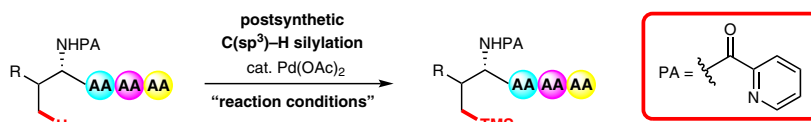
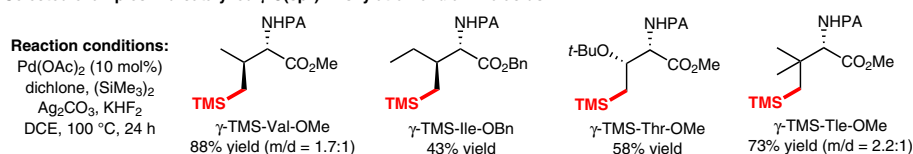


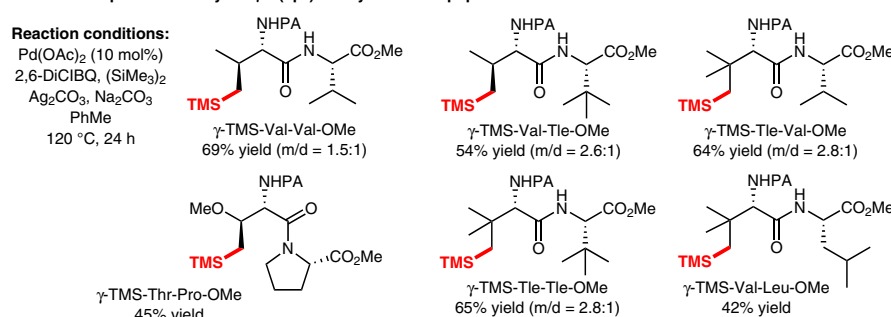
Palladium-Catalyzed Site-Selective γ -C(sp³)-H Silylation of Peptides



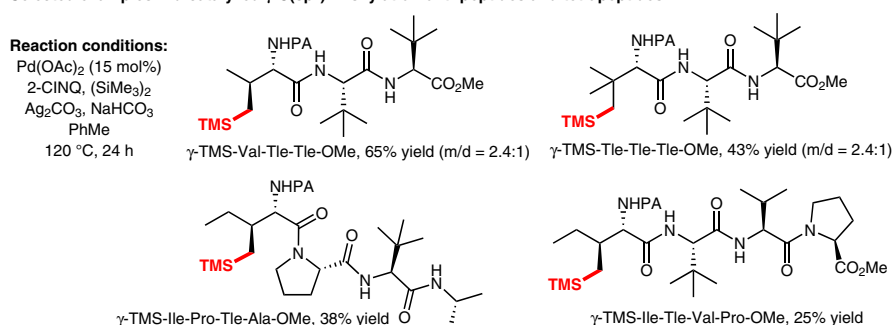
Selected examples: Pd-catalyzed γ -C(sp³)-H silylation of α -amino acids:



Selected examples: Pd-catalyzed γ -C(sp³)-H silylation of dipeptides:



Selected examples: Pd-catalyzed γ -C(sp³)-H silylation of tripeptides and tetrapeptides:



Significance: Chemically modified unnatural peptides are often endowed with improved biological and pharmacokinetic properties and are therefore valuable in the drug-discovery process. Modification by silicon-containing groups appears to be promising, because the presence of a silicon moiety in amino acids or peptides can help to improve permeation through membranes and increase proteolytic stability.

Comment: Shi and co-workers have developed an efficient procedure for the synthesis of various γ -silyl- α -amino acids and oligopeptides by palladium(II)-catalyzed γ -C(sp³)-H silylation. The present site-specific late-stage C(sp³)-H functionalization is assisted by a picolinamide auxiliary and uses cheap and commercially available hexamethyldisilane as a silylating agent. Compatibility with a broad range of amino acid residues and the facile removal of the picolinamide auxiliary are noteworthy features of the present protocol.