NATURAL PRODUCTS

Crowdsourcing drug discovery

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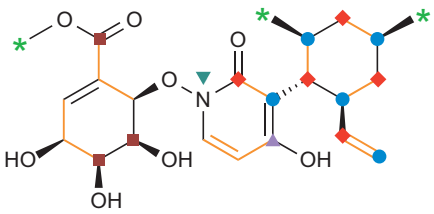

Fungal natural products include a diverse range of chemical structures and often possess interesting biological properties — such as anticancer or antimicrobial activity. However, it is difficult to collect and isolate a large range of fungal species to analyse, and so far only a small percentage of metabolites from fungal species has been tested for bioactivity. Taking a collaborative approach to this problem, a team led by Susan Mooberry and Robert Cichewicz from the University of Texas Health Science Center and the University of Oklahoma respectively, enlisted the help of 'citizen scientists' to collect soil samples from different regions. Crowdsourcing sample collection enabled them to isolate and analyse metabolites from a greater range of fungal species.

This approach led to the discovery of a previously unknown natural product, which the team called maximiscin. They found that by altering the culture medium for a strain of crowdsourced *Tolypocladium*, or by co-culturing the strain with a species of bacteria, they could switch on an otherwise silent biosynthetic pathway that led to this natural product. The team probed the biosynthetic origins of maximiscin by including isotope-labelled precursors in the culture medium and identifying where they were incorporated into the structure. These labelling experiments revealed that maximiscin consists of two moieties that are synthesized by different biosynthetic pathways. One moiety is produced via the known 'shikimate pathway', and the other via a route that includes a polyketide synthase and a non-ribosomal peptide synthetase. These two moieties are linked by an unusual O=C–N–O–C bridge.

Maximiscin was shown to possess useful anticancer properties. Screening tests revealed that the natural product inhibited the growth of several cancer cell lines. Follow-up studies using a mouse model of cancer demonstrated that it can also significantly inhibit tumour growth in mice. The team say that crowdsourcing approaches can enable research teams to obtain information that would otherwise be inaccessible, whilst also engaging the public in the scientific process. *RJ*

CARBOHYDRATE CHEMISTRY

Through the looking glass

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Naturally occurring sugars are a readily available, cheap source of chirality and have frequently been used as the starting point for stereoselective syntheses. They are often, however, only easily available in one mirror-image form, with their respective enantiomers being scarce and expensive. Moreover, the unnatural isomers may be endowed with interesting and potentially useful biological properties. Now, Sarah Jenkinson and co-workers from the University of Oxford, alongside colleagues from Kagawa University, have reported a rapid and easily scalable conversion of natural D-glucose to either L-glucose or L-glucoronic acid.

D-Glucose has a six-carbon chain and four stereocentres, but Jenkinson and co-workers planned a synthetic conversion to the enantiomer by forming a new carbon–carbon bond at one end of the chain, and breaking one at the other. The first step in the sequence is a Felkin–Anh Kiliani ascension — a reaction known since the 1930s — in which cyanide is diastereoselectively added to the aldehyde before hydrolysis of the nitrile to produce a seven-carbon sodium carboxylate. Reduction of the carboxylate would lead to a *meso*-intermediate, but Jenkinson and co-workers avoid this with a short and highly effective protecting group sequence. In one step, the six hydroxy groups (three diols) are protected as a triacetonide group and the carboxylate is converted to an ester. Only one of three possible triacetonide isomers is formed, and then one acetonide is unmasked in preparation for the key carbon–carbon cleavage reaction. Reduction of the ester, oxidative cleavage of the diol and global deprotection leads to L-glucose. A small change to the sequence, with oxidative cleavage of the diol first, before an unmasking of the hydroxy groups and cleavage of the ester leads to L-glucoronic acid.

The L-enantiomer of glucose is known to be almost as sweet as its natural counterpart, but has no calorific value. Some nasty side-effects, however, will prevent use in food, but this synthesis will provide a useful starting point for that of other L-sugars and investigations of their biological properties. *SD*

Written by Stuart Cantrill, Stephen Davey, Russell Johnson and Paul MacLellan.

blogroll

Creative chemistry

Bloggers combine chemistry and the arts for striking results.

'Creative' may not be the first adjective that comes to mind when describing chemists. Despite comparisons one might make between chemical synthesis and the 'dark arts', the stereotype of a chemist is that of a methodical, analytical thinker rather than a creative and artistic one. Several chemistry bloggers are helping to dispel this myth, however, by sharing their science in the form of photographs, digital art or poetry.

Kristof Hegedüs blogs at Pictures from an Organic Chemistry Laboratory, where each day he shares a photograph of something from his lab. Subjects range from crystals (http://go.nature.com/CxM6IS), to experimental set-ups (http://go.nature.com/28sdhR) and interesting reagents (http://go.nature.com/GsSeaR). Each post is accompanied by a short description to explain what is shown in the picture. Nevertheless, the focus is primarily on the photography, with the simple aesthetics of laboratory glassware a recurring theme.

A recent post (http://go.nature.com/QDORoS) from the Picture it... Chemistry blog featured the opium poppy *Papaver somniferum*, popularly known for its psychoactive alkaloids. The blog post begins on a surreal note, with a picture of a poppy growing out of an Allihn condenser used to demonstrate a laboratory extraction of opioids. The post concludes with discussion of total syntheses of morphine and codeine, incorporating some classics of synthetic chemistry such as the Diels–Alder reaction and reductive amination.

Finally, to transition from pictures back to words, Mark Lorch at Chemistry Blog recently hosted a number of limerick poems written by Nicholas Dawson. With topics ranging from Viagra (http://go.nature.com/6CEGOM) to the vulcanization of rubber (http://go.nature.com/46taoR) to phlogiston theory (http://go.nature.com/UBt6bc), it was a refreshing and whimsical way to rediscover some of the milestones of chemical history.

Written by Renée Webster, who blogs at www.lostinscientia.wordpress.com