Principal Researcher	Yasuyuki Kita	**Number of Researchers**	4
Research Institution・Department・Title	Professor, Graduate School of Pharmaceutical Sciences, Osaka University	**Location of Institution**	Suita

Title of Project	Environmentally benign reactions for large-scale syntheses of bioactive natural products and their application to drug discovery
Abstract of Research Project	In the last two decades, biologically active natural products with unique, highly complex molecular skeletons have been used as leading compounds for raw materials of the new drugs. Due to the limitation on natural supply, the highly efficient large-scale syntheses and molecular design have been sought in drug discovery. With that purpose in mind, we have focused on a synthetic strategy effective to develop novel reactions and reagents, as well as to apply them for the total synthesis of target molecules. To date, utilizing our new methods, we achieved the total synthesis of anticancer marine alkaloid discorhabdin A, which has a unique sulfur-containing spirocyclic enone system, and the asymmetric total synthesis of antitumor antibiotic, fredericamycin A for the first time. To develop environmentally benign synthetic methods has been our goal for more than ten years. For example, the use of less toxic hypervalent iodine reagents as a replacement for toxic heavy metal oxidants enabled us to establish novel activation methods of iodine reagents to generate aromatic cation radicals, in consequence, which have resulted in the development of various new oxidation reactions. Recently, we succeeded in the radical reactions of hydrophobic compounds in water and the new asymmetric reactions utilizing natural hydrolytic enzymes. In this project, we improve our methodology for rational new drug discovery based on the total syntheses of complicated natural products by developing environmentally benign synthetic methods, establishing the large-scale production, and utilizing computer-supported chemistry .
References	Enantioselective Total Synthesis of a Potent Antitumor Antibiotic, Fredericamycin A, *J. Am. Chem. Soc.* **2001**, *123*, 3214-3222. Efficient Oxidative Biaryl Coupling Reaction of Phenol Ether Derivatives Using Hypervalent Iodine(III) Reagents, *Tetrahedron* **2001**, *57*, 345-352. Novel and Efficient Synthesis of *p*-Quinones in Water via Oxidative Demethylation of Phenol Ethers Using Hypervalent Iodine(III) Reagents, *Tetrahedron Lett.* **2001**, *42*, 6899-6902. Enantiodivergent Synthesis of Either Enantiomer of ABCDE-Ring Analog of Antitumor Antibiotic, Fredericamycin A via Intramolecular [4+2] Cycloaddition Approach, *Org. Lett.* **2001**, *3*, 4015-4018. Facile and Efficient Sulfenylation Method Using Quinone Mono *O,S*-Acetals under Mild Conditions, *J. Org. Chem.***2001**, *66*, 2434-2441. A Novel and Efficient Methodology for the C-C Bond Forming Radical Cyclization of Hydrophobic Substartes in Water, *Org. Lett.* **2001**, *3*, 1157-1160. An Efficient Lipase-Catalyzed Enantioselective Desymmetrization of Prochiral 2,2-Disubstituted 1,3-Propanediols and Meso 1,2-Diols Using 1-Ethoxyvinyl 2-Furoate, *J. Org. Chem.* **2002**, *67*, 411-419. Synthetic Studies on Sulfur Cross-linked Core of Antitumor Marine Alkaloid, Discorhabdins: Total Synthesis of Discorhabdin A, *Angew. Chem. Int. Ed.* **2002**, *41*, 348-350.
Term of Project	Fiscal years 2001-2005. (5 years)

Budget Allocation (in thousand of yen)	FY2001	FY2002	FY2003	FY2004	FY2005	Total
	19,100	18,100	18,100	18,100	18,100	91,500