Study on Visible-light-driven Photocatalytic Carbon-Carbon Cross-couplings by Vitamin B12 Derivative for Green Organic Synthesis

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論文の要約

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論 文 名：Study on Visible-light-driven Photocatalytic Carbon-Carbon Cross-couplings by Vitamin B_{12} Derivative for Green Organic Synthesis（グリーン有機合成を志向したビタミンB_{12}誘導体による可視光駆動型の炭素-炭素カップリング反応に関する研究）

Organometallic B_{12} compounds are unique metal complexes having a cobalt-carbon σ-bond present in biological systems, playing various important roles in the metabolism of microorganisms, animals and humans. Cleavage of the cobalt-carbon σ-bond could initiate many B_{12}-dependent enzymatic reactions. The alkylated Co(III)-complex, which is the key factor in such reactions, is generally formed by the reaction of the Co(I) species of the B_{12} complex with electrophiles, such as organic halides, *in vivo*. Therefore, the reductive formation of the Co(I) species and the followed oxidative addition of the organic halide to form the alkylated Co(III)-complex are the key steps for the development of the B_{12}-mediated enzymatic reactions. The visible light-driven formation of the Co(I) species of the B_{12} derivative, heptamethyl cobyrinate perchlorate, in the presence of photosensitizer (such as $[Ru(bpy)_3]Cl_2$, cyclometalated Ir(III)-complexes, *etc.*), catalyzed various B_{12} model reactions (1,2-migration of the functional group, methyl-transfer reaction, dichlorination reaction, *etc.*). These B_{12}-based visible light-driven photocatalytic systems have promising significance in organic synthesis, from the viewpoint of green and sustainable chemistry, because of their advantages of being clean, low-cost, sustainable, and environmentally benign. As expanding application of such B_{12}-based photocatalytic system, in this work, the visible light-driven photocatalytic Mizoroki-Heck-type reaction and Sonogashira-type reaction catalyzed by vitamin B_{12} derivative (**Scheme 1**) was investigated for the C-C bond elaboration in green organic synthesis. The details of this work were described as below.

Chapter 1 A brief overview of the vitamin B_{12}-based chemistry and C-C bond cross-couplings was outlined. In the part of vitamin B_{12}-based chemistry, the general function and corresponding catalytic systems of vitamin B_{12} and its derivatives were introduced. The part of C-C bond cross-couplings mainly focused on the significance and development of Mizoroki-Heck-reaction and Sonogashira-reaction.

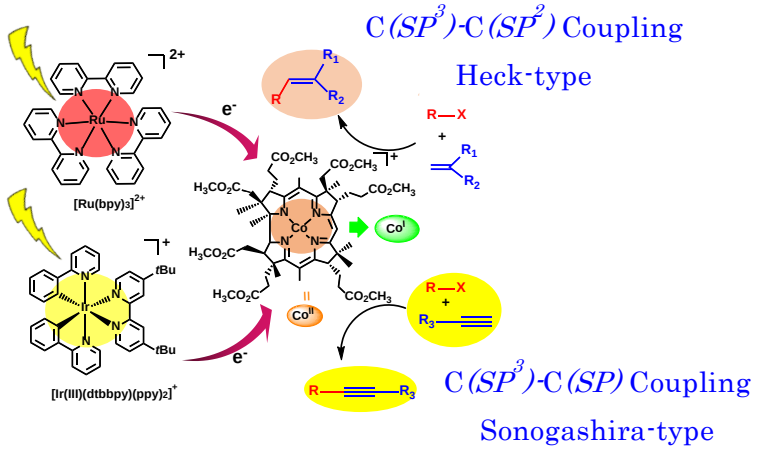
Chapter 2 The photo-driven Mizoroki-Heck-type reaction catalyzed by vitamin B_{12} derivative in the presence of $[Ru(bpy)_3]Cl_2$ as photosensitizer was described. In this work, the reaction proceeded through a radical intermediate to react with an alkene, and the *β*-elimination problem encountered in conventional Pd-catalysis could be well avoided. The catalytic efficiencies of the B_{12} catalyst were compared to that of other cobalt complexes (cobaloxime, *etc.*). A variety of control experiments supported a radical-based mechanism similar with those for typical B_{12} model reactions. A unique coupling reaction combined with 1,2-migration of the functional group was also conducted. The most probable mechanism was proposed. With the vitamin B_{12} derivative as one efficient catalyst in this study, the B_{12}-based

enzyme reaction was advanced to develop C-C bond formation between organic halide and alkene in synthetic organic chemistry.

Chapter 3 The vitamin B_{12} derivative-mediated photo-driven catalytic Sonogashira-type reaction in the presence of $[Ir(dtbbpy)(ppy)_2][PF_6]$ as photosensitizer at room temperature was investigated. In this study, with the vitamin B_{12} derivative as catalyst and $[Ir(dtbbpy)(ppy)_2][PF_6]$ as photosensitizer, such B_{12}-based visible light-driven photocatalytic system showed excellent efficiency with remarkable high turnover in the C_{Sp^3}-C_{Sp} bond formation between organic halides and alkynes. The most preferable mechanism was proposed. Compared with the conventional Pd- and Cu- mediated heating method, this B_{12}-catalyzed visible-light-driven system showed the clear advantage of being clean, low-cost, sustainable, and environmentally benign, furthermore, this straightforward protocol avoided the homocoupling reaction of alkynes.

Chapter 4 Redox active ionic liquid as efficient media and solvent for vitamin B_{12} derivative-catalyzed photo-driven Mizoroki-Heck-type reaction and Sonogashira-type reaction was discovered. In this chapter, the redox active ionic liquid, 1-ethyl-4-(methoxycarbonyl)pyridinum bis(trifluoromethanesulfonyl)amide (**RIL**), was synthesized from its iodide form by an anion exchange reaction of $Li(NTf_2)$ as one viscos liquid (η = 122 cp at 25 °C), and characterized by NMR, and elemental analysis. The **RIL** showed reversible redox couples at -0.65 V and -1.48 V vs. Ag/AgCl, worked as an electron mediator in the B_{12} derivative catalyzed Mizoroki-Heck-type reaction and Sonogahsira-reaction under visible-light irradiation. The catalytic efficiency in the **RIL** was higher than those in MeOH and the redox inactive ionic liquid, 1-butyl-3-methyl imidazolium bis(trifluoromethylsulfonyl)amide. To the best of our knowledge, this is the first example of the Mizoroki-Heck-type reaction/Sonogashira-type reaction combined with the cobalt-mediated IL-system.

Chapter 5 The summary of this work and perspective of the future work were depicted. Such environmentally benign vitamin B_{12} derivative, which derived from the natural B_{12}, catalyzed visible-light-driven C-C bond cross-couplings provided one promising and practical pathway for the green organic synthesis.



Scheme 1