To Whom It May Concern,

Attached is the chapter of Jisun Lee's thesis that deals with the work supported by the NIJ graduate research fellowship (Award number: 2012-IJ-CX-0019). The dissertation has been successfully defended on July 21st, 2014. Chapters 1-4 are unrelated to the subject supported by the NIJ and were completed prior to the NIJ fellowship, supported by other funding agencies (NSF, Novartis, University of Pennsylvania). A delay of publication of the thesis was requested to University of Pennsylvania and accepted. This delay is a formal, binding agreement between the author of the thesis and the University of Pennsylvania, and it holds for two years after the degree is granted (August, 2016). For further inquiries, please contact Jisun Lee (jlsun@sas.upenn.edu).

Thank you,

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PART I. SYNTHETIC INVESTIGATIONS OF HETEROCYCLIC NATURAL AND UNNATURAL COMPOUNDS

PART II. NEW APPROACH TO LATENT FINGERPRINT DETECTION ON PAPER

Jisun Lee

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ABSTRACT

PART I. SYNTHETIC INVESTIGATIONS OF HETEROCYCLIC NATURAL AND UNNATURAL COMPOUNDS

PART II. NEW APPROACH TO LATENT FINGERPRINT DETECTION ON PAPER

Jisun Lee

Madeleine M. Joullié

Since the discovery and isolation of the didemnin family of marine depsipeptides in 1981, the synthesis and biological activity of its congeners have been of great interest to the scientific community. Of those, didemnin B was the first marine natural product to reach phase II clinical trials, stimulating many analogue syntheses to date. Almost two decades later, tamandarins A and B were reported and found to possess a structure similar to that of the didemnins. Significant efforts have been devoted to the syntheses of tamandarin analogues to find whether they behaved as didemnin mimics or as individual therapeutic agents. The biological and synthetic significance of the didemnins, tamandarins, and related natural products are discussed in Chapter 1.

The improved second-generation synthesis of the tamandarin B macrocycle and its successful application to the syntheses of three novel tamandarin B side chain analogues are presented in Chapter 2. The results of these investigations could help elucidate the structure-activity relationship as well as mode of action of these natural products.

Chapter 3 deals with the generation of structurally intriguing azabicyclic [3.1.0]- and [4.1.0]aminocyclopropanes and their application in an unprecedented ring-opening

conditions to afford corresponding 3-piperidinone and 3-azepinone derivatives which are important pharmaceutical motifs.

Chapter 4 introduces a rapidly growing family of natural diketopiperazine alkaloids: epipolythiodiketopiperazine (ETP) alkaloids, and related synthetic efforts in the generation of these alkaloids. Extensive synthetic investigation towards the formal synthesis of (−)-epicoccin G and other related epidithiodiketopiperazine alkaloids have been conducted. A novel methodology to access the 6-5-6-5-6 pentacyclic framework present in many ETP alkaloids is presented. Further application of this methodology in total synthesis could provide ETP alkaloids that have not been synthesized.

Chapter 5 deals with the development and successful application of 1,2-indanedione functionalized gold nanoparticles in a modified multi-metal deposition process for the development of latent fingerprints on paper. Although a wide variety of ninhydrin-like compounds have been developed as chemical agents for this process over the years, considerable portions of latent fingerprints still escape detection. The new approach provides an alternative method of fingerprint detection that could be utilized in challenging situations.

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Chapter 5: Development of novel 1,2-indanedione fingerprint reagents

5.1) Significance and background of latent fingerprint detection

The central dogma of forensic science: "Every contact leaves a trace" was first introduced by Edmond Locard, a pioneer of forensic science (also regarded as the Sherlock Holmes of France), in what is known as the Locard's exchange principle.[1] Needless to say, fingerprint detection is a crucial area in forensic science. A variety of physical and chemical methods have been developed over the years for the visualization of latent (hidden) fingerprints.[2] Chemical techniques are amongst the most sensitive techniques available today, and can be applied on many surfaces, porous or non-porous and on a large variety of materials (paper, plastic, wood, etc.). Of considerable importance are chemical techniques applied for paper and related cellulosic materials, since our society relies heavily on such materials for official documents, currency printing, wrapping, packaging, etc. More specifically, these methods rely upon the detection of the amino acids present in natural skin secretions. When a fingerprint is deposited on paper substrates, the amino acids are believed to bind to the cellulose of the paper, which preserves an impression of the friction ridge patterns.[2] These impressions are classified into two main groups—visible and latent. Visible marks are remnants of colored contaminant on the skin (blood, oil, ink), which leaves a positive visible impression. Latent marks, on the other hand, are invisible friction ridge impressions that are the result of transfer of skin secretions and non-visible surface contaminants on the porous substrates. Of the two, latent fingerprints are the most common type of evidence

found at crime scenes, and the most problematic, because they require methods to develop fingerprints that can be visualized and recorded.

For the purpose of latent fingerprint detection, eccrine and sebaceous glands are the most important glands that are responsible for skin secretions within the dermis.[2] Eccrine (sweat) glands are found on the palms of the hands, consequently contributing as the major aqueous component of a latent fingerprint. The palms also contain sebaceous secretions as a contaminant due to interactions with the face and hair. Varying degrees of combination of eccrine and sebaceous glands are present in latent deposits depending on the individual (Table 5.1). Human sweat contains a wide range of amino acids, where the exact composition depends upon the individual and a variety of other factors including general health, diet, gender and age.[3] When transferred to the surface of a paper substrate, amino acids have a great affinity for cellulose and tend to be stable over a prolonged period of time (>20 years).[2]

Table 5.1. Summarized constituents of eccrine and sebaceous skin secretions.[2,3]

Secretion	**Constituents**	
	Organic	**Inorganic**
Eccrine	Amino acids	Water (>98%)
	Proteins	Chloride
	Urea	Metal ions (Na^+, K^+, Ca^{2+})
	Uric acid	Sulfate
	Lactic acid	Phosphate
	Sugars	Hydrogen carbonate
	Creatinine	Ammonia
	Choline	
Sebaceous	Glycerides	
	Fatty acids	
	Wax esters	
	Squalene	
	Sterol esters	
	Sterols	

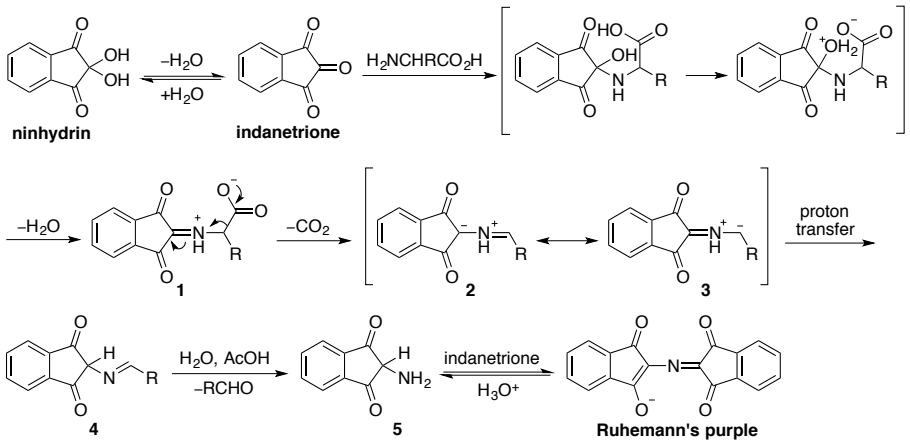
Since the amino acid composition of a fingerprint could vary depending on the individual, non-specific amino acid sensitive reagents are often considered for fingerprint detection.

According to Bramble and Brennan, there are three key requirements that any successful fingerprint detection reagent should have: (1) a suitable medium for the reagent (2) a method of transport for the reagent onto the item of interest (spraying, dipping) (3) using suitable reaction conditions (without destroying the evidence).[4] Generally, amino acid sensitive reagents are dissolved in a carrier solvent with or without additives (acetic acid, metal salts). An ideal solvent is volatile (to readily dry the substrate), non-toxic, non-flammable, and non-polar in order to avoid dissolving inks on treated documents.[2] For these reasons, 1-methoxynonafluorobutane (HFE 7100) is usually the carrier solvent of choice, although depending on the reagent, combination of formulations could be used to allow dissolution of the reagent. Most known reagents often require heat to develop latent fingerprints. Depending on the reagent, the method of heating could be varied, such as using an oven, domestic iron, or laundry press.[2] Furthermore, in certain cases, humidity was found to improve the development of fingerprints.[2] Finally, the developed latent fingerprint is then examined and recorded for identification. The method of examining and recording the developed prints could vary depending on the characteristics of the reagent employed. For instance, photoluminescence could be measured by illuminating the developed fingerprint with a filtered light source (or laser) and visualizing through appropriate filters.[2] Although such visualization methods may allow detection of even weak prints, it is not favorable, due to utilization of highly specialized and expensive instrumentation that are not readily accessible.

5.2) Common amino acid sensitive reagents

5.2.1) Ninhydrin

Although ninhydrin was synthesized and discovered by Ruhemann in 1910,[5] it was not until the mid 1950s when it was applied as the first amino acid sensitive reagent for the detection of latent fingerprints.[6] Ruhemann observed a color change after ninhydrin came in contact with his skin, leaving a purple mark.[5] This purple compound was subsequently known as "Ruhemann's purple."[2] The accepted general mechanism for the reaction of ninhydrin and an amino acid was proposed by Friedman and Williams,[7] and was later confirmed by Grigg[8] using X-ray studies (Scheme 5.1). Condensation of the amine portion of the amino acid on the central carbonyl of ninhydrin affords Schiff's base **1**, which then undergoes decarboxylation (Strecker degradation) to yield resonance-stabilized 1,3-dipolar species **2** and **3**. Subsequent proton transfer followed by hydrolysis affords 2-amino intermediate **5**. Condensation with another molecule of ninhydrin then furnishes Ruhemann's purple.

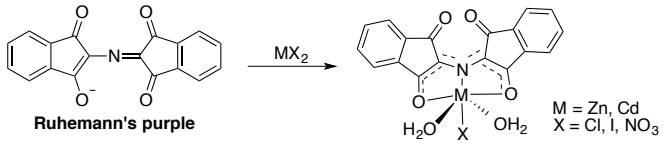


Scheme 5.1. Mechanism of Ruhemann's purple synthesis.

Ninhydrin can be applied to paper substrates by several different ways, but the most popular method is dipping the paper into a solution of ninhydrin. Upon exposure to

ninhydrin, heat and humidity are applied to accelerate the development process. Since prolonged exposure to light could fade ninhydrin developed prints, samples are usually allowed to develop in the dark at room temperature in order to obtain maximum sensitivity and minimal background staining.[9] The main limitation to this procedure is that full development of prints could often take weeks. In order to address this issue, initial efforts were made to alter the formulation of carrier solvent used to dissolve ninhydrin. However, unsatisfactory improvements were made by simple change of formulation methods, which ultimately ushered a wide variety of synthetic efforts towards generation of ninhydrin analogues.[9] Introduction of various substituents and extension of the conjugated system in such analogues showed for the first time that these modifications could produce an increase in molar extinction coefficients, resulting in more sensitive reagents and inducing shifts in the absorption maxima which resulted in change in the color of the Ruhemann's purple complex.[9,10] Alternatively, Ruhemann's purple prints could be complexed with various metal salts which could alter the color of the print. In 1982, Herod and Menzel observed that ninhydrin developed fingerprints changed color as well as became highly fluorescent (observed under an argon laser) when treated with zinc chloride solutions.[11] This was a pivotal discovery in the realm of fingerprint detection. Converting nonfluorescent ninhydrin developed prints into highly fluorescent prints allowed for improvement in contrast on a variety of backgrounds as well as heightened sensitivity (photoluminescence). Such post-treatment of Ruhemann's purple prints with metals has been widely used since then, especially in the detection of weak ninhydrin prints. It has been shown that zinc(II) and cadmium (II) salts complex with Ruhemann's purple to give luminescent products with slightly different properties

(Scheme 5.2). Soon thereafter, it was discovered that the intensity of the luminescence could be further improved if the prints are cooled in liquid nitrogen prior to observation.[12]

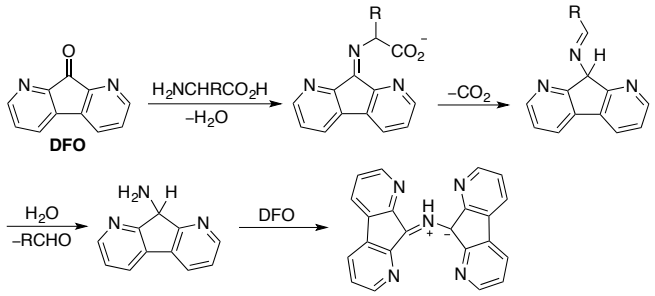


Scheme 5.2**.** Complexation of Ruhemann's purple with metals.

Although the use of fluorescence-based detection methods on ninhydrin/metal treated prints have been popular since its discovery, much attention was given to the synthesis of novel ninhydrin analogues, with the intention of obtaining highly colored Ruhemann's purple species that also exhibit fluorescence without secondary metal treatment, in order to simplify the visualization process. Of the various ninhydrin analogues that were synthesized, the most prominent analogues were 1,8-diazafluorene-9-one (DFO) and 1,2-indanedione, since they produced both color and intense luminescence upon reaction with amino acids in fingerprints without requiring further treatment.[2]

5.2.2) 1,8-Diazafluoren-9-one (DFO)

Although DFO was known since 1950,[13a] it was not until 1990[14] when Grigg and Pounds introduced DFO as an alternative amino acid detecting reagent. Although DFO is not a direct analogue of ninhydrin, it behaves similarly when reacting with amino acids (Scheme 5.3). DFO has only one central carbonyl moiety that is adjacent to two fused pyridine rings on each side that act similarly as neighboring dipoles of the 1,3-diketones in ninhydrin. Upon reaction with amino acids, it produces a red product, which is analogous to Ruhemann's purple.[9,14]



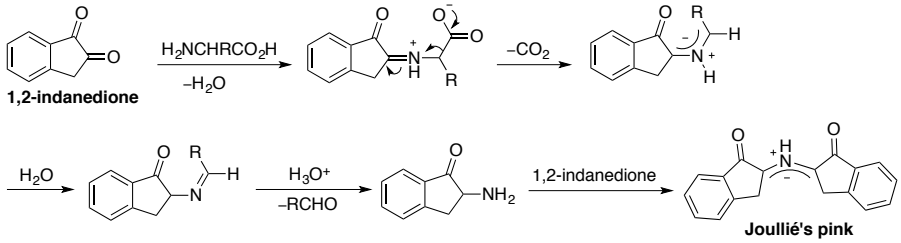
Scheme 5.3. Proposed reaction mechanism of DFO with an amino acid.

Unlike ninhydrin, DFO developed fingerprints were found to be highly fluorescent without secondary post-treatment with metal salts. Although the sensitivity was increased, there were practicality issues related with using DFO as a reagent. For instance, although commercially available, DFO is significantly more expensive than ninhydrin and requires the use of specialized light sources (prints viewed and photographed with a 520 nm (green) excitation filter and 590 nm (red) observation filter) for observation of fingerprints.[9] Furthermore, the development of DFO treated fingerprints requires carefully timed application of relatively high temperature (100-180 ^{o}C) and dry heat in order to avoid thermal decomposition.[2,9] In certain cases, DFO failed to develop all the prints and hence necessitated a secondary treatment with ninhydrin in order to maximize the number and quality of fingerprints. These shortcomings are believed to be the result of a slower reaction with amino acids when compared to ninhydrin. Moreover, efforts toward developing DFO analogues have not resulted in significant improvements.[9,14]

5.2.3) 1,2-Indanedione

In 1997, Joullié reported the ability of 1,2-indanedione to react with amino acids present in latent fingerprints.[15] The reaction results in a pale pink color with intense room-temperature luminescence comparable to that of DFO.[2,15] Extensive mechanistic studies were conducted[16,17] in order to elucidate the reaction pathway. In particular, the

involvement of 1,3-dipolar species of various geometries has been unequivocally confirmed through subsequent cycloaddition studies with *N*-methylmaleimide.[17] The proposed mechanism involves similar reaction pathway to that of DFO and ninhydrin that involves formation of imine intermediate followed by Strecker degradation to obtain 2-amino-1-indanone, which could then react further with another equivalent of 1,2-indanedione to produce a pink Ruhemann's purple analogue referred to as Joullié's pink (Scheme 5.4).[2,18]



Scheme 5.4. Proposed reaction mechanism of 1,2-indanedione and an amino acid.

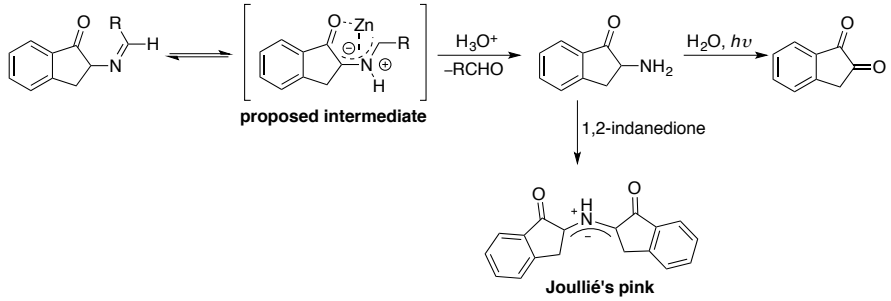
As was the case for ninhydrin, when 1,2-indanedione developed fingerprints were treated with zinc or cadmium chloride, the luminescence intensity of the corresponding product was increased, and the color of the product became a darker pink color, improving contrast.[15] Alternatively, zinc chloride could be added in the solution of 1,2-indanedione to provide similar results.[15a] However, inconsistencies in the formulation of 1,2-indanedione solutions across research labs in the world necessitated an optimized protocol that would be universally accepted.[2] It was found that depending on the formulation, varying results were obtained, suggesting usefulness or lack there of, of using 1,2-indanedione as an alternative to ninhydrin or DFO. Moreover, the observed discrepancy was suggested to be the result of differing climate of the research labs (it was believed that humidity plays a big role on development of fingerprints) and/or varying constituents of paper.[19] Formulations from early investigations used methanolic

solutions,[15] although later research recommended limiting the amount of methanol or other alcohols in 1,2-indanedione solutions due to resultant hemiketal formation that could interfere in the desired reaction with amino acids.[2,17,20] Furthermore, fingerprints developed using methanolic solutions often resulted in smudging of the image, thereby reducing the detail of the ridges.[21] Investigations on the effect of different carrier solvents (methanol, petroleum ether, HFE 7100, etc.) on the development of latent fingerprints strongly suggested the use of HFE 7100 over other solvents due to increased luminescence and lower health and safety risks.[2,19,20] In contrast, in some studies, petroleum ether based formulation was found to develop fingerprints that were darker in color and stronger in luminescence in comparison to HFE 7100 based formulation.[22] However, as suggested from the proposed mechanism of action (Scheme 5.4) use of acetic acid as an acidic additive to the formulation is less debated, and is rather well accepted to date to produce better results.[2] Furthermore, studies suggested the importance of relative humidity and moisture content of the paper substrate on the development of latent fingerprints, which may explain the observed results obtained from various countries with differing climatic conditions.[2,19] Although heating of 1,2-indanedione treated fingerprints is not necessary (24-48 h at room temperature for development), the reaction could be accelerated by heating with either an oven or dry heat/laundry press.[2,21] The most accepted conditions to obtain optimum development is to treat 1,2-indanedione developed fingerprints with laundry press at 160-165 ^{o}C for 10 seconds.[2]

In 2011, a study was conducted to elucidate the role of zinc(II) ions and cellulose substrates in the reaction of 1,2-indanedione and amino acids.[23] As was the case for

Ruhemann's purple, zinc(II) ions were initially thought to form a complex with Joullié's pink upon post treatment.[15] However, concentration studies of zinc chloride and its effect on development of fingerprints suggested that the primary role of zinc(II) ions in the 1,2-indanedione-amino acid reaction is that of a Lewis acid catalyst.[24] More specifically, a minor red shift in the absorption spectrum as well as decrease in luminescence and color intensity was observed at high concentrations of zinc chloride, which suggests the catalytic role of zinc chloride.[24] This hypothesis was formulated primarily through anecdotal observations of fingerprints developed using 1,2-indanedione-zinc chloride in various forensic laboratories and have not been confirmed in the literature.[23] Therefore, a careful investigation was conducted[23] in order to determine if the reaction of 1,2-indanedione with amino acids on cellulose proceeds *via* the same mechanism proposed earlier[17] which was done in solution. Three amino acids (L-alanine, L-phenylalanine, and L-leucine) were chosen for the study and were mixed with cellulose to produce amino acid-impregnated cellulose that would mimic the conditions observed on paper substrates.[23] A solution of 1,2-indanedione with or without catalytic amount of zinc chloride (1:2:0 or 10:10:1, or 10:20:1 molar ratios of amino acid-1,2-indanedione-zinc chloride was used) was added to the amino acid-impregnated cellulose and was mixed at room temperature in the dark for 1 h. The resulting reaction products were extracted and analyzed by mass spectrometry (ESI-MS), ^{13}C-MAS-NMR, and UV-Vis.[23] Of the three amino acids studied, the reaction between L-leucine and 1,2-indanedione/zinc(II) (10:10:1 ratio) resulted in the greatest reaction rate, which was implied from the low relative abundance of ions attributable to 1,2-indanedione and early stage reaction intermediates (the ESI-MS results were obtained *via* direct injection immediately

following extraction of reaction mixture from cellulose).[23] Furthermore, an increase in the relative abundance of the Joullié's pink ion was observed with the addition of zinc chloride dramatically improving the reaction rate.[23] The involvement of a new intermediate was subsequently proposed (Scheme 5.5).[23] Since the presence of the proposed intermediate was never detected in any of the reaction conditions that had zinc chloride as an additive, it was suggested that the addition of zinc(II) ions leads to the rapid conversion of the proposed intermediate to 2-amino-1-indanone.[23] From their results, they claimed that zinc chloride acts as a Lewis acid catalyst that stabilizes the 1,3-dipole intermediate during the hydrolytic conversion to 2-amino-1-indanone in low humidity environments.[23] Addition of stoichiometric amount of zinc chloride did not result in improved luminescence through complex formation, but decreased the rate of the reaction and overall yield of Joullié's pink instead.



Scheme 5.5. Proposed reaction pathway to Joullié's pink from the imine intermediate.[23]

In order to further support the involvement of 2-amino-1-indanone moiety in the reaction pathway, 2-amino-1-indanone was synthesized using known methods and reacted with 1,2-indanedione in solution on cellulose at room temperature in a 160 ^{o}C oven. UV-Vis spectroscopy, fluorescence spectroscopy, and NMR spectroscopy (HSQC) confirmed the formation of Joullié's pink.[23] When 2-amino-1-indanone was added to cellulose and heated under the same conditions, an unexpected formation of Joullié's pink was

observed, indicating a possible secondary reaction pathway that occurs by slow deamination of 2-amino-1-indanone to form 1,2-indanedione under warm humid conditions (Scheme 5.5).[23] Taken together, these results support the generally accepted reaction mechanistic pathway of 1,2-indanedione and amino acids, and suggest a specific role of zinc chloride as a Lewis acid catalyst. Furthermore, the success of the 1,2-indanedione reaction is dependent upon the relative humidity of the laboratory environment, since decomposition of Joullié's pink was observed under excessive humidity (nearing saturation of the paper substrate). Prolonged heating at relatively high temperatures (70-100 ^{o}C) in low humidity conditions was also found to be detrimental in the development of fingerprints, as the only products that were formed were non-fluorescence oligomeric byproducts.[23] Finally, the role of cellulose was found to be similar to that of a surface catalyst, since it is believed to orient the intermediates in the optimum reaction geometry (through hydrogen bonding), and retain water molecules close to the reaction site to improve the reaction rate.[23] Trace metals present in the commercial paper stocks may also act as a Lewis acid catalyst in the same manner as zinc(II) ions. Although the presence of Joullié's pink was identified by mass, UV, and fluorescence,[23] full characterization still needs to be accomplished in order to validate various hypotheses that were proposed to date. For instance, the initial hypothesis of complexation of zinc with Joullié's pink[15] cannot be completely disregarded.

In terms of determining the overall performance of 1,2-indanedione as a fingerprint detection reagent in comparison to ninhydrin and DFO, there seems to be no clear answer. Using a sequence of combination of reagents has been popularized as well, and in certain

cases, performed better than using a single reagent.[2] A recent study conducted in Australia[25] evaluated two particular fingerprint detection sequences on porous surfaces: 1) 1,2-indanedione—$ZnCl_2$ followed by ninhydrin, physical developer (PD) and the lipid stain Nile red; and 2) DFO followed by ninhydrin, PD and Nile red. The obtained results indicated negligible difference in the performance between the two sequences across all paper types and all time periods evaluated. However, when considering individual reagents, 1,2-indanedione—$ZnCl_2$ developed better quality fingerprints than DFO.[25] In terms of enhancement, ninhydrin had a greater enhancement effect on DFO developed prints rather than 1,2-indanedione—$ZnCl_2$. Although the use of Nile red was proposed in the beginning of the trials, since Nile red did not develop any additional fingerprints at the end of each sequence, it was excluded in the sequences.[25] The optimum sequence that was suggested was the use of 1,2-indanedione—$ZnCl_2$ followed by ninhydrin and PD for development of fingerprints on Australian paperstock.[25]

5.3) Development of alternative fingerprint detecting methods

Although a wide variety of ninhydrin-like compounds have been developed since its discovery, considerable portions of latent fingerprints still escape detection. The main limitation of the existing methods is their stoichiometric nature: as long as the reaction assumes a stoichiometric pathway, there is an upper limit to the sensitivity. Furthermore, latent fingerprints often do not contain enough amino acids (or other relevant components such as lipids), so even the most sensitive reagents fail to produce a sufficiently meaningful mark through a direct chemical reaction with fingerprint components. Although much attention has been given to developing optimal formulation conditions,

success of developing latent fingerprints seems to depend heavily on environmental factors (relative humidity of the laboratory, paper stock of the country, sweat content of individual's fingerprint, etc.) that are difficult to control. Moreover, apart from ninhydrin, amino acid sensitive reagents that have been identified thus far[26] rely on luminescence in order to view latent fingerprints, significantly limiting general accessibility (Table 5.2).

Table 5.2. Conditions for observing photoluminescence of latent fingerprints using common amino acid sensitive reagents.[2]

Reagent	Excitation band	Viewing conditions
Ninhydrin—$ZnCl_2$	490 nm	Orange goggles
DFO	505 nm	Orange goggles
	530 nm	Red goggles
	555 nm	Red goggles
1,2-Indanedione—$ZnCl_2$	505 nm	Orange goggles

There are methods other than using amino acid sensitive chemical reagents in developing latent fingerprints. One notable method is the use of silver physical developer (Ag-PD), which is a process that utilizes metastable silver colloid that develops latent prints on wet, porous surfaces such as paper and cardboard.[27] The developer deposits a black silver precipitate along the fingerprint ridges by associating or reacting with the lipid material present in the fingerprint residue. In a typical formulation, a solution of ferrous and ferric ions, also containing citric acid and a detergent, is mixed with a solution of silver nitrate to generate a citrate-stabilized silver colloid through an electroless reaction in which the Fe^{2+} ions reduce the Ag^{+} ions *in situ*.[27] As already mentioned, Ag-PD could be used after ninhydrin or other amino acid sensitive reagent processing in order to amplify the obtained image or obtain more prints. Prints developed using Ag-PD appear as dark ridges on lighter/white background, creating enough contrast that allows visualization under visible light. Although the process negates the use of expensive, specialized light sources for visualization, it suffers from instability of the developing solution (shelf-life

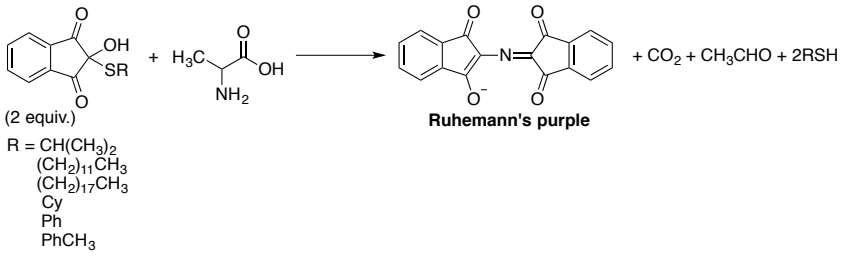
of Ag-PD solution is limited and should be freshly prepared for best results) and poor reproducibility.

Multimetal deposition (MMD)[28] is a variation of the process, in which a latent fingerprint is enhanced by gold nanoparticles stabilized by citrate ions in aqueous medium, and then treated with Ag-PD. The gold nanoparticles adhere to the fingerprint residue and are believed to catalyze the precipitation of metallic silver from the Ag-PD solution.[28] The affinity of gold nanoparticles to the fingerprint residue is thought to be the result of an ionic interaction between the negatively charged gold colloids and the positively charged components of the fingerprint residue at low pH.[28] Advantages of using MMD is based on its sensitivity, specifically with aged fingerprints, and in the fact that it works on porous as well as non-porous surfaces. However, the main drawback of the process is that it is considered to be labor-intensive (involving several steps to obtain working solution, exposure of prints to six different solutions) and it only produces dark grey to black fingerprints, which could be problematic when dealing with dark and/or patterned surfaces. Therefore, a modification of the process known as single-metal deposition (SMD) was developed, where the enhancement of gold colloids by precipitation of silver was replaced by gold-based growth of the nanoparticles.[29] Efforts towards discovering improved fingerprint development techniques that are based on nanochemical processes are ongoing, and they all suggest the involvement of adherence of nanoparticles to fingerprint residues.[30]

Based on earlier reports by Vijayamohanan,[31] in which dodecanethiol stabilized gold nanoparticles were found to be adsorbed onto activated hydrophobic surfaces *via* hydrophobic interactions, Almog reported[32] that sebum-rich fingerprint deposits could serve as hydrophobic surface for such interactions with various alkanethiol stabilized gold nanoparticles. Ag-PD was used as a post-treatment process, in which the gold nanoparticles that have been adsorbed onto the fingerprint ridges catalyzes silver reduction from the Ag-PD solution, allowing the precipitation of Ag^0 on the ridges, significantly enhancing the developed fingerprints as a result.[32] Although the two step development process is similar to MMD, since the nanoparticles adsorb onto the fingerprint ridges *via* hydrophobic interactions rather than ionic interactions, the underlying mechanism is considered to be different. Moreover, the average size of the gold nanoparticles that were synthesized were of 2-3 nm, which is smaller than the gold nanoparticles often used in MMD process (~14 nm).[32] Best results were obtained using a 0.04% (w/v) solution of the alkanethiol stabilized gold nanoparticle solutions in petroleum ether. Of the three different lengths of the alkanethiol chain tested (10-, 14-, and 18-carbon chains), the longest chain, octadecanethiol, provided the best result, where the aggregation of gold nanoparticles occurred fastest and in greatest amount as observed by scanning electron microscopy (SEM).[32] However, all three chains resulted in positive latent fingerprint detection after post treatment with Ag-PD. The obtained results using paper substrates translated well onto non-porous surfaces (silicon wafers). To test the generality of using metallic nanoparticles, petroleum ether solution of CdSe/ZnS nanoparticles (~3 nm size) stabilized by octadecaneamine were synthesized.[32] Although successful development of fingerprints were obtained for non-porous, silicon wafer

substrates, the process did not work for paper substrates. Interestingly, post treatment with Ag-PD was unnecessary as the CdSe/ZnS treated fingerprints were fluorescent, and consequently visible under UV illumination using optical microscopy.[32]

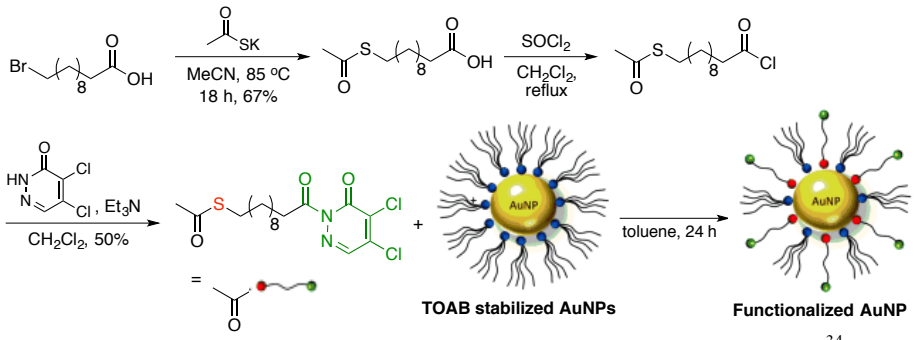
In 2010, with the intension of extending his previous findings, Almog reported the synthesis of various thiohemiketals of ninhydrin and 1,2-indanedione as potential fingerprint developing reagents.[18] The premise of the study was to use the known reaction of ninhydrin and 1,2-indanedione with amino acids that would furnish the corresponding colored Ruhemann's purple or Joullié's pink, and by having thioether linkages on the compounds, the overall reaction would expel the corresponding thiol alkyl chain that would then presumably stay on the fingerprint ridges and react with gold nanoparticles, further enhancing the contrast.[18] With regards to the synthesis of thiohemiketals, formation of thioketals were not observed in the case of ninhydrin even in the presence of excess thiol. However, in the case of 1,2-indanedione, formation of only thioketals was observed under the same conditions. Several thiohemiketal analogues of ninhydrin were synthesized and reported, however, none of the presumably synthesized thioketal of 1,2-indanedione was reported or characterized.[18] A possible reason for this discrepancy may be due to the fact that the thioketal version of 1,2-indanedione presumably did not react with amino acids or latent fingerprints on paper.[18] Nonetheless, the thiohemiketal analogues of ninhydrin did react with alanine (stereochemistry not specified) to produce Ruhemann's purple (noticed visually), and the presence of thiols in the reaction mixture was detected by GCMS (Scheme 5.6).



Scheme 5.6. Reaction of thiohemiketals of ninhydrin and alanine.

Amongst the analogues, there was an apparent difference in the rate of the reaction (monitored visibly). For instance, analogues containing longer alkyl chains reacted slowly in comparison to shorter chains. Furthermore, the thiohemiketal analogues of ninhydrin developed latent fingerprints on paper that was comparable to that of ninhydrin.[18] The use of ketals of ninhydrin in the reaction with amino acids is not entirely unprecedented, since another group reported the reaction of hemiketals of ninhydrin with amino acids to form Ruhemann's purple and two equivalents of alcohol per amino acid as early as 1991.[33] Nonetheless, since the proposed hypothesis of using the thiohemiketal analogues of ninhydrin in conjugation with gold nanoparticles was not tested, the viability of this approach remains uncertain.

Shortly thereafter, Almog reported yet another approach[34] to develop latent fingerprints on paper using a similar protocol, but with a different reagent. A bifunctional reagent was devised, in which it is composed of an active polar head (acyl pyridazine) that has high affinity to cellulose (main ingredient of paper), and a long alkyl chain tail containing a sulfur group at the terminal end that could stabilize gold nanoparticles (Scheme 5.7).



Scheme 5.7. Almog's synthesis of functionalized gold nanoparticles.[34]

Since the head portion of the molecule that has a long alkylthiol chain adheres preferentially to the paper rather than to the sebaceous fingerprint material, further treatment with Ag-PD would darken the paper, leaving the fingerprint ridges uncolored, resulting in a white on black fingerprint image. This so-called "negative image" was hypothesized to be superior in comparison to conventional methods, since the current approach is based on interactions with cellulose rather than the sebaceous fingerprint, which could be varied depending on the sweat content of the individual (Figure 5.1). Although their previous work with octadecanethiol stabilized gold nanoparticles[32] produced good quality fingerprints using conventional methods (gold nanoparticle exposure followed by Ag-PD, targeting sebaceous fingerprints, thereby producing black on white image), they claim that their process lacked consistency due to variability in fingerprint residue composition.[34] The desired fingerprint image was obtained rather quickly using the new process, where the image was obtained after 5 min of treatment with the gold nanoparticles followed by 40-60 s with Ag-PD. Prolonged exposure to Ag-PD solution resulted in darkening of the entire paper, where the silver eventually precipitated on the fingerprint ridges as well. Since the method is based on sebaceous fingerprints (lipid containing hydrophobic prints), eccrine fingerprints (amino acid containing prints) did not work under the same reaction conditions.

Figure 5.1. Comparison between conventional fingerprint image (left) and "negative" image (right) obtained by Almog *et al*.[34]

In an attempt to provide an explanation of the particular interaction that could be occurring with acyl pyridazine moiety of the reagent and cellulose of the paper, two particular classes of gold nanoparticle ligands were synthesized. The first class had functional end groups that are known to form hydrogen bonds (glucose, acetylthioalkoxy benzaldehydes, etc.), while the second class had polar end groups that cannot hydrogen bond (tetrachlorobenzene). Each compound was functionalized with gold nanoparticles and was tested for visualization of sebaceous fingerprints on paper using the same methodology. The authors found that negative fingerprint images were obtained by the first class (ligands with hydrogen bonding motifs), while conventional, positive fingerprint images were obtained by the second class (non-hydrogen bonding motifs). None of the aforementioned obtained images or any of the gold nanoparticle derivatives (other than their main acyl pyridazine reagent) were characterized or referenced in the article.[34] Nonetheless, the fingerprint image that was obtained using their bifunctional ligand containing an acyl pyridazine moiety suggested successful application of this protocol.

More recently, Almog reported another example of negative development of latent fingerprints using a slightly different set of reagents.[35] The method utilized commercially available mercaptocarboxylic acids as ligands to gold nanoparticles rather than the

previously mentioned acyl pyridazine containing ligand. There are apparent advantages in using commercially available mercaptocarboxylic acids—namely the fact that they are commercially available, thus not requiring synthesis and purification to obtain the ligand. Furthermore, the solvent mixture (CH_3CN/DMSO) utilized for the formulation of their previous ligand[34] was an undesirable system for document examinations, since it dissolved ink.[35] Since most mercaptocarboxylic acids that were examined are soluble in water, such problem was not encountered (Figure 5.2). Mercaptocarboxylic acids retain the desired bifunctional behavior of the ligand, since the carboxylic acid serves as the active head that hydrogen bonds to cellulose, and the thiol serves as the active tail that binds to gold nanoparticles, resulting in negative fingerprint images. Although seemingly unconventional, there is precedent[36] in using a variety of mercatocarboxylic acids as ligands to gold nanoparticles.

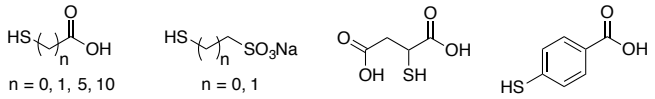


Figure 5.2. Mercaptocarboxylic acids and salts examined by Almog.[35]

All the gold nanoparticle functionalized mercaptocarboxylic ligands were dissolved in water (in the case of 10-carbon chain mercaptocarboxylic ligand, minimal amount of THF was used for dissolution and was further diluted with water to obtain 5% v/v THF in water) for the formulation. Apart from functionalized gold nanoparticles of 5-carbon and 10-carbon chain mercaptocarboxylic ligands, the desired negative fingerprint image was obtained after post treatment with Ag-PD. Best results were obtained using 3-mercaptopropionic acid as the ligand, since fresh and 14 month old latent sebaceous fingerprints were developed with good contrast and resolution. However, gold nanoparticles capped with 6-mercaptohexanoic acid (5-carbon chain ligand) failed to

develop fingerprints, as the entire paper was stained without any distinction. Interestingly, gold nanoparticles capped with 11-mercaptoundecanoic acid produced a positive fingerprint image, in which the gold nanoparticles was preferentially bound to the sebaceous ridges of the fingerprint rather than to the cellulose, which was in line with their previous studies.[32] Although there was no explanation provided for the failure of 6-mercaptohexanoic acid as a ligand for fingerprint development, the obtained results suggested that the appearance of the fingerprint as positive or negative could be tuned *via* the length of ligand on gold nanoparticles.[35]

5.4) Design and synthesis of novel 1,2-indanedione reagents

5.4.1) Proposed methodology and design of novel bifunctional reagent

As discussed in previous sections, the use of amino acid detecting reagents alone for the development of latent fingerprints on paper is not advantageous due to their stoichiometric nature. Since amino acids and the sweat content on a given fingerprint varies drastically depending on the individual and the climate, this prevents even the most sensitive reagents from producing sufficiently meaningful mark through direct chemical reaction. As long as the reaction assumes a stoichiometric pathway, where an equivalent of the reagent (i.e. ninhydrin) reacts with an equivalent of the substrate (amino acid), there is an upper limit to the sensitivity. Furthermore, other factors such as relative humidity of the laboratory in which the development is conducted, formulation conditions, accessibility to specialized equipment (light sources such as lasers) could

affect the outcome. Therefore, utilization of nanotechnology, such as the MMD process, for the development of latent fingerprints could be a promising alternative.

In this context, development of a new highly sensitive, non-stoichiometric gold nanoparticle-based technology following the basic principle of MMD was envisioned. In particular, employing bifunctional reagents similar to that of Almog's[34,35] where one end of the reagent would react with the fingerprint ridges, while the other end would react with gold nanoparticles were envisaged. Since these novel reagents would act as ligands on the gold nanoparticles, in theory, each gold nanoparticle could have many of these ligands appended on them, where the opposite end would seek out amino acids of the fingerprint, thereby increasing the sensitivity *via* catalytic amplification. The resulting ternary complex could then catalyze silver deposition from the Ag-PD, generating a high-contrast fingermark that could be visualized without the use of specialized light source.

In terms of the bifunctional reagent design, based on the well-known use of 1,2-indanedione and our particular familiarity of the reagent, 1,2-indanedione was selected as the "head" portion of the bifunctional reagent. The "tail" portion would be a long alkylthiol chain that is connected to the aromatic ring of 1,2-indanedione. Taken together, the 1,2-indanedione portion would react with amino acids of the fingerprint, and long alkylthiol chain would act as stabilizing ligands on gold nanoparticles (Figure 5.3). Unlike previously mentioned bifunctional reagents that could only target either amino acids or hydrophobic lipids, this reagent could in theory react with both amino acids

(eccrine) as well as lipids (sebaceous) of the fingerprint, increasing the likelihood of latent fingerprint detection on paper substrates.

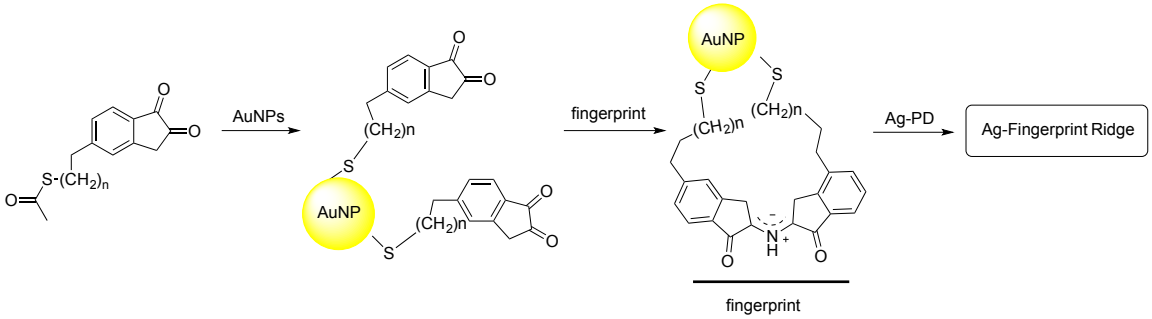
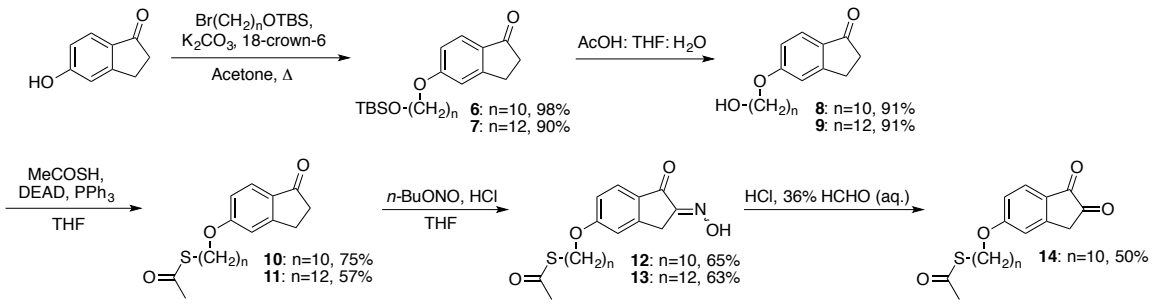


Figure 5.3. General schematic for proposed development of latent fingerprints.

5.4.2) First-generation synthesis

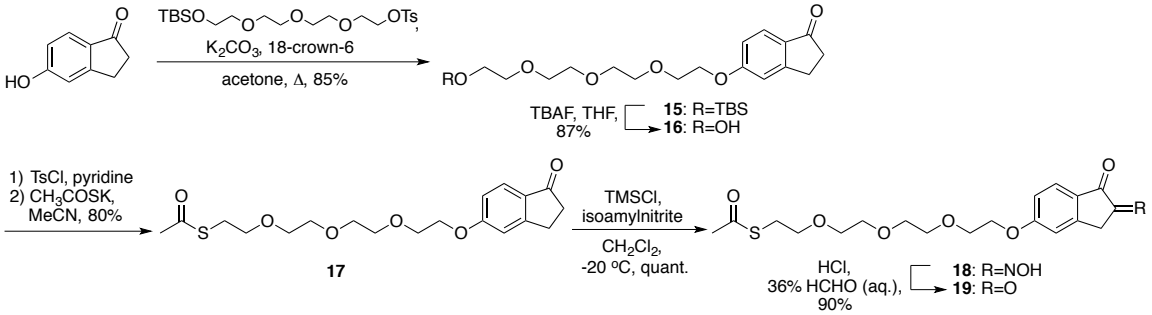
A general route for synthesizing 1,2-indanedione derivatives was developed using commercially available 5-hydroxyindanone as the starting material (Scheme 5.8). Side chain attachment followed by removal of TBS group afforded the corresponding alchols **6** and **7**, which was subsequently transformed into the thioester **8** and **9** by Mitsunobu reaction. Oxime formation using previously developed methods[15,17] followed by conversion to the corresponding ketone[15,17] furnished the functionalized 1,2-indanedione derivative **14**. Although generation of three particular derivatives with varying side chain lengths (n = 10, 12, 14) was envisioned using this methodology, unexpected problems were encountered during the last two steps of the synthesis, thereby limiting the overall efficiency of the synthetic sequence.



Scheme 5.8. First generation synthesis of 1,2-indanedione analogues.

In particular, for the oxime formation step, various solvents were screened (CH_2Cl_2, THF, EtOH, EtOH:CH_2Cl_2), and the best result was obtained using THF. In terms of the reagent, comparable results were obtained using isopentyl nitrite instead of *n*-butyl nitrite. The main side reactions that were in competition with the desired transformation were the cleavage of the C-O bond in the molecule and removal of the thioacetate group. These unfavorable processes could be attributed to the presence of protic acid (HCl) in the reaction. Similar problems were encountered in the final step of the synthetic sequence, since HCl in aqueous conditions was used. Furthermore, the final product was found to be unstable on silica gel during the duration of the column chromatography, which did not allow effective separation of the desired product from the side products. Other reactions using different set of reagents were explored in hopes of avoiding the use of protic acids. In particular, oxidative deoximating reactions[37] were investigated using Dess-Martin periodinane (DMP), MnO_2, and dichloramine-T.[38] Oxidation by MnO_2 proved to be sluggish and did not result in full conversion of the starting material. As for DMP and dichloramine-T, although the desired product was detected in the reaction mixture (verified by ^{1}H NMR, ^{13}C NMR, and LRMS), the pure product was unable to be isolated *via* silica gel chromatography (due to instability) from the side products of the oxidation. As an alternative, resin bound pyridinium dichromate [poly(vinylpyridinium dichromate)] was synthesized[39] and tested, but the reaction failed to reach full conversion even after prolonged period of time (1 week). Other deoximation methods, such as deoximation by hydrolysis with copper chloride[40] only resulted in side chain cleaved material.

Interestingly, when the present protocol was applied to a derivative bearing a polyethylene glycol (PEG) side chain (Scheme 5.9), side chain cleavage was not observed for the last two steps of the synthesis. This could be attributed to hydrogen bonding interactions in solution that may orient the PEG chain in a manner to protect the C-O bond linkage. Based on previous synthesis, minor changes were made in the synthetic sequence to ensure good yields. For instance, the Mitsunobu step was not utilized due to inconsistency in yield amongst the analogues (Scheme 5.8). Instead, alcohol **16** was converted to the tosylate, which was then substituted by thioacetate to afford **17** (Scheme 5.9). Use of TMSCl in place of HCl for the oxime formation step furnished the desired oxime **18** in excellent yield. Subsequent deoximation under the same conditions used in prior synthesis afforded the desired 1,2-indanedione analogue **19** in good yield. Silica gel column chromatography was not required for the last two steps, since a simple aqueous work-up allowed the isolation of pure material. Although side chain cleaved side product was not observed, minor presence of acetate removed thiol 1,2-indanedione product was observed by NMR and LCMS. However, removal of the acetate group was not a major concern, since such process takes place in the following step (functionalizing gold nanoparticles with 1,2-indanedione analogue as ligand) *in situ*.

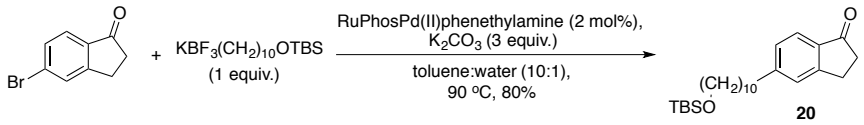


Scheme 5.9. Synthesis of 1,2-indanedione PEG analogue.

Although the 1,2-indanedione PEG side chain analogue afforded synthetically good results, an improved protocol for attaching alkyl side chains was desired. The PEG side chain could display enhanced solubility in water or other polar solvents, while as long alkyl side chains could display the opposite solubility, which would ultimately allow the investigation of various formulations for development of latent fingerprints.

5.4.3) Second-generation synthesis

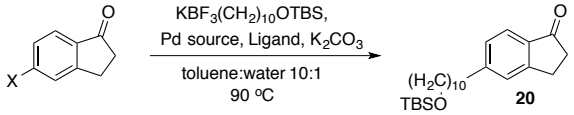
Variation in the bond linkage between the phenyl ring of 1,2-indanedione and the side chain was deemed necessary, in order to circumvent the undesirable side reactions that were occurring under aqueous protic acid conditions in the last step of the synthesis. An alternative solution to the problem was devised, in which a C-C bond linkage was substituted for the problematic C-O bond. The well-known Suzuki-Miyaura reaction was employed to form the desired C-C bond between the sp^2 carbon of the aromatic ring and the sp^3 carbon of the alkyl chain using a known protocol.[41] In particular, commercially available 5-bromo-1-indanone was coupled with a 10-carbon chain potassium alkyltrifluoroborate using slightly modified version of the palladium catalyst (Scheme 5.10). The requisite side chain was synthesized following the synthetic sequence used by Dreher and Molander.[41] The use of Buchwald's 1st generation preformed palladium catalyst (RuPhosPd(II)phenethylamine)[42] was of particular interest due to ease of operation. Aryl bromide was used instead of aryl chloride, since aryl bromides are generally considered to be more reactive as an electrophile in comparison to aryl chlorides. The desired coupled product **20** was obtained in comparable yields using the modified version of the protocol.[41]



Scheme 5.10. Suzuki-Miyaura coupling of 5-bromo-1-indanone and alkyltrifluoroborate.

Since 5-bromo-1-indanone was more expensive than the chloro- derivative at the time, quick optimization of the reaction was conducted (Table 5.3). Although the original protocol was proved to be general[41] in terms of the nature of the electrophile (Br, Cl, I, OTf), a clear difference between the aryl bromide and the chloride was observed in the present case, especially when the 1st generation RuPhos precatalyst was used (Entries 1 & 2, Table 5.3). The aryl chloride was unable to react even under higher preformed catalyst loadings (Entry 3, Table 5.3). Interestingly, when palladium acetate was used instead, the reaction was able to proceed with the aryl chloride as the substrate. Minor differences were observed amongst the different types of phosphine catalyst, although SPhos gave the best yield (Entries 4,6,7, Table 5.3). Increasing the amount of palladium acetate did not improve the yield (Entry 5, Table 5.3). The 2nd generation SPhos precatalyst[43] afforded comparable results, suggesting the improved reactivity in comparison to the 1st generation preformed catalyst (Entry 8, Table 5.3).

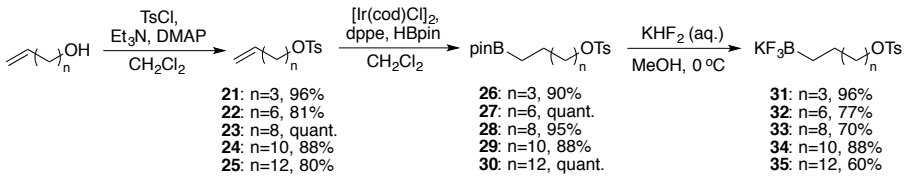
Table 5.3. Optimization of cross-coupling reaction.



Entry	X	Pd source	Ligand (mol%)	Yield[b]
1	Br	1st generation RuPhos precatalyst (2 mol%)	-	80%
2	Cl	1st generation RuPhos precatalyst (2 mol%)	-	No reaction
3	Cl	1st generation RuPhos precatalyst (10 mol%)	-	No reaction
4	Cl	$Pd(OAc)_2$ (2 mol%)	RuPhos (4 mol%)	62%
5	Cl	$Pd(OAc)_2$ (4 mol%)	RuPhos (8 mol%)	49%
6	Cl	$Pd(OAc)_2$ (2 mol%)	SPhos (4 mol%)	70%
7	Cl	$Pd(OAc)_2$ (2 mol%)	XPhos (4 mol%)	49%
8	Cl	2nd generation SPhos precatalyst[c] (2 mol%)	-	57%

[a] Reaction conditions: 1 equiv. electrophile, 1 equiv. trifluoroborate, 3 equiv. K_2CO_3, at 0.25 M concentration.
[b] Isolated yield.
[c] Chloro(2-dicyclohexylphosphino-2′,6′-dimethoxy-1,1′-biphenyl)[2-(2′-amino-1,1′-biphenyl)]palladium(II).

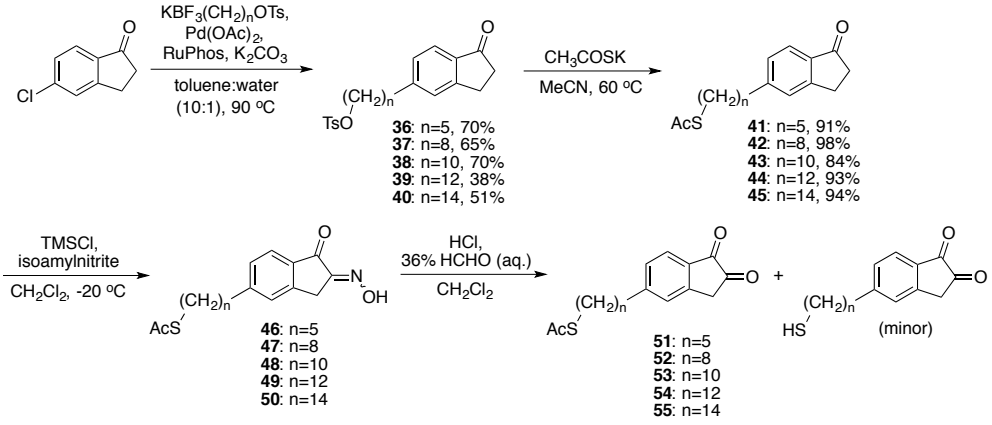
With the optimized condition in hand, synthesis of potassium alkyltrifluoroborate side chains of varying lengths was commenced. Based on the PEG side chain analogue synthesis (Scheme 5.9), appending a tosylate moiety at the opposite end of the alkyl trifluoroborate chain was desired in order to achieve synthetic efficiency. Accordingly, following the general procedure,[41] various alkyl side chains were synthesized in good yields (Scheme 5.11). Apart from 12- and 14-carbon chain starting materials, commercially available alcohols were used as starting materials. Tosylation of the alcohol followed by iridium-mediated borylation afforded the corresponding pinacol boronate esters in good yields. Conversion of the boronate esters to the corresponding potassium trifluoroborates resulted in acceptable yields of the final side chain products.



Scheme 5.11. Synthesis of potassium trifluoroborate alkyl side chains.

With the requisite alkyl side chains, the synthesis of 1,2-indanedione analogues was conducted following the general synthetic sequence (Scheme 5.12). Slight variability in terms of yield was observed for the cross-coupling reaction, which may be attributed to the various side chain lengths. In general, longer side chains afforded modest yields in comparison to shorter ones. Subsequent displacement of the tosylate with potassium thioacetate generated analogues **41**-**45** in good yields. Formation of the oxime followed by conversion to the desired 1,2-indanedione occurred in near quantitative yields without the need of performing silica gel column chromatography purifications. Similar to

previous syntheses (Scheme 5.9), removal of thioacetate group was observed as a minor side product in the last step.



Scheme 5.12. Second generation synthesis of 1,2-indanedione analogues.

The second-generation synthesis was proved to be more synthetically efficient in comparison to the first-generation synthesis not only in terms of number of steps (5 steps *vs.* 4 steps), but also in terms of overall yield. Furthermore, by changing the linkage between the aromatic ring of the 1,2-indanedione and the side chain, the undesired side reactions were not observed, allowing ease of isolation of the desired material by simple aqueous work-up conditions rather than column chromatography purification.

5.5) Progress towards developing latent fingerprints using 1,2-indanedione analogues

In order to assess the ability of the newly generated 1,2-indanedione analogues to detect amino acids, a spot test was performed. The spot test consisted of using a strip of Whatman filter paper that has been impregnated with drops of a weak solution of L-leucine (0.2% w/v in a mixture of 3:7 dioxane/water), which was air-dried. The paper substrate was then dipped into solutions containing either ninhydrin (0.05% w/v solution of ninhydrin in petroleum ether with a drop of AcOH), 1,2-indanedione (0.05% w/v

solution of 1,2-indandione in petroleum ether with a drop of AcOH and catalytic amount of $ZnCl_2$), or the 10-carbon chain analogue **53** (0.05% w/v solution of **53** in petroleum ether with a drop of AcOH and catalytic amount of $ZnCl_2$). The treated paper strip was then air-dried and heated using a steam iron until the spots were visible (1 min). As expected, the ninhydrin treated substrates displayed the characteristic purple colored spots where L-leucine was present (Figure 5.4b). 1,2-Indanedione treated substrates displayed light orange to pink colored spots in comparison. However, paper substrates treated with **53** initially showed almost no visible color development (Figure 5.4a). The spots were made visible only after subsequent post treatment with ninhydrin (Figure 5.4b). Such practices are well-documented in the literature,[2] where weakly developed fingerprints are augmented by post treatment with ninhydrin. Likewise, when 1,2-indanedione treated substrate was post treated with ninhydrin, the color of the spots changed to a darker hue (Figure 5.4b). In all cases, the observed contrast for the developed spots increased over time when the samples were place in an environment away from light (Figure 5.4c).

Figure 5.4. Spot test results; **a)** Initial treatment with **53** (left), post treatment with ninhydrin (right) **b)** Ninhydrin (left), 1,2-indanedione with ninhydrin post treatment (middle), **53** with ninhydrin post treatment (right) **c)** After 24 h.

The results obtained from the spot test with L-leucine suggest that the activity of 1,2-indanedione portion of **53** with amino acids is retained in the presence of a long alkyl side

chain. With this promising result in hand, **53** was chosen as the representative ligand to be functionalized onto gold nanoparticles. Functionalization of gold nanoparticles with **53** was first attempted following a modified Brust protocol[44] used by Almog.[34] Although the synthesis of gold nanoparticles stabilized by tetraoctylammonium bromide was evident (observation of characteristic deep red color upon reduction with $NaBH_4$), subsequent ligand exchange with **53** was unsuccessful. An alternative protocol[45] to synthesize gold colloids stabilized by dodecyldimethylammonium bromide (DDAB) followed by ligand exchange was tested. The protocol was part of a study that was conducted to test the efficacy of digestive ripening with various alkanethiols. Since digestive ripening is a method used to transform highly polydispersed gold nanoparticles to monodispersed gold nanoparticles of decreased average particle size, relatively lower concentration of the surfactant (DDAB) was purposefully used for the study. The authors reasoned that by using a low concentration of DDAB, the removal of DDAB would be easier before the digestive ripening step, and it would also lead to highly polydispersed gold nanoparticles that could be used to observe the decrease in polydispersity after disgestive ripening. Likewise, for the present system, the use of lower concentration of DDAB could allow the subsequent ligand exchange with **53** to occur more easily. However, the digestive ripening step was not followed, since the effect of polydispersity of gold nanoparticles on the development on latent fingerprints on paper has not been determined. Nonetheless, when the protocol was applied in the current system using **53**, the desired functionalized gold nanoparticles were successfully obtained, albeit with prolonged reaction time for ligand exchange. Longer reaction time was expected, since majority of **53** still contained the thioacetate moiety as opposed to the thiol group, which

readily forms strong bonds with gold nanoparticles.[46] Various attempts were made for the removal of the acetate group with no success. Conditions used to convert thioesters to thiols require the use of aqueous media in protic acid or nucleophilic conditions, which only led to the formation of undesired corresponding acetals or decomposition of the material. The precise size of the acquired gold nanoparticles was not determined, since it was assumed that highly polydispersed gold colloids would be obtained. UV-Vis data (λ_{max} = ~530 nm) supported the presence of gold nanoparticles, since the observed λ_{max} was in the region that is characteristic of gold nanoparticles.

With the promising result in hand, detection of latent fingerprint on paper was attempted, following Almog's general procedure.[34] Fingerprints were deposited on a paper substrate (fingerprints that are not "charged" with oily residue (sebaceous) and the paper was subsequently soaked in an aqueous solution of maleic acid for about 5 min to eliminate calcium carbonate on paper. If the calcium carbonate is not removed, the entire paper turns black upon treatment with Ag-PD (i.e. spontaneous silver deposition). The treated paper substrate was air-dried, and dipped into a solution of the functionalized gold nanoparticles in acetonitrile for about 10 min. Subsequent post treatment with Ag-PD solution for 1-2 min gave rise to visible fingerprint ridges (Figure 5.5).

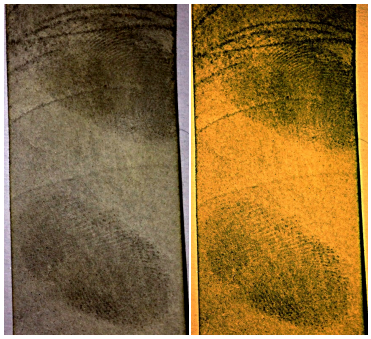


Figure 5.5. Latent fingerprints developed on paper substrate (original image-left, photo enhanced contrast image-right).

Since a "positive" fingerprint image was obtained, in which the silver deposition was more apparent on the ridges of the fingerprint in comparison to the background, the desired reaction of the 1,2-indanedione portion of **53** with the amino acid residue of the fingerprint may be taking precedence over the reaction of 1,2-indanedione with cellulose. Furthermore, although fingerprints that were not "charged" (eccrine fingerprints) were deposited, due to the presence of along alkyl chain on **53**, the observed image could be further amplified by hydrophobic interactions as well.[34,35]

5.6) Conclusions

Novel 1,2-indanedione analogues were successfully synthesized using a concise, four-step protocol. The 10-carbon chain 1,2-indanedione analogue **53** was functionalized onto gold nanoparticles and used to develop latent fingerprints on paper substrates. With the promising preliminary results at hand, further efforts toward optimization of the development protocol will be made. For instance, the effect of gold nanoparticle dispersity on fingerprint development could be studied using the 1,2-indanedione analogues of varying chain lengths. Formulation of the functionalized gold nanoparticle could be optimized as well in order to use solvents that will produce acceptable images without dissolving ink. Use of other sulfur containing compounds as ligands to gold

nanoparticles could be investigated, since the use of thioacetates resulted in prolonged reaction times. Moreover, much work remains to be done in order to fully elucidate the mechanism in which the newly developed reagents are undergoing with residues of latent fingerprints.

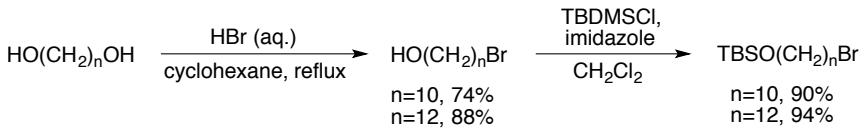
Development of latent fingerprints on paper is still an ongoing research area, since there is no universal reagent that detects fingerprints. The outcome of the developed fingerprint could vary on many external factors that are difficult to control. For instance, a recent study using 1,2-indanedione with $ZnCl_2$ suggested that there is a correlation between the grade and the age of the developed print, age of the donor, and the washing of hands.[47] In order to address such issues, existing fingerprint developing processes, such as Ag-PD,[48] are still evolving to achieve optimal formulation conditions. With the rapid advances in nanotechnology, there is a high demand for developing methods using modified MMD processes. Therefore, the proposed current approach in using functionalized 1,2-indanedione analogues as tunable ligands on gold nanoparticles followed by Ag-PD processing could be an important contribution to the area of latent fingerprint detection on paper.

5.7) Experimental results

General Methods. All reactions were performed under an argon atmosphere except where otherwise noted. Tetrahydrofuran was distilled over sodium-benzophenone, dichloromethane was distilled over calcium hydride, DMF in Acroseal bottles were used without further purification prior to use. Flash chromatography was carried out on Merck silica gel 60 (240-400 mesh) using the solvent conditions listed under individual

experiments. Analytical thin-layer chromatography was performed on Merck silica gel (60F-254) plates (0.25 mm). Visualization was effected with ultraviolet light or phosphomolybdic acid (PMA) stain. Proton magnetic resonance spectra (^{1}H NMR), Carbon magnetic resonance spectra (^{13}C NMR), Fluorine magnetic resonance spectra (^{19}F NMR), and Boron magnetic spectra (^{11}B NMR) were performed on a Bruker NMR operating at 500, 125, 470, and 128 MHz respectively. All ^{11}B chemical shifts were referenced to external BF_3•OEt_2 (0.0 ppm) with a negative sign indicating an upfield shift. Infrared spectra (IR) were obtained on a Perkin-Elmer 281-B spectrometer. High resolution mass spectra (HRMS) were obtained on a Micromass Autospec or a Waters LCTOF-Xe premier. Optical rotations were measured on a Jasco P-1010 polarimeter. 5-hydroxy-1,2-indanedione was prepared following the procedure by Petrovskaia.[i] All other starting materials and reagents were purchased from Sigma-Aldrich, TCI, Acros, or Strem unless specified.

General procedure for alkyl side chain synthesis for first generation synthesis



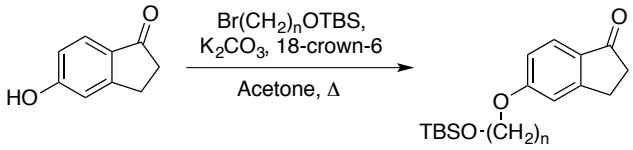
Following the protocol reported by Suzuki *et al*,[ii] to a solution of the diol (5.74 mmol) dissolved in cyclohexane (25 mL) at room temperature was added aqueous HBr (141.4 mmol). The resulting mixture was brought to reflux with stirring for 6 h or until

[i] O. G. Petrovskaia, "Design and synthesis of chromogenic and fluorogenic reagents for amino acid detection." University of Pennsylvania, Philadelphia, PA, 1999.
[ii] Luu, B., Bagnard, D., Hanibali, M., Yamada, M., Suzuki, H. Hydroquinone long-chain derivative and/or phenoxy long-chain derivative and pharmaceutical preparation comprising the same. EP1854777 (A1), November 14, 2007.

completion (monitored by TLC). The reaction mixture was cooled to room temperature and extracted with diethyl ether. The organic layers were combined and washed with aqueous sat. $NaHCO_3$, brine, and dried over $MgSO_4$. Filtration followed by concentration under vacuum afforded a clear oil. Further purification by silica gel chromatography afforded the desired product. ^{1}H NMR spectra of the 10- and 12-carbon derivative were in good accordance with the reported data.[1]

To a solution of the bromoalcohol (4.216 mmol) in anhydrous CH_2Cl_2 (10 mL) was added TBDMSCl (6.324 mmol) followed by imidazole (6.324 mmol) at room temperature. The resulting solution was left to stir for 48 h at room temperature. After removal of the solvent, the residue was dissolved in ethyl acetate and washed with aqueous 10% $KHSO_4$ and dried over Na_2SO_4, filtered, and concentrated. Silica gel chromatography purification afforded the desired product as a clear, colorless oil. ^{1}H NMR spectra of 10- and 12-carbon derivative were in good accordance with the reported data.[iii,iv]

General procedure for chain attachment for first generation synthesis

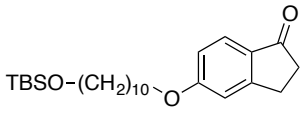


To a stirred solution of 5-hydroxy-1-indanone (100 mg, 0.675 mmol) in anhydrous

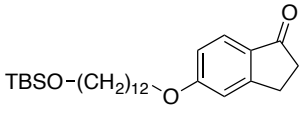
[iii] Goulaouic-Dubois, C., Guggisberg, A., Hesse, M. "Samarium diiodide induced ring enlargement of azidocyclododecanones to various marocyclic lactams." *Tetrahedron* **1995**, *51*, 12035-12046.

[iv] Maharvi, G. M., Edwards, A. O., Fauq, A. H. "Chemical synthesis of deuterium-labeled and unlabeled very long chain polyunsaturated fatty acids." *Tetrahedron Lett.* **2010**, *51*, 6426-6428.

acetone (20 mL) was added the 10-carbon chain (261 mg, 0.742 mmol), K_2CO_3 (233 mg, 1.687 mmol), and 18-crown-6 (1.3 mg, 0.005 mmol). The resulting mixture was brought to reflux and left to stir for 24 h. The solvent was evaporated, dissolved in CH_2Cl_2 (30 mL), washed with H_2O (10 mL), back-extracted the aqueous layer with CH_2Cl_2 (10 mL, 3 times). The organic layers were combined and dried over $MgSO_4$, filtered, and concentrated. Silica gel chromatography purification (10% Ethyl acetate/Hexanes) afforded the chain attached indanone **6**.



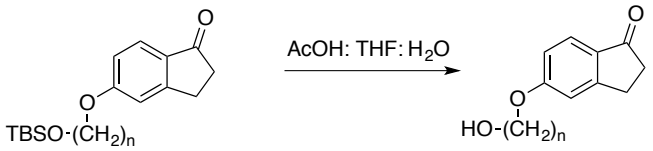
10-Carbon chain TBS ether (6). R_f 0.28 (10% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 9.13 Hz, 1H), 6.91 (dd, *J* = 6.1, 2.1 Hz, 2H), 4.05 (t, *J* = 6.5 Hz, 2H), 3.64 (t, *J* = 6.5 Hz, 2H), 3.09 (dd, *J* = 7.46, 4.21 Hz, 2H), 2.70-2.67 (m, 2H), 1.86-1.81 (m, 2H), 1.61-1.44 (m, 6H), 1.44-1.28 (m, 8H), 1.04 (s, 9H), 0.13 (s, 6H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 205.2, 164.9, 158.1, 130.2, 125.3, 115.6, 110.3, 68.4, 63.3, 63.0, 36.4, 32.84, 32.79, 29.5, 29.45, 29.38, 29.3, 29.0, 25.9, 25.8, 25.76, 25.71, 18.35; IR (cm^{-1}): 2929, 2856, 1709, 1601, 1489, 1471, 1443, 1406, 1388, 1360, 1332, 1303, 1257, 1143, 1100, 1006, 836, 812, 775; HRMS (ESI) *m/*z calculated for $C_{25}H_{42}O_3Si$ $(M + Na)^+$: 441.2801, found: 441.2808.



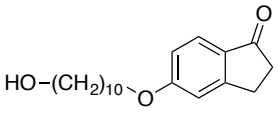
12-Carbon chain TBS ether (7). R_f 0.57 (20% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.71-7.69 (m, 1H), 6.92-6.90 (m, 2H), 4.04 (t, *J* = 6.51 Hz, 2H), 3.61 (td, *J* = 6.63, 0.98 Hz, 2H), 3.11-3.09 (m, 2H), 2.70-2.67 (m, 2H), 1.84-1.81 (m, 2H), 1.54-1.47 (m, 4H), 1.39-1.27 (m, 14H), 0.91 (s, 9H), 0.06 (s, 6H); ^{13}C NMR: (125

MHz, $CDCl_3$) δ 205.2, 164.9, 158.1, 130.2, 125.3, 115.6, 110.3, 68.5, 63.3, 36.4, 32.9, 29.6, 29.5, 29.4, 29.3, 29.1, 26.0, 25.9, 25.86, 25.81, 18.4; IR (cm^{-1}): 2924, 2853, 1701, 1608, 1583, 1475, 1438, 1388, 1329, 1259, 1244, 1146, 1101, 1019, 875, 835, 773; HRMS (ESI) *m/z* calculated for $C_{27}H_{46}O_3Si$ $(M + Na)^+$: 469.3114, found: 469.3120.

General procedure for TBS removal for first generation synthesis

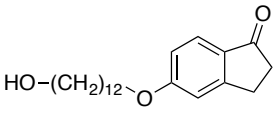


A solution of 10-carbon chain TBS ether **6** (2.7 g, 6.544 mmol) in 3:3:1 mixture of acetic acid:THF:H_2O (170 mL) was stirred at room temperature overnight. Ethyl acetate (200 mL) was added to the reaction mixture. The organic layer was carefully washed with 5% aq. $NaHCO_3$ (100 mL) to neturalize the solution (checked by pH). The organic layer was then washed with 1M HCl (100 mL), brine, dried over $MgSO_4$, filtered and concentrated. Silica gel chromatography purification (30% → 50% EtOAc/Hexanes) afforded the desired alcohol **8**.



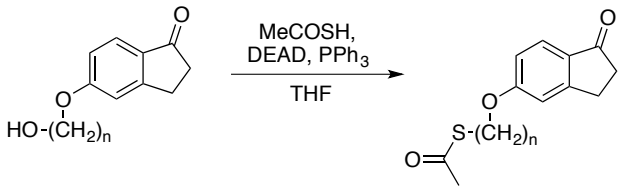
10-Carbon chain alcohol (8). R_f 0.72 (30% Acetone/Hex); ^1H NMR: (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 9.14 Hz, 1H), 6.92-6.90 (m, 2H), 4.05 (t, *J* = 6.54 Hz, 2H), 3.66 (td, *J* = 6.63, 0.93 Hz, 2H), 3.11-3.09 (m, 2H), 2.70-2.68 (m, 2H), 1.85-1.80 (m, 2H), 1.61-1.56 (m, 2H), 1.50-1.44 (m, 4H), 1.41-1.32 (m, 10H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 205.2, 164.9, 158.1, 130.3, 125.3, 115.6, 110.3, 68.4, 63.0, 36.4, 32.8, 29.51, 29.46, 29.4, 29.3, 29.0, 25.9, 25.8, 25.7; IR (cm^{-1}): 3411, 2916, 2851, 1686,

1672, 1607, 1595, 1469, 1439, 1401, 1339, 1305, 1259, 1106, 1092, 1049, 1019, 859, 836, 811, 716; HRMS (ESI) *m/*z calculated for $C_{19}H_{28}O_3$ $(M + H)^+$: 305.2117, found: 305.2129.

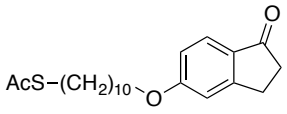


12-Carbon chain alcohol (9). R_f 0.21 (2% EtOAc/CH_2Cl_2); ^1H NMR: (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 9.33 Hz, 1H), 6.92-6.90 (m, 2H), 4.04 (t, *J* = 6.54 Hz, 2H), 3.69-3.65 (m, 2H), 3.11-3.09 (m, 2H), 2.72-2.67 (m, 2H), 1.87-1.80 (m, 2H), 1.62-1.56 (m, 4H), 1.52-1.45 (m, 2H), 1.42-1.28 (m, 14H), 1.26-1.21 (m, 1H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 205.3, 164.8, 158.1, 130.1, 125.3, 115.6, 110.2, 68.4, 63.0, 36.4, 32.7, 29.6, 29.5, 29.4, 29.3, 29.0, 25.9, 25.8, 25.7; IR (cm^{-1}): 3420, 2915, 2851, 1686, 1672, 1605, 1583, 1473, 1439, 1401, 1336, 1305, 1258, 1147, 1107, 1094, 1055, 1039, 1023, 1000, 860, 834, 810, 715, 651, 568; HRMS (ESI) *m/*z calculated for $C_{21}H_{32}O_3$ $(M + Na)^+$: 355.2249, found: 355.2255.

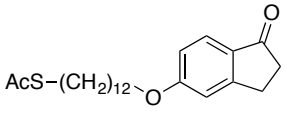
General procedure for Mitsunobu reaction for first generation synthesis



To a mixture of the 10-carbon chain alcohol **8** (90 mg, 0.2956 mmol) and PPh_3 (116 mg, 0.4435 mmol) in anhydrous THF was added drop-wise DEAD (70 mL, 0.4435 mmol). After 5 min, thioacetic acid (42 mL, 0.5913 mmol) was added, and the resulting mixture was stirred at room temperature for 20 h. The solvent was concentrated. Silica gel column chromatography purification (30% EtOAc/Hexanes) afforded the desired product **10**.

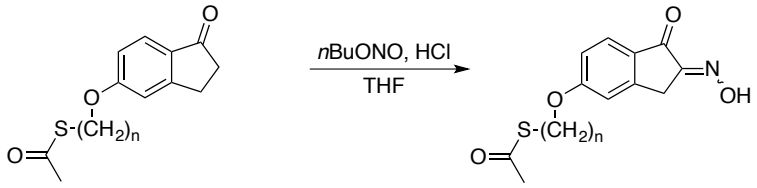


10-Carbon chain thioacetate (10). R_f 0.62 (30% Acetone/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 9.06 Hz, 1H), 6.89 (t, *J* = 2.23 Hz, 2H), 4.03 (t, *J* = 6.52 Hz, 2H), 3.08 (t, *J* = 5.82 Hz, 2H), 2.86 (t, *J* = 7.36 Hz, 2H), 2.68-2.65 (m, 2H), 2.23, (s, 3H), 1.84-1.76 (m, 2H), 1.57 (dt, *J* = 14.59, 7.30 Hz, 2H), 1.49-1.42 (m, 2H), 1.36-1.24 (m, 12H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 205.1, 195.9, 164.8, 158.0, 130.1, 125.2, 115.5, 110.2, 68.4, 36.3, 30.5, 29.4, 29.37, 39.30, 29.2, 29.1, 29.0, 28.7, 28.3, 25.9, 25.8, 24.9, 14.0; IR (cm^{-1}): 2918, 2851, 1755, 1698, 1607, 1594, 1470, 1433, 1414, 1305, 1254, 1141, 1119, 1089, 1043, 1014, 968, 855, 830, 807, 717, 636; HRMS (ESI) *m/z* calculated for $C_{21}H_{30}O_3S$ $(M + H)^+$: 363.1994, found: 363.1984.

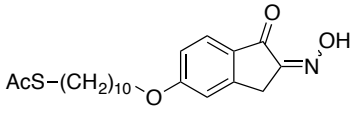


12-Carbon chain thioacetate (11). R_f 0.65 (2% EtOAc/CH_2Cl_2); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.99 Hz, 1H), 6.92-6.90 (m, 2H), 4.04 (t, *J* = 6.55, 2H), 3.11-3.09 (m, 2H), 2.88 (t, *J* = 7.35, 2H), 2.68 (ddd, *J* = 5.96, 4.08, 1.83 Hz, 2H), 2.33 (s, 3H), 1.86-1.80 (m, 2H), 1.61-1.55 (m, 2H), 1.51-1.45 (m, 2H), 1.43-1.25 (m, 14H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 205.2, 195.9, 164.8, 158.0, 130.1, 125.2, 115.5, 110.2, 68.4, 63.9, 38.9, 36.3, 30.5, 29.47, 29.40, 29.2, 29.1, 29.05, 29.03, 28.9, 28.8, 28.7, 28.3, 25.9, 25.8, 24.9, 14.0; IR (cm^{-1}): 2915, 2850, 1755, 1698, 1606, 1487, 1470, 1433, 1414, 1354, 1329, 1305, 1254, 1141, 1089, 1038, 1021, 987, 951, 853, 830, 807, 716, 634, 595; HRMS (ESI) *m/z* calculated for $C_{23}H_{34}O_3S$ $(M + Na)^+$: 413.2126, found: 413.2140.

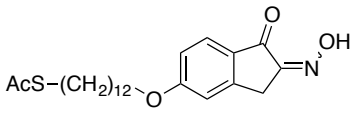
General procedure for oxime formation for first generation synthesis



To a solution of 10-carbon thioacetate **10** (86 mg, 0.2372 mmol) in THF (0.5 mL) was added conc. HCl (0.13 mL, 4.278 mmol) followed by *n*Butyl nitrite (77 mL, 0.658 mmol). The resulting mixture was left to stir at room temperature for 2 h (or until completion monitored by TLC). Ethyl acetate (5 mL) was added to the reaction mixture, and the organic layer was washed with H_2O (1 mL), washed with brine (1 mL), dried over $MgSO_4$, filtered, and concentrated. Silica gel chromatography purification (30% EtOAc/Hexanes → 40% → 50%) afforded the desired product **12**.



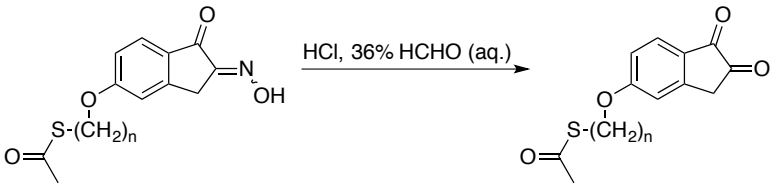
10-Carbon chain oxime (12). R_f 0.28 (40% EtOAc/Hex); ^1H NMR: (500 MHz, $CDCl_3$) δ7.85 (d, *J* = 8.5 Hz, 1H), 6.97-6.94 (m, 2H), 4.08 (t, *J* = 6.5 Hz, 2H), 3.82 (s, 2H), 2.88 (t, *J* = 7.4 Hz, 2H), 2.34 (s, 3H), 1.87-1.81 (m, 2H), 1.61-1.46 (m, 14H), 1.41-1.29 (m, 19H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 196.2, 187.7, 165.8, 155.2, 149.9, 131.0, 136.6, 116.1, 110.5, 68.6, 30.5, 29.4, 29.3, 29.2, 29.1, 29.0, 28.9, 28.7, 28.4, 25.8; IR (cm^{-1}): 3232, 2925, 2853, 1692, 1601, 1578, 1468, 1344, 1278, 1248, 1108, 1037, 905, 770, 686, 628; HRMS (ESI) *m/*z calculated for $C_{21}H_{29}NO_4S$ $(M + H)^+$: 392.1896, found: 392.1882.



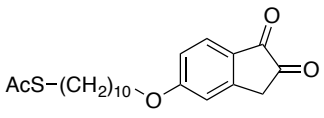
12-Carbon chain oxime (13). R_f 0.36 (40% EtOAc/Hex); ^1H

NMR: (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.4 Hz, 1H), 6.96 (s, 1H), 6.94 (s, 1H), 4.08 (t, *J* = 6.5 Hz, 2H), 3.82 (s, 2H), 2.88 (t, *J* = 7.4 Hz, 2H), 2.34 (s, 3H), 1.87-1.81 (m, 2H), 1.57 (sextet, *J* = 6.4 Hz, 2H), 1.51-1.45 (m, 2H), 1.38-1.29 (m, 15H).; ^{13}C NMR: (125 MHz, $CDCl_3$) δ 196.2, 187.7, 166.0, 155.5, 149.9, 131.1, 126.7, 116.2, 110.6, 68.7, 30.6, 29.49, 29.43, 29.29, 29.15, 29.13, 29.08, 28.99, 28.81, 28.4, 25.92, 25.90; IR (cm^{-1}): 2923, 2852, 1692, 1645, 1601, 1579, 1489, 1471, 1343, 1297, 1248, 1109, 1095, 1037, 771, 684, 628; HRMS (ESI) *m/z* calculated for $C_{23}H_{33}NO_4S$ $(M + Na)^+$: 442.2028, found: 442.2038.

General procedure for synthesis of 1,2-indanedione derivative for first generation synthesis



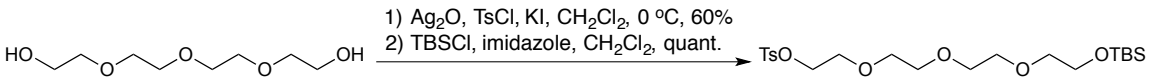
To a suspension of the 10-carbon chain oxime **12** (893 mg, 2.281 mmol) in aqueous formaldehyde (37% in water) (8.6 mL, 116.3 mmol), was added conc. HCl (17 mL, 559.5 mmol). The resulting suspension was vigorously stirred at room temperature overnight. The reaction mixture was diluted with CH_2Cl_2 (20 mL), basified until pH ~5 using aqueous $NaHCO_3$. The aqueous layer was separated and extracted with CH_2Cl_2 (10 mL, 3 times). The organic layers were combined and washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated.



10-Carbon chain 1,2-indanedione analogue (14). R_f 0.6 (40% EtOAc/Hex); ^1H NMR: (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.6 Hz, 1H), 7.00-6.95 (m, 2H),

4.11 (t, J = 6.5 Hz, 2H), 3.57 (s, 2H), 2.87 (t, J = 7.4 Hz, 2H), 2.33 (s, 3H), 1.88-1.82 (m, 2H), 1.57 (dt, J = 14.6, 7.3 Hz, 2H), 1.49-1.45 (m, 2H), 1.37-1.31 (m, 10H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 200.4, 196.0, 184.6, 166.7, 149.7, 131.3, 128.2, 116.9, 110.7, 69.9, 36.7, 30.6, 29.6, 29.4, 29.38, 29.32, 29.1, 29.09, 29.03, 28.8, 28.7, 25.8; IR (cm^{-1}): 3413, 2826, 2853, 1710, 1691, 1599, 1261, 1105.

Synthesis of functionalized PEG chain

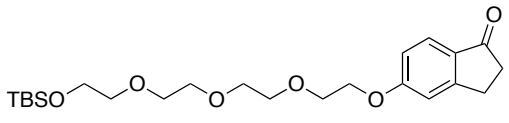


To a stirred solution of tetraethyleneglycol (1 mL, 5.766 mmol) in anhydrous CH_2Cl_2 (58 mL) at 0 ^{o}C was added Ag_2O (2 g, 8.649 mmol) and KI (0.19 mg, 1.154 mmol) followed by portion-wise addition of TsCl (1.2 g, 6.343 mmol). The resulting mixture was kept at 0 ^{o}C for 10 min. The reaction mixture was then filtered through a pad of silica gel and evaporated. Silica gel chromatography purification (30% Acetone/CH_2Cl_2) afforded the tosylated PEG chain as a colorless oil (1.21 g, 60%). ^{1}H NMR spectra obtained was in good accordance with the reported data.[v]

To a stirred solution of tosylated PEG chain (1.11 g, 3.186 mmol) in anhydrous CH_2Cl_2 (16 mL) was added TBSCl (0.72 g, 4.779 mmol) followed by imidazole (0.33 g, 4.779 mmol). The resulting mixture was left to stir at room temperature overnight. The reaction was diluted with ethyl acetate (40 mL), washed with aqueous 10% $KHSO_4$ (15 mL). The organic layer was separated, and dried over Na_2SO_4, filtered, and concentrated. Silica gel

[v] Rubinshtein, M., James, C. R., Young, J. L., Ma, Y. J., Kobayashi, Y., Gianneschi, N. C., Yang, J. "Facile procedure for generating side chain functionalized poly(α-hydroxy acid) copolymers from aldehydes via a versatile passerini-type condensation." *Org. Lett.* **2010**, *12*, 3560-3563.

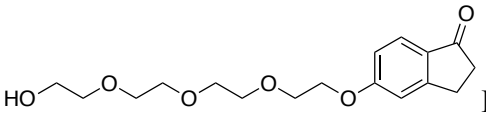
chromatography purification (40% EtOAc/Hexanes) afforded the desired functionalized PEG chain as a colorless oil (1.47 g, quant.). ^{1}H NMR spectra obtained was in good accordance with the reported data.[vi]



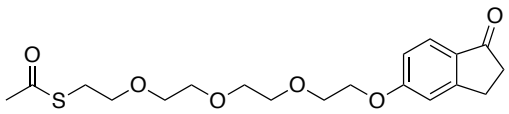
TBS ether PEG chain indanone (15). To a stirred solution of 5-hydroxy-1-indanone (300 mg, 2.025 mmol) in anhydrous acetone (61 mL) was added the functionalized PEG chain (1.0 g, 2.227 mmol), K_2CO_3 (0.7 g, 5.06 mmol), and 18-crown-6 (4 mg, 0.014 mmol). The resulting mixture was brought to reflux and left to stir overnight. The solvent was evaporated, dissolved in CH_2Cl_2 (30 mL), washed with H_2O (10 mL), back-extracted the aqueous layer with CH_2Cl_2 (10 mL, 3 times). The organic layers were combined and dried over $MgSO_4$, filtered, and concentrated. Silica gel chromatography purification (40% EtOAc/Hexanes) afforded the desired product as a yellow oil (759 mg, 85%). R_f 0.23 (40% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 9.19, 1.88 Hz, 1H), 6.93 (dd, *J* = 7.20, 1.87 Hz, 2H), 4.23-4.21 (m, 2H), 3.90 (td, *J* = 4.80, 1.45 Hz, 2H), 3.79-3.74 (m, 4H), 3.71 (dd, *J* = 2.85, 1.64 Hz, 2H), 3.67 (d, J = 1.82 Hz, 4H), 3.57 (td, J = 5.43, 1.88 Hz, 2H), 3.09 (t, *J* = 5.39 Hz, 2H), 2.68 (ddt, *J* = 5.75, 3.95, 1.96 Hz, 2H), 0.90 (d, *J* = 1.96 Hz, 9H), 0.07 (d, *J* = 1.95 Hz, 6H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 205.2, 164.4, 158.0, 130.5, 125.2, 115.6, 110.4, 72.6, 70.8, 70.7, 70.68, 70.63, 69.4, 67.7, 62.6, 36.3, 25.9, 25.8, 25.6, 18.3, -5.2; IR (cm^{-1}): 2928, 1705, 1601, 1488, 1471, 1462, 1443, 1407, 1388, 1360, 1350, 1332,

[vi] Gutiérrez-Nava, M., Masson, P., Nierengarten, J.-F. "Synthesis of copolymers alternating oligophenylenevinylene subunits and fullerene moieties." *Tetrahedron Lett.* **2003**, *44*, 4487-4490.

1304, 1258, 1103, 1030, 1006, 953, 835, 811, 778, 710, 660, 592; HRMS (ESI) *m/*z calculated for $C_{23}H_{38}O_6Si$ $(M + H)^+$: 439.2516, found 439.2523.

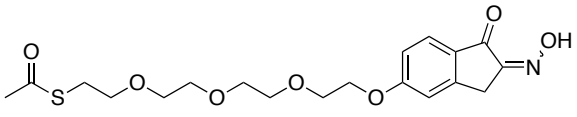


PEG chain indanone (16). To a stirred solution of the TBS ether **15** (659 mg, 1.502 mmol) in anhydrous THF (8 mL) at 0 °C was added TBAF (1M in THF, 3.76 mL, 3.756 mmol). The resulting mixture was kept at 0 °C for 2 h then slowly warmed to room temperature for additional 2 h. The reaction mixture was diluted with ethyl acetate (20 mL), washed with H_2O (10 mL) and brine (10 mL). The organic layer was separated and dried over Na_2SO_4, filtered, and concentrated. Silica gel chromatography purification afforded the alcohol (425 mg, 87%). R_f 0.23 (40% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 9.24 Hz, 1H), 6.95-6.93 (m, 2H), 4.23 (t, *J* = 4.82 Hz, 2H), 3.90 (t, *J* = 4.81 Hz, 2H), 3.77-3.67 (m, 11H), 3.63 (dd, *J* = 5.12, 3.96 Hz, 2H), 3.10 (t, *J* = 5.91 Hz, 2H), 2.70-2.68 (m, 2H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ; 205.2, 164.4, 158.0, 130.5, 125.3, 115.7, 110.4, 72.4, 70.8, 70.7, 70.6, 70.3, 69.5, 67.7, 61.7, 36.4, 25.8; IR (cm^{-1}): 3449, 3062, 3023, 2919, 2872, 1701, 1599, 1488, 1442, 1406, 1348, 1334, 1305, 1259, 1198, 1127, 1104, 1090, 1032, 953, 885, 837, 809, 710, 650, 592; HRMS (ESI) *m/*z calculated for $C_{17}H_{24}O_6$ $(M + Na)^+$: 347.1471, found: 347.1464.



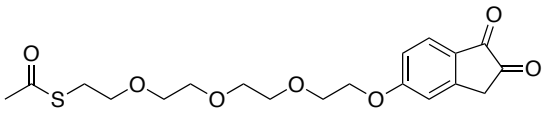
Thioacetate PEG chain indanone (17). To a stirred mixture of the alcohol **16** (420 mg, 1.294 mmol) in pyridine (13 mL) at −5 °C was added TsCl (617 mg, 3.237 mmol). The resulting mixture was kept at −5 °C for 1 h, then

warmed to room temperature over 4 h. The reaction was quenched with 1N HCl (10 mL), and extracted with ethyl acetate (30 mL). The organic layer was washed with 1N HCl (10 mL, three times), aqueous $NaHCO_3$ (10 mL), and brine (10 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated to afford the crude tosylated product, which was carried on to the next step without further purification. To a stirred solution of the tosylate in anhydrous acetonitrile (78 mL) was added potassium thioacetate (286 mg, 2.504 mmol) in one portion. The resulting mixture was brought to 60 ^oC and left to stir overnight. The reaction was quenched with H_2O (160 mL), and the aqueous layer was extracted with CH_2Cl_2 (200 mL, two times). The combined organic layers were washed with brine (100 mL) and dried over Na_2SO_4, filtered, and concentrated. Silica gel chromatography purification (70% EtOAc/Hexanes) afforded the product as a yellow oil (370 mg, 77%). R_f 0.6 (80% EtOAc/Hex); ^1H NMR: (500 MHz, $CDCl_3$) δ 7.66 (d, J = 9.13 Hz, 1H), 6.91 (t, J = 2.97 Hz, 2H), 4.20 (t, J = 4.79 Hz, 2H), 3.88 (dd, J = 5.17, 4.39 Hz, 2H), 3.74-3.57 (m, 10H), 3.09-3.06 (m, 4H), 2.67-2.64 (m, 2H) 2.31 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 205.1, 195.3, 164.3, 157.9, 130.4, 125.2, 115.6, 110.3, 70.8, 70.6, 70.4, 70.2, 69.6, 69.4, 67.7, 36.3, 30.4, 28.7, 25.7; IR (cm^{-1}): 2920, 2869, 1701, 1691, 1599, 1487, 1441, 1353, 1332, 1303, 1257, 1196, 1102, 1088, 1055, 1030, 953, 868, 836, 808, 709, 626, 592; HRMS (ESI) *m/z* calculated for $C_{19}H_{26}O_6S$ $(M + Na)^+$: 405.1348, found: 405.1332.



Thioacetate PEG chain oxime (18). To a flask charged with **17** (100 mg, 0.261 mmol) and a stir bar at −20 ^oC was added TMSCl

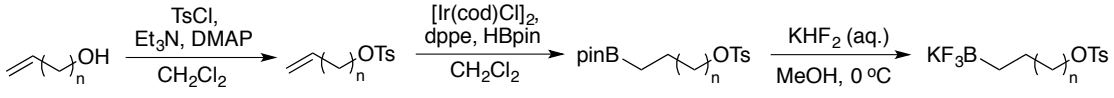
(33 mL, 0.261 mmol) followed by drop-wise addition of isoamyl nitrite (35 mL, 0.261 mmol). The resulting mixture was left to stir at −20 °C for 30 min. The reaction was quenched with H_2O (1 mL), extracted with ethyl acetate (3 mL), dried over Na_2SO_4, filtered, and concentrated to afford the desired product. R_f 0.2 (80% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 10 Hz, 1H), 6.94 (d, *J* = 10 Hz, 1H), 6.88 (s, 1H), 4.26 (t, *J* = 5 Hz, 2H), 3.89 (t, *J* = 5 Hz, 2H), 3.74-3.53 (m, 13H), 3.06 (t, *J* = 5 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 195.5, 187.7, 165.4, 155.2, 149.7, 131.3, 136.5, 116.2, 110.7, 70.8, 70.7, 70.5, 70.2, 69.7, 69.4, 67.9, 41.6, 30.5, 28.7, 28.3, 22.5; HRMS (ESI) *m/z* calculated for $C_{19}H_{25}NO_7S$ $(M + Na)^+$: 434.1249, found: 434.1261.



Thioacetate PEG chain 1,2-indanedione (19). To a flask charged with **18** (25 mg, 0.061 mmol) and a stir bar was added formaldehyde (37% in water) (500 mL) and conc. HCl (0.1 mL). The resulting suspension was vigorously stirred overnight. The reaction mixture was diluted with CH_2Cl_2 (2 mL), basified until pH ~5 using aqueous $NaHCO_3$. The aqueous layer was separated and extracted with CH_2Cl_2 (1 mL, 3 times). The organic layers were combined and washed with brine (1 mL), dried over $MgSO_4$, filtered, and concentrated. R_f 0.4 (80% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.58 Hz, 1H), 7.04-7.00 (m, 2H), 4.29 (t, *J* = 4.44 Hz, 2H), 3.93 (t, *J* = 4.28 Hz, 2H), 3.76-3.58 (m, 12H), 3.08 (t, *J* = 6.49 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 200.3, 195.4, 184.7, 166.3, 149.7, 131.3, 128.1, 116.9, 111.0, 70.9, 70.6, 70.5, 70.2, 70.0, 69.7, 69.2, 68.2, 36.7, 30.5, 29.6, 28.7; IR (cm^{-1}): 2871, 1761, 1713, 1600, 1489, 1452, 1350, 1257, 1104, 1052, 954,

841; HRMS (ESI) *m/z* calculated for $C_{19}H_{24}O_7S$ $(M + H)^+$: 397.1321, found: 397.1318.

General procedure for synthesis of potassium alkyltrifluoroborate side chains



21: n=3, 96%
22: n=6, 81%
23: n=8, quant.
24: n=10, 88%
25: n=12, 80%

26: n=3, 90%
27: n=6, quant.
28: n=8, 95%
29: n=10, 88%
30: n=12, quant.

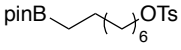
31: n=3, 96%
32: n=6, 77%
33: n=8, 70%
34: n=10, 88%
35: n=12, 60%

To a stirred solution of 9-decen-1-ol (3 mL, 16.702 mmol) in anhydrous CH_2Cl_2 (30 mL) was added triethylamine (3.5 mL, 25.053 mmol) followed by DMAP (82 mg, 0.668 mmol) and TsCl (3.18 g, 16.702 mmol). The resulting mixture was left to stir at room temperature overnight. The reaction was diluted with water (10 mL) and extracted with chloroform (10 mL, three times). The combined organic layers were washed with aqueous sat. NH_4Cl (10 mL), separated, dried over $MgSO_4$, filtered, and concentrated. Silica gel column chromatography purification (30% EtOAc/Hexanes) afforded **23** as an oil (4.73, 91%).

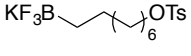
A 100 mL round bottom flask was charged with $[Ir(cod)Cl]_2$ (146 mg, 0.217 mmol), dppe (173 mg, 0.434 mmol), and a stir bar in a glovebox. The flask was then removed and to it was added a solution of the tosylate **23** (4.5 g, 14.495 mmol) in anhydrous CH_2Cl_2 (48 mL) via cannula addition. The resulting mixture was brought to 0 ^oC, followed by drop-wise addition of pinacolborane (3.15 mL, 21.742 mmol). The reaction mixture was left to stir and allowed to warm to room temperature overnight. The reaction was quenched by water (15 mL), left to stir for 5 min, and the resulting mixture was separated. The aqueous layer was extracted with diethyl ether (15 mL, three times). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Purification by silica

gel chromatography (15% EtOAc/Hexanes) afforded the product **28** as an oil (6.12 g, 97%).

To a stirred solution of **28** (4.5 g, 10.357 mmol) in acetonitrile (14 mL) was added aqueous 4.5 M KHF_2 (14 mL). The resulting mixture was left to stir at room temperature for 1 h. The solution was concentrated, and put under vacuum overnight. Hot acetonitrile (100 mL) was added to the solid and filtered by hot gravity filtration (or alternatively, soxhlet extraction). The filtrate was evaporated, re-dissolved in small amount of cold diethyl ether (20 mL) and filtered to afford the desired potassium alkyltrifluoroborate salt **33**.

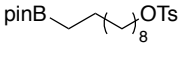


8-Carbon chain pinacolboronate ester (27). R_f 0.65 (20% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.31 Hz, 2H), 7.35 (d, *J* = 8.51 Hz, 2H), 4.04-4.00 (m, 2H), 2.45 (s, 3H), 1.69-1.59 (m, 4H), 1.39-1.22 (m, 20H), 0.75 (t, *J* = 7.82 Hz, 2H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 144.5, 133.1, 129.7, 127.8, 82.8, 70.6, 32.1, 31.6, 29.0, 28.9, 28.8, 28.7, 25.2, 24.7, 23.8, 22.5, 21.5, 14.0; ^{11}B NMR (128.4 MHz, $CDCl_3$) δ 33.68; IR (cm^{-1}): 2977, 2928, 2857, 1598, 1495, 1466, 1363, 1320, 1272, 1213, 1188, 1177, 1145, 1098, 1019, 966, 936, 845, 815, 664, 577, 555; HRMS (ESI) *m/*z calculated for $C_{21}H_{35}BO_5S$ $(M + H)^+$: 411.2377, found: 411.2372.

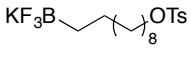


8-Carbon chain potassium trifluoroborate salt (32). ^{1}H NMR: (500 MHz, acetone-d_6) δ 7.81 (d, *J* = 8.18 Hz, 2H), 7.50 (d, *J* = 8.29 Hz, 2H), 4.05 (t, *J* = 6.41 Hz, 2H), 2.47 (s, 3H), 1.63 (dt, *J* = 14.26, 6.90 Hz, 2H), 1.38-1.15 (m, 10H), 0.88 (t, *J* = 7.05 Hz, 2H); ^{13}C NMR: (125 MHz, acetone-d_6) δ 145.7, 134.6, 130.9, 128.7, 83.5, 71.6,

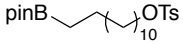
32.9, 32.5, 26.1, 25.3, 25.29, 25.25, 24.8, 23.3, 21.5, 14.4; ^{11}B NMR (128.4 MHz, acetone-d_6) δ 6.03; IR (cm^{-1}): 2916, 2850, 1362, 1175, 1095, 964, 944, 835, 810, 720, 669, 650; HRMS (ESI) *m/*z calculated for $C_{15}H_{23}BF_3O_3S$ $(M - K^+)^+$: 351.1413, found: 351.1406.



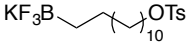
10-Carbon chain pinacolboronate ester (28). R_f 0.43 (10% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.36 Hz, 2H), 7.34-7.32 (m, 2H), 3.99 (t, *J* = 6.52 Hz, 2H), 2.42 (s, 3H), 1.60 (dt, *J* = 14.42, 6.99 Hz, 2H), 1.40-1.34 (m, 2H), 1.26-1.18 (m, 24H), 0.73 (t, *J* = 7.79 Hz, 2H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 114.5, 133.0, 129.6, 127.7, 82.7, 70.5, 32.2, 31.7, 29.25, 29.23, 29.1, 28.7, 28.6, 25.1, 24.6, 23.8, 22.5, 21.5; ^{11}B NMR (128.4 MHz, $CDCl_3$) δ 33.87; IR (cm^{-1}): 2977, 2855, 1598, 1495, 1466, 1371, 1320, 1271, 1212, 1188, 1177, 1145, 1098, 1019, 1004, 966, 920, 882, 832, 815, 790, 776, 723, 688, 664, 577, 555; HRMS (ESI) *m/*z calculated for $C_{23}H_{39}BO_5S$ $(M + H)^+$: 439.2690, found: 439.2685.



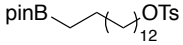
10-Carbon chain potassium trifluoroborate salt (33). ^{1}H NMR: (500 MHz, acetone-d_6) δ 7.84-7.81 (m, 2H), 7.52-7.49 (m, 2H), 4.06 (dt, J = 10.63, 5.0 Hz, 2H), 2.47 (s, 3H), 1.66-1.60 (m, 2H), 1.29-1.18 (m, 14H), 0.15-0.12 (m, 2H); ^{13}C NMR: (125 MHz, acetone-d_6) δ 145.8, 134.5, 130.9, 128.7, 74.8, 71.6, 34.6, 30.8, 30.5, 26.6, 26.1, 25.3, 25.2, 21.6; ^{11}B NMR (128.4 MHz, acetone-d_6) δ 6.06; ^{19}F NMR (470.8 MHz, acetone-d_6) δ −140.95; IR (cm^{-1}): 2918, 2852, 1358, 1188, 1175, 1094, 965, 904, 836, 809, 784, 627.



12-Carbon chain pinacolboronate ester (29). R_f 0.34 (10% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.32 Hz, 2H), 7.32 (d, *J* = 8.51 Hz, 2H), 4.00 (t, *J* = 6.54 Hz, 2H), 2.43 (s, 3H), 1.61 (dt, *J* = 14.43, 7.00 Hz, 2H), 1.40-1.17 (m, 30H), 0.74 (t, *J* = 7.77, 2H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 144.4, 133.2, 129.6, 127.7, 82.7, 70.5, 32.2, 29.5. 29.4, 29.3, 29.2, 28.8, 28.7, 25.2, 24.7, 23.8, 21.4; ^{11}B NMR (128.4 MHz, $CDCl_3$) δ 33.68; IR (cm^{-1}): 2977, 2925, 2853, 1598, 1466, 1364, 1319, 1212, 1188, 1176, 1145, 1098, 1019, 966, 912, 846, 814, 790, 763, 732, 688, 665, 651, 641, 625; HRMS (ESI) *m/*z calculated for $C_{25}H_{43}BO_5S$ $(M + Na)^+$: 489.2822, found: 489.2825.

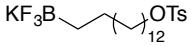


12-Carbon chain potassium trifluoroborate salt (34). ^{1}H NMR: (500 MHz, DMSO-*d*$_6$) δ 7.78 (d, *J* = 8.1 Hz, 2H), 7.49 (d, *J* = 7.9 Hz, 2H), 4.00 (t, *J* = 6.2 Hz, 2H), 2.43 (s, 3H), 1.53 (t, *J* = 6.7 Hz, 2H), 1.19 (s, 18H), -0.04--0.10 (m, 2H); ^{13}C NMR: (125 MHz, DMSO-*d*$_6$) δ 144.8, 132.5, 130.1, 127.5, 70.8, 33.1, 29.4, 29.2, 29.1, 28.9, 28.8, 28.1, 28.0, 25.6, 24.6, 21.0; ^{11}B NMR (128.4 MHz, DMSO-*d*$_6$) δ 6.42; IR (cm^{-1}): 2917, 2850, 1598, 1468, 1363, 1298, 1248, 1188, 1175, 1096, 1021, 965, 946, 918, 836, 809, 793, 720, 669, 642, 626.

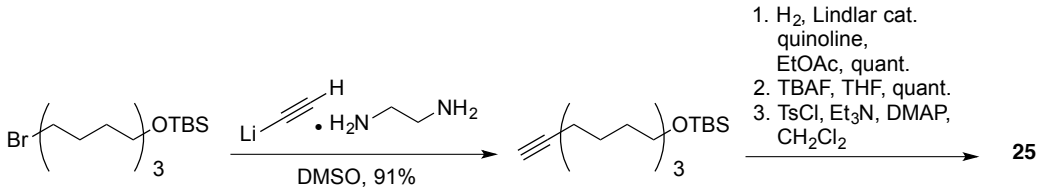


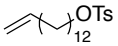
14-Carbon chain pinacolboronate ester (30). R_f 0.67 (20% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.80 Hz, 2H), 7.35 (d, *J* = 7.98 Hz, 2H), 4.05-4.02 (m, 2H), 2.46 (s, 3H), 1.67-1.61 (m, 2H), 1.41 (ddd, *J* = 12.36, 6.78, 6.30 Hz, 2H), 1.30-1.22 (m, 32H), 0.77 (t, *J* = 7.75 Hz, 2H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 144.5, 133.3, 129.7, 129.5, 127.8, 127.0, 82.8, 70.6, 41.9, 32.4, 29.6, 29.58, 29.55, 29.4, 29.38, 29.36, 28.9, 28.7, 25.3, 24.7, 23.9, 21.5, 14.1; IR (cm^{-1}): 2977, 2925, 2854, 1598, 1466,

1367, 1321, 1188, 1177, 1145, 1097, 1020, 966, 814, 714, 663, 577, 554; HRMS (ESI) *m/z* calculated for $C_{27}H_{47}BO_5S$ $(M + H)^+$: 494.3316, found: 495.3318.



14-Carbon chain potassium trifluoroborate salt (35). ^{1}H NMR: (500 MHz, DMSO-d_6) δ 7.78 (d, J = 8.2 Hz, 2H), 7.48 (d, J = 7.8 Hz, 2H), 4.00 (t, J = 6.3 Hz, 2H), 2.42 (s, 3H), 1.57-1.52 (m, 2H), 1.21-1.16 (m, 22H), -0.06--0.12 (m, 2H); ^{13}C NMR: (125 MHz, DMSO-d_6) δ 144.7, 132.5, 130.1, 127.5, 89.7, 84.5, 70.8, 33.1, 29.4, 29.2, 29.1, 29.0, 28.9, 28.8, 28.7, 28.1, 28.0, 25.6, 24.9, 24.6, 21.0; ; ^{11}B NMR (128.4 MHz, acetone) δ 4.63; IR (cm^{-1}): 2916, 2850, 1364, 1176, 1095, 965, 923, 835, 809, 793, 719, 670.

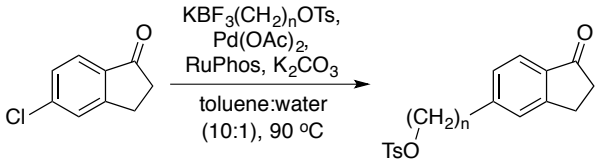




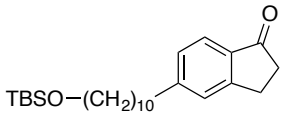
14-Carbon alkene tosylate (25). To a stirred solution of 12-carbon chain bromoalkane (3.57 g, 9.407 mmol) in anhydrous DMSO (21 mL) was added lithium acetylide ethylenediamine complex (1.12 g, 12.229 mmol). The resulting mixture was left to stir at room temperature for 6 h. The reaction was quenched with aqueous sat. NH_4Cl (10 mL). The aqueous layer was extracted with diethyl ether (20 mL, three times). The combined organic layers were washed with water (10 mL), brine (10 mL), and dried over $MgSO_4$, filtered, and concentrated. Purification by silica gel chromatography (100% Hexanes → 5% EtOAc/Hexanes) afforded the known alkyne (2.79 g, 91%). To a solution of the alkyne (2.79 g, 8.595 mmol) in ethyl acetate (43 mL) was added Lindlar's catalyst

(249 mg, 1.203 mmol) followed by quinoline (1 mL, 8.595 mmol). The resulting mixture was stirred under H_2 at room temperature overnight. The reaction mixture was filtered through a bed of Celite and washed with ethyl acetate (10 mL, three times). The filtrate was concentrated. Purification by silica gel chromatography (100% Hexanes → 5% EtOAc/Hexanes) afforded the known alkene as a yellow oil (2.8 g, quant.). To a stirred solution of the TBS ether alkene (2.13 g, 6.521 mmol) in anhydrous THF (44 mL) was added TBAF (1M in THF, 13 mL, 13.042 mmol). The resulting solution was stirred at room temperature for 3 h. The solvent was concentrated and directly loaded onto a silica gel column (20% EtOAc/Hexanes) and afforded the corresponding alcohol (1.38 g, quant.). The desired tosylate **25** was synthesized using the first step of the general procedure to synthesize potassium alkyltrifluoroborate side chains. R_f 0.53 (10% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.80 (d, J = 7.92 Hz, 2H), 7.36 (d, J = 8.24 Hz, 2H), 5.87-5.79 (m, 1H), 5.03-4.93 (m, 2H), 4.03 (td, J = 6.53, 0.72 Hz, 2H), 2.46 (s, 3H), 2.08-2.03 (m, 2H), 1.68-1.62 (m, 2H), 1.41-1.23 (m, 18H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 144.5, 139.2, 133.3, 129.7, 127.8, 114.0, 70.6, 33.7, 29.5, 29.4, 29.3, 29.1, 28.9, 28.8, 25.6, 25.3, 21.6; IR (cm^{-1}): 2977, 2918, 2850, 1641, 1597, 1495, 1474, 1397, 1357, 1309, 1294, 1190, 1174, 1097, 1042, 1019, 984, 956, 930, 917, 840, 816, 794, 718, 707, 668, 578, 555, 531, 503; HRMS (ESI) *m/*z calculated for $C_{21}H_{34}O_3S$ $(M + H)^+$: 367.2307, found: 367.2306.

General procedure for side chain coupling for second generation synthesis

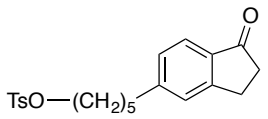


A microwave tube was charged with 5-chloro-1-indanone (100 mg, 0.600 mmol), 10-carbon-potassium alkyltrifluoroborate chain **33** (240 mg, 0.600 mmol), $Pd(OAc)_2$ (3 mg, 0.012 mmol), RuPhos (12 mg, 0.025 mmol), K_2CO_3 (249 mg, 1.801 mmol), and a stir bar. The cap was sealed, and evacuated and purged with Ar (3 cycles). Degassed toluene:H_2O mixture (3 mL) was then added to the microwave tube via syringe and the resulting reaction mixture was heated to 90 ^oC for 36 h. (For larger scale operation, the reaction was set up in a glovebox.) H_2O (1 mL) was added to the reaction, stirred for 5 min, and the resulting layers were separated. The aqueous layer was extracted with ethyl acetate (2 mL, three times). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated. Purification by silica gel chromatography (20% EtOAc/Hexanes) afforded the coupled product **38** as an amorphous solid (178 mg, 67%).

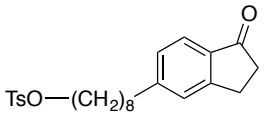


10-Carbon chain TBS ether indanone (20). R_f 0.37 (40% EtOAc/Hex); 1H NMR: (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.84 Hz, 1H), 7.28 (s, 1H), 7.20 (d, *J* = 7.76 Hz, 1H), 3.61 (t, *J* = 6.31 Hz, 2H), 3.12 (t, *J* = 5.77 Hz, 2H), 2.69 (dd, *J* = 10.17, 4.62, 4H), 1.64 (q, *J* = 7.08, 2H), 1.51 (q, *J* = 6.55 Hz, 2H), 1.33-1.29 (m, 12H), 0.90 (s, 9H), 0.05 (s, 6H); ^{13}C NMR: (125 MHz, $CDCl_3$) δ 206.5, 155.6, 150.7, 135.0, 127.9, 126.3, 123.5, 63.2, 36.4, 32.8, 31.2, 29.5, 29.45, 29.42, 29.3, 29.2, 25.9, 25.7, 25.6, 18.3, -5.0; IR (cm^{-1}): 2928, 2855, 1714, 1609, 1470, 1463, 1442, 1406, 1387, 1329, 1280,

1254, 1230, 1098, 1029, 1006, 835, 813, 775, 711; HRMS (ESI) *m/*z calculated for $C_{25}H_{42}O_2Si$ $(M + Na)^+$: 425.2852, found: 425.2849.

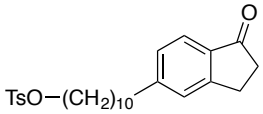


5-Carbon chain tosylate indanone (36). R_f 0.23 (20% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.30 Hz, 2H), 7.67 (d, *J* = 7.85 Hz, 1H), 7.36-7.34 (m, 2H), 7.25 (s, 1H), 7.15 (d, *J* = 7.86 Hz, 1H), 4.03 (t, *J* = 6.41 Hz, 2H), 3.11 (t, *J* = 5.86 Hz, 2H), 2.70-2.65 (m, 4H), 2.45 (s, 3H), 1.76-1.59 (m, 4H), 1.45-1.36 (m. 2H); ^{13}C NMR: (125 MHz, $CDCl_3$) 206.5, 155.7, 149.8, 144.6, 135.1, 133.1, 129.7, 127.9, 127.8, 126.8, 123.6, 70.2, 36.8, 36.0, 30.4, 28.6, 25.6, 24.9, 21.6; IR (cm^{-1}): 2932, 2860, 1708, 1608, 1494, 1440, 1403, 1357, 1281, 1188, 1176, 1097, 1030, 948, 903, 815, 663, 576, 554; HRMS (ESI) *m/*z calculated for $C_{21}H_{24}O_4S$ $(M + H)^+$: 373.1474, found: 373.1473.

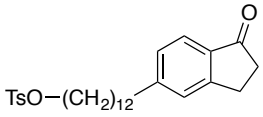


8-Carbon chain tosylate indanone (37). Rf 0.24 (20% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 2H), 7.19 (d, *J* = 7.9 Hz, 1H), 4.03 (t, *J* = 6.5 Hz, 2H), 3.12 (t, *J* = 5.9 Hz, 2H), 2.68 (dd, *J* = 10.3, 4.8 Hz, 4H), 2.46 (s, 3H), 1.64 (dq, *J* = 14.4, 7.2 Hz, 4H), 1.35-1.25 (m, 9H).; ^{13}C NMR: (125 MHz, $CDCl_3$) 206.5, 155.6, 150.5, 144.5, 135.0, 133.2, 129.7, 127.9, 127.8, 126.3, 123.5, 70.5, 36.3, 36.2, 31.1, 29.1, 29.0, 28.8, 28.7, 25;6, 25.2, 21.5; IR (cm^{-1}): 2928, 2856, 1709, 1608, 1495, 1441, 1403, 1359, 1289, 1229, 1188, 1176, 1097, 1030, 941, 815, 664, 577, 555; HRMS (ESI) *m/*z calculated for

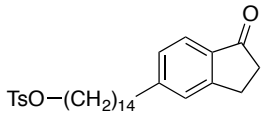
$C_{24}H_{30}O_4S$ $(M + H)^+$: 414.1943, found: 414.1943.



10-Carbon chain tosylate indanone (38). R_f 0.26 (20% EtOAc/Hex); ^1H NMR: (500 MHz, $CDCl_3$) δ 7.70, (d, *J* = 8.27 Hz, 2H), 7.64 (d, *J* = 7.85 Hz, 1H), 7.32 (d, *J* = 8.29 Hz, 2H), 7.26 (s, 1H), 7.17 (d, *J* = 7.85 Hz, 1H), 4.00 (t, *J* = 6.50 Hz, 2H), 3.08 (t, *J* = 5.82 Hz, 2H), 2.68-2.64 (m, 4H), 2.42 (s, 3H), 1.65 (dt, *J* = 14.25, 6.95 Hz, 4H), 1.29-1.21 (m, 12H); ^{13}C NMR: (125 MHz, $CDCl_3$) 206.5, 155.6, 150.6, 144.5, 134.8, 133.0, 129.6, 127.8, 127.6, 126.2, 123.3, 70.5, 36.3, 36.2, 31.1, 29.2, 29.1, 29.0, 28.7, 28.6, 25.5, 25.1, 21.4; IR (cm^{-1}): 2927, 2854, 1709, 1609, 1495, 1465, 1441, 1404, 1359, 1282, 1188, 1176, 1097, 1030, 1020, 957, 927, 814, 664, 576, 555; HRMS (ESI) *m/*z calculated for $C_{26}H_{34}O_4S$ $(M + Na)^+$: 465.2076, found: 465.2079.

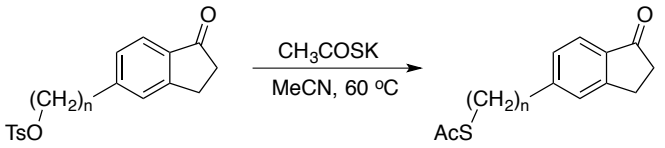


12-Carbon chain tosylate indanone (39). R_f 0.39 (20% EtOAc/Hex); ^1H NMR: (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 7.8 Hz, 1H), 4.04-4.02 (m, 2H), 3.12 (t, *J* = 5.8 Hz, 2H), 2.71-2.68 (m, 4H), 2.46 (s, 3H), 1.69-1.62 (m, 4H), 1.32-1.23 (m, 17H); ^{13}C NMR: (125 MHz, $CDCl_3$) 206.6, 155.6, 150.7, 144.5, 135.0, 133.2, 129.7, 127.9, 127.8, 126.3, 123.5, 70.6, 36.3, 31.2, 29.5, 29.45, 29.4, 29.3, 29.2, 28.8, 28.7, 25.6, 25.2, 21.5; IR (cm^{-1}): 2977, 2922, 2849, 1704, 1607, 1470, 1434, 1393, 1356, 1323, 1296, 1281, 1246, 1186, 1173, 1097, 1030, 949, 837, 815, 670, 576, 556, 532; HRMS (ESI) *m/*z calculated for $C_{28}H_{38}O_4S$ $(M + H)^+$: 471.2569, found: 471.2550.

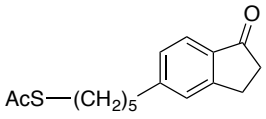


14-Carbon chain tosylate indanone (40). R_f 0.45 (20% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.36-7.34 (m, 2H), 7.28 (d, *J* = 0.8 Hz, 1H), 7.19 (d, *J* = 7.9 Hz, 1H), 4.02 (t, *J* = 6.5 Hz, 2H), 3.11 (t, *J* = 5.9 Hz, 2H), 2.71-2.67 (m, 4H), 2.45 (s, 3H), 1.69-1.59 (m, 6H), 1.36-1.18 (m, 18H).; ^{13}C NMR: (125 MHz, $CDCl_3$) 206.6, 155.6, 150.7, 144.5, 134.9, 133.1, 129.7, 127.9, 126.3, 123.4, 70.6, 36.3, 31.2, 29.6, 29.5, 29.47, 29.41, 29.39, 29.3, 29.2, 28.8, 28.7, 25.6, 25.2, 21.5; IR (cm^{-1}): 2917, 2851, 1712, 1607, 1472, 1433, 1360, 1228, 1186, 1171, 1095, 1030, 977, 955, 832, 807, 794, 719, 689, 668, 644; HRMS (ESI) *m/*z calculated for $C_{30}H_{42}O_4S$ $(M + Na)^+$: 521.2702, found: 521.2698.

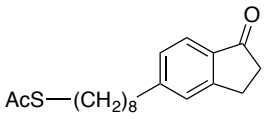
General procedure for thioacetate synthesis



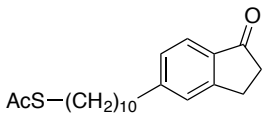
To a stirred solution of tosylate **38** (173 mg, 0.391 mmol) in anhydrous acetonitrile (25 mL) was added potassium thioacetate (89 mg, 0.782 mmol) in one portion. The resulting mixture was then brought to 60 ^{o}C and left to stir overnight. The reaction was quenched by addition of H_2O (40 mL), and extracted with CH_2Cl_2 (50 mL, three times). Organic layers were then combined, washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by silica gel chromatography (15% EtOAc/Hexanes) afforded **43** as an amorphous solid (114 mg, 84%).



5-Carbon chain thioacetate indanone (41). R_f 0.39 (20% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.8 Hz, 1H), 7.26 (s, 1H), 7.16 (dd, *J* = 7.8, 0.6 Hz, 1H), 3.09 (t, *J* = 5.9 Hz, 2H), 2.84 (t, *J* = 7.3 Hz, 2H), 2.69-2.64 (m, 4H), 2.30 (s, 3H), 1.68-1.56 (m, 4H), 1.43-1.37 (m, 2H).; ^{13}C NMR: (125 MHz, $CDCl_3$) 206.6, 195.9, 155.7, 150.2, 135.1, 127.9, 126.4, 123.6, 36.4, 36.1, 30.68, 30.63, 29.3, 28.9, 28.3, 25.7; IR (cm^{-1}): 2930, 2857, 1710, 1608, 1435, 1353, 1330, 1284, 1230, 1134, 1104, 1030, 956, 813, 627, 586; HRMS (ESI) *m/*z calculated for $C_{16}H_{20}O_2S$ $(M + H)^+$: 277.1262, found: 277.1264.

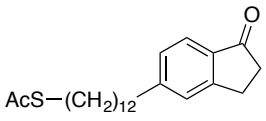


8-Carbon chain thioacetate indanone (42). R_f 0.65 (30% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.8 Hz, 1H), 7.26 (s, 1H), 7.17 (d, *J* = 7.8 Hz, 1H), 3.09 (t, *J* = 5.7 Hz, 2H), 2.84 (t, *J* = 7.3 Hz, 2H), 2.66 (q, *J* = 6.7 Hz, 4H), 2.30 (s, 3H), 1.62 (q, *J* = 7.1 Hz, 2H), 1.55 (quintet, *J* = 7.2 Hz, 2H), 1.31-1.23 (m, 8H); ^{13}C NMR: (125 MHz, $CDCl_3$) 206.3, 195.7, 155.5, 150.4, 134.9, 127.8, 126.2, 123.4, 36.3, 36.2, 31.0, 30.4, 30.0, 29.3, 29.1, 29.0, 28.9, 28.8, 28.5, 25.5; IR (cm^{-1}): 3009, 2926, 2854, 1694, 1608, 1439, 1353, 1330, 1282, 1245, 1230, 1192, 1133, 1105, 1030, 954, 886, 835, 814, 763, 724, 673, 627, 586; HRMS (ESI) *m/*z calculated for $C_{19}H_{26}O_2S$ $(M + H)^+$: 319.1732, found: 319.1729.

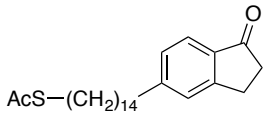


10-Carbon chain thioacetate indanone (43). R_f 0.57 (20%

EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.9 Hz, 1H), 7.28 (s, 1H), 7.19 (d, *J* = 7.9 Hz, 1H), 3.11 (t, *J* = 5.8 Hz, 2H), 2.86 (t, *J* = 7.4 Hz, 2H), 2.69-2.66 (m, 4H), 2.32 (s, 3H), 1.63 (dt, *J* = 14.7, 7.4 Hz, 2H), 1.56 (dq, *J* = 14.3, 7.0 Hz, 2H), 1.31 (dd, *J* = 21.5, 15.0 Hz, 10H); ^{13}C NMR: (125 MHz, $CDCl_3$) 206.5, 195.9, 155.6, 150.6, 134.9, 127.9, 126.2, 123.4, 36.3, 31.2, 30.5, 29.4, 29.3, 29.1, 29.0, 28.9, 28.7, 25.6; IR (cm^{-1}): 2921, 2851, 1697, 1686, 1608, 1469, 1444, 1352, 1334, 1294, 1234, 1132, 1106, 1031, 958, 818, 766, 721, 638; HRMS (ESI) *m/*z calculated for $C_{21}H_{30}O_2S$ $(M + Na)^+$: 369.1864, found: 369.1865.



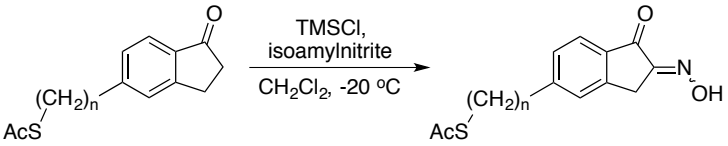
12-Carbon chain thioacetate indanone (44). R_f 0.63 (20% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.8 Hz, 1H), 7.29 (s, 1H), 7.21 (d, *J* = 7.8 Hz, 1H), 3.13 (dd, *J* = 7.6, 4.1 Hz, 2H), 2.88 (t, *J* = 7.4 Hz, 2H), 2.72-2.69 (m, 4H), 2.34 (s, 3H), 1.72-1.62 (m, 2H), 1.61-1.54 (m, 2H), 1.37-1.28 (m, 16H); ^{13}C NMR: (125 MHz, $CDCl_3$) 206.6, 196.0, 155.6, 150.7, 135.0, 128.0, 126.3, 123.5, 36.4, 31.2, 30.6, 29.6, 29.5, 29.49, 29.43, 29.2, 29.1, 29.0, 28.8, 25.7; IR (cm^{-1}): 2917, 2851, 1701, 1686, 1607, 1470, 1443, 1352, 1334, 1295, 1273, 1231, 1193, 1135, 1106, 1031, 959, 903, 818, 766, 719, 639; HRMS (ESI) *m/*z calculated for $C_{23}H_{34}O_2S$ $(M + Na)^+$: 397.2177, found: 397.2177.



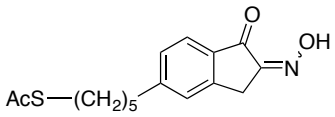
14-Carbon chain thioacetate indanone (45). R_f 0.5 (20% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.8 Hz, 1H), 7.29 (s, 1H), 7.21

(d, J = 7.8 Hz, 1H), 3.12 (dd, J = 5.9, 5.7 Hz, 2H), 2.88 (t, J = 7.4 Hz, 2H), 2.71-2.69 (m, 4H), 2.34 (s, 3H), 1.71-1.62 (m, 2H), 1.61-1.55 (m, 4H), 1.38-1.27 (m, 18H); ^{13}C NMR: (125 MHz, $CDCl_3$) 206.6, 196.0, 155.6, 150.8, 135.0, 128.0, 126.3, 123.5, 36.4, 31.3, 30.6, 29.6, 29.56, 29.53, 29.49, 29.46, 29.2, 29.15, 29.11, 28.8, 25.7; IR (cm^{-1}): 2916, 2849, 1701, 1686, 1607, 1469, 1442, 1428, 1234, 1120, 1030, 958, 818, 654; HRMS (ESI) m/z calculated for $C_{25}H_{38}O_2S$ $(M + Na)^+$: 425.2490, found: 425.2498.

General procedure for oxime synthesis

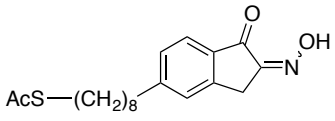


To a stirred solution of indanone **43** (398 mg, 1.148 mmol) in anhydrous CH_2Cl_2 (5 mL) at −20 °C was added TMSCl (0.15 mL, 1.148 mmol) followed by drop-wise addition of isoamy nitrite (0.15 mL, 1.148 mmol). The resulting mixture was left to stir at −20 °C for 1 h. The reaction was quenched by addition of H_2O (1 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 mL, three times), and the organic layers were combined. The organic layer was washed with brine (2 mL), dried over $MgSO_4$, filtered, and concentrated to afford the oxime **48** (420 mg, quant.).

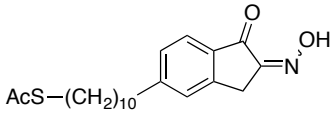


5-Carbon chain thioacetate oxime (46). R_f 0.3 (40% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.82 (d, J = 7.9 Hz, 1H), 7.34 (s, 1H), 7.27 (d, J = 8.0 Hz, 1H), 3.85 (s, 2H), 2.88 (t, J = 7.3 Hz, 2H), 2.73 (t, J = 7.7 Hz, 2H), 2.34 (s, 3H), 1.73-1.60 (m, 5H), 1.47-1.42 (m, 2H).; ^{13}C NMR: (125 MHz, $CDCl_3$) δ 196.1, 189.2,

155.4, 152.3, 147.4, 135.8, 128.7, 126.5, 124.7, 36.4, 30.67, 30.56, 29.3, 28.9, 28.32, 28.26; IR (cm^{-1}): 3497, 3386, 2925, 2858, 1707, 1688, 1649, 1608, 1491, 1340, 1279, 1139, 1112, 1043, 948, 922, 910, 843; HRMS (ESI) *m/z* calculated for $C_{16}H_{19}NO_3S$ $(M + Na)^+$: 328.0983, found: 328.0993.

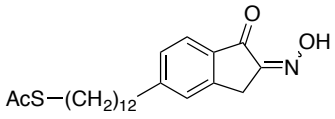


8-Carbon chain thioacetate oxime (47). R_f 0.36 (40% EtOAc/Hex); ^1H NMR: (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.9 Hz, 1H), 7.33 (s, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 3.85 (s, 2H), 2.87 (t, *J* = 7.4 Hz, 2H), 2.72 (t, *J* = 7.7 Hz, 2H), 2.34 (s, 3H), 1.69-1.63 (m, 2H), 1.60-1.54 (m, 2H), 1.34-1.28 (m, 9H); ^{13}C NMR: (125 MHz, $CDCl_3$) 196.2, 189.0, 155.4, 152.6, 147.2, 135.7, 128.6, 126.4, 124.6, 36.6, 31.0, 30.6, 29.4, 29.2, 29.1, 29.0, 28.9, 28.6, 28.2; IR (cm^{-1}): 3247, 2922, 2852, 1726, 1686, 1655, 1608, 1469, 1434, 1407, 1332, 1302, 1273, 1126, 1109, 1037, 959, 946, 924, 905, 832, 773, 755, 691, 634; HRMS (ESI) *m/z* calculated for $C_{19}H_{25}NO_3S$ $(M + Na)^+$: 370.1453, found: 370.1453.

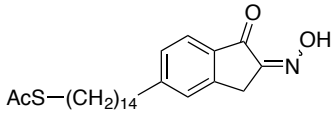


10-Carbon chain thioacetate oxime (48). R_f 0.39 (40% EtOAc/Hex); ^1H NMR: (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.9 Hz, 1H), 7.33 (s, 1H), 7.26 (d, *J* = 7.9 Hz, 1H), 3.85 (s, 2H), 2.87 (t, *J* = 7.4 Hz, 2H), 2.71 (t, *J* = 7.7 Hz, 2H), 2.34 (s, 3H), 1.66 (dq, *J* = 13.8, 6.9 Hz, 3H), 1.60-1.54 (m, 3H), 1.34-1.28 (m, 11H).; ^{13}C NMR: (125 MHz, $CDCl_3$) 196.2, 189.2, 155.3, 152.8, 147.3, 135.6, 128.7, 126.4, 124.5, 36.6, 31.1, 30.6, 29.4, 29.37, 29.34, 29.2, 29.1, 29.0, 28.7, 28.2; IR (cm^{-1}): 3248, 2919, 2851,

1725, 1685, 1655, 1609, 1581, 1469, 1435, 1409, 1352, 1331, 1302, 1269, 1201, 1132, 1111, 1037, 958, 923, 907, 833, 774, 755, 690, 665, 637; HRMS (ESI) *m/z* calculated for $C_{21}H_{29}NO_3S$ $(M + Na)^+$: 376.1922, found: 376.1940.



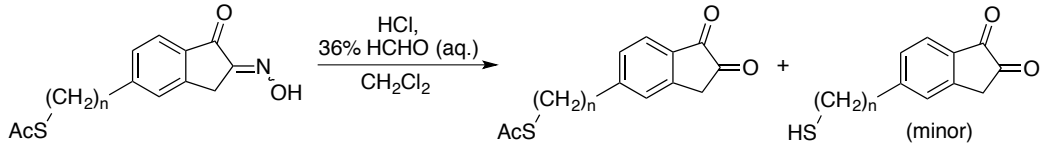
12-Carbon chain thioacetate oxime (49). R_f 0.5 (40% EtOAc/Hex); ^1H NMR: (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.9 Hz, 1H), 7.34 (s, 1H), 7.26 (s, 1H), 3.85 (s, 2H), 2.88 (t, *J* = 7.4 Hz, 2H), 2.72 (t, *J* = 7.7 Hz, 2H), 2.34 (s, 3H), 1.70-1.64 (m, 2H), 1.60-1.54 (m, 2H), 1.36-1.27 (m, 17H); ^{13}C NMR: (125 MHz, $CDCl_3$) 196.2, 189.0, 155.4, 152.7, 147.2, 135.7, 128.7, 126.4, 124.5, 36.6, 31.1, 30.6, 29.53, 29.5, 29.46, 29.42, 29.3, 29.2, 29.1, 29.0, 28.7, 28.2; IR (cm^{-1}): 3258, 2916, 2851, 1726, 1685, 1655, 1610, 1581, 1470, 1406, 1353, 1332, 1303, 1272, 1113, 1037, 960, 922, 906, 832, 755, 756, 689, 640; HRMS (ESI) *m/z* calculated for $C_{23}H_{33}NO_3S$ $(M + Na)^+$: 426.2079, found: 426.2081.



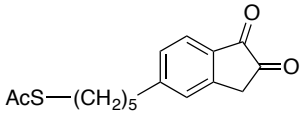
14-Carbon chain thioacetate oxime (50). R_f 0.53 (40% EtOAc/Hex); ^1H NMR: (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.8 Hz, 1H), 7.33 (s, 1H), 7.28 (d, *J* = 2.7 Hz, 1H), 3.85 (s, 2H), 2.87 (t, *J* = 7.2 Hz, 2H), 2.72 (t, *J* = 7.3 Hz, 2H), 2.33 (s, 3H), 1.67-1.63 (m, 2H), 1.60-1.54 (m, 2H), 1.34-1.32 (m, 21H); ^{13}C NMR: (125 MHz, $CDCl_3$) 196.2, 189.1, 155.3, 152.7, 147.3, 135.7, 128.7, 126.4, 124.5, 36.6, 31.1, 30.6, 29.57, 29.53, 29.4, 29.3, 29.2, 29.1, 29.0, 28.7, 28.2; IR (cm^{-1}): 3252, 2916, 2849, 1726, 1685, 1655, 1609, 1470, 1435, 1353, 1332, 1303, 1270, 1139, 1120, 1037, 959, 923, 907,

833, 774, 754, 690, 663, 639; HRMS (ESI) *m/*z calculated for $C_{25}H_{37}NO_3S$ $(M + Na)^+$: 454.2392, found: 454.2387.

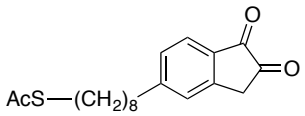
General procedure for 1,2-indanedione synthesis



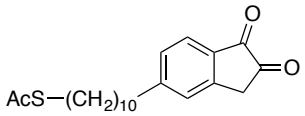
To a stirred solution of **47** (189 mg, 0.543 mmol) in CH_2Cl_2 (5.4 mL) was added aqueous formaldehyde (37% in water, 0.3 mL) followed by conc. HCl (0.6 mL). The resulting mixture was left to stir at room temperature overnight. The reaction was quenched with cold H_2O (5 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (5 mL, three times), and the organic layers were combined. The organic layer was washed with brine (5 mL), dried over $MgSO_4$, filtered, and concentrated to afford **52** as a mixture with thioacetate removed thiol, which was used without further purification.



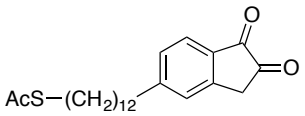
5-Carbon chain thioacetate 1,2-indanedione (51). R_f 0.52 (40% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.9 Hz, 1H), 7.37 (s, 1H), 7.31 (d, *J* = 7.9 Hz, 1H), 3.60 (s, 2H), 2.87 (t, *J* = 7.3 Hz, 2H), 2.75 (t, *J* = 7.7 Hz, 2H), 2.33 (s, 3H), 1.74-1.60 (m, 6H), 1.48-1.41 (m, 4H); ^{13}C NMR: (125 MHz, $CDCl_3$) 200.2, 195.8, 186.4, 154,0, 146.9, 135.1, 129.2, 126.9, 125.7, 36.6, 36.5, 30.5, 30.3, 29.2, 28.7, 28.2; IR (cm^{-1}): 2932, 2858, 1764, 1719, 1688, 1609, 1437, 1391, 1353, 1263, 1134, 949, 837, 752, 627; HRMS (ESI) *m/*z calculated for $C_{16}H_{18}O_3S$ $(M + H)^+$: 291.1055, found: 291.1060.



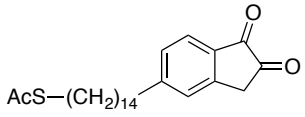
8-Carbon chain thioacetate 1,2-indanedione (52). R_f 0.6 (40% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.9 Hz, 1H), 7.37 (s, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 3.60 (s, 2H), 2.85 (t, *J* = 7.4 Hz, 2H), 2.74 (t, *J* = 7.7 Hz, 2H), 2.32 (s, 3H), 1.70-1.64 (m, 3H), 1.56 (dt, *J* = 14.6, 7.3 Hz, 3H), 1.35 (dd, *J* = 13.3, 5.8 Hz, 6H).; ^{13}C NMR: (125 MHz, $CDCl_3$) 200.3, 195.9, 186.4, 154.4, 146.8, 135.1, 129.2, 126.9, 125.6, 36.8, 36.5, 30.8, 30.5, 29.4, 29.1, 29.0, 28.9, 28.8, 28.6; IR (cm^{-1}): 3520, 2421, 3354, 3050, 2921, 2852, 2254, 1900, 1768, 1714, 1613, 1580, 1468, 1434, 1386, 1354, 1329, 1304, 1261, 1203, 1118, 1099, 951, 824, 755, 724, 667, 632; HRMS (ESI) *m/*z calculated for $C_{19}H_{24}O_3S$ $(M + H)^+$: 333.1524, found: 333.1521.



10-Carbon chain thioacetate 1,2-indanedione (53). R_f 0.65 (40% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.9 Hz, 1H), 7.38 (s, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 3.61 (s, 2H), 2.89-2.86 (m, 2H), 2.76 (t, *J* = 7.7 Hz, 2H), 2.34 (s, 3H), 1.72-1.64 (m, 3H), 1.62-1.54 (m, 3H), 1.38-1.28 (m, 10H); ^{13}C NMR: (125 MHz, $CDCl_3$) 200.3, 196.0, 186.4, 154.6, 146.8, 135.1, 129.2, 126.9, 125.7, 36.9, 36.6, 30.9, 30.6, 29.6, 29.4, 29.37, 29.34, 29.2, 29.1, 29.0, 28.7; IR (cm^{-1}): 2920, 2851, 1765, 1715, 1686, 1612, 1468, 1435, 1352, 1331, 1302, 1268, 1201, 1117, 1098, 954, 923, 907, 833, 774, 755, 690, 637; HRMS (ESI) *m/*z calculated for $C_{21}H_{28}O_3S$ $(M + Na)^+$: 383.1657, found: 383.1644.



12-Carbon chain thioacetate 1,2-indanedione (54). R_f 0.71 (40% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.9 Hz, 1H), 7.38 (s, 1H), 7.33-7.32 (m, 1H), 3.61 (s, 2H), 2.87 (t, *J* = 7.3 Hz, 2H), 2.75 (t, *J* = 7.7 Hz, 2H), 2.34 (s, 3H), 1.71-1.65 (m, 3H), 1.60-1.54 (m, 3H), 1.36-1.27 (m, 14H).; ^{13}C NMR: (125 MHz, $CDCl_3$) 200.4, 196.0, 186.4, 154.6, 146.8, 135.1, 129.2, 126.9, 125.7, 36.9, 36.5, 30.9, 30.6, 29.5, 29.49, 29.45, 249.41, 29.3, 29.2, 29.1, 29.0, 28.7; IR (cm^{-1}): 2918, 2850, 1766, 1716, 1694, 1611, 1469, 1434, 1384, 1353, 1328, 1304, 1267, 1136, 1118, 951, 8223, 718, 630; HRMS (ESI) *m/*z calculated for $C_{23}H_{32}O_3S$ $(M + Na)^+$: 411.1970, found: 411.1973.



14-Carbon chain thioacetate 1,2-indanedione (55). R_f 0.7 (40% EtOAc/Hex); ^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.0 Hz, 1H), 7.38 (s, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 3.61 (s, 2H), 2.87 (t, *J* = 7.4 Hz, 2H), 2.75 (t, *J* = 7.7 Hz, 2H), 2.33 (s, 3H), 1.71-1.54 (m, 8H), 1.36-1.27 (m, 16H); ^{13}C NMR: (125 MHz, $CDCl_3$) 200.4, 196.0, 186.4, 154.6, 146.8, 135.1, 129.2, 126.9, 125.7, 36.9, 36.5, 30.9, 30.6, 29.6, 29.5, 29.47, 29.43, 29.3, 29.2, 29.1, 29.0, 28.7; IR (cm^{-1}): 2919, 2849, 1765, 1719, 1693, 1610, 1470, 1437, 1385, 1351, 1328, 1262, 1118, 948, 823, 718, 630; HRMS (ESI) *m/*z calculated for $C_{25}H_{36}O_3S$ $(M + Na)^+$: 439.2283, found: 439.2278.

General procedure for synthesis and functionalization of AuNPs with 1,2-indanedione analogues

Following Klabunde's procedure,[45] a solution of dodecyldimethylammonium bromide (0.02 M) was prepared in 2.5 mL of anhydrous toluene. To this was added $AuCl_3$ (8.5

mg), and the resulting mixture was sonicated until complete dissolution was evident (homogeneous dark orange solution). Freshly prepared 9.4 M aqueous solution of $NaBH_4$ (50 μL) was quickly added to the vortex of the vigorously stirring solution. The resulting mixture was left to stir vigorously for additional 15-20 min to afford the "as-prepared" gold colloid. In a separate vial containing **53** (151 mg, 0.420 mmol) dissolved in anhydrous toluene (2 mL) was added to the solution containing gold colloid via syringe. The resulting mixture was left to stir vigorously for 24 h at room temperature to allow ligand exchange. The functionalized AuNPs were isolated by precipitation with ethanol (10 mL). The tube containing the functionalized AuNPs were centrifugated at 5000 rpm for 5 min cycles three times. After each cycle, the supernatant was decanted and discarded, and fresh EtOH (10 mL) was added. After final centrifugation, the supernatant was decanted, and the resulting AuNPs were dried under vacuum. The dried AuNPs were redispersed in acetonitrile (2.5 mL) to be used as part of the working solution for fingerprint development.

General procedure for development of fingerprints on paper

Following Almog's procedure,[34] the paper substrate containing latent fingerprint deposits was immersed in an aqueous solution of maleic acid (2.5% w/v in water) for 10 min or until no bubbles were apparent. The paper was then air-dried, and subsequently immersed in the working solution containing functionalized AuNPs (5 min-30 min). The paper was air-dried, and immersed in the Ag-PD solution (Arrowhead Scientific Inc.) until visible marks appeared (1-2 min). The paper substrate was then removed and washed with two successive water baths: Milli-Q followed by tap water.

5.8) References

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