Poster Presentation

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Exploring the salt-cocrystal continuum with ssNMR using natural abundance samples

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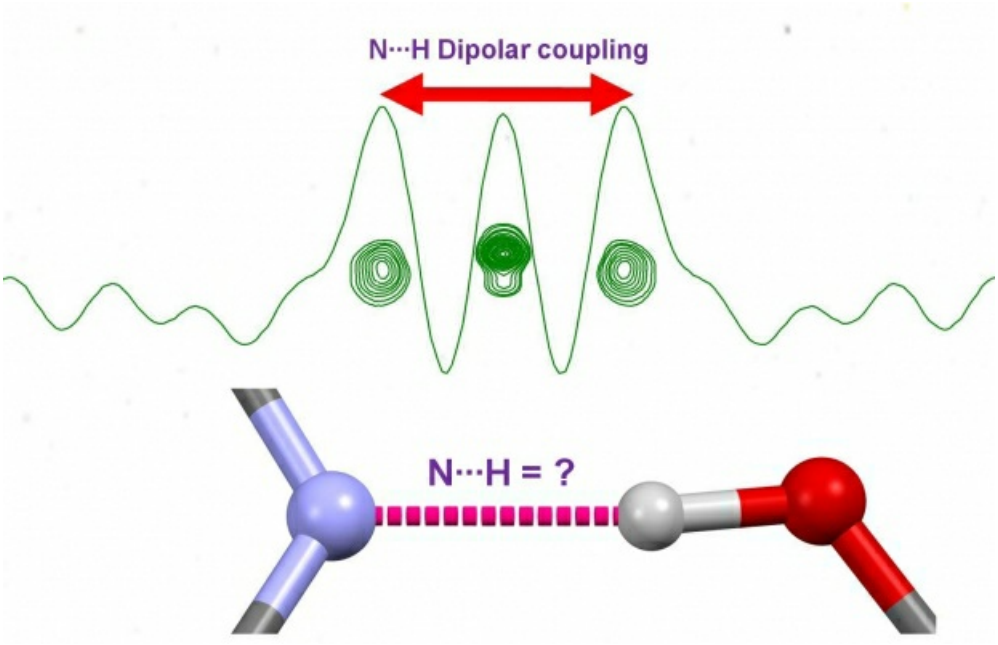
There is a significant recent interest in differentiating multi-component solid forms such as salt, cocrystal, and their continuum, owing to the direct relationship of property to clinical, regulatory and legal requirements for an active pharmaceutical ingredient (API). In this context, detection of the H-atom position in a hydrogen bond X–H•••A–Y is a matter of fundamental and practical importance.[1] In the present study, solid forms of simple cocrystals/salts were investigated by high field (700 MHz) solid-state NMR (ssNMR) technique using the samples with naturally abundant 15N nuclei. Several model compounds in a series of prototypical salt/cocrystal/continuum systems exhibiting the {PyN•••H–O–}/{PyN+–H•••O-} type of hydrogen bonds were selected and prepared. The crystal structures were determined at low temperature and room temperature using X-ray diffraction. Accurate H-atom positions were determined by measuring the 15N–1H distances through 15N-1H dipolar interactions using 2D inversely proton-detected cross-polarization with variable contact-time (invCP-VC) 1H→15N→1H experiments at ultra-fast (vR ≥ 60–70 kHz) magic angle spinning (MAS) frequency.[2] The experiment is sensitive enough to determine the proton position even in a continuum where an ambiguity of terminology for the solid form often arises[3] and can be performed on minimum amounts of microcrystalline or even amorphous solids with natural abundance 15N samples. The crystal structures of the relevant solids have also been determined at a high level of accuracy and the results of the X-ray and NMR experiments are compared. This work has implications in the pharmaceutical industry where the salt/cocrystal/continuum condition of the APIs is seriously considered.

[1] Desiraju, G. R. & Steiner, T. (1999). The Weak Hydrogen Bond in Structural Chemistry and Biology. Oxford University Press.

[2] Nishiyama, Y. et al. (2016). Solid State Nucl. Magn. Reson. 73, 15–21.

[3] Aitipamula, S, et al. (2012). Cryst. Growth Des. 12, 2147–2152.



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