【Grant-in-Aid for Transformative Research Areas（B)】

Section II

Title of Project : Highly organized catalytic reaction chemistry realized by low entropy reaction space

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Number of Research Area : 21B202 Researcher Number : 00548943

【Purpose of the Research Project】

Catalysts play an important role in synthetic organic chemistry by reducing activation energy, resulting in less environmental load and less material consumption. On the other hand, catalytic reactions for synthetic organic chemistry made reaction media more complex, because various chemical species, reaction intermediates, catalytically active species, co-products, exist in the same reaction space. Therefore, suppression of attendant side-reactions and deactivation of catalysts is key for efficient catalysis. We will construct a theory to design an appropriate reaction space for a particular catalytic organic reaction by understanding its reaction mechanism in molecular level, focusing on entropy of the reaction space. Thus, establishment of order of reaction pathways will realize unpreceded difficult transformation and complex reaction systems, such as cooperative catalysis and synergistic catalysis.

We defined ‘A reaction space where reaction species exist highly in order’ as ‘Low entropy reaction space’. This reaction space can be constructed in continuous-flow systems in various sizes from micrometer to bulk size (Fig. 1). **1. Spatially separated catalysts and substrates** and **2. Space-specific temperature controlling** will lower the energy barrier for desired reaction as well as raise the energy barrier for undesired reactions. This will result in suppression of decomposition of catalysts and intermediates, and side-reactions as well as increasing selectivity of reaction pathway toward desired product. **3. Flash mixing** and **4. Heterogeneous catalyst flow** will realize highly selective and fast transformation to isolate pure product, keeping highly ordered reaction environment. **5. Sequential multi-step reaction** and **6. Cooperative catalysis where different catalysts work in distinct timeline** will realize difficult transformation and complex catalysis. **8. Flash quenching strategy and inline analysis** of continuous-flow system will enable an analysis of unstable intermediates and kinetic study of ultra-fast reactions.

【Content of the Research Project】

We will construct a basic theory to control low entropy reaction space and will develop difficult transformation and complex catalysis based on the newly designed catalytic reaction based on the theory. More specifically, we will develop instructive theory to design continuous-flow systems that can provide low entropy reaction space where reaction pathways of catalytic organic reaction are well controlled. The research is divided to following 4 steps.

Step 1) Measurements of kinetic parameters of reactions involving fast mixing under flow conditions as key

Step 2) Measurements of kinetic parameters of ultra-fast reactions and step-by-step of catalytic reaction

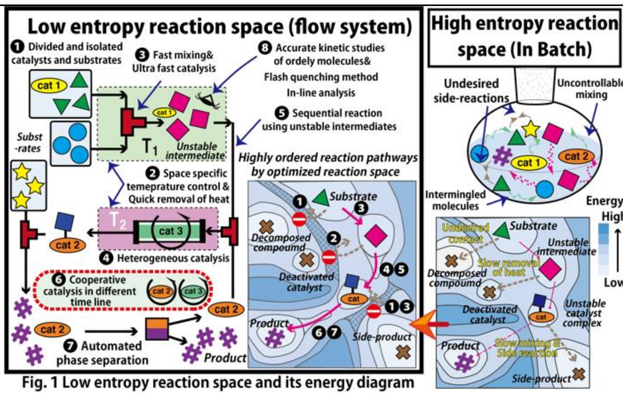

Fig. 1 Low entropy reaction space and its energy diagram

Step 3) Construction of systems providing negative entropy and catalytic systems keeping low entropy

Step 4) Development of suitable reaction space for heterogeneous catalysis, cooperative catalysis and sequential multi-step catalysis

A01 Nagaki is mainly responsible for steps 1 and 3, A02 Fuse is responsible for steps 1 and 2, A03 Miyamura is responsible for steps 3 and 4, and A04 Asano is responsible for steps 1, 2 and 4.

【Expected Research Achievements and Scientific Significance】

It is expected to realize new difficult transformations, highly selective and efficient catalytic reactions, and practical continuous-flow synthetic methods thorough this research project. They will result in elimination of environmental load during synthetic process of APIs and organic materials. In addition, efficiency and reliability in high-throughput screening based on synthesis of small quantity and many varieties will be improved.

【Key Words】

Low entropy: Thermodynamic definition of entropy was given $dS=dQ/T$ by R. J. E. Clausius. Statistical (macro) definition of entropy was given $S=k\log W$ by L. Boltzmann. The Second Law of thermodynamics is formulated as absolute law – Entropy always increases in a spontaneous process in an isolated system. Increase of entropy is intuitively understood as disorder, spreading, missing information, and maximum of probability distribution. E. Schrödinger described that ‘Living organisms feed negative entropy upon itself from environment to compensate the entropy increase that it produces by living, and thus to maintain itself on a stationary and fairly low entropy level’ in ‘What is life?’.

【Term of Project】 FY2021-2023

【Budget Allocation】 105,000 Thousand Yen

【Homepage Address and Other Contact Information】

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