# Catalytic 1,1-Diazidation of Alkenes

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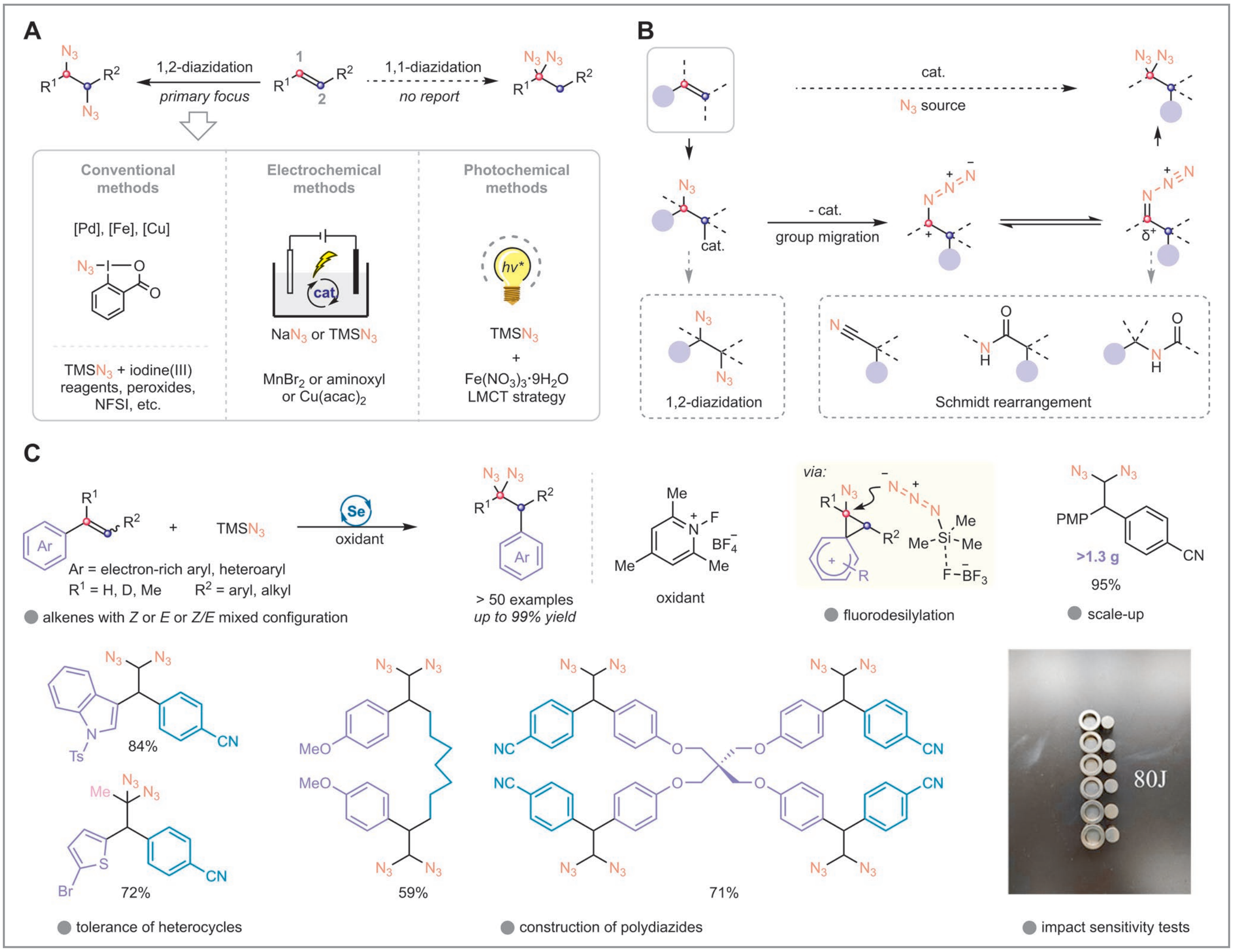
Organic azides are of great importance in synthetic, materials, and biorthogonal chemistries. Azidative functionalization of alkenes is an important way to produce organic azides, especially alkyl azides. In a recent publication in *Nature Communications*, the group of Professors Xiaodan Zhao and Lihao Liao at Sun Yat-Sen University (P. R. of China) developed a selenium-catalyzed migratory 1,1-diazidation of aryl alkenes for the efficient synthesis of geminal diazides (Schemes 1B and 1C). "Compared to well-developed catalytic 1,2-diazidation of alkenes, the 1,1-diazidation version has not been realized (Scheme 1A), although the obtained geminal diazides can serve as energetic molecules and act as valuable synthetic precursors," said Professor Zhao. "Developing an efficient approach for 1,1-diazidation of alkenes has been a challenging task in the field of azide chemistry."

Professor Zhao explained to SYNFORM the background of their work. "One of our research interests is to realize challenging transformations via selenium redox catalysis. Different from other electrophilic catalysts, the involved electrophilic selenium species exhibited the unique properties



**Scheme 1** Catalytic diazidation of alkenes

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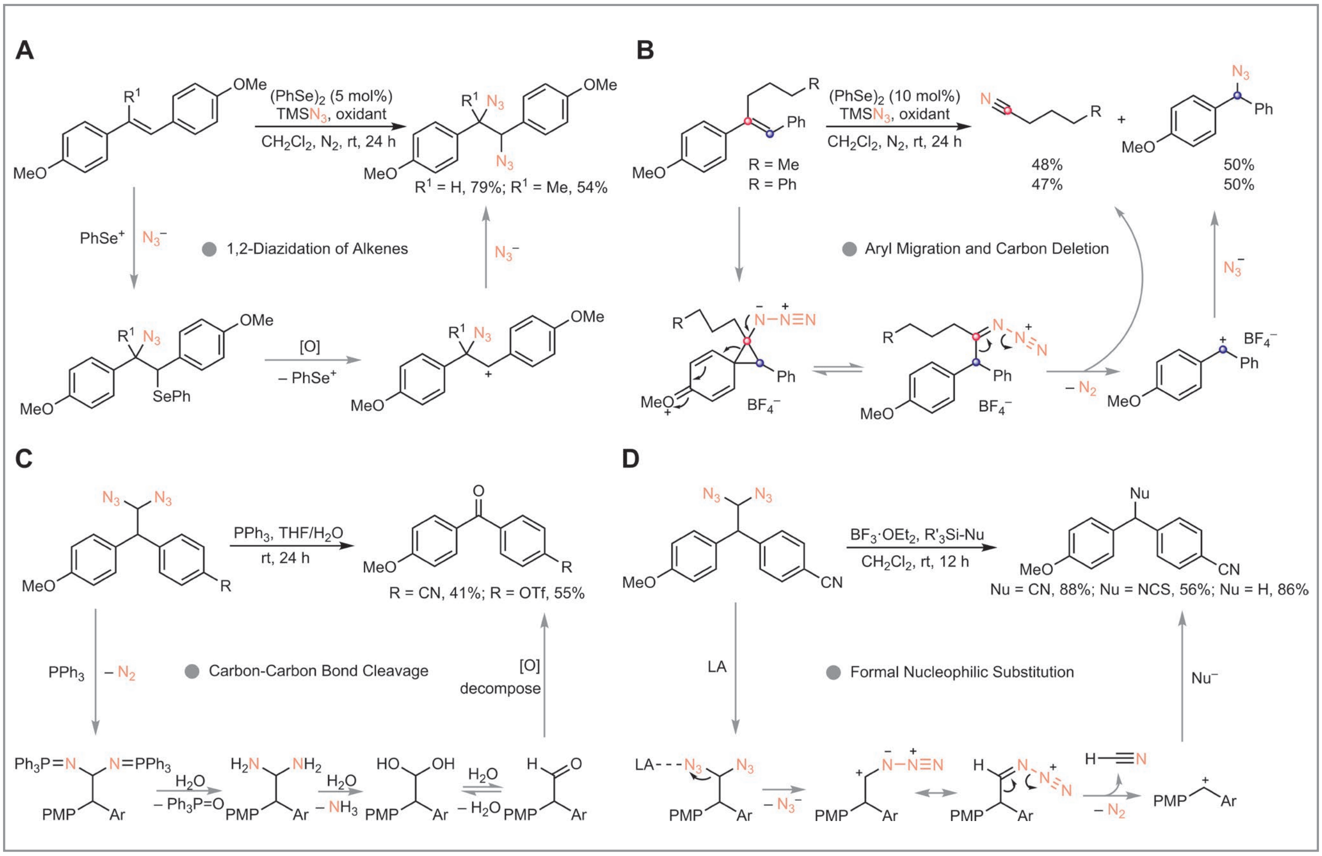
of carbophilicity toward the alkene π bond and a convenient release from the intermediates. As an emerging aspect of main-group-element-based organocatalysis, this technique has become a powerful tool for functionalization of alkenes, especially in allylic functionalization, direct alkenyl C–H functionalization, and 1,2-difunctionalization," he said, continuing: "Considering the great importance of geminal diazides, we wondered whether these molecules might be constructed in selenium-catalyzed 1,1-diazidation fashion (Scheme 1B), although this type of catalysis had remained elusive for the 1,1-difunctionalization of alkenes. It is gratifying that we have indeed achieved it (Scheme 1C)."

During the evaluation of reaction conditions, the authors discovered some interesting phenomena. "Tetrafluoborate anion-bearing oxidants were found significantly better than triflate-bearing ones, suggesting that tetrafluoborate anion might facilitate the release of azide anions from azidotrimethylsilane via fluorodesilylation," said Professor Liao, adding: "In addition, both *Z*- or *E*-alkenes could be converted into the desired products efficiently, which is of great significance for practical organic synthesis, owing to the easy availability of *Z*/*E* alkene isomers."

With the optimized conditions in hand, the scope of substrates was evaluated systematically. "1,2-Disubstituted or trisubstituted alkenes with electron-rich aryl or heteroaryl groups could go through the migratory 1,1-diazidation to afford the geminal diazides smoothly," graduate student Wangzhen Qiu said, continuing: "Besides, oligomeric alkenes could yield polydiazides in this catalytic system without difficulties, which might be attractive in materials science."

"Compared to the well-developed 1,2-difunctionalization of alkenes, the corresponding 1,1-difunctionalization of alkenes is more challenging," said Professor Zhao, adding: "It was found that the hypervalent iodine system, an important tool for 1,1-difunctionalization, could not furnish the desired geminal diazides no matter how catalysis or stoichiometry were varied, reflecting the advantages and uniqueness of selenium redox catalysis."

As the simplest geminal diazide derivative, diazidomethane $CH_2(N_3)_2$ is highly explosive and vibration-sensitive.



**Scheme 2** Some interesting reactions

To figure out whether the obtained geminal diazides are also so dangerous, the authors conducted a safety evaluation. “TGA-DSC analysis showed that some representative geminal diazides with relatively lower $(N_C+N_O)/N_N$ were stable under 118 °C, and standard fall hammer tests revealed that the most likely ‘dangerous’ sample was insensitive to impact (IS > 80 J),” remarked graduate student Qiu, who continued: “These results indicated that the obtained geminal diazides are relatively safe for conventional use, which might be the reason why the scale-up reactions (using alkenes in several hundred milligrams to one gram scale) could be handled routinely.”

In addition to the pursued catalytic 1,1-diazidation, the authors also observed other interesting reactions when using different substrates. “1,2-Diazidation occurred instead of 1,1-diazidation when stilbene derivatives with two electron-rich aryl groups were utilized as substrates (Scheme 2A), while aryl migration plus carbon deletion was observed when some trisubstituted alkenes were used, and the products were identified as diarylmethyl azides and nitriles (Scheme 2B),” said Professor Liao, adding: “These two reactions further enrich the field of selenium-catalyzed azidations of alkenes.”

Moving away from the conventional reactivities of organic azides, the unique reactivities of geminal diazides were also investigated. “Ketones were formed via carbon–carbon bond cleavage when geminal diazides were treated with triphenylphosphine under Staudinger reduction conditions (Scheme 2C),” Professor Liao said, continuing: “Interestingly, the geminal diazidomethyl moiety could act as a formal leaving group in the presence of a Lewis acid, facilitating the subsequent nucleophilic substitution (Scheme 2D).” The authors believe that these new reactivities might promote new applications of geminal diazides.

“This work represents the first successful example of catalytic 1,1-diazidation of alkenes, which is greatly complementary to the fields of alkene chemistry and azide chemistry,” Professor Zhao concluded, continuing: “It also exhibits the unique advantage of selenium redox catalysis, which offers a basis for the design of new reactions.”

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