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Crystal engineering of *N*-salicylideneanilines as a tool to study solid-state photochromism and to develop photochromic solid-state materials

Abstract

N-salicylideneaniline derivatives are among the most studied man-made photochromic systems. However, due to the volume requirements of the cis-trans photoisomerization at the basis of the photoswitching, not every *N*-salicylideneaniline forms photochromic solids. Herein, we report our findings on cocrystallization employed as an elegant technique (of crystal engineering) to induce photochromism in non-photochromic *N*-salicylideneaniline dyes. The focus is put on the formation and characterization of isomorphous solids and their solid solutions, with the aim to gain insights on the structural factors controlling the expression of photochromism in this family of derivatives.

Keywords

Multicomponent crystalline solids, cocrystallization, photochromism, *N*-salicylideneanilines, isostructural solids, solid solutions.

1. Introduction

Cocrystallization is the combination of two, or more, chemical entities in the same crystal lattice.

Herein, beyond the existing semantic debates around the term “cocrystal”, cocrystallization is intended in its broadest sense of “formation of multicomponent solids” regardless the nature of the two cocrystal partners. Over the past decade, we have witnessed a growing interest in the development of cocrystallization procedures to address poor solubility issues of non-ionizable pharmaceutical molecules, or to improve other physicochemical properties such as melting point or hygroscopicity [1-3]. Cocrystallization has also been employed as a resolution tool to resolve a racemic mixture of drug substances and, more recently, attention has been prompted to drug-drug formulations [4-5]. Recent advances of cocrystallization lie in its use as a design element in the creation of **multipurpose materials** [6]. Luminescent [7-9] or smart materials responding to various external stimuli such as light [10-12] or heat [13, 14], or even mechano-[15], solvato-[16], and vapo-responsive [17] solids are few examples of multicomponent materials designed by cocrystallization.

In this renewed framework, our work deals with the use of **cocrystallization to develop**

photochromic crystalline materials [10, 18-20]. In a photochromic material, the color change occurs due to reversible transformation of chemical entities following the absorption of electromagnetic radiation [21]. For example, in *N*-salicylideneanilines the switching mechanism can be induced by thermal means (thermochromism) or by light irradiation (photochromism). Thermochromism is due to a temperature dependent ground-state keto-enol tautomerization via intramolecular proton transfer between a colorless enol form and a yellow *cis*-keto form [22, 23]. Light irradiation (~ 365 nm for the enol form and ~ 450 nm for the *cis*-keto form), induces an isomerization toward a red *trans*-keto form (~ 560 nm, Figure 1), the photochromic product [24-27]. However, due to steric effects that molecules experience in the constrained solid media, the photochromic

transformation is not always observed. Herein, cocrystallization is used with the aim to induce photochromism in non-photochromic *N*-salicylideneaniline chromophores.

Understanding the relationship between the nature of the two components of the cocrystal (the cofomer and the dye molecule), the crystal structure and the optical properties is also a scope of our work. Fulfillment of this goal might lead to a better understanding of the structure-optical relationships of solid materials and help designing new ones with improved photochromism. To this purpose, cocrystallization is suitable for the creation of libraries of crystalline solids with modulated properties. One can potentially build an infinite number of cocrystal forms for the same dye of interest (by varying the cocrystal former, Figure 2) [28].

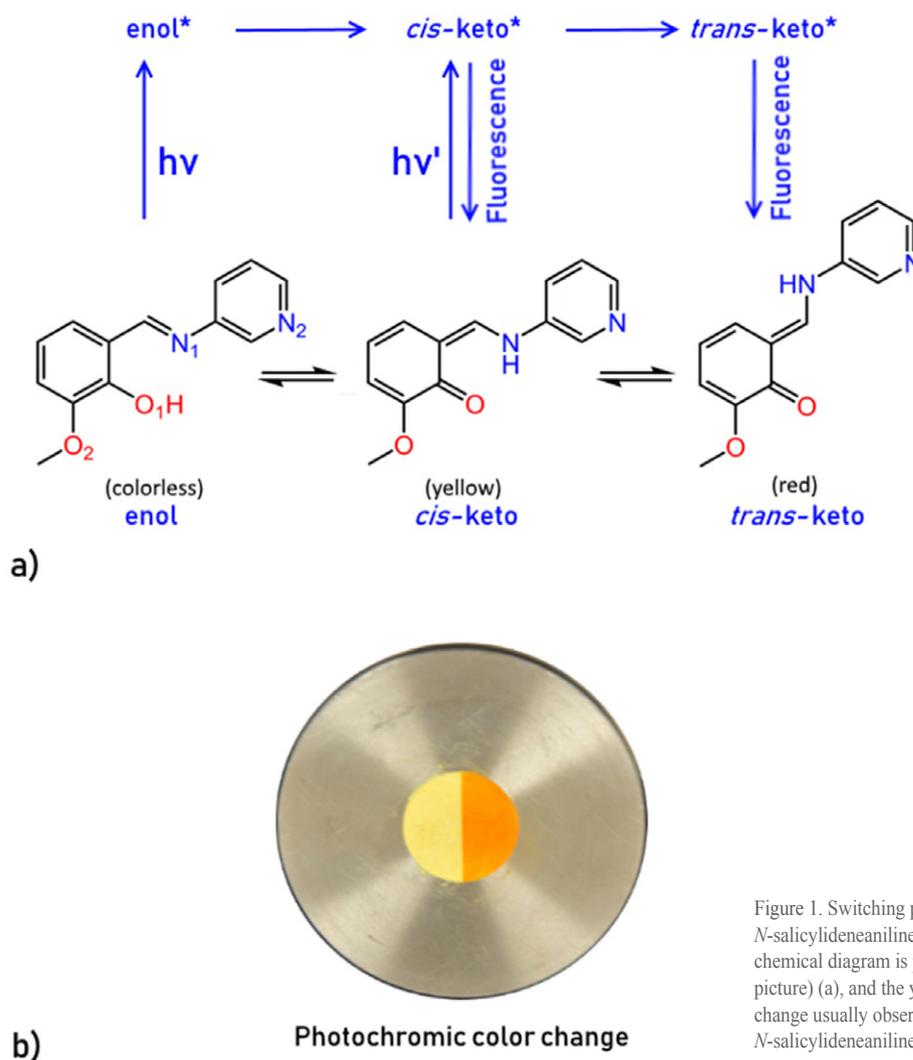


Figure 1. Switching pathway of *N*-salicylideneaniline derivatives (3AP chemical diagram is provided in the picture) (a), and the yellow-to-red color change usually observed in crystalline *N*-salicylideneanilines (b)

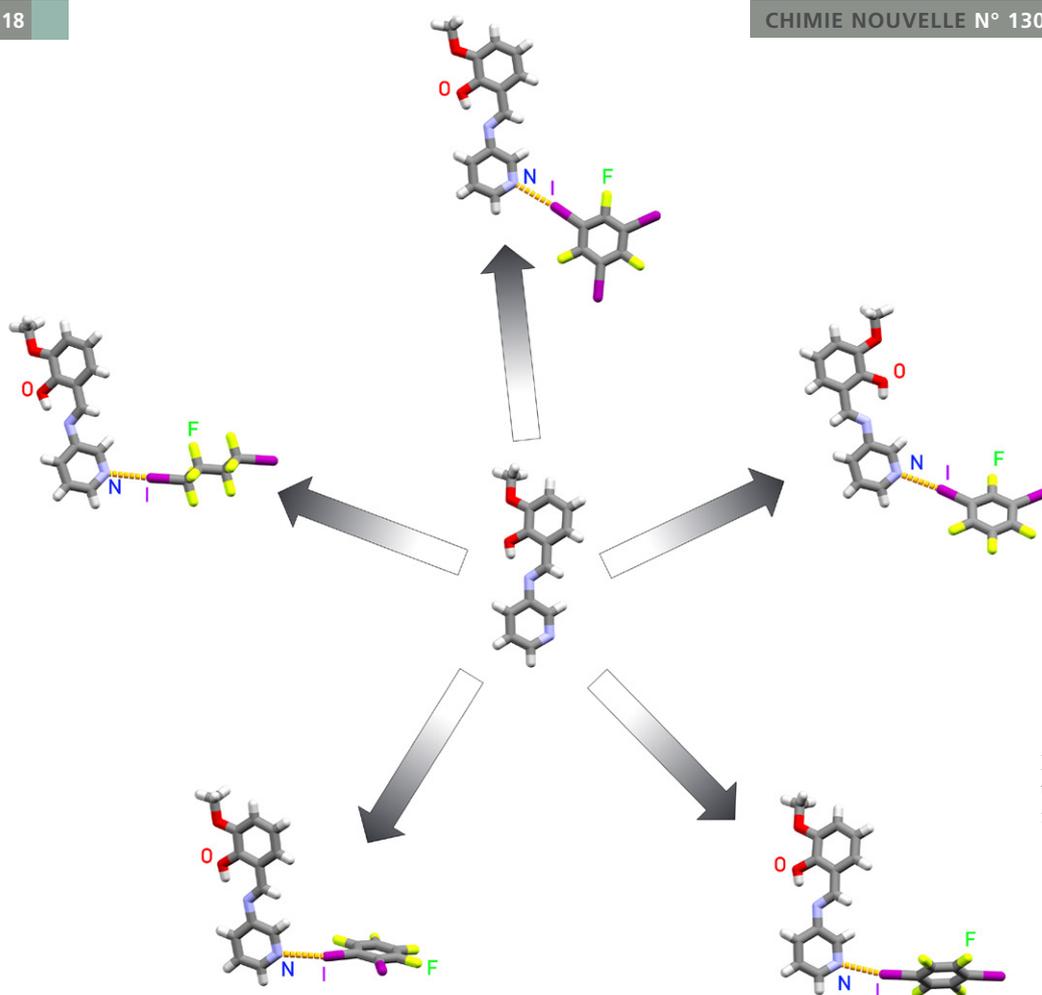


Figure 2. Cocrystallization as a strategy to generate libraries of crystalline solids for a dye of interest

However, despite the large number of cocrystals that can be synthesized, the task of discovering features linking the crystal structure to the bulk properties is not simple. In which cases can cocrystals differing by both composition and crystal structure be compared? How can they be defined as similar or dissimilar? Which one of these dissimilarities will mostly affect their physicochemical properties [29]?

As a matter of fact, comparison of crystal structures is not always straightforward. To simplify the problem, one should restrict the comparison to solids having either same composition or same crystal structure. Solids having same composition but different crystal structure are called **polymorphs** (Figure 3a). The most known polymorphic system is diamond vs graphite. They are made of the same atoms, but behave (and look) very different.

Solids having same crystal structure but different composition are called **isostructural solids** (Figure 3a). The **cocrystallization-**

induced isostructurality (Figure 3b) describes the use of cocrystallization as a tool to force two chemically different molecules, which possess distinct packing preferences, to form isostructural cocrystals. In other words, cocrystallization overcomes the molecular dissimilarities that determine the selection of the crystal packing [30-33]. Within the frame of designing isostructural photochromic materials, **two strategies** can be defined depending on which one of the two cocrystal partners (dye or coformer) is changed (Figure 3c) [10, 14, 34].

On the one hand, the strategy “**same dye / different coformer**”, permits to evaluate the supramolecular effects of the surroundings on a given chromophore embedded in several highly similar architectures (isostructural) which differ by subtle, systematic and predictable modifications (“single-point” modifications). On the other hand, the complementary production and evaluation of isostructural cocrystals obtained through the strategy “**same coformer / different dye**” would allow for corroboration

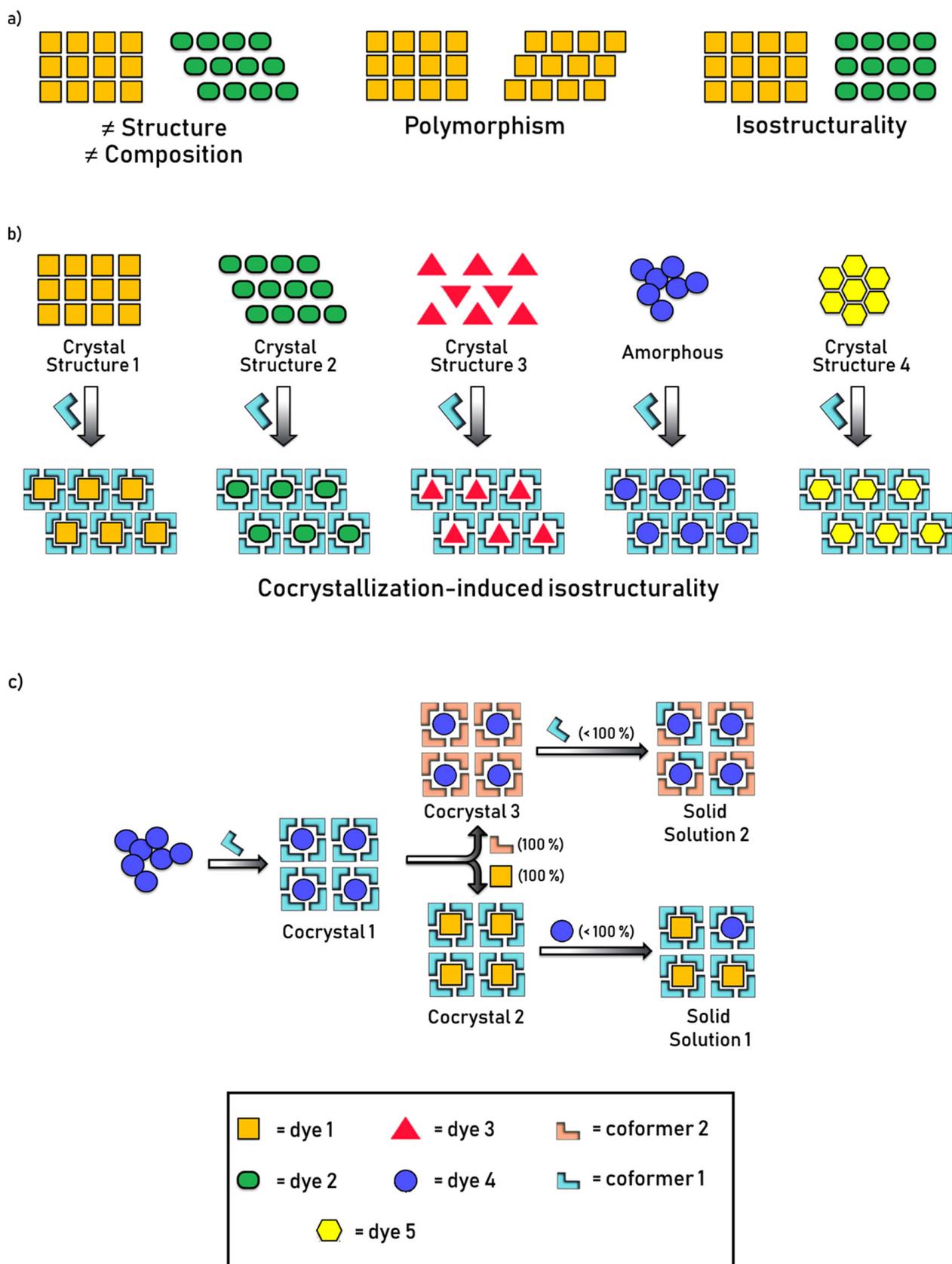


Figure 3. Polymorphism and isostructurality (a), cocrystallization-induced isostructurality (b) and the two main strategies (“same coformer / different dye” (cocystal 2, bottom) and “same dye / different coformer” (cocystal 3, top)) to form isostructural cocrystals and their solid solutions (c)

of the hypotheses formulated in the first place. The achieved isostructurality allows for another interesting property of solids: the solid solubility (Figure 3c) [35-38]. Solid solutions are multicomponent solids which do not obey Dalton's law of multiple proportion. Their stoichiometry is not limited to integral values but can be varied in continuum (in a limited range of concentrations) [35-38]. Crystallographically speaking, the components of a solid solution are not characterized by specific crystallographic positions, therefore, their structure is disordered. The two (or more) constituents of a solid solution may be soluble over a broad range of relative concentrations producing a crystalline solid with physical properties varying continuously over this concentration range or which shows characteristics of the combined substances [35-38]. Solid solutions have been applied to various fields of crystal engineering to study optical, electrical, and photochemical properties of molecular and ionic crystals [39-42]. It is in our interest to understand (thanks to solid solutions) as composition affects photochromism by keeping crystal structure constant (Figure 3c).

The results are divided into two main sections in accordance to the strategy put in place to obtain/study the materials. In the first section, we will report a case of strategy “**same dye / different cofomer**” while, in the second section, we will report a case of strategy “**same cofomer / different dye**”.

2. Results

2.1. Strategy I – “same dye / different cofomer” [10, 28]

We describe the effects of cocrystallization on the expression of solid-state photochromism in four cocrystals of an *N*-salicylideneaminopyridine derivative (labelled as **3AP**). The derivative **3AP** was synthesized by mechanochemical synthesis performed in a ball mill at 30 Hz in 10 min from condensation reaction of 3-aminopyridine and *o*-vanillin. The recovered product **3AP** is a light orange crystalline powder. Single crystal

structure was determined by X-ray diffraction. **3AP** crystallizes in the orthorhombic $P2_12_12_1$ space group. In this crystalline form, the derivative is non-photochromic *i.e.* it does not change its coloration after light irradiation.

The N-atom of the pyridine moiety can act as a strong hydrogen or halogen bond acceptor making the formation of cocrystals easier through these interactions [14, 43, 44]. Alternatively, the N-atom can be easily alkylated to form various pyridinium salts (see next section) [34].

In this first section, the **3AP** derivative is cocrystallized with four compounds: fumaric acid (**FA**), succinic acid (**SA**), 1,4-diiidotetrafluorobenzene (**I2F4**) and octafluoro-1,4-diiidobutane (**I2F8**). Synthesis of these cocrystals can be performed in two steps (*i.e.* cofomer is added to preformed **3AP** in the grinding jar) or in a one-step process (a one-pot mechanochemical synthesis) which allows the concomitant formation of the “imino” covalent bond as well as the non-covalent bonds needed for cocrystallization.

Strategically, to obtain isostructural cocrystals, we chose cofomers having similar size (of about 7 Å for **FA** and **SA** and of about 7.5 Å for **I2F4** and **I2F8**) and similar number and disposition of the interacting groups (all are 180° ditopic cofomers). Interestingly, all four cocrystals have a 2:1 stoichiometry and exhibit structures belonging to the $P2_1/c$ space group. Unit cell parameters show similar values. Piles of stacked molecules of **3AP**, propagating along the *b*-axis, form the common structural motif of their crystal structures (2D-isostructurality). Those piles of molecules are interconnected to other adjacent piles via bridges of cofomers (Figure 4). An in-depth look at the crystal packing reveals that structures are isostructural in pairs: a 3D-isostructurality is found for the group $(\mathbf{3AP})_2 \cdot \mathbf{FA} / (\mathbf{3AP})_2 \cdot \mathbf{SA}$ and for $(\mathbf{3AP})_2 \cdot \mathbf{I2F4} / (\mathbf{3AP})_2 \cdot \mathbf{I2F8}$. One group differs from the other by the orientation of the cofomer bridges. Studies of photochromism were conducted on microcrystalline powders of the cocrystals. Solids of the first group

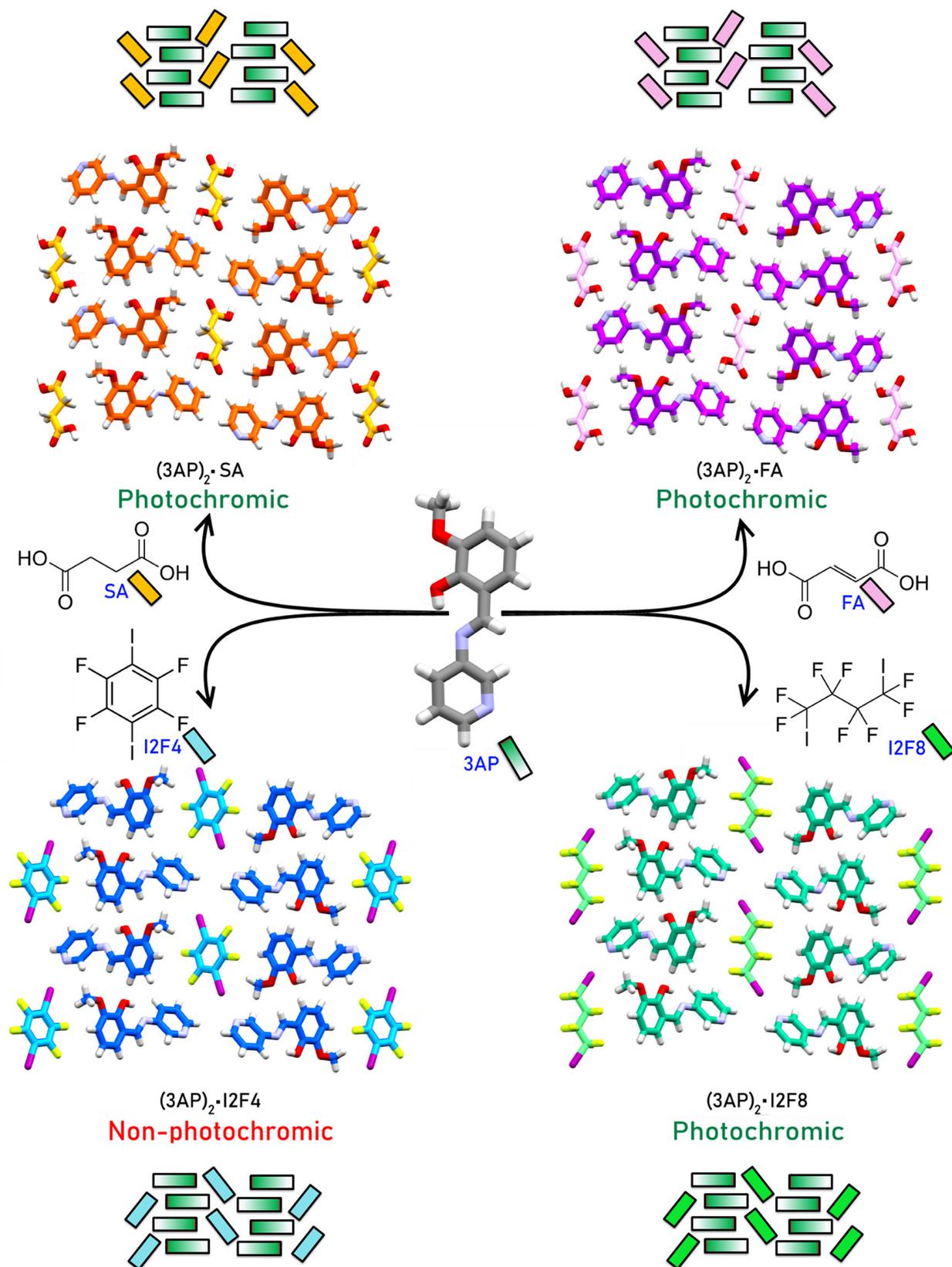


Figure 4. 3D-isostructurality in 3AP-based cocrystals. The found 3D-isostructural cocrystal are (3AP)₂·FA vs (3AP)₂·SA and (3AP)₂·I2F4 vs (3AP)₂·I2F8. The two cocrystal pairs ((3AP)₂·FA / (3AP)₂·SA and (3AP)₂·I2F4 / (3AP)₂·I2F8) share a 2D-isostructurality due to the common structural motif constituted by piles of stacked dye molecules propagating along the *b*-axis (green rectangles)

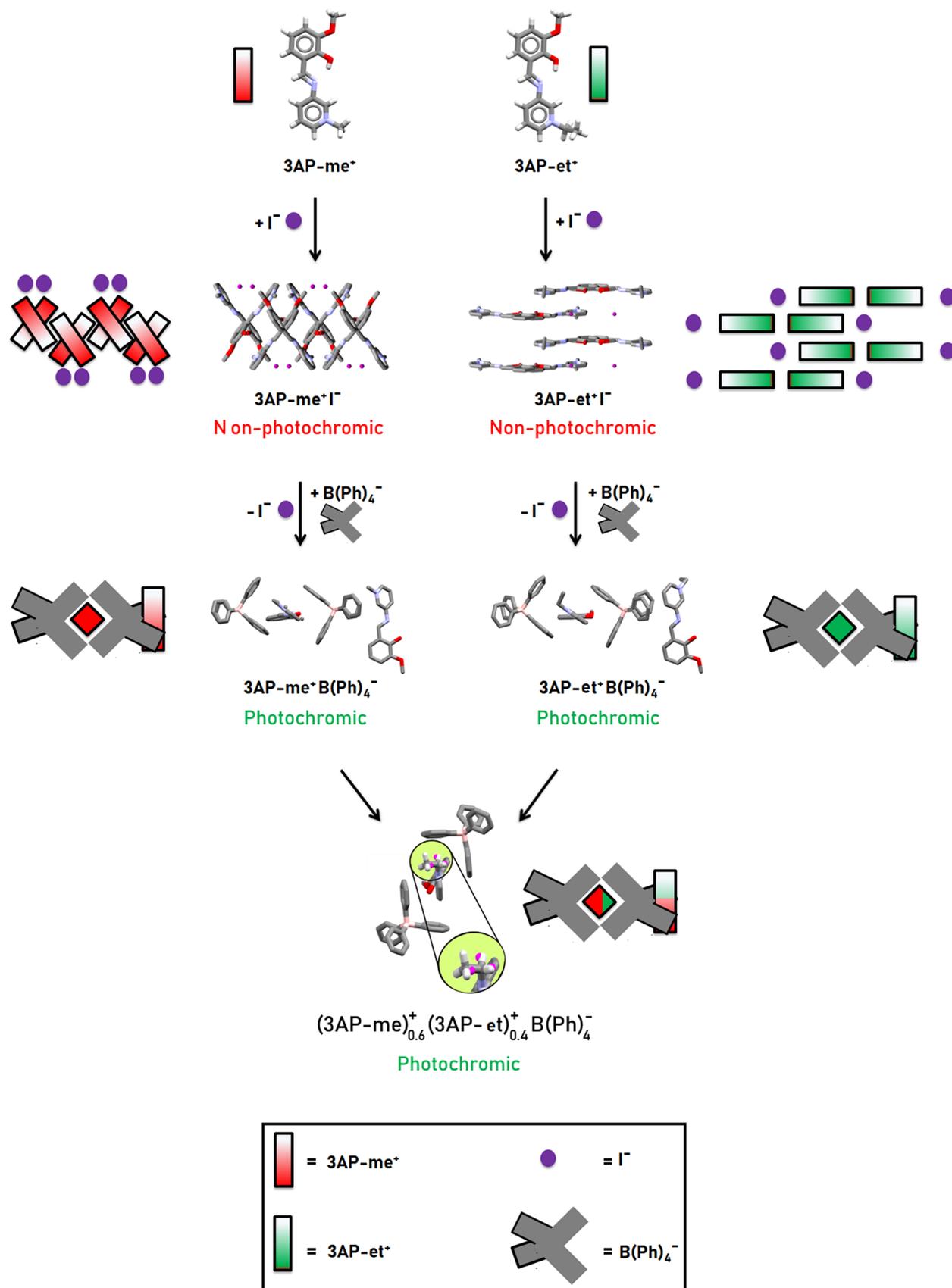


Figure 5. Co-crystallization-induced isostructurality and solid solubility in *N*-salicylideneamino-1-alkylpyridinium cations as tetraphenylborate salts. Disorder in the alkyl chain (due to the simultaneous presence of ethyl and methyl groups) is highlighted (in magenta) in the structure of the solid solution

((**3AP**)₂·FA / (**3AP**)₂·SA) were found to be both photochromic. Their color transition is from pale yellow to red and lasts for about four days. This result highlights a non-photochromic-to-photochromic transformation induced to **3AP** by cocrystallization with dicarboxylic acids. It indicates how the photochromic behavior is not due to the molecule itself but to the crystal structure. However, counterintuitively, solids of the second group ((**3AP**)₂·I2F4 / (**3AP**)₂·I2F8) show a divergent behavior: compound (**3AP**)₂·I2F8 is photochromic while (**3AP**)₂·I2F4 is not. This result reveals for the first time how in a given molecular arrangement, photochromism of *N*-salicylideneanilines is highly sensitive to volume variations.

2.2. Strategy II "same cofomer / different dye"

Two *N*-salicylidenealkylpyridinium derivatives obtained from *N*-alkylation of **3AP**. The two derivatives differ in the alkylation of the pyridine with iodoalkanes: in one case, the alkyl group is a methyl (this derivative is labeled here as **3AP-me⁺I**) while in the second case an ethyl (**3AP-et⁺I**).

3AP-me⁺I and **3AP-et⁺I** are non-photochromic solids. Their crystal packing is different with **3AP-me⁺I** dominated by a *herringbone* structure while **3AP-et⁺I** showing a *layered* structure. However, both solids are characterized by a dense packing and by the presence of head-to-tail dimers with short interplanar distances. Those features might account for non-photochromism. The replacement of iodide, in **3AP-me⁺I** and **3AP-et⁺I**, by a bulky tetraphenylborate anion (solids **3AP-me⁺B(Ph)₄⁻** and **3AP-et⁺B(Ph)₄⁻**) leads to a multiplicity of effects (Figure 5).

First, photochromism: solids **3AP-me⁺B(Ph)₄⁻** and **3AP-et⁺B(Ph)₄⁻** are both photochromic due to disruption of head-to-tail stacking structural motifs.

Secondly, isostructurality: we found how an ethyl in place of a methyl substitution dramatically changes the structure from a *herringbone* arrangement to a *layered* one in solids **3AP-**

me⁺I and **3AP-et⁺I**. This lack of isostructurality suggests that the protruding ethyl group of **3AP-et⁺I** cannot be fitted in the compact structure of **3AP-me⁺I**. Instead, tetraphenylborate salts, **3AP-me⁺B(Ph)₄⁻** and **3AP-et⁺B(Ph)₄⁻**, are isostructural. Their isostructurality is due to formation of tetra-aryl boxes which constitute a loose region of the packing permitting the accommodation of the protruding alkyl groups (methyl for **3AP-me⁺B(Ph)₄⁻** and ethyl for **3AP-et⁺B(Ph)₄⁻**) overcoming molecular differences.

Thirdly, solid solubility: **3AP-me⁺B(Ph)₄⁻** and **3AP-et⁺B(Ph)₄⁻** could be mixed in a (**3AP-me**)_{0.6}⁺(**3AP-et**)_{0.4}⁺**B(Ph)₄⁻** solid solution isostructural to the starting tetraphenylborate salts. Attempts to obtain a solid solution of (**3AP-me**)_x⁺(**3AP-et**)_(1-x)⁺**I** type have, instead, been unsuccessful. All three isostructural solids (**3AP-me⁺B(Ph)₄⁻**, **3AP-et⁺B(Ph)₄⁻** and (**3AP-me**)_{0.6}⁺(**3AP-et**)_{0.4}⁺**B(Ph)₄⁻**) are photochromic. The study of kinetics (bi-exponential decay) of thermal fading reveals that **3AP-me⁺B(Ph)₄⁻** undergoes the slowest process ($t_1 = 78.5 \pm 1.9$ min, $t_2 = 470.4 \pm 6.9$ min) while **3AP-et⁺B(Ph)₄⁻** is of about 1.6 times faster ($t_1 = 45.3 \pm 0.6$ min, $t_2 = 476.4 \pm 3.2$ min). Remarkably, the (**3AP-me**)_{0.6}⁺(**3AP-et**)_{0.4}⁺**B(Ph)₄⁻** solid solution is also photochromic and shows a conversion time ($t_1 = 55.0 \pm 1.7$ min, $t_2 = 471.2 \pm 7.8$ min) which is intermediate between the one of **3AP-me⁺B(Ph)₄⁻** and **3AP-et⁺B(Ph)₄⁻**. This trend is consistent with structure data and shows that the ethyl group acts by slightly opening the tetra-aryl boxes of the structure and by slightly increasing distances between dye ions, two favorable factors for photoisomerization. It is noteworthy that the thermal decay of (**3AP-me**)_{0.6}⁺(**3AP-et**)_{0.4}⁺**B(Ph)₄⁻** is closer to the one of **3AP-et⁺B(Ph)₄⁻** although this latter is the minor component of the solid solution. Overlay of the three tetraphenylborate crystal structures reveals that the solid solution is structurally closer to **3AP-et⁺B(Ph)₄⁻** than **3AP-me⁺B(Ph)₄⁻** even though the former is the minor constituent (40 %). This result suggests that it is not the major component that determines the photochromic behavior but the combined effect that both components (in a given composition) have on the crystal structure.

3. Conclusions

We have shown herein a crystal engineering approach applied to photochromic materials. Isostructural solids and their solid solutions have been obtained by using bulky templating anions (*i.e.* tetraphenylborates) or by replacement of the ditopic 180° tectons (dicarboxylic acid or diiodoperfluoroalkanes). Cocrystallization has been discovered to be a suitable approach to modify or unlock photochromic properties in crystalline *N*-salicylideneaniline materials which can be used complementary/alternatively to the chemical modification of the dyes. In our hands, we observed how embedding a dye in different crystalline networks affects both its photoresponsiveness (photochromic solids and non-photochromic solids) as well as the retention of the photochromic coloration [28].

The single-step mechanochemical synthesis of cocrystals allowing for short reaction times, along with the low cost of the reactants and limited use of solvents represent an added value to this approach.

Indeed, the way along the discovery of structure-property relationships is still complex and will require extensive yet focused experiments on isostructural cocrystals and solid solutions to be refined and extended (hopefully) to the whole family of *N*-salicylideneaniline solids. This aspect represents the main future perspective of this work.

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