

Young Career Focus: Dr. Zhong Wang (University of Southampton, UK)

Background and Purpose. SYNFORM regularly meets young up-and-coming researchers who are performing exceptionally well in the arena of organic chemistry and related fields of research, in order to introduce them to the readership. This Young Career Focus presents postdoctoral researcher Dr. Zhong Wang (University of Southampton, UK). Zhong Wang was recently awarded the Best Poster prize at The 22nd International Symposium on Fluorine Chemistry (ISFC-22, July 22–27, 2018) in Oxford (UK).

Biographical Sketch



Dr. Zhong Wang

Zhong Wang was born in 1986 in Nantong (P.R. of China) and studied at Donghua University (Shanghai, P.R. of China) and Hochschule Reutlingen (Baden-Württemberg, Germany) obtaining a BSc in chemistry with marketing in 2010. He then moved to University of Southampton (UK) where he completed his MSc (2011) in the synthesis of fluorinated 5-HT₄R ligands and the synthesis of rigid fluorohydrins as models for the investigation of hydrogen-bond donating capacity. In 2016, he received his PhD in chemistry under the supervision of Professor Bruno Linclau. His other experience includes an internship in 2009 at Benecke-Kaliko, Hannover (Germany), conducting research on the coating systems based on NMP-free aliphatic anionic polyurethane dispersions. In 2012 he worked as a marketing supervisor at Shanghai Rainbow Chemistry (P. R. of China), mainly working on overseas market penetration and in 2015 he completed an industrial placement at Dextra Laboratories (Reading, UK) on the synthesis of fluorinated bioactive compounds. He has also attended various conferences, where he has had poster presentations and given oral presentations, and has co-authored several academic papers.

INTERVIEW

SYNFORM *What is the focus of your current research activity?*

Dr. Z. Wang Fluorine introduction is an attractive and effective strategy to modulate chemical and physicochemical properties of organic compounds. Currently, our research interest includes the investigation of the influence of fluorination on molecular lipophilicity and on hydrogen-bond donating capacity of aliphatic fluorohydrins and deoxyfluorinated carbohydrates. I am currently continuing my second postdoctoral research position on these topics in the group of Professor Bruno Linclau at University of Southampton (UK).

SYNFORM *When did you get interested in organofluorine chemistry?*

Dr. Z. Wang I already was interested in chemistry when I was in high school, and I chose chemistry and physics as optional subjects to study for national college entrance examination in P. R. of China. This was then followed by two years of studies in natural sciences in Donghua University (P. R. of China) and a further two years of training in polymer chemistry in Hochschule Reutlingen (Germany). Up until that moment, I was still a stranger to organofluorine chemistry. However, during a research project (synthesizing fluorinated serotonin 5-HT₄R ligands¹) for my Master's degree at the University of Southampton (UK), I was introduced to fluorine chemistry by my supervisor Professor Linclau and was instantly amazed by fluorine's impact on molecular and biological properties. My interest in fluorine chemistry was further enhanced by our unexpected finding of the influence of fluorination on hydrogen-bond donating capacities of conformationally restricted fluorohydrins (Figure 1).² Since then, I have

been exploring the surprising effects of fluorination in model compounds and in bioactive compounds.

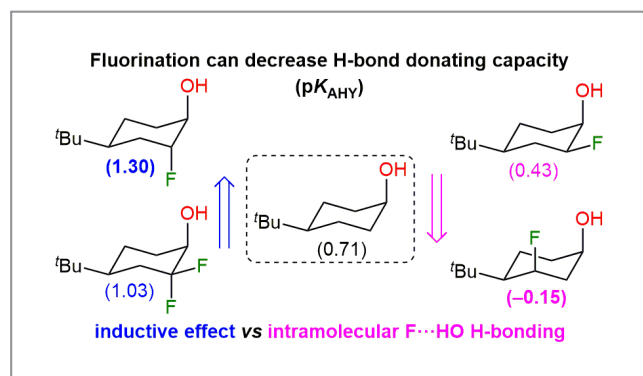


Figure 1 Impact of fluorination on H-bond donating capacity of model compounds²

SYNFORM What do you think about the modern role and prospects of fluorine chemistry?

Dr. Z. Wang From my perspective, organofluorine chemistry is still a vibrant and thriving field. It plays an important role in chemical industry. An obvious example of its success is the application in pharmaceutical industry for drug property optimization. Fluorinated compounds also find key applications in agrochemicals, fine chemicals and materials. In addition, it is worth mentioning that ^{18}F -labelled radiotracers are commonly used in positron emission tomography (PET)

imaging for disease diagnosis and for monitoring treatment effects. During the last few decades, many new fluorinating reagents and new methodologies for the introduction of fluorine atoms and fluorinated motifs have been reported with increasing frequency. This provides even more opportunities for chemists to explore organofluorine chemistry and its applications. Therefore, I think the best era for fluorine chemistry is yet to come.

SYNFORM Could you tell us more about the work that was awarded the Best Poster prize at ISFC-22?

Dr. Z. Wang First of all, I would like to thank the ISFC-22 organizing committee for such an incredible conference, gathering so many great minds from the fluorine chemistry community across the globe. It was truly my honour to present our work at such a conference in Oxford (UK), and also I want to thank all the poster judges for their recognition of our work.

The work I presented in my poster regards our recent findings on the influence of deoxyfluorination on the lipophilicity ($\log P$) of fluorinated monosaccharides and their derivatives, using a straightforward method to determine $\log P$ values based on ^{19}F NMR spectroscopy that we have developed (Figure 2).³ We were able to measure the lipophilicity of a wide range of fluorinated carbohydrates and their derivatives, and we identified interesting trends (comparing numbers of fluorination sites, fluorine motif, and stereochemistry) on carbohydrate lipophilicity. For the first time, we also investigated the $\log P$ differences between anomers of methyl glycosides

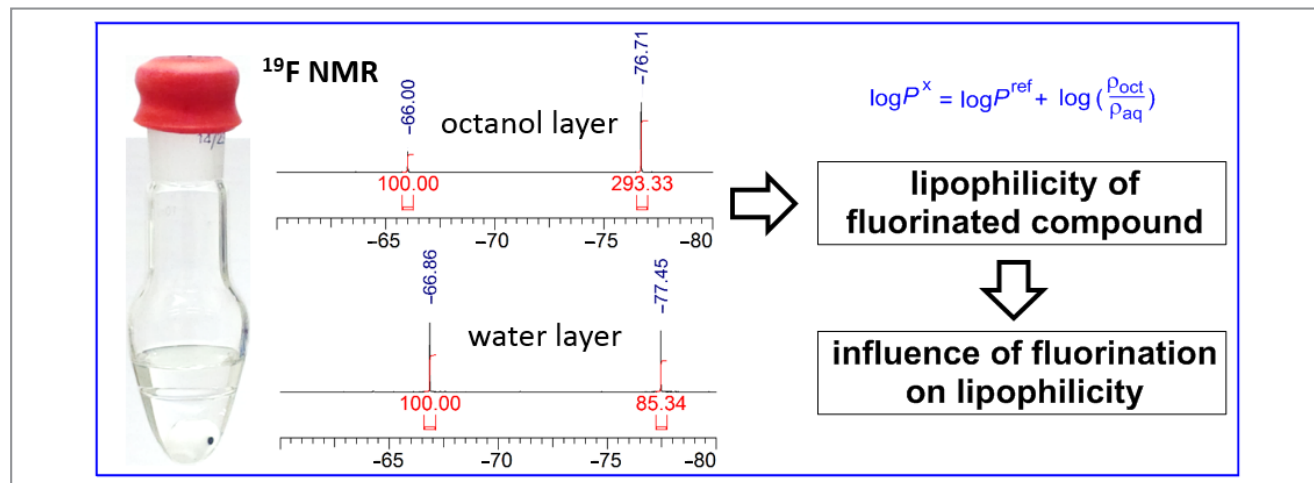


Figure 2 Investigation of fluorination effect on lipophilicity by using a ^{19}F NMR-based method for $\log P$ measurement.³ Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Adapted with permission.

and glycosyl fluorides. As expected, we found that α -anomers of methyl glycosides and glycosyl fluorides are more lipophilic than their respective β -anomers. We have also been able to measure lipophilicities of equilibrating species, such as the anomers of reducing sugars. We will publish the detailed results shortly.

SYNFORM *What are the most important aspects of this work and why?*

Dr. Z. Wang Fluorinated carbohydrates have been used as probes for sugar epitope mapping, mechanism-based inhibitors and for kinetic studies of membrane transport rate in human red blood cells. However, it is difficult to properly interpret the changes in binding data without knowing the lipophilicity difference due to deoxyfluorination. Currently, there is very little information regarding the effect of deoxyfluorination on carbohydrate lipophilicity, which is cumbersome to measure due to the difficulty in quantifying concentrations of non-UV-active compounds. This is why our NMR method, which works equally as well for hydrophilic as for lipophilic compounds (within a $\log P \pm 3$ range), is of interest. While carbohydrates are very hydrophilic and for this reason are perceived as of less interest in drug discovery, we show that deoxyfluorinations rapidly bring their $\log P$ to acceptable ranges: monodeoxyfluorination increases their lipophilicity by 1 $\log P$ unit, dideoxy-difluorination by 2 $\log P$ units, and dideoxy-tetrafluorination by three $\log P$ units. Interestingly, the lipophilicity difference between α - and β -anomers, including between anomers of reducing sugars, can be very large (up to ca. 1.0 $\log P$ units). The findings from this work will contribute to insights into the data interpretation of binding studies involving fluorinated carbohydrates. More broadly, together with our work on other aliphatic fluorination motifs and equilibrating species, an improved and more detailed understanding of the influence of fluorination on lipophilicity will be beneficial in general medicinal chemistry, where control of lipophilicity is one of the most important aims in the drug development process.



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