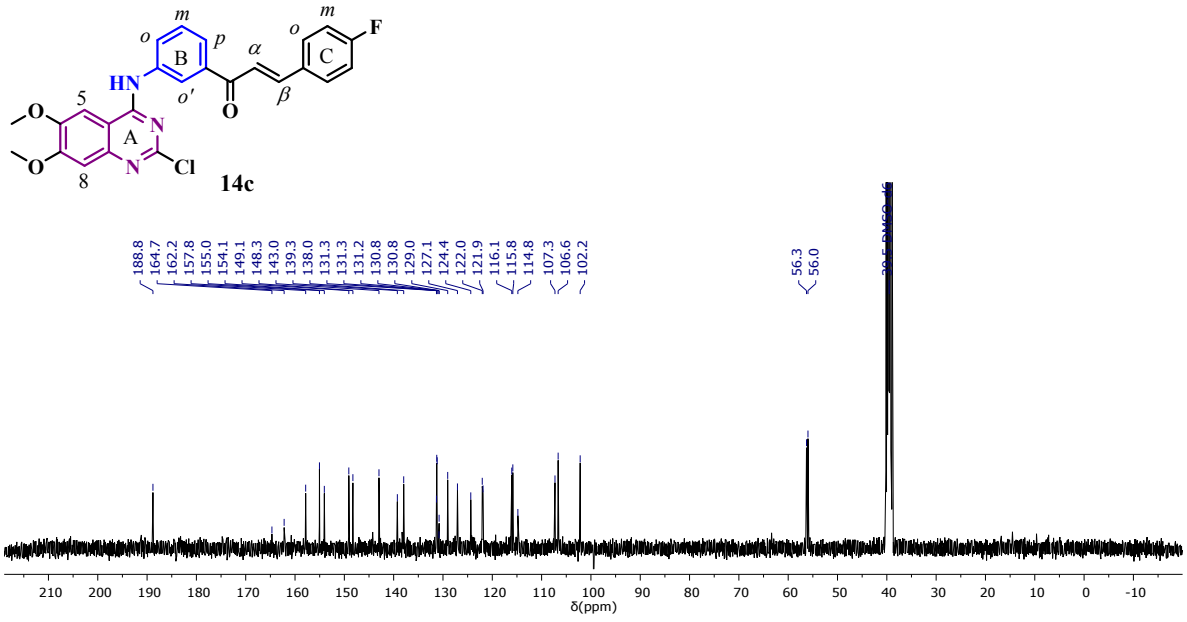


^{13}C NMR (100 MHz, DMSO-d_6) spectrum of **14a**.

Compound 14c

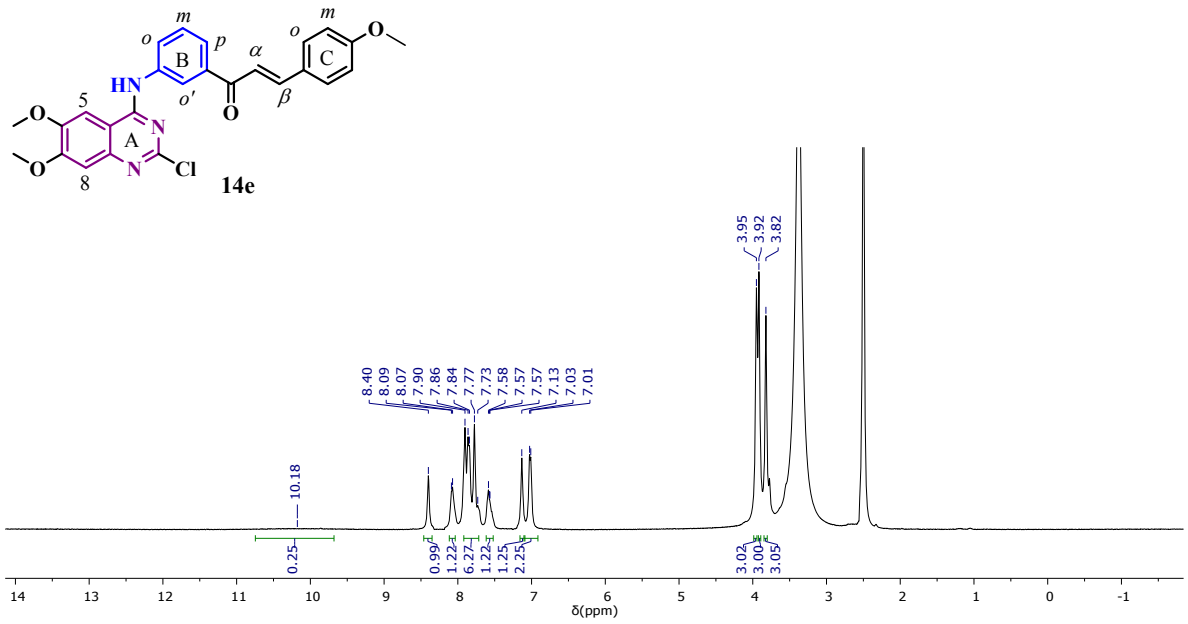


^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **14c**.

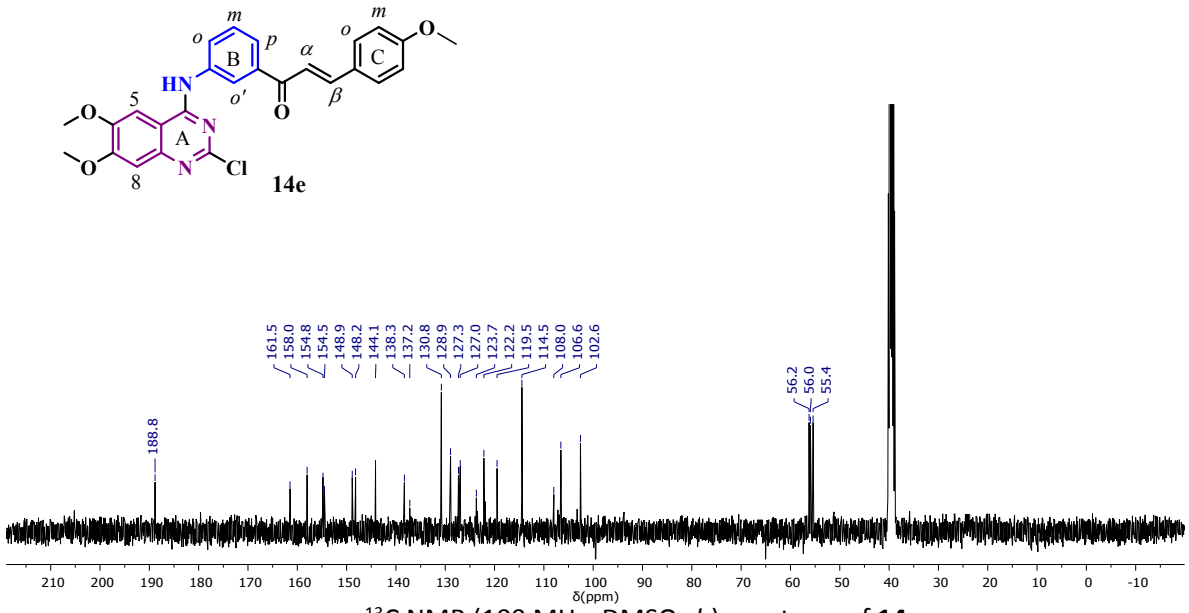


^{13}C NMR (100 MHz, DMSO-d_6) spectrum of **14c**.

Compound 14e

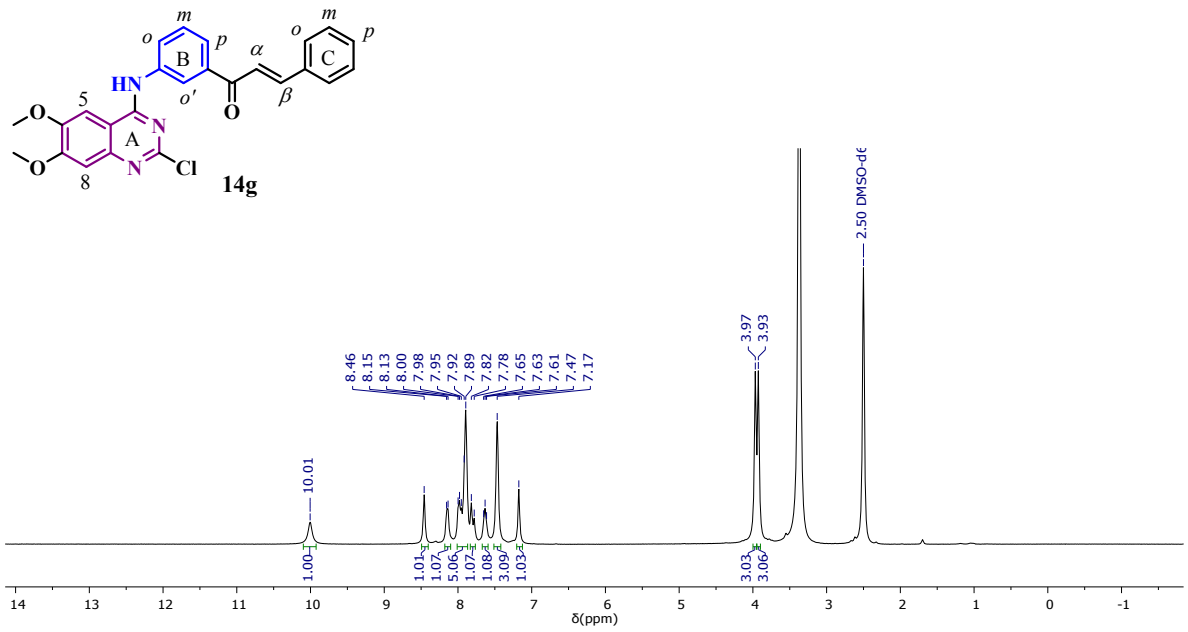


^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **14e**.

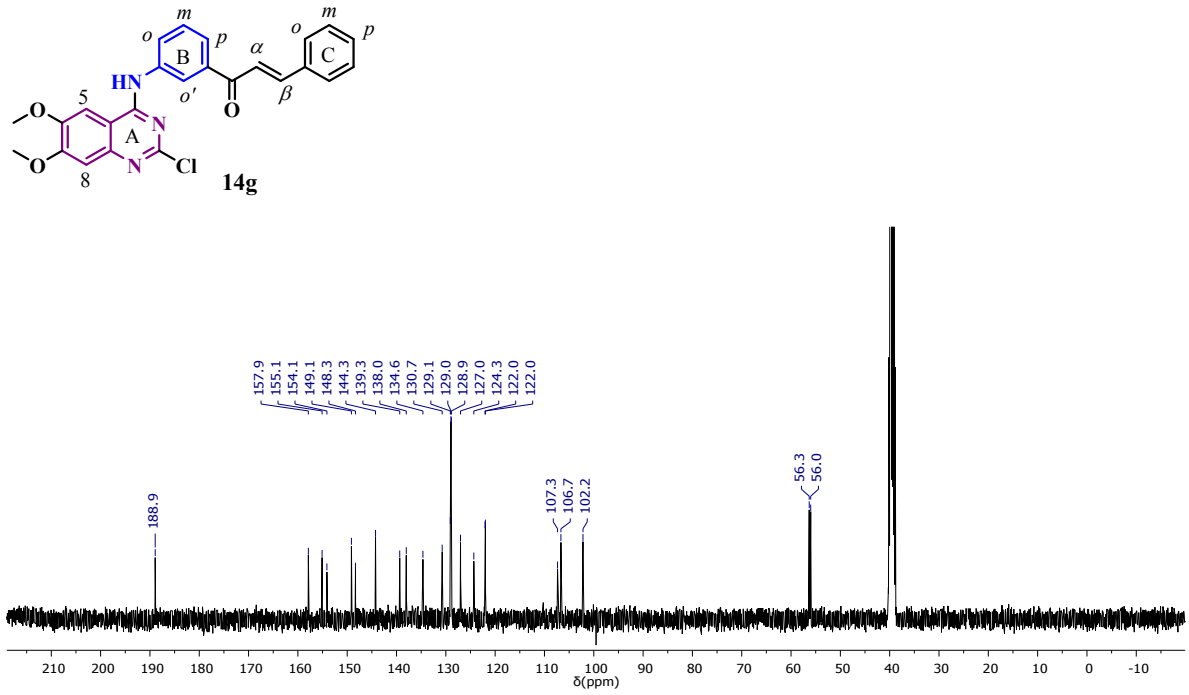


^{13}C NMR (100 MHz, DMSO-d_6) spectrum of **14e**.

Compound 14g

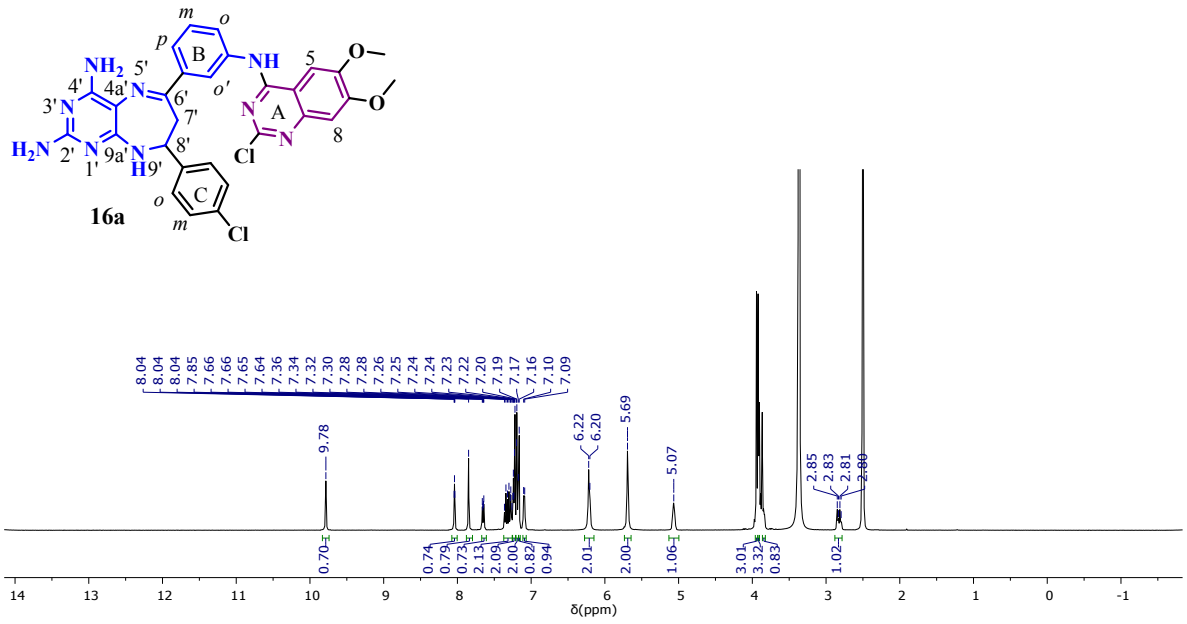


^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **14g**.

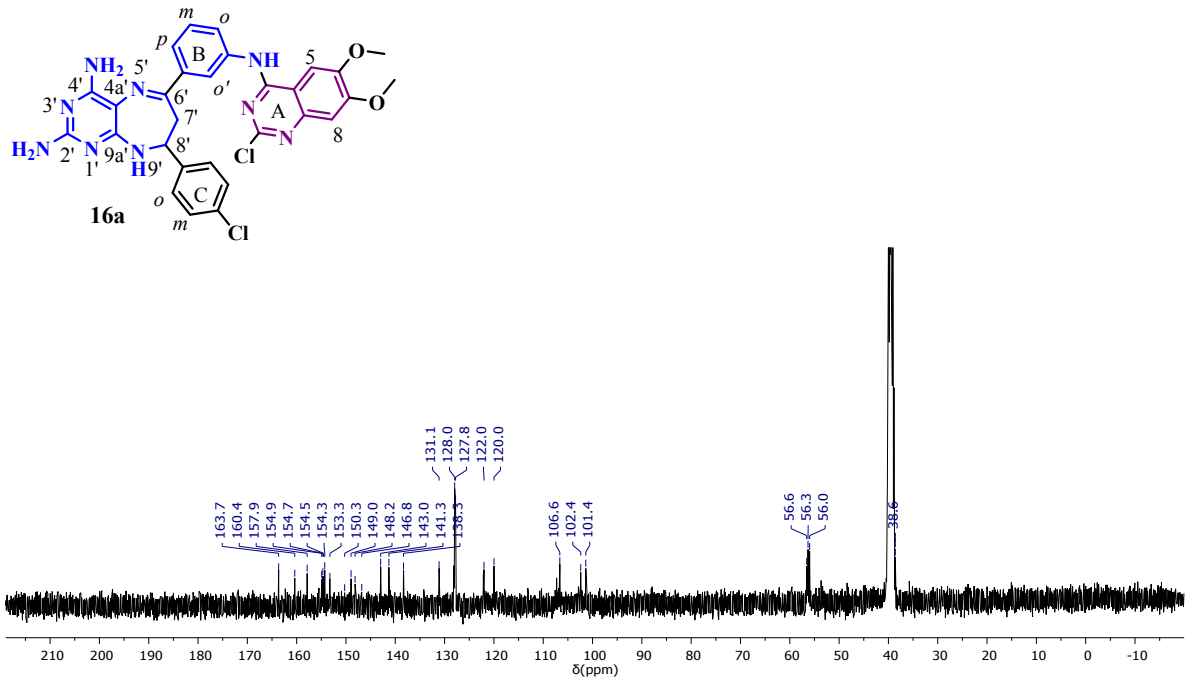


^{13}C NMR (100 MHz, DMSO-d_6) spectrum of **14g**.

Compound 16a

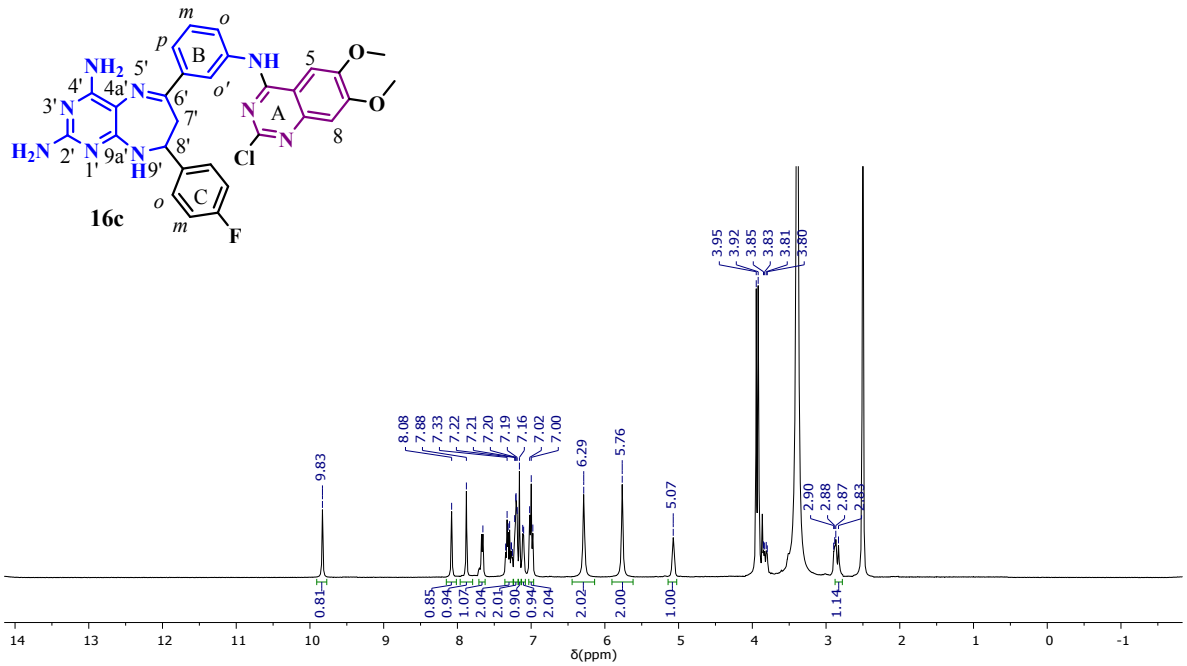


^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **16a**.

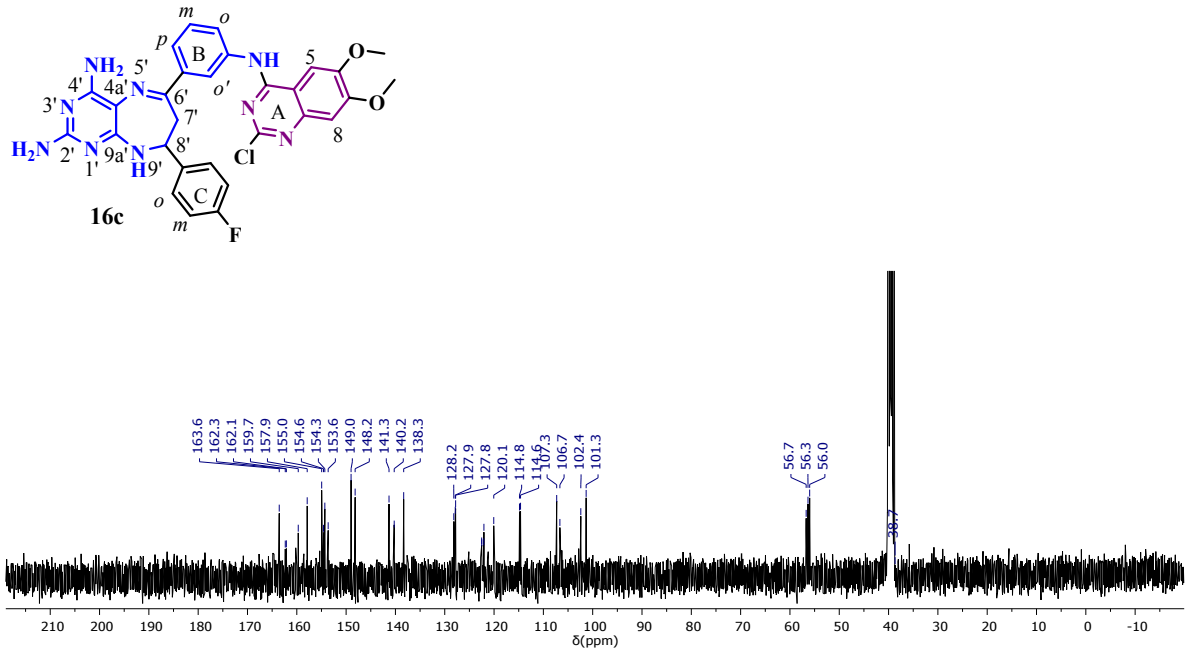


^{13}C NMR (100 MHz, DMSO-d_6) spectrum of **16a**.

Compound 16c

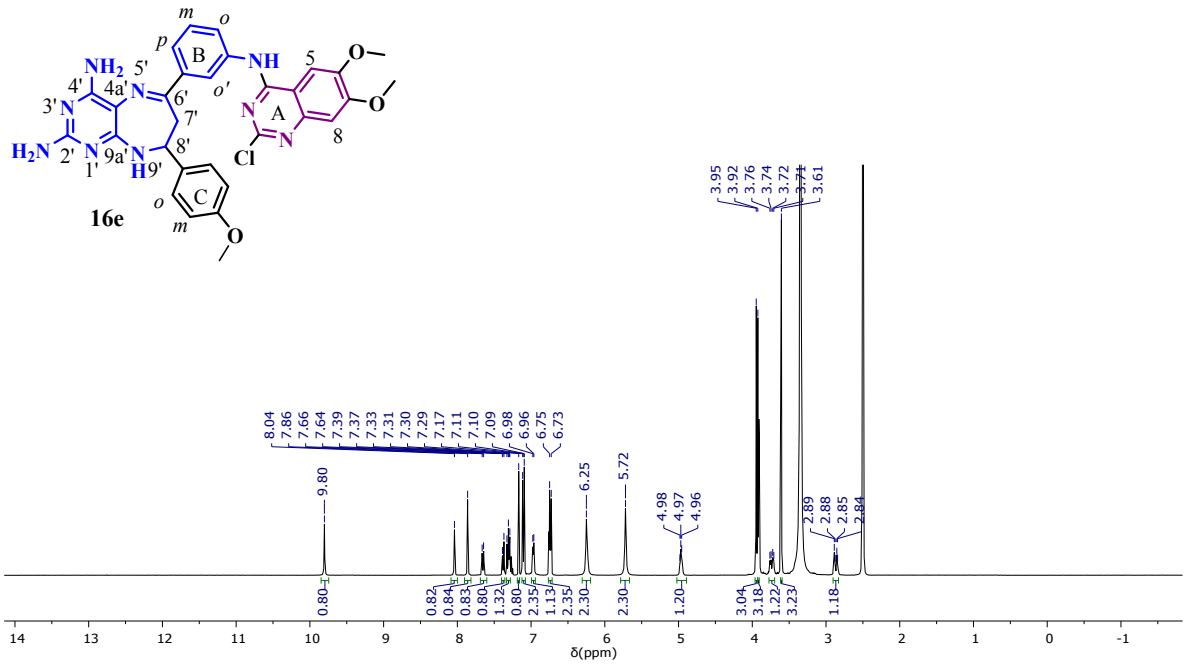


^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **16c**.

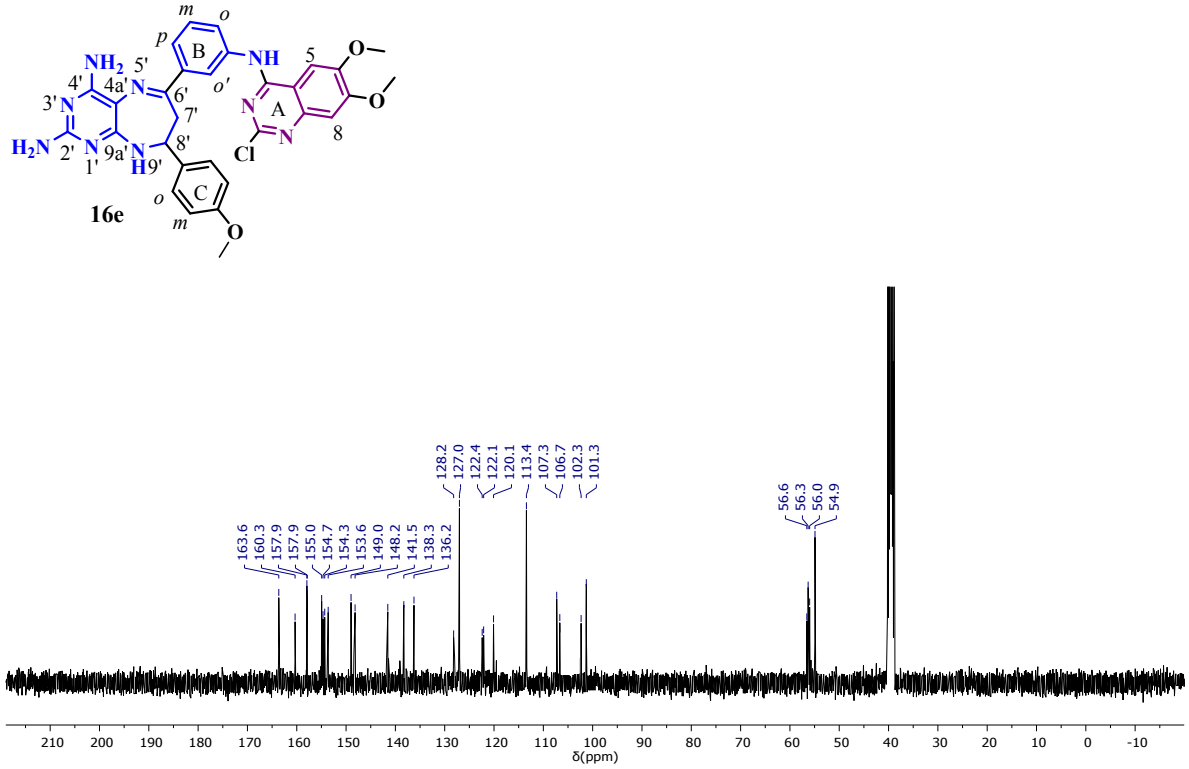


^{13}C NMR (100 MHz, DMSO-d_6) spectrum of **16c**.

Compound 16e

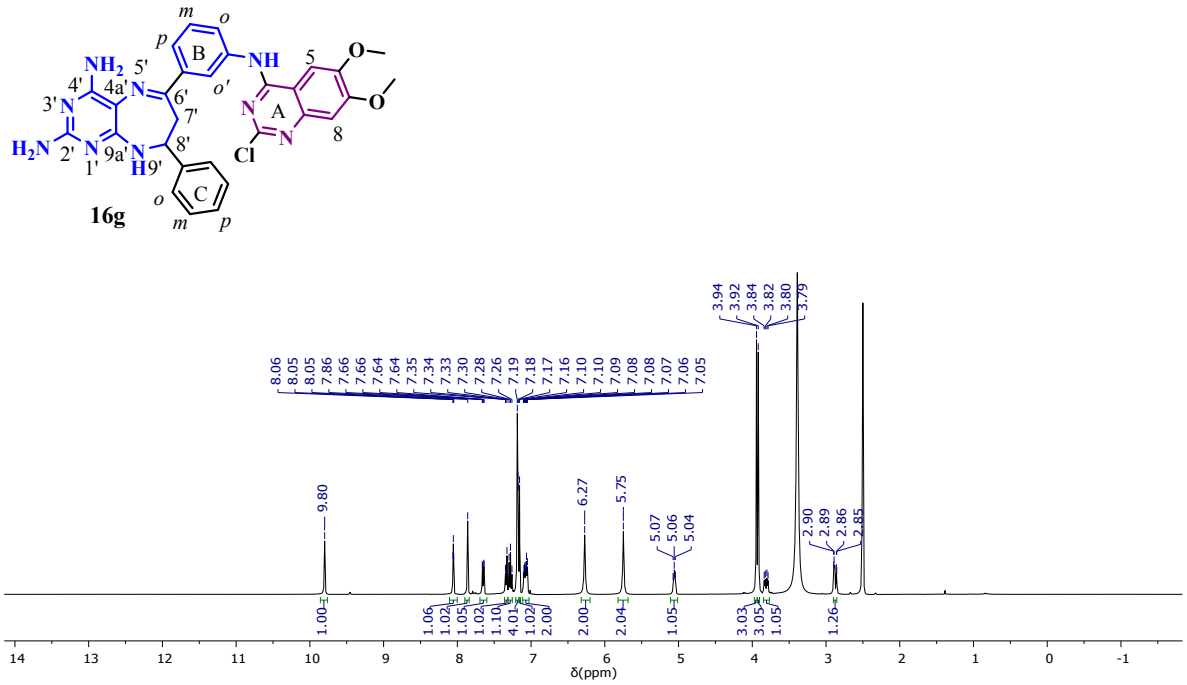


^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **16e**.

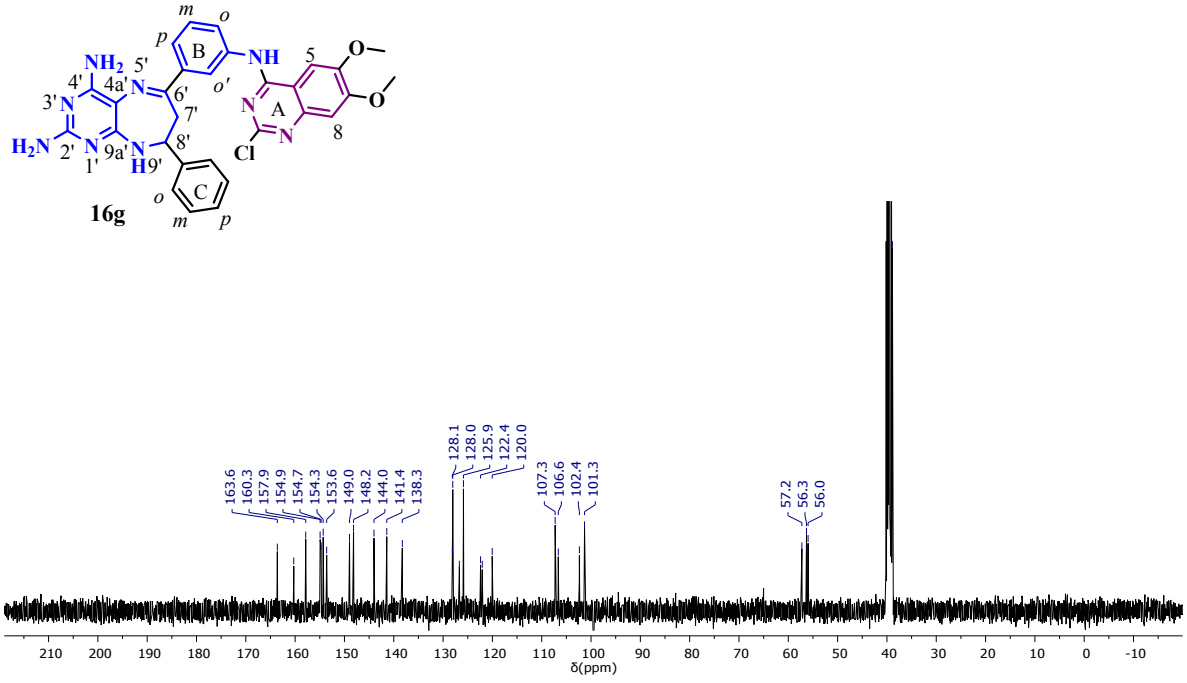


^{13}C NMR (100 MHz, DMSO-d_6) spectrum of **16e**.

Compound 16g



^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **16g**.



^{13}C NMR (100 MHz, DMSO-d_6) spectrum of **16g**.