Basic chemicals, Pharmaceuticals

Positive oxygen enabled by designed peroxides

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Abstract

Oxygen is an essential bioelement for our daily lives and biological activities. The synthesis of oxygen-containing compounds, such as water, plays a vital role across a vast spectrum of fields—from basic chemicals to high-value-added compounds like pharmaceuticals. From a chemical perspective, one defining characteristic of oxygen is its high electronegativity. This property makes negatively charged oxygen anions common and familiar chemical species. In contrast, positively charged oxygen cations are almost impossible and highly unstable species. Recently, we succeeded in pioneering the creation of designed peroxides capable of realizing this otherwise unattainable "positive" oxygen, and we demonstrated its potential applications in synthetic chemistry—a groundbreaking achievement.

Background & Results

Peroxides are a general class of chemical species characterized by an oxygen-oxygen bond. The most familiar example in our daily lives is hydrogen peroxide (HO–OH), commonly used as the active ingredient in disinfectant solutions like antiseptic hydrogen peroxide. In industrial applications, peroxides are often utilized as initiators for radical polymerization reactions, which are essential for synthesizing polymers. Generally, oxygen-oxygen bonds have low bond energy, making them prone to homolytic cleavage under external stimuli such as heat or light, yielding corresponding oxygen radical species (Figure 1). Over the years, various peroxides suitable for different polymerization reactions have been developed.

Focusing on the cleavage modes of oxygen-oxygen bonds, we recognize that in addition to homolytic cleavage, heterolytic cleavage is theoretically possible. Heterolytic cleavage would produce an oxygen anion and an oxygen cation instead of oxygen radicals. While oxygen anions are very well-known and common due to oxygen's high electronegativity, oxygen cations are expected to be extremely unstable species, making efforts to utilize them in chemical synthesis exceedingly rare.

Intrigued by the potential of these rare oxygen cations, we started exploring their chemistry. Recently, we successfully developed a designed peroxide capable of generating "positive" oxygen, equivalent to an oxygen cation (Figure 2). When paired with an appropriate copper catalyst, this designed peroxide behaves as an oxygen cation and enables the introduction of oxygen functional groups into alkene molecules. Furthermore, we achieved high asymmetric induction, which conventional oxygen radical chemistry cannot accomplish. Specifically, we utilized optically active copper complexes as catalysts, successfully achieving the catalytic asymmetric synthesis of optically active ethers (Figure 3).

Significance of the research and Future perspective

Achieving the realization of "positive" oxygen species, which conventional chemistry deemed impossible, represents significant scientific and academic advancement. Furthermore, we have developed a novel method for incorporating this biologically essential element into organic molecules, which holds the promise of substantial contributions to fields such as drug discovery and pharmaceuticals. Moving forward, we aim to further refine the design of these "positive" oxygen species, making them more user-friendly and offering unique selectivity, with industrial applications in sight.

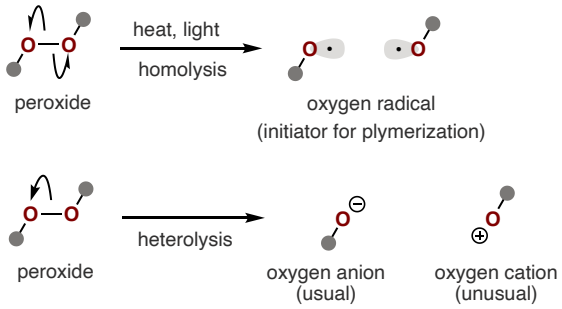

Fig.1: Cleavage patterns of O–O bond of peroxides

Fig. 2: Designed peroxide as an oxygen cation equivalent

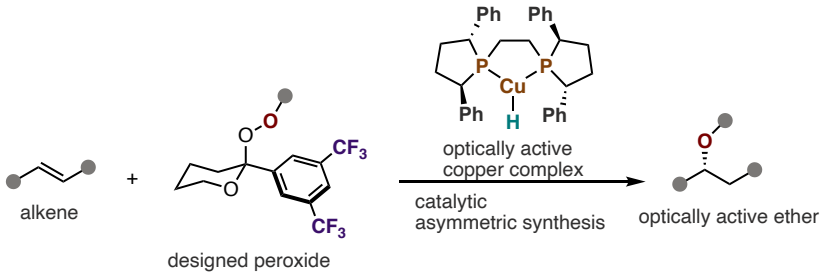

Fig. 3: Copper-catalyzed stereoselective hydroalkoxylation of alkenes with designed peroxides

Patent
Treatise Hirano, Koji et al. CuH-catalyzed regio-and stereoselective hydroalkoxylation of styrenes with acetal-based peroxides. ACS Catalysis. 2025, 15(10), 8353-8360. doi: 10.1021/acscatal.5c02202
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