# UCR chemists prepare molecules that accelerate chemical reactions for manufacturing drugs

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***New molecules help make stable catalysts that work at room temperature***

Chemists at the University of California, Riverside have synthesized a new class of carbenes – molecules that have unusual carbon atoms – that is expected to have wide applications in the pharmaceutical industry, ultimately resulting in a reduction in the price of drugs.

Called cyclic alkyl amino carbenes or CAACs, the molecules attach themselves to metals, such as palladium, to form highly efficient catalysts that allow chemical transformations otherwise considered impossible. The carbenes modulate the properties of the metals to which they are bound and can facilitate and speed up reactions involving their use.

Study results appear in the Angewandte Chemie International Edition, and were published online Aug. 1.

A carbene is a molecule that has a carbon atom with six electrons instead of the usual eight. Because of the electron deficiency, carbenes are highly reactive and usually unstable in nature.

In their paper, the UCR chemists discuss a set of chemical reactions involving the use of catalysts other than those that are CAAC-based. The

authors note that these catalysts need strong heating to be effective. They add that the CAAC-based catalysts, on the other hand, can be used not only at room temperature but also in smaller amounts than is necessary for the other catalysts.

"For more than a century, most catalysts were prepared using chemical compounds called phosphines," said Guy Bertrand, the lead author of the study and Distinguished Professor of chemistry. "But in the 1990s, carbenes were found to be useful to make catalysts. The new carbenes we have prepared in the laboratory are such that they protect the metals to which they bind, making the metal catalysts more stable and longer lasting."

Because nitrogen atoms stabilize a carbene when they are adjacent to it, chemists believed until now that two nitrogen atoms were necessary in a carbene to make efficient catalysts. But having two nitrogen atoms also imposes structural limitations at the center of the carbene.

The carbenes synthesized by the UCR chemists has only one nitrogen atom, which lends the molecule a far more flexible structure. In effect, the carbenes are bigger at the metallic center of the catalyst, a feature that improves the efficiency of the catalyst.

"We started this project nearly two years ago," said Vincent Lavallo, an undergraduate researcher in Bertrand's laboratory and the first author of the paper. "The carbene-based catalysts we report can simplify complex chemical preparations. Further, just mild temperatures are needed for the catalyst to be effective. Because of the catalyst's longevity, you need only a small amount to achieve your final product. All of this can dramatically reduce the cost of manufacturing drugs, given that pharmaceutical companies are increasingly using carbene-supported catalysts for their chemical reactions."

Bertrand's research group plans to continue to modify the new carbenes to find more efficient catalysts. "We're looking also for new catalytic reactions facilitated by these new carbene metal complexes," Lavallo said. "The CAACs have made the field of carbene chemistry more exciting than ever."

Yves Canac, Carsten Präsang and Bruno Donnadieu of UCR assisted with the study. The National Institutes of Health and the chemicals manufacturer Rhodia provided support.

Source: University of California, Riverside