THE SUMMARY OF Ph. D. DISSERTATION

Major		SURNAME, Firstname
Fundamental Science & Technology		SUZUKI, Tamotsu

Title

Total Synthesis of Spicamycin, a Novel Anti-tumor Nucleoside

Abstract

This dissertation describes the first total synthesis of spicamycin, a natural anti-tumor nucleoside possessing novel and unusual N^6-glycosylated adenine structures, starting from carbohydrates, in which the palladium catalyzed coupling reaction between glycosylamines and 6-halopurine derivatives was employed as the key reaction.

Chapter 1 describes the isolation, the structure determination, and biological activities of spicamycin and its related compounds.

In chapter 2, after surveying precedents for preparation of *N*-glycosides and N^6-substituted adenines, a development of a new and efficient methodology to construct N^6-glycosylated adenine structures using palladium catalyzed coupling reaction between glycosylamines and 6-halopurine derivatives are described .

In chapter 3, thermodynamic and kinetic analyses of the anomerization of *N*-glycosides are discussed.

Chapter 4 describes the total synthesis of spicamycin starting from *myo*-inositol. A chiral cyclitol derivative, prepared from *myo*-inositol in 15 step reactions involving optical resolution, was converted into an acyclic aldehyde intermediate. Stereoselective carbon elongation and an introduction of a nitrogen function into anomeric position afforded a heptopyranosylamine with L-*glycero*-L-*manno* configuration. Palladium catalyzed coupling reaction of the glycosylamine with a 6-chloropurine derivative generated adenine N^6-glycoside in moderate yield. Deprotection and subsequent introduction of an acyl side chain completed the first total synthesis of spicamycin.

Chapter 5 disclosed the new and efficient synthesis of a heptopyranose moiety of spicamycin. An enofuranoside prepared from D-ribose by stereoselective carbon elongation was transglycosylated to give an enopyranoside derivative. Stereoselective dihydroxylation and subsequent introduction of an azide group furnished the heptopyranose, an important intermediate for the synthesis of spicamycin.

Chapter 6 is a summary of the dissertation. This study revealed that the palladium catalyzed coupling reaction of glycosylamines and 6-halopurine derivatives is a useful method for the construction of unusual *N*-glycoside structures found in spicamycin. This study also provides a practical method for the synthesis of spicamycin and its novel derivatives, which are expected to show clinically interesting activities.