Project 18: ***Supramolecular solid state switches*** Date: **20/08/10**	Author: **Carla A. Daly** Strand: **Particle Engineering** Institute: **University College Cork**

Title: The rational design of a hydrogen bond molecular switch directed by the oxidation level of sulfur.

The solid state physical properties of organic compounds are critically important to their application as pharmaceuticals. Solid pharmaceuticals exist as polymorphs, solvates or amorphous forms which gives rise to measureable differences in physical properties and processing. The particular form determines the physicochemical properties of the drug such as its hygroscopicity, bioavailability, solubility, stability and dissolution rate.[1]

Advances in crystal engineering and supramolecular chemistry has lead us to consider new perspectives of the various solid state forms that molecules may adopt in terms of molecular assemblies. Control of the physical properties demands an understanding of the nature of interactions between molecules in the solid state at a fundamental level.[2, 3]

Principle Focus: This research focuses on the solid state properties of API-like molecules, with the objective of developing an understanding of how the molecular structure of the compounds impact upon the solid state crystalline structure and, in particular, to probe the relative importance of different intermolecular non-covalent interactions. The work focuses specifically on a series of organosulfur compounds – these were selected for two reasons: firstly systematic variation of the sulfur functional group for example through oxidation alters the molecular properties in a predictable manner thereby providing an interesting series of related compounds for investigation; secondly many API's are organosulfur compounds and therefore the insight produced is directly relevant to the field of pharmaceutical solids.

Previous research in the group reported that terminal alkynes acted as the key H-bond donor in sulfides but in sulfoxides/sulfones the hydrogens α to the sulfur were involved. When a methyl substituent was introduced at the α-position, it blocked the competing H-bond donor and the terminal alkyne re-emerged as the H-bond donor.[4, 5]

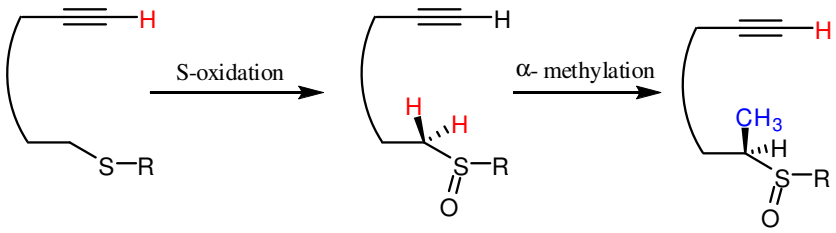

Figure 1: Solid State interactions between alkynes and sulfoxides.

Discussion: The design and synthesis of compounds containing terminal alkynes, sulfur moieties and hydrogen bond acceptors were successfully achieved. The solid state interactions of these novel compounds were also explored.

Future Work: The design and synthesis of further compounds based on knowledge acquired from previous compounds synthesized will be explored so that intramolecular hydrogen bonding can be studied. Also the impact of chirality will be investigated e.g. sulfoxides.

References:

1. Huang, L.F.; Tong, W.Q.; *Advanced Drug Delivery Reviews*, **2004**, 56, 321–334.
2. Snider, D.A.; *Advanced Drug Delivery Reviews*, **2004**, 56, 391–395.
3. Rodrıguez-Spong, B.; *Advanced Drug Delivery Reviews*, **2004**, 56, 241–27.
4. Lehane, N.K.; Moynihan, E.J.; Brondel, N.; Lawrence, S.E.; Maguire, A.R.; *CrystEngComm*, **2007**, 9,1041-1050.
5. Brondel, N.; Moynihan, E.J.; Lehane, N.K.; Eccles, K.S.; Elcoate, C.J.; Coles, S.J.; Lawrence, S.E.; Maguire, A.R.; *CrystEngComm*, **2010**. **DOI:** 10.1039/c000371a