

NATURAL PRODUCTS

Weapon of ash destruction

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Over the past two decades the European ash tree has been severely afflicted by a disease called ash dieback. Caused by the pathogenic fungus *Hymenoscyphus pseudoalbidus*, ash dieback is characterized by loss of leaves, necrotic lesions, suppression of new growth, and normally the eventual death of the tree. Regions affected by dieback have lost up to 90% of their ash trees and germination of new seeds is also inhibited by the fungus.

The fungal metabolite viridiol — a known toxin — has been proposed as one of the virulence factors responsible. However, when isolated from different fungal strains the concentration of viridiol does not correlate with the pathogenicity of the fungi, suggesting that other molecules must also be involved.

Now, in an effort to discover more about the compounds responsible for the pathogenicity of this fungus, a team led by Jeroen S. Dickschat at Technische Universität Braunschweig has analysed the volatile metabolites it produces. Their first step was to collect the metabolites released into the air. These compounds were then analysed by gas chromatography and identified by a combination of mass spectrometry and comparisons to reference compounds. Once the compounds' identities were known, the team tested their bioactivity using ash seeds germinated on agar. One volatile lactone, 3,4-dimethylpentan-4-olide, showed concentration-dependent bioactivity against ash. At higher concentrations this lactone completely inhibited germination and also caused necrotic lesions on the seeds.

The lactone contains a chiral centre, so the team synthesized both enantiomers to determine whether they had different activities. Surprisingly, the racemic mixture was found to be more potent than either enantiomer alone, although the reason for this is unclear as the molecular target of 3,4-dimethylpentan-4-olide is not known. Nevertheless this volatile lactone seems to be an important virulence factor; however, as with viridiol, it does not fully account for the toxic effects of ash dieback, because although the lactone was produced by most of the pathogenic fungal strains tested, it was not synthesized by all of them. *RJ*

METAL-ORGANIC FRAMEWORKS

Patterning with a light touch

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Metal-organic frameworks (MOFs) are often synthesized as free-standing crystalline solids. However, to take advantage of their intrinsic porosity for sensing applications it would be beneficial to form them as

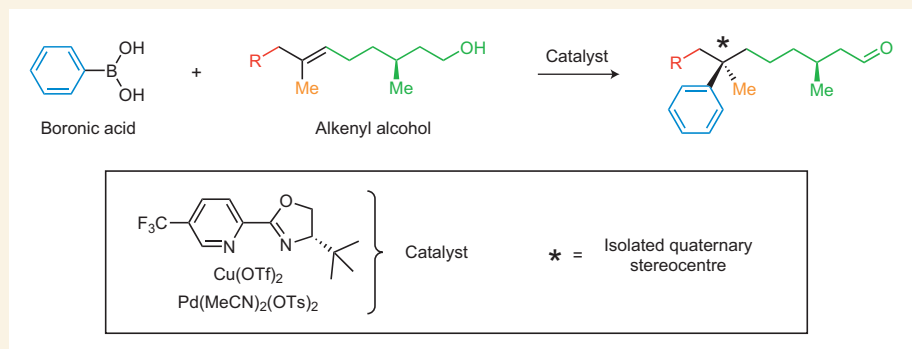
ASYMMETRIC SYNTHESIS

Carbons all round

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Enantioselectivity is an important consideration for synthetic chemists because two stereoisomers can have marked differences in terms of their chemical and physical properties. The specificity of binding sites within enzymes and cell receptors, for example, means that enantiomers can have very different biological effects. There are classic examples of enantiomers displaying different scents or tastes, and where one isomer might be therapeutically beneficial, its mirror image may be inactive or possibly toxic.

Asymmetric catalysis can be used to promote various enantioselective transformations; however, its application in the synthesis of quaternary stereocentres is challenging. This is due to the difficulty of adding an additional carbon to an already crowded tertiary centre, while also requiring a suitable catalyst able to produce an enantiomerically pure product. Previous approaches have involved the use of neighbouring functional groups to install this final C–C bond, such as α - and β -carbonyls. However, subsequent carbonyl deprotection may be necessary and these strategies are not applicable



to the synthesis of quaternary centres at remote sites.

To get around these limitations, a team of researchers led by Matthew Sigman from The University of Utah have developed a catalytic and enantioselective reaction for the installation of more-isolated quaternary centres. They found that by using a palladium catalyst in an intermolecular Heck-type reaction of aryl boronic acids with trisubstituted alkenyl alcohols, incorporation of the aryl group was promoted at the more substituted alkene carbon with very good enantioselectivity. This bond formation led

to the migration of unsaturation along the alkyl chain to the alcohol, which was then converted to a carbonyl. Importantly, they found that this migration was preserved over long chain lengths, thus allowing the enantioselective synthesis of quaternary β -, γ -, δ -, ϵ - or ζ -aryl carbonyl compounds. They also found that pre-existing stereocentres along the alkyl chain are preserved during alkene relay to the alcohol. Although currently limited to aryl groups, it is possible that various other groups may be reacted with the tertiary alkene, furthering the synthetic possibilities of the technique. *JH*