学位論文の要旨

Abstract of Thesis

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専　攻 Division	地球生命物質科学専攻
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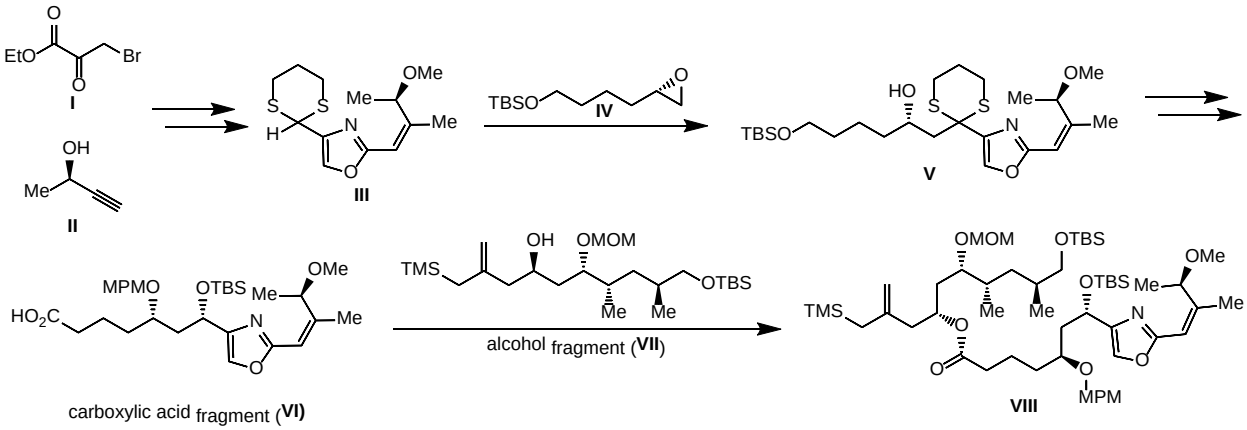
学位論文題目 Title of Thesis（学位論文題目が英語の場合は和訳を付記）

Study of the Convergent Synthesis of Enigmazole A, Neopeltolide and Ciguatoxin 3C

(Enigmazole A、Neopeltolide及びCiguatoxin 3Cの収束的合成についての研究)

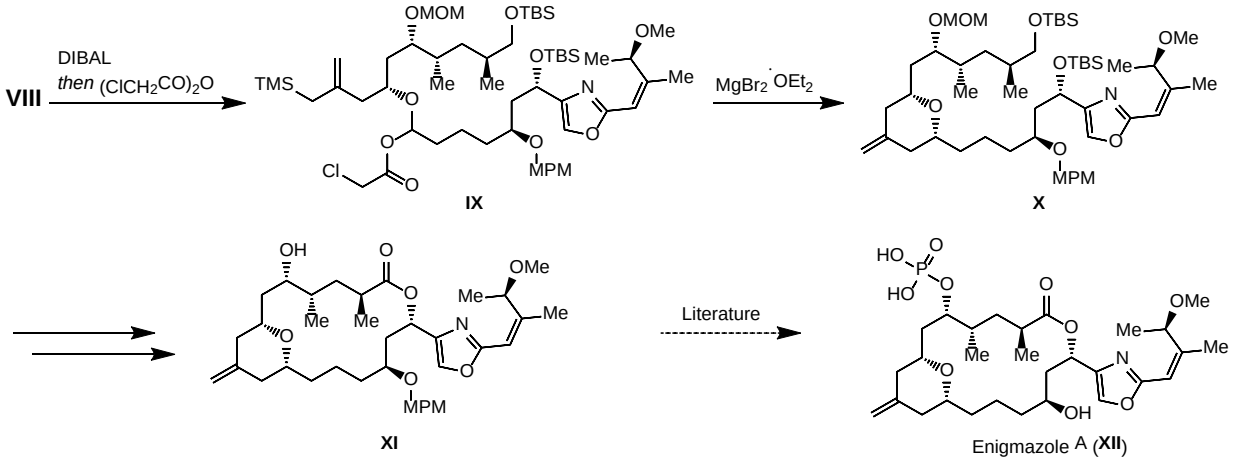
学位論文の要旨 Abstract of Thesis

This thesis consists of two parts. In the first part, synthetic studies of the two macrolides enigmazole A and neopeltolide are described. Enigmazole A was isolated from the marine sponge *cinachyrella enigmatica* and gained much interest due to its strong cytotoxicity and complex structure, resulting in five total syntheses to date. The synthesis presented in this thesis started from ethyl bromopyruvate **I** and chiral propargylic alcohol **II**. Following a literature procedure, dithiane **III** was prepared and coupled to chiral epoxide **IV** to give chiral alcohol **V** which was converted to the carboxylic acid fragment **VI**. Esterification of **VI** with alcohol fragment **VII** under Shiina conditions furnished ester **VIII**.

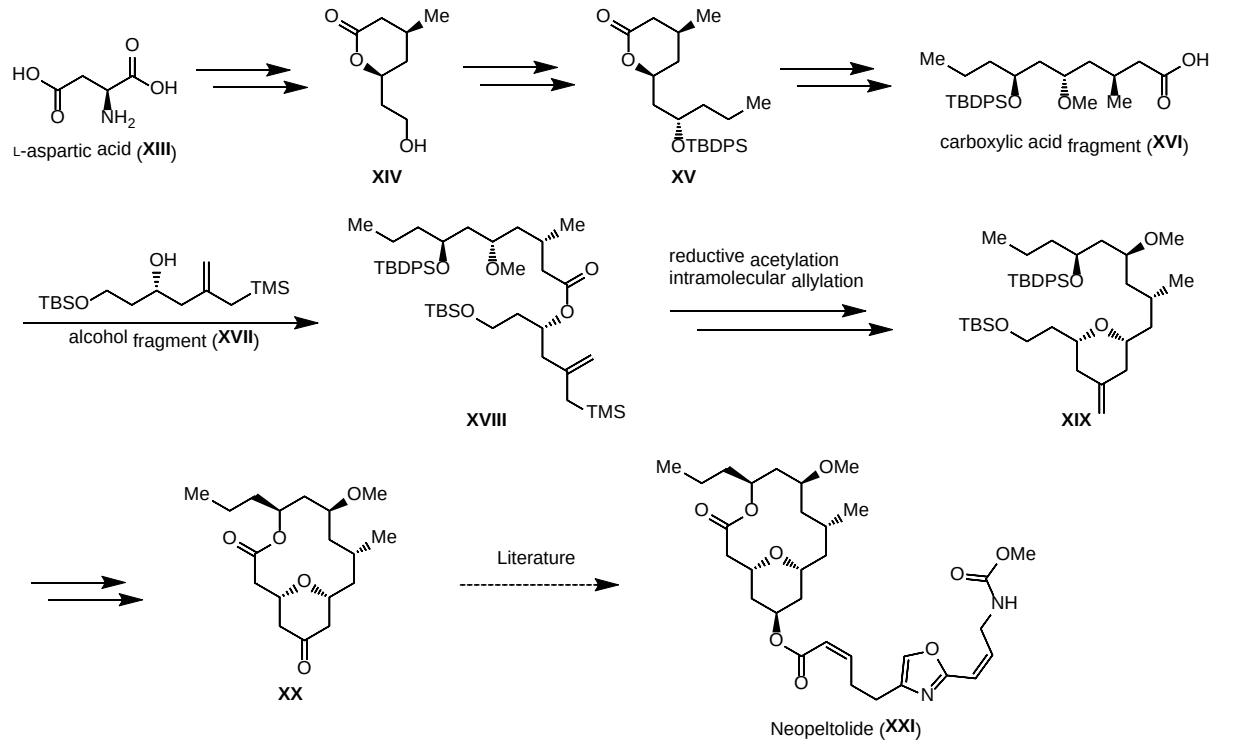


Reductive acetylation of the ester **VIII** gave α-acetoxy ether **IX**. The cyclization precursor **IX** was subjected to the intramolecular allylation with $MgBr_2 \cdot OEt_2$ to provide THP derivative **IX** was prepared and converted to lactone **X** by Yamaguchi`s conditions. Selective deprotection of the MOM group delivered alcohol **XI**, a known synthetic intermediate of enigmazole A **XII.**

Name	Andreas Meissner



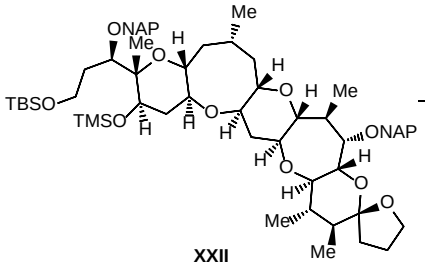
Next, the synthesis of the macrolactone core of neopeltolide, isolated from the marine sponge of *Daedalopelta* is described. Since its isolation, neopeltolide became a quite famous target for synthetic chemists. To date, more than 20 formal and total syntheses are published. Using L-aspartic acid **XIII** as the starting material, alcohol **XIV** was prepared according to a literature procedure. Subjection to a reaction sequence involving chiral allylation gave lactone **XV**. Further transformation led to the carboxylic acid fragment **XVI**. The acid was coupled to alcohol fragment **XVII** under Shiina`s conditions to give ester **XVIII**. Reductive acetylation and intramolecular allylation installed the desired THP ring of derivative **XIX**. This compound was transformed to the macrolactone **XX** which is a known synthetic intermediate of neopeltolide **XXI**.



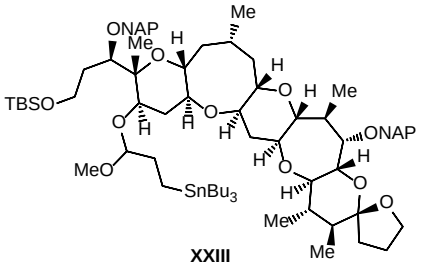
The second part of this thesis discusses research towards the polyether ciguatoxin 3C, isolated from the dinoflagellate *Gambierdiscus toxicus*. Two syntheses are published from Hirama`s group which gave fundamental insights in the reactivity of the protecting groups. The synthetic study was based on H-M ring fragment **XXII**. The stannane containing acetal was prepared via reductive acetylation and acetal exchange to give **XXIII**. Conversion to

Name	Andreas Meissner

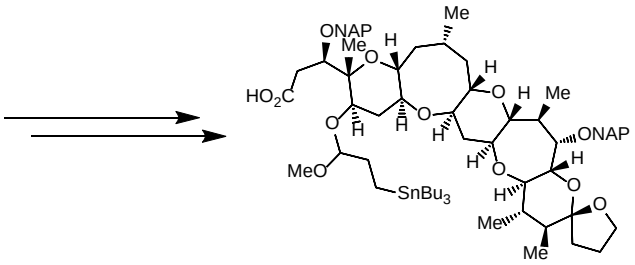
the carboxylic acid fragment **XXIV** and coupling to A-E alcohol fragment **XXV** under Shiina`s conditions delivered ester **XXVI**. Treatment with TMSI/HMDI furnished an allyl stannane which was subjected to reductive acetylation and intramolecular allylation to install the desired G-ring of compound **XXVII.**



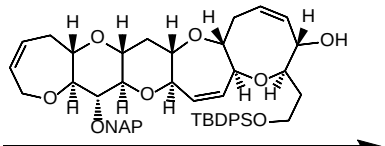
XXII



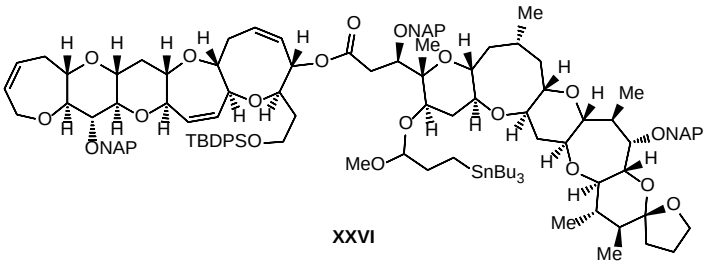
XXIII



carboxylic acid fragment (**XXIV**)

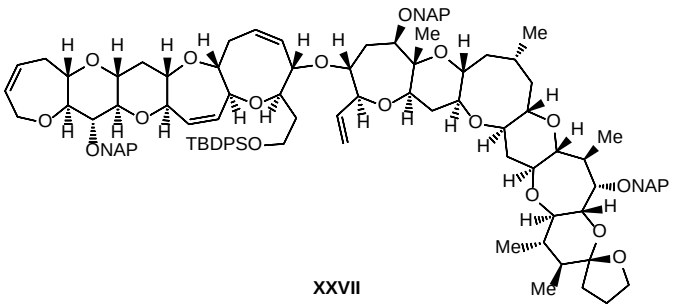


alcohol fragment (**XXV**)



XXVI

reductive acetylation
intramolecular allylation



XXVII