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SYNFACTS Highlights in Chemical Synthesis

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X.-Y. DONG*, Z.-J. ZHOU, Z.-L. LI, P.-F. WANG, J. WANG, X.-Y. LIU* (GREAT BAY UNIVERSITY, DONGGUAN, AND SOUTHERN UNIVERSITY OF SCIENCE AND TECHNOLOGY, SHENZHEN, P. R. CHINA)

Ligand-Enabled Cu-Catalyzed Deoxyalkynylation of α-Unfunctionalized Alcohols with Terminal Alkynes
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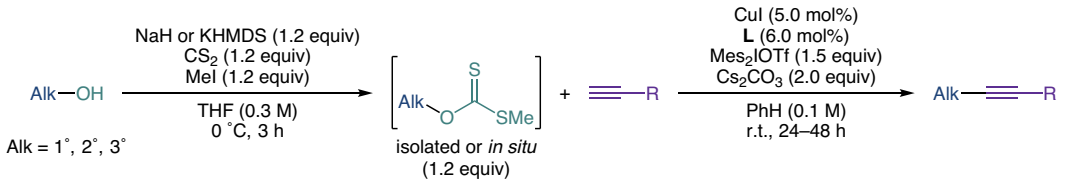
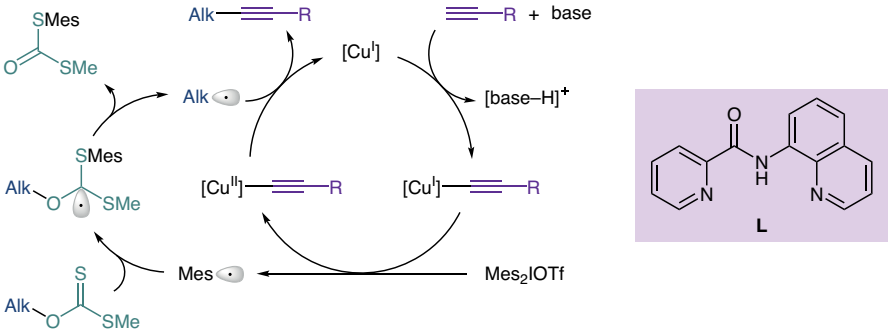
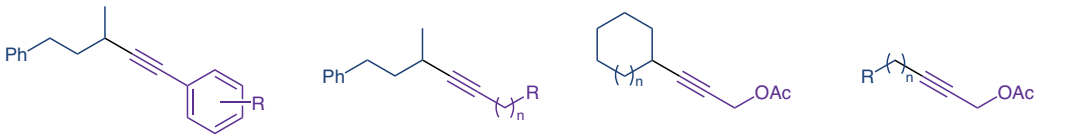
Copper-Catalyzed Radical Deoxyalkynylation of Unactivated Aliphatic Alcohols



Proposed mechanism:



Selected examples:



R = H: 80% yield
R = 4-CHO: 63% yield
R = 4-CN: 70% yield
R = 4-Cl: 78% yield
R = 3-Me: 81% yield
R = 3-CO_2Me: 77% yield
R = 3-F: 75% yield

n = 0, R = *c*-Pr: 71% yield
n = 1, R = Cy: 65% yield
n = 1, R = *n*-Bu: 77% yield
n = 1, R = OAc: 83% yield
n = 1, R = NHBoc: 66% yield
n = 1, R = Br: 50% yield
n = 1, R = N(SO_2Ph)$_2$: 77% yield
n = 2, R = CO_2Me: 82% yield
n = 2, R = NHBoc: 70% yield
n = 3, R = Cl: 75% yield

n = 1: 72% yield
n = 2: 64% yield
n = 7: 85% yield

52% yield

n = 1, R = *n*-Oct: 51% yield
n = 2, R = Ph: 52% yield
n = 2, R = 2-Naph: 52% yield
n = 2, R = 2-pyridyl: 53% yield
n = 2, R = 2-thienyl: 50% yield
n = 2, R = CN: 52% yield
n = 5, R = Br: 41% yield

Significance: A ligand-enabled copper-catalyzed protocol for the deoxyalkynylation of unactivated aliphatic alcohols with terminal alkynes is reported. This method features excellent functional group tolerance, providing various coupling products in high yields using primary, secondary and tertiary alcohols.

Comment: Mechanistic studies support the shown catalytic cycle. The key to this transformation was the use of a rigid quinolin-8-amine-derived tridentate *N,N,N*-ligand, which allowed both improving the yield and suppressing the formation of undesired by-products.

SYNFACTS Contributors: Martin Oestreich, Hendrik F. T. Klare, Sergiu Bicic
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Metals in Synthesis

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