

論文の内容の要旨

論文題目 **Development of Transition Metal-Catalyzed Hydroarylation and Acyloxyalkylation of Unsaturated Molecules**

(遷移金属触媒による不飽和分子の

ヒドロアリアル化及びアシロキシアルキル化反応の開発)

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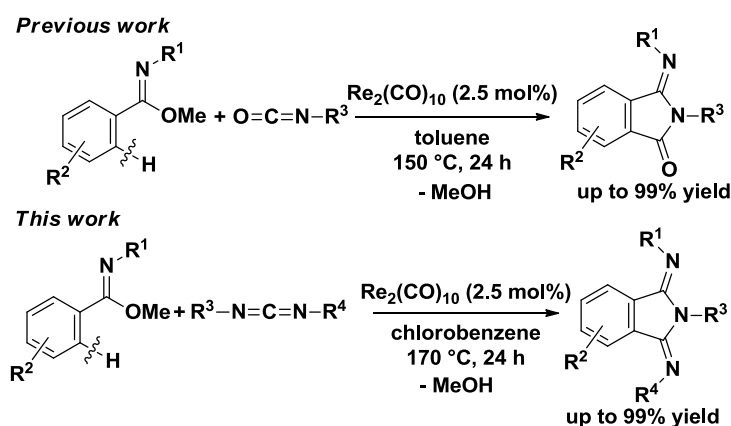
Research background

Transition metal-catalyzed addition reaction to unsaturated molecules has emerged as an increasingly important method for organic synthesis. Likewise, hydroarylation and acyloxyalkylation of unsaturated molecules could efficiently build more complicated compounds with multifunctional groups. However, unavoidable mixtures of products are almost always obtained. Therefore, a solution of the pressing problem about regioselectivity in addition reactions to unsaturated molecules brooks no delay.

(1) Rhenium-Catalyzed Synthesis of 1,3-Diiminoisoindolines via Insertion of Carbodiimides into a C-H Bond of Aromatic and Heteroaromatic Imidates

1,3-Diiminoisoindolines are diimidated phthalimides and partial structures of phthalocyanines and their metal complexes. However, synthetic reactions of 1,3-diiminoisoindolines are still rare. Representative synthetic routes for synthesis of 1,3-diiminoisoindolines is the treatment of 2,3-dicyanoarenes with sodium metal and ammonia gas. However, these reactions require harsh conditions and only symmetrical 1,3-diiminoisoindolines are obtained. Therefore, it is necessary to develop a new synthetic method for 1,3-diiminoisoindolines.

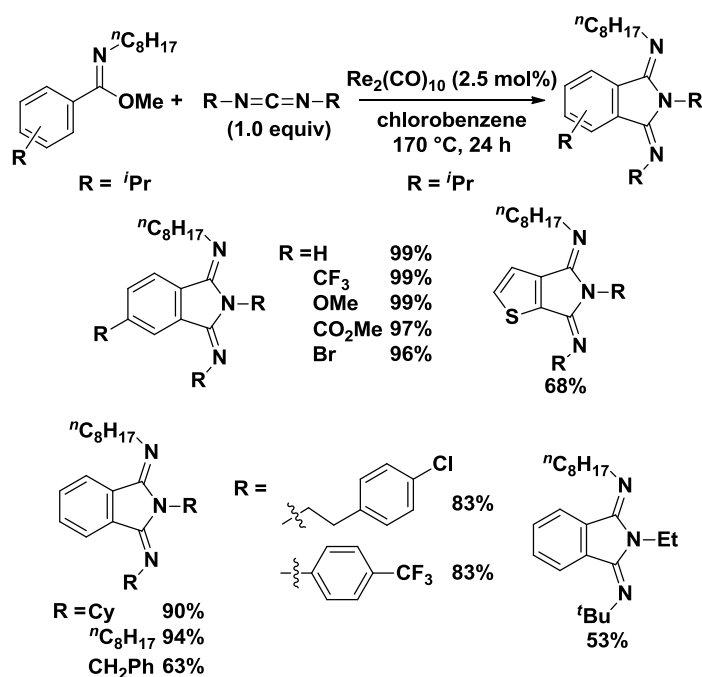
Our group recently reported a rhenium-catalyzed synthesis of 3-iminoisoindolinones using aromatic imidates and isocyanates. Due to the methoxy leaving group, a C=N double bond of the directing groups remains after the reaction (Scheme 1).^[1]



Scheme 1. C-H Insertion-Cyclization Sequence.

We investigated several reactions of imidates with other unsaturated molecules, such as carbodiimides. As a result, I found that a rhenium complex catalyzed a reaction between aromatic imidates and carbodiimides efficiently to give 1,3-diiminoisoindolines (Table 1).^[2]

Table 1. Scope of Imidates and Carbodiimides



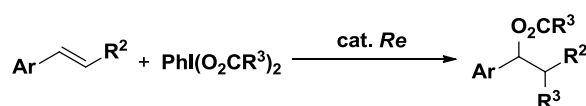
Next, I investigated the substrate scope of the reaction between imidates and carbodiimides (Table 1). A reaction of *N*-alkylimidates with diisopropylcarbodiimide proceeded to give the corresponding 1,3-diiminoisoindolines quantitatively. 1,3-Diiminoisoindolines with electron-withdrawing or -donating groups were obtained in excellent yields. It is notable that a methoxycarbonyl group and bromine atom were tolerated under the reaction conditions. This reaction system is applicable to the reaction of a heteroaromatic imidate. Then, the substrate scope for carbodiimides with respect to an imidate was assessed. The reaction of DCC proceeded to give 1,3-diiminoisoindoline in spite of the steric hindrance. In this reaction, a primary alkyl, benzyl, and chlorophenylethyl carbodiimides were applicable. A diarylcarbodiimide with electron-withdrawing groups provided the corresponding product in good yields.

Interestingly, when the reaction of *N*-alkylimidate with unsymmetrical carbodiimide was carried out, the corresponding 1,3-diiminoisoindoline was obtained as a single product regioselectively.

(2) Iron-Catalyzed Acyloxyalkylation of Styrenes Using Hypervalent Iodine Reagents

Transition metal-catalyzed difunctionalization of alkenes is a hot subject of intense investigation because the reactions can introduce two new functional groups only in one step. However, acyloxyalkylation of alkenes is still challenging and the examples are quite rare.

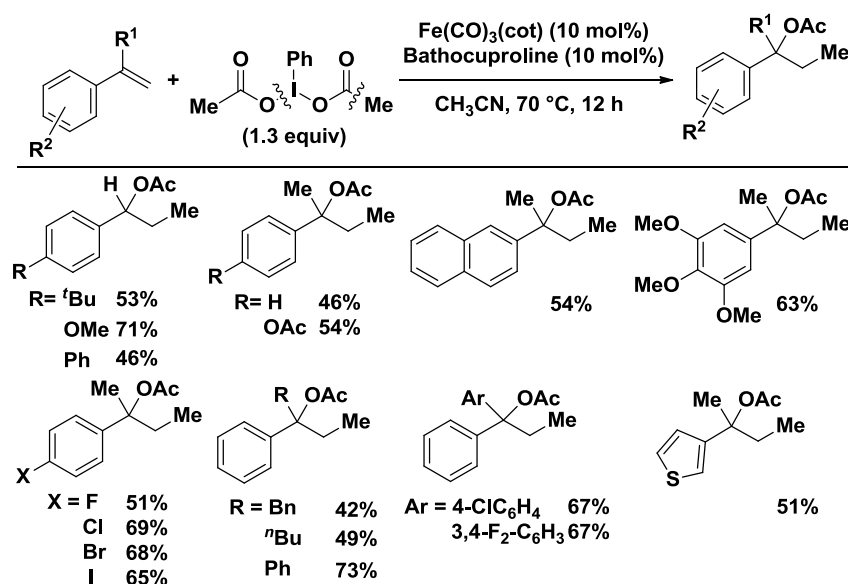
Wang and co-workers recently reported the first example of rhenium-catalyzed acyloxyalkylation of styrenes with hypervalent iodine reagents, in which hypervalent iodine reagents act as both oxidant and alkylation reagent in difunctionalization of styrenes (Scheme 2).^[3] But visible light irradiation is required in many cases. Therefore, we develop iron-catalyzed acyloxyalkylation of styrene derivatives using various types of hypervalent iodine reagents (HIRs).^[4]



Scheme 2. Re-Catalyzed Regioselective Oxyalkylation.

We examined the reactivity of various styrenes with $\text{PhI}(\text{OAc})_2$. Among them, styrenes bearing *t*Bu, methoxy, or phenyl group at the *para*-position gave the desired products in moderate to good yields (Table 2). α -Methyl styrenes including ester, naphthalene, or strong electron-donating group also reacted smoothly with $\text{PhI}(\text{OAc})_2$. Halogen atoms on the aromatic ring of styrenes, including an iodine atom, remained unchanged under the reaction conditions. Styrenes with a benzyl, *n*-butyl, or substituted aromatic group at the α -position delivered the corresponding products in moderate yields. Those reaction conditions were applicable to the heteroaromatic system.

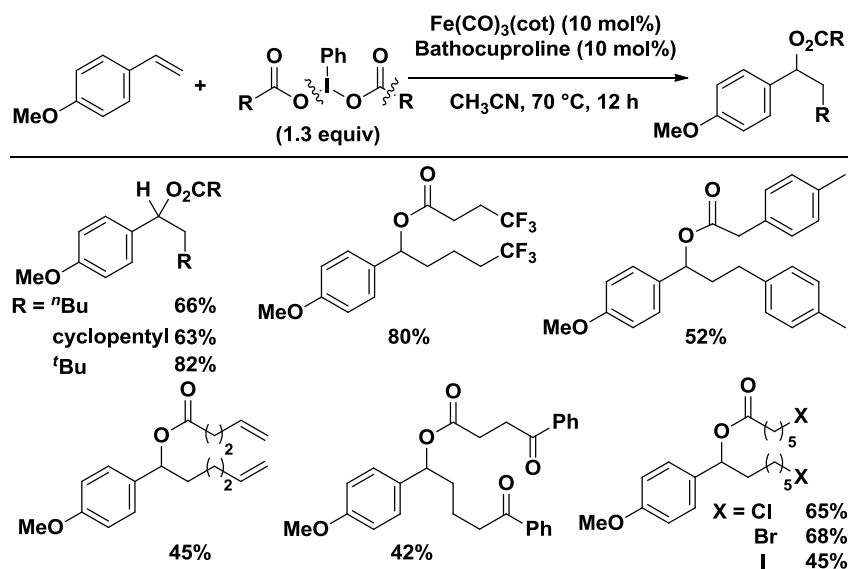
Table 2. Scope of Styrenes



Next, a range of HIRs were tested (Table 3). Specifically, HIRs derived from

primary, secondary, and tertiary aliphatic carboxylic acids were well compatible with the styrene acyloxyalkylation. HIRs with trifluoromethyl or benzyl groups tolerated under the reaction conditions. HIRs bearing C=C double bonds or carbonyl groups provided the products in moderate yields. I finally checked hypervalent iodine(III) reagents with chlorine, bromine, or iodine atoms to give the desired products.

Table 3. Scope of Hypervalent Iodine Reagents



Summary

I developed rhenium-catalyzed synthesis of 1,3-diiminoisindolines from aromatic imidates and carbodiimides via C-H activation. To the best of my knowledge, this reaction is the first example of a transition metal-catalyzed insertion of carbodiimides into an aromatic C-H bond. I also succeeded in the development of iron-catalyzed acyloxyalkylation of styrenes. The acyloxyalkylation reaction proceeded using various types of styrenes and several kinds of hypervalent iodine reagents. The products were obtained in moderate to good yields without loss of the functional groups.

References

- [1] Sueki, S.; Guo, Y.; Kanai, M.; Kuninobu, Y. *Angew. Chem. Int. Ed.* **2013**, *52*, 11879.
- [2] Wang, Z.; Sueki, S.; Kanai, M.; Kuninobu, Y. *Org. Lett.* **2016**, *18*, 2459. [3] Wang, Y.; Zhang, L.; Yang, Y.; Zhang, P.; Du, Z.; Wang, C. *J. Am. Chem. Soc.* **2013**, *135*, 18048. [4] Wang, Z.; Kanai, M.; Kuninobu, Y. *Org. Lett.* **2017**, *19*, 2398.