The development of novel ninhydrin analogues

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Received 30th November 2004
First published as an Advance Article on the web 11th February 2005
DOI: 10.1039/b315496n

Following its discovery by Siegfried Ruhemann in 1910, ninhydrin rapidly became a practical analytical tool. In 1954 it was found to be an important reagent to develop fingerprints on porous surfaces. Since its use in forensic chemistry, many efforts have focused on improving the reagent. Many of the shortcomings of ninhydrin have been met by the synthesis of a variety of ninhydrin analogues. This *tutorial review* provides a short introduction to ninhydrin and highlights the different synthetic approaches used in the development of analogues for the detection of latent fingerprints.

Introduction

The history of ninhydrin

Ninhydrin was first synthesized in 1910 by Siegfried Ruhemann, a professor of chemistry at the University Chemical Laboratories at Cambridge University. In an effort to synthesize dicarbonyl compounds by the reaction of 1-indanone with *p*-nitrosodimethylaniline, he isolated 1,2,3-indanetrione (ninhydrin) instead of the desired 1,2-indanedione (Scheme 1). Ninhydrin (**1**) exists as a stable hydrate (**2**) and the tricarbonyl is only present under rigorously anhydrous conditions.[1] In a further stroke of serendipity Ruhemann discovered that this compound reacted with ammonia and amines to yield coloured products. Due to ninhydrin's structural similarities to another cyclic triketone alloxan (**3**) and its ability to react with amino acids to yield a blue compound (**4**), murexide (Scheme 2), Ruhemann was able to deduce that the product of the reaction between ninhydrin and amino acids, should have a similar structure. The years following the discovery of ninhydrin's reaction with amino acids saw its use proliferate for the detection and quantification of amino acids but it was not until 1954 that two Swedish scientists, Oden and von Hofsten recognized that it was a useful reagent for developing fingerprints.[2]

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The chemistry of Ruhemann's purple

The structure of Ruhemann's Purple was originally established by Ruhemann in 1911 but the mechanism for its formation has been investigated by many groups for over 90 years. An extensive assessment of the mechanistic studies on the formation of Ruhemann's purple can be found in an earlier review.[3] The accepted mechanism to account for the formation of Ruhemann's purple was first proposed by Friedman and Williams as depicted in Scheme 3.[4,5] Although the mechanism appears simple, depending on the conditions, especially the pH of the solution, it may be more complex than that shown. Other products such as hydrindantin may be formed and ninhydrin has been shown to react with a large variety of

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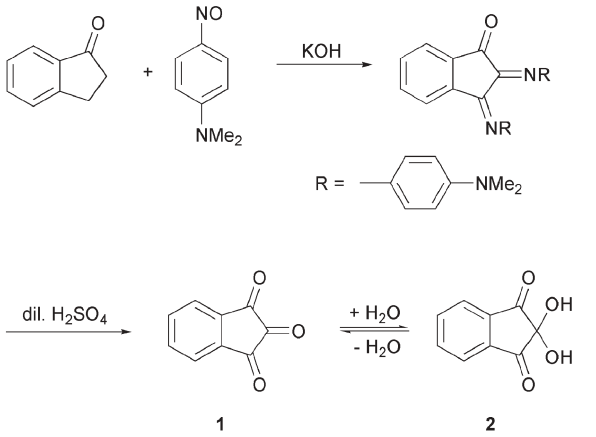
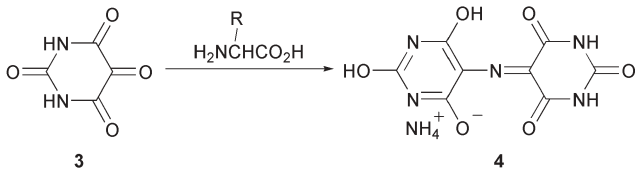


Scheme 1



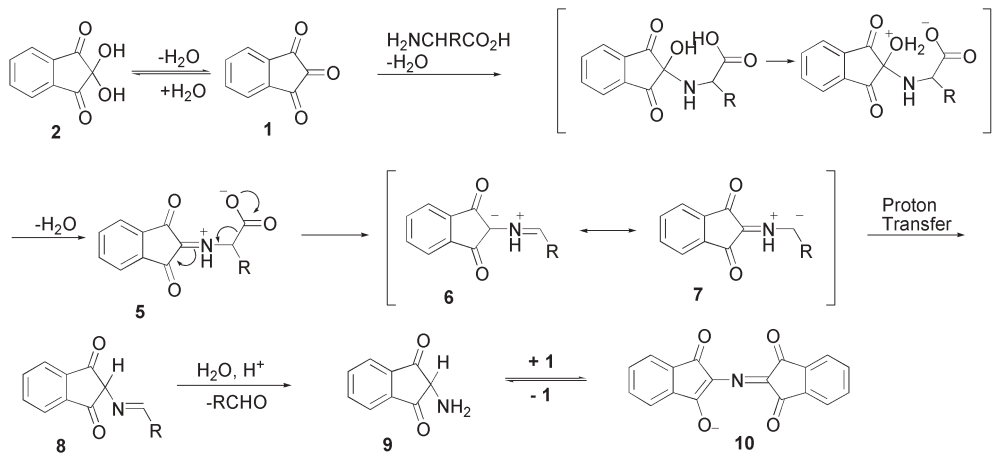
Scheme 2

compounds and to form a variety of different chromogenic products.[5] The reaction involves an initial Schiff's base condensation involving attack of the amine on the central carbonyl of the anhydrous keto (**1**) form, which is in constant equilibrium with the hydrated form of ninhydrin. The resulting Schiff's base (**5**) then undergoes decarboxylation to yield a resonance-stabilized 1,3-dipolar species (**6 and 7**). Proof of the 1,3-dipolar species was demonstrated by Grigg who trapped it with *N*-phenylmaleimide to form a cycloadduct.[6] Proton transfer yields an intermediate aldimine (**8**) that is hydrolyzed to the aldehyde and a 2-amino intermediate (**9**), which then condenses with another molecule of ninhydrin to yield Ruhemann's purple (**10**). X-Ray studies of Ruhemann's purple by Grigg and co-workers further confirmed the structure of the final product.[7]

The principles of latent fingerprint development

Fingerprints are still one of the most useful forms of physical evidence in identification. There are three major types of fingerprints: visible prints, impression prints and latent prints. Latent prints are normally invisible without some form of development. The techniques used for fingerprint identification vary according to the surface to which the fingerprints are applied. The development of latent fingerprints on porous surfaces such as paper and cardboard are particularly well suited for chemical development. The choice of chemicals used for development is dependent on the composition of latent fingerprints. Fingerprints result from the bodily fluids on the skin surface that are secreted from various glands located in the skin. The eccrine glands compose the majority of the sweat glands located on the fingers. The composition of eccrine sweat is 99% water in addition to minor amounts of inorganic and organic compounds.[8] Of particular interest to ninhydrin-based development is the concentration of amino acids, which has been reported to be between 0.3 to 2.59 mg L^{-1} of sweat. This value corresponds to an average amino acid content of about 250 ng per print. Small concentrations of amino acids in sweat are sufficient for development on paper. Amino acids are stable over a great period of time. Since amino acids have a high affinity for cellulose, the main component of paper, they do not bleed from/on the paper's surface. It is possible to obtain sharp fingerprints even after extended periods of time but the best results are usually obtained within several weeks.

The early forensic research groups tried to develop many different formulations of ninhydrin but were plagued by numerous problems. Early solvent mixtures of ninhydrin contained one or more of the following solvents; acetone, diethyl ether, isopropanol and ethanol in addition to various concentrations of ninhydrin and other additives to improve performance. These early formulations suffered from several shortcomings including low sensitivity, high background staining, and solvent mixtures that were often highly flammable. Many of the organic solvent mixtures caused ink and dye in the paper to run, thereby obscuring the fingerprints. Several of these problems were corrected by using 1,1,2,-trifluorotrichloroethane, more commonly known as Freon113



Scheme 3

or CFC113. This formulation became known as NFN (nonflammable ninhydrin) and was an improvement over earlier solvent mixtures. The new solvent system was also non-toxic and did not dissolve ink on paper. However, by 1992 CFC113 was banned in most countries because it caused the depletion of the ozone layer. More recently, 3M™ Novec™ HFE-7100, a hydrofluoroether, has been introduced as a non-ozone depleting replacement for chlorofluorocarbon solvents.[9,10] Research is still on going to develop suitable solvent systems and new ninhydrin derivatives with improved formulation properties.

Ninhydrin can be applied and developed in a number of different ways. The most popular methods of application are spraying a mist, dipping or swabbing the formulation on the paper. While each method has certain attributes dipping seems to be the most popular method available. After application of ninhydrin, the prints need to be developed. Most development methods use a combination of heat and humidity to accelerate the process. For maximum sensitivity and less background staining, samples should be allowed to develop in the dark at room temperature because light can fade ninhydrin developed prints. The main drawback to this procedure is that full development can take weeks, which is unacceptable for a forensic laboratory.

New developments

Since ninhydrin's first use as a reagent for developing latent fingerprints there have been investigations focused on improving this technique. Initial research was aimed at meeting the demands of forensic scientists for a more sensitive reagent with less background staining and safer solvent mixtures. Many formulation improvements were made over a period of forty years but these changes did not address all the shortcomings of ninhydrin. The problem of improved contrast and visualization could not be overcome solely by formulation and, in addition, the need for chemical development of latent fingerprints on dark surfaces and paper containing certain coatings did not allow for the necessary contrast between the developed print and the background coloration to allow for visualization.

The limitations of improved formulations were met by the development of new reagents. The first three ninhydrin analogues specifically synthesized for fingerprint development (Fig. 1) were reported by Almog *et al.* in 1982 and showed that

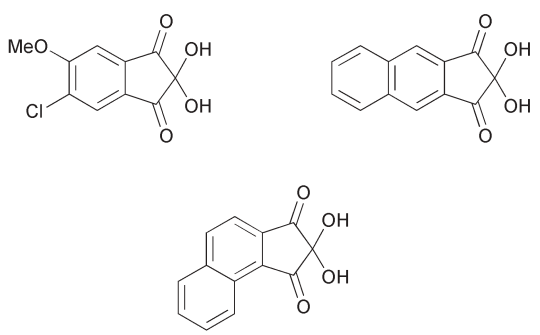


Fig. 1 First ninhydrin analogues.

modification of the aromatic ring could favourably alter the optical properties of ninhydrin while preserving the reactivity of the cyclic triketone.[11] The introduction of various substituents and extension of the conjugated system caused an increase in molar extinction coefficients yielding more sensitive reagents and induced shifts in the absorption maxima resulting in some variation in the colour of the Ruhemann's purple product. A variety of ninhydrin-based reagents would allow for the optimal development of fingerprints over a range of background colours and surfaces. The development of a more hydrophobic reagent would allow for easier formulation in less polar solvent systems.

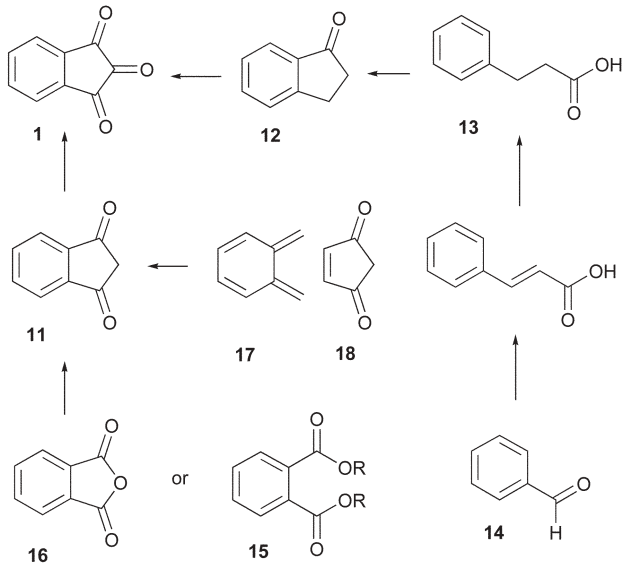
Fluorescent observation of latent fingerprints by secondary metal salts

It was known for a long time that Ruhemann's purple prints could be complexed with various metal salts resulting in colour changes from the original purple colour. In 1982 Herod and Menzel discovered that ninhydrin developed fingerprints not only changed colour when treated with zinc chloride solutions but also became highly fluorescent when examined under an argon laser.[12] This discovery was an important breakthrough in fingerprint detection. The ability to convert nonfluorescent ninhydrin developed prints into highly fluorescent prints allowed for improved contrast on a variety of backgrounds and increased the number of prints that could be visualized because fluorescence-based detection methods are more sensitive than traditional absorption methods. The use of fluorescence-based detection methods is now common practice in the forensic community. While significant sensitivity gains have been made with the combination of ninhydrin/zinc chloride development, the ability to develop analogues with improved absorption and emission spectrum would allow for cheaper light sources, making the technique more accessible. In addition analogues that produced highly coloured Ruhemann's purple species that also exhibited fluorescence without secondary metal treatment would simplify the visualization of latent fingerprints and benefit the forensic community.

Synthesis of ninhydrin analogues

Retrosynthetic analysis

To better understand the development of new ninhydrin analogues a short outline of the general synthetic approaches used in constructing ninhydrin will be reviewed. Most syntheses of ninhydrin are composed of similar reactions centered around the oxidation of 1,3-indanedione (**11**) or 1-indanone (**12**) to 1,2,3-indanetriones (**1**). A second common feature is ring formation of the fused five-membered ring from an aromatic precursor (Scheme 4). Most approaches toward 1-indanones (**12**) are based on a Friedel–Crafts cyclization of the 3-phenylpropionic acids (**13**), which are synthesized from the corresponding aromatic aldehyde (**14**). Another major approach utilizes 1,3-indanedione (**11**) intermediates which are most commonly formed from the corresponding *ortho*-diesters (**15**) or phthalic anhydrides (**16**) and Diels–Alder based approaches of a transient *o*-xylylene (**17**) and



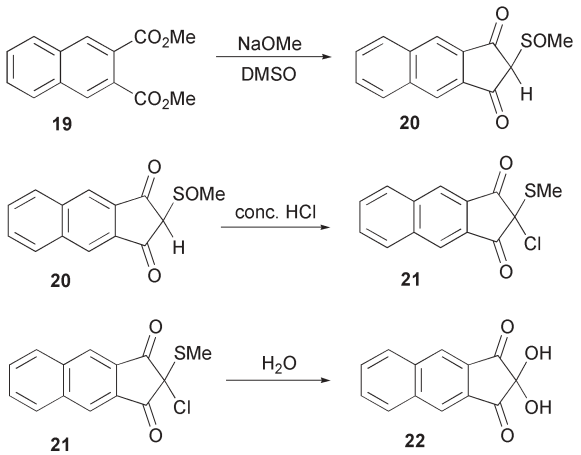
Scheme 4

4-cyclopentene-1,3-dione (**18**). A more exhaustive examination of the synthetic approaches to ninhydrin has appeared in an early review.[3]

Nearly 100 ninhydrin analogues have been synthesized since Ruhemann's initial attempts to develop compounds with improved solubility in organic solvents.[13] This review will cover some of the newest analogues and methods developed to date; a more extensive recent review contains a comprehensive list of over 80 compounds that have been synthesized.[14] While the early ninhydrin analogues were developed for the study of reaction kinetics, preparation of charge transfer complexes and as intermediates in natural products syntheses, most compounds are currently prepared for forensic evaluation.

Benzo[*f*]ninhydrin

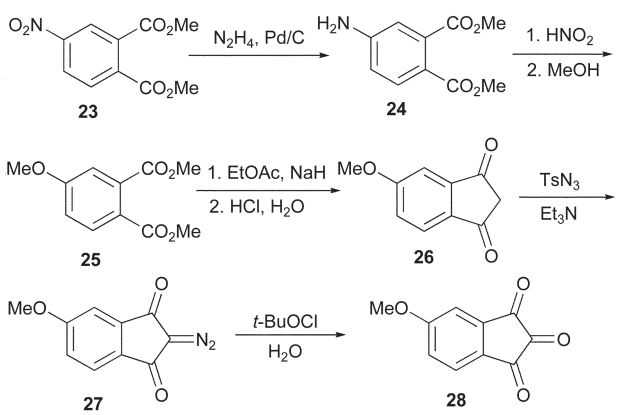
One of the earliest analogues that showed promise was benzo[*f*]ninhydrin. This compound had been previously synthesized by several investigators in modest yield[15] and then by Almog in 1982[11] from the condensation of dimethyl naphthalene-2,3-dicarboxylate (**19**) with dimethyl sulfoxide (Scheme 5). The intermediate sulfoxide (**20**) was then treated with concentrated hydrochloric acid causing a Pummerer rearrangement to yield 2-chloro-2-(methylthio)-1,3-indanedione (**21**) which was subsequently hydrolyzed in boiling water to yield benzo[*f*]ninhydrin (**22**). This analogue's properties were different from those of ninhydrin. Prints developed with this reagent provided dark green marks with a similar sensitivity to that of ninhydrin and provided better contrast on a variety of pink to purple backgrounds.[16] The most important quality of this new reagent was that treatment of benzo[*f*]ninhydrin-developed prints with zinc chloride caused the formation of a complex that exhibited luminescence properties that were far superior to the zinc–ninhydrin complex.[17]



Scheme 5

5-Methoxyninhydrin

Lennard and co-workers have synthesized many of the early substituted ninhydrin analogues, including 5-methoxyninhydrin (**28**).[18] The synthesis began with commercially available dimethyl 4-nitrophthalate (**23**) (Scheme 6). Reduction of the nitro group to the amine **24**, was followed by diazotization with nitrous acid in methanol to yield 4-methoxyphthalate (**25**). Reaction of this compound (**25**) with ethyl acetate and sodium hydride afforded the Claisen ester condensation product, which was treated with aqueous hydrochloric acid to yield the desired 1,3-diketone (**26**). Treatment with *p*-toluenesulfonyl azide in triethylamine delivered the 2-diazo intermediate (**27**) that was subsequently hydrolyzed with refluxing aqueous *tert*-butyl hypochlorite to yield 5-methoxyninhydrin (**28**). The reagent develops prints with a more intense fluorescence than ninhydrin-developed prints. Joullié and co-workers later developed an alternative route to 5-substituted ninhydrins. They used this method to synthesize 5-(methylthio)ninhydrin, which was shown to possess superior properties to those of 5-methoxyninhydrin.[19]



Scheme 6

Nucleophilic aromatic substitution designed ninhydrin analogues

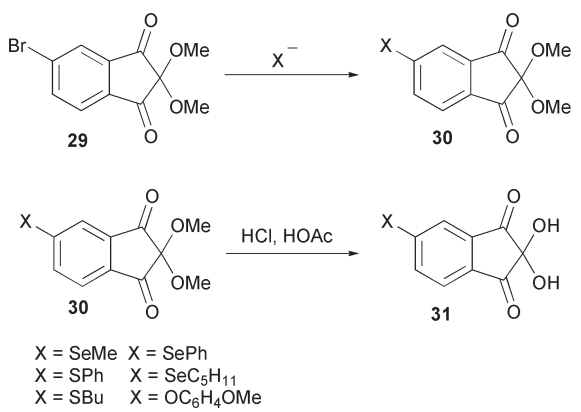
The success of 5-methoxyninhydrin prompted the further development of analogues with substitution at the C-5 position. Using the same intermediate devised by Joullié 5-bromo dimethyl ketal (**29**), Della and co-workers developed a more direct route to a variety of analogs.[20] This intermediate (**29**) was also an ideal substrate for nucleophilic aromatic substitution reactions (Scheme 7). Treatment of the bromo ketal with a variety of phenolates, thiolates, and selenides afforded the corresponding products (**30**) in good yields. All attempts to extend the method to the aliphatic alkoxides failed resulting only in decomposition of the starting material. Further treatment of the ketals with dilute hydrochloric acid in acetic acid furnished the ninhydrin analogues (**31**). Evaluation of these analogues was disappointing, having on average lower intensity of colour and offering no advantages over ninhydrin.[21]

Thieno[*f*]ninhydrin

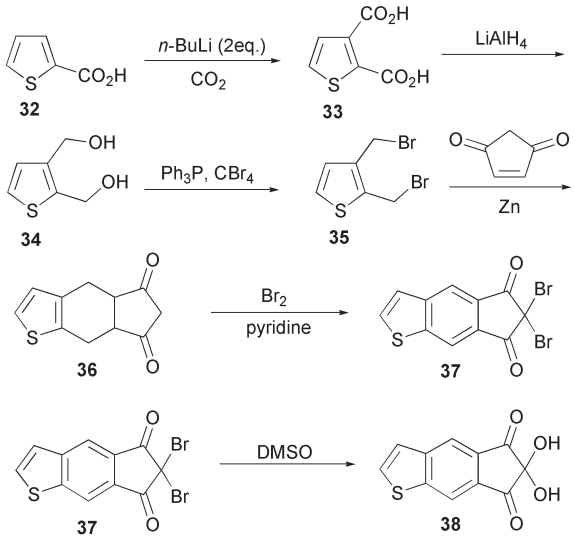
Joullié and co-workers devised a conceptually different approach to the synthesis of benzo[*f*]ninhydrin and related fused aromatic analogues (Scheme 8) such as thieno[*f*]ninhydrin (**38**).[22] Commercially available thiophene-1-carboxylic acid (**32**) was deprotonated, then lithiated at the 2-position and added to carbon dioxide to yield thiophene-2,3-dicarboxylic acid (**33**). The diacid was reduced with lithium aluminium hydride to the diol (**34**), which was converted to the dibromide (**35**). Sonication of the dibromide with activated zinc provided the *in situ* generation of a transient highly reactive diene which was subsequently trapped with 4-cyclopentene-1,3-dione *via* a Diels–Alder reaction to provide intermediate **36** in excellent yield. Exposure to bromine in pyridine resulted in aromatization of the six-membered ring and oxidation of the 2-position to the geminal dibromide (**37**) followed by treatment with dimethyl sulfoxide yielded thieno[*f*]ninhydrin (**38**). This compound displayed a combination of good chromogenic and fluorogenic properties after zinc chloride treatment.

Naphtho[*f*]ninhydrin

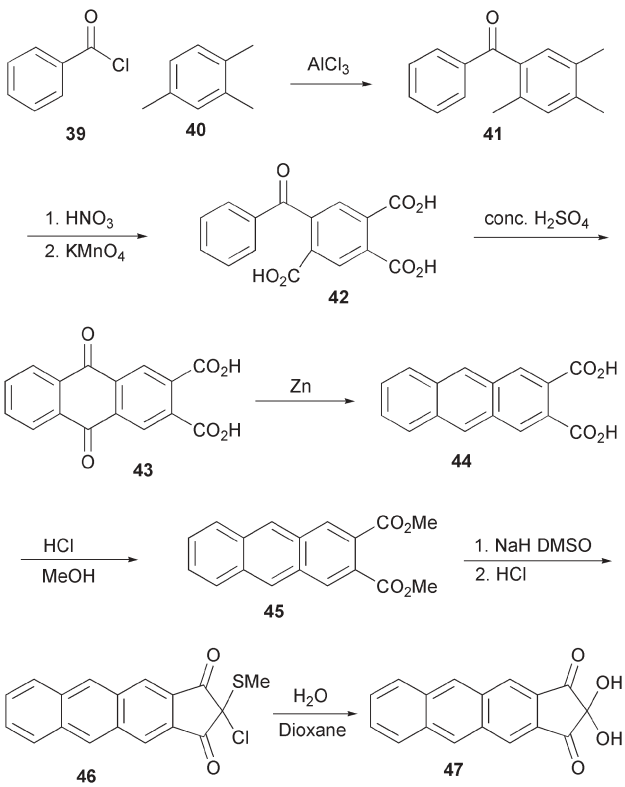
Attempts to apply the Diels–Alder method of Joullié by Bartsch and co-workers failed in the synthesis of naphtho[*f*]ninhydrin (**47**).[23] A revised scheme was developed around the method utilized by Almog in the synthesis of benzo[*f*]ninhydrin (Scheme 9). Friedel–Crafts acylation of 1,2,4-trimethylbenzene (**40**) with benzoyl chloride (**39**) and $AlCl_3$ gave ketone **41**. Oxidation of all three methyl groups with a combination of HNO_3 followed by $KMnO_4$ gave the triacid (**42**) which was cyclized to quinone **43** in sulfuric acid. Reduction of the quinone was accomplished with zinc to yield 2,3-anthracenedicarboxylic acid (**44**), which was then esterified



Scheme 7



Scheme 8



Scheme 9

in methanol to give the diester **45**. Condensation with DMSO in the presence of sodium hydride followed by treatment with hydrochloric acid produced intermediate **46** that was hydrolyzed in aqueous dioxane to give naphtho[*f*]ninhydrin (**47**). Evaluation of this analogue has yet to be published and cannot be compared with ninhydrin.

Bis-ninhydrin analogues

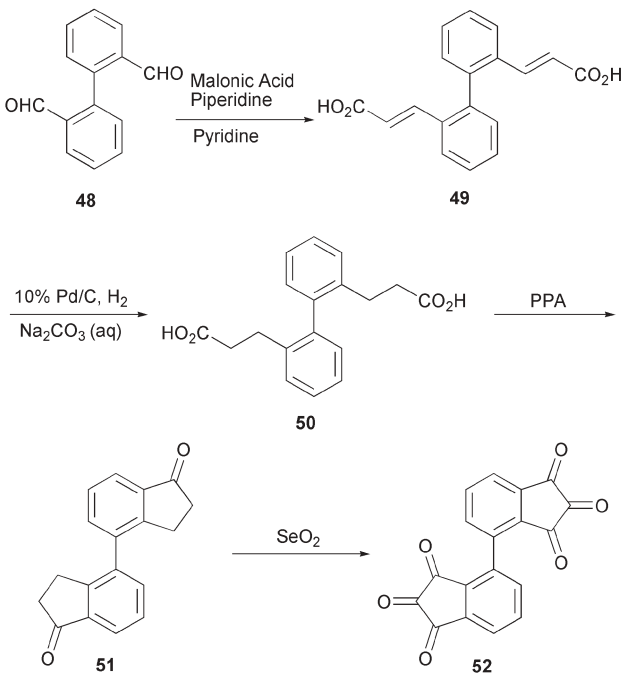
The success of both benzo[*f*]ninhydrin and thieno[*f*]ninhydrin spurred a development of analogues that contained extended conjugation and sulfur-containing heterocycles (Schemes 10 and 11). Hark *et al.* prepared a series of compounds that would meet the criteria of extended conjugation by synthesis of bis-ninhydrin analogues that contain two cyclopenta-1,2,3-trione moieties.[13] Commencing from dialdehyde **48**, Knoevenagel condensation of malonic acid yielded diacid **49**. Hydrogenation of **49** followed by Friedel–Crafts cyclization with polyphosphoric acid yielded bis-1,1′-indanone (**51**). Selenium dioxide oxidation gave a modest yield of the desired bis-ninhydrin (**52**). Initial studies regarding the ability of the bis-ninhydrin to develop fingerprints showed similar colour development to that of ninhydrin, but there was no improvement in the optical properties compared to that of ninhydrin. The authors suggested that the two aromatic rings were not coplanar and therefore not in conjugation and that each half was essentially behaving as an isolated ninhydrin molecule. This class of analogues does allow for the potential formation of a polymeric Ruhemann's purple species.

Aryl and heteroaryl ninhydrin analogues

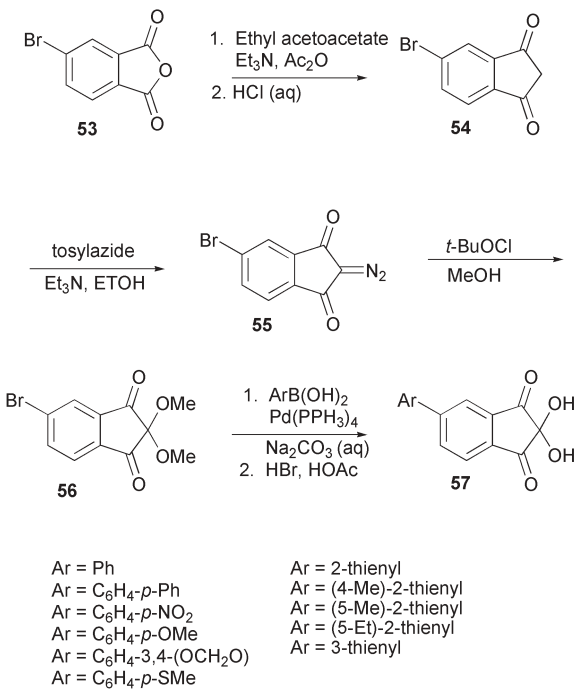
In order to streamline the synthesis of a variety of ninhydrin analogues Joullié and co-workers developed an advanced intermediate that would allow for the palladium catalysed coupling of a large number of aryl substituents.[13] The Suzuki cross-coupling was selected because a large variety of aryl boronic acids were commercially available (Scheme 11). 2,2-Dimethoxy-1,3-indanedione (**56**) was chosen as the coupling partner because the basic reaction conditions used in the Suzuki coupling would have destroyed most intermediates commonly used to prepare the trione moiety. Claisen–Dieckmann condensation of 4-bromophthalic anhydride (**53**) and ethyl acetoacetate in the presence of triethylamine followed by acidic work up yielded 5-bromo-1,3-indanedione (**54**) that was oxidized to the diazo compound (**55**) by tosylazide and then treated with *tert*-butyl hypochlorite in methanol to yield 2,2-dimethoxy-1,3-indanedione (**56**). Various substituted aryl and thiophene boronic acids were coupled with intermediate **56** and the resulting dimethyl ketals were hydrolyzed in a mixture of hydrobromic acid and acetic acid to yield the desired ninhydrin analogues. Evaluation of the analogues indicated that 2-thienyl and 3-thienyl were promising new analogues that exhibited fluorogenic properties without secondary treatment with metal salts.

Ninhydrin hemiketals

The high polarity of ninhydrin often requires the addition of a small percentage of a polar solvent to solubilize it. Even a small percentage of a polar solvent has been shown to cause a high degree of background staining when used to develop fingerprints on some materials such as thermal paper. To overcome this problem a ninhydrin analogue with improved solubility was needed. Efforts to append additional alkyl groups to the aromatic ring were largely ineffective. These analogues have shown improved solubility but decreased sensitivity.[24] Another approach to overcome this problem was developed by Takatsu and co-workers by the use of



Scheme 10



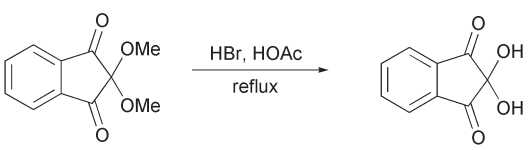
Scheme 11

hemiketal derivatives.[25] Ketal derivatives were proven to be too robust requiring refluxing hydrobromic acid in acetic acid to deliver ninhydrin (Scheme 12). It is well-known that hemiketals are less stable than ketals and that this fact may allow for the balancing of reactivity and improved solubility. A variety of alkyl alcohols were mixed with ninhydrin and heated to produce a series of hemiketal analogues. The ninhydrin-hemiketal **58** derived from 3,5,5-trimethyl-1-hexanol and ninhydrin (Scheme 13) is currently used and is commercially available. Formulations with this analogue can be prepared in hexane and used to detect latent fingerprints on thermal paper without background staining.

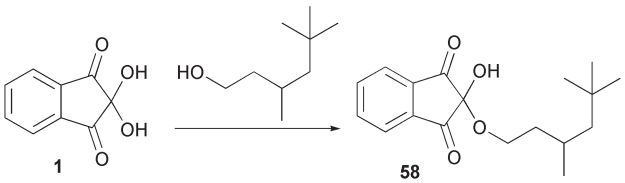
Metal complexes of Ruhemann's purple

The reaction of metal salts with Ruhemann's purple to provide products that have strong luminescent properties has been essential in the detection of weak ninhydrin prints. The resulting complex between Ruhemann's purple and metal salts has been a subject of growing interest. It has been shown that both zinc(II) and cadmium(II) salts complex with Ruhemann's purple to provide luminescent products with slightly different properties (Scheme 14). The intensity of the luminescence can be further improved if the prints are cooled in liquid nitrogen before observation.

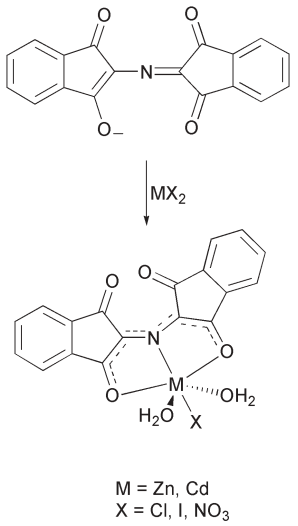
The complexes formed are very sensitive to the development conditions and can form species with either 1 : 1 or 1 : 2 metal : ligand ratio. In polar solvents it has been shown that a red 1 : 2 metal : ligand complex is formed while in less polar solvents the formation of an orange 1 : 1 metal : ligand complex is favored.[26] The complexes each show different emission spectrum that may be beneficial depending on the background present. On paper surfaces it has been shown that products are mainly determined by the concentration of Ruhemann's purple. Strong fingerprints induced the formation of a 1 : 2 complex while weak fingerprints favored the formation of a 1 : 1 complex. As secondary metal treatment is used primarily for the detection of weak fingerprints, it stands to reason that 1 : 1 complexes will be preferred, making it less likely that 1 : 2 complexes will be effectively utilized.



Scheme 12



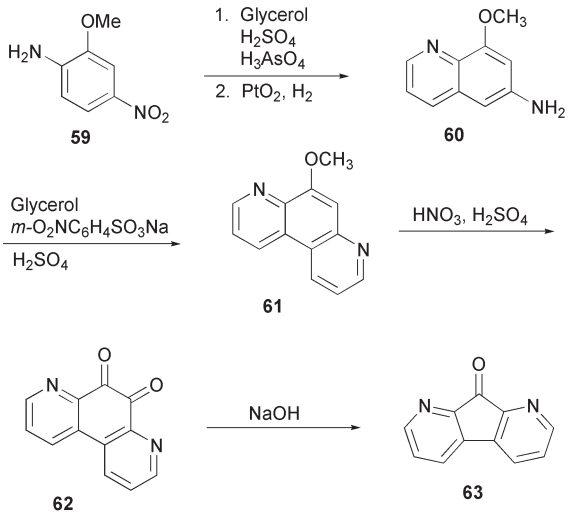
Scheme 13



Scheme 14

1,8-Diazafluorene-9-one (DFO)

A major achievement in the advancement of ninhydrin analogues with increased sensitivity was met by the development of a related compound that is in fact not a direct analogue of ninhydrin at all (Scheme 15). In 1990 Grigg and Pounds prepared 1,8-diazafluorene-9-one[27] (DFO) by the method of Druey and Schmidt.[28] 2-Methoxy-4-nitroaniline (**59**) was subjected to Skraup quinoline synthesis and then reduced by catalytic hydrogenation to amine **60** and subjected to Skraup quinoline conditions again to yield 5-methoxy-4,7-phenanthroline (**61**). Oxidation of **61** with acids provided diketone **62**, which, when exposed to aqueous sodium hydroxide, yielded DFO (**63**). Unlike ninhydrin, DFO has only one central carbonyl that is now flanked by two fused pyridine rings that act similarly as neighbouring dipoles of the 1,3-diketones in ninhydrin. This compound was found to react with α-amino acids to give a red product. Further analysis determined that the product was analogous to that of



Scheme 15

Ruhemann's purple. DFO, unlike ninhydrin, developed fingerprints that were highly fluorescent without secondary treatment with metal salts.

These improvements have quickly made DFO a popular addition for the development of latent fingerprints although it only forms a weakly coloured print. The increased sensitivity has been shown on average to reveal more fingerprints than ninhydrin. The increased sensitivity does not come without certain disadvantages. DFO, while commercially available, is significantly more expensive than ninhydrin and requires the use of specialized light sources for correct observation (Fig. 2). The development of DFO is more demanding, requiring a carefully timed application of relatively high temperature and dry heat to avoid thermal decomposition of developed prints. It has also been shown that DFO does not develop all of the latent prints and that secondary treatment of DFO-developed prints with ninhydrin has been necessary to maximize the number and quality of fingerprints. While the reason for this shortcoming is still under examination it has been speculated that DFO reacts with amino acids more slowly than ninhydrin and in certain instances the reaction with DFO does not proceed to completion. Development of DFO analogues has not resulted in any significant improvements.[27]

1,2-Indanediones

The ability to prepare fluorogenic prints directly continues to drive the development of newer ninhydrin analogues. Joullié and co-workers, while investigating different oxidation strategies, synthesized a variety of 1,2-indanediones instead of the more common 1,3-indanedione precursors. Their discovery that 1,2-indanediones could react with amino acids to yield fluorogenic products led to the development of a new class of fluorescent ninhydrin analogues.[29] The synthesis of 1,2-indanedione (**69**) is shown in Scheme 16. Knoevenagel condensation of benzaldehyde (**64**) with malonic acid in the presence of catalytic piperidine in pyridine yielded cinnamic acid (**65**) that was hydrogenated over 10% palladium on carbon to give dihydrocinnamic acid (**66**). Cyclization with polyphosphoric acid gave the desired 1-indanone (**67**).

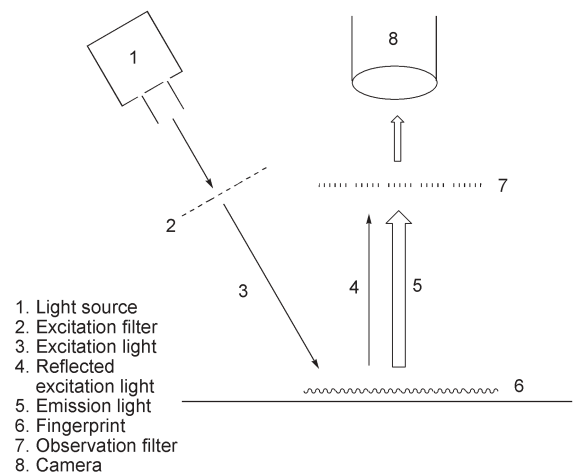
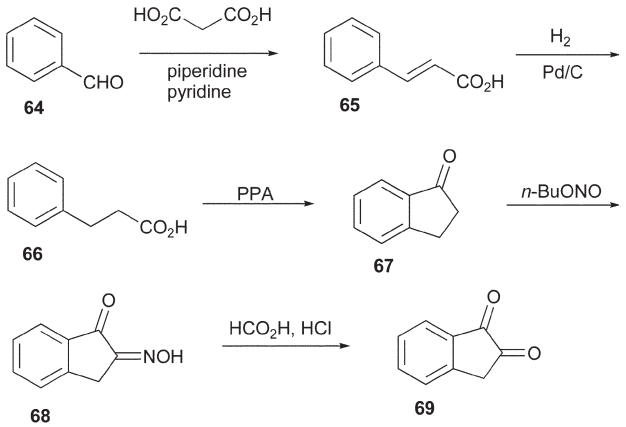


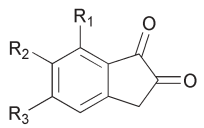
Fig. 2 Prints are viewed and photographed with a 520 nm (green) excitation filter and 590 nm (red) observation filter.



Scheme 16

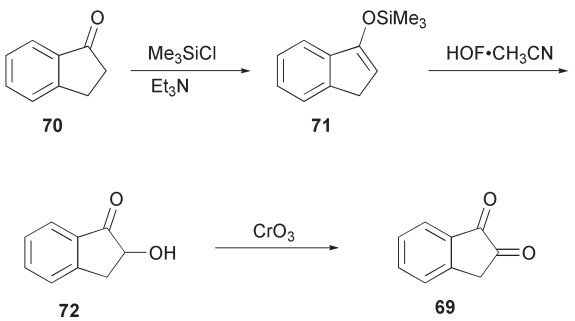
Oxidation of the 2-position was accomplished with *n*-butyl nitrite to yield an intermediate oxime **68** that was hydrolyzed to 1,2-indanedione (**69**) in an aqueous mixture of formic and hydrochloric acid. In an analogous fashion, an additional nine substituted 1,2-indanedione derivatives were synthesized (Fig. 3).

Initial evaluation of this class of analogues has shown great promise.[30] While several researchers reported improved performance of 1,2-indanedione and some of its analogues over that of DFO, other groups claim that DFO gives better results.[31] This discrepancy is currently under investigation.[32] The reaction of 1,2-indanedione with amino acids is similar to that of ninhydrin and has been shown to proceed through a 1,3-dipole that can be trapped with *N*-methylmaleimide.[33] The 1,2-indanediones are more sensitive than DFO and react faster



1. R_1 = H; R_2 = H; R_3 = F
2. R_1 = H; R_2 = SMe; R_3 = H
3. R_1 = H; R_2 = NO_2; R_3 = H
4. R_1 = H; R_2 = H; R_3 = MeO
5. R_1 = H; R_2 = Br; R_3 = H
6. R_1 = H; R_2 = H; R_3 = Cl
7. R_1 = H; R_2 = MeO; R_3 = MeO
8. R_1 = MeO; R_2 = MeO; R_3 = MeO
9. R_1 = H; R_2, R_3 = OCH_2O

Fig. 3 Substituted 1,2-indanediones.



Scheme 17

revealing more overall prints. In addition to being more sensitive, the cost of the reagent is less than DFO and does not require such precise development conditions to prevent thermal decomposition. The prints can be viewed and photographed with existing DFO light sources, avoiding the need for additional equipment for forensic laboratories working with DFO. Formulations and optimum development conditions are currently being worked out to improve the practical utility of 1,2-indanediones in the development of latent fingerprints.

The interest in 1,2-indanediones has inspired the creation of several analogues by Dayan and co-workers.[34] The method used by Joullié and co-workers was successful for the synthesis of several substituted 1,2-indanediones (**73** and **74**) but the oxidation of the 1-indanone failed when attempted on more complex analogues **75** and **76** (Fig. 4). Alternatively, formation of the silyl enol ether (**71**) and subsequent exposure to $HOF{\cdot}CH_3CN$ delivered the 2-hydroxy-1-indanone **72**, which was oxidized with Jones reagent to the corresponding 1,2-indanedione (**69**) analogues. This method allowed for the preparation of an additional four 1,2-indanedione analogues including benzo[*f*]indan-1,2-dione (**75**) and 3-methyl-1,2-indanedione (**76**).

Computational design

Despite the number of ninhydrin analogues that have been synthesized there has yet to be a substantial improvement to warrant the replacement of ninhydrin. Without the ability to predict the efficacy of novel ninhydrin analogues, a large majority of the analogues produced to date have shown no improved optical properties. Elber and Almog have tried to solve this problem with the use of semi-empirical calculations.[35] A comparison of the calculated absorption spectrum of Ruhemann's purple with that of a large number of previously synthesized analogues of Ruhemann's purple derivatives showed that there were few differences in the absorption spectra and that the data correlated well with the fact that many derivatives developed colours similar to that of Ruhemann's purple. Further calculations to examine electron densities showed a profound effect by varying the heteroatoms at the 1,3 position. Two compounds were proposed for examining the effects of modifying the 1-position, by replacing the oxygen either with a sulfur (**77**) or carbon (**79**) atom. Calculations of the absorption spectra of the two Ruhemann's purple analogues (**78, 80**) showed significant differences in their absorption spectra. Not surprisingly in view of the known instability of thioketones attempts to synthesize thiono analogue **77** have failed and currently the calculations cannot be compared to the experimental values.

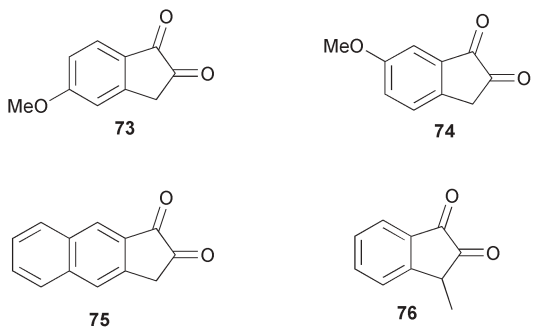
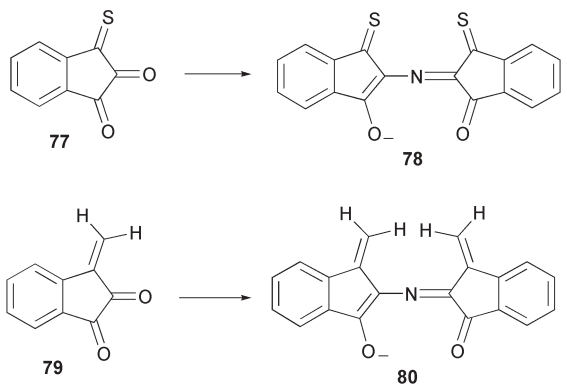


Fig. 4 1,2-Indanedione analogues.



Scheme 18

Conclusions

The continued importance of latent fingerprints as physical evidence in forensic science has created a demand for improved reagents for fingerprint development. The synthetic analogues highlighted here have shown that reagents with enhanced properties are still needed. While ninhydrin analogues have shown improved properties they have yet to replace ninhydrin as the standard reagent for latent fingerprint development.

Acknowledgements

The authors would like to thank the many co-workers over the years that have contributed to the chemistry presented here. We additionally thank Dr Joseph Almog, Dr Antonio A. Cantu, Dr Diane B. Hauze, Prof. Richard R. Hark and Dr Jan Zonjee for their helpful discussions and review of this manuscript.

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