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Study of Water Adsorption on Organics Crystal Surfaces Using a Modified X-ray Photoelectron Spectroscopy Instrument

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S Supporting Information

ABSTRACT: The coupling of a high partial pressure water vapor system to a conventional X-ray photoelectron spectroscopy instrument for use with both organic powders and single crystals is described. The modified chamber serves a dual purpose as both a treatment and sample preparation apparatus. The design utilizes the high- and cryo-temperature capabilities of the existing system to allow investigation of various states of surface water, as well as the interplay between temperature, water, and surface structure of the substrate. Sample handling and methods for compatibility testing are detailed, and data illustrating the application of the modified and integrated capabilities are summarized, detailing novel studies on the state of water on the surface of model organic pharmaceutical salts. In addition to facilitating investigation of the presence of various states of water at the surface of organic material, namely, dissociated versus molecular water, the setup allows the investigation of structural effects of the surface on the state of water.
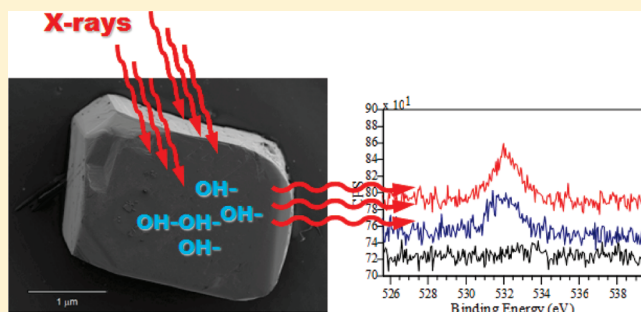
The presence of water at surfaces or interfaces is an important issue across a diverse range of fields,[1−4] from atmospheric aerosols to food chemistry to catalysis to biomaterials, due to its influence on surface chemistry and properties. The polar nature of water, its ability to ionize, and its unique properties as a solvent and adsorbate are all important properties that need to be considered. Surface water plays a major role in instabilities of crystalline pharmaceutical solids, aiding or catalyzing reactions such as hydrolysis, oxidation, and deamidation, as well as phase transformations.[5−8] Since control of these reactions is essential for the successful development of new therapies, knowledge of the state of surface water, the role of substrate and the mechanistic role of surface water as a mediator of physical and chemical stability of the substrate is crucial. Despite this importance, the state of water on the crystalline organic surfaces is a largely unexplored field, due in large part to incompatibilities of such materials with ultra high-vacuum techniques. The need to develop techniques which accommodate organic and biological materials cannot be overstated.

In recent decades, the state of water has been extensively studied on the surfaces of various metals, metal oxides, and certain inorganic salts, with many studies providing evidence for the existence of a chemisorbed dissociated state of water.[1,2] X-ray photoelectron spectroscopy (XPS) is a surface technique frequently used to investigate the interaction of water with various surfaces. Its prominence in the surface science field is due to its excellent quantitative ability as well as its powerful ability to provide intricate detail on the chemical environment of surface atoms. One of the underlying problems specific to XPS is the tendency for X-ray beam damage of organic samples.

Further difficulties are encountered with the accompanying intention of studying the effects of adsorbed moisture under controlled conditions of gaseous water. One of the foremost reasons for the incompatibility of XPS, likewise other surface techniques, with high gas pressures is the attenuation of the signal by inelastic collisions with gas-phase molecules at pressures above ultrahigh vacuum conditions. Also, there exists a "pressure gap" between the modeling of the kinetics of adsorption and catalytic reactions under high vacuum and those experienced at high pressure conditions;[9−11] normally pressures of at least a few Torr but frequently higher (∼1 atm) are required for activation or sufficient reaction rates to be observed.[12,13] This gap has been bridged in recent years by using differentially pumped stages in the analysis chamber,[10,11,14−24] allowing operating pressures above 5 Torr. However, such systems cannot inherently be used to investigate surface effects or chemical states "activated" at vapor pressures relevant for samples exposed to ambient conditions, particularly organic solids. This is not a trivial issue since organic surfaces are very different energetically from their inorganic counterparts, and the system design described herein depends critically on the existence of adsorbed water stable at UHV conditions either at room temperature or at cryo-temperatures. Herein we describe the design and construction of, as well as results from an experimental setup for analysis of the state of surface adsorbed water on organic surfaces and possible effects of the surface structure.

■ METHODS AND MATERIALS

For details of the synthesis of single crystals of clonidine HCl and crystalline clonidine HBr, as well as information on the XPS instrumentation, the reader is referred to the Supporting Information.

■ RESULTS AND DISCUSSION

In order to overcome limitations of traditional XPS instrumentation for successful realization of the goal of probing surface water on organic salts, the following capabilities were sought: (a) perform exposures of organic samples to elevated water vapor pressures (up to 98% relative humidity) typical of relevant ambient conditions; (b) high- and low-temperature analysis of samples coupled with the capabilities of part a; (c) cleave single crystals within an ultrahigh vacuum environment to give new, clean surfaces without the presence of oxygen-containing species which may interfere with the O 1s signal of water species; and (d) pre- and post-treatment analysis without exposure to ambient air. The above objectives were met via successful design and implementation of an ambient-pressure compartment in-line with the analysis chamber as well as a suitable sample holder and cleaving apparatus, with details provided in the Supporting Information. Three organic pharmaceutical salts, the hydrochloride and hydrobromide salts of clonidine, an α-adrenergist agonist, and the dihydrochloride salt of trifluoperazine, an antipsychotic, were selected for use in this work. The following describes application of the modified system described above to investigate the state of water and the effect of surface structure for these model organic salts.

Investigation of Dissociated Water. In a recent study, the presence of chemisorbed, dissociated water adsorbed on the surface of two organic hydrochloride salts, clonidine HCl and trifluoperazine di-HCl was demonstrated.[25] As a much more reactive species,[1] the dissociated form may have a role in initiating some of the surface degradations common for pharmaceutical compounds. Therefore it is important to further investigate this phenomenon. It was of particular interest to probe the ability of the surface of an alternate halide salt to potentially induce dissociation upon exposure to water vapor. The presence or absence of dissociated water on clonidine HBr was inferred from the binding energy of the O(1s) peak. While molecular water typically shows an O(1s) peak with a BE in the range of 533−535 eV, dissociated water has a peak at a lower BE (530−532 eV) due to the reduced Coulombic interaction between the photoemitted electron and the ion core of oxygen. Initial analysis of a freshly prepared powder sample of clonidine HBr showed no evidence of the presence of either form, based on the absence of any O(1s) signal. The absence of molecular water is to be expected at ambient temperature under UHV. After transfer to the LC, exposure to high vapor pressure (90% RH) for 2 h, subsequent degassing, and transfer to the analysis chamber, analysis showed the emergence of a peak indicative of dissociated water at approximately 532 eV (see Figure 1), corresponding to a level of 0.6%, similar to levels observed previously for the HCl salt. Also shown in Figure 1 is the O(1s) peak for a powdered sample of clonidine HCl after exposure at 90% RH. The observation of the presence of the dissociated species of water on a second halide salt of clonidine is important since it illustrates that this phenomenon is not restricted only to HCl salts but in fact is likely to be a more widespread phenomenon.

Effect of Temperature on Dissociated Water. As stated previously, molecularly adsorbed water, which interacts with
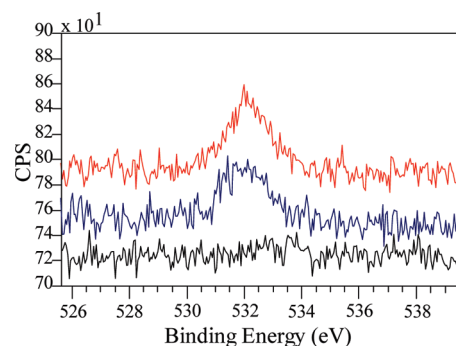

Figure 1. O(1s) photoelectron spectra of a powder sample of clonidine HBr: initial spectrum (black), spectrum following exposure for 2 h at 90% RH (blue), and spectrum for clonidine HCl after exposure at 90% RH (red).

Table 1. Elemental Compositions (%) of Oxygen for Powder and Cleaved Samples of the [100] Face of Clonidine HCl, before and after Exposure to Moisture Both with and without Preannealing

no annealing pre-exposure	initial	after exposure to 90% RH for 60 min	after heating to 353 K	after heating to 413 K
powder	0.07	0.45	0.59	1.17
cleaved [100]	0.24	0.73	0.83	1.38

annealed at 373 K pre-exposure	initial (after annealing)	after exposure to 90% RH for 60 min	after heating to 413 K
powder	0.26	0.59	0.62
cleaved [100]	0.24	0.87	0.86

organic surfaces via interactions such as hydrogen bonds, dipole—dipole interactions, and van der Waals forces, does not form sufficiently strong interactions with the surface to remain adsorbed under UHV conditions. In contrast, dissociatively adsorbed moisture can be detected even at ambient temperature as a consequence of the much stronger interactions with the surface. It is thus of interest to probe the effects of temperature on surface dissociated water in order to evaluate its persistence or lack thereof at elevated temperatures. To do this, clonidine HCl was investigated both as freshly prepared powder and a single crystal cleaved (under ambient conditions) parallel to the [100] face. Following exposure to moisture at 90% RH within the LC for 1 h, the samples were heated to 353 K then 413 K for periods of 1 h. Analyses were performed initially and again following each treatment; thus, no exposure to ambient gases following the initial analysis occurred. Initially minimal amounts of oxygen characteristic of dissociative water adsorption were present on both the powder and single crystal samples (see Table 1). Significant increases of similar magnitude were observed for both following water exposure, and interestingly, the level again increased noticeably after each temperature increment, albeit heating occurred under vacuum. This increase at elevated temperatures suggests not only that dissociated water is able to persist at the temperatures studied but also that there was migration of additional dissociated water species. The lack of desorption of the adsorbed species at temperatures as high as 413 K confirms the chemisorbed nature of the interaction.

To further probe these observations, fresh powder and cleaved samples were preheated at 373 K, in an attempt to anneal surface defects thought to be responsible for the dissociation and subsequent migration. Again, a small amount of surface oxygen was initially present, with a BE characteristic of dissociatively adsorbed water. While significant increases, similar in level to the unannealed samples, were still observed upon exposure to the identical vapor pressure (Table 1), neither sample showed noticeable changes in the levels following heating postexposure to 373 K. The results presented above suggest either (a) the annealing, during preheating, of subsurface regions containing active defect sites; these defects may have been responsible for the increase in level of dissociative adsorption, during postexposure heating, observed for the unannealed samples due to subsequent migration of the dissociated species or (b) the migration of active sites for dissociation such as an F or H center, under annealing conditions, from a subsurface region into the surface analysis region. Water has been estimated using density functional theory to be highly mobile on the surface of alkali-earth fluorides[26] and may lower the energy barrier for diffusion of vacancies to the surface. Both the large XPS analysis area and the inherent homogeneity of the powder sample suggest the observance of increased OH levels with heating is not due to migration along the surface.

The processing of pharmaceutical organic crystalline materials has been shown to influence the extent of moisture sorption,[27,28] with the results often attributed to the presence of bulk disordered regions. Quantifying the levels of disorder believed to be responsible is nearly impossible below levels of 1%, due to the limitations of commonly used techniques such as X-ray powder diffraction (XRPD). The results here attest to the possibility of defective regions present below the first few molecular layers of the surface, although the effect here may be considered separate or at least more specific than that of bulk mechanically induced disorder. The qualitative similarity in the results between the powder and cleaved samples was somewhat surprising; despite being subjected to less mechanical abrasion, the surfaces produced by cleavage apparently have similar levels of defects active to dissociation. These results highlight the importance of surface and subsurface defects which may be extremely difficult to control despite careful processing techniques; the presence of dissociated water persists regardless of the sample preparation method or attempts to anneal defects.

Investigation of Various States of Adsorbed Water. A cryo-temperature experiment was performed on trifluoperazine diHCl with the primary aim of capturing molecular water on the surface. A freshly recrystallized powder sample was exposed to 60% RH in the load-lock chamber at ambient temperature for 1 h, followed by evacuation of moisture from the chamber using dry nitrogen and then pumpdown, with immediate cooling to 110 K to minimize degassing of the surface water. The sample was transferred immediately to the analysis chamber, also precooled to 110 K, with minimal degassing observed by inspection of the chamber pressure. Pre-exposure analysis had revealed a minor amount of dissociated water, based on the BE of the O(1s) peak at 531.9 eV (Table 2). Analysis following ambient-pressure moisture exposure showed a dramatically increased O(1s) peak with an elemental concentration nearly 2 orders of magnitude larger than initially observed (see Table 2).

In addition, the BE was 533.5 eV, indicative of adsorbed molecular water. This contrasts with previous experiments with the three salts conducted completely at ambient temperature, where solely the dissociated species was observed. Upon equilibration of the sample at ambient temperature, analysis showed

Table 2. O(1s) Elemental Compositions for Recrystallized Sample of Trifluoperazine diHCl

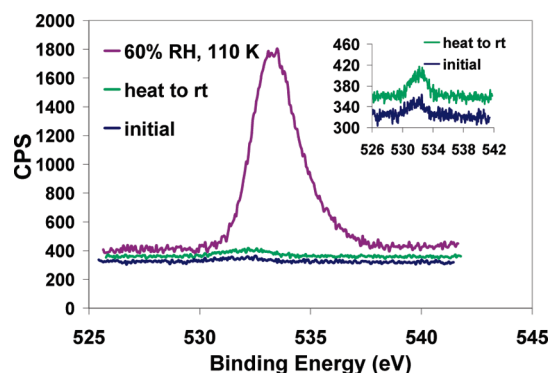|	O(1s)	
	elemental %	O(1s) BE
initial	0.25	531.9
after exposure to 60% RH, then cooled to 110 K	16.9	533.5
heat to 298 K	0.53	532.0

Figure 2. O(1s) photoelectron spectra of a recrystallized powder sample of trifluoperazine di-HCl, analyzed initially, after exposure to 60% RH and cooling to 110 K and finally after warming to room temperature; inset depicts the initial and final spectra after heating to ambient temperature.

the molecular water degassed (see Figure 2), while degassing of the dissociated species, as expected, did not occur. The inset in Figure 2 suggests the electronic identity of the dissociated species, based on binding energy, was unchanged. This instrumental system has thus demonstrated the capability of examining both molecularly and dissociatively adsorbed water present due to adsorption at controlled water pressures representative of ambient conditions. Furthermore, the identification of molecular water provides material-specific evidence differentiating molecular water from the dissociated species.

CONCLUSIONS

The system modifications to the XPS instrumentation described herein have enabled the successful investigation of water on the surface of three model crystalline organic salts, confirming the previous studies identifying dissociated water and providing further investigations. By utilizing the added capabilities, we have succeeded at capturing separate states of water on the surface of the model pharmaceutical salts, making the investigation of surface chemistry and/or structure influenced by moisture adsorbed at the surface a possibility. With the aid of the variable-temperature capabilities coupled with the application of the modified high vapor pressure chamber, annealing experiments highlighted the importance of surface defects capable of inducing dissociation, particularly the existence of sites active for dissociation even with minimally abrasive preparation of surfaces and targeted annealing treatments

ASSOCIATED CONTENT

S **Supporting Information.** Additional information as noted in text. This material is available free of charge via the Internet at http://pubs.acs.org.

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