Ruthenium-catalyzed Hydrocarboxylation of Alkynes: A Highly Efficient and Selective Access to Enol Esters

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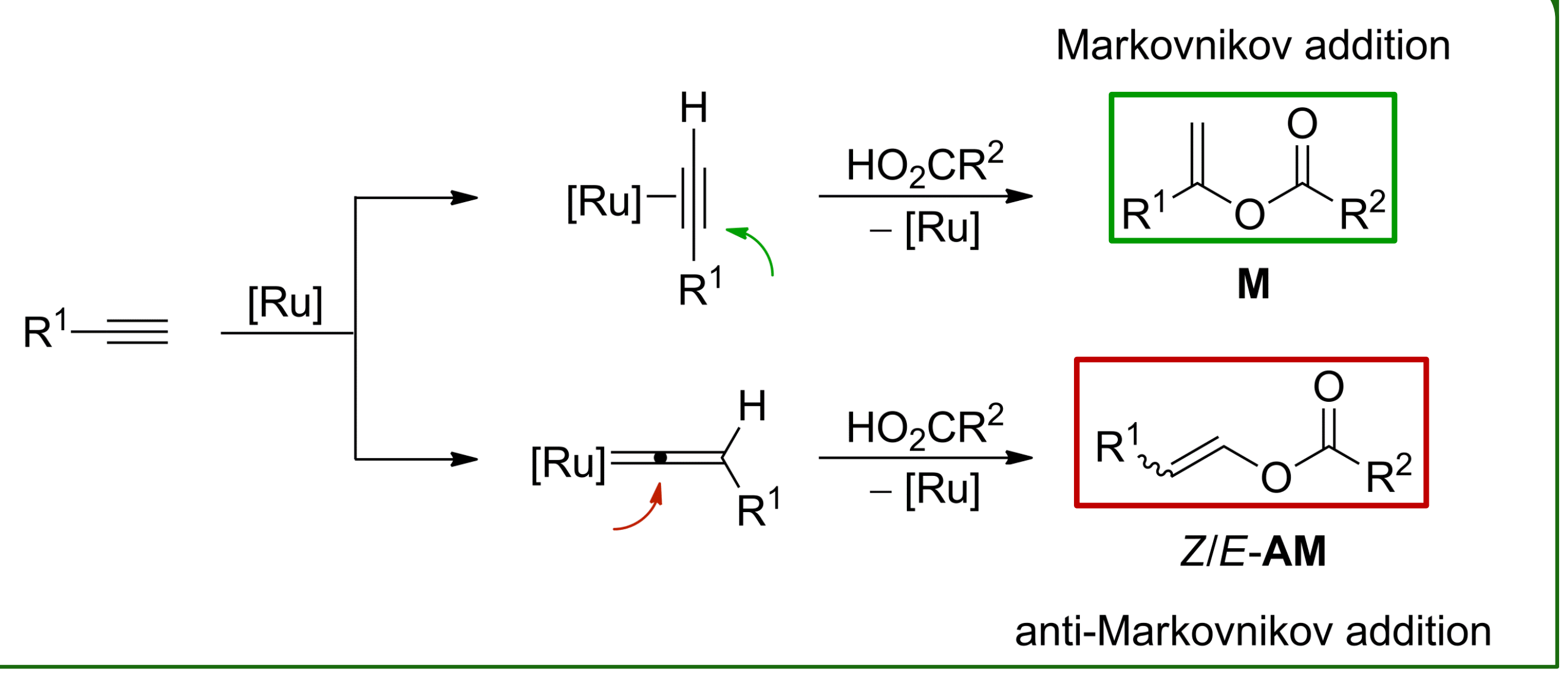
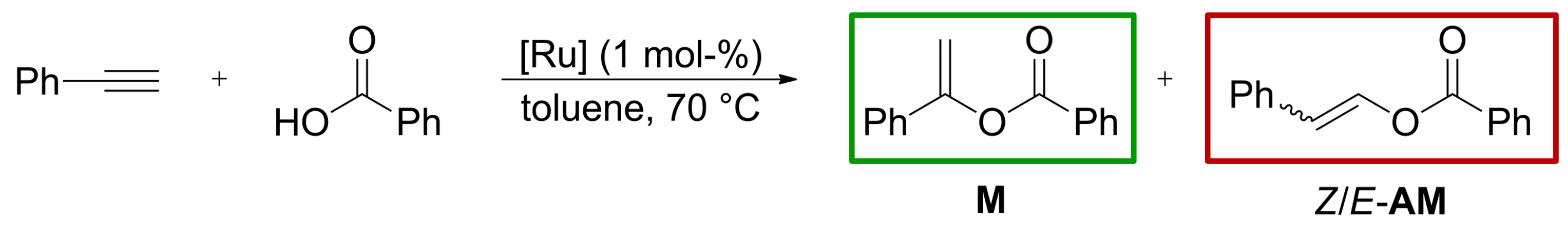
Motivation

Enol esters are important monomers in olefin polymerization[1] (*e.g.* vinyl acetate) and intermediates in organic synthesis.[2,3] Since the first reports on the atom-economic Ru-catalyzed addition of carboxylic acids to alkynes in the 1980s[4–6], a variety of Ru-catalysts has been developed.[7–9] Depending on the tautomerization between η^2-alkyne and vinylidene binding mode the Ru-catalyst either promotes the Markovnikov or anti-Markovnikov addition.[10,11] However, there are only few examples of catalysts that selectively promote the formation of the Markovnikov products.

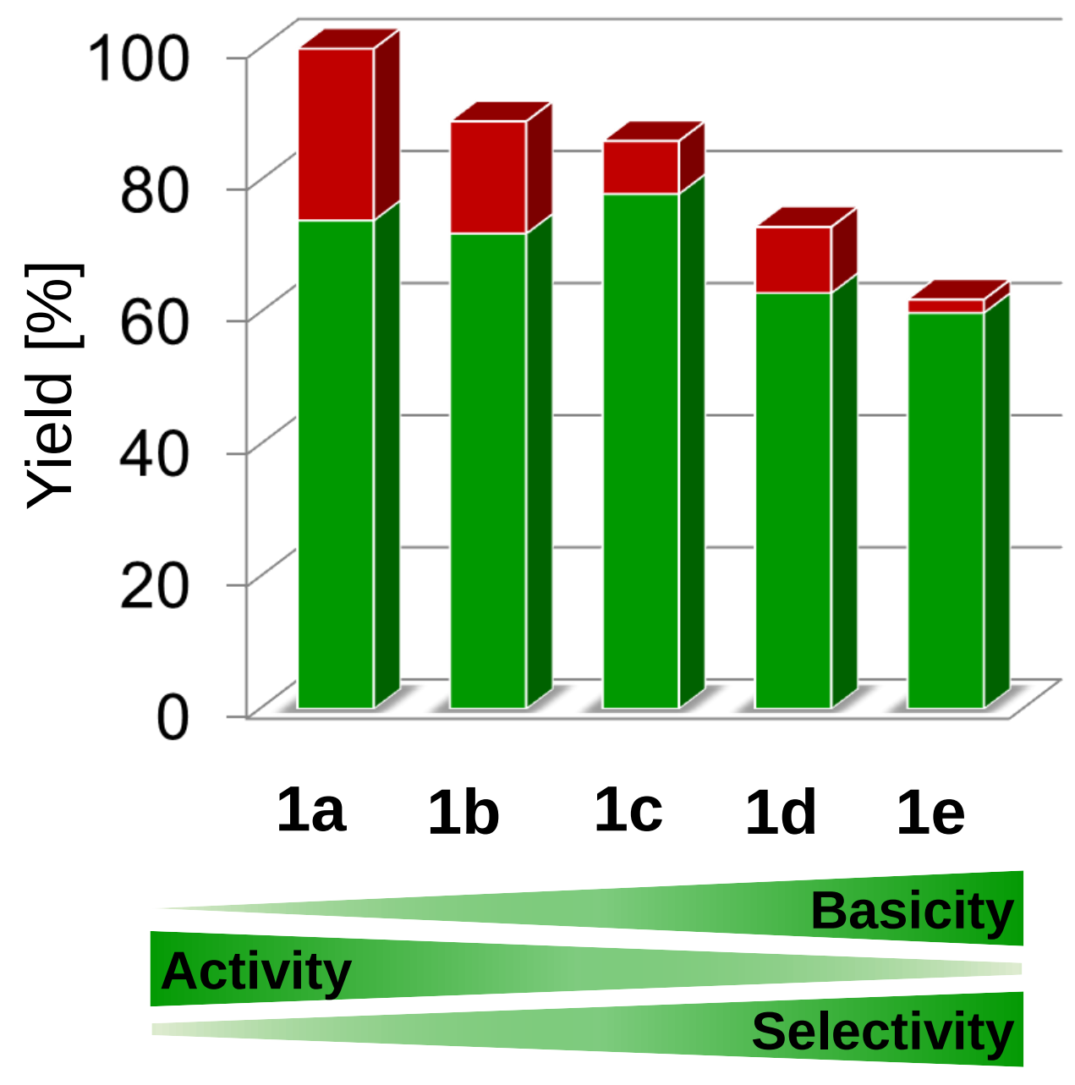
We herein present the application of Ru-complexes of type $[Ru(CO)_2(P[p\text{-}C_6H_4\text{-}X]_3)_2(O_2CPh)_2]$ (**1a**, X = CF_3; **1b**, X = Cl; **1c**, X = H; **1d**, X = Me; **1e**, X = OMe) in the catalytic formation of enol esters under mild reaction conditions.[12,13] These complexes have already demonstrated their suitability to selectively favor the Markovnikov products in the related synthesis of β-oxo esters by addition of carboxylic acids to propargylic alcohols.[14,15]



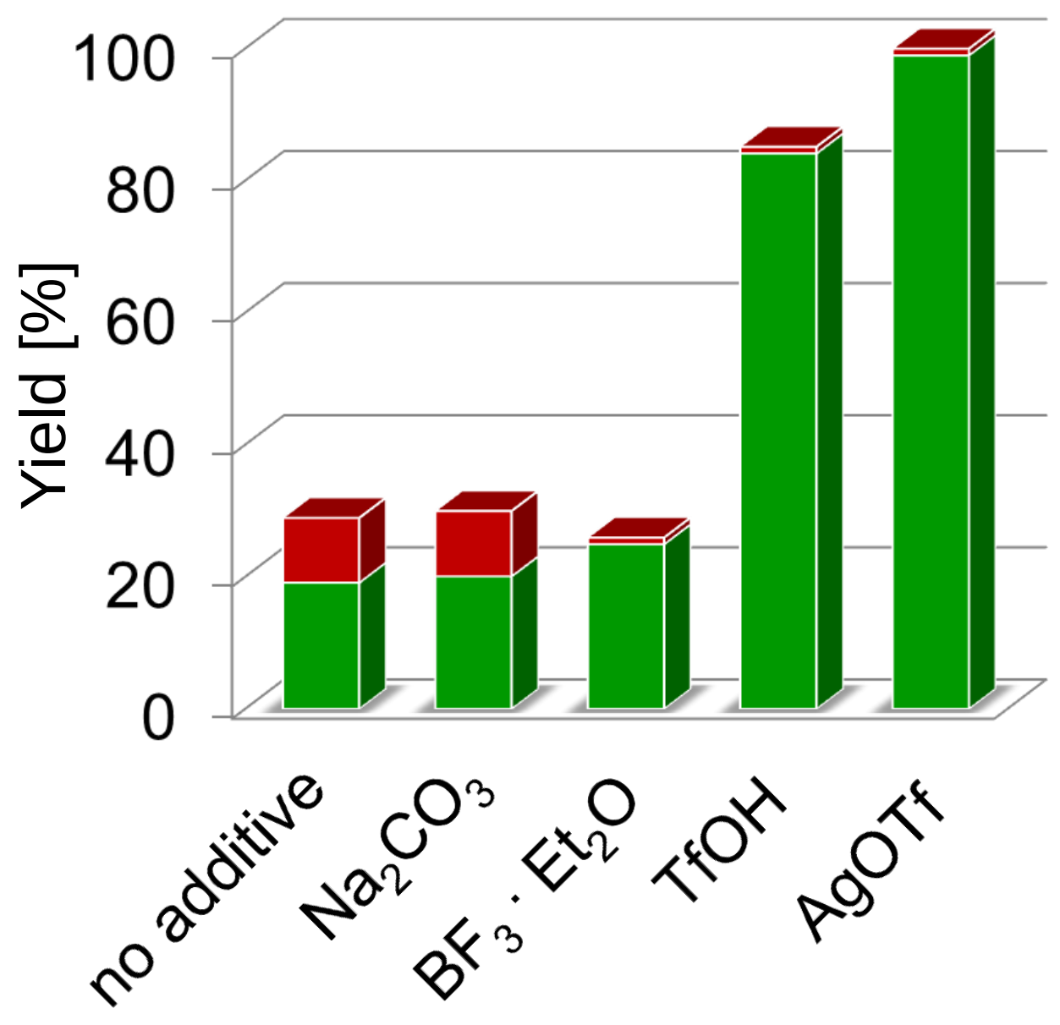
Catalyst Screening & Optimization



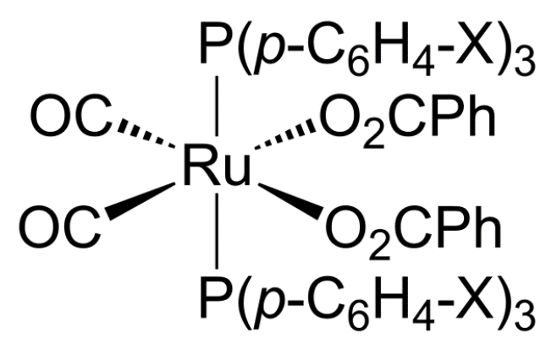
Catalyst Screening



Influence of Additives

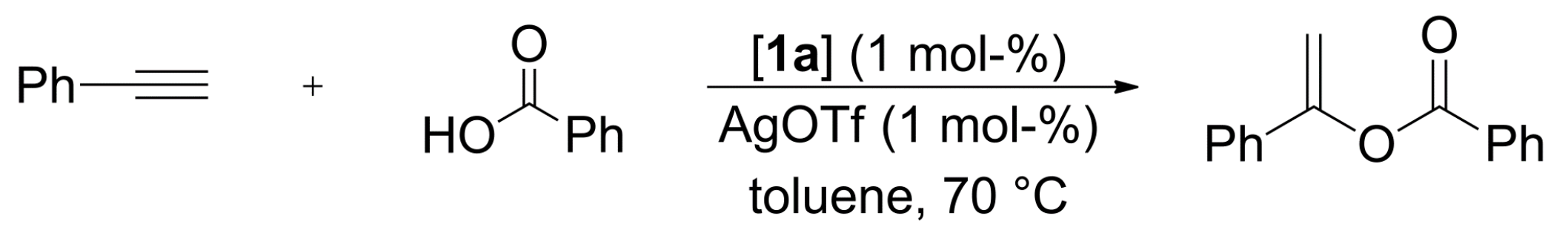


Catalysts

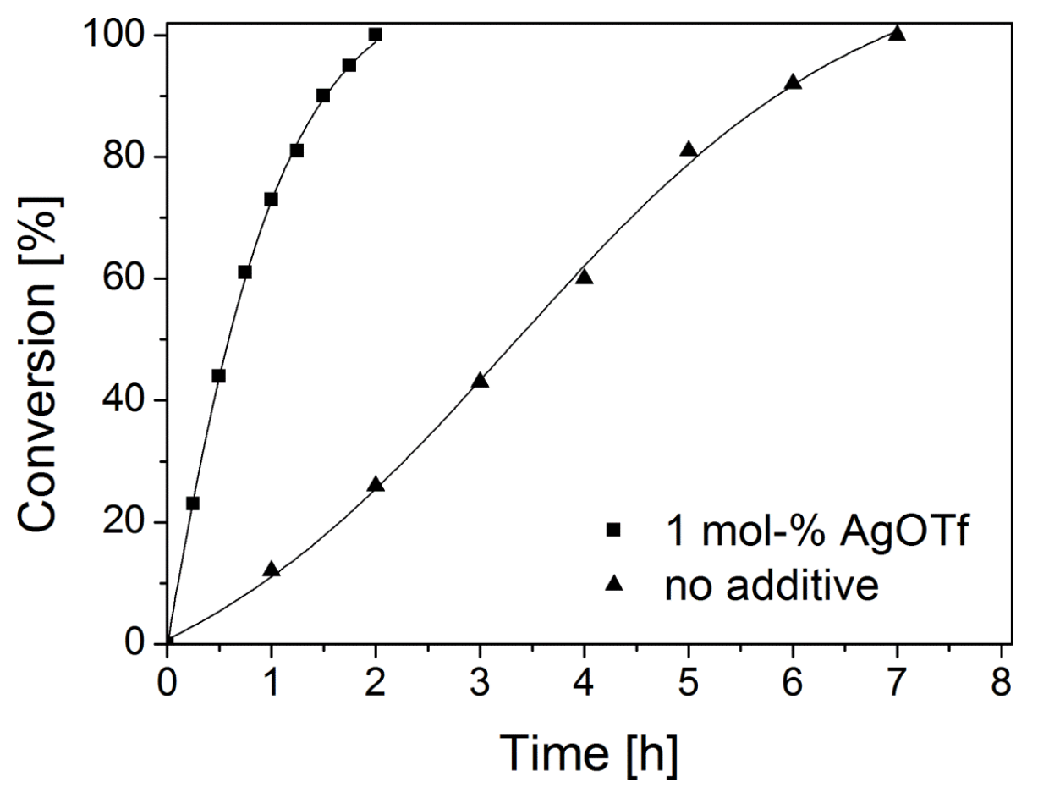


1a–e

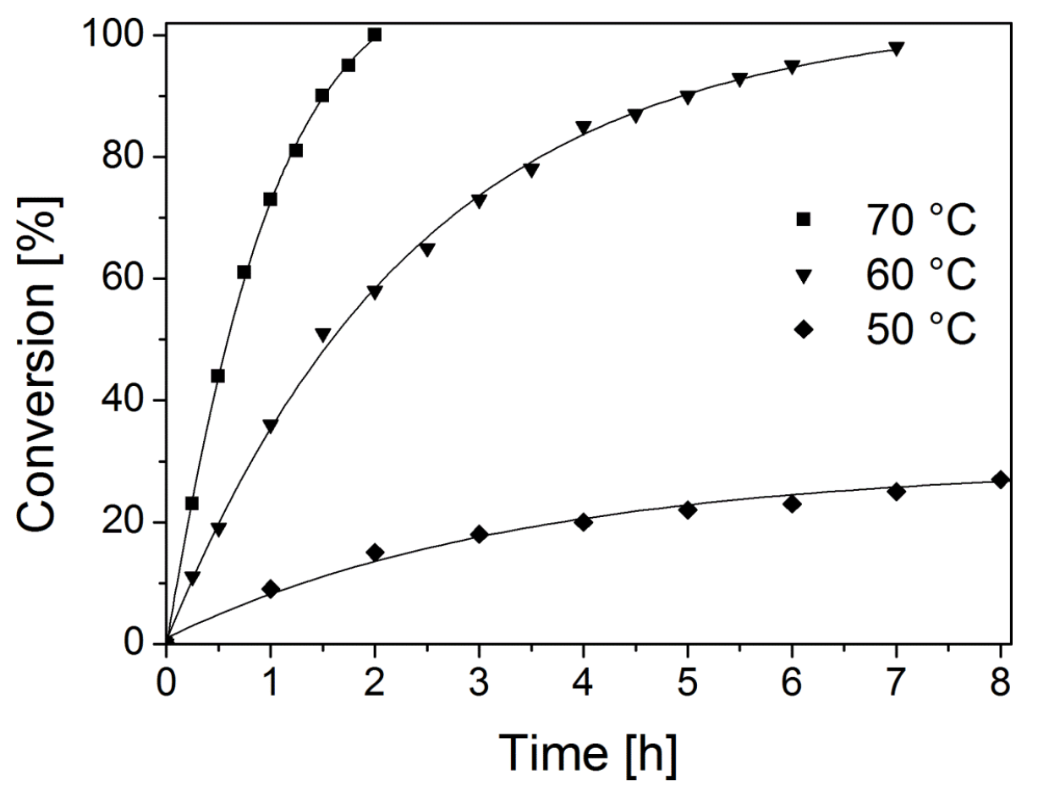
1a, X = CF_3
1b, X = Cl
1c, X = H
1d, X = Me
1e, X = OMe



Reaction Profile – Addition of AgOTf –

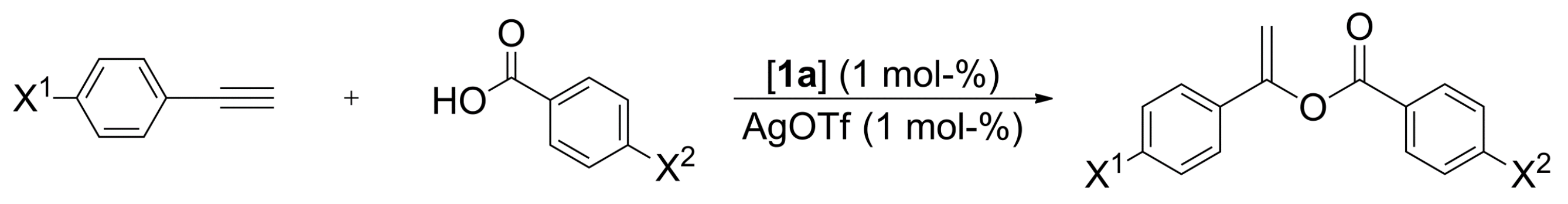


Reaction Profile – Temperature –

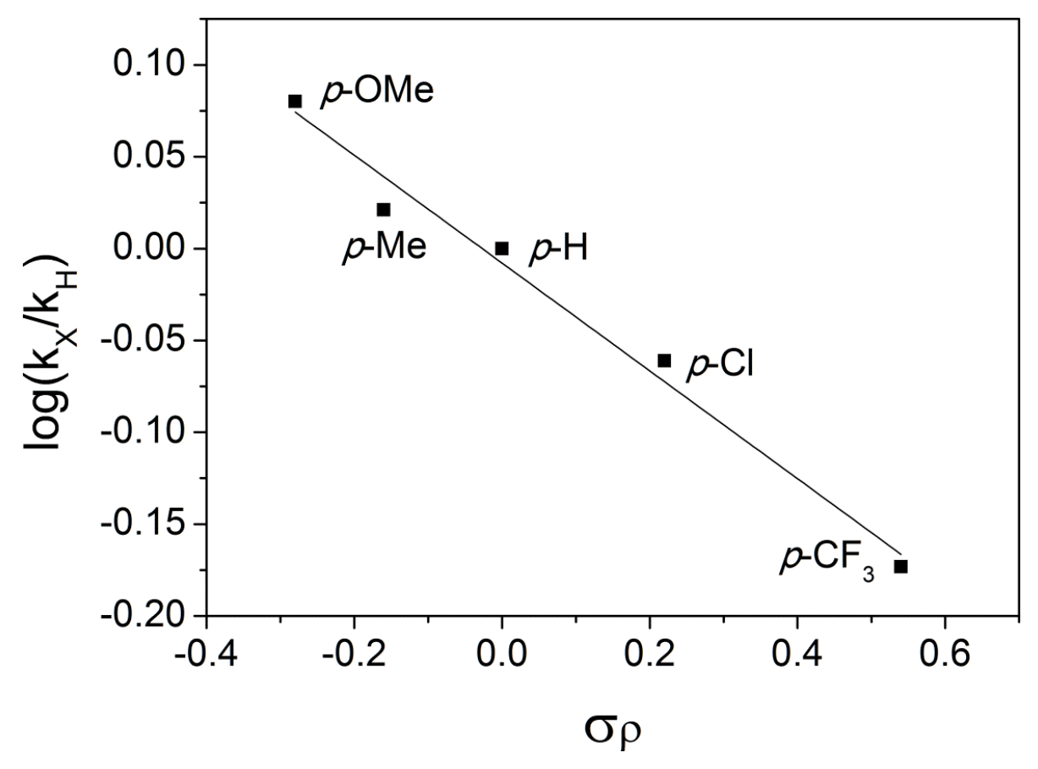


The reaction profiles demonstrate the increased activity of catalyst **1a** by the addition of catalytic amounts of AgOTf (■) compared to the absence of any additive (▲) at 70 °C.

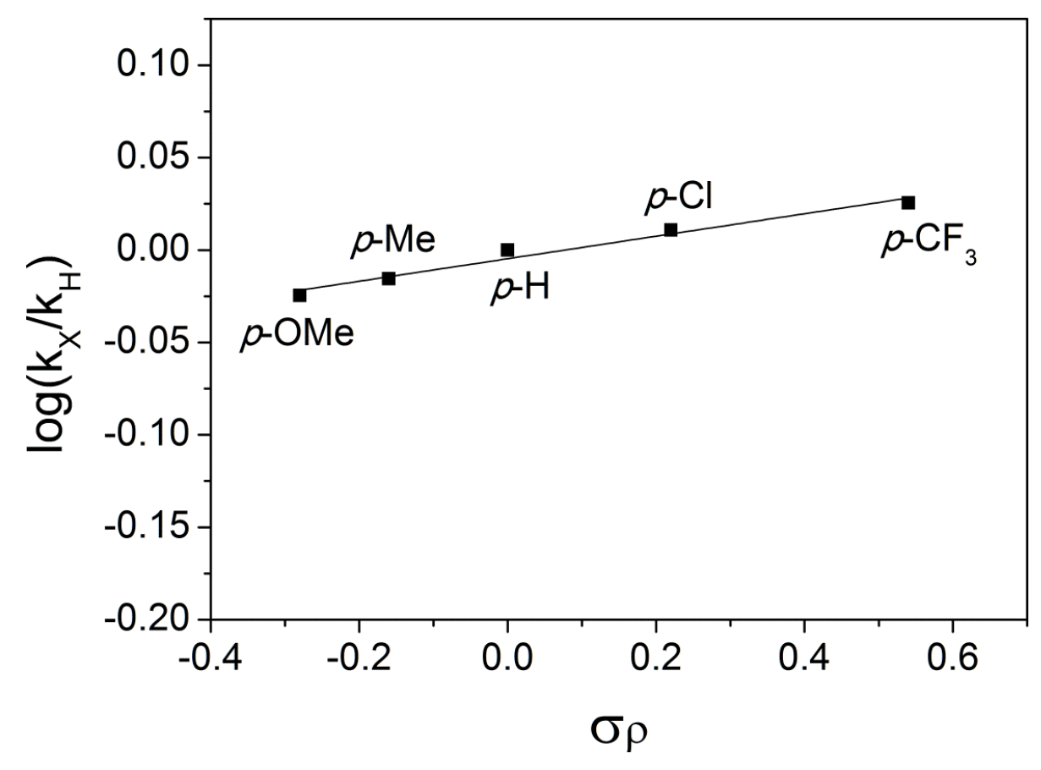
Hammett Study & Substrate Screening



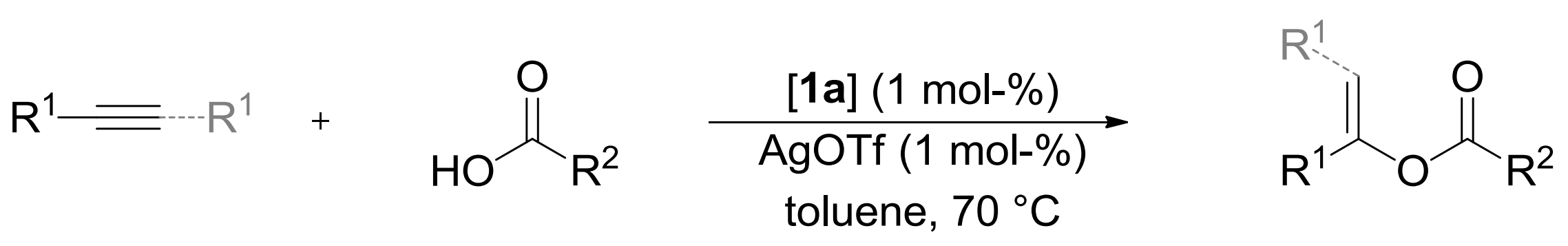
Alkyne

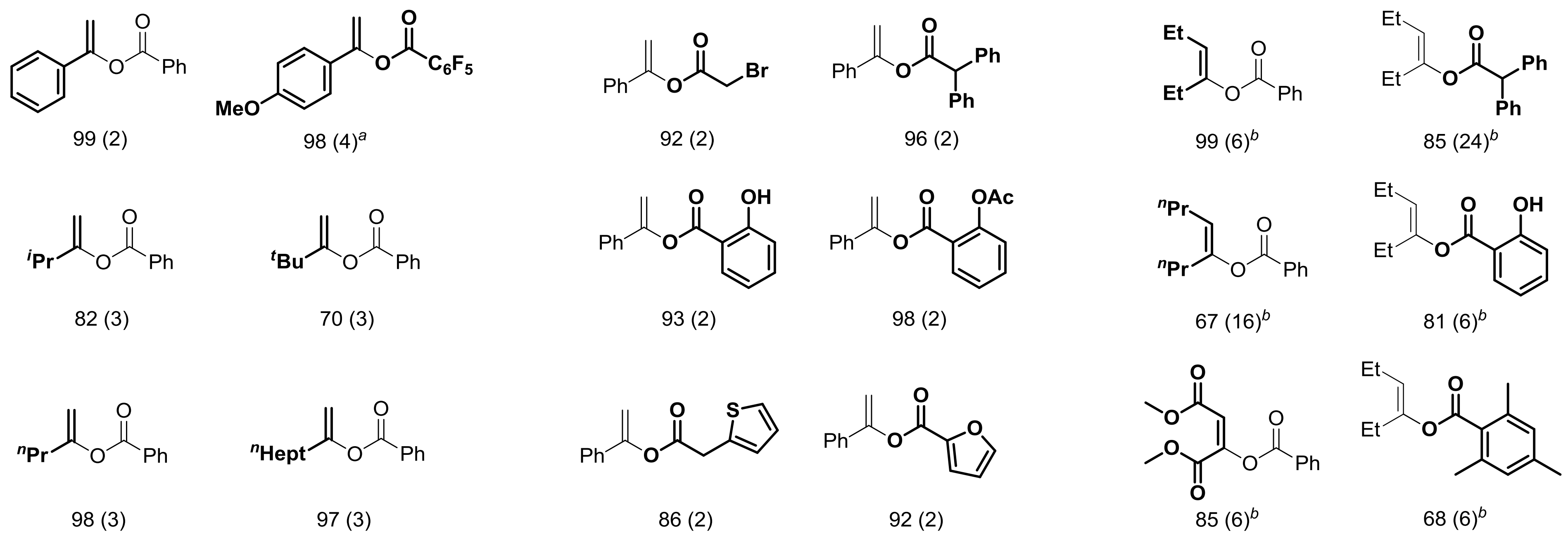


Carboxylic Acid



The Hammett studies demonstrate that electron-donating groups at the phenylacetylene (X^1, ρ = –0.29) or electron-withdrawing groups at the benzoic acid (X^2, ρ = +0.06) increase the reaction rate.





99 (2)
98 (4)[a]
92 (2)
96 (2)
99 (6)[b]
85 (24)[b]
82 (3)
70 (3)
93 (2)
98 (2)
67 (16)[b]
81 (6)[b]
98 (3)
97 (3)
86 (2)
92 (2)
85 (6)[b]
68 (6)[b]

Isolated yields. Optimized reaction times are given in parentheses. [a] Reaction performed at 25 °C. [b] Reaction performed at 140 °C.

Summary

- ✓ Successful application of Ru-catalysts **1a–e** in the enol ester synthesis
- ✓ The addition of catalytic amounts of AgOTf increases activity and selectivity
- ✓ Selective formation of Markovnikov addition products (up to 99 %)
- ✓ Best reported activities and selectivities for the conversion of aromatic alkynes
- ✓ Mild reaction conditions (25–70 °C) for the conversion of terminal alkynes
- ✓ Successful conversion of internal alkynes

References and Acknowledgements

[1] G. Roscher, *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley VCH, Weinheim, **2002**. [2] H. Schröder *et al*., *Adv. Synth. Catal*. **2013**, *355*, 1799. [3] P. Kleman *et al*., *ACS Catalysis* **2014**, *4*, 4398. [4] M. Rotem, Y. Shvo, *Organometallics* **1983**, *2*, 1691. [5] C. Ruppin, P. H. Dixneuf, *Tetrahedron Lett.* **1986**, *27*, 6323. [6] Y. Hori, T.-A. Mitsudo, Y. Watanabe, *J. Organomet. Chem*. **1987**, *321*, 397. [7] L. J. Gooßen, J. Paetzold, D. Koley, *Chem. Commun*. **2003**, 706. [8] F. Nicks, R. Aznar, D. Sainz, G. Muller, A. Demonceau, *Eur. J. Org. Chem*. **2009**, 5020. [9] C. S. Yi, R. Gao, *Organometallics* **2009**, *28*, 6585. [10] V. Cadierno, J. Francos, J. Gimeno, *Organometallics* **2011**, *30*, 852. [11] O. J. S. Pickup *et al*., *Organometallics* **2014**, *33*, 1751. [12] J. Jeschke, C. Gäbler, H. Lang, *J. Org. Chem.* **2016**, *81*, 47. [13] J. Jeschke, T. B. Engelhardt, H. Lang, *Eur. J. Org. Chem*. **2016**, doi: 10.1002/ejoc.201501583. [14] J. Jeschke, C. Gäbler, M. Korb, T. Rüffer, H. Lang, *Eur. J. Inorg. Chem.* **2015**, 2939. [15] J. Jeschke, M. Korb, T. Rüffer, C. Gäbler, H. Lang, *Adv. Synth. Catal*. **2015**, *357*, 4069.

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