REGIOSELECTIVE C-H HYDROARYLATION of INTERNAL ALKYNES with ARENECARBOXYLATES: CARBOXYLATES AS DECIDING DIRECTING GROUPS

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Abstract
In the presence of catalytic [Ru(η-cym)]2+, and the base guanidine carbonate, benzoic acids react with internal alkynes to give the corresponding 2-vinylbenzoic acids. This alkyne hydroarylation is generally applicable to diversely substituted benzoic and acrylic acids. Aryl/alkylacetylenes react regioselectively with formation of the alkyl-branch hydroarylation products, and propargylic alcohols are converted into γ-alkyldiene-δ-lactones. The hydroarylation can also be conducted decarboxylatively with a different choice of catalyst and conditions, opening up a regioselective, waste-minimized synthetic entry to vinylarenes.

Versatility of COOH as Directing Group
Arguably, the most advantageous directing groups are carboxylates. Benzoic acids are widely available in great structural diversity and at low cost, and can subsequently be derivatized further, utilized as leaving groups in decarboxylative couplings,10 or removed tracelessly by protodecarboxylation.2

COOH Directed Hydroarylation of Alkynes
In continuation of our research on the use of carboxylic acids as substrates in transition metal catalysis,11-13 we explored whether carboxylate groups could be utilized as directing groups in redox-neutral intermolecular hydroarylations of alkynes A). The desired process would have to be initiated by a carboxylate-directed ortho-C–H alkyne insertion step. The resulting vinyl–metal species would then need to be forced towards a reductive elimination step yielding alkényl/benzoic acids despite the abundance of facile pathways leading to cyclized products B).13-14

Conclusion and Outlook
In conclusion, the carboxylate-directed C–H hydroarylation of internal alkynes with benzoic or acrylic acids catalyzed by the inexpensive, easy-to-handle [Ru(η-cym)]2+, complex opens up a convenient and waste-free entry to a wide variety of 2-vinylbenzoic acids or aromatic δ-lactones from abundant precursors. In a less polar solvent mixture and at higher temperatures, the carboxylate group is removed directly within the hydroarylation process. Beyond being removable, the carboxylates thus become deciding directing groups, intrinsically preventing substitution in this directed C–H functionalization.

Aryl/alkylacetylenes do not react under the decarboxylative hydroarylation conditions. Further investigations to convert these asymmetrically substituted internal alkynes in a regioselective way are currently running in our laboratory.

Moreover, the development of further application of deciding directing groups, as a novel concept, is highly desired and is part of our current research. See Poster P299 for an inversion of the classical regioselectivity in a Mizoroki-Heck reaction via a decarboxylative shed of the carboxylate directing group.