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Degree in Chemistry

Final Year Project

Development of a photosensitive organocatalyst for the ring-opening
polymerization of ϵ -Caprolactone

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Summary

Biodegradable polyesters and polycarbonates are one of the main families of biodegradable polymers and are widely synthesized by ring opening polymerization (ROP) of lactones. An important field of use of these polyesters is the medical field, where there is great interest in being able to fabricate 3D object like tissue scaffolds or prostheses with these materials. Stereolithography or the 3D impression by controlled photopolymerization is an area of fast development, but the range of available monomers and photocatalysts is still very narrow. In the last years research on organocatalysis for lactone ROP has been intense, with many organic acids catalysing the cationic polymerization of these cyclic esters. The deactivation of these organic acids to form photoacid generators, and the employability of these compounds for stereolithography is a subject of great interest.

The goal of this project is to develop a photocatalyst able to catalyse a ROP reaction with short reaction times. To find the best monomer, catalyst and conditions, a screening work was done and several catalysts were tried in different conditions. The fastest ones were selected to develop a photosensitive photocatalyst. This new compounds were photoacid generators, an inactive catalyst with the ability to decompose under UV light into the original organic acid. Finally, these photoacid generators was tried to examine its behaviour under different conditions and its catalytic power after decomposition.

Resumen

Los poliésteres y policarbonatos biodegradables son una de las principales familias de polímeros biodegradables y biocompatibles, y son habitualmente sintetizados por polimerización de apertura de anillo (ROP) de lactonas. Un ámbito importante de uso de estos poliésteres es la medicina, donde hay un gran interés en la posibilidad de fabricar objetos 3D como andamiajes para tejidos o prótesis. La estereolitografía o la impresión 3D por fotopolimerización controlada es un área de rápido desarrollo, pero el rango de monómeros y fotocatalizadores disponibles es muy estrecho todavía. En los últimos años la investigación en la organocatálisis de la ROP de las lactonas ha sido muy intensa, con múltiples ácidos orgánicos catalizando la polimerización catiónica de estos ésteres cíclicos. La desactivación de dichos ácidos para formar fotogeneradores ácidos, y la empleabilidad de estos compuestos para la estereolitografía es un campo de gran interés.

El objetivo de este proyecto es desarrollar un fotocatalizador capaz de catalizar una reacción ROP con breves tiempos de reacción. Para encontrar el mejor monómero, catalizador y condiciones se llevó a cabo un trabajo de screening y se probaron múltiples catalizadores en distintas condiciones. Los catalizadores más rápidos fueron escogidos para desarrollar fotocatalizadores fotosensitivos. Los nuevos compuestos eran fotogeneradores ácidos, unos catalizadores inactivos con la habilidad de descomponerse bajo radiación ultravioleta y liberar el ácido original. Finalmente, se estudió el comportamiento de los fotogeneradores ácidos bajo diferentes condiciones y su potencial catalítico durante y tras la descomposición.

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1.- Introduction

The technique of polymer 3D printing was born in the early 1980s, with the invention of localized photo-curing of polymers and the 3D System Corporation patent for an early stereolithography (SLA) system in 1984. In 1988 the company Stratasys commercialized the first Fused Deposition Modelling (FDM) system, based on the extrusion and deposition of molten polymer. During the 1990s the patents for FDM processes expired and the technique was perfected; during this time other processes like Selective Laser Melting (SLM) and Selective Laser Sintering (SLS) were developed. These first systems were cumbersome, slow and expensive; the applications of this early 3D printing were restricted to high-end objects like design models and rapid prototyping. However, the new century came with an increase in miniaturization and affordability of the machines, and desktop printers like the RepRap project in 2005 and the Makerbot in 2009 and the foundation of the file library Thingiverse made of the 3D printing systems a consumer product. Nowadays there is a very broad range of 3D printing systems and applications, from inexpensive desktop printers to high-precision industrial machines aimed at rapid prototyping and high added value objects like prosthesis components.

There are several available processes for 3D printing, and although a continuous curing technology was developed in 2014 by Carbon3D, all commercial systems work by the creation of a new layer of material over the previous layer to build the object. The creation of the new layer may be by deposition of molten polymer (e.g. FDM), the aggregation of smaller particles (e.g. SLM and SLS) or the synthesis of the polymer by an external stimulus. The deposition of molten polymer is the simplest of the techniques, and as such is the easiest to execute and the cheapest. However, it also comes with disadvantages: the range of polymers adequate for 3D printing is increasing but is not very broad yet, the polymer chains may degrade due to the thermal and mechanical stress of the extrusion, and the resolution of the technique is limited by the practical nozzle size limits and the thermal expansion and contraction of the polymers.

On the other hand, in SLA the new layer is synthesised by photopolymerization; a laser is focused in a single point inside the monomer liquid triggering the photopolymerization, and the focal point is displaced through the previous surface creating a new layer. As the focal point of the laser may be significantly smaller than the smallest extrusion nozzle, SLA offers higher resolution and surface smoothness than FDM, making it more suitable in fields where this accuracy is worth the extra cost of the technique e.g. medical applications. What is more, the lack of thermal or mechanical stress reduces the degradation of the polymer, and the wider variety of possible liquid formulations opens up the possibility of impression of copolymers.

This light triggered photopolymerization requires of polymerization processes that can stay deactivated for long periods of time, and then be precisely activated with irradiation. To be able to achieve this, photosensitive molecules able to rapidly catalyse the polymerization of the monomer liquid have to be developed. Over the last years, light-triggered polymerization has experienced a fast development, with many monomers and catalysts available. However, most of the research done in this field has been on photoinduced radical polymerization^[1], suffering the common problems of radical polymerization such as deactivation by atmospheric O₂. Light-induced ionic polymerization is also possible through photoacid (PAG) and photobase (PBG) generators; however, even though photo-ionic processes are undergoing intense research^{[2][3]}, the range of monomers and catalysts available is much narrower.

Biodegradable polyesters and polycarbonates are one of the main families of biodegradable polymers and are widely synthesized by ring opening polymerization (ROP) of lactones. These polyesters are widely used in prostheses and as support scaffolds^[4] for engineered tissue, applications where custom-made 3D printed designs may suppose a great improvement. The American FDA has approved many types of polyester for biomedical use such as polycaprolactone (PCL) and polylactic acid (PLA). However, most of the photopolymerization research on ROP reactions of lactones has been on metal-catalysed ROP reactions^{[5][6]}; many organometallic catalysts are not suitable for biological applications due to the acute toxicity and difficulty of removal. Opposed to this, organocatalysis provides various advantages, including but not limited to lower biotoxicity and lower sensitivity to O₂ or moisture^{[7][8]}. On the same note, ionic

catalysts are less sensitive to atmospheric conditions, and present lower toxicity than their radical counterparts.

This project was carried out at the Innovative Polymers Group of the BERC-POLYMAT, located at the Faculty of Chemistry of EHU/UPV in Donostia-San Sebastián, Spain. The project was supervised by Dr. Nicolas Zivic and Prof. Haritz Sardón.

1.1.- Objectives

The objective of this project is to expand the library of monomers and catalysts available for SLA 3D printing, focusing on lactones and carbonates polymerized by organocatalyzed ROP.

First, based on previous research on polymerization by photosensitive organocatalysts^[7], a bibliographical study will be conducted to identify the reagents and conditions under which the polymerization would be fast enough to be useful in 3D printing. This study will focus on ring opening cationic polymerization reactions catalysed by organic acids.

Afterwards, an experimental study of the reaction speed under 3D printing conditions will be carried out with different catalysts and molar ratios to determine the optimal reagents and conditions.

Finally, a photocatalyst will be developed from the original organocatalyst and its characteristics such as photosensitivity and catalytic power will be studied. The objective for the photocatalyst is to obtain conversion values of >80% at 15 minutes of reaction in bulk and at room temperature, with a maximum initiator and catalyst molar ratio of 5%.

1.2.- Glossary and Abbreviations

- E-CL: ϵ -Caprolactone monomer
- MSA: Methanesulfonic Acid catalyst
- TfOH: Triflic Acid, Trifluoromethanesulfonic Acid catalyst
- TMC: Trimethylene carbonate monomer
- PCL: Polycaprolactone polymer
- PDM: p-Phenylene dimethanol initiator
- TEA: Triethylamine base

1.3.- Monomer Selection

2 different monomers were studied: Trimethylene carbonate (TMC) and ϵ - Caprolactone (ϵ -CL) (Fig.1); following a collaboration agreement, the group of Prof. Andrew Dove would be studying L-Lactide. A review article published in 2015^[6] proved to be very useful as a summary of different catalysts and conditions for ROP of cyclic esters and carbonates, as well as a gate to relevant literature. The goal of the study was to find the theoretical conditions under which the ROP was fast (high conversions at <15 minutes) at bulk polymerization and with maximum 5% molar percentage of both organic catalyst and initiator.

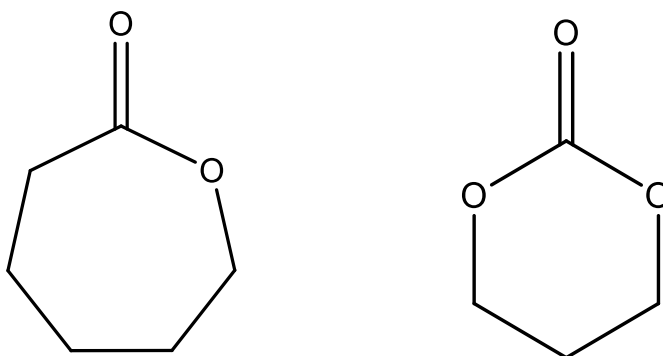


Fig. 1. Structure of monomers ϵ -Caprolactone (ϵ -CL) and Trimethylene carbonate (TMC), respectively.

The major problem that was encountered during the literature review was the lack of scientific papers describing the bulk ring-opening polymerization of polyesters. Most (if not all) of the research described in the literature is about in solution polymerization, with very low amounts of catalyst and very long reaction times (between 8 and 72 hours, very long compared to the 15-30 minutes this project is aiming for). Due to this lack of data, the literature review proved useful mostly for the selection of the catalysts and monomers, but it was not useful for the establishment of the reaction conditions.

The first monomer to be studied was TMC. Poly(trimethylene carbonate) (PTMC) is very useful as a homopolymer or copolymerized with L-Lactide and ϵ -CL in medical applications. These polymers degrade *in-vivo* without releasing acidic byproducts^[9], making them ideal for temporal applications such as suture. However, the polymerization described in the articles was very slow for our purposes. AS TMC is solid at room temperature, instead of bulk polymerization the reaction is usually performed in 1M solution. The polymerization times ranged from the very slow 22h (10% catalyst molar percentage 1% initiator in CH_2Cl_2 , r.t.)^[10] and 6h (5% catalyst and initiator in toluene, r.t.)^[11] to the faster 45' (15% catalyst molar percentage 2.5% initiator in toluene, 30°C)^[12]. The usual catalysts were methanesulfonic acid (MSA), triflic acid (TfOH) or diphenyl phosphate (DPP); the usual initiators were the monofunctional n-pentanol or the bifunctional water and 1,4-phenylene dimethanol (PDM).

The second monomer to be studied was ϵ -CL. Polycaprolactone (PCL) is very used as a biodegradable and biocompatible polymer as a homopolymer or copolymerized with other polyesters. Again, almost all literature on PCL described in-solution polymerization. The polymerization described in the literature is faster than the reactions of TMC, ranging from 90' (2.5% catalyst molar percentage and initiator in toluene, 30°C)^[13] to 30' (5% catalyst molar percentage and initiator in toluene, 30°C)^[13]. The most used catalysts were MSA and TfOH; Tf_2NH was mentioned in a paper with long reaction times, but very low catalyst ratio (0.2% catalyst molar percentage 2% initiator in CH_2Cl_2)^[14]. Again, the usual initiators were n-pentanol, water and PDM.

For this project, ϵ -CL was chosen as the appropriate monomer. The reaction times described in the literature were longer than desired but not as long as the ones of TMC and polymerization in bulk usually have shorter reaction times. For TMC, the reaction times were too slow to be used in 3D printing and it was discarded as a viable monomer for this project.

ϵ -CL is a cyclic ester (lactone) that undergoes ring opening polymerization to form polycaprolactone, a polyester. Both radical and ionic polymerization are possible with ϵ -CL; as mentioned before, cationic polymerization (especially if catalysed by organic acids) have important advantages over free-radical catalysis including but not limited to lower sensitivity to oxygen and lower biotoxicity of the catalysts. The cationic ROP of ϵ -CL is therefore catalysed by Brønsted acids, and initiated by an hydroxyl-containing initiator.

The mechanism of the cationic ROP of ϵ -CL is well known (Fig.2). The carbonyl is protonated by the acid, and the resulting carbocation suffers the nucleophilic attack of the hydroxyl group of the initiator/the end of the elongating chain. In this position, the trivalent oxygen is positively charged, although through tautomerism the proton may be transferred to the oxygen of the cycle. Finally, the hydroxyl group formed by the protonation of the carbonyl releases the proton and the ring opens, releasing the catalyst's proton and elongating the chain. The protonated oxygen of the cycle is now a terminal hydroxyl group after the opening of the cycle, and it is this hydroxyl group that may be used to open another cycle and elongate the chain ever further.

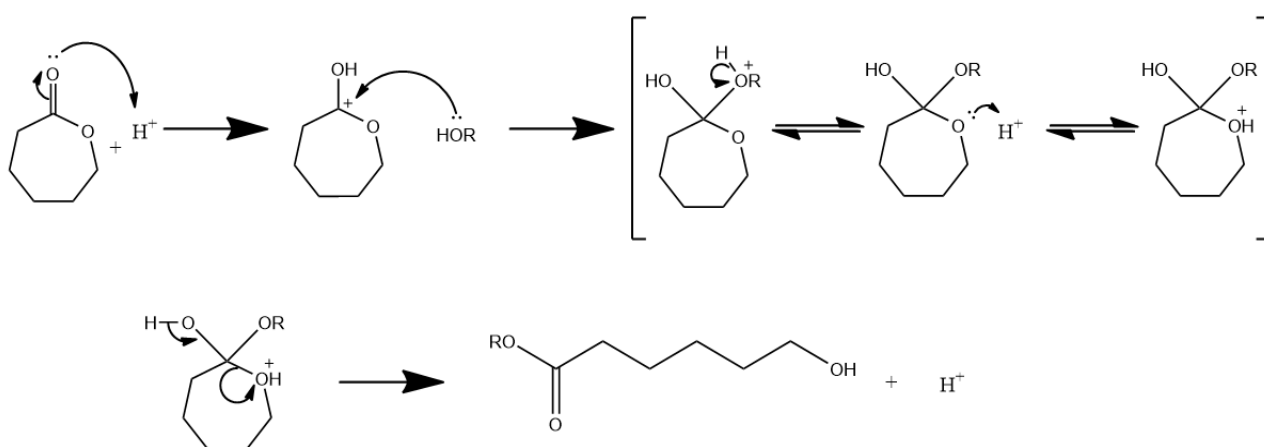


Fig. 2. Mechanism of the initiation or the elongation of the chain in the Ring Opening Polymerization of ϵ -CL.

1.4.- Photoacid Generators (PAG)

Photoacid generators are a subgroup of catalysts that are sensitive to irradiation. These photosensitive molecules are able to generate an acid upon irradiation. Unlike other triggers like heat, light can be applied with great spatial and temporal control and in combination with PAGs allows for localized and controlled catalysis.

PAGs are usually sensitive to ultraviolet and/or visible light. Photons of that wavelength contain enough energy to promote an electron from the ground state of the molecule (HOMO) to a state with higher energy; this state is usually the first possible excited state (LUMO)^[15]. According to quantum mechanics, only photons with the same energy as the energy gap between the two states is able to promote an electron; thus, the molecule is able to absorb light of certain wavelengths (therefore, of certain energy) and each molecule has a characteristic absorption spectra.

Molecules are generally not stable at this singlet excited state, and seek to relax into a state of lower energy. This relaxation can happen through multiple different and competing processes, including but not limited to internal conversion (releasing the energy as heat), emission of electromagnetic radiation with or without intersystem crossing to a triplet state (fluorescence and phosphorescence, respectively) or decomposition of the triplet state (after the change of spin multiplicity from singlet to triplet) through different processes such as electron transfer or proton transfer^[15].

Photoacid generators are photosensitive compounds that, upon irradiation, undergo a proton transfer process and yield an acid. As discussed previously, this acid can be used as a catalyst to perform light-controlled cationic polymerizations.

Depending on the structure and the nature of the molecule, PAGs can be classified in two major groups.

Ionic Photoacid Generators^[7]

Ionic PAGs are composed of two or more ions that form a salt. These salts are usually composed of a photosensitive cation, and the conjugated anion of an acid. Upon irradiation, the cation decomposes into smaller molecules, releasing a proton in the process. This proton is released alongside the conjugated anion to yield an acid. One of the most common ionic PAG families is the iodonium photoacid family, with a photosensitive cation containing a positive divalent iodine atom.

Due to their ionic nature, many of the ionic PAGs are hardly soluble in organic solvents and monomers, limiting their usefulness to be employed as polymerization catalysts.

Non-Ionic Photoacid Generators^[7]

Non-ionic PAGs are neutral molecules that decompose into smaller molecules upon irradiation, including a Brönsted or Lewis acid. In these molecules, the acid-to-be is linked to the chromophore by an ester, sulfonic ester, phosphate ester... that is broken upon irradiation. The resulting ion or radical (depending on the cleavage process) takes a proton from another of the decomposition molecules or the solvent, forming an acid. Based on the chromophore, the main families of non-ionic PAGs are the benzyl esters, the imino esters and the conjugated imino esters (Fig. 3).

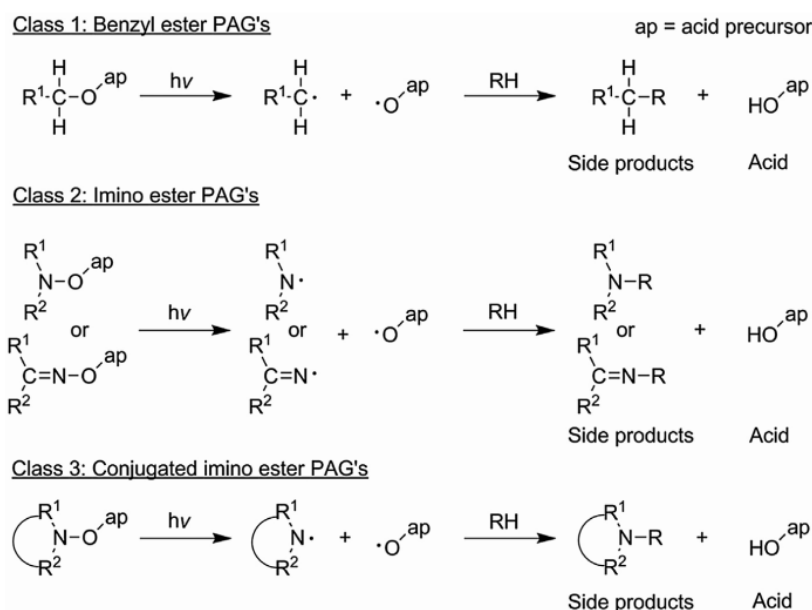


Fig. 3. Structure and decomposition of the main non-ionic PAG families^[7]

1.4.1.- Iodonium Salt Photocatalysts

Iodonium salts are a family of photoactive compounds that decompose under UV light into neutral organic compounds and the protonated acid. The first use for cationic polymerization of iodonium salts was described by Crivello in 1984^[16]. These salts consist of a positively charged iodine atom bonded to 2 aromatic substituents. One of the substituents is usually highly conjugated and able to absorb UV light, and when this chromophore absorbs a photon the molecule transitions into an excited state. This excited state is unstable and causes the decomposition of the molecule; the bond between the iodine atom and the non-chromophore substituent suffers a homolytic cleavage (Fig. 4)^{[17][18.a]}. This process yields a phenyl radical and a cationic iodine radical. Then the system can recombine back into the iodonium salt or it can undergo an electron transfer process to link the phenyl radical and the chromophore; after this linkage the system undergoes a proton transfer process, releasing the protonated acid and a neutral organic molecule.

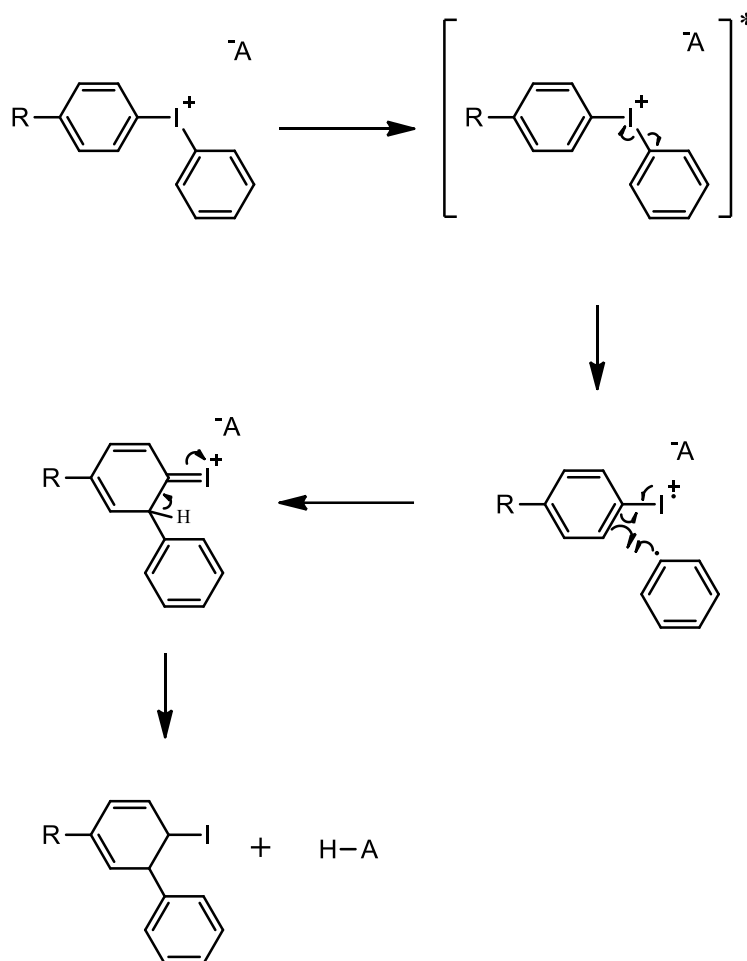


Fig. 4. Decomposition mechanism of Iodonium salts under UV light, following the homolytic cleavage route described by Dektar et al.^[17]

The Iodonium salts used in this project were based on naphthalimide, and synthesized following the process described in the doctoral theses of Dr. Zivic^[18.b]. Naphthalimide-based chromophores are used instead of simpler chromophores because of their ability to absorb UV-A light, the least energetic wavelengths of the UV range; for example, typical iodonium salts are only able to absorb irradiation with a wavelength shorter than 300nm^[17]. The best approach to the synthesis of these salts is by the synthesis of the photosensitive cationic part first, and then the linkage with the conjugated base of TfOH. After the salt with the trifluoromethanesulfonate is synthesized, then the counteranion may be replaced by the counteranion of another acid.

In our project, the “parent” catalyst developed was (4-(6-Bromo-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)phenyl)(phenyl)iodonium trifluoromethanesulfonate; this compound was named Iodonium-TfOH (Fig 5). Then, trifluoromethanesulfonate was substituted by methanesulfonate, MSA’s counteranion, forming Iodonium-MSA.

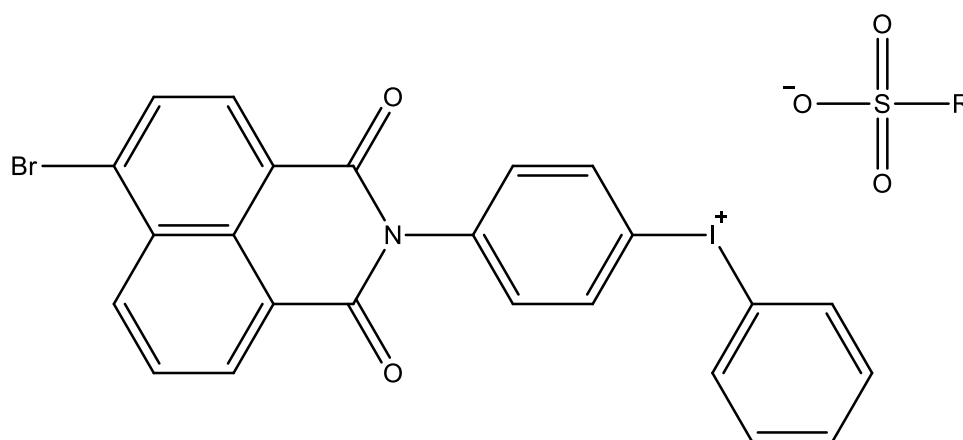


Fig. 5. Naphthalimide based Iodonium Salts.

R= CF₃ -> Iodonium-TfOH

R=CH₃ -> Iodonium-MSA

1.4.2.- Non Ionic Naphthalimide Photocatalysts

Non-ionic photocatalysts based on naphthalimide have been already reported in the literature^[19]. These catalysts are composed of the naphthalimide chromophore and an additional chain that is released upon decomposition. These chains can be designed during synthesis and depending on the chain introduced the acidity of the decomposition products can be tuned. In this project, methanesulfonate was introduced as the substituent chain.

According to Ortica et al. the mechanism of decomposition of the imidosulfonates develops through heterolytic cleavage of the N-O bond (Fig. 7), although the homolytic cleavage has also been described^[20] (Fig. 6). The heterolytic cleavage is favoured over the homolytic in cases where the resultant anion is stable and a good leaving group.

In the more probable heterolytic cleavage, upon irradiation the imidosulfonates decompose yielding a sulfonate anion and an ammonium cation. This positive nitrogen reacts afterwards with water, forming N-hydroxy-naphthalimide and releasing a proton; thus, the previously inactive acid is released.

In order to increase the solubility of 4-bromo-1,8-naphthalic anhydride another photocatalyst was proposed for synthesis, with an alkoxy chain linked to the chromophore instead of the bromine.

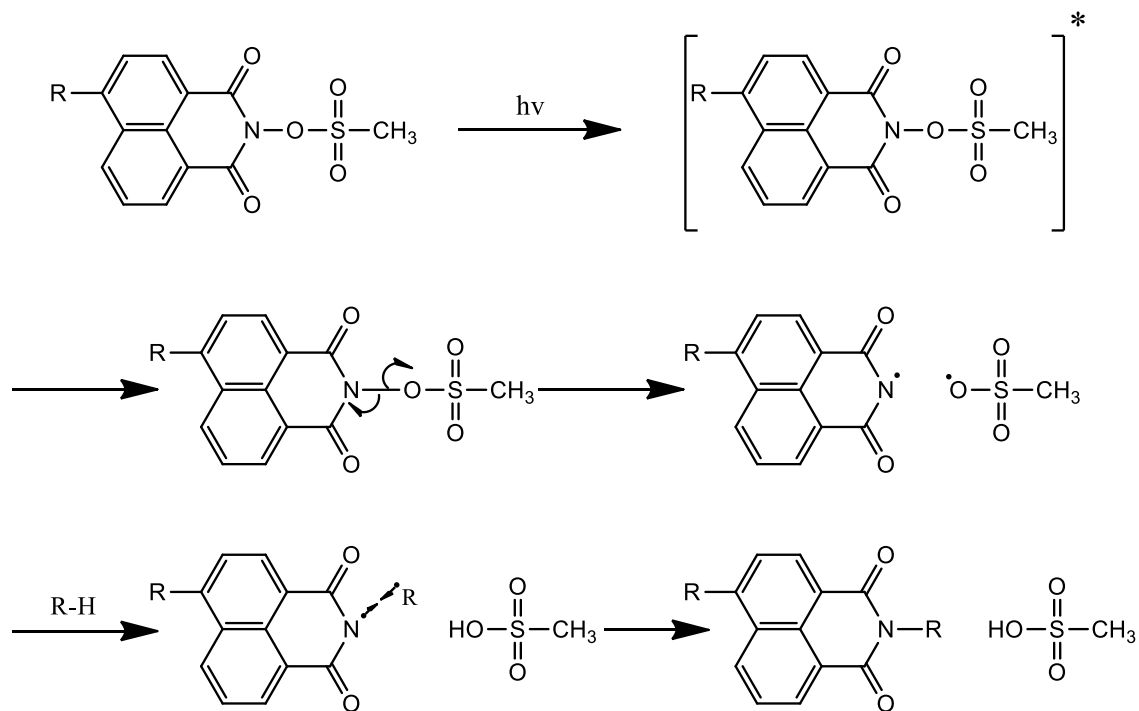


Fig. 6. Decomposition mechanism of naphthalimide-based sulfonylesters, following the homolytic cleavage described by Ortica et al.^[20]

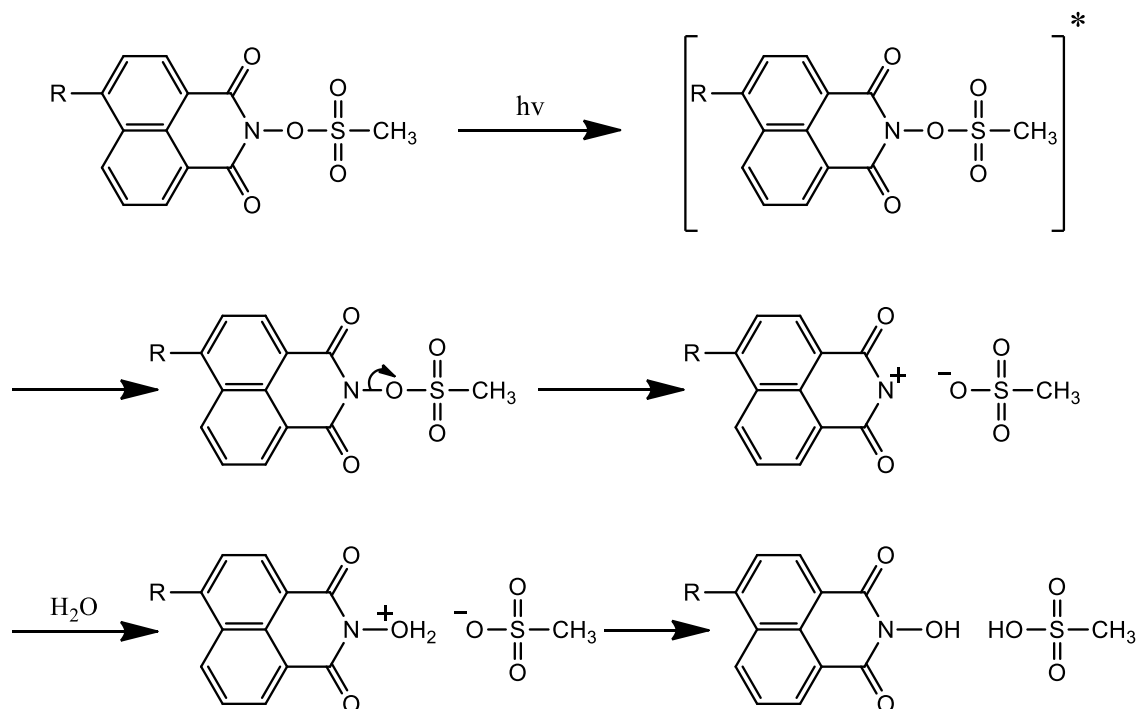


Fig. 7. Decomposition mechanism of naphthalimide-based sulfonylesters, following the heterolytic cleavage and hydration described by Ortica et al.^[20]

1.4.3.- Non Ionic Anthrone Photocatalysts

In order to complement the two previous families a third group of photocatalysts was proposed. Based on anthrone iminosulfonates, these photocatalysts are similar to the naphthalimide-based catalysts, with an aromatic chromophore and a leaving acid connected by the iminosulfonate bridge^[21]. In contrast with the naphthalimide-based imidosulfonates, which decompose mainly through heterolytic cleavage of the N-O bond, the main decomposition pathway of the iminosulfonates is the homolytic cleavage^[21] (Fig. 8). Upon irradiation, this bridge is broken and the acid is released.

The leaving acid is introduced during the synthesis of the photocatalyst, and different acids can be linked to the precursor molecule. In this project, methanesulfonic acid was used as its acid chloride is widely available and more stable than trifluoromethanesulfonyl chloride.

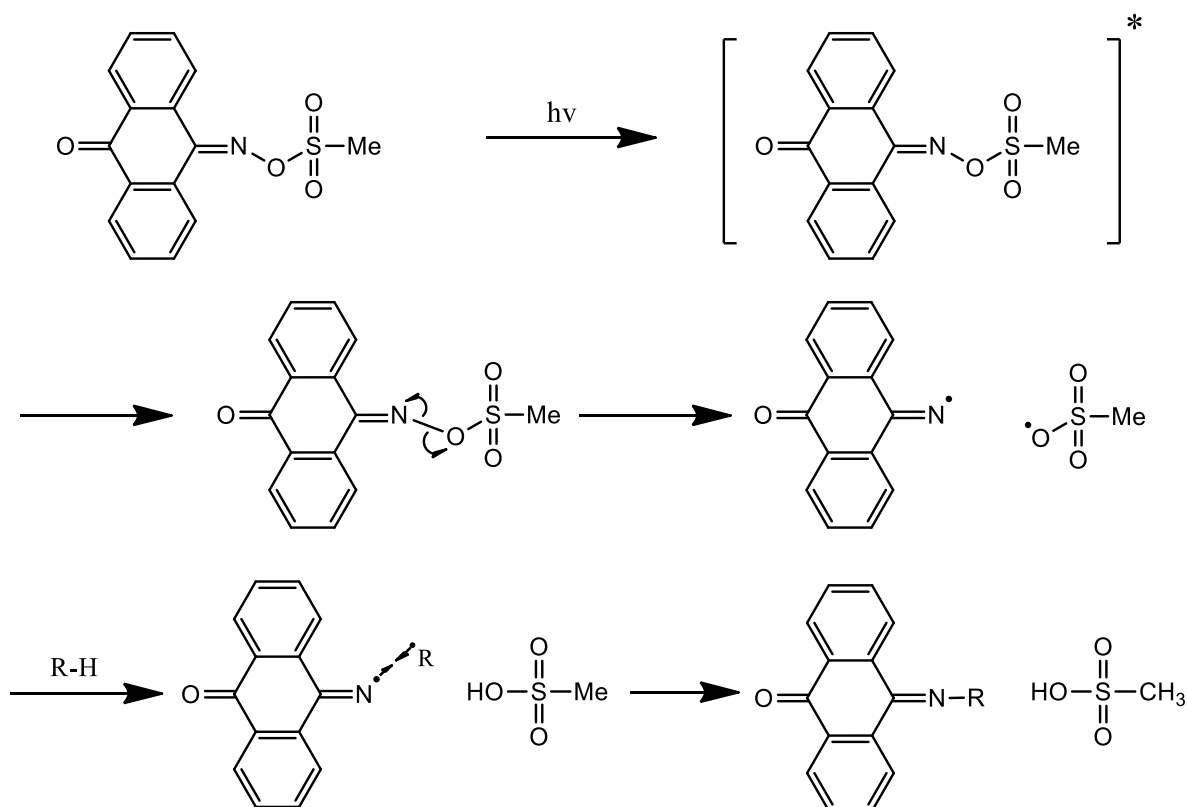


Fig. 8. Decomposition mechanism of anthrone-based sulfonylesters, following the homolytic cleavage described by Sun et al.^[21]

2.- Experimental Procedure

2.1.- Materials Used

The monomer used was ϵ -Caprolactone (97%, bought at Sigma-Aldrich) CAS: 502-44-3. Its density is 1.07 g/mL. The molecular weight is 114.144 g/mol. It is a viscous, pale yellow liquid.

The initiator used was *p*-phenylenedimethanol (>99%, bought at TCI) CAS: 589-29-7. The molecular weight is 138.11 g/mol. It is a white solid.

The acid catalysts used were:

- Methanesulfonic Acid (>99%, bought at Sigma-Aldrich) CAS: 75-75-2. The molecular weight is 96.1 g/mol. Its density is 1.48 g/mL. It is a viscous, pale yellow liquid.
- Triflic Acid (98%, bought at Sigma-Aldrich). CAS: 1493-13-6. The molecular weight is 150.08 g/mol. Its density is 1.696 g/mL. It is a fumant, viscous liquid.

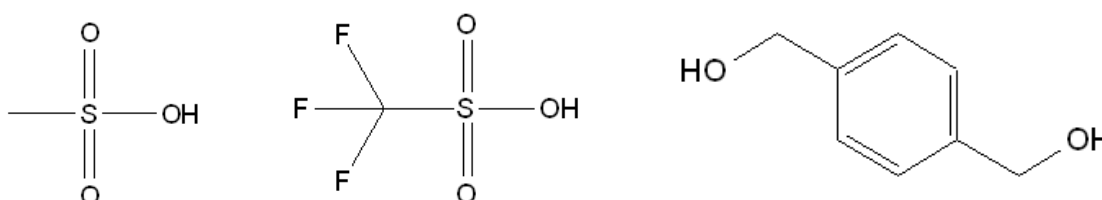


Fig. 9. Structure of the reagents used in the screening: Methanesulfonic acid (MSA), Triflic acid (TfOH) and *p*-phenylenedimethanol (PDM), respectively

2.2.-Model Reactions and Catalyst Screening

The conversion values for the kinetics experiments were calculated by H-NMR. The best signal to monitor the conversion of the monomer is the signal at 4.1 ppm (in CDCl_3), a triplet corresponding to 2 protons with an unclearly-defined triplet shape. As the polymerization occurs, the signal of these two protons, now part of the chain of the polymer, appears shifted slightly downwards, giving a well-defined triplet around 3.9 ppm (Fig. 11).

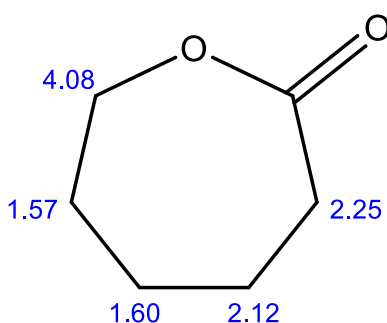


Fig. 10. Prediction of the H-NMR shifts of ϵ -CL using the ChemDraw Ultra software.

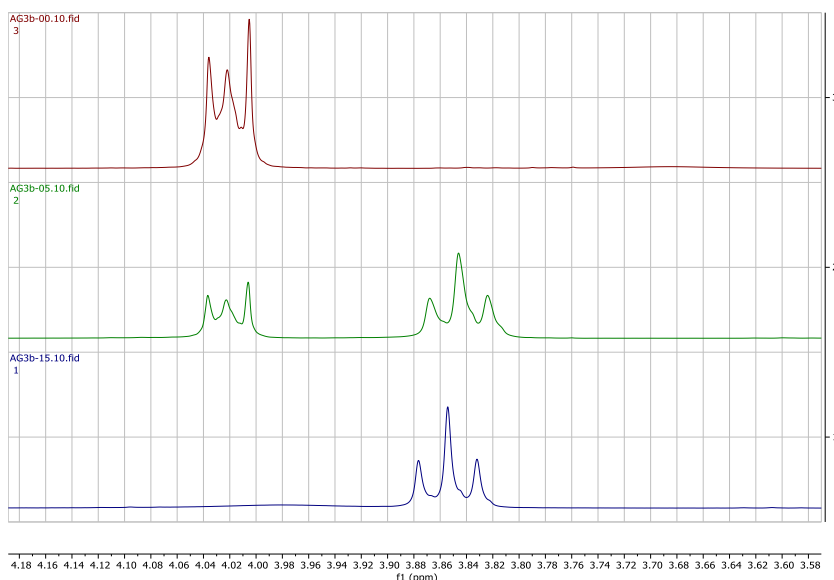


Fig. 11. H-NMR shifts (in CDCl_3) and shapes of ϵ -Caprolactone (in red), Polycaprolactone (in blue) and a mid-polymerization stage at $\sim 65\%$ conversion (in green) in the 4.0ppm region.

As both signals correspond to two protons, the following equation was used to calculate the conversion:

$$\text{Conversion (\%)} = \frac{\text{Area}_{3.9\text{ppm}}}{\text{Area}_{4.1\text{ppm}} + \text{Area}_{3.9\text{ppm}}} * 100 \quad \text{Eq. 1}$$

In-Solution Polymerization

A 0.56% molar ratio of both PDM initiator (8.9 mg, 0.064 mmol) and MSA catalyst (8 μL , 0.123 mmol) were mixed with $\epsilon\text{-CL}$ (2.4 mL, 22 mmol) in 19.5 mL (1.1 M) of toluene in a 50 mL vial. The initiator and monomer were dissolved in the toluene inside a heat-dried vial and placed under a N_2 atmosphere. The mixture was stirred at room temperature. Samples were taken, dissolved in CDCl_3 and the reaction quenched with TEA.

The molar ratios of both the catalyst and the initiator were increased to the maximum desired value. 5% molar ratio of both PDM (77.8 mg, 0.56 mmol) and MSA catalyst (71.5 μL , 1.225 mmol) were mixed with $\epsilon\text{-CL}$ (2.4 mL, 22 mmol) in 19.5 mL (1.1 M) of CH_2Cl_2 in a 50 mL heat dried vial, and placed under a N_2 atmosphere. The catalyst was added and the mixture was stirred at room temperature. Samples were taken, dissolved in CDCl_3 and the acid catalysis quenched with TEA.

Bulk Polymerization – Ideal Conditions

ϵ -CL (2.4 mL, 22 mmol) was placed in a heat-dried 7 mL vial and the vial was placed under a N₂ atmosphere. Then, 5% molar percentage initiator (PDM 75.4 mg, 0.55 mmol) was added to the vial, and the mixture was stirred for 5' to achieve a homogeneous solution. Then, 5% of either catalyst (MSA: 71.5 μ L, 1.225 mmol // TfOH: 99.5 μ L, 1.125 mmol) was added, and the mixture was stirred at room temperature. Samples of the mixture were taken until 15' had passed; then, the samples were dissolved in CDCl₃ and the acid catalysis was quenched with TEA.

Bulk Polymerization – Open System

As mentioned before, the environment on which stereolithography is performed is not as controlled as in the laboratory. In order to have a standard with which the activity of the photocatalysts could be compared, bulk polymerization was also performed in non-controlled conditions.

ϵ -CL (2.4 mL, 22 mmol) was placed in an undried 7 mL vial. Then, 5% molar percentage initiator (PDM 75.4 mg, 0.55 mmol) was added to the vial, and the mixture was stirred for 5' to achieve a homogeneous solution. Then, 5% of either catalyst (MSA: 71.5 μ L, 1.125 mmol // TfOH: 99.5 μ L, 1.125 mmol) was added, and the mixture was stirred at room temperature. Samples of the mixture were taken until 15' had passed; then, the samples were dissolved in CDCl_3 and the acid catalysis was quenched with TEA.

Also, the experiment was repeated using 2.5% molar percentage of initiator and catalyst. ϵ -CL (2.4 mL, 22 mmol) was placed in an undried 7 mL vial and 2.5% molar percentage initiator (PDM 37.7 mg, 0.275 mmol) and 2.5% of either catalyst (MSA: 35.8 μ L, 0.563 mmol // TfOH: 49.8 μ L, 0.563 mmol) were added, and the mixture was stirred at room temperature. Samples of the mixture were taken until 15' had passed; then, the samples were dissolved in CDCl_3 and the acid catalysis was quenched with TEA.

Stability of Monomer-Initiator Pair

The final characteristic we were looking for in our system was the stability of the mixture of the monomer and initiator; in order to be able to store the mixture, the polymerization must not start before the addition of the catalyst. To check the stability of the mixture ϵ -CL and 5% molar ratio of PDM were mixed in the vial, but no catalyst was added. Then, the mixture was left stirring for 24h. As in the previous reactions, samples were analysed by H-NMR.

2.3.- Synthesis of Photocatalysts

2.3.1.- Iodonium Salt Photocatalysts

Iodonium Salts Precursor Synthesis^[18.b]

As mentioned previously, the family of Iodonium salts is synthesized from the trifluoromethanesulfonate salt. On the first step, the precursor (4-Bromo-N-(p-iodophenyl)-1,8-naphthalimide) (Fig. 12) is synthesized.

4-bromo-1,8-naphthalic anhydride (1.5 g, 5.41 mmol, 1eq, MW = 277.07), 4-iodoaniline (2.37 g, 10.83 mmol, 2eq, MW = 219.02 g/mol) and imidazole (7.735 g, 108,33 mmol, 20eq, MW = 68.08 g/mol) were mixed in 45 mL of CHCl₃. The mixture was stirred at reflux temperature for 3h.

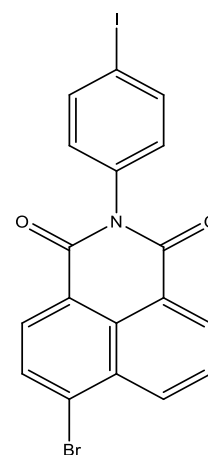


Fig. 12. Structure of the Iodonium Salt precursor

After cooling, the solvent was removed using a rotary evaporator and then washed with absolute ethanol. The heterogeneous mixture was stirred for 30' and then filtered under vacuum. The obtained solid was washed with more absolute ethanol and dried under vacuum to provide an off-white solid. An average yield of $\approx 85\%$ was obtained.

H-NMR (CDCl₃): 7.29 (2H), 7.92 (2H), 8.06 (1H), 8.29 (1H), 8.46 (1H), 8.71 (2H)

Iodonium-TfOH Salt Synthesis^[18.b]

The precursor (1 g, 2.09 mmol, 1eq, MW = 478.08 g/mol), m-CPBA (77%, 515 mg, 2.30 mmol, 1.1 eq, MW = 172.57 g/mol) and benzene (200 μ L, 179.5 mg, 2.30 mmol, 1.1 eq, MW = 78.11 g/mol) were mixed in 25 mL of CH₂Cl₂. TfOH was added (350 μ L, 595 mg, 3.96 mmol, 1.9 eq) until the solution became transparent with a non-dissolved precipitate on the bottom.

The mixture was then stirred for 1h30' at room temperature. Then 25 mL of diethyl ether were added to the mixture, and the solid was filtered and washed with more ether; it was then dried under vacuum to provide a pale orange solid. The final structure of Iodonium-TfOH is shown in Fig. 13.

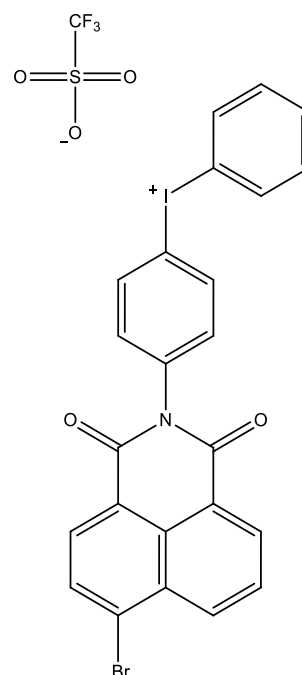


Fig. 13. Structure of the Iodonium-TfOH catalyst.

H-NMR (d-Acetone): 7.78 (5H), 8.09 (1H), 8.29 (1H), 8.51 (5H), 8.70 (2H)

F-NMR (d-Acetone): -78.9 ppm

Iodonium-MSA Salt Synthesis^[18.b]

Iodonium-TfOH (240 mg, 0.34 mmol, 1 eq, MW = 704.25 g/mol) was mixed with 6 mL of CH₃CN and stirred under a N₂ atmosphere. Then, MSA (133 μL, 197 mg, 2.05 mmol, 6 eq) is added with a micropipette, and the mixture is stirred at room temperature and under N₂ atmosphere for 24h.

After this time, the solvent was eliminated using a rotatory evaporator, and the solid washed with water to get rid of the excess of acid. It was then dried under vacuum to provide an off-white solid. The yield of this reaction was of 57%. The final structure of Iodonium-MSA is shown in Fig. 14.

H-NMR (d-Acetone): , 2.80 (3H), 7.31 (1H), 7.73 (2H), 7.95 (1H), 8.06 (1H), 8.26 (1H), 8.51 (3H), 8.69 (2H)

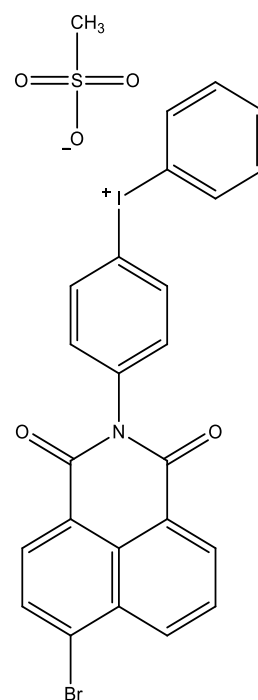


Fig. 14. Structure of the Iodonium-MSA catalyst

2.3.2.- Non Ionic Naphthalimide Photocatalysts

Naphthalimide Based Bromo-Precursor Synthesis^[19]

4-bromo-1,8-naphthalic anhydride (1 g, 3.43 mmol, 1eq, MW = 277.07), hydroxylamine hydrochloride (337.25 mg, 4.8 mmol, 1.4eq, MW = 69.49 g/mol) were mixed in 7mL of pyridine and placed in a N₂ inert atmosphere. The mixture was stirred at 100°C for 16h.

After cooling, the mixture was added onto 70mL 1M HCl, and the precipitate was filtrated and washed with water under vacuum. The obtained solid was then recrystallized in hot ethanol. A deep brown solid was obtained, with an average yield of ≈45% was obtained. The final structure of the precursor for Naphthalimide based non-ionic catalysts is shown in Fig. 15.

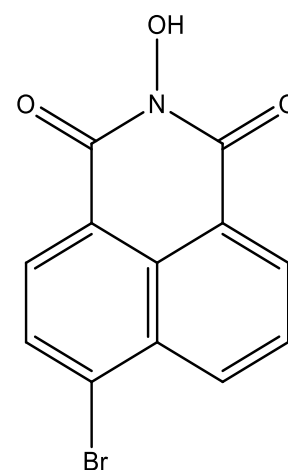


Fig. 15. Structure of the bromo-precursor

H-NMR (CDCl₃): 7.92 (1H), 8.13 (1H), 8.51 (1H), 8,72 (2H)

TLC (CH₂Cl₂): Rf of the product: 0,0

Rf of the naphthalimide: 0,7

NonINaph-MSA Synthesis^[19]

The bromine containing precursor (600 mg, 2.05 mmol, 1eq, MW = 292.9 g/mol) was mixed with methanesulfonyl chloride (158.5 mg, 2.05 mmol, 1eq, MW = 114.55 g/mol) and TEA (286 μ L, 207.4 mg, 2.05 mmol, 1eq, MW = 101, 2 g/mol) in 8 mL of toluene. The mixture was placed under a N₂ protective atmosphere, and stirred at room temperature for 16h.

The mixture was then filtered under vacuum and washed with 4x25 mL saturated NaHCO₃, and then with 2x25 mL deionized water. Then, the organic phase was dried with MgSO₄ and the solvent removed with a rotatory evaporator. Finally, the collected yellow solid was then recrystallized in dichloromethane and dried under vacuum. A yield of 57% was achieved. The structure of NonINaph-MSA is shown in Fig. 16.

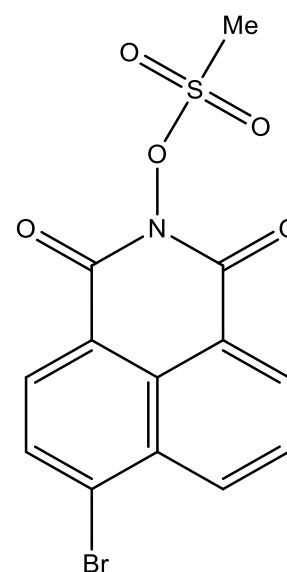


Fig. 16. Structure of the NonINaph-MSA catalyst

H-NMR (CDCl₃): 3.61 (3H), 7.92 (1H), 8.11 (1H), 8.49 (1H), 8,73 (2H)

TLC (CH₂Cl₂): Rf of the product: 0,0

Rf of the naphthalimide: 0,7

2.3.3.- Non Ionic Anthrone Photocatalysts

Anthrone-MSA Synthesis

The precursor obtained by Quinten Thijssen (Fig. 17), 10-(hydroxyimino)anthracen-9(10H)-one (504 mg, 2.25 mmol, 1 eq., MW = 224 g/mol) is dissolved in 50 mL of acetone, in a heat dried flask and under a protective N₂ atmosphere. The solution was placed in an ice bath, and TEA was added (312 μL, 2.24 mmol, 1 eq, MW = 101.2 g/mol). Finally, methanesulfonyl chloride was added (175 μL, 259 mg, 2.26 mmol, 1 eq., MW = 114.55 g/mol). The mixture was left stirring for 16 hours.

The solution was then filtered and the solvent was eliminated using a rotatory evaporator. The obtained solid was washed with water to get rid of the ammonium chloride salt. The catalyst and the starting material were separated using a chromatographic column in pure CH₂Cl₂. The isolated catalyst was dried under vacuum. A yield of 26% was achieved. The final structure of NonlAnth-MSA is shown in Fig. 18.

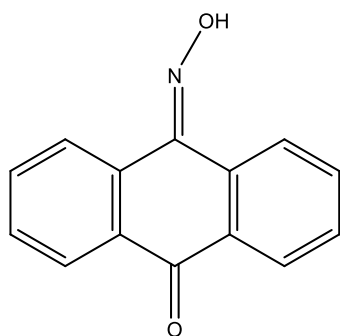


Fig. 17. Structure of the anthrone based precursor

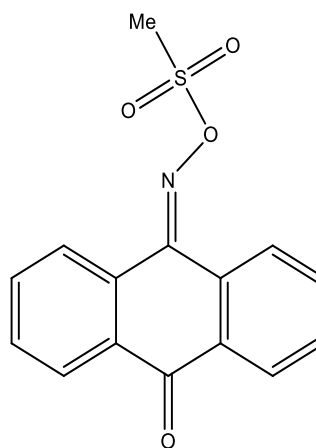


Fig. 18. Structure of the NonlAnth-MSA

H-NMR (CDCl₃): 3.34 (3H), 7.74 (4H), 8.28 (2H), 8.55 (2H)

TLC (CH₂Cl₂): R_f of the product: 0,7
R_f of the precursor: 0,3

2.4.- Photocatalyst Testing

As the final step of the project, we wanted to measure the catalytic power of the photocatalysts synthesized. In order to be able to compare the results with the ones obtained with the pure acids, the same conditions of temperature, atmosphere and molar ratios were employed.

The testing experiments consisted of two different phases with two different goals:

- First, the monomer-photocatalyst-initiator mixture was prepared and left stirring for 24h. Samples were taken periodically to monitor the polymerization reaction. The idea behind this experiment is to check if the mixture is stable and if it could be prepared beforehand and stored prior to use.
- The second part of the experiment tested the response of the mixture to UV irradiation. The mixture was exposed to UV irradiation while stirring, and samples were taken periodically to monitor the polymerization reaction.

The UV source used for these irradiation experiments was a LightiningCure™ LC-L1V3 UV-LED light source. According to the manufacturer, the light source has an output of 450 mW at 365 nm. The light source was placed at 10 cm over the mixture surface.

2.4.1.- Iodonium Salt Photocatalysts

Stability and Irradiation with 2.5% Iodonium-TfOH

Iodonium-TfOH (102.4 mg, 0.1454 mmol, 5 eq, MW = 704.25 g/mol) was mixed in a undried vial and not-inert atmosphere with PDM (11.0 mg, 0.0796 mmol, 2.5 eq) and ϵ -CL (320 μ L, 342.4 mg, 2.595 mmol, 100 eq). This 5% molar ratio mixture was not homogeneous, and after stirring there were two separated phases with the catalyst precipitated on the bottom of the vial. The same amount (320 μ L, 342.4 mg, 2.595 mmol, 100 eq) of additional ϵ -CL was added, increasing the amount of monomer to 200 eq, and achieving a 2.5% molar ratio of catalyst and initiator.

This experiment was performed twice. In the first try, as the photocatalyst proved to be non-soluble, the mixture was sonicated on ice to avoid thermal degradation, but no solubilisation was obtained. The mixture was then dissolved in acetone and then the solvent was eliminated using a rotatory evaporator. However, during the evaporation the catalyst precipitated from the solution. What is more, the amount of acetone needed to dissolve the amount of catalyst used was 4 or 5 times the volume of the monomer. The mixture was left stirring at room temperature and non-inert atmosphere for 24h, taking samples at 0, 1, 2, 4 and 24h.

In the second try, as there were concerns about the premature degradation that these solubilisation methods may cause, the mixture was only stirred with a Vortex machine to achieve a homogeneous suspension.

During this stability test, the sample was kept away from any UV source, covering the vial with aluminium foil and keeping it inside the UV chamber. The conversion was followed by H-NMR, using the same 4.2ppm and 4.0ppm signals (for ϵ -CL and PCL respectively) used during the screening process; the samples were dissolved in $CDCl_3$ and quenched with TEA.

After 24h, the sample was placed in a UV chamber. Due to the size of the vial, the mixture was around 2 mm thick. The surface of the mixture was placed 10 cm away from the lamp. The sample was irradiated by UV light, and samples were taken after 1, 2, 5, 10 and 15 minutes of irradiation. The samples were dissolved in CDCl_3 and quenched with TEA.

Another method was also tried in order to solubilize the catalyst. The catalyst was dissolved in acetone, mixed with the monomer and initiator, and then the acetone was eliminated using a rotatory evaporator. However, during the evaporation the catalyst precipitated from the solution. What is more, the amount of acetone needed to dissolve the amount of catalyst used was often 4 or 5 times the volume of the monomer. Thus, it was decided that the sonication/vortex stirring method was the best way to obtain a uniform distribution of catalyst in the sample.

2.4.2.- Non-Ionic Naphthalimide Photocatalysts

Stability and Irradiation with 2.5% NonINaph-MSA

NonINaph-MSA (100.4 mg, 0.2595 mmol, 2.5 eq, MW = 386.9 g/mol) was mixed in a undried vial and not-inert atmosphere with PDM (18.2 mg, 0.132 mmol, 1.25 eq) and ϵ -CL (1010 μ L, 1081 mg, 9.47 mmol, 100 eq). This 2.5% molar ratio mixture was not homogeneous as the catalyst was not soluble in the monomer, and the mixture was shaken in a Vortex machine to obtain a uniform suspension.

The mixture was left stirring at room temperature and non-inert atmosphere for 24h, taking samples at 0, 1, 2, 4 and 24h. During this stability test the sample was kept away from any UV source, covering the vial with aluminium foil and keeping in inside the UV chamber. The samples were dissolved in CDCl₃ and quenched with TEA. The conversion was followed by H-NMR, using the same 4.2ppm and 4.0ppm signals (for ϵ -CL and PCL respectively) used during the screening process.

After 24h, the sample was placed in a UV chamber. Due to the size of the vial, the mixture was around 3 mm thick. The surface of the mixture was placed 10 cm away from the lamp. The sample was irradiated by UV light, and samples were taken after 1, 2, 5, 10 and 15 minutes of irradiation. The samples were dissolved in CDCl₃ and quenched with TEA.

2.4.3.- Non-Ionic Anthrone Photocatalysts

Photolysis of 0.2M NonIAnth-MSA

NonIAnth-MSA (60.8 mg, 0.2026 mmol, MW = 300 g/mol) was dissolved in 1.0 mL of chloroform to make a solution with a concentration of catalyst similar to the used in the polymerization experiments; this concentration of catalyst is around 0.2M (0.22 mmol in 1.01 mL of caprolactone).

The solution was placed 10 cm away from the UV light source. Samples were taken after 10, 20, 40, 80, 160, 320, 640 and 1280 seconds, and put in vials in the dark to evaporate the solvent. Then the solid samples were dissolved in CDCl₃ and an H-NMR analysis was performed.

To calculate the degree of degradation of the catalyst, the peaks at 3.35 ppm and 2.95 ppm were compared (Fig 19). The protons from the methyl group had a shift of 3.35 ppm, whereas those protons had a shift of 2.95 ppm when the acid was released (as seen at an H-NMR spectrum of pure MSA).

$$\text{Conversion (\%)} = \frac{\text{Area}_{2.95 \text{ ppm}}}{\text{Area}_{3.35 \text{ ppm}} + \text{Area}_{2.95 \text{ ppm}}} * 100 \quad \text{Eq. 2}$$

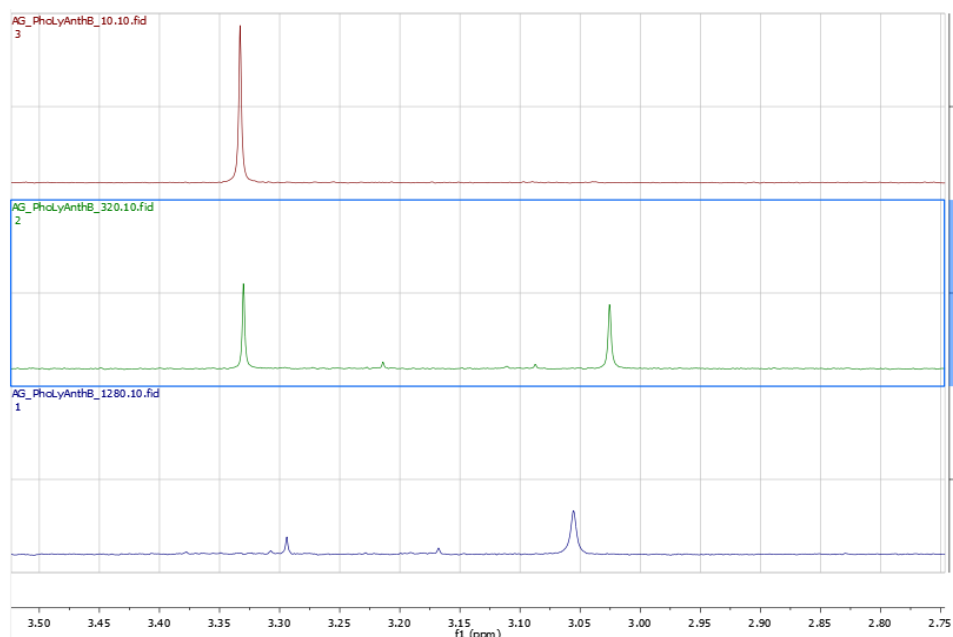


Fig. 19. H-NMR signals at 3.3 ppm and 3.0 ppm corresponding to the protons of the methyl group attached to the photocatalyst and as free MSA, respectively.

Photolysis of 0.01M NonIAnth-MSA

The same experiment was repeated but at much lower concentration. NonIAnth-MSA (4.6 mg, 0.015 mmol, MW = 300 g/mol) was dissolved in 1.5 mL of chloroform to make 1M solution.

The solution was placed 10 cm away from the UV light source. Samples were taken after 10, 20, 40, 80, 160, 320, 640 and 1280 seconds, and put in vials in the dark to evaporate the solvent. Then the solid samples were dissolved in CDCl₃ and an H-NMR analysis was performed. The percentage of acid released was measured the same way.

Stability and Irradiation with 2.5% NonIAnth-MSA

NonIAnth-MSA (75.8 mg, 0.253 mmol, 2.5 eq, MW = 300 g/mol) was mixed in a undried vial and with a not-inert atmosphere with PDM (35.4 mg, 0.256 mmol, 2.5 eq) and ϵ -CL (1078 μ L, 1153 mg, 10.10 mmol, 100 eq). The catalyst was not soluble at first, but after being shaken for 30" with a Vortex machine the catalyst dissolved in the monomer.

The mixture was left stirring at room temperature and non-inert atmosphere for 24h, taking samples at 0, 1, 2, 4 and 24h. During this stability test the sample was kept away from any UV source, covering the vial with aluminium foil and keeping in inside the UV chamber. The samples were dissolved in CDCl₃ and quenched with TEA. The conversion was followed by H-NMR, using the same 4.2ppm and 4.0ppm signals (for ϵ -CL and PCL respectively) used during the screening process.

After 24h, the sample was placed in a UV chamber. Due to the size of the vial, the mixture was around 3 mm thick. The surface of the mixture was placed 10 cm away from the lamp. The sample was irradiated by UV light, and samples were taken after 1, 2, 5, 10 and 15 minutes of irradiation. The samples were dissolved in CDCl₃ and quenched with TEA.

3.- Results and Discussion

3.1.- Model Reactions and Catalyst Screening

The reactions described in the literature are quite different from the conditions on which 3D printing is carried out. Most articles describe in-solution polymerizations with very long reaction times. Almost all of them carry out the ROP reactions under an inert atmosphere. The goal of our project was the development a catalyst for bulk polymerization with fast reaction times and flexible condition requirements; because of that, the results described in the literature are useful as a starting point but are not valid as a standard with which the results yielded by the photocatalyst experiments could be compared.

These series of experiments would serve as model reactions for the ring opening polymerization of model reactions for ϵ -CL, as well as to establish a framework with which to compare the data obtained from the experiments with the photocatalysts. First, we tried to replicate an in-solution reaction described in the literature. As the results of the reaction were not successful, another in-solution reaction was designed and carried out with better results.

Then, bulk polymerization was carried out using both MSA and TfOH as catalysts, monitoring the conversion rate using H-NMR. The bulk-polymerization reactions were performed using the maximum acceptable catalyst and initiator molar ratio, 5%. These reactions were performed in controlled conditions of humidity and under an inert atmosphere. However, in a 3D printing setup, the control the humidity and the reactivity of the atmosphere are less controlled; under real conditions, the catalytic power of our compounds could be different. In order to have a standard with which the activity of the photocatalysts could be compared, bulk polymerization was also performed in non-controlled conditions with 2 different catalyst and initiator molar ratios: 5% and 2.5%.

Finally, we wanted to check the stability of the monomer and initiator mixture without the catalyst, to check if the combination used in our experiments was suitable for storage.

In solution, polymerization was performed under the conditions described in the literature^[22]. We were not able to replicate the polymerization in solution described in the literature^[22] using only 0.56% of molar percentage of catalyst, as after 2h the conversion values were still negligible. In the second reaction, with 5% of catalyst and initiator molar percentage, the reaction speed was obviously faster than the speed described in the paper, obtaining an 80% conversion at 30' (Table 1).

Tab. 1. Conversion vs Time data from the In Solution Polymerization experiment using 5% molar percentage of MSA and PDM.

In Solution Polymerization							
Time (m)	0	10	30	50	70	90	24h
Conversion (%)	0	21.9	79.7	95.2	≈100	≈100	≈100

We performed bulk polymerization of ϵ -CL with both of the catalysts described in the literature: MSA and TfOH. First, the bulk polymerization was performed under ideal conditions, under a N₂ atmosphere and in a dry environment. Under these conditions, the ROP would be faster than under use-conditions, but it would give us a value against other results would be compared. The reactions for both catalysts were performed following the same procedure and under the same conditions. In bulk, the ROP was much faster (Table 2):

- Under inert atmosphere and in a dry environment, 63% conversion was achieved by MSA and ≈100% by TfOH by 5' with a 5% molar ratio of both the catalyst and the initiator.
- When the reaction was performed without an inert atmosphere and without drying the reaction environment the reaction speed was slower. However, >80% conversion was obtained with both catalysts at 10' (Fig. 20).
- When the catalyst and initiator ratios were reduced to 2.5% the overall reaction speed slowed down even more, with MSA not being able to achieve the 80% threshold by 15' and TfOH struggling to achieve 100% conversion (Fig. 21).

Also, quite different qualitative macroscopic behaviour was observed for both catalysts. With MSA the mixture got progressively more viscous, especially after the 7th minute (at 5% ratio); this increase in viscosity is approximately related to the increase of the conversion. At around 11'20" the magnetic stirrer stopped rotating due to the high

viscosity of the mixture. On the other hand, with TfOH the viscosity increased only after the 5th minute (at 5% catalyst molar ratio), and the qualitative change in viscosity happened in a short span of time; by that time 100% of conversion had been long achieved.

Tab. 2. Conversion vs Time data from the different Bulk Polymerization experiments

Times (min)	Conversion (%)					
	5% MSA	5% TfOH	5% MSA Open	5% TfOH Open	2.5% MSA Open	2.5% TfOH Open
0	0.0	0.0	0.0	0.0	0.0	0
1	5.7	93.0	3.0	19.4	10.7	21.3
2	17.4	100.0	9.0	49.5	13.8	37.5
5	63.2	100.0	35.5	100.0	23.7	87.9
10	100.0	100.0	80.9	100.0	42.5	93.4
15	100.0	100.0	100.0	100.0	62.55	100

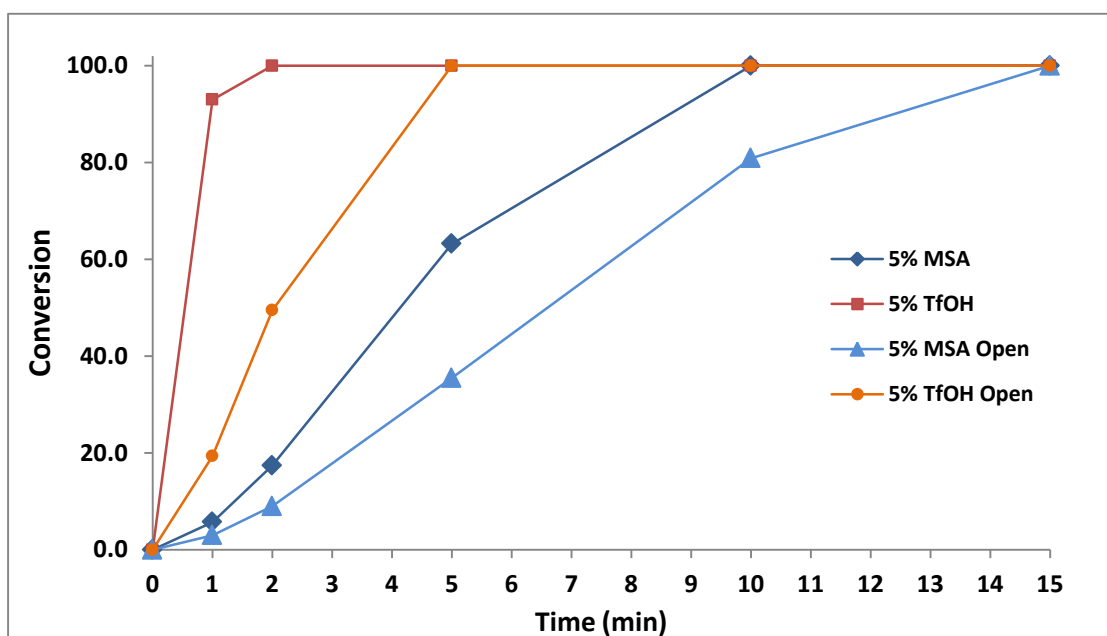


Fig. 20. Conversion vs Time comparison graph of the different 5% initiator and catalyst molar percentage experiments

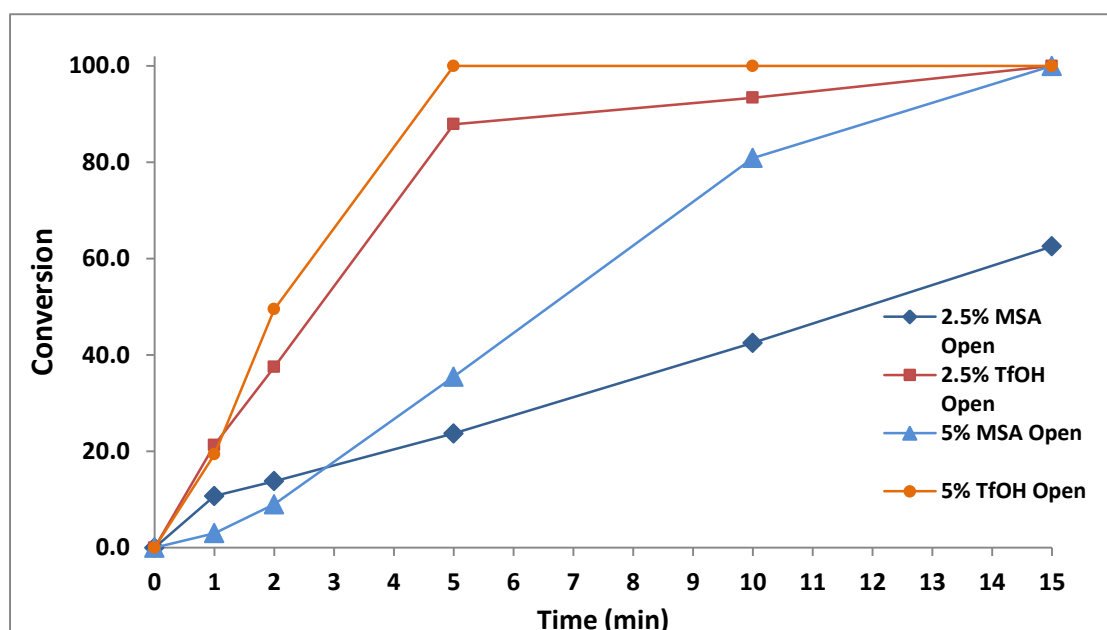


Fig. 21. Conversion vs Time comparison graph of the different experiments performed in open air.

According to these results, it is clear that TfOH is strongly more active than MSA when catalysing the ROP of ϵ -CL; it could easily be related to the difference between the pKa of both acids (-14.7 of TfOH against the -1.9 of MSA). However, in the literature it has been reported that the relationship between the pKa of an acid and its catalytic activity is not clearly related^[13], and that the activity of the catalysts is probably related to the catalyst: initiator ratio. According to Gazeau-Bureau *et al.*, the optimal ratio for TfOH would be the 1:1 ratio used during our experiments, and MSA could be more active when the ratio is favourable to the initiator. This would be caused by the excessive acidity of TfOH, causing competitive protonation of the initiator as well as the monomer. However, the exploration of multiple monomer/catalyst/initiator ratios and their behaviour with both catalysts is beyond the scope of this project.

The difference between inert atmosphere/open air was the same for MSA and TfOH; both reactions were slower under air. TfOH is known to be hygroscopic and more sensitive to water than MSA, but no significant differences were found on the behaviour of MSA and TfOH.

However, high conversion values were obtained with the 2.5% molar ratio at the first few minutes. With both TfOH and MSA the conversion values were higher using a 2.5% molar ratio of catalyst and initiator than when 5% ratios were used. This phenomenon could be related to the experimental results obtained by Gazeau-Bureau *et al.* The low concentration of acid and initiator could speed up the reaction in the beginning. After 2 minutes, in the 5% ratio experiments the higher amount of catalyst and active chains (created because of a higher concentration of initiator) is enough to overcome the initial lead and yield higher conversions.

Thus, both acid catalyst could be used for our project, as both catalysts are able to obtain >80% conversion values at 15' when a molar ratio of 5% is used. However, the catalytic power of MSA is not strong enough to obtain the threshold of 80% conversion when 2.5% molar ratio is used.

3.2.- Synthesis of Photocatalysts

According to the results of the model reactions (see p. 34), both MSA and TfOH are able to catalyse the ROP of caprolactone within acceptable time values. It has been reported in the literature^{[1][17]} that there are different options to transform these acids into photosensitive catalysts. In our project, two of these options were contemplated:

The first option would be to create a binary salt formed by a photosensitive cation and the deprotonated acid counteranion. When irradiated with UV light, the photosensitive cation would decompose, freeing the protonated acid ready for catalysis. The most usual photosensitive cations are highly conjugated aromatic compounds containing a positive iodine atom; this family of salts is called the iodonium family.

The second option was to create a single photosensitive molecule based on the same naphthalimide ring. The naphthalimide ring acts as a UV-A chromophore, and the protoacid would be covalently linked to this ring. Upon irradiation, these molecules undergo cleavage processes that break that link, releasing the acid ready to catalyse the reaction. Naphthalimide is chosen as the base to build the chromophore because of its ability to absorb low energy ultraviolet irradiation, UV-A.

3.2.1.- Iodonium Salt Photocatalysts

As mentioned above, the family of Iodonium salts is synthesized from the trifluoromethanesulfonate salt, and the synthesis of this salt is carried out in two steps. On the first step, the precursor (4-Bromo-N-(p-iodophenyl)-1,8-naphthalimide) is synthesized from 4-bromo-1,8-naphthalic anhydride, 4-iodoaniline and imidazole following the work described by Dr. Zivic^[18.b]. This reaction yields a trisubstituted, cyclic imide with an average yield of 85%. This first compound acts as the precursor to the different catalysts of the Iodonium Salts family (Fig. 22).

This precursor contains a terminal monovalent iodine atom. Once the precursor is synthesized the next step is to oxidize the iodine atom to form a cation, and then stabilize the positive charge through conjugation. To oxidize the iodine atom a strong oxidizer is needed, and in our case m-CPBA was used. To stabilize the positive charge a benzene ring was linked to form divalent iodine, so alongside m-CPBA benzene was also added, stabilizing the iodine cation. With the addition of triflic acid, a salt is formed between the cation and the conjugated base of TfOH.

This free-radical reaction proved to be quite complicated to perform, as the addition of the triflic acid yielded very different results depending on unknown factors. Triflic acid was added until noticeable changes in the solution occurred (the solution became green and transparent with a non-dissolved precipitate on the bottom); however, depending on those unknown factors this change happened after between 2 or 4 equivalents of triflic acid were added, or sometimes did not happen at all. Also, the compound precipitated from the reaction solution, but sometimes the solvent of the liquid phase had to be eliminated using a rotatory evaporator, and re-dissolved in CH₂Cl₂. It was then precipitated with ether, filtered and dried under vacuum again.

These problems made that this second step had an average yield of 30%, with some batches having a yield of 60-65% and other reactions failing to synthesize the compound. The purity of the obtained compound also varied greatly, but it could be purified by recrystallization in chloroform.

Iodonium-MSA is not synthesized following this route, but by anion substitution. In order to change the anion of the salt, Iodonium-TfOH is dissolved and excess amounts of MSA are added. This reaction was performed following the similar anion substitution performed by Dr. Zivic^[18.b], although the substitution described in his work used *p*-toluenesulfonic acid as the substituting anion. The reaction had a yield of 57%, but the purity of the off-white solid obtained was not measured. The H-NMR spectrum shows multiple peaks that could not be identified, and the F-NMR spectra showed contamination by fluorine, indicating the presence of triflate anions. Recrystallization proved futile, and no chromatographic column could be performed.

As this mixture of compounds was not soluble in ϵ -CL, the compound was abandoned in favour of the exploration of non-ionic photocatalysts.

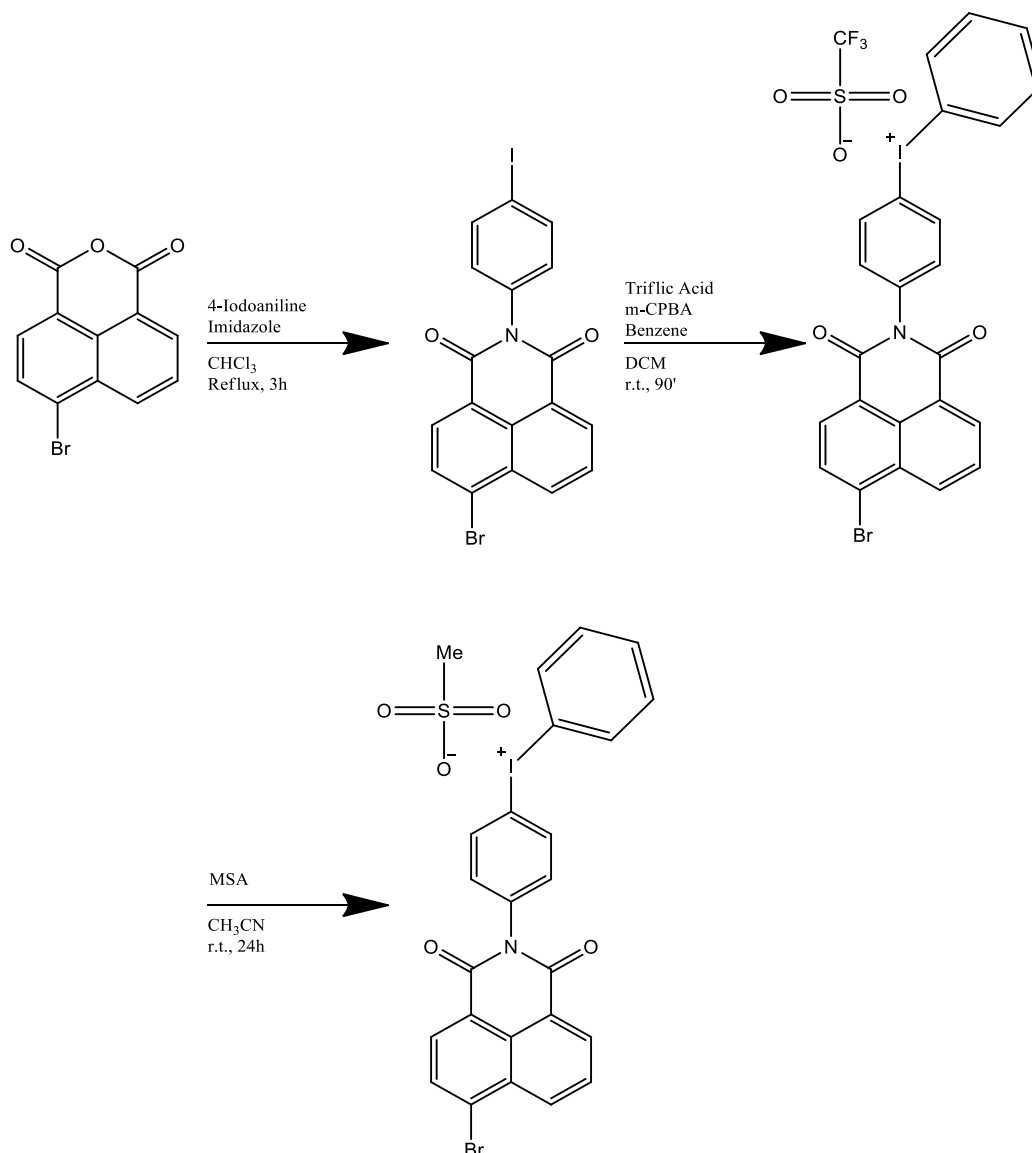


Fig. 22. Overview of the synthetic process of the Iodonium Salt family catalysts.

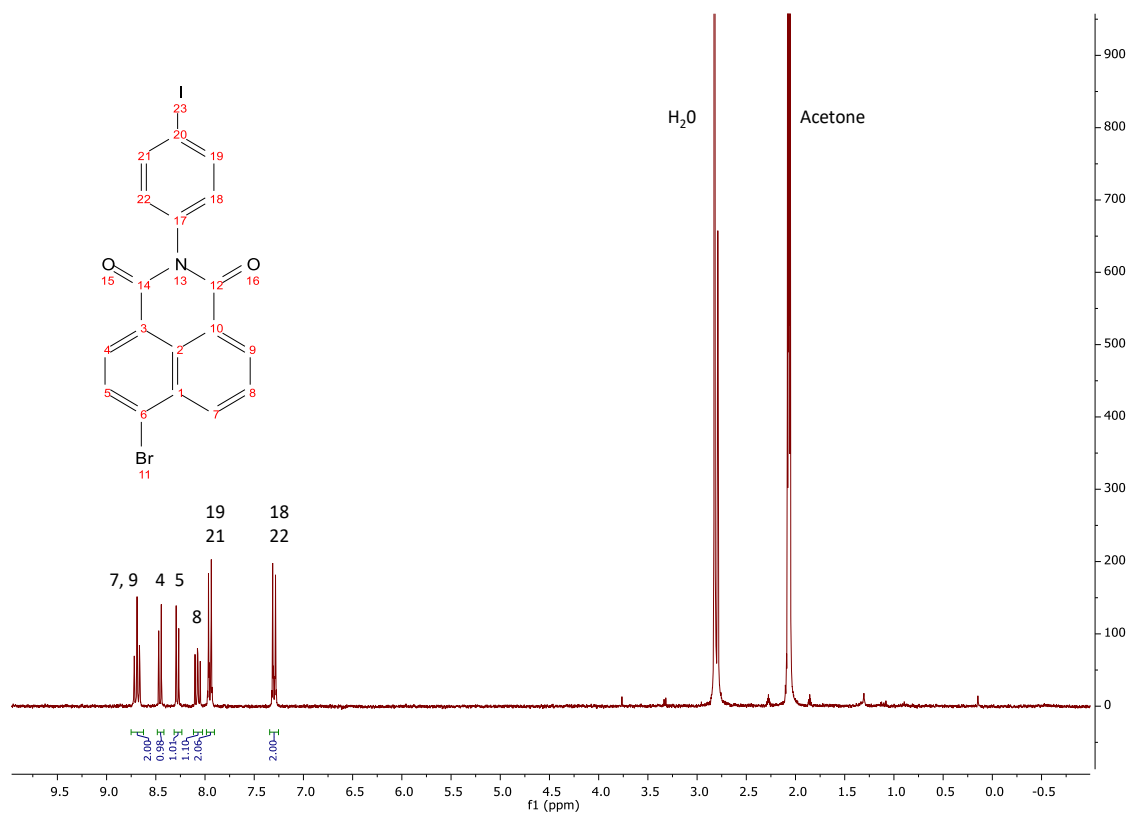


Fig. 23. H-NMR spectra and assignments of the precursor for the Iodonium Salt family. Performed in d-Acetone.

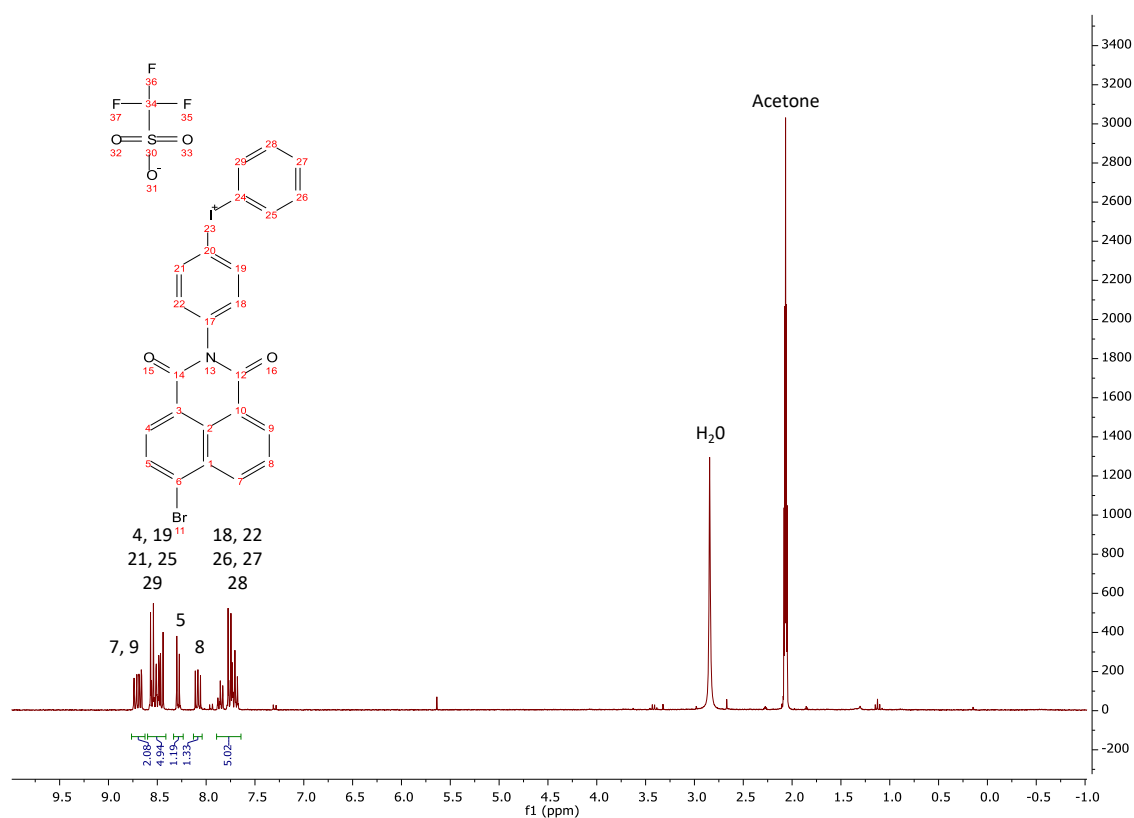


Fig. 24. H-NMR spectra and assignments of Iodonium-TfOH. Performed in d-Acetone.

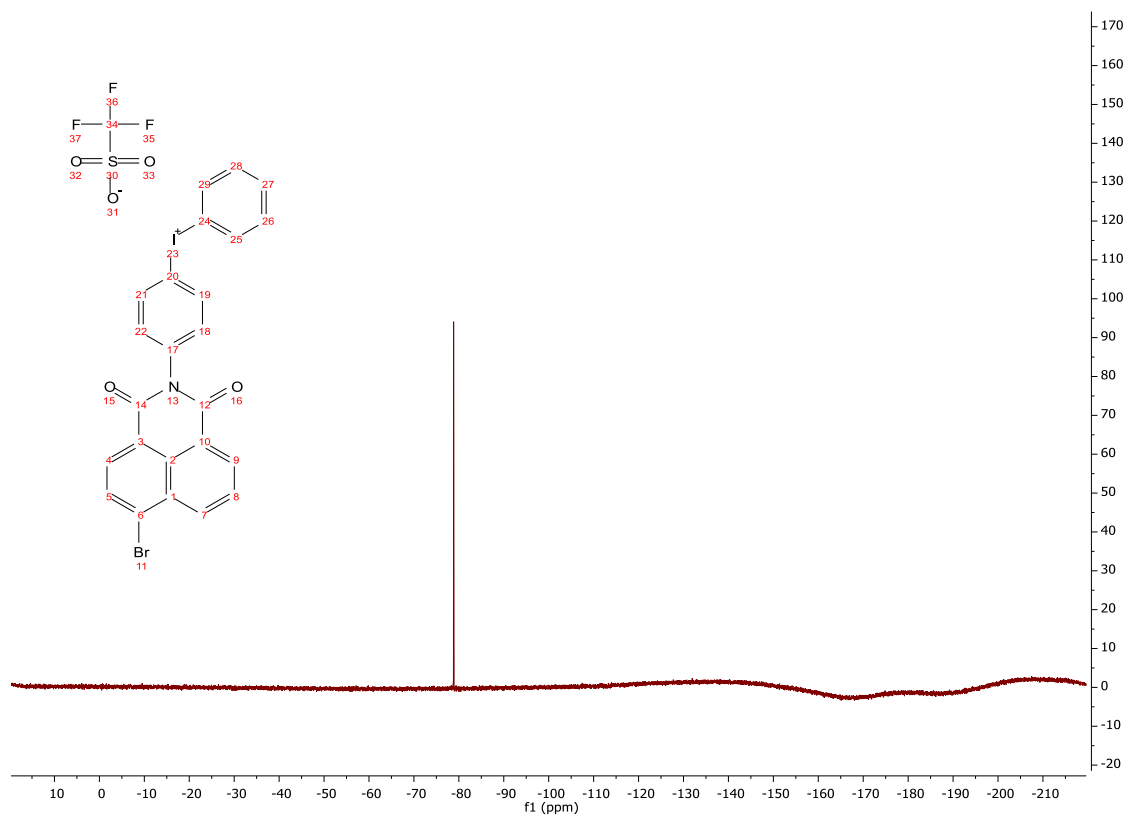


Fig. 25. F-NMR spectra of Iodonium-TfOH. Performed in d-Acetone.

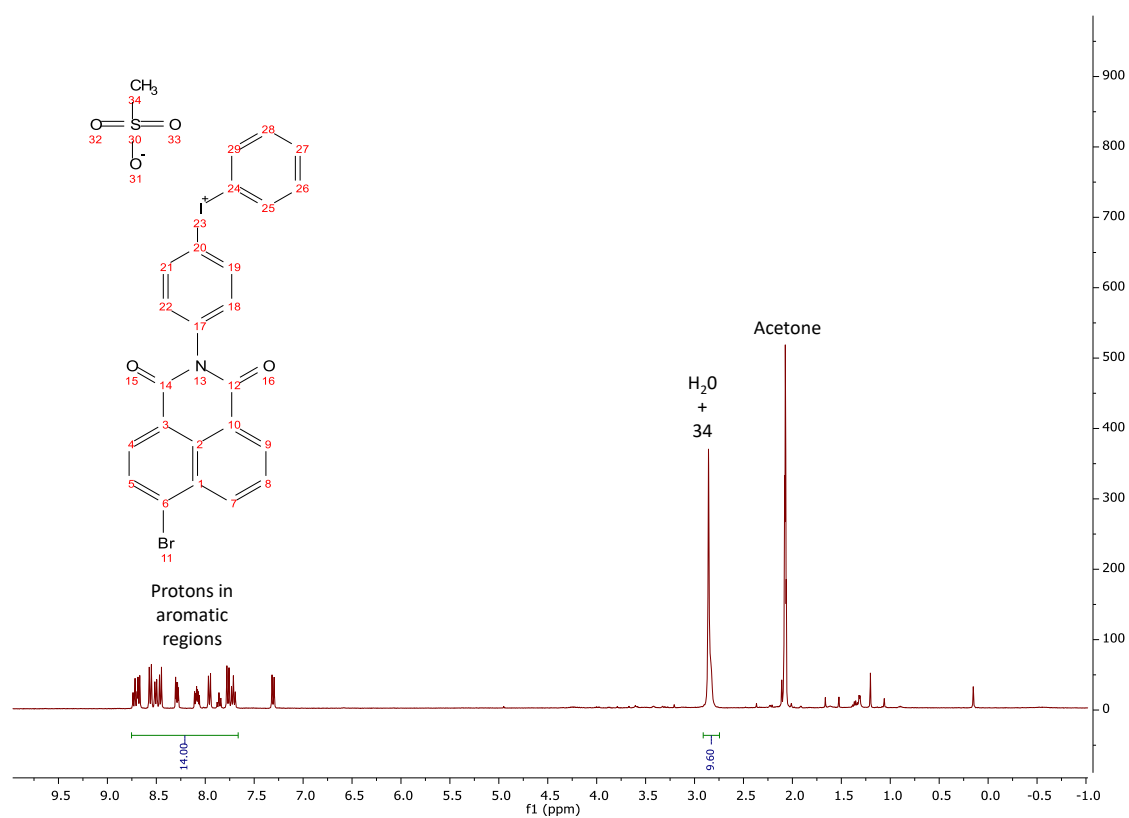


Fig. 26. H-NMR spectra and assignments of Iodonium-MSA. Performed in d-Acetone.

Due to the contamination of the solid, there are too many signals in the aromatic region of the H-NMR spectrum. The predictions of the spectra by MestReNova and ChemDraw were not helpful, and no assignment could be done on those peaks. Also, the signal for the methyl group of the methanesulfonate anion and the signal for the water impurities on the solvent overlap, yielding an integral way over its true value and creating the “belly” on the right of the peak.

3.2.2.- Non Ionic Naphthalimide Photocatalysts

Again, the family of these naphthalimide-based photocatalysts is synthesized from a common precursor (Fig. 27). On the first step, the precursor (6-Bromo-2-hydroxy-1H-benzo[de]isoquinoline-1,3(2H)-dione) is synthesized from 4-bromo-1,8-naphthalic anhydride, hydroxylamine hydrochloride and pyridine. The reaction is performed following the work described by Iwashima et al^[19]. A deep brown solid is obtained, with an average yield of $\approx 45\%$ was obtained.

After this precursor is synthesized, NonINaph-MSA is synthesized by the nucleophilic substitution of methanesulfonyl chloride. The precursor is mixed with methanesulfonyl chloride in solution, and TEA is added to neutralize the HCl released; this shifts the equilibrium forward and should increase the yield. The final yield of this reaction is 68%, forming a pale yellow solid.

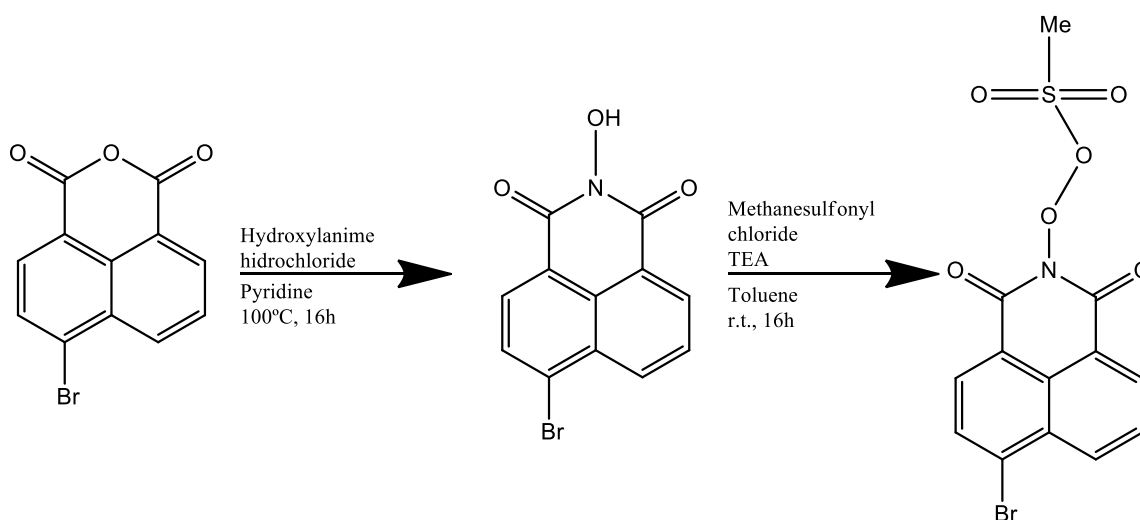


Fig. 27. Overview of the synthetic process of the NonINaph-MSA.

Due to solubility problems in ϵ -CL of the bromo-substituted NonINaph-MSA (see p. 52), another version of the precursor was prepared. This new version would have an alkoxy substituent instead of bromine, and the solubility in ϵ -CL may improve (Fig. 28). The reaction was performed in two steps as the reactivity of the N-hydroxylamine could be problematic. The introduction of a hexyl chain was performed through an Ullman condensation. Sodium hexylate was prepared from 1-Hexanol using metallic sodium, and after the bubbling stopped the precursor, copper (I) bromide and ethyl acetate were added to perform the condensation following the description of the work of Sambigiato et al^[23]. However, the product did not precipitate from the hexanol, and evaporating the solvent without degrading the compound proved impossible; precipitating the compound using other solvents was also useless. After two consecutive chromatographic columns the amount of hexanol was reduced greatly, but the amount of compound left was negligible too. As it was deemed inviable to continue with the isolation of that compound, and taking into account that the process to create the alkoxy-precursor had taken up to ten days with no real possibility of obtaining a significative amount of product, this line was given up.

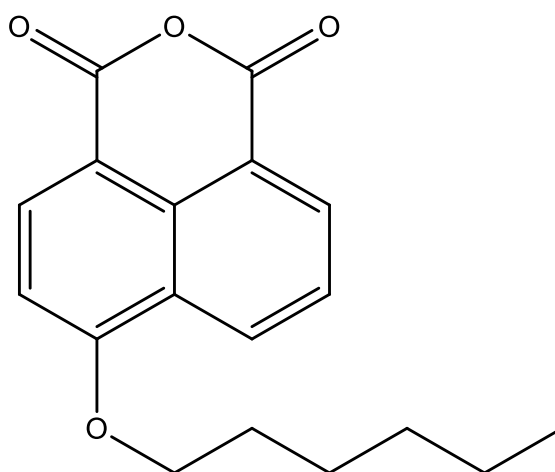


Fig. 28. Structure of the Non Ionic precursor containing the alkoxy chain.

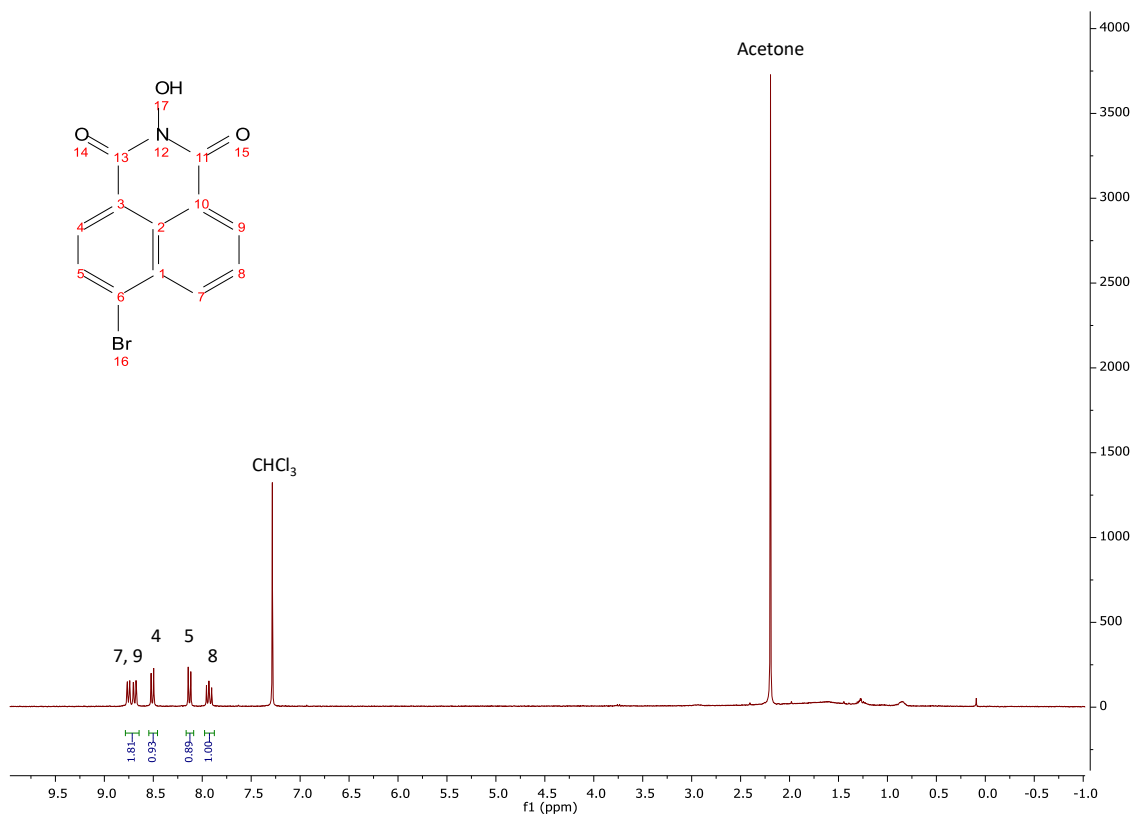


Fig. 29. H-NMR spectra and assignments of the precursor for the naphthalimide family. Performed in CDCl₃.

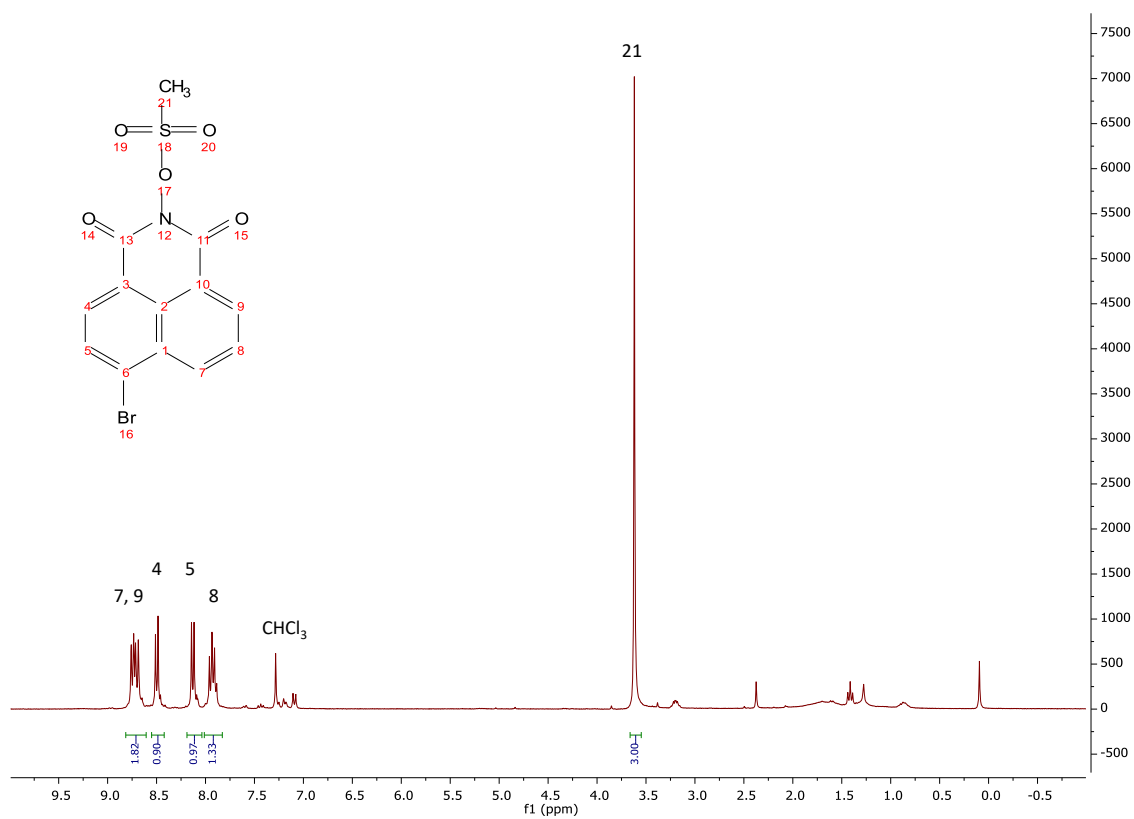


Fig. 30. H-NMR spectra and assignments of NonINaph-MSA. Performed in CDCl₃.

3.2.3.- Non Ionic Anthrone Photocatalysts

Again, the family of these naphthalimide-based photocatalysts is synthesized from a common precursor, 10-(hydroxyimino)anthracenone. This common precursor is synthesized from anthrone and t-butyl nitrite using metallic sodium and ethanol as described by Surkau et al.^[24] However, this precursor was synthesized and kindly provided by a fellow student of the research group, Quinten Thijssen (Fig. 31).

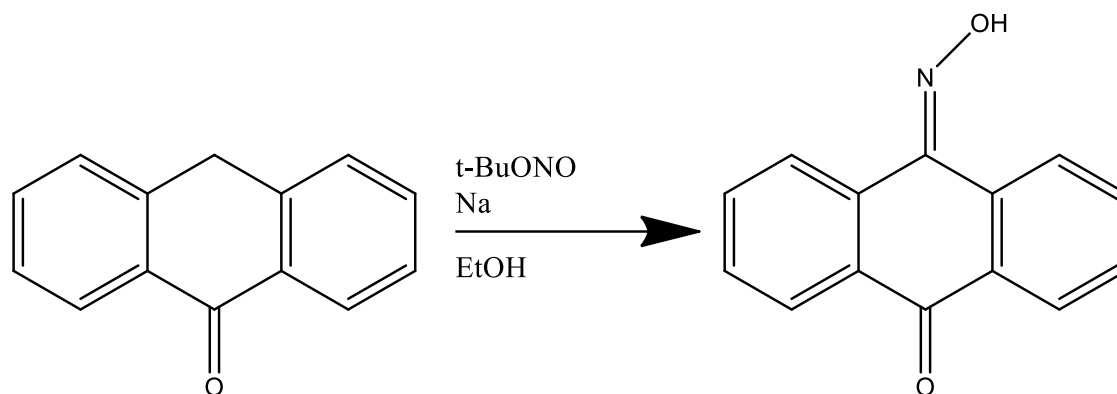


Fig. 31. Synthesis of the 10-(hydroxyimino)anthracenone precursor, performed by Quinten Thijssen

After the precursor was obtained, it was mixed with methanesulfonyl chloride and TEA in acetone to perform a nucleophilic substitution very similar to the one performed to create NonINaph-MSA.

The solid was a mixture of the starting product and the catalyst; recrystallization in both ethanol and ethyl acetate proved futile, so the two compounds were separated using a chromatographic column in pure CH_2Cl_2 . The isolated catalyst was dried under vacuum and an H-NMR spectrum was obtained in CDCl_3 . The obtained product was a pale yellow solid, with a yield of 26% (Fig. 32).

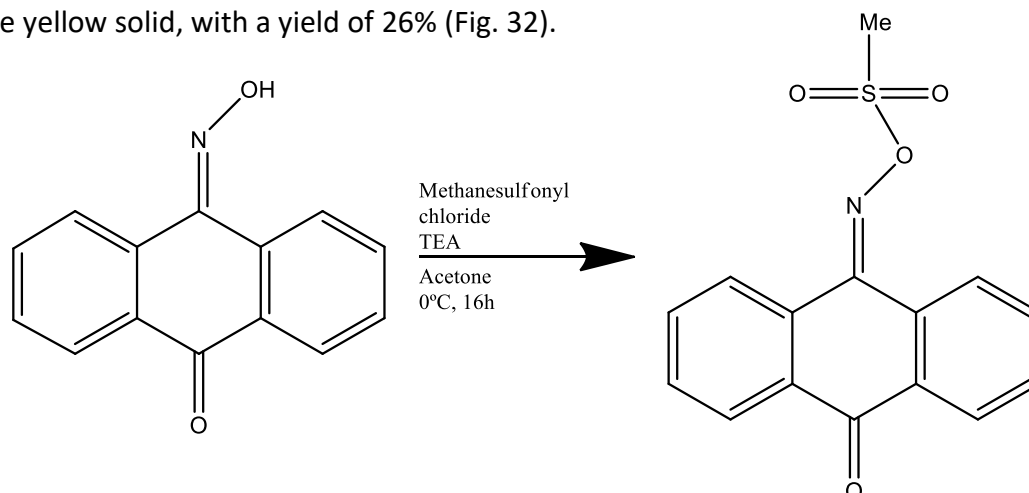


Fig. 32. Synthesis of NonIAnth-MSA.

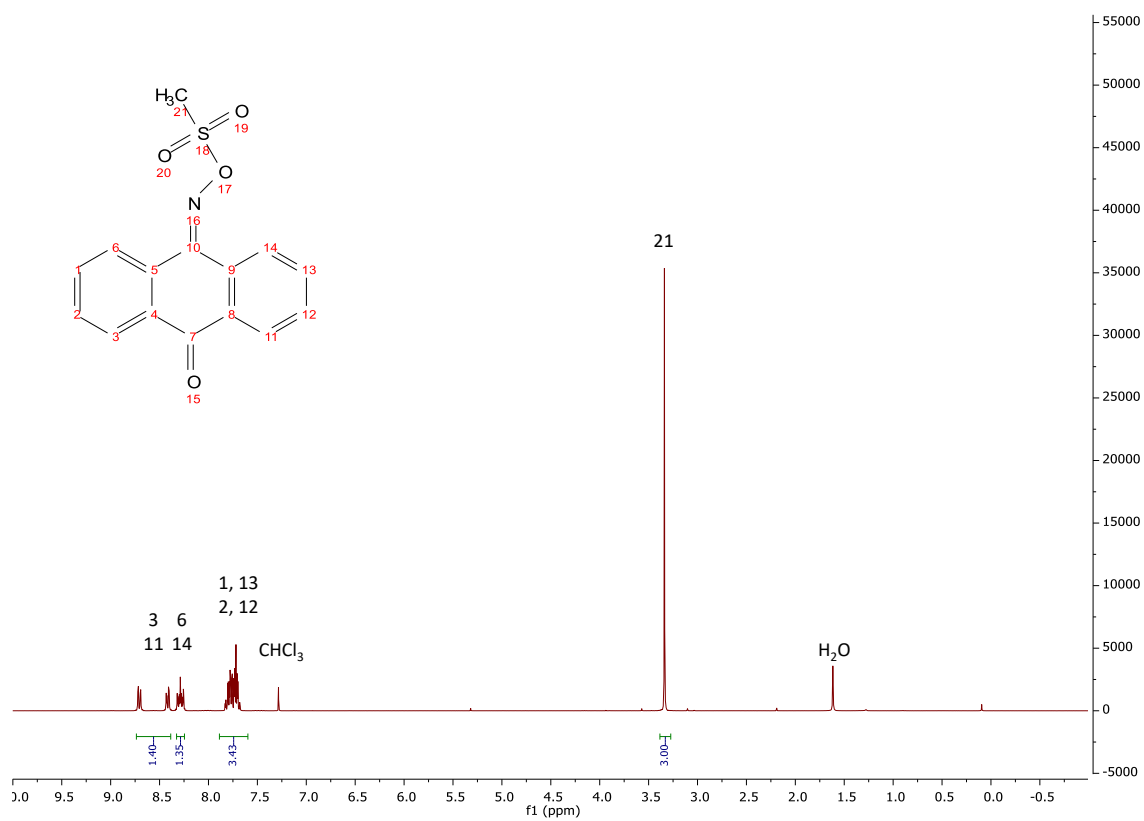


Fig. 33. ¹H-NMR spectra and assignments of NonIAnth-MSA. Performed in CDCl₃.

3.3.- Photolysis

A photolysis experiment was performed with NonIAnth-MSA. As it is described in p. 52, NonIAnth-MSA is the only compound from the 4 synthesized that was soluble in the monomer, and thus it is the only one chosen for the photolysis experiment. The goal of this experiment was to monitor the degradation and acid release of the photocatalyst upon being irradiated by UV light. As it was expected, the photolysis of the 0.01M sample was faster than the process for 0.2M.

The signal at 2.95 ppm at the 0.01M sample was measurable after 20'' of irradiation. The degradation increased steadily for 5 minutes, and then it slowed down for another 5 minutes; finally, it remained almost constant for another 10 minutes until the experiment was stopped after 21' 20'', with a final conversion of 83.1%. During the irradiation, the colour of the solution and the obtained solid changed: they turned from almost colourless to bright yellow during the first ~20 seconds, and then darker yellow after minutes of irradiation.

At the 0.2M sample the degradation was slower (Table 3) (Fig. 34). The signal at 2.95 ppm was first measurable after 80'', and the error margin for that measurement was huge due to the tiny size of the peak. The conversion continued to be very low for 10 minutes, and the experiment ended after 21'20'' with a final conversion of 3.8%. However, the colour change was very noticeable, as during the irradiation, the colour of the solution and the obtained solid turned from pale yellow to dark orange.

Tab. 3. Conversion vs Time data from the photolysis experiments at different concentrations

Photolysis of NonIAnth-MSA								
Time	10''	20''	40''	1' 20''	2' 40''	5' 20''	10' 40''	21' 20''
0.01M (%)	0.0	2.9	5.7	7.5	14.7	49.2	81.4	83.1
0.2M (%)	0.0	0.0	0.0	1.0	1.0	1.0	2.0	3.8

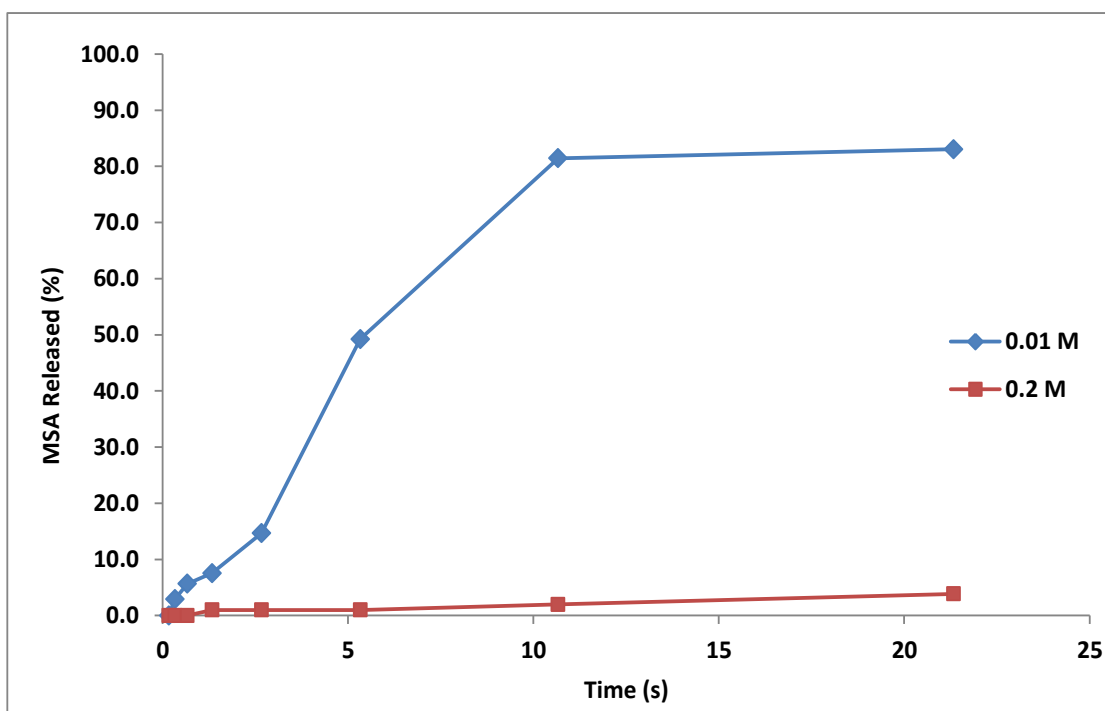


Fig. 34. Conversion (Acid Release) vs Time comparison graph from the photolytic experiments at the two different concentrations

Upon looking closely to the NMR spectra obtained from the 0.2M experiment we saw that the signals from the protons at the aromatic regions of the molecule (between 8.8 and 7.6 ppm) had changed; some little peaks appeared after irradiation, and slowly but steadily grew in size (Fig 35).

Thus, we concluded that the photocatalyst did indeed degrade during the 0.2M experiment, but it degraded in a way we did not expect. If the concentration of the photocatalyst is low enough, the degradation follows the pathway described in the literature and it degrades releasing MSA. However, if the catalyst is concentrated enough the decomposition follows an unknown pathway that does not yield MSA, but creates side-products of very intense color. We cannot explain the mechanism that inhibits the decomposition pathway that yields MSA, but we think that may be related to the accessibility to the solvent (in order to neutralize the formed radicals by protonating the acid and alkylating the chromophore, as explained in Fig. 8) or some interaction between the catalyst molecules. At lower concentrations, the amount of solvent is higher and the possible interactions between catalyst molecules will be rarer.

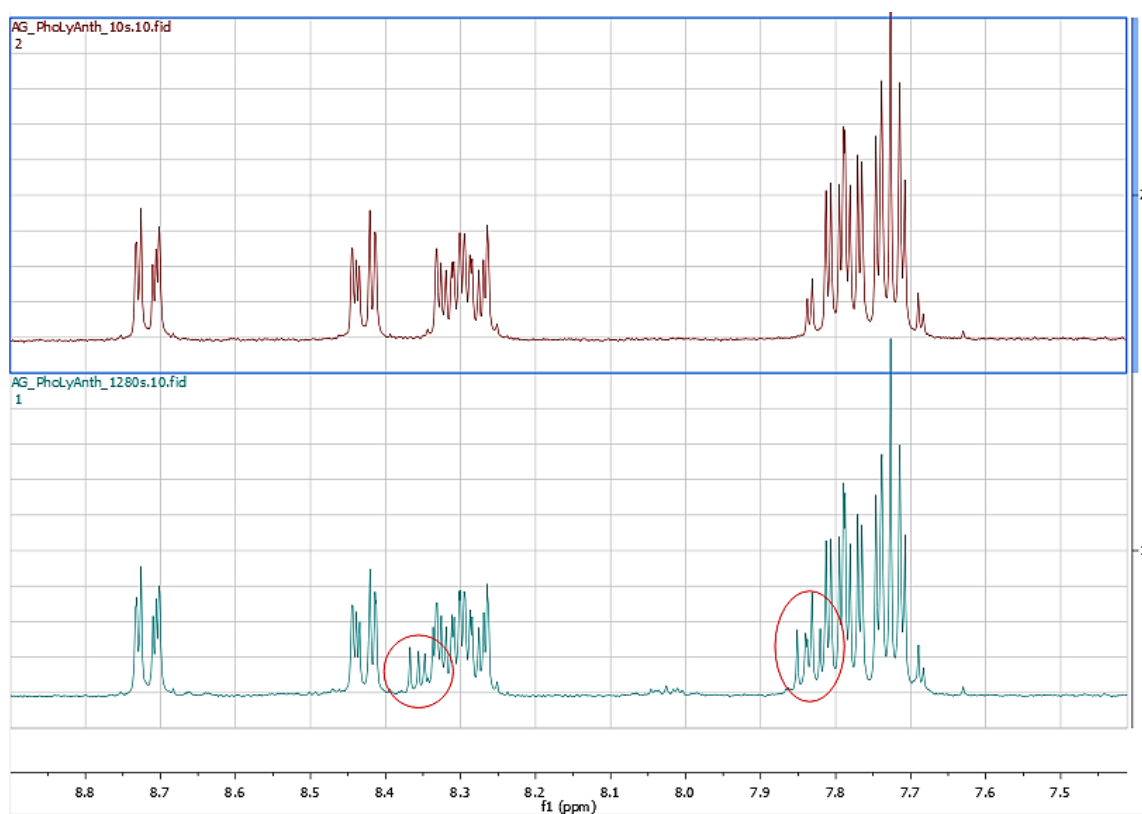


Fig. 35. Signals (marked in red) that appeared in the aromatic region during the photolysis experiment of the 0.2M sample of NonAnth-MSA. The 2 spectra correspond to 10" of irradiation (upper) and 21'20" of irradiation (lower).

3.4.- Polymerization by Photocatalysts

Finally, the compounds were used to try to catalyse the ROP of ϵ -CL. As the final goal of these compounds is the controlled catalysis of the cationic ROP of ϵ -CL, this final experiment was designed to test the catalytic power of the photocatalyst when irradiated with UV light. These results would provide information about the behaviour of the photocatalysts under irradiation when mixed with the monomer-initiator formulation, and about the possible viability of the compounds for stereolithography techniques. As described in the experimental procedure, the stability experiment was repeated twice for Iodonium-TfOH. In both cases, the sample taken just after sonication showed that the polymerization had already begun; in the first experiment, with the different efforts to try to solubilize the photocatalyst, the initial conversion had a value of 75%. After 1h without irradiation the conversion value increased to 99%, and after 2h the polymerization conversion was of 100%. Because of this, the irradiation had no effect on the conversion as every sample reported 100% of conversion. In the second experiment, the starting conversion was of 41%, and it constantly increased after 1, 2 and 4h of stirring without irradiation. After 24h the conversion was complete, with 100% of the monomer having reacted, and again the irradiation had no effect on the conversion as every sample reported 100% of conversion. The colour of the yellow suspension did not change during the 24h of stirring without irradiation neither after 15 minutes under UV light.

NonINaph-MSA was not soluble in ϵ -CL; after mixing it with a Vortex machine a uniform suspension was obtained. This 2.5% molar ratio mixture of NonINaph-MSA, monomer and initiator was stable for 24h without irradiation: the conversion did not increase during that time. However, it proved not sensitive to UV irradiation, as after 15 minutes of irradiation the conversion did not increase. The base conversion was \sim 13%. The colour of the yellow suspension did not change during the 24h of stirring without irradiation neither after 15 minutes under UV light.

NonIAnth-MSA was soluble in ϵ -CL after mixing it for 30" with a Vortex machine. The mixture proved stable for 24h, as the conversion did not increase (barring the error from the analysis of the H-NMR spectra) during the first 24h without irradiation.

However, polymerization did not begin upon irradiation, and the conversion did not increase. The colour of the solution did not change visibly during the 24h of stirring without irradiation; when it was irradiated, however, the colour changed from pale yellow to bright yellow, and then the solution darkened until it was dark orange after 15 minutes of irradiation.

Tab. 4. Conversion vs Time data from the polymerization experiments with different catalysts. The first 24h correspond to the period without irradiation, and afterwards they were irradiated for 15 minutes.

Time	Iodonium-TfOH			NonINaph-MSA	NonIAnth-MSA
	1st Exp. (%)	2nd Exp (%)	Avg. (%)	Avg (%)	Avg (%)
0h	75	41	58	13.04	0.00
1h	99	64	81.5	11.50	0.00
2h	100	83	91.5	11.50	0.00
4h	100	99	99.5	11.50	0.99
24h	100	100	100	11.50	1.01
1'	100	100	100	11.50	0.00
2'	100	100	100	11.50	0.00
5'	100	100	100	11.50	0.00
10'	100	100	100	11.50	0.00
15'	100	100	100	12.28	0.00

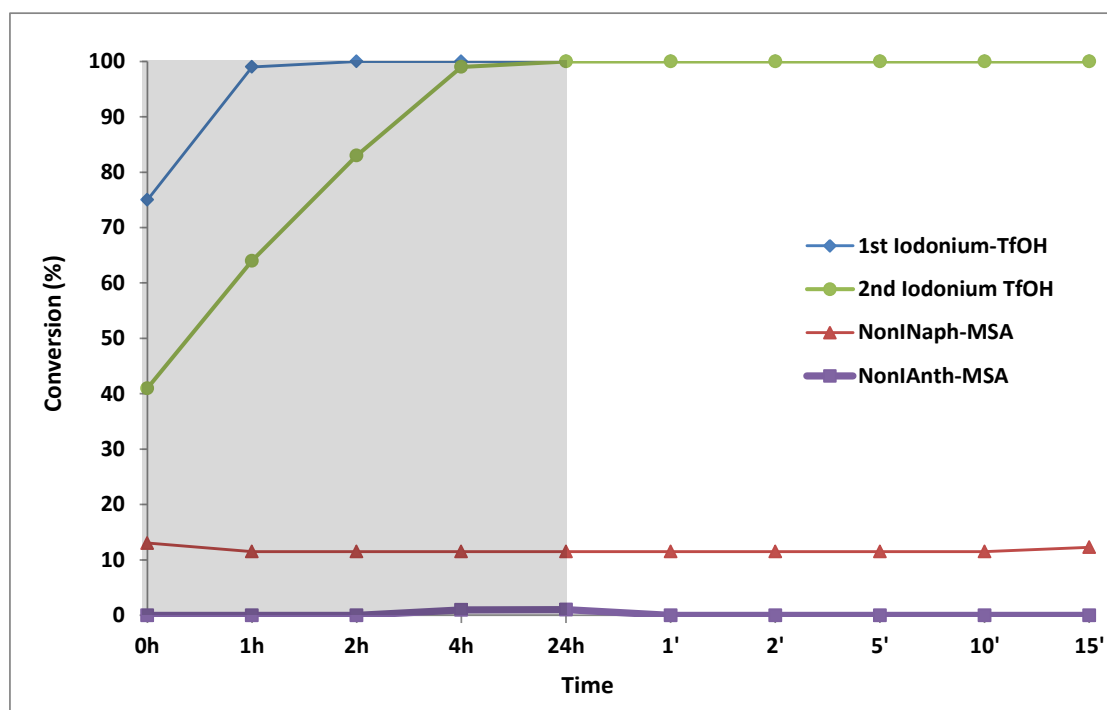


Fig. 36. Conversion vs Time comparison graph of Iodonium-TfOH, NonINaph-MSA and NonIAnth-MSA catalysts. The shadowed area corresponds to the non-irradiated period, and the clear area corresponds to the irradiated time.

In the Iodonium-TfOH tests, it is clear that the compound decomposed before irradiation. As mentioned above, the methods tried to solubilize the compound accelerated its decomposition. With a conversion of 83% at 2 hours without irradiation, the mixture of photocatalyst, initiator and monomer at 2.5% molar ratio is too unstable to be used properly. The mixture stayed liquid probably due to the short length of the polymer chains, but with the NMR method used in this project it could not be measured or proved; by comparing the peaks at 4.1 and 3.9 ppm we can only measure how much of the monomer has and has not reacted; this technique does not give information on the length of the chains or its' distribution.

In the NonINaph-MSA test, it can be seen that the mixture was stable but not sensitive to irradiation. The base conversion value of 13% was caused by a contaminated monomer; an H-NMR spectrum of the pure monomer was made and it showed the same conversion value.

The same thing happened with NonIAnth-MSA: the mixture was stable without irradiation, but it did not initiate polymerization when exposed to the UV light. As in the photolysis experiment with the 0.2M sample, it could be said that the photocatalyst degraded (due to the change in colour and the visibly different NMR spectra in the aromatic region) but following a pathway that did not yield MSA, and thus did not catalyse the polymerization.

4.- Conclusions

During this project four new compounds have been synthesized. These new compounds have been purified, characterized and studied for their application in ROP processes for ϵ -CL. However, during the tests these compounds have not been able to catalyse the polymerization. These results show the importance of solubility and make evident one of the big problems with bulk polymerization. Of the 4 compounds that were developed, only one was soluble in ϵ -Caprolactone, and the best that could be achieved with the other three was to form a uniform suspension in the monomer. Apart from the clear storage problems that an heterogeneous mixture presents (with non-uniform distribution and precipitation issues), the inability to dissolve the catalysts may result in problems with the release of the acid into the monomer medium, or the inefficient photolysis due to a reduced surface/mass ratio. With thermal stability and long shelf life in their favour, the usefulness for bulk polymerization of ionic PAGs may be greatly reduced by their low solubility in the monomers.

The described decomposition pathways of the photocatalyst seem like are only valid in low concentrations, and that those pathways may be inhibited in some way in higher concentrations. This alone may not be a problem, and using lower concentrations of catalyst may help with its distribution in the monomer and the final properties of the obtained material. However, one of the disadvantages of organocatalysts compared to metallic/organometallic catalysts is the high amount of catalyst needed to perform the same reaction or achieve similar reaction speeds. One the goals of the project was to find a photocatalyst that could achieve high conversion values in short timespans, preferably under 15 minutes; the active catalysts were able to obtain those values when used to perform bulk polymerizations with a molar percentage of 5% and 2.5% but no tests were performed using a concentration as low as 0.1% (the equivalent of 0.01M). Lowering even more the reducing even more the amount of photocatalyst would result in too long polymerization times, so long that it would not be useful for 3D printing or lithography.

The following steps on the development of organic photocatalyst for bulk ionic polymerizations oriented to 3D printing should be directed to exploring the catalysts that are known to be soluble in monomers (such as the anthrone-based iminosulfates) They also should be directed to the development and optimization of polymerization reactions in conditions of low catalyst ratios to prevent the problems of high-concentration-photolysis encountered during this project, and check if fast enough polymerizations under those conditions are possible.

4.- Conclusiones

A lo largo de este proyecto cuatro nuevos compuestos han sido sintetizados. Estos compuestos han sido purificados, caracterizados y se ha estudiado la posibilidad de utilizarlos en la ROP de la ϵ -CL. No obstante, durante las pruebas ninguno de los compuestos ha sido capaz de catalizar la polimerización. Estos resultados demuestran la importancia de la solubilidad, y evidencian uno de los mayores problemas de la polimerización en masa. De los 4 compuestos desarrollados en este proyecto, solamente uno de ellos era soluble en ϵ -Caprolactona, y lo mejor que se pudo conseguir con los demás fue la formación de una suspensión heterogénea pero uniforme en el monómero. Más allá del evidente problema de almacenamiento que presentan las mezclas heterogéneas (con posibles distribuciones no uniformes y problemas de precipitación del catalizador), la imposibilidad de disolver los catalizadores puede resultar en problemas de liberación del ácido ya generado al medio del monómero y en absorciones poco eficientes de la radiación UV debido a un ratio superficie/masa reducido. Aún con una buena estabilidad térmica y una larga vida de almacenamiento a su favor, la utilidad para la polimerización en masa de los fotogeneradores ácidos iónicos puede verse significativamente reducida por su escasa solubilidad en los monómeros a utilizar.

Las vías de descomposición descritas parecen válidas solamente en condiciones de baja concentración, y que dichas vías se ven inhibidas en condiciones de mayor concentración. Esto por sí mismo puede no ser un problema, y utilizar menores concentraciones de catalizador puede mejorar la distribución de éste en el medio y las propiedades finales del material obtenido. No obstante, una de las desventajas de la organocatálisis comparada con los catalizadores metálicos y organometálicos es la necesidad de emplear cantidades mayores de catalizador para llevar a cabo las mismas reacciones o alcanzar velocidades de reacción similares. Uno de los objetivos de este proyecto era el desarrollo de un fotocatalizador capaz de obtener altos valores de conversión en breves tiempos de reacción, preferiblemente por debajo de los 15 minutos; los catalizadores activos eran capaces de llevar a cabo polimerizaciones en masa y obtener dichas conversiones en esas franjas de tiempo cuando se usaron en

proporciones de 5% y 2.5% molar. No se hicieron pruebas con concentraciones de catalizador tan bajas como 0.1% (el equivalente de 0.01M en ϵ -Caprolactona) Reducir todavía más la cantidad de fotocatalizador podría resultar en tiempos de polimerización demasiado largos; tan largos que no serían útiles para impresión 3D o litografía.

Los próximos pasos en el desarrollo de fotocatalizadores orgánicos para la polimerización iónica en masa orientada a impresión 3D debería centrarse en explorar los catalizadores cuya capacidad de disolverse en el monómero es conocida (como los iminosulfatos basados en antrona). También centrarse en el desarrollo y optimización de polimerizaciones en condiciones de muy bajo ratio de catalizador para evitar los problemas de fotólisis asociados a altas concentraciones hallados durante este proyecto, para ver si dichas condiciones permiten una polimerización lo suficientemente rápida.

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