Yasuyuki Kita
Professor, Graduate School of Pharmaceutical Sciences, Osaka University

**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**


**Term of Project**
Fiscal years 2001-2005. 5 years

<table>
<thead>
<tr>
<th>Principal Researcher</th>
<th>Number of Researchers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yasuyuki Kita</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Research Institution</th>
<th>Location of Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Professor, Graduate School of Pharmaceutical Sciences, Osaka University</td>
<td>Suita</td>
</tr>
</tbody>
</table>

**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**


**Term of Project**
Fiscal years 2001-2005. 5 years

**Budget Allocation**

<table>
<thead>
<tr>
<th>Year</th>
<th>Amount (in thousand of yen)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FY2001</td>
<td>19,100</td>
</tr>
<tr>
<td>FY2002</td>
<td>18,100</td>
</tr>
<tr>
<td>FY2003</td>
<td>18,100</td>
</tr>
<tr>
<td>FY2004</td>
<td>18,100</td>
</tr>
<tr>
<td>FY2005</td>
<td>18,100</td>
</tr>
<tr>
<td>Total</td>
<td>91,500</td>
</tr>
</tbody>
</table>