SUMMARY OF Ph.D. DISSERTATION

School	Student Identification Number	SURNAME, First name
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Title

Synthetic study of diaryl ether compounds using electrochemical direct / indirect oxidation methodologies

Abstract

The diaryl ether is the common key structure of a variety of isodityrosine, diarylheptanoid, diarylchalcone natural products, such as vancomycin, K-13, eurypamide, galleon, and verbenachalcone. These natural products exhibit a wide range of biological activity. Therefore, synthetic studies of natural products carrying the diaryl ether moieties have been reported by many synthetic chemists around the world. Our laboratory has studied application of oxidative phenol-coupling reaction as a part of biomimetic synthesis of a wide range of natural products. In this thesis, anodic oxidation and thallium (III) oxidation have been investigated in particular.

Based on the strategy mentioned above, total synthesis of verbenachalcone and its SAR (structure activity relationship) study of NGF (nerve growth factor)-mediated neurite outgrowth of PC12D cells were investigated. In addition, thallium (III)-mediated electrochemical oxidation was investigated to develop its catalytic usage.

(1) Total synthesis of verbenachalcone and its SAR study using electrochemical construction of diaryl ether moiety.

Verbenachalcone was isolated from the aerial part of *Verbena littoralis* H. B. K. The typical dimeric chalcone structure connected with a diaryl ether linkage, provides enhancement of the NGF -mediated neurite outgrowth of PC12D cells. Our electrochemical phenolic oxidation methodology enabled successful construction of the core diaryl ether by dimerization of the corresponding *o,o*-dihalogenated phenol derivatives, followed by introduction of an alkoxy function. Based on this methodology, total synthesis of verbenachalcone and its SAR study using newly synthesized 17 derivatives were executed.

(2) Electrochemical regeneration of thallium (III) ion, toward catalytic thallium (III) mediated oxidation.

In thallium(III) trinitrate (TTN)-mediated phenolic coupling to provide diaryl ether macrocyclic compounds, utilization of *o,o-di*halogenated phenol is essential to control the oxidation potential and the regioselectivity. The versatile availability of the TTN oxidation for intramolecular oxidative cyclization was proved by the successful total synthesis of OF-4949, K-13, and eurypamides. Even so, a disadvantage of this method is the limitation of the reaction yield and toxicity of thallium (III) salts. To conquer these weak points of the thallium-mediated intramolecular oxidative cyclization method, elaboration of the reaction conditions was carried out to optimize the yield. Furthermore, electrochemical generation of the thallium (III) from (I) and *in situ* reaction with phenols or olefinic compounds were parformed as an approach to the ultimate goal, which will be an environmentally benign catalytic cycle.