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Gabriel M. Mercier<sup>†</sup>, Koen Robeyns <sup>†</sup>, Tom Leyssens <sup>†</sup>\*

*†* Institute of Condensed Matter and Nanosciences, Université catholique de Louvain, 1348 Louvain-la-Neuve, Belgium.

\* Corresponding author: tom.leyssens@uclouvain.be.

#### Abstract

In this work photochromic properties of N-Salicylideneanilines were modified using a crystal engineering approach. Co-crystallization allowed to modify the structural arrangement and electronic properties of the target compounds altering its photochromic behavior without having to change the nature of the molecule. A co-crystal of N-Salicylideneaniline and citraconic acid characterized by a zwitterionic anil character and showing inverted photochromic behavior when compared to the parent anil is reported here for the first time.



ORTEP representation of the crystal structure of co-crystal between anil N-Salicylidenaniline and citraconic acid co-former. Dashed blue line represent the  $D_2^2(4)$  synthon with two hydrogen atoms shared between the three electronegative atoms. Right: 2-d scheme of the structure showing the zwitterionic character of anil moiety.

\*Corresponding author:

Tom Leyssens Institute of Condensed Matter and Nanosciences Molecules, Solids and Reactivity Université Catholique de Louvain Place Louis Pasteur 1, bte L4.01.03 B-1348 Louvain-La-Neuve Tel: +32 10 47 2811 Fax: +32 10 47 27 07 tom.leyssens@uclouvain.be http://www.uclouvain.be/leyssens-group

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*†* Institute of Condensed Matter and Nanosciences, Université catholique de Louvain, 1348Louvain-la-Neuve, Belgium

\* Corresponding author: tom.leyssens@uclouvain.be

#### Keywords

N-Salicylideneaniline, photochromism, crystal engineering, co-crystal.

#### Abstract

In this work photochromic properties of N-Salicylideneanilines were modified using a crystal engineering approach. Co-crystallization allowed to modify the structural arrangement and electronic properties of the target compounds altering its photochromic behavior without having to change the nature of the molecule. A co-crystal of N-Salicylideneaniline and citraconic acid characterized by a zwitterionic anil character and showing inverted photochromic behavior when compared to the parent anil is reported here for the first time.

#### 

#### Introduction

Within the race to novel technologies, chromotropic materials have gained an increasing amount of attention over the last few decades, from industrial as well as academic point of view [1]. Photochromism is likely the most sought chromotropic property, and is defined as a light induced reversible color change of a material. Most often photochromism is associated to a compound, which can occur in two specific forms absorbing at different wavelengths [2].

Among photochromic materials, N-Salicylideneaniline (anils) derivatives have been widely studied since 1939 [3] as they present multiple advantages: they are relatively straightforward to synthesize [4,5], easy to handle and use in the solid state, and resistant to fatigue [6,7,8]. N-Salicylideneanilines belong to the group of Schiff bases as they contain an azomethine (imine) bond [9]. The ortho-hydroxyl (phenol) group can undergo a keto-enol equilibrium through a temperature induced proton transfer to the nitrogen of the azomethine bond [4,10-12] (Figure 1). At room temperature in general both the enol and *cis*-keto forms are present in equilibrium. In some cases, upon UV-visible irradiation, both undergo transition to a third form, the *trans*-keto form [4-12] as presented in Figure 1.



Figure 1: Photo and thermo-induced transitions in N-Salicylideneaniline [13].

The enol form (usually the most stable form) is usually colorless whereas the *cis*-keto form, which becomes more populated at high temperature, exhibits more often a deep yellow to orange coloration. Finally, the *trans*-keto form obtained after light irradiation is usually deep red-colored [3,4]. As mentioned, color changes can either be thermally or photo-induced, allowing to classify anil compounds as thermochromic and/or photochromic. Figure 2 shows the overall mechanisms believed to occur upon photo-irradiation [6,14-16]. In the most simple scheme, excitation of the enol form, will lead to an exited enol state, which either returns to the ground state by fluorescence, or which undergoes non-radiative transition to an exited *cis*-keto state. This latter can undergo a radiative relaxation to the ground *cis*-keto state, or undergo a non-radiative transition to an excited *trans*-keto state. Non-radiative relaxation of this latter is believed to lead to the red-colored ground state *trans*-keto species. Recent theoretical and ultra-fast laser spectroscopy studies have shown this scheme to be over simplified, with a more complex situation involving multiple transient species being more likely [17,18].

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Figure 2: Simplified scheme of transition pathways for anils upon light irradiation.

From a structural point of view, photochromic anils usually present a non-planar shape with a dihedral angle between aromatic rings  $\varphi > 25^{\circ}$  [12,16,19,20]. When the molecule is planar the anil tends to be only thermochromic. Recent work, however, suggest that planarity or non-planarity of the anil molecules is not the determining factor for thermochromic or photochromic behavior of those compounds [21]. The thermo and/or photochromic character of the anil strongly depends on the overall structural environment, explaining why different polymorphs of the same compound can exhibit different thermo/photochromic properties [4].

Although sought for, only a limited number of anils show photochromism at the solid state. In general, identification of novel photochromic anils focuses on the synthesis of new compounds by inserting or combining different functional groups. Alternatively, the photochromic compound can be inserted in a different environment such as polymers and rigid glasses [19] or porous materials [22] and zeolite [23]. In a final approach, a crystal engineering approach, the crystal environment of the compound can be impacted. By adding a metal component, metal organic frameworks (MOFs) can be obtained [13,24]. In a recent contribution, a novel

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methodology was used, consisting in co-crystallizing the molecule of interest with another organic molecule. This approach allows combining properties of different materials rendering them for instance more stable or less reactive to external factors. More specifically, co-crystallization allows the creation of novel crystalline forms, even for those compounds for which no salts or solvates can be formed [25,26].

In the case of N-Salicylideneanilines, co-crystallization could allow to increase the space available in the crystal structure required for the "pedal motion" involved in the photochromic mechanism [20]. Doing so non-photochromic materials have been shown to be transformable into photochromic ones [27]. In their contribution, Johmoto *et al.* studied acid-base co-crystallization [27], with a proton transfer occurring between the co-former and the anil of interest, hereby obtaining two charged species. Another recent research succeeded in obtaining a photochromic co-crystal coming from a non-photochromic anil [28]. Hutchins *et al.* used a phenolic derivative which was hydrogen bonded with 4,4-Bipyridin [28]. We used a similar approach but aimed not only to avoid acid-base co-crystallization, but also to impact the photochromically active site directly by changing its hydrogen bonding pattern. To do so, we focused on two model compounds (see experimental section) that do not contain any basic or acidic group other than the ones at the photochromically active site.

By allowing hydrogen bonding to the photochromic site of the anil, the goal of this study was to directly impact the photochromic behavior of these reference compounds.

#### **Experimental Section**

#### **Starting Materials.**

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Carboxylic acids used as co-formers, solvents and starting materials for synthesis were all purchased and used as such. Product codes are given in the brackets. From Accros Organic: 1hvdroxv-2-naphtoic acid (149231000); 2,5-dihydroxybenzoic acid (165200500): 4hvdroxvbenzoic acid (120995000); Acetylsalicylic acid (158185000); Citric acid (110450010); Fumaric acid (119750010); Maleic acid (125230010); Mandelic acid R (101691137); Oxalic acid (186432500); Succinic acid (158745000); Tartaric acid D (137871000); 4-fluoro-aniline (119290250). Sigma Aldrich: 2,3-dihydroxybenzoic From acid (206-135-5); 2,4dihvdroxvbenzoic acid (101527441); 3,4-dihydroxybenzoic acid (100986520): 3.5dihydroxybenzoic acid (202-730-7); Salicylaldehyde (101669521). From Alfa Aesar: 2,2dimethylsuccinic acid (209-899-6). From U.C.B. s.a.: Salicylic acid (4388); Aniline (1163-4944). From Janssen Chimica: Acetic acid (14.893.52). From TCI: Citraconic acid (207-858-7). From VWR Chemicals: Acetonitrile (200-835-2); Diethyl ether (200-467-2); Ethanol (200-578-6); Ethyl acetate (205-500-4). From Fisher Chemicals: Acetone (200-662-2).

**Synthesis.** Compound **A** (N-Salicylideneaniline) was prepared by hand grinding (ten minutes) of salicylaldehyde (10 mmol) with aniline (10 mmol) in presence of a catalytic amount of acetic acid (0.2 mmol) and dried for 48 h at 45 °C and used as such (yield: 98%, purity: 99%)<sup>1</sup>. Compound **B** (4-fluoro-Salicylideneaniline) was prepared by grinding (5 minutes) of salicylaldehyde (10 mmol) with 4-fluoro-aniline (10 mmol) and dried for 48 h at 45°C and used as such (yield: 98%, purity: 99%).

**Mechanochemical co-crystal screen.** The experimental co-crystal screening procedure was performed as follows: in a first stage, solvent-drop grinding (10 µl of acetonitrile) was performed

<sup>&</sup>lt;sup>1</sup> The photochromically active polymorph of this compound was obtained using this procedure.

using an equimolar (10<sup>-3</sup> mol) mixture of starting materials. Samples were ground in a RETSCH Mixer Mill MM 400 for 90 min with a beating frequency of 30 Hz. The resulting powders were characterized using X-ray Powder Diffraction. Upon co-crystal identification, attempts were made to obtain a single crystal of suitable size and quality for single crystal X-ray diffraction measurement. As a chemical reaction can occur during solvent-drop grinding, <sup>1</sup>H-NMR was used to eliminate samples were degradation/reaction occurred.

**Single Crystal formation attempts.** Single crystals of **A-C10** were grown by MeCN vapor diffusion in a furnace at 45 °C for 1 week after grinding. Standard slow solvent evaporation at room temperature was tried for each positive hit with acetone, acetonitrile, diethylether, ethanol, ethylacetate but did not yield successful results. MeCN vapor diffusion at 45 °C was tested for **B** co-crystals but did not yield single crystals suitable for analysis.

**X-ray Powder Diffraction (XRPD).** X-ray diffraction measurements were performed on a Siemens D5000 diffractometer equipped with a Cu X-ray source operating at 40 kV and 40 mA and a secondary monochromator allowing to select the K $\alpha$  radiation of Cu ( $\lambda$ =1.5418 Å). A 20 scanning range from 2° to 50° at a scan rate of 0.6° min<sup>-1</sup> was applied. Simulated patterns of the known starting compounds were calculated from their single crystal structures with Mercury 3.1 and plotted with WinPLOTR (version: September 2015). For each reported mixture diffraction pattern (in blue) is superimposed onto simulated patterns of its components (in red for the corresponding anil and green for the co-former). All data are normalized at 100 for the highest peak. We assume formation of new phases when at least 2 new peaks appear and at least 2 reference peaks are missing.

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**Single crystal X-Ray diffraction.** The structure of **A-C10** was solved from single-crystal synchrotron X-ray diffraction data, which were collected on the Swiss-Norwegian Beam Line BM01A at the European Synchrotron Radiation Facility (ESRF) (Grenoble, France), using a PILATUS 2M hybrid pixel detector at a wavelength of 0.82103 Å. Prior to the data collection the sample was flash-cooled to 100(2) K using an Oxford Cryostream 700 system. The data were converted with the SNBL toolbox software [29] for integration with the CrysAlisPro software [30].

Structure was integrated with the CrysalisPro software and the implemented multi-scan absorption correction procedure was applied. The structure was solved by direct methods, SHELXS-97 [30] and was refined by full-matrix least squares on  $|F|^2$  using SHELXL-2014 [31] Non-hydrogen atoms were refined anisotropically and hydrogen atoms were either placed on calculated positions in riding mode with temperature factors fixed at 1.2 times U<sub>eq</sub> of the parent atoms and 1.5 times U<sub>eq</sub> for methyl groups, or located in the Fourier difference maps when involved in H-bonds.

**NMR analysis.** <sup>1</sup>H NMR spectra were recorded on Bruker-300 MHz. <sup>1</sup>H NMR chemical shifts are reported relative to CD<sub>3</sub>CN (1.94 ppm).

Compound A:  $\delta$  (ppm): 13.26 (s, 1H); 8.82 (s, 1H); 7.56-7.31 (m, 7H); 7.03-6.98 (dt, 2H, J<sub>1</sub>=7.8Hz, J<sub>2</sub>=1.2Hz).

Diffuse Reflectance Spectroscopy measurements. DRS spectra were obtained on a Varian Cary 5E spectrometer using PTFE as a reference. Spectra were measured on pure solid. Diffuse Reflectance spectra were normalized (value at  $\lambda$ =395 nm set at 1). Signal assignment was supported by reported band range for N-salicylideneaniline derivatives [15]. Light irradiations

were carried out with a LOT-ORIEL 200 W high-pressure mercury arc lamp combined with selected band pass filter. Kubelka-Munk spectra were taken before and after irradiation (irradiation time is described in the text).

CSD statiscal analysis. Reference bond lengths of interest were obtained by statistical analysis of the data available in the CSD: we searched all reported organic structure (with R factor  $\leq 0.05$ ) containing at least two bonds corresponding to critical bonds of the two forms (enol and keto: Figure 3) studied. A search was performed in order to specifically describe bond lengths in the case of anil derivatives and to be more accurate than average values already reported by Frank H. Allen et al. [32]. Reference structures used to approximate enol-imine and conjugated-ketone form are presented in Figure 4. Doing so, reference bond lengths were obtained (noted as bond 2, 3, 4 and 5 in Figure 3) in various environments regardless of temperature. Results of average bond lengths are reported in table 1 with standard deviation and number of CSD hits. As shown by this table, there is a clear cut difference between enol-imine and ketone bond lengths, with a slightly more narrow distribution in the case of the enol-imine form. Bond lengths obtained for Conjugated Ketone 1 are different from bond lengths of Conjugated Ketone 2 and Amine 1 (Figure 4). We considered Conjugated Ketone 1 already partially displaced toward Enol-Imine 1 and furthermore there are only a few hits (126) meaning results on this form are less accurate. We therefore used both forms, Conjugated-Ketone 2 and Amine 1 (for bond 5), to better describe the conjugated ketone character. To describe the enolimine character we selected bond length values of Enol-Imine 1 as it is the closest to the anil A structure and they are in good agreement with the results observed in Phenol 1 and Imine 1.



Figure 3: Common structure of all anils considered. Important bonds are noted from 1 to 6.



Figure 4: Structures with bond lengths researched through CSD to approach enol-imine form (Enol-Imine 1, Phenol 1, Imine 1) and ketone form (Conjugated Ketone 1, 2 and Amine 1) bond lengths. Non described bonds/atoms were not defined during the search.

Table 1: bond lengths and standard deviations for each pattern researched with its number of hits in the CSD

Pattern	Bond 2, $\sigma$ (Å)	Bond 3, $\sigma$ (Å)	Bond 4, $\sigma$ (Å)	Bond 5, $\sigma$ (Å)
Enol-Imine 1	1 344 0 022	1 406 0 017	1 450 0 021	1 286 0 021
Hits = 2652	1.344, 0.022	1.400, 0.017	1.430, 0.021	1.280, 0.021
Phenol 1	1 364 0 020	1 200 0 017	1 400 0 210	/
Hits = 10000	1.304, 0.020	1.399, 0.017	1.499, 0.310	/
Imine 1	/	/	1.443, 0.023	1.283, 0.021

Hits = 10000				
Conj. Ketone 1 Hits = 126	1.291, 0.015	1.431, 0.013	1.414, 0.014	1.303, 0.015
Conj. Ketone 2 Hits = 881	1.249, 0.034	1.463,0.032	1.375, 0.040	/
Amine 1 Hits = 10000	/	/	1.356, 0.026	1.358, 0.027

#### Results

**Co-crystal screening.** Two very basic, well-described model anil derivatives were chosen as well as 18 common carboxylic acid co-former candidates (Figure 5). A first anil is N-Salicylideneaniline (**A**, reported with crystal structures REFCOD SALCAN to SALCAN04 in the CSD [34,35,36]) known to show strong photochromism; the second one is 4-fluoro-N-Salicylideneaniline (**B**, reported as CAVQAR in the CSD [37]) known to show only thermochromism in the solid-state. Both compounds have been extensively studied [4,38,39].With the principal functionality available on classical anils being the hydroxyl function, carboxylic acids have been tested in order to form a hydrogen bridge as this type of hydrogen bonding is strong and regularly encountered in co-crystals [25,26]. A typical synthon occurring between an alcohol and carboxylic acid group is the synthon  $D_2^2(4)$  (according to Etter Nomenclature [33]) shown in Figure 6. Another common synthon is  $R_2^2(6)$  (which would extend to  $R_2^2(10)$  in the case of anils) but wasn't observed here.





Figure 5: Compounds studied (IUPAC name in Table 1).



Figure 6: Expected  $D_2^2(4)$  supramolecular interaction [33] between N-Salicylideneaniline and a carboxylic acid (R1 stands for alkyl group).

Co-crystals were identified using a mechanochemical approach (see experimental details). All possible combinations of 1:1 molar ratio between the co-formers and the anils were tested. A change in XRPD pattern (Figure 7) is expected to be related to either a change in polymorphic nature of one of the compounds, degradation (=reaction) or co-crystal formation. When degradation occurred (usually dissociation of anil in amine and aldehyde), the result was discarded.

Table 2: XRPD and H-NMR comparison results between ground compounds and reference. X implies a perfect superposition of XRPD data, XX implies reaction/degradation of products and v means a structural change without degradation of starting materials (co-crystal or polymorph)<sup>2</sup>.

<sup>&</sup>lt;sup>2</sup> Screening was limited to grinding methods, so the possibility exists that some co-crystals might have been overlooked.

	Salicylideneaniline)	Salicylideneaniline)
C1 (1-hydroxy-2-naphtoic acid)	X	X
C2 (2,2-dimethylsuccinic acid)	X	X
C3 (2,3-dihydroxybenzoic acid)	X	X
C4 (2,4-dihydroxybenzoic acid)	XX	V
C5 (2,5-dihydroxybenzoic acid)	X	X
C6 (3,4-dihydroxybenzoic acid)	XX	V
C7 (3,5-dihydroxybenzoic acid)	X	X
C8 (4 hydroxybenzoic acid)	X	X
C9 (acetylsalicylic acid)	X	X
C10 (citraconic acid)	V	XX
C11 (citric acid)	X	X
C12 (fumaric acid)	X	X
C13 (maleic acid)	XX	V
C14 (mandelic acid R)	X	X
C15 (oxalic acid)	XX	V
C16 (salicylic acid)	X	X
C17 (succinic acid)	X	X
C18 (tartaric acid D)	X	X

As shown in table 2, a positive hit was obtained when working with N-Salicylideneaniline (entry **A**) and citraconic acid (Entry **C10**). Figure 7 shows that the XRPD patterns of the ground material is different from any of the known polymorphic forms of **A**, as well as from the XRPD pattern of citraconic acid. NMR analysis confirmed no degradation occurred, leaving co-crystal formation as the likely outcome, as confirmed by single crystal analysis. This result shows how co-crystallization can effectively occur even when a limited amount of functional groups is

present on the target compound. For compound **B**, a total of 4 positive results were identified, using 2,4-dihydroxybenzoic acid, 3,4-dihydroxybenzoic acid, maleic acid, or oxalic acid as a co-former.

#### **Co-crystals of 4-fluoro-N-Salicylideneaniline**

Although 4 novel co-crystals of 4-fluoro-N-Salicylideneaniline are suspected based on the data in Table 2, no single crystals of these have been obtained so far. One reason could be the sensitivity of anil to hydrolysis catalyzed by acids (co-formers). As solvent used are all slightly hygroscopic process like slow evaporation could lead to the degradation of anil and recombination of amine with the co-former to make a salt. Such a process should then be performed under water-free atmosphere to avoid this.

Furthermore, DRS analyses on the ground co-crystal powders did not show significant differences with respect to the reference compound, nor did irradiation at different wavelengths for prolonged periods. These co-crystals, are thus, like the reference parent compound, expected to be thermochromic, with no significant difference between the keto-enol equilibrium found in the parent compound as compared to that within the co-crystals.

#### **Co-Crystal between N-Salicylideneaniline (A) and citraconic acid (C10)**



Figure 7: XRPD pattern of A-C10 powder versus references: the ground mixture (blue spectra) is clearly different from all references of A (four polymorphs) and C10 (black).

A single crystal was successfully grown and structural analysis shows both compounds to cocrystallize in the P2<sub>1</sub>/c space group (structural details are presented in table 3), with the expected  $D_2^2(4)$  synthon (which is a combination at the binary level of S(6) and D patterns) forming between the carboxylic acid group and the phenolate function (Figure 8). To the best of our knowledge, we are the first to report on a direct impact of co-crystallization on the functional groups that are involved in the thermochromic and photochromic nature of the anils by impacting the hydrogen bonding pattern. The co-crystal is not a salt as the carboxylic proton was clearly visible in the density maps and the carbon-oxygen bond lengths in the carboxylic group are significantly different, identifying them as a C=O double bond (1.223(2) Å) and a single C-O bond (1.298(2) Å), opposed to the salt form where equal bond distances are expected.



Figure 8 left: ORTEP projection of crystal structure of co-crystal between anil A and co-former C10. Dashed blue line represent the  $D_2^2(4)$  synthon with two hydrogen atoms shared between the three electronegative atoms. Right: schematic representation of the structure showing the zwitterionic character of anil moiety.

To study the impact of co-crystallization on the keto-enol equilibrium, we compare the main bond lengths involved in the **A-C10** co-crystal with those of the free anil (**A**), as well as with a statistical analysis as specified in the experimental details of similar derivatives available in the CSD (Figure 5). Results are given in table 3.

Table 3: Expected values with their standards deviations<sup>3</sup> for bond lengths 2 to 5 of Enol-Imine and Keto-form (regardless to the temperature) based on CSD statistical analysis and comparison with **A-C10** co-crystal (bond lengths measured and their standard deviations) and **A** (SALCAN01).

	Bond 2, $\sigma$ (Å)	Bond 3, $\sigma$ (Å)	Bond 4, $\sigma$ (Å)	Bond 5, $\sigma$ (Å)
Enol-Imine	1.344, 0.022	1.406, 0.017	1.45, 0.021	1.286, 0.021
Conj. Ketone	1.249, 0.034	1.463, 0.032	1.375, 0.04	1.358, 0.027
Α	1.352, 0.003	1.419, 0.003	1.455, 0.003	1.280, 0.003

<sup>&</sup>lt;sup>3</sup> The errors of the CSD search are one order of magnitude higher compared to the error on a single structure, as they are derived from an ensemble of structure.

(120K)				
A-C10 (100K)	1.316, 0.002	1.424, 0.003	1.407, 0.003	1.309, 0.002

Table 3 clearly shows **A** to exist in an enol/*cis*-keto equilibrium which is strongly displaced towards the enol form. An important structural variation is observed when **A** co-crystallizes with **C10** (crystal data and structure refinement are given in table 4), as bond lengths indicate the equilibrium is shifted in favor of the keto form. As data were collected at 120 K for **A** and 100 K for **A**-**C10** we expect only a neglectible temperature effect on the bond lengths. Bonds 2 and 4 are shorter within the co-crystal, whereas the length of bond 5 increases.

Even though these bond lengths indicate a displacement towards the keto form, at this stage, the use of the term 'keto'-form does seem inappropriate. The 'keto'-form can actually be represented under two resonance structures, either using a charge neutral keto representation or through a zwitterionic representation. This latter seems much more pertinent in the current case: the hydrogen of the enol is clearly transferred to the nitrogen atom as shown by the Xray density maps. Even though, this clear transfer of the hydrogen atom, bond 2 (1.316 Å) is intermediate between a pure C=O double bond (1.344 Å) and a C-OH single bond (1.249 Å) as shown in table 3. Furthermore the C-C bond 3 (1.424 Å) is almost not affected whereas a clear increase up to 1.46 Å would be observed (according to table 3) if one would expect a more keto character. Finally, the C-N bond 5 length (1.309 Å) is closer to that of a C-N (1.286 Å) single bond, than that of a C=N double bond (1.358 Å). These combined observations suggest to consider the 'keto'-form rather as a 'zwitterionic form' in this case, and the keto-enol equilibrium should rather be presented as the "enol-zwitterionic" equilibrium shown in Figure 9. This zwitterionic form was already reported for anils inserted into zeolites however in that case no photochromism was observed [23].

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The displacement from the enol form towards the zwitterionic form upon co-crystallization is likely induced by the hydrogen donating effect of the co-former (synthon  $D_2^2(4)$ ). The directionalized interaction of the co-former hydrogen towards the alcohol function, could allow for a better hydrogen transfer of this latter to the imine function, and stabilizes the negative charge on the oxygen atom, create by doing so. This displacement also induces a change in optical properties as illustrated in Figure 10 showing the color change between the original compound and the co-crystals, at room temperature and at 50 °C. At room temperature co-crystal **A-C10** has a more intense yellow color compared to the reference **A** which can be explained by an increased amount of *zwitterionic* form. When heated up to 50 °C anil **A** starts to melt and is characterized by a more intense brown color whereas **A-C10** remains solid, exhibiting a more intense yellow color (melting occurs at 80 °C). When cooled to -80 °C anil **A** turns to pale yellow whereas no change is observed for **A-C10**.



Figure 9: New equilibrium pattern based on structural analysis



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Figure 10: Comparison between **A** and **A-C10** at room temperature (left) and upon heating at 50 °C (right).

To study the effect of co-crystallization on the photochromic properties of the parent anil, Kubelka-Munk spectra of the anil **A** and co-crystal **A-C10** were measured under standard conditions (room temperature and pressure) as shown in Figure 11. Data are normalized to 1 for the peak at 395 nm. Spectra of the two compounds clearly differ. No such difference is found when comparing the spectra of reference **A** (polymorph alpha 2) with that of a physical mixture (see supporting information) between **A** and **C10**. Both the parent anil **A** as well as the co-crystal **A-C10** show a strong absorption band at 375 nm, attributed to the absorption of the enol form [4]. The strongest difference for the co-crystal comes from the very strong absorption band centered on 488 nm which is typically attributed to the keto form (or the zwitterionic form in our case) of the product. This form appears to be strongly populated which is in line with the structural analysis, pointing towards an increased amount of zwitterionic form in the equilibrium. The weak absorption at 450 nm clearly shows why the parent anil, was labeled nonthermochromic.

When zooming into the 525-700 nm range both forms present a small shoulder centered on 600nm, attributed to the *trans*-keto form.



Figure 11: Kubelka-Munk spectra of anil A and co-crystal A-C10 at room temperature.

The photochromic effect of both forms was studied by comparing variation of the absorption spectra upon prolonged irradiation (30 minutes to 1 hour). Irradiation of **A** at 365 nm leads to an increase in cis-keto and trans-keto form, whereas an irradiation at 436 nm leads to a depopulation of the already small amount of *cis*-keto form in favor of the *trans*-keto form, in agreement with the earlier work by Fujiwara *et al.* [15]. However in the case of **A-C10** a surprisingly different behavior is observed. Irradiation at 365 nm, leads to both a strong depletion of the *cis*-zwitterionic form (centered at 450 nm) and *trans*-keto (600 nm) forms relatively to the enol form (centered at 380 nm). Subsequent irradiation at 546 nm (+/- 20 minutes) restores the original situation contrary to what is observed for the parent anil (Figure 12). Another difference observed is irradiation at 436 nm which has no observable effect on the zwitterion/enol equilibrium in this case. These results might indicate that the *trans*-keto form is also impacted by co-crystallization, and might also show a strong zwitterionic character, although this remains to be proven.

After prolonged irradiation, the initial equilibrium can be restored thermally (without irradiation), but at room temperature, one requires about 8 hours to return to original levels.



Figure 12: Kubelka-Munk spectra of **A-C10** after irradiation at 365 nm (blue) for 20 minutes and reference (red).

From the results above, it is clear that co-crystallization strongly affects the photochromic behavior of anils, likely due to the impact on the hydrogen bonding pattern which is affected. To fully understand the underlying mechanism, one would have to review the scheme as presented in Figure 2. A future full investigation using e.g. femtosecond spectroscopy could be interesting to elucidate this behavior.

Our results clearly show that tackling the structure of anils through co-crystallization and more specifically through alteration of the hydrogen bonding pattern directly involved in the keto (zwitterion)/enol equilibrium, offers new possibilities for varying the photochromic behavior of anils, and might lead to promising results on future candidates.

Table 4: Crystal	data and structur	re refinement for	co-crystal A-C10
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	Co-crystal A-C10
Empirical formula	$C_{18}H_{17}NO_5$
М	327.32
<i>T</i> [K] Crystal system	100(2) Monoclinic
Space group	$P2_{1}/c$ (no.14)
<i>a</i> [Å]	10.7434(4)
<i>b</i> [Å]	8.3025(2)
<i>c</i> [Å]	19.0548(7)
β [°]	113.813(3)
V [ų]	1554.94(10)
Z	4
$ ho_{calcd}  [\mathrm{Mgm}^{-3}]$	1.398
F(000)	688
$\mu \ [\mathrm{mm}^{-1}]$	0.142
Crystal size [mm]	0.15x0.10x0.10
$\theta_{max}$ [°]	31.2129
Reflection collected/unique	7945/2471
R <sub>int</sub>	0.0393
$R_1 [I \ge 2\sigma(I)]$	0.0401
$wR_2$	0.0926

Largest diff. Peak/hole [e Å<sup>-3</sup>] 0.152/-0.223

#### Conclusion

We have crystallized a co-crystal of N-Salicylideneaniline and Citraconic acid which shows new and unexpected photochromic behavior. A careful structural analysis reveals cocrystallization affected bond lengths and electronic structure of the photochromic center in such a manner to suggest viewing the classical keto-enol equilibrium rather as an enol-zwitterionic equilibrium. This effect is due to the co-formers we chose for synthon creation in order to build the co-crystal. By altering the hydrogen bonding pattern of the alcohol functionality, we are able to impact the photochromic mechanism directly. To do so, we added a hydrogen donor to the alcohol group, creating a push-and-pull effect on the hydrogen involved in the enol-zwitterionic equilibrium. For the parent N-Salicylideneaniline, co-crystallization not only led to a substantial change in the classical view of the keto/enol equilibrium, which is in our case described as an enol-zwitterionic equilibrium, but furthermore to some unexpected photochromic behavior, which up to now remains unexplained by the classical scheme. These findings open new ways to fine-tune photochromism of N-Salicylideneaniline derivatives: one can not only increase the space available in the crystal structure through co-crystallization (allowing cis-trans isomerization), but one can also directly impact the electronic behavior of the centers involved in the photochromic and thermochromic behavior.

**Supporting Information**. Structures described in this contribution have been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition numbers CCDC 1448718

for A-C10. Supporting information also contains TGA, DSC, XRPD and DRS patterns of discussed compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

#### **Corresponding Author**

\* Email: tom.leyssens@uclouvain.be.

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#### **Crystal Growth & Design**

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## For Table of Contents Use Only

## Altering the photochromic properties of N-Salicylideneanilines using a crystal engineering approach

Gabriel M. Mercier, Koen Robeyns, Tom Leyssens.



A new co-crystal of N-Salicylideneaniline with citraconic acid was reported and studied through Diffuse Reflectance Spectroscopy and X-Ray Diffraction. Co-crystallization strongly altered the electronic structure as well as photochromic properties.