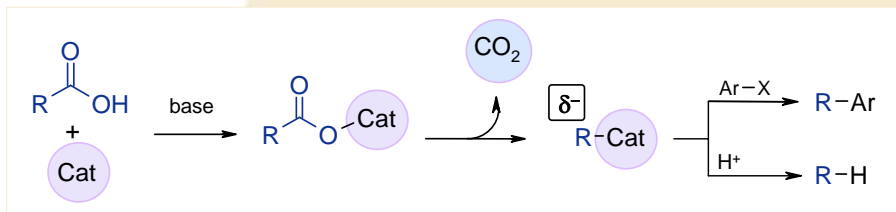
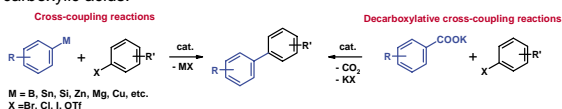


Concept: In decarboxylative cross-couplings, metal salts of carboxylic acids are converted into carbon nucleophiles by extrusion of CO₂ and are directly coupled with carbon electrophiles. This approach combines the key benefit of regioselectivity that cross-couplings have over reactions under C–H activation, e.g. Friedel-Crafts or metal-catalyzed reactions of arenes, with the broad availability, low cost, and easy handling of carboxylate substrates. The concept was first proven with a biaryl synthesis from activated carboxylates and aryl bromides.¹ Using this novel coupling, expensive and delicate organometallic compounds are replaced by inexpensive, broadly available carboxylic acids. Liberation of the aryl group from the copper to a palladium(II) species formed by oxidative addition of an aryl halide. Liberation of the biaryl closes the catalytic cycle for the palladium, while the original copper(I) carboxylate is regenerated by ligand exchange between the copper(I) halide and fresh potassium carboxylate.

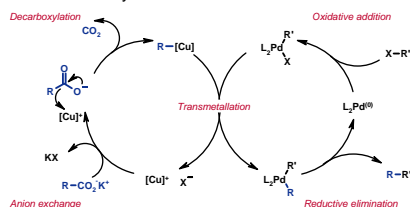


Pd/Cu-Catalyzed Decarboxylative Cross-Couplings

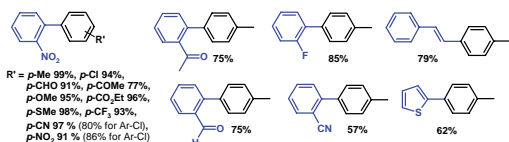
A bifunctional Pd/Cu catalyst system has been developed that efficiently catalyzes the decarboxylation of aromatic carboxylates and the cross-coupling of the resulting organometallic species with aryl halides to give biaryls.¹ Using this novel coupling, expensive and delicate organometallic compounds are replaced by inexpensive, broadly available carboxylic acids.



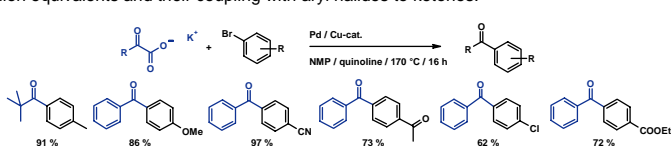
Its initial step, the extrusion of CO₂ under formation of arylcopper species, is mediated by copper-phenanthroline complexes. While these intermediates are converted into the corresponding arenes in the presence of protons,² aprotic conditions allow the transfer of the aryl group from the copper to a palladium(II) species formed by oxidative addition of an aryl halide. Liberation of the biaryl closes the catalytic cycle for the palladium, while the original copper(I) carboxylate is regenerated by ligand exchange between the copper(I) halide and fresh potassium carboxylate.



The viability of this concept has been confirmed by coupling various aryl iodides, bromides, and chlorides with a broad range of aromatic carboxylic acids.³ Its synthetic potential has been demonstrated for industrially important biaryls, e.g. boscalid, valsartan and telmisartan.⁴

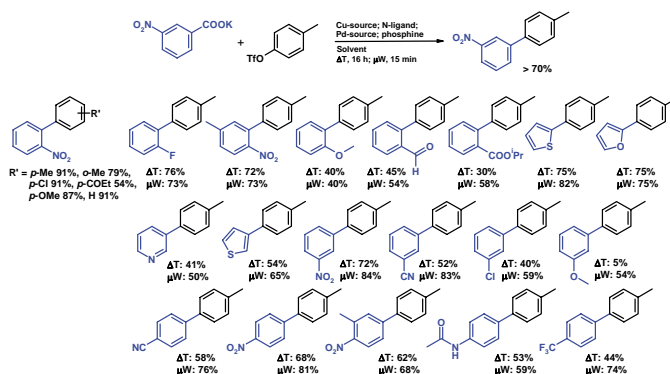


A particularly useful application is the decarboxylation of α -oxocarboxylic acid salts to acyl anion equivalents and their coupling with aryl halides to ketones.⁵



Decarboxylative Cross-Couplings of Non-Activated Carboxylates

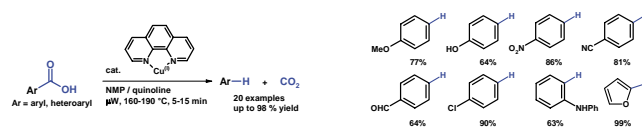
The initial reaction protocol remained limited to certain *ortho*-substituted or heterocyclic carboxylic acids, but using aryl triflates as coupling partners, the reaction is now applicable to the full range of carboxylates including *meta*- and *para*-substituted derivatives. Such electrophiles with non-coordinating leaving groups that do not compete for coordination sites at the decarboxylation catalyst requires a specially developed cross-coupling catalyst with electron-rich, chelating phosphines such as Tol-BINAP. The use of microwave irradiation has led to a particularly effective protocol.⁶



With our latest catalyst generation, encouraging turnover was recently achieved also for the inexpensive aryl tosylates as carbon electrophilic coupling partners.

Decarboxylations of Non-Activated Carboxylates

Having established that the initial limitations were mainly caused by the presence of halide ions and that halide-free protocols have a much broader scope, the optimization of a new generation of decarboxylation catalysts capable of operating at lower temperatures is currently in the focus of our interest. In the course of these investigations, a protocol has been developed that allows the smooth protodecarboxylation of diversely functionalized aromatic carboxylic acids within 5-15 min in the microwave using at most 5 mol% of an inexpensive Cu(I) oxide / 1,10-phenanthroline catalyst.⁷



Further progress has been made over the last months, and we have recently succeeded in performing protodecarboxylations of non-activated benzoic acids at temperatures of only 120 °C with a silver-based catalyst. The use of these new decarboxylation systems as components of decarboxylative cross-coupling catalysts is currently under investigation.

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

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