

Chemists use oxygen, copper 'scissors' to make cheaper drug treatments possible

November 22 2023, by Holly Ober



Credit: Gio Bartlett/Unsplash

Drugs to treat cancer are often very expensive to produce, resulting in high costs for the patients who need them. Thanks to pathbreaking research by UCLA chemists, led by organic chemistry professor Ohyun



Kwon, the price of drug treatments for cancer and other serious illnesses may soon plummet.

One chemical used in some <u>anti-cancer drugs</u>, for example, costs <u>pharmaceutical companies</u> \$3,200 per gram—50 times more than a gram of gold. The UCLA researchers devised an inexpensive way to produce this drug molecule from a chemical costing just \$3 per gram. They were also able to apply the process to produce many other chemicals used in medicine and agriculture for a fraction of the usual cost.

This feat, <u>published in the journal *Science*</u>, involves a process known as "aminodealkenylation." Using oxygen as a reagent and copper as a catalyst to break the carbon-carbon bonds of many different organic molecules, the researchers replaced these bonds with carbon-nitrogen bonds, converting the molecules into derivatives of ammonia called <u>amines</u>.

Because amines interact strongly with molecules in living plants and animals, they are widely used in pharmaceuticals, as well as in agricultural chemicals. Familiar amines include nicotine, cocaine, morphine and amphetamine, and neurotransmitters like dopamine. Fertilizers, herbicides and pesticides also contain amines.

Industrial production of amines is therefore of great interest, but the <u>raw</u> <u>materials</u> and reagents are often expensive, and the processes can require many complicated steps to complete. Using fewer steps and no expensive ingredients, the process developed at UCLA can produce valuable chemicals at a much lower cost than current methods.

"This has never been done before," Kwon said. "Traditional metal catalysis uses expensive metals such as platinum, silver, gold and palladium, and other precious metals such as rhodium, ruthenium and iridium. But we are using oxygen and copper, one of the world's most



abundant base metals."

The new method uses a form of oxygen called ozone, a potent oxidant, to break the <u>carbon-carbon bond</u> in hydrocarbons called alkenes, and a copper catalyst to couple the broken bond with nitrogen, turning the molecule into an amine. In one example, the researchers produced a c-Jun N-terminal kinase inhibitor—an anti-cancer drug—in just three <u>chemical</u> steps, instead of the 12 or 13 steps previously needed. The cost per gram can thus be reduced from thousands of dollars to just a few dollars.

In another example, the protocol took just one step to convert adenosine—a neurotransmitter and DNA building block that costs less than 10 cents per gram—into the amine N6-methyladenosine. The amine plays crucial roles in controlling <u>gene expression</u> in cellular, developmental and disease processes, and its production cost has previously been \$103 per gram.

Kwon's research group was able to modify hormones, pharmaceutical reagents, peptides and nucleosides into other useful amines, showing the new method's potential to become a standard production technique in drug manufacturing and many other industries.

More information: Zhiqi He et al, Aminodealkenylation: Ozonolysis and copper catalysis convert C(sp 3)-C(sp 2) bonds to C(sp 3)-N bonds, *Science* (2023). DOI: 10.1126/science.adi4758

Provided by University of California, Los Angeles

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