only allows higher doses to be administered at the site of need, but also increases patient compliance. Targeted or 'smart' drug-delivery is a means of consigning a therapeutic payload to specific locations within the body, and metal-organic frameworks (MOFs) appear ideal candidates for such a purpose: they can be made relatively easily, they have large pores capable of hosting drug molecules and have well-defined molecular structures. What's more, frameworks with extra functionalities can be created by carrying out further chemistry after their initial fabrication in a process termed post-synthetic modification (PSM).

Now, in a collaboration between Jilin University and Beijing Institute of Technology, Ying-Wei Yang, Bo Wang and co-workers have fabricated just such a material. Following self-assembly of zinc ions and dicarboxylate ligands into nanosized MOFs, the team covalently decorated the outer surfaces with pyridinium pendants through PSM. Their pores were charged with an active payload — either rhodamine 6G (a fluorescent dye) or doxorubicin hydrochloride (an anticancer drug) — and then capped by anionic 'pillarenes', which are bulky macrocycles. The binding of these anions was through encapsulation around the cationic pyridinium pendants. This capping was sufficiently effective that the pore openings were blocked and release of the payload in this state was negligible.

Exposure of the MOFs to an acidic environment, such as is present in the vicinity of tumour cells, causes protonation of the pillarenes and their dissociation from the framework surface. With the pores uncapped, the active payload is released into the surrounding medium. Additionally, the MOF possesses properties that are key for *in vivo* implementation, namely, low cytotoxicity with good biodegradability and good biocompatibility. The nanosized crystals are also small enough to be taken up by cells.

## NATURAL PRODUCTS

## **Re-examining resveratrol**

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The apparent health benefits of polyphenolic compounds — such as resveratrol and its oligomers — have attracted a great deal of attention. Their biological activity has been attributed to their ability to act as radical traps — but systematic studies, particularly on the kinetics of these reactions, have not been performed. Now, Derek Pratt and Corey Stephenson from the Universities

of Ottawa and Michigan, respectively, and their co-workers have described a scalable synthesis of two resveratrol dimers — (±)-pallidol and (±)-quadrangularin A — and used the products to evaluate their antioxidant activity.

Biomimetic syntheses of related oligomeric natural products have proved difficult to control. Thus Pratt, Stephenson and co-workers resorted to the use of a resveratrol starting material with two of its phenols protected as ethers and two of its aryl C–H groups — those *meta* to the remaining phenol — masked as tert-butyl groups. On treatment with a ferrocenium oxidant a remarkably chemoselective dimerization occurs, producing a mixture of three diastereomers. Two of these three products — the enantiomers (and not the *meso* product) — undergo two subsequent Lewis acid-catalysed cyclization reactions to produce the 5,5-fused ring system of  $(\pm)$ -pallidol. To gain access to (±)-quadrangularin A, dimerization was followed by a base-induced tautomerization, resulting in the loss of one stereocentre and the E-selective formation of a stilbene-type double bond. The synthesis was completed by Lewis acid-catalysed cyclization followed by removal of the ether and tert-butyl protecting groups.

With these compounds, and their tetrabutylated intermediates, in hand, studies on their radical trapping activities were undertaken. In organic solution - using the alkylated derivatives (for solubility reasons) as a proxy for the natural products — they were found to be no better than the common food additive BHT (butylated hydroxytoluene). When studied in a lipid bilayer the alkylated derivatives were found to be most active, followed by another well-known antioxidant (α-tocopherol) and the natural products themselves coming in third. All of this suggests that the radical-trapping ability of these natural products is not at the heart of their bioactivity. SD

Written by Stephen Davey, Thomas Faust, James Hennessy and Russell Johnson.

## blog<sub>roll</sub>

## **Tasty chemistry**

Chemistry usually conjures up images of sterile or hazardous environments, but there's a mouth-watering side too.

Almost a quarter of the way through the year, the resolutions that many of us made just a few months ago are probably starting to lose their appeal. Food is almost certainly a focus for many of the promises that we made to ourselves, but we shouldn't forsake all thoughts of delicious treats.

Esther Inglis-Arkell, writing at i09, describes (http://go.nature.com/WmfWT2) how chemistry can fool our senses into tasting apple pie even when there is no fruit to be found in the recipe. With some cream of tartar, Ritz crackers and cinnamon, you can create an 'almost real' apple pie despite the fact that real apples are just budding in the orchard.

Over at Food Chem Blog, Emily Buehler covers (http://go.nature.com/6xs76q) how bread goes stale, including some tips on how to store your bread for maximum shelf-life. Importantly, she also highlights the Twitter hashtag #breadchat for all bread enthusiasts. At the same time, Compound Interest's Andy Brunning published a handy graphic on the Maillard reaction (http://go.nature.com/T7MUKD) showing how it affects the flavours, aromas and colours of food during cooking.

Getting out of the kitchen and into the fresh air, Justin Brower at Nature's Poisons recounts his hijinks with growing horseradish and the chemistry behind why it smells so spicy (http://go.nature.com/1FudVm). He ropes his unwitting father into his experiment and outlines some of the reactions that happen in the plant as it gets turned into a condiment.

Everyone is familiar with cooking and baking on some level and these posts demonstrate that the connection between cooking and chemistry can help to explain basic scientific concepts to a wider audience.

Written by Joseph Meany, who blogs at http://jsphmeany.blogspot.com