Visiting Professors

Visiting Professor
OGOSHI, Sensuke *(from Osaka University)*

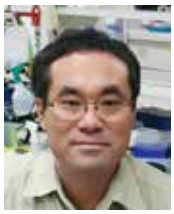
Transformation of Tetrafluoroethylene via Oxycupration

Organofluorine compounds have attracted much attention, mostly on account of their applications in a variety of research areas, including pharmaceutical, agrochemical, and materials science, and consequently substantial efforts have been devoted to the development of novel strategies for the construction of fluorinated organic compounds. Among these, fluoroalkyl ethers such as Ar–OCF_2CF_2–Ar' (Ar/Ar' = aryl) have garnered special attention, as they represent key structures in insecticides and lubricants. In addition, this structural motif is fascinating with respect to perfluoroalkoxylation of aromatic compounds. Most of practical approaches to the construction of Ar–OCF_2CF_2–Ar' moieties have to use the fluorinated starting materials that have very high greenhouse gas effect. Under these circumstances, we have to develop new reactions to allow us to produce those chemicals without using such starting materials. We have been focusing on the synthesis of a variety of fluorinated compounds by using tetrafluoroethylene (TFE) of which greenhouse gas effect is almost zero. So far, we have reported the transformation of TFE by Palladium catalyzed coupling reaction with aryl metals (Zn, B, Si) to give α,β,β-trifluorostyrene and nickel-catalyzed co-trimerization with ethylene and aldehyde. Although the introduction of both oxygen and carbon into TFE is the one of the most difficult reactions, the oxycupration of TFE allows us to the construction of Ar–OCF_2CF_2–Ar' moieties.

Visiting Associate Professor
SHOJI, Osami *(from Nagoya University)*

Gaseous Alkane and Benzene Hydroxylation Catalyzed by Cytochrome P450BM3 with the Assistance of Decoy Molecules

Cytochrome P450BM3 (P450BM3) is one of the most promising P450s for construction of biocatalysts because of its high monooxygenase activity. Because the substrate binding is crucial for the generation of active species of P450BM3 (Compound I), substrates whose structures are largely different from that of its native substrates (long-alkyl-chain fatty acids) cannot be hydroxylated by P450BM3. However, we found that P450BM3 starts to catalyze hydroxylation of nonnative substrates in the presence of perfluorinated carboxylic acids (PFCs) as inert dummy substrates (decoy molecules). Recently, we have succeeded in developing the next generation of decoy molecules by modifying the carboxylate of PFCs with amino acids and succeeded in enhancing the catalytic activity for gaseous alkanes. Furthermore, we have succeeded in crystallizing the *N*-perfluorononanoyl-*L*-tryptophan (PFC9-*L*-Trp)-bound form of P450BM3. The crystal structure analysis of PFC9-*L*-Trp-bound form of P450BM3 showed that the terminal of alkyl chain does not reach to the active site owing to the multiple hydrogen bonding interactions between the carboxyl and carbonyl groups of PFC9-*L*-Trp and amino acids located at the entrance of P450BM3. More recently, we have demonstrated that various carboxylic acids modified with amino acids (*N*-acyl amino acids) as well as amino acid dimers having a completely different structure from fatty acids can serve as decoy molecules. Benzene was more efficiently hydroxylated in the presence of these decoy molecules. Furthermore, we have succeeded in controlling the enantioselectivity of benzylic hydroxylation using these decoy molecules.



Visiting Associate Professor
TOSHA, Takehiko *(from RIKEN SPring-8 Center)*

Elucidation of Mechanism for Effective Chemical Reactions by Supracomplex Formation

Nitric Oxide (NO) plays diverse and significant roles in biological processes such as signal transduction, vasodilation and memory consolidation, despite its high cytotoxicity, raising the essential question of how biological systems control the action of NO to minimize its cytotoxic effect in cells. To answer this, we focus on microbial denitrification in which cytotoxic NO is produced as an intermediate product. However, denitrifying bacteria can grow without any damage from NO, suggesting that there is a system for effective NO elimination. As a possible system, we found from X-ray crystallography, mutagenesis and molecular dynamics simulation that NO-generating nitrite reductase (NiR) forms a complex with NO-decomposing nitric oxide reductase (NOR) to suppress the diffusion of NO. To further elucidate how the proteins involved in denitrification effectively catalyze the consecutive chemical reactions, we explore the possibility of their supracomplex formation using cryo-electron microscopic technique.