The Development of New Automated Flow Chemistry Approaches to Synthesise Porous Organic Molecules

Diana Zele

Porous materials with high surface areas and tuneable pore structure can exhibit interesting host–guest behaviour and selective molecular adsorption properties. Most emerging classes of porous materials have coordinatively bonded or covalent extended framework structures, such as metal-organic frameworks[1], and it is often challenging to very finely tune pore size and shape in these materials. Porous organic molecules, in contrast, offer greater synthetic structural tunability, however, their assembly into porous materials is more challenging to control because they assemble via weaker, non-covalent interactions[2].

This project focuses on the development of new porous molecules with bimodal pore structures that can be used as building blocks in the assembly of selectively porous materials.

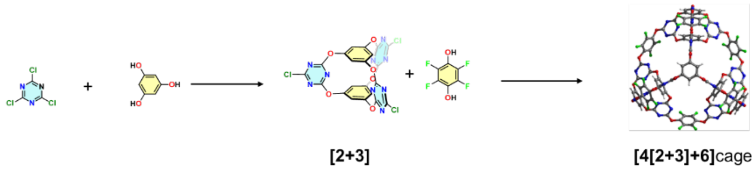

Figure 1 *Two-step hierarchical assembly of "cage of cages".*

The concept builds on a previously reported "cage of cages", synthesised by a two-step hierarchical assembly[2] (Figure 1). In the **[4[2+3]+6]**cage, the smaller **[2+3]** cage is non-porous to gases due to the small pore size. It will be shown that the **[2+3]** cage can be replaced with organic macrocycles, to create a hierarchical assembly with two pores: one from the pre-synthesised organic macrocycles and the other from their assembly into a larger hierarchical macrocyclic assembly. Three derivatives of these macrocycle hierarchical assemblies were successfully isolated.

Further optimisation of the organic macrocycle synthesis using machine learning achieved 64% product conversion after only 10 minutes of residence time, while byproduct formation was significantly reduced under flow (7% vs. 25% in batch).

Future work will integrate on-line HPLC into a closed-loop, self-optimising flow system for the synthesis of porous molecules.

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Automating the Vortex Fluidic Device for Photocatalytic Transformations

Fiona Gordon

The Vortex Fluidic Device (VFD) is a microfluidic continuous flow reactor consisting of a high-speed rotating tube (2000 – 9000 rpm).[1] As the rotation speed increases, centrifugal forces push the reaction mixture up the tube, forming thin films on the walls, which create high shear forces resulting in accelerated reaction rates.[1] Previous applications of the VFD include pharmaceutical synthesis,[2] biodiesel production[3] and famously 'unboiling an egg' via protein folding, which won an Ig Nobel Prize.[1]

At Heriot-Watt University, we have automated the injection and recovery of solvent from the VFD to enable the device to operate in continuous reaction mode. We have applied this approach to optimise photochemical reactions, including the oxidation of triphenylphosphine *via* singlet oxygen using a novel heterogeneous photosensitiser coating formed from the visible light catalyst, benzo[*c*][1,2,5]thiadiazole (BTZ). It has been previously shown that singlet oxygen generation with a BTZ polymer can accelerate oxidation reactions.[4] Here, it will be shown that combining BTZ polymer for singlet oxygen production with the VFD's high mass transfer abilities resulted in a substantial decrease in reaction time, from 18 hours for coated glass beads to 6 minutes in the VFD.[5] Furthermore, future work to automate the variation of the VFD's reaction parameters (*e.g.*, tilt angle and rotation speed) with integrated machine learning tools for reaction optimisation will be demonstrated.

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Scotch Whisky: From ground to glass, a chemical analysis of the whisky journey.

Lilian Karim

Scotch Whisky, Scotland's second most productive sector, contributed £5.4 billion to global exports in 2024.[1] At least 3 of our 5 senses are engaged when we pour and enjoy a glass of whisky, these responding to the many different congeners, such as syringaldehyde, furfural and vanillin that enter the headspace; all of which contribute to the experience one has when nosing a glass.[2] Scotch whisky can only be called such once it meets specific criteria outlined in The Scotch Whisky Act 1988 and The Scotch Whisky Order 1990.[3]

This project has been divided into three parts, each contributing to the journey of Scotch Whisky from the ground to the glass.

Part I: Seaweed for peat. Scotland's coastline is home to a diverse array of seaweed.[4] For analysis, a variety of seaweed samples, including sugar kelp, were collected from a beach on the Isle of Harris. Seaweed has been used in numerous food and drink products, such as Harris Gin, which is infused with hand-picked sugar kelp. The analysis of seaweed could potentially reveal whether it can serve as a peat replacement or an additional additive.

Part II: Fermentation tracking by NMR. Fermentation samples were collected from an undisclosed distillery every eight hours, including low wines and the spirit collected at the end of pre-maturation. Using solvent suppression NMR sequences, we dive into the chemical intricacies of whisky, revealing the congeners that develop during the fermentation process.

Part III: Ethanol-water clusters, when experimental meets computational. Congeners may be trapped within ethanol-water clusters, affecting the aromas released when you nose your glass. DOSY NMR confirmed this clustering of ethanol-water around the common ABV% of whisky (40-70%) by showing a lower diffusion value. Using open-sourced Molecular Simulation Design Framework (MoSDeF), we develop extensible molecular simulation workflows for high-throughput screening of water, ethanol and congener mixtures.

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