Physicochemical properties of molecular crystals are significantly influenced by non-covalent interactions and proton transfer. A well known application is the tuning of solubility, bioavailability and stability of pharmaceutical actives through co-crystal (hydrogen-bonding) or salt (ionic, Brønsted acceptors) formation. X-ray Photoelectron Spectroscopy (XPS) is an intrinsically local structural probe, providing information on the chemical state and chemical environment of atoms in molecules and crystals through the photoemission of core level electrons. We have recently studied a wide range of acid-base complexes in molecular crystals and found that analyzing the chemical shifts of N1s core level binding energies provides a facile route for characterizing the chemical and structural changes at functional groups involved in hydrogen bonding and proton transfer [1]. Very importantly, XPS unequivocally distinguishes protonated (salt) from hydrogen-bonded (co-crystal) nitrogen moieties. We have complemented our results for nitrogen species with 15N Solid-State Nuclear Magnetic Resonance (ssNMR) chemical shifts, which reveal low frequency shifts with protonation, but the magnitude of these shifts is additionally influenced by the wider chemical environment [2]. When crystallographic structure information is available, ssNMR shifts can be computationally predicted and thereby related to H-bond lengths, giving a measure of H-bond strength (NMR crystallography). The wide variety of donor/acceptor systems we have investigated has covered a large range of pKa values and demonstrates the generic nature of taking an XPS/ssNMR/XRD approach to organic molecule crystallography (Fig 1). The excellent agreement between the conclusions drawn by XPS and combined ssNMR/CASSET investigations opens up a reliable avenue for local structure characterization in molecular systems even in the absence of crystal structure information, for example with non-crystalline or amorphous matter.