

New method for late-stage functionalization of carbon-hydrogen bonds

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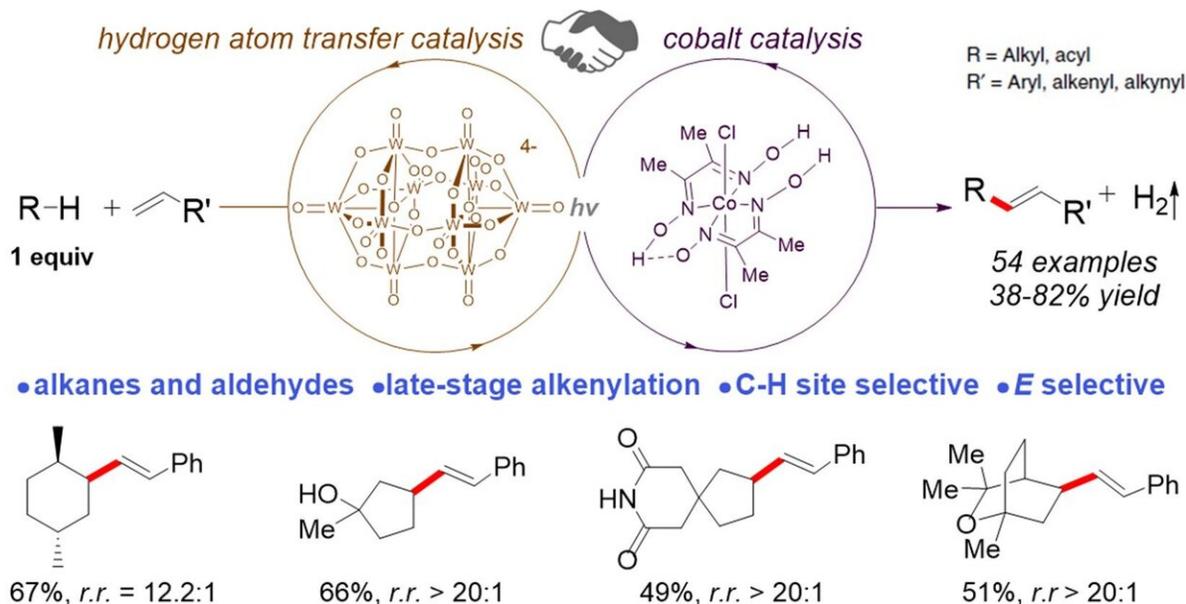


Illustration showing (top) the site-selective late-stage C-H alkenylation through the use of synergistic hydrogen atom transfer and cobalt catalysis in the presence of light ($h\nu$). (Bottom) Selection of chemical products that can be synthesised from this method. Credit: Nature Communications

National University of Singapore chemists have developed a photo-induced method for late-stage functionalization of carbon-hydrogen (C-H) bonds in organic molecules.

The replacement of H in C-H bonds with other atoms or substituents is one of the most coveted ways to create new and useful [molecules](#). While the C-H [bond](#) can be found in almost all organic molecules, it is typically inactive and therefore difficult to functionalise. Direct transformation of C-H bonds to versatile alkene [functional groups](#) represents an economical approach for olefin synthesis and molecular editing. In [drug discovery](#) and development, late-stage C-H functionalisation offers an efficient way to facilitate the preparation of structural analogs of targets with enhanced structure-activity relationships or other desired physicochemical properties without de novo approaches.

A research team led by Prof Wu Jie from the Department of Chemistry, NUS, has developed a photocatalytic process for direct alkenylation of C-H bonds in alkanes and aldehydes. In recent decades, transition-metal-catalyzed alkenylations of arenes and heteroarenes have been extensively studied. However, analogous transformations of alkanes and aldehydes remain challenging. The existing methods generally suffer from the use of noble metal, stoichiometric amounts of oxidants and large excess of C-H substrates. To solve these issues, the research group used a combination of two types of catalytic methods, the direct hydrogen atom transfer catalysis (with a decatungstate anion, $[W_{10}O_{32}]^{4-}$) and the cobaloxime catalysis, for the direct activation and alkenylation of alkanes and aldehydes. When these two catalysts work synergistically in the presence of light, a diverse range of cheap feedstocks can be easily transformed into valuable olefins. Other advantages of this strategy include a broad substrate scope, high C-H site selectivity, excellent trans selectivity of the alkene products, and the use of the C-H substrate as the limiting reagent. Moreover, this strategy can be applied in the selective late-stage functionalisation of natural products and important pharmaceutical molecules.

Prof Wu said, "The site-selective late-stage functionalisation of C-H bonds in complex molecules developed from our studies is a very useful

class of reactions. This method could potentially find broad application in olefin synthesis, structural modification of pharmaceuticals and natural product synthesis."

The research team plans to develop more advanced catalytic processes for the late-stage functionalisation of carbon-hydrogen bonds.

More information: Hui Cao et al. Photoinduced site-selective alkenylation of alkanes and aldehydes with aryl alkenes, *Nature Communications* (2020). [DOI: 10.1038/s41467-020-15878-6](https://doi.org/10.1038/s41467-020-15878-6)

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