The Backbone Constitution Drives Passive Permeability Independent of Side Chains in Depsipeptide and Peptide Macrocycles Inspired by *ent*-Verticilide

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Supporting Information

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Section 1. Synthesis of Analogs in Series 1-5

The analogs were prepared using procedures similar to those described previously[1] and have been published elsewhere.[2]

Section 2. PAMPA Assay

2.1 Experiment Procedure

PAMPA was conducted using a 96-well donor plate with 0.45 µm hydrophobic Immobilon-P membrane supports (Millipore), and a 96-well Teflon acceptor plate. 1000 µM stock solutions were made up of 1-4 mg of compound (dependent on molecular weight) and 100% DMSO. The donor solutions were prepared using 1.25 mL stock, 1.25 mL PBS (pH 7.4 – prepared as a 1L solution, Millipore P3813) and 80.0 mg D-α-Tocopherol polyethylene glycol 1000 succinate (TPGS, Millipore 57668). The donor concentration is 500 µM due to the limit of detection on the LC/MS system. The donor solutions were prepared using 38.4 mg TPGS and 5% DMSO in PBS (192 µL DMSO, 3684 µL PBS). A solution of 1% (w/v) of lecithin in *n*-dodecane was prepared, which acts to activate the membrane. Prior to setting up the experiments, each membrane was visually assessed to ensure no cracking has occurred, which would skew the experiments. It is important to load the wells carefully to ensure the membranes don't become punctured. It is worth noting that once solutions are added working quickly is recommended to prevent evaporation. 5 µL of the lecithin solution was carefully applied to the membrane supports in the wells of the donor plate. The membrane should begin white and after application should be more transparent. The acceptor plate was prepared by adding 300 µL of the acceptor solution to each well. The donor plate was then placed on top of the acceptor plate and the acceptor solution should touch the membrane. It is important to begin recording times, to the second, as the donor solutions are added. Without allowing evaporation, 150 µL of the donor solution was added to each well. Once complete, the lid was placed on top of the donor plate, and the system was placed in a chamber with wet paper towels to prevent evaporation. It was incubated at room temperature for 14-18 hours and exact times were recorded to the second.

Once complete, the solutions were prepared to run on the LC/MS. 1-mL glass mass spectroscopy vials were labeled and the solutions were added to them. Rather than taking an aliquot of solution from each well, the entire solution was pulled up (either 150 µL or 300 µL) and placed in the vial. Then, the relative concentrations were analyzed by LC/MS performed on an Agilent 6130 single quadrupole LC-MS system. Chromatographic separation was performed on an Agilent Eclipse XD-C18 column (4.6x150mm, 5 µm) with 0.1% (vol) TFA in deionized water (mobile phase A) and 0.1% (vol) TFA in acetonitrile (mobile phase B). The following elution gradient was used: 30% B for 0.5 min, 30-75% linear gradient for 0.5 min, 75-88% linear gradient for 1 min, 88-90% linear gradient for 8 min, 90-100% linear gradient for 3 min, 100-30% linear gradient for 2 min. The flow rate was 1 mL/min. The column temperature was 23°C and the injection volume was 100 µL. The ion source parameters of the mass spectrometer include gas temperature of 300°C, gas flow of 12 L/min, nebulizer gas pressure of 30 psi, and sheath gas temperature of 200°C. All peak-picking and integration bounds were manually entered for each spectrum.

2.2 Materials and Suppliers

- *n*-Dodecane: Oakwood Chemical – 099221
- Dimethyl sulfoxide: Sigma – D2650
- Phosphate buffered saline pH 7.4 powder (PBS): Millipore – P-3813
- MultiScreen-IP PAMPA assay plates: Millipore – MAIPNTR10
- PTFE Acceptor plates: Millipore – MATRNPS50 or MSSACCEPT0R

- L-∂-phosphatidylcholine, egg lecithin: Sigma – P3556
- D-α-tocopheryl polyethylene glycol 1000 succinate (TPGS): Millipore – 57668
- Polysorbate 80 (TWEEN 80): Sigma – 1547969

2.3 Optimization: Technique and Surfactants

Prior to running the analogs in series 1-5 of unknown permeability, rigorous optimization was completed. To ensure proper technique and reproducibility two standards of different molecular weights were subjected to the PAMPA conditions: propranolol and cyclosporin A. Literature values for these two positive controls were reproduced successfully.

a. Positive Control: Propranolol Variables from Calculations and Standard Curve

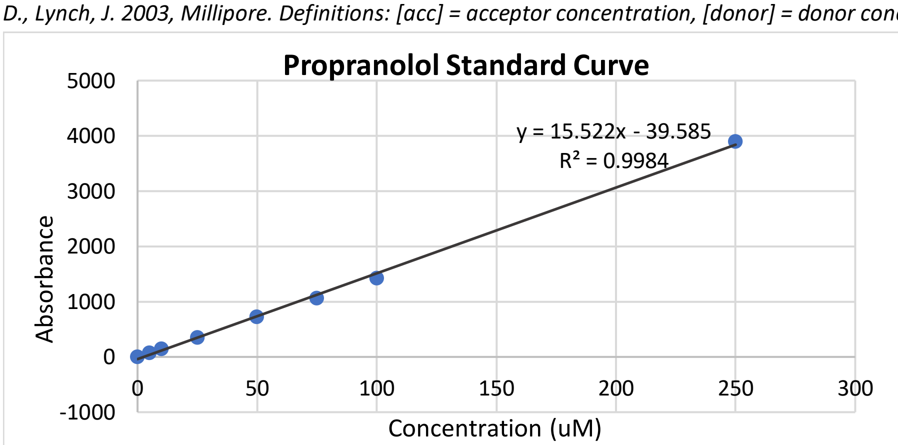
(*S*)-Propranolol (Millipore, catalog number P-0884) was subjected to standard PAMPA conditions listed above. Data was quantified using a UV trace, 254 nm. Each experiment included 5 replicates at a specified concentration (1: 10 uM, 2: 50 uM, 3: 100 uM, 4: 200 uM). The PAMPA data is shown below:

Experiment	MW (g/mol)	Ave RT (min)	C ($x10^{-9}$)	Well 1		Well 2		Well 3		Well 4		Well 5		Ave %R ± SD
				%T	%R	%T	%R	%T	%R	%T	%R	%T	%R	
1	259.34	3.85	3.23	0.81	91	0.80	90	0.81	89	0.83	90	0.77	90	93.1 ± 2.8
2			3.29	0.77	94	0.76	93	0.80	96	0.76	99	0.78	95	
3			3.04	0.55	93	0.60	91	0.59	94	0.59	90	0.61	99	
4			3.24	0.70	93	0.76	95	0.74	94	0.74	94	0.75	92	

Supplement Table 2. Variables from Calculations for (S)-Propranolol. *Data is summarized for 4 experiments with 5 replicates (20 total). The molecular weight is 259.34 g/mol and with a retention time of 3.9 minutes. Variable C and %T were calculated using Supplement Equation 1. The mean % recovery was 93%. Definitions: MW = molecular weight, RT = retention time, %R = % recovery, Ave %R = mean ± standard deviation.*

Exp	Ave. P_{app} (x 10^{-6})	Literature P_{app} [a] (x 10^{-6})	Well 1		Well 2		Well 3		Well 4		Well 5		C_0 (uM)	% diff. ± SD
			[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]		
1	9.4 ± 0.6	10.0 ± 0.0	4.05	5.06	3.97	5.05	3.95	4.94	4.03	4.97	3.92	5.13	10	37.1 ± 0.02
2	9.1 ± 0.4		18.26	28.51	17.46	29.06	18.31	29.83	18.07	31.26	18.09	29.62	50	
3	9.7 ± 0.4		37.89	55.45	33.45	57.74	36.13	58.01	35.56	54.55	39.92	58.91	100	
4	10.0 ± 0.3		72.80	113.27	71.05	118.47	73.31	115.52	71.12	116.80	71.60	112.16	200	

Supplement Table 1. Final Experimental Data for (S)-Propranolol. *The mean calculated P_{app} was 9.55 ± 0.4 cm/s. The acceptor and donor well concentrations were calculated using a standard curve. The initial concentrations are listed under C_0. The mean % diffusion is 37.1% ± 0.02. [a]Evaluation of the reproducibility of Parallel Artificial Membrane Permeation Assays (PAMPA). Schmidt, D., Lynch, J. 2003, Millipore. Definitions: [acc] = acceptor concentration, [donor] = donor concentration, % diff = % diffusion.*



Conc. (uM)	Absorbance
250	3895.32
100	1426.7
75	1059.5
50	720.9
25	353.6
10	145.6
5	75.3
0	0

Supplement Graph 1. *The standard curve for absorbance vs. concentration (uM) of (S)-propranolol utilizing UV detection (254 nm).*

b. Positive Control: Cyclosporine A Variables from Calculations and Standard Curve

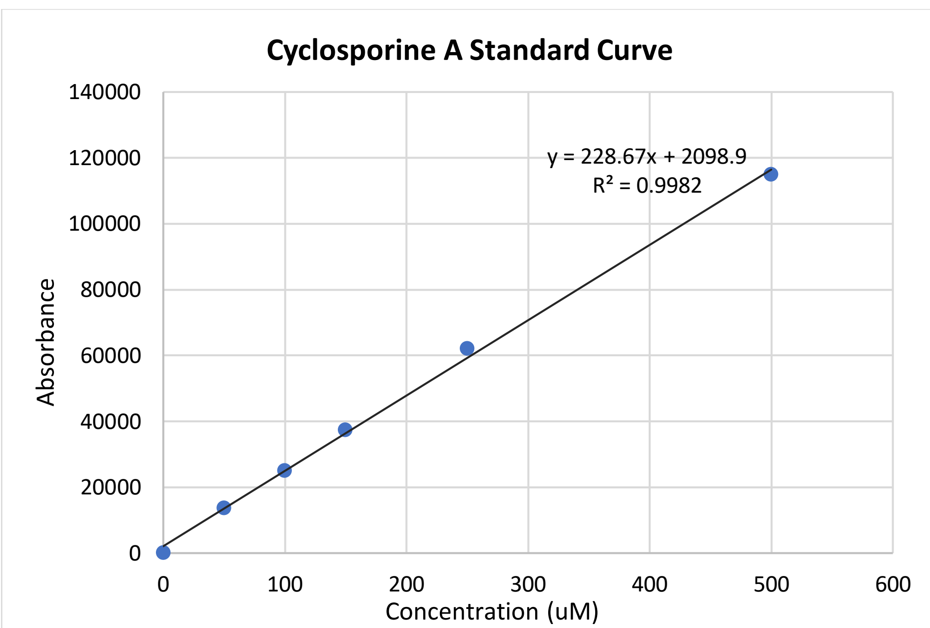
Cyclosporine A (Sigma Aldrich, catalog number C1832-5MG) was subjected to standard PAMPA conditions listed above. Data was quantified using a UV trace, 210 nm. Each experiment included 5 replicates at a concentration of 500 uM. This higher concentration was chosen following running samples at 50, 100, 250 uM and seeing weak peak absorbance. The limit of detection is 25 uM. The PAMPA data is shown below:

Experiment	MW (g/mol)	Ave RT (min)	C ($x10^{-9}$)	Well 1		Well 2		Well 3		Well 4		Well 5		Ave %R ± SD
				%T	%R	%T	%R	%T	%R	%T	%R	%T	%R	
1	1202.6	12.03	3.20	0.70	92	0.71	100	0.69	93	0.69	94	0.70	91	88.4 ± 5.9
2			3.11	0.65	97	0.65	89	0.67	92	0.67	90	0.65	86	
3			3.03	0.78	78	0.81	83	0.78	82	0.80	82	0.81	81	
4			3.21	0.74	84	0.74	92	0.77	82	0.72	93	0.74	87	

Supplement Table 3. Variables from Calculations for Cyclosporine A. *Data is summarized for 4 experiments with 5 replicates (20 total). The molecular weight is 1202.6 g/mol with a retention time of 12.03 minutes. Variable C and %T were calculated using Supplement Equation 1. The mean % recovery was 88%. Definitions: MW = molecular weight, RT = retention time, %R = % recovery, Ave %R = mean ± standard deviation.*

Exp	Ave. $LogP_{app}$ (x 10^{-6})	Literature $LogP_{app}$[a] (x 10^{-6})	Well 1		Well 2		Well 3		Well 4		Well 5		C_0 (uM)	% diff. ± SD
			[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]		
1	-5.06 ± 0.04	-5.01 ± 0.00	163.80	297.69	162.17	338.49	169.34	295.21	172.82	295.43	154.85	299.69	500	30.1 ± 0.02
2	-5.07 ± 0.03		163.89	321.67	149.84	293.96	154.98	306.98	160.44	291.70	151.52	277.27		
3	-5.08 ± 0.02		142.63	248.95	148.56	266.18	144.96	265.25	143.42	266.25	144.67	261.44		
4	-5.10 ± 0.02		135.17	285.46	146.79	312.02	138.79	270.43	141.78	321.87	139.48	293.97		

Supplement Table 4. Final Experimental Data for Cyclosporine A. *The mean calculated $LogP_{app}$ was -5.07 ± 0.03 cm/s, calculated using Supplement Equation 1. The acceptor and donor well concentrations were calculated using a standard curve. The initial concentration is 500 uM. The mean % diffusion is 30%. Definitions: [acc] = acceptor concentration, [donor] = donor concentration, % diff = % diffusion ± standard deviation. [a]Seo, J., et. al., J. Med. Chem.* ***2021****, 64, 8272.*



Conc. (uM)	Absorbance
500	114765.9
250	62031.8
150	37323.4
100	24980.1
50	13597.2
0	0

Supplement Graph 2. *The standard curve for absorbance vs. concentration (uM) of Cyclosporine A utilizing UV detection (210 nm).*

c. PAMPA Assay Optimization: Concentration and Surfactants

Concentration:

Next, *ent*-verticilide was ran in the PAMPA assay using literature conditions. In literature, a PAMPA assay is usually ran with 2-10 uM of analyte. After preparing stock solutions and gathering HPLC data for varying concentrations, it was found that the limit of detection for the available system is around 50 uM for *ent*-verticilide. Using this information, initial donor concentration subjected to the PAMPA conditions was 100 uM. Due to adherence of compound to the PAMPA plate, the recoveries for experiments were < 30%. It was evident that running these assays at higher concentrations could provide easier detection and quantification of data. Next, numerous assays were run at 100, 250 and 500 uM concentrations. Through this optimization it was found that the highest donor concentration provided the most reproducible results, so moving forward each assay was run at 500 uM. Although this improved quantification and absorbances were closer to ideal, a large loss in mass recovery was still noted.

Surfactants:

Early in the experimentation, it was noted that 50% of the material was being lost to the membrane and/or the plastic surrounding the wells (**Supplement Table 5, entry 1**). The highly lipophilic compound, *ent*-verticilide, adhered to the sides of the wells and the membrane, preventing collection of reproducible data. This was a major problem that needed to be resolved before testing the first series of analogs. Surfactants were introduced as they are known to help prevent the adherence with lipophilic compounds in the PAMPA assay.[3] Many experiments were completed using TPGS and/or polysorbate 80. In **entry 2**, it is evident that the 1% TPGS is insufficient at preventing the adherence, but about a 10% improvement in recovery was noted. Adding 2.5% of polysorbate 80 (**entries 3 & 4**), boosted the recoveries but proved to be irreproducible. The final conditions included using 2% TPGS in the donor well (entries **5-7**), which provided yields in the desired range (>85%) and consistent % diffusions. It is worth noting that the acceptor well has 1% TPGS, but there was no optimization of this.

Experiment	Donor Surfactant	% Diffusion	$LogP_{app}$	% Recovery
1	None	15%	-5.54	50
2	1% TPGS	19%	-5.43	61
3	2.5% Polysorbate 80	19%	-5.42	68
4	2.5% Polysorbate 80	20%	-5.39	95
5	2% TPGS	24%	-5.23	97
6	2% TPGS	26%	-5.18	92
7	2% TPGS	26%	-5.19	87
Optimized Cond.	2% TPGS	26%	-5.18	90

Supplement Table 5. Surfactant Optimization with ent-Verticilide. *Each entry is the mean of 5 replicates within each experiment. The optimized conditions are listed in the final entry of the table, these conditions are used for all analogs in series 1-5.* $LogP_{app}$ *is calculated using Supplement Equation 1.*

2.4 Calculations

a. Ratio Method Calculations ($LogP_{app}$ and P_{app})

PAMPA permeability parameters were calculated by the following formulas:

$$C_{equilibrium} = \frac{(C_D V_D) + (C_A V_A)}{V_D + V_A}$$

$$\%T = \frac{C_A}{C_{equilibrium}} \times 100 = \frac{R_A}{\left(\frac{R_A V_A + R_D V_D}{V_A + V_D}\right)} \times 100$$

$$LogP_{app} = \log\left\{-\frac{V_D V_A}{V_D V_A} \times \frac{\ln(1\text{-}\%T)}{area \times time}\right\}$$

$$\%\,Recovery = \frac{(C_D V_D + C_A V_A)}{C_0 V_D} \times 100$$

Supplement Equation 1. Equations for Calculating P_{app}. *Utilizing a ratio-based method of final concentrations (donor and acceptor wells), the following variables can be calculated - C_D: relative concentration in donor well, C_A: relative concentration in acceptor well, C_0: relative concentration of initial test solution added to donor well, V_D: volume of donor well (0.15 cm^3), V_A: volume of acceptor well (0.30 cm^3), Area: membrane area (0.24 cm^2), Time: actual elapsed time in second.*

b. Standard Curve Method Calculations (LogP)

Experimental LogP values were calculated by leveraging a standard curve to obtain concentrations in the donor and acceptor wells, then utilizing the following equation:

$$Log\,P = \log\left\{C \times \ln\left(1 - \frac{[analyte]_{acceptor}}{[analyte]_{donor}}\right)\right\} \quad where\ C = \frac{V_D \times V_A}{(V_D + V_A) \times area \times time}$$

Supplement Equation 2. Equation for Calculating LogP. *LogP utilizes a standard curve-based method, where V_D = donor solution initial volume (300 uL) and V_A = acceptor solution initial volume (150 uL). LogP is the log of the effective permeability.*

c. Percent Recovery (%R)

Sample percent recovery was calculated using the following equation:

$$Percent\ Recovery = \frac{[acceptor] + [donor]}{500} \times 100$$

Supplement Equation 3. Percent Recovery Equation. *Total concentration of analyte detected after incubation divided by C_0.*

d. Percent Diffusion (% diff.)

Percent diffusion is the amount of compound that diffused across the membrane:

$$Percent\ Diffusion = \frac{[acceptor]}{500} \times 100$$

Supplement Equation 4. Percent Diffusion Equation. *Percent diffusion is the [acceptor]/500 uM (C_0).*

2.5 LC/MS Optimization

a. Quantification Methods

To ensure rigorous experimental design, 3 different forms of quantification were utilized, *when possible,* for calculating the LogP and $LogP_{app}$ values. A Varian 380-ELSD, an Agilent 6130 single quadrupole LC-MS system and an Agilent 1100 series HPLC were used for the data collection. For the quantification of the HPLC traces, a 210 nm wavelength spectrum was used, which provided the sharpest signals. For some macrocycles, only 2 of the 3 methods of quantification showed peaks, so in those cases the traces with no peaks to quantify were excluded. The reported logP and $logP_{app}$ values within this supporting information are means of the 2-3 traces, providing between 20-45 experiments per analog. This extra level of rigor provided a method to further verify the results for each analog.

In cases where peak absorbance was strong, multiple detection methods were used to add another level of rigor to the study. Prior to running the PAMPA assay, standard curves were produced for each of the analogs. Many of the analogs were detected with UV, ELSD and MS: analogs 2.3, 2.5, 4.1-4.6, and 5.6. Some of the analogs could only be detected by UV and ELSD: *ent*-vert, 1.1-1.5, 2.1, 2.2, 3.1, 5.4, and 5.5. Finally, the remaining analogs were only detected by UV and MS: 2.4, 3.2-3.5 and 5.1-5.3.

Detection Method	Series 1					Series 2					Series 3					Series 4						Series 5					
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	6	1	2	3	4	5	6
UV	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
ELSD	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓					✓	✓	✓	✓	✓	✓				✓	✓	✓
MS								✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓

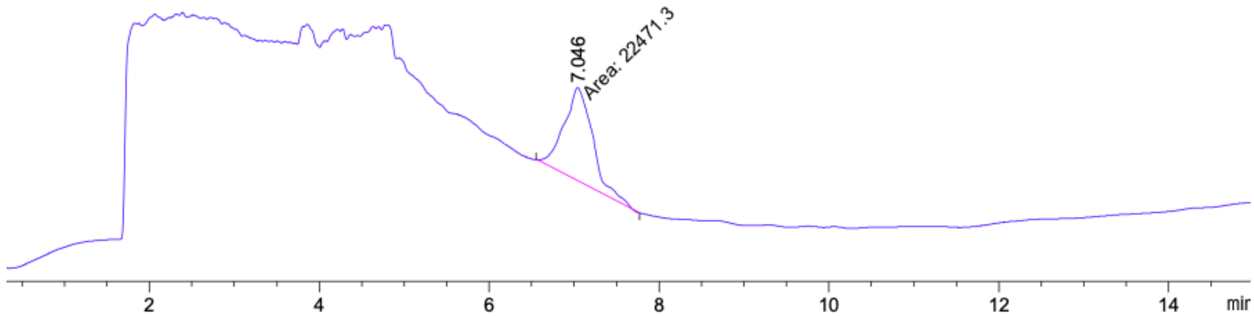
Supplement Table 6. Methods of Quantification. *Each of the series were quantified using multiple detection methods. For series 1 through series 5, this summarizes the different methods and data to be reported within this supporting information. Due to lack of peaks in the experimental traces, not all methods could be used for every analog.*

Although 2-3 methods of quantification were documented for all analogs, the constant detection method present with all analogs was **UV absorption (210 nm)**. This renders UV as the final method of detection to be used to compare data between series and within series. The additional data collected for some analogs has been reported only in this supporting information. By reporting ELSD and/or MS data, the final UV data can be supported by showing consistency with calculations across different methods.

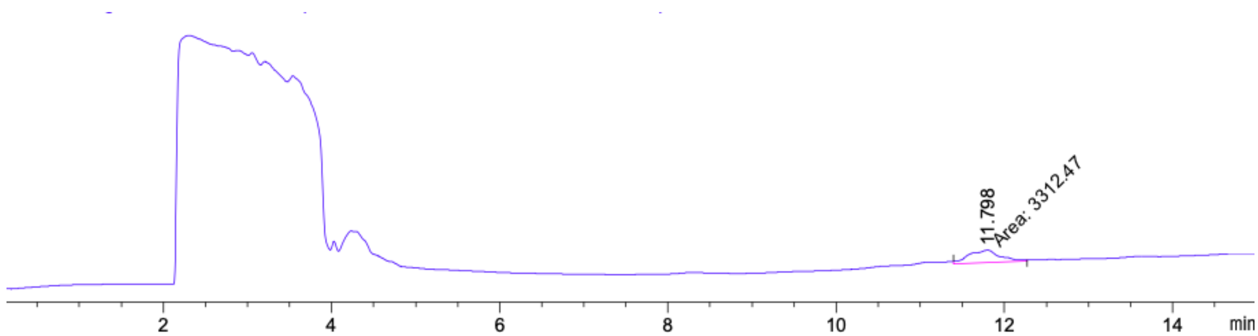
b. Optimization of the Traces

Shown below is an example trace that was used to optimize the eluent gradient for *ent*-verticilide and analogs. Both of the following traces are 50 uM *ent*-verticilide in DMSO. The following elution gradients were used. The initial gradient (pre-optimization) was 30%-90% linear gradient of B (MeCN) for 5 min, 90-100% linear gradient for 8 min, 100-30% linear gradient for 2 min. The trace shown below is at 210 nm and the macrocycle elutes around 7 minutes. Many different gradients were tested, and the final conditions are as follows: 30% B for 0.5 min, 30-75% linear gradient for 0.5 min, 75-88% linear gradient for 1 min, 88-90% linear gradient for 8 min, 90-100% linear gradient for 3 min, 100-30% linear gradient for 2 min. The trace shown below is at 210 nm and the macrocycle elutes around 12 minutes. All analogs produced similar traces to the following example:

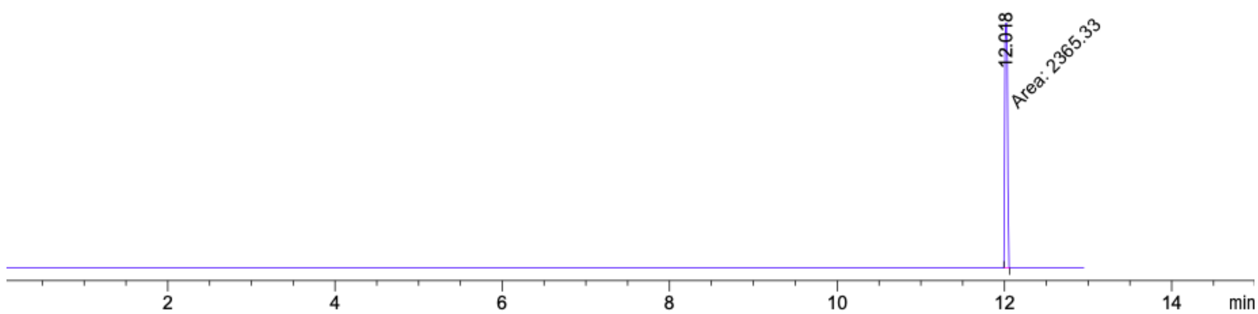
A. HPLC trace pre-optimization (λ = 210 nm):



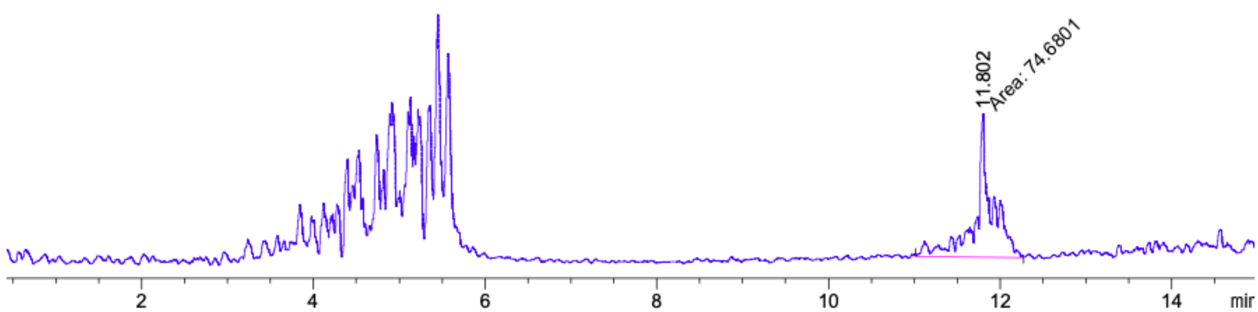
B. HPLC trace post-optimization (λ = 210 nm):



C. MS trace:



D. ELSD trace:



Supplement Figure 1. Traces from a 50 uM sample of ent-Verticilide in DMSO. *Analyte peaks are integrated in each spectrum.* ***A*** *includes the trace using pre-optimization conditions, where there is visible overlap of peaks, making accurate quantification difficult. Analyte is found at 7 minutes.* ***B*** *is the HPLC trace using post-optimization conditions.* ***C*** *is the MS trace using post-optimization conditions.* ***D*** *is the ELSD trace using post-optimization conditions. B-C shows the analyte eluting around 12 minutes.*

2.6 PAMPA Results

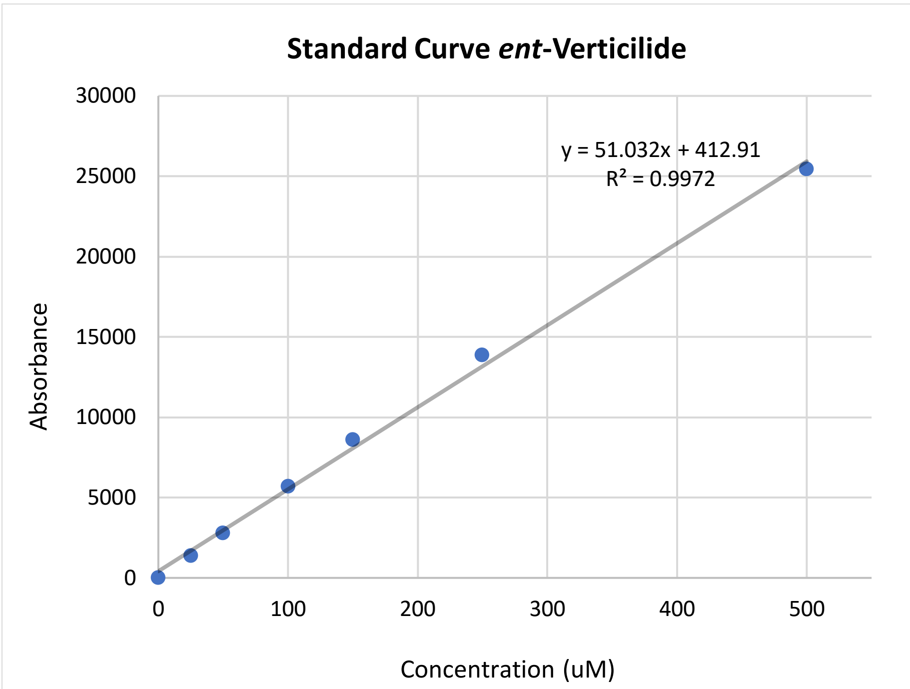
a. *ent*-Verticilide: PAMPA Data and Standard Curves

Experiment	MW (g/mol)	Ave RT (min)	C ($x10^{-9}$)	Well 1		Well 2		Well 3		Well 4		Well 5		Ave %R
				%T	%R	%T	%R	%T	%R	%T	%R	%T	%R	
1			3.27	0.71	86	0.72	98	0.53	98	0.72	92	0.58	89	
2			3.20	0.66	99	0.62	94	0.72	88	0.67	96	0.75	86	
3			3.28	0.68	90	0.75	84	0.70	84	0.71	85	0.70	87	
4			3.27	0.74	88	0.71	87	0.72	84	0.53	93	0.72	93	
5	853.15	11.80	3.23	0.58	86	0.66	96	0.62	88	0.72	76	0.67	97	89.85 ± 5.64
6			3.28	0.75	86	0.67	83	0.75	86	0.70	87	0.71	77	
7			3.05	0.70	88	0.74	83	0.71	84	0.72	99	0.53	97	
8			3.20	0.72	96	0.58	99	0.66	97	0.62	95	0.72	85	
9			3.21	0.67	91	0.75	87	0.68	87	0.75	87	0.70	91	
10			3.24	0.71	91	0.70	88	0.74	93					

Supplement Table 7. The Variables from Calculations for ent-Verticilide. *ent-Verticilide was subjected to the optimized PAMPA conditions comprised of 6 experiments, each with 8 replicates run in tandem (total of 48 individual experiments). Dark grey boxes are unused. The molecular weight of ent-verticilide is 853.15 g/mol and the mean retention time seen via HPLC (210 nm) is 10.1 minutes. The C and %T values are calculated using Supplement Equation **1**. The mean percent recovery is 90%. Definitions: MW = molecular weight, RT = retention time, %R = % recovery, Ave %R = mean ± standard deviation.*

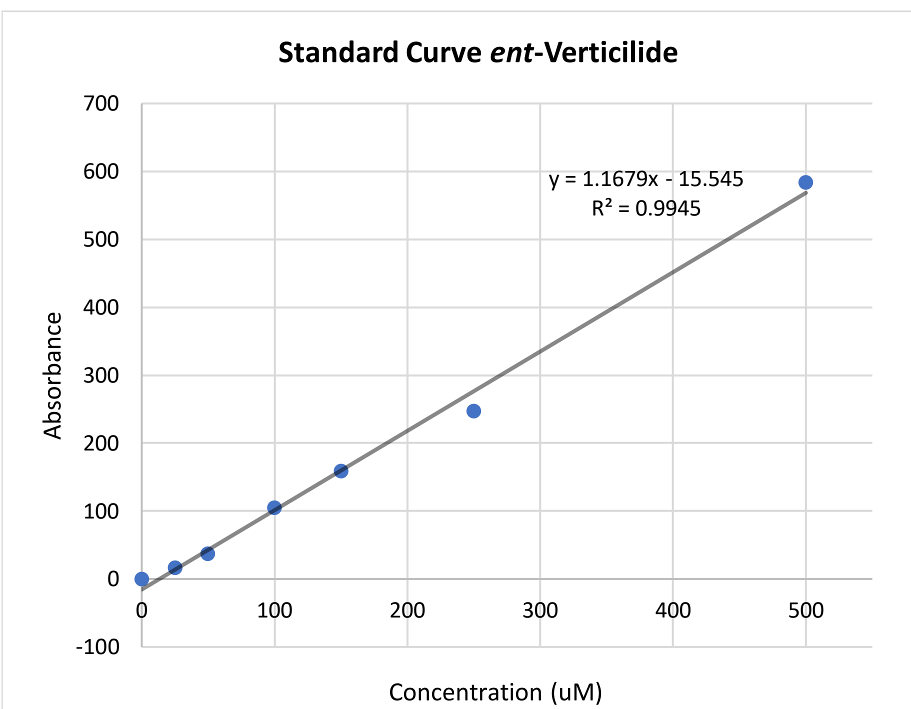
Exp	Ave. $logP_{app}$	Ave. logP	Well 1		Well 2		Well 3		Well 4		Well 5		Ave. [acc]
			[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	
1	-5.24	-9.00	137.13	294.39	156.71	332.05	109.93	380.22	150.20	310.31	139.99	305.40	
2	-5.13	-9.01	144.38	350.10	141.87	327.23	141.97	299.17	136.43	346.04	141.66	290.02	
3	-5.14	-8.99	128.70	322.90	136.90	283.18	123.79	295.27	128.35	294.44	129.00	307.89	
4	-5.14	-8.99	140.70	301.64	106.52	328.03	100.02	317.70	100.46	365.47	135.43	328.64	
5	-5.37	-9.17	102.73	327.69	98.16	381.51	105.23	334.48	108.92	271.94	140.94	346.20	127.56 ± 17.17 uM (26%)
6	-5.28	-9.21	141.38	289.87	94.39	323.10	144.66	284.12	141.48	295.46	91.72	294.34	
7	-5.26	-9.01	130.11	307.71	110.98	301.95	113.63	308.73	144.25	350.73	130.30	354.17	
8	-5.20	-9.03	133.07	348.96	119.98	375.87	159.32	323.79	151.74	321.96	115.39	360.24	
9	-5.19	-9.02	122.26	332.46	123.39	312.41	121.37	314.63	143.42	313.52	125.44	329.94	
10	-5.20	-9.00	147.93	304.65	125.61	312.06	124.96	337.91					

Supplement Table 8. Final Experimental Data for ent-Verticilide. *The mean calculated $LogP_{app}$ is -5.22 ± 0.07 cm/s, calculated using Supplement Equation **1**. The mean logP is -9.04 ± 0.08, calculated using Supplement Equation 2. The acceptor and donor well concentrations were calculated using a standard curve. The initial concentration is 500 uM for all experiments. The mean acceptor concentration is 128 uM, yielding a percent diffusion of 26%. The dark grey boxes in the table are unused. There was a total of 48 experiments (6 individual experiments x 8 replicates run in tandem). Definitions: [acc] = acceptor concentration after incubation, [donor] = donor concentration after incubation, mean [acc] = mean acceptor concentration ± standard deviation.*



Conc. (uM)	Area
500	25422.4
250	13857.9
150	8604.07
100	5690.66
50	2784.89
25	1389.67
0	0

Supplement Graph 3. *The standard curve for absorbance vs. concentration (uM) of ent-verticilide utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	583.193
250	247.036
150	158.758
100	104.47
50	37.2842
25	15.9836
0	0

Supplement Graph 4. *The standard curve for absorbance vs. concentration (uM) of ent-verticilide utilizing* ***ELSD*** *detection.*

b. Series 1: Acceptor Concentration, $LogP_{app}$ and LogP

Acceptor Concentration											
ent-vert		1.1		1.2		1.3		1.4		1.5	
137.13	**MPT-4-098 (UV)**	84.24	**MPT-4-090 (UV)**	88.57	**MPT-4-096 (UV)**	21.95	**MPT-5-091 (ELSD)**	23.15	**MPT-4-011 (ELSD)**	62.39	**MPT-5-092 (ELSD)**
144.38		99.21		92.89		21.95		21.14		54.35	
128.7		92.51		80.00		21.95		38.05		60.03	
140.7		106.35		94.37		21.95		32.12		69.66	
102.73		106.66		91.90		21.95		33.42		52.75	
141.38		89.86	**MPT-4-090 (ELSD)**	101.67		23.72	**MPT-5-091 (UV)**	26.24	**MPT-4-011 (UV)**	87.72	**MPT-5-092 (UV)**
130.11		83.09		67.68		23.72		18.03		51.08	
133.07		85.35		98.01		24.29		27.68		71.98	
122.26	**MPT-4-098 (ELSD)**	103.35		106.71	**MPT-4-096 (ELSD)**	22.58		36.01		64.95	
147.93		91.19		101.76		23.72		31.29		52.10	
156.71		85.35	**MPT-4-090 (UV)**	103.64		21.95	**MPT-5-097 (ELSD)**	22.52	**MPT-4-012 (ELSD)**	49.21	**MPT-5-098 (ELSD)**
141.87		98.58		97.75		21.95		18.70		47.24	
136.9		94.20		98.44		21.95		33.80		44.27	
106.52		97.18		101.43		21.95		28.04		53.80	
98.16		105.85		102.06		21.95		31.62		43.95	
94.39		95.63	**MPT-4-097 (ELSD)**	94.02		27.03	**MPT-5-097 (UV)**	7.65	**MPT-4-012 (ELSD)**	52.29	**MPT-5-098 (UV)**
110.98	**MPT-4-141 (UV)**	102.11		102.56	**MPT-4-097 (UV)**	27.03		2.97		56.14	
119.98		122.39		90.06		27.03		11.04		64.50	
123.39		108.21		105.15		27.03		16.22		58.20	
125.61		99.01		102.20		27.03		16.04		46.04	
109.93				105.06							
141.97		**97.52**	**Mean**	92.16		**23.12**	**Mean**	**28.47**	**Mean**	**57.49**	**Mean**
123.79		**9.85**	**Std Dev**	98.64		**1.44**	**Std Dev**	**6.37**	**Std Dev**	**10.49**	**Std Dev**
100.02				105.17							
105.23	**MPT-4-141 (ELSD)**			87.59	**MPT-4-097 (ELSD)**						
144.66				82.25							
113.63				70.25							
159.32				79.92							
121.37				84.24							
124.96				77.27							
150.2				81.85							
136.43				75.69							
128.35	**MPT-4-148 (UV)**										
100.46				**92.53**	**Mean**						
108.92				**10.99**	**Std Dev**						
141.48											
144.25											
151.74											
123.42											
139.99											
141.66	**MPT-4-148 (ELSD)**										
129.00											
135.43											
140.94											
91.72											
130.3											
115.39											
125.44											
127.56	**Mean**										
17.17	**Std Dev**										

Supplement Table 9. *Acceptor concentration experimental values for ent-vert and analogs in series 1 using all detection methods.*

LogP$_{app}$											
***ent*-vert**		**1.1**		**1.2**		**1.3**		**1.4**		**1.5**	
-5.15	**MPT-4-098 (UV)**	-6.49	**MPT-4-096 (UV)**	-5.30	**MPT-4-096 (UV)**	-5.87	**MPT-5-091 (ELSD)**	-6.29	**MPT-4-011 (ELSD)**	-5.49	**MPT-5-092 (ELSD)**
-5.14		-6.46		-5.32		-5.32		-5.66		-5.53	
-5.37		-6.44		-5.28		-5.88		-5.96		-5.50	
-5.13		-6.44		-5.32		-5.86		-6.07		-5.44	
-5.30		-6.44		-5.32		-5.83		-5.94		-5.50	
-5.21		-5.31	**MPT-4-096 (ELSD)**	-5.30		-5.96	**MPT-5-091 (UV)**	-5.93	**MPT-4-011 (UV)**	-5.43	**MPT-5-092 (UV)**
-5.25		-5.30		-5.30		-5.36		-5.79		-5.62	
-5.14		-5.30		-5.34		-5.96		-5.90		-5.48	
-5.19	**MPT-4-098 (ELSD)**	-5.24		-5.49	**MPT-4-096 (ELSD)**	-5.96		-5.85		-5.52	
-5.10		-5.27		-5.43		-5.96		-5.90		-5.58	
-5.19		-6.49	**MPT-4-097 (UV)**	-5.48		-5.85	**MPT-5-097 (ELSD)**	-6.18	**MPT-4-012 (ELSD)**	-5.59	**MPT-5-098 (ELSD)**
-5.11		-6.47		-5.44		-5.85		-5.59		-5.62	
-5.17		-6.48		-5.37		-5.82		-5.71		-5.61	
-5.15		-6.44		-5.31		-5.88		-6.07		-5.50	
-5.16		-6.44		-5.53		-5.86		-5.95		-5.58	
-5.12		-5.27	**MPT-4-097 (ELSD)**	-5.35		-5.30	**MPT-5-097 (UV)**	-5.82	**MPT-4-012 (ELSD)**	-5.61	**MPT-5-098 (UV)**
-5.35	**MPT-4-141 (UV)**	-5.29		-5.27	**MPT-4-097 (UV)**	-5.26		-6.42		-5.60	
-5.33		-5.17		-5.34		-5.27		-6.00		-5.68	
-5.39		-5.26		-5.32		-5.27		-5.81		-5.57	
-5.16		-5.26		-5.33		-5.29		-5.85		-5.57	
-5.36				-5.27							
-5.42		**-5.86**	**Mean**	-5.31		**-5.68**	**Mean**	**-5.93**	**Mean**	**-5.55**	**Mean**
-5.33		**0.61**	**Std Dev**	-5.34		**0.29**	**Std Dev**	**0.20**	**Std Dev**	**0.07**	**Std Dev**
-5.22				-5.29							
-5.24	**MPT-4-141 (ELSD)**			-5.51	**MPT-4-097 (ELSD)**						
-5.24				-5.45							
-5.44				-5.57							
-5.20				-5.52							
-5.23				-5.53							
-5.46				-5.46							
-5.25				-5.53							
-5.32				-5.52							
-5.26	**MPT-4-148 (UV)**										
-5.21				**-5.39**	**Mean**						
-5.26				**0.09**	**Std Dev**						
-5.24											
-5.32											
-5.12											
-5.14											
-5.32											
-5.22	**MPT-4-148 (ELSD)**										
-5.19											
-5.2											
-5.19											
-5.21											
-5.1											
-5.18											
-5.21											
-5.23	**Mean**										
0.09	**Std Dev**										

Supplement Table 10. *LogP$_{app}$ experimental values for ent-vert and analogs in series 1 using all detection methods, calculated using Supplement Equation 1.*

LogP											
ent-vert		1.1		1.2		1.3		1.4		1.5	
-8.98	MPT-4-098 (UV)	-9.19	MPT-4-096 (UV)	-9.10	MPT-4-096 (UV)	-9.84	MPT-5-091 (ELSD)	-9.81	MPT-4-011 (ELSD)	-9.37	MPT-5-092 (ELSD)
-8.91		-9.23		-9.13		-9.84		-9.85		-9.43	
-9.09		-9.22		-9.12		-9.84		-9.59		-9.38	
-8.93		-9.12		-9.15		-9.84		-9.66		-9.31	
-9.12		-9.19		-9.14		-9.84		-9.64		-9.44	
-8.95		-9.19	MPT-4-096 (ELSD)	-9.13		-9.80	MPT-5-091 (UV)	-9.75	MPT-4-011 (UV)	-9.21	MPT-5-092 (UV)
-9.04		-9.23		-9.13		-9.81		-9.92		-9.46	
-8.96		-9.22		-9.17		-9.79		-9.73		-9.30	
-8.98	MPT-4-098 (ELSD)	-9.12		-9.20	MPT-4-096 (ELSD)	-9.82		-9.61		-9.35	
-8.96		-9.19		-9.23		-9.80		-9.67		-9.30	
-9.01		-9.22	MPT-4-097 (UV)	-9.30		-9.84	MPT-5-097 (ELSD)	-9.82	MPT-4-012 (ELSD)	-9.48	MPT-5-098 (ELSD)
-8.98		-9.15		-9.24		-9.84		-9.90		-9.49	
-9.03		-9.17		-9.22		-9.84		-9.64		-9.52	
-9.01		-9.15		-9.26		-9.84		-9.72		-9.43	
-9.01		-9.11		-9.23		-9.84		-9.67		-9.53	
-8.97		-9.16	MPT-4-097 (ELSD)	-9.27		-9.10	MPT-5-097 (UV)	-10.3	MPT-4-012 (ELSD)	-9.45	MPT-5-098 (UV)
-9.09	MPT-4-141 (UV)	-9.13		-9.12	MPT-4-097 (UV)	-8.98		-10.7		-9.42	
-9.14		-9.04		-9.19		-8.99		-10.1		-9.52	
-9.13		-9.10		-9.11		-9.00		-9.97		-9.39	
-9		-9.15		-9.13		-9.01		-9.97		-9.42	
-9.12				-9.11							
-9.14		**-9.16**	**Mean**	-9.17		**-9.81**	**Mean**	**-9.89**	**Mean**	**-9.41**	**Mean**
-9.11		**0.05**	**Std Dev**	-9.14		**0.03**	**Std Dev**	**0.27**	**Std Dev**	**0.08**	**Std Dev**
-9.09				-9.11							
-8.97	MPT-4-141 (ELSD)			-9.20	MPT-4-097 (ELSD)						
-8.97				-9.23							
-9.16				-9.30							
-8.95				-9.24							
-8.99				-9.22							
-9.18				-9.26							
-9.00				-9.23							
-9.21				-9.27							
-9.07	MPT-4-148 (UV)										
-8.95				**-9.19**	**Mean**						
-9				**0.06**	**Std Dev**						
-8.99											
-9.05											
-8.9											
-8.93											
-9.06											
-9.04	MPT-4-148 (ELSD)										
-9.03											
-9.04											
-9.03											
-9.02											
-8.93											
-9.02											
-9.03											
-9.03	**Mean**										
0.07	**Std Dev**										

Supplement Table 11. *LogP experimental values for ent-vert and analogs in series 1 using all detection methods, calculated using Supplement Equation 2.*

c. Series 1: Variables from Calculations and Percent Recoveries

Cmpd	MW (g/mol)	Ave RT (min)	C ($x10^{-9}$)	Well 1		Well 2		Well 3		Well 4		Well 5		Ave. %R
				%T	%R	%T	%R	%T	%R	%T	%R	%T	%R	
1.1	839.08	12.60	3.23	0.57	88	0.58	80	0.58	82	0.63	87	0.62	82	91.45 ± 6.80
1.1			3.24	0.54	98	0.59	101	0.62	89	0.62	99	0.62	99	
1.1			3.23	0.61	86	0.59	94	0.69	88	0.61	93	0.61	87	
1.1			3.23	0.55	97	0.58	100	0.57	101	0.62	91	0.63	87	
1.2	825.05	10.55	3.28	0.43	95	0.47	89	0.44	83	0.46	93	0.52	80	87.72 ± 5.66
1.2			3.27	0.57	80	0.40	76	0.54	83	0.58	92	0.56	92	
1.2			3.28	0.60	86	0.56	88	0.56	88	0.58	88	0.58	87	
1.2			3.28	0.59	88	0.41	98	0.47	81	0.39	85	0.42	89	
1.2			3.27	0.40	97	0.45	77	0.40	93	0.41	84	0.61	83	
1.2			3.27	0.54	85	0.56	94	0.55	94	0.62	85	0.57	94	
1.2			3.23	0.50	91	0.44	89							
1.3	825.05	12.28	3.24	0.17	95	0.18	90	0.17	90	0.17	94	0.17	94	91.15 ± 3.10
1.3			3.23	0.22	93	0.20	90	0.21	95	0.22	91	0.23	84	
1.3			3.18	0.58	93	0.62	91	0.61	91	0.61	90	0.59	94	
1.3			3.23	0.22	89	0.22	90	0.23	84	0.21	94	0.22	91	
1.4	811.03	11.80	3.28	0.09	96	0.32	90	0.17	96	0.14	98	0.18	77	90.65 ± 7.88
1.4			3.28	0.19	84	0.24	78	0.20	80	0.22	93	0.20	90	
1.4			3.27	0.11	73	0.35	94	0.29	98	0.14	97	0.18	93	
1.4			3.28	0.14	96	0.46	90	0.22	96	0.20	97	0.24	97	
1.5	797.00	12.32	3.23	0.48	99	0.34	89	0.44	89	0.41	88	0.44	85	87.35 ± 4.65
1.5			3.24	0.43	88	0.41	84	0.43	86	0.48	77	0.43	86	
1.5			3.23	0.53	91	0.46	88	0.50	90	0.51	83	0.46	83	
1.5			3.24	0.36	93	0.35	92	0.35	89	0.42	83	0.37	84	

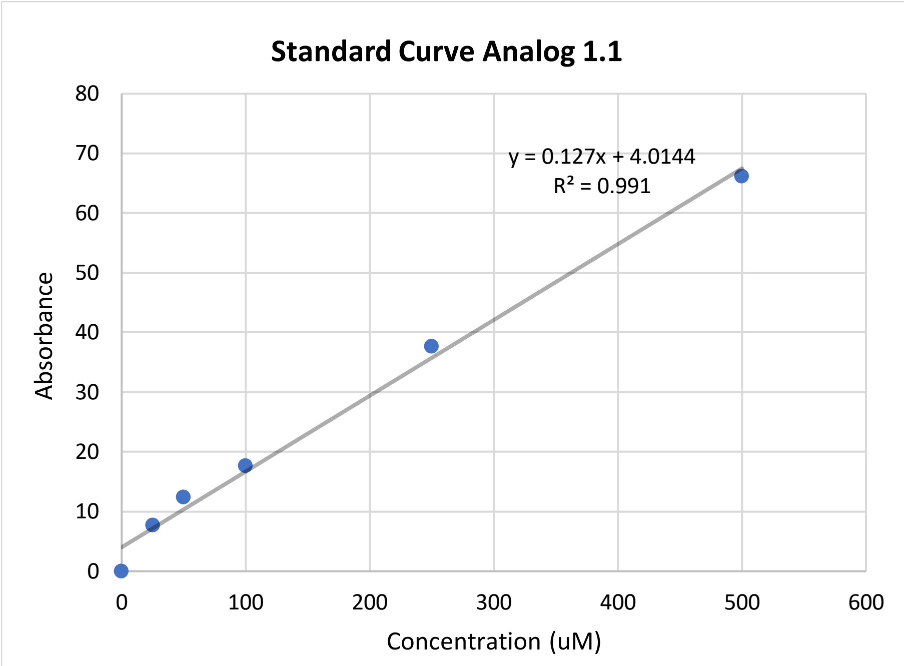
Supplement Table 12. Series 1 Variables from Calculations. *Analog 1.1 data is comprised of 4 experiments, each with 5 replicates run in tandem (20 total). Analog 1.2 data is comprised of 4 experiments each, with 8 replicates run in tandem (32 total). The dark grey boxes were unused. Analog 1.3 data is comprised of 4 total experiments, each with 5 replicates run in tandem (20 total). Analog 1.4 and 1.5 were subjected to 4 experiments each, with 5 replicates run in tandem (20 total each). The molecular weights and the mean retention time seen via HPLC (210 nm) are listed. The C values and %T values are calculated using Supplement Equation **1**. The mean percent recoveries are listed. Definitions: MW = molecular weight, RT = retention time, %R = % recovery, Ave %R = mean ± standard deviation.*

Cmpd	Ave. $logP_{app}$	Ave. logP	Well 1		Well 2		Well 3		Well 4		Well 5		Ave. [acc]
			[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	
1.1	-5.29	-9.19	89.86	348.27	83.09	317.20	85.35	326.37	103.35	329.65	91.19	316.78	97.52 ± 9.85 uM (20%)
1.1	-5.29	-9.15	84.24	405.86	99.21	405.83	92.51	352.93	106.35	391.63	106.66	390.98	
1.1	-5.25	-9.12	95.63	332.48	102.11	366.64	122.39	315.35	108.21	357.23	99.01	333.52	
1.1	-5.29	-9.16	85.35	399.02	98.58	414.89	94.20	411.12	97.18	361.22	105.85	383.02	
1.2	-9.19	-5.42	88.57	387.42	92.89	353.80	80.00	334.42	94.37	371.51	91.90	307.53	92.53 ± 10.99 uM (19%)
1.2	-9.19	-5.41	101.67	299.11	67.68	311.11	98.01	314.82	106.71	351.67	101.76	357.46	
1.2	-9.13	-5.31	103.64	323.81	97.75	343.38	98.44	339.78	101.43	336.40	102.06	335.25	
1.2	-9.14	-5.32	94.02	345.08	87.59	402.58	82.25	322.93	70.25	353.96	79.92	364.38	
1.2	-9.24	-5.51	84.24	402.98	77.27	308.10	81.85	386.71	75.69	345.88	102.56	314.47	
1.2	-9.14	-5.31	90.06	334.19	105.15	366.92	102.20	367.75	105.06	321.07	92.16	375.72	
1.2	-9.14	-5.30	98.64	356.60	105.17	340.35							
1.3	-5.96	-9.81	23.72	452.14	23.72	427.88	24.29	428.34	22.58	445.33	23.72	448.86	23.11 ± 1.44 uM (5%)
1.3	-5.86	-9.84	21.95	442.78	21.95	427.54	21.95	455.30	21.95	433.69	21.95	399.49	
1.3	-5.93	-9.78	23.50	441.53	25.68	428.47	26.22	429.02	23.77	427.38	25.68	444.18	
1.3	-5.85	-9.84	21.95	424.85	21.95	427.93	21.95	394.97	21.95	450.63	21.95	433.14	
1.4	-5.91	-9.71	23.15	455.24	21.14	94.82	38.05	444.12	32.12	455.90	33.42	352.16	27.62 ± 9.77 uM (5%)
1.4	-5.86	-9.74	26.24	391.65	18.03	370.15	27.68	370.40	36.01	426.97	31.29	418.57	
1.4	-6.18	-9.75	22.52	340.71	18.70	451.56	33.80	455.93	28.04	459.40	31.62	431.62	
1.4	-5.94	-9.71	23.15	455.24	21.14	427.82	38.05	444.12	32.12	455.90	33.22	452.16	
1.5	-5.50	-9.32	87.72	405.48	51.08	393.46	71.98	375.42	64.95	376.26	52.10	371.98	57.14 ± 10.79 uM (11%)
1.5	-5.49	-9.39	62.39	377.92	54.35	367.84	60.03	371.36	69.66	358.54	52.75	334.29	
1.5	-5.41	-9.24	52.29	360.96	56.14	372.81	64.50	365.68	58.20	333.88	46.04	373.76	
1.5	-5.58	-9.49	49.21	418.16	47.24	432.70	44.27	402.27	53.80	359.31	43.95	378.52	

Supplement Table 13. Final Experimental Data for Series 1. *The mean $logP_{app}$ (calculated from Supplement Equation **1**) and logP values (calculated from Supplement Equation 2) are listed. The acceptor and donor concentrations are calculated using a standard curve and the units are uM, and the initial concentration is 500 uM for all experiments. The total mean acceptor concentration and percent diffusion (in parentheses) are listed in the final column. The dark grey boxes for analog 1.2 are unused (32 total experiments total). Definitions: [acc] = acceptor concentration after incubation, [donor] = donor concentration after incubation, Ave. [acc] = mean acceptor concentration ± standard deviation.*

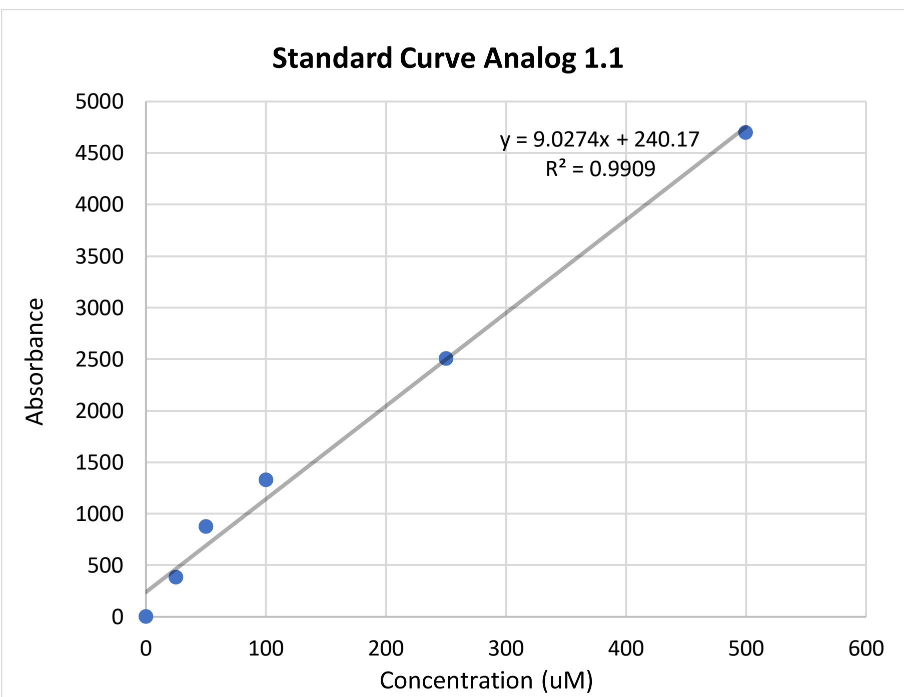
d. Standard Curves for Series 1

Analog 1.1



Conc. (uM)	Area
500	66.132
250	37.6433
100	17.6377
50	12.39
25	7.7168
0	0

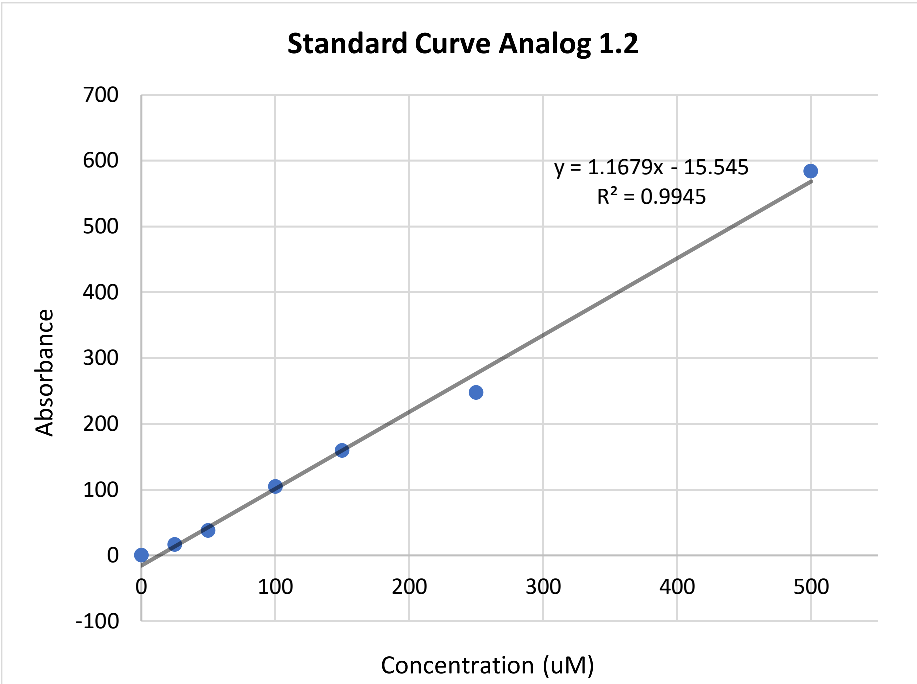
Supplement Graph 5. *The standard curve for absorbance vs. concentration (uM) of analog 1.1 utilizing* ***ELSD detection****.*



Conc. (uM)	Area
500	4698.31
250	2505.02
100	1329.35
50	876.23
25	382.507
0	0

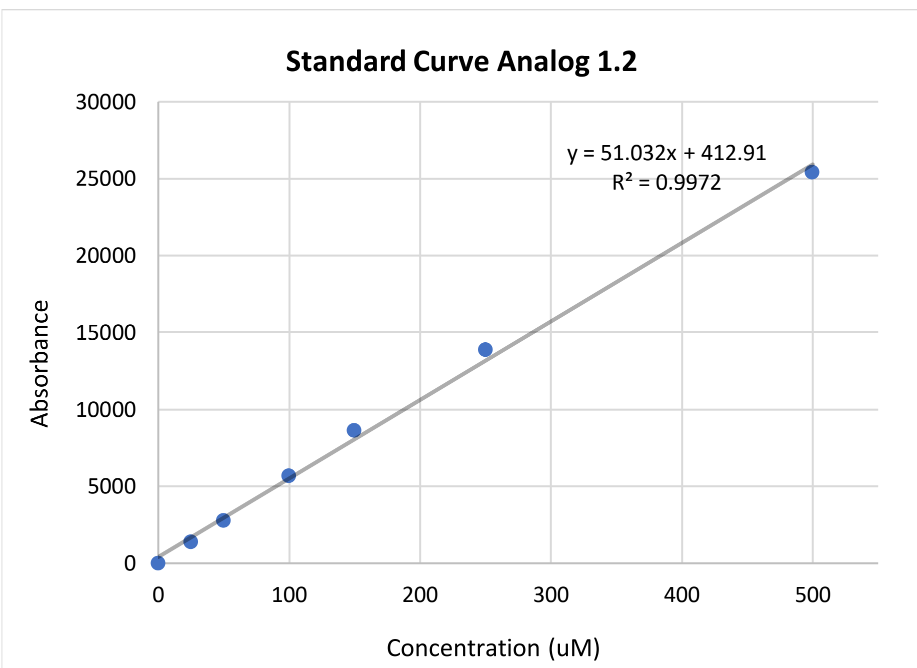
Supplement Graph 6. *The standard curve for absorbance vs. concentration (uM) of analog 1.1 utilizing* ***UV detection*** *(210 nm).*

Analog 1.2



Conc. (uM)	Area
500	583.193
250	247.036
150	158.758
100	104.47
50	37.2842
25	15.9836
0	0

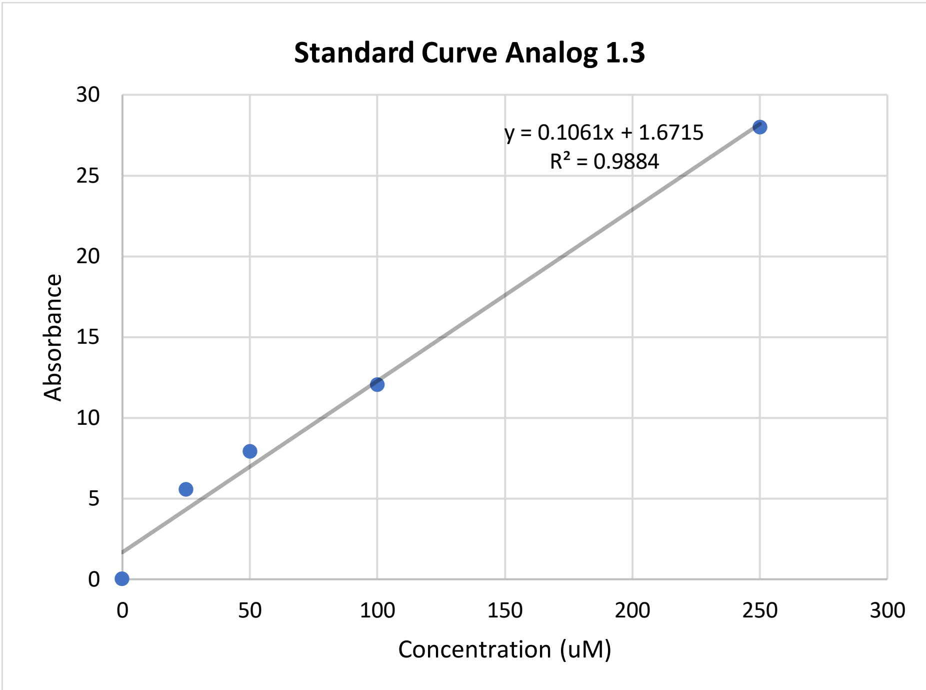
Supplement Graph 7. *The standard curve for absorbance vs. concentration (uM) of analog 1.2 utilizing* ***ELSD detection.***



Conc. (uM)	Area
500	25422.4
250	13857.9
150	8604.07
100	5690.66
50	2784.89
25	1389.67
0	0

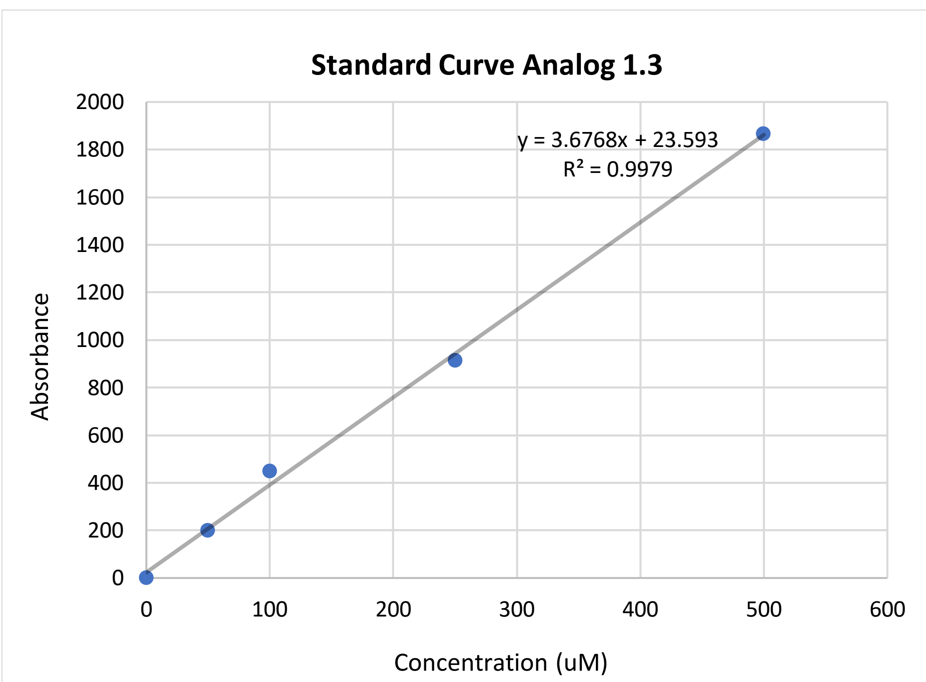
Supplement Graph 8. *The standard curve for absorbance vs. concentration (uM) of analog 1.2 utilizing* ***UV detection*** *(210 nm).*

Analog 1.3



Conc. (uM)	Area
500	58.6659
250	27.99
100	12.0189
50	7.901
25	5.532
0	0

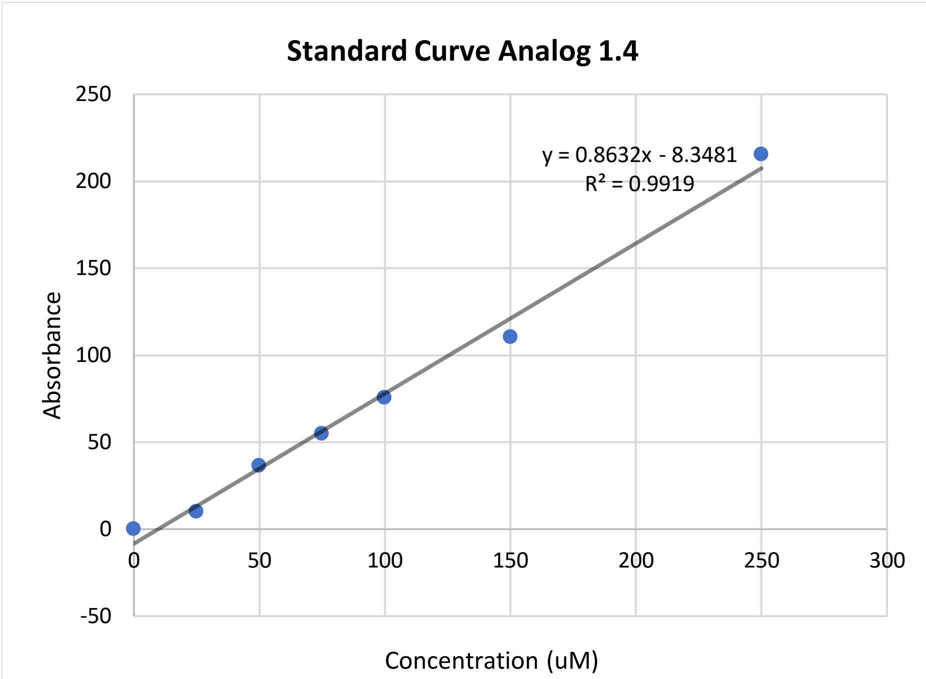
Supplement Graph 9. *The standard curve for absorbance vs. concentration (uM) of analog 1.3 utilizing **ELSD detection.***



Conc. (uM)	Area
500	1865.84
250	913.992
100	448.012
50	199.2
0	0

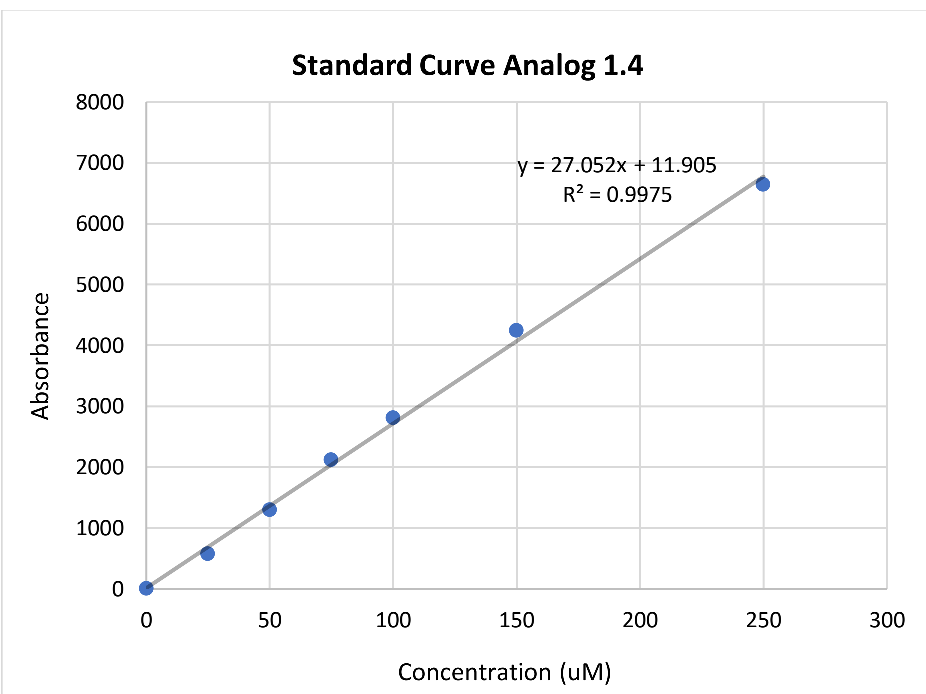
Supplement Graph 10. *The standard curve for absorbance vs. concentration (uM) of analog 1.3 utilizing **UV detection** (210 nm).*

Analog 1.4



Conc. (uM)	Area
250	262.182
200	221
150	165
100	110
75	79.226
50	36.2222
25	10.1405
0	0

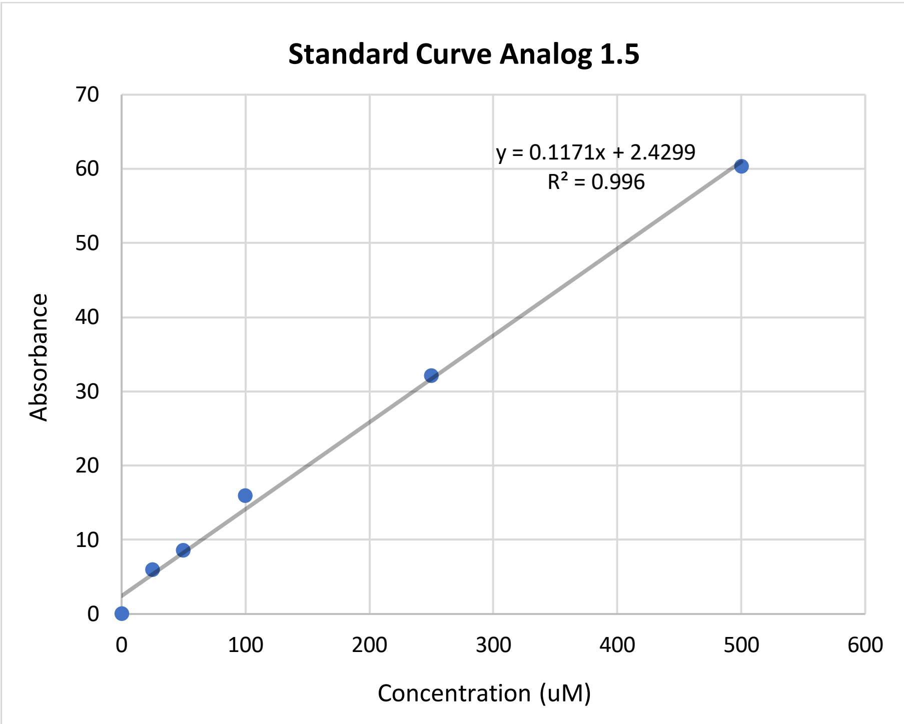
Supplement Graph 11. *The standard curve for absorbance vs. concentration (uM) of analog 1.4 utilizing* ***ELSD detection.***



Conc. (uM)	Area
250	6639.55
150	4242.1
100	2802.53
75	2118.98
50	1294.82
25	568.899
0	0

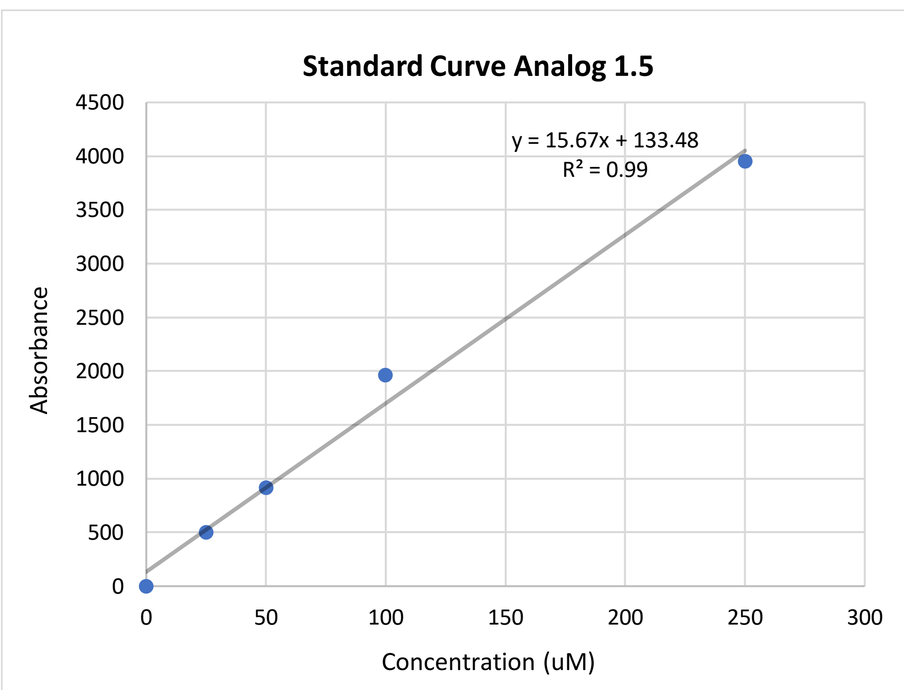
Supplement Graph 12. *The standard curve for absorbance vs. concentration (uM) of analog 1.4 utilizing* ***UV detection*** *(210 nm).*

Analog 1.5



Conc. (uM)	Area
500	60.33
250	32.1199
100	15.9528
50	8.5339
25	5.9225
0	0

Supplement Graph 13. *The standard curve for absorbance vs. concentration (uM) of analog 1.5 utilizing* ***ELSD detection.***



Conc. (uM)	Area
250	3948.8
100	1962.74
50	916.65
25	499
0	0

Supplement Graph 14. *The standard curve for absorbance vs. concentration (uM) of analog 1.5 utilizing* ***UV detection*** *(210 nm).*

e. Statistical Analysis Series 1

LogPapp			Percent Diffusion			LogP		
Pair	P-value	Inference	Pair	P-value	Inference	Pair	P-value	Inference
A vs B	1.64E-8	**	A vs B	0.0183	*	A vs B	0.00133	**
A vs C	1.89E-5	**	A vs C	1.22E-4	**	A vs C	3.26E-6	**
A vs D	1.94E-9	**	A vs D	4.39E-19	**	A vs D	4.54E-12	**
A vs E	1.24E-16	**	A vs E	1.46E-18	**	A vs E	1.65E-19	**
A vs F	9.47E-9	**	A vs F	4.26E-10	**	A vs F	1.89E-11	**
B vs C	1.0	NS	B vs C	1.0	NS	B vs C	1.0	NS
B vs D	1.0	NS	B vs D	7.00E-6	**	B vs D	0.0680	NS
B vs E	0.530	NS	B vs E	1.23E-5	**	B vs E	8.05E-5	**
B vs F	1.0	NS	B vs F	0.0598	NS	B vs F	0.112	NS
C vs D	0.507	NS	C vs D	7.03E-6	**	C vs D	0.117	NS
C vs E	5.06E-4	**	C vs E	1.31E-5	**	C vs E	7.78E-5	**
C vs F	0.875	NS	C vs F	0.124	NS	C vs F	0.199	NS
D vs E	1.0	NS	D vs E	1.0	NS	D vs E	1.0	NS
D vs F	1.0	NS	D vs F	0.461	NS	D vs F	1.0	NS
E vs F	0.634	NS	E vs F	0.604	NS	E vs F	0.913	NS

Supplement Table 14. Data Analysis for Series 1. *Kruskal-Wallis test with Dunn's multiple comparisons post hoc analysis using GraphPad Prism v10.1.1. Definitions: A = ent-verticilide, B = 1.1, C = 1.2, D = 1.3, E = 1.4, F = 1.5 and ** $p < 0.01$, * $p < 0.05$, NS = not significant.*

f. Series 2: Acceptor Concentration, $LogP_{app}$ and LogP

Acceptor Concentration											
***ent*-vert**		**2.1**		**2.2**		**2.3**		**2.4**		**2.5**	
137.13	**MPT-4-098 (UV)**	157.96	**MPT-5-109 (UV)**	155.43	**MPT-5-119 (UV)**	145.68	**MPT-5-143 (ELSD)**	81.99	**MPT-5-134 (MS)**	83.50	**MPT-5-129 (ELSD)**
144.38		157.26		161.52		131.55		78.79		89.39	
128.7		160.13		152.32		124.46		74.20		91.58	
140.7		154.26		147.77		125.36		67.85		96.13	
102.73		154.94		145.18		124.24		73.48		92.96	
141.38		119.85	**MPT-5-109 (ELSD)**	164.59	**MPT-5-119 (ELSD)**	117.64	**MPT-5-143 (UV)**	101.28	**MPT-5-134 (UV)**	99.38	**MPT-5-129 (UV)**
130.11		156.14		163.85		128.36		86.95		115.70	
133.07		168.56		156.21		135.24		87.57		100.79	
122.26	**MPT-4-098 (ELSD)**	171.88		137.44		128.27		81.86		103.19	
147.93		169.30		152.60		138.44		92.97		115.29	
156.71		192.18	**MPT-5-119 (UV)**	189.23	**MPT-5-125 (UV)**	108.39	**MPT-5-143 (MS)**	108.76	**MPT-5-135 (MS)**	71.30	**MPT-5-129 (MS)**
141.87		193.02		183.57		100.51		104.76		69.52	
136.9		201.37		169.70		81.88		106.75		66.92	
106.52		196.32		178.46		84.35		104.68		70.93	
98.16		193.76		165.14		80.77		108.47		69.28	
94.39		207.95	**MPT-5-119 (ELSD)**	158.41	**MPT-5-125 (ELSD)**	136.41	**MPT-5-144 (ELSD)**	109.80	**MPT-5-135 (UV)**	80.44	**MPT-5-030 (ELSD)**
110.98	**MPT-4-141 (UV)**	188.63		152.88		131.34		98.01		75.82	
119.98		181.68		148.58		124.22		97.59		89.06	
123.39		191.76		149.50		116.18		83.73		94.85	
125.61		188.77		149.22		116.45		87.57		89.83	
109.93		203.78	**MPT-5-120 (UV)**			134.02	**MPT-5-144 (UV)**	86.02	**MPT-5-142 (MS)**	99.14	**MPT-5-130 (UV)**
141.97		224.03		**159.08**	**Mean**	133.44		99.84		103.11	
123.79		172.21		**13.24**	**Std Dev**	127.46		95.92		91.18	
100.02		208.83				112.79		83.82		102.37	
105.23	**MPT-4-141 (ELSD)**	197.12				124.65		84.81		115.12	
144.66		224.65	**MPT-5-120 (ELSD)**			87.76	**MPT-5-144 (MS)**	109.87	**MPT-5-142 (UV)**	68.15	**MPT-5-130 (MS)**
113.63		208.33				121.13		109.08		73.16	
159.32		216.77				115.64		112.92		72.44	
121.37		164.48				103.77		93.22		74.67	
124.96		223.02				101.19		77.16		75.92	
150.2						135.63	**MPT-5-145 (ELSD)**			88.53	**MPT-5-131 (ELSD)**
136.43		**184.96**	**Mean**			129.80		**92.99**	**Mean**	91.07	
128.35	**MPT-4-148 (UV)**	**21.82**	**Std Dev**			125.12		**12.85**	**Std Dev**	92.98	
100.46						118.24				99.06	
108.92						112.53				86.01	
141.48						116.97	**MPT-5-145 (UV)**			107.84	**MPT-5-131 (UV)**
144.25						121.47				99.08	
151.74						123.60				75.07	
123.42						114.84				83.98	
139.99						115.66				93.56	
141.66	**MPT-4-148 (ELSD)**					88.47	**MPT-5-145 (MS)**			72.93	**MPT-5-131 (MS)**
129.00						118.22				72.08	
135.43						119.91				70.51	
140.94						99.25				75.49	
91.72						103.02				77.42	
130.3											
115.39						**117.43**	**Mean**			**87.26**	**Mean**
125.44						**15.74**	**Std Dev**			**13.92**	**Std Dev**
127.56	**Mean**										
17.17	**Std Dev**										

Supplement Table 15. *Acceptor concentration experimental values for ent-vert and analogs in series 2 using all detection methods.*

LogP$_{app}$											
***ent*-vert**		**2.1**		**2.2**		**2.3**		**2.4**		**2.5**	
-5.15	**MPT-4-098 (UV)**	-4.75	**MPT-5-109 (UV)**	-5.12	**MPT-5-119 (UV)**	-5.12	**MPT-5-143 (ELSD)**	-5.50	**MPT-5-134 (MS)**	-5.37	**MPT-5-129 (ELSD)**
-5.14		-4.85		-5.10		-5.13		-5.50		-5.37	
-5.37		-4.95		-5.08		-5.21		-5.53		-5.37	
-5.13		-4.88		-5.10		-5.19		-5.56		-5.33	
-5.30		-4.88		-5.07		-5.20		-5.54		-5.34	
-5.21		-5.13	**MPT-5-109 (ELSD)**	-4.98	**MPT-5-119 (ELSD)**	-5.24	**MPT-5-143 (UV)**	-5.31	**MPT-5-134 (UV)**	-5.33	**MPT-5-129 (UV)**
-5.25		-5.03		-5.01		-5.22		-5.41		-5.27	
-5.14		-4.93		-5.05		-5.19		-5.40		-5.32	
-5.19	**MPT-4-098 (ELSD)**	-4.99		-5.10		-5.22		-5.38		-5.31	
-5.10		-5.00		-5.07		-5.18		-5.30		-5.26	
-5.19		-4.68	**MPT-5-119 (UV)**	-4.87	**MPT-5-125 (UV)**	-5.29	**MPT-5-143 (MS)**	-5.35	**MPT-5-135 (MS)**	-5.49	**MPT-5-129 (MS)**
-5.11		-4.92		-4.89		-5.35		-5.34		-5.52	
-5.17		-4.86		-4.99		-5.42		-5.28		-5.57	
-5.15		-4.87		-5.01		-5.39		-5.37		-5.51	
-5.16		-4.87		-5.04		-5.37		-5.30		-5.55	
-5.12		-4.82	**MPT-5-119 (ELSD)**	-5.00	**MPT-5-125 (ELSD)**	-5.12	**MPT-5-144 (ELSD)**	-5.27	**MPT-5-135 (UV)**	-5.99	**MPT-5-030 (ELSD)**
-5.35	**MPT-4-141 (UV)**	-4.85		-5.05		-5.13		-5.32		-6.01	
-5.33		-4.95		-5.08		-5.16		-5.31		-5.95	
-5.39		-4.88		-5.06		-5.22		-5.42		-5.91	
-5.16		-4.88		-5.08		-5.21		-5.38		-5.94	
-5.36		-4.79	**MPT-5-120 (UV)**			-5.15	**MPT-5-144 (UV)**	-5.37	**MPT-5-142 (MS)**	-5.33	**MPT-5-130 (UV)**
-5.42		-4.59		**-5.04**	**Mean**	-5.18		-5.31		-5.31	
-5.33		-4.86		**0.06**	**Std Dev**	-5.20		-5.33		-5.35	
-5.22		-4.73				-5.25		-5.38		-5.32	
-5.24	**MPT-4-141 (ELSD)**	-4.74				-5.20		-5.39		-5.26	
-5.24		-4.82	**MPT-5-120 (ELSD)**			-5.37	**MPT-5-144 (MS)**	-4.98	**MPT-5-142 (UV)**	-5.53	**MPT-5-130 (MS)**
-5.44		-4.79				-5.21		-5.01		-5.53	
-5.20		-4.86				-5.29		-5.05		-5.56	
-5.23		-4.84				-5.33		-5.10		-5.53	
-5.46		-4.91				-5.31		-5.07		-5.53	
-5.25						-5.11	**MPT-5-145 (ELSD)**			-5.95	**MPT-5-131 (ELSD)**
-5.32		**-4.90**	**Mean**			-5.16		**-5.39**	**Mean**	-5.94	
-5.26	**MPT-4-148 (UV)**	**0.10**	**Std Dev**			-5.17		**0.09**	**Std Dev**	-5.93	
-5.21						-5.21				-5.90	
-5.26						-5.21				-5.96	
-5.24						-5.29	**MPT-5-145 (UV)**			-5.25	**MPT-5-131 (UV)**
-5.32						-5.25				-5.30	
-5.12						-5.25				-5.41	
-5.14						-5.26				-5.36	
-5.32						-5.28				-5.33	
-5.22	**MPT-4-148 (ELSD)**					-5.36	**MPT-5-145 (MS)**			-5.45	**MPT-5-131 (MS)**
-5.19						-5.22				-5.54	
-5.2						-5.25				-5.56	
-5.19						-5.35				-5.52	
-5.21						-5.33				-5.44	
-5.1											
-5.18						**-5.24**	**Mean**			**-5.50**	**Mean**
-5.21						**0.08**	**Std Dev**			**0.23**	**Std Dev**
-5.23	**Mean**										
0.09	**Std Dev**										

Supplement Table 16. *LogP$_{app}$ experimental values for ent-vert and analogs in series 2 using all detection methods, calculated using Supplement Equation 1.*

LogP											
***ent*-vert**		**2.1**		**2.2**		**2.3**		**2.4**		**2.5**	
-8.98	**MPT-4-098 (UV)**	-8.91	**MPT-5-109 (UV)**	-8.92	**MPT-5-119 (UV)**	-8.95	**MPT-5-143 (ELSD)**	-9.24	**MPT-5-134 (MS)**	-9.23	**MPT-5-129 (ELSD)**
-8.91		-8.91		-8.90		-9.01		-9.26		-9.20	
-9.09		-8.90		-8.93		-9.03		-9.28		-9.18	
-8.93		-8.92		-8.94		-9.03		-9.33		-9.16	
-9.12		-8.92		-8.95		-9.03		-9.29		-9.18	
-8.95		-9.05	**MPT-5-109 (ELSD)**	-8.89	**MPT-5-119 (ELSD)**	-9.06	**MPT-5-143 (UV)**	-9.14	**MPT-5-134 (UV)**	-9.15	**MPT-5-129 (UV)**
-9.04		-8.92		-8.89		-9.02		-9.21		-9.07	
-8.96		-8.88		-8.92		-8.99		-9.21		-9.14	
-8.98	**MPT-4-098 (ELSD)**	-8.86		-8.98		-9.02		-9.24		-9.13	
-8.96		-8.87		-8.93		-8.98		-9.18		-9.07	
-9.01		-8.80	**MPT-5-119 (UV)**	-9.00	**MPT-5-125 (UV)**	-9.10	**MPT-5-143 (MS)**	-9.10	**MPT-5-135 (MS)**	-9.30	**MPT-5-129 (MS)**
-8.98		-8.80		-8.90		-9.14		-9.12		-9.31	
-9.03		-8.78		-8.93		-9.24		-9.11		-9.33	
-9.01		-8.79		-8.94		-9.22		-9.12		-9.30	
-9.01		-8.80		-8.95		-9.24		-9.10		-9.32	
-8.97		-8.76	**MPT-5-119 (ELSD)**	-8.91	**MPT-5-125 (ELSD)**	-8.99	**MPT-5-144 (ELSD)**	-9.10	**MPT-5-135 (UV)**	-9.25	**MPT-5-030 (ELSD)**
-9.09	**MPT-4-141 (UV)**	-8.81		-8.93		-9.01		-9.15		-9.27	
-9.14		-8.84		-8.94		-9.03		-9.15		-9.20	
-9.13		-8.80		-8.94		-9.07		-9.23		-9.17	
-9		-8.81		-8.94		-9.07		-9.20		-9.19	
-9.12		-8.77	**MPT-5-120 (UV)**			-9.00	**MPT-5-144 (UV)**	-9.21	**MPT-5-142 (MS)**	-9.15	**MPT-5-130 (UV)**
-9.14		-8.72		**-8.93**	**Mean**	-9.00		-9.14		-9.13	
-9.11		-8.86		**0.03**	**Std Dev**	-9.02		-9.16		-9.19	
-9.09		-8.76				-9.08		-9.23		-9.13	
-8.97	**MPT-4-141 (ELSD)**	-8.79				-9.03		-9.22		-9.07	
-8.97		-8.72	**MPT-5-120 (ELSD)**			-9.21	**MPT-5-144 (MS)**	-9.10	**MPT-5-142 (UV)**	-9.32	**MPT-5-130 (MS)**
-9.16		-8.76				-9.05		-9.10		-9.29	
-8.95		-8.74				-9.07		-9.08		-9.30	
-8.99		-8.89				-9.12		-9.17		-9.28	
-9.18		-8.72				-9.13		-9.26		-9.27	
-9.00						-8.99	**MPT-5-145 (ELSD)**			-9.20	**MPT-5-131 (ELSD)**
-9.21		**-8.86**	**Mean**			-9.01		**-9.19**	**Mean**	-9.19	
-9.07	**MPT-4-148 (UV)**	**0.07**	**Std Dev**			-9.03		**0.07**	**Std Dev**	-9.18	
-8.95						-9.06				-9.15	
-9						-9.08				-9.21	
-8.99						-9.06	**MPT-5-145 (UV)**			-9.11	**MPT-5-131 (UV)**
-9.05						-9.05				-9.15	
-8.9						-9.04				-9.28	
-8.93						-9.07				-9.22	
-9.06						-9.07				-9.17	
-9.04	**MPT-4-148 (ELSD)**					-9.20	**MPT-5-145 (MS)**			-9.29	**MPT-5-131 (MS)**
-9.03						-9.06				-9.30	
-9.04						-9.05				-9.31	
-9.03						-9.14				-9.28	
-9.02						-9.13				-9.26	
-8.93											
-9.02						**-9.06**	**Mean**			**-9.21**	**Mean**
-9.03						**0.08**	**Std Dev**			**0.08**	**Std Dev**
-9.03	**Mean**										
0.07	**Std Dev**										

Supplement Table 17. *LogP experimental values for ent-vert and analogs in series 2 using all detection methods, calculated using Supplement Equation 2.*

g. Series 2: Experimental Variables from Calculations and Percent Recoveries

Cmpd	MW (g/mol)	Ave RT (min)	C ($x10^{-9}$)	Well 1		Well 2		Well 3		Well 4		Well 5		Ave. %R
				%T	%R	%T	%R	%T	%R	%T	%R	%T	%R	
2.1			3.20	0.31	89	0.31	85	0.36	83	0.33	86	0.30	90	
2.1			3.22	0.49	79	0.55	88	0.61	84	0.58	91	0.58	91	
2.1	851.56	11.68	3.24	0.30	89	0.34	87	0.38	93	0.35	91	0.35	90	87.90 ± 4.33
2.1			3.21	0.40	80	0.41	95	0.33	94	0.35	92	0.37	91	
2.1			3.13	0.75	86	0.74	82	0.73	87	0.60	86	0.70	96	
2.1			3.23	0.41	90	0.40	87	0.49	81	0.48	89	0.39	85	
2.2			2.70	0.83	86	0.82	88	0.78	89	0.76	83	0.77	89	
2.2	851.14	11.55	2.91	0.67	98	0.71	99	0.70	92	0.81	86	0.77	92	88.55 ± 5.55
2.2			2.79	0.70	81	0.80	80	0.67	87	0.68	84	0.79	84	
2.2			2.89	0.55	92	0.76	90	0.78	88	0.60	84	0.65	99	
2.3			2.69	0.59	91	0.54	95	0.49	89	0.51	86	0.52	80	
2.3			2.69	0.73	94	0.72	87	0.66	93	0.68	91	0.67	92	
2.3			2.68	0.64	89	0.65	94	0.67	95	0.65	95	0.69	96	
2.3			2.69	0.53	85	0.66	88	0.60	96	0.56	94	0.57	88	
2.3	851.14	11.06	2.63	0.71	88	0.69	91	0.67	91	0.63	88	0.67	89	90.44 ± 3.85
2.3			2.70	0.73	89	0.73	86	0.70	87	0.65	89	0.66	89	
2.3			2.99	0.54	84	0.65	87	0.63	93	0.55	92	0.56	94	
2.3			2.90	0.60	98	0.63	95	0.63	96	0.62	91	0.60	95	
2.3			2.77	0.74	87	0.70	90	0.70	88	0.66	89	0.66	86	
2.4			3.13	0.43	98	0.43	95	0.40	95	0.38	93	0.40	96	
2.4			3.14	0.58	89	0.49	94	0.50	93	0.52	83	0.58	81	
2.4	850.16	11.37	3.04	0.55	97	0.55	93	0.60	85	0.53	97	0.58	90	88.67 ± 5.54
2.4			3.04	0.61	89	0.57	88	0.58	85	0.49	92	0.52	88	
2.4			3.10	0.53	80	0.58	83	0.56	84	0.52	80	0.51	83	
2.4			3.11	0.83	83	0.81	84	0.79	85	0.75	86	0.77	91	
2.5			3.04	0.52	82	0.53	86	0.53	88	0.56	85	0.55	86	
2.5			3.05	0.56	86	0.61	91	0.57	86	0.58	87	0.62	88	
2.5			3.05	0.43	83	0.41	86	0.38	91	0.42	86	0.39	83	
2.5			3.09	0.40	86	0.41	92	0.39	80	0.41	93	0.40	81	
2.5	849.17	11.29	3.05	0.56	86	0.58	87	0.54	83	0.57	88	0.62	80	86.16 ± 4.79
2.5			3.04	0.17	91	0.16	90	0.18	92	0.19	90	0.18	81	
2.5			3.05	0.46	79	0.40	92	0.38	95	0.41	93	0.48	82	
2.5			3.06	0.37	82	0.41	82	0.50	76	0.47	78	0.44	80	
2.5			3.05	0.18	92	0.18	91	0.18	92	0.20	89	0.18	80	

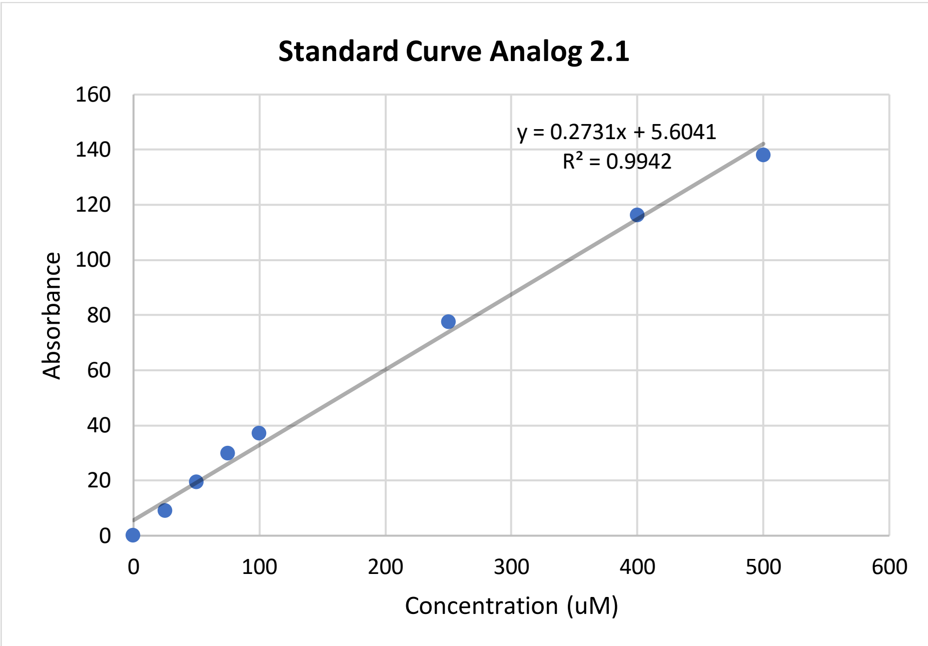
Supplement Table 18. The Variables from Calculations for Analogs in Series 2. *Analog 2.1 data is comprised of 6 experiments, each with 5 replicates run in tandem (30 total). Analog 2.2 data is comprised of 4 experiments, each with 5 replicates run in tandem (20 total). Analog 2.3 data is comprised of 9 experiments, each with 5 replicates run in tandem (45 total). Analog 2.4 data is comprised of 6 experiments, each with 5 replicates run in tandem (30 total). Analog 2.5 data is comprised of 9 experiments, each with 5 replicates run in tandem (45 total). The molecular weights and mean retention times seen via HPLC (210 nm) are listed. The C values and %T values are calculated using Supplement Equation **1**. The mean percent recoveries are listed. Definitions: MW = molecular weight, RT = retention time, %R = % recovery, Ave. %R = mean ± standard deviation.*

Cmpd	Ave. $logP_{app}$	Ave. logP	Well 1		Well 2		Well 3		Well 4		Well 5		Ave. [acc]
			[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	
2.1	-4.86	-8.91	157.96	287.03	157.26	268.64	160.13	254.77	154.26	277.97	154.94	295.82	184.9 ± 21.82 uM (37%)
2.1	-5.02	-8.92	119.85	276.22	156.14	284.99	168.56	251.35	171.88	286.17	169.30	284.98	
2.1	-4.84	-8.80	192.18	208.33	193.02	281.28	201.37	267.34	196.32	264.11	193.76	262.26	
2.1	-4.88	-8.80	207.95	238.47	188.63	245.28	181.68	281.49	191.76	263.40	188.77	259.46	
2.1	-4.74	-8.78	203.78	245.81	224.03	213.05	172.21	230.71	208.83	235.63	197.12	226.02	
2.1	-4.84	-8.76	224.65	207.22	208.33	202.02	216.77	219.56	164.48	263.39	223.02	258.46	
2.2	-5.09	-8.92	155.43	338.89	161.52	336.11	152.32	309.58	147.77	312.61	145.18	289.50	159.08 ± 13.24 uM (31%)
2.2	-5.04	-8.95	164.59	239.99	163.85	236.15	156.21	278.78	137.44	282.53	152.60	267.40	
2.2	-4.96	-8.85	189.23	272.48	183.57	266.74	169.70	245.46	178.46	255.68	165.14	292.41	
2.2	-5.05	-8.93	158.41	264.39	152.44	277.24	148.58	288.98	149.50	278.63	149.22	292.42	
2.3	-5.17	-9.01	145.68	324.14	131.55	301.23	124.46	342.51	125.36	328.73	124.24	333.33	117.43 ± 15.74 uM (23%)
2.3	-5.19	-9.03	117.64	329.63	128.36	343.78	135.24	341.19	128.27	348.72	138.44	339.34	
2.3	-5.21	-9.04	108.39	345.17	100.51	372.02	81.88	361.74	84.35	346.30	80.77	318.29	
2.3	-5.21	-9.03	136.41	306.51	131.34	298.84	124.22	308.81	116.18	331.01	116.45	327.99	
2.3	-5.21	-9.02	134.02	307.35	133.44	324.47	127.46	326.19	112.79	329.61	124.65	318.04	
2.3	-5.21	-9.01	87.76	337.03	121.13	317.29	115.64	362.26	103.77	366.61	101.19	340.88	
2.3	-5.22	-9.02	135.63	297.33	129.80	321.73	125.12	315.06	118.24	328.74	112.53	318.08	
2.3	-5.25	-9.05	116.97	371.81	121.47	352.82	123.60	353.88	114.84	341.84	115.66	360.11	
2.3	-5.29	-9.09	88.47	332.36	118.22	318.47	119.91	345.24	99.25	361.32	103.02	365.02	
2.4	-5.52	-9.28	81.99	408.11	78.79	396.37	74.20	402.56	67.85	396.69	73.48	404.22	92.99 ± 12.85 uM (19%)
2.4	-5.49	-9.26	101.28	346.17	86.95	381.58	87.57	374.93	81.86	331.75	92.97	313.79	
2.4	-5.47	-9.25	108.76	377.90	104.76	359.87	106.75	319.53	104.68	382.03	108.47	340.31	
2.4	-5.44	-9.23	109.80	334.86	98.01	342.14	97.59	329.67	83.73	374.30	87.57	352.82	
2.4	-5.41	-9.22	86.02	315.05	99.84	317.63	95.92	324.80	83.82	317.52	84.81	329.22	
2.4	-5.36	-9.19	109.87	303.72	109.08	311.45	112.92	313.78	93.22	336.21	77.16	346.28	
2.5	-5.36	-9.19	83.50	325.14	89.39	342.29	91.58	348.30	96.13	330.51	92.96	335.24	87.26 ± 13.92 uM (17%)
2.5	-5.35	-9.17	99.38	329.76	115.70	338.41	100.79	331.04	103.19	332.12	115.29	326.73	
2.5	-5.33	-9.15	71.30	342.87	69.52	359.65	66.92	386.13	70.93	360.84	69.28	383.36	
2.5	-5.32	-9.14	80.44	373.48	75.82	372.61	89.06	369.70	94.85	353.24	89.83	359.18	
2.5	-5.31	-9.13	99.14	332.03	103.11	330.45	91.18	324.58	102.37	337.25	115.12	325.57	
2.5	-5.30	-9.11	68.15	362.19	73.16	385.60	72.44	407.29	74.67	391.26	75.92	404.74	
2.5	-5.33	-9.14	88.53	370.12	91.07	363.55	92.98	369.31	99.06	348.10	86.01	365.30	
2.5	-5.38	-9.19	107.84	300.14	99.08	310.08	75.07	304.37	83.98	305.76	93.56	313.89	
2.5	-5.43	-9.23	72.93	321.05	72.08	388.56	70.51	405.00	75.49	388.67	77.42	326.87	

Supplement Table 19. Final Experimental Data for Analogs in Series 2. *The mean $logP_{app}$ (calculated from Supplement Equation 1) and logP values (calculated from (Supplement Equation 2) are listed. The acceptor and donor concentrations are calculated using a standard curve and the units are uM. The initial concentration is 500 uM for all experiments. The total mean acceptor concentrations are listed in the final column. The dark grey boxes for analog 1.2 are unused (32 total experiments). Definitions: [acc] = acceptor concentration after incubation, [donor] = donor concentration after incubation, mean [acc] = mean acceptor concentration ± standard deviation.*

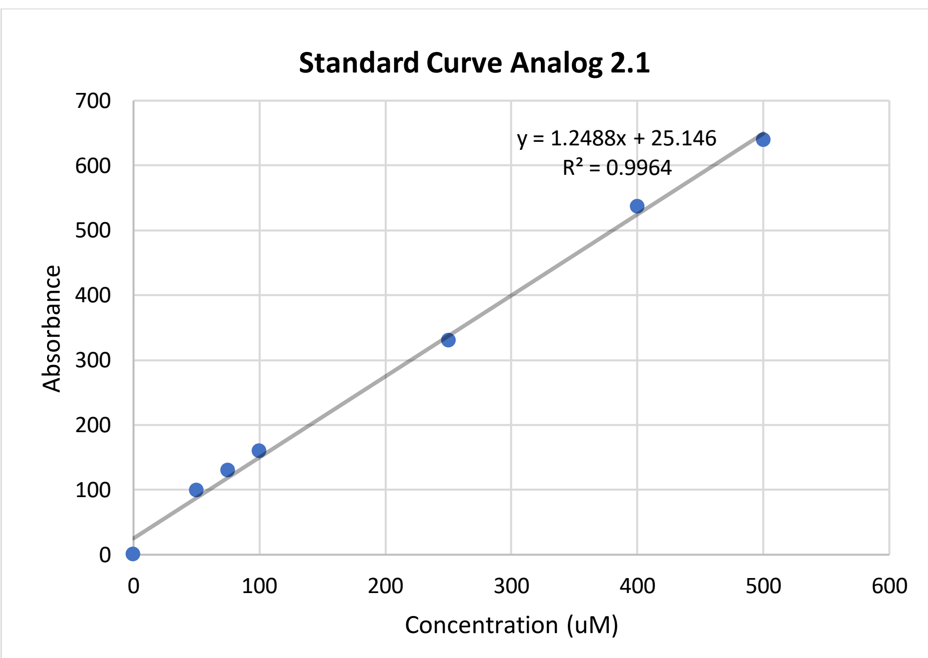
h. Standard Curves for Series 2

Analog 2.1



Conc. (uM)	Area
500	137.9328
400	116.3233
250	77.432
100	37.0039
75	29.9394
50	19.4774
25	9.0455
0	0

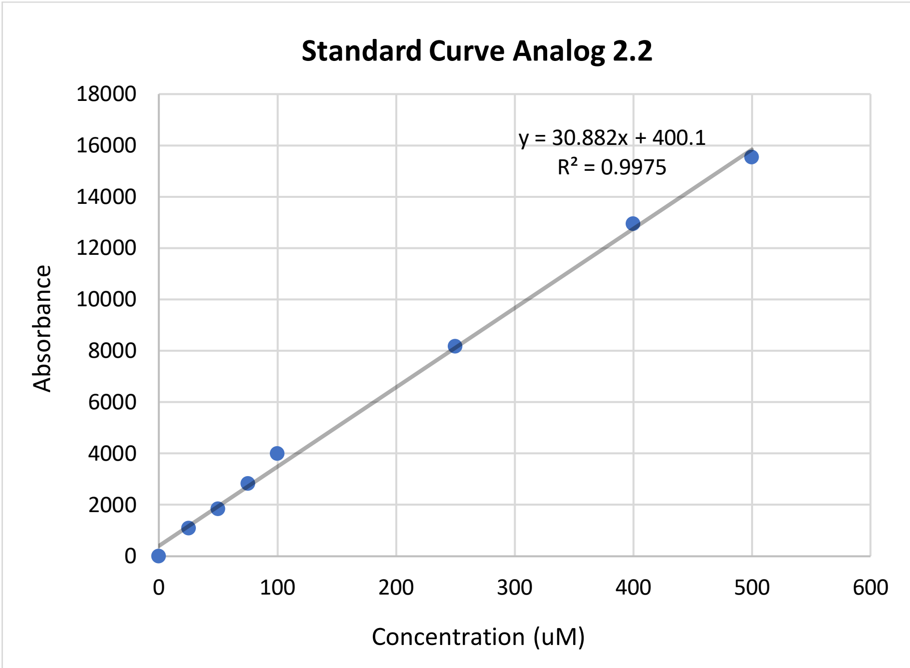
Supplement Graph 15. *The standard curve for absorbance vs. concentration (uM) of analog 2.1 utilizing* ***ELSD detection.***



Conc. (uM)	Area
500	639.412
400	536.085
250	330.263
100	158.951
75	129.3793
50	98.993
0	0

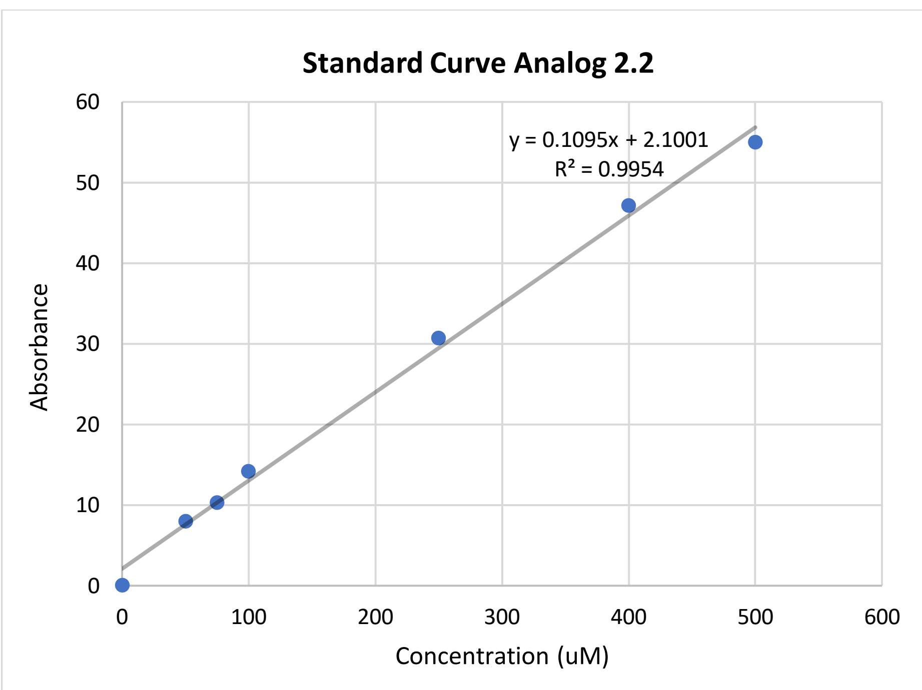
Supplement Graph 16. *The standard curve for absorbance vs. concentration (uM) of analog 2.1 utilizing* ***UV detection*** *(210 nm).*

Analog 2.2



Conc. (uM)	Area
500	54.9999
400	47.121
250	30.674
100	14.1722
75	10.2932
50	7.987
0	0

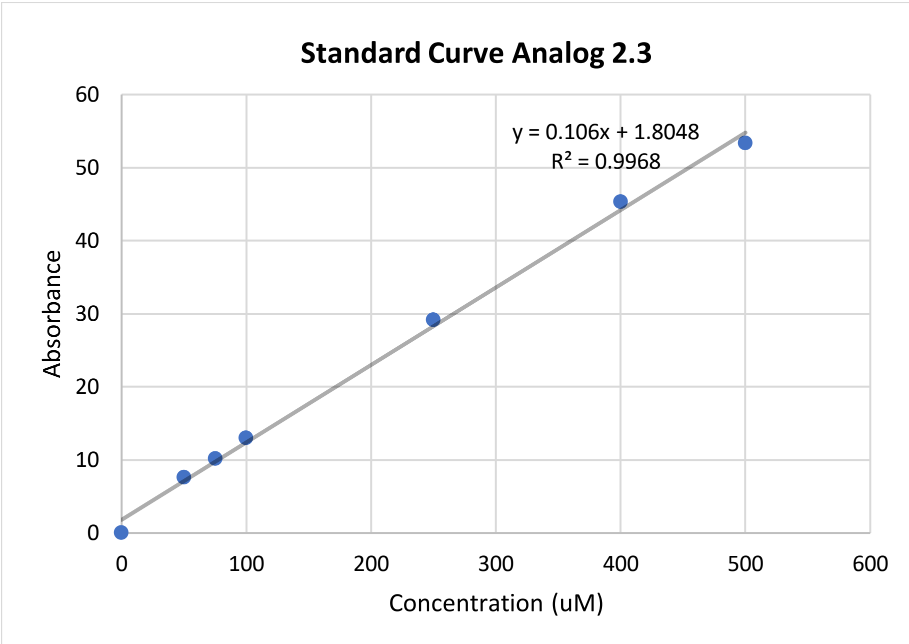
Supplement Graph 17. *The standard curve for absorbance vs. concentration (uM) of analog 2.2 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	15547.7
400	12950.3
250	8178.66
100	4004.7
75	2840.26
50	1834.2
25	1079.48
0	0

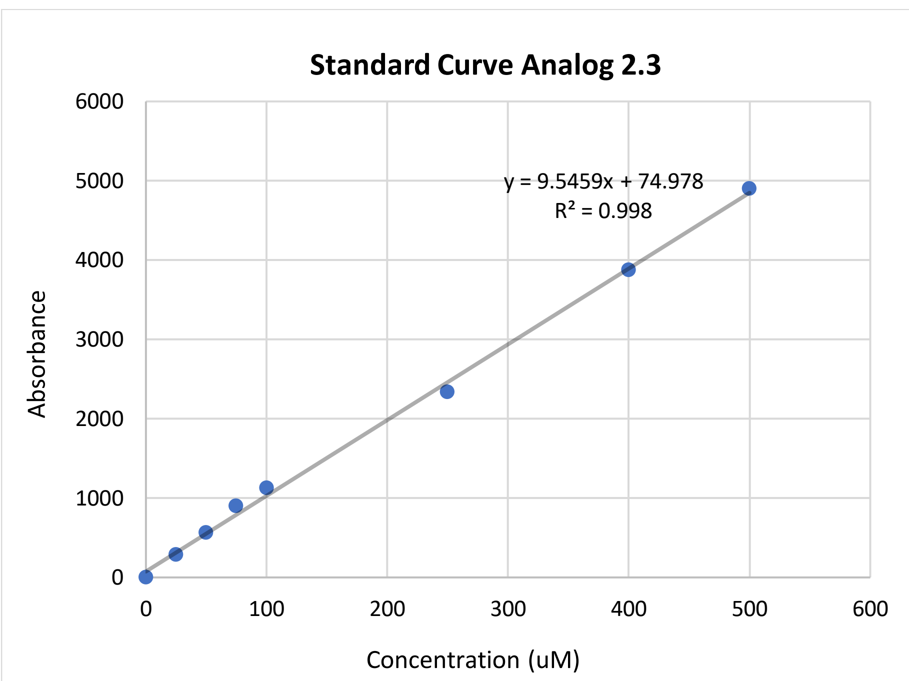
Supplement Graph 18. *The standard curve for absorbance vs. concentration (uM) of analog 2.2 utilizing* ***ELSD detection.***

Analog 2.3



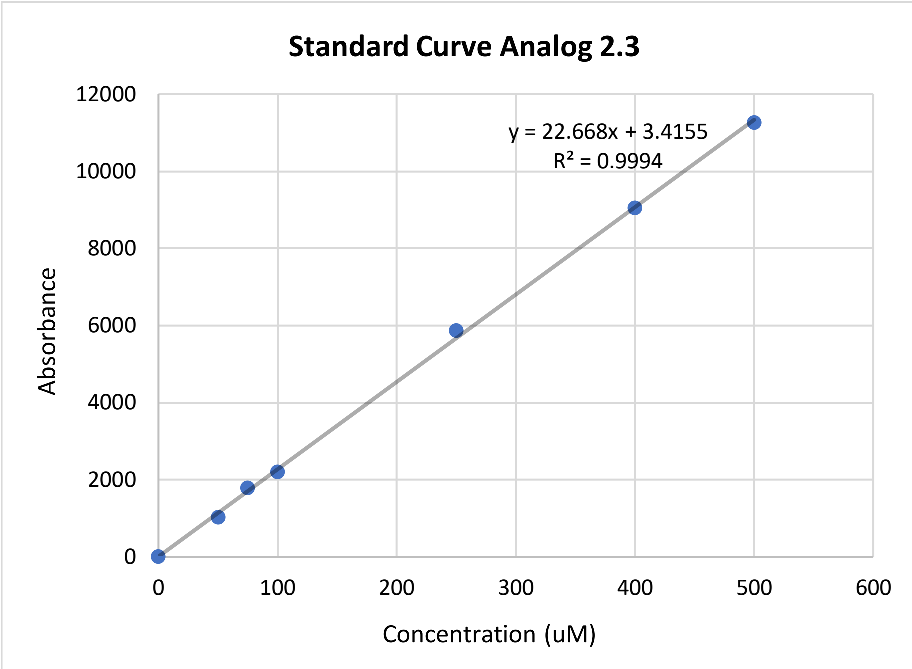
Conc. (uM)	Area
500	53.283
400	45.288
250	29.112
100	12.977
75	10.102
50	7.567
0	0

Supplement Graph 20. *The standard curve for absorbance vs. concentration (uM) of analog 2.3 utilizing* ***ELSD detection.***



Conc. (uM)	Area
500	4898.56
400	3867.86
250	2333.72
100	1120.07
75	899.778
50	557.215
25	286.835
0	0

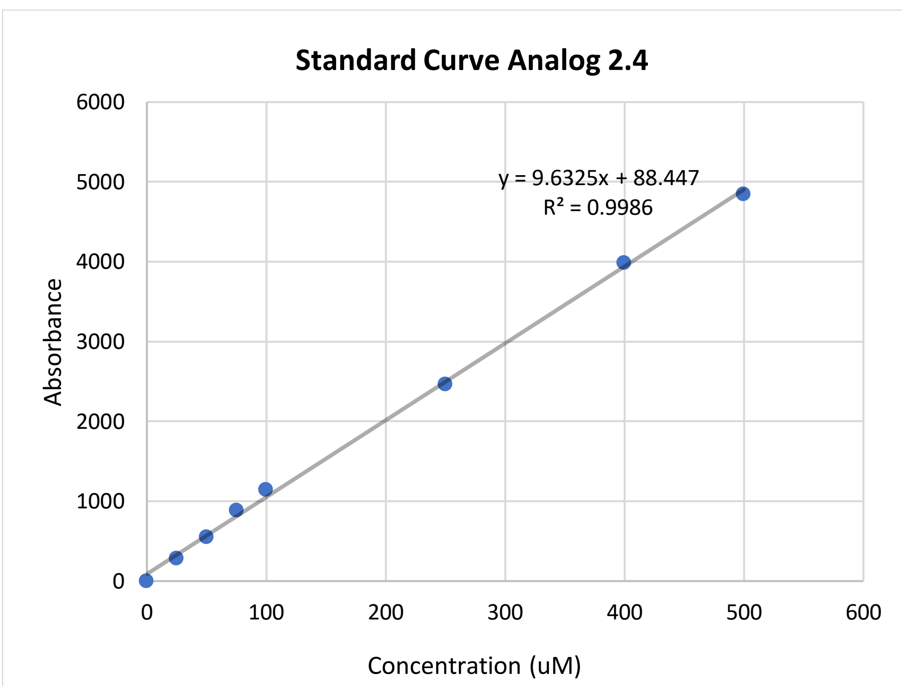
Supplement Graph 19. *The standard curve for absorbance vs. concentration (uM) of analog 2.3 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	11272.7
400	9045.42
250	5866.71
100	2199.12
75	1783.33
50	1024.9
0	0

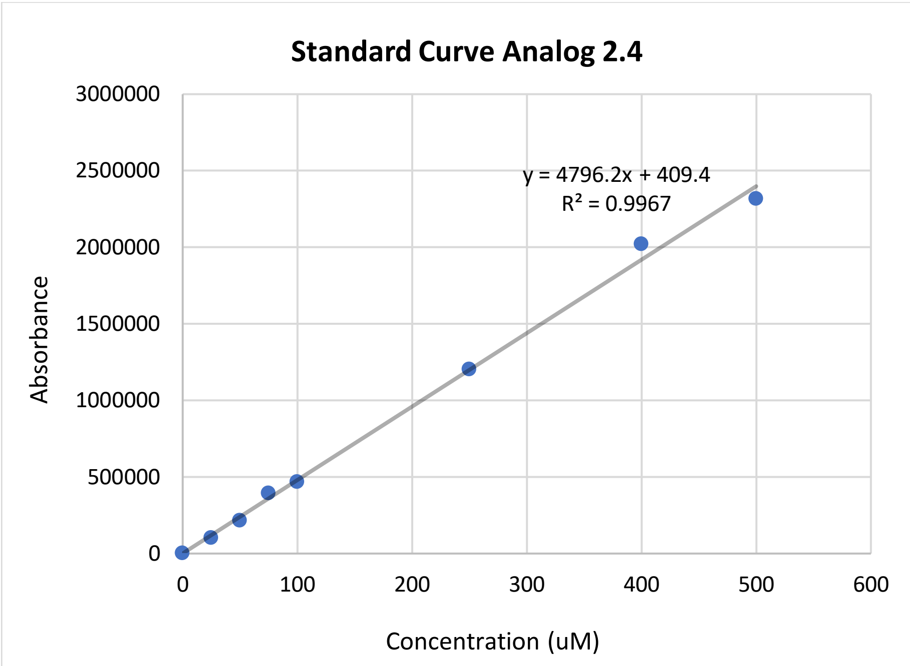
Supplement Graph 21. *The standard curve for absorbance vs. concentration (uM) of analog 2.3 utilizing* ***MS detection.***

Analog 2.4



Conc. (uM)	Area
500	4852
400	3991
250	2467
100	1147
75	892
50	557.215
25	286.835
0	0

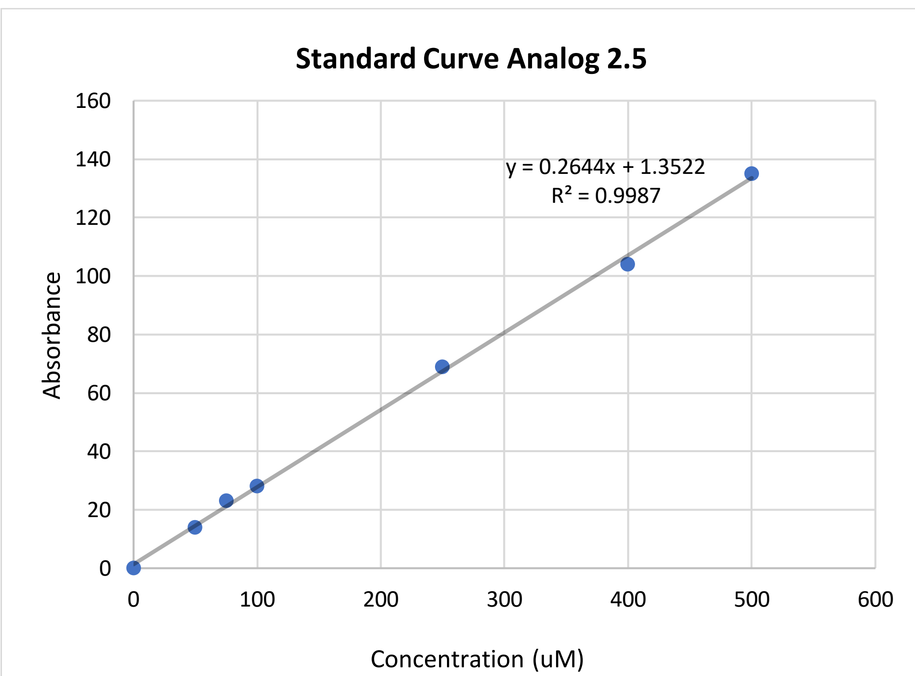
Supplement Graph 22. *The standard curve for absorbance vs. concentration (uM) of analog 2.4 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	2316260
400	2019807
250	1204510
100	468320
75	391472
50	215551
25	102019
0	0

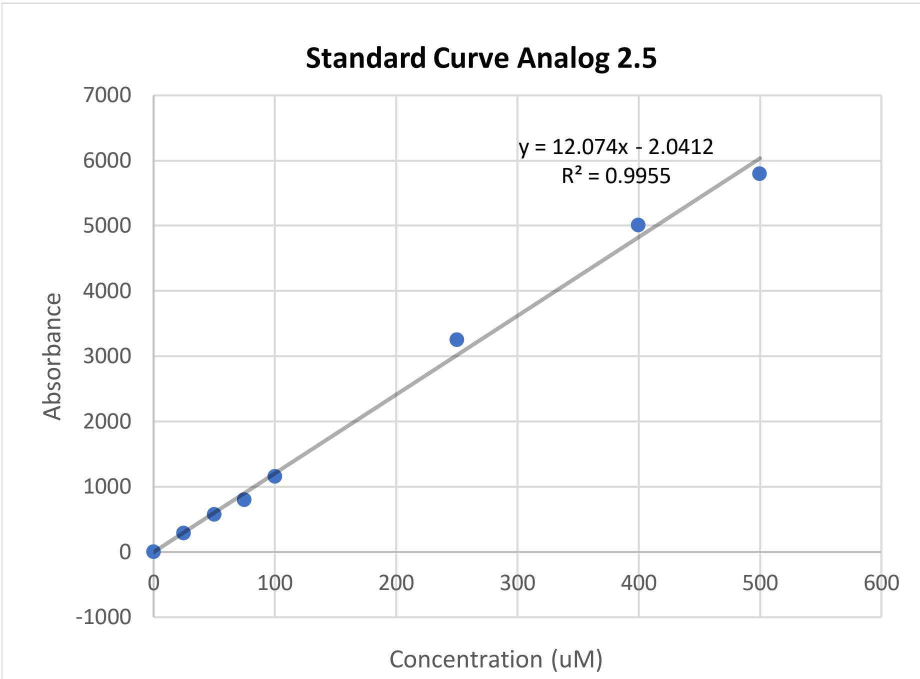
Supplement Graph 23. *The standard curve for absorbance vs. concentration (uM) of analog 2.4 utilizing* ***MS detection.***

Analog 2.5



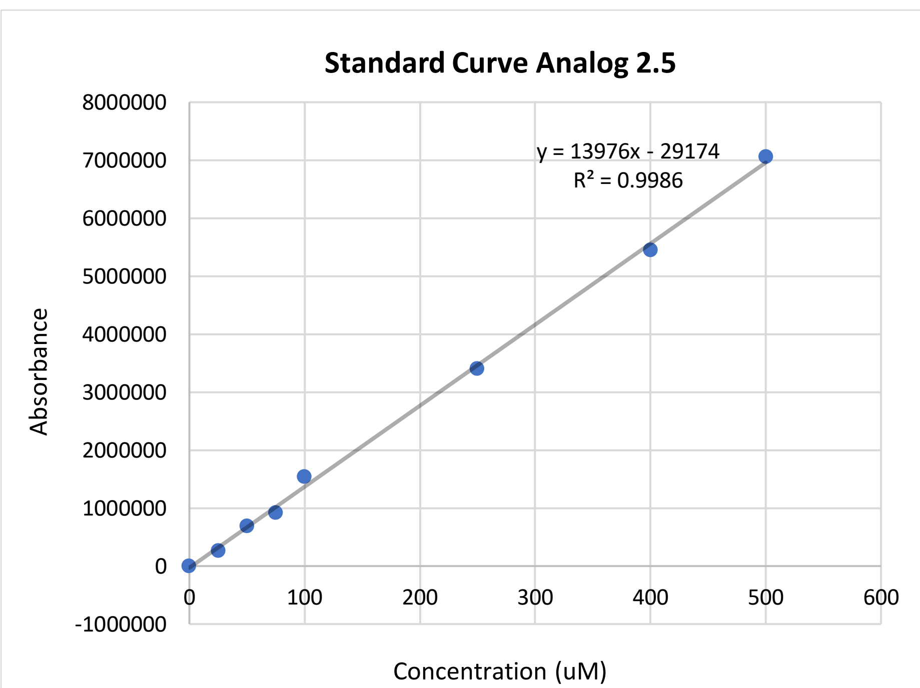
Conc. (uM)	Area
500	135
400	104
250	69
100	28
75	23
50	14
0	0

Supplement Graph 24. *The standard curve for absorbance vs. concentration (uM) of analog 2.5 utilizing* ***ELSD detection.***



Conc. (uM)	Area
500	5795
400	5013
250	3256
100	1154
75	803
50	577
25	289
0	0

Supplement Graph 25. *The standard curve for absorbance vs. concentration (uM) of analog 2.5 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	7056560
400	5450970
250	3409460
100	1537100
75	916804
50	696154
25	266246
0	0

Supplement Graph 26. *The standard curve for absorbance vs. concentration (uM) of analog 2.5 utilizing* ***MS detection.***

i. Statistical Analysis Series 2

LogPapp			**Percent Diffusion**			**LogP**		
Pair	P-value	Inference	Pair	P-value	Inference	Pair	P-value	Inference
A vs B	4.33E-6	**	A vs B	2.84E-5	**	A vs B	5.12E-4	**
A vs C	0.0298	*	A vs C	0.0237	*	A vs C	0.468	NS
A vs D	0.663	NS	A vs D	1.0	NS	A vs D	0.0574	NS
A vs E	0.00259	**	A vs E	3.23E-6	**	A vs E	2.18E-8	**
A vs F	1.62E-10	**	A vs F	2.88E-10	**	A vs F	3.30E-13	**
B vs C	1.0	NS	B vs C	1.0	NS	B vs C	1.0	NS
B vs D	1.21E-10	**	B vs D	1.41E-8	**	B vs D	4.77E-10	**
B vs E	1.72E-14	**	B vs E	4.49E-18	**	B vs E	5.99E-19	**
B vs F	3.34E-27	**	B vs F	3.87E-25	**	B vs F	4.32E-26	**
C vs D	5.86E-5	**	C vs D	1.87E-4	**	C vs D	1.89E-4	**
C vs E	6.19E-8	**	C vs E	1.96E-11	**	C vs E	1.01E-10	**
C vs F	1.44E-15	**	C vs F	1.42E-15	**	C vs F	1.44E-14	**
D vs E	0.791	NS	D vs E	0.00316	**	D vs E	0.00915	**
D vs F	3.75E-5	**	D vs F	7.43E-6	**	D vs F	4.48E-5	**
E vs F	0.344	NS	E vs F	1.0	NS	E vs F	1.0	NS

Supplement Table 20. Data Analysis of Series 2. *Kruskal-Wallis test with Dunn's multiple comparisons post hoc analysis using GraphPad Prism v10.1.1. Definitions: A = ent-verticilide, B = 2.1, C = 2.2, D = 2.3, E = 2.4, F = 2.5 and ** p < 0.01, * p < 0.05, NS = not significant.*

j. Series 3: Acceptor Concentration, $LogP_{app}$ and LogP

Acceptor Concentration											
***ent*-vert**		**3.1**		**3.2**		**3.3**		**3.4**		**3.5**	
137.13		67.09		84.42		83.62		56.05		43.19	
144.38		119.78		124.10		65.68		56.26		46.24	
128.7		125.17	**MPT-5-150 (UV)**	90.10	**MPT-5-156 (UV)**	81.29	**MPT-5-163 (MS)**	60.64	**MPT-5-198 (MS)**	51.46	**MPT-5-206 (MS)**
140.7	**MPT-4-098 (UV)**	123.80		90.59		80.77		66.86		48.20	
102.73		133.97		89.63		84.81		63.93		57.92	
141.38		65.61		92.01		91.31		70.31		61.70	
130.11		124.12		95.59		86.85		69.25		59.76	
133.07		139.88	**MPT-5-150 (ELSD)**	105.01	**MPT-5-156 (MS)**	83.82	**MPT-5-163 (UV)**	62.73	**MPT-5-198 (UV)**	45.12	**MPT-5-206 (UV)**
122.26		112.79		99.96		84.30		57.57		62.29	
147.93		120.75		98.21		82.70		58.19		72.35	
156.71		96.62		98.50		73.86		74.19		46.07	
141.87	**MPT-4-098 (ELSD)**	116.55		83.20		81.34		75.09		47.42	
136.9		113.47	**MPT-5-151 (UV)**	94.77	**MPT-5-157 (UV)**	81.02	**MPT-5-164 (MS)**	89.29	**MPT-5-199 (MS)**	48.29	**MPT-5-207 (MS)**
106.52		86.75		84.56		80.02		71.83		49.97	
98.16		110.13		89.95		81.33		76.77		52.04	
94.39		140.47		98.48		87.91		60.19		72.00	
110.98		119.71		108.07		90.94		64.08		60.65	
119.98		98.70	**MPT-5-151 (ELSD)**	96.28	**MPT-5-157 (MS)**	77.28	**MPT-5-164 (UV)**	60.61	**MPT-5-199 (UV)**	57.23	**MPT-5-207 (UV)**
123.39		98.76		92.21		85.04		61.18		62.35	
125.61	**MPT-4-141 (UV)**	108.34		91.61		82.28		62.11		43.59	
109.93		115.31				77.96		59.11		38.58	
141.97		111.54		**95.36**	**Mean**	80.12		63.49		39.64	
123.79		106.76	**MPT-5-152 (UV)**	**9.35**	**Std Dev**	75.32	**MPT-5-165 (MS)**	66.19	**MPT-5-200 (MS)**	35.39	**MPT-5-208 (MS)**
100.02		92.73				80.61		67.47		38.55	
105.23		112.25				76.74		66.13		37.55	
144.66		138.82				96.20		62.29		43.59	
113.63		106.95				82.86		68.86		55.00	
159.32	**MPT-4-141 (ELSD)**	106.89	**MPT-5-152 (ELSD)**			82.59	**MPT-5-165 (UV)**	66.16	**MPT-5-200 (UV)**	38.18	**MPT-5-208 (UV)**
121.37		115.24				86.69		70.60		46.12	
124.96		114.21				87.86		69.30		43.29	
150.2											
136.43		**111.12**	**Mean**			**82.44**	**Mean**	**65.86**	**Mean**	**50.15**	**Mean**
128.35		**20.70**	**Std Dev**			**5.76**	**Std Dev**	**8.41**	**Std Dev**	**10.02**	**Std Dev**
100.46											
108.92											
141.48	**MPT-4-148 (UV)**										
144.25											
151.74											
123.42											
139.99											
141.66											
129.00											
135.43											
140.94	**MPT-4-148 (ELSD)**										
91.72											
130.3											
115.39											
125.44											
127.56	**Mean**										
17.17	**Std Dev**										

Supplement Table 21. *Acceptor concentration values for ent-vert and analogs in series 3 using all detection methods.*

$LogP_{app}$											
***ent*-vert**		**3.1**		**3.2**		**3.3**		**3.4**		**3.5**	
-5.15	**MPT-4-098 (UV)**	-5.45	**MPT-5-150 (UV)**	-5.37	**MPT-5-156 (UV)**	-5.48	**MPT-5-163 (MS)**	-5.71	**MPT-5-198 (MS)**	-5.82	**MPT-5-206 (MS)**
-5.14		-5.20		-5.22		-5.59		-5.71		-5.77	
-5.37		-5.17		-5.32		-5.50		-5.67		-5.74	
-5.13		-5.16		-5.34		-5.53		-5.62		-5.74	
-5.30		-5.15		-5.35		-5.46		-5.64		-5.67	
-5.21		-5.52	**MPT-5-150 (ELSD)**	-5.39	**MPT-5-156 (MS)**	-5.45	**MPT-5-163 (UV)**	-5.43	**MPT-5-198 (UV)**	-5.53	**MPT-5-206 (UV)**
-5.25		-5.26		-5.33		-5.47		-5.43		-5.52	
-5.14		-5.13		-5.37		-5.51		-5.45		-5.61	
-5.19	**MPT-4-098 (ELSD)**	-5.24		-5.40		-5.50		-5.49		-5.52	
-5.10		-5.23		-5.32		-5.52		-5.48		-5.46	
-5.19		-5.30	**MPT-5-151 (UV)**	-5.32	**MPT-5-157 (UV)**	-5.58	**MPT-5-164 (MS)**	-5.68	**MPT-5-199 (MS)**	-5.79	**MPT-5-207 (MS)**
-5.11		-5.18		-5.35		-5.50		-5.65		-5.77	
-5.17		-5.22		-5.34		-5.53		-5.62		-5.74	
-5.15		-5.33		-5.34		-5.50		-5.62		-5.72	
-5.16		-5.24		-5.33		-5.50		-5.63		-5.70	
-5.12		-5.12	**MPT-5-151 (ELSD)**	-5.33	**MPT-5-157 (MS)**	-5.46	**MPT-5-164 (UV)**	-5.39	**MPT-5-199 (UV)**	-5.46	**MPT-5-207 (UV)**
-5.35	**MPT-4-141 (UV)**	-5.17		-5.33		-5.43		-5.41		-5.51	
-5.33		-5.26		-5.39		-5.51		-5.34		-5.52	
-5.39		-5.26		-5.40		-5.49		-5.40		-5.50	
-5.16		-5.23		-5.44		-5.52		-5.37		-5.60	
-5.36		-5.23	**MPT-5-152 (UV)**			-5.50	**MPT-5-165 (MS)**	-5.65	**MPT-5-200 (MS)**	-5.86	**MPT-5-208 (MS)**
-5.42		-5.23		**-5.35**	**Mean**	-5.49		-5.64		-5.83	
-5.33		-5.29		**0.04**	**Std Dev**	-5.49		-5.67		-5.86	
-5.22		-5.30				-5.41		-5.66		-5.86	
-5.24	**MPT-4-141 (ELSD)**	-5.27				-5.43		-5.63		-5.87	
-5.24		-5.28	**MPT-5-152 (ELSD)**			-5.42	**MPT-5-165 (UV)**	-5.43	**MPT-5-200 (UV)**	-5.62	**MPT-5-208 (UV)**
-5.44		-5.25				-5.50		-5.42		-5.55	
-5.20		-5.30				-5.49		-5.44		-5.66	
-5.23		-5.07				-5.49		-5.41		-5.59	
-5.46		-5.26				-5.47		-5.42		-5.62	
-5.25											
-5.32		**-5.24**	**Mean**			**-5.49**	**Mean**	**-5.54**	**Mean**	**-5.66**	**Mean**
-5.26	**MPT-4-148 (UV)**	**0.10**	**Std Dev**			**0.04**	**Std Dev**	**0.13**	**Std Dev**	**0.13**	**Std Dev**
-5.21											
-5.26											
-5.24											
-5.32											
-5.12											
-5.14											
-5.32											
-5.22	**MPT-4-148 (ELSD)**										
-5.19											
-5.2											
-5.19											
-5.21											
-5.1											
-5.18											
-5.21											
-5.23	**Mean**										
0.09	**Std Dev**										

Supplement Table 22. *$LogP_{app}$ experimental values for ent-vert and analogs in series 3 using all detection methods, calculated using Supplement Equation 1.*

LogP											
ent-vert		3.1		3.2		3.3		3.4		3.5	
-8.98	MPT-4-098 (UV)	-9.33	MPT-5-150 (UV)	-9.22	MPT-5-156 (UV)	-9.23	MPT-5-163 (MS)	-9.42	MPT-5-198 (MS)	-9.53	MPT-5-206 (MS)
-8.91		-9.05		-9.03		-9.34		-9.41		-9.50	
-9.09		-9.03		-9.19		-9.24		-9.38		-9.45	
-8.93		-9.04		-9.19		-9.24		-9.33		-9.48	
-9.12		-9.00		-9.19		-9.22		-9.35		-9.40	
-8.95		-9.34	MPT-5-150 (ELSD)	-9.18	MPT-5-156 (MS)	-9.19	MPT-5-163 (UV)	-9.31	MPT-5-198 (UV)	-9.37	MPT-5-206 (UV)
-9.04		-9.03		-9.16		-9.21		-9.32		-9.39	
-8.96		-8.97		-9.12		-9.23		-9.36		-9.51	
-8.98	MPT-4-098 (ELSD)	-9.08		-9.14		-9.22		-9.40		-9.37	
-8.96		-9.05		-9.15		-9.23		-9.40		-9.30	
-9.01		-9.16	MPT-5-151 (UV)	-9.15	MPT-5-157 (UV)	-9.29	MPT-5-164 (MS)	-9.39	MPT-5-199 (MS)	-9.51	MPT-5-207 (MS)
-8.98		-9.07		-9.23		-9.24		-9.36		-9.49	
-9.03		-9.08		-9.17		-9.24		-9.34		-9.48	
-9.01		-9.21		-9.22		-9.25		-9.33		-9.47	
-9.01		-9.09		-9.19		-9.24		-9.34		-9.45	
-8.97		-8.97	MPT-5-151 (ELSD)	-9.15	MPT-5-157 (MS)	-9.20	MPT-5-164 (UV)	-9.28	MPT-5-199 (UV)	-9.30	MPT-5-207 (UV)
-9.09	MPT-4-141 (UV)	-9.05		-9.10		-9.19		-9.28		-9.38	
-9.14		-9.15		-9.16		-9.26		-9.20		-9.40	
-9.13		-9.15		-9.18		-9.22		-9.30		-9.36	
-9		-9.10		-9.18		-9.23		-9.27		-9.53	
-9.12		-9.07	MPT-5-152 (UV)			-9.26	MPT-5-165 (MS)	-9.38	MPT-5-200 (MS)	-9.59	MPT-5-208 (MS)
-9.14		-9.09		**-9.17**	**Mean**	-9.25		-9.35		-9.57	
-9.11		-9.11		**0.04**	**Std Dev**	-9.28		-9.38		-9.62	
-9.09		-9.18				-9.24		-9.37		-9.59	
-8.97	MPT-4-141 (ELSD)	-9.08				-9.27		-9.37		-9.60	
-8.97		-8.98	MPT-5-152 (ELSD)			-9.16	MPT-5-165 (UV)	-9.37	MPT-5-200 (UV)	-9.53	MPT-5-208 (UV)
-9.16		-9.11				-9.23		-9.32		-9.42	
-8.95		-9.11				-9.23		-9.34		-9.59	
-8.99		-9.07				-9.21		-9.31		-9.50	
-9.18		-9.08				-9.20		-9.32		-9.53	
-9.00											
-9.21		**-9.09**	**Mean**			**-9.24**	**Mean**	**-9.34**	**Mean**	**-9.47**	**Mean**
-9.07	MPT-4-148 (UV)	**0.10**	**Std Dev**			**0.03**	**Std Dev**	**0.06**	**Std Dev**	**0.09**	**Std Dev**
-8.95											
-9											
-8.99											
-9.05											
-8.9											
-8.93											
-9.06											
-9.04	MPT-4-148 (ELSD)										
-9.03											
-9.04											
-9.03											
-9.02											
-8.93											
-9.02											
-9.03											
-9.03	**Mean**										
0.07	**Std Dev**										

Supplement Table 23. *LogP experimental values for ent-verticilide analogs in series 3 using all detection methods, calculated using Supplement Equation 2.*

k. Series 3: Experimental Variables from Calculations and Percent Recoveries

Cmpd	MW (g/mol)	Ave RT (min)	C ($x10^{-9}$)	Well 1		Well 2		Well 3		Well 4		Well 5		Ave. %R
				%T	%R	%T	%R	%T	%R	%T	%R	%T	%R	
3.1	866.15	12.00	2.90	0.55	94	0.50	99	0.64	90	0.63	89	0.53	92	85.90 ± 4.53
3.1			2.94	0.42	80	0.62	86	0.73	85	0.63	84	0.65	89	
3.1			2.94	0.59	89	0.69	83	0.65	80	0.56	81	0.63	83	
3.1			2.91	0.74	84	0.69	81	0.62	85	0.62	81	0.65	86	
3.1			2.99	0.65	85	0.64	81	0.59	83	0.58	84	0.61	87	
3.1			2.93	0.66	87	0.70	85	0.64	91	0.64	82	0.66	91	
3.2	879.19	11.86	3.24	0.53	96	0.66	99	0.57	93	0.55	96	0.54	97	93.60 ± 5.00
3.2			3.20	0.51	90	0.56	84	0.52	99	0.50	100	0.57	84	
3.2			3.19	0.57	98	0.55	91	0.56	99	0.55	91	0.57	93	
3.2			3.20	0.56	85	0.56	94	0.51	95	0.51	91	0.48	97	
3.3	879.19	12.21	3.44	0.44	92	0.37	87	0.43	93	0.40	98	0.46	91	90.70 ± 3.52
3.3			3.40	0.46	91	0.45	88	0.42	92	0.43	91	0.41	93	
3.3			3.33	0.37	98	0.43	92	0.49	98	0.42	92	0.43	92	
3.3			3.41	0.46	88	0.48	87	0.42	84	0.44	89	0.41	91	
3.3			3.39	0.43	89	0.43	90	0.40	84	0.49	93	0.42	93	
3.3			3.30	0.48	91	0.43	88	0.44	86	0.43	91	0.45	89	
3.4	892.24	12.09	2.99	0.44	93	0.37	94	0.43	93	0.40	95	0.45	94	92.50 ± 2.24
3.4			2.90	0.61	94	0.55	93	0.64	90	0.61	90	0.63	92	
3.4			2.94	0.52	94	0.55	96	0.54	94	0.55	95	0.51	94	
3.4			2.98	0.71	91	0.67	95	0.61	95	0.66	89	0.67	90	
3.4			2.87	0.64	90	0.65	94	0.60	94	0.63	94	0.64	89	
3.4			2.94	0.70	87	0.67	91	0.66	92	0.71	91	0.69	92	
3.5	905.28	11.98	3.23	0.21	95	0.21	93	0.22	97	0.28	92	0.25	95	92.54 ± 2.90
3.5			3.20	0.31	98	0.29	93	0.30	92	0.35	96	0.34	96	
3.5			3.31	0.22	96	0.20	94	0.21	91	0.23	91	0.23	90	
3.5			3.26	0.28	96	0.30	92	0.28	89	0.28	93	0.30	88	
3.5			3.24	0.21	92	0.22	90	0.21	85	0.19	93	0.20	91	
3.5			3.25	0.29	92	0.29	93	0.33	92	0.31	89	0.32	90	

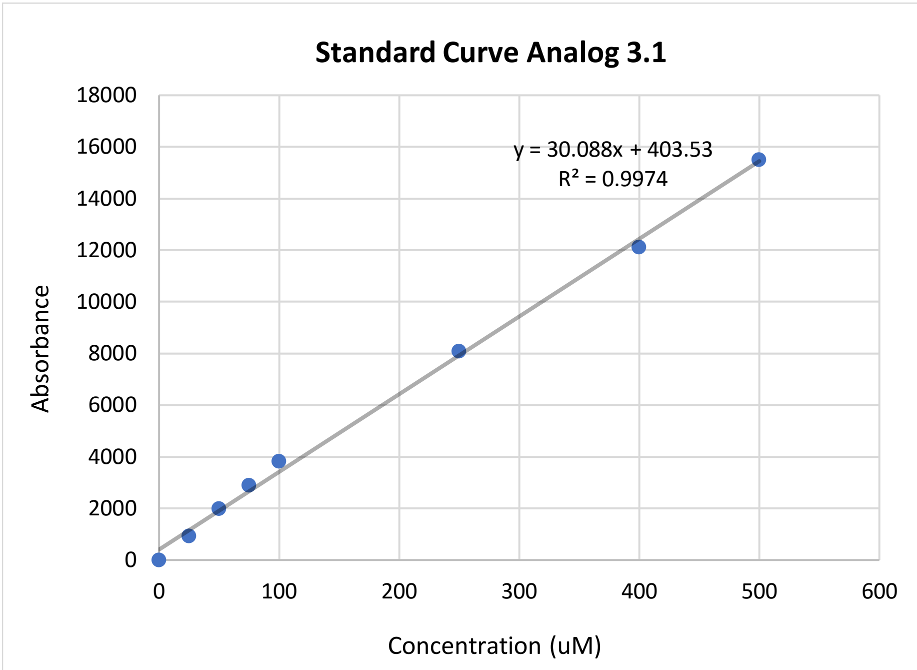
Supplement Table 24. The Variables from Calculations for Analogs in Series 3. *Analog 3.1 data is comprised of 6 experiments, each with 5 replicates run in tandem (30 total). Analog 3.2 data is comprised of 4 experiments, each with 5 replicates run in tandem (20 total). Analog 3.3 data is comprised of 6 experiments, each with 5 replicates run in tandem (30 total). Analog 3.4 data is comprised of 6 experiments, each with 5 replicates run in tandem (30 total). Analog 3.5 data is comprised of 6 experiments, each with 5 replicates run in tandem (30 total). The molecular weights and mean retention times seen via HPLC (210 nm) are listed. The C values and %T values are calculated using Supplement Equation* ***1****. The mean percent recoveries are listed. Definitions: MW = molecular weight, RT = retention time, %R = % recovery, Ave. %R = mean ± standard deviation.*

Cmpd	Ave. $logP_{app}$	Ave. logP	Well 1		Well 2		Well 3		Well 4		Well 5		Ave. [acc]
			[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	
3.1	-5.28	-9.10	65.61	403.01	124.12	372.41	139.88	310.24	112.78	330.71	120.63	340.68	111.4 ± 20.70 uM (23%)
3.1	-5.23	-9.09	67.09	332.40	119.78	311.21	125.17	300.70	123.79	295.35	133.97	312.47	
3.1	-5.21	-9.08	140.47	305.61	119.71	296.29	98.70	302.54	98.76	305.90	108.34	307.91	
3.1	-5.25	-9.12	96.62	322.94	116.55	289.24	113.47	311.50	86.75	316.04	110.13	319.38	
3.1	-5.20	-9.06	138.82	287.64	106.95	296.32	106.89	307.78	115.24	304.74	114.21	320.35	
3.1	-5.26	-9.11	115.31	321.87	111.54	313.65	106.76	347.84	92.73	315.07	112.25	342.73	
3.2	-5.32	-9.17	84.42	396.22	124.10	372.83	90.10	372.62	90.59	388.63	89.63	396.96	95.36 ± 9.35 uM (19%)
3.2	-5.37	-9.15	92.00	358.98	95.58	321.97	105.01	390.86	99.96	399.47	98.21	324.20	
3.2	-5.33	-9.19	98.50	392.89	83.20	373.20	94.77	399.96	84.55	370.12	89.96	375.96	
3.2	-5.38	-9.15	98.48	326.30	108.07	360.95	96.28	376.51	92.21	362.26	91.61	395.10	
3.3	-5.51	-9.25	83.62	375.04	65.68	371.71	81.29	382.23	80.77	411.27	84.81	367.92	82.44 ± 5.76 uM (16%)
3.3	-5.49	-9.22	91.31	361.13	86.85	352.90	83.82	374.26	84.30	369.58	82.70	380.43	
3.3	-5.52	-9.25	73.86	415.50	81.33	379.86	81.02	410.48	80.01	379.46	81.32	380.08	
3.3	-5.48	-9.22	87.91	353.85	90.93	342.53	77.27	344.82	85.03	361.61	82.28	374.31	
3.3	-5.50	-9.26	77.96	367.60	80.12	369.33	75.31	342.70	80.61	384.27	76.74	386.19	
3.3	-5.47	-9.21	96.20	358.90	82.86	359.33	82.59	349.55	86.69	369.64	87.86	358.05	
3.4	-5.67	-9.38	56.05	409.52	56.25	414.82	60.64	404.18	66.86	407.84	63.93	405.80	65.89 ± 8.41 uM (13%)
3.4	-5.45	-9.36	70.31	400.19	69.25	397.26	62.73	389.29	57.57	393.11	58.19	400.13	
3.4	-5.64	-9.35	59.11	409.52	63.49	414.82	66.19	404.18	67.47	407.84	66.13	405.80	
3.4	-5.38	-9.27	74.19	380.31	75.09	399.12	89.29	383.85	71.83	375.26	76.77	372.90	
3.4	-5.64	-9.37	60.19	389.72	64.08	405.17	60.61	407.15	61.18	403.00	62.11	380.66	
3.4	-5.43	-9.33	62.29	372.56	68.86	387.61	66.16	395.19	70.60	386.82	69.30	388.90	
3.5	-5.75	-9.48	43.19	432.53	46.24	420.51	51.46	431.50	48.20	409.50	57.92	418.93	50.15 ± 10.01 uM (10%)
3.5	-5.53	-9.39	61.70	428.94	59.76	407.70	45.12	417.29	62.30	416.76	72.35	408.06	
3.5	-5.74	-9.48	46.07	432.20	47.42	424.49	48.30	405.30	49.97	405.38	52.04	397.51	
3.5	-5.52	-9.40	72.00	406.18	60.65	401.82	57.23	389.53	62.35	404.88	43.59	396.29	
3.5	-5.86	-9.60	38.58	421.30	39.64	410.70	35.39	390.39	38.55	424.17	37.55	419.15	
3.5	-5.61	-9.52	43.59	417.94	55.00	411.00	38.18	419.65	46.12	399.23	43.30	408.06	

Supplement Table 25. Final Experimental Data for Analogs in Series 3. *The mean $logP_{app}$ (calculated from Supplement Equation 1) and logP values (calculated from (Supplement Equation 2) are listed. The acceptor and donor concentrations are calculated using a standard curve and the units are uM. The initial concentration is 500 uM for all experiments. The total mean acceptor concentrations are listed in the final column. Definitions: [acc] = acceptor concentration after incubation, [donor] = donor concentration after incubation, mean [acc] = mean acceptor concentration ± standard deviation.*

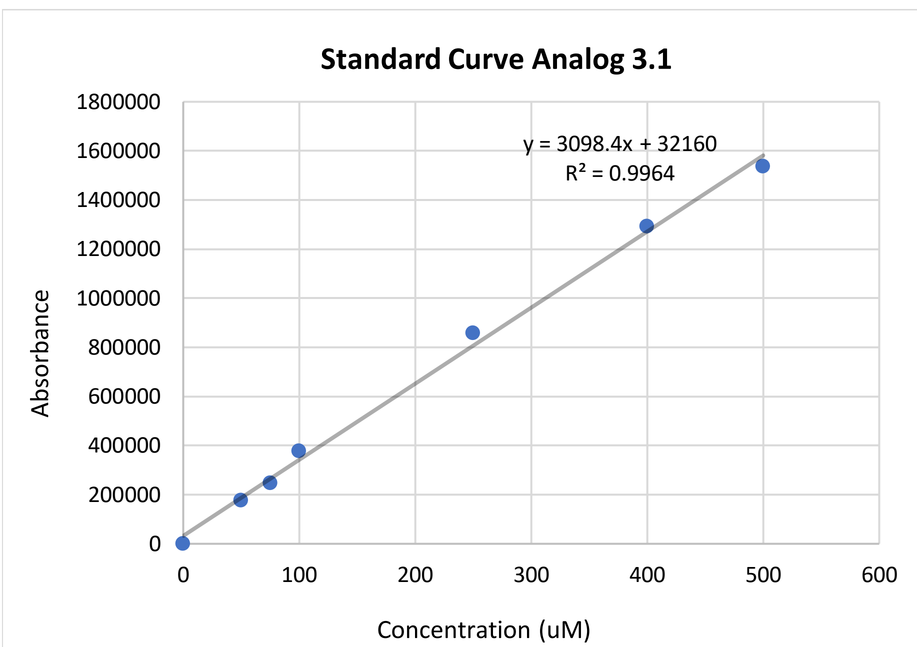
I. Standard Curves Series 3

Analog 3.1



Conc. (uM)	Area
500	15506.4776
400	12119.323
250	8094.3233
100	3810.97
75	2894.004
50	1998.324
25	928.455
0	0

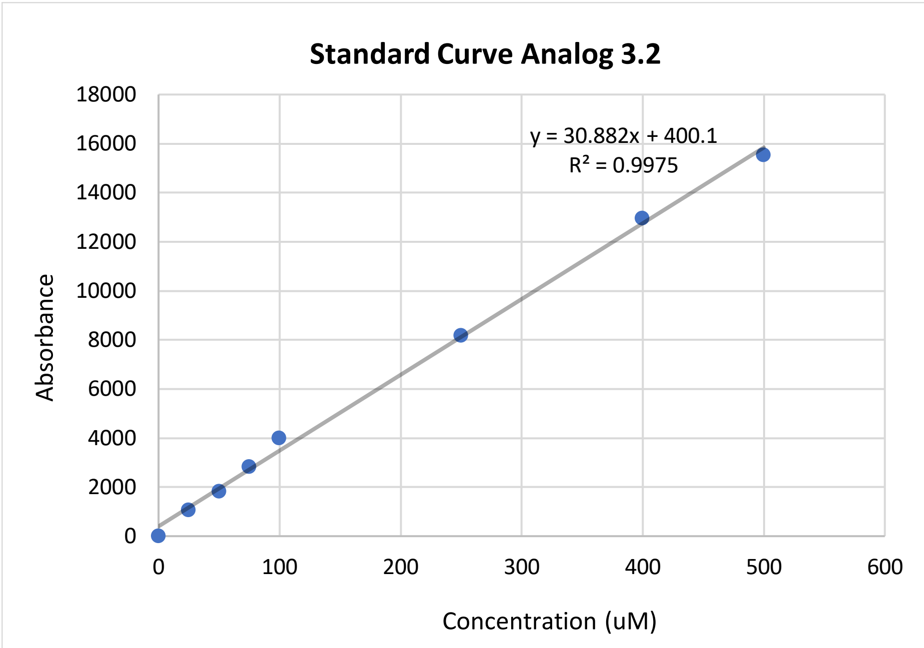
Supplement Graph 27. *The standard curve for absorbance vs. concentration (uM) of analog 3.1 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	1536400
400	1292300
250	857118
100	376535
75	246367
50	176676
0	0

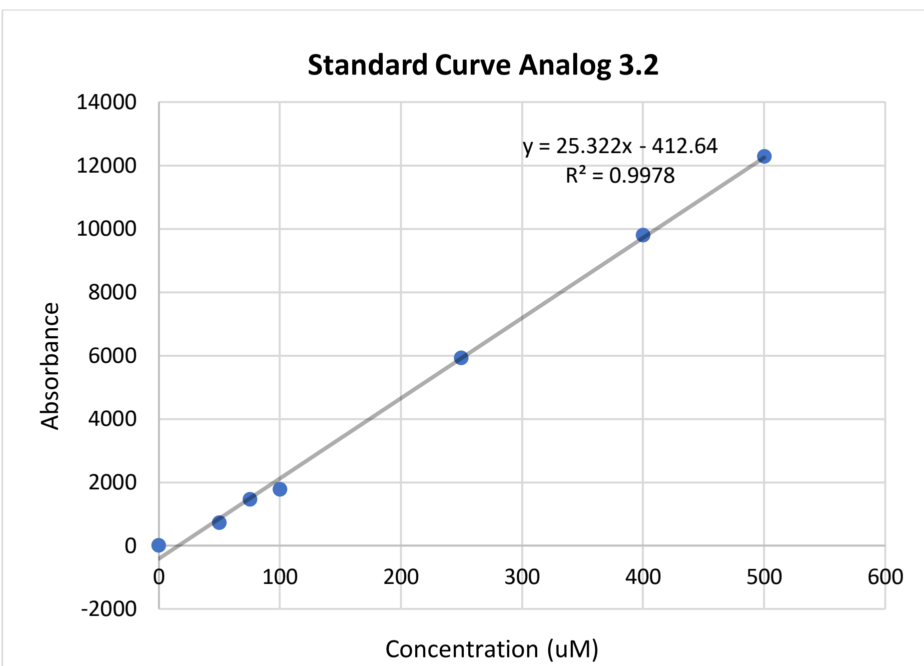
Supplement Graph 28. *The standard curve for absorbance vs. concentration (uM) of analog 3.1 utilizing* ***MS detection.***

Analog 3.2



Conc. (uM)	Area
500	15547.7
400	12950.3
250	8178.66
100	4004.7
75	2840.26
50	1834.2
25	1079.48
0	0

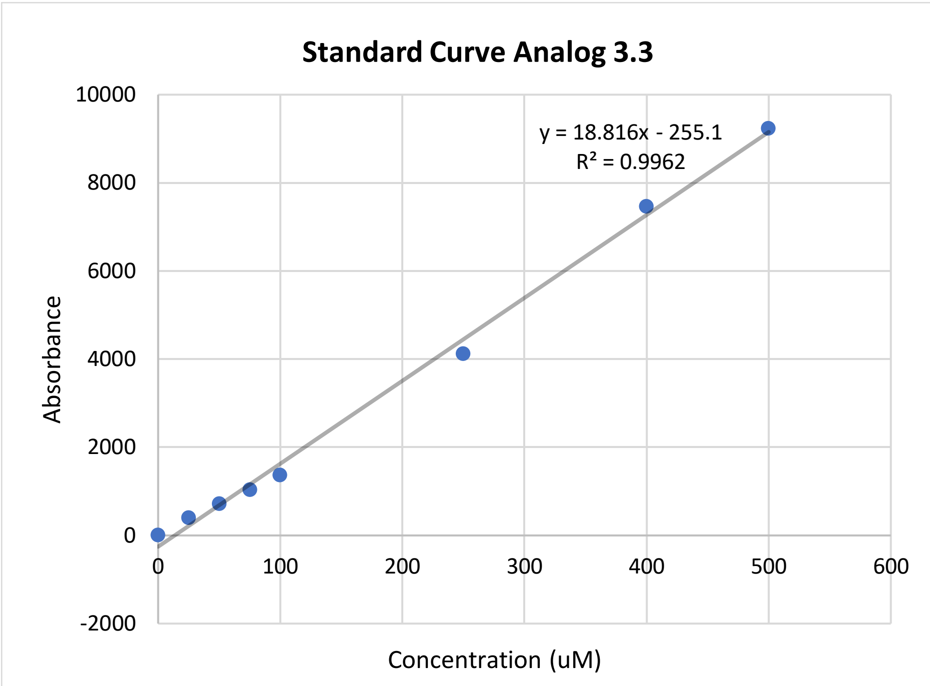
Supplement Graph 29. *The standard curve for absorbance vs. concentration (uM) of analog 3.2 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	12272.7
400	9792.552
250	5921.94
100	1775.4344
75	1457.577
50	708.894
0	0

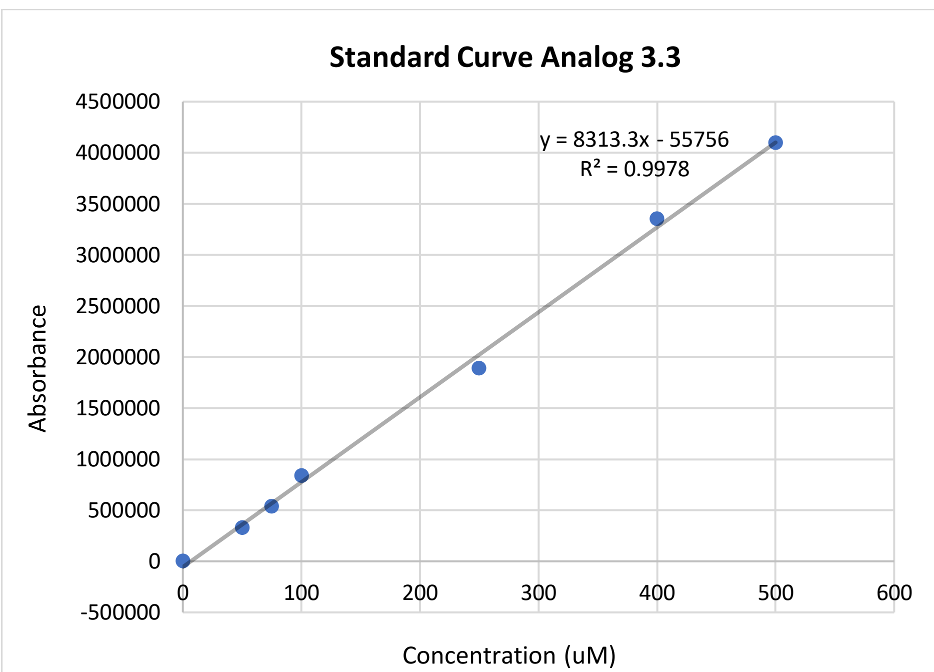
Supplement Graph 30. *The standard curve for absorbance vs. concentration (uM) of analog 3.2 utilizing* ***MS detection.***

Analog 3.3



Conc. (uM)	Area
500	9227
400	7464
250	4110.97
100	1368.185
75	1024.84
50	718.228
25	388.15
0	0

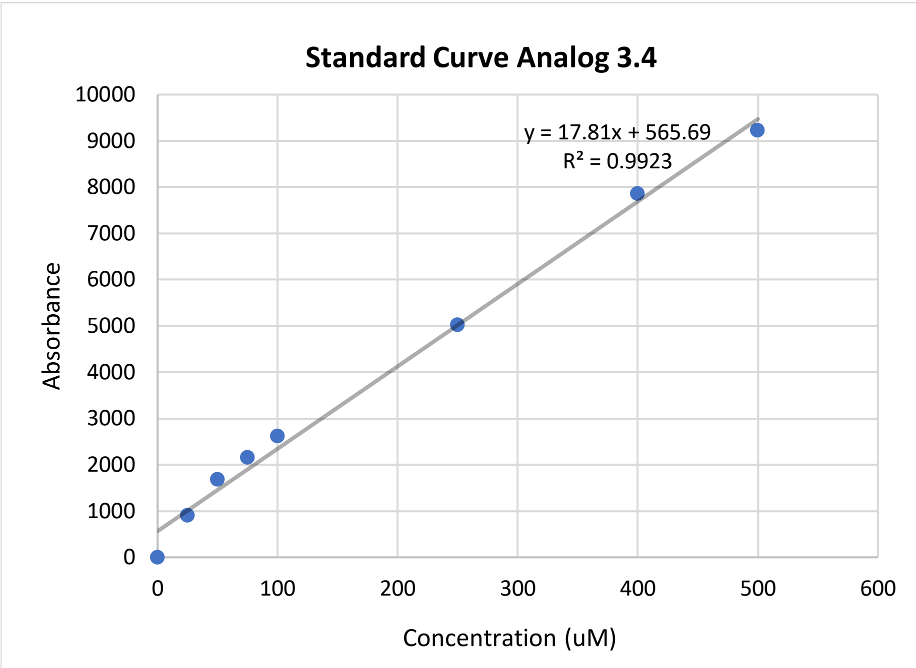
Supplement Graph 31. *The standard curve for absorbance vs. concentration (uM) of analog 3.3 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	4098273
400	3350280
250	1889170
100	839858
75	534824
50	328073
0	0

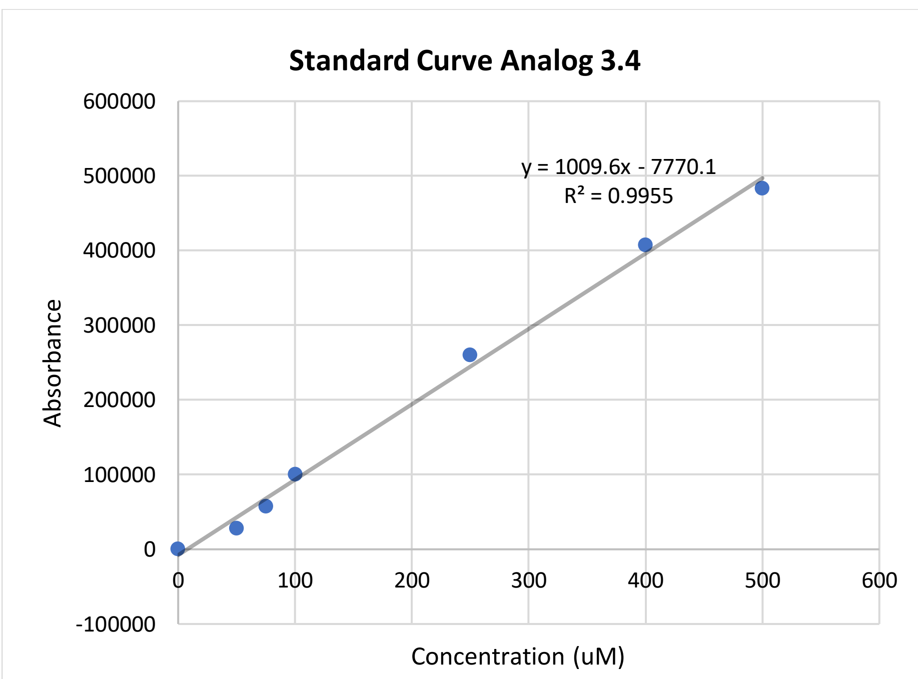
Supplement Graph 32. *The standard curve for absorbance vs. concentration (uM) of analog 3.3 utilizing* ***MS detection.***

Analog 3.4



Conc.(uM)	Area
500	9227
400	7854
250	5023
100	2621
75	2151
50	1684
25	899
0	0

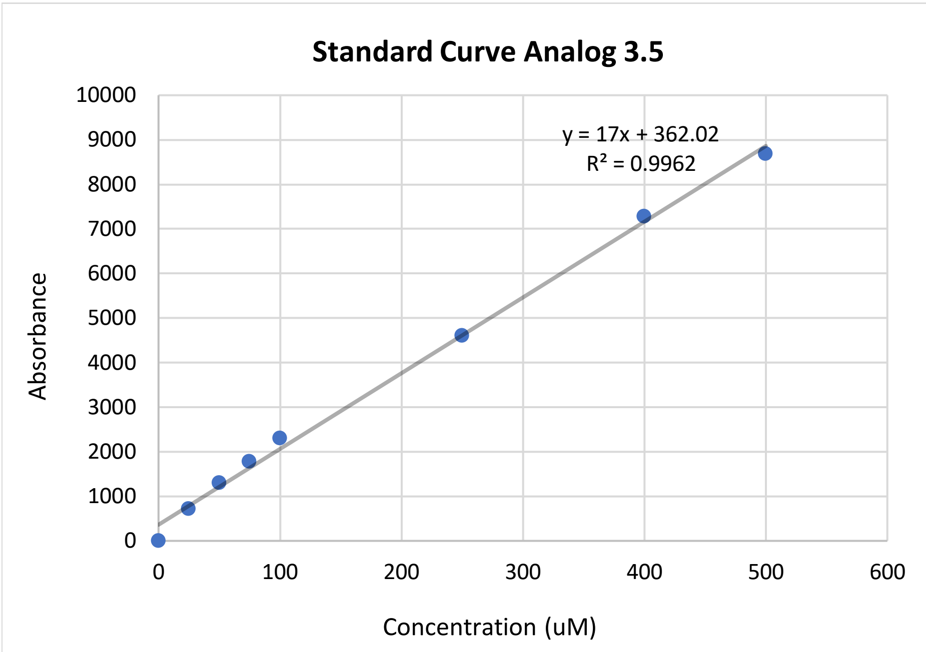
Supplement Graph 33. *The standard curve for absorbance vs. concentration (uM) of analog 3.4 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	482526
400	407205
250	259321
100	100328
75	56982
50	27457
0	0

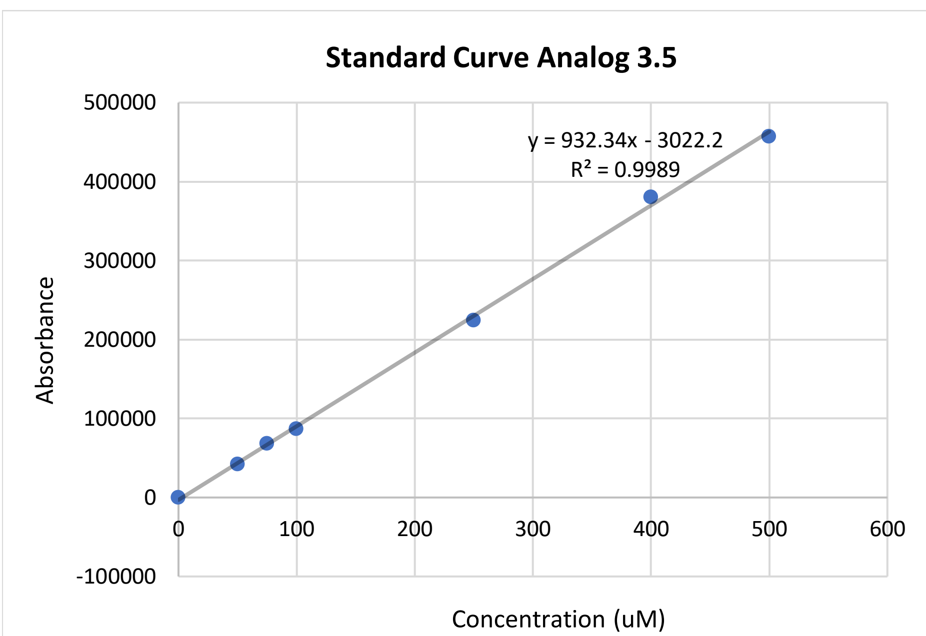
Supplement Graph 34. *The standard curve for absorbance vs. concentration (uM) of analog 3.4 utilizing* ***MS detection.***

Analog 3.5



Conc. (uM)	Area
500	8685
400	7290
250	4610
100	2304
75	1778
50	1302
25	727
0	0

Supplement Graph 35. *The standard curve for absorbance vs. concentration (uM) of analog 3.5 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	457740
400	380938
250	224223
100	87240
75	68575
50	42093
0	0

Supplement Graph 36. *The standard curve for absorbance vs. concentration (uM) of analog 3.5 utilizing* ***MS detection.***

m. Statistical Analysis Series 3

LogPapp			Percent Diffusion			LogP		
Pair	P-value	Inference	Pair	P-value	Inference	Pair	P-value	Inference
A vs B	1.0	NS	A vs B	3.40E-6	**	A vs B	0.118	NS
A vs C	0.00601	**	A vs C	1.33E-13	**	A vs C	0.00204	**
A vs D	7.08E-13	**	A vs D	7.42E-14	**	A vs D	1.38E-9	**
A vs E	1.24E-14	**	A vs E	7.42E-14	**	A vs E	1.55E-18	**
A vs F	2.01E-23	**	A vs F	7.42E-14	**	A vs F	1.75E-27	**
B vs C	0.921	NS	B vs C	3.60E-4	**	B vs C	1.0	NS
B vs D	2.43E-6	**	B vs D	1.57E-13	**	B vs D	0.00857	**
B vs E	1.81E-7	**	B vs E	7.42E-14	**	B vs E	1.03E-7	**
B vs F	2.56E-13	**	B vs F	7.42E-14	**	B vs F	3.93E-13	**
C vs D	0.0732	NS	C vs D	0.00824	**	C vs D	1.0	NS
C vs E	0.0188	*	C vs E	3.43E-12	**	C vs E	0.00210	**
C vs F	9.02E-6	**	C vs F	7.42E-14	**	C vs F	8.11E-7	**
D vs E	1.0	NS	D vs E	2.21E-5	**	D vs E	0.282	NS
D vs F	0.225	NS	D vs F	1.28E-13	**	D vs F	4.55E-4	**
E vs F	0.729	NS	E vs F	6.24E-5	**	E vs F	1.0	NS

Supplement Table 26. Data Analysis of Series 3. *Kruskal-Wallis test with Dunn's multiple comparisons post hoc analysis using GraphPad Prism v10.1.1. Definitions: A = ent-verticilide, B =3.1, C = 3.2, D = 3.3, E = 3.4, F = 3.5 and ** p < 0.01, * p < 0.05, NS = not significant.*

n. Series 4: Acceptor Concentration, $LogP_{app}$ and LogP

Acceptor Concentration											
4.1		**4.2**		**4.3**		**4.4**		**4.5**		**4.6**	
43.19		84.55		79.53		63.75		41.00		19.76	
46.24		68.00		67.31		58.93		38.22		18.06	
51.46	**MPT-5-206 (MS)**	62.29	**MPT-5-264 (MS)**	64.91	**MPT-5-267 (MS)**	50.72	**MPT-5-270 (MS)**	37.78	**MPT-5-277 (MS)**	17.76	**MPT-5-280 (MS)**
48.20		74.41		73.56		52.37		36.93		17.45	
57.92		81.42		83.29		51.52		35.44		18.13	
61.70		87.47		89.12		61.86		49.65		17.27	
59.76		96.31		84.52		55.71		48.51		24.22	
45.12	**MPT-5-206 (UV)**	97.01	**MPT-5-264 (UV)**	77.49	**MPT-5-267 (UV)**	56.97	**MPT-5-270 (UV)**	36.50	**MPT-5-277 (UV)**	21.75	**MPT-5-280 (UV)**
62.29		90.69		78.35		56.89		50.65		20.31	
72.35		96.13		88.08		59.64		46.86		18.52	
46.07		98.25		90.75		57.18		37.67		29.46	
47.42		74.35		95.65		54.30		34.46		23.04	
48.29	**MPT-5-207 (MS)**	90.21	**MPT-5-264 (ELSD)**	93.24	**MPT-5-267 (ELSD)**	51.92	**MPT-5-270 (ELSD)**	32.99	**MPT-5-277 (ELSD)**	20.19	**MPT-5-280 (ELSD)**
49.97		101.78		80.15		56.94		36.72		20.25	
52.04		110.10		87.56		57.17		33.92		19.90	
72.00		82.07		86.97		56.30		46.38		16.26	
60.65		74.25		77.38		66.18		39.93		26.16	
57.23	**MPT-5-207 (UV)**	84.73	**MPT-5-265 (MS)**	90.06	**MPT-5-268 (MS)**	67.75	**MPT-5-271 (MS)**	37.19	**MPT-5-278 (MS)**	16.59	**MPT-5-281 (MS)**
62.35		97.53		83.38		59.93		34.08		19.59	
43.59		71.55		83.10		65.37		31.47		22.87	
38.58		97.33		94.61		56.89		43.51		11.35	
39.64		104.86		96.17		50.22		42.71		20.31	
35.39	**MPT-5-208 (MS)**	118.37	**MPT-5-265 (UV)**	97.03	**MPT-5-268 (UV)**	56.97	**MPT-5-271 (UV)**	38.64	**MPT-5-278 (UV)**	16.73	**MPT-5-281 (UV)**
38.55		101.33		94.46		57.75		40.30		13.86	
37.55		104.37		98.06		50.81		50.65		17.09	
43.59		97.45		68.36		55.89		40.07		21.59	
55.00		106.52		70.75		53.18		34.30		17.50	
38.18	**MPT-5-208 (UV)**	105.76	**MPT-5-265 (ELSD)**	72.79	**MPT-5-268 (ELSD)**	58.86	**MPT-5-271 (ELSD)**	40.71	**MPT-5-278 (ELSD)**	15.55	**MPT-5-281 (ELSD)**
46.12		98.53		75.59		59.66		38.35		15.41	
43.29		105.28		79.02		59.81		39.18		15.21	
50.15	**Mean**	**92.10**	**Mean**	**83.37**	**Mean**	**58.07**	**Mean**	**39.83**	**Mean**	**19.07**	**Mean**
10.02	**Std Dev**	**13.76**	**Std Dev**	**9.54**	**Std Dev**	**4.55**	**Std Dev**	**5.37**	**Std Dev**	**3.71**	**Std Dev**

Supplement Table 27. *Acceptor concentration experimental values for ent-vert and analogs in series 4 using all detection methods.*

LogPapp											
4.1		4.2		4.3		4.4		4.5		4.6	
-5.82	**MPT-5-206 (MS)**	-5.37	**MPT-5-264 (MS)**	-5.33	**MPT-5-267 (MS)**	-5.55	**MPT-5-270 (MS)**	-5.89	**MPT-5-277 (MS)**	-5.93	**MPT-5-280 (MS)**
-5.77		-5.45		-5.34		-5.56		-5.93		-5.92	
-5.74		-5.49		-5.36		-5.63		-5.87		-5.95	
-5.74		-5.42		-5.33		-5.59		-5.93		-5.93	
-5.67		-5.40		-5.33		-5.60		-5.98		-5.93	
-5.53	**MPT-5-206 (UV)**	-5.38	**MPT-5-264 (UV)**	-5.42	**MPT-5-267 (UV)**	-5.57	**MPT-5-270 (UV)**	-5.63	**MPT-5-277 (UV)**	-6.18	**MPT-5-280 (UV)**
-5.52		-5.41		-5.42		-5.65		-5.62		-6.01	
-5.61		-5.34		-5.48		-5.63		-5.73		-6.06	
-5.52		-5.39		-5.48		-5.60		-5.60		-6.09	
-5.46		-5.38		-5.43		-5.61		-5.65		-6.13	
-5.79	**MPT-5-207 (MS)**	-5.32	**MPT-5-264 (ELSD)**	-5.37	**MPT-5-267 (ELSD)**	-5.68	**MPT-5-270 (ELSD)**	-5.83	**MPT-5-277 (ELSD)**	-6.12	**MPT-5-280 (ELSD)**
-5.77		-5.40		-5.43		-5.71		-5.85		-6.24	
-5.74		-5.36		-5.43		-5.71		-5.82		-6.32	
-5.72		-5.28		-5.41		-5.68		-5.86		-6.33	
-5.70		-5.29		-5.39		-5.68		-5.91		-6.30	
-5.46	**MPT-5-207 (UV)**	-5.35	**MPT-5-265 (MS)**	-5.40	**MPT-5-268 (MS)**	-5.62	**MPT-5-271 (MS)**	-5.83	**MPT-5-278 (MS)**	-5.98	**MPT-5-281 (MS)**
-5.51		-5.44		-5.48		-5.54		-5.90		-5.86	
-5.52		-5.38		-5.42		-5.52		-5.94		-5.98	
-5.50		-5.33		-5.45		-5.54		-5.98		-5.92	
-5.60		-5.44		-5.45		-5.52		-6.02		-5.89	
-5.86	**MPT-5-208 (MS)**	-5.33	**MPT-5-265 (UV)**	-5.33	**MPT-5-268 (UV)**	-5.60	**MPT-5-271 (UV)**	-5.64	**MPT-5-278 (UV)**	-6.28	**MPT-5-281 (UV)**
-5.83		-5.32		-5.34		-5.67		-5.66		-6.08	
-5.86		-5.31		-5.33		-5.63		-5.69		-6.17	
-5.86		-5.36		-5.36		-5.62		-5.70		-6.25	
-5.87		-5.34		-5.35		-5.66		-5.63		-6.17	
-5.62	**MPT-5-208 (UV)**	-5.34	**MPT-5-265 (ELSD)**	-5.40	**MPT-5-268 (ELSD)**	-5.69	**MPT-5-271 (ELSD)**	-5.79	**MPT-5-278 (ELSD)**	-6.31	**MPT-5-281 (ELSD)**
-5.55		-5.28		-5.37		-5.71		-5.86		-6.45	
-5.66		-5.31		-5.35		-5.65		-5.76		-6.59	
-5.59		-5.34		-5.38		-5.63		-5.78		-6.53	
-5.62		-5.30		-5.40		-5.61		-5.80		-6.56	
-5.66	**Mean**	**-5.36**	**Mean**	**-5.34**	**Mean**	**-5.61**	**Mean**	**-5.80**	**Mean**	**-6.15**	**Mean**
0.13	**Std Dev**	**0.05**	**Std Dev**	**0.28**	**Std Dev**	**0.06**	**Std Dev**	**0.12**	**Std Dev**	**0.21**	**Std Dev**

Supplement Table 28. *LogP$_{app}$ experimental values for ent-vert and analogs in series 4 using all detection methods, calculated using Supplement Equation 1.*

LogP											
4.1		4.2		4.3		4.4		4.5		4.6	
-9.53	**MPT-5-206 (MS)**	-9.22	**MPT-5-264 (MS)**	-9.14	**MPT-5-267 (MS)**	-9.36	**MPT-5-270 (MS)**	-9.56	**MPT-5-277 (MS)**	-9.89	**MPT-5-280 (MS)**
-9.50		-9.33		-9.15		-9.39		-9.59		-9.92	
-9.45		-9.37		-9.17		-9.46		-9.59		-9.93	
-9.48		-9.28		-9.12		-9.45		-9.60		-9.94	
-9.40		-9.24		-9.12		-9.45		-9.62		-9.92	
-9.37	**MPT-5-206 (UV)**	-9.21	**MPT-5-264 (UV)**	-9.20	**MPT-5-267 (UV)**	-9.37	**MPT-5-270 (UV)**	-9.47	**MPT-5-277 (UV)**	-9.94	**MPT-5-280 (UV)**
-9.39		-9.16		-9.22		-9.42		-9.48		-9.79	
-9.51		-9.16		-9.26		-9.41		-9.61		-9.84	
-9.37		-9.19		-9.26		-9.41		-9.46		-9.87	
-9.30		-9.16		-9.20		-9.39		-9.50		-9.91	
-9.51	**MPT-5-207 (MS)**	-9.15	**MPT-5-264 (ELSD)**	-9.14	**MPT-5-267 (ELSD)**	-9.41	**MPT-5-270 (ELSD)**	-9.60	**MPT-5-277 (ELSD)**	-9.71	**MPT-5-280 (ELSD)**
-9.49		-9.28		-9.16		-9.43		-9.64		-9.82	
-9.48		-9.19		-9.18		-9.45		-9.66		-9.87	
-9.47		-9.13		-9.14		-9.41		-9.61		-9.87	
-9.45		-9.09		-9.14		-9.40		-9.64		-9.88	
-9.30	**MPT-5-207 (UV)**	-9.24	**MPT-5-265 (MS)**	-9.21	**MPT-5-268 (MS)**	-9.41	**MPT-5-271 (MS)**	-9.50	**MPT-5-278 (MS)**	-9.97	**MPT-5-281 (MS)**
-9.38		-9.28		-9.26		-9.34		-9.57		-9.76	
-9.40		-9.22		-9.19		-9.33		-9.60		-9.96	
-9.36		-9.15		-9.23		-9.38		-9.64		-9.89	
-9.53		-9.30		-9.23		-9.34		-9.68		-9.82	
-9.59	**MPT-5-208 (MS)**	-9.16	**MPT-5-265 (UV)**	-9.17	**MPT-5-268 (UV)**	-9.41	**MPT-5-271 (UV)**	-9.53	**MPT-5-278 (UV)**	-10.13	**MPT-5-281 (UV)**
-9.57		-9.12		-9.16		-9.47		-9.54		-9.87	
-9.62		-9.06		-9.16		-9.41		-9.58		-9.96	
-9.59		-9.13		-9.17		-9.40		-9.56		-10.04	
-9.60		-9.12		-9.15		-9.46		-9.46		-9.95	
-9.53	**MPT-5-208 (UV)**	-9.15	**MPT-5-265 (ELSD)**	-9.15	**MPT-5-268 (ELSD)**	-9.42	**MPT-5-271 (ELSD)**	-9.57	**MPT-5-278 (ELSD)**	-9.85	**MPT-5-281 (ELSD)**
-9.42		-9.11		-9.14		-9.44		-9.64		-9.94	
-9.59		-9.11		-9.13		-9.39		-9.56		-9.99	
-9.50		-9.15		-9.13		-9.39		-9.59		-9.99	
-9.53		-9.12		-9.15		-9.38		-9.58		-10.00	
-9.47	**Mean**	**-9.19**	**Mean**	**-9.17**	**Mean**	**-9.41**	**Mean**	**-9.57**	**Mean**	**-9.90**	**Mean**
0.09	**Std Dev**	**0.07**	**Std Dev**	**0.04**	**Std Dev**	**0.04**	**Std Dev**	**0.06**	**Std Dev**	**0.08**	**Std Dev**

Supplement Table 29. *LogP experimental values for ent-verticilide analogs in series 4 using all detection methods, calculated using Supplement Equation 2.*

o. Series 4: Experimental Variables from Calculations and Percent Recoveries

Cmpd	MW (g/mol)	Ave RT (min)	C $(x10^{-9})$	Well 1		Well 2		Well 3		Well 4		Well 5		Ave. %R
				%T	%R	%T	%R	%T	%R	%T	%R	%T	%R	
4.1	905.28	11.98	3.23	0.21	95	0.21	93	0.22	97	0.28	92	0.25	95	92.54 ± 2.90
4.1			3.20	0.31	98	0.29	93	0.30	92	0.35	96	0.34	96	
4.1			3.31	0.22	96	0.20	94	0.21	91	0.23	91	0.23	90	
4.1			3.26	0.28	96	0.30	92	0.28	89	0.28	93	0.30	88	
4.1			3.24	0.21	92	0.22	90	0.21	85	0.19	93	0.20	91	
4.1			3.25	0.29	92	0.29	93	0.33	92	0.31	89	0.32	90	
4.2	891.25	11.80	3.01	0.74	83	0.74	83	0.72	85	0.72	82	0.75	83	87.63 ± 2.71
4.2			3.03	0.68	89	0.69	89	0.72	88	0.72	89	0.71	85	
4.2			3.03	0.73	91	0.74	89	0.74	91	0.70	88	0.68	89	
4.2			3.05	0.78	87	0.77	86	0.79	88	0.78	89	0.74	87	
4.2			3.06	0.71	87	0.68	91	0.70	93	0.71	89	0.68	85	
4.2			3.08	0.72	90	0.73	90	0.72	89	0.71	88	0.70	86	
4.3	877.23	11.93	3.33	0.49	90	0.49	85	0.44	87	0.44	88	0.48	91	91.20 ± 3.22
4.3			3.35	0.56	93	0.55	91	0.54	93	0.56	95	0.56	95	
4.3			3.30	0.53	90	0.52	95	0.48	93	0.49	98	0.51	94	
4.3			3.30	0.50	85	0.44	87	0.49	91	0.47	89	0.47	89	
4.3			3.31	0.56	87	0.55	90	0.56	91	0.54	93	0.54	94	
4.3			3.29	0.50	94	0.53	91	0.54	89	0.52	94	0.50	94	
4.4	877.23	11.87	3.23	0.34	100	0.40	97	0.41	96	0.39	90	0.41	92	91.80 ± 3.29
4.4			3.28	0.35	87	0.31	90	0.34	92	0.34	92	0.32	89	
4.4			3.23	0.51	95	0.55	90	0.61	92	0.52	88	0.51	89	
4.4			3.25	0.30	96	0.29	94	0.33	92	0.33	91	0.35	86	
4.4			3.27	0.47	91	0.49	90	0.47	92	0.46	88	0.49	89	
4.4			3.29	0.39	89	0.44	96	0.41	91	0.53	95	0.55	95	
4.5	863.20	11.76	3.49	0.20	94	0.19	94	0.21	81	0.19	89	0.17	94	91.33 ± 4.80
4.5			3.47	0.33	90	0.34	86	0.28	85	0.36	84	0.33	88	
4.5			3.48	0.22	91	0.22	86	0.23	78	0.22	95	0.20	97	
4.5			3.45	0.23	96	0.20	93	0.18	92	0.17	90	0.15	89	
4.5			3.48	0.33	82	0.32	84	0.30	83	0.29	88	0.34	91	
4.5			3.47	0.25	89	0.22	88	0.27	84	0.25	83	0.24	89	
4.6	849.17	11.64	3.25	0.19	94	0.19	88	0.18	93	0.19	88	0.18	89	88.43 ± 4.22
4.6			3.26	0.11	95	0.16	91	0.14	92	0.13	90	0.12	92	
4.6			3.23	0.12	101	0.10	92	0.08	88	0.08	90	0.08	83	
4.6			3.26	0.17	94	0.22	96	0.17	95	0.19	93	0.20	94	
4.6			3.25	0.09	81	0.13	90	0.11	89	0.09	91	0.11	93	
4.6			3.29	0.11	96	0.13	91	0.14	98	0.11	85	0.13	88	

Supplement Table 30. The Variables from Calculations for Analogs in Series 4. *The data for series 4 analogs are comprised of 6 experiments, each with 5 replicates run in tandem (30 total). The molecular weights and mean retention times seen via HPLC (210 nm) are listed. The C values and %T values are calculated using Supplement Equation **1**. The mean percent recoveries are listed. Definitions: MW = molecular weight, RT = retention time, %R = % recovery, Ave. %R = mean ± standard deviation.*

Cmpd	Ave. $logP_{app}$	Ave. logP	Well 1		Well 2		Well 3		Well 4		Well 5		Ave. [acc]
			[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	
4.1	-5.75	-9.48	43.19	432.53	46.24	420.51	51.46	431.50	48.20	409.50	57.92	418.93	50.15 ± 10.01 uM (10%)
4.1	-5.53	-9.39	61.70	428.94	59.76	407.70	45.12	417.29	62.30	416.76	72.35	408.06	
4.1	-5.74	-9.48	46.07	432.20	47.42	424.49	48.30	405.30	49.97	405.38	52.04	397.51	
4.1	-5.52	-9.40	72.00	406.18	60.65	401.82	57.23	389.53	62.35	404.88	43.59	396.29	
4.1	-5.86	-9.60	38.58	421.30	39.64	410.70	35.39	390.39	38.55	424.17	37.55	419.15	
4.1	-5.61	-9.52	43.59	417.94	55.00	411.00	38.18	419.65	46.12	399.23	43.30	408.06	
4.2	-5.43	-9.29	84.55	347.31	67.99	351.85	62.29	361.44	74.41	358.14	81.42	365.01	92.10 ± 13.76 uM (18%)
4.2	-5.38	-9.17	87.47	331.80	96.31	395.35	97.01	340.46	90.69	356.15	96.13	363.54	
4.2	-5.33	-9.17	98.25	343.29	74.35	323.77	90.21	347.91	101.78	327.34	110.10	352.69	
4.2	-5.39	-9.24	82.07	324.21	74.25	368.35	84.73	361.44	97.53	358.14	71.55	358.41	
4.2	-5.33	-9.12	97.33	332.43	104.86	348.76	118.37	386.38	101.33	371.67	104.37	360.85	
4.2	-5.31	-9.13	97.44	359.43	106.52	338.31	105.76	360.72	98.53	365.26	105.28	349.19	
4.3	-5.34	-9.14	79.53	364.89	67.31	359.49	64.91	368.64	73.56	372.61	83.28	370.32	83.37 ± 9.54 uM (17%)
4.3	-5.44	-9.22	89.12	359.71	84.52	342.64	77.49	358.55	78.35	363.53	88.08	367.50	
4.3	-5.40	-9.15	90.64	349.42	95.64	380.01	93.24	371.57	80.15	388.75	87.56	369.57	
4.3	-5.44	-9.22	86.96	340.35	77.38	359.08	90.06	365.24	83.38	362.35	83.10	363.42	
4.3	-5.34	-9.16	94.61	342.61	96.17	355.79	97.03	356.47	94.45	369.48	98.05	372.36	
4.3	-5.38	-9.14	68.36	372.16	70.75	354.87	72.79	343.07	75.59	367.57	79.02	371.09	
4.4	-5.58	-9.42	63.75	412.60	58.93	389.99	50.72	411.42	52.37	387.78	51.52	393.18	57.38 ± 4.55 uM (11%)
4.4	-5.61	-9.40	61.86	380.58	55.71	421.72	56.97	407.63	56.89	373.33	59.64	401.37	
4.4	-5.69	-9.42	57.18	422.87	54.30	427.45	51.92	404.03	56.94	418.11	57.17	417.01	
4.4	-5.55	-9.36	56.30	443.40	66.18	420.22	67.75	411.42	59.93	387.78	65.37	393.18	
4.4	-5.64	-9.43	56.89	380.24	50.22	399.18	56.97	402.04	57.75	400.33	50.81	392.51	
4.4	-5.66	-9.40	55.88	422.40	53.17	417.61	58.86	400.10	59.66	395.34	59.81	370.44	
4.5	-5.92	-9.59	41.00	431.13	38.22	432.22	37.78	369.28	36.93	409.82	35.44	436.40	39.83 ± 5.373 uM (8%)
4.5	-5.65	-9.50	49.65	400.20	48.51	382.02	36.50	388.82	50.65	371.22	46.86	393.99	
4.5	-5.85	-9.63	37.67	417.03	34.46	397.28	32.98	358.95	36.72	436.25	33.92	450.10	
4.5	-5.93	-9.60	46.38	431.46	39.93	424.33	37.19	420.71	34.08	418.30	31.48	412.52	
4.5	-5.67	-9.54	43.51	365.00	42.71	375.08	38.64	372.32	40.29	399.65	50.65	402.27	
4.5	-5.79	-9.59	40.07	403.04	34.30	407.20	40.70	378.31	38.35	376.44	39.18	406.31	
4.6	-5.93	-9.92	19.76	448.80	18.06	423.45	17.76	447.11	17.45	421.23	18.13	427.24	19.07 ± 3.708 uM (4%)
4.6	-6.09	-9.87	17.27	459.34	24.22	429.21	21.74	436.38	20.31	429.21	18.52	441.40	
4.6	-6.26	-9.83	29.46	474.24	23.04	435.48	20.18	420.82	20.25	430.53	19.90	396.08	
4.6	-5.93	-9.88	16.26	451.55	26.16	454.82	16.59	459.32	19.59	444.39	22.87	446.91	
4.6	-6.19	-9.99	11.35	391.19	20.31	427.78	16.73	430.29	13.86	442.12	17.09	446.79	
4.6	-6.49	-9.95	21.59	457.15	17.50	435.60	15.54	473.98	15.41	410.50	15.21	424.59	

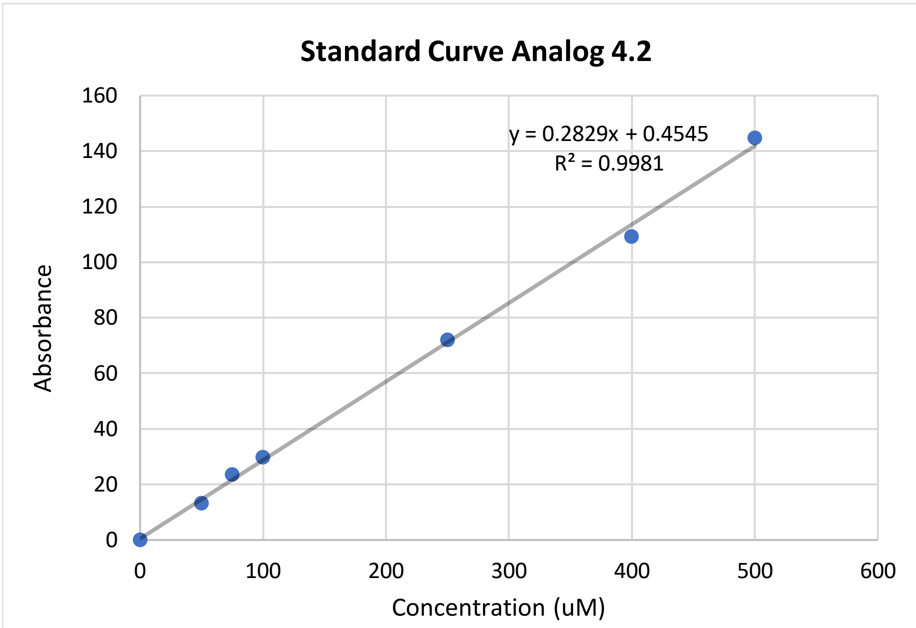
Supplement Table 31. Final Experimental Data for Analogs in Series 4. *The mean $logP_{app}$ (calculated from Supplement Equation 1) and logP values (calculated from (Supplement Equation 2) are listed. The acceptor and donor concentrations are calculated using a standard curve and the units are uM. The initial concentration is 500 uM for all experiments. The total mean acceptor concentrations are listed in the final column. Definitions: [acc] = acceptor concentration after incubation, [donor] = donor concentration after incubation, mean [acc] = mean acceptor concentration ± standard deviation.*

p. Standard Curves for Series 4

Analog 4.1

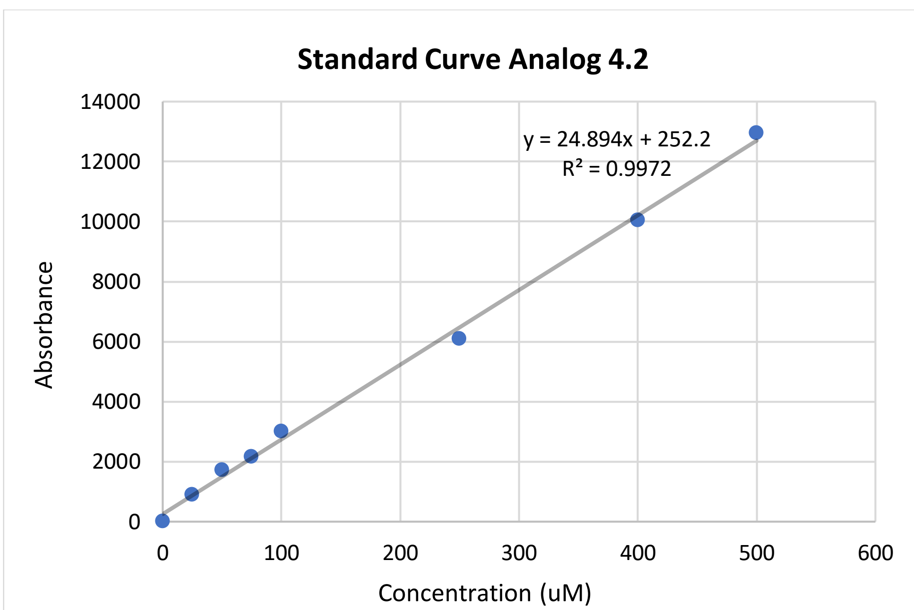
- Same as analog 3.5/5.1

Analog 4.2



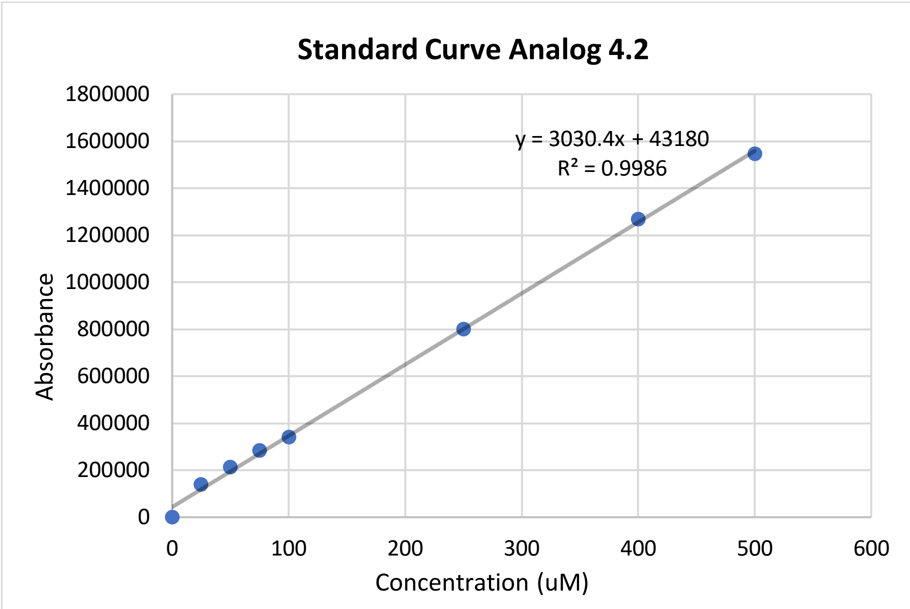
Conc. (uM)	Area
500	144.65
400	109.323
250	71.929
100	29.7709
75	23.424
50	13.076
0	0

Supplement Graph 37. *The standard curve for absorbance vs. concentration (uM) of analog 4.2 utilizing* ***ELSD detection****.*



Conc. (uM)	Area
500	12946.411
400	10033.36
250	6096.09
100	3012.85
75	2155.79
50	1721.3
25	903.2
0	0

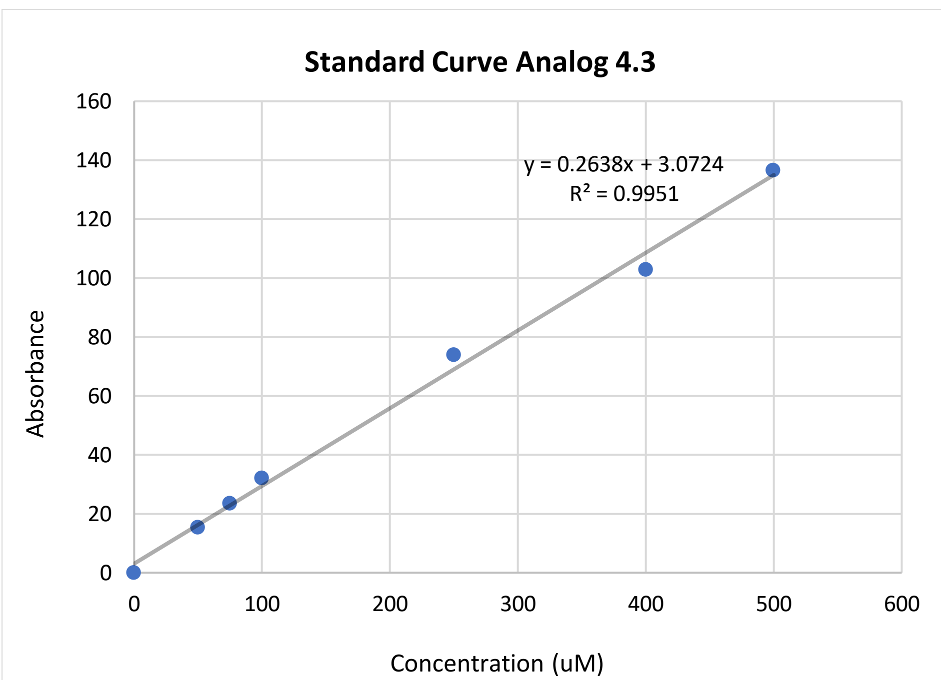
Supplement Graph 38. *The standard curve for absorbance vs. concentration (uM) of analog 4.2 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	1544958
400	1268530
250	799584
100	339632
75	283279
50	213664
25	138361
0	0

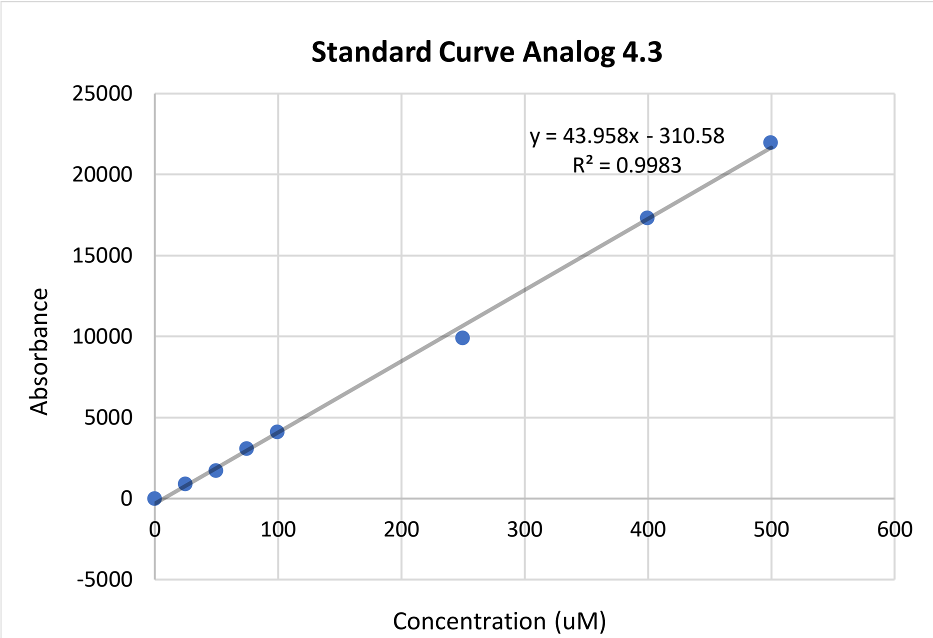
Supplement Graph 39. *The standard curve for absorbance vs. concentration (uM) of analog 4.2 utilizing* ***MS detection.***

Analog 4.3



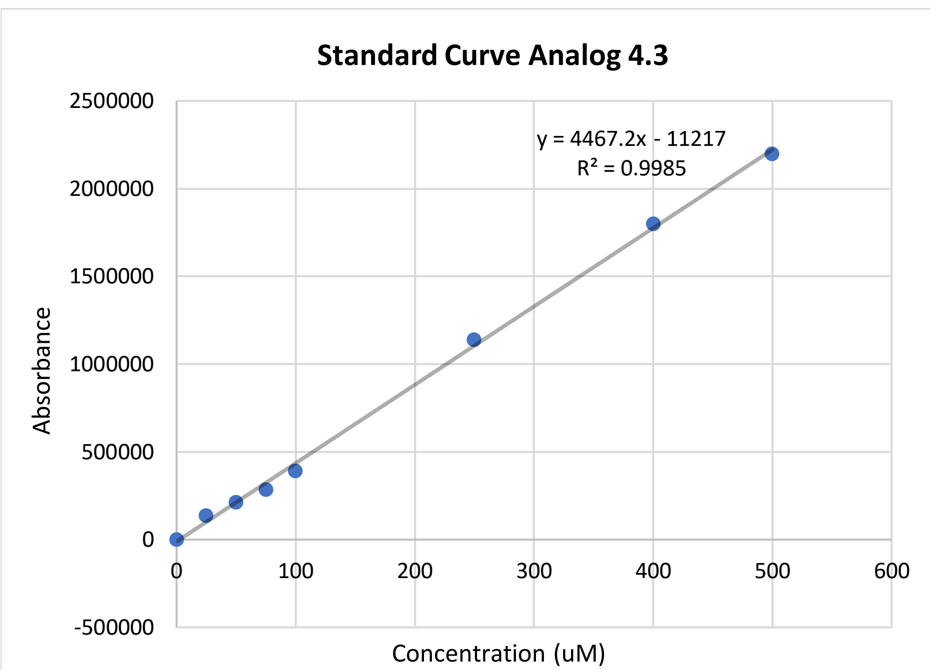
Conc. (uM)	Area
500	136.56
400	102.9
250	73.88
100	32.121
75	23.424
50	15.33
0	0

Supplement Graph 40. *The standard curve for absorbance vs. concentration (uM) of analog 4.3 utilizing* ***ELSD detection****.*



Conc. (uM)	Area
500	21992
400	17328.2
250	9928.3
100	4102.56
75	3095.61
50	1709.3
25	901.22
0	0

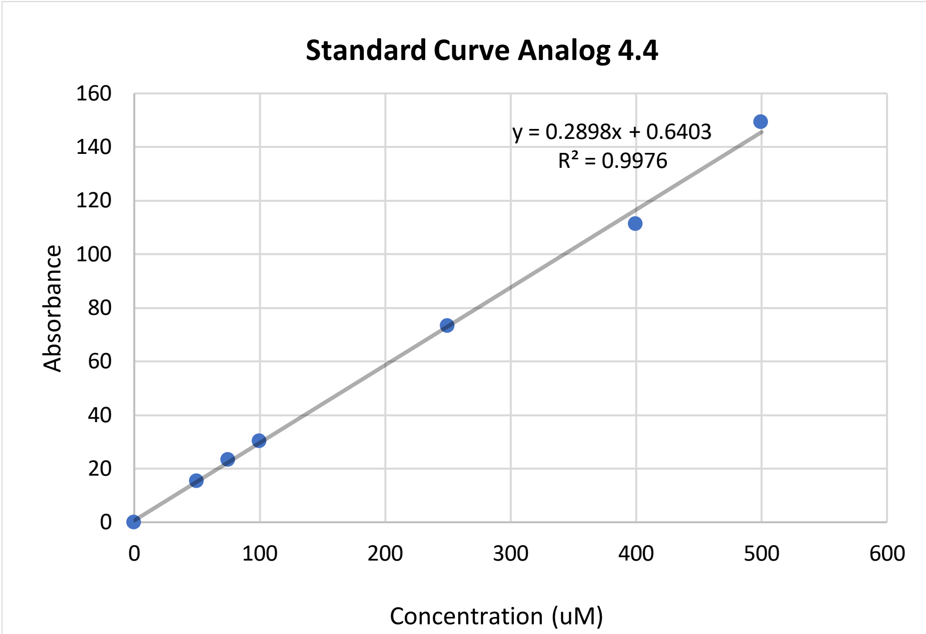
Supplement Graph 41. *The standard curve for absorbance vs. concentration (uM) of analog 4.3 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	2199503
400	1799308
250	1139403
100	390778
75	283279
50	213664
25	138361
0	0

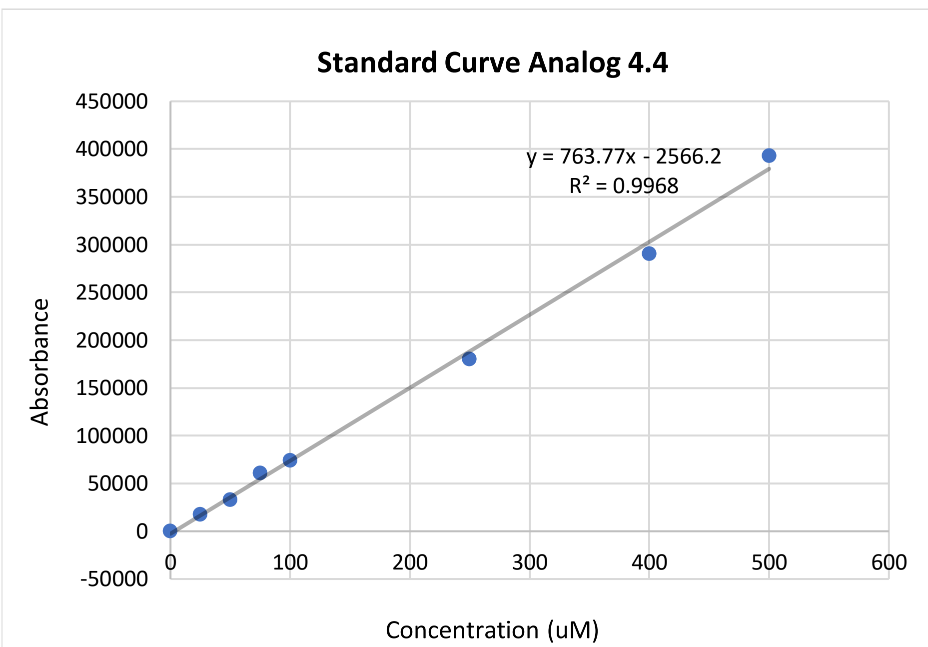
Supplement Graph 42. *The standard curve for absorbance vs. concentration (uM) of analog 4.3 utilizing* ***MS detection.***

Analog 4.4



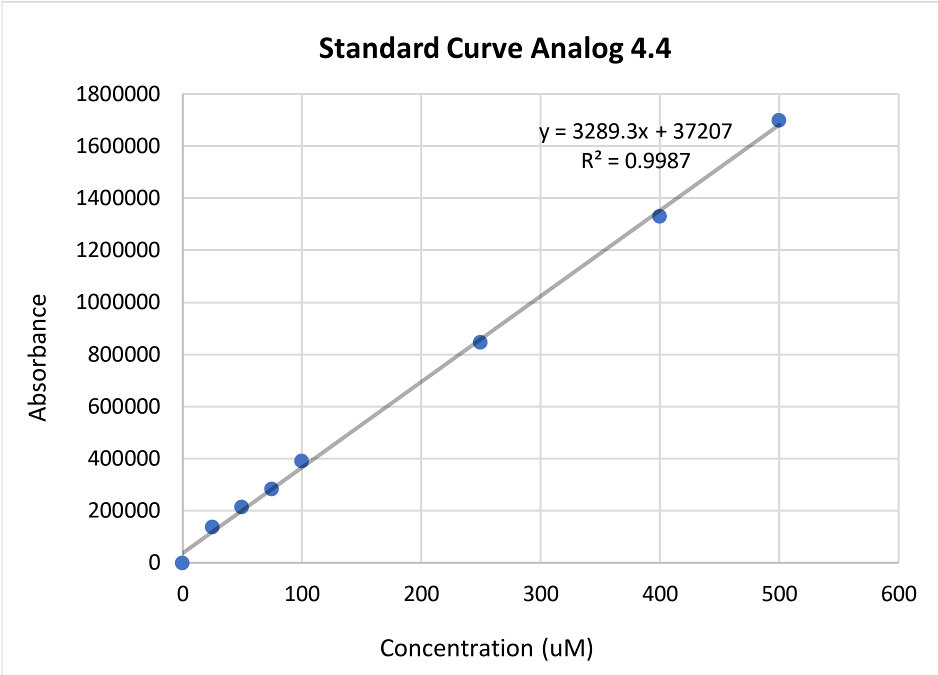
Conc. (uM)	Area
500	149.34
400	111.3
250	73.39
100	30.23
75	23.424
50	15.33
0	0

Supplement Graph 43. *The standard curve for absorbance vs. concentration (uM) of analog 4.4 utilizing* ***ELSD detection****.*



Conc. (uM)	Area
500	392843
400	290395
250	179909
100	73808
75	60951
50	33209
25	17636
0	0

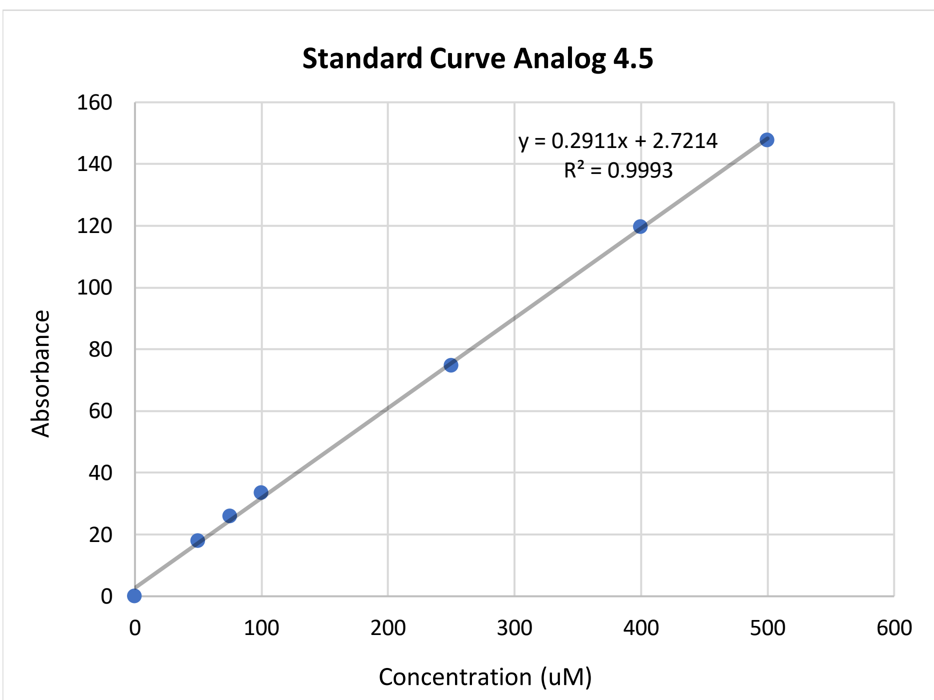
Supplement Graph 44. *The standard curve for absorbance vs. concentration (uM) of analog 4.4 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	1699435
400	1329934
250	847273
100	390778
75	283279
50	213664
25	138361
0	0

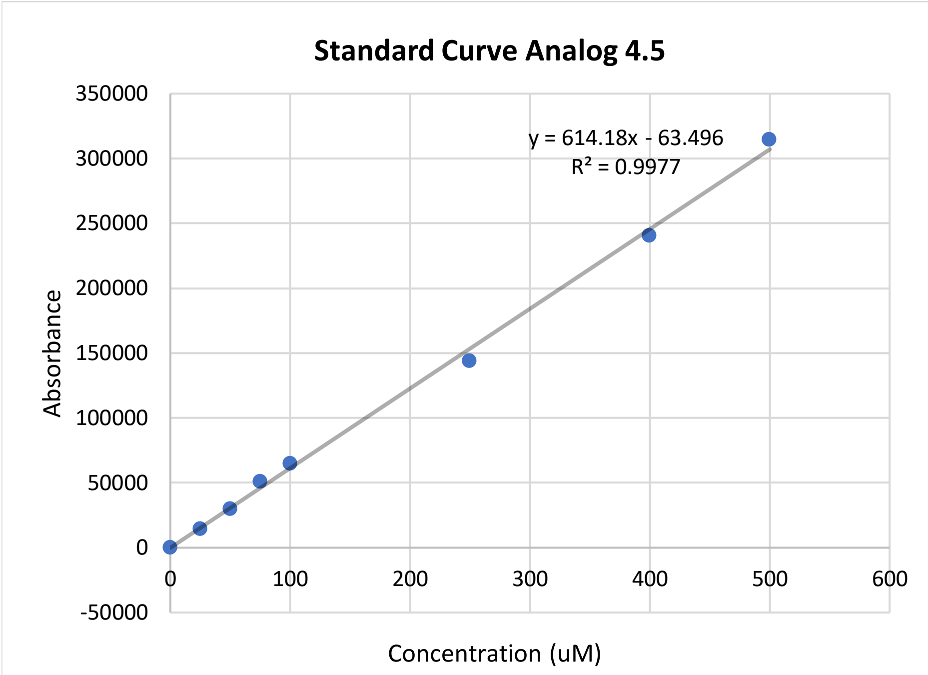
Supplement Graph 45. *The standard curve for absorbance vs. concentration (uM) of analog 4.4 utilizing* ***MS detection.***

Analog 4.5



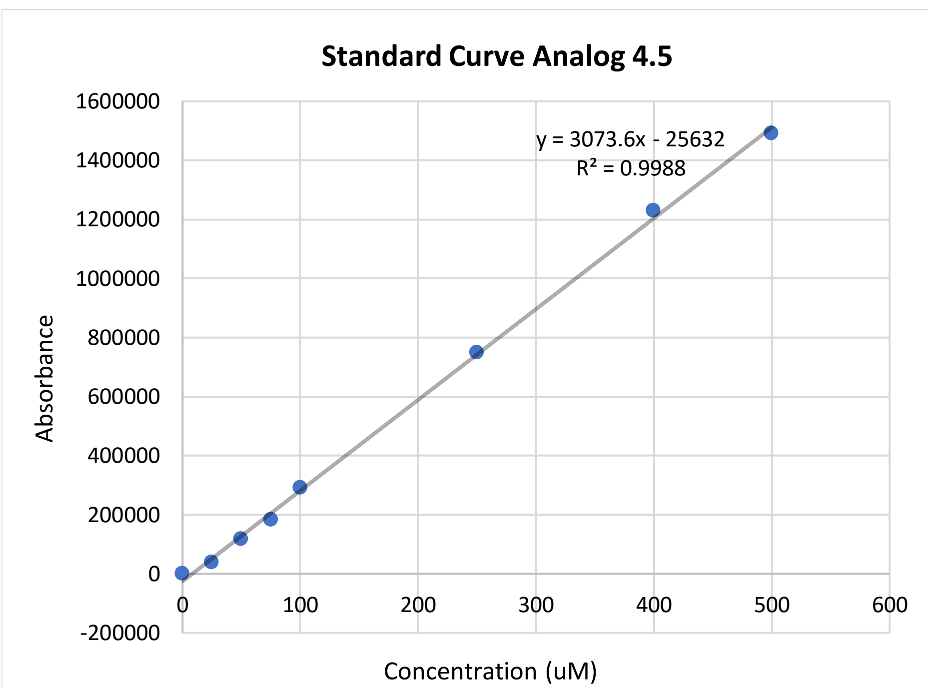
Conc. (uM)	Area
500	147.76
400	119.63
250	74.67
100	33.49
75	25.88
50	17.95
0	0

Supplement Graph 46. *The standard curve for absorbance vs. concentration (uM) of analog 4.5 utilizing* ***ELSD detection.***



Conc. (uM)	Area
500	314492
400	240539
250	143940
100	64857
75	51233
50	29898
25	14392
0	0

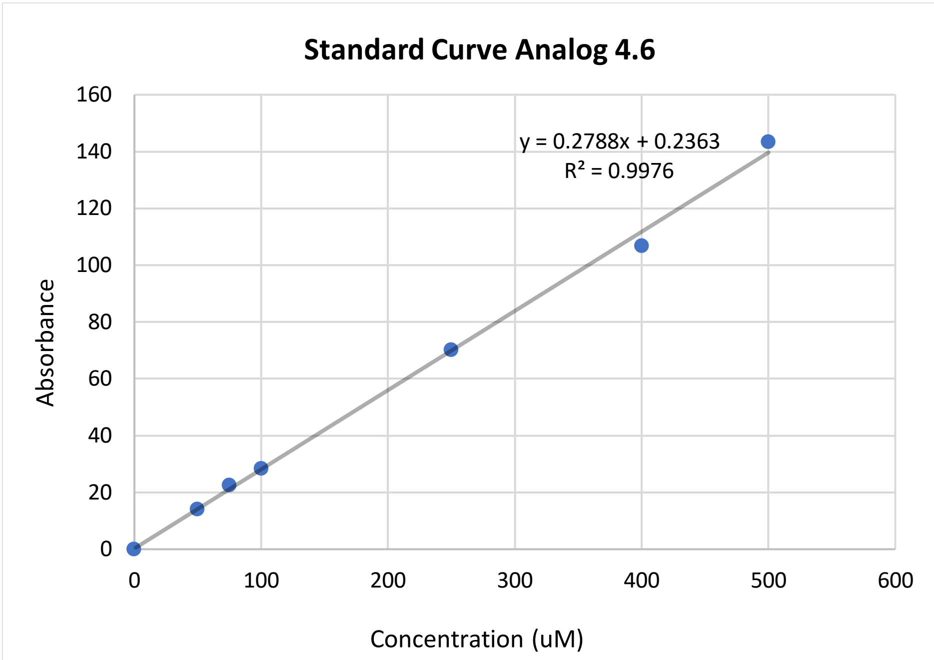
Supplement Graph 47. *The standard curve for absorbance vs. concentration (uM) of analog 4.5 utilizing **UV detection** (210 nm).*



Conc. (uM)	Area
500	1490635
400	1229376
250	749376
100	291545
75	182289
50	116651
25	38118
0	0

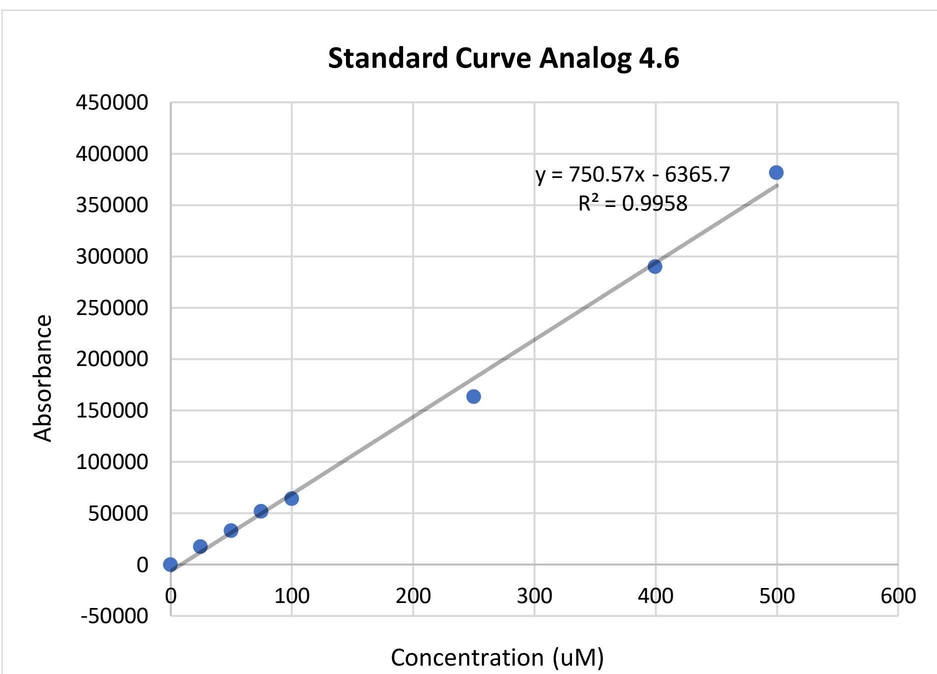
Supplement Graph 48. *The standard curve for absorbance vs. concentration (uM) of analog 4.5 utilizing **MS detection.***

Analog 4.6



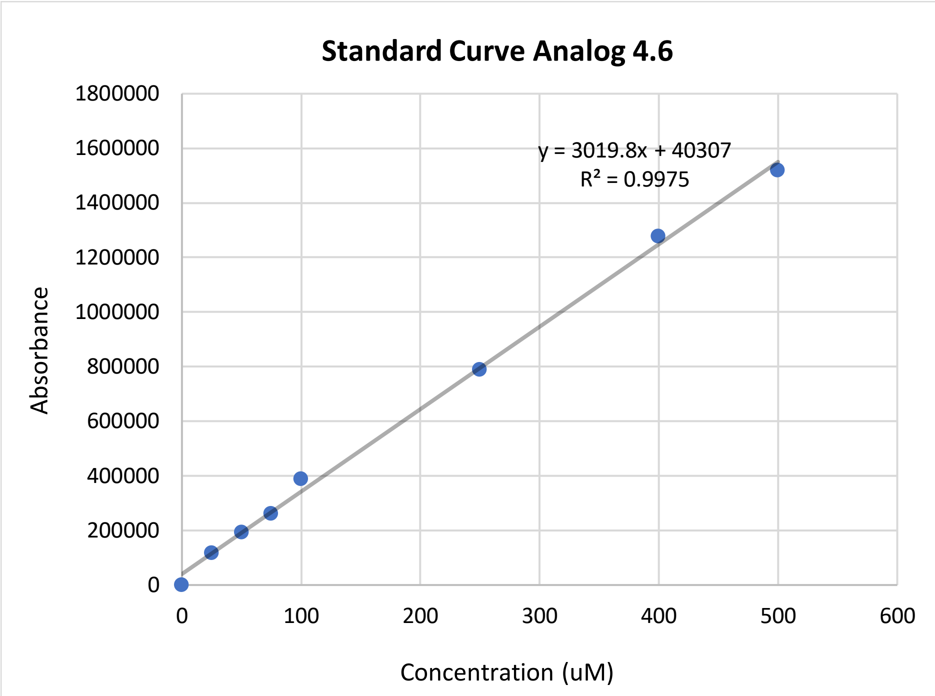
Conc. (uM)	Area
500	143.33
400	106.76
250	70.09
100	28.38
75	22.45
50	14
0	0

Supplement Graph 49. *The standard curve for absorbance vs. concentration (uM) of analog 4.6 utilizing* ***ELSD detection.***



Conc. (uM)	Area
500	381293
400	290037
250	163284
100	63999
75	51382
50	32942
25	16938
0	0

Supplement Graph 50. *The standard curve for absorbance vs. concentration (uM) of analog 4.6 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	1519328
400	1278893
250	790394
100	388475
75	261532
50	193098
25	118429
0	0

Supplement Graph 51. *The standard curve for absorbance vs. concentration (uM) of analog 4.6 utilizing* ***MS detection.***

q. Statistical Analysis Series 4

LogPapp			Percent Diffusion			LogP		
Pair	P-value	Inference	Pair	P-value	Inference	Pair	P-value	Inference
A vs B	5.19E-7	**	A vs B	8.96E-8	**	A vs B	1.45E-6	**
A vs C	2.72E-5	**	A vs C	1.90E-5	**	A vs C	9.78E-7	**
A vs D	1.0	NS	A vs D	1.0	NS	A vs D	1.0	NS
A vs E	0.640	NS	A vs E	0.642	NS	A vs E	0.681	NS
A vs F	3.20E-5	**	A vs F	4.43E-5	**	A vs F	4.88E-5	**
B vs C	1.0	NS	B vs C	1.0	NS	B vs C	1.0	NS
B vs D	1.64E-5	**	B vs D	1.81E-4	**	B vs D	0.00156	**
B vs E	6.87E-13	**	B vs E	6.60E-14	**	B vs E	3.37E-12	**
B vs F	1.62E-23	**	B vs F	1.42E-24	**	B vs F	2.63E-22	**
C vs D	5.42E-4	**	C vs D	0.00995	**	C vs D	0.00116	**
C vs E	1.57E-10	**	C vs E	9.59E-11	**	C vs E	1.97E-12	**
C vs F	2.77E-20	**	C vs F	2.62E-20	**	C vs F	1.27E-22	**
D vs E	0.114	NS	D vs E	0.00792	**	D vs E	0.00834	**
D vs F	1.10E-6	**	D vs F	1.45E-8	**	D vs F	1.54E-8	**
E vs F	0.0999	NS	E vs F	0.121	NS	E vs F	0.120	NS

Supplement Table 32. Data Analysis of Series 4. *Kruskal-Wallis test with Dunn's multiple comparisons post hoc analysis using GraphPad Prism v10.1.1. Definitions: A = 4.1, B = 4.2, C = 4.3, D = 4.4, E = 4.5, F = 4.6 and ** $p < 0.01$, * $p < 0.05$, NS = not significant.*

r. Series 5: Acceptor Concentration, $LogP_{app}$ and LogP

Acceptor Concentration											
5.1		**5.2**		**5.3**		**5.4**		**5.5**		**5.6**	
43.19	**MPT-5-206 (MS)**	115.43	**MPT-5-216 (MS)**	84.39	**MPT-5-198 (MS)**	72.82	**MPT-5-256 (ELSD)**	56.26	**MPT-5-283 (ELSD)**	83.50	**MPT-5-129 (ELSD)**
46.24		140.51		110.40		73.46		40.64		89.39	
51.46		117.49		87.40		72.68		62.91		91.58	
48.20		112.09		103.67		77.46		46.8		96.13	
57.92		115.77		87.13		72.54		49.73		92.96	
61.70	**MPT-5-206 (UV)**	120.82	**MPT-5-216 (UV)**	113.18	**MPT-5-198 (UV)**	86.71	**MPT-5-256 (UV)**	46.86	**MPT-5-283 (UV)**	99.38	**MPT-5-129 (UV)**
59.76		111.93		108.29		93.69		54.91		115.70	
45.12		127.84		103.74		60.11		51.14		100.79	
62.29		121.41		121.32		93.5		78.89		103.19	
72.35		124.05		88.51		80.13		54.2		115.29	
46.07	**MPT-5-207 (MS)**	114.96	**MPT-5-217 (MS)**	84.06	**MPT-5-199 (MS)**	81.66	**MPT-5-257 (ELSD)**	57.4	**MPT-5-284 (ELSD)**	71.30	**MPT-5-129 (MS)**
47.42		118.41		102.34		71.09		44.28		69.52	
48.29		107.44		96.93		83.77		49.62		66.92	
49.97		123.76		95.50		76.1		34.66		70.93	
52.04		119.42		100.48		83.49		60.53		69.28	
72.00	**MPT-5-207 (UV)**	110.94	**MPT-5-217 (UV)**	92.40	**MPT-5-199 (UV)**	60.08	**MPT-5-257 (UV)**	41.16	**MPT-5-284 (UV)**	80.44	**MPT-5-030 (ELSD)**
60.65		116.76		99.40		83.91		55.56		75.82	
57.23		120.88		92.61		88.07		43.94		89.06	
62.35		103.44		117.55		78.27		46.38		94.85	
43.59		129.92		97.42		70.1		48.6		89.83	
38.58	**MPT-5-208 (MS)**	117.68	**MPT-5-218 (MS)**	119.65	**MPT-5-200 (MS)**	92.42	**MPT-5-258 (ELSD)**	53.83	**MPT-5-285 (ELSD)**	99.14	**MPT-5-130 (UV)**
39.64		118.85		87.79		70.1		37.32		103.11	
35.39		116.9		96.39		73.9		49.51		91.18	
38.55		117.95		103.67		58.48		37.02		102.37	
37.55		114.55		104.74		85.89		54.05		115.12	
43.59	**MPT-5-208 (UV)**	130.55	**MPT-5-218 (UV)**	99.85	**MPT-5-200 (UV)**	60.95	**MPT-5-258 (UV)**	40.3	**MPT-5-285 (UV)**	68.15	**MPT-5-130 (MS)**
55.00		117.43		122.99		90.49		60.31		73.16	
38.18		115.09		98.68		84.98		36.85		72.44	
46.12		114.73		105.75		86.64		39.9		74.67	
43.29		117.2		105.15		77.46		50.69		75.92	
										88.53	**MPT-5-131 (ELSD)**
50.15	**Mean**	**118.47**	**Mean**	**101.04**	**Mean**	**78.03**	**Mean**	**49.48**	**Mean**	91.07	
10.02	**Std Dev**	**7.18**	**Std Dev**	**10.81**	**Std Dev**	**10.07**	**Std Dev**	**9.49**	**Std Dev**	92.98	
										99.06	
										86.01	
										107.84	**MPT-5-131 (UV)**
										99.08	
										75.07	
										83.98	
										93.56	
										72.93	**MPT-5-131 (MS)**
										72.08	
										70.51	
										75.49	
										77.42	
										87.26	**Mean**
										13.92	**Std Dev**

Supplement Table 33. *Acceptor concentration experimental values for ent-vert and analogs in series 5 using all detection methods.*

LogPapp											
5.1		5.2		5.3		5.4		5.5		5.6	
-5.82	**MPT-5-206 (MS)**	-5.27	**MPT-5-216 (MS)**	-5.38	**MPT-5-198 (MS)**	-5.48	**MPT-5-256 (ELSD)**	-5.71	**MPT-5-283 (ELSD)**	-5.37	**MPT-5-129 (ELSD)**
-5.77		-5.26		-5.27		-5.33		-5.63		-5.37	
-5.74		-5.26		-5.31		-5.42		-5.76		-5.37	
-5.74		-5.26		-5.24		-5.39		-5.65		-5.33	
-5.67		-5.27		-5.26		-5.39		-5.71		-5.34	
-5.53	**MPT-5-206 (UV)**	-5.26	**MPT-5-216 (UV)**	-5.3	**MPT-5-198 (UV)**	-5.43	**MPT-5-256 (UV)**	-5.58	**MPT-5-283 (UV)**	-5.33	**MPT-5-129 (UV)**
-5.52		-5.26		-5.3		-5.50		-5.58		-5.27	
-5.61		-5.27		-5.36		-5.41		-5.55		-5.32	
-5.52		-5.28		-5.33		-5.44		-5.62		-5.31	
-5.46		-5.27		-5.31		-5.51		-5.57		-5.26	
-5.79	**MPT-5-207 (MS)**	-5.27	**MPT-5-217 (MS)**	-5.36	**MPT-5-199 (MS)**	-5.43	**MPT-5-257 (ELSD)**	-5.66	**MPT-5-284 (ELSD)**	-5.49	**MPT-5-129 (MS)**
-5.77		-5.24		-5.24		-5.38		-5.62		-5.52	
-5.74		-5.25		-5.34		-5.37		-5.70		-5.57	
-5.72		-5.25		-5.25		-5.33		-5.74		-5.51	
-5.70		-5.25		-5.23		-5.32		-5.75		-5.55	
-5.46	**MPT-5-207 (UV)**	-5.45	**MPT-5-217 (UV)**	-5.33	**MPT-5-199 (UV)**	-5.42	**MPT-5-257 (UV)**	-5.53	**MPT-5-284 (UV)**	-5.99	**MPT-5-030 (ELSD)**
-5.51		-5.47		-5.38		-5.36		-5.45		-6.01	
-5.52		-5.51		-5.39		-5.48		-5.52		-5.95	
-5.50		-5.50		-5.39		-5.44		-5.53		-5.91	
-5.60		-5.52		-5.33		-5.36		-5.53		-5.94	
-5.86	**MPT-5-208 (MS)**	-5.48	**MPT-5-218 (MS)**	-5.34	**MPT-5-200 (MS)**	-5.48	**MPT-5-258 (ELSD)**	-5.66	**MPT-5-285 (ELSD)**	-5.33	**MPT-5-130 (UV)**
-5.83		-5.59		-5.39		-5.42		-5.69		-5.31	
-5.86		-5.50		-5.32		-5.40		-5.68		-5.35	
-5.86		-5.53		-5.33		-5.43		-5.75		-5.32	
-5.87		-5.46		-5.3		-5.39		-5.64		-5.26	
-5.62	**MPT-5-208 (UV)**	-5.19	**MPT-5-218 (UV)**	-5.28	**MPT-5-200 (UV)**	-5.34	**MPT-5-258 (UV)**	-5.63	**MPT-5-285 (UV)**	-5.53	**MPT-5-130 (MS)**
-5.55		-5.20		-5.34		-5.40		-5.54		-5.53	
-5.66		-5.21		-5.35		-5.35		-5.58		-5.56	
-5.59		-5.21		-5.31		-5.49		-5.61		-5.53	
-5.62		-5.22		-5.31		-5.42		-5.68		-5.53	
										-5.95	**MPT-5-131 (ELSD)**
-5.66	**Mean**	**-5.33**	**Mean**	**-5.32**	**Mean**	**-5.41**	**Mean**	**-5.63**	**Mean**	-5.94	
0.13	**Std Dev**	**0.13**	**Std Dev**	**0.05**	**Std Dev**	**0.05**	**Std Dev**	**0.08**	**Std Dev**	-5.93	
										-5.90	
										-5.96	
										-5.25	**MPT-5-131 (UV)**
										-5.30	
										-5.41	
										-5.36	
										-5.33	
										-5.45	**MPT-5-131 (MS)**
										-5.54	
										-5.56	
										-5.52	
										-5.44	
										-5.50	**Mean**
										0.23	**Std Dev**

Supplement Table 34. *LogP$_{app}$ experimental values for ent-vert and analogs in series 5 using all detection methods, calculated using Supplement Equation 1.*

LogP											
5.1		5.2		5.3		5.4		5.5		5.6	
-9.53		-9.07		-9.22		-9.29		-9.56		-9.23	
-9.50		-9.07		-9.10		-9.38		-9.46		-9.20	
-9.45	**MPT-5-206 (MS)**	-9.06	**MPT-5-216 (MS)**	-9.16	**MPT-5-198 (MS)**	-9.27	**MPT-5-256 (ELSD)**	-9.63	**MPT-5-283 (ELSD)**	-9.18	**MPT-5-129 (ELSD)**
-9.48		-9.06		-9.06		-9.31		-9.48		-9.16	
-9.40		-9.07		-9.12		-9.38		-9.56		-9.18	
-9.37		-9.05		-9.09		-9.29		-9.41		-9.15	
-9.39		-9.06		-9.12		-9.17		-9.42		-9.07	
-9.51	**MPT-5-206 (UV)**	-9.05	**MPT-5-216 (UV)**	-9.16	**MPT-5-198 (UV)**	-9.23	**MPT-5-256 (UV)**	-9.47	**MPT-5-283 (UV)**	-9.14	**MPT-5-129 (UV)**
-9.37		-9.06		-9.15		-9.26		-9.50		-9.13	
-9.30		-9.06		-9.14		-9.21		-9.43		-9.07	
-9.51		-9.06		-9.21		-9.29		-9.50		-9.30	
-9.49		-9.05		-9.04		-9.17		-9.43		-9.31	
-9.48	**MPT-5-207 (MS)**	-9.05	**MPT-5-217 (MS)**	-9.14	**MPT-5-199 (MS)**	-9.23	**MPT-5-257 (ELSD)**	-9.56	**MPT-5-284 (ELSD)**	-9.33	**MPT-5-129 (MS)**
-9.47		-9.06		-9.05		-9.18		-9.60		-9.30	
-9.45		-9.06		-9.04		-9.19		-9.61		-9.32	
-9.30		-9.19		-9.13		-9.26		-9.36		-9.25	
-9.38		-9.21		-9.2		-9.25		-9.26		-9.27	
-9.40	**MPT-5-207 (UV)**	-9.23	**MPT-5-217 (UV)**	-9.18	**MPT-5-199 (UV)**	-9.38	**MPT-5-257 (UV)**	-9.38	**MPT-5-284 (UV)**	-9.20	**MPT-5-030 (ELSD)**
-9.36		-9.22		-9.2		-9.31		-9.43		-9.17	
-9.53		-9.23		-9.15		-9.22		-9.38		-9.19	
-9.59		-9.23		-9.21		-9.30		-9.50		-9.15	
-9.57		-9.34		-9.23		-9.24		-9.52		-9.13	
-9.62	**MPT-5-208 (MS)**	-9.24	**MPT-5-218 (MS)**	-9.14	**MPT-5-200 (MS)**	-9.23	**MPT-5-258 (ELSD)**	-9.53	**MPT-5-285 (ELSD)**	-9.19	**MPT-5-130 (UV)**
-9.59		-9.24		-9.16		-9.29		-9.60		-9.13	
-9.60		-9.22		-9.11		-9.21		-9.46		-9.07	
-9.53		-9.01		-9.08		-9.21		-9.47		-9.32	
-9.42		-9.05		-9.13		-9.30		-9.40		-9.29	
-9.59	**MPT-5-208 (UV)**	-9.04	**MPT-5-218 (UV)**	-9.17	**MPT-5-200 (UV)**	-9.20	**MPT-5-258 (UV)**	-9.42	**MPT-5-285 (UV)**	-9.30	**MPT-5-130 (MS)**
-9.50		-9.05		-9.12		-9.39		-9.47		-9.28	
-9.53		-9.02		-9.12		-9.26		-9.57		-9.27	
										-9.20	
-9.47	**Mean**	**-9.11**	**Mean**	**-9.14**	**Mean**	**-9.26**	**Mean**	**-9.48**	**Mean**	-9.19	
0.09	**Std Dev**	**0.09**	**Std Dev**	**0.05**	**Std Dev**	**0.06**	**Std Dev**	**0.09**	**Std Dev**	-9.18	**MPT-5-131 (ELSD)**
										-9.15	
										-9.21	
										-9.11	
										-9.15	
										-9.28	**MPT-5-131 (UV)**
										-9.22	
										-9.17	
										-9.29	
										-9.30	
										-9.31	**MPT-5-131 (MS)**
										-9.28	
										-9.26	
										-9.21	**Mean**
										0.08	**Std Dev**

Supplement Table 35. *LogP experimental values for ent-verticilide analogs in series 5 using all detection methods, calculated using Supplement Equation 2.*

s. Series 5: Experimental Variables from Calculations and Percent Recoveries

Cmpd	MW (g/mol)	Ave RT (min)	C ($x10^{-9}$)	Well 1		Well 2		Well 3		Well 4		Well 5		Ave. %R
				%T	%R	%T	%R	%T	%R	%T	%R	%T	%R	
5.1	905.28	11.98	3.23	0.21	95	0.21	93	0.22	97	0.28	92	0.25	95	92.54 ± 2.90
5.1			3.20	0.31	98	0.29	93	0.30	92	0.35	96	0.34	96	
5.1			3.31	0.22	96	0.20	94	0.21	91	0.23	91	0.23	90	
5.1			3.26	0.28	96	0.30	92	0.28	89	0.28	93	0.30	88	
5.1			3.24	0.21	92	0.22	90	0.21	85	0.19	93	0.20	91	
5.1			3.25	0.29	92	0.29	93	0.33	92	0.31	89	0.32	90	
5.2	891.25	11.95	2.99	0.33	92	0.41	87	0.37	93	0.38	98	0.40	91	91.13 ± 2.45
5.2			3.10	0.45	95	0.44	87	0.44	85	0.48	91	0.43	92	
5.2			3.02	0.34	94	0.34	92	0.31	92	0.33	91	0.35	90	
5.2			3.00	0.30	90	0.31	88	0.29	92	0.29	93	0.34	91	
5.2			2.98	0.45	92	0.51	91	0.46	91	0.47	92	0.50	92	
5.2			2.99	0.51	91	0.46	89	0.46	91	0.43	91	0.49	90	
5.3	877.23	9.96	3.27	0.22	90	0.21	92	0.21	90	0.23	94	0.22	88	90.02 ± 4.22
5.3			3.25	0.30	91	0.33	86	0.31	89	0.32	85	0.30	83	
5.3			3.26	0.45	90	0.52	97	0.51	97	0.52	98	0.46	96	
5.3			3.24	0.55	91	0.61	85	0.62	90	0.57	86	0.57	86	
5.3			3.23	0.52	86	0.55	93	0.53	94	0.52	93	0.56	96	
5.3			3.24	0.35	90	0.33	91	0.36	83	0.37	87	0.33	89	
5.4	877.23	11.40	2.76	0.44	97	0.56	89	0.47	97	0.51	86	0.51	94	89.57 ± 4.59
5.4			2.79	0.48	90	0.43	87	0.50	88	0.47	87	0.41	92	
5.4			2.82	0.48	87	0.52	99	0.53	88	0.56	89	0.57	85	
5.4			2.81	0.49	91	0.54	83	0.44	85	0.47	87	0.54	88	
5.4			2.87	0.44	98	0.49	95	0.50	93	0.48	89	0.51	93	
5.4			2.83	0.56	85	0.51	81	0.55	89	0.43	84	0.49	91	
5.5	863.20	11.34	3.02	0.37	95	0.37	94	0.39	80	0.35	88	0.38	91	88.27 ± 4.63
5.5			3.11	0.29	85	0.34	86	0.26	81	0.33	87	0.29	85	
5.5			3.09	0.40	95	0.46	97	0.41	88	0.41	82	0.40	91	
5.5			3.07	0.32	86	0.34	91	0.29	84	0.27	84	0.27	85	
5.5			3.06	0.34	96	0.40	88	0.37	95	0.35	92	0.31	91	
5.5			3.03	0.32	87	0.30	87	0.31	85	0.27	84	0.33	88	
5.6	849.17	11.29	3.04	0.52	82	0.53	86	0.53	88	0.56	85	0.55	86	86.16 ± 4.79
5.6			3.05	0.56	86	0.61	91	0.57	86	0.58	87	0.62	88	
5.6			3.05	0.43	83	0.41	86	0.38	91	0.42	86	0.39	83	
5.6			3.09	0.40	86	0.41	92	0.39	80	0.41	93	0.40	81	
5.6			3.05	0.56	86	0.58	87	0.54	83	0.57	88	0.62	80	
5.6			3.04	0.17	91	0.16	90	0.18	92	0.19	90	0.18	81	
5.6			3.05	0.46	79	0.40	92	0.38	95	0.41	93	0.48	82	
5.6			3.06	0.37	82	0.41	82	0.50	76	0.47	78	0.44	80	
5.6			3.05	0.18	92	0.18	91	0.18	92	0.20	89	0.18	80	

Supplement Table 36. The Variables from Calculations for Analogs in Series 5. *The data for series 5 analogs (5.1-5.6) are comprised of 6 experiments, each with 5 replicates run in tandem (30 total). The data for analog 5.6 is comprised of 45 experiments. The molecular weights and mean retention times seen via HPLC (210 nm) are listed. The C values and %T values are calculated using Supplement Equation* ***1****. The mean percent recoveries are listed. Definitions: MW = molecular weight, RT = retention time, %R = % recovery, Ave. %R = mean ± standard deviation.*

Cmpd	Ave. $logP_{app}$	Ave. logP	Well 1		Well 2		Well 3		Well 4		Well 5		Ave. [acc]
			[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	[acc]	[donor]	
5.1	-5.75	-9.48	43.19	432.53	46.24	420.51	51.46	431.50	48.20	409.50	57.92	418.93	50.15 ± 10.01 uM (10%)
5.1	-5.53	-9.39	61.70	428.94	59.76	407.70	45.12	417.29	62.30	416.76	72.35	408.06	
5.1	-5.74	-9.48	46.07	432.20	47.42	424.49	48.30	405.30	49.97	405.38	52.04	397.51	
5.1	-5.52	-9.40	72.00	406.18	60.65	401.82	57.23	389.53	62.35	404.88	43.59	396.29	
5.1	-5.86	-9.60	38.58	421.30	39.64	410.70	35.39	390.39	38.55	424.17	37.55	419.15	
5.1	-5.61	-9.52	43.59	417.94	55.00	411.00	38.18	419.65	46.12	399.23	43.30	408.06	
5.2	-5.51	-9.25	115.43	377.85	111.93	368.27	107.44	380.50	103.44	377.37	114.55	377.37	118.47 ± 7.18 uM (24%)
5.2	-5.22	-9.01	140.51	333.19	127.84	308.27	123.76	300.50	129.92	322.88	130.55	327.37	
5.2	-5.26	-9.05	117.49	352.20	121.41	340.16	119.42	342.51	117.68	337.33	117.43	334.56	
5.2	-5.49	-9.21	112.09	379.57	124.05	364.08	110.94	371.03	118.85	363.44	115.09	368.44	
5.2	-5.27	-9.07	115.77	345.18	114.96	339.76	116.76	338.72	116.90	341.39	114.73	344.18	
5.2	-5.27	-9.06	120.82	332.61	118.41	326.11	120.88	336.12	117.95	335.60	117.20	330.37	
5.3	-5.30	-9.13	84.39	364.90	108.29	351.20	96.93	353.46	117.55	351.79	104.74	332.95	101.0 ± 10.81 uM (20%)
5.3	-5.32	-9.14	110.40	344.79	103.74	326.85	95.50	347.43	97.42	328.89	99.85	315.73	
5.3	-5.29	-9.10	87.40	362.29	121.32	366.06	100.48	384.47	119.65	367.89	122.99	358.36	
5.3	-5.37	-9.17	103.67	349.96	88.51	337.29	92.40	357.51	87.79	340.33	98.68	332.63	
5.3	-5.34	-9.17	87.13	344.31	84.06	381.40	99.40	368.48	96.39	369.77	105.75	373.00	
5.3	-5.32	-9.13	113.18	337.04	102.34	355.08	92.61	322.66	103.67	328.87	105.15	337.91	
5.4	-5.40	-9.23	72.82	411.71	93.69	352.75	83.77	401.72	78.27	353.26	85.89	383.81	78.03 ± 10.07 uM (16%)
5.4	-5.46	-9.33	73.46	378.18	60.11	376.96	76.10	366.33	70.10	366.65	60.95	396.57	
5.4	-5.37	-9.21	72.68	364.71	93.50	399.75	83.49	354.72	92.42	353.26	90.49	336.81	
5.4	-5.41	-9.28	77.46	378.18	80.13	336.91	60.08	365.32	70.10	366.65	84.98	356.52	
5.4	-5.43	-9.25	72.54	415.82	81.66	393.87	83.91	380.48	73.90	373.05	86.64	379.87	
5.4	-5.40	-9.28	86.71	340.38	71.09	334.87	88.07	355.05	58.48	363.97	77.46	377.82	
5.5	-5.58	-9.45	56.26	420.83	54.91	414.46	49.62	350.67	46.38	395.88	54.05	400.52	49.48 ± 9.49 (10%)
5.5	-5.69	-9.54	40.64	382.19	51.14	381.33	34.66	372.68	48.60	385.79	40.30	382.71	
5.5	-5.51	-9.36	62.91	411.54	78.89	404.25	60.53	381.94	53.83	358.07	60.31	394.31	
5.5	-5.70	-9.54	46.80	384.42	54.20	399.22	41.16	379.27	37.32	382.28	36.85	386.19	
5.5	-5.61	-9.47	49.73	429.96	57.40	384.37	55.56	420.35	49.51	409.60	39.90	415.81	
5.5	-5.68	-9.52	46.86	386.66	44.28	390.96	43.94	378.98	37.02	383.25	50.69	391.67	
5.6	-5.36	-9.19	83.50	325.14	89.39	342.29	91.58	348.30	96.13	330.51	92.96	335.24	87.26 ± 13.92 uM (17%)
5.6	-5.35	-9.17	99.38	329.76	115.70	338.41	100.79	331.04	103.19	332.12	115.29	326.73	
5.6	-5.33	-9.15	71.30	342.87	69.52	359.65	66.92	386.13	70.93	360.84	69.28	383.36	
5.6	-5.32	-9.14	80.44	373.48	75.82	372.61	89.06	369.70	94.85	353.24	89.83	359.18	
5.6	-5.31	-9.13	99.14	332.03	103.11	330.45	91.18	324.58	102.37	337.25	115.12	325.57	
5.6	-5.30	-9.11	68.15	362.19	73.16	385.60	72.44	407.29	74.67	391.26	75.92	404.74	
5.6	-5.33	-9.14	88.53	370.12	91.07	363.55	92.98	369.31	99.06	348.10	86.01	365.30	
5.6	-5.38	-9.19	107.84	300.14	99.08	310.08	75.07	304.37	83.98	305.76	93.56	313.89	
5.6	-5.43	-9.23	72.93	321.05	72.08	388.56	70.51	405.00	75.49	388.67	77.42	326.87	

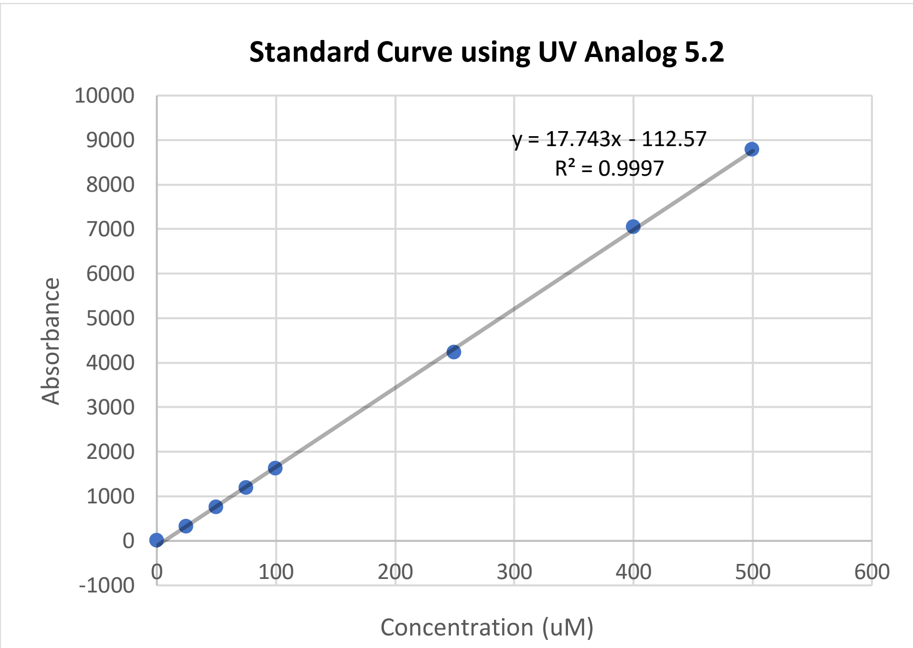
Supplement Table 37. Final Experimental Data for Analogs in Series 5. *The mean $logP_{app}$ (calculated from Supplement Equation 1) and logP values (calculated from (Supplement Equation 2) are listed. The acceptor and donor concentrations are calculated using a standard curve and the units are uM. The initial concentration is 500 uM for all experiments. The total mean acceptor concentrations are listed in the final column. Definitions: [acc] = acceptor concentration after incubation, [donor] = donor concentration after incubation, mean [acc] = mean acceptor concentration ± standard deviation.*

t. Standard Curves Series 5

Analog 5.1

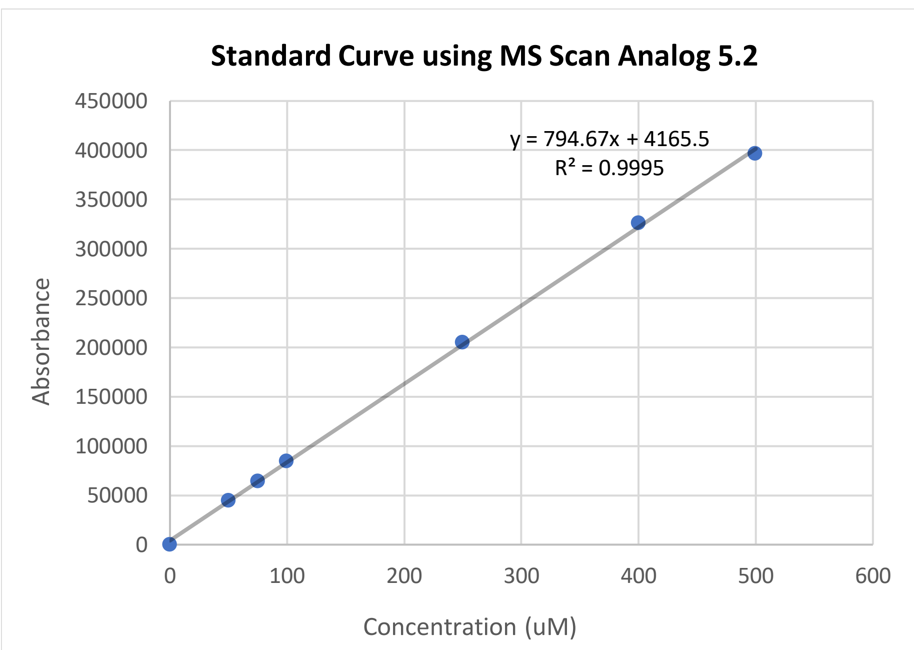
- Same as analog 3.5, 4.1 (see above)

Analog 5.2



Conc. (uM)	Area
500	8775.57
400	7037.97
250	4231.57
100	1625.17
75	1190.77
50	756.37
25	321.97
0	0

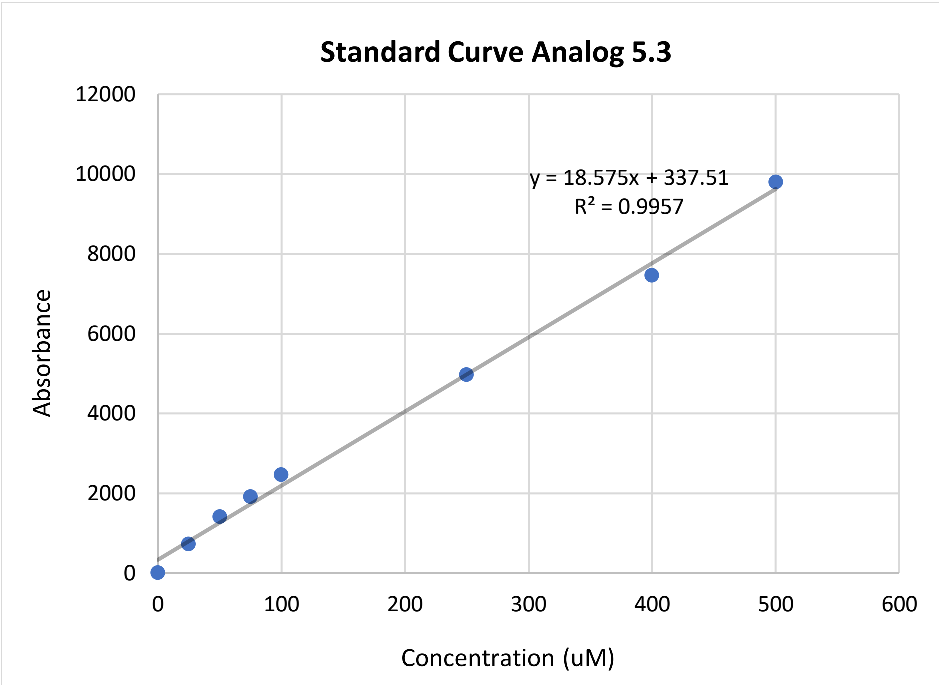
Supplement Graph 52. *The standard curve for absorbance vs. concentration (uM) of analog 5.2 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	396566.7
400	326100.7
250	205401.7
100	84702.7
75	64586.2
50	44469.7
0	0

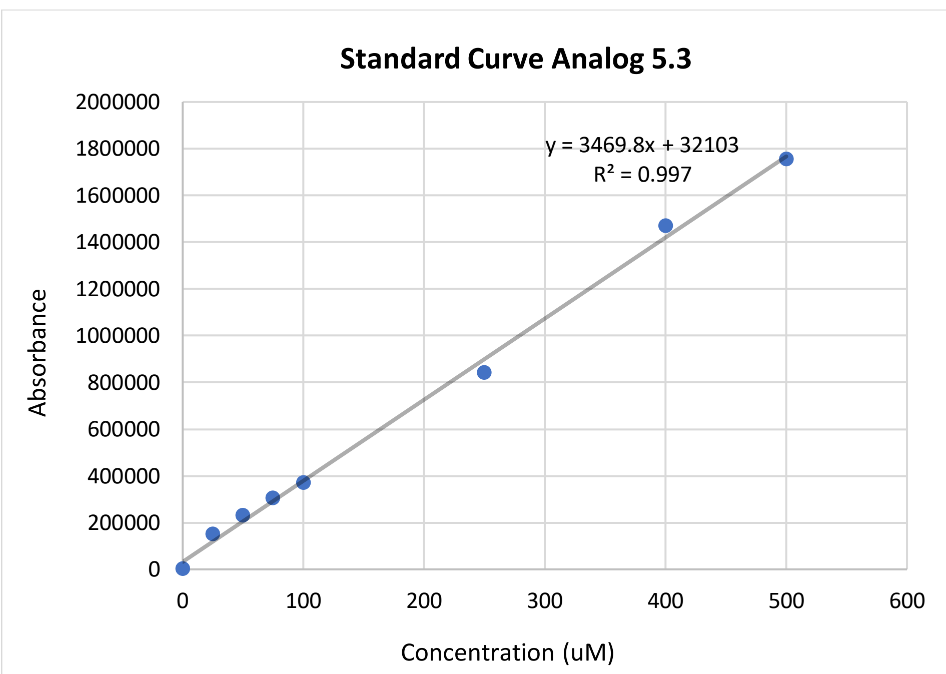
Supplement Graph 53. *The standard curve for absorbance vs. concentration (uM) of analog 5.2 utilizing* ***MS detection.***

Analog 5.3



Conc. (uM)	Area
500	9792
400	7460
250	4960
100	2460
75	1910
50	1405
25	718
0	0

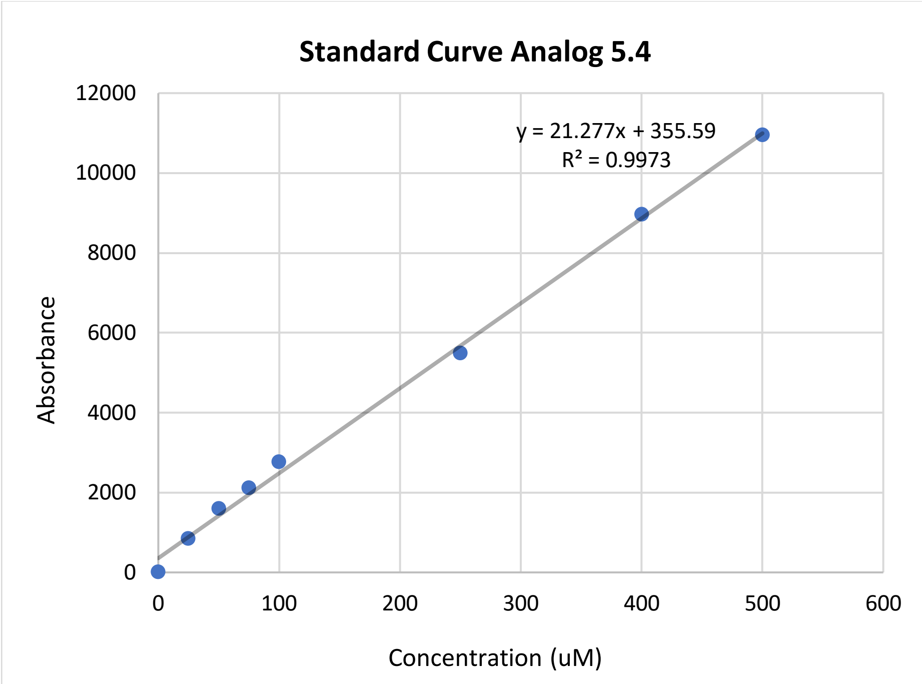
Supplement Graph 54. *The standard curve for absorbance vs. concentration (uM) of analog 5.3 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	1754470
400	1468400
250	839584
100	369962
75	303299
50	230302
25	148463
0	0

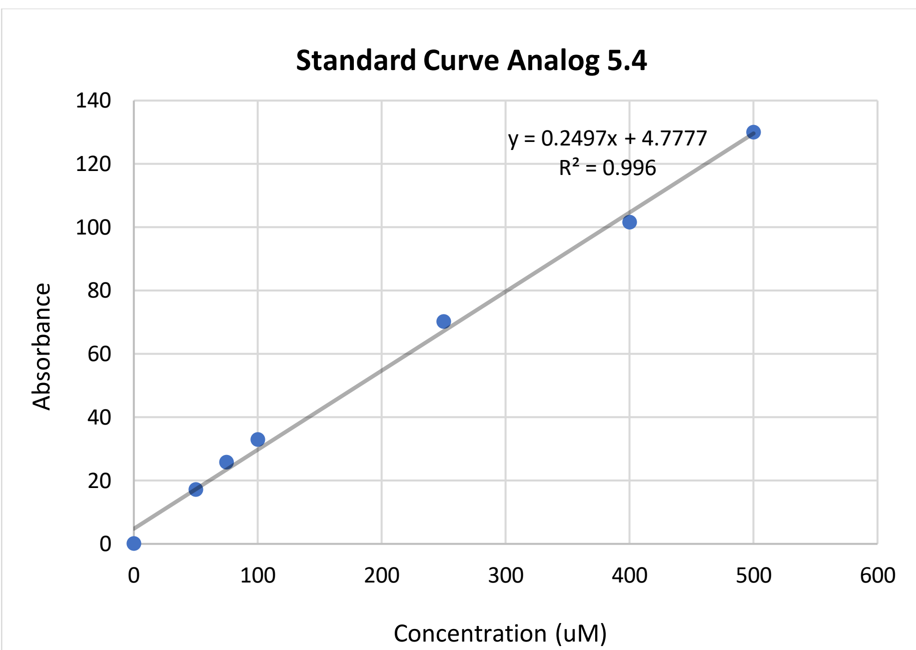
Supplement Graph 55. *The standard curve for absorbance vs. concentration (uM) of analog 5.3 utilizing* ***MS detection.***

Analog 5.4



Conc. (uM)	Area
500	10938
400	8949
250	5476
100	2748
75	2103
50	1589
25	830
0	0

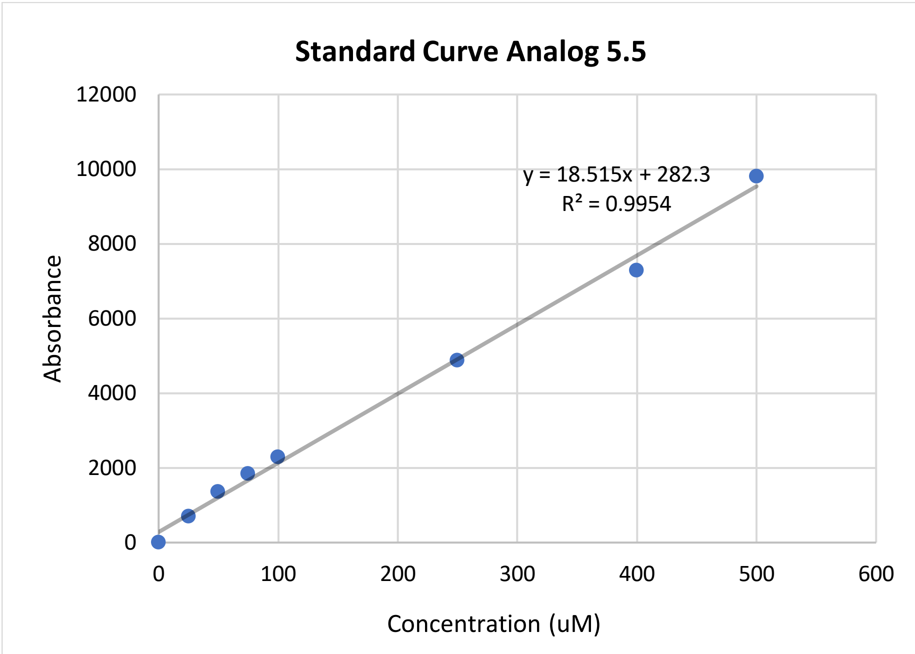
Supplement Graph 56. *The standard curve for absorbance vs. concentration (uM) of analog 5.4 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	129.9
400	101.4
250	70.1
100	32.8
75	25.6
50	17
0	0

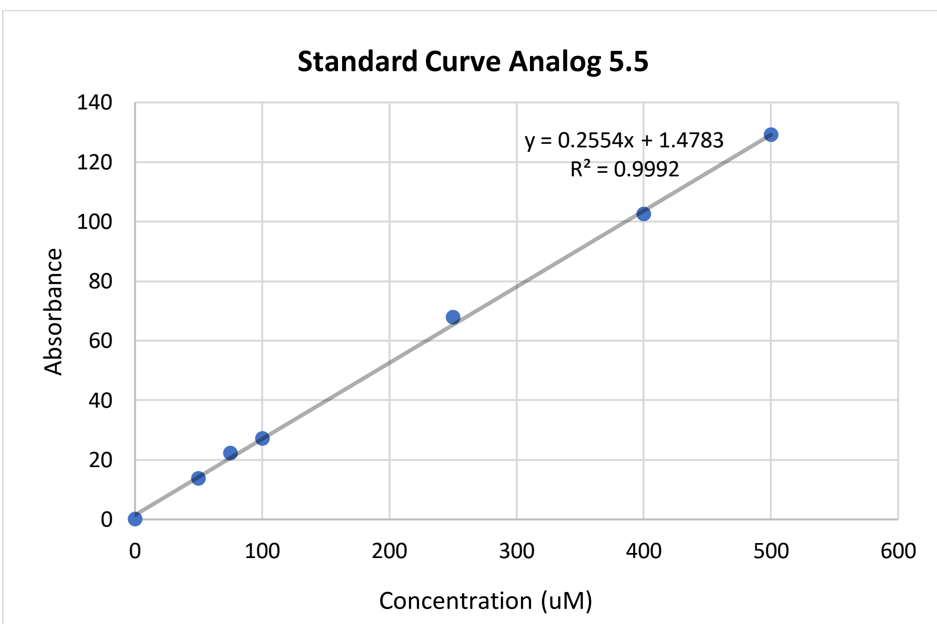
Supplement Graph 57. *The standard curve for absorbance vs. concentration (uM) of analog 5.4 utilizing* ***MS detection.***

Analog 5.5



Conc. (uM)	Area
500	9801
400	7293
250	4876
100	2301
75	1837
50	1369
25	702
0	0

Supplement Graph 58. *The standard curve for absorbance vs. concentration (uM) of analog 5.5 utilizing* ***UV detection*** *(210 nm).*



Conc. (uM)	Area
500	128.9
400	102.3
250	67.7
100	27.1
75	22
50	13.5
0	0

Supplement Graph 59. *The standard curve for absorbance vs. concentration (uM) of analog 5.5 utilizing* ***ELSD detection.***

Analog 5.6

- same as analog 2.5 (see above)

u. Statistical Analysis Series 5

LogPapp			Percent Diffusion			LogP		
Pair	P-value	Inference	Pair	P-value	Inference	Pair	P-value	Inference
A vs B	9.71E-24	**	A vs B	7.36E-25	**	A vs B	1.11E-27	**
A vs C	0.00636	**	A vs C	1.0	NS	A vs C	0.0181	*
A vs D	0.00871	**	A vs D	0.00799	**	A vs D	0.00250	**
A vs E	4.18E-8	**	A vs E	3.25E-11	**	A vs E	2.09E-12	**
A vs F	4.59E-23	**	A vs F	5.20E-25	**	A vs F	6.23E-28	**
A vs G	5.77E-15	**	A vs G	3.07E-9	**	A vs G	2.03E-10	**
B vs C	2.79E-8	**	B vs C	5.12E-17	**	B vs C	3.21E-11	**
B vs D	1.75E-8	**	B vs D	4.88E-9	**	B vs D	8.28E-10	**
B vs E	0.00191	**	B vs E	0.0322	*	B vs E	0.0159	*
B vs F	1.0	NS	B vs F	1.0	NS	B vs F	1.0	NS
B vs G	0.0556	NS	B vs G	3.18E-5	**	B vs G	9.77E-6	**
C vs D	1.0	NS	C vs D	0.347	NS	C vs D	1.0	NS
C vs E	0.662	NS	C vs E	5.45E-7	**	C vs E	0.00445	**
C vs F	6.40E-8	**	C vs F	3.95E-17	**	C vs F	2.30E-11	**
C vs G	0.00579	**	C vs G	4.07E-5	**	C vs G	0.143	NS
D vs E	0.548	NS	D vs E	0.0320	*	D vs E	0.0252	*
D vs F	4.06E-8	**	D vs F	4.04E-9	**	D vs F	6.07E-10	**
D vs G	0.00421	**	D vs G	0.690	NS	D vs G	0.589	NS
E vs F	0.00331	**	E vs F	0.0291	*	E vs F	0.0135	*
E vs G	1.0	NS	E vs G	1.0	NS	E vs G	1.0	NS
F vs G	0.0895	NS	F vs G	2.71E-5	**	F vs G	7.50E-6	**

Supplement Table 38. Data Analysis of Series 5. *Kruskal-Wallis test with Dunn's multiple comparisons post hoc analysis using GraphPad Prism v10.1.1. Definitions: A = ent-verticilide, B = 5.1, C = 5.2, D = 5.3, E = 5.4, F = 5.5, G = 5.6 and ** p < 0.01, * p < 0.05, NS = not significant.*

2.7 Summary of Reported P_{app} Values from Calculations (UV only)

low permeability Papp < 2 x 10^{-6} cm/s

moderate permeability Papp 2-10 x 10^{-6} cm/s

high permeability Papp > 10 x 10^{-6} cm/s

Series 1: P_{app} (UV only)					
ent-vert	**1.1**	**1.2**	**1.3**	**1.4**	**1.5**
6.39	4.86	4.14	1.07	0.83	2.39
7.95	4.97	4.53	1.09	0.84	3.05
6.48	4.99	4.57	1.10	0.85	3.33
7.85	5.12	4.62	1.11	1.13	3.37
6.83	5.32	4.63	1.14	1.17	3.52
7.11	5.37	4.74	1.15	1.22	3.54
6.85	5.46	4.75	1.17	1.26	3.67
7.63	5.49	4.76	1.18	1.26	3.92
4.68	5.70	4.83	1.22	1.41	4.02
4.63	6.82	5.01	1.24	1.42	4.29
4.05		5.02			
6.98		5.06			
4.62		5.12			
3.79		5.30			
4.66		5.39			
5.98		5.41			
6.44					
7.86					
4.86					
6.27					
6.77					
5.18					
5.55					
6.05					
6.58 ± 0.83	**5.41 ± 0.56**	**4.87 ± 0.35**	**1.15 ± 0.06**	**1.14 ± 0.23**	**3.51 ± 0.54**
moderate	**moderate**	**moderate**	**low**	**low**	**moderate**

Supplement Table 39. Final Experimental P_{app} Values for Series 1. *The calculated P_{app} values are listed in this table. This data was calculated using Supplement Equation 1 and utilizes UV absorption HPLC data (210 nm). Units are x 10^{-6} (cm/s).*

Series 2: P_{app} (UV only)					
ent-vert	**2.1**	**2.2**	**2.3**	**2.4**	**2.5**
6.39	7.40	8.29	5.14	3.84	3.90
7.95	9.26	8.36	5.25	3.87	4.33
6.48	10.10	8.49	5.34	3.88	4.42
7.85	10.22	8.66	5.49	3.97	4.68
6.83	11.13	8.76	5.60	4.20	4.68
7.11	11.70	8.81	5.68	4.26	4.73
6.85	12.41	9.01	5.80	4.65	4.76
7.63	13.03	9.74	5.97	4.84	4.78
4.68	13.03	9.90	6.05	4.86	4.87
4.63	13.80	10.36	6.13	4.96	4.89
4.05	14.16		6.15	5.00	5.01
6.98	14.60		6.41	5.40	5.35
4.62	15.01		6.45	5.76	5.52
3.79	15.27		6.59	5.91	5.53
4.66	16.16		6.84	5.94	5.61
5.98					
6.44					
7.86					
4.86					
6.27					
6.77					
5.18					
5.55					
6.05					
6.58 ± 0.83	**12.49 ± 2.49**	**9.04 ± 0.71**	**5.93 ± 0.51**	**4.76 ± 0.75**	**4.87 ± 0.48**
moderate	**high**	**moderate**	**moderate**	**moderate**	**moderate**

Supplement Table 40. Final Experimental P_{app} Values for Series 2. *The calculated P_{app} values are listed in this table. This data was calculated using Supplement Equation 1 and utilizes UV absorption HPLC data (210 nm). Units are x 10^{-6} (cm/s)*

Series 3: P_{app} (UV only)					
ent-vert	**3.1**	**3.2**	**3.3**	**3.4**	**3.5**
6.39	1.37 (outlier)	3.67	3.01	3.31	2.18
7.95	5.30	3.95	3.04	3.34	2.38
6.48	5.48	4.01	3.07	3.56	2.43
7.85	5.53	4.03	3.10	3.63	2.44
6.83	5.72	4.04	3.17	3.68	2.50
7.11	5.91	4.23	3.19	3.72	2.58
6.85	5.91	4.65	3.27	3.73	2.82
7.63	6.71	4.69	3.27	3.79	2.94
4.68	7.09	4.73	3.27	3.80	3.01
4.63	7.57	4.75	3.42	3.86	3.05
4.05			3.43	3.91	3.05
6.98			3.46	4.01	3.09
4.62			3.54	4.05	3.13
3.79			3.72	4.22	3.46
4.66			3.78	4.57	3.46
5.98					
6.44	**with outlier:**				
7.86	5.66 ± 1.68				
4.86					
6.27					
6.77					
5.18					
5.55					
6.05					
6.58 ± 0.83	**6.14 ± 0.80**	**4.28 ± 0.40**	**3.32 ± 0.24**	**3.81 ± 0.32**	**2.83 ± 0.40**
moderate	**moderate**	**moderate**	**moderate**	**moderate**	**moderate**

Supplement Table 41. Final Experimental P_{app} Values for Series 3. *The calculated P_{app} values are listed in this table. This data was calculated using Supplement Equation 1 and utilizes UV absorption HPLC data (210 nm). Units are x 10^{-6} (cm/s).*

Grubbs' test was used to detect the presence of one outlier within the experimental data set for analog 3.1 (P_{app} of 1.37). Excel was used to calculate both G and $G_{critical}$.

$$G = \frac{\text{mean} - \text{minimum}}{\text{standard deviation}}$$

$$G_{critical} = \frac{(\#\text{ samples} - 1) \times t_{critical}}{\sqrt{[\#\text{ samples} \times (\text{deg freedom} + t_{critical}^2)]}}$$

if $G > G_{critical}$, then minimum is an outlier and can be excluded.

Supplement Equation 5. *Calculations for Grubbs' Statistical test used to calculate the data found in the table below.*

Minimum	Mean	SD	G	α	# samples	Sig Value	Deg freedom	$t_{critical}$	$G_{critical}$	Significance?
1.37	5.66	1.68	2.55	0.05	10	0.005	8	3.36	2.18	outlier

Supplement Table 42. *Grubbs' test for outliers for analog 3.1.*

Series 4: P_{app} x 10^{-6} cm/s (UV only)					
4.1	**4.2**	**4.3**	**4.4**	**4.5**	**4.6**
2.18	3.99	3.74	1.95	1.24	0.26
2.38	4.40	3.75	1.95	1.38	0.27
2.43	4.55	3.85	1.97	1.38	0.29
2.44	4.56	3.94	2.03	1.42	0.31
2.50	4.80	3.99	2.08	1.48	0.32
2.58	4.89	4.07	2.10	1.50	0.33
2.82	5.03	4.17	2.11	1.58	0.36
2.94	5.19	4.24	2.26	1.62	0.37
3.01	5.19	4.30	2.32	1.66	0.38
3.05	5.23	4.47	2.48	1.75	0.49
3.05					
3.09					
3.13					
3.46					
3.46					
2.83 ± 0.40	**4.78 ± 0.41**	**4.05 ± 0.24**	**2.13 ± 0.17**	**1.50 ± 0.15**	**0.34 ± 0.07**
moderate	**moderate**	**moderate**	**moderate**	**low**	**low**

Supplement Table 43. Series 4 Experimental Papp Values. *The calculated Papp values are calculated using UV only (210 nm).*

Series 5: P_{app} x 10^{-6} cm/s (UV only)					
5.1	**5.2**	**5.3**	**5.4**	**5.5**	**5.6**
2.18	5.30	3.31	3.28	2.08	3.90
2.38	5.35	3.34	3.32	2.35	4.33
2.43	5.36	3.56	3.68	2.42	4.42
2.44	5.43	3.63	3.70	2.46	4.68
2.50	5.47	3.68	3.78	2.61	4.68
2.58	5.47	3.72	3.79	2.62	4.73
2.82	5.60	3.73	3.99	2.63	4.76
2.94	5.61	3.79	4.04	2.68	4.78
3.01	5.64	3.80	4.05	2.84	4.87
3.05	5.73	3.86	4.11	2.90	4.89
3.05	6.04	3.91	4.16	2.92	5.01
3.09	6.10	4.01	4.24	2.95	5.35
3.13	6.23	4.05	4.63	2.96	5.52
3.46	6.28	4.22	4.68	3.04	5.53
3.46	6.41	4.57	4.76	3.55	5.61
2.83 ± 0.40	**5.74 ± 0.38**	**3.81 ± 0.32**	**4.01 ± 0.45**	**2.73 ± 0.35**	**4.87 ± 0.48**
moderate	**moderate**	**moderate**	**moderate**	**moderate**	**moderate**

Supplement Table 44. Series 5 Experimental Papp Values. *The calculated Papp values are calculated using UV only (210 nm).*

2.8 Summary of Reported $LogP_{app}$ Values from Calculations (UV only)

Series 1: $LogP_{app}$ (UV only)					
ent-vert	**1.1**	**1.2**	**1.3**	**1.4**	**1.5**
-5.19	-5.31	-5.38	-5.97	-6.08	-5.62
-5.10	-5.30	-5.34	-5.96	-6.08	-5.52
-5.19	-5.30	-5.34	-5.96	-6.07	-5.48
-5.11	-5.29	-5.34	-5.95	-5.95	-5.47
-5.17	-5.27	-5.33	-5.94	-5.93	-5.45
-5.15	-5.27	-5.32	-5.94	-5.91	-5.45
-5.16	-5.26	-5.32	-5.93	-5.90	-5.44
-5.12	-5.26	-5.32	-5.93	-5.90	-5.41
-5.35	-5.24	-5.32	-5.91	-5.85	-5.40
-5.33	-5.17	-5.30	-5.91	-5.85	-5.37
-5.39		-5.30			
-5.16		-5.30			
-5.36		-5.29			
-5.42		-5.28			
-5.33		-5.27			
-5.22		-5.27			
-5.24					
-5.24					
-5.44					
-5.20					
-5.23					
-5.46					
-5.25					
-5.32					
-5.21 ± 0.09	**-5.27 ± 0.04**	**-5.31 ± 0.03**	**-5.94 ± 0.02**	**-5.95 ± 0.09**	**-5.46 ± 0.07**
moderate	**moderate**	**moderate**	**low**	**low**	**moderate**

Supplement Table 45. Final Experimental $LogP_{app}$ Values for Series 1. *The calculated $LogP_{app}$ values are listed in this table. This data was calculated using Supplement Equation 1 and utilizes UV absorption HPLC data (210 nm).*

Series 2: $LogP_{app}$ (UV only)					
ent-vert	**2.1**	**2.2**	**2.3**	**2.4**	**2.5**
-5.19	-5.13	-5.08	-5.29	-5.42	-5.41
-5.10	-5.03	-5.08	-5.28	-5.41	-5.36
-5.19	-5.00	-5.07	-5.27	-5.41	-5.35
-5.11	-4.99	-5.06	-5.26	-5.40	-5.33
-5.17	-4.95	-5.06	-5.25	-5.38	-5.33
-5.15	-4.93	-5.06	-5.25	-5.37	-5.33
-5.16	-4.91	-5.05	-5.24	-5.33	-5.32
-5.12	-4.89	-5.01	-5.22	-5.32	-5.32
-5.35	-4.89	-5.00	-5.22	-5.31	-5.31
-5.33	-4.86	-4.98	-5.21	-5.30	-5.31
-5.39	-4.85		-5.21	-5.30	-5.30
-5.16	-4.84		-5.19	-5.27	-5.27
-5.36	-4.82		-5.19	-5.24	-5.26
-5.42	-4.82		-5.18	-5.23	-5.26
-5.33	-4.79		-5.16	-5.23	-5.25
-5.22					
-5.24					
-5.24					
-5.44					
-5.20					
-5.23					
-5.46					
-5.25					
-5.32					
-5.21 ± 0.09	**-4.91 ± 0.09**	**-5.05 ± 0.03**	**-5.23 ± 0.04**	**-5.33 ± 0.07**	**-5.31 ± 0.04**
moderate	**high**	**moderate**	**moderate**	**moderate**	**moderate**

Supplement Table 46. Final Experimental $LogP_{app}$ Values for Series 2. *The calculated $LogP_{app}$ values are listed in this table. This data was calculated using Supplement Equation 1 and utilizes UV absorption HPLC data (210 nm).*

Series 3: LogP_{app} (UV only)

ent-vert	3.1	3.2	3.3	3.4	3.5
-5.19	-5.86 (outlier)	-5.44	-5.52	-5.48	-5.66
-5.10	-5.28	-5.40	-5.52	-5.48	-5.62
-5.19	-5.26	-5.40	-5.51	-5.45	-5.61
-5.11	-5.26	-5.39	-5.51	-5.44	-5.61
-5.17	-5.24	-5.39	-5.50	-5.43	-5.60
-5.15	-5.23	-5.37	-5.50	-5.43	-5.59
-5.16	-5.23	-5.33	-5.49	-5.43	-5.55
-5.12	-5.17	-5.33	-5.49	-5.42	-5.53
-5.35	-5.15	-5.33	-5.49	-5.42	-5.52
-5.33	-5.12	-5.32	-5.47	-5.41	-5.52
-5.39			-5.46	-5.41	-5.52
-5.16			-5.46	-5.40	-5.51
-5.36			-5.45	-5.39	-5.50
-5.42			-5.43	-5.37	-5.46
-5.33			-5.42	-5.34	-5.46
-5.22					
-5.24					
-5.24	**with outlier:**				
-5.44	**-5.28 ± 0.21**				
-5.20					
-5.23					
-5.46					
-5.25					
-5.32					
-5.21 ± 0.09	**-5.22 ± 0.05**	**-5.37 ± 0.04**	**-5.48 ± 0.03**	**-5.42 ± 0.04**	**-5.55 ± 0.06**
moderate	**moderate**	**moderate**	**moderate**	**moderate**	**moderate**

Supplement Table 47. Final Experimental LogP_{app} Values for Series 3. *The calculated LogP_{app} values are listed in this table. This data was calculated using Supplement Equation 1 and utilizes UV absorption HPLC data (210 nm). Units are x 10^{-6} (cm/s).*

Grubbs' test was used to detect the presence of one outlier within the experimental data set for analog 3.1 (LogP_{app} of -5.86). Excel was used to calculate both G and $G_{critical}$.

$$G = \frac{\text{mean} - \text{minimum}}{\text{standard deviation}}$$

$$G_{critical} = \frac{(\#\ \text{samples} - 1) \times t_{critical}}{\sqrt{[\#\ \text{samples} \times (\text{deg freedom} + t_{critical}^2)]}}$$

if $G > G_{critical}$, then minimum is an outlier and can be excluded.

Supplement Equation 6. *Calculations for Grubbs' Statistical test used to calculate the data found in **Supplement Table 48**.*

Minimum	Mean	SD	G	α	# samples	Sig Value	Deg freedom	$t_{critical}$	$G_{critical}$	Significance?
-5.86	-5.28	0.21	22.5	0.05	10	0.005	8	3.35	2.18	outlier

Supplement Table 48. *Grubbs' test for outliers for analog 3.1.*

Series 4: $LogP_{app}$ (UV only)					
4.1	**4.2**	**4.3**	**4.4**	**4.5**	**4.6**
-5.66	-5.40	-5.43	-5.71	-5.91	-6.59
-5.62	-5.36	-5.43	-5.71	-5.86	-6.57
-5.61	-5.34	-5.41	-5.71	-5.86	-6.54
-5.61	-5.34	-5.40	-5.69	-5.85	-6.51
-5.60	-5.32	-5.40	-5.68	-5.83	-6.49
-5.59	-5.31	-5.39	-5.68	-5.82	-6.48
-5.55	-5.30	-5.38	-5.68	-5.80	-6.44
-5.53	-5.28	-5.37	-5.65	-5.79	-6.43
-5.52	-5.28	-5.37	-5.63	-5.78	-6.42
-5.52	-5.28	-5.35	-5.61	-5.76	-6.31
-5.52					
-5.51					
-5.50					
-5.46					
-5.46					
-5.55 ± 0.06	**-5.32 ± 0.04**	**-5.39 ± 0.03**	**-5.67 ± 0.04**	**-5.83 ± 0.04**	**-6.48 ± 0.08**
moderate	**moderate**	**moderate**	**moderate**	**low**	**low**

Supplement Table 49. Final Experimental $LogP_{app}$ Values for Series 4. *The calculated $LogP_{app}$ values are listed in this table.*

Series 5: $LogP_{app}$ (UV only)					
5.1	**5.2**	**5.3**	**5.4**	**5.5**	**5.6**
-5.66	-5.28	-5.48	-5.48	-5.68	-5.41
-5.62	-5.27	-5.48	-5.48	-5.63	-5.36
-5.61	-5.27	-5.45	-5.43	-5.62	-5.35
-5.61	-5.27	-5.44	-5.43	-5.61	-5.33
-5.60	-5.26	-5.43	-5.42	-5.58	-5.33
-5.59	-5.26	-5.43	-5.42	-5.58	-5.33
-5.55	-5.25	-5.43	-5.40	-5.58	-5.32
-5.53	-5.25	-5.42	-5.39	-5.57	-5.32
-5.52	-5.25	-5.42	-5.39	-5.55	-5.31
-5.52	-5.24	-5.41	-5.39	-5.54	-5.31
-5.52	-5.22	-5.41	-5.38	-5.53	-5.30
-5.51	-5.21	-5.40	-5.37	-5.53	-5.27
-5.50	-5.21	-5.39	-5.33	-5.53	-5.26
-5.46	-5.20	-5.37	-5.33	-5.52	-5.26
-5.46	-5.19	-5.34	-5.32	-5.45	-5.25
-5.55 ± 0.06	**-5.24 ± 0.03**	**-5.42 ± 0.04**	**-5.40 ± 0.05**	**-5.57 ± 0.06**	**-5.31 ± 0.04**
moderate	**moderate**	**moderate**	**moderate**	**moderate**	**moderate**

Supplement Table 50. Final Experimental $LogP_{app}$ Values for Series 5. *The calculated $LogP_{app}$ values are listed in this table.*

2.9 Summary of Reported LogP Values from Calculations (UV only)

Series 1: LogP (UV only)					
ent-vert	**1.1**	**1.2**	**1.3**	**1.4**	**1.5**
-8.98	-9.19	-9.10	-9.80	-9.75	-9.21
-8.96	-9.23	-9.13	-9.81	-9.92	-9.46
-9.01	-9.22	-9.12	-9.79	-9.73	-9.30
-8.98	-9.12	-9.15	-9.82	-9.61	-9.35
-9.03	-9.19	-9.14	-9.80	-9.67	-9.30
-9.01	-9.22	-9.13	-9.10	-10.3	-9.18
-9.01	-9.15	-9.13	-8.98	-10.7	-9.27
-8.97	-9.17	-9.17	-8.99	-10.1	-9.22
-9.09	-9.15	-9.12	-9.00	-9.97	-9.26
-9.14	-9.11	-9.19	-9.01	-9.97	-9.27
-9.13		-9.11			
-9		-9.13			
-9.12		-9.11			
-9.14		-9.17			
-9.11		-9.14			
-9.09		-9.11			
-8.97					
-8.97					
-9.16					
-8.95					
-8.99					
-9.18					
-9.00					
-9.21					
-9.02 ± 0.07	**-9.18 ± 0.04**	**-9.14 ± 0.03**	**-9.82 ± 0.02**	**-9.72 ± 0.11**	**-9.36 ± 0.08**
moderate	**moderate**	**moderate**	**low**	**low**	**moderate**

Supplement Table 51. Final Experimental LogP Values for Series 1. *The calculated LogP values are listed in this table. This data was calculated using Supplement Equation 2 and utilizes UV absorption HPLC data (210 nm).*

Series 2: LogP (UV only)					
ent-vert	**2.1**	**2.2**	**2.3**	**2.4**	**2.5**
-8.98	-8.91	-8.92	-9.06	-9.14	-9.15
-8.96	-8.91	-8.90	-9.02	-9.21	-9.07
-9.01	-8.90	-8.93	-8.99	-9.21	-9.14
-8.98	-8.92	-8.94	-9.02	-9.24	-9.13
-9.03	-8.92	-8.95	-8.98	-9.18	-9.07
-9.01	-8.80	-9.00	-9.00	-9.10	-9.15
-9.01	-8.80	-8.90	-9.00	-9.15	-9.13
-8.97	-8.78	-8.93	-9.02	-9.15	-9.19
-9.09	-8.79	-8.94	-9.08	-9.23	-9.13
-9.14	-8.80	-8.95	-9.03	-9.20	-9.07
-9.13	-8.77		-9.06	-9.10	-9.11
-9	-8.72		-9.05	-9.10	-9.15
-9.12	-8.86		-9.04	-9.08	-9.28
-9.14	-8.76		-9.07	-9.17	-9.22
-9.11	-8.79		-9.07	-9.26	-9.17
-9.09					
-8.97					
-8.97					
-9.16					
-8.95					
-8.99					
-9.18					
-9.00					
-9.21					
-9.02 ± 0.07	**-8.82 ± 0.07**	**-8.94 ± 0.03**	**-9.03 ± 0.03**	**-9.17 ± 0.06**	**-9.14 ± 0.05**
moderate	**high**	**moderate**	**moderate**	**moderate**	**moderate**

Supplement Table 52. Final Experimental LogP Values for Series 2. *The calculated LogP values are listed in this table. This data was calculated using Supplement Equation 2 and utilizes UV absorption HPLC data (210 nm).*

Series 3: LogP (UV only)					
ent-vert	**3.1**	**3.2**	**3.3**	**3.4**	**3.5**
-8.98	-9.33 (outlier)	-9.22	-9.19	-9.31	-9.37
-8.96	-9.05	-9.03	-9.21	-9.32	-9.39
-9.01	-9.03	-9.19	-9.23	-9.36	-9.51
-8.98	-9.04	-9.19	-9.22	-9.40	-9.37
-9.03	-9.00	-9.19	-9.23	-9.40	-9.30
-9.01	-9.16	-9.15	-9.20	-9.28	-9.30
-9.01	-9.07	-9.23	-9.19	-9.28	-9.38
-8.97	-9.08	-9.17	-9.26	-9.20	-9.40
-9.09	-9.21	-9.22	-9.22	-9.30	-9.36
-9.14	-9.09	-9.19	-9.23	-9.27	-9.53
-9.13	-9.07		-9.16	-9.37	-9.53
-9	-9.09		-9.23	-9.32	-9.42
-9.12	-9.11		-9.23	-9.34	-9.59
-9.14	-9.18		-9.21	-9.31	-9.50
-9.11	-9.08		-9.20	-9.32	-9.53
-9.09					
-8.97					
-8.97	**with outlier:**				
-9.16	**-9.11 ± 0.08**				
-8.95					
-8.99					
-9.18					
-9.00					
-9.21					
-9.02 ± 0.07	**-9.09 ± 0.06**	**-9.18 ± 0.06**	**-9.21 ± 0.02**	**-9.32 ± 0.05**	**-9.43 ± 0.09**
moderate	**moderate**	**moderate**	**moderate**	**moderate**	**moderate**

Supplement Table 53. Final Experimental LogP Values for Series 3. *The calculated LogP values are listed in this table. This data was calculated using Supplement Equation 2 and utilizes UV absorption HPLC data (210 nm).*

Grubbs' test was used to detect the presence of one outlier within the experimental data set for analog 3.1 ($LogP_{app}$ of -5.86). Excel was used to calculate both G and $G_{critical}$.

$$G = \frac{\text{mean} - \text{minimum}}{\text{standard deviation}}$$

$$G_{critical} = \frac{(\#\text{samples} - 1) \times t_{critical}}{\sqrt{[\#\text{samples} \times (\text{deg freedom} + t_{critical}^{2})]}}$$

if $G > G_{critical}$, then minimum is an outlier and can be excluded.

Supplement Equation 7. *Calculations for Grubbs' Statistical test used to calculate the data found in **Supplement Table 54**.*

Minimum	Mean	SD	G	α	# samples	Sig Value	Deg freedom	$t_{critical}$	$G_{critical}$	Significance?
-9.33	-9.11	0.08	102.2	0.05	15	0.003	13	3.22	2.41	outlier

Supplement Table 54. *Grubbs' test for outliers for analog 3.1.*

Series 4: LogP (UV only)					
4.1	4.2	4.3	4.4	4.5	4.6
-9.37	-9.21	-9.20	-9.37	-9.47	-9.94
-9.39	-9.16	-9.22	-9.42	-9.48	-9.79
-9.51	-9.16	-9.26	-9.41	-9.61	-9.84
-9.37	-9.19	-9.26	-9.41	-9.46	-9.87
-9.30	-9.16	-9.20	-9.39	-9.50	-9.91
-9.30	-9.16	-9.17	-9.41	-9.53	-10.13
-9.38	-9.12	-9.16	-9.47	-9.54	-9.87
-9.40	-9.06	-9.16	-9.41	-9.58	-9.96
-9.36	-9.13	-9.17	-9.40	-9.56	-10.04
-9.53	-9.12	-9.15	-9.46	-9.46	-9.95
-9.53					
-9.42					
-9.59					
-9.50					
-9.53					
-9.43 ± 0.09	**-9.15 ± 0.04**	**-9.20 ± 0.04**	**-9.42 ± 0.03**	**-9.52 ± 0.05**	**-9.93 ± 0.10**
moderate	**moderate**	**moderate**	**moderate**	**low**	**low**

Supplement Table 55. Final Experimental LogP Values for Series 4. *The calculated LogP values are listed in this table.*

Series 5: LogP (UV only)					
5.1	**5.2**	**5.3**	**5.4**	**5.5**	**5.6**
-9.37	-9.05	-9.09	-9.29	-9.41	-9.15
-9.39	-9.06	-9.12	-9.17	-9.42	-9.07
-9.51	-9.05	-9.16	-9.23	-9.47	-9.14
-9.37	-9.06	-9.15	-9.26	-9.50	-9.13
-9.30	-9.06	-9.14	-9.21	-9.43	-9.07
-9.30	-9.19	-9.13	-9.26	-9.36	-9.15
-9.38	-9.21	-9.20	-9.25	-9.26	-9.13
-9.40	-9.23	-9.18	-9.38	-9.38	-9.19
-9.36	-9.22	-9.20	-9.31	-9.43	-9.13
-9.53	-9.23	-9.15	-9.22	-9.38	-9.07
-9.53	-9.01	-9.08	-9.21	-9.47	-9.11
-9.42	-9.05	-9.13	-9.30	-9.40	-9.15
-9.59	-9.04	-9.17	-9.20	-9.42	-9.28
-9.50	-9.05	-9.12	-9.39	-9.47	-9.22
-9.53	-9.02	-9.12	-9.26	-9.57	-9.17
-9.43 ± 0.09	**-9.10 ± 0.09**	**-9.14 ± 0.04**	**-9.26 ± 0.06**	**-9.42 ± 0.07**	**-9.14 ± 0.06**
moderate	**moderate**	**moderate**	**moderate**	**moderate**	**moderate**

Supplement Table 56. Final Experimental LogP Values for Series 5. *The calculated LogP values are listed in this table.*

2.10 Summary of Reported Percent Diffusion Values from Calculations (UV only)

Series 1: Percent Diffusion (UV only)					
ent-vert	**1.1**	**1.2**	**1.3**	**1.4**	**1.5**
27.29	16.85	17.71	4.74	5.25	17.54
28.33	19.84	18.58	4.74	3.61	10.22
25.74	18.50	16.00	4.86	5.54	14.40
27.38	21.27	18.87	4.52	7.20	12.99
24.76	21.33	18.38	4.74	6.26	10.42
25.67	17.07	20.33	5.41	4.63	10.46
25.80	19.72	13.54	5.41	4.23	11.23
28.14	18.84	19.60	5.41	7.61	12.90
21.30	19.44	20.51	5.41	6.42	11.64
20.00	21.17	18.01	5.41	6.64	9.21
20.09		21.03			
27.09		20.44			
20.55		21.01			
19.63		18.43			
21.05		19.73			
21.78		21.03			
28.19					
28.28					
18.88					
28.93					
28.30					
18.34					
26.02					
22.20					
25.63 ± 2.83	**19.40 ± 1.62**	**18.95 ± 2.03**	**5.06 ± 0.37**	**5.74 ± 1.31**	**12.10 ± 2.47**
moderate	**moderate**	**moderate**	**low**	**low**	**moderate**

Supplement Table 57. Final Experimental Percent Diffusion Values for Series 1. *The calculated % diffusion values are listed in this table. This data was calculated using Supplement Equation 4 and utilizes UV absorption HPLC data (210 nm).*

Series 2: Percent Diffusion (UV only)					
ent-vert	**2.1**	**2.2**	**2.3**	**2.4**	**2.5**
27.29	31.59	31.09	23.53	20.26	15.88
28.33	31.45	32.30	25.67	17.39	18.14
25.74	32.03	30.46	27.05	17.51	16.16
27.38	30.85	29.55	25.65	16.37	14.64
24.76	30.99	29.04	27.69	18.59	15.06
25.67	38.44	29.85	26.80	21.96	19.83
25.80	38.60	26.71	26.69	19.60	20.62
28.14	40.27	33.94	25.49	19.52	18.24
21.30	39.26	27.69	22.56	16.75	14.47
20.00	38.75	33.03	24.93	17.51	18.22
20.09	40.76		23.39	21.97	21.57
27.09	44.81		24.29	21.82	19.82
20.55	34.44		24.72	22.58	15.01
19.63	41.77		22.97	18.64	16.80
21.05	39.42		23.13	15.43	18.71
21.78					
28.19					
28.28					
18.88					
28.93					
28.30					
18.34					
26.02					
22.20					
25.63 ± 2.83	**36.90 ± 4.57**	**30.37 ± 2.29**	**24.97 ± 1.64**	**19.06 ± 2.28**	**17.54 ± 2.31**
moderate	**high**	**moderate**	**moderate**	**moderate**	**moderate**

Supplement Table 58. Final Experimental Percent Diffusion Values for Series 2. *The calculated % diffusion values are listed in this table. This data was calculated using Supplement Equation 4 and utilizes UV absorption HPLC data (210 nm).*

Series 3: Percent Diffusion (UV only)					
ent-vert	**3.1**	**3.2**	**3.3**	**3.4**	**3.5**
27.29	13.42 (outlier)	16.88	18.26	14.06	12.34
28.33	23.96	24.82	17.37	13.85	11.95
25.74	25.03	18.02	16.76	12.55	9.02
27.38	24.76	18.12	16.86	11.51	12.46
24.76	26.79	17.93	16.54	11.64	14.47
25.67	19.32	19.70	17.58	12.04	14.40
25.80	23.31	16.64	18.19	12.82	12.13
28.14	22.69	18.95	15.46	12.12	11.45
21.30	17.35	16.91	17.01	12.24	12.47
20.00	22.03	17.99	16.46	12.42	8.72
20.09	23.06		19.24	12.46	8.72
27.09	22.31		16.57	13.77	11.00
20.55	21.35		16.52	13.23	7.64
19.63	18.55		17.34	14.12	9.22
21.05	22.45		17.57	13.86	8.66
21.78					
28.19					
28.28					
18.88	**with outlier:**				
28.93	**21.76 ± 3.39**				
28.30					
18.34					
26.02					
22.20					
25.63 ± 2.83	**22.35 ± 2.58**	**18.60 ± 2.38**	**17.18 ± 0.92**	**12.85 ± 0.90**	**10.98 ± 2.18**
moderate	**moderate**	**moderate**	**moderate**	**moderate**	**moderate**

Supplement Table 59. Final Experimental Percent Diffusion Values for Series 2. *The calculated % diffusion values are listed in this table. This data was calculated using Supplement Equation 4 and utilizes UV absorption HPLC data (210 nm).*

Grubbs' test was used to detect the presence of one outlier within the experimental data set for analog 3.1 (LogP_{app} of -5.86). Excel was used to calculate both G and $G_{critical}$.

$$G = \frac{\text{mean} - \text{minimum}}{\text{standard deviation}}$$

$$G_{critical} = \frac{(\#\text{ samples} - 1) \times t_{critical}}{\sqrt{[\#\text{ samples} \times (\text{deg freedom} + t_{critical}^{2})]}}$$

if $G > G_{critical}$, then minimum is an outlier and can be excluded.

Supplement Equation 8. *Calculations for Grubbs' Statistical test used to calculate the data.*

Minimum	Mean	SD	G	α	# samples	Sig Value	Deg freedom	$t_{critical}$	$G_{critical}$	Significance?
-9.33	-9.11	0.08	102.2	0.05	15	0.003	13	3.22	2.41	outlier

Supplement Table 60. *Grubbs' test for outliers for analog 3.1.*

Series 4: Percent Diffusion (UV only)					
4.1	**4.2**	**4.3**	**4.4**	**4.5**	**4.6**
12.34	17.49	17.82	12.37	9.93	3.45
11.95	19.26	16.90	11.14	9.70	4.84
9.02	19.40	15.50	11.39	7.30	4.35
12.46	18.14	15.67	11.38	10.13	4.06
14.47	19.23	17.62	11.93	9.37	3.70
14.40	19.47	18.92	11.38	8.70	2.27
12.13	20.97	19.23	10.04	8.54	4.06
11.45	23.67	19.41	11.39	7.73	3.35
12.47	20.27	18.89	11.55	8.06	2.77
8.72	20.87	19.61	10.16	10.13	3.42
8.72					
11.00					
7.64					
9.22					
8.66					
10.98 ± 2.18	**19.88 ± 1.72**	**17.96 ± 1.52**	**11.27 ± 0.71**	**8.96 ± 1.04**	**3.63 ± 0.75**
moderate	**moderate**	**moderate**	**moderate**	**low**	**low**

Supplement Table 62. Final Experimental Percent Diffusion Values for Series 4. *The calculated % diffusion values are listed.*

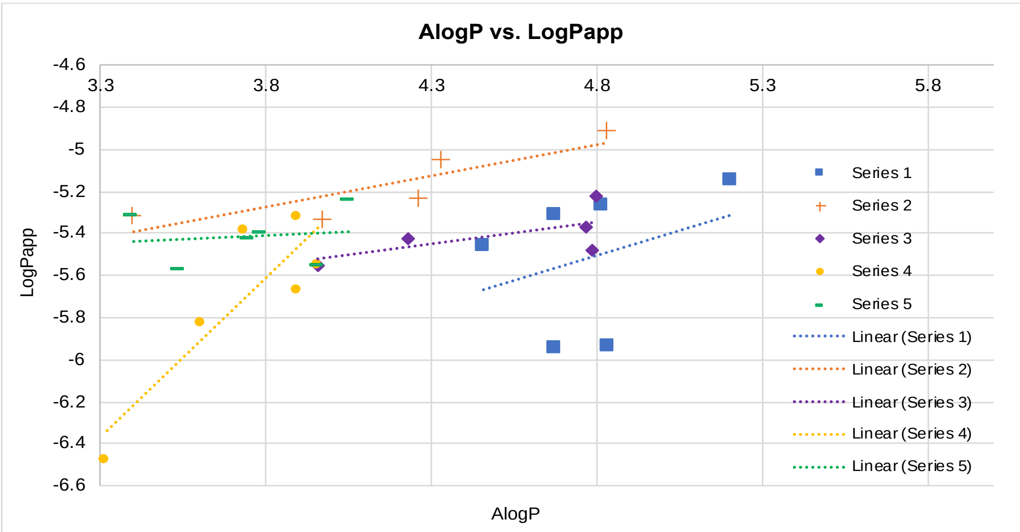
Series 5: Percent Diffusion (UV only)					
5.1	**5.2**	**5.3**	**5.4**	**5.5**	**5.6**
12.34	24.16	22.64	17.34	9.37	15.88
11.95	22.39	21.66	18.74	10.98	18.14
9.02	25.57	20.75	12.02	10.23	16.16
12.46	24.28	24.26	18.70	15.78	14.64
14.47	24.81	17.70	16.03	10.84	15.06
14.40	22.19	18.48	12.02	8.23	19.83
12.13	23.35	19.88	16.78	11.11	20.62
11.45	24.18	18.52	17.61	8.79	18.24
12.47	20.69	23.51	15.65	9.28	14.47
8.72	25.98	19.48	14.02	9.72	18.22
8.72	26.11	19.97	12.19	8.06	21.57
11.00	23.49	24.60	18.10	12.06	19.82
7.64	23.02	19.74	17.00	7.37	15.01
9.22	22.95	21.15	17.33	7.98	16.80
8.66	23.44	21.03	15.49	10.14	18.71
10.98 ± 2.18	**23.77 ± 1.48**	**20.89 ± 2.11**	**15.93 ± 2.35**	**10.00 ± 2.09**	**17.54 ± 2.31**
moderate	**moderate**	**moderate**	**moderate**	**moderate**	**moderate**

Supplement Table 61. Final Experimental Percent Diffusion Values for Series 5. *The calculated % diffusion values are listed.*

2.9 Calculated AlogP Values

Molecule	Formula	MW	# Rotatable bonds	HBA	HBD	TPSA	AlogP	LogPapp
ent-verticilide	C44H76N4O12	853.09	16	12	0	186.44	5.21	-5.21
1.1	C43H74N4O12	839.07	16	12	1	195.23	4.82	-5.27
1.2	C42H72N4O12	825.04	16	12	2	204.02	4.68	-5.31
1.3	C42H72N4O12	825.04	16	12	2	204.02	4.84	-5.94
1.4	C41H70N4O12	811.01	16	12	3	212.81	4.68	-5.95
1.5	C40H68N4O12	796.99	16	12	4	221.6	4.46	-5.46
2.1	C44H77N5O11	852.11	16	11	1	189.24	4.83	-4.91
2.2	C44H78N6O10	851.12	16	10	2	192.04	4.33	-5.05
2.3	C44H78N6O10	851.12	16	10	2	192.04	4.26	-5.23
2.4	C44H79N7O9	850.14	16	9	3	194.84	3.97	-5.33
2.5	C44H80N8O8	849.15	16	8	4	197.64	3.4	-5.31
3.1	C45H79N5O11	866.14	16	11	0	180.45	4.8	-5.22
3.2	C46H82N6O10	879.18	16	10	0	174.46	4.77	-5.37
3.3	C46H82N6O10	879.18	16	10	0	174.46	4.79	-5.48
3.4	C47H85N7O9	892.22	16	9	0	168.47	4.23	-5.42
3.5	C48H88N8O8	905.26	16	8	0	162.48	3.96	-5.55
4.1	C48H88N8O8	905.26	16	8	0	162.48	3.96	-5.55
4.2	C47H86N8O8	891.23	16	8	1	171.27	3.9	-5.32
4.3	C46H84N8O8	877.21	16	8	2	180.06	3.74	-5.39
4.4	C46H84N8O8	877.21	16	8	2	180.06	3.9	-5.67
4.5	C45H82N8O8	863.18	16	8	3	188.85	3.61	-5.83
4.6	C44H80N8O8	849.15	16	8	4	197.64	3.32	-6.48
5.1	C48H88N8O8	905.26	16	8	0	162.48	3.96	-5.55
5.2	C47H86N8O8	891.23	16	8	1	171.27	4.05	-5.24
5.3	C46H84N8O8	877.21	16	8	2	180.06	3.75	-5.42
5.4	C46H84N8O8	877.21	16	8	2	180.06	3.79	-5.4
5.5	C45H82N8O8	863.18	16	8	3	188.85	3.54	-5.57
5.6	C44H80N8O8	849.15	16	8	4	197.64	3.4	-5.31

Supplement Table 63. *Comparison of molecular formula and weight (MW = g/mol), rotatable bonds, HBDs and HBAs, topological polar surface area, calculated AlogP and experimental LogPapp. Calculated TPSA and AlogP found using Swiss ADME calculator http://www.swissadme.ch.*



Supplement Graph 60. *Comparison of AlogP and LogPapp.*

Section 3. Caco-2 Assay

3.1 Experimental Procedure

Caco-2 assays were performed by Inotiv. Polarized human colorectal adenocarcinoma-derived (Caco-2) cells were differentiated (passage 55 to 65) for 21 days in 24 Transwell® inserts with a semiporous polystyrene membrane (0.4 µm; CORNING Cat#3378) at a density of 150,000 – 180,000 cells per well in Dulbecco's Modified Eagle's Medium (glucose 1 g/L, fetal bovine serum 10% v/v, L-glutamine 2 mM, penicillin 110 U/mL, and streptomycin 100 µg/mL). Transepithelial electrical resistance (TEER) measurements greater than 1000 Ω x cm2 between the apical and basal compartments were used to identify inserts with cell monolayers suitable for transport studies. Hank's balanced salt solution (HBSS; pH 7.4) was used as the standard transport buffer for all permeability experiments. Final concentrations of test and reference compounds were prepared in HBSS and run in duplicate to assess permeability. Test compounds were diluted to a final concentration of 10 uM with less than 1% of DMSO in the assay buffer. Reference compounds (10 uM) used as positive controls included atenolol and metoprolol as low and high permeability compounds along with digoxin as a known substrate for the efflux transporter, p-glycoprotein.

Prior to starting transport experiments, cell culture media was gently aspirated from both sides of the cell monolayer inserts and washed twice by adding 250 ul and 750 ul of Hank's balanced salt solution (HBSS; pH 7.4) pre-warmed to 37°C to the apical and basal compartment, respectively. Following the second wash, the plate was returned to the cell incubator (37 °C, 5 % CO2) for 30 minutes. For apical-to-basal (A-B) permeability studies, the plate was removed from the cell incubator and the HBSS was gently aspirated from the basal compartment and replaced with fresh, pre-warmed HBSS (750 ul). Test compounds prepared in pre-warmed HBSS (275 ul) were applied to the apical compartment (donor side) and each insert was immediately placed into the basal compartment (receiver side). For basal-to-apical (B-A) permeability studies, a second plate was removed from the cell incubator and the HBSS was gently aspirated from the basal compartment and replaced with fresh, pre-warmed HBSS (775 ul) containing test compounds. Pre-warmed HBSS (250 ul) was applied to the apical compartment (receiver side) and each insert was immediately placed into the basal compartment containing test compounds (donor side). A 25 ul sample was immediately removed from the donor side of the plate (apical for A-B studies; basal for B-A studies) and transferred to a separate 96-well plate for subsequent LC-MS/MS analysis at the end of the experiment. After collecting samples at time zero (T0), plates were placed in the cell incubator to allow mass transport of test and reference compounds to cross the cell monolayer from the donor side to the receiver side. Plates were removed from the cell incubator after 2 hours (T2) and a 25 ul sample from both the donor and receiver side was transferred to the 96-well plate for LC-MS/MS analysis. Samples collected at both time points (T0 and T2) were analyzed by liquid chromatography coupled to tandem mass spectrometry to assess the initial compound donor concentration, overall compound recovery, and the bidirectional permeability (A-B and B-A) of each compound. Permeability for each test and reference compound was calculated according to the following equation:

$$Papp = \frac{dQ}{dt} \times \frac{1}{A \times C_{donor,T0}}$$

where Papp represents the coefficient of apparent permeability (cm/sec), which corresponds to the proportion of compound that crosses the cell monolayer at each time point (dQ/dt; nmol/sec) divided by the product of the cell monolayer surface area and the initial concentration of the compound in the donor side at time zero ($C_{donor,T0}$; nmol/ml).

An efflux ratio (ER) for the bidirectional transport of each compound across the cell monolayer was used as a general measure to evaluate the involvement of passive and active transport processes using the following equation:. An ER was calculated for each compound by dividing the Papp in the B-A direction (P by the Papp in the A-B direction:

$$ER = \frac{P_{app\ B-A}}{P_{app\ A-B}}$$

where $P_{appB\text{-}A}$ and $P_{appA\text{-}B}$ refers to the permeability of each compound in the B-A and A-B directions, respectively.

Compound recovery for each transwell experiment was determined using the following mass balance equation:

$$\%\ Recovery = \frac{(C_{A,T2} \times V_A) + (C_{B,T2} \times V_B)}{C_{donor,T0} \times V_{donor}} \times 100$$

where $C_{A,T2}$ and $C_{B,T2}$ correspond to compound concentrations at timepoint 2 hours in the apical and basal compartments, respectively. The term $C_{donor,T0}$ is the initial concentration of the compound in the donor compartment at time zero. The terms V_A, V_B, and V_{donor} correspond to the volume of buffer in the apical, basal, and donor compartments, respectively.

Cell monolayer integrity for each well was also evaluated at the end of experiments by measuring the A-B permeability of lucifer yellow. HBSS was gently aspirated from the basal compartment and replaced with fresh, pre-warmed HBSS (750 ul). Pre-warmed HBSS (250 ul) containing lucifer yellow (100 uM) was applied to the apical compartment (donor side) and each insert was immediately placed into the basal compartment (receiver side). Plates were protected from light and placed in the cell incubator (at 37 °C and 5 % CO2) for 1 hour. At the end of the incubation period, a 200 ul sample was collected from the basal compartment and transferred to 96-well plate for fluorescence-based assays. Fluorescence intensity of samples and a standard curve prepared from the lucifer yellow working solution was measured in a fluorometer at 485/527 excitation/emission wavelengths. Lucifer yellow paracellular flux values ≤ 0.5 % was used as a strong indicator of cell barrier integrity.

3.2 Caco-2 Experimental Data

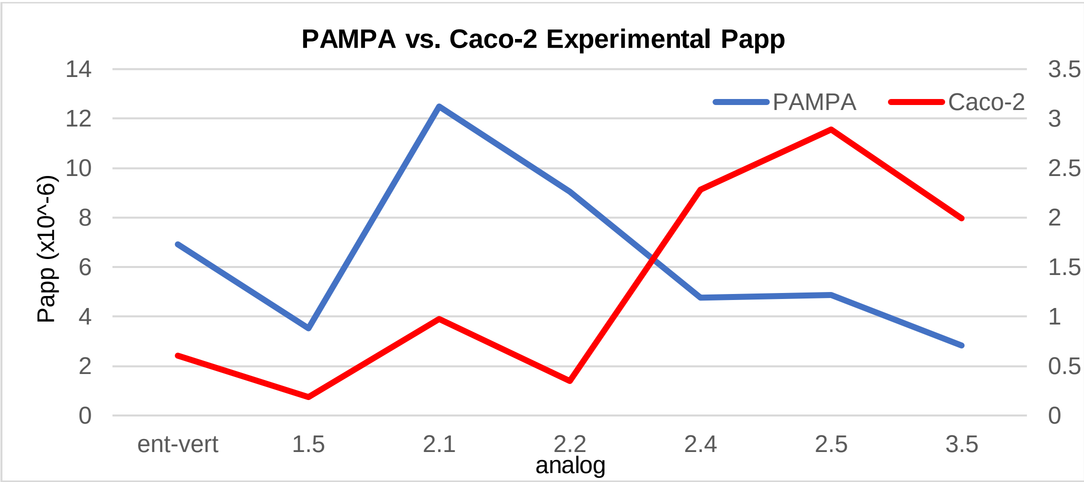
Compound	Donor Concentration	Papp (x 10^{-6} cm/sec)		ER
		A-B	B-A	
Atenolol	10 µM	0.121	0.482	3.98
Metoprolol	10 µM	19.8	15.4	0.78
Digoxin	10 µM	1.59	12.2	7.68
MPT-6-108	10 µM	0.604	0.964	1.60
MPT-6-109 1.5	10 µM	0.186	0.0896	0.48
MPT-6-110 2.1	10 µM	0.978	1.16	1.18
MPT-6-111 2.2	10 µM	0.349	2.12	6.09
MPT-6-112 2.3	10 µM	ND	ND	ND
MPT-6-113 2.4	10 µM	2.28	4.32	1.89
MPT-6-114 2.5	10 µM	2.89	6.82	2.36
MPT-6-115 3.5	10 µM	1.99	1.85	0.93

Supplement Table 64. *Final Experimental data for the Caco-2 assays.*

	PAMPA			Caco-2			
Analog	**Papp**	**% R**	**Permeability**	**Papp (A-B)**	**Papp (B-A)**	**Efflux Ratio**	**Permeability**
***ent*-vert**	6.92 ± 0.66	90	moderate	0.604	0.964	1.6	moderate
1.5	3.51 ± 0.54	87	moderate	0.186	0.0896	0.48	low
2.1	12.49 ± 2.49	88	high	0.978	1.16	1.18	moderate
2.2	9.04 ± 0.71	89	moderate	0.349	2.12	6.09	moderate
2.3	5.93 ± 0.51	90	moderate	ND	ND	ND	ND
2.4	4.76 ± 0.75	89	moderate	2.28	4.32	1.89	moderate
2.5	4.87 ± 0.48	86	moderate	2.89	6.82	2.36	moderate
3.5	2.83 ± 0.40	93	moderate	1.99	1.85	0.93	moderate

Supplement Table 65. *Side-by-side comparison of final experimental data for the PAMPA and Caco-2 assays. ND = not detectable.*

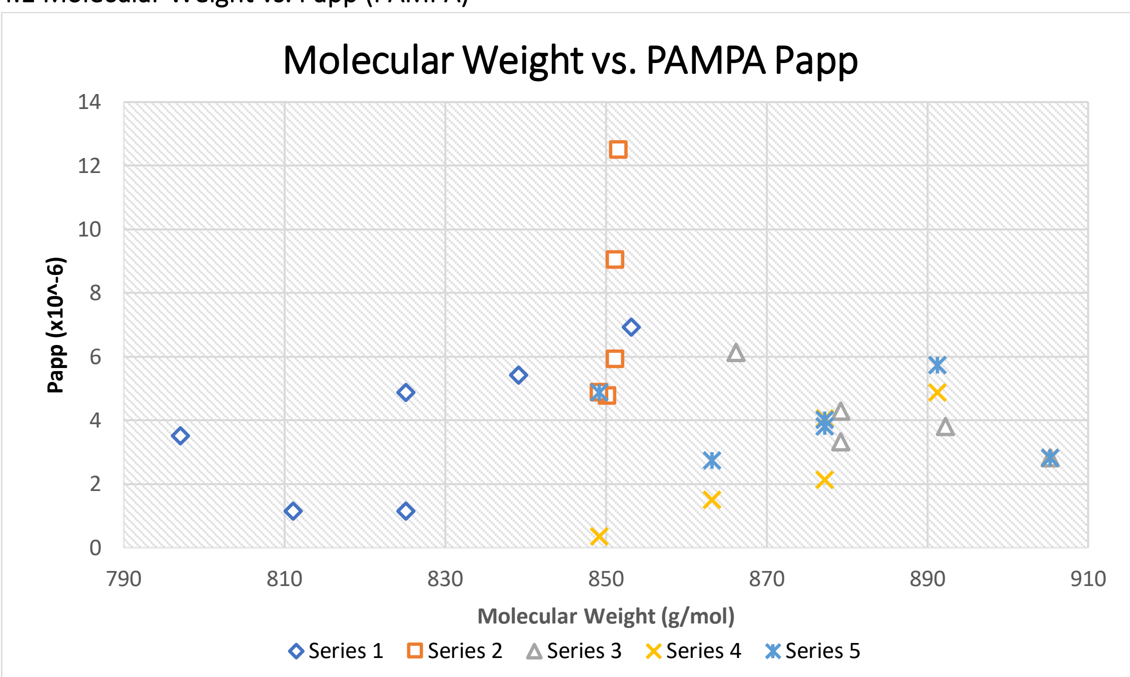
3.3 Comparison of Caco-2 and PAMPA Data



Supplement Graph 61. *Comparison of PAMPA and Caco-2 Experimental Papp.*

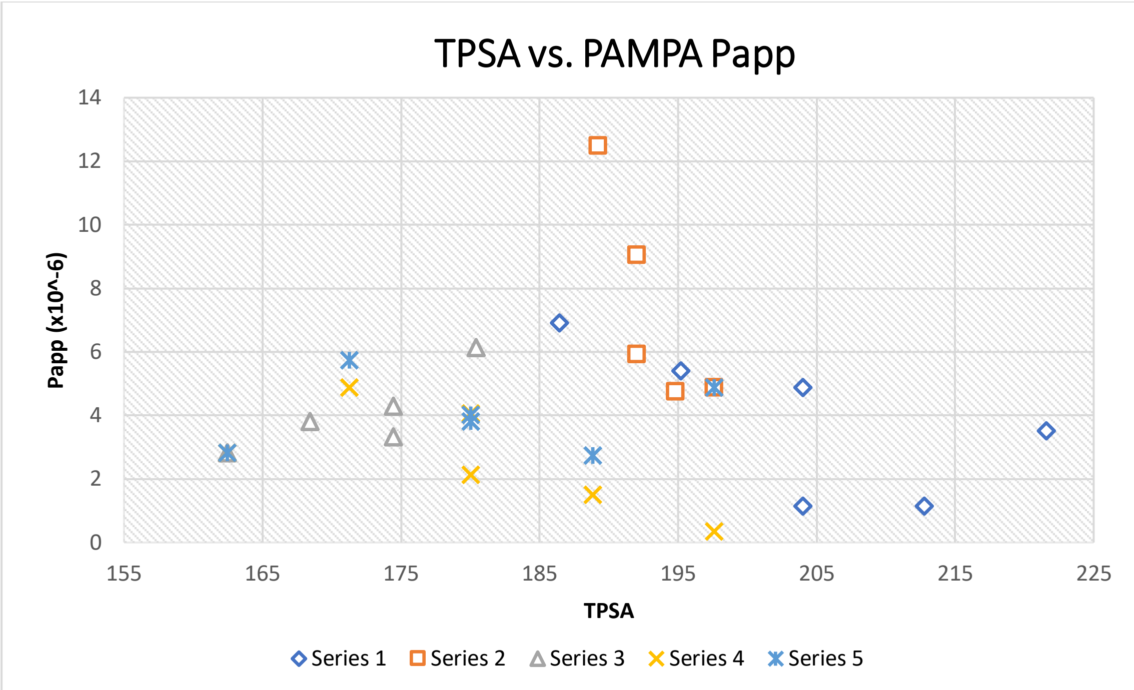
Section 4. Correlation Plots

4.1 Molecular Weight vs. Papp (PAMPA)



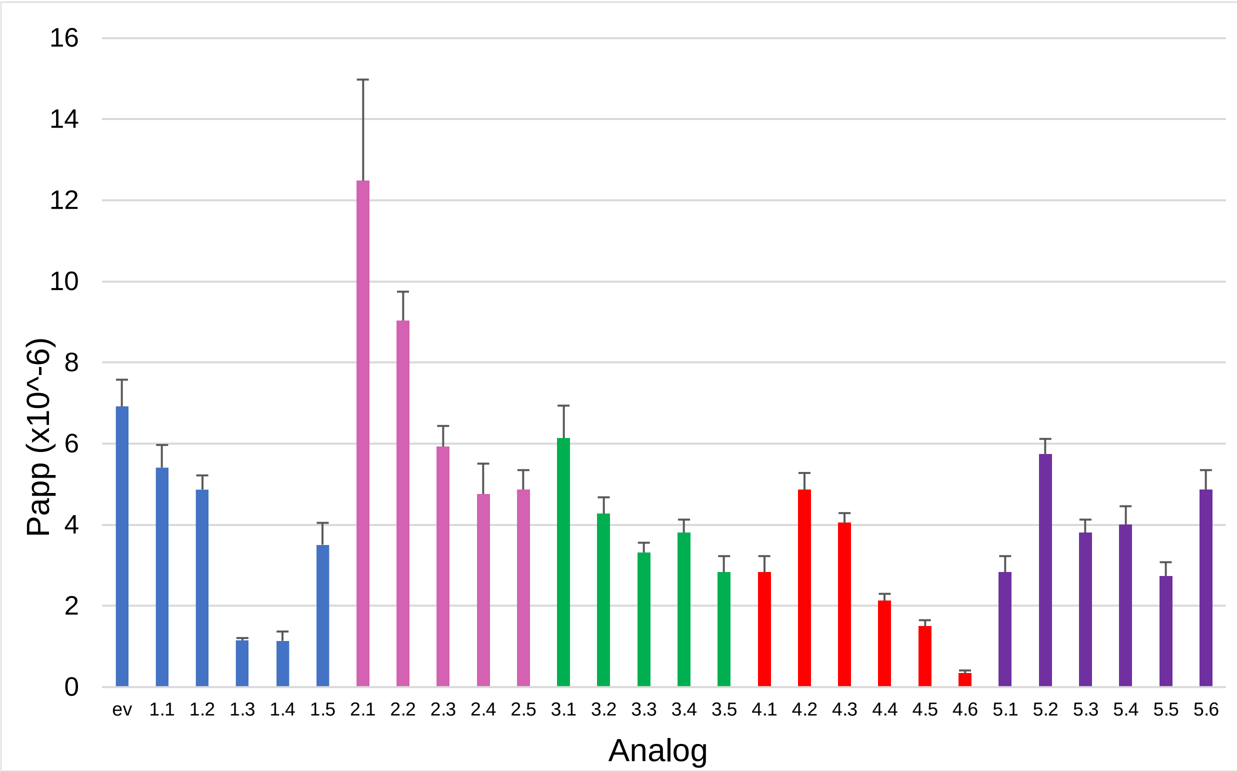
Supplement Graph 62*. Molecular weight versus experimental Papp.*

4.2 Topological Polar Surface Area vs. Papp (PAMPA)



Supplement Graph 63. *Topological polar surface (calculated) area versus experimental Papp.*

4.3 Comparison of Papp Data Across Series 1-5



Supplement Graph 64. *Experimental Papp values for Series 1 (blue), 2 (pink), 3 (green), 4 (red) and 5 (purple).*

Section 5. NMR Experiments

^{1}H NMR: Titration of 1.5 with DMSO-d_6 to investigate the nature of hydrogen bonding.

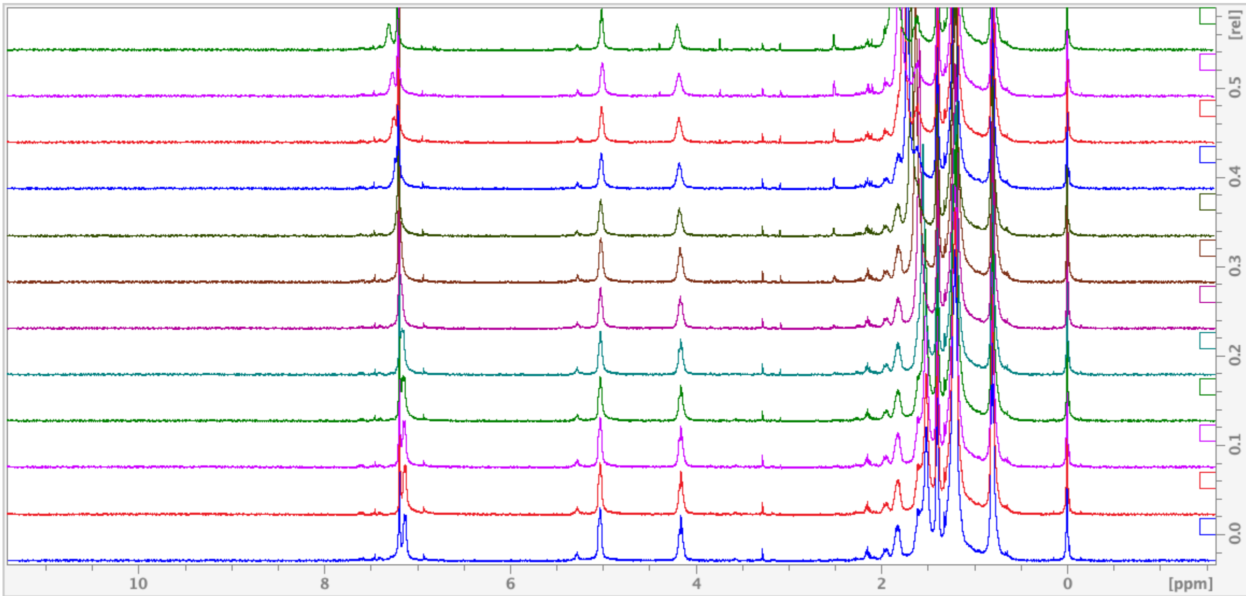
The macrocycle (**1.5**, 6.6 mg) was dissolved in 500 µL of $CDCl_3$ and the solution was sonicated. A ^{1}H NMR was recorded (experiment 0), and DMSO-d_6 was added in increments. After each addition, the NMR tube was sonicated for 30 seconds. To more accurately measure the amount of DMSO-d_6 added, a stock solution was made using $CDCl_3$. The 5 mol % additions came from a stock of 3 µL DMSO-d_6 in 1000 µL $CDCl_3$. The 10 mol % additions came from a stock of 6 µL DMSO-d_6 in 1000 µL $CDCl_3$. The 50 mol % additions came from a stock of 30 µL DMSO-d_6 in 1000 µL $CDCl_3$. The 100 mol % additions came from a stock of 60 µL DMSO-d_6 in 1000 µL $CDCl_3$. There was a total of 21 ^{1}H NMR experiments completed in this study, with the addition of 5 to 2007 mol % of DMSO-d_6 added. The experiments spanned 3 days, with 0-11 being on the first day, 12-18 on the second day and 19-21 on the final day. The solution was stored in the NMR tube at -20 °C between days, and no solubility issues were noted.

experiment #	total mol% DMSO-d_6	total volume (µL)	mmol/mL	*N*-H chemical shift (ppm)
0*	0	500	0.016562108	7.199
1	5	510	0.016237361	7.2
2*	10	520	0.015925104	7.204
3	15	530	0.01562463	7.206
4*	20	540	0.015335285	7.207
5	30	550	0.015056462	7.211
6*	40	560	0.014787596	7.219
7	57	563.33	0.014700183	7.223
8*	107	573.33	0.014443783	7.232
9	157	583.33	0.014196174	7.238
10*	207	593.33	0.013956911	7.244
11	257	603.33	0.01372558	7.246
12*	307	613.33	0.013501792	7.249
13*	357	623.33	0.013285184	7.259
14	407	633.33	0.013075417	7.266
15*	457	643.33	0.012872171	7.271
16	507	653.33	0.012675147	7.292
17*	607	663.33	0.012484064	7.304
18	807	673.33	0.012298656	7.324
19*	1207	683.33	0.012118675	7.34
20	1607	693.33	0.011943885	7.351
21*	2007	703.33	0.011774066	7.36

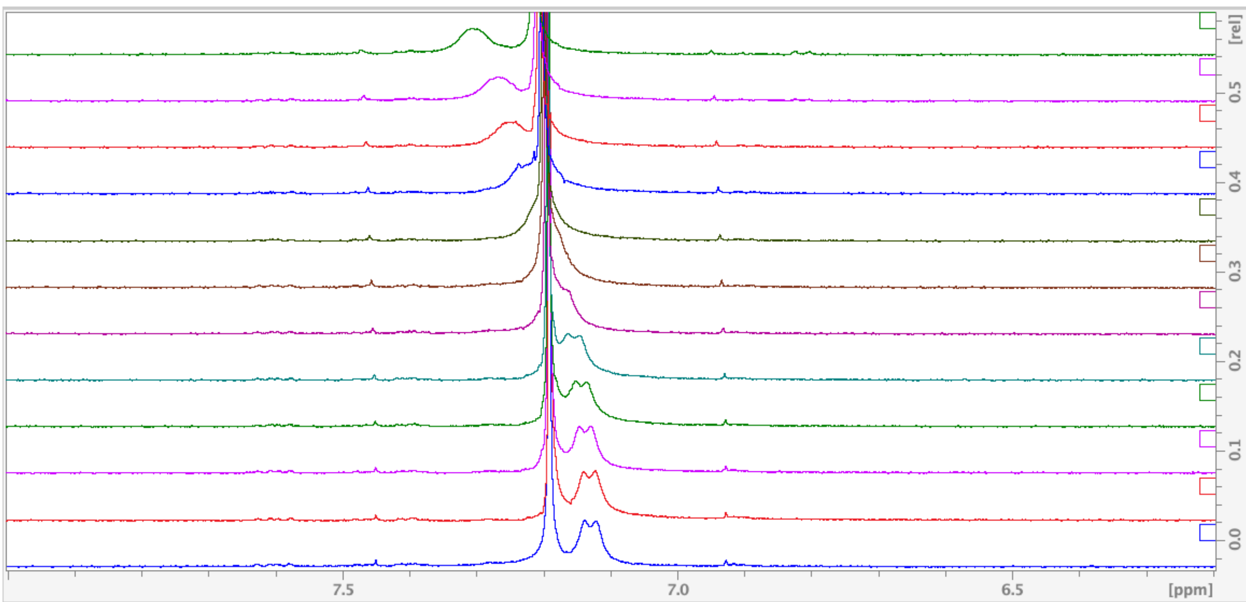
Supplement Table 66. *Experimental data for the DMSO titration experiment of analog* ***1.5*** *in* $CDCl_3$*. The chemical shifts are referenced to TMS at 0.000 ppm. * = ^{1}H NMR shown on following page.*

Supplement Figure 2. *[1]H NMR of analog **1.5** in $CDCl_3$: **A**) Experiment number from bottom to top: 0, 2, 4, 6, 8, 10, 12, 13, 15, 17, 19, 21; **B**) N-H region; **C**) experiment 0 (bottom) vs. experiment 21 (top).*

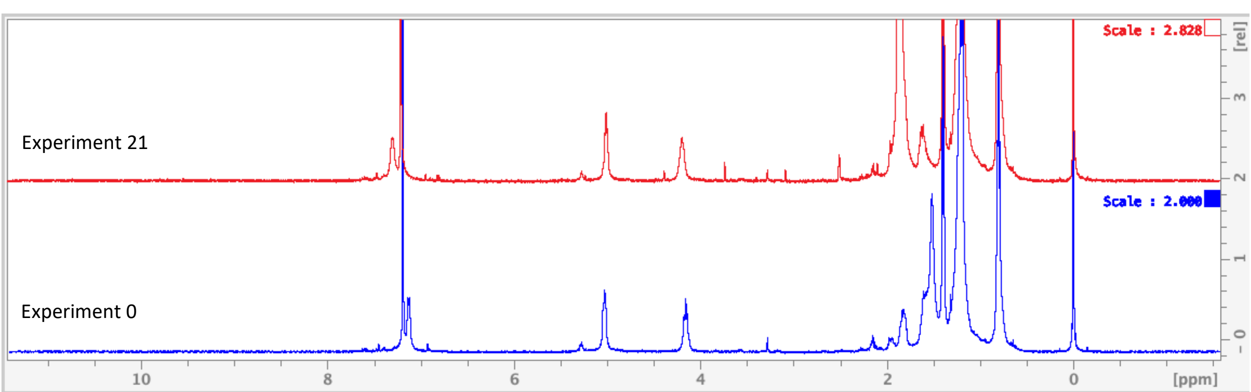
A)



B)



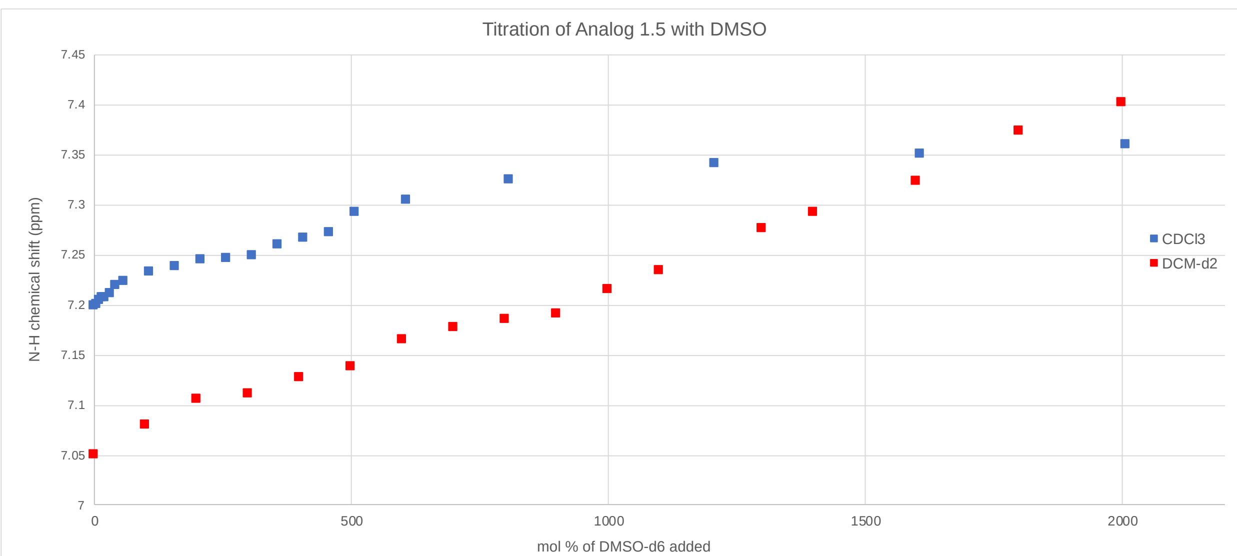
C)



A similar study using DCM-d_2 was completed to verify the results found in the first study.

experiment #	total mol% DMSO-d6	total volume (μL)	mmol/mL	*N*-H chemical shift (ppm)
0*	0	500	0.0165621	7.05
1	100	510	0.016237353	7.079
2*	200	520	0.015925096	7.105
3	300	530	0.015624623	7.111
4*	400	540	0.015335278	7.126
5	500	550	0.015056455	7.137
6*	600	560	0.014787589	7.164
7	700	570	0.014528158	7.177
8*	800	580	0.014277672	7.185
9	900	590	0.014035678	7.19
10*	1000	600	0.01380175	7.214
11	1100	610	0.013575492	7.233
12*	1300	620	0.013356532	7.276
13	1400	630	0.013144524	7.2913
14*	1600	640	0.012939141	7.323
15	1800	650	0.012740077	7.373
16*	2000	660	0.012547045	7.401

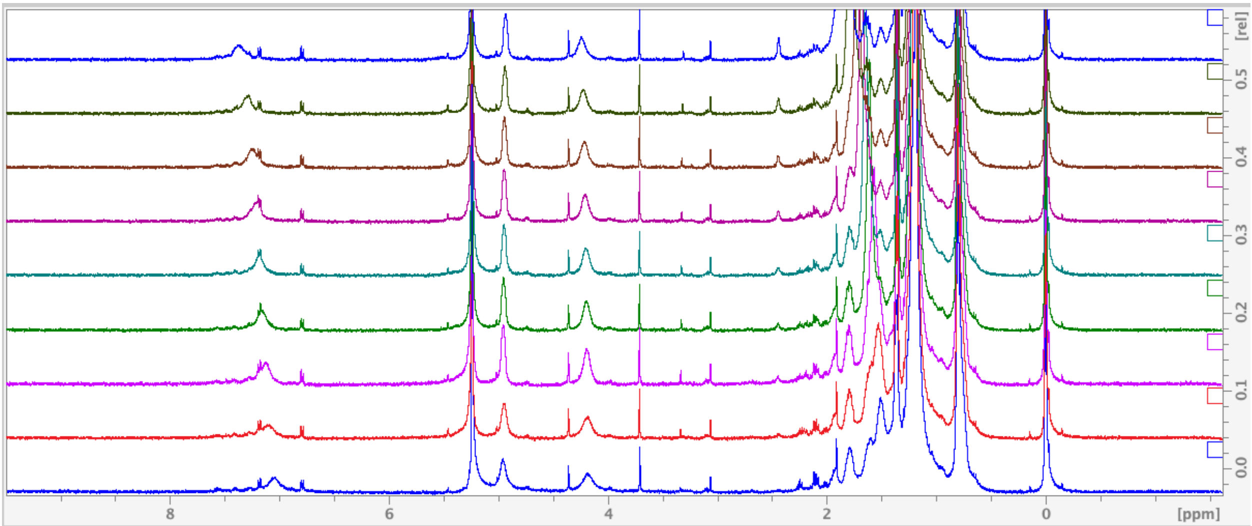
Supplement Table 67. *Experimental data for the DMSO titration experiment of analog* ***1.5*** *in DCM-d_2. The chemical shifts are referenced to TMS at 0.000 ppm. * = ^{1}H NMR shown on following page.*



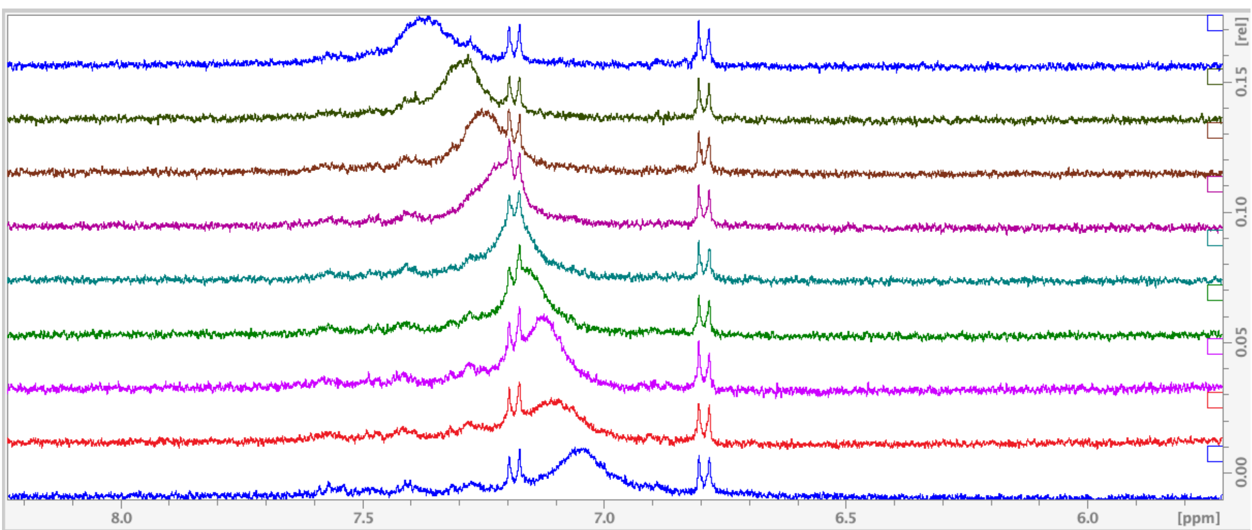
Supplement Graph 65. *Experimental data for the DMSO titration experiment of analog* ***1.5****: A comparison between the N-H chemical shift and amount of DMSO-d_6. Blue = solvent is $CDCl_3$, Red = solvent is DCM-d_2. The chemical shifts are referenced to TMS at 0.000 ppm.*

Supplement Figure 3. *[1]H NMR of analog **1.5** in DCM-d$_2$: **A**) Experiment number from bottom to top: 0, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20; **B**) N-H region.*

A)



B)



[1] Smith, A. N.; Thorpe, M. P.; Blackwell, D. J.; Batiste, S. M.; Hopkins, C. R.; Schley, N. D.; Knollmann, B. C.; Johnston, J. N.; *ACS Med. Chem. Lett.* **2022** *13*, 1755.
[2] Thorpe, M. P.; Blackwell, D. J.; Knollmann, B. C.; Johnston, J. N.; *J. Med. Chem.* **2024** *67*, 12205.
[3] Oh, M. H.; Lee, H. J.; Jo, S. H.; Park, B. B.; Park, S.-B.; Kim, E.-y.; Zhou, Y.; Jeon, Y. H.; Lee, K.; *Biological and Pharmaceutical* Bulletin **2017** *40*, 419.