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Supramolecular Hair Dyes: A New Application of Cocrystallization

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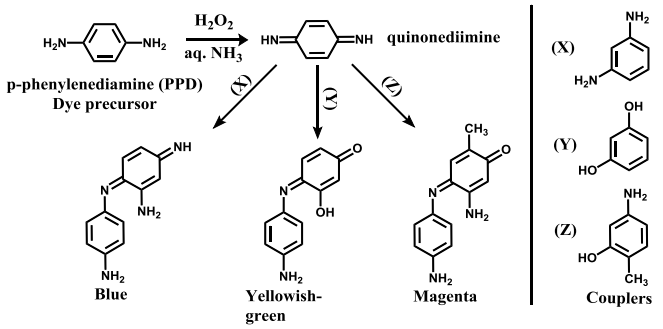
Abstract: The manuscript presents the first report of hair dyes of various colors formed by the cocrystallization reactions. Unlike the most popular oxidative hair dye (**OHD**) products, these dyes are NH_3 free and do not require H_2O_2 as a color developer. The importance of these new hair dyes products is further enhanced by recent reports which indicate that some of the **OHD**s may be carcinogenic.

Introduction

OHDs hold a dominant share of the multi-billion dollar hair dye industry (70-80%).[1] These dyes are marketed in their colorless form and the dye molecules are synthesized by the end users via simply mixing the contents of the two tubes provided, widely known as colorant and developer tubes. While the colorant tube contains color components i.e. dye precursor and coupler in a basic media, the developer tube contains H_2O_2. By altering the precursor-coupler combination, hair dyes of different colors can be obtained as shown in **Scheme 1**.[2]



Scheme 1. Coupling reaction used in **OHD**s.

OHDs contain some harsh chemicals such as ammonium hydroxide (i.e. NH_4OH) and H_2O_2, which have been further linked with increase in hair porosity,[3, 4] hair loss,[3, 5, 6] dermatitis[5, 7] and chemical burns.[7] H_2O_2 and NH_4OH are the constituents of piranha base, which is well known for its corrosive nature especially with regard to organic matter including hairs which are largely proteinaceous.[2] H_2O_2-NH_4OH combination, present in **OHD**s, breaks the disulphide bond of the cystine moiety of hair proteins, which compromises the mechanical strength of the hairs.[4, 8] Further concerns about the safety of the **OHD**s have been raised in the past 20 years due to their potential carcinogenic nature.[9]

Each of the additives have their place, H_2O_2 oxidizes the phenylenediamine to form quinonediimine for reaction with the couplers. NH_4OH creates the basic environment and also lifts the scales of the hairs for the easier penetration of dye molecules before conditioners are used to reverse this effect.[10, 11] Scales may lose their elasticity on repetitive use of **OHD**s (by a combination of repetitive scale lifting-smoothening cycles and chemical degradation by H_2O_2-NH_4OH mixture) resulting in hairs that are permanently damaged and porous. Porous hairs absorb significantly higher amount of water which accelerates the hair loss due to sheer weight of the absorbed water.[3, 5, 12] Further problems arise from this effect where the hairs are prone to moisture loss as well as the loss of the hair dye molecules themselves.[10]

Despite the negative attributes of **OHD**s they hold a dominant share of the hair-dye industry due to the unavailability of equally durable and economical permanent hair dye products. Here we show how crystal engineering can be used to create H_2O_2 and NH_4OH free hair dyes by cocrystallization. Cocrystallization reactions are known for their ease and have been well explored to improve the physical properties such as solubility,[13, 14] phase transition temperatures,[15] melting points,[14] tableting properties,[16] stability,[17] fluorescence,[18] elasticity,[19] color[18, 20, 21] etc. In a hunt for molecules which can form colored cocrystals/salts, we chose p-Phenylenediamine (**PPD**) and N-Phenyl-p-phenylenediamine (**NPPPD**), as these molecules are already precursors for many **OHD**s (**Scheme 2**). Though **NPPPD** itself is colored, the freshly prepared **PPD** is colorless but oxidizes in air causing a change to a light-pink color.

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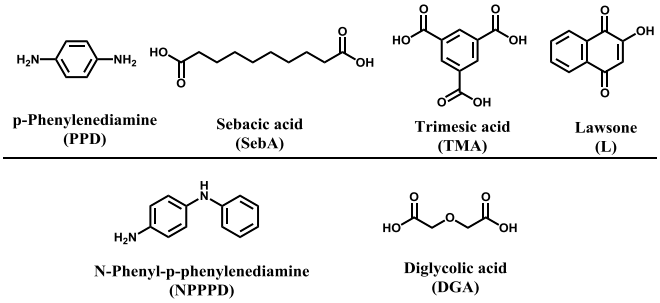

Scheme 2. Chemical structure of reactants used for cocrystallization.

The cocrystallization reactions were initially carried out in 1:1 ratio from methanol and were accompanied by the color changes. The color changes were characterized using UV-visible spectrophotometer, which revealed a bathochromic shift with respect to their respective amines (see **Figure 1**).

To determine whether a chemical or supramolecular reaction had occurred, all the materials were characterized structurally via single crystal X-ray diffraction. They all showed that salt formation had occurred, where the deprotonated coformer interacted with the amine/ammonium group of protonated amines through N-H···O, N-H···O^-, N^+-H···O, N^+-H···O^- hydrogen bonds, using carboxylic acid/carboxylate/keto/O^- functionalities (**Figure 2**). The structures revealed that while **PPD-SebA** and **PPD-L** form in 2:1 and 1:2 respectively, reactants of all the other salts preferred to interact in 1:1 (see supplementary information (**SI-1**) for crystallographic tables). **NPPPD-DGA** exists in 2 forms, both of which were obtained from a cocrystallization reaction in methanol. Form 2 of **NPPPD-DGA** has only been obtained once.

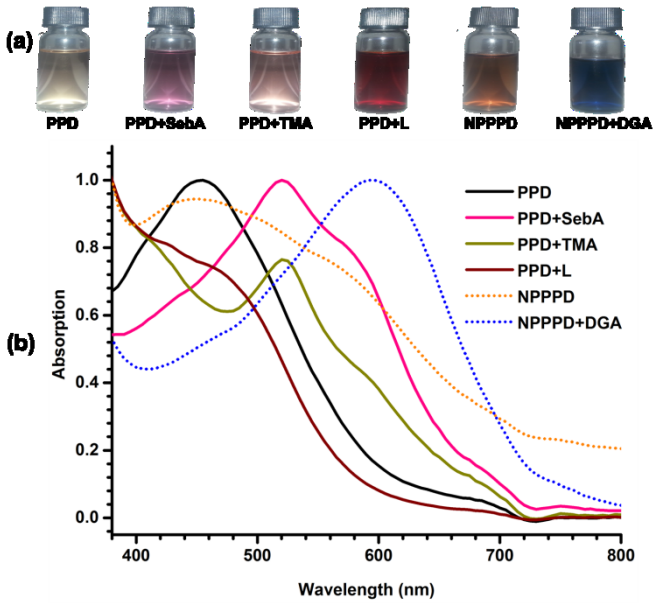

Figure 1. a) Color change and (b) bathochromic shift observed in salts of **PPD** and **NPPPD**.

Using the stoichiometric information from the solution chemistry we have been able to synthesize the salts by a greener liquid-assisted grinding (LAG) route, which makes use of minimal amount of solvent. Powder diffraction patterns of all the materials obtained by LAG were Pawley-fitted using the unit cell obtained from their respective crystal structures and revealed that we were successful in synthesizing all the three salts of **PPD** and Form 1 of **NPPPD-DGA** (See **SI-3**).

The colored solutions formed during cocrystallization were investigated for their hair dyeing performance. For this test we chose to dye grey hairs to allow a clear indication of the dyeing potential i.e. failure to dye would be clearly apparent (**Figure 3a**). This was performed by immersing 200mg of grey hairs in 15ml of 6.67 % (w/v) methanolic solutions of the salts before letting the solutions evaporate to dryness. The excess hair dye that adhered to the surface of hair was removed with an excess of hot water (50°C). After dyeing the sample hairs were initially washed for 30 minutes, and later for a more prolonged 24 hours by stirring in 200 ml of hot soapy water (50°C); the latter experiment as an extreme test of color fastness. All the hair dyes worked well and retained their color (**Figure 3b & c**). In these experiments the water was changed 5 and 20 times respectively during 30 minutes and 24 hour washings.

Figure 3. (a) Undyed hairs. (b and c) Dyed hairs after washing for 30 minutes and 24 hours respectively.

Comparison of the SEM images of undyed hairs (**Figure 4a**) with the hairs dyed with supramolecular hair dyes (**SHD**s) revealed no significant change in the surface properties of the hairs after dyeing (**Figure 4 (c-f)**), indicating that these dyes are not harsh on the hair surface.

From an industrial perspective, scalability and ease of processing are very important factors. Considering this in mind, one of the hair dyes (**PPD-SebA**) was chosen for scale up, based upon the cost and availability of the chemicals. The system was scaled up to 275g scale both by LAG and solution methods (**SI-2c** and **2d**). The materials obtained from LAG (pinkish-white) and solution crystallizations (dark bluish-black) differ in color, but PXRD analysis shows that the products of both these methods are the same (**Figure 5**). Such differences in color of the materials obtained by grinding and solution crystallizations have been reported by some other groups too.[20, 22] These color differences indicate that solvent plays an important role in color generation probably via affecting the extent of crystallization and crystal size.

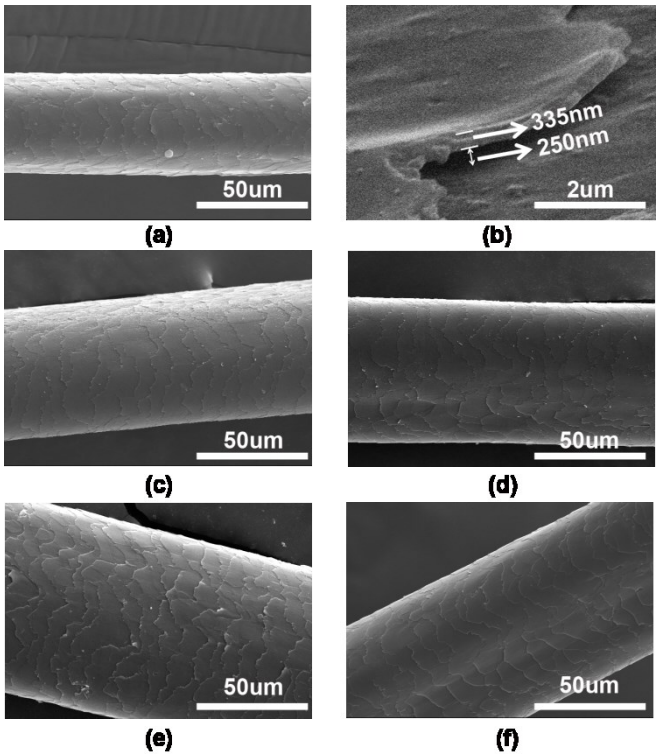

Figure 4. (a) Surface of a hair sample before dyeing showing the scales. (b) measurement of the thickness of scales on the hair samples and pore size. Hairs dyed with (c) **PPD- SebA** (d) **PPD- TMA** (e) **PPD-L** and (f) Form 1 of **NPPPD-DGA**.

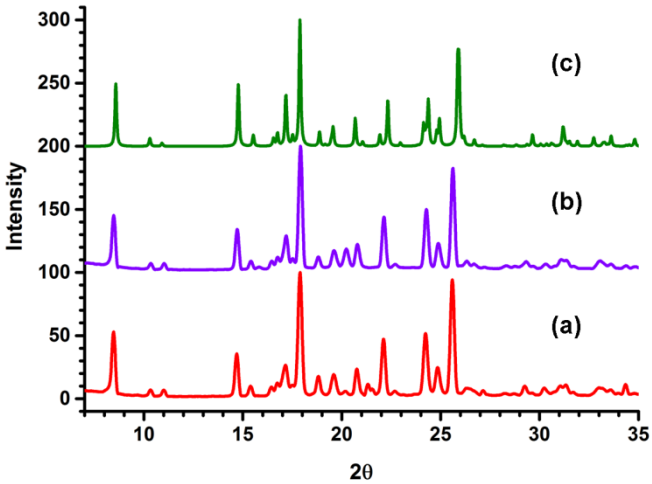

Figure 5. Comparison of the PXRD patterns of **PPD-SebA** salts obtained from (a) LAG and (b) solution crystallization with (c) its PXRD pattern simulated from its crystal structure.

After bulk preparation, we attempted to formulate the **PPD-SebA** salt into a formulation that could be applied to hairs directly on potential customers. For this purpose, 4ml of a concentrated solution of **PPD-SebA** in methanol (**SI-2e**) was diluted with the addition of 2 ml of water to form a solution. To this 6g of solid **PPD-SebA** (obtained from solution crystallization from methanol (**SI-2d**)) was added to form a paste. During the paste formation the mixture was kneaded to break up the solid that had agglomerated (**Figure 6a**). This paste was used to dye the wet grey hairs (soaked in water for 2 minutes to swell the hair) for 30 minutes. The excess hair dye, which was adhering to the surface of the hairs, was easily recovered by rubbing the hairs between the finger tips. Interestingly, even this simple formulation dyed the hairs reasonably well (**Figure 6c**). The dyed hairs were tested for their dying performance by washing them 25 times with soapy water and found to retain the color (Figure 6d). To investigate the reusability of this **SHD** for dying, 3g of the recovered material was again converted to a paste by adding 1ml of water and 2 ml of concentrated solution of **PPD-SebA**. Dyeing was done for 30 minutes, which was followed by 25 washings with soapy water. The dyeing performance of the recovered material was same as that of dye used for the first time. It is noteworthy to mention that **OHD**s are not reusable and any hair dye left after use is simply discarded.

Figure 6. (a) Strong color observed during **PPD-SebA** paste formation. (b) Undyed hairs (c) Hairs dyed with paste formulation after (c) first washing (d) twenty fifth washing.

Diffusion of the dye molecules into hairs is an important parameter and is directly related to the dyeing times. The relative dimensions of dye molecules and pores of the hairs dictate this diffusion process.[10] While the dimension of the molecules is a fixed quantity, pore size can be increased to a great extent by a phenomenon known as swelling. [23] Swelling is induced by the addition of chemical additives (such as solvents, amines, organic and inorganic acids, salts, urea, formamide etc.), [5, 10, 24] which can disrupt the hydrogen bonding present in hairs. In **OHD**s, NH_4OH is added to swell the hairs. NH_4OH also serve to generate the basic environment which is required for the proper functioning of **OHD**s.[2] The swelling action of amines increases with the increase of pH however the decomposition of keratin also takes place at high pH, so the ideal environment for **OHD**s is to operate between pH range 9-10.[2] In our paste formulation we used water which is a well-known swelling agent.[23] Water increases the pore size by couple of hundred of nanometers in little as 5 minutes.[23, 25] Before applying the paste formulation to hairs, they were submerged in water for 2 minutes to induce swelling and hence increase the rate of dye intake. Since the dimensions of the molecules used for our study were only few angstrom in size (<15 Å) we expected the dyeing process to be rapid which is what we observed.

Hair dye performance is determined by the binding forces between hairs and dye. The dye molecules primarily bind the hairs using hydrogen bonds.[2, 26] Hair dye companies aim at increasing the strength of these hydrogen bonds for better product performance. The **SHD**s presented in this paper are ionic and hence have the potential to form stronger charge assisted

hydrogen bonds with the hairs in comparison to the neutral molecules formed via the oxidative reaction.

One of the prime requirements of the hair dye industry is to produce a range of colors. **OHD** industries rely on changing the dye precursor-coupler combination to achieve the same. The precursors and couplers are chosen in such a way that they can form the more conjugated colored end product. Unfortunately, **OHD** industry is limited in terms of the number of approved safe molecules (around 100) which they can use as dye precursors and couplers.[2, 27] **SHD**s appear to have an edge over **OHD**s in terms of the number of safe molecules (thousands of safe coformers for **SHD** can be chosen from EAFUS[28] and GRAS[29] lists), but also a major drawback in terms of control of outcome of cocrystallization reaction.

Conclusion: A technological breakthrough has been achieved in synthesizing the H_2O_2 and NH_3 free hair dyes by using a cocrystallization based hair dye technology. The dyeing performance of the hairs dyes presented in this paper is comparable to the permanent hair dyes which last for more than 24 washings. SEM analysis revealed that the application of these hair dyes did not appear to have a detrimental effect on the hairs themselves. The scalability of these hair dyes was demonstrated by taking a representative example, in which **PPD-SebA** salt was scaled up to a 275g scale and used to dye hair samples with relative ease.

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Keywords: Cocrystallization, colored salts • supramolecular hair dye • permanent hair dye • supramolecular chemistry • H_2O_2-NH_4OH free hair dye

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