Electronic Supplementary Material (ESI) for Medicinal Chemistry Communications.

Supporting information

An imidazole-based derivative shows anti cancer potential by inducing apoptosis and cellular senescence

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Contents

Table 01: Antitumor activity (GI_{50}/□M)[a] and toxicity (LC_{50}/□M)[b] data of **771432** selected for 5 dose studies for the NCI60-cell lines screen.

Cell lines	GI_{50} (□M)	LC_{50} (□M)
Leukemia		
CCRF-CEM	7.540	>100
HL-60(TB)	21.20	>100
K-562	6.370	>100
MOLT-4	18.00	>100
RPMI-8226	27.40	>100
SR	7.770	>100
Non-Small Cell Lung Cancer		
A549/ATCC	9.020	>100
HOP-62	15.30	>100
NCI-H226	21.30	>100
NCI-H23	28.50	>100
NCI-H322M	21.40	>100
NCI-H460	32.10	>100
NCI-H522	31.40	>100
Colon Cancer		
COLO 205	52.20	>100
HCT-116	7.350	>100
HCT-15	6.720	>100
HT29	35.30	>100
KM12	11.10	>100
SW-620	42.00	>100
CNS		

SF-268	43.80	>100
SF-295	9.560	>100
SF-539	33.80	>100
SNB-19	30.20	>100
SNB-75	24.00	>100
U251	20.60	>100
Melenoma		
LOX IMVI	26.10	>100
M14	22.70	>100
MDA-MB-435	31.30	>100
SK-MEL-2	38.40	>100
SK-MEL-28	38.70	>100
SK-MEL-5	11.40	>100
UACC-257	26.20	>100
Ovarian Cancer		
IGROV1	11.50	>100
OVCAR-3	30.30	>100
OVCAR-4	32.30	>100
OVCAR-5	26.50	>100
OVCAR-8	17.30	>100
NCI/ADR-RES	6.960	>100
SK-OV-3	27.60	>100
Renal Cancer		
786-0	48.70	>100
A498	16.50	>100
ACHN	6.920	>100
CAK-1	7.440	>100
SN12C	24.50	>100

UO-31	7.430	>100
Prostate Cancer		
PC-3	11.10	>100
DU-145	23.30	>100
Breast Cancer		
MCF7	6.580	>100
MDA-MB-231ATCC	18.20	>100
HS 578T	9.700	>100
BT-549	50.00	>100
T-47D	9.730	>100
MDA-MB-468	38.40	>100

[a]GI_{50}: 50% Growth inhibition, concentration of drug resulting in a 50% reduction in net protein increase compared with control cells. [b]LC_{50}: Lethal concentration, concentration of drug lethal to 50% of cells.

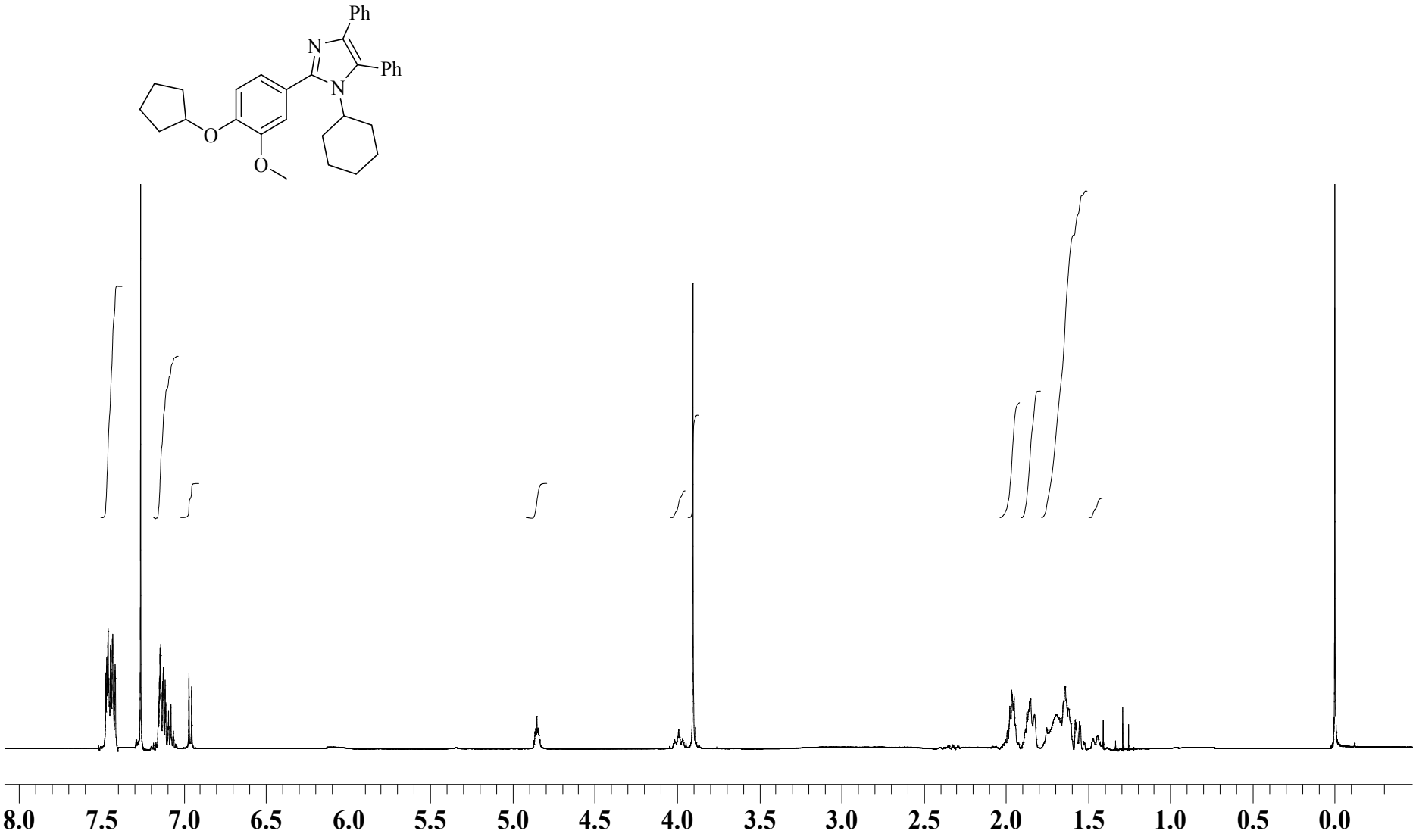


Figure 1: ^{1}H NMR spectrum of **3** (300 MHz, $CDCl_3$, 298K).

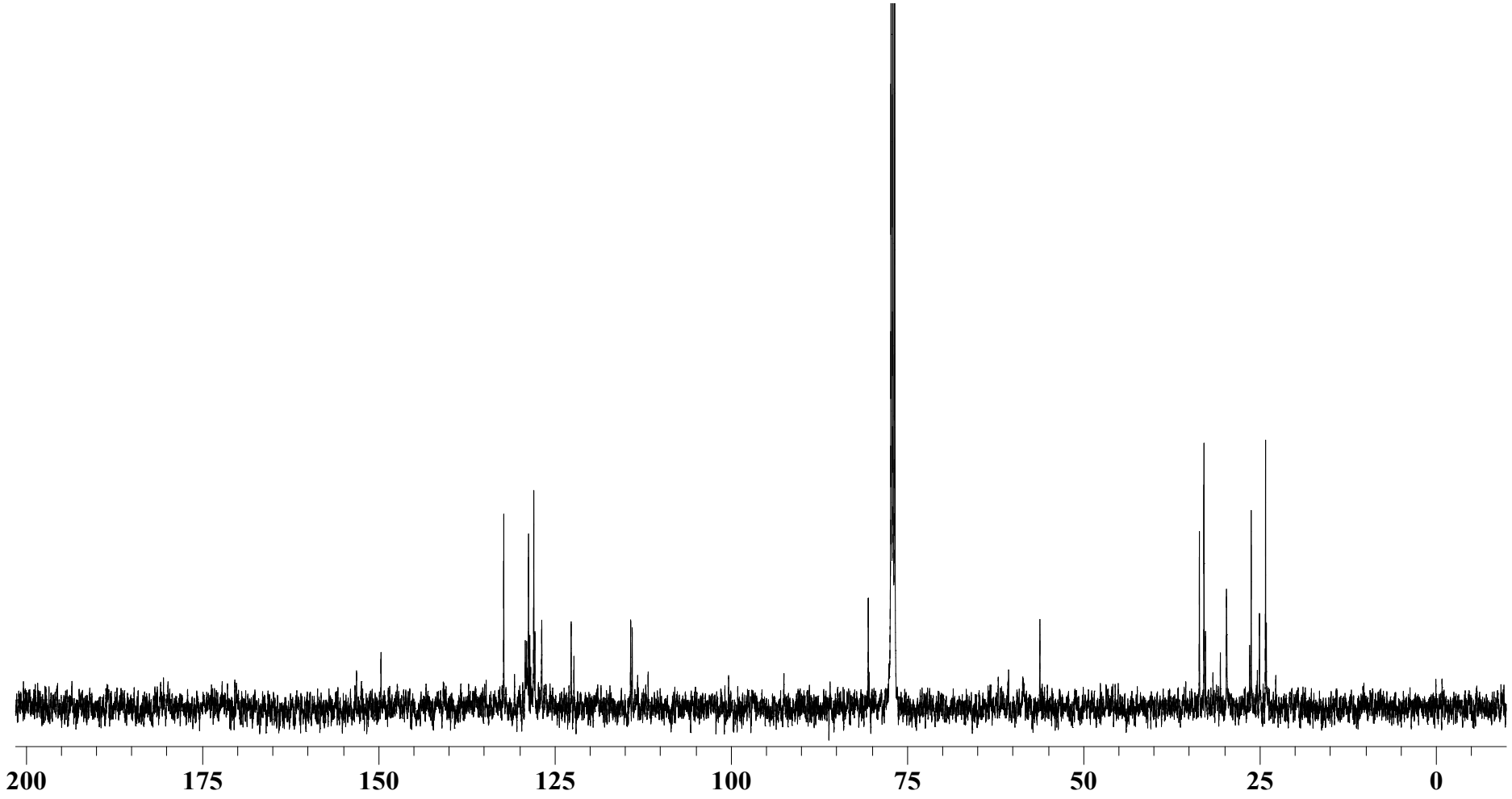


Figure 2. ^{13}C NMR Spectrum of 3 (75MHz, $CDCl_3$, 298K).

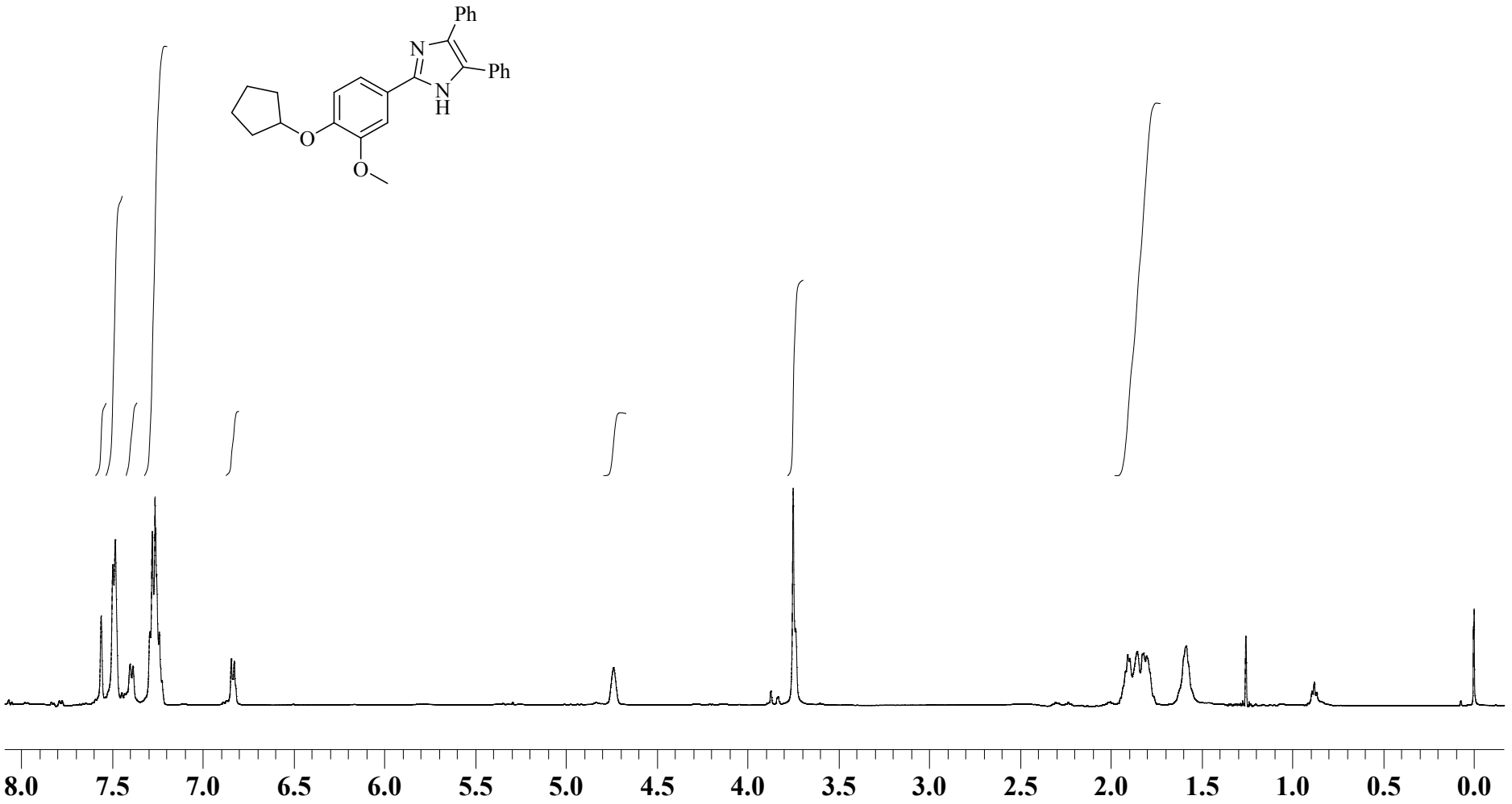


Figure 3. ^{1}H NMR Spectrum of 4 (300 MHz, $CDCl_3$, 298K).

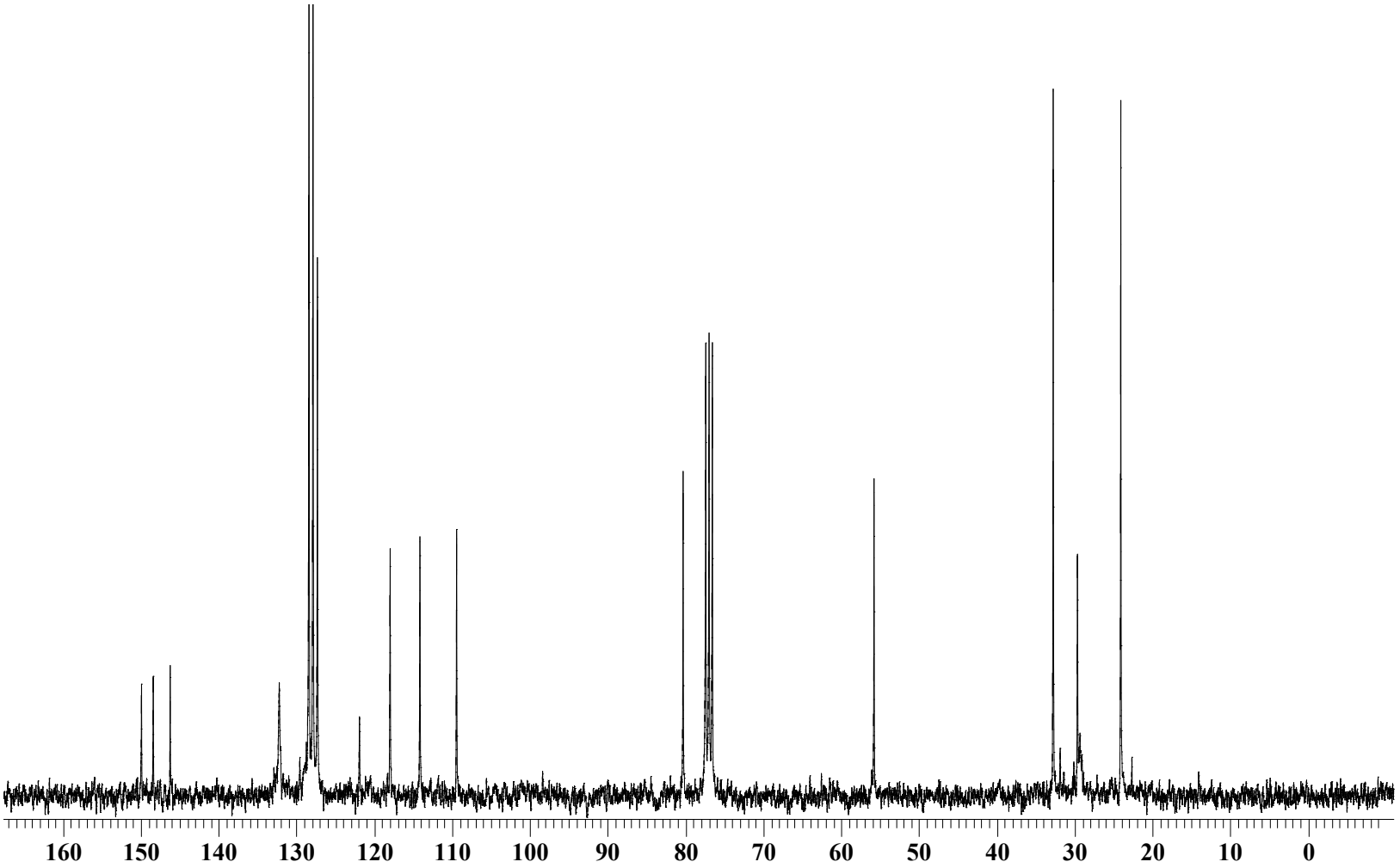


Figure 4. ^{13}C NMR Spectrum of 4 (75MHz, $CDCl_3$, 298K).

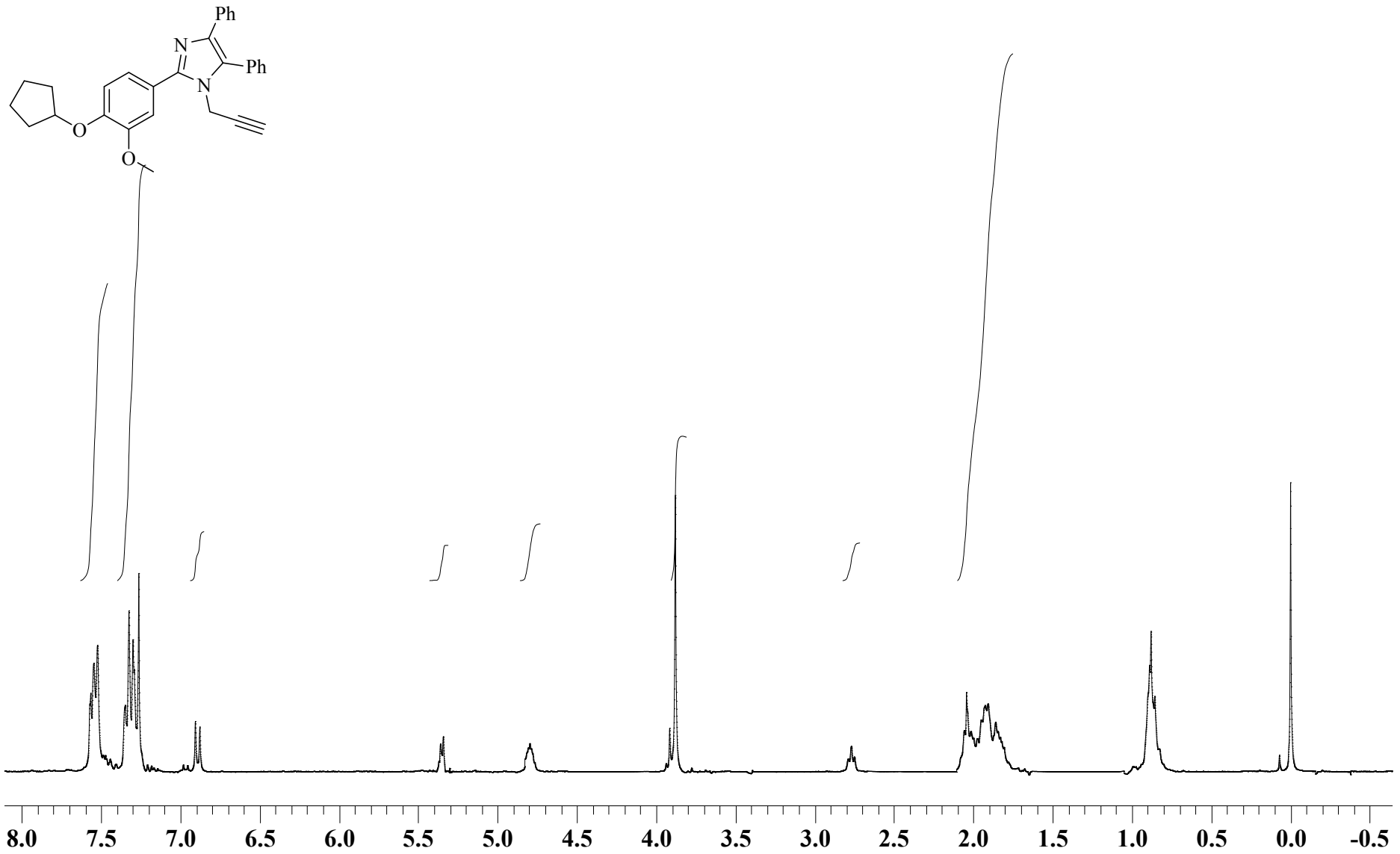


Figure 5. ^{1}H NMR Spectrum of 5 (300 MHz, $CDCl_3$, 298K).

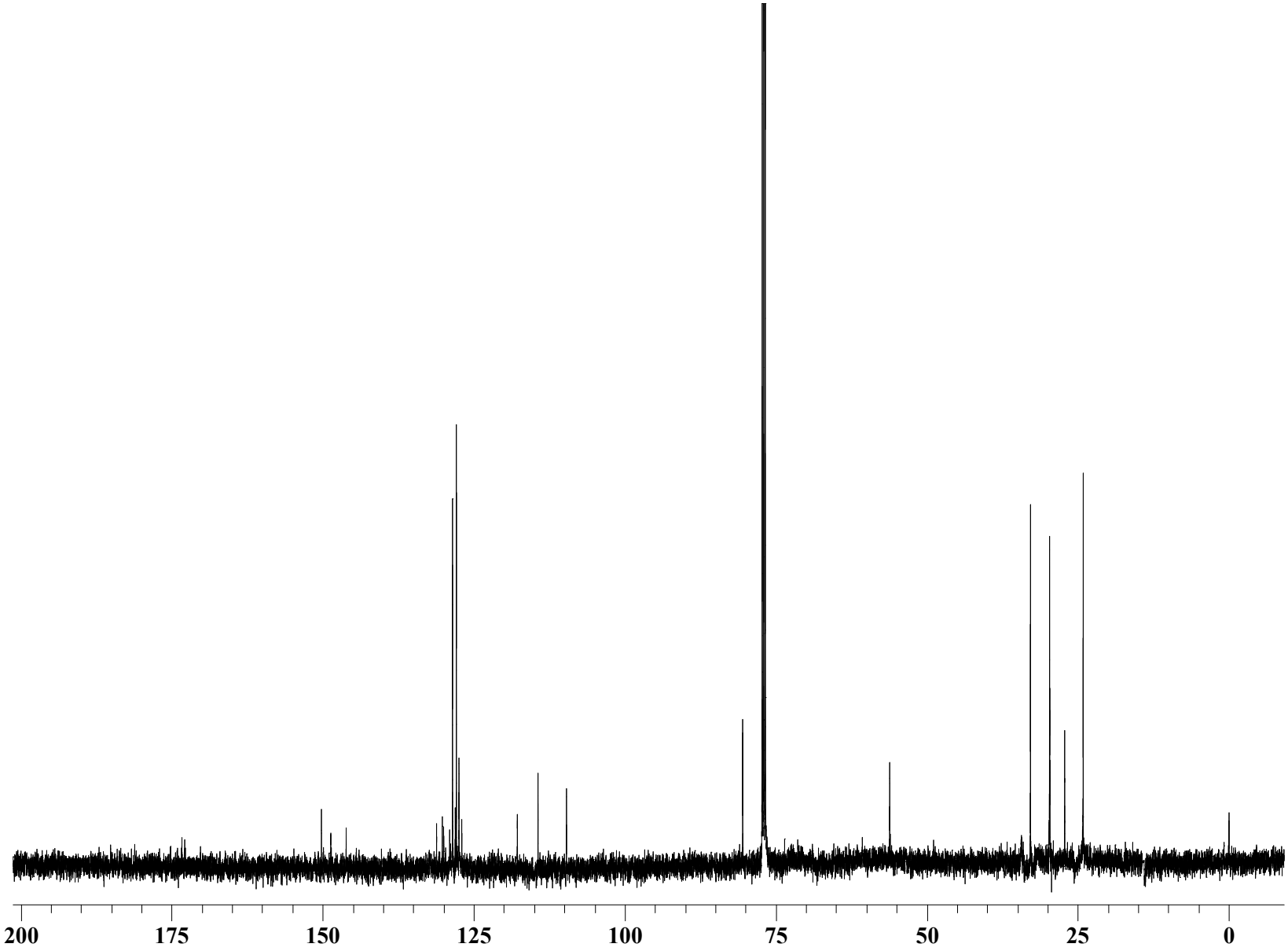


Figure 6. ^{13}C NMR Spectrum of 5 (75MHz, $CDCl_3$, 298K).

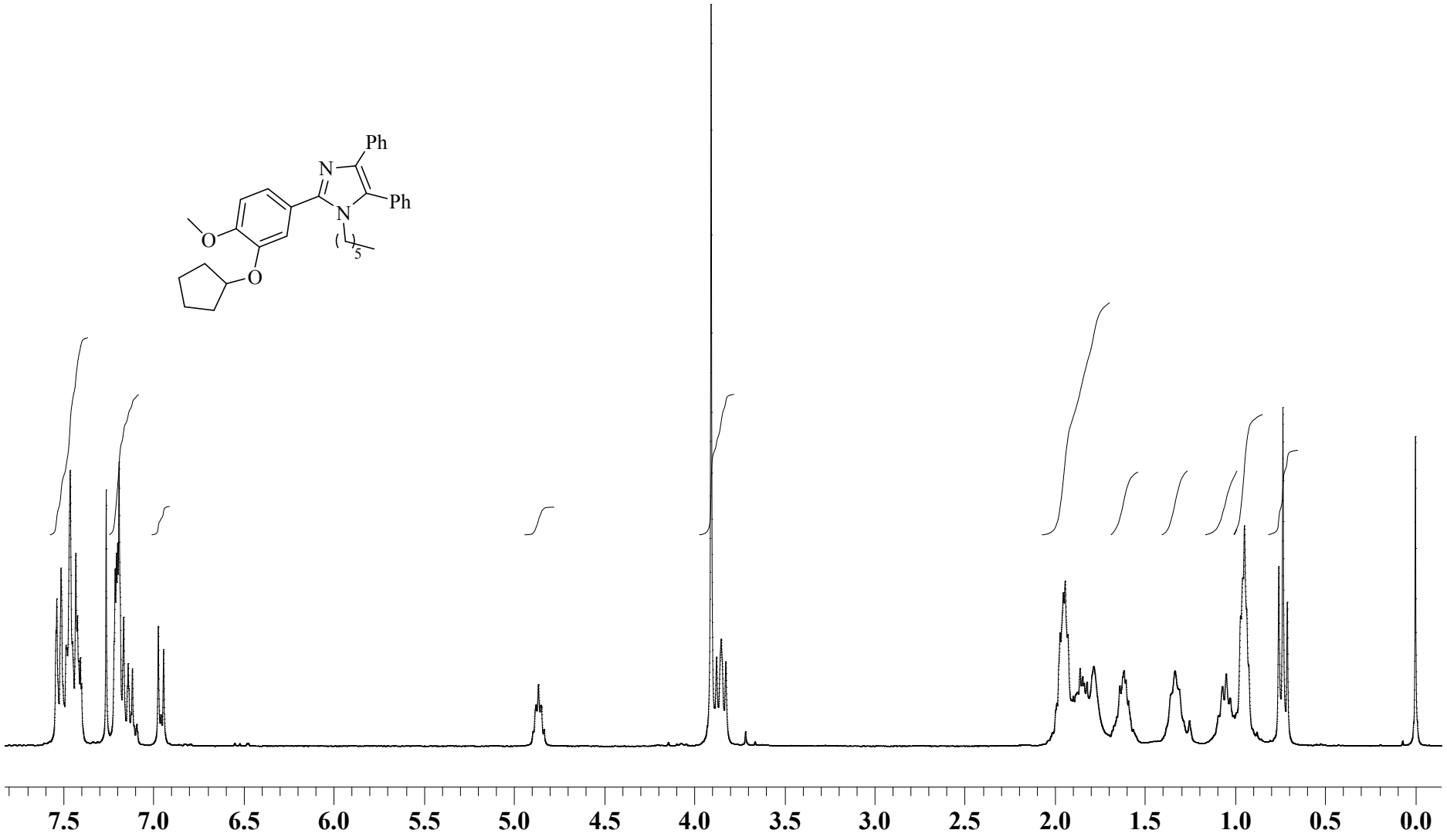


Figure7. ^{1}H NMR Spectrum of 6 (300 MHz, $CDCl_3$, 298K).

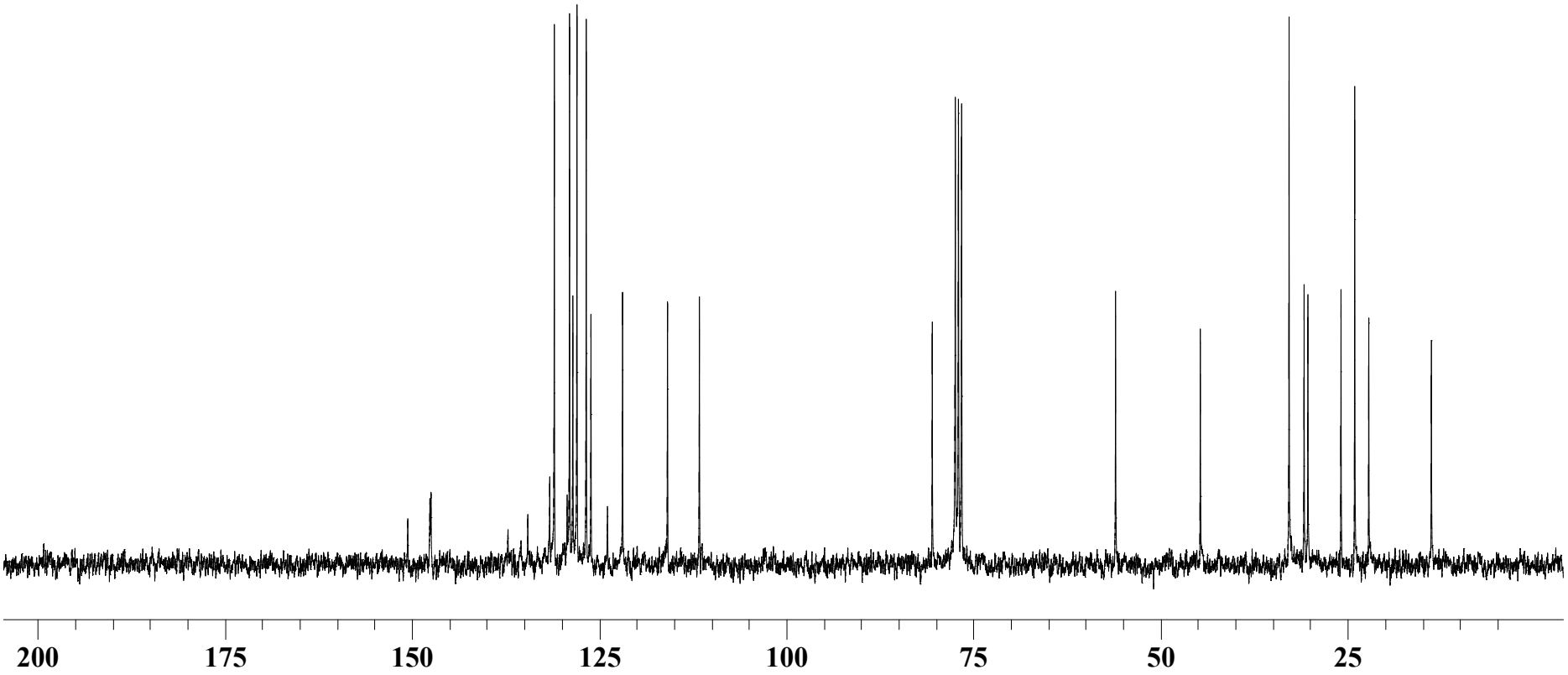


Figure 8. ^{13}C NMR Spectrum of 6 (75MHz, $CDCl_3$, 298K).

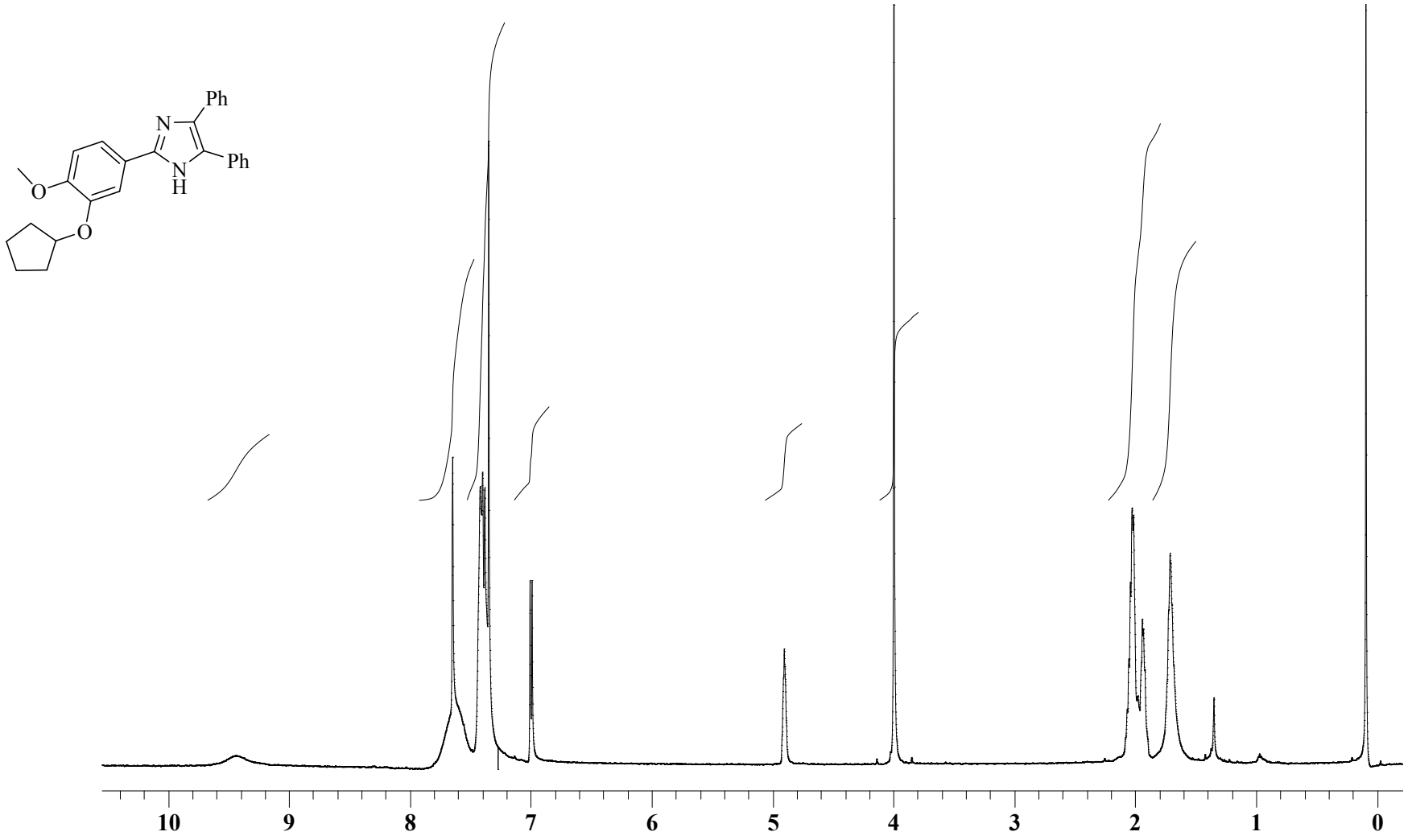


Figure 9. ^{1}H NMR Spectrum of 7 (300 MHz, $CDCl_3$, 298K).

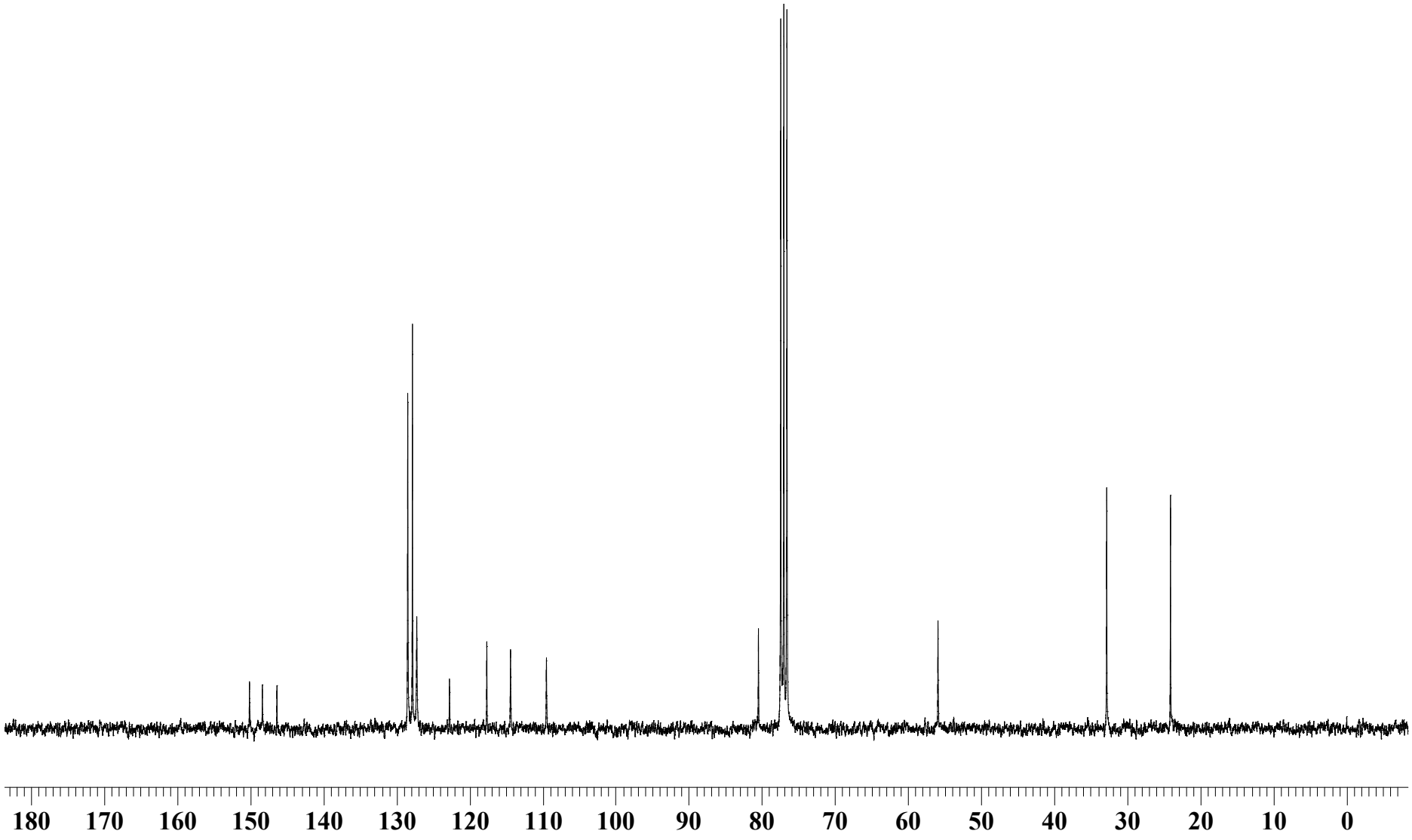


Figure 10. ^{13}C NMR Spectrum of 7 (75MHz, $CDCl_3$, 298K).

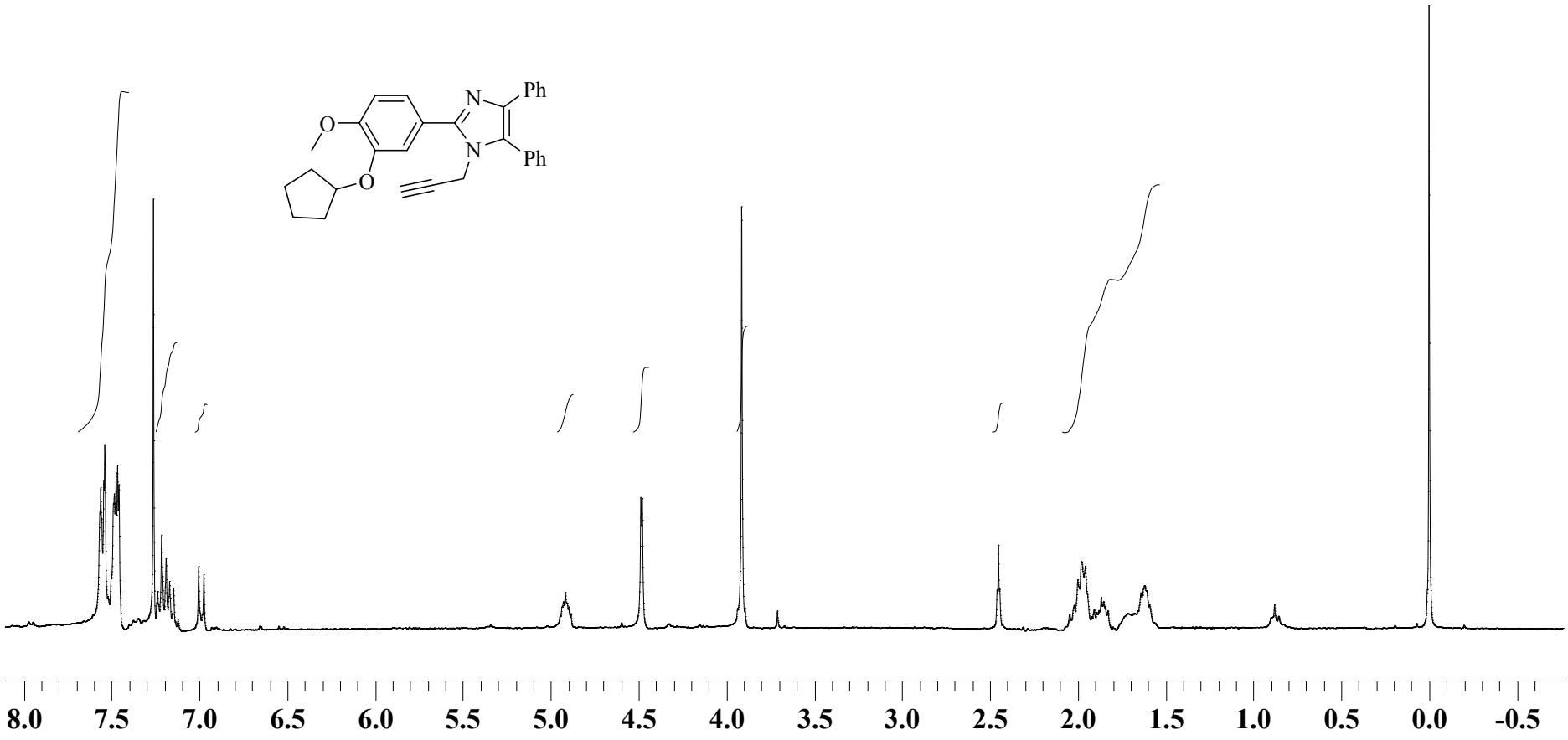


Figure 11. ^{1}H NMR Spectrum of 8 (300 MHz, $CDCl_3$, 298K).

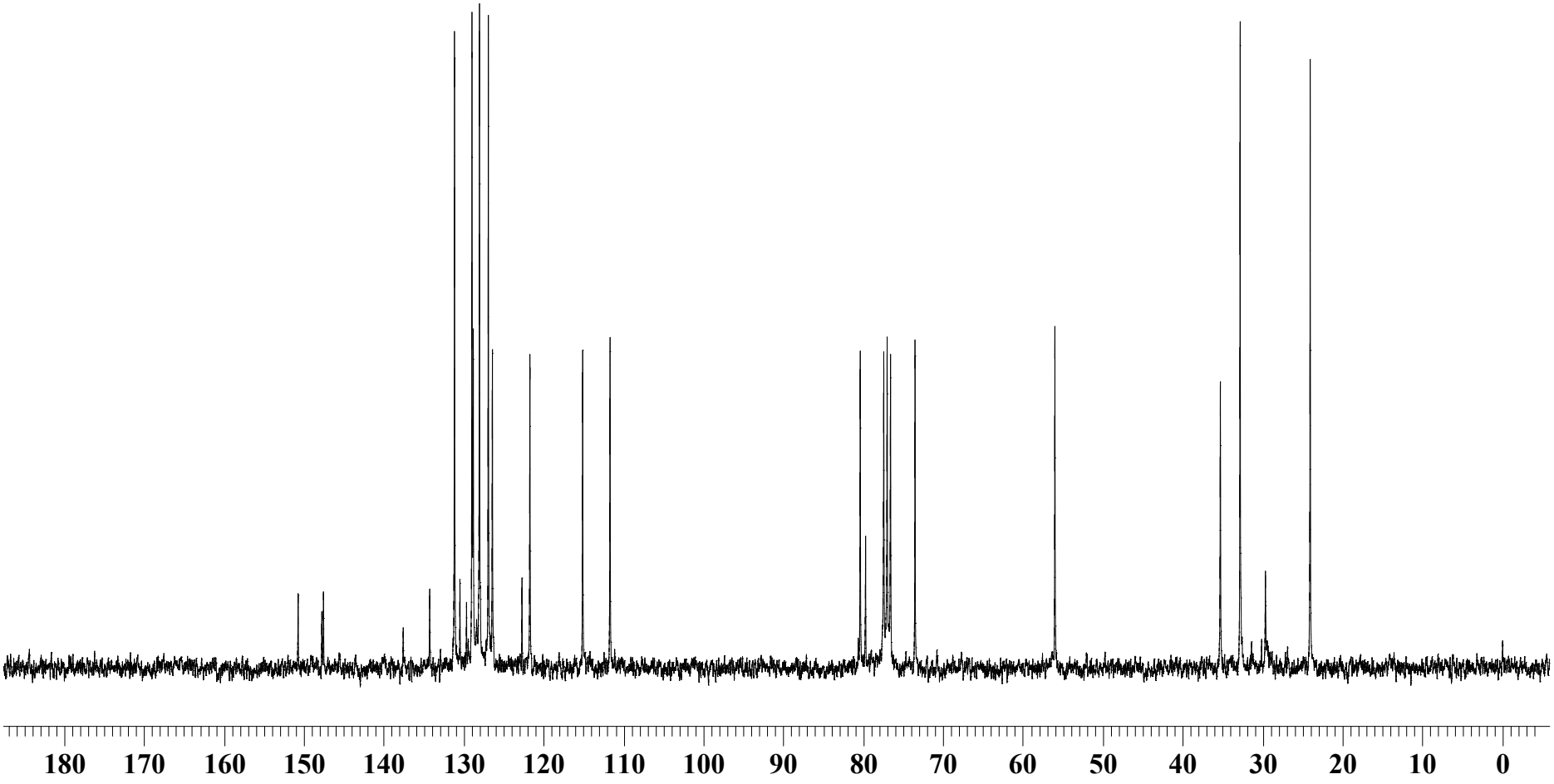


Figure 12. ^{13}C NMR Spectrum of 8 (75MHz, $CDCl_3$, 298K).

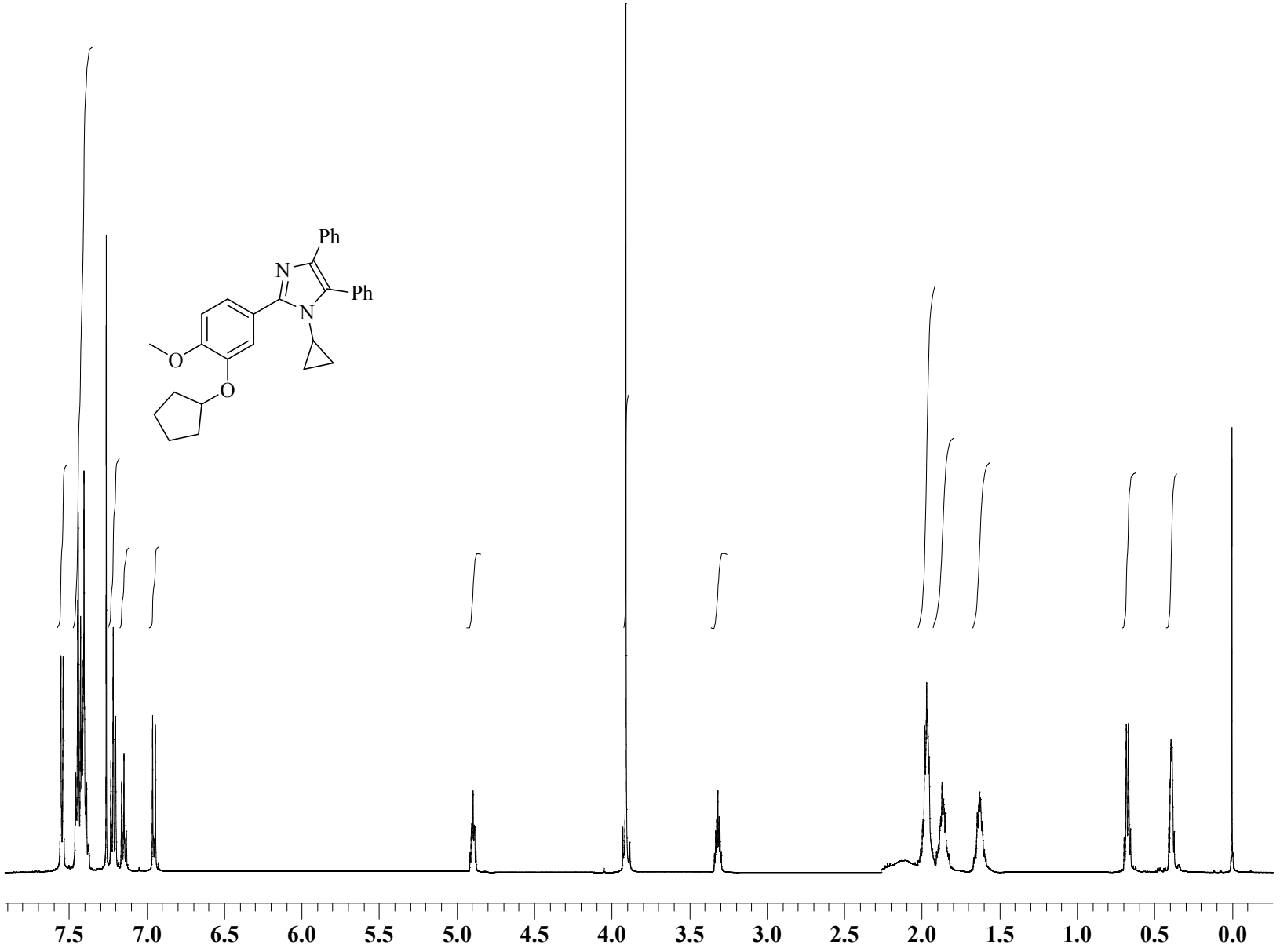


Figure 13. ^{1}H NMR Spectrum of 9 (300 MHz, $CDCl_3$, 298K).

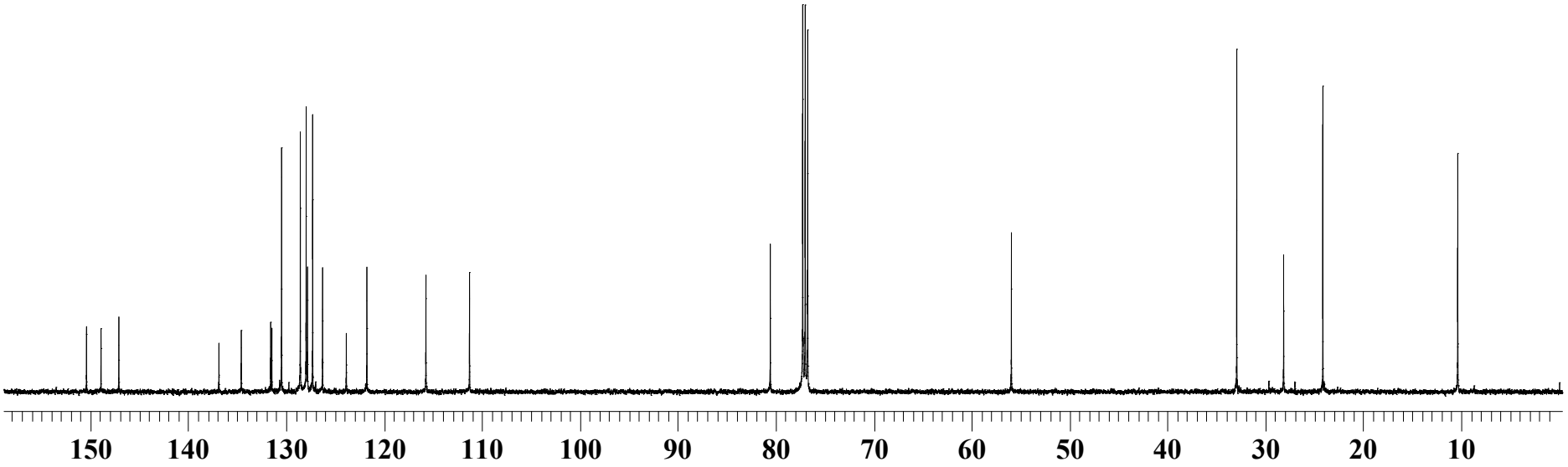


Figure 14. ^{13}C NMR Spectrum of 9 (75MHz, $CDCl_3$, 298K).

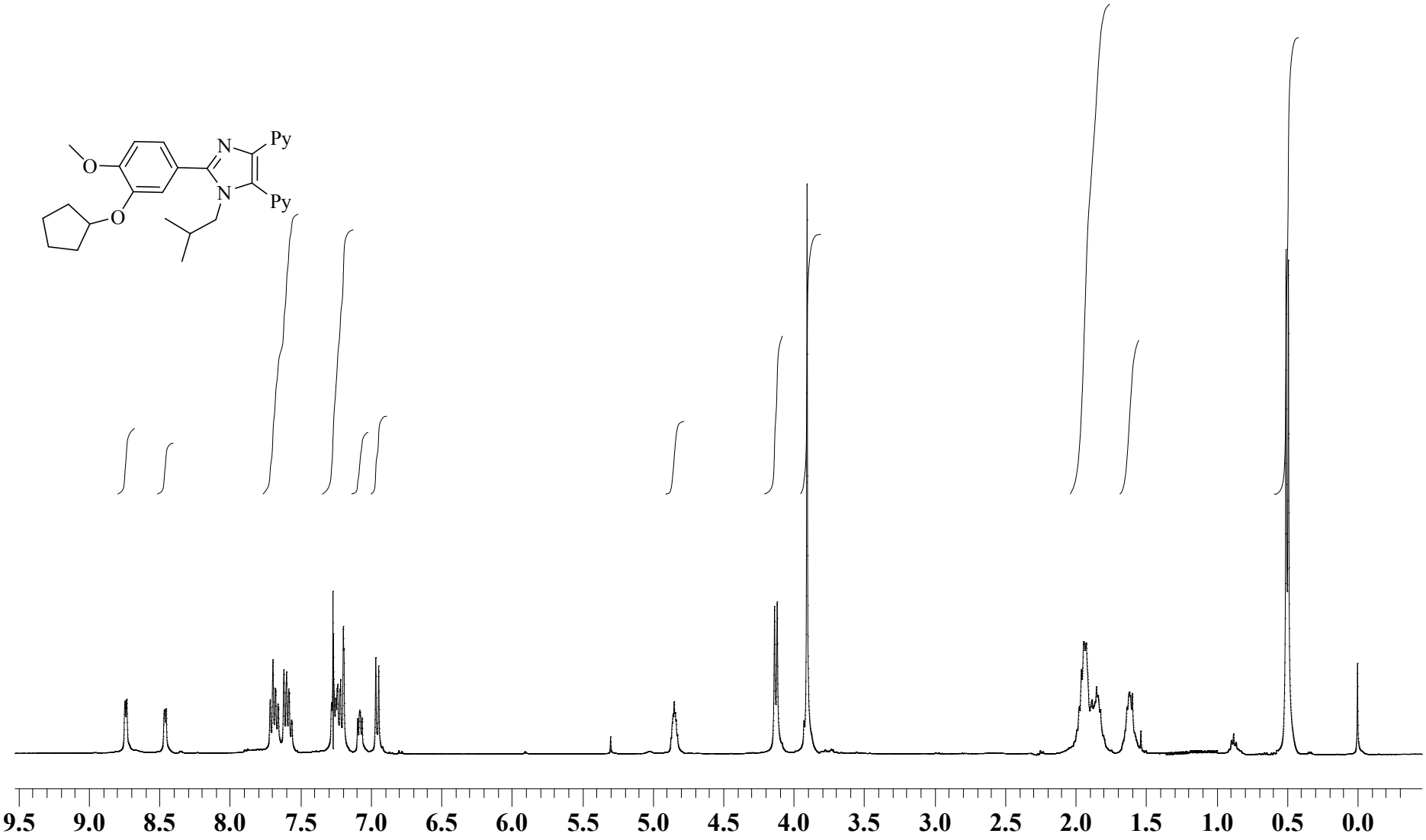


Figure 15. ^{1}H NMR Spectrum of 10 (400 MHz, $CDCl_3$, 298K).

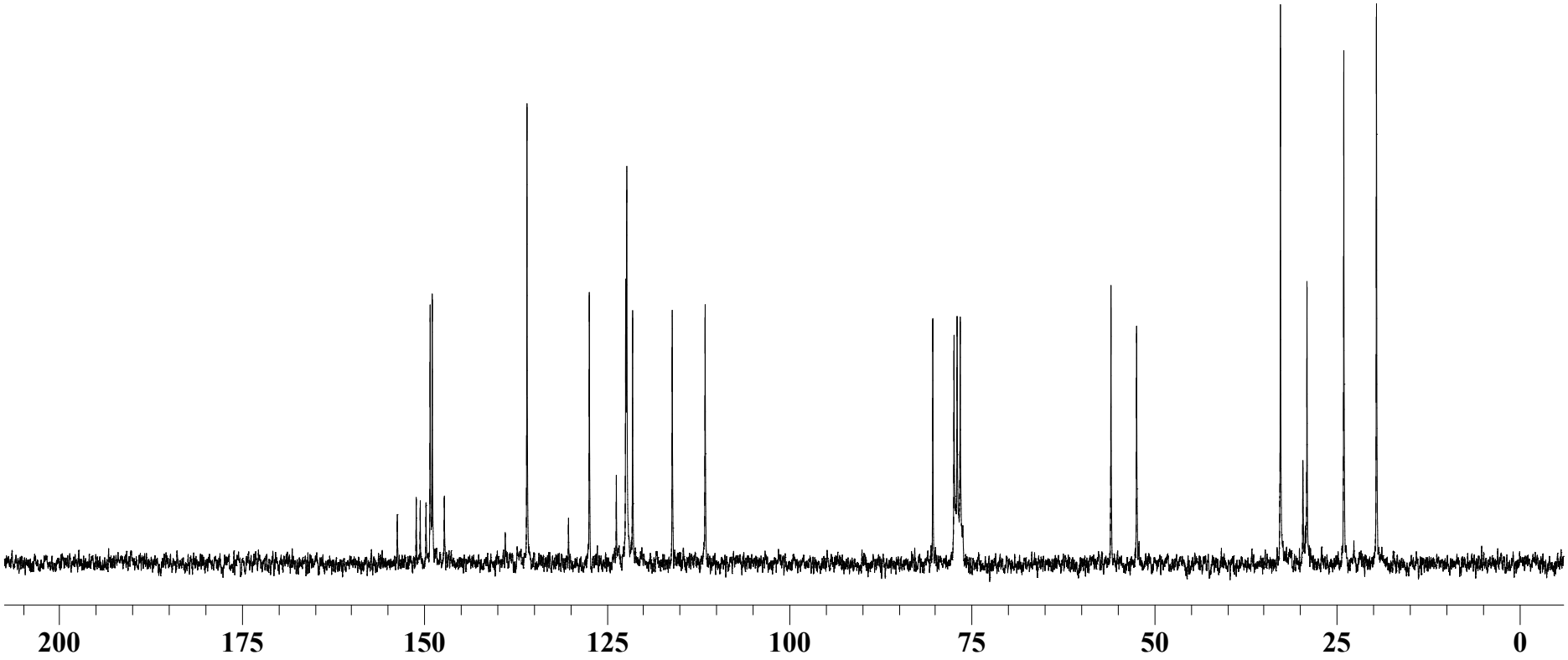


Figure 16. ^{13}C NMR Spectrum of 10 (75MHz, $CDCl_3$, 298K).

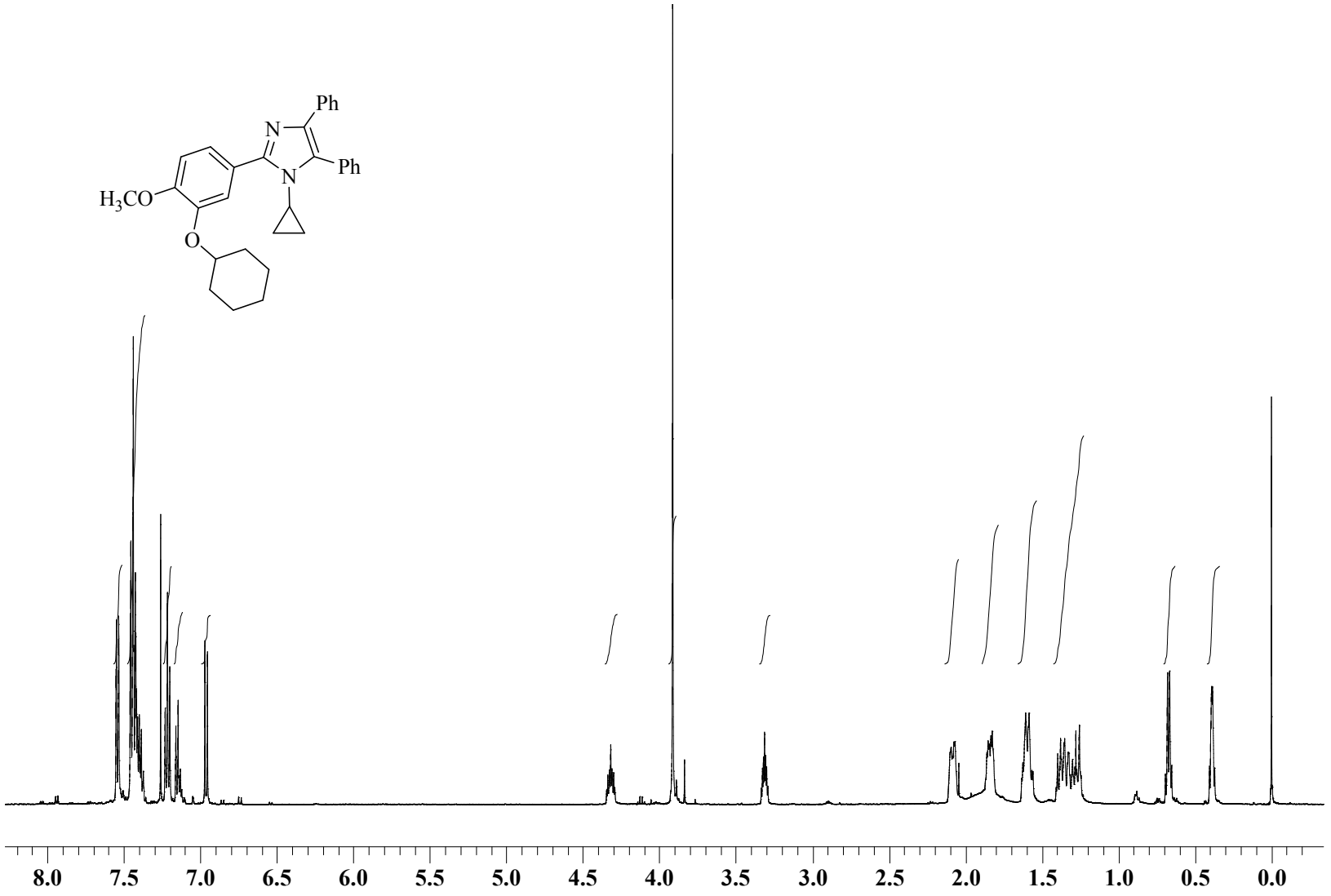


Figure 17. ^{1}H NMR Spectrum of 11 (300 MHz, $CDCl_3$, 298K).

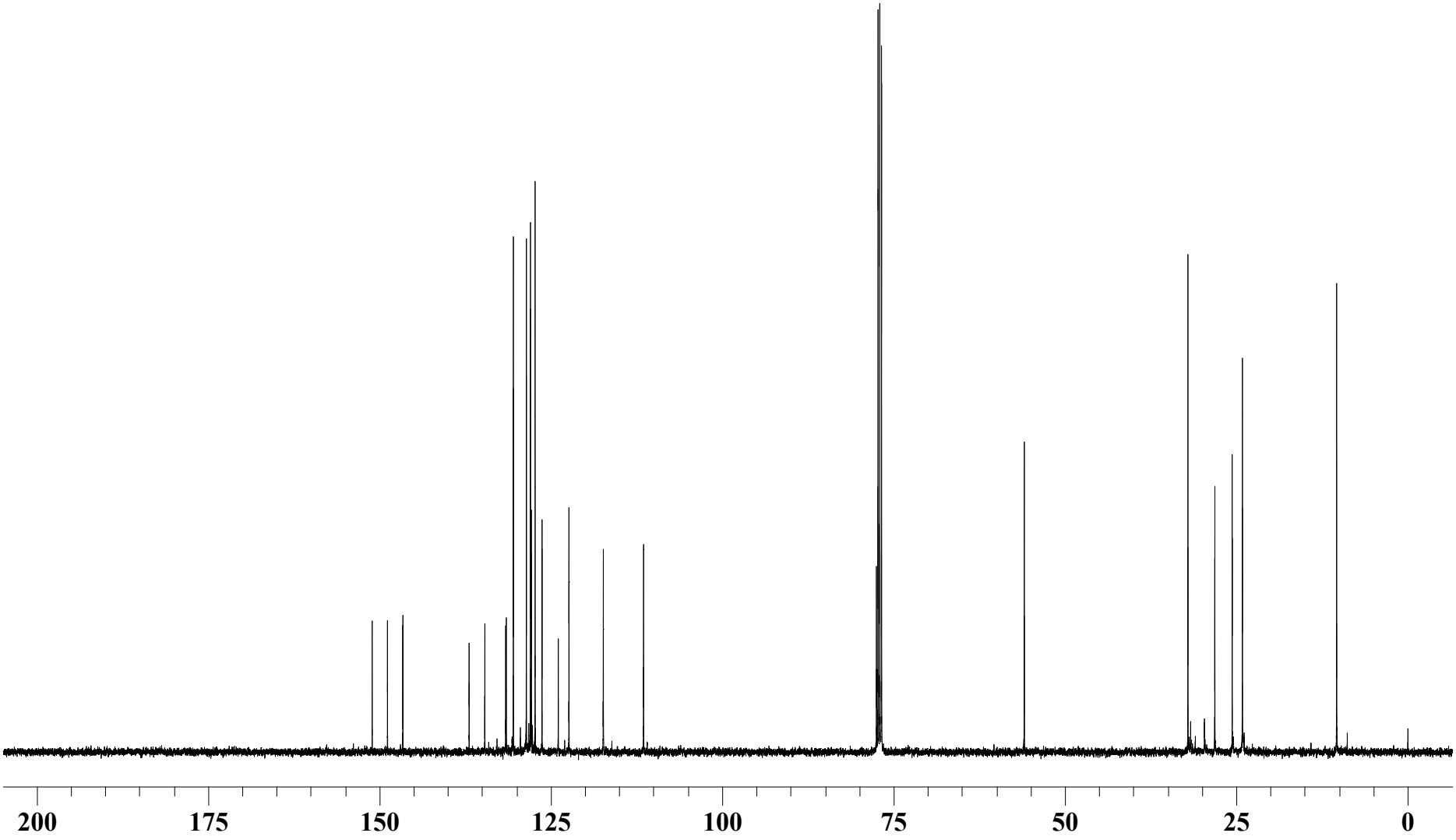


Figure 18. ^{13}C NMR Spectrum of 11 (75 MHz, $CDCl_3$, 298K).

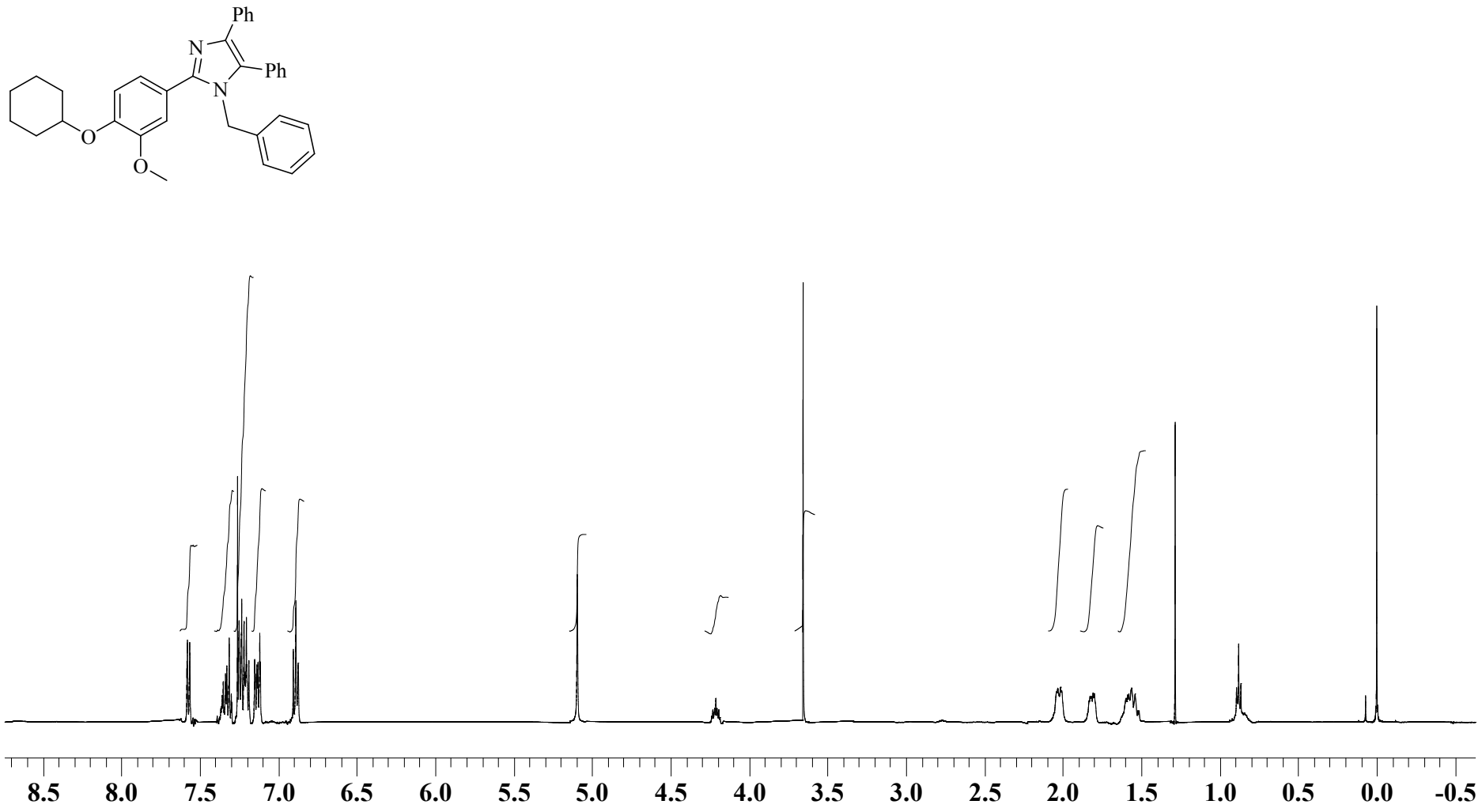


Figure 19: ^{1}H NMR Spectrum of 12 (300 MHz, $CDCl_3$, 298K).

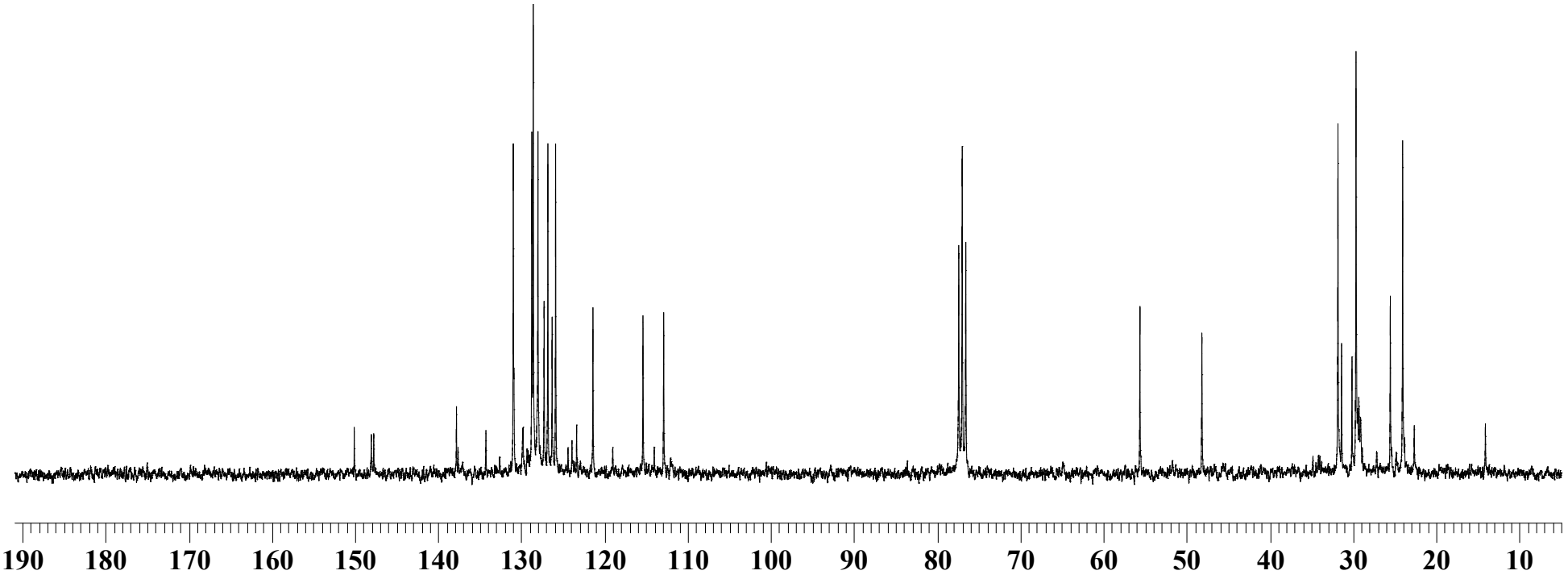
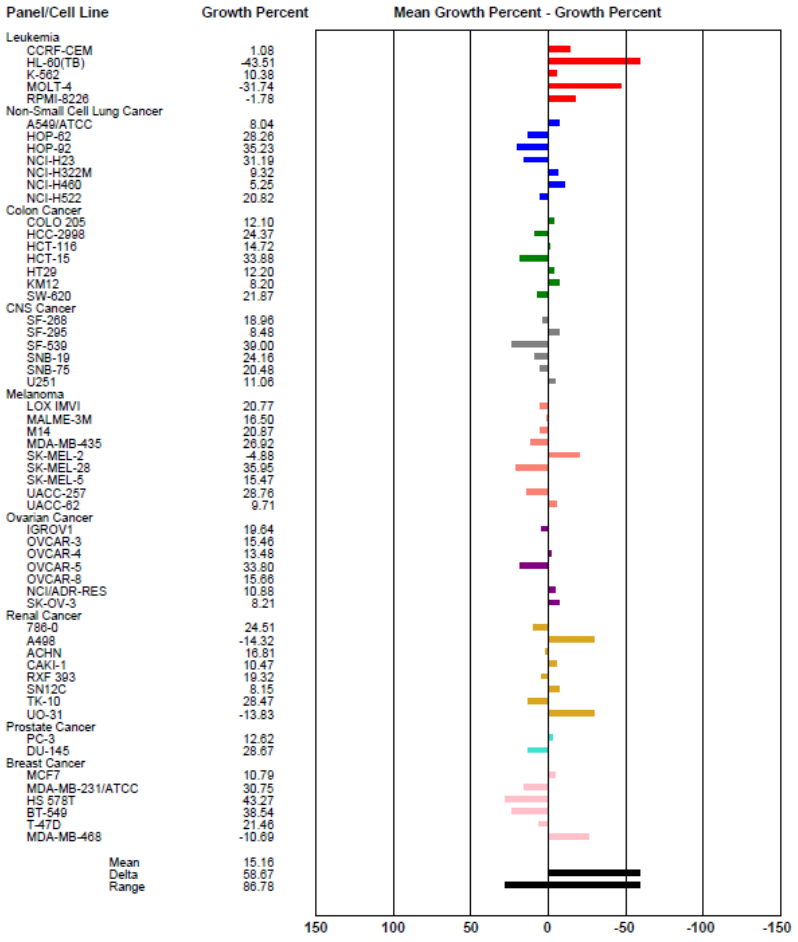


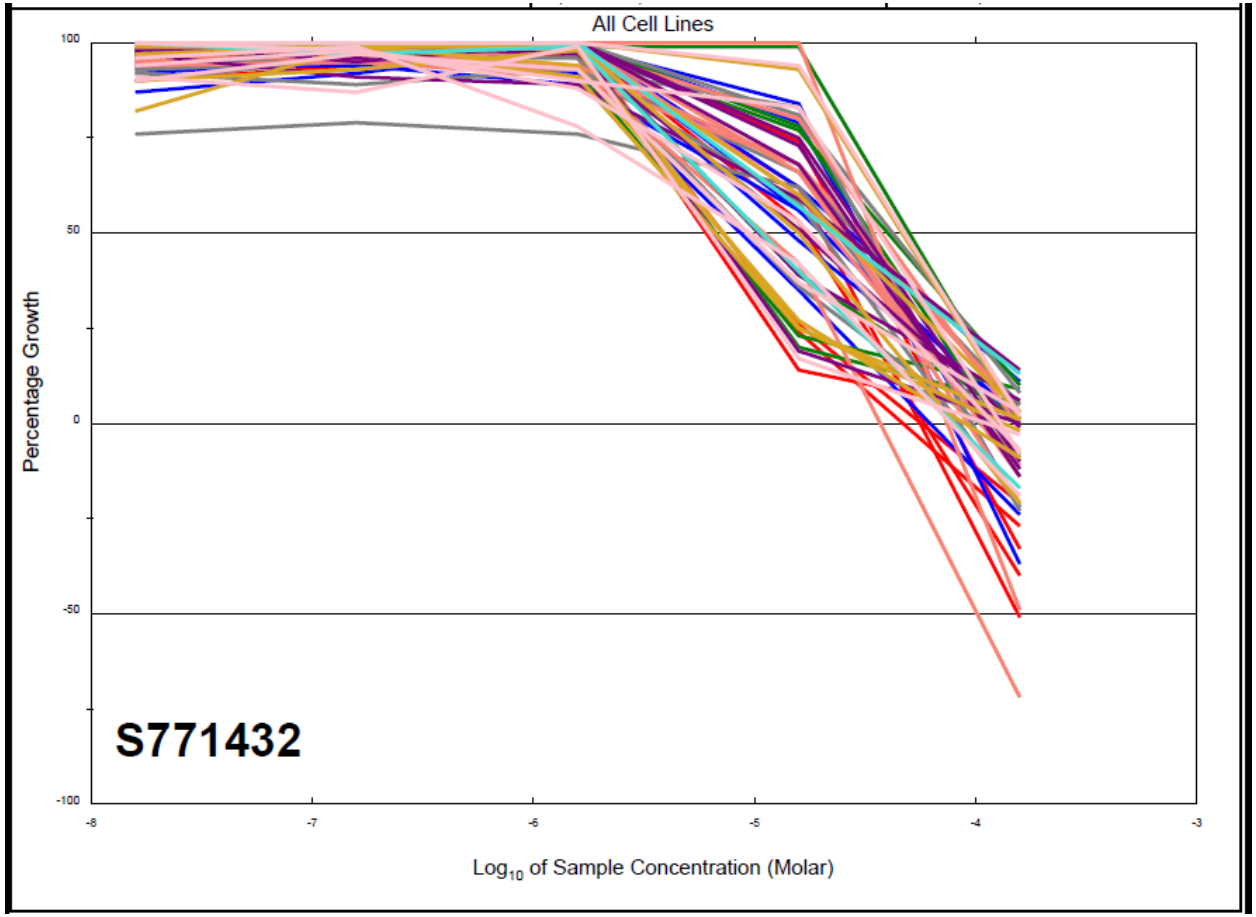
Figure20. ^{13}C NMR Spectrum of 12 (75MHz, $CDCl_3$, 298K).

One dose study data (NSC771432)



Five dose study data (NSC771432)

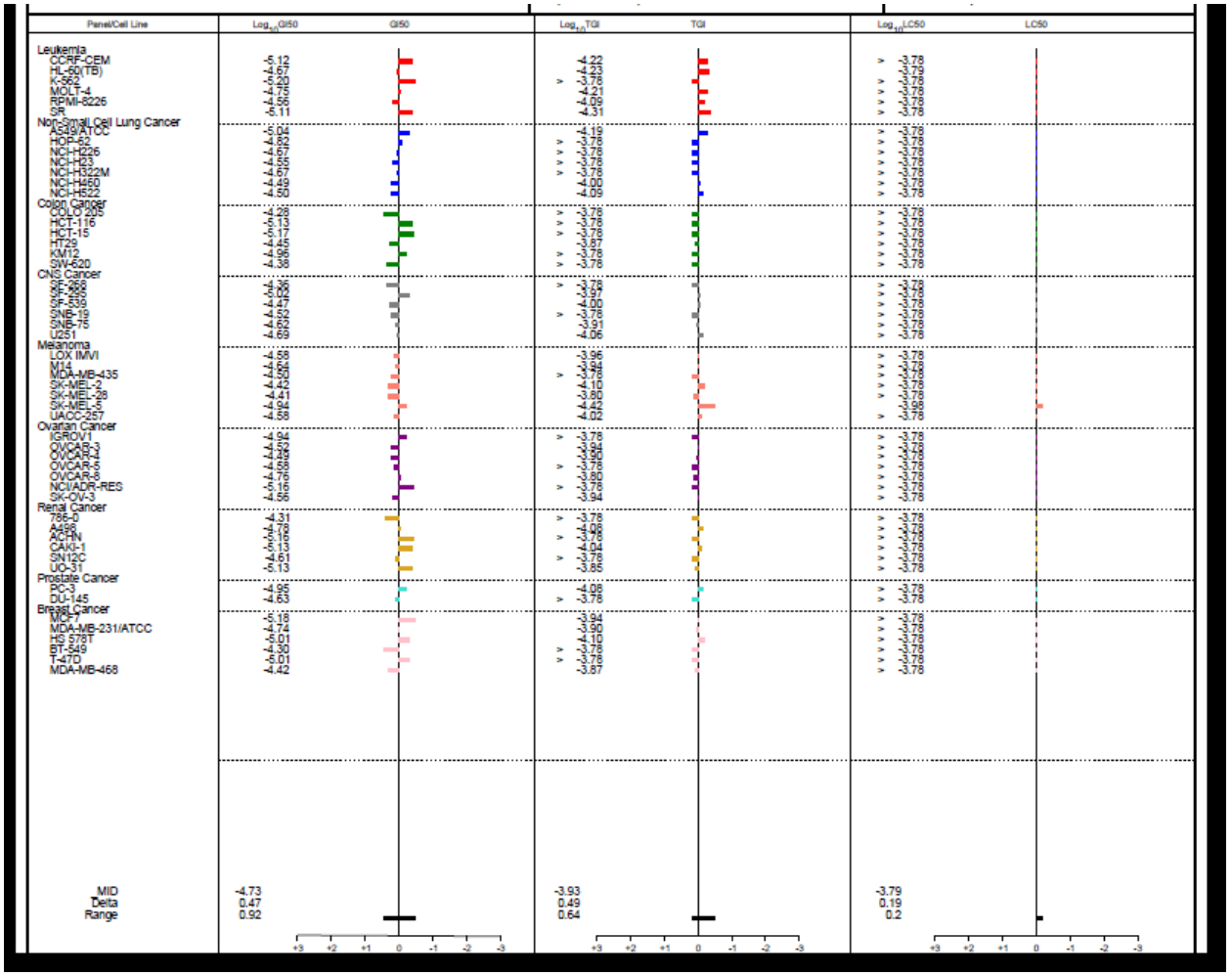
Dose Response Curves [NSC 771432]



Five dose/concentration results (NSC771432)

			Log10 Concentration											
	Time		Mean Optical Densities					Percent Growth						
Panel/Cell Line	Zero	Ctrl	-7.8	-6.8	-5.8	-4.8	-3.8	-7.8	-6.8	-5.8	-4.8	-3.8	GI50	TGI	LC50
Leukemia															
CCRF-CEM	0.841	3.273	3.238	3.275	3.176	1.481	0.667	99	100	96	26	-21	7.54E-6	5.98E-5	> 1.65E-4
HL-60(TB)	0.904	3.026	2.950	2.941	2.997	2.226	0.447	96	96	99	62	-51	2.12E-5	5.88E-5	1.63E-4
K-562	0.250	2.015	1.981	1.918	2.040	0.493	0.288	98	95	101	14	2	6.37E-6	> 1.65E-4	> 1.65E-4
MOLT-4	0.962	3.090	3.021	3.056	3.116	2.100	0.578	97	98	101	53	-40	1.80E-5	6.16E-5	> 1.65E-4
RPMI-8226	1.191	2.925	2.928	2.986	2.971	2.467	0.795	100	103	103	74	-33	2.74E-5	8.05E-5	> 1.65E-4
SR	0.365	1.899	1.742	1.803	1.942	0.739	0.267	90	94	103	24	-27	7.77E-6	4.92E-5	> 1.65E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.308	1.400	1.314	1.345	1.309	0.693	0.235	92	95	92	35	-24	9.02E-6	6.51E-5	> 1.65E-4
HOP-62	0.631	1.922	1.901	1.895	1.911	1.255	0.644	98	98	99	48	1	1.53E-5	> 1.65E-4	> 1.65E-4
NCI-H226	1.066	2.469	2.388	2.386	2.320	1.855	1.069	94	94	89	56		2.13E-5	> 1.65E-4	> 1.65E-4
NCI-H23	1.097	2.972	2.872	2.874	2.998	2.262	1.303	95	95	101	62	11	2.85E-5	> 1.65E-4	> 1.65E-4
NCI-H322M	0.715	1.677	1.608	1.706	1.758	1.256	0.726	93	103	108	56	1	2.14E-5	> 1.65E-4	> 1.65E-4
NCI-H460	0.344	3.141	3.231	3.202	3.190	2.566	0.268	103	102	102	79	-22	3.21E-5	9.97E-5	> 1.65E-4
NCI-H522	1.210	2.163	2.035	2.091	2.158	2.010	0.760	87	92	99	84	-37	3.14E-5	8.13E-5	> 1.65E-4
Colon Cancer															
COLO 205	0.565	2.307	2.259	2.276	2.286	2.298	0.575	97	98	99	99	1	5.22E-5	> 1.65E-4	> 1.65E-4
HCT-116	0.210	1.762	1.667	1.754	1.860	0.513	0.289	94	99	106	20	5	7.35E-6	> 1.65E-4	> 1.65E-4
HCT-15	0.260	1.969	1.931	1.912	1.846	0.647	0.418	98	97	93	23	9	6.72E-6	> 1.65E-4	> 1.65E-4
HT29	0.703	2.635	2.661	2.684	2.755	2.219	0.649	101	103	106	78	-8	3.53E-5	1.34E-4	> 1.65E-4
KM12	0.510	2.568	2.496	2.522	2.624	1.313	0.528	97	98	103	39	1	1.11E-5	> 1.65E-4	> 1.65E-4
SW-620	0.346	2.438	2.394	2.435	2.406	1.966	0.550	98	100	98	77	10	4.20E-5	> 1.65E-4	> 1.65E-4
CNS Cancer															
SF-268	0.587	2.084	2.026	2.027	2.091	1.794	0.713	96	96	100	81	8	4.38E-5	> 1.65E-4	> 1.65E-4
SF-295	0.706	2.610	2.428	2.526	2.536	1.385	0.647	90	96	96	36	-8	9.56E-6	1.06E-4	> 1.65E-4
SF-539	0.935	2.715	2.643	2.621	2.594	2.417	0.717	96	95	93	83	-23	3.38E-5	9.97E-5	> 1.65E-4
SNB-19	1.047	2.519	2.400	2.362	2.422	2.018	1.124	92	89	93	66	5	3.02E-5	> 1.65E-4	> 1.65E-4
SNB-75	1.108	1.939	1.741	1.765	1.736	1.620	1.007	75	79	76	62	-9	2.40E-5	1.23E-4	> 1.65E-4
U251	0.546	1.946	1.854	1.882	1.843	1.354	0.425	93	95	93	58	-22	2.06E-5	8.69E-5	> 1.65E-4
Melanoma															
LOX IMVI	0.549	2.785	2.698	2.732	2.838	2.026	0.471	96	98	102	66	-14	2.61E-5	1.10E-4	> 1.65E-4
M14	0.421	1.630	1.572	1.593	1.629	1.145	0.373	95	97	100	60	-11	2.27E-5	1.14E-4	> 1.65E-4
MDA-MB-435	0.627	2.667	2.676	2.631	2.536	2.016	0.691	101	98	94	68	3	3.13E-5	> 1.65E-4	> 1.65E-4
SK-MEL-2	0.745	1.152	1.165	1.199	1.239	1.182	0.380	103	111	121	107	-49	3.84E-5	8.02E-5	> 1.65E-4
SK-MEL-28	0.809	1.860	1.872	1.820	1.838	1.652	0.799	101	96	98	80	-1	3.87E-5	1.59E-4	> 1.65E-4
SK-MEL-5	0.524	2.975	2.922	2.855	2.810	1.547	0.147	98	95	93	42	-72	1.14E-5	3.84E-5	1.06E-4
UACC-257	0.826	1.690	1.641	1.650	1.615	1.414	0.650	94	95	91	68	-21	2.62E-5	9.53E-5	> 1.65E-4
Ovarian Cancer															
IGROV1	0.662	1.949	1.975	2.070	2.075	1.164	0.746	102	109	110	39	6	1.15E-5	> 1.65E-4	> 1.65E-4
OVCAR-3	0.460	1.599	1.624	1.621	1.598	1.297	0.414	102	102	100	73	-14	3.03E-5	1.14E-4	> 1.65E-4
OVCAR-4	0.718	1.607	1.620	1.566	1.623	1.382	0.647	101	95	102	75	-10	3.23E-5	1.26E-4	> 1.65E-4
OVCAR-5	0.527	1.435	1.412	1.366	1.335	1.067	0.653	97	91	89	59	14	2.65E-5	> 1.65E-4	> 1.65E-4
OVCAR-8	0.598	2.191	2.166	2.171	2.147	1.411	0.592	98	99	97	51	-1	1.73E-5	1.58E-4	> 1.65E-4
NCI/ADR-RES	0.866	2.738	2.695	2.656	2.786	1.213	0.875	98	96	103	19		6.96E-6	> 1.65E-4	> 1.65E-4
SK-OV-3	0.610	1.300	1.316	1.303	1.324	1.079	0.535	102	100	103	68	-12	2.76E-5	1.16E-4	> 1.65E-4
Renal Cancer															
786-0	0.720	2.613	2.599	2.589	2.622	2.465	0.743	99	99	100	93	1	4.87E-5	> 1.65E-4	> 1.65E-4
A498	1.610	2.476	2.317	2.467	2.465	2.043	1.265	82	99	99	50	-21	1.65E-5	8.27E-5	> 1.65E-4
ACHN	0.392	1.873	1.881	1.840	1.736	0.768	0.405	101	98	91	25	1	6.92E-6	> 1.65E-4	> 1.65E-4
CAKI-1	0.757	2.807	2.723	2.785	2.689	1.302	0.686	96	99	94	27	-9	7.44E-6	9.02E-5	> 1.65E-4
SN12C	0.750	2.726	2.676	2.701	2.708	1.929	0.813	97	99	99	60	3	2.45E-5	> 1.65E-4	> 1.65E-4
UO-31	0.612	1.866	1.746	1.777	1.841	0.920	0.602	90	93	98	25	-2	7.43E-6	1.42E-4	> 1.65E-4
Prostate Cancer															
PC-3	0.798	2.152	2.155	2.114	2.135	1.338	0.666	100	97	99	40	-17	1.11E-5	8.38E-5	> 1.65E-4
DU-145	0.393	1.615	1.651	1.635	1.714	1.085	0.548	103	102	108	57	13	2.33E-5	> 1.65E-4	> 1.65E-4
Breast Cancer															
MCF7	0.200	0.766	0.713	0.691	0.762	0.298	0.194	91	87	99	17	-3	6.58E-6	1.15E-4	> 1.65E-4
MDA-MB-231/ATCC	0.709	1.499	1.557	1.484	1.404	1.124	0.659	107	98	88	53	-7	1.82E-5	1.25E-4	> 1.65E-4
HS 578T	1.410	2.660	2.606	2.653	2.381	1.932	1.136	96	99	78	42	-19	9.70E-6	7.94E-5	> 1.65E-4
BT-549	1.117	2.135	2.156	2.178	2.295	2.079	1.138	102	104	116	94	2	5.00E-5	> 1.65E-4	> 1.65E-4
T-47D	0.632	1.668	1.567	1.635	1.599	1.017	0.663	90	97	93	37	3	9.73E-6	> 1.65E-4	> 1.65E-4
MDA-MB-468	0.789	1.675	1.623	1.660	1.586	1.529	0.728	94	98	90	63	-6	3.84E-5	1.36E-4	> 1.65E-4

Mean Graph


Panel/Cell Line
Log10GI50
GI50
Log10TGI
TGI
Log10LC50
LC50
Leukemia
CCRF-CEM -5.12 -4.22 > -3.78
HL-60(TB) -4.67 -4.23 > -3.79
K-562 -5.00 > -3.78 > -3.78
MOLT-4 -4.75 -4.21 > -3.78
RPMI-8226 -4.56 -4.09 > -3.78
SR -5.11 -4.31 > -3.78
Non-Small Cell Lung Cancer
A549/ATCC -5.04 -4.19 > -3.78
HOP-62 -4.82 > -3.78 > -3.78
NCI-H226 -4.57 > -3.78 > -3.78
NCI-H23 -4.55 > -3.78 > -3.78
NCI-H322M -4.67 > -3.78 > -3.78
NCI-H460 -4.49 -4.00 > -3.78
NCI-H522 -4.50 -4.09 > -3.78
Colon Cancer
COLO 205 -4.28 > -3.78 > -3.78
HCT-116 -5.13 > -3.78 > -3.78
HCT-15 -5.17 > -3.78 > -3.78
HT29 -4.45 -3.87 > -3.78
KM12 -4.96 > -3.78 > -3.78
SW-620 -4.38 > -3.78 > -3.78
CNS Cancer
SF-268 -4.36 > -3.78 > -3.78
SF-295 -5.02 -3.97 > -3.78
SF-539 -4.47 -4.00 > -3.78
SNB-19 -4.63 > -3.78 > -3.78
SNB-75 -4.60 -3.91 > -3.78
U251 -4.69 -4.06 > -3.78
Melanoma
LOX IMVI -4.58 -3.96 > -3.78
M14 -4.64 -3.94 > -3.78
MDA-MB-435 -5.01 > -3.78 > -3.78
SK-MEL-2 -4.42 -4.10 > -3.78
SK-MEL-28 -4.41 -3.80 > -3.78
SK-MEL-5 -4.94 -4.42 -3.96
UACC-257 -4.58 -4.02 > -3.78
Ovarian Cancer
IGROV1 -4.94 > -3.78 > -3.78
OVCAR-3 -4.62 -3.94 > -3.78
OVCAR-4 -4.49 -3.90 > -3.78
OVCAR-5 -4.58 > -3.78 > -3.78
OVCAR-8 -4.75 -3.80 > -3.78
NCI/ADR-RES -5.16 > -3.78 > -3.78
SK-OV-3 -4.56 -3.94 > -3.78
Renal Cancer
786-0 -4.31 > -3.78 > -3.78
A498 -4.78 -4.06 > -3.78
ACHN -5.16 > -3.78 > -3.78
CAKI-1 -5.13 -4.04 > -3.78
SN12C -4.61 > -3.78 > -3.78
UO-31 -5.13 -3.85 > -3.78
Prostate Cancer
PC-3 -4.95 -4.09 > -3.78
DU-145 -4.63 > -3.78 > -3.78
Breast Cancer
MCF7 -5.18 -3.94 > -3.78
MDA-MB-231/ATCC -4.74 -3.90 > -3.78
HS 578T -5.01 -4.10 > -3.78
BT-549 -4.30 > -3.78 > -3.78
T-47D -5.01 > -3.78 > -3.78
MDA-MB-468 -4.42 -3.87 > -3.78
MID -4.73 -3.93 -3.79
Delta 0.47 0.49 0.19
Range 0.92 0.64 0.2
+3 +2 +1 0 -1 -2 -3