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## 学位論文内容の要旨

博士の専攻分野名称：博士（農学）

氏 名： Zetryana Puteri Tachrim

## 学位論文題名

Comprehensive studies of organic synthesis by utilizing chemical features of  
natural products

(天然物の化学的特性を活かした有機合成反応の網羅的検討)

Natural products possess a unique chemical diversity which its individual scaffolds has different reactivity and stability. Organic synthesis can give opportunity for exploring new synthetic strategies for wider ranges of research and development. In this study, organic syntheses by utilizing chemical features of natural products are optimized comprehensively.

### 1. Direct halogenations of carbohydrate

Regioselective halogenation of unprotected alcohols is the prior approaches to simplicity synthesis of carbohydrate-based products. Appel reaction—by the used of carbon tetrahalide and triphenylphosphine—is one of efficient method to convert primary hydroxyl groups to halide. Sucrose, the most abundant carbohydrate, was introduced by limited proportion of Appel reagents. Selective halogenation was occurred at 6- or 6'-position of sucrose's primary alcohols, which 1'-position considerably more hindered position. 1-kestose, one of potential fructooligosaccharide (FOS) with additional fructose moiety of sucrose at 1'-position, is also subjected into Appel reaction. Selective halogenation was occurred at 6-, 6', and 6''-position of 1-kestose's primary alcohols, which ensuring the least reactive primary alcohols at 1-position of fructose moiety, in line with sucrose utilization. Structural analysis of all halogenated derivatives can be completed by NMR analyses, which lead into revision of previous ambiguous interpretation of halogenated sucrose and introduction of the first halogenated FOS of 1-kestose.

## 2. $\alpha$ -Amino acids extensive acylation

*N*-Protected  $\alpha$ -amino aryl-ketone is known as a precursor in the synthesis of biologically active compounds. Friedel–Crafts acylation is one of favorable strategy to synthesize  $\alpha$ -amino aryl-ketone. *N*-hydroxysuccinimide ester (OSu) derivatives of  $\alpha$ -amino acids have high storage stability and showed no racemization during amide bond construction. In this study, aliphatic and aromatic *N*-trifluoroacetyl (TFA)-protected  $\alpha$ -amino acid-OSu derivatives were introduced for Friedel–Crafts acylation. The demonstration of optically active isoleucine, which has two chiral centers in the molecules, and its diastereomer *allo*-isoleucine to identify chirality of the Friedel–Crafts acylation product's offered more efficient method. Chirality retarded acylated product of isoleucine derivatives  $\alpha$ -proton can be directly observed by  $^1\text{H}$ -NMR. The introduction of these stereochemical features as a representative acyl donor can broaden the extensive acylation for revisiting  $\alpha$ -amino acid chloride formation and application. The comprehensive study of TFA- $\alpha$ -amino acid chloride for Friedel–Crafts acylation can be used to explore the synthesis of  $\alpha$ -amino aryl-ketone without loss of chirality.

## 3. Hydrogen/deuterium (H/D) exchange of aromatic compounds

In the demand of deuterated pharmaceuticals, development of efficient methods for H/D exchange has been increase rapidly. CycloDOPA (5,6-dihydroxy-indoline-2-carboxylic acid) is one of intermediate in melanin formation and betanidin main skeleton. Synthesis of deuterated cycloDOPA via H/D exchange by utilization of deuterium chloride and deuterated triflic acid are studied. The novel fully deuterated aromatic cycloDOPA derivative can be formed depending on temperature and time of H/D exchange condition. The complete study of H/D exchange resulted in the selective deuterium between 4- or 7-position of aromatic hydrogen of cycloDOPA.