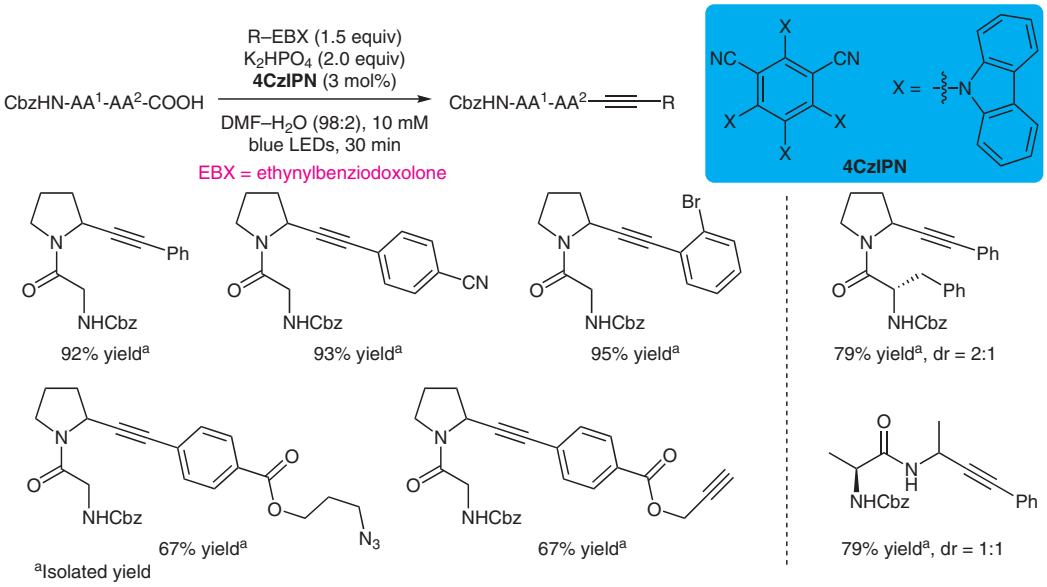
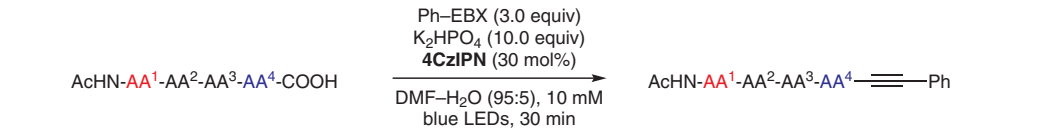
M. GARREAU, F. LE VAILLANT, J. WASER* (ECOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE, SWITZERLAND)

C-Terminal Bioconjugation of Peptides through Photoredox Catalyzed Decarboxylative Alkynylation
Angew. Chem. Int. Ed. **2019**, *58*, 8182–8186.

Photoredox-Catalyzed Decarboxylative Alkynylation of Peptides





A) Scope at the N-terminus

AcHN-AA[1]-Phe-Gly-Pro—Ph

AA[1] = Ala, >95% yield[b]; Arg, >95% yield[b]; His, 84% yield[b]; Lys, 47% yield[b]

S—Ph (>95% yield[b])

AcHN-Cys-Phe-Gly-Pro—Ph

B) Scope at the C-terminus

AcHN-Ala-Phe-Gly-AA[4]—Ph

AA[4] = Ala, >95% yield[b]; Phe, >95% yield[b]; Ser, >95% yield[b]; Met, >95% yield[b]; Asn, >95% yield[b]; Gly, >95% yield[b]; Glu, >95% yield[b]; His, 76% yield[b]; Asp, 37% yield[b]

C) Internal selectivity: C-terminus vs side chain

AcHN-AA[1]-Phe-Gly-AA[4]—Ph

AA[1] = Asp, AA[4] = Pro, >95% yield[b]; Ala, >95% yield[b]; Gly, 48% yield[b]

AA[1] = Glu, AA[4] = Pro, >95% yield[b]; Gly, 75% yield[b]

[b]Yield measured by HPLC as the ratio of the area of the product over remaining starting material and possible side products at 214 nm

Significance: This paper provides a decarboxylative strategy for the alkynylation of the C-terminus of peptides, starting from free carboxylic acids. C-Terminal selectivity can be achieved in the presence of carboxylic acid side chains, and a broad range of functional groups are tolerated in the reaction system.

Comment: The authors have developed a metal-free decarboxylative alkynylation of the C-terminus of peptides. The reaction proceeds rapidly and cleanly and might be useful for modifying peptides.

SYNFACTS Contributors: Hisashi Yamamoto, An Wu
Synfacts 2019, 15(07), 0817 Published online: 17.06.2019
DOI: 10.1055/s-0039-1689776; **Reg-No.:** H04719SF

Category
Peptide Chemistry

Key words
photoredox catalysis
decarboxylation
alkynylation
C-terminal selectivity
hypervalent iodine reagents
metal-free

Synfact of the Month