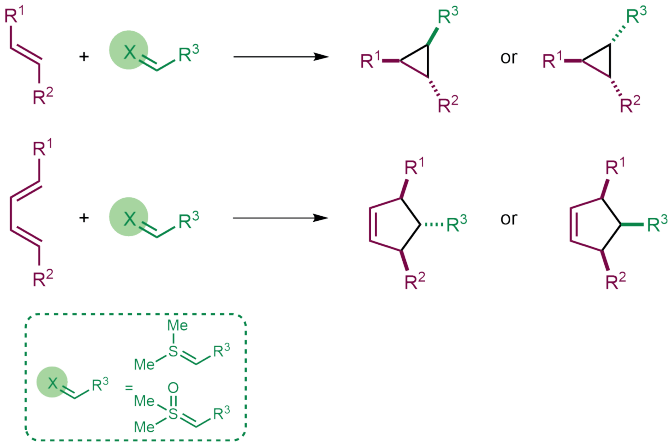
Enantioselective Cycloadditions Involving Sulfur Ylides

Clara Meilhac | Institut de Chimie Moleculaire et des Matériaux d'Orsay (ICMMO), CNRS, Université Paris-Saclay, France

Clara Meilhac obtained her M.Sc. from the University of Caen (France) in 2025. She is currently a PhD student in the group of Dr. Aurélien de la Torre, where she works on the generation of sulfur ylide derivatives and their reactivity in cycloaddition reactions.

Abstract

Our team is involved in various research projects, with a current particular focus on the development of new cycloaddition methodologies. Over the past few years, we have developed enantioselective [4+2]-cycloaddition reactions between diverse dienes and suitable partners, enabling access to molecular scaffolds that can be further manipulated through ring-opening or retro-cycloaddition processes. However, these methods are limited to a specific range of substrates. Sulfur ylides are interesting one-carbon partners for cycloaddition reactions, with an inherent nucleophilic character. While commonly employed in (2+1) cycloadditions, their involvement in enantioselective (4+1) cycloaddition is more limited (Scheme 1). The successful development of such approaches requires a thorough understanding of the synthesis and reactivity of these one-carbon species. *Science of Synthesis* represents a reliable and data-rich resource, providing rapid access to a large body of articles and reviews.

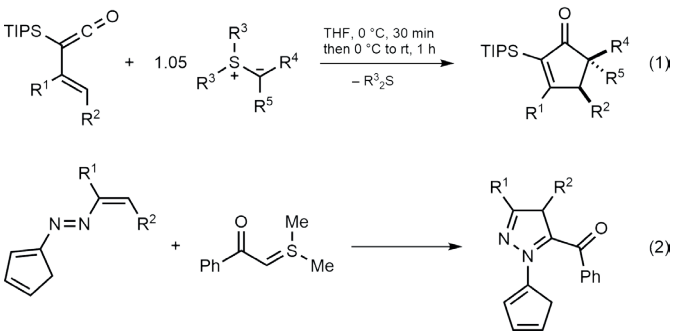


Scheme 1 Cycloadditions Involving Sulfur Ylides

Discussion

Personally, I have found *Science of Synthesis* to be useful throughout the entire project. At the outset, this platform allowed me to gather all the necessary information on one-carbon, sulfur-based reacting partners. Initially, I focused on the reactivity and synthesis of sulfur ylides, discussed in Section 27.1.2[1] (on sulfoxonium ylides) and Section 27.1.3[1] (on sulfonium ylides) in a contribution by Aggarwal and Richardson that covers all types of sulfur ylides. These sections give an overview of the generation of sulfur ylides from sulfonium salts. Their generation under basic conditions is also described in Section 8.2.4.1.4[2] by Kowalkowska and Jonczyk in a subsection on the "Generation and Reaction of Ylides" using sodium hydroxide. Taken together, these summaries provided the necessary background to prepare and select suitable ylides for cycloaddition studies.

With methods for preparing the two types of substrates in hand, I then focused on the cycloaddition reaction itself and was interested in finding previously reported conditions that could be applied in our studies. Once again, *Science of Synthesis* offers several sections discussing this type of reaction, giving examples (Scheme 2) and providing access to many key references.



Scheme 2 Examples of (4+1) Cycloadditions Involving Mono-Carbon Partners

Beyond the specific reactivity of sulfur ylides described in the chapter written by Aggarwal and Richardson on sulfur ylides, other articles provide valuable background information relevant to other types of cycloaddition reaction. For example, Section 47.1.3.1[3] offers a comprehensive overview on Diels–Alder reactions, including inverse-electron-demand processes using electron-deficient dienes. This section was especially useful for understanding general reactivity patterns and orbital considerations governing such transformations, which could be applied to other cycloadditions involving dienes.

General discussion of enantioselective approaches for [4+2]-cycloaddition reactions[4,5] and other types of cycloadditions (excluding [4+2])[6] are also covered in dedicated separate

reviews. In addition, stereochemical aspects of cycloadditions of aldehyde derivatives are notably discussed in Section 25.1.16.6,[7] including interesting discussion about enantioselective Diels–Alder reactions.

These chapters provided a general overview of strategies used to control enantio- and diastereoselectivity, including the use of chiral catalysts and auxiliaries. Together, they offered a solid conceptual framework for the design of enantioselective cycloaddition reactions between electron-deficient dienes and one-carbon partners.

Conclusion

For me, *Science of Synthesis* is an incredibly useful resource. Even with its vast range of topics, the user-friendly search and logical organization allow me to quickly locate what I need. The exceptional quality of each review makes it the first place I turn to when beginning a new project, or when simply exploring a fascinating area to discover new chemistry.

References

[1] Aggarwal, V. K.; Richardson, J., *Science of Synthesis*, (2004) **27**, 21; DOI: 10.1055/sos-SD-027-00002.

[2] Jonczyk, A.; Kowalkowska, A., *Science of Synthesis*, (2006) **8**, 1040; DOI: 10.1055/sos-SD-008-00826.

[3] Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L., *Science of Synthesis*, (2010) **47**, 561; DOI: 10.1055/sos-SD-047-00252.

[4] Ishihara, K.; Sakakura, A., *Science of Synthesis: Stereoselective Synthesis*, (2011) **3**, 67; DOI: 10.1055/sos-SD-203-00046.

[5] Du, H., *Science of Synthesis: Metal-Catalyzed Cyclization Reactions*, (2016) **2**, 205; DOI: 10.1055/sos-SD-222-00111.

[6] Jiang, G.; Wang, Y.; Yu, Z., *Science of Synthesis: Stereoselective Synthesis*, (2011) **3**, 7; DOI: 10.1055/sos-SD-203-00002.

[7] Witulski, B.; Alayrac, C., *Science of Synthesis*, (2007) **25**, 405; DOI: 10.1055/sos-SD-025-00268.

Contact
Science of Synthesis Editorial Office | Georg Thieme Verlag KG
Oswald-Hesse-Str. 50 | 70469 Stuttgart | Germany
https://sos-chemistry.thieme.com

Thieme