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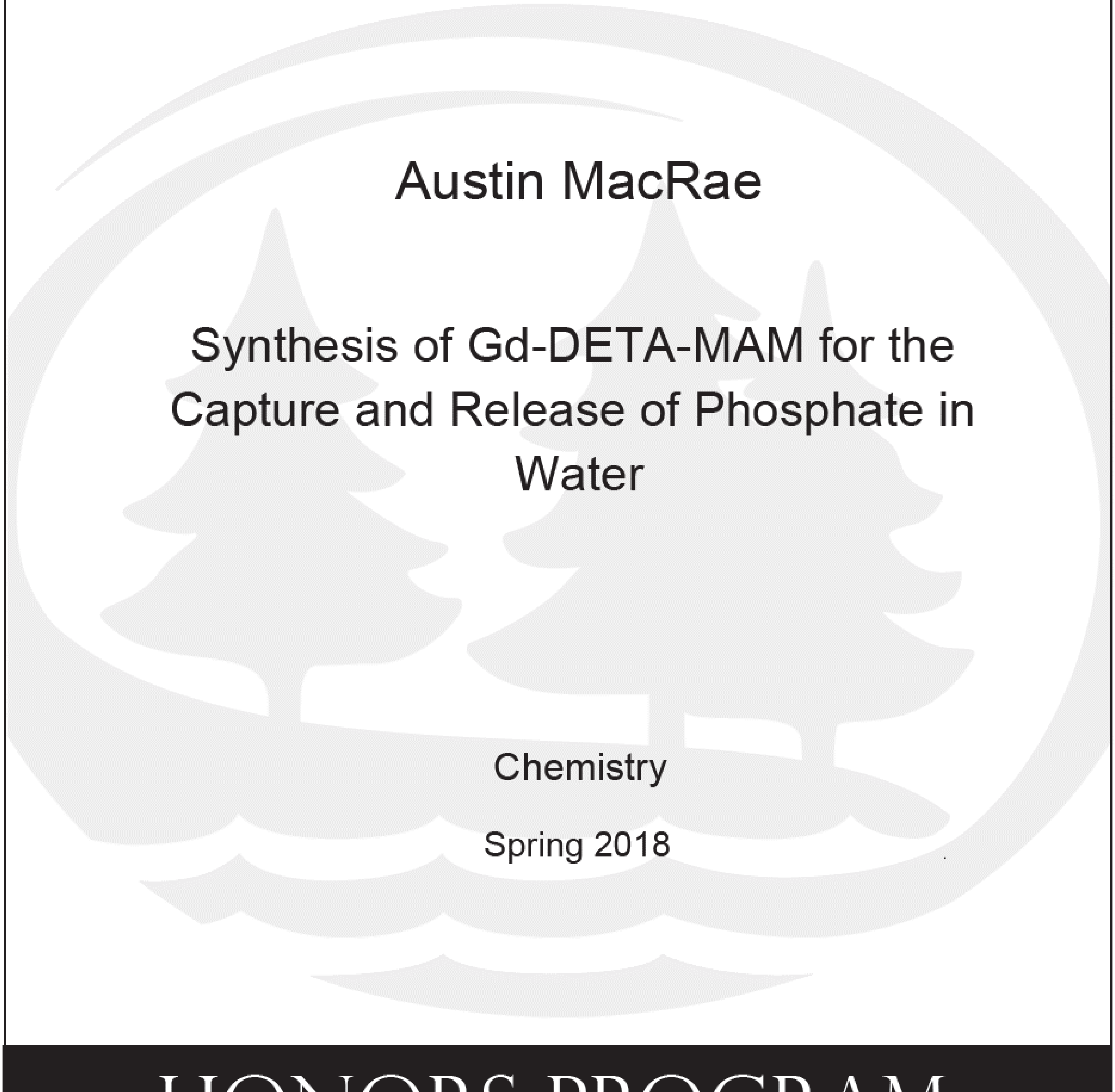

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Synthesis of Gd-DETA-MAM for the Capture and Release of Phosphate in Water

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Synthesis of Gd-DETA-MAM for the Capture and Release of Phosphate in Water

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Abstract

Excess phosphorus in lakes from fertilizer runoff causes eutrophication, which in turn promotes algal blooms. These algal blooms can produce toxins that pollute drinking water for entire cities. A catch and release system for phosphate is proposed that features Gd-DETA-MAM, which is a derivative of Gd-TREN-MAM. Gd-TREN-MAM has been shown to selectively and reversibly bind phosphate in a pH dependent manner. The derivation aims to increase the binding affinity of phosphate by reducing steric hinderance around the gadolinium atom. The rational for this hypothesis is that the linear DETA backbone will have increased accessibility compared to a TREN backbone. The first three reactions in the synthesis of Gd-DETA-MAM have been successfully performed in lab, and varying reaction parameters have been tested to increase yields of each reaction step. Each reaction was monitored by TLC, and synthetic intermediates were be characterized via ^{1}H NMR. DFT calculations have been performed to determine the lowest average structures of both Gd-DETA-MAM and Gd-TREN-MAM. The calculated energy values for the hydrated and phosphorylated complexes were used to calculate theoretical binding affinities for the complexes.

Background

In 2014, Lake Erie was overtaken by algal blooms in a process called eutrophication. The large blooms led to the pollution of the lake with toxins such as microcystin.[1] Microcystin is a toxin that the World Health Organization has deemed be toxic to humans at 1 ppm or higher.[2] In 2014, Lake Erie's water had levels above 2.5 ppm for microcystin so surrounding cities were forced to shut down their water supplies.[1] In 2015, the city of Toledo, which provides water to 400,000 residents, had to shut down their water supply for 4 days due to high levels of the toxin.[3] In 2017, Lake Erie was covered by more than 700 square miles of algae, which could lead to increasing levels of toxins to return to the lake.[4]

The growth of algae in lakes is exacerbated by high levels of phosphate and nitrogen in the water, which is caused by fertilizer runoff from nearby field.[1,5] Capturing phosphate in natural bodies of water is a good approach to reduce eutrophication. Gadolinium complexes have been known to bind to phosphate due to previous research on MRI contrast agents.[6] Dr. Valerie Pierre at the University of Minnesota - Twin Cities has proposed a membrane with a gadolinium complex appended to it could be used in water to bind and release phosphate with pH dependency. Dr. Pierre has been working alongside Bemidji State University on this project under supervision of Dr. Katie Peterson. At a low pH such as 4.0, phosphate would be released from the proposed membrane complex, but at a more neutral pH around 7.4, phosphate would be tightly bound to gadolinium complexes on the membrane (Figure 1). This pH dependency will allow for the capture of phosphate in lake water, which can then be released in a well-known, industrial method that lowers the pH of a solution and facilitates the crystallization of phosphate in the form of struvite, a commercial fertilizer.[7-10]

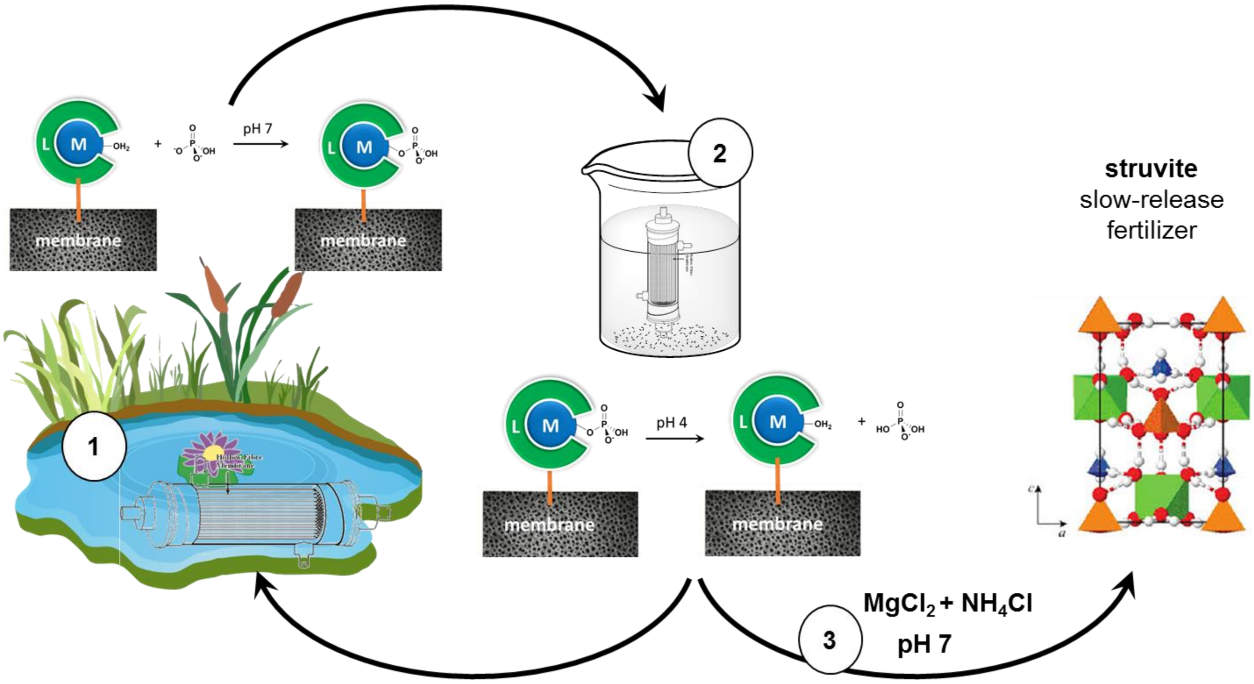


Figure 1. The recycling process of phosphate in natural water sources using a metal-ligand complex to uptake phosphate. Phosphate is collected in a reduced pH, and struvite is produced via popular commercial reactions.[7-10]

The recycling process of using a membrane-appended complex to capture phosphate is important due to the depletion of economically mineable phosphorus. The prices of phosphorus have increased 310.5% between the years of 2006 and 2016.[7] The skyrocketing price of phosphorus is due to the depletion of current mines that are safe and feasible for supplying phosphorus with current industry practices. Understanding the pricing of phosphorus is important to this project because fertilizer uses approximately 80% of the phosphorus that is mined.[11] To conclude, this project is environmentally friendly as well as economically important because the capture and release process proposed will produce a commercial fertilizer that can be sold and reused.

Introduction

This project aimed synthesize gadolinium complexes. Specifically, the aim was to work out the small details and problems that arise when synthesizing benzyl-maltol-carboxylic acid, which is also known as Bn-MAM (Figure 2). Literature about an MRI contrast agent, [Gd(TREN-MAM)(H_2O)$_2$)] (Figure 3), has shown that phosphate binds to gadolinium complexes at neutral pH, and the MAM moiety is an important component of the gadolinium complexes.[6] Alongside the investigation of synthesizing MAM, this project aimed to synthesize [Gd(DETA-MAM)(H_2O)$_2$)] (Figure 4), which has been hypothesized to bind phosphate at neutral pH better than [Gd(TREN-MAM)(H_2O)$_2$)] due to the reduced steric hinderance.

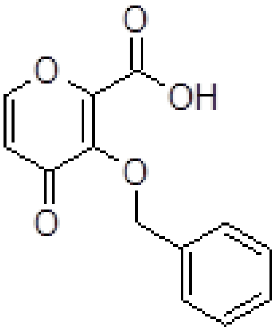


Figure 2. Chemical structure of 3-(benzyloxy)-4-oxo-4H-pyran-2-carboxylic acid, Bn-MAM.

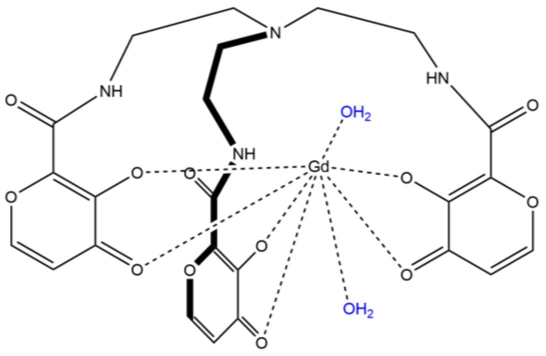


Figure 3. Chemical structure of the complex [Gd(TREN-MAM)(H_2O)$_2$)].

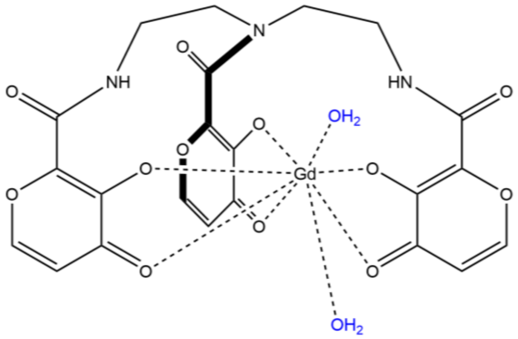


Figure 4. Chemical structure of the complex [Gd(DETA-MAM)(H_2O)$_2$)].

Normally, [Gd(TREN-MAM)(H_2O)$_2$)] allows for a gadolinium atom to bind to two water molecules (these are replaced by phosphate molecules), but the other portions of the ligand "clutter" or hinder access to the metal center.[6] It is proposed that the DETA backbone, versus TREN, will be more open and create more space for phosphate to replace water. This hypothesis will be tested using computational chemistry to calculate the phosphate binding affinity to each of the complexes. A higher binding affinity of phosphate on Gd-DETA-MAM from calculations would prove that the hypothesis of this project is valid. The computational portion of this project was led by Dr. Bob Quandt.

Methods

The synthesis scheme of [Gd(DETA-MAM)(H_2O)$_2$)] will follow the same pathway that has been published in literature for [Gd(TREN-MAM)(H_2O)$_2$)], but the addition of the DETA backbone instead of TREN must be modified via trial and error.[12]

Synthesis of Benzyl-Maltol

The synthesis of benzyl-maltol is well documented.[13-15] Maltol (3.1123 g, 24.679 mmol, 1 eq.) and potassium carbonate (8.5521 g, 61.882 mmol, 2.5 eq.) was dissolved in DMF (45 mL). Benzyl bromide (7.3284 mL, 61.698 mmol, 2.5 eq.) was diluted in 5 mL of DMF and added dropwise to the reaction flask. The reaction mixture was heated to 80˚C for 24 hours under a constant flow of nitrogen gas. The reaction was monitored with TLC (SiO_2, eluent: 50% dichloromethane and 50% hexane). Additionally, TLC plates were stained with an iron(III) chloride solution to test for phenols. The final TLC plate showed an absence of maltol (Fe(III)Cl_3 test stained red). Potassium carbonate was filtered off the solution before the DMF solvent was removed under reduced pressure. The reaction was filtered to remove excess potassium carbonate, and then the DMF solvent was evaporated under reduced pressure to produce the crude product as a thick, orange oil.

The crude product was dissolved in DCM (35 mL) and washed with distilled water (3 x 35 mL). The lower organic layer was retrieved after each wash. The organic layer was then washed with 5% NaOH (2 x 35 mL) and brine (1 x 35 mL). This final organic layer was dried with an excess amount of $MgSO_4$, filtered, and the DCM solvent was evaporated off under reduced pressure to yield a thick yellow oil (5.2815 g, 24.425 mmol, 99.03% yield). The product was characterized via ^{1}H NMR (60 MHz, DMSO-d^6) δ: 2.09 (s, 3H, $-CH_3$), 5.04 (s, 2H, $-CH_2$), 6.36 (d, 1H, Pyridinone), 7.38 (s, 6H, Ar), 8.04 (d, 1H, Pyridinone C_6-H).

Synthesis of Benzyl-Maltol-Aldehyde

The synthesis of benzyl-maltol-aldehyde is well documented, and additional contact with the University of Minnesota - Twin Cities has been used for additional synthetic parameters. [15] Benzyl-maltol (0.4950 g, 2.289 mmol, 1 eq.) was dissolved in bromobenzene (5 mL), and SeO_2 (1.1044 g, 9.9531 mmol, 4 eq.) was added in two separate additions. The reaction vessel was attached to a Dean-Stark apparatus to remove water biproduct. The mixture was heated to 130˚C and stirred vigorously for 24 hours. Half of the SeO_2 was added initially to the reaction while the other half of the SeO_2 was added after an hour of applying heat to the reaction. The reaction was monitored with TLC (SiO_2, eluent = 50% hexane and 50% ethyl acetate); plates were treated with a DNP stain, which stains yellow in the presence of an aldehyde. SeO_2 was filtered off the reaction and the solvent was removed under vacuum. The crude product was purified via column chromatograph (SiO_2, eluent gradient: 25 to 50% ethyl acetate in hexane). The last compound to emerge through the column was tested via TLC (SiO_2, eluent = 50% hexanes and 50% ethyl acetate) and a DNP stain. The TLC spot for this compound stained yellow. The product was present in fractions 40-55. Fractions 40-55 were combined, and the solvent was removed under vacuum to yield a thick, orange oil (0.2441 g, 1.060 mmol, 46.3% yield). The product was characterized via ^{1}H NMR (60 MHz, $CDCl_3$) δ: 5.36 (s, 2H, $-CH_2$), 6.25 (d, 1H, Pyridinone), 7.41 (s, 5H, Ar), 8.19 (d, 1H, Pyridinone C_6-H), 9.86 (s, 1H, CHO).

Synthesis of Benzyl-Maltol-Carboxylic Acid (MAM)

The synthesis of benzyl-maltol-carboxylic acid, MAM, used a well-documented synthesis.[16] Benzyl-maltol-aldehyde (0.0672 g, 0.292 mmol, 1 eq.) was dissolved in acetone. To a separate beaker, $NaClO_2$ (0.0570 g, 0.632 mmol, 2 eq.) and sulfamic acid (0.0520 g, 0.845 mmol, 3 eq.) were dissolved in water. The $NaClO_2$ and sulfamic acid solution was cooled in an ice bath before it was added dropwise to the benzyl-maltol-aldehyde solution. The reaction proceeded at room temperature with vigorous stirring overnight. The reaction was monitored via TLC (SiO_2, eluent = 50% hexanes and 50% ethyl acetate), which was treated with a DNP stain to show the presence of the aldehyde reactant. The solvent was removed under reduced pressure and the crude product was washed with water. The solution was filtered to collect the product as white crystals (0.0382 g, 0.155 mmol, 53.129% yield). The product was characterized via ^1H NMR (400 MHz, DMSO-d^6) δ: 5.11 (s, 2H, Ar-CH_2), 6.54 (d, 1.H, Pyridinone), 7.33-7.44 (s, 5H, Ar), 8.20 (d, 1H, Pyridinone C_6-H).

Energy Calculations

Structures of Gd-DETA-MAM and Gd-TREN-MAM were built in the modeling software named Avogadro. From here, the XYZ coordinate plane for each atom in the complex was exported from Avogadro and imported into another program named Gabedit. Gabedit was used to open each complex, which had to be corrected since the XYZ coordinate plane doesn’t correctly draw bonds. Once corrected, a rough molecular structure of each complex was calculated using the Amber potential from David E. Condon et al.[17] Fifty to 100 conformers were found for each complex, and the lowest energy conformer was selected to be optimized. The final XYZ coordinate plane is exported from Gabedit, and an input file was created for the complex in which the coordinate plane could be input. Each complex, with or without water/phosphate bound, was run through a calculation that treated the complex as either a gas or as an aqueous compound.

Each complex was refined using NWCHEM and B3LYP-DFT calculations. Each complex was refined with either two waters or two phosphates present. The final COSMO potential calculations, the calculations that consider the complexes in a solvent of water, were unable to finish in time due to how long each calculation takes; the COSMO calculations are expected to take another few weeks. The basis set for each atom was 6-31G except for gadolinium, which had to use a special basis named *Stuttgart RSC 1997 ECP*. The final energies for the complexes can be used to manually calculate the binding affinity of the phosphate groups to the complexes.

Results

The products of each synthesis in this project were characterized after they were purified. Product 1, benzyl-maltol, was purified via washes to yield an orange oil at 99.03% of the predicted yield. Benzyl-Maltol was characterized via ^{1}H NMR (Figure 5).

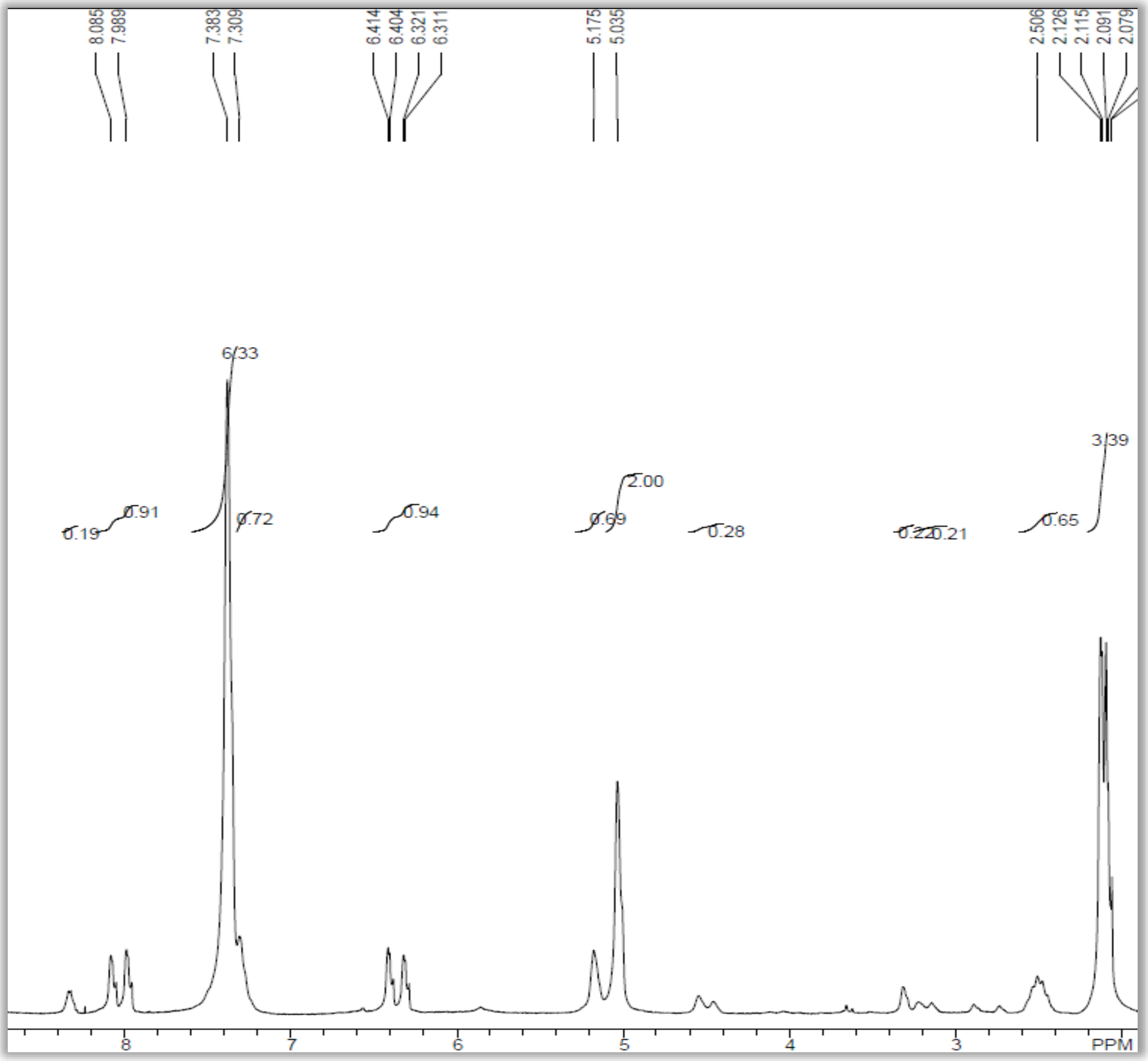


Figure 5. ^{1}H NMR (60 MHz, DMSO-d^6) spectrum of Benzyl-Maltol (1).

In the second synthesis, benzyl-maltol-aldehyde was purified using column chromatography to yield a dark orange oil at 46.3% of the predicted yield. The product was characterized via ^{1}H NMR (Figure 6).

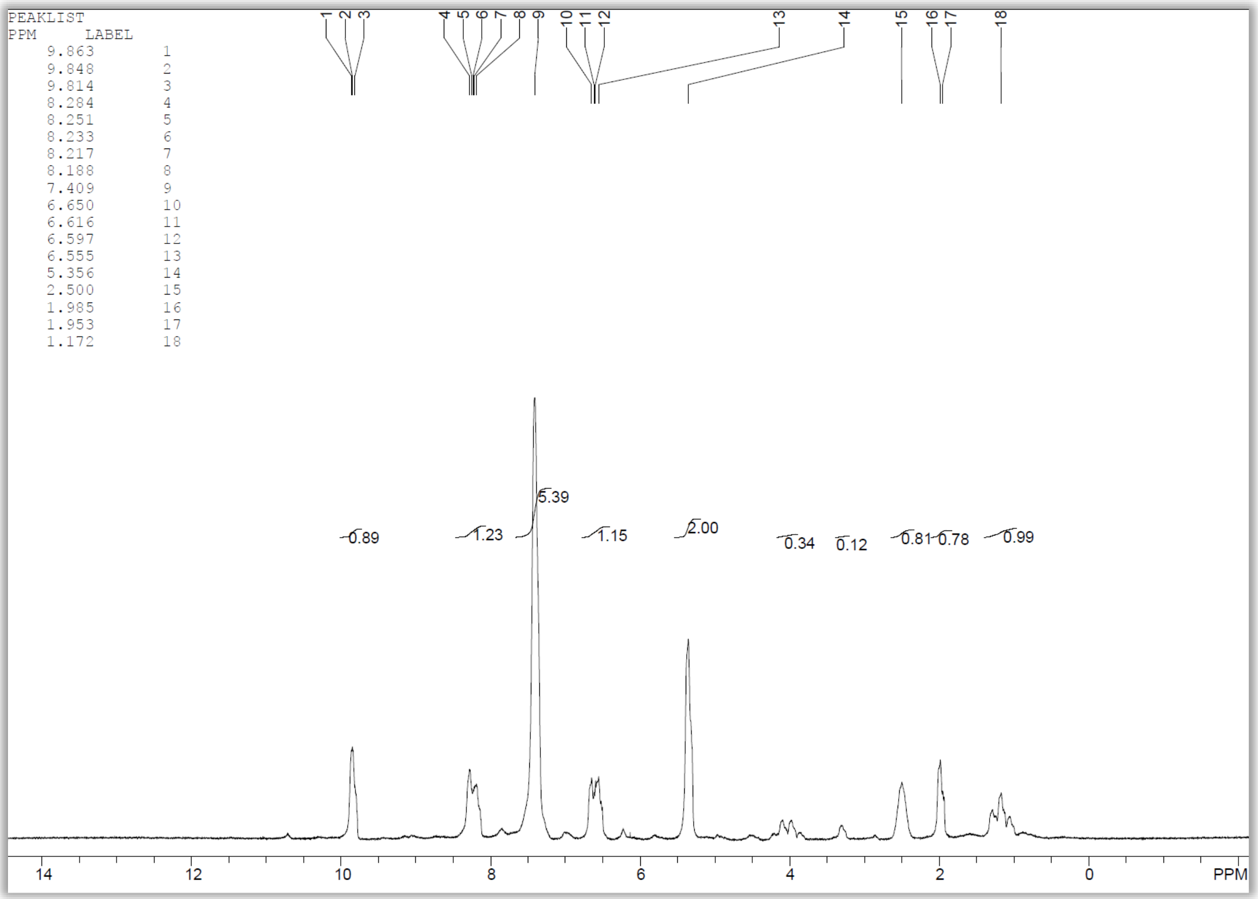


Figure 6. ^{1}H NMR (60 MHz, $CDCl_3$) spectrum of Benzyl-Maltol-Aldehyde (2).

In the third synthesis, benzyl-maltol-carboxylic acid was purified via vacuum filtration to yield white crystals at 47.2% of the predicted yield. The product was characterized at the University of Minnesota - Twin Cities via ^{1}H NMR (Figure 7).

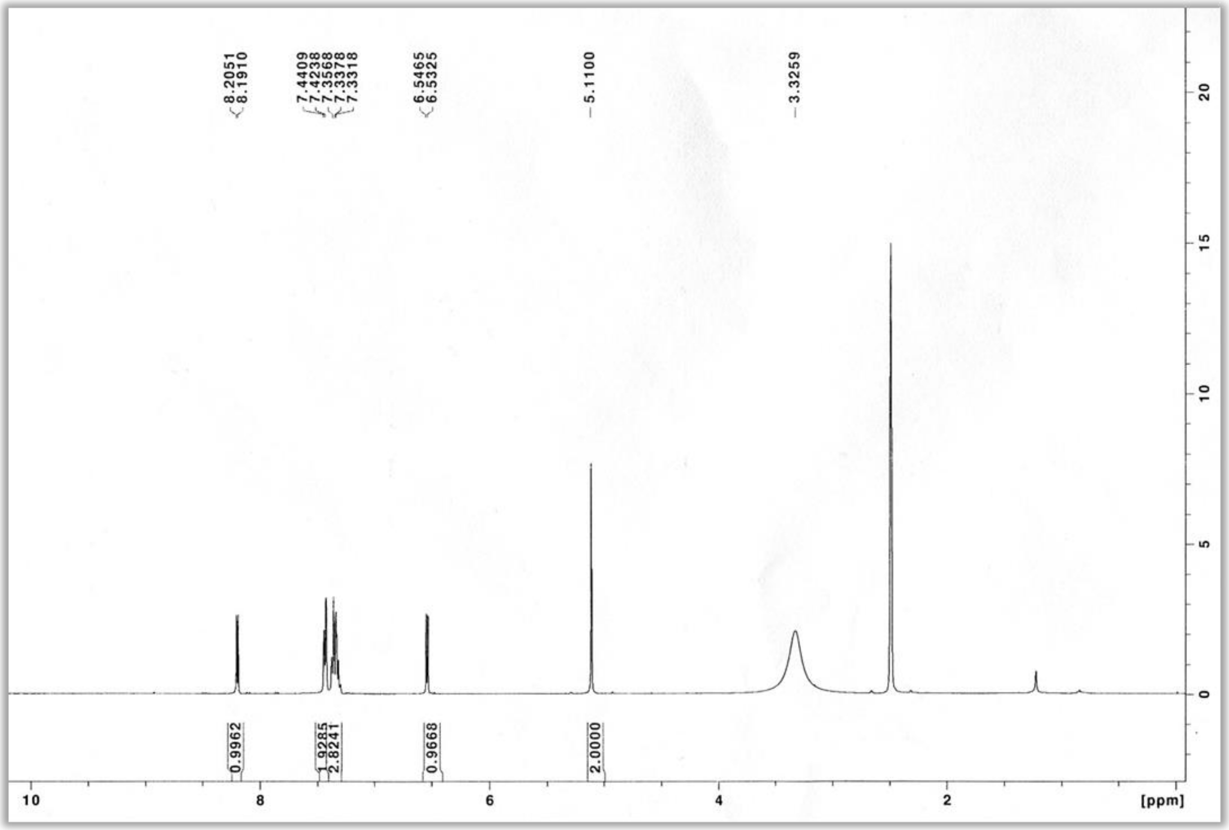
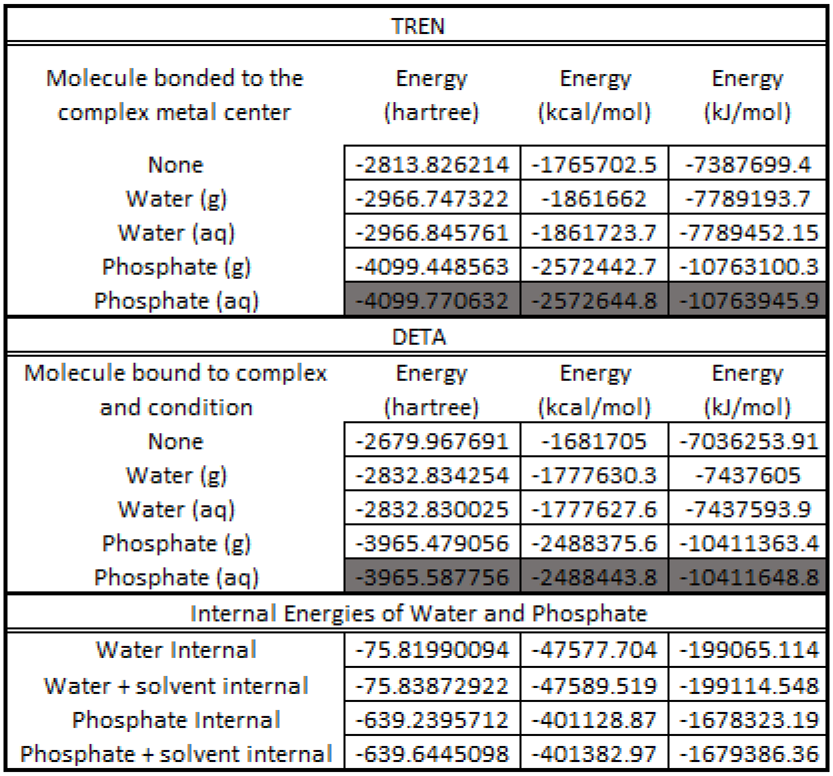


Figure 7. ^{1}H NMR (400 MHz, DMSO-d^{6}) spectrum of Benzyl-Maltol-Carboxylic Acid (3).

The geometry optimization calculations for Gd-TREN-MAM and Gd-DETA-MAM found a stable conformer for each complex bound to either water or phosphate. The calculations for each complex are output in an energy unit called hartrees. This energy value represents the total internal energy of the complete structure. The energies for each complex, water, and phosphate have been tabulated (Table 1). The internal energy of phosphate and water are required to calculate the bonding affinity for phosphate to the complex. Each calculation was performed in either the aqueous or gas phase.



TREN			
Molecule bonded to the complex metal center	Energy (hartree)	Energy (kcal/mol)	Energy (kJ/mol)
None	-2813.826214	-1765702.5	-7387699.4
Water (g)	-2966.747322	-1861662	-7789193.7
Water (aq)	-2966.845761	-1861723.7	-7789452.15
Phosphate (g)	-4099.448563	-2572442.7	-10763100.3
Phosphate (aq)	-4099.770632	-2572644.8	-10763945.9
DETA			
Molecule bound to complex and condition	Energy (hartree)	Energy (kcal/mol)	Energy (kJ/mol)
None	-2679.967691	-1681705	-7036253.91
Water (g)	-2832.834254	-1777630.3	-7437605
Water (aq)	-2832.830025	-1777627.6	-7437593.9
Phosphate (g)	-3965.479056	-2488375.6	-10411363.4
Phosphate (aq)	-3965.587756	-2488443.8	-10411648.8
Internal Energies of Water and Phosphate			
Water Internal	-75.81990094	-47577.704	-199065.114
Water + solvent internal	-75.83872922	-47589.519	-199114.548
Phosphate Internal	-639.2395712	-401128.87	-1678323.19
Phosphate + solvent internal	-639.6445098	-401382.97	-1679386.36

Table 1. Calculated internal energies of Gd-TREN-MAM, Gd-DETA-MAM, water, and phosphate. *Darkened boxes are values that have not finished calculating.*

Discussion

Benzyl-Maltol

Benzyl-maltol was synthesized with a yield of 99.03%, but the ^{1}H NMR shows some impurities. Figure 6 has five peaks at 2.5 ppm, which corresponds to the DMSO-d^6 residual solvent peak, but there are also additional impurity peaks that can be found around 4.4 ppm to 4.5 ppm and a small peak around 7.25. These impurities could be from the benzyl bromide reactant that was used in the reaction. Benzyl bromide has a 5-hydrogen peak at 4.440 ppm and a 2-hydrogen peak at 7.09 ppm to 7.51 ppm.[18] There is also a small peak at 3.3 ppm, which corresponds to water. The water most likely comes from the purification washes. The last impurity on the NMR spectrum at 5.175 ppm, which shows that the product is not 100% pure. Initially, the peak was expected to be dichloromethane, but dichloromethane would show up around 5.76 ppm in a DMSO-d^6 NMR spectrum.[19]

The synthesis of benzyl-maltol has been performed many times in the Peterson research lab, and every synthesis reaction parameters have been fine tuned in attempt to increase product yields. Initially, the synthesis of benzyl-maltol was done at 60˚C to 80˚C for 2 hours with 2 equivalents of benzyl bromide. However, TLC analysis of the reaction flask showed that the reaction was not fully complete, and the benzyl bromide reactant was no longer present. More recent syntheses showed that the yields increased as a result of increasing the equivalents of benzyl bromide to 2.5 while also letting the reaction go for 24 hours. It should also be noted that the presence of a nitrogen atmosphere has been used in the syntheses that have had yields above 90%.

Benzyl-Maltol-Aldehyde

The ^{1}H NMR of benzyl-maltol-aldehyde in figure 7 shows that the product that was isolated with 46.3% yield was close to pure. The additional impurity peaks around 1.3, 2.0, and 4.2 ppm are ethyl acetate that was used as an eluent in the SiO_2 column.[19] However, the peaks for the ethyl acetate are small in comparison to the aldehyde peaks so it can be assumed that the purified product is mainly the desired aldehyde.

The synthesis of benzyl-maltol-aldehyde has consistently provided Peterson research lab between 22% and 28% yield. Initial yields for this reaction were lower than 10%, but it was found that yields could be increased by changing a few reaction parameters. Ramakrishna Raju from the University of Minnesota: Twin Cities suggested to add more SeO_2 in two separate additions to increase yields. Half of the SeO_2 should be added initially to the reaction and the other half should be added an hour later for an increase in yields. These suggestions along with applying an inert atmosphere to the reaction have increased the aldehyde yields to be close to 25%. Changing the reaction setup to using a Dean-Stark apparatus along with grinding the SeO_2 into a fine powder has increased the yield to the 46.3%. It should be noted that literature has shown that these reactions have been performed around 70% yield in only two hours, but the Peterson lab has found the most success in a 24-hour reaction.[15]

Benzyl-Maltol-Carboxylic Acid

The ^{1}H NMR of benzyl-maltol-carboxylic acid contains four signal peaks, which show the presence of acid (MAM). In the spectrum two other peaks are present. The first peak at 2.5 ppm was the DMSO-d^6 solvent peak, and the second peak is at 3.3 ppm. A solvent peak of 3.3 ppm in a DMSO-d^6 NMR spectrum indicates the presence of water.[19] Water in the sample indicated that longer dry times are required. Thus, it is a relatively pure sample. It should also be noted that the benzyl bromide peaks are not present in this ^{1}H NMR spectrum which indicates that the benzyl bromide impurities from the benzyl-maltol-aldehyde reactant were purified out when the solution was filtered.

Ramakrishna Raju suggested that the Peterson lab should use minimal amounts of solvent for acid conversion, and he suggested that the $NaClO_2$ should be swapped for NaOCl to allow for optimal yields. These new reaction procedures have yet to be tested due to an inability to obtain NaOCl in a timely manner. Current reaction parameters have produced a pure product with a 47.2% yield, which is acceptable, but future experiments with NaOCl could be performed to try to improve yields further.

Benzyl-maltol-aldehyde and benzyl-maltol-carboxylic acid yields could possibly be increased more by Bemidji State University students by performing these reactions in rapid succession to reduce the amount of time that a product, albeit crude or pure, is in a form that could break down over time.

Energy Calculations

The energy values from Table 1 were used to calculate the binding affinity for phosphate to the gadolinium complexes by using a balanced chemical equation (equations 1 and 2).

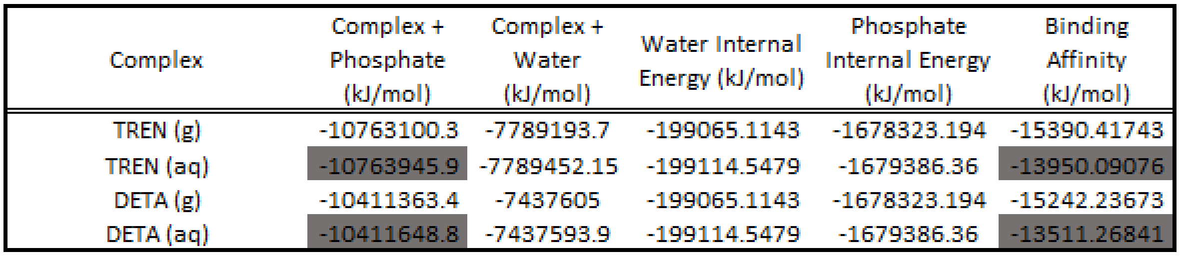
$$Gd\text{-}TREN\text{-}MAM{\cdot}2H_2O + 2HPO_4^{2-} \rightarrow Gd\text{-}TREN\text{-}MAM{\cdot}2HPO_4^{2-} + 2H_2O \qquad \textbf{(equation 1)}$$

$$Gd\text{-}DETA\text{-}MAM{\cdot}2H_2O + 2HPO_4^{2-} \rightarrow Gd\text{-}DETA\text{-}MAM{\cdot}2HPO_4^{2-} + 2H_2O \qquad \textbf{(equation 2)}$$

The binding affinity is calculated from the equations by comparing the energy in the products to the energy in the reactants (equation 3).

$$\sum \Delta H_{products} - \sum \Delta H_{reactants} = Binding\ Affinity$$ **(equation 3)**

The results of calculating the binding affinities for each complex in both the gas and aqueous phase have been tabulated (Table 2). It should be noted that the aqueous phase calculations for the complexes bound to two phosphate molecules have not yet been completed, but the energies in should be relatively close since they were taken from their most recent iteration. The calculations are expected to take at least another month.



Complex	Complex + Phosphate (kJ/mol)	Complex + Water (kJ/mol)	Water Internal Energy (kJ/mol)	Phosphate Internal Energy (kJ/mol)	Binding Affinity (kJ/mol)
TREN (g)	-10763100.3	-7789193.7	-199065.1143	-1678323.194	-15390.41743
TREN (aq)	-10763945.9	-7789452.15	-199114.5479	-1679386.36	-13950.09076
DETA (g)	-10411363.4	-7437605	-199065.1143	-1678323.194	-15242.23673
DETA (aq)	-10411648.8	-7437593.9	-199114.5479	-1679386.36	-13511.26841

Table 2. Energy calculations for the binding affinity of phosphate to Gd-TREN-MAM and Gd-DETA-MAM. *Darkened boxes are values that have not finished calculating.*

The energies that were calculated using equation 3 were found to all be negative values that were all in the order of mega-joules. The negative sign on all these binding affinities conclude that these reactions are exothermic, and they would likely be favorable, spontaneous reactions. The values of the binding affinities were expected to around the order of kilo-joules, but the calculated values were all on the order of mega-joules, which means that these calculations are likely incorrect. To put these values into comparison, the amount of energy given off by 1.00L of isooctane, gasoline, is roughly 33,100kJ, which is enough energy to melt about 218 pounds of ice.[20] Further investigation into the calculations by Dr. Quandt found that the input files for the calculations were using a multiplicity of 2. This is an issue because gadolinium's ground state configuration is [Xe] $4f^7 5d^1 6s^2$ which means there are 8 unpaired electrons. There are 7 unpaired electrons in the f orbital and 1 in the d orbital. The total spin of gadolinium in this state is $8 * \frac{1}{2} = 4$. The final conclusion this makes is that the multiplicity is then $2S + 1 = 2(4) + 1 = 9$. This means that every calculation of both complexes was performed with the incorrect multiplicity, which means that the reported calculations were much higher in energy than expected because they optimized an excited state of gadolinium.

The final energies were retrieved only hours before the final draft of this report, which means that there is no way to recalculate them all for this report, but future students will be able to use the current input files to reperform each calculation. In the end, the incorrect multiplicity is suspected to be the main factor in the high energies, and recalculations should produce more accurate binding affinities.

Conclusion

In conclusion, the first three steps towards the synthesis of Gd-DETA-MAM have been completed. The calculations for these complexes are inconclusive, but if the negative nature of the binding affinities is correct it could be concluded that Gd-DETA-MAM$\cdot$2H_2O would bind two phosphate molecules. These calculations could be completed and peer reviewed relatively quickly by future students. The finalized calculations took roughly 1 week to complete when the computer was running constantly. Also, future students will be able to use the parameters that were found in this set of experiments to synthesize Bn-MAM in less than a month, and then the students can use a coupling agent such as PyBOP to attach a backbone, or addition to the ligand, of their choice. This will allow Bemidji State University to progress in the search to find an optimized ligand that can hold a gadolinium atom while binding phosphate in a strong but reversible manner. Future work will need to be performed on the synthesis of benzyl-maltol-aldehyde since the yields are still low, but further collaboration with the Pierre lab may offer additional assistance as needed. In the end, the identification of a metal complex that can adequately bind phosphate in a strong, reversible manner is a long process, but the work being performed by the Peterson and Pierre labs is helping to solve the problem of eutrophication of lakes that is contributed by fertilizers.

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Glossary

Aldehyde – A chemical functional group that consists of a carbon group that is doubly bound to an oxygen, hydrogen, and carbon-based “R” group. Example: R-CHO.

Amber Protocol – Assisted Model Building with Energy Refinement (AMBER) is a collaboration of programs that is used to find the lowest energy of a molecules structure. The advantage to Amber over NWChem procedures is that Amber is very quick in comparison, but the accuracy is limited. The Amber conformation search gives a good starting point for higher level calculations.

Avogadro – A shareware modeling software that allows users to build molecules and conduct simple force-field optimizations.

Binding affinity – The strength of a molecular interaction.

Bromobenzene – A nonpolar organic solvent used to dissolve chemical reactants.

Brine – Saturated salt water.

B3LYP – An implementation of Density Functional Theory (DFT) that is used to determine the lowest energy structure of a molecule. Advantages of B3LYP include that it works for most molecules and that it is fast, but B3LYP only partially compensates for correlation energy of charges, which is a major issue in computational chemistry.

Carboxylic Acid – A chemical functional group that consists of a carbon group that is doubly bound to an oxygen, alcohol, and carbon-based “R” group. Example: R-COOH.

Column Chromatography – A purification method to separate chemicals in a solution based on their relative polarity.

Conformer – A molecule that has the same chemical composition as another molecule, but a different molecular orientation.

Coupling Agent – A chemical compound that is used in organic synthesis to activate a carboxylic acid and facilitate the formation of a new chemical bond. This is used to couple each molecule with a chemical backbone.

DCM – Dichloromethane; a polar organic solvent used to dissolve chemical reactants.

Dean-Stark apparatus – This is a distilling apparatus that is used in synthetic chemistry to remove water or other biproducts during a reaction.

DETA – A linear compound that is composed of thrice nitrogen atoms separated by two CH_2 groups.

DFT Calculations – Density Functional Theory (DFT) is used to determine the lowest energy of a molecular structure.

DMF – Dimethylformamide; an organic solvent used to dissolve chemical reactants.

DNP – 2,4-Dinitrophenyl – An organic compound that allows aldehydes and other compounds to be identified visually on a TLC plate.

Eluent – A solvent system used to separate compounds in a column or TLC plate.

Eutrophication – Growth of plants and algae in lakes due to excess nutrients.

Gabedit – A freeware program that allows users to build molecules, optimize the structure using force-fields, and perform conformer searches.

Gd-DETA-MAM – Gadolinium-based complex that is proposed to have increased binding affinity for phosphate.

Gd-TREN-MAM – Gadolinium-based complex that is known to bind phosphate.

^{1}H NMR – Proton Nuclear Magnetic Resonance; a method of analyzing the structure and atomic connectivity in organic compounds, such as the products in the synthesis of MAM.

Hexane – a nonpolar organic solvent.

Ligand – A molecule that binds metal ions through coordinating bonds.

Maltol – An organic food-grade sweetener.

MAM – Benzyl-Maltol-Carboxylic Acid in this project. Technically this compound is a modified version of MAM that has it's -OH (alcohol) group protected by a non-reactive "benzyl" (cyclic carbon ring) group.

Microcystin – A toxin that can be caused by excess amounts of algae in a lake.

NMR – An instrument that uses nuclear resonance to detect certain nuclei in a molecule.

Phenol – A benzene (6-membered carbon ring) with an -OH (alcohol) group.

PyBOP – A coupling agent that is used commonly in organic synthesis.

SciFinder – A chemical website that acts as a large database of chemical syntheses and is searchable by chemical structure.

SiO_2 – Silica dioxide is a type of medium for TLC plates and purification columns. The polarity of SiO_2 allows for separation of compounds based on their relative polarity.

Steric hinderance – Interruption or decrease of chemical processes that are caused by a crowded molecular structure.

Struvite – ($NH_4MgPO4\cdot 6H_2O$) – A common commercial fertilizer.

Stuttgart RSC 1997 ECP – A series of mathematical functions used to model electrons in atoms or molecules. This specific set of functions uses relativistic corrections for inner shell electrions which is useful for computational chemistry involving large atoms.

Sulfamic Acid **–** An organic compound that is used as an acid in organic synthesis. The chemical formula of sulfamic acid is H_3NSO_3.

TLC – Thin layer chromatography; a method of analysis that separates compounds in a solution based on their relative polarity. Normally TLC is used to view components of a reaction mixture.

TREN – A 3-dimensional compound that is composed of four nitrogen atoms separated by three CH_2 groups. One of the nitrogen groups is surrounded by the other three "arms" of the molecule.

6-31G – A series of mathematical functions used to model electrons in atoms or molecules. This set adds extra functions to model the outer shell electrons which are most important in determining the chemistry of an atom or molecule.