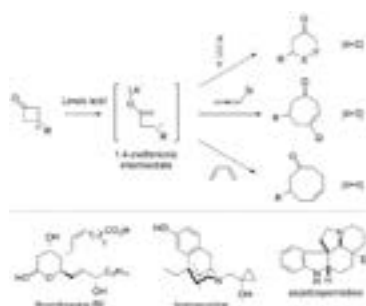


Development of cycloaddition reactions using 1, 4-zwitterionic intermediates

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Cyclobutane derivatives show characteristic reactivities in organic reactions based on release of their high strained energy, and have been used as a useful C₄ building block in organic synthesis. We found a new method for generation of 1,4-zwitterionic intermediates by Lewis-acid catalyzed ring cleavage of cyclobutanones which had a cation-stabilizing group at the 3-position.¹ Regioselectivity for the ring cleavage was predicted and controlled by the structure of cyclobutanones. Formed 1, 4-zwitterionic intermediates reacted with compounds which had various types of unsaturated bonds such as C=C, C≡C, C=O, C=N, C≡N, N=N, N=O to give the corresponding six-membered compounds by formal [4+2] cycloaddition reaction.^{2,3} Reactions of the 1,4-zwitterionic intermediates with allenylsilanes and diene derivatives afforded seven- and eight-membered carbocyclic compounds by formal [4+3] and [4+4] cycloaddition reactions, respectively. Racemic total syntheses of thromboxane B₂, bremazocine,⁴ and aspidospermidine⁵ were performed by using intra- and intermolecular cycloaddition of cyclobutanones. High reactivity of the zwitterionic intermediates for cycloaddition will be applicable to synthesis of multiply substituted cyclic compounds.



Recent publications

1. Kuzuguchi T, Yabuuchi Y, Yoshimura T and Matsuo J (2017) Synthesis of multisubstituted phenols by formal [4+2] cycloaddition of nucleophilic alkynes with 3ethoxycyclobutanones. *Org. Biomol. Chem* 15:5268-5271.
2. Matsuo J (2014) 1, 4-Zwitterionic intermediates formed by cleavage of a cyclobutane ring and their cycloaddition reactions. *Tetrahedron Lett* 55:2589-2595.
3. Kawano M, Kiuchi T, Negishi S, Tanaka H and Hoshikawa T, (2013) Regioselective Inter- and Intramolecular Formal [4+2] Cycloaddition of Cyclobutanones to Indoles and Total Synthesis of (±)-Aspidospermidine. *Angew. Chem., Int. Ed.* 52:906-910.
4. Matsuo J, Okado R and Ishibashi H (2010) A new synthesis of 2,3-di- or 2,3,3-trisubstituted 2,3-dihydro-4-pyridones by reaction of 3-ethoxycyclobutanones and *N-p*-toluenesulfonyl imines using titanium(IV) chloride: Synthesis of (±)-bremazocine. *Org. Lett.* 12:3266-3268.
5. Matsuo J, Sasaki S, Tanaka H and Ishibashi H (2008) Lewis acid-catalyzed intermolecular [4+2] cycloaddition of 3-alkoxycyclobutanones to aldehydes and ketones. *J. Am. Chem. Soc.* 130:11600-11601.

Biography

Jun-ichi Matsuo received his PhD from Tokyo University under the direction of Prof. Kenji Koga and Prof. Shū Kobayashi (1999). After his Postdoctoral research, he became an Assistant Professor at Tokyo University of Science (Prof. Teruaki Mukaiyama) in 2000. In 2002, he moved to the Kitasato Institute (Prof. Teruaki Mukaiyama and Prof. Satoshi Ōmura). He moved to Kanazawa University as an Associate Professor in 2005, and was promoted to a Professor in 2014. His research interests include discovery and development of new organic reaction methodology.

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