SYNLETT
Spotlight 127

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Synthetic Applications of Stryker's Reagent

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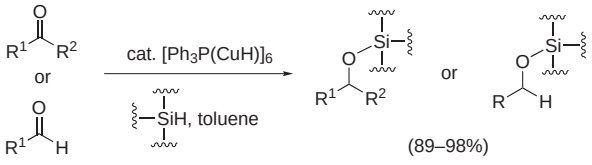
Introduction

Hexa-μ-hydrohexakis(triphenylphosphine) hexacopper, also known as Stryker's reagent, is a well-characterized copper(I) hydride reagent for chemoselective conjugate reduction of α,β-unsaturated ketones,[1–7] esters,[1,4] lactones,[8] nitriles,[9] aldehydes,[3] sulfones, and sulfonates.[6] The reaction is highly chemoselective, and isolated alkenes, halogens, and typical oxygenated functionalities are not reduced under the reaction conditions.[1–7] In the presence of several silanes and a catalytic quantity of Stryker's reagent, ketones and aldehydes are reduced to the corresponding alcohols.[10] The conjugated reduction can be performed either stoichiometrically or catalytically in the presence of reducing agents, and the reaction intermediates can be used for further C–C bond formations.[9,11–14] Stryker's reagent is commercially available, but various methods have been developed over the years for its preparation.[15–19]

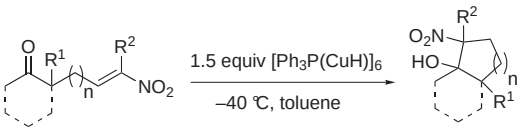
Abstract

(A) A catalytic quantity (≤ 5 mol% in copper) of Stryker's reagent in the presence of silanes [$PhMe_2SiH$, $MePh_2SiH$, or (*t*-Bu)Ph_2SiH] is an efficient reaction condition for the reduction of non-conjugated aldehydes or ketones to the corresponding silyl ethers or alcohols (basic workup is necessary) in high yields (89–98%).[10]



R^1 = Alkyl and aryl
R^2 = CH_3, C_2H_5

(B) With Stryker's reagent, the conjugate reduction of nitroalkenes is followed by intramolecular aldol reaction (Henry reaction) to produce β-nitroalcohols in modest to good yield.[12]



n = 1, 2, 3

R^1 = CH_3, H and R^2 = H (62–79%)
R^1 = H and R^2 = CH_3 (25–75%)
R^1 = R^2 = CH_3 reaction not observed

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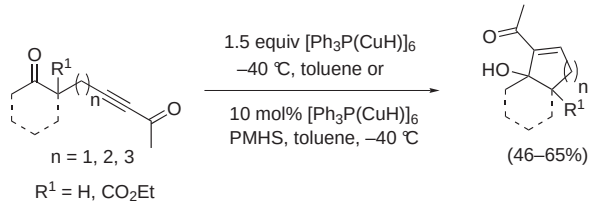
(C) Stoichiometric or catalytic amounts of Stryker's reagent can be used with polymethylhydrosiloxane to promote the tandem conjugate reduction–intramolecular aldol reaction of alkynones to generate β-hydroxyenones.[11]

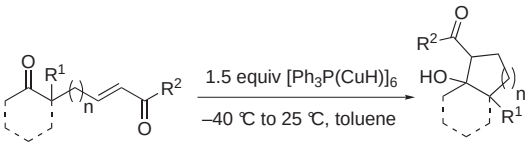


n = 1, 2, 3

R^1 = H, CO_2Et

PMHS = Polymethylhydrosiloxane

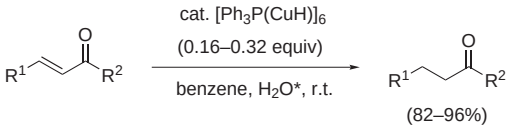
(D) A conjugate reduction with Stryker's reagent to form copper enolates, followed by an intramolecular aldol reaction, was used in the efficient one-pot generation of five- and six-membered carbocycles. This methodology has provided β-hydroxyketones diastereoselectively, and in good yields, at low temperatures and without the need for a dehydration step.[14]



n = 1, 2

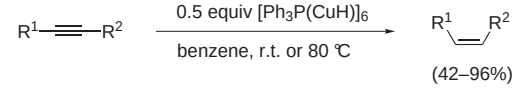
R^1 = H and R^2 = CH_3 (72–81%)
R^1 = CH_3, CO_2Et and R^2 = CH_3 (66–93%)
R^1 = CO_2Et and R^2 = CO_2Et, CN (41–84%)

(E) Stryker's reagent allows for the stoichiometric conjugate reduction of α,β-unsaturated ketones or lactones without affecting isolated alkenes, carbonyl groups, halogens or typical oxygenated functionalities under the reaction conditions.[1–8]



* = at least 1 equiv per hydride equiv

(F) Selective reduction of alkynes to the corresponding alkenes can also be achieved with Stryker's reagent. Terminal alkynes are reduced at room temperature, while unactivated internal alkynes react only at elevated temperatures. Protection of propargylic alcohol functionality is usually unnecessary, although in sterically hindered cases, fragmentation is sometimes competitive.[20]



R^1 = H, Ph, C_3H_7, C_6H_{13}, Bn, CH_2OH, $PhC(CH_3)OH$
R^2 = H, Ph, C_3H_7, CH_2OH, $C_6H_{13}C(OH)$

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