Division of Synthetic Chemistry
– Synthetic Organic Chemistry –

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Selected Publications


Scope of Research

The research interests of the laboratory include the development of advanced molecular transformation, total synthesis of biologically active products, and molecular recognition. Programs are active in the areas of asymmetric alkylation of carbonyl compounds based on “memory of chirality”, organocatalysis for fine organic syntheses, synthesis of unusual amino acids and nitrogen heterocycles, regioselective functionalization of carbohydrates, and the structural and functional investigation of heterochiral oligomers.

KEYWORDS

Organocatalysis
Regioselective Functionalization
Dynamic Chirality
Unusual Amino Acid
Molecular Recognition

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Functional Group Tolerance in Organocatalytic Regioselective Acylation of Carbohydrates

Organocatalytic regioselective acylation of mono- and disaccharides with various functionalized acid anhydrides has been developed. Acylation of octyl β-D-glucopyranoside with acid anhydrides derived from α-amino acids, cinnamic acid, and gallic acid took place at C(4)-OH in 78-94% regioselectivity in the presence of catalyst 1. Especially, a disaccharide with seven free hydroxy groups (X=OH, R’=H) underwent acylation at C(4)-OH in 78% regioselectivity in the presence of catalyst 1. The 4-O-acylates of the glucose moiety were universally obtained as the major acylate in the acylation of various carbohydrates with various functionalized acid anhydrides. The functional group tolerance in the regioselective acylation catalyzed by 1 was found to be high. This seems surprising because the hydrogen-bonding interactions (yellow rectangles) between C(6)- and C(3)-OH of the glucose moiety and the catalyst, which was proposed to be responsible for the selective 4-O-acylation, are supposed to be specifically operative even in the presence of many other hydrogen bond donors and acceptors (pink circles).

Axially Chiral Binaphthyl Surrogates with a Metal Center Directly Connected the Chiral C-N Axis

Chiral binaphthyls have been extensively used in asymmetric synthesis. In particular, metal complexes of 2,2'-disubstituted-1,1'-binaphthyls have been shown to be extremely effective catalysts for a variety of asymmetric transformations. While the catalytically active metal center (M) in 4 is located far from the chiral axis (C(1)-C(1')) by three bonds, it is quite effective for asymmetric induction in many cases. The ultimate structure to minimize the distance between the metal center and the chiral axis is shown as 5 and 6 in which a metal center (Al) is directly connected to the chiral C(1')-X axis. X-ray analysis of 6 indicates that the complex adopts a conformation similar to that of 1,1'-binaphthyl. The racemization barrier of 5 was determined to be 23.0 kcal/mol, which was found to be higher by ~4 kcal/mol than the corresponding biaryl amine precursor with an N-H-N hydrogen bond.

Perfectly Regioselective and Sequential Protection of Glucopyranosides

Regioselective manipulation of one of the multiple hydroxy groups of carbohydrates has been a fundamental challenge in organic synthesis. We have developed a perfectly regioselective and sequential method for the preparation of orthogonally protected glucopyranosides starting from alkyl and thioalkyl β-D-glucopyranosides. An acyl group was introduced at C(4)-OH by organocatalysis in >99% regioselectivity. TBDPS, Boc, and BOM groups were sequentially introduced into the 4-O-acyl-glucopyranoside at C(6)-OH, C(2)-OH, and C(3)-OH, respectively, in >99% regioselectivity in each step. Each of the protective groups (PG1~PG4) was readily removed to give the corresponding mono-ols with three different protective groups, which are possible intermediates for the synthesis of natural and modified oligosaccharides.