Palladium-Catalyzed Trimethylenemethane (TMM) Cycloaddition

Biography

Dr. Chao Zheng studied chemistry at Shanghai Jiao Tong University and earned his B.Sc. degree in 2007. He obtained his Ph.D. at Shanghai Institute of Organic Chemistry (SIOC) in 2012 under the supervision of Prof. Shu-Li You and Prof. Yu-Xue Li. He is currently an Associate Professor in the group of Prof. Shu-Li You at SIOC. His research interests are focused on understanding reaction mechanisms and developing new synthetic methodology with the assistance of theoretical calculations.

Institution

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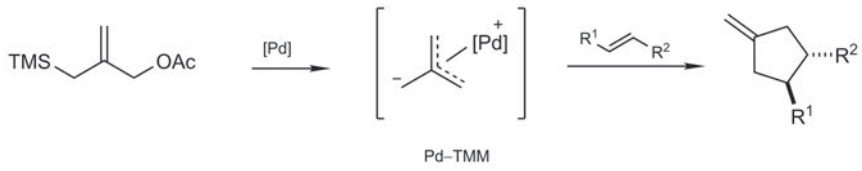
Abstract

In this case study, a literature survey on palladium-catalyzed trimethylenemethane (TMM) cycloaddition reactions was conducted with *Science of Synthesis* Online (Scheme 1). The search was carried out using the text search query tool. The hit list results are quite concise, informative, and useful.



Scheme 1 Palladium-Catalyzed Cycloaddition of Trimethylenemethane

Discussion

The transition-metal-catalyzed asymmetric allylic substitution reaction is among the major research interests of this group. Recently, we wanted to exploit the possibility of integrating a transition-metal-catalyzed asymmetric allylic substitution reaction into multistep cascade reactions to provide novel synthetic routes to complex targets with polycyclic skeletons. Before beginning this program in the laboratory, we decided to conduct a literature survey of palladium-catalyzed trimethylmethylene cycloaddition reactions.

Palladium–trimethylenemethane, a zwitterionic intermediate that can be easily generated from 2-[(trimethylsilyl-methyl]allyl acetate with a palladium(0) catalyst, can react with a wide variety of dipolarophiles such as imines, aldehydes, ketones, and electron-deficient alkenes to afford various [3 + 2]-cycload-dition products. This protocol was originally developed by Trost and co-workers several decades ago. The corresponding enantioselective variants have also emerged recently.

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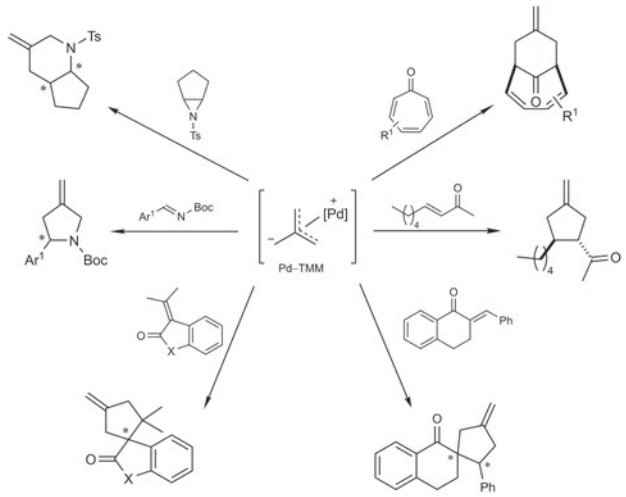
The chapter-based search was executed by simply typing “trimethylenemethane” in the full text query box. A total of 28 hits appear, all of which are subchapters from *Science of Synthesis*, e.g. Section 1.2.2.62 on the synthesis of methylenecyclopentanes within the chapter on ‘Palladium–Allyl Complexes’ or Section 48.4.1.4.4 describing the synthesis of larger-ring cycloalkanes from trimethylenemethanes, *Science of Synthesis*: *Stereoselective Synthesis* Section 3.1.2.2 on asymmetric [3+2]-cycloaddition reactions using trimethylenemethane, and more recent material from the *Science of Synthesis Knowledge Updates*. The [3+2] cycloaddition of palladium–trimethylenemethane with imines, α,β-unsaturated ketones, amides, [3+3] cycloaddition of palladium–trimethylenemethane with *N*-tosylaziridines (Section 40.1.5.2.1.6.1), and [6+2] cycloaddition of palladium–trimethylenemethane with tropones (*Stereoselective Synthesis*, Section 3.1.7.1) are all covered (Scheme 2). In addition, the thermally-induced [3+2] cycloaddition of trimethylenemethane as well as the use of trimethylenemethane as an η^4-ligand in low-valent iron complexes are also discussed.



Scheme 2 Representative Examples of Cyclization Reactions Using Palladium–Trimethylenemethane

The search results are very user-friendly. All the reactions are described by very concise texts accompanied with clear reaction equations and a brief summary of reaction conditions and results in tables. More importantly, typical experimental procedures are also given at the end of the section. The relevant original references can be accessed easily via hyperlinks. Users can save the subchapter or the whole chapter of *Science of Synthesis* by simply clicking the “print page” or “print chapter” button. The hit list can be saved and reloaded in one’s future search task using “MySOS”.

Conclusion

Science of Synthesis Online is an excellent alternative tool for organic researchers to quickly identify useful and reliable synthetic information to given molecules. I would be willing to recommend it to my colleagues and friends.

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