Periodic DFT study of the effects of co-crystallization on a N-salicylideneaniline molecular switch.

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Abstract

This work aims at better understanding the complex effects of co-crystallization on a single salicylideneaniline molecular switch, (E)-2-methoxy-6-(pyridine-3-yliminomethyl)phenol (PYV3), which can tautomerize between an enol and a keto form. A combination of periodic boundary conditions DFT and molecular wavefunction calculations has been adopted for examining a selection of PYV3 co-crystals, presenting hydrogen bonds (H-bonds) or halogen bonds (X-bonds), for which X-ray diffraction data are available. Three aspects are targeted: i) the energy (H-bond strength, enol to keto relative energy, and geometry relaxation energies), ii) the geometrical structure (PYV3 to co-crystal and enol to keto geometrical variations), and iii) the electron distribution (PYV3 to co-crystal and enol to keto Mulliken charge variations). These allow i) explaining the preference for forming H-bonds with the nitrogen of the pyridine of PYV3 with respect to the oxygens and the importance of the crystal field, ii) distinguishing the peculiar behavior of the SulfonylDiPhenol (SDP) coformer, which stabilizes the keto form of PYV3, iii) describing the relative stabilization of the enol form upon co-crystallization (with the exception of SDP) and therefore iv) substantiating the co-crystallization-induced reduction of thermochromism observed for several PYV3 co-crystals.

1 Introduction

In order to tune solid state properties of organic and inorganic compounds, many methods have been developped, such as doping[1, 2, 3, 4] or substitution[5, 6, 7, 8, 9]. Among them, co-crystallization, *i.e.* the crystallization of at least two different compounds together, is studied in both medicinal [10, 11, 12, 13] and materials science [14, 15, 16, 17, 18, 19, 20]. For the latter, it has been used to optimize optical properties such as absorption[16], fluorescence[19], phosphorescence[14, 20], and second harmonic generation [15, 17, 18]. Although any non-bonded interaction can be used to generate co-crystals (e.g. π - π stacking, Coulombic interactions, etc), directional interactions —hydrogen and halogen bonds (denoted Hbonds and X-bonds, respectively)— allow for a better control over the interactions found in the resulting co-crystals. Previously, some of us have shown experimentally that co-crystallization affects the thermo- and photochromic behaviors of N-salicylideneanilines (or anils), depending on the coformer (the secondary compound) [21, 22, 23]. Anils are dynamical compounds, whose color changes when triggered by external stimuli [24, 25, 26]. They are able to switch between an enol (E) and a keto (K) form and each ought to be affected differently by the coformer. This work aims at evaluating and understanding the influence of the two classes of coformers, those forming H-bonds and those making X-bonds by employing quantum chemistry methods and by focusing on the relative energies, the geometries, and the Mulliken charges of a selected anil, (E)-2-methoxy-6-(pyridine-3-yliminomethyl)phenol (PYV3, see Scheme 1a). The H-bond coformers, succinic acid (SA), fumaric acid (FA), dihydroxylbiphenyl (DHBP), and sulfonyldiphenol (SDP), are shown Schemes 1b, c, d, and e, respectively. The X-bond coformers are 1,4-diiodo-octafluorobutane (I2but), 1,4-diiodotetrafluorobenzene (I2F4), and 1,3,5-triiodo-2,4,6-trifluorobenzene (I3F3), and are given in Schemes 1f, g, and h, respectively.



Scheme 1: Structures of the compound and coformers under investigation, (a) anil and its enol-keto equilibrium; coformers interacting by H-bonding (b)-(e) or X-bonding (f)-(h).

This paper is organized as follows. In the next Section, the computational details are described. Section 3 first analyzes the two H-bond interaction sites of PYV3. Then, the effect of co-crystallization on the energies is broken down, followed by its geometrical changes and the analysis of the Mulliken charges, before ending with the conclusions.

2 Methods and Computations

Full geometry optimizations (including of the unit cell parameters) were performed with the CRYSTAL14 package[27] using periodic boundary conditions (PBC) with

density functional theory (DFT). As we have shown in previous works (see Ref. 28 and 29), the PBEsol0 exchange-correlation functional (XCF) (based on PBEsol[30] with 25% of exact exchange) in combination with Pople's 6-31G(d,p) basis set (as taken from Basis Set Exchange[31, 32]) is an efficient method to reproduce the unit cell parameters and molecular geometry of salicylideneanilines as obtained by single crystal X-ray diffraction. This particular XCF does not require empirical dispersion corrections to perform well as it is tailored to crystals (see Ref. 29 for more details on that particular issue and 30 for the details on the conception of the XCF). Iodine atoms were described with the LANL2DZ effective core potential and basis set, as taken from Basis Set Exchange[31, 32]. The default convergence parameters were used with a shrinking factor of the irreducible Brillouin zone of 6 (yielding between 64 and 112 k-points of integration) and tolerance criteria for the exchange and correlation integrals (TOLINTEG keyword) of "8 8 8 8 16". More details on the CRYSTAL14 calculations are given in Ref. 28. These calculations provide the limit forms of the anil, as there are no dynamic aspects (such as disorder). Gas phase potential energy scans were generated and analyzed with the DRAWMOL suite[33] and performed at the MP2/aug-cc-pVDZ level of approximation using the GAUSSIAN16 package[34].

3 Results and discussion

The combination of PYV3 with the 7 selected coformers (see Scheme 1) has yielded 8 co-crystals, for which Figure 1 shows the main intermolecular interaction(s) between PYV3 and each coformer. The asymmetric units are composed of one molecule of PYV3 and one coformer, except I3F3. In the later case, it contains

two molecules of PYV3 and one molecule of coformer: one PYV3 interacts through both the N_2 and the O_1 and O_2 atoms (I3F3-O), while the second PYV3 interacts only through N_2 (I3F3-N) (see Scheme 2 for the atom numbering and Figure 1h for the representation of I3F3-N/-O). In all cases, the nitrogen of the pyridine moiety (N_2) interacts with the coformer either by H-bonding or by X-bonding. Fumaric acid yielded two polymorphic co-crystals, noted FA1 and FA2, the former being isostructural to the SA co-crystal. The second and last stand-out co-crystal is SDP as it interacts through both the N_2 nitrogen and the O_1 and O_2 oxygen atoms. Comparing the optimized structures with the single crystal X-ray diffraction (XRD) data (taken from the Cambridge Structural Database[35], CSD refcodes EDEQAG01 (PYV3), IRALUK (PYV3·FA 1), IRALUK01 (PYV3·FA 2), IRAMEV (PYV3·SA), JOBROK (PYV3·DHBP), JOBRUQ (PYV3·SDP), NIN-MAB (PYV3·I2but), SEDFIT (PYV3·I2F4), and NINPIM (PYV3·I3F3)), the root mean square deviation averaged over all crystals amounts to 0.398 Å (2.7%) for the unit cell lengths, 1.90° (2.0%) for the unit cell angles, and 29.0Å³ (1.9%) for the unit cell volumes. The averaged RMSD on the bond lengths that do not contain hydrogen atom amounts to 0.013 Å. Overall, the optimized structures are in good agreement with experiment and the performance of the method is consistent with our recent investigations [28, 29].



Scheme 2: Atom numbering of PYV3.



Figure 1: Representation of the PYV3-coformer synthons as extracted from the cocrystal structure optimized at the PBC/PBEsol0/6-31G(d,p)/I(LANL2DZ) level of approximation. The enol form was considered for all co-crystals. The corresponding references to the X-ray diffraction structures are also provided.

3.1 Interaction sites of PYV3

All coformers interact with the N₂ atom of PYV3 while only two interact with its oxygens. To elucidate the situation observed for H-bonding systems, a molecule of hydrofluoric acid, H-F (bond length sets to 0.917 Å), was used as a rigid probe to compare both interaction sites (Figure 2a). The geometry of PYV3 was kept fixed to the one obtained from its crystal optimization geometry. Figure 2b shows the N_2 ...HF scans for both the enol and keto forms while Figures 2c and 2d show the corresponding 2D scans for the oxygens, respectively. On the N_2 scans, both the enol and keto forms have their minimum at 1.74 Å. The stabilization energy for the enol amounts to $52 \,\mathrm{kJ}\,\mathrm{mol}^{-1}$ while for the keto form, it is slightly smaller, by $3 \,\mathrm{kJ}\,\mathrm{mol}^{-1}$. For both the enol and keto forms, the probe molecule interacts more strongly with the oxygen involved in the intramolecular H-bond, O_1 , than the one from the methoxy group, O_2 . Consequently, for the enol form, the minimum on the potential energy surface is characterized by a O_1 -H distance of 1.81Å, in comparison to 2.60 Å for O_2 -H. For the keto form, the first distance gets even smaller with a d_{O_1-H} value of 1.72 Å while $d_{O_2-H} = 2.63$ Å. Thus, for the keto, the HF probe gets closer to O_1 (by 0.09 Å) and further to O_2 (by 0.03 Å), and subsequently, its stabilization energy gets larger than for the enol, $-54 \,\mathrm{kJ \, mol^{-1}}$ $vs. -42 \,\mathrm{kJ \, mol^{-1}}$. Comparing both acceptor sites, for the enol form, the interaction with the probe is stronger with the nitrogen than with the oxygen pair, by $10 \,\mathrm{kJ \, mol^{-1}}$. By opposition, in the case of the keto, the H-bonding with the oxygens leads to more stable situations than with the nitrogen, by 15 kJ mol^{-1} .

The same conclusions can be drawn for the X-bond interactions (probed with CF_3I , see Figure S1 in the Supporting Informations): the enol form favors the interaction on N_2 with respect to the oxygens (by 5 kJ mol⁻¹) while it is the opposite for the keto (by 7 kJ mol⁻¹).



Figure 2: Potential energy scans for the PYV3[PYV3]···H–F complex using a H–F molecule as a probe, computed at MP2/aug-cc-pVDZ level of approximation. (a) sketch of the molecules and interactions with H–F for the N₂ (along the blue arrow) and O₁ and O₂ (along the red arrows); (b) N₂···HF potential energy scans, for the enol, the minimum is at $(1.74 \text{ Å}, -51.6 \text{ kJ mol}^{-1})$ while for the keto, at $(1.74 \text{ Å}, -49.0 \text{ kJ mol}^{-1})$; (c) O₁···HF and O₂···HF 2D potential energy scans for the enol form, minimum at $(1.81 \text{ Å}, 2.60 \text{ Å}, -41.6 \text{ kJ mol}^{-1})$ and (d) for the keto form, minimum at $(1.72 \text{ Å}, 2.63 \text{ Å}, -54.2 \text{ kJ mol}^{-1})$.

3.2 Relative energy of the enol and keto forms

The accurate determination of the correct enol/keto proportion remains an important challenge as shown by some of us in a study focusing on the evaluation of the enol/keto ratio in solution by combining TDDFT simulations of absorption spectra with experiment (Ref 38). Table 1 shows the enol to keto relative energies per asymmetric unit, $\Delta E_{\rm EK}^{\rm as.u.} = [E_{\rm K}^{\rm cell} - E_{\rm E}^{\rm cell}]/[$ number of as.u. per cell], for PYV3 and its co-crystals (as obtained after crystal geometry optimization). With the exception of PYV3·SDP, the enol crystals are more stable than the keto ones: $\Delta E_{\rm EK}^{\rm as.u.} >$ 0. Then, the switching process requires more energy for the co-crystals than for the PYV3 crystal (ignoring the kinetics): $\Delta E_{\rm EK}^{\rm as.u.}$ [co-crystals] > $\Delta E_{\rm EK}^{\rm as.u.}$ [PYV3], highlighting the role of the coformer to stabilize the enol form and/or destabilize the keto one. These results are in agreement with the experimental evidence that the thermochromism is reduced in FA1, FA2, and SA[21]. For SDP, the keto cocrystal is more stable than the enol one, by $15 \, \text{kJ} \, \text{mol}^{-1}$, in agreement with XRD data where the major observed form is the keto at both low $(105 \pm 2 \text{ K})$ and room $(293 \pm 2 \text{ K})$ temperatures [36]. $\Delta E_{\text{EK}}^{\text{as.u.}}$ of FA2 is smaller by a marginal amount, $0.5 \,\mathrm{kJ \, mol^{-1}}$, with respect to FA1. Another noticeable value is that of I3F3 with the largest $\Delta E_{\rm EK}^{\rm as.u.}$ (31.1 kJ mol⁻¹), which also corresponds to the asymmetric unit containing not one but two PYV3 (so two PYV3 enols are switching to the keto form). In this particular case, the average switching energy per chromophore is $15.5 \,\mathrm{kJ \, mol^{-1}}$ which is well within the trend of the other co-crystals.

In order to understand the effect of the coformer on the PYV3 E/K equilibrium, additional single point calculations were performed on the isolated PYV3 species using its geometries in the crystals. First, the gas phase enol to keto relative energy, $\Delta E_{\rm EK}^{\rm isolated} = E_{\rm K}^{\rm isolated} - E_{\rm E}^{\rm isolated}$, was computed at the PBEsol0/6-31G(d,p) level of approximation. For PYV3, the $\Delta E_{\rm EK}^{\rm isolated}$ is much larger than $\Delta E_{\rm EK}^{\rm as.u.}$, showing the role of the crystal field and of the interactions in better stabilizing the keto form than the end one. The same trend is observed for the co-crystals with a noticeable difference for PYV3·SDP for which $\Delta E_{\rm EK}^{\rm isolated}$ is smaller, by about 10 kJ mol⁻¹, but favoring the end form, contrary to what is observed in the co-crystal.

In addition to the effect on the E/K equilibrium, co-crystallization also impacts the geometry of PYV3, either because the crystal packing is different from the pure PYV3 crystal or because of the PYV3-coformer interactions. Thus, the energy of geometrical relaxation, ΔE^{relax} , when PYV3 (in its E or K form) goes from its geometry in the PYV3 crystal (PYV3[PYV3]) to its geometry in the different co-crystals (PYV3[co-crystal]) was calculated. It reads:

$$\Delta E_{\rm E}^{\rm relax} = E_{\rm E}^{\rm isolated}({\rm PYV3[co-crystal]}) - E_{\rm E}^{\rm isolated}({\rm PYV3[PYV3]})$$
(1)

$$\Delta E_{\rm K}^{\rm relax} = E_{\rm K}^{\rm isolated}({\rm PYV3[co-crystal]}) - E_{\rm K}^{\rm isolated}({\rm PYV3[PYV3]}).$$
(2)

 $\Delta \Delta E_{\rm EK}^{\rm relax}$ is then defined as their differences:

$$\Delta \Delta E_{\rm EK}^{\rm relax} = \Delta E_{\rm K}^{\rm relax} - \Delta E_{\rm E}^{\rm relax}.$$
(3)

All these values are given in Table 1 and summarized in Figure S2 (see the supporting informations). The $\Delta E_{\rm E}^{\rm relax}$ values highlight the systematic stabilization of the enol form when it switches from its geometry in the crystal to its geometry in the co-crystal, except for the SDP co-crystal. For the keto form, this modification of geometry can be accompanied either by a destabilization or a stabilization but in the latter case, always by a smaller amount than for the enol. This leads to positive $\Delta \Delta E_{\rm EK}^{\rm relax}$ values, again, except for SDP, for which the enol is destabilized and the keto stabilized. Thus, taking the PYV3 crystal as reference, its $\Delta E_{\rm EK}^{\rm isolated}$ value of 37 kJ mol⁻¹ slightly increases when it adopts its co-crystal geometry (except with SDP). This appears to be related to the stronger geometry relaxation of the E vs. K forms. This foresees, qualitatively, the increase of $\Delta E_{\rm ex}^{\rm as.u.}$ from PYV3

		$\Delta E_{\rm EK}^{\rm as.u.}$	$\Delta E_{\rm EK}^{\rm isolated}$	$\Delta E_{\rm E}^{\rm relax}$	$\Delta E_{\rm K}^{\rm relax}$	$\Delta \Delta E_{\rm EK}^{\rm relax}$
Crystal	PYV3	7.1	36.8	0.0	0.0	0.0
Co envetala	SA FA1 FA2 DHBP SDP	$18.2 \\ 18.2 \\ 17.7 \\ 12.7 \\ -15.3$	$ \begin{array}{c cccc} 41.4 \\ 41.2 \\ 39.5 \\ 41.0 \\ 29.0 \\ \end{array} $	-6.2 -6.5 -0.1 -4.2 7.2	-1.5 -2.1 2.7 0.1 -0.6	$ \begin{array}{r} 4.7 \\ 4.4 \\ 2.8 \\ 4.2 \\ -7.8 \end{array} $
	I2but I2F4 I3F3 I3F3-N I3F3-O	12.5 12.2 31.1 	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	-4.4 -1.2 	2.4 3.5 -4.3 -7.3	$6.9 \\ 4.6 \\ \\ 0.5 \\ 3.9$

Table 1: Crystal enol to keto relative energies per asymmetric unit (as.u.), $\Delta E_{\rm EK}^{\rm as.u.} = (E_{\rm K}^{\rm cell} - E_{\rm E}^{\rm cell})/(\text{number of as.u. per cell}).$ Isolated enol to keto relative energies, $\Delta E_{\rm EK}^{\rm isolated} = E_{\rm K}^{\rm isolated} - E_{\rm E}^{\rm isolated}$, geometry relaxation energies from PYV3[PYV3] to PYV3[co-crystal] for the enol and keto forms, $\Delta E_{\rm E}^{\rm relax} = E_{\rm E}^{\rm isolated}(\text{PYV3[co-crystal]}) - E_{\rm E}^{\rm isolated}(\text{PYV3[PYV3]})$ and $\Delta E_{\rm K}^{\rm relax} = E_{\rm K}^{\rm isolated}(\text{PYV3[co-crystal]}) - E_{\rm K}^{\rm isolated}(\text{PYV3[PYV3]})$, and their differences, $\Delta \Delta E_{\rm EK}^{\rm relax} = \Delta E_{\rm K}^{\rm relax} - \Delta E_{\rm E}^{\rm relax}$. All values were obtained at the PBC/PBEsol0/6-31G(d,p)/I(LANL2DZ) level of approximation and are given in kJ mol⁻¹.

to its co-crystals. On the other hand, for SDP, there is a clear stabilization of the keto *vs.* the enol form and the results show that it originates from an increase of the enol form energy when PYV3 adopts its co-crystal geometry.

3.3 Geometry variations upon enol-keto transformation

Table 2 lists the PYV3 bond lengths and intramolecular H-bond angle as well as their variations upon co-crystallization for both the enol and keto forms. Our aim consists in highlighting the key geometrical changes that could explain the ΔE^{relax} values discussed in the previous paragraph.

Starting from the enol forms, SA and FA1 are identically affected, e.g. the

 O_1-H and the H-bond angle $(O_1-H\cdots N_1)$ get smaller $(-0.02 \text{ Å} \text{ and } -2.2^\circ, \text{ re-})$ spectively) while $N_1 \cdots H$ and $O_1 \cdots N_1$ are larger by 0.09 Å and 0.06 Å, respectively. Variations of similar amplitude are obtained for I3F3-O, despite the supplementary interaction on O_1 and O_2 . A stronger covalent O_1 -H bond stabilizes the enol form, consistently with the negative $\Delta E_{\rm E}^{\rm relax}$ values obtained for these crystals (SA and FA1: -6 kJ mol^{-1} , I3F3-O: -11 kJ mol^{-1}). In FA2, the N₁…H and O₁…N₁ distances also get shorter but the variations are smaller (-0.02 Å) with negligible change of the O_1 -H bond length. In addition, O_1 - C_0 is shorter by less than 0.01 Å and $C_O - C_{N\beta}$ is larger by about the same amount. These latter changes are consistent with an increased keto character with respect to PYV3, balanced by a strong H-bond, leading to almost negligible stabilization $(-0.1 \, \text{kJ} \, \text{mol}^{-1})$. SDP co-crystal displays an even shorter $N_1 \cdots H$ bond length than FA2, characterized by variations of -0.03 Å with respect to -0.02 Å and the $O_1 \cdots N_1$ distance further decreases (-0.02 Å), in addition to a longer O_1 -H bond (0.02 Å) and a shorter H-bond angle (-1.2°) . The O₁-H elongation and N₁...H shortening correspond to a displacement of the hydrogen towards the N_1 atom and to the destabilization of the enol form ($\Delta E_{\rm E}^{\rm relax} = 7 \, \rm kJ \, mol^{-1}$). Upon co-crystallization with DHBP, the $N_1 \cdots H$ and $O_1 \cdots N_1$ distances become larger by 0.03 Å and 0.02 Å, respectively, with a small shortening of the O_1 -H bond length (-0.01 Å). This again corresponds to a stronger enol character and a higher stability, as previously computed ($\Delta E_{\rm E}^{\rm relax}$ $= -4 \,\mathrm{kJ \, mol^{-1}}$). I3F3-N is similarly modified to DHBP ($\Delta E_{\mathrm{E}}^{\mathrm{relax}} = -5 \,\mathrm{kJ \, mol^{-1}}$) but the elongation of the bonds is smaller $(-0.02 \text{ Å } vs. -0.03 \text{ Å for } N_1 \cdots H \text{ and } V_1 \cdots H \text{ and } V_2 \cdots H \text{$ -0.01 Å vs. -0.02 Å for $O_1 \cdots N_1$), as well as a slight shortening of the $O_1 - C_0$ bond (-0.01 Å). I2but is also similar to DHBP, explaining the similar $\Delta E_{\rm E}^{\rm relax}$ value (-4 kJ mol^{-1}) . Finally, I2F4 is barely affected, in agreement with the very small $\Delta E_{\rm E}^{\rm relax}$ value $(-1 \, \rm kJ \, mol^{-1})$.

Concerning the geometrical variations of the keto form, in general, the carbon-

carbon bonds of the enol/keto ring are more affected than in the case of the enol form. Again, SA and FA1 present similar variations upon co-crystallization: the $O_1 \cdots H$ H-bond gets longer by 0.06 Å and, in parallel, the $O_1 \cdots N_1$ distance increases by 0.03 Å while the angle is smaller by 3°. In addition, the $O_1 = C_0$ and $C_{N\beta} = C_{N\alpha}$ bonds are shorter by 0.01 Å and $C_{N\alpha} - N_1$ is longer by 0.01 Å, which is consistent with a stronger keto character — although the $C_O = C_{N\beta}$ is barely increased (by less than 0.01 Å). This corroborates the negative $\Delta E_{\rm K}^{\rm relax}$ value $(-2 \, \rm kJ \, mol^{-1})$. FA2 is affected in the opposite way: the $O_1 \cdots H$ and $O_1 \cdots N_1$ distances get shorter by 0.10 Å and 0.05 Å, respectively, while the N_1-H bond length and the $O_1\cdots H-N_1$ bond angle increase by 0.02 Å and 3.0°. Unlike FA1, the FA2 non-hydrogen containing bonds are merely affected. These geometrical variations are consistent with the destabilization of the keto form of FA2 with respect to pure PYV3 ($\Delta E_{\rm K}^{\rm relax}$ = $3 \,\mathrm{kJ \, mol^{-1}}$). For DHBP, the co-crystallization has a small impact on the keto geometry since the largest bond length variation, for the O_1 ...H bond, attains only -0.01 Å, in agreement with the calculated relative energies (small destabilization of $0.1 \,\mathrm{kJ \, mol^{-1}}$). In the case of SDP, the geometrical changes are much larger, though $\Delta E_{\rm K}^{\rm relax}$ only amounts to $-0.6\,{\rm kJ\,mol^{-1}}$. Indeed, the O₁...H distance increases by 0.12 Å and the $O_1 \cdots N_1$ one by 0.05 Å, which favors the K form. On the other hand the $C_O - C_{N\beta}$ bond is shortened by 0.01 Å, stabilizing the enol form. This explains the small $\Delta E_{\rm K}^{\rm relax}$ value. Concerning the X-bond co-crystals, I2but and I2F4 are similarly affected: a decrease of the $O_1 \cdots H$ and $O_1 \cdots N_1$ bond lengths by 0.06 Å and 0.03 Å, respectively, and an increase of the $\rm N_1-H$ bond and $\rm O_1\cdots H-N_1$ angle by 0.01 Å and 3°. I2F4 differs itself from I2but by a slightly longer $C_{N\alpha} - N_1$ bond length variation: 0.007 Å vs. 0.004 Å, meaning a slightly larger keto character and destabilization, as previously shown $(2 \text{ kJ mol}^{-1} \text{ for I2but and } 3 \text{ kJ mol}^{-1} \text{ for}$ I2F4). For I3F3-N, the H-bond distances are less impacted by the co-crystallization $(O_1 \cdots H \text{ and } N_1 - H \sim 0.02 \text{ Å or less})$. On the other hand, the $O_1 = C_0$ bond length

decreases (-0.01 Å), which corresponds to a stabilization of the K form. Finally, I3F3-O's O₁...H bond is larger by 0.02 Å while O₁...H-N₁, O₁=C_O, and C_{N\beta}=C_{Nα} are all smaller by 2.1°, 0.01 Å, and 0.01 Å, respectively. The latter changes are typical of an increased keto contribution and thus, stabilization with respect to the pure keto PYV3, in agreement with the $\Delta E_{\rm K}^{\rm relax}$ calculation (-7 kJ mol⁻¹).

For the enol to keto bond lengths variations, all co-crystals follow the same trends as PYV3 (Figure 3). In particular, in the keto/enol delocalization ring $(H-O_1-C_0=C_{N\beta}-C_{N\alpha}=N_1)$ single bonds shorten and double bonds lengthen. Note that the $O_1\cdots N_1$ distance decreases when going from the enol to keto form, except for SDP where it increases by 0.07 Å (which is also consistent with the Mulliken charges, see next section). Furthermore, the amplitudes of the $O_1\cdots N_1$ shortening are much larger for the co-crystals, ranging between -0.03 Å and -0.06 Å, than for PYV3 with -0.01 Å. Finally, for all crystal/co-crystals, the $N_1-C_{N\gamma}$ bond is very weakly impacted by the proton transfer, despite the fact that N_2 interacts with the coformer.



Figure 3: Selected bond length variations (in Å) in PYV3 when switching from the enol to keto forms, as a function of the nature of the coformer. The geometries were obtained at the PBC/PBEsol0/6-31G(d,p)/I(LANL2DZ) level of approximation.

	($C_{N\beta}$	- C _{Nα}				$C_{N\beta} = C_{N\alpha}$	/	_	
	0_{2}	\sim C_0 O_1	$N_1 - C_N$ — H	γN2		$-O_2$	$\begin{array}{ccc} C_{O} & N \\ & & \swarrow \\ O_{1} & H \end{array}$	$C_1 - C_{N\gamma}$	N ₂	
		Enol								
	PYV3	SA	FA1	FA2	DHBP	SDP	I2but	I2F4	I3F3-N	I3F3-O
O ₁ -H	1.020	-0.016	-0.015	-0.003	-0.006	0.016	-0.009	-0.005	-0.005	-0.016
$N_1 \cdots H$	1.597	0.090	0.088	-0.023	0.026	-0.030	0.030	0.003	0.015	0.086
$O_1 \cdots N_1$	2.536	0.061	0.059	-0.027	0.017	-0.021	0.018	-0.002	0.007	0.052
$O_1 - H \cdots N_1$	150.7	-2.2	-2.2	-0.4	-0.4	-1.2	-0.5	-0.1	-0.4	-2.9
$O_1 - C_O$	1.332	-0.003	-0.003	-0.006	-0.001	0.004	-0.002	-0.002	-0.005	-0.006
$C_O = C_{N\beta}$	1.409	-0.001	-0.001	0.005	-0.001	-0.004	-0.001	-0.002	0.000	-0.001
$\mathrm{C}_{\mathrm{N}eta}\!-\!\mathrm{C}_{\mathrm{N}lpha}$	1.441	-0.003	-0.002	0.001	-0.003	0.000	-0.003	-0.003	-0.001	-0.002
$C_{N\alpha}\!=\!N_1$	1.291	0.001	0.001	0.002	0.001	0.000	0.003	0.004	-0.002	-0.004
$ m N_1 - C_{N\gamma}$	1.393	0.001	0.001	-0.003	-0.001	0.000	-0.001	-0.003	0.000	0.000
	Keto									
	PYV3	SA	FA1	FA2	DHBP	SDP	I2but	I2F4	I3F3-N	I3F3-O
O ₁ …H	1.598	0.060	0.064	-0.095	-0.014	0.118	-0.061	-0.057	-0.018	0.019
$N_1 - H$	1.060	-0.005	-0.005	0.021	0.004	-0.018	0.012	0.012	0.003	0.000
$O_1 \cdots N_1$	2.527	0.032	0.034	-0.052	-0.006	0.053	-0.028	-0.027	-0.008	0.004
$O_1 \cdots H - N_1$	143.1	-3.0	-3.2	3.0	0.6	-5.8	3.0	2.6	1.1	-2.1
$O_1 \!=\! C_O$	1.274	-0.009	-0.010	0.000	-0.002	0.003	-0.002	-0.002	-0.007	-0.012
$C_O - C_{N\beta}$	1.442	0.003	0.003	0.001	0.000	-0.008	-0.001	-0.002	0.003	0.005
$C_{N\beta} = C_{N\alpha}$	1.403	-0.010	-0.010	-0.003	-0.004	0.001	-0.003	-0.005	-0.003	-0.008
$C_{N\alpha}\!-\!N_1$	1.316	0.008	0.008	0.004	0.004	0.000	0.004	0.007	0.000	0.005
$\mathrm{N}_1\!-\!\mathrm{C}_{\mathrm{N}\gamma}$	1.394	0.000	0.000	-0.003	-0.002	0.001	-0.005	-0.005	-0.002	0.001

Table 2: Key bond lengths and H-bond angle for PYV3 crystal and their variations [$\Delta \alpha = \alpha$ (co-crystal) – α (PYV3) with α a distance or an angle] when forming co-crystals (bond lengths and bond length variations in Å; angle and angle variations in °). Large values are highlighted in bold. The geometries were obtained at the PBC/PBEsol0/6-31G(d,p)/I(LANL2DZ) level of approximation.

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3.4 Mulliken charges analysis

Table 3 shows the relevant Mulliken atomic charges of PYV3 and their variations with respect to the PYV3 crystal, for all co-crystals, as determined at the PBC/PBEsol0/6-31G(d,p)/I(LANL2DZ) level of approximation. Table S2 in the Supporting Informations compares the Mulliken and Hirshfeld charges and shows that the enol to keto differences globally follow the same trends. The Hirshfeld charges have been obtained using the iterative Hirshfeld method[39, 40] with Crystal17[41] at the PBC/PBEsol0/6-31G(d,p) level of approximation with the XXL integration grid). Considering only the Mulliken values in Table 3, the variations with respect to PYV3 are small for both the enol and keto forms, with a few exceptions: firstly, for the N₂ atom and secondly, on SDP. Concerning N₂, the negative Mulliken charges are significantly larger for all enol and keto co-crystals. H-bonded co-crystals are the most affected with an increase of 0.11 e to 0.16 e (26 %

Enol										
PYV3	SA	FA1	FA2	DHBP	SDP	I2but	I2F4	I3F3-N	I3F3-O	
0.40	-0.00	-0.00	0.00	0.00	0.11	0.00	0.01	-0.01	0.01	
-0.59	0.02	0.03	0.02	0.01	-0.15	0.02	0.01	0.03	0.02	
-0.60	0.00	0.01	-0.01	-0.00	-0.03	-0.01	-0.01	0.03	0.00	
-0.41	-0.16	-0.16	-0.14	-0.12	-0.13	-0.06	-0.06	-0.06	-0.05	
Keto										
PYV3	SA	FA1	FA2	DHBP	SDP	I2but	I2F4	I3F3-N	I3F3-O	
0.38	0.00	0.00	0.02	0.01	0.09	0.01	0.01	0.01	0.01	
-0.63	0.03	0.03	0.01	0.01	-0.05	0.01	0.01	0.01	0.04	
-0.59	-0.02	-0.02	-0.04	-0.02	-0.12	-0.03	-0.03	-0.01	-0.01	
-0.42	-0.15	-0.15	-0.14	-0.12	-0.11	-0.05	-0.05	-0.05	-0.05	
	PYV3 0.40 -0.59 -0.60 -0.41 PYV3 0.38 -0.63 -0.59 -0.42	PYV3 SA 0.40 -0.00 -0.59 0.02 -0.60 0.00 -0.41 -0.16 PYV3 SA 0.38 0.00 -0.63 0.03 -0.59 -0.02 -0.42 -0.15	PYV3 SA FA1 0.40 -0.00 -0.00 -0.59 0.02 0.03 -0.60 0.00 0.01 -0.41 -0.16 -0.16 PYV3 SA FA1 0.38 0.00 0.00 -0.63 0.03 0.03 -0.59 -0.02 -0.02 -0.42 -0.15 -0.15	PYV3 SA FA1 FA2 0.40 -0.00 -0.00 0.00 -0.59 0.02 0.03 0.02 -0.60 0.00 0.01 -0.01 -0.41 -0.16 -0.16 -0.14 PYV3 SA FA1 FA2 0.38 0.00 0.00 0.02 -0.63 0.03 0.03 0.01 -0.59 -0.02 -0.04 -0.04 -0.42 -0.15 -0.15 -0.14	$\begin{tabular}{ c c c c c } \hline F \\ \hline PYV3 & SA & FA1 & FA2 & DHBP \\ \hline 0.40 & -0.00 & -0.00 & 0.00 & 0.00 \\ \hline -0.59 & 0.02 & 0.03 & 0.02 & 0.01 \\ \hline -0.60 & 0.00 & 0.01 & -0.01 & -0.00 \\ \hline -0.41 & -0.16 & -0.16 & -0.14 & -0.12 \\ \hline \hline $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $$	$\begin{array}{ c c c c c c } \hline FA2 & FA1 & FA2 & DHBP & SDP \\ \hline PYV3 & SA & FA1 & FA2 & DHBP & SDP \\ \hline 0.40 & -0.00 & -0.00 & 0.00 & 0.01 & -0.59 \\ \hline 0.02 & 0.03 & 0.02 & 0.01 & -0.15 \\ \hline -0.60 & 0.00 & 0.01 & -0.01 & -0.00 & -0.03 \\ \hline -0.41 & -0.16 & -0.16 & -0.14 & -0.12 & -0.13 \\ \hline \hline PYV3 & SA & FA1 & FA2 & DHBP & SDP \\ \hline 0.38 & 0.00 & 0.00 & 0.02 & 0.01 & 0.09 \\ \hline -0.63 & 0.03 & 0.03 & 0.01 & 0.01 & -0.05 \\ \hline -0.59 & -0.02 & -0.02 & -0.04 & -0.02 & -0.12 \\ \hline -0.42 & -0.15 & -0.15 & -0.14 & -0.12 & -0.11 \\ \hline \end{array}$	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	

Table 3: Mulliken charges and variations with respect to PYV3 calculated at the PBC/PBEsol0/6-31G(d,p)/I(LANL2DZ) level of approximation (in e). Large values are highlighted in bold.

to 39%) while for the X-bonded co-crystals, the increase varies between 0.05 e and 0.06 e (12% and 15%). The charges of all the other atoms barely change except for SDP H and O₁ in its enol form [variations of 0.11 e (27%) and -0.15 e (25%), respectively] and H and N₁ for the keto form [variations of 0.09 e (24%) and -0.12 e (20%), respectively]. The very large charge variation of the hydrogen might explain SDP's O₁...N₁ different behavior compared to all other crystals, *i.e.* a large increase instead of the opposite (see previous section).

About the enol to keto charge distribution differences, represented in Figure 4, only some of the atoms follow the same trend amongst all crystals: H, for which the charge decreases by about 0.02 e (as it becomes bonded to a less electronegative atom); C_O, where the charge is more positive by about 0.07 e (since it is no longer aromatic and the charge on O₁ is usually more negative); the charge on



Figure 4: Enol to keto Mulliken charges differences calculated at the PBC/PBEsol0/6-31G(d,p)/I(LANL2DZ) level of approximation (in e).

 $C_{N\beta}$ becomes more negative by about 0.05 e (because it is bonded to the positive C_{O} atom and loses its aromaticity); $C_{N\gamma}$ charge becomes more positive by about 0.03 e, except for I3F3-N with a much larger increase of 0.09 a.u.; and for O_2 , the charge increases only by 0.01 e even for the co-crystals where it is involved in intermolecular interactions (SDP and I3F3-O). O_1 charge decreases as one would have expected when going from an enol to a keto by about 0.03 e, except for two co-crystals: I3F3-O, which is less affected with a decrease of only 0.01 e and SDP, for which the charge increases by 0.06 e. This highlights that the interaction between the coformer and PYV3 O_1 is much stronger for SDP than for I3F3. About $C_{N\alpha}$, the charge becomes less positive by about 0.02e except for FA2 for which it increases slightly (0.01 e). The charge of PYV3 N₁ increases by 0.01 e while it decreases weakly/strongly depending on the co-crystal (except for I3F3-O with a slight increase of 0.003 e): -0.005 e for DHBP and I2F4 and up to -0.08 e for SDP. This is the largest qualitative difference between PYV3 and its co-crystals regarding the Mulliken charges. Finally, the charge differences for N_2 are not systematic and vary between -0.005 for DHBP and 0.009 e for SDP.

4 Conclusions

Co-crystallization has extremely complex effects on the structures and properties of organic chromophores, as illustrated in this investigation on the PYV3 salicylideneaniline, which switches between an enol and a keto form. In our attempt to decipher them, using theoretical chemistry methods, we broke them down in three categories associated with the energy (H-bond strength, enol to keto relative energy, and geometry relaxation energies), the geometrical structure (PYV3 to co-crystal and enol to keto geometrical variations), and the electron distribution (PYV3 to co-crystal and enol to keto Mulliken charge variations). First, potential energy scans of a HF probe molecule with the nitrogen and oxygen interaction sites shows that the enol form favors the interaction on the nitrogen (N₂) by about 6 kJ mol^{-1} with respect to the oxygens while the opposite is obtained for the keto form by an even larger amount (12 kJ mol^{-1}). This correlates with the fact that among the studied co-crystals, only two show interactions between the coformer and the oxygens of the anil while the interaction with the nitrogen of the pyridine ring (N₂) is always present. Subsequently, since the enol form of PYV3 is mostly present in solution, the interaction on the nitrogen is thus the most probable in both liquid and crystalline states. This suggests that cocrystallization under the keto form could be favored by increasing its population in solution with careful control of the conditions impacting the enol/keto equilibrium (specific intermolecular interactions with the solvent, substituents, temperature, and light exposure).

Looking at the relative keto/enol energy, the enol crystals are more stable than the keto ones, except for the SDP co-crystal, in agreement with experiment. Furthermore, the switching requires more energy for the co-crystals than for the pure PYV3 crystal (ignoring the kinetics), which is also in agreement with the experimental data. Indeed for the co-crystals with FA1, FA2, and SA, the thermochromism was found to be reduced with respect to the pure PYV3 crystal[21]. Calculations on isolated PYV3 molecules have then highlighted the role of the crystal field and of the geometry relaxations on the enol/keto relative energies. In particular, with the exception of the SDP co-crystal, where the keto form is dominant, the geometry relaxation induced by co-crystallization better stabilizes the enol form than the keto one. These geometry relaxation energies are associated to geometrical variations within the keto/enol delocalization ring $(H-O_1-C_0=C_{N\beta}-C_{N\alpha}=N_1)$, which follow the same trends for all crystals, again, with the exception of PYV3·SDP. These have been analyzed in parallel with the Mulliken charge distribution, showing that the interaction with the coformer makes the N_2 charge more negative.

Overall, we have showed that the effect of co-crystallization can not be singularly characterized but is a collective effect. The change of packing (short-range intermolecular interactions and long-range crystal field interactions) affects the geometry, the electronic distribution, and the energy of a target molecule in different ways, despite the key compound-coformer interaction being the same. *e.g.* the SA, FA, and DHBP coformers, forming a single H-bond on N₂, yield three "types" of co-crystals, PYV3·SA/FA1, PYV3·FA2, and PYV3·DHBP. Moreover, the study of the PYV3·SDP co-crystal shows how the interaction with the coformer modifies the structure and electron distribution, stabilizing the ever so elusive crystalline keto form.

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Tuning thermochromism! Using periodic density functional theory, we show how co-crystallization affects the keto/enol populations of a N-salicylideneaniline molecular switch. Depending on the chosen coformer, the equilibrium is reversed (see figure) or reinforced. This behavior is then correlated to bond lengths and charges variations.

6 Keywords

Crystals; co-crystals; molecular switch; N-salicylideneaniline; geometry; relative energy

7 TOC

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