MS31-P15

Steroids as coformers in cocrystallization of PAHs and heterocycles

Filip Topić [1], Davin Tan[1], Tomislav Friščić[1]

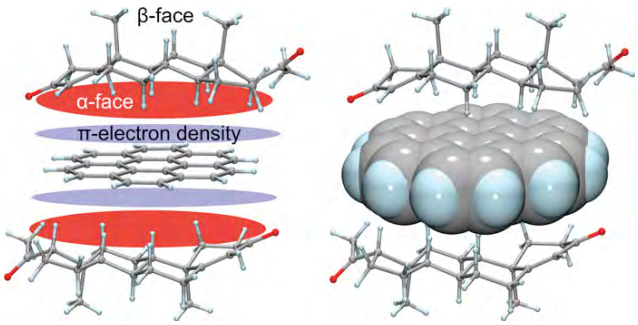
1. Department of Chemistry, McGill University, Montreal, Canada

email: filip.topic@mcgill.ca

Currently, function and biological behaviour of steroids are believed to be mainly determined by terminal chemical groups attached to their backbone. Recently, however, mechanochemical solid-state screening techniques developed by our group revealed there may be another way for steroids to recognize and bind other molecules, named the α···π interaction, so far observed in solid-state complexes of the steroid sex hormone progesterone with electron-rich, planar aromatic molecules (arenes).[1] This interaction takes place specifically between one side of the progesterone molecule, known as the α-face, and the π-electron cloud above the plane of the aromatic molecule. Importantly, the small number of other steroids explored so far suggest that such supramolecular assembly is highly dependent on the fine detail of the steroid backbone,[1,2] thus paralleling their behaviour in biological systems, where small differences in steroid structures are immediately reflected in their biological activities. In the context of supramolecular chemistry, the assembly by α···π interaction can enable the rational design of new solid-state materials with potential use in drug delivery.

We set out to explore the limits of the cocrystallization strategy with progesterone, using larger PAHs such as perylene and coronene, and polyaromatic heterocycles such as phenanthridine, phenanthroline and others. The cocrystal screening was conducted mechanochemically, i.e. by liquid-assisted grinding, and the successful formation of a cocrystal established by powder X-ray diffraction and ATR-IR spectroscopy. A number of cocrystals were successfully obtained and their structures determined by single-crystal X-ray diffraction.

Our results so far demonstrate impressive reliability of the α···π interaction, witnessed by a relatively high rate of successful cocrystallization within the investigated coformers. On the other hand, the stoichiometry of the cocrystals could so far not be accurately predicted in all cases, with all of 1:1, 2:1 and 3:1 steroid-to-coformer stoichiometries observed.



References:

[1] Friščić, T. et al. (2010). Proc. Natl. Acad. Sci. U.S.A. 107, 13216-13221.

[2] Ardila-Fierro, K. J. et al. (2015). Cryst. Growth Des. 15, 1492-1501.

Keywords: steroid, arene, cocrystal