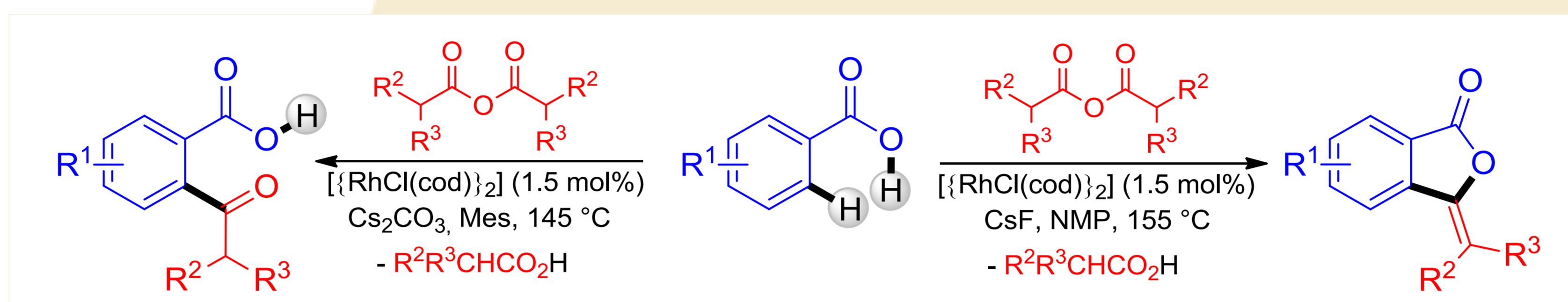


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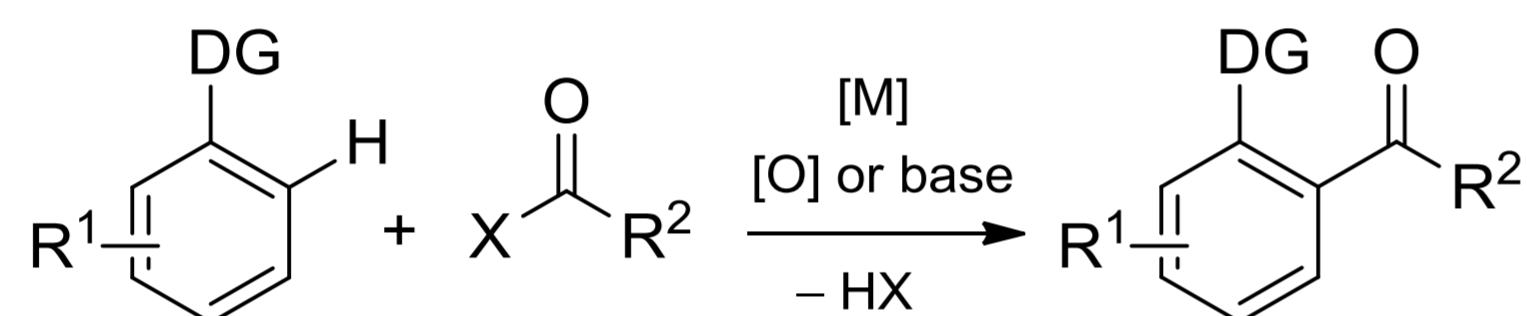
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Abstract: In the presence of a rhodium catalyst, the carboxylate group directs the acylation of arenes with carboxylic anhydrides into their *ortho*-position. This *ortho*-acylation is complementary to the meta selectivity of classical Friedel–Crafts reactions. The resulting products can undergo protodecarboxylation to deliver an aryl ketone. Moreover, this transformation leads, after small adjustments of the reaction conditions, to alkylidenephthalides and presents a good alternative to the limited *ortho*-olefination / annelation of carboxylic acids.

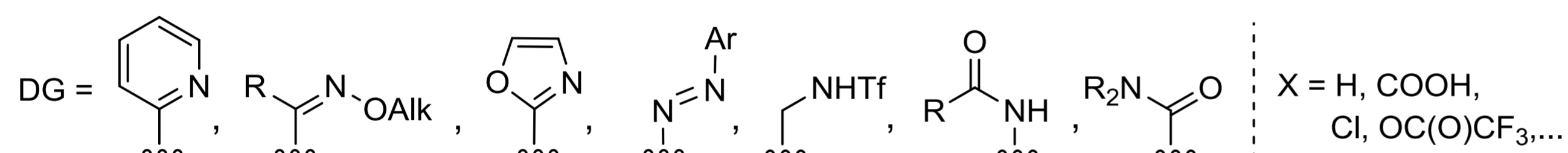


ortho-Acylation

Transition metal-catalyzed directed *ortho*-functionalizations of arenes constitute modern and sustainable tools for the regiospecific formation of carbon–carbon and carbon–heteroatom bonds. In these transformations, directing groups such as pyridine, amide, oxime, etc.... are employed.^[1] The carboxylate group is one of the most useful directing groups for C–H activations because it can subsequently be utilized as a leaving group in further functionalization steps, or tracelessly removed by protodecarboxylation.^[2]

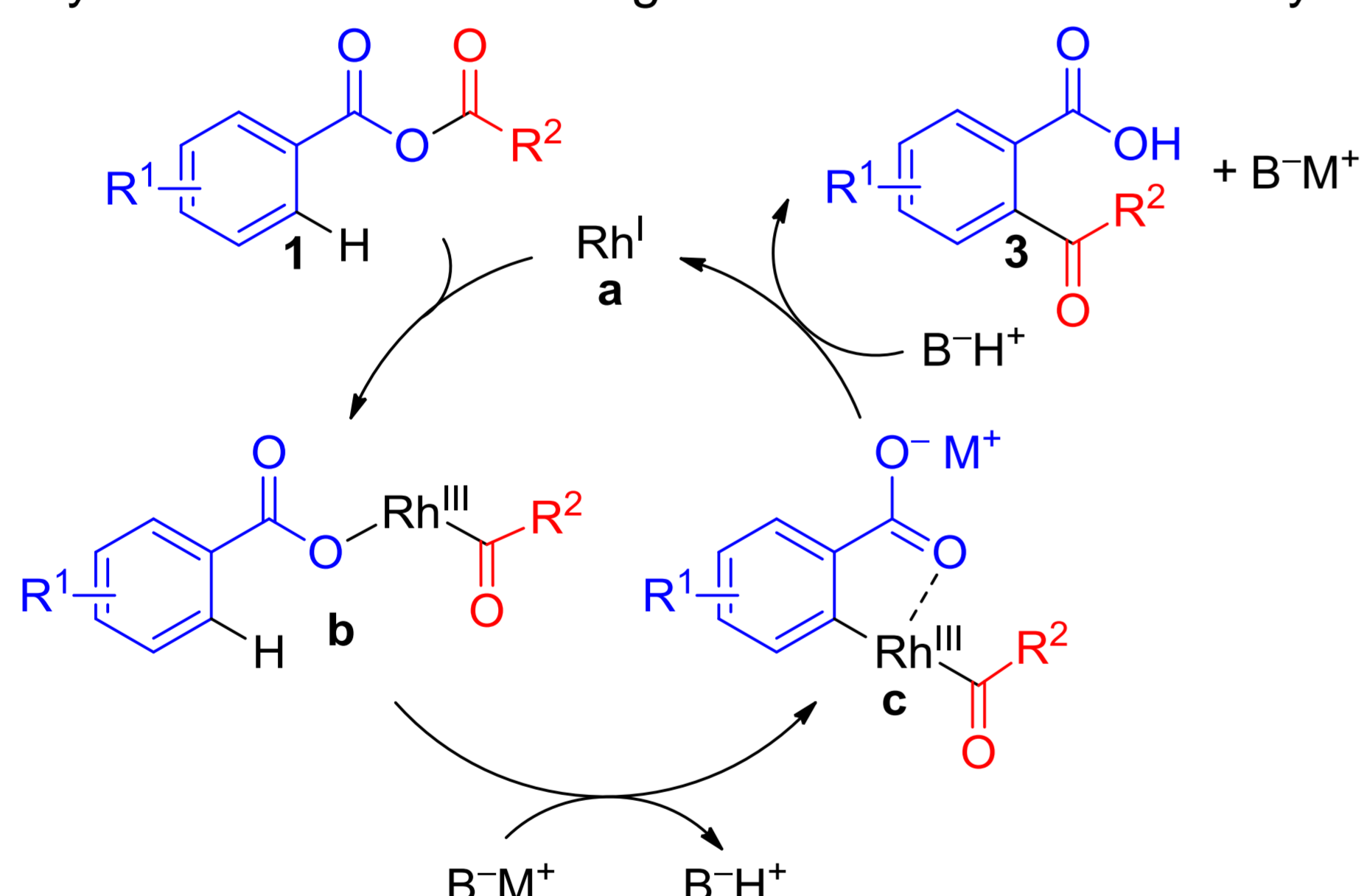


Previous work



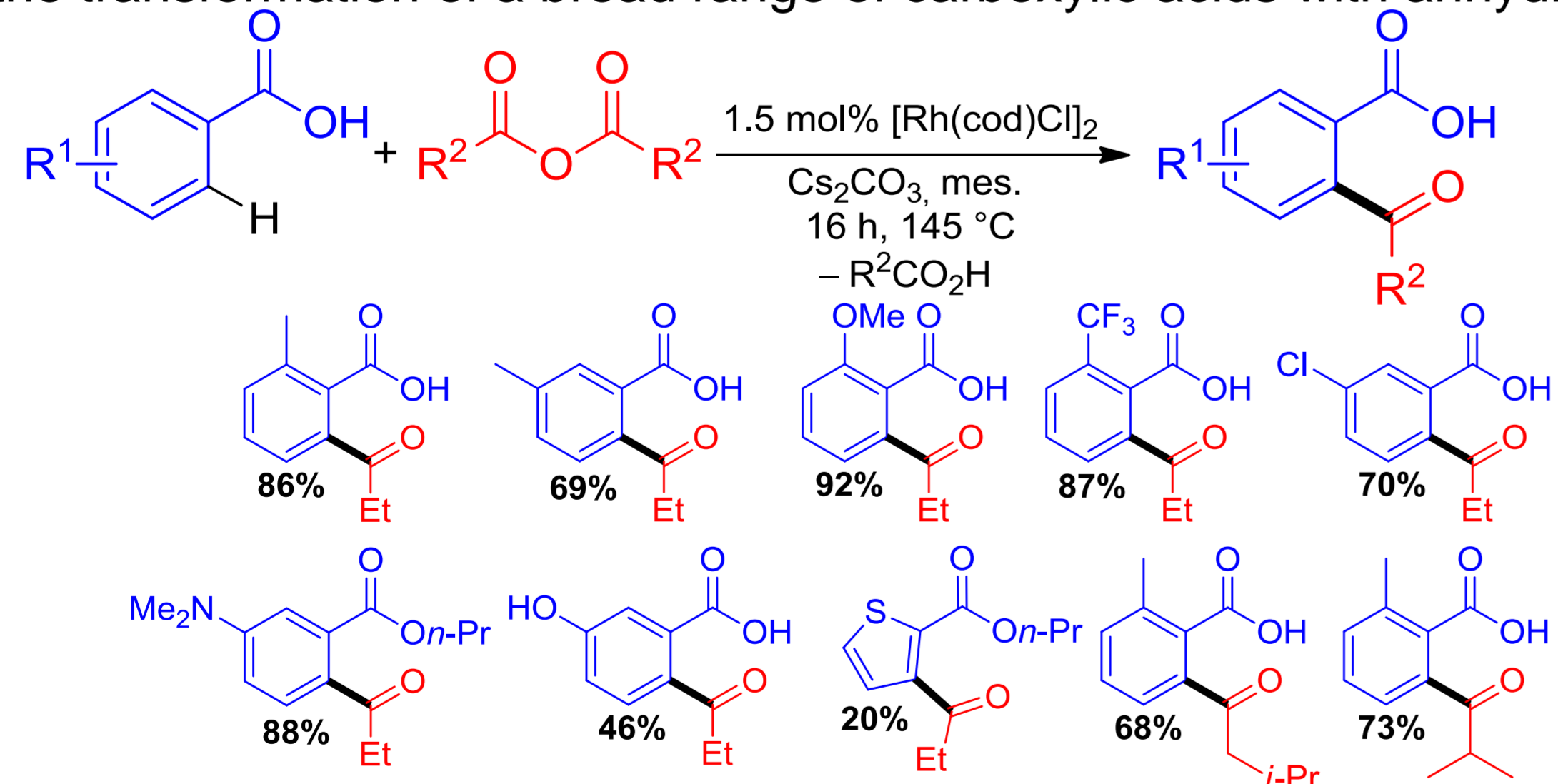
The Mechanistic Concept

Mixed or symmetrical anhydrides should allow the intramolecular *ortho*-acylation in the presence of a rhodium (I) catalyst. The Rh-catalyst should insert into the acyl–O bond of the anhydride **1** leading to the benzoate **b**. Assisted by a base, the rhodium should then insert intramolecularly into the *ortho*-C–H bond to give **c**. Reductive elimination would furnish the *ortho*-acylbenzoic acid **3** and regenerate the rhodium catalyst **a**.



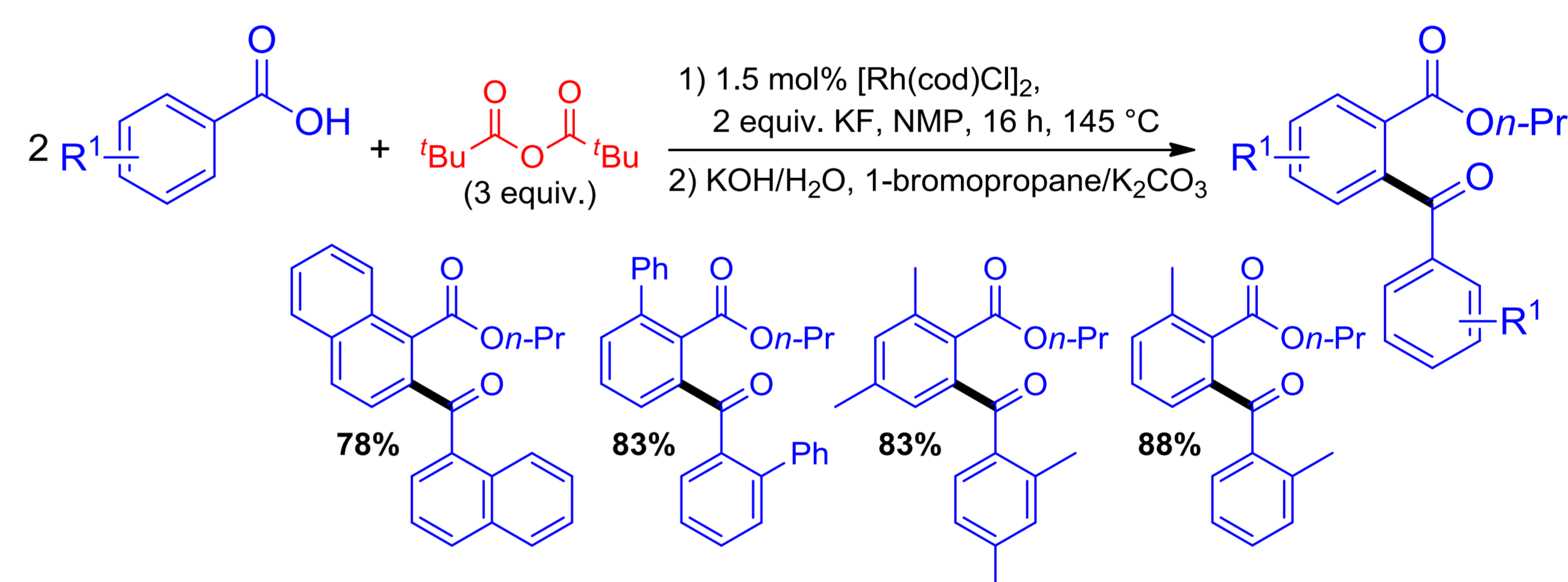
Scope of the *ortho*-Acylation of Benzoic Acids

Indeed, a combination of [RhCl(cod)]₂ as catalyst and Cs₂CO₃ as base in mesitylene allows the transformation of a broad range of carboxylic acids with anhydrides.^[3]



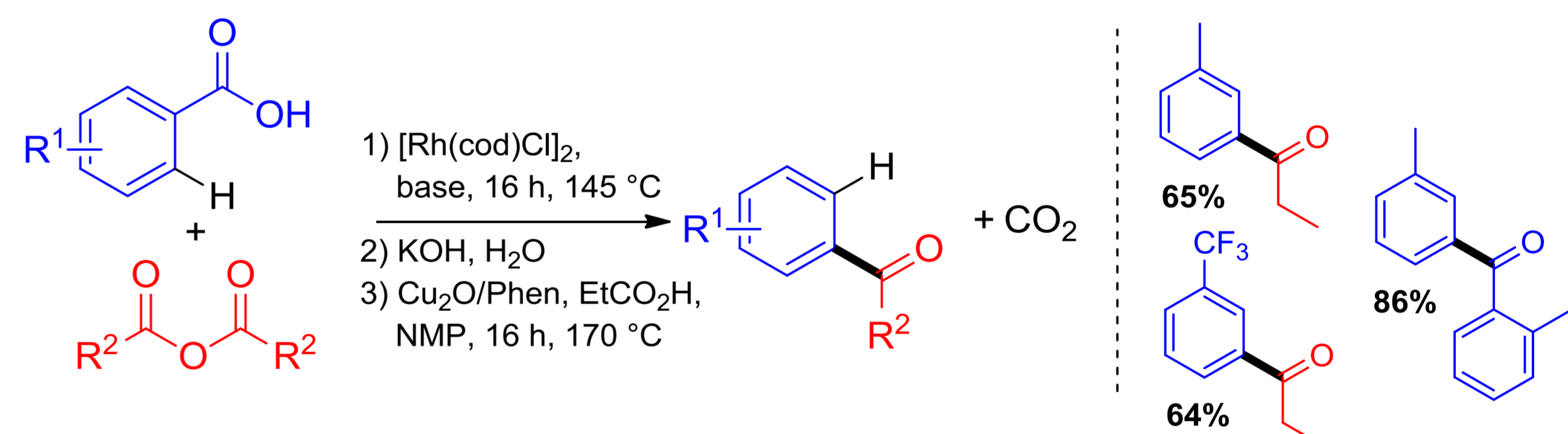
Self-Acylation of Aromatic Benzoic Acids

Treating benzoic acids with an excess of pivalic anhydride in the presence of a rhodium catalyst, *ortho*-aroylbenzoic acids are formed in high yields and selectivities.



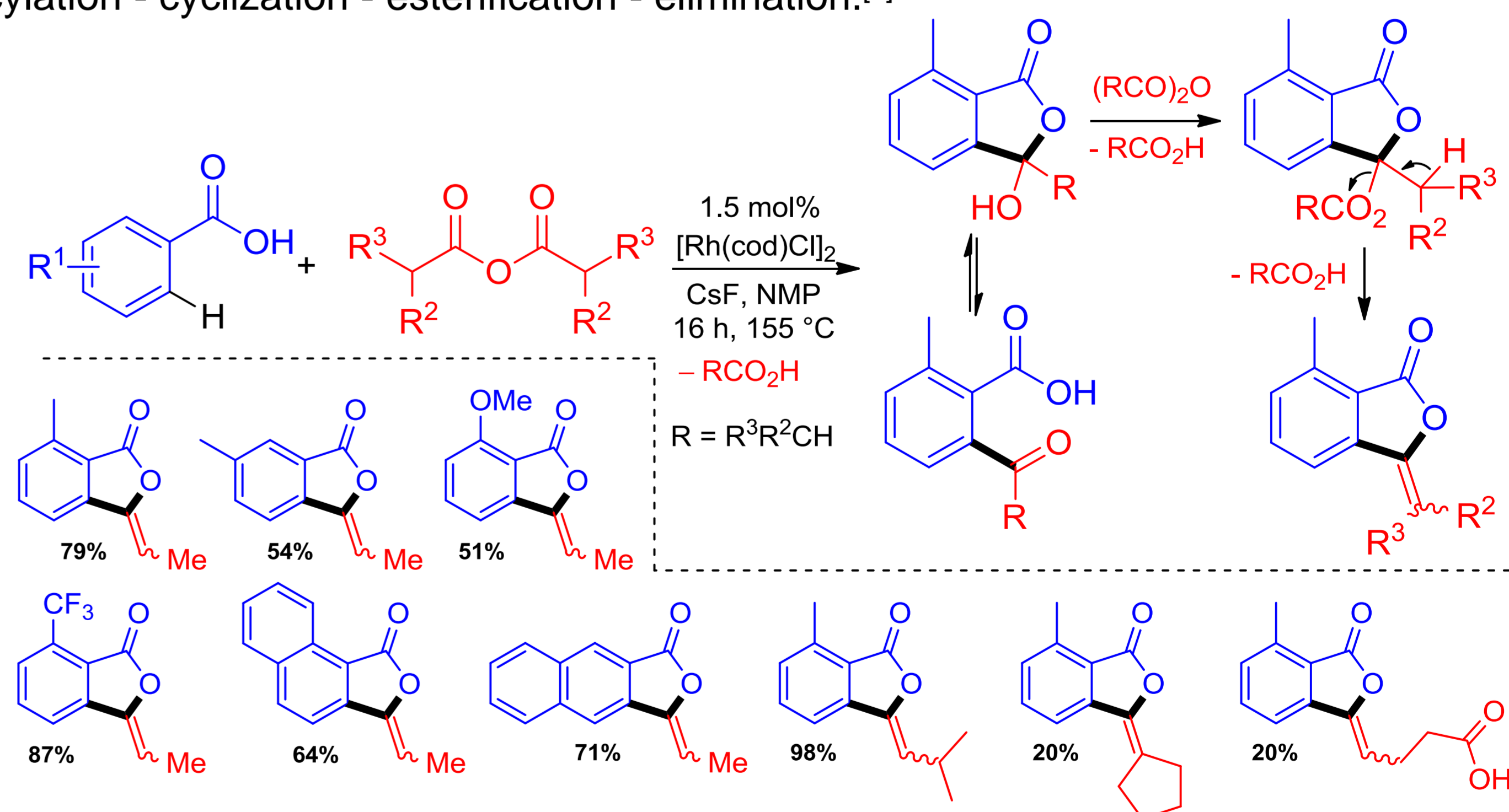
ortho-Acylation Followed by Protodecarboxylation

The carboxylate group can optionally be removed by an in situ-protodecarboxylation. However, the rhodium complex mediates this step only at temperatures above 200 °C. Higher yields were obtained by using a copper-mediated protodecarboxylation in a sequential one-pot procedure.^[4]



Synthesis of Alkylidenephthalides via C–H Activation

A similar catalyst system with CsF as base in NMP at 155 °C allows the formation of alkylidenephthalides starting from benzoic acids and anhydrides via a sequential *ortho*-acylation - cyclization - esterification - elimination.^[5]



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

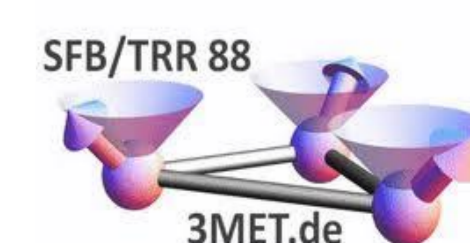
- [1] For a review, see: C. Pan, X. Jia, J. Cheng, *Synthesis* **2012**, *44*, 677–685.
- [2] a) L. J. Goossen, N. Rodríguez, K. Goossen, *Angew. Chem., Int. Ed.* **2008**, *47*, 3100; b) N. Rodríguez, L. J. Goossen, *Chem. Soc. Rev.* **2011**, *40*, 5030.
- [3] P. Mamone, G. Danoun, L. J. Goossen, *Angew. Chem. Int. Ed.* **2013**, *52*, 6704.
- [4] a) G. Dougherty, *J. Am. Chem. Soc.* **1928**, *50*, 571–573; b) L. J. Goossen, N. Rodríguez, C. Linder, P. P. Lange, A. Fromm, *ChemCatChem* **2010**, *2*, 430–442; c) L. J. Goossen, F. Manjolinho, B. A. Khan, N. Rodríguez, *J. Org. Chem.* **2009**, *74*, 2620–2623.
- [5] G. Danoun, P. Mamone, L. J. Goossen, manuscript in preparation.

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