Palladium-Catalyzed Site-Selective $\gamma$-C(sp$^3$)–H Silylation of Peptides

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 $\gamma$-silyl-$\alpha$-amino acids and oligopeptides by palladium(II)-catalyzed $\gamma$-C(sp$^3$)–H silylation. The present site-specific late-stage C(sp$^3$)–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.

SYNFACTS Contributors: Hisashi Yamamoto, Sachin Suresh Bhojgude

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