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Visible Light-Mediated Diastereoselective Synthesis of Novel C-Glycopeptides

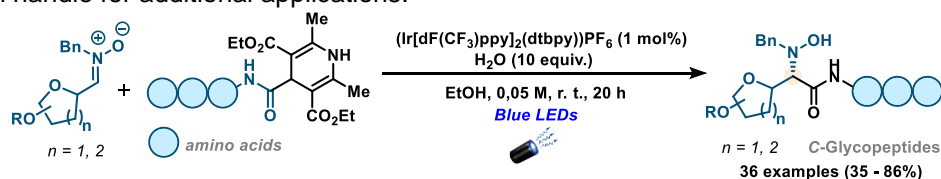
Jeimy A. C. Vélez,^{1*} Renan. O. Gonçalves,¹ Pedro H. R. Oliveira,¹ Robert Forster,² Stefanie I. Demel,² Till Opatz,² and Márcio W. Paixão¹

1) Department of Chemistry, Federal University of São Carlos, UFSCar
2) Department of Chemistry, Johannes Gutenberg-University Mainz, JGU
*e-mail: jacvelez@estudante.ufscar.br

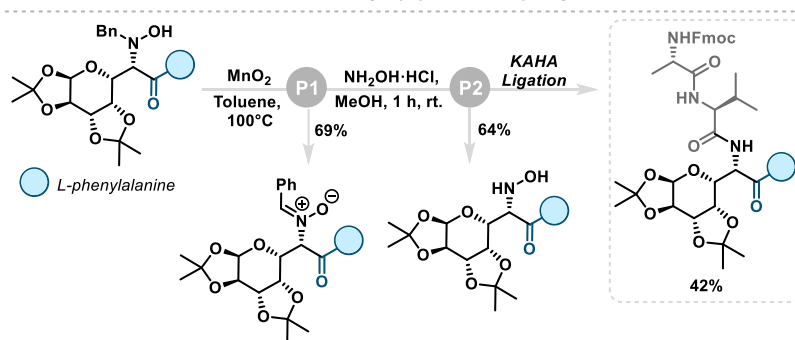
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ABSTRACT

The incorporation of carbohydrates into peptides can significantly enhance their pharmacological properties, including metabolic stability, target selectivity, and membrane permeability.¹ Despite some advances, synthetic methods for C-glycosylation of peptides and amino acids continue to present a significant challenge, with most methods relying on multistep preparations, harsh conditions, and a lack of stereocontrol.² To tackle this challenge, we decided to investigate the synergy between a range of glycosyl nitrones and the 4-amido 1,4-dihydropyridine (1,4-DHPs) derived from amino acids and peptides – two highly versatile synthons – employing a photocatalytic radical addition approach. Therefore, we have developed a mild and operationally simple photocatalytic protocol for synthesizing novel glycopeptides. This protocol demonstrates good stereoselectivity and performs well across a wide variety of substrates, including modified glycosides and peptides. Additionally, the resulting products possess a versatile hydroxylamine group that can be further modified, serving as a bioconjugation handle for additional applications.



Derivatization of Glycopeptide from L-phenylalanine



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