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Synthesis and Characterization of Photochromic Copolymers Containing 3-Indolylfulgides/ Indolylfulgimides

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SYNTHESIS AND CHARACTERIZATION OF PHOTOCHROMIC COPOLYMERS CONTAINING 3-INDOLYLFULGIDES/INDOLYLFULGIMIDES

A dissertation submitted in partial fulfillment of

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by

Changjun Fan

2015

To: Dean Michael R. Heithaus
College of Arts and Sciences

This dissertation, written by Changjun Fan, and entitled Synthesis and Characterization of Photochromic Copolymers Containing 3-Indolylfulgides/Indolylfulgimides, having been approved in respect to style and intellectual content, is referred to you for judgment.

We have read this dissertation and recommend that it be approved.

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Kathleen Rein

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Watson J. Lees, Major Professor

Date of Defense: October 13, 2015

The dissertation of Changjun Fan is approved.

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University Graduate School

Florida International University, 2015

DEDICATION

I dedicate this work to my wife Ping Jiang, my mother Yujie Lu, my father Shiqin Fan and sister Lin Fan. Without their understanding, encouragement, support and love, the completion of this work would not have been possible.

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ABSTRACT OF THE DISSERTATION

SYNTHESIS AND CHARACTERIZATION OF PHOTOCHROMIC COPOLYMERS CONTAINING 3-INDOLYLFULGIDES/INDOLYLFULGIMIDES

by

Changjun Fan

Florida International University, 2015

Miami, Florida

Professor Watson J. Lees, Major Professor

Fulgides and fulgimides are important organic photochromic compounds and can switch between the open forms and the closed forms with light. The 3-indolylfulgides and 3-indolylfulgimides exhibit promising photochromic properties and have great potential in optical memory devices, optical switches and biosensors. Copolymers containing 3-indolylfulgides/indolylfulgimides synthesized via free radical polymerizations increase conformation changes and allow the photochromic compounds to be uniformly distributed in the polymer matrix.

A trifluoromethyl 3-indolylfulgide and two trifluoromethyl 3-indolylfulgimides with one or two polymerizable *N*-stryryl group(s) were prepared. Copolymerization with methyl methacrylate provided two linear copolymers or a cross-linked copolymer. The properties of the monomeric fulgide/fulgimides and copolymers in toluene or as thin films were characterized. In general, the photochromic monomers and copolymers revealed similar photochromic properties and exhibited good thermal and photochemical stability. All compounds absorb visible light in both open forms and closed forms. The closed form copolymers were more stable than the open form copolymers and showed little or no degradation after 400 h. The photochemical degradation rate was less than 0.03% per cycle. In films, conformational restrictions were observed for the open forms suggesting that the preparation of films from the closed forms is advantageous.

Two novel methyl 3-indolylfulgimides with one or two polymerizable *N*-stryryl group(s) were prepared. Copolymerization of acrylamide with the methyl indolylfulgimides or the trifluoromethyl indolylfulgimides yielded two aqueous soluble linear copolymers and two photochromic hydrogels. The closed form copolymers containing trifluoromethyl indolylfulgimides were hydrolyzed in aqueous solution by replacing the trifluoromethyl group with a carboxylic acid group. The resulting carboxylic copolymers were also photochromic. The copolymers containing methyl fulgimides were stable in aqueous solutions and did not hydrolyze. Both methyl and carboxylic copolymers exhibited good stability in aqueous solutions. In general, the open form copolymers were more stable than the closed form copolymers, and the copolymers revealed better stability in acidic solution than neutral solution. The linear copolymers displayed better photochemical stability in neutral solution and degraded up to 22% after 105 cycles. In contrast, the hydrogels showed enhanced fatigue resistance in acidic condition and underwent up to 60 cycles before degrading 24%.

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1. INTRODUCATION

1.1 Photochromic compounds

Photochromic compounds are well known because of their successful application in photochromic lenses. The lenses are coated with photochromic compounds, which darken in sunlight because of the absorption of UV photons and then become clear in diffused light. The phenomenon is called photochromism, which is defined as a reversible transformation of chemical species between two forms having different absorption spectra induced by a certain type of electromagnetic radiation.[1]

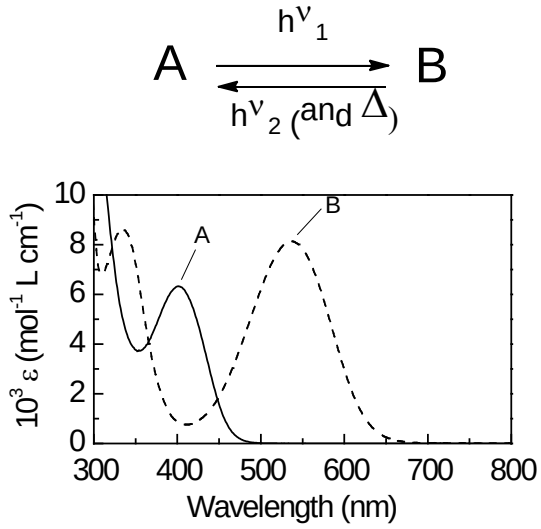


Figure 1. Photochromic reactions and absorption spectra of a photochromic compound

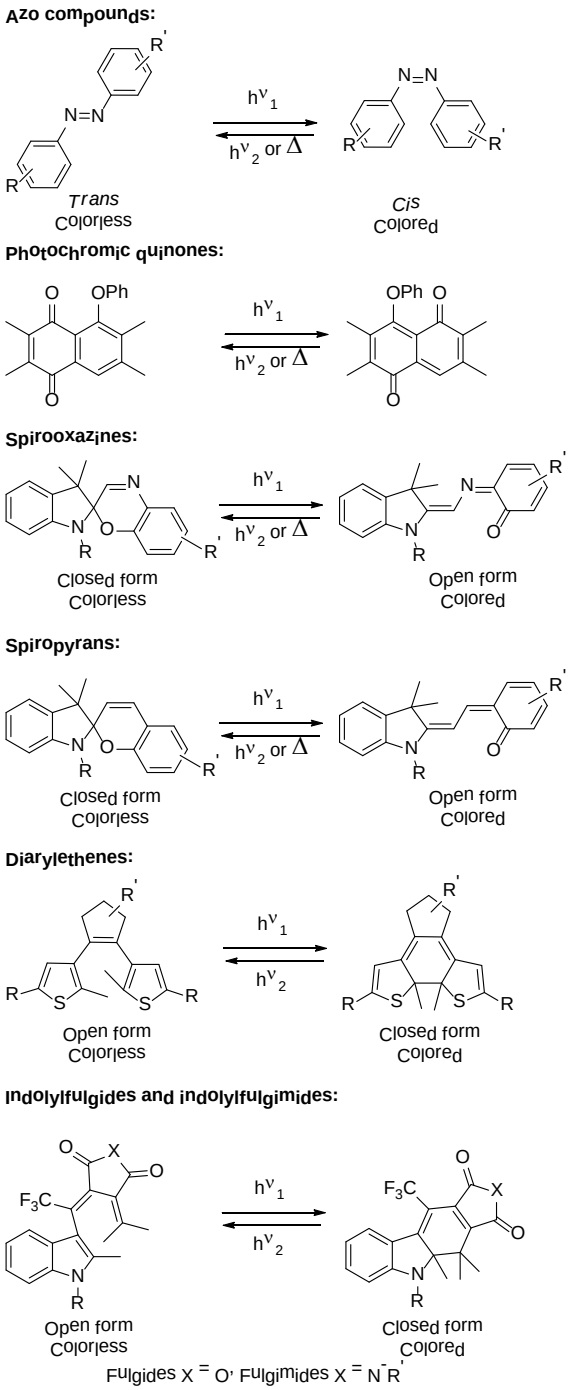
In the past several decades, many organic photochromic compounds were synthesized, and their photochromic properties were thoroughly studied.[1] In general, organic photochromic compounds have two forms, A and B. Figure 1 shows that the A form is thermally stable and the forward reaction (A to B) occurs photochemically. For some photochromic compounds, such as spiropyrans and spirooxazines, the B form is thermally unstable, and the reverse reaction occurs photochemically and thermally. For other photochromic compounds, such as fulgides, the B form is thermally stable, and the reverse reaction occurs only photochemically. For almost all organic photochromic compounds, the longest wavelength absorption maximum (λ_{max}) of the B form

occurs at a longer wavelength than that of the A form, and the system involves unimolecular reaction.[1] Normally, the A form is colorless and B form is colored. Therefore, the forward reaction (A to B) is referred as a coloration reaction, and the reverse reaction is a decoloration reaction, even if both forms are colored.[1]

The early organic photochromic compounds were limited by their fast photodegradation. From 1980 onwards, researchers focused on the development of organic photochromic compounds with good photochemical stability, and many new photochromic compounds were synthesized. For example, the most photochemically stable indolylfulgide can be interconverted between the open form and the closed form for 10000 photochemical cycles before degrading by 13% in toluene.[2]

Among organic photochromic compounds, there are several important species that have attracted more attention than others because of their promising photochromic properties. Scheme 1 shows the photochromism of azo compounds, photochromic quinones, spirooxazines, spiropyrans, diarylethenes with heteroaryl groups, fulgides and fulgimides. There are several different chemical reactions involved in photochromism, for example, pericyclic reactions occur in spirooxazines, spiropyrans, diarylethenes, fulgides and fulgimides; cis-trans isomerizations take placed in azobenzenes; and quinones undergo proton and group transfer reactions. These organic photochromic compounds have been extensively studied because of their successful or potential applications in photochromic lenses, optical memory devices, dyes, optical switches, logic gates, biological imaging, and sensors.[1,3-14] However, only diarylethenes, fulgides and fulgimides have a thermally stable colored form, which makes them suitable for applications in optical memory devices where thermal irreversibility is essential.

Scheme 1. Photochromism of photochromic compounds

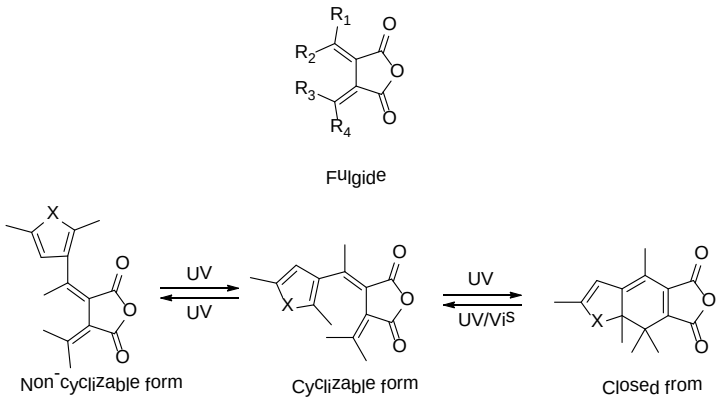


1.2 Fulgide and fulgimides

Fulgides are derivatives of 1,3-butadiene-2,3-dicarboxylic acid anhydride, which was synthesized by Stobbe in 1905.[15] As illustrated in scheme 2, if one of the R groups is aromatic or

contains a double bond, the fulgide may be photochromic. Photochromic fulgides have three forms, two open forms and one closed form. The two open forms can be interconverted by irradiation with UV light and in some cases visible lights. But only one of the open forms, the cyclizable form of the fulgide, can be converted to the closed form via a photochemical 6π-electrocyclization. For the early fulgides, the closed form was thermally unstable and the reverse reaction (ring-opening reaction) occurred thermally.[1] In 1981, Heller synthesized the first thermally irreversible fulgide, a furylfulgide with a 2,5-dimethyl-3-furyl as the aromatic group.[16,17] Since 1981, different fulgides with different substituents, such as thienylfulgide, pyrrylfulgide, and indolylfulgide were successfully prepared to improve the thermal stability and photochromic properties.[2]

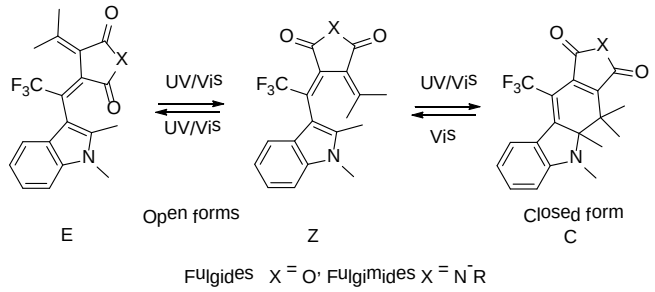
Scheme 2. Fulgide structure and photochromism



Among these different fulgides, indolylfulgides have attracted particular attention because of their promising properties, such as increased fatigue resistance, enhanced thermal stability, high efficiency of photoreactions, and visible wavelength absorption.[2,18] These excellent properties allow fulgides to be used as optical switches and optical information storage media.[19] However, previous reports indicated that fulgides were unstable in protic solvents (hydroxylic media) because the succinic anhydride ring can be easily hydrolyzed.[20,21] Therefore, fulgimides, as the

most important fulgide derivatives, were synthesized to improve the hydrolytic stability by replacing the succinic anhydride ring with a succinimide ring (Scheme 3).[2,22]

Scheme 3. Photochromism of indolylfulgides and indolylfulgimides



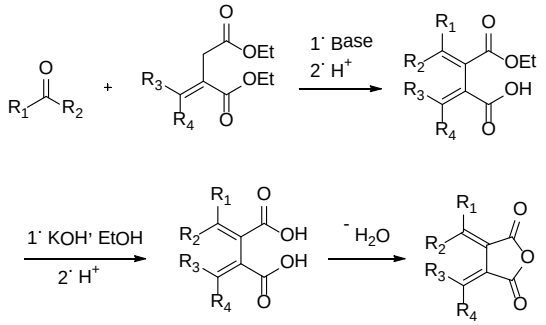
In general, fulgimides, which have similar photochromic properties with the corresponding fulgides, exhibit hypsochromic shift in UV-Vis absorption spectra relative to the fulgides.[1] Beside hydrolytic stability, another major advantage of fulgimides is that the succinimide ring allows another substituent (such as a polymerizable group) to be attached without any significant change in photochromic properties. Recently, the applications of fulgimides in many fields have been reported. Moore *et al.* designed an optoelectronic device on the basis of a fulgimide–porphyrin–dithienylethene triad that can displays different functions of logic gates with photonic inputs and outputs.[23] Also, fulgimides can be used as molecular switches to photocontrol a variety of photochemical processes. Moore *et al.* reported a porphyrin covalently linked fulgimide moiety that efficiently switch the porphyrin excited states "on" and "off".[24] In addition, fulgimides have been used to control biological activities. Willner *et al.* synthesized a thiophenefulgimide that controlled the binding of 4-nitrophenyl α-D-mannopyranoside to the protein Concanavalin A photochemically.[25] Furthermore, polymerizable groups on the succinimide ring allow the fulgimide incorporation into polymers. The resulting copolymers were photoresponsive and had similar absorption spectra with the monomeric fulgimides. For example, Rentzepis *et al.* synthesized a thermally stable 2-indolylfulgimide-MMA cross-linked copolymer, and Lees *et al.*

prepared a linear and a cross-linked copolymer containing 3-indolyfulgimide-MMA copolymer. The cross-linked copolymers exhibited excellent thermal stability and fatigue resistance.[26,27]

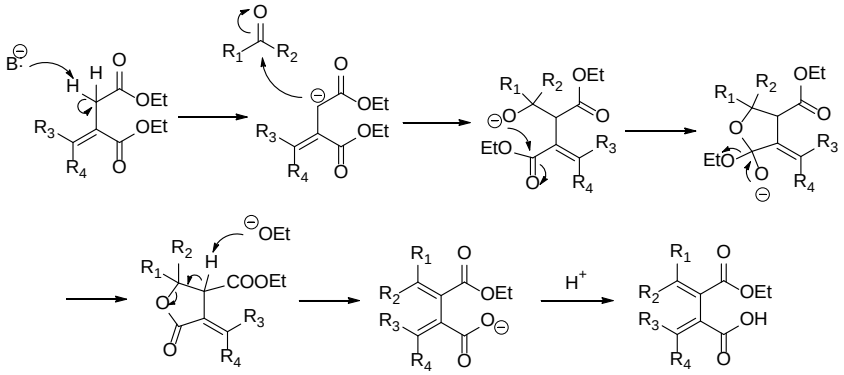
1.3 Synthesis

1.3.1 Synthesis of fulgides

Scheme 4.General synthetic pathway of fulgides via Stobbe condensation[1]



Scheme 5. Mechanism of Stobbe condensation[1]

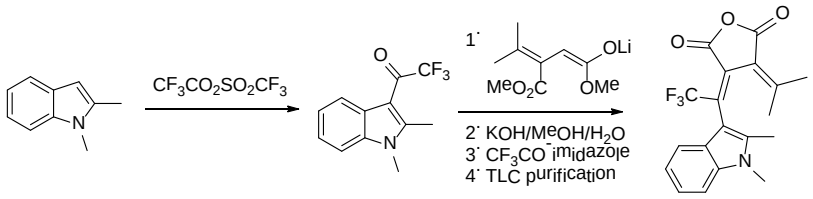


The main reaction to synthesize a fulgide is Stobbe condensation, where a ketone or an aryl aldehyde reacts with a succinate derivative to form a half ester. Then the fulgide can be prepared after ester hydrolysis and an dehydration process (Scheme 4). The synthesis of fulgide is usually low yielding and difficult to scale up in the chemical industry.[28,29] The mechanism of the Stobbe condensation which is the key step in fulgide synthesis is shown in Scheme 5.[1] The first step is deprotonation of the diethyl succinate at the α-carbon to form an ester enolate. Then the enolate undergoes aldol reaction with the carbonyl compound (ketone or aryl aldehyde) to form a β-alkoxy ester intermediate. The following intramolecular acyl substitution gives a lactone

intermediate. Then, the lactone is opened via an elimination reaction to an ester at basic condition. Finally, the ester is hydrolyzed to a diacid and dehydrated to obtain the fulgide. Therefore, to improve the overall yield of fulgide, an efficient method to prepare the lactone needs to be developed.

In 1996, Yokoyama *et al.* reported the first synthesis of trifluoromethyl indolylfulgide (Scheme 6). The synthesis started with the reaction of 1,2-dimethyl indole with trifluoroacetyl trifluoromethanesulfonate to form 1,2-dimethyl-3-trifluoroacetylindole in 42% yield. Then the Stobbe condensation was performed by treating the 1,2-dimethyl-3-trifluoroacetylindole with dimethyl isopropylidene succinate. The hydrolysis reaction was performed in KOH/MeOH/H_2O solution followed by dehydration in the presence of imidazole-trifluoroacetate to afford the indolylfulgide in a yield of 3%. The overall reaction yield is only 1%. Although the trifluoromethyl indolylfulgide showed remarkable photochemical and thermal stability, the low yielding synthesis hampered further research and potential applications.

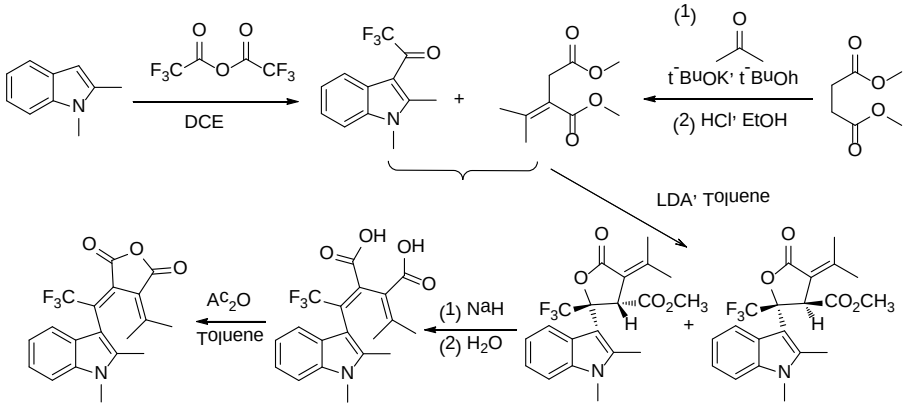
Scheme 6. Synthetic pathway of indolylfulgide by Yokoyama *et al.*[28]



An improved synthetic route to prepare the trifluoromethyl indolylfulgide was introduced by Lees *et al.* in 2001 (Scheme 7).[18] The synthesis of indolylfulgide employed two Stobbe condensations. The first condensation involved the reaction of diethyl succinate with acetone to afford diethyl isopropylidene succinate in 75% yield. Another starting material, 1,2-dimethyl-3-trifluoroacetylindole, was prepared in 96% yield by treating 1,2-dimethylindole with trifluoroacetic anhydride in 1,2-dichloroethane. The second Stobbe condensation combined diethyl isopropylidene succinate and 1,2-dimethylindole in the presence of LDA in toluene at -78 °C. The resulting *cis*/*trans* lactones were isolated in 38% yield. In the hydrolysis step,

cis/*trans* lactones was treated with NaH and followed by addition of water in DMF to form the dicarboxylic acid intermediate. Then dehydration of the dicarboxylic acid intermediate in acetic anhydride provided the trifluoromethyl indolylfulgide in 83% yield from the lactones. The new methodology improved the overall yield of trifluoromethyl indolylfulgide from 1% to 29%. Lees *et al.* demonstrated that the new method improved the yield of not only fluorinated but also non-fluorinated indolylfulgide derivatives and the method is expected to be applicable to most cis lactone derivatives. By using the method, a trifluoromethyl indolylfulgide was prepared on a large scale (10 g) with an overall yield of 18%. The new methodology allows enough preparation of significant amounts of numerous indolylfulgides, which permits investigation of photochromic properties and the potential applications.

Scheme 7. Synthetic pathway of CF_3 indolylfulgide by Lees *et al.*[18]

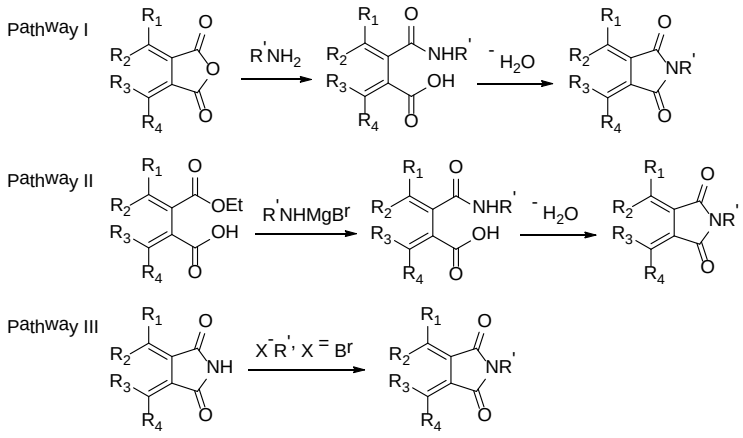


1.3.2 Synthesis of fulgimides

Fulgimides are the most important fulgide derivatives and are synthesized by replacing the succinate anhydride ring of the fulgides with a succinimide ring. Synthesis of fulgimides is low yielding in most cases. Numerous studies have been undertaken to explore preparation of fulgimides. In general, fulgimides can be prepared using the following three different methods (Scheme 8). In synthetic pathway I, fulgimide is prepared by treating fulgide with a primary amine to form a succinamic acid intermediate then followed by dehydration. The succinamic acid

intermediate also could be synthesized by the reaction of a succinic half-ester with the Grignard salt of the amine as shown in pathway II. In the third method, a non-*N*-substituted fulgimide is prepared from a fulgide and then the substituent is added by treating the fulgimide with brominated compounds. According to previous reports, synthetic pathway I is the most common way and numerous fulgimides were prepared on the basis of the first method.[1,2,27,29-34]

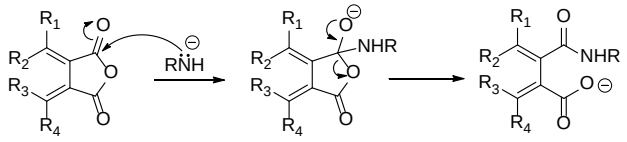
Scheme 8. General synthetic pathway of fulgimides from fulgides[1]



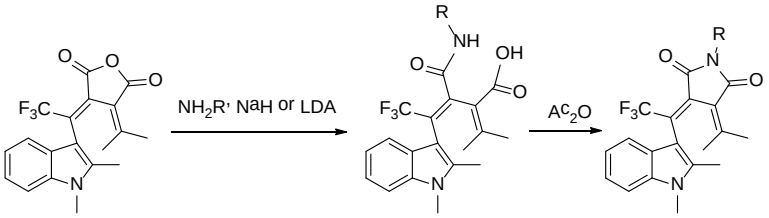
The key step in synthetic pathway I is the formation of a succinamic acid intermediate. Generally, the reaction is conducted by using a base to deprotonate a primary amine and then the substantial amine with a negative charge attacks the carbonyl carbon on the succinate anhydride ring to undergo a ring opening reaction (Scheme 9). Finally, the resulting succinamic acid intermediate was dehydrated to yield a fulgimide.

Several studies demonstrated that fulgimides can be synthesized in high yield following pathway I. A series of fluorinated indolylfulgimides were synthesized by Lees *et al*. from the precursor fulgide.[35] As shown in Scheme 10, the fulgide was reacted with substituted anilines in the presence of a base, such as of NaH or LDA, to obtain succinamic acid intermediates. Then the succinamic acid intermediates underwent dehydration in acetic anhydride to form the corresponding fulgimides in the overall yield of up to 64%.

Scheme 9. Mechanism of formation of succinamic acid intermediate in basic conditions

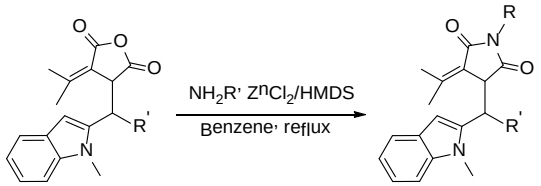


Scheme 10. Synthetic pathway of CF_3 indolylfulgimides by Lees *et al.*[35]



Rentzepis *et al.* synthesized a series of 2-indolylfulgimides using a similar method. The fulgimides were prepared in excellent yield (over 80%) from a Lewis acid and hexamethyldisilazane (HMDS)-promoted one-pot reaction (Scheme 11). The method was first introduced by Toru *et al.* who indicated that the anhydride first reacted with amine to form an succinamic acid intermediate then followed by dehydration with Lewis acid and HMDS.[36] The proposed cyclization mechanism involved the Lewis acid and HMDS-promoted silylation of the succinamic acid intermediate to form a labile trimethylsilyl ester and followed by thermal deoxysilylation to yield an imide. The reaction can be conducted under mild conditions and without forming undesired isoimides.

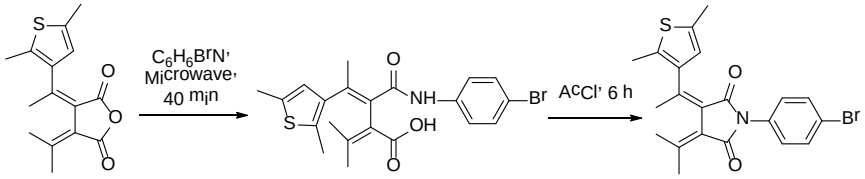
Scheme 11. Synthetic pathway of fulgimides by Rentzepis *et al.*[32]



Moreover, Lee *et al.* reported a microwave-assisted synthesis method to prepared thienylfulgimide.[37] First, the succinamic acid intermediates were formed by subjecting the mixture of precursor thienylfulgides and bromo-amines to microwave radiation by using a

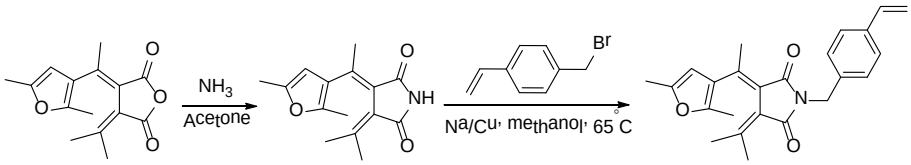
conventional microwave oven. Then the succinamic acid intermediates underwent dehydration in acetic anhydride to obtain the corresponding fulgimides in up to 85% yield (Scheme 12). The microwave-assisted synthesis provides an efficient way to make fulgimides in a shorter time and less solvent than the traditional mothed.

Scheme 12. Microwave-assisted synthesis of fulgimides by Lee *et al*.[37]



Smets *et al*. demonstrated that furylfulgimides can be prepared via the synthetic pathway III.[38] As shown in Scheme 13, a non-N-substituted furyfulgimide was synthesized in 58% yield from a reaction of a corresponding furylfulgide with ammonia in acetone. Then the non-*N*-substituted furyfulgimide was treated with 4-vinylbenzyl bromide in the presence of Cu-powder to obtain the *N*-*p*-methylstyryl furyfulgimide in a yield of 68%.

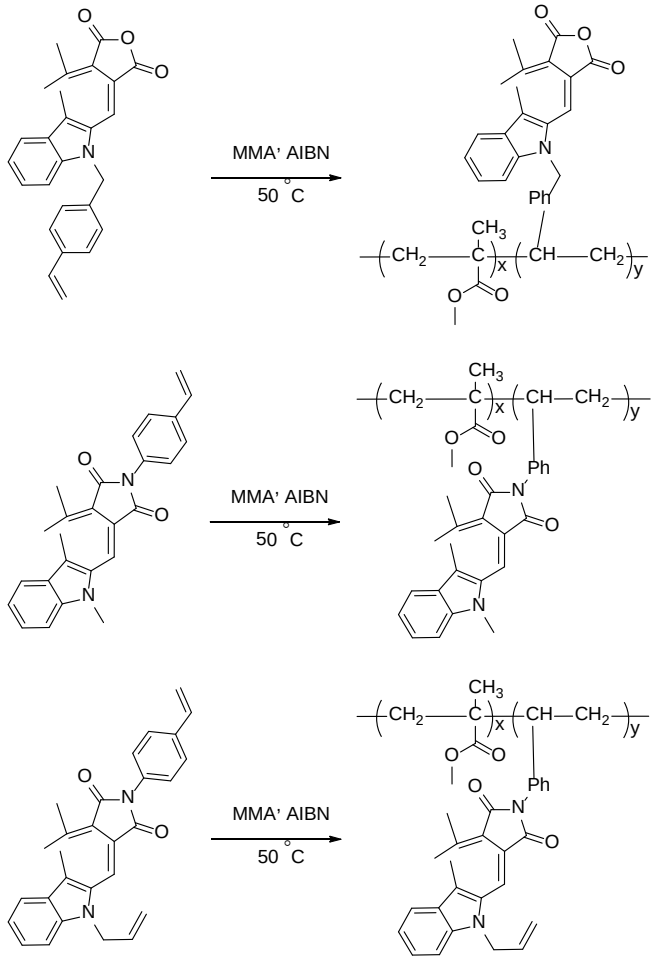
Scheme 13. Synthetic pathway of fulgimides by Smets *et al*[38]



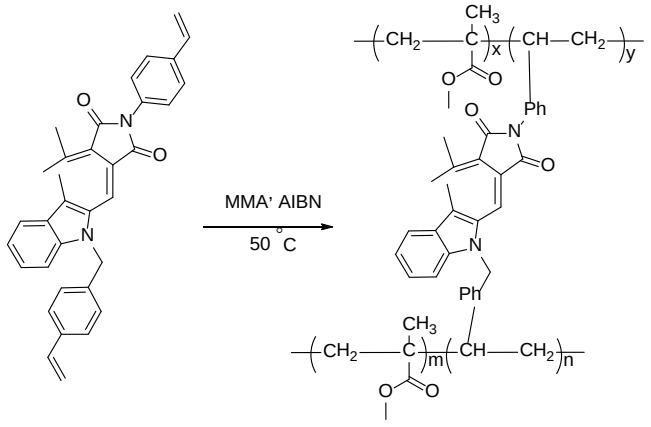
1.3.3 Synthesis of copolymers containing fulgides or fulgimides

Generally, photochromic molecules for applications in optical devices must be uniformly dispersed at relatively high concentration in a condensed phase.[26,39] For example, 3D optical memory devices on the basis of two photon absorption usually need photochromic molecules in concentrations of 0.1 M and higher to perform at the required writing and reading efficiencies.[9] Photochromic fulgides and fulgimides have been incorporated into synthetic polymers to meet the demands of technological devices.

Scheme 14. Linear PMMA copolymers containing 2-indolylfulgides or 2-indolylfulgimides[39]

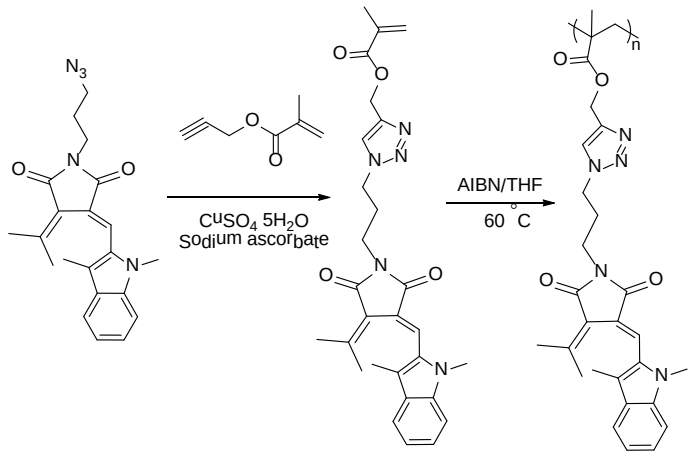


Scheme 15. Cross-linked PMMA copolymers containing 2-indolylfulgimides[26]



Rentzepis *et al*. synthesized a series of photochromic copolymers containing 2-indolylfulgides or 2-indolylfulgimides.[26,39] The fulgide or fulgimides with one or two polymerizable styrene group copolymerized with methyl methacrylate (MMA) via a free radical reaction with azobisisobutyronitrile (AIBN) to form linear or cross-linked copolymers (Scheme 14 and 15). The linear copolymers can be dissolved in organic solvent but cross-linked copolymers were insoluble in any solvents. Both kinds of copolymers are stable at room temperature and displayed similar photochromic properties as their monomeric fulgides or fulgimides. Another polymer containing triazole-linked 2-indolylfulgimide was synthesized using a similar method (Scheme 16).[40] The monomeric fulgimide with triazole ring prepared via "click chemistry" increased the thermal stability of the polymer.

Scheme 16. Pendant triazole-linked indolylfulgimide polymer[40]



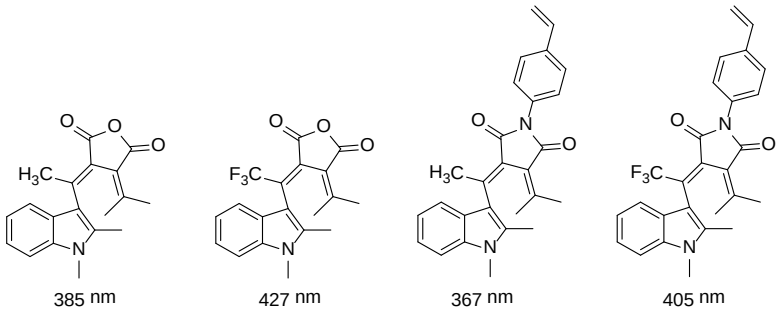
1.4 Photochromic properties of indolylfulgides and indolylfulgimides

Understanding of photochromic properties is essential to explore the potential applications of photochromic compounds. Photochromic properties include UV-Vis absorption spectra, quantum yield, photostationary state (PSS), photochemical stability (fatigue resistance), thermal stability, and hydrolytic stability. Indolylfulgides and indolylfulgimides are among the most promising photochromic compounds and their photochromic properties need to be thoroughly studied. In general, indolylfulgides, indolylfulgimides and their copolymers exhibit similar photochromic

properties. However, fulgimides are more promising than fulgides because of enhanced hydrolytic stability, which is an important characteristic for biological applications.

1.4.1 UV-Vis Spectroscopy

Scheme 17. Absorption maxima of open form indolylfulgides and indolylfulgimides



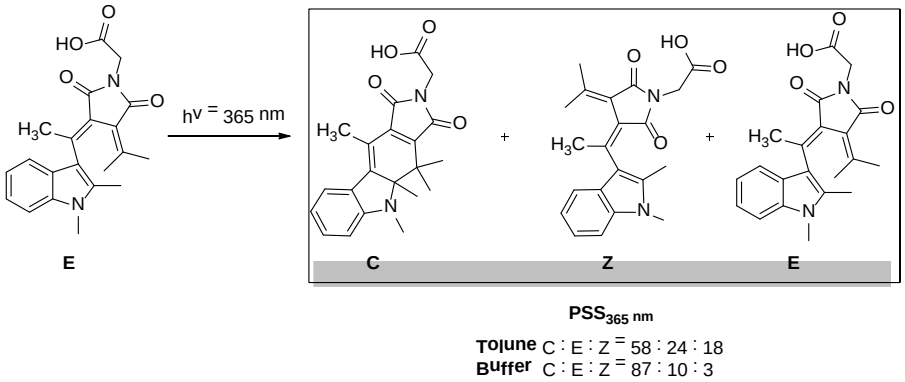
Usually, indolylfulgides and indolylfulgimides have one closed form with an absorption maximum in the visible region and two open forms that absorb in the visible region or near UV region. The absorption maxima can be affected by the substituent on the bridging position. The electron withdrawing group will shift the absorption spectra of the open form towards a longer wavelength than that of fulgimides with a electron donating group.[41] For example, the absorption maxima of the open *E*-form of CH_3 fulgide is at 385 nm in toluene (Scheme 17). The absorption maximum of the CF_3 indolylfulgide red shifts 42 nm to the visible region by replacing a CH_3 group with a CF_3 group on the bridging position. A similar observation was made for indolylfulgimides. The CH_3 indolylfulgimide absorbs at 367 nm and the absorbance of the CF_3 indolylfulgimides red shifts to 405 nm. However, compared to indolylfulgides, indolylfulgimides shift the absorption spectra of the open form towards shorter wavelength. In biological applications, visible light is preferred to be used to control the conformation of photochromic compounds because UV light can be damaging to living organism and materials.[42]

1.4.2 Photostationary state

Photostationary state (PSS) is the equilibrium composition of a photochemical reaction under a specific wavelength of electromagnetic irradiation. The PSS is important because it describes

the extent of the photochemical reaction. The ideal photochromic material in practical applications needs to contain a high percentage of the desired product at PSS. The composition of PSS is affected by wavelength of light used, the extinction coefficient of the chemical species at that wavelength, and the quantum yields of the reactions.

Scheme 18. $PSS_{365\ nm}$ of a carboxylic acid fulgimide in buffer and toluene



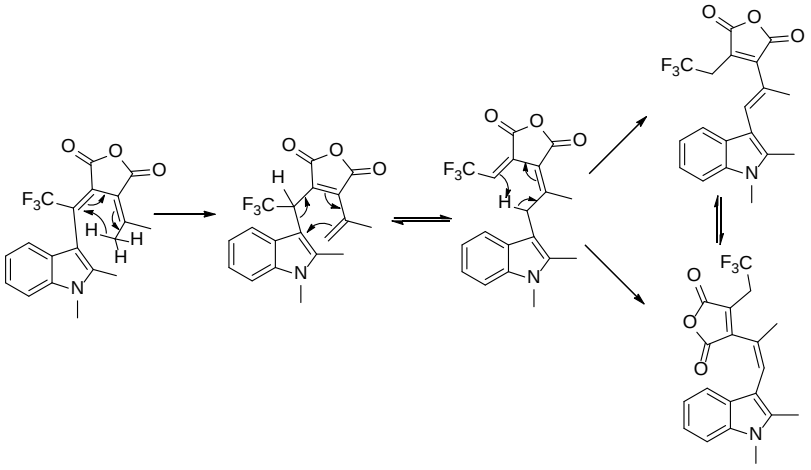
Generally, percentage of the desired product at PSS for the indolylfulgides and indolylfulgimide is relatively high, especially for CF_3 indolylfulgides and indolylfulgimides.[27,33] Photochemical reaction from the closed form to the open form can yield 100% of open form and the reversed reaction can reach up to 90% of the closed form. Solvents also play an important role in photochemical reactions. For example, the ring closing reaction of a carboxylic acid fulgimide produced 87% of *C*-form in aqueous solution, however, there was only 58% of *C*-form found at PSS after switching the solvent to toluene (Scheme 18).[34] The reason is that the ratio of quantum yields (***ΦE-C***/***ΦC-E***) is relative higher in polar solvent to provide more *C*-form fulgimides.[31,43]

1.4.3 Thermal stability

Thermal stability is essential in the application of photochromic compounds in storage devices which requires the materials to endure 50 °C for prolonged periods.[18] Indolylfulgides and indolylfulgimides are regarded as promising candidates to be used in optical data storage devices because they usually display great thermal stability in solvents and polymer films.[18,27,28,34] A previous study found that the fluorinated indolylfulgides had outstanding resistance to thermal

stress in the closed form, however, the open form was less stable and degraded rapidly at 80°C.[41] A mechanism for the thermal degradation of the open form in toluene was proposed (Scheme 19). The initial step involves a 1,5-hydrogen shift from the isopropylidene group to the bridging position to break the conjugation of the anhydride ring with the indole group. The final stable products are formed via a formal 1,5-indolyl migration and a final 1,5-hydrogen shift. The first 1,5-hydrogen shift was demonstrated to be the rate determining step of the thermolysis processes.[44]

Scheme 19. Proposed thermal degradation mechanism of a CF_3 Indolylfulgide[18]



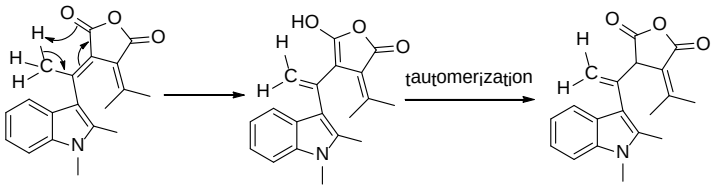
On the basis of the mechanism, a series of cycloalkylidene indolylfulgides were synthesized to improve the photochromic properties by replacing the isopropylidene group with a cycloalkylidene group.[45]

1.4.4 Photochemical stability

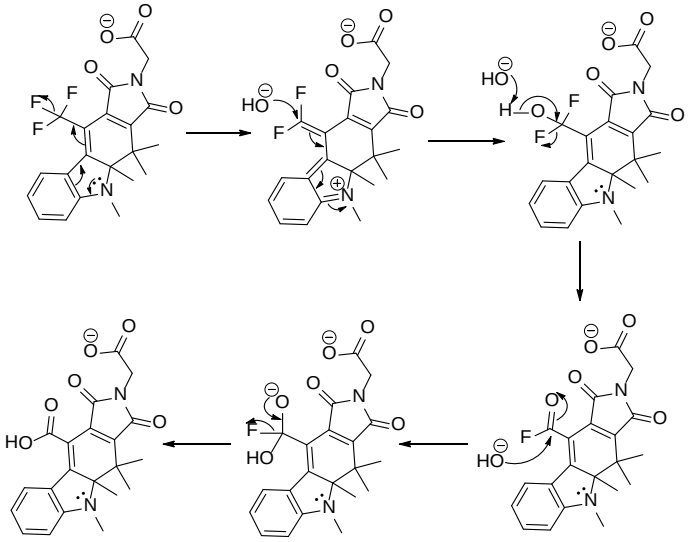
Photochemical stability, which is also know as fatigue resistance, can be measured by comparing initial absorption with remaining absorption of a photochromic compound after a certain number of photochromic cycles.[46] Indolylfulgides and indolylfulgimides can endure hundreds to thousands of photochemical cycles (back and forth conversion between the two key forms) before degrading by 20%.[2,27-29,41] A mechanism of photochemical degradation for a methyl indolylfulgide was proposed by Yokoyama (Scheme 20).[28] The major degradation pathway

involves a 1,5-hydrogen migration from a methyl group to the carbonyl oxygen on the anhydride ring. The research demonstrated that an indolylfulgide with a CF_3 group instead of a CH_3 group on the bridging position exhibited enhanced photochemical stability.

Scheme 20. Proposed mechanism of photochemical degradation for a methyl indolylfulgide



Scheme 21. Mechanism for the Hydrolysis of CF_3 fulgimide*[33]*



1.4.5 Hydrolytic stability of indolylfulgimides

Hydrolytic stability, which is defined as the ability of photochromic compounds to resist solvolysis in aqueous solutions, is important for applications in biological systems and humid conditions.[34] Contrary to the high thermal stability in aprotic solvents, fulgides show rapid degradation in aqueous solution because the succinate anhydride ring can be easily hydrolyzed to a half-ester.[20,21] By replacing the succinate anhydride ring with a succinimide ring, fulgimides exhibit enhanced hydrolytic stability.[20,34] However, a previous study found that *C*-form

fulgimides with a CF_3 group on the bridging position can be rapidly hydrolyzed to a COOH fulgimides via a proposed mechanism shown in Scheme 21.[33] The CH_3 fulgimides with a methyl group instead of a CF_3 group on the bridging position showed increased hydrolytic stability. In 50 mM sodium phosphate buffer (pH 7.4) at 37 °C, there was no obvious degradation observed for the open form fulgimide, and the *C*-form fulgimide degraded only 22% after 500 h.[34]

1.5 Potential applications of polymer containing fulgimides

Fulgides, fulgimides, and their copolymers are promising materials for optical informational storage media, photochromic dyes, logic gates, photoswitches, and biosensors.[10-13,19,25,43,47-52] Fulgimides with enhanced hydrolytic stability are suitable for applications in biological system, such as enzyme immobilization and controlled drug release.[14,53-63]

1.5.1 Enzyme immobilization

Enzymes, which are ubiquitous in living organisms, are naturally biocompatible and biodegradable catalysts that accelerate many biochemical and chemical reactions.[58] Enzymatic processes usually occur with high rates and selectivities, and can be operated in aqueous solutions under mild conditions (close to room temperature, atmospheric pressure and physiological pH).[61] In addition, enzymes are sustainable, environmentally friendly and cost-effective, and can meet the increasing demand for green manufacturing, particularly in food processing, pharmaceuticals, textiles, and waste treatment.[59,64-69]

Enzymes have been used in food processing throughout human history, when no concept of an enzyme even existed. People found that spoiled food could have some surprising flavors. The process of ‘spoilage’ (or fermentation) could give beneficial results. Dating back thousands of years, Chinese produced soy sauce by enzymatic fermentations of soybean.[70] In the past two decades, the application of enzymes in different industries has been continuously increasing thanks to developments in biotechnology and protein engineering. However, there are some drawbacks of conventional operations of enzymes. First, enzymes in aqueous solutions are

difficult to recover and reuse. Second, most enzymes are very sensitive to temperature and pH, and lack long-term operational stability.[58,71-73] One successful method to overcome these drawbacks is to use an enzyme immobilization strategy. The insoluble immoblized enzymes are more stable and less sensitive toward environmental changes than the soluble form of enzymes. In addition, immobilized enzymes can be easily recycled.[57,58,60]

Enzyme immobilization methods include binding to a support (carrier), cross-linking, and entrapment (Figure 2).[61] Binding to a support can be because of physical (hydrophobic and van der Waals forces), ionic, or covalent interactions. Physical binding is usually too weak to keep the enzyme fixed to the carrier. On the other hand, ionic and covalent bonds are too strong and may alter the conformational structure and active site of the enzyme. Cross-linking of enzymes provides a carrier-free immobilization by using biofunctional reagents. In addition, entrapment involves the synthesis of a polymeric network in the presence of an enzyme.[57,61]

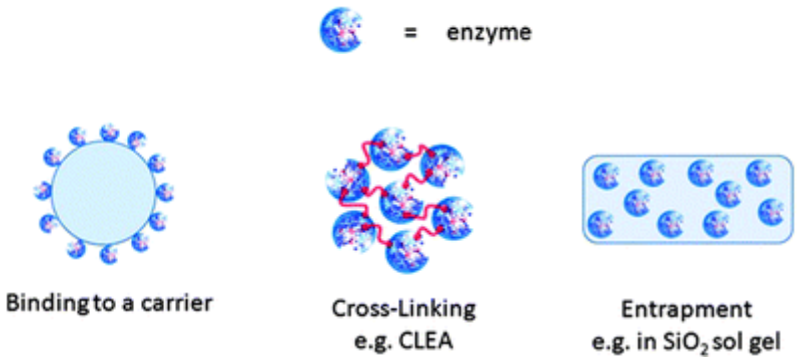


Figure 2. Different methods for immobilizing enzymes[61]

Copolymers containing photochromic compounds can be used in enzyme immobilization via the entrapment method. For example, immobilization of α-chymotrypsin was studied in a cross-linked copolymer containing azobenzene.[74] The azobenzene can be interconverted between the *cis* form and the *trans* form with lights.[74] Switching the conformation of the azobenzene led to changes of the permeability of the copolymer matrix towards the substrate. Therefore, the α-chymotrypsin immobilized in a photochromic copolymer can be photo-regulated. It is beneficial

to photo-control an enzymatic reaction, because light can be imposed instantly and precisely in the desired intensity. I expect that cross-linked copolymers containing fulgimides as cross-linkers will be more effective to photo-regulate an immobilized enzyme because of the enhanced conformation changes. As shown in Figure 3, the copolymer can switch between the rigid form and the flexible form as the fulgimide is interconverted between the closed form and open form with light. The enzymatic activity will be affected because the conformation of the enzyme or the substrate accessibility to the active site will be altered. So the activity of the enzyme can be photocontrolled "on" and "off".

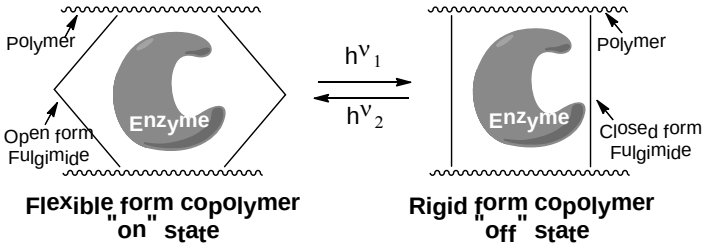


Figure 3. Enzyme immobilization by using polymer containing fulgimide

1.5.2 Controlled drug delivery

Besides enzyme immobilization, hydrogels containing fulgimide can be used in controlled drug delivery systems, which are designed to release drugs at predetermined rates for predefined periods of time controlled by external stimuli, such as temperature, pH, and light. [53-56] Compared to other stimuli, light stimulus can be imposed instantly and precisely to deliver drugs in specific amounts.[54] The photoresponsive hydrogels have great potential in encapsulation or release of drug molecules because of light-induced volume changes. Many studies about controlled drug release using photoresponsive systems have been reported.[14,53-56] For example, Ohya *et al*. synthesized a photochromic lipid, SP-16A, having a spiropyran group on the terminal.[75] They found that SP-16A molecule can form liposomes with dipalmitoyl phosphatidylcholine, and the resulting photochromic liposomes were able to release the previously entrapped carboxyfluorescein after irradiation with UV light.[75] In another study, Peng *et al*. demonstrated that in a light-responsive

hemicellulose-based hydrogel containing photochromic azobenzene, the cumulative release rate of vitamin B12 was higher under UV irradiation than that without UV irradiation.[56]

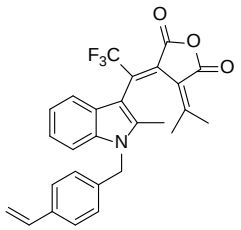
Hydrogels with fulgimides as cross-linkers have many advantages in biological systems, such as water compatible, good photochemical stability, and enhanced conformation changes. I expect that the polymer matrices will be changed significantly as the fulgimides switch between the closed form and the open form. Herein, it is necessary to synthesize copolymers containing fulgimides, and their stability and photochromic properties, such as UV-Vis absorption and fatigue resistance, need to be carefully characterized.

2. OBJECTIVES

The overall aim of my research is to synthesize a series of photochromic copolymers with advanced properties by using polymerizable fulgides and fulgimides.

I. Synthesis of linear fulgimide-co-PMMA copolymers

A 3-indolylfulgide and a 3-indolylfulgimide with a polymerizable styrene attached to the indole nitrogen atom were synthesized. Copolymerization with methyl methacrylate (MMA) provided linear copolymers.



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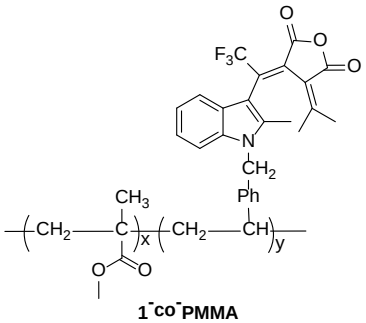
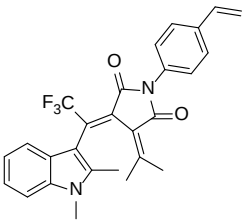


1-co-PMMA



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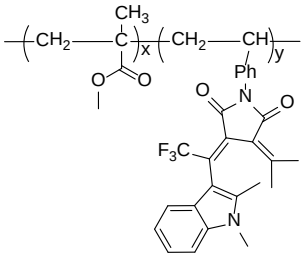
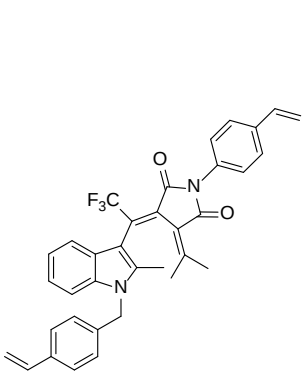


2-co-PMMA

II. Synthesis of cross-linked fulgimide-co-PMMA copolymers

A 3-indolylfulgimide with two polymerizable styrene groups attached on the two nitrogen atoms was synthesized. Copolymerization with MMA provided cross-linked copolymers.



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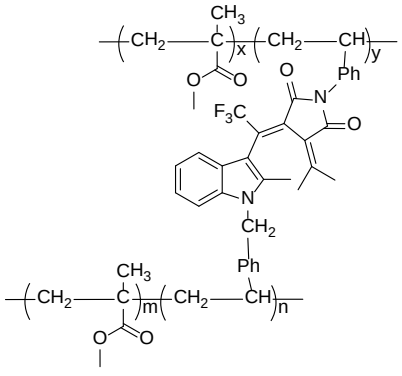
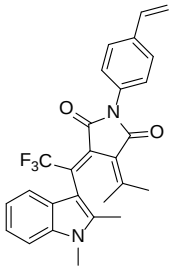


3-co-PMMA

III. Synthesis of aqueous soluble linear fulgimide-co-PAA copolymers

Two 3-indolylfulgimides with a polymerizable styrene attached on the succinimide nitrogen atom were synthesized. Copolymerization with acrylamide provided water soluble linear copolymers.



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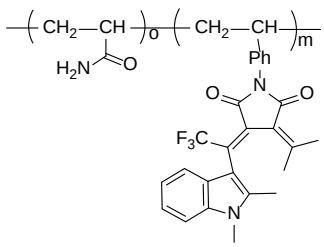
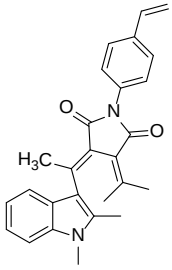


2-co-PAA



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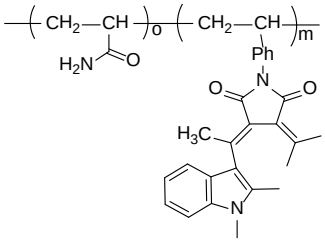
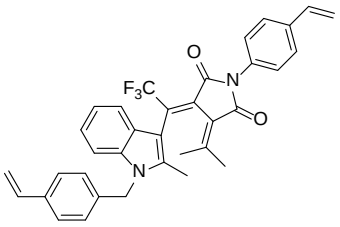


4-co-PAA

IV. Synthesis of cross-linked fulgimide-co-PAA hydrogels

A 3-indolylfulgimide with two polymerizable styrene groups attached on the two nitrogen atoms was synthesized. Copolymerization with acrylamide provided cross-linked hydrogels.



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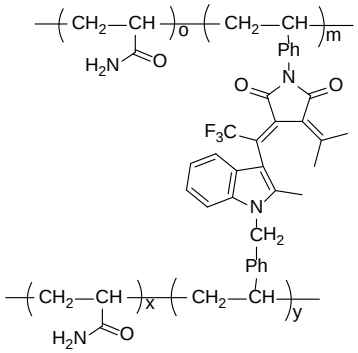
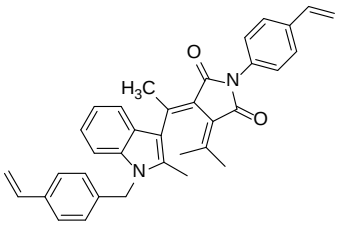


3-co-PAA



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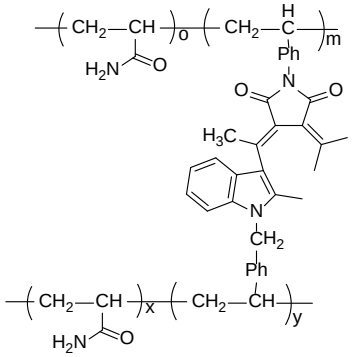


5-co-PAA

All fulgimides and their copolymers were characterized by measuring UV-Vis spectra, thermal stability, and photochemical stability.

3. SYNTHESIS OF 3-INDOLYLFULGIDE/INDOLYLFULGIMIDE-CO-PMMA LINEAR COPOLYMERS

3.1 Abstract

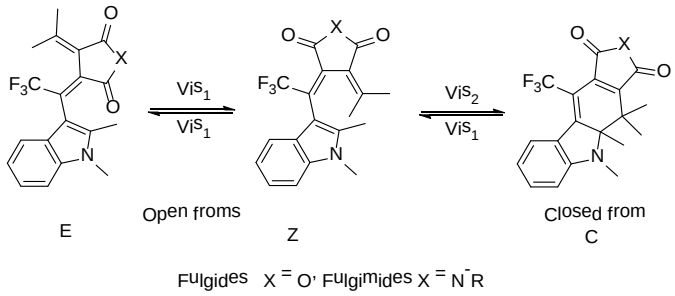
Photochromic polymers containing indolylfulgides or indolylfulgimides have many beneficial properties for application in optical switches. A fluorinated indolylfulgide and a fluorinated indolylfulgimide with a polymerizable *N*-stryryl group attached on the succinimide ring were synthesized. The new compounds were copolymerized with methyl methacrylate (MMA) to provide two linear copolymers. The photochromic properties of monomeric fulgide and fulgimide in toluene and the corresponding copolymers in both toluene and films were measured. All compounds were photochromic and exhibited strong absorption in the visible region of the spectrum for both closed forms and open forms. All copolymer films were found to be very stable at room temperature and showed no loss of absorbance after 5 weeks. At 80 °C, in either toluene or as films, the copolymers exhibited similar thermal stability pattern with their monomeric fulgide or fulgimide. The closed forms displayed excellent stability and there was no obvious thermolysis observed after 400 h. However, the open forms were less stable and may undergo 1,5-hydrogen shift from the isopropylidene group to form an non-photochromic product. Moreover, all new compounds displayed good photochemical stability and underwent thousand(s) of photochromic cycles (ring-opening/ring-closing) in toluene or as films before degrading 20% of absorbance.

3.2 Introduction

Fulgides and fulgimides are important species in the organic photochromic compound family because of their advanced properties and potential applications. The first fulgide was synthesized by Stobbe in 1905, and the first thermally irreversible fulgide, a furylfulgide with a 2,5-dimethyl-3-furyl as the aromatic group, was synthesized by Heller In 1981.[15-17] Thermally irreversible fulgides exhibit good thermal stability and high photochemical stability.[19,26] Fulgimides as the

most important fulgide derivatives not only exceed the photochromic properties of parent fulgides but also improved the hydrolytic stability in aqueous solutions. Fluorinated 3-indolylfulgides and indolylfulgimides are the most promising because of their high thermal and photochemical stability, large quantum yields, large molar absorption coefficients, and absorption maxima in the visible region.[2,28,41] As shown in Scheme 22, the fulgide/fulgimide has two open forms and one closed form. The two open forms can be interconverted with light. But only one of the open forms, the cyclizable-form can be converted to the closed form via a photochemical 6π-electrocyclization. The reversible changes between two thermally stable states with different conformation and UV-Vis absorption spectra allow fulgides and fulgimides to be used in optical information storage devices and biological sensors.[19]

Scheme 22. The Photochromism of fluorinated 3-indolylfulgides and indolylfulgimides



Usually, the photochromic compounds are attached to polymer to meet the requirements for various applications because of their good photoresponsive behavior in the solid state.[76] Covalent attachment to synthetic polymers can minimize aggregation and diffusion of the photochromic molecules compared to dispersion in a polymer matrix.[26,39,77,78] Previously, many polymers containing photochromic fulgimides have been synthesized and photochromic properties have been studied. Rentzepis et al. reported a series of linear and cross-linked photochromic copolymers prepared from methyl methacrylate (MMA) and 2-indolylfulgimides with a polymerizable styrene group on the succinimide ring.[26,39] These copolymers exhibited similar photochromic properties as the corresponding monomeric 2-indolylfulgimide and displayed good

thermal stability at room temperature and lost less than 10% of absorption after 100 photochemical cycles. Kannan et al. synthesized a linear MMA copolymer containing two different photochromic units: thermally reversible azobenzenes and thermally irreversible 2-indolylfulgimide.[79] The conformation of the copolymer can be controlled with light and temperature. Ramamurthy et al. prepared a 2-indolylfulgimide with a pendant MMA via click chemistry, and then a linear polymer was prepared. The resulting polymer was photochromic and exhibited enhanced thermal resistance. In practical applications, thermal stability, efficiency, and photochemical stability are all important. However, there was no study reported about thermal stability of the fulgimide in the open form and the closed form at elevated temperature. In addition, the photochemical stability of the copolymers needs to be improved.

Herein, a fluorinated 3-indolylfulgide and a fluorinated 3-indolylfulgimide with a pendant styrene group on the succinimide ring were synthesized. The new compounds were polymerized with MMA to obtain linear copolymers in both closed forms and open forms. Optical properties, thermal stability, and photochemical stability of monomers and copolymer were measured in toluene and as films.

3.3 Experimental section

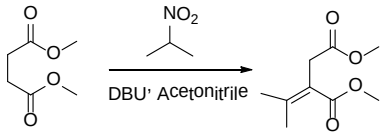
3.3.1 General procedures and materials

All commercially available materials were used without purification. The NMR spectra were recorded on a Brücker 400 MHz NMR spectrometer. The ^{1}H and ^{13}C NMR samples were internally referenced to TMS. The UV-vis spectra were recorded with a Cary 300 spectrophotometer. The HRMS were obtained at the University of Florida. Flash chromatography was performed with 230-400 mesh silica gel. Illumination was provided by a 1000 W Hg (Xe) arc lamp with a water filter went through a hot mirror (a dichroic filter reflecting infrared light back into the light source and allowing visible light to pass), and then through either a band pass filter (436 nm (for fulgide)/405 nm (for fulgimides)) or a cutoff filters (>570 nm (for fulgide)/515 nm

(for fulgimides)). The molecular weights of copolymers were determined by gel permeation chromatography.

3.3.2 Synthesis of trifluoromethyl *N*-stryryl indolylfulgide (1)

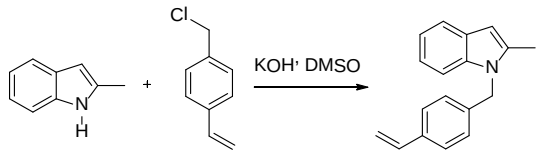
3.3.2.1 Synthesis of dimethyl isopropylidene succinate (6)[80]



5 **6** (67%)

2-nitropropane (**5**) (76.60 g, 0.860 mol) was dissolved in 3.6 L of acetonitrile followed by addition of dimethyl maleate (135.70 g, 0.942 mol). The mixture was stirred for 10 min and of DBU (201.56 g, 1.320 mol) was added. The reaction mixture was stirred overnight and then concentrated in vacuo. The residue was quenched with 1 L of 1 M HCl and the extracted with of diethyl ether (3 × 1.5 L). The combined organic layers were washed with water (2 × 500 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by vacuum distillation to provide 107.50 g (67%) of dimethyl isopropylidenesuccinate.

3.3.2.2 Synthesis of 2-methyl-1-(4-vinylbenzyl)indole (8)[39]

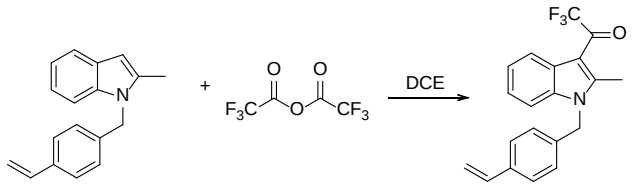


7 **8** (62%)

2-Methylindole (**7**) (20.96 g, 160 mmol) was added to a suspension of potassium hydroxide (40.80 g, 728 mmol) in 320 mL of DMSO. The mixture was stirred at room temperature for 45 min and then cooled to 0 ºC. 4-vinylbenzyl chloride (26.25 g, 172 mmol) was added and the reaction mixture was stirred at room temperature. After 1.5 h, the mixture was poured onto 100 g of crushed ice in an Erlenmeyer flask and left to stand for 24 h at room temperature. The mixture then was diluted with 2.5 L of water, and the aqueous layer was extracted with methylene

chloride (3 × 500 mL). The combined organic layers were washed with 1 L of water, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography (hexane as a solvent) to afford a white solid (24.44 g, 62%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.58-7.53 (m, 1H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.21-7.16 (m, 1H), 7.12-7.04 (m, 2H), 6.92 (d, *J* = 8.2 Hz, 2H), 6.65 (dd, *J* = 17.6, 10.9 Hz, 1H), 6.32 (s, 1H), 5.68 (dd, *J* = 17.5, 0.5 Hz, 1H), 5.28 (s, 2H), 5.20 (dd, *J* = 10.9, 0.4 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.5, 137.2, 136.73, 136.65, 136.3, 128.2, 126.6, 126.2, 120.8, 119.7, 119.5, 113.9, 109.2, 100.5, 46.3, 12.7. $C_{18}H_{17}N$ HRMS (ESI) *m/z*: 248.1436 [obtained M + H]$^+$, 248.1434 [calculated M + H]$^+$.

3.3.2.3 Synthesis of 2-methyl-1-(4-vinylbenzyl)-3-trifluoroacetylindole (9)

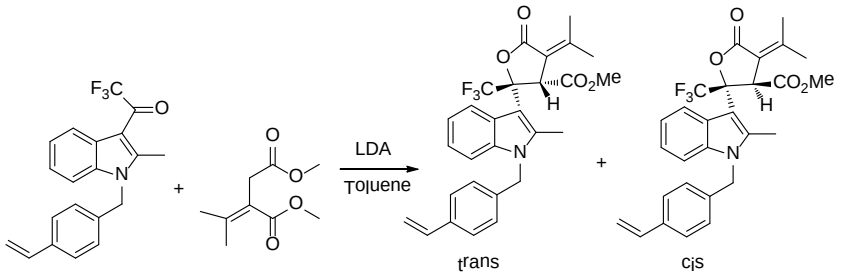


8 **9** (89%)

Trifluoroacetic anhydride (TFAA) (31.10 g, 148.3 mmol) was dissolved in 170 mL of 1,2-dichloroethane (DCE). The mixture was cooled to 0 °C and followed by addition of 2-Methyl-1-(4-vinylbenzyl)indole (**6**) (24.44 g, 98.9 mmol) dissolved in 100 mL of DCE dropwise via an addition funnel. Then the reaction mixture was allowed to warm to room temperature and stirred for 1 h under argon. The mixture was quenched with a saturated $NaHCO_3$ solution (300 mL) and then extracted with methylene chloride (2 × 150 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. A white solid was afforded (30.09 g, 89%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.09 (d, *J* = 8.2 Hz, 1H), 7.40 -7.20 (m, 5H), 6.97 (d, *J* = 8.2 Hz, 2H), 6.66 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.71 (d, *J* = 17.6 Hz, 1H), 5.40 (s, 2H), 5.25 (d, *J* = 11.0 Hz, 1H), 2.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.7 (q, *J* = 36 Hz), 150.0, 137.6, 136.7, 136.0, 134.5, 127.0, 126.2, 125.3, 123.5, 123.4, 121.1 (q, *J* = 4 Hz), 117.2 (q, *J* = 290 Hz), 114.6, 110.2,

108.5, 46.7, 13.3. $C_{20}H_{16}F_3NO$ HRMS (ESI) *m/z*: 344.1262 [obtained M + H]$^+$, 344.1257 [calculated M + H]$^+$.

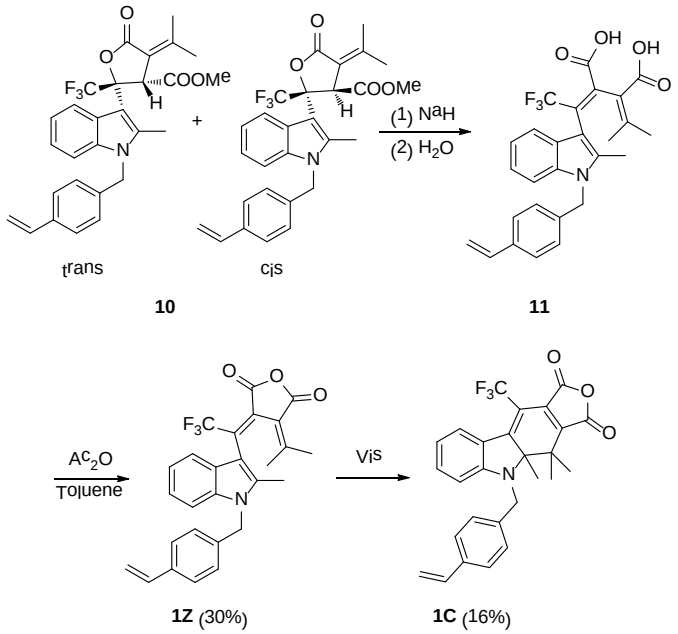
3.3.2.4 Synthesis of trifluoromethyl isopropylidene indolelactone (10)



9 **6** **10** (83 %)

Dimethyl isopropylidenesuccinate (**6**) (13.6 g, 73 mmol) was dissolved in 400 mL of toluene in a 1 L round-bottom flask, and then the solution was concentrated to 300 mL to remove water via a rotavapor. To the stirred solution under argon, lithium diisopropylamide (LDA) (29.2 mL of a 2 M solution in THF, 58.4 mmol) was added dropwise via an addition funnel. A cannula was used to transfer LDA into the addition funnel to avoid moisture. To the succinate/LDA/toluene solution, 2-methyl-1-(4-vinylbenzyl)-3-trifluoroacetylindole (**9**) (5.0 g, 14.6 mmol) dissolved in toluene (50 mL) was added dropwise via an addition funnel, and the reaction mixture was stirred under argon. After 1.5 h, the mixture was quenched with 200 mL of 5% H_2SO_4, and the acidic layer was extracted with diethyl ether (3 × 300 mL). The organic layers were combined, extracted with water (2 × 300 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography (3:1 methylene chloride/hexane as eluent) and then recrystallized from ethanol to provide 5.9 g (83%) of a cis/trans mixture of indolelactones (**10**).

3.3.2.5 Synthesis of trifluoromethyl *N*-stryryl indolylfulgide (1)

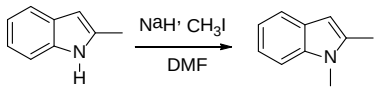


The cis/trans mixture of indolelactones (**10**) (2.0 g) was dissolved in 100 mL of and cooled to 0 ºC in an ice bath. Sodium hydride (60% dispersion in oil, 0.64 g, 16.08 mmol) was added to the mixture and stirred for 1.5 h at room temperature. Then water (300 μL) was added, and the reaction mixture was left to react for 12 h. The mixture was concentrated in vacuo until only solid remained, and the solid was partitioned between 0.1 M NaOH (100 mL) and EtOAc (100 mL). The aqueous layer was acidified with 5% H_2SO_4 and extracted with EtOAc (3 × 150 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo to afford 2.20 g of the crude diacid (**11**). Then the diacid was suspended in 50 mL of toluene. Acetic anhydride (20 mL, 210 mmol) was added, and the mixture was left to react at 35 ºC for 1 h and then concentrated in vacuo. The resulting crude fulgide was purified by column chromatography with toluene as the eluent to provide a *Z*/*E* mixture. To prepare pure *Z*-form, the *Z*/*E* mixture in toluene was illuminated with 436 nm light until photostationary state (PSS) was reached. The PSS solution in toluene was then illuminated with 570 nm light to obtain the crude *Z*-form solution. Toluene was removed in vacuo and recrystallization from CH_2Cl_2/hexane provided 0.68

g of the *Z*-form fulgide (30%). *Z*-form: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36 -7.25 (m, 4H), 7.25 - 7.16 (m, 2H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.66 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.71 (d, *J* = 17.6 Hz, 1H), 5.36 (d, *J* = 16.8 Hz, 1H), 5.26 (d, *J* = 10.9 Hz, 1H), 5.25 (d, *J* = 16.8 Hz, 1H), 2.19 (s, 3H), 2.09 (s, 3H), 1.00 (s, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 161.7, 160.6, 159.5, 137.5, 137.3, 136.8, 135.9, 135.8, 132.8 (q, *J* = 35 Hz), 128.6, 126.8, 126.5, 124.9, 122.8, 122.0 (q, *J* = 278 Hz), 121.6, 120.4, 119.6, 114.6, 109.8, 107.8, 47.0, 26.9, 23.1, 12.2. $C_{27}H_{22}F_3NO_3$ HRMS (ESI) *m/z*: 466.1646 [obtained M + H]$^+$, 466.1625 [calculated M + H]$^+$. Pure *C*-form was prepared from the PSS solution, toluene was removed in vacuo, and the *C*-form was purified by column chromatography (toluene as an eluent) followed by the recrystallization from CH_2Cl_2/hexane to provide 0.48 g of the *C*-form fulgide (16%). *C*-form: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82 (d, *J* = 8.1 Hz, 1H), 7.44 (d, *J* = 8.1 Hz, 2H), 7.34 (td, *J* = 7.3, 1.1 Hz, 1H), 7.26 (d, *J* = 7.1 Hz, 2H), 6.89 (t, *J* = 7.6 Hz, 1H), 6.73 (dd, *J* = 17.6, 10.9 Hz, 1H), 6.52 (d, *J* = 8.3 Hz, 1H), 5.77 (d, *J* = 17.6 Hz, 1H), 5.32 (d, *J* = 11.0 Hz, 1H), 4.60 (d, *J* = 17.6 Hz, 1H), 4.19 (d, *J* = 17.5 Hz, 1H), 1.58 (s, 3H), 1.46 (s, 3H), 1.25 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.8, 162.5 (q, *J* = 3.6 Hz), 160.9, 159.7, 141.8, 138.1 (q, *J* = 1.5 Hz), 137.0, 136.32, 136.24, 136.16, 128.7 (q, *J* = 7 Hz), 126.9, 126.6, 122.2 (q, *J* = 273 Hz), 120.4, 119.3, 114.3, 110.9, 105.6 (q, *J* = 38 Hz), 76.7, 50.8, 39.1, 19.5, 18.2, 16.4. $C_{27}H_{22}F_3NO_3$ HRMS (ESI) *m/z*: 466.1641 [obtained M + H]$^+$, 466.1625 [calculated M + H]$^+$.

3.3.3 Synthesis of trifluoromethyl *N*-stryryl indolylfulgimide 2

3.3.3.1 Synthesis of 1,2-dimethylindole 12

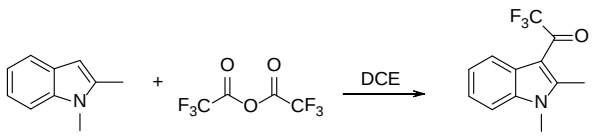


7 **12** (75%)

2-Methylindole **7** (0.117 mmol, 15.40 g) was added in 200 ml of DMF and stirred for 30 min. The mixture was cooled to 0 °C followed by addition of NaH (6.01 g of 60 % dispersion in oil,

0.150 mmol). After stirring for 10 min, methyl iodide (8.0 ml, 0.129 mmol) was added. The reaction mixture was warmed to room temperature and left to react under argon gas for 5 h. The mixture was then concentrated in vacuo. The residue was dissolved in 500 ml of EtOAc and extracted with H_2O (2 x 200 ml) and brine (200 ml). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. Further purification via column chromatography (1:1 hexane/EtOAc) provided 12.74 g (75%) of 1,2-dimethylindole.

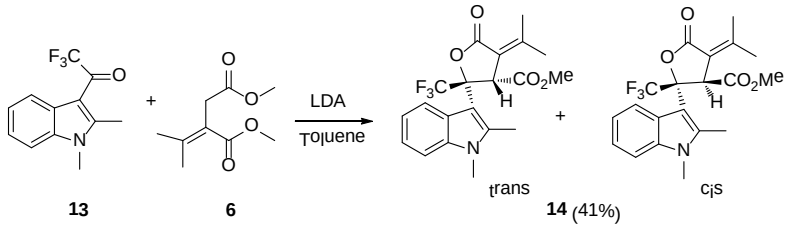
3.3.3.2 Synthesis of 3-acetyl-1,2-dimethylindole 13



12 **13** (99%)

Trifluoroacetic anhydride (54.01 g, 0.48 mol) was disslived in 300 mL of 1,2-dichloroethane at 0 °C followed by addition of a solution of 1,2-dimethylindole (24.52 g, 0.34 mol) dissolved in 150 mL of 1,2-dichloroethane dropwise. The mixture was stirred for 2 h at room temperature and then concentrated in vacuo. The purple residue was quenched with 250 mL of saturated aqueous $NaHCO_3$and extracted with CH_2Cl_2 (3 × 300 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo to provide 45.65 g of 1,2-dimethyl-3-trifluoroacetylindole **13** (99%).

3.3.3.2 Synthesis of trifluoromethyl isopropylidene indolelactone 7

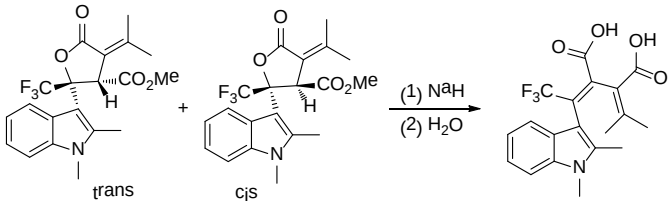


13 **6** trans **14** (41%) cis

Lithium diisopropylamide (LDA) (60 mL of a 2 M solution, 120 mmol) was added dropwise from an addition funnel to a stirred solution of dimethyl isopropylidene succinate 15 (22.82 g, 123 mmol) in 200 mL of dried toluene. To avoid moisture, the LDA was filled the addition funnel

via a cannula under argon gas. The mixture was stirred for 20 min and 1,2-dimethyl-3-trifluoroacetylindole 16 (12.20 g, 51 mmol) dissolved in 50 ml of dried toluene was added dropwise. After 2 h, the reaction was quenched with 100 mL of 5% H_2SO_4 solution and extracted with EtOAc (3 × 150 mL). The combined organic layers were dried over MgSO4, filtered and concentrated in vacuo. The residue was purified by silica gel chromatography (4:1 hexanes/EtOAc followed by 3:1 hexanes/EtOAc) and recrystallized from ethanol to provide 8.12 g (41%) of cis/trans isopropylidene indolelactone **14**.

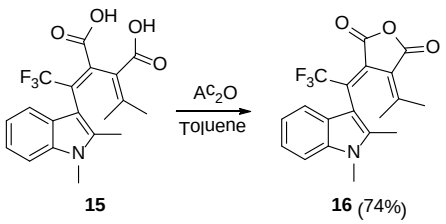
3.3.3.3 Synthesis of diacid 15



14 **15** (65%)

The cis/trans indolelactone **14** (6.90 g, 17.5 mmol) was dissolved in 200 mL of DMF at 0 °C followed by addition of NaH (60% dispersion in oil, 3.02 g, 75 mmol). The mixture was stirred for 1 h at 0 °C and 4 mL of water was added. The mixture was allowed to warm to room temperature and stirred overnight. Then the mixture was concentrated in vacuo and the residue was then partitioned between in 200 mL of water and extracted with 200 mL of EtOAc. The aqueous layer was acidified with 5% H_2SO_4 and extracted with EtOAc (3 × 150 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo to afford 4.50 g (61%) of the crude diacid **15** as a white solid.

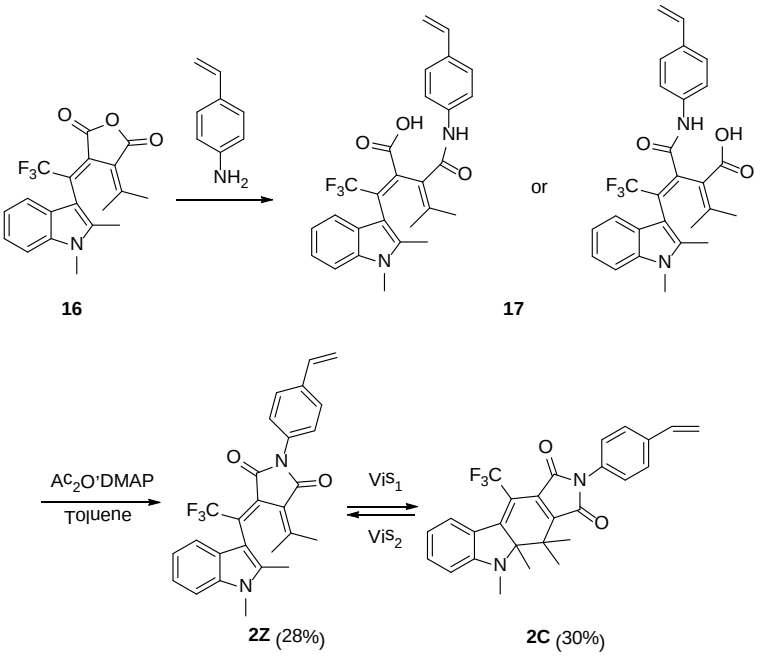
3.3.3.4 Synthesis of trifluoromethyl indolylfulgide 16



15 **16** (74%)

The resulting diacid intermediate **15** (4.50 g, 12 mmol) was suspended in 50 mL of toluene. Acetic anhydride (46.75 mL, 500 mmol) was added to the mixture and stirred for 2 d under argon gas. The solution was then concentrated in vacuo. The residue was quenched with 200 mL of water and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. Recrystallization from CH_2Cl_2/hexane provided 3.18 g of trifluoromethyl indolylfulgide **16** (74%).

3.3.3.5 Synthesis of trifluoromethyl *N*-stryryl indolylfulgimide 2



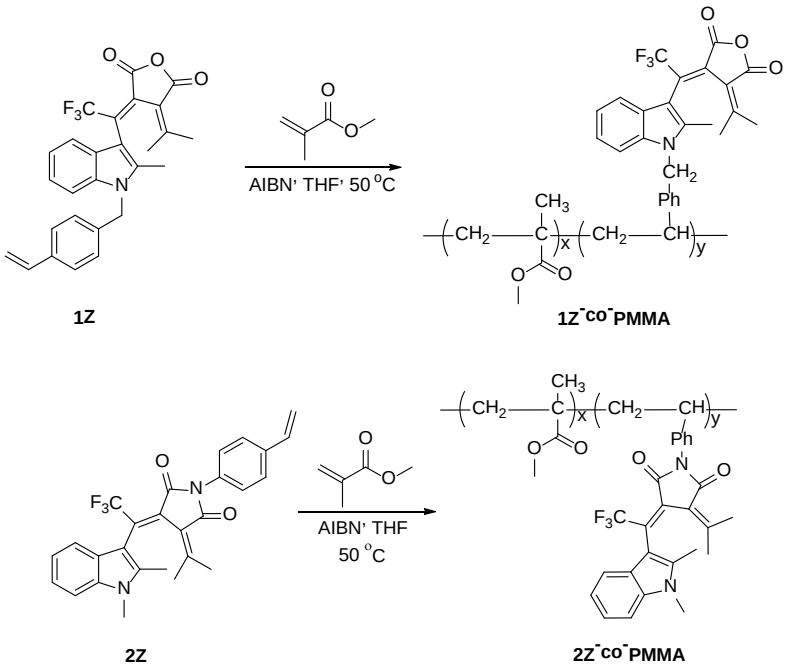
4-Vinylaniline (0.70 g, 5.9 mmol) was added to the open form solution of trifluoromethyl indolylfulgide (**4**) (1.50 g, 4.13 mmol) in 250 mL of toluene at room temperature. The reaction mixture was heated to 50 °C and stirred for 2 h. The solution was then concentrated in vacuo. The residue was quenched with 100 mL of 1 M HCl and extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with H_2O (100 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo to provide the crude acid intermediate. Acetic anhydride (100 mL) was added to the crude acid intermediate in 125 mL of toluene. The reaction mixture was allowed to stir at room temperature for 10 min and 4-dimethylaminopyridine

(DMAP) (10 mg) was added. The reaction mixture was concentrated in vacuo after 40 min. The residue was dissolved in 250 mL of EtOAc and extracted with saturated $NaHCO_3$ (2 × 100 mL) and H_2O (100 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The orange residue was purified by column chromatography with toluene. The resulting E/Z mixture was dissolved in 100 mL of toluene and illuminated with 405 nm light until PSS was reached, and then illuminated with visible light >515 nm to obtain crude *Z*-form solution. Toluene was removed in vacuo, and recrystallization from CH_2Cl_2/hexanes provided 0.54 g (28% from fulgide) of the *Z*-form vinyl trifluoromethyl indolylfulgimide **2**. *Z*-form: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 7.9 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.23 (td, *J* = 7.1, 1.2 Hz, 1H), 7.16 (td, *J* = 7.5, 1.0 Hz, 1H), 6.75 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.80 (d, *J* = 17.6 Hz, 1H), 5.31 (d, *J* = 11.0 Hz, 1H), 3.72 (s, 3H), 2.28 (s, 3H), 2.16 (s, 3H), 1.00 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.3, 164.1, 154.4, 137.7, 137.0, 136.9, 136.1, 132.6 (d, *J* = 2 Hz), 130.9, 129.3 (q, *J* = 35 Hz), 126.8, 126.6, 125.4, 122.6, 122.5 (q, *J* = 278 Hz), 122.0, 121.0, 119.6, 115.0, 109.2, 107.6 (d, *J* = 2 Hz), 30.0, 26.7, 22.4, 12.0. $C_{27}H_{23}F_3N_2O_2$ HRMS (ESI) *m/z*: 465.1796 [obtained M + H]$^+$, 465.1784 [calculated M + H]$^+$. The *C*-form was obtained by irradiating pure *Z*-form solutions of **2** (0.13 g) with 405 nm light followed by purification via flash column chromatography with toluene and recrystallization from CH_2Cl_2/hexanes (0.04 g, 30% yield). *C*-form: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.76 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.40 -7.36 (m, 3H), 6.80 (t, *J* = 7.6 Hz, 1H), 6.73 (dd, *J* = 17.6, 10.9 Hz, 1H), 6.65 (d, *J* = 8.4 Hz, 1H), 5.77 (d, *J* = 17.6 Hz, 1H), 5.29 (d, *J* = 10.8 Hz, 1H), 2.95 (s, 3H), 1.83 (s, 3H), 1.39 (s, 3H), 1.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.2, 165.0, 160.0, 159.9, 139.3, 136.8, 136.1, 135.8 (q, *J* = 1 Hz), 135.1, 131.1, 128.6 (q, *J* = 7 Hz), 126.7, 126.1, 122.6 (q, *J* = 273 Hz), 119.6, 119.0, 114.7, 109.5, 106.2 (q, *J* = 37 Hz), 75.9, 39.3, 32.6, 19.7, 19.1, 14.8. $C_{27}H_{23}F_3N_2O_2$ HRMS (ESI) *m/z*: 465.1799 [obtained M + H]$^+$, 465.1784 [calculated M + H]$^+$.

3.3.4 Synthesis of linear copolymers 1-co-PMMA and 2-co-PMMA

Free-radical solution addition polymerization technique was used. The monomer, fulgide **1** or fulgimide **2** (*Z*- or *C*-form), (4.6 mg, 0.01 mmol)) was dissolved in 2 mL of THF. Methyl methacrylate (0.40 g, 4 mmol) was added to the solution followed by the addition of initiator AIBN (1 wt% of MMA). The glass ampoule was sealed under vacuum and kept at 50 ºC for 48 h. The ampoule was cooled to room temperature and 2 mL of hexane was added. The copolymer was precipitated and filtered. Molecular weights (g/mol): **1Z-co-PMMA** $M_n = 6.4 \times 10^4$, **1C-co-PMMA** $M_n = 6.0 \times 10^4$; **2Z-co-PMMA** $M_n = 5.9 \times 10^4$, **2C-co-PMMA** $M_n = 6.6 \times 10^4$.

3.3.5 Preparation of copolymer films



The copolymer (**1Z/C-co-PMMA** or **2Z/C-co-PMMA**) (30-50 mg) was dissolved in CH_2Cl_2 (1 mL), and the solution was deposited via a pipet onto a circular glass slide (Escoproducts) and allowed to spread over the surface of the slide. The sample was allowed to dry overnight inside a glass Petri dish at room temperature. The resulting films were used to study the photochromic properties.

3.3.6 Spectra determination in toluene

1Z, ***2Z*** *(general procedure):* A concentrated stock solution was prepared from 10 mg of *Z*-form compounds followed by dilution into 5 solutions with concentrations between 0.05 to 0.20 mM. UV-Vis spectra of these solutions were acquired. Concentration versus absorbance was plotted, and absorption coefficient at λ_{max} was determined.

1C, ***2C****:* A concentrated stock solution was diluted to 5 solutions of different unknown concentrations, and their UV-Vis spectra were obtained. Each of the five *C*-form solutions was then quantitatively converted to a *Z*-form solution by illumination with 515 nm light and the UV-Vis spectrum was measured. Using the predetermined *Z*-form extinction coefficient, concentrations of the *Z*-form solutions, which are equivalent to the initial *C*-form solutions, were obtained and plotted versus the *C*-form absorbencies at λ_{max} thus allowing the determination of the extinction coefficient for the *C*-form.

3.3.7 PSS measurements

The photostationary state (PSS) was measured using NMR spectroscopy. An NMR tube containing *Z*-form of fulgide (or fulgimide) in toluene-d_8 was illuminated with 436 nm light (or 405 nm for fulgimides) until PSS was reached. A ^{1}H NMR spectrum was then acquired and integrated.

3.3.8 Photochemical stability

For each compound, *Z*-form sample (solutions or films) was prepared with an initial absorbance of 0.6-0.8 at the absorption maxima. Sample was irradiated to PSS after prolonged irradiation at 436 nm for fulgide (PSS_{436nm}) or 405 nm for fulgimides (PSS_{405nm}). Then the UV-Vis spectrum of PSS was acquired and another sample of pure *Z*-form was irradiated to 90% of the PSS. The reaction time was obtained. The 90% PSS mixture was then back irradiated with light >570 nm (for fulgide) or >515 nm (for fulgimides) and again the reaction time was obtained. Once the duration of irradiation reactions was established, the system was automated through the

use of a filter switch. After a designated number of irradiation cycles, the sample was fully converted to PSS and UV-Vis spectrum scanned. The photochemical fatigue was determined by comparison with the initial PSS absorption spectrum. The cycling times in toluene were: 40 s (*Z* -*C*) and 30 s (*C* -*Z*) for **1**, 70 s (*Z* -*C*) and 60 s (*C* -*Z*) for **1-co-PMMA**; 60 s (*Z* -*C*) and 40 s (*C* -*Z*) for **2** and **2-co-PMMA**; as films: 300 s (*Z* -*C*) and 180 s (*C* -*Z*) for **1-co-PMMA**, 150 s (*Z* -*C*) and 60 s (*C* -*Z*) for **2-co-PMMA**.

3.3.9 Thermal stability

Polymer-based study: Thin films of **1-co-PMMA** and **2-co-PMMA** (*Z*- and *C*-forms) were wrapped in aluminum foil and placed in an oven maintained at 80 °C. The films were removed at prescribed intervals and their UV-Vis spectra measured.

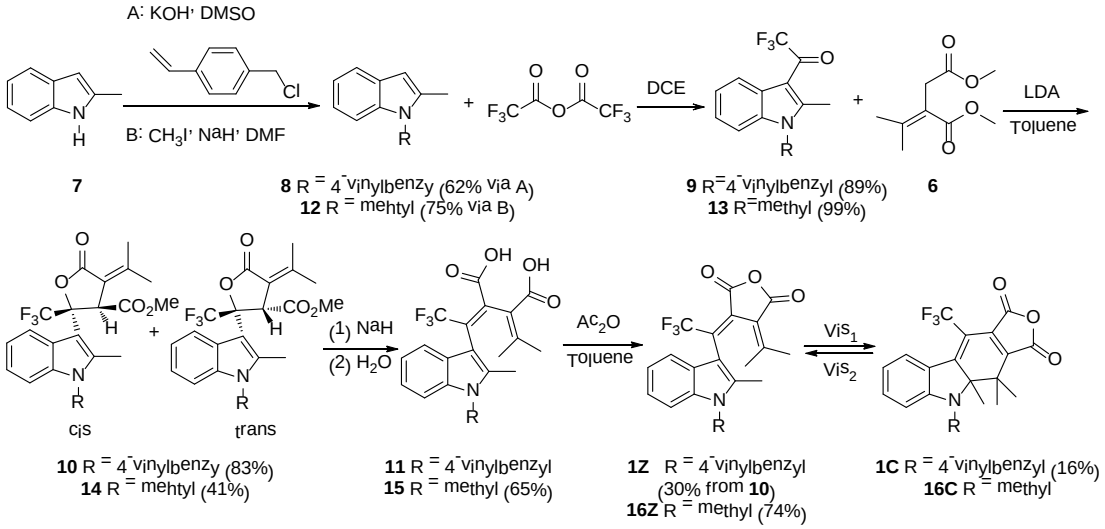
Solution-based study: The thermal stability of fulgide **1**, fulgimides **2**, copolymers **1-co-PMMA,** and **2-co-PMMA** (*Z*- and *C*-forms) in toluene was measured using UV-Vis spectroscopy. Thermal stability of monomers **1** and **2** was also followed by ^{1}H NMR spectroscopy. The solutions were prepared in toluene or its deuterated analog and transferred into several ampoules or NMR tubes, respectively. UV-Vis and ^{1}H NMR spectra of these initial samples were then acquired. Ampoules and NMR tubes were sealed and submersed in a water bath maintained at 80 °C. At predetermined times, ampoules and NMR tubes were removed, and their contents analyzed by UV-Vis or ^{1}H NMR spectroscopy. All the photochemical and thermal measurements were performed by Dr. Islamova in Dr. Lees' group.

3.4 Results and discussion

3.4.1 Synthesis

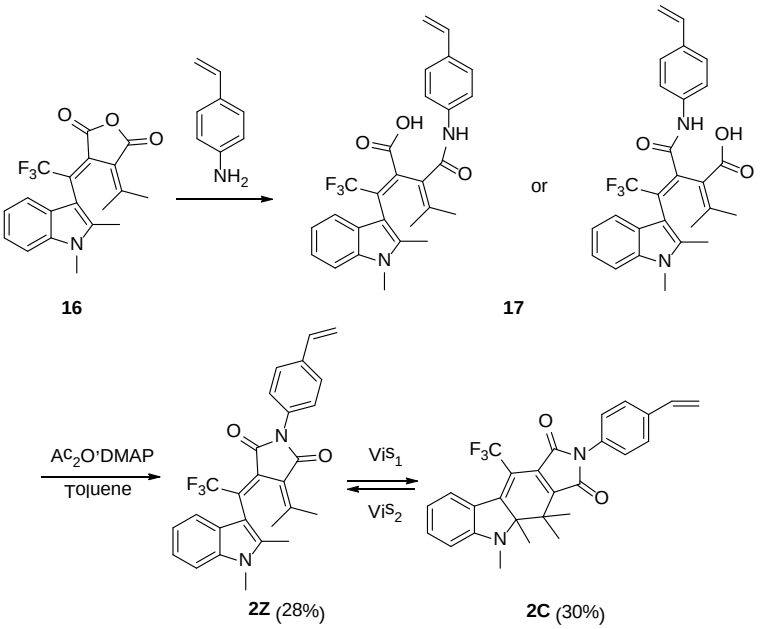
Two new photochromic compounds 3-indolylfulgide **1** and 3-indolylfulgimide **2** with a polymerizable styrene group were synthesized. Fulgide **1** was prepared via a Stobbe condensation of 3-trifluoroacetylindole **9** with a substituted methylene succinate **6**, followed by hydrolysis and dehydration (Scheme 23).

Scheme 23. Synthesis of fulgides 1 and 16



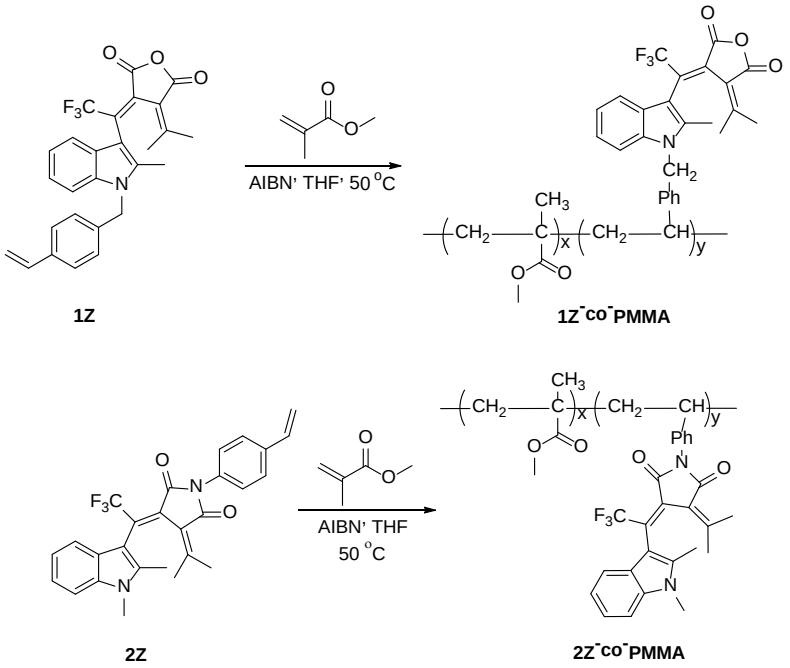
Fulgimide **2** was synthesized from the corresponding fulgide **16** which was prepared via a similar method to make fulgide **1**. By treatment of fulgide **16** with 4-vinylaniline, an amide acid intermediate was obtained. Then the amide acid intermediate was dehydrated in acetic anhydride to provide fulgimide **2** (Scheme 24).

Scheme 24 Synthesis of fulgimide 2



Two linear copolymer **1-co-PMMA** and **2-co-PMMA** were synthesized form free radical polymerization of methyl methacrylate with polymerizable fulgide **1** or fulgimide **2** in the presence of AIBN as an initiator (Scheme 24). The ratios of monomers (photochromic molecule to MMA) were selected to ensure that the copolymers were suitable for UV-vis measurements (absorbance approx. 1). Copolymer films **1-co-PMMA** and **2-co-PMMA** were prepared using drop casting. The fulgide, fulgimide, and their copolymers were found to be photochromic and stable at room temperature.

Scheme 25. Synthesis of copolymers 1-co-PMMA and 2-co-PMMA



3.4.2 UV-Vis absorption spectra

The UV-Vis absorption spectra of fulgide 1 and fulgimide 2 were measured in toluene (Figure 4). The absorption maxima (λ_{max}) of both open forms and closed forms were observed in the visible region. In practical applications, visible lights have many advantages over UV lights to control the conformation of the compounds, such as low cost and no damage to the living materials. As shown in Table 1. Fulgide **1** displayed a similar λ_{max} as fulgide **16** for the open form

but blue shifted approx. 20 nm for the closed form. The fulgimide **2** exhibited a hypsochromic shift of approx. 20 nm relatively to the fulgide **16** for open form by replacing the succinate anhydride ring with a succinimide ring. After polymerization with MMA, the resulting linear copolymers displayed a similar UV-Vis absorption pattern in toluene and films. Moreover, fulgides and fulgimide exhibited similar extinction coefficients and ratios of *C/Z/E*-forms in PSS. The high percentage of closed form in PSS makes the photochromic compounds promising in practical applications.

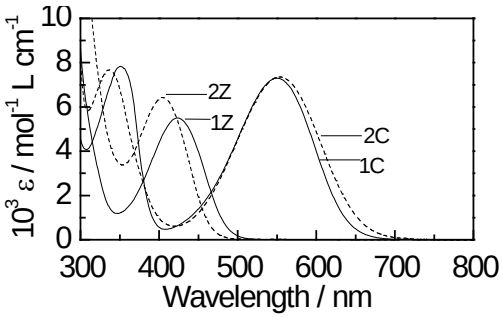


Figure 4. UV-Vis absorption spectra of fulgide **1** and fulgimides **2**

Table 1. Extinction coefficients at λ_{max} of fulgide 1, 16, fulgimide 2 and λ_{max} of copolymers

Compound (Medium)	λ_{max}/nm (ε_{max}/mol^{-1} L cm^{-1})		PSS$_{436\ nm\ (405\ nm)}$ [a]
	Z-form	*C*-form	*C*:*Z*:*E*
1 (Toluene)	424 (5.5×10^3)	549 (7.3×10^3)	94:5:1
2 (Toluene)	405 (6.4×10^3)	554 (7.4×10^3)	93:4:3
16 (Toluene) [b]	427 (5.8×10^3)	571 (7.0×10^3)	95:3:2
1-co-PMMA (Toluene)	424	550	-
2-co-PMMA (Toluene)	405	554	-
1-co-PMMA (Film)	425	554	-
2-co-PMMA (Film)	405	557	-

[a]Photostationary state. [b]The data taken from ref. 7.

3.4.3 Thermal stability

The thermal stability of monomers fulgide **1** and fulgimide **2** was measured in Toluene at 80 ^{o}C via UV-Vis spectroscopy and ^{1}H NMR spectroscopy. The closed form compounds exhibited

excellent thermal stability, and there is no obvious degradation observed after 400 h (Figure 5a). However, the open form compounds were less stable which is consistent with previous study for fluorinated indolylfulgides and indolylfulgimides.[2] According to the ^{1}H NMR data, there was no polymerization of **1** and **2** occurred during thermolysis. The ^{1}H NMR data were fit for a single exponential decay for both closed form and open form compounds which is analogous to the UV-Vis spectroscopy results.

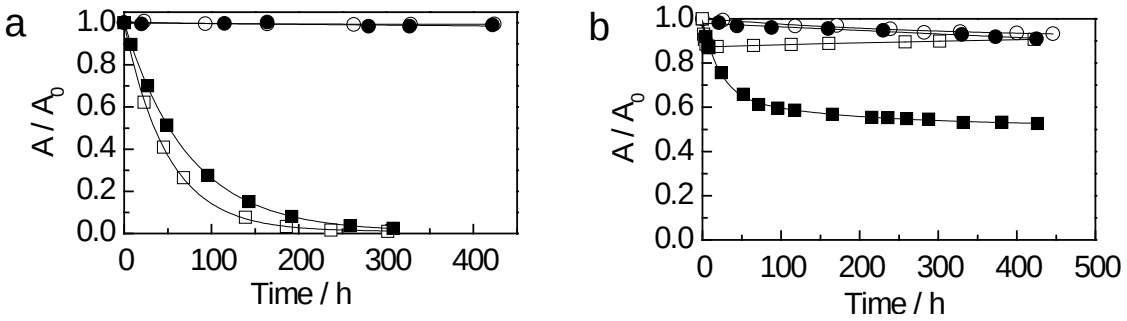


Figure 5. Thermal decomposition of fuligmides and coplymers: (a) fulgimides in toluene at 80 ºC measured by NMR: **1Z** (□), **2Z** (■), **1C** (○), and **2C** (●); (b) copolymers in films at 80 ºC measured by UV-Vis spectroscopy: **1Z-co-PMMA** (□), **2Z-co-PMMA** (■), **1C-co-PMMA** (○), and **2C-co-PMMA** (●)

The UV-Vis spectroscopy results showed that **2Z** degraded by an initial drop at the λ_{max} then followed by a bathochromic shift and subsequent increase in absorbance (Figure 6a). The absence of the isosbestic point indicated the presence of an intermediate. The pattern was similar to the pervious results of fulgide 1**6Z** which degraded via a 1,5-hydrogen shift from the isopropylidene group to form an intermediate and then rearranges to a mixture of two products (Scheme 19 in Chapter 1).[18] The electron withdrawing CF_3 group, on the bridging position can accelerate 1,5-hydrogen shift processes, which makes the open form fulgimides relatively unstable. Therefore, the thermal stability of fulgimides can be improved by replacing the CF_3 group with an electron donating group, such as a CH_3 group.

All copolymers are very stable at room temperature in toluene and films (no loss of absorption within experimental error after 5 weeks). The thermal stability of copolymers in

toluene and films at 80 °C is similar with their monomers. The closed form copolymers were more stable than open form copolymers. Compare to the degradation pattern of open from monomers, the open form copolymers exhibited decreased absorbance of the red shifted peak after longer time (>100-200 h) in toluene at 80 ºC (Figure 6b). It potentially indicated decomposition of thermolysis product(s). Thus, the data were only fitted for the first 200 h (Table 2).

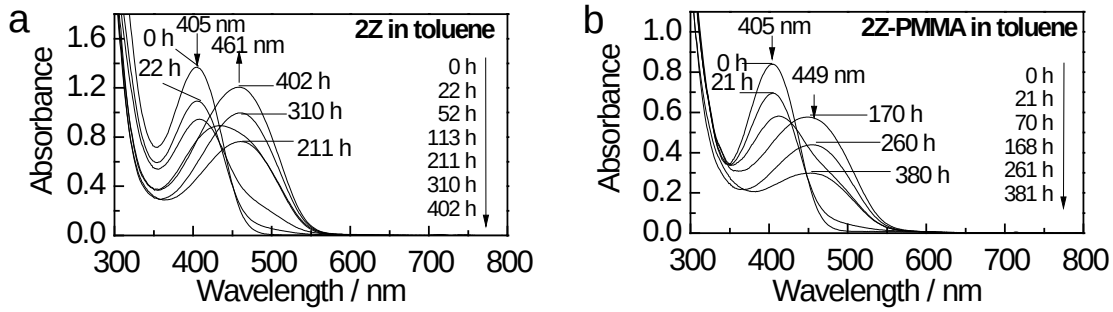


Figure 6. Thermal decomposition of fulgimide **2Z** and copolymer **2Z-co-PMMA**: (a) **2Z** in toluene; (b) **2Z-co-PMMA** in toluene by UV-Vis at 80 °C

Table 2. Thermal decomposition rrate constants ($\times 10^3$, h^{-1}) for 1, 2, and their copolymers at 80 ºC

Compound (Medium)	UV-Vis		^{1}H NMR	
	Z-form[a]	*C*-form[b]	*Z*-form[c]	*C*-form[b]
1 (Toluene)	53[d]	< 0.05	20	< 0.05
2(Toluene)	18[c]	< 0.05	14	< 0.05
1-co-PMMA(Toluene)	105[d]	0.19		
2-co-PMMA(Toluene)	88[d]	0.21		
1-co-PMMA(Film)	543[d]	0.15	-	
2-co-PMMA(Film)	32[c]	0.16		

[a]The first 200 h data were fit only. [b] Fit to a single exponential excluding 0 h data point. [c]Fit to a single exponential. [d]Fit to a sequential decay.

3.4.4 Photochemical stability

Photochemical stability is also referred as fatigue resistance and can be defined as the percentage loss in absorbance per photochemical cycle (ring-opening/ring-closing) during the

first approx. 20% of degradation. Photochromic fulgide **1** displayed excellent fatigue resistance and degraded only 0.005 % per cycle in toluene, which is comparable with fulgide **16** (3000 times before degrading by 21%, 0.007% per cycle).[41] After polymerization, the photochemical stability was affected by the substitution pattern around the indole ring (Figure 7). Copolymer **1-co-PMMA** degraded 0.012% per cycle in toluene, and 0.017% per cycle in film (Table 3). One possible reason is because of the longer cycling times in the polymer state. The fulgimide **2** showed slightly less photochemical stability compared to fulgides **1** and **16**, however, the polymerization state in toluene or film did not affect the fatigue resistance.

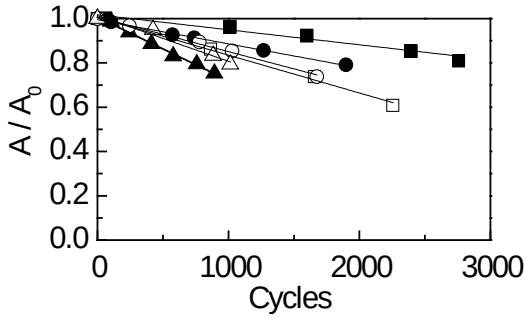


Figure 7. Photochemical decomposition of **1**, **2**, **1-co-PMMA** and **2-co-PMMA**: **1** (■) and **2** (□) in toluene, **1-co-PMMA** (●) and **2-co-PMMA** (○) in toluene, and **1-co-PMMA** (▲) and **2-co-PMMA** (Δ) in films

Table 3. Photochemical fatigue resistance of 1, 2, 3 and their copolymers

Compound (Medium)	Cycling time (s)		Photochemical decomposition		
	Z-C	C-Z	Number of cycles	A/A_0	% per cycle
1 (Toluene)	40	30	2760	0.809	0.0050
2 (Toluene)	60	40	1660	0.738	0.016
1-co-PMMA (Toluene)	70	60	1898	0.791	0.012
2-co-PMMA (Toluene)	60	40	1674	0.738	0.014

1-co-PMMA (Film)	300	180	760	0.794	0.030
2-co-PMMA (Film)	150	60	1014	0.794	0.017

3.5 Conclusion

I have synthesized two new photochromic compounds with a polymerizable pendant styrene group, 3-indolylfulgide **1** and 3-indolylfulgimide **2**. The compounds were copolymerized with MMA to obtain two linear copolymers, **1-co-PMMA** and **2-co-PMMA**. The resulting copolymers were found to be photochromic in toluene and films and showed good stability at room temperature. All monomeric photochromic compounds and copolymers absorb in the visiable region of the spectrum for both closed forms and open forms. The closed form monomers and copolymers exhibited similar thermal degradation pattern at 80 °C. The closed form compounds exhibited excellent thermal stability and the open form compounds were less stable. All compounds can cycle between open forms and closed forms for thousand(s) time before degrading 20% in toluene. The cycling times were longer in films than in toluene for the copolymers. Ultimately, copolymers in solution and films maintained all the promising photochromic properties as their monomers but are still limited by their less stable open forms.

4. SYNTHESIS OF INDOLYLFULGIMIDE-CO-PMMA CROSS-LINKED COPOLYMERS

4.1 Abstract

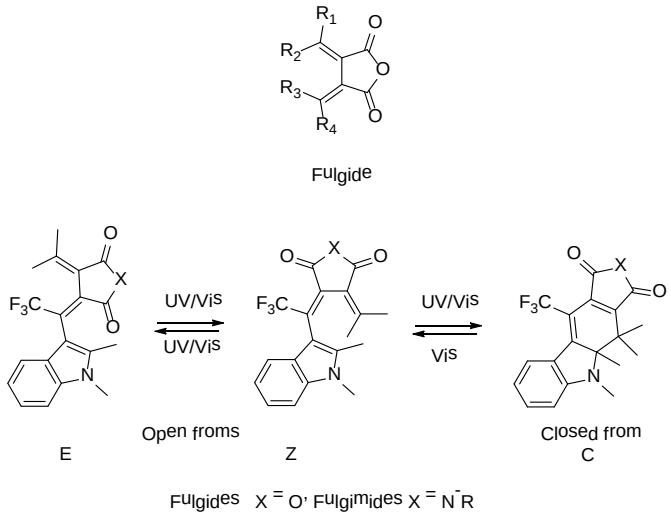
Fulgimides are the most important fulgide derivatives and have great potential to be used as optical switches in information storage devices and biological sensors.[19] A new 3-indolylfulgimide with two pendant styrene groups was synthesized, and the fulgimide was used as a cross-linker in the polymerization reaction with MMA to obtain a cross-linked copolymer. The photochromic properties of fulgimide and copolymer including UV-Vis spectra, thermal stability at 80 °C, and photochemical stability were characterized. I found that the compounds absorbed the light in the visible region for both closed forms and open forms which is beneficial in the practical applications. At 80 °C, the closed forms were more stable than the open forms, and the open forms degraded via an intermediate. The new compounds exhibited excellent photochemical stability during repeated photochemical cycles (ring-opening/ring-closing). The degradation rates were only 0.005% per cycle for both fulgimide and copolymer.

4.2 Introduction

Fulgides and fulgimides are important organic photochromic compounds because of their potential applications in optical information storage devices and biological sensors.[19] Fulgides are derivative of 1,3-butadiene-2,3-dicarboxylic acid anhydride first synthesized by Stobbe in 1905 and the first thermally stable fulgide, a furylfulgide with a 2,5-dimethyl-3-furyl group, was synthesized by Heller In 1981. [15-17] As shown in Scheme, if one of the substituent R groups is aromatic or contains a double bond, the fulgide may be photochromic. The indolylfulgides, with an aromatic indole as the R group, are the most promising photochromic fulgides. Previous studies demonstrated that indolylfulgides have many advantages, such as enhanced thermal stability, increased photochemical stability, high efficiency of photoreactions, and large molar absorption coefficients.[22,27,35,39,81] For example, the most photochemically stable indolylfulgide

can be interconverted between the open form and the closed form for 10000 times before degrading by 13% in toluene.[2] However, previous studies indicated that fulgides were unstable in protic solvents because the succinic anhydride ring can be rapidly hydrolyzed.[20,21] To meet the demands of applications in humid environment and biological systems, hydrolytic stability is required. Therefore, fulgimides were synthesized by replacing the succinic anhydride ring with a more hydrolytically stable succinimide ring (Scheme 26).

Scheme 26. General structure of fulgides and the photochromism of indolylfulgides and indolylfulgimides



Generally, photochromic compounds for applications in optical devices must be uniformly dispersed at relatively high concentration in a condensed phase.[26,39] Photochromic fulgimides have been incorporated into synthetic polymers to meet technological devices demands. Rentzepis et al. synthesized a series of photochromic copolymer containing 2-indolylfulgides or 2-indolylfulgimides.[26,39] The fulgide or fulgimides with one or two polymerizable styrene group copolymerized with MMA via a free radical reaction with azobisisobutyronitrile (AIBN) to form linear or cross-linked copolymers. Thermal stability, efficiency, and photochemical stability are all important for practical applications. However, there is no report of thermal stability of the fulgimide copolymers at elevated temperatures or a comparison of polymers prepared in the open

and closed forms. In addition, the photochemical stability of the copolymers to cycle back and forth could be improved.

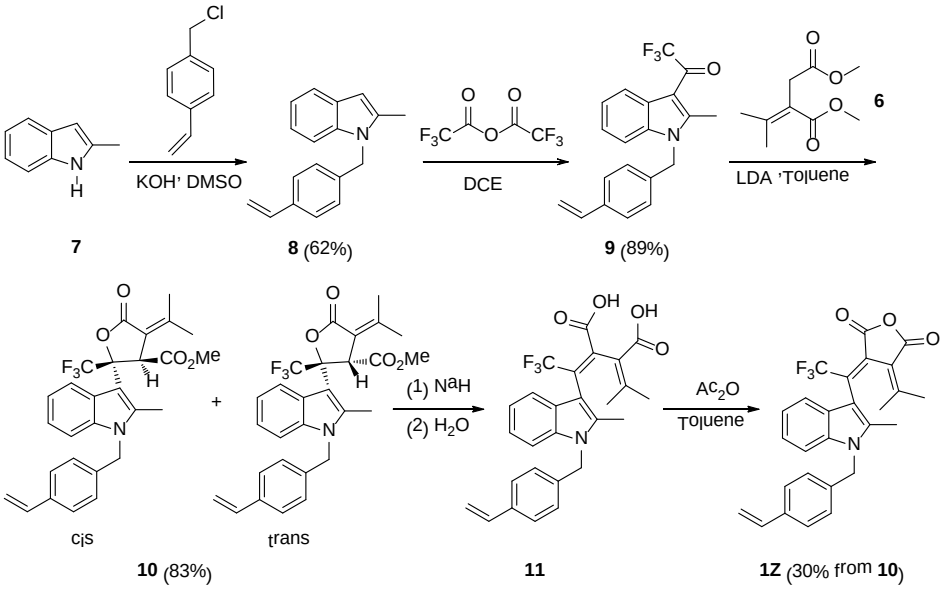
Herein, a 3-indolylfulgimide with two pendant styrene groups on the nitrogen atoms was synthesized. The new fulgimide was polymerized with MMA to obtain a cross-linked copolymer film in both the closed form and the open form. Optical properties, thermal stability, and photochemical stability of the fulgimide and the copolymer were measured.

4.3 Experimental section

4.3.1 General procedures and materials

All commercially available materials were used without purification. The NMR spectra were recorded on a Brücker 400 MHz NMR spectrometer. The ^{1}H and ^{13}C NMR samples were internally referenced to TMS. The UV-vis spectra were recorded with a Cary 300 spectrophotometer. The HRMS were obtained at the University of Florida. Flash chromatography was performed with 230-400 mesh silica gel. Illumination was provided by a 1000 W Hg (Xe) arc lamp with a water filter passed through a hot mirror followed by either a 405 nm band pass filter or a 515 nm cutoff filter.

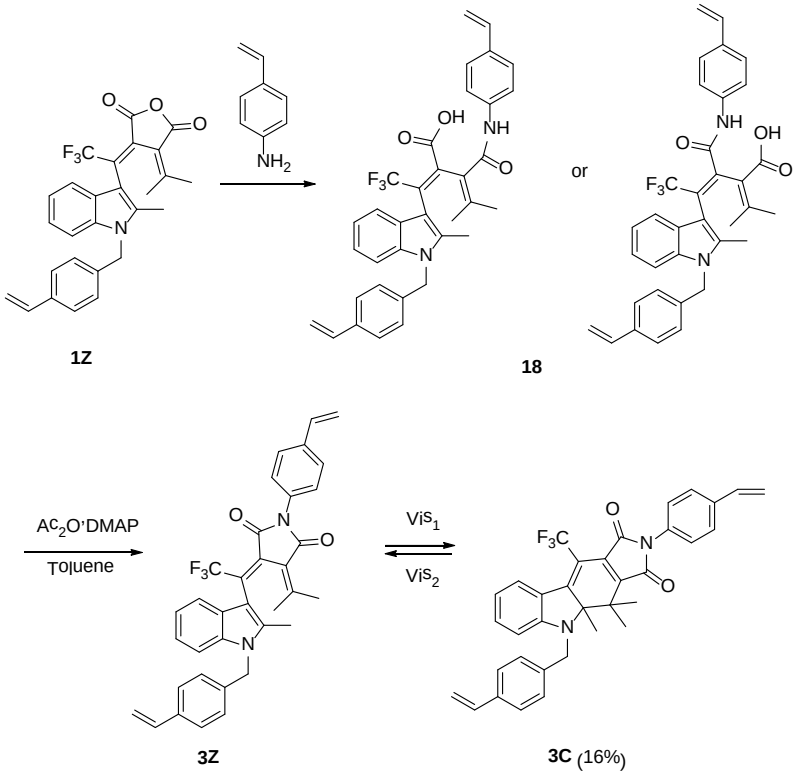
Scheme 27. Synthesis of CF_3 fulgide 1



4.3.2 Synthesis of CF_3 fulgide 1

Trifluoromethyl 3-indolylfulgide **1** was prepared as a precursor to trifluoromethyl 3-indolylfulgimide **3** in five steps from 2-methyl indole followed the procedure described in Chapter 3 (Scheme 27).

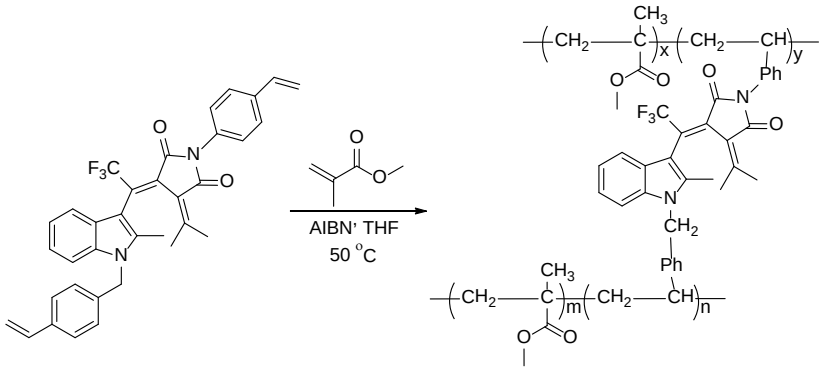
4.3.3 Synthesis of CF_3 fulgimide 3



4-Vinylaniline (0.10 g, 0.84 mmol) was added to a solution of trifluoromethyl indolylfulgide **1Z** (0.30 g, 0.65 mmol) in 60 mL of toluene at room temperature. The reaction mixture was heated to 50 °C and stirred for 2 h. The solution was then concentrated in vacuo. The residue was quenched with 100 mL of 1 M HCl and extracted with EtOAc (3 × 75 mL). The combined organic layers were washed with 50 mL H_2O. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo to provide the crude acid intermediate. Acetic anhydride (75 mL) was added to the crude acid intermediate in 100 mL of toluene. The reaction mixture was allowed to stir at room temperature for 10 min and DMAP (4 mg) was added. After 30 min, the reaction

mixture was concentrated in vacuo. The residue was dissolved in 150 mL of EtOAc and extracted with saturated $NaHCO_3$ (3 × 50 mL) and H_2O (75 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The orange residue was dissolved in 125 mL of toluene and illuminated with 405 nm light until the PSS was reached, and then the *C*-form was purified by column chromatography with toluene. Recrystallization from CH_2Cl_2/hexanes provided 0.11 g (30% from fulgide) of the *C*-form divinyl trifluoromethyl indolylfulgimide (**3**). *C*-form: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82 (d, *J* = 8.1 Hz, 1H), 7.48 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.32 -7.27 (m, 3H), 6.88 (td, *J* = 7.6, 0.9 Hz, 1H), 6.74 (dd, *J* = 17.8, 10.8 Hz, 1H), 6.73 (dd, *J* = 17.7, 10.9 Hz, 1H), 6.48 (d, *J* = 8.3 Hz, 1H), 5.77 (d, *J* = 17.5 Hz, 1H), 5.76 (d, *J* = 17.8 Hz, 1H), 5.29 (d, *J* = 10.8 Hz, 1H), 5.27 (d, *J* = 10.9 Hz, 1H), 4.63 (d, *J* = 17.5 Hz, 1H), 4.15 (d, *J* = 17.6 Hz, 1H), 1.64 (s, 3H), 1.49 (s, 3H), 1.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.9, 165.0, 160.4, 159.6 (q, *J* = 4 Hz), 140.5, 136.9, 136.8, 136.7, 136.3, 136.0, 135.6 (q, *J* = 1 Hz), 135.1, 130.1, 128.5 (q, *J* = 7 Hz), 126.8, 126.7, 126.6, 126.1, 122.6 (q, *J* = 273 Hz), 119.9, 114.7, 114.0, 110.6, 106.8 (q, *J* = 37 Hz), 77.04, 51.1, 39.3, 20.1, 18.6, 15.8. $C_{35}H_{29}F_3N_2O_2$ HRMS (ESI) *m/z*: 589.2094 [obtained M + Na]$^+$, 589.2073 [calculated M + Na]$^+$. The *Z*-form was prepared by illuminating the *C*-form in $CDCl_3$ with visible light >515 nm to quantitatively convert it to the *Z*-form. *Z*-form: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52 (d, *J* = 8.6 Hz, 2H), 7.46 -7.38 (m, 3H), 7.36 -7.28 (m, 3H), 7.24 -7.15 (m, *J* = 6.4, 1.4 Hz, 2H), 6.98 (d, *J* = 8.1 Hz, 2H), 6.75 (dd, *J* = 17.6, 11.0 Hz, 1H), 6.67 (dd, *J* = 17.5, 10.9 Hz, 1H), 5.79 (d, *J* = 17.6 Hz, 1H), 5.71 (d, *J* = 17.6 Hz, 1H), 5.37 (d, *J* = 16.9 Hz, 1H), 5.31 (d, *J* = 10.8 Hz, 1H), 5.26 (d, *J* = 16.6 Hz, 1H), 5.25 (d, *J* = 11.0 Hz, 1H), 2.20 (s, 3H), 2.09 (s, 3H), 1.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.2, 163.9, 154.5, 137.7, 137.3, 136.7, 136.6, 136.2, 136.1, 136.0, 133.1 (q, *J* = 2 Hz), 130.9, 129.3 (q, *J* = 35 Hz), 126.8, 126.7, 126.6, 126.4, 125.7, 122.6, 122.5 (q, *J* = 278 Hz), 122.4, 121.2, 119.8, 115.0, 114.5, 109.6, 108.4 (q, *J* = 2 Hz), 46.9, 26.9, 22.3, 12.1. $C_{35}H_{29}F_3N_2O_2$ HRMS (ESI) *m/z*: 589.2097 [obtained M + Na]$^+$, 589.2073 [calculated M + Na]$^+$.

4.3.4 Synthesis of cross-linked copolymers film 3-co-PMMA



3 **3-co-PMMA**

To the solution of monomer **3** (*Z*- or *C*-form) (1.0 mg, 0.002 mmol) in methyl methacrylate (1.0 g, 10 mmol), AIBN (1 wt% of MMA) was added. The polymerization was performed between two 1 inch diameter circular glass slides with a 2 mm plastic spacer at 50 ºC for 12 h. The resulting rigid thin films containing cross-linked copolymers were cooled to room temperature and directly utilized to investigate their stability.

4.3.5 Spectra determination in toluene

A concentrated stock solution of the *C*-form was prepared using 10 mg of solid sample followed by the preparation of 5 dilute solutions with concentrations between 0.05 to 0.20 mM. UV-Vis spectra of these solutions were obtained, and concentration versus absorbance was plotted to determine the extinction coefficient. The diluted *C*-form solutions were irradiated with 515 nm light to quantitatively convert to *Z*-form solutions. UV-Vis spectrum of each freshly converted *Z*-form solution was measured and then the extinction coefficient was determined.

4.3.6 PSS measurements

The photostationary state (PSS) was measured using NMR spectroscopy. An NMR tube containing *Z*-form fulgimide in toluene-d_8 was illuminated with 405 nm light until PSS was reached. A ^{1}H NMR spectrum was then acquired and integrated.

4.3.7 Photochemical stability

The *Z*-form sample (solution or film) was prepared with an initial absorbance of 0.6 -0.8 at the absorption maxima. Sample was irradiated to PSS and an UV-Vis spectrum was acquired after prolonged irradiation at 405 nm. Another sample of pure *Z*-form was irradiated to 90% of the PSS, and the reaction time (coloration) was obtained. The 90% PSS mixture was then back irradiated to the yellow form, and again the reaction time (decolorization) was obtained. Once the duration of irradiation reactions (coloration-decolorization) was established, the system was automated through the use of a filter switch. After a designated number of photochemical cycles, the sample was converted to PSS and UV-Vis spectrum scanned. The photochemical stability was determined by comparison with the initial PSS absorption spectrum. The cycling times in toluene were: 60 s (*Z* - *C*) and 40 s (*C* - *Z*) for **3**; 80 s (*Z* - *C*) and 90 s (*C* - *Z*) for **3-co-PMMA**.

4.3.8 Thermal stability

The thermal stability of fulgimide **3** (*Z*- and *C*-forms) in toluene was measured using both UV-Vis spectroscopy and ^{1}H NMR spectroscopy. The solutions were prepared in toluene or its deuterated analog and transferred into several ampoules or NMR tubes, respectively. UV-Vis and ^{1}H NMR spectra of these initial samples were measured. Ampoules and NMR tubes were sealed and submersed in a water bath maintained at 80 °C. At predetermined times, ampoules and NMR tubes were removed, and their contents analyzed by UV-Vis or ^{1}H NMR spectroscopy. For the copolymer **3-co-PMMA**, the thin films (*Z*- and *C*-forms) were wrapped in aluminum foil and placed in an oven maintained at 80 °C. The films were removed at prescribed intervals and their UV-Vis spectra measured. All the photochemical properties measurements were performed by Dr. Islamova in Dr. Lees' group.

4.4 Results and discussion

4.4.1 Synthesis

A new 3-indoleylfulgimide **3** with two pendant styrene groups on nitrogen atoms was synthesized in two steps form the precursor fulgide **1**. The first step involved an anhydride ring opening reaction via addition of 4-vinylaniline to generate an amide acid intermediate. In the following step, subsequent dehydration of the succinamic acid intermediate was taken place with acetic anhydride to yield the fulgimide **3**. The fulgimide was then copolymerized with MMA to provide a cross-linked polymer **3-co-PMMA** via a free radical polymerization between two glass slides. The ratio of monomers (fulgimide to MMA) was selected to ensure that the copolymers were suitable for UV-Vis measurements (absorbance approx. 1). The resulting **3-co-PMMA** was found to be insoluble in THF, CH_2Cl_2, DCE, or toluene and very rigid, optically clear, and difficult to break. The photochromic properties of monomeric fulgimide and copolymer were studied in toluene and as film, respectively. Both monomer and copolymer are photochromic and stable (in both forms) at room temperature.

4.4.2 UV-Vis absorption spectra

The UV-Vis absorption spectrum of fulgimide **3** was measured in toluene and the extinction coefficient was calculated (Figure 8, Table 4). Both *Z*-form and *C*-form absorbed the light in the visible region. The *C*-from fulgimide **3C** showed larger extinction coefficient and blue shifted 17 nm of the absorbance maximum relative to the *C*-from fulgimide **2C**, however, the substitution of a styrene group does not significantly change the absorbance maximum or extinction coefficient of the Z-form. As expected, the absorbance maxima of the *Z*-form fulgimide **3Z** exhibited a hypsochromic shift of 23 nm relative to the precursor fulgide **1Z**.[1,39] The photostationary state (PSS) achieved upon irradiation with 405 nm light contained 95% *C*-form. After polymerization with MMA, **3-co-PMMA** displayed a similar UV-Vis absorption pattern with the fulgimide **3**. The advantageous properties include the absorption maxima in the visible region of the spectrum

and high conversion in both directions that makes the compounds promising for practical applications.

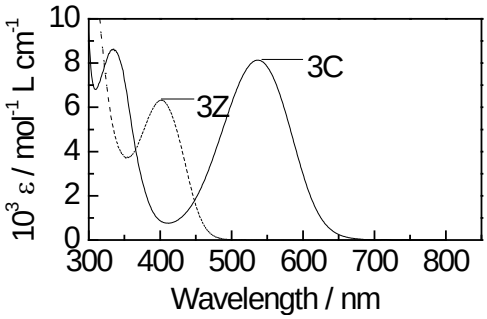


Figure 8. UV-Vis absorption spectra fulgimide **3C** and **3Z** in toluene

Table 4. Extinction coefficients at λ_{max} for 3 in toluene and λ_{max} for copolymer 3-co-PMMA in thin film.

Compound (Medium)	λ_{max}/nm (ε_{max}/mol^{-1} L cm^{-1})		$PSS_{405\ nm}$[a]
	Z-form	*C*-form	*C*:*Z*:*E*
1 (Toluene)[b]	424 (5.5×10^3)	549 (7.3×10^3)	94:5:1
2 (Toluene)[b]	405 (6.4×10^3)	554 (7.4×10^3)	93:4:3
3 (Toluene)	401 (6.3×10^3)	537 (8.1×10^3)	95:4:1
3-co-PMMA (Film)	402	540	-

[a]Photostationary state. [b]The data taken from Chapter 2.

4.4.3 Thermal Stability

Thermal stability is essential for fulgimides in the application of optical memory devices or optical switches.[2,20,28] To make the data comparable, the thermal stability of fulgimide **3** was tested in toluene at 80 °C, which is the same condition used in the previous research.[2,33,34,82] Both ^{1}H NMR and UV-Vis spectroscopy were used to measure the thermal decomposing of fulgimide **3**. The cross-linked polymer **3-co-PMMA** was studied as film at 80 °C and followed by UV-Vis spectroscopy.

In toluene, the closed form **3C** was more stable than the open form **3Z** which is consistent with previous results for fluorinated indolylfulgimides (Figure 9).[2] All the data were fit to a single

exponential decay for both forms excluding the first data point for the *C*-form as there is an initial 1-2% loss in the absorbance followed by a slow decomposition. The *Z*-form degraded 0.018 h^{-1} and 0.011 h^{-1} by UV-Vis and ^{1}H NMR spectroscopy, respectively. The values are comparable to that previously found for the parent fulgide **1** and the analogous fulgimide **2** (Table Table 5).

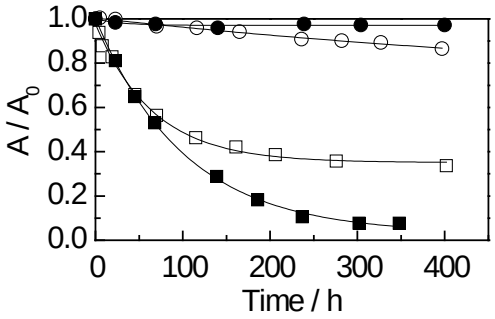


Figure 9. Thermal decomposition of fuligmides **3** and coplymers **3-co-PMMA**: (a) fulgimides in toluene at 80 ºC measured by NMR: **3C** (●) and **3Z** (■); (b) copolymers as films at 80 ºC measured by UV-Vis spectroscopy: **3C-co-PMMA** (○) and **3Z-co-PMMA** (□) at 80 ºC

Table 5. Thermal decomposition rate constants (×10^3, h^{-1}) for 3 and 3-co-PMMA at 80 ºC

Compound (Medium)	UV-Vis		^{1}H NMR	
	Z-form[a]	*C*-form[b]	*Z*-form[a]	*C*-form[b]
1 (Toluene)[c]	53[d]	< 0.05	20	< 0.05
2 (Toluene)[c]	18[c]	< 0.05	14	< 0.05
3 (Toluene)	18	< 0.05	11	< 0.05
3-co-PMMA (Film)	16	0.37	-	-

[a]Fit to a single exponential decay. [b]Fit to a single exponential excluding 0 h data point. [c]The data taken from Chapter 3.

The UV-Vis spectrum of **3Z** in toluene displayed an initial drop in absorbance followed by a red shift and subsequent increase in absorbance and the absence of the isosbestic points indicated the presence of an intermediate (Figure 10a). The pattern is similar to the pervious results of fulgimide **2Z** in chapter 3 which degraded possibly via a 1,5-hydrogen shift from the isopropylidene group to form an intermediate and then rearranges to a mixture of two products.[18] However, in the case of the open form copolymer **3Z-co-PMMA**, the UV-Vis spectrum exhibited

decreased absorbance of the red shifted peak after 70 h in toluene at 80 ºC (Figure 10b). It potentially indicated decomposition of a thermolysis product(s). Similar to its monomeric fulgimide, the copolymer was much more stable in closed form at 80 ºC, and there is no decomposition occurred at room temperature for both closed form and open form.

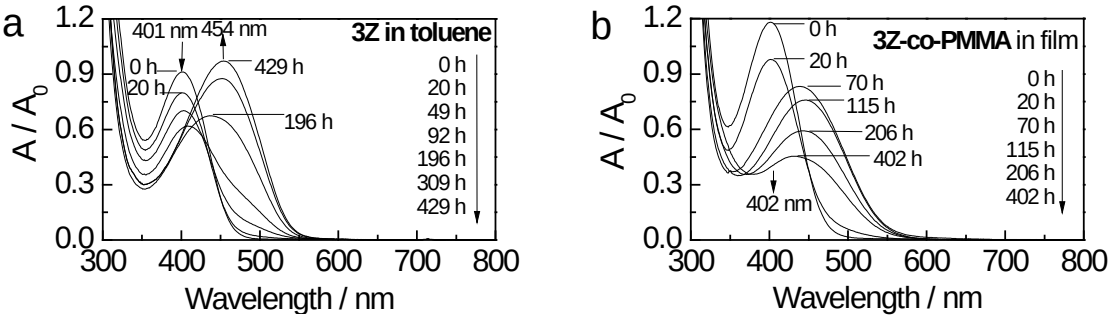


Figure 10. Thermal decomposition of fulgimide **3Z** and copolymer **3Z-co-PMMA**: (a) **3Z** in toluene and (b) **3Z-co-PMMA** in film at 80 °C by UV-Vis

4.4.4 Photochemical stability

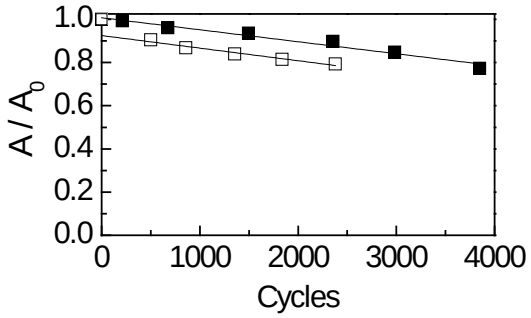


Figure 11. Photochemical decomposition of fulgimide **3** and copolymer **3-co-PMMA**: **3** (■) in toluene and **3-co-PMMA** (□) in film

Table 6. Photochemical fatigue resistance of 3 and 3-co-PMMA

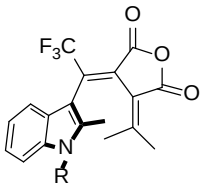
Compound (Medium)	Cycling time (s)		Photochemical decomposition		
	Z-C	C-Z	Number of cycles	A/A_0	% per cycle
3 (Toluene)	60	40	2990	0.848	0.0050
3-co-PMMA (Film)	80	90	2378	0.793	0.0050[a]

[a]From 500 cycles onwards.

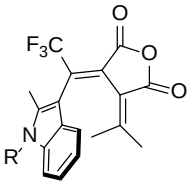
Photochemical stability was measure by determining the percentage loss in absorbance per photochemical cycle (ring-opening/ring-closing) during approx. the first 20% of degradation. The fulgimide was tested in toluene and its copolymer was measured as film. Fulgimide **3** showed excellent photochemical stability in toluene, degrading only 0.005% pre photochemical cycle (Figure 11). After polymerization, the copolymer film degraded at the same rate as its monomeric fulgimide (Table 6). The initial drop in absorbance followed by a linear decomposition as shown in Figure 11, possibly results from polymer reorganization at the beginning.

4.4.5 Conformational restrictions

I found that when the copolymer films **1-co-PAA, 2-co-PAA** (in Chapter 3)**,** and **3-co-PAA** initially prepared in the open form were converted to $PSS_{436/405\ nm}$, the absorbance at λ_{max} decreased. However, when copolymer films prepared in the closed form were converted to the open form and then converted back to $PSS_{436/405\ nm}$, the absorbance at λ_{max} changed slightly. This behaviour just like diarylethenes which was reported previously.[83] Diarylethenes in open forms have two conformations, antiparallel conformation and parallel conformation. The two conformations can be interconverted in solution. But in films, the interconversion is limited and only the antiparallel conformation can be converted to closed form. Similar with diarylethenes, the copolymers films initially prepared in the open form contains two conformations, a reactive conformation and a unreactive conformation. Only the reactive conformation can convert to the closed form, so the conversion of the open form to the closed form is lower. However, the copolymer films prepared in the closed form and then converted to the open form only contains reactive conformation. The conversion between the open form and the closed form was more complete. As a result, it is recommended that polymer films better to be prepared in the closed forms.



Reactive conformation



Unreactive conformation

4.5 Conclusion

I have synthesized a 3-indolylfulgimide 3 with two pendant styrene groups and copolymerized it with MMA to obtain cross-linked copolymer films (in the Z- and C-forms). The fulgimide and copolymer were found to be photochromic and very stable at room temperature. For both fulgimide and copolymer, the C-forms exhibited excellent thermal stability at 80 °C, however, the Z-forms were less stable decomposing through intermediates. Fulgimide and copolymer exhibited similar photochemical stability only degrading 0.005% per cycle. In films, the open Z-form fulgimide was conformationally restricted, so preparation of photochromic films in the closed C-forms is preferred.

5. SYNTHESIS OF AQUEOUS SOLUBLE 3-INDOLYLFULGIMIDE-CO-PAA LINEAR COPOLYMERS

5.1 Abstract

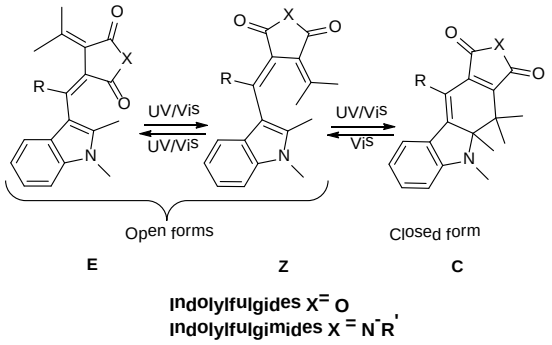
Aqueous soluble polymers containing photochromic indolylfulgimides are promising materials for optical molecular switches and biological sensors. A new CH_3 indolylfulgimide **4** with an *N*-stryryl on the succinimide ring was synthesized. Copolymerization of the CH_3 indolylfulgimide **4** or CF_3 indolylfulgimide **2** with acrylamide provided linear copolymers **4-co-PAA** or **2-co-PAA**, respectively. The resulting linear copolymers were aqueous soluble and photochromic. The CH_3 fulgimide was characterized in toluene. The open form CH_3 fulgimide **4E** exhibited excellent thermal stability and no degradation was observed after 400 h at 80 °C. The *C*-form fulgimide **4C** was less stable and degraded about 30% after 220 h at 80 °C. Photochemical stability was measured by repeatedly interconverting the fulgimide between the open form and the closed form. The CH_3 fulgimide **4** decomposed 0.018% per cycle in toluene. The copolymers were studied in three different aqueous solutions: a sodium acetate buffer (pH 5.0), water, and a sodium phosphate buffer (pH 7.4). The closed form **2C-co-PAA** was rapidly hydrolyzed probably by replacing the CF_3 group on the bridging position of the fulgimide to COOH group in aqueous solutions. The resulting **hydrolyzed-2-co-PAA** was also photochromic. In general, both **4-co-PAA** and **hydrolyzed-2-co-PAA** exhibited enhanced stability in acidic solution. The open form copolymers were more stable than the closed form copolymers. All copolymers were able to undergo at least 16 cycles before degrading 20% in aqueous solutions.

5.2 Introduction

Photochromic compounds are known for their ability to interconvert between two isomers upon irradiation. Within organic photochromic compounds, photochromic fulgides and fulgimides have been extensively studied.[1,2,19,27,33,34] Indolylfulgides have many advantages, such as enhanced thermal stability, increased photochemical stability, highly efficient photoreactions,

and large molar absorption coefficients (Scheme 1).[22,27,35,39,81] These promising characteristics make indolylfulgides useful in optical information storage devices and as optical molecular switches.[19,25,43,47,48] The most photochemically stable indolylfulgide can be interconverted between the open form and the closed form 10000 times before degrading by 13% in toluene.[2] However, fulgides are unstable in protic solvents.[20,21] Hydrolytic stability is essential for the applications in humid environment and biological systems. Thus, fulgimides were synthesized to improve the hydrolytic stability by replacing the succinic anhydride ring with a succinimide ring (Scheme 28).

Scheme 28. Photochromism of indolylfulgides and indolylfulgimides



Manipulation of the functional groups on fulgimides which control their photochemical properties is essential to the development of functional materials. For example, the absorption maximum of a indolylfulgimide will be in the visible region in both the open form and the closed form with a trifluoromethyl group at the bridging position (R in Scheme 28).[27] Using visible lights instead of UV lights in biological systems is preferred, because the UV lights can be damaging to the living organisms. Replacing the trifluoromethyl group with a methyl group shifts the absorption maxima of the open form to the UV region. However, the resulting indolylfulgimides will have enhanced hydrolytic stability.[33,34] The other functional group, R' on the succinimide ring, can also be modified for specific purposes. A series of fulgimides with an acetic acid as R' group were synthesized. These fulgimides with a pendant hydrophilic group can be dissolved not only in organic solutions but also in aqueous solutions.[33,34] The ability to be

aqueous soluble will make the fulgimides more practical for applications in biological systems. The R' group can also be a polymerizable group, for example, a fulgimide with a pendant *N*-stryryl on the succinimide ring was synthesized.[27] The fulgimide was then copolymerized with the methyl methacrylate (MMA) to obtain a photochromic linear copolymer. The resulting copolymer retained the photochromic properties as the monomeric fulgimide and exhibited good thermal and photochemical stabilities in toluene. Covalent incorporation instead of embedding into copolymers allowed the fulgimide distributed uniformly in the polymer matrix to minimize aggregation and diffusion.[26,39,78] For the applications in biological systems, such as bioimaging and biosensors, aqueous solubility is preferred. Therefore, aqueous soluble copolymers containing a photochromic fulgimide will be promising. However, to the best of my knowledge, no example of such a photochromic copolymer was reported.

Herein, I synthesized a CF_3 indolylfulgimide and a CH_3 indolylfulgimide with an *N*-stryryl on the succinimide ring were synthesized and incorporated into water soluble polymers. The linear copolymers were aqueous soluble and photochromic. The photochromic properties of the fulgimides were measured in toluene and the copolymers were studied in three aqueous solutions: water, a 50 mM sodium phosphate buffer (pH 7.4), and a 50 mM sodium acetate buffer (pH 5.0).

5.3 Experimental section

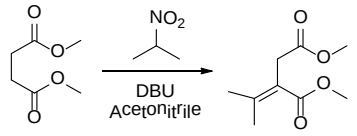
5.3.1 General procedures and materials

All commercially available materials were used without purification. The NMR spectra were recorded on a Brücker 400 MHz NMR spectrometer. The ^{1}H and ^{13}C NMR samples were internally referenced to TMS. The UV-Vis spectra were recorded with a Cary 300 spectrophotometer. The HRMS were obtained at the University of Florida. Flash chromatography was performed with 230-400 mesh silica gel. Illumination was provided by a 1000 W Hg (Xe) arc lamp. The light first went through a water filter, then through a hot mirror, and finally through

either a band pass filter (365 nm (for CH_3 fulgimide)/405 nm (for CF_3 fulgimides)) or a cutoff filters (> 515 nm). Trifluoromethyl indolylfulgimide **2** was synthesized as reported previously.[27]

5.3.2 Synthesis of methyl fulgimides

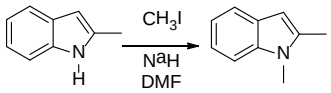
5.3.2.1 Synthesis of dimethyl isopropylidenesuccinate 6 [80]



5 **6** (67%)

2-Nitropropane **5** (76.60 g, 0.860 mol) was dissolved in 2.4 L of acetonitrile, then followed by addition of dimethyl maleate (135.70 g, 0.942 mol) and 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) (201.56 g, 1.32 mol). The reaction mixture was stirred at room temperature. After 16 h, the mixture was concentrated in vacuo. The residue was poured into a 4 L separatory funnel and quenched with 600 mL of HCl. The mixture was extracted with 1.5 L of diethyl ether and washed with water (2 x 600 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was then purified by vacuum distillation to yield 107.50 g (67%) of dimethyl isopropylidenesuccinate **6**.

5.3.2.2 Synthesis of 1,2-dimethylindole 12

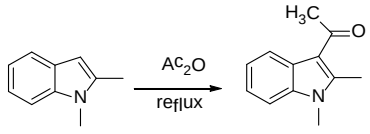


7 **12** (81%)

2-Methylindole **7** (0.117 mmol, 15.40 g) was added in 200 mL of DMF and stirred for 30 min. The mixture was cooled to 0 °C followed by addition of NaH (6.01 g of 60 % dispersion in oil, 0.150 mmol). After stirring for 10 min, methyl iodide (8.0 mL, 0.129 mmol) was added. The reaction mixture was warmed to room temperature and left to react under argon gas for 5 h. The mixture was then concentrated in vacuo. The residue was dissolved in 500 mL of EtOAc and extracted with water (2 x 200 mL) and brine (200 mL). The organic layer was dried over $MgSO_4$,

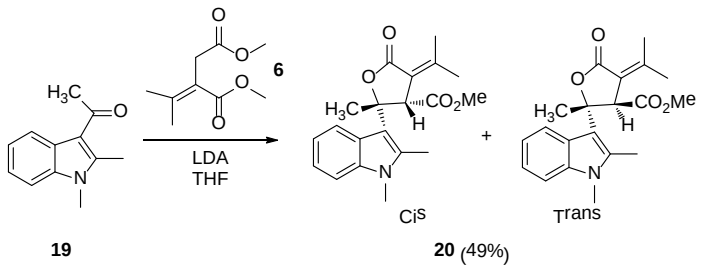
filtered, and concentrated in vacuo. Further purification via column chromatography (1:1 hexane/EtOAc) provided 13.76 g (81%) of 1,2-dimethylindole **12**.

5.3.2.3 Synthesis of 3-acetyl-1,2-dimethylindole 19[18]



1,2-dimethylindole **12** (9.50 g, 65.4 mmol) was dissolved in 160 mL of acetic anhydride (172.8 g, 1.692 mol). The mixture was heated to reflux under argon gas for 36 h. After concentrating in vacuo, the brown residue was purified by recrystallization from hexane/CH_2Cl_2 to yield 7.86 g (64%) of 3-acetyl-1,2-dimethylindole **19**.

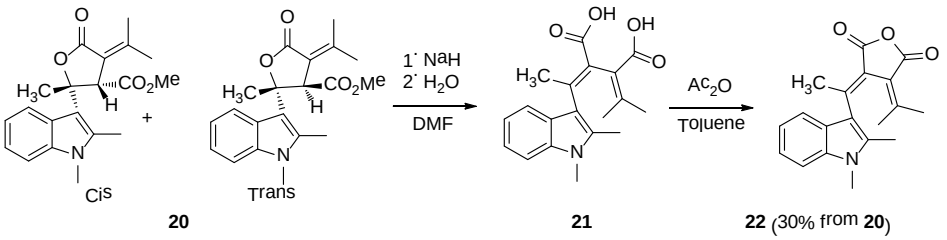
5.3.2.4 Synthesis of cis/trans indolelactones 20[18]



Dimethyl isopropylidenesuccinate **6** (23.86 g, 69 mol) was dissolved in 60 mL of dry THF and cooled to -78 °C under argon gas. Lithium diisopropylamide (LDA) (40 mL of a 1.5 M solution in THF, 60 mmol) was added dropwise via an addition funnel to the solution and stirred for 30 min at -78 °C under argon gas. To the mixture, a solution of 3-acetyl-1,2-dimethylindole **19** (5.75 g, 30.8 mmol) in dry THF was added dropwise via an addition funnel. To avoid moisture in the reaction mixture, a cannula was used to fill the addition funnel. The mixture was warmed to room temperature and allowed to react for 48 h. The solution was then concentrated in vacuo. The residue was quenched with 200 mL of water and acidified with 5% H_2SO_4 solution. The aqueous layer was extracted with diethyl ether (3 x 100 mL). The combined organic layers were washed

with brine (2 x 100 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography (2:1 hexanes/ether) and then recrystallized from ethanol to provide 5.20 g (49%) of cis/trans mixture of indolelactones **20**.

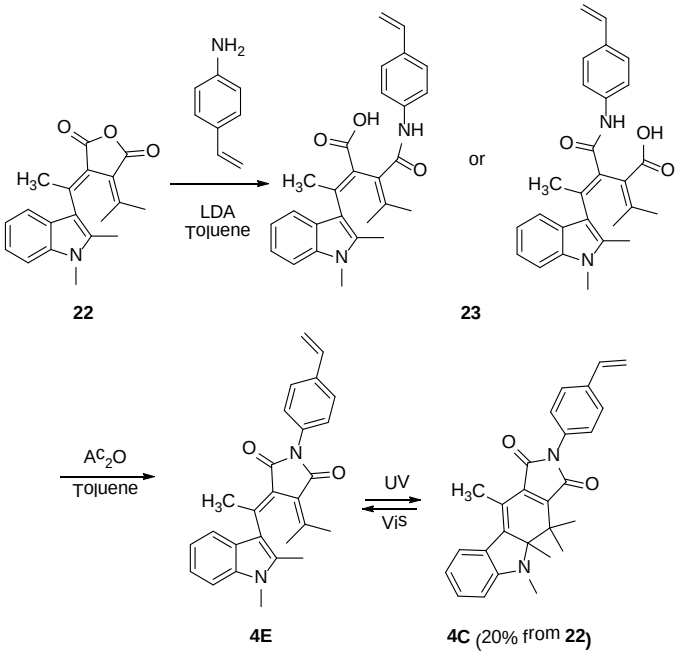
5.3.2.5 Synthesis of methyl indolylfulgide 22[18,84]



20 **21** **22** (30% from **20**)

Sodium hydride (60% dispersion in oil, 0.84 g, 21 mmol) was added to a solution of cis/trans indolelactones **20** (2.90 g, 8.50 mmol) in 250 mL of DMF at 0 °C. The mixture was warmed to room temperature and stirred for 1 h. Then, the mixture was cooled back again to 0 °C, and water (2.5 mL, 139 mmol) was added. After stirring overnight, the mixture was then concentrated in vacuo. The residue was dissolved in 150 mL of water and washed with EtOAc (3 x 100 mL). The aqueous layer was then acidified with 10% HCl to pH 2 and extracted with EtOAc (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo to provide crude diacid intermediate **21**. The resulting diacid was suspended in 100 mL of toluene. Acetic anhydride (50 mL, 0.53 mol) was added, and the reaction mixture was heated to reflux for 2 h under argon gas. The mixture was then concentrated in vacuo. The residue was partitioned between water (200 mL) and CH_2Cl_2 (100 mL). The aqueous layer was then extracted with CH_2Cl_2 (2 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography with CH_2Cl_2 and recrystallized from CH_2Cl_2/hexanes to provide 0.78 g (30%) of methyl indolylfulgide **22**.

5.3.2.6 Synthesis of methyl styrene indolylfulgimide 4



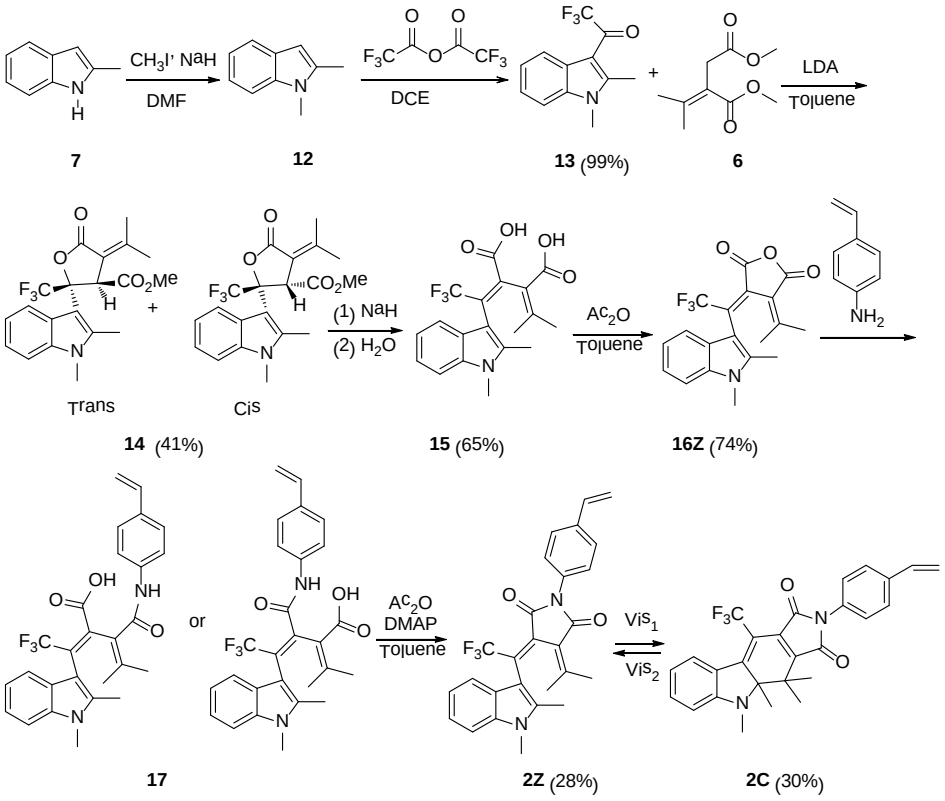
To a stirred solution of 4-vinylaniline (0.316 g, 2.65 mmol) in 50 mL of dry THF, lithium diisopropylamide (LDA) (3.0 mL of a 1.5 M solution in THF, 4.5 mmol) was added dropwise via a syringe. The mixture was left to react for 5 min, and methyl indolylfulgide **20** (0.316 g, 1.08 mmol) was added. The reaction mixture was then stirred overnight. The mixture was quenched with 10% H_2SO_4 (100 mL) and extracted with EtOAc (3 x 100 mL). The combined organic layers were washed with brine (100 mL) and water (100 mL). Then, the solution was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by column chromatography to provide the crude amide acid intermediate **23**. Acetic anhydride (50 mL) was added to the solution of **23** in 60 mL of toluene. The mixture was stirred for 10 min and followed by addition of 10 mg of 4-dimethylaminopyridine (DMAP). The reaction mixture was allowed to react overnight at 50 °C. Then, the mixture was concentrated in vacuo. The residue was dissolved in EtOAc (100 mL) and extracted with $NaHCO_3$ (2 x 50 mL) and water (50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by silica gel chromatography (1:1 EtOAc/hexanes). The resulting open form of methyl

styrene indolylfulgimide **4E** was illuminated with 365 nm light in toluene until the photostationary state (PSS) was reached, and then the *C*-form was purified by silica gel chromatography (1:1 CH_2Cl_2/hexanes). Recrystallization from CH_2Cl_2/hexanes yielded 92 mg (20%) of *C*-form methyl styrene indolylfulgimide **4C**. The *E*-form was prepared by illuminating the *C*-form in toluene with visible light > 515 nm and recrystallized from CH_2Cl_2/hexanes. *C*-form ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.60 (d, *J* = 7.5 Hz, 1H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.23 (t, *J* = 7.7 Hz, 1H), 6.77-6.70 (m, 2H), 6.57 (d, *J* = 8.1 Hz, 1H), 5.77 (dd, *J* = 17.3, 0.5 Hz, 1H), 5.28 (d, *J* = 10.9 Hz, 1H), 2.92 (s, 3H), 2.47 (s, 3H), 1.81 (s, 3H), 1.33 (s, 3H), 1.23 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 168.3, 157.3, 150.9, 138.2, 136.6, 136.2, 136.0, 131.7, 131.3, 126.6, 126.2, 126.0, 124.6, 118.0, 115.1, 114.5, 108.1, 72.6, 40.3, 31.8, 20.0, 19.0, 15.7, 13.7. $C_{27}H_{26}N_2O_2$ HRMS (ESI) *m/z*: 411.2072 [obtained M + H]$^+$, 411.2067 [calculated M + H]$^+$. *E*-form: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.31-7.24 (m, 2H), 7.14 (td, J = 7.3, 1.1 Hz, 1H), 6.75 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.78 (dd, *J* = 17.6, 0.6 Hz, 1H), 5.29 (dd, *J* = 10.9, 0.6 Hz, 1H), 3.69 (s, 3H), 2.82 (s, 3H), 2.22 (s, 3H), 2.20 (s, 3H), 0.97 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.1, 167.7, 148.5, 144.8, 137.2, 137,1, 136.3,134.3, 131.7,127.1, 126.6, 125.5, 123.8, 122.7, 121.7, 120.4, 119.7, 118.3, 114.6, 109.0, 29.8, 26.4, 23.1, 22.2, 12.1. $C_{27}H_{26}N_2O_2$ HRMS (ESI) *m/z*: 411.2076 [obtained M + H]$^+$, 411.2067 [calculated M + H]$^+$, 433.1894 [obtained M + Na]$^+$, 433.1886 [calculated M + Na]$^+$.

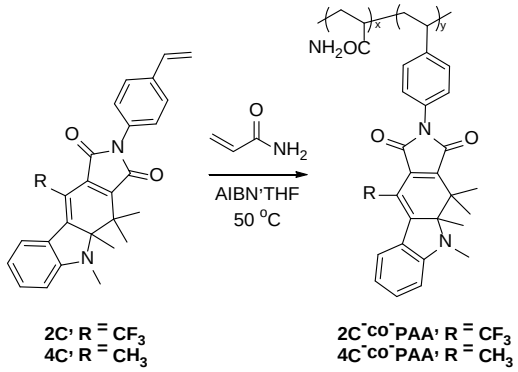
5.3.2.7 Synthesis of trifluoromethyl styrene indolylfulgimide 2

Trifluoromethyl styrene indolylfulgimide **2** was synthesized following the procedure described in Chapter 3 (Scheme 29). Trifluoromethyl 3-indolylfulgide **16** was prepared in five steps from 2-methyl indole.[22] Then, fulgimide **2** was obtained by addition of 4-vinylaniline to the succinate ring of fulgide **16** followed by dehydration in acetic anhydride.

Scheme 29. Synthesis of trifluoromethyl styrene indolylfulgimide 2



5.3.3 Synthesis of linear copolymers 2-co-PAA and 4-co-PAA



2C, R = CF_3
4C, R = CH_3

2C-co-PAA, R = CF_3
4C-co-PAA, R = CH_3

The *C*-form indolylfulgimide **2C** or **4C** (4.5 mg, 0.01 mmol) were dissolved in 2 mL of DMSO. Acrylamide (0.35 g, 4.9 mmol) was added to the solution followed by the addition of initiator azobisisobutyronitrile, AIBN (1 wt% of PAA). The solution was stirred until all solids dissolved. The solution was transferred to a resealable glass ampule. The ampule was sealed under vacuum and kept at 50 °C. After 48 h, a blue polymeric gel was formed. The polymeric gel

was dissolved in 30 mL water and transferred to a dialysis bag (M.W. cutoff: 6000-8000). Dialysis was performed four times against 3.5 L of water each time. The copolymer solution was lyophilized to provide the *C*-form copolymers **2C-co-PAA** and **4C-co-PAA**.

5.3.4 Stability of fulgimides in toluene at 80 °C and Stability of copolymers in aqueous solutions at 37 °C

The thermal stability of fulgimides and copolymers were measured in both the open and closed forms. Solutions of fulgimides in toluene and copolymers in aqueous solutions (50 mM sodium phosphate buffer (pH 7.4), 50 mM sodium acetate buffer (pH 5.0), and water) were prepared and each solution was transferred into several ampoules. The ampoules were then sealed and incubated in a water bath maintained at 80°C and 37 °C for fulgimides and copolymers, respectively. At predetermined times, ampoule were removed and the solution was analyzed by UV-Vis spectroscopy.

5.3.5 Photostationary state (PSS) measurements

The Fulgimide **4C** in toluene-d8 was converted to **4E** with >515 nm light and then the **3E** was illuminated with 365 nm light until a constant Z/E/C ratio was obtained. The reaction was monitored via ^{1}H NMR spectroscopy.

5.3.6 Photochemical stability

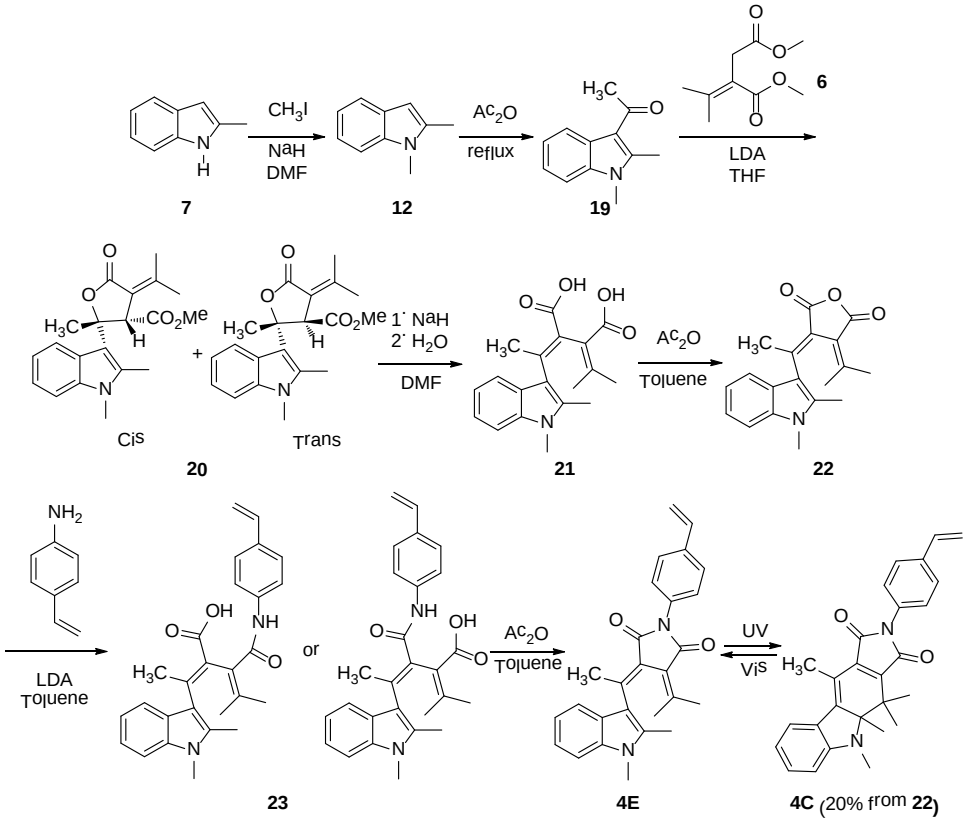
Solution of closed form fulgimides in toluene and copolymers in aqueous solutions (50 mM sodium phosphate buffer (pH 7.4), 50 mM sodium acetate buffer (pH 5.0), and water) were quantitatively converted to solutions of open form by irradiating with visible light >515 nm. The open form solutions were converted to the photostationary state (PSS) with prolonged irradiation of 365 nm light for **4** and **4-co-PAA** and 405 nm light for **2** and **hydrolyzed 2-co-PAA**. A UV-Vis spectrum was acquired and the absorbance at λ_{max} in the visible region was determined. The time taken to achieve 90% of the absorbance at λ_{max} of $PSS_{365\ nm\ (405\ nm)}$ was then recorded. Then, the solutions of $PSS_{365\ nm\ (405\ nm)}$ were irradiated with visible light >515 nm again until the *C*-form

solutions were < 1% in absorbance at λ_{max} of the *C*-form, and the reaction time was measured. Once the duration of the irradiation reactions was established, the solutions were converted back and forth with an automated filter switch. After a designated number of irradiation cycles, the sample was fully converted to $PSS_{365\ nm\ (405\ nm)}$ with prolonged irradiation and the UV-Vis spectrum was scanned. The photochemical stability was determined by comparison with the absorbance at the λ_{max} of the *C*-form obtained from the initial $PSS_{365\ nm(405\ nm)}$ absorption spectrum.

5.4. Results and discussion

5.4.1 Synthesis

Scheme 30.Synthesis of methyl styrene 3-indolylfulgide 4



A new 3-indolylfulgimide **4** with an *N*-stryryl on the succinimide ring was synthesized from the precursor indolylfulgide **22**. Preparation of fulgide started from commercial available 2-methylindole. After methylation and acetylation, 1,2-dimethyl-3-acetylindole was obtained. Then

the resulting indole was reacted with a dimethyl isopropylidene succinate to yield cis/trans indolelactones via a Stobbe condensation. The indolelactones were then hydrolyzed to a dicarboxylic acid by using NaH as a base and followed with water in DMF. The methyl indolylfulgide **22** was afforded in 30% yield from the indolelactones after dehydration of the dicarboxylic acid in refluxing acetic anhydride (Scheme 30). Fulgide **22** was then used as a starting material for synthesis of CH_3 fulgimide **4**. The anhydride ring of **22** was opened via addition of 4-vinyl aniline. The resulting succinamic acid, one of the two possible regioisomers, was then dehydrated in acetic anhydride to yield open form CH_3 fulgimide **4E**. The closed form fulgimide **4C** was prepared by illuminated **4E** with UV light. The CF_3 fulgimide **2** was synthesized by using the method described in Chapter 3 (Scheme 29). Two linear copolymers (**2-co-PAA** and **4-co-PAA**) were prepared from the corresponding fulgimides and acrylamide via free-radical polymerization with AIBN as the initiator. The ratio of monomers (fulgimide to acrylamide) was selected to ensure that the copolymers were suitable for UV-Vis measurements (absorbance approx. 1). All linear copolymers were soluble in aqueous solutions and photochromic. The copolymer **2-co-PAA** was studied by ^{19}F NMR spectroscopy in D_2O (Figure 12). For the **2Z-co-PAA**, , which contains the open form CF_3 fulgimide, only one resonance at -56 ppm in the spectrum was observed and the resonance is consistent with the fluorines of a CF_3 group. However, after converting to the closed form **2C-co-PAA**, the resonance at -56 ppm disappeared, and a new signal appeared at -146 ppm, which corresponds to the chemical shift of a fluoride anion. As expected, after irradiating back to the open form, the signal at -146 ppm persisted. The result suggests that **2C-co-PAA** was not stable in aqueous solutions and rapidly hydrolyzed to lose the fluorines. A similar conclusion was found in a previous model study, in which a *C*-form water soluble CF_3 fulgimide was rapidly hydrolyzed in buffer by replacing the CF_3 group on the bridging position with a carboxylic acid group.[33]

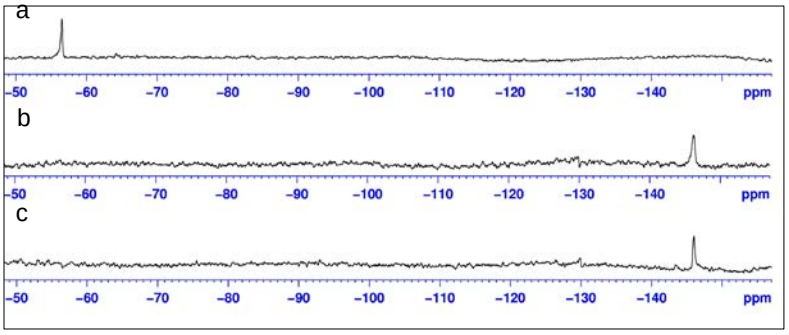
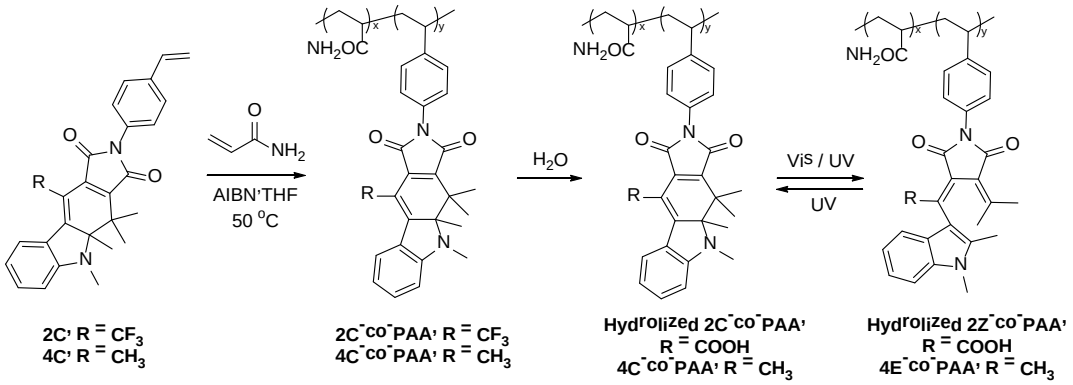


Figure 12. ^{19}F NMR spectra of copolymer (a) original **2Z-co-PAA**, (b) **hydrolyzed-2C-co-PAA**, and (c) **hydrolyzed-2Z-co-PAA** in D_2O

I also found that the resulting **hydrolyzed-2C-co-PAA** was also photochromic and can be converted to open form **hydrolyzed-2Z-co-PAA** with light. However, the open form copolymer prepared from open form fulgimide **2Z** was stable in aqueous solutions and can not be degraded to **hydrolyzed-2Z-co-PAA** directly. This result is also consistent with the model study.[33] The thermal and photochemical stabilities of **2-co-PAA** were studied in their hydrolyzed forms. By replacing the CF_3 group with a CH_3 group on the bridging position, the copolymer **4-co-PAA** containing CH_3 fulgimide **4** was relatively stable in aqueous solutions for both closed form and open form (Scheme 31).

Scheme 31.Synthesis of linear copolymers 2-co-PAA and 4-co-PAA



5.4.2 UV-Vis absorption spectra

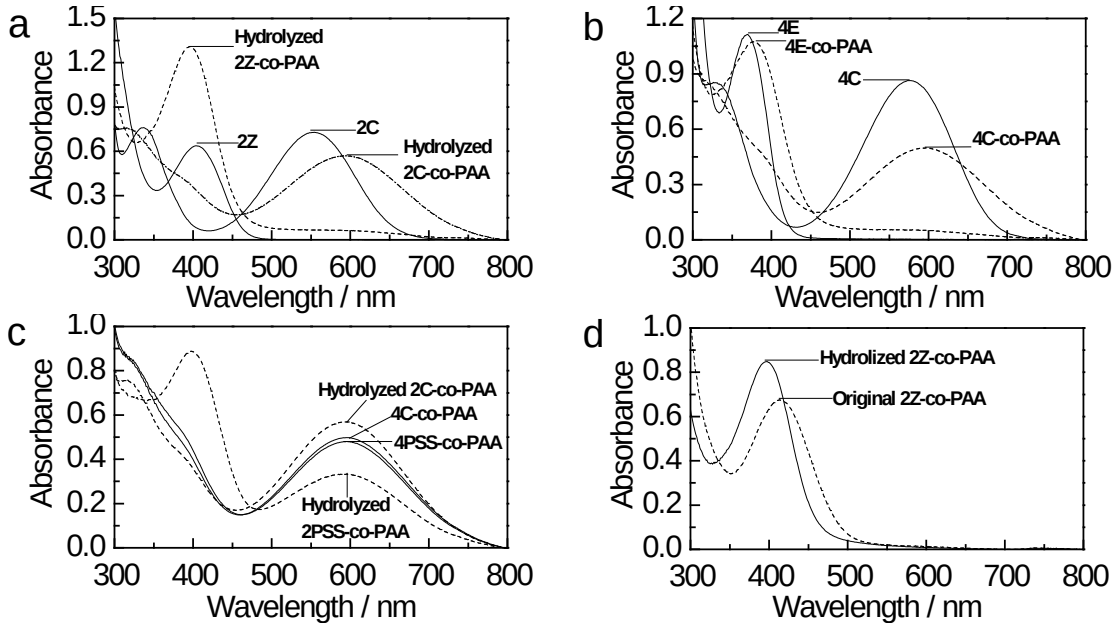


Figure 13. UV-Vis absorption spectra of fulgimide **2** and copolymers **2-co-PAA** and **4-co-PAA**: (a) fulgimide **2** in toluene (solid) and copolymer hydrolyzed **2-co-PAA** in 50 mM sodium acetate buffer (pH 5.0) (dashed); (b) fulgimide **4** in toluene (solid) and copolymer **4-co-PAA** in 50 mM sodium acetate buffer (pH 5.0) (dashed); (c) copolymers in initial closed forms and in PSS in 50 mM sodium acetate buffer (pH 5.0); (d) original **2Z-co-PAA** and hydrolyzed **2Z-co-PAA** in water.

The UV-Vis absorption spectra of fulgimides and copolymers in *C*-form, *E*-form and $PSS_{365nm\ (405\ nm)}$ were measured (Figure. 13(a), Table 7 Table 8). The longest wavelength absorption maxima (λ_{max}) of CF_3 fulgimide **2** is in the visible region for both the open and closed forms. After replacing the CF_3 group with a CH_3 group at the bridging position, a hypsochromic shift of 38 nm for *E*-form and a bathochromic shift of 20 nm for *C*-form were observed for CH_3 fulgimide **4** in toluene. The extinction coefficients were similar in both forms for fulgimides **2** and **4**. After polymerization, the resulting polymers displayed similar UV-Vis absorption patterns as their corresponding monomeric fulgimides. The λ_{max} of the copolymers in the aqueous solutions exhibited bathochromic shift relative to fulgimide**s** in toluene (Table 8, Figure 13a, and 13b).

A relatively low percentage of *C*-form in $PSS_{365\ nm}$ of **4** was observed in toluene (66%, Table 7). However, after polymerization, the copolymer in aqueous solution provided higher *C*-form

percentage (96%, Figure 13c). The conversion of open form to the closed form could be improved by increasing solvent polarity.[34] In contrast, the **hydrolyzed 2-co-PAA** only has 58% of *C*-form at PSS. The enhanced PSS will make the copolymer **4-co-PAA** more promising for practical applications.

Table 7. Extinction coefficients at λ_{max} for fulgimides in toluene

Compound (Medium)	λ_{max}/nm (ε_{max}/mol^{-1} L cm^{-1})		$PSS_{365\ nm\ (405\ nm)}$ [a]
	Z/E-form	*C*-form	*C*:*Z*:*E*
CF_3 fulgimide 2 (Toluene) [b]	405 (6.4×10^3)	554 (7.4×10^3)	93:4:3
CH_3 fulgimide 4 (Toluene)	367 (6.6×10^3)	574 (6.0×10^3)	66:12:22

[a]Photostationary state. [b]The data taken from ref.[27].

Figure 13d shows UV-Vis absorbance spectrum of original **2Z-co-PAA** (made directly from *Z*-from fulgimide **2**) was different from that of **hydrolyzed-2Z-co-PAA** (initially prepared from *C*-from fulgimide **2** followed by irradiation of **2C-co-PAA** with light). The **hydrolyzed-2Z-co-PAA** was hypsochromic shift of approx. 15 nm relative to the original **2Z-co-PAA** which is consistent with the water soluble fulgimides in previous report.[33] As expected, replacing the CF_3 group on the bridging position of fulgimide with CH_3 group increased stability of **4-co-PAA** in aqueous solutions, and there was no corresponding hydrolyzed form observed.

Table 8. λmax for copolymers hydrolyzed-2-co-PAA and 4-co-PAA in aqueous solutions

Copolymer (Medium)	λ_{max}/nm	
	Z/E-form (Original Z-from)	*C*-form
Hydrolyzed-2-co-PAA (Water)	398 (413)	596
Hydrolyzed-2-co-PAA (Phosphate buffer)	397 (412)	595
Hydrolyzed-2-co-PAA (Acetate buffer)	400 (414)	592
4-co-PAA (Water)	376	596
4-co-PAA (Phosphate buffer)	379	590
4-co-PAA (Acetate buffer)	377	596

5.4.3 Stability of fulgimides in toluene at 80 °C and Stability of copolymers in aqueous solutions at 37 °C

To be used as optical information storage media, biological sensors, or optical molecular switches, the stability of fulgimides and their copolymers is important. In this research, the stability of fulgimides and copolymers was studied in toluene at 80 °C and in the aqueous solutions at 37 °C, respectively. Decomposition rate constants of fulgimides and their copolymers are summarized in Table 9. For all compounds, the UV-Vis data were fit to a single exponential decay except **hydrolyzed 2-co-PAA** in acetate buffer which degraded in a sequential decomposition pathway. Double exponential fit was applied since a relatively rapid decomposition of <20% was observed followed by a slow decomposition. The reason of the initial drop in absorbance may be polymer reorganization. The rate constant for the slow decomposition was reported.

Table 9. Decomposition rate constants ($\times 10^3$, h^{-1}) of fulgimides at 80 °C and their copolymers at 37 °C.

Compound (Medium)	Decomposition rate ($\times 10^3$, h^{-1})	
	Open forms [a]	Closed forms [a]
2 (Toluene) [b]	18	< 0.05
4 (Toluene)	0	9.1
Hydrolyzed-**2-co-PAA** (Water)	1.8	15
Hydrolyzed-**2-co-PAA** (Acetate buffer)	2.0[c]	3.0
Hydrolyzed-**2-co-PAA** (Phosphate Buffer)	3.8	71
Original Z-from **2-co-PAA** (Acetate buffer)	5.6	-
Original Z-from **2-co-PAA** (Phosphate Buffer)	28	-
4-co-PAA (Water)	4.2	12
4-co-PAA (Acetate buffer)	1.1	3.0
4-co-PAA (Phosphate Buffer)	4.1	97

[a]Fit to a single exponential. [b]Data taken from ref. [27]. [c]Fit to a sequential decay.

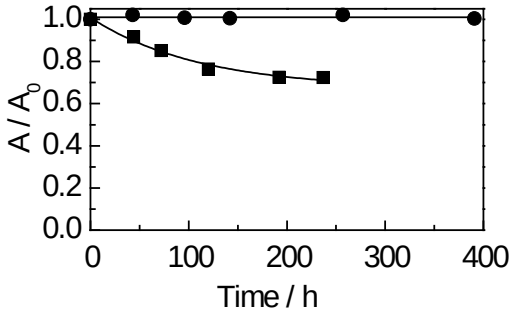


Figure 14. Thermal decomposition of fulgimide **4**: **4C** (■) and **4E** (●) in toluene at 80 ºC

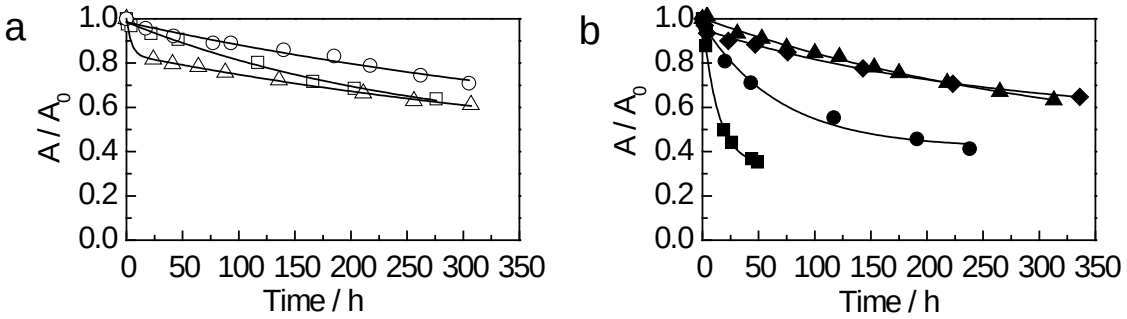


Figure 15. Decomposition of **hydrolyzed-2-co-PAA**: (a) *Z*-form in 50 mM phosphate buffer (pH 7.4) (□), in 50 mM sodium acetate buffer (pH 5.0) (Δ), and in water (○) at 37 °C; (b) *C*-form in water at 37 °C (●) and at 25 °C (♦), in 50 mM phosphate buffer (pH 7.4) (■), and in 50 mM sodium acetate buffer (pH 5.0) (▲) at 37 °C

In toluene at 80 °C, the *E*-form CH_3 fulgimide **4** was very stable and there was no degradation observed after about 391 h. The *C*-forms were less stable and degraded about 30% after 220 h (Figure 14). The UV-Vis data of *C*-form copolymers were fit to a single exponential decay, the decomposition products were assumed not to have absorbance at the λ_{max} of the *C*-forms. On the other hand, studies in Chapter 3 indicated that *C*-form CF_3 fulgimide **2** was more stable than the *Z*-form (open form) in toluene at 80 °C.

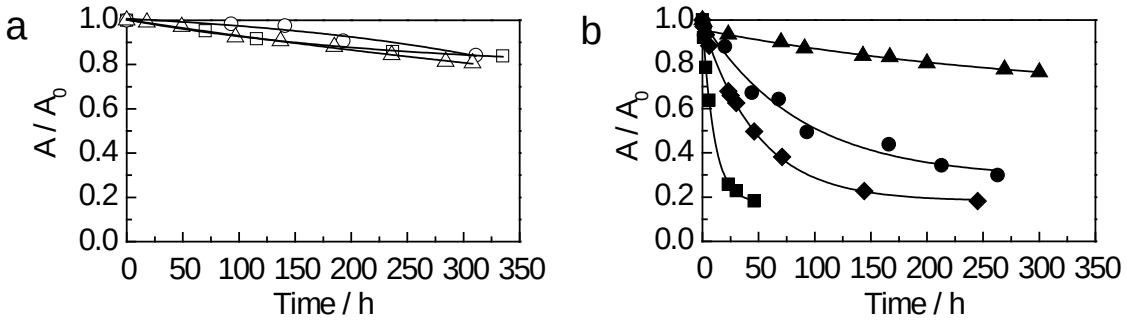


Figure 16. Decomposition of **4-co-PAA**: (a) *E*-form in 50 mM phosphate buffer (pH 7.4) (□), in 50 mM sodium acetate buffer (pH 5.0) (Δ), and in water (○) at 37 °C; (b) *C*-form in 50 mM phosphate buffer (pH 7.4) at 37 °C (■) and at 25 °C (♦), in 50 mM sodium acetate buffer (pH 5.0) (▲), and in water (●) at 37 °C

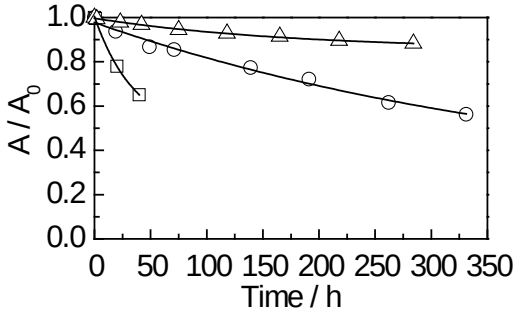


Figure 17. Decomposition of *Z*-form original **2-co-PAA**: in water at 25 °C (○), in 50 mM phosphate buffer (pH 7.4) (□), and in 50 mM sodium acetate buffer (pH 5.0) (Δ) at 37 °C

The stability of both forms of copolymers was measured in three different aqueous solutions, 50 mM sodium acetate buffer (pH 7.4), water, and 50 mM sodium acetate buffer (pH 5.0) (Figures 15 and 16). Stability of copolymers with fulgimide in closed form was affected by the pH of the aqueous solutions. **Hydrolyzed-2C-co-PAA** and **4C-co-PAA** exhibited enhanced stability in sodium acetate buffer (pH 5.0), however, a rapid degradation was observed in phosphate buffer (pH 7.4) (Figure 15b and 16b). For the open forms, **4E-co-PAA** exhibited better stability than **hydrolyzed-2-co-PAA**. Both **hydrolyzed-2Z-co-PAA** and **4E-co-PAA** displayed similar degradation patterns in the three different aqueous solutions, and the overall stability was better than that of their closed forms (Figure 15a and 16a). Moreover, the stability of the original **2Z-co-PAA** was also studied, and a better thermolysis resistance was observed in acid solution

than in neutral solution (Figure 17). In general, the copolymers in open forms were more stable than in closed forms. The copolymers were more stable in acidic solution than in neutral solution for both forms, possibly because the *N*-stryryl succinimide ring of the fulgimides hydrolyzed to the succinamic acid at lower rate in a lower pH solution.[85]

5.4.4 Photochemical stability

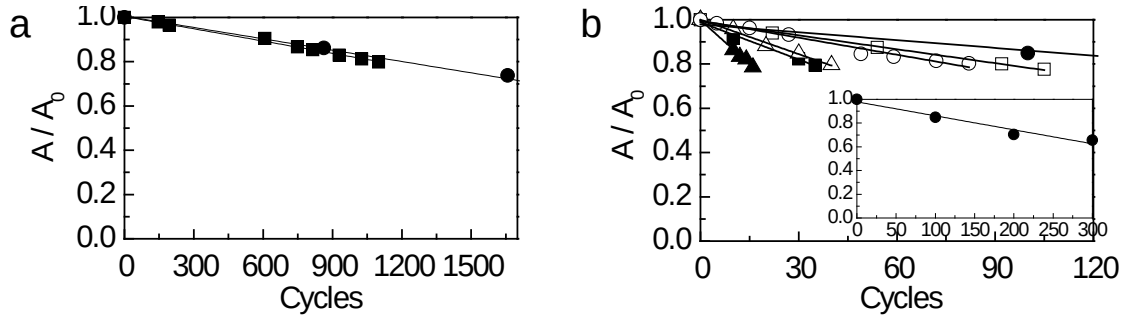


Figure 18. Photochemical decomposition of fulgimides and linear copolymers: (a) fulgimides **2** (●) and **4** (■) in toluene; (b) **hydrolyzed-2-co-PAA** in 50 mM phosphate buffer (pH 7.4) (■), in 50 mM sodium acetate buffer (pH 5) (▲), and in water (●); **4-co-PAA** in 50 mM phosphate buffer (pH 7.4) (□), in 50 mM sodium acetate buffer (pH 5) (Δ), and in water (○)

The photochemical stability of fulgimides and their copolymers were studied in toluene and aqueous solutions, respectively. The copolymer **2-co-PAA** was studied in its hydrolyzed form. In toluene, the CH_3 fulgimide **4** underwent 871 photochemical cycles before degrading by 20% (Figure 18a). The decomposition rate is 0.022% per cycle which is comparable with that of CF_3 fulgimide **2** (0.016% per cycle). Compared to their monomeric fulgimides in toluene, the copolymers exhibited faster decomposition rate in aqueous solutions, potentially because of longer cycling time (Table 10). The observation is consistent with previous studies which pointed out that fulgimides have relatively lower quantum yields (longer cycling times) in aqueous solutions.[31,33,34] The copolymers degraded at least twice as fast in the acid solution (acetate buffer) as in neutral solutions (phosphate buffer) (Figure 18b). Among the three aqueous solutions tested, the best solution for **hydrolyzed-2-co-PAA** was water and for **4-co-PAA** was phosphate buffer.

Both copolymers underwent close to 100 photochemical cycles before degrading 20%. One possible reason is that the photochromic reaction requires relatively shorter irradiation time.

Table 10. Photochemical fatigue resistance of fulgimides and their copolymers at room temperature

Compound (Medium)	Cycling time (s)		Photochemical decomposition		
	C-Z/E	Z/E-C	Cycles	A/A_0	% Per cycle
2 (Toluene) [a]	40	60	1660	0.74	0.016
4 (Toluene)	20	100	871	0.81	0.022
Hydrolyzed-**2-co-PAA** (Water)	720	120	200	0.70	0.15
Hydrolyzed-**2-co-PAA** (Acetate buffer)	1080	600	16	0.79	1.3
Hydrolyzed-**2-co-PAA** (Phosphate buffer)	1500	600	35	0.79	0.60
4-co-PAA (Water)	840	840	82	0.80	0.24
4-co-PAA (Acetate buffer)	720	720	40	0.80	0.51
4-co-PAA (Phosphate Buffer)	120	300	105	0.78	0.21

[a]The data taken from ref. [27].

5.5 Conclusion

I have successfully synthesized a new CH_3 fulgimide **4** with a pendant styrene group and two linear copolymers **2-co-PAA** and **4-co-PAA** containing CF_3 fulgimide **2** and CH_3 fulgimide **4**, respectively. All fulgimides and copolymers were found to be photochromic. In toluene at 80 °C, the *E*-form fulgimide **4E** showed very good stability with no decomposition after 392 h, but the *C*-form fulgimide **4C** was less stable and degraded 28% after 237 h. The linear copolymers **2-co-PAA** and **4-co-PAA** can be dissolved in aqueous solutions. The closed form **2C-co-PAA** was converted to the **hydrolyzed-2C-co-PAA** in aqueous solutions, and the resulting **hydrolyzed-2-co-PAA** was also photochromic. In general, both **hydrolyzed-2-co-PAA** and **4-co-PAA** were more stable in acidic solution. In the open form copolymers, **4E-co-PAA** exhibited better stability

than **hydrolyzed-2Z-co-PAA.** Both copolymers showed better stability in the open forms than in closed form. For the photochemical stability, fulgimide **4** degraded 0.022% per cycle in toluene and the copolymers underwent up to 100 photochemical cycles in aqueous solutions before degrading 20%. Ultimately, the linear copolymers showed better photochemical stability in neutral solution than in acidic solution but their stability was limited. In the acidic solution, the stability of copolymers was enhanced and their photochemical stability could be improved. Replacing the CF_3 group on the bridging position of fulgimide with CH_3 group increased the stability of copolymer **4-co-PAA** in aqueous solutions.

6. SYNTHESIS AND CHARACTERIZATION OF INDOLYLFULGIMIDE CO-PAA HYDROGELS

6.1 Abstract

Hydrogels using photochromic indolylfulgimides as cross-linkers have great potential for applications in the modulation of biological systems. A new CH_3 indolylfulgimide **5** with two polymerizable styrene groups on the nitrogen atoms was synthesized. Copolymerization of the CH_3 indolylfulgimide **5** and CF_3 indolylfulgimide **3** with acrylamide provided cross-linked copolymers **5-co-PAA** and **3-co-PAA**, respectively. The resulting **5-co-PAA** and **3-co-PAA** were found to be photochromic hydrogels, which were compatible with water. The CH_3 indolylfulgimide **5** was characterized in toluene. The open form CH_3 fulgimide **5E** exhibited excellent thermal stability, and there was no degradation after 350 h at 80 °C. The *C*-form was less stable, which degraded 30% after 220 h. Also, the fulgimide **5** displayed good photochemical stability in toluene, only decomposing 0.018% per cycle. The copolymers were studied in three different aqueous solutions: a sodium acetate buffer (pH 5.0), water, and a sodium phosphate buffer (pH 7.4). Copolymer **3-co-PAA** in the closed form was rapidly hydrolyzed in aqueous solution to provide photochromic **hydrolyzed 3C-co-PAA**. Replacing the CF_3 group on the bridging position of fulgimide with CH_3 group increased the stability of **5-co-PAA** in aqueous solutions. In general, both **hydrolyzed 3-co-PAA** and **5-co-PAA** exhibited enhanced stability at 37 °C in acidic solution than in neutral solution. And **5-co-PAA** was more stable than **hydrolyzed 3-co-PAA**. All copolymers displayed enhanced photochemical stability in acidic conditions and underwent 60 cycles of photochromic reactions before degrading 24%.

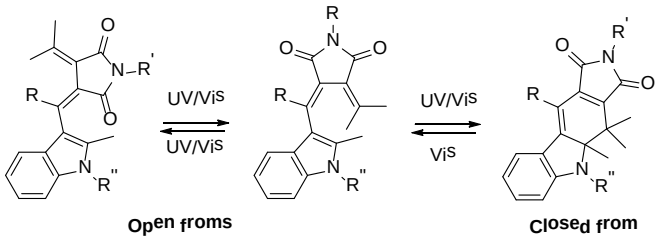
6.2 Introduction

Hydrogels are highly-hydrated three dimensional cross-linked polymer networks. Stimuli-responsive ‘‘smart’’ hydrogels able to respond to external stimuli, such as light-irradiation or changes in pH value, temperature, ionic strength, etc. are promising materials suitable for

numerous applications.[55,86] Compare to other stimuli, the light stimulus can be imposed instantly and precisely. The light-responsive hydrogels containing photochromic compounds with photoinduced conformational change have great potential for applications in biological systems, such as enzyme immobilization and controlled drug release.[54]

Many studies on synthesis of novel light-responsive hydrogel systems have been reported. For example, Willner et al. synthesized a series of hydrogels by radical copolymerization of acrylamide, *N*,*N*'-methylenebis(acrylamide) (as a cross-linker), and a photochromic compound, such as azobenzene, spiropyran, or triphenylmethane leucohydroxide derived monomer.[74,87] The cross-linked copolymers were tested for immobilization of α-chymotrypsin by embedding the enzyme into the polymer matrix. The activity of the enzyme can be photo-control because the permeability of the copolymers to the substrate was altered as the structures of the photochromic compounds changed with light. Peng et al. synthesized a hemicellulose-based light-responsive hydrogel containing photochromic azobenzene and the hydrogel under UV irradiation showed higher cumulative release rate of vitamin B12 than that without UV irradiation.[56]

Scheme 32. Photochromism of 3-indolylfulgimides



Among photochromic compounds, 3-indolylfulgimides are promising because of their enhanced photochromic properties, such as enhanced thermal stability, increased photochemical stability (fatigue resistance), highly efficient photoreactions, large molar absorption coefficients and hydrolytic stability.[22,27,35,39,81] The photochromism of methyl and trifluoromethyl-3-

indolylfulgimides was shown in Scheme 32, where the fulgimides can be converted between the open forms and the closed form reversibly by light.

Compared to the hydrogels containing a photochromic compound as a pendant, I expect that the hydrogels with photochromic fulgimides as cross-linkers will be more efficient because of the enhanced conformation changes. UV-Vis absorption, stability in aqueous solutions, and fatigue resistance are essential to the development of advanced materials for applications in biological systems. Therefore, the properties of the light-responsive hydrogels also need to be characterized.

Herein, a CF_3 indolylfulgimide and CH_3 indolylfulgimide with doubly substituent styrene groups were synthesized. The fulgimides were then copolymerized with acrylamide to prepare two photochromic hydrogels. The photochromic properties of fulgimides were measured in toluene, and their copolymers were studied in three different aqueous solutions: water, 50 mM sodium phosphate buffer (pH 7.4), and 50 mM sodium acetate buffer (pH 5.0).

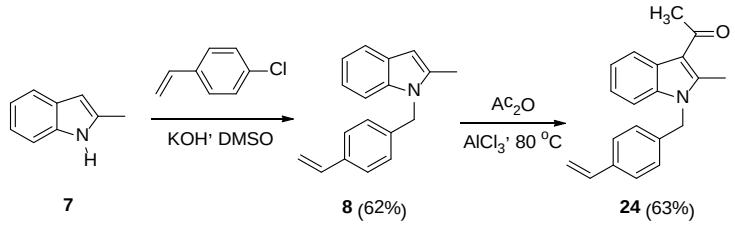
6.3 Experimental section

6.3.1 General procedures and materials

All commercially available materials were used without purification. The NMR spectra were recorded on a Brücker 400 MHz NMR spectrometer. The ^{1}H and ^{13}C NMR samples were internally referenced to TMS. The UV-Vis spectra were recorded with a Cary 300 spectrophotometer. The HRMS were obtained at the University of Florida. Flash chromatography was performed with 230-400 mesh silica gel. Illumination was provided by a 1000 W Hg (Xe) arc lamp and first pass through a water filter, then a hot mirror, and lastly, either a band pass filter (365 nm (for CH_3 fulgimide)/405 nm (for CF_3 fulgimides)) or a cutoff filter (> 515 nm).

6.3.2 Synthesis of methyl distyrene fulgimide

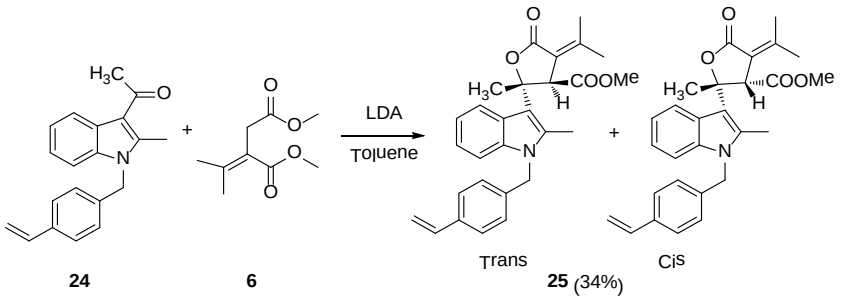
6.3.2.1 Synthesis of 2-Methyl-1-(4-vinylbenzyl)-3-acetylindole



7 **8** (62%) **24** (63%)

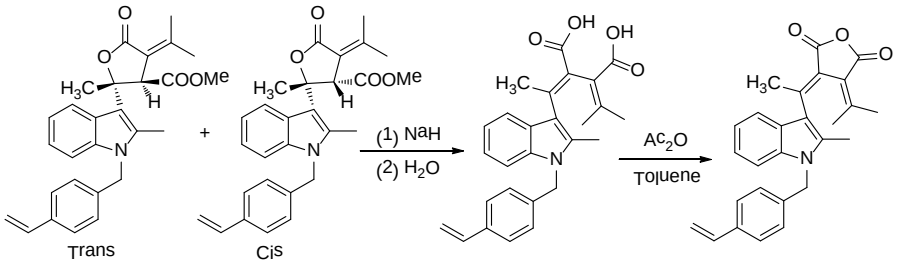
2-Methyl-1-(4-vinylbenzyl)indole **8** (8.00 g, 32.3 mmol) was synthesized as described in chapter 4. The indole **8** was then dissolved in acetic anhydride (120 mL, 1.27 mol). Anhydrous aluminium chloride (0.60 g, 4.5 mmol) was added to the solution, and then the reaction mixture was heated to 80 °C and stirred for 3 d. The mixture was concentrated in vacuo, and the residue was quenched with a saturated $NaHCO_3$ solution (200 mL) and then extracted with methylene chloride (3 × 100 mL). The combined organic layers were then dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography (1:2 hexanes/EtOAc) and followed by recrystallization from hexanes/EtOAc to provide 5.93 g of 2-methyl-1-(4-vinylbenzyl)-3-acetylindole **24** (63%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.02 (d, *J* = 8.3 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.29-7.27 (m, 2H), 7.23-7.19 (m, 1H), 6.94 (d, *J* = 8.2 Hz, 2H), 6.66 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.70 (dd, *J* = 17.5, 0.8 Hz, 1H), 5.37 (s, 2H), 5.23 (dd, *J* = 10.8, 0.6 Hz, 1H), 2.74 (s, 3H), 2.72 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.8, 144.8, 137.3, 136.5, 136.1, 135.6, 126.8, 126.5, 126.2, 122.3, 122.1, 120.8, 114.8, 114.4, 110.0, 46.2, 31.8, 12.7. $C_{20}H_{19}NO$ HRMS (ESI) *m/z*: 290.1553 [obtained M + H]$^+$, 290.1539 [calculated M + H]$^+$, 312.1370 [obtained M + Na]$^+$, 312.1359 [calculated M + Na]$^+$.

6.3.2.2 Synthesis of styrene methyl fulgide 12



24 **6** **25** (34%)

Dimethyl isopropylidenesuccinate **6** (16.0 g, 74.1 mmol) was dissolved in 150 mL of dry toluene under argon. The solution was cooled to -78 °C and lithium diisopropylamide (LDA) (50 mL of 1.5 M solution in cyclohexane, 75 mmol) was added dropwise via an addition funnel. Then the mixture was stirred for 30 min and warmed to 0 °C. A solution of 2-methyl-1-(4-vinylbenzyl)-3-acetylindole **24** (5.0 g 17.3 mmol) in 50 mL of toluene was added into the mixture of dimethyl isopropylidenesuccinate/LDA/toluene dropwise via an addition funnel. The reaction mixture was warmed to room temperature and stirred under argon for 3 d. Then the mixture was quenched with 300 mL of 5% H_2SO_4, and the aqueous layer was extracted with diethyl ether (3 × 200 mL). The combined organic layers were washed with water (3 × 100 mL). Then the organic phase was dried over $MgSO_4$ and concentrated in vacuo. The crude lactone was purified by column chromatography (1:2 diethyl ether/hexanes) and recrystallized from diethyl ether/hexanes to provide a mixture of cis/trans indolelactones **25** (2.6 g) in 34% yield.



25 **26** **27** (12% from **24**)

The mixture of cis/trans indolelactones **25** (2.0 g) was dissolved in 150 mL of DMF, and then sodium hydride (60% dispersion in oil, 0.51 g, 12.8 mmol) was added and the reaction was

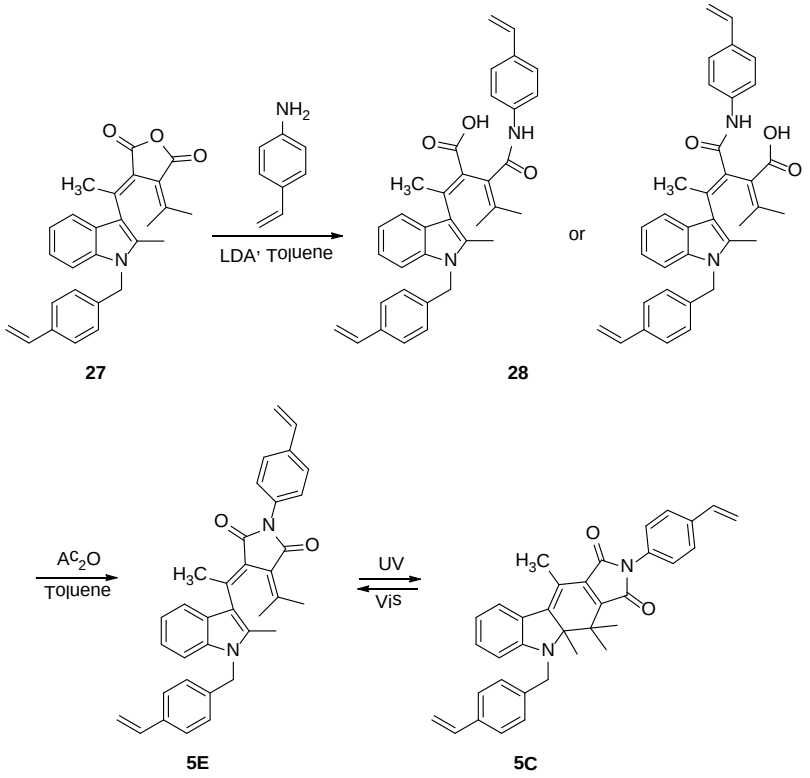
cooled to -78 °C. The reaction mixture was allowed to warm to room temperature and then stirred for 1.5 h. To the mixture, water (2.0 mL, 110 mmol) was added. The mixture was stirred for 12 h and then concentrated in vacuo. The residue was quenched with 0.1 M NaOH (100 mL) and extracted with EtOAc (100 mL). The aqueous layer was acidified with conc. H_2SO_4 to pH 2. Then the aqueous phase was extracted with EtOAc (3 × 100 mL). The organic phase was dried over $MgSO_4$ and concentrated in vacuo to provide crude diacid intermediate **26**. The crude diacid was then dissolved in 50 mL of acetic anhydride. The mixture was heated to reflux and stirred for 2 h. After concentrating in vacuo, the residue was mixed with 50 mL of water and extracted with methylene chloride (3 × 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo to provide crude fulgide. The crude fulgide was purified by column chromatography (1:1 methylene chloride/hexanes) and recrystallized from methylene chloride /hexanes to afford yellow crystals **27** (0.66 g, 12% from **24**). *E*-form fulgide: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.44 (d, *J* = 7.8 Hz, 1H), 7.34-7.30 (m, 3H), 7.22 (td, *J* = 7.7, 1.3 Hz, 1H), 7.17 (td, *J* = 7.8, 1.2 Hz, 1H), 6.98 (d, *J* = 8.1 Hz, 2H), 6.67 (dd, *J* = 17.5, 10.9 Hz, 1H), 5.71 (d, *J* = 17.5 Hz, 1H), 5.34 (d, *J* = 16.8 Hz, 1H), 5.25 (d, *J* = 11.3 Hz, 1H), 5.24 (d, *J* = 16.0 Hz, 1H), 2.82 (s, 3H), 2.13 (s, 3H), 2.11 (s, 3H), 0.95 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 164.0, 163.7, 153.3, 149.3, 137.4, 137.0, 136.1, 136.0, 134.8, 126.7, 126.5, 125.1, 122.4, 121.5, 121.0, 119.7, 119.6, 117.3, 114.5, 109.7, 46.8, 26.4, 23.6, 22.5, 12.4. $C_{27}H_{25}NO_3$ HRMS (ESI) *m/z*: 412.1916 [obtained M + H]$^+$, 412.1907 [calculated M + H]$^+$, 434.1732 [obtained M + Na]$^+$, 434.1727 [calculated M + Na]$^+$.

6.3.2.3 Synthesis of methyl distyrene fulgimide 5

To a solution of 4-vinylaniline (0.47 g, 3.9 mmol) in 50 mL of dry toluene, LDA (5.0 mL of 1.5 M solution in cyclohexane, 7.5 mmol) was added dropwise. The mixture was stirred for 5 min, and then methyl styrene fulgide **27** (0.23 g, 0.56 mmol) was added. The mixture was stirred under argon at room temperature. After 12 h, the solution was concentrated, and the residue was treated with 50 mL of 10% H_2SO_4. The aqueous layer was extracted with EtOAc (3 × 50 mL). The

combined organic layers were washed with brine (100 mL), dried over $MgSO_4$, and concentrated in vacuo to provide crude amide acid intermediate **28**. 4-Dimethylaminopyridine (DMAP 2 mg) was added to the solution of amide acid, which was dissolved in 50 mL of acetic anhydride. The mixture was heated to 50 °C and stirred for 12 h. The solution was then concentrated in vacuo. The residue was extracted with a saturated aqueous solution of $NaHCO_3$ (50 mL) and methylene chloride (3 × 50 mL). The combined organic layers were washed with brine (100 mL), dried over $MgSO_4$, and concentrated in vacuo. The organic residue was then dissolved in 100 mL of toluene and illuminated with 365 nm light to reach the photostationary state (PSS). The *C*-form was purified by column chromatography (1:1 methylene chloride /hexanes) and recrystallized from methylene chloride/hexanes to provide 0.072 g of *C*-form fulgimide **5** (25% from fulgide). *C*-form: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67 (d, *J* = 7.5 Hz, 1H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.17 (td, *J* = 7.8, 1.1 Hz, 1H), 6.83 (td, *J* = 7.6, 0.9 Hz, 1H), 6.73 (dd, *J* = 17.5, 11.0 Hz, 2H), 6.42 (d, *J* = 8.2 Hz, 1H), 5.76 (d, *J* = 17.6 Hz, 2H), 5.28 (d, *J* = 11.1 Hz, 1H), 5.25 (d, *J* = 11.1 Hz, 1H), 4.65 (d, 17.6 Hz, 1H), 4.19 (d, *J* = 17.6 Hz, 1H), 2.51 (s, 3H), 1.62 (s, 3H), 1.44 (s, 3H), 1.23 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.8, 168.2, 158.0, 150.6, 138.1, 137.6, 137.2, 136.6, 136.5, 136.4, 136.1, 131.7, 131.3, 126.9, 126.6, 126.1, 126.2, 125.9, 124.9, 119.0, 115.5, 114.5, 113.8, 109.6, 73.8, 50.7, 40.5, 20.5, 18.4, 16.7, 13.8. $C_{35}H_{32}N_2O_2$ HRMS (ESI) *m/z*: 513.2525 [obtained M + H]$^+$, 513.2537 [calculated M + H]$^+$, 535.2346 [obtained M + Na]$^+$, 535.2356 [calculated M + Na]$^+$. The *E*-form was prepared quantitatively by illuminating the *C*-form in toluene with visible light>515 nm. *E*-form: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53 – 7.50 (m, 3H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.34-7.30 (m, 3H), 7.22-7.15 (m, 2H), 6.99 (d, *J* = 8.1 Hz, 2H), 6.75 (dd, *J* = 17.6, 10.9 Hz, 1H), 6.69 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.78 (d, *J* = 17.6 Hz, 1H), 5.71 (d, *J* = 17.6 Hz, 1H), 5.34 (d, *J* = 16.8 Hz, 1H), 5.29 (d, *J* = 11.1 Hz, 1H), 5.25 (d, *J* = 16.4 Hz, 1H), 5.24 (d, *J* = 11.2 Hz, 1H), 2.84 (s, 3H), 2.15 (s, 3H), 2.12 (s, 3H), 1.00 (s,3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.0, 167.6, 148.6, 144.6,

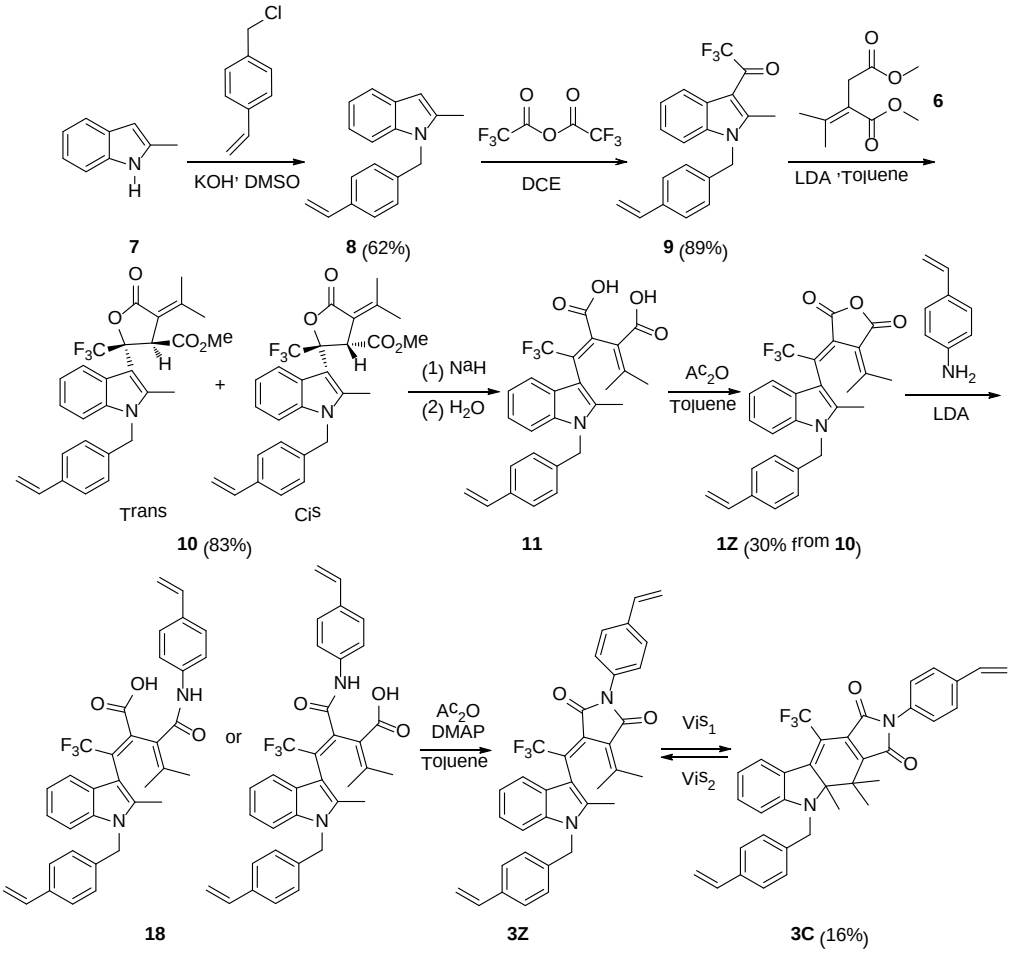
137.2, 137.2, 137.0, 136.5, 136.2, 136.1, 133.9, 131.6, 127.0, 126.7, 126.6, 126.5, 125.6, 123.7, 123.0, 122.0, 120.6, 119.8, 117.8, 114.7, 114.4, 109.4, 46.7, 26.6, 22.9, 22.0, 12.3. $C_{35}H_{32}N_2O_2$ HRMS (ESI) *m/z*: 513.2525 [obtained M + H]$^+$, 513.2537 [calculated M + H]$^+$. 535.2339 [obtained M + Na]$^+$, 535.2346 [calculated M + Na]$^+$.



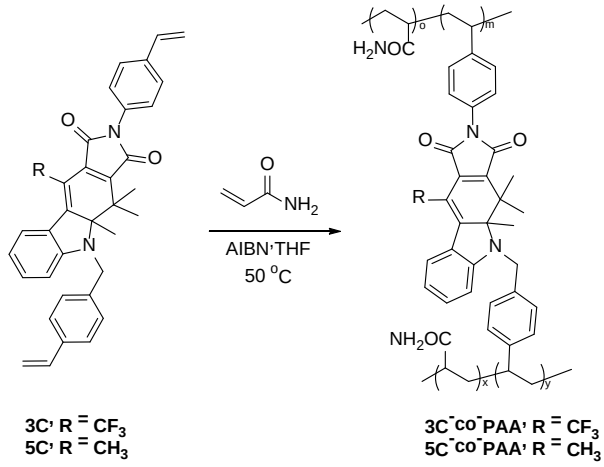
6.3.2.4 Synthesis of trifluoromethyl distyrene fulgimide 3

Trifluoromethyl styrene indolylfulgimide **3** was synthesized followin the procedure described in Chapter **4** (Scheme 33). First, the trifluoromethyl 3-indolylfulgide **1Z** was prepared as a precursor in five steps from 2-methyl indole. Then fulgimide **3Z** was obtained by adding 4-vinylaniline to the succinate anhydride ring of fulgide **1Z**, followed by dehydration in acetic anhydride.

Scheme 33. Synthesis of trifluoromethyl distyrene fulgimide 5



6.3.3 Synthesis of cross-linked PAA copolymer gel



The monomer, fulgimides **3C** or **5C** (2.26 mg, 0.004 mmol), was dissolved in 2 mL of DMSO. Acrylamide (284 mg, 3.99 mmol) and azobisisobutyronitrile, AIBN (1 wt% of PAA) were added to the solution. The mixture was stirred until all solids were dissolved. The solution was transferred to a resealable glass ampule. The ampule was sealed under vacuum and kept at 50 °C. After 48 h, a blue polymeric gel was formed. The polymeric gel was suspended in water and transferred to a dialysis bag (M.W. cutoff: 6000-8000). Dialysis was performed four times against 3.5 L of H_2O each time. The copolymer solution was dried under vacuo to provide the *C*-form cross-linked polymers.

6.3.4 Spectra determination for fulgimide 5 in toluene

From a concentrated stock solution of CH_3 fulgimides **5C** in toluene, five solutions with concentrations between 0.05 and 0.20 mM were obtained by dilution with toluene. The UV-Vis spectra of these diluted solutions with different known concentrations of fulgimide were obtained. After λ_{max} was determined, the concentration vs. absorbance at λ_{max} was plotted, and the extinction coefficient was calculated. Each *C*-form solution was then quantitatively converted to the *E*-form with >515 nm light. The UV-Vis spectra of the *E*-form solutions were measured, and the extinction coefficients and λ_{max} of **5E** were determined.

6.3.5 Photostationary state (PSS) measurements

The fulgimide **5C** in toluene-d8 was illuminated with >515 nm light to form **5E**, and then the **5E** was converted back with prolonged illumination of 365 nm light until a constant Z/E/C ratio was obtained. The reaction was monitored via ^{1}H NMR spectroscopy.

6.3.6 Stability of fulgimide in toluene at 80 °C and stability of copolymers in aqueous solutions at 37 °C

The thermal stability of *C/E* forms of CH_3 fulgimides **5**, and copolymers **3-co-PAA and 5-co-PAA** were measured using UV-Vis spectroscopy. A solution of fulgimides **5** in toluene were transferred into several ampoules. The ampoules were then sealed and incubated in a water bath

maintained at 80 °C. At predetermined times, ampoules were removed, and their contents analyzed by UV-Vis spectroscopy. The swollen cross-linked hydrogels **3-co-PAA** and **5-co**-PAA, which absorbed the aqueous solutions, were placed between two 2.54 cm diameter circular glass slides with a 2 mm plastic spacer. The glass slides were fixed in an optical mount and wrapped in aluminum foil. Then the hydrogels were maintained at 37 °C and analyzed by UV-Vis spectroscopy at predetermined times.

6.3.7 Photochemical stability

Solution of closed form fulgimide in toluene and copolymers in aqueous solutions (50 mM sodium phosphate buffer (pH 7.4), 50 mM sodium acetate buffer (pH 5.0), and water) were quantitatively converted to solutions of open form by irradiating with visible light >515 nm. The open form solutions were converted to the photostationary state (PSS) with prolonged irradiation of 365 nm light for **5** and **5-co-PAA** and 405 nm light for **3** and **hydrolyzed 3-co-PAA**. A UV-Vis spectrum was acquired and the absorbance at λ_{max} in the visible region was determined. The time taken to achieve 90% of the absorbance at λ_{max} of $PSS_{365\ nm\ (405\ nm)}$ was then recorded. Then, the solutions of $PSS_{365\ nm\ (405\ nm)}$ were irradiated with visible light >515 nm again until the *C*-form solutions were < 1% in absorbance at λ_{max} of the *C*-form, and the reaction time was measured. Once the duration of the irradiation reactions was established, the solutions were converted back and forth with an automated filter switch. After a designated number of irradiation cycles, the sample was fully converted to $PSS_{365\ nm\ (405\ nm)}$ with prolonged irradiation and the UV-Vis spectrum was scanned. The photochemical stability was determined by comparison with the absorbance at the λ_{max} of the *C*-form obtained from the initial $PSS_{365\ nm(405\ nm)}$ absorption spectrum.

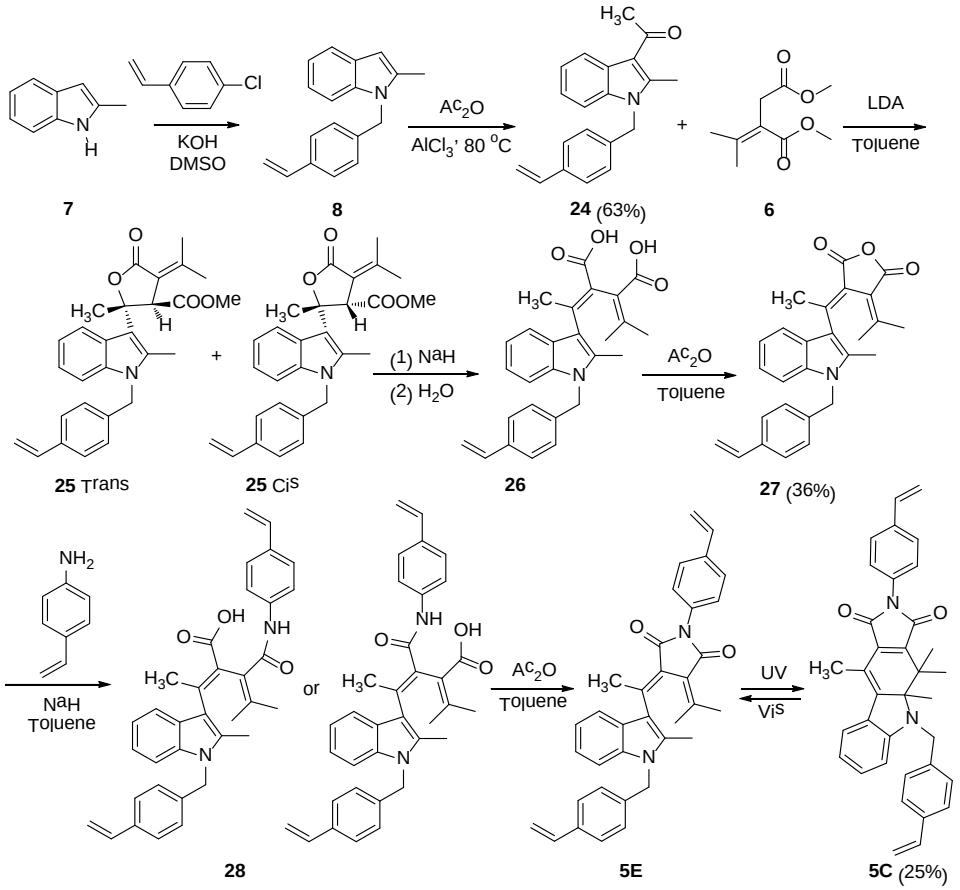
6.4 Results and discussion

6.4.1 Synthesis

A new CH_3 indolylfulgimide **5** with a double polymerizable styrene groups on both nitrogens was synthesized. The fulgimide was prepared by reacting the corresponding fulgide with 4-

vinylaniline and followed by dehydration in acetic anhydride (Scheme 34). The preparation of the fulgide involved a series of precursors. The most important intermediates are the indolelactones, which were synthesized by a Stobbe condensation of the corresponding indole-3-carboxaldehydes and dimethyl isopropylidenesuccinate.

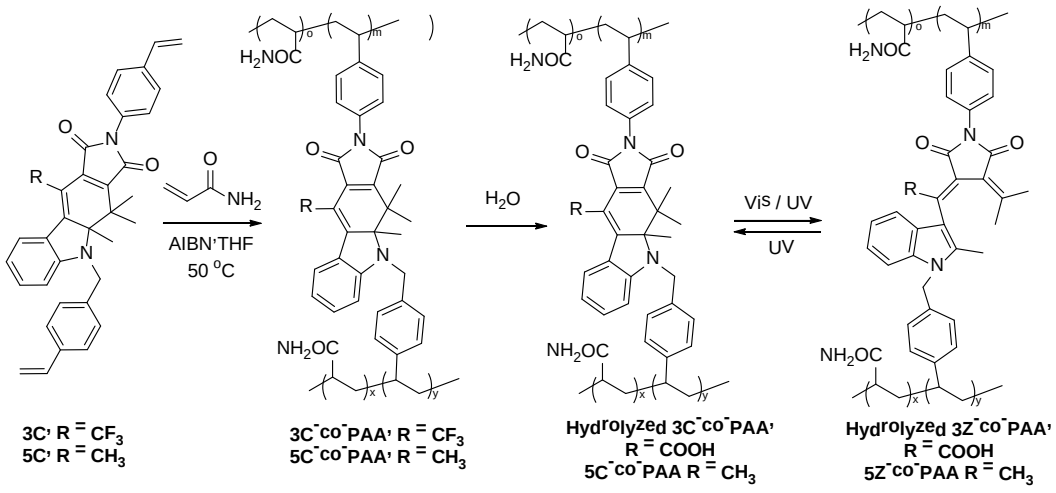
Scheme 34. Synthesis of trifluoromethyl distyrene fulgimide 5



Two cross-linked copolymers (**3-co-PAA** and **5-co-PAA**) were prepared from the corresponding fulgimides and acrylamide via free-radical polymerization with AIBN as the initiator. The ratio of monomers (fulgimide to acrylamide) was selected to ensure that the copolymers were suitable for UV-Vis measurements (absorbance approx. 1). The copolymers were found to be photochromic hydrogels. The dried hydrogels were rigid and glassy and became swollen and soft after absorbing aqueous solutions. The closed form copolymers were prepared

from closed form fulgimides, and the open form copolymers were made by irradiation of the corresponding closed form copolymers with light. Similar with linear copolymer **2C-co-PAA** in Chapter 5, the closed form copolymer **3C-co-PAA** hydrolyzed in aqueous solution, probably because the CF_3 fulgimide were rapidly converted to a carboxylic acid fulgimide in aqueous solutions as described in a previous report.[33] The resulting hydrolyzed copolymers were also photochromic. The thermal and photochemical stabilities of hydrolyzed **3-co-PAA** were studied (**Error! Not a valid bookmark self-reference.**).

Scheme 35.Synthesis of cross-linked copolymers 3-co-PAA and 5-co-PAA



6.4.2 UV-Vis absorption spectra

The UV-Vis absorption spectra of fulgimides in tolunene and their copolymer in aqueous solutions were measured (Figure. 19, Table 11 and Table 12). The wavelengths of the absorbance maxima (λ_{max}) and the extinction coefficients at λ_{max} of fulgimides are shown in Table 11. Compared to CF_3 fulgimide, the CH_3 fulgimide **5** exhibited a hypsochromic shift of 35 nm for the *E*-form and a bathochromic shift of 24 nm for the *C*-form at λ_{max} by replacing the CF_3 group with a CH_3 group on the bridging position. The extinction coefficients were same for in both fulgimides in the open forms. For the closed forms, the CH_3 fulgimide **5C** showed decreased extinction coefficient relavtive to the CF_3 fulgimide **3C**. After polymerzation, the copolymer retained the

photochromic properties of the monomer and displayed similar UV-Vis spectra (Figure 19a and 19b). The λ_{max}s of the copolymers in aqueous solutions were shifted to longer wavelengths. The PSS of the CH_3 fulgimide **5** at 365 nm contained a low percentage of *C*-form (66%) (Table 11). However, after polymerization, the copolymer **5-co-PAA** in aqueous solution provided higher *C*-form percentage (92%) at PSS (Figure 19c). The conversion of the open form to the closed form could be improved by increasing the solvent polarity because of enhanced ratio of quantum yields (***ΦE-C*/*ΦC-E***). The result is consistent with previous reports.[31,34,43] The enhanced PSS will make the copolymer more promising for practical applications.

Table 11. Extinction coefficients at λ_{max} for fulgimides in toluene

Compound (Medium)	λ_{max}/nm (ε_{max}/mol^{-1} L cm^{-1})		PSS$_{365\ nm\ (405\ nm)}$ [a]
	Z/E-form	*C*-form	*C*:*Z*:*E*
Fulgimide **3** (Toluene) [b]	401 (6.3×10^3)	537 (8.1×10^3)	95:4:1
Fulgimide **5** (Toluene)	366 (6.3×10^3)	561 (5.0×10^3)	64:16:20

[a]Photostationary state. [b]The data taken from ref.[27]

The copolymer prepared from *C*-from CF_3 fulgimide **3** followed by irradiation to *Z*-form exhibited different absorption maximum with the **3Z-co-PAA** made from *Z*-from CF_3 fulgimide 3 directly (Figure 19d). The reason is that the copolymer **3-co-PAA** in closed form, **3C-co-PAA**, was rapidly hydrolyzed in aqueous solution to provide **hydrolyzed 3C-co-PAA**. The resulting **hydrolyzed 3C-co-PAA** was also photochromic and can be converted to **hydrolyzed 3Z-co-PAA** with light. However, the original **3Z-co-PAA** was relatively stable and was not directly converted to **hydrolyzed 3Z-co-PAA** in aqueous solutions. **Hydrolyzed 3Z-co-PAA** can be obtained by illuminating the original **3Z-co-PAA** to the closed form followed by irradiation back to the open form. The **hydrolyzed 3Z-co-PAA** exhibited a hypsochromic shift of 8 nm relative to the original **3Z-co-PAA**, which is less compared to the water soluble fulgimides in a previous report.[33] As ex**p**ected, replacing the CF_3 group on the bridging position of fulgimide with a CH_3

group increased stability of **5-co-PAA** in aqueous solutions, and there was no corresponding hydrolyzed form observed.

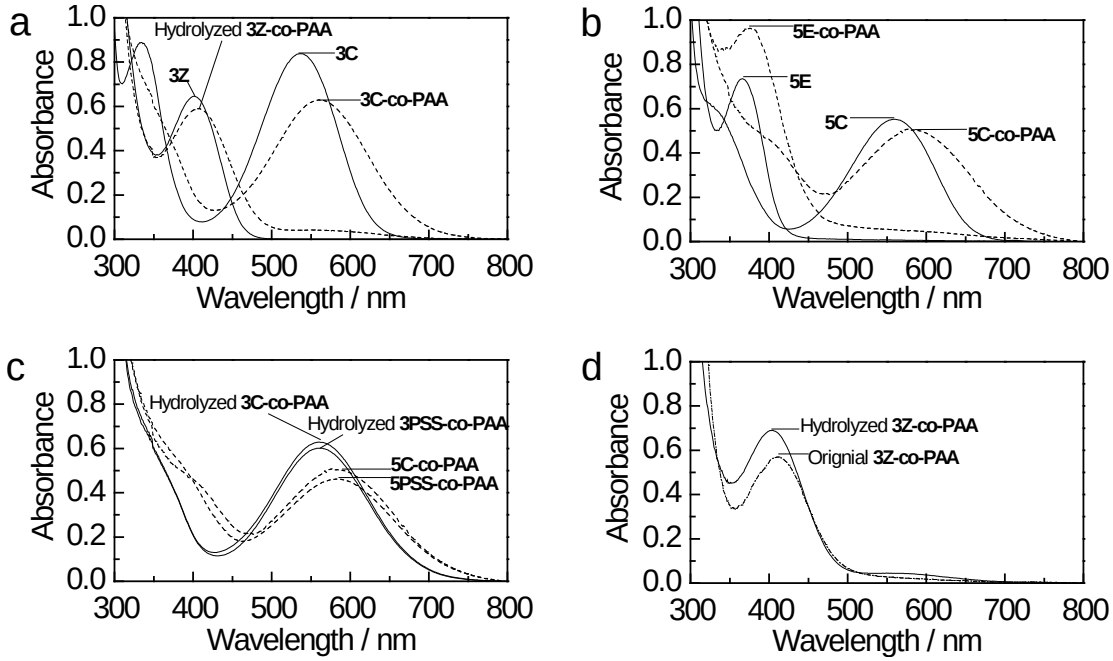


Figure 19. UV-Vis absorption spectra of fulgimide **3** and **5** and cross-linked copolymers: (a) fulgimide **3** in toluene (solid) and copolymer **hydrolyzed-3-co-PAA** in 50 mM sodium acetate buffer (pH 5.0) (dashed); (b) fulgimide **5** in toluene (solid) and copolymer **5-co-PAA** in 50 mM sodium acetate buffer (pH 5.0) (dashed); (c) copolymers in initial closed forms and in PSS in 50 mM sodium acetate buffer (pH 5.0); (d) original **3Z-co-PAA** and hydrolyzed **3Z-co-PAA** in 50 mM sodium acetate buffer (pH 5.0)

Table 12. λ_{max} for copolymers in aqueous solutions

Copolymer (Medium)	λ_{max}/nm	
	Z/E-form (Original Z-from)	*C*-form
Hydrolyzed 3-co-paa (Water)	403(411)	559
Hydrolyzed 3-co-paa (Phosphate buffer)	403 (411)	559
Hydrolyzed 3-co-paa (Acetate buffer)	405 (412)	560
5-co-paa (Water)	379	584
5-co-paa (Phosphate buffer)	379	586
5-co-paa (Acetate buffer)	374	585

6.4.3 Stability of fulgimides in toluene at 80 °C and Stability of copolymers in aqueous solutions at 37 °C

The stability of fulgimides and their copolymers is important for their practical application as optical information storage media, biological sensors, or optical molecular switches in biological system. The stability of fulgimides and copolymers was studied in toluene at 80 °C and in aqueous solutions at 37 °C, respectively. Decomposition rate constants of fulgimides and their copolymers are summarized in Table 13. For all compounds, the UV-Vis data were fit to a single exponential decay or a sequential decomposition pathway. Double exponential fit was applied for **hydrolyzed 3-co-PAA** in water and acetate buffer, because of a relatively rapid decomposition of <30% was observed followed by a slow decomposition. The possible reason of the initial drop in absorbance is polymer reorganization. The rate constant for the slow decomposition was reported.

For the CH_3 fulgimide **5**, the *E*-form copolymers were very stable, and there was no degradation after 350 h in toluene. The *C*-forms were less stable and degraded 30% after 220 h (Figure. 20). The UV-Vis data of *C*-form copolymers were fitted to a single exponential decay. The decomposition products were assumed not to have absorbance at the λ_{max} of the *C*-forms. On the other hand, CF_3 fulgimide **3** has opposite characteristics where the *Z/E*-forms were less stable than the *C*-form on the basis of previous report.[27]

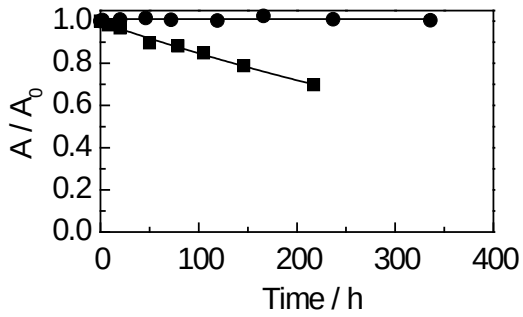


Figure 20. Thermal decomposition of CH_3 fulgimide **5**: **5C** (■) and **5E** (●) in toluene at 80 ºC

The stability of both forms of copolymers was measured in three different aqueous solutions, 50 mM sodium acetate buffer (pH 7.4), water, and 50 mM sodium acetate buffer (pH 5.0). The

pH of aqueous solutions affected the stability of copolymers at 37 °C. The copolymers in acidic solution (pH 5.0) exhibited enhanced stability than in neutral solution (Figure. 21). Probably because the hydrolysis rate of *N*-stryryl succinimide ring of the fulgimides to a succinamic acid is decreased in a lower pH solution.[85] In general, copolymers in open forms were more stable than in closed forms, and copolymer **5-co-PAA** displayed better stability than the **hydrolyzed 3-co-PAA**. The enhanced stability makes the **5-co-PAA** more promising for applications in acidic conditions.

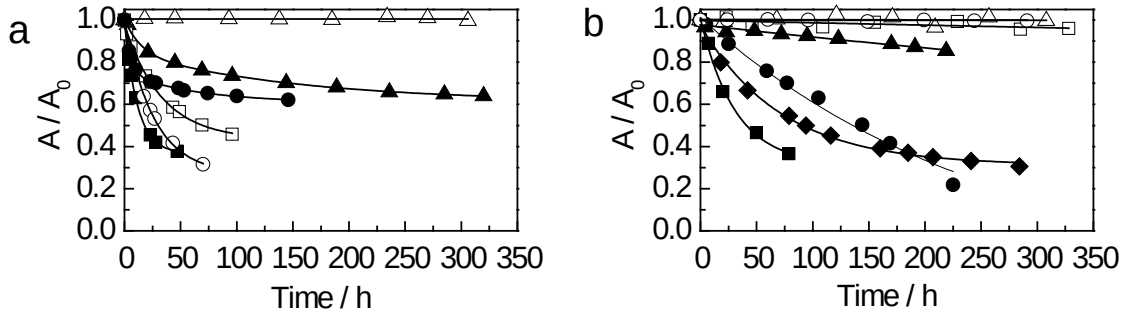


Figure 21. Decomposition of cross-linked copolymers: (a) closed form **hydrolyzed-3-co-PAA** in 50 mM phosphate buffer (pH 7.4) (■), in 50 mM sodium acetate buffer (pH 5.0) (▲), and in water (●) at 37 °C; and open form **hydrolyzed-3-co-PAA** in 50 mM phosphate buffer (pH 7.4) (□), in 50 mM sodium acetate buffer (pH 5) (Δ), and in water (○) at 37 °C; (b) closed form **5-co-PAA** previously immersed in 50 mM phosphate buffer (pH 7.4) at 37 °C (■) and at 25 °C (♦), in 50 mM sodium acetate buffer (pH 5.0) (▲), and in water (●) at 37 °C; and open form **5-co-PAA** previously immersed in 50 mM phosphate buffer (pH 7.4) (□), in 50 mM sodium acetate buffer (pH 5.0) (Δ), and in water (○) at 37 °C

Table 13. Decomposition rate constants ($\times 10^3$, h^{-1}) of fulgimides at 80 °C and their copolymers at 37 °C.

Compound (Medium)	Decomposition rate ($\times 10^3$, h^{-1})	
	Open-form [a]	Closed form [a]
Fulgimide **3** (Toluene) [b]	18	< 0.05
Fulgimide **5** (Toluene)	0	1.4
Hydrolyzed **3-co-PAA** (Water)	38	15 [c]
Hydrolyzed **3-co-PAA** (Acetate buffer)	0	6.7 [c]
Hydrolyzed **3-co-PAA** (Phosphate	30	91

Buffer)		
5-co-PAA (Water)	0	3.8
5-co-PAA (Acetate buffer)	0	1.1
5-co-PAA (Phosphate Buffer)	< 0.05	32

[a]Fit to a single exponential. [b]The data taken from ref.[27]. [c] Fit to a sequential decay.

6.4.4 Photochemical stability

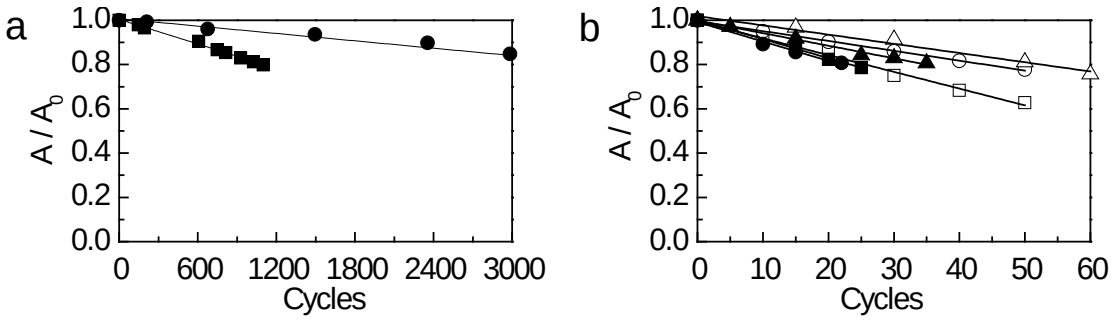


Figure 22. Photochemical decomposition of fulgmides (**3** and **5**) and crosslinked copolymers (**hydrolyzed 3-co-PAA** and **5-co-PAA**): (a) fulgimide **3** (●) and **5** (■) in toluene; (b) **hydrolyzed 3-co-PAA** previously immersed in 50 mM phosphate buffer (pH 7.4) (■), in 50 mM sodium acetate buffer (pH 5) (▲), and in water (●); **5-co-PAA** previously immersed in 50 mM phosphate buffer (pH 7.4) (□), in 50 mM sodium acetate buffer (pH 5) (Δ), and in water (○)

Table 14. Photochemical fatigue resistance of fulgimides and their copolymers at room temperature

Compound (Medium)	Cycling time		Photochemical decomposition		
	C-Z/E	*Z/E- C*	Cycles	A/A_0	% Per cycle
Fulgimide **3 (**Toluene)[a]	40	60	2990	0.85	0.005
Fulgimide **5** (Toluene)	20	200	1100	0.80	0.018
Hydrolyzed **3-co-paa** (Water)	900	420	22	0.81	0.86
Hydrolyzed **3-co-paa** (Acetate buffer)	1080	600	35	0.81	0.55
Hydrolyzed **3-co-paa** (Phosphate Buffer)	540	360	25	0.78	0.88
5-co-paa (Water)	900	1140	50	0.78	0.45
5-co-paa (Acetate buffer)	480	780	60	0.76	0.41
5-co-paa (Phosphate Buffer)	900	1140	30	0.75	0.83

The photochemical stability, also known as fatigue resistance, of fulgimides and copolymers was studied in toluene and aqueous solutions, respectively. The photochromic cycles were measured during the first approx. 20% loss in absorbance at λ_{max}. The CH_3 fulgimide **5** displayed a good photochemical stability in toluene, only decomposing 0.018% per cycle (Table 14). My previous study indicated that the CF_3 fulgimide **3** has better fatigue resistance than **5**.[27] For the copolymers in aqueous solutions, the cycle numbers were lower and the cycling times were longer than their monomers in toluene, probably because the fulgimides have lower quantum yields in more polar solution.[31] Copolymer **5-co-PAA** displayed better photochemical stability than the **hydrolyzed 3-co-PAA**. In my current study, **hydrolyzed 3-co-PAA** and **5-co-PAA** exhibited the greater photochemical stability in sodium acetate buffer, where the copolymers underwent up to 60 photochromic cycles before degrading 24% (Figure. 22), possibly because of relatively shorter irradiation times required during the photochromic reaction.

6.5 Conclusion

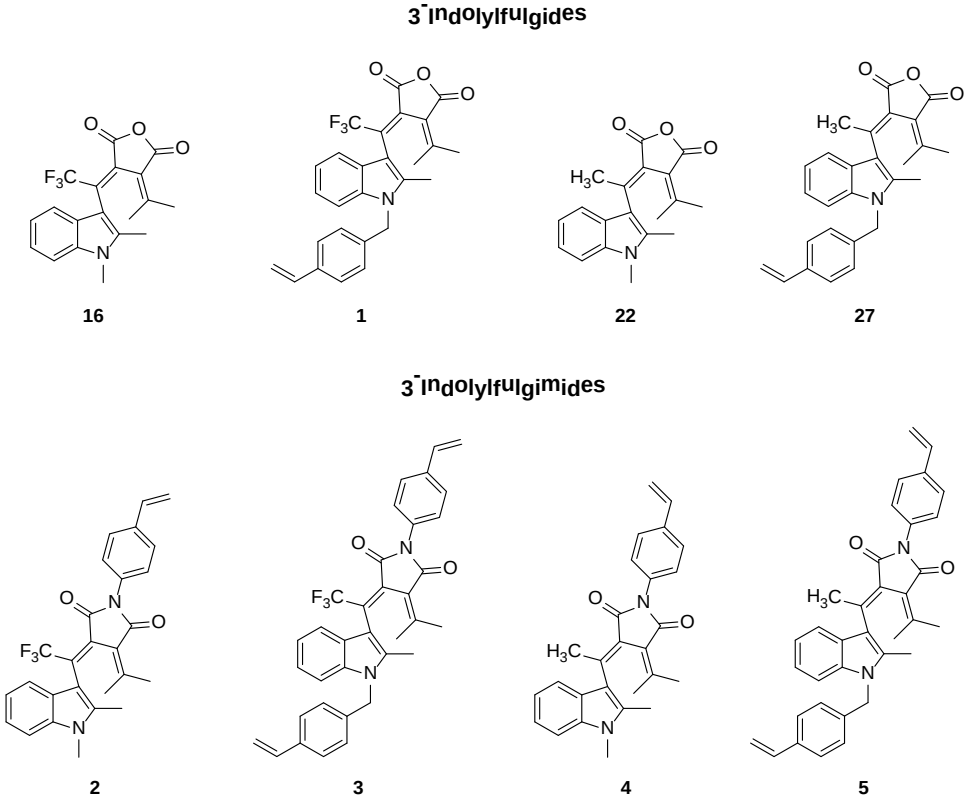
In summary, a new CH_3 fulgimide **5** with two pendant styrene groups was successfully synthesized from a CH_3 vinylbenzyl fulgide. In toluene, the open form fulgimide **5E** exhibited excellent stability at 80 °C with no degradation after 350 h. The *C*-form was less stable and degraded 30% after 220 h. Also, the fulgimide displayed good photochemical stability and underwent 1100 photochemical cycles before degrading by 20%. Two cross-linked copolymers **3-co-PAA** and **5-co-PAA** containing the CF_3 fulgimide **3** and CH_3 fulgimide **5** were synthesized, respectively. The copolymers were water compatible photochromic hydrogels. The copolymer containing CF_3 fulgimide in the closed form, **3C-co-PAA,** was converted to **hydrolyzed 3C-co-PAA** in aqueous solutions. The resulting **hydrolyzed 3-co-PAA** was also photochromic. In general, the **5-co-PAA** was more stable than **hydrolyzed 3-co-PAA** in aqueous solutions. The copolymers exhibited enhanced stability in acid solution than in neutral solution at 37 °C. Also,

similar with fulgimide **5**, the copolymers in the open forms were more stable than in the closed forms. All copolymers can undergo dozens of cycles before degrading 20%. The copolymers exhibited better fatigue resistance in acidic solution than in neutral solution and underwent up to 60 photochromic reactions before degrading 24%. Moreover, copolymer **5-co-PAA** displayed better photochemical stability than the **hydrolyzed 3-co-PAA**. Because of the enhanced photochromic properties in acidic solution, the hydrogels will be better at modulating biological systems in acidic condition compared to neutral condition.

7. CONCLUSION

The overall goal of the project was to develop thermally and hydrolytically stable photochromic copolymers containing 3-indolylfulgides/indolylfulgimides to meet the demands for applications in optical information storage devices or molecular switch in biological systems.

Scheme 36. 3-Indolylfulgides/indolylfulgimides synthesized in this project.

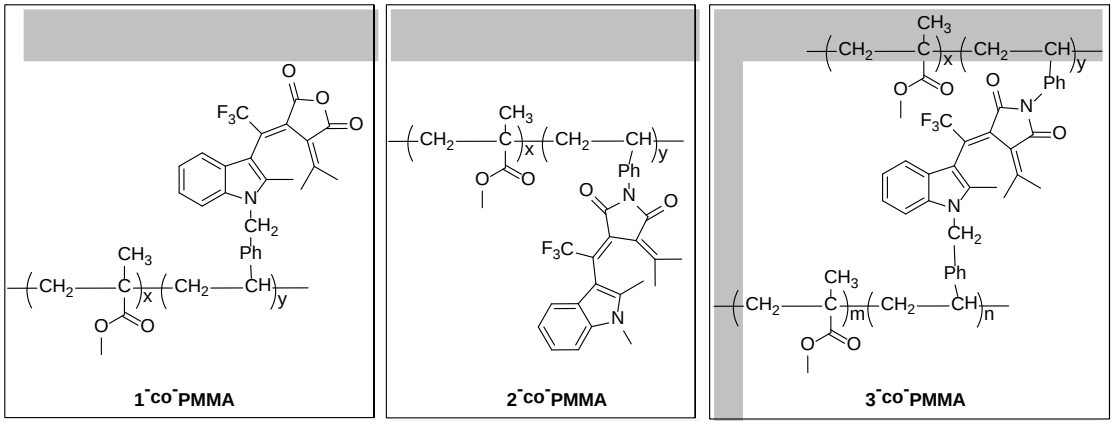


I have successfully synthesized several indolylfulgides and indolylfulgimides with enhanced thermal and photochemical stabilities (Scheme 36). The fulgides were generally prepared via Stobbe condensation of the corresponding indoles with a dimethyl succinate derivative followed by hydrolysis and dehydration. Fulgide **1** and **27** with a pendant styrene group were synthesized for the first time. The new fulgimides **2**, **3**, **4**, and **5** with one or two pendant styrene group(s) were synthesized by reacting their precursor fulgides with 4-vinylaniline followed by dehydration.

A series of copolymers were prepared via a free radical polymerization of polymerizable trifluoromethylfulgides/fulgimides with MMA (Scheme 37). The photochromic properties of

linear copolymers **1-co-PMMA** and **2-co-PMMA** were characterized in toluene and as films. Cross-linked copolymer **3-co-PMMA** was studied as a film. The copolymers, especially the *C*-forms exhibited excellent thermal stability at 80 °C. The degradation rate because of repeated photochemical cycles (ring-closing/ring opening) was less than 3% per 100 cycles. The advantageous properties make the copolymer promising in applications as optical information storage devices.

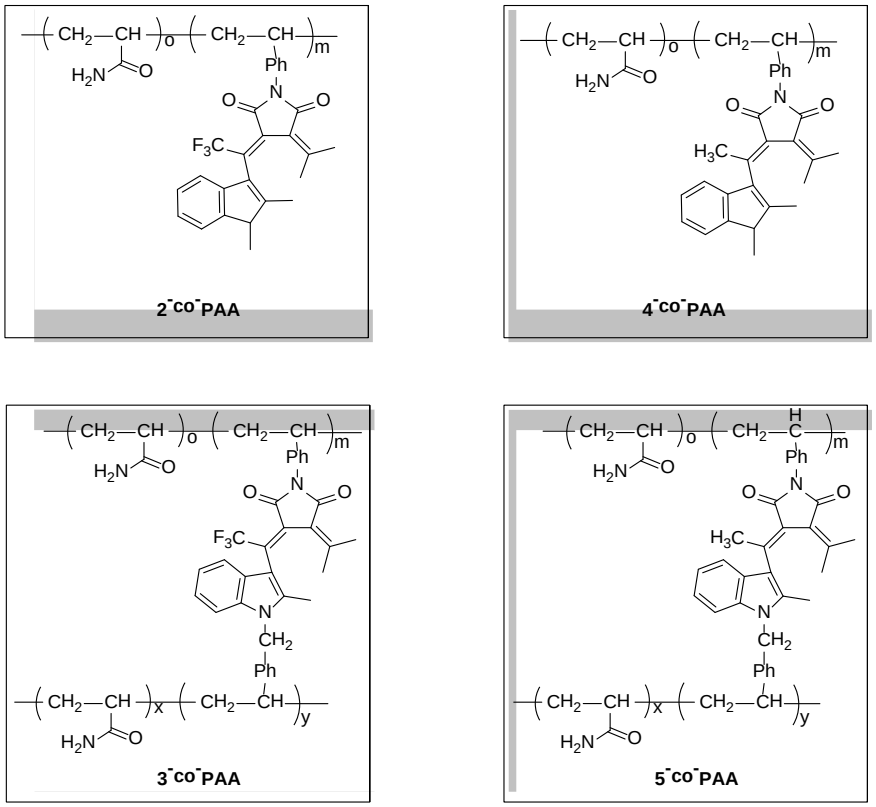
Scheme 37. 3-Indolylfulgide/indolylfulgimides co-PMMA copolymers synthesized in this project.



Polymerizing the fulgimides with acrylamide provided two linear copolymers, **2-co-PAA** and **4-co-PAA**, and two cross-linked copolymers, **3-co-PAA** and **5-co-PAA** (Scheme 38). The linear copolymers were found to be water soluble and photochromic, and the cross-linked copolymers are photochromic hydrogels. The copolymers were characterized in water, sodium phosphate buffer (pH 7.4), and sodium acetate buffer (pH 5.0). I found that the *C*-form copolymers, **2-co-PAA** and **3-co-PAA**, containing trifluoromethylfulgimides were hydrolyzed in aqueous solution by replacing the trifluoromethyl group with a carboxylic acid group on the bridging position. The resulting hydrolyzed **2-co-PAA** and **3-co-PAA** were also photochromic and exhibited better stability in acid solutions than in neutral solutions. The copolymers **4-co-PAA** and **5-co-PAA** containing methyl fulgimides with a methyl group at the bridging position of the fulgimide

significantly increased the hydrolytic stability and overcame the rapid hydrolysis of the trifluoromethyl group. Similar to the hydrolyzed **2-co-PAA** and hydrolyzed **3-co-PAA**, **4-co-PAA** and **5-co-PAA** displayed enhanced thermal stability in acidic conditions which makes the copolymer suitable for application in biological system, such as enzyme immobilization and controlled drug release.

Scheme 38. 3-Indolylfulgimides-co-PAA copolymers synthesized in this project.



8. FUTURE RESEARCH

The future work includes two objectives. First, applications of the copolymers synthesized in Chapter 6 in biological systems need to be investigated. For example, experiments can be performed to study enzyme immobilization using the copolymer **5-co-PAA** to photo-control enzymatic reactions. Second, the stability of **5-co-PAA** in basic condition needs to be improved to meet the demands of wider variety of applications. One solution could be to replace the styrene group on the succinimide ring of the fulgimide with a vinylbenzyl group.

8.1 Regulation of enzymatic reactions using copolymer 5-co-PAA

The cross-linked copolymer **5-co-PAA** is a photochromic hydrogel and can change its conformation between the rigid form and the flexible form as the fulgimide is interconverted between the closed form and open form with light. An enzyme can be embedded into the hydrogel in the polymerization process. And the immobilized enzyme will be photo-regulated in the hydrogel because the conformation of the enzyme or the substrate accessibility to the active site will be altered by light (Figure 23).

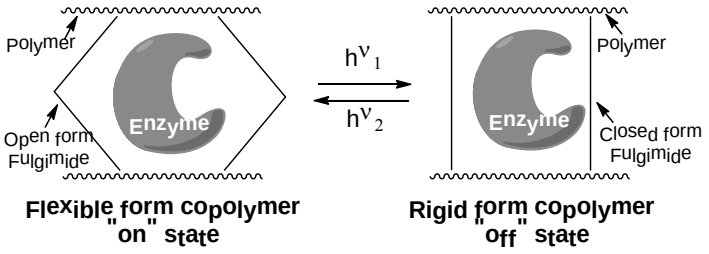


Figure 23. Enzyme immobilization by using polymer containing fulgimide

An experiment could be performed using lactase as the enzyme, because the optimum pH of lactase is 6.0, a PH where the hydrogel displays good stability.[88] The substrate used in the lactase assay will be *o*-nitrophenyl-D galactoside (ONPG), which can be hydrolyzed into galactose and *o*-nitrophenol (ONP) (λ_{max} = 420 nm, $\varepsilon_{max} = 4.9 \times 10^3$ mol^{-1} L cm^{-1}).[89] The lactase will be embedded into the hydrogel in the polymerization process. Then, the mixture will be suspended in buffer (pH 6.0) and incubated for 10 min at 37 °C. The substrate, ONPG, will be added and the

formation rate of ONP will be monitored by UV-Vis spectrometer. The assay of lactase will be conducted in both flexible form and rigid form hydrogel, and the activities of lactase will be compared. A control test will be performed under the same conditions but without the hydrogel. Finally, the loading degree of the fulgimide will be optimized by comparing the photo-regulation effects in hydrogels prepared with different ratios of the fulgimide and acrylamide.

In practical use, there are many advantages to use a photochromic hydrogel as a carrier to immobilize an enzyme. First, the enzymatic reaction can be photo-controlled, that is beneficial because light can be imposed instantly and precisely in the desired intensity. Second, hydrogel can be removed immediately when the reaction is complete because the hydrogel is a cross-linked polymer and insoluble in water. Third, the system can be used repeatedly because the hydrogel has good thermal stability and photochemical stability. Moreover, the enzyme embedded in the polymer matrix can be protected from contamination and easily stored.

8.2 Controlled drug release behavior of hydrogel 5-co-PAA

Hydrogels with hydrophilic polymer chains have the ability to swell and absorb aqueous solutions. So drugs can be loaded into the hydrogels during the swelling process. The rate of drug release depends on the permeability of the polymer matrix towards the drug. Photochromic hydrogel **5-co-PAA** has great potential to be used as a “smart” drug delivery carrier because of polymer matrix permeability can be modulated by interconversion of the fulgimide between the open form and the closed form with light. So I expect that the rate of drug release will be affected when the hydrogel switches conformations (Figure 24). The photo-induced system will be promising because light stimulus can be controlled precisely and has no or little harmful effect on the activity of most proteins.

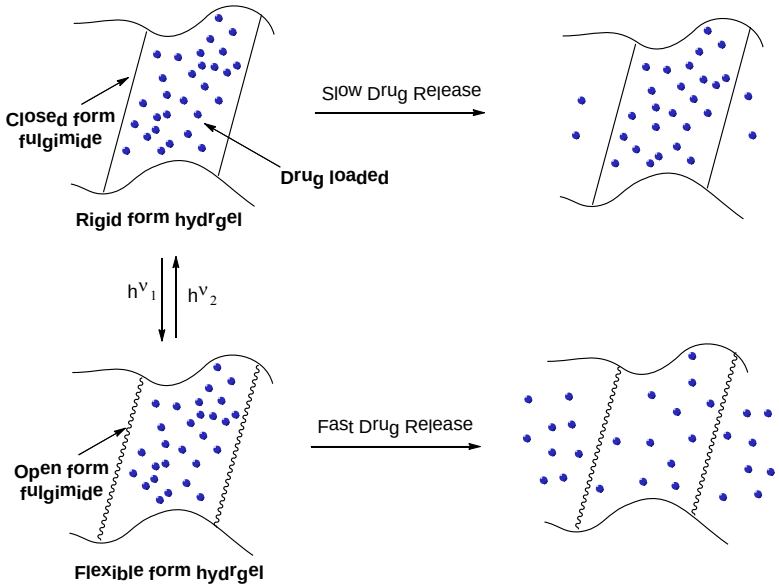


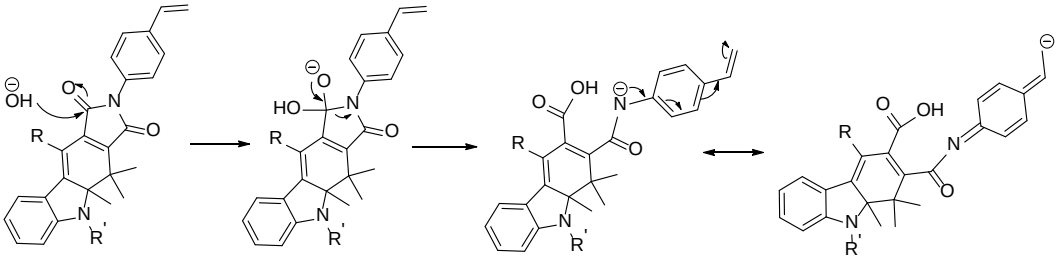
Figure 24. Photo-controlled drug release behavior of hydrogel 5-co-PAA

Vitamin B_{12} (VB_{12}) (λ_{max} = 361 nm, $\varepsilon_{max} = 2.75 \times 10^4$ mol^{-1} L cm^{-1}) can be used as a model drug to study the release behavior of the hydrogel **5-co-PAA** in *vitro*. The pre-weighed dried hydrogel will be put into a solution with sufficient VB_{12} and freeze-dried after swelling. Then the dried hydrogel loaded with VB_{12} will be immersed into a buffer and the release rate of VB_{12} will be monitored by UV-Vis spectrometer. The tests will be conducted using both forms of hydrogel, and VB_{12} release rates will be compared.[56]

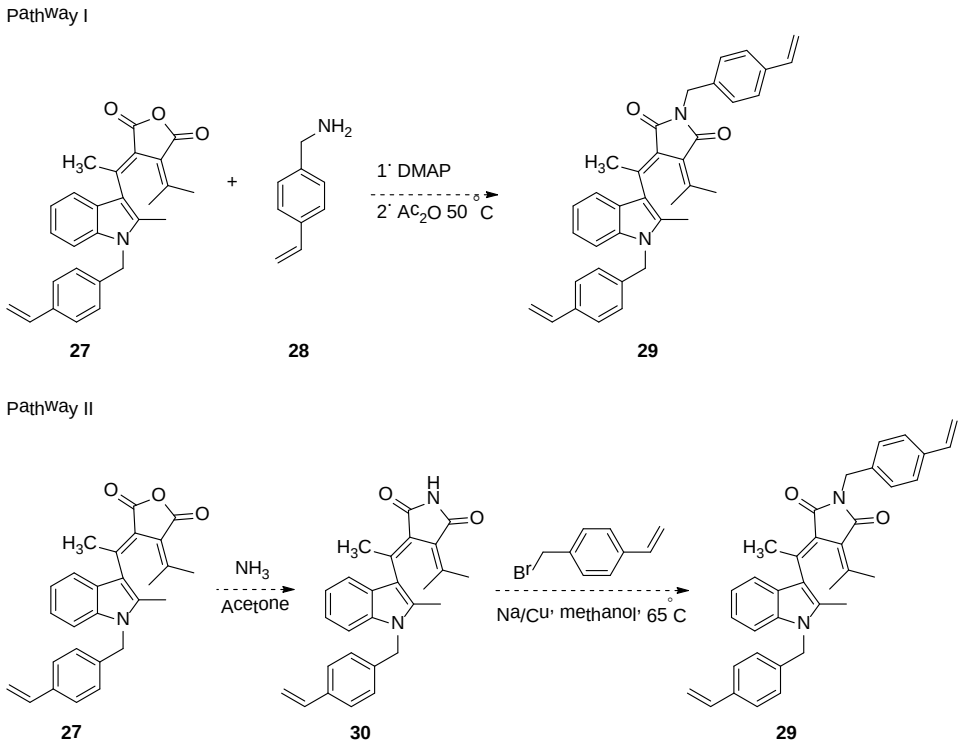
8.3 Synthesis of methyl fulgimide with doubly substituted vinylbenzyl groups

My results showed that copolymer **5-co-PAA** is more stable in acidic solution than in neutral solution. A possible reason is that the fulgimide with a styrene group on the succinimide ring can be easily hydrolyzed in the presence of hydroxide ions. As shown in Scheme 39, in basic solutions, hydroxide ions can attack the carbonyl carbon on the succinimide ring. The excess electrons will force the ring open and form a negative charge on the nitrogen. Then the negative charge can be delocalized by the styrene group on the nitrogen. As a result, the ring opening reaction can be accelerated by the resonance structures.

Scheme 39.Proposed mechanism for hydrolysis of fulgimide in basic condition



Scheme 40. Proposed synthetic pathways of methyl fulgimide 29[38,90]



To enhance the stability of fulgimide in basic solution, the styrene group needs to be replaced. A previous study pointed out that the half-life time of *N*-ethylmaleimide is 20 times that of *N*-phenylmaleimide at pH 7.0.[85] I expect that the fulgimide with an aliphatic substituent group on the nitrogen will be more stable. Therefore, two synthetic pathways are proposed to prepare the fulgimide with a vinylbenzyl group on the succinimide ring **29** (Scheme 40). Both pathways employ the corresponding fulgide **27** as the starting material. Pathway I involves the reaction of fulgide **27** with 4-(aminomethyl)styrene **28** to form an succinamic acid intermediate, then the

fulgimide **29** will be obtained following dehydration. In pathway II, the precursor fulgide **27** is treated with ammonia to prepare a non-*N*-substituted fulgimide **30**, and then the fulgimide will be reacted with 4-vinylbenzyl bromide in the presence of Cu-powder to obtain the desired fulgimide **29**. Copolymers containing fulgimide **29** are expected to be stable in both acidic solution and basic solution.

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