Abstracts of Oral Presentations

Lecture1

Transition-Metal-Catalyzed Synthesis of Organoheteroatom Compounds

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Key words: Organoheteroatom compounds, Catalysis, Equilibrium

Organoheteroatom compounds are used for biological active substances and functional materials, and it is necessary to develop efficient methods for their synthesis. Compared with the second-row heteroatoms such as oxygen and nitrogen, the element of sulfur and phosphorus in the third-row are larger, polarizable, and oxidizable, and the synthesis of these organoheteroatom compounds needs different methods. Although substitution reactions of organohalogen compounds with various heteroatom reagents generally have been employed for the carbon-heteroatom bond formation, it was considered that the C-H substitution reaction of heteroatom reagents would be more favorable from the environmental viewpoint. It was found that transition-metal complexes could be used as catalyst for the synthesis and transformation of organoheteroatom compounds, and that a variety of reactions involving cleavage of heteroatom bonds such as C-H, C-S, C-F, C-C, S-S bonds were developed. The development of efficient catalysts, which decreases the activation energy of the reaction, provides equilibrium reactions, when the relative thermodynamic stabilities of the substrates and products are close. Then, equilibrium control method using organic co-substrates/co-product system was developed.[1]

For example, using appropriate co-substrates and co-products, a series of rhodium-catalyzed organothiolation reactions were developed for the synthesis of organosulfides using C-H functionalization, which employed substrates such as nitroalkanes, ketones, and heterocyclic compounds with pKa values 16–29 (Fig. 1). The method employing the combination of transition-metal catalysis and equilibrium control can be generally used for the synthesis of organosulfur compounds. Related carbon-heteroatom bond formation reactions will also be discussed.

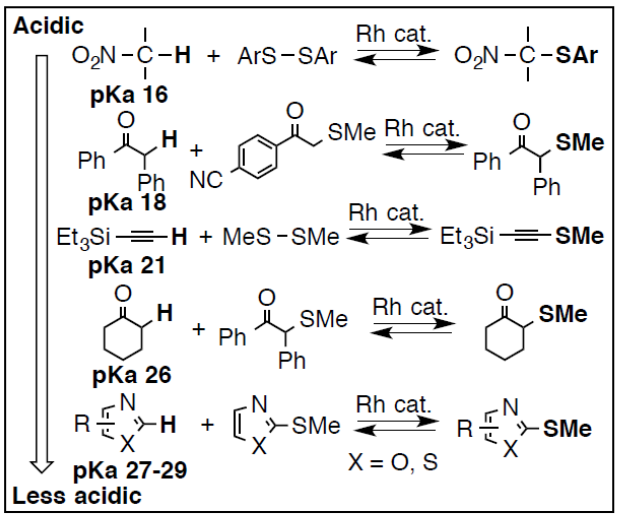

Fig. 1. Rhodium-catalyzed thiolation reactions.

References

[1] *Review*: M. Arisawa, *Tetrahedron Lett.*, **2014**, *55*, 3391-3399.

O-1(Invited)

Enantioselective and Regiodivergent Copper-Catalysed Electrophilic Arylation of Allylic Amides with Diaryliodonium Salts

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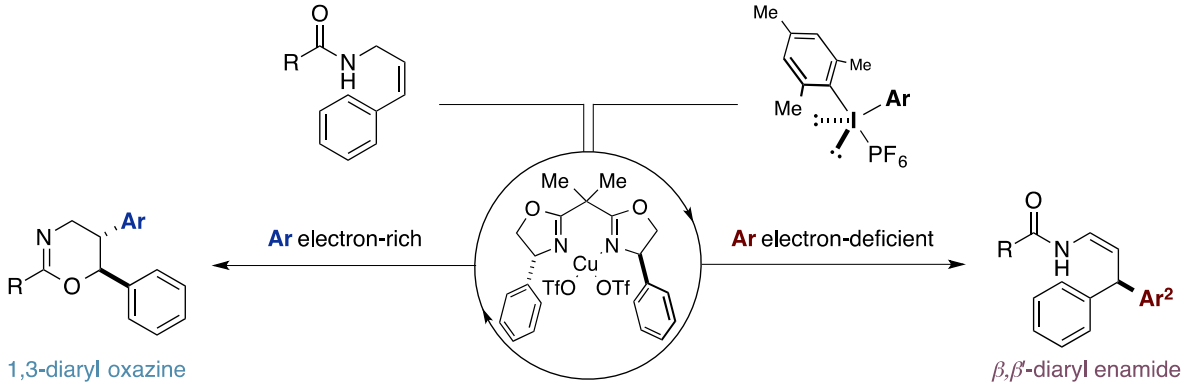
Key words: enantioselectivity, regiodivergence, iodonium salts

The catalytic asymmetric addition of carbon-based electrophiles to simple alkenes represents a strategically important bond-forming process that, despite several important examples,[1] remains largely under-investigated in contemporary organic synthesis.

Over the last seven years our laboratory has developed methodologies employing the reactivity of a putative copper(III)-aryl intermediate as an aromatic electrophile equivalent. These reactive species can be generated by the union of simple copper sources and diaryliodonium salts, and have been shown to functionalise a range of latent nucleophiles.[2] Furthermore, both our group and the MacMillan group have shown that the use of asymmetric bisoxazoline ligands in these systems can provide a platform for the enantioselective arylation of electron-rich alkene equivalents.[2c,3]

With these developments in mind, we describe an enantioselective and regiodivergent copper-catalysed alkene arylation process, generating 1,3-diaryl oxazines and β,β'-diaryl enamides from one substrate class (Scheme 1). The selectivity of the arylation is observed to be controlled by the electronic properties of the transferred aryl-group of the employed diaryliodonium salt.



Scheme 1. Copper-catalysed enantioselective and regiodivergent arylation of allylic amides

[1] (a) Sigman *et al. Nature* **2014**, *508*, 340; (b) Wolfe *et al. J. Am. Chem. Soc.* **2010**, *132*, 12157.
[2] Gaunt *et al.* (a) *J. Am. Chem. Soc.* **2008**, *130*, 8172; (b) *Science*, **2009**, *323*, 1593; (c) *J. Am. Chem. Soc.* **2011**, *133*, 13778; (d) *Angew. Chem. Int. Ed.* **2013**, *52*, 9284.
[3] MacMillan *et al.* (a) *J. Am. Chem. Soc.* **2011**, *133*, 13782; (b) *J. Am. Chem. Soc.* **2012**, *134*, 17702.

O-2(Invited)

Radiation-Induced Defects in Si after High Dose Proton Irradiation

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Key words: positron, annihilation, radiation defects, proton irradiation, silicon

Primary radiation defects (vacancies and interstitials) in Si single crystals are rather mobile; so, just after proton radiation, interstitial Si atoms disappear in sinks or outer boundaries, but vacancies become decorated by impurities forming vacancy-impurity complexes: monovacancy-oxygen (A-centers), monovacancy-phosphorus (E-centers) or just Si divacancies [1]. Previous experiments with low dose proton irradiation (~10^{14} cm^{-2}) [2] showed that the concentration of radiation-induced defects is proportional to the radiation dose. [1]

In the present work we have studied Si single crystals with moderate concentrations of impurities ([P] ≈ 10^{15} cm^{-3}, [O] ≈ 8×10^{17} cm^{-3}, [C] ≈ 2.5×10^{16} cm^{-3}) irradiated by protons (21.5 - 22 MeV) with a dose ~10^{16} cm^{-2}. The protons passed through a set of eight Si wafers with thickness of 0.4 mm each.

The LT spectra are fitted and processed (fig. 1) with the help of a 4 state trapping model (with A-centers, 225 ps, E-centers, 270 ps, and divacancies, 320 ps). Oxygen complexes are effectively dissociated at T > 100°C. So, after annealing at 200°C the positron lifetime in defects dramatically increases (up to 500 ps) and the short-lived defect components completely disappear. Concentration of these defects (formed after annealing) is comparable with the concentration of phosphorus. This may indicate that initial A-centers dissociate and the released vacancies attach to E-centers forming complexes of 5 and more vacancies. The number density of these complexes is comparable with the concentration of phosphorus.

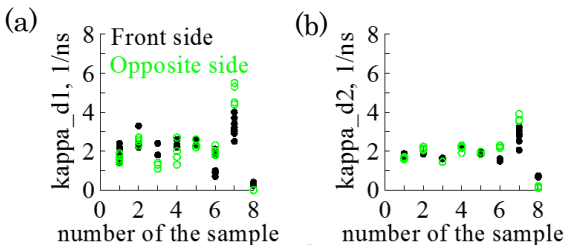

Fig. 1. Results of the processing of the annihilation spectra with the assumption of trapping e^+ in different types of defects

Ref. [1] Reinhard Krause-Rehberg, Hartmut S. Leipner, Positron Annihilation in Semiconductors: Defect Studies. Springer, (1999)

[2] N. Yu. Arutyunov, M. Elsayed, R. Krause-Rehberg, V.V. Emtsev, G.A. Oganesyan, V.V. Kozlovski , J. Phys.: Condensed Matter **25**, 035801 (2013)

O-3(Invited)

Investigating a Binary Solvent Mixture at the Liquid-Solid Interface via Molecular Dynamics

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Key words: interface, hydrogen bonding, molecular dynamics

Recent experimental and simulation work has investigated the organization and dynamics of binary solvent mixtures at the hydrophilic silica-liquid interface.[1,2] Molecular behavior at interfaces is often quite dissimilar from the bulk and when one of these phases is a multicomponent liquid, the interfacial liquid mole fraction region can also differ dramatically from the bulk value. In this study we examine the nonequilibrium orientation and dynamics of an acetonitrile-methanol mixture at a hydrophilic silica surface. Since acetonitrile and methanol interact with a fully hydroxylated silica surface in distinct manners, a binary mixture results in the solvent molecules competing to occupy interfacial silica sites. At all observed mole fractions methanol dominates the interfacial liquid mole fraction. We use nonequilibrium molecular dynamics simulations to gain molecular insight into the mechanism by which liquid methanol approaches and displaces acetonitrile from the silica surface.

Our first study of this process involves placing one methanol molecule in the vicinity of the neat acetonitrile-silica interface. After diffusing to the surface, methanol can hydrogen bond with the silica and displace an acetonitrile molecule by one of two mechanisms, dictated by the orientation of the approach. Two reaction coordinates are isolated and the deviation from transition state theory is investigated.

Ref [1] Gobrogge, E. A.; Walker, R. A. *J. Phys. Chem. Lett.* **2014**, 5 (15), 2688–2693.
Ref [2] Melnikov, S. M.; Höltzel, A.; Seidel-Morgenstern, A.; Tallarek, U. *J. Phys. Chem. C* **2014**, 119 (1), 512–523.

O-4

Fabrication of Ultrafine Titanate Nanowires as Highly Efficient Ion Exchanger Using a Dealloying Method

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Key words: nanowires, ion exchangers, titanium oxide, dealloying,

Sodium titanates have gained a great attention due to their ion exchange properties for decontamination of radioactive cations. Radioactive Sr^{2+} and Ra^{2+} ions are strongly captured to titanate and the resulting adsorbed ions can be immobilized, leading to safe disposal. A variety of titanate nanostructures have been prepared by hydrothermal, sol-gel, and other methods. However, it was difficult to make nanowires with a diameter of a few nanometers because they need high-temperature treatments that lead to crystal growth. To enhance ion capturing abilities of sodium titanate, new mild synthetic way is required. Herein, we report a new synthetic method involving a nonthermal process, allows the formation of ultrafine titanate nanowires [1].

Sodium titanate nanowires were readily fabricated by the treatment of Ti_6Al_{94} alloy with aqueous NaOH at room temperature (Figure 1). In this process, Al leaching and Ti oxidation occurred simultaneously to form nanowire structures. HRTEM image clearly shows the fine nanowire structure with a diameter of around 3 nm. The crystal structure of this nanowire is lepidocrocite type in which sodium ion layers are sandwiched between TiO_6 octahedra layers and its interlayer distance was 9.1 Å.

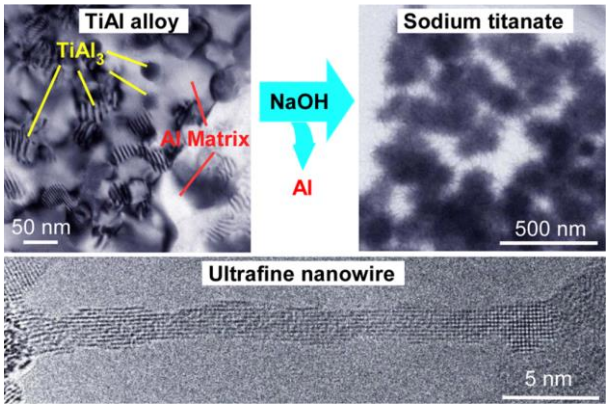

Fig. 1, Reaction scheme and TEM image

Using this nanowire, we examined the ion capturing ability of Sr^{2+} ions in solution. As a result, our nanowire can adsorb 3.8 meq/g of Sr ions within 5 min. The amount of captured Sr is three times higher and the adsorption rate is over 500 times faster than those of previously reported titanate nanowires [2]. The high capacity and adsorption rate is ascribed from small diameter and wide interlayer distance of metastable crystal structure.

1) Y. Ishikawa, S. Tsukimoto, K. S. Nakayama, N. Asao *Nano Lett.*, **2015**, *15*, 2980

2) D. Yang, Z. F. Zhang, H. Y. Zhu, H. W. Liu, X. P. Gao *Adv. Mater.*, **2008**, *20*, 2777

O-5

Novel separation method of vitamin E and free fatty acids using ion-exchange resin

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Key words: ion-exchange, purification, selective adsorption, vitamin E

Abstract: Vitamin E (V_EH) is conventionally recovered from vegetable oils by multi-stage molecular distillation at high temperature (100~250°C) and then purified by chromatographic separation. We have constructed a novel recovery method by adsorption/desorption using strongly basic anion-exchange resin at low temperature (50°C) and the recovery ratio is reported to be 75%, higher than that of conventional one, 50%. In the V_EH rich fraction obtained by our method, there exists only 22wt% free fatty acid (FH) as an impurity (there exist 65wt% several components in the conventional one). If FH can be completely removed from the V_EH rich fraction, the pure product will be obtained without chromatographic separation.

In this study, we propose a separation method based on differences in acidity between FH (pKa=4.8) and V_EH (pKa=13.1). When the ion-exchange resin with acidity between those of FH and V_EH can be used as an adsorbent, only FH with higher acidity can be ionized and adsorbed on the resin via Eq.(1). So, a weakly basic ion-exchange resin Diaion WA21J (pKa=7~9) was packed into the separation column and maintained at 50°C. The model V_EH rich fraction, mixture of FH and V_EH in ethanol, was fed to the bottom of the column at 0.25 cm^3/min. Then, the concentrations of FH and V_EH in the effluent from the top of the column were measured.

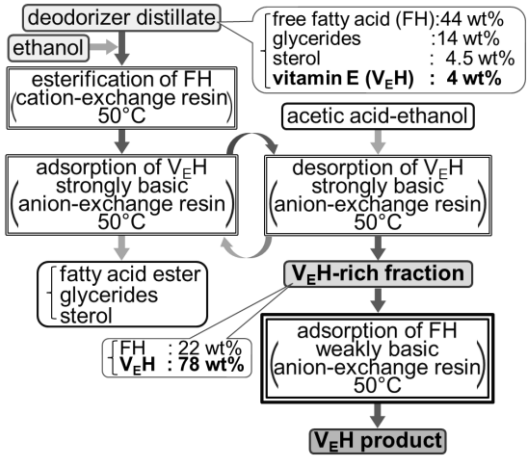
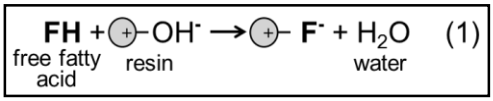


Fig. 1 Novel recovery and separation method of V_EH



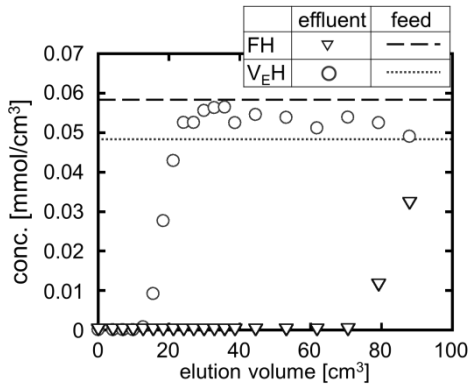


Fig. 2 Concentration profiles of FH and V_EH in the effluent

Figure 2 shows the concentration profiles in the effluent with elution volume. Up to 71 cm^3, FH was not detected in the effluent. Thus, we succeeded in obtaining the V_EH solution without the impurity at recovery ratio of 85%.

[1]B.B.Aggarwal *et al.,Biochem.Pharmacol.*,**80**,1613(2010) [2]S.T.Jiang *et al.,Biosyst.Eng.*,**93**, 383(2006), [3]K.Hiromori, *et al., 106th AOCS* #62186, Orlando, May(2015)

Lecture-2

Synergy between Metal and Ligand for Molecular Probes Aimed at Biomedical Applications

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Key words: Lanthanide luminescence, Diradical complex, Near infrared, Molecular probe, Medical diagnostics

Modern medical diagnostics rely on imaging techniques such as X-ray, PET, and MRI enabling highly resolved visualization of organs locating deep inside the body. By contrast, molecular imaging using fluorescence and absorption in visual wavelength region is still in its infancy, suffering from scattered light, auto-fluorescence, and low ability to penetrate into tissues. To circumvent the problems, we have engaged in a study to use metal-ligand complexes exhibiting signaling such as long-lifetime emission and one in near-infrared (NIR) region, which cannot be afforded by organic dyes relying on π-π* transition. In this talk, two metal complex systems will be presented to highlight the synergistic effect between metal ions and ligands to lead to signaling suitable for medical diagnostics.

Lanthanide(III)–thiacalixarene complexes - Thiacalix[4]arene-*p*-sulfonate (TCAS, Fig. 1) forms various types of heteronuclear cluster complexes with Ag^{I} and lanthanides(III) with characteristic luminescence properties. For example, $Ag_2Tb_1TCAS_2$ exhibited exceptionally long-lived luminescence (τ = 4.6 ms), owing to a supramolecular cage surrounding Tb^{III} to expel coordinating water responsible for the luminescence quenching [1]. Nd^{III} afforded $Ag_4Nd_1TCAS_2$ having luminescence quantum yield of 4.9×10^{-4}, which is the second largest ever reported in H_2O [2].

Platinum(II)–o-diiminobenzosemiquinonato complexes - Water-soluble *o*-phenylenediamine ligands affords a diradical complex (**1**, Fig. 1), exhibiting a strong NIR absorption band ($\varepsilon \approx 10^5$ $M^{-1}cm^{-1}$) [3]. The oxidized dimer **2** in the NIR-off state was introduced into cells to exhibit NIR absorption by reduction to **1** with glutathione in the cell. This could lead to an NIR probe to selectively stain cancer cells with the aid of a suitable targeting substance.

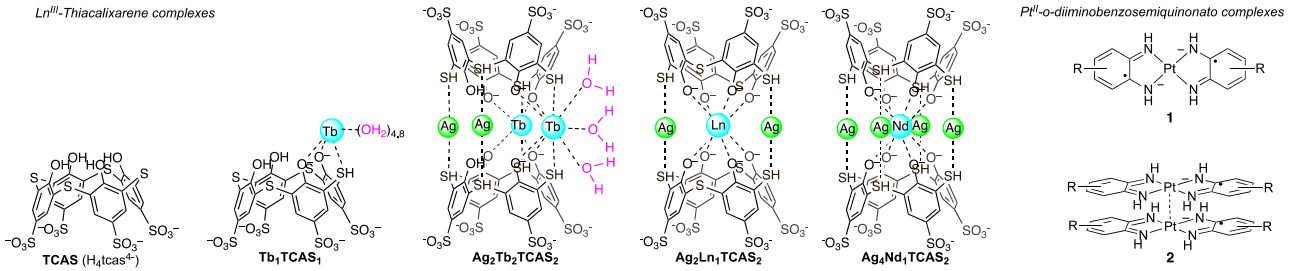

Fig. 1. Structures of the complexes.

[1] *Chem. Asian J.*, **2008**, *3*, 849. [2] *Inorg. Chem.*, **2012**, *51*, 1648. [3] *Chem. Commun.*, **2013**, *49*, 4812 (2013).

O-6

Formation of a Tungsten Complex Having a Metal–Silicon Triple Bond and Its Monomer-dimer Dissociation Equilibrium

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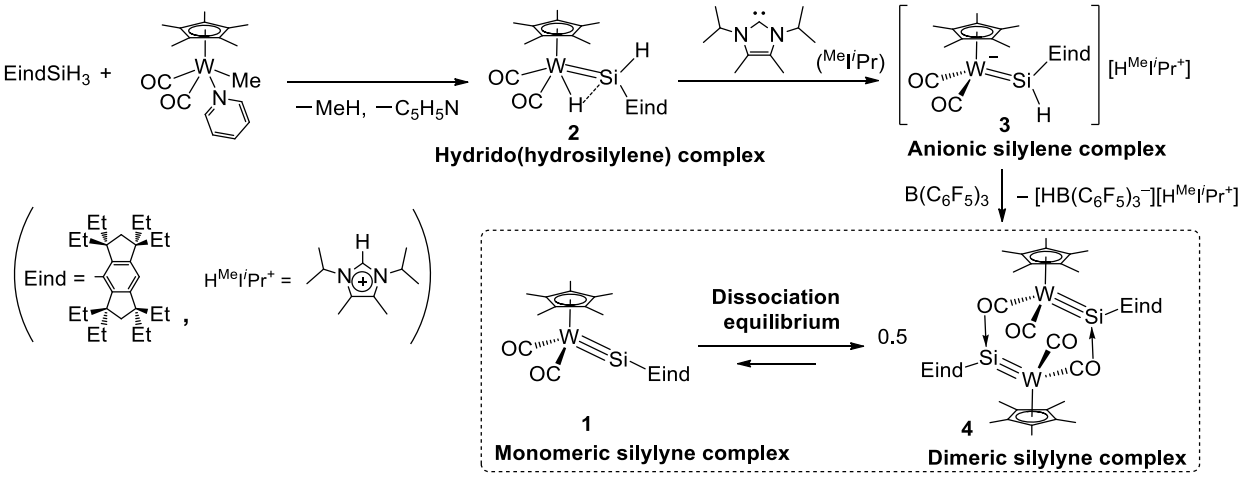
Key words: silicon, triple bond, dissociation equilibrium, tungsten, silylyne complex

Silylyne complexes have a polarized transition metal(δ–)–silicon(δ+) triple bond, and are expected to be very reactive. Therefore, research on their reactivity attracts large interest. The number of their examples and reactivity studies are, however, very small so far. A possible stumbling block in their research is instability of current starting materials (divalent silicon species) toward air, which causes troubles in handling and storing them. In addition, the current starting materials make it inevitable that the silicon atom of the product has a very bulky substituent, which may reduce reactivity of the triple bond by its steric hinderance.

This time, I synthesized a tungsten silylyne complex **1** having an Eind group, a plate-shaped aryl substituent, from $EindSiH_3$, an air-stable silicon compound (*Scheme 1*). First, a hydrido-(hydrosilylene) complex **2** was synthesized according to a synthetic method for similar complexes, and it was then treated with $^{Me}I^{i}Pr$. This led to proton abstraction from **2** to give an anionic silylene complex **3**. Finally, a reaction of **3** with $B(C_6F_5)_3$ instantly brought about hydride abstraction to yield a monomeric silylyne complex **1**, which was isolated as its dimer **4**. Interestingly, it was revealed that **4** is in dissociation equilibrium with a monomer **1** in solution. This clearly demonstrates that the triple bond of **1** readily accept attack of relatively large molecules.



Scheme 1

O-7(Invited)

Phenalenyl-fused Porphyrin Biradicaloids

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Key words: biradicaloids, porphyrins, polycyclic aromatic hydrocarbon

Mono- and *bis*- phenalenyl fused porphyrin biradicaloids **1** and **2** were synthesized. It was found that **1** has a closed-shell structure while **2** exists as a triplet diradical in the ground state. Compound **1** underwent reductive hydrogenation during the crystal growing process while compound **2** was easily oxidized in air to give two dioxo-porphyrin isomers, which can be correlated to their unique biradical character and spin distribution. Difference raises the curiosity about their ground state, chemical reactivity and physical properties. Like all other biradicaloids, kinetic blocking of the high spin density sites is necessary to obtain stable/persistent materials, thus the bulky mesityl-blocked, *mono*- and *bis*-phenalenyl fused Ni-porphyrins **1** and **2** were synthesized and investigated in this work (Figure 1)[1].

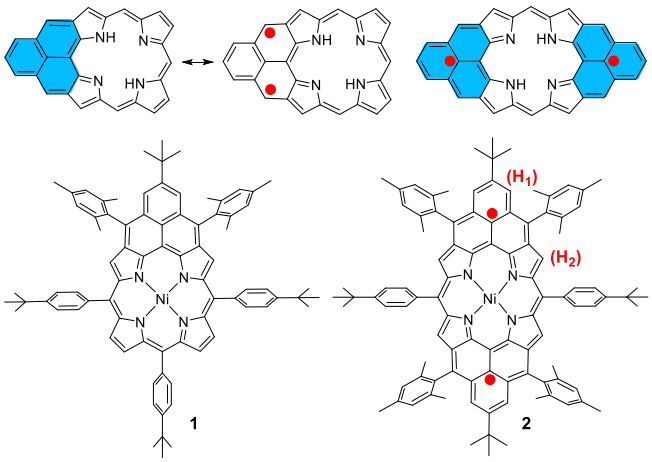
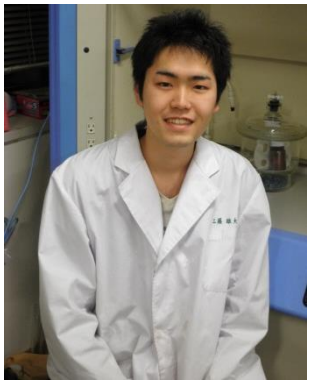


Fig. 1. Structures of *mono*- and *bis*- phenalenyl fused porphyrin biradicaloids and their derivatives **1** and **2**.

[1] W. Zeng et al., *Chem. Sci.* **2015**, *6*, 2427-2433.

O-8

Identification of analogues and biosynthetic intermediates of tetrodotoxin aimed at elucidating its biosynthesis



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Key words: biosynthesis, tetrodotoxin, LC-MS, structure elucidation

Tetrodotoxin (TTX; **1**), a potent neurotoxin, causes worldwide fatal food poisoning. TTX has been found in various marine and terrestrial animals. The biosynthesis of TTX, consisting of an unique 2,4-dioxaadamantane skeleton and a guanidine moiety, is an attractive mystery in natural products chemistry. We have determined the structures of natural TTX analogues to obtain insights for its biosynthetic pathway.[1] Through a structure-based screening using a LC–MS/MS method focusing on the characteristic fragment ions of TTX analogues (i.e. *m/z* 162), an unknown compound (**2**) showing characteristic fragment ion was found from toxic newts (Figure 1). Compound **2** was identified as the first C5–C10 directly bonded TTX analogue, 4,9-anhydro-10-hemiketal- 5-deoxyTTX. Based on its chemical structure and wide distribution of **2** among the toxic newts, we proposed a monoterpene (geranyl pyrophosphate) origin for TTX (Figure 2).[2]

On the basis of the proposed biosynthetic pathway, further screening of biosynthetic intermediates of TTX ("Next target" in Figure 2) was performed using LC-MS. A candidate compound (**3**) was detected in the toxic newts and isolated by several column chromatographies. The structure of **3** was elucidated based on the spectroscopic analysis, and it suggests that **3** would be an intermediate or a shunt of TTX and also would support our hypothetic pathway.

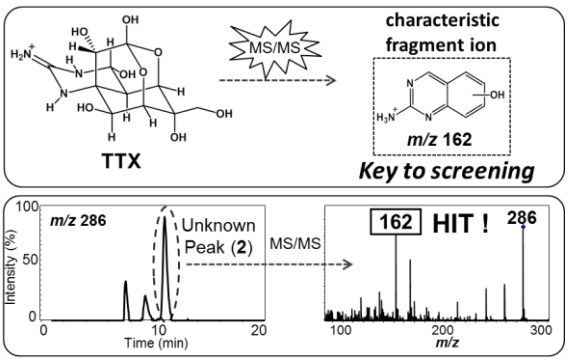

Figure 1. Summary of the structure-based screening using LC-MS/MS.

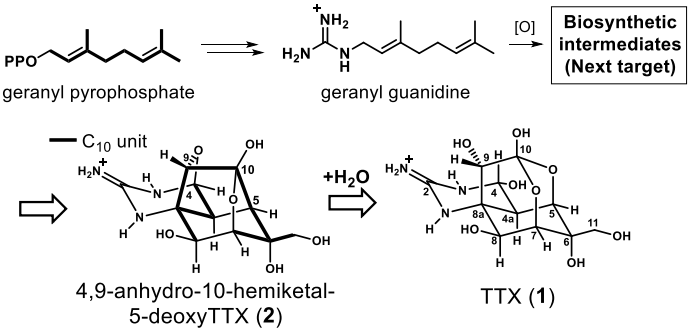

Figure 2. Proposed biosynthetic pathway towards TTX based on the structure of **2** obtained from the toxic newts.

Ref. [1] (a) Yotsu-Yamashita, M; *et al. Mar. Drugs* **2013**, *11*, 2799−2813. (b) Kudo, Y.; Yotsu-Yamashita, M.; *et al. J. Nat. Prod.* **2014**, *77*, 1000–1004. [2] Kudo, Y.; Yotsu-Yamashita, M.; *et al. Angew. Chem. Int. Ed.* **2014**, *53*, 14546–14549.

O-9

Eu(OTf)$_3$-Catalyzed Regioselective Ring Opening Reactions of Epoxy Alcohols: Application to the Synthesis of Bioactive Compounds

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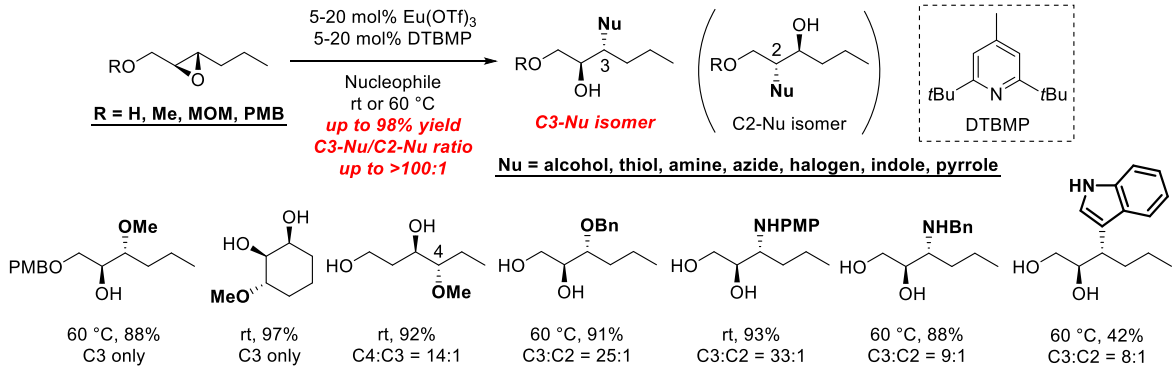
Key words: lanthanoid, asymmetric epoxidation, total synthesis

The strategy employing the asymmetric epoxidation of allylic alcohols followed by the nucleophilic ring opening of 2,3-epoxy alcohols provides chemists with a reliable latitude for the design and synthesis of optically active compounds with multiple stereogenic centers. However, the reported methods require stoichiometric amounts of Lewis acids to achieve regioselective ring opening of epoxy alcohols.[1] In our study of the total synthesis of (+)-irciniastatin A, we found a method that enables a C3-selective nucleophilic ring opening of 2,3-epoxy alcohol by MeOH using the catalytic amounts of Eu(OTf)$_3$ and 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP).[2] This time, I'll introduce the applicable scope and limitation of the protocol that effects a highly regioselective nucleophilic ring opening of 2,3-epoxy alcohols.

I found that this method has the following advantages: (1) excellent regioselectivities are achieved with various epoxides, including unprotected and protected 2,3-epoxy alcohols, 3,4-epoxy alcohols, and cyclic epoxy alcohols; (2) not only MeOH, but also various *O*-, *S*-, *N*-, and *N*-heterocyclic-nucleophiles can be used; (3) the reaction conditions are not sensitive to water or air; (4) the reaction is induced using commercially available europium salt. The present protocol can therefore be widely applied to the synthesis of complex molecules with continuous stereocenters.[3]

In this presentation, the details of applied research toward the efficient synthesis of bioactive compounds will be described.



1) Sharpless, K. B. *et al. J. Org. Chem*. **1985**, *50*, 1557. 2) Iwabuchi, Y. *et al. Org. Lett*. **2010**, *12*, 1040. 3) Iwabuchi, Y. *et al. Org. Lett*. **2014**, *16*, 4408.

O-10(Invited)

Visible-Light-Induced, Enantioselective Reactions of α-Aminoalkyl Radicals with α,β-Unsaturated Oxindoles.

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Key words: photochemistry, photocatalysis, hydrogen bonding

Prochiral lactams, such as 2-pyridones, isoquinolones and oxindoles are excellent precursors for hydrogen bond mediated, enantioselective photoreactions.[1] Chiral template **1**, which was developed in our group allows face differentiation *via* hydrogen bonding to its lactam binding site and thus shielding of one face (see Fig. 1). Depending on the reaction conditions (solvent, temperature, concentration), high yields and excellent enantiomeric excesses can be achieved. Based on our interest in photoinduced electron transfer (PET)-catalyzed reactions,[2] this study, focuses on visible light induced formation of α-aminoalkyl radicals and subsequent reactions with α,β-unsaturated oxindoles in a stereoselective fashion applying template **1**. The formation of α-aminoalkyl radicals can be achieved *via* photoinduced electron transfer from an amine to an excited oxidant upon loss of a cationic leaving group (H^+, TMS^+). Oxindole precursors **2** were synthesized *via* Knoevenagel condensation of parent oxindoles with various symmetric and asymmetric ketones. Next, the synthesized oxindoles were reacted with aniline derivative **3** in the presence of $[Ir(ppy)_2(dtbbpy)]BF_4$ upon irradiation with visible light to form Michael-type addition products **4** in good to excellent yields (up to 99%).

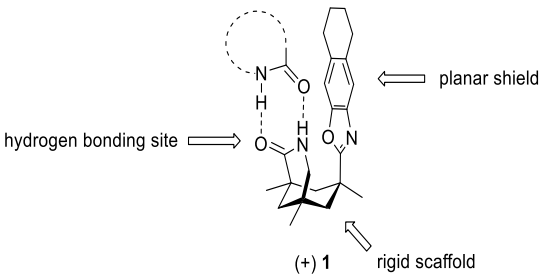

Fig. 1. Concept of face differentiation *via* hydrogen bonding to template (+)-1.

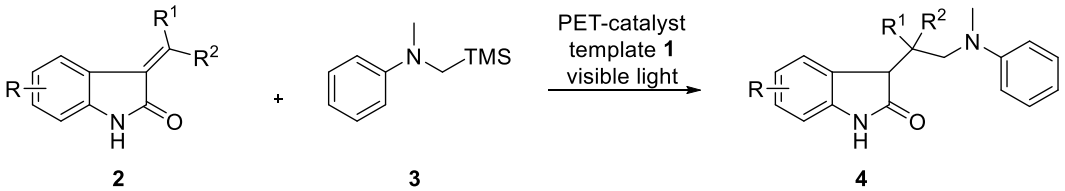

Fig. 2. General reaction design.

First attempts of stereoselective reactions showed significant enantiomeric excesses, but the procedure needs further optimization since a strong impact of the applied wavelength was observed.

Ref.: [1] M. M. Maturi, T. Bach, *Angew. Chem. Int. Ed*. **2014**, *53*, 7661-7664; S. C. Coote, A. Pöthig, T. Bach, *Chem. Eur. J*. **2015**, *21*, 6906-6912. [2] D. Lenhart, T. Bach, *Beilstein J. Org. Chem*. **2014**, *10*, 890-896; A.Bauer, F. Westkämper, S. Grimme, T. Bach, *Nature* **2005**, *436*, 840.843.

O-11

Synthesis of Catechol Functional Group Contained Polysiloxane

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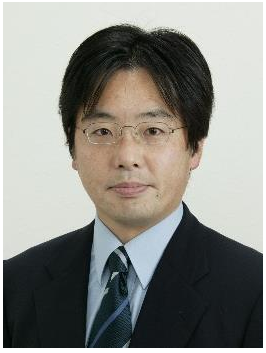
Key words: Hybrid polymer, Catechol, Siloxane,

Heterogeneities structure of marine mussels endows byssus threads a remarkable ability, both hard and stretchy, to withstand the periodic mechanical shocks of waves and the eroding action of seawater particles. By studying the structure and chemical composition of byssus, DOPA, a catecholic amino acid, was found as a critical substance related with such unique mechanical property. Catechol-Fe^{3+} complex on one hand can severed as cross-linker which makes cuticle hard in the condition of high density, on the other hand let the material able to elastically recover to its initial length and stiffness after being strained by as much as 100% because of the noncovalent and reversible character of the complex. Inspired by this mechanism, researchers synthesized plenty of polymers which contain catecholic repeating units with multiple functions for instance tunable adhesive property, self-healing property and so on. And it is still a promising structure that can be designed into novel monomers, surfactants or nano-particles applied in polymer matrix and assemblies.

Silicones, as a general class of materials, are ubiquitous in technology, with applications ranging widely from electrical materials to biomaterials as a result of their unique properties, such as low glass transition temperature ,a flexible backbone, good thermal and oxidative stability, excellent dielectric properties, water repellency, physiological inertness and biocompatibility. Various siloxane-based components are commercially available as multifunctional building blocks. These components consist of a molecular structure of alternating silicon and oxygen atoms as an inorganic backbone (–Si–O–) and an organic substituent (R) attached to each silicone atom. Although it is possible using such multifunctional degree siloxane monomers to prepare three dimensional cross-linking polymers, antiadhesive properties as well as difficulty of controlling of cross-linking degree during thermal curing restrain its application as wet adhesive materials. Herein, we design a facile synthetic strategy to introduced catechol group into silicone backbone based on a readily available precursor (eugenol) and efficient chemistries [tris(pentafluorophenyl)borane-catalyzed silation and hydrosilylation] using a post functionalization method. Cathechol functional silicone can be served as versatile adhesive layer to bind various inorganic materials such as nanocarbons, metal oxide nanomaterials. This biomimic polymer with high content of cathechol functional groups are anticipated as a polymers assemble to prepare adhesive nanocomposites film.

Lecture-3

World of Oxide Electronics



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Key words: oxide electronics, oxide spintronics, functional oxides, material design, thin film epitaxy

Recent discovery of functional oxides such as high temperature superconductivity and colossal magnetoresistance surprisingly developed physics and chemistry of oxides [1]. Thanks to recently emerging thin film epitaxy, we can synthesize high quality oxides and also tailor unexpected functionality such as room temperature ferromagnetism (Fig. 1) [2,3] and high electron mobility heterointerface between different oxides [3]. Owing to these state-of-the-art techniques, we have achieved various functionalities leading to future green innovations. In this talk, we shall talk about plenty of possibilities in oxides for future innovations: this is why silicon is not enough in our world and what a wonderful world of oxides.

Fig. 1. Photograph of semitransparent, electrically conducting, room temperature ferromagnetic, and chemically durable cobalt-doped TiO_2 thin film.

References

[1] *Functional Metal Oxides: New Science and Novel Applications*, ed. by S. Ogale, M. Blamire, T. Venkatesan, (Wiley-VCH, Weinheim, 2013).
[2] Y. Matumoto et al., *Science* **2001**, 291, 854-856.
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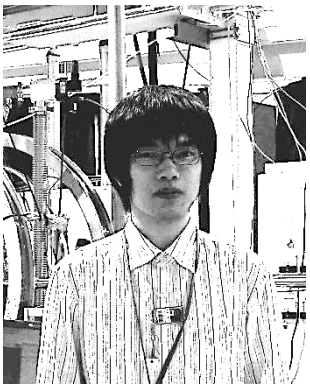
[4] J. Heber, *Nature* **2009**, 459, 28-30.

O-12

IR laser induced photoelectron rescattering experiment on hydrocarbon molecules



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Key words: rescattering photoelectron, tunneling ionization, intense laser field, electron-ion scattering

When atoms or molecules are irradiated with a linearly-polarized intense near-IR laser (~10^{14} W/cm^2), a part of the electrons released by tunneling ionization will be driven back by the oscillating laser field into recollisions with their parent ions. Elastically scattered electrons have structural information of the molecular ions. The rescattering process completes within one optical cycle of the laser (about 2.7 fs at 800 nm), which may enable ultrafast molecular imaging with a femtosecond time resolution. In our laboratory, we have measured rescattering photoelectron spectra of atoms and molecules using laser pulses at 800 nm [1]. In this study, we measured rescattering photoelectron spectra of hydrocarbon molecules using IR laser pulses at longer wavelengths to increase the momentum of the recolliding electron.

An optical parametric amplifier pumped by Ti:Sapphire laser pulses at 800 nm (100 fs, 1.5 mJ, 1 kHz) is used to obtain IR laser pulses at 1200-1650 nm. The IR pulses are focused onto a sample gas effusively introduced in a vacuum chamber. Angular distributions of photoelectrons are obtained by continuously rotating the polarization direction of the optical fields using a half wave plate.

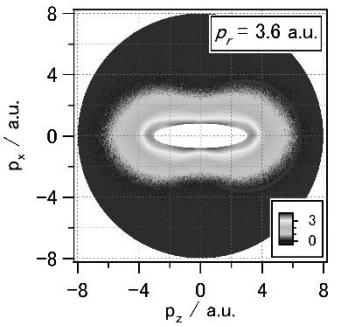

Fig. 1. Angle-resolved rescattering photoelectron spectrum of C_6H_6.

Fig. 1 shows an angle-resolved rescattering photoelectron spectrum of C_6H_6 measured using the 1650 nm laser light. We could extend the recolliding momentum of the electrons around 3.6 a.u. It corresponds to 176 eV in the energy and 0.92 Å in the de Broglie wavelength, which is shorter than 1.39 Å, the C-C bond length of C_6H_6 molecules.

Ref. [1] M. Okunishi *et al*., Phys. Rev. Lett. **100**, 143001 (2008); M. Okunishi *et al*., Phys. Rev. Lett. **106**, 063001 (2011); C. Wang *et al*., J. Phys. B: At. Mol. Opt. Phys. **45**, 131001 (2012).

O-13

Investigating the Interatomic Coulombic Decay Process Induced by Two-photon Double Excitation in Ne Dimer Using XUV pump-UV probe Measurements

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Key words: interatomic coulombic decay, pump-probe experiments, free-electron laser

Interatomic Coulombic decay (ICD) is a relaxation process of an electronically excited atoms and molecules in the environment [1]. These excited species decay non-radiatively by releasing the excess energy via electron emission of the neighboring species. Numerous theoretical and experimental studies on ICD have been carried out in many different systems in the past. Recently, a new ICD process induced by two-photon double excitation in Ne dimer (Ne_2) was proposed (Equation 1) [2].

$$Ne_2 + 2h\nu \rightarrow [Ne^*(2p^{-1}3s)]_2 - ICD \rightarrow Ne^+(2p^{-1})\text{-}Ne + e_{ICD}^- \qquad (1)$$

To produce this doubly excited state, we used seeded free-electron laser (FEL) facility "FERMI". We measured Ne_2^+ yield as a function of FEL photon energy. Ne_2^+ is produced via the ICD process from the doubly excited state $[Ne^*(2p^{-1}3s)]_2$. The resonant enhancement of Ne_2^+ yield could be seen around the photon energy 16.39 eV, in good agreement with the theoretical prediction [2].

The doubly excited state can be quenched before the ICD process occurs by photoionization of the 3s electron using the probe UV laser. By scanning the FEL-UV laser delay time we were able to estimate the ICD lifetime with the help of *ab initio* calculations.

Ref. [1] L.S. Cederbaum *et al*., *Phys. Rev. Lett.* **1997**, *79*, 4778-4781.

[2] Ph. V. Demekhin *et al*., *J. Phys. B: At. Mol. Opt. Phys*. **2013**, 46, 021001.

O-14(Invited)

Glutathione transport across the ER membrane

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Key words: glutathione, disulphide bonds, roGFP, microsomes, endoplasmic reticulum

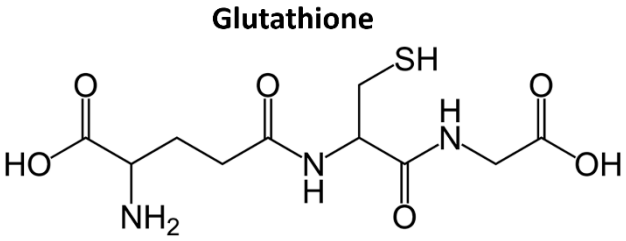

Fig 1. Structure of glutathione

Introduction of disulphide bonds into nascent polypeptide chain stabilises protein structure and ensures correct folding. Disulphide bonds formation takes place in a separated environment inside the lumen of the ER. Glutathione is a tripeptide synthesised in the cytosol that plays important role in the formation of disulphide bonds. However, it is still unknown how glutathione is transported to the ER and other organelles. To establish an assay for glutathione transport we have taken advantage of the properties of a redox sensitive Green Fluorescent Protein (roGFP). We used microsomes prepared from cells expressing roGFP in the ER. The transport assay relies on the selective permeability of membranes. Biological membranes allow some reducing agents to go through while other compounds are impermeable. The overall change in roGFP redox state measured over time reflects the rate of transport of reducing agents. By using this system we demonstrated that the ER membrane constitutes a barrier for GSH. We have also shown that GSH does not simply diffuse through the ER membrane and transport is necessary for GSH to cross the ER membrane. This assay is not limited to reducing agents only and can be used to monitor the transport of any compounds able to alter the redox status of roGFP. An inhibitor of GSH transport is the necessary key needed to validate the assay and to progress further with the project.

O-15(Invited)

Preparation of novel biomaterials from linear-type and cyclomatrix-type polyphosphazenes

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Key words: polyphosphazene, biomaterials, hydrogels, nano-particles

Polyphosphazenes-based materials are a class of inorganic–organic hybrid polymers that consist of an inorganic main structure (-P=N-) with two organic side groups attached to each phosphorus atom. There are two types of polyphosphazene materials. The linear one is prepared from ring opening polymerization of hexachlorocyclo-triphosphazene (HCCP). While the cyclomatrix one is synthesized directly from HCCP via precipitation polymerization reaction (Figure 1). These polymers are very designable and exhibit versatile characteristics depending on their substituents which are employed by nucleophilic substitution reaction. According to the reports and our studies, amino acid ester substituted polyphosphazene-based materials have shown significant potential as biomaterials due to their excellent biocompatibility, tunable biodegradation and nontoxic degradation products. Here, we present two of our works as follows:

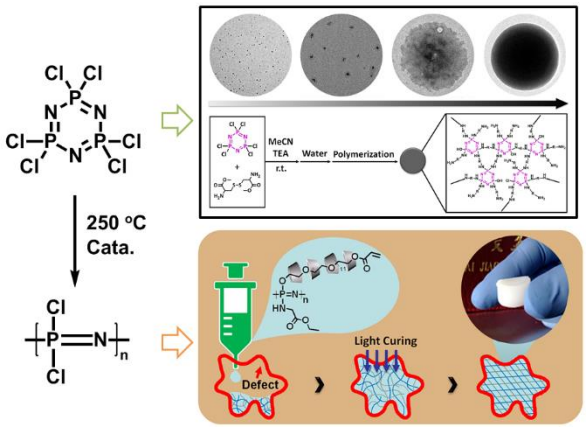

Fig. 1. Polymerization of linear polyphosphazene from HCCP, and the synthesis of cyclomatrix polyphosphazene nanoparticles and injectable linear polyphosphazene hydrogel.

1) We synthesized and self-assembled an injectable hydrogel from biodegradable mixed-substituted linear type polyphosphazene and natural organic molecule α-cyclodextrin (αCD) by host-guest inclusion. Photo-crosslinking was then employed to enhance mechanical property and anti-water solubility. In addition, the surface of the cured hydrogel can be readily tuned from cell-philic to cell-phobic by changing the substituted ratio of amino acid ester.[1]
2) Water-triggered self-assembly polycondensation was proposed for preparation of cyclomatrix polyphosphazene nanoparticle from amino acid esters, and found a critical solubility parameter to determine whether the nanoparticles were formed. Based on this rule, we also investigated the control of the size of its nanoparticles.[2]

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O-16(Invited)

In Situ Growth of Polyphosphazene Nanoparticles Coating on Honeycomb Surface: Facilely Forming Hierarchical Structure for Bioapplication

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Key words: breath figure, cell adhesion, hierarchical structures, polyphosphazene, surface chemistry

The cellular physiological conditions usually rely on hierarchical structure at both nanoscale and microscale. Thus, it is of significant sense to provide a hierarchical stucture for the cell culture which is more approximate to the real cells physiological environment than those with only single scale ones. Honeycomb structured surface, featured with highly ordered hexagonal pore array and obtained via breath figure method, has been widely applied as the cell substrates. However, the nano/microhierarchical honeycomb for cell cultrue is still a blank area. Even there are some achievements on hybrid or hierarchical honeycomb structures, it is a challenge to solve the problems on their biocompatiblity and facility. A potential strategy to address these issues is growing an organic nanostructure in situ from a honeycomb surface.

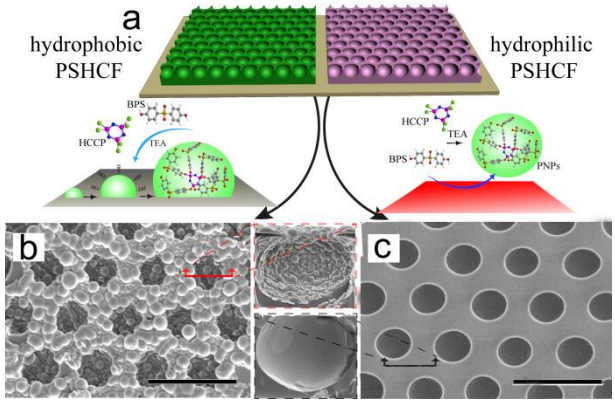

Fig. 1. Schematic of the process of decoration of PSHCF with polyphosphazene.

In this study, we developed a quite simple and facile method to prepare the cyclomatrix polyphosphazene coating. The polyphosphazene nanoparticles can be modulated and patterned to form hierarchical structures on honeycomb surface. This approach is unique in two aspects: 1) it can provide a rapid generation of phosphorus-containing hierarchical surface for cell scaffold; 2) the parameters of polyphosphazene coating were controllable without laboriously chemical modification. [1] The hierarchical substrate has good biocompatibility and markedly enhances cell adhesion, spreading, and proliferation. The method presented in this work opens new opportunities in the design and development of hierarchical, PS-based cell scaffolds for biomedical applications.

Ref. [1] S. Chen et al., *Chem. Commun*. **2015**, 51, 5698-5701.

O-17(Invited)

4-arm PEG based polyurethane hydrogels with high strength and sensitivity to stimulus

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Key words: pulyurethane, hydrogels, high strength, sensitivity to heavy metal ions, degradable

Hydrogels have been considered as promising materials in myriad applications. For various practical applications, hydrogels should not only hold good mechanical strength, but also possess functionalities.

Herein, we take 4-arm PEG not only as the skeletion of hydrogel with high mechanical strength, for its homogeneous network, but also as crosslinker. And HDI was chose as the hard segment of polyurethane. In this base, we prepared two kinds of functional hydrogels with outstanding compressive strength, one is rapidly sensitive to low concentration of specific heavy metal ions(the first work), and the other one is degradable in reducing environment and biocompatible(the second work).

In the first work(Fig 1), due to the high reactivity and efficiency of -NCO on HDI, it plays the role of reactive site to introduce functional chain extender, TPP-(OH)4. TPP-(OH)4 have been proven sensitive to certain metal ions, and reported to act as both ion receptors and signaling fluorophores. Through tuning the mole ratio of -NCO/-OH in the system, excess -NCO terminal groups are remained to react with TPP-(OH)4. Finally, the obtained PEG-HDI$_X$-TPP hydrogels has outstanding compressive strength and rapid detection to low concentration of metal ions. Noteworthily, the hydrogel can be recycled.

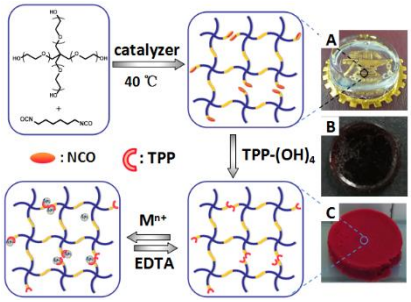

Fig 1. Process map of PEG-HDI$_X$-TPP

In the second work(Fig 2), Cys was chosen as chain extender and become the hard segment after end-capped by HDI. Since Cys has S-S bonds, this polyurethane hydrogels can be rapidly degraded in the presence of reducing DTT. Furthermore, controlling the proportion of Cys and HDI, the number of Cys introduced between each two arms of PEG can be manipulated. As a result, degradation rate of the hydrogels can be flexibly adjusted. Eventually, the obtained PEG-(S-S)$_X$-HDI hydrogels has adjustable degradation rate, excellent compressive strength and outstanding biocompatibility.

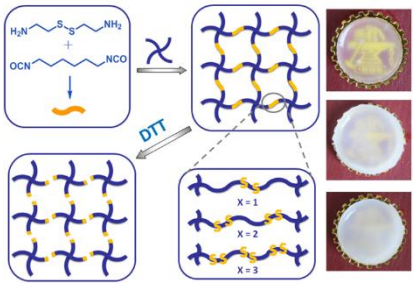

Fig 2. Process map of PEG-(S-S)$_X$-HDI

Lecture-4

Biotechnology meets inorganic nanomaterials

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Key words: protein engineering, nanobiotechnology

Advance in molecular biology has supplied us vast resources of functional molecules (proteins) and various experimental technologies to generate recombinant proteins with a non-native function and structure can be generated by means of molecular evolutional techniques and fusion protein engineering. In this molecular biology background, we are proposing the concept of "smart nano-bio design" for generating functional nanodevices from various protein modules together with organic and inorganic materials.

Protein structural and functional information of proteins are stored by the unit of domain (module) which can be expressed in *E. coli*, and molecular evolutional techniques prefer to functionalize proteins by the units. Further, in the field of materials, "Nanotechnology" came in use from 1980s, so that various organic and inorganic materials are downsized to nano-meter which is comparable to the size of the protein domain and modules. In the smart nano-bio design, the protein module and various organic/ inorganic nanomaterials are considered as "functional nanomaterials" with no distinction of matters. Present fusion protein engineering can design the giant recombinant proteins fused from several modules, but the structural complexity and increase of molecular size cause little expression of protein in host cells or lead to high-cost protein production. In the "smart nano-bio design", the protein modules with desired function are identified from protein data base or generated by means of molecular evolution technique. The smart proteins with only functional protein modules are economically prepared in bacterial cells, and they are constructively built up in vitro on a scaffold structure of organic or inorganic nanomaterial without being bound to the limitation of structural design using amino acid sequence. By using this concept, we are trying to generate a novel and unique chimera nanodevices which can be used in the therapy, material, and environmental Fields.

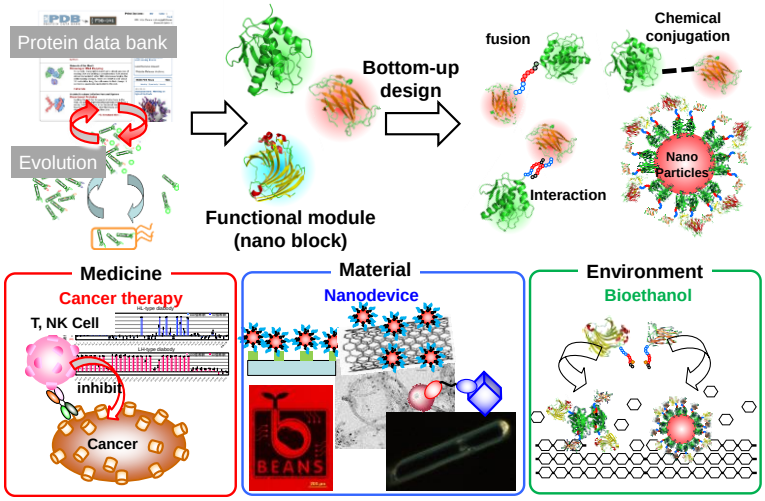
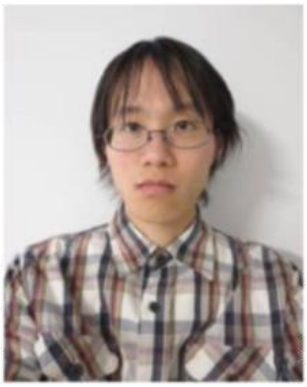


Figure. Smart nano-bio design

O-18

Observation of the Search Dynamics of p53 Mutants for the Target DNA Sequence by Single-molecule Fluorescence Microscopy



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Key words: p53, DNA, anisotropy measurement, single-molecule measurement, binding probability

p53 slides along DNA, binds to the target DNA sequence, and promotes the expression of proteins required for tumor suppression. Previous studies revealed that only one posttranslational modification or mutation can change the activity of p53 drastically. The objective of my research is to understand the activation mechanism of p53 by comparing the sliding dynamics of several mutants based on single-molecule fluorescence microscopy. We constructed the pseudo-wild type (WT) [1], activated, and inactive mutants of p53, and compared their dynamics.

First, GST-tagged p53 was constructed with *E. coli* and purified by passing through GST and heparin columns. Second, the equilibrium dissociation constants of the pseudo-WT, activated, and inactive mutants of p53 from the target DNA were examined by fluorescence anisotropy measurements and were 1.3, 0.76, and 6.2 nM, respectively. Third, the dissociation rate constants of p53 from the target DNA were obtained by stopped-flow experiments. The obtained rate constants suggest that the activated p53 possesses the longer binding time to the target sequence.

We next conducted the single-molecule fluorescence microscopy measurements and observed the sliding dynamics of p53 along DNA containing a target sequence. The binding and the pass-through events of p53 to the target sequence were observed (Fig.1). The binding probabilities (BP) of pseudo-WT, activated, and inactive mutants were respectively 10, 15, and 4%, indicating that BP is correlated with the activity of p53. We suggest that p53 may regulate its function by altering BP based on posttranslational modifications.

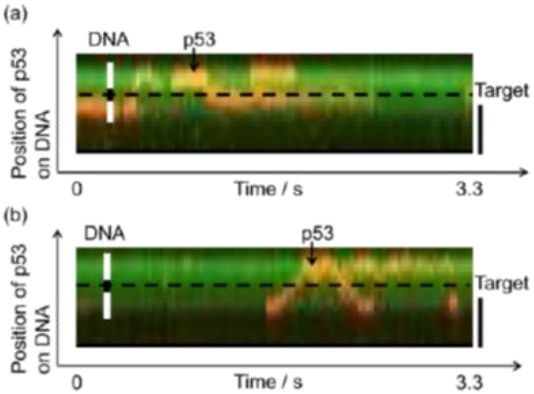

Fig. 1. Sliding dynamics of p53 along DNA. (a) Binding and (b) pass-through events. Scale bar: 1μm.

Ref. [1] Petty, T. J. *et al*., *EMBO J*., **2011**, *30*, 2167.

O-19(Invited)

Measuring translation rates *in vivo* by single molecule microscopy

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Key words: translation, ribosomes, single molecule microscopy, nanoscopy, translation rate.

Protein synthesis is a very extensivly studied field, and we now have detailed knowledge about ribosomal structure and it's mechanism. However, much less is known about ribosomal dynamics inside living cells. Certain parameterns, such as number of ribosomes or average translation rate, have since long been calculated from external observations or bulk experiments. These do, however, not nesscarily tell us very much about what translation actually looks like in it's natural environment. For example, magnitude differences in translation rates have been observed in vitro. Is this also a phenomenon in living cells, which are crowded and might even have yet unknown players taking part in translation?

By using *in vivo* single molecule microscopy we can now take both the step to study single molecules and thus see the spectrum of variation instead of just the average, and study the reactions in the environment they evolved for. By imaging cells under strong laser illumination, single diffusing fluorophores can be resolved at a high frame rate, located by automated image analysis and connected into trajectories over time. Particles bound in different complexes can be distinguished by measuring their diffusion rates, and it's variation over time indicates the lifelength of the complexes.

To apply these methods to the problem of translation rates, we are developing an assay to study single ribosomes translating known mRNAs. Labeling a subset of the cellular ribosomes that translates a subset of mRNAs would allow us to in effect perform a single molecule experiment inside a growing cell but independent of other cellular processes except the translation machinery. For this we need 1. an orthogonal ribosome that only translates a matching mRNA, and 2.the ability to label this ribosome. We have modified a rRNA locus to express small subunits with these properties and by expressing a orthogonal mRNA, electroporate in a label and observing under the microscope we can measure now diffusion rates and thus binding-unbinding events of the orthogonal subunit in living cells.

O-20

Fabrication of π-Conjugated Polymer Nanofibers and Their Formation Processes

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Key word: Organic nanocrystal / Polydiacetylene / Surfactant

Organic third-order nonlinear optical (NLO) materials are powerful and useful candidates for highly efficient optoelectronic devices. π-Conjugated polymers such as polydiacetylene (PDA) possess fast third-order NLO response. NLO and physical properties of PDA such as poly[1,6-di(*N*-carbazolyl)-2,4-hexadiyne (DCHD)] are strongly dependent on crystal size and shape in nanocrystal state. Although it has been reported that some surfactants such as CTAB, and SDS [1] could produce the fibrous PDA nanocrystal by using the reprecipitation method [2], there are still no clear understanding of the formation mechanism.

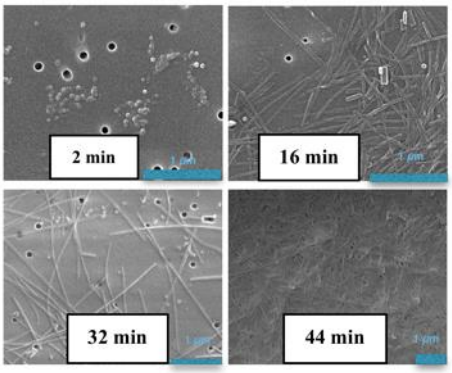


Figure 1. SEM images of poly-DCHD nanocrystals prepared at room temperature by adding Triton X-100 under different retention time

So far, it was so difficult to monitor the formation process of fibrous PDA nanocrystals prepared at the elevated temperature (e.g., 333 K), and the surfactants used were commonly added into DA solution in the previous reprecipitation method.

In the present study, we have developed the new way to fabricate fibrous PDA nanocrystal at room temperature by using Triton-X *etc*. on the basis of reprecipitation process. After the retention time of about 40 minutes, the shape of PDA nanocrystals has been dramatically changed from cubic-like to fibrous as shown in Fig. 1. In addition, it has become apparent that the resulting DA nanocrystals became solid-state polymerizable with the retention time, according to the extinction spectral changes (Fig. 2) and the photographs of the dispersion liquids (Fig. 3).

Attempted to fully understand the effect of added surfactants in the reprecipitation method will fundamentally contribute to further control the size and shape of organic and polymer nanocrystals.

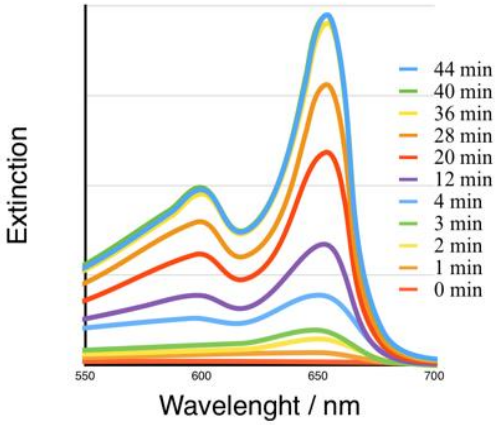


Figure 2. Extinction spectra of poly-DCHD nanocrystals under different retention time

Figure 3. Dispersion liquid of poly-DCHD nanocrystal prepared by adding Triton X-100 under different retention times (from left: 1,2,3,4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44 minute)

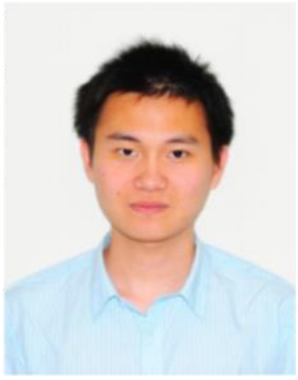
[Reference]

[1] T. Onodera *et al., J. Cryst. Growth,* **229**, 586 (2001).

[2]H. Kasai *et al., Jpn. J. Appl. Phys.*, **31**, 1132 (1992).

O-21

Investigation of the Roles of the Intrinsically Disordered Region of a Tumor Suppressor p53 in the DNA Binding



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Key words: tumor suppressor p53, single molecule measurement, DNA binding, intrinsically disordered region

A tumor suppressor p53 can search for and bind to the specific target sequences of DNA, which results in cell cycle arrest, apoptosis and DNA repair. The intrinsically disordered region (IDR) of p53, which connects the core and tetramerization domains of p53, has been considered as just a flexible linker; however, considering that the length and sequence of IDR are highly reserved across different species, a possible involvement of IDR is suggested in the activities of p53 such as the target search. To address the roles of IDR, we prepared a mutant of p53, in which the IDR region is repeated twice (DL-p53), and investigated the affinity to the target and non-target sequences of DNA and the one-dimensional (1D) sliding dynamics along DNA.

We first observed the 1D-sliding dynamics of DL-p53 on stretched DNA by using a home-made single-molecule fluorescence microscopy, and obtained the diffusion coefficient, D, by fitting the averaged mean-square displacement of DL-p53. The coefficient for DL-p53 (D= 0.076±0.002 $\mu m^2/s$) decreased significantly compared to that of wild-type p53 (D= 0.181±0.006 $\mu m^2/s$). We next examined the affinities of DL-p53 to the target and non-target sequences of DNA by using fluorescence anisotropy measurements. The DL-p53 showed similar affinities to the target and non-target DNAs, indicating the loss of sequence specificity (Fig. 2). We also conducted stopped-flow experiments and obtained that the dissociation rate constant of DL-p53 (k_d = 42 s^{-1}) from the non-target DNA is almost half of that of WT-p53 (k_d = 77 s^{-1}). On the other hand, gel electrophoresis results suggest that the elongation of the linker IDR causes the p53 to aggregate easier in the presence of DNA compared to WT-p53.

In this study, we found that the elongation of the IDR dramatically affects the binding ability and the sliding dynamics of p53. The effect of elongating the IDR might be caused by the increased amount of positively charged residues in IDR, which results in the stronger non-specific interaction between p53 and DNA. Thus, we suggest that the IDR may affect the search dynamics of p53 by directly interacting with DNA and that the length of IDR might be optimized to facilitate the search process for the target sequence.

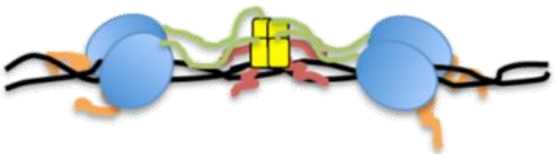

Fig. 1 . Schematic representation of DL-p53 and DNA complex. The circle, square, and the line connecting the two are respectively the core domain, tetramerization domain, and linker region. Black line represents DNA.

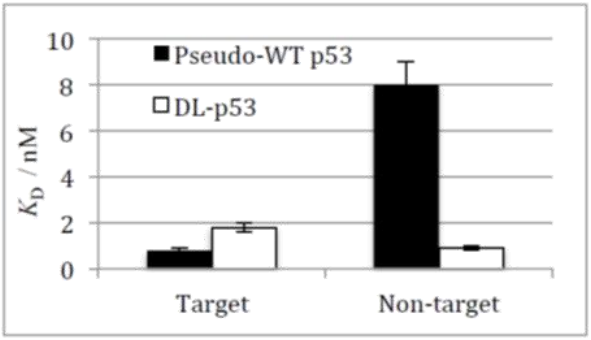

Fig. 2 . Dissociation constants of pseudo-WT and DL-p53 from target and non-target DNA.

O-22

Supramolecular asymmetric photochirogenesis mediated by synthetic antibody: *In the ground and excited states interaction studies of synthetic antibody with 2-anthracenecarboxylate monomer and dimers*

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Key words: asymmetric photoreaction, supramolecular, synthetic antibody, phage display technique, anthracenecarboxylate

We have reported the supramolecular enantiodifferentiating photocyclodimerization of 2-antharcenecarboxylate (AC) mediated by mammalian serum albumins, including bovine, human, porcine, and canine (BSA, HSA, PSA, and CSA), as a chiral reaction media to render the cyclodimers with high enantioselectivities of up to 97 % enantiomeric excess (ee). Contrarily, synthetic antibody has never been used as a chiral catalytic media in asymmetric photochirogenesis, although it is widely used in thermal reaction as catalytic antibody. Based on the background, we have attempted to utilize synthetic antibody as a novel chiral reaction media for supramolecular asymmetric photochirogenesis (SMAP).

In this work, we focused on synthesizing single-chain antibody using a conventional phage display technique and studying the interaction of synthetic antibody with AC. The ligand consisted with target AC dimer, polyethylene glycol (PEG) spacer, and biotin was synthesized by solid phase peptide synthesis strategy, and applied as a hapten in a phage display technique. After three rounds of selection, we successfully isolated several candidate phages showing high affinity to a target AC dimer. The candidate antibodies were selected by ELISA selective experiments of target AC dimer from 4 kinds of dimer mixture. The sequence of synthetic antibody was determined by DNA sequencer and subcloned into an expression vector. The synthetic antibody was expressed in *E.coli*, and purified with Ni-NTA column and gel permeation chromatography (GPC) with a high purity. The ground- and excited-state interactions of synthetic antibody against desired target AC dimer and AC monomer were discussed. We also studied these interactions in the competitive environment, which is the mixture of all four AC dimers to determine the selective recognition properties of the antibody.

O-23(Invited)

NMR Analysis of Terbium(III)─Phthalocyaninato Single Molecule Magnets

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Key words: paramagnetic NMR, solution, magnetic anisotropy, single-molecule magnets

Single-molecule magnets (SMMs) are molecular materials displaying stable magnetization below a blocking temperature (T_B).[1,2] The prerequisite for SMM behaviour is a high spin quantum number combined with a large magnetic anisotropy ($\Delta\chi$). Magnetic measurements, performed on solid samples and conducted at temperatures close to zero degrees Kelvin are usually used for characterization of SMMs.[3] Solution studies at room temperature have been reported in rare cases only.[4–6] However, NMR spectroscopy can provide valuable information for predicting SMM properties, as the mean paramagnetic susceptibility.[7] and the anisotropy of the magnetic susceptibility tensor can be easily obtained. The studied Tb(III)–phthalocyaninato SMMs $Tb(obPc)_2$, $Tb_2(obPc)_3$ and the slipped triple-decker (obPc)Tb(Fused-Pc)Tb(obPc) (obPc = 2,3,9,10,16,17,23,24-octabutoxyphthalocyaninato) show different NMR phenomena. In $Tb_2(obPc)_3$, we focused on the analysis of pseudocontact shifts and residual dipolar couplings (RDCs) for the purpose of obtaining the solution structure of this complex and for studying the mobility of the alkoxy chains.[8] The ligand-radical containing, neutral $[Tb(obPc)_2]^0$, along with its cationic and anionic counterparts, was used in a combined NMR and DFT study of the various contributions to the hyperfine terms of the ^1H and ^{13}C resonances in the phthalocyaninato moieties. Furthermore, ferromagnetic coupling of the ligand- and metal-centered radicals in $[Tb(obPc)_2]^0$ was shown. The 49 signals observed in the ^1H NMR spectrum of the C_{2h} symmetric slipped triple-decker were assigned with paramagnetic COSY and NOESY spectra and used for determining the rotation barrier of the phthalocyaninato ligand and the coordination geometry of the Tb(III) ions.

References: [1] A. Caneschi et al., *J. Am. Chem. Soc.* **1991**, *113*, 5873–5874; [2] N. Ishikawa et al., *J. Am. Chem. Soc.* **2003**, *125*, 8694–8695; [3] D. N. Woodruff et al., *Chem. Rev.* **2013**, *113*, 5110–5148; [4] N. Ishikawa, *J. Phys. Chem. A* **2003**, *107*, 5831–5835; [5] K. R. Meihaus et al., *J. Am. Chem. Soc.* **2014**, *136*, 6056–6068; [6] A. G. Martynov et al., *Inorg. Chim. Acta* **2009**, *362*, 11–18; [7] D. F. Evans, *J. Chem. Soc.* **1959**, 2003–2005; [8] M. Damjanović et al. *J. Am. Chem. Soc.* **2013**, *135*, 14349–14358.

O-24(Invited)

A novel time scale of dynamic heterogeneity in a supercooled liquid system

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Keywords: Supercooled liquid, Dynamic heterogeneity, Dynamic susceptibility, Characteristic time scale.

A normal liquid state matter becomes a “supercooled liquid” state when it is cooled very rapidly. It is also known that there is a phase transition to glass state when the material reaches the critical temperature. The dynamic heterogeneity is important concept to understand the properties of this phase transition. However, common correlation functions used for studying the phase transition of normal liquid cannot demonstrate the dynamic heterogeneity. Multi-point density correlation function and multi-time correlation function are alternatives for previous correlation functions, which contain the characteristic length scale and time scale of dynamic heterogeneity, respectively. We noticed that the dynamic susceptibility, which is derived from the spatial integration of the four-point density correlation function, could also have the characteristic time scale. To verify this, the MD simulations using the Lennard-Jones binary mixture model system are employed to find the time scale of dynamic heterogeneity. We introduce the new time scale τ_4 by integrating the dynamic susceptibility with time and find the scaling factor with other time scales(Figure 1). We finally confirm that τ_4 has the same scaling with τ_{DH}, which comes from the three-time density correlation function.

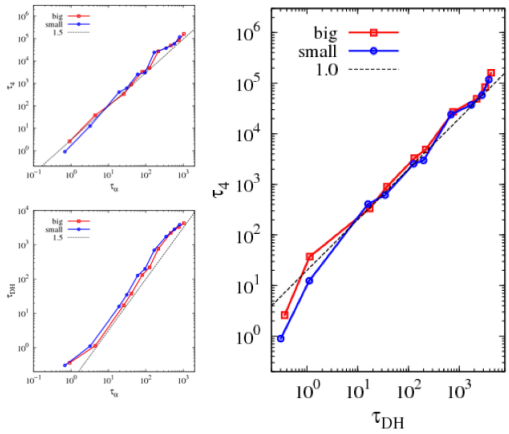

Fig 1. Scaling relation between each time scales. $\boldsymbol{\tau_\alpha}$ is the spatial relaxation time, derived from the intermediate scattering function. Because we used two different size particle, there are two curves.

O-25

Relationship between Structural Flexibilities and Gas Adsorption Properties of One-Dimensional Copper(II) Polymers with Paddle-Wheel Units

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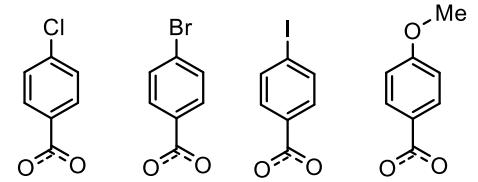
Keywords: Copper(II) complex, Gas adsorption-desorption property, Interchain interaction

Tuning of structural flexibilities and gas adsorption properties plays an important role to design new gas adsorption metal-organic materials. We have been already reported the crystal structures, CO_2-, and N_2-gas adsorption-desorption properties of four kinds of paddle-wheel shaped binuclear copper(II) complexes of $[Cu_2(p\text{-ClBA})_4(pz)]_n$, $[Cu_2(p\text{-BrBA})_4(pz)]_n$, $[Cu_2(p\text{-IBA})_4(pz)]_n$, and $[Cu_2(p\text{-MeOBA})_4(pz)]_n$ (*p*-ClBA= *p*-chlorobenzoate, *p*-BrBA= *p*-bromobenzoate, *p*-IBA= *p*-iodobenzoate, *p*-MeOBA= *p*-methoxybenzoate, and pz = pyrazine), which did not have sufficient void space to include the crystallized solvents.[1] From the X-ray crystallographic analyses, the interchain interactions and gas-adsorption properties were depended on the *para*-substituents of BA ligands. However, the relationship between the magnitude and types of interchain interactions and gas adsorption properties is still under the consideration. Herein, we discussed the relationship between gas adsorption properties and interchain interactions using a Hirshfeld surface analysis.



p-ClBA *p*-BrBA *p*-IBA *p*-MeOBA

Fig. 1. Molecular structures of four kinds of benzoate ligands in Cu(II) complexes.

Hirshfeld surface analysis indicated that the structural flexibility of the complexes was decreased in larger halogen atom. On the other hand, $[Cu_2(p\text{-MeOBA})_4(pz)]_n$ had a different type of interchain interactions from the others. Detail correlation between the structural flexibilities and gas adsorption properties will be discussed.

[1] K. Takahashi et al, "Intermolecular Interactions and Physical Properties of One-Dimensional Cu(II) Complex Bearing Bulky Benzoate Ligands", The 64th Conference of Japan Society of Coordination Chemistry, 2Fa-07, Tokyo, Japan (September 2014).

O-26(Invited)

Xylem-Like Honeycomb Monoliths Constructed from Cellulose Nanofibers and Studies on the Monolith Component Control

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Key words: unidirectional freeze drying; TEMPO-mediated oxidized cellulose nanofibers; xylem-like monoliths; component control

"Biomimetics" has proved to be an effective way to design newly advanced materials. The tree-xylem, which is featured by its honeycomb patterned cross-section and straightly stretching channels (Fig. 1), is considered as a valuable mimicking target for its structural merits such as high strength-to-weight ratio, high surface area and low pressure drop.

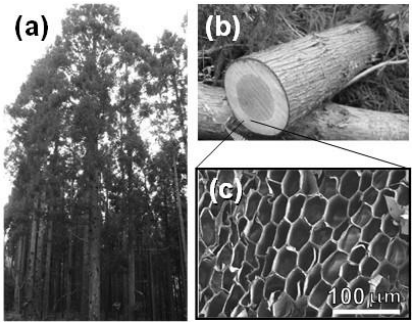

Fig. 1 (a) Cryptomeria japonicas and (b) its log. (c) SEM image of the xylem of a cryptomeria japonica.

In this work, we have found that with a water dispersion of 2,2,6,6-tetramethylpiperidine-1-oxyl radical (TEMPO)-mediated oxidized cellulose nanofibers (TOCNs), xylem-like honeycomb monoliths (XMs) can be constructed via a unidirectional freeze drying (UDF) method.

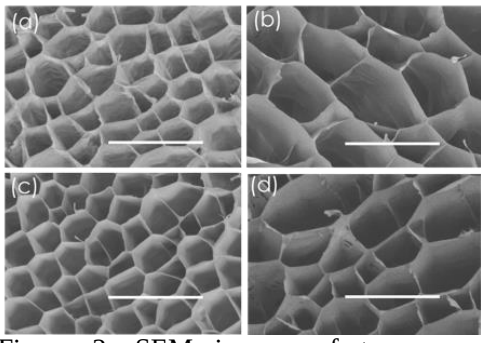

Figure 2. SEM images of transverse section for XMs prepared from (a) TOCNs sol, (b) vinyltrimethoxysilane modified TOCNs sol, (c) a polyurethane mixed TOCNs sol, and (d) graphene-oxide mixed TOCNs sol. Scale bars: 50 μm.

Superior to the real xylem structure, the XMs are free from channel blockage and chemical component of their channel walls could be easily controlled at the precursor preparing stage. It was found that the as-prepared TOCNs sol is miscible with many a chemical and could form homogeneous multi-component hybrid precursor sols, which could lead to composite xylem-like honeycomb monoliths (CXMs) in the subsequent UDF procedure (Fig. 2). The resulting CXMs appear with many more intriguing manifestations such as high water stability, high elasticity, and possession of electrical conductivity. All these behaviors have extended the versatility of the XM and may give rise to its potential practical application.

O-27

What are critical factors for highly cytotoxic smart antibody ?

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Key words: antibody engineering, protein engineering, tumor, immune therapy

Antibody has a hierarchical structure constructed from structurally-independent domains, and various recombinant antibodies with artificial structural formats are designed from the domains. Bispecific Diabody (BsDbs) is a small antibody designed only from two kinds of the fragments of variable region (Fvs) **(Fig. 1)**, and the diabody composed of the Fvs from anti-cancer and anti-lymphocyte antibodies can form a bridge between cancer and T-lymphocyte to make an effective damage on cancer cells **(Fig. 2)**. The cytotoxicity of diabody can be dramatically changed by Fv used; however which the physical properties of Fv used have correlations with cytotoxicity remain unknown. Therefore, it is important to reveal the cytotoxic mechanism in order to design the highly cytotoxic diabody. Here, we propose a methodology for high throughput screening of the most effective bispecific antibody of more than 100 diabodies designed from several anti-cancer and anti-lymphocyte IgG type antibodies.

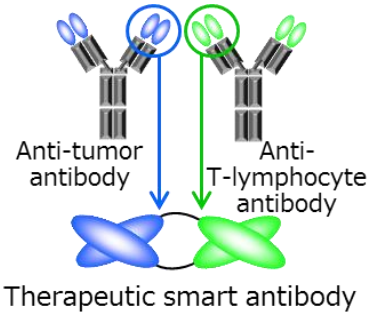

Fig. 1 Structure of smart antibody

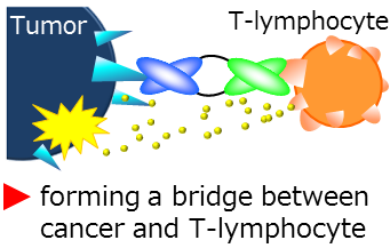

Fig. 2 Cytotoxic activity of smart antibody against for cancer

We applied each medium fraction to immobilized metal affinity chromatography (IMAC) to purify expressed diabodies. We step-wisely measured the cytotoxicity of IMAC-refined diabodies at the various diabody concentrations by MTS assay. In this assay, all samples were prepared to less than 50 mM imidazole concentration, because imidazole showed the cytotoxicity against cancer cells at more than 75 mM. In the result of step-wise screening, we got 6 high cytotoxic diabodies which damaged at cancer cells at 100 fM concentration. By means of the screening, we found some rules of high cytotoxicity of the diabody, specific domain order, target molecules, and epitopes of the targets. These results imply that high cytotoxic diabodies have universal rules of structure and using antibodies for diabody.

O-28

Fabrication of Nano-Prodrugs of cholesterol-modified SN-38 and their Anticancer Activities

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Key words: nano-prodrugs, SN-38, drug delivery system, reprecipitation method

Nanometer-sized drugs (nanodrugs) have been received considerable attention for their potential application as a therapeutic agent for cancer, due to their tumor targeting efficacy. Various types of nanocarriers have been proposed to fabricate nanodrugs. The introduction of drug into nanocarriers, however, would cause several problems, such as low drug loading (less than 10wt%), side effects by themselves, and so on. In order to solve these problems, we have proposed "nano-prodrugs", which are composed of prodrug molecules without using nanocarriers as a novel designed nanodrugs.

In the present study, we have selected SN-38 as a model compound so as to obtain nano-prodrugs. SN-38 is the biologically active metabolite of irinotecan, which is commercially available, and exhibits potent antitumor activity. First, prodrugs of SN-38 with various substituents were synthesized through biodegradable ester bond. Next, the nano-prodrugs of SN-38 prodrug were fabricated by using the reprecipitation method. When the hydrophobic substituents such as saturated alkyl chain and/or cholesterol were employed, nano-prodrug with less than 100 nm in size could be obtained successfully (Fig. 1). Finally, the antitumor properties were surveyed by evaluating *in vitro* cell viabilities and *in vivo* antitumor effects, after treated with cholesterol conjugated SN-38 nano-prodrug (SN-38-chol NPs) or irinotecan. As a result, all SN-38-chol NPs exhibited higher activities than irinotecan against 4T1-Luc cells (Fig. 2, 3).

In conclusion, we have succeeded in synthesizing SN-38 prodrug and fabricating the corresponding nanoparticles, that is, nano-prodrugs. The pharmacological efficiency of SN-38 nano-prodrugs was confirmed evidently by *in vitro* and *in vivo* assay.

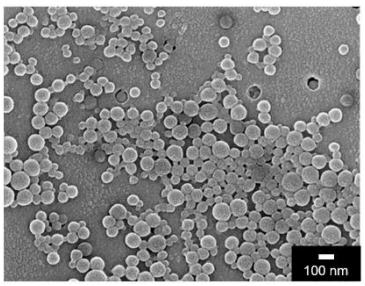

Fig. 1 SEM image of SN-38 –chol NPs.

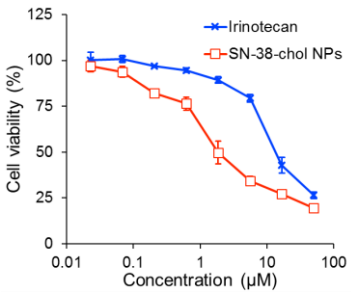

Fig. 2 *In vitro* cytotoxic activities against 4T1-Luc cells.

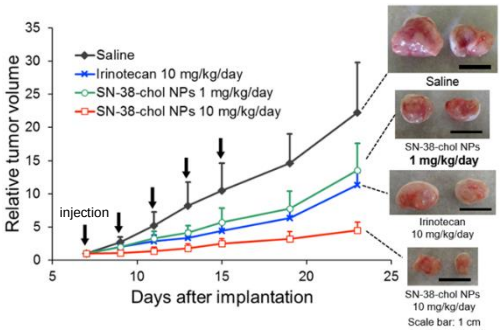

Fig. 3 *In vivo* antitumor activities against 4T1-Luc-beared nude mice.

O-29(Invited)

pH-Responsive Supramolecular Vesicles Assembled by Water-Soluble Pillar[5]arene of BODIPY Photosensitizer for Chemo-Photodynamic Dual Therapy

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Email: lidongqi1984@163.com
Key words: supramolecular vesicles,drug delivery system, photodynamic therapy

Pillararenes, a new generation of macrocyclic hosts with unique symmetric pillar frameworks and π-rich cavities, have excited great interest in fabricating many interesting supramolecular complexes and assemblies with various types of guests, which can be further applied as multifarious functional materials.[1]-[3] Recently, our group have pioneered the development of stimuli-responsive supramolecular nanocarriers and reported a series of **WP6**/**WP5**-based pH/Ca^{2+}/UV/GSH-responsive supramolecular nanoparticles for the controlled delivery of chemotherapic drugs to a variety of tumor cells.[4]-[5] In order to take advantages of combined modality therapy, herein we designed and prepared a BODIPY-functionalized quaternary ammonium derivative **G** which played a dual role in constructing supramolecular vesicles with **WP5**, acting not only as a guest molecule, but also a photosensitizer for photodynamic therapy. To the best of our knowledge, this is the first example of pillararene-based supramolecular nanocarrier for potent combined cancer treatment.

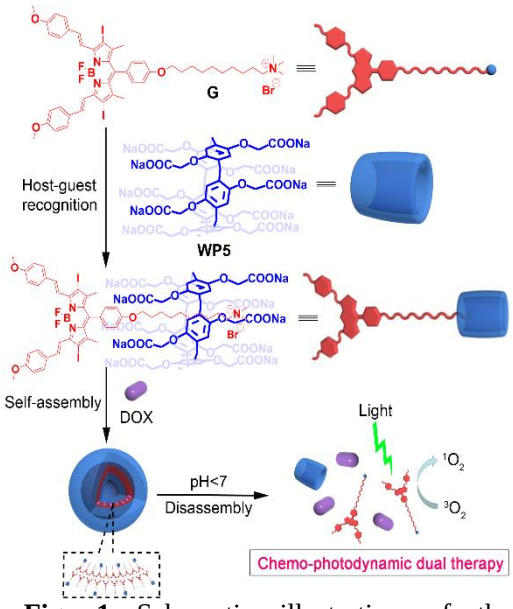

Fig. 1 Schematic illustration of the formation of **WP5** ⊃ **G** supramolecular vesicles and their pH-responsive drug release for chemo-photodynamic dual therapy.

Ref.
[1] Ogoshi, T.; Kanai, S.; Fujinami, S.; Yamagishi, T.-a.; Nakamoto, Y. *J. Am. Chem. Soc.* **2008**, *130*, 5022-5023.
[2] Hu, X.-Y.; Xiao, T.; Lin, C.; Huang, F.; Wang, L. Acc. Chem. Res. **2014**, 47, 2041-2051.
[3] Duan, Q.; Cao, Y.; Li, Y.; Hu, X.; Xiao, T.; Lin, C.; Pan, Y.; Wang, L. *J. Am. Chem. Soc.* **2013**, *135*, 10542-10549.
[4] Cao, Y.; Hu, X.-Y.; Li, Y.; Zou, X.; Xiong, S.; Lin, C.; Shen, Y.-Z.; Wang, L. *J. Am. Chem. Soc.* **2014**, *136*, 10762-10769.
[5] Hu, X.-Y.; Jia, K.; Cao, Y.; Li, Y.; Qin, S.; Zhou, F.; Lin, C.; Zhang, D.; Wang, L. *Chem. – Eur. J.* **2015**, *21*, 1208-1220.

O-30

Copper(I) Stabilization in the Extracellular N-terminal Domain of Ctr4

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Key words: membrane protein, metal transporter, spectroscopy

Copper is one of the trace elements essential for living cells. It serves as a cofactor of various redox enzymes because it is easily reduced and oxidized between Cu^{+} and Cu^{2+}. Therefore, copper transport across the plasma membrane and the distribution of copper to cupro-proteins are crucial for cell to live. The CXXSMXWNWYXXDXC motif with a symmetrical arrangement of Cys/Trp residues is conserved in extracellular N-terminal region of various fungi and yeast copper transporter proteins. This motif is hence likely to have important role in copper transportation.

We synthesized a peptide corresponding to this region of copper transporter Ctr4, and measured fluorescence, UV-visible absorption and Raman spectra in the presence and absence of copper.

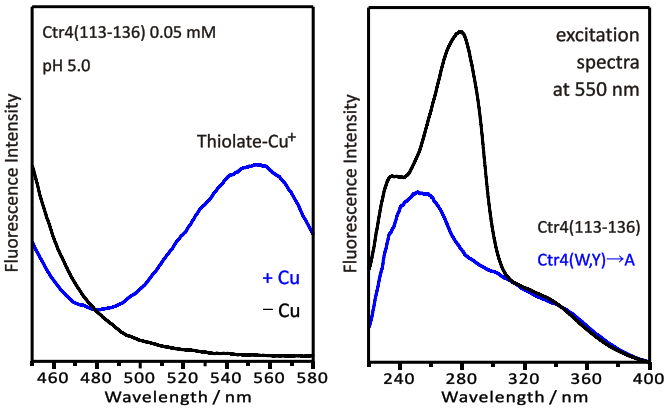

Figure 1. The fluorescence spectra of Ctr4(113-136) in equimolar $CuCl_2$ addition and its fluorescence excitation spectrum at 550 nm.

From the measurement of fluorescence spectra in Cu^{2+} addition, a peak was observed around at 550 nm, which is assigned to thiolate-Cu^{+} bond. It is revealed that this domain readily reduces Cu^{2+} and traps Cu^{+} through thiolate-Cu^{+} bond. This thiolate-Cu^{+} bond is stable even in air-saturated condition. Moreover, fluorescence excitation spectra at 550 nm have a peak at 280 nm as well as 300 nm. Förster resonance energy transfer (FRET) from tryptophan to thiolate-Cu^{+} bond seems to occur. At least one of the tryptophan residues is considered to be absolutely close to thiolate-Cu^{+} bond. That is not only cysteine but also tryptophan interacts to Cu^{+}. UVRR spectra show that the π-electrons of tryptophan indole ring may contribute to stabilization of the thiolate-Cu^{+}.

This tryptophan- and cysteine-based Cu^{+} stabilization is possibly crucial in primitive copper transporter.

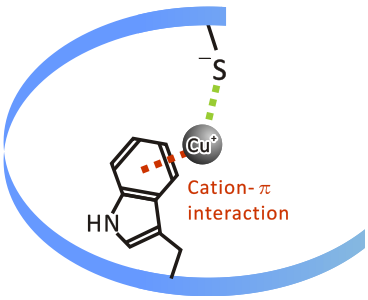

Figure 2. Cu^{+} stabilization by thiolate and tryptophan.

Abstracts of Poster Presentations

P-1

Investigation of Al_2O_3 growth behaviors on ultraviolet cured resin for establishment of ultraviolet nanoimprinting-atomic layer deposition

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Key words: atomic layer deposition (ALD), Al_2O_3, UV nanoimprinting,

UV nanoimprinting is a next generation nanoscale figuration technology.[1] UV nanoimprinting enables easy fabrication of sub-100 nm resin patterns. Atomic layer deposition (ALD) is a method for fabricating uniform inorganic material layers through sequential chemical synthesis. We demonstrate UV nanoimprinting-atomic layer deposition (UVN-ALD) process by combining UV nanoimprinting with ALD to fabricate 3-dimensional inorganic nanostructures as shown in Figure 1.[2] In this study, Al_2O_3 deposition behaviors on UV-cured resin patterns by ALD were investigated.

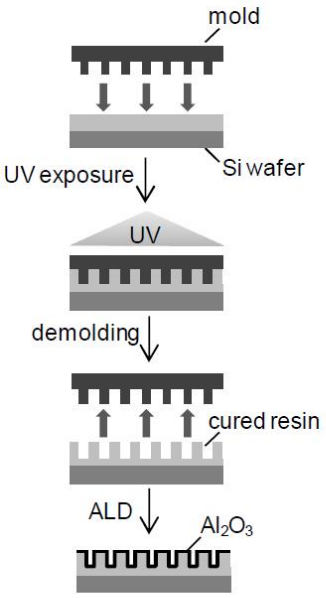

Figure 1. Schematic illustration of UVN-ALD .process.

A 100-nm-thick layer of UV-curable resin containing bisphenol A glycerolate dimethacrylate (BPAGDM) as a base monomer was formed on a Si substrate by spin-coating. Line&space (L&S) patterns were transformed by UV nanoimprinting. Trimethylaluminum (TMA) and H_2O were used as a precursor and an oxidizing agent, respectively. Al_2O_3 was deposited on the resin patterns under conditions; a substrate temperature of 120 °C and a cycle number of 150. The conditions were set as an ALD condition on a Si substrate.

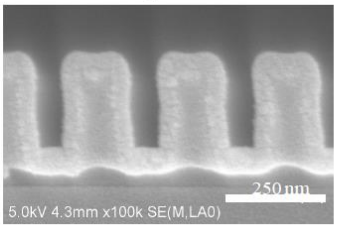

Figure 2. Cross-sectional FE-SEM image of 100 nm L&S cured resin pattern after ALD of Al_2O_3.

Figure 2 showed across-sectional FE-SEM image of 100 nm L&S cured resin pattern after Al_2O_3ALD. Bright and dark regions showed Al_2O_3rich region and UV-cured resin rich region, respectively. A uniform Al_2O_3 layer was formed on the resin surface. A40-nm-thick Al_2O_3 layer was obtained along sidewall of the pattern although the theoretical calculated thickness of 150-cycle-ALD was 15 nm on Si substrate. The resin pattern width of 100 nm decreased to 80 nm. These results suggested that TMA penetrated into resin. Therefore, UVN-ALD with a control of TMA penetration is a promising process to fabricate targeted 3-dimentional structures.

[1] J. Haisma et al., *J. Vac. Sci. Technol. B* **14**, 4124 (1996).
[2] S. Kuroyanagi et al., 2014 高分子学会東北支部研究発表会. A19

Synthesis and Monolayer Assembly of Titanium-Containing Amphiphilic Copolymer

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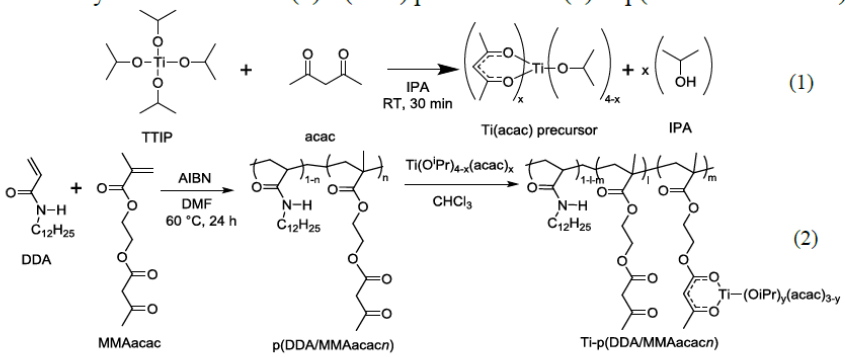
Key words: Polymer-titanium complex, Amphiphilic copolymer, Langmuir-Blodgett technique

Group 4(Ti, Zr, Hf) dioxide thin films are known to high-dielectric and semiconductor materials applicable for thin film transistor and photocatalyst. To fabricate ultrathin oxide films, mineralization of organic-inorganic hybrid film provides benefits for yielding fine patterns at room temperature under atmospheric pressure. The aim of this study is to synthesize Ti-containing amphiphilic copolymer and fabricate the Langmuir-Blodgett(LB) film capable of fabricating high-quality TiO_2 ultrathin film.

Scheme 1 Synthetic scheme of(1)Ti(acac) precursor and (2)Ti-p(DDA/MMAacac*n*).



We synthesized Ti-containing copolymer through three step processes (Scheme 1). Figure 1 shows elution curves of Ti-containing amphiphilic copolymer. The result shows that Ti complexes were successfully introduced to the copolymer because the high-molecular-weight component had absorbance at 330 nm, at which Ti(acac) precursor has absorbance due to LMCT. The monolayer stability of the Ti-containing amphiphilic copolymer at the air-water interface was confirmed by surface-area isotherm measurement; the curve had steep rise in pressure and high collapse pressure. Fig.2 shows the UV spectra of the thin film of amphiphilic copolymer with Ti complexes and the plot of absorbance at 320 nm as a function of the number of layers. This indicates that Ti was successfully introduced in this film and the monolayers were transferred regularly on solid substrates by LB technique.

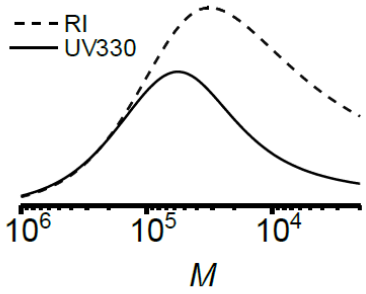


Fig. 1 Elution curves of Ti-p(DDA/MMAacac21).

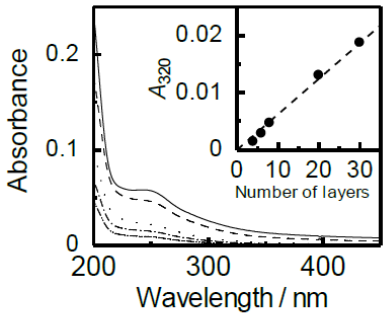


Fig. 2 UV-Vis absorption spectra of Ti-p(DDA/MMAacac30) LB film on SiO_2 substrate (4, 6, 8, 20, and 30 layers). The inset shows the relationship between absorbance at 320 nm and the number of layers.

P-3

Bioconversion of putative biosynthetic intermediates of paralytic shellfish toxins in the cyanobacterium *Anabaena circinalis* (TA04)

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Key words: saxitoxin, paralytic shellfish toxins, biosynthetic intermediates, metabolites

Saxitoxin (**1**) and its analogues, known as the strong Voltage-gated sodium channels blocker, are paralytic shellfish toxins (PSTs). We previously reported synthesis of the predicted biosynthetic intermediates (Int-A' (**2**), Int-C'2 (**3**) and Cylic-C' (**4**)).[1,2] These compounds were identified and quantified in the toxic cyanobacterium *Anabaena circinalis* (TA04) and dinoflagellate *Alexandrium tamarense* (Axat-2).

However, it has not been completely proved that **2**, **3** and **4** are the true biosynthetic precursors of PSTs. They are still suspectable to be just shunt compounds.

Therefore, we synthesized stable isotope (^{15}N) labeled **2**, **3** and **4**, and attempted to conduct a precursor incorporation experiments using *A. circinalis* (TA04). The results whether these labeled compounds are incorporated into C1/C2 (**5**, **6**), the major toxins of *A. circinalis* (TA04), will be reported.

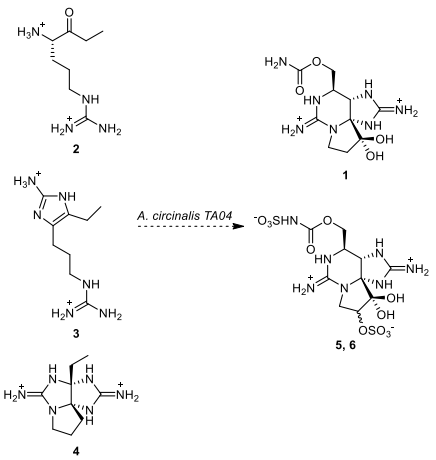

Fig. 1. The chemical structures of PSTs and biosynthetic intermediates

Ref.

[1] S. Tsuchiya, Y. Cho, K. Konoki, K. Nagasawa, Y. Oshima, M. Yotsu-Yamashita, *Org. Biomol. Chem.*, **2014**, *12*, 3016-3020.

[2] S. Tsuchiya, Y. Cho, K. Konoki, K. Nagasawa, Y. Oshima, M. Yotsu-Yamashita, *Chem. Eur. J.*, **2015**, *21*, 7835-7840.

P-4

Tetrodotoxin study in pufferfish and screening of bioactive compounds in marine invertebrates from Solomon Islands

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Key words: tetrodotoxin, pufferfish, invertebrates, bioactive compounds

Marine environment is a source of toxins and bioactive compounds. Screening of tetrodotoxin (TTX) (**Fig. 1**), a potent neurotoxin, in pufferfish from Solomon Islands was conducted for the first time in this study. Investigation of three species of pufferfish, *Arothron hispidus*, *A. nigropunctatus* and *Diodon holocanthus* using LC-FLD (fluorescence detection) and LC-MS [1] revealed *A. hispidus* and *A. nigropunctatus* to be toxic. The skin accumulates more TTX which presumably relate to their protection in predator-prey relationship, a role believed to be replaced by thorny spikes in *D. holocanthus*, the nontoxic species. Despite a significant difference in TTX content of Okinawan *A. nigropunctatus* and Solomon Islands toxic species, all toxic pufferfish possess similar toxin distribution profile for TTX analogues including 4,9-anhydroTTX, 5,6,11-trideoxyTTX and 4,9-anhydro-5,6,11-trideoxyTTX along with a few minor analogues 6,11-dideoxyTTX, 5,11-dideoxyTTX and 11-norTTX-6(*S*)-ol. Interestingly, 11-oxoTTX, an uncommon but highly toxic analogue was also observed in almost all toxic species in this study. Presence of TTX in pufferfish suggests that TTX distribution in other marine organisms within Solomon Islands is also possible.

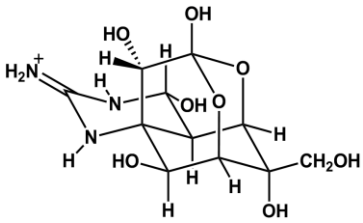


Fig. 1. The structure of TTX

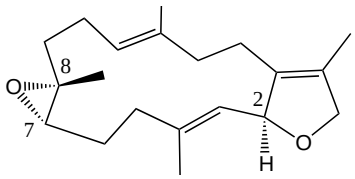


Fig. 2. The structure of (2*R*,7*S*,8*S*)-sarcophytoxide

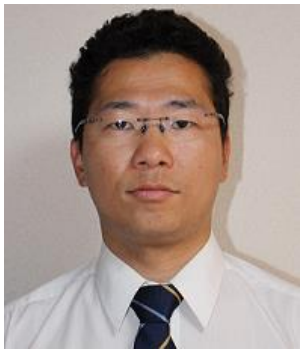
In an attempt to explore bioactive compounds from thirty marine invertebrates collected in Solomon Islands, a cell-based screening method was performed and revealed that three sponges (*Haliclona* sp., *Agelas* sp. and *Gelliodes* sp.), four corals (three *Lobophytum* sp., one *Montipora* sp.) and one starfish (*Acanthaster* sp.) were cytotoxic against Neuro-*2a* (mouse *neuroblastoma) cell* line, *P388* (murine leukaemia) *cell* line and Jurkat (human T-*cell* leukaemia) cell line. First two candidates that were semi-purified from a soft coral *Lobophytum* sp. were estimated to be known cembrane compounds, (2*R*,7*S*,8*S*)-sarcophytoxide (**Fig. 2**) and its isomer. [2] The isolation and structural elucidation of the potential bioactive compounds using HPLC, LC/MS, MS/MS and NMR are currently in progress.

Ref. [1] Yotsu-Yamashita, M. *et al*. *Mar. Drugs*, **2013**, *11*, 2799−2813.

[2] Bowden, B. *et al*., *J. Nat. Prod.*, **1987**, *50*, 4, 650–659.

P-5

Efficient Total Synthesis of the Potent Anti-HIV Nucleoside EFdA



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[1] Graduate School of Agricultural Sciences, Tohoku University, Sendai 980-8555, Japan.
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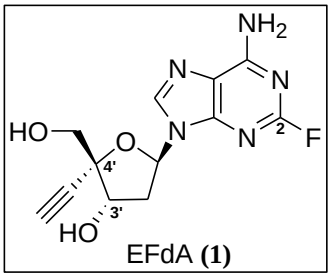
Key words: Anti-HIV agent, 4'-Ethynyl nucleoside, NRTI

4'-*C*-Substituted nucleosides have attracted much attention because of their remarkable biological activities. EFdA(4'-Ethynyl-2-fluoro-2'-deoxyadenosine **1**) is a nucleoside reverse transcriptase inhibiter (NRTI) created by collaborative studies among the Ohrui group, Mitsuya group and Yamasa Corp. The structure of **1** differ substantially from other NRTIs clinically approved for the treatment of human immunodeficiency virus (HIV) infection, since it retains the 3'-OH functionality of 2'-deoxyadenosine. The installation of an ethynyl group and a fluoro substituent at the C4' and C2 positions of the parent natural nucleoside, respectively, while maintaining the 3'-hydroxy group, endowed 1 with highly promising pharmacological profiles as an anti- HIV agent including (i) exceptionally potent antiviral activity against both wild-type and multidrug-resistant HIV-1 strains (ED_{50}, low nM to pM level), (ii) no acute toxicity in ICR mice at a dose of 100 mg/kg and (iii) longer intracellular half-life ($t_{1/2}$, 17.2 h) of its active form (EFdA-5'-triphosphate) than that of zidovudine triphosphate (AZT-5'-triphosphate, $t_{1/2}$, 2.8 h), which may enable a once- or twice-daily regimen and thereby improve the quality of life (QOL) of people suffering from AIDS. Because of these favorable characteristics of **1** in terms of potency, safety, and pharmacokinetics, detailed mechanistic as well as clinical studies have been carried out on 1.



EFdA **(1)**

We report an enantioselective total synthesis of EFdA **1** accomplished in an excellent overall yield of 37% from diacetone-D-glucose by a 14-step sequence that features the diastereoselective installation of the tetrasubstitured stereocenter at the C4' position, chemoselective acetonide hydrolysis, followed by concomitant oxidative cleavage of the resulting diol to form aldehyde, and a one-pot 2'-deoxygenation. Of value is the fact that the present synthesis requires only four chromatographic purifications, mainly because every reaction that could potentially produce diastereomers proceeded with virtually perfect stereoselection. From these favorable features, as well as the use of diacetone-D-glucose as an inexpensive starting material, the new synthesis described herein is considered to be more efficient and practical than previous syntheses.

Ref. K. Fukuyama, H. Ohrui, S. Kuwahara, *Org. Lett.*, **2015**, *17*, 828.

Development of accurate LC-MS/MS quantification method for phosphoethanolamine plasmalogen

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Key words: plasmalogen, LC-MS/MS, organic synthesis

Phosphoethanolamine plasmalogen, PE-Pls (**1a** - **1f**; Fig.1), are glycerophospholipids present in human brain. They have a *Z* - vinyl ether functionality in common, and the chain lengths of the vinyl ether and the fatty acid moieties show considerable structural diversity. It is suggested that PE-Pls are associated with the onset and progress of Alzheimer's disease (AD) because AD brains exhibit 20~30% deficiency of PE-Pls as compared to healthy brains[1)]. However, detailed functions of PE-Pls are not yet clear due to the lack of reliable analytical methods of sufficient specificity and quantitativity. Thus, we undertook the development of an accurate LC-MS/MS quantification method for brain PE-Pls at the molecular species level using specific fragment ion of PE-Pls[2)] (Fig. 2).

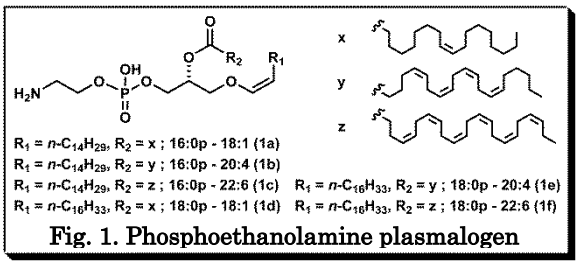


Fig. 1. Phosphoethanolamine plasmalogen

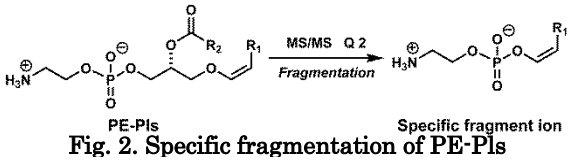
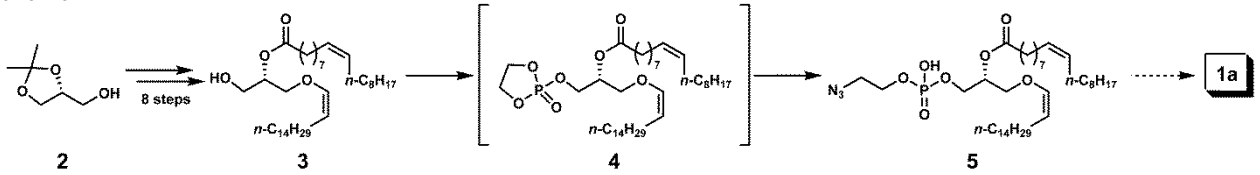


Fig. 2. Specific fragmentation of PE-Pls

For evaluating specificity, phospholipids extracts from rat brain were subjected to LC-MS/MS MRM analysis and conditions were optimized. As a result, the peak of PE-Pls was found specifically. Furthermore, because no ionsuppression effect was observed, this method was found to be useful for accurate PE-Pls quantification. Next, to obtain PE-Pls species standard necessary for quantification, the total synthesis of **1a** was conducted (Scheme 1). Commercially available alcohol **2** was converted in 8 steps into vinyl ether **3**, which was then transformed into **5** via cyclic phosphate **4**. The Staudinger reaction of azide **5** is now on progress.

1) L. Ginsberg *et al.*, *Brain Res.* **1995**, *698*, 223. 2) R. C. Murphy *et al.*, *J. Am. Soc. Mass Spectrom.* **2004**, *15*, 1499.

Scheme 1



P-7

Synthetic Study on Strigol

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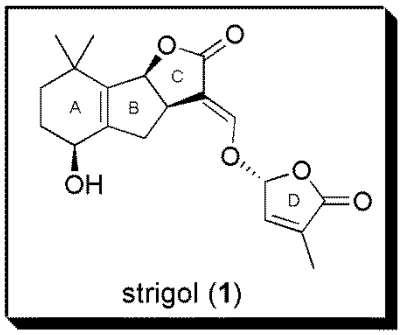
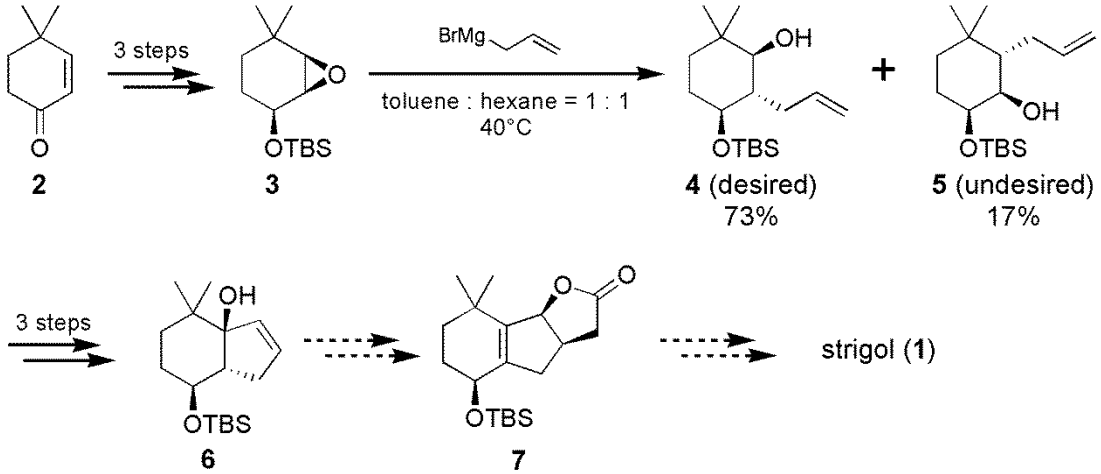
Email: aiko.takahashi.0109@gmail.com
Key words: total synthesis, Strigolactones, plant hormone



Parasitic weeds of the genera *Striga* cause serious crop yield losses in the world. Strigol (**1**) is a kind of strigolactone which was isolated from host plants of *Striga*, such as maize, proso millet, and sorghum[1]. Strigolactones are shown to be a strong stimulant for the germination of parasitic weed seeds[2]. In addition, they have activities of inhibiting plants shoot branching[3] and promoting host-recognition for arbuscular mycorrhizal fungi[4]. Therefore, strigolactones are expected to be useful for promoting agricultural production. In this poster, we present our efforts to establish an efficient synthetic route to **1**.

Epoxide **3** was synthesized from enone **2** in three steps. Treatment of **2** with allylmagnesium bromide in toluene/hexane gave alcohol **4** regioselectively. Oxidation of **4** followed by the addition of vinyllithium and ring-closing olefin metathesis afforded tertiary alcohol **6**. Thus, the construction of the A and B rings has been completed. We are now working on the installation of the C ring.



Ref. [1] B. A. Siame *et al.*, *J. Agric. Food Chem*. **1993**, *41*, 1486-1491.
Ref. [2] C. E. Cook *et al.*, *J. Am. Chem. Soc*. **1972**, *94*, 6198-6199.
Ref. [3] M. Umehara *et al.*, *Nature* **2008**, *455*, 195-200.
Ref. [4] K. Akiyama *et al.*, *Nature* **2005**, *435*, 824-827.

Synthetic Study of Indole Diterpens

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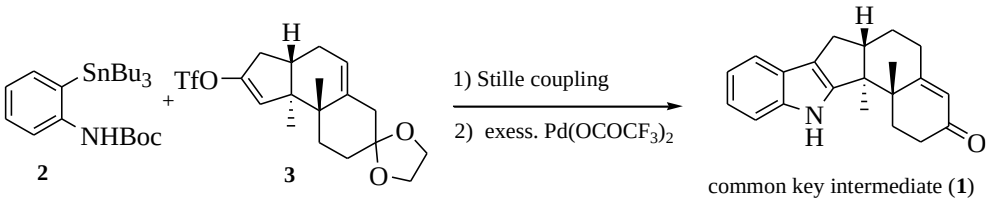
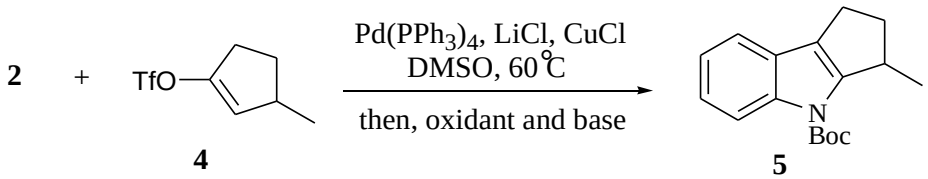
Key words: total synthesis, indole diterpen, indole synthesis

Indole diterpens are a family of natural product which shows various biological activities such as insecticidal, anticancer, anti-MRSA mainly isolated from fungi. Owing to their impressive polycyclic ring system as well as the pharmacologically and agriculturally important biological activities, they have long attracted great deal of attention from synthetic chemists. In our effort toward total synthesis of several indole diterpens, we achieved highly stereoselective construction of a common key intermediate **1**[1]. However, this synthetic route contains a serious problem: key reaction of the route, oxidative ring closure, required excessive amount of expensive reagent, $Pd(OCOCF_3)_2$. Thus we investigated more effective method to synthesise **1**.



Scheme 1. Previous work.

Considering that Pd^0 was used in the first coupling reaction, Pd^{II} species could be prepared *in situ* by the addition of the suitable oxidant following the first reaction. In model experiment, enol triflate **4** was subjected to the Stille coupling reaction with the *o*-stannylated aniline derivative **2** under Corey's conditions[2] to give *o*-alkenyl aniline derivative followed by addition of oxidants and bases successfully furnished indole derivative **5**. This is a new method to assemble indole structure in one-pot. Optimization of reaction conditions and application to synthesis of **1** are now in progress.



oxidant: $Cu(OAc)_2$, $Cu(OCOCF_3)_2$ etc.
base: AcONa, AcOK, Na_2CO_3, K_2CO_3 etc.

Scheme 2. Present work.

1) Enomoto, M.; Morita, A.; Kuwahara, S. *Angew. Chem. Int. Ed*. **2012,** *51*, 12833-12836.
2) Han, X.; Stoltz, B. M.; Corey, E. J. *J. Am. Chem. Soc.* **1999,** *121*, 7600-7605.

P-9

Synthetic studies toward strophasterol A

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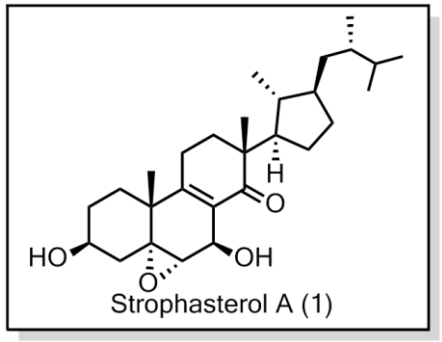
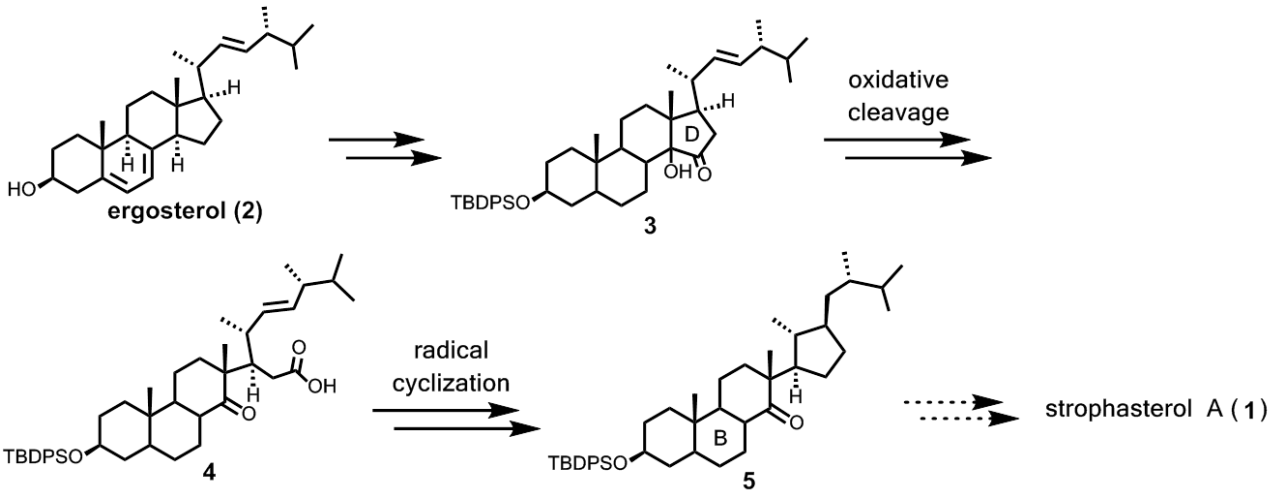
Key word: strophasterol A, mushroom

Strophasterol A (**1**), isolated from the mushroom *Stropharia rugosoannulata* [1)], is a steroidal compound with an unprecedented carbon skeleton that features a highly functionalized tricyclic steroidal ABC-ring system linked through a single bond to a cyclopentane ring bearing two alkyl substituents. This novel steroid is known to be contained in many species of mushrooms and to exhibit fruiting body-inducing activity in several species of mushrooms tested, which might suggest that strophasterol A could be a hormone that has never been found in mushrooms so far. We are now working on its synthesis to secure a sufficient amount of strophasterol A for detailed biological studies. Until now, we have succeeded in obtaining a key intermediate **5** .





The preparation of **5** began with the isomerization of the two double bonds on the B ring of ergosterol (**2**) and the oxidation of the product to a γ-hydroxy-α,β-unsaturated ketone intermediate. Two successive metal reductions of the intermediate followed by α-hydroxylation of the D-ring ketone gave **3.** Oxidative cleavage of **3** afforded a D-seco keto carboxylic acid **4**, which was transformed into **5** via selenoester radical cyclization followed by chemoselective reduction of a newly formed ketone functionality. Functionalization of the B ring to obtain **1** is now in progress.

1) H. Kawagishi *et al.*, *Angew. Chem. Int. Ed.* **2012**, *51*, 10820-10822

P-10

Synthesis of the tumor cell invasion inhibitor BU-4664L

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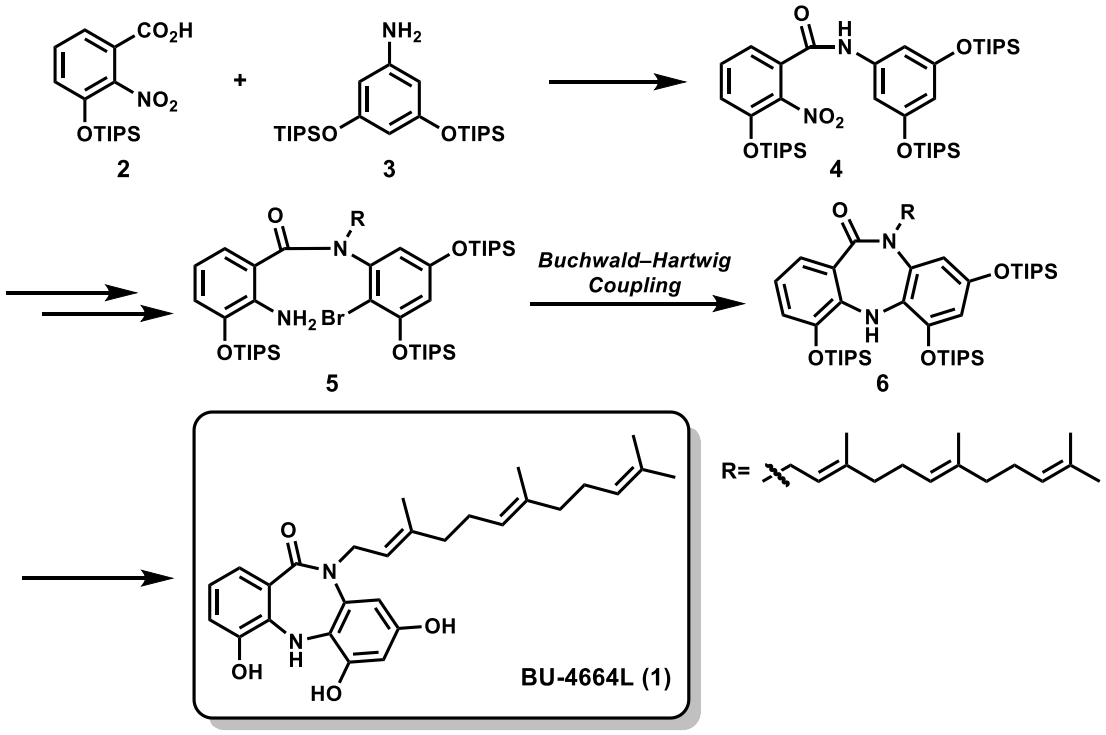
Key words: total synthesis, BU-4664L

BU-4664L (**1**), isolated from the actinomycetes *Micromonospora* sp. M990-6, has a farnesyl side chain on a naturally rare dibenzodiazepinone skeleton. [1] This compound is known to possess an anti-invasive activity against colon 26-L5 carcinoma cells and an anti-angiogenic activity against HUVEC (IC_{50} = 1.0 μg/ml, 0.7 μg/ml respectively).[2] We have achieved the first total synthesis of **1**.

Our synthesis commenced with condensation of carboxylic acid **2** and aniline **3**, both of which were prepared from commercially available materials, to afford amide **4**. Its bromination followed by installation of a farnesyl chain to the amide nitrogen atom and subsequent reduction of the nitro group gave **5**. The intramolecular Buchwald–Hartwig coupling of **5** to form **6** with the dibenzodiazepinone ring followed by removal the three silyl protecting groups completed our total synthesis of **1**.



1) Igarashi, Y. *et al.*, *J. Antibiot.* **2005**, *58*, 350-352.
2) Miyashita, S. *et al.*, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 963-965.

P-11

Kinetic analysis of sugar oxazoline hydrolysis catalyzed by Lacto-*N*-biosidase from *Bifidobacterium bifidum*

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Key words: glycosides, glycoside hydrolase, oxazoline, kinetic analysis

Human milk oligosaccharides (HMOs) have been known to show positive effects on the infant's well-being as the prebiotics. Lacto-*N*-biosidase (LNBase) liberates Lacto-*N*-biose (LNB) from nonreducing end of HMOs. LNBase belongs to the glycoside hydrolase family 20, and a hydrolysis machanism involving an oxazolinium ion intermidiate named as 'substrate-assisted catalysis' (Fig.1). The glycoside hydrolase-catalyzed transglycosylation has become a vivid topic in glycotechnology. Sugar oxazolines have been successfully utilized as glycosyl donors for glycoside hydrolase-catalyzed transglycosylation. However, kinetic analysis using sugar oxazoline substrates has not been well studied. So, we calculated kinetic parameters (K_m, k_{cat}) of LNB-oxazoline (LNB-oxa) hydrolysis catalyzed by LNBase. LNBase-catalyzed hydrolysis of LNB-oxa was performed in 10 mM

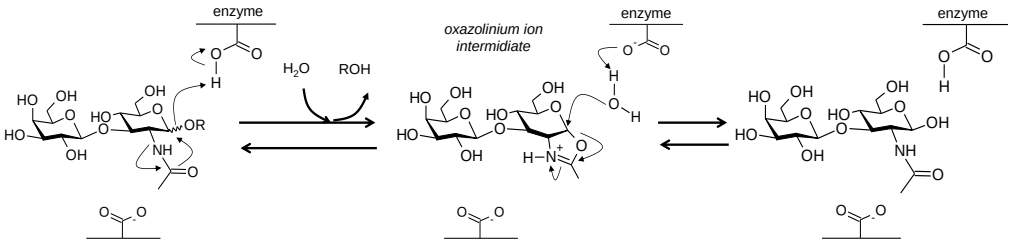

Fig. 1 Substrate-assisted catalysis

carbonate/bicarbonate buffer (pH 10.6) at 25 °C and was monitored by detecting the degradation amount of LNB-oxa using HPLC. The K_m value for LNB-oxa were $1.0\pm0.2\times10^{2}$ mM, the k_{cat} value for LNB-oxa were $5.3\pm0.5\times10^{2}$ s^{-1}, respectively. Further kinetic analysis by using *p*-nitrophenyl LNB (conventional substrate) catalyzed by LNBase will also be discussed.

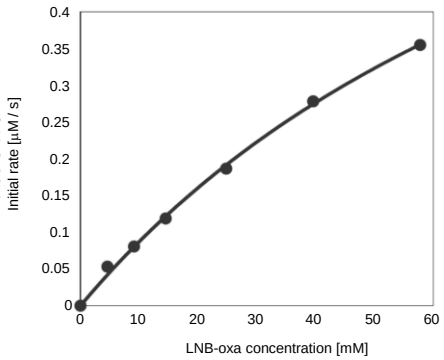

Fig. 2 The dependence of hydrolysis initial rate on LNB-oxa concentration

P-12

One-Step Preparation of 1,6-Anhydro Sugars Using 2-Chloro-1,3-dimethyl-1*H*-benzimidazolium Chloride

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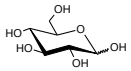
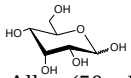
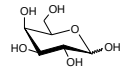
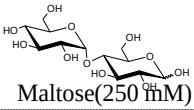
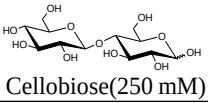
Key words: dehydration-condensation agent, 1,6-Anhydro sugar, one-step preparation

1,6-Anhydro sugars have fused-ring framework by intramolecular dehydrative condensation between C1 and C6 hydroxy group. 1,6-Anhydro sugars have been used as the important intermediates for preparation of various sugars, *C*-glycosides, *N*-glycosides, *S*-glycosides, glycosyl halides, hyperbranched polysaccharides. The conventional synthetic method of 1,6-anhydro sugars has been achieved via multi-step reactions involving protection and deprotection of hydroxy groups. We have reported a novel method for preparation of 1,6-anhydro sugars from unprotected sugars by using 2-chloro-1,3-dimetylimidazolinium chloride (DMC) as a dehydration-condensation agent in aqueous solution[1]. However, DMC is difficult to handle due to its higher hygroscopicity and difficulty of removing the by-product of DMI.

Recently, the drawback of DMC was improved by using 2-chloro-1,3-dimethyl-1*H*-benzimidazolium chloride (CDMBI) as a dehydration-condensation agent instead of DMC. Here, we report the direct synthesis of 1,6-anhydro sugars by using CDMBI.

Table 1. The synthesis of 1,6-unhydro sugars from unprotected sugars using dehydration-condensation agent.

Entry	Sugar	Condensing agent(eq.)	TEA(eq.)	Yield(%)[1)]
1	 D-Glucose(50 mM)	CDMBI (3)	45	89
2		DMC (3)		80
3	 D-Allose(50 mM)	CDMBI (5)	30	73
4		DMC (5)		51
5	 D-Galactose(50 mM)	CDMBI (5)	15	85
6		DMC (5)		70
7	 Maltose(250 mM)	CDMBI (3)	9	96
8	 Cellobiose(250 mM)	CDMBI (3)	9	96

1) Determined by ^{1}H NMR spectra of reaction mixtures using sodium mesitylenesulfonate as internal standard.

Ref. [1] T.Tanaka *et al. Tetrahedron Lett.*, **2009**, *50*, 2154-2157

P-13

Kinetic model for esterification of free fatty acid with methanol catalyzed by cation-exchange resin

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Key words: kinetics, esterification, ion-exchange resin, fatty acid, biodiesel

Abstract: Recently, esterification of free fatty acid with methanol has received much attention as an economical route to produce biodiesel from waste acid oil. The conventional homogeneous acid catalyst generally requires the excess methanol addition (20 times of the stoichiometric molar ratio) to obtain over 90% conversion[1]. However, we have reported that the cation-exchange resin has a high catalytic activity to obtain the complete conversion without adding excess methanol[2]. For construction of industrial production system, it is important to design the appropriate size apparatus and to determine the optimum operating conditions. In this study, we have proposed a kinetic model that describes the esterification behavior under various conditions. The batch experiments for esterification of model oleic acid and methanol were performed using the porous type strongly acidic cation-exchange resin, Diaion PK208LH. The reaction temperature, resin amount and molar ratio were varied.

Figure 1 shows the conceptual diagram of the model. The esterification proceeds via the following three steps:①distribution from the bulk liquid phase to the resin surface, ②diffusion in the resin liquid phase, ③adsorption and reaction on the resin solid phase via Langmuir-Hinshelwood mechanism. On the basis of this concept, the model equations are derived and the model constants are estimated by fitting the equations with the experimental data. An example of the experimental and calculated results is shown in Figure 2. The fitted lines are in agreement with the experimental symbols. The similar agreement was obtained under other conditions. Thus, the model can predict the esterification behavior under various conditions.

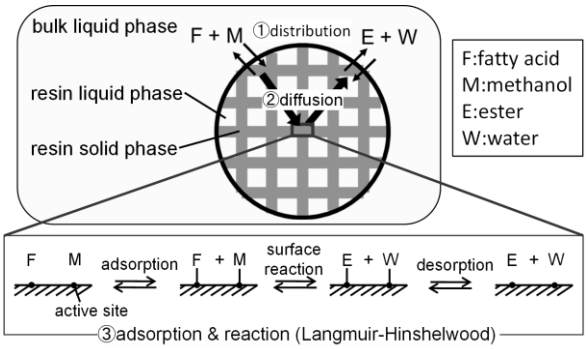

Fig. 1 Conceptual diagram of esterification in batch system with cation-exchange resin

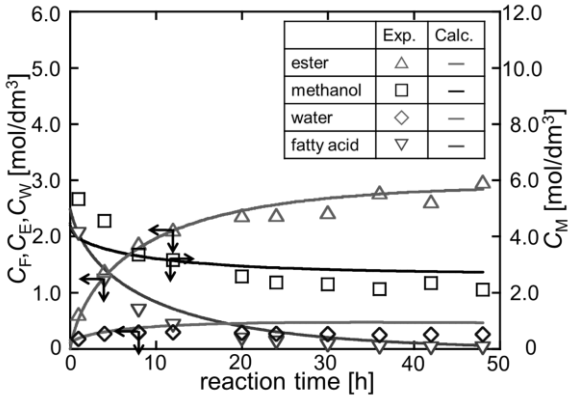

Fig. 2 Experimental and calculated results for batch esterification at 50°C, resin loading of 33.3wt%, and oleic acid : methanol =1:1

[1]K.N.P.Rani *et al.*,*Eur.J.Lipid Sci.Technol.*, **115**, 691 (2013) [2]N.Shibasaki-Kitakawa *et al.*,*Fuel*,**139**,11(2015)

P-14

Optimized Conditions for the Aerobic Alcohol Oxidation Using Nitroxyl Radical/Copper Catalysis

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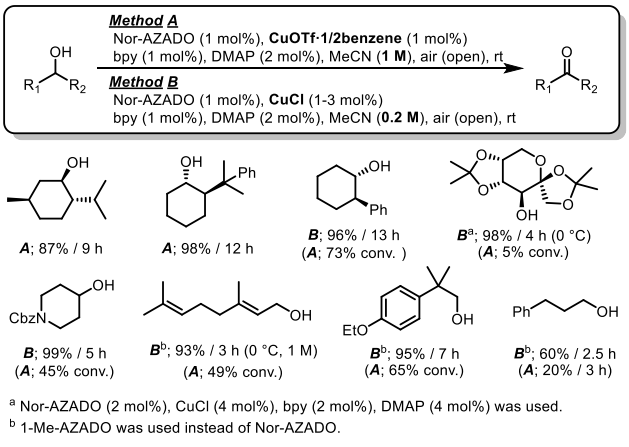
Key words: alcohols, copper, homogeneous catalysis, oxidation, radicals

Aerobic oxidation is an ideal process for alcohol oxidation to give the corresponding carbonyl compound, the development of which has attracted attention in current organic chemistry. We recently reported that 2-azaadamantane *N*-oxyl (AZADO)[1]/copper catalysis promoted the highly chemoselective aerobic oxidation of unprotected amino alcohols into amino carbonyl compounds under mild conditions.[2] With our ambition to expand the scope of AZADO/copper catalysis to not only unprotected amino alcohols but also other various alcohols including highly hindered and heteroatom-rich substrates, we embarked on this study.

During close examination of the reaction conditions using several alcohols, we identified two distinct reaction conditions, the selection of which is roughly estimated by the presence or absence of coordinating groups in the substrate (Table).

Method A: if the substrate "does NOT contain" coordinating groups, CuOTf is used as copper salt,
Method B: if the substrate "contains" coordinating groups, CuCl is used as copper salt,
in which optimum nitroxyl radical depends on whether the substrate is a primary or secondary alcohol. Nor-AZADO [3] should be used for secondary alcohols, whereas 1-Me-AZADO should be used for primary alcohols. With sets of optimum conditions in hands, we applied to examine the substrate scope. Various alcohols, including highly hindered and heteroatom-rich substrates, were efficiently oxidized to give the corresponding carbonyl compounds under mild conditions.[4] Interestingly, AZADO/Cu catalysis did not efficiently oxidize 3-phenylpropanol, because of deactivation of the catalyst. The detail will be discussed in this presentation.



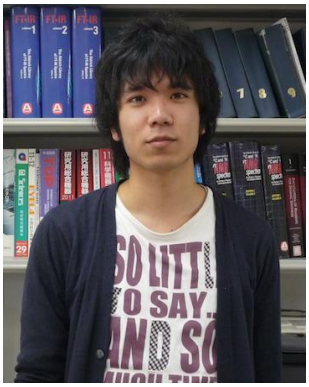
[a] Nor-AZADO (2 mol%), CuCl (4 mol%), bpy (2 mol%), DMAP (4 mol%) was used.
[b] 1-Me-AZADO was used instead of Nor-AZADO.

Table: Optimized conditions and substrate scope

Ref. [1] Iwabuchi, Y. *et al. J. Am. Chem. Soc.* **2006**, *128*, 8412. [2] Iwabuchi, Y. *et al. Angew. Chem. Int. Ed.* **2014**, *53*, 3236-3240. [3] Iwabuchi, Y. *et al. Chem. Pharm. Bull.* **2011**, *59*, 1570-1573. [4] Iwabuchi, Y. *et al. Chem. Asian J.* **2015**, *10*, 1004-1009.

P-15

Total Synthesis of (+)-MPC1001B



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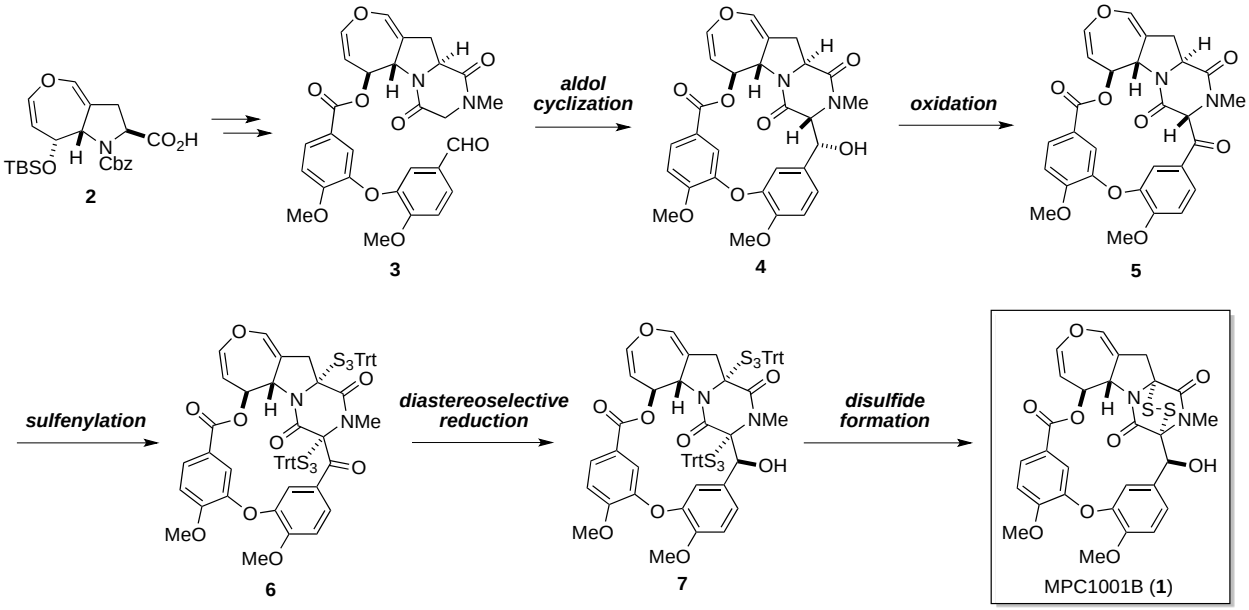
Key words: dihydrooxepine, 15-membered ring, dithiodiketopiperazine, total synthesis, aldol

MPC1001B (**1**), isolated from the fungus *Cladorrhinum* sp. KY4922 by Kanda and co-workers, exhibits potent antiproliferative activity against DU145 human prostate cancer cell line (IC_{50} = 39 nM).[1a, b] The promising activity and the unique macrocyclic structure have attracted considerable attention in the synthetic community; however, total synthesis of this compound has not been achieved so far. Herein I report the first construction of the framework of MPC1001s and the total synthesis of MPC1001B (**1**). The synthesis commenced with preparation of the substrate for the formation of the 15-membered ring. Thus, dihydrooxepine **3**[2] was converted to aldehyde **4** via construction of a diketopiperazine. Intramolecular Aldol reaction was performed to provide the corresponding aldol product **5** as a sole isomer, however, **5** possessed the different stereochemistries to those of MPC1001s. After the oxidation of the hydroxyl group, the introduction of the sulfur functionality was effected by the stepwise formation of bis(trisulfide) **6**. Finally, chemo- and diastereoselective reduction of the carbonyl group in **6** and subsequent formation of disulfide[3] provided MPC1001B (**2**).



Ref. [1] (a) Y. Yamashita *et al*., *J. Antibiot.* **2004**, *57*, 532. (b) Y. Kanda *et al*., *Org. Lett.* **2004**, *6*, 4101. [2] H. Tokuyama *et al*., *Angew. Chem. Int. Ed*. **2012**, *51*, 13062. [3] S. J. Danishefsky *at al*., *Angew*. *Chem*. *Int. Ed*. **2004**, *43*, 2557.

Synthetic Studies on Aconitine Alkaloids

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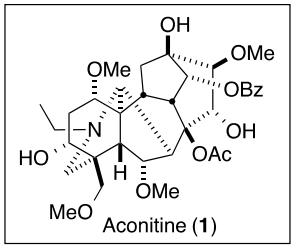
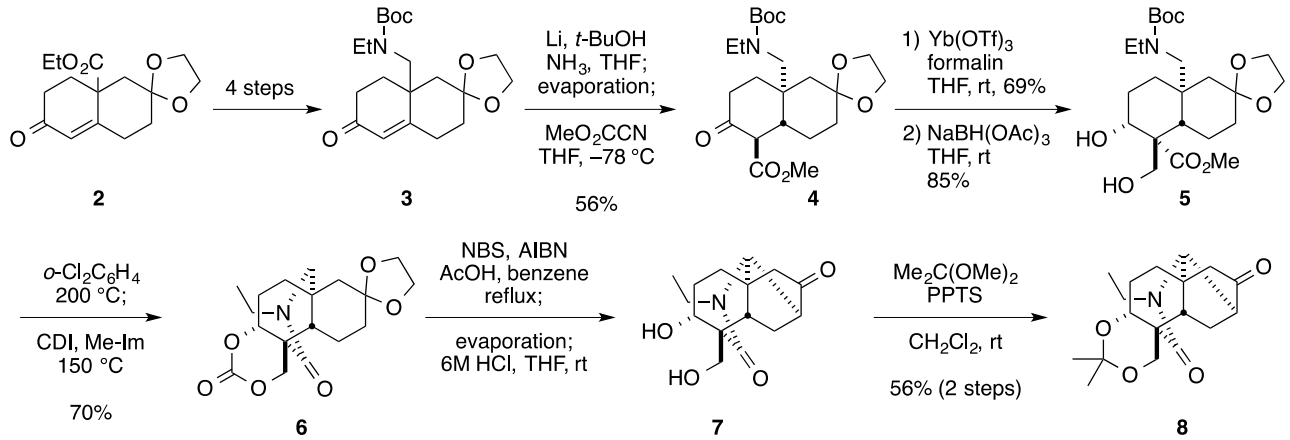
Key words: Natural Product, Mannich Reaction, C-H Oxidation, Total Synthesis



Aconitine (**1**)

Aconitine (**1**), which was first isolated from *Aconitam napellus* by Hesse and Geiger, has attracted a number of synthetic chemists due to its unique cage-like skeleton and significant neurotoxicity.[1a,b] Among the related alkaloids, this compound has not been synthesized because of its unique structure having mine oxygen functionalities on the complex framework. Herein, we report a novel strategy for construction of A/E/F framework of aconitine (**1**) utilizing radical-mediated trans-annular reaction.

The synthesis commenced with transforming bicyclic ester **2** into carbamate **3** over four steps. Subsequent Birch reduction and acylation of the resulting enolate gave β-keto ester **4**. After conversion to **5**, the resulted diol **5** was heated at 200 °C followed by addition of CDI and Me-imidazole in one-pot to furnish lactam **6**. Upon treatment with a combination of NBS and AIBN in the presence of AcOH, oxidation of the methylene adjacent to nitrogen and subsequent Mannich reaction occurred to construct tetracyclic core. After deprotection of carbonate and ketal, diol **7** was protected as its acetonide **8**.



References

1) (a) Geiger, P. L.; Hesse, O. *Eur. J. Org. Chem.* **1832**, *4*, 66. (b) Wang, S.-Y.; Wang, G. K. *Cell. Signal.* **2003**, *15*, 151.

Total Synthesis of (–)-Histrionicotoxin by Radical Translocation-Cyclization Reaction

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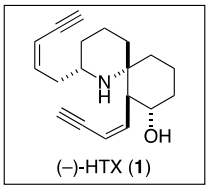
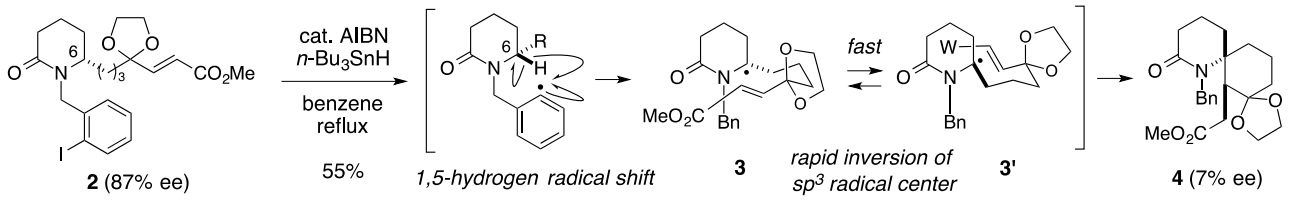
Key words: radical reaction, azaspirocyclic ring, natural product synthesis

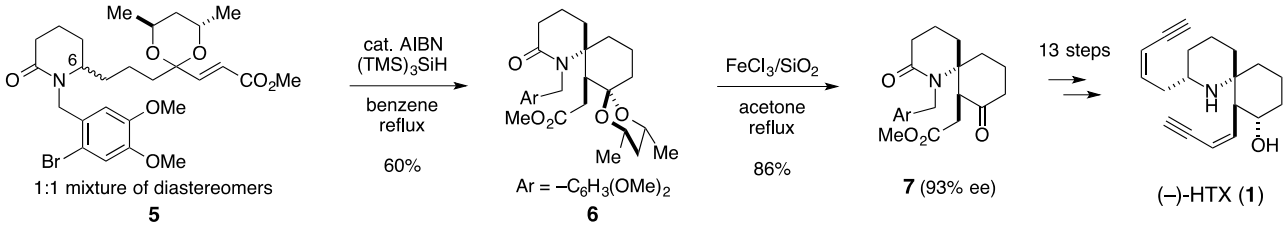
Histrionicotoxin (**1**: HTX), isolated from the arrow poison frog, *Dendrobates histrionicus* by Daly and co-workers in 1971,[1] possesses activity as a non-competitive blocker of nicotinic acetylcholine-acceptors. Although several racemic and formal syntheses have been described, only three asymmetric total syntheses were accomplished by Stork,[2] Holmes,[3] and Fukuyama.[4] Herein we report a recently accomplished total synthesis of (–)-**1** based on diastereoselective construction of the core six-membered spirolactam utilizing a radical translocation-cyclization strategy.



Initially, we examined the key radical reaction[5] using chiral lactam **2**. While the reaction provided the corresponding azaspirocyclic compound **4** in moderate yield, the optical purity was significantly decreased to 7%. This result indicated that inversion of the sp^3 radical center generated via 1,5-hydrogen shift should be much faster than cyclization.



Based on these results, we planed a stereoselective radical reaction using a substrate having a chiral ketal moiety. We found that the cyclic ketal **5**, which was 1:1 mixture of diastereomers at the C6 position, provided the desired azaspirocyclic compound **6** in high diastereomeric ratio. Furthermore, optical purity of the major diastereomer was determined to be 93% ee after removal of the ketal moiety. Finally, additional transformations led to the total synthesis of (–)-HTX (**1**).



(1) Daly, J. W.; Karle, I.; Myers, C. W.; Tokuyama, T.; Waters, J. A.; Witkop, B. *Proc. Natl. Acad. Sci. USA* **1971**, *68*, 1870. (2) Stork, G.; Zhao, K. *J. Am. Chem. Soc.* **1990**, *112*, 5875. (3) Williams, G. M.; Roughley, S. D.; Davies, J. E.; Holmes, A. B. *J. Am. Chem. Soc.* **1999**, *121*, 4900. (4) Adachi, Y.; Kamei, N.; Yokoshima, S.; Fukuyama, T. *Org. Lett.* **2011**, *13*, 4446. (5) (a) Takasu, K.; Ohsato, H.; Ihara, M. *Org. Lett.* **2003**, *5*, 3017. (b) Fujitani, M.; Tsuchiya, M.; Okano, K.; Takasu, K.; Ihara, M.; Tokuyama, H. *Synlett* **2010**, 822.

Concentration Threshold and Amplification Phenomena during Helix-dimer Formation of Sulfonamidohelicene Tetramer

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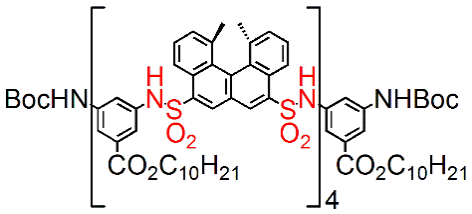
Key words: Sulfonamides • Helical structure • Concentration amplification • Self-catalysis

Chemical studies on molecular sensing system are essential to understand biological mechanisms and to develop synthetic sensing systems, which require high sensitivities to environmental changes. Previously, we reported molecular thermal hysteresis during the structural change of the sulfonamidohelicene tetramer (*M*)-**1** in solution between the random-coil **X** and the helix-dimer $\mathbf{X}_2$ involving self-catalysis.[1,2] In this work, we discovered the concentration threshold and amplification phenomena during helix-dimer formation of (*M*)-**1**, which sensitively responded to a small concentration increase of **X**.[3]



(*M*)-**1**

A random-coil **X** solution (*m*-difluorobenzene, 0.5 mM) of (*M*)-**1** was prepared at 50 °C, which remained unchanged for 200 min. To the random-coil solution was added another random-coil **X** in toluene (6.6 mM) to increase the concentration of random-coil **X** to 0.7 mM (Fig. 1). Then, concentration of helix-dimer $\mathbf{X}_2$ started to increase, which exhibited concentration threshold and amplification phenomena. Below the threshold concentration, no helix-dimer formation is observed, and once the concentration of random-coil **X** exceeds the threshold concentration, helix-dimer formation occurs in an amplified manner.

In the presentation, a proposal of such phenomena in biological concentration sensing will also be described.

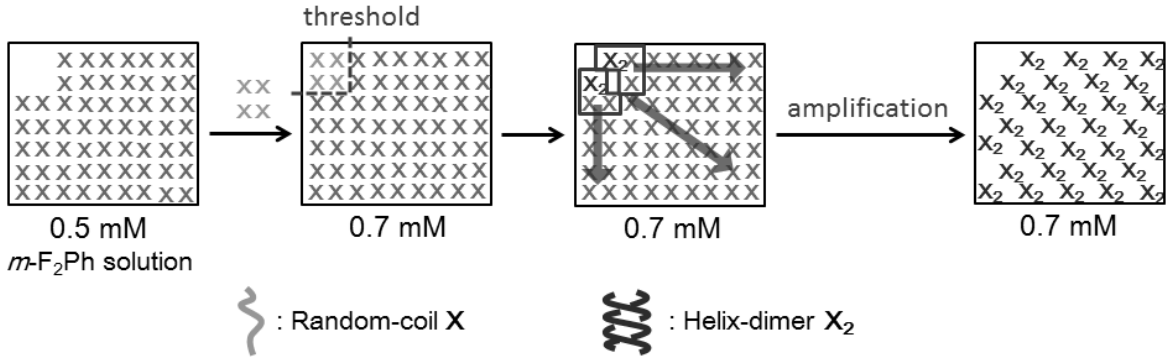


Fig. 1. Concentration threshold and amplification phenomena

(1) M. Shigeno, Y. Kushida, M. Yamaguchi. *Chem. Eur. J.* **2013**, *19*, 10226; (2) M. Shigeno, Y. Kushida, M. Yamaguchi. *Chem. Commun.* **2015**, *51*, 4040; (3) Y. Kushida, M. Shigeno, M. Yamaguchi. *Chem. Eur. J.* Accepted.

P-19

Double Helix Formation of Amphiphilic Ethynylhelicene Oligomer with Tri(Ethylene Glycol) Terminal Groups Induced by Heating

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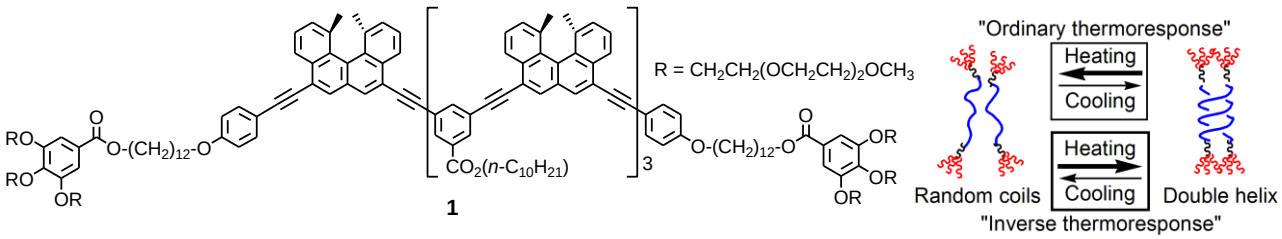
Key words: Helicene, Oligomer, Reversible Structural Change, Dimeric Aggregate, Thermoresponse

Dimeric-aggregate-forming molecules exhibit various functions, where aggregation occurs upon cooling, and disaggregation occurs upon heating. Such behavior is termed “ordinary” thermoresponse in this study. In principle, molecules which exhibits the “inverse” thermoresponse are also conceivable, where dimeric aggregation occurs upon heating and disaggregation occurs upon cooling, although such synthetic molecules essentially have not been known. Molecular systems exhibiting the “inverse” thermoresponse is applicable to novel thermal sensing system. Here, we report the synthesis and the “inverse” thermoresponse of an ethynylhelicene oligomer **1** with tri(ethylene glycol) moieties at the termini.

CD spectra of **1** (10 μM, acetone) showed strong Cotton effect at −10 °C, and dimeric aggregation was indicated by vapor pressure osmometry (acetone, 40 °C). Therefore, **1** formed double helix in acetone. The Cotton effect decreased upon heating the solution to 40 °C, which indicated the disaggregation of double helix. “Ordinary” thermoresponse was observed in acetone.

In the mixture of acetone/water/triethylamine (1/2/1), CD spectra of **1** (10 μM) showed weak Cotton effects at −10 °C. Upon heating the solution to 40 °C, the Cotton effects were enhanced, which indicated the formation of double helix. This is an unprecedented example of the “inverse” thermoresponse. The phenomenon can be explained by the hydration/dehydration of terminal tri(ethylene glycol) groups and the formation of condensed triethylamine domain by heating.



P-20

Palladium-Catalyzed Addition Reaction of Thioesters to Norbornene Derivatives

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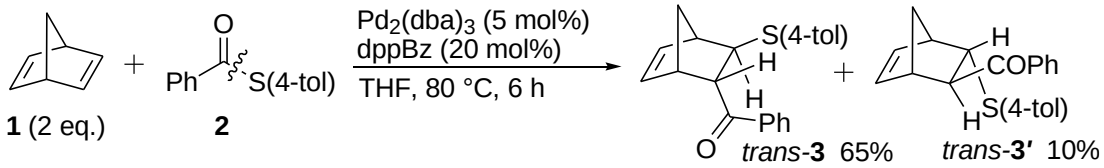
Key words: Palladium, Acylation, Thioester, Norbornene

Ketones are widely used for drugs and materials, and it is necessary to develop efficient methods of synthesizing such functionalized ketones. Addition reaction of carboxylic acid derivatives RCOX to alkenes via C-X bond cleavage are convenient method to synthesize β-heteroatom functionalized ketones, which are useful synthetic precursors, for example, for conjugated enones. However, such addition reaction of RCO and X groups to isolated double bond are limited. The Friedel-Crafts reaction of acid chlorides with alkenes in the presence of strong Lewis acid in some cases gives β-chloro ketones. The transition-metal-catalyzed addition reaction of carboxylic acid derivatives to alkenes can be an attractive method because of mild reaction conditions and functional group tolerances. Such reaction however, has not been developed.

Described here is the palladium-catalyzed addition reaction of thioesters and norbornenes giving 2-acyl-3-organothionorbornane[1]. We have recently reported a palladium-catalyzed addition reaction of acid anhydride[2]. Compared with acid anhydride, thioesters are easy to handle and stable, and thioesters functionalized either at the acyl or organothio group are available.

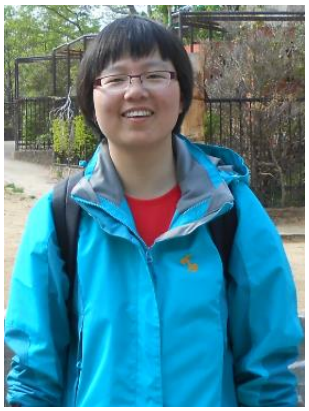
When norbornadiene **1** and thiotolyl benzoate **2** were reacted in refluxing THF for 6 h in the presence of $Pd_2(dba)_3$ (5 mol%) and $[2,4,6\text{-}(MeO)_3C_6H_2]_3P$ (20 mol%), 2-benzoyl-3-tolylthionorbornene *trans*-**3** and *trans*-**3'** were obtained in 65% and 10% yield. The catalytic cleavage of the CO-S bond of thioesters and addition to the alkenes is a novel method for the synthesis of β-heteroatom functionalized ketones.



References:
(1) M. Arisawa, S. Tanii, T. Yamada, M. Yamaguchi, *Tetrahedron*, **2015,** in press. (2) M. Arisawa, S. Tanii, M. Yamaguchi, *Chem.Commun.*, **2014**, *50*, 15267.

P-21

Synthetic Study of Asperterrestide A



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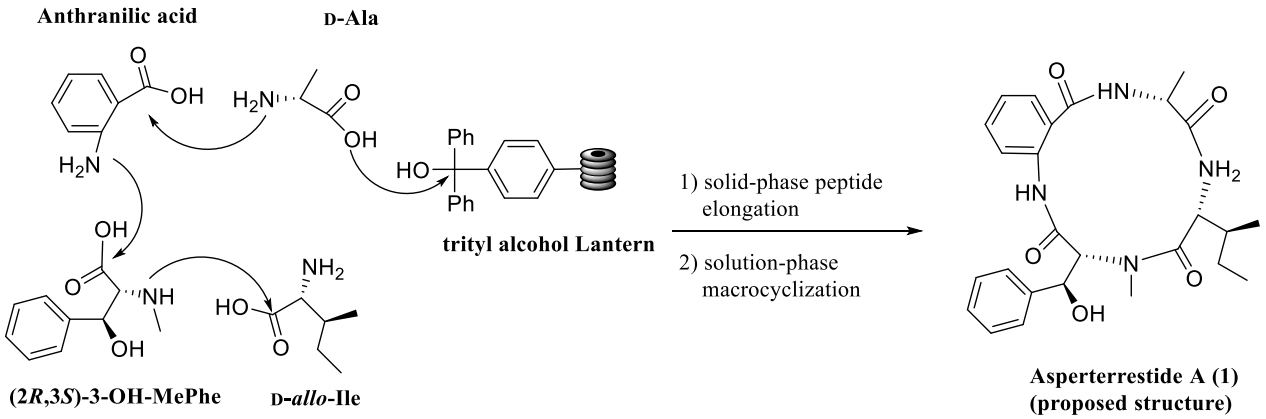
Key words: cyclic peptide, solid-phase synthesis

Asperterrestide A was isolated from the fermentation broth of the marine-derived fungus *Aspergillus terreus* SCSGAF0162[1]. Asperterrestide A is a cyclic tetrapeptide containing D-Ala, anthranilic acid (Ant), (2*R*,3*S*)-3-hydroxy-*N*-methylphenylalanine (3-OH-MePhe) and D-*allo*-Ile, whose absolute structure was proposed by chiral-phase HPLC and Marfey's analysis. Asperterrestide A was reported to have cytotoxicity against U937 and MOLT 4 human carcinoma cell lines and inhibitory effects on influenza virus strains H1N1 and H3N2. Toward structure-activity relationship study, we synthesized the proposed structure of asperterrestide A (**1**).

After attachment of the Fmoc-D-Ala onto trityl alcohol lanterns, peptide elongation was performed by solid-phase peptide synthesis using Fmoc-Ant, Fmoc-3-OH-MePhe and Fmoc-D-*allo*-Ile to afford the linear peptide. After cleavage of the peptide from the lanterns, macrolactamization was conducted using HATU and DIEA under dilution condition to give the desired macrocycle **1**. However, spectroscopic data of **1** did not coincide with those of the natural product. This indicates that the stereochemistry is different from the proposed structure. Now we are synthesizing the diastereoisomers of **1** with the other stereochemistries of 3-OH-MePhe.



Scheme Synthesis of asperterrestide A (**1**)

Ref. 1) He, F.; Bao, J.; Zhang, X. Y.; Tu, Z. C.; Shi, Y. M.; Qi, S. H. *J. Nat. Prod*. **2013**, *76*, 1182-1186.

P-22

Synthesis of substituted 3-hydroxypyridines via ‘anti-Wacker’-type cyclization

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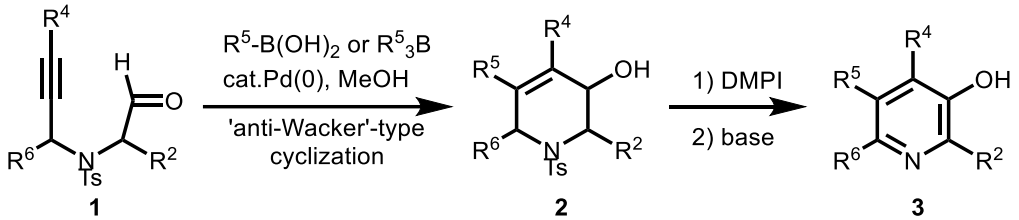
Key words: 3-hydroxypyridines, ‘anti-Wacker’-type cyclization, alkyne-aldehydes, tetrahydropyridine, organoboron reagents.

[Purpose] Pyridines are important structural units found in numerous bioactive compounds. Although many diverse methods have been developed to synthesize pyridines, it is still difficult to introduce multiple substituents around the ring in a regioselective manner. 3-Hydroxypyridine is a useful intermediate to prepare substituted pyridines, because the electron-donating hydroxyl group not only helps electrophilic substitutions at the 2-, 4-, and/or 6-positions but also can be substituted by a wide variety of nucleophiles under palladium catalysis through its trifluoromethanesulfonate ester formation. Here, we report a new preparative method for 3-hydroxypyridines via the palladium(0)-catalyzed alkylative cyclization (‘anti-Wacker’-type cyclization) of alkyne-aldehyde **1** that we previously developed.[1)]

[Methods and Results] *p*-Toluenesulfonamide-tethered alkyne-aldehydes **1**, readily prepared from amino acid derivatives, propargyl alcohols, and aryl- or alkynyl-halides (R^4), were employed for our ‘anti-Wacker’-type cyclization leading to tetrahydropyridines **2** (Scheme 1). While organoboron reagents could introduce sp^2- or sp^3-carbones at the C-5 position in **2**, a terminal alkyne in combination with a catalytic amount of CuI could set sp-carbon for R^5. As a ligand for the catalyst, triphenylphosphine and tricyclohexylphosphine were essential for cyclization of terminal alkyne-aldehydes (R^4 = H) and internal alkyne-aldehydes (R^4 = aryl or alkynyl), respectively. Tetrahydropyridines **2** were successfully converted to 3-hydroxypyridines **3** via oxidation of allylic alcohol with Dess-Martin reagent and subsequent elimination of *p*-toluenesulfinic acid with DBU[2)]. The reaction sequence furnished 15 examples of 3-hydroxypyridines with substituents at 3,5-, 2,3,5-, 3,4,5-, 3,5,6-, 2,3,5,6- and 2,3,4,5-positions.



Scheme 1

1) Tsukamoto, H.; Ueno, T.; Kondo, Y. *J. Am. Chem. Soc.* **2006**, *128*, 1407.

2) Yoshida, K.; Kawagoe, F.; Hayashi, K.; Horiuchi, S.; Imamoto, T.; Yanagisawa, A. *Org, Lett.* **2009**, *11*, 515.

P-23

Synthesis and Conformational Analysis of Spiruchostatin Analogues

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Key words: Cyclopeptide, HDAC, Conformational analysis

Spiruchostatin A (**1**), isolated from *Pseudomonas sp*.[1)], is a potent histone deacetylase (HDAC) inhibitor, and **1** consists of the bicyclic depsipeptide structure having a bridged disulfide bond. Because of its unique structure and HDAC inhibitory activity, spiruchostatin A (**1**) can be a novel drug candidate for cancer therapeutics. We have reported the total synthesis of spiruchostatin A[2)] (1) and its analogues toward elucidation of the structure-activity relationships. We are next interested in the effect of the macrocyclic structure for inducing HDAC inhibitory activity, therefore we planned to synthesize spiruchostatin lactam analogue **2** and compare its conformation of **2** with that of the natural product.

Synthesis of the lactam analogue **2** was performed in the same manner as in the synthesis of **1** we previously reported. β-Amino acid derivative **4**, a key segment for the synthesis of **2**, was successfully prepared by diastereoselective Mannich reaction, and peptide elongation in the solution-phase afforded tetrapeptide **3**. After removal of the protecting groups at the *N*- and *C*-terminus, macrolactamization under high dilution conditions, followed by a formation of disulfide bond furnished desired lactam analogue **2**. Details of the synthesis and conformational analysis of **2** will be discussed.

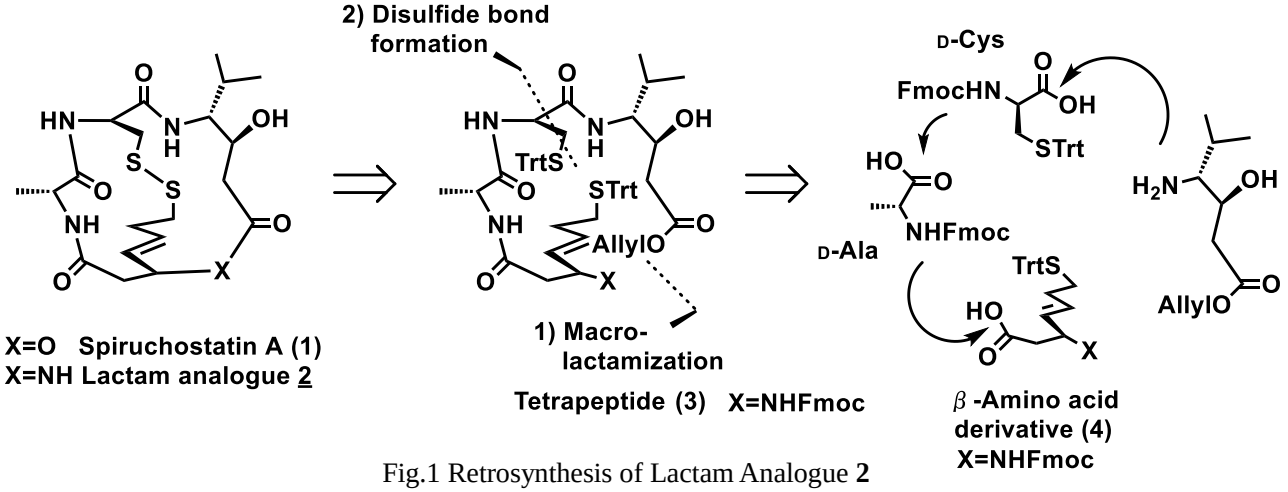

Fig.1 Retrosynthesis of Lactam Analogue **2**

Ref. 1) Matsuoka, Y.; Nagai, A.; Shin-ya, K.; Furihata, K.; Nagai, K.; Suzuki, K.; Hayakawa, Y.; Seto, H. *Tetrahedron Lett.* **2001**, 42, 41–44. 2) a) Doi, T.; Iijima, Y.; Shin-ya, K.; Ganesan, A.; Takahashi, T. *Tetrahedron Lett.* **2006**, 47, 1177–1180. b) Iijima, Y.; Munakata, A.; Shin-ya, K.; Ganesan, A.; Doi, T.; Takahashi, T. *Tetrahedron Lett*. **2009**, 50, 2970–2972.

P-24

Synthetic Studies for Spiromamakone A

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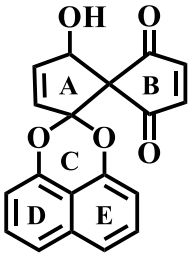
Key words: spiromamakone A, anti-tumor, double oxa-Michael addition, naphthalene acetal, spirononadiene skeleton

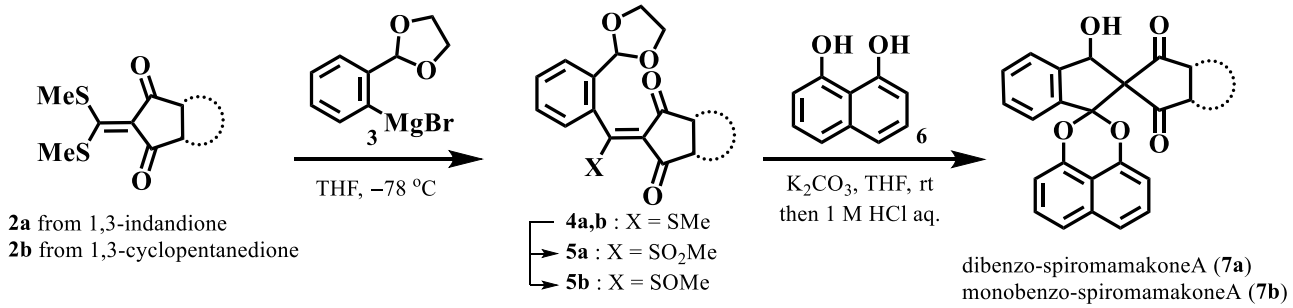
[Purpose] Spiromamakone A (**1**), exhibiting cytotoxicity to P388 murine leukemia cell line (IC_{50} 0.33 μM), was isolated from New Zealand native trees *Knightia excelsa* (Fig. 1). Its highly oxidized and unique structure features two contiguous spiro-carbons consisting of cyclopentenedione (B ring) and naphthalene acetal (C ring) on cyclopentenol (A ring).[1] The attractive biological activity and chemical structure let us to initiate our own research for the first total synthesis of **1**. The synthesis of **1** requires an efficient method to build the naphthalene acetal part, which is difficult to construct under conventional acid catalysis.



spiromamakone A (**1**)

Fig. 1. Structure of **1**.

[Methods and Results] Prior to the synthesis of natural product **1**, benzannulated spiromamakones **7a**, **b** were chosen as the target molecules to synthesize (Scheme 1). The preparation of **7a, b** commenced with addition-elimination reactions between α-oxo ketene dithioacetals **2a, b** and arylmagnesium bromide **3**. [2] Oxidation of sulfides **4a, b** provided sulfone **5a** and sulfoxide **5b**, repspectively, both of which became susceptible to the following double oxa-Michael addition of 1,8-dihydroxynaphthalene **6** for the C-ring formation. The oxa-Michael addition of **6** under basic conditions and chemoselective acid hydrolysis of the 1,3-dioxolane moiety proceeded in a one-pot fashion to give **7a, b** via intramolecular aldol reactions. Now, the synthetic study for **1** is underway.

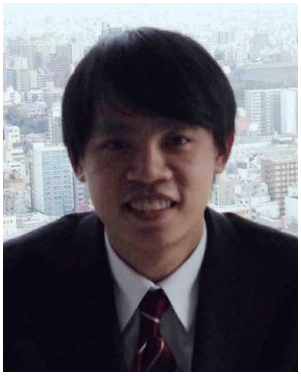


Scheme. 1. Synthetic route of model compound

Ref. [1] van der Sar, S. A.; Blunt, J. W.; Munro, M. H. G. *Org. Lett.* **2006**, *8*, 2059.
[2] Huang, X.; Chen, B.-C. *Synthesis* **1987**, 480

P-25

$ZnCl_2$-induced production of novel metabolites in the cellular slime mold *Dictyostelium bruneum*



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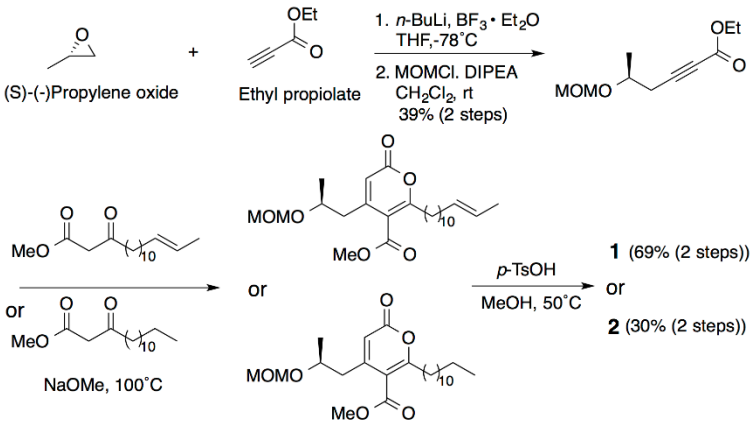
Key words: cellular slime mold, natural product, secondary metabolite

The cellular slime molds are excellent model organisms for research of cell and developmental biology because of their simple pattern of development. However, few secondary metabolites of them were reported. In recent years, we have explored the diversity of the secondary metabolites of cellular slime molds and demonstrated the utility of them as novel resources for natural product chemistry.[1,2]

Recently, it was revealed that addition of $ZnCl_2$ to the medium could induces the production of new metabolites of cellular slime molds.[3] This result encourgaed us to evaluate the effect of $ZnCl_2$ and isolate metabolites from various cellular slime molds.

In this study, we found that 0.5 mM $ZnCl_2$ promoted the production of some metabolites in *Dictyostelium bruneum*. From the methanol extract of their fruiting bodies, we isolated two new compounds **1** and **2** (Figure 1). We synthesized these compounds to confirm their structures including absolute configurations (Scheme 1). Compounds **1** and **2** possess a unique fused bispyrone structure which has not been seen in nature. This result showed that addition of $ZnCl_2$ to the medium is useful method to collect new compounds from cellular slime molds.



Scheme 1. Synthesis of compounds **1** and **2**.

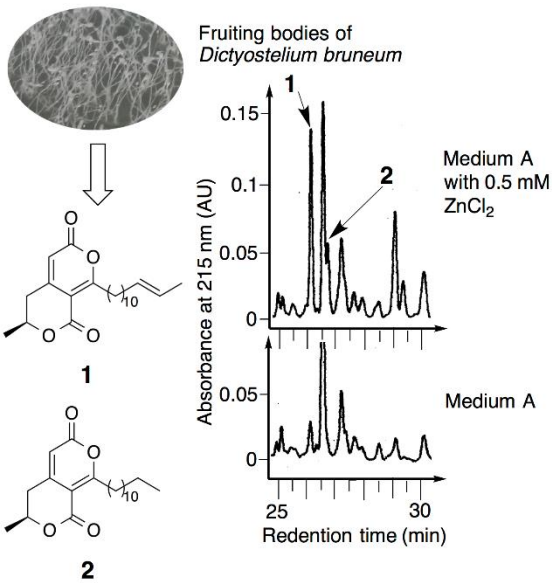


Figure 1. HPLC charts of methanol extracts of *D.bruneum*.

References

[1] H. Kikuchi et. al., *Tetrahedron* **2012**, *68*, 8884-8889.
[2] H. Kikuchi et. al., *Yakugaku Zasshi* **2007**, *127*, 1431-1439.
[3] R. R. Kay et. al., *Dev. Biol.* **2005**, *282*, 432-441.

Pd-catalyzed C(sp^2)–H Selective Aminocarbonylation of 2-Bromo phenethylamines

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Key words: C–H Functionalization, Carbon monoxide, Palladium

Since Heck and co-workers first reported in 1974, extensive efforts have been made to develop transition-metal-catalyzed carbonylation of aryl/binyl halides using carbon monoxide (CO) as the most important and simplest C1 building block. From atom-economic and environmentally benign points of view, it is attractive to develop methods for direct C-H aminocarbonylation reactions. The first Pd-catalyzed intramolecular oxidative aminocarbonylation of aryl C(sp^2)–H bonds with amines was described by Orito and co-workers in 2004, which enabled to access five- or six-membered benzolactams.[1] They also reported that aminocarboylation of *N*-alkyl-*ω*-arylalkylamines which contains C–H and C–Br bonds as competing reactive site provided mixtures of C–H and C–Br carbonylated benzolactam in poor selectivity (**Fig. a**). To date, there is no effective method for C–H aminocarbonylation preferentially in competition with C–X (X = Br, I *etc.*) aminocarbonylation.

In our study of transition-metal catalyzed carbonylation,[2] we found Pd-catalyzed C–H aminocarbonylation of **1a** proceeded in excellent selectivity, which provided C–Br containing product (**2a**) (**Fig. b**). This six-membered benzolactams has been known as a core structure of PARP1 inhibitors; furthermore, the remaining highly reactive C–Br bond enables further Pd-catalyzed coupling reactions. Herein, we wish to show Pd(TFA)$_2$-catalyzed C–H selective aminocarbonylation, by BINOL/Ag_3PO_4 as an effective combination of ligand and oxidant. Details of the reaction will be presented.

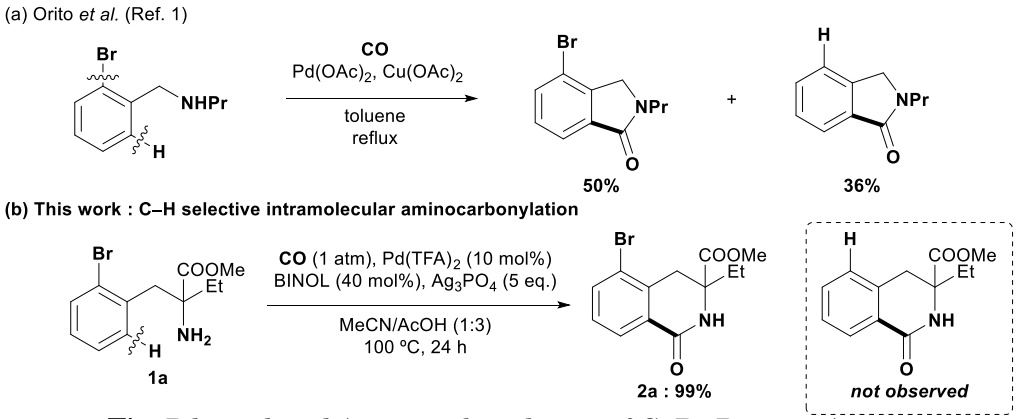

Fig. Pd-catalyzed Aminocarbonylation of C–Br Bearing Amine.

Ref. [1] K. Orito *et al.*, *J. Am. Chem. Soc.*, 2004, **126**, 14342-14343.
[2] K. Inamoto, J. Kadokawa and Y. Kondo, *Org. Lett.*, 2013, **15**, 3962-3965.

P-27

Development of Deoxygenative Cyclization of 2-Nitrobiphenyls by Silylborane

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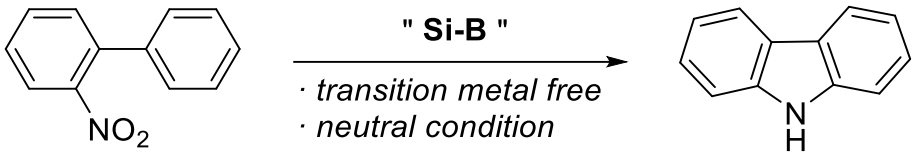
Key words: carbazole, silylborane

Cadogan synthesis, which is the deoxygenative cyclization of 2-nitrobiphenyls to carbazoles, is one of the most versatile methods for the preparation of carbazoles because of the widespread availability of nitrobiphenyls. This cyclization is traditionally achieved using excess amounts of a reductant such as phosphite, zinc dust, Grinard reagent, or high pressures of carbon monoxide, which convert the nitro-group into an electrophilic nitrogen species. These methods, however, often suffer from severed drawbacks such as purification, scope limitation, toxicity of reagents *etc*. Therefore, there is still demand for alternative reducing agents for this transformation.



Scheme Synthesis of carbazole by silyborane

Recently, silylborane is focused by many organic chemists owing to its interesting nature. While silylborane is often utilized for various transformation including silylation, borylation, and silaborylation,[1] it has not been applied to deoxgenative reaction. We envisioned that silylborane could have the property of deoxgenation. Indeed, we disclosed that silylborane is effective for deoxgenative cyclization of 2-nitrobiphenyls to carbazoles. Herein, we report a novel and convenient method for the synthesis of carbazoles by using silylborane. The detail on this reaction will be discussed.

Reference

[1] Oestreich, M.; Hartmann. E.; Mewald, M. *Chem. Rev.* **2013**, *113*, 402.

Ferroelasticity of Two-Dimensional Hydrogen-Bonding Boric Acid Crystal

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Key words: Ferroelasticity, Hydrogen-bonding, Hysteresis

Ferroelastic crystal has several domain orientations in single crystal, which orientations can be changed to each other by the application of outer stimuli of mechanical stress. Although the ferroelastic property of boric acid; $B(OH)_3$, crystals has been reported by Wadhawan,[1] there was no report about the detail analyses on the domain switching phenomena and mechanical hysteresis. Herein, we noticed the two-dimensional hydrogen-bonding layer structure of boric acid crystal, and its ferroelastic domain switching behavior was examined in detail.

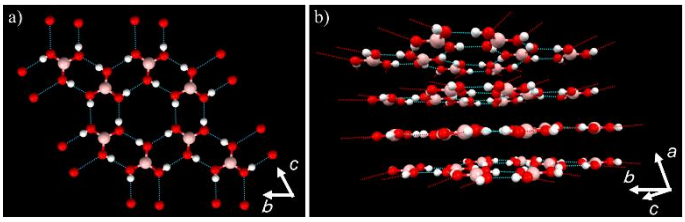

Fig. 1. Two-dimensional layer structure of boric acid in the *bc* plane (a) and its stack along the *a* axis (b)

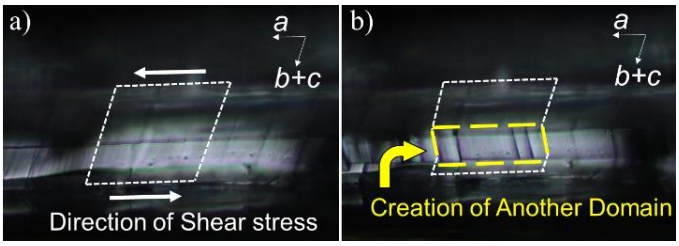

Fig. 2. Microscopic images of boric acid crystal (a) and domain switching by shear stress (b)

Hexagonal-prism-shaped boric acid crystals were easily obtained from aqueous solution. X-ray single crystal structural analysis showed the two-dimensional O-H•••O hydrogen-bonding layer was existed in the *bc* plane (Fig. 2a), which was stacked along the *a* axis (Fig. 2b). Domain boundary was observed along the *a* axis under the optical microscope images, and the domain switching behavior was confirmed along the *a* axis by the application of shear stress (Fig. 3). After the application of the shear force, domain boundary was directly moved and area of each domain was changed according to the magnitude of shear stress. Both the crystal structural and domain orientation observations revealed that the domain orientation was elongated along the *a* axis.

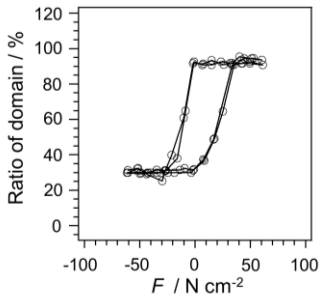

Fig. 3. Mechanical hysteresis

Ref. [1] V. Wadhawan, *Mat. Res. Bull.* **1978**, *13*, 1-8.

Ferroelectricity, Electric Conductivity and Fluorescence of Alkylamide-Substituted Pyrene Derivative

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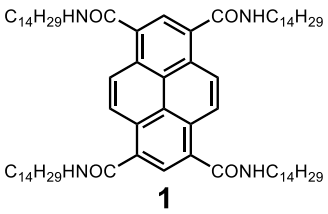
Key words: Ferroelectricity, Hydrogen-bond, Molecular aggregation, Pyrene, Electric Conductivity

Alkylamide-substituted benzene derivatives showed hydrogen-bonding molecular aggregations, nanofiber networks, hexagonal columnar liquid crystalline phase (Col_h), and ferroelectricity.[1, 2] On the other hand, the π-expanded pyrene derivative point to interesting concentration-dependent optical responses such monomer and excimer fluorescence. Herein, we could obtained novel alkylamide-substituted pyrene derivative (**1**).[3] The liquid crystalline properties, organogellation ability, optical responses, and dielectric responses through the molecular aggregations of **1** were examined.



1

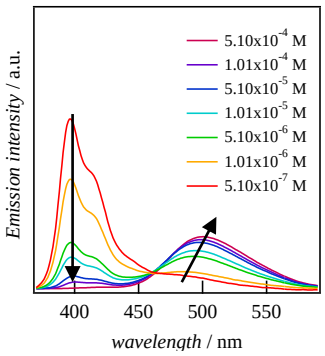


Fig.1 Fluorescence spectra

The molecular aggregation in $CHCl_3$ was investigated by the concentration-dependent fluorescence spectra (Fig. 1). Fluorescence maximum at ~400 nm was ascribed to the monomer emission at 5.10×10^{-7} M. Increasing in the concentration decreased the fluorescence band at 400 nm and was red-shifted to ~500 nm with excimer emission band. The concentration of excimer emission of **1** was observed at the concentration over 5×10^{-6} M, which was three orders of magnitude lower than that of pyrene. Both of the π–π stacking and hydrogen-bonding interaction played an important role to show high molecular aggregation ability. The molecule **1** also showed Col_h at 300 ~ 473 K based on DSC, POM, and XRD. The polarization – electric filed (*P-E*) hysteresis curve at Col_h phase was evaluated at 0.5 Hz, indicating typical ferroelectric behavior (Fig. 2). Electric conductivity will be discussed in this conference.

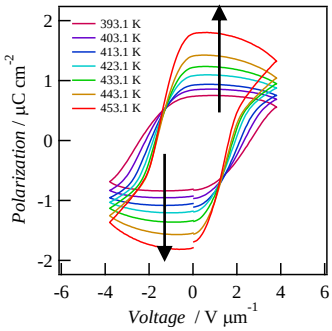


Fig. 2 *P-E* hysteresis

Ref. [1] R. P. Sijibesma, *et al.*, *J. Am. Chem. Soc*. **2010**, *132*, 6892.

Ref. [2] Y. Shishido, *et al.*, *J. Phys. Chem. C* **2014**, *118*, 21204.

Ref. [3] H. Anetai, *et al.*, *J. Phys. Chem. Lett.* **2015**, *6*, 1813.

Ferroelastcic Phase Transition Mechanism of *n*-Alkylammonium Dihydrogen Phosphate

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Key words: Ferroelasticity, Phase Transition, Ionic crystal

Molecular ferroelastic materials have been attracted much attentions from the viewpoint of molecular mechanical devices. Phase transition behaviours and ferroelasticity at room temperature have been reported in *n*-alkylammonium dihydrogen phosphate for various lengths of alkyl chain.[1] Herein, we examined the detail mechanism of ferroelastic phase transitions of pentylammonium dihydrogen phosphate (C_5ADP) crystal.

Preparation of single crystals C_5ADP was followed by the literature,[1] and the deuterated crystals C_5ADP-*d* were prepared by slow cooling of D_2O solution including stoichiometric amount of pentylamine and D_3PO_4. Single crystal X-ray crystal structural analysis of C_5ADP showed the two-dimensional O-H•••O hydrogen-bonding sheet of $H_2PO_4^-$ anions, whereas cationic $C_5H_{12}NH_3^+$ chains were arranged at the direction normal to the hydrogen-bonding sheet. The alternate cation-anion layer was observed along the *b* axis. Figure 1 showed the DSC chart of C_5ADP and C_5ADP-*d*. The difference of ferroelastic-paraelastic (FE-PE) phase transition temperature was only 3.0 K showing that the hydrogen-bonding sheet does not associate with the phase transition. Temperature-dependent PXRD patterns of C_5ADP showed the change in the crystal structures around the FE-PE phase transition temperature (Figure 2). The (020) reflection was safely assigned to the interlayer spacing along the *b* axis. The interlayer spacing at 299 and 380 K were 13.6 and 15.1 Å, respectively. The dynamic characteristics and dielectric responses will be discussed in detail.

[1] J. Kroupa, A. Fuith, *Phys. Rev. B*, **1993**, *48*, 4119-4121.

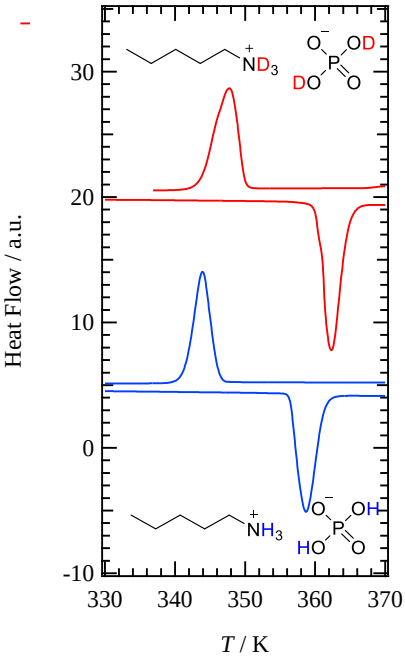

Figure 2 DSC charts of C_5ADP

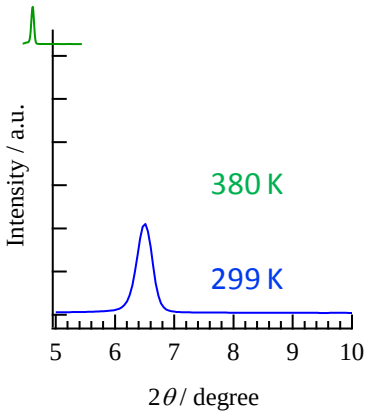

Figure 3 PXRD patterns of C_5ADP

P-31

Synthesis with *in situ* surface modification of cerium oxide using L-glutamic acid

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Key words: subcritical hydrothermal reaction, cerium oxide, *in situ* surface modification

Cerium oxide (CeO_2) is an important catalyst, catalyst promoter, and supporter. A noble and green process for the synthesis of metal oxide nanoparticles (NPs) is the supercritical hydrothermal reaction. Beside the fast reaction, an advantage of this method is the *in situ* surface modification of NPs that controls the shape and dimension of particles depending on applied organic surfactant such as oleic acid**.** However, a complex phase behavior of the organic phase, water phase and supercritical water complicates the observation of the surface modification mechanism in detail. In this study, we simplified the reaction system to a single phase synthesis with the introduction of a water-soluble surfactant, kinetic information as well as new CeO_2 structures can be obtained. We studied the effect of L-glutamic acid (Glu) as capping agent on the cerium oxide structure depending on the cerium to modifier ratio and reaction time. Electron microscopy images in Fig.1 identify the surface modification from octahedral shapes, in the absence of the amino acid, to spherical self-assemblies with increased modifier concentration. As the molar ratio of cerium to Glu and the reaction time rises, the assembly grows to uniform 80 nm particles. The reaction rate of the solid-forming reaction estimated on the base of a first order assumption decelerates drastically with increasing amount of Glu. From the results, L-glutamic acid has a high impact on the CeO_2 reaction system as it alters the morphology and slows the reaction rate.

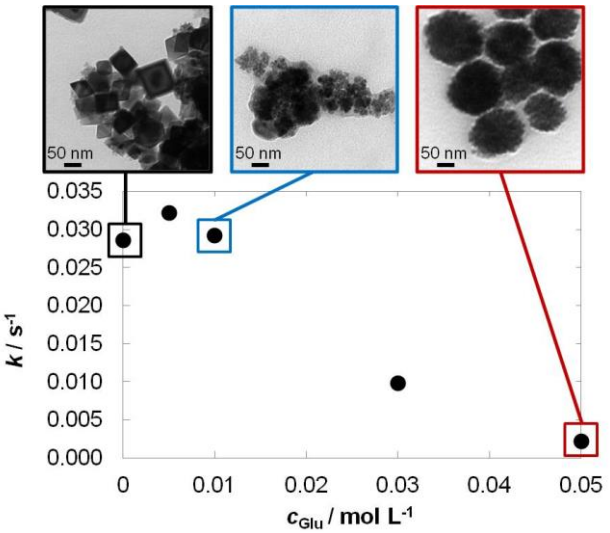

Fig. 1: Reaction constant dependency on the modifier concentration and the corresponding TEM images of the synthesized particles

P-32

Evaluation of pH at the mica-water interface using SFA fluorescence spectroscopy

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Key words: Surface Force Measurement, Fluorescence Probe, Electric Double Layer, Solid-Liquid Interface, pH

Local pH at the solid-liquid interface is important for many research fields such as electrochemistry and catalytic chemistry. Surface forces apparatus (SFA) fluorescence spectroscopy (Fig. 1) enables us to evaluate local properties of the confined liquid from a signal of a fluorescence probe[1), 2)]. Using this apparatus, we evaluated the local pH of water between mica surfaces from the fluorescence spectrum measurement of pH probe (C. SNARF-4F in Fig. 2).

11 μM C. SNARF-4F and 96 μM NaOH were dissolved in water (pH 6.8 ± 0.3) and used as a sample solution. The fluorescence spectra of the sample solution between mica surfaces at various surface separations (*D*) were measured as shown in Fig. 3 inset. When *D* decreased, the fluorescence intensity of the peak at 590 nm (I_{590}) attributed to the acidic form of C. SNARF-4F increased while the intensity of the peak at 645 nm (I_{645}) attributed to the basic form decreased. From these changes of the spectra, we evaluated pH of water between mica surfaces, as shown in Fig. 3. The pH values were constant at $D \geqq 200$ nm and decreased sharply with decreasing *D* below 200 nm. This result suggests that pH decreases due to protons concentrated at the interface between the negatively charged mica and water.

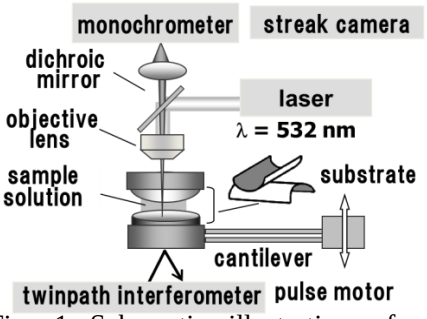

Fig. 1 Schematic illustration of experimental setups of SFA fluorescence spectroscopy.

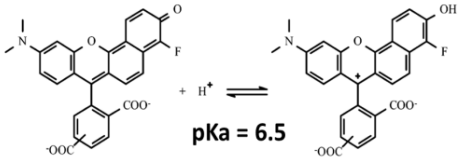

Fig. 2 Acid-base equilibrium of C. SNARF-4F.

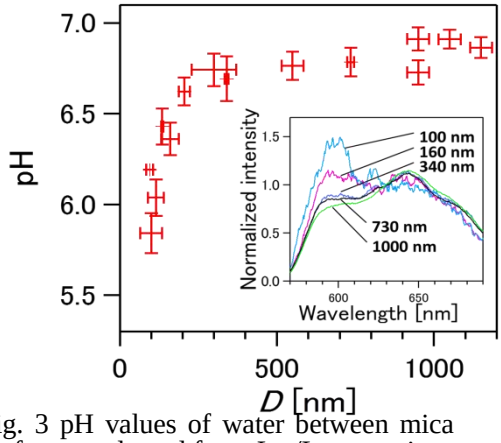

Fig. 3 pH values of water between mica surfaces evaluated from I_{590}/I_{645} at various *D*.Inset : Fluorescence spectra of C. SNARF-4F in water between mica surfaces at varius *D*.

[Reference] 1) D. Fukushi, M. Kasuya, H. Sakuma, and K. Kurihara, *Chem. Lett.* **40**, 776 (2011).
2) Y. Saito, M. Kasuya, K. Kurihara, *Chem. Lett.* **41**, 1282 (2012).

Interatomic Coulombic Decay Following Ar 2p Photoexcitation and Photoionization in Ar Clusters.

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Key words: interatomic Coulombic decay, electron-ion coincidence, synchrotron radiation

Auger decays after core-level photoexcitation and photoionization are well known. If an excited ion after the Auger decay neighbor other species, energy transfers can happen from excited ion to the other species and the other species emit the valence electron. This relaxation process is called Interatmoic Coulombic Decay (ICD) [1]. In this study, we have observed the ICD in Ar clusters with changing the size of clulsters and excitation photon energies.

The experiments were carried out on the beam line BL17SU and BL27SU at SPring-8. We used linearly polarized light at several photon energies around Ar 2p excitation region. We used three-dimensional momentum-resolved electron-ion coincidence techniques[2].

Figure 1(a) shows electron spectra in coincidence with Ar^+-Ar_2^+, Ar^+-Ar_2^+-Ar_2^+. The photon energy is 246.7 eV and the cluster size <n> is ~36. Figure 1(b) shows a different between two spectra in Fig. 1(a). The peak around 3 eV corresponds to the ICD electrons.

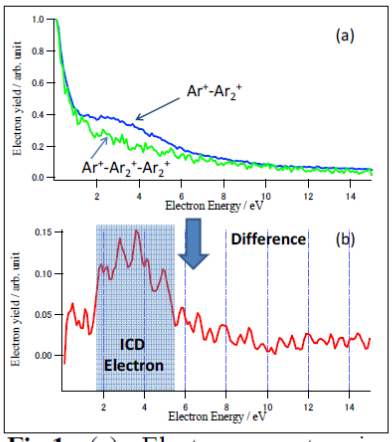

Fig.1 (a) Electron spectra in coincidence with Ar^+-Ar_2^+ and Ar^+-Ar_2^+-Ar_2^+ at the photon energy of 246.7eV in cluster size <n> of ~36. (b) Different spectrum between two spectra in Fig. 1(a)

Ref. [1] L. S. Cederbaum *et al*., *Phys. Rev. Lett.* **1997**, 79, 4778-4781

[2] T. Jahnke *et al*., *Phys. Rev. Lett*. **2004**, 93, 163401

P-34

Infrared Spectroscopy of Warm and Neutral Phenol–Water Clusters

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Key words: Gas phase, Molecular cluster, Infrared spectroscopy, Structural conversion, Temperature control

Molecular clusters in the gas phase have been widely used as a microscopic model for condensed phase. Recent studies on hydrogen-bonded clusters have greatly developed by means of various advanced spectroscopic techniques and high–precision quantum chemical calculations. Although many studies have been reported on structures of neutral water clusters, most of experimental information has been restricted to their most stable structures. With elevation of temperature, however, transient structures as well as higher energy stable structures can be formed, as recently demonstrated in small–sized neat warm water clusters by Zischang and Suhm[1]. They concluded the structural change from the most stable cyclic type to the transient chain type in water trimer and tetramer.

In the present study, we performed infrared spectroscopy of warm phenol–$(H_2O)_2$, which is an analogue of $(H_2O)_3$ concerning the hydrogen–bond structure, in order to overcome the size uncertainty in the neat water cluster study[1]. This cluster size is at the minimum size to form the most stable cyclic structure, which is composed by three OH…O hydrogen bonds. This hydrogen bonds are, however, highly distorted. Therefore, it is expected that a higher energy chain–type structure might be formed by thermal excitation. The strict cluster size selection was achieved by infrared–ultraviolet double–resonance spectroscopy combined with mass spectrometry. The temperature control of the cluster was accomplished by the reduction of the stagnation pressure of the jet expansion and the internal energy selective detection of the cluster. Observed and calculated spectra are shown in Figure 1. A remarkable shift to higher frequency of the phenolic OH stretch band (band **P** showed in Fig.1) was observed with elevation of temperature, suggesting deformation of the cluster from the most stable cyclic structure to the transient chain–type structure.

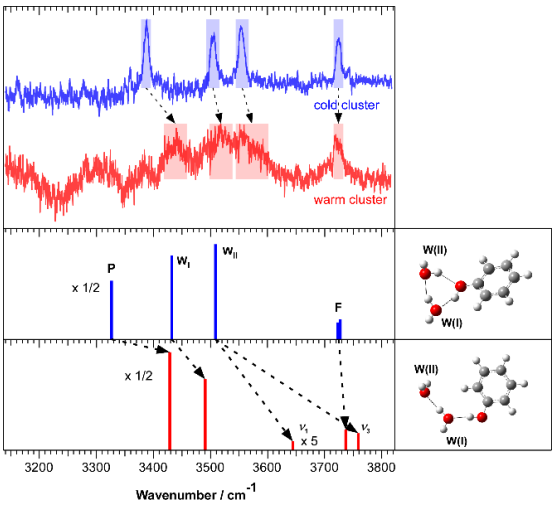

Fig. 1. Comparison between the experimental (upper box) and calculated spectra (lower box).

[1] Zischang, J. *et al.*, *J. Chem. Phys*. **2014**, 140, 064312

P-35

Model potential approach to positronic noble gas diatoms

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Key words: positron, noble gas atom, few-body system

A positron (e^+) having an equal mass and opposite charge of an electron forms unique states with atoms. Because of the Colombic repulsion between the positron and atomic nucleus, the positron cannot intrude inside the atom. This characteristic has allowed the positron to be a useful probe for materials for several decades. Structures and energy levels of positronic atoms have attracted many researchers on atomic physics and molecular chemistry because the positron, which delocalizes in the low electron density region of atomic systems, can represent interesting quantum phenomena.

Until now, scattering states of a positron and an atom have been studied both theoretically and experimentally [1]. A system composed of a positron and noble gas atoms is one of the most fundamental research subjects. A lot of experiments of positron scattering by a noble gas atom have been done [2]. Although the results of elastic scattering cross sections show a good agreement with theoretical calculations, the low energy scattering phenomena have not been revealed [3]. Recently, some experiments utilizing positron thermalization in dense Ar gas have been done to investigate the mechanism of low energy positron scattering by a noble gas atom [4]. In the dense gas, bubble structures and snow-ball effects, which are correlations between a positron and a number of atoms, should be taken into account.

Recently, we have examined structures and binding energies of positronic alkali atoms [5]. In this work, we adapt the model potential used in alkali atoms [6] to noble gas atoms (X=He, Ne, Ar) and calculate the quasi-three-body system e^+X_2. The main interactions between the positron and noble gas atom consist of a short-range static repulsion and middle-range polarization attraction. Since the wavefunction of positron spreads outside the atom, the polarization interaction plays an important role to bind the positronic atoms. On the other hand, the main interactions between an electron and the noble gas atom rise from a short-range static, an exchange and a polarization attraction. We compare the e^-X_2 with e^+X_2 and reveal the uniqueness of the positron-diatomic molecular structure.

Ref. [1] C. M. Surko, G. F. Gribakin and S. J. Buckman, *J. Phys. B: At. Mol. Opt. Phys.* **38**, R57 (2005). [2] D. G. Green, J. A. Ludlow, and G. F. Gribakin, *Phys. Rev.* A **90**, 032712 (2014). [3] C. M. Surko and F. A. Gianturco, "*New Directions in Antimatter Chemistry and Physics*," (Kluwer Academic Publisher). [4] Y. Sano, Y. Kino, T. Oka, and T. Sekine, *JJAP Conf. Proc.* **2**, 011004 (2014). [5] T. Yamashita, A. Irisawa and Y. Kino, *JJAP Conf. Proc.* **2**, 011005 (2014). [6] T. Yamashita and Y. Kino, *J. Phys. Conf. Ser.* (accepted, 2015).

P-36

Study of Ion Transport through Liquid Interface by using Molecular Dynamics Simulation.

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Key words: ion transport, molecular dynamics, free energy, water finger

Ion transport through liquid interfaces is often discussed in many fields such as interfacial chemistry, reaction engineering, electrochemistry, atmospheric chemistry, and biochemistry. Ion transfer can be investigated with electrochemical and thermodynamic measures, but it is difficult to connect these results with the microscopic pictures. To fill the gap between them, Molecular dynamics (MD) simulation is one of the valid methods.

The first important insight about ion transports from MD simulation is that the characteristic interfacial fluctuation, called water finger, may have a great effect of ion transport.[1] This finding inspired the following theoretical and studies[2, 3] and these researches was shown that the water finger may control the rate of ion transport.

In these theoretical analyses, the transfer free energy profiles of ions as functions of ion positions and interfacial fluctuations are required. However, knowledge of the free energy profiles, especially about interfacial fluctuations, are quite limited and this makes the role of water finger uncertain. So the aims of our study are to calculate the shapes of free energy profiles by using MD simulations and reveal the role of interfacial fluctuations in ion transports.

In the poster presentation of the summer school, I will explain the calculation method of the 2-dimmentional free energy profiles and the result of the calculation. The frictions on these profiles may be also discussed.

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Distribution of hydrated ion clusters transported through water-oil interface.

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Key words: liquid-liquid interface, water finger, free energy

Transport of ions through liquid-liquid interfaces, often called the interface between two immiscible electrolyte solutions (ITIES), plays versatile roles in a number of phenomena, but the elementary kinetics and mechanism of the ion transport at ITIES remain largely unknown.

The widely accepted ion transport mechanism includes the formation and break of the water finger, a finger like structure formed by water molecules surrounding transported ion.[1] The hydration number of ion clusters throughout the ion transport process is of particular importance to its free energy nature. In order to understand the effect of hydration on the ion transport process, we adopt the picture of free energy surface in relation to the hydration number of the ion and the distance between transported ion and the interface. This research tries to gain knowledge on the distribution of different hydrated ion clusters by free energy calculation. It is found that when near the interface, particular position of ion (distance from the surface) favors particular hydration number of the ion cluster. When the ion moves into the oil phase, the hydrated water molecules around the ion evaporate and the distribution of the ion cluster changes drastically. This research shows that coupling of water finger formation/destruction near the interface and the change in the distribution of hydration number of ions plays a key role to the ion transport process.

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Molecular dynamics simulation of strand break processes in a model duplex DNA

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Key words: DNA strand break, density functional tight binding method

Today, much attention is focused on the effects of radioactive decays on a human body, especially on DNA. It has been reported that the cleavage of the sugar-nucleobase bond (base loss) occurs followed by that of the sugar-phosphate bond (strand break) in a near-UV irradiated single-strand DNA (Fig. 1).[1] The mechanism of strand break processes in a duplex DNA, however, remains unclear at a molecular level, leading to difficulties in detailed scientific discussions on the radioactive effects on DNA.

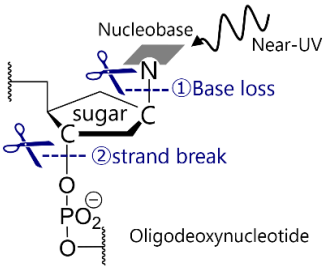

Fig. 1. Single-strand break processes analyzed by MALDI/TOF MS in a previous work. [1]

A variety of model DNAs which have a small number of base pairs and two linkers bridging the ends of the short strands has been synthesized as prototypes of DNAs. [2] In this study, we performed molecular dynamics (MD) simulations of the model DNA illustrated in Fig. 2 to investigate the dynamics of strand break processes.

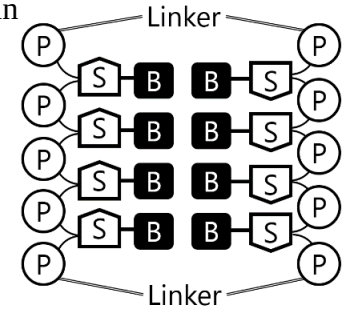

Fig. 2.
Structure of model DNAs.
B = nucleobase, S = sugar,
P = phosphate group

We used the Self-Consistent Charge Density Functional Tight Binding (SCC-DFTB) method[3], which is based on the Density Functional Theory (DFT) and allows for charge fluctuations in electronic state calculations. It is as accurate as and much faster than the DFT. In a MD calculation the model DNA was initially given a thermal energy of 0.4 eV/atom and the results were analyzed from the viewpoint of energy and charge transfers.

The same strand break process as in the case of a single-strand DNA was observed for the double-strand model DNA (Fig. 3). We also found long-range energy and charge transfers in elementary processes of base loss and strand break. The detailed discussions will be presented in the poster.

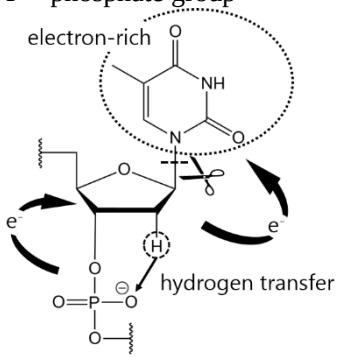

Fig. 3. Base loss requires electron flow to the nucleobase caused by hydrogen transfer

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Analyses of the solvation free energies due to electron density fluctuation using QM/MM method combined with a theory of solutions

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Key word: QM/MM method, theory of solutions, energy representation, OH/π interaction

XH/π interactions (X = C, N, or O) occurring between XH groups and π-electrons are observed in aromatic compounds and proteins and play a key role in hydration or organizing their structures and functionalities. Thus, XH/π interaction attracts broad interests in recent years. However, the effect of the XH/π interactions on the hydration properties is not investigated on the quantitative basis. In this work, we address the issue of the hydration of benzene, which shows a negative hydration free energy (–0.87 kcal/mol) in spite of its non-polarity, by utilizing the hybrid QM/MM simulation technique combined with a theory of solutions (QM/MM-ER)[1]. The hydration free energy contribution $\delta\mu$ due to the electron density fluctuation is decomposed into the contributions of σ and π electrons to elucidate the microscopic hydration mechanism of benzene.

In the QM/MM-ER method, solvation free energy $\Delta\mu$ of a solute is given by sum of the free energy $\Delta\bar{\mu}$ due to the two-body interactions and the residual many-body contribution $\delta\mu$. We apply the perturbation theory in the QM/MM simulation to realize the polarization of the solute[2,3]. Then, $\delta\mu$ can be readily decomposed into the free energies $\delta\mu_\pi$ and $\delta\mu_\sigma$ due to the fluctuations of π and σ electrons, respectively, by virtue of the density functional theory of solutions.

Computed solvation free energies are presented in Table 1[4]. The free energy contribution $\delta\mu_\pi$ arising from the π-electrons fluctuation (–0.94 kcal/mol) is about 3 times as large as $\delta\mu_\sigma$ (–0.35 kcal/mol) and found to be the major source of affinity of benzene to water. We also decompose $\delta\mu$ into contributions due to electron density fluctuation that are parallel and perpendicular to the molecular plain of benzene. We will present detail of the method and results of this decomposition.

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	$\Delta\bar{\mu}$	$\delta\mu_\pi$	$\delta\mu_\sigma$	$\Delta\mu$	$\Delta\mu_{\mathrm{E}\xi\pi\mathrm{t.}}$
Benzene	0.84	–0.94	–0.35	–0.47	–0.87

Table 1. Computed hydration free energy $\Delta\mu$ and its components for a benzene in units of kcal/mol. $\Delta\mu_{\mathrm{E}}$is the experimental value.

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Magnetic Properties of π-Stacked Pillared Layer Frameworks with Decamethylmetallocenium Cations

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Key words: Donor/Acceptor, Magnetic property, Paddlewheel-type diruthenium unit, Metallocene

Metal-organic frameworks constructed from electron-donor (D) and -acceptor (A) building blocks: we call as D/A-MOFs, are intriguing targets for inducing electronic and magnetic correlations through the frameworks.[1] D_2A-type layered compounds composed of a paddlewheel-type diruthenium complexes ($[Ru_2^{II,II}]$ as the electron donor) and 7,7,8,8-tetracyano-*p*-quinodimethane (TCNQ as the electron acceptor) derivatives allowed to be magnets with accompanying one-electron transfer of $(D_2)\rightarrow A$. However, many of compounds had an antiferromagnetic ground state due to the presence of antiferromagnetic dipole interactions between ferrimagnetically ordered layers. Hence, we had an idea on the control of interlayer magnetic ordering that the presence of one paramagnetic intercalator between the layers would provide a ferromagnetic spin arrangement between layer's ordered spins independent of interaction between intercalator and each layer whether ferromagnetic or antiferromagnetic.

In this study, we synthesized the novel 3-*D* network compound $[FeCp^*_2][\{Ru_2(2,3,5,6\text{-}F_4PhCO_2)_4\}_2TCNQ]\cdot n(solv)$ (**1**), in which a paramagnetic decamethylferrocenium cation ($[Fe^{III}Cp^*_2]^+$ with $S = 1/2$) was intercalated between the layers composed of $[Ru_2^{II,II}]$ ($S = 1$) and $TCNQ^{\bullet-}$ ($S = 1/2$) units. This type of frameworks was named as π-stacked pillared layer framework (π-stacked PLF) (Figure 1).[2] Compound **1** exhibited a ferrimagnetic phase transition at $T_C = 82$ K.

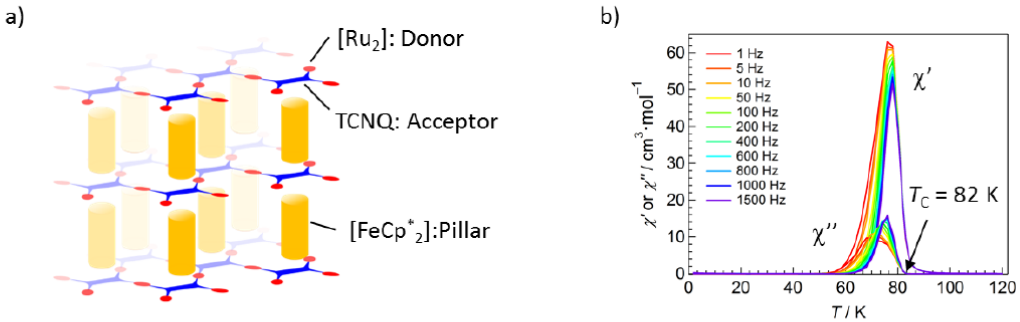

Figure 1. a) The illustration of π-stacked PLF b) the ac susceptibilities of **1**.

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P-41

Fabrication of thin film composed of paddlewheel type Ru dimer and organic linker.

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Key words: Thin film, Metal Organic Framework, donor-acceptor systems.

The fabrication of thin films composed of metal complexes have gained much attentions due to the attractive physical properties attributed to the difference in form to the bulk state and the component metal ions.[1] Especially, metal-organic framework (MOF), which allows well-ordered specific structure and exhibit several functionalities such as gas storage/adsorption, can be the attractive candidate of thin film. Recently, our group have reported that the donor acceptor MOF (D/A MOF) composed of the paddlewheel type Ru dimer ([Ru_2]) as electron donor and 7,7,8,8-tetracyano-p-quinodimethane (TCNQ) or *N*,*N*-dicyanoquinodiimine (DCNQI) as electron acceptor exhibited the interesting magnetic and/or conductive properties.[2] Since the [Ru_2] unit and DCNQI are coordination bonding building blocks with liner direction, the complexation of the building block in 1:1 ratio selectively resulted in the formation of the chain compounds. Thus the creation of the thin film composed of the D/A unit were expected to construct well-defined structure and exhibit unique physical properties as thin film.

In this poster, we investigated the synthetic methods for the fabrication of the novel D/A MOF thin film on ITO (indium tin oxide) substrate. The layer-by-layer assembly of thin films has been of considerable interest because of its ability to exert nanometer control over film thickness. The alternating immersion of the solution including the [Ru_2] unit and DCNQI yielded a flat thin film on the ITO substrate. AFM and XPS measurements confirmed that the gradual growth of the nano-architecture composed of the donor/acceptor units upon the increasing the cycle number. Further characterization and investigation of physical properties for obtained thin film will be discussed.

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C–H Silylation and Hydroalkenylation Reactions of Arylalkynes Catalyzed by Ruthenium Bis(silyl) Complexes

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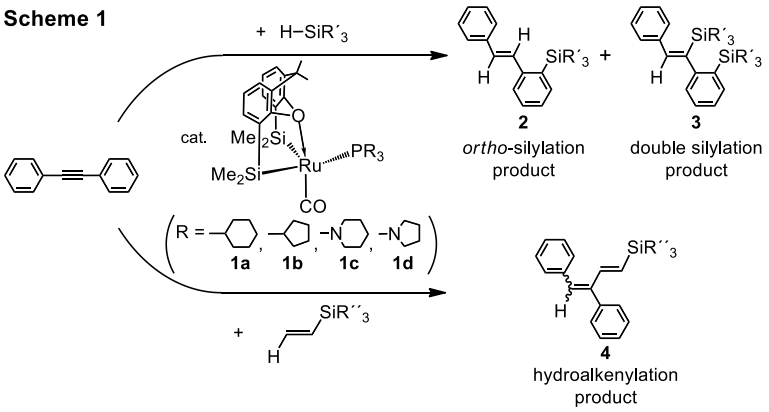
Key words: C–H silylation, Hydroalkenylation, Ruthenium complex, Bis(silyl) ligand, Arylalkyne

[Introduction] Transition metal–silyl complexes can serve as highly active catalysts for C–H bond activation because they can generate coordinatively unsaturated intermediates whose metal centers are electron-rich due to the strong σ-donating ability of the silyl ligands. Our group is studying the synthesis and catalytic performance of complexes having a xanthene-based bis(silyl) chelate ligand "xantsil" and has found that a 16-electron ruthenium–xantsil complex Ru{κ^3(*Si*,*O*,*Si*)-xantsil}(CO)(PCy_3) (**1a**) catalyze a one-step C–H silylation/hydrogenation (*ortho*-silylation) of diphenylacetylene to give (*E*)-2-silylstilbenes (**2**) (Scheme 1).[1] This time, we report the development of a unique one-step C–H silylation/hydrosilylation (double silylation) of arylalkynes with tertiary silanes and also hydroalkenylation of arylalkynes with silylalkenes catalyzed by **1a** or its related complexes **1b–d** bearing different phosphine (PR_3) ligands [R = Cyp (**1b**), NC_5H_{10} (**1c**), NC_4H_8 (**1d**)].

[Results and Discussion] Reactions of diphenylacetylene with several tertiary silanes in the presence of trialkylphosphine complexes **1a,b** afforded *ortho*-silylated products **2** exclusively (Scheme 1). On the other hand, the corresponding reactions catalyzed by triaminophosphine complexes **1c,d** gave unprecedented doubly silylated products (*Z*)-2,α-bis(silyl)stilbenes (**3**) together with **2** (Scheme 1). Bis(silyl)stilbenes **3** are considered to form via dehydrogenative silylation of an aromatic C–H bond and hydrosilylation of the C≡C triple bond. We investigated the effect of silane substituents on the reactions and found that silanes with electron-withdrawing groups such as $HSiMe(OSiMe_3)_2$ improve the selectivity for the double silylation.

Complexes **1a–d** were also found to catalyze hydroalkenylation of diphenylacetylene with silylalkenes to give silylated 1,3-dienes **4** under mild conditions (Scheme 1). For this reaction, complex **1c** with a relatively bulky and weakly electron-donating phosphine ligand, $P(NC_5H_{10})_3$, showed the highest catalytic activity.

Scheme 1



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P-43

Test for Estimation of total contamination of Cs-137 in abandoned cattle from that in tooth

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Key words: Cs-137, tooth, cattle, Fukushima Daiichi Nuclear Power Plant (FNPP) accident

It is known that radionuclides are incorporated into tooth only the formation period of the tooth. The radionuclides remain the tooth until the tooth is extracted. The tooth is a good indicator for incorporation of radionuclides into the body [1]. In this study, we focused on the relationship between Cs-137 in tooth and in body. Cs-137 is still remained in environment because its half-life is 30.2 yeas. We examined the ratio of Cs-137 tooth to organ for estimation of Cs-137 in body from Cs-137 concentration in tooth.

We collected 6 cattle (Young1, 2, Adult1, 2 and Old1, 2) in evacuation zone located 20 km southwest from the FDNPP. Cs-137 in tooth and organ was measured by an HP-Ge detector.

Table 1 shows Cs-137 concentrations and the ratio of Cs-137 organ to tooth. It is known that Cs-137 is more incorporated into muscle rather than other organ. The Cs-137 concentration in femoral muscle is higher than that of the other organ [2]. Ratio of Cs-137 in muscle to that in tooth should be a constant value when the intake and discharge of Cs-137 reaches equilibrium. We found age dependence of the constant. In order to estimate the Cs-137 in body from that in tooth, we require to increase the number of samples.

Table 1 Cs-137 concentration and ratio of Cs-137

Body parts	Cs-137 concentration / Bq kg					
	Young1	Young2	Adult1	Adult2	Old1	Old2
Tooth	52.8±1.9	24.6±0.5	17.3±0.4	23.8±0.4	13.9±0.5	20.4±0.8
Femoral muschle	436±9	591±10	299±5	490±8	549±11	535±14
	Ratio of Cs-137 femoral muscle to tooth					
	8.26±0.35	24.0±0.6	17.3±0.5	20.6±0.5	39.4±1.6	26.2±1.3

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P-44

Single-Molecule Magnet Properties of a Tetranuclear Dy(III)–Fused Phthalocyaninato Quintuple-Decker Complex

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Key words: Single-molecule magnet, Phthalocyanine

In 2003, lanthanoid(III)–phthalocyaninato double-decker complexes $[LnPc_2]^-(TBA)^+$ (Ln = Tb, Dy) were reported to be single-molecule magnets (SMMs).[1] Recently, our group has shown that SMM properties of these complexes highly depend on the spatial arrangements of the metal centers.[2] Thus, we can control the SMM properties by changing the spatial arrangements of the metal ions in the molecules and crystal lattices.

Previously, we have reported the Tb(III)–fused phthalocyaninato quintuple-decker complex $[Tb(obPc)_2]Tb(Fused\text{-}Pc)Tb[Tb(obPc)_2]$ (abbreviated as **[Tb$_4$]**; obPc = 2,3,9,10,16,17,23,24-octabutoxyphthalocyaninato, Fused-Pc = bis{7^2,8^2,12^2,13^2,17^2,18^2-hexabutoxytribenzo[*g*,*l*,*q*]-5,10,15,20-tetraazaporphirino}[*b*,*e*]benzenato), which contains four Tb(III) ions in one molecule, as shown in the figure.[3] In the complex, two different magnetic dipole-dipole interactions, *i.e.*, that in triple-decker moiety (0.352 nm) and that through the fused phthalocyaninato ligand (1.131 nm), occur. The latter is much weaker than the former is. In other words, the magnetic properties of **[Tb$_4$]** correspond to a dimer of tripe-decker complexes.

Here we report the Dy(III)–fused phthalocyaninato quintuple-decker complex (**[Dy$_4$]**) (ESI-MS: 2274.0432[M^{3+}]). Electronic structures of Tb(III) and Dy(III) ions are significantly different. For example, Tb(III) ions behave as a non-Kramers system, whereas Dy(III) ions are a Kramers system. In addition, the magnetic properties of Dy(III) complexes are affected by the coordination geometries around the metal ions. In this presentation, we will discuss the relationship between the magnetic properties of Dy(III) complexes and their coordination geometries.

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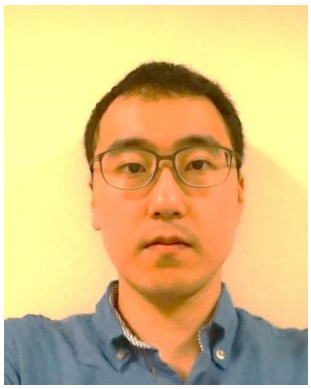
P-45

Magnetic properties of Dysprosium(III)-Yttrium(III) Phthalocyaninato Quadruple-Decker Complexes



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Key words: Single-Molecule Magnet

In this presentation, we will discuss the relationship between f-f interactions and the magnetic relaxation processes in Dy(III)-phthalocyaninato multiple-decker complexes. The Dy^{III}-Y^{III} hetero quadruple-decker complex DyCdY* was synthesized, and its SMM properties were compared with those of triple-decker DyDy, quadruple-decker DyCdDy, and quintuple-decker complexes DyCdCdDy.[1,2] From single crystal X-ray analysis, the coordination geometries around the Dy^{III} ion in DyCdY* are similar to those in DyCdDy and DyCdCdDy.

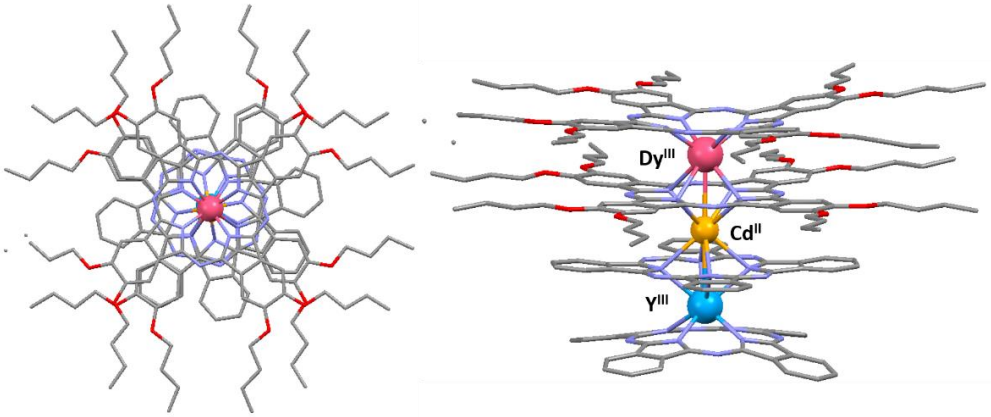

Fig.1. Crystal structure of DyCdY*.

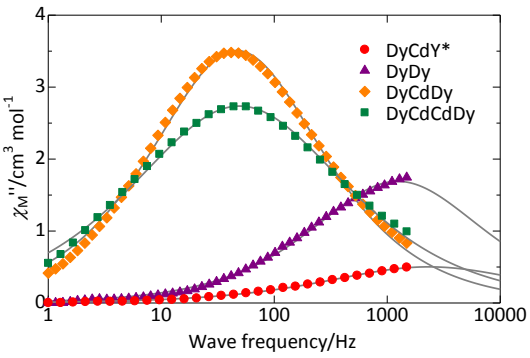

Fig.2. AC magnetic susceptibilities of Dy^{III} complexes at 2.2 K.

AC magnetic susceptibilities of DyCdY* measured at 2.2 K (Fig.2) showed no clear peaks due to fast relaxation processes, as compared to DyCdDy and DyCdCdDy, which show weak Dy^{III}-Dy^{III} interactions. On the other hand, DyDy, in which there are strong Dy^{III}-Dy^{III} interactions, underwent fast relaxation like DyCdY* did. Our results suggest that the weak Dy^{III}-Dy^{III} interactions effectively suppress quantum tunneling of the magnetization (QTM) and thus slow the relaxations, whereas strong Dy^{III}-Dy^{III} interactions induce fast relaxations.

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P-46

Research for the Relationship between Structure and Spin Crossover Phenomena in Iron(III) Dithiocarbamato Complex

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Key words: Spin Crossover, Fe(III)

[Research Background] Spin crossover (SCO) compounds have attracted much attention in a wide variety of phase transitions as well as their potential applications. In SCO phenomena, the entropy difference serves as a driving force of the spin transition. There are three important sources contributing to the entropy difference in solid states. One is a change in the spin manifold between the low- and high-spin states. Two is the metal to ligand bond length changes and last is the changes in lattice phonons. In 1991, Oshio *et al*. reported the temperature-dependent crystallographic studies on ferric SCO complexes with different spin transition rates[1]. In their study, they concluded that SCO phenomena in their complexes mainly depend on the metal to ligand bond length. So in our study, in order to tune the effect of intermolecular vibration, we synthesized iron(III) dithiocarbamato complexes which have alkyl chain with different lengths . Herein we discuss the relationship between molecular packing and spin transition in iron(III) dithiocarbamato complexes.

[Result] Fe(1-methoxycarbonyl-piperidine-4-carbodithiorate)$_3$ (**C1**) and the derivatives which have ethoxy group (**C2**), propoxy group (**C3**), butoxy group (**C4**), pentoxy group (**C5**) and hexoxy group (**C6**) were synthesized and determined the crystal structure by means of X-ray crystallographic analysis. In all complexes, iron(III) ions were surrounded by six S atoms and the Fe-S length and coordination symmetries were quite similar at 98 K. From direct current magnetic susceptibility measurements, all complexes showed gradual decreasing of $\chi_M T$ value in *T*. Despite of the similar coordination environment, they exhibited different $\chi_M T$ value at 93 K. It seems that there are some contribution except for the metal to ligand bond length changes in SCO phenomena. In order to investigate the detail of their electronic states, we plan to measure the ^{57}Fe Mössbauer spectra.

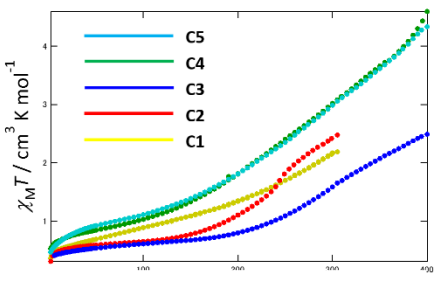

Fig.1 $\chi_M T$ vs T plot of **C1–C5**

[1] H.Oshio *et al*., *Inorg. Chem*., 1991, **30**, 4252-4260

P-47

Reductive Solid Phase Epitaxy and Physical Properties of Layered Y_2O_2Bi Thin Film with Bi^{2-} Square Net

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Key words: layered oxide, unusual valence, solid phase epitaxy, two-dimensional electronic system

Layered compounds with Bi square net show fascinating electronic properties such as anisotropic Dirac Fermions [1] and superconductivity [2]. Recently, a new series of layered compounds R_2O_2Bi (R: rare earth or Y) with unusual Bi^{2-} square net was synthesized in polycrystalline powder form [3]. In order to investigate the intrinsic properties of the R_2O_2Bi, single crystal or epitaxial thin film is indispensable, but their fabrication has not been reported due to the extreme reductive state of Bi. In this study, we report on the fabrication of Y_2O_2Bi epitaxial thin film by newly developed reductive solid phase epitaxy [4].

The multilayered precursor composed of Bi, Y, and Y_2O_3 layers were deposited on a lattice matched CaF_2 substrate at room temperature by sputtering, followed by *in situ* heating in order to promote the solid phase epitaxy of Y_2O_2Bi. In XRD pattern (Fig. 1), Y_2O_2Bi 00*l* diffraction peaks were observed along the CaF_2 00*n* diffraction peaks without impurities, representing successful epitaxial growth of the Y_2O_2Bi thin film. The angular dependence of magnetoresistance at 2 K and 9 T showed $|\cos\theta|$ dependence as shown in Fig. 2, where I is the in-plane current and θ is the angle between film normal and magnetic field H. This result demonstrates two-dimensional electronic transport owing to the conductive Bi^{2-} square net. In the presentation, we shall report on the details of novel fabrication techniques and physical properties of Y_2O_2Bi.

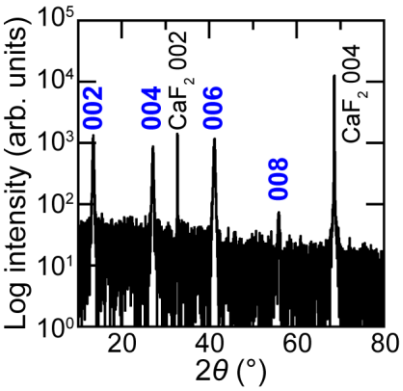


Fig. 1. XRD pattern of Y_2O_2Bi epitaxial thin film.

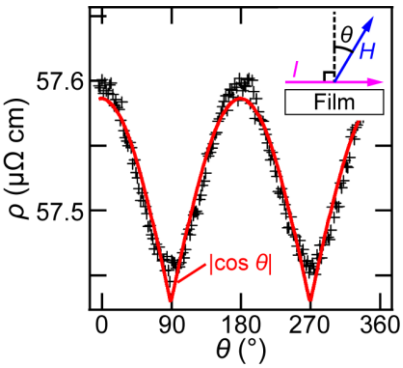
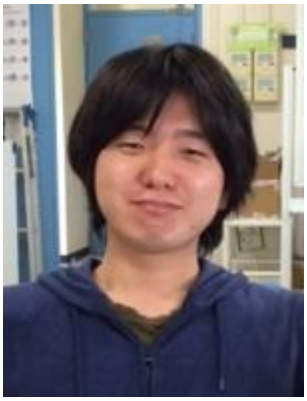


Fig. 2. Angular dependence of magnetoresistance of Y_2O_2Bi epitaxial thin film.

Ref. [1] J. Park *et al.*, *Phys. Rev. Lett.* **2011**, *107*, 126402-1-4. [2] H. Mizoguchi *et al.*, *Phys. Rev. Lett.* **2011**, *106*, 057002-1-4. [3] H. Mizoguchi *et al.*, *J. Am. Chem. Soc.* **2011**, *133*, 2394-2397. [4] R. Sei *et al.*, *Cryst. Growth Des.* **2014**, *14*, 4227-4229.

P-48

Nonequilibrium Synthesis of Solid State Yttrium Monoxide



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Key words: pulsed laser deposition, rare earth oxide

Yttrium sesquioxide (Y_2O_3) has been investigated as a gate insulator in field effect transistors owing to the high permittivity and robust insulating properties [1]. This result reflects high stability of trivalent yttrium ion in solid phase oxides. Indeed, yttrium monoxide (YO) with divalent yttrium ion exists only as a gaseous phase [2]. In this study, we report the first synthesis of rock salt structure YO solid phase in a form of epitaxial thin film by pulsed laser deposition (PLD) method. YO films were grown at 350°C on CaF_2 (100) substrates with Y_2O_3 pellet target. The oxygen partial pressures (P_{O2}) were varied from 10^{-11} to 10^{-8} Torr by introducing Ar and O_2 mixed gas in order to control the amount of oxygen vacancy.

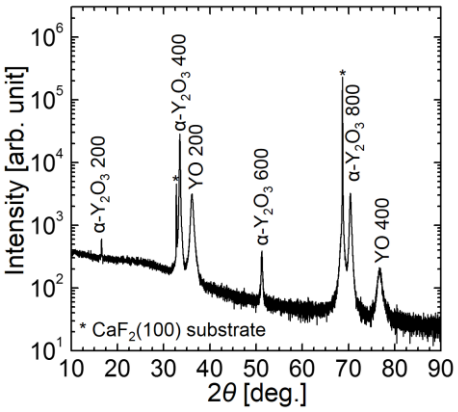


Fig. 1. XRD pattern of YO film.

Figure 1 shows an out-of-plane XRD pattern of YO film. Rock salt structure YO *h*00 peaks were clearly observed representing the formation of YO (100) epitaxial thin film. The presence of Y_2O_3 phase suggests the surface oxidation of YO into Y_2O_3.

Figure 2 shows temperature dependence of resistivity (ρ) for YO films deposited at different P_{O2}. The carrier density (n) in YO was controllable with the amount of oxygen vacancy that serves as an electron donor. The range of resistivity at 300 K was 10^{-3} – 10^{1} Ωcm, which is much lower than that of Y_2O_3, 10^{13} – 10^{14} Ωcm [3]. Insulator to metal transition was observed around at n ~10^{20} cm^{-3}. Metallic transport was observed at $n \geq 10^{20}$ cm^{-3}. A slight upturn of resistivity below 20 K reminiscent of the Kondo effect and rather low electron mobility imply heavy Fermionic nature of this compound.

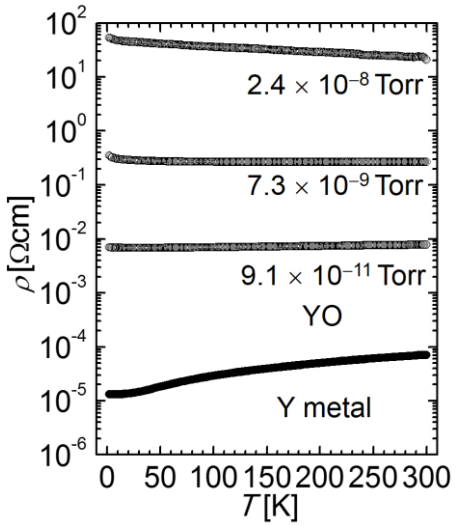
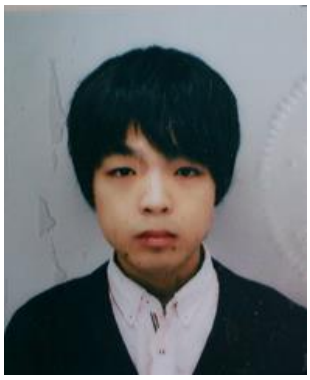


Fig. 2. ρ-T curves of YO films deposited at different P_{O2}.

Ref. [1] H. Yabuta *et al.*, *Appl. Phys. Lett.* **89**, 112123 (2006). [2] J.M. Badie *et al.*, *Chem. Phys. Lett.* **364**, 550 (2002). [3] R. Ivanic *et al.*, *J. Electr. Eng.* **54**, 83 (2003).

P-49

Thin film growth of HP-PdF_2 type RuO_2



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Key words: thin film, solid state chemistry

Ruthenium dioxide (RuO_2) is tetragonal rutile structure at ambient pressure and transforms into cubic structure (HP-PdF_2) at high pressure and temperature.[1] HP-PdF_2 RuO_2 is expected to show remarkable electromagnetic properties like superconducting CuS_2 because of the similar crystal structure and *U/W* value, where *U* and *W* are the Coulomb repulsion energy and the bandwidth, respectively. However, only polycrystalline HP-PdF_2 RuO_2 mixed with rutile RuO_2 impurity phase has been synthesized at high pressure, thus intrinsic properties of HP-PdF_2 RuO_2 have been unveiled. In this study, we try to synthesize HP-PdF_2 RuO_2 thin film by pulsed laser deposition method.

Figure 1 shows $2\theta/\theta$ X-ray diffraction patterns of films grown on CaF_2 (100) substrates at 600−900°C in oxygen partial pressure of 1.0×10^{-3} Torr. The films grown at 600 and 700°C and at 900°C were rutile RuO_2 and Ru metal, respectively. This result is plausible from the viewpoint of thermodynamics because RuO_2 was reported to decompose into Ru at high temperature under reductive atmosphere.[2][3] On the other hand, the film grown at 800°C was HP-PdF_2 RuO_2 phase. This result shows that polycrystalline HP-PdF_2 RuO_2 film can be grown without high pressure condition, although the synthesis condition was limited on a boundary between rutile RuO_2 and Ru metal phases in the Ellingham diagram.

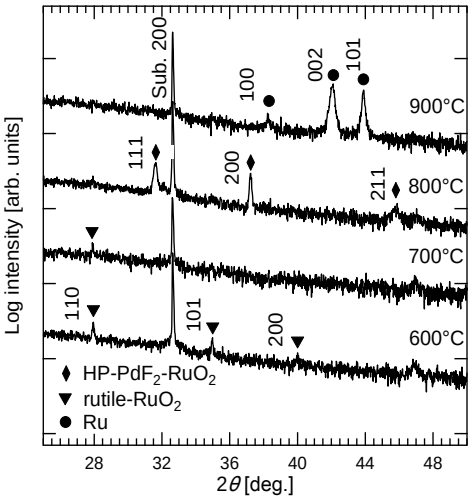

Fig.1 X-ray diffraction patterns of samples grown at different temperatures.

Ref. [1] Y. Shirako *et al., Inorg. Chem.* **53**, 11616 (2014). [2] S. Pizzini at al., *Z. Naturforsch., A: Phys. Sci.*, **26A** 177 (1971). [3] K. T. Jacob et al., *J. Am. Ceram. Soc.*, **83** 1745 (2000)

P-50

Positron annihilation study on nanostructure change of polyethylene induced by electron beam irradiation

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Key words: polyethylene, positron annihilation, free volume, oxidation, cross-linking

Polyethylene (PE) is one of the most useful polymers. Since PE is widely used in various radiation environments such as nuclear power plants and accelerators, the irradiation effect of PE is important for safety of these facilities. In this work, to investigate the irradiation effect of PE, changes of chemical structures, degree of cross-linking, and nanostructures were measured by FT-IR spectroscopy, gel fraction measurement, and positron annihilation lifetime spectroscopy (PALS), respectively. PALS is a powerful tool to measure sub-nanometer holes in polymers called "free volume". [1]

High density polyethylene (HDPE) was used as a sample. HDPE was irradiated with different absorbed doses up to 1000 kGy under vacuum at room temperature. After the irradiation, samples were exposed to air.

The amount of carbonyl groups increased during long-term storage (Fig. 1), indicating that the oxidation of irradiation HDPE underwent with elapsed time after the irradiation due to hydroperoxide produced from allyl radical. On the other hand, the degree of cross-linking did not change with time. It suggests that hydroperoxide induced oxidation during the long-term storage, but it gives little contribution to the cross-linking. Free volume sizes estimated by Tao-Eldrup model[2] was comparable in two samples: one is measured just after irradiation and the other is kept in air for 5 months. Especially it appears to decrease for higher absorbed dose samples (Fig. 2). The post-irradiation effects of the samples are required to measure continuously.

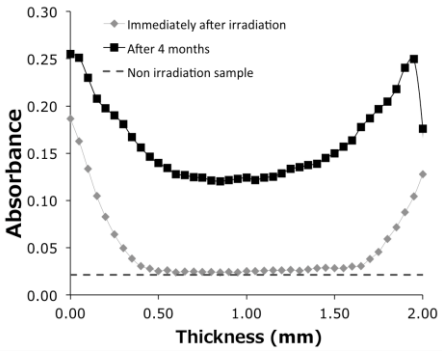

Fig. 1. Depth profile of the carbonyl absorbance for HDPE

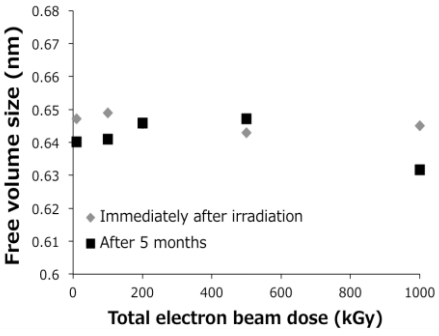

Fig. 2. Free volume size as a function

Ref. [1] T. Oka *et al., Appl. Phys. Lett.* **2012**, 101, 203108.
[2] K. Eldrup *et al., Chem. Phys.*, **1981**, 63, 51.

P-51

Kinetic Effect of Cationic Species on Self-assembly of Thiacalix[4]arene-*p*-tetrasulfonate – Lanthanide Cluster Complex

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Key words: Thiacalix[4]arene-*p*-tetrasulfonate, Cluster complex, f-f communication, Self-assembly

[Introduction] We recently found that thiacalix[4]arene-*p*-tetrasulfonate (TCAS, **Fig. 1**) with different lanthanide(III) species (Ln, Ln') forms hetero-nuclear cluster complex ($Ln_{3-x}Ln'_xTCAS_2$, x = 1, 2) by self-assembly. In the case of Tb and Yb pair, the hetero-nuclear complex ($Tb_{3-x}Yb_xTCAS_2$, x = 1, 2) exhibited Tb→Yb energy transfer by f-f communication in the complex. However, mixtures of homo- and hetero-nuclear complex were produced under the conventional self-assembly conditions. The selective formation of each complex species is needed to investigate luminescence properties of the hetero-nuclear complex. On the other hand, the self-assembly process proceeds via step-wise manner (eqs. 1–3).[1]

$$Ln + TCAS \rightarrow Ln_1TCAS_1 \quad (1)$$

$$2\ Ln_1TCAS_1 \rightarrow Ln_2TCAS_2 \quad (2)$$

$$Ln_2TCAS_2 + Ln \rightarrow Ln_3TCAS_2 \quad (3)$$

If we could decrease the rate of step (2), selective formation of the hetero-nuclear species may be possible. In this presentation, we will show the control of the self-assembly rate by addition of cationic species as monitored with HPLC analysis.

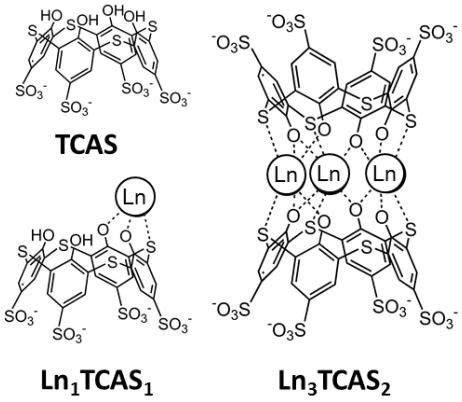


Fig. 1 Structure of TCAS, Ln_1TCAS_1, and Ln_3TCAS_2.

[Results & Discussion] At pH 7.4, peaks of Tb_1TCAS_1 and Tb_3TCAS_2 appeared at 1 hour after mixing. Eventually, the peak of Tb_1TCAS_1 disappeared and one of Tb_3TCAS_2 increased after 1 day. In the case of addition of tetrabutylammonium bromide (TBABr), the peak of Tb_1TCAS_1 was observed after 1 day (**Fig. 2**). Hence, the rate of step (2) in the self-assembly could be decelerated by addition of TBABr. In comparison with various bromides salts, the peak height of the remaining Tb_1TCAS_1 was higher in the order: none < Na^+ < tetramethylammonium$^+$ < TBA^+. It is likely that the hydrophobicity of cationic species affects the rate of step (2).

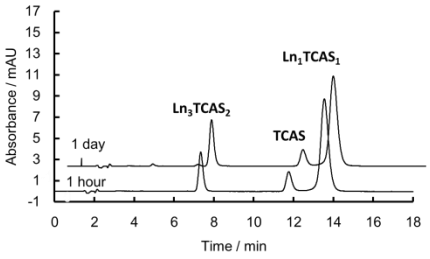
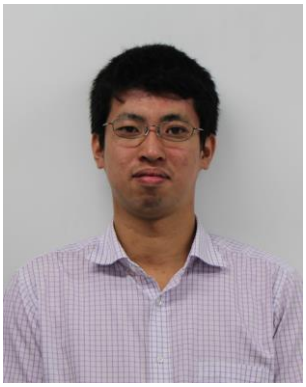


Fig. 2 Chromatograms of Tb-TCAS system with TBABr.
Sample: [Tb^{III}] = [TCAS] = 20 μM, [HEPES] = 0.01 M, pH 7.4, [TBABr] = 0.02 M, λ: 316 nm.

[Reference] 1 N. Iki, S. Hiro-oka, M. Nakamura, T. Tanaka, H. Hoshino, *Eur. J. Inorg. Chem.* **2012**, 3541.

P-52

Synthesis and photoluminescence properties of Mn^{4+}-doped the Ruddlesden-Popper type $SrLa_nAl_nO_{3n+1}$ (n = 1, 2, ∞)



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Key words: Mn^{4+}-doped phosphor, Ruddlesden-Popper, solid-state reaction

White light emitting diode (wLED) is expected to be a white light source because of its long life and high efficiency. High color rendering wLED combined near-UV or blue LED and phosphors is proposed to improve the color rendering. Mn^{4+} phosphors are expected to be candidates of red phosphor for wLED because they exhibit red photoluminescence (PL) by excitation of near-UV or blue LED. In this study, we have focused on difference in stacking of the Ruddlesden-Popper (RP) type layered perovskite $SrLa_nAl_nO_{3n+1}$ as host materials. The number of perovskite layers increase with increasing n because the RP phase $A_{n+1}B_nO_{3n+1}$ consists of stacked rock salt AO and perovskite $(ABO_3)_n$ layer. Thus, PL properties influenced by the coordination environment can be changed by perovskite layer stack. In the RP phase of $SrO\text{-}La_2O_3\text{-}Al_2O_3$ system, $SrLaAlO_4$, $SrLa_2Al_2O_7$, and $LaAlO_3$ have been reported as n = 1, 2, and ∞, respectively. In addition, $SrLaAlO_4$[1] and $LaAlO_3$[2] have been reported as host materials of Mn^{4+}-doped phosphor. Therefore, $SrLa_2Al_2O_7$ is expected to be a candidate of host material. In the present study, we synthesized Mn^{4+}-doped the RP type $SrLa_nAl_nO_{3n+1}$ (n = 1, 2, ∞), and compared PL properties for each host materials.

$SrLaAlO_4:Mn^{4+}$, $SrLa_2Al_2O_7:Mn^{4+}$, and $LaAlO_3:Mn^{4+}$ were synthesized by solid-state reaction. The starting materials were powder of $SrCO_3$, La_2O_3, Al_2O_3, and MnO_2. These powders were weighed and mixed on the composition of $SrLa_n(Al_{0.999}Mn_{0.001})_nO_{3n+1}$ (n = 1, 2, ∞). The mixtures were calcined at 1000 ºC for 12 h in air. The pellets of calcined sample were then placed on an alumina plate and heated at 1100 - 1400 ºC for 12 h in air. The obtained samples were characterized by XRD and PL measurement.

$SrLa_nAl_nO_{3n+1}:Mn^{4+}$($n$ = 1, 2, ∞) were synthesized as the main phase by firing at 1400 ºC. Fig. 1 shows PL emission spectra of these samples. The emission spectra were narrow band between 660 and 790 nm due to the $^2E \rightarrow {}^4A_2$ transition of Mn^{4+}. However, the spectral shape was significantly different for each host structure. The results suggested that change of the coordination environment of perovskite layers influenced PL properties.

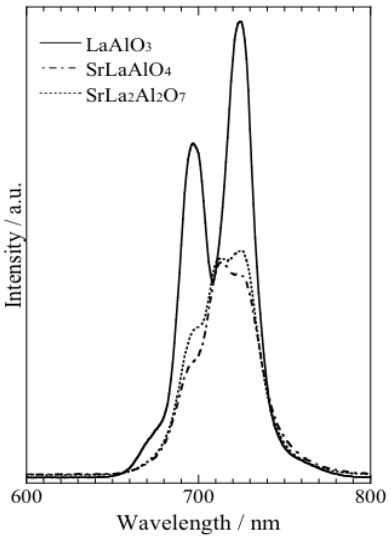

Fig. 1. PL emission spectra of $SrLa_nAl_nO_{3n+1}:Mn^{4+}$($n$ = 1, 2, ∞)

[1] Y. Zhydachevskii *et al*., *Opt. Mater.* **35** 1664 (2013).
[2] M.E. van Ipenburg *et al*., *Mater. Chem. Phys.* **39** 236 (1995).

P-53

Identification of Protein Disulfide Isomerases that Directly Interact with Insulin

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Key words: protein folding, insulin

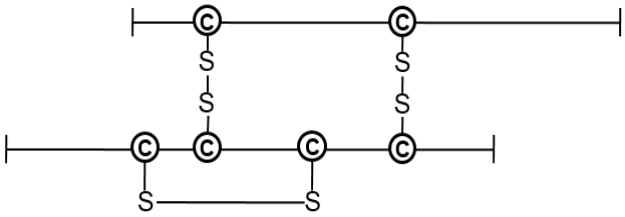


Fig. 1. Disulfide bonds in insulin

Insulin is a peptide hormone secreted from pancreatic beta cells and plays an important role in the regulation of glucose concentration in blood. Insulin has three disulfide bonds (Fig. 1). Failure to form these disulfides between correct pairs of cysteines leads to the development of diabetes. Therefore, it is important to elucidate the mechanism of disulfide bond formation in insulin. Nevertheless, the order in which three disulfide bonds are formed in insulin and the enzymes involved in the reactions are not known. Thus, we aimed to identify the enzymes.

In the endoplasmic reticulum (ER), protein disulfide isomerase (PDI) family enzymes introduce disulfide bonds into proteins. More than twenty PDI family member proteins have so far been identified in mammalian cells. During catalysis of disulfide bond formation, these enzymes form disulfide-linked complexes with their substrates. We took advantage of this chemical property of the enzymes to identify PDI family members involved in insulin biogenesis.

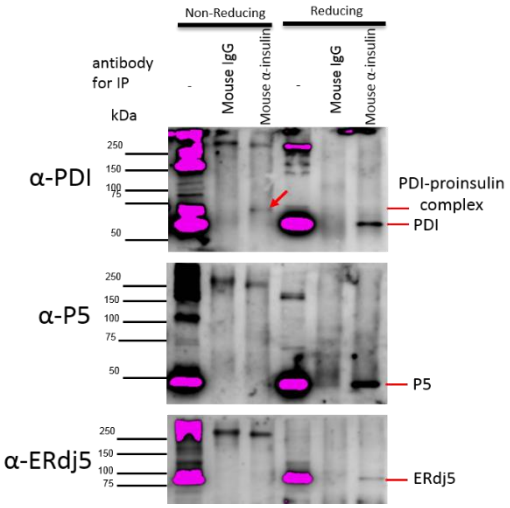
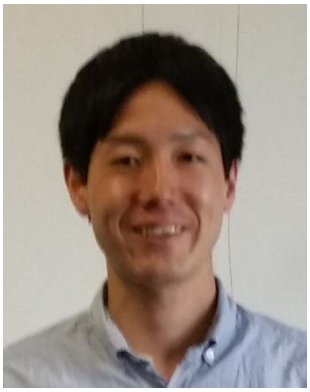


Fig. 2. Three PDI family proteins

By treating a mouse insulin-producing pancreatic beta cell line, MIN6, with 10% trichloroacetic acid and N-ethylmaleimide, we successfully prepared the stable disulfide-linked complexes that involve in proinsulin (the precursor protein of insulin localized in the ER). We then purified the complexes using antibody for proinsulin and analyzed them by mass spectrometry. Consequently, we discovered three PDI family members that directly interacted with proinsulin via intermolecular disulfide bonds (Fig .2). We are currently exploring the roles of these PDI family proteins in the biosynthesis of insulin.

P-54

Physiological function of pancreas-specific protein disulfide isomerase family protein (PDIp)



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Key words: protein quality control, protein folding, chaperone

Formation of disulfide bridges is an important step in the folding of secretory proteins. In the endoplasmic reticulum, the formation, reduction and isomerization of disulfide bridges are catalyzed by protein disulfide isomerase (PDI) family proteins. In mammals, about 20 PDIs are known (Fig. 1). However, physiological function of each enzyme is still unclear. This is in part due to the lack of information on the physiological substrates of each enzyme. Therefore, we aim to identify the physiological substrates of PDIs to elucidate their functions. We had particular interest in pancreas-specific PDI family protein (PDIp) among the PDIs, since pancreas produces large quantities of important secretory proteins including endocrine hormones such as insulin and digestive enzymes such as α-amylase.

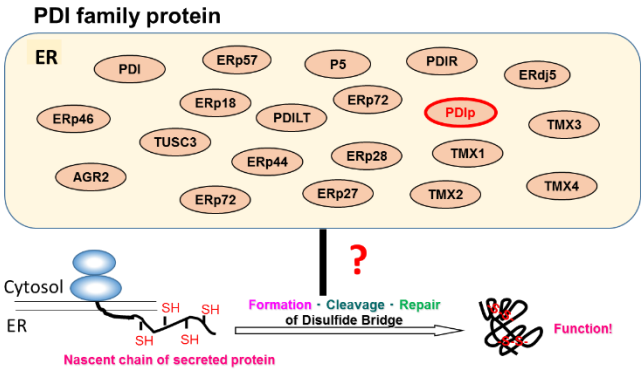

Fig. 1. PDI family proteins and their presumed functions

Thiol-disulfide exchange reaction catalyzed by PDIs proceeds through a disulfide-linked intermediate between PDIs and their substrates. We utilized the characteristics to identify physiological substrates of PDIp. To stabilize the disulfide-linked complexes, mouse pancreas tissue was directly treated with 10% trichloroacetic acid, and free cysteines were blocked with N-ethylmaleimide. The samples were then immunoprecipitated with antibody for PDIp, and subjected to the mass analysis. We thus identified digestive enzymes such as α-amylase as potential substrates of PDIp(Table 1). We are currently investigating the role of PDIp in the biosynthesis of identified substrates.

Type	Name	Coverage(%)
Digestive enzymes	α −Amylase	68
	Chymotrypsinogen B	44
	Trypsin−1	36
	Chymopasin	32
	Elastase−1	31
	Pancreatic triacylglycerol lipase	31
	Elastase−2	29
	Trypsin−4	29
	Inactive pancreatic lipase−related protein 1	13
Zymogen granule excytosis enhancer	Syncollin	26
PDI family protein oxidase	Prx4	61
	ERO1β	41
PDI family protein	P5	45
	ERp46	25

Table 1. Identified potential substrates of PDIp

P-55

Preparations and Crystallizations of ER calcium storage protein Calsequestrin, its anchor protein Junctin and their complex.

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Key words: Calcium homeostasis, X-ray crystallography, Endoplasmic reticulum
Ryanodine receptor, protein crystallization

The endoplasmic reticulum (ER) stores high concentration of Ca^{2+} within the cell. Various stimulations induce release of Ca^{2+} from the ER into the cytoplasm. This Ca^{2+} release is mainly mediated by ER calcium channels, Ryanodine receptor (RyR) and/or inositol-trisphosphate receptor. The opening and closing of RyR is controlled by a variety of factors. For example, the change in cellular Ca^{2+} concentration and the binding of some regulatory proteins are involved in this control. In the lumen of the ER, single transmembrane protein Junctin (JCT) and Triadin (TRD), and Calsequestrin (CSQ) play important roles in the regulation of RyR. CSQ is a calcium binding protein with three thioredoxin-like domains. JCT and TRD are membrane-anchored proteins that interact with RyR. Presumably, CSQ binds the inner luminal side of JCT and TRD, forming a CSQ-JCT-TRD ternary complex. Previous studies suggested that the calcium concentration affects the association between CSQ and the other two proteins. However, little is known about the mechanism by which these three proteins assemble to the ternary complex. The purpose of this study is to clarify the above issue using biochemical and crystallographic approaches. Recombinant human CSQ was overexpressed in *Escherichia coli* BL21 (DE3) and was purified by Ni-affinity, ion exchange and gel filtration chromatographies. Gel filtration chromatography analysis suggested that CSQ exists in a tetramer in the absence of Ca^{2+} and we succeeded in crystallization of the tetrameric form of CSQ. The diffraction data were collected at the BL44XU beamline, SPring8, at cryogenic temperature (100K). The diffraction images were processed with HKL2000. The structure was determined by the molecular replacement method, and was refined by several cycles of manual rebuilding and refinement with Coot and Phenix (Fig.1).

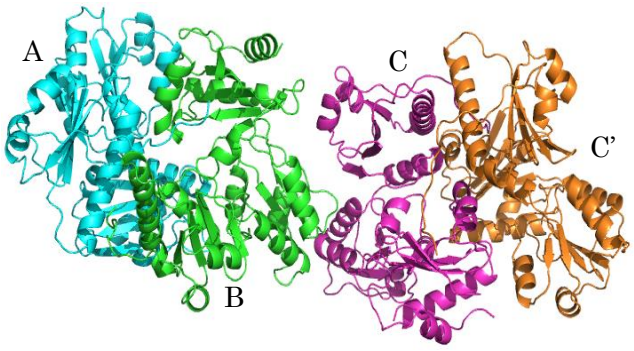

Fig.1 The overall structure of the CSQ tetramer.

We also constructer several versions of the luminal domain of human JCT and purified them by Ni-affinity and ion exchange chromatographies. We are now searching conditions optimal for the interaction between CSQ and JCT, in order to obtain the stable CSQ-JCT complex toward its crystallization.

P-56

Method for selective clearance of cytosolic proteins via autophagy

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Key words: autophagy, 8-nitro-cGMP, orotein *S*-guanylation

Autophagy is an intracellular degradation system conserved among eukaryotes, which is generally considered nonselective, whereas specific cargos such as damaged organelles, protein aggregates and intracellular bacteria are known to be excluded by highly selective and tightly regulated autophagy. Recently, we reported 8-nitro-cGMP as novel endogenous inducer of autophagy[1]. A post-translational protein modification (protein *S*-guanylation[2]) at cystein residues by 8-nitro-cGMP was suggested to play a role. In this work, a summary of our recent efforts toward elucidation of the molecular mechanism of 8-nitro-cGMP-mediated autophagy, as well as its application for selective clearance of specific proteins via autophagy are presented.

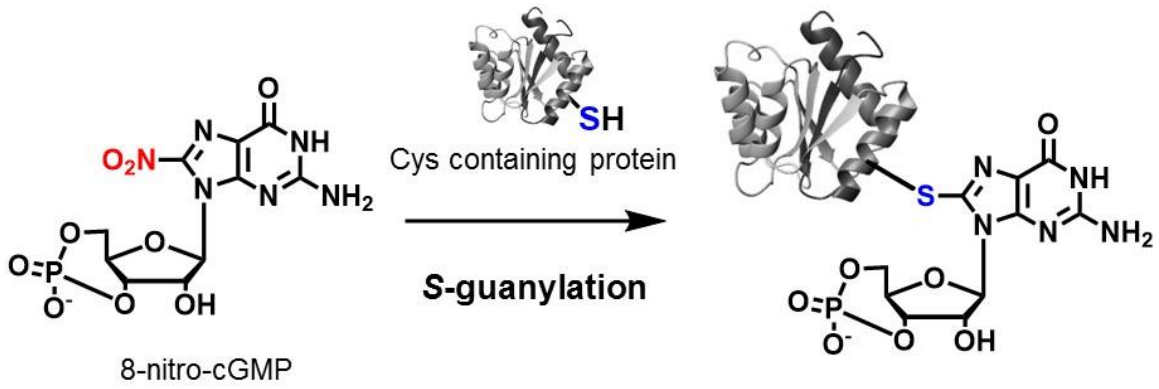

Fig. protein *S*-guanylation

Ref.
1.Ito, C. *et al.* Endogenous nitrated nucleotide is a key mediator of autophagy and innate defense against bacteria. *Mol. Cell* **52,** 794–804 (2013).
2.Sawa, T. *et al.* Protein S-guanylation by the biological signal 8-nitroguanosine 3’,5’-cyclic monophosphate. *Nat. Chem. Biol.* **3,** 727–735 (2007).

Effect of lipid-soluble antioxidant tocotrienol on oxidation of biomembrane lipids

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Key words: tocotrienol, antioxidant activity, lipid oxidation

Abstract: Tocotrienol (T_3H), novel vitamin E, has an unsaturated side chain with three double bonds, and higher antioxidant activity than tocopherol (T_0H), conventional vitamin E. [1] After oral intake of vitamin E, they are accumulated in the biomembrane, which is lipid bilayer consisting of phospholipid (LH) and cholesterol (ChH), and prevent the lipid oxidation induced by water-soluble free radicals. However, there is little knowledge about the mechanisms of anti-oxidation by T_3H. In this research, with model biomembrane system, T_3H is enclosed in liposome (lipid bilayer vesicle, Fig. 1) and the oxidation experiments are performed in the presence of water-soluble radicals. For comparison, the oxidation experiments of liposomes with T_0H or without antioxidants are also performed.

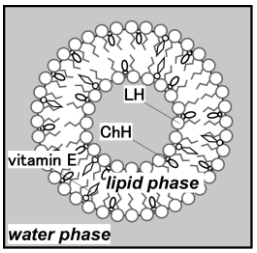

Fig. 1 Schematic diagram of liposome

Figure 2 shows the experimental results for three kinds of liposomes. In the case without antioxidants (○), the concentrations of LH (a) and ChH (b) quickly decreased, suggesting that the oxidation of LH and ChH proceeded. In the case with T_0H (△), the concentrations of LH and ChH hardly decreased up to 25 h and then rapidly decreased after T_0H concentration (c) became almost zero. This meant that the lipid oxidation progress was suppressed as long as T_0H remained in the system. In the case with T_3H (◇), T_3H concentration became almost zero at 50 h, but the concentrations of LH and ChH started to rapidly decrease after 75 h. Thus, the lipid oxidation progress was still suppressed after T_3H disappeared from the system. T_0H is known to react with the radical and to change itself to the stable tocopheroxyl radical.[2] Similarly, T_3H reacts with the radical, but the formed tocotrienol radical with unsaturated side chain also reacts with another radical, so that the antioxidant effect can continue for a longer time.

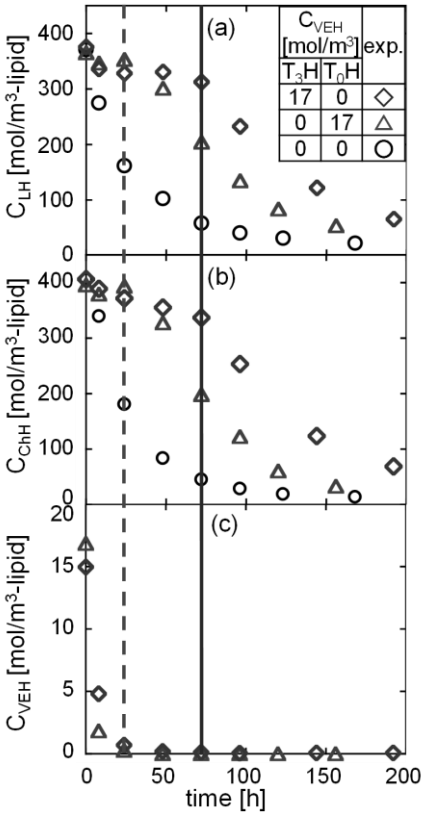

Fig. 2 Time courses of LH (a), ChH (b) and T_3H orT_0H

[1] T. Eitsuka *et al.*, *Biochem. Bioph. Res. Co.*, **348**,170-175(2006)

[2] S. Nagaoka et al., *Chem. Phys. Lipids*, **146**,26-32(2007)

Optimum condition for the preparation of homogeneous antibody-drug conjugate

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Key words: antibody-drug-conjugate (ADC), chemical conjugate

The antibody with cytotoxic molecule conjugated (Antibody-drug-conjugate, ADC) can critically make damages on the solid tumors which are hardly damaged only by normal antibody functions. For chemical conjugation on proteins, the use of the thiol group in cystein residue is a simple approach for site-specific conjugation; however, in the case of antibody, the activation of thiol groups lead to instabilities of antibody structures, because the disulfide linkages in each domain of antibody are critical for the structural stability of antibody. Especially, structural stability of the recombinant small antibody, which is built up from the faragment of variable region in antibody, is seriously dependent on the formation of the disulfide linkages. In this study, we applied the amino group in lysine residue for the site-specific chemical conjugation of organic molecule on recombinant small antibody and we tried to control the organic molecules to antibody ratio by changing the experimental conditions of mixture ratio of antibody and organic molecule, reaction time, and reaction pH.

In this study, fluorescence and biotin molecules are applied instead of drug. Quantitative binding amount of fluorescence to antibody was calculated from the absorbance at 555 nm. Binding amount of biotin to antibody was estimated by HABA assay. By using these analysis, we tried to correlate reaction condition with the number of conjugated organic molecules.

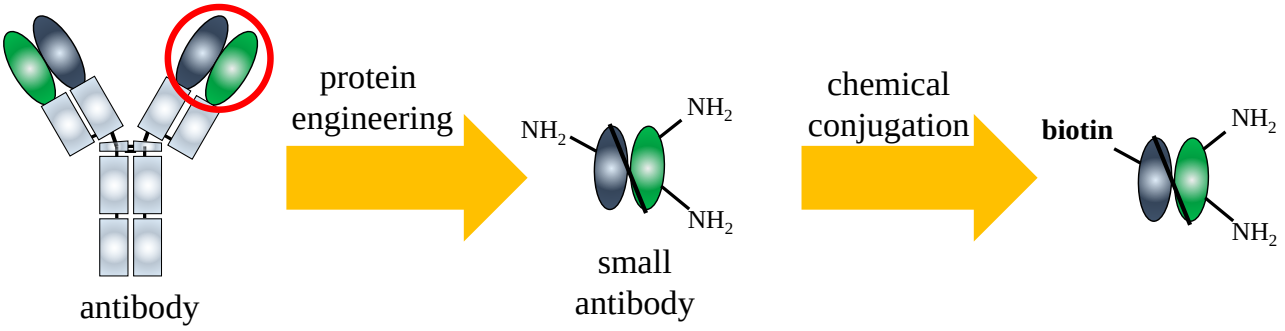

Fig.1 strategy of chemical conjugate

P-59

Improving multi-specificity of an anti-mutated IDH1 antibody by directed evolution

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Key words: Protein engineering, Directed evolution, Isocitrate dehydrogenase 1, Multi-specificity

Gliomas are the tumors formed in brain, and the mutations at functional arginine residues in isocitrate dehydrogenase 1/2 (IDH1/2) have a clear correlation with the prognosis of glioma patients. In the case of IDH1, mutation of the arginine 132 residues (R132) have been reported and the patients with the mutated IDH1 have shown good prognosis[1]. The R132-mutated IDH1 can be a promising prognostic marker in gliomas. Recently, multi-specific anti-mutated IDH1 monoclonal antibody (MsMab-1) has been generated: MsMab-1 has the specific affinity for three R132-mutated IDH1 (R132H, R132S, R132G)[2]. More increment of multi-septicity is expected to completely find all the patients with good prognostic markers. In this study, we attempted to prepare the fragments of variable region (Fv) from MsMab-1 and the single chain Fv (scFv) by means of *E.coli* expression to improve multi-specificity of MsMab-1 by directed evolution.

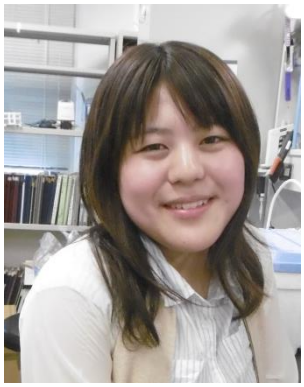
First, we transformed *E. coli* with the vectors encoding Fv and scFv of MsMab-1, respectively. MsMab-1 Fv was expressed as insoluble aggregate in *E. coli*, whereas MsMab-1 scFv was expressed as soluble protein. To improve the expressed yield of soluble MsMab-1 scFv, we then sought to optimize the cultivation and purification conditions. Culturing transformed *E. coli* at low temperature for 12 hours after induction led to the most effective expression of the scFv in soluble fraction, and use of BL21 (DE3) star that enhances mRNA stability was suited for expressing soluble scFv. For purification, high salt concentration in the scFv-containing solutions resulted in the increase of absorbed scFv on the carriers for immobilized metal ion affinity chromatography; consequently, the yield of the purified protein was increased.

In conclusion, we have succeeded in expressing the MsMab-1 in soluble fraction by optimizing the conditions of cultivation and purification process. Evaluation of binding function of scFv is in progress. In the future, we will try to give further multi-specificity by directed evolution.

[1] H.Yan *et al*., *New England Journal of Medicine*, **360**, 763-73, 2009.
[2] Y. Kato, *Brain Tumor Pathology,* **32**, 3-11, 2015.

P-60

Production of single chain antibody using baculovirus-silkworm expression system



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Key word: silkworm express system, scFv, vaculovirus,

Phase display method is the technique to select the antibodies with affinity for a target molecule from the library of the phases displaying a large variety of antibody fragments on the surfaces. However, in the situation where the phases with low affinity are selected, accidently-bound phases are possibly selected due to non-specific interaction between phases and target molecules. To overcome this problem, the antibody fragment from each clone should be prepared as recombinant protein to analyze correct affinity, and the rapid protein preparation method for achieving the analysis should be prepared. Here, we focused on the protein production by means of silkworm, which can produce relatively large amount of proteins in small scale with high cellular density. (Fig.1)

We attempted to produce single chain fragments of variable region (scFv), where heavy chain of variable region (VH) and light chain of variable region (VL) are linked via apeptide linker. First, we inserted the scFv gene from the antibody with affinity for CD3 on lymphocyte cell and with affinity for epidermal growth factor receptor (EGFR) on cancer cells into vaculovirus vectors and we transduced silkworm pupae with thevectors. The pupas were smashed and then ultracentrifuged. From the supernatant after ultracentrifugation, the scFv were purified by means of immobilized metal affinity chromatography and size exclusion chromatography. Finally, we measured the binding affinity of scFvs for each target molecule by means of flow cytometry and surface plasmon resonance.

In this study, 1 and 5 kinds of scFvs were prepared from anti-CD3 and anti-EGFR antibody, respectively. The scFvs were purified from the supernatant after ultracentrifugation, although the expressed amounts were varied. We confirmed that all of 6 scFvs bound to each target molecule. From these results, we concluded that scFvs can be prepared from silkworms.

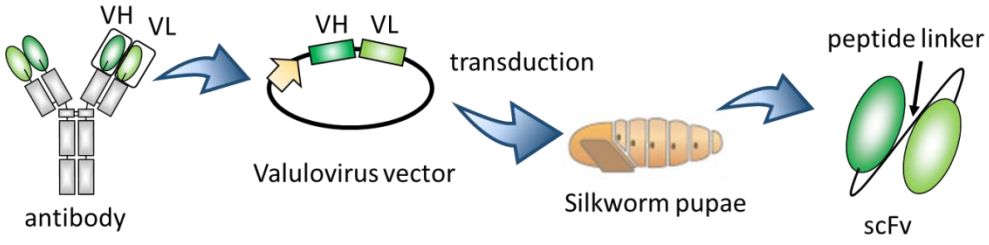

Fig. 1 production of scFv by means of silkworm

P-61

Therapeutic Peptide Format Toward Antibody

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Key words: peptide medicines, evolution technology, phage display

Biological medicines, such as peptides and antibodies, have been expected to substitute for chemical medicines, because biomolecules have higher specificity for target molecules than chemical compounds. Peptide medicines with target specificity are more easily selected by in vitro evolution technology than antibody, but they tend to be degraded in vivo. On the other hand, antibody medicines have high specificity and selectivity for target molecules and long biological half-life.

Here, we designed peptide format which can be used not only for peptide medicines, but also for the grafting into antibody: the grafting of the peptide into complementarity determining region (CDR) of antibody molecules to express the function of grafted peptide in antibody. These peptide formats could provide various biological drugs and flexible therapeutic strategies. In this study, we selected the camel-type single variable antibody fragment (VHH) as a scaffold for grafting peptide.

First, we measured the length of α-carbon atoms between N- and C-terminus of CDR loop based on protein crystal structure. This result showed that the N- and C-terminus could be linked by disulfide bond formation between cysteine residues fused at each terminus (Fig. 1). In order to construct phage library where the Cys-sandwiched randomized peptide with the same number of amino acid residues as CDR3 loop is displayed, the gene was constructed by two approaches: ligation reaction of phage vector fragment and library fragment, and inverse polymerase chain reaction (inverse PCR) using the primers with randomized sequence. By using two methods, libraries with a complexity of ~10^3 clones were acquired. We are in progress of increasing the scale of library.

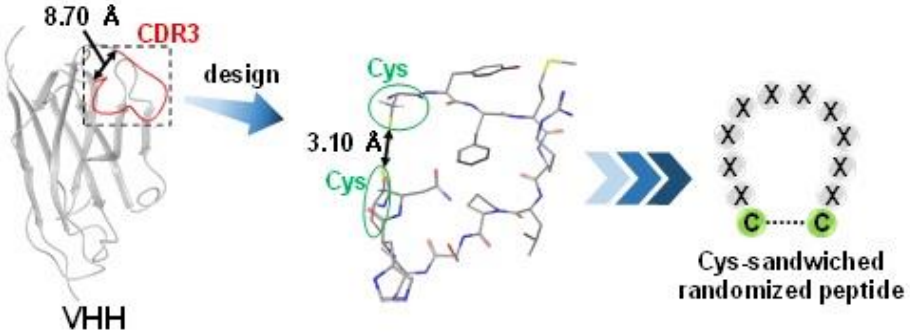

Fig.1 Construction of peptide format for the grafting into antibody

P-62

Structural analysis for Cu^{2+}-binding sites of the denatured apo-SOD1

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Key words: Cu,Zn-Superoxide dismutase, pro-oxidant activity

The metal-depleted apo form of H43R mutant of SOD1 misfolds into a denatured structure, which results in the acquisition of the pro-oxidant activity upon binding of Cu^{2+} at the two sites composed of His residues [1, 2]. In this study, we have assigned His residues in the two Cu-binding sites of the denatured apo- H43R to clarify the origin of the pro-oxidant activity.

We measured the absorption spectra of the denatured apo-H43R binding to the one equivalent Co^{2+}. The strong absorption was clearly observed around at 580 nm, which was assigned to the d-d transition of Co2+. The absorption of the d-d transition of Co^{2+} was markedly reduced when one of His63, 71, or 80, which constitute the Zn-binding site of the native SOD1, was replaced with Ala (Fig. 1). This result indicates that these three His residues remain to construct one of the two Cu^{2+}-binding sites of the denatured apo-H43R.

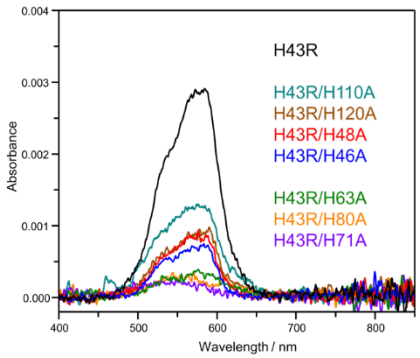


Fig. 1 The d-d absorption spectra of Co^{2+}

Besides to the His residues constituting to Co^{2+} binding site, H43R contains 4 His residues, His46, 48, 110, and 120. We therefore measured the pro-oxidant activity of the denatured H43R/HxA. His46 and 48 were important for the pro-oxidant activity but His110 and 120 were not, which leads us to a conclusion that His46 and His48 constitute one site having the pro-oxidant activity.

From the obtained results, the structure of the Cu-binding sites of the denatured H43R can be proposed as shown in Fig. 2. The His residues constituting the two metal binding sites remain unchanged through the denaturation except for His120 that constitutes the Cu site in native SOD1. It is therefore suggested that the origin of the pro-oxidant activity is derived from the absence of His120.

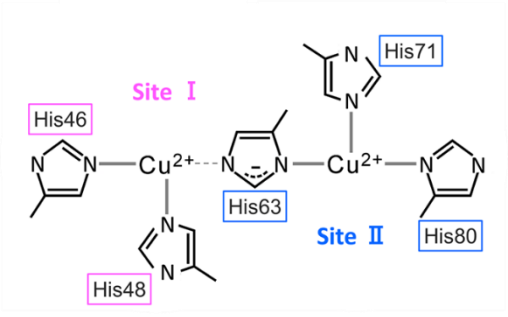
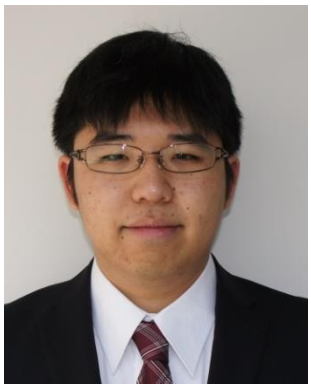


Fig. 2 The structural model of the Cu-binding sites of the denatured H43R

Ref. [1] Kitamura, F., et al. (2011) Biochemistry 50, 4245-4250.

[2] Fujimaki, N., et al. (2013) Biochemistry 52, 5184-5194.

Development of Bioactivity-controlled Molecular Probe to Reveal the Mechanism of Stomatal Reopening Caused by Phytotoxin Coronatine



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Key words: natural product, bioactivity control, molecular probe, target identification

Coronatine (COR), a well-known phytotoxin produced by bacterial pathogens, causes stomatal reopening by affecting the guard cells to acquire the infection route. [1] However, the target protein of COR has not been identified, and therefore, the molecular mechanism is still unclear. On the other hand, COR is also known as a mimic of plant hormone 7-*epi*-jasmonoyl-L-isoleucine, which induces various biological responses such as plant wounding response or senescence, through formation of protein-protein interaction between COI1 and JAZ proteins.

In this report, we newly designed and synthesized a COR-based photoaffinity probe (**1**) to identify the target protein involved in stomatal reopening. From the several biological assays using *A. thaliana*, **1** kept stomatal reopening activity, whereas the binding affinity of **1** with COI1-JAZ complex significantly reduced. These results clearly indicated that we succeeded in uncoupling of the dual bioactivities of COR (stomatal reopening and the ligand for COI1-JAZ), and **1** would be a useful molecular probe for identification of the unknown target protein involved in stomatal reopening caused by COR.

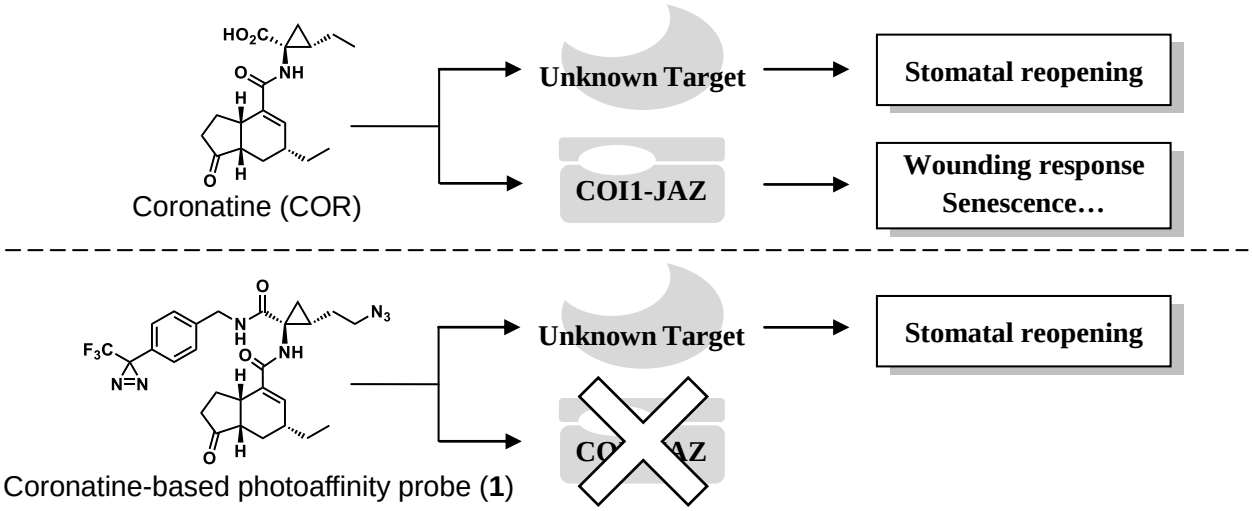

Fig. 1. Bioactivity-uncoupled coronatine-based photoaffinity probe (**1**) to identify the unknown target involved in stomatal reopening.

Ref. [1] S. Y. He *et al.*, *Cell* **2006**, *126*, 969-980.

p-4

A Multi-reactive Molecule for Imprinting of Peptides and Proteins

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Key words: Molecular Imprinting, Biomolecules

Molecular imprinting is a powerful methodology to develop a synthetic receptor for molecular recognition. The typical method of imprinting is to polymerize a monomer in the presence of a target substrate such as small synthetic molecules and biomarcromolecules, followed by removal of the target to obtain polymerized products containing imprinted cavities. Although the reaction is carried out in a solution phase, the products are usually insoluble solid, which is useful as filler particles for affinity chromatography and so on.

In this study, we have been developing soluble imprinting materials, where the solubility is advantageous for processing properties and post-modification. We chose peptides and proteins as the targets for bio-related applications of the imprinting products. As the polymerizing material to imprint the target, poly(ethylene glycol) was chosen because of its high solubility in both aqueous and organic media and high biocompatibility.[1] For the molecular imprinting of a peptide, it is required for the poly(ethylene glycol) to contain multi-reactive points for binding with the target and polymerization. We designed a multi-functional poly(ethylene glycol) derivative with two orthogonal pairs of reactive points as the monomer. Detailed results about the synthesis of the imprinting monomer and some preliminary results about the imprinting process will be presented.

[1] T. Muraoka, K. Kinbara *et al.*, *Angew. Chem. Int. Ed.* **2013**, *52*, 2430–2434; T. Muraoka, K. Kinbara *et al.*, *Biochem. Eng. J.* **2014**, *86C*, 41–48; T. Muraoka, K. Kinbara *et al.*, *Chem. Lett.* **2014**, *43*, 1055–1057; T. Muraoka, K. Kinbara *et al.*, *Chem. Asian J.* **2014**, *9*, 2778–2788; T. Muraoka, K. Kinbara *et al.*, *Chem. Commun.* **2015**, *51*, 8457–8460.

Fabrication of Charge-Transfer Complex Nanocrystals and Chemical Doping Effects to Optoelectronic Properties

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Key words: Charge-transfer complex, Reduction-coprecipitation method, Chemical doping

Charge-transfer complexes composed of donor (D) and acceptor (A) are an interesting research subject because of their versatile characteristics such as optical properties, conductivity, and magnetism. These physical properties are determined by the degree of charge transfer γ($D + A \rightarrow D^{+\gamma}A^{-\gamma}$) and crystal structure. So far, we have developed the coprecipitation method with chemical reduction, in which nanocrystallization proceeds, involving chemical doping process so as to control the γ. This method has been employed to copper 7,7,8,8-tetracyanoquinodimethane (Cu-TCNQ)[1] (Fig.1), and insoluble complexes of Cu^+ and $TCNQ^-$ were first formed, and then excess amount of Cu atoms was taken into nanocrystals (NCs) as a dopant during growth of NCs. In the present study, how to control the crystal size and amount of dopants, and the doping effects for the physical properties have been investigated in detail.

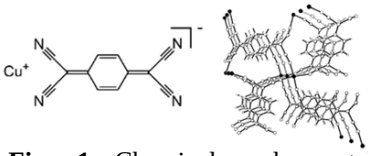

Fig. 1 Chemical and crystal structure of Cu-TCNQ complex

Cu-TCNQ NCs have been fabricated successfully by the coprecipitation method with chemical reduction. The crystal size and amount of dopant Cu^+ increased with raising temperature. As a result, we were able to control crystal size of Cu-TCNQ NCs with a rod-like shape in the range of 50 nm to 800 nm along the longitudinal axis (Fig. 2). Next, the composition ratio of Cu to TCNQ was investigated by elemental analysis. The Cu-TCNQ NCs fabricated at 15°C and 30°C were found to be Cu:TCNQ = 1.3:1 and 1.7:1, respectively. On the other hand, the powder X-ray diffraction patterns show that both Cu-TCNQ NCs were assigned to the segregated stacking structure (Fig.1), being identical to bulk crystal (Cu:TCNQ = 1:1), in spite of the different composition. Therefore, the resulting Cu-TCNQ NCs can be regarded as doped Cu-TCNQ NCs.

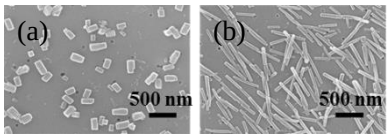

Fig. 2 SEM images of Cu-TCNQ nanocrystals prepared at (a) 15°C and (b) 30°C

Figure 3 shows Vis-NIR extinction spectra of doped Cu-TCNQ NCs. The doped Cu-TCNQ NCs exhibited a new strong extinction peak in NIR region. Interestingly, the peak strength and positions were dependent on crystal size of the NCs. The detail of chemical doping process and effects will be discussed on that day.

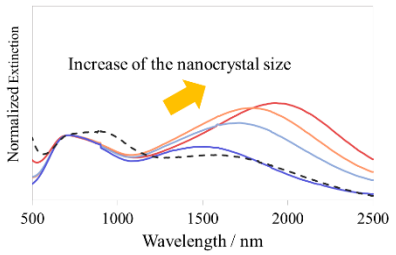

Fig. 3 Vis-NIR extinction spectra of doped Cu-TCNQ NCs (solid lines) and Cu-TCNQ bulk crystal (a broken line)

Ref : 1. R.A. Heintz *et al.*, *Inorg. Chem.*, **1999**, *38*, 144-156

Nonlinear Optical Response of Polydiacetylene Nanomaterials

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Key words: organic nanocrystals, nonlinear optical property, reprecipitation method

Polydiacetylene (PDA), classified as a one-dimensional π-conjugated polymer, has been known as one of the most promising materials for photonic devices, due to high third-order nonlinear optical (NLO) susceptibility $\chi^{(3)}$ and ultrafast NLO response in femto-second region. On the other hand, recently PDA nanomaterials have been intensively studied for realizing superior properties to bulk materials. For example, excitonic absorption (EA) peak position in nanofiber (NF) of poly[1,6-di(*N*-carbazolyl)-2,4-hexadiyne] (polyDCHD) [Fig. 1] (λ_{max} = 660 nm) was interestingly red-shifted, compared with that in the corresponding bulk crystal (λ_{max} = 655 nm)[1], which is expected to enlarge $\chi^{(3)}$, according to simplified three-level model. In the viewpoint of application into photonic devices, it is very important to fabricate assembled thin film with highly optical quality. PolyDCHD NFs could provide oriented thin films with low scattering loss, which would enable us to overcome the problem in processability of organic bulk crystals. In the present research, we have fabricated well-defined polyDCHD nanocrystals (NCs) and NFs and their assembled thin films, and tried to investigate the size-dependence of $\chi^{(3)}$ in polyDCHD NCs and NFs.

We succeeded in fabricating various polyDCHD NCs and NFs [Fig. 2] by the reprecipitation method[2] under various conditions such as temperature, concentration and addition of surfactant, and their polyvinyl alcohol (PVA) composite thin films. Transient transmittance spectroscopy has clarified the size-dependence of NLO response in polyDCHD NCs and NFs for the first time [Fig. 3]. The measurement of complex refractive index with ellipsometry is now in progress for analyzing $\chi^{(3)}$ of polyDCHD NCs and NFs.

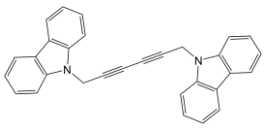

Fig.1. Structure of DCHD

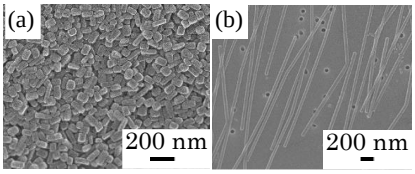

Fig.2. SEM images of polyDCHD nanocrystals

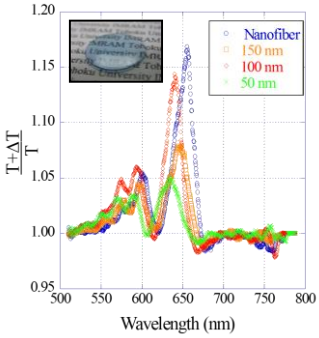

Fig.3. Transient transmission spectrum of various sizes of polyDCHD

Ref.1. Onodera *et al.*, *M&BE.* 2014, **25**(2), 97-100., and under preparation.
Ref.2. H. Kasai *et al.*, *Jpn. J. Appl. Phys.* 1992, **31**, 1132-1134.

Synthesis of 1,3-*syn*-diol using asymmetric al1dol reaction and oxy-Michael reaction

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Key words: Diarylprolinol, Asymmetric aldol reaction, Oxy-Michael reaction, 1,3-*syn*-diol

1,3-*syn*-diol is a useful building block found in natural products and medicines. Therefore, the development to the synthesize 1,3-*syn*-diol structure is very important. Recently, we have found trifluoromethyl substituted diarylprolinol **1** to be an effective organocatalyst in asymmetric, catalytic direct aldol reaction with alkynyl aldehyde. Evans' group reported the synthesis of 1,3-*syn*-diol using oxy-Michael reaction with bismuth nitrate with high selectivity (Fig. 1).[1] In our synthesis of 1,3-*syn*-diol, asymmetric aldol reaction and oxy-Michael reaction using bismuth proceeded smoothly to give the acetal compound **4** with a diastereomeric ratio of 1:1. These aldol and oxy-Michael reactions can theoretically provide four isomers **4a**, **4b**, **4c** and **4d**, but those relative configurations have not been determined (Scheme 1). Therefore, we are converting oxy-Michael product **4** to **5** to determine the newly generated chiral center (Scheme 2).

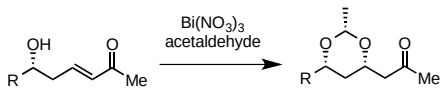
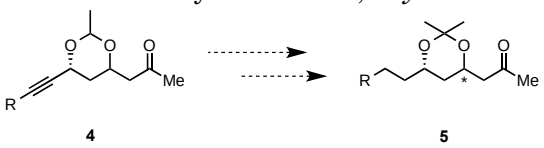
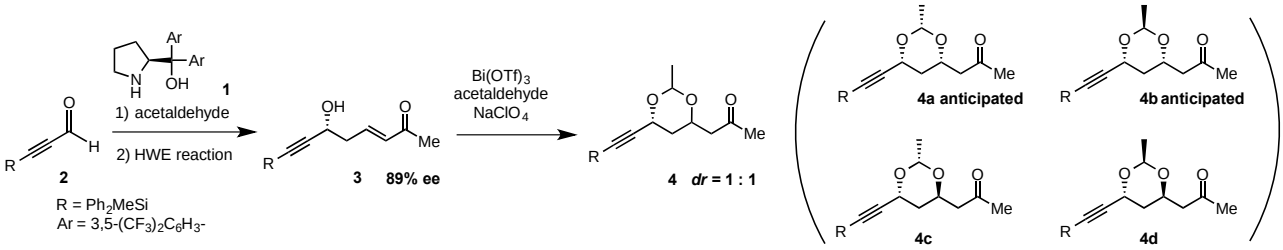


Fig. 1. Evans' method of 1,3-*syn*-diol

Scheme 1. Synthesis of 1,3-*syn*-diol



Scheme 2. Determination of the stereochemistry of



Reference, 1) P. A. Evans *et al., J. Am. Chem. Soc.*, **2012**, *134*, 2856.

Synthesis of chiral di-substituted cyclopentenone via diphenylprolinol silyl ether mediated asymmetric Michael reaction as a key step

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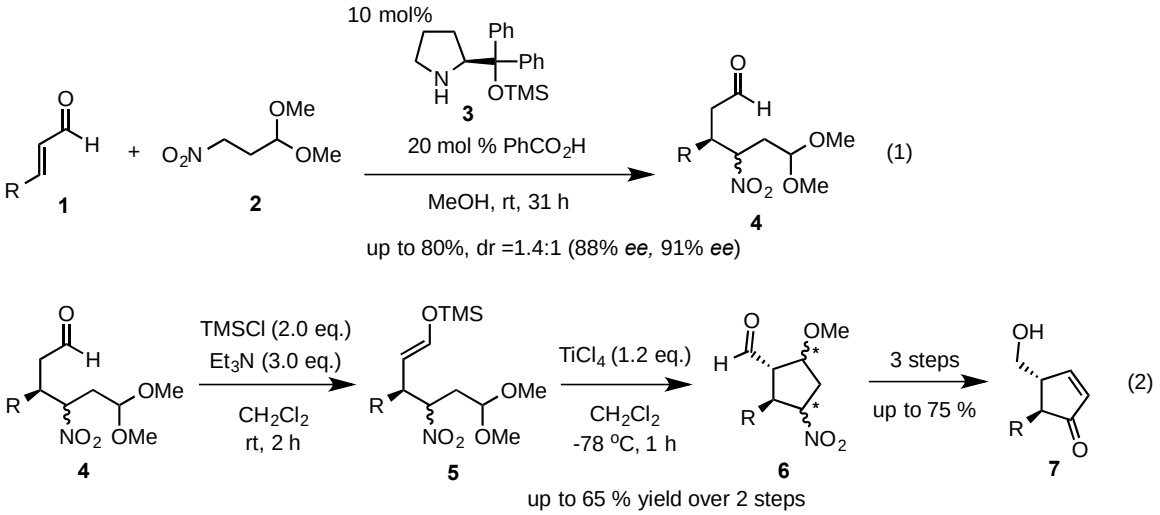
Key Words: Organocatalyst, Diphenylprolinol silyl ether,
Asymmetric Michael reaction, Cyclopentenone, Mukaiyama aldol reaction

Cyclopentane skeleton is an important framework in organic chemistry because there are many natural products and drugs possessing this structure. The field of Organocatalyst has grown very rapidly and there are several reports to prepare this skeleton using organocatalyst. I have been investigating the synthesis of cyclopentane via organocatalyst mediated asymmetric Michael reaction with nitro compound.[1]

I examined asymmetric Michael reaction of β-substituted propenal **1** and 3-nitropropanal dimethyl acetal (**2**) in the presence of diphenylprolinol silyl ether **3** as a catalyst (Eq. 1). Desired aldehyde **4** was obtained in good yield and good ee. Michael adduct **4** was converted to silyl enol ether **5**, which was subjected to Mukaiyama aldol reaction using titanium chloride as a Lewis acid. These two steps afforded cyclopentane compound **6** in moderate to good yield. After reduction, Nef reaction using dimethyldioxirane (DMDO) and elimination reaction, di-substituted cyclopentenone **7** was obtained as a single isomer (Eq. 2).



Scheme 1. Synthetic route of cyclopentenone **7**

Ref. [1] H. Gotoh, H. Ishikawa, and Y. Hayashi, *Org. Lett.*, **9**, 5307 (2007).

Asymmetric aldol reaction of dichloroacetaldehyde catalyzed by diarylprolinol

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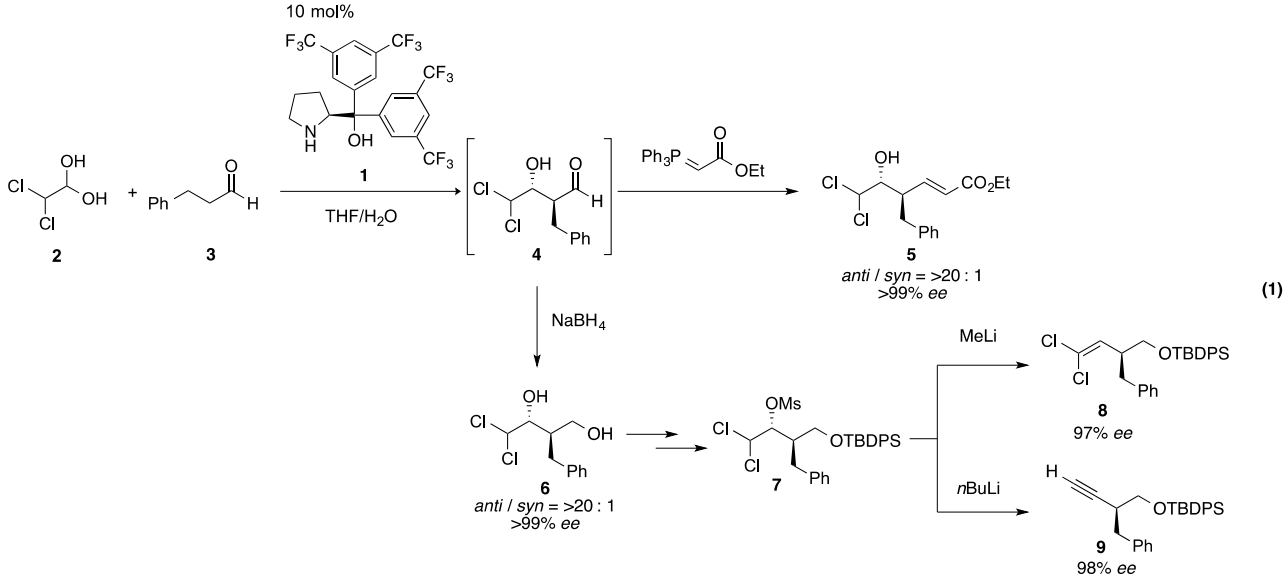
Key words: Organocatalyst, asymmetric synthesis, aldol reaction, dichloroacetaldehyde

The asymmetric cross-aldol reaction is a useful method to obtain chiral β-hydroxy carbonyl compounds.[1,2] In particular, the cross aldol reaction of dichloroacetaldehyde provides synthetically useful γ,γ-dichloro-β-hydroxy aldehydes, whereby the dichloromethyl moiety can be transformed into several other functional groups. We found that diarylprolinol **1**, developed by our group, acts as an effective catalyst in the asymmetric aldol reaction of dichloroacetaldehyde, to provide corresponding γ,γ-dichloro-β-hydroxy aldehydes in good yield with excellent enantioselectivity (Eq. 1). The reaction was performed by employing dichloroacetaldehyde hydrate **2**, nucleophilic aldehyde **3**, and catalyst **1** at room temperature. Aldol product **4** was directly converted into α,β-unsaturated ester **5** and diol **6**. Products **5** and **6** showed good diastereomeric ratio and excellent enantiomeric excess. Diol **6** was converted into dichloroolefin **8** and alkyne **9**, which would be a useful chiral building block, without erosion of enantiomeric excess.



Reference:

1) Y. Hayashi *et al*. *Angew. Chem. Int. Ed.*, **2008**, *47*, 2082-2084.
2) Y. Hayashi *et al*. *ChemCatChem*, **2015**, *5*, 2887-2892.

Synthesis of Phenanthrene Derivatives Utilizing [1,2]-Phospha-Brook Rearrangement Catalyzed by Brønsted Base

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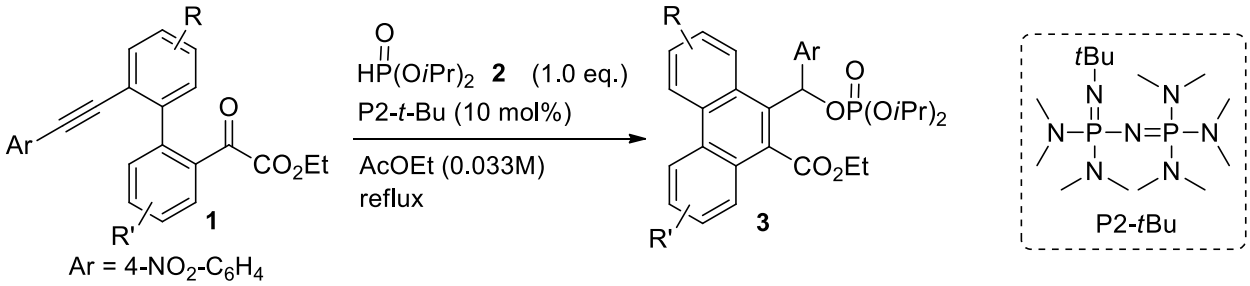
Key words: Phospha-Brook Rearrangement, Base Catalysis, Intramolacular Cyclization, Tandem Reaction, Phenanthrene

[Introduction]

Phenanthrene derivatives have attracted great attention because of their presence in numerous natural products as well as their interesting biological activities. They are also an important structural motif in material science. Therefore, development of general and efficient methods for the synthesis of highly functionalized phenanthrene derivatives is imperative in organic synthesis, and massive efforts have been undertaken over the years. However, there still remained some limitations on introduction of functionalities into the resulting phenanthrene skeleton in a regioselective manner. Therefore, the new efficient methodology that can expand the scope of the accessible phenanthrene derivatives would be highly valuable.

[Result]

In this context, we designed a new method for the synthesis of highly functionalized phenanthrene derivatives utilizing the [1,2]-phospha-Brook rearrangement under Brønsted base catalysis. Treatment of biaryl compounds **1** having an α-ketoester moiety and an alkyne moiety at 2 and 2' position with diisopropyl phosphate (**2**) in the presence of a catalytic amount of phosphazene base P2-*t*Bu provided 9,10-disubstituted phenanthrene derivatives **3** in high yields. This reaction involves the generation of an ester enolate via umpolung process, that is the addition of diisopropyl phosphate to a keto moiety followed by the [1,2]-phospha-Brook rearrangement, intramolecular addition to an alkyne, and [3,3]-rearrangement of allylic phosphate moiety in a consecutive fashion.



Gold-Catalyzed Skeletal Rearrangement of *O*-Propargylic Formaldoximes via Intermolecular Methylene Group Transfer

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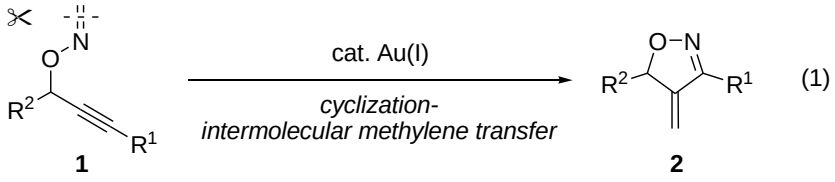
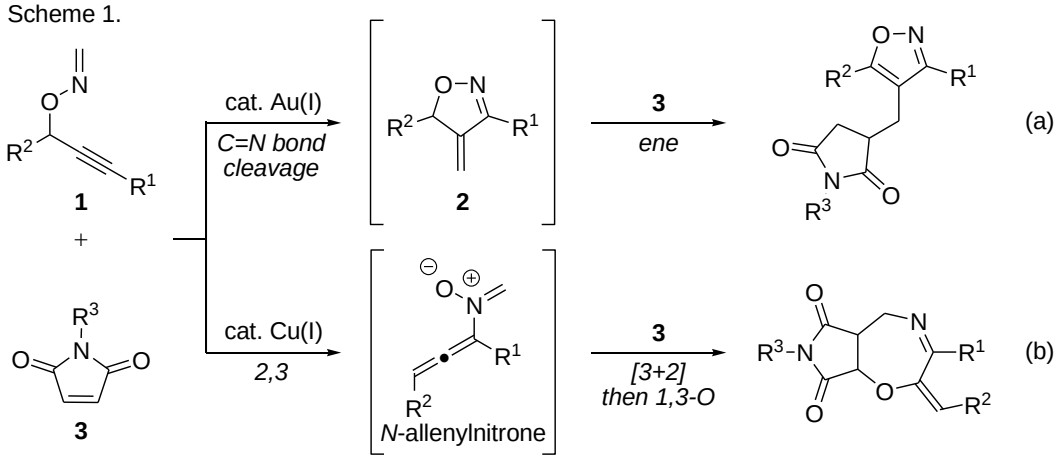
Key words: rearrangement, gold catalyst, heterocycles, cascade reaction, ene reaction

Skeletal rearrangement reactions have served as attractive transformations constructing highly functionalized molecular frameworks in a single step. Recently, we have reported that copper catalyzed skeletal rearrangement of *O*-propargylic oximes proceeds via C-O bond cleavage.[1] In this work, we reported that gold catalyzed skeletal rearrangement of *O*-propargylic formaldoximes afforded 4-methylene-2-isoxazolines in good to excellent yields via C=N bond cleavage (eq. 1).[2] The reaction proceeds through cyclization/intermolecular methylene group transfer. In addition, the cascade reaction with maleimide in the presence of a gold catalyst afforded isoxazole derivatives by cyclization/intermolecular methylene group transfer and a subsequent ene reaction (scheme 1a), whereas that using a copper catalyst gave oxazepines through 2,3-rearrangement/[3+2] cycloaddition/1,3-oxygen migration (scheme 1b).[3] These results indicate that the reaction pathway of the π-acidic metal-catalyzed cascade reactions can be controlled by selecting the appropriate metal catalysts.



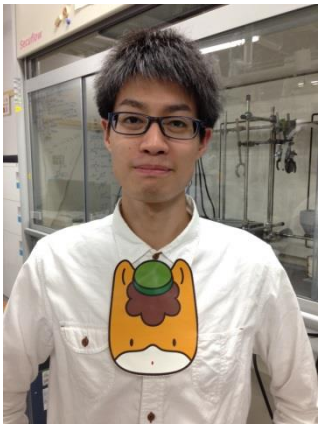
Scheme 1.



[1] Nakamura, I.; Zhang, D.; Terada, M. *J. Am. Chem. Soc*. **2010**, *132*, 7884.
[2] Nakamura, I.; Gima, S.; Kudo, Y.; Terada, M. *Angew. Chem., Int. Ed.* **2015**, *54*, 7154.
[3] Nakamura, I.; Kudo, Y.; Terada, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 7536.

p-15

Efficient Synthesis of 3-Aryloxindoles Utilizing [1,2]-Phospha-Brook Rearrangement and Palladium-Catalyzed Cross-Coupling Reaction



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Key words: Oxindole Derivatives, Phospha-Brook Rearrangement, Cross-Coupling, Palladium Catalyst, Relay Catalysis

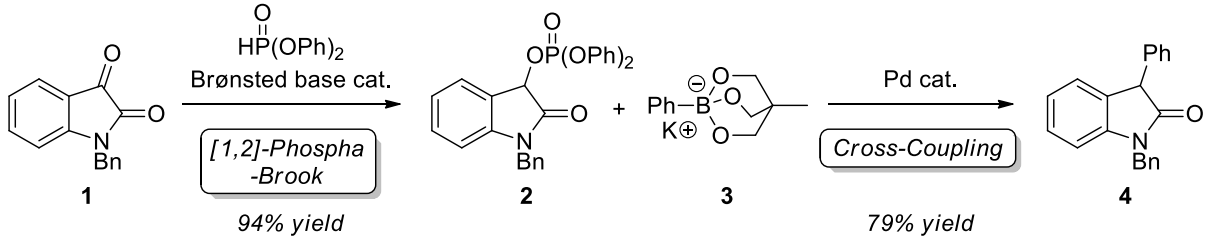
[Introduction]

Oxindole derivatives with C-3 functionalities are common motifs in biologically active natural product as well as pharmaceuticals. Among them, C-3 aryl oxindoles are not only one of privileged subclasses but also serve as valuable building blocks in organic syntheses. Generally the synthesis of C-3 aryl oxindoles involves arylation of isatin derivatives using aryl metal reagents, such as aryl lithium reagents and aryl Grignard reagents, followed by dehydroxylation. The alternative approach is palladium-catalyzed C-3 arylation of oxindoles, which are generally synthesized by reduction of isatin derivatives. Although both approaches are reliable, they include harsh reductive conditions for the synthesis of C-3 aryl oxindoles from isatin and thus there remains the issue on the functional group tolerance. In this context, we investigated a new approach toward C-3 aryl oxindoles from isatin derivatives, that is [1,2]-phospha-Brook rearrangement of isatin derivatives under Brønsted base catalysis followed by cross-coupling reaction under palladium catalysis (Scheme 1).

[Result and Discussion]

The first step of our synthesis was the transformation of isatin derivatives **1** into phosphate **2** by treatment of **1** with diphenyl phosphite in the presence of a catalytic amount of Brønsted base. Phosphate **2** thus synthesized was then subjected to the conditions for cross-coupling with aryl boron reagents **3** to provide the desired 3-aryloxindole derivatives **4** in good yield.

Scheme 1. A new approach towards the synthesis of 3-aryloxindole.



Synthesis of Nucleoside Analogues as Jointing Units for Chimeric Oligonucleotides with Triazole Linkages toward Functional RNA Molecules

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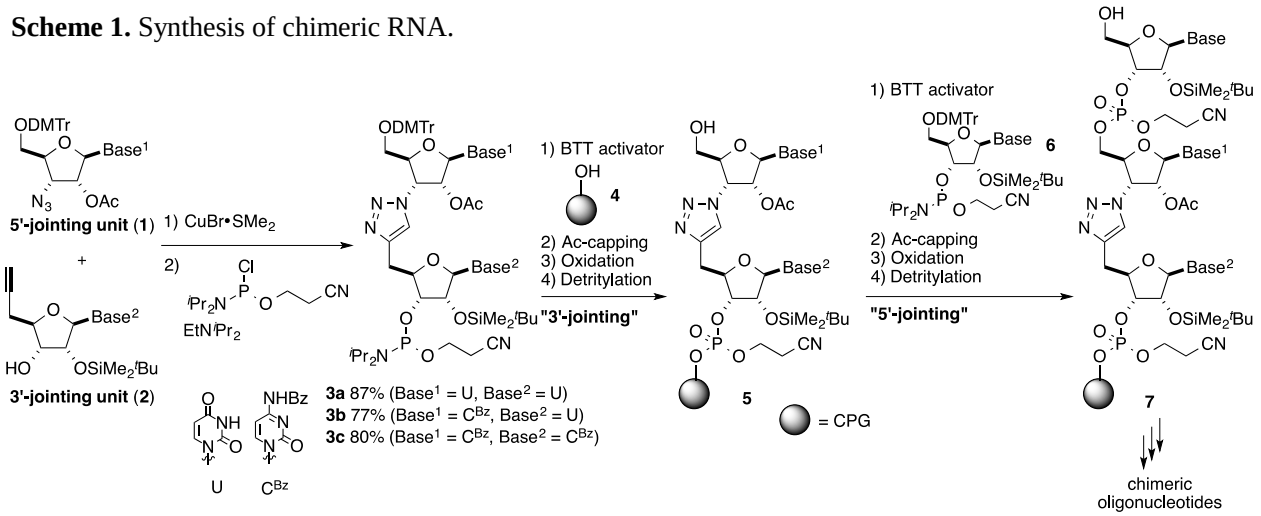
Key words: RNA, chimeric oligomer, triazole, phosphoramidite method, siRNA

Phosphate-replaced RNA analogues possessing furanose rings are attracting interest as a biological tool, because they can serve as substrates for enzymatic reactions despite their inertness toward nuclease hydrolysis. The phosphate-replaced RNA analogue with triazole linkers (^{TL}RNA) has been developed in our group.[1] The ^{TL}RNA analogues, however, were not proven useful for any biological functions, because of the poor solubility of oligomers. In this study, we revised the structure to incorporate the triazole linkers in chimeric oligonucleotide structures with a combination with natural phosphate linkers.

The fundamental units in this study were 5'- and 3'-jointing units (**1**, **2** in Scheme 1). The jointing units were then coupled by copper-catalyzed Huisgen reaction, and the dinucleotide was converted to phosphoramidites **3**. The phosphoramidites were tolorated in automated synthesis protocols for natural RNA, and a series of chimeric oligonucleotides was prepared using the phosphoramidite method. The chimeric oligonucleotides were examined for a screening study of RNA interference to clarify the preference of the modifications.

Scheme 1. Synthesis of chimeric RNA.



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Development of Synthetic Chiral Transmembrane Molecule

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Key words: Protein mimics, Self-assembly, Transmembrane protein

Multipass transmembrane protein is known to perform important biological functions such as ion transportation and signal transduction. These functions are known to be regulated by external stimuli such as light, ligands and chemical reactions. The multipass transmembrane structure, a fundamental higher-order structure of membrane proteins, is developed by folding of a multiblock amphiphile with repeating hydrophilic and hydrophobic parts. The hydrophobic parts penetrate a hydrophobic layer of a bilayer membrane while the hydrophilic parts protrude from the lipid bilayer, allowing formation of the folded conformation in a bilayer. Inspired by such natural systems, we have been developing synthetic molecules, consisting of hydrophobic aromatic parts and hydrophilic oligoethylene glycol chains to form a multipass transmembrane structure.[1] It has been revealed that the synthetic multipass transmembrane molecule is capable of ion transportation by the formation of supramolecular ion channels.[2] Furthermore, in our recent study, the first synthetic ion channel whose ion transportation function could be reversibly regulated by attachment and detachment of an organic ligand has been successfully developed.[3]

To realize such dynamic function, detection of the conformational changes at the membrane-penetrating parts is of importance. In this study, we have developed a chiral multiblock amphiphile, where the chirality at the hydrophobic parts is expected to give the conformational information in the membrane by circular dichroism spectroscopy. In this presentation, we report details about the synthesis of the chiral transmembrane amphiphiles as well as their spectroscopic and microscopic characterization.

[1] T. Muraoka, K. Kinbara *et al*., *Chem. Commun.* **2011**, *47*, 194–196 (Hot Article).
[2] T. Muraoka, K. Kinbara *et al.*, *J. Am. Chem. Soc*. **2012**, *134*, 19788–19794.
[3] T. Muraoka, K. Kinbara *et al*., *J. Am. Chem. Soc*. **2014**, *136*, 15584–15595.

p-20

Development of Photoresponsive Functional Material Utilizing the Engineered Photoactive Yellow Protein

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Key words: Photoactive Yellow Protein, Photoreceptor Protein, Photoresponsive Material

Proteins are expected to be applied in a wide range of fields because of their high functionality, biocompatibility, biodegradability, and molecular size. Photoactive yellow protein (PYP) is known as a photoreceptor and exhibits a photocycle in response to visible light. PYP contains a *p*-coumaric acid derivative as a chromophore, which binds to Cys69 via a thioester bond. This chromophore undergoes *trans*-to-*cis* photoisomerization by irradiation with blue light, which causes unfolding of the protein, followed by thermal *cis*-to-*trans* isomerization to recover the initial trans configuration at room temperature. [1,2] Application of PYP to hybrid materials using site-specific modification via cysteine residues is limited because PYP contains a cysteine residue which is the important part for bearing the chromophore. Here, we constructed a specifically-modified PYP with hydrophilic synthetic compound and applied it to functional materials. In this presentation, we report details about the synthesis of hydrophilic synthetic compounds and properties of the modified PYP and functional materials.

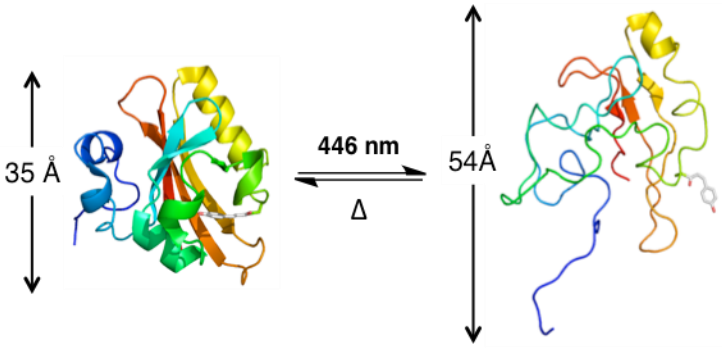

Figure 1. Photoinduced structural change of PYP

[1] Michael A. Cusanovich, Terry E. Meyer, *Biochemistry* **2003**, *42*, 4759–4770.

[2] Pradeep L. Ramachandran, Jasper J. van Thor, *J. Am. Chem. Soc.* **2011**, *133*, 9395–9404.

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Construction of PEG-incorporated Synthetic Protein

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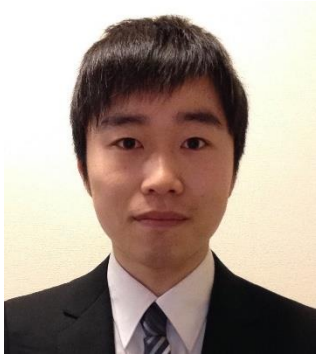
Key words: Synthetic Protein, Polyethylene glycol, PEGylation,

Proteins are attractive molecules as biomaterials and therapeutic reagents due to its highly sophisticated functions and possible design of its amino acid sequence by well-developed gene-engineering technology. One of the problems to use proteins for such applications is its poor stability, where proteins tend to denature upon physical and chemical stresses and be degraded by enzymes. To enhance their stability, surface modification of proteins by cross-linking reagents or water-soluble polymers such as poly(ethylene glycol) with large excluded volumes has been developed.
As a new approach to enhance the stability, we have been trying to replace a part of protein molecule with a synthetic component.[1] It is expected that the synthetic part would not be hydrolyzed by protease, so that the semi-synthetic protein could acquire longer lifetime than the native molecule. Bovine carbonic anhydrase II was chosen as the target protein for demonstration, because of the known crystallographic structure and activity assay. We combine synthetic reactions in aqueous media and gene-engineering technology conducted in *E. coli* for the development of a semi-synthetic protein. Details on the research concept, synthesis and characterizations will be presented.

[1] M. Ui, K. Kinbara *et al. Mol. BioSyst.* **2014**, *10*, 3199–3206.

Development of chemically reactive threading intercalator targeting RNA



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Key words: RNA, intercalator, rotaxane, click reaction

Interlocked molecular architectures such as rotaxanes and catenanes have the property that two constituent molecules cannot be separated without bond cleavage although they do not form covalent bond directly (Fig. 1). We focus on this unique property, and are developing the method for forming the interlocked structure targeting nucleic acids, especially RNA.[1] Formation of the interlocked structure targeting RNA with small molecules would be a new tool to inhibit the generation of miRNA and for DNA/RNA nanotechnology.

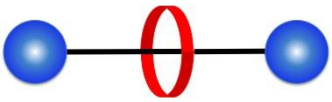

Fig. 1. Graphical representation of a rotaxane.

In this research, we designed a chemically reactive threading intercalator to bind to the bulge structure in RNA. We expect that the intercalator threading into dsRNA will react with the reactive linker via click and S_N2 reaction, and form an interlocked architecture as shown in Fig. 2. First, we synthesized 9-anilinoacridine-4-carboxamide derivative (**1**) with a chloroacetoamide group and an azide group as reactive parts (Fig. 3A). The reactive linker with a thiol group and a DBCO group was synthesized as a disulfide precursor (**2**) which can be generated the nucleophilic thiol by using DTT or gluthathione *in situ* (Fig. 3B). The interlocked formation targeting RNA using **1** and **2** is now ongoing. In this poster, we would like to report the synthesis and the result of the interlocked structure formation with RNA.

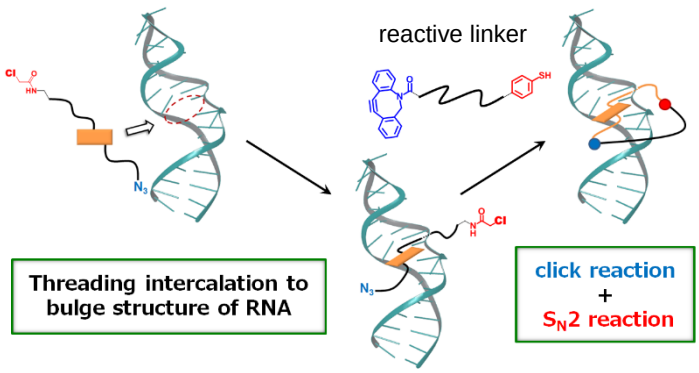

Fig. 2. Reaction for the Interlocked structure formation

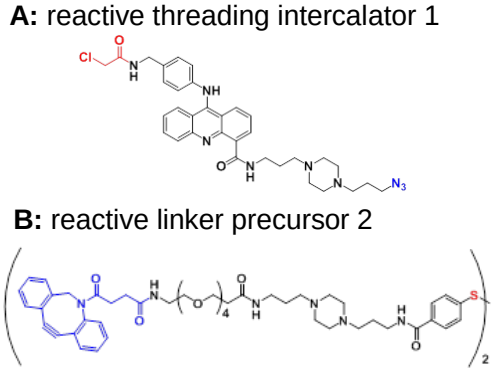

Fig. 3. Structure of reactive molecules.

[1] K. Onizuka, F. Nagatsugi, Y. Ito, H. Abe, *J. Am. Chem. Soc.* **2014**, *136*, 7201.

Synthesis and Evaluation of the Reactivity of 7-Deaza-6-vinylguanosine Derivatives

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Key words: Organic synthesis, Nucleic acid chemistry, Chemical biology

Various synthetic oligonucleotides have been developed to inhibit gene expressions by binding to the target DNA or mRNA. Recently, we have developed 2′-OMe-RNA containing 2-amino-6-vinyl purine (2-AVP) to induce uridine (U)-selective interstrand cross-linking formation (Fig. 1) [1].

However, the slow cross-linking (CL) reactions of AVP with the target uracil could be one of the obstacles to perform intra-cellular crosslinking. We assumed that the slow reaction rate of AVP can be attributed to the equilibrium between two conformations, s-cis and s-trans. Based on this hypothesis, we designed the 7-deazaguanine derivative anticipating to be fixed the s-cis conformation with favorable for the crosslinking reaction by the steric repulsion between vinyl group and the substituent at 7 position (Fig. 2). The 7-deazaguanine can be introduced the 7-substituents stably, and 7-alkynyl- 7-deaza-AVP would make it possible to synthesize a variety of compounds with substituted at the 7-position via Huisgen reaction.

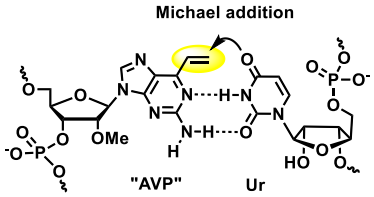

Fig. 1 Cross-link AVP with

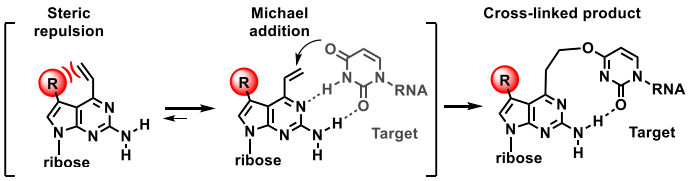

Fig. 2 Control of the orientation of vinyl group by steric effect of 7-substituents.

The ribonucleoside (**3**) was prepared by glycosylation of acyl-protected ribose (**1**) with halogenated base (**2**) [2]. After deprotection nucleoside **(4)** and substitution of chlorine with sodium methoxide, the selective methylation of 2′-hydroxy group was performed to produce **5**. The chemical functionalization of the nucleobase of **6** was successfully carried out by Sonogashira cross-coupling, Stille coupling to produce **6**. The synthesis of **CFO1** is now ongoing. We would like to present the synthesis and the reactivity of **CFO1**

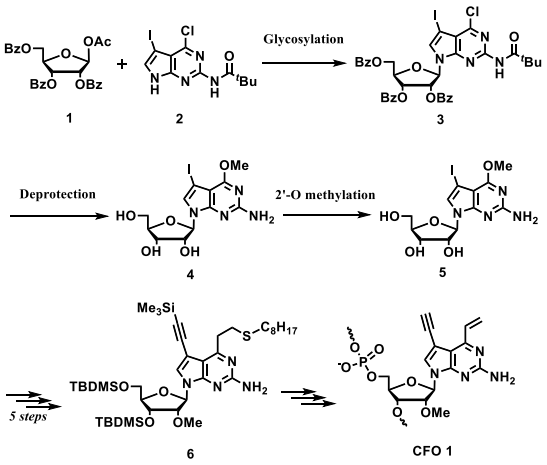

Fig. 3 Synthetic scheme of CL-nucleoside

Reference: [1] Hagihara, S. *et al*, *Bioorg. Med. Chem. Lett.* **2012**, 3870-3872 [2] Seela, F. *et. al*., *J. Org. Chem.* **2006**, *71*, 81-90

Synthesis of vinyltriazine derivatives aiming at alkylation to U–U mismatch structure in RNA.

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Key words: RNA, Alkylation, Mismatched base pair, Molecular recognition

Myotonic dystrophy type 1 (DM1) is one of the genetic disorders caused by RNA with aberrantly expanded CUG triplet repeats (r(CUG)^{exp}), which inactivates the alternative splicing regulators such as muscleblind-like 1 (MBNL1) (**Fig. 1**). Recently, some researches showed that U-U mismatches can be formed as a high-order structure of r(CUG)^{exp}.[1] Accordingly, the development of the U–U mismatch structure-recognizing and -binding molecules is important for discovery of a new therapy of DM1. Zimmerman's group has developed triaminotriazine-acridine conjugates as the U–U mismatch recognizing molecules.[2]

In this study, we have designed and synthesized the acridine-conjugated 2-vinyl-4,6-diamino-s-triazine (VDAT) derivative (**1**) aiming at the selective alkylation to the U–U mismatch base pairs in RNA (**Fig. 2**). We expected that the molecules formed five hydrogen bonds in the U–U mismatch and induced the selective alkylation to U by the proximity effect (**Fig. 3**).

The reactivity of VDAT derivative (**1**) was evaluated using duplex DNAs containing one mismatch base pair and full-matched DNA. The probe (**1**) reacted to T–T mismatch structure with high selectivity and did not react to full-matched DNA (**Fig. 4**). On the other hand, probe (**1**) showed low reactivity to the duplex RNAs. In this poster, we will report the detail of these experiments on the alkylation using VDAT derivatives to the duplex DNA and RNA.

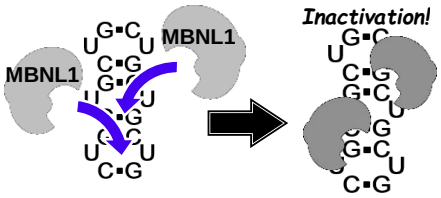

Fig. 1. Formation of CUG–MBNL1 complex and deactivation of MBNL1.

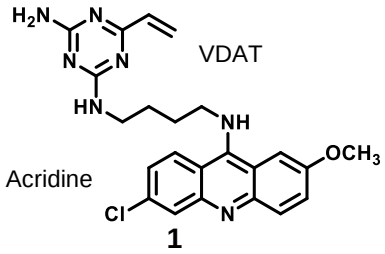

Fig. 2. VDAT derivative (**1**).

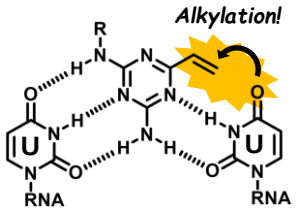

Fig. 3. Hydrogen bonding recognition and reaction to U–U mismatch.

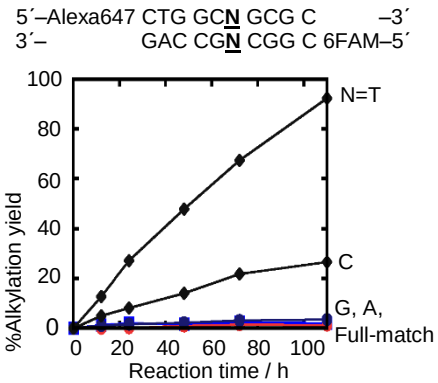

Fig. 4. Alkylation yields using DNA.

1. Berglund, J. A. et al. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, 102, 16626–16631.
2. Zimmerman, S. C. et al. *Proc. Natl. Acad. Sci. U.S.A.* **2009**, 106, 16068–16073.

Development of small molecular probes for selective alkylation in the higher-order structure of nucleic acids.

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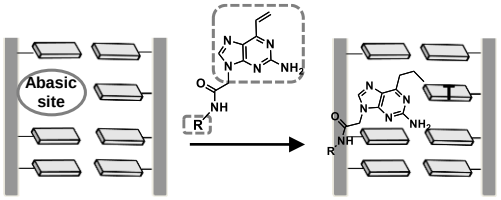
Key words: AP site, DNA alkylation

Recently, the higher-order structure of nucleic acids is known to play an important role in the regulation of gene expressions. The chemical probes to react specifically with such a regulatory structure of nucleic acids should be beneficial tools for controlling gene expressions. We designed the new probes for reactions involving an abasic site (AP site) in duplex DNA. This probe consisted of 2-amino-6-vinylpurine (AVP) as a reactive molecule activated by forming hydrogen bond to target base[1] and Hoechst 33258 as a DNA binding molecule. The Hoechst-AVP probe exhibited high selectivity and efficient reactivity to thymine bases at the site opposite an AP site in DNA (**Fig. 1**). In this study, we developed Hoechst-7-deaza-2-amino-6-vinylpurine (DAVP) probe, which enabled to introduce the functional group at a 7 position. This probe was expected to be selective labeling in the AP site after crosslinking formation (**Fig. 2**).



R = Hoechst

Fig. 1. Alkylation of the thymine at the opposite site of an AP site

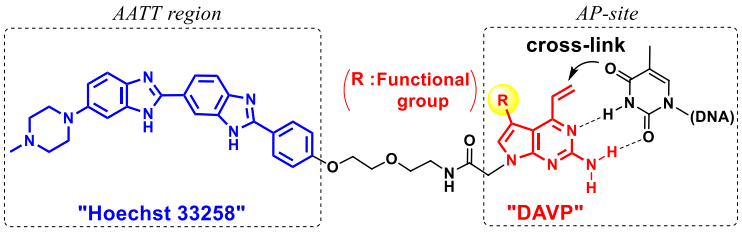
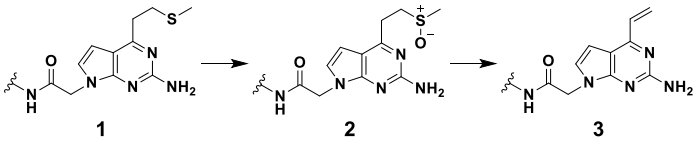


Fig. 2. Structure of Hoechst-DAVP

The chemically stable precursor **1** was successfully synthesized. The sulfide-protected derivative was oxidized by magnesium monoperphthalate (MMPP) following an alkaline treatment to produce an activated form of the conjugate **3** (**Scheme 1**). The reactivity of probe **3** was evaluated using duplex DNA containing an AP site and fully-matched DNA. Our probe **3** selectively reacted with thymine base in AP site under neutral condition. We will report these results in detail.

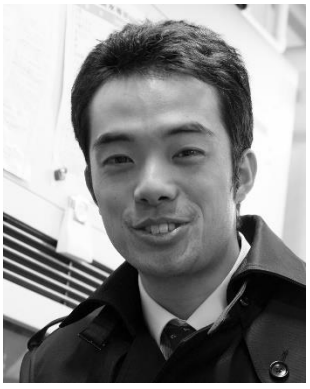


Scheme 1. Regenerate vinyl group of the probe **3**

[1] S. Hagihara, S. Kusano, W. C. Lin, X. G. Chao, T. Hori, S. Imoto and F. Nagatsugi, *Bioorg. Med. Chem. Lett.*, 2012, **22**, 3870.

[1] Fujino, T.; Endo, K.; Yamazaki, N.; Isobe, H. *Chem. Lett.* **2012**, *41*, 403-405.

Synthetic study of organic catalysts containing Lewis acidic moieties and Lewis basic moieties



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Key words: asymmetric catalyst, Lewis acid, Lewis base

In recent years, activation of less reactive small molecules, such as molecular hydrogen, carbon dioxide and so on, by use of combination of bulky Lewis acids and Lewis bases (frustrated Lewis pairs, FLPs) is attracting attention of many organic chemists. In such systems, the Lewis acids and Lewis bases cannot interact directly each other because of their steric factor, therefore, both Lewis acids and Lewis bases can effectively activate substrate molecules (**Fig.** 1). This methodology seems powerful, however, successful examples especially application to asymmetric reaction are still limited.

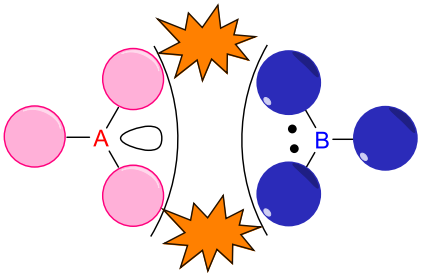
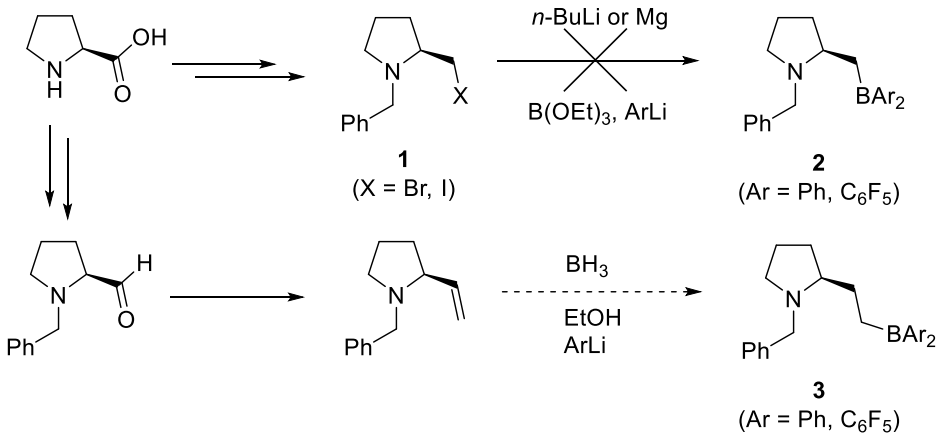


Fig. 1. Concept of FLPs

Our group have been developing chiral discriminating agents which can form host-guest complexes through multiple Lewis acids –base interactions and we examine to apply these agents for the use as chiral FLPs with slight modification.

We designed chiral FLPs **2**, **3**. The Lewis acid moieties of these molecules are covalently bonded to the chiral backbone, therefore, improvement in handiness was expected. Synthesis of **2** was planned via the compound **1**, however, metalation of **1** did not successfully proceed by alkyllithium reagent nor under Grignard conditions. The reason of these results can be attributed to the instability of the compound **1** itself. Degradation of **1** takes place in several days even at –30 °C. We then put our hand to preparation of another candidate. Currently, synthesis of **3** is undergoing.



Substituent Effects on the Structures of 1,3-Disilabicyclo[1.1.0]butanes

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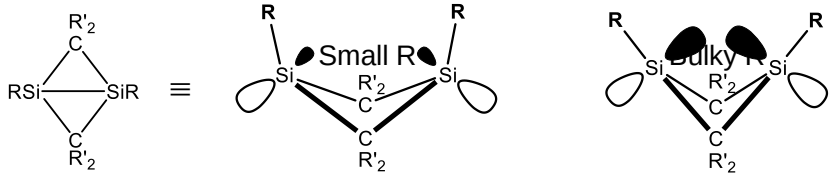
Key words: silicon, bicyclobutane, molecular structure, substituent effects

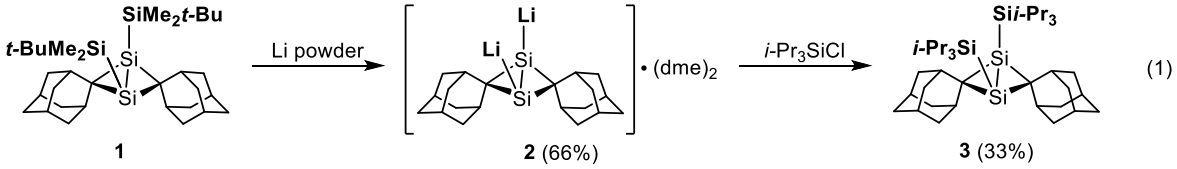
Theoretical studies of 1,3-disilabicyclo[1.1.0]butanes have predicted the existence of the bond-stretch isomers which differ primarily in the distance between the bridgehead silicon atoms, a short bond isomer (SB) and a long bond isomer (LB) (Chart 1). [1-4] The relative energy between the SB and LB isomers is predicted to depend on the steric bulkiness of substituents on the bridgehead atoms, which have not been investigated experimentally. Previously, we synthesized 1,3-disilabicyclo[1.1.0]butane with *t*-BuMe_2Si groups (**1**) as a LB isomer. We report herein synthesis and structures of novel 1,3-disilabicyclo[1.1.0]butane with bulky silyl substituents and found that structural characteristics of 1,3-disilabicyclo[1.1.0]butane are dependent on the steric bulkiness of substituents.

Chart 1. Bond-stretch Isomers of 1,3-Disilabicyclo[1.1.0]butane



Long Bond Isomer (LB) Short Bond Isomer (SB)

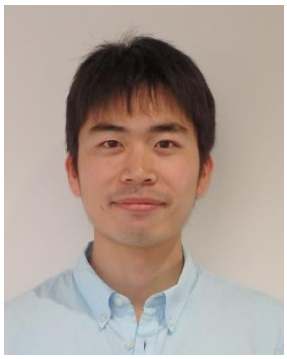
Reduction of **1** by lithium powder in THF gave 1,3-dilithio derivative **2** as red crystals. Then, reaction of **2** with *i*-Pr_3SiCl gave **3** as bright-yellow crystals in 33% yield (eq. 1). X-ray crystal structural analysis revealed the SB character of **3**. The bridgehead Si–Si bond length is 2.230 Å, which is much shorter than that of **1** (2.412 Å). A hexane solution of **3** showed an absorption band at 384 nm, which is significantly blue-shifted to that of **1** (λ_{max} = 420 nm). The blue-shift suggests the stronger interactions between the bridgehead silicon atoms of **3**. Details of the synthesis and properties of **3** will be discussed.



1 **2** (66%) **3** (33%)

Ref. [1] P. v. R. Schleyer, A. F. Sax, J. Kalcher, R. Janoschek, *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 364. [2] S. Nagase, T. Kudo, *J. Chem. Soc., Chem. Commun.* **1988**, 54. [3] J. A. Boatz, M. S. Gordon, *J. Phys. Chem.* **1989**, *93*, 2888. [4] D. Kitchen, J. E. Jackson, L. C. Allen, *J. Am. Chem. Soc.* **1990**, *112*, 3408. [5] T. Iwamoto, D.Yin, C. Kabuto, M. Kira, *J. Am. Chem. Soc.* **2001**, *123*, 12730.

Syntheses and Structures of Silicon-Silicon Doubly-Bonded Compounds with Polycyclic Silicon Frameworks



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Key words: oligosilane, disilene

Silicon-silicon doubly-bonded compounds, disilenes, are very attractive π-electron systems because they have various structures and electronic properties which are different from those of alkenes. The structures and properties of disilenes are largely affected by substituents. Recently we have reported that bicyclo[1.1.1]pentasilanyl (BPS) group works as an σ-conjugation unit (Fig. 1a).[1] The silicon framework of BPS group has two-degenerate σ orbitals similar to two π orbitals of alkynes (Fig. 1b). Accordingly BPS group is expected to conjugate with π-electron systems. We are focusing on disilenes bearing BPS groups to create the σ-π conjugation system between σ(BPS) and π(Si=Si) electrons constituted by the all silicon skeleton. In the present study, we synthesized a new disilene with two BPS groups and isopropyl groups (**1**) which is thermally unstable and undergoes thermal rearrangement to isomer **2**. When methyl groups are used instead of isopropyl groups, isomer **3** was obtained. Detailed structures, properties, and formation mechanism for disilene **2** and **3** will be discussed.

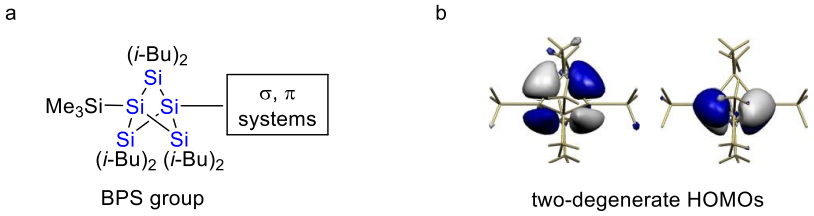


Fig. 1. Schematic diagrams of BPS group and possible σ-σ or σ–π conjugation (a) and two-generate HOMOs of model compound of BPS–$SiMe_3$ (b).

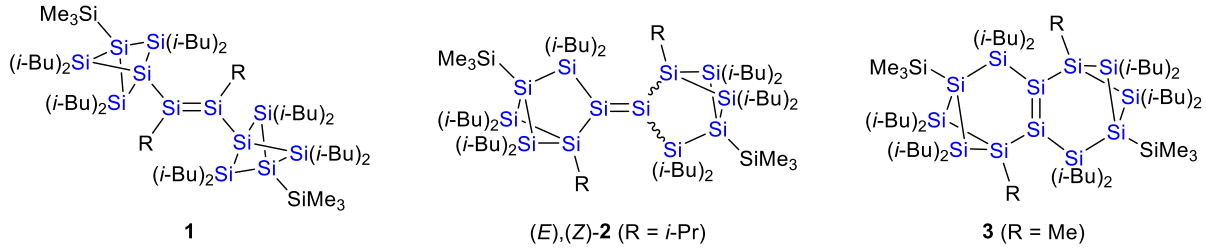
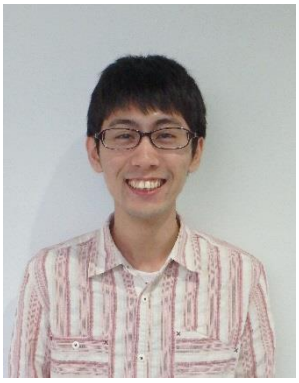


Fig. 2. Structures of disilenes **1**, **2** and **3**.

Ref. 1) Iwamoto, T.; Tsushima, D.; Kwon, E.; Ishida, S.; Isobe, H. *Angew. Chem. Int. Ed.* **2012**, *51*, 2340.

Isolable Two Coordinate Antimony-centered Radical



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Key words: radical, antimony, group 15 elements

Neutral two coordinate antimony-centered radical $R_2Sb•$ is recognized as one of the important reactive intermediates of antimony compounds. Recently we have successfully observed antimony-centered radical **1** in solution spectroscopically.[1] However, **1** exists as its dimer, distibine **2** in the solid state and equilibrates with **2** in solution (Scheme 1). In this work, we report synthesis and properties of antimony-centered radical **3** bearing more bulky alkyl group as an isolable compound (Chart 1).

Scheme 1. Equilibrium between **1** and **2**

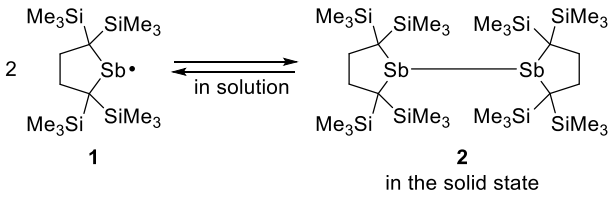
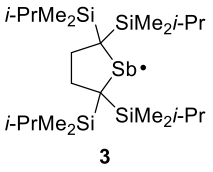
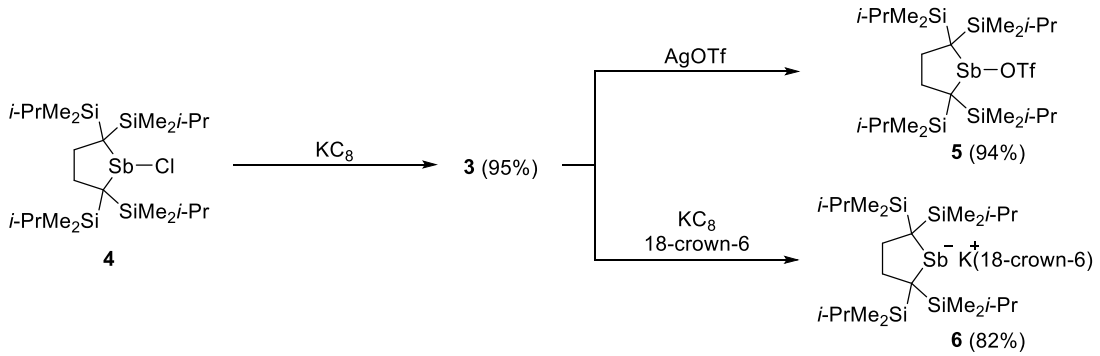


Chart 1. First Isolable Antimony-centered Radical **3**



Isolable antimony-centered radical **3** is readily synthesized by the reduction of chlorostibine **4** with KC_8 (Scheme 2). The shortest Sb–Sb distance (7.392 Å) in the single crystals is much longer than the sum of van der Waals radii of two antimony atoms (4.12 Å), therefore radical **3** exists as a monomer in the solid state. UV–vis absorption spectrum of **3** in 3-methylpentane at 298 K shows a broad band at 506 nm assigned to the n(Sb)→5p(Sb) (HOMO→SOMO) transition of antimony-centered radical. Since the UV–vis absorption spectra do not change significantly in various temperatures, no dimerization of **3** would occur. The one-electron chemical oxidation and reduction of **3** gave **5** and **6**, respectively (Scheme 2).

Scheme 2. Synthesis and One-electron Redox Reactions



[1] Ishida, S.; Hirakawa, F.; Furukawa, K.; Yoza, K.; Iwamoto, T. *Angew. Chem. Int. Ed.* **2014**, *53*, 11172-11176.

Creation of hypoxia specific oligonucleotide therapeutics system with intracellular environment-responsible Peptide Ribonucleic Acids (PRNAs): — *Tuning of on - off switching pH of PRNA for optimization of hypoxia cell specificity* —

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Key words: hypoxia, oligonucleotide therapeutics, peptide ribonucleic acid (PRNA), pH-dependent

Recently, hypoxia, which is specific states of cell under low oxygen concentration, has received much attention. Hypoxia is mostly induced by various kinds of diseases, such as cerebral infarction and nephritis. Hypoxia responsible oligonucleotide therapeutics (ONT) systems must be one of the most promising candidates of ONT strategy. Under hypoxic cellular condition, intracytoplasmic pH is reported lowering down to *ca*. 6.2 in general.

We have proposed and reported novel artificial nucleic acids named peptide ribonucleic acids (PRNAs), as cancer cell specific ONT. The advantages of PRNA are precise recognition and complexation with target RNAs. Additionally, intracellular environment condition responsible *on* to *off* function switching induced by *anti* to *syn* orientation change triggered by intramolecular cyclic borate ester formation with incorporated phenyl boronic acid (PBA) moiety is unique advantage of PRNA. Under hypoxia specific intracytoplasmic condition (pH = 6.2), PRNAs prefer *anti* orientation and form stable complex with target RNA, therefore expect to work as effective ONT. In contrast, under normal cellular conditions, PRNA's furanose moiety forms intramolecular cyclic borate ester with 2',3' *cis* diol, and the nucleobase orientation changes from *anti* to *syn*. The *syn* orientated nucleobase is not suitable for complexation. Thus PRNAs are expected to show no side effects and no toxicity.

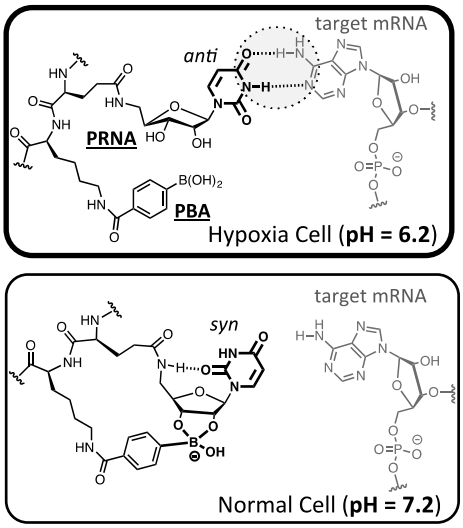
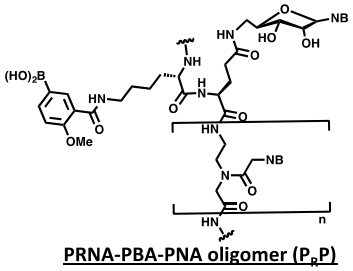


Figure. 1 pH dependent responsibility of PRNA

In this study, we tried to tune and optimize the switching pH range of PRNA-PBA-PNA oligomer (P_RP) by introduction of various types of substituent groups into PBA moiety discussed with CD & UV-vis spectroscopic studies. Moreover, precise *on-off* switching in complexation behavior with target RNA is also discussed in the poster.



Creation of the hypoxia-specific oligonucleotide therapeutics system with intracellular environment-responsible Peptide Ribonucleic Acids (PRNAs): Synthesis and properties of new type of chimeric PRNA derivatives with 3'-DNA moiety introduced at *N*-terminus of PRNA

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Key words: Peptide Ribonucleic Acid (PRNA), Chimeric Artificial Nucleic Acid, Hypoxia Cell Specific Oligonucleotide Therapeutics, RNase H Activity

Hypoxia is low O_2 concentration situation of cells related with various kinds of diseases such as cerebral infraction, cardiac infraction, diabetic retinopathy and cancer cells under rapid growth phase. We have reported the synthesis and properties of peptide ribonucleic acids (PRNAs) for the hypoxia cells specific oligonucleotide therapeutics. Under hypoxic cellular condition, intracytoplasmic pHs are reported lowering down to *ca.* 6.2, therefore we have demonstrated that complexation behavior of PRNA with target RNA could be *off* to *on* switched by intracellular condition change from normal (pH 7.2) to hypoxic state (～pH 6.2). Moreover, we have reported the design and synthesis of chimeric PRNA derivatives (P_RPDs) consisted with PRNA, PNA and DNA moieties by module strategy. In the P_RPDs, PRNA-PNA moiety introduced at amino modified 5'-end of DNA moiety with an amide bond of *C*-terminus of PRNA-PNAs. P_RPDs showed remarkably enhanced RNase H mediated target mRNA cleavage activity up to 200 times compared with that of DNA/RNA complexes. Based on this encouraging result presented, PRNAs should be one of the most promising candidates of hypoxia specific oligonucleotide therapeutics.

Recently, the gapmer type DNA derivatives were reported, *e.g.*, LNA/DNA and 2'-*O*-methyl RNA/DNA systems, as more efficient strategies for the oligonucleotide therapeutics. Thus, the synthesis of 3'-end DNA modified chimeric DNA-PRNA-PNA has received much attention.

In this paper, the novel method for the synthesis of new type of chimeric PRNAs with 3'-DNA moiety introduced at *N*-terminus of PRNA (DP_RPs) was discussed. In the DP_RPs, a phosphoramidate bond was introduced at junction of 3'-end of DNA and *N*-terminus of PRNA-PNA moiety. The synthesis, recognition properties with DNA/RNA, and antisense activities of DP_RPs were discussed in details.

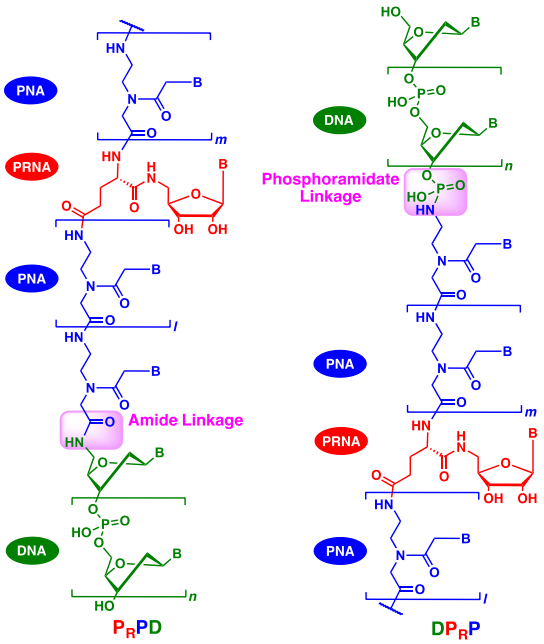

Fig 1. Chimeric DNA-PNA-PRNA Derivatives. (B = Nucleobase residues)

Studies on the excited state dynamics of cyclodextrin-aromatic compound complex by high sensitive/high time-resolved Circular Dichroism (CD) measurement system

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Key words: Circular Dichroism, Cyclodextrin, Time-resolved spectroscopy

Circular Dichroism (CD) is one of the most powerful and versatile tools for detection of structural information and interaction of bio- and biorelated molecules, since these molecules are consisted of chiral molecules/unit modules. Thus, these conformational and structural change and/or variety could be observed by CD spectra with high sensitivities. Nevertheless, it is well known that the $\Delta\varepsilon$ values are mostly three order-reduced magnitude than those of the UV/Vis (ε). In order to improve the sensitivity drawback, a Lock in Detection System with a Photo-Elastic Modulator (PEM) has been successfully employed in modern CD instruments. However, the modulation frequencies of PEM (~50 KHz) make a limitation of time-resolution of CD measurements (~ msec order). Then, a proposal of novel strategy of CD detection methods for higher time-resolution with high sensitivity for observing first events, such as protein folding (~μsec order) has been desired.

In this study, a novel high sensitive CD detection method based on a new control method of elliptically polarized light was developed aimed to construction of high time-resolve CD measurement system.[1] The constructed time-resolve CD measurement system was applied for investigation of photo-excited state dynamics of cyclodextrin included aromatic compounds.

Several report suggested that cyclodextrin inclusion complex tended to dissociate by photo excitation.[2] The driving force of photoirradiation induced dissociation would be differences of properties in the ground state and in the excited state, especially triplet state. We considered the time-resolved CD measurement could observe this dynamics of the event of chiral CDx with achiral guest molecules. In this work, the photo-dynamics of the cyclodextrin encapsulated aromatic compound, such as xanthone and methyl orange were discussed with time-resolved CD signal in sub-microsecond time scale by original CD measurement system.

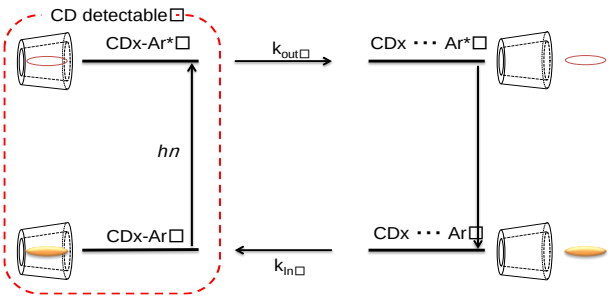

Fig. 1. Photodynamics of cyclodextrin-aromatic compound complex.

Ref.

[1] M. Murakami *et al*. *Chem. Lett.* **2013**, 42, 261-262.
[2] C. Bohne *et al*. *J. Am. Chem. Soc.* **1990**, 112, 8075-8079.

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Supramolecular Enantiodifferentiating Photocyclo - dimerization of 2-Anthracenecarboxylate (AC) with Proteins & Polymer Hybrids as Chiral Reaction Media - PEG modified BSA -

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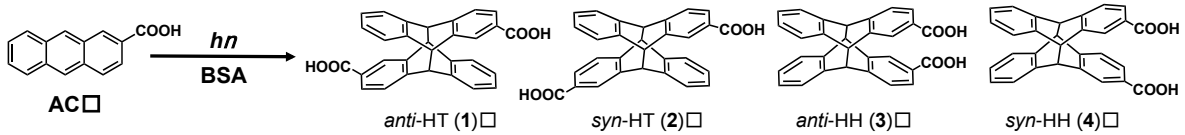
Key words: Serum Albumin, Supramolecular Asymmetric Photochirogenesis, Polyethylene Glycol, Asymmetric Photoreaction, Bovine Serum Albumin (BSA)

Increasing attention has recently been directed toward the new methodology of asymmetric photochemistry using various supramolecules. In this paper, we will present the novel strategy and recent results of supramolecular asymmetric photochirogenesis (SMAP) with protein and polymer modified protein, such as bovine serum albumins and polyethylene glycol (PEG) modified albumins as chiral reaction medias.

The biopolymers, especially proteins, possessing chiral binding pockets for guest, are of particular interest as potential chiral reaction cavities and/or fields for SMAP, although such an approach has not extensively been investigated. Serum albumins are the most abundant and well-characterized water-soluble plasma proteins, which transport hydrophobic compounds. We have employed bovine, human, porcine, and canine serum albumin (BSA, HSA, PSA and CSA) as a chiral supramolecular host and 2-anthracenecarboxylate (AC) as a substrate. The photocyclodimerization of AC was performed in aqueous buffer solutions in the presence of SAs to give the [4+4] cyclodimers with high enantioselectivities of up to 97% ee. However, little is reported about the positive design and active control of supramolecular photochirogenesis with biomolecules used as chiral reaction media.

In this study, effects of PEG modification of BSA upon in the ground state and excited state interaction with AC were discussed. Additionally supramolecular asymmetric photodimerization of AC mediated by a variety of PEG modified BSA will be discussed.



Scheme 1. Enantiodifferentiating photocyclodimerization of 2-anthracenecarboxylic acid (AC) mediated by bovine serum albumin.