

SNAPSHOTS OF SOME TOPICS OF INTEREST OF RECENT NOTABLE ADVANCES IN CHEMISTRY

- *De Novo* synthetic approach toward β -2,6-dideoxypyranoglycosides
- Silanized liquid-gallium nanoparticles
- Construction of 5-, 6-, and 7-membered Cyclic Carbamate Derivatives
- Hydrogen boride sheets as reductants for metal ions

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Snapshots of some topics of interest of recent notable advances in chemistry

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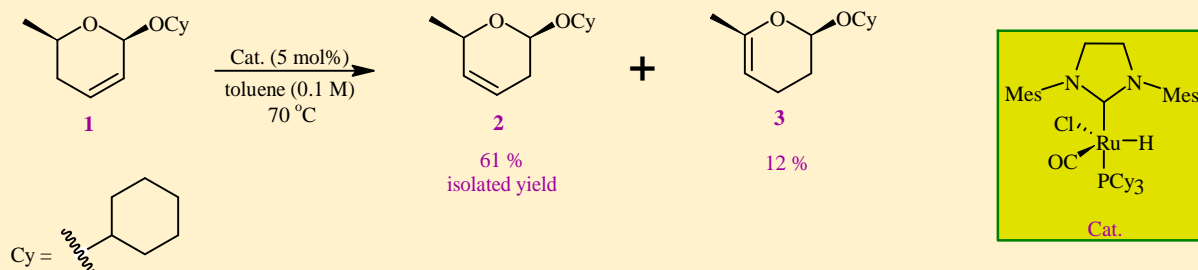
Managing Director / Founder

De Novo Synthetic Approach Toward β -2,6-dideoxypyranoglycosides

A *de novo* synthetic strategy toward β -2,6-dideoxypyranoglycosides is described. The key step of the strategy is the ruthenium-catalyzed regioselective olefin migration of dihydropyran allylic acetals to homoallylic acetals.

The stereoselective synthesis of β -2,6-dideoxypyranoglycosides, an important unit of oligosaccharide portion in natural products, is a great challenge due to the lack of stereodirecting neighboring groups at 2-position.

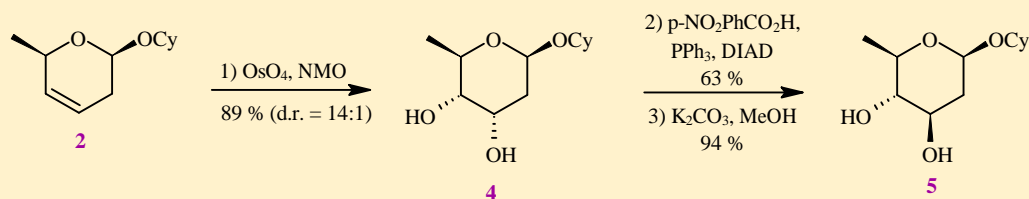
In this context, Seo and Rhee developed *de novo* synthetic method that aims to regioselective migration of cyclohexyl allylic acetal **1** to homoallylic acetal **2** employing *in situ* generated Ru-H complex. The desired homoallylic acetal **2** along with enol acetal **3** were obtained at 70 °C in 63% NMR yield and 12%, respectively (Scheme 1).



Scheme 1. Preparation of homoallylic acetal *via* regioselective migration of cyclohexyl allylic acetal.

This migration reaction proved to be compatible with highly sensitive 2,3,6-trideoxyglycoside moieties regardless of their structural differences.

The synthesis of cyclohexyl digitoxose **4**, a monosaccharide compound, was achieved from the homoallylic acetal **2** using osmium-catalyzed dihydroxylation reaction. The inversion of the C3-OH group in **4** gave olivose glycoside **5** (Scheme2).



Scheme 2. Synthesis of cyclohexyl digitoxose **4** and olivose glycoside **5**.

This strategy can allow to construct the challenging oligomeric form of *cis*-2,6-dideoxy-glycosides without the need of common glycosyl donors and activating group.

Review

K. Seo, Y. H. Rhee, *Org. Lett.*, **2020**, *22*, 2178 – 2181.

Silanized Liquid-Gallium Nanoparticles

A method of silanizing liquid gallium alloy particles is highlighted. The advantages of introducing alkoxysilane ligands have been demonstrated by orthogonal functionalization to produce chemically diverse, multifunctional hybrid liquid-metal nanoparticles. Furthermore, fabrication of architected stretchable conductors, called polymerized liquid-metal networks, is outlined. These conductors were fabricated using hitherto inaccessible chemistries with enhanced electrochemical performance.

There has been a burgeoning interest in room temperature liquid-gallium metal particles due to their extraordinary material properties such as metallic conductivity ($3.4 \times 10^4 \text{ S cm}^{-1}$), low viscosity, and nontoxicity. They are involved in a wide range of applications including stimuli-responsive electronics, self-healing devices, drug delivery, and microfluidic antennas and switches. Among their alloys, eutectic gallium-indium alloy (EGaIn) is composed of 75% Ga and 25% In by mass, that its melting point is 15 °C (ranked the second to gallium-indium-tin alloy – with a melting point of 10 °C). One of the features of this class of alloys is their spontaneous formation of a passivating oxide as their exposure to an ambient atmosphere, resulting in the formation of a native, amorphous gallium oxide layer (about 3 nm in thickness). This protective oxide skin exhibits a huge influence on the behavior of liquid-metal systems. The ability to modify the oxide skin or add chemical functionality to liquid-metal particles is very important for many applications. The current modification of the oxide skin is based on phosphoric acid, which leads to many drawbacks in terms of limited chemical functionality and being costly.

In this context, Farrell *et al.* have reported a method to fabricate silanizable EGaIn particles, which allows simple one-step additions of a wide range of moieties. Under water-free conditions, EGaIn particles were prepared using ultrasonication in ethanol under exposure to an ambient atmosphere to produce hydroxylated surface sites via either homolytic cleavage of water or production of ethanolic radicals that go on to react with gallium oxide surfaces. Then, the particles were functionalized with excess trialkoxysilane ligands to produce silanized EGaIn particles (Figure 1).

Multifunctionalization of EGaIn particles

The preparation of multifunctionalization of EGaIn particles were accomplished by sonication of the particles in the presence of 10:90 water/ethanol solution, which resulted in growing high-aspect-ratio crystalline GaOOH spikes from the surfaces of the particles to form hedgehog-like particles. These spiky hedgehog particles have shown enhanced colloidal stability as the spikes reduce van der Waals forces and decrease particle-particle attraction forces. In addition, they exhibited increased surface area providing additional surface sites for silanization. Sequential functionalization with alkoxysilane (e.g. (3-aminopropyl)-

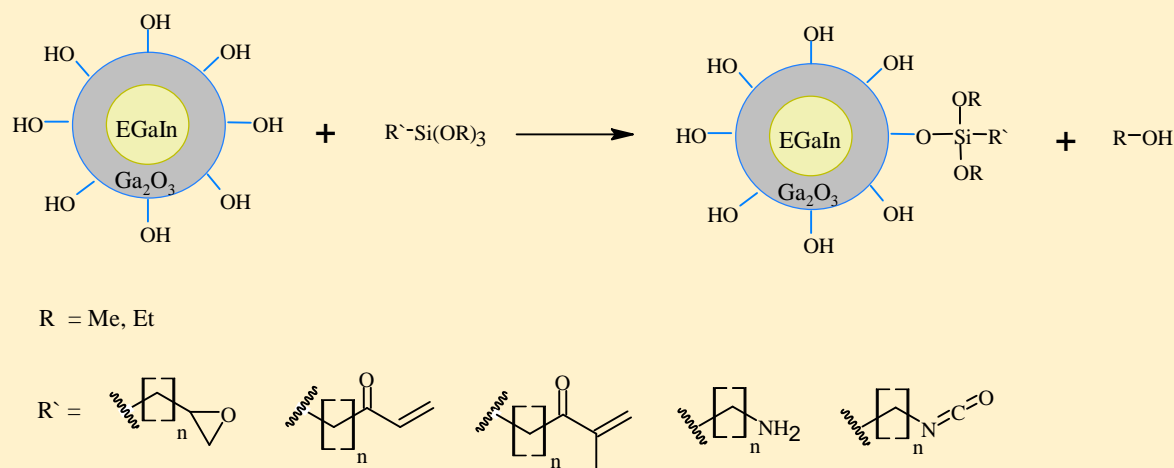


Figure 1. Silanization of EGaIn particles.

triethoxysilane) under water-free conditions, followed by phosphoric acid ligands (e.g. 2,6-difluorobenzylphosphonic acid) produced multifunctional EGaIn particle systems with controllable morphology (Figure 2).

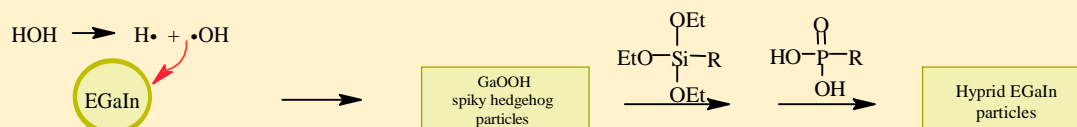


Figure 2. Multifunctionalization of EGaIn particles functionalized with both alkoxy-silane and phosphoric acid ligands.

The ability to introduce multiple functional groups on the spiky EGaIn particles with bioorthogonal reactivity could benefit theranostics and drug delivery. Furthermore, fabrication of architected polymerized liquid-metal networks (Poly-LMNs) functionalized with silanized EGaIn particles with polymerization of 3-(glycidyloxypropyl)-trimethoxysilane (GLYMO) and 3-(acryloxypropyl)-trimethoxysilane (AcTMS) enabled these stretchable conductors to be formed from particles over an order of magnitude smaller than previously possible, with appropriate tailorability of electromechanical properties (Figure 3). Poly-LMNs are mechanically responsive stretchable conductors generated from the functionalization and subsequent polymerization of liquid-metal particles to themselves to form mechanoresponsive networks. They exhibit characteristic electromechanical behavior under strain. This significant advancement in stretchable conductors should add new manufacturing techniques in aerosol-jet and inkjet printing.

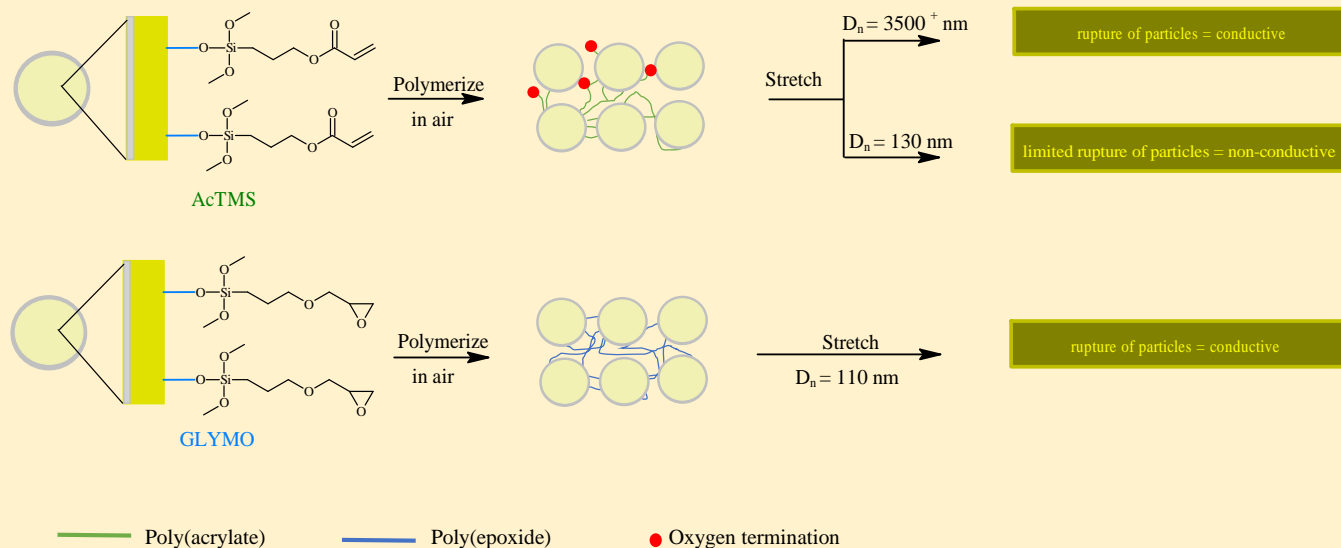


Figure 3. Polymerized liquid-metal network formation. EGAIn particles functionalized with multifunctional ligands are polymerized together with high ratios of EGAIn to ligand such that they create a trace of connected liquid-metal particles. If sufficient connectivity is achieved, the oxide shells containing liquid EGAIn will rupture when strained. This releases the liquid to connect and create a percolated conductive network. Poly-LMNs formed with cationically polymerizing epoxides show strain-induced rupture at much smaller particle sizes than the oxygen-inhibited free-radical polymerization of acrylates.

The development in the chemical space available within silanizable ligands and their economic viability would pave the way for further development of engineered devices and technologies.

Review

Z. J. Farrell, C. J. Thrasher, A. E. Flynn, C. E. Tabor, *ACS Appl. Nano Mater.*, **2020**, 3, 6297-6303.

Construction of 5-, 6-, and 7-membered Cyclic Carbamate Derivatives

Synthesis of multisubstituted oxazolidinones, oxazinanones, oxazepanones and their thio and sulfur scaffolds are highlighted. Two-step synthetic route is involved based on a multicomponent reaction followed by cyclization. The strategy demonstrated the capability of the transition from basic moieties to charge neutral cyclic derivatives.

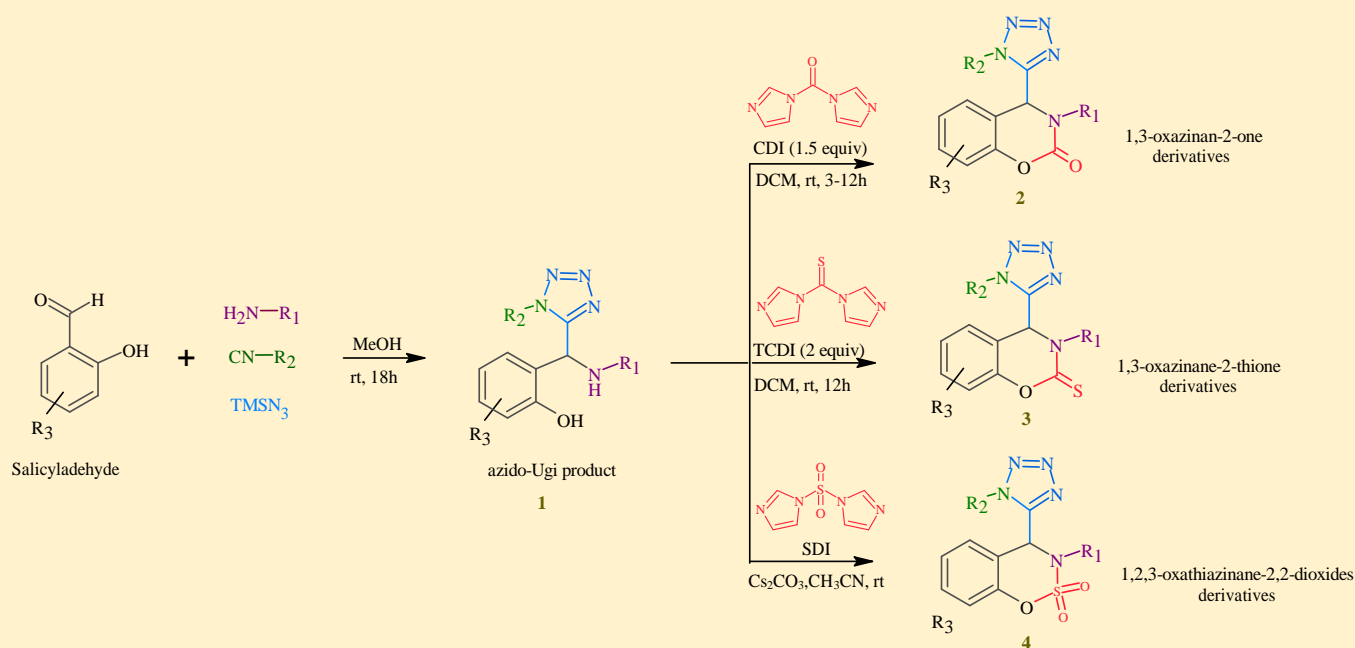
Multicomponent reactions (MCRs) are considered as privileged one-pot processes involving high complexity and a large of chemical diversity in the product from simple starting materials with easy operation. These important advantages of MCRs have promoted their application in interrelated fields, such as the synthesis of functional molecular libraries, medicinal chemistry and so on. In order to impose a physicochemical property (e.g., passive permeability, 3D distribution of lipophilic, charges, or neutrality) in a compound, cyclization constitutes a key factor in determining the conformational structure of the compound.

In achieving the goal of modifying chemical space in order to synthesize multi-heterocyclic biomolecules with different properties than that of the related compounds, Li *et al.* reported an elegant procedure which based on two-step approach involving MCR followed by cyclization. The strategy aims to perform the transition from basic moieties to charge neutral cyclic derivatives.

Taking into account of the importance of cyclic carbamate moieties in medicinal and industrial applicability, there are many different and elegant MCRs have been developed for the synthesis of various heterocyclic products. In this context, the authors employed both of the azido-Ugi reaction and Groebke Blackburn-Bienaymé reaction (GBB reaction) as versatile tools for the construction of multisubstituted 5-, 6-, and 7-membered cyclic carbamate derivatives using bifunctional orthogonal amino and hydroxyl aldehydes followed by cyclization.

The azido-Ugi reaction

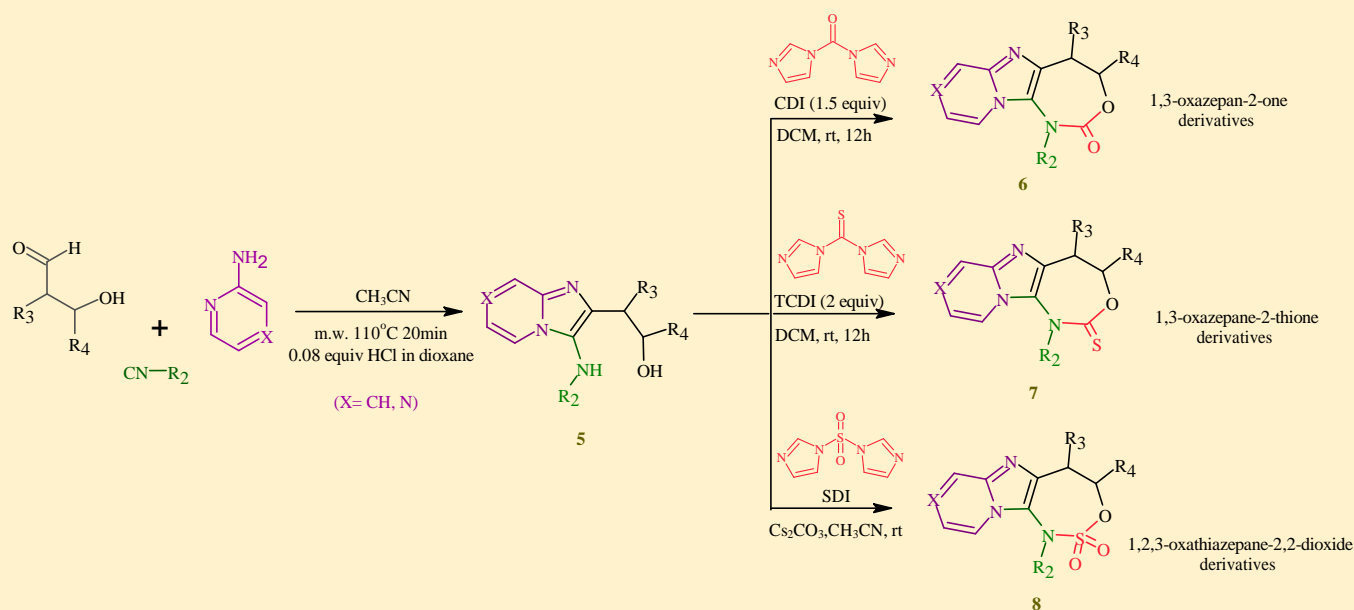
In this azido-Ugi reaction, salicylaldehyde was chosen as the source of free hydroxyl group. 1,1'-carbonyldiimidazole (CDI), or its analog 1,1'-thiocarbonyldiimidazole (TCDI) in the case of synthesis of cyclic thio-carbamates, serving as a coupling reagent, was added to a solution of the azido-Ugi product **1** in DCM at room temperature under air to afford the corresponding 1,3-oxazinan-2-ones **2**, or 1,3-oxazinane-2-thiones **3**, respectively, in high yield (Scheme 1). Whereas the synthesis of sulfamate derivatives were accomplished using 1,1'-sulfonyldiimidazole (SDI), as the sulfonyl donor, in the presence of excess amount of Cs₂CO₃ to afford 1,2,3-oxathiazinane-2,2-dioxides **4** (Scheme 1).



Scheme 1. Synthesis of the Ugi products **1** and 6-membered cyclized carbamates and their thio- and sulfur derivatives.

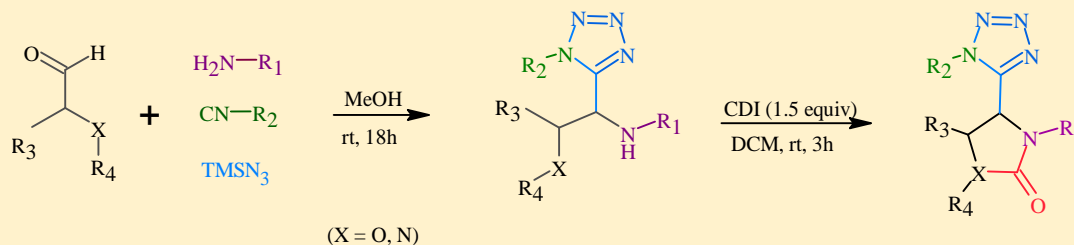
Groebke Blackburn-Bienaymé reaction (GBB reaction)

The scaffold three component GBB reactions, (GBB-3CR), which form secondary amines on imidazole heterobicyclic rings, were accomplished by the reaction of equimolar amounts of aldehyde, amino amine, isocyanide and HCl/dioxane in CH_3CN in a microwave to yield the corresponding imidazole-heterobicyclic product **5** (Scheme 2). Cyclization of **5** in the presence of the coupling reagents, CDI, TCDI, or SDI, afforded the corresponding 7-membered cyclic thiocarbamate derivatives **6-8** (Scheme2).



Scheme 2. Preparation of the 7-membered cyclic thiocarbamate derivatives.

Extending the methodology to prepare 5-membered cyclic carbamate and urea, the glycolaldehyde dimer, as supplier of a free hydroxyl group, was utilized in the azido-Ugi reaction which reacted with CDI to afford oxazolidine-2-one ($X = O$) (Scheme 3). The heterobicyclic ureas ($X = N$) were obtained using pyrrole-2-carboxaldehyde and 2-imidazolecarboxaldehyde as suppliers of secondary amines (Scheme 3).



Scheme 3. Synthesis of 5-membered cyclic carbamates and ureas.

This protocol is scalable and efficient employing mild reaction conditions and readily available building blocks.

Review

J. Li, V. D. Lorenzo, P. Patil, A. J. Ruiz-Moreno, K. Kurpiewska, J. Kalinowska-Thuścik, M. A. Velasco-Velázquez, A. Dömling, *ACS Comb. Sci.*, **2020**, 22, 356–360.

Hydrogen Boride Sheets as Reductants for Metal Ions

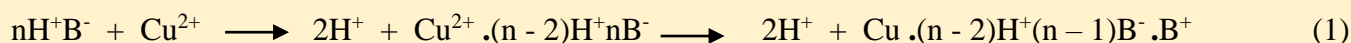
A new role of hydrogen boride sheets as reductants for metal ions is outlined. Based on this reduction property, the reported study demonstrated the facile formation of hydrogen boride sheet nanocomposites with metal nanoparticles.

Hydrogen boride (HB) sheets are characterized by their large H₂ content, unique electronic properties, catalytic properties as solid acid catalysts, and a light-responsive hydrogen release function. They have been synthesized as two-dimensional materials composed of hydrogen and boron in a 1:1 stoichiometric ratio. Extended to the properties of these hydrogenated borophene, Ito and his colleagues reported a new property of HB sheets as reductants for metal ions.

They have investigated a range of metal salts to demonstrate the formation of HB sheet nanocomposites with the metal nanoparticles of these salts. Their study showed that the UV-vis measurements before and after the addition of HB sheets to the CH₃CN solution containing Pt(NO₂)₂(NH₃)₂, Pd(C₅H₇O₂)₂ or Ni(C₅H₇O₂)₂ were changed, indicating the reduction of metal ions in the presence of HB sheets. In contrast, the addition of HB sheets to Zn(C₅H₇O₂)₂ and Co(C₅H₇O₂)₂ showed no clear change in UV-vis spectrum, indicating that Zn and Co ions were not reduced.

Based on the redox potential of these metal ions, they estimated that the redox potential of HB sheets was between -0.277 and -0.257 V versus standard hydrogen electrode (SHE). In view of this fact, HB sheets can be employed as catalysts for CO₂ conversion, *e.g.* conversion of CO₂ to HCOOH or CO₃²⁻ to HCHO.

Based on the reducing property of HB sheets, they demonstrated the formation of nanocomposites of HB sheets with Cu metal nanoparticles through the addition of a solution of CH₃CN containing Cu(CH₃COO)₂ to HB sheets. In such reaction, the Cu²⁺ cations were first exchanged with protons in HB, and then the Cu²⁺ was reduced to Cu⁰ on the HB sheets at the expense of an electron from negatively charged boron. Then, the metal Cu⁰ atoms form nanoparticles with a diameter of 2.0 nm on the HB sheets (eq 1).



The size and density of nanoparticles on HB sheets can be controlled by the initial prepared amount of metal ions and HB. Also, the immersion time, temperature, and the employed solution may play an important role in controlling these parameters.

Review

S. Ito, T. Hirabayashi, R. Ishibiki, R. Kawamura, T. Goto, T. Fujita, A. Yamaguchi, H. Hosono, M. Miyauchi, T. Kondo, *Chem. Lett.*, **2020**, *49*, 789–793.