

Catalytic vinylene transfer reaction for the direct construction of multi-ring systems

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Abstract

Transition-metal-catalyzed C–H activation and subsequent oxidative cyclization with alkynes has been a powerful tool for the synthesis of polycyclic aromatic compounds. Despite the substantial progress in this field, it is still a significant challenge to establish synthetic methodologies for the construction of non-substituted vinylene-fused aromatics. We have developed a catalytic “vinylene transfer strategy” adopting vinylene carbonate as an acetylene surrogate. Vinylene carbonate also acts as an internal oxidant to regenerate the catalytically active species in situ; thus, no external oxidant is required to trigger the oxidative annulation. This protocol is applicable to the direct synthesis of various polycyclic heteroaromatics.

Background & Results

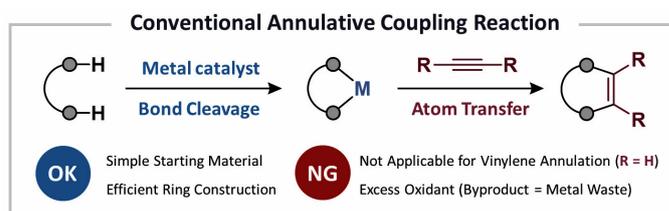
Polycyclic heteroaromatic scaffolds are ubiquitous in many natural compounds and have been a key motif in a wide range of manufactured functional molecules. Accordingly, tremendous research interest has been focused on the development of new and efficient synthetic methods for constructing fused-ring skeletons. Transition-metal-catalyzed C–H activation and subsequent oxidative annulation with alkynes or their equivalents have emerged as promising synthetic tools for the assembly of heterocycles. This method allows us to construct various fused-ring systems with simple manipulations; however, most of these reactions are only applicable to internal alkynes. This limitation significantly takes from the practical value of the annulative coupling reaction because a non-substituted vinylene fragment cannot be installed via the catalysis. Moreover, a stoichiometric amount of external oxidant is usually required to ensure the catalytic turnover, leading to the formation of undesired byproducts.

To address this issue, we envisioned using vinylene carbonate as an oxidizing acetylene surrogate. Vinylene carbonate is a bench-stable reagent with bulk production as an electrolyte and for polymer chemistry. Upon liberation of the $[\text{CO}_3]^{2-}$ anion (formal two-electron reduction), vinylene carbonate might act as a two-electron internal oxidant under proper reaction conditions to establish a redox-neutral reaction system. Overall, only H_2CO_3 (or $\text{H}_2\text{O} + \text{CO}_2$) would form as a byproduct. With this picture in mind, we investigated the annulative coupling using vinylene carbonate as a coupling partner and, to our delight, various vinylene-fused heteroaromatic compounds were successfully synthesized through the C–H/N–H, C–H/C–H, and C–H/O–H oxidative cyclization.

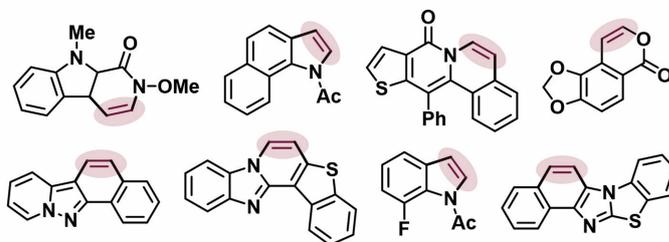
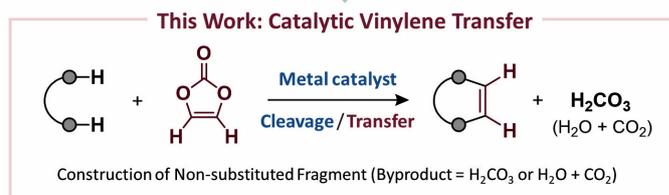
Significance of the research and Future perspective

Notable features of this reaction system are that (1) non-substituted vinylene-fused cyclic compounds can be obtained directly, without any pre-functionalization, and (2) no external oxidant nor base is required for the catalytic turnover because the vinylene carbonate fulfills both the functions. Considering a wide prevalence

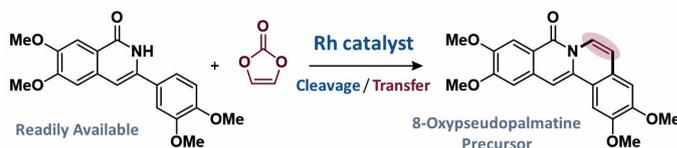
of such polycyclic molecules in various biologically active compounds (pharmaceuticals, agrochemicals, etc.) and manufactured functional molecules (luminescence materials, semiconductor, solar cells, etc.), these new reaction systems would highly reinforce the synthetic utility of the direct annulation strategy.



As useful synthetic methodology



Representative Examples for the Scope of Developed Reaction System



Synthetic Application: Concise Synthesis of a Natural Alkaloid

Patent

Ghosh, Koushik; Nishii, Yuji; Miura, Masahiro; Rhodium-Catalyzed Annulative Coupling Using Vinylene Carbonate as an Oxidizing Acetylene Surrogate. *ACS Catalysis*. 2019; 9: 11455-11460. doi: 10.1021/acscatal.9b04254.

Treatise

Ghosh, Koushik; Nishii, Yuji; Miura, Masahiro; Oxidative C–H/C–H Annulation of Imidazopyridines and Indazoles through Rhodium-Catalyzed Vinylene Transfer. *Organic Letters*. 2020; 22: 3547-3550. doi: 10.1021/acs.orglett.0c00975.

Mihara, Gen; Nishii, Yuji; Miura, Masahiro et al. Concise Synthesis of Isocoumarins through Rh-Catalyzed Direct Vinylene Annulation: Scope and Mechanistic Insight. *Organic Letters*. 2020; 22: 5706-5710. doi: 10.1021/acs.orglett.0c02112.

URL

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Keyword

catalysis, organic electronics, coupling reaction