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Palladium-Catalysed C(sp³)–H Glycosylation for Synthesis of C-Alkyl Glycoamino Acids

Synthesis of C-Alkyl Glycoamino Acids via Palladium-Catalyzed C(sp³)–H Glycosylation

**Significance:** The authors report a highly efficient, regio- and diastereoselective palladium-catalyzed glycosylation of inert β-C(sp³)–H bonds of N-phthaloyl α-amino acids under mild conditions. The method utilizes a combination of silver carbonate and trifluoroacetic acid in a polar solvent (THF), which enabled the activation cycle of this C–H bond. The reaction has a high tolerance towards functional groups and a broad scope, providing over 30 β-substituted C-alkyl glycoamino acids with up to 88% yield.

**Comment:** This method allows for the first time to activate C(sp³)–H bonds for glycosylation reactions, thus advancing the state-of-the-art techniques in carbohydrate chemistry. Liu and co-workers propose a mechanistic cycle for the C–H activation, based on experimental studies. Therein, the formation of a palladacycle via cyclometallation plays a key role in the activation and the resulting diastereoselectivity.

**Proposed mechanism:**

![Proposed mechanism diagram]

**Selected examples:**

- 76% yield, dr > 20:1
- 72% yield, dr > 20:1

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SYNFACTS 2020, 16(03), 0291 Published online: 18.02.2020
DOI: 10.1055/s-0039-1690382; Reg-No.: P00120SF

Category: Metals in Synthesis
Key words: palladium catalysis, glycosylation, amino acids