Photo- vs Mechano-Induced Polymorphism and Single Crystal to Single Crystal [2 + 2] Photoreactivity in a Bromide Salt of 4-Amino-Cinnamic Acid

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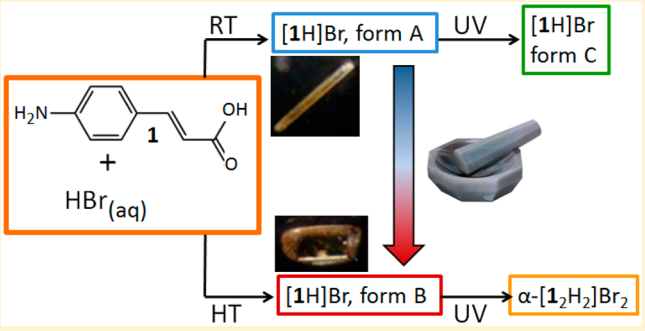
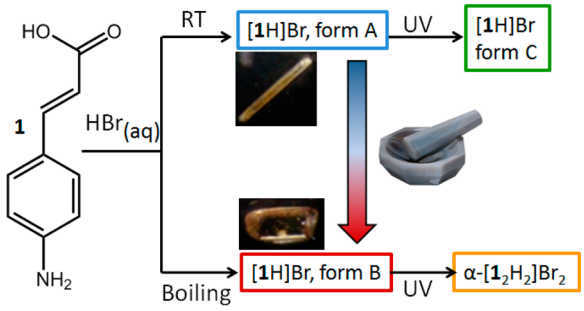
ABSTRACT: The new molecular salt [**1**H]Br (**1** = 4-amino-cinnamic acid) was obtained in two polymorphic modifications, forms A and B. While mechanical stress induces transformation of form A into form B, an unexpected effect of UV irradiation is observed on form A, i.e., a single crystal to single crystal (SCSC) transformation to a third polymorph, form C. Form B, on the contrary, responds to UV irradiation by undergoing a stepwise SCSC [2 + 2] photodimerization to α-[$\mathbf{1}_2H_2$]Br_2, via formation of a solid state solutions in the whole compositional range. All transformations were followed by a combination of solid-state techniques, i.e., single crystal and powder X-ray diffraction, FTIR, and FT-Raman, and by solution ^{1}H NMR. All structural changes also resulted in variations in crystal morphology/texture, and these were monitored via SEM analysis.



Following the pioneering work of Schmidt and Cohen[1] which delineated the "topochemical principle" for [2 + 2] photoreactions in the solid state, there has been increasing interest for such reactions, which became paradigmatic in crystal engineering studies[2,3] and solid state organic chemistry.[4,5] Although a maximum center-to-center bond separation (d) of 4.2 Å is often claimed as a necessary condition for [2 + 2] photoreactions to occur, either positive or negative exceptions to this rule have been reported in the literature[6] and additional geometrical criteria,[7] mechanical properties,[8,9] or alternative mechanisms[6,10,11] have been proposed to influence the photoreactivity. However, such an empirical rule remains very useful in the prediction and rationalization of topotactic reactions, which occur with the least molecular motion and are also prone to undergo single crystal to single crystal (SCSC) photoconversion.[4,12−14] Additional key points are (i) the symmetry conservation of the reactant lattice during the reaction,[15,17] which also implies that the interaction patterns detectable within the reactant do not change appreciably, (ii) the constancy of lattice parameters during the photoconversion process,[15−17] and (iii) the use of wavelengths covering the absorption tail region of the molecule, which ensures more homogeneous light penetration into each crystallite, and not simply absorption from its surface,[18−20] and minimum crystal disintegration.[21,22,23] Several strategies[24−27] have been devised and employed in the last decades to perform solid state [2 + 2] reactions. In addition to pure theoretical considerations, there is also considerable interest in the exploitation of such transformations for the production of UV-filters/sunscreens[28−30] and polymers[31−34] synthesized from raw materials derived from natural molecules (i.e., cinnamates), and in the conversion of light energy into mechanical work.[4,35] To this end SCSC transformations are promising and widely investigated. In a recent paper we reported on a clean and efficient strategy based on molecular salt formation as a means to activate the solid state photoreactivity of 4-aminocinnamic acid derivatives via SCSC reactions.[24,36]

In this communication we report our findings on the solid-state [2 + 2] photoreactivity and behavior of two polymorphs of the hydrobromide salt of 4-aminocinnamic acid, namely, [**1**H]Br forms A and B, which display quite different photochemical behavior. Upon photoirradiation form B undergoes a SCSC [2 + 2] dimerization via formation of solid solutions in the whole range of compositions, while form A undergoes a SCSC transition to a third polymorph of [**1**H]Br, form C. This kind of behavior, i.e., polymorphic transformation induced by UV light, has, to these authors' knowledge, never been observed before in organic molecular crystals. In addition to this, the mechanically induced transformation of form A into form B has been monitored via X-ray powder diffraction and analyzed with Rietveld refinements. The overall process is summarized in Scheme 1.

Scheme 1. Photo- and Mechano-Triggered Polymorphism and UV-Induced Cycloaddition Reaction in Crystalline [1H]Br[a]



[a]The partial or complete conversion from form A to form B via grinding depends on the grinding time.

Needle-like crystals of [1H]Br form A were grown from an aqueous solution obtained sonicating **1** at room temperature in the presence of a few drops of HBr, while form B was obtained as block-shaped crystals when the same solution was boiled for 2−3 min (see Scheme 1). Structural characterization of both polymorphs via single-crystal X-ray diffraction (see SI) showed that in both forms A and B the relative arrangement of double bonds in neighboring molecules [distances between bond centers are 4.425(6) and 3.618(6)Å, respectively; see Scheme SI-1 and Table SI-2)] should favor the cycloaddition reaction. The same single crystals used for structure determination were thus irradiated overnight with an LED source (λ = 365 nm). Subsequent X-ray diffraction analysis showed that (i) crystallinity had been preserved, and (ii) a significant expansion (+3.5%) and contraction (−3.8%) of the unit cell volumes had occurred for irradiated crystals of forms A and B, respectively (see Table SI-1).

The effect of UV irradiation on crystalline [1H]Br form A was quite unexpected: instead of promoting the cycloaddition reaction, it triggered a polymorphic transformation to a third polymorphic form C (Figure 1). Form C retains the monoclinic

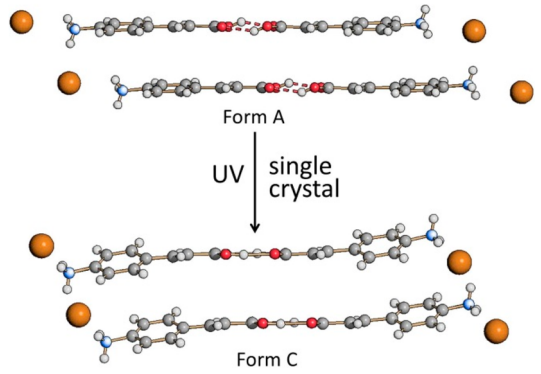


Figure 1. Light-induced polymorphic transition from [1H]Br form A to [1H]Br form C.

symmetry $P2_1/c$ with small but significant changes in the a and b axes (−4.9% and 5.2%, respectively), in the β angle (−11.6%), and it is characterized by a packing slightly stretched out along the [010] direction with respect to A and with slightly shorter, hence expectedly more favorable for cycloaddition, distances between double bonds (d = 4.210(1)Å, see Table SI-2).

To exclude a possible heating effect of the LED on the A to C transformation, we performed a Hot Stage Microscopy (HSM) experiment (Figure 2). A fresh single crystal of form A

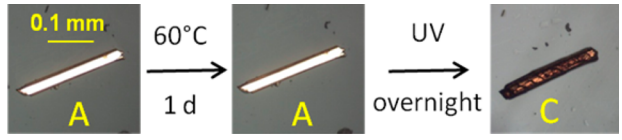


Figure 2. Cross-polarized HSM pictures showing single crystals of [1H]Br form A before and after thermal treatment and after UV irradiation.

was kept at 60 °C (i.e., at a temperature ca. 20 °C higher than that experienced by the crystal under the LED source) for 24 h on the HSM plate; X-ray data were then collected on the single crystal thus treated, which produced an unaltered result. Conversion from A to C was obtained only upon UV irradiation, and was accompanied by partial amorphization of the crystal surface and partial fragmentation. Each fragment, analyzed with SCXRD, corresponded to form C. This process can described as a single crystal to single crystal (SCSC) polymorphic transformation.

A comparison between SEM micrographs (Figure 3) taken before and after overnight irradiation on form A clearly shows

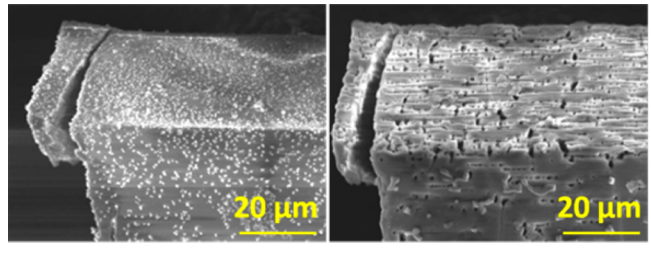


Figure 3. SEM micrographs of a single crystal of [1H]Br form A before (left) and after (right) UV irradiation. The crystal on the right corresponds to [1H]Br form C.

how the crystal is cracked and its surface damaged, as a result of a marked internal molecular motion leading to the structural change.

To exclude the formation of side-products during the irradiation process, we selected a dozen single crystals of A and irradiated them in order to obtain form C. We then carried out FT-Raman analyses, which confirmed that no side reaction had taken place and that amorphization accompanied the A → C transition, as revealed by the broadening of several bands (Figure 4), according to what was observed with optical microscopy. On the same irradiated samples we also ran ^{1}H NMR in solution, which confirmed that the chemical identity was maintained (see SI) between form A and form C, since no new peaks appeared in the spectrum.

Therefore, we are observing a polymorphic transition triggered by light. In our case, we first thought that this polymorphic transition (A → C) might be driven by the molecular movements necessary to optimize the overall crystal geometry to bring together the reacting molecules. Surprisingly, however, this new form does not undergo cycloaddition reaction even after prolonged exposure (72 h) to UV light. The lack of reactivity might be due to the presence of strong carboxylic acid homosynthons $R_2^2(6)$ (see Figure SI-2), which would have to be broken in order to allow cyclobutane

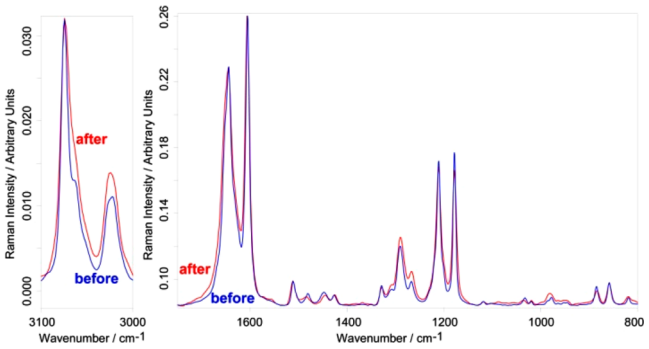


Figure 4. Raman spectra of crystalline [**1**H]Br form A before (blue line) and after (red line) UV irradiation.

formation, thus making the energetic balance unfavorable with respect to cycloaddiction product formation. The difficulty in rearranging the distribution of anions and cations, hence the pattern of electrostatic attraction and repulsions within the lattice, might also play a role in hampering the approach of the molecules for photoreaction. A combination of both factors ought also to be considered.

The solid state behavior of form A is also peculiar, since upon grinding it progressively converts to form B. Rietveld analysis was used to evaluate the relative amounts of polymorphs during this process (see SI for difference patterns and details). "Soft" grinding (the crystals where gently tapped) leads to a pattern which contained about 57% of form B. Further soft grinding leads to an increase in form B (ca. 93%), while upon ca. 30 s of normal grinding the conversion into form B was quantitative.

The behavior of crystalline [**1**H]Br form B upon UV irradiation is analogous to that of the previously reported[36] hydrochloride salt. As demonstrated by SCXRD analysis and cross-polarized optical and SEM images (see SI), the photoreaction (Figure 5) proceeds quantitatively in a SCSC

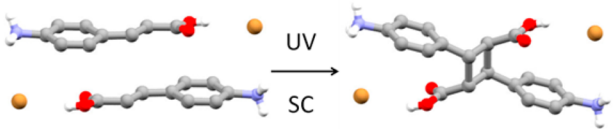


Figure 5. Photodimerization of [**1**H]Br form B to α-[$\mathbf{1}_2H_2$]Br_2.

fashion, and is accompanied by variations in the unit cell constants, while the hydrogen bond distances remain almost unaltered (see SI for details).

Inspection of the interaction patterns for [**1**H]Br and α-[$\mathbf{1}_2H_2$]Br_2, evaluated by Hirshefeld surface analysis[37] and 2D Fingerprint plots[38] (see SI), reveals that for these crystals the interaction patterns are nearly constant. This should enable solid state solutions. Accordingly, UV irradiation was repeated stepwise for subsequent short time intervals. After each exposure, single crystal data were collected and the structure redetermined. The presence of the product α-[$\mathbf{1}_2H_2$]Br_2 in the crystal was confirmed, and its percentage increased up to complete conversion and with a sigmoidal dependence of the dimer content vs irradiation time.[4,13,39] Single crystals with the following compositions were progressively obtained: (i){[**1**H]-Br}$_{0.88}$·{α-[$\mathbf{1}_2H_2$]Br_2}$_{0.12}$; (ii) {[**1**H]Br}$_{0.58}$·{α-[$\mathbf{1}_2H_2$]Br_2}$_{0.42}$ and {[**1**H]Br}$_{0.14}$·{α-[$\mathbf{1}_2H_2$]Br_2}$_{0.86}$. For each stage the hydrogen bonding interactions were maintained nearly constant (see SI).

Interestingly, as evidenced by SCXRD analysis on samples obtained after recrystallization of partially reacted crystals, i.e., {[**1**H]Br}$_{0.58}$·{α-[$\mathbf{1}_2H_2$]Br_2}$_{0.42}$, complete separation of the solid solution components was invariably achieved, indicating that solid solution formation is attained only through UV irradiation of solid state samples (see Figure 6).

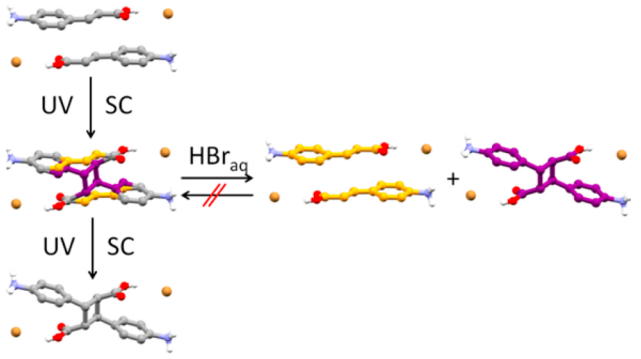


Figure 6. Formation of partially reacted crystals, which after recrystallization give single crystals of [**1**H]Br and α-[$\mathbf{1}_2H_2$]Br_2.

Photochemical behavior of [**1**H]Br form B was also investigated in polycrystalline samples. Upon overnight irradiation, both the FTIR[31−33] and FT-Raman[40−43] spectra (see SI) showed changes consistent with completion of the [2 + 2] photodimerization: the marker bands of the olefinic moiety disappeared, while those assignable to the dimer (α-truxillic acid derivative) were detected. The occurrence of the reaction was also confirmed by ^{1}H NMR solution spectroscopy, which showed unequivocally the disappearance of the olefinic peaks and the emergence of cyclobutane protons (see SI). Changes, corresponding to complete photoconversion, were noticed also in the XRPD pattern (see SI).

In summary, in this communication we have described the synthesis and structural characterization of two polymorphs of the hydrobromide salt of 4-aminocinnamic acid, namely, [**1**H]Br forms A and B. Conversion from form A to form B was obtained upon grinding and was followed by powder X-ray diffraction.

The solid state photoreactivity of both polymorphs has been investigated, although the mutual arrangement of the double bonds in crystalline form A is not strictly favorable.

In the case of form B, as demonstrated by SCXRD analysis, cross-polarized optical and SEM micrographs, the [2 + 2] photoreaction was found to proceed quantitatively and topotactically, i.e., with the least motion and conservation of crystal outer shape and symmetry, namely, in a SCSC fashion to generate the corresponding truxillic acid derivative α-[$\mathbf{1}_2H_2$]Br_2. The behavior of a polycrystalline sample of form B was also investigated via FTIR, FT-Raman, and ^{1}H NMR spectroscopy which confirmed the quantitative conversion in the corresponding α-dimer. Solid solutions with general formula {[**1**H]Br}$_x$·{α-[$\mathbf{1}_2H_2$]Br_2}$_{1-x}$, were also achieved by progressively irradiating the same single crystal specimen of form B. Concerning the partially reacted crystals, we found the complete separation of the solid solution components upon recrystallization indicating thus that solid state solutions can only be attained specifically via UV irradiation.

Surprisingly, irradiation of form A, instead of photoreaction, causes conversion into a third polymorph, denoted as C. Form C retains the monoclinic symmetry $P21/c$ with small but

significant changes in the *a* and *b* axes and in the β angle, which are accompanied by partial fragmentation of the starting single crystal into several smaller single crystals (SCSCs). Hot stage microscopy combined with SCXRD and spectroscopic techniques (FTIR, FT-Raman, and ^{1}H NMR) were applied to exclude the heating effect of the LED source and the presence of side reactions, respectively. To the best of these authors' knowledge, the transformation of form A into form C is the first case of a polymorphic transition triggered by UV irradiation. Further studies are required to shed light on this peculiar behavior.

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