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Polymorphism in 4'-hydroxyacetophenone: A vibrational analysis

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HIGHLIGHTS

G R A P H I C A L A B S T R A C T

- Two polymorphs of 4'hydroxyacetophenone were distinguished by DRIFT spectroscopy.
- Differences in H-bonding found by XRD were also captured by the DRIFT spectra.
- ATR studies suggest a link between the solution species and the crystallized form.

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ABSTRACT

In this work we show that the two known polymorphs of 4'-hydroxyacetophenone (form I, monoclinic, $P2_1/c$, Z'/Z = 1/4; form II, orthorhombic, $P2_12_12_1$, Z'/Z = 2/8) can be clearly distinguished by diffuse reflectance infrared Fourier-transform infrared (DRIFT) spectroscopy. The experimental studies were complemented by density functional theory calculations (DFT) carried out at the B3LYP/cc-pVTZ level of theory on the *E* and *Z* molecular conformers present in the solid forms I and II, respectively. Comparison between the calculated and experimental spectra allowed understanding the influence of polymorphism on the main intermolecular interactions. It was concluded that the differences in the hydrogen bond (H-bond) patterns of the two forms previously highlighted by X-ray diffraction were also captured by the vibrational spectra. Finally, attenuated total reflectance (ATR) spectra suggested that there is a direct connection between the predominant solvent-induced molecular conformation of 4'-hydroxyacetophenone (*E* or Z) and the selective nucleation of form I from water and form II from ethanol. © 2013 Elsevier B.V. All rights reserved.

1. Introduction

Polymorphism, the ability of a given compound to crystallize in diverse crystal forms that may coexist under the same pressure and temperature conditions, is a common phenomenon in organic molecular solids [1–3]. Distinct polymorphs may exhibit significantly different physical (e.g. density, fusion temperature, solubility) and spectroscopic properties (e.g. color) and,

consequently, their selective and reproducible preparation allows, in principle, the production of new materials without changing the molecule involved. This achievement finds very important practical applications, for example, in the dye and pharmaceutical industries [1–3]. The lack of control over polymorphism can, on the other hand, significantly interfere with the end uses of a given product. Well characterized polymorphic systems are also relevant to fundamental science, in areas such as the assessment of crystallization theories [4–6] and the development of force-fields that are used to rationalize and predict the structural and energetic properties of organic molecular solids [7,8]. Such facts justify the considerable attention that the phenomenon of polymorphism in organic

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Fig. 1. Conformation and atom labeling scheme of the molecules in the crystal lattices of the two polymorphic forms of 4'-hydroxyacetophenone suggested by the single crystal X-ray diffraction analysis [9]: (a) form I (monoclinic; HAP molecule in a *E* conformation); (b) form II (orthorhombic; HAP molecule in a *Z* conformation).

molecular solids has received in recent years. One key aspect of these studies is the ability to unequivocally discriminate polymorphs. Since variations in conformation or environment of the molecules in different solid forms necessarily affect their vibrational spectra, infrared spectroscopy can be used to qualitatively or even quantitatively analyze polymorphs.

We recently found that 4'-hydroxyacetophenone (HAP) can be reproducibly obtained as two different polymorphs [9,10]: form I, which crystallizes in the monoclinic space group $P2_1/c$, and has Z'/Z = 1/4, and form II, previously isolated [11–13], which crystallizes in the orthorhombic crystal system with space group $P2_12_12_1$, and Z'/Z = 2/8. Crystallization from water leads to form I while crystallization from ethanol leads to form II [9]. These forms were structurally, morphologically, and thermodynamically characterized by using a variety of experimental methods, such as Xray diffraction, microscopy, solubility and crystallization studies, combustion and solution calorimetry, differential scanning calorimetry (DSC), Calvet-drop sublimation calorimetry, and the Knudsen effusion method [9–13]. They were also investigated by molecular dynamics simulations [14]. Overall these studies indicated that [9,10,14]: (i) the system is enantiotropic, with form II being more stable than form I at 298 K, with $\Delta_{trs}H_m^o(II \rightarrow I) = 0.49 \pm 0.13 \text{ kJ mol}^{-1}$; (ii) despite this small enthalpy difference compared to the thermal energy at that temperature $(RT \sim 2.5 \text{ kJ mol}^{-1})$, a sample of form I could be stored at ambient temperature, for at least one year, without change; (iii) form II first transforms into form I at a temperature below 351.2 ± 2.7 K [10], followed by fusion of form I at 381.9 ± 0.1 K; (iv) the HAP system obeys Kitaigorodskii's "density rule", according to which the most stable polymorph should correspond to the structure with the highest density [1,15]; and (v) the fact that the more stable form II has a greater Z' than the less stable form I contradicts the proposal that high Z' polymorphs are metastable precursors of lower Z' forms along the crystallization pathway [16,17].

Analysis of the crystal structure indicated that, at the molecular level, the two forms differ by the relative orientation of the OH and CO groups (Fig. 1), which adopt an E conformation in form I and a Z conformation in form II. The hydrogen bond patterns in the crystal

packing of the two phases at 298 K are also rather different (Fig. 2). Although in both cases the 1D motif consists of an infinite linear chain C(8) sustained by "head-to-tail" bonding between the hydroxyl group of one molecule (donor) and the carbonyl group of an adjacent molecule (acceptor), O1H···O2, the chains are planar in form I and helicoidal in form II (see also Figs. 5 and 6 of Ref. [9]). In form I the O1H...O2 hydrogen bonds are of a single type $(d_{O1H\dots O2} = 1.82 \pm 0.02 \text{ Å}; d_{O1\dots O2} = 2.676 \pm 0.002 \text{ Å})$ and adjacent chains do not interact among themselves. The chains of form II involve two different O1H···O2 bonds ($d_{O1H···O2} = 1.64 \pm 0.03$ Å, $d_{O1\dots O2} = 2.707 \pm 0.002$ Å and $d_{O1H\dots O2} = 1.80 \pm 0.03$ Å, $d_{O1\dots O2} =$ 2.739 ± 0.003 Å), which result from the existence of two nonequivalent molecules in the asymmetric unit. They also interact with their adjacent counterparts through C5H···O1 ($d_{C5H···O1}$ = 2.49 ± 0.02 Å), C8H···O1 ($d_{CH···O}$ = 2.68 ± 0.01 Å), and C8H···O2 $(d_{CH\dots O} = 2.66 \pm 0.01 \text{ Å})$ contacts forming a 3D supramolecular structure. Efficient π - π stacking is absent in both polymorphs.

Here we investigate how these structural differences are reflected by their Fourier-transform infrared spectra, which, to the best of our knowledge, was not taken into account in the previous characterization of 4'-hydroxyacetophenone by Raman and infrared spectroscopies [18]. Also addressed is the relationship between the molecular conformations of HAP predominant in ethanol or water solution and the polymorph formed upon crystallization.

2. Materials and methods

2.1. Materials

The samples of forms I and II HAP used in this work were prepared and characterized as previously reported [9]. In brief, crystals of form I were obtained by heating commercial HAP (Aldrich, 98%, sublimed prior to use) in an oven, at 363 K, under nitrogen atmosphere (1 bar), during six days. Form II was produced by cooling without stirring a saturated ethanol solution from 333 K to 277 K at a rate of 0.01 K min⁻¹.

The form I HAP deuterated at the hydroxyl group was prepared by cooling 50 cm^3 of a solution with concentration 56 g kg^{-1} of HAP in deuterium oxide (D₂O, Aldrich, 99.9 atom% D) from 343 K to 283 K at 5 K min⁻¹. The obtained sample was dried in an oven for 48 h at 363 K. ¹H NMR analysis (Fig. 3), carried out at 293 ± 2 K, on a Bruker Ultrashield 400 MHz spectrometer using CDCl₃ (Aldrich 99.80%, <0.01% H₂O) as solvent led to: δ / ppm = 2.57 (s, 3.00H, CH₃), 6.90 (d, 1.98H, CH), 7.91 (d, 1.99H, CH). These results are in good agreement with those obtained for a non-deuterated sample, δ /ppm = 2.58 (s, 3.00H, CH₃), 6.92 (d, 2.01H, CH), 7.91 (d, 1.97H, CH). This indicates that selective deuteration at the hydroxyl group was achieved. The X-ray powder diffraction (XRPD) analysis were carried out at 296 ± 3 K in a Philips Analytical X'Pert PRO apparatus set with a vertical PW 3050/60 goniometer and a X'Celerator detector. Automatic data acquisition was performed by means of the X'Pert Data Collector v2.0b software package. The instrument operated in the θ -2 θ mode, using a Cu K α radiation source, with the tube amperage set to 30 mA



Fig. 2. Molecular packing and hydrogen bonding pattern in the crystal structures of form I (a) and form II (b) 4'-hydroxyacetophenone, at 298 K.

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Fig. 3. Overlay of the ¹H NMR spectra of non-deuterated (black line) and deuterated (red line) 4'-hydroxyacetophenone at 293 ± 2 K. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

and the tube voltage to 40 kV. The diffractograms were recorded by continuous scanning in the 2θ range $5-35^{\circ}$, with 2θ step sizes of 0.017° and scan step times of 20 s, respectively. The samples were mounted on aluminum sample holders. The powder pattern was indexed with the program Celref [19] as monoclinic, space group $P2_1/c$, with $a = 7.703 \pm 0.022$) Å, $b = 8.335 \pm 0.013$ Å, $c = 11.244 \pm 0.024$ Å, $\beta = 95.04 \pm 0.65^{\circ}$. These results are in good agreement with those obtained for the non-deuterated form I by single crystal X-ray diffraction at 298 ± 2 K [9], indicating that deuteration did not significantly affect the packing arrangement: $a = 7.720 \pm 0.002$ Å, $b = 8.360 \pm 0.002$ Å, $c = 11.280 \pm 0.002$ Å, $\beta = 95.02 \pm 0.03)^{\circ}$ [9].

2.2. Diffuse Reflectance Infrared Fourier Transform (DRIFT) and attenuated total reflectance (ATR) spectroscopies

A Nicolet 6700 spectrometer (Thermo Electron Corp., Madison, WI) equipped with a deuterated triglycine sulfate (DTGS) detector (4000–400 cm⁻¹) and a Smart Diffuse Reflectance (SDR) kit (Thermo Electron Corp.) was used for scanning the spectra of the HAP polymorphs in diffuse reflectance mode. The spectra were collected with a resolution of 2 cm⁻¹, by using 512 scans for the sample and background experiments. The sample preparation consisted simply on grinding a mixture of KBr (Sigma–Aldrich, FTIR grade) and each sample powder, in appropriate weight proportions to obtain spectral absorbance in the range of applicability of the Kubelka–Munk transformation [20]. The amount of sample in the sample-holder was consistent with infinite thickness. The background spectra were recorded with pure KBr. X-ray powder diffraction (XRPD) analysis indicated that grinding of the HAP crystals did not induce any polymorphic transition between forms I and II.

The spectra of saturated solutions of HAP in D₂O (D₂O, Aldrich, 99.9 atom% D) and ethanol (Merck, Uvasol, >99.9 wt%) at 293 ± 2 K, were obtained in a Mattson RS1 FTIR spectrometer, equipped with a wide band mercury cadmium telluride (MCT) detector (4000–400 cm⁻¹), using a horizontal attenuated total reflectance (HATR) accessory with a ZnSe crystal (10 reflections, 4000–600 cm⁻¹). The spectra were scanned at 2 cm⁻¹ resolution, and result from the ratio of the sample single beam to the background single beam obtained for the pure solvent (500 scans each). All solutions were filtered prior to use with a Millex-GV (0.22 μ m) filter.

2.3. Density functional theory (DFT) calculations

To guide the proposed band assignments of solid state spectra of the two HAP polymorphs, DFT calculations on the isolated E and Z conformers (Fig. 1) were performed using the Gaussian-03

3

package [21]. Full geometry optimizations and vibration frequency predictions were made using Becke's three-parameter hybrid method [22] with the Lee, Yang, and Parr (LYP) [23] correlation functional (B3LYP), and the cc-pVTZ [24,25] basis set. The corresponding molecular energies (*E*) were obtained from Eq. (1) [26]:

$$E = V_{\rm NN} + H^{\rm CORE} + V_{\rm ee} + E_{\rm X}[\rho] + E_{\rm C}[\rho]$$
⁽¹⁾

where $V_{\rm NN}$ is the nuclear–nuclear interaction, $H^{\rm CORE}$ is a mono–electronic contribution to the total energy, including electron kinetic and electron–nuclear interaction energies, and $V_{\rm ee}$ is the coulombic interaction between the electrons. The terms $E_{\rm X}[\rho]$ and $E_{\rm C}[\rho]$ represent the exchange and correlation energies, respectively, functionals of the electronic density ρ . The calculated frequencies were used without scaling. Total energy distribution (TED) analysis of the theoretical vibration spectra was performed by using the VEDA 4 program [27].

3. Results and discussion

3.1. Vibrational analysis of the solid phase spectra

Fig. 4 shows an overlay of the DRIFT spectra of both forms of 4'hydroxyacetophenone in the whole mid infrared range. Table 1 includes the proposed band assignment, as well as the comparison of the experimental band positions with those calculated by DFT for the isolated *E* and *Z* molecular conformations (Fig. 1). Full assignment of the calculated vibrational modes and the corresponding total energy distribution (TED) are given as Supporting Information (Table S1).

The different relative orientations of the OH and CO groups hardly affect the calculated frequencies for the isolated molecules, with very few exceptions, assigned majorly to HCCC out-of-plane deformations of the ring (see Table S1 given as Supporting Information), at 818/830, 867/855, 959/977, and 1012/1000 cm⁻¹ for conformers E/Z respectively. On the other hand, the different packing motifs in the two crystalline forms originate striking differences between the spectra of the two polymorphs. These deserve a general comment.

As predicted by the DFT calculations, the position of the OH stretching band is expected well above 3600 cm⁻¹ for free or weakly interacting hydroxyl groups. The shifts towards much lower wavenumbers observed in the spectra of the solid phases indicate that these groups are involved in hydrogen bonds, stronger



Fig. 4. DRIFT spectra of the two forms of 4'-hydroxyacetophenone, taken at 293 ± 2 K: form I corresponds to the red line and form II to the black line. The spectra were normalized at the carbonyl stretching mode (1661 and 1645 cm⁻¹, respectively, for forms I and II). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)





Fig. 5. Enhanced spectral regions between (a) 1750 and 900 cm⁻¹ and (b) 900 and 400 cm⁻¹. Form I, red line; form II, black line. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

in form II (the band maximum occurs at 3124 cm^{-1} , instead of 3308 cm^{-1} for form I) and in a wider diversity (the band is much broader: $\sim 380 \text{ cm}^{-1}$ of full width at half maximum, compared with $\sim 270 \text{ cm}^{-1}$ for form I) [28]. These may be, in principle, OH···OH or OH···O=C intermolecular hydrogen bonds, where the basicity of the acceptor oxygen is enhanced by electron delocalization of the π system in the adjacent benzene ring. Resonance-assisted hydrogen bonding (RAHB) occurs in systems where electron delocalization is responsible for decreasing the electron density of the donor and increasing the basicity of the acceptor [28,29].

The observation that the H-bonds are more diverse and stronger in form II than in form I agrees with the single crystal X-ray diffraction results mentioned in the Introduction, which indicate that [9]: (i) form I exhibits a single type of O1H...O2 H-bond while two types are present in form II; (ii) albeit slightly shorter $d_{01...02}$ bond lengths are observed in form I ($d_{O1...O2}$ = 2.676 ± 0.002 Å in form I and $d_{O1...O2} = 2.707 \pm 0.002$ Å or 2.739 ± 0.003 Å in form II), the $O1H \cdots O2$ angles are closer to 180° in form Π $(O1H \cdots O2 = 160 \pm 2^{\circ}$ in form I and $O1H \cdots O2 = 166 \pm 3^{\circ}$ or 178 ± 3° in form II); (iii) in form II the O1H...O2 H-bonds are reinforced by C8H···O2 intermolecular contacts, which are absent in form I. Stronger H-bonds may also be reflected by the finding that the lattice energy of form II at 298 K, obtained from solution calorimetry measurements, is 0.49 ± 0.13 kJ mol⁻¹ higher than that of form I [9].

In the wavenumber range between \sim 3100 and \sim 2800 cm⁻¹, the DRIFT spectra of both forms present a number of bands, overlapped with the vOH band. They are assigned to CH stretching modes,



Fig. 6. Comparison of the DRIFT spectra of form I HAP (red line) and its deuterated isotopomer (black line) in the wavenumber ranges: (a) $3800-2040 \text{ cm}^{-1}$; (b) $1750-1050 \text{ cm}^{-1}$; (c) $1100-400 \text{ cm}^{-1}$. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

both of the ring and of the CH₃ group; in the case of the methyl group, the presence of overtones of the symmetrical deformation enhanced by Fermi resonance with the stretching modes renders the assignments tentative [30]. The frequency of the $v_{as}CH_3$ mode has been related to the H–C–H angle, wider angles corresponding to higher stretching frequencies. The interactions of the methyl group with a lone electron pair of a neighbor atom may be responsible for lowering the stretching frequencies, and a preferential interaction of one CH bond may render the three bonds non-equivalent, resulting in multiple stretching bands [31]. Taking into account that the calculated frequencies are very similar for both conformers, any shifts observed in the spectra are due to intermolecular effects. Relying on the proposed assignments (Table 1), the frequencies and relative intensities of the methyl stretching bands of the two forms of HAP indicate that the vicinity of these groups is very different. The much lower wavenumber of the $v_{as}CH_3$ mode in

Table 1

Proposed band assignment of the DRIFT spectra of forms I and II HAP. Comparison with the unscaled wavenumbers calculated at the B3LYP/cc-pVTZ level of theory for the corresponding *E* and *Z* molecular conformations in the gas phase^a.

E conformation	Form I	Z conformation	Form II	Assignments
B3LYP/cc-pVTZ	Exp ^b	B3LYP/cc-pVTZ	Exp ^b	
427	418 _w	427	439/432 _w	γ CCC (ring, op def.)
473	490 _m	474	483 _w	δCCC
509	498 _m	509	500 _w	γOCC (op def.)
579	569 _s	578	574 _m	δO=CC (ip def.)
602	590 _m	602	593 _m	$\gamma O = CCC(ring, op def), \tau CH_3$
653	637 _w	653	638 _w	δCC (ring, ip def.)
694	668/690 _m	693	698 _w	γCOH (op def.), vCC
818	727 _w	830	725 _w	γHCCC (ring, op def.)
848	817 _m	848	785 _{m,br}	vC===C(ring)
867	849 _s	855	837 _{VS} /822 _{sh}	γHCCC (ring)(op def.)
958	963 _s	959	966s	ρCH ₃
1012	1005 _{vw}	1000		γHCCC (ring)(op def.)
1050	1022 _m	1050	1026 _w	τCH ₃
1093	1075 _m	1093	1084 _m	vC—C
1131	1108 _m	1132	1115 _m	δHCC (ring, ip def.)
1284	1167 _{VS}	1284	1171 _s	vCC, vC===C(ring)
1191	1219 _{VS}	1195	1235 _s	δHOC (ip def.), δHCC (ring, ip def.)
1301	1260 _w /1279 _{VS}	1299	1252 _m /1282 _{VS}	vC—O (phenol)
1338	1302 _w	1338	1309 _m	δHC (ring)
1390	1357 _{VS}	1391	1365 _s	$\delta_s CH_3$
1473	1427 _m	1473	1437 _s	$\delta_{as}CH_3$
1472	1444 _m	1469	1441 _s	vC===C(ring)
1547	1513 _s	1546	1514 _m	δHC (ring)
1623	1577 _{VS}	1627	1584 _s	vC===C (ring)
1649	1602 _{VS}	1647	1597 _s	vC===C (ring)
1744	1661 _{VS}	1744	1645 _s /1628 _w	νC=0
	1800-2800		1800-2800	Overtones, combinations
3035	2799 _w	3036	2816 _m	v _s CH ₃
3090	2997 _m	3090	2964 _w	v _{as} CH ₃
3142	3045 _w	3143		v _{as} CH ₃
3156	3071 _w	3153	3016 _m	vCH (ring)
3194	$\sim 3214_{sh}$	3201		vCH (ring)
3812	3308 _s	3811	3124 _s	νОН

^a Data in cm⁻¹.

^b DRIFT spectra, this work: VS – very strong; S – strong; m – medium; w – weak; vw – very weak; op def. – out of plane deformation; ip def. – in plane deformation.

form II (2964 vs 2997 cm⁻¹ in form I) suggests stronger intermolecular interactions, in good agreement with the C8H····O contacts proposed by X-ray diffraction [32].

Other spectral details are better analyzed by enhancing the lower wavenumber regions (Fig. 5). The frequency of the vC=O mode is very sensitive to the group involvement in hydrogen bonds as electron donor [33]. In the free HAP molecule, this mode is typically expected above 1700 cm⁻¹, as obtained by DFT calculations, even taking into account the participation of the group in the resonant system. In the spectrum of form II, the vC=O band presents the largest shift towards lower wavenumbers (1645 cm⁻¹), which means a stronger involvement in hydrogen bonds than in form I (where it appears at 1661 cm^{-1}). This is consistent with the analysis of the OH stretching bands presented above. It is not, however, reflected by a longer C=O distance in form I than in form II, possibly due to a charge compensation by resonance with the aromatic ring. Note that the differences in the $d_{C7...O2}$ bond distances for the two polymorphs $(1.231 \pm 0.002 \text{ Å} \text{ and } 1.224 \pm 0.003/$ 1.226 ± 0.003 Å, respectively for forms I and II) are essentially within their combined uncertainty intervals.

Because the vC=O bands are narrow (the FWHH is 16 cm⁻¹ in form I and 19 cm⁻¹ in form II), it appears that the hydrogen bonds of the carbonyl groups in each individual polymorph are almost identical. The very slight broadening of the C=O band in form II relative to form I, as well as the presence of a second weak component, may be explained by the existence of the C8H…O2 intermolecular contact ($d_{C8H...O2} = 3.582 \pm 0.004$ Å), which is absent in form I.

Different vC—C bands are expected, since these modes are responsive to distortions of the benzene ring, to the character of

the substituents and the resulting charge density distribution [34]: the doublet at \sim 1580/ \sim 1600 cm⁻¹ is characteristic of para substituted aromatic rings and the splitting is known to gain importance when the two substituent groups have different electron donor/acceptor nature [35]; although the two groups are the same in both HAP forms, (COCH₃ and OH), the doublet is much better defined in the spectrum of form I; it appears that the same substituent groups acquire different electron donor/acceptor character in this spatial arrangement, yielding an asymmetric electronic distribution. The vC==-C and $\delta_{as}CH_3$ modes are well resolved in the spectrum of form I, at 1444 and 1427 cm⁻¹, respectively, the assignment being confirmed by comparison with the deuterated form I (see below). In form II, these modes appear overlapped at 1441/1437 cm⁻¹. This is due to a significant shift of the $\delta_{as}CH_3$ mode to higher wavenumbers, in good agreement with the shift observed in the $v_{as}CH_3$ induced by selective interactions of C8H.

In the two forms there are bands characteristic of *para* substituted phenols [36,37]. The stronger ones are assigned to the vC–O, δ HOC and γ COH modes of phenol, that appear at 1279/1260, 1219 and 668/690 cm⁻¹ in form I, respectively, and at 1282/1252, 1235 and 698 cm⁻¹ for form II. Confirmation that the OH groups of form I are involved in stronger hydrogen bonds than those of form I is obtained from the analysis of the COH deformation modes: the in plane (δ COH) mode, with maximum at 1219 cm⁻¹ for form I, appears shifted to 1235 cm⁻¹ in phase II, partially overlapped with the vC–O mode at 1252 cm⁻¹; the out-of-plane (γ COH) mode in the spectrum of form I is very broad, relatively much stronger (more allowed due to larger distances between neighbor molecules), and shifted to a lower wavenumber (668 cm⁻¹ instead of 698 cm⁻¹ for form II). In addition, the splitting of the vC–O mode



Fig. 7. Comparison of the ATR spectra of HAP in D_2O (blue line) and in ethanol (green line) solution with the DRIFT spectra of forms I (red line) and II (black line) in two spectral regions. The spectra were normalized to the carbonyl stretching band. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

is clear in form II, probably due to the diversity of hydrogen bonds, whereas in form I the two components are partially overlapped.

So far, the observations from the DRIFT spectra suggest that strong intermolecular hydrogen bonds are established between the carbonyl and hydroxyl groups in both HAP forms. These bonds are clearly stronger in form II: the carbonyl groups establish soft interactions with C8H, in good agreement with the X-ray diffraction results, and the hydroxyl groups form different types of hydrogen bonds with OH and CO, and also establish weak contacts with other CH groups.

In order to confirm the band assignments proposed in Table 1, the DRIFT spectrum of form I deuterated at the OH was analyzed. The two spectra of form I are compared in Fig. 6.

The efficiency of deuteration is demonstrated by the appreciable intensity loss of the bands related with the OH groups: vOH at 3308 cm⁻¹, δ HOC at 1219 cm⁻¹, and γ COH at 668/690 cm⁻¹. The vOH band does not shift and becomes much narrower, which shows that the small fraction of remaining OH groups is involved in fewer types of hydrogen bonds. The new strong band that appears at 2464 cm⁻¹ is assigned to hydrogen bonded OD groups [38]. The assignments of the CH₃ and of the aromatic CH modes are confirmed and their frequencies do not shift beyond spectral resolution.

3.2. Vibrational analysis of the spectra in solution

As previously mentioned, the crystallization of HAP from water leads to form I while form II is obtained when the solvent is ethanol [9]. These forms differ not only in packing but also in the conformation adopted by the HAP molecule (Fig. 1): E in form I and Z in form II. To analyze if there was a relationship between the molecular conformation of HAP present in solution and the obtained polymorph, the ATR spectra of saturated solutions of HAP in heavy water and in ethanol were compared. Deuterated water was preferred, to avoid the OH bands of water. Cancellation of the solvent bands was achieved by using the spectrum of the corresponding solvent as background, and further subtracting the ATR spectrum of the solvent multiplied by the appropriate factor. The correlation of the species in solution with each HAP polymorph is not straightforward, because the H-bond interactions of HAP with the solvent may replace those between the HAP molecules in the crystal phase and modify the spectra. Keeping in mind that the bands related to the hydroxyl and to the carbonyl groups are the most affected by H-bonding, the comparison between the spectra in solution and those of the two HAP forms was made in two regions related with the CC stretching modes and the CH (ring) deformations, namely $1550-1630 \text{ cm}^{-1}$ and $800-880 \text{ cm}^{-1}$ (Fig. 7).

The splitting of the vC—C bands at 1577/1602 cm⁻¹ is extremely clear in the spectrum of form I, and the same is true for HAP in D₂O solution (1578/1601 cm⁻¹), whereas the smaller splitting in ethanol solution (1582/1600 cm⁻¹) is more similar to that in form II (1584/1597 cm⁻¹). The out of plane γ HCCC and vC—C (ring) modes, at 849 and 817 cm⁻¹ in form I, appear at close frequencies in D₂O solution (843 and 814 cm⁻¹). In form II and in ethanol solution the patterns are comparable: the out of plane γ HCCC mode appears at 837 or 839 cm⁻¹, with a shoulder at 821 or 820 cm⁻¹. Therefore, the ATR results indicate that the molecular conformation of form I (*E*) prevails in ethanol. This suggests that there is indeed a relationship between the nature of the predominant solution species and the nucleation of a specific HAP polymorph.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.molstruc.2013. 11.050.

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