DEVELOPMENT OF A SYNTHETIC METHOD OF *C*-ACYL GLYCOSIDE VIA PHOTOREDOX COUPLING

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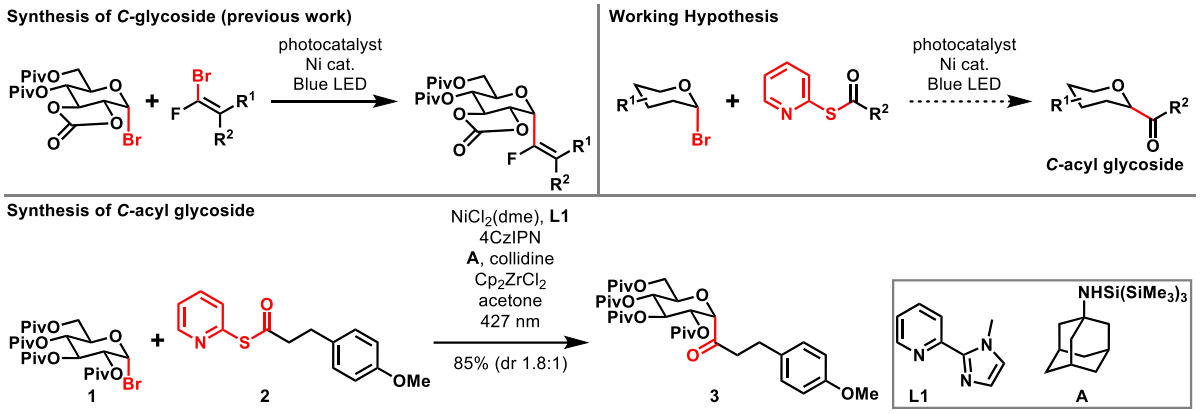
Glycoconjugates are biologically important molecules, yet their precise roles in many biological processes remain poorly understood due to their instability under conditions such as acidic and enzymatic hydrolysis. *C*-glycosides, which feature a *C*-glycosidic bond in place of the *O*-glycosidic bond, are attractive analogs of native glycans because they are resistant to hydrolysis. Recently, we demonstrated that *C*-glycosides can enhance or modify the biological activities of their parent molecules [1]. While numerous synthetic methods for *C*-glycosides have been developed, reports on *C*-acyl glycosides remain scarce. To address this, we developed a novel method for the synthesis of *C*-acyl glycosides.

We have developed a photoredox/Ni-catalyzed reductive cross-coupling strategy to synthesize fluorovinyl *C*-glycosides from Br-sugars [1]. We hypothesized that replacing the alkenyl bromide with a suitable acyl donor could produce *C*-acyl glycosides.

Inspired by Weix and Kishi's reports [2,3], we explored the cross-coupling reaction between Br-sugar and pyridyl thioester. Through optimization, we found that Br-sugar **1** and thioester **2** gave desired coupling adduct **3** under photoirradiation with blue LED in the presence of $NiCl_2$(dme), **L1**, 4CzIPN, aminosilane **A**, collidine, and Cp_2ZrCl_2. This protocol proved to be broadly applicable for various Br-sugars and thioesters, enableing the synthesis of *C*-acyl glycosides.



References:
1. Kato, N.; Hirai, G. *et al. J. Chem. Am. Soc.* **2024**, *146,* 2237.
2. Weix, D. J. *et al. Org. Lett.* **2012**, *14*, 1476.
3. Umehara, A. and Kishi, Y. *Chem. Lett.* **2019**, *48*, 947.