Mechanochemical reactivity of halogen-bonded materials: computational prediction of reaction outcome and spectroscopic monitoring

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Halogen bonding interactions formed between electrophilic region of the halogen atom (σ-hole) and electrophilic acceptor atom or functional group, have become a prominent force in crystal engineering, and an alternative to widely-used hydrogen bonding. Design of halogen-bonded molecular multicomponent crystals (cocrystals) has gained traction, with a great potential for constructing new supramolecular architectures, involving elements from the lower rows of the Periodic Table.

This presentation will show how computational methods, specifically periodic density-functional theory (DFT) calculations offer wide opportunities in predicting and rationalizing solid-state reactivity of halogen-bonded materials, provide insights into their electronic structures and facilitate spectroscopic *in situ* monitoring of mechanochemical transformations.

The presentation will commence with the demonstration of how periodic DFT calculations in combination with experimental dissolution calorimetry measurements can be used to predict the thermodynamic possibility of mechanochemical coformer exchange reactions in halogen-bonded two- and three-component cocrystals.[1,2] It will be shown that the sign of the DFT-calculated reaction energy is an excellent predictor for the possibility of the reaction occurring under experimental conditions, while comparison with the calorimetric data provides quantitative verification of the accuracy of the DFT-calculated energies.

The presentation will continue with the discussion of the accuracy of periodic DFT calculations, depending on the choice of the functional and dispersion correction scheme. Since the fundamental property modelled in a DFT calculation is electron density distribution, it will be shown how experimental charge density analysis by X-ray diffraction can be used to assess the accuracy of charge density distributions in halogen-bonded materials calculated by DFT.

Finally, it will be shown how low-frequency Raman spectroscopy in conjunction with periodic DFT calculations, provide a new approach for *in situ* monitoring of mechanochemical cocrystal reactions.[3] The low-frequency Raman spectroscopy, defined as the 0-200 cm^{-1} frequency range, corresponds to intermolecular vibrations, which makes the spectral signal very sensitive towards changes in crystal packing. Yet, assignment of individual low frequency Raman bands to particular types of atomic motion, is far more challenging than in the fingerprint region. With the aid of dispersion-corrected periodic DFT calculations, however, normal mode vectors corresponding to each Raman band can be directly visualized, making for an excellent aid in assigning the experimental spectra and gaining microscopic insights into the dynamic behaviour of molecules in solid state, and monitoring the evolution of crystal packing in real time.

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[2] Kumar, L., Dash, S. G., Leko, K., Trzybiński, D., Bregović, N., Cinčić, D. & Arhangelskis, M. (2023). *Phys. Chem. Chem. Phys.* **25**, 28576.

[3] Borchers, T. H., Topić, F., Arhangelskis, M., Ferguson, M., C. B. Lennox, C. B., Julien, P. A. & Friščić, T. (2025). *Chem* , **11**, 102319.