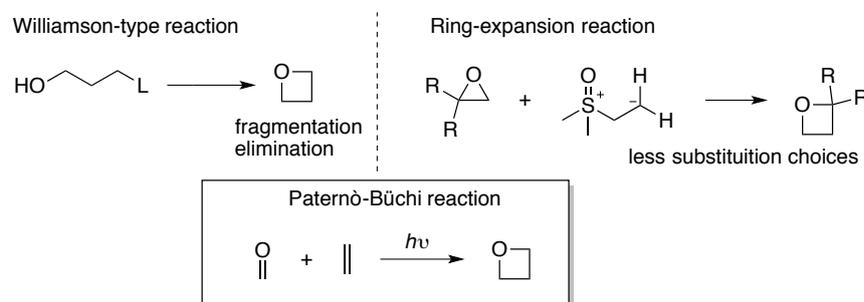


Thesis Summary

Regio- and stereoselectivity in the photochemical [2+2] cycloaddition reaction of carbonyl compounds with pyrrole derivatives
(カルボニル化合物とピロール誘導体の光[2+2]付加環化反応における位置及び立体選択性に関する研究)

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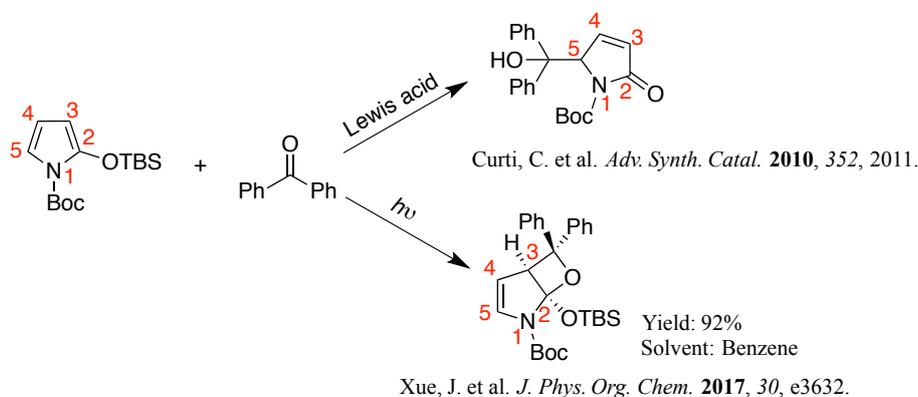
In recent years, the application of photochemistry in organic synthesis have attracted much attention.¹ For example, Paternò-Büchi reaction (PB reaction), one of the photochemical [2+2] cycloaddition reaction, is widely applied in the synthesis of oxetane, that is four-membered ring structure found in many biologically active compounds.² It is possible to prepare oxetane using thermal reactions, such as Williamson-type reaction or ring-expansion reaction at the expense of side reactions or less substitution choices (Scheme 1). Comparatively, PB reaction is straightforward for the oxetane formation without any other additive, which makes it become the most efficient method in the oxetane synthesis.



Scheme 1. Comparison of oxetane formation using thermal reaction and Paternò-Büchi reaction (PB reaction)

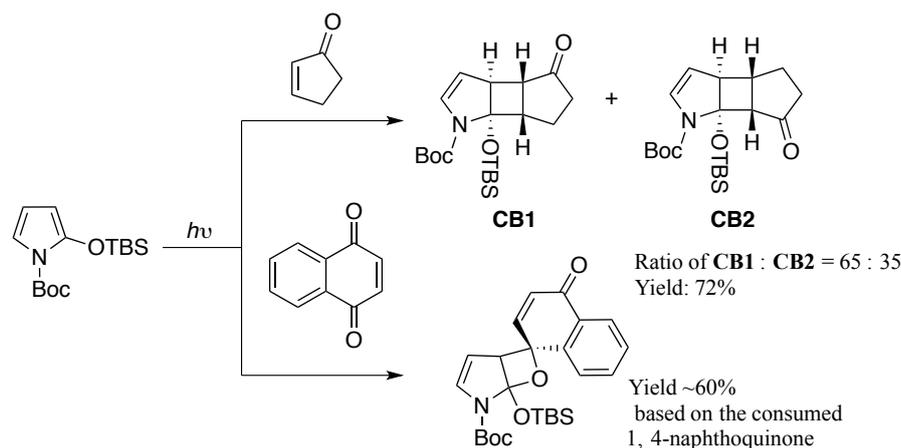
Even though many studies have been done in the PB reactions using furan derivatives,³ the pyrrole derivatives are barely addressed because of the instability of product. In this thesis, the reactivity and mechanism exploration of pyrrole derivatives in PB reactions and other photochemical [2+2] cycloaddition reactions were discussed in details.

As shown in Scheme 2, the pyrrole derivative was designed that the siloxyl group (OTBS) is used for the regioselectivity exploration and increase of reactivity of pyrrole; meanwhile, the electron-withdrawing group, *tert*-butyloxycarbonyl (Boc), was introduced to the nitrogen atom of the pyrrole ring to stabilize the bicyclic oxetane product. In the Lewis-acid promoted reaction of the pyrrole and benzophenone, newly



Scheme 2. Comparison of reactions of pyrrole and benzophenone induced by Lewis acid and light

formed C-C bond was formed at the most nucleophilic position of pyrrole (C5). However, if the benzophenone is excited to electrically excited state under photo irradiation, the oxygen atom in the carbonyl group will be switched from nucleophilic to electrophilic character that newly formed C-C bond is at C3 of pyrrole ring. The corresponding oxetane product was isolated successfully at the yield of over 90%. In addition, the laser flash photolysis study indicated that almost all of the benzophenone at excited state is quenched by pyrrole though the quantum yield was measured to be 0.02. The computation study showed that another regioisomer was not isolated because 1,4-diradical intermediate is not productive, which also explained why only one regioisomer was obtained.



Scheme 3. Photochemical [2+2] cycloaddition reaction of pyrrole with 2-cyclopenten-1-one and 1,4-naphthoquinone

Furthermore, similar photochemical [2+2] cycloaddition reactions of pyrrole derivatives with 2-cyclopenten-1-one and 1,4-naphthoquinone were also investigated and cyclobutane and oxetane product were obtained respectively in moderate yields (Scheme 3). Additionally, the product selectivity, cyclobutane *versus* oxetane, is largely depended on the occurrence of photoinduced electron transfer (PET). Although the estimation based on Rehm-Weller equation calculated by cyclic voltammetry analysis and excitation energy computation indicates that PET in both cases are exothermic, the computations on energies of the 1,4-diradicals intermediates and spin density of the excited enones imply that 2-cyclopenten-1-one favors the cyclobutane product while 1,4-naphthoquinone favors the oxetane product because of the stability of 1,4-diradical intermediates that is consistent with the findings in experiment.

In conclusion, efforts have been made on the photochemical [2+2] cycloaddition reactions using pyrrole derivatives that oxetane and cyclobutane containing pyrrole moiety were isolated in moderate yields successfully and structures were confirmed by 2D-NMR; meanwhile, the related mechanisms were elucidated by physical chemistry studies.

References

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List of Publications

1. Xue, J.; Abe, M.; Takagi, R. *J. Phys. Org. Chem.* **2017**, *30*, e3632.
2. Xue, J.; Takagi, R.; Abe, M. *Arkivoc*, **2018**, part ii, 192.