Chem Soc Rev

REVIEW ARTICLE

View Article Online
View Journal | View Issue

Cite this: *Chem. Soc. Rev.*, 2024, **53**, 2326

Metal-catalyzed asymmetric reactions enabled by organic peroxides

Nengbo Zhu,[a] Huijie Yao,[abd] Xiyu Zhang[a] and Hongli Bao *[abcd]

As a class of multifunctional reagents, organic peroxides play vital roles in the chemical industry, pharmaceutical synthesis and polymerization reactions. Metal-catalyzed asymmetric catalysis has emerged as one of the most straightforward and efficient strategies to construct enantioenriched molecules, and an increasing number of metal-catalyzed asymmetric reactions enabled by organic peroxides have been disclosed by researchers in recent years. Despite remarkable progress, the types of asymmetric reactions facilitated by organic peroxides remain limited and the catalysis systems need to be further broadened. To the best of our knowledge, there is still no review devoted to summarizing the reactions from this perspective. In this review, we will endeavor to highlight the advances in metal-catalyzed asymmetric reactions enabled by organic peroxides. We hope that this survey will summarize the functions of organic peroxides in catalytic reactions, improve the understanding of these compounds and inspire future developments in this area.

Received 2nd September 2023

DOI: 10.1039/d3cs00735a

rsc.li/chem-soc-rev

1. Introduction

Organic peroxides are derived from hydrogen peroxide, where one or both hydrogen atoms are replaced by organic groups, such as alkyl, aryl, acyl groups, and so on. The general formula of organic peroxide is R^1–O–O–R^2, and it can be classified into several categories including alkyl hydroperoxide, dialkyl peroxide, diacyl peroxide, peroxyester, peroxide carbonate, peroxide ketal, *etc.* according to the structure (Scheme 1a).[1] Organic peroxide contains a weak covalent O–O bond the dissociation energy of which is mostly between 125 and 150 kJ mol^{-1}.[2] Upon heating, O–O bond homolysis occurs forming radicals that initiate the reaction (their 10 hour half-life temperature ranges detailed in Scheme 1a).[3,4] On the other hand, the metal catalyst can also facilitate the catalytic decomposition of organic peroxides through a single electron transfer (SET) pathway, leading to the generation of radical species under milder reaction conditions.[5] Organic peroxides can be used as oxidants, radical initiators, radical relay reagents and multifunctional reagents. After about 160 years of development, a large number of organic peroxides with diverse structures are readily available

[a] *State Key Laboratory of Structural Chemistry, Key Laboratory of Coal to Ethylene Glycol and Its Related Technology, Center for Excellence in Molecular Synthesis, Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences, 155 Yangqiao Road West, Fuzhou, Fujian 350002, P. R. China. E-mail: hlbao@fjirsm.ac.cn*

[b] *Fujian College, University of Chinese Academy of Sciences, 155 Yangqiao Road West, Fuzhou, Fujian 350002, P. R. China*

[c] *University of Chinese Academy of Sciences, Beijing 100049, P. R. China*

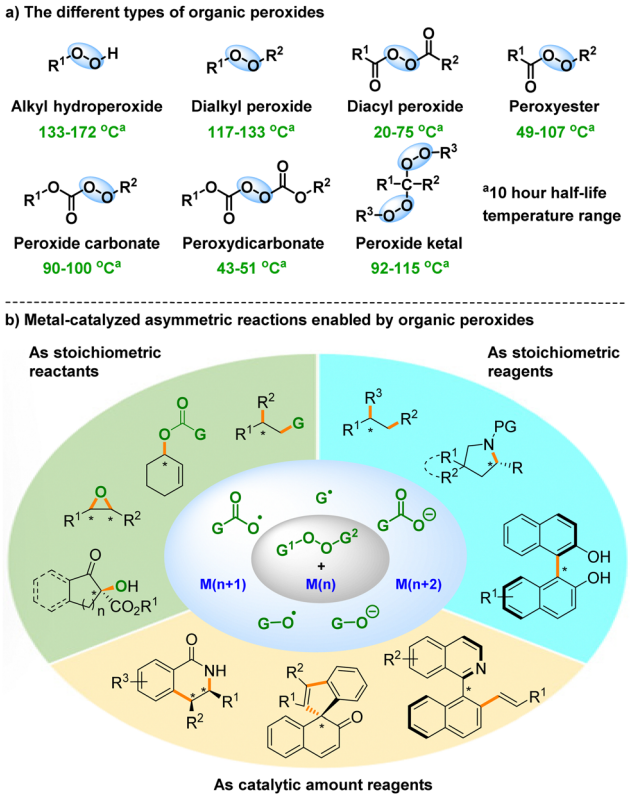
[d] *College of Chemistry, Fuzhou University, Fuzhou, Fujian 350108, P. R. China*

Nengbo Zhu

Nengbo Zhu received his PhD degree in organic chemistry from the University of Chinese Academy of Sciences in 2018 under the supervision of Prof. Hongli Bao. He is currently an engineer at the Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences. His current research interests include radical chemistry, asymmetric catalysis and functional polymers.

Huijie Yao

Huijie Yao was born in 2000 in Shandong Province (China). She received her BS degree in chemical engineering and technology from the Liaocheng University. Currently, she is carrying out her master studies at Fujian Institute of Research on the Structure of Matter and Fuzhou University under the supervision of Prof. Hongli Bao. Her research focuses on radical chemistry, asymmetric catalysis and new polymerization methodology.



Scheme 1 The types of organic peroxides and application in asymmetric reactions.

from hydrogen peroxides, carboxylic acids and alcohols, acyl chlorides, ketones, aldehydes, *etc.*[6,7] and these compounds become the commonly used raw materials in the chemical industry, medicinal chemistry and polymer chemistry.[2,8]

The first organic peroxide (Benzoyl Peroxide, BPO) was synthesized by Brodie in 1858. Initially, peroxides were only used as bleach and oxidants. The Baeyer–Villiger oxidation, which was first reported in 1899, forms an ester from a ketone or a lactone from a cyclic ketone, using peroxyacids or peroxides as the oxidant.[9] In the early 20th century, with the development of the polymerization industry, peroxides were widely used as initiators for radical polymerization. Although organic peroxides are widely used as free radical initiators and oxidants with more than 500 000 reports, the study of organic peroxides as radical relay reagents is less developed. Organic peroxides can undergo cleavage to generate oxygen-centered radicals, which can abstract hydrogen atoms to generate new radical species (radical relay), such as acyl radicals,[10] phosphinoyl radicals,[11] alkyl radicals,[12,13] *etc.* The decomposition of organic peroxides can also produce carbon-centered radicals after the release of CO_2 or acetone. Different to oxygen-centered radicals, carbon-centered radicals possess the unique capability of abstracting halogen atoms as well as electron poor hydrogen atoms,[14] leading to the generation of new desired radicals, such as haloalkyl radicals,[15,16] acetic carbon radicals,[17] α-cyanoalkyl radicals,[18,19] tris(trimethylsilyl)silyl radicals,[20] *etc.* As a result, by utilizing a radical relay strategy enabled by organic peroxides,[21,22] the sources of free radicals have been greatly expanded to organic compounds containing hydrogen elements (R–H) or organic halides (R–X), and the types of free radicals are enriched. These new radicals can then participate in further reactions, resulting in the desired transformations. In addition to radical relay reagents, the oxygen- or carbon-center radicals generated from organic peroxides can also serve as stoichiometric reactants to react with substrates and appear in the final products.[23] The classical reaction of peroxide as an oxyfunctionalization reagent is the Kharasch–Sosnovsky reactions, which is a useful tool for synthesizing allylic esters.[24] The first example of peroxides as alkylation reagents was reported by Fieser and Oxford in 1942.[25] However, the utilization of organic peroxides as alkylation reagents in organic synthesis is limited due

Xiyu Zhang

Xiyu Zhang was born in 1998 in Gansu Province (China). He received his BS degree in biopharmaceuticals from the Longdong University. Currently, he is carrying out his master studies at the Fujian Institute of Research on the Structure of Matter and Fujian Normal University under the direction of Prof. Hongli Bao. His current research interests include asymmetric catalysis and biofunctional materials.

Hongli Bao

Hongli Bao received her BS degree in chemistry from the University of Science & Technology of China in 2002. She obtained her PhD from the joint program of the Shanghai Institute of Organic Chemistry (SIOC, China) and the University of Science & Technology of China in 2008 with Professor Kuiling Ding and Professor Tianpa You. She joined the Tambar lab in 2009 and received the UT Southwestern Chilton Fellowship in Biochemistry in 2012. She started her independent career in 2014 at the Fujian Institute of Research on the Structure of Matter, Chinese Academy of Science. She is interested in developing metal-catalyzed new reactions and asymmetric catalysis.

to the chaotic cleavage of organic peroxides. Until the past decade, several types of reactions employing peroxides as oxidation type alkylation reagents under metal catalysis were developed by the Li,[26] Dirocco,[27] Bao,[28–30] and Stahl groups.[31]

The metal-catalyzed asymmetric reaction is one of the most efficient and economical approaches to construct optically pure molecules in pharmaceutical, agrochemical and materials industries.[32–36] Organic peroxides could play multiple roles in one catalytic cycle due to the multiple components therein, therefore, they are also widely applied in asymmetric reactions. Metal catalysts, such as Cu, Fe, Ti, Pd, and so on, generally have multiple oxidation states and can react with the organic peroxides through electron transfer processes. Compared with thermal cracking, the reactions of metal-catalyzed cleavage of organic peroxides are more controllable and easier to regulate the generation and following reactions of radical species under mild conditions. Several types of active species, including high-valent metal complexes, acyloxyl radicals, alkoxy radicals, alkyl radicals, acyloxy anions, and alkoxy anions, will be generated in the reaction system (Scheme 1b). These active species will enable various types of asymmetric reactions, such as asymmetric difunctionalized unsaturated C–C bond reactions,[37,38] Kharasch–Sosnovsky reactions,[39–43] asymmetric epoxidation,[44] *etc.* In these reactions, the organic peroxides can be used as oxidants, functionalization reagents, radical relay reagents, or ligand exchange promoters. More importantly, organic peroxides, as multifunctional reagents, can play multiple roles in a reaction cycle.[45] Therefore, an increasing number of metal-catalyzed asymmetric reactions enabled by organic peroxides have been reported by researchers in recent years.[37,42] In summary, the organic peroxides can be used as: (1) stoichiometric reactants (their components appear in the final product), (2) stoichiometric reagents (their components do not appear in the final product), and (3) catalytic amount reagents (such as oxidizing a lower valent pre-catalyst to the reactive high-valent metal species) (Scheme 1b). Hence, we will endeavor to highlight the advances in metal-catalyzed asymmetric reactions enabled by organic peroxides and emphasize reaction mechanisms and the role of organic peroxides in this review.

2. Organic peroxides as stoichiometric reactants

Organic peroxides can be used as stoichiometric oxidants to achieve asymmetric reactions, such as epoxidation of alkenes, sulfoxidation, *etc.* Moreover, the oxygen- or carbon-center radicals generated from organic peroxides can serve as stoichiometric reactants to react with substrates. In this section, we focus on the asymmetric reactions with organic peroxides as stoichiometric reactants (their components appear in the final product) under different metal catalysis.

2.1. Copper catalysis

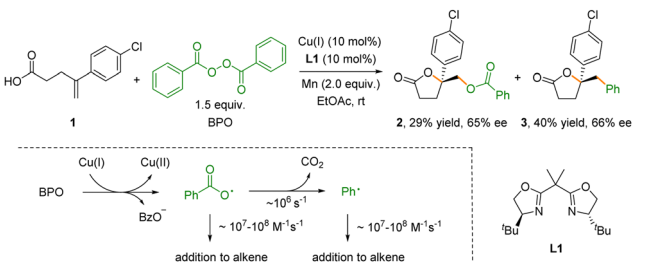
Copper ($3d^{10}4s^1$) has four oxidation states and is often used as a single-electron transfer catalyst. The copper catalyst facilitates the efficient decomposition of organic peroxides through a single electron transfer (SET) pathway, leading to the generation of the desired radical species. Therefore, the chiral copper catalysts are good candidates for the asymmetric reactions enabled by organic peroxides.

2.1.1. Asymmetric difunctionalization of unsaturated C–C bonds. The stereoselective transformation of unsaturated bonds through difunctionalization reactions provides an economical and efficient method to achieve enantioenriched building blocks. The unsaturated C–C bonds include unsaturated double and triple bonds, such as alkenes, alkynes, enynes and allenes. In the past decade, significant progress has been achieved in the field of metal-catalyzed asymmetric difunctionalization of unsaturated C–C bonds using organic peroxides as stoichiometric reactants.

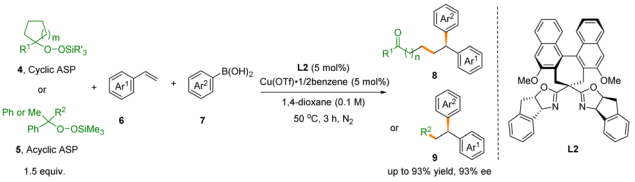
In 2015, Buchwald and co-workers pioneeringly developed a copper catalyzed asymmetric oxyfunctionalization of alkenes based on an enantioselective C–O bond forming process (Scheme 2).[46] It was found that in the presence of dibenzoyl peroxide, chiral catalyst and manganese(0), the reaction delivered two products, diacyloxylation product **2** (29% yield, 65% ee) and oxyarylation product **3** (40% yield, 66% ee) which were generated from benzoyloxyl O-radical or phenyl C-radical. The phenyl radical is presumably derived from the decarboxylation of the benzoyloxyl radicals. The rate constants of the addition of aroyloxyl radicals to the substrate and decarboxylation processes have been discussed in this work.

The chiral 1,1-diarylalkane structures are found in a variety of bioactive molecules. In 2020, Maruoka *et al.* reported a Cu-catalyzed highly enantioselective alkylarylation of vinylarenes using alkylsilyl peroxides as alkyl radical sources and arylboronic acids as aryl group sources (Scheme 3).[47] The reaction proceeds under practical reaction conditions by employing a novel set of binaphthyl-bis(oxazoline) (BN-BOX) hybrid ligands. The asymmetric 1,1-diarylalkane structures were obtained with excellent yield (up to 93%) and enantioselectivity (up to 93% ee)

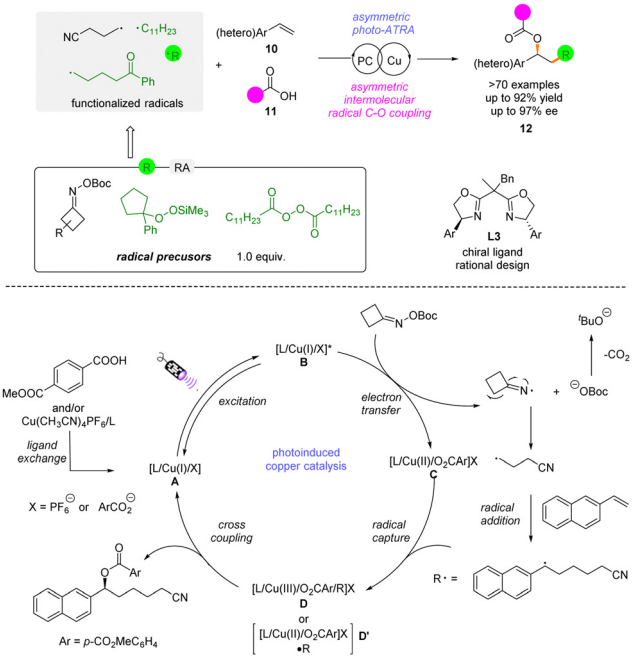
Visible light can also promote the metal-catalyzed asymmetric difunctionalization of alkenes. In 2022, Chen *et al.* reported a visible-light-induced copper-catalyzed asymmetric three-component photo-ATRA-type (ATRA: atom transfer radical addition) reaction of alkenes using oxime esters, alkylsilyl peroxide or lauroyl peroxide as ATRA reagents (Scheme 4).[48] This reaction exhibits broad substrate scope and high functional group tolerance with respect to each component (>70 examples;



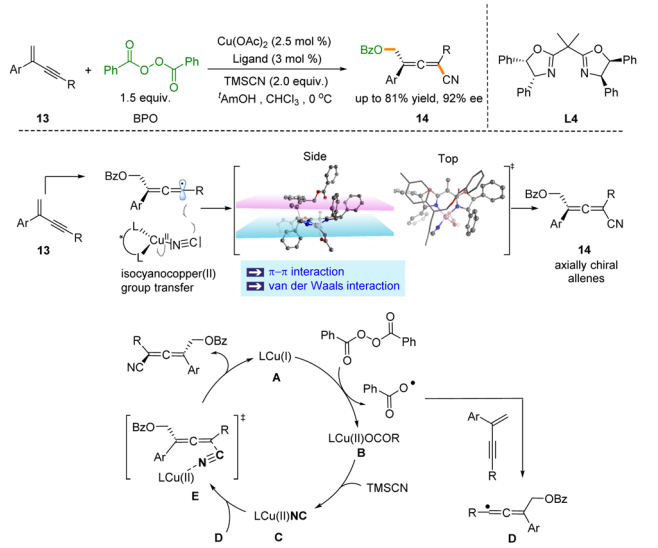
Scheme 2 Copper-catalyzed asymmetric oxyfunctionalization of alkenes.



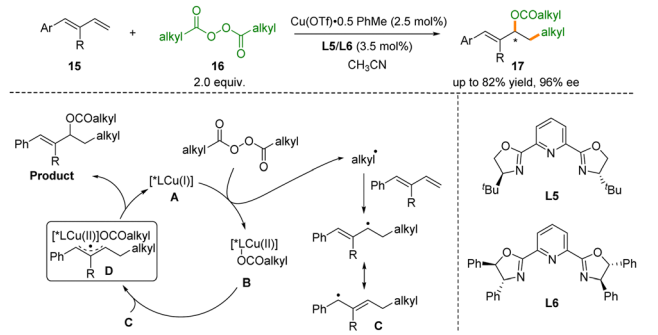
Scheme 3 Cu-catalyzed enantioselective alkylarylation of vinylarenes.



Scheme 4 Visible-light-induced copper-catalyzed asymmetric photo-ATRA-type reaction of alkenes.



Scheme 5 Asymmetric radical 1,4-difunctionalization of 1,3-enynes to chiral allenes *via* an outer-sphere pathway.



Scheme 6 Copper-catalyzed regioselective and enantioselective carboesterification of dienes.

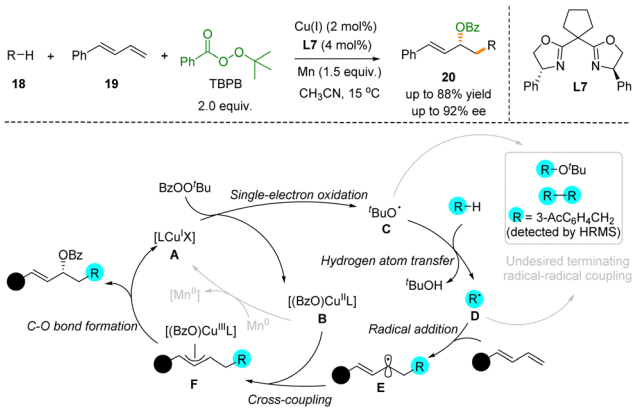
up to 97% ee). The experimental and theoretical studies revealed that highly enantioselective intermolecular C–O cross-coupling was enabled by the formation of the aryl π-bond-engaged [σ + π]-copper complex.

In 2020, Bao *et al.* disclosed the first radical enantioselective allene formation *via* a group transfer pathway in the context of copper-catalyzed radical 1,4-difunctionalization of 1,3-enynes (Scheme 5).[49] In this reaction, organic peroxides serve as acyloxyl radical sources to functionalize the enynes delivering the enantioselective allenes. Based on the experimental and theoretical studies, the π–π and van der Waals interactions may account for the observed enantioselective control of the allenyl radical and the cyanation reaction proceeds by an allenyl radical pathway rather than an allenyl cation pathway.

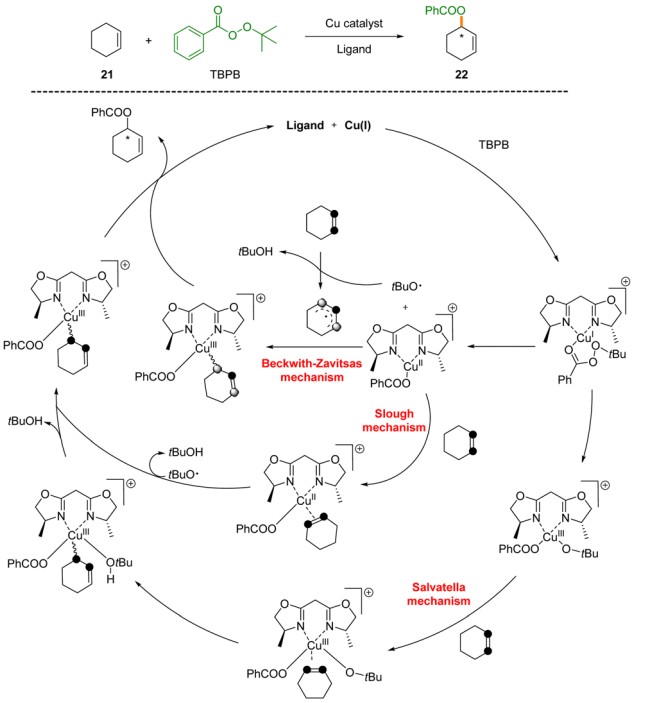
In addition to monoene, Bao *et al.* further disclosed a copper-catalyzed regioselective and enantioselective carboesterification of substituted dienes using alkyl diacyl peroxides as a source of both carbon and oxygen substituents in 2021 (Scheme 6).[50] In this reaction, the alkyl diacyl peroxide reacts with copper(I) complex (**A**) by SET to deliver the alkyl radical and copper(II) species (**B**). Based on the copper species observed and experimental results obtained, a possible reaction pathway involving alkyl radical and allylic radical intermediates was proposed. This work provided an important strategy for stereocontrol at free radical centers and may lead to the discovery of other asymmetric radical reactions.

Recently, Gong and co-workers developed an asymmetric 1,2-oxidative alkylation of conjugated dienes based on direct functionalization of strong and neutral C(sp^3)–H bonds enabled by the combination of hydrogen atom transfer and copper catalysis (Scheme 7).[13] This approach affords chiral allylic esters in high yields and enantioselectivities. The amount of toluene has a significant effect on the yield. In this reaction, the single-electron oxidation of Cu(I) with benzoperoxoate is the key step to generate the alkoxyl radical and Cu(II) benzoate complexes, which are responsible for the subsequent hydrogen atom transfer (HAT) and radical coupling. It represents a conceptually new alternative to processes that use prefunctionalized alkyl radical precursors.

2.1.2. Asymmetric Kharasch–Sosnovsky reactions. The allylic oxidation of alkenes to give allylic benzoates catalyzed by copper complexes with peroxides as oxidants was named the



Scheme 7 Asymmetric 1,2-oxidative alkylation of conjugated dienes.



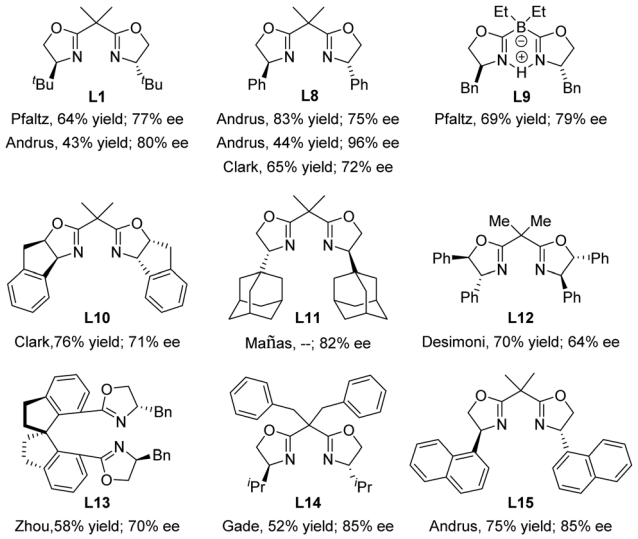
Scheme 8 The possible mechanism of the asymmetric Kharasch–Sosnovsky oxidation reaction.

Kharasch–Sosnovsky reaction. Since the first example reported in 1958 by Kharasch, various Kharasch–Sosnovsky reactions were developed.[24] The asymmetric version (known as the enantioselective Kharasch–Sosnovsky reaction) using chiral Cu complexes as catalysts was reported in the early 1990s. This method has become a useful tool for the synthesis of chiral allylic esters which will hydrolysis to valuable chiral allylic alcohols. Peroxides, usually *tert*-butyl peroxybenzoate (TBPB), have been employed as the standard stoichiometric oxidants in the asymmetric Kharasch–Sosnovsky reaction. Additionally, an alternative oxidation system is *tert*-butyl hydroperoxide (TBHP) in the presence of a carboxylic acid.[39,42,43]

Although many papers concerning the asymmetric Kharasch–Sosnovsky reaction have been reported, two pivotal points of the mechanism are still unclear up to now. One is the detailed steps of the mechanism, another one is the factors that determine the enantiocontrol of the reaction. Based on the mechanistic experiments and theoretical studies, three different reaction mechanisms have been proposed by the Beckwith–Zavitsas, Slough and Salvatella groups (Scheme 8). Beckwith–Zavitsas *et al.* proposed that the *tert*-butoxyl radical abstracts the allylic hydrogen, resulting in the formation of a cyclohexenyl radical. The cyclohexenyl radical then binds to the copper atom of the benzoate-copper(II) cation to generate the corresponding allyl-copper(III) key reaction intermediate.[51] In 2005, Slough *et al.* reported a different mechanism that involves formal π-bond migration in the organometallic species. They proposed that hydrogen abstraction occurs between the *tert*-butoxyl radical and the ligand-bound benzoate-cyclohexene-copper(I) ion. In a subsequent step, a Cu–C δ-bond was given in an intermolecular reaction.[52] In 2008, Salvatella *et al.* discussed the above two mechanisms and proposed a new reaction mechanism by investigating the reaction path using DFT calculations with the B3LYP/6-31G* theory. The authors suggested that the rate-limiting step of the reaction consists of an intramolecular step involving the abstraction of an allylic hydrogen from cyclohexene which is π-bound to the copper(III) complex.[53]

Asymmetric Kharasch–Sosnovsky oxidation is frequently used as a benchmark reaction to evaluate the performance of copper complexes that incorporate various chiral ligands. The results of enantioselectivity and yield are highly dependent on the ligand structure. The structural type of ligands used in this reaction mainly focuses on several categories, including oxazoline-type, amino acid-type, bipyridine-type, and a few other types. Oxazoline ligands are often used in the asymmetric Kharasch–Sosnovsky oxidation and have shown excellent enantioselectivity control. The reactions with amino acid-type ligands, such as prolines and bicyclic amino acids, afforded the optically active allylic esters with moderate enantioselectivities and yields. Most of the reactions with the bipyridine-type ligands required excessively long reaction times to give products with moderate enantioselectivities and conversions. In this section, we focus on the asymmetric Kharasch–Sosnovsky oxidation with different types of ligands using organic peroxides as stoichiometric oxidants. To ease the reading, the ligands have been divided into five categories: (1) bisoxazoline type, (2) trisoxazoline and multioxazoline type, (3) bipyridine and phenanthroline type, (4) amino-acid type, and (5) other types. First, we discussed the reaction of cyclic olefins using various ligands, and then, acyclic alkenes were viewed. Additionally, when available, this review was primarily focused on describing the reaction results using cyclohexene as a substrate in order to compare the enantioselectivity and efficiency of the catalyst system.

2.1.2.1. Bisoxazoline ligands. Chiral bisoxazoline ligands with different linking groups are often employed in the asymmetric Kharasch–Sosnovsky oxidation. The earliest example was reported by Pfaltz and co-workers adopting Cu(I)OTf with a C_2-symmetric bisoxazoline ligand as a catalyst. The reaction

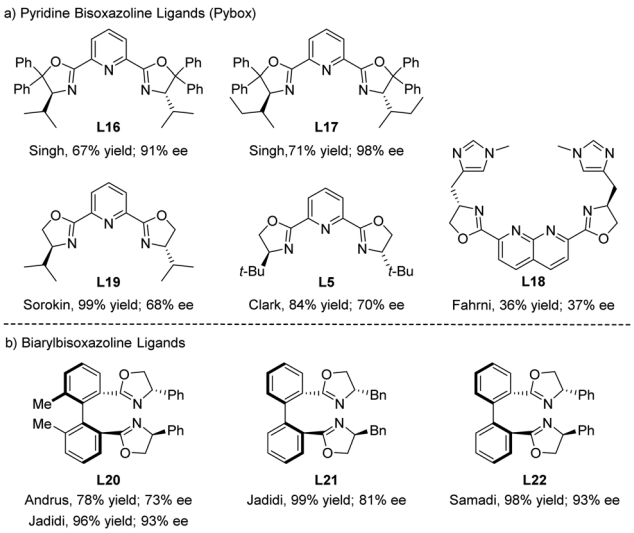


Scheme 9 Bisoxazoline ligands employed in the asymmetric Kharasch–Sosnovsky oxidation.

afforded optically active 2-cycloalkenyl benzoates from cyclohexene in 64% yield and 77% ee in the presence of *tert*-butyl perbenzoate (Scheme 9, **L1**).[54] Following this, the copper catalysts coordinating with various bisoxazoline ligands were developed for asymmetric Kharasch–Sosnovsky oxidation. In 1995, Andrus *et al.* reported a copper(I) catalyst system to form chiral 2-cycloalkenyl benzoates in 43% yield and 80% ee (Scheme 9, **L1**) using cyclohexene as a substrate.[55] Then, the new peresters with the different substituent groups were investigated. Cyclohexene reacted with *para*-chloro *tert*-butylperbenzoate in the presence of diphenylbisoxazoline-copper(I) hexafluorophosphate affording the allylic benzoate esters in 83% yield and 75% ee (Scheme 9, **L8**).[56] In 2002, a highly enantioselective process using bisoxazoline ligands with *tert*-butyl *p*-nitroperbenzoate to produce enantiomerically enriched ester with cyclohexene in 44% yield and 96% ee (Scheme 9, **L8**) was developed by Andrus and co-workers.[57] The asymmetric allylic oxidation of cyclohexene with bisoxazoline ligands using a new peroxycarbamate as an oxidant providing the corresponding chiral ester in 65% yield and 72% ee (Scheme 9, **L8**) was reported by Clark *et al.* in 2005.[58] A chiral boron-bridged bisoxazoline ligand was designed and prepared by Pfaltz *et al.* in 2008, which was tested in oxidation of cyclohexene affording the ester with 69% yield and 79% ee (Scheme 9, **L9**).[59]

Several different structures of bisoxazoline ligands were examined by researchers. The copper complexes of bisoxazolines, prepared from (1*S*,2*R*)-aminoindanol, have been studied as catalysts for the allylic oxidation of cyclohexene with TBPB by Clark *et al.* in 1998 and the reaction afforded the enantiomerically enriched ester in 76% yield and 71% ee (Scheme 9, **L10**).[60] The bisoxazoline featuring two adamantane skeletons (AdamBox, **L11**) was prepared and the enantioselective induction properties in allylic oxidation of cyclopentene with TBPB was investigated by Mañas *et al.* in 2002, providing the chiral ester in 82% ee (Scheme 9, **L11**).[61] The copper(I) triflate-catalyzed asymmetric allylic oxidation of cyclohexene with 4,5-diphenyl substituted bisoxazoline affording the ester in 70% yield and 64% ee (Scheme 9, **L12**) was reported by Desimoni and co-workers in 2001.[62] Zhou *et al.* disclosed a new type of SpiroBOX ligands which were applied to the Cu-catalyzed asymmetric allylic oxidation of cyclohexene with *tert*-butyl perbenzoate giving the ester in 58% yield and 70% ee (Scheme 9, **L13**).[63] The sidearm functionalized bisoxazoline ligand has been synthesized by Gade *et al.* in 2006 and tested in the copper catalyzed asymmetric Kharasch–Sosnovski reaction of cyclohexene with *tert*-butyl *p*-nitroperbenzoate giving the allylic ester in 52% yield and 85% ee (Scheme 9, **L14**).[64] The application of naphthyl substituted bisoxazoline in oxidation of cyclohexene with *t*-butyl *p*-nitroperbenzoate has been performed by Andrus *et al.* in 2012, achieving good reactivity (75% yield) while maintaining high enantioselectivity (85% ee) (Scheme 9, **L15**).[65]

The asymmetric Kharasch–Sosnovsky reactions based on the pyridine bisoxazoline ligands (Pybox) were published independently by Singh, Fahrni, Sorokin, and Clark groups. The investigations of copper complexes coordinated with chiral pybox ligands were carried out by Singh *et al.* and the cyclohexene reacted with *tert*-butyl perbenzoate in the presence of phenylhydrazine providing the ester up to 67% yield and 91% ee at 25 °C in 1 hour (Scheme 10, **L16**).[66–68] Various peresters were investigated in allylic oxidation of cyclohexene using pybox as a ligand to achieve high asymmetric induction (up to 71% yield and 98% ee) (Scheme 10, **L17**) and the authors found that the asymmetric induction in this reaction strongly depended on the identity of the substituents attached to the aryl ring of peresters.[69,70] Allylic oxidation of cyclohexene catalyzed by dinuclear copper complexes with chiral ligand giving the ester products with 36% yield and 37% ee was reported by Fahrni *et al.* (Scheme 10, **L18**).[71] Another pybox ligand was examined in the allylic oxidation of cyclohexene by Sorokin *et al.* in 2007 and the high product yield (99%) and moderate enantioselectivity (68% ee) were obtained (Scheme 10, **L19**).[72] Enantioselective



Scheme 10 Pyridine bisoxazoline and biarylbisoxazoline ligands.

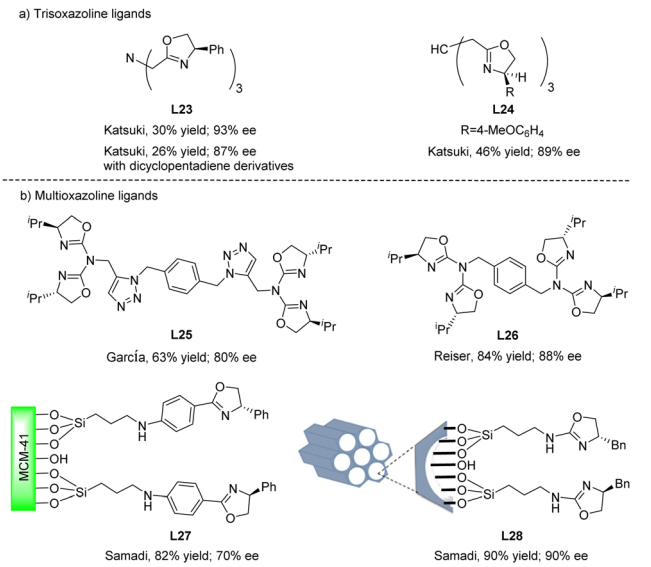
allylic oxidation of racemic bridged bicyclic alkene using the pybox ligand was explored by Clark *et al.* with good yields (84%) and moderate asymmetric induction (70% ee) (Scheme 10, **L5**).[73]

The new bi-*o*-tolyl bisoxazolines were prepared by Andrus *et al.* and examined in the asymmetric allylic oxidation reaction employing peroxyesters with different substituents as oxidants. The reaction afforded the corresponding ester with up to 78% yield and 73% ee (Scheme 10, **L20**).[74,75] The chiral bi-*o*-tolyl bisoxazoline (Scheme 10, **L20**)[76] and biphenylbisoxazoline (Scheme 10, **L21**)[77] ligands were also investigated by Jadidi and co-workers. They found that the addition of SBA-15 mesoporous silica as an additive significantly increased the enantioselectivity and efficiency of the reaction, resulting in 96% yield and 93% ee. Recently, a range of *t*-butyl perbenzoates bearing electron-withdrawing and electron-donating substitutions on the phenyl ring were studied by Samadi *et al.* with HZSM-5 zeolites as a porous additive using the biphenylbisoxazoline ligands. The enantioenriched allylic esters were obtained with excellent enantioselectivities (93% ee) and yields (98%) adopting *t*-butyl *p*-nitroperbenzoate as the oxidant and cyclohexene as the substrate (Scheme 10, **L22**).[78]

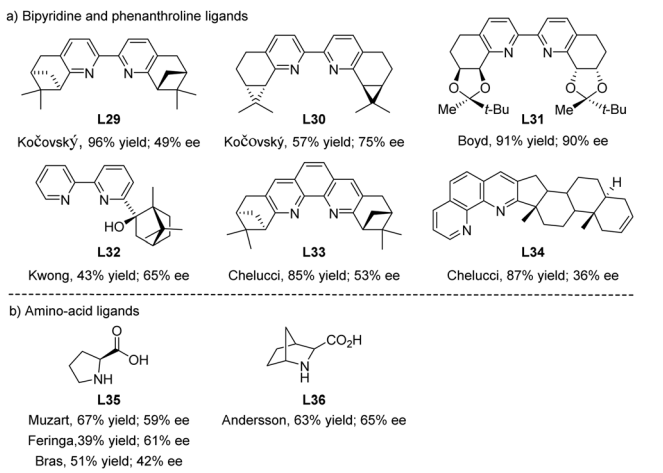
2.1.2.2. Trisoxazoline or multioxazoline ligands. The C_3-symmetric tris(oxazoline) ligands were designed and synthesized by Katsuki and co-workers. These ligands were investigated in the enantioselective allylic C–H oxidation of cyclopentene and the reaction with **L23** as the ligand showed high enantioselectivity (up to 93% ee) (Scheme 11, **L23**).[79,80] Additionally, asymmetrization of racemic dicyclopentadiene derivatives was reported by using copper complexes coordinated with chiral tris(oxazoline) as catalysts. It is worth noting that optically active acyloxylated dicyclopentadiene derivatives which are useful building blocks bearing multiple asymmetric centers were obtained in a highly enantioselective manner (up to 87% ee) (Scheme 11, **L23**).[81] A newly introduced C_3-symmetric trisoxazoline ligand was synthesized from methanetriacetic acid and optically pure β-amino alcohol by Katsuki and co-workers. It was used in the copper-mediated asymmetric allylic oxidation of cyclopentene affording the product with 46% yield and 89% ee (Scheme 11, **L24**).[82]

Several examples of recoverable heterogenous enantioselective catalytic systems with multioxazoline core ligands for the Kharasch–Sosnovsky oxidation of cycloalkenes were reported. The ditopic azabisoxazoline ligands were investigated by García *et al.* in 2012 and the best result with cyclohexene as substrate was obtained in 63% yield and 80% ee with the glycerol-derived solvent (Scheme 11, **L25**).[83] This reaction system has shown good catalyst recovery properties, allowing up to four uses with good yields and enantioselectivities. An easily recoverable and reusable enantioselective catalytic system based on a new ditopic chiral ligand was developed by Reiser *et al.* in 2012 (Scheme 11, **L26**).[84] **L26** is able to form insoluble coordination polymers with copper salts, and good enantioselectivities and yields were obtained in seven successive cycles. A series of chiral 4-oxazolinylaniline ligands were covalently grafted onto the mesoporous silicas MCM-41 (Scheme 11, **L27**)[85] or SBA-15 (Scheme 11, **L28**)[86] and their catalytic and induced asymmetric effects on the asymmetric allylic oxidation of cycloolefins were investigated by Samadi and co-workers. These heterogeneous catalysts were easily recoverable and could be reused five or eight times without remarkable loss in reactivity, yield, and enantioselectivity. It is noteworthy that, these reaction results are a significant step in the advancement of green chemistry.

2.1.2.3. Bipyridine and phenanthroline ligands. The C_2-symmetrical bipyridine ligands (Scheme 12, **L29**[87] and **L30**[88]) were prepared by Kočovský *et al. via* a *de novo* construction of the pyridine ring and investigated in the Kharasch–Sosnovsky reaction. The reaction resulted in the allylic oxidation of the cyclohexene product with excellent yield (96%) and moderate enantioselectivity (49% ee) (Scheme 12, **L29**) in less than 30 minutes at room temperature. The results showed that these



Scheme 11 Trisoxazoline and multioxazoline ligands.

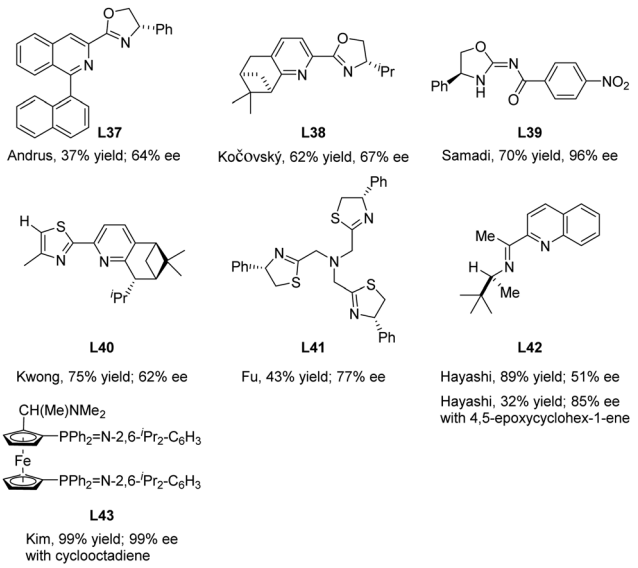


Scheme 12 Bipyridine, phenanthroline and amino-acid ligands.

ligands shortened reaction times considerably, while most of the other ligands required excessively long reaction times to achieve moderate yield. Several new 2,2′-bipyridine ligands have been designed by Boyd *et al.* and proved to be useful ligands for asymmetric allylic oxidation with high efficiency (91% yield) and excellent enantioselectivity (90% ee) (Scheme 12, **L31**).[89] A series of C_1-symmetric bipyridine ligands were synthesized by Kwong and co-workers. They found that the asymmetric Kharasch–Sosnovsky reaction with the C_1-symmetric ligands was slightly slower compared to C_2-symmetric bipyridine ligands. In the case of cyclohexene, the reaction with the C_1-symmetric bipyridine ligand achieved modest yield (43%) and moderate enantioselectivity (65% ee) (Scheme 12, **L32**).[90] A general procedure for the preparation of a new chiral C_2-symmetric 1,10-phenanthroline derived from pinene was developed by Chelucci and co-workers. The ligand (**L33**) was assessed in allylic oxidation of cyclohexene affording the chiral ester in 86% yield and 53% ee (Scheme 12, **L33**).[91] C_1-symmetric 1,10-phenanthrolines were also investigated and the results indicated that the topological property of at least a substituent close to the heterocyclic nitrogen is necessary to obtain an effective enantioselective catalytic system (Scheme 12, **L34**).[92]

2.1.2.4. Amino-acid ligands. The amino-acid ligands were investigated in the asymmetric allylic oxidation of cycloalkenes using *tert*-butyl peroxybenzoate as the oxidant. These reactions delivered the chiral allylic ester with moderate enantioselectivities and yields. The proline (Scheme 12, **L35**) was examined by the Muzart,[93–95] Feringa,[96,97] and Bras[98] groups and the best enantioselectivity with cyclohexene as substrate was achieved with 61% ee. Bicyclic α-amino acids were also examined by Andersson *et al.* and cyclohexene was oxidized to the corresponding benzoate in 63% yield and 65% ee (Scheme 12, **L36**).[99] It is worth noting that amino acid ligands have been rarely investigated in the enantioselective version of the Kharasch–Sosnovsky reaction in the recent decade, presumably because of the higher enantioselectivity and efficiency of oxazoline type ligands.

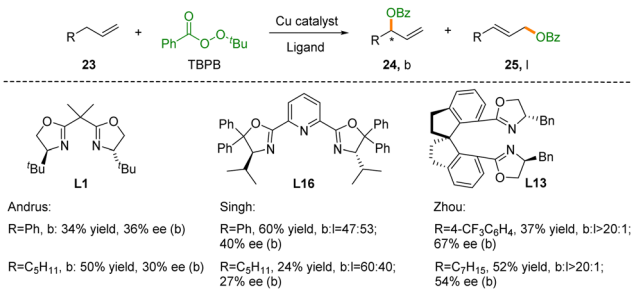
2.1.2.5. Other type ligands. The oxazoline ligand with the 1-naphthylisoquinoline group was prepared using the Pictet–Gams reaction by Andrus and co-workers. It is worth noting that the use of phenylhydrazine as a reducing additive gave much faster reaction times with improved enantioselectivity (64% ee) in the asymmetric copper catalyzed allylic oxidation of cyclohexenes (Scheme 13, **L37**).[100] New pinene-derived pyridines as bidentate chiral ligands were achieved from the readily available β-pinene by Kočovský and co-workers. The copper complex in cooperation with the pyridine-oxazoline ligand (**L38**) was found to catalyze the enantioselective esterification of allylic C–H bonds of cyclopentene in 62% yield and 67% ee (Scheme 13, **L38**).[101] A new amido-oxazoline ligand was investigated in the asymmetric Kharasch–Sosnovsky reaction of cyclohexene with *tert*-butyl-4-nitrobenzoperoxoate by Samadi *et al.* and the reaction afforded the ester in good yield (70%) and excellent enantioselectivity (96% ee) (Scheme 13, **L39**).[102]



Scheme 13 Other types of ligands employed in the asymmetric Kharasch–Sosnovsky oxidation.

Two types of thiazoline ligands, **L40**[103] and **L41**[104] (Scheme 29), were synthesized by the Kwong and Fu groups, respectively. And, moderate yields and enantioselectivities were obtained in the allylic oxidation of cycloalkenes with these ligands. A new *N*,*N*-bidentate Schiff base ligand (Scheme 13, **L42**) was exploited in the allylic oxidation of cycloalkene[105] and 4,5-epoxycyclohex-1-ene[106] by Hayashi and co-workers. Interestingly, prolonged reaction time (40 h) increased the *trans*/*cis* isomer ratio up to >99/1 with 4,5-epoxycyclohex-1-ene as substrate. Furthermore, the chiral (iminophosphoranyl)ferrocenes were proved to be efficient ligands with high reactivity and enantioselectivity in the allylic oxidation of various cyclic olefins by Kim and co-workers. Even more remarkably, excellent enantioselectivity (99% ee) and yield (99%) were obtained from the reaction of cyclooctadiene (Scheme 13, **L43**).[107]

2.1.2.6. The asymmetric Kharasch–Sosnovsky reaction of acyclic alkenes. The asymmetric intermolecular asymmetric allylic C–H oxidation of cyclic alkenes has seen significant development with high enantioselectivity. However, the results for acyclic olefins, such as allylbenzene and 1-octene, have been unsatisfactory in terms of efficiency, enantioselectivity and regioselectivity. The first asymmetric Kharasch–Sosnovsky reaction of acyclic olefins was reported by Andrus *et al.* in 1995. This reaction adopted copper(I) triflate and a C_2-symmetric bisoxazoline ligand (Scheme 14, **L1**) as a catalyst in the presence of *tert*-butyl perbenzoate.[55] It is worth noting that the enantioselectivities of the allylic oxidation of allylbenzene and 1-octene were improved to 36% and 30% ee, respectively, at higher temperatures (55 °C) with benzene as the solvent. The chiral tridentate pybox ligand (Scheme 14, **L16**) was also examined in allylic oxidation of acyclic olefins by Singh and co-workers.[68,69] The result for allylbenzene showed a mixture of branched and linear products with a ratio of 47 : 53 and moderate enantioselectivity (40% ee). 1-Octene also afforded a mixture of benzoate products (b : l = 3 : 2) in 24% yield and 27% ee.

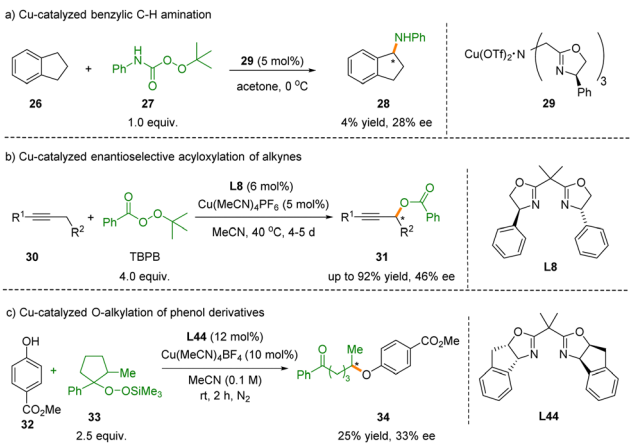


Scheme 14 Asymmetric Kharasch–Sosnovsky oxidation for acyclic alkenes.

The oxidation of various acyclic alkenes by allylic C–H activation with the complexes of copper and chiral spiro bisoxazoline ligands as catalysts was developed by Zhou *et al.* in 2013 (Scheme 14, **L13**).[108] This work achieved excellent regioselectivity (>20 : 1 in most cases). The enantioselectivities of *n*-decene and 1-allyl-4-(trifluoromethyl)benzene were up to 54% and 67% ee, respectively. These results represent the best results for the asymmetric Kharasch–Sosnovsky reaction of acyclic olefins up to now.

A considerable amount of asymmetric allylic oxidation of alkene reactions with copper complexes incorporating chiral ligands as catalysts have been reported in the last three decades. High yields and enantioselectivities can be achieved with cyclic olefins under suitable conditions; however, no single ligand has emerged as superior for all substrates and a prolonged reaction time (up to several days at room temperature) is typically required. Moreover, the efficiency and enantioselectivity of the asymmetric Kharasch–Sosnovsky reaction of acyclic olefins did not give satisfactory results and it remains a longstanding challenge.

2.1.3. Other asymmetric reactions. Copper catalysis plays a significant role in metal-catalyzed asymmetric reactions. In addition to the aforementioned reactions, there are some other asymmetric reactions promoted by organic peroxides. In 1997, Katsuki *et al.* disclosed a copper catalyzed allylic or benzylic C–H amination by treating alkenes or alkylarenes with *t*-butyl *N*-(*p*-toluenesulfonyl)peroxycarbamate (Scheme 15a).[109]



Scheme 15 Cu-catalyzed other asymmetric reactions enabled by organic peroxides.

The reaction afforded the amination products in moderate yield. When attempting the asymmetric version of this reaction using the $Cu(OTf)_2$-tris(oxazoline) complex at 0 °C, the reaction afforded products in 4% yield and 28% ee.

In 1998, a direct copper-catalyzed acyloxylation of alkynes with *t*-butyl peroxybenzoate in an enantioselective manner was developed by Clark and co-workers (Scheme 15b).[110] The corresponding propargylic oxidation products were obtained upon the oxidation of non-terminal alkynes with excess perester using copper-bisoxazoline complexes as catalysts with high yield (up to 92%) and moderate enantioselectivity (46% ee).

Recently, a Cu-catalyzed *O*-alkylation of phenol derivatives using alkylsilyl peroxides as alkyl radical sources was described by Maruoka and co-workers. This catalyst system can be applied to the asymmetric reaction and it afforded the corresponding product in 25% yield with 33% ee (Scheme 15c).[111] The control experiment suggested that this reaction proceeds *via* a radical mechanism.

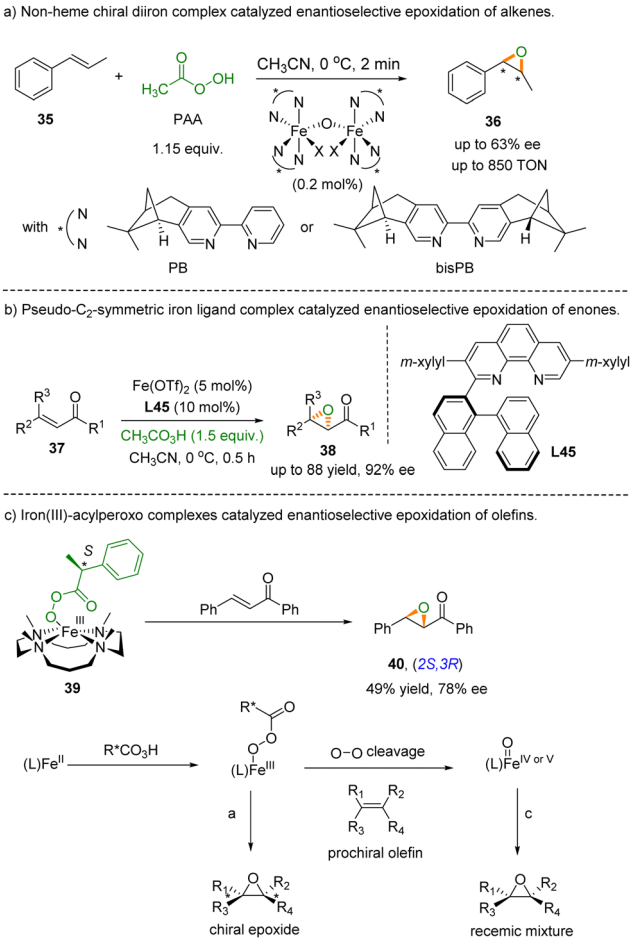
2.2. Iron catalysis

Iron is an inexpensive and low toxicity transition metal catalyst and is abundant in nature, which makes it very attractive to asymmetric catalytic reactions.[112] Iron ($3d^64s^2$) spans formal oxidation states ranging from −II to +VI and often used as an electron transfer catalyst in redox reactions.

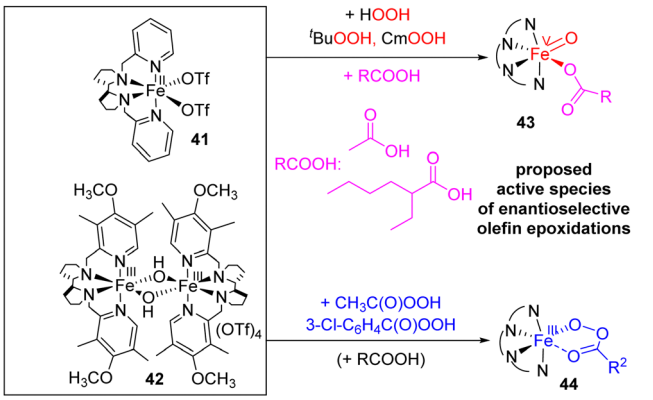
2.2.1. Asymmetric epoxidation of alkenes. Among various practical asymmetric epoxidation of alkene approaches, the development of an iron catalyst system is particularly attractive due to its low cost and environmentally friendly nature. Furthermore, understanding the fundamental aspects of the chemistry and mechanism of iron-catalyzed oxidations, which play important roles in biological metabolism, may help in the understanding of enzymatic oxidations and lead to new insights in biocatalysis.

In 2007, Ménage *et al.* pioneeringly disclosed the example of a non-heme chiral diiron complex $Fe_2O(bisPB)_4(X)_2(ClO4)_4$ (X = H_2O or CH_3CN) catalyzed enantioselective epoxidation of alkenes (Scheme 16a).[113] The reaction favors electron deficient alkenes with high efficiency (up to 850 TON) and moderate enantioselectivity (63%) by employing peracetic acid as an oxidant. The authors demonstrated that the dinuclear iron catalyst is necessary for this reaction. It is worth noting that its simple preparation and high efficiency may serve as a good alternative for asymmetric oxidations of terminal and electron-deficient alkenes.

In 2011, Yamamoto and co-workers reported an iron complex with the combination of $Fe(OTf)_2$ and novel phenanthroline ligands (Scheme 16b).[114] This pseudo-C_2-symmetric orthophenanthroline ligand-based catalyst, revealed by X-ray crystallography, enables the catalytic asymmetric epoxidation of acyclic β,β-disubstituted enones giving highly enantioenriched β,β-epoxyketones (up to 92% ee). Moreover, these β,β-epoxyketones can be further converted to functionalized β-ketoaldehydes with an all-carbon quaternary center. The use of peracetic acid as a terminal oxidant is crucial for the production of epoxides in this work. This work provides a



Scheme 16 Iron catalyzed enantioselective epoxidation of alkenes.



Scheme 17 Fe(PDP) complexes with various oxidants in the enantioselective epoxidation of olefin reactions.

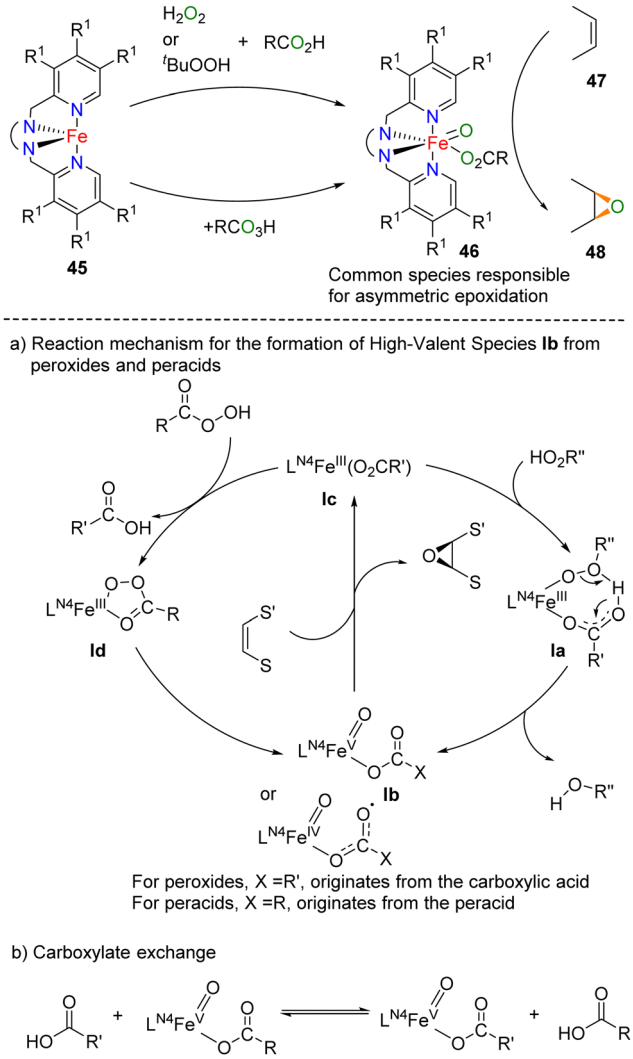
new strategy for designing pseudo-C_2-symmetric orthophenanthroline ligand-based catalysts.

The groups of Nam, Talsi and Costas developed different iron catalytic systems and investigated the reaction mechanisms independently. In 2016, Nam *et al.* synthesized a mononuclear nonheme high-spin iron(III)–acylperoxo complexes bearing an *N*-methylated cyclam ligand (Scheme 16c).[115] Epoxides were yielded as the major products with high chemo-, stereo-, and enantioselectivities in the epoxidation of olefins by using chiral iron(III)–acylperoxo complexes, indicating that iron(III)–acylperoxo species are the epoxidizing agents. Based on the ^{18}O-labeled water experiments, the authors proposed that mononuclear nonheme high-spin iron(III)–acylperoxo complexes act as strong oxidants capable of oxygenating hydrocarbons prior to their conversion into iron-oxo species *via* O–O bond cleavage. Furthermore, they hypothesized that the spin states or the structures of iron(III)–acylperoxo complexes are key factors that control the reactivities of the nonheme iron(III)–acylperoxo complexes.

In the same year, Talsi and co-workers investigated the mechanistic landscape of the Fe(PDP) catalyst family with various oxidants, including H_2O_2, organic hydroperoxides, and peracids (Scheme 17).[116] The combined data of EPR (electron paramagnetic resonance) spectroscopy, enantioselectivity, Hammett, *Z*-stilbene epoxidation stereoselectivity, and ^{18}O labeling suggested that the same oxoiron complexes [(L)FeV = O(OC(O)R)]$^{2+}$species are the actual epoxidizing acids in both catalyst systems (L)Fe/H_2O_2/carboxylic acid and (L)Fe/AlkylOOH/carboxylic. On the contrary, the epoxidation is predominantly conducted by the acylperoxo–iron(III) intermediates [(L)FeIII(OOC(O)R_2)]$^{2+}$ in a concerted fashion in the systems (L)Fe/R^2C(O)OOH (R^2 = CH_3 or 3-Cl–C_6H_4). And the plausible mechanisms of epoxidations with different oxidants were proposed in this article.

The enantioselectivities obtained under different reaction conditions for two iron catalysts (*S*,*S*)-[Fe(CF_3SO_3)$_2$(^{Me2N}pdp)] ((*S*,*S*)^{Me2N}1Fe) and (*S*,*S*)-[Fe(CF_3SO_3)2(^{dMM}pdp)] ((*S*,*S*)^{dMM}1Fe) have been analyzed by Costas *et al.* in 2017 (Scheme 18).[117] The enantioselectivities of reactions with a series of peracids were compared with those obtained by combining peroxides and carboxylic acids. These results indicated that the same oxidant is responsible for the asymmetric epoxidation reaction in both scenarios. And the experimental data provided conclusive evidence that the reaction formed the same oxygen atom transfer species The authors suggested that the putative oxidant is a Fe^{V}(O)(O_2CR) (or Fe^{IV}(O)($^{\bullet}O_2$CR)) (**Ib**) species.

2.2.2. Asymmetric carboazidation of alkenes. Carboazidation of alkenes is an efficient protocol for the synthesis of organic azides. In 2021, Feng and co-workers disclosed an efficient enantioselective radical carboazidation of α, β-unsaturated ketones catalyzed by chiral *N*,*N*′-dioxide/Fe(OTf)$_2$ complexes (Scheme 19).[118] Alkyl peroxides were used as ideal carbon radical sources or radical relay reagents to generate more carbon radical intermediates for alkylazidation of alkenes. Mechanistic studies and DFT calculations suggest that the radical pathway is involved in the reaction process and the azido transfers to the radical intermediate *via* an intramolecular five-membered transition state with the internal nitrogen of the Fe–N_3 species. A wide array of chiral α-azido carbonyl derivatives, which could be further transformed into highly valuable chiral amino ketones, amino alcohols, and vicinal diamines, were synthesized by this efficient protocol.

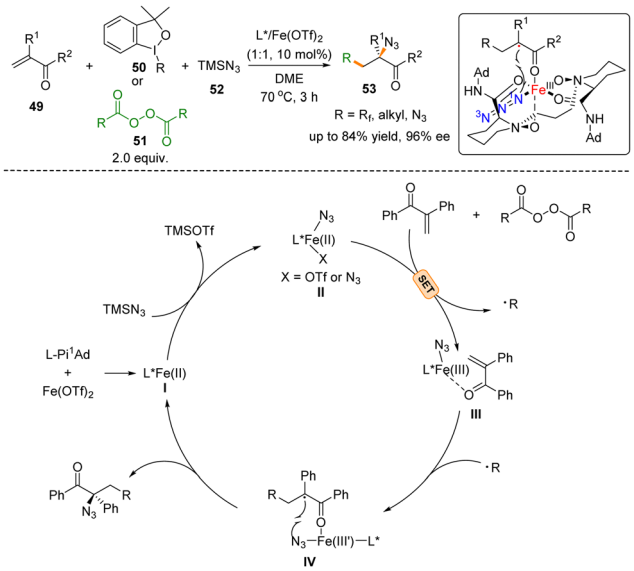


Scheme 18 Common species responsible for asymmetric epoxidation of alkenes and reaction mechanisms.

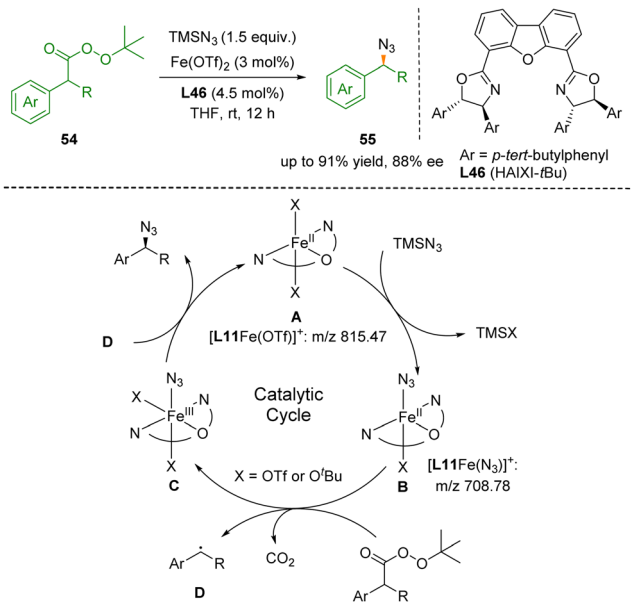
2.2.3. Asymmetric benzylic azidation reaction. Radical azidation has been recognized as a promising tool for the construction of organic azides. Recently, Bao *et al.* developed an iron(II)-catalyzed radical asymmetric azidation of benzylic peresters with trimethylsilyl azide ($TMSN_3$) as an azido source (Scheme 20).[119] The authors proposed that the weak interactions, such as π interaction and van der Waals interaction, between the catalytic chiral center and the heteroatom-free benzylic carbon-centered radicals, are crucial for the enantiocontrol in this asymmetric reaction. A variety of benzylic peresters can be used as substrates to afford enantioenriched benzylic azides under mild conditions. Interestingly, several types of further transformations of the chiral products were successfully carried out due to the diverse reactivities of the azido group.

2.3. Titanium catalysis

Titanium catalysts have high activity and selectivity in asymmetric reactions, which can promote the reaction process and improve the quality and purity of the products. Therefore, Ti-catalysts are widely used in asymmetric reactions, such as epoxidation of alkene and sulfoxidation reactions.



Scheme 19 Enantioselective radical carboazidation of α, β-unsaturated keto.



Scheme 20 Iron(II)-catalyzed radical asymmetric azidation of benzylic peresters.

2.3.1. Asymmetric epoxidation of alkenes. Ti-catalyzed asymmetric epoxidation of alkenes plays an important role in organic chemistry because the optically active epoxides are important building blocks for the production of chiral drugs, bioactive compounds and functional molecules. This study began with the pioneering work by Sharpless in the early 1980s. He was awarded the 2001 Nobel Prize for his contribution to

asymmetric oxidation reactions (epoxidation, dihydroxylation and oxyamination). Since then, this field has evolved rapidly and numerous efficient protocols for the Ti-catalyzed asymmetric epoxidation of a wide range of substrates containing vinyl groups have been exploited. Organic peroxides, such as *tert*-butyl hydroperoxide (TBHP) and cumyl hydroperoxide (CHP), and inorganic peroxides, such as hydrogen peroxide, are often used as oxidants in the asymmetric epoxidation of olefins. Researchers have made great efforts to explore the chiral metal catalysts capable of performing asymmetric epoxidation. The method developed by Sharpless and co-workers, which utilizes titanium tartrate complexes and alkyl hydroperoxides, is probably one of the most well-known.

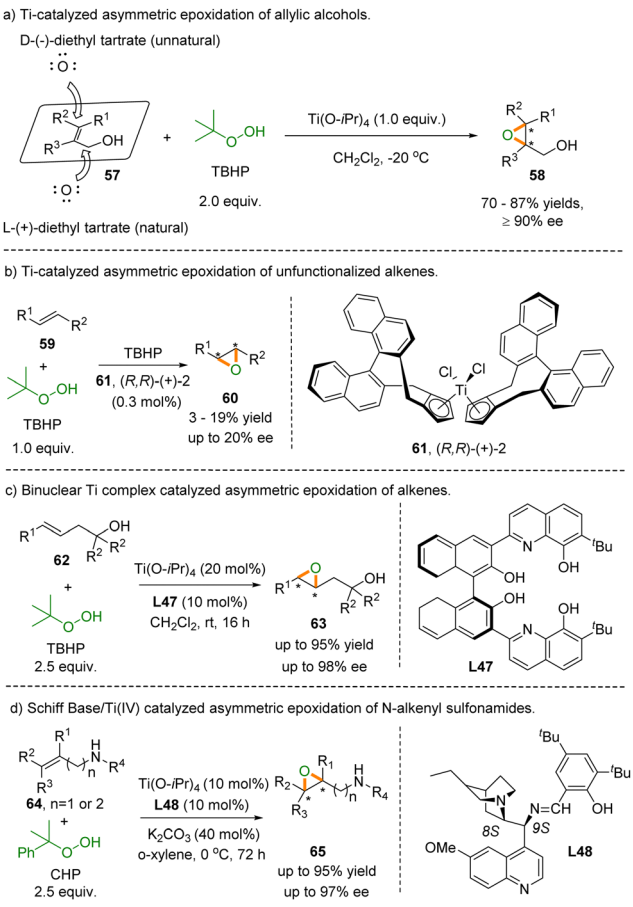
In 1980, Sharpless *et al.* discovered a new titanium-catalyzed asymmetric epoxidation process that exhibited significantly higher selectivity compared to previously described methods (Scheme 21a).[120,121] The required components including alkene, titanium tetraisopropoxide and *tert*-butyl hydroperoxide are all commercially available at low to moderate cost, and the reaction conditions are simple, making this new method attractive and practical.

In 1993, an asymmetric epoxidation of unfunctionalized alkenes was reported by Halterman and co-workers. The reaction was conducted by using titanocene peroxide complexes incorporating the C_2-symmetrical binaphthylcyclopentadienyl ligand (BpDMCp, **61**) as a catalyst (Scheme 21b).[122] The reaction afforded enantiomerically enriched epoxides with up to 20% ee and activities of up to 55 turnovers with TBHP as oxidants. It is worth noting that a significant decrease in enantioselectivity for the epoxidation of *trans*-3-hexene was observed when the metal was switched from titanium to niobium in these binaphthyl-derived C_z-symmetrical complexes.

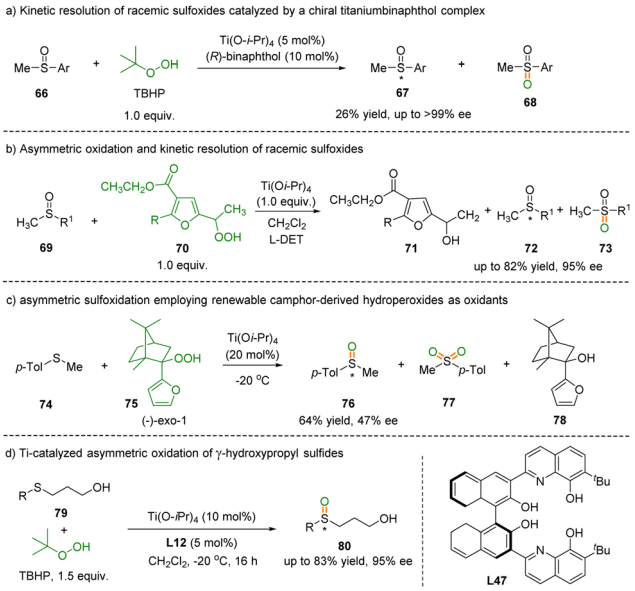
In 2015, Yamamoto *et al.* disclosed a new class of chiral tethered 8-quinolinol-based ligands which can accommodate two "independent" titanium centers in the active site (Scheme 21c).[123] The binuclear Ti-complex allows for high regio- and stereoselective epoxidation of primary and tertiary homoallylic alcohols (up to 98% ee) processes using TBHP as an oxidant, as well as first examples of 2-allylic phenols (up to 92% ee). This novel binuclear catalyst, which contains two independent metal centers and one metal center binds the substrate in close proximity to the second metal center, will accelerate reactivity and facilitate the enantioselective process. Interestingly, the new catalyst system also promotes the asymmetric oxidation of γ-hydroxypropyl sulfides giving chiral sulfoxides (up to 95% ee).

A highly enantioselective novel Schiff Base/Ti(IV) catalyst derived from hydroquinine and Ti(Oi-Pr)$_4$ for the catalytic asymmetric epoxidation of *N*-alkenyl sulfonamides was further developed by He and co-workers in 2016 (Scheme 21d).[124] The reaction with cumyl hydroperoxide as oxidants afforded the chiral epoxy sulfonamides in good yields (up to 95%) with excellent enantioselectivities (up to 97% ee) under mild conditions. Significantly, the configuration of the epoxide product was determined by the configuration of the C8 and C9 positions of the cinchona alkaloid.

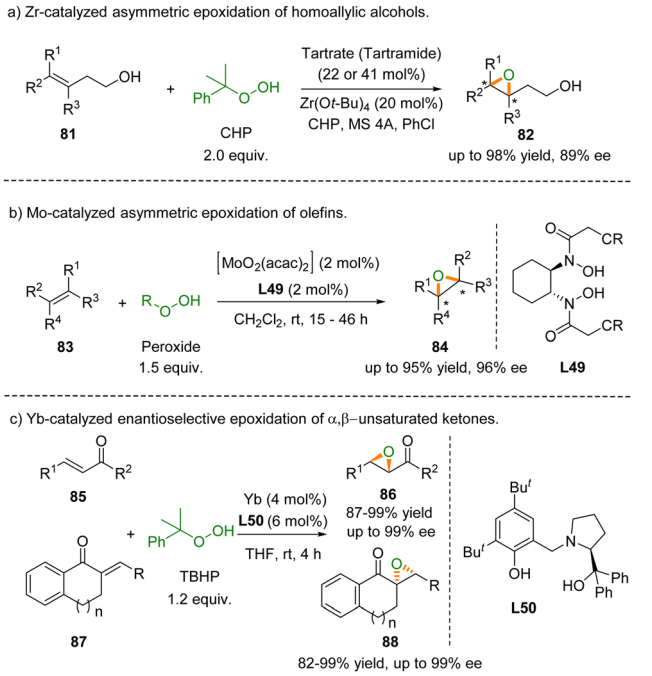
2.3.2. Asymmetric sulfoxidation reactions. Chiral sulfoxides are valuable auxiliaries in asymmetric reactions, and their preparation methods include the Andersen synthesis and asymmetric oxidation of sulfides. In 1993, a kinetic resolution of racemic sulfoxides catalyzed by a chiral titaniumbinaphthol complex providing optically pure sulfoxides (up to 99% ee) was developed by Uemura and co-workers (Scheme 22a).[125] This is a facile and convenient method to obtain optically pure sulfoxides using commercially available 70% aqueous *tert*-butyl hydroperoxide (TBHP) as the oxidant. In 1997, an asymmetric oxidation and kinetic resolution of racemic sulfoxides with furylhydropcroxide as an oxygen donor was reported by Scettri and co-workers (Scheme 22b).[126] This methodology provided an alternative route to obtain chiral sulfoxides with high enantioselectivity (up to 95% ee) under simple reaction conditions. In 2004, Lattanzi *et al.* developed a chemoselective process of asymmetric sulfoxidation employing easily accessible and renewable camphor-derived hydroperoxides as stereoselective oxidants in the presence of Ti(Oi-Pr)$_4$ (Scheme 22c).[127] The reaction afforded aryl methyl sulfoxides of both absolute configurations with enantioselectivities of up to 47%. The camphor-derived hydroperoxides can be prepared in one-step from furyl alcohols which are the by-products of the asymmetric sulfoxidation, with the advantage of providing a less-consuming chiral reagent protocol. Moreover, Yamamoto *et al.* reported a new class of optically active ligands capable of



Scheme 21 Ti-catalyzed asymmetric epoxidation of alkenes.



Scheme 22 Ti-catalyzed asymmetric sulfoxidation enabled by organic peroxides.



Scheme 23 Catalytic asymmetric epoxidation of alkene by other metals.

accommodating two "independent" titanium centers in the active site in 2015 (Scheme 22d).[123] This new catalyst system enables the asymmetric oxidation of γ-hydroxypropyl sulfides reaction using TBHP as an oxidant to afford an important class of chiral sulfoxides (up to 95% ee).

2.4. Other metal catalysis

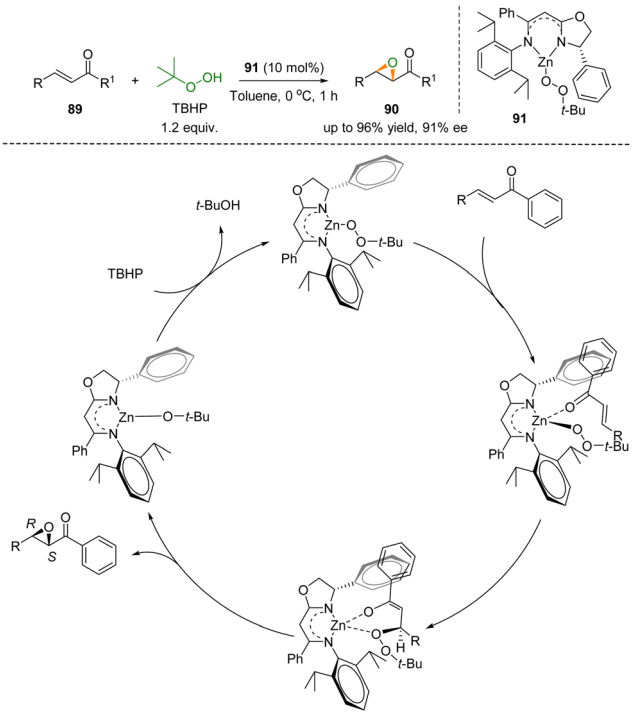
2.4.1. Asymmetric epoxidation of alkenes. Several other metals, such as Zr, Mo, Yb and Zn, have been exploited for the asymmetric epoxidation of alkenes. In 2003, Onaka *et al.* reported the catalytic asymmetric epoxidation of homoallylic alcohols using $Zr(Ot\text{-}Bu)_4$ and tartrate ester (or tartramide) (Scheme 23a).[128] The reaction afforded the epoxides with high yield (up to 98%) and excellent enantioselectivity (up to 89% ee) by using cumene hydroperoxide (CHP) as an oxidant reagent. Additionally, it was observed that the enantiofacial selectivity was reversed depending on the Zr/ligand ratio in this work. It is worth noting that molecular sieves probably play a key role in promoting the exclusive formation of the active catalyst.

In addition to the homoallylic alcohols, the catalytic asymmetric oxidation of mono-, di-, and trisubstituted olefins using chiral molybdenum catalysts was described by Yamamoto and co-workers in 2006 (Scheme 23b).[129] The reaction afforded epoxides in high yields (up to 98%) and excellent selectivity (up to 96% ee) adopting peroxides (THP, CHP or TBHP) (THP: trityl hydroperoxide) as oxidants. The authors suggested that the Mo-BHA (BHA: bishydroxamic acid) complex, in combination with the achiral oxidant, oxidizes the olefin in a concerted fashion by transfer of oxygen from the metal peroxide to the olefin and the mechanism follows the concerted metal alkylperoxide mechanism.

In 2015, Yao *et al.* further developed a simple and efficient catalytic enantioselective epoxidation method for α, β-unsaturated ketones (Scheme 23c).[130] The reaction provided epoxides with high yield (up to 99%) and excellent enantiomeric excess (up to 99% ee) when catalyzed by rare-earth metal amides in the presence of phenoxy-functionalized chiral prolinols, using *tert*-butylhydroperoxide (TBHP) as an oxidant. Interestingly, the central metals significantly influenced the enantiometric excess of epoxides with the decreasing tendency of Yb > Y > Lu > Sm > La.

Shortly after this, Lewiński *et al.* reported a zinc *tert*-butyl peroxide-based catalytic system for the asymmetric epoxidation of enones using *tert*-butyl hydroperoxide as an oxidant (Scheme 24).[131] Different chiral monoanioninc *N*,*N*′-bidentate ligands, including C_2-symmetric bisoxazolinates and C_1-symmetric enaminooxazolinates, were compared in this catalytic system. The results revealed that the C_1-symmetric enaminooxazolinates exhibited excellent performance as auxiliary ligands in the catalytic asymmetric epoxidation of enones (up to 96% yield and 91% ee). These results demonstrated that the steric effects of the substituents in close proximity of the binding site had a major influence on the enantioselectivities.

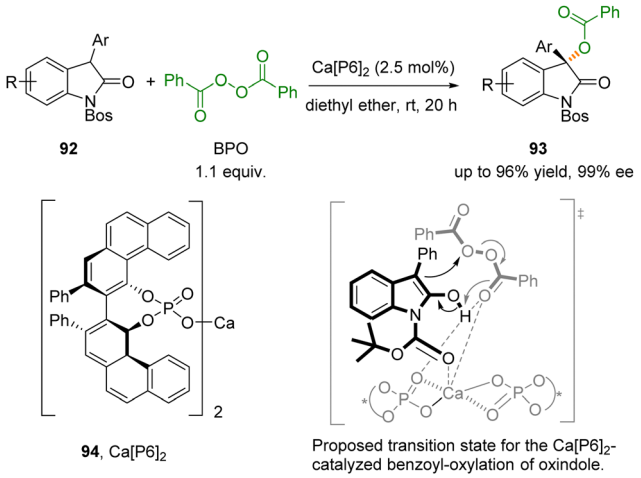
2.4.2. Asymmetric benzylic functionalization reaction. Enantioenriched compounds with a chiral center in the benzylic position, such as chiral benzyl amines and alcohols, are structural motifs present in plenty of pharmaceuticals and natural products.[132,133] Many endeavors dedicated to this area of chemistry, and the classical example is the enantioselective cyanation of benzylic C–H bonds using *N*-fluorobenzenesulfonimide (NFSI) as a radical relay reagent reported by Liu and co-workers.[134] Organic peroxides are an important class of radical precursors that are often used to abstract the hydrogen atom in the functionalization of the $C(sp^3)$–H bond. However, only a limited number of approaches to asymmetric benzylic



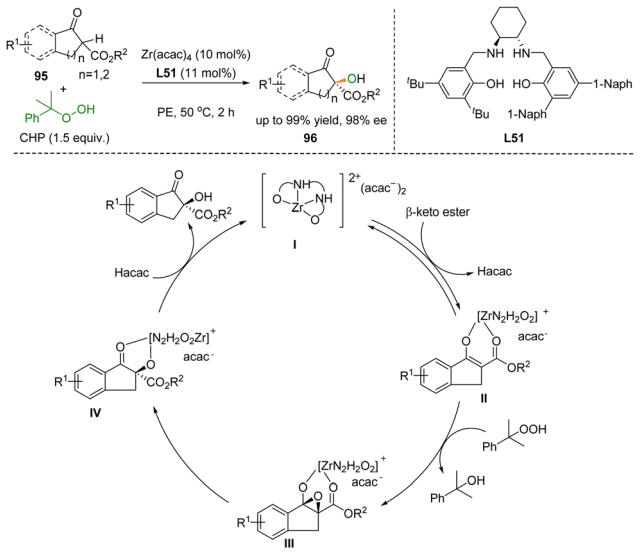
Scheme 24 Zn-catalyzed asymmetric epoxidation of enones.

functionalization enabled by organic peroxides have been reported and the development of this field has proven a formidable challenge. A remarkable breakthrough was achieved by Antilla and co-workers in 2011. They successfully developed a novel asymmetric benzoyloxylation of oxindole with BPO catalyzed by a chiral VAPOL calcium phosphate salt (**94**). Various 3-aryl-3-benzoyloxindoles were obtained in good yields (up to 96%) and excellent enantioselectivities (up to 99% ee), utilizing readily available BPO as the benzoyloxylation reagent (Scheme 25).[135] The authors proposed that the bifunctional nature of the chiral calcium phosphate salt allows for the activation of both the nucleophile and the electrophile. The coordination between calcium and the carbonyl oxygens of both BPO and the Boc-group of the oxindole forces the two substrates to be in closer proximity to one another in the chiral environment. These interactions coupled with the hydrogen-bonding interactions between the hydroxy group of the oxindole tautomer and the P═O moiety of the catalyst can be used to rationalize the high enantiocontrol in this transform.

2.4.3. Asymmetric hydroxylation reaction. Enantioenriched α-hydroxy β-keto esters are important structural cores in natural products. In 2016, the highly enantioselective α-hydroxylation of β-keto esters was achieved by employing a modified salen–Zr(IV) catalyst with cumene hydroperoxide (CHP) as the oxidant by Meng and co-workers. The reaction afforded a series of chiral α-hydroxy β-keto esters in excellent yields (up to 99%) and enantioselectivities (up to 98% ee) (Scheme 26).[136] The authors proposed a possible mechanism and suggested that the catalyst system containing a tetradentate ligand with two distinct bulky benzene rings and a chiral cyclohexanediamine core is crucial for



Scheme 25 Ca-catalyzed asymmetric benzoyloxylation of oxindole.



Scheme 26 Zr-catalyzed enantioselective α-hydroxylation of β-keto esters.

controlling the stereoselectivity of α-hydroxylation efficiently. It is worth noting that this reaction can be performed in a gram scale affording the corresponding chiral products in excellent yield and enantioselectivity.

3. Organic peroxides as stoichiometric reagents

The organic peroxides can be used as stoichiometric terminal oxidants. Furthermore, the oxygen- or carbon-center radicals generated from organic peroxides can also serve as radical relay reagents to promote the reactions. In this section, we focus on the organic peroxides as stoichiometric reagents (their components do not appear in the final product) in asymmetric reactions with different metal catalysis.

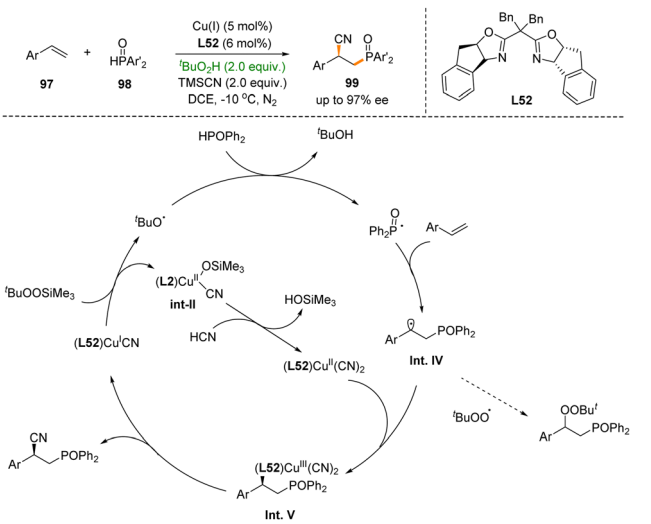
3.1. Copper catalysis

3.1.1. Asymmetric difunctionalization of alkenes. Organic peroxides can undergo cleavage to generate oxygen- or carbon-centered radicals, which can abstract hydrogen atoms or halogen atoms to generate new radical species. These new radicals can then participate in further reactions, resulting in the desired transformations. In 2019, Liu *et al.* developed a Cu(I)-catalyzed enantioselective phosphinocyanation of styrenes reaction affording various phosphine-containing alkylnitriles with up to 95% yield and 97% ee by a tandem radical relay strategy (Scheme 27).[11] In this strategy, the alkylsilyl peroxide (^{t}BuOOSiMe$_3$) generated *in situ* from ^{t}BuOOH serves as a radical initiator to trigger *t*-butoxy radical production upon oxidization of L*Cu(I) species *via* a proton-coupled-electron transfer (PCET) pathway. Then, the *t*-butoxy radical led to sequential formations of phosphinoyl radicals and benzyl radicals.

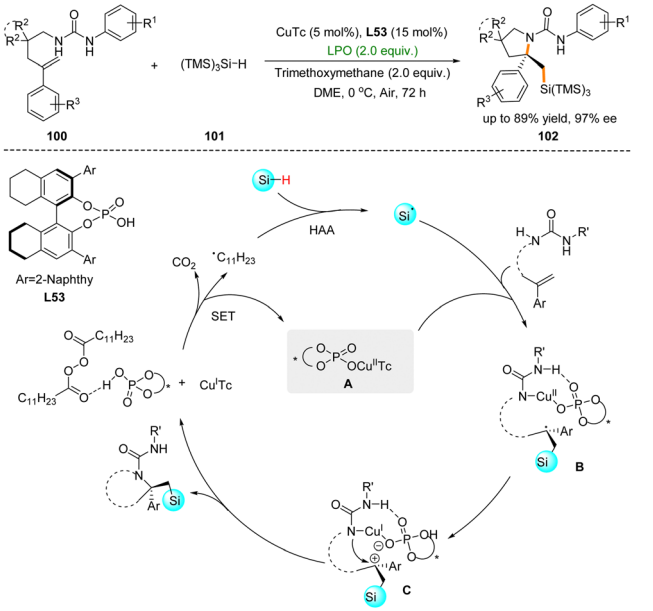
In the same year, the catalytic radical-initiated asymmetric 1,2-aminosilylation of alkenes with high enantioselectivity under the Cu(I)/CPA cooperative catalyst was developed by Liu and co-workers (Scheme 28).[20] The desired 1,2-aminosilylation product was obtained with up to 89% yield and 97% ee using lauroyl peroxide (LPO) as the external oxidant and radical relay reagent. In this reaction, LPO was activated by CPA and reacted with Cu(I) *via* O–O bond heterolysis, followed by the loss of CO_2 to afford highly reactive alkyl radical accompanied by the crucial chiral Cu(II) phosphate complex **A**. The hydrogen-bonding interactions and ion–pair interactions are critical factors contributing to the excellent enantioselective control observed in this reaction.

Later on, a chiral bisoxazoline/Cu(I) catalyzed highly enantioselective three-component fluoroalkylcyanation reaction of alkenes has been developed by Bao and co-workers (Scheme 29).[45] In this radical relay strategy, the alkyl radical generated from LPO is sufficiently reactive to abstract the iodine atom from fluoroalkyl iodides, affording electrophilic fluoroalkyl radicals. The products could be easily further converted into amides, acids, oxazoles, and other derivatives.

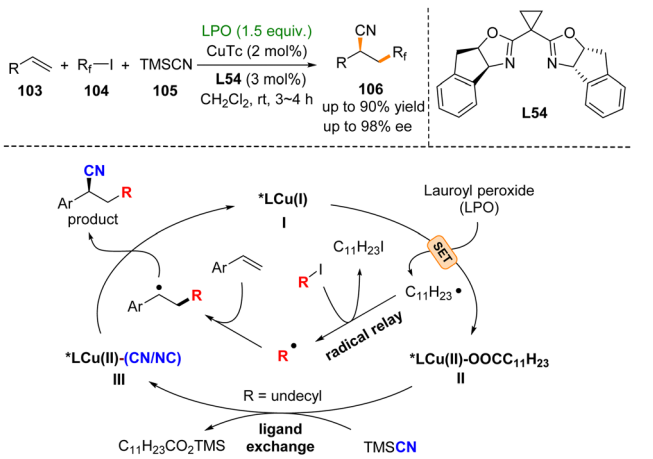
Inspired by recent work of radical asymmetric carboazidation of olefins *via* an iron-catalysed group transfer mechanism,[16] an efficient catalytic radical enantioselective carbo-esterification of styrenes enabled by the Cu^I-perfluoroalkylated PyBox system was developed by Bao and co-workers (Scheme 30).[17] The LPO reacts with copper(I) catalyst by SET, delivering the Cu^{II}O$_2$CR intermediate with the alkyl radical, which then abstracts the iodine atom from the iodoacetic acid to form the acetic carbon radical by radical relay. The acetic carbon radical subsequently adds to styrene to produce the butyric benzylic radical. The mechanistic studies reveal that this reaction is a rare example of an efficient ligand decelerated system.



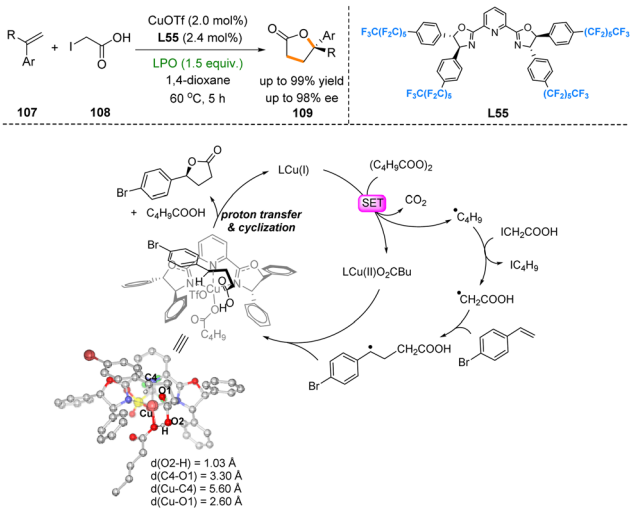
Scheme 27 Cu(I)-catalyzed enantioselective phosphinocyanation of styrenes.



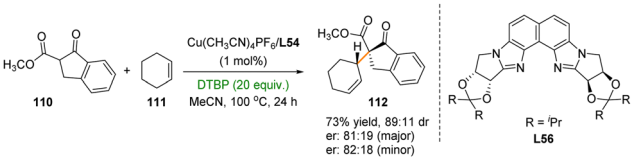
Scheme 28 Cu(I)/CPA-catalyzed asymmetric 1,2-aminosilylation of alkene of alkenes.



Scheme 29 Bisoxazoline/Cu(I)-catalyzed enantioselective cyano-(fluoro)alkylation of alkenes.



Scheme 30 Cu-catalyzed radical asymmetric carboazidation of olefins.



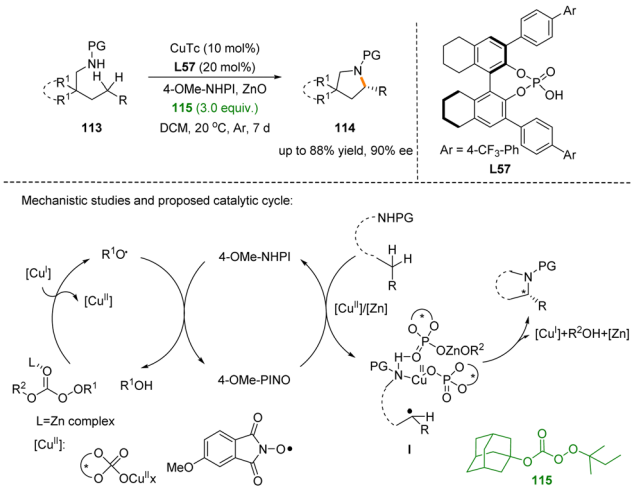
Scheme 31 Cu-catalyzed asymmetric allylic alkylation reaction.

3.1.2. Asymmetric allylic alkylation reaction. In 2018, a Cu(I) complex catalyzed coupling between 1,3-dicarbonyl compounds and simple cyclic alkenes using di-*tert*-butyl peroxide (DTBP) as an oxidant affording *C*-allylation products with a high diastereomer ratio was disclosed by Kitamura and co-workers (Scheme 31).[137] This reaction system has been applied to the asymmetric *C*-allylation giving the products with up to 81 : 19 enantiomer ratio with chiral Naph-diPIM ligand (**L56**).

3.1.3. Asymmetric allylic and benzylic amination reaction. Radical-involved enantioselective C(sp^3)–H bond functionalization *via* a hydrogen atom transfer (HAT) process enables the direct transformation of hydrocarbon feedstocks into optically pure products. In 2019, Liu *et al.* disclosed a Cu(I)/CPA (**L57**) catalytic system for radical-involved enantioselective intramolecular C(sp^3)–H amination of benzylic and allylic substrates with peroxide as an oxidant and radical relay reagent (Scheme 32).[138] Mechanistic studies revealed that a crucial benzylic or allylic radical intermediate resulting from a HAT process is involved and the use of 4-OMe-*N*-hydroxyphthalimide (4-OMe-NHPI) as a stable and chemoselective HAT mediator is crucial for this transformation. This is the first example of construction of C–N bonds giving chiral α alkenyl/α-aryl pyrrolidines with excellent enantioselectivity (up to 94% ee) through asymmetric radical oxidative C–H bond amination.

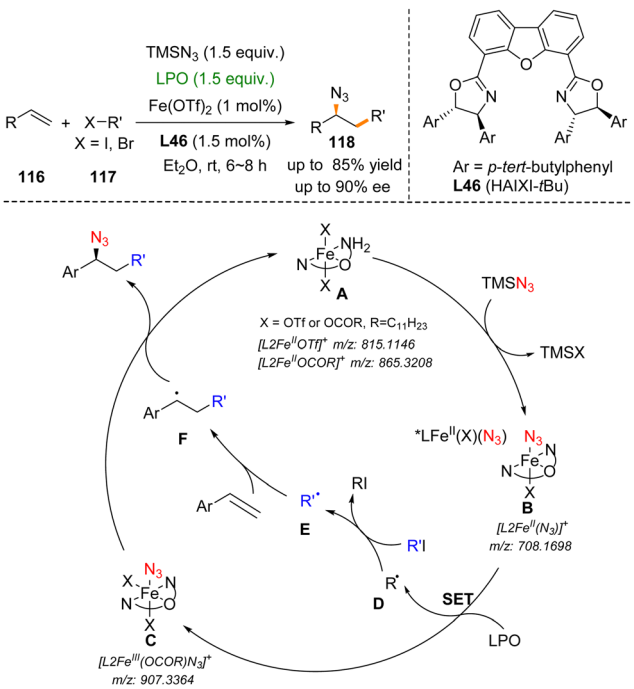
3.2. Iron catalysis

3.2.1. Asymmetric difunctionalization of alkenes. Carboazidation of olefins is an efficient method to convert hydrocarbon feedstocks directly into nitrogen-containing molecules.

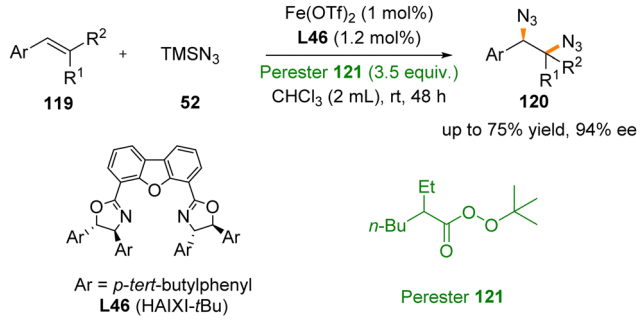


Scheme 32 Cu(I)/CPA catalytic system for enantioselective amination of benzylic and allylic substrates.

In 2020, Bao *et al.* disclosed a radical asymmetric carboazidation of olefins *via* an iron-catalysed group transfer mechanism (Scheme 33).[16] This reaction involves the generation of carbon radicals through a radical relay process using LPO as a radical precursor. The carbon radical then adds to the double bond, followed by group transfer of the azido group from the Fe(III)–N_3 species to the benzylic radical. Mechanistic and DFT studies revealed that the stereocontrol on the radical center is realized *via* the synergistic effects of van der Waals and π interactions in the rigid chiral space created by the tridentate chiral NON-pincer ligand and the iron salt. And, the radical azidation reaction in this process is supported by mechanistic studies.



Scheme 33 Radical asymmetric carboazidation of olefins.



Scheme 34 Iron-catalyzed asymmetric diazidation of styrenes.

Valuable chiral halogenated organoazides were synthesized from alkenes with this method. This strategy will provide a set of tools for asymmetric incorporation of carbon and nitrogen functionalities, and spur the development of an asymmetric radical method that proceeds through a group transfer pathway.

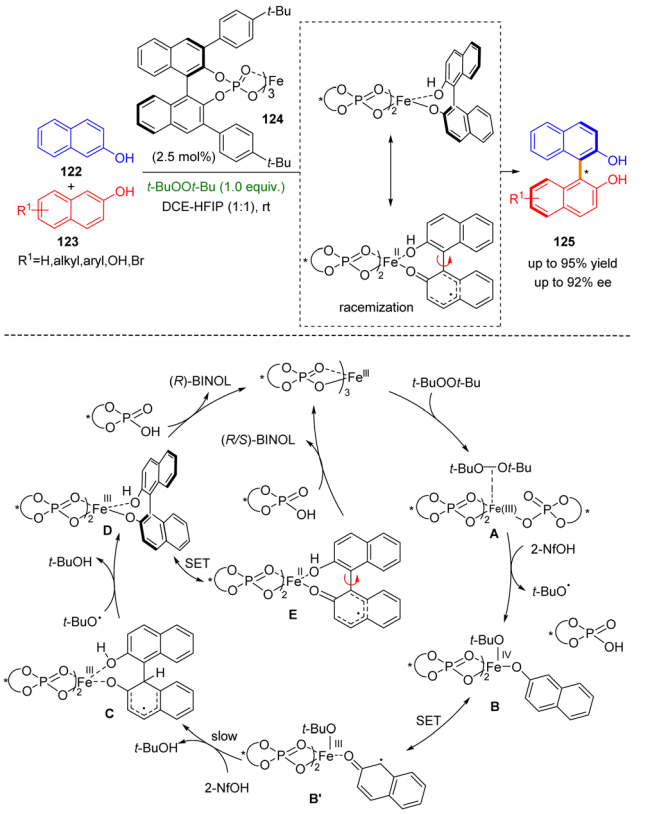
In 2021, Bao *et al.* further developed an iron-catalyzed intermolecular asymmetric diazidation of disubstituted or trisubstituted styrenes (Scheme 34).[139] A range of otherwise inaccessible chiral diazidation products, which can further transform into various useful nitrogen-containing compounds, were synthesized by using alkyl peresters as oxidant reagents. Studies on the mechanism of the reaction suggest that the reaction proceeds *via* a radical pathway. The stereocontrol of an acyclic free radical probably takes place through a group transfer mechanism.

3.2.2. Asymmetric oxidative coupling reactions. Optically pure C_1-and C_2-symmetric 1,1′-bi-2-naphthol (BINOLs) can serve as auxiliaries and ligands for asymmetric transformations. In 2016, a novel class of chiral iron phosphate complexes for asymmetric oxidative coupling reactions affording enantioenriched C_1- and C_2-symmetric binaphthols (BINOLs) with DTBP as the oxidant was reported by Pappo and co-workers (Scheme 35).[140] The mechanism experiments revealed that the reaction takes place *via* an oxidative radical-anion coupling mechanism. Importantly, the ligand was successfully recovered from the large-scale reactions in 74% yield.

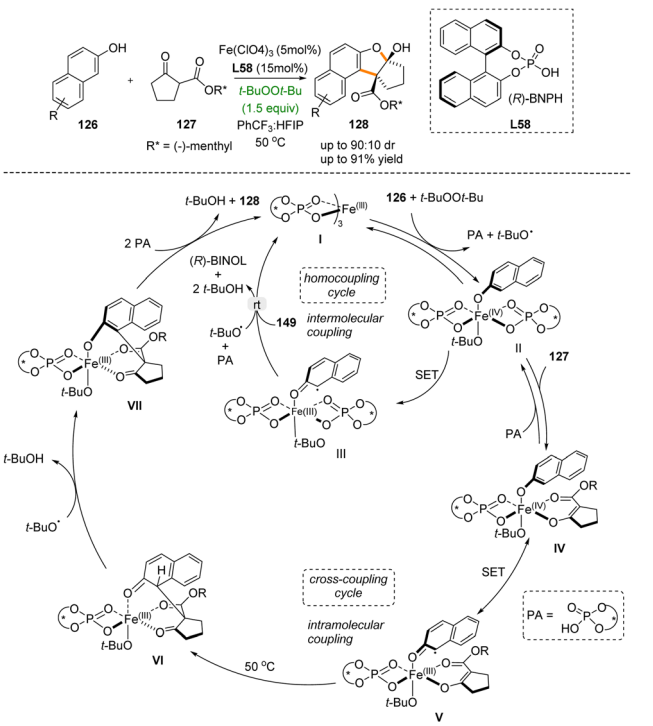
Inspired by the above work, chiral iron phosphate complexes catalyzed asymmetric cross-dehydrogenative coupling reactions between 2-naphthols and β-ketoester derivatives affording polycyclic hemiacetals with di-*tert*-butyl peroxide (DTBP) as the oxidant was further developed by Pappo *et al.* in 2017 (Scheme 36).[141] Kinetic studies revealed that chiral iron phosphate complexes induce stereoselectivity during the carbon–carbon bond formation step. On the basis of mechanistic investigations, the homocoupling and cross-coupling cycles were proposed depending on different reaction temperatures.

3.3. Palladium catalysis

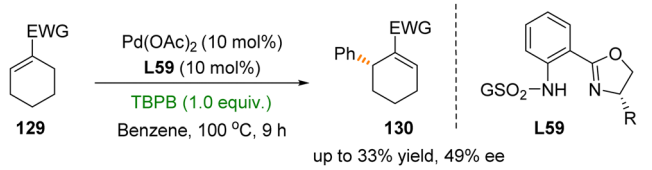
In 1999, Mikami *et al.* reported the first example of an asymmetric Fujiwara–Moritani reaction catalyzed by Pd(II) complexes with a chiral sulfonylamino-oxazoline ligand (Scheme 37).[142] The reaction afforded the coupling products in modest yields and



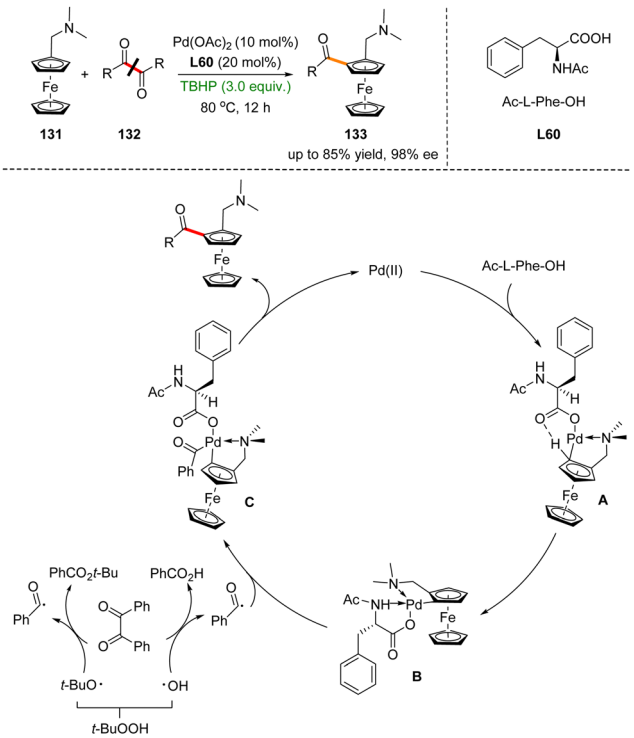
Scheme 35 Fe-catalyzed asymmetric oxidative coupling of phenol derivatives.



Scheme 36 Fe-catalyzed asymmetric cross-dehydrogenative coupling of 2-naphthols and β-ketoester.



Scheme 37 Asymmetric Fujiwara–Moritani reaction catalyzed by Pd(II) complexes.



Scheme 38 Pd-catalyzed asymmetric C–H bonds direct acylation of ferrocene derivatives.

enantioselectivities in the presence of *t*-butyl perbenzoate as an oxidant. This work represents a catalytic aromatic C–H bond activation and asymmetric olefin coupling reaction.

A novel and convenient protocol to achieve the 2-acyl-1-dimethylaminomethylferrocenes with planar chirality *via* Pd-catalyzed asymmetric C–H bond direct acylation of ferrocene derivatives was developed by Wu *et al.* in 2014 (Scheme 38).[143] Various corresponding products were afforded under highly efficient and concise one-pot conditions with up to 85% yield and 98% ee using commercially available and cheap mono-protected amino acids as a chiral ligand. In this reaction, the benzoyl radical was generated by the reaction of diphenyl diketone with TBHP.

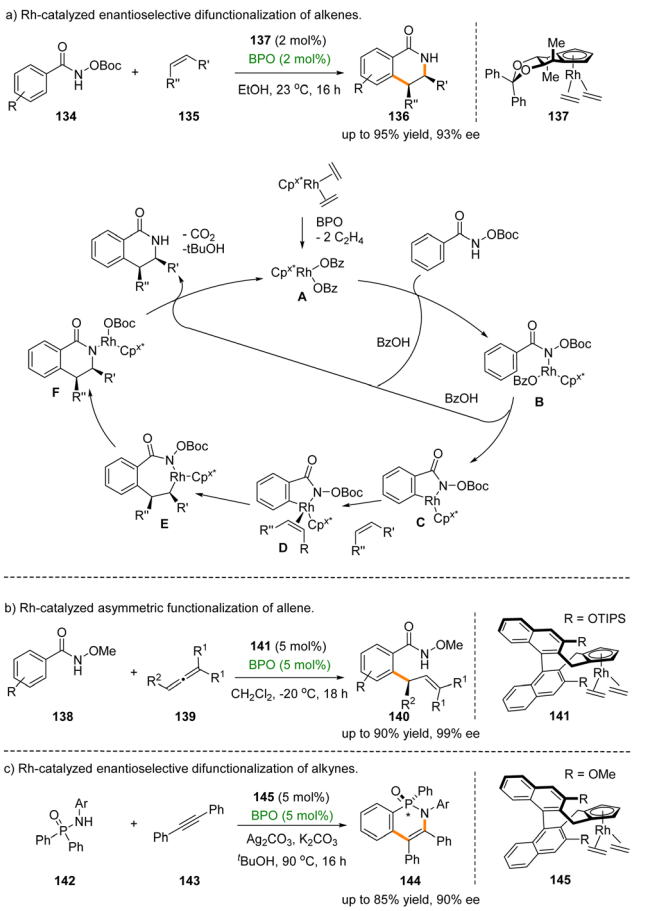
4. Organic peroxides as catalytic amount reagents

Organic peroxides have a wide range of applications as catalytic amount reagents in the chemical industry. For instance, they are utilized as initiators in polymerization reactions and as oxidants to convert a lower valent pre-catalyst into reactive high-valent metal species.

4.1. Asymmetric difunctionalization of unsaturated C–C bonds

A series of chiral cyclopentadienyl (Cp) ligands and rhodium(III) complexes were developed by the Cramer[144] and You groups,[145] and these complexes were used in the reaction of asymmetric difunctionalization of unsaturated C–C bonds enabled by organic peroxides. The organic peroxides often serve as oxidants to oxidize the Rh(I) complexes to the catalytically active Rh(III) species.

First, the highly enantioselective rhodium(III) complex catalysts bearing simple C_2-symmetric Cp derivatives for the directed functionalization of the carbon–hydrogen (C–H) bond in hydroxamic acid derivatives was described by Cramer *et al.* in 2012 (Scheme 39a).[144] The authors found that the new chiral Cp* analogs can finely control the spatial arrangement of the transiently coordinated reactants around the central metal atom. In this reaction, the catalytic cycle is presumably initiated by oxidation of the Cp*Rh(I) complex **137** by peroxide (BPO) to the Rh(III) bis-benzoate complex *in situ*. The reaction afforded



Scheme 39 Rh-catalyzed enantioselective functionalization of unsaturated C–C bonds.

alkene difunctionalization products with high yield (up to 95%) and enantioselectivity (up to 93% ee) under mild conditions.

Having established this approach, Cramer and co-workers further reported a class of chiral Cp ligands with sterically adjustable biaryl backbones and the corresponding Rh(I) complexes in 2013, which are shown to be excellent catalysts for enantioselective allylation of *N*-methoxybenzamides *via* directed C–H functionalization under very mild conditions (Scheme 39b).[146] Coordinated to transition metals, the chiral Cp ligands are able to imprint its chirality onto the metal by creating a well-defined chiral pocket. The dibenzoyl peroxides were used as oxidants to oxidize the Rh(I) olefin complexes to the Rh(III) carboxylate species. The reaction of methyl hydroxamate **134** and trisubstituted allene **138** provided the monoallylated product **139** in good yield (up to 90%) and excellent enantioselectivity (up to 99% ee).

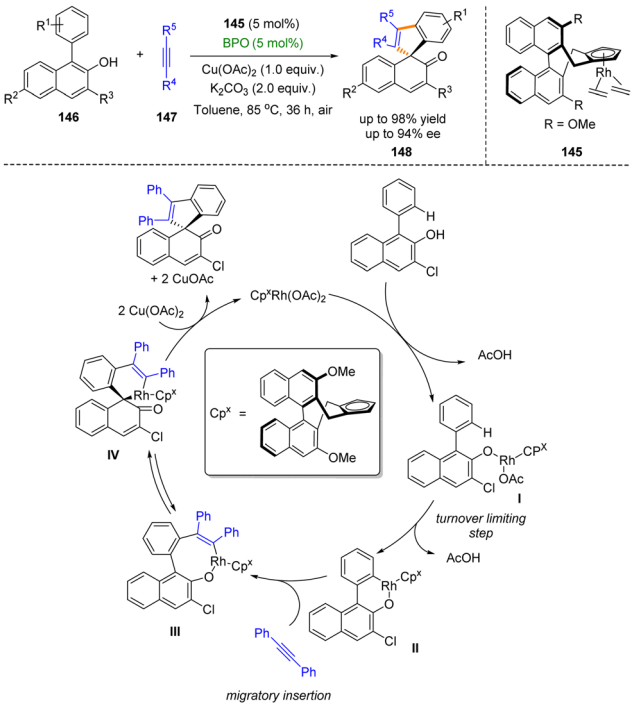
In addition to the double bond, alkynes can also be difunctionalized by using $Cp^xRh(III)$ complex **144** as a catalyst. In 2016, a direct catalytic enantioselective method for the synthesis of P-chiral compounds, which are frequently used as ligands for transition-metals as well as organocatalysts, from easily accessible diaryl phosphinamides has been developed by Cramer and co-workers (Scheme 39c).[147] Upon trapping with alkynes, the reaction afforded various cyclic phosphinamides with a stereogenic phosphorus(V) atom in high yields and enantioselectivities. This transformation was catalyzed by the $Cp^xRh(III)$ complex **145**, which is equipped with a suitable atropochiral cyclopentadienyl ligand that enables an enantiodetermining C–H activation step. Moreover, these P-chiral phosphorus(V) can be reduced enantiospecifically to P-chiral phosphorus(III) compounds, making this method attractive to access P-chiral phosphine ligands. The dibenzoyl peroxide and silver carbonate were used as combined oxidants to oxidize Rh(I) to Rh(III).

In 2015, You *et al.* developed a Rh-catalyzed enantioselective dearomatization of β-naphthol derivatives with internal alkynes *via* the C–H functionalization reaction (Scheme 40).[145] Various highly enantioenriched spirocyclic enones bearing an all-carbon quaternary stereogenic center were synthesized from simple naphthol derivatives in 33–98% yields with up to 94% ee. $Cu(OAc)_2$, air (oxygen), and BPO were used as combined oxidants in this reaction.

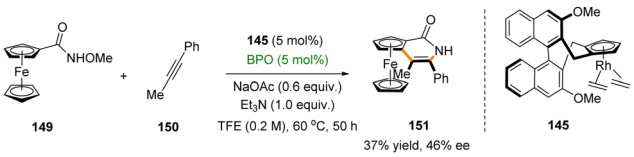
An Rh(III)-catalyzed C–H bond annulation of ferrocenecarboxamide with internal alkyne using a directing group as an internal oxidant was further disclosed by You and co-workers in 2016 (Scheme 41).[148] Various substituted groups on alkynes and ferrocenecarboxamides can be tolerated and the reaction delivers ferrocene-based pyridinones generally in moderate to good yields. Furthermore, the asymmetric reaction was achieved in moderate yield (37%) and enantioselectivity (46% ee) in the presence of the chiral catalyst **145** and BPO.

4.2. Other asymmetric reactions

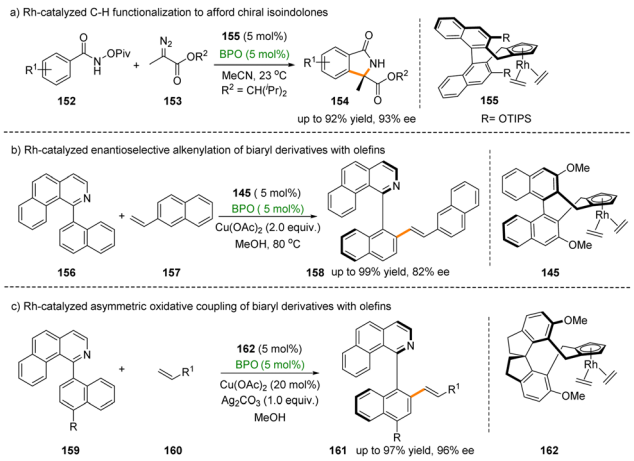
BPO was often used as an oxidant to oxidize Rh(I) to Rh(III) in rhodium catalyzed C–H functionalization reactions. In 2014, Cramer *et al.* reported an enantioselective rhodium(III)-catalyzed C–H functionalization to construction of chiral



Scheme 40 Rh-catalyzed enantioselective dearomatization of β-naphthol derivatives with internal alkynes.



Scheme 41 Rh-catalyzed C–H bond annulation of ferrocenecarboxamide with internal alkynes.



Scheme 42 Ru-catalyzed other asymmetric reactions enabled by organic peroxides.

isoindolones with BPO as the oxidant (Scheme 42a).[149] The rhodium complex guided the substrates with a high double

facial selectivity giving the functionalized isoindolones in good yields (up to 94%) and excellent enantioselectivities (up to 93% ee) with a chiral, atropchiral biaryl backbone Cp ligand.

In the same year, You *et al.* developed an asymmetric rhodium (III)-catalyzed direct alkenylation of biaryl derivatives with olefins affording the novel axially chiral biaryls in good to excellent yields and enantioselectivities employing BPO, Ag_2CO_3, and $Cu(OAc)_2$ as combined oxidants (Scheme 42b).[150] Moreover, the obtained axially chiral biaryls have been demonstrated as suitable ligands for rhodium-catalyzed asymmetric conjugate addition reactions. With a similar strategy, You *et al.* further disclosed a series of novel cyclopentadienyl ligands based on 1,1′-spirobiindane scaffolds in 2016. The Rh(I) complexes with these ligands behaved as superior catalysts in the asymmetric oxidative coupling of biaryl derivatives with olefins at room temperature, providing axially chiral biaryls in 19–97% yield with up to 98 : 2 er (Scheme 42c).[151]

5. Conclusion

Since the first organic peroxide (Benzoyl Peroxide, BPO) was synthesized in 1858, various types of organic peroxides have been exploited by researchers. Organic peroxides are commercially available and low price industrial raw materials, which play vital roles in the chemical industry, pharmaceutical synthesis, and polymerization chemistry by now. The metal-catalyzed asymmetric reaction enabled by organic peroxides has emerged as one of the most straightforward and efficient strategies to construct enantioenriched molecules in pharmaceutical, agrochemical and material industries in the past few decades. In these reactions, organic peroxides can be used as stoichiometric reactants, stoichiometric reagents, and catalytic amount reagents. This review has summarized the development of the metal-catalyzed asymmetric reaction enabled by organic peroxides and highlighted the reaction mechanisms and the role of organic peroxides.

The advantage of organic peroxides is that they can be used as multifunctional reagents, such as oxidants, functionalization reagents, radical relay reagents, and ligand exchange promoters. Moreover, the organic peroxides can play multiple roles in a reaction cycle due to the multiple components therein. The asymmetric reactions, including difunctionalization of unsaturated C–C bonds, Kharasch–Sosnovsky oxidation, epoxidation of olefins, *etc.*, were successfully developed using organic peroxides as stoichiometric reactants. The metal-catalyzed asymmetric difunctionalization of unsaturated C–C bonds enabled by organic peroxides can rapidly assemble otherwise difficult-to-access optically pure molecules. Consequently, a remarkable development was achieved in the recent ten years. As a benchmark reaction, asymmetric Kharasch–Sosnovsky oxidation has been often used to test catalytic systems with the alkenes and organic peroxides. High yields and enantioselectivities can be successfully achieved with cyclic olefins. Since the pioneering work reported by Sharpless in the early 1980s, organic peroxides have been often used as oxidants in asymmetric epoxidation of olefins, and significant progress has indeed been achieved. As stoichiometric reagents, the organic peroxides were used as terminal oxidants or radical relay reagents. The radical relay strategy was exploited to expand the sources of free radicals. The oxygen- or carbon-center radicals generated from organic peroxides will abstract the hydrogen or halides atom to deliver the new radical species which can then participate in further reactions, such as asymmetric difunctionalization of alkenes, allylic alkylation, and benzylic amination. In addition, the organic peroxides can also serve as catalytic amount reagents to oxidize a lower valent pre-catalyst to reactive high-valent metal species in asymmetric reactions, such as the Rh-catalyzed functionalization of unsaturated C–C bonds.

Notwithstanding these exciting advances, challenges still remain: (1) the cleavage of organic peroxides is relatively complicated, and a variety of radicals are generated simultaneously. The interaction between these radicals can lead to the formation of undesired compounds. The key point to solve this issue is an exploitation of a new metal catalyst system that can control the catalytic cracking of organic peroxides under mild conditions and regulate the radical species generated. The pivotal issue is how to make the cleavage of organic peroxides selective and orderly to generate the desired active species. (2) Organic peroxides are widely used as free radical initiators and oxidants; however, the metal-catalyzed asymmetric reactions by employing organic peroxides as alkylating reagents or radical relay reagents are less developed. (3) The reactions enabled by organic peroxides often involve radical intermediates. However, achieving enantioselectivity control in free radical reactions remains a significant challenge. How to control the stereochemistry of an unconstrained free radical center atom is crucial to successfully realize the asymmetric free radical reactions. In recent years, asymmetric radical reactions with high enantioselectivity *via* the inner-sphere mechanism and the outer-sphere mechanism have been developed. Although breakthrough progress has been made in this area, the reaction types are still limited and need to be further expanded, such as asymmetric Kharasch–Sosnovsky oxidation of acyclic olefins, organoperoxide-promoted asymmetric C–H bond activation reactions, *etc.*

To solve the aforementioned challenges in this field, future opportunities rely on the development of new metal catalysts and chiral ligands to control the cleavage of organic peroxides, regulate radical species, and improve enantioselectivity. In addition, organic peroxides can generate several types of carbon-centered radicals, such as phenyl radicals, methyl radicals, primary alkyl radicals, secondary alkyl radicals and so on. The metal-catalyzed asymmetric reactions enabled by organic peroxides utilizing these carbon-centered radicals as functionalization reagents or radical relay reagents is also an opportunity for the future. As a unique class of alkylating reagents or carbon-centered radical relay reagents, organic peroxides are complementary to classic reagents and will become an important tool for rapid assembly of otherwise difficult-to-access chiral molecules. We hope that this review will attract more

researchers dedicated to this challenging field and inspire future developments in this area.

Caution

Organic peroxide containing a weak covalent O–O bond is in principle thermally unstable. In the presence of heat, acids, or metals, organic peroxides can undergo cleavage for producing free radicals, which is a strong exothermic reaction. If the heat generation occurs at a faster rate than its dissipation, it can result in a rise in temperature, which further intensifies the rate of exothermic decomposition. This may create a dangerous situation known as a self-accelerating decomposition. Furthermore, the decomposition of certain organic peroxides, such as diacyl peroxide, peroxyester, peroxide carbonate, and peroxydicarbonate, may release carbon dioxide gas, resulting in an increase in pressure within the reaction system. Therefore, improper handling of organic peroxides can potentially lead to explosions.[152] Different types of organic peroxides have varying decomposition temperatures, and their 10 hour half-life temperature ranges were presented in Scheme 1a. In general, the lower the decomposition temperature of organic peroxides, the higher the potential risk associated with their use. In conclusion, the proper usage, storage, transportation, and disposal of organic peroxides should comply with the corresponding safety operational regulations to ensure safety and prevent potential hazards.[3,153]

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We acknowledge the generous financial support of National Natural Science Funds for Distinguished Young Scholar (Grant No. 22225107).

Notes and references

1 S. Pata, *The chemistry of peroxides*, John Wiley & Sons Ltd., 1983.
2 M. Locklear and P. H. Dussault, *Eur. J. Org. Chem.*, 2020, 4814–4840.
3 *Safety and Handling of Organic Peroxides, Retrieved from*: **https://www.americanchemistry.com/content/download/5324/file/Safety-and-Handling-of-Organic-Peroxides.pdf**.
4 *List of Organic peroxides*, *Retrieved from*: **https://image.ec21.com/company/c/ch/che/chemex/upfile/2_1.pdf**.
5 H. Liu, J. T. Yu and C. Pan, *Chem. Commun.*, 2021, **57**, 6707–6724.
6 H. Gandhi, K. O'Reilly, M. K. Gupta, C. Horgan, E. M. O'Leary and T. P. O'Sullivan, *RSC Adv.*, 2017, **7**, 19506–19556.
7 M. Klussmann, *Chem. – Eur. J.*, 2018, **24**, 4480–4496.
8 S. Wang, Y. Zhao, A. W. H. Chan, M. Yao, Z. Chen and J. P. D. Abbatt, *Chem. Rev.*, 2023, **123**, 1635–1679.
9 A. Baeyer and V. Villiger, *Ber. Dtsch. Chem. Ges.*, 1899, **32**, 3625–3633.
10 W. Liu, Y. Li, K. Liu and Z. Li, *J. Am. Chem. Soc.*, 2011, **133**, 10756–10759.
11 G. Zhang, L. Fu, P. Chen, J. Zou and G. Liu, *Org. Lett.*, 2019, **21**, 5015–5020.
12 D. Liu, C. Liu, H. Li and A. Lei, *Angew. Chem., Int. Ed.*, 2013, **52**, 4453–4456.
13 L.-F. Fan, R. Liu, X.-Y. Ruan, P.-S. Wang and L.-Z. Gong, *Nat. Synth.*, 2022, **1**, 946–955.
14 F. Parsaee, M. C. Senarathna, P. B. Kannangara, S. N. Alexander, P. D. E. Arche and E. R. Welin, *Nat. Rev. Chem.*, 2021, **5**, 486–499.
15 H. Xiong, N. Ramkumar, M. F. Chiou, W. Jian, Y. Li, J. H. Su, X. Zhang and H. Bao, *Nat. Commun.*, 2019, **10**, 122.
16 L. Ge, H. Zhou, M.-F. Chiou, H. Jiang, W. Jian, C. Ye, X. Li, X. Zhu, H. Xiong, Y. Li, L. Song, X. Zhang and H. Bao, *Nat. Catal.*, 2020, **4**, 28–35.
17 Z. Nie, M. F. Chiou, J. Cui, Y. Qu, X. Zhu, W. Jian, H. Xiong, Y. Li and H. Bao, *Angew. Chem., Int. Ed.*, 2022, **61**, e202202077.
18 N. Zhu, T. Wang, L. Ge, Y. Li, X. Zhang and H. Bao, *Org. Lett.*, 2017, **19**, 4718–4721.
19 X. Wu, J. Riedel and V. M. Dong, *Angew. Chem., Int. Ed.*, 2017, **56**, 11589–11593.
20 Y. Zeng, X.-D. Liu, X.-Q. Guo, Q.-S. Gu, Z.-L. Li, X.-Y. Chang and X.-Y. Liu, *Sci. China: Chem.*, 2019, **62**, 1529–1536.
21 L. Chang, Q. An, L. Duan, K. Feng and Z. Zuo, *Chem. Rev.*, 2022, **122**, 2429–2486.
22 H. Yi, G. Zhang, H. Wang, Z. Huang, J. Wang, A. K. Singh and A. Lei, *Chem. Rev.*, 2017, **117**, 9016–9085.
23 S. Kawamura, S. Mukherjee and M. Sodeoka, *Org. Biomol. Chem.*, 2021, **19**, 2096–2109.
24 M. S. Kharasch and G. Sosnovsky, *J. Am. Chem. Soc.*, 1958, **80**, 756.
25 L. F. Fieser and A. E. Oxford, *J. Am. Chem. Soc.*, 1942, **64**, 2060–2065.
26 Y. Zhang, J. Feng and C. J. Li, *J. Am. Chem. Soc.*, 2008, **130**, 2900–2901.
27 D. A. Dirocco, K. Dykstra, S. Krska, P. Vachal, D. V. Conway and M. Tudge, *Angew. Chem., Int. Ed.*, 2014, **53**, 4802–4806.
28 N. Zhu, J. Zhao and H. Bao, *Chem. Sci.*, 2017, **8**, 2081–2085.
29 B. Qian, S. Chen, T. Wang, X. Zhang and H. Bao, *J. Am. Chem. Soc.*, 2017, **139**, 13076–13082.
30 W. Jian, L. Ge, Y. Jiao, B. Qian and H. Bao, *Angew. Chem., Int. Ed.*, 2017, **56**, 3650–3654.
31 A. Vasilopoulos, S. W. Krska and S. S. Stahl, *Science*, 2021, **372**, 398–403.
32 R. Giri, B. F. Shi, K. M. Engle, N. Maugel and J. Q. Yu, *Chem. Soc. Rev.*, 2009, **38**, 3242–3272.
33 J. H. Xie, S. F. Zhu and Q. L. Zhou, *Chem. Rev.*, 2011, **111**, 1713–1760.
34 C. X. Zhuo, C. Zheng and S. L. You, *Acc. Chem. Res.*, 2014, **47**, 2558–2573.

35 A. H. Cherney, N. T. Kadunce and S. E. Reisman, *Chem. Rev.*, 2015, **115**, 9587–9652.
36 F. D. Lu, J. Chen, X. Jiang, J. R. Chen, L. Q. Lu and W. J. Xiao, *Chem. Soc. Rev.*, 2021, **50**, 12808–12827.
37 Z. L. Li, G. C. Fang, Q. S. Gu and X. Y. Liu, *Chem. Soc. Rev.*, 2020, **49**, 32–48.
38 T. Xiong and Q. Zhang, *Chem. Soc. Rev.*, 2021, **50**, 8857–8873.
39 J. Eames and M. Watkinson, *Angew. Chem., Int. Ed.*, 2001, **40**, 3567–3571.
40 M. B. Andrus and J. C. Lashley, *Tetrahedron*, 2002, **58**, 845–866.
41 D.-W. Gao, J. Zheng, K.-Y. Ye, C. Zheng and S.-L. You, *Asymmetric Functionalization of C-H Bonds*, The Royal Society of Chemistry, 2015, vol. 25, pp. 141–213.
42 L. Bayeh and U. K. Tambar, *ACS Catal.*, 2017, **7**, 8533–8543.
43 S. Samadi, H. Arvinnezhad, S. Nazari and S. Majidian, *Top Curr. Chem.*, 2022, **380**, 20.
44 A. Lattanzi and A. Scettri, *J. Organomet. Chem.*, 2006, **691**, 2072–2082.
45 M. Israr, H. Xiong, Y. Li and H. Bao, *Adv. Synth. Catal.*, 2020, **362**, 2211–2215.
46 R. Zhu and S. L. Buchwald, *J. Am. Chem. Soc.*, 2015, **137**, 8069–8077.
47 S. Sakurai, A. Matsumoto, T. Kano and K. Maruoka, *J. Am. Chem. Soc.*, 2020, **142**, 19017–19022.
48 P.-Z. Wang, Y.-J. Liang, X. Wu, W. Guan, W.-J. Xiao and J.-R. Chen, *ACS Catal.*, 2022, **12**, 10925–10937.
49 Y. Zeng, M. F. Chiou, X. Zhu, J. Cao, D. Lv, W. Jian, Y. Li, X. Zhang and H. Bao, *J. Am. Chem. Soc.*, 2020, **142**, 18014–18021.
50 X. Zhu, W. Jian, M. Huang, D. Li, Y. Li, X. Zhang and H. Bao, *Nat. Commun.*, 2021, **12**, 6670.
51 A. L. J. Beckwith and A. A. Zavitsas, *J. Am. Chem. Soc.*, 1986, **108**, 8230–8234.
52 K. Smith, C. D. Hupp, K. L. Allen and G. A. Slough, *Organometallics*, 2005, **24**, 1747–1755.
53 J. A. Mayoral, S. Rodríguez-Rodríguez and L. Salvatella, *Chem. – Eur. J.*, 2008, **14**, 9274–9285.
54 A. S. Gokhale, A. B. E. Minidis and A. Pfaltz, *Tetrahedron Lett.*, 1995, **36**, 1831–1834.
55 M. B. Andrus, A. B. Argade, X. Chen and M. G. Pamment, *Tetrahedron Lett.*, 1995, **36**, 2945–2948.
56 M. B. Andrus and X. Chen, *Tetrahedron*, 1997, **53**, 16229–16240.
57 M. B. Andrus and Z. Zhou, *J. Am. Chem. Soc.*, 2002, **124**, 8806–8807.
58 J. S. Clark and C. Roche, *Chem. Commun.*, 2005, 5175–5177.
59 V. Kohler, C. Mazet, A. Toussaint, K. Kulicke, D. Haussinger, M. Neuburger, S. Schaffner, S. Kaiser and A. Pfaltz, *Chem. – Eur. J.*, 2008, **14**, 8530–8539.
60 J. S. Clark, K. F. Tolhurst, M. Taylor and S. Swallow, *J. Chem. Soc., Perkin Trans. 1*, 1998, 1167–1170.
61 J. Clariana, J. Comelles, M. Moreno-Mañas and A. Vallribera, *Tetrahedron: Asymmetry*, 2002, **13**, 1551–1554.
62 J. Bayardon, D. Sinou, M. Guala and G. Desimoni, *Tetrahedron: Asymmetry*, 2004, **15**, 3195–3200.
63 B. Liu, S.-F. Zhu, L.-X. Wang and Q.-L. Zhou, *Tetrahedron: Asymmetry*, 2006, **17**, 634–641.
64 M. Seitz, C. Capacchione, S. Bellemin-Laponnaz, H. Wadepohl, B. D. Ward and L. H. Gade, *Dalton Trans.*, 2006, 193–202, DOI: 10.1039/b512570g.
65 Z. Zhou and M. B. Andrus, *Tetrahedron Lett.*, 2012, **53**, 4518–4521.
66 A. DattaGupta and V. K. Singh, *Tetrahedron Lett.*, 1996, **37**, 2633–2636.
67 G. Sekar, A. DattaGupta and V. K. Singh, *J. Org. Chem.*, 1998, **63**, 2961–2967.
68 S. K. Ginotra and V. K. Singh, *Tetrahedron*, 2006, **62**, 3573–3581.
69 S. K. Ginotra and V. K. Singh, *Org. Biomol. Chem.*, 2006, **4**, 4370–4374.
70 P. K. Singh and V. K. Singh, *Pure Appl. Chem.*, 2010, **82**, 1845–1853.
71 C. J. Fahrni, *Tetrahedron*, 1998, **54**, 5465–5470.
72 L. X. Alvarez, M. L. Christ and A. B. Sorokin, *Appl. Catal., A*, 2007, **325**, 303–308.
73 J. S. Clark, M.-R. Clarke, J. Clough, A. J. Blake and C. Wilson, *Tetrahedron Lett.*, 2004, **45**, 9447–9450.
74 M. B. Andrus, D. Asgari and J. A. Sclafani, *J. Org. Chem.*, 1997, **62**, 9365–9368.
75 M. B. Andrus and D. Asgari, *Tetrahedron*, 2000, **56**, 5775–5780.
76 S. Samadi, S. Nazari, H. Arvinnezhad, K. Jadidi and B. Notash, *Tetrahedron*, 2013, **69**, 6679–6686.
77 S. Samadi, K. Jadidi and B. Notash, *Tetrahedron: Asymmetry*, 2013, **24**, 269–277.
78 S. Samadi, H. Arvinnezhad, S. Mansoori and H. Parsa, *Sci. Rep.*, 2022, **12**, 15038.
79 K. Kawasaki, S. Tsumura and T. Katsuki, *Synlett*, 1995, 1245–1246.
80 K.-i Kawasaki and T. Katsuki, *Tetrahedron*, 1997, **53**, 6337–6350.
81 Y. Kohmura and T. Katsuki, *Synlett*, 1999, 1231–1234.
82 Y. Kohmura and T. Katsuki, *Tetrahedron Lett.*, 2000, **41**, 3941–3945.
83 L. Aldea, J. I. Garcia and J. A. Mayoral, *Dalton Trans.*, 2012, **41**, 8285–8289.
84 L. Aldea, I. Delso, M. Hager, M. Glos, J. I. García, J. A. Mayoral and O. Reiser, *Tetrahedron*, 2012, **68**, 3417–3422.
85 S. Samadi, K. Jadidi, B. Khanmohammadi and N. Tavakoli, *J. Catal.*, 2016, **340**, 344–353.
86 S. Samadi, A. Ashouri and M. Samadi, *ACS Omega*, 2020, **5**, 22367–22378.
87 A. V. Malkov, M. Bella, V. V. Langer and P. Kocovsky, *Org. Lett.*, 2000, **2**, 3047–3049.
88 A. V. Malkov, D. Pernazza, M. Bell, M. Bella, A. Massa, F. Teply, P. Meghani and P. Kocovsky, *J. Org. Chem.*, 2003, **68**, 4727–4742.
89 D. R. Boyd, N. D. Sharma, L. Sbircea, D. Murphy, T. Belhocine, J. F. Malone, S. L. James, C. C. Allen and J. T. Hamilton, *Chem. Commun.*, 2008, 5535–5537.
90 W.-S. Lee, H.-L. Kwong, H.-L. Chan, W.-W. Choi and L.-Y. Ng, *Tetrahedron: Asymmetry*, 2001, **12**, 1007–1013.

91 G. Chelucci, G. Loriga, G. Murineddu and G. A. Pinna, *Tetrahedron Lett.*, 2002, **43**, 3601–3604.
92 C. Giorgio, I. Anna, M. Daniele and S. Antonio, *J. Mol. Catal. A: Chem.*, 2003, **191**, 29–33.
93 J. Muzart, *J. Mol. Catal.*, 1991, **64**, 381–384.
94 A. Levina and J. Muzart, *Tetrahedron: Asymmetry*, 1995, **6**, 147–156.
95 A. Levina and J. Muzart, *Synth. Commun.*, 1995, **25**, 1789–1794.
96 M. T. Rispens, C. Zondervan and B. L. Feringa, *Tetrahedron: Asymmetry*, 1995, **6**, 661–664.
97 C. Zondervan and B. L. Feringa, *Tetrahedron: Asymmetry*, 1996, **7**, 1895–1898.
98 J. Le Bras and J. Muzart, *Tetrahedron: Asymmetry*, 2003, **14**, 1911–1915.
99 M. J. Södergren and P. G. Andersson, *Tetrahedron Lett.*, 1996, **37**, 7577–7580.
100 M. B. Andrus and B. B. V. S. Sekhar, *J. Heterocyclic Chem.*, 2001, **38**, 1265–1271.
101 A. V. Malkov, A. J. P. Stewart-Liddon, F. Teplý, L. Kobr, K. W. Muir, D. Haigh and P. Kočovský, *Tetrahedron*, 2008, **64**, 4011–4025.
102 S. Samadi, K. Jadidi, M. Samadi, A. Ashouri and B. Notash, *Tetrahedron*, 2019, **75**, 862–867.
103 P.-F. Teng, C.-S. Tsang, H.-L. Yeung, W.-L. Wong, H.-L. Kwong and I. D. Williams, *J. Organomet. Chem.*, 2006, **691**, 2237–2244.
104 X.-M. Cheng, Z.-B. Zheng, N. Li, Z.-H. Qin, B. Fu and N.-D. Wang, *Tetrahedron: Asymmetry*, 2008, **19**, 2159–2163.
105 Q. Tan and M. Hayashi, *Adv. Synth. Catal.*, 2008, **350**, 2639–2644.
106 Q. Tan and M. Hayashi, *Org. Lett.*, 2009, **11**, 3314–3317.
107 V. D. M. Hoang, P. A. N. Reddy and T.-J. Kim, *Organometallics*, 2008, **27**, 1026–1027.
108 B. Zhang, S.-F. Zhu and Q.-L. Zhou, *Tetrahedron Lett.*, 2013, **54**, 2665–2668.
109 Y. Kohmura, K. Kawasaki and T. Katsuki, *Synlett*, 1997, 1456–1458.
110 J. Clark, K. Tolhurst, M. Taylor and S. Swallow, *Tetrahedron Lett.*, 1998, **39**, 4913–4916.
111 S. Sakurai, T. Kano and K. Maruoka, *Chem. Commun.*, 2021, **57**, 81–84.
112 K. Gopalaiah, *Chem. Rev.*, 2013, **113**, 3248–3296.
113 C. Marchi-Delapierre, A. Jorge-Robin, A. Thibon and S. Menage, *Chem. Commun.*, 2007, 1166–1168.
114 Y. Nishikawa and H. Yamamoto, *J. Am. Chem. Soc.*, 2011, **133**, 8432–8435.
115 B. Wang, Y. M. Lee, M. Clemancey, M. S. Seo, R. Sarangi, J. M. Latour and W. Nam, *J. Am. Chem. Soc.*, 2016, **138**, 2426–2436.
116 A. M. Zima, O. Y. Lyakin, R. V. Ottenbacher, K. P. Bryliakov and E. P. Talsi, *ACS Catal.*, 2016, **7**, 60–69.
117 O. Cussó, J. Serrano-Plana and M. Costas, *ACS Catal.*, 2017, **7**, 5046–5053.
118 W. Liu, M. Pu, J. He, T. Zhang, S. Dong, X. Liu, Y. D. Wu and X. Feng, *J. Am. Chem. Soc.*, 2021, **143**, 11856–11863.
119 K. Wang, Y. Li, X. Li, D. Li and H. Bao, *Org. Lett.*, 2021, **23**, 8847–8851.
120 T. Katsuki and K. B. Sharpless, *J. Am. Chem. Soc.*, 1980, **102**, 5974–5976.
121 V. S. Martin, S. S. Woodard, T. Katsuki, Y. Yamada, M. Ikeda and K. B. Sharpless, *J. Am. Chem. Soc.*, 1981, **103**, 6237–6240.
122 S. L. Colletti and R. L. Halterman, *J. Organomet. Chem.*, 1993, **455**, 99–106.
123 S. Bhadra, M. Akakura and H. Yamamoto, *J. Am. Chem. Soc.*, 2015, **137**, 15612–15615.
124 N. Ji, J. Yuan, M. Liu, T. Lan and W. He, *Chem. Commun.*, 2016, **52**, 7731–7734.
125 N. Komatsu, M. Hashizume, T. Sugita and S. Uemura, *J. Org. Chem.*, 1993, **58**, 7624–7626.
126 A. Lattanzi, F. Bonadies, A. Senatore, A. Soriente and A. Scettri, *Tetrahedron: Asymmetry*, 1997, **8**, 2473–2478.
127 A. Lattanzi, P. Iannece and A. Scettri, *Tetrahedron: Asymmetry*, 2004, **15**, 413–418.
128 T. Okachi, N. Murai and M. Onaka, *Org. Lett.*, 2003, **5**, 85–87.
129 A. U. Barlan, A. Basak and H. Yamamoto, *Angew. Chem., Int. Ed.*, 2006, **45**, 5849–5852.
130 C. Zeng, D. Yuan, B. Zhao and Y. Yao, *Org. Lett.*, 2015, **17**, 2242–2245.
131 A. Raheem Keeri, I. Justyniak, J. Jurczak and J. Lewiński, *Adv. Synth. Catal.*, 2016, **358**, 864–868.
132 C. G. Newton, S. G. Wang, C. C. Oliveira and N. Cramer, *Chem. Rev.*, 2017, **117**, 8908–8976.
133 E. L. Lucas, N. Y. S. Lam, Z. Zhuang, H. S. S. Chan, D. A. Strassfeld and J. Q. Yu, *Acc. Chem. Res.*, 2022, **55**, 537–550.
134 W. Zhang, F. Wang, S. D. McCann, D. Wang, P. Chen, S. S. Stahl and G. Liu, *Science*, 2016, **353**, 1014–1018.
135 Z. Zhang, W. Zheng and J. C. Antilla, *Angew. Chem., Int. Ed.*, 2011, **50**, 1135–1138.
136 F. Yang, J. Zhao, X. Tang, G. Zhou, W. Song and Q. Meng, *Org. Lett.*, 2017, **19**, 448–451.
137 S. Tanaka, G. Ramachandran, Y. Hori and M. Kitamura, *Chem. Lett.*, 2018, **47**, 1486–1489.
138 L. Ye, Y. Tian, X. Meng, Q. S. Gu and X. Y. Liu, *Angew. Chem., Int. Ed.*, 2020, **59**, 1129–1133.
139 D. Lv, Q. Sun, H. Zhou, L. Ge, Y. Qu, T. Li, X. Ma, Y. Li and H. Bao, *Angew. Chem., Int. Ed.*, 2021, **60**, 12455–12460.
140 S. Narute, R. Parnes, F. D. Toste and D. Pappo, *J. Am. Chem. Soc.*, 2016, **138**, 16553–16560.
141 S. Narute and D. Pappo, *Org. Lett.*, 2017, **19**, 2917–2920.
142 K. Mikami, M. Hatano and M. Terada, *Chem. Lett.*, 1999, 55–56.
143 C. Pi, X. Cui, X. Liu, M. Guo, H. Zhang and Y. Wu, *Org. Lett.*, 2014, **16**, 5164–5167.
144 B. Ye and N. Cramer, *Science*, 2012, **338**, 504–506.
145 J. Zheng, S. B. Wang, C. Zheng and S. L. You, *J. Am. Chem. Soc.*, 2015, **137**, 4880–4883.
146 B. Ye and N. Cramer, *J. Am. Chem. Soc.*, 2013, **135**, 636–639.
147 Y. Sun and N. Cramer, *Angew. Chem., Int. Ed.*, 2017, **56**, 364–367.

148 S.-B. Wang, J. Zheng and S.-L. You, *Organometallics*, 2016, **35**, 1420–1425.
149 B. Ye and N. Cramer, *Angew. Chem., Int. Ed.*, 2014, **53**, 7896–7899.
150 J. Zheng and S. L. You, *Angew. Chem., Int. Ed.*, 2014, **53**, 13244–13247.
151 J. Zheng, W. J. Cui, C. Zheng and S. L. You, *J. Am. Chem. Soc.*, 2016, **138**, 5242–5245.
152 D. C. Noller and D. J. Bolton, *Anal. Chem.*, 1963, **35**, 887–893.
153 J. Varjavandi and O. L. Mageli, *J. Chem. Educ.*, 1971, **48**, A451–A456.