A green route to key molecular building blocks delivers a continuous stream of products

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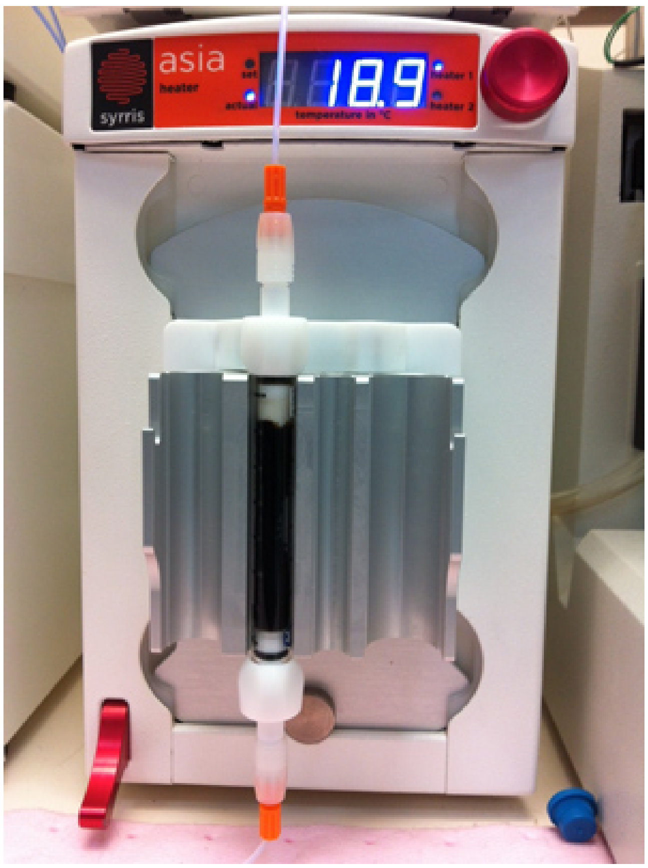


A ruthenium catalyst packed into a reaction column can help to produce a steady stream of useful products. Credit: A*STAR Institute of Chemical and Engineering Sciences

An efficient catalyst has opened up an environmentally benign route to a family of molecular building blocks found in many pharmaceuticals and agrochemicals, a study shows.

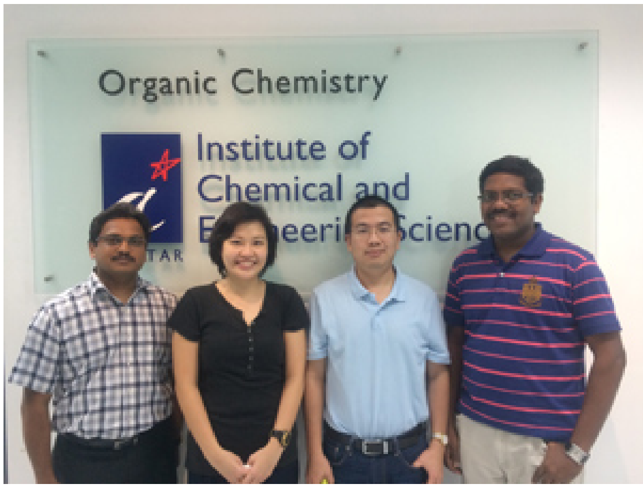
Molecular building blocks known as substituted amines contain a nitrogen atom bonded to at least two carbon atoms. They are often made by reacting nitrogen-containing amines with carbon-based molecules bearing a halogen atom such as chlorine, but this process tends to produce significant amounts of toxic waste.

Cleaner synthesis processes use a catalyst to connect the carbon chain of an alcohol molecule to the amine. But these catalysts, which contain metals such as ruthenium and iridium, usually dissolve in solution with the reactants. This makes it difficult to separate them from the products once the reaction is completed, wasting precious catalyst and increasing processing costs.

Balamurugan Ramalingam and colleagues at the A*STAR Institute of Chemical and Engineering Sciences have now developed a ruthenium catalyst that does not dissolve in solution, potentially making this reaction greener and more efficient.

The team used linker molecules containing phosphorus atoms to attach the ruthenium compound [Ru(p-cymene)2Cl2]2 to tiny polystyrene beads or granules of silica. These particles are easily filtered from the reaction mixture.

The researchers optimized the catalyst's activity by testing different types of linker and varying the amount of ruthenium compound on each particle. They then used the best catalyst to join together a wide range of amines and alcohols, producing various substituted amines in good yields. The catalyst could be recycled over five reactions without much loss in activity, and very little ruthenium leached from the solid particles into solution. Ramalingam's team then exploited the catalyst to produce a drug molecule called piribedil (used to treat Parkinson's disease) in almost 100 per cent yield.



Left to right: Abdul Majeed Seayad, Siah Pei Shan, Tuan Thanh Dang and Balamurugan Ramalingam. Credit: A*STAR Institute of Chemical and Engineering Sciences

The catalyst beads can also be packed into hollow columns (see image) so that reagents flow over them to deliver a stream of products. Such continuous-flow systems are increasingly used to make pharmaceuticals or other high-value chemicals, as a more efficient and sustainable alternative to conventional 'batch-by-batch' processes.

The scientists slowly pumped an amine and an alcohol through the loaded column at a temperature of 120 °C. This delivered a continuous flow of product in 60–70 per cent yields for 21 hours, with virtually no loss of ruthenium. "In principle, the reaction could be scaled up to production scale, and the complete conversion could be achieved by recycling the reagents," says Ramalingam. The team is now using the catalyst to make amine-based polymers.

More information: Shan, S. P., Dang, T. T., Seayad, A. M. & Ramalingam, B. Reusable supported ruthenium catalysts for the alkylation of amines by using primary alcohols. *ChemCatChem* 6, 808–814 (2014). dx.doi.org/10.1002/cctc.201300971

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