A green transformation for pharmaceuticals

November 21 2014

Credit: AI-generated image (disclaimer)

Waste is reduced through the cheap and green development of a catalyst for the transformation of a commercially important functional group

A more sustainable approach to a bond-forming reaction extensively used in the pharmaceutical and fine chemical industries has been developed by an international research team led by A*STAR. The team used the solvent-free, catalytic reaction to produce high yields of a wide

range of amides, including the antidepressant moclobemide and other drug-like molecules.

"Amide groups are widely found in pharmaceuticals," explains Anqi Chen from the A*STAR Institute of Chemical and Engineering Sciences who led this research with the National University of Singapore (NUS). Examples include moclobemide, the cholesterol-lowering drug Lipitor, the anticancer drug Velcade and the anti-HIV drug Isentress. Current routes used to synthesize amide-containing molecules are expensive and generate lots of waste, prompting the need for cheaper, greener approaches.

An attractive alternative to conventional methods is transamidation—the catalytic reaction of a primary amide with an amine to make a secondary or tertiary amide. One of its advantages is that ammonia is the only byproduct. A range of organocatalysts and metal catalysts have recently been trialed for reactions of this type.

Now, Chen and his team have demonstrated that the solid-state catalyst mesoporous niobium oxide is suitable for transamidation in the absence of any solvent. "Compared with other reported transamidation catalysts, the niobium catalyst has the advantages of a broad substrate scope, a good functional group tolerance and high yields of amide products," says Chen.

The team's collaborators at NUS had previously developed the catalyst for other reaction types. The catalyst is simple and inexpensive to synthesize and does not require any noxious solvents. It has a highly regular spherical structure with a diameter of approximately 500 nanometers and an acidity comparable to that of sulfuric acid. "The catalyst can also be conveniently recovered after the reaction and reused several times without appreciable loss of activity," explains Chen.

The team tested the niobium oxide catalyst in reactions of a wide range of primary amides with various primary and secondary amines. The corresponding amides were all obtained in high yields. To further showcase the utility of the catalyst in this type of reaction, the team used it to synthesize the antidepressant moclobemide and other drug-like molecules in gram quantities with excellent yields.

The only downside is that the reactions require a relatively high temperature (around 150 degrees Celsius). "The promising results from this work should promote the development of more efficient catalysts that allow this valuable transformation to be carried out at lower temperatures to facilitate its application," says Chen.

More information: Ghosh, S. C., Li, C. C., Zeng, H. C., Ngiam, J. S. Y., Seayad, A. M. & Chen, A. "Mesoporous niobium oxide spheres as an effective catalyst for the transamidation of primary amides with amines." *Advanced Synthesis & Catalysis* 356, 475–484 (2014). DOI: 10.1002/adsc.201300717

Provided by Agency for Science, Technology and Research (A*STAR), Singapore