A new method cuts the cost of drug-building chemicals

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EPFL scientists design a new method to cheaply produce some of the most important chemical compounds in the pharmaceutical industry - the amines.

The amines are one of the most important classes of chemical compounds today. Amines that contain a ring-like structure - called an "aryl" group - are used widely in pharmaceuticals, such as the top-selling drugs Abilify, Crestor, Gleevec, and Lidoderm. EPFL scientists have now developed a method to produce aryl-containing amines in a cheap and easily scalable way. The work is published in *Nature Communications*.

Amines with an aromatic aryl ring in their structure are collectively referred to as "hetero aryl amines" and are widely used in medicinal chemistry. This process involves connecting an amine to an organic molecule - what is known as a "functional group".

Currently, making these amines requires a three-step process that produces toxic compounds called anilines. These are often used in industry, e.g. to make polyurethane. Chemists make hetero aryl amines by treating anilines with hydrogen.

Xile Hu and Chi Wai Cheung at EPFL have now developed a new method for making hetero aryl amines without needing to go through the aniline step first. Using a simple iron catalyst, the researchers were able to couple amines to organic compounds that are widely used in

commercial products, including pharmaceuticals.

The method, which bypasses the aniline step, produces hetero aryl amines that have a high tolerance to functional groups, and match the amines produced with the conventional aniline method in terms of versatility and usefulness for a broad range of chemical applications. Some of those functional groups actually require protection under conventional amine synthesis, meaning that the hetero aryl amines produced with the new method are also safer to produce.

The new method allows chemists to synthesize amines from starting compounds that are often cheaper and easier to produce and more readily available than anilines, which have to be produced from such compounds to begin with anyway.

The authors state: "From these points of view, the current method can be considered as a valuable alternative to the conventional amination methods such as direct alkylation and reductive amination."

More information: Cheung CW, Hu X. Amine Synthesis via Iron Catalyzed Reductive Coupling of Nitroarenes with Alkyl Halides. *Nature Communications* 12 August 2016. DOI: 10.1038/NCOMMS12494

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