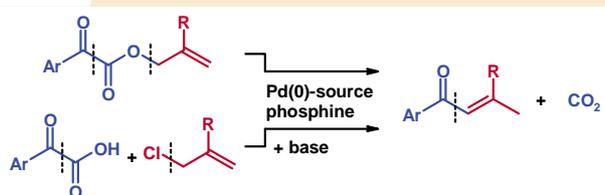


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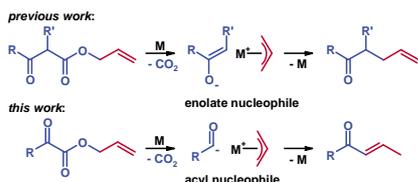
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A palladium / phosphine system has been developed that catalyzes the extrusion of carbon dioxide from α -oxocarboxylic acid allyl esters, leading to α,β -unsaturated ketones. The palladium complex activates the substrate and mediates the carbon-carbon bond formation to intermediate allyl ketones, as well as their double bond isomerization. The actual decarboxylation step with formation of the acyl nucleophile is promoted by the phosphine.



Decarboxylative Allylation

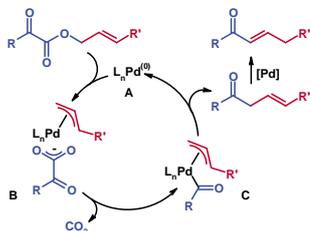
Within recent years, the field of decarboxylative allylation reactions has undergone tremendous development.^[1] The foundations for this area were laid by Carroll in 1940 with his report that allyl β -oxocarboxylates extrude CO_2 to give γ,δ -unsaturated alkyl ketones when heated in the presence of a base.^[2] In the 1980s, Pd-catalyzed versions of this transformation that proceed under neutral conditions were discovered by Saegusa^[3] and Tsuji.^[4] This concept was decisively advanced by Tunge and Stoltz.^[1]



We herein report the Pd/phosphine-catalyzed decarboxylative allylation of allyl α -oxocarboxylates as the first example of a decarboxylative allylation involving destabilized carbon nucleophiles.^[5] This reaction provides an expedient synthetic entry to α,β -unsaturated ketones, privileged structures in biologically active natural products.^[6]

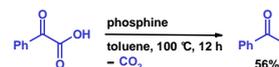
Mechanism

The decarboxylative allylation of α -oxocarboxylates proceeds via a different mechanism than bimetallic decarboxylative cross-coupling reactions.^[1] Coordination and oxidative addition of the substrate to a Pd(0) precursor (A) lead to the formation of covalent or ionic π -allyl-Pd carboxylate complexes (B). The phosphine promoted extrusion of CO_2 forms the acyl π -allyl-Pd complex C and subsequent reductive elimination gives the allyl ketone, which can be expected to rapidly isomerize to the conjugated vinyl ketone in the presence of palladium.^[7]



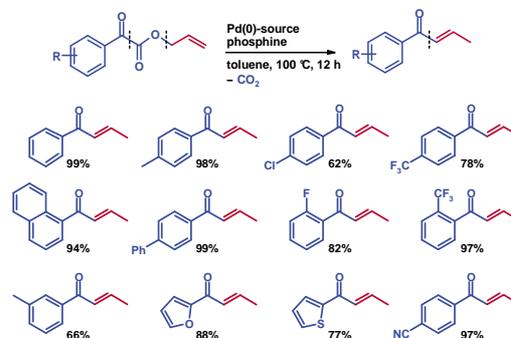
We performed a cross-over experiment in which a mixture of two different allyl α -oxocarboxylates were subjected to the optimized reaction conditions. The fact that all possible products were formed in comparable quantities shows that after the oxidative addition step, the carboxylate ions can dissociate and exchange with other salts, even in the nonpolar solvent toluene.

Further mechanistic investigations revealed that the phosphine acts as an organocatalyst for the decarboxylation step, and also stabilizes the palladium cross-coupling catalyst.

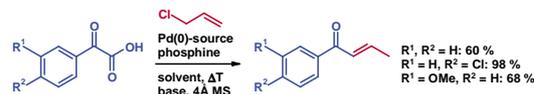


Scope of the Decarboxylative Coupling

α -Oxocarboxylic acid allyl esters can be seen as acyl anion synthons that can be released under the influence of the appropriate catalyst. We have demonstrated the viability of this concept by applying it to a broad range of arylglyoxylic esters. Substrates with electron-rich and -deficient aryl substituents react similarly well, various functional groups are tolerated, and even heterocyclic derivatives could be converted. The reaction also gave a high yield when conducted on gram-scale.



Analogous decarboxylative allylations can also be performed starting from α -oxocarboxylic acids, allyl chlorides and potassium carbonate as the base. Spectroscopic studies confirmed that this reaction variant proceeds via an intermediate formation of the allyl esters.



Ongoing work

Ongoing work is directed towards combining the phosphine-catalyzed decarboxylation of α -oxocarboxylates with other synthetic transformations that require acyl anion equivalents. Ultimately, this strategy may become a general alternative to established syntheses involving the umpolung of aldehydes.

Literature and Further Reading (see also www.chemie.uni-kl.de/goossen)

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