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The Response of a Biocompatible Liquid Crystal to Ions and Chemistry on Nanostructured Surfaces

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APPROVED

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Abstract:

Traditional lyotropic liquid crystals are composed of amphiphilic molecules forming assemblies in water. Disodium cromoglycate (cromolyn or DSCG) – an antiasthmatic drug – is a novel and unusual lyotropic liquid crystal because it is not amphiphilic, and yet, it exhibits large birefringence (shininess) when dissolved in water forming lyotropic liquid crystal. In the work, DSCG liquid crystal is doped with different types of salt such as sodium chloride and sodium perchlorate, and the response in the changes of birefringence and liquid crystal transition temperature is studied. We find that addition of certain type of salts enhance the propensity of formation of liquid crystal phase of DSCG, whereas other type inhibit the formation of liquid crystal. This discovery is pleasantly perplexing because it contradicts the general observation that addition of salt often disrupts the tendency of structure formation – for example, spreading salt in the winter time to help melt the ice on the roadway. In another effort to control the structural organization of the molecules within this liquid crystal phase – so-called liquid crystal orientation, I synthesized oligo-ethylene glycol (OEG)-terminated alkanethiols and overlay them to form self-assembled monolayers (SAM) on a nanostructured gold film. We use this unique combination of chemistry and surface nanotopography to control the liquid crystal orientation. The hypothesis, promising results and interpretation will be presented. Because of DSCG is an antiasthmatic drug and has been shown not to denature protein folding at the concentrations that give rise to liquid crystal phases, this work imparts both fundamental understanding of a novel liquid crystal and explore application of detecting presence of toxic ions and protein binding events.

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Preface

During my four years at Syracuse University, I have contradicted myself numerous times with decisions I have made regarding my academic career. First off, I never imagined I will spend my last semester at Syracuse University writing my Senior Thesis. The idea of a thesis was never appealing to me. All my past encounters with thesis and honors program were not too pleasant. To me, a thesis involves a lot of determination, hard work, and frustration of the individual who is writing one and extremely time consuming. But with all that said and my thesis done, my view of it still remains the same, but I can proudly add on it is definitely worthwhile and rewarding.

There were many things I have done and accomplished during my stay here that I never dreamt of. One of them was joining a research group and the other – writing the thesis. Literally, each time an opportunity was presented to me, I ran the other way. Why? Simple. I was lazy and didn't want to spend long hours researching. But in the end, I have contradicted myself and look at where I am now. I must say I am very fortunate to join Professor Luk's lab in the spring semester of my junior year; join the Honors Thesis Program the beginning of my senior year; and being able to complete this thesis.

As a science major, I definitely encourage all fellow science majors to take the time to join a research group whether at Syracuse University or SUNY Upstate. It may be time consuming, but you can always work something out with your research advisor. From my experience, I learned much more hands on experience than I would from my introductory lab courses and enjoyed the idea of

flexible lab hours, where I can work at my own pace without having the worry of completing my tasks in a limited amount of time. In addition, being part of the research lab, I gave more thought process in what I was doing and had the opportunity to be creative at the same time. I also encourage those who do research to write a thesis. It is almost the equivalent of a lab report in Organic Chemistry lab or Biochemistry Lab. But with the Senior Thesis, there is much more content involved, everything that is being put into this "lab report" requires more thought and consideration. It's challenging at times because of the language style that I need to write it so I can properly communicate to the reader. Nonetheless, it is a great achievement and wonderful experiences have gained from my research and writing this thesis.

I hope for those in doubt about research and/or a thesis, go give it a try! Because you'll never know until you try like me. Plus, it's never too late!

Advice for Future Honors Students:

Always start early!!! It's never too early to start writing or even compiling data for your research. Keep a weekly, monthly, or even semester summary of what you have done. Present them in an informal lab report. When I was doing research, I had to submit a lab report of what I had done as an independent research credit. I thought it was the most tedious thing to do, another lab report? But in the end, when I was writing my thesis, those lab reports came in extremely handy! Also, it's hard to convert your work into the science language.

Try to get them done before Spring break or sometimes right after. Because when April is around the corner, the sun is out, and all you want to do is go out and play! Plus, our advisors and second reader are busy people too! They need time to read them!

Good luck to all of you!

Acknowledgments:

First and foremost, I want to thank my research advisor and mentor Professor Yan-Yeung Luk. I remembered when I first emailed him about research opportunities, he responded me right away and offered a position in his lab after learning my background with research which I acquired previously in general chemistry laboratory and organic chemistry laboratory. Basically, I went in there with very limited knowledge of organic synthesis and he was willing to help me learn and accumulate more of such skills. Professor Luk is absolutely an amazing person to work with. He's very kind, caring, and always manage to find time to fit me in his busy schedule to find out how things are going with the research and how I am doing in general outside the lab. Not only that, but he responds emails quickly and will always listen to your ideas. He shares his experiences with me and provides many opportunities for me outside the lab which he thinks will be beneficial in the long run of my future career. Not only that, but Professor Luk always encouraged everybody to ask questions to help us learn. In addition to Professor Luk, I have to thank everybody in his research group during my stay, especially the graduate students: Erik Burton, Preeti Sejwal, and Karen Simon. They were all very patient with me especially with the simple calculations for the experiments, which I often have difficulty with. They answered my questions regarding applications and procedures I did not understand.

Besides my research advisor, I must also thank my academic advisor Dr. James Dabrowiak. He was always there for me, kept me back on track of things, and even introduced Professor Luk to me. Also, I thank him for taking time off his busy schedule to become my second reader for this thesis and putting up with me. He was always the one who would lecture me, constantly questioning what I plan to do with my life, and encourage me to give research a try. I learned a lot from him inside the classroom and a lot about writing a good lab report.

Finally, I have to thank Dr. Belote and Dr. Wolfe who let me participate in BIO 419 even though I decided to write my thesis at the beginning of my senior year.

Thank you all and everybody who helped me reach this point, without you guys, I don't think I can reach this far.

Chapter 1: Detection of Toxic Ions through Lyotropic Liquid Crystal

1.1 Introduction:

Liquid crystal is a unique class of substance which exhibits a phase of matter that has both the properties of both a liquid and a solid. It flows like a liquid but its molecules are arranged in a crystal-like way. Liquid crystals can also be viewed as phases between isotropic liquid and crystals, which exhibit both the fluidic property of an isotropic liquid and the optical properties of a crystal. There are many types of liquid crystal and they can be easily distinguished based on birefringence – optical properties – under a microscope or under polarized light. The distinct texture the liquid crystal possesses corresponds to the direction in which the molecules are oriented.

There are two types of liquid crystals: thermotropic and lyotropic liquid crystals. Thermotropic liquid crystals are crystals which orient based on temperature in phase transition. Lyotropic liquid crystals (LLCs) are liquid crystals which orient based on the concentration of the solute. They have been separated into three sub-groups, which exhibit the following mesophases: amphiphilic, chromonic, and polymeric mesophases.[1] Lyotropic chromonic liquid crystals (LCLCs) have an unusual type of mesomorphism.[2] Chromonic refers to a "lyotropic mesophase formed by soluble aromatic mesogens." The aromatic mesogens are isotropic and rigid in chemical structures and have high hydrophilic residues.[1]

Lyotropic liquid crystals exhibit different phase transitions based on the concentration of the solution in which they are placed. In fact, LLCs have a more significant role than thermotropic liquid crystals. Lyotropic liquid crystals are found to be composed of amphiphilic molecules. Amphiphilic compounds are also known as surfactants – surface active agents.[3] Amphiphilic compounds are encountered in our daily lives. For example, the 'goo' that collects on the bottom of our soap dish in the kitchen or bathroom is an example of LCC; the 'goo' is a mixture of soap and water. In terms of biological applications, LCC is present within our bodies as well. The cell membrane in our body has its own liquid crystal nature due to the phospholipids and water mixture.

Disodium cromoglycate (cromolyn or DSCG) is an antiasthmatic drug (widely known as Intal) which exhibits liquid crystal properties. It is a novel and unusual LLC due to the fact it is not amphiphilic and yet exhibits a large birefringence. This contradicts the normal state of LLC where it is amphiphilic compounds. Addition of certain salts such as sodium chloride and potassium bromide enhance the formation of the liquid crystal phase of DSCG, while others inhibit the formation of the liquid crystal phase.

In the following experiments, different types of salt additives of various concentrations will be added into a fixed concentration of 10 wt% DSCG with varying amounts of water, to maintain a total weight of 0.750 g. This will allow us to observe the transition phase temperatures. A special liquid glass holder was fabricated for this particular experiment. The purpose of the experiments is to find if certain salt additives such as sodium chloride and sodium perchlorate will

enhance, inhibit or have no effect on the transition phase temperature of DSCG; and if the crystal structures of such salts are similar when they interact with DSCG.

1.2 Experimental Section

Materials:

Cromolyn sodium salt, lithium chloride (99+% purity), potassium chloride, and potassium nitrate (99.999% purity) were purchased from Aldrich Chemicals (Milwaukee, WI). Sodium phosphate and sodium chloride were purchased from Fisher Scientific (Pittsburg, PA). Lithium sulfate (99% purity), potassium bromide reagent, tetrabutylammonium fluoride (98+% purity), and sodium sulfate (granular), sodium perchlorate (98% purity), and acetone were purchased from Acros Organics (Suwanee, GA). All samples were prepared using deionied water having a resistivity of 18MΩ cm (Milli-Q^{plus} Millipore, Bedford, MA). A dual-channel thermometer with offsets and traceable wires was purchased from Fisherbrand (Pittsburg, PA).

DSCG Holder:

A special liquid crystal holder was fabricated after learning that the slide sandwich method was not sufficient to detect temperature changes throughout the experiment. A diamond or tear drop glass holder was created from the glass shop at Syracuse University. The narrow neck allowed the insertion of a temperature

measuring device into the holder to measure the transition temperature of the liquid crystal sample inside the hollow well of the holder. This prevented the sample from leaking out of the holder. A Dual-Channel thermometer with offsets (Range -50º to +1300º/ -58º to +1999ºF) purchased from FisherScientific was used to monitor the change in temperature.

Figure 1: A fabricated tear-shaped glass holder in lab. The narrow neck allows the temperature probe to be inserted and prevention of sample from leaking out. It is wide enough to allow the insertion of the sample into the deeper part of the glass holder.

Inserting Sample/Cleaning Glass Holder:

A sterile disposable pipette was used to transfer the sample into the fabricated glass holder. The probe from the temperature reader was inserted into the narrow neck. Parafilm was used to wrap around the probe and narrow neck to prevent leaking. After observations under the microscope, the sterile disposable pipette was used to retrieve as much as of the sample as possible. When done, the glass was washed with water, rinsed with acetone, and dried with a stream of N_2 gas. This washing procedure was repeated at least three times to make sure all the content inside the glass holder is out and thoroughly clean. A stream of N_2 was used to dry it and was left in the incubator to dry completely.

DSCG Sample:

Samples of DSCG and salt addictive were prepared through the following table:

Table 1: DSCG and Desire Salt Preparation table.

Targeted DSCG		Targeted Salt		Targeted Water (g)	Targeted Total Weight (g)
wt%	Grams	Wt%	Grams		
10 wt %	0.0750	0 wt %	0.0000	0.6750	0.7500
10 wt %	0.0750	1 wt %	0.0075	0.6675	0.7500
10 wt %	0.0750	3 wt %	0.0225	0.6525	0.7500
10 wt %	0.0750	5 wt %	0.0375	0.6375	0.7500
10 wt %	0.0750	7 wt %	0.0525	0.6225	0.7500
10 wt %	0.0750	9 wt %	0.0675	0.6075	0.7500
10 wt %	0.0750	11 wt %	0.0825	0.5925	0.7500
10 wt %	0.0750	12 wt %	0.0900	0.5850	0.7500
10 wt %	0.0750	13 wt %	0.0975	0.5775	0.7500

Cromolyn and various salt samples were usually prepared at 1 wt% and 3 wt% to test whether or not that particular salt concentration would allow liquid crystal formation. If liquid crystal formation was allowed, the salt concentration was increased to the next higher level. If no crystal formation occurred, that particular salt was terminated to prevent wasting the expensive DSCG compound.

Once the sample is prepared in a vial and parafilmed to prevent evaporation, the vial is left alone for several hours in order to allow DSCG to completely dissolve in the solution. Once DSCG is completely dissolved, a clean pipette or syringe is used to inject a portion of the sample into the liquid crystal holder. Parafilm is used to seal the opening of the holder to prevent leaking of the sample before inserting the thermometer device in. The sample is placed under the polarizing microscope and the transition phase observed under various magnifications of the microscope. If needed, ice water and a heat gun are used to

decrease or increase the temperature of the liquid crystal sample. This helps to control the temperature at which the phase transition occurs.

1.3 Results:

DSCG Result and Transition Temperature Range

Table 2. Cromolyn (DSCG) and Sodium Chloride (NaCl)

DSCG		NaCl		Water (g)	Total Weight (g)	Transition Temperature (˚C)	Description of solution
Wt %	Grams	Wt %	Grams				
DSCG and NaCl Liquid Crystal Formation							
10.0	0.0755	0.0	0.000	0.6768	0.7523	21.1-23.2	Clear
10.0	0.0755	1.0	0.0077	0.6723	0.7555	24.9-27.7	Cloudiness with no precipitate
10.0	0.0756	3.0	0.0234	0.6532	0.7522	31.4-34.3	Cloudiness with no precipitate
DSCG and NaCl that did not form Liquid Crystal							
10.0	0.0754	5.0	0.0380	0.6409	0.7543	-	Clear. White precipitates on the bottom of vial
10.0	0.0754	7.2	0.0544	0.6252	0.7550	-	Clear. White precipitates on the bottom of vial
10.0	0.0756	9.1	0.0678	0.6079	0.7522	-	Clear. White precipitates on the bottom of vial
10.0	0.0760	11.0	0.0833	0.5941	0.7534	-	Clear. White precipitates on the bottom of vial
9.9	0.0754	11.9	0.0906	0.5928	0.7588	-	Clear. White precipitates on the bottom of vial
10.0	0.0757	12.9	0.0977	0.5822	0.7556	-	Clear. White precipitates on the bottom of vial

Table 3: Cromolyn (DSCG) and Sodium perchlorate ($NaClO_4$):

DSCG		$NaClO_4$		Water (g)	Total Weight (g)	Transition Temperature (˚C)	Description of solution
wt%	Grams	Wt%	Grams				
10.0	0.0754	1.0	0.0080	0.6684	0.7518	24.3 – 27.2	Clear
10.0	0.0755	3.0	0.0227	0.6546	0.7528	27.4 – 31.3	Tint of cloudiness
10.0	0.0752	5.0	0.0376	0.6394	0.7520	29.1 – 33.9	Tint of cloudiness. Thick
10.0	0.0753	7.0	0.0528	0.6235	0.7516	-	Precipitation. Very little solution present.

Table 4: Cromolyn (DSCG) and Tetrabutylammonium fluoride (TBAF):

DSCG		TBAF		Water (g)	Total Weight (g)	Transition Temperature (˚C)	Description of solution
wt%	Grams	Wt%	Grams				
DSCG and TBAF Liquid Crystal Formation							
10.0	0.0753	0.0	0.0000	0.6753	0.7506	19.2 - 22.6	Clear
10.0	0.0758	1.0	0.0078	0.6694	0.7530	15.5 - 20.9	Clear. Small amount of white powder on bottom of vial.
DSCG and TBAF that did not form Liquid Crystal							
10.0	0.0756	3.05	0.0231	0.6579	0.7566	-	Clear with TBAF floating on top.
10.0	0.0753	5.1	0.0386	0.6395	0.7534	-	Clear with TBAF floating on top.
10.0	0.0755	7.0	0.0528	0.6266	0.7549	-	Clear with TBAF floating on top.

Table 5: Cromolyn (DSCG) and Sodium Phosphate (NaH_2PO_4):

DSCG		NaH_2PO_4		Water (g)	Total Weight (g)	Transition Temperature (˚C)	Description of solution
wt%	Grams	Wt%	grams				
10.0	0.0756	1.0	0.0076	0.6706	0.7538	22.7 – 25.4	Clear with few visible particles floating.
10.0	0.0753	3.0	0.0230	0.6587	0.7569	25.9 – 29.2	Clear. Little cloudiness.

Table 6: Cromolyn (DSCG) and Lithium Chloride (LiCl):

DSCG		LiCl		Water (g)	Total Weight (g)	Transition Temperature (˚C)	Description of solution
wt%	Grams	Wt%	grams				
10.0	0.0753	1.0	0.0076	0.6690	0.7519	-	Not soluble. Two distinct layers visible
9.9	0.0751	3.0	0.0228	0.6601	0.7580	-	No solution. Uniform white solid layer.
10.0	0.0752	5.0	0.0376	0.6383	0.7511	-	No solution. White solid.

Table 7: Cromolyn (DSCG) and Lithium Sulfate ($LiSO_4$):

DSCG		$LiSO_4$		Water (g)	Total Weight (g)	Transition Temperature (˚C)	Description of solution
wt%	Grams	Wt%	grams				
10.1	0.0755	0.0	0.0000	0.6750	0.7502	17.1 – 22.0	Clear
10.0	0.0753	1.0	0.0077	0.6703	0.7533	21.5 – 23.9	Clear and tiny tints of gel like solution
10.0	0.0753	3.0	0.0226	0.6532	0.7511	-	Cloudy. Not soluble.
10.0	0.0755	5.3	0.0399	0.6366	0.7520	-	Cloudy. Not soluble.
9.9	0.0754	7.0	0.0525	0.6256	0.7534	-	Cloudy. Not soluble.
10.0	0.0758	9.1	0.0686	0.6083	0.7527	-	Cloudy. Not soluble.

Table 8: Cromolyn (DSCG) and Potassium Chloride (KCl)

DSCG		KCl		Water (g)	Total Weight (g)	Transition Temperature (˚C)	Description of solution
wt%	Grams	Wt%	grams				
10.0	0.0748	1.0	0.0072	0.6682	0.7517	23.1 – 24.9	Clear
10.0	0.0758	3.0	0.0231	0.6537	0.7546	-	Little precipitates.

Table 9: Cromolyn (DSCG) and Potassium Bromide (KBr):

DSCG		KBr		Water (g)	Total Weight (g)	Transition Temperature (˚C)	Description of solution
wt%	Grams	Wt%	grams				
10.0	0.0753	1.0	0.0079	0.6691	0.7523	15.4 - 18.1	Clear
10.0	0.0752	3.0	0.0227	0.6537	0.7516	25.5 – 29.3	Clear

Pictures based on Similar Temperature Range:

Sodium Chloride vs. Sodium perchlorate

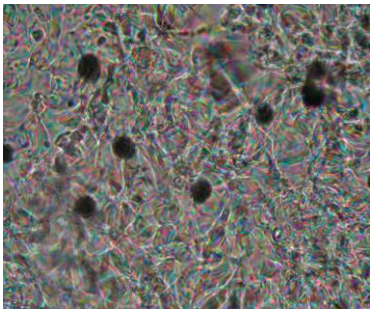
(a)  (b) 

Figure 2: (a) 1wt%NaCl taken at 22.3°C. (b) 1wt%$NaClO_4$ taken at 22.3°C. Both solutions were taken under 10x magnifications at the same temperature. The only difference between these two chemicals is the chloride ion and the perchlorate ion.

Sodium Chloride vs. Sodium Phosphate

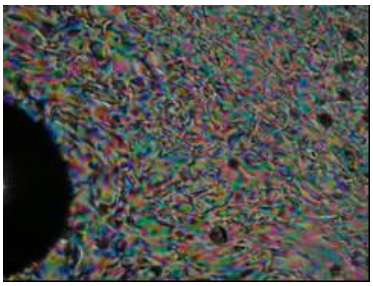
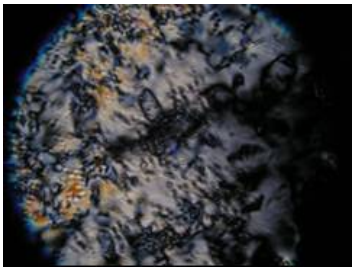
(a)  (b) 

Figure 3: (a) 1wt%NaCl taken at 24.2°C. (b) 1wt% NaH_2PO_4 taken at 24.3°C. Pictures of the two samples were taken under the temperature listed above at different days. The difference between the two is the anion.

Sodium Chloride vs. Potassium Chloride

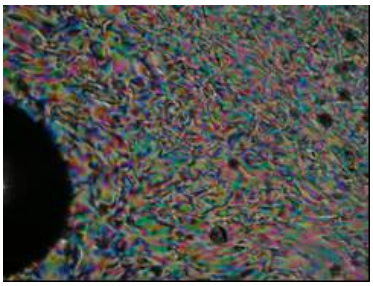
(a)  (b) 

Figure 4: (a) 1wt%NaCl taken at 24.2°C. (b) 1wt%KCl taken at 23.1°C. Pictures of the two samples were taken under 10X magnification.. The difference between these two chemicals is the anion. The pictures display drastic changes in ion crystal formation.

Pictures of Liquid Crystal Formation at Room Temperature

Sodium Chloride vs. Sodium Bromide

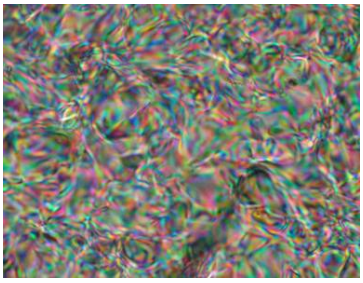
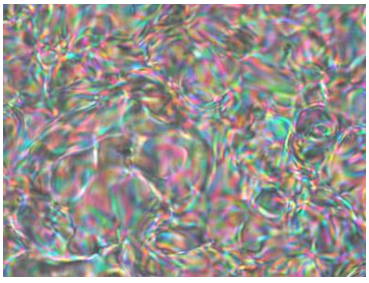
(a)  (b) 

Figure 5: (a) 1 wt % NaCl. (b) 1 wt % NaBr. Both are taken at the room temperature: 23.0ºC 15 minutes after the insertion of the sample into the liquid crystal holder glasses under 20X magnification. NaBr picture is adjusted +55 brightness and +35 contast through the aid of Adobe Photoshop.

Postassium Bromide vs. Sodium Bromide

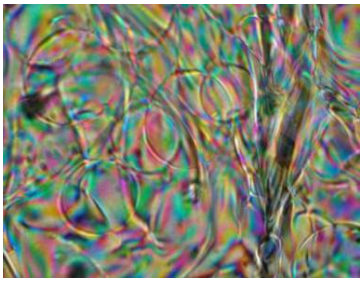
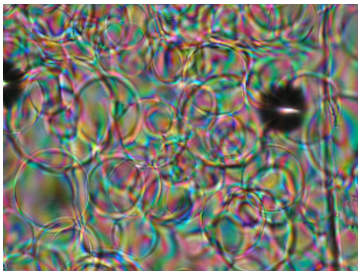
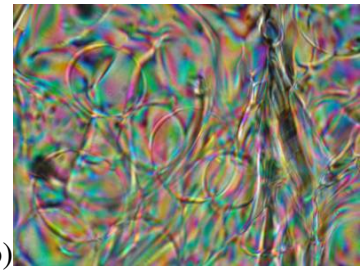
(a)  (b) 

Figure 6: (a) 1 wt % KBr. (b) 1 wt % NaBr. Both pictures were taken at room temperature 22.7ºC 15 minutes insertion of samples into liquid crystal holder glasses under 20X magnifications.

Potassium Chloride and Potassium Bromide

(a)  (b) 

KCl 1 wt % DSCG 9.9 wt % KBr 1 wt% DSCG 9.9 wt %

Figure 7: (a) 1 wt % KCl. (b) 1 wt% KBr. Both pictures were taken at room temperature 23.3ºC 15 minutes after insertion of samples into the liquid crystal glass holder under 20X magnification.

Potassium Sulfate vs. Sodium Sulfate

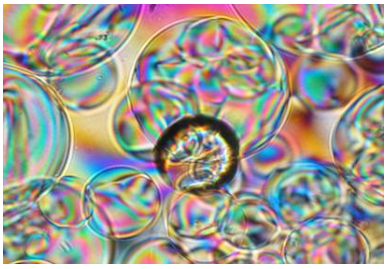
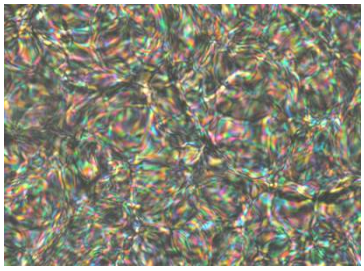
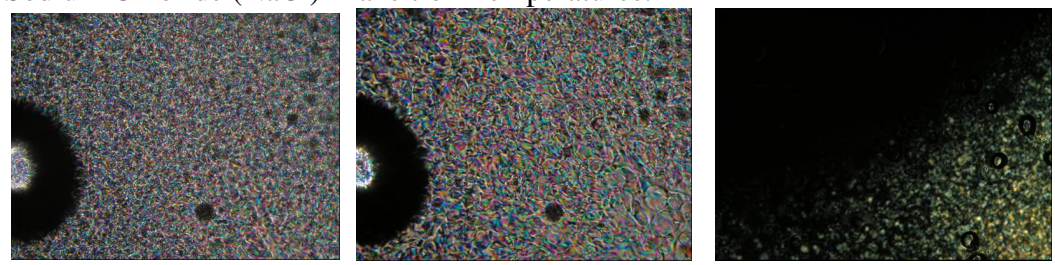
(a)  (b) 

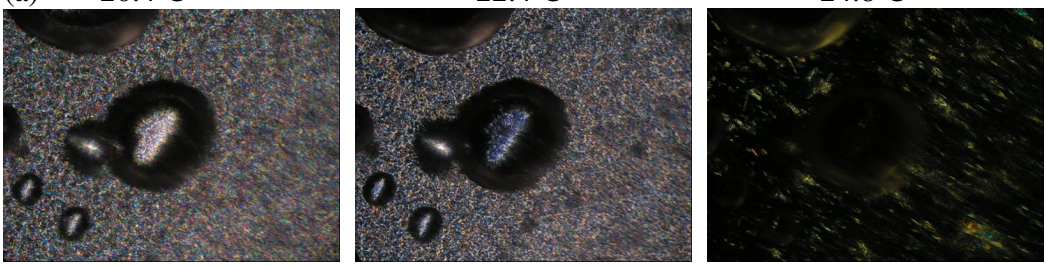
Figure 8: (a) 1.05 wt % K_2SO_4. (b) 1.05 wt % Na_2SO_4. Both pictures were taken at room temperature 24.5ºC 15 minutes after insertion of samples into the liquid crystal glass holder under 20X magnification.

Pictures of Salt though Transition Temperature:

Sodium Chloride (NaCl) Transition Temperatures:



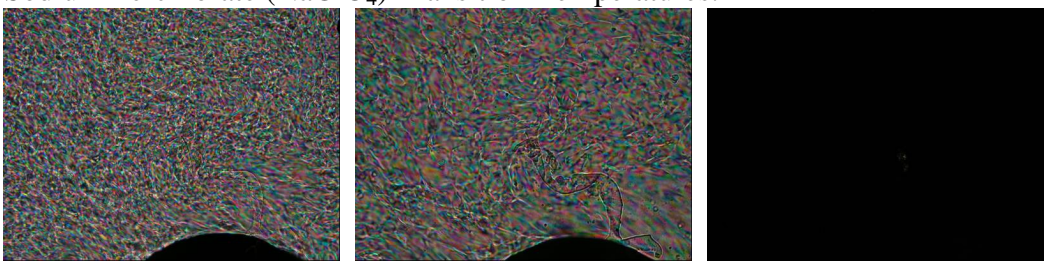
(a) 20.4ºC 22.4ºC 24.8ºC



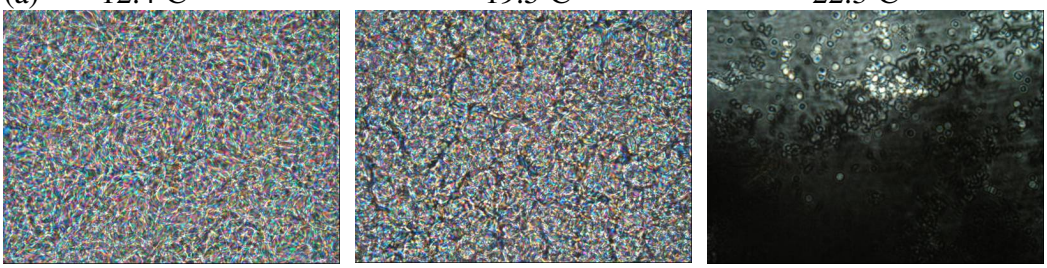
(b) 24.3ºC 29.7ºC 32.7ºC

Figure 9: (a) 1 wt % NaCl in 10 wt % DSCG solution. (b) 3 wt % NaCl in 10 wt % DSCG solution. In both samples, liquid crystal formation is visible at low temperature, but becomes isotropic at a higher temperature.

Sodium Perchlorate ($NaClO_4$) Transition Temperatures:



(a) 12.4ºC 19.5ºC 22.3ºC



(b) 25.8ºC 29.0ºC 31.2ºC

Figure 10: (a) 1 wt % NaClO4 in 10 wt % DSCG solution. (b) 3 wt % $NaClO_4$ in 10 wt % DSCG solution. In both samples, liquid crystal formation is visible at low temperature, but becomes isotropic at higher temperatures.

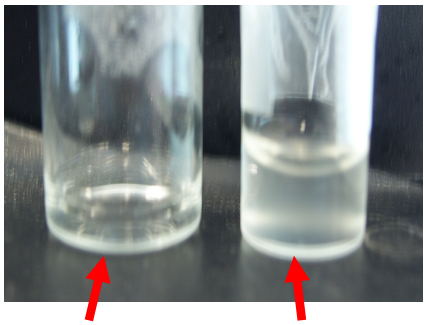


Figure 11: Vial on left is clear solution which is isotropic under microscope. Vial on the right has a cloudy solution, when placed under microscope, liquid crystals can be observed.

1.4 Discussion:

For most of the salt additives, weight concentrations higher than 1 wt % were not able to be observed under the polarizable microscope due to precipitation. From this observed trend, samples up to 3 wt % were usually prepared at the initial step before continuing with the preparation at higher weight percent in order to be more efficient and conservative of the expensive compound DSCG.

Some salt additives such as NaCl and $NaClO_4$ were found to be close in transition temperature. Based on this observation, it can be assumed that the two salts have a great probability to display similar liquid crystal formation in texture, size, and/or shape. However, this assumption was proven to be false. Although these two chemical compounds have the same cation but different anion, the pictures taken (Figure 2) clearly indicate vast differences between the two salts at

1 wt % concentration. There is no similarity of their structure based on the common ion the two salts have.

Sodium phosphate, compared to other sodium compounds, has a much more defined structure and more noticeable color difference in terms of crystal formation. Potassium bromide and potassium chloride are other cases in which the results were dramatic, and no similarity seems to be possessed by the two (Figure 7). Potassium bromide has a transition temperature that is significantly higher than KCl. Potassium chloride is in isotropic form at room temperature as indicated in Figure 7. Different cations were also considered. In NaCl and KCl, there is a noticeable change in both the color and the texture of the liquid crystal formation (Figure 4). Sodium chloride produces a sharper and a greater variety of colors compared to KCl, which is already in the isotropic stage in a similar temperature range.

In terms of transition temperature, with each salt at a different concentration (i.e. 1 wt %, 3 wt %, and 5 wt %) relative to the fixed amount of DSCG concentration (10 wt %) sample, it is found that liquid crystal formation occurs at a relatively lower temperature range in a positive correlated ion with lowered salt concentration (i.e. 1 wt %). Liquid crystal formation occurs at a higher temperature as the combination increases. For example, NaCl (Figure 9), at 1 wt %, becomes isotropic at around 24.8ºC and under 3 wt % it becomes isotropic at 32.7ºC. The same trend was observed for $NaClO_4$ (Figure 10). Higher concentrations were not observed due to formation of precipitates (Table

3). The same trend was observed for other salts such as KBr and NaH_2PO_4 as well.

All of the samples were prepared in a clear and transparent vial. After preparation, the vial was often left to stand for one day to allow DSCG and salt to completely dissolve in water. Upon the addition of the water to the DSCG and salt, the solution is clear and transparent, and maintains water-like properties in terms of fluidity. After the salt and DSCG dissolve in the water, the clear solution changes in texture, it is less fluid and becomes more of a gel-like solution. Precipitation and cloudiness may develop. A correlation can be made that when cloudiness occurs in the solution; liquid crystals are likely to occur for that particular concentration of salt. Under solely 10 wt % of DSCG and no added salt, the solution is clear and transparent indicating there is no liquid crystal at that solution composition (Figure 11). This phenomenon shows the lack of polarization under a microscope indicating the absence of a liquid crystal phase.

Many methods were also used to observe the DSCG liquid crystal formation phenomenon in the presence of various salt types. One of the methods involved many layers of scotch tape on top of a microscope slide. Other types of tape were also used such as duct tape and masking tape. Another factor considered was the different amount of layers applied on the first ply of tape on top of the microscope slide. After sufficient layers of tape, a hole-puncher was used to create several holes before mounting the pile of tape on top of a microscope slide. Small portion of various DSCG and salt solution combination was placed into each of the hole-punched region. Another microscope slide was

placed onto all the layers of tape using binder clips to hold the slides together tightly. However, this method was ineffective due to the air bubbles formed for each additional layer of tape applied onto the previous layer. In addition, the liquid sample would soak into the scotch tape. Another method used to replace the tape was to create our own microscope slides with holes already carved out. This also failed due to the difficult process needed to create them, since the thin microscope slides are very sensitive when placed under extreme heat environment.

1.5 Conclusion:

Each salt exhibits its own effect on liquid crystal formation, and independent of the different cation or anion it contains. In some cases, the different salts may have similar transition temperatures, but this does not indicate correlation between the transition temperature and the crystal structure. The concentration of salt is found to play an important role in terms of liquid crystal formation as shown with 3 wt % $NaClO_4$, in which higher concentration intensifies liquid crystal formation. Low salt concentrations such as 1 wt % $NaClO_4$ inhibit liquid crystal formation. The naked eye can also be used to detect whether or not liquid crystal formation has occurred. If DSCG liquid crystal formation is allowed, the clear and transparent solution in the vial will become cloudy and exhibit gel-like liquid more than a smooth, clear, and transparent liquid it was originally was.

The measure of birefringence of the liquid crystal can readily differentiate the types of ions present in the water and DSCG. For example, $NaClO_4$ can be detected if it is present in water. This will be very helpful since $NaClO_4$ is used as pesticides and found to be harmful to pregnant women if consumed in large amounts. This approach can be used to detect toxic ions at low concentrations.

Along with the results, there needs to be a more developed and convenient technique to observe multiple samples at the same time at specific temperature. This will save a lot of time over the current method, where a number of self-synthesized tear-shaped glass holder is used at a time to observe the liquid crystal formation. Also it eliminates the possibility of heat radiating off from your hand and affecting the liquid crystal formation when you have to hold the glass holder to place it under the microscope.

Chapter 2: Synthesis of Oligo(ethylene glycol)-Terminated Alkanethiol Self-Assembled Monolayers for the Study of ODD-EVEN Orientation of Disodium Cromoglycate

2.1 Introduction:

A self-assembled monolayer (SAM) is a unidirectional, highly stable single layer of molecules on a solid surface. A SAM is composed of three main components: a headgroup, which binds strongly to the substrate; a tailgroup that constitutes the outer surface on film; and a chainlike spacer which separates headgroups and tailgroups (Figure 1).[4] The headgroup provides the most exothermic process due to chemisorption on the substrate surface.[5] The chainlike spacer is supported by interchain van der Waals interactions, independent of the chain length.[5] It has a high degree of flexibility allowing simple modification at the molecular level.

Figure 1: SAM attaching to surface

A SAM can be easily prepared by adding a solution of the desired molecule onto the substrate surface and washing off the excess solution. A very common example is alkanethiol on gold film surface. Its sulfur ending group has a particular binding affinity on gold and alkane with a thiol head group that can

adhere to the gold surface easily with its tail pointing away, as shown in the diagram.

Oligo(ethylene glycol) $(OEG)_n$, $HS(CH_2)_{11}(OCH_2CH_2)_nOH$ (n= 3, 4, 5, and 6) is a type of SAM which has been found to exhibit protein resistant properties, especially $OEG_{2\text{-}7}$, demonstrating prevention of direct contact between the surface and the protein.[6] It is often used as a biomaterial for its low toxicity property, low immunogenicity, and poor binding of proteins and cells. It has excellent protein and cell repelling properties. Oligo(ethylene glycol) structure plays an important role in a SAM. The terminal hydroxyl group or methyl group does not significantly affect protein resistance of OEG-SAM.

The orientation of SAM is highly sensitive to the number of methylene units involved. The alteration of a single methylene unit can result in a difference in the orientation of methyl groups being present at the surface of SAM.[7] When an odd alkanethiol (n = 3, 5, 7 …) is present, the molecule is perpendicular to the direction of deposition of gold on SAM and the surface is aligned parallel to the surface (Figure 2). When it is an even alkanethiol (n = 2, 4, 6 …), the direction of deposition of gold on SAM and the surface align in parallel (Figure 3).[8] The different orientation each alkanethiol molecule exhibits produces an odd-even effect based on the number of methylene unit the molecule has, which influences its direction of orientation when interacting with the surface. $HS(CH_2)_{11}$-, an odd number alkanethiol, is the basic foundation of a stable SAM.[9]

Currently, SAM is the best defined system available for examining protein interactions on surfaces, and provides a mean for evaluating the many hypotheses

regarding the mechanisms of protein-protein interactions and how it binds to the surface.[10] Self-assembled monolayers have been applied to the development of various detection systems such as electrochemical and optical detection.

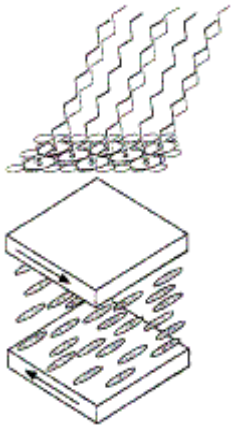


Figure 2: Odd alkanethiol SAM

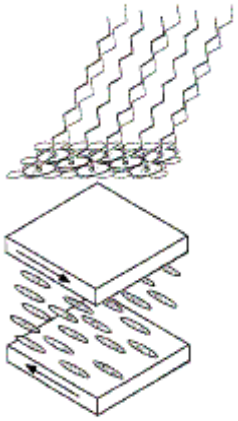


Figure 3: Even alkanethiol SAM

The interaction of SAMs with gold films is used to control nanometer-scale topography of surfaces. The orientation of liquid crystals depends on the specific terminals groups of SAMs; this gives information about how the SAM is functioning and the topography of the surface.

When a gold surface comes into contact with a liquid crystal or SAM molecule, it can exhibit either maximum roughness or minimum roughness. The minimum roughness is aligned parallel to the gold deposition onto the glass slide. The maximum roughness is perpendicularly aligned to the gold deposition onto the glass.

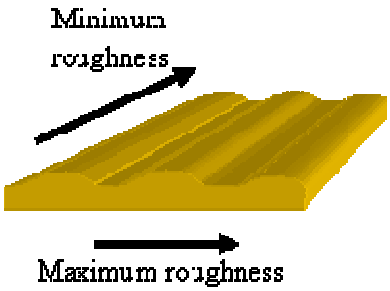


Figure 4: The gold surface has a topography with hill and valley corrugation. Minimum roughness and maximum roughness are perpendicular to each other.

2.2 Experimental Section:

Materials

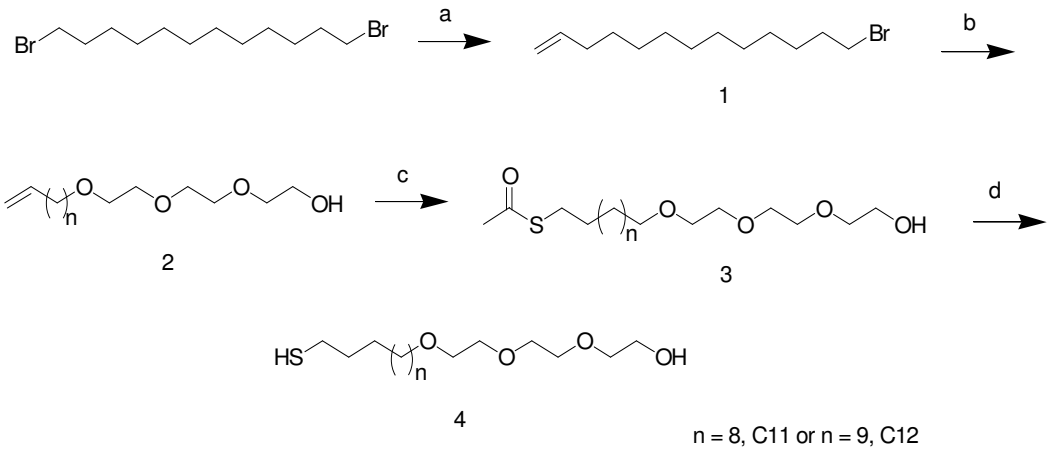
Triethylene glycol (EG_3OH, 99% purity), tetraethylene glycol (EG_4OH, 99.5% purity), 1,12-dibromododeance (96% purity), thioacetic acid (98% purity), hydrochloric acid 1N (standard solution), sodium sulfate (anhydrous), hexane, ethyl acetate, pentane, and THF were purchased from Acros Organics (Suwanee, GA). 11-bromo-1-undecene (95% purity), cromolyn sodium salt (95% purity), 2,2'-Azobis(2-methylproprionitrile) (AIBN, 98% purity), and diethyl acetate were purchased from Aldrich Chemicals (Milwaukee, WI). Hexamethylphosphoramide (HMPA, 98& purity) was purchased from Fluka (Allentown, PA). Ethanol (absolute) was purchased from Pharmco-AAPER (Brookfield, CT). The glass microscope slides were Fisher's Finest, premium grade, obtained from Fisher Scientific (Pittsburg, PA).

Methods

Synthesis of (1-Mercapto-n-yl)tri(ethylene glycol)

Two types of **4** were synthesized. The 11 methylene unit 1-Mercaptoundec-1-yl-tri(ethylene glycol) (Compound **4**, n = 8) was synthesized using the procedures from Pale-Grosdemange and co-workers.[8]

12-bromododecane was not commercially available and thus was synthesized from 1, 12-dibromododecance. The synthesis was done after modifying the HMPA-promoted elimination by Hoye and co-workers.[11]



a. HMPA, Distill at 175°C for 0.5 h; b. Triethylene glycol at 70°-80°C for 24 h; c. Thioacetic acid, AIBN in THF under ultraviolet light for 1.5 h; d. HCl, methanol and reflux.

Synthesis of Odd methylene unit triethylene glycol SAM:

$HS(CH_2)_{11}(OCH_2CH_2)_3OH$ ($C_{11}EG_3$)

*Synthesis of Undec-1-en-11-yltri(ethylene glycol) (Compound **2**, n = 8)*

A mixture of 0.102 mL of 50% aqueous sodium hydroxide and 5 mL of triethylene glycol (11.23 mmol) were placed inside a round bottomed flask and stirred for 0.5 h in triethylene glycol oil bath, at 70ºC - 80ºC. Upon heating the solution, it turned from a colorless liquid to a bright yellow color. To the resulting yellow solution, 11-bromoundec-1-ene (0.5 mL, 2.3 mmol) was slowly added through the use of a syringe in a drop-wise fashion. Upon completion, the reaction was heated for 24 h and then cooled at room temperature. After cooling, a combined mixture of hexane and diethyl ether (ratio 2:3) was added to the reaction with the addition of water and 1N HCl drop-wise until pH 7 was achieved. The organic layer was extracted three times with hexane and diethyl ether mixture (ratio 2:3) to ensure most, if not all, of the aqueous waste was gone. The resulting crude product was yellow in color. Column chromatography on silica gel (eluent: 10% ethyl acetate and 90% hexane) was used to purify before the next synthesis step.

Synthesis of [1-(Methylcarbonyl)thio]undec-11-yl]oligo-(ethylene glycol) **3**

A mixture of undec-1-en-11-yltri(ethylene glycol) (Compound 2) and 30.0 mg of AIBN (0.18 mmol), the catalyst, was dissolved in tetrahydrofuran (THF). Thioacetic acid (2.5 mol equivalent) was added to the reaction and the resulting

solution was exposed to ultraviolet light for 1.5 h. After the photochemical reaction, the solution was evaporated until dried. Column chromatography on silica gel using an ethyl acetate and hexane (7:3) mixture was used to obtain pure OEG terminated alkanethiol. Fractions obtained from the column were checked for purity using TLC, with the solvent ethyl acetate and hexane mixture (7:3); m/z = 379 $(M+H)^+$, 401 $(M+Na)^+$.

Synthesis of (1-Mercaptoundec-11-yl)oligo(ethylene glycol) **4**

With the [1-(Methylcarbonyl)thio]undec-11-yl]oligo-(ethylene glycol) product, 5 drops of HCl in methanol solvent were added to it, and it was refluxed for 2 h. The thioacetates were deprotected under this condition. The resulting solution was evaporated under a Rotorvap until dried. The final product was pure yellow oil.

Synthesis of EVEN methylene unit triethylene glycol SAM:

$HS(CH_2)_{12}(OCH_2CH_2)_3OH$ ($C_{12}EG_3$)

Synthesis of 12-bromododecane (Compound **1**, n = 9)

In a three-necked 100 mL round-bottom flask, 5.80 g (18.3 mmol) of **1**, 12-dibromododecance was placed inside the flask along with a spin bar. The first neck was sealed with a rubber septum, the middle neck of the flask was connected to a pressure-equalizing funnel, and the third neck was attached to a short-path

distillation head that was insulated with cotton. The distillation head was equipped with a water inlet, water outlet, and a vacuum outlet with 15 Torr of applied pressure. At the end of the distillation head, it was connected to a 10 mL receiving flask that was soaked in acetone-ice water bath. A silicon oil bath was preheated to 200°C before placing in the three necked-flask with 1, 12-dibromoalkane. The round-bottom flask was lowered into the oil bath until the oil level was 1 cm away from the joint of the flask. The solution was rapidly stirred through the distillation process. Upon the melting of 1, 12-dibromododecance (~175°C), 6.40 mL HMPA (36.5 mmol) was added dropwise at the rate within 30 minutes to completion through the aid of a funnel. The reaction was cooled at room temperature for 12 h. The residue, HMPA-HBr, was black-brown in color. The distillate was clear when allowed to warm to room temperature with some suspended HMPA. HMPA dissolved to give a colorless liquid. The cooled distillate was diluted with 10 mL of hexane and washed twice with water, dried with $NaSO_4$, and filtered to completely rid of HMPA. The organic layer was evaporated to dryness. Thin layer chromatography was preformed in the solvent system of ethyl acetate and hexane mixture (9:1); m/z = 248 $(M+H)^+$, 217 $(M+Na)^+$. 288 $(M+K)^+$; ^1H NMR (300 MHz, CDCl3) δ: 1.35 (m, 12H), 1.41 (quintet, 2H, *J* = 7.5, 14.4 Hz), 1.540 (2H, s), 1.86 (quintet, 2H, *J* = 6.9, 14.7 Hz), 2.03 (q, 2H, *J* = 7.5, 6.6, 14.1 Hz), 3.41 (t, 2H, *J*=6.9), 4.96 (m, 1H), 5.02 (q, 1H), 5.805 (t, 1H, *J* = 0.6, 10.2 Hz).

Synthesis of Dodec-1-en-12-yltri(ethylene glycol) **2**

The above procedure was used for the synthesis of ODD carbon triethylene glycol ($C_{11}EG_3$). The procedure for synthesizing dodec-1-en-12-yltri(ethylene glycol) is as follows: 0.182 mL of 50% aqueous sodium hydroxide (1 equivalent), 10 mL of triethylene glycol (22.275 mmol), and 0.559 mL 12-bromoundec-1-ene (2.275 mmol) were heated at 70 - 80ºC for 0.5 h. The reaction was cooled at room temperature for 24 h after heating. Extraction was performed under the same conditions. The crude was purifed using silica gel chromatography with the eluent mixture of ethyl acetate and hexane (9:1), followed by a dichloromethane and methanol mixture (3:2).

Synthesis of [1-(Merthylcarbonyl)thio]dodec-12-yl]oligo-(ethylene glycol) **3**

The above procedure for [1-(Merthylcarbonyl)thio]dodec-11-yl]oligo-(ethylene glycol) was used. In this photochemical reaction, the following amounts of compounds used were the same as for ODD carbon triethylene glycol, along with 30 mg of AIBN as the catalyst. The reaction gave off yellow oil and went through the same purification process as above. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.30 (m, 16H), 1.56 (t, 2H, J = 6.9 Hz), 2.49 (t, 2H), 3.35 (s, 3H), 3.46 (t, 2H, J = 6.6 Hz), 3.64 (m, 12H).

Synthesis of 1-(Mercaptododec-12-yl) triethylene glycol) **4**

The same procedure applies when synthesizing 1-(Mercaptododec-11-yl) triethylene glycol) ($C_{11}EG_3$) with the exception of the reflux. The reaction was refluxed for 5 h. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.30 (m, 20H), 1.56 (broad, t, 2H, *J* = 6.9 Hz), 2.49 (t, 2H), 3.35 (m, 2H), 3.46 (t, 2H, *J* = 6.6 Hz), 3.64 (m, 12H). m/z = 351 $(M+H)^+$, 371 $(M+Na)^+$.

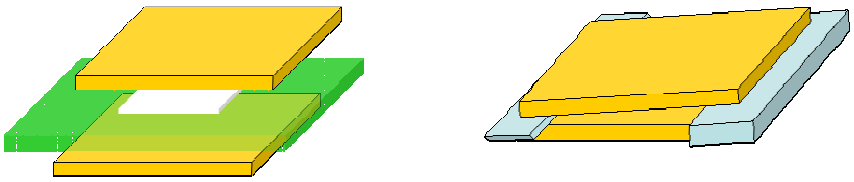
Preparation of $C_{11}EG_3$ and $C_{12}EG_3$ SAM

Sterile forceps were used to handle already prepared deposited gold at a 45º angle. The forceps were also used for support when cutting the gold slide with a glass cutter. Additional forceps were used to bend the gold slide and break it into smaller gold pieces. When completed, stream of N_2 was used to blow away the dust that had gathered through the process. Only sterile forceps were used to handle the gold slides. A Petri dish cover was used to cover the gold slides to prevent dust from gathering. The slides were rinsed extensively with water and ethanol, and dried with stream of N_2. This process was repeated several times until the gold slide was thoroughly clean. The slide was then placed into the appropriate soaking solution. The remaining slides that had been cut went through the same procedures above. Two small pieces of gold slides can be fitted in each vial (of 2mM of targeted SAM solution in ethanol) by having the non-gold slide facing back to back of each other. Slides were soaked for 12 h. It was dried with stream of N_2 when taken out of the vial, followed by extensively rinsing with ethanol and dried with stream of N_2. When the slides are placed down, have the

gold surface facing up and covered with Petri disk when not in use. A small rectangular shape was cut out from a small piece of saran wrap, large enough to cover the gold slide with a hole-puncher in it for DSCG insertion. The diameter of the hole-punched region must not exceed the gold slide. In this region, 13 wt % DSCG was inserted, and covered with another gold slide where the gold surface facing the liquid crystal. Binder clips were used to bind both sides and to prevent air bubbles formation. This is known as the sandwiching technique (Figure 5a). Once the DSCG-SAM was fully prepared, it was placed under a polarizable microscope for observation. The sample was rotated at every 45º to observe the orientation.

Preparation of wedge DSCG-SAM slide

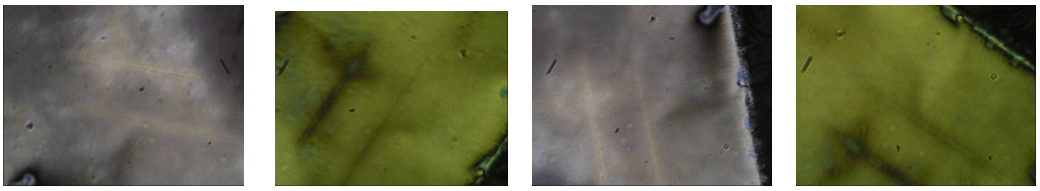
The set-up for a wedge slide was the same as before, except the cut-out rectangular area of saran wrap needed to be more narrow and longer, till it will not come in contact with binder clips when binded together. In addition, a spacer was placed on one side of the slide to create a wedge (three-ply saran wrap was used create the spacer). A small portion of the DSCG sample was placed into the rectangular area; gold slides were aligned together (facing each other); and clipped together using binder clips. The wedged cell was placed under a polarizable microscope to observe. It was rotated 45º each time to observe the orientation of DSCG when DSCG came into contact with SAM.



(a) (b)

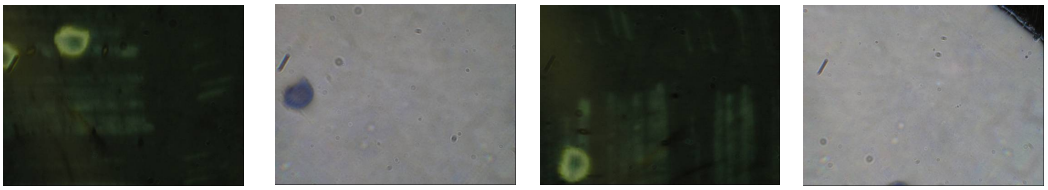
Figure 5: (a) A regular liquid crystal and SAM cell set up. The gold films are aligned face-to-face with each other with a thin layer of saran wrap separating them. (b) A wedged cell where there is a spacer at one end to separate the two gold slides to induce an inclined.

2.3 Results:



350° 35° 80° 125°

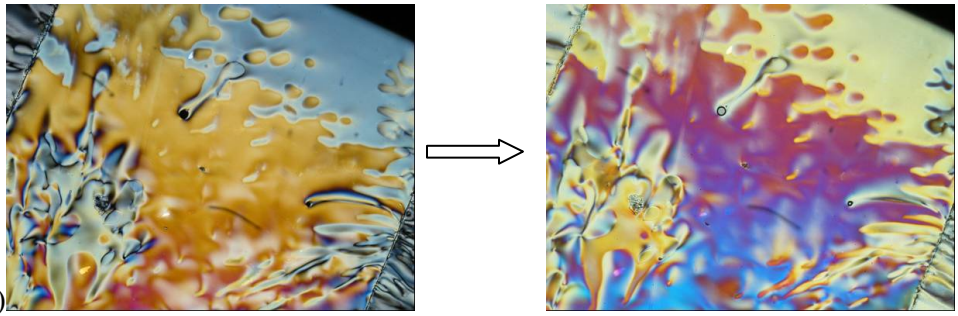
Figure 6: Liquid crystal on C11EG3 SAM at every 45° rotation on the polarizable microscope under 10X magnification



350° 35° 80° 125°

Figure 7: DSCG on C12EG3 SAM at every 45° rotation on the polarizable microscope under 10X magnification.

(a)



(b)

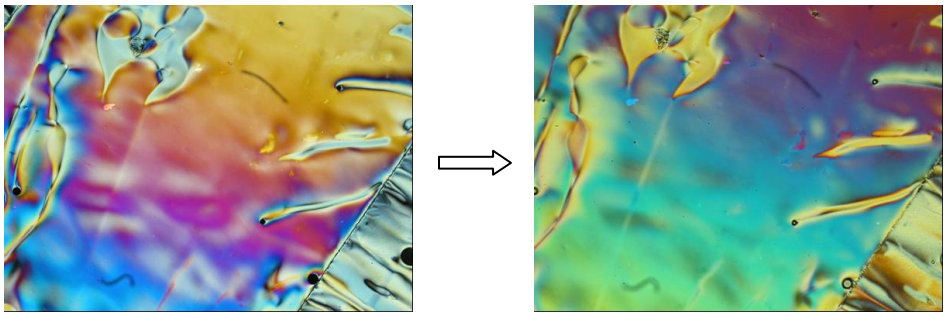


Figure 8: DSCG on C12EG3 SAM under 10x magnification. On the left, represent slides taken with QWP. At the right, pictures of slides are taken at the same degree angle, but without the QWP. (a) and (b) represents different position of the wedge cell it was taken under.

2.4 Discussion:

Synthesis of Odd methylene unit triethylene glycol SAM:

$HS(CH_2)_{11}(OCH_2CH_2)_3OH$ ($C_{11}EG_3$)

Each intermediate product was purified through column chromatography to obtain a pure product before proceeding to the next synthesis step. ^{1}H NMR analysis was performed to verify product and whether or not reactants were used up to obtain the desire intermediate product. Mass spectrometry was also performed, if necessary. Column chromatography for the first intermediate product went well; the resulting purified product was yellow and transparent in color. AIBN was

recrystallized with dioxane and dried before use. All reactions involving thioacetic acid were handled under the hood due to the horrid odor it produced. A large beaker filled with bleach was placed under the hood. All syringes, vials, pipettes, and any disposable equipment, that came in contact with thioacetic acid were thrown into the beaker to neutralize the smell. After the photochemical reaction, column chromatography was performed, along with ^{1}H NMR. In addition, the reaction was often stopped at this step and the flask was placed in the refrigerator before further synthesis into an amine-terminated SAM. This is mainly because the amine-terminated SAM is very unstable and highly reactive. It is often further synthesized when one is ready to proceed further with the experiment.

Synthesis of EVEN methylene unit triethylene glycol SAM:

$HS(CH_2)_{12}(OCH_2CH_2)_3OH$ ($C_{12}EG_3$)

Due to the fact that 12-bromo-1-undecene is not commercially available, the synthesis of $C_{12}EG_3$ was more difficult to achieve. The operational set-up required two people to help set up the apparatus. One person kept three-necked, round-bottomed flask steady on the stand, while another person attached a receiving flask to the end of the distillation head. This particular synthesis was done several times, due to poor apparatus set-up, before 12-bromo-1-undecene was successfully synthesized. Once this product was synthesized, it followed the same procedures as the $C_{11}EG_3$, and less complication occurred.

Observations of DSCG-SAM:

Two types of OEG-SAM were observed: $HS(CH_2)_{11}(OCH_2CH_2)_3OH$ ($C_{11}EG_3$) and $HS(CH_2)_{12}(OCH_2CH_2)_3OH$ ($C_{12}EG_3$), each interacting with 13 wt % DSCG in Millipore water on gold films, that were deposited at 45º, through the use of a self-fabricated liquid crystal cell (Figure 5a). Observations were made at every 45º rotation under the polarized light of the microscope at different magnifications. Pictures were taken. Observations of $HS(CH_2)_{11}(OCH_2CH_2)_3OH$ ($C_{11}EG_3$) were made under 4x and 10x magnification. Under 10X magnifications, pictures were taken at 350º, 35º, 80º, and 125º, a 45º rotation from original point (Figure 6). At 35º and 125º the liquid crystal displayed a yellow color and uniform texture. At 80º and 350º, a gray and black image was seen compared to the two previous rotations, and the content on the slide had a uniform texture as well. These were the results of optical images and cross polarizer of DSCG on tri-ethylene glycol SAM. Upon each 45º rotation, a change in light intensity was observed; the texture remained uniform. It indicated DSCG under $C_{11}EG_3$ possessed a uniform orientation on the surface. The same applies when observations were made with $C_{12}EG_3$, except the optical images were either white or black under each rotation (Figure 7).

The sample, $C_{12}EG_3$ was furthermore observed with the change in interference color created by the light when observing under a wedge-shaped cell, and the insertion of quarter wave plate (QWP). A wedge-shaped cell had a spacer at one end which separated the two gold films to produce an incline (Figure 5b).

When QWP was inserted into the microscope pathway and taken out, the colors from the liquid crystal images changed from red to blue and yellow to red as the pictures indicated (Figure 8). From the picture below, when light passes through QWP, there are significant changes in color, such that it shifts from green to yellow, from blue to green, and from white to yellow. The QWP of interference colors were created by the white light transmission upon the sample (Figure 9).[12] This is a similar pattern as indicated in earlier pictures form the observations made under $C_{12}EG_3$.

Figure 9: A wedge-shaped cell when placed under a polarizable microscope, expects to see certain results when there is no QWP and change in interference color when inserted QWP.

$C_{11}EG_3$ did not show as promising a result when compared to $C_{12}EG_3$ under the same set of conditions. This is likely due to the poor preparation technique of DSCG on wedged slide and having DSCG leaking out of its designated area when observing under the microscope.

2.5 Conclusion and Perspective:

Through the measurements of liquid crystal birefringence between SAMs, that were either composed of $HS(CH_2)_{11}(OCH_2CH_2)_3OH$ ($C_{11}EG_3$) and $HS(CH_2)_{12}(OCH_2CH_2)_3OH$ ($C_{12}EG_3$)**,** (odd and even carbon number), it can be concluded that the antiasthmatic drug DSCG had a uniform orientation when DSCG came into contact with the SAM on the gold surface. The liquid crystal of DSCG was aligned in parallel to the gold surface at minimum roughness, when comes into contact with $C_{11}EG_3$. The liquid crystal of DSCG is perpendicular aligned to the gold surface at maximum roughness when it comes into contact with $C_{12}EG_3$. In conclusion, DSCG's orientation on the gold surface reinforces the idea that EVEN methylene units are parallel and ODD methylene units are perpendicular to the gold surface. For future studies, this can help one to understand protein-protein interactions of liquid crystal's orientation upon SAM molecules. It will also further our understanding of cell signaling in the human body.

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