DESIGN AND APPLICATIONS OF 4-YL-(METHYL)COUMARINS AND THEIR DERIVATIVES

BY

JOSHUA A. RITCHEY

DISSELINEATION

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Doctoral Committee:

Professor Jeffrey S. Moore, Chair
Professor Jennifer A. Lewis
Professor Ralph G. Nuzzo
Professor Kenneth S. Suslick
ABSTRACT

Surface chemistry is a well-established area of research and is required in many commercial applications. However, most surface modifications are static in nature meaning a single treatment will produce a single, fixed surface state (e.g.: hydrophobic, hydrophilic, etc.). Dynamic systems, those that respond to stimuli, have become an active area of surface chemistry because they provide a means to vary surface properties. Responsive dynamic systems are classified as either reversible or irreversible. When light is used as a stimulus, the chemical moieties that produce the reversible and irreversible responses are known as photoswitches and photofuses, respectively.

The o-nitrobenzyl photofuse, which was initially used as a biological caging group, has been utilized in various surface applications with great success. However, this photofuse can be problematic due to the long exposure times required for full conversion and the reactive byproducts that form upon UV exposure. Another photofuse, known as the 4-yl-(methyl)coumarin, is of particular interest because of its rapid photochemical response, lack of reactive products upon UV exposure, and many different photofuses are readily prepared from inexpensive, commercially available starting materials.

A divergent synthetic scheme was developed that allows access to a variety of coumarin photofuses, via similar synthetic pathways, that enable multiple surface modifications. After establishing this synthetic pathway, various coumarin photofuses were prepared and applied to surfaces to demonstrate the utility of this convenient and efficient photofuse. Prepared photofuses provide transitions including hydrophobic-to-
negative, hydrophobic-to-positive, negative-to-positive, positive-to-negative, and hydrophobic-to-neutral transitions.

Multiple photofuses were then utilized to probe chemical greyscale transitions by combining the photoresponsive coumarin monolayer with novel greyscale photolithography masks. The versatility of the coumarin photofuse was demonstrated through simple modifications of the coumarin core to provide access to characterization techniques such as secondary ion mass spectrometry (SIMS) and fluorescence microscopy. Chemical gradients were successfully patterned and characterized. The patterned gradients were then used to produce pressure sensitive microfluidic gates based on the variation in surface hydrophobicity. Correlation of mask transparency to resulting surface hydrophobicity provided a predictive curve of gating pressures that were in excellent agreement with theoretically predicted values.

The coumarin photofuse was then utilized to pattern substrates based on the changes in surface composition. Monolayer templating has been reported previously, but the photoresponsive nature of the coumarin monolayers reported herein provides unique patterning capabilities within three-dimensional structures such as artificial opals by taking advantage of the photonic properties of these materials. Functionalization, photochemical conversion, and labeling within inverse opals was performed and characterized using confocal fluorescence microscopy. Alternative labeling and patterning schemes were also successfully performed on planar substrates including atomic layer deposition and selective metallization.
To Mom and Dad
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# TABLE OF CONTENTS

CHAPTER 1: Controlling Surface Chemistry with Light .................................................. 1
  1.1 Introduction ............................................................................................................. 1
  1.2 Reversible Photoresponsive Surfaces ................................................................. 4
  1.3 Irreversible Photoresponsive Surfaces ................................................................. 19
  1.4 Conclusions/Future Outlook .................................................................................. 31
  1.5 Scope of Thesis ..................................................................................................... 33
  1.6 Figures ................................................................................................................... 35
  1.7 References ............................................................................................................. 41

CHAPTER 2: Surface Analysis Techniques ....................................................................... 51
  2.1 Introduction ............................................................................................................. 51
  2.2 Contact Angle Analysis ......................................................................................... 52
  2.3 Ellipsometry .......................................................................................................... 54
  2.4 Secondary Ion Mass Spectrometry (SIMS) ............................................................ 55
  2.5 Scanning Electron Microscopy (SEM) .................................................................. 57
  2.6 Light, Fluorescence, and Confocal Microscopy ..................................................... 58
  2.7 Zeta Potential Measurement .................................................................................. 59
  2.8 Thermal Analysis Methods .................................................................................... 61
  2.9 Figures ................................................................................................................... 63
  2.10 References .......................................................................................................... 65

CHAPTER 3: Coumarin Photofuses ................................................................................ 66
  3.1 Introduction ............................................................................................................. 66
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.2 Photochemistry of o-Nitrobenzyl Photofuse</td>
<td>67</td>
</tr>
<tr>
<td>3.3 Photoresponsive Coumarins</td>
<td>69</td>
</tr>
<tr>
<td>3.4 Surface Chemistry Toolbox</td>
<td>72</td>
</tr>
<tr>
<td>3.5 Establishing Divergent Synthetic Routes</td>
<td>74</td>
</tr>
<tr>
<td>3.6 Future Work: Negative-to-Neutral and Positive-to-Neutral Transitions</td>
<td>84</td>
</tr>
<tr>
<td>3.7 Conclusions</td>
<td>84</td>
</tr>
<tr>
<td>3.8 Experimental</td>
<td>86</td>
</tr>
<tr>
<td>3.9 Figures</td>
<td>104</td>
</tr>
<tr>
<td>3.10 References</td>
<td>113</td>
</tr>
</tbody>
</table>

CHAPTER 4: Greyscale Photolithography Monitored by Coumarin Monolayers and Applications ................................................. 117
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1 Introduction</td>
<td>117</td>
</tr>
<tr>
<td>4.2 Photofuse Selection: 4-yl-methyl Coumarins</td>
<td>119</td>
</tr>
<tr>
<td>4.3 Fabrication of Greyscale Photolithography Masks</td>
<td>122</td>
</tr>
<tr>
<td>4.4 Binary Patterning of Coumarin Monolayers</td>
<td>123</td>
</tr>
<tr>
<td>4.5 Greyscale Patterning of Coumarin Monolayers</td>
<td>131</td>
</tr>
<tr>
<td>4.6 Microfluidic Gating using Greyscale Surface Modification</td>
<td>135</td>
</tr>
<tr>
<td>4.7 Conclusions</td>
<td>138</td>
</tr>
<tr>
<td>4.8 Experimental</td>
<td>139</td>
</tr>
<tr>
<td>4.9 Figures</td>
<td>148</td>
</tr>
<tr>
<td>4.10 References</td>
<td>161</td>
</tr>
</tbody>
</table>

CHAPTER 5: Photochemical Modification within Three-Dimensional Structures and Applications for Novel Fabrication Schemes ........................................... 164
5.1 Introduction .................................................................................................................. 164
5.2 Photonic Crystals: Opals and Inverse Opals ......................................................... 166
5.3 Optical Properties of Photonic Crystals .................................................................. 168
5.4 Functionalization and Characterization within Inverse Opal Structures .... 170
5.5 Coumarin Templating for Novel Fabrication of Complex Structures ...... 175
5.6 Conclusions and Future Work .................................................................................. 180
5.7 Experimental .............................................................................................................. 182
5.8 Figures .......................................................................................................................... 194
5.9 References ................................................................................................................... 203

CHAPTER 6: Conclusions ................................................................................................. 205

APPENDIX A: Mechanophore Discovery Aided by a Turn-on Fluorescence Probe .. 208
   A.1 Initial Efforts for Coumarin Mechanophore ......................................................... 208
   A.2 Redesign of Coumarin Mechanophore ................................................................. 212
   A.3 Conclusions .............................................................................................................. 215
   A.4 Figures ....................................................................................................................... 216
   A.5 References .............................................................................................................. 220
CHAPTER 1

Controlling Surface Chemistry With Light†

1.1 Introduction

The chemistry of interactions of surfaces or phase boundaries, also known as interfacial chemistry, can be utilized to control a variety of material properties including friction, adhesion, wetting, reflectivity, and conductivity. The ability to understand, design, and tailor these interactions has led to advances in research areas including heterogeneous catalysis, optics, and tribology. Many examples of modified surface chemistries have been developed for commercial use, from the non-stick properties of Teflon, to anti-corrosion and anti-reflective coatings.

The development of dynamic surface chemistries is of recent interest due to the control of surface properties upon exposure to a desired external stimulus. Dynamic systems change a surface’s composition or molecular orientation after exposure to a stimulus, (e.g. changes in pH, ionic strength, temperature, or light) which results in a change in the interfacial properties. Careful synthesis combined with appropriate surface modification can produce a surface that changes either reversibly or irreversibly between two desired states. For example, a dynamic surface may be altered to decrease light transmission after exposure to a stimulus, much like the commercially available Transitions lenses. Some of the realized and potential changes in surface characteristics include transitions from electrostatically repellent to attractive, colorless

† This chapter was written in collaboration with Dr. Elizabeth M. Glogowski for submission in Advanced Materials as a Progress Report.
to colored, and absorbent to non-absorbent; the number and types of transitions can be specifically tailored with different chemical moieties to meet the need of various applications. Applications range from biointerfaces\textsuperscript{2} to semi-permeable membranes, \textsuperscript{3} and photonics, \textsuperscript{4} among others.

Direct chemical methods are commonly used for surface modification. These methods involve either chemisorption (\textit{e.g.}, of polymer brushes or self-assembled monolayers) or physisorption of an organic moiety (\textit{e.g.}, layer-by-layer assembly or Langmuir-Blodgett films) (Table 1.1). Selection of a method for surface modification is dependent on the surface properties required for the desired application. Additionally, each method requires special preparation of both the surface and the dynamic moiety. Thus, the surface modification method demands careful consideration from both synthetic and processing perspectives.

Once a functional layer has been deposited on the substrate, many methods are available to induce changes at the surface. First, solvent-based methods can change pH, ionic strength, and solvent composition. Solvent-based modifications can also result in swelling/deswelling of a hydrogel, change in hydrodynamic radius of grafted polymer chains, chemical modification of grafted molecules, and/or a change in molecular conformation. Each of these solvent-based methods is inherently systemic and not exclusive to the regions of interest. These non-specific methods limit the scale and scope of applications of these resulting surfaces. Therefore, methods that induce change with a high degree of spatial control are highly desirable.

Significant progress has been made towards the synthesis of molecules that respond to various forms of electromagnetic radiation. Specifically, light is a natural
stimulus for surface modification because of its high spatial-temporal control. Additionally, surfaces are readily accessible to photon flux, and complications resulting from scattering or absorption can be minimized. The spatial and temporal aspects of the response can be controlled while not affecting the entire non-irradiated surface. Utilization of this remote surface modification provides a level of control that was not previously accessible in a direct manner. Controlled dynamic surface functionalization has the potential to create more complex systems such as three-dimensional structures in devices that require fine pattern control such as biological sensors.

This introduction is organized into two general classes of photoresponsive systems. The first class of systems is a photoswitch, which exhibits a change on exposure to light, but ultimately returns to its original state in response to another stimulus such as another wavelength of light, or through thermal relaxation. Photoswitches generally undergo a conformational change or a ring opening/closing in response to light. The reversibility of photoswitches enables repeated responses to multiple exposures. The second class of systems is a photofuse, which – as its name implies – undergoes a non-reversible change in response to light. Photofuses undergo bond cleavage, either heterolytic or homolytic, to produce a different molecule after exposure to specific wavelengths of light. For some applications, a non-reversible change is desirable to allow for further chemical modification. The ability to provide reversible responses has been demonstrated widely in applications such as optical storage, light-induced topographical changes, and rewritable paper. Demonstrated irreversible systems include controlled self-assembly, photolithography, and drug delivery from surfaces.
Herein we discuss the progression and recent advances of some light-responsive groups and their incorporation into both planar and colloidal surfaces. We discuss both photoswitches (reversible) and photofuses (non-reversible) that have been used successfully for surface modifications. Our own work in this field will be discussed in the context of previous work on the topic of photoresponsive materials. This report will conclude with a discussion of the potential applications of photoresponsive materials, and the outlook of the field. The literature is vast and this report is by no means a comprehensive review. We direct readers to the many reviews or texts available for each photoresponsive unit.  

1.2 Reversible Photoresponsive Surfaces

Photoswitches, i.e. photochromic molecular switches, undergo a reversible response to light that can be accompanied by a corresponding color change. Photoswitches encompass a wide range of organic and inorganic materials that respond to light by various mechanisms. While a large variety of photoswitchable moieties have been reported, we will limit our discussion to those with demonstrated applications in colloids and planar substrates; these systems include azobenzenes, spiropyran, spiroxazines, fulgides, stilbenes, and diarylethenes.

1.2.1 Azobenzene Photoswitches – Planar Substrates

Azobenzene-containing materials, which have been thoroughly studied as photoswitches, undergo a reversible trans to cis isomerization upon exposure to UV light, corresponding to the π-π* transition of the azobenzene moiety. The reverse
reaction, a cis to trans isomerization, occurs upon exposure to visible light – corresponding to the n-π* transition – or by thermal relaxation. The change in geometry results in a decrease in distance of the carbons para to the diazo group from 9.0 Å in the trans isomer to 5.5 Å in the cis isomer. This change in geometry results in a measurable dipole moment of the azobenzene-containing functional group; the less thermally stable cis isomer has a dipole moment of 3.0 D whereas the more thermally stable trans isomer has a negligible dipole moment. The photoisomerizations occur on the picosecond timescale, while the thermal back reaction rates depend on the composition of the photochromic moiety (e.g. the azobenzene thermal relaxation is slow, while the aminoazobenzene and the pseudo-stilbene thermal relaxation is fast). The quantum yields of isomerization are generally high, and the resultant photochemical processes are efficient, which is partially attributable to the non-emissive characteristics of the azobenzene excited states.

Azobenzene derivatives absorb strongly in the visible region (ε = 22,387 M⁻¹cm⁻¹ at 319 nm for unsubstituted azobenzene) and are relatively thermally and photochemically stable. For these reasons, azobenzenes have been widely studied and constitute one of the largest class of synthetic dyes (the so-called azo dyes). More recently, azobenzenes have been incorporated into responsive materials such as liquid crystalline materials, nonlinear optical materials, rewritable memory devices, and biological applications. Incorporation of azobenzene derivatives into polymer chains directly affects the resulting material properties. Azobenzene-functionalized polymers have been studied extensively, including their photochemical properties, molecular motions, and alignment in liquid crystalline polymers. Because these
materials have been reviewed previously, we have chosen to focus our discussion toward the utilization of these materials on surfaces.

The functionalization of planar substrates with azobenzene derivatives has been achieved by the deposition of either small molecule monolayers or thin polymer films containing azobenzene moieties. In one example, the wafers were functionalized either directly with an triethoxysilane-containing azobenzene or indirectly by reacting an acid chloride-containing azobenzene with an amine-terminated silicon substrate. These examples showed incomplete monolayer formation; both methods resulted in a change in contact angle of ca. 9º upon irradiation with 354 nm light where the trans to cis isomerization occurs. In another example, a silicon wafer was functionalized with 3-aminopropylmethyldiethoxysilane, and an azobenzene carboxylic acid was attached. Upon irradiation with UV light, the contact angle of the azobenzene-functionalized surface changed from 100-102º to 88-89º. The difference in contact angle before and after irradiation was used to direct the movement of liquids on the surface by creating a wettability gradient based on a UV-visible optical gradient. Other substrates, including gold, have been modified with azobenzenes to give monolayers. In one study, gold surfaces modified with thiol-functionalized azobenzenes were photoswitched and were monitored by the change in current between the gold surface and a mercury drop electrode. The ability to create a wettability gradient via controlled photoswitching may be useful in the development of microfluidic systems.

In addition to functionalization of surfaces with small molecule azobenzenes, thin polymer films containing azobenzenes have been utilized as photoswitches on planar substrates. In one example, a liquid-crystalline azobenzene monomer and a diacrylate
cross-linker were polymerized to form an elastomeric liquid-crystalline network with random orientation of azobenzenes. Using linearly polarized 366 nm light, the film was reversibly curled parallel to the polarized light, and returned to the flat conformation upon exposure to visible light. Because of the random orientation of the azobenzene moieties, photoswitching of the groups aligned with polarized UV light contract result in a macroscopic volume contraction in any direction.\textsuperscript{24}

Irradiation of surfaces functionalized with azobenzenes generally exhibit small changes in contact angle (< 10º).\textsuperscript{21-22} An exception is a nanoporous, multilayer organic-inorganic hybrid film.\textsuperscript{25} Poly(allylamine hydrochloride) (PAH) and silica nanoparticles were deposited layer-by-layer. A fluorinated azobenzene was attached via coupling to primary amine-functionalized silica. By increasing the number of PAH/SiO\textsubscript{2} bilayers, the surface roughness and nanoporosity were increased. This enlarged surface area resulted in an effectively higher azobenzene concentration, yielding a greater change in contact angle upon UV irradiation as compared to previous examples. After nine bilayer depositions, the contact angle switched from 152 ± 3º to < 5 ± 1º upon UV irradiation. The change in contact angle was cycled with UV–visible irradiation, and the surface was patterned using an aluminum mask, selectively switching irradiated regions from hydrophobic to hydrophilic.

Because birefringence can be induced and erased optically in azobenzene-containing films, one potential application for these photoswitches is surface relief gratings. These gratings can be produced by irradiating the film with an interference pattern, inducing a sinusoidal volume change, which results in a sinusoidal change in height of the polymer film. This application is limited to polymeric thin films due to the
mass transport required for grating formation. The grating pattern can be erased upon heating the polymer above its glass transition temperature. A variety of polymer thin films have been used for surface relief gratings, including an epoxy-based polymer, polyesters, polyacrylates, polymethacrylates, and other polymers.

1.2.2 Azobenzene Photoswitches – Colloidal Substrates

Azobenzene functionalization has been extended to colloids, both by surface functionalization and by controlled colloid formation from azobenzene-containing polymers. Gold nanoparticles have been functionalized with azobenzene-containing ligands that undergo photoisomerization. The photoisomerization was used to control nitrogen gas permeance in a gas separation membrane consisting of azobenzene-functionalized gold nanoparticles. Azobenzene-functionalized calix [4] resorcinarene groups were adsorbed onto the surface of silica particles. Upon UV irradiation of a suspension of particles in cyclohexane, the particles precipitated; the particles re-dispersed upon visible light exposure, which demonstrates the reversibility of this system.

Azobenzenes functionalized with aromatic polyether dendrons have been grafted to silica particles previously functionalized with 3-triethoxysilylpropylisocyanate via carbamate formation, and the rate constant of cis to trans isomerization was shown to decrease by a factor of four with increasing dendron size from the first to third generation. The confinement of azobenzenes within the nanopores of the silica particles resulted in a noticeable effect of the dendron tether size on the mobility of the
azobenzene groups upon light exposure.\textsuperscript{34} Effecting a dramatic change in molecule movement could be used in potential applications such as light-induced encapsulation.

The photoreversibility of azobenzenes also has been utilized within colloidal crystals, combining the properties and structure of the crystal with the photoswitchability of azobenzenes. In one example, a crystalline colloidal array was polymerized within a hydrogel matrix in which an azobenzene moiety was attached covalently.\textsuperscript{4b} Photochemical analysis of the photonic crystal demonstrated a photochemically driven diffraction switching upon irradiation with UV light. Azobenzene photoisomerization resulted in a change in dipole moment, which increased the free energy of mixing, leading to a red shift of ca. 15 nm of the embedded diffraction. This is the first example of direct control over the wavelength of photonic crystal diffraction using light in water. While response of the material is relatively slow, and the diffraction shift is small, the material functions as a novel recordable and erasable memory device. In another example, the incorporation of azobenzene groups as cross-linking agents reverses the observed effect; conversion to the \textit{cis} isomer resulted in a blue-shift of ca. 10 nm of the photonic crystal diffraction.\textsuperscript{35} Incorporating an azobenzene-containing polymer layer during colloidal crystal growth resulted in a planar defect that could be controlled using UV irradiation.\textsuperscript{36} Including azobenzenes at the surfaces of photonic crystals could potentially be used in recordable and erasable memory devices, although the thermal back reaction would limit temperatures at which memory storage would be preserved.

Azobenzene-containing polymers can be condensed into latex particles by the slow addition of a poor solvent, resulting in gradual aggregation promoted by hydrophobic interactions. In one example, the particles were deposited on a silicon
wafer. Subsequent exposure to 488 nm plane-polarized light resulted in a deformation of the spheres into ellipsoids in line with the polarization direction of the expanded laser beam.\textsuperscript{37} Exposure of an azobenzene-containing polymer to plane-polarized light resulted in a deformation in alignment with the polarized light as shown in Figure 1.1. Varying the ratio of the two polymers allowed for tailoring of the photoresponse. The colloidal spheres were thought to have a core-shell structure: the hydrophobic (poly(2-[4-(4-ethoxyphenylazo)]acrylate)-co-poly(acrylic acid)) PEAPE forms the core while the hydrophilic (a bisphenol-azo epoxy) BP-AZ-CA forms the shell. The degree of deformation depends on the ratio of the two polymers, increasing with increasing BP-AZ-CA composition.\textsuperscript{38} Ultimately, azobenzene polymer colloids can be synthesized in a controlled manner with an attenuable response to irradiation, yielding photoresponsive building blocks for further incorporation into more complex materials.

Lambeth and Moore utilized the functional group compatibility of ring-opening metathesis polymerization (ROMP) to synthesize polymers incorporating nitro-substituted azobenzenes.\textsuperscript{39} A norbornene-based monomer was prepared from coupling of exo-2-norbornene-5-carboxylic acid with a terminal alcohol-functionalized azobenzene. The monomer was polymerized with 3\textsuperscript{rd} generation Grubbs’ catalyst to form the azobenzene-containing polynorbornene. The polymer was cast as a thin film and irradiated with plane-polarized light with a periodic interference pattern. A sinusoidal diffraction grating was observed by atomic force microscopy (AFM). Isotropic particles cast onto a glass slide were transformed to ellipsoid-shaped particles upon irradiation with plane-polarized light. The particles were characterized by scanning electron microscopy (SEM) before and after irradiation, and were observed to elongate
in the direction of polarization with exposure time. This method combines the versatility of ROMP with the photoresponsive behavior of azobenzenes, opening the door to a variety of azobenzene-containing polymers to tailor response of the materials for incorporation into more complex structures.

Although azobenzene is widely used as a photoswitch, the thermal back reaction can impose limitations for using azobenzenes in applications. It may be possible, however, to lock the cis conformation through hydrogen bonding, steric effects, or covalent bonding of the azobenzene terminus. Preparation of the “locked” cis conformer would be useful due to the added degree of control. Progress towards this goal has been reported, although no complete inhibition of the cis-trans isomerism has been observed. ⁴⁰

1.2.3 Spiropyran Photoswitches† – Planar Substrates

Spiropyrans (SPs) have been studied as reversible photochromic systems in which exposure to UV light (ca. 366 nm) initiates a ring opening isomerization of the

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† In the preparation of a variety of SP derivatives, the authors have developed some useful methods for synthesis and purification of SP derivatives. Some of these methods have been published, but we feel it necessary to bring attention to them, the first of which is the synthesis of indolenine salts. Typically, these are prepared on large scale (multi-gram), and the use of a Soxhlet extractor for repeated rinsing of the bromide salt is a simple means to obtain reasonably pure material on a large scale. On the synthesis of spiropyran, one may choose to use an ethyl alcohol linker from the indolenine nitrogen. While this route can be used to obtain SP monomer in reasonable yield, the propionic acid linker is much easier to recrystallize (using small amounts of methanol in hexane) and ultimately can yield excellent crystals of the product monomer with less autopolymerization issues (using methacrylic acid vs. methacryloyl chloride to prepare SP monomer). The ability to scale these molecules is a requirement for extending their applications to functional materials. While previous work has shown the utility of SP-functionalized colloids and surfaces for patterned substrates on the small scale, a reproducible and scaleable synthesis is required to make the materials more readily accessible.
colorless SP to the highly colored merocyanine (MC) form.\textsuperscript{41} This ring opening is reversible both by heating and upon exposure to visible light (ca. 550-600 nm). A large body of research has been focused on incorporating SPs into functional materials. SPs have been incorporated into various polymeric materials to yield a wide range of photoresponsive materials.\textsuperscript{17b, 19c, 42} SPs have been utilized in biological applications,\textsuperscript{43} nonlinear optics,\textsuperscript{16a} reversible optical memory,\textsuperscript{44} and optoelectronics.\textsuperscript{45}

Incorporating photoreversible groups within a polymer matrix, a photoresponsive polymer membrane was synthesized by grafting a copolymer of ca. 5 mol % SP monomer onto a porous membrane. Irradiation of the SP resulted in a chain contraction from the ring opening isomerization, which altered the pore size and increased the permeability of the membrane. A polytetrafluoroethylene (PTFE) membrane was grafted by conventional free radical polymerization with a methacrylate-functionalized SP and acrylamide.\textsuperscript{3a} Irradiation with UV light resulted in an increase in permeability of 125\% for a 10 vol \% solution of water in methanol, suggesting that the pore sizes of the membrane are larger upon conversion to the MC form. The permeability of the membrane was reversed six times upon alternating exposure to UV and visible light. To achieve a photoresponsive membrane for organic solvents, a copolymer of SP and MMA was grafted from a porous glass filter.\textsuperscript{3b} Upon UV irradiation, the membrane was permeable to toluene, due to the collapse of the polymer chains. Because both the SP and MC non-grafted polymers are soluble in DMF, the polymer-grafted filter showed no change in permeability for DMF upon irradiation. In another example, a molecular valve – a channel protein from \textit{E. coli} modified with SPs – was imbedded in a membrane, and showed reversible opening and closing upon UV and visible irradiation, respectively.\textsuperscript{46}
Controlled free radical polymerization reactions, such as atom transfer radical polymerization (ATRP), have been used to graft random copolymers of SP monomers with MMA onto surfaces to obtain photoswitchable planar substrates and colloids. In one example, polymer brushes were grafted onto glass surfaces to create reversible photoswitchable optical sensors by utilizing the complexation of the open MC zwitterion with metal ions. The irradiated polymers were exposed to 25 mM metal ion solutions and were air-dried. When the complex was irradiated with visible light in a non-polar solvent, the metal ion dissociated and the ring closed. The UV-vis absorption spectrum of the MC polymer decreased and blue shifted depending upon the metal ion complex, and thus the color of the polymer film changed. The system was reported to be reversible through three cycles.

Bell and Braun have characterized the photoresponsive properties of SP-functionalized surfaces. Both silica colloids and quartz cover slips were coated by grafting a random copolymer of a methacrylate-functionalized SP with MMA (SP-co-MMA) for surface patterning as shown in Figure 1.2. The photoswitching of SP to MC was accomplished using a laser scanning confocal microscope either by standard one-photon absorption of 366 nm light or by two-photon absorption of 780 nm light. After patterning, the refractive index and thickness of the polymer film changes. Confocal microscopy can be used in reflectance mode to image the resulting pattern. Reflectance imaging was performed at 458 nm, to utilize the minimum in the MC absorption spectrum and thus minimize the ring-closing back reaction. The patterned substrates were exposed to SP-co-MMA functionalized colloids at very low flow rates over the patterned quartz cover slip, resulting in settling and diffusion of the colloids. To remove
non-adsorbed colloids, the substrate was rinsed with toluene and dried under a nitrogen stream prior to imaging. Particles were adsorbed selectively on the irradiated MC areas on the substrate as shown in Figure 1.2.

1.2.4 Spiropyran Photoswitches – Colloidal Substrates

Colloids have been functionalized with SP groups, either by small molecule functionalization or incorporation of a grafted polymer. In one example, aminopropyl-functionalized silica colloids were functionalized with small molecule SPs. The SP-functionalized particles were stable in organic solvents, and reversibly aggregated upon exposure to UV light. Altering the alkyl spacer between the SP group by changing the silica surface from ethyl to decyl resulted in an increase in the thermal decoloration rate by a factor of ten due to increased mobility of the SP.

Bell, Lewis, and Braun have used two-photon directed laser writing to create 3D structures from photoswitchable colloids. SP-co-MMA-functionalized silica colloids formed a dense suspension by sedimentation of the particles dispersed in toluene. Upon irradiation with a near-IR laser (780 nm) at high intensity, the SP moieties switched to the MC conformation under two-photon absorption, resulting in particle flocculation. Unexposed particles could be washed away to give a 3D structure, as shown in Figure 1.3. Even after reversal of the photoswitching, the particle aggregates remained stable without significant mechanical agitation. The photoisomerization was limited to the focal volume of the Ti/Sapphire laser where the flux was sufficiently intense for two-photon absorption to occur, which allowed for 3D control of the structure. Non-irradiated particles were removed by rinsing, and thus a continuous path was
required for their removal. The particles were imaged by reflectance mode confocal microscopy due to the change in index of refraction, absorption coefficient, polymer-brush conformation upon irradiation, and fluorescence of the MC form in glassy media. The structures could be transferred to tetrahydrofuran, ethanol, or water, and were broken apart slowly with agitation in toluene or tetrahydrofuran due to slow conversion of the MC to the SP form. The structures were dispersed by vigorous agitation, and the particles could be harvested and reused. The minimum feature size achievable by this technique was ca. 5 µm, which was limited by colloid diameter and adhesion coefficient (preference for non-irradiated particles to adhere to irradiated surfaces).

Although SPs have been utilized successfully in functional materials, their conformational reversibility may limit their use in some applications. The MC form relaxes thermally to the SP form; however, this process can be eliminated by chelating divalent metals or in some cases by performing the ring opening in the presence of a strong base. Thus, in some applications, a reversible system may be made non-reversible. Additionally, SPs in general are not commercially available, and complex systems must be prepared through multi-step syntheses. Complicated syntheses can be used to tailor the chemistry of functionalized surfaces; however, it may limit the accessibility of some applications.
1.2.5 Other Reversible Photoswitches – Planar Substrates

Other photoactive reversible compounds have been synthesized and studied. Here we will discuss briefly stilbenes, spirooxazines, fulgides, and diarylethenes.

Stilbenes undergo a *trans* to *cis* photoisomerization similar to azobenzenes. The $\pi$ to $\pi^*$ excitation from the *trans* configuration results in twisting about the ethylenic bond to produce the *cis* configuration. Stilbenes have been studied extensively as small molecules\(^{56}\) and in polymeric materials where the stilbene is incorporated in a random copolymer,\(^{57}\) as well as and other systems.\(^{58}\) Langmuir-Blodgett films have been used to study changes of the pressure-area isotherm as a function of photoisomerization of a stilbene amphiphile.\(^{59}\) Interestingly, the photoisomerization process induced a monolayer melting process that was monitored by fluorescence microscopy.

Photoisomerization of stilbene SAMs on Au\(^{60}\) has been reported to compete with photodimerization.\(^{61}\) Both processes can provide control over electrochemical and surface energy properties of the substrate.

Spirooxazines (SOs) have garnered interest due to their optical response because it is comparable to spiropyrans.\(^{44}\) SOs also have been investigated because they have higher fatigue lifetimes relative to SPs, and have much faster ring opening and ring closing reaction rates, the closing reaction of which is immediate upon the removal of UV light.\(^{62}\) In one example, blended SO and PMMA were cast as a thin film. The MC form was aligned by irradiation with a 632.8 nm laser to create a photo-induced birefringent film.\(^{63}\) This alignment was used to create polarization holographic gratings.\(^{64}\) The polymer thin film also has been used as a UV optical waveguide-type sensor.\(^{65}\) In another example, SO was encapsulated in mesoporous organosilica films,
resulting in the combined photoresponsive properties of the SO groups and the mechanical properties of the silica films.\textsuperscript{66}

Fulgides have been investigated due to their “true” photoreversibility. The back reaction is thermally forbidden by orbital symmetry rules, so both the ring opening and ring closing reactions only occur upon light irradiation. However, fulgides exhibit a non-desirable side reaction – an \textit{E}-to-\textit{Z} isomerization – which competes with the desired reaction that results in color change from ring closure.\textsuperscript{12} Fulgides have been investigated as molecular switches\textsuperscript{67} and in optical recording memory as small molecules and in polymer films.\textsuperscript{68} Fulgides have been incorporated into polymer films as dopants in polymers such as PMMA.\textsuperscript{69} Using three fulgides as dyes in a PMMA film coated on poly(ethylene-terephthalate), a full-color rewritable film was prepared. Full color images were prepared by irradiation with white light using a positive mask and could be erased in under ten minutes with UV light.\textsuperscript{70} The films were repatterned using a different mask, and significant degradation was not observed until 18 cycles.

Diarylethenes with heterocyclic rings, such as dithienylethene, have been developed as thermally irreversible and fatigue-resistant photochromic compounds.\textsuperscript{67b} The introduction of 2-substituted heteroarene moieties eliminates the low thermal stability of the dihydro form, which had previously limited the applicability of the reversible photocyclization reaction. Dithienylethenes undergo a ring closing upon exposure to UV light. The cyclization and ring-opening reactions can be repeated $10^4$ times while maintaining the photochromic functions.\textsuperscript{12} The properties of dithienylethenes have facilitated their incorporation into materials as molecular switches.\textsuperscript{67a}
1.2.6 Other Reversible Photoswitches – Colloidal Substrates

Other reversibly photoactive moieties have been used to functionalize colloids. A dithienylethene was used to create organic nanoparticles that demonstrated reversible photochromism. Gold nanoparticles have been capped with a stilbene ligand. In another example, a thin film of fulgides was deposited onto a patterned substrate. A templated substrate with cylindrical holes was used, and controlled dewetting resulted in formation of fulgide nanodots of < 500 nm diameter. The dots were imaged using a confocal microscope. The fulgide dots formed a regular hexagonal array arrangement, and each location could be photoisomerized and read for memory applications with a higher density of memory than current optical storage technology.

Colloids have been functionalized with SOs, or the comparable SPs. In one example, either SP or SO was covalently bound in the pores of mesoporous silica particles. The particles were incorporated into latex films that became colored upon UV irradiation, indicating a transition to the open MC form. In another example, SO was encapsulated with the dye 4-(dicyanomethylene)-2-methyl-6-(p-dimethyl-aminostyryl)-4H-pyran, and an emissive assistant molecule (1,3-di(pyren-1-yl) propane), and was formed into particles by rapid injection into water. Upon UV irradiation, the SO opened to the MC form, effectively quenching the emission from the encapsulated dye. With visible light irradiation, the MC reverted back to the closed SO form and became fluorescent. The particles also can be dispersed in a polymer film. SO-functionalized methacrylate was copolymerized with methyl methacrylate by emulsion polymerization to prepare microspheres. The SO groups were located on the surface of the particles, as determined by XPS, which allowed for a change in the surface charge upon
conversion of the SO groups to their MC form. This property allowed for selective adsorption of bovine serum albumin to the MC form, demonstrating the potential utility of control over surface charge and polarity for biological applications.\textsuperscript{76}

In general, these photochromic moieties have not been studied extensively for film and colloid applications. It is possible however, that these molecular switches and others not mentioned here could be useful for a variety of applications involving the modification of thin films and colloids, ranging from optical to biological materials. While some of these photophores are not commercially available, generally the syntheses are not difficult, and the chromophores have been studied thoroughly in solution.

1.3 Irreversible Photoresponsive Surfaces

In addition to reversible surface modifiers, irreversible photoactive modifiers – or molecular photofuses – are important targets for responsive systems. While several examples of chemical moieties have been demonstrated as molecular photofuses, only two have seen widespread use in photoresponsive materials. The first is the o-nitrobenzyl group, which has been incorporated in a diverse array of applications. These molecular photofuses are activated by UV light, whereupon cleavage of the benzyl carbon-oxygen bond occurs, leaving a carboxylic acid group and a nitrosaldehyde (Table 1.3).\textsuperscript{77} Coumarin molecular fuses, a subset of the general class of arylmethyl photofuses, also undergo heterolytic bond cleavage of the 4-methyl carbon-oxygen bond. The mechanism has been characterized as solvent-assisted photoheterolysis\textsuperscript{78} and produces highly fluorescent 4-(hydroxymethyl) coumarin as well
as a carboxylic acid, sulfonic acid, or phosphonic acid from the corresponding carboxylate ester, sulfonate ester or phosphonate ester, respectively. Other molecular fuses have been studied in solution, which also display the potential for applications in photoresponsive materials. These alternative fuses will be discussed briefly.

1.3.1 O-nitrobenzyl Photofuses – Planar Substrates

Previous use of o-nitrobenzyl (NB) derivatives as photodeprotection moieties in biological applications prompted a large number of studies on its photocleavage mechanism in solution. The NB group is a useful protecting group in organic synthesis due to its mild, UV light-assisted deprotection conditions, which are orthogonal to most other protecting groups. It is thus used to protect a variety of functional groups, including carboxylic acids, phosphates, alcohols, thiols, phenols, and amines. In biological systems, the NB group has been used to protect sugars, adenosine triphosphate (ATP), peptide residues, and other biologically relevant compounds effectively. For surface modification, these protected functionalities can provide an array of masked reaction sites and surface charges, as well as vehicles for the control of self-assembly. Here we highlight the development of the NB photofuse for its use in surface modification.

The first reported use of NB photofuses in surface modification involved the preparation of an array of various peptide sequences on a planar substrate. Using the nitroveratryloxycarbonyl (NVOC) photofuse, masked primary amines were liberated on NB cleavage upon exposure to 365 nm light. The free amines reacted the NVOC-peptides via N-hydroxybenzotriazole (HOBt) peptide coupling. This sequence was
repeated to create pentapeptides grafted from the surface. Fluorescence microscopy was used to detect fluorescently labeled antibodies that selectively coupled to specific peptide sequences, thus confirming proper sequencing. The technique then was extended using a complex series of masking and HOBt couplings to fabricate a 1.6 cm² area containing 1024 different peptide sequences, as imaged by fluorescence microscopy (Fig. 1.4). Selectively photopatterning and subsequently reacting modified regions on a substrate dramatically increases the number of detectable analytes in a given area. The premise of this work is promising for multi-analyte detection in small devices.

In addition to solid phase applications, NB photofuses also have been used in the manipulation of cells. Maeda et al. used the photochemical reactions of NB groups to alter the cell adhesion properties of surfaces. In this work, an NB-modified surface was covered with bovine serum albumin\textsuperscript{90} or a pluronic\textsuperscript{91} which both resisted cellular adhesion. Exposure of the surface to 365 nm light was followed by treatment with the cellular adhesive fibronectin, which allowed for site-selective adhesion and mobility of cells only in the areas exposed to UV light. The ability to control cellular deposition onto a substrate can potentially aid in the study of intracellular communication, cellular dynamics, and other related multicellular processes.

Although NB photofuses have been primarily used for biochemical protecting groups or for control of the deposition of biological systems on surfaces, these fuses have also been used in device fabrication in nonbiological systems. One such case by Zhao used the NB photofuse to control surface energy within microfluidic devices.\textsuperscript{92} Controlling the difference in surface energy at specific locations using functionalized
NB-modified surfaces permitted the fabrication of a “virtual” barrier that allowed for the control of laminar flow and liquid/air interfaces within the confined microfluidic channels. Fabrication of such a system could have been accomplished with a simple flow-through approach, but alignment issues of the final assembly would have proven very difficult. Utilizing the photochemical response of the NB system along with simple photolithographic techniques permits a high degree of control over spatial orientation in a single UV exposure, thus greatly simplifying fabrication.

1.3.2 O-Nitrobenzyl Photofuses – Colloidal Substrates

To the best of the authors’ knowledge, the only report of a directly NB-functionalized colloid is work by Moore and coworkers. This demonstration utilized the photochemical cleavage of the NB photofuse to control electrostatic colloid-colloid interactions.¹ The photofuse was designed to undergo a charge inversion (positive to negative) upon exposure to UV light. The positive charge is created by a protonated terminal amine, which was originally protected with the acid-labile tert-butoxycarbonyl (Boc) group during the deposition process and subsequently deprotected and protonated after deposition. The opposite end of the NB photofuse contained a terminal alkene that was hydrosilylated using Karstedt’s catalyst and chlorodimethylsilane. Colloidal silica was then modified with the NB-modified silane. After acid-promoted deprotection and protonation of the Boc-protected amine, analysis of a binary mixture of positively charged particles and bare, negatively charged silica by confocal microscopy indicated a self-supported, open, gel-like network. Sedimentation of this binary mixture was limited due to the electrostatic attraction of the oppositely charged particles. Upon
UV exposure, the photocleavage reaction produced negatively charged silica particles due to the newly formed surface carboxylate groups. The particle charge inversion eliminated the particle-particle attraction, thus forming a fluid-like suspension, as supported by further sedimentation (relative to the non-exposed system) as well as confocal microscopy studies of the sediment.

Although the photocleavage of NB moieties is generally selective, there are a few problems associated with their use. First, the aldehyde resulting from photocleavage can potentially react with various functional groups, leading to unwanted byproducts. The phenylnitroso product formed during photocleavage is highly reactive and can limit the application of this photofuse in biologically compatible systems. In addition, the phenylnitroso group can dimerize to form an azobenzene moiety, which strongly absorbs at the same wavelength as the photofuse (365 nm), leading to reduction in quantum efficiency. Secondly, the exposure times required for complete conversion of a NB-modified surface can be quite long compared to more efficient photochemical reactions — sometimes on the order of minutes under the same exposure conditions. A more ideal photofuse would react rapidly and efficiently to produce products which are chemically inert to the relevant application. Pfleiderer and co-workers have reported a 10-fold increase in photocleavage reaction rate by addition of a methyl group on the benzyl carbon. They proposed that the α-methyl group increases the efficiency of the proton transfer.
1.3.3 Coumarin-based photofuses – Planar Substrates

The historical progression from biological protecting groups to photochemical surface modifiers is clear for NB systems. Given the similar progression of photolabile coumarins from solution-based studies to biochemical protecting groups, the coumarin is a likely candidate for use in surface modifications as a photoresponsive agent. Understanding the solution-based reactivity of these photofuses is a prerequisite to using them on surfaces where characterization methods for chemical reactions are often limited in comparison. Therefore, it is not surprising to see the same general pattern of development for new photofuses with more favorable characteristics. The 4-yl-methyl coumarin moiety is a well-established photolabile protecting group.\textsuperscript{77, 93, 97} Recently, 4-yl-methyl coumarin photofuses have been explored as surface modifiers.\textsuperscript{8} Here, we briefly describe the solution based studies, which is followed by the incorporation of these coumarin photofuses onto planar surfaces and colloids.

The photochemical reactivity of coumarins in solution has been well-documented by Bendig \textit{et al.}\textsuperscript{78, 98} Excitation of the weakly fluorescent 4-yl-methyl coumarin ester derivative at 330 nm results in heterolytic bond cleavage of the 4-methylene carbon and the attached heteroatom. The mechanism was initially thought to be homolytic,\textsuperscript{99} but more recently there has been significant evidence to the contrary.\textsuperscript{78, 98a, 100} Specifically, when the photocleavage was performed in the presence of H\textsubscript{2}\textsuperscript{18}O, only the 4-(hydroxymethyl) coumarin contained the isotopically labeled oxygen atom after photocleavage, which is suggestive of an ion pair mechanism. In addition, if the homolytic mechanism were active, H-abstraction from solvent would form 4-(methyl) coumarin; however, this product is not observed in any appreciable quantity. The
increasing leaving group ability of the resulting alcohol is also suggestive of the heterolytic mechanism. Despite the consistency of these experimental results with a heterolytic cleavage mechanism, these data do not preclude a mechanism in which homolytic bond cleavage is followed by a single electron transfer to create the proposed caged-ion pair.

Upon photoexcitation of the coumarin ester, the excited-state intermediate escapes from the solvent cage, and the coumarin undergoes solvolysis with any nucleophilic solvent; water is most commonly employed. The resulting photopродuct, 4-(hydroxymethyl) coumarin, is highly fluorescent and is generally water soluble. Other products of photocleavage depend on the desired functionality, similar to the NB photofuse. Protected functional groups have included amines (via a carbamate linkage),\textsuperscript{101} alcohols (via a carbonate linkage),\textsuperscript{102} acetals,\textsuperscript{103} carboxylic acids,\textsuperscript{78, 101a} sulfonic acids (via a sulfonate ester linkage),\textsuperscript{104} and phosphonates (via a phosphonic ester linkage).\textsuperscript{95, 105}

The photocleavage reaction of coumarins in solution occurs quickly, with rate constants that are typically 2-3 orders of magnitude faster than the NB systems (ca. $10^6$ s\textsuperscript{-1} for NBs and ca. $10^9$ s\textsuperscript{-1} for coumarins).\textsuperscript{97b} The overall rate is a function of the quantum yield and light intensity, polarity of the environment, and structural features of the photofuse. Generally, coumarins are thought to react more quickly due to the direct conversion of the excited singlet state to the solvolysis product as opposed to going through the long-lived acid-nitro intermediate, as is the case for NB photofuses.\textsuperscript{97b} The absence of reactive products and the increase in reaction rate make the coumarin system rather appealing for use in surface modification.
A few papers have reported the incorporation of coumarin photofuses onto surfaces. Only recently have coumarins been used on surfaces in conjunction with NB groups to create a dual-wavelength responsive monolayer. The (7-diethylaminocoumarin-4-yl) derivative was used because it has a maximum absorption intensity at 390 nm that does not overlap significantly with the absorption of the NB group at 345 nm. Irradiation at 412 nm selectively cleaved the coumarin monolayer generating a free amine labeled with a fluorescent dye. Further exposure at 345 nm cleaved the NB group that was also tagged with a dye. The resulting bifunctional substrate was imaged using fluorescence microscopy. Although the coumarin and NB have a significant absorption coefficient at 345 nm, selective photocleavage was possible at 412 nm.

Expanding on this previous report, the efforts in our labs are intended to broaden the current uses of surface modification using the coumarin photofuse. Using a divergent synthetic scheme, both the initial and final surface functionalities can be easily incorporated to accommodate specific applications. For example, the simple case of the change from a hydrophobic to hydrophilic surface involves functionalizing the coumarin core with a hydrophobic tail at the C7-position. Further modification at the 4-methyl position of the coumarin to form an ester (carboxylate or sulfonate) with a terminal alkene attached renders the coumarin photoactive and allows for surface modification. The terminal alkene can undergo hydrosilylation with silane coupling agents (trichloro, chlorodimethyl, triethoxy, etc.). After monolayer formation, the contact angle of the hydrophobic surface (ca. 106 °C) changes upon UV exposure to a more hydrophilic surface (ca. 45 °C). By utilizing a divergent synthesis along with different
termini that are relatively easy to prepare, a wide variety of transitions are possible, *i.e.* a surface chemistry toolbox (Fig 1.5). These photochemical transitions can be used to produce a variety of surface-based transitions for simple patterning, biological labeling/isolation, microfluidics, or applications requiring controlled conversion of a light-accessible surface.

Using the scheme described above, an application–specific coumarin core was designed to be easily monitored. In this case, a coumarin-functionalized substrate was switched from a hydrophobic surface to a hydrophilic surface upon irradiation. 6-Bromo-7-hydroxy-4-methyl-2H-chromen-2-one was used as the central moiety; the bromine atom on the coumarin allowed for imaging of the coumarin moiety via secondary ion mass spectrometry (SIMS). Although the absorption properties of the brominated vs. the non-brominated derivative are slightly different ($\lambda_{\text{max}} = 375$ vs. 330 nm for the brominated and non-brominated coumarins, respectively), the quantum efficiencies and rates of photocleavage are similar. A hydrophobic tail was used to functionalize the 7-position of the coumarin to create an initially hydrophobic surface. The 4-methyl position was oxidized to the corresponding alcohol and was subsequently esterified with prop-2-ene-1-sulfonyl chloride. A trichlorosilane derivative was prepared through hydrosilylation using Karstedt’s catalyst and trichlorosilane, and monolayers of the coumarin-modified silane were deposited onto silicon wafers.

Exposure of the monolayer on silicon through a binary photomask with a 365 nm light source (20mW/cm$^2$) followed by sonication in MeOH yields the expected patterning (Fig. 1.6). Analysis of contact angles before and after irradiation suggest that photocleavage of the surface-bound coumarin occurs ca. two orders of magnitude faster.
than a surface with a similar NB system which required ca 2 min of UV exposure (20 mW/cm²). A bromine ion SIMS image clearly showed regions of high bromine concentration where no photocleavage occurred and regions of low bromine where exposure resulted in photocleavage. Analysis of SIMS spectroscopy data also indicates the sulfur remains bound at the surface, suggesting photodegradation at the surface does not occur under these conditions. Additionally, the hydrophobic to hydrophilic conversion is easily monitored by condensation microscopy (Fig. 1.6). The behavior of these functionalized planar substrates also was supported by contact angle and ellipsometry measurements. Ellipsometry of the unexposed surface is consistent with a near monolayer with a thickness of ca. 16 Å, which is slightly less than the expected 20 Å and is presumably due to the alkyl chain tilt. After complete photoconversion, measurement of the same substrate gave a thickness of ca. 4 Å, which is consistent with the size of the remaining propylsulfonate. These results demonstrate the ability of the coumarin to be incorporated onto model surfaces. The rapid response and apparent lack of reactive products show distinct advantages over the NB systems.

1.3.4 Other Irreversible Photofuses – Planar Substrates

As previously mentioned, published work on non-reversible photoresponsive surfaces has been primarily limited to NB-based systems. Aside from work on the coumarin photofuse, alternative photoresponsive moieties are known although their surface applications have been limited thus far. Benzoin, for example, has been used as a surface-bound photoinitiator for “grafting-from” polymer brush preparation. Its incorporation into monolayer applications may be limited due to radical-forming
photodecomposition reactions. Used as a photofuse, the reactive radical formed from benzoin on the surface can inhibit complete monolayer removal by radical recombination or H-abstraction from the surrounding photofuses or solvent. Similarly, photocleavage of the phenacyl group proceeds through a radical pathway but has been successfully incorporated into polymeric thin films for patterning applications.\textsuperscript{110}

Alternative photofuses are available, but work involving their incorporation onto surfaces is still to come. For example, xanthone acetic acid derivatives have high reaction quantum yields ($\Phi > 0.6$), no detectable reaction byproducts, sub-nanosecond release rates, and molar absorptivity of 5600 M$^{-1}$cm$^{-1}$ at $\lambda = 348$ nm.\textsuperscript{111} Utilizing photofuses with faster, more easily accessible transitions, and simplified synthetic schemes promises to make useful advances for photoresponsive surfaces.

1.3.5 Other Irreversible Photofuses – Colloidal Substrates

Moore and Braun have utilized acid-labile grafted colloids for microfluidics in opal structures.\textsuperscript{112} A two-photon absorbing photoacid generator was used to alter the surface hydrophobicity of polymer-functionalized particles, resulting in high-resolution 3D microfluidic structures. Silica particles functionalized with poly(tetrahydropyranyl methacrylate) were formed into colloidal crystals. The acid-sensitive tetrahydropyran (THP) groups on the polymer cleaved, resulting in a change in surface properties from hydrophobic to hydrophilic. A small molecule photoacid generator (PAG) (octoxyphenyphenyliodonium hexafluoroantimonate) was added after the colloidal crystal formation in addition to a sensitizer and a copolymer of poly(methyl methacrylate) (PMMA) and poly(ethylene glycol methacrylate) (PEGMA) to dissolve the
PAG and sensitizer, and to index match the silica to minimize scattering from the particles. The activation of the PAG was limited to the focal volume of the Ti-Sapphire laser, allowing for 3D control and patterning. The photoacid cleaved the THP groups of the grafted polymer, and the resulting PMMA-functionalized colloids created a hydrophilic channel within the hydrophobic structure as seen in Figure 1.7. Confocal microscopy was used to image the hydrophilic channel by flowing an aqueous dye (8-hydroxypyrene-1,3,6-trisulfonate) in water through the sample. The aqueous dye selectively penetrated the hydrophilic channel, while dodecane was used in the hydrophobic areas to minimize scattering as shown in Figure 1.7. Increasing laser power resulted in an increase in effective spot size and also greater photoacid generation. Thus the actual feature width increased relative to the focal point with increasing laser power. The feature size limit is approximately 3 µm, perhaps due to the diameter of the colloids used. Although this work utilizes an acid responsive group rather than a photoresponsive group, it could easily be made directly photoresponsive by utilizing any of the photoresponsive units mentioned above.

Continued progress with non-reversible colloidal systems is underway within our group. This work involves the incorporation of a coumarin photofuse into colloidal surfaces to generate a variety of surface transitions. The variety of photofuses will create colloidal suspensions capable of fluid-to-gel, gel-to-fluid, or gel-to-crystal phase transitions. In addition, these photoresponsive colloids can be used to fabricate patterned colloids such as Janus particles or “patchy” particles with an assortment of “patch chemistries.”
1.4 Conclusions/Future Outlook

As the demand for intricacy and level of control for objects become ever smaller and more finely-tuned, so must the techniques used to create the next generation of materials and technology. The need for micro- and nano-scopic control combined with creating structures on the macroscopic level in systems ranging from biology (sensing, engineering, etc.) to optics and technology (photonics, electronics, etc.) creates a challenge that branches materials science, chemistry, and engineering and must utilize a combination of the skills of all of these areas. Top-down methods have resulted in patterned materials of undeniable function. However, as features become increasingly smaller, it will be necessary to pursue the elegance and sophistication of the bottom-up approach. While synthetic approaches currently focus on the building blocks, it is also necessary to tailor how these building blocks assemble into larger, complex, 3-dimensional structures.

Colloids are an example of one building block that has been the subject of intense investigation. The versatility of colloid synthesis and functionalization lends itself to the potential incorporation in structured materials. Highly ordered colloidal assemblies are theorized to have interesting material and optical properties. For example, the diamond lattice colloidal crystal is reported to have an unprecedented photonic bandgap. Unfortunately, the fabrication of these structures can be complicated, and resulting structures often have limited long-range order. Several recently published perspectives have highlighted the concept of self-directed assembly
of these 3D structures.\textsuperscript{115} Utilizing self-assembly may provide access to structures not previously possible and may simplify current fabrication techniques.

In order to create self-assembling systems of colloidal building blocks, a high degree of control needs to be exhibited over the regions (i.e., patches) on the particles that will drive self-assembly as well as the surface properties of these patches. The spatial orientation of patches likely will be controlled by the fabrication method used. Multiple methods are available to create patchy particles, some of which are similar to those used for creating Janus particles, (i.e., masking/unmasking, directional depositions, microcontact printing, or embedding.\textsuperscript{116} The surface composition of the patches however is currently limited to static surface modifications (i.e., permanent positive charge or hydrophobic patches). These static surface chemistries have been utilized in many reports of Janus particle preparation. The ability to control the patch composition through some external stimuli is highly desirable since it opens up many other fabrication possibilities. Of specific interest are light-responsive surfaces that can lead to a change in surface chemistry in selectively irradiated areas of particles. Utilizing the above-mentioned photoresponsive groups may lead to the development of the needed building blocks heretofore inaccessible. This is an opportunity for organic chemists, materials scientists, and engineers to collaborate their efforts to creating potentially interesting new photoresponsive materials, both from a perspective of the design of appropriate photoresponsive chemical groups, incorporation of the chemical groups onto surfaces, and design of new types of surfaces to be created.
1.5 Scope of Thesis

This thesis highlights the developments of the 4-yl-methyl coumarin photofuse as a viable alternative to the o-nitrobenzyl system. The overview of light-controlled surface chemistry was provided in this chapter. The systems are classified as either photoswitches (reversible) or photofuses (irreversible) in terms of their response to light. Each section highlights published reports utilizing the change in surface chemistry for various applications. Chapter 2 is a brief overview of surface analysis techniques. It is not intended to be a comprehensive treatment of surface analysis or a complete discussion of each individual technique. Chapter 2 simply provides background information about the techniques used within this work and provides references for further reading. Chapter 3 describes the development of the synthetic strategies and the various coumarin photofuses that were prepared to complete the surface “toolbox.” This toolbox provides multiple transitions (e.g., hydrophobic-to-negative, positive-to-negative, etc.) upon exposure with UV light. Experiments are presented which demonstrate proof-of-concept for these various transitions. Chapter 4 is a collaborative work with the Nuzzo group that utilized greyscale photolithography masks in combination with the coumarin photofuse to create chemical gradients. Various imaging techniques were used, some of which required specific design of the coumarin core, to demonstrate these chemical gradients. Additionally, the chemical gradients were used to create pressure sensitive microfluidic gates that agreed remarkably well with theoretically predicted values. Chapter 5 is also a collaborative work with the Braun group in which photonic crystals were functionalized and patterning was attempted. It
describes the efforts to functionalize and characterize inverse opal structures modified with the coumarin photofuses. Also, it describes the use of these inverse opals to create novel three-dimensional fabrication schemes using the coumarin photofuse as a molecular resist/template. Chapter 6 summarizes the complete works described above and briefly discusses some possible future work.
1.6 Figures

**Figure 1.1** Left – structures of azobenzene-containing polymers. Right – TEM images of colloids prepared from (a) PEAPE, (b) BP-AZ-CA, and (c) PEAPE/BP-AZ-CA after exposure to 150 mW/cm$^2$ of 488 nm Ar$^+$ laser. Copyright

**Figure 1.2** Left – grafting-from chemistry of SP-co-MMA and ring opening of SP to MC form. Right – Reflectance mode confocal images of SP-co-MMA coated cover slip (A) in toluene, (B) patterned with two-photon process, (C) after exposure to SP-co-MMA coated colloids, and (D) after drying. Copyright
Figure 1.3 Top – schematic of direct laser writing of SP-co-MMA functionalized silica colloids. Bottom – reflectance mode confocal images of 3D reconstructions of (a) colloids near the substrate, (b) after rinsing, and (c) the 3D reconstruction. Scale bars = 10 µm. Copyright

Figure 1.4 Fluorescence scan of 1024 peptide array generated by iterative coupling/masking scheme (shown on right). Copyright
**Figure 1.5** Divergent photoresponsive coumarin synthesis produces multiple transitions.

**Figure 1.6** Schematic of patterned monolayer (left), Br ion SIMS image (center), and condensation microscopy image of patterned substrate (right). \(^{106}\)

**Figure 1.7** Top – schematic of polymer functionalized colloids into crystal and subsequent patterning. Bottom – hydrophilic areas dyed green showing limit of feature sizes. \(^{119}\)
<table>
<thead>
<tr>
<th>Method</th>
<th>Process</th>
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<tr>
<td>Self-assembled Monolayer</td>
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<td>Vapor Deposition</td>
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<tr>
<td>Polymer “Grafting from”</td>
<td></td>
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<tr>
<td>Polymer “Grafting to”</td>
<td></td>
<td>123</td>
</tr>
<tr>
<td>Layer-by-layer</td>
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<td>124 125 126 127 128 129</td>
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<tr>
<td>Langmuir-Blodgett</td>
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**Table 1.1** Surface modification methods
<table>
<thead>
<tr>
<th>Photoswitch</th>
<th>Applications</th>
<th>Comments</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azobenzene</td>
<td><img src="image" alt="Azobenzene Structure" /></td>
<td>- Incomplete monolayers; reproducible contact angle changes</td>
<td>21-22</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Light-controlled water droplet motion</td>
<td></td>
</tr>
<tr>
<td></td>
<td><img src="image" alt="Azobenzene Structure" /></td>
<td>- Change in layer thickness used to “lift” Hg drop</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Controlled omnidirectional film bending with polarized UV exposure</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Controlled sedimentation due to isomerization</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Multistep preparation used to control N₂ gas permeation of glass substrate</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Polyelectrolyte defect layer results in optically tunable colloidal photonic crystals</td>
<td>36</td>
</tr>
<tr>
<td>Spiropyran</td>
<td><img src="image" alt="Spiropyran Structure" /></td>
<td>- Controls pore size of membrane</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Incorporated into channel protein to control liposome pore size</td>
<td>46</td>
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<tr>
<td></td>
<td></td>
<td>- Used as divalent metal chelator</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Colorimetric detection of various metals possible</td>
<td></td>
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**Table 1.2** Reversible photoresponsive surface applications.
<table>
<thead>
<tr>
<th>Photoswitch</th>
<th>Applications</th>
<th>Comments</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>o-nitrobenzyl</td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
<td>- BSA adheres to o-nitrobenzyl to prevent cellular adhesion</td>
<td>90-91</td>
</tr>
<tr>
<td></td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
<td>- Photocleavage of o-nitrobenzyl leaves carboxylic acid which binds fibronectin (cellular adhesive)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
<td>- Low surface energy perfluorinated monolayer to high surface energy carboxylic acid</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
<td>- Can direct fluid flow in microfluidic channels</td>
<td></td>
</tr>
<tr>
<td></td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
<td>- Binary mixture of negative and positive particles forms gel</td>
<td>1</td>
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<tr>
<td></td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
<td>- Photocleavage generates negatively charged surface, melting colloidal gel</td>
<td></td>
</tr>
<tr>
<td>4-yl-methyl coumarin</td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
<td>- Amine produced after UV exposure used to tether fluorophore for imaging</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
<td>- Hydrophobic to hydrophilic transition</td>
<td>106</td>
</tr>
<tr>
<td></td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
<td>- Bromine easily observed by SIMS</td>
<td></td>
</tr>
<tr>
<td></td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
<td>- Hydrophobic to hydrophilic transition</td>
<td>106</td>
</tr>
<tr>
<td></td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
<td>- Resulting amine can be used for post-exposure functionalization</td>
<td></td>
</tr>
</tbody>
</table>

**Table 1.3** Non-reversible photoresponsive surface applications.
1.7 References


75. Sheng, X.; Peng, A.; Fu, H.; Liu, Y.; Zhao, Y.; Ma, Y.; Yao, J., Nanotech. 2007, 18, 145707.


CHAPTER 2
Surface Analysis Techniques

2.1 Introduction

Unambiguous characterization of a surface presents an interesting analytical problem because of the small amount of material present. In the context of this work, the problem is exacerbated because initial characterization of the substrates is essential, but perhaps more important is the characterization of materials that have undergone photochemical modification on the surface. Extraordinary efforts spanning decades of research have provided some solutions to this grand challenge. However, there is no single technique that provides a complete analysis of monolayer composition; while each technique can provide useful information about the surface (i.e., spatial distribution of analyte, overall composition, or quantification of surface coverage), none produce a complete representation of the surface. In other words, no one technique will provide chemical composition, thickness, and spatial distribution of analyte contained in a monolayer; multiple techniques are required to produce a composite understanding of the surface properties. Therefore, this chapter is intended to outline and discuss the advantages and limitations of the surface analysis techniques used in this work. While some techniques are not inherently surface specific (e.g. light microscopy), modification of the substrate or special techniques used can provide information about the surface. A brief overview of each technique is provided including
the strengths and weaknesses of each method. A summary table has been provided at the end of this chapter to provide a quick-reference.

2.2 Contact Angle Analysis

The wettability of a monolayer on a non-porous surface provides a surprising amount of qualitative information about the chemical composition and structure. The ability to determine this information is based on the differences in surface energy between the substrate being probed, a droplet of liquid on the substrate, and the vapor phase surrounding the system. The well established Young’s Equation is derived from thermodynamic first principles and is defined as

$$\gamma_{SL} + \gamma_{LV} \cos \theta_c = \gamma_{SV}$$

where $\gamma$ is the surface interfacial tension (force per unit length in mN/m), $\theta_c$ is the equilibrium contact angle between the droplet and the surface, and SL, LV, and SV represent the solid-liquid, liquid-vapor, and solid-vapor boundaries respectively. This relationship assumes the surface is completely flat since surface roughness will influence the apparent contact angle. There are two different modes of measurement; advancing and receding contact angle. Advancing mode is measured by the angle on the advancing side of a rolling droplet and receding mode is measured from the receding side. Both values can be measured and the equilibrium contact angle can be calculated. However, the advancing contact angle is normally sufficient for most studies.
Commercially available systems contain a movable stage that controls the substrate position, a device to image the droplet on the surface (either a eyepiece or CCD camera), a backlight to illuminate the analysis area, and a microliter syringe to deposit a liquid onto the surface in a controlled manner. A droplet is deposited and the advancing or receding angle is measured at the tangent from the droplet surface where the droplet and surface meet (Fig 2.1). This measurement is repeated never less than three times per substrate to ensure uniform behavior across the entire sample.

Contact angle analysis provides information about surface functionalization (e.g. hydrophobicity, surface microstructure, acidic/basic group presence) through the behavior of the droplet on the substrate. For example, a surface modified with long aliphatic chains (low \( \gamma \) material) will have a high contact angle with water as the probe droplet. Conversely, a surface with polar end groups such as a carboxylic acid (high \( \gamma \)) will have a low contact angle. At times, the surface can be completely “wetted”. In other words, the surface is so polar that a contact angle is not measurable because the droplet immediately spreads over the entire substrate. Alternatively, the probe liquid can be changed to determine composition on the surface. For example, using different pH aqueous solutions can provide information about the presence of acidic groups on the surface. Additionally, contact angle hysteresis (difference between advancing and receding contact angles) can be measured to determine chemical heterogeneity on the surface.\(^1\) Although these techniques were not used in this work, many texts are available that describe their use.\(^2\)
2.3 Ellipsometry

Film thickness can be especially difficult to characterize when the dimensions in question are on the molecular order. In this case, direct observation methods become impossible and alternatives are required. Ellipsometry is a commonly used technique that measures thicknesses in the monolayer dimension by exploiting the change in the phase of polarized light after interacting with a surface. Many texts are available on the fundamentals and applications of ellipsometry including a well developed web tutorial from a major instrument manufacturer.\(^3\)

Ellipsometry requires that substrates are reflective and have well defined layers that are optically homogeneous and parallel to each other. The change in polarization is a function of the surface’s optical properties including the thickness and refractive index (simple substrates require the real portion of the complex refractive index). With these values known, an incident beam of polarized light is reflected from the sample surface. The polarization components of the reflected light are deconvoluted into parallel (p) and perpendicular (s) components. The amplitude of each component is then substituted into the fundamental ellipsometry equation,

\[
\rho = \frac{r_p}{r_s} = \tan\Psi e^{i\Delta}
\]

where \(\rho\) is the complex reflectance ratio, \(r_p\) and \(r_s\) are the amplitudes of parallel and perpendicular light respectively, \(\tan\Psi\) is the amplitude ratio between parallel and perpendicular components, and \(\Delta\) is the change in phase between incident and reflected light. There is no direct calculation from determined values of \(\Psi\) or \(\Delta\) unless the sample is isotropic, homogeneous, and infinitely thick. In most cases, a layer model
is created of the system being probed and an iterative calculation is used to compare the measured values with those calculated from known optical constants of the substrate. Since this method depends only on the phase change of light, it is not diffraction limited and permits near molecular resolution of film thicknesses. Additionally, since the measurement is based on a comparison of the phases rather than an absolute phase, it is generally regarded as robust, accurate, and reproducible.

2.4 Secondary Ion Mass Spectrometry (SIMS)

Chemical speciation of thin films is a particularly difficult analytical problem. Determining the composition of organic materials is straightforward using standard techniques such as mass spectrometry, NMR and elemental analysis. However, these techniques require the sample to be soluble or combustible, which normally prevents analysis of thin films deposited on substrates. Therefore, to analyze patterned substrates, new imaging and analysis routines are required.

Secondary Ion Mass Spectrometry (SIMS) is a surface specific technique that sputters material from a surface using a focused ion beam (e.g.: C_{60}^+, Au^+, O^-, Cs^+) and analyzes the ejected material by mass spectrometry. The sputtering process can operate in either static or dynamic mode, which refers to the ion flux at the surface. Static mode typically receives less than 10^{12} ions/cm^2 and dynamic is much higher at 10^{18} ions/cm^2. The less destructive static mode is typically used for monolayer analysis and provides both atomic and molecular fragment information. Dynamic mode is used for bulk materials and provides only atomic information. Many factors determine the
sensitivity including ion beam used, using a pulsed or non-pulsed beam, and the detector used (time-of-flight, magnetic sector, quadrupole). For example, $\text{O}^-$ primary beams are used to probe electropositive elements but have a poor focus compared to Au liquid metal ion guns (LMIGs) which can be used to probe both electropositive and electronegative elements (not simultaneous) with much higher beam focus. This results in higher spatial resolution of the LMIG primary ion beams. Additionally, the detector determines the sensitivity of acquisition; a quadrupole detector can only acquire data for single m/z ratios at once while the time-of-flight (TOF) detector is capable of simultaneous acquisition of all m/z ratios. The low secondary ion yield from static SIMS (because of the low primary ion flux required) essentially requires use of a TOF detector to maximize the collectable signal. Moreover, the transmission through a quadrupole detector is lower than TOF, resulting in a $10^4$ decrease in sensitivity relative to the TOF detector.

A system comprised of a pulsed, high-mass primary ion beam provides high atomic and molecular mass resolution (typically mAMU). When the pulsed primary ion beam is coupled with the TOF analyzer, a more detailed analysis is possible. The primary beam can be controllably rastered across the surface and reconstructed after mass detection to produce ion images rather than mass spectra alone. Each pixel of the resulting images represents an entire mass spectrum. This allows each spectrum to be processed and recompiled to show distributions of single masses. The ability to resolve the distribution of atomic and molecular species in a planar substrate has demonstrated utility in elucidating various chemical processes occurring within a monolayer.
There are few substrate limitations for SIMS since charge compensation is possible through careful control of the extraction current and focused ion beam current. The primary limitation of TOF-SIMS is the spatial resolution in the XY direction and the detection limit of the analyte. While variations of SIMS provide increases in resolution, standard operating conditions typically provide 1 \( \mu \)m resolution in the XY direction.

2.5 Scanning Electron Microscopy (SEM)

Electron microscopy techniques are generally used to probe surface topology, composition, and a variety of other surface properties. Acceleration of an electron beam onto the substrate produces multiple types of signals including x-rays or backscattered electrons (BSE), both of which provide information about the composition of the bulk material. The most common mode of operation is detection of secondary electron imaging (SEI) which detects electrons that are ejected from the substrate atoms through inelastic scattering of the incident electron beam providing primarily topographical information. Low-energy secondary electrons (<50 eV) are only emitted from the first few nanometers of the sample substrate. Thus, SEI is not surface specific but it can be used for surface analysis assuming the signal from the underlying substrate does not interfere.

Previous reports using SEM have demonstrated the utility of this technique by imaging and quantifying monolayer coverage based on the intensity of the secondary electron signal. It has been proposed that these differences arise from either a change in the work function \( (W) \) of the underlying substrate or merely to diminution of the
secondary electron yield due to a difference in the monolayer thickness. Regardless, the exact nature of these differences is still debated and differences in secondary electron intensity can be determined and compared to the monolayer coverage and composition. Therefore, SEM techniques can be used quite reliably to image monolayer patterns or in some cases quantify coverage.

2.6 Light, Fluorescence, and Confocal Microscopy

Optical microscopy is a commonly used simple imaging technique for samples requiring color imaging and do not require resolution below the optical diffraction limit. Resolution as low as 200 nm is possible with highly refined optics and special acquisition methods but 1 µm is a practical limit of the technique. While optical light uses white light as an illumination source, fluorescence microscopy typically uses UV or monochromatic visible wavelengths to selectively excite a fluorophore bound within the sample. If a surface can be selectively modified with such a dye, it can be used to indirectly determine composition in a monolayer. Alternatively, electrostatic attraction of oppositely charged particles can be used to probe surface chemical heterogeneity.

In addition to using different illumination sources, controlling the sample environment also enables unique imaging possibilities. For example, placing the sample in a high humidity environment and cooling the sample stage below the dew point can image a sample that exhibits different regions of hydrophobicity. Water condenses at different rates for the hydrophobic and hydrophilic regions. A dramatic contrast is observed between the larger droplets that are formed in the hydrophilic areas.
compared to the small droplets that form in the hydrophobic areas. This technique, known as condensation microscopy, allows one to analyze surfaces of different composition in a simple and cost-effective manner.

Efforts to increase the spatial resolution, contrast and overall image quality of standard light microscopy initially produced a more advanced imaging technique known as confocal microscopy. By excluding unfocused light from above and below the focal plane, the depth of field is severely restricted. However, acquiring images while moving the focal plane up through the sample produces images with higher overall depth of view. In some cases, the sample can be scanned over large depths (20-30 µm) to produce three-dimensional representations. The increased depth of field comes at a cost of reduction in the signal arriving at the detector since much of the light is excluded at the pinhole aperture. Typically, samples require longer exposure times to obtain good signal-to-noise ratios.

Confocal microscopy is generally used for only those samples that require a three-dimensional perspective. This includes biological samples, composites, colloidal suspensions and similar systems with information contained in three-dimensions.

2.7 Zeta Potential Measurement

When investigating colloidal systems, some standard methods of surface characterization become unavailable because the surface is curved rather than planar. This presents yet another analytical difficulty. Methods such as elemental analysis can be used, but they require either large sample sizes of a modified colloid or very high
surface area to volume ratios (which can be achieved by using smaller colloid substrates). SIMS can also be used to provide speciation at the surface using special sample mounting techniques, but it provides an incomplete understanding of the colloidal behavior in solution.

A widely used technique for measuring stability of colloidal suspensions is electrokinetic potential, also known as zeta (ζ) potential. It represents the electric potential within the double-layer that compares the slipping plane to the bulk fluid in which the colloid is suspended. For electrostatically stabilized systems, this value describes the degree of repulsion between particles. Higher values of ζ (positive or negative) indicate highly repulsive particles whereas lower values of ζ suggest electrostatic stabilization may be overcome. Therefore, it is unlikely that the suspension will flocculate if the ζ potentials are high and *vice versa*.

The measurement of ζ potentials is an electrokinetic method; it involves placing a suspension of particles in an electric field and monitoring the particle movement as a function of the applied voltage. It is not a direct measurement because raw data must be fit to theoretical models (ie: Smoluchowski theory) to obtain ζ. In the presence of an applied electric field, the particle migrates toward the electrode of positive charge with a velocity proportional to ζ. This velocity is measured using laser Doppler anemometry, which measures the frequency shift of an incident laser beam. The measured frequency shift is then related to the particle mobility, which in turn is used to determine ζ.
2.8 Thermal Analysis Methods

Due to the limited amount of analyte, thermal methods are not typically used for surface analysis; they simply do not have the mass resolution needed to detect monolayer changes. However, when applied appropriately they can provide useful information about thin films on colloidal substrates (use for planar substrates is impractical due to the limited amount of analyte). Thermal Gravimetric Analysis (TGA) monitors mass changes as a function of temperature. Applying sufficient heat to a polymer coated inorganic colloid results in oxidation of the organic material thus providing information about the amount of organic material in the sample. This of course assumes that the inorganic substrate is not simultaneously oxidized. The acquired TGA data can be used to approximate surface coverage per particle and grafting density of the polymeric material. Similarly, Dynamic Scanning Calorimetry (DSC) can detect the polymeric phase transitions on the colloid surface given a sufficient sample size. This can provide indirect polymer information as well as confirm surface functionalization.

One may also consider elemental analysis for heterogenous samples such as functionalized colloidal materials. As a general rule, elemental analysis of large particles by combustion requires more analyte on the substrate than available. However, alternative methods such as ICP-MS and halogen titrations can be used to determine extent of surface modification. For example, a bromine containing monolayer is deposited on 1 \( \mu \)m silica particles and submitted for halogen analysis. Based on the surface area of each particle, density of the particle, and initial assumptions about the
surface available for modification, one can calculate approximate grafting density of the monolayer that agrees quite well with predicted values.
2.9 Figures

Figure 2.1 Schematic of droplet on surface indicating the contact angle \( \theta_c \)
<table>
<thead>
<tr>
<th>Technique</th>
<th>Information Provided</th>
<th>Advantages</th>
<th>Limitations</th>
<th>Ref.</th>
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</thead>
<tbody>
<tr>
<td>Contact Angle</td>
<td>Surface functionality, coverage</td>
<td>Rapid, inexpensive, non-destructive</td>
<td>Surfaces cannot be rough, incomplete information</td>
<td>7</td>
</tr>
<tr>
<td>Ellipsometry</td>
<td>Film thickness</td>
<td>Accuracy, non-destructive, surface specific</td>
<td>Requires smooth, reflective surface</td>
<td>8</td>
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<tr>
<td>Secondary Ion Mass Spectrometry</td>
<td>Surface composition/distribution</td>
<td>High atomic/molecular mass resolution, imaging</td>
<td>1 µm spatial resolution (practical limit), expensive, destructive</td>
<td></td>
</tr>
<tr>
<td>Secondary Electron Microscopy</td>
<td>Surface modification, topographical info</td>
<td>Rapid analysis, may be used for quantitation</td>
<td>Contrast is function of substrate, destructive to thin films</td>
<td>4b</td>
</tr>
<tr>
<td>Optical Microscopy</td>
<td>Presence of probe modified surface, imaging</td>
<td>Good contrast, demonstrates surface modification</td>
<td>Requires surface treatment (fluorescence) or special setup (condensation)</td>
<td>6</td>
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<tr>
<td>Confocal Microscopy</td>
<td>Presence of fluorophore modified surface, imaging</td>
<td>Scanning in 3D</td>
<td>Requires surface treatment if non-fluorescent</td>
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<tr>
<td>Zeta Potential</td>
<td>Electrokinetic behavior, surface charge</td>
<td>Provides info about non-planar surfaces (colloids)</td>
<td>Variable results, “black box”, destructive</td>
<td>6</td>
</tr>
<tr>
<td>Thermal-Gravimetric Analysis</td>
<td>mass loss as a function of temperature</td>
<td>Mass coverage estimates of non-planar surfaces</td>
<td>Destructive, detection limit</td>
<td></td>
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<tr>
<td>Dynamic Scanning Calorimetry</td>
<td>Thermal transition temperatures</td>
<td>Phase change behavior on non-planar substrates</td>
<td>Destructive, detection limit</td>
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</table>

**Table 2.1** Summary of various techniques used highlighting their advantages and limitations in the context of surface analysis.
2.10 References


3.1 Introduction

Controlling colloidal surface chemistry is of general interest for applications ranging from ceramics, coatings, inks, photonics, and pharmaceuticals. Through control of the colloid surface chemistry, many material properties can be modified including electrophoretic, electrokinetic, and rheological properties. A recent demonstration, and the preliminary motivation for work contained in this chapter, was control over the electrostatic interactions between colloids.

Utilizing an o-nitrobenzyl photofuse (NB) monolayer, Plunkett et al. functionalized colloids that respond to UV light (See Chapter 1 for discussion of photofuses). Initially, the photofuse contained a primary amine that provided a positive charge at neutral pH. Upon UV exposure at 365 nm, the NB photofuse cleaved to produce a negatively charged carboxylic acid terminus on the surface. The resulting change in surface charge was used to control the aggregation state of a binary colloidal suspension. Negatively-charged rhodamine-labeled silica was mixed with the positively charged o-nitrobenzyl-modified particles to form an open gel-like suspension. The suspension was exposed with UV light at 365 nm to produce the negatively charged particles. Due to electrostatic repulsion, the suspension became more fluid-like and resulted in more densely packed sediments. However, the NB photofuse is somewhat limited in its
application for a variety of reasons. To understand these limitations, a discussion of this photofuse and its properties is necessary.

3.2 Photochemistry of o-Nitrobenzyl Photofuse

The NB group is a useful protecting group in organic synthesis due to its mild, UV light-initiated deprotection conditions, which are orthogonal to many other protecting groups. It is thus used to protect a variety of functional groups, including carboxylic acids, phosphates, alcohols, thiols, phenols, and amines. In biological systems, the NB group has been used to protect sugars, adenosine triphosphate (ATP), peptide residues, and other biologically relevant compounds effectively.

The widespread use of the NB photofuse in biological applications ultimately prompted a significant amount of work probing the mechanism of the o-nitrobenzyl photocleavage (Figure 3.1). All reported mechanisms agree on the first phototautomerization step, although the remainder of the mechanism was not fully understood until flash-photolysis studies were performed. Even with these results, some ambiguity remains in the mechanistic details. An excellent review of the o-nitrobenzyl photocleavage mechanism is presented by Givens et al. that will be summarized here. First, UV excitation of the o-nitrobenzyl ester (1) induces a hydrogen abstraction (a redox reaction) from the benzyl carbon to the nitro group to form the aci-nitro intermediate (2) via a singlet excited state. The aci-nitro intermediate was assigned by monitoring the transient absorption spectrum (both formation and decay) as a function of pH and confirmed later through time-resolved infrared (TRIR)
The existence of an equilibrium between the nitronic acid and the nitro anion (3) is consistent with the observed increase in overall rate due to the shift to reactants during low pH conditions.\textsuperscript{20h}

The next step in the proposed mechanism is the irreversible cyclization of the aci-nitro intermediate to the benzisoxazoline intermediate (4). The cyclic intermediate was determined by TRIR and laser flash photolysis studies\textsuperscript{20h} and is consistent with computational results.\textsuperscript{20e} The benzisoxazoline rapidly forms a hemiacetal (5) which quickly undergoes elimination of the leaving group resulting in the nitrosoaldehyde product (6).

Given the reactive nature of the photocleavage byproduct, it is unsurprising that there are documented examples of side reactions that occur. The original work by Barltrop reported only a 17% yield for the photorelease of the desired benzoic acid (8). This decreased yield was attributed to the dimerization of the byproduct nitroso (9) to form the highly absorbing azo compound (10) (Figure 3.2).\textsuperscript{10, 23} The azo compound competes for incident light, effectively reducing the photocleavage quantum yield. This dimerization process is likely active in most o-nitro systems. Additionally, the nitrosoaldehyde photoproduct (9) can react via nucleophillic additions with the aldehyde or via radical pathways with the nitroso group.

Efforts to reduce the nucleophillic byproducts have been reported through $\alpha$-alkylation of the benzyl carbon.\textsuperscript{23-24} The resulting photoproduct in this case is a nitrosoketone which is less susceptible to nucleophillic additions. Further complications for the use of NB photofuses arise when one considers the longer exposure times required for complete conversion as compared to other photofuses such as the 4-yl-
methyl coumarins and anthraquinone derivatives. There has been one report of a 10-fold photofuse rate enhancement of an o-nitrobenzyl photofuse through the previously mentioned α-alkylation of the benzyl carbon. The authors propose the α-group facilitates the first proton transfer step, however the rates achieved are still 2 orders of magnitude lower than other systems.

3.3 Photoresponsive Coumarins

As previously mentioned, alternative photofuses are available that do not have the same complications as the o-nitrobenzyl derivatives. Of notable interest is the 4-ylmethyl coumarin derivatives. They produce almost no reactive byproducts and have much faster rates of cleavage. The uncleaved coumarins are essentially non-fluorescent and the coumarin photoproduct is highly fluorescent (Figure 3.3, R = Me, R’ – SO₂Me Φₖ = 0.30), which provides simple access to photocleavage information through fluorescence spectroscopy. Most importantly, the coumarin core is readily prepared on large scale from inexpensive starting materials and can be modified at the 4- and 7- positions to produce a wide variety of photofuses. A divergent synthetic pathway that allows access to a variety of transitions, via similar synthetic pathways, can thus be envisaged that will enable a variety of surface modifications to be possible through this efficient and convenient photofuse (Figure 3.4).

The coumarin core can be functionalized at the 4-methyl position to produce a structure that responds irreversibly to UV exposure. Products of photocleavage depend on the desired functionality, similar to the NB photofuse. Protected functional groups
have included amines (via a carbamate linkage),\textsuperscript{28} alcohols (via a carbonate linkage),\textsuperscript{29} acetals,\textsuperscript{30} carboxylic acids,\textsuperscript{28a, 31} sulfonic acids (via a sulfonate ester linkage),\textsuperscript{32} and phosphonates (via a phosphonic ester linkage).\textsuperscript{25, 33} The general class of 4-yl-methyl coumarins are also commonly used in photodeprotection of biologically relevant compounds including glycine\textsuperscript{34}, glutamic acid\textsuperscript{35}, cyclic-(adenosinemonophosphate)\textsuperscript{25}, and other nucleobases\textsuperscript{27}.

The photochemical reactivity of coumarins in solution has been well-documented by Bendig \textit{et al.}.\textsuperscript{31, 36} Excitation of the weakly fluorescent (R = Me, R’ – SO\textsubscript{2}Me $\Phi_f = 0.007$)\textsuperscript{31} 4-yl-methyl coumarin ester derivative (11) at its $\lambda_{max}$ (in this case, 330 nm) results in heterolytic bond cleavage of the 4-methylene carbon and the attached heteroatom. The mechanism was initially thought to be homolytic,\textsuperscript{37} but recently significant evidence to suggest a heterolytic pathway has been reported.\textsuperscript{31, 36a, 38} Photocleavage of 11 performed in the presence of $\text{H}_2^{18}$O, formed exclusively the $^{18}$O-labeled the 4-(hydroxymethyl) coumarin (17), consistent with nucleophilic addition of $\text{H}_2\text{O}$ into the proposed 4-methyl carbocation-like intermediate (16) (Figure 3.3). Additionally, if the homolytic cleavage mechanism were active, H-abstraction from solvent would form 4-(methyl) coumarin (14); however, this product is not observed in any appreciable quantity.\textsuperscript{31, 38b} Studies in which the starting ester at the 4-methyl position is varied (carboxylate, phosphonate, sulfonate),\textsuperscript{31} indicate a dependence on pK$_a$ of the leaving group on rate of photocleavage consistent with the proposed heterolytic mechanism\textsuperscript{31} shown in Figure 3.3. Despite the consistency of these experimental results with a heterolytic cleavage mechanism, these data do not preclude
a mechanism in which homolytic bond cleavage (13) is followed by a single electron transfer to create the proposed caged-ion pair.

As mentioned previously, the photocleavage reaction of coumarins in solution occurs quickly, with rate constants that are typically 2-3 orders of magnitude faster than the NB systems (ca. $10^6$ s$^{-1}$ for NBs and ca. $10^9$ s$^{-1}$ for coumarins). Generally, coumarins are thought to react more quickly due to the direct conversion of the excited singlet state to the solvolysis product as opposed to going through the long-lived aminonitro intermediate, as is the case for NB photofuses.

Briefly, the photolysis mechanism is as follows: upon photoexcitation of the coumarin ester (11), the excited-state intermediate (12) undergoes the proposed heterolytic bond cleavage to form a caged ion pair (15), escapes from the solvent cage (16), and the coumarin undergoes solvolysis with any nucleophilic solvent; water is most commonly employed. The resulting photoproduct, 4-(hydroxymethyl) coumarin (17), is highly fluorescent and is generally water soluble. The overall rate is a function of the quantum yield ($\Phi$) and light intensity, polarity of the environment, and structural features of the photofuse.

Although external factors such as light intensity and polarity of solvent are readily controlled, the quantum yield of photocleavage is also dependent on the structure of the coumarin in question. There are multiple structural variations that affect the absorption maximum ($\lambda_{\text{max}}$), molar absorptivity ($\varepsilon_{\text{max}}$), and $\Phi$. With each electron-donating substituent added, the molar absorptivity increases and a corresponding red shift in the absorption max occurs. The photochemical quantum yields for all 6- and 7-alkoxy derivatives have reported values ca. 0.1, but the 7-diethylamino coumarins increase to
ca. 0.3. Similarly, the 6- and 7-alkoxycoumarins have measured photochemical cleavage rate constants of ca. $10^8 \text{s}^{-1}$ and the 7-diethylamino coumarins are slightly higher at $10^9 \text{s}^{-1}$. (See Table 3.1.) Note that these photophysical properties are directly governed by the substituents on the coumarin (most of which are reported at the 6- and 7- positions), not by the ester that is attached to the 4-methyl position.

Table 3.1 illustrates the wide range of currently available classes of 4-yl-methyl coumarins. They span a wide range of wavelengths compared to the o-nitrobenzyl derivatives and demonstrate the first level of tunability of the coumarin photofuse. As Section 3.5 describes, functionalization of both the 7- and 4-methyl positions provide the ability to directly tune surface properties of materials functionalized with these coumarins. The ability to select the desired photochemical properties as well as the final surface properties using a divergent synthetic scheme makes its ultimate incorporation into materials applications very attractive. In addition, the absence of reactive products and the increase in reaction rate compared to the o-nitrobenzyl system offer significant improvements over other photofuses.

### 3.4 Surface Chemistry Toolbox

In order to provide full control over surface composition (and alternative applications discussed in Chapters 4 and 5), initial approaches were focused on creating a “toolbox” of chemical transitions. These would produce changes in the net surface charge from hydrophobic to negative, hydrophobic to positive, positive to negative, as well as others (Figure 3.4). These light induced transitions could be used
to control the phase of the colloidal suspension, surface hydrophobicity, or surface charge. Just as previous work has shown, a binary mixture of positively and negatively charged particles would aggregate into a gel-like state. However, if one induced a surface transition from negative to positive, all particles would have a net positive charge. The electrostatic repulsion between particles would form a fluid-like colloidal suspension. Extension of this toolbox concept from uniform to non-uniform photoconversion of the surface could be used to create attractive or repulsive patches on each particle. In principle, these chemistries could then be used to drive self-assembly of supramolecular colloidal materials or provide unique access to fabrication schemes that have not been reported to date.

The toolbox is comprised of three different levels of control. First, is the photochemical properties defined by the structure of the coumarin core as outlined in Section 3.3. Next, functionalization at the 7-position and 4-methyl position defines the properties to be provided such as negative or positive charges. Finally, the surface modification method can range from monolayer chemistry (through silane-on-silica or thiol-on-gold approaches) to polymer brushes (through surface bound initiators and polymerization of a coumarin monomer from the surface). For initial demonstration of this approach, all work contained herein utilized the silane monolayer chemistry although few modifications are required to obtain the polymeric or thiol-on-gold surfaces.
3.5 Establishing Divergent Synthetic Routes

Due to the number of desired transitions, ideally the synthetic route developed would be divergent; the coumarin core could be modified in a minimal number of steps at both the 4 and 7 positions to provide any transition. Initially, functionalization of a phenol derivative which could then be used in a Pechmann condensation to form a coumarin core was considered. However, this route is not divergent and it required that the modified phenol was stable in concentrated sulfuric acid; most groups being considered were not. Alternatively, 7-hydroxy-4-(hydroxymethyl)-2H-chromen-2-one (35) was prepared and selective functionalization of the phenol vs. the benzylic alcohol could be used to prepare the target substrates. Not surprisingly, this route suffered significant losses due to the undesired di-substitution product. This route did provide access to targets in some cases but was generally not useful. Ultimately, modification of the commercially available 4-methyl-umbellifurone was chosen which requires oxidation of the 4-methyl position using SeO₂. This route is more accessible but also limiting due to the typically low yields obtained from the oxidation reaction. The following sections discuss the synthesis and characterization of resulting surfaces that provide these UV induced transitions.

3.5.1 Hydrophobic-to-Negative Transition

A photofuse-containing substrate capable of hydrophobic-to-negative transition was selected as an initial group of target substrates. They did not require protecting group chemistry of terminal groups and seemed more likely to withstand later reaction
conditions. In the interest of providing multiple transitions a few different hydrophobic-to-negative transitions were attempted. It will be shown that these experiments proved useful in understanding the photochemistry that is possible with these coumarin derivatives and determining optimal synthetic routes.

First, a simple 7-methoxy derivative was prepared via the commercially available 7-methoxy-4-(bromomethyl)-coumarin. Hydrolysis of the bromine generated the 7-methoxy-4-(hydroxymethyl)-coumarin which could then be used to prepare the sulfonate ester (20) (Figure 3.5). The sulfonate ester was chosen since the rate of photolysis is predicted to be faster than that of the carboxylate ester.**{}**

31 Hydrosilylation of the terminal alkene produced a trichlorosilane which was used for surface modification. Planar substrates were used to optimize deposition conditions, which indicated near-monolayer coverage by ellipsometry. Subsequent deposition onto monodisperse colloidal silica produced the first photoresponsive coumarin modified particles.

The freshly prepared particles treated with coumarin (21) were analyzed by zeta potential analysis (see Chapter 2 for details on zeta potential analysis) to monitor photochemical conversion. As a baseline comparison, the zeta potential $\zeta$ of the bare silica particles in Milli-Q water measured -23 mV due to the partial ionization of the surface silanols. Particles modified with coumarin (21) had measured $\zeta$ values of -26 mV. To ensure the unreacted silanol groups on the silica surface would not interfere with the $\zeta$ measurement, coumarin-modified colloids were also treated with trimethylchlorosilane to passivate the underlying silica surface. No statistically significant change in $\zeta$ was observed. After exposure of particle suspensions in water, the uncapped and capped silica measured $\zeta$ of -40 mV and -44 mV, respectively. This
large increase is consistent with the increase in negative charge from the newly formed sulfonic acid on the surface after UV exposure. These results demonstrated, at least initially, that photochemical conversion of the surface occurred. A time series was attempted to monitor the progress of the surface conversion, but even very short UV exposure times resulted in the same $\zeta$, regardless of exposure time. One of three problems was occurring: $\zeta$ measurements were inherently flawed ($\zeta$ results are not always reliable due to unexplained variations in measurement), the $\zeta$ measurement is unable to resolve these small changes (a positive to negative $\zeta$ transition would be easier to observe), or photochemical reaction at the surface was not occurring as expected.

Attempts were made to monitor the photochemical reaction of the particle suspensions by UV-Vis spectroscopy. An index-matched suspension of the methoxy-coumarin modified colloids was placed into a microcuvette and a spectrum was obtained. Another suspension (same concentration) was exposed to UV light (60 sec, 20 mW/cm$^2$), centrifuged and rinsed with water three times. Subsequent UV-Vis analysis of these particles showed an increase in absorbance at 260 nm and a decrease in the coumarin absorption at 330 nm. Although the decrease in absorption at 330 nm can be explained by photocleavage of the coumarin from the surface, the increase in absorption at 260 nm could not be explained readily, but a [2+2] cycloaddition process in either an intra- or interparticle manner is currently the most likely explanation. Exposure of the particle suspension to 254 nm light increased the absorption at 330 nm, consistent with a reversible [2+2] cycloaddition. However, the absorption never returned to its initial value suggesting that some cleavage occurred.
and the [2+2] process competes with the photosolvolysis reaction. Interestingly, the [2+2] process is known\textsuperscript{40} but there are no reports of this pathway occurring with the 4-yl-methyl coumarin derivatives and its apparent competition with the photosolvolysis reaction.

Increasing the alkyl chain length was attempted to minimize the cycloaddition product. Since the [2+2] cycloaddition process is highly dependent on the orientation of the double bond close to the surface, modification of the coumarin with anything to disrupt this organization at the surface may be sufficient to minimize this photocyclization. Increasing the methyl group size to a decyl chain that can provide intramolecular van der Waals stabilization was hypothesized to eliminate the undesired cyclization.

Synthesis of the decyl derivative (25) was achieved by Williamson etherification of bromodecane with the commercially available and inexpensive 4-methyl-umbelliferone. Subsequent oxidation and same-pot reduction of the 4-methyl position\textsuperscript{†} produced the 4-(hydroxymethyl) derivative (23) that could then be esterified as previously reported. Formation of the silane (25) followed by the surface modification of colloids was performed exactly as the methoxy derivative. The UV-Vis spectrum (Figure 3.8) of the decyl-modified colloids shows the same absorption at 330 nm that decreases with exposure at 365 nm. However, exposure at 254 nm for extended periods of time (> 120 min) does not result in the increase of the signal at 330 nm. This

\textsuperscript{†} SeO\textsubscript{2} oxidation is one of few reported methods to selectively oxidize the 4-methyl group. One report used activated MnO\textsubscript{2}, however all attempts using this method failed. There are limitations of the SeO\textsubscript{2} oxidation method. Due to the active oxidant (selenious acid)\textsuperscript{41} acid sensitive species cannot be oxidized by this route without significant decrease in yield. Additionally, there are a significant number of selenium containing by-products; yields seldom exceed 50%.
suggests that no reversible cyclization is occurring. More experiments are required to determine if the alkyl chain is indeed responsible.

The decyl-coumarin particles were used to qualitatively demonstrate the faster response time of the coumarin photofuse modified silica. A suspension of the modified silica in toluene was placed over an immiscible water layer. The suspension was exposed with UV light (~ 50 mW/cm², 60 sec). Immediately, the particles aggregate out of the toluene layer and settle at the toluene-water interface. Upon standing, or mild agitation, the particles migrate into the water layer. This behavior is consistent with the non-polar decyl derivative being stabilized in toluene but destabilized (as evidenced by aggregation) after UV exposure where the particles become negatively charged.

Attempts were made to create a perfluorinated version of coumarin 25 for potential applications that will be discussed in Chapters 4 and 5. However, the etherification of 4-methyl umbellifurone with 1H,1H,2H,2H-perfluoro-1-iododecane under various reaction conditions did not yield the desired product. This is likely due to elimination occurring rather than the desired $S_n2$ reaction or the lack of driving force for the equilibrium reaction to occur. Increasing the distance between the iodo- and fluoro-groups would minimize the elimination reaction, however the relevant perfluoro compounds are limited. Alternatively, a carboxylic acid group placed at the coumarin 7-position of the coumarin (28) could enable an esterification of the perfluoro-alcohol through multiple esterification reactions after deprotection.

After preparation of 28, the esterification reaction was successfully attempted using Steglich conditions (DCC/DMAP). Unfortunately, the subsequent oxidation step was unsuccessful, yielding only starting material. Potential alternative routes were
entertained, but all had complications such as requirements for protecting groups. As a result, the preparation of a perfluorinated version of 25 was abandoned to pursue alternative transitions.

3.5.2 Positive-to-Negative Transition

One method to create a positive charge on a surface is through a primary or quaternary amine. Experience from the Section 3.5.1 assisted in the design of the synthetic pathway show in Figure 3.11. Three targets were chosen to provide the terminal amine. The first was a tertiary amine (33c) that could be converted to a quaternary amine and the other targets both provide a primary amine (33a and b) differing only by the protecting groups used (Cbz vs. BOC, respectively). First, attempts to synthesize the N,N-dimethylamino derivative involved direct etherification with N,N-dimethylaminoethyl bromide. All attempts resulted in no product formation, presumably due to the loss of starting material to form the stable ammonium bromide salt. Next, synthesis of 30c was attempted through a Mitsunobu reaction between the N,N-dimethylaminoethyl alcohol and 4-methylumbellifurone. Once again, no product was obtained and the reason for this is not immediately obvious.

Esterification of the tertiary amine has been reported although all substrates have been with carboxylic acids, not phenols. Since the previous coupling of the perfluorinated alkyl chain was successful when the electronics of the coumarin were isolated, a similar effort was made for target 30c. However, esterification of 28 with N,N-dimethylaminoethyl alcohol again resulted in no reaction. Based on the inability to
prepare the N,N-dimethylamino derivative through any pathway, the similar target substrate 32b was attempted.

First, direct esterification of the 4-methyl-umbelliferone was attempted with a commercially available N-BOC-aminoethylbromide (b) and the prepared N-Cbz-aminoethylbromide (a) using Williamson ether conditions. Both reactions proceeded as expected to produce the ethers 30a and 30b in good yield. Parallel attempts were made to prepare the extended linker (28 coupled with b) with similar success. Complications arose when attempting the SeO₂ oxidation of the resulting products. In all three cases, significant losses occurred during the oxidation step. This is unsurprising if one considers the in situ formation of seleninic acid during the oxidation has a pKₐ = 2.6. Presence of acid at temperatures > 100°C is known to remove both BOC and Cbz protected amines. However, utilization of protecting groups that are stable to these acidic conditions would complicate the ultimate deprotection once these materials were deposited on substrates. For this reason, the decrease in yield was deemed necessary and the intermediates 30a and 30b were subjected to the sulfonylation conditions to form the sulfonate esters. Sulfonylation of both the BOC and Cbz derivatives proceeded with high yields.

Formation of silane derivatives of 32a and 32b provided further synthetic complications due to either the presence of an amine or the acid-labile nature of the groups present. Hydrosilylation using trichlorosilane required fractional distillation of the starting silane to remove any residual acid. Frequently, the hydrosilylation resulted in polymerization of the resulting silane. Initially, this was attributed to in situ formation of acid due to hydrolysis of the starting trichlorosilane. However, similar complications
occurred when attempts at hydrosilylation of a triethoxysilane that does not form acid upon hydrolysis. Hydrosilylation conditions are reported to perform reductions of amides\textsuperscript{42}, however this is highly dependent on the substrate, silane, catalyst, and reaction temperature. From the above results, it appears that further investigation into the hydrosilylation reaction could result in successful synthesis of the silane for surface coupling.

Despite the limited success in preparing both 32a and 32b using the above pathway, an alternative route was explored to determine if the limiting oxidation step could be avoided. This was achieved by preparing the 7-hydroxy-4-(hydroxymethyl)-coumarin (35) prior to any modification of the 7 position. Multi-gram synthesis of the 7-hydroxy-4-(chloromethyl)-coumarin (34) is achieved through the typical Pechmann condensation of 4-chloromethyl-acetoacetate with resorcinol. Subsequent hydrolysis in refluxing water produces large quantities of the desired diol which can then be subjected to Williamson etherification conditions to prepare 31b. Not surprisingly, di-functionalized products are present but are easily removed. The advantage to this route is scalability, however losses are comparable between the oxidation and diol methods and the BOC-aminoethylbromide is quite expensive. Thus, further preparations continued using the oxidation route (Figure 3.11).

3.5.3 Negative-to-Positive Transition

Preparation of the negative-to-positive transition is straightforward using the synthetic scheme provided in Figure 3.13. Esterification of 4-methyl-umbelliferone with tert-butyl 2-bromoacetate provides 27 in high yield. Oxidation and subsequent
reduction yields the 4-(hydroxymethyl) derivative (36) in moderate yields. Treatment of this substrate with catalytic dibutyl tin dilaureate in the presence of 3-isocyanato-propyl triethoxysilane produces the desired product (37) in high yield.

To demonstrate the change in surface composition, 37 was deposited on silicon wafers and analyzed by contact angle measurements and ellipsometry. Water contact angles of as-deposited substrates measured 80° and ellipsometry indicated film thicknesses of 20 ± 5 Å. Treatment of the substrate with trifluoroacetic acid in CH₂Cl₂ caused a decrease in contact angle to 45°, consistent with the presence of a more polar group on the surface. These results suggest the acid-catalyzed deprotection of the carboxylic acid were successful.

The deprotected surfaces were then subjected to UV exposure (365 nm, 20 mW/cm², 120 sec) through a chrome photolithography mask with 5 µm lines. Immediately following exposure, the samples were rinsed with water, methanol, and blown dry with N₂. Since the exposed regions should be positively charged at neutral pH, and the surrounding regions should still be negatively charged, electrostatically labeling the substrates would indicate patterning did or did not occur. The patterned substrates were then submersed in a suspension of carboxylated 800 µm SiO₂ particles to selectively adhere in the positive regions and imaged by optical microscopy. Figure 3.14 shows the resulting image that confirm patterning occurred as intended. Conditions were not optimized for this labeling and the selectivity of labeling is not 100%, but these results are consistent with the intended charge inversion at the surface. Additionally, the application of this coumarin for photochemically patterned
monolayer resists is discussed further in Chapter 5 where its selectivity was increased to nearly 100%.

3.5.4 Hydrophobic-to-Neutral Transition

The aforementioned transitions were of primary interest due to the large change in surface composition. However, less dramatic changes in surface composition may be of interest as well. The hydrophobic-to-neutral transition was prepared to attempt direct observation of the surface heterogeneity by fluorescence microscopy. As described in Section 3.3, the uncleaved coumarin is essentially non-fluorescent but once cleaved, the 4-(hydroxymethyl)-coumarin is highly fluorescent and may be imaged directly. Synthesis of 38 required use of the diol pathway described in Section 3.5.2 because of the expected complications of oxidizing a terminal olefin. Etherification of the diol with allyl bromide yielded the desired ether in excellent yields. The alcohol was then subjected to the sulfonylation conditions to produce the hydrophobic 39. Patterning was performed through a chrome photolithography mask using standard UV exposures (20 mW/cm², 30 sec). After rinsing with hexane, CH₂Cl₂ and drying under a stream of N₂, the expected patterns were visible using the “breath test.” However, because the fluorescence microscopes available are not fitted with the correct dye filters, the fluorescent patterns could not be observed. The fluorescence emission intensity of the coumarin ca. 400 nm is well below the detectable range of the microscope used. Alternative detection schemes were not explored due to the lack of an immediate application for this photofuse.
3.6 Future Work: Negative-to-Neutral and Positive-to-Neutral Transitions

In order to complete the “toolbox” of possible transitions, the charged-to-uncharged transitions are required (Figure 16). Although preparation of these moieties was not performed, their possible synthetic routes were developed. These routes are based on the synthetic routes developed above but will require some effort to prepare the terminal charged groups. In both cases, the vinyl ether of the coumarin will be prepared as discussed above. Deprotection on the surface should be performed with TFA:CH₂Cl₂ solutions.

Synthesis of the requisite sulfonyl chlorides requires an oxidative chlorination step, which has been reported for similar systems. Both retro-synthetic pathways are shown in Figure 3.17. The thiol required for the oxidative chlorination step can be prepared simply from the di-acid which is BOC protected using standard methods and then reduced to the free thiol. The BOC-amine thiol is commercially available.

3.7 Conclusions

The o-nitrobenzyl photofuse, while firmly established in the literature, has some significant limitations as a surface modification agent. These include reactive byproducts and long exposure times required for full conversion. An attractive replacement for the o-nitrobenzyl photofuse is the general class of 4-yl-methyl coumarins. These coumarin photofuses provide no byproducts, achieve full conversion with short exposure times, and can be prepared through a divergent pathway. The
divergent pathway is especially important since it allows facile preparation of many different UV-induced transitions from the same starting materials.

This chapter discusses the photochemical cleavage mechanisms of both o-nitrobenzyl and 4-yl-methyl derivatives and provides an important comparison between them, justifying their incorporation into surface applications. Synthetic schemes for multiple photofuses for surface modification are presented along with some demonstrations of their utility. The ability to control surface chemistry using light has been demonstrated with the o-nitrobenzyl system, but significant advances are also possible with the coumarin photofuse.
3.8 Experimental

**Materials.** All materials were used as received unless otherwise noted. Anhydrous toluene and DMF was purchased from Sigma Aldrich. All water used was deionized (resistivity < 18 MΩ) and obtained from a Millipore water purification system.

**Characterization.** All $^1$H and $^{13}$C spectra were obtained on a Varian Unity 500 MHz spectrometer in the VOICE NMR laboratory, School of Chemical Sciences (SCS), University of Illinois. Chemical shifts are reported in ppm ($\delta$) using residual solvent protons as internal standards. Coupling constants ($J$) are reported in Hertz (Hz) and splitting patterns are expressed as s (singlet), d (doublet), t (triplet), q (quartet), or m (multiplet). Mass spectra were obtained on a Micromass 70-VSE using an EI source, performed by the Mass Spectrometry Labs, School of Chemical Sciences, University of Illinois. Broadband UV exposures were performed with a Novacure Spot Cure system equipped with a liquid filled light guide coupled to a collimating lens to yield a spot size of 1.3 cm. The intensity of light, normalized by the area, was determined by an exterior Ophir radiometer equipped with a spot detector. Ellipsometry measurements were performed on a Gaertner L116C Single Wavelength ellipsometer with a 632.5 nm laser and an incident angle of 70°. Contact angle measurements were performed on a Rame-Hart Goniometer using Milli-Q water as the probe droplet.
Prop-2-ene-1-sulfonyl chloride

2-propene-1-sulfonic acid sodium salt (1g, 8.76 mmol) was added to a flame dried sealed tube. Freshly distilled phosphorous oxychloride (2.68g, 17.5 mmol) was added and the tube sealed. The reaction was stirred at 120°C for 4hrs. To the resulting grey suspension, 12.5mL of deionized water was added dropwise at 0°C and allowed to sit for 10 minutes to completely hydrolyze excess POCl₃. The solution was extracted with CH₂Cl₂ and dried with Na₂SO₄. The brown oil was distilled under vacuum by Kugelrohr distillation (90°C, ~20 torr). Obtain 0.419g of a colorless oil. NMR and MS agree with literature reports.

![Chemical structure](attachment:image.png)

4-(hydroxymethyl)-7-methoxy-2H-chromen-2-one (19)

4-(bromomethyl)-7-methoxy-2H-chromen-2-one (250 mg, 0.9 mmol) was added to a 50 mL round bottom flask with 25 mL of deionized water. The suspension was refluxed overnight, at which point all solids had dissolved. The solution was extracted with EtOAc (3 x 20 mL), the organic fractions were combined, and dried with Na₂SO₄. After removal of solvent, the solids were recrystallized from hot ethanol to yield 0.191g of needle-like crystals (100%). NMR and MS agree with literature reports.
(7-methoxy-2-oxo-2H-chromen-4-yl)methyl prop-2-ene-1-sulfonate (20)

To a flame dried round bottom flask, 19 (35 mg, 0.17 mmol) and anhydrous THF (2 mL) were added with a stir bar. While stirring to dissolve, the mixture was cooled to 0 °C. The prop-2-ene-1-sulfonyl chloride (48 mg, 0.34 mmol) was dissolved in 2 mL of anhydrous THF. Addition of the sulfonyl chloride solution was followed by dropwise addition of freshly distilled Et₃N. The solution was stirred at 0 °C for 1 hr and then allowed to warm to room temperature and stirred for an additional 1 hr. After diluting with 5 mL THF, the solution was washed with water and extracted with CH₂Cl₂. The organic layer was dried with Na₂SO₄ and the solvent removed en vacuo. Purification of the resulting residue by column chromatography (SiO₂ 1:1 hexane:EtOAc, Rf = 0.2) yielded 25 mg of a white solid (47%). MP 155-156 °C. ¹H NMR (500 MHz, CDCl₃) δ = 7.43 (d, J = 8.7 Hz, 1H), 6.90 (dd, J = 8.7, 2.5 Hz, 1H), 6.88 (d, J = 2.5, 1H), 6.41 (s, 1H), 5.92 (m, 1H), 5.51 (m, 2H), 5.36 (d, J = 1.1, 2H), 3.96 (d, J = 7.2 Hz, 2H), 3.91 (s, 3H). EI-MS (m/z): calcd for C₁₄H₁₄O₆S, 310.05; found, 310.05.
Terminal alkene 20 (11 mg, 0.036 mmol) was added to a flame dried sealed tube under a flow of N₂. The coumarin was then dissolved in anhydrous toluene (2.5 mL). An excess of trichlorosilane (50 \( \mu \)L, 0.5 mmol) was added followed by 3 drops of Karstedt’s Catalyst. The reaction is allowed to stir under N₂ overnight. The excess solvent and silane is removed \emph{en vacuo} and used directly for surface modification. \(^1\)H NMR indicates complete conversion by the disappearance of the terminal alkene protons.

7-decyloxy-4-methyl-chromen-2-one (22)

K₂CO₃ (314 mg, 2.27 mmol) was added to a flask and flame dried with the solid present. Under flowing N₂, 4-methyl-umbeliferone (200 mg, 1.13 mmol) was added and then the mixture was dissolved in anhydrous DMF (11.3 mL). After the mixture turns yellow and no more solids appear to dissolve, 1-bromodecane (502 mg, 2.27 mmol) was added drop-wise. The mixture was stirred for 13 hr at 80°C followed by
neutralization with HCl (0.1M) and extraction with CH₂Cl₂. After washing multiple times with water to remove residual DMF, the organic phase was dried with Na₂SO₄. Purification by flash chromatography (SiO₂ 3:1 Hexanes: Ethyl Acetate Rᵣ = 0.37) provided 283 mg (78% yield) of a white solid. MP 44-46°C. ¹H NMR (500 MHz, CDCl₃) δ = 7.49 (d, J = 8.3 Hz, 1H), 6.86 (dd, J = 8.5, 2.7 Hz, 1 H), 6.81 (d, J = 2.7, 1H), 6.13 (d, J = 1.2 Hz, 1H), 4.02 (t, J = 6.8 Hz, 2H), 2.40 (d, J = 1.2 Hz, 3H), 1.82 (quint, J = 8.1 Hz, 2H), 1.47 (quint, J = 7.6 Hz, 2H), 1.4-1.24 (m, 12H), 0.89 (t, J = 7.3, 3H). ¹³C NMR (500 MHz, CDCl₃) δ = 216.2, 162.4, 161.6, 155.5, 152.8, 125.6, 113.6, 112.9, 112.0, 101.5, 68.8, 32.1, 29.7, 29.6, 29.5, 29.2, 26.2, 22.9, 18.9, 14.3. EI-MS (m/z): calcd for C₂₀H₂₈O₃ 316.2; found, 316.1.

7-decyloxy-4-hydroxymethyl-chromen-2-one (23)

22 (252 mg, 0.79 mmol) was dissolved in xylenes (7.9 mL) and SeO₂ (133 mg, 1.2 mmol) was added. The solution was allowed to reflux for 18 hr. Xylenes were removed by azeotropic distillation with EtOH until dry. The remaining residue was dissolved in absolute EtOH (5 mL) and NaBH₄ (30 mg, 0.79 mmol) was added in portions. After stirring for 15 min, the reaction was complete by TLC. The solution was diluted with water and HCl (1M) was added until bubbling stopped. The mixture was extracted with hexanes (2 x 10 mL) followed by CH₂Cl₂ (1 x 10 mL). Purification by column chromatography (SiO₂ 9:1 CH₂Cl₂:Ethyl Acetate, Rᵣ = 0.2) yielded 134mg (50%
yield) of a white solid. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.40 (d, $J = 9.2$, 1.3 Hz, 1H), 6.84 (d, $J = 2.6$ Hz, 1H), 6.83 (t, $J = 1.3$ Hz, 1H), 6.48 (t, $J = 1.5$ Hz, 1H), 4.89 (dd, $J = 6.0$, 1.5 Hz, 2H), 4.0 (t, $J = 6.6$ Hz, 2H), 1.9 (t, $J = 6.0$ Hz, 1H), 1.81 (quint, $J = 7.5$ Hz, 2H), 1.46 (quint, $J = 7.7$ Hz, 2H), 1.39-1.21 (m, 10H), 0.88 (t, $J = 7.3$ Hz, 3H). EI-HRMS ($m/z$): calcd for C$_{20}$H$_{28}$O$_4$, 332.1988; found, 332.1988.

Prop-2-ene-1-sulfonic acid 7-decyloxy-2-oxo-2H-chromen-4-ylmethyl ester (24)

23 (100 mg, 0.30 mmol) was added to a flame dried flask under flowing N$_2$. Anhydrous THF (3 mL) was added, followed by the 2-propene-1-sulfonyl chloride (84.5 mg, 0.60 mmol). After cooling to 0°C, Et$_3$N was added dropwise and stirred for 1 hr. After stirring at room temperature for an additional hour, the reaction mixture was diluted with water and extracted with CH$_2$Cl$_2$. The organic portions were dried with Na$_2$SO$_4$ and purified by flash chromatography (SiO$_2$ 99% CH$_2$Cl$_2$: 1% MeOH to 98% CH$_2$Cl$_2$: 2% MeOH $R_f = 0.7$). Combining appropriate fractions yields 119 mg (91%) of a white solid. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.40 (d, $J = 8.8$ Hz, 1H), 6.88 (d, $J = 8.8$, 2.4 Hz, 1H), 6.85 (d, $J = 2.4$ Hz, 1H), 6.38 (dd, $J = 1.2$ Hz, 1H), 5.92 (m, 1H), 5.51 (m, 2H), 5.35 (s, 2H), 4.03 (t, $J = 6.1$ Hz, 2H), 3.96 (d, $J = 6.8$ Hz, 2H), 1.82 (quint, $J = 6.8$ Hz, 2H), 1.47 (quint, $J = 8.3$ Hz, 2H), 1.40-1.22 (m, 12H), 0.89 (t, $J = 7.3$ Hz, 3H).
(7-(decyloxy)-2-oxo-2H-chromen-4-yl)methyl 3-(trichlorosilyl)propane-1-sulfonate (25)

Terminal alkene 24 (0.024 mmol) and toluene (2 mL) were added to a flame dried tube equipped with a stir bar. Under N₂, HSiCl₃ (0.24 mmol) was added, followed by 3 drops of Karstedt’s Catalyst. The solution immediately turned yellow and was covered with foil and stirred overnight. The toluene and excess silane is removed in vacuo leaving only a fluorescent orange solid. NMR suggests reaction is complete by the disappearance of the alkene protons. The material was used without further purification.

tert-butyl 2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)acetate (27)

t-butyl bromoacetate (4.98 g, 25 mmol), 4-methyl-umbellifurone (4.5 g, 25 mmol), potassium iodide (6.3 g, 37 mmol), and potassium carbonate (7.3 g, 52 mmol), and 100 mL of acetone were added to a round bottom flask. The stirring suspension was refluxed for 5 hrs, cooled to room temperature and diluted with 1M HCl to acidify. The solution was extracted with CH₂Cl₂, the organic portions dried with MgSO₄, and solvent
removed en vacuo. The resulting residue was purified by column chromatography (SiO₂ 1:1 hexane:EtOAc Rf = 0.3) to yield 4 g of a white solid (55%). \(^1\)H NMR (500 MHz, CDCl₃) δ = 7.51 (d, J = 8.8, 1H), 6.90 (dd, J = 8.8, 2.5 Hz, 1H), 6.75 (d, J = 2.5 Hz, 1H), 6.15 (q, J = 1.2 Hz, 1H), 4.57 (s, 2H), 1.60 (s, 2H), 1.49 (s, 9H). EI-HRMS (m/z): calcd for C₁₆H₁₈O₆, 290.1154; found, 290.1155.

2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)acetic acid (28)

Coumarin 27 was dissolved in CH₂Cl₂ (6 mL) and trifluoroacetic acid (2 mL) was added. After stirring for 2 hrs at room temperature, the reaction was complete as determined by TLC. Solvent was removed en vacuo to produce a white solid in quantitative yield. The material was carried on to the next step without further purification. \(^1\)H NMR (500 MHz, CDCl₃) δ = 7.67 (d, J = 9.0, 1H), 6.96 (dd, J = 8.0, 2.5 Hz, 1H), 6.95 (s, 1H), 6.21 (q, J = 1.2 Hz, 1H), 4.82 (s, 2H), 2.38 (d, J = 2.0 Hz, 3H).

Benzyl (2-bromoethyl)carbamate\(^{45}\)

2-bromo-ethylamine bromide (2.07 g, 10 mmol) was dissolved in a solution of 5 mL deionized water and 5 mL 1,4-dioxane. A solution of 5 mL 1,4-dioxane and carbobenzoxy chloride (2.10 g, 12.1 mmol) was added dropwise alternating with 3.5 M
K$_2$CO$_3$ in water to keep pH between 7 and 8. After addition, the solution was stirred for 1 hr. NaOH (1mL, 2M) was added to quench remaining carbobenzoxy chloride. The solution was extracted with diethyl ether, dried with Na$_2$SO$_4$ and purified by column chromatography (SiO$_2$ 10:1 hexane:EtOAc R$_f$ = 0.6) to yield 1.17 g (45%). NMR and MS agree with literature reports.

![Chemical Structure](image)

**Benzyl (2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)ethyl)carbamate (30a)**

4-methyl-umbelliferone (100 mg, 0.5 mmol) and (2-bromoethyl)carbamate (293 mg, 1.1 mmol) was added to a round bottom flask containing dimethylformamide (5 mL) and potassium carbonate (156 mg). The suspension was stirred overnight at room temperature and the reaction deemed complete by TLC. The solution was quenched by the addition of water and extracted with CH$_2$Cl$_2$. After drying with Na$_2$SO$_4$ and removal of the solvent en vacuo, the residue was purified by column chromatography (SiO$_2$ 1:1 hexane:EtOAc) to yield 104 mg (52%) of the desired material. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.50 (d, J = 9.8, 1H), 7.39-7.35 (m, 5H), 6.85 (dd, J = 8.8, 2.3), 6.80 (d, J = 2.3 Hz, 1H), 6.16 (q, J = 1.2 Hz, 1H), 5.13 (s, 2H), 4.11 (t, J = 5.0 Hz, 2H), 3.66 (q, J = 5.4 Hz, 2H), 2.40 (d, J = 1.1 Hz, 3H).
tert-butyl (2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)ethyl)carbamate (30b)

Commercially available BOC-N-ethyl bromide (567 mg, 25 mmol), 4-methyl-umbelliferone (223 mg, 12.7 mmol), potassium carbonate (351 mg, 25 mmol), and anhydrous N,N-dimethylformamide (13 mL) was added to a round bottom flask. The suspension was stirred at 80 °C overnight. HCl was added (10 mL, 0.5M) to remove excess K$_2$CO$_3$ and the solution was extracted with CH$_2$Cl$_2$. The organic portions were combined and dried using Na$_2$SO$_4$ followed by removal of the solvent en vacuo. The residue was purified by column chromatography (SiO$_2$ 1:1 CH$_3$Cl:EtOAc R$_f$ = 0.5) to yield 305 mg (75%) of a white solid. MP 122-123.5 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ = 7.41 (d, J = 8.8, 1H), 6.82 (dd, J = 8.8, 2.5 Hz, 1H), 6.76 (d, J = 2.5 Hz, 1H), 6.47 (s, 1H), 5.09 (bs, 1H), 4.05 (t, J = 5.2 Hz, 2H), 3.57 (q, J = 4.9 Hz, 2H), 2.40 (s, 3H), 1.45 (s, 9H). El-HRMS (m/z): calcd for C$_{17}$H$_{20}$NO$_5$, 319.1420; found, 319.1419.

Benzyl (2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)ethyl)carbamate (31a)

Coumarin 30a (100 mg, 0.2 mmol) was added to a round bottom with 1,4-dioxane (25 mL) along with recrystallized SeO$_2$ (47 mg, 0.4 mmol). The solution was
allowed to reflux overnight. Xylenes were removed by azeotropic distillation with EtOH until dry. The remaining residue was dissolved in absolute EtOH (25 mL) and NaBH₄ (10.7 mg, 0.28 mmol) was added in portions. After stirring for 30 min, the reaction was complete by TLC. The solution was diluted with water and HCl (1M) was added until bubbling stopped. The mixture was extracted with CH₂Cl₂. Purification by column chromatography (SiO₂ 95:5 CH₂Cl₂:MeOH, Rf = 0.31) yielded 98 mg (93% yield) of a white solid. ¹H NMR (500 MHz, CDCl₃) δ = 7.42 (d, J = 8.6, 1H), 7.37 (m, 5H), 6.82 (m, 2H), 6.48 (s, 1H), 5.13 (bs, 1H), 4.88 (d, J = 1.4 Hz, 2H), 4.10 (t, 2H), 3.65 (q, 2H). EI-HRMS (m/z): calcd for C₂₀H₁₉NO₆, 353.1263; found, 353.1214.

Synthesis of tert-butyl (2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)ethyl)carbamate (31b)

Coumarin 30b (1.0 g, 3.1 mmol) was added to a round bottom with 1,4-dioxane (30 mL) along with recrystallized SeO₂ (521 mg, 4.6 mmol). The solution was allowed to reflux overnight. Xylenes were removed by azeotropic distillation with EtOH until dry. The remaining residue was dissolved in absolute EtOH (30 mL) and NaBH₄ (118 mg, 3.1 mmol) was added in portions. After stirring for 30 min, the reaction was complete by TLC. The solution was diluted with water and HCl (1M) was added until bubbling stopped. The mixture was extracted with CH₂Cl₂. Purification by column chromatography (SiO₂ 9:1 EtOAc:hexane, Rf = 0.4) yielded 668 mg (63% yield) of an
off-white solid. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.42 (d, $J = 8.7$ Hz, 1H), 6.84 (dd, $J = 8.7$, 2.5 Hz, 1H), 6.81 (d, $J = 2.5$ Hz, 1H), 6.48 (t, $J = 1.5$ Hz, 1H), 4.97 (bs, 1H), 4.88 (dd, $J = 6.0$, 1.5 Hz, 2H), 4.07 (t, $J = 5.0$ Hz, 2H), 3.57 (q, $J = 5.3$ Hz, 2H), 1.45 (s, 9H). EI-HRMS ($m/z$): calcd for C$_{17}$H$_{21}$NO$_6$, 335.1369; found, 335.1369.

(7-(2-(((benzyloxy)carbonyl)amino)ethoxy)-2-oxo-2H-chromen-4-yl)methyl prop-2-ene-1-sulfonate (32a)

Coumarin 31a (50 mg, 0.13 mmol) was added to a flame dried flask under flowing N$_2$. Anhydrous THF (2 mL) was added, followed by the 2-propene-1-sulfonyl chloride (28 mg, 0.20 mmol). After cooling to 0°C, Et$_3$N (20.5 mg, 0.20 mmol) was added dropwise and stirred for 1 hr. After stirring at room temperature for an additional hour, the reaction mixture was diluted with water and extracted with CH$_2$Cl$_2$. The organic portions were dried with Na$_2$SO$_4$ and purified by flash chromatography (SiO$_2$ 3:1 EtOAc:hexane $R_f = 0.7$). Combining appropriate fractions yields 43 mg (84%) of a yellow oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.42 (d, $J = 8.8$ Hz, 1H), 7.36 (m, 5H), 6.86 (m, 2H), 6.41 (t, $J = 1.2$ Hz, 1H), 5.93 (m, 1H), 5.51 (m, 2H), 5.35 (d, $J = 1.3$, 2H), 5.14 (s, 2H), 4.13 (t, 2H), 3.97 (dt, $J = 7.3$, 1.0 Hz, 2H), 3.68 (q, $J = 5.3$ Hz, 2H). EI-HRMS ($m/z$): calcd for C$_{23}$H$_{23}$NO$_6$S, 473.1144; found, 473.1110.
(7-(2-((tert-butoxycarbonyl)amino)ethoxy)-2-oxo-2H-chromen-4-yl)methyl prop-2-ene-1-sulfonate (32b)

Coumarin 32a (42 mg, 0.12 mmol) was added to a flame dried flask under flowing N₂. Anhydrous THF (1.5 mL) was added, followed by the 2-propene-1-sulfonyl chloride (35 mg, 0.25 mmol). After cooling to 0°C, Et₃N (31.6 mg, 0.31 mmol) was added dropwise and stirred for 1 hr. After stirring at room temperature for an additional hour, the reaction mixture was diluted with water and extracted with CH₂Cl₂. The organic portions were dried with Na₂SO₄ and purified by flash chromatography (SiO₂ 99:1 CHCl₃ Rᶠ = 0.3). Combining appropriate fractions yields 37 mg (69%) of a yellow oil. ¹H NMR (500 MHz, CDCl₃) δ = 7.41 (d, J = 8.8, 1H), 6.87 (dd, J = 2.4, 8.8 Hz, 1H), 6.83 (d, J = 2.4 Hz, 1H), 5.95-5.86 (m, 1H), 5.52-5.46 (m, 2H), 5.33 (d, J = 1.2 Hz, 2H), 4.99 (broad s, 1H), 4.08 (t, J = 5.1 Hz, 2H), 3.95 (dt, J = 7.1, 1.0 Hz, 2H), 3.57 (q, J = 5.6 Hz, 2H), 1.45 (s, 9H). EI-HRMS (m/z): calcd for C₂₀H₂₅NO₈S, 439.1301; found, 439.1294.
4-(chloromethyl)-7-hydroxy-2H-chromen-2-one\textsuperscript{46} (34)

Resorcinol (1.01 mg, 6.0 mmol) and ethyl 4-chloroacetoacetate (1.35 g, 12 mmol) were added slowly to concentrated sulfuric acid (7 mL). After stirring overnight (no less than 12 hr), the conc. acid solution was added slowly to a stirring ice slurry. The precipitated yellow solid was gravity filtered and dried under vacuum to provide 945 mg (75\%) of a pale yellow solid. \(^1\)H NMR (500 MHz, DMSO) \(\delta = 7.66 \ (d, \ J=8.6\text{Hz}, \ 1H), 6.82 \ (dd, \ J=2.4, 8.6\text{Hz}, \ 1H), 6.73 \ (d, \ J=2.4\text{Hz}, \ 1H), 6.40 \ (s, \ 1H), 4.94 \ (s, \ 2H).\) El-HRMS \((m/z): \) calcd for C\(_{10}\)H\(_7\)ClO\(_3\), 210.0083; found, 210.0084.

7-hydroxy-4-(hydroxymethyl)-2H-chromen-2-one \((35)\)

Coumarin 34 (543 mg, 2.5 mmol) was added to 30 mL deionized water and refluxed overnight. Approx. 50\% of the water was distilled off under vacuum and allowed to cool to room temperature. Upon cooling, the product crystallized from solution. Recrystallization from water provided 35 in quantitative yield (496 mg). \(^1\)H NMR (500MHz, DMSO) \(\delta = 10.53 \ (s, \ 1H), 7.5 \ (d, \ J=8.4\text{Hz}, \ 1H), 6.77 \ (dd, \ J=2.8, 8.4\text{Hz}, \)
tert-butyl 2-((4-(hydroxymethyl)-2-oxo-2H-chromen-7-yl)oxy)acetate (36)

Coumarin 27 (4.5 g, 15.5 mmol) was added to a round bottom with 1,4-dioxane (150 mL) along with recrystallized SeO₂ (2.57 mg, 23.2 mmol). The solution was allowed to reflux overnight. Xylenes were removed by azeotropic distillation with EtOH until dry. The remaining residue was dissolved in absolute EtOH (150 mL) and NaBH₄ (586 mg, 15.5 mmol) was added in portions. After stirring for 30 min, the reaction was complete by TLC. The solution was diluted with water and HCl (1M) was added until bubbling stopped. The mixture was extracted with CH₂Cl₂. Purification by column chromatography (SiO₂ 99:1 CH₂Cl₂:MeOH to 98:2 CH₂Cl₂:MeOH) yielded 2.69 g (56% yield) of a white solid. ¹H NMR (500 MHz, CDCl₃) δ = 7.43 (d, J = 8.8 Hz, 1H), 6.88 (dd, J = 8.8, 2.5 Hz, 1H), 6.77 (d, J = 2.5 Hz, 1H), 6.48 (s, 1H), 4.87 (s, 2H), 4.57 (s, 2H), 1.5 (s, 9H). EI-HRMS (m/z): calcd for C₁₆H₁₈O₆, 306.1103; found, 306.1103.
tert-butyl 2-((2-oxo-4-(((3-(triethoxysilyl)propyl)carbamoyl)oxy)methyl)-2H-chromen-7-yl)oxy)acetate (37)

In a flame dried round bottom flask, coumarin 36 (300 mg, 0.97 mmol) was dissolved in anhydrous THF under flowing Ar. 2-isocyanato-propyl triethoxysilane (242 mg, 0.97 mmol) was then added followed by a catalytic amount of dibutyltin dilaureate (30 mg, 0.048 mmol). The solution was allowed to stir under Ar overnight (16 hr) at which point the solvent was removed en vacuo. The residue was purified by column chromatography (SiO$_2$ 1:1 hexane:EtOAc, R$_f$ = 0.5) to collect 487 mg (90%) of a white waxy residue. $^1$H NMR (500 MHz, CDCl$_3$) $\delta = 7.44$ (d, J = 8.8 Hz, 1H), 6.89 (dd, J = 8.8, 2.4 Hz, 1H), 6.78 (d, J = 2.4 Hz, 1H), 6.33 (s, 1H), 5.23 (s, 2H), 4.57 (s, 2H), 3.83 (q, J = 6.9 Hz, 6H), 3.24 (q, J = 6.5 Hz, 2H), 1.67 (m, 2H), 1.49 (s, 9H), 1.23 (t, J = 7.0, 9H). El-HRMS (m/z): calcd for C$_{16}$H$_{18}$O$_6$, 306.1103; found, 306.1103.

7-(allyloxy)-4-(hydroxymethyl)-2H-chromen-2-one (38)

Potassium carbonate (140 mg, 1.0 mmol) and coumarin 35 (100 mg, 0.5 mmol) were added to a flame dried round bottom flask. Anhydrous DMF (5 mL) was added
followed by allyl bromide (123 mg, 1.0 mmol). The reaction was heated to 75 °C for 2.5 hr at which point the reaction was complete by TLC. The solution was cooled to room temperature, extracted with CH₂Cl₂ and the organic portions dried with Na₂SO₄. The solvent was removed en vacuo and the residue purified by column chromatography (SiO₂ 1:1 hexane:EtOAc Rₖ = 0.25) to yield 83 mg of a yellow solid (70%). ¹H NMR (500 MHz, CDCl₃) δ = 7.42 (d, J = 8.8 Hz, 1H), 6.87 (dd, J = 8.8, 2.4 Hz, 1H), 6.84 (d, J = 2.4 Hz, 1H), 6.48 (t, J = 1.5 Hz, 1H), 6.04 (m, 1H), 5.39 (m, 2H), 4.89 (dd, J = 6.2, 1.7 Hz, 2H), 4.60 (dt, J = 5.4, 1.5 Hz, 2H), 1.98 (t, J = 6.2 Hz, 1H).

(7-(allyloxy)-2-oxo-2H-chromen-4-yl)methyl dodecyl-1-sulfonate (39)

Coumarin 38 (49 mg, 0.2 mmol) was added to a flame dried flask under flowing N₂. Anhydrous THF (2 mL) was added, followed by the 1-dodecanesulfonyl chloride (85 mg, 0.31 mmol). After cooling to 0°C, Et₃N (32 mg, 0.31 mmol) was added dropwise and stirred for 1 hr. After stirring at room temperature for an additional hour, the reaction mixture was diluted with water and extracted with CH₂Cl₂. The organic portions were dried with Na₂SO₄ and purified by flash chromatography (SiO₂ 99:1 CHCl₃ Rₖ = 0.3). Combining appropriate fractions yields 76 mg (77%) of an off-white solid. ¹H NMR (500 MHz, CDCl₃) δ = 7.43 (d, J = 8.8 Hz, 1H), 6.90 (dd, J = 2.4, 8.8 Hz, 1H), 6.87 (d, J = 2.4 Hz, 1H), 6.39 (s, 1H), 6.04 (m, 1H), 5.40 (m, 1H), 5.32 (s, 2H), 4.62 (d, J = 5.3, 2H),
3.17 (m, 2H), 1.87 (m, 2H), 1.55 (s, 2H), 1.42 (m, 2H), 1.32-1.22 (m, 18H), 0.87 (t, J = 7.0 Hz, 3H). El-HRMS (m/z): calcd for C_{25}H_{36}O_6S, 464.2233; found, 464.2233.
3.9 Figures

**Figure 3.1** Reported photochemical cleavage mechanism for o-nitrobenzyl derivatives.

**Figure 3.2** First reported photochemical cleavage of a o-nitrobenzyl group with subsequent byproduct formation.
Figure 3.3 Proposed general mechanism of photocleavage of 4-yl-methyl coumarin derivatives.\textsuperscript{31}
Table 3.1 Compiled values for some photophysical properties of various 4-yl-coumarin derivatives.\textsuperscript{39}

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Figure 3.4 Various transitions possible with 4-yl-methyl coumarin photofuse.

Figure 3.5 Synthetic route for the preparation of the first hydrophobic to negative coumarin photofuse.
Figure 3.6 UV-Vis suggesting [2+2] occurrence. The first exposure of 365 nm causes a decrease in absorbance at 330 nm. Subsequent exposure at 254 nm results in an increase in absorbance at 330 nm.

Figure 3.7 Synthesis of second hydrophobic-to-negative coumarin
**Figure 3.8** UV-Vis of colloidal suspension of (25) indicating no [2+2] reaction.

**Figure 3.9** Phase migration of colloids modified with (25) before and after UV exposure.
Figure 3.10 Attempted synthesis of perfluorinated coumarins.

Figure 3.11 Attempted synthesis of positive-to-negative transitions.
Figure 3.12  Pechman Condensation to prepare multi-gram quantities of 4-(hydroxymethyl)-7-hydroxy coumarin.

Figure 3.13  Synthetic route for negative-to-positive transition.

Figure 3.14  Optical image of silicon wafer, modified with 37, patterned through a chrome photolithography mask, then treated with carboxylated 800 \( \mu \)m SiO\(_2\) particles. The patterned vertical lines show some selective adhesion of the SiO\(_2\) particles.
Figure 3.15 Synthetic route for preparation of hydrophobic to neutral transition.

Figure 3.16 Proposed synthetic route to charged-to-neutral coumarins.
Figure 3.17  Retrosynthetic pathways for required sulfonyl chlorides for preparation of 40 and 41.
3.10 References


CHAPTER 4

Greyscale Photolithography Monitored by Coumarin Monolayers and Applications†

4.1 Introduction

The ability to control surface chemistry is of significant importance in applications such as microfluidic devices\textsuperscript{1} and self-assembling systems\textsuperscript{2}. Much work has been reported on controlling surface functionality\textsuperscript{3}, however these reports are limited to binary, or on/off functionality meaning the surface is in one state or another. Controlling functionality between these states, otherwise known as greyscaling, is a developing area of study. Chemical gradients can be used for cellular control and growth studies\textsuperscript{4} in addition to modulating surface hydrophobicity or composition\textsuperscript{5}. However, the methods to generate such surfaces generally require difficult and often expensive fabrication techniques such as fabrication of complex greyscale photolithography masks or complex deposition conditions.

Multiple techniques are available to create greyscale photolithography masks, but most of these methods are costly and/or time intensive. The most common greyscale photolithography masks are fabricated using High Energy Beam Sensitive (HEBS) glass.\textsuperscript{6} Silver ion-doped glass is subject to electron beam irradiation which reduces the silver salt to elemental silver, thus rendering the region optically opaque. The opacity of the feature can be controlled by the length and power of the beam

† The work contained in this chapter was performed in collaboration with Audrey Bowen of the Nuzzo Group. At the time of this writing, it is being prepared for publication.
exposure. Although this process creates high quality masks of high resolution and multiple levels of greyscale, the glass is expensive and the mask writing procedure is serial in nature and thus a time intensive process. Alternatively, deep reactive ion beam etching (DRIE) can be used in combination with chrome-on-glass (COG) greyscale masks to create three-dimensional features in Si that can be used as greyscale lithography masks for X-ray exposures.\textsuperscript{7} Briefly, using a commercially available COG mask, photoresist was patterned and developed on a Si wafer. The resulting 3D greyscale feature is etched into the Si using SF\textsubscript{6} RIE with O\textsubscript{2} passivation with the photoresist features acting as a mask. Again, the high cost associated with the fabrication of such masks is high due to the time-intensive processing steps and the processes used.

Greyscale masks, while traditionally used for photoresist patterning, can also be used to create chemical gradients. The ability to create chemical gradients has been demonstrated in both thin films and monolayers by vapor diffusion of reactive species,\textsuperscript{5b, 5g, 8} variable composition deposition solutions,\textsuperscript{9} microcontact printing,\textsuperscript{5d} programmed desorption,\textsuperscript{5a} or gradient polymerization.\textsuperscript{10} However, it is difficult to create gradients of monolayers with a high degree of spatial control without using expensive greyscale lithography masks. Control over both chemical gradients and spatial orientation would be useful for a variety of applications, but has not yet been demonstrated.

Recently, developments have been reported that dramatically decrease the cost of greyscale fabrication. A report from Folch et al. used microfluidic arrays of dye solutions that varied in concentration as a photomask.\textsuperscript{11} This approach is particularly appealing due to the low cost of fabrication and the ability to reprogram each mask.
element by simply emptying and refilling the desired microfluidic channel. The mask was used to pattern photoresist resulting in different heights from a single UV exposure. However, fluid-filled microchannels raise concerns such as compromised channel sealing and consequently limited flexibility. Additionally, the mask elements are limited to microfluidic features. Thus, a more robust and versatile solid-state greyscale photomask is desirable.

This work presents a mechanically flexible PDMS-based greyscale photolithography mask fabrication scheme that is inexpensive and extremely simple. These greyscale photolithography masks were used to pattern a rapidly responding coumarin-based monolayer. The coumarin core is readily modified to incorporate a variety of terminal functionalities (see Chapter 3) and provides ways to monitor the surface chemistry through use of atomic labels, fluorophores, etc. Additionally, the greyscale mask and surface chemical gradients were used to fabricate pressure sensitive microfluidic gates and pattern on highly curved surfaces.

4.2 Photofuse Selection: 4-yl-methyl Coumarins

Designing a photofuse for surface modification is critical as monolayer films have small amounts of material and greyscaling using this photochemistry would require monitoring small changes within that limited amount of material. The ideal photofuse produces no reactive byproducts, provides a large observable change after UV exposure, is easily modified to produce a variety of surface composition transitions, and
produces a reactive “handle” at the surface to allow post-exposure modification of the surface.

The photochemical reactivity of 4-yl-methyl coumarins has been studied in depth by Bendig et al\textsuperscript{12}. Excitation of the weakly fluorescent 4-yl-methyl coumarin ester derivative at 330 nm results in heterolytic bond cleavage of the 4-methylene carbon and the attached heteroatom. The mechanism was initially thought to be homolytic,\textsuperscript{13} but recently there has been significant evidence to the contrary.\textsuperscript{12a, 12d-f} Specifically, when the photocleavage was performed in the presence of H\textsubscript{2}\textsuperscript{18}O, only the 4-(hydroxymethyl) coumarin contained the isotopically labeled oxygen atom after photocleavage, which is suggestive of an ion pair mechanism. In addition, if the homolytic mechanism were active, H-abstraction from solvent would form 4-(methyl) coumarin; however, this product is not observed in any appreciable quantity. The increasing leaving group ability of the resulting alcohol (the lower pK\textsubscript{a} = -2 of the sulfonic acid makes it a better leaving group than the carboxylic acid with a pK\textsubscript{a} of ~4-5) is also suggestive of the heterolytic mechanism. Despite the consistency of these experimental results with a heterolytic cleavage mechanism, this data does not preclude a mechanism in which homolytic bond cleavage is followed by a single electron transfer to create the proposed caged-ion pair.

Upon photoexcitation of the coumarin ester, the excited-state intermediate escapes from the solvent cage, and the coumarin undergoes solvolysis with any nucleophilic solvent; water is most commonly employed. The resulting photoproduct, 4-(hydroxymethyl) coumarin, is highly fluorescent and is generally water soluble. Other products of photocleavage depend on the desired functionality, similar to the o-
nitrobenzyl (NB) photofuse. Protected functional groups have included amines (via a carbamate linkage),\textsuperscript{14} alcohols (via a carbonate linkage),\textsuperscript{15} acetals,\textsuperscript{16} carboxylic acids,\textsuperscript{12d, 14a} sulfonic acids (via a sulfonate ester linkage),\textsuperscript{17} and phosphonates (via a phosphonic ester linkage).\textsuperscript{12c, 18}

The photocleavage reaction of coumarins in solution occurs quickly, with rate constants that are typically 2-3 orders of magnitude faster than the NB systems (ca. $10^6$ s$^{-1}$ for NBs and ca. $10^9$ s$^{-1}$ for coumarins).\textsuperscript{19} The overall rate is a function of the quantum yield and light intensity, polarity of the environment, and structural features of the photofuse. Generally, coumarins are thought to react quicker due to the direct conversion of the excited singlet state to the solvolysis product as opposed to the long-lived acid-nitro intermediate, in the case for NB photofuses.\textsuperscript{19} The absence of reactive products and the increase in reaction rate make the coumarin system appealing for use in surface modification.

The 4-yl-methyl coumarins lend themselves well to divergent synthetic methods and are readily accessible from commercially available starting materials. The ease of modification of the coumarin core greatly expands the number of methods that can be used to characterize surfaces functionalized with these coumarins. A variety of transitions are easily prepared to permit facile imaging of coumarin modified surfaces. Examples include hydrophobic to hydrophilic transitions that can be observed by eye,\textsuperscript{20} presence of atomic labels to monitor surface composition before and after exposure, as well as formation of primary amines after exposure to be for post-exposure modification.
4.3 Fabrication of Greyscale Photolithography Masks

All mask fabrication and characterization performed by Audrey M. Bowen.²¹

First, soft lithographic masters were created by photolithographic methods using SU8-50 photoresist. Following fabrication, the masters were treated with UV-ozone for 3 min and immediately treated with tridecafluoro-1,1,2,2,-tetrahydroxytyl-1-trichlorosilane (No-Stick) vapor in a closed container for 1 h. The masters were then used to create PDMS stamps by mixing commercially available PDMS prepolymer and initiator in a 10:1 w/w ratio, pouring the prepolymer mixture on the masters and placing in a vacuum oven (50 torr) at room temperature to remove air bubbles from the liquid PDMS. The stamps were then cured at 70 °C for 3 h and removed from the masters, using a scalpel to cut around the channel pattern, and carefully separated from the pattern.

For positive-tone greyscale mask fabrication, a 3 mm biopsy punch was used to create a reservoir hole on one end of the PDMS channel pattern. On the opposite end, a 2 mm biopsy punch was used to create an outlet hole. The PDMS stamp was then laminated onto a piece of No-Stick treated polyimide (Kapton). Sylgard 170 (carbon black infused PDMS) was mixed in different weight ratios with Sylgard 184 (clear PDMS) and dropped into the respective reservoirs via syringe. Direct application of vacuum (aspirator pump) at the outlet pulled the PDMS prepolymer mixtures through the channels. Once the channels were filled, the sample was cured at 70 °C for 1 h and then peeled from the supporting Kapton film.
For negative-tone greyscale mask fabrication, degassed PDMS was spin-coated onto a piece of No-Stick treated Kapton and cured at 70 °C for 2 h. Next, the PDMS film was subjected to a 30 sec O₂ plasma reactive-ion etch (RIE) treatment and immediately placed in an e-beam metal deposition chamber to deposit a 2 nm Ti adhesion layer followed by an optically dense 100 nm Au film. Mercaptopropyltrimethoxysilane (MTPMS) was spin-coated onto the Au film (3000 rpm, 30 sec). A patterned PDMS channel stamp with inlet/outlet holes, as described above, was treated with UV-ozone for 3 min and immediately bonded to the MPTMS on Au. The composite stamp was cured at 70 °C for 1 h to facilitate bonding between the PDMS stamp and the MPTMS on Au. A potassium iodide based gold etch was aspirated through all channels, thus opening windows in the optically dense Au film. After flushing the channels with water, degassed solutions of the various mixtures of black PDMS were used to fill as described above. The mask was cured at 70 °C for 3 h, at which point the masks were peeled off of the Kapton support film.

4.4 Binary Patterning of Coumarin Monolayers

Initially, coumarin 1 was designed for surface modification through a hydrophobic to hydrophilic transition upon UV exposure. The synthesis of 1 can be completed in 4 steps from commercially available materials to provide the stable terminal alkene.
Hydrosilylation of the terminal alkene produces the trichlorosilane used to deposit the coumarin monolayer. Surface deposition onto freshly piranha cleaned silicon substrates was performed under anyhydrous conditions to minimize oligomerization in solution. Contact angle measurements of 98-100° are consistent with literature values for terminal methyl groups at the surface.\textsuperscript{22} Ellipsometry measurements indicate a film thickness of 16 ± 0.7 Å, consistent with near monolayer coverage. Assuming an all-trans configuration would produce ca. 22 Å thick monolayers, but the observed lower values are likely due to both the alkyl chain tilt as well as the inherently more disordered silicon substrates resulting from the lower density of silanol groups available for bonding compared to alkanethiols on gold.\textsuperscript{23}

Before any patterning was performed, confirmation of photochemical conversion at the surface was essential. Exposures were performed using a Novacure spot cure system with a high pressure Hg lamp. Exposure intensities can be controlled with iris settings and illumination geometry (spot size, height from sample) and exposure times are microprocessor controlled. The lamp has a broadband emission with a major output at 365 nm. Using flood exposures (uniform exposure of entire surface) of 20 mw/cm\textsuperscript{2}, the contact angle was measured as a function of exposure time, shown in Figure 4.3. The substrates were exposed in 0.5 second intervals and analyzed after each exposure. The minimum contact angle measured occurred after ca. 30 seconds was 45°, slightly higher than previous reports of a sulfonic acid terminated surface on silicon.\textsuperscript{24} Additionally, ellipsometry of the exposed surface indicated film thicknesses of 4.3 ± 1.3 Å, consistent with the approximated thickness of a propyl sulfonic acid modified substrate. The linear response in the first 10 seconds of exposure indicates a high
degree of control over the surface photoresponse and suggests greyscale is possible using a single UV exposure.

After demonstrating the photochemical conversion on the surface, patterning was attempted through a binary photolithography mask to develop the surface characterization techniques. Monolayers were deposited on a silicon wafer and characterized using contact angles and ellipsometry. Then, the substrates were covered with a small amount of water and the binary mask was placed in conformal contact. Exposure at 20 mW/cm² for 30 sec followed by a methanol rinse and blown dry with N₂ resulted in features that can be seen when the surface is breathed upon.²⁰

The qualitative “breath test” did confirm the desired photocleavage occurred, however more rigorous methods were desired. SEM has been used to image monolayer patterns on both gold substrates²⁵ as well as silicon²⁶. Figure 4.4 is an SEM image of the patterned substrate; the inset is an optical image of the photomask. The bright regions in the SEM image are where photocleavage has occurred and the dark regions where it has not. This is consistent with the thinner layer producing a higher secondary electron yield, hence brighter features. However, the contrast obtained by SEM images is limited since the range of intensity in the resulting image is small. Although SEM will provide some information, it will likely not provide the necessary contrast between regions within a greyscale pattern.

Similar to the “breath test,” condensation microscopy²⁰ can be used to image surfaces with differences in hydrophobicity. Briefly, the patterned substrate is placed on a Peltier stage in a controlled, high humidity environment and the stage is cooled below the dew point. Ambient moisture condenses on the substrate, uniformly at first, until the
differences in surface energy cause the droplets in different regions to coalesce at different rates. The contrast seen in Fig 4.5 is caused by the droplet coalescence that occurs more slowly in the regions that remain hydrophobic (lighter regions) than the regions that are hydrophilic (darker regions). The resulting contrast appears sufficient to discriminate between small differences in hydrophobicity, and therefore greyscale; a significant improvement over SEM.

Surface characterization using SEM and condensation microscopy confirmed patterning by film thickness changes and differences in surface energy, respectively. However, a more direct imaging scheme that probes atomic or molecular distributions in the monolayer composition would be ideal. Time-of-Flight Secondary Ion Mass Spectrometry (TOF-SIMS) yields surface specific mass spectral data and can also provide images that represent both atomic and molecular distributions on the surface with ppm resolution. SIMS has been widely used to characterize similar surfaces with great success.\textsuperscript{20, 27}

\begin{center}
\includegraphics[width=\textwidth]{monolayer.pdf}
\end{center}

SIMS is capable of imaging monolayers of coumarin 2 by monitoring the molecular ion and molecular fragments, however labeling with a heavy atom such as bromine provides a more direct characterization of the surface. In this case, Br would be present before exposure and absent (or in lower quantities) in the exposed regions. This also highlights the versatility of the coumarin core; its ability to be easily modified for particular applications or characterization methods. Coumarin photofuse 2 was
synthesized similarly to 1 to provide a Br at the 6-position on the coumarin core. Contact angle and ellipsometry measurements of the Br containing monolayer were similar to 1 at 96° and 17 ± 1.1 Å, respectively. Contact angle as a function of exposure time shows the same optimal exposure times as coumarin 1. SEM images of the patterned bromocoumarin monolayers were obtained and the contrast is similar to the non-brominated version (Figure 4.6).

SIMS imaging of the same surfaces was performed and ion maps were generated from the acquired data. Figure 4.7 shows the 79Br and 81Br combined and 16O. The Br ion map illustrates the intended patterning; the circular regions have been cleaved and have little Br remaining. The contrast between regions is excellent without noticeable feature broadening. The oxygen ion image was unexpected in terms of its high contrast; the higher quantities of oxygen being observed in the cleaved regions. It was initially thought that adventitious water was present in higher quantities in the hydrophilic (circular) regions. Alternatively, the apparent amplification of the oxygen ion yield is most likely due to the lower energy required to sputter the sulfonic acid from the surface relative to the entire coumarin molecule.

In order to probe the surface composition more completely, SIMS data was processed by region of interest analysis. Selecting specific cleaved regions within the image allowed for summation of all mass spectra of the included areas. As expected, the mass spectrum of the cleaved region contained a significant amount of Br as shown in Figure 4.8. Conversely, the cleaved regions exhibited a smaller amount of Br. Continued exposure did not eliminate the Br signal so its presence was due either to adsorption of cleaved material, suggesting that post-processing will require rigorous
cleaning, or some extraneous process was preventing the complete removal of material. Previous reports of photochemically modified surfaces had similar complications,\textsuperscript{3c-e, 28} so efforts remained focused on characterizing these patterned substrates and the residual material was assumed to negligibly impact surface properties.

Further ROI analysis was also performed to illustrate the difference between cleaved and uncleaved areas. Subtraction of the ROI spectra produced a difference spectra where signals above $y = 0$ represent a surplus and below represent a deficiency. For example, in Figure 4.9, the Br is clearly in abundance in the uncleaved region as compared to the uncleaved. Additionally, the amount of carbon, present as the m/z = 15 amu fragment peak, is present in lower quantities in the cleaved region relative to the uncleaved region. Also shown in Figure 4.9 is a mass spectrum of the higher mass region of the uncleaved area. Present in this spectrum is the expected molecular fragments containing the coumarin core, consistent with the presence of this molecule on the surface.

Dependence on photoexposure times was also investigated. With increased exposure times, the features were expected to broaden and possibly increase contrast. This behavior would be consistent with overexposure that is observed with standard photolithographic techniques. Bromocoumarin monolayers were exposed for the optimal 30 sec or overexposed for 60 sec. SIMS images of the Br and O ion maps are shown in Figure 4.10. As expected, the small cross figure that was exposed for 30 sec is 40 microns across with sharp edge resolution corresponding exactly with the photomask used during the exposure. The features of the 60 sec exposed surface are clearly broadened and the edge resolution is degraded. In addition, there is no
significant increase in contrast between the 30 and 60 sec exposure in both the Br and O ion maps. This suggests that all Br containing material has been removed by photocleavage and no further removal occurred with increased exposure time. Thus the macroscopic determination of optimum photocleavage by contact angle analysis agrees well with SIMS analysis.

In addition to exposure times, the post-exposure treatment protocol was investigated to ensure the photocleaved material was completely removed from the surface. Initially, the substrates were rinsed after photoexposure using CH$_2$Cl$_2$ because the resulting alcohol is soluble. Both the Br and Cl ion maps were collected on patterned, rinsed, and dried substrates. Interestingly, the Cl ion map indicates the presence of Cl in the unpatterned regions (Figure 4.11). These results suggest that CH$_2$Cl$_2$ is being retained within the hydrophobic patterns on the substrate. By subjecting the same substrates to a rapid heat treatment (130° t = 0 min, 5 min, 10 min), a decrease in the Cl presence at the surface is observed. These results suggest that the CH$_2$Cl$_2$ can be easily removed by heating to drive off solvent. Alternative rinsing schemes were investigated since CH$_2$Cl$_2$ does not rinse the surface well and is trapped in the monolayer.

Methanol also solubilizes the resulting photoproduct. Interestingly, rinsing with methanol followed by SIMS imaging (monitoring Br only) still shows some aggregates on the surface (Figure 4.12). This phenomenon has been reported previously and was attributed to re-adsorption of monolayer materials from solution. Sonication of the sample in methanol improves the contrast and removes nearly all aggregates present. Sonication in toluene yielded similar results. From these results, post exposure
cleaning requires sonication in a low boiling, polar solvent. The removal of the surface features within the exposed regions as well as the increased contrast after cleaning suggests this post-exposure treatment is well-suited for these substrates.

After demonstrating the ability to image the binary patterned substrates using SIMS, an alternate coumarin core was explored. This alternate core was designed to provide a reactive site on the surface that enables post-exposure functionalization of the patterned monolayer. Successful functionalization provides information about the surface chemistry as well as pathways to alternative applications such as biologically modified surfaces, imaging schemes, etc. The resulting sulfonic acid produced after exposure of 1 or 2 is not easily modified without first performing multiple surface reactions, therefore something more accessible such as a primary amine was desired. Coumarin 3 produces a carbamic acid anion after exposure with UV light that undergoes rapid decarboxylation to produce a primary amine.

First, the new monolayer of 3 was deposited on silicon wafer. Contact angles of the freshly deposited monolayer measured 90°, which was slightly lower than expected. Ellipsometry measurements determined the film thickness to be 23 ± 2 Å that is consistent with a full monolayer. Although the contact angles were slightly lower, the measured film thickness suggested the monolayer was acceptable for patterning. Optimal photochemical exposure times were obtained by contact angle analysis using the same intensities (20 mW/cm²) as previously reported (Figure 4.13). The contact angle approaches a minimum of 75° after 60 seconds.
Once the monolayers were characterized and the optimal exposure times determined, binary patterning was performed through standard photolithography masks, as before. Exposure intensities were kept at 20 mW/cm² for 60 seconds. Once patterned, the substrates were sonicated in methanol and blown dry with N₂. The patterned substrates were immediately placed in a dilute solution (0.1 mg/mL) of dansyl chloride in anhydrous DMF for 1 h. After removing the substrates, they were rinsed with copious amounts of DMF followed by CH₂Cl₂, methanol, and then blown dry. The patterned and dye treated substrates were then imaged using fluorescence microscopy. This is shown schematically in Figure 4.14a. Figure 4.14b contains an optical image of the photolithography mask used and characteristic fluorescence images. Figure 4.14c is a standard acquisition image and Fig 4.14d, a false color mosaic tiled image, both showing successful incorporation of the fluorescent dansyl moiety.

### 4.5 Greyscale Patterning of Coumarin Monolayers

Once these surface characterization methods were proven to be effective, the greyscale patterning and characterization was attempted. First, the exposure intensity through the greyscale mask must be determined to understand how much light reaches the coumarin monolayer through each greyscale mask element. This response was directly measured with large area masks of the same thickness (80 µm), concentration of black PDMS, and thus the same %T as each greyscale mask element. Flood exposures of 30 seconds were performed through these masks onto freshly prepared monolayers and the resulting contact angles were measured. As expected, with
increasing concentration of black PDMS the intensity of transmitted light decreased and the surface had a lower contact angle. Repeating these exposures at various black PDMS concentrations produces a predictive curve for the design of greyscale masks with a high degree of control over the resulting contact angle (Figure 4.15). Based on the curve, the largest changes in contact angle appear to occur between black PDMS content of 30 and 0%.

After determining optimal greyscale levels within the mask, a microfluidic mask was created with black PDMS concentrations of 0, 100, 25, 12.5, and 6.25% by weight mixed with clear PDMS. Exposures through these masks using the optimal exposure conditions produced greyscale features that were visible by a “breath test”. These substrates were imaged using SEM to confirm greyscale modification. As Figure 4.16 shows, greyscale patterning was successful but is difficult to discriminate without post-image processing. This confirms the hypothesis of poor contrast by SEM imaging. Clearly alternative imaging schemes were required to confirm greyscale patterning.

Next, condensation microscopy was used to image the greyscale patterns. Using the negative-tone mask and the same concentrations of black PDMS, substrates were exposed using the same conditions (20 mW/cm²) followed by sonication in methanol. The substrates were then subjected to the condensation microscopy imaging conditions (as described in section 4.8); the resulting micrograph is shown in Figure 4.17. The feature labelled 0% received a complete exposure due to the absence of black PDMS, as it is the most hydrophilic. Conversely, the feature labelled 100% received no UV exposure since the mask is optically dense (0 %T). The 100% black PDMS feature cannot be seen in this image as the condensate in this hydrophobic area
has significantly smaller droplets. Interestingly, all features from 25 to 6.25% black PDMS show a clear difference in nucleation between them that indicates successful greyscale patterning. Moreover, very small differences in surface chemistry can be discriminated, as evidenced by the contrast between 0% and 6.25% features. The ability to resolve these small differences in surface chemistry illustrates the utility of condensation microscopy. This is the first demonstrated case of chemical greyscale imaging using this technique.

To highlight the flexible nature of the greyscale masks, patterning was attempted on surfaces of small radius of curvature; in this case, Pasteur pipettes. Initial attempts were performed on standard 5 inch pipettes, but resolving the patterned features was quite difficult because the substrate surface is transparent and non-reflective. To aid in imaging, the Pasteur pipettes were sealed at the narrow end and treated with Tollen's reagent to create a silver mirror finish on the interior. After rinsing with copious amounts of water, the silvered pipettes were blown dry with N\textsubscript{2}, flame sealed and the outer surface of the pipette was cleaned using standard Pirhanna conditions. Flame sealing was essential to prevent the oxidation of the deposited Ag layer. The coumarin monolayer was deposited using the normal monolayer deposition conditions (described in Section 4.8). Flexible greyscale masks were laminated onto the outer surface onto the outer surface of the silvered substrates, the surface was exposed, rinsed, dried and then imaged by condensation microscopy. Figure 4.18 (right) shows an optical image of the silvered pipettes that were patterned. Fig 4.18 (left) is the resulting condensation micrograph of the patterned area. Imaging of such highly curved surfaces is difficult
without an objective lens with a large focal depth. However, it is clear from Figure 4.18 that the intended patterning occurred on the highly curved surfaces.

that were modified with coumarin 1 and patterned through a negative-tone flexible greyscale photolithography mask.

Next, SIMS was used to characterize the chemical greyscale patterns. Based on the success of the condensation microscopy imaging, the number of greyscale features was increased to demonstrate the versatility of the mask and the degree of control over the greyscale features. A positive-tone mask with 8 discrete greyscale features was used to pattern monolayers of 2 using the same exposure conditions as outlined above. An optical image of the greyscale mask is shown in Figure 4.19 (A) along with a simulation of the expected intensity of Br (B), and the resulting SIMS images (C and D). The different levels of greyscale are apparent in the SIMS image, but a linescan across the patterned features more clearly shows all levels of greyscale. From this linescan plot, differences in Br concentration can be seen between all features; even between 22 and 25 % black PDMS. Similar to the binary patterning results, O ion map images were obtained. These images also suggest greyscale between all desired levels. These results suggest that the SIMS technique is capable of imaging these small differences between features and the range of possible greyscale can be expanded to more levels.

In addition to directly imaging greyscale using SIMS, the use of coumarin 2 permits post-exposure modification of greyscale features. Exposure of monolayers of 3 through a negative-tone mask creates a greyscale pattern of primary amines that can be modified with a fluorophore and imaged using fluorescence microscopy. Figure 4.20 shows a mosaic-tiled fluorescence micrograph of a dye labelled greyscale pattern with a
corresponding linescan to highlight the difference in dye incorporation between the different regions. Aperture effects (the dark corners of each tile) are difficult to eliminate completely, although the intended greyscale is still visible.

4.6 Microfluidic Gating using Greyscale Surface Modification

Chemical gradients have a number of applications, some of which have not been realized up until this point. Numerous reports of monolayer chemical gradients have been reported with applications ranging from simple control over water droplet movement\textsuperscript{5b, 5f} to complex control over cellular adhesion\textsuperscript{4a}. However, using surface energy gradients to control liquid flow within a microfluidic channel has not been reported. Binary patterning permits control over laminar flow within such a device\textsuperscript{3c, d, 28b}, but gating using this type of system is less useful because of the requirement of a liquid/liquid boundary. Additionally, this type of gating has not yet been demonstrated due to the difficulty of patterning chemical gradients with controllable spatial orientation and reliably controlling the greyscale levels. The greyscale masks described above combined with the photochemical reactivity of the coumarin systems permits such control.

Patterning greyscale features within a single microfluidic channel provides a simple demonstration of surface energy control of fluid flow. According to the Young-Laplace equation, the capillary pressure difference between two fluids (in this case, water and air) is a function of surface tension. Therefore, creating different surface energies within a microfluidic channel will affect the interfacial energy between the water
in the microchannel and the patterned substrate. The patterned surface will form virtual boundaries that require different pressures of water within the channel to allow flow; in other words, a pressure sensitive gate.

Understanding the Young-Laplace equation and the photochemical response of the coumarin monolayers, when patterned through the greyscale masks, provides an analytical foundation for this application. Knowing the contact angles after exposure through mask features of known transparency (as discussed in section 4.5) permits the calculation of threshold pressure values that can be compared with experimentally observed values. The Young-Laplace equation can be written as

$$\Delta p = \gamma \left( \frac{1}{R_1} + \frac{1}{R_2} \right)$$

where $\Delta p$ represents the pressure difference across a surface, $\gamma$ is the surface tension of the fluid, and $R_1$ and $R_2$ are the principal radii of curvature of the liquid interface. This relationship can be modified to describe a pressure difference within a rectangular channel and comprised of surfaces of different composition; in this case a glass substrate with a PDMS microfluidic channel. The modified Young-Laplace equation is as follows:

$$\Delta p = \left| P_2 - P_1 \right| = \left( \gamma_{water/air} \cos \theta_{PDMS} \frac{2h + w}{hw} + \gamma_{water/air} \cos \theta_{uncleaved} \frac{w}{hw} \right) - \left( \gamma_{water/air} \cos \theta_{PDMS} \frac{2h + w}{hw} + \gamma_{water/air} \cos \theta_{cleaved} \frac{w}{hw} \right)$$

where $P_2$ is the pressure (or resistance of liquid flow) required to move water over a hydrophobic boundary, $P_1$ is the capillary pressure from water within a hydrophilic channel. In this case, $P_1$ represents the uncleaved hydrophobic coumarin surface. Expansion gives the equation in its final form, where $\gamma_{water/air}$ is the surface tension of
water (constant at RT, 0.073 J/m²), \(\cos \theta_{\text{PDMS}}\) is the cosine of the contact angle of water on PDMS (measured at 105°), and \(h\) and \(w\) are the height and width of the microfluidic channel sides. Substitution of contact angles of partially cleaved surfaces for \(\theta_{\text{uncleaved}}\) for each level of greyscale (defined by the % black PDMS used) provides the predicted threshold pressures at which a given gate is expected to fail. Table 4.1 shows the tabulated threshold values.

A single microfluidic channel was fabricated by molding PDMS to a traditional soft lithography master. Alignment markers were etched into glass slides, which were then subjected to monolayer deposition. The alignment markers were used to properly align the greyscale mask on the substrate and provide visual indicators of the location of each gate after patterning. The sample was exposed at 20 mW/cm² for 30 sec, rinsed with methanol and dried with \(\text{N}_2\). The microfluidic channel was placed perpendicularly across the patterned gates. A disposable plastic pipette was marked with mm increments to measure the applied pressure (in mm H₂O) and act as a reservoir on the inlet side of the device. Figure 4.21 shows a cartoon representation of the completed device. The reservoir and channel were first primed with water, meaning the inlet and channel to the first gate were filled with water. Gradually, water was added until the water inside of the channel reached the first gate and stopped. The height of water was measured and allowed to sit for a period of at least 3 hrs to ensure the gate had actually ceased to flow. This process was repeated for all gates and images were collected at each point to document the gating process. Figure 4.22 shows each gate during the “stopped flow” state. The alignment markers to the left of the channel are colored to indicate an active gate. The applied pressure values are listed above each image.
It is important to note that the meniscus shape of the liquid within each gate is comparatively flat. This suggests it is experiencing a resistance to flow, just as the Young-Laplace equation predicts. As a comparison, a free-flowing meniscus of typical curvature is shown at the far right. Table 4.1 shows very good agreement between the observed threshold values and the calculated values from the modified Young-Laplace Equation.

4.7 Conclusions

Photoresponsive 4-yl-methyl coumarins have been prepared to fabricate chemical greyscale features using solid-state flexible greyscale masks. The versatility of the photoresponsive coumarins is highlighted through application-oriented synthesis that allows access to various characterization schemes of the resulting surfaces. First a hydrophobic to hydrophilic transition was used to demonstrate the ability to photochemically modify the surface energy of a coumarin monolayer. Next, a bromocoumarin derivative was used to monitor surface patterning directly by SIMS. Post-exposure modification was demonstrated using a coumarin designed to provide a primary amine, thus enabling further functionalization of the surface. This work used a simple dye, however many other modifications are possible including DNA, biomolecules, or any other small molecule that can be coupled through peptide or sulfonamide coupling schemes. After demonstrating binary patterning of the various photoresponsive coumarin monolayers, chemical gradients were patterned and characterized by SEM, condensation microscopy, SIMS, and fluorescence microscopy.
Additionally, the flexible masks were used to pattern chemical gradients on highly curved surfaces. This is the first report of such greyscale patterning. The change in surface energy between different levels of greyscale was used to demonstrate pressure-sensitive microfluidic gating. Theoretically predicted values from a modified Young-Laplace equation are in excellent agreement with experimentally observed values.

4.8 Experimental

Materials. All materials were purchased from Sigma Aldrich and used without purification unless otherwise noted. All water used was deionized (resistivity < 18 MΩ) and obtained from a Millipore water purification system. All silicon used was <111> orientation, 228-330 μm thick, P-doped test-grade wafers. Glass coverslips used for fluorescence microscopy were # 1.5, 22 mm x 22 mm. All substrates were cleaned using Pirhanna solution (3:1 conc. sulfuric acid:30% H₂O₂)

Characterization. All \(^1\)H and \(^{13}\)C spectra were obtained on a Varian Unity 500 MHz spectrometer in the VOICE NMR laboratory, School of Chemical Sciences (SCS), University of Illinois. Chemical shifts are reported in ppm (δ) using residual solvent protons as internal standards. Coupling constants (J) are reported in Hertz (Hz) and splitting patterns are expressed as s (singlet), d (doublet), t (triplet), q (quartet), or m (multiplet). Mass spectra were obtained on a Micromass 70-VSE equipped with an EI source, performed by the Mass Spectrometry Labs, School of Chemical Sciences, University of Illinois. Secondary Electron Microscopy (SEM) images were collected on a
JOEL-6060LV General Purpose SEM in the Center for Microanalysis of Materials, Materials Research Laboratories (MRL), University of Illinois. Broadband UV exposures were performed with a Novacure Spot Cure system equipped with a liquid filled light guide coupled to a collimating lens to yield a spot size of 1.3 cm. The intensity of light, normalized by the area, was determined by an exterior Ophir radiometer equipped with a spot detector. Ellipsometry measurements were performed on a Gaertner L116C Single Wavelength ellipsometer with a 632.5 nm laser and an incident angle of 70°. Optical constants were assumed for silicon (n = 3.86, thickness = 1 mm) and measured for all other overlayers. Contact angle measurements were performed on a Rame-Hart Goniometer using Milli-Q water as the probe droplet. Fluorescence microscopy was performed on a Zeiss Axiovert 200M equipped with a Roper Scientific Cascade 512B EMCCD camera and a DAPI dye filter set. SIMS imaging was performed on a Physical Electronics TRIFT III TOF-SIMS equipped with a Au LMIG operating at 22 KeV and extracting current of 2.6 μA. All spectra were acquired in negative ion mode, unbunched, with a molecular weight cutoff of 600 AMU. All mosaic tile images used a 250 μm x 250 μm scan area to acquire a 2 mm x 2 mm image.

Prop-2-ene-1-sulfonyl chloride (1)\textsuperscript{30}

2-propene-1-sulfonic acid sodium salt (1g, 8.76 mmol) was added to a flame dried sealed tube. Freshly distilled phosphorous oxychloride (2.68g, 17.5 mmol) was added and the tube sealed. The reaction was stirred at 120°C for 4hrs. To the resulting grey suspension, 12.5mL of deionized water was added dropwise at 0°C and allowed to
sit for 10 minutes to completely hydrolyze excess POCl$_3$. The solution was extracted with CH$_2$Cl$_2$ and dried with Na$_2$SO$_4$. The brown oil was distilled under vacuum by Kugelrohr distillation (90°C, ~20 torr). Obtain 0.419g of a colorless oil. NMR and MS agree with literature reports.

7-decyloxy-4-methyl-chromen-2-one

K$_2$CO$_3$ (314 mg, 2.27 mmol) was added to a flask and flame dried with the solid present. Under flowing N$_2$, 4-methyl-umbeliferone (200 mg, 1.13 mmol) was added and then the mixture was dissolved in anhydrous DMF (11.3 mL). After the mixture turns yellow and no more solids appear to dissolve, 1-bromodecane (502 mg, 2.27 mmol) was added dropwise. The mixture was stirred for 13 hr at 80°C followed by neutralization with HCl (0.1M) and extraction with CH$_2$Cl$_2$. After washing multiple times with water to remove residual DMF, the organic phase was dried with Na$_2$SO$_4$. Purification by flash chromatography (SiO$_2$ 3:1 Hexanes: Ethyl Acetate $R_f = 0.37$) provided 283 mg (78% yield) of a white solid. MP 44-46°C $^1$H NMR (500 MHz, CDCl$_3$) $\delta = 7.49$ (d, $J = 8.3$ Hz, 1H), 6.86 (dd, $J = 8.5$, 2.7 Hz, 1 H), 6.81 (d, $J = 2.7$, 1H), 6.13 (d, $J = 1.2$ Hz, 1H), 4.02 (t, $J = 6.8$ Hz, 2H), 2.40 (d, $J = 1.2$ Hz, 3H), 1.82 (quint, $J = 8.1$ Hz, 2H), 1.47 (quint, $J = 7.6$ Hz, 2H), 1.4-1.24 (m, 12H), 0.89 (t, $J = 7.3$, 3H). $^{13}$C NMR (500 MHz, CDCl$_3$) $\delta = 216.2, 162.4, 161.6, 155.5, 152.8, 125.6, 113.6, 112.9, 112.0, 101.5, 68.8, 32.1, 29.7, 29.6, 29.5, 29.2, 26.2, 22.9, 18.9, 14.3$. El-MS ($m/z$): calcd for C$_{20}$H$_{28}$O$_3$ 316.2; found, 316.1.
7-decyloxy-4-hydroxymethyl-chromen-2-one

7-decyloxy-4-methyl-chromen-2-one (252 mg, 0.79 mmol) was dissolved in xylenes (7.9 mL) and SeO$_2$ (133 mg, 1.2 mmol) was added. The solution was allowed to reflux for 18 hr. Xylenes were removed by azeotropic distillation with EtOH until dry. The remaining residue was dissolved in absolute EtOH (5 mL) and NaBH$_4$ (30 mg, 0.79 mmol) was added in portions. After stirring for 15 min, the reaction was complete by TLC. The solution was diluted with water and HCl (1M) was added until bubbling stopped. The mixture was extracted with hexanes (2 x 10 mL) followed by CH$_2$Cl$_2$ (1 x 10 mL). Purification by column chromatography (SiO$_2$ 9:1 CH$_2$Cl$_2$:Ethyl Acetate, R$_f$ = 0.2) yielded 134mg (50% yield) of a white solid. $^1$H NMR (500 MHz, CDCl$_3$) δ = 7.40 (d, J = 9.2, 1.3 Hz, 1H), 6.84 (d, J = 2.6 Hz, 1H), 6.83 (t, J = 1.3 Hz, 1H), 6.48 (t, J = 1.5 Hz, 1H), 4.89 (dd, J = 6.0, 1.5 Hz, 2H), 4.0 (t, J = 6.6 Hz, 2H), 1.9 (t, J = 6.0 Hz, 1H), 1.81 (quint, J = 7.5 Hz, 2H), 1.46 (quint, J = 7.7 Hz, 2H), 1.39-1.21 (m, 10H), 0.88 (t, J = 7.3 Hz, 3H). EI-HRMS (m/z): calcd for C$_{20}$H$_{28}$O$_4$, 332.1988; found, 332.1988.

Prop-2-ene-1-sulfonic acid 7-decyloxy-2-oxo-2H-chromen-4-ylmethyl ester

7-decyloxy-4-hydroxymethyl-chromen-2-one (100 mg, 0.30 mmol) was added to a flame dried flask under flowing N$_2$. Anhydrous THF (3 mL) was added, followed by
the 2-propene-1-sulfonyl chloride (84.5 mg, 0.60 mmol). After cooling to 0°C, Et₃N was added dropwise and stirred for 1 hr. After stirring at room temperature for an additional hour, the reaction mixture was diluted with water and extracted with CH₂Cl₂. The organic portions were dried with Na₂SO₄ and purified by flash chromatography (SiO₂ 99% CH₂Cl₂: 1% MeOH to 98% CH₂Cl₂: 2% MeOH Rᵣ = 0.7). Combining appropriate fractions yields 119 mg (91%) of a white solid. ¹H NMR (500 MHz, CDCl₃) δ = 7.40 (d, J = 8.8 Hz, 1H), 6.88 (d, J = 8.8, 2.4 Hz, 1H), 6.85 (d, J = 2.4 Hz, 1H), 6.38 (dd, J = 1.2 Hz, 1H), 5.92 (m, 1H), 5.51 (m, 2H), 5.35 (s, 2H), 4.03 (t, J = 6.1 Hz, 2H), 3.96 (d, J = 6.8 Hz, 2H), 1.82 (quint, J = 6.8 Hz, 2H), 1.47 (quint, J = 8.3 Hz, 2H), 1.40-1.22 (m, 12H), 0.89 (t, J = 7.3 Hz, 3H).

(7-(decyloxy)-2-oxo-2H-chromen-4-yl)methyl 3-(trichlorosilyl)propane-1-sulfonate

Prop-2-ene-1-sulfonic acid 7-decyloxy-2-oxo-2H-chromen-4-ylmethyl ester (0.024 mmol) and toluene (2 mL) were added to a flame dried tube equipped with a stir bar. Under N₂, HSiCl₃ (0.24 mmol) was added, followed by 4 drops of Karstedt’s Catalyst. The solution immediately turned yellow and was covered with foil and stirred overnight. The toluene and excess silane is removed in vacuo leaving only a fluorescent orange solid. NMR suggests reaction is complete by the disappearance of the alkene protons.
6-bromo-7-hydroxy-4-methyl-2H-chromen-2-one

4-bromo-resorcinol (1.98 g, 10.5 mmol), ethyl acetoacetate (2.0 g, 2.0 mL, 15.8 mmol), p-toluene sulfonic acid (300 mg, 1.58 mmol), and toluene (30 mL) was added into a 50 mL round bottom flask. The flask was equipped with a Dean-Stark trap, a condenser and allowed to reflux overnight. The resulting suspension was filtered and rinsed with toluene. After drying en vacuo, 2.37 g of a fine brown solid were obtained. 

$^1$H NMR (500 MHz, $d_6$-DMSO) $\delta = 11.37$ (s, 1H), 7.85 (s, 1H), 6.85 (s, 1H), 6.16 (s, 1H), 2.35 (s, 3H). $^{13}$C NMR (500 MHz, $d_6$-DMSO) $\delta = 160.46, 157.85, 154.25, 153.45, 129.76, 114.10, 111.90, 106.60, 103.65, 18.76$. EI-HRMS (m/z): calcd for C$_{10}$H$_7$BrO$_3$, 253.9579; found, 253.9583.

6-bromo-7-(decyloxy)-4-methyl-2H-chromen-2-one

6-bromo-7-hydroxy-4-methyl-2H-chromen-2-one (500 mg, 1.96 mmol), bromodecane (650 mg, 610 µL, 2.94 mmol), potassium carbonate (541 mg, 3.92 mmol), and DMF (20 mL) was added to a 50 mL round bottom flask. The reaction was heated with stirring for 2 hrs, at which point the reaction was complete by TLC. After cooling to room temperature, 1M HCl was added until the solution was acidic and then extracted with CH$_2$Cl$_2$. The collected organic phase was washed with H$_2$O five times to remove excess DMF followed by brine. The organic layer was dried with MgSO$_4$ and purified by
column chromatography. (SiO₂, 3:1 hexane:ethyl acetate, Rₜ = 0.4) Isolated 0.405 g (52%) of a white solid. ¹H NMR (500 MHz, CDCl₃) δ = 7.76 (s, 1H), 6.82 (s, 1H), 6.17 (s, 1H), 4.09 (t, J = 6.5 Hz, 2H), 2.40 (s, 3H), 1.89 (m, 1H), 1.53 (m 2H), 1.43-1.26 (m, 12H), 0.90 (t, J = 7.0 Hz, 3H). El-HRMS (m/z): calcd for C₂₀H₂₇BrO₃, 394.1144; found, 394.1142.

6-bromo-7-(decyloxy)-4-(hydroxymethyl)-2H-chromen-2-one

6-bromo-7-(decyloxy)-4-methyl-2H-chromen-2-one (100 mg, 0.25 mmol), SeO₂ (42 mg, 0.38 mmol), and 1,4-dioxane (2.5 mL) was added to a 10 mL round bottom flask equipped with a stir bar and a reflux condenser. The reaction mixture was heated at reflux overnight. The suspension was hot-filtered through a plug of silica which was then rinsed with ethanol. After removing all solvent en vacuo, the residue was redissolved in ethanol (2.5 mL) and NaBH₄ (9.5 mg, 0.25 mmol) was added at once. After stirring at room temperature for 15 min, the reaction was complete by TLC. The reaction was quenched with 0.1M HCl and extracted with CH₂Cl₂. After drying with Na₂SO₄, the solvent was removed en vacuo and residue purified by column chromatography (SiO₂, 1:9 ethyl acetate: CH₂Cl₂ Rₜ = 0.3). Collecting appropriate fractions yielded 87 mg of an off-white solid. ¹H NMR (500 MHz, CDCl₃) δ = 7.67 (s, 1H), 6.77 (s, 1H), 6.47 (s, 1H), 6.31 (s, 2H), 4.84 (d, J = 1.3 Hz, 1H), 4.05 (t, J = 6.5 Hz, 2H), 1.86 (m, 2H), 1.50 (m, 2H), 1.40-1.23 (m, 12H), 0.89 (t, J = 6.8 Hz, 3H). El-HRMS (m/z): calcd for C₂₀H₂₇BrO₄, 410.1093; found, 410.1096.
(6-bromo-7-(decyloxy)-2-oxo-2H-chromen-4-yl)methyl prop-2-ene-1-sulfonate

6-bromo-7-(decyloxy)-4-(hydroxymethyl)-2H-chromen-2-one (87.5 mg, 0.21 mmol) was added to a flame dried flask under flowing N₂. Anhydrous THF (2 mL) was added, followed by the 2-propene-1-sulfonyl chloride (44.8 mg, 0.31 mmol). After cooling to 0°C, Et₃N was added dropwise and stirred for 1 hr. The solution was allowed to warm to room temperature and stir for an additional hour, at which point it was diluted with water and extract with CH₂Cl₂. The organic layer was dried with Na₂SO₄ and purified by flash chromatography (SiO₂ 99% CH₂Cl₂:1% MeOH to 98% CH₂Cl₂:2% MeOH Rf = 0.7). Combining appropriate fractions yields 57.7 mg (52%) of a light tan colored solid. ᵃH NMR (500 MHz, CDCl₃) δ = 7.67 (s, 1H), 6.86 (s, 1H), 6.43 (s, 1H), 5.93 (m, 1H), 5.54 (m, 2H), 5.32 (s, 2H), 4.10 (t, J = 6.5 Hz, 2H), 3.98 (m, 2H), 1.90 (m, 2H), 1.54 (m, 2H), 1.43-1.25 (m, 12H), 0.90 (t, J = 6.9 Hz, 3H). EI-HRMS (m/z): calcd for C₂₃H₃₁BrO₆S, 514.1025; found, 514.1029.

(6-bromo-7-(decyloxy)-2-oxo-2H-chromen-4-yl)methyl (3-(triethoxysilyl)propyl)carbamate

(6-bromo-7-(decyloxy)-2-oxo-2H-chromen-4-yl)methyl prop-2-ene-1-sulfonate (200 mg, 0.5 mmol) was dissolved in anhydrous THF (5 mL). 3-(Triethoxysilyl)propyl
isocyanate (125 mg, 0.5 mmol) was then added followed by a catalytic amount of dibutyltin dilaureate (15 mg, 0.025 mmol). After stirring overnight, the solvent was removed en vacuo. The residue was purified by column chromatography (SiO$_2$ 99:1 CH$_2$Cl$_2$:MeOH) to yield 320 mg (93%) of a white solid. $^1$H NMR (500 MHz, CDCl$_3$) $\delta = 7.67$ (s, 1H), 6.77 (s, 1H), 6.47 (s, 1H), 6.24 (s, 2H), 4.84 (d, J = 1.3 Hz, 1H), 4.05 (t, J = 6.5 Hz, 2H), 3.70, (q, 6H), 2.90 (q, 2H), 2.15 (t, 2H), 1.86 (m, 2H), 1.50 (m, 2H), 1.40-1.23 (m, 14H), 1.26 (t, 9H), 0.89 (t, J = 6.8 Hz, 3H) FD (m/z): calcd for C$_{30}$H$_{48}$BrNO$_8$Si, 657.23; found, 658.3.
4.9 Figures

**Figure 4.1** The fabrication scheme for positive tone greyscale masks (left) and optical image of the resulting greyscale mask (right).

**Figure 4.2** The fabrication scheme for negative tone greyscale masks (left) and optical image of the resulting greyscale mask (right).
Figure 4.3  Contact angle of surfaces modified with coumarin 1 as a function of exposure time ($I = 20 \text{ mW/cm}^2$). The rapid decrease in contact angle is consistent with the expected formation of sulfonic acid groups on the surface.

Figure 4.4  SEM image of silicon substrate modified with coumarin 1 following UV exposure through a photolithography mask (inset). The lighter regions are regions that received UV exposure and underwent photocleavage, hence the higher secondary electron yield.
**Figure 4.5** Condensation micrograph of silicon surface functionalized with coumarin 1 and patterned with a photolithograph mask (shown at right). The darker regions condense more water than the lighter regions. This is caused by the difference in surface hydrophobicity from the photolithographic patterning.

**Figure 4.6** SEM image of silicon substrate modified with coumarin 2 following UV exposure through a photolithography mask (see inset in Figure 4.4). The lighter regions are regions that received UV exposure and underwent photocleavage, lending to higher secondary electron yield.
**Figure 4.7** SIMS ion maps of $^{79}\text{Br}$ (left) and $^{16}\text{O}$ (right) showing circular regions of lower Br concentration, consistent with photocleavage occurring in these regions. The inverse of this is observed in the O ion map and is due to either the increased presence of water in the hydrophilic regions or the difference in energy required to cleave the smaller sulfonic acid relative to the entire monolayer. All SIMS images are plotted on a hot-cold false-color scale where yellow represents higher counts and red represents low counts. All images are 400 µm x 400 µm.

**Figure 4.8** Region of interest analysis of the Br ion map shown in Figure 4.7. The top spectrum is a summation of all spectra from the cleaved regions and the bottom is the summation of all spectra from the uncleaved regions. Notably, there is a large difference in the presence of Br relative to a normalization peak at 16 m/z.
Figure 4.9 Subtraction spectrum from the difference illustrating the difference in Br quantity between the cleaved and uncleaved regions (top). Signals above y=0 represent surplus relative to the uncleaved regions. The mass spectrum (bottom) of the uncleaved region shows higher molecular weight fragments consistent with the expected presence of the coumarin monolayer.
Figure 4.10  Zoomed Br ion map (top, left) of Br ion map (top, center) and O ion map (top, right) of surface after 30 sec of exposure. Increasing exposure time to 60 sec results in broadening of the feature in the zoomed image (bottom, left) from the Br ion map (bottom, center). Similar broadening was observed in the O ion map (bottom, right). The zoomed images are 50 µm x 50 µm and all others are 400 µm x 400 µm.
Figure 4.11  SIMS Br ion maps (top) and Cl ion maps (bottom) that were rinsed with CH$_2$Cl$_2$ and dried in a 130°C oven (from left to right) for 0 min, 5 min, and 10 min. Longer drying times resulted in complete removal of the Cl from residual CH$_2$Cl$_2$. Each image is 400 µm x 400 µm.

Figure 4.12  SIMS Br ion maps of patterned monolayers that were subjected to varying sonication times in MeOH. From left to right, sonication time = 0 min, 1 min, 5 min.
Figure 4.13 Contact angle of surfaces modified with coumarin 3 as a function of exposure time ($I = 20 \text{ mW/cm}^2$). The less rapid decrease in contact angle compared to Figure 4.3 is expected since the sulfonic acid of 2 is a better leaving group than the carbamate from 3. The optimal exposure time according to this data is ca. 60 sec.

Figure 4.14 A) Photopatterning and fluorescence labelling scheme used for post-exposure modification. B) Optical microscopy image of chrome mask used for patterning. C) Fluorescence microscopy image of patterned and dyed substrate. D) Mosaic tiled, false colored image of same substrate shown in C.
Figure 4.15 Contact angle of surfaces modified with coumarin 2 as a function of % clear PDMS mask in black PDMS after exposure through each mask. Each surface was flood exposed ($I = 20 \text{ mW/cm}^2$) for 30 sec to determine the effect of transmission of each greyscale mask. The maximum control over greyscale appears between 100% and 30% clear PDMS.

Figure 4.16 SEM image of silicon surface modified with coumarin 2 and exposed through a negative-tone greyscale mask. Greyscale features can be seen, however the contrast between different regions of exposure is limited.
Figure 4.17  Condensation micrograph of silicon surface modified with coumarin 2 and patterned through a negative-tone greyscale mask. The values shown represent the % black PDMS contained in each greyscale feature. A difference in surface hydrophobicity can be observed between all levels of greyscale.

Figure 4.18  Condensation micrographs (left) of 5 inch, silvered, Pasteur pipettes (right)
Figure 4.19  A) Optical image of greyscale mask used to pattern silicon surfaces modified with coumarin 2. Scale bar = 150 µm. B) Simulated linescan approximated from the % black PDMS within each feature. C) Br ion map with corresponding line scan. D) O ion map image with corresponding line scan.
Figure 4.20  Fluorescence microscopy image of a cover slip modified with coumarin 3 and patterned through a negative-tone greyscale mask. The surface was subsequently labelled with dansyl chloride which selective reacts with the newly formed primary amines on the surface. A line scan across the image indicates the differences in incorporation of the fluorophore onto the surface.

Table 4.1 Contact angle following flood exposure of each known % black PDMS. Corresponding threshold pressures to overcome flow resistance were calculated as a function of this contact angle and compared to the experimentally observed threshold values. The theoretically obtained values show excellent agreement with the experimentally observed values.
**Figure 4.21** Schematic representation of the microfluidic gating device used to determine pressure thresholds. Water was added to the reservoir where its height was measured to determine the applied pressure in the microfluidic channel.

**Figure 4.22** Optical images of microfluidic gating at each “stopped flow” state at each gate. The shape of the meniscus appears much more flat during resistance to flow at each gate compared to that of free flow in the image at $P >> 33$ mm H$_2$O.
4.10 References


CHAPTER 5

Photochemical Modification within Three-Dimensional Structures and Applications for Novel Fabrication Schemes

5.1 Introduction

Solar cell technology has been an area of extensive research due to the potential gains of reducing fossil fuel consumption and minimizing harmful greenhouse gas components. One particularly new field of solar cell technology is that of dye sensitized solar cells (DSSCs). Work by O’Brien and Gratzel\textsuperscript{1} first demonstrated this system using a nanocrystalline TiO\textsubscript{2} charge carrier and a ruthenium based dye as the absorber. DSSCs have a few advantages over Si solar cells such as ease of fabrication, low cost and transparency at visible wavelengths. Additionally, due to the nature of the charge injection into the TiO\textsubscript{2} matrix, they can operate under low-light conditions unlike current monocrystalline silicon solar cells. However, their efficiencies are still only ca. 12\%. These low efficiencies are due to multiple factors, mainly the low photon absorption of the ruthenium dye at longer wavelengths and the charge conduction of the TiO\textsubscript{2} matrix.

Efforts to increase efficiency of DSSCs have been reported through the use of photonic crystals coupled with the typical TiO\textsubscript{2} nanocrystalline matrix.\textsuperscript{2} The authors reported a 26\% enhancement in photocurrent compared to a standard DSSC. The origins of this phenomenon were unclear until work by Mihi and Miguez determined the optical coupling of the titania layer to the photonic crystal was responsible\textsuperscript{3}. This coupling results in the generation of standing waves within the absorbing layer coupled
to the photonic crystal that enhances absorption due to the increased dwell time of the incident photons and partial localization of light within the titania layer.

Extension of this photonic coupling led to further understanding of similar standing waves within the photonic crystal. In other words, light can be concentrated at certain regions of the photonic structure. This localization is a direct result of the unique photonic crystal response at wavelengths equal to or lower than the lattice parameter, \( a/\lambda \), rather than the commonly used low energy region. The localized light can be used to perform photochemical modification selectively within the photonic crystal depending on the wavelengths used. Site-specific surface modification could then be achieved through covalent attachment of any dye or absorber such as the Ru dye or quantum dots. Therefore, using different wavelengths of light could enable the placement of multiple absorbers within the photonic crystal. Similar efforts to this end using TiO\(_2\) nanotubes have been proposed but not achieved. These “rainbow cells” can be a significant improvement over current solar cells because the usable spectral window extends into the visible and theoretically increases the overall efficiency of the devices.

Using the unique optical properties of the inverse opal in combination with the utility of the coumarin photofuse, a novel approach to improve upon current DSSC technology was attempted. If modification of the surface chemistry within the inverse opal is possible at a single wavelength, the surface could be covalently modified with a high efficiency absorber. Using multiple coumarins that photocleave at different wavelengths, different positions within the inverse opal surface could be selectively
functionalized with different absorbers theoretically increasing the overall efficiency of the device.

This chapter discusses efforts towards this goal of integrating multiple absorbers into the inverse opal geometry. A brief discussion of photonic crystals, artificial and inverse opals, and properties of photonic crystals is presented followed by initial work demonstrating its feasibility as a templating agent both in inverse opals for DSSC applications as well as new fabrication schemes within three-dimensional structures.

5.2 Photonic Crystals: Opals and Inverse Opals

A photonic crystal (PC) is defined as a material in which the refractive index is periodically variable through regular arrangements of high and low refractive index materials.\(^8\) This periodic arrangement has the ability to affect the propagation of light much like semiconducting materials affect the flow of electricity.\(^9\) Propagation through a photonic crystal is either allowed or disallowed based on the wavelength of light used. Wavelengths and thus energies of light that are not permitted to propagate through the photonic crystal are part of the photonic band gap (PBG). This phenomenon was originally reported simultaneously by two groups\(^10\) and their reports are generally considered the origin of the photonic crystal or photonic band gap materials.\(^9\)

The PBG is dependent on many features of the photonic crystal; the most important properties include dimensionality, symmetry, topology, lattice parameter and scalability. Dimensionality defines where the periodic elements are located in space relative to one another. A photonic crystal can be either one (1D), two (2D), or three
dimensional (3D). Symmetry defines the position and packing of the periodic structures. Examples of symmetry in 3D PCs include simple cubic (sc), face-centered-cubic (fcc), and hexagonal close-packed (hcp) structures. Topology of a given symmetry describes the extent of “touching” between dielectric features. Very close features, or interpenetrated features, are known as a network topology and isolated features are known as a Cermet topology. The lattice parameter defines the distance between dielectric elements. In the common case of a 3D fcc structure, the lattice parameter \(a\) is equal to \((\sqrt{2})d\) where \(d\) is the diameter of the dielectric element. Scalability is a result of the lack of fundamental length scales or dielectric constants in equations describing the optical properties of PCs. Therefore, scalability allows a solution at one length scale (in other words, one lattice parameter value) to provide solutions at all other length scales merely by correcting by a scalar quantity. Other important properties include filling fraction, effective refractive index, and refractive index contrast. Excellent reviews on PC properties have been reported which discuss these properties in depth.\(^{8-9,11}\)

Photonic crystal structures take many forms, but of primary interest in this work are opal and inverse opal structures. The naturally occurring opal structure is a highly ordered array of silicate particles and can be found in rock fissures. The regularly ordered silicate in the naturally occurring material provides its characteristic iridescence and spectrum of colors. These natural opals can be mimicked in the laboratory setting and are known as artificial opals. They have been created from both inorganic\(^{12}\) and polymeric\(^{13}\) materials through a variety of methods.\(^{11}\) Their photonic properties can be controlled by regulating the symmetry of packing, the particle size and the particle material (in other words, its refractive index). Similarly, filling the interstitial spaces of
artificial opals followed by the removal of the opal by dissolution or sintering creates the inverse opal structure. By definition, artificial opals and inverse opals are photonic crystals due to their periodic variation of refractive index. Additionally, their formation and materials properties, and thus their photonic properties, can be engineered to create photonic crystals with specific properties.

5.3 Optical Properties of Photonic Crystals

With the knowledge of the aforementioned PC features, it is possible to determine the photonic band structure (PBS) and the light propagating through a PC. The PBS is a representation of the available energy states for propagation plotted as a function of the propagation direction. The PBS provides information about how light propagates through a PC and which energies or wavelengths are affected in a given photonic crystal. An example of a calculated PBS along with its corresponding reflectance spectrum is shown in Figure 5.1. The frequency in reduced units \( \frac{a}{\lambda} \) is plotted on the y-axis and the reflectance and Brillouin zone direction \( \Gamma \text{L} \) on the left and right x-axis, respectively. The \( \Gamma \text{L} \) direction corresponds to incident irradiation on the <111> face of an hcp array of spheres.

From the calculated PBS on the right, the accessible photonic bands (or wave-vectors) appear at all frequencies except those centered at \( \frac{a}{\lambda} = 0.6 \). The grey area where no wave-vector is present is a PBG. In this case, since the band gap is not present in all directions (not shown), it is called a pseudo band gap. Comparison to the reflectance spectrum indicates a high reflectance at the same photon energies of \( \frac{a}{\lambda} = 
0.6, consistent with inability of the PC to pass photons of these energies. Above and below this band gap, the PBS diagram shows highly sloped bands. The slope of the wave-vector is related to the group velocity, or speed of light through the material.

Interesting behavior appears at higher energies \((a/\lambda > 1.0)\) where increased reflectivity is observed in the reflectance spectrum. Comparison to the PBS diagram reveals no photonic band gaps; in fact, many photonic bands occur in this region with high dispersion. The group velocity (in other words, the slope of the bands in the PBS) in this high-energy region is quite low compared to the low energy region indicating light will propagate very slowly at these energies along the \(\Gamma L\) direction.

This slowing of light as well as the localization of light can be modeled by solving Maxwell equations in a discrete temporal window within the opal structure using the MIT Electromagnetic Equation Propogation (MEEP) computational package; a finite-difference time-domain program used to model electromagnetic systems.\(^\dagger\) The time-averaged electric field intensity, or photon density of selected energies \((a/\lambda)\) is shown in Figure 5.2 where the light is propagating from left to right and the inverse opal structure cross section (shown as circular structures) begins at the center of the figure. As the energy is increased, the localization of photons appears as the red regions. Also in Figure 5.2 is a three-dimensional representation of the same model at \(a/\lambda = 1.35\) that illustrates the “hotspots,” or regions of localized photon density.

With this theoretical foundation of “hotspots” that can be generated within the inverse opal structure, this work set out to utilize the coumarin photofuse as a templating agent for surface functionalization. Tuning the optical properties of the opal

\(^\dagger\) All calculations performed and interpreted by Dr. Agustin Mihi
and the coumarin together provided a narrow window of wavelengths to generate the “hotspots” with. Using the localization of light within the inverse opal, the generated hotspots could be used to locally convert the coumarin-modified interior of the inverse opal. By taking advantage of the ability to selectively change the surface chemistry within the 3D structure, selective labeling schemes could be used to demonstrate the existence of the hotspots empirically; the first attempt of its kind. If these efforts proved successful, the concept could be extended into more advanced applications such as DSSCs and novel 3D fabrication schemes.

5.4 Functionalization and Characterization within Inverse Opal Structures

All initial surface modifications and labeling studies were performed on planar substrates. These planar studies ensured optimal deposition conditions, proper UV exposure and labeling conditions where they could be appropriately characterized. Characterization within the desired three-dimensional structures is difficult so it is assumed that all surface modifications and labeling schemes used are essentially identical to those on planar substrates.

A triethoxysilane modified 7-diethylamino coumarin derivative (1) was deposited onto thin films (~50 nm) of titania on both glass and silicon wafer (Figure 5.3). This particular coumarin moiety was chosen because its $\lambda_{\text{max}} = 370$ nm closely matched the desired $a/\lambda$ bands where photochemical switching was expected for the inverse opal structure. Also, after UV exposure the coumarin produces a terminal amine which can be used for labeling. Ellipsometry indicated coverage of 27 Å, corresponding to
approximately two monolayers. Contact angle measurement provided contact angles of 0° for the unmodified titania and 73° for the coumarin modified substrate, which is consistent with previously published values for this monolayer.14

Planar coumarin modified substrates were then subjected to UV exposure using broadband emission from a high-pressure Hg lamp. Intensity was calibrated using an external radiometer to provide 20 mW/cm² at the substrate surface. Contact angle analysis as a function of exposure time was performed to determine the optimal exposure conditions. A substrate was exposed for 10 seconds, rinsed with methanol, blown dry with N₂, and the contact angle was measured. This process was repeated until no further change in the contact angle was detected. As shown in Figure 5.4, the optimal exposure time occurs when the contact angle does not change with increased exposure, or ca. 40 seconds. A parallel experiment was performed using a lower dose of 10 mW/cm² to determine if the intensity affected the rate of change as determined by contact angle. The rate of change appears to be very similar between the two doses, suggesting that the intensities currently used are above the reaction threshold.

Once photochemical conversion was confirmed on the surface, patterning studies were performed to determine the feasibility of selective labeling after exposure. Two different labeling schemes were selected: covalent bonding of a fluorophore to monitor by fluorescence microscopy and electrostatic labeling with negatively charged particles to be imaged by either SEM or optical microscopy. Fluorescent labeling demonstrates the ability to modify the substrates post-exposure; this will be critical for the end application when quantum dots are to be incorporated as covalent bonding will ensure the absorber is fixed within the structure. Electrostatic labeling will provide
further confirmation that the surface chemistry is indeed a positively charged amine and can be labeled with carboxylated and/or sulfonated polystyrene spheres for simple verification of surface conversion. Ultimate analysis of the three dimensional structures would require labeling of very small regions. Thus, carboxylated Au nanoparticles could be used to electrostatically label the photochemically converted regions and would show contrast in a cross-sectional SEM image.

Preliminary fluorescent labeling was performed by exposing substrates through a chrome mask of various line features. Exposure times of 60 seconds at 20 mW/cm$^2$ were used to ensure complete conversion, as determined in the contact angle study above. After exposures, the samples were sonicated in methanol, blown dry and placed into a dilute solution of dansyl chloride in N,N-dimethyl formamide (DMF). After sitting in the dye solution for 1 hr, they were removed, sonicated in DMF, rinsed with DMF then methanol, and blown dry. Fluorescent images were collected on a Zeiss Axiovert 200M microscope with an electron multiplying CCD camera using a DAPI filter cubeset. Figure 5.5 clearly shows patterning of the substrate and selective labeling of the photochemically converted regions. The feature sizes of the patterns agree with the mask features indicating good pattern fidelity.

Electrostatic labeling was then attempted using carboxylated and sulfonated polystyrene. After exposure through a chrome photolithography mask, the samples were sonicated in methanol, blown dry, and placed vertically into an aqueous suspension of either carboxylated or sulfonated 1 µm polystyrene spheres overnight. The substrates were then rinsed with water and allowed to air dry. Imaging by optical microscopy, the formed patterns suggest that the positively charged amine moiety that
is present in the photochemically deprotected areas attracts the negatively charged polystyrene spheres as intended. Interestingly, the carboxylated particles are less dense compared to the sulfonated particles. This is likely due to the large difference in the pK<sub>a</sub> values between the carboxylate and sulfonate groups on the surface.

Similar labeling was attempted with carboxylated Au nanoparticles, however the image quality was quite poor. Initially, the cause was thought to be the purity of the Au nanoparticle solution. Further investigation suggested that the Au was deposited non-specifically on the patterned surface resulting in low contrast difference between the patterned and non-patterned regions. Therefore, the Au does not provide enough contrast by SEM to provide useful data using coumarin 1 and the Au nanoparticle approach was abandoned to pursue the alternative labeling schemes.

Titania inverse opals were prepared by the Braun group. Briefly, this process involves slow evaporation of a monodisperse, 300 nm polystyrene colloidal suspension in water/ethanol mixtures to form a highly ordered colloidal crystal. The colloidal crystal is then subjected to atomic layer deposition (ALD, see Section 5.4) to deposit ca. 6 nm of alumina in the interstitial spaces. The polystyrene spheres are then removed either by pyrolysis at 500 °C 1 hour or dissolved in THF. The resulting structure was subject to ALD again to deposit ca. 10 nm titania on the inverse structure. The resulting inverse opal is then sintered at 450 °C to crystallize the amorphous titania into its anatase form. Optical properties were measured by FTIR analysis measuring the reflectance and absorption properties of the inverse opal structure.

The photoresponsive coumarin was deposited using the same deposition conditions as the planar substrates. When the surfaces were removed from the
deposition solution, they were rinsed well with toluene, dichloromethane, then methanol and allowed to air dry. Since almost normal incidence monochromatic light is essential for the desired optical response (accessing the appropriate photonic band) of the inverse opal, exposures were performed with a mode-locked Tsunami Ti:Saphire laser equipped with a frequency-doubler tuned to 390 nm and a beam expander to provide a \( \sim 1 \text{ cm} \) spot size. The incident light intensity measured 0.2 \( \mu \text{W/cm}^2 \). The monochromatic UV source was used to expose both water-immersed and air-filled inverse opals. Exposure time as determined by contact angle analysis using the UV laser was found to be \( \text{ca.} 5 \text{ minutes} \). After exposure, the inverse opals were rinsed well with methanol (sonication was attempted but it destroys the inverse opal structure) and placed into a dilute solution of dansyl chloride in DMF. The dyed inverse opals were then removed, rinsed extensively with DMF, dichloromethane, and methanol and allowed to air dry.

Confocal microscopy was used to visualize the labeled regions within the inverse opals. Although the \( \sim 80 \text{ nm} \) features to be imaged are below the resolution of the microscope (\( \sim 200 \text{ nm} \)), these imaging experiments serve two purposes. First, detection of any modification within the inverse opal structure demonstrates the ability to photochemically modify and label within a three dimensional structure. Second, even if the features to be detected are below the XY resolution, post-acquisition analysis could yield useful information about the intensity distribution and indirectly the hotspot distribution in the inverse opal. Figure 5.7 shows a characteristic image where the fine structure of the inverse opal can be seen. As expected, the intensity appears uniform throughout the image – a consequence of the resolution limitations. Control
experiments were performed to confirm this photochemical modification. An inverse opal that was exposed to UV but received no dye treatment and another inverse opal not exposed to UV but did receive dye treatment both showed no fluorescence signals by confocal microscopy. These control experiments in combination with the initial result suggest that the interior of the inverse opal was indeed modified photochemically and was successfully labeled with the dansyl chloride fluorophore. Interestingly, a z-stack image set was collected and there are clearly variations of intensity in both the xy-plane as well as the z-direction (Figure 5.7). It remains unclear if this is the desired hotspot labeling or simply defects within the inverse opal structure that produce scattering events.

5.5 Coumarin Templating for Novel Fabrication of Complex Structures

Given the complications of characterizing the current inverse opal structures, alternative applications were investigated. Monolayers have been utilized in a variety of masking schemes but until now have typically been used in microcontact printing approaches as molecular resist materials. Recent efforts by Bent et al. have focused on microcontact-printed monolayers as ALD resists. Due to the large difference in surface energy between the deposited hydrophilic monolayer and underlying substrate, a selective ALD deposition is possible.

ALD is similar to chemical vapor deposition (CVD) in that it is an epitaxial growth of material. Rather than using a single precursor like CVD, ALD requires two precursors to be cycled sequentially. Oxide materials such as titania, silica, and alumina use water
as the first precursor and a water reactive precursor such as titanium isopropoxide, silicon tetrachloride, and trimethylaluminum, respectively. The ALD process can be described in four sequential steps. First, the first precursor (in this case, water) is cycled into the deposition chamber where it is chemisorbed onto the substrate. The current approach of selective deposition exploits this step by depending on the preference for water to deposit on the hydrophilic regions rather than the hydrophobic ones. Continuing the deposition process, the deposition chamber is then purged or evacuated. The second precursor is then introduced where it reacts with the first precursor on the substrate. This process is self-limiting since only the reactive material is present at the surface. The chamber is then purged or evacuated again to prepare for the next complete cycle. This process is repeated until the requisite amount of material has been deposited.

Based on the reports of selective ALD deposition, the possibility of using a photochemically switchable surface as a molecular resist was explored. The coumarin systems described in Chapter 4 can be used to photochemically switch a surface from hydrophobic to hydrophilic. Switchable surfaces have a distinct advantage over simple monolayers since they can be used in conjunction with the light harvesting properties of opals and inverse opals. This unique extension into three-dimensional materials can produce previously inaccessible structures in a bottom-up approach.

Initial attempts using the photochemically templated ALD deposition were performed on planar substrates to first determine the feasibility of this approach. As mentioned previously, planar substrates allow for screening of surface reactions since characterization inside of an opal or inverse opal requires special sample handling to
probe the interior structures. Monolayers of coumarin 2 were deposited on silicon wafer (Figure 5.8). Contact angle measurement of the deposited monolayer was ~110° which is consistent with a terminal methyl group at the surface. Ellipsometry indicated a film thickness of 23 Å that agrees well with the expected monolayer thickness. Monolayers were then exposed to UV light (365 nm, 20 mW/cm²) for 60 seconds through a chrome mask to generate a hydrophobic/hydrophilic pattern. Flood exposures (non-patterned) on parallel samples provided contact angles of 57° and ellipsometry indicated film thicknesses of 5 Å, which suggests a removal of the hydrophobic coumarin to create a more hydrophilic surface.

The photochemically patterned substrates were then subjected to alumina ALD conditions. The process conditions for a 6 nm film was as follows: 80 cycles, 80 °C, 10 sccm, H₂O pulse 0.03 s, exposure 3 s, purge 65 s, trimethylaluminum pulse 0.03 s, exposure 2 s, purge 65 s. The resulting substrates were imaged using SEM and are shown in Figure 5.9. Initial images have some regions where deposition appeared selective and the feature definition is very good. However, the overall pattern replication was poor as indicated by the pattern irregularities. Efforts were made to improve the large area pattern replication. Sonication of the substrate resulted only in partial removal of the sacrificial material, and carbon tape pull-off was also attempted which gave similar results. After exhausting many possible deposition conditions, it was determined that the difference in surface energy between the cleaved and uncleaved regions of the patterned substrate was simply not enough to provide selective deposition. Even if sonication or the tape lift-off were successful in removing the excess material, its ultimate application in 3D structures would prove impossible. Thus, the use
of more targeted deposition methods such as seeded growth techniques were investigated to produce patterned three-dimensional structures.

Electroless deposition is a chemical deposition method used to deposit metal thin metal films on surfaces.\textsuperscript{18} It involves depositing a catalyst material or reagent on a substrate followed by treatment with a metal salt. The catalyst or reagent reduces the metal salt at the surface resulting in metal deposition. Work by Mewe et al. has advanced the scope of this process by selectively patterning a catalyst material followed by electroless deposition to produce patterned metal structures.\textsuperscript{19} Using the coumarin photofuse, a catalyst can be selectively patterned and in theory selectively metalized. Again, the unique photochemical properties of opals and inverse opals can be harnessed to provide novel methods of patchy particles and other unique three-dimensional structures.

Attempts at selective metallization began with selection of a coumarin photofuse. Primary amines had provided good results when labeling with a fluorophore, therefore it was the ideal starting point. Additionally, previous reports using aminopropyl triethoxysilane (APTES) microcontact printed surfaces produced excellent selectivity when labeled with Au nanoparticles for electroless deposition. Briefly, silicon wafers were microcontact printed with APTES followed by treatment with a solution of citrate-stabilized Au nanoparticles. The nanoparticles are thought to selectively deposit through an electrostatic interaction with the protonated primary amine at the surface. The subsequent electroless deposition of Ag produced the desired patterns with a high degree of selectivity. Thus, a coumarin that produced a primary amine following UV
exposure was chosen. Additionally, the coumarin was designed to be hydrophobic prior to UV exposure to facilitate the selective Au nanoparticle deposition.

Monolayers of the hydrophobic-to-amine coumarin photofuse (3) were deposited through a triethoxysilane coupling to a silicon wafer (Figure 5.10). UV exposure (365 nm, 20 mW/cm²) through a chrome mask for 60 seconds produced the intended patterning of the surface. The substrates were then allowed to sit in a dilute solution of citrate stabilized Au nanoparticles overnight. After removal, the substrate was placed in a silvering bath for 60 mins. SEM was used to confirm deposition on the substrate and showed low selectivity (Figure 5.11). The 5 µm line pattern could be observed as slight density variations in the surface. However, sonication of this substrate removed the undesired material and produced the intended 5 µm line pattern (Figure 5.11). The space between the Ag lines remains free of any Ag deposits. Although the feature definition was poor, the newly fabricated structures appeared to be a promising result.

Based on the apparent lack of selectivity in Figure 5.11, another coumarin photofuse was used for patterning to possibly increase the selectivity of the deposited silver. Coumarin 4 is capable of a charge inversion since it begins with a carboxylate anion terminus (after surface deprotection) and produces a primary amine after exposure to UV light (Figure 5.12). It was thought that the initial negative charge would repel the negatively charged Au nanoparticles better than the non-charged hydrophobic tail in the previous patterning scheme. Monolayer deposition and exposure conditions remained the same. Figure 5.13 contains SEM images of the un-sonicated samples after Ag deposition. Figure 5.13A shows the overall pattern where the dark and light areas are regions with low and high amounts of Ag, respectively. Figure 5.13B is a
zoomed image of the unexposed circular region showing a low amount of Ag deposited compared to the exposed region (Fig 5.13C) where a large amount of Ag is present. From these results, it is clear that the deposition selectivity is significantly higher; in fact, it seems quite close to being completely selective. In addition to the difference in coverage, the grain size is much smaller in the unpatterned area. This is consistent with a higher concentration of Au nanoparticles in the seeding step.

5.6 Conclusions and Future Work

Functionalization of the interior of an inverse opal structure has been demonstrated. First, modification of the titania surface was obtained through standard silane coupling schemes. Monochromatic exposure followed by selective fluorescent dye labeling enabled confocal fluorescent imaging of the labeled structure. The resulting images proved inconclusive due to the small features sizes to be viewed. However, it did confirm that modification, photoexposure, and post-exposure modification all within an inverse opal were possible. Upon reevaluation of the project, a unique fabrication scheme for three-dimensional structures by using the coumarin as a molecular resist was developed. Initial efforts focused on ALD deposition, but ultimately selective metallization through electroless deposition proved successful. Initial results demonstrated very high selectivity between cleaved and un-cleaved regions of a planar substrate.

Based on the results from this selective metallization, it appears the fabrication of metalized structures inside the opals is feasible. This would involve the monolayer
modification of either an opal or inverse opal with coumarin 4 followed by normal incidence irradiation using a UV laser source. The opal or inverse opal structure would then be treated with the Au nanoparticle solution followed by treatment with the silver bath. With the intact three-dimensional structures, the deposition should be selective enough that the structure can be cross-sectioned and analyzed by SEM to visualize the “hotspots.”

Alternatively, a simple method to create patchy particles can be realized using a similar approach. First, the opal would be modified with the same charge inversion coumarin 4. Rather than exposure of the opal directly, the opal can be exposed through a chrome mask with features on the order of the colloid dimension. If the opal is index matched, scattering and light harvesting effects are eliminated so the UV exposure will produce a response only below the transparent regions of the mask. The opal would then be subjected to the Au nanoparticles and silver deposition. At that point, the opal could be disassembled by sonication to release the patchy particles from the substrates. SEM imaging and optical microscopy could be used to confirm the patchy structure. Similar attempts to fabricate patchy particles suffered from characterization difficulties. The metalized patches should be comparatively simple to image by both SEM and optical microscopy. From this work, alternative patterning could be used, including the previously proposed PnP mask to create more complex patch structures.
5.7 Experimental

**Materials.** All materials were used as received unless otherwise noted. Anhydrous toluene and DMF was purchased from Sigma Aldrich. All water used was deionized (resistivity < 18 MΩ) and obtained from a Millipore water purification system.

**Characterization.** All $^1$H and $^{13}$C spectra were obtained on a Varian Unity 500 MHz spectrometer in the VOICE NMR laboratory, School of Chemical Sciences (SCS), University of Illinois. Chemical shifts are reported in ppm (δ) using residual solvent protons as internal standards. Coupling constants (J) are reported in Hertz (Hz) and splitting patterns are expressed as s (singlet), d (doublet), t (triplet), q (quartet), or m (multiplet). Mass spectra were obtained on a Micromass 70-VSE using an EI source, performed by the Mass Spectrometry Labs, School of Chemical Sciences, University of Illinois. Secondary Electron Microscopy (SEM) images were collected on a Hitachi S-4800 High Resolution SEM in the Center for Microanalysis of Materials, Materials Research Laboratories (MRL), University of Illinois. Broadband UV exposures were performed with a Novacure Spot Cure system equipped with a liquid filled light guide coupled to a collimating lens to yield a spot size of 1.3 cm. The intensity of light, normalized by the area, was determined by an exterior Ophir radiometer equipped with a spot detector. Monochromatic UV exposures were performed with a pulsed, mode-locked Tsunami Ti:Saphire laser equipped with a frequency doubler and tuned to 390 nm in the Laser and Spectroscopy Facility, MRL, University of Illinois. Ellipsometry measurements were performed on a Gaertner L116C Single Wavelength ellipsometer with a 632.5 nm laser and an incident angle of 70°. Contact angle measurements were
performed on a Rame-Hart Goniometer using Milli-Q water as the probe droplet. Fluorescence microscopy was performed on a Zeiss Axiovert 200M equipped with a Roper Scientific Cascade 512B EMCCD camera and a DAPI dye filter set. Confocal microscopy was performed on a Leica Microsystems TCS SP2 RBB visible laser confocal microscope.

Prop-2-ene-1-sulfonyl chloride

2-propene-1-sulfonic acid sodium salt (1g, 8.76 mmol) was added to a flame dried sealed tube. Freshly distilled phosphorous oxychloride (2.68g, 17.5 mmol) was added and the tube sealed. The reaction was stirred at 120°C for 4hrs. To the resulting grey suspension, 12.5mL of deionized water was added dropwise at 0°C and allowed to sit for 10 minutes to completely hydrolyze excess POCl₃. The solution was extracted with CH₂Cl₂ and dried with Na₂SO₄. The brown oil was distilled under vacuum by Kugelrohr distillation (90°C, ~20 torr). Obtain 0.419g of a colorless oil. NMR and MS agree with literature reports.

7-(diethylamino)-4-(hydroxymethyl)-2H-chromen-2-one

7-(diethylamino)-4-methyl-coumarin (4.77g, 0.02 mol) was added to a round bottom flask equipped with a stir bar. After dissolving the coumarin in 1,4-dioxane (120 mL), SeO₂ (3.43 g, 0.03 mol) was added and the vessel was heated at reflux overnight.
The dark solution was filtered through a SiO$_2$ plug to remove elemental selenium. The solvent was removed en vacuo to leave a dark brown residue. The residue was redissolved in absolute ethanol (130 mL) and NaBH$_4$ (0.380 g) was added in portions and the reaction was stirred overnight. 1M HCl was added until slightly acidic and the reaction was extracted with CH$_2$Cl$_2$. After the organic fractions were combined and dried with Na$_2$SO$_4$, the mixture was purified by column chromatography (SiO$_2$ 5:1 CH$_2$Cl$_2$:acetone). NMR and MS agree with literature reports.

![Chemical Structure](image)

(7-(diethylamino)-2-oxo-2H-chromen-4-yl)methyl (3-(triethoxysilyl)propyl)carbamate (1)$^{14}$

7-(diethylamino)-4-(hydroxymethyl)-2H-chromen-2-one (250 mg, 1 mmol) was dissolved in anhydrous THF (10 mL). 3-(Triethoxysilyl)propyl isocyanate (265 mg, 1 mmol) was then added followed by a catalytic amount of dibutyltin dilaureate (10 µL). After stirring overnight, the solvent was removed en vacuo. The residue was purified by column chromatography (SiO$_2$ 1:1 hexane:EtOAc) to yield 345 mg (70%) of a pale-yellow solid. $^1$H NMR (500 MHz, CDCl$_3$) δ = 7.29 (d, J = 8.9 Hz, 1H), 6.57 (dd, J = 8.9, 2.6 Hz, 1H), 6.50 (d, J = 2.6 Hz, 1H), 6.12 (s, 1H), 5.21 (s, 2H), 4.12 (q, J = 7.1 Hz, 2H), 3.83 (q, J = 7.0 Hz, 6H), 3.41 (q, J = 7.1 Hz, 4H), 3.23 (q, J = 6.5 Hz, 2H), 1.66 (m, 2H), 1.22 (m, 15H).
Surface deposition of (7-(diethylamino)-2-oxo-2H-chromen-4-yl)methyl (3-triethoxysilyl)propyl)carbamate

Coumarin 1 (75 mg, 0.1 mmol) was dissolved in 10 mL of anhydrous toluene in an I-CHEM vial equipped with custom Teflon substrate holders. The solution was heated at 60 °C for 8 hrs. After the solution cooled, the substrates were individually removed, rinsed with a large amount of toluene, CH₂Cl₂, and methanol. Film thickness was measured by ellipsometry for silicon substrates. All surfaces were analyzed by contact angle to approximate deposition quality prior to further analysis. If the deposition solution was kept closed, the same solution could be used for multiple depositions.

7-decyloxy-4-methyl-chromen-2-one

K₂CO₃ (314 mg, 2.27 mmol) was added to a flask and flame dried with the solid present. Under flowing N₂, 4-methyl-umbeliferone (200 mg, 1.13 mmol) was added and then the mixture was dissolved in anhydrous DMF (11.3 mL). After the mixture turns yellow and no more solids appear to dissolve, 1-bromodecane (502 mg, 2.27 mmol) was added drop-wise. The mixture was stirred for 13 hr at 80°C followed by neutralization with HCl (0.1M) and extraction with CH₂Cl₂. After washing multiple times with water to remove residual DMF, the organic phase was dried with Na₂SO₄. Purification by flash chromatography (SiO₂ 3:1 Hexanes: Ethyl Acetate Rf = 0.37) provided 283 mg (78% yield) of a white solid. MP 44-46°C ¹H NMR (500 MHz, CDCl₃)
δ = 7.49 (d, J = 8.3 Hz, 1H), 6.86 (dd, J = 8.5, 2.7 Hz, 1H), 6.81 (d, J = 2.7, 1H), 6.13 (d, J = 1.2 Hz, 1H), 4.02 (t, J = 6.8 Hz, 2H), 2.40 (d, J = 1.2 Hz, 3H), 1.82 (quint, J = 8.1 Hz, 2H), 1.47 (quint, J = 7.6 Hz, 2H), 1.4-1.24 (m, 12H), 0.89 (t, J = 7.3, 3H).

13C NMR (500 MHz, CDCl3) δ = 216.2, 162.4, 161.6, 155.5, 152.8, 125.6, 113.6, 112.9, 112.0, 101.5, 68.8, 32.1, 29.7, 29.6, 29.5, 29.2, 26.2, 22.9, 18.9, 14.3.  EI-MS (m/z): calcd for C20H28O3 316.2; found, 316.1.

7-decyloxy-4-hydroxymethyl-chromen-2-one

7-decyloxy-4-methyl-chromen-2-one (252 mg, 0.79 mmol) was dissolved in xylenes (7.9 mL) and SeO2 (133 mg, 1.2 mmol) was added. The solution was allowed to reflux for 18 hr. Xylenes were removed by azeotropic distillation with EtOH until dry. The remaining residue was dissolved in absolute EtOH (5 mL) and NaBH4 (30 mg, 0.79 mmol) was added in portions. After stirring for 15 min, the reaction was complete by TLC. The solution was diluted with water and HCl (1M) was added until bubbling stopped. The mixture was extracted with hexanes (2 x 10 mL) followed by CH2Cl2 (1 x 10 mL). Purification by column chromatography (SiO2 9:1 CH2Cl2:Ethyl Acetate, Rf = 0.2) yielded 134mg (50% yield) of a white solid. 1H NMR (500 MHz, CDCl3) δ = 7.40 (d, J = 9.2, 1.3 Hz, 1H), 6.84 (d, J = 2.6 Hz, 1H), 6.83 (t, J = 1.3 Hz, 1H), 6.48 (t, J = 1.5 Hz, 1H), 4.89 (dd, J = 6.0, 1.5 Hz, 2H), 4.0 (t, J = 6.6 Hz, 2H), 1.9 (t, J = 6.0 Hz, 1H), 1.81 (quint, J = 7.5 Hz, 2H), 1.46 (quint, J = 7.7 Hz, 2H), 1.39-1.21 (m, 10H), 0.88 (t, J = 7.3 Hz, 3H). EI-HRMS (m/z): calcd for C20H28O4, 332.1988; found, 332.1988.
Prop-2-ene-1-sulfonic acid 7-decyloxy-2-oxo-2H-chromen-4-ylmethyl ester

7-decyloxy-4-hydroxymethyl-chromen-2-one (100 mg, 0.30 mmol) was added to a flame dried flask under flowing N₂. Anhydrous THF (3 mL) was added, followed by the 2-propene-1-sulfonyl chloride (84.5 mg, 0.60 mmol). After cooling to 0°C, Et₃N was added dropwise and stirred for 1 hr. After stirring at room temperature for an additional hour, the reaction mixture was diluted with water and extracted with CH₂Cl₂. The organic portions were dried with Na₂SO₄ and purified by flash chromatography (SiO₂ 99% CH₂Cl₂: 1% MeOH to 98% CH₂Cl₂: 2% MeOH Rᵣ = 0.7). Combining appropriate fractions yields 119 mg (91%) of a white solid. ¹H NMR (500 MHz, CDCl₃) δ = 7.40 (d, J = 8.8 Hz, 1H), 6.88 (d, J = 8.8, 2.4 Hz, 1H), 6.85 (d, J = 2.4 Hz, 1H), 6.38 (dd, J = 1.2 Hz, 1H), 5.92 (m, 1H), 5.51 (m, 2H), 5.35 (s, 2H), 4.03 (t, J = 6.1 Hz, 2H), 3.96 (d, J = 6.8 Hz, 2H), 1.82 (quint, J = 6.8 Hz, 2H), 1.47 (quint, J = 8.3 Hz, 2H), 1.40-1.22 (m, 12H), 0.89 (t, J = 7.3 Hz, 3H).
Terminal alkene prop-2-ene-1-sulfonic acid 7-decyloxy-2-oxo-2H-chromen-4-ylmethyl ester (0.024 mmol) and toluene (2 mL) were added to a flame dried tube equipped with a stir bar. Under N₂, HSiCl₃ (0.24 mmol) was added, followed by 4 drops of Karstedt’s Catalyst. The solution immediately turned yellow and was covered with foil and stirred overnight. The toluene and excess silane is removed in vacuo leaving only a fluorescent orange solid. NMR suggests reaction is complete by the disappearance of the alkene protons.

**Surface deposition of (7-(decyloxy)-2-oxo-2H-chromen-4-yl)methyl 3-(trichlorosilyl)propane-1-sulfonate**

The solid residue remaining from the previous step is dissolved in anhydrous toluene (10 mL). Freshly deposited or cleaned (depending on the substrate) were then immersed in the solutions under N₂ atmospheres for 30-45 mins (deposition time varied with ambient humidity and needed to be optimized approx. once every month). After deposition, the surfaces were rinsed with toluene under N₂ atmosphere before removing from the glove bag. The rinsing was continued outside of the glovebag with CH₂Cl₂ and methanol. Ellipsometry and contact angle analysis was performed on every planar substrate to determine surface quality.
6-bromo-7-hydroxy-4-methyl-2H-chromen-2-one

4-bromo-resorcinol (1.98 g, 10.5 mmol), ethyl acetoacetate (2.0 g, 2.0 mL, 15.8 mmol), p-toluenesulfonic acid (300 mg, 1.58 mmol), and toluene (30 mL) was added into a 50 mL round bottom flask. The flask was equipped with a Dean-Stark trap, a condenser and allowed to reflux overnight. The resulting suspension was filtered and rinsed with toluene. After drying en vacuo, 2.37 g of a fine brown solid were obtained. $^1$H NMR (500 MHz, $d_6$-DMSO) $\delta = 11.37$ (s, 1H), 7.85 (s, 1H), 6.85 (s, 1H), 6.16 (s, 1H), 2.35 (s, 3H). $^{13}$C NMR (500 MHz, $d_6$-DMSO) $\delta = 160.46, 157.85, 154.25, 153.45, 129.76, 114.10, 111.90, 106.60, 103.65, 18.76$. El-HRMS (m/z): calcd for C$_{10}$H$_7$BrO$_3$, 253.9579; found, 253.9583.

6-bromo-7-((decyloxy)-4-methyl-2H-chromen-2-one

6-bromo-7-hydroxy-4-methyl-2H-chromen-2-one (500 mg, 1.96 mmol), bromodecane (650 mg, 610 $\mu$L, 2.94 mmol), potassium carbonate (541 mg, 3.92 mmol), and DMF (20 mL) was added to a 50 mL round bottom flask. The reaction was heated with stirring for 2 hrs, at which point the reaction was complete by TLC. After cooling to room temperature, 1M HCl was added until the solution was acidic and then extracted with CH$_2$Cl$_2$. The collected organic phase was washed with H$_2$O five times to remove excess DMF followed by brine. The organic layer was dried with MgSO$_4$ and purified by
column chromatography. (SiO$_2$, 3:1 hexane:ethyl acetate, $R_f = 0.4$) Isolated 0.405 g (52%) of a white solid. $^1$H NMR (500 MHz, CDCl$_3$) $\delta = 7.76$ (s, 1H), 6.82 (s, 1H), 6.17 (s, 1H), 4.09 (t, $J = 6.5$ Hz, 2H), 2.40 (s, 3H), 1.89 (m, 1H), 1.53 (m 2H), 1.43-1.26 (m, 12H), 0.90 (t, $J = 7.0$ Hz, 3H). EI-HRMS (m/z): calcd for C$_{20}$H$_{27}$BrO$_3$, 394.1144; found, 394.1142.

6-bromo-7-(decyloxy)-4-(hydroxymethyl)-2H-chromen-2-one

6-bromo-7-(decyloxy)-4-methyl-2H-chromen-2-one (100 mg, 0.25 mmol), SeO$_2$ (42 mg, 0.38 mmol), and 1,4-dioxane (2.5 mL) was added to a 10 mL round bottom flask equipped with a stir bar and a reflux condenser. The reaction mixture was heated at reflux overnight. The suspension was hot-filtered through a plug of silica which was then rinsed with ethanol. After removing all solvent en vacuo, the residue was redissolved in ethanol (2.5 mL) and NaBH$_4$ (9.5 mg, 0.25 mmol) was added at once. After stirring at room temperature for 15 min, the reaction was complete by TLC. The reaction was quenched with 0.1M HCl and extracted with CH$_2$Cl$_2$. After drying with Na$_2$SO$_4$, the solvent was removed en vacuo and residue purified by column chromatography (SiO$_2$, 1:9 ethyl acetate: CH$_2$Cl$_2$ $R_f = 0.3$). Collecting appropriate fractions yielded 87 mg of an off-white solid. $^1$H NMR (500 MHz, CDCl$_3$) $\delta = 7.67$ (s, 1H), 6.77 (s, 1H), 6.47 (s, 1H), 4.84 (d, $J = 1.3$ Hz, 1H), 4.05 (t, $J = 6.5$ Hz, 2H), 1.86 (m, 2H), 1.50 (m, 2H), 1.40-1.23 (m, 12H), 0.89 (t, $J = 6.8$ Hz, 3H). EI-HRMS (m/z): calcd for C$_{20}$H$_{27}$BrO$_4$, 410.1093; found, 410.1096.
(6-bromo-7-(deoxy)-2-oxo-2H-chromen-4-yl)methyl (triethoxysilyl)propyl carbamate (3)

6-bromo-7-(deoxy)-4-(hydroxymethyl)-2H-chromen-2-one (200 mg, 0.5 mmol) was dissolved in anhydrous THF (5 mL). 3-(Triethoxysilyl)propyl isocyanate (125 mg, 0.5 mmol) was then added followed by a catalytic amount of dibutyltin dilaureate (15 mg, 0.025 mmol). After stirring overnight, the solvent was removed en vacuo. The residue was purified by column chromatography (SiO$_2$ 99:1 CH$_2$Cl$_2$:MeOH) to yield 320 mg (93%) of a white solid. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.67 (s, 1H), 6.77 (s, 1H), 6.47 (s, 1H), 6.24 (s, 2H), 4.84 (d, J = 1.3 Hz, 1H), 4.05 (t, J = 6.5 Hz, 2H), 3.70 (q, 6H), 2.90 (q, 2H), 2.15 (t, 2H), 1.86 (m, 2H), 1.50 (m, 2H), 1.40-1.23 (m, 14H), 1.26 (t, 9H), 0.89 (t, J = 6.8 Hz, 3H) FD (m/z): calcd for C$_{30}$H$_{48}$BrNO$_8$Si, 657.23; found, 658.3.

**tert-butyl 2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)acetate**

t-butyl bromoacetate (4.98 g, 25 mmol), 4-methyl-umbellifurone (4.5 g, 25 mmol), potassium iodide (6.3 g, 37 mmol), and potassium carbonate (7.3 g, 52 mmol), and 100 mL of acetone were added to a round bottom flask. The stirring suspension was refluxed for 5 hrs, cooled to room temperature and diluted with 1M HCl to acidify. The solution was extracted with CH$_2$Cl$_2$, the organic portions dried with MgSO$_4$, and solvent
removed en vacuo. The resulting residue was purified by column chromatography (SiO\textsubscript{2} 1:1 hexane:EtOAc R\textsubscript{f} = 0.3) to yield 4 g of a white solid (55\%). \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta = 7.51\) (d, \(J = 8.8\), 1H), 6.90 (dd, \(J = 8.8, 2.5\) Hz, 1H), 6.75 (d, \(J = 2.5\) Hz, 1H), 6.15 (q, \(J = 1.2\) Hz, 1H), 4.57 (s, 2H), 1.60 (s, 2H), 1.49 (s, 9H). El-HRMS (m/z): calcd for C\textsubscript{16}H\textsubscript{18}O\textsubscript{6}, 290.1154; found, 290.1155.

tert-butyl 2-((4-(hydroxymethyl)-2-oxo-2H-chromen-7-yl)oxy)acetate

tert-butyl 2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)acetate (4.5 g, 15.5 mmol) was added to a round bottom with 1,4-dioxane (150 mL) along with recrystallized SeO\textsubscript{2} (2.57 mg, 23.2 mmol). The solution was allowed to reflux overnight. Xylenes were removed by azeotropic distillation with EtOH until dry. The remaining residue was dissolved in absolute EtOH (150 mL) and NaBH\textsubscript{4} (586 mg, 15.5 mmol) was added in portions. After stirring for 30 min, the reaction was complete by TLC. The solution was diluted with water and HCl (1M) was added until bubbling stopped. The mixture was extracted with CH\textsubscript{2}Cl\textsubscript{2}. Purification by column chromatography (SiO\textsubscript{2} 99:1 CH\textsubscript{2}Cl\textsubscript{2}:MeOH to 98:2 CH\textsubscript{2}Cl\textsubscript{2}:MeOH) yielded 2.69 g (56% yield) of a white solid. \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta = 7.43\) (d, \(J = 8.8\) Hz, 1H), 6.88 (dd, \(J = 8.8, 2.5\) Hz, 1H), 6.77 (d, \(J = 2.5\) Hz, 1H), 6.48 (s, 1H), 4.87 (s, 2H), 4.57 (s, 2H), 1.5 (s, 9H). El-HRMS (m/z): calcd for C\textsubscript{16}H\textsubscript{18}O\textsubscript{6}, 306.1103; found, 306.1103.
tert-butyl 2-((2-oxo-4-(((3-(triethoxysilyl)propyl)carbamoyl)oxy)methyl)-2H-chromen-7-yl)oxy)acetate (4)

In a flame dried round bottom flask, tert-butyl 2-((4-(hydroxymethyl)-2-oxo-2H-chromen-7-yl)oxy)acetate (300 mg, 0.97 mmol) was dissolved in anhydrous THF under flowing Ar. 2-isocyanato-propyl triethoxysilane (242 mg, 0.97 mmol) was then added followed by a catalytic amount of dibutyltin dilaureate (30 mg, 0.048 mmol). The solution was allowed to stir under Ar overnight (16 hr) at which point the solvent was removed en vacuo. The residue was purified by column chromatography (SiO₂ 1:1 hexane:EtOAc, R_f = 0.5) to collect 487 mg (90%) of a white waxy residue. ¹H NMR (500 MHz, CDCl₃) δ = 7.44 (d, J = 8.8 Hz, 1H), 6.89 (dd, J = 8.8, 2.4 Hz, 1H), 6.78 (d, J = 2.4 Hz, 1H), 6.33 (s, 1H), 5.23 (s, 2H), 4.57 (s, 2H), 3.83 (q, J = 6.9 Hz, 6H), 3.24 (q, J = 6.5 Hz, 2H), 1.67 (m, 2H), 1.49 (s, 9H), 1.23 (t, J = 7.0, 9H). EI-HRMS (m/z): calcd for C₁₆H₁₈O₆, 306.1103; found, 306.1103.
5.8 Figures

Figure 5.1 Calculated absorbance spectrum (left) and photonic band structure diagram along the Γ-L direction (right) of the <111> face of a polystyrene opal.
Figure 5.2 MEEP calculations of the spatial distribution of the electric field intensity indicating the formation of “hotspots” (shown in red) in inverse opals structures at a) different frequencies of the incoming light, illustrating how light is distributed in the structure depending on the photonic band at which the light propagates b) a 3D representation at $a/\lambda = 1.3$. The red regions represent areas where the electric field intensity is greater than or equal to 4x the blue regions.
Figure 5.3 Deposition of coumarin 1 onto substrate followed by photolysis of the coumarin to provide the primary amine.

Figure 5.4 Contact angle as a function of exposure time indicating controlled photochemical conversion of the coumarin modified TiO$_2$ substrates. Lower doses resulted in similar changes in contact angle, suggesting that the conditions used were above the threshold exposure levels required for photoconversion of the coumarin photofuse.
Figure 5.5  Fluorescence micrographs of a glass slide modified with the diethylaminocoumarin, patterned, and treated with dansyl chloride as a covalent fluorophore. The image on the left was enhanced to increase contrast between patterned and non-patterened regions.

Figure 5.6  Optical micrograph of patterned substrates labeled with carboxylated (left) and sulfonated (right) polystyrene spheres. The patterned lines are 90 µm and the spaces are 180 µm wide.
Figure 5.7  Confocal microscopy image of inverse titania opal that was exposed with UV light to cleave the surface and treated with dansyl chloride. A-D) Various z-slices through the inverse opal. Inset images highlight variations in intensity. E) Compiled z-stack (observed along the xy-plane, the bottom of the image is the supporting slide) that shows some regions of higher intensity along the z-direction. In all images, some regions of increased intensity can be seen but it remains unclear if these regions are the intended “hotspots.”
Figure 5.8 Surface modification using coumarin 2 and subsequent UV exposure to provide hydrophobic to negative transition.

Figure 5.9 SEM images of patterned coumarin monolayers subjected to TiO₂ ALD conditions. Initial attempts showed promising results (A and B), but it was discovered later that sonication (C) and carbon tape pull-off (D) removed the sacrificial material.
Figure 5.10 Surface modification using coumarin 3 and subsequent UV exposure to produce the primary amine on the surface.

Figure 5.11 SEM images of patterned coumarin monolayers subjected to Ag electroless deposition conditions. Initially, there appears to be very low selectivity (left) but following sonication, the patterned features appear quite clear.
Figure 5.12 Charge inversion coumarin 4 deposited on surface with subsequent deprotection to provide a net negative charge. Exposure with UV light induces the photolysis of the coumarin core to produce the primary amine.
**Figure 5.13** SEM images of patterned coumarin 4 monolayer which was subjected to Ag electroless deposition. A shows the pattern which did not require any sonication. B and C are zoomed regions of the exposed and unexposed areas, respectively. With this nearly 100% selective deposition, the as-deposited films are expected to be conductive and non-conductive, respectively.
5.9 References


CHAPTER 6

Conclusions

Work contained within this thesis describes the development of photofuses, known as the 4-yl-(methyl)coumarins, as a unique method to modify surfaces using light. The class of 4-yl-(methyl)coumarins offer significant improvements over the commonly used o-nitrobenzyl systems (NB), as well as some other simple photofuses (See Chapter 1). The coumarins have rates of photocleavage that are roughly 2 orders of magnitude faster than that of NB, produce no reactive byproducts, are readily prepared from commercially available starting materials, and have the added advantage of becoming fluorescent upon photocleavage.

A synthetic scheme is described which takes advantage of inexpensive starting materials and a divergent pathway, thus enabling facile synthesis of many different coumarin photofuses. The synthetic route used here depends primarily on the SeO$_2$ oxidation of the 4-methyl position, which is the major limiting factor in terms of yield. Alternative oxidation schemes may allow further simplification of the proposed synthetic schemes. As Chapter 3 outlines, many transitions are possible and the application of such photoresponsive molecules are limited only by the applications in which they are used. Due to the unique ability to tune the photochemical properties of the coumarin core, the surface properties based on the linkers used, as well as the methods in which the photofuse is incorporated onto a surface (i.e., monolayer formation vs. polymer thin films via silane coupling or polymerization of coumarin monomers, respectively), the 4-
yl-(methyl)coumarin is capable of dramatically changing how functional surfaces are prepared and used.

The photochemistry of the coumarin produces no reactive byproducts on exposure to UV light. However, the initial results concerning the [2+2] side-reaction presented in Chapter 3 do require further investigation. When the 7-position is a methoxy group, UV-Vis analysis suggests the [2+2] process is active and is reversible as expected. Interestingly, when the 7-position is lengthened to a decyl derivative, the [2+2] is no longer observed. Systematic variation of the alkyl chain followed by UV-Vis analysis may provide insight into this possible competitive reaction pathway that has not been previously reported.

Synthesis of the “toolbox” would be useless if the transitions could not be used in an application. The remainder of the work contained in this thesis highlights the ability to tune the coumarin photofuse to desired wavelengths of photocleavage as well as using the changes in surface chemistry to generate functional surfaces. The photochemical greyscaling utilized the mechanically robust, flexible PDMS masks to generate variable levels of UV light at the surface. Incorporation of the coumarin photofuse created a method by which the surface energies could be controlled to ultimately produce pressure sensitive microfluidic gates. In addition, the preparation of a 4-methyl-carbamate to produce a primary amine at the surface provides a means to post-exposure modification. This naturally inspires biological sensing applications but there is seemingly no limit to the types of applications for this “caged” surface.

The application of coumarins as molecular photoresists in two dimensions is interesting, but having the same level of control within three-dimensional structures is
clearly more appealing. Utilization of the coumarins coupled with the unique optical properties of opals and inverse opals creates a method by which to confirm the theoretically predicted hotspots. Although, for this direct observation, significant efforts will need to be made to observe such small features contained within a three-dimensional structure. Once this occurs, the concept of a rainbow DSSC solar cell (Chapter 5) is much more feasible. In the interim, the optical properties of the opals can be used to generate three-dimensional structures within the opal using the coumarin as a templating agent; a technique that until this point has not been reported. Of specific interest is the negative-to-positive coumarin transition that provides nearly 100% selectivity when subject to Ag electroless depositions. This particular coumarin photofuse may be useful in many similar surface labeling studies.

It is the hope of the author that the 4-yl-(methyl)coumarin becomes as widely used as it’s predecessor, the NB photofuse. The progression from biological caging group to surface modifier appears to be how both will eventually become widely used for their various properties. Moreover, the coumarins are not limited to just surface chemistry, but can be used in a wide variety of materials systems. Therefore, the 4-yl-(methyl)coumarins can be tailored to provide certain specifications very well and are thus quite amenable to use in materials applications.
APPENDIX A

Mechanophore Discovery Aided by a Turn-on Fluorescence Probe

A.1 Initial Efforts for Coumarin Mechanophore

The mechano-activation of covalent bonds is an area of considerable current interest due to its potential applications in catalysis and in materials science for self-sensing and self-healing polymers. The incorporation of a mechanophore near the mid-point of a polymer chain emerged as an extremely powerful tool for controlling the specific bond activation of the polymer. In general, mechanophores easily undergo a reaction in response to mechanical force. However, due to the large size of macromolecules, it is challenging to investigate chemical changes that occur at one specific unit. New probes are needed to explore and discover new mechano-activity, an aspect of chemical reactivity that remains poorly investigated. Here we describe a strategy based on a turn-on fluorescent probe which led to the discovery of a new mechanochemical activation process.

Our strategy for the detection of the bond activation process relies on the selective activation of a mechanophore containing a coumarin unit, which is incorporated near the center of a polymer chain. Upon applying mechanical force, the mechanophore is specifically activated to generate a fluorescent coumarin-ended polymer chain. The fluorescence change during the mechanoactivation can then be

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† This work was originally suggested and developed by J. Ritchey. This appendix is intended to catalogue progress of the coumarin mechanophore project and summarize recent work towards understanding its mechanism of mechanochemical cleavage. Work contained within section A.1 was performed by Dr. Qilong Shen, Dr. Hideo Enozawa and Chrissy Weaver. Subsequent work in section A.2 was performed by J. Ritchey with sonication and fluorescence studies performed by Q. Shen.
monitored and quantitatively analyzed. Several mechanophores with the coumarin unit were synthesized (Chart 1).

Single electron transfer living radical polymerization (SET-LRP) was employed for the synthesis of mechanophore-linked polymers, as this method has been shown to generated high molecular weight polymers with narrow polydispersity indices (PDIs).\textsuperscript{11,6} Coumarin-sulfonate mechanophore 1 incorporated polymer (PMA-CS-PMA, 122 kDa, PDI = 1.2) and coumarin-carboxylic ester 3 incorporated polymer (PMA-CC-PMA, 121 kDa, PDI = 1.3) were synthesized and subjected to an acoustic field to probe for mechanical activity. Initial attempts to polymerize coumarin-sulfonate 4, however, did not result in polymer formation.

The responses of the polymers with different coumarin mechanophores to the acoustic field differed greatly. When 7.5 mg of PMA-CS-PMA (122 kDa) was subjected to pulsed ultrasound in the presence of 600 equivalents of radical trap 2,6-di-\textit{tert}-butyl-4-methylphenol (BHT) in CH\textsubscript{3}CN/H\textsubscript{2}O (9:1) for 30 min under an argon atmosphere at 6-9 °C, fluorescence intensity increase significantly. The molecular weight of the polymer after sonication (78.0 kDa) was slightly higher than half of the original molecular weight of the polymer. In contrast, sonication of PMA-CC-PMA (121 kDa) under the same conditions only leads to slightly increased fluorescence intensity. The disparity for the two polymers in responses to pulsed ultrasound strongly indicates that the sulfonate group is critical to the fluorescence change during sonication and the activation of the coumarin-sulfonate mechanophore is induced by mechanical force.

In order to confirm the mechanochemical nature of the activation of the coumarin-sulfonate mechanophore, two additional control experiments were performed.
A mono-functional coumarin-sulfonate initiator 2 was synthesized and used to prepare end-terminated polymer (CS-PMA, 122 kDa, PDI = 1.3). Sonication of this polymer for 30 min leads to a slight increase in fluorescence, although the polymer chains were cleaved during sonication, as indicated by the GPC analysis. In a second control, a mixture of homopolymer PMA with small molecule 1 were subjected to sonication under the same conditions, the increase in fluorescence intensity was minimal. In addition, PMA-CS-PMA is reasonably stable even at 90 °C. In fact, refluxing the polymers in CH₃CN/H₂O (9:1) for 24 h resulted in only a slight (ca. 10%) increase in fluorescence intensity. These control experiments combining with thermal stability of the mechanophore indicate that the activation of coumarin-sulfonate mechanophore is stress-induced and not the result of thermal effects.

To determine the kinetics of the mechano-activation process, we next studied the fluorescence of PMA-CS-PMA over the sonication time. Fluorescence spectra were acquired for aliquots of the sonicated solution removed at timed intervals. Over time, fluorescence signal increased in intensity. The fluorescence reached a plateau after 80 min, which suggested that the activation of the CS mechanophore reached a maximum but was not necessarily 100% complete (See Sect A.2). In contrast, the activation of the mechanophore in two control experiments occurred to less than half conversion even after 4.5 h (Figure 3-B).

To evaluate the effect of the polymer molecular weight on the rate of the activation, a series of PMA-CS-PMA with different molecular weights were synthesized and the kinetics of the sonication reactions of these polymers were studied. The rate constant (k) of the mechanophore activation for various molecular weights of PMA-CS-
PMA was calculated using a simple first order kinetic model. The dependence of the rate constants on polymer molecular weight for the activation of the coumarin-sulfonate is shown in Figure 3-C. It was found that the rate constants were linearly dependent on polymer molecular weight; PMA-CS-PMA samples with higher molecular weights underwent faster bond cleavage. PMA-CS-PMA under 16.6 kDa could not be activated, which is lower than previous reported limiting molecular weights in other sonicated polymers.\(^7\) The chain-length dependence is additional strong evidence that supports the mechanochemical reactivity of the coumarin-sulfonate mechanophore.

To determine which covalent bond of the CS mechanophore was cleaved during sonication, we synthesized two \(^{13}\)C labeled CS mechanophores (Figure 4). If the C-O bond of the labeled carbon in these mechanophores were cleaved during sonication, we would expect that the chemical shift of these labeled carbons in the \(^{13}\)C NMR spectra would change before and after sonication. However, in both cases there is no change in chemical shift after sonication. Based on these observations, it remains unclear which bond is activated under mechanical stress.

Efforts were made to characterize the small molecule mechanophores shown in Chart A.1 to compare with the mechanophore incorporated-polymer. Small molecules 1 and 4 were subjected to UV irradiation (365 nm, 20 mW/cm\(^2\)) for various times and monitored by fluorescence microscopy (Figure A.5). Exposure was continued until the maximum fluorescence intensity was observed. The samples were then submitted for LC-MS. Both 1 and 4 experienced increases in fluorescence intensity following UV exposure, but two notable differences between the two were observed. First, the fluorescence intensity increases much faster for 4 than 1. This is consistent with
previously published reports on the rates of photochemical cleavage.\textsuperscript{8} Second, there is a reproducible red-shift in the fluorescence emission spectra for 1 following UV exposure. The cause of this red-shift has not been explained. LC-MS spectra showed some differences between the exposed and unexposed samples, however none provided conclusive evidence of conversion. Moreover, the LC separation was poor due to the very polar solvent systems used in the mass spectrometry facility.

\textbf{A.2 Redesign of Coumarin Mechanophore}

New design elements were considered based on the difficulties in determining the details of mechanical cleavage with the above coumarin mechanophores. Electronically, the CS and CC mechanophores are quite different than the original designs which placed the sulfonate ester at the 4-methyl position and the ether at the 7-position. This electronic consideration is essential to the success of this project for multiple reasons. The most important of which is photochemistry of the 4-yl-methyl coumarins is dramatically inhibited when electron withdrawing substituents are placed at the 7-position.

The photochemical cleavage of 4-yl-methyl coumarins is well-understood\textsuperscript{8a, 9} (See Chapter 3 for a complete discussion of the photochemistry of coumarins). The 4-(hydroxymethyl)coumarin produced upon UV exposure is dramatically more fluorescent than the uncleaved esters, therefore the increase in fluorescence intensity can be used to monitor the extent of reaction. This method is commonly used in photochemical
applications, but can be useful in mechanochemical applications as well. Moreover, if one assumes that the photochemical products are the same as the mechanochemical products, the fluorescence change can be used to estimate the extent of mechanochemical activation as compared to photochemical activation. The reversible nature of previous mechanophores such as the spiropyran, have made approximating extent of activation impossible. Therefore, the structural features of the mechanophore must be chosen carefully to facilitate this comparative study of mechanochemical and photochemical behavior.

The first of two mechanophores was prepared as illustrated in Figure A.6. Using synthetic schemes similar to those presented in Chapter 3, first the coumarin diol 5 was prepared so the subsequent esterification using the α-bromo-isobutyryl bromide could provide the desired diester in one step. This coumarin is expected to undergo photochemical and mechanochemical cleavage of the benzyl carbon-oxygen bond as outlined in Chapter 3 and previous publications.⁸a,⁹

Mechanophore 6 was subject to SET-LRP polymerization conditions with methyl methacrylate to produce the chain-centered mechanophore. The resulting polymer (126 kDa, PDI = 1.3) was then subject to an acoustic field. Monitoring the fluorescence response as a function of sonication time indicated no changes in the intensity, suggesting the mechanophore 6 is not mechanochemically active. This result is unsurprising considering the leaving group ability of the carboxylate compared to the sulfonic acid from the photochemical cleavage pathway. Although the mechanisms are not likely to be the same, as a first approximation we will use the photochemical mechanism as a guide to develop new mechanophores.
Based on these results, the most likely mechanophore candidate (7) is similar to 4 but does not have the electron withdrawing ester moiety at the 7-position. Electron withdrawing moieties at both the 6- or 7- position have significant influences on the photochemical cleavage due to the destabilization of the carbocation-like intermediate (See Figure 3.3, 15). Coumarin 5 however indicated that the ether alone is not sufficient to activate the mechanochemical pathway. The sulfonic acid is a better leaving group than the carboxylic acid and may be necessary for a successful mechanophore.

A proposed synthetic pathway is shown in Figure A.7. Following the design rules presented in Chapter 3, a divergent pathway is presented which may facilitate multi-gram synthesis of the di-functional initiator, as well as the necessary end-group controls. TMS protection of the bromoethanol using typical protecting conditions should provide the 7-position linker.\(^\text{10}\) Coupling of the TMS protected alcohol to the coumarin diol can be achieved through Williamson ether conditions. The sulfonyl chloride would require an oxidative chlorination reaction from the disulfide\(^\text{11}\) or possibly using sulfuryl chloride in the presence of a metal nitrate on the thiol.\(^\text{12}\) Subsequent esterification using 2-bromo-isobutyryl bromide followed by formation of the sulfonate ester could then be isolated. Finally, deprotection of the TMS protected alcohol followed by another esterification with 2-bromo-isobutyryl bromide will yield the target di-functional initiator. The limiting step in this proposed pathway will likely be the generation of the sulfonyl chloride because the reaction typically uses chlorine gas and generates multiple byproducts, although alternative preparations have been reported that may provide the desired product.
A.3 Conclusions

In conclusion, we have shown multiple coumarin mechanophores for use as a turn-on fluorescence probe for the discovery of new mechanophores. However, current results suggest careful design factors are required. Currently one coumarin (1) appears to be mechanically active, but the cleavage location is not well understood. The $^{13}\text{C}$ labeling experiments previously reported are certainly useful to identify new mechanophores.\textsuperscript{1h, 1k} Unfortunately, the labeling experiments remain too time-consuming and costly for routine use. The availability of a sensitive fluorescence probe method to accurately measure the response to the mechano-activation of one covalent bond in a mechanophore offers a novel approach for the discovery of new mechanophores and may provide many insights into the mechanochemical process.
A.4 Figures

Chart A.1 Mechanophores containing coumarin unit.

Figure A.1 Schematics of a bifunctional mechanophore (a) and control molecules containing a mechanophore linkage at the polymer chain end (b) or a mixture of small molecule mechanophore and a polymer chain (c). The mechanophore is colored in red for emphasis.
Figure A.2 Fluorescence change for sonication of (A) PMA-CS-PMA (122 kDa) and (B) PMA-CC-PMA (121 kDa) and control experiments including: (C) Coumarin-sulfonate ended polymer CS-PMA (121 kDa) and (D) A mixture of PMA (160 kDa) and small molecule 1.

Figure A.3 Fluorescence spectra of 122 kDa PMA-CS-PMA over sonication time (A); Fluorescence change at 400 nm over time for sonication of PMA-CS-PMA (O), PMA-CC-PMA (■), and a mixture of PMA + 1 (▲) (B); Rate constant versus molecular weight of PMA-CS-PMA (C).
Figure A.4 $^{13}$C labeled coumarin-sulfonate mechanophores and their $^{13}$C NMR spectra before and after sonication.

Figure A.5 Fluorescence emission spectra for the photochemical conversion of 1 (top) and 4 (bottom).

Figure A.6 Synthetic route to difunctional coumarin initiator 6.
Figure A.7 Proposed synthesis of mechanophore 7.
A.5 References


9. (a) Eckardt, T.; Hagen, V.; Schade, B.; Schmidt, R.; Schweitzer, C.; Bendig, J., 

