Electronic Supplementary Material (ESI) for MedChemComm.

Electronic Supplementary Information

Design, synthesis and anticancer activity evaluation of irreversible allosteric inhibitors of ubiquitin-conjugating enzyme Ube2g2

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NCI-60 screening methodology

The human tumor cell lines are grown in RPMI 1640 medium containing 5% fetal bovine serum (FBS) and 2 mM L-glutamine. Typically, cells are inoculated into 96-well microtiter plates in 100 µL at plating densities of 5000 to 40000 cells per well depending on the doubling time of individual cell lines. Then, the plates are incubated at 37 °C, 5% CO_2, 95% air, and 100% relative humidity for 24 h before the addition of experimental drugs. After 24 h, two plates of each cell line are fixed *in situ* with trichloroacetic acid (TCA), to represent a measurement of the cell population for each cell line at the time of drug addition (T_z). Experimental drugs are dissolved in DMSO at 400-fold the desired final maximum test concentration and stored frozen prior to use. An aliquot of frozen drug is thawed and diluted to twice the desired final maximum test concentration with complete medium containing 50 µg ml^{-1} gentamicin. For five-dose screen, additional four, 10-fold and three serial 1/10 dilutions are made to provide a total of five drug concentrations plus control. Aliquots of 100 µl of these different drug dilutions are added to the appropriate microtiter wells already containing 100 µl of medium, resulting in the required final drug concentrations (0.01, 0.1, 1, 10, and 100 µM). After the addition of experimental drugs, the plates are incubated for an additional 48 h. The assay is terminated by the addition of cold TCA for adherent cells. Cells are fixed *in situ* by the addition of 50 µl of cold 50% (w/v) TCA (final concentration, 10% TCA) and incubated for 1 h at 4 °C. The supernatant is removed, and the plates are washed five times with tap water and air dried. Sulforhodamine B (SRB) solution (100 µl) at 0.4% (w/v) in 1 % acetic acid is added to each well, followed by a 10 min incubation at room temperature. After staining, the unbound dye is removed by washing five times with 1 % acetic acid and the plates are air dried. The bound stain is subsequently solubilized with 10 mM trizma base, and the absorbance is read on an automated plate reader at a wavelength of 515 nm. For suspension cells, the methodology is identical except that the assay is terminated by fixing settled cells at the bottom of the wells by adding 50 µl of 80 % TCA (final concentration, 16 % TCA).

For one-dose screen, data are reported as a mean graph of the percent growth of treated cells and are similar in appearance to mean graphs from the five-dose assay. The number reported for the one-dose assay is growth relative to the no-drug control, and relative to T_z number of cells. This allows detection of both growth inhibition (0 - 100) and lethality (< 0). This is the same as for the five-dose assay. For example, a value of 100 means no growth

inhibition. A value of 30 means 70% growth inhibition. A value of 0 means no net growth over the course of the experiment. A value of -30 means 30% lethality. A value of -100 means all cells are dead.

For five-does screen, seven absorbance measurements of T_z, control growth (C), and test growth in the presence of drugs at five different concentrations (T_i), will be used to calculate the percentage growth. Percentage growth inhibition is calculated as:

$[(T_i-T_z)/(C-T_z)] \times 100$ for concentrations of which $T_i >/= T_z$ or

$[(T_i-T_z)/T_z] \times 100$ for concentrations of which $T_i < T_z$.

Three dose response parameters are calculated for each experimental drug. Growth inhibition of 50 % (GI50) is calculated from $[(T_i-T_z)/(C-T_z)] \times 100 = 50$, which is the drug concentration resulting in a 50% reduction in the net protein increase (as measured by SRB staining) in control cells during the drug incubation. The drug concentration resulting in total growth inhibition (TGI) is calculated from $T_i = T_z$. The LC50 (concentration of drug resulting in a 50% reduction in the measured protein at the end of the drug treatment as compared to that at the beginning) indicating a net loss of cells following treatment is calculated from $[(T_i-T_z)/T_z] \times 100 = -50$. Values are calculated for each of these three parameters if the level of activity is reached; however, if the effect is not reached or is exceeded, the value for that parameter is expressed as greater or less than the maximum or minimum concentration tested.

For additional information, see https://dtp.cancer.gov/discovery_development/nci-60/methodology.htm.

Table S1 One-Dose (10 μM) NCI 60 Tumor Cell Line Screen for CW2 through CW20

Panel/Cell Line	Growth Percent																		
	CW2	CW3	CW4	CW5	CW6	CW7	CW8	CW9	CW10	CW11	CW12	CW13	CW14	CW15	CW16	CW17	CW18	CW19	CW20
Leukemia																			
CCRF-CEM	125.67	17.19	57.86	90.58	88.12	88.44	95.11	80.20	53.71	103.17	108.71	79.27	74.44	95.37	102.20	104.66	104.10	105.20	109.19
HL-60(TB)	96.71	-27.39	50.50	81.58	88.98	86.59	96.53	108.83	96.96	101.21	93.96	76.45	63.68	100.09	100.88	98.00	90.91	95.86	87.88
K-562	115.73	8.57	49.28	85.50	84.99	80.72	86.08	85.00	100.14	105.99	99.27	89.43	74.01	97.03	96.74	101.64	90.02	100.59	93.28
MOLT-4	117.42	1.95	44.82	71.88	72.22	65.54	81.53	101.99	109.26	83.39	84.40	74.32	56.46	99.57	91.24	98.54	97.68	93.30	87.96
RPMI-8226	111.95	-2.44	43.18	76.33	76.07	82.41	83.69	82.65	97.03	100.21	98.21	73.80	56.26	98.10	96.60	104.09	102.41	104.55	104.84
SR	110.68	7.26	42.85	77.29	71.85	77.90	79.36	81.59	110.46	84.72	90.59	68.67	56.30	90.49	82.01	95.60	94.06	92.83	91.87
Non-Small																			
A549/ATCC	95.42	11.55	56.89	74.21	72.34	88.24	76.53	72.02	69.15	76.48	56.31	76.42	69.53	84.57	76.90	84.79	75.87	78.98	79.23
EKVX	90.39	19.96	67.64	101.60	89.64	94.23	90.32	90.04	97.90	84.36	91.14	90.98	80.85	97.29	95.90	98.05	94.18	93.04	98.48
HOP-62	98.19	35.97	70.18	83.12	74.28	81.24	83.22	87.33	85.61	72.45	65.59	88.38	76.45	87.30	82.01	86.88	81.93	79.04	71.41
HOP-92	123.49	14.82	63.17	78.05	81.51	76.33	84.28	84.44	87.57	79.37	94.97	73.73	72.28	93.58	96.42	93.77	96.54	93.87	96.86
NCI-H226	86.78	10.84	50.31	61.32	75.09	71.48	91.61	71.35	76.52	58.79	82.18	68.91	67.90	88.35	86.19	82.50	82.89	84.91	99.23
NCI-H23	95.45	15.61	62.01	81.26	83.08	91.40	93.61	93.58	89.56	85.18	90.66	76.10	68.04	95.31	92.74	94.90	92.50	99.88	92.80
NCI-H322M	92.81	58.87	84.47	95.94	83.27	92.42	96.75	100.25	98.34	80.67	74.67	92.85	93.94	98.88	101.29	96.97	92.72	104.57	93.52
NCI-H460	100.39	9.25	60.03	85.85	80.51	91.81	90.12	94.94	99.93	99.67	100.50	98.66	95.10	104.69	99.56	104.44	106.46	104.96	102.33
NCI-H522	103.87	3.13	45.30	66.74	57.45	77.15	73.30	59.06	79.56	58.90	58.18	51.11	45.82	63.61	70.71	72.27	61.67	67.67	74.76
Colon Cancer																			
COLO 205	107.62	6.63	62.66	96.32	98.27	92.19	101.14	91.89	97.95	98.31	NG	95.79	83.01	100.87	95.73	106.47	102.08	NG	96.81
HCC-2998	102.42	41.57	92.88	98.76	94.29	96.68	102.48	108.52	104.20	97.63	86.28	94.64	100.53	96.87	101.18	97.11	82.63	87.28	78.31
HCT-116	88.25	11.07	44.97	63.94	68.78	79.15	62.06	75.51	91.81	87.41	74.13	72.07	57.45	98.43	82.48	92.21	75.21	91.51	73.38
HCT-15	95.42	15.15	64.22	83.89	89.58	95.60	94.91	96.00	104.46	96.34	98.18	79.22	79.62	97.92	98.08	115.54	94.75	104.05	101.48
HT29	93.30	20.30	56.31	82.16	81.31	82.81	74.14	81.46	88.33	80.43	78.95	86.87	76.46	88.24	97.78	89.11	84.46	87.86	92.43
KM12	96.83	24.16	70.80	93.14	87.47	100.29	98.92	99.33	100.31	93.52	89.23	89.83	78.00	103.46	98.53	101.48	95.68	101.65	103.30
SW-620	94.53	11.74	70.93	95.25	92.39	94.19	93.86	98.08	104.50	101.06	103.77	91.66	76.66	107.73	103.92	102.83	105.97	100.79	107.95
CNS Cancer																			
SF-268	98.20	32.07	70.31	84.52	87.79	97.04	94.21	102.17	94.59	83.00	86.42	84.66	81.88	100.50	98.71	92.68	94.00	100.55	96.36
SF-295	93.58	21.84	55.88	85.55	76.72	95.58	90.00	82.80	100.41	85.97	91.51	83.13	66.55	98.30	100.59	102.94	90.56	100.07	97.26
SF-539	88.70	56.77	87.33	96.45	98.32	96.72	97.91	99.58	94.57	98.12	100.48	99.89	94.24	96.27	94.58	99.00	98.16	94.86	96.42
SNB-19	102.23	33.94	90.31	104.43	97.66	99.37	98.09	99.54	97.71	87.47	102.04	91.14	86.80	88.71	97.90	104.79	93.82	98.08	105.37
SNB-75	74.14	40.30	81.45	89.65	101.47	85.25	82.60	86.98	92.31	82.77	90.87	82.53	90.32	86.07	87.01	92.04	85.49	103.82	86.62
U251	102.56	20.19	58.24	79.59	76.17	88.82	85.83	80.20	85.74	79.24	82.05	78.99	70.81	93.17	82.99	91.84	95.12	92.08	94.34
Melanoma																			
LOX IMVI	96.59	36.58	68.43	90.21	81.09	86.10	93.40	95.59	98.13	86.58	92.51	86.68	75.43	100.52	96.93	95.11	97.85	98.43	98.28
MALME-3M	76.70	4.14	82.34	86.90	103.22	89.24	87.39	90.08	103.26	99.44	89.12	87.58	72.13	98.58	99.95	98.53	94.28	96.60	96.89
M14	99.48	24.67	69.68	96.95	88.68	91.09	89.02	86.31	96.58	91.69	100.36	88.66	79.71	95.65	92.25	104.82	97.73	99.44	97.48
MDA-MB-435	97.18	1.71	58.63	95.44	93.49	100.47	94.26	101.97	112.70	102.37	104.21	96.11	81.73	102.71	102.71	108.02	103.14	101.62	109.29
SK-MEL-2	112.53	14.05	67.42	91.70	83.32	96.16	95.75	90.00	102.35	94.80	96.86	90.38	80.74	91.27	101.09	98.27	94.16	96.96	104.78
SK-MEL-28	100.75	39.85	84.57	98.56	98.33	108.12	105.97	106.23	107.25	102.99	109.13	113.15	101.35	109.36	111.97	107.58	107.56	107.24	107.24
SK-MEL-5	104.37	-88.19	35.93	71.84	71.81	86.22	96.50	91.57	101.31	91.38	96.39	72.76	64.37	99.35	95.68	99.46	96.78	99.33	97.71
UACC-257	112.84	-2.68	62.28	82.50	87.36	91.79	90.68	74.41	75.85	94.13	86.41	75.46	68.92	87.74	89.51	86.45	89.11	80.56	93.98
UACC-62	89.67	9.00	48.87	66.68	60.36	NG	NG	NG	NG	74.71	75.53	60.94	51.06	88.75	86.77	98.51	87.76	89.26	93.54
Ovarian Cancer																			
IGROV1	96.58	36.16	76.00	92.07	98.67	97.38	97.84	96.72	105.35	94.21	92.63	93.00	87.58	107.37	114.48	106.97	104.46	104.81	107.37
OVCAR-3	99.92	13.53	49.09	80.76	83.17	101.54	98.21	101.46	103.00	88.34	97.63	89.55	77.95	115.33	108.15	110.01	102.08	114.19	111.97
OVCAR-4	98.92	10.73	43.29	75.52	74.43	94.19	87.08	96.87	107.51	91.21	88.09	83.55	63.08	100.32	98.57	100.93	99.61	99.87	106.36
OVCAR-5	83.93	55.85	91.52	96.68	94.39	98.64	94.23	95.96	90.89	75.43	79.11	95.49	97.11	100.62	92.01	94.73	86.65	86.78	83.35
OVCAR-8	105.68	16.82	60.04	67.11	81.67	92.80	97.24	90.89	83.49	85.05	86.99	76.62	79.85	95.12	92.69	99.72	97.09	85.85	98.49
NCI/ADR-RES	101.56	8.70	64.54	82.99	89.17	97.43	98.59	100.93	92.45	84.05	85.49	81.78	80.41	83.36	106.54	96.90	98.29	95.63	106.76
SK-OV-3	106.97	26.74	62.60	93.88	92.29	75.65	81.91	78.63	97.11	91.73	103.51	94.61	80.06	88.42	87.31	95.96	92.25	91.61	86.08
Renal Cancer																			
786-0	106.27	11.83	83.25	99.47	90.01	99.71	93.85	92.22	94.26	102.03	96.96	96.03	94.31	102.88	98.37	105.65	104.86	98.63	95.55
A498	68.48	NG	NG	NG	NG	65.29	64.34	80.63	85.49	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG
ACHN	98.36	26.73	75.88	92.75	89.56	101.48	101.22	101.26	99.52	91.53	97.43	90.11	89.39	103.59	101.65	104.78	99.75	100.14	103.03
CAKI-1	90.78	35.90	69.69	88.39	82.23	84.74	80.58	84.01	90.54	83.78	85.69	79.38	70.80	91.41	86.27	92.48	90.56	91.57	95.37
RXF 393	101.76	-10.14	47.97	83.30	80.55	81.35	96.22	100.81	101.03	NG	NG	NG	NG	NG	NG	NG	NG	NG	NG
SN12C	106.47	3.95	80.31	86.15	82.27	94.48	92.40	98.46	94.86	82.61	99.00	88.61	85.52	96.32	100.45	98.33	94.98	95.73	106.27
TK-10	82.18	6.04	63.66	80.76	73.40	69.99	67.34	81.70	91.36	71.83	84.50	89.10	74.22	99.53	103.73	82.87	85.09	99.32	90.96
UO-31	74.81	14.16	46.73	67.06	69.02	76.42	79.15	86.79	84.81	60.85	67.16	56.73	60.08	92.83	80.97	83.86	80.30	84.04	86.10
Prostate Cancer																			
PC-3	94.57	16.90	38.45	73.15	63.68	66.09	67.27	63.88	80.30	78.02	64.84	60.71	53.55	87.38	80.65	87.50	66.47	89.40	71.96
DU-145	102.67	16.94	68.83	79.06	85.49	101.48	96.57	101.74	103.83	94.24	96.17	91.15	91.85	106.13	106.12	107.04	97.57	109.26	101.35
Breast Cancer																			
MCF7	87.93	4.06	48.33	77.00	77.74	88.92	89.66	87.01	103.44	87.11	94.04	82.84	77.01	92.33	92.75	96.36	94.73	93.51	99.27
MDA-MB-231/ATC(	93.98	9.36	57.07	86.11	84.44	95.91	94.00	98.85	99.02	84.99	90.25	72.86	68.49	93.13	97.91	105.95	95.95	103.79	104.01
HS 578T	102.04	40.31	93.86	101.76	97.51	94.89	93.32	95.52	111.87	90.44	100.70	94.84	91.38	102.90	97.02	98.79	111.45	92.92	108.23
BT-549	100.38	4.23	62.36	84.91	85.32	96.15	87.02	87.45	98.65	92.02	72.31	84.58	77.88	93.98	92.00	103.16	87.60	91.91	89.11
T-47D	88.39	-4.93	31.46	61.31	58.04	54.04	71.73	89.95	66.22	68.85	75.87	57.66	45.29	89.24	81.02	88.76	85.16	96.14	76.13
MDA-MB-468	98.86	1.83	39.53	75.85	82.30	73.48	82.19	85.51	103.22	83.88	88.75	88.04	81.95	80.15	101.48	97.84	92.37	100.59	109.79
Mean	98.07	15.35	62.50	84.27	83.26	88.15	88.87	90.32	94.82	87.35	88.96	83.25	75.80	95.64	94.96	97.59	93.06	95.74	95.70

Table S2 Five-Dose NCI 60 Tumor Cell Line Screen for CW3

			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															
HL-60(TB)	1.008	3.270	3.117	3.173	3.026	2.057	0.875	93	96	89	46	-13	8.22E-6	6.00E-5	> 1.00E-4
K-562	0.553	2.872	2.900	2.944	3.126	1.990	0.582	101	103	111	62	1	1.57E-5	> 1.00E-4	> 1.00E-4
MOLT-4	0.806	3.150	3.019	2.968	2.878	1.824	0.855	94	92	88	43	2	7.14E-6	> 1.00E-4	> 1.00E-4
SR	0.391	1.985	1.925	1.766	1.728	1.009	0.310	96	86	84	39	-21	5.63E-6	4.48E-5	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.566	1.810	1.710	1.740	1.800	1.393	0.569	92	94	99	66	.	1.77E-5	> 1.00E-4	> 1.00E-4
EKVX	0.686	2.300	2.162	2.130	2.154	1.535	0.701	91	89	91	53	1	1.12E-5	> 1.00E-4	> 1.00E-4
NCI-H226	1.510	2.656	2.477	2.436	2.381	2.284	1.338	84	81	76	68	-11	1.67E-5	7.17E-5	> 1.00E-4
NCI-H23	0.602	1.970	1.861	1.872	1.778	1.336	0.623	92	93	86	54	1	1.18E-5	> 1.00E-4	> 1.00E-4
NCI-H460	0.319	3.067	3.068	3.046	2.829	1.842	0.154	100	99	91	55	-52	1.12E-5	3.28E-5	9.60E-5
NCI-H522	0.897	1.995	1.900	1.894	1.827	1.395	0.279	91	91	85	45	-69	7.60E-6	2.49E-5	6.83E-5
Colon Cancer															
COLO 205	0.431	1.540	1.564	1.480	1.496	1.156	0.328	102	95	96	65	-24	1.48E-5	5.38E-5	> 1.00E-4
HCC-2998	0.850	2.280	2.225	2.230	2.331	2.026	0.630	96	97	104	82	-26	1.99E-5	5.76E-5	> 1.00E-4
HCT-116	0.268	2.359	2.262	2.259	2.251	0.956	0.191	95	95	95	33	-29	5.29E-6	3.42E-5	> 1.00E-4
HCT-15	0.293	2.007	1.980	1.898	1.870	1.074	0.307	98	94	92	46	1	8.01E-6	> 1.00E-4	> 1.00E-4
HT29	0.363	1.840	1.821	1.802	1.891	1.258	0.230	99	97	103	61	-37	1.28E-5	4.19E-5	> 1.00E-4
KM12	0.428	1.936	1.920	1.971	1.891	1.405	0.420	99	102	97	65	-2	1.66E-5	9.37E-5	> 1.00E-4
SW-620	0.320	2.009	1.975	1.883	1.879	1.447	0.302	98	93	92	67	-6	1.70E-5	8.32E-5	> 1.00E-4
CNS Cancer															
SF-268	0.632	1.962	1.914	1.914	1.821	1.463	0.647	96	96	89	62	1	1.60E-5	> 1.00E-4	> 1.00E-4
SF-295	0.740	2.193	2.084	2.013	2.060	1.586	0.704	92	88	91	58	-5	1.35E-5	8.35E-5	> 1.00E-4
SF-539	0.680	2.310	2.302	2.257	2.259	1.973	0.309	99	97	97	79	-55	1.66E-5	3.91E-5	9.25E-5
SNB-19	0.708	2.181	2.110	2.119	2.058	1.641	0.737	95	96	92	63	2	1.65E-5	> 1.00E-4	> 1.00E-4
SNB-75	0.806	1.781	1.728	1.654	1.594	1.314	0.729	95	87	81	52	-10	1.08E-5	7.00E-5	> 1.00E-4
U251	0.397	1.825	1.763	1.750	1.756	1.302	0.495	96	95	95	63	7	1.72E-5	> 1.00E-4	> 1.00E-4
Melanoma															
LOX IMVI	0.429	2.675	2.585	2.539	2.449	1.981	0.188	96	94	90	69	-56	1.42E-5	3.56E-5	8.91E-5
MALME-3M	0.752	1.300	1.257	1.228	1.206	1.046	0.398	92	87	83	54	-47	1.09E-5	3.41E-5	> 1.00E-4
M14	0.544	2.165	2.190	2.256	2.075	1.629	0.507	102	106	94	67	-7	1.70E-5	8.07E-5	> 1.00E-4
MDA-MB-435	0.438	2.140	2.130	2.027	2.064	1.234	0.350	99	93	96	47	-20	8.58E-6	5.01E-5	> 1.00E-4
SK-MEL-2	1.045	2.444	2.363	2.337	2.389	2.143	0.459	94	92	96	78	-56	1.63E-5	3.83E-5	9.01E-5
SK-MEL-28	0.790	2.327	2.300	2.331	2.270	1.866	0.730	98	100	96	70	-8	1.81E-5	7.98E-5	> 1.00E-4
SK-MEL-5	0.268	1.570	1.485	1.527	1.412	0.653	0.020	93	97	88	30	-93	4.46E-6	1.75E-5	4.48E-5
UACC-257	0.798	1.553	1.452	1.512	1.530	1.300	0.643	87	95	97	66	-19	1.55E-5	5.93E-5	> 1.00E-4
UACC-62	0.762	2.569	2.357	2.415	2.091	1.449	0.332	88	91	74	38	-56	4.60E-6	2.52E-5	8.54E-5
Ovarian Cancer															
IGROV1	0.651	2.208	2.134	2.173	2.044	1.509	0.760	95	98	89	55	7	1.28E-5	> 1.00E-4	> 1.00E-4
OVCAR-3	0.513	1.681	1.700	1.678	1.575	1.020	0.429	102	100	91	43	-16	7.27E-6	5.31E-5	> 1.00E-4
OVCAR-4	0.896	2.139	2.151	2.081	1.973	1.339	0.849	101	95	87	36	-5	5.22E-6	7.44E-5	> 1.00E-4
OVCAR-5	0.643	1.623	1.547	1.541	1.473	1.307	0.788	92	92	85	68	15	2.16E-5	> 1.00E-4	> 1.00E-4
OVCAR-8	0.475	1.892	1.803	1.779	1.782	1.151	0.520	94	92	92	48	3	8.89E-6	> 1.00E-4	> 1.00E-4
NCI/ADR-RES	0.399	1.494	1.503	1.457	1.381	0.998	0.365	101	97	90	55	-9	1.19E-5	7.33E-5	> 1.00E-4
SK-OV-3	0.996	2.123	2.112	2.140	2.163	1.877	0.802	99	101	104	78	-20	1.94E-5	6.31E-5	> 1.00E-4
Renal Cancer															
786-0	0.574	2.244	2.331	2.319	2.216	1.798	0.556	105	105	98	73	-3	2.02E-5	9.10E-5	> 1.00E-4
ACHN	0.529	2.191	2.160	2.098	2.023	1.572	0.546	98	94	90	63	1	1.61E-5	> 1.00E-4	> 1.00E-4
CAKI-1	0.961	3.348	3.304	3.341	3.181	2.572	1.315	98	100	93	67	15	2.15E-5	> 1.00E-4	> 1.00E-4
RXF 393	0.781	1.345	1.290	1.283	1.262	1.041	0.484	90	89	85	46	-38	7.96E-6	3.53E-5	> 1.00E-4
SN12C	0.795	2.589	2.441	2.501	2.560	1.601	0.313	92	95	98	45	-61	8.04E-6	2.66E-5	7.93E-5
TK-10	1.304	2.404	2.260	2.250	2.144	2.143	1.294	87	86	76	76	-1	2.19E-5	9.77E-5	> 1.00E-4
UO-31	0.829	2.481	2.276	2.265	2.091	1.416	0.824	88	87	76	36	-1	4.42E-6	9.62E-5	> 1.00E-4
Prostate Cancer															
DU-145	0.638	2.285	2.329	2.312	2.212	1.591	0.550	103	102	96	58	-14	1.29E-5	6.42E-5	> 1.00E-4
Breast Cancer															
MCF7	0.359	1.923	1.801	1.776	1.782	0.952	0.330	92	91	91	38	-8	5.92E-6	6.64E-5	> 1.00E-4
MDA-MB-231/ATCC	0.469	1.279	1.237	1.290	1.205	0.949	0.344	95	101	91	59	-27	1.28E-5	4.88E-5	> 1.00E-4
HS 578T	0.985	1.825	1.756	1.735	1.716	1.536	0.909	92	89	87	66	-8	1.63E-5	7.84E-5	> 1.00E-4
BT-549	0.790	1.775	1.782	1.773	1.719	1.348	0.540	101	100	94	57	-32	1.19E-5	4.38E-5	> 1.00E-4
T-47D	0.883	1.670	1.620	1.510	1.563	1.018	0.697	94	80	86	17	-21	3.35E-6	2.80E-5	> 1.00E-4
MDA-MB-468	0.840	1.648	1.609	1.619	1.611	1.097	0.716	95	96	95	32	-15	5.17E-6	4.81E-5	> 1.00E-4

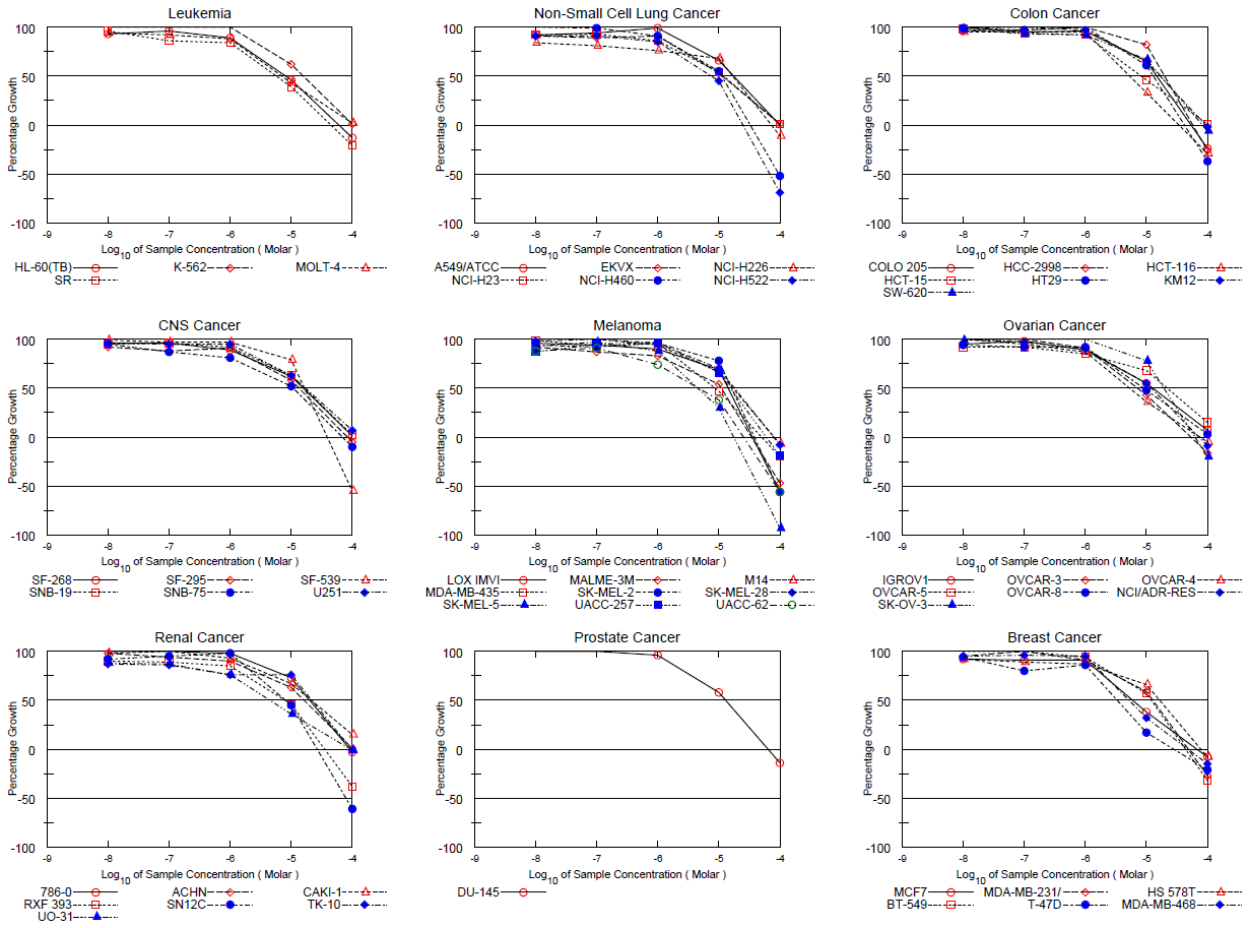


Fig. S1 The NCI 60 tumor cell line five-dose testing results of CW3. As shown, CW3 exhibited a clear dose dependence against every cell line. In terms of cancer types, CW3 showed the highest lethiferous activity against Melanoma cancer cells.

Synthesis of compounds 2 to 7 and 9 to 40

*(R)-2-((tert-butoxycarbonyl)amino)-3-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)propanoic acid (**2**).* Compound **1** (5.00 g, 12.78 mmol), 3,5-dichlorophenylboronic acid (3.66 g, 19.18 mmol) and Na_2CO_3 (8.13 g, 76.68 mmol) were combined in a 500 mL flask and filled with argon. $Pd(PPh_3)_4$ (0.15 g, 0.13 mmol), THF (80 mL) and H_2O (40 mL) were introduced into the flask under argon atmosphere and the mixture was heated with stirring at 70 °C for 48 h. After cooling to room temperature, the pH value was adjusted to 3.0 using a 1 M HCl aqueous solution. The THF was removed with a rotary evaporator and resulting liquid was extracted with CH_2Cl_2. The combined organics was dried with anhydrous $MgSO_4$, filtered and concentrated to a colourless colloid, which was purified by liquid chromatography (Teledyne ISCO Combiflash Rf system, EtOAc in hexane) to afford a white solid (4.72 g, 90% yield). NMR δ H (400 MHz; $CDCl_3$), 1.43 (9H, s), 3.12–3.26 (2H, m), 4.64 (1H, d), 4.96 (1H, d), 7.28 (2H, d), 7.32 (1H, s), 7.42 (2H, s), 7.46 (2H, d). ^{13}C NMR ($CDCl_3$) 175.88, 155.40, 143.69, 137.31, 136.35, 135.28, 130.08, 127.22, 127.14, 125.48, 80.52, 54.25, 37.51, 28.29. MS (ESI): *m*/*z* Calcd for $C_{20}H_{22}Cl_2NO_4$ $[M + H]^+$ 410.09, found 310.0 + 100.05 (Boc group).

*Methyl (R)-2-((tert-butoxycarbonyl)amino)-3-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)propanoate (**3**).* Compound **2** (4.72 g, 11.50 mmol) was dissolved in 40 mL DMF, followed by the addition of 2.90g (34.50 mmol) $NaHCO_3$ and 2.87 mL (46.00 mmol) CH_3I. The solution was stirred at room temperature for 12 h. The solvent was removed with a rotary evaporator and resulting mixture was added 30 mL H_2O and extracted with EtOAc. The combined organics was dried with anhydrous $MgSO_4$, filtered and concentrated to a light yellow solid (4.46 g, 92% yield). NMR δ H (400 MHz; $CDCl_3$), 1.42 (9H, s), 3.05–3.20 (2H, m), 3.73 (3H, s), 4.62 (1H, d), 5.06 (1H, d), 7.21 (2H, d), 7.30 (1H, s), 7.41 (2H, s), 7.45 (2H, d). ^{13}C NMR ($CDCl_3$) 172.18, 155.04, 143.75, 137.23, 136.56, 135.27, 130.02, 127.16, 127.12, 125.50, 80.05, 54.35, 52.32, 38.06, 28.30. MS (ESI): *m*/*z* Calcd for $C_{21}H_{24}Cl_2NO_4$ $[M + H]^+$ 424.11, found 324.0 + 100.05 (Boc group).

*Tert-butyl (R)-(1-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-3-hydroxypropan-2-yl)carbamate (**4**).* Compound **3** (3.00 g, 7.08 mmol) was dissolved in 50 mL CH_2Cl_2, followed by the dropwise addition of 21.30 mL 1 M DIBAL in PhMe. The solution was stirred at room temperature for 12 h, before being quenched by the dropwise addition of MeOH (8 mL). The mixture was evaporated using a rotary evaporator to remove the solvent and then added 40 mL EtOAc and 30 mL saturated Rochelle's salt aqueous solution. The mixture was stirred until the appearance of two distinct layers. The organic layer was separated and the aqueous layer was extracted with EtOAc for three times. The combined organics were dried by anhydrous $MgSO_4$, filtered and concentrated to a colourless colloid, which was purified by HPLC to afford a colourless solid (1.96 g, 70% yield). NMR δ H (400 MHz; $CDCl_3$), 1.42 (9H, s), 2.89 (2H, d), 3.56–3.71 (2H, m), 3.89 (1H, s), 4.77 (1H, s), 7.29–7.32 (3H, m), 7.43 (2H, s), 7.47 (2H, d). ^{13}C NMR ($CDCl_3$) 156.13, 143.84, 138.46, 136.73, 135.25, 130.02, 127.14, 127.03, 125.44, 79.83, 64.11, 53.65, 37.12, 28.36. MS (ESI): *m*/*z* Calcd for $C_{20}H_{24}Cl_2NO_3$ $[M + H]^+$ 396.11, found 296.0 + 100.05 (Boc group).

*Tert-butyl (R)-(1-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-3-oxopropan-2-yl)carbamate (**5**).* Compound **4** (1.30 g, 3.28 mmol) was dissolved in 50 mL CH_2Cl_2, followed by the addition of 1.39 g (3.28 mmol) Dess-Martin periodinane. The solution was stirred at room temperature for 5 h, before being quenched by 1.5 mL saturated $Na_2S_2O_3$ aqueous. The resulting mixture was added 30 mL H_2O and extracted with CH_2Cl_2. The combined organics was dried with anhydrous $MgSO_4$, filtered and concentrated to a yellow colloid, which was purified by HPLC to afford a light yellow solid (1.25 g, 97% yield). NMR δ H (400 MHz; $CDCl_3$), 1.45 (9H, s), 3.18 (2H, t), 4.47 (1H, d), 5.08 (1H, d), 7.26 (2H, d), 7.33 (1H, t), 7.43 (2H, d), 7.48 (2H, d). ^{13}C NMR ($CDCl_3$) 198.99, 155.32, 143.61, 137.34, 136.29, 135.32, 130.05, 127.38, 127.21, 125.51, 60.75, 50.16, 35.09, 28.29. MS (ESI): *m*/*z* Calcd for $C_{20}H_{22}C_{l2}NO_3$ $[M + H]^+$ 394.10, found 294.0 + 100.05 (Boc group).

*Ethyl (R,E)-4-((tert-butoxycarbonyl)amino)-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)pent-2-enoate (**6**).* Triethyl phosphonoacetate (0.43 mL, 2.18 mmol) was added into a solution of NaH (52.00 mg, 2.18 mmol) in DMF (30 mL) at 0 ºC. The mixture was stirred at 0 ºC for 1 h and then was added 0.66 g (1.68 mmol) compound **5**. Then, the solution was warmed to room temperature and stirred at room temperature for 2 h. 5mL 1 M HCl aqueous solution was added to the resulting mixture and then the solvent was removed with a rotary evaporator. The mixture was added 20 mL H_2O and extracted with CH_2Cl_2. The combined organics was dried with anhydrous $MgSO_4$, filtered and concentrated to a colourless colloid, which was purified by HPLC to afford a colourless solid (0.75 g, 96% yield). NMR δ H (400 MHz; $CDCl_3$), 1.28 (3H, t) 1.40 (9H, s), 2.95 (2H, d), 4.17–4.22 (2H, m), 4.53 (1H, d), 4.65 (1H, s), 5.86–5.91 (1H, m), 6.89–6.95 (1H, m), 7.26 (2H, d), 7.33 (1H, s), 7.44 (2H, s), 7.48 (2H, d). ^{13}C NMR ($CDCl_3$) 165.73, 157.71, 149.60, 143.89, 137.38, 136.85, 135.24, 130.21, 127.06, 127.01, 125.46, 121.35, 79.84, 60.36, 50.52, 39.87, 27.99, 14.24. MS (ESI): *m*/*z* Calcd for $C_{24}H_{28}Cl_2NO_4$ $[M + H]^+$ 464.14, found 364.1+ 100.05 (Boc group).

*Ethyl (R,E)-4-amino-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)pent-2-enoate (**7**).* Compound **6** (0.60g, 1.29 mmol) was dissolved in 30 mL EtOH, followed by the dropwise addition of 7.0 mL 4 M HCl in dioxane. The solution was stirred at room temperature for 6 h. The solvent was removed with a rotary evaporator and the resulting mixture was added 10 mL H_2O and extracted with CH_2Cl_2. The combined organics was dried with anhydrous $MgSO_4$, filtered and concentrated to a colourless solid (0.46 g, 98% yield). NMR δ H (400 MHz; $CDCl_3$), 1.21 (3H, t), 3.06–3.26 (2H, d), 4.08–4.14 (2H, m), 4.16 (1H, s), 5.98 (1H, d), 6.89 (1H, s), 7.28 (2H, s), 7.32 (1H, t), 7.39 (2H, d), 7.46 (2H, d). ^{13}C NMR ($CDCl_3$) 165.70, 143.30, 140.58, 137.97, 135.35, 134.41, 130.08, 127.65, 127.35, 125.84, 125.47, 61.38, 53.85, 38.67, 13.92. MS (ESI): *m*/*z* Calcd for $C_{19}H_{20}Cl_2NO_2$ $[M + H]^+$ 364.09, found 364.1.

*Ethyl (R,E)-4-(but-3-enamido)-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)pent-2-enoate (**9, CW4**).* Compound **9** was synthesized using the same experimental procedure as compound **8** except that acrylic acid was replaced by 3-butenoic acid. A white solid was obtained after purification by HPLC (0.13 g, 55% yield). NMR δ H (400 MHz; $CDCl_3$), 1.27 (3H, t), 1.85 (2H, d), 3.00 (2H, d), 4.15–4.21 (2H, m), 5.07 (1H, t), 5.50 (1H, d), 5.77 (1H, d), 5.86 (1H, d), 6.26

(1H, d), 6.91–6.96 (1H, m), 7.27 (2H, s), 7.33 (1H, t), 7.44 (2H, d), 7.47 (2H, d). ^{13}C NMR ($CDCl_3$) 166.04, 165.39, 146.55, 143.63, 141.29, 137.18, 136.70, 135.29, 130.01, 127.27, 127.15, 125.49, 124.36, 121.72, 60.61, 50.58, 39.97, 17.80, 14.22. MS (ESI): *m*/*z* Calcd for $C_{23}H_{24}Cl_2NO_3$ $[M + H]^+$ 432.11, found 432.0.

*(R,E)-4-acrylamido-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)pent-2-enoic acid (**10, CW5**).* A mixture of compound **8** (60 mg, 0.14 mmol), MeOH (5 mL) and H_2O (5 mL) was added 29 mg (0.72 mmol) NaOH and stirred at room temperature for 12 h. The pH value of the resulting solution was adjusted to 3.0 using a 1 M HCl aqueous solution. The MeOH solvent was removed with a rotary evaporator, followed by the extraction with EtOAc. The combined organics were dried with anhydrous $MgSO_4$, filtered and concentrated to a white solid (42 mg, 77% yield). NMR δ H (400 MHz; $CDCl_3$), 2.94 (2H, d), 5.01 (1H, s), 5.60 (1H, d), 5.80 (1H, d), 6.00 (1H, m), 6.21 (1H, d), 6.91–6.97 (1H, m), 7.18 (2H, d), 7.24 (1H, s), 7.34 (2H, s), 7.36 (2H, d). ^{13}C NMR ($CDCl_3$) 169.57, 164.97, 148.64, 143.53, 137.40, 136.32, 135.32, 130.08, 129.99, 127.72, 127.39, 127.23, 125.51, 121.05, 50.78, 28.86. MS (ESI): *m*/*z* Calcd for $C_{20}H_{18}Cl_2NO_3$ $[M + H]^+$ 390.07, found 390.0.

*(R,E)-4-(but-3-enamido)-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)pent-2-enoic acid (**11, CW6**).* Compound **11** was synthesized using the same experimental procedure as compound **10**, except that compound **8** was replaced with compound **9** (60 mg, 0.14 mmol). 45 mg white solid was obtained (80% yield). NMR δ H (400 MHz; $CDCl_3$), 1.86 (2H, d), 3.01 (2H, d), 5.09 (1H, d), 5.35–5.43 (1H, m), 5.76–5.89 (2H, m), 6.92–6.97 (1H, m), 7.00–7.05 (1H, m), 7.25 (2H, s), 7.33 (1H, t), 7.44 (2H, d), 7.48 (2H, d). ^{13}C NMR ($CDCl_3$) 169.79, 165.69, 148.92, 143.55, 141.84, 137.32, 136.41, 135.30, 129.96, 127.35, 127.20, 125.49, 124.12, 120.95, 50.72, 39.79, 17.83. MS (ESI): *m*/*z* Calcd for $C_{21}H_{20}Cl_2NO_3$ $[M + H]^+$ 404.08, found 404.0.

*(R)-2-amino-3-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)propan-1-ol (**12**).* Compound **12** was synthesized using the same experimental procedure as compound **7**, except that compound **6** was replaced with compound **4** (0.60 g, 1.52 mmol). 0.43 g white solid was obtained (96% yield). NMR δ H (400 MHz; $CDCl_3$) 2.70–2.89 (2H, m), 3.26 (1H, s), 3.48 (2H, m), 7.27–7.30 (3H, m), 7.39 (2H, s), 7.44 (2H, d). ^{13}C NMR ($CDCl_3$) 143.04, 137.98, 135.36, 134.68, 129.60, 127.69, 127.42, 125.34, 60.86, 54.84, 34.98. MS (ESI): *m*/*z* Calcd for $C_{15}H_{16}Cl_2NO$ $[M + H]^+$ 296.06, found 296.1.

*(R)-N-(1-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-3-hydroxypropan-2-yl)acrylamide (**13, CW1**).* Compound **13** was synthesized using the same experimental procedure as compound **8**, except that compound **7** was replaced with compound **12** (0.16 g, 0.55 mmol). 0.12 g white solid was obtained (62% yield). NMR δ H (400 MHz; $CDCl_3$), 2.93 (2H, s), 3.63–3.69 (2H, d), 4.27 (1H, s), 5.62 (1H, d), 6.05–6.12 (1H, m), 6.25 (1H, d), 6.36 (1H, s), 7.28 (3H, m), 7.37 (2H, s), 7.41 (2H, d). ^{13}C NMR ($CDCl_3$) 166.09, 143.61, 138.14, 136.83, 135.25, 130.63, 129.91, 127.20, 127.08, 125.39, 63.48, 52.80, 36.58. MS (ESI): *m*/*z* Calcd for $C_{18}H_{18}Cl_2NO_2$ $[M + H]^+$ 350.07, found 350.1.

*(R)-N-(1-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-3-hydroxypropan-2-yl)but-3-enamide (**14, CW2**).* Compound **14** was synthesized using the same experimental procedure as compound **9**,

except that compound **7** was replaced by compound **12** (0.16 g, 0.55 mmol). 0.13g white solid was obtained (65% yield). NMR δ H (400 MHz; $CDCl_3$), 1.80 (2H, d), 2.94 (2H, d), 3.59–3.71 (2H, m), 4.28 (1H, s), 5.81 (1H, d), 6.44 (1H, d), 6.76–6.85 (1H, m), 7.27 (2H, m), 7.30 (1H, s), 7.35 (2H, d), 7.40 (2H, d). ^{13}C NMR ($CDCl_3$) 166.66, 143.64, 140.65, 138.37, 136.69, 135.23, 129.93, 127.13, 127.03, 125.35, 124.87, 63.53, 52.74, 36.64, 17.79. MS (ESI): *m*/*z* Calcd for $C_{19}H_{20}Cl_2NO_2$ $[M + H]^+$ 364.09, found 364.0.

*Ethyl (2S,3R,4R)-4-((tert-butoxycarbonyl)amino)-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-2,3-dihydroxypentanoate (**15**).* A mixture of methanesulfonamide (82 mg, 0.86 mmol), $K_3Fe(CN)_6$ (0.85 g, 2.58 mmol), OsO_4 (2.2 mg, 8.6 μmol), $(DHQD)_2PHAL$ (13.4 mg, 17 mmol) and K_2CO_3 (0.36 g, 2.58 mmol) in t-BuOH (10 mL) and H_2O (10 mL) was treated with compound **6** (0.40 g, 0.86 mmol) and stirred at room temperature for 12 h. The resulting solution was cooled to 0 ºC and then treated with 1.25 g Na_2SO_3, followed by stirred at 0 ºC for 30 min and at room temperature for 1 h. The mixture was extracted with EtOAc. The combined organics were washed with brine, dried with anhydrous $MgSO_4$, filtered and concentrated to a white solid, which was purified by HPLC to afford a white solid (0.28 g, 65% yield). NMR δ H (400 MHz; $CDCl_3$), 1.29 (3H, t), 1.39 (9H, s), 2.93–3.12 (2H, m), 3.83 (1H, s), 4.26 (2H, m), 4.36 (1H, s), 4.79 (1H, d), 7.33 (3H, m), 7.44 (2H, t), 7.47 (2H, d). ^{13}C NMR (MeOD) 172.92, 156.31, 143.87, 136.62, 135.46, 135.20, 130.09, 127.10, 127.03, 125.39, 80.34, 72.79, 71.51, 62.08, 53.66, 36.78, 28.27, 14.13. MS (ESI): *m*/*z* Calcd for $C_{24}H_{30}Cl_2NO_6$ $[M + H]^+$ 498.15, found 398.1 + 100.05 (Boc group).

*Ethyl (2S,3R,4R)-4-amino-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-2,3 dihydroxypentanoate (**16**).* Compound **16** was synthesized using the same experimental procedure as compound **7**, except that compound **6** was replaced with compound **15** (0.25g, 0.50 mmol). 0.19 g white solid was obtained (95% yield). NMR δ H (400 MHz; $CDCl_3$), 1.18 (3H, t), 3.07 (2H, s), 3.75 (1H, s), 4.15 (2H, s), 4.32 (1H, s), 4.73 (1H, s), 7.32 (3H, m), 7.38 (2H, d), 7.46 (2H, d). ^{13}C NMR ($CDCl_3$) 172.49, 143.30, 137.95, 137.84, 135.36, 130.08, 127.69, 127.35, 125.42, 73.83, 67.68, 62.53, 56.38, 37.15, 13.81. MS (ESI): *m*/*z* Calcd for $C_{19}H_{22}Cl_2NO_4$ $[M + H]^+$ 398.09, found 398.1.

*Ethyl (2S,3R,4R)-4-acrylamido-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-2,3-dihydroxypentanoate (**17**).* Compound **17** was synthesized using the same experimental procedure as compound **8**, except that compound **7** was replaced with compound **16** (85 mg, 0.21 mmol). 64 mg white solid was obtained (67% yield). ^1H NMR δ H (400 MHz; $CDCl_3$), 1.26 (3H, t), 3.04 (2H, m), 3.78 (1H, d), 3.89 (1H, s), 4.22 (2H, m), 4.33 (1H, s), 5.65 (1H, t), 6.04–6.11 (1H, m), 6.24 (1H, d), 7.32 (3H, m), 7.42 (2H, s), 7.45 (2H, d). ^{13}C NMR ($CDCl_3$) 172.92, 166.57, 143.71, 137.93, 136.93, 135.26, 130.39, 129.92, 127.36, 127.22, 127.08, 125.45, 72.38, 70.91, 62.34, 52.96, 37.25, 14.05. MS (ESI): *m*/*z* Calcd for $C_{22}H_{24}Cl_2NO_5$ $[M + H]^+$ 452.10, found 452.1.

*Ethyl (2S,3R,4R)-4-(but-3-enamido)-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-2,3-dihydroxypentanoate (**18**).* Compound **18** was synthesized using the same experimental procedure as compound **9** except that compound **7** was replaced with compound **16** (85 mg, 0.21 mmol). 63 mg white solid was obtained (64% yield). NMR δ H (400 MHz; $CDCl_3$), 1.34 (3H, t), 1.82 (2H,

d), 3.04 (2H, m), 3.18 (2H, m), 3.87 (1H, t), 4.25 (2H, m), 5.75 (1H, t), 5.89 (1H, m), 6.82 (1H, m), 7.31 (3H, m), 7.42 (2H, d), 7.45 (2H, d). ^{13}C NMR ($CDCl_3$) 172.26, 167.27, 143.76, 141.97, 141.14, 137.01, 135.29, 129.92, 127.34, 127.20, 125.45, 124.07, 73.37, 70.90, 62.83, 54.84, 36.36, 17.80, 14.19. MS (ESI): *m*/*z* Calcd for $C_{23}H_{26}Cl_2NO_5$ $[M + H]^+$ 466.12, found 466.1.

*(2S,3R,4R)-4-acrylamido-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-2,3-dihydroxypentanoic acid (**19, CW9**).* A mixture of compound **17** (35 mg, 0.077 mmol), THF (5 mL), MeOH (5 mL) and H_2O (5 mL) was added 15 mg (0.38 mmol) NaOH and stirred at room temperature for 12 h. The pH value of the resulting solution was adjusted to 3.0 using a 1 M HCl aqueous solution. The THF and MeOH solvent was removed with a rotary evaporator, followed by the extraction with EtOAc. The combined organics were dried with anhydrous $MgSO_4$, filtered and concentrated to a white solid (23 mg, 70% yield). NMR δ H (400 MHz; $CDCl_3$), 2.88–3.22 (2H, m), 4.16 (1H, s), 4.38 (2H, s), 5.69 (1H, d), 6.10–6.27 (2H, m), 7.24 (2H, s), 7.28 (1H, s), 7.32-7.37 (4H, m). ^{13}C NMR (MeOD) 176.19, 169.19, 149.02, 139.56, 138.87, 134.97, 129.91, 127.72, 126.46, 125.39, 124.94, 124.34, 74.03, 73.06, 54.54, 37.44. MS (ESI): *m*/*z* Calcd for $C_{20}H_{20}Cl_2NO_5$ $[M + H]^+$ 424.07, found 424.1.

*(2S,3R,4R)-4-(but-3-enamido)-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-2,3-dihydroxypentanoic acid (**20, CW10**).* Compound **20** was synthesized using the same experimental procedure as compound **19**, except that compound **17** was replaced with compound **18** (35 mg, 0.075 mmol). 25 mg white solid was obtained (76% yield). NMR δ H (400 MHz; $CDCl_3$), 1.63 (2H, t), 2.86–2.98 (2H, m), 3.12 (1H, s), 3.92 (1H, d), 4.24 (2H, d), 5.65–5.75 (1H, m), 6.56–6.69 (2H, m), 7.14–7.17 (3H, m), 7.19 (2H, s), 7.24 (2H, d). ^{13}C NMR ($CDCl_3$) 174.82, 168.38, 143.43, 137.46, 136.85, 136.65, 135.19, 129.72, 127.18, 125.27, 125.16, 123.58, 73.43, 71.71, 52.63, 37.03, 17.86. MS (ESI): *m*/*z* Calcd for $C_{21}H_{22}Cl_2NO_5$ $[M + H]^+$ 438.09, found 438.1.

*(S)-2-((tert-butoxycarbonyl)amino)-3-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)propanoic acid (**22**).* Compound **22** was synthesized using the same experimental procedure as compound **2**, except that compound **1** was replaced with compound **21.** Final product was 5.14 g at a yield of 98%. NMR δ H (400 MHz; $CDCl_3$), 1.42 (9H, s), 3.09–3.26 (2H, m), 4.65 (1H, d), 5.00 (1H, d), 7.28 (2H, s), 7.31 (1H, s), 7.41 (2H, s), 7.46 (2H, d). ^{13}C NMR ($CDCl_3$) δ 175.88, 155.40, 143.69, 137.31, 136.35, 135.28, 130.08, 127.22, 127.14, 125.48, 80.51, 54.25, 37.51, 28.29. MS (ESI): *m*/*z* Calcd for $C_{20}H_{22}Cl_2NO_4$ $[M + H]^+$ 410.09, found 310.0 + 100.05 (Boc group).

*Methyl (S)-2-((tert-butoxycarbonyl)amino)-3-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)propanoate (**23**).* Compound **23** was synthesized using the same experimental procedure as compound **3**, except that compound **1** was replaced with compound **21.** Final product was 5.10 g at a yield of 96%. NMR δ H (400 MHz; $CDCl_3$), 1.42 (9H, s), 3.05–3.20 (2H, m), 3.74 (3H, s), 4.62 (1H, d), 5.09 (1H, d), 7.21 (2H, d), 7.30 (1H, s), 7.41 (2H, s), 7.44 (2H, d). ^{13}C NMR ($CDCl_3$) 172.21, 155.13, 143.70, 137.17, 136.55, 135.25, 130.00, 127.14, 127.09, 125.45, 80.12, 54.39, 52.34, 38.02, 28.30. MS (ESI): *m*/*z* Calcd for $C_{21}H_{24}Cl_2NO_4$ $[M + H]^+$ 424.11, found 324.0 + 100.05 (Boc group).

*Tert-butyl (S)-(1-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-3-hydroxypropan-2-yl)carbamate (**24**).* Compound **24** was synthesized using the same experimental procedure as compound **4**,

except that compound **1** was replaced with compound **21.** Final product was 3.71 g at a yield of 78%. NMR δ H (400 MHz; $CDCl_3$), 1.40 (9H, s), 2.89 (2H, d), 3.55–3.68 (2H, m), 3.91 (1H, s), 5.07 (1H, s), 7.27–7.30 (3H, m), 7.37 (2H, s), 7.41 (2H, d). ^{13}C NMR ($CDCl_3$) 156.20, 143.80, 138.59, 136.58, 135.21, 130.05, 127.06, 126.97, 125.38, 79.74, 63.79, 53.61, 37.11, 28.39. MS (ESI): *m*/*z* Calcd for $C_{20}H_{24}Cl_2NO_3$ $[M + H]^+$ 396.11, found 296.0 + 100.05 (Boc group).

*Tert-butyl (S)-(1-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-3-oxopropan-2-yl)carbamate (**25**).* Compound **25** was synthesized using the same experimental procedure as compound **5**, except that compound **1** was replaced with compound **21.** Final product was 1.66 g at a yield of 90%. NMR δ H (400 MHz; $CDCl_3$), 1.44 (9H, s), 3.17 (2H, t), 4.47 (1H, d), 5.08 (1H, d), 7.26 (2H, d), 7.33 (1H, t), 7.43 (2H, d), 7.48 (2H, d). ^{13}C NMR ($CDCl_3$) 198.99, 155.46, 143.62, 137.35, 136.28, 135.33, 130.06, 127.38, 127.22, 125.52, 60.81, 50.31, 35.62, 28.28. MS (ESI): *m*/*z* Calcd for $C_{20}H_{22}C_{l2}NO_3$ $[M + H]^+$ 394.10, found 294.0 + 100.05 (Boc group).

*Ethyl (S,E)-4-((tert-butoxycarbonyl)amino)-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)pent-2-enoate (**26**).* Compound **26** was synthesized using the same experimental procedure as compound **6**, except that compound **1** was replaced with compound **21.** Final product was 1.90 g at a yield of 97%. NMR δ H (400 MHz; $CDCl_3$), 1.28 (3H, t) 1.40 (9H, s), 2.94 (2H, d), 4.16–4.22 (2H, m), 4.63 (2H, s), 5.89 (1H, d), 6.90–6.95 (1H, m), 7.26 (2H, d), 7.31 (1H, t), 7.42 (2H, d), 7.46 (2H, d). ^{13}C NMR ($CDCl_3$) 166.09, 154.96, 147.22, 143.73, 137.07, 136.98, 135.27, 130.09, 127.18, 127.10, 125.47, 121.35, 79.98, 60.54, 52.25, 40.56, 28.30, 14.23. MS (ESI): *m*/*z* Calcd for $C_{24}H_{28}Cl_2NO_4$ $[M + H]^+$ 464.14, found 364.1+ 100.05 (Boc group).

*Ethyl (S,E)-4-amino-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)pent-2-enoate (**27**).* Compound **27** was synthesized using the same experimental procedure as compound **7**, except that compound **1** was replaced with compound **21.** Final product was 0.74 g at a yield of 99%. NMR δ H (400 MHz; $CDCl_3$), 1.21 (3H, t), 3.02–3.28 (2H, m), 4.08–4.13 (2H, m), 4.16 (1H, s), 5.97 (1H, d), 6.86–6.91 (1H, m), 7.26 (2H, d), 7.32 (1H, t), 7.39 (2H, d), 7.46 (2H, d). ^{13}C NMR ($CDCl_3$) 165.68, 143.31, 140.58, 137.96, 135.35, 134.44, 130.07, 127.64, 127.35, 125.85, 125.47, 61.36, 53.84, 38.68, 13.92. MS (ESI): *m*/*z* Calcd for $C_{19}H_{20}Cl_2NO_2$ $[M + H]^+$ 364.09, found 364.1.

*Ethyl (S,E)-4-acrylamido-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)pent-2-enoate (**28, CW13**).* Compound **28** was synthesized using the same experimental procedure as compound **8**, except that compound **1** was replaced with compound **21.** Final product was 0.25 g at a yield of 59%. NMR δ H (400 MHz; $CDCl_3$), 1.19 (3H, t), 2.92 (2H, d), 4.07–4.13 (2H, m), 4.99 (1H, s), 5.58 (1H, d), 5.81 (1H, d), 5.93 (1H, s), 6.01 (1H, m), 6.20 (1H, d), 6.86 (1H, m), 7.17 (2H, d), 7.23 (1H, t), 7.34 (2H, d), 7.38 (2H, d). ^{13}C NMR ($CDCl_3$) 165.01, 164.03, 145.26, 142.54, 136.17, 135.62, 134.25, 129.20, 128.95, 126.44, 126.24, 126.13, 124.43, 120.84, 59.65, 49.83, 38.91, 13.18. MS (ESI): *m*/*z* Calcd for $C_{22}H_{22}Cl_2NO_3$ $[M + H]^+$ 418.10, found 418.0.

*Ethyl (S,E)-4-(but-3-enamido)-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)pent-2-enoate (**29, CW14**).* Compound **29** was synthesized using the same experimental procedure as compound **9**, except that compound **1** was replaced with compound **21.** Final product was 0.30 g at a yield of 68%. NMR δ H (400 MHz; $CDCl_3$), 1.27 (3H, t), 1.86 (2H, d), 3.00 (2H, d), 4.16–4.21 (2H, m),

5.08 (1H, t), 5.32 (1H, d), 5.76 (1H, d), 5.86 (1H, d), 6.86 (1H, m), 6.94 (1H, m), 7.26 (2H, d), 7.33 (1H, s), 7.44 (2H, s), 7.48 (2H, d). ^{13}C NMR ($CDCl_3$) 164.97, 164.25, 145.50, 142.60, 140.22, 136.18, 135.44, 134.27, 128.98, 126.26, 126.07, 124.46, 123.35, 120.70, 59.57, 49.51, 38.96, 16.77, 13.19. MS (ESI): *m/z* Calcd for $C_{23}H_{24}Cl_2NO_3$ $[M + H]^+$ 432.11, found 432.0.

*(S,E)-4-acrylamido-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)pent-2-enoic acid (**30, CW15**).* Compound **30** was synthesized using the same experimental procedure as compound **10**, except that compound **1** was replaced with compound **21.** Final product was 0.17 g at a yield of 74%. NMR δ H (400 MHz; $CDCl_3$), 3.02 (2H, d), 5.10 (1H, s), 5.69 (1H, d), 5.87 (1H, d), 6.08 (1H, m), 6.29 (1H, d), 7.03 (1H, m), 7.24 (2H, d), 7.33 (1H, s), 7.43 (2H, s), 7.48 (2H, d). ^{13}C NMR ($CDCl_3$) 169.53, 164.98, 148.63, 143.53, 137.40, 136.32, 135.32, 130.08, 129.99, 127.72, 127.39, 127.22, 125.51, 121.05, 50.78, 28.86. MS (ESI): *m/z* Calcd for $C_{20}H_{18}Cl_2NO_3$ $[M + H]^+$ 390.07, found 390.0.

*(S,E)-4-(but-3-enamido)-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)pent-2-enoic acid (**31, CW16**).* Compound **31** was synthesized using the same experimental procedure as compound **11**, except that compound **1** was replaced with compound **21.** Final product was 0.22 g at a yield of 80%. NMR δ H (400 MHz; $CDCl_3$), 1.76 (2H, d), 2.92 (2H, d), 5.00 (1H, t), 5.63 (1H, d), 5.69–5.80 (2H, m), 6.75–6.80 (1H, m), 6.92–6.97 (1H, m), 7.18 (2H, d), 7.24 (1H, s), 7.34 (2H, s), 7.38 (2H, d). ^{13}C NMR ($CDCl_3$) 169.14, 164.54, 147.83, 142.52, 140.52, 136.21, 135.51, 134.26, 128.95, 126.29, 126.14, 124.44, 123.24, 120.07, 49.68, 38.83, 16.80. MS (ESI): *m/z* Calcd for $C_{21}H_{20}Cl_2NO_3$ $[M + H]^+$ 404.08, found 404.0.

*(S)-2-amino-3-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)propan-1-ol (**32**).* Compound **32** was synthesized using the same experimental procedure as compound **12**, except that compound **1** was replaced with compound **21.** Final product was 1.37 g at a yield of 99%. NMR δ H (400 MHz; $CDCl_3$) 2.90–2.96 (2H, m), 3.61–3.82 (3H, m), 7.20 (2H, d), 7.29 (1H, s), 7.33 (2H, s), 7.41 (2H, d). ^{13}C NMR ($CDCl_3$) 143.08, 138.07, 135.37, 134.59, 129.62, 127.76, 127.43, 125.38, 60.98, 54.89, 34.99. MS (ESI): *m/z* Calcd for $C_{15}H_{16}Cl_2NO$ $[M + H]^+$ 296.06, found 296.1.

*(S)-N-(1-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-3-hydroxypropan-2-yl)acrylamide (**33, CW11**).* Compound **33** was synthesized using the same experimental procedure as compound **13**, except that compound **1** was replaced with compound **21.** Final product was 0.57 g at a yield of 99%. NMR δ H (400 MHz; $CDCl_3$), 2.92 (2H, d), 3.60–3.73 (2H, m), 4.28 (1H, s), 5.59 (1H, d), 6.06–6.13 (1H, m), 6.22 (1H, d), 6.50 (1H, d), 7.28 (3H, m), 7.36 (2H, d), 7.39 (2H, d). ^{13}C NMR ($CDCl_3$) 166.32, 143.63, 138.19, 136.74, 135.22, 130.60, 129.89, 127.28, 127.15, 127.04, 125.36, 63.59, 52.80, 36.54. MS (ESI): *m/z* Calcd for $C_{18}H_{18}Cl_2NO_2$ $[M + H]^+$ 350.07, found 350.1.

*(S)-N-(1-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-3-hydroxypropan-2-yl)but-3-enamide (**34, CW12**).* Compound **34** was synthesized using the same experimental procedure as compound **14**, except that compound **1** was replaced with compound **21.** Final product was 0.63 g at a yield of 75%. NMR δ H (400 MHz; $CDCl_3$), 1.78 (2H, d), 2.92 (2H, d), 3.59–3.72 (2H, m), 4.28 (1H, s), 5.82 (1H, d), 6.62 (1H, d), 6.73–6.83 (2H, m), 7.28 (3H, m), 7.36 (2H, d), 7.39 (2H, d). ^{13}C NMR ($CDCl_3$) 166.89, 143.69. 140.65, 138.44, 136.57, 135.19, 129.92, 127.07, 126.97, 125.34,

124.81, 63.55, 52.70, 36.59, 17.76. MS (ESI): *m*/*z* Calcd for $C_{19}H_{20}Cl_2NO_2$ $[M + H]^+$ 364.09, found 364.0.

*Ethyl (2R,3S,4S)-4-((tert-butoxycarbonyl)amino)-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-2,3-dihydroxypentanoate (**35**).* Compound **35** was synthesized using the same experimental procedure as compound **15**, except that compound **1** was replaced with compound **21.** Final product was 0.68 g at a yield of 75%. NMR δ H (400 MHz; $CDCl_3$), 1.28 (3H, t), 1.37 (9H, s), 2.90–3.16 (2H, m), 3.83 (1H, t), 4.26 (2H, m), 4.39 (1H, d), 4.92 (1H, d), 7.30 (3H, m), 7.41 (2H, s), 7.44 (2H, d). ^{13}C NMR ($CDCl_3$) 172.86, 156.40, 143.87, 137.94, 136.71, 135.23, 130.07. 127.08, 127.00, 125.42, 80.49, 72.75, 71.00, 62.19, 53.69, 36.78, 28.27, 14.13. MS (ESI): *m*/*z* Calcd for $C_{24}H_{30}Cl_2NO_6$ $[M + H]^+$ 498.15, found 398.1 + 100.05 (Boc group).

*Ethyl (2R,3S,4S)-4-amino-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-2,3-dihydroxypentanoate (**36**).* Compound **36** was synthesized using the same experimental procedure as compound **16**, except that compound **1** was replaced with compound **21.** Final product was 0.46 g at a yield of 84%. NMR δ H (400 MHz; $CDCl_3$), 1.19 (3H, t), 3.07 (2H, s), 3.77 (1H, s), 4.15 (2H, s), 4.33 (1H, s), 4.73 (1H, s), 7.32 (3H, m), 7.38 (2H, d), 7.46 (2H, d). ^{13}C NMR ($CDCl_3$) 172.48, 143.29, 138.00, 137.90, 135.37, 130.06, 127.74, 127.38, 125.43, 73.79, 68.20, 62.57, 56.42, 36.04, 13.80. MS (ESI): *m*/*z* Calcd for $C_{19}H_{22}Cl_2NO_4$ $[M + H]^+$ 398.09, found 398.1.

*Ethyl (2R,3S,4S)-4-acrylamido-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-2,3-dihydroxypentanoate (**37, CW17**).* Compound **37** was synthesized using the same experimental procedure as compound **17**, except that compound **1** was replaced with compound **21.** Final product was 0.15 g at a yield of 59%. ^1H NMR δ H (400 MHz; $CDCl_3$), 1.25 (3H, t), 3.09 (2H, m), 3.92 (1H, s), 4.20 (2H, m), 4.27 (1H, d), 5.35 (1H, s), 5.63 (1H, d), 6.07–6.14 (1H, m), 6.23 (1H, d), 6.43 (1H, d), 7.32 (3H, m), 7.41 (2H, d), 7.44 (2H, d). ^{13}C NMR ($CDCl_3$) 172.87, 166.58, 143.74, 138.11, 136.78, 135.23, 130.52, 129.95, 127.23, 127.14, 127.02, 125.42, 72.48, 71.54, 62.18, 53.02, 37.18, 14.05. MS (ESI): *m*/*z* Calcd for $C_{22}H_{24}Cl_2NO_5$ $[M + H]^+$ 452.10, found 452.1.

*Ethyl (2R,3S,4S)-4-(but-3-enamido)-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-2,3-dihydroxypentanoate (**38, CW18**).* Compound **38** was synthesized using the same experimental procedure as compound **18**, except that compound **1** was replaced with compound **21.** Final product was 0.23 g at a yield of 85%. ^1H NMR δ H (400 MHz; $CDCl_3$), 1.25 (3H, t), 1.79 (2H, m), 3.02 (2H, m), 3.91 (1H, m), 4.17–4.27 (2H, m), 4.31 (1H, d), 5.31 (1H, s), 5.77 (1H, t), 6.20 (1H, m), 6.78 (1H, m), 7.30 (3H, m), 7.39 (2H, s), 7.43 (2H, d). ^{13}C NMR ($CDCl_3$) 172.95, 167.31, 143.71, 141.22, 138.09, 136.75, 135.23, 129.92, 127.25, 127.14, 125.39, 124.52, 72.79, 71.58, 62.18, 52.95, 37.16, 17.78, 14.05. MS (ESI): *m*/*z* Calcd for $C_{23}H_{26}Cl_2NO_5$ $[M + H]^+$ 466.12, found 466.1.

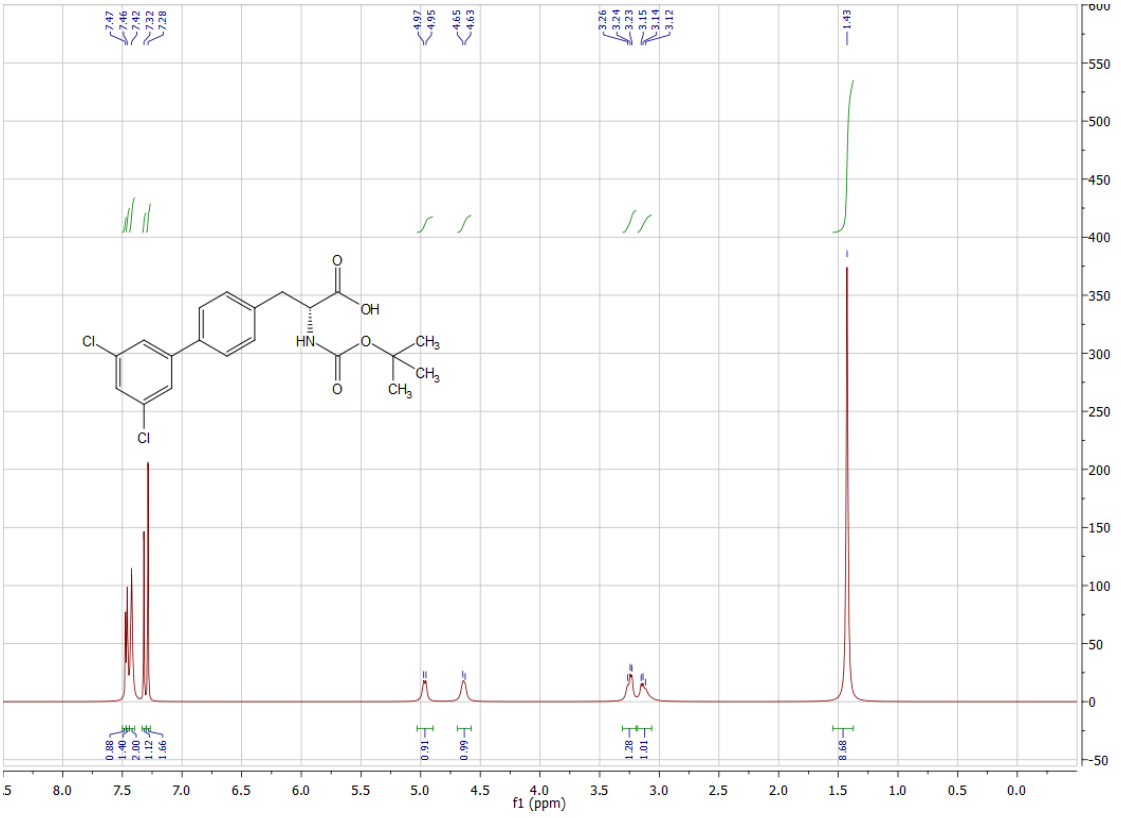
*(2R,3S,4S)-4-acrylamido-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-2,3-dihydroxypentanoic acid (**39, CW19**).* Compound **39** was synthesized using the same experimental procedure as compound **19**, except that compound **1** was replaced with compound **21.** Final product was 0.10 g at a yield of 68%. NMR δ H (400 MHz; $CDCl_3$), 3.01–3.20 (2H, m), 4.13–4.21 (1H, m), 4.43 (2H, s), 5.56 (1H, d), 6.08–6.17 (2H, m), 7.22 (3H, d), 7.27–7.39 (4H, m). ^{13}C NMR (MeOD) 176.19, 169.19, 149.02, 139.56, 138.87, 134.97, 129.79, 127.72, 126.46, 125.39, 124.94, 124.34,

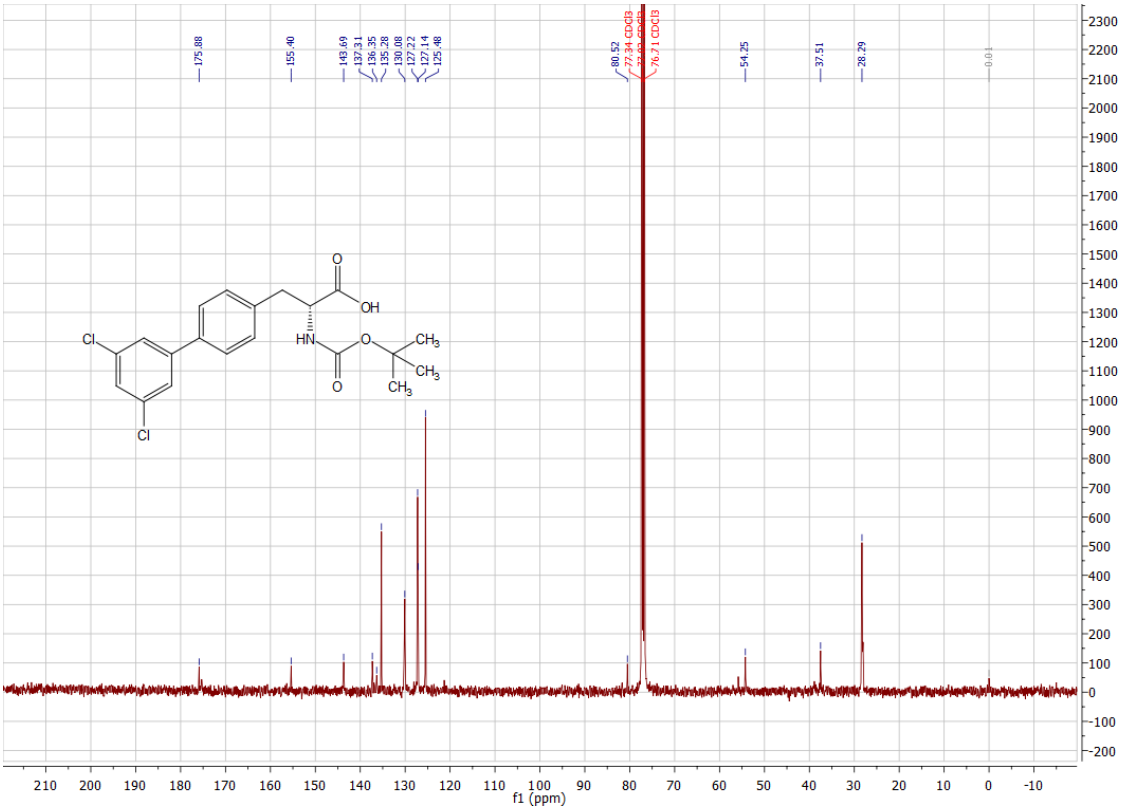
74.18, 73.42, 54.92, 37.45. MS (ESI): *m*/*z* Calcd for $C_{20}H_{20}Cl_2NO_5$ $[M + H]^+$ 424.07, found 424.1.

*(2R,3S,4S)-4-(but-3-enamido)-5-(3',5'-dichloro-[1,1'-biphenyl]-4-yl)-2,3-dihydroxypentanoic acid (**40, CW20**).* Compound **40** was synthesized using the same experimental procedure as compound **20**, except that compound **1** was replaced with compound **21.** Final product was 0.14 g at a yield of 64%. NMR δ H (400 MHz; $CDCl_3$), 1.68 (2H, t), 2.83–3.04 (2H, m), 3.20 (1H, s), 4.01 (1H, d), 4.37 (2H, d), 5.72–5.82 (1H, m), 6.61–6.78 (2H, m), 7.20 (3H, m), 7.23 (2H, s), 7.28 (2H, d). ^{13}C NMR ($CDCl_3$) 175.19, 168.26, 143.41, 137.67, 136.69, 136.54, 135.16, 129.76, 127.08, 125.21, 125.12, 123.88, 73.54, 71.73, 52.75, 36.96, 17.81. MS (ESI): *m*/*z* Calcd for $C_{21}H_{22}Cl_2NO_5$ $[M + H]^+$ 438.09, found 438.1.

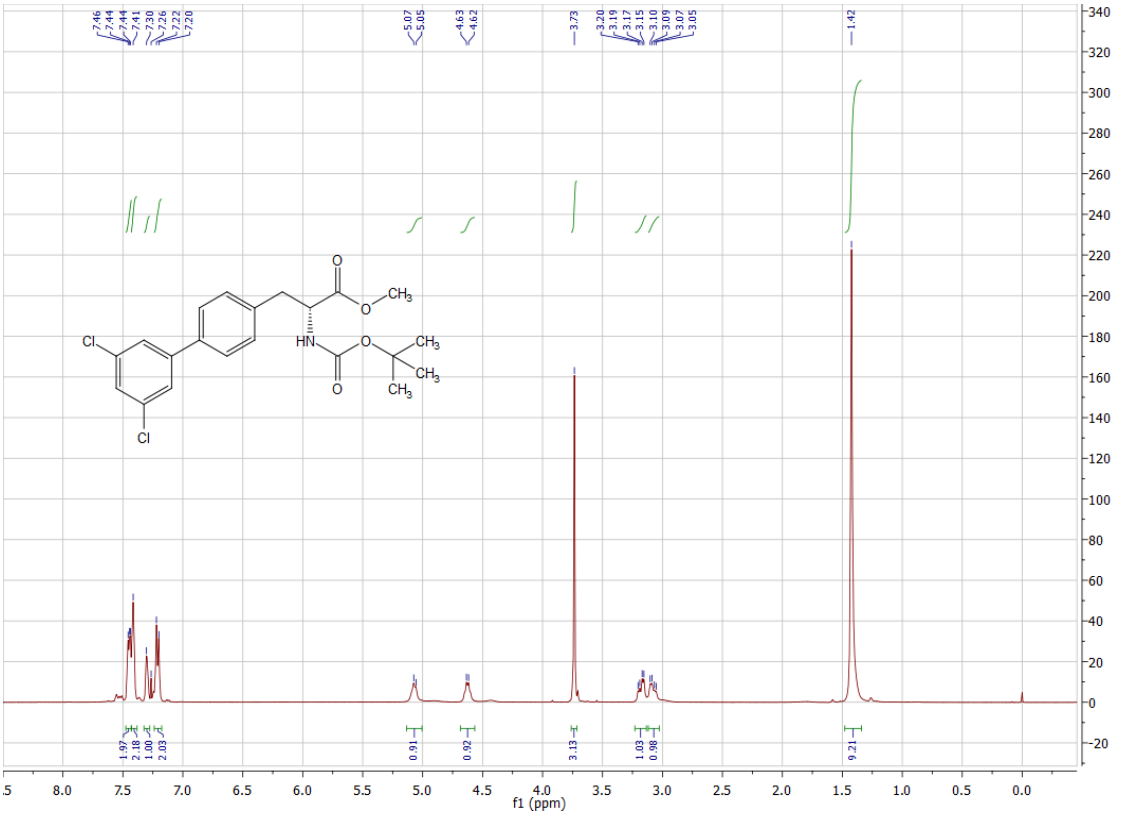
^{1}H and ^{13}C NMR spectra of compounds **2-20**, **22-40**

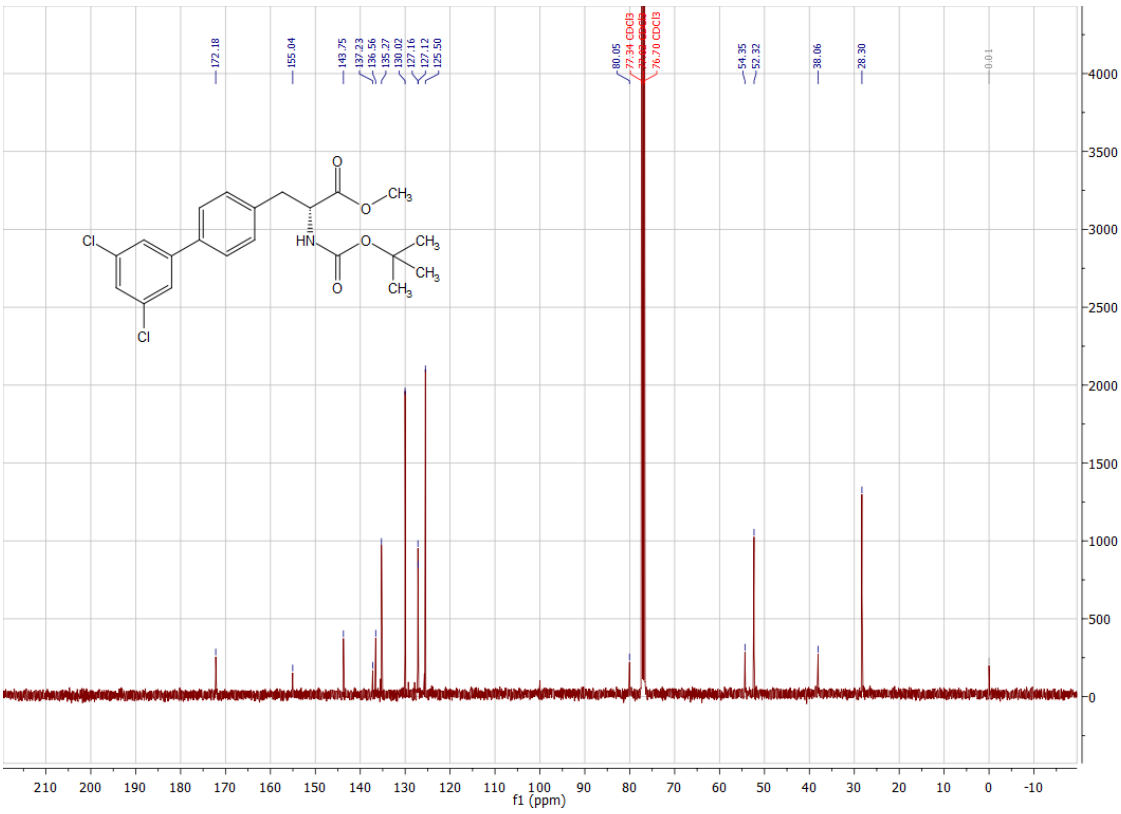
Compound **2**


7.47
7.46
7.42
7.32
7.28
4.97
4.95
4.65
4.63
3.26
3.24
3.23
3.15
3.14
3.12
1.43
0.88
1.40
2.00
1.12
1.66
0.91
0.99
1.28
1.01
8.68
f1 (ppm)

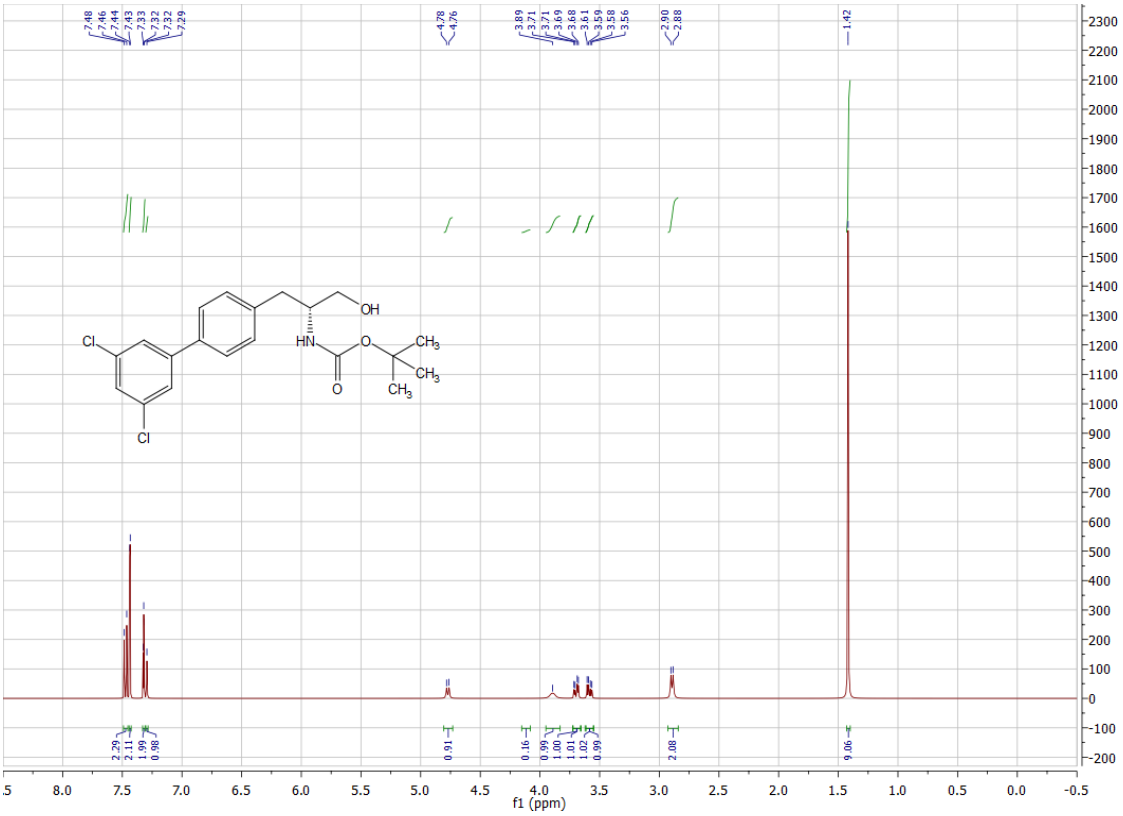

175.88
155.40
143.69
137.31
136.35
135.28
130.00
127.22
127.14
125.48
80.52
77.34 CDCl3
76.71 CDCl3
54.25
37.51
28.29
f1 (ppm)

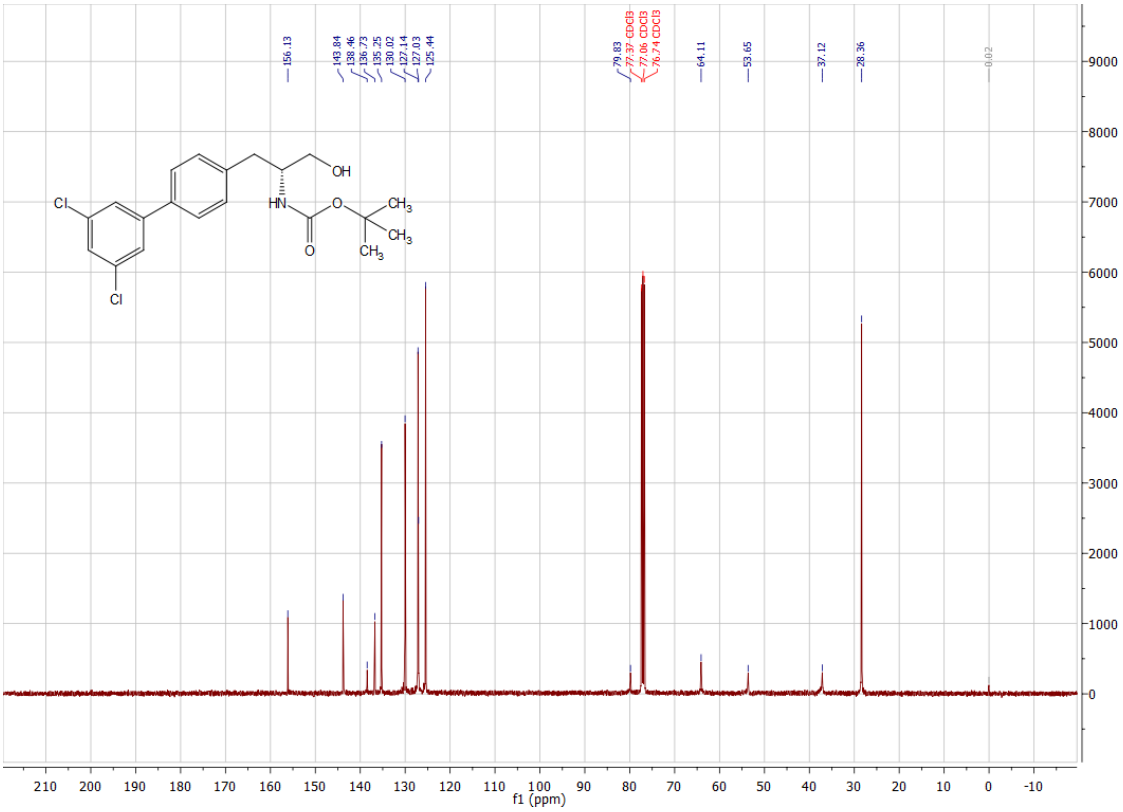
Compound **3**


7.46
7.44
7.44
7.41
7.30
7.26
7.23
7.22
7.20
5.07
5.05
4.63
4.62
3.73
3.20
3.19
3.17
3.15
3.10
3.09
3.07
3.05
1.42
Cl
HN
O
CH3
Cl
1.97
2.18
1.00
2.03
0.91
0.92
3.13
1.03
0.98
9.21
f1 (ppm)

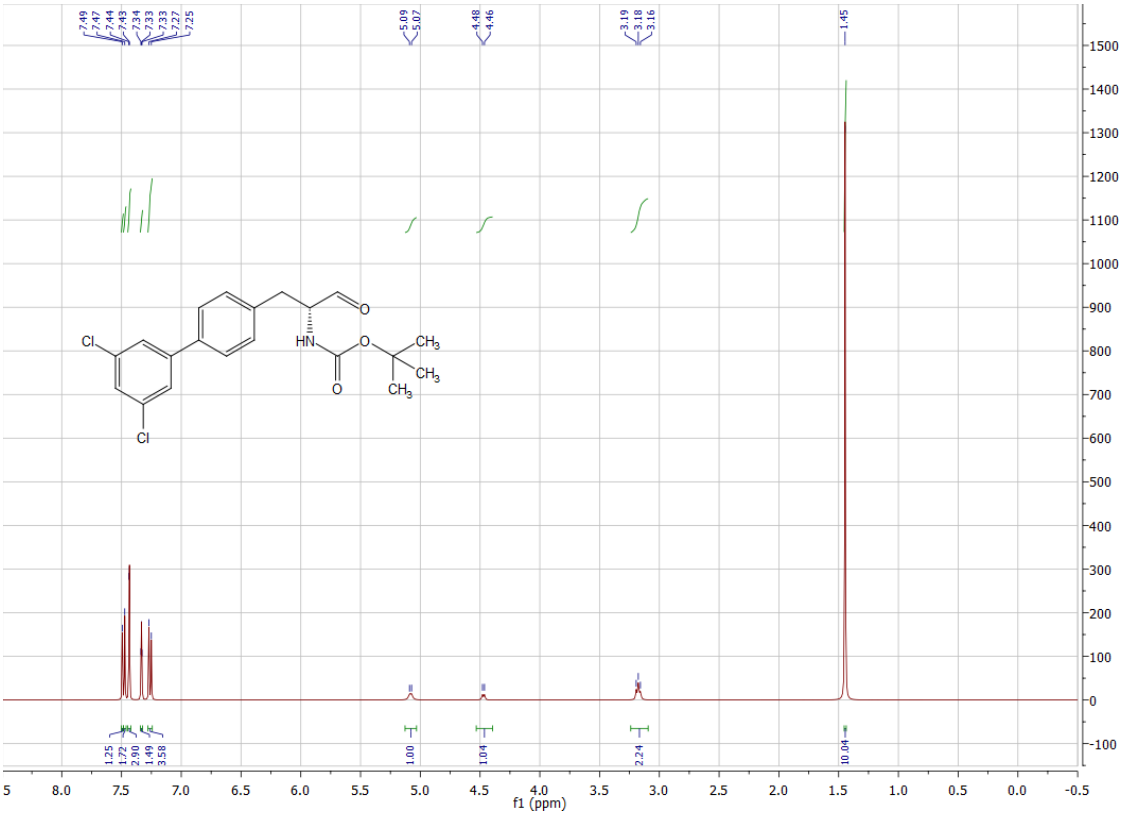

172.18
155.04
143.75
137.23
136.56
135.27
130.02
127.16
127.12
125.50
80.05
77.34 CDCl3
76.70 CDCl3
54.35
52.32
38.06
28.30
0.01
Cl
HN
O
CH3
f1 (ppm)

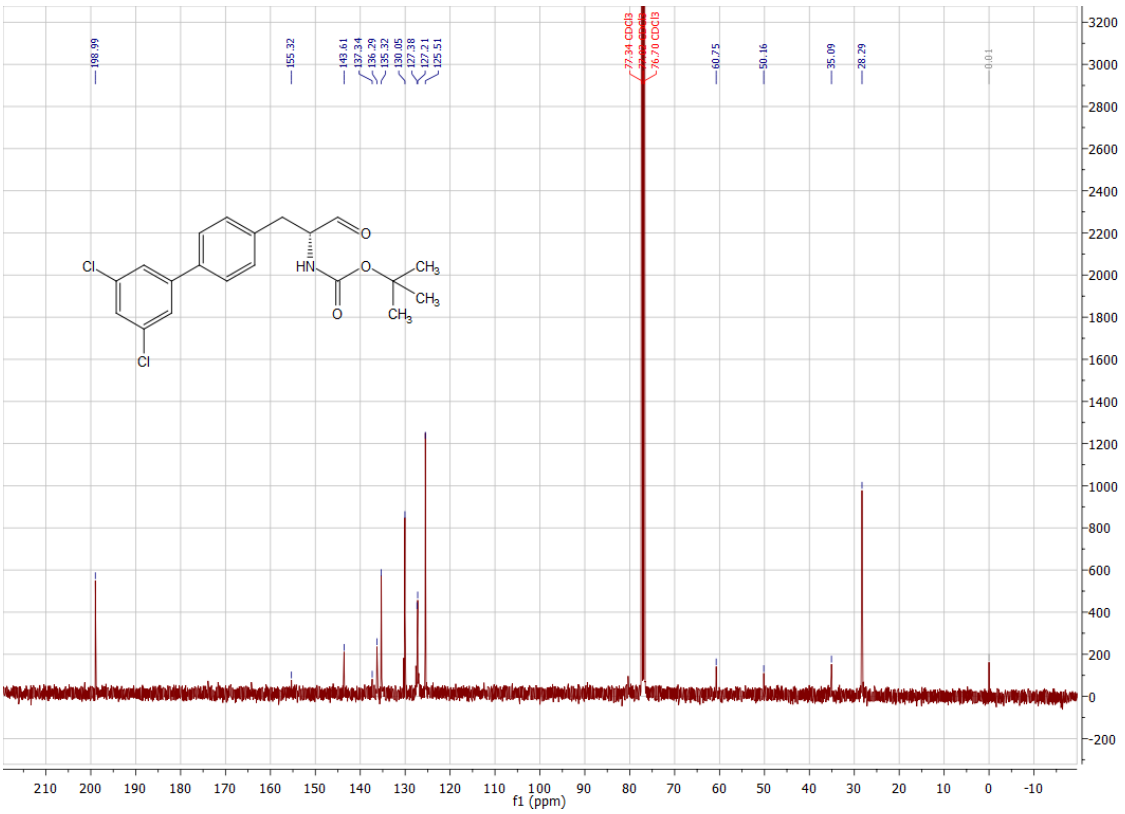
Compound **4**


7.48
7.46
7.44
7.43
7.33
7.32
7.32
7.29
4.78
4.76
3.89
3.71
3.71
3.69
3.68
3.61
3.59
3.58
3.56
2.90
2.88
1.42
OH
HN
O
CH3
CH3
CH3
Cl
Cl
2.29
2.11
1.99
0.98
0.91
0.16
0.99
1.00
1.01
1.02
0.99
2.08
9.06
f1 (ppm)

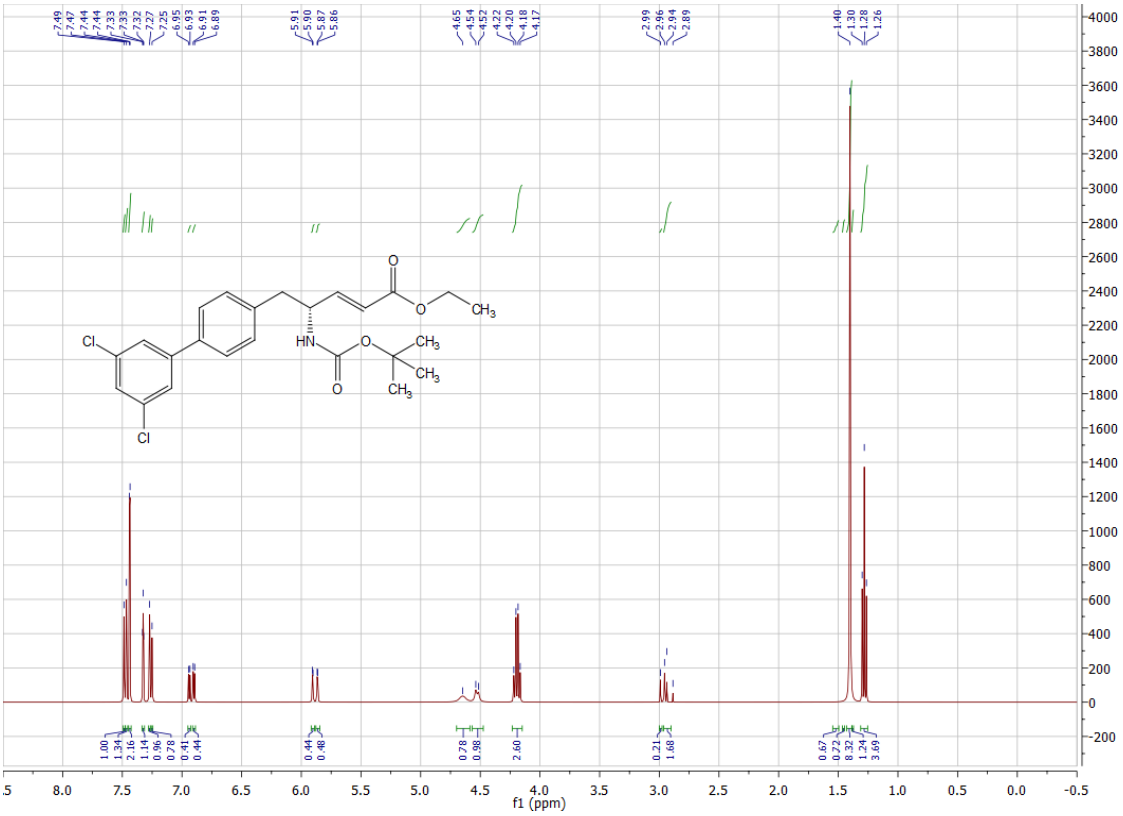

156.13
143.84
138.46
136.73
135.25
130.02
127.14
127.03
125.44
79.83
77.37 CDCl3
77.06 CDCl3
76.74 CDCl3
64.11
53.65
37.12
28.36
0.02
OH
HN
O
CH3
CH3
CH3
Cl
Cl
f1 (ppm)

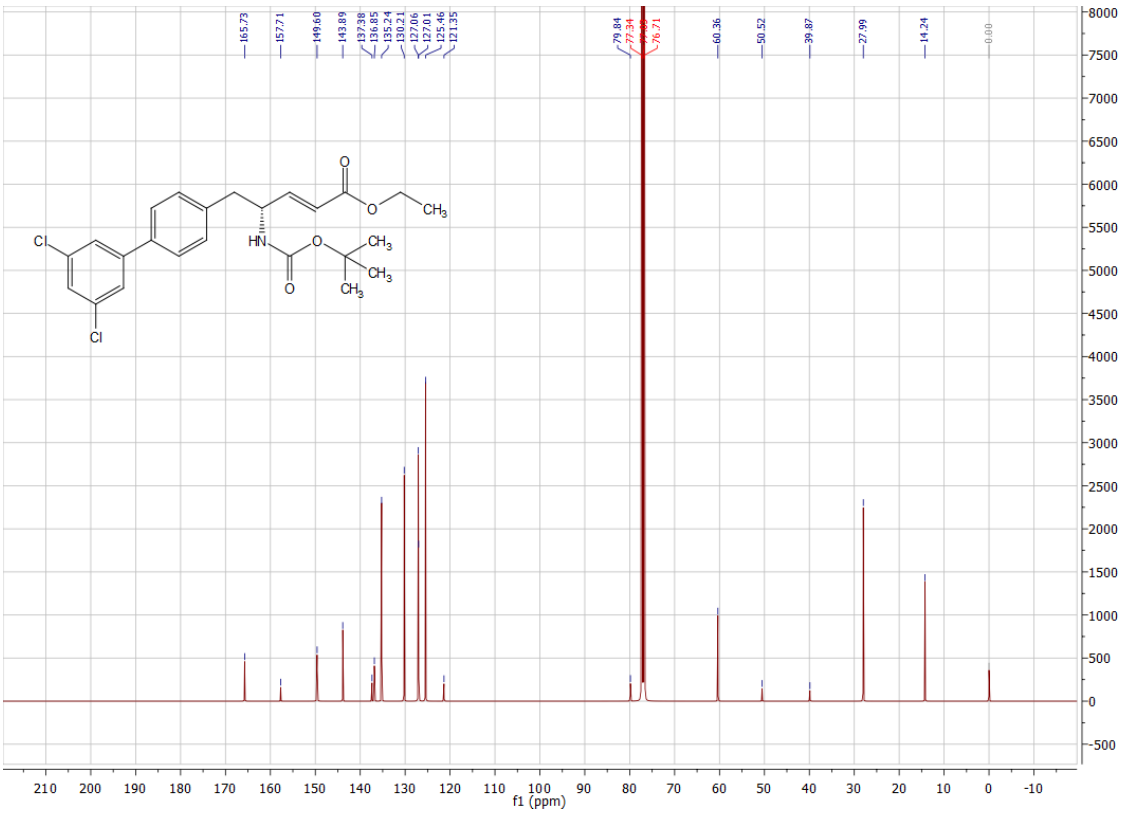
Compound **5**


7.49
7.47
7.44
7.43
7.34
7.33
7.27
7.25
5.09
5.07
4.48
4.46
3.19
3.18
3.16
1.45
Cl
HN
O
CH3
Cl
1.25
1.72
2.90
1.49
3.58
1.00
1.04
2.24
10.04
f1 (ppm)

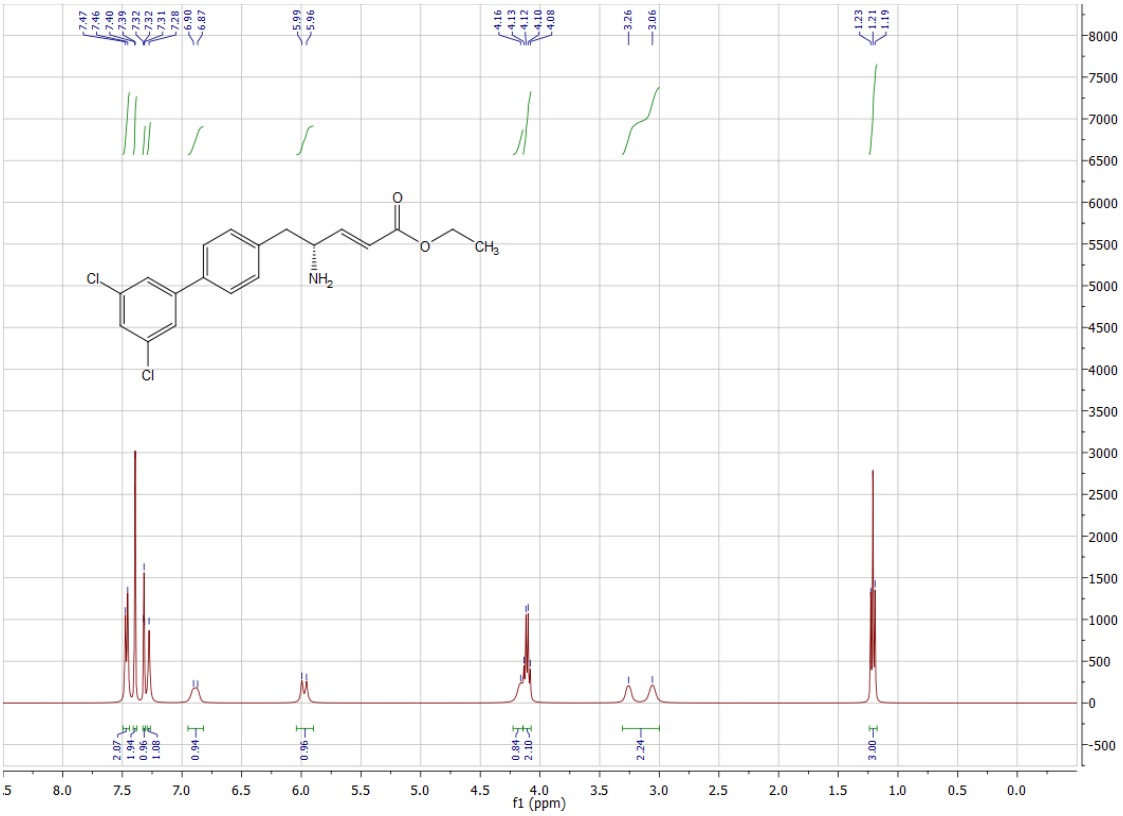

198.99
155.32
143.61
137.34
136.29
135.22
130.05
127.38
127.21
125.51
77.34 CDCl3
76.70 CDCl3
60.75
50.16
35.09
28.29
Cl
HN
O
CH3
f1 (ppm)

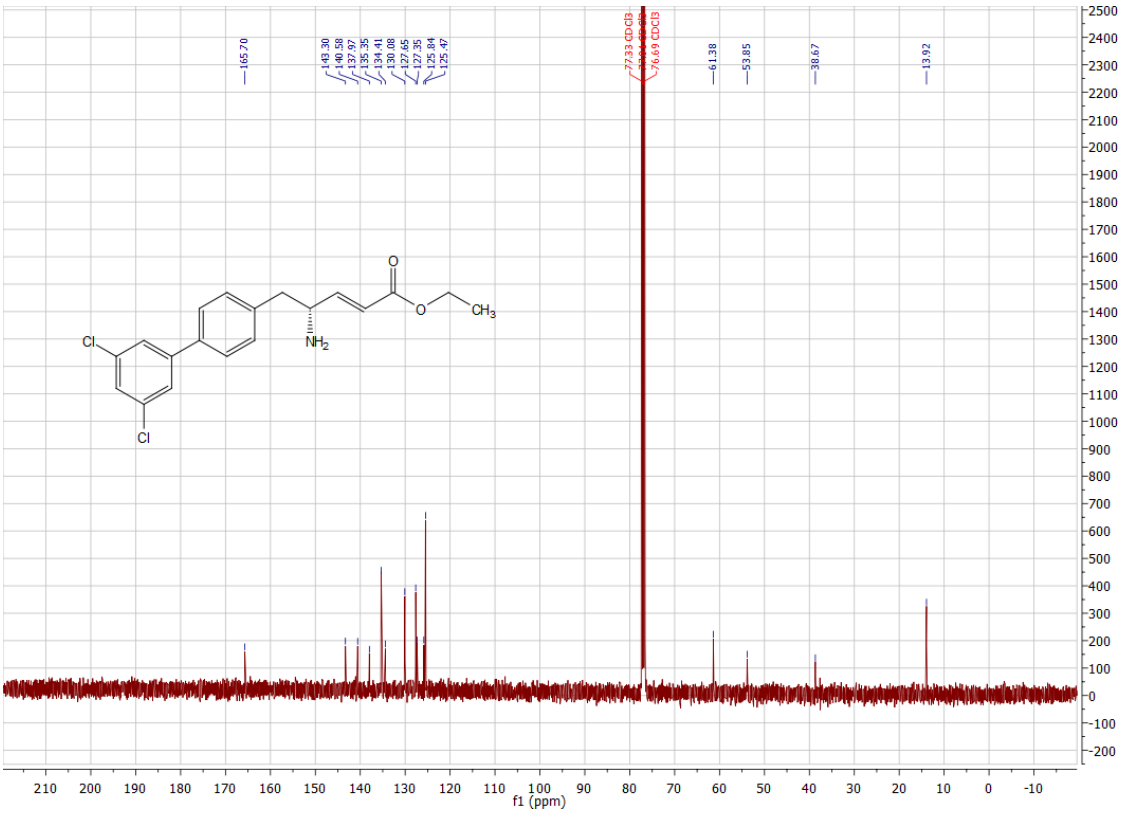
Compound **6**


7.49
7.47
7.44
7.44
7.33
7.33
7.32
7.27
7.25
6.95
6.93
6.91
6.89
5.91
5.90
5.87
5.86
4.65
4.54
4.52
4.22
4.20
4.18
4.17
2.99
2.96
2.94
2.89
1.40
1.30
1.28
1.26
Cl
HN
O
CH3
f1 (ppm)

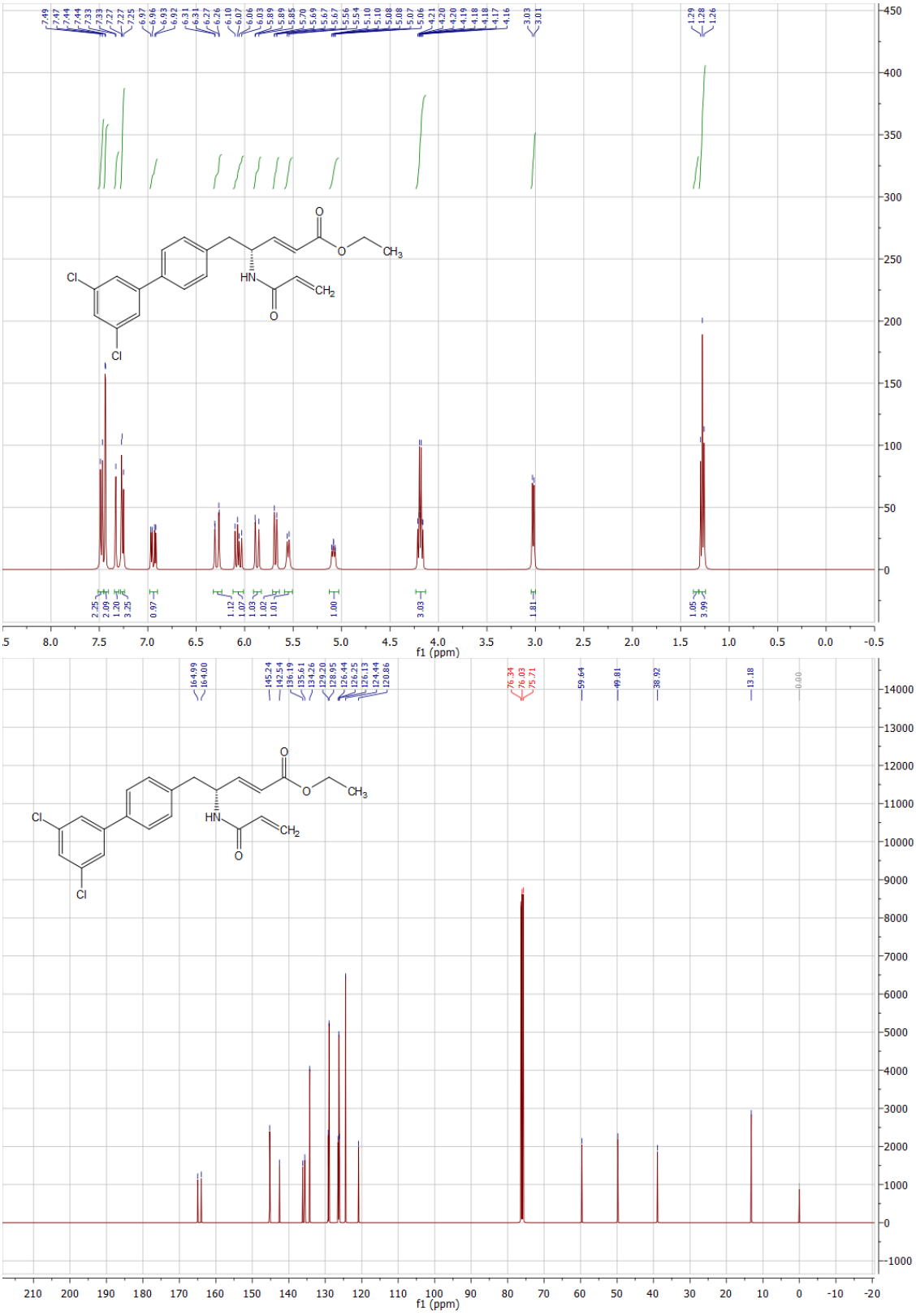

165.73
157.71
149.60
143.89
137.38
136.85
135.24
130.21
127.06
122.01
121.46
121.35
79.84
77.34
76.71
60.36
50.52
39.87
27.99
14.24
0.00
Cl
HN
O
CH3
f1 (ppm)

Compound **7**

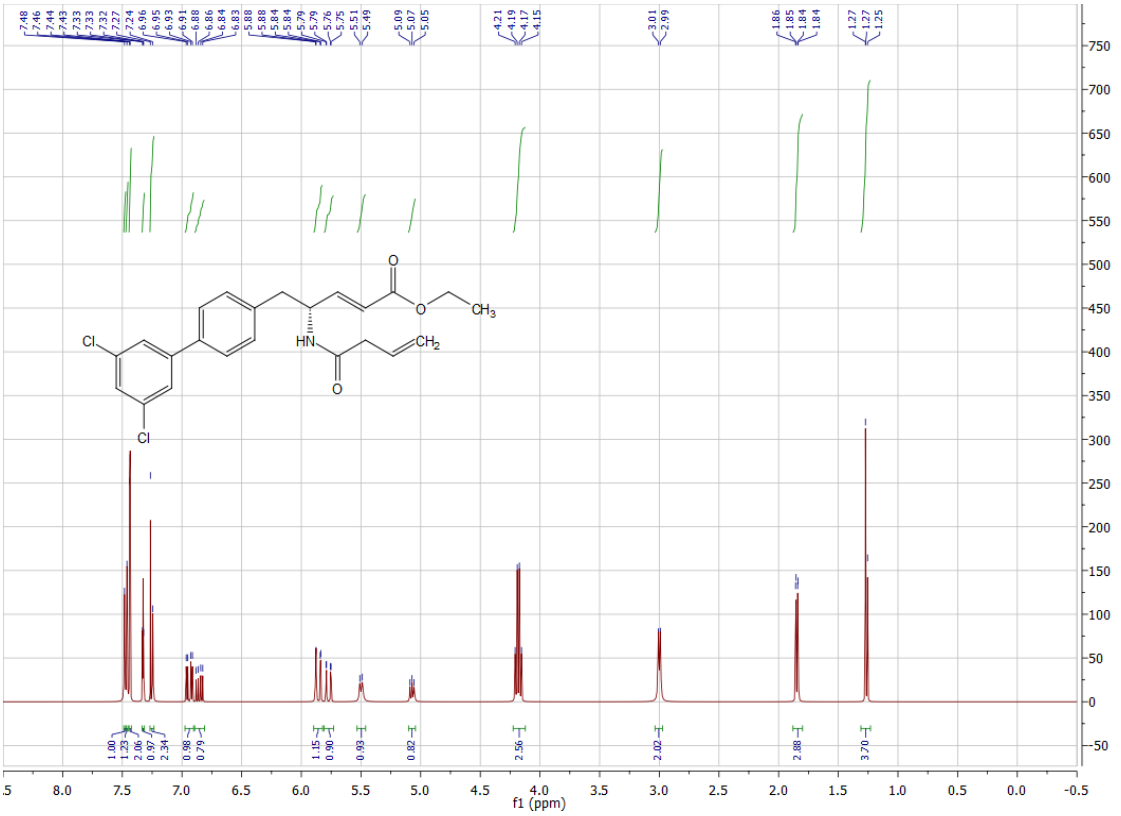

7.47
7.46
7.40
7.39
7.32
7.32
7.31
7.30
6.89
6.87
5.99
5.96
4.16
4.13
4.12
4.10
4.08
3.26
3.06
1.23
1.21
1.19
Cl
Cl
O
O
CH3
NH2
f1 (ppm)

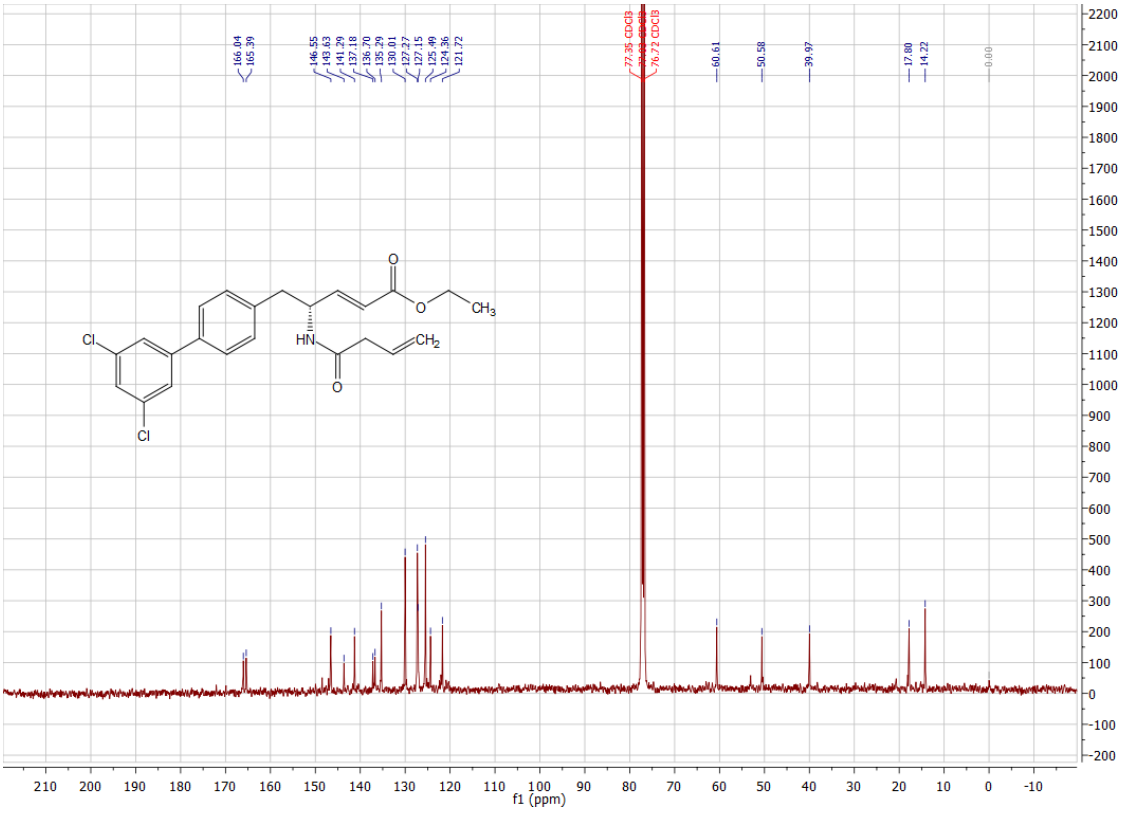

165.70
143.30
140.58
137.97
135.35
134.41
130.08
127.65
127.35
125.84
125.47
77.33 CDCl3
76.69 CDCl3
61.38
53.85
38.67
13.92
Cl
Cl
O
O
CH3
NH2
f1 (ppm)

Compound **8** (CW3)

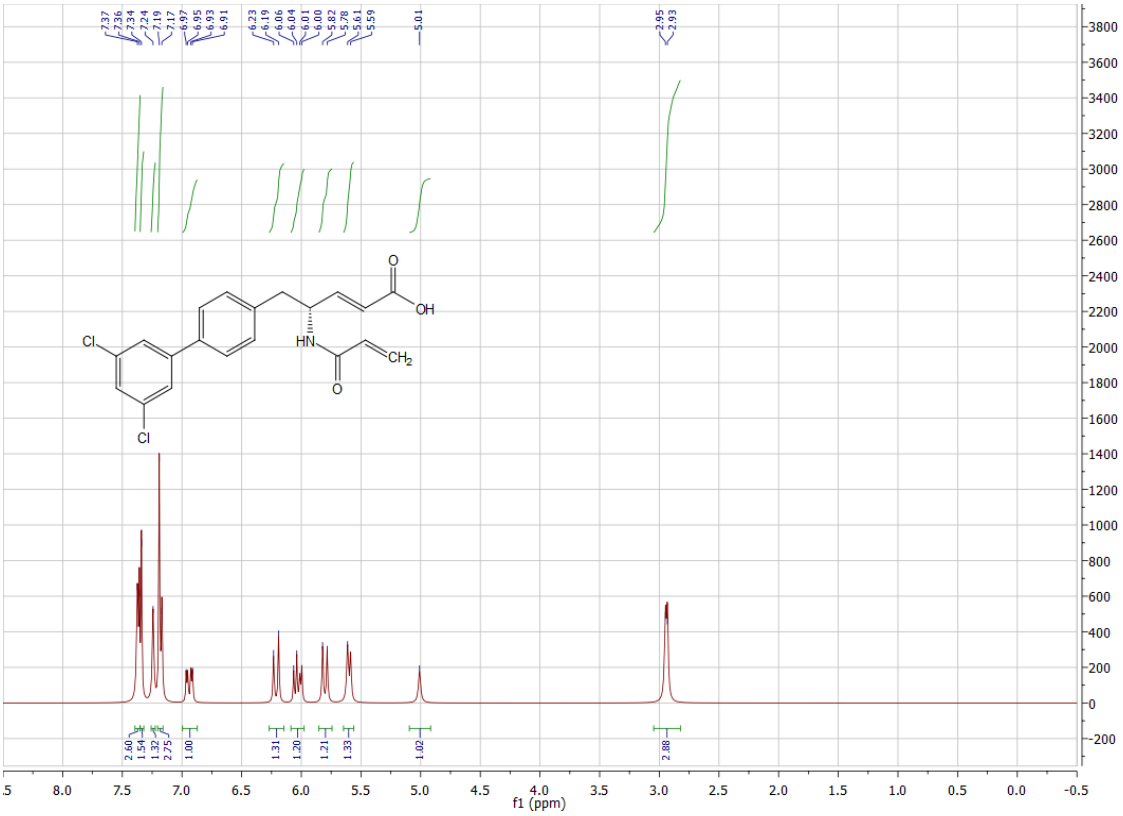


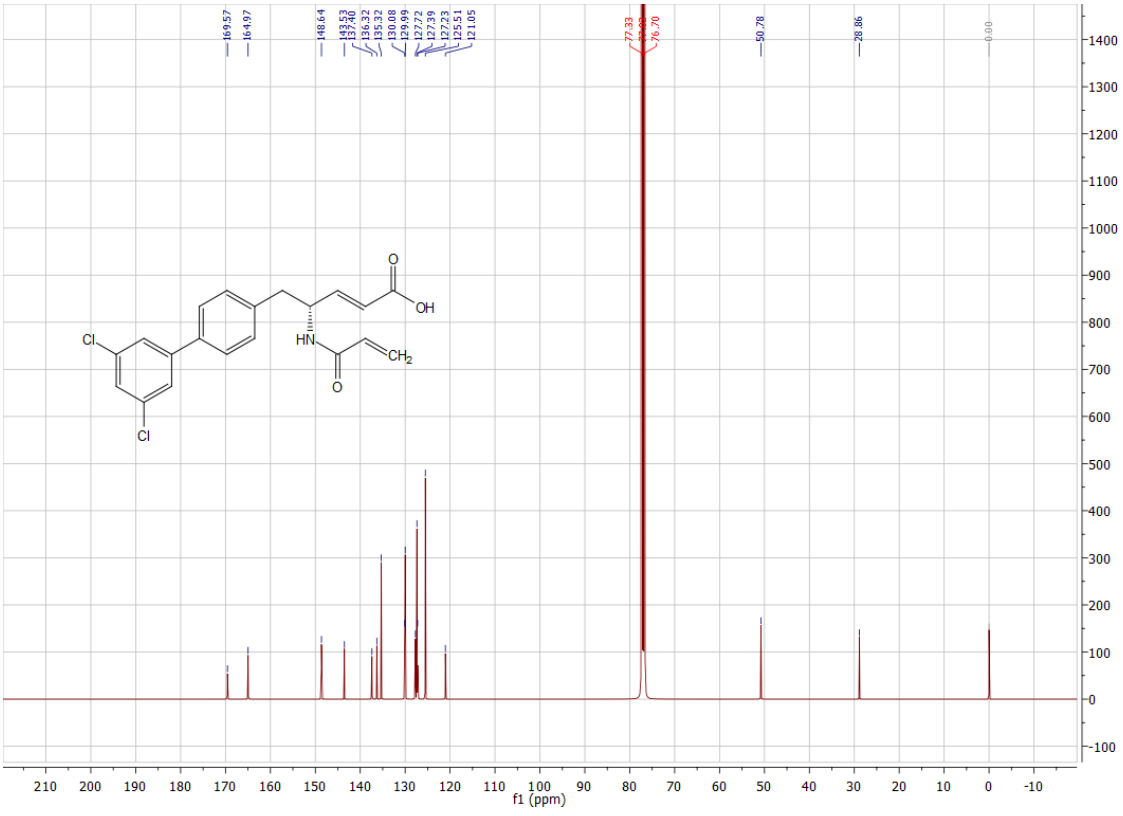
Compound **9** (CW4)



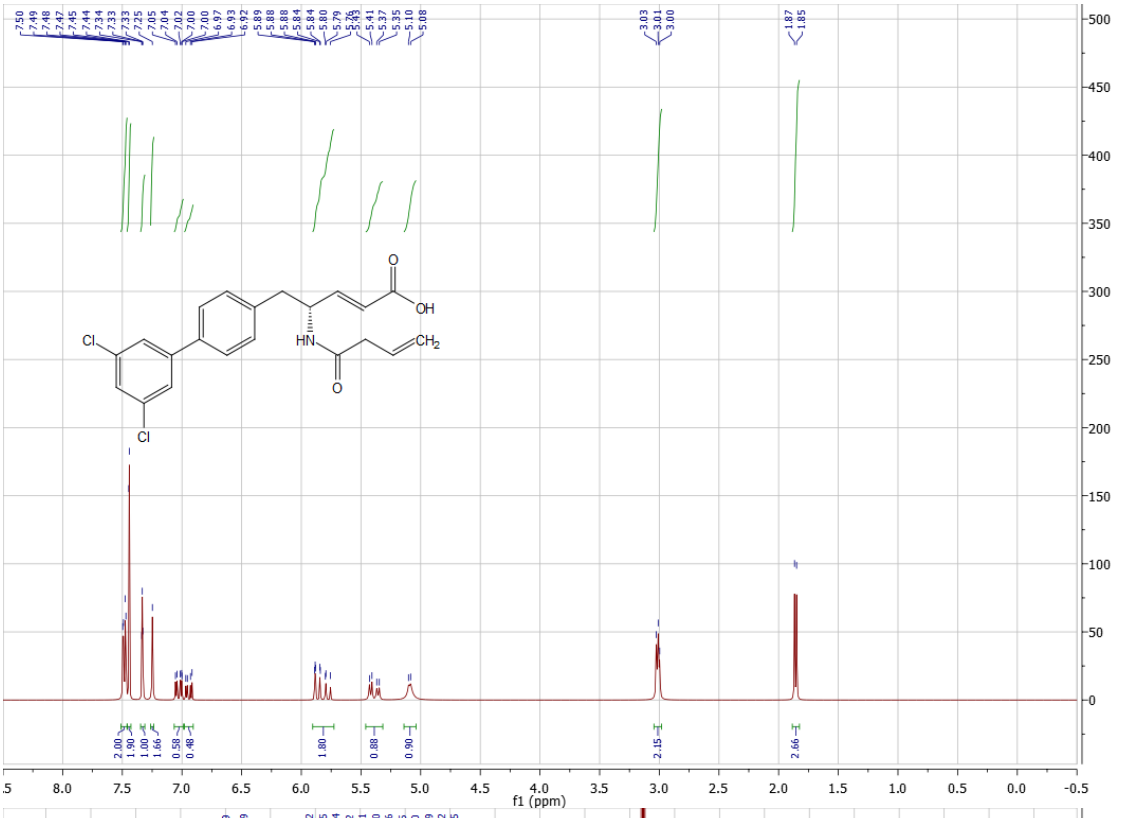


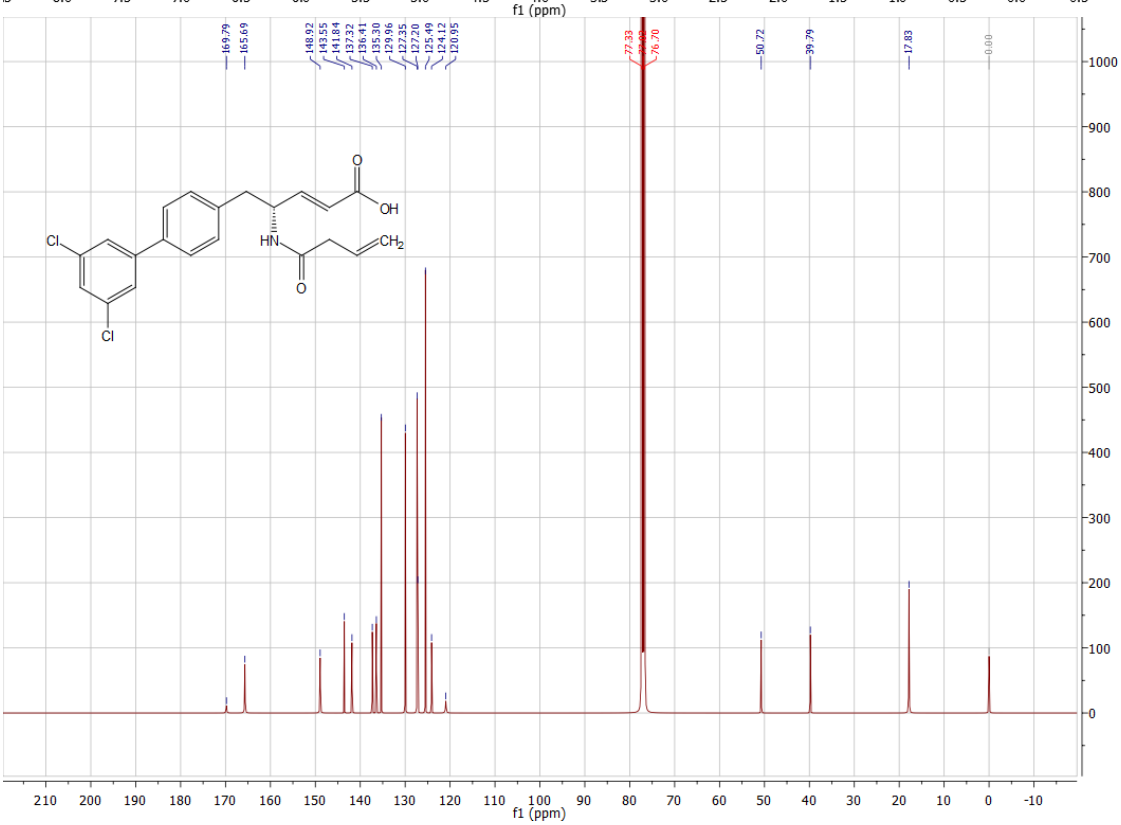
Compound **10** (CW5)



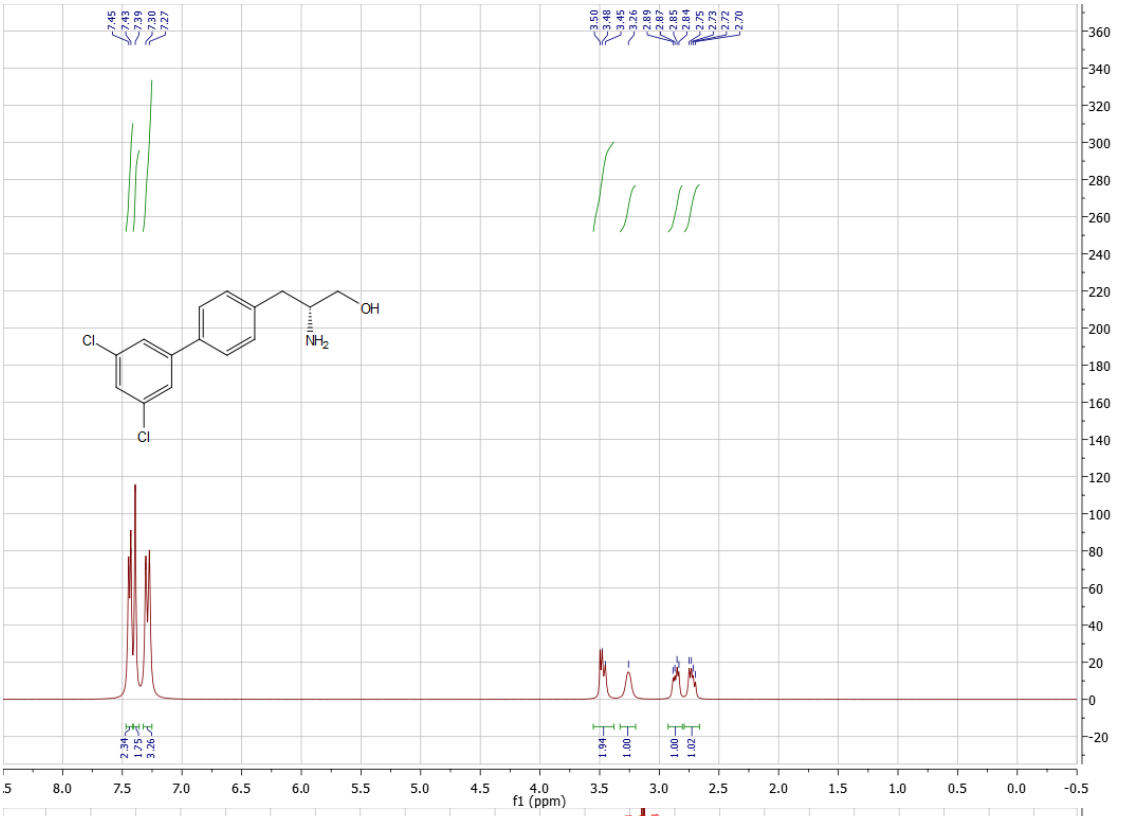


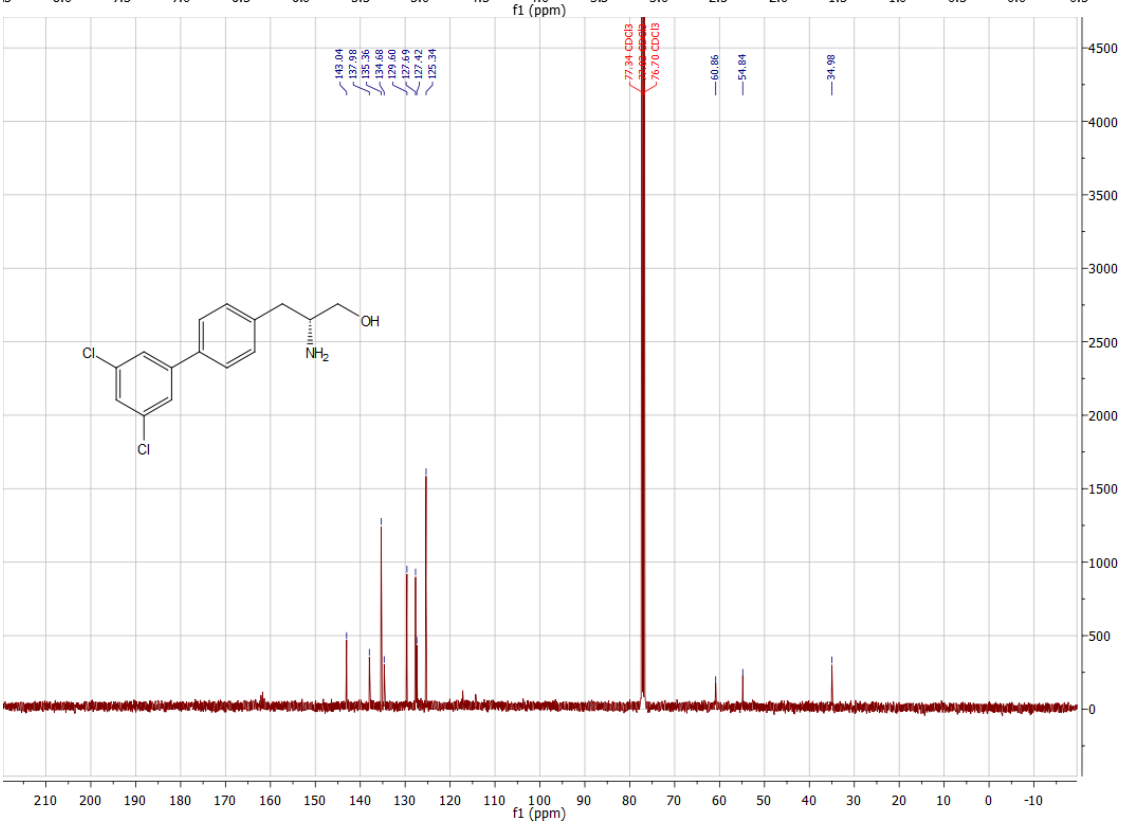
Compound **11 (**CW6)



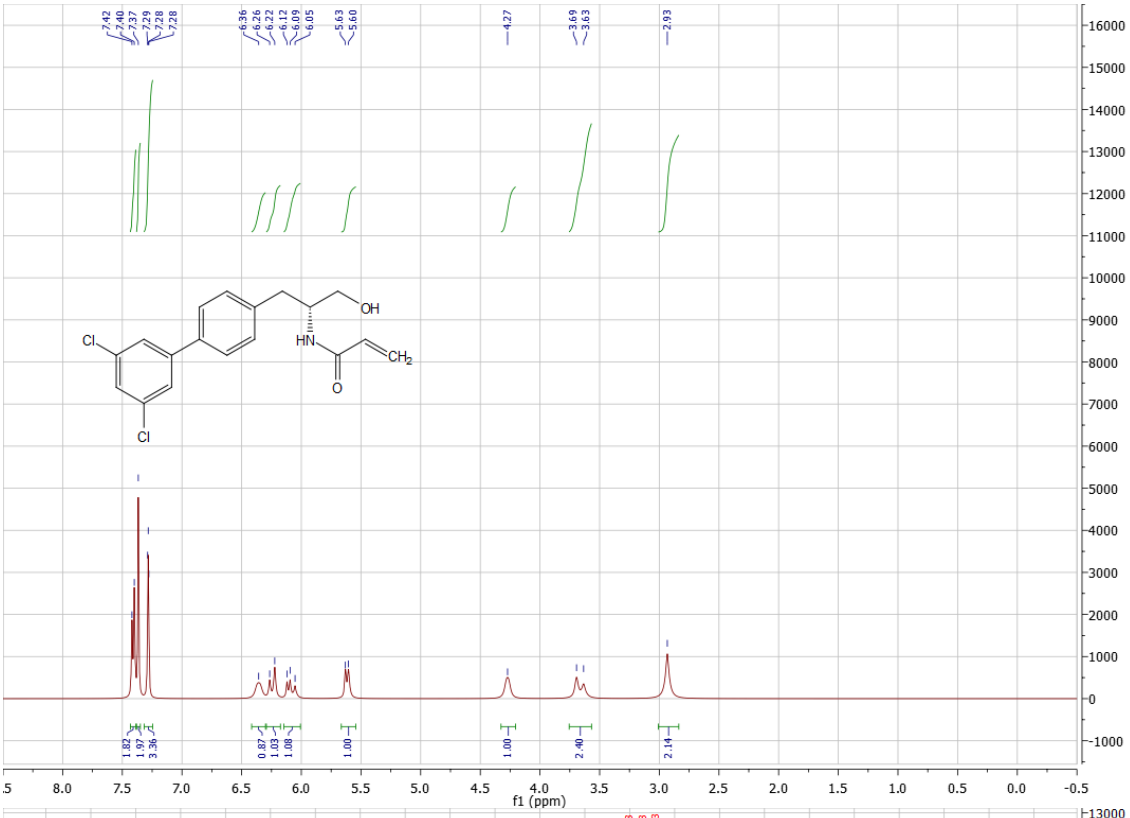


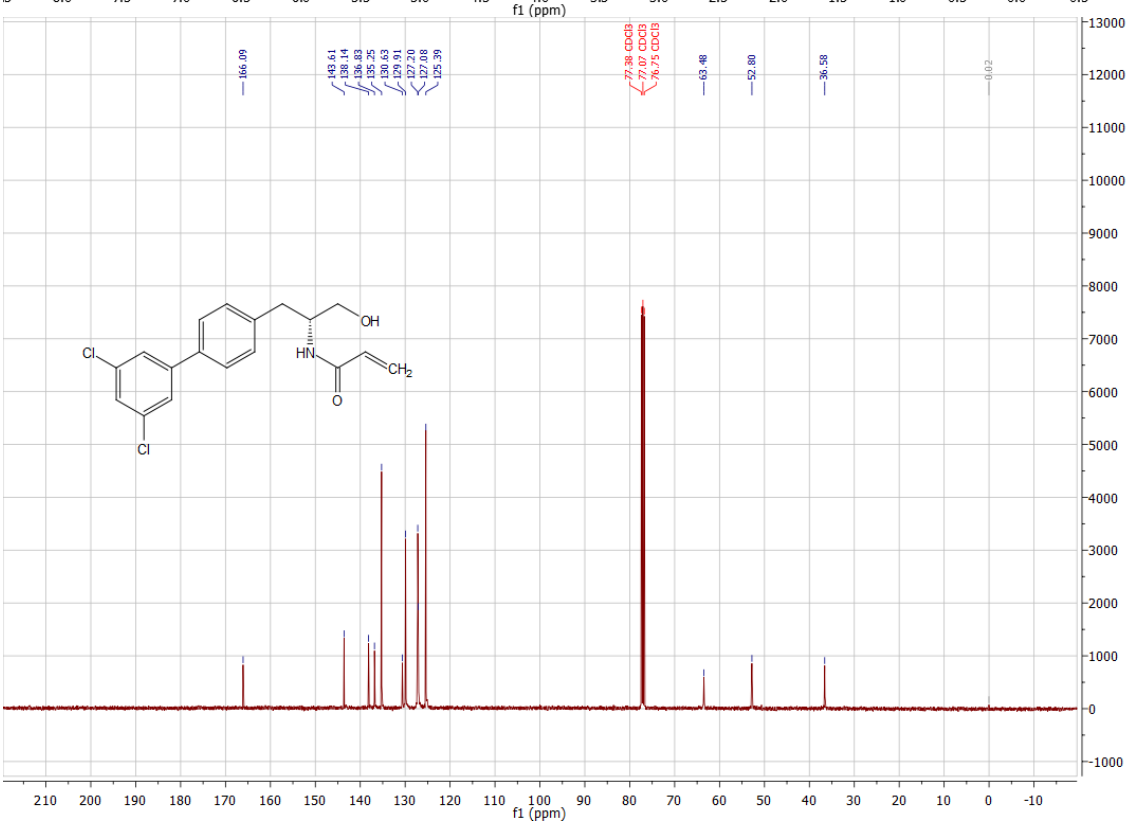
Compound **12**


7.45
7.43
7.39
7.30
7.27
3.50
3.48
3.45
3.26
2.89
2.87
2.85
2.84
2.75
2.73
2.72
2.70
OH
NH2
Cl
Cl
2.34
1.75
3.26
1.94
1.00
1.00
1.02
f1 (ppm)

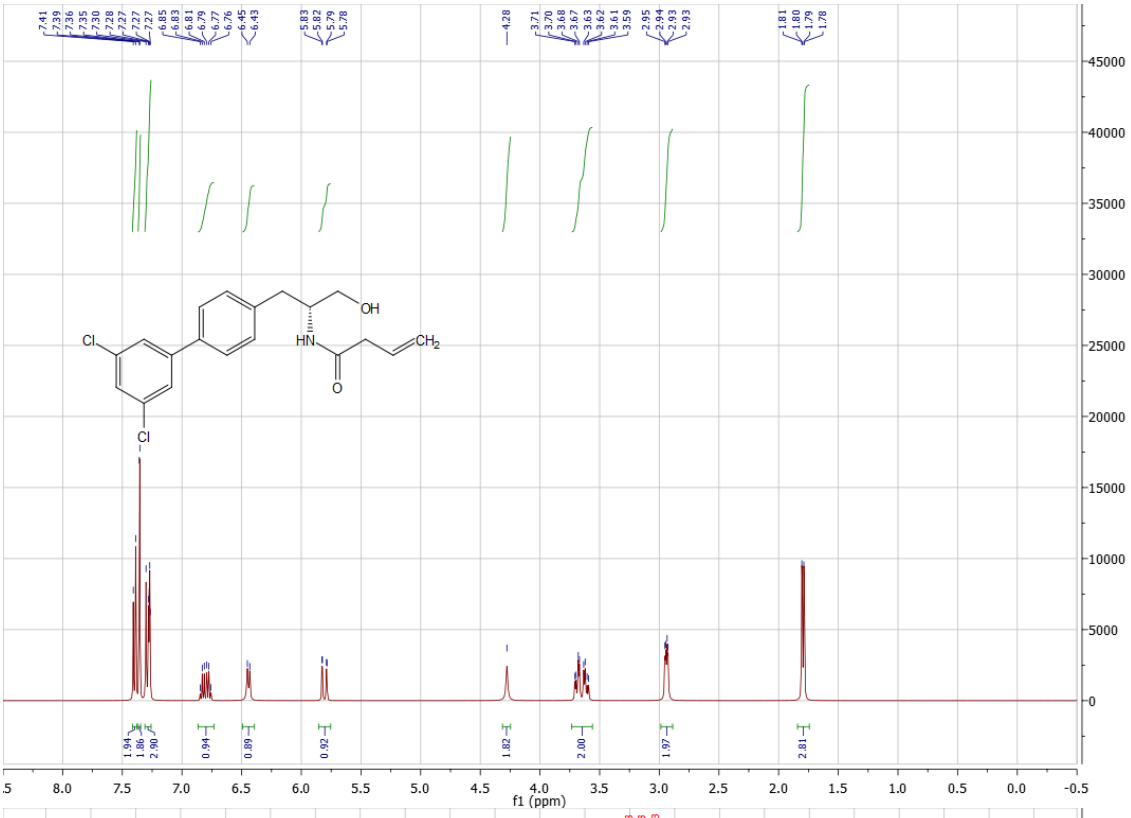

143.04
137.98
135.36
134.68
129.60
127.69
127.42
125.34
77.34 CDCl3
76.70 CDCl3
60.86
54.84
34.98
OH
NH2
Cl
Cl
f1 (ppm)

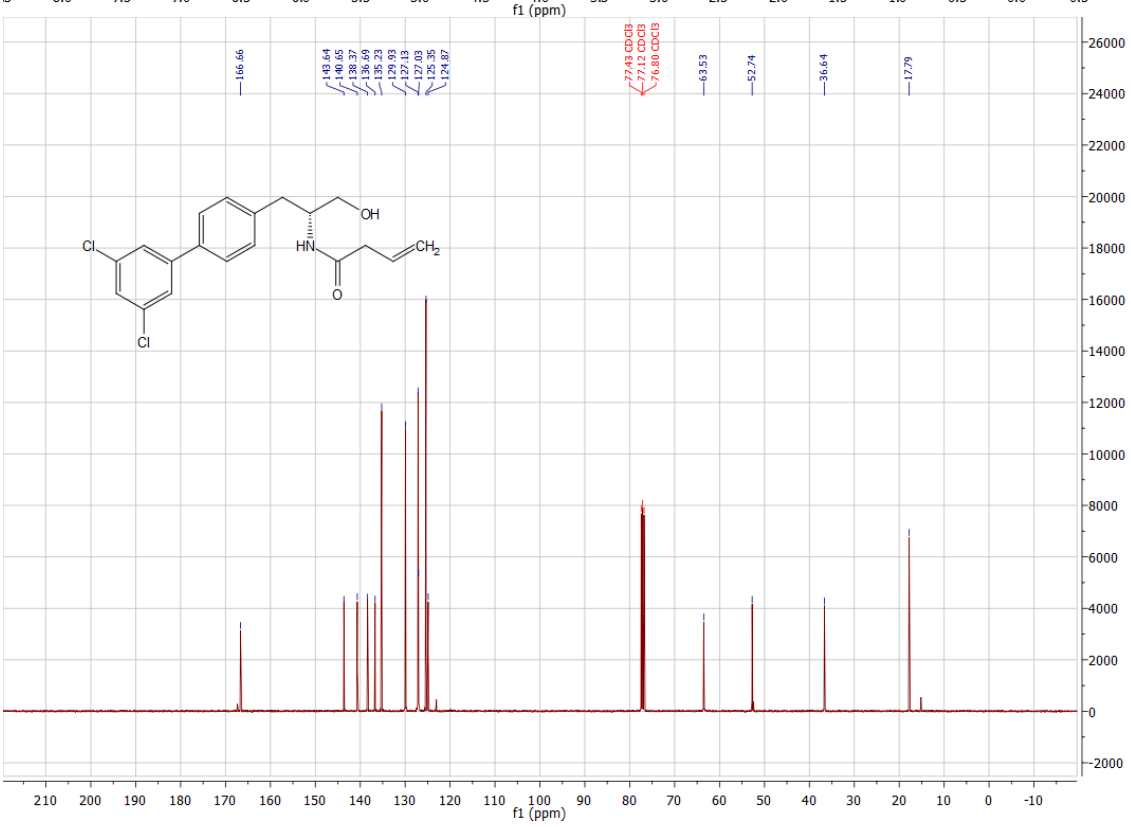
Compound **13** (CW1)



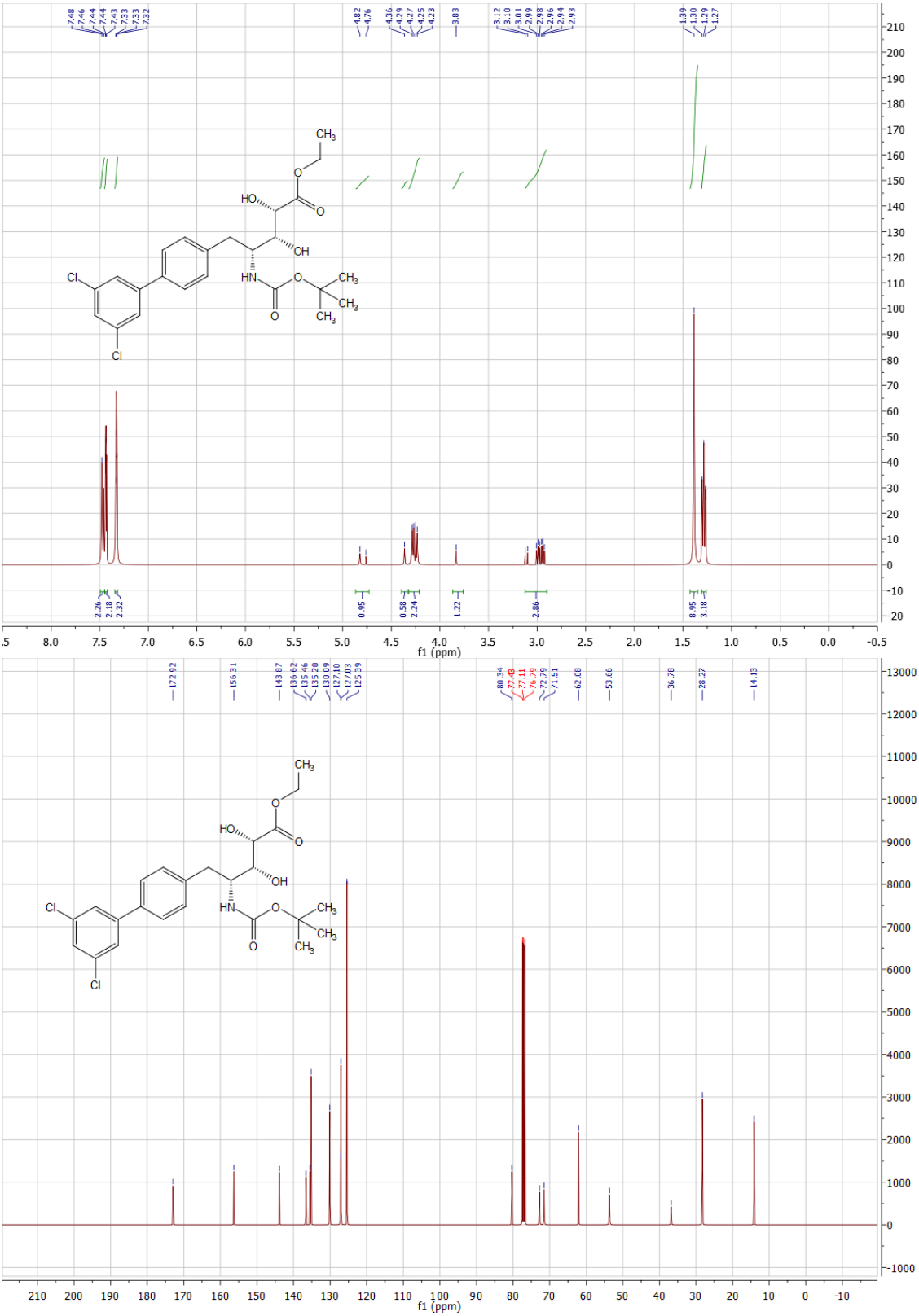


Compound **14** (CW2)

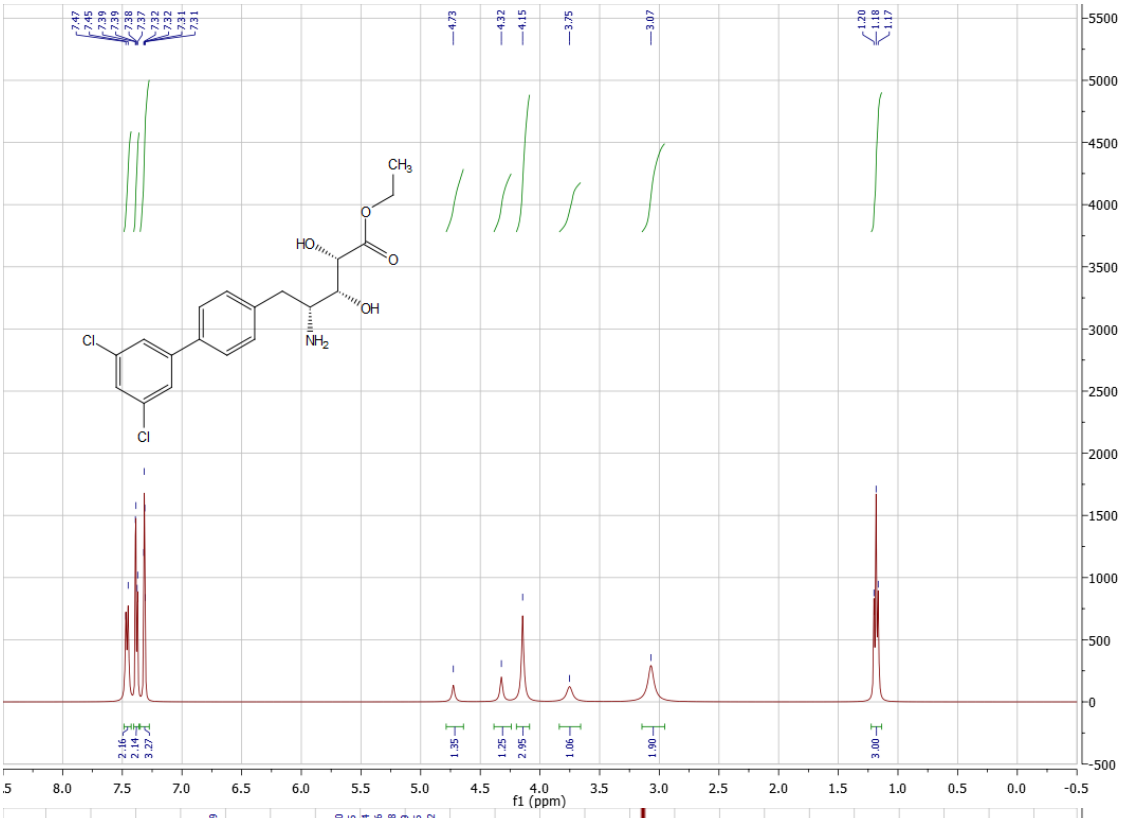


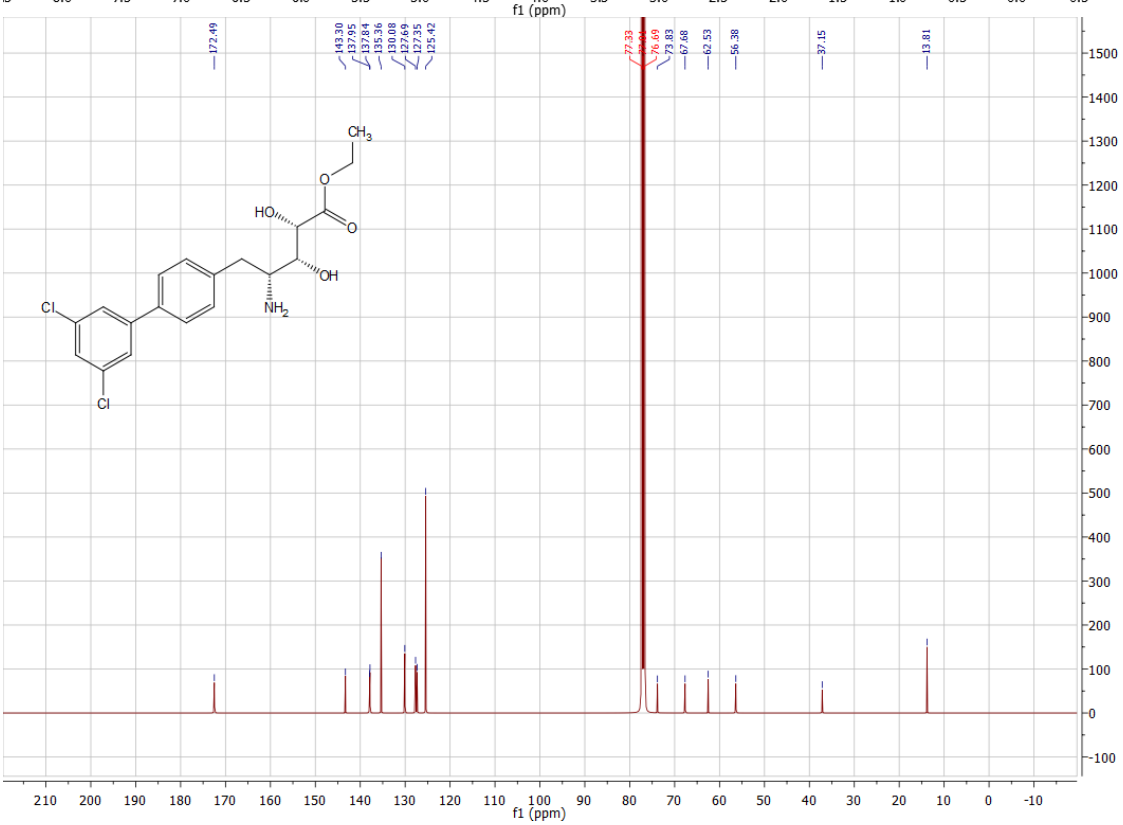


Compound **15**

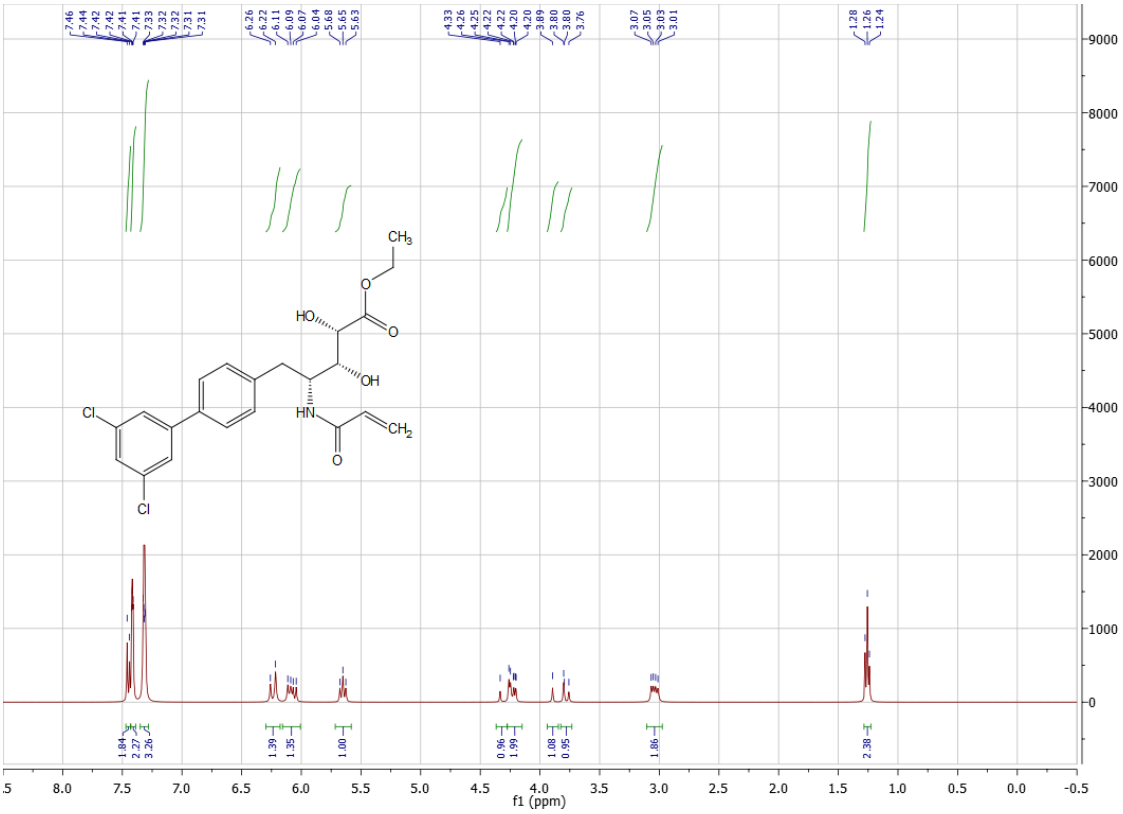

7.48
7.46
7.44
7.44
7.43
7.33
7.33
7.32
4.82
4.76
4.36
4.29
4.27
4.25
4.23
3.83
3.12
3.10
3.01
2.99
2.98
2.96
2.94
2.93
1.39
1.30
1.29
1.27
2.26
2.18
2.32
0.95
0.58
2.24
1.22
2.86
8.95
3.18
f1 (ppm)
172.92
156.31
143.87
136.62
135.46
135.20
130.09
127.10
127.03
125.89
80.34
77.43
77.11
76.79
72.79
71.51
62.08
53.66
36.78
28.27
14.13
f1 (ppm)

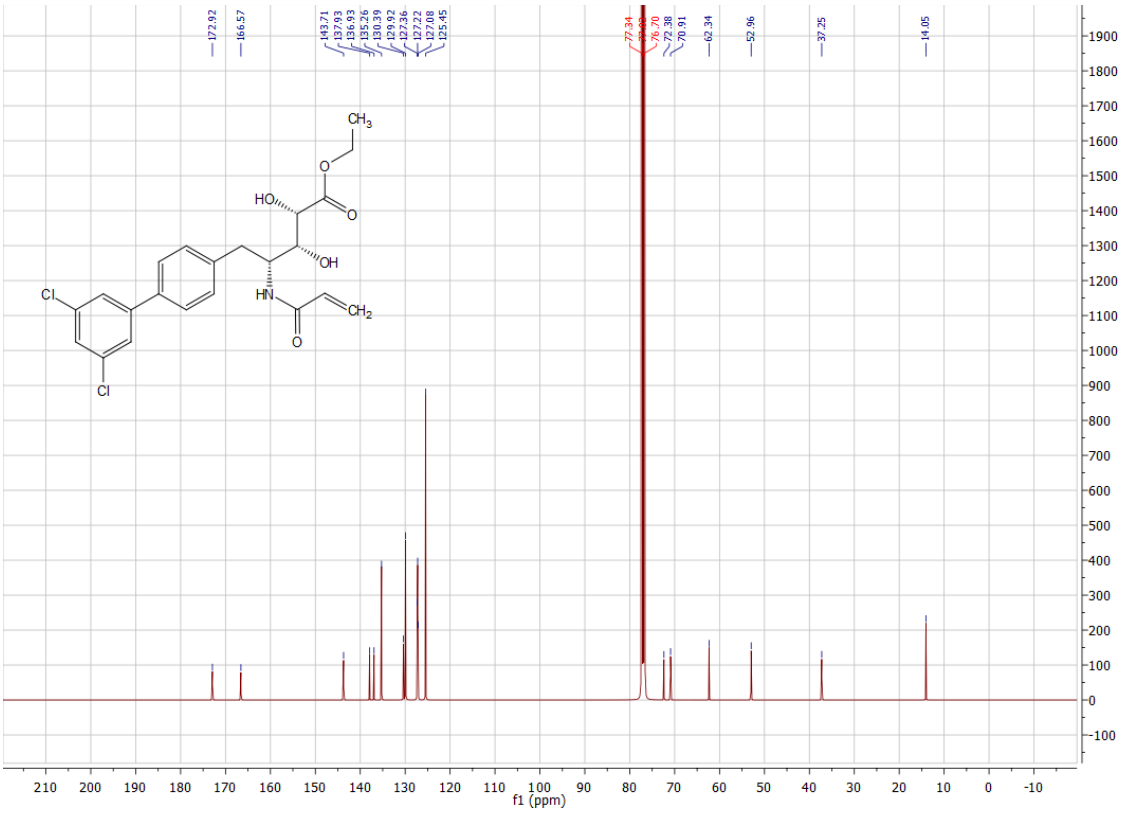
Compound **16**


7.47
7.45
7.39
7.39
7.38
7.37
7.32
7.32
7.31
7.31
4.73
4.32
4.15
3.75
3.07
1.20
1.18
1.17
CH3
O
HO
O
OH
NH2
Cl
Cl
2.16
2.14
3.27
1.35
1.25
2.95
1.06
1.90
3.00
f1 (ppm)

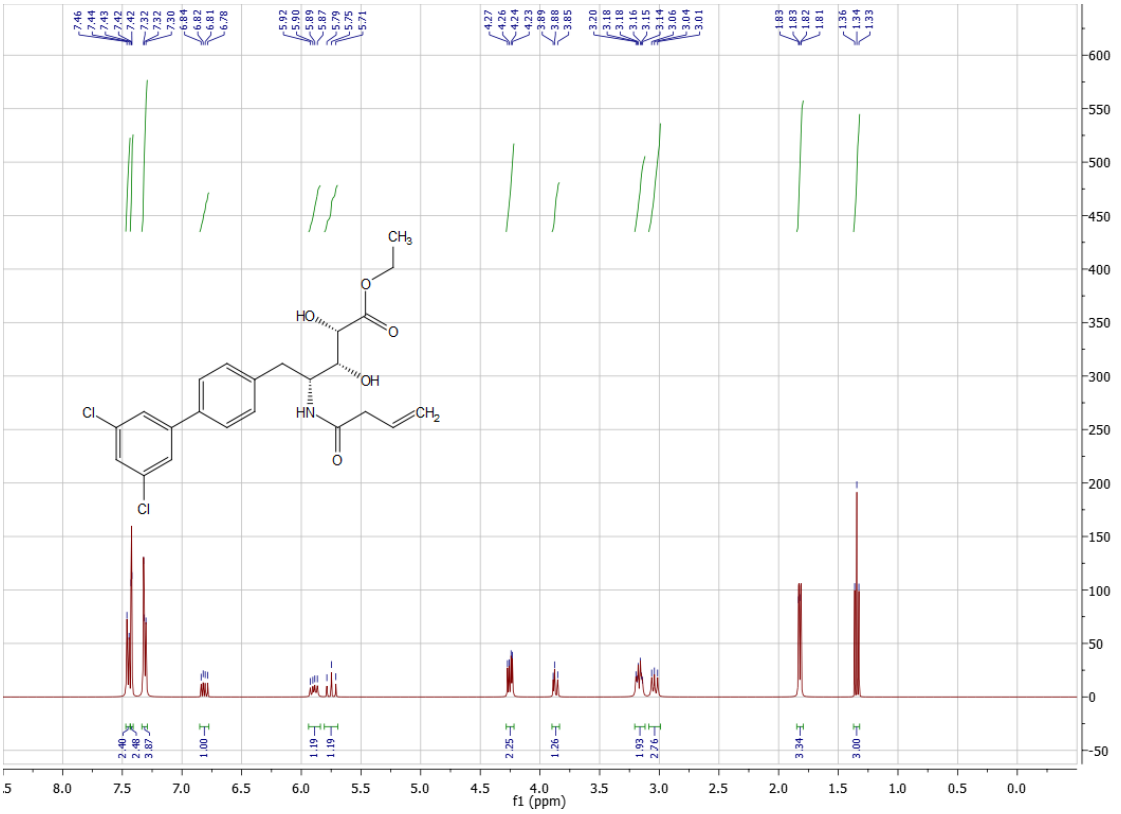

172.49
143.30
137.95
137.84
135.36
130.08
127.69
127.35
125.42
77.33
77.04
76.69
73.83
67.68
62.53
56.38
37.15
13.81
CH3
O
HO
O
OH
NH2
Cl
Cl
f1 (ppm)

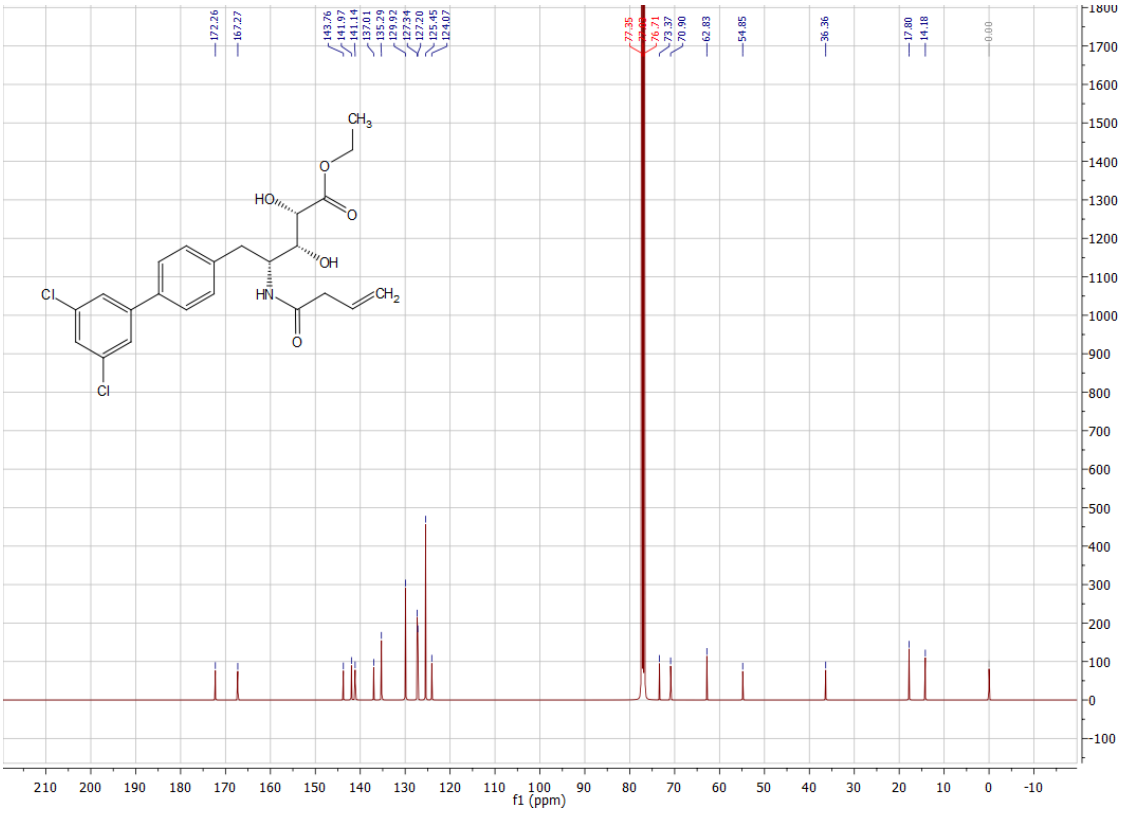
Compound **17** (CW7)



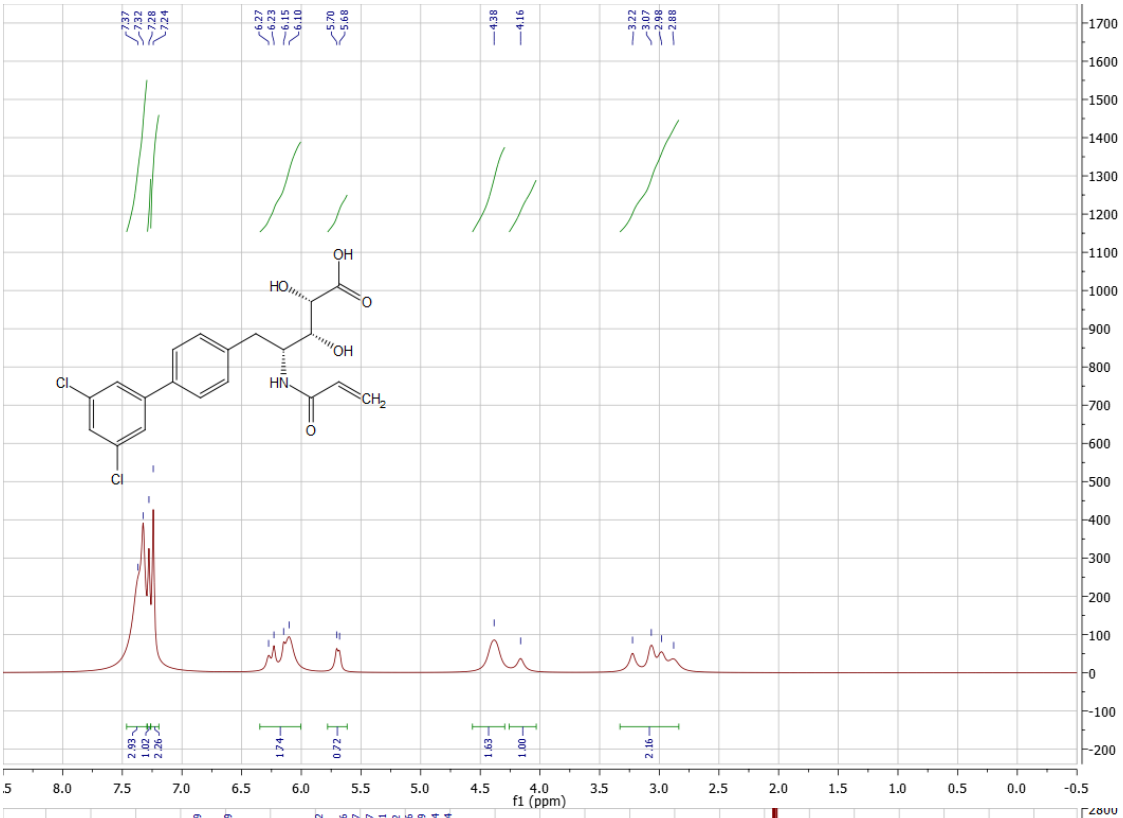


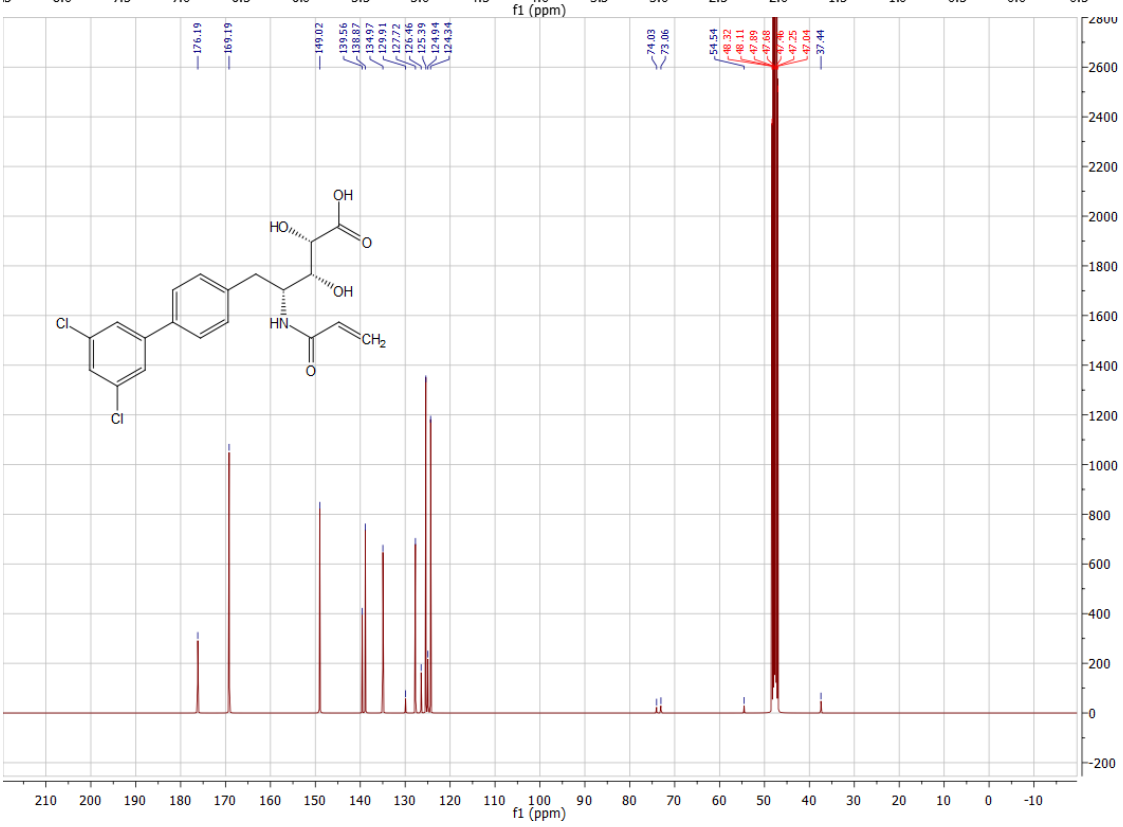
Compound **18** (CW8)



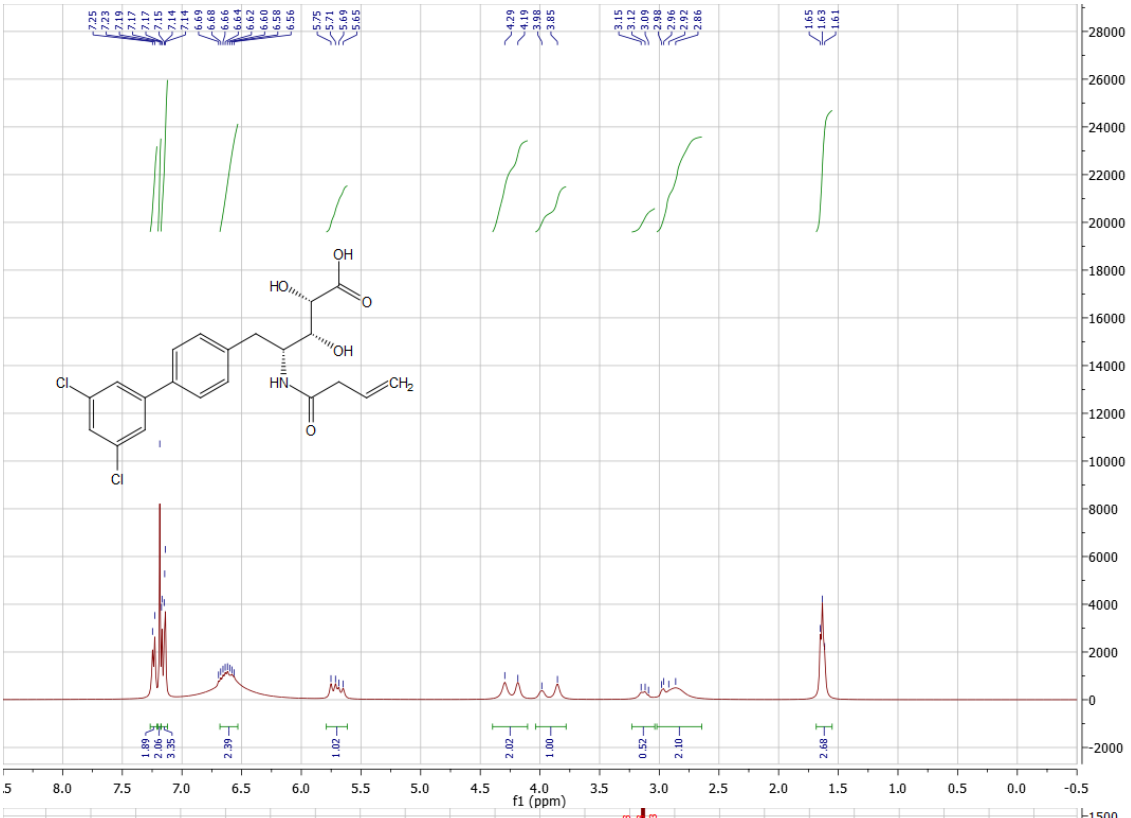


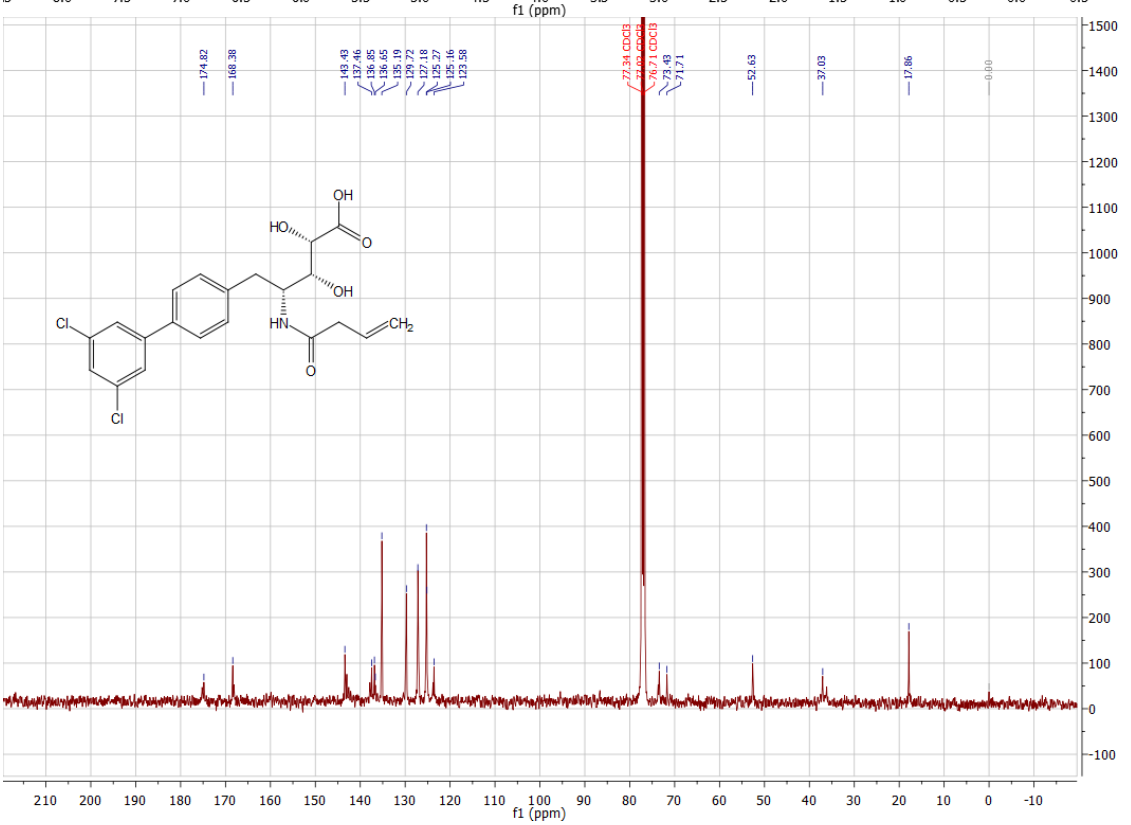
Compound **19** (CW9)



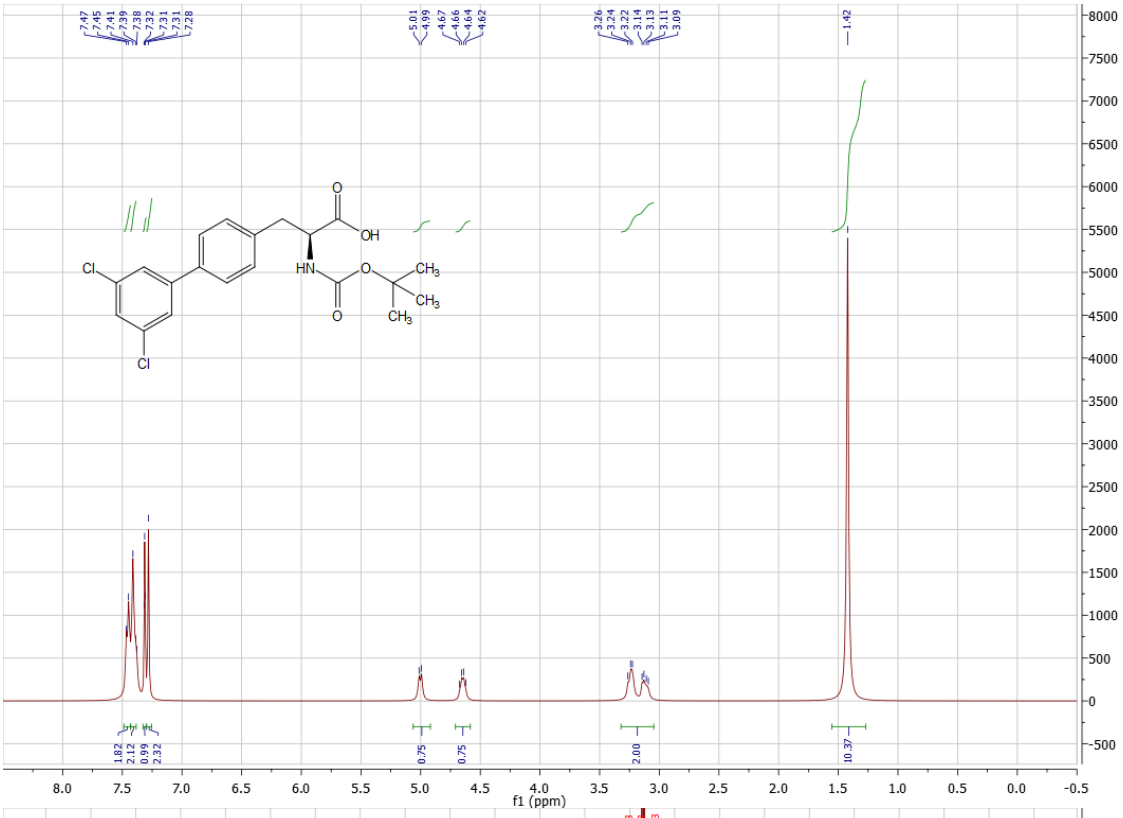


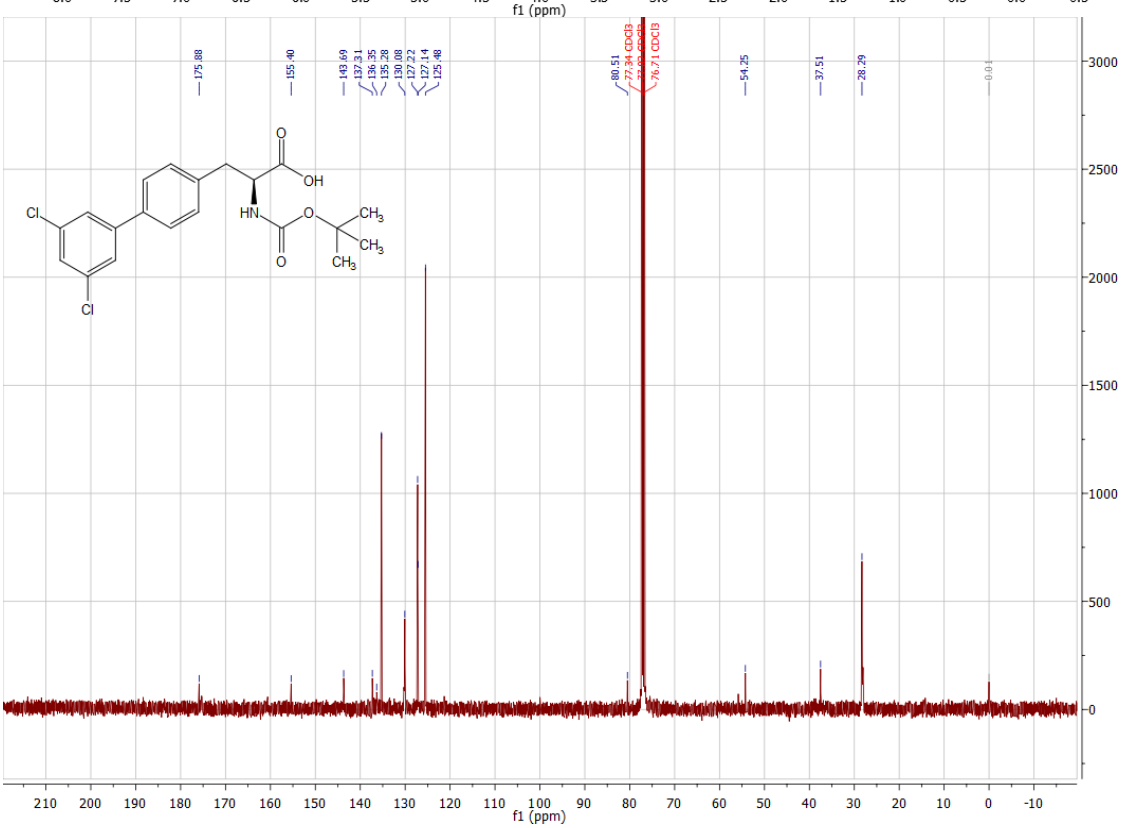
Compound **20** (CW10)



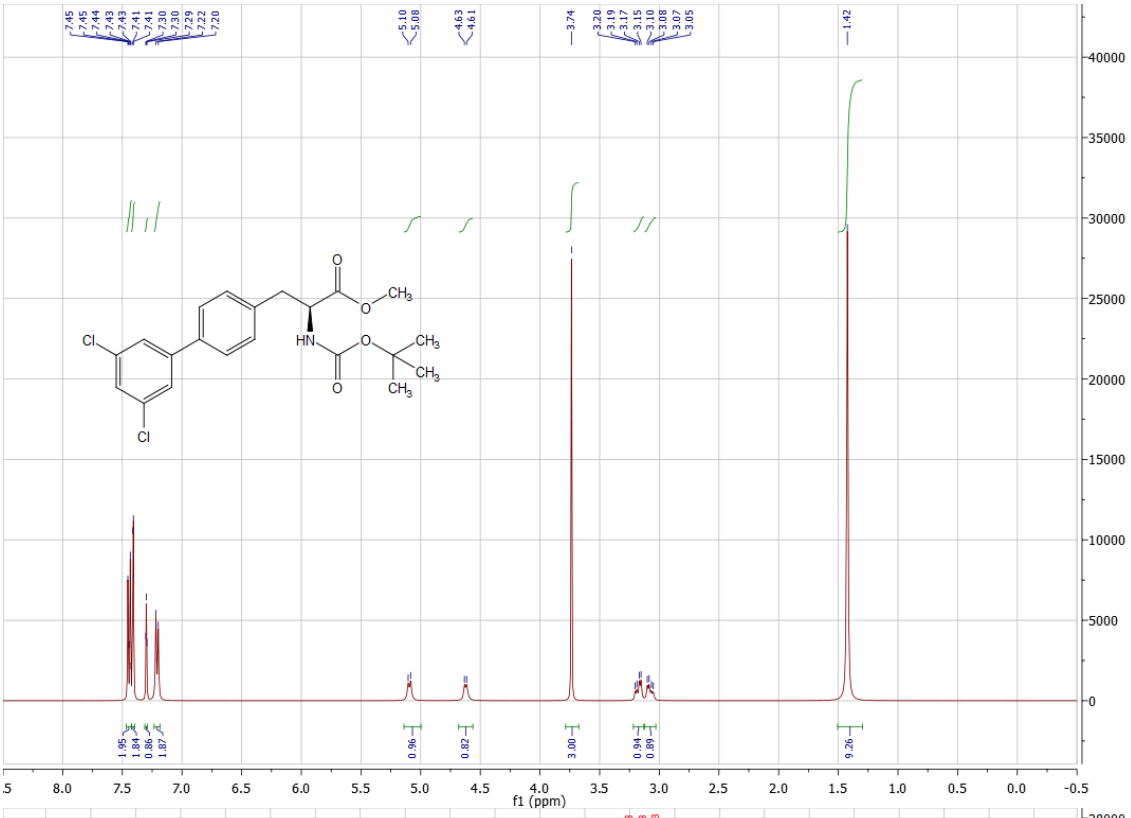


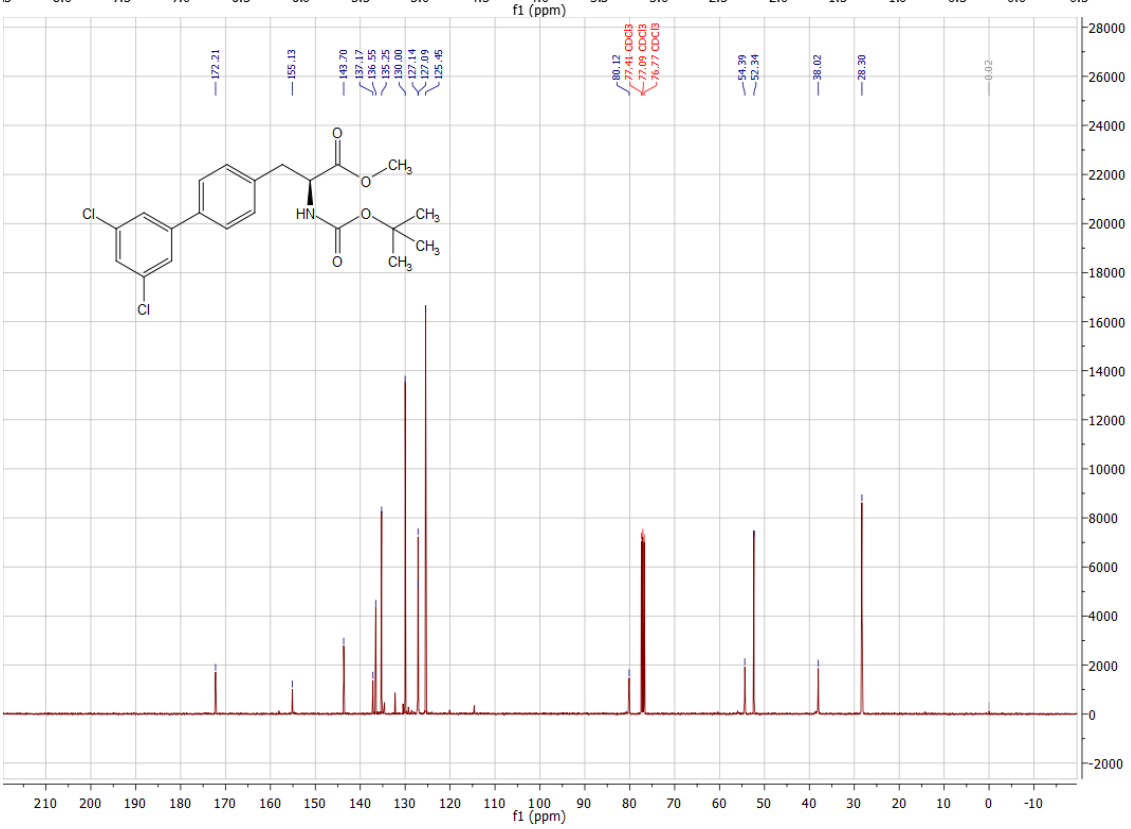
Compound **22**


7.47
7.45
7.41
7.39
7.38
7.32
7.31
7.31
7.31
7.28
5.01
4.99
4.67
4.66
4.64
4.62
3.26
3.24
3.22
3.14
3.13
3.11
3.09
1.42
Cl
Cl
O
OH
HN
O
O
CH3
CH3
CH3
1.82
2.12
0.99
2.32
0.75
0.75
2.00
10.37
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500

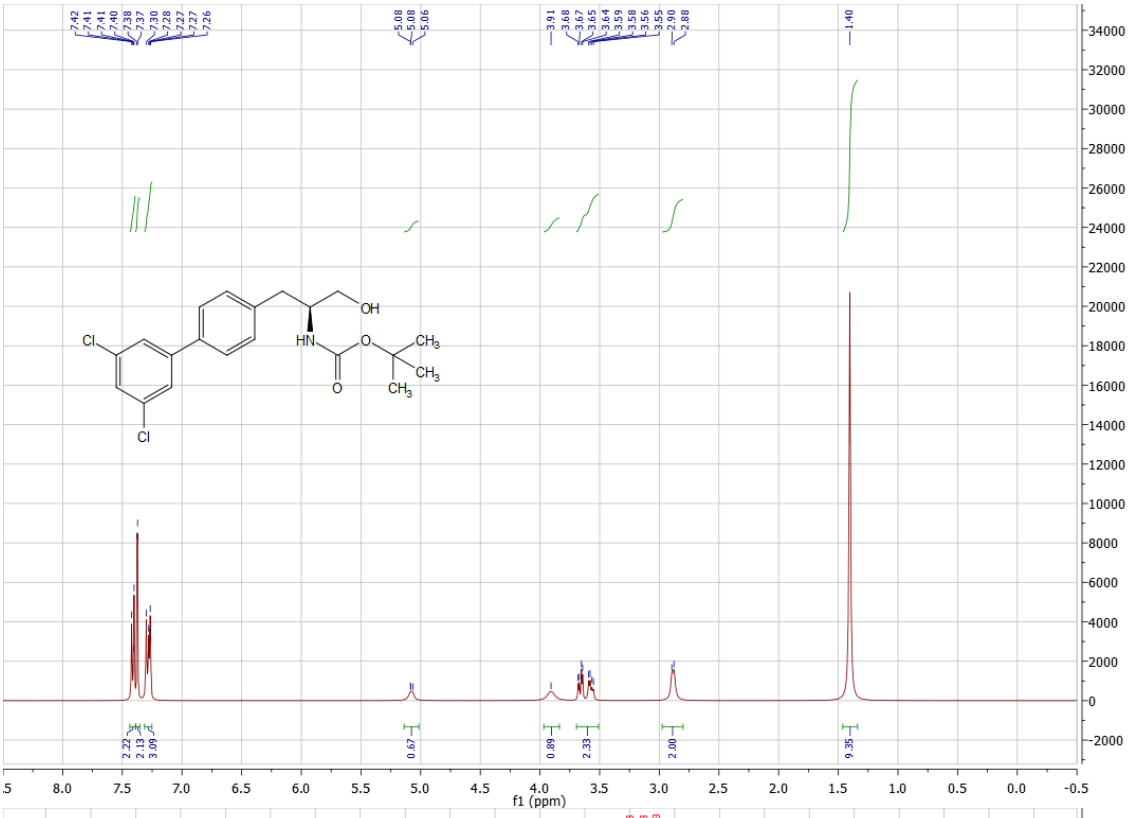

175.88
155.40
143.69
137.31
136.35
135.28
130.08
127.22
127.14
125.48
80.51
77.34 CDCl3
76.71 CDCl3
54.25
37.51
28.29
0.04
Cl
Cl
O
OH
HN
O
O
CH3
CH3
CH3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
3000
2500
2000
1500
1000
500
0

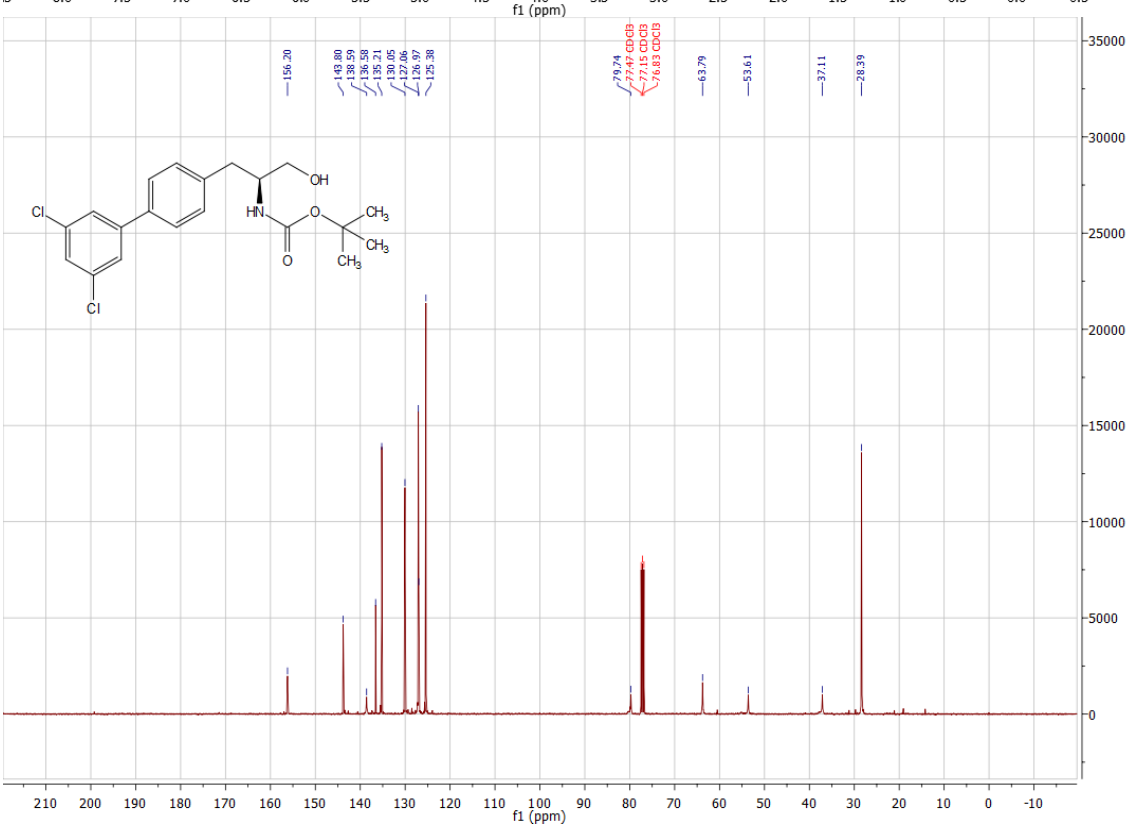
Compound **23**


7.45
7.45
7.44
7.43
7.43
7.41
7.41
7.30
7.30
7.29
7.22
7.20
5.10
5.08
4.63
4.61
3.74
3.20
3.19
3.17
3.15
3.10
3.08
3.07
3.05
1.42
1.95
1.84
0.86
1.87
0.96
0.82
3.00
0.94
0.89
9.26
f1 (ppm)


172.21
155.13
143.70
137.17
136.55
135.25
130.00
127.14
127.09
125.45
80.12
77.41 CDCl3
77.09 CDCl3
76.77 CDCl3
54.39
52.34
38.02
28.30
0.02
f1 (ppm)

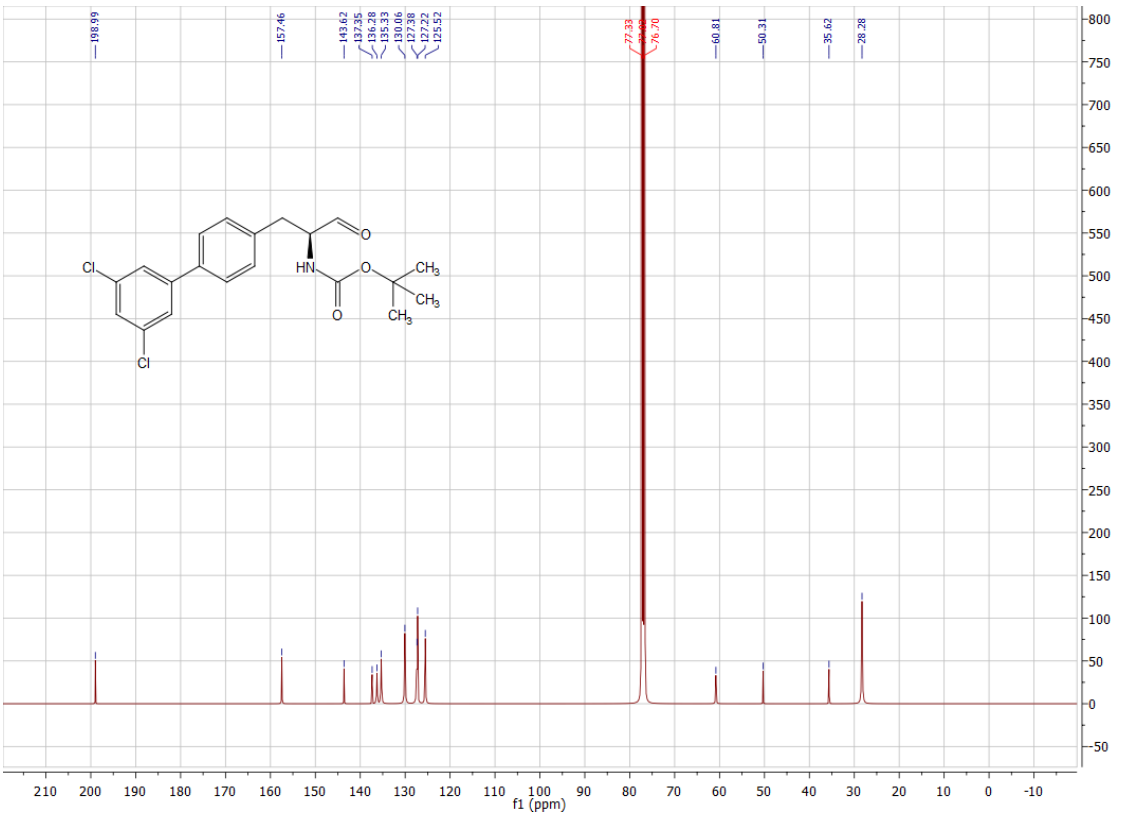
Compound **24**


7.42
7.41
7.41
7.40
7.38
7.37
7.30
7.28
7.27
7.27
7.26
5.08
5.08
5.06
3.91
3.68
3.67
3.65
3.64
3.59
3.58
3.56
3.55
2.90
2.88
1.40
OH
HN
O
O
CH3
CH3
CH3
Cl
Cl
2.22
2.13
3.09
0.67
0.89
2.33
2.00
9.35
f1 (ppm)

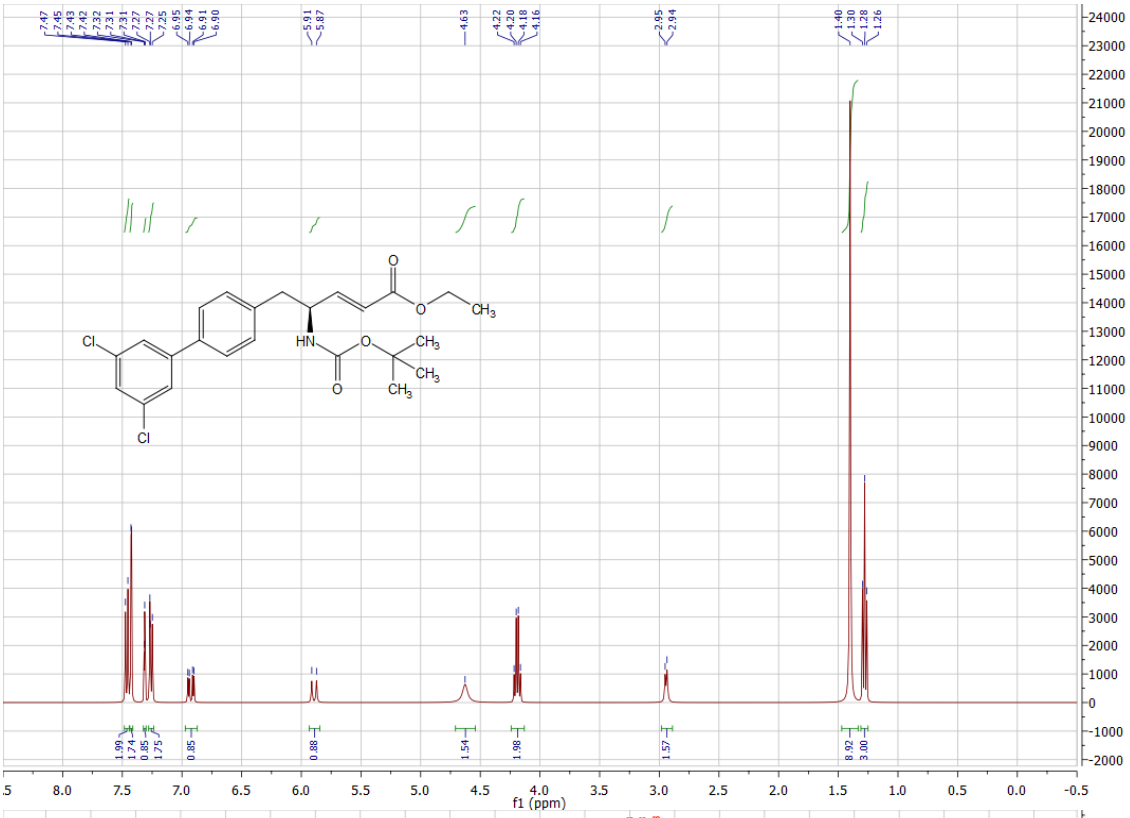

156.20
143.80
138.59
136.58
135.21
130.05
127.06
126.97
125.38
79.74
77.47 CDCl3
77.15 CDCl3
76.83 CDCl3
63.79
53.61
37.11
28.39
OH
HN
O
O
CH3
CH3
CH3
Cl
Cl
f1 (ppm)

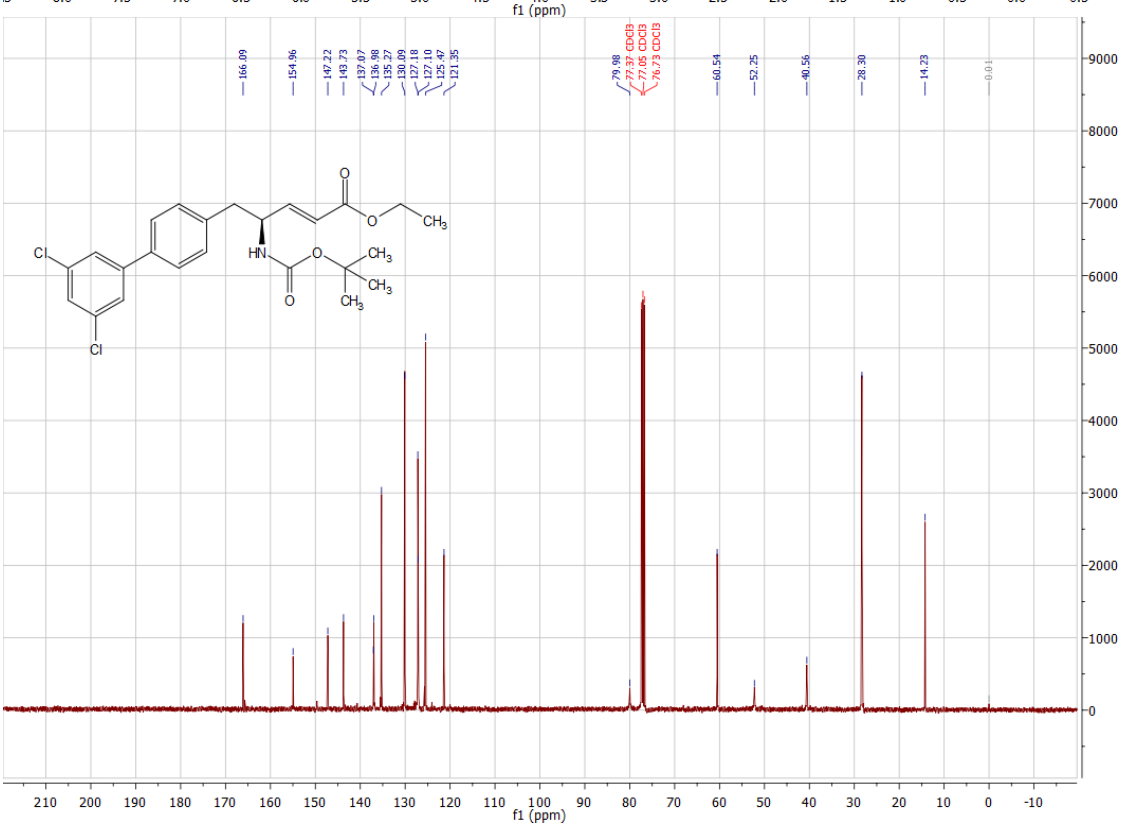
Compound **25**


7.49
7.47
7.44
7.43
7.34
7.33
7.33
7.27
7.26
5.09
5.07
4.48
4.46
3.19
3.17
3.16
1.44
Cl
HN
O
O
O
CH3
CH3
CH3
Cl
2.50
2.36
1.30
2.21
1.00
0.96
1.88
8.59
f1 (ppm)

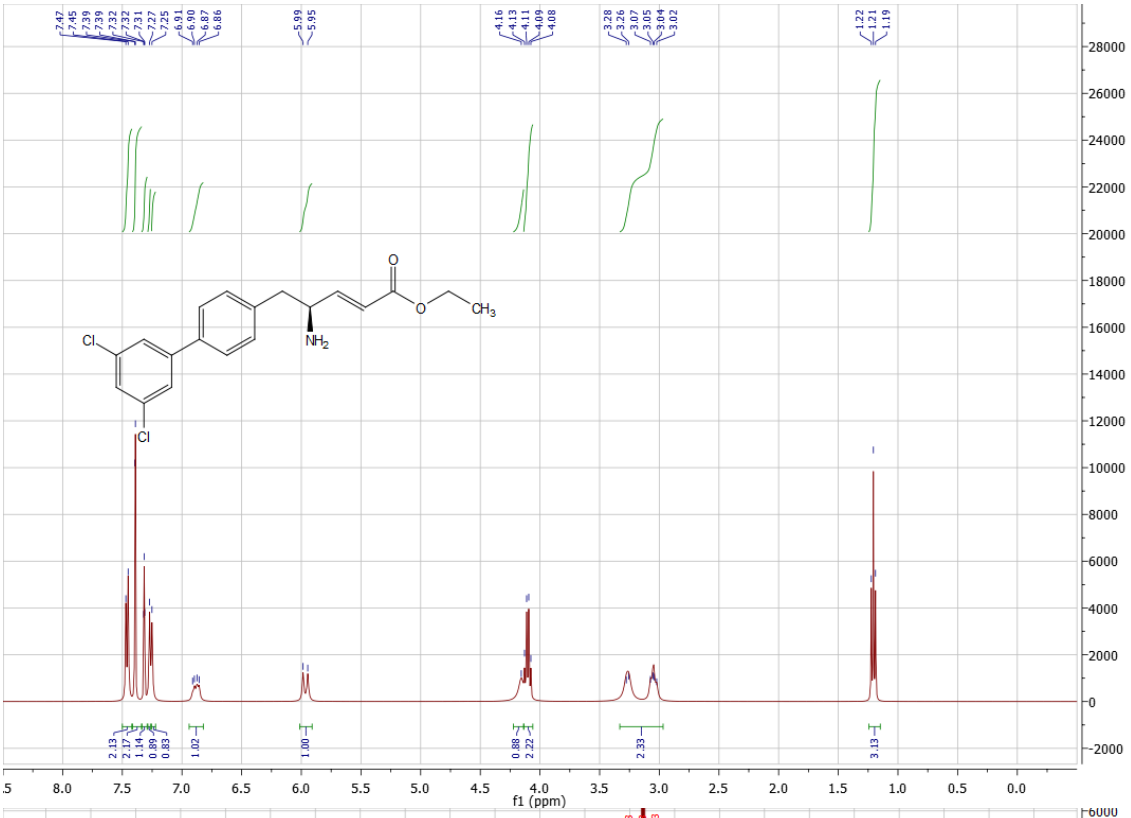

198.99
157.46
143.62
137.35
136.28
135.33
130.06
127.38
127.22
125.52
77.33
77.08
76.70
60.81
50.31
35.62
28.28
Cl
HN
O
O
O
CH3
CH3
CH3
Cl
f1 (ppm)

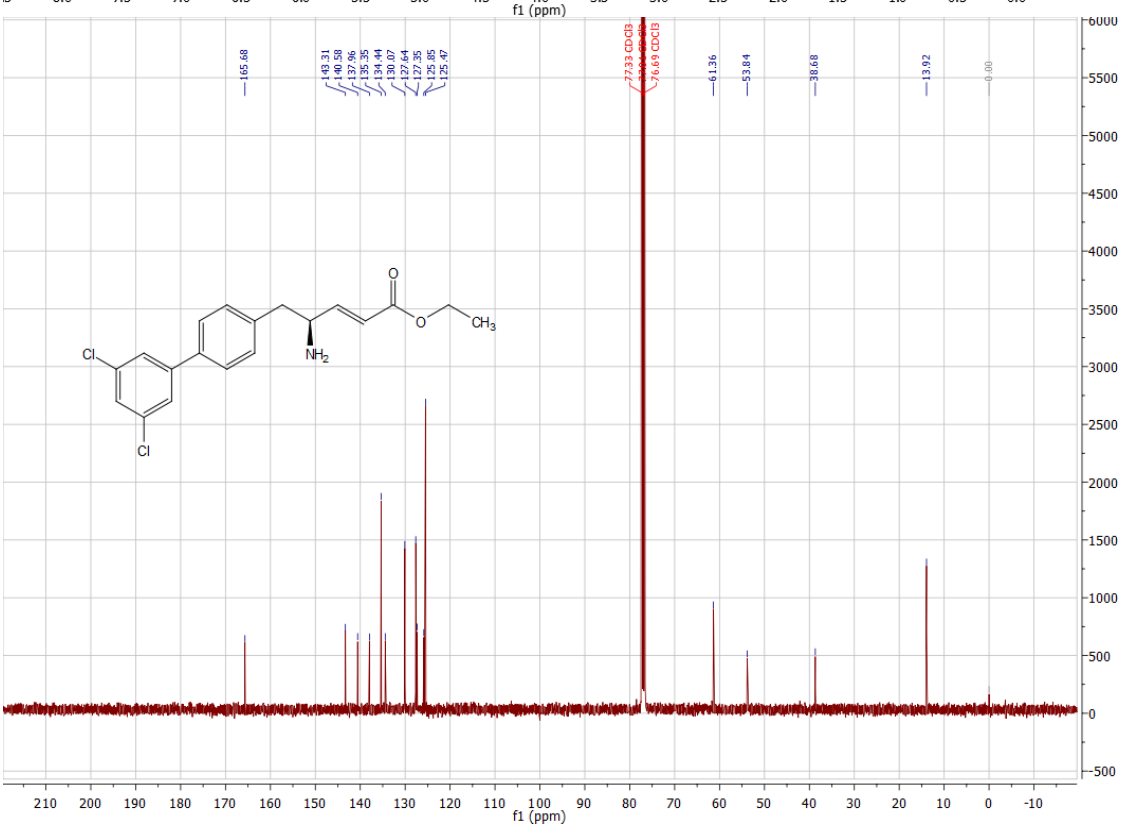
Compound **26**


7.47
7.45
7.43
7.42
7.32
7.31
7.31
7.27
7.27
7.25
6.95
6.94
6.91
6.90
5.91
5.87
4.63
4.22
4.20
4.18
4.16
2.95
2.94
1.40
1.30
1.28
1.26
Cl
HN
O
CH3
Cl
1.99
1.74
0.85
1.75
0.85
0.88
1.54
1.98
1.57
8.92
3.00
f1 (ppm)

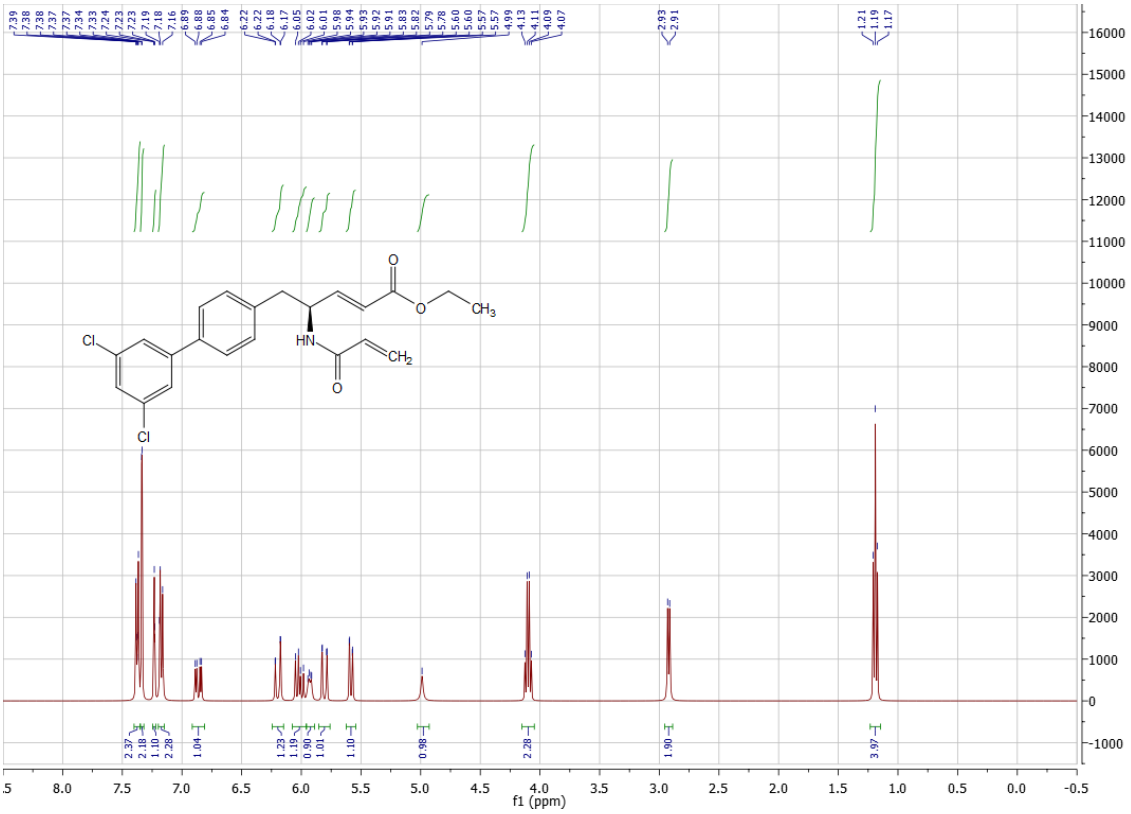

166.09
154.96
147.22
143.73
137.67
136.88
135.27
130.09
127.18
127.10
125.47
121.35
79.98
77.37 CDCl3
77.05 CDCl3
76.73 CDCl3
60.54
52.25
40.56
28.30
14.23
Cl
HN
O
CH3
f1 (ppm)

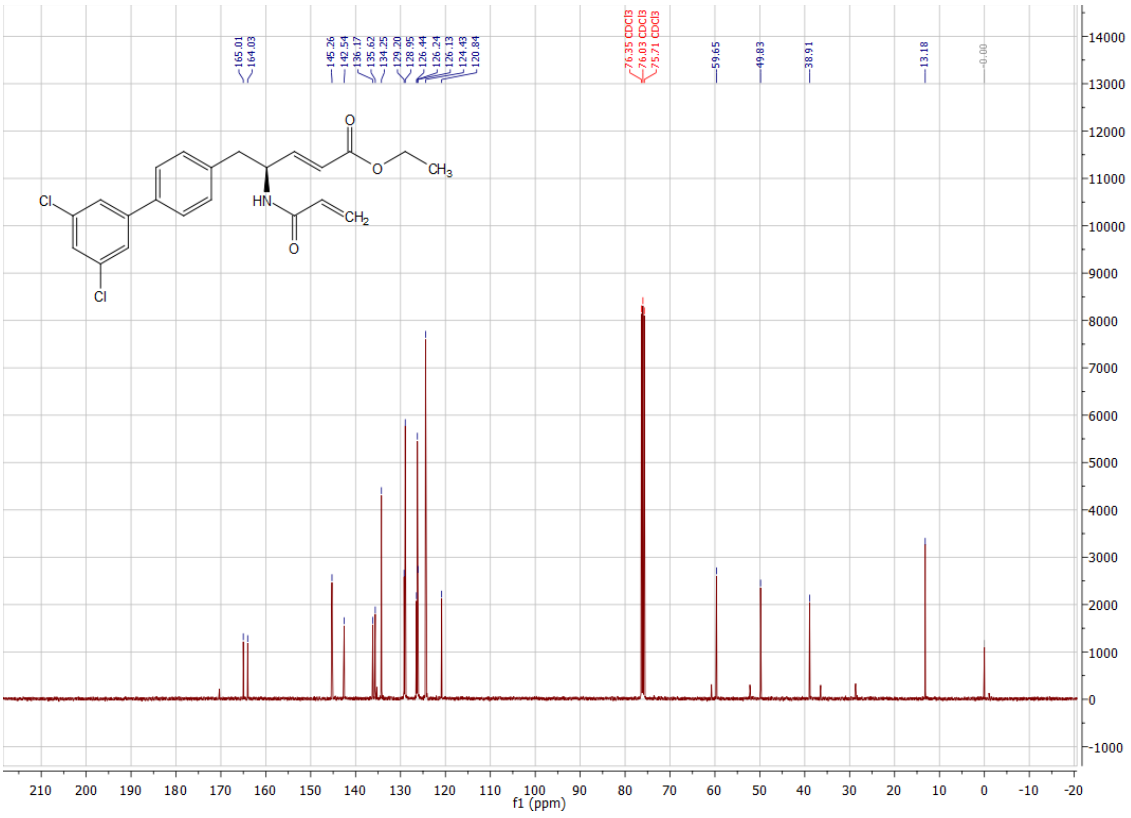
Compound **27**


7.47
7.45
7.39
7.39
7.32
7.32
7.31
7.27
7.25
6.91
6.90
6.87
6.86
5.99
5.95
4.16
4.13
4.11
4.09
4.08
3.28
3.26
3.07
3.05
3.04
3.02
1.22
1.21
1.19
Cl
O
O
CH3
NH2
Cl
2.13
2.17
1.14
0.89
0.83
1.02
1.00
0.88
2.22
2.33
3.13
f1 (ppm)

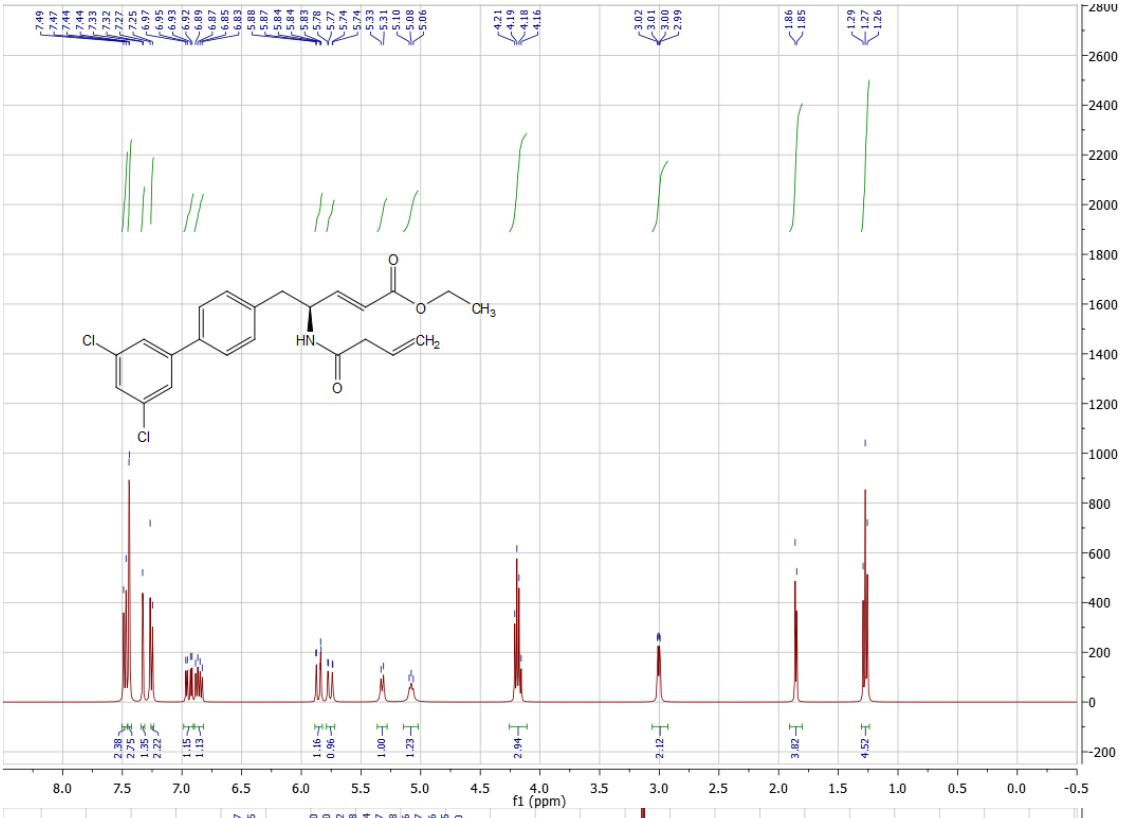

165.68
143.31
140.58
137.96
135.35
134.44
130.07
127.64
127.35
125.85
125.47
77.33 CDCl3
76.69 CDCl3
61.36
53.84
38.68
13.92
0.00
Cl
O
O
CH3
NH2
Cl
f1 (ppm)

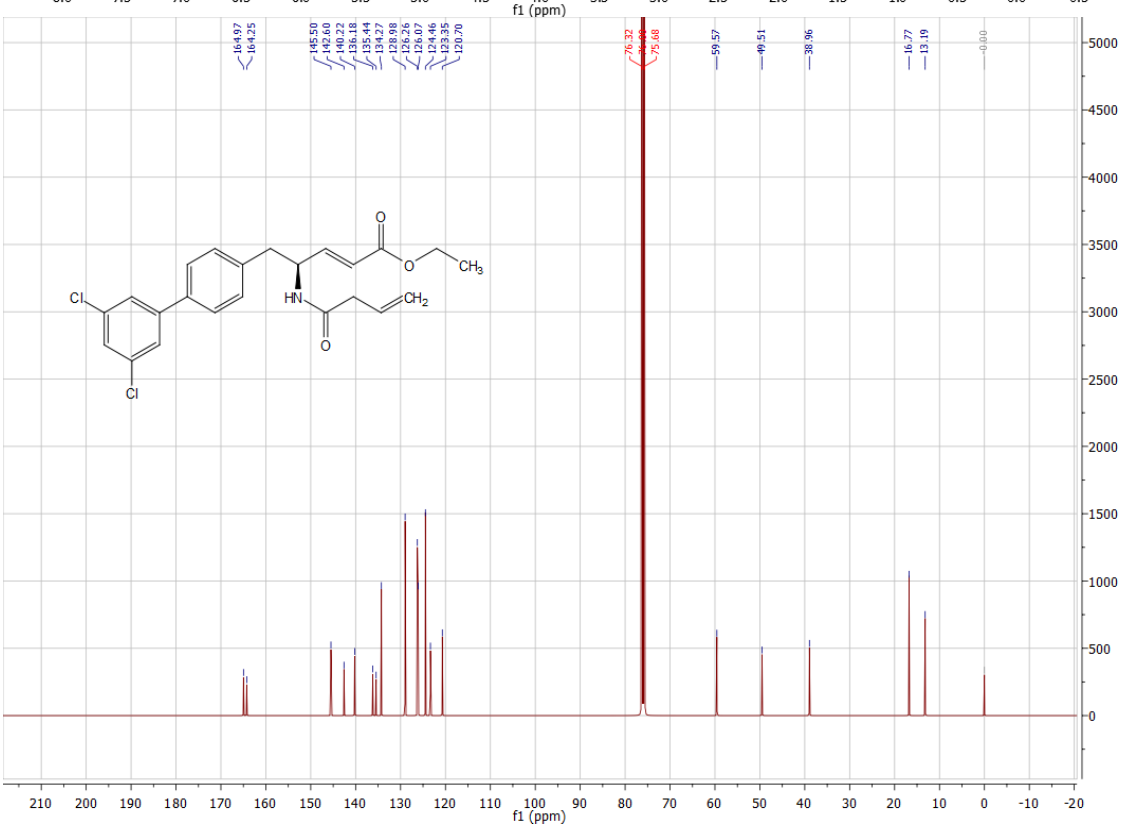
Compound **28** (CW13)



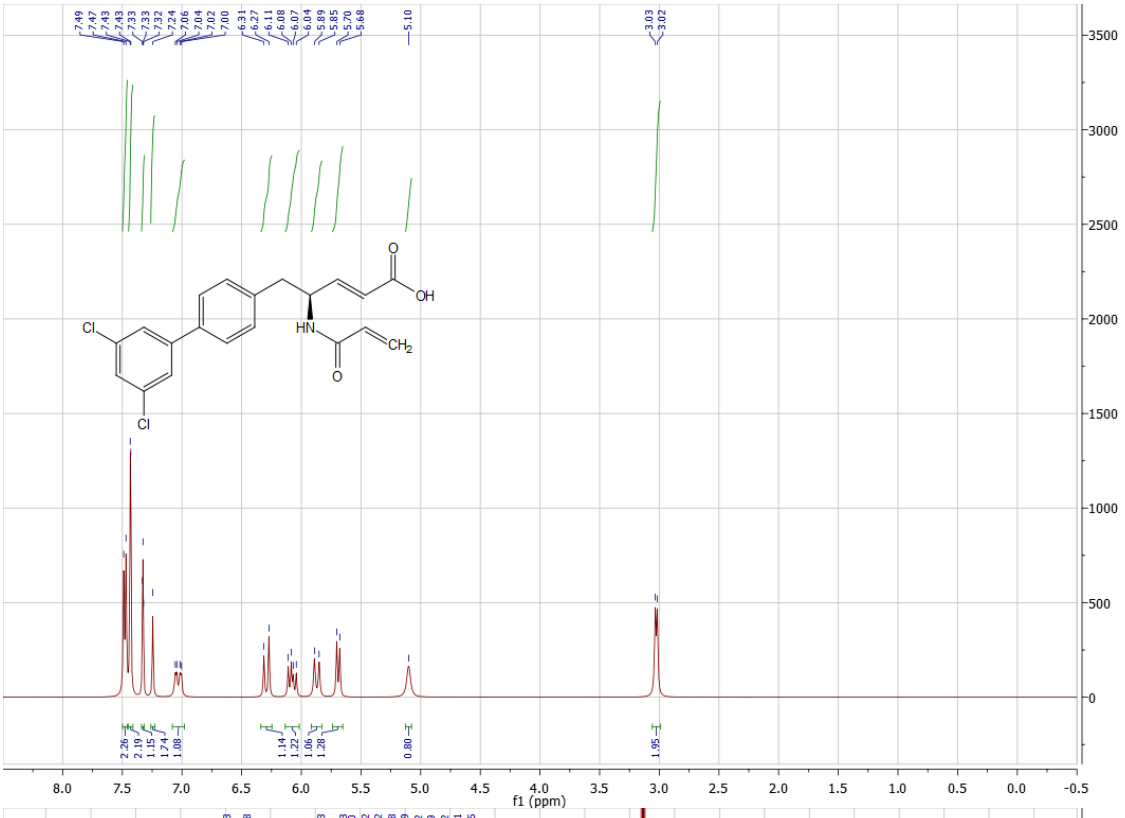


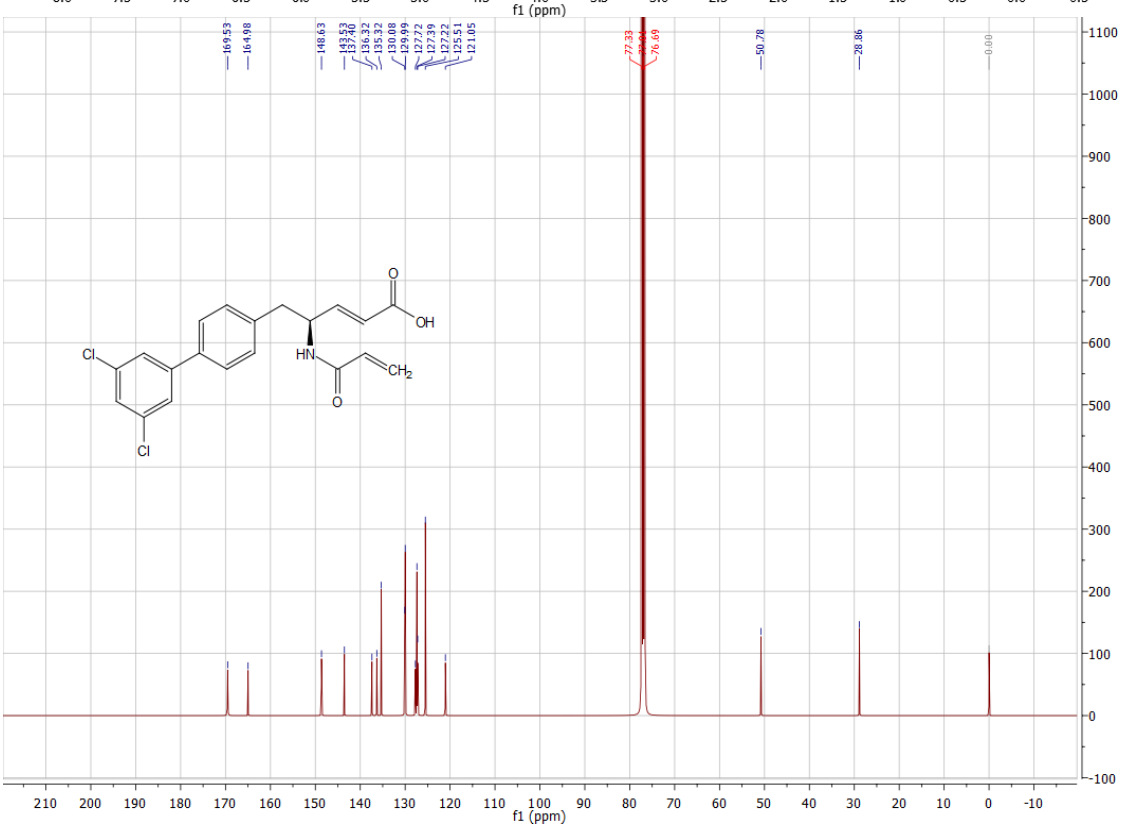
Compound **29** (CW14)



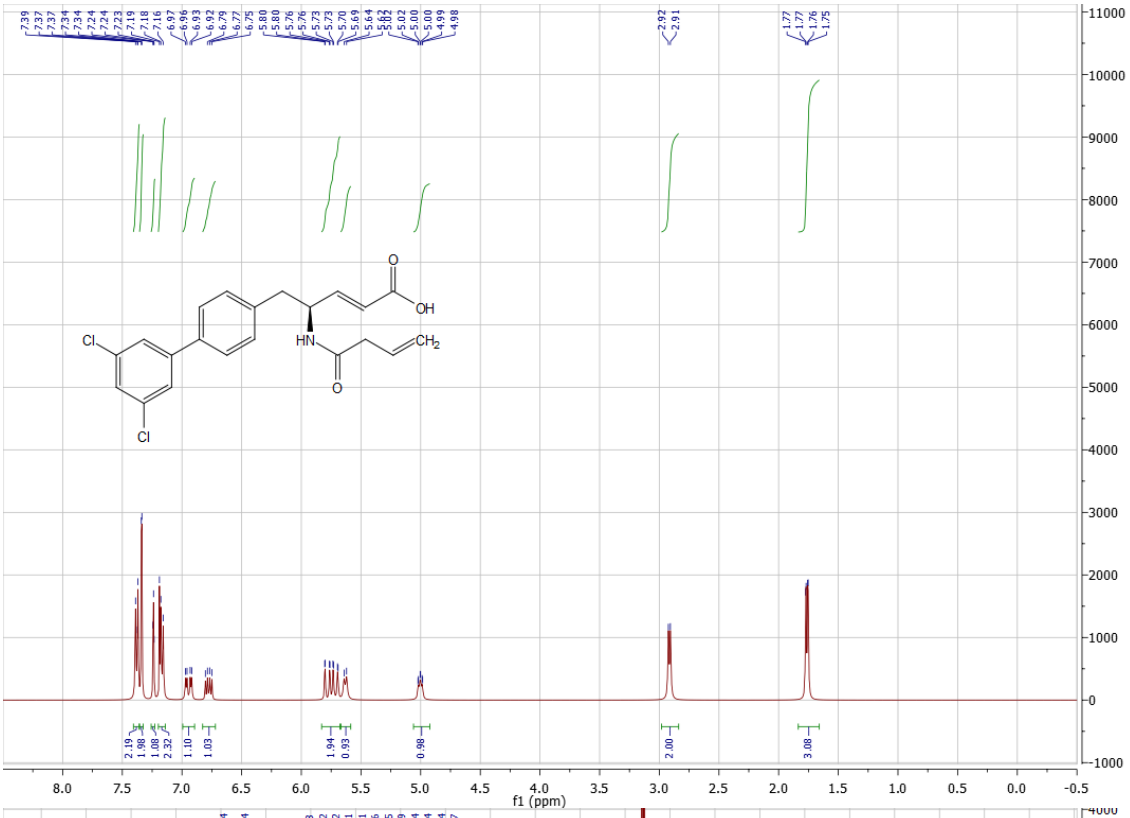


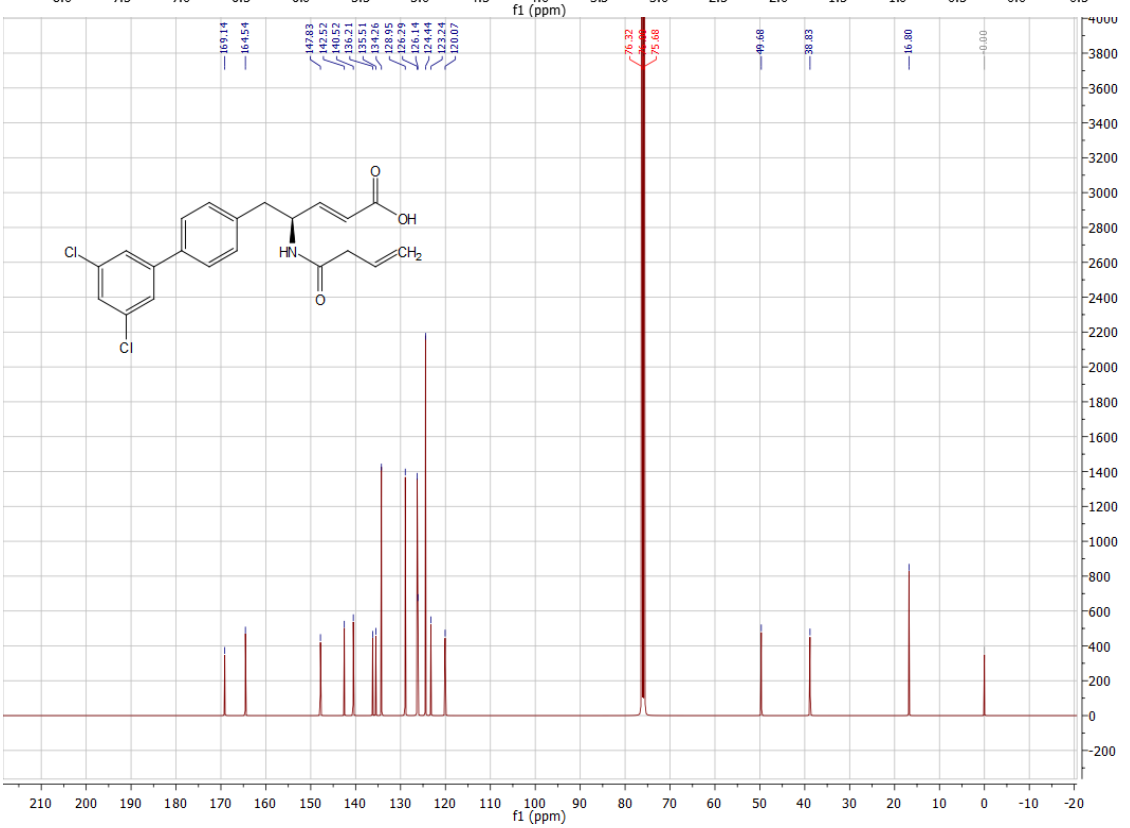
Compound **30** (CW15)



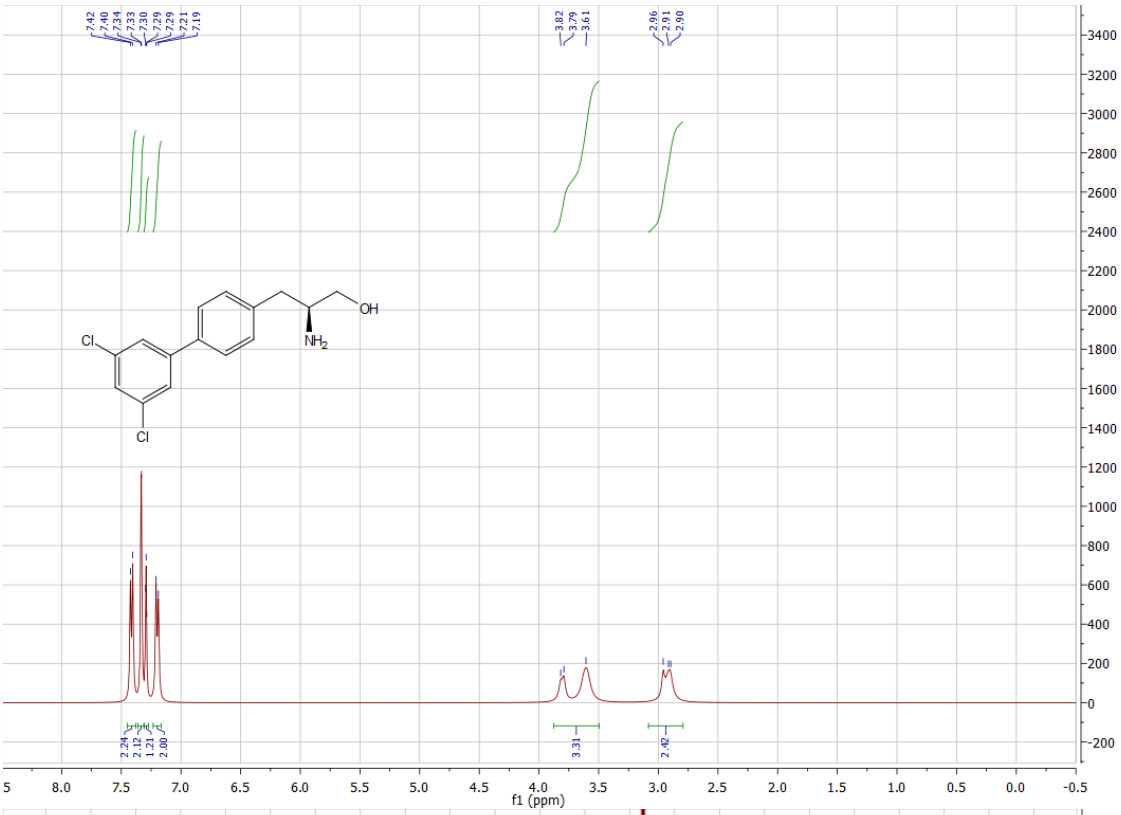


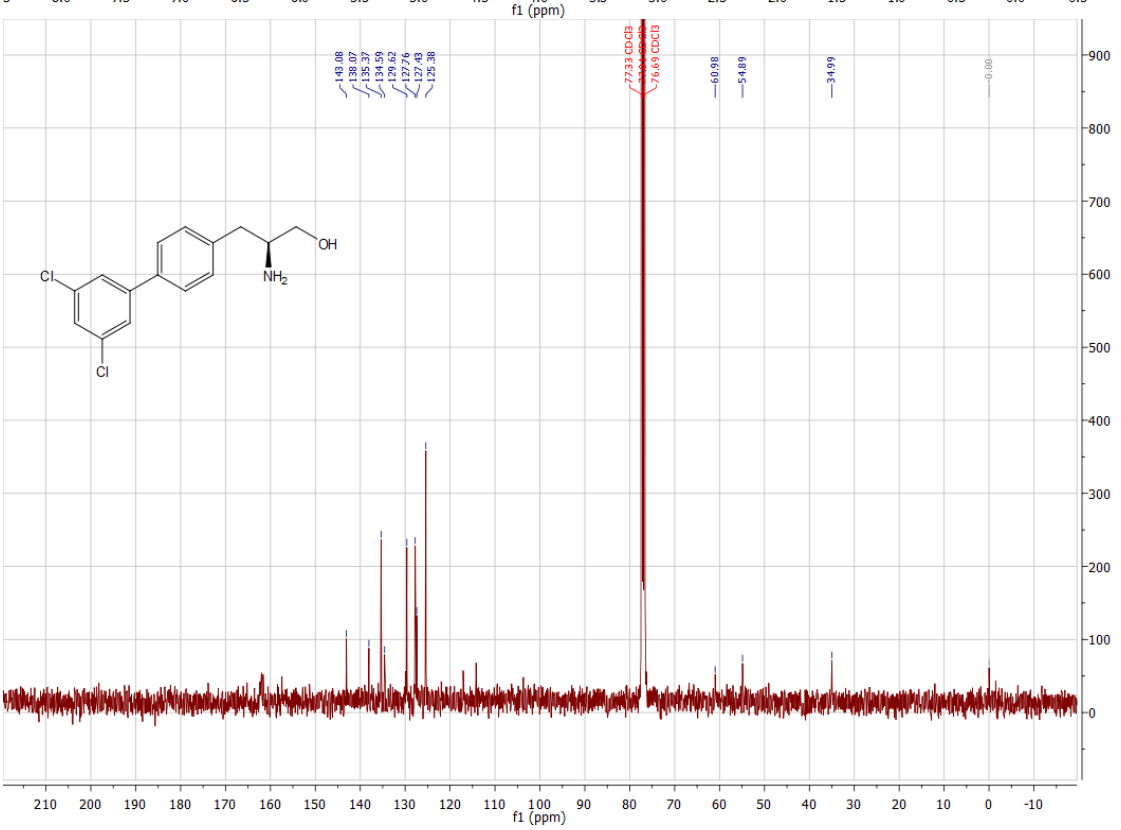
Compound **31** (CW16)



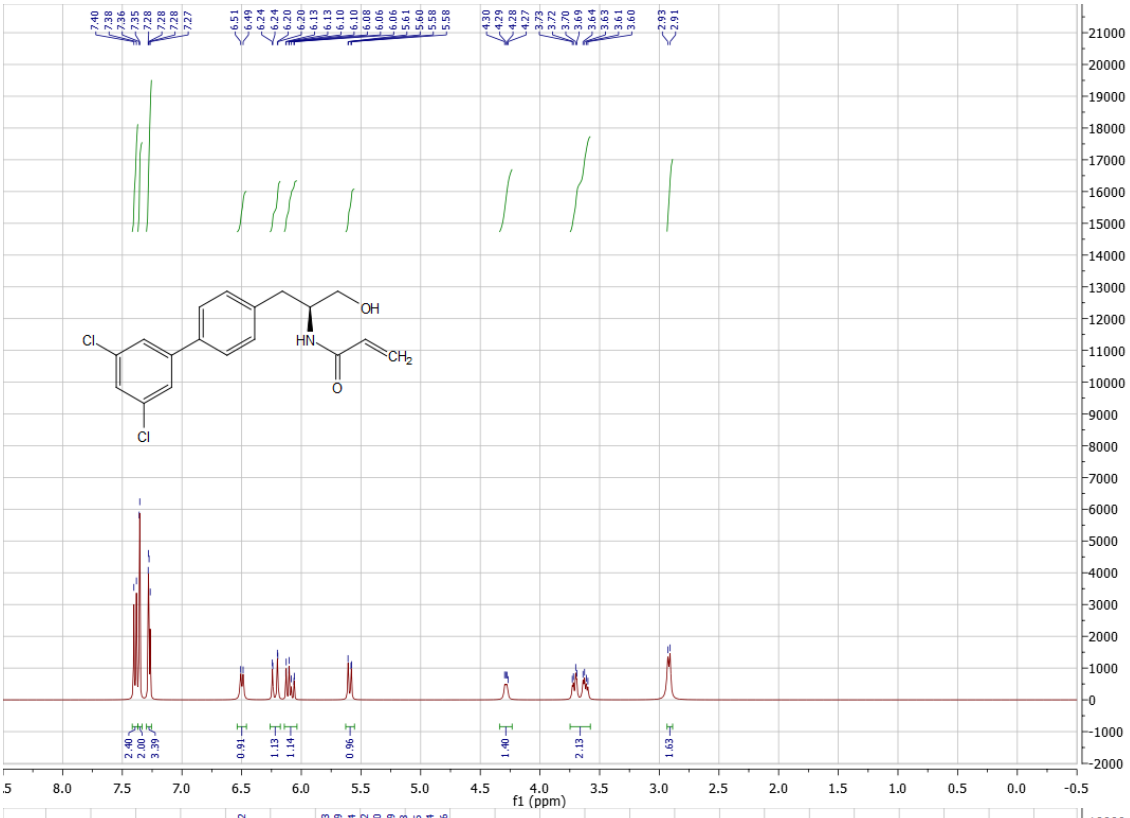


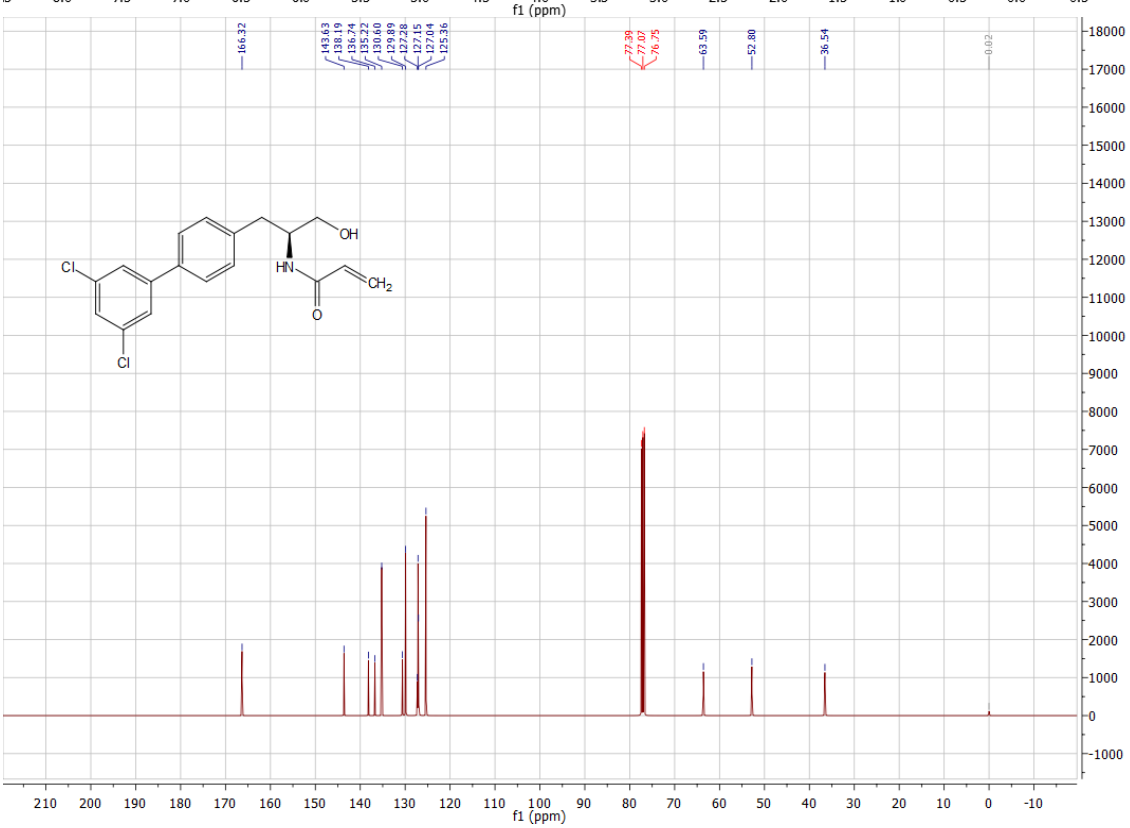
Compound **32**


7.42
7.40
7.34
7.33
7.30
7.29
7.29
7.21
7.19
3.82
3.79
3.61
2.96
2.91
2.90
OH
NH2
Cl
Cl
2.24
2.12
1.21
2.00
3.31
2.42
f1 (ppm)

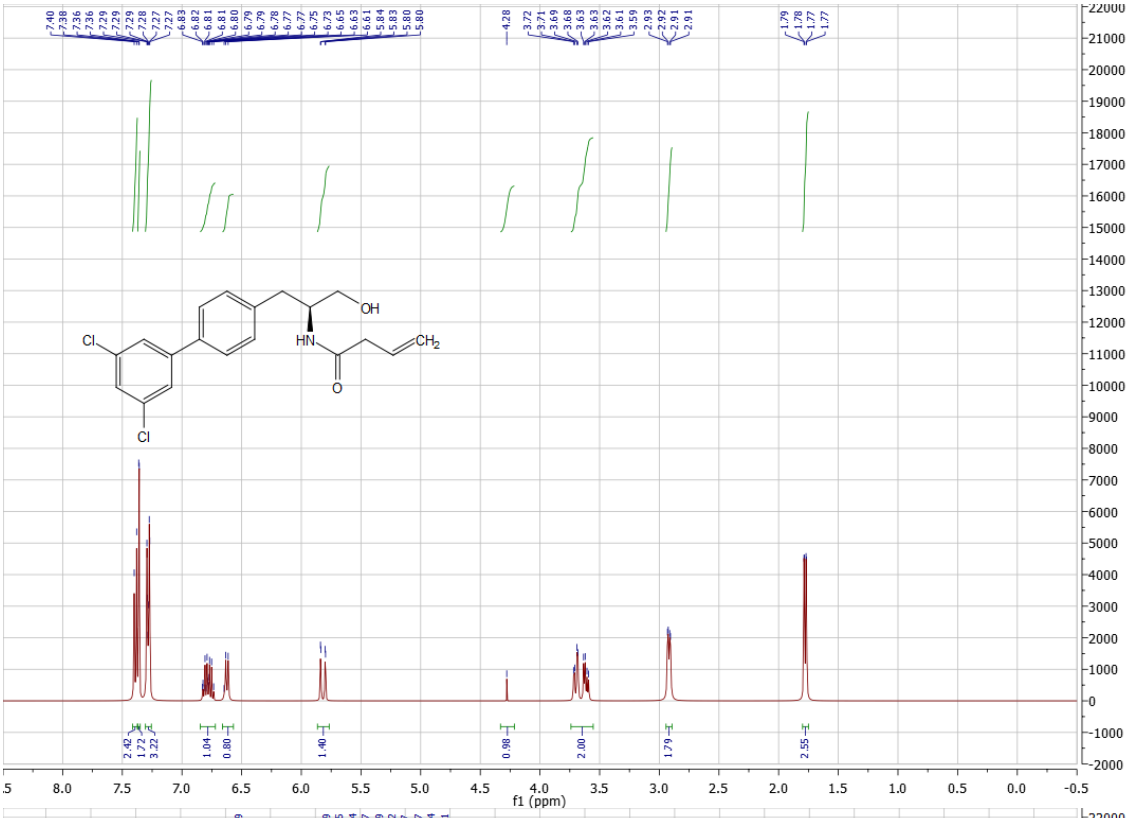

143.08
138.07
135.37
134.59
129.62
127.76
127.43
125.38
77.33 CDCl3
76.69 CDCl3
60.98
54.89
34.99
0.00
OH
NH2
Cl
Cl
f1 (ppm)

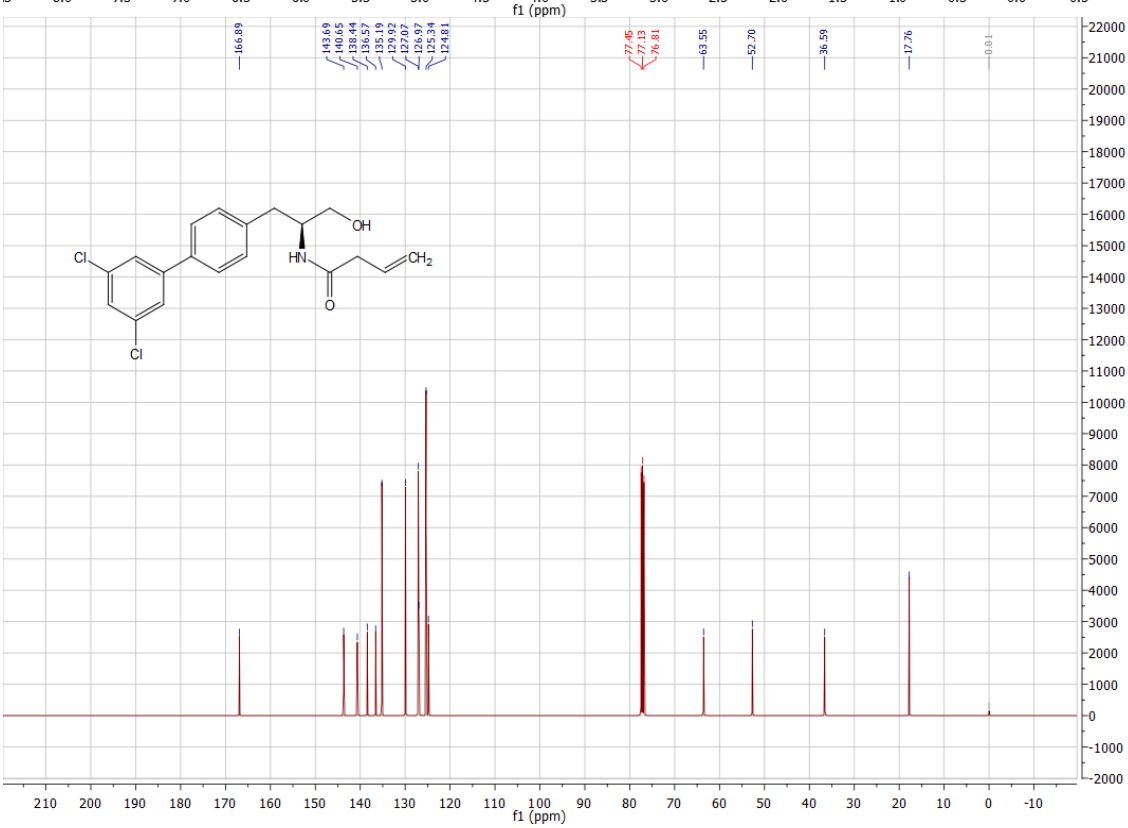
Compound **33**


7.40
7.38
7.36
7.35
7.28
7.28
7.28
7.27
6.51
6.49
6.24
6.24
6.20
6.20
6.13
6.10
6.08
6.06
6.06
5.61
5.60
5.58
5.58
4.30
4.29
4.28
4.27
3.73
3.72
3.70
3.69
3.64
3.63
3.61
3.60
2.93
2.91
OH
HN
CH2
O
Cl
Cl
2.40
2.00
3.39
0.91
1.13
1.14
0.96
1.40
2.13
1.63
f1 (ppm)

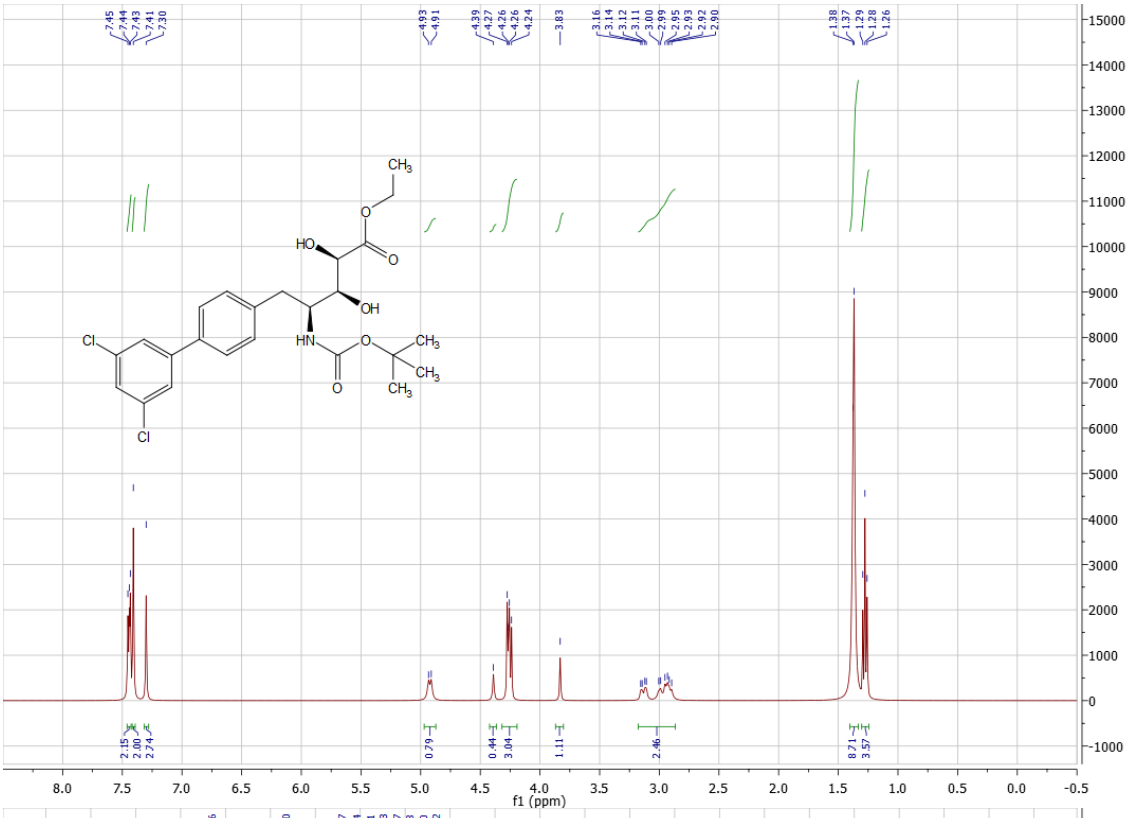

166.32
143.63
138.19
136.74
135.22
130.60
129.89
127.28
127.15
127.04
125.36
77.39
77.07
76.75
63.59
52.80
36.54
0.02
OH
HN
CH2
O
Cl
Cl
f1 (ppm)

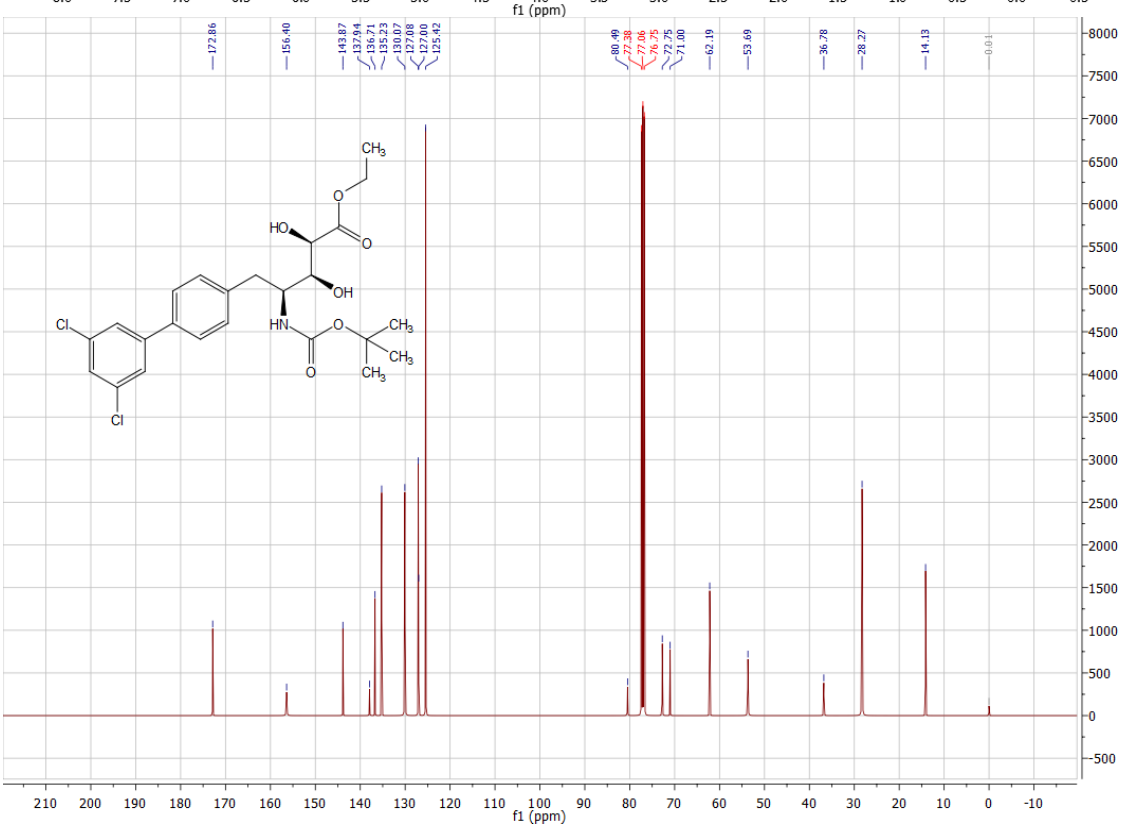
Compound **34**



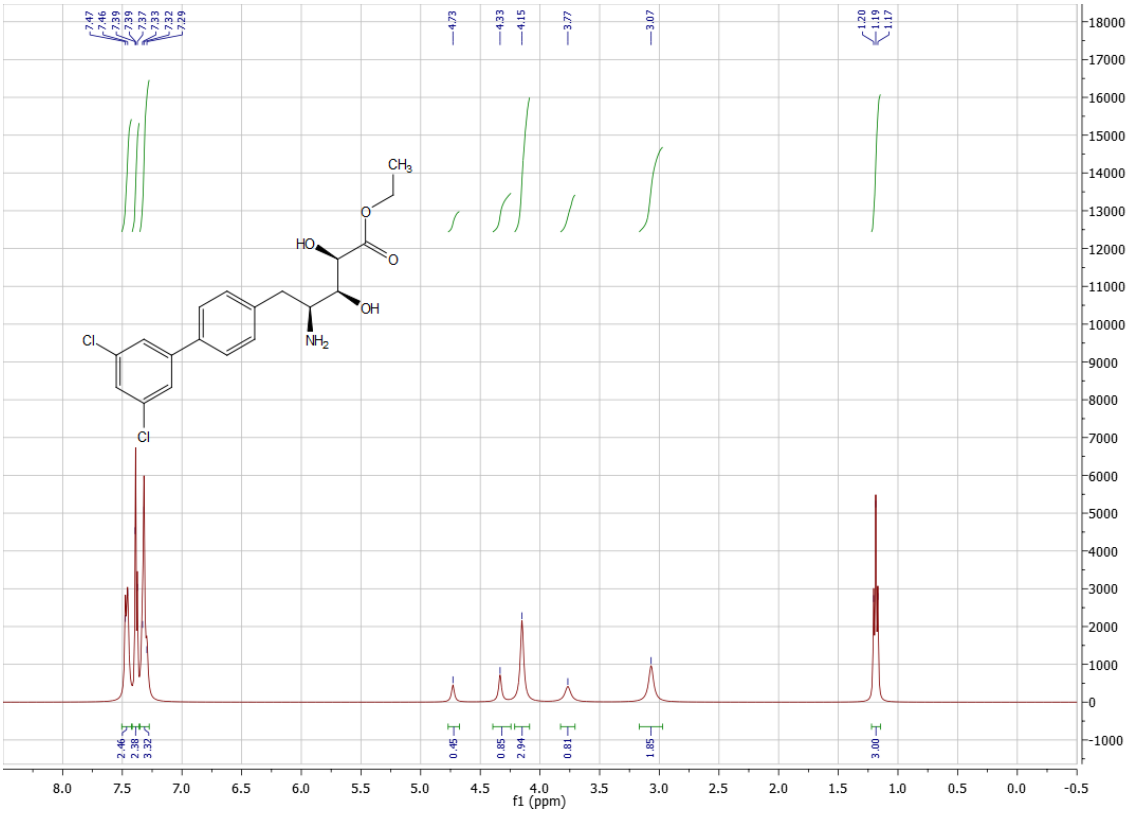


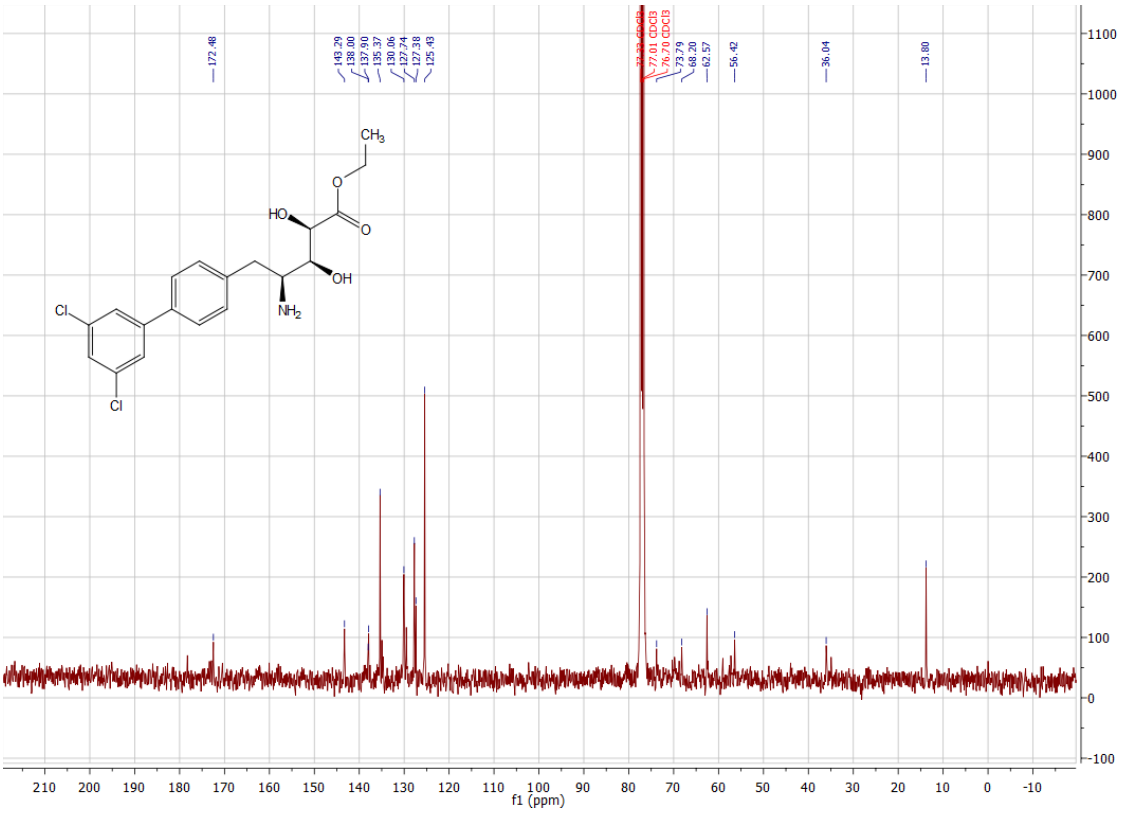
Compound **35**


7.45
7.44
7.43
7.41
7.30
4.93
4.91
4.39
4.27
4.26
4.26
4.24
3.83
3.16
3.14
3.12
3.11
3.00
2.99
2.95
2.93
2.92
2.90
1.38
1.37
1.29
1.28
1.26
CH3
O
HO
O
OH
HN
O
CH3
CH3
CH3
O
Cl
Cl
2.15
2.00
2.74
0.79
0.44
3.04
1.11
2.46
8.71
3.57
f1 (ppm)

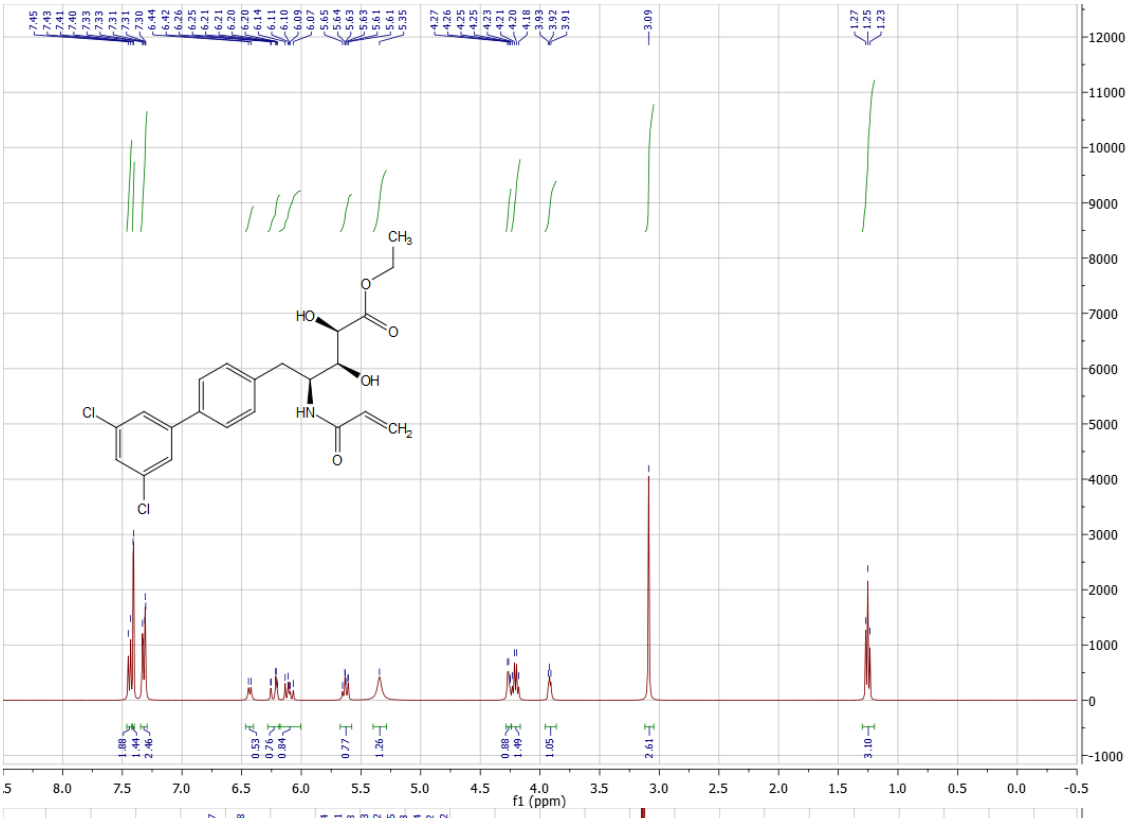

172.86
156.40
143.87
137.84
136.71
135.23
130.07
127.68
127.00
125.42
80.49
77.38
77.06
76.75
72.75
71.00
62.19
53.69
36.78
28.27
14.13
CH3
O
HO
O
OH
HN
O
CH3
CH3
CH3
O
Cl
Cl
f1 (ppm)

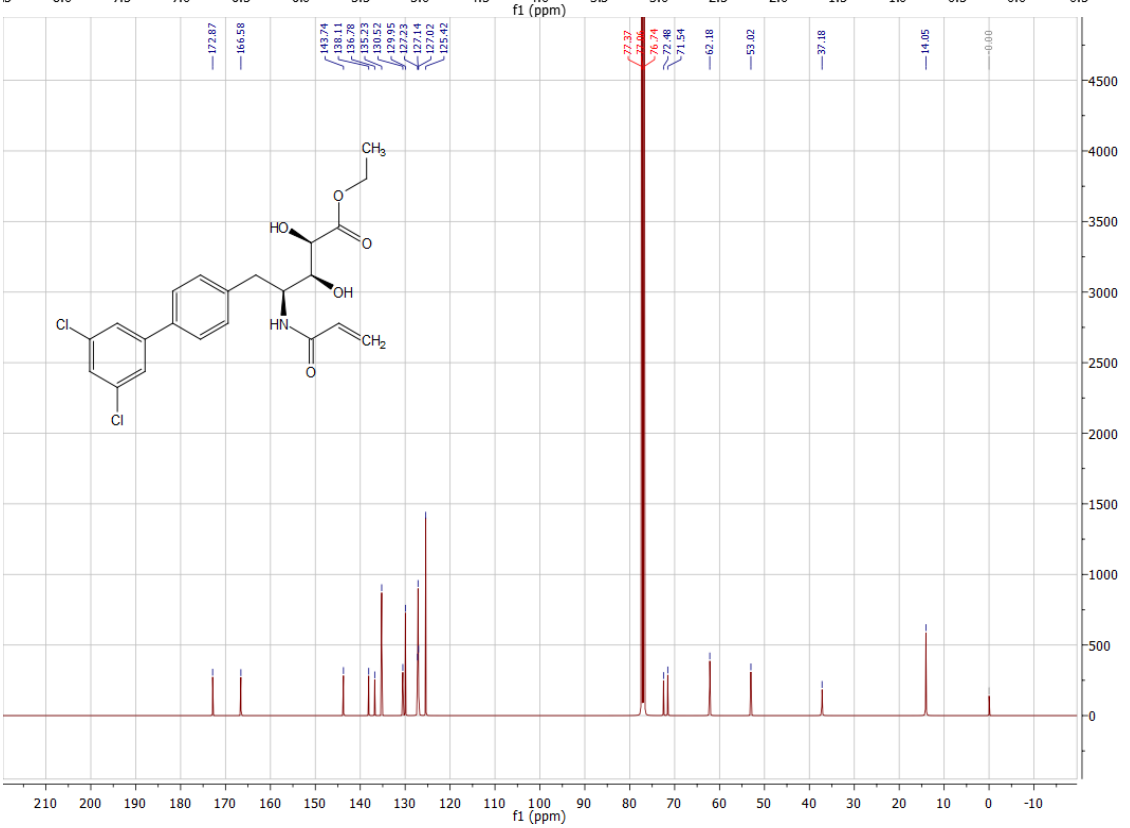
Compound **36**


7.47
7.46
7.39
7.39
7.37
7.33
7.32
7.29
4.73
4.33
4.15
3.77
3.07
1.20
1.19
1.17
CH3
O
HO
O
OH
NH2
Cl
Cl
2.46
2.38
3.32
0.45
0.85
2.94
0.81
1.85
3.00
f1 (ppm)

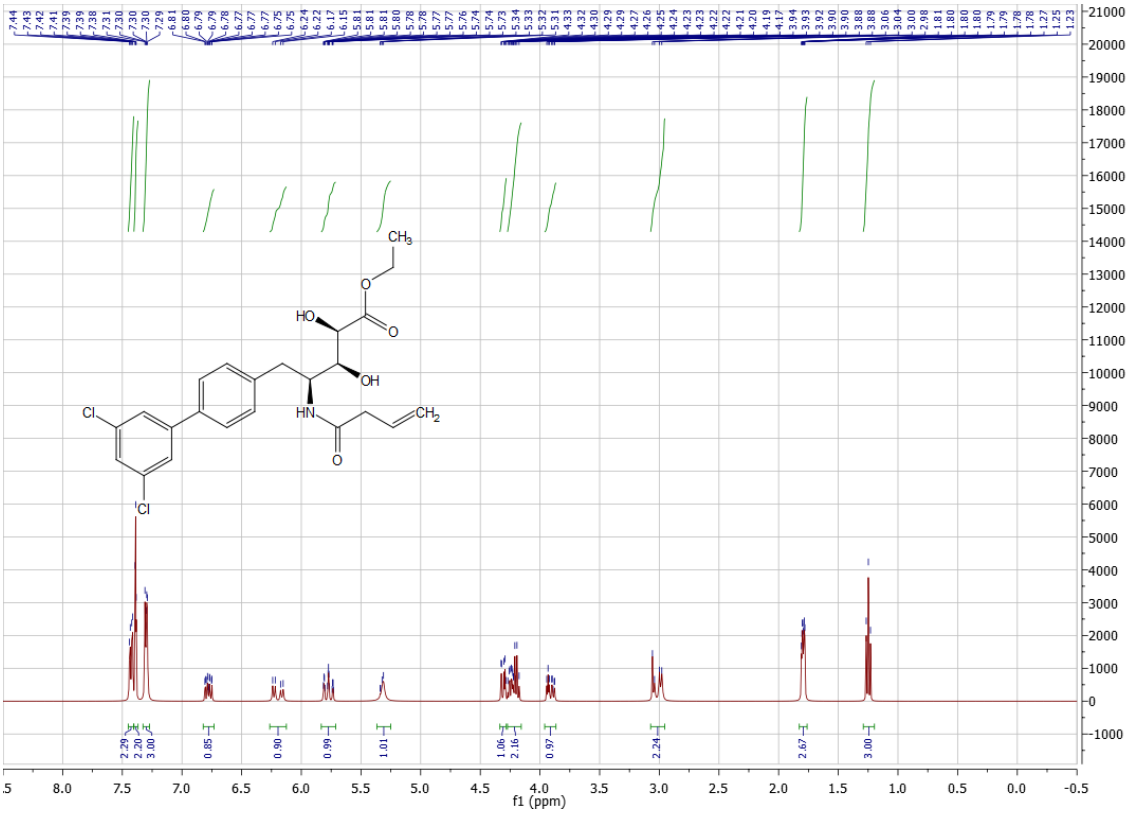

172.48
143.29
138.00
137.90
135.37
130.06
127.74
127.38
125.43
77.01 CDCl3
76.70 CDCl3
73.79
68.20
62.57
56.42
36.04
13.80
CH3
O
HO
O
OH
NH2
Cl
Cl
f1 (ppm)

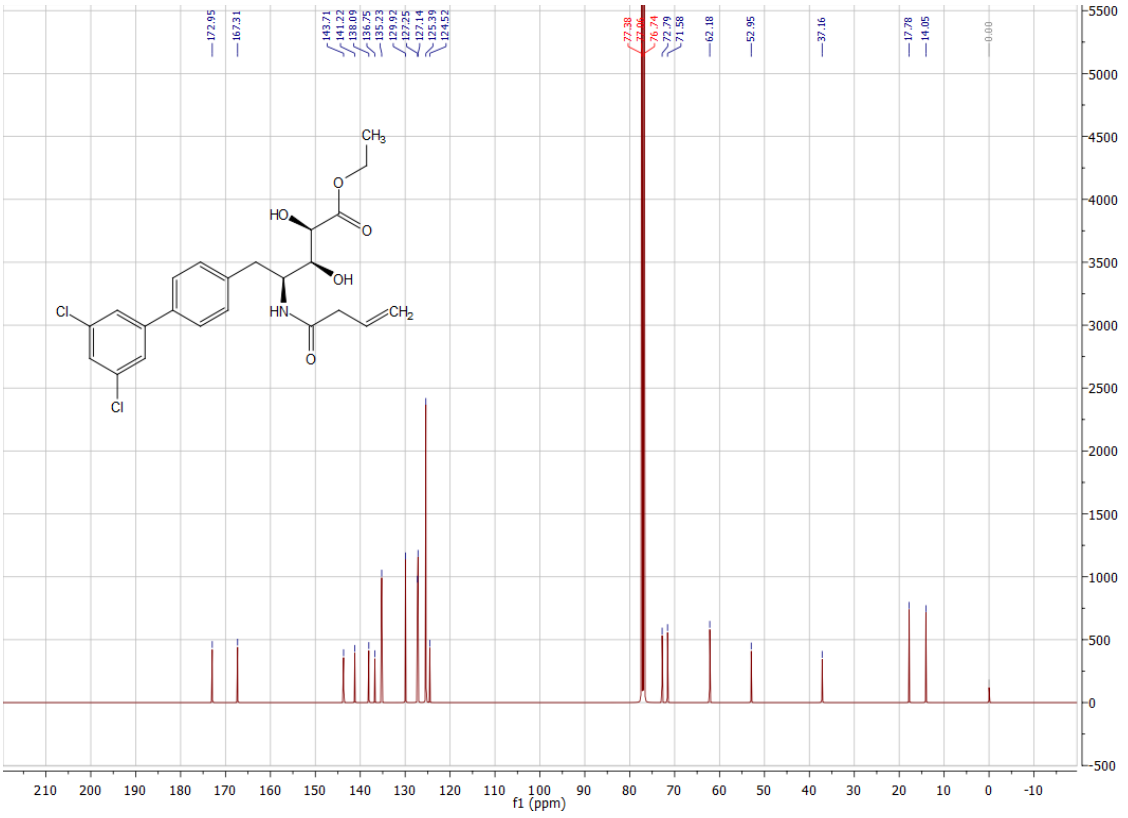
Compound **37** (CW17)



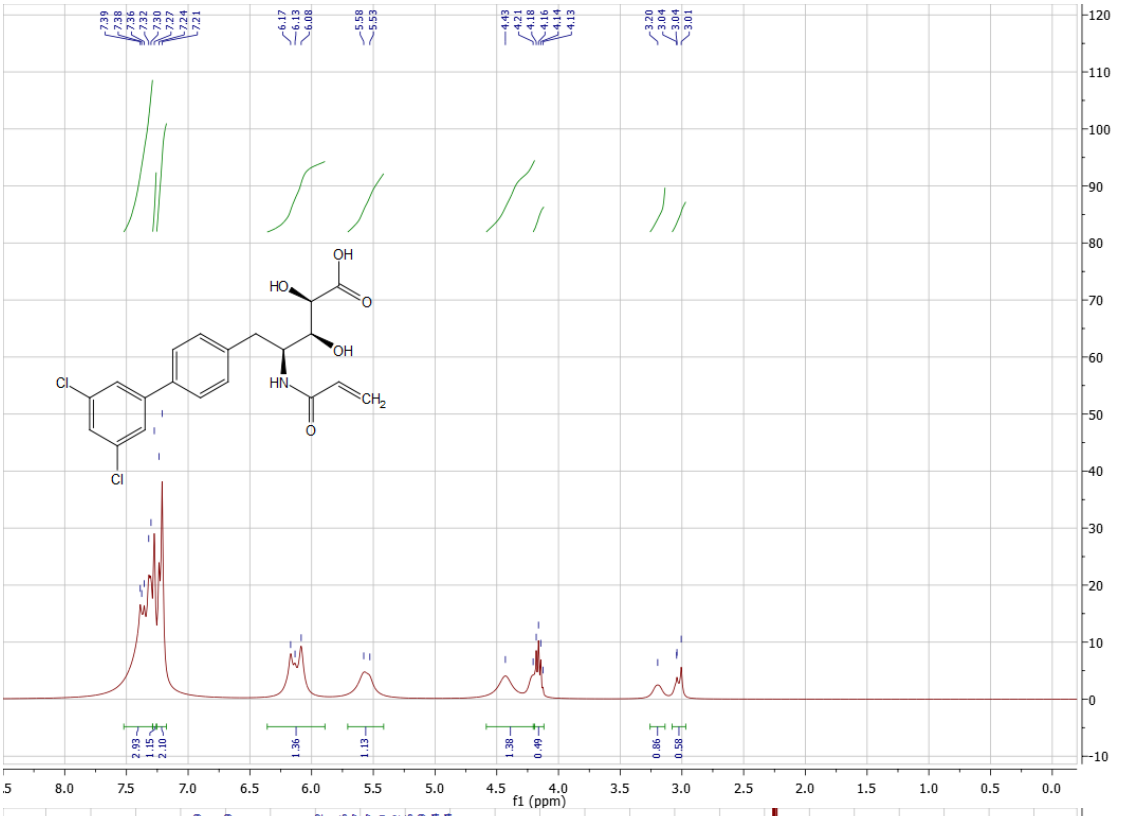


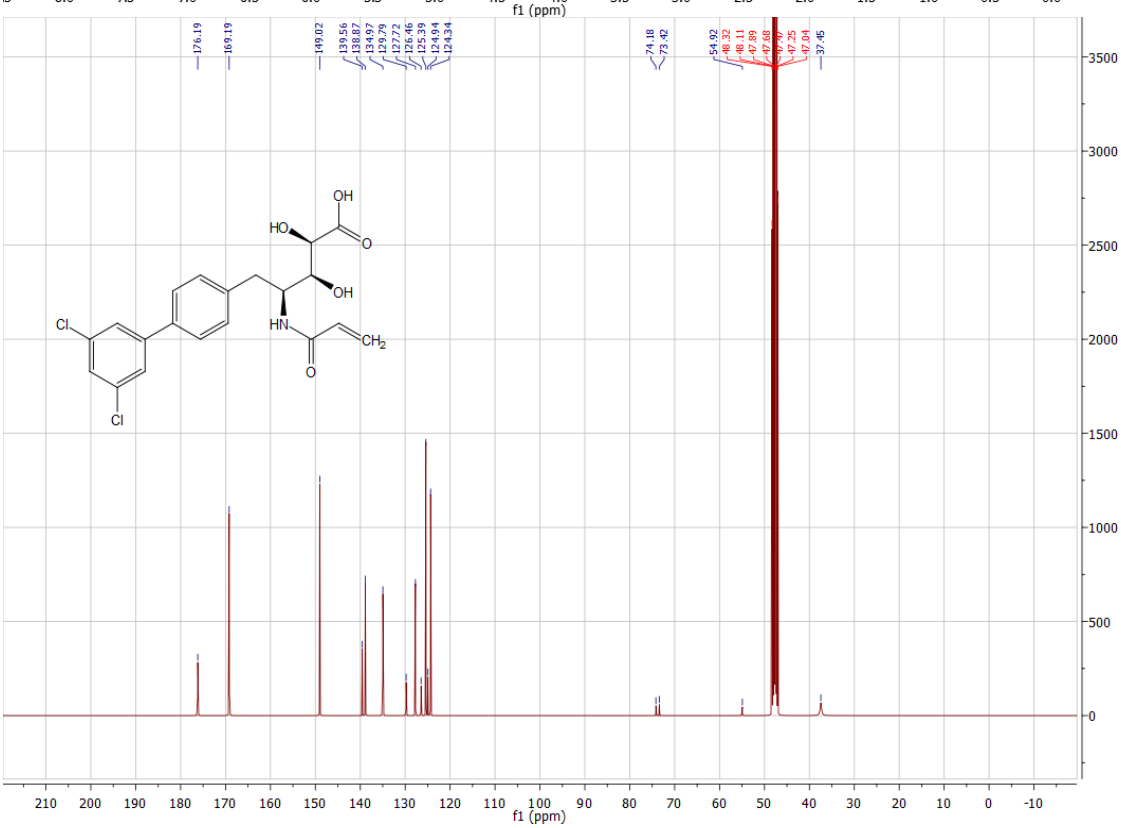
Compound **38** (CW18)





Compound **39** (CW19)





Compound **40** (CW20)