論文の内容の要旨

論文題目

Development of a Catalytic Aminoalkynylation Reaction to Unprotected Aldoses for the Efficient Synthesis of Carbohydrate Derivatives

（糖誘導体の効率的合成を指向した無保護のアルドースに対する触媒的アミノアルキニル化反応の開発）

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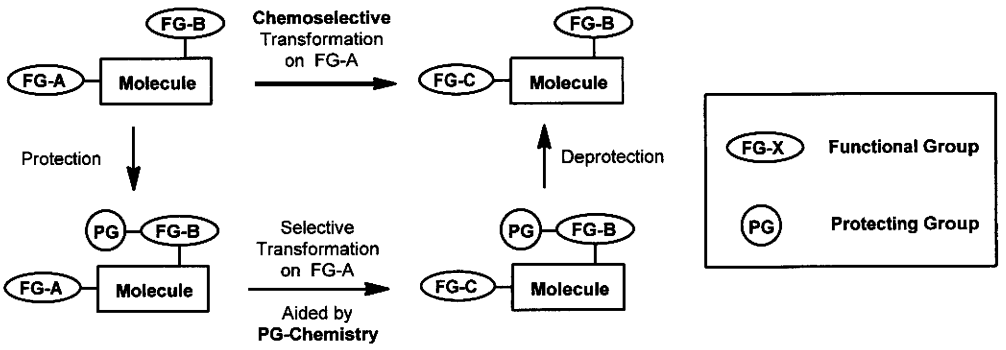
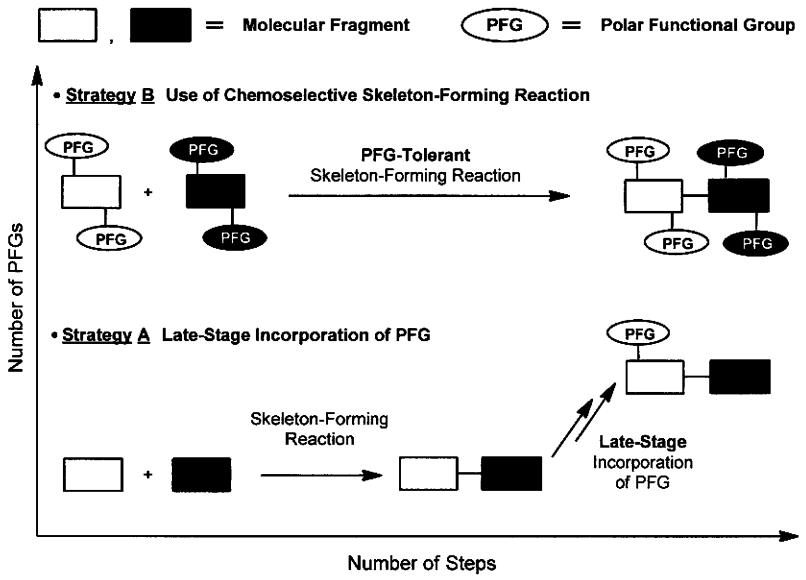
Chemoselectivity[1] issues have been major obstacles to the synthesis of highly complex molecules. Chemistry of protecting groups (PGs) has provided reliable solutions to these issues. However, the use of PGs generally impairs the synthetic efficiency in terms of atom[2]- and step economy[3] (Figure 1).

Figure 1. Chemoselectivity issues and protecting groups



Generally speaking, there are two major strategies to minimize the use of PGs in complex molecule synthesis (Figure 2): **A.** To introduce polar functional groups to the molecules at the late stage of the synthesis; **B.** To use highly chemoselective skeleton forming reactions.

Figure 2. Two major strategies to minimize the use of protecting groups in complex molecule synthesis

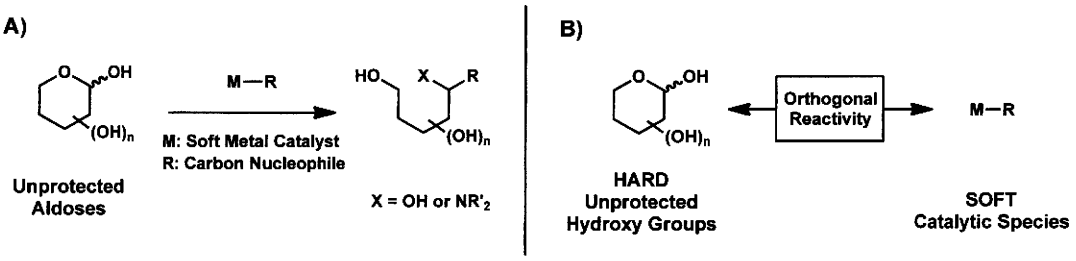


In light of the recognition that the later strategy is suitable especially for the synthesis of highly polar compounds such as carbohydrate derivatives, with which the significant biological activities are normally associated, I planned to develop a *catalytic* C-C bond forming reaction to unprotected aldoses (Scheme 1A). In order to ensure orthogonal reactivity of the catalytic species and the substrates, the use of soft metal catalyst was strategically adopted (Scheme 1B).

Scheme 1.

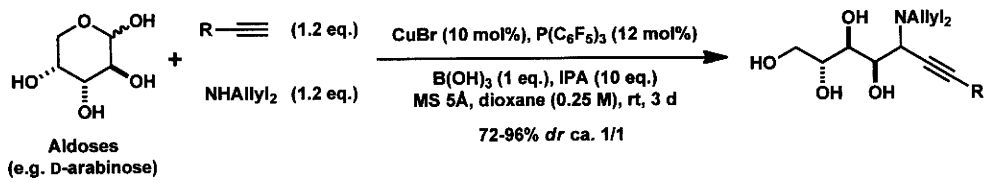
A) General objective: development of carbon-carbon forming reactions to unprotected aldoses

B) Conceptual outline of the strategy: orthogonal reactivity of the substrates and catalytic species



Additionally, by considering the synthetic utility of the products, I defined the soft Cu(I)-catalyzed aminoalkynylation reaction[4] to unprotected aldoses as the target reaction in this study. (Scheme 2.) After intensives studies for the optimal conditions, it was found that the use of boric acid was essential for the target reaction to proceed.

Scheme 2. A general equation of the developed aminoalkynylation to unprotected aldoses



Under the optimized conditions, many kinds of synthetically useful alkynes and several aldoses including a disaccharide were applicable to give the propargylamines with moderate or high molecular complexity by a single-step transformation (Scheme 2). Based on the scope of aldoses, it was speculated that the specific stereochemical motif of aldose substrates is important for high reactivity. A control reaction with a protected derivative of arabinose (the most reactive aldose), did not afford the corresponding propargylamine even in the presence of boric acid. These results suggest that boric acid does not simply act as protecting groups for the free hydroxy groups and that *the innate reactivity*[5] *of unprotected hydroxy group is essential for the target reaction to proceed.*

Although diastereoselectivity and the scope of aldose substrates need to be improved, this reaction can be regarded as an important step to the ultimate goal: to streamline the synthesis of polar molecules with minimum use of PGs, by making use of highly chemoselective skeleton forming reactions. Attempts to improve diastereoselectivity and to apply the developed reaction to the synthesis of a complex molecule are now undergoing.

References

(1) Trost, B. M. *Science* **1983**, *219*, 245.

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(4) A reported reaction with aldehydes without polar functional groups: Gommermann, N.; Koradin, C.; Polborn, K.; Knochel, P. *Angew. Chem. Int. Ed.* **2003**, *42*, 5763.

(5) Shenvi, R. A.; O'Malley, D. P.; Baran, P. S. *Acc. Chem. Res.* **2009**, *42*, 530.