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Review

# Recent Advances in Reductive Desymmetrization of Diketones

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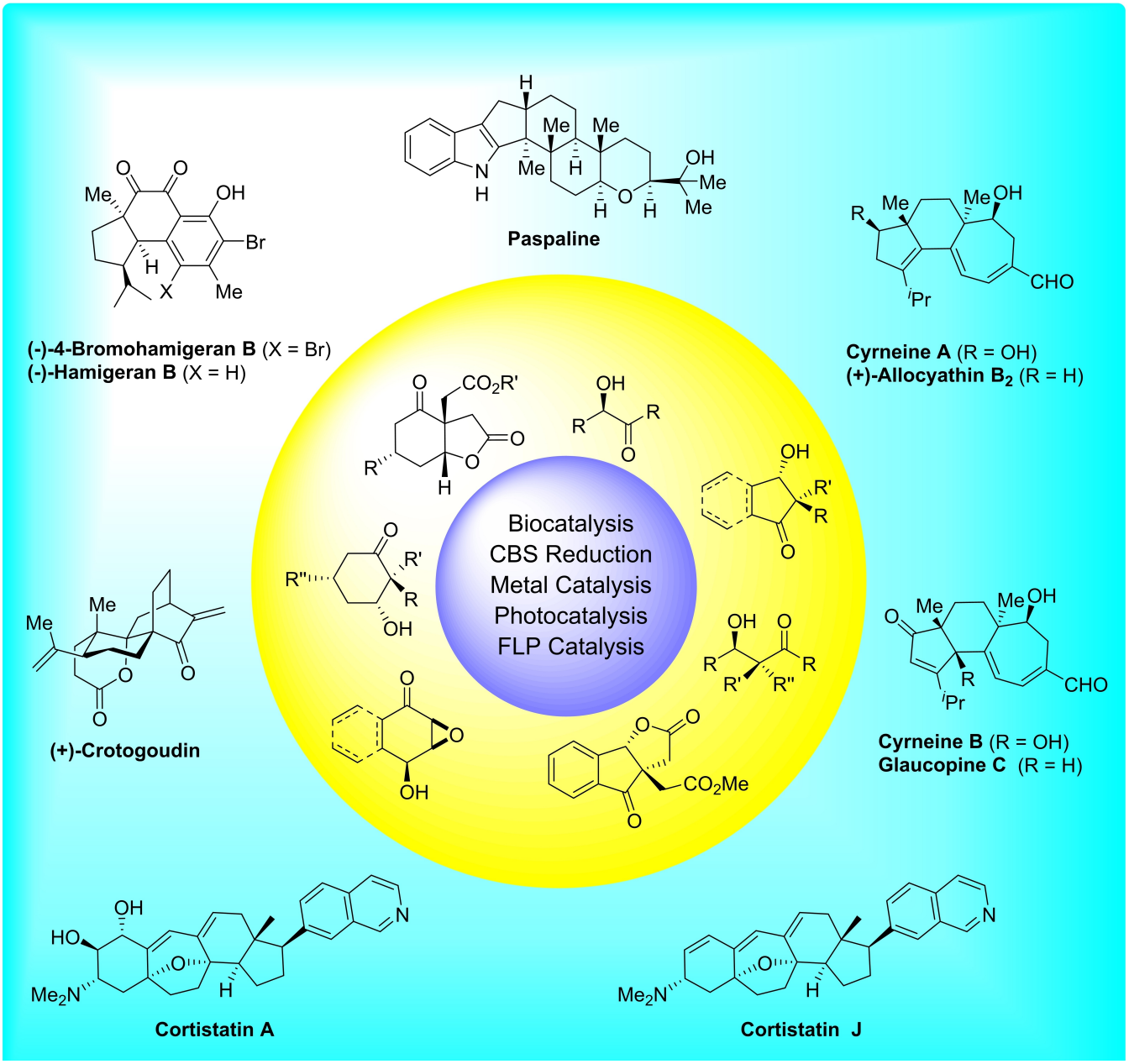

**Abstract:** Reductive desymmetrization of achiral or meso diketones has attracted considerable attention due to these motifs which play important roles in organic synthesis, pharmaceuticals and functional materials. This review focuses on recent advances in homogeneous reductive desymmetrization of 1,2-, 1,3- and 1,4-diketones, which provides an efficient and practical access to structurally diverse chiral α-, β- or γ-hydroxy ketone derivatives.

## 1. Introduction

Due to the importance of chiral hydroxy ketones for natural products synthesis and drug discovery,[1] much attention has been paid to the development of their synthetic methods. In most cases, chiral α-hydroxy ketones could be obtained by enzymatic or *N*-heterocyclic carbene-catalyzed benzoin condensation, and β-hydroxy ketones could be mainly acquired by classical aldol reactions. However, in the above methods, sometimes it is difficult to control enantioselectivity, which may be accompanied by problems such as poor yield and large catalyst loading. Therefore, it seems particularly important to start from simple and cheap raw materials, and develop a simple and efficient method to synthesize optically active hydroxy ketones, which have important scientific value and potential application prospects.

Enantioselective desymmetrization of achiral or meso diketones has become one of the versatile and powerful tools for synthesizing enantioenriched hydroxy ketones, which should overcome the following potential challenges:[2] 1) two carbonyl groups have similar reduction reactivity. 2) diketones, especially 1,3-diketones, serve as good ligands, which can lead to catalyst poisoning or deactivation easily in the presence of base. 3) β-hydroxy ketones are prone to easy racemization through reversible aldol condensation reaction (Figure 1). This review is designed to give an overview of enantioselective reductive desymmetrization, highlighting and detailing the most efficient transformations that have been reported in the past ten years, including biocatalyzed reduction, metal-catalyzed asymmetric hydrogenation (AH) and asymmetric transfer hydrogenation (ATH), CBS catalyzed reduction, FLP catalyzed and photoinduced asymmetric reduction. Asymmetric aldol reaction and other catalytic/stoichiometric enantioselective desymmetriz-ation are not discussed here.

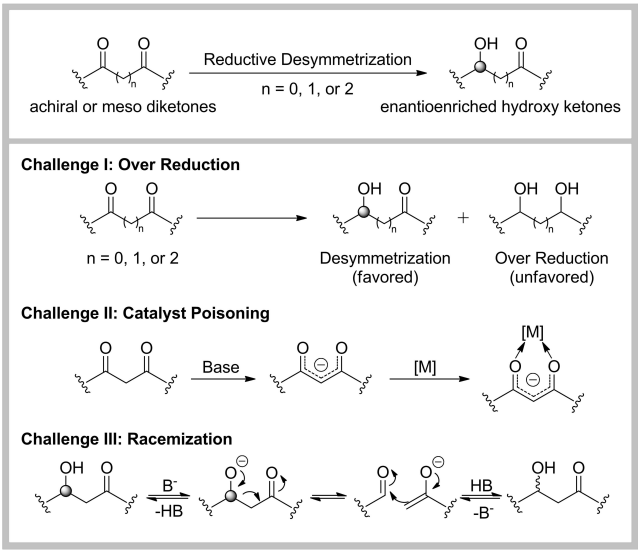


**Figure 1.** The challenges of reductive desymmetrization of diketones.

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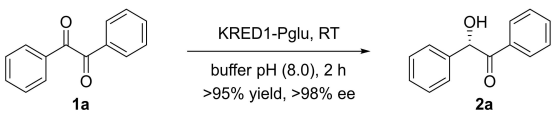
## 2. Biocatalyzed Reductive Desymmetrization

The asymmetric microbial reduction of the carbonyl functional group is a viable preparative method because of the variety and the specificity of dehydrogenase in microorganisms. In the past decades, some progresses have been made in biocatalysis for the enantioselective desymmetrization of 1,2-, 1,3- or 1,4-diketones[3–5] *via* stereoselective reduction of one of the two enantiotopic ketone moieties.

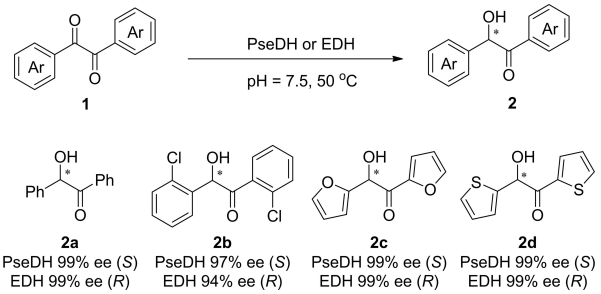
### 2.1. Desymmetrization of 1,2-Diketones

Optically active α-hydroxy ketones constitute a useful group of major chiral building blocks for asymmetric synthesis. Although some such building blocks can be derived from natural products such as lactic acid, asymmetric synthesis of unnatural type compounds is still desirable. Microbial reduction of 1,2-diketones to optically active α-hydroxy ketones has been identified as one of the most effective methods. In 2016, Romano and coworkers[6] reported KRED1-Pglu, a new NAD(P)H-dependent reductase, could reduce benzil to (*S*)-benzoin with >95% yield and >98% ee value, which gave a simple and efficient way to the synthesis of optical pure aromatic hydroxy ketones (Scheme 1).

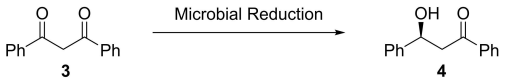
Later, Ansorge-Schumacher's group[7] disclosed an efficient bioreduction of 1,2-diarylketones to chiral α-hydroxy ketones with up to 99% ee values by using NAD(P)H-dependent




**Scheme 1.** Reduction of Benzil with KRED1-Pglu.

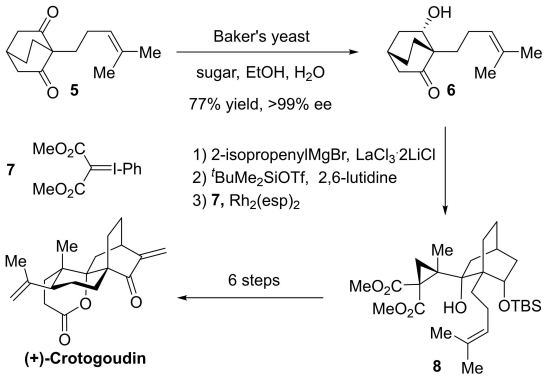



**Scheme 2.** Reduction of 1,2-Diketones with PseDH or EDH.




| Biocatalyst | Yield (%) | Ee (%) |
|---|---|---|
| Saccharomyces cerevisiae (GC) | 50 | 58 |
| Kluyveromyces marxianus (GC) | 12 | 36 |

**Scheme 3.** Bioreduction of 1,3-Diphenyl-1,3-propandione.




**Scheme 4.** Enantioselective Synthesis of (+)-Crotogoudin.

pseudoephedrine or ephedrine dehydrogenases (PseDH or EDH) (Scheme 2). Both of PseDH and EDH, from Arthrobacter sp. TS-15, were NADH-dependent members of oxidoreductase superfamily. Because of the wide substrate spectrum and high regio- and enantioselectivity, these dehydrogenases showed

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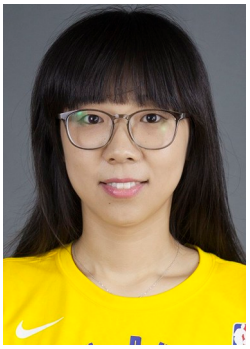

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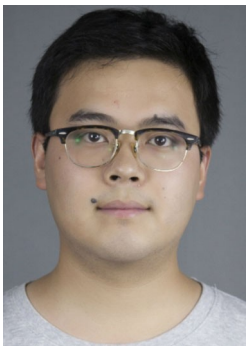

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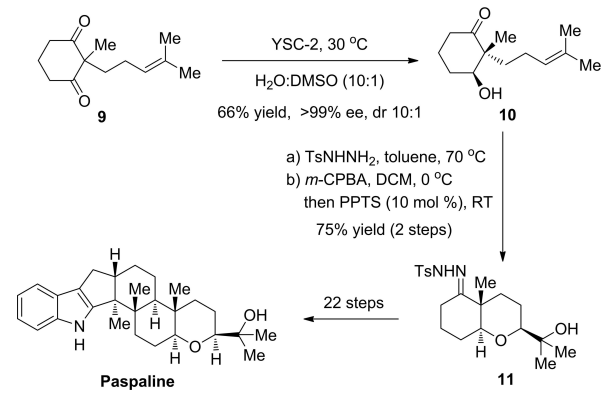
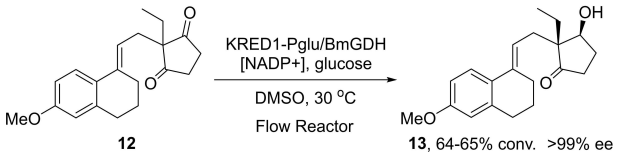
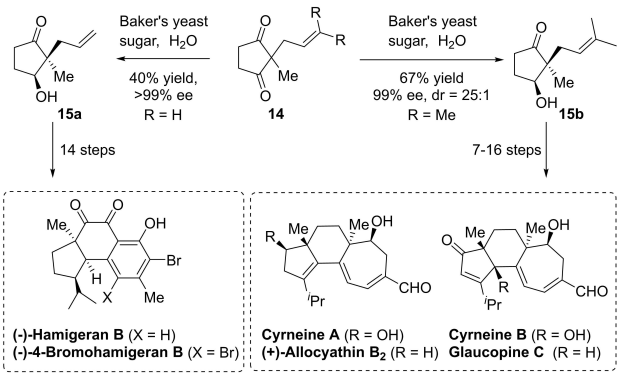
*Yong-Gui Zhou was born in Hubei Province, China. He received a B.S. degree from Huaibei Coal Industrial Teachers' College in 1993 and earned his Ph.D. from Shanghai Institute of Organic Chemistry under supervision of Prof. Li-Xin Dai and Xue-Long Hou in 1999. He joined Xumu Zhang's group at Pennsylvania State University as a postdoctoral fellow that same year, and in 2002 he began his independent research career at Dalian Institute of Chemical Physics, Chinese Academy of Sciences, where currently he is professor of organic chemistry. His research interests include the development of asymmetric reactions, mechanistic elucidation and asymmetric synthesis.*



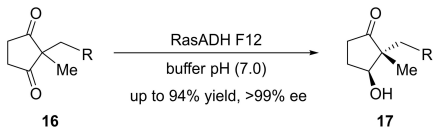

**Scheme 5.** Enantioselective Synthesis of Paspaline.




**Scheme 6.** Immobilized KRED1-Pglu/BmGDH in Flow Reactor.

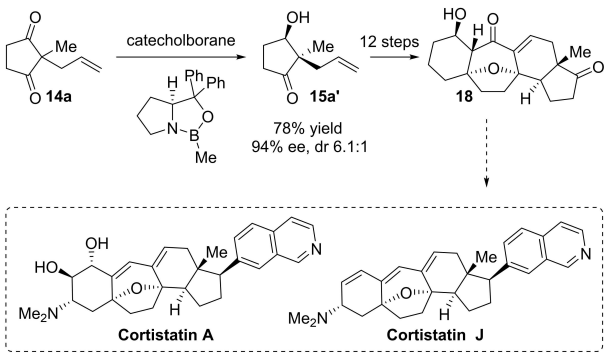



**Scheme 7.** Enantioselective Synthesis of Diterpenoids.

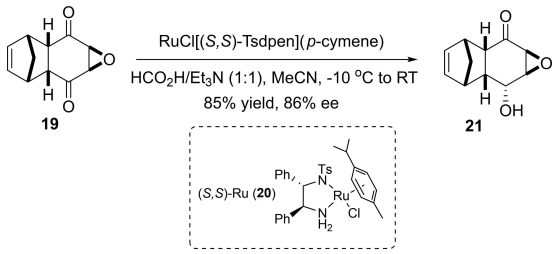



**Scheme 8.** RasADH F12 Catalyzed Reductive Desymmetrization of **16**.

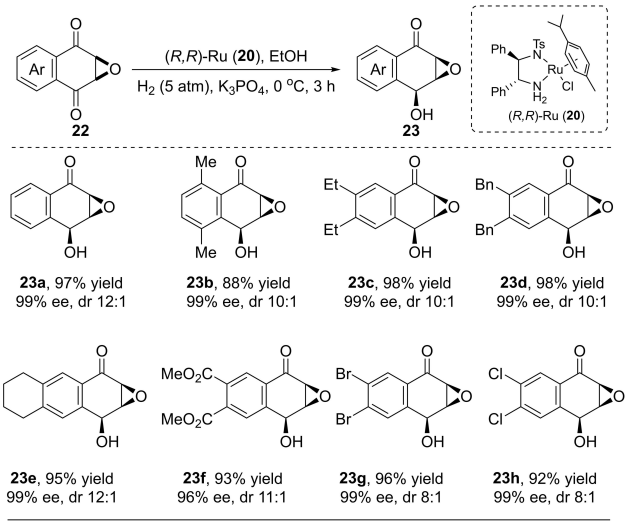
great potential in the industrial production of valuable chiral compounds. Interestingly, these two dehydrogenases had strict stereoselectivity in the reduction. For example, in the reduction of α-diketones **1a**, (*S*)-**2a** and (*R*)-**2a** could be given by PseDH and EDH, respectively.




**Scheme 9.** Enantioselective Synthesis of Cortistatins A and J.




**Scheme 10.** Ru-catalyzed Desymmetrization of Meso-epoxy Diketone.

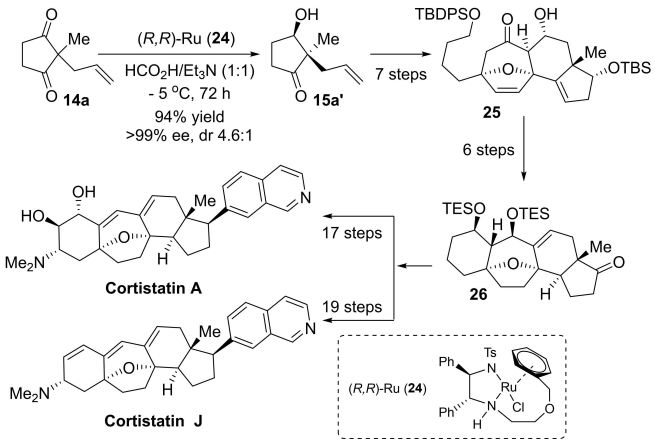



**Scheme 11.** Ru-catalyzed Desymmetrization of Meso-epoxy Diketones.

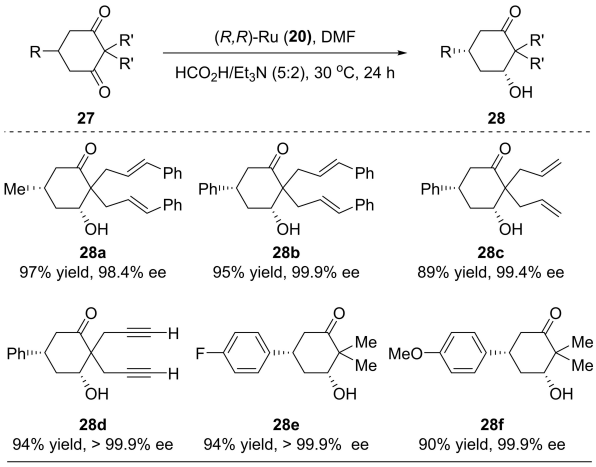
## 2.2. Desymmetrization of 1,3-Diketones

### *2.2.1. Acyclic 1,3-Diketones*

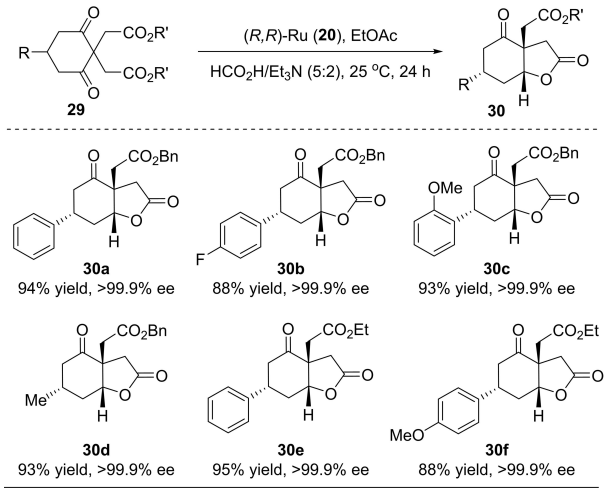
Apart from 1,2-diketones, bioreduction of linear 1,3-diketones has also attracted wide attention. In 2016, Vitale and co-workers[8] reported that a bacterium in a nutrient medium could regio- and stereoselectively reduce substituted 1,3-diphenyl-1,3-propandione **3** in the presence of different whole cell micro-organisms, affording the chiral 3-hydroxy-1,3-diphenylpropan-1-one in moderate yields and ee values (Scheme 3).



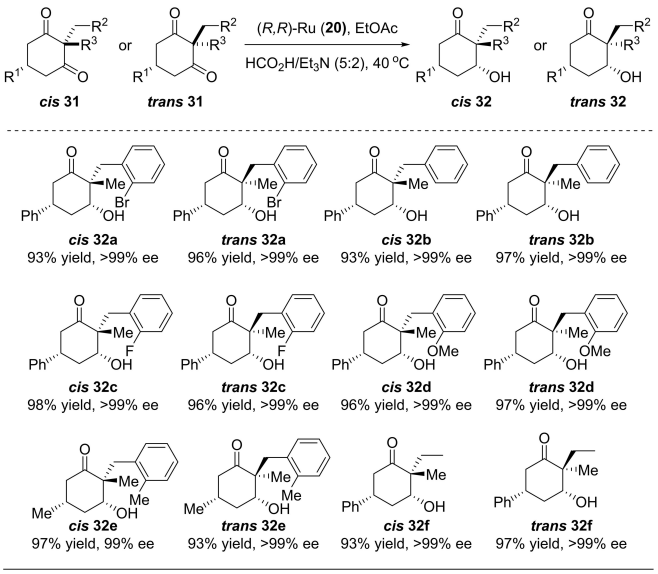

**Scheme 12.** Enantioselective Synthesis of Cortistatins A and J.



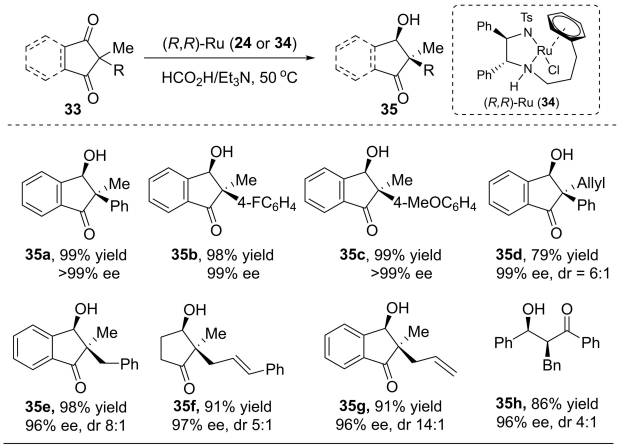

**Scheme 13.** Ru-catalyzed Desymmetrization of 1,3-Cyclohexanediones.



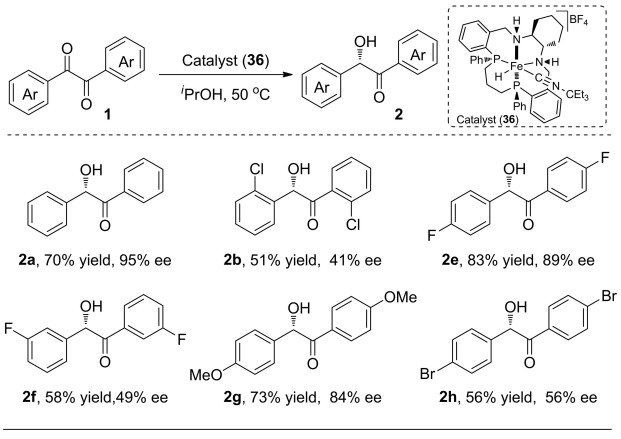

**Scheme 14.** Ru-catalyzed Desymmetrization of 1,3-Cyclohexanediones.



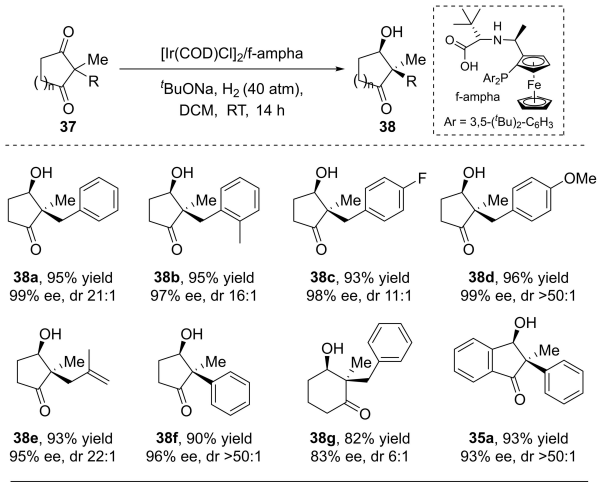

**Scheme 15.** Ru-catalyzed Desymmetrization of 1,3-Cyclohexanediones.



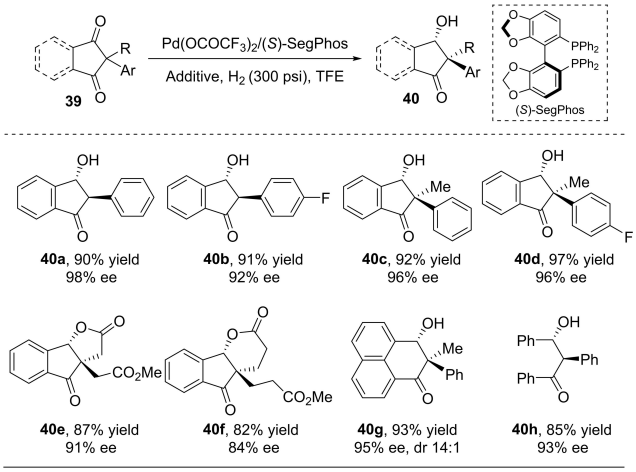

**Scheme 16.** Desymmetrization of 1,3-Indanediones.



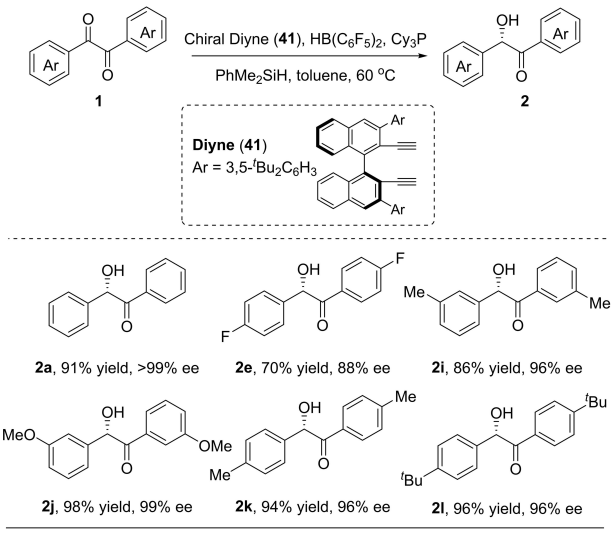

**Scheme 17.** Fe-catalyzed Hydrogenative Desymmetrization of 1,2-Diketones.



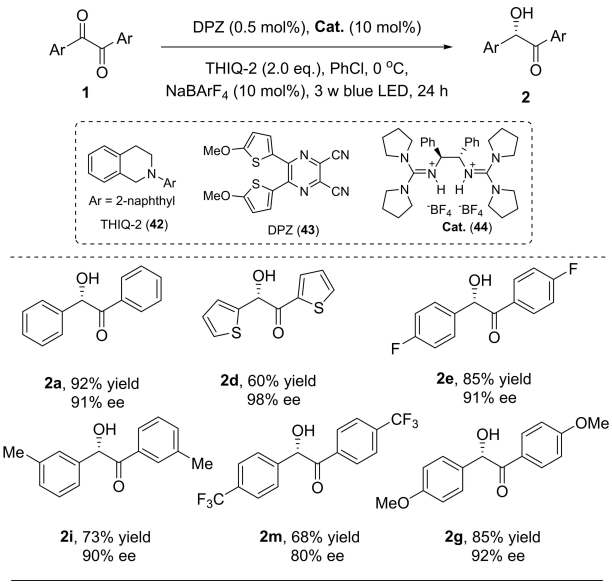

**Scheme 18.** Ir-catalyzed Hydrogenative Desymmetrization.



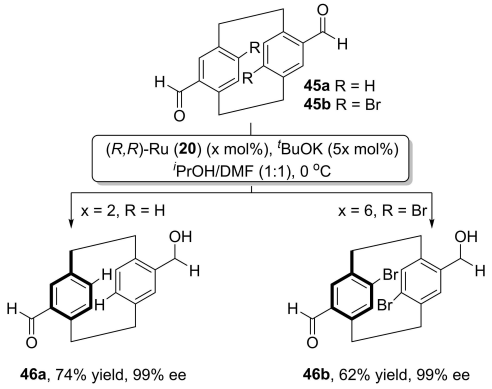

**Scheme 19.** Pd-catalyzed Hydrogenative Desymmetrization.




**Scheme 20.** FLP Catalyzed Desymmetrization.




**Scheme 21.** Photoreduction of 1,2-Diketones.




**Scheme 22.** Desymmetrization of Centrosymmetric Dialdehydes

### *2.2.2. Cyclic 1,3-Diketones*

The desymmetrization of 2,2-disubstituted 1,3-cyclic diketones *via* stereoselective monoreduction of diketones is a useful approach to furnish the hydroxy ketones. Many research groups have applied the methodology to the synthesis of natural products. For example, in 2013, Carreira's group[9] reported a total synthesis of *ent*-crotogoudin. Salient features of their total synthesis included an efficient access which could obtain the key hydroxy ketone intermediate alcohol **6** as a single diastereomer and enantiomer in 77% yield by the reduction of 1-substituted bicyclo[2.2.2]octa-2,6-dione **5** (Scheme 4) with Baker's yeast. The intermediate **6** could be converted to **8**, a key synthon in the total synthesis of (+)-crotogoudin, through nucleophilic addition of 2-isopropenyl magnesium bromide, selective TBS-protection of the secondary alcohol and Rh-catalyzed cyclopropanation of the newly introduced olefin using phenyliodonium malonates.

Later, Johnson and co-workers[10] utilized the same strategy to total synthesis of paspaline. Biocatalytic mono-

reduction of **9**, a key step in this procedure, was promoted by Saccharomyces cerevisiae, providing the desired **10** with excellent enantioselec-tivity and good diastereoselectivity. With the desired hydroxy ketone **10** in hand, *cis*-pyran **11** was obtained by a simple conversion of the carbonyl group followed by a stereoselective epoxidation/intramolecular etherification sequence in 75% yield and >20:1 dr. Then, pyran **11** underwent further transformations including a selective C–H acetoxylation as another key step to give the final natural product paspaline (Scheme 5).

Very recently, Serra group[11] found that a robust two-enzyme system composed of an immobilized ketoreductase (KRED1-Pglu) and a glucose dehydrogenase (BmGDH) could be used continuously for weeks to stereoselective reduction of diketones in a flow reactor. For example, the reaction of 1,3-diketone **12** gave the moderate conversion and excellent enantioselectivity by using the immobilized system (Scheme 6).

Most recently, two notable examples of enzymatic reductive desymmetrization of diketones were disclosed by Han's group[12] in the enantioselective total synthesis of a series of natural products (Scheme 7). It was found that, when treated with a Baker's yeast and sugar in water, prochiral diketone **14** was readily converted to the desired hydroxy ketone **15a** in >99% ee, and **15b** in 67% yield, 25:1 dr and 99% ee, respectively. Another advantage of this enzymatic reduction was that the reaction could be very simply performed on multigram scales, which made the following transformations more easily. The remaining ketone moiety of compound **15a** or **15b** served as a necessary synthetic handle for synthesis of the target products.

Although the research on the biocatalytic desymmetric reduction of diketones started relatively early, the reduction is far from efficiency due to the low substrate concentration (3–5 g/L) and long conversion time (3–7 days). In 2019, Wu and co-workers[13] engineered the Ralstonia sp. alcohol dehydrogenase (RasADH) to achieve the desymmetrization of 2,2-disubstituted-1,3-cyclopentanedione derivatives. Filtered by a series of conditions, they found the final five-site mutant I91V/I187S/I188L/Q191N/F205A (F12) could finish the desymmetrization of 2,2-disubstituted-1,3-cyclopentanediones in high yields and diastereomeric ratio values in 24 hours (Scheme 8).

## 3. CBS-Catalyzed Reductive Desymmetrization

Compared with biocatalysis, synthetic catalysts have shown more practical utility in the desymmetric reduction of the prochiral diketones. In the past decades, Corey-Bakshi-Shibata reduction has also been applied in desymmetrization of 1,3-diketones.[14] In 2011, Chiu's group[15] reported a desymmetrization of 2-allyl-2-methylcyclopentane-1,3-diones with (*S*)-CBS-*B*-Me, providing the mono reduction product cyclopentanol (2*R*,3*R*)-**15a′** in 94% ee, 6.1:1 dr, which was a key step during asymmetric synthesis of the pentacyclic framework of cortistatin A and J (Scheme 9).

## 4. Metal-Catalyzed Hydrogenative Desymmetrization

Metal-catalyzed asymmetric (transfer) hydrogenation has been extensively studied over the past decades and achieved great success.[16] In sharp contrast, due to the equivalent activity of two carbonyl groups of diketone substrates, its application in asymmetric monoreduction of diketones has been rarely explored.[17] Nevertheless, chiral iridium, ruthenium, and palladium catalysts were successfully developed for the asymmetric hydrogenation leading to desymmetrization of diketones.

### 4.1. Ruthenium-Catalyzed Hydrogenative Desymmetrization

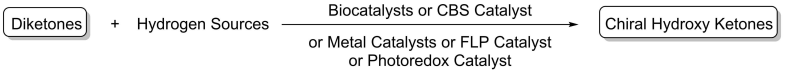
The *trans*-epoxy quinol moiety is widely present in natural products and biologically active molecules. In the past decades, several methods have been developed including Baker's yeast reduction, asymmetric epoxidation, stoichiometric and catalytic asymmetric Diels-Alder reactions. In 2011, McIntosh and co-workers[18] developed an efficient scalable synthetic protocol for chiral epoxy alcohol **21** using Noyori's Ru catalyst system *via* transfer hydrogenative desymmetrization of meso-epoxy diketone **19** with 85% yield and 86% ee (Scheme 10).

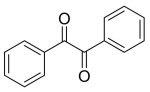
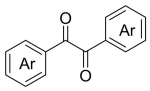
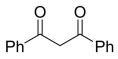
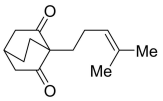
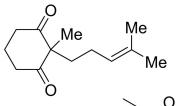
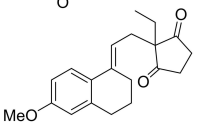
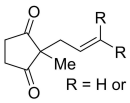
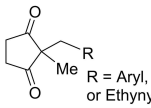
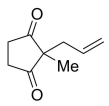
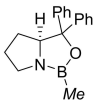
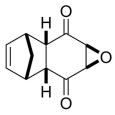
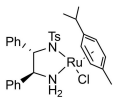
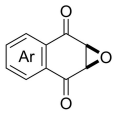
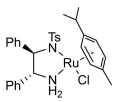
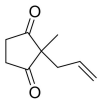
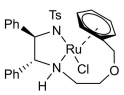
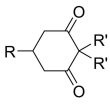
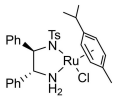
Considering the great value of epoxy quinol moiety, Zhang and co-workers[19] synthesized various chiral *cis*-epoxy naphthoquinols with excellent enantioselectivities and diastereoselectivities *via* a strategy of reductive desymmetrization (Scheme 11). To gain a better understanding of the reaction mechanism, they conducted some control experiments. The results showed that transfer hydrogenation played a dominant role, although the transformation proceeded *via* a combination of asymmetric hydrogenation/transfer hydrogenation mode both catalyzed by TsDPEN-Ru (**20**) catalyst.

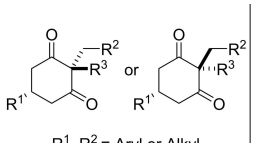
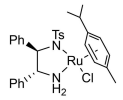
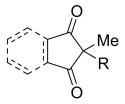
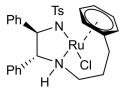
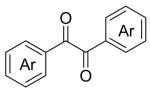
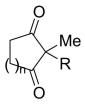
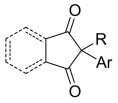
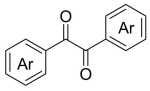
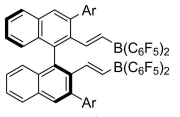
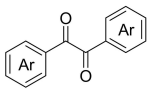
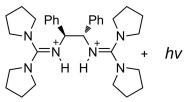
The ruthenium-catalyzed hydrogenative desymmetrization of prochiral 1,3-diketones with an α-tertiary or quaternary carbon is probably one of the most streamlined reactions to construct β-hydroxy ketone derivatives. The desymmetrization was applied to the synthesis of (+)-cortistatin A and J by Chiu and co-workers[20] in 2015. Substrate 2-allyl-2-methylcyclopentane-1,3-dione **14a** in the presence of Noyori's Ru transfer hydrogenation catalyst was converted to the key intermediate β-hydroxy ketone **15a′** on gram scale, the synthetic utility of which was demonstrated in the natural products synthesis (Scheme 12).

Multi-substituted chiral cyclohexanes are a series of important structural motifs in natural products and biologically active molecules. Therefore, their synthetic studies have attracted substantial interest. Recently, Zhou's group[21] reported the construction of multi-substituted chiral cyclohexane skeletons through a ruthenium-catalyzed hydrogenative desymmetrization of 2,2,5-trisubstituted 1,3-cyclohexanediones, affording the chiral 5-substituted 3-hydroxycy-

**Table 1.** Typical Catalytic Systems for Desymmetrization of Diketones.




| Catalytic systems | Substrates | Catalysts | Hydrogen Sources | Ee (%) | Schemes | References |
|---|---|---|---|---|---|---|
| Biocatalysts |  | KRED1-Pglu | NADPH | >98% ee | Scheme 1 | 6 |
| |  | PseDH or EDH | NADH | up to 99% ee | Scheme 2 | 7 |
| |  | Saccharomyces cerevisiae or Kluyveromyces marxianus | EtOH | 58% ee or 36% ee | Scheme 3 | 8 |
| |  | Baker's yeast | EtOH | >99% ee | Scheme 4 | 9 |
| |  | YSC-2 | $H_2O$ | >99% ee | Scheme 5 | 10 |
| |  | KRED1-Pglu/BmGDH | NADPH | >99% ee | Scheme 6 | 11 |
| |  R = H or Me | Baker's yeast | $H_2O$ | ≥99% ee | Scheme 7 | 12 |
| |  R = Aryl, Vinyl or Ethynyl | RasADH F12 | NADPH | up to >99% ee | Scheme 8 | 13 |
| CBS Catalyst |  |  | catecholborane | 94% ee | Scheme 9 | 15 |
| Metal Catalysts |  |  | $HCO_2H/NEt_3$ (1:1) | 86% ee | Scheme 10 | 18 |
| |  |  | $H_2$ | up to 99% ee | Scheme 11 | 19 |
| |  |  | $HCO_2H/Et_3N$ (1:1 | >99% ee | Scheme 12 | 20 |
| |  R = Aryl or Alkyl, R' = Alkyl |  | $HCO_2H/Et_3N$ (5:2 | up to >99% ee | Scheme 13 Scheme 14 | 21 |

| | | | | | | |
|---|---|---|---|---|---|---|
| |  R$^1$, R$^2$ = Aryl or Alkyl; R$^3$ = Me, Et or Allyl |  | $HCO_2H/Et_3N$ (5:2) | up to >99% ee | Scheme 15 | 22 |
| |  R = Aryl or Alkyl |  | $HCO_2H/Et_3N$ (5:2) | up to >99% ee | Scheme 16 | 23 |
| Metal Catalysts |  | $[FeH(CNCEt_3)L^*]BF_4$ | $^i$PrOH | up to 99% ee | Scheme 17 | 24 |
| |  n = 1 or 2 | $[Ir(COD)Cl]_2$/f-ampha | $H_2$ | up to 99% ee | Scheme 18 | 25 |
| |  R = H or Alkyl | $Pd(OCOCF_3)_2$/(*S*)-SegPhos | $H_2$ | up to 98% ee | Scheme 19 | 27 |
| FLP Catalyst |  |  Ar = 3,5-$^t$Bu$_2$C$_6$H$_3$ | $PhMe_2SiH$ | up to >99% ee | Scheme 20 | 28 |
| Photoredox Catalyst |  |  | THIQ-2 | up to 98% ee | Scheme 21 | 29 |

clohexanones bearing two discrete stereogenic centers. The mild reaction conditions were well compatible with a wide range of functionalities, including alkenyl and alkynyl, offering the useful handles for further synthetic manipulations (Scheme 13).

Notably, when an ester group was introduced to the 2-position, a hydrogenative desymmetrization/transesterification cascade occurred, affording the chiral bicyclic lactones which provided a potential opportunity for synthesis of optically active polycyclic compounds (Scheme 14).

Then, Zhou's group[22] reported a hydrogenative desymmetri-zation of 2,2,5-trisubstituted cyclohexane-1,3-diones with the different groups at the 2-position, constructing three stereogenic centers including two one-carbon-separated chiral centers and a quaternary chiral carbon. Both *cis* and *trans* isomers could give the desirable products with excellent diastereoselectivities, yields, and enantioselectivities regardless of the steric and electronic effect of the substituents (Scheme 15). To their surprise, the configuration of the hydroxy group related to the 5-substituent was irrelevant with the substituents at the 2-position.

Very recently, the same group[23] found that the *cis* β-hydroxy ketones could be conveniently obtained through hydrogenative desymmetrization of 1,3-indanediones with chiral ruthenium-diamine catalyst system (**34**). The reaction had wide functional group tolerance and could be carried out on gram scale. The synthesis of the key intermediate of the bioactive molecule (+)-estrone was also conducted (Scheme 16).

### 4.2. Iron-Catalyzed Hydrogenative Desymmetrization

In 2016, the first Fe-catalyzed asymmetric hydrogenative desymmetrization of 1,2-diketones was reported by Mezzetti and Luca.[24] A hydride isonitrile iron complex, in the presence of 2-propanol as hydrogen donor, was used to catalyze asymmetric transfer hydrogenation (ATH) of benzil to benzoin which contained a base-labile stereocenter. Benzoins were formed in up to 83% isolated yield with enantioselectivity reaching 95% (Scheme 17).

### 4.3. Iridium-Catalyzed Hydrogenative Desymmetrization

Besides the above metal catalyst systems, iridium catalyst was also applied in the hydrogenative desymmetrization of cyclic 1,3-diketones. In 2019, Zhang's group[25] reported the Ir/f-ampha catalyzed hydrogenative desymmetrization of cyclic α,α-disubstituted 1,3-diketones, giving mono-reduced products with high enantio- and diastereoselectivities. Simultaneously, the above method has been successfully applied in the synthesis of the key intermediate of (+)-estrone (Scheme 18).

### 4.4. Palladium-Catalyzed Hydrogenative Desymmetrization

The field of Pd(II)-catalyzed asymmetric hydrogenation was significantly developed in the past years.[26] Inspired by these works, Zhou's group[27] reported a Pd-catalyzed hydrogenative desymmetrization of cyclic and acyclic 1,3-diketones, providing a series of chiral β-hydroxy ketones containing two adjacent stereocenters with high enantio- and diastereoselectivity. In the reaction, an unprecedented *trans* reductive products was observed. To shed some light on the plausible mechanism to explain the phenomenon, they conducted some control experiments and DFT calculations. Due to the charge-charge interaction between the palladium and the aromatic ring on the substrate, not only the diastereoselectivity was reversed, but also the reactivity was obviously improved (Scheme 19).

## 5. FLP Catalyzed Desymmetrization

Besides the above successful examples of asymmetric hydrogenative desymmetrization of diketones with various metal catalysts, frustrated Lewis pair catalyst (FLP) was also developed for the reduction of these substrates in 2016. Du and co-workers[28] utilized the combination of tricyclohexylphosphine and chiral alkenylborane derived *in situ* from diyne as a frustrated Lewis pair catalyst, realizing the hydrogenative desymmetrization of 1,2-dicarbonyl compounds with up to 98% yields and 99% ee (Scheme 20). This methodology offered an alternative access to the synthesis of optically active α-hydroxy ketones.

## 6. Photo Reduced Desymmetrization

Reductive desymmetrization of 1,2-diketones can also be realized by visible light. In 2017, the first enantioselective photoreduction of 1,2-diketones under visible light was reported by Jiang and co-workers.[29] A series of chiral α-hydroxy ketones with excellent enantioselectivity were obtained by using dicyanopyrazine derived chromophore (DPZ) as the photoredox catalyst and a non-covalent chiral organocatalyst. In the reaction process, the chiral Brønsted acid coordinated the alkoxy radical/carbanion intermediate generated by the electron transfer to benzil from the exicited THIQ-2 to control the protonation facial selectivity and induced the observed enantioselectivity (Scheme 21).

## 7. Desymmetrization of Dialdehydes

It is well known that the carbonyl groups of aldehydes and ketones have approximate chemical properties. Recently due to the configurational and chemical stability, good tolerance to the acids and bases, the planar chiral [2.2]paracyclophanes (pCps) have received widespread attention which could be used as building blocks for the polarized light-emitting materials. Inspired by Noyori's asymmetric transfer hydrogenations (ATH), Micouin and co-workers[30] achieved the desymmetrization of a centrosymmetric pseudo-para-diformyl[2.2]paracyclophane **45 a** by using ruthenium complex with 74% isolated yield and 99% ee. The following year, the same research group completed the desymmetricalization of polysubstituted pCps **45 b** with 62% isolated yield and 99% ee (Scheme 22).

## 8. Conclusion

This mini review has presented some efficient methods for catalytic reductive desymmetrization of achiral and meso substrates by enzyme, transition-metal catalysis, organocatalysis, frustrated Lewis pairs catalysis and photoredox catalysis for nearly a decade (Table 1). They offered a straightforward and facile access to a wide range of chiral hydroxy ketones which were widespread in nature and considered as significant motifs in drugs owing to the pharmaceutical and biological activities.[9,10,12,15,20] The desymmetrization of diketones also provided a novel and highly efficient strategy for the construction of all carbon quaternary stereocenters and multiple stereogenic centers.[9–13,15,18–23,25,27]

Despite that significant achievements have been made in recent years, it is especially significant to indicate that this area is still far from being mature and full of challenges. For instance, in the presence of various catalysts, modest to good yields, and enantio- and diastereoselectivities were achieved for this challenging desymmetrization, whereas the substrate scopes were relatively narrow. Moreover, in some cases catalyst loadings were high and the reactions took a long time. Conclusively, In order to meet the growing demands of a variety of optically pure compounds, the substrate scope of the desymmetrization reaction such as fluorine compounds or multifunctional compounds also need to be extended. In addition, efficient, economical and environmentally friendly access to hydroxy ketones is still desirable. Therefore, the development of highly efficient and concise synthetic methodologies is in great demand in the future study such as photocatalytic, electro-catalytic, and earth-abundant metal-catalyzed desymmetrization of diketones.

## Acknowledgements

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## Conflict of Interest

*The authors declare no conflict of interest.*

**Keywords:** Desymmetrization · Asymmetric Hydrogenation · Diketones · Enzyme · Photocatalysis

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