SUMMARY OF Ph.D. DISSERTATION

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Title

Synthetic studies on sesquiterpenoids from the liverwort possessing the bicyclo[4.3.0]nonane framework

Abstract

Liverworts produce a variety of sesquiterpenoids, possessing the bicyclo[4.3.0]nonane moiety such as chiloscyphone, pinguisenol, and acutifolone. These natural products have unique structures including the *cis*-oriented continuous-substitutions in the bicyclo[4.3.0]nonane structure, which provide anticancer, antimicrobial, and antifeedant activities. We undertook an efficient synthesis of these sesquiterpenoids by our original approach varied from the conventional methodologies. We developed a synthetic method of the bicyclo[4.3.0]nonane system by using the intramolecular Diels-Alder reaction. Availability of the intermediate was demonstrated by the total synthesis of chiloscyphone and isochiloscyphone through the Michael addition and desulfurization of the cyclic sulfide as key steps. Furthermore, we accomplished the first total synthesis of acutifolone and formal total synthesis of pinguisenol by the Mukaiyama aldol reaction. The chiral intermediate was synthesized by using the intramolecular Diels-Alder reaction started from D-mannitol. In this reaction, it was considered that the stereoselectivity of the cycloadducts might be effected by electric interaction between the allylic substituent and the diene moiety. This protocol enables us not only to synthesize the bicyclo[4.3.0]nonane framework, but also to introduce a variety of functional groups into desired positions. The synthetic intermediates were assessed for various antimicrobial activities such as Gram positive or Gram negative bacteria. Among them, methicillin resistant *Staphyrococcus aureus* (MRSA) has been known as one of the drug resistant bacteria, which caused the serious infections. Therefore, compound with significant potential as leads for development anti bacterial drugs has been desired. The intermediate possessing the tricyclic structure exhibited the biological activity against MRSA and/or potentiation of the imipenem activity. It has been expected that these results contribute to the development of the new anti-MRSA drug.