Trends in Chemistry | **Mechanism of the Month**

Asymmetric radical cyclopropanation of alkenes

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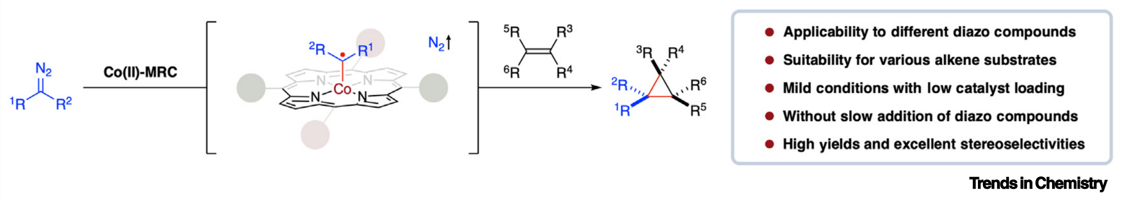

- Applicability to different diazo compounds
- Suitability for various alkene substrates
- Mild conditions with low catalyst loading
- Without slow addition of diazo compounds
- High yields and excellent stereoselectivities

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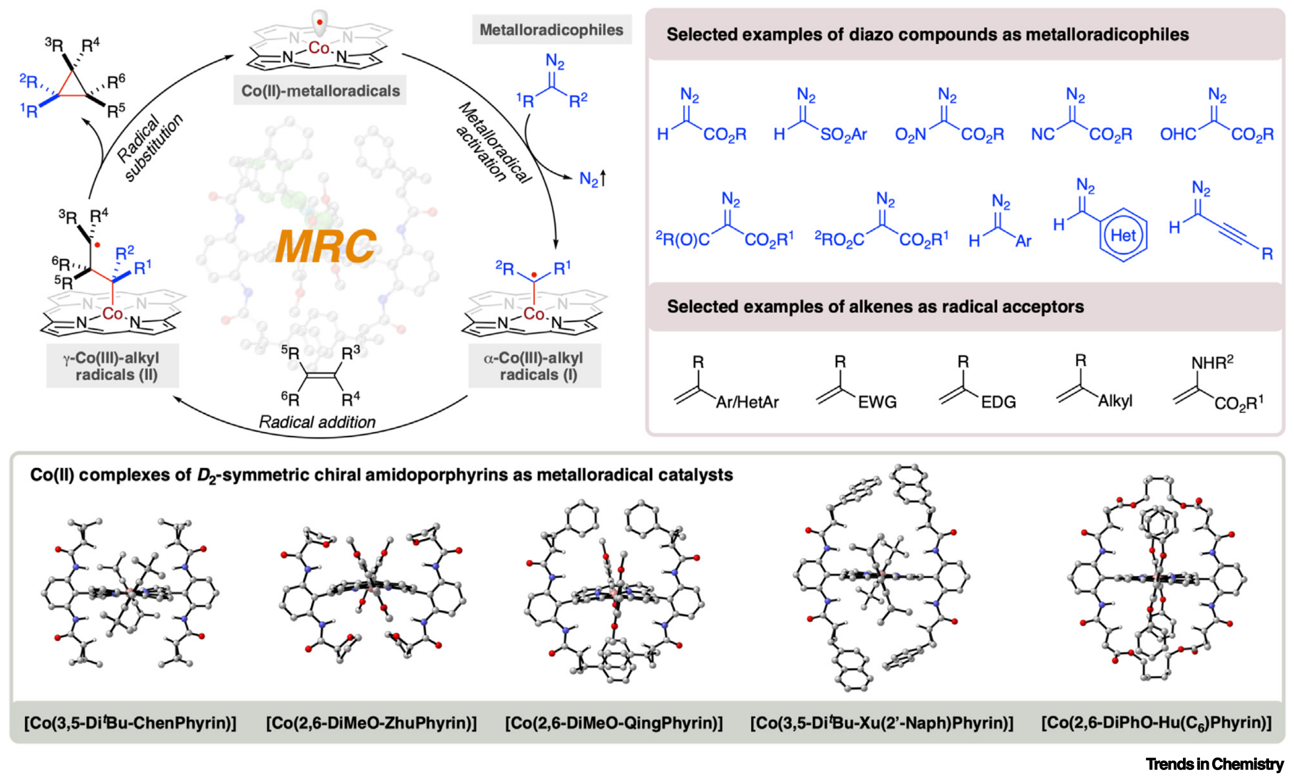
ORIGIN

Metalloradical catalysis (MRC), which utilizes metal-centered radicals to homolytically activate substrates for catalytic generation of metal-stabilized organic radicals as key intermediates, has emerged as a conceptually new approach for controlling both reactivity and stereoselectivity of radical reactions. As the first application of MRC, Co(II) complexes of chiral porphyrins, as stable 15e-metalloradicals, have been demonstrated as effective catalysts for asymmetric cyclopropanation of alkenes with diazo compounds via a stepwise radical mechanism.

REACTION MECHANISM

With the support of D_2-symmetric chiral amidoporphyrin ligands, the Co(II)-based metalloradical system, which operates under mild conditions with low catalyst loadings, can activate various classes of diazo compounds without the need of slow addition for asymmetric cyclopropanation of diverse types of alkenes as the limiting reagents. The corresponding cyclopropanes can be synthesized in high yields with excellent control of both diastereoselectivity and enantioselectivity. The broad substrate scope and the unique catalytic profile of the Co(II)-catalyzed cyclopropanation are attributed to the underlying stepwise radical mechanism that has been established through combined experimental and computational studies. The Co(II) complexes of porphyrins as metalloradical catalysts can activate diazo compounds homolytically while translocating the original radical character from the metal center to the α-carbon atom upon releasing dinitrogen gas, resulting in the generation of α-Co(III)-alkyl radicals **I**. The initially generated α-Co(III)-alkyl radical intermediates **I**, which represent a fundamentally new class of metal-stabilized organic radicals, are kinetically competent to undergo radical addition to alkenes, leading to the generation of γ-Co(III)-alkyl radicals **II** while forming the first C–C bond. Since Co–C bonds are significantly weaker than C–C bonds, the resulting γ-Co(III)-alkyl radical intermediates **II** preferentially proceed with intramolecular radical substitution (*3-exo-tet* radical cyclization) over intermolecular radical addition to another alkene molecule, giving rise to selective production of the cyclopropanes by forming the second C–C bond while regenerating the Co(II)-metalloradical catalysts. Different from the well-known concerted mechanism, the Co(II)-based radical cyclopropanation controls enantioselectivity and diastereoselectivity separately during two consecutive steps of C–C bond formation.



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IMPORTANCE

As the first demonstration of MRC to harness the potential of radical chemistry for stereoselective organic synthesis, the Co(II)-based metalloradical system for radical cyclopropanation provides a fundamentally different and practically attractive method for asymmetric synthesis of chiral cyclopropanes. Due to its distinctive stepwise radical mechanism involving unprecedented α-Co(III)-alkyl radical and γ-Co(III)-alkyl radical intermediates, Co(II)-catalyzed cyclopropanation enables some long-standing problems in asymmetric cyclopropanation to be addressed.

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https://doi.org/10.1016/j.trechm.2022.06.003

Acknowledgments

We are grateful for financial support by the National Institutes of Health (R01-GM102554) and National Science Foundation (CHE-1900375).

Declaration of interests

No interests are declared.

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https://doi.org/10.1016/j.trechm.2022.06.003