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Recent progress in selective functionalization of diols *via* organocatalysis

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Polyols bearing multiple hydroxyl groups present persistent challenges for site-selective functionalization due to their inherent reactivity similarity. As minimal polyol systems, diols offer a practical and conceptually rich platform for developing regioselective catalytic strategies. This review highlights recent progress in organocatalyzed diol functionalization, with a survey of organocatalysts incorporating boron, nitrogen, and phosphorus-based motifs, as well as emerging photoredox methodologies. These systems enable selective transformation under mild conditions, avoiding stoichiometric activation and minimizing reaction complexity. Steric and electronic effects, along with noncovalent interactions, are examined in detail to rationalize the observed selectivity and guide the rational design of catalysts. This review offers a conceptual foundation for advancing sustainable, selective methods in diol derivatization.

1. Introduction

Hydroxyl groups are among the most fundamental and ubiquitous functional groups in organic chemistry, frequently found in biologically important molecules.[1,2] Their chemical versatility allows transformations *via* oxidation, reduction, and substitution, however, achieving regio- and stereoselective functionalization in highly functionalized environments remains a major challenge. A seminal contribution in this field came from the Miller group, who developed small-peptide catalysts for the enantioselective kinetic resolution of alcohols *via* hydrogen bonding, selectively acylating hydroxyl groups over amides.[3] This work exemplified the potential of non-enzymatic catalysts for selective hydroxyl functionalization in complex settings.

Polyols, which contain multiple hydroxyl groups, are widespread in both natural and synthetic compounds, including carbohydrates,[4] glycosides,[5] and other biomolecules,[6] and are key intermediates in pharmaceutical,[7] agrochemical,[8] and materials science.[9] The dense presence of hydroxyl groups often necessitates complex protecting group strategies to achieve site selectivity.[10] To address this, direct and site-selective functionalization approaches have emerged. In another pioneering example, the Miller group achieved desymmetrization of myo-inositol through site-selective phosphorylation,[11,12] and later extended this concept to the selective modification of erythromycin A, a complex natural product polyol.[13,14] These studies placed a premium on selective catalysis and functional group tolerance in high-complexity environments, setting the stage for today's late-stage functionalization strategies. More recent approaches further advance selectivity through the strategic use of non-covalent interactions,[15] minimizing undesired over-functionalization.

Diols represent an essential subclass within the broader polyol family and serve as a critical platform for advancing selective functionalization methodologies.[16] Despite possessing fewer hydroxyl groups compared to higher-order polyols, diols still pose the fundamental challenge of distinguishing between two closely similar OH functionalities. Consequently, diols act as practical model systems for developing innovative site-selective transformations, potentially extendable to more structurally complex polyols. Modern catalytic strategies are designed to achieve not only regioselectivity, by selectively modifying one hydroxyl group over the other, but also stereoselectivity and chemoselectivity, thereby broadening the synthetic versatility and application potential of diol-based transformations.[17]

From a synthetic standpoint, diols are easily accessible *via* well-established methods, including the dihydroxylation of alkenes,[18] hydrolysis of epoxides,[19] carbonyl reduction,[20] and cascade aldol/reduction sequences,[21] rendering them both cost-effective and widely available building blocks (Fig. 1a). Beyond their synthetic accessibility, diols possess notable biological significance due to their widespread occurrence in natural products and bioactive molecules (Fig. 1b). Prominent examples include (1*R*,2*S*)-Goniodiol, known for its antibacterial activity; Zephyranthine, utilized in respiratory treatments; and Fluvastatin, an anti-hypercholesterolemic agent.[22–25] Targeted diol manipulation *via* functional group interconver-

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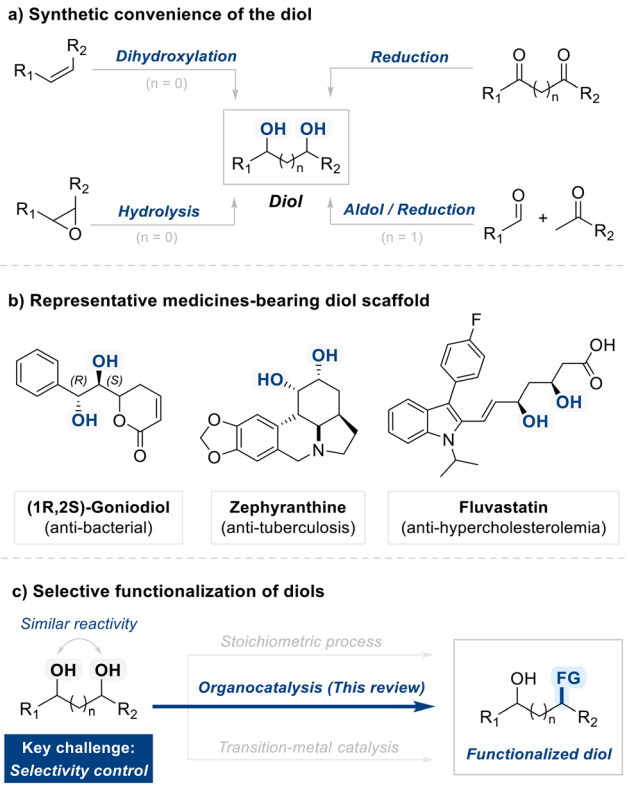


Fig. 1 Overview of diol substrate: synthetic accessibility, pharmaceutical relevance, and the thematic focus of this review.

sion, ring formation, or derivatization can dramatically alter biological activity or streamline synthetic pathways. These attributes highlight the critical importance of selective diol functionalization in contemporary organic synthesis.

However, these manipulations demand precise control, and achieving regioselective functionalization of diol remains a persistent challenge due to the similar reactivity of hydroxyl groups (Fig. 1c). Traditional solutions often involve multi-step protection and stoichiometric activation, which can inflate the length and cost of a synthetic sequence while generating undesirable waste.[26,27] Over the past few decades, researchers have made substantial progress in developing more direct and sustainable processes.[28] Regiodivergent reactions, for instance, allow a single diol to give different regioisomers by modulating reaction parameters, thereby offering a potent means to generate structural diversity in fewer steps.[29]

A broad array of catalytic paradigms has been developed to realize this objective. Early efforts predominantly utilized organometallic or tin-based reagents,[30,31] whereas enzymatic approaches[32] leveraged the remarkable selectivity of biological catalysts. Transition-metal complexes, with palladium,[33] ruthenium,[34] and copper[35] among popular choices, continue to demonstrate impressive regio- and stereoselectivities in diol functionalization. More recently, organocatalysts have gained prominence owing to their mild conditions, minimal toxicity, and straightforward reaction setups. Through the integration of hydrogen-bond donor frameworks (*e.g.*, peptides, thioureas), Lewis and Brønsted acid catalysis (*e.g.*, boron-based species, phosphoric acids), and photoredox platforms, organocatalytic methods have achieved high selectivity in the direct modification of diols, significantly reducing the need for protective groups and harsh reagents.

While the selective functionalization of carbohydrate systems has been extensively explored and reviewed,[28,36–46] contemporary research increasingly turns to non-carbohydrate diols as platforms for testing new catalytic concepts. These investigations have not only yielded streamlined synthetic pathways, but also critical mechanistic insights, revealing how subtle variations in sterics, electronics, and reaction conditions can bias reactivity toward one hydroxyl group over another. A detailed understanding of these control factors provides the foundation for designing next-generation catalysts that enable highly selective functionalization of diols and structurally complex polyols.

This review provides an overview of recent advancements in the organocatalyzed selective functionalization of diol substrates. Selective transformations of carbohydrates are deliberately excluded, as they have been comprehensively covered in previous reviews.[28,36–46] Likewise, transition metal-catalyzed approaches to diol functionalization are beyond the scope of this discussion.[31,47–52] Our focus is confined to organocatalytic strategies, reflecting their significance in selective diol derivatization. The literature is systematically categorized based on the nature of the organocatalyst, with particular emphasis on systems, incorporating nitrogen, boron, or phosphorus centers, as well as emerging photoredox methodologies. Throughout, we highlight key mechanistic insights and showcase representative synthetic applications that underscore the potential and versatility of these catalytic platforms (Fig. 2). By contextualizing these recent advances within a broader historical and conceptual framework, this review aims to guide practitioners toward innovative and sustainable solutions for this enduring challenge in organic synthesis.

2. Organoboron catalytic systems

Boron is a main-group element uniquely characterized by its electron deficiency, possessing only three valence electrons and commonly adopting sp^2 and sp^3 hybridizations. These features give rise to tricoordinate, planar geometries with an empty p-orbital, allowing boron compounds to act as Lewis acids capable of engaging nucleophiles (Fig. 3a).[53] Upon coordination, tetracoordinate boron species are formed, which often serve as key intermediates in organic transformations.[54]

Organoboron compounds are classified into borane, borinic acids, boronic acids, and boric acid according to their oxidation states[55] (Fig. 3b). While each of these boron species has demonstrated substantial utility in organic synthesis, their differing oxidation states impart distinct electronic properties. These variations in electronic nature strongly influence their reaction mechanisms and acidity profiles.[56] Among them,

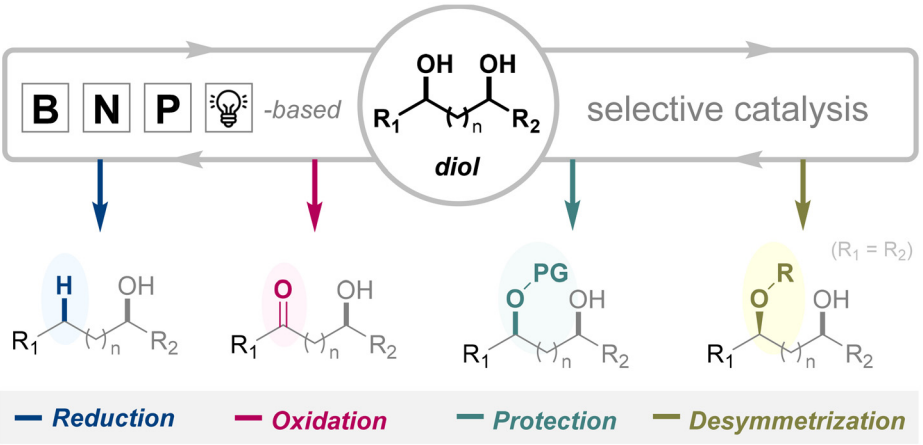


Fig. 2 Selective functionalization of diol *via* organocatalysis.

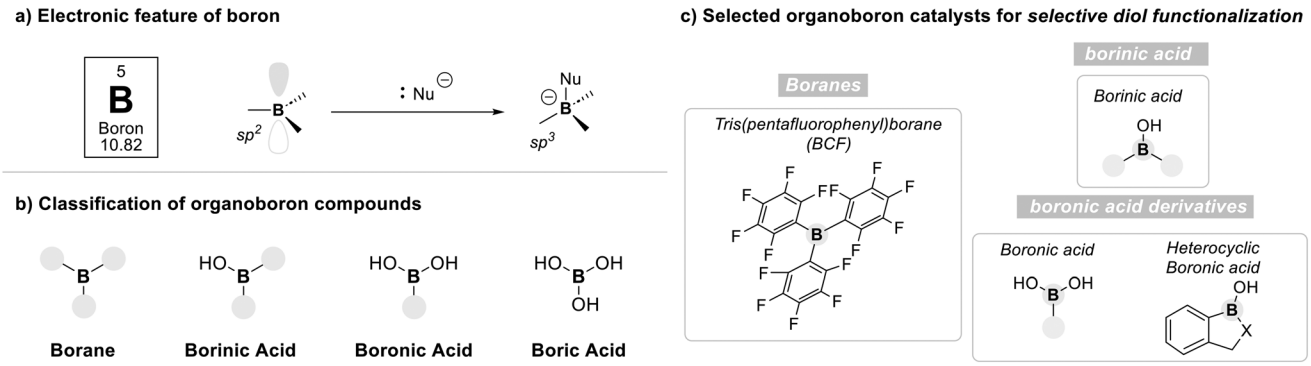


Fig. 3 Overview of boron-based organocatalyst.

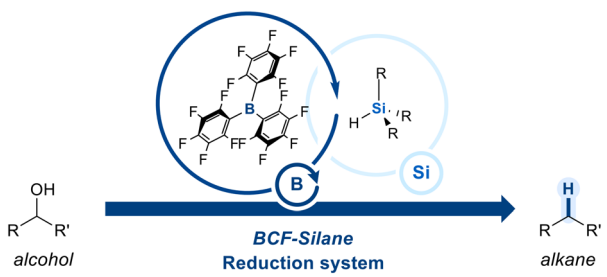
boranes, borinic acids, and boronic acids possess at least one organic substituent, allowing for structural and electronic tunability.[57,58] In contrast, boric acid consists solely of hydroxyl groups, offering limited flexibility for such modifications, and is therefore excluded from further discussion in this review.

In the following sections, four representative classes of organo-boron catalysts, such as boranes, borinic acids, boronic acids, and heterocylic boronic acid derivatives, are introduced with a focus on their characteristic activation modes and their application to the selective functionalization of diol substrates (Fig. 3c).

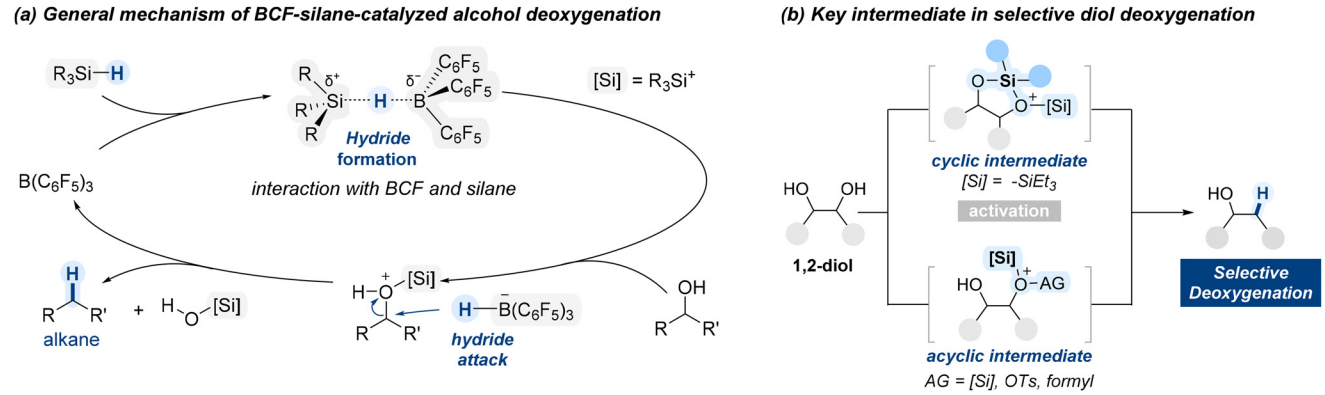
2.1. Borane catalysis

Boranes have a trivalent boron center bonded to three organic groups and no hydroxyl groups, which makes them highly electron-deficient and Lewis acidic. To further enhance their electrophilicity, strong electron-withdrawing groups are introduced onto the borane framework. A prominent example is tris(pentafluorophenyl)borane (BCF), an exceptionally electron-deficient Lewis acid owing to the strong inductive and resonance effects of the pentafluorophenyl groups. BCF has found widespread utility in organic synthesis, particularly in combination with hydrosilanes for the deoxygenation of alcohols (Scheme 1).[59]

The deoxygenation mechanism initiates when BCF interacts with a hydrosilane, leading to polarization of the Si–H bond (Scheme 2a).[60] The electron-deficient boron center withdraws electron density from silicon, resulting in partial positive charge on silicon and partial negative charge on boron. Next, oxygen atom of an alcohol coordinate to the electrophilic silicon center, forming a transient oxonium ion. Concurrently, this interaction facilitates the transfer of a hydride ion (H^-) from the silane to the boron center, resulting in the formation



Scheme 1 The BCF-silane catalytic reduction system.

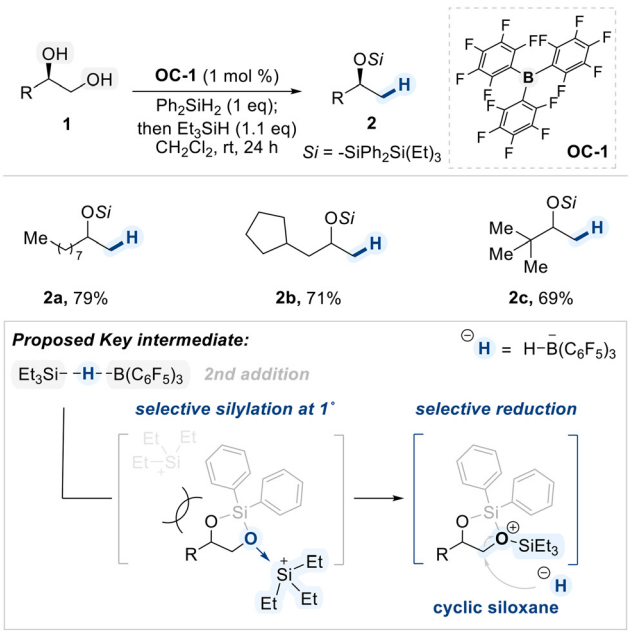


Scheme 2 General mechanism for BCF-catalysed deoxygenation of alcohols.

of a reactive boron–hydride species. The resultant hydride is then delivered to the α-carbon to substitute the oxonium leaving group, leading to cleavage of the C–O bond.

When diol substrates are treated with the BCF/hydrosilane system, selective deoxygenation can proceed through either cyclic or acyclic intermediates, as illustrated in Scheme 2b. The nature of the intermediate, cyclic or acyclic, depends on the substrate's structure and the reaction conditions, influencing both selectivity and efficiency. In the following section, we will explore examples demonstrating how the BCF/silane system enables selective deoxygenation of diol substrates.

In a 2015 study, Morandi demonstrated a BCF (**OC-1**)-catalyzed regioselective deoxygenation of terminal 1,2-diols with a preference on 1°-hydroxyl group reduction (Scheme 3).[61] In this reaction, two types of silane sources were employed. The



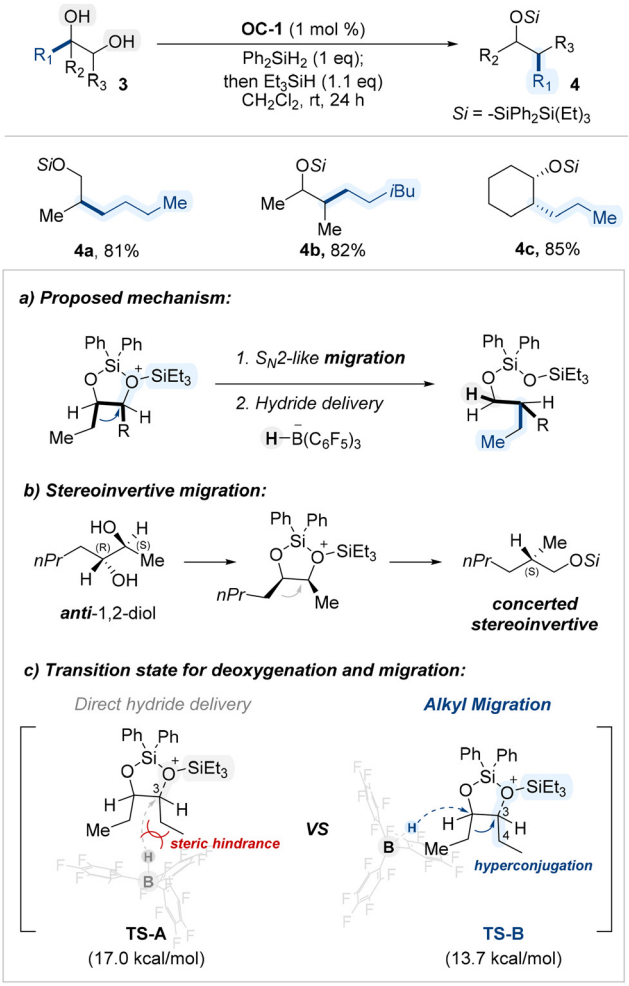
Scheme 3 BCF-catalyzed regioselective deoxygenation of terminal 1,2-diols.

first, Ph_2SiH_2, which contains two equivalents of hydride, is sacrificially consumed to generate the key cyclic siloxane intermediate. In the subsequent addition of the second silane, Et_3SiH, the more sterically accessible primary alcohol coordinates to the electrophilic silicon center, forming an oxonium intermediate. Subsequently, the hydride was selectively delivered to the activated carbon center resulting in high primary regioselectivity. From their DFT calculation study, the authors proposed that the cyclic siloxane pathway is energetically favored, providing a rationale for the observed selectivity.[62]

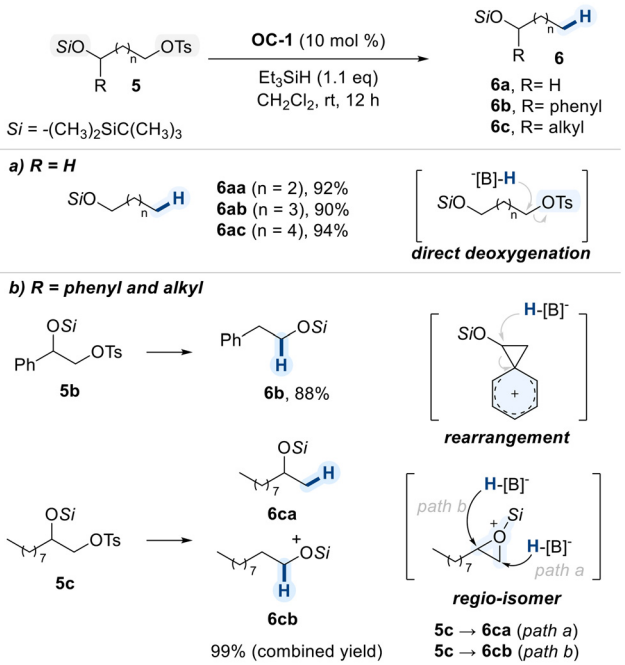
Extending their earlier findings, the Morandi group applied the previously established $B(C_6F_5)_3$/silane conditions to internal 1,2-diols, rather than terminal ones, and observed distinct reactivity, leading to a catalytic reductive pinacol-type rearrangement (Scheme 4a).[63] This transformation enabled stereoinvertive migration of alkyl groups from secondary–secondary diols (Scheme 4b), efficiently affording rearranged alcohols. Computational studies indicated that steric hinderance between BCF scaffold and alkyl substituents of a cyclic siloxane intermediate prohibited direct hydride insertion (TS-A, Scheme 4c) and that hyperconjugative effects from the migrating group stabilize the transition state, thereby favoring rearrangement over direct hydride deoxygenation (TS-B, Scheme 4c).

Oestreich and co-workers reported a $B(C_6F_5)_3$-catalyzed chemoselective reduction of primary alkyl tosylates under mild conditions (Scheme 5).[64] In this study, remote diols, in which one hydroxyl group was converted into a *tert*-butyldimethylsilyl (TBDMS) ether and the other into a tosylate, were examined for evaluating the leaving group aptitudes of these two different groups. Upon addition of BCF/hydrosilane, *in situ* generated boron–hydride species was found to be preferentially delivered to tosylated position for the chemoselective deoxygenation (Scheme 5a).

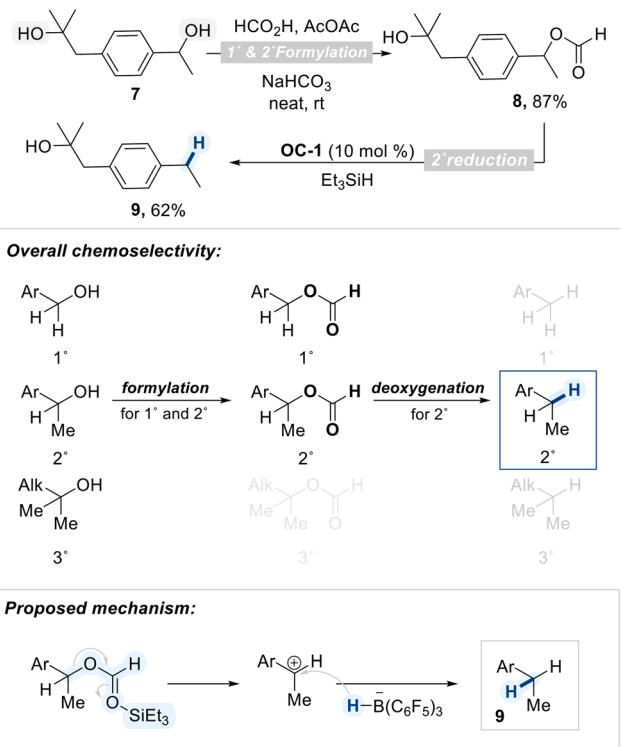
This strategy was further applied to terminal 1,2-diols bearing a primary tosylate (Scheme 5b). Notably, the product outcome varied significantly depending on the nature of the secondary substituent. In aryl-substituted substrates (**5b**), the benzene π-system participates as a neighboring group, facilitating the formation of a spirocyclic phenonium ion intermediate. The resulting three-membered ring was then opened by



Scheme 4 BCF-catalyzed reductive pinacol-type rearrangement of internal 1,2-diols.



Scheme 5 Chemoselective deoxygenation of tosylated diols.

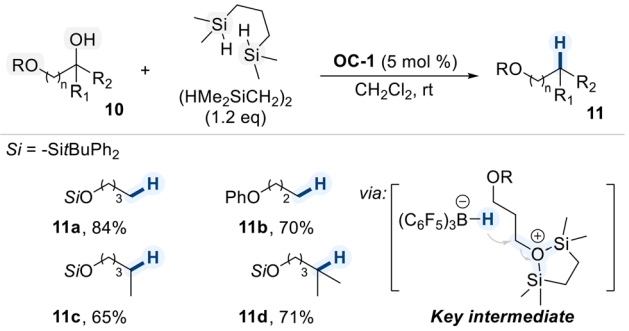


Scheme 6 BCF-catalyzed tandem activation–reduction sequences for selective deoxygenation of remote diols.

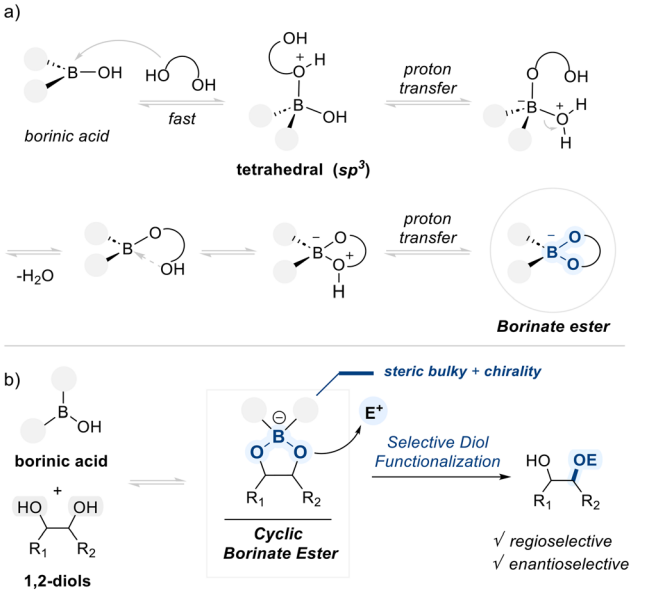
hydride delivery from the boron species, affording the rearranged product (**6b**).

In contrast, alkyl-substituted diols (**5c**) underwent intramolecular attack of the tosyl group by the oxygen atom on *vicinal* silyl ether to form a silyl oxonium ion. This intermediate was reduced by hydride attack at either ring carbon (path a or path b), resulting in a nearly 1 : 1 mixture of regioisomeric products (**6ca** and **6cb**). These results demonstrate that distinct reaction pathways can emerge from subtle changes in substrate structure, highlighting the mechanistic flexibility of this catalytic system.

Following this investigation, the same group presented a BCF/silane-stimulated selective deoxygenation, particularly designed for secondary benzylic alcohols from remote diol substrates (Scheme 6).[65] The process is associated with a tandem formylation and deoxygenation sequence. The prior formylation reactions take place only for primary or secondary alcohol substrates due to steric accessibility to formyl group, and the latter deoxygenation proceeds *via* presupposed carbocation formation followed by hydride delivery. In the second step, secondary benzylic selectivity was achieved given that carbocation is more stable in secondary position than primary position. This result implied that the rationale design of substrates with proper understanding of reaction mechanism would facilitate the development intriguing selective functionalization on unsymmetrical diol substrates.



Scheme 7 BCF-catalyzed chemoselective deoxygenation of naked hydroxyl group in diols containing diverse ether functionalities.



Scheme 8 (a) Formation of borinate ester, (b) borinic acid-mediated selectivity control.

In light of the research by Song and Lu, a $B(C_6F_5)_3$-catalyzed deoxygenation protocol was developed for mono-protected diols using a uniquely structured bis(silyl) reductant, $(HMe_2SiCH_2)_2$ (Scheme 7).[66] The reaction displayed high selectivity for free hydroxyl groups over aryl and silyl ethers, as well as other functional groups. The remarkable chemoselectivity is attributed to the dual coordination mode of the bis(silyl) reagent. $(HMe_2SiCH_2)_2$ features two atom-centered silicon units capable of simultaneously coordinating to a single hydroxyl group, thereby enhancing the leaving group ability of the oxygen and facilitating hydride transfer from the *in situ* generated boron–hydride species. This mode of activation preferentially engages naked hydroxyl groups over sterically hindered silyl ethers, allowing for selective deoxygenation even in the presence of multiple oxygen-containing functionalities. Notably, the method was also extended to more hindered secondary and tertiary alcohols, which were efficiently converted to the corresponding hydrocarbons, **11c** and **11d**, respectively.

2.2. Borinic acid catalysis

Borinic acids, featuring one hydroxyl group and two organic substituents bound to a trivalent boron center, possess a vacant p-orbital, rendering them moderately Lewis acidic. The electrophilic boron center of borinic acids can reversibly interact with the electron-rich hydroxyl groups of diols. This interaction facilitates a reversible alcoholysis, leading to the formation of a key cyclic borinate ester intermediate (Scheme 8a).[67] The formation of this cyclic borinate intermediate not only enhances the nucleophilicity of the coordinated oxygen, but also creates a tunable spatial and electronic environment that allows for precise control over site-selectivity in subsequent transformations.

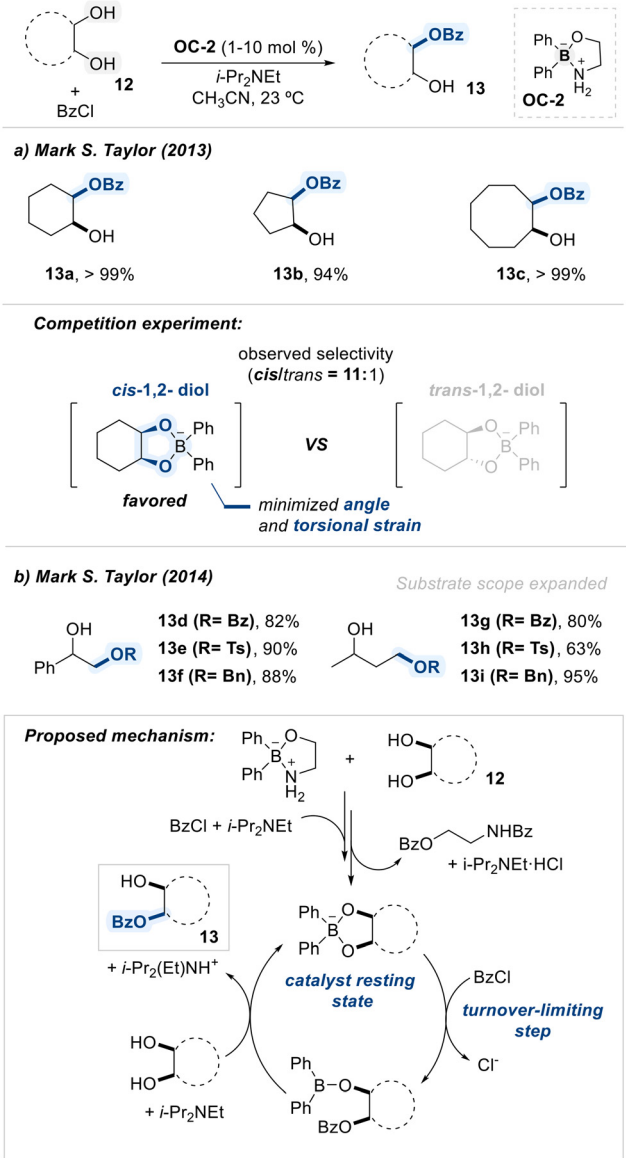
The selectivity of borinic acid-mediated transformations can be modulated by altering the nature of the substituents on the boron center (Scheme 8b). When sterically bulky groups are introduced, the reaction is directed toward the more accessible hydroxyl group in unsymmetric diols. Alternatively, attaching chiral substituents can restrict the spatial approach of electrophiles, thereby promoting functionalization in an enantioselective manner. In this section, we introduce examples of diol functionalization using borinic acid catalysts, focusing on how steric and electronic features of the catalyst structure influence selectivity.

Taylor and coworkers employed a diphenylborinic acid ethanolamine complex (**OC-2**) as a catalyst for the monobenzoylation of *vicinal*-1,2-diol substrates (Scheme 9a).[68] The catalyst **OC-2** was turned out to form the key cyclic borinate intermediate preferentially with *cis*-1,2-diols over *trans*-diols (*cis*/*trans* = 11 : 1), which was owing to the less angle and torsional strain in *cis*-intermediate.

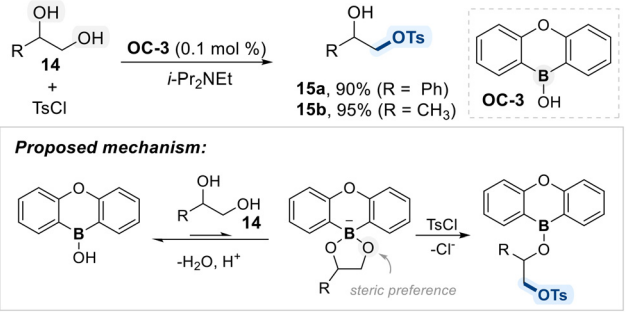
Diphenylborinic acid ethanolamine catalyst (**OC-2**) forms a reversible complex with the diol substrate, which subsequently undergoes nucleophilic attack on benzoyl chloride to furnish the monobenzoylated products with high selectivity. Importantly, the reaction exhibits a strong preference for *cis*-*vicinal* diols, whose adjacent hydroxyl groups adopt a chelating geometry conducive to the formation of a stable five-membered borinate ring. This preference is attributed to the reduced dihedral angle and torsional strain associated with the *cis* conformation.

Building on this strategy, Taylor and co-workers expanded the scope of the borinic acid-catalyzed monofunctionalization to include sulfonylation and alkylation of non-carbohydrate diols (Scheme 9b). The proposed catalytic cycle begins with the activation of catalyst (**OC-2**) *via* irreversible bis-benzoylation of the ethanolamine ligand, followed by coordination of the resulting boron center with the diol substrate to form a stable borinate adduct. The nucleophilic intermediate then undergoes a turnover-limiting benzoylation step, forming a monobenzoylated intermediate. This species is readily displaced by another diol substrate, yielding the desired product and regenerating the resting-state borinate complex.

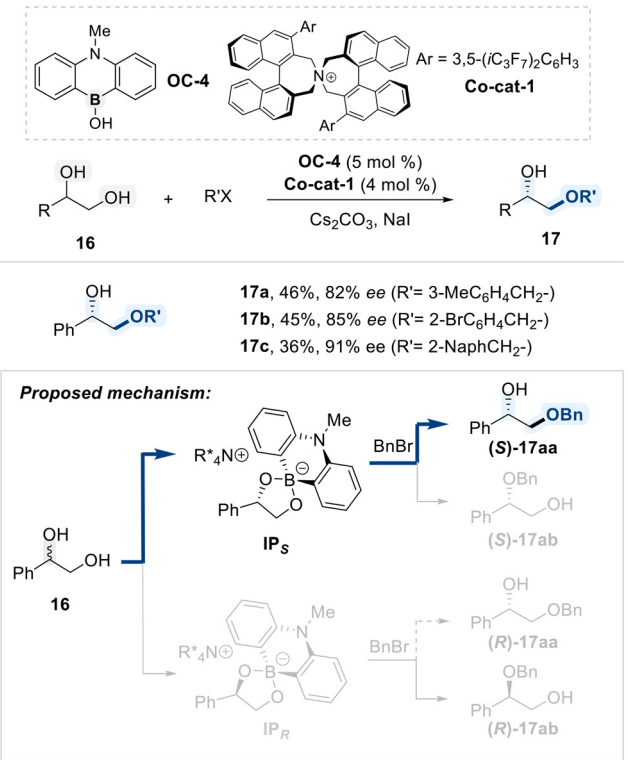
As a part of their ongoing studies on borinic acid catalysis, the Taylor group introduced a heteroboraanthracene-derived catalyst (**OC-3**) for the 1°-alcohol selective mono-functionali-



Scheme 9 Borinic acid-catalyzed regioselective acylation of diols.



Scheme 10 Borinic acid (OC-3)-catalyzed regioselective tosylation of terminal 1,2-diol.

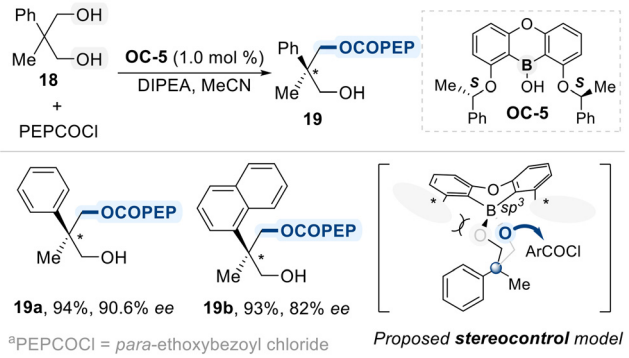


Scheme 11 Alkylative functionalization of *vicinal* diols catalyzed by a chiral ammonium borinate.

zation of terminal 1,2-diols (Scheme 10).[69] The system exhibited high selectivity for primary alcohols, which was attributed to both electronic and steric factors favoring activation at the less hindered hydroxyl group. Mechanistically, the catalyst forms a borinate intermediate with the diol substrate, which then undergoes nucleophilic attack on the electrophile to furnish the functionalized product. Although the interaction between the catalyst and diol is relatively weak, the resulting borinate species is sufficiently nucleophilic to ensure efficient transformation and high selectivity.

Maruoka and Hashimoto demonstrated that a combination of a borinic acid catalyst (**OC-4**) and a chiral ammonium salt (**Co-cat-1**) can induce an enantioselective benzylation of terminal *vicinal* diols selectively targeting the primary hydroxyl group (Scheme 11).[70] In this catalytic process, a borinate ester intermediate, formed between catalyst **OC-4** and the diol substrate, interacts with the chiral ammonium salt, generating ion-pair complex labeled, $\mathbf{IP}_S$ and $\mathbf{IP}_R$. Stoichiometric experiments indicated that the formation of the $\mathbf{IP}_S$ intermediate is kinetically favored; however, the subsequent benzylation step was proposed as the enantio-determining event. While nucleophilic attack by $\mathbf{IP}_S$ on benzyl chloride is kinetically accessible, nucleophilic substitution involving the $\mathbf{IP}_R$ intermediate is kinetically disfavored. This kinetic difference results in an effective kinetic resolution of the racemic diol.

Zheng designed a C_2-symmetric chiral borinic acid catalyst (**OC-5**) for the enantioselective desymmetrization of 2,2-di-



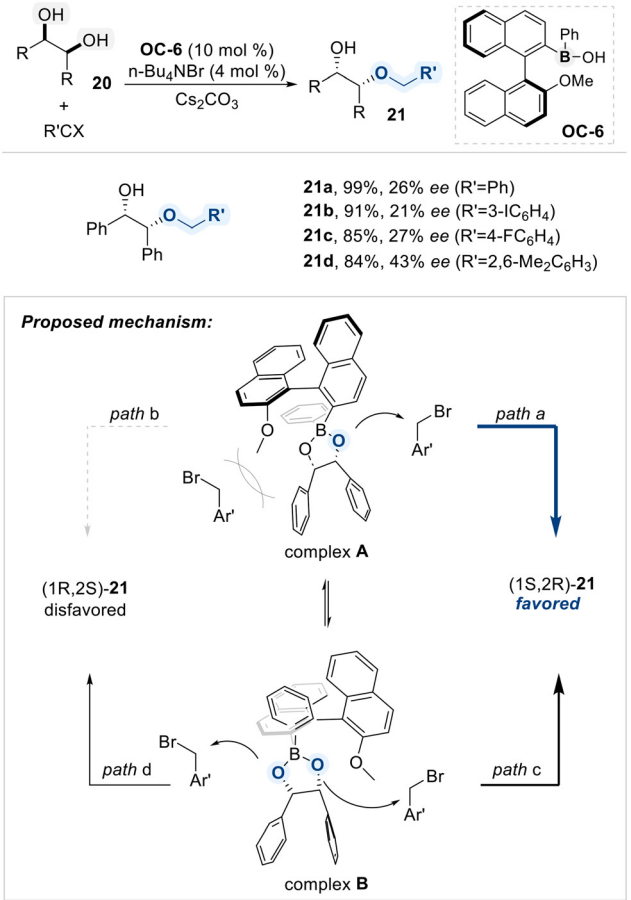
[a]PEPCOCl = *para*-ethoxybezoyl chloride

Scheme 12 Asymmetric desymmetrization using chiral borinic acid.

substituted-1,3-propanediols (Scheme 12).[71] The catalyst features a rigid oxaboraanthracene core with two chiral side arms, which adopt a twisted C_2-symmetric conformation upon diol binding. This conformation generates a well-defined asymmetric cleft that enforces a fixed geometry on the bound diol. Within this cleft, the two enantiotopic hydroxyl groups are differentiated by their spatial environments, one is deeply buried and sterically shielded by the catalyst framework, while the other remains accessible for reaction. As a result, nucleophilic attack occurs selectively at the exposed site, enabling high levels of enantioselectivity. This cleft-based differentiation is key to the catalyst's ability to control stereochemical outcome, even with sterically hindered diol substrates bearing quaternary centers.

Arisawa and Sako presented an enantioselective alkylative desymmetrization of *meso*-1,2-diols (**20**) using an axially chiral boronic acid catalyst (**OC-6**) (Scheme 13).[72] The catalyst featured a C_2-symmetric biaryl scaffold that established a chiral environment upon coordination with the diol substrate. This interaction generated a cyclic borinate intermediate, positioning the two enantiotopic hydroxyl groups unsymmetrically within the catalyst's architecture. Consequently, one hydroxyl group became sterically shielded, while the other remained accessible for nucleophilic attack, enabling asymmetric induction.

According to their mechanistic study *via* DFT calculations using (*R*,*R*)-butane-2,3-diol ((1*R*,2*R*)-**20**), coordination to the chiral boronic acid catalyst **OC-6** generates two borinate complexes (complex **A** and **B**), resulting in a total of four possible transition states (paths a–d). For complex A, path a is energetically favored, as minimal steric interference between the oxygen and the electrophile leads to the (1*S*,2*R*)-product. In contrast, path b is disfavored due to steric congestion from the catalyst's methoxy group. The other conformational complex B proceeds through paths c and d, which compete and reduce overall enantioselectivity. Path c, despite nearby steric bulk, benefits from a twisted geometry that enables effective nucleophilic attack, forming the major enantiomer, (1*S*,2*R*)-product. Path d, though free from steric hindrance, suffers from a stereoelectronic mismatch and leads to the minor (1*R*,2*S*)-product. These features collectively account for the modest enantioselectivity observed.



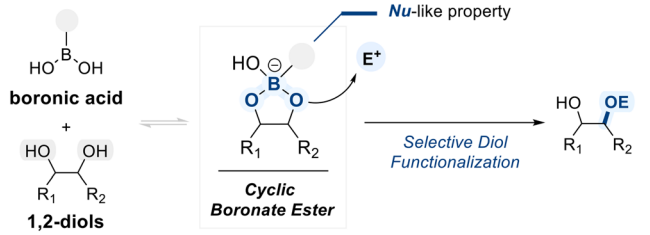
Scheme 13 Alkylative desymmetrization of 1,2-diols catalyzed by chiral borinic acid.

2.3. Boronic acid catalysis

Boronic acids are well known for their utility as synthetic building blocks in a variety of bond-forming reactions, such as the Suzuki–Miyaura coupling,[73] Petasis reaction,[74] and Chan–Lam coupling,[75] where they typically function in a stoichiometric manner. However, their role as catalytic reagents, particularly in the context of diol functionalization, is comparatively less developed and remains distinct from that of other boron-based species such as borinic acids, which offer greater structural tunability and catalytic versatility.

This limitation is closely linked to the structural simplicity of boronic acids, which possess a trivalent boron center bound to two hydroxyl groups and a single organic substituent. While this architecture is well suited for reversible covalent interactions with diol substrates, a key feature in dynamic covalent catalysis, it inherently restricts opportunities for fine-tuning steric and electronic environments. As a result, in boronic acid-catalyzed selective functionalization of diols, regio- or chemoselectivity is rarely dictated by the catalyst itself and instead arises from the intrinsic electronic or steric bias within unsymmetric diol substrates (Scheme 14).

While numerous methods employing boronic acids have been developed for diol modification, this review focuses



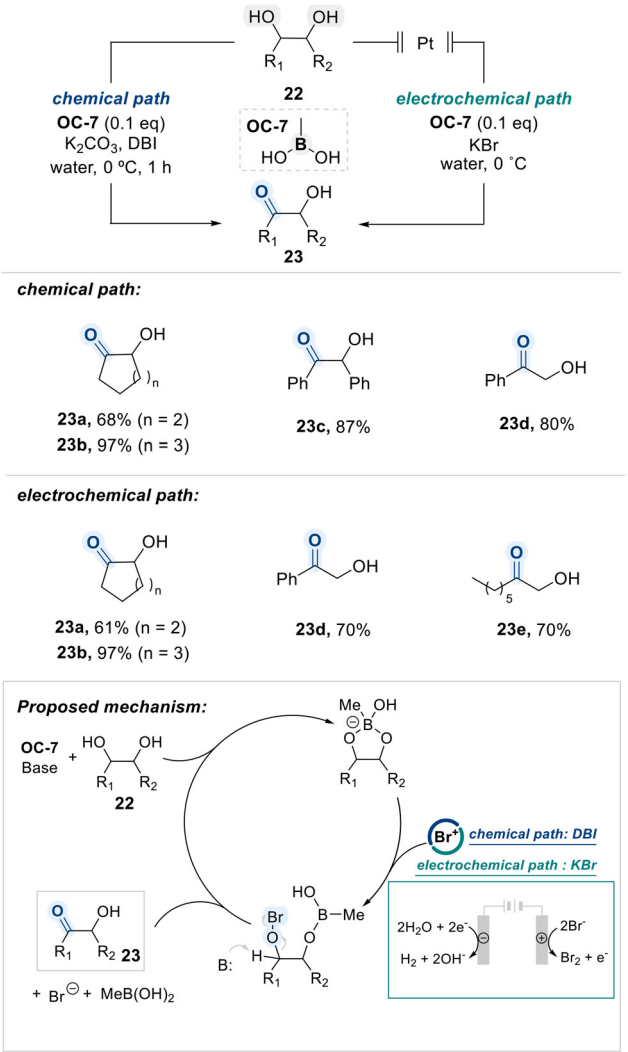
Scheme 14 Boronic acid-catalyzed selective functionalization of diol.

specifically on catalytic approaches. Accordingly, systems requiring stoichiometric or excess amounts of boronic acids are excluded.[76,77] In the following section, we highlight representative examples in which boronic acid-derived catalysts have enabled selective diol functionalization, with particular attention to the underlying reaction mechanisms.

Onomura's group reported that a boronic acid catalyst (**OC-7**) efficiently facilitates the selective oxidation of *vicinal*-diols to α-hydroxyketones under aqueous conditions, performing in both chemical and electrochemical reaction systems (Scheme 15).[78] According to their proposed mechanism, the 1,2-diol substrate is first activated by the boronic acid catalyst **OC-7** *via* formation of a boronate ester intermediate. In the chemical pathway, the cyclic boronate undergoes nucleophilic attack on an Br^+ species, generated *in situ* from DBI. This transformation ultimately affords the ketone product **23** through an elimination process. The authors further demonstrated that a combination of $KBrO_3$ and $KHSO_4$ can also serve as an electrophilic bromine source for this transformation.[79] In the electrochemical pathway, Br^+ is produced at the anode from KBr, while OH^- ions formed at the cathode and subsequently act as the base in the elimination step.

In this context unsymmetrical terminal diol substrates exhibited selective oxidation at the secondary hydroxyl group, highlighting a preference over the primary site under the optimized conditions.

In 2021, Taylor and co-workers reported a site-selective intramolecular cyclization of remote diols utilizing a pentafluorophenylboronic acid catalyst (**OC-8**) and oxalic acid co-catalyst (**Co-cat-2**) (Scheme 16).[80] The reaction proceeds *via* the formation of a Brønsted acid-like boron species (**I**), generated through dynamic association between **OC-8** and **Co-cat-2**, which acts as the active catalyst. Upon exposure to the diol substrate, species (**I**) functions as a proton donor toward the benzylic hydroxyl group, thereby promoting the elimination of water and generating a benzylic carbocation intermediate. This intermediate subsequently undergoes intramolecular nucleophilic attack by the pendant hydroxyl group, resulting in formation of the cyclic ether. Concurrently, the conjugate base boron species (**II**), generated in the initial proton transfer step, accepts the proton released during ether formation to afford the protonated boron species (**III**). Rehydration of (**III**) under aqueous conditions restores the active species (**I**), thus completing the catalytic cycle. The observed regioselectivity is



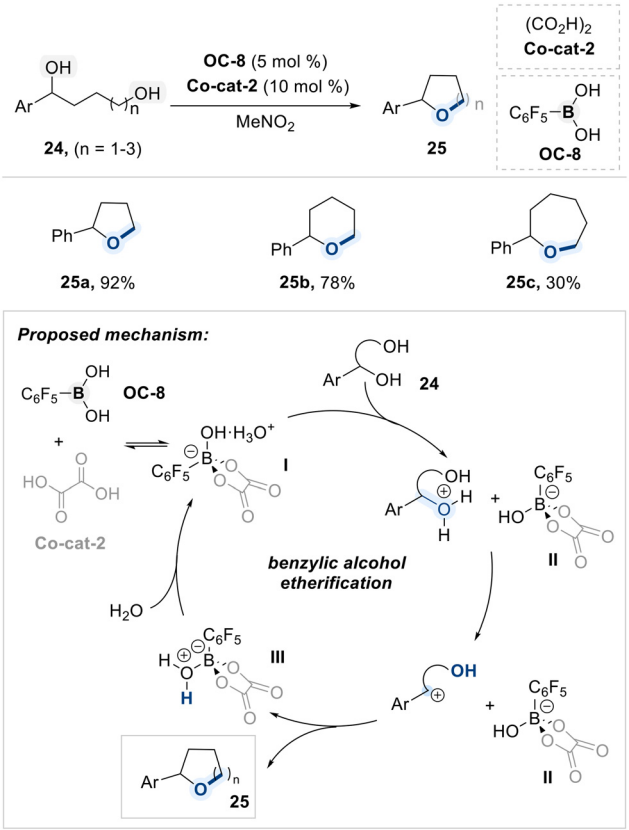
Scheme 15 Boronic acid-catalyzed selective oxidation of 1,2-diols to α-hydroxyl ketones.

attributed to the involvement of a carbocation intermediate, as benzylic positions provide sufficient stabilization to allow efficient cyclization.

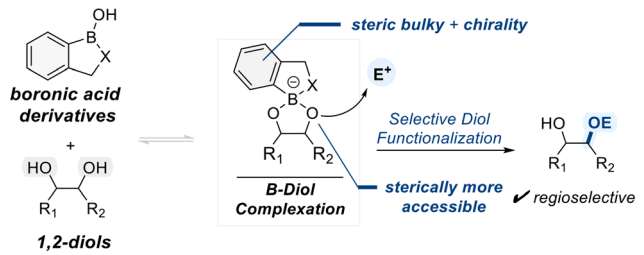
2.4. Catalysis by heterocyclic boronic acid derivatives

Heterocyclic boronic acid derivatives have gained attention as promising catalysts for selective polyol functionalization due to their customizable properties in catalyst desgin.[81] A subset of these catalysts possesses boron-containing heterocycles incorporating oxygen or nitrogen atoms within the ring, which provide stable rigidity and sufficient Lewis acidity for effective diol binding (Scheme 17).[82] These heterocyclic frameworks often feature unsymmetric geometries distinct from classical boronic or borinic acids, allowing differentiation between the two hydroxyl groups in diol substrates during complexation.

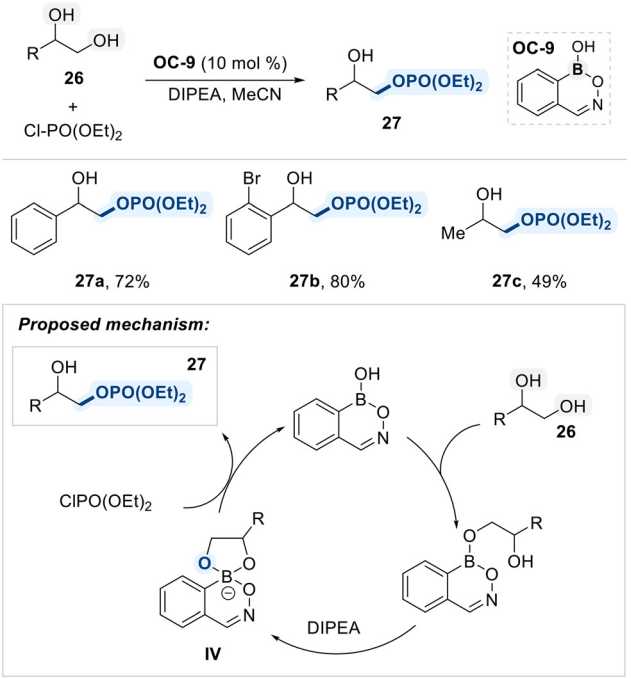
Incorporating steric hindrance or chiral elements into the heterocyclic backbone can further enhance the selectivity of electrophilic reactions mediated by such boron–diol com-



Scheme 16 Intramolecular cyclization of remote diols.



Scheme 17 General mechanism for heterocyclic boronic acid-catalyzed selective functionalization of diols.



Scheme 18 Monophosphorylation reaction of *vicinal* diols catalyzed by benzoxazaborine scaffold.

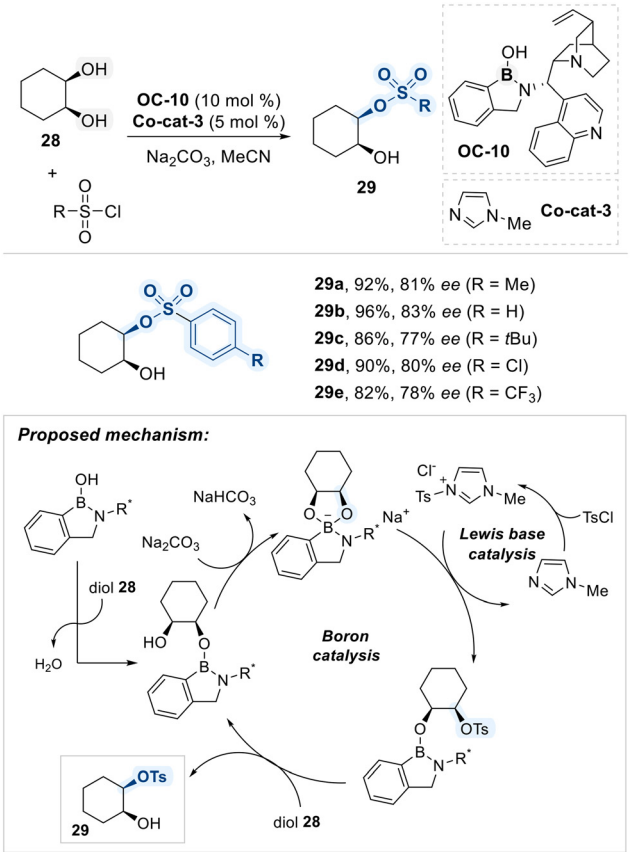
plexes. The following section highlights representative examples of selective diol functionalization, with a particular focus on catalysts based on benzoxaborole scaffolds. This section presents various examples of selective diol functionalization, focusing on catalysts derived from heterocyclic boron-based scaffolds.

Hall and Rygus developed a neutral benzoxazaborine-based organocatalyst (**OC-9**) for the regioselective functionalization of *vicinal*-diols (Scheme 18).[83] Upon reversible formation of a tetracoordinate boronate species (**IV**), the sterically accessible oxygen, originating from the primary alcohol, selectively attacks chlorophosphate electrophiles, affording the desired products in high yields with excellent site-selectivity.

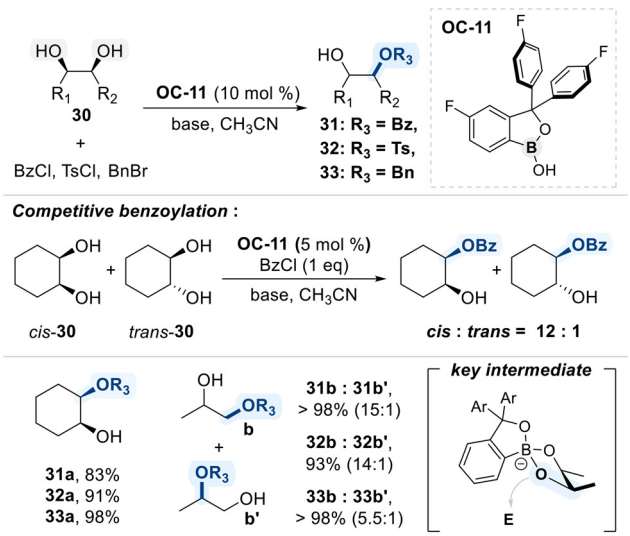
Kuwano and Arai unveiled that a chiral benzazaborole catalyst (**OC-10**), in combination with an *N*-methylimidazole (NMI) co-cataylst (**Co-cat-3**), effectively induced the enantio-selective sulfonylation of *cis*-1,2-diols (Scheme 19).[84] The benzazaborole scaffold of **OC-10** facilitates the stepwise formation of a key boronate intermediate upon binding to the *cis*-diol substrate. Meanwhile, the NMI co-catalyst activates sulfonyl chloride by generating a tosyl imidazolium species, which serves as the actual electrophile. The conformationally more accessible oxygen atom within the cyclic boronate intermediate then performs a nucleophilic attack on the activated tosyl electrophile, providing the enantioriched tosylated product. Finally, the boronate ester is regenerated as the catalytic boron center is displaced by another incoming diol substrate, thus completing the catalytic cycle.

The Kusano research group presented a benzoxaborole-based catalytic platform for the site-selective functionalization of 1,2-diols (Scheme 20).[81] The catalyst features a benzoxaborole core bearing electron-withdrawing aryl substituents, which increase the binding affinity toward diol substrates and promote the formation of catalytically active boronate intermediates. This conformational advantage was experimentally shown to confer high selectivity for *cis*-1,2-diols over their *trans*-isomers, as evidenced by competitive benzoylation reactions in which preferential functionalization of the *cis*-isomer was observed. In substrates bearing both primary and secondary hydroxyl groups, functionalization predominantly occurs at the primary site, likely due to its lower steric hindrance.

In a follow-up study, the same research group developed an improved bifunctional benzoxaborole catalyst (**OC-12**) bearing

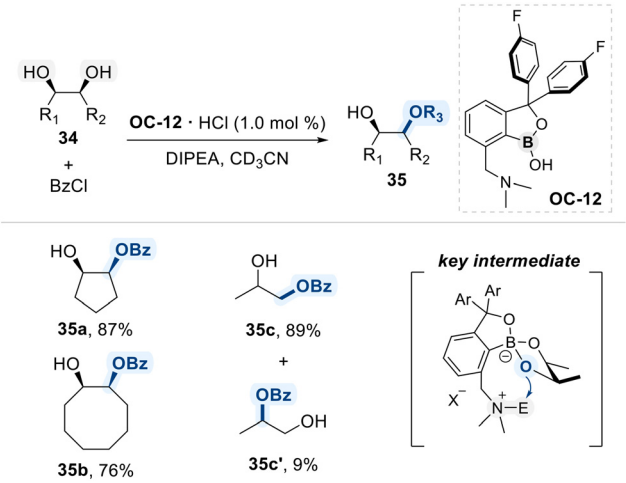


Scheme 19 Chiral benzazaborole-catalyzed enantioselective sulfonylation of *meso*-1,2-diol.



Scheme 20 Site-selective modification of diols catalyzed by **OC-11**.

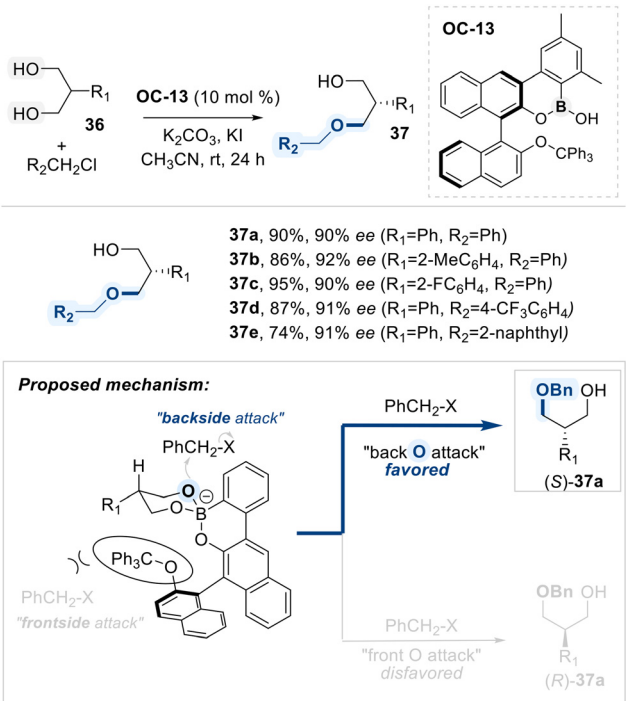
a pendant *N*,*N*-dimethylamino group for the regioselective benzoylation of 1,2-diols (Scheme 21).[85] The catalyst engages in bifunctional activation, wherein the benzoxaborole moiety selectively forms a tetrahedral boronate intermediate with *cis*-1,2-diols due to their favorable geometry for cyclic ester formation, while



Scheme 21 Selective *cis*-1,2-diol modification using the benzoxaborole catalyst embedded with Lewis base.

the pendant *N*,*N*-dimethylamino group simultaneously performs nucleophilic activation of the benzoyl chloride, enabling an intramolecular acyl transfer to the coordinated diol. This cooperative mechanism not only enhances catalytic efficiency but also confers high regioselectivity, favoring monobenzoylation at the less hindered primary alcohol of the terminal 1,2-diol substrate.

Hall and co-workers described a method for the desymmetrization of *meso*-1,3-diols *via* an enantioselective alkylation, employing a chiral hemiboronic acid catalyst (**OC-13**) (Scheme 22).[86] A boroxarophenanthrene core from a BINOL-



Scheme 22 Enantioselective alkylation of 1,3-diols with a chiral hemiboronic acid catalyst.

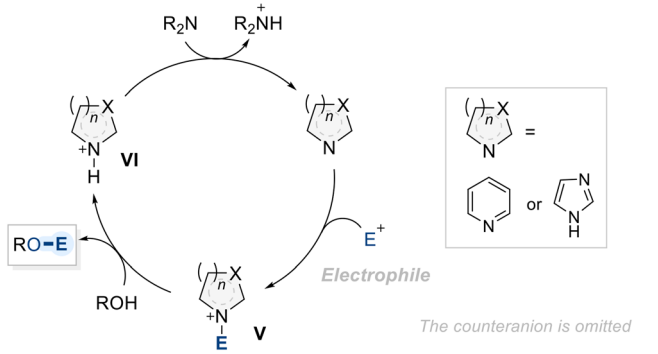
derived backbone, along with steric elements such as a trityl ether and two methyl groups, confers the catalyst (**OC-13**) for having conformational-biased environment when reactants approach to them. Complexation of **OC-13** catalyst with the 1,3-diol forms a six-membered borinate ester, positioning the two hydroxyl groups in distinct spatial orientations. Selective alkylation occurs at the less hindered hydroxyl group, located away from the bulky trityl substituent, furnishing the enantioriched alkylated product.

3. Nitrogen-based organocatalytic systems

In recent years, nitrogen-containing organocatalysts have played a crucial role in modern organic synthesis, offering versatile reactivity, favorable electronic properties, and enhanced catalytic efficiency.[87] In the context of selective diol functionalization, various types of nitrogen-containing catalytic systems have been employed, including N-heterocycles, diamines, peptides and N-heterocyclic carbenes (NHCs), and others, each operating through distinct mechanistic pathways. The continued application of these catalysts to a broader range of diol substrates has enabled value-added structural modifications with high selectivity.[88]

3.1. N-Heterocycle catalysis

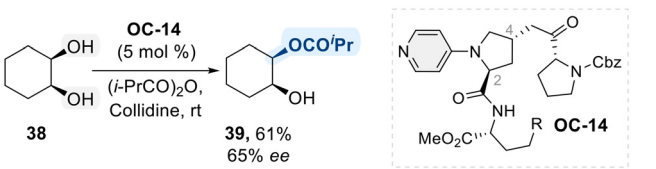
Aromatic N-heterocycles are widely recognized as efficient catalysts for the functionalization of alcohols.[89] The mechanism underlying their catalytic activity in hydroxyl group functionalization is well understood (Scheme 23).[90] It begins with the activation of the N-heterocycle by an electrophilic species, leading to the formation of a key ammonium intermediate (**V**), which acts as a new electrophile, for the subsequent nucleophilic attack by the alcohol. This nucleophilic attack leads to the functionalization of the alcohol, forming a desired product with a second ammonium intermediate (**VI**). Consequently, intermediate **VI** undergoes deprotonation by an external base, regenerating the catalyst and completing the catalytic cycle.[91]



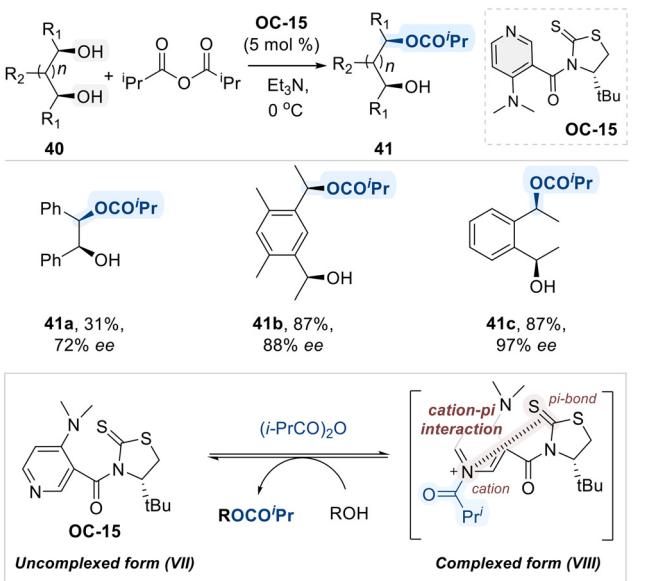
Scheme 23 General mechanism of N-heteroycle-catalyzed alcohol functionalization.

With these mechanistic features in hand, researchers have explored the potential of N-heterocycles in selective catalysis for diol functionalization. Notably, chiral 4-amino pyridine structures have been widely considered as an asymmetric catalyst in the context of enantioselective acylation of diol substrates. In 2003, Kawabata *et al.* introduced a chiral 4-pyrrolidinopyridine catalyst (**OC-14**), featuring two distinct functional side chains at C2 and C4 of the pyrrolidine ring, to perform enantioselective isopropanoylation of *meso*-1,2-cyclohexane diol (Scheme 24).[92] As outlined in the general mechanism (Scheme 23), forming a chiral isopropyl acyl-pyridinium intermediate was identified as a key step in achieving enantioselectivity. Despite moderate yield (61%) and enantioselectivity (65% ee), the successful sterochemical induction achieved by introducing chiral substituents onto the N-heterocycle offers pioneering insights and establishes a foundation for advancing chiral pyridine-based catalysts in the selective functionalization of diols.

Building on these insights, Yamada and co-workers designed a novel class of chiral 4-(dimethylamino)pyridine (DMAP) catalyst (**OC-15**) for the asymmetric isopropanoylation of *meso*-diols (Scheme 25).[93] A distinctive feature of this catalyst is its unique conformation switch system, which is based



Scheme 24 Desymmetrization of *meso*-1,2-cyclohexane diol using organo-catalyst (**OC-14**).



Scheme 25 Enantioselective isopropanoylation of *meso*-diols using chiral-DMAP catalyst (**OC-15**).

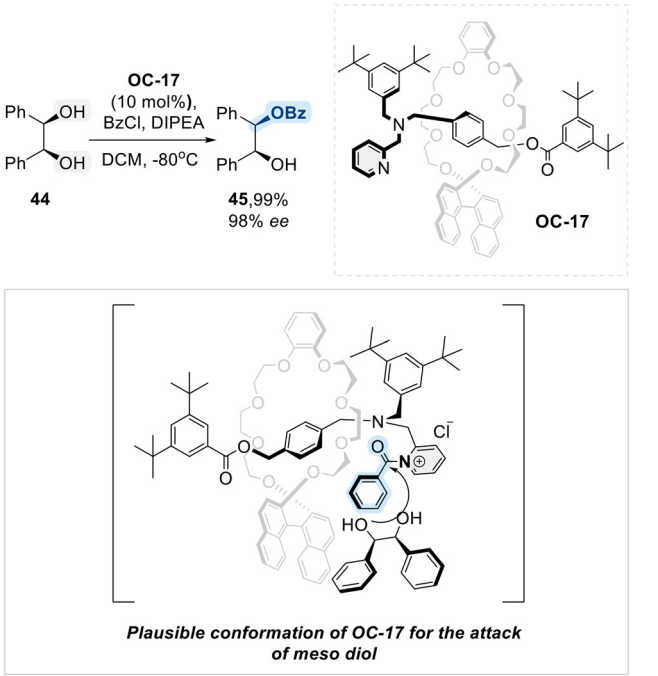
on the interconversion between the uncomplexed form (**VII**) and the self-complexed form (**VIII**), induced by *N*-acylation. The proposed mechanistic model suggests that self-complexation, driven by an intramolecular cation–π interaction between the pyridinium ring and a thiocarbonyl group, creates a chiral environment around the active site, which is used for discriminating symmetric diols.

Furthermore, a study by Mandai *et al.* made a significant contribution to the chiral 4-amino pyridine catalytic system by introducing a 1,1′-binaphthyl containing two 3° hydroxyl units (**OC-16**) (Scheme 26).[94] The study highlighted that the two 3° hydroxyl units were crucial for achieving high catalytic activity and enantioselectivity in desymmetrization of 1,3-diols, though their specific role in the reaction mechanism has not yet elucidated.

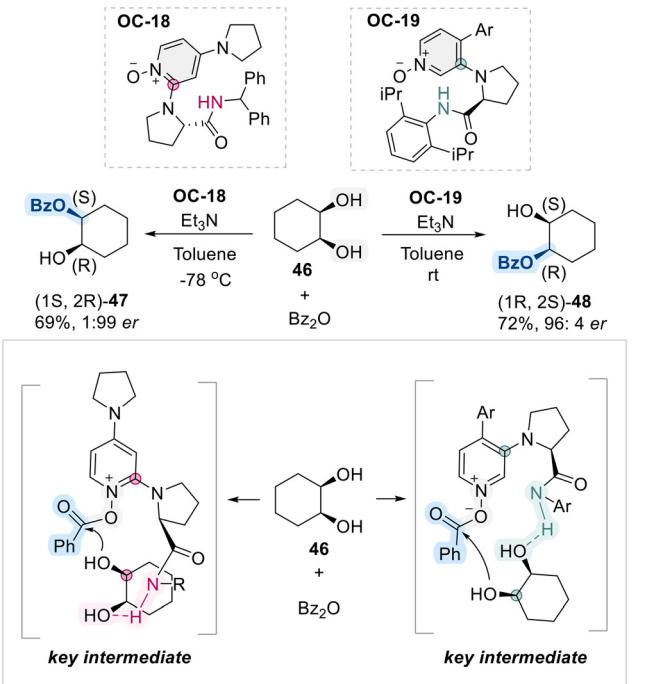
In 2018, Takata and his colleagues disclosed a novel rotaxane-type catalyst (**OC-17**) to undergo *O*-benzoylative asymmetric desymmetrization of *meso*-1,2-diol (Scheme 27).[95] The rotaxane-type catalyst **OC-17** exhibited a cooperative effect between its crown ether wheel bearing (*R*)-binaphthyl group (back structure of **OC-17**, Scheme 27) and its axle containing *N*-pyridylmethyl substituent (front structure of **OC-17**, Scheme 27). As described in Scheme 23, the reaction initiated with the formation of an *N*-acylpyridinium intermediate, followed by the enantioselective approach of the diol substrate. The proximity effect, driven by the localization of the chiral wheel around the *N*-benzoyl pyridinium intermediate, facilitated this selectivity.

As a further contribution, Lian *et al.* recently developed a chiral C2-substituted aminopyridine-*N*-oxide (**OC-18**) and a chiral C3-substituted arylpyridine-*N*-oxide (**OC-19**), enabling enantio-divergent benzoyl transfer in the desymmetrization of *meso*-1,2-diols (Scheme 28).[96] Depending on the choice of chiral catalyst (**OC-18** or **OC-19**), benzoylation of *meso*-diol **46** proceeded selectively to afford either enantiomer, **47** or **48**. DFT calculations further elucidated the reaction mechanism, revealing that it proceeded through a bifunctional activation, where the benzoyl-activated *N*-oxide and the proton of the amides played pivotal roles in both catalytic reactivity and enantio-control.

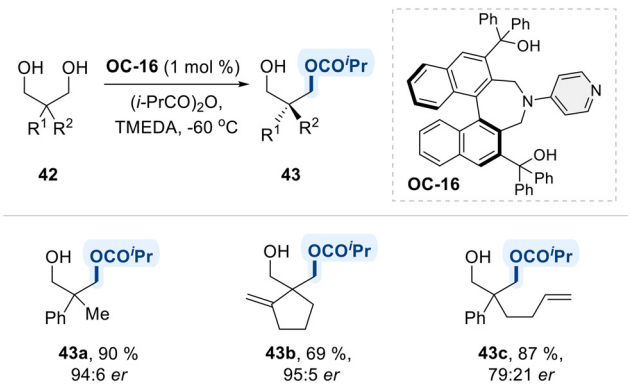
Selective functionalization has been achieved using not only pyridine-based organocatalysts but also imidazole-derived



Scheme 27 Rotaxane-based catalyst (**OC-17**) for asymmetric regioselective benzoylation of *meso*-1,2-diol.



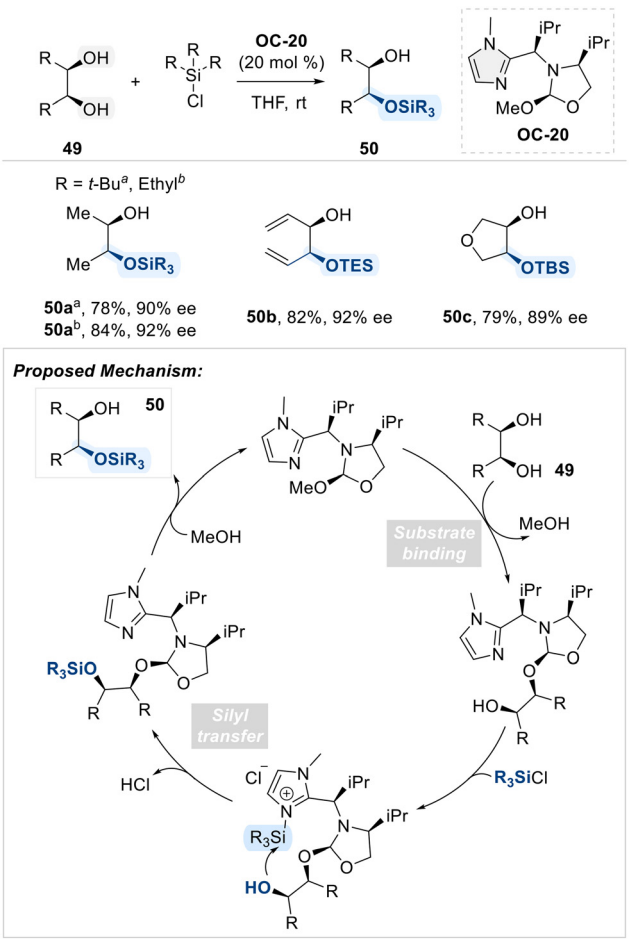
Scheme 28 Desymmetrization of *meso*-diols catalyzed by chiral pyridine-*N*-oxide (**OC-18** and **OC-19**).



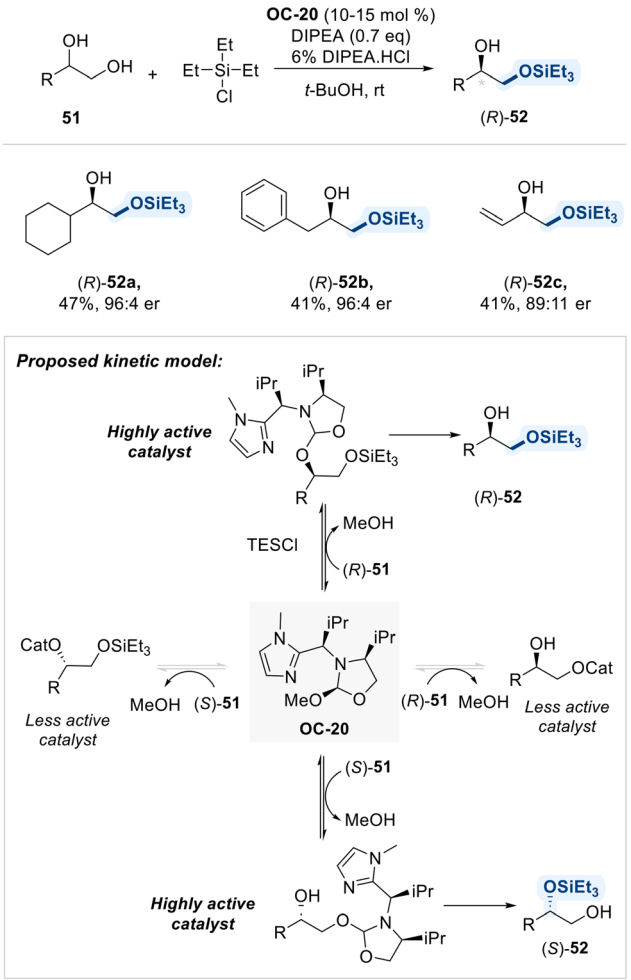
Scheme 26 Enantioselective isopropylation of 1,3-diols *via* chiral-DMAP catalyst (**OC-16**).

catalysts. In the context of imidazole-based selective organocatalysis, Tan and coworkers demonstrated that an imidazole bearing a chiral substituent at the C2-position (**OC-20**) effectively catalyzed the enantioselective silylation of *meso*-1,2-diols (Scheme 29).[97] This catalyst exhibits bifunctional properties: a 2-methoxy oxazolidine moiety functions as the diol-binding site, while the imidazole group serves as the silyl-binding site. This arrangement enables efficient and selective transfer of silyl groups to diols in an enantioselective manner.

In the following year, the same group presents a regiodivergent kinetic resolution of terminal 1,2-diols through asymmetric silyl transfer, utilizing the same chiral catalyst **OC-20** (Scheme 30).[98] This strategy enables selective silylation of either the primary or secondary hydroxyl group in each enantiomer, thereby achieving both chemical differentiation and enantiomeric resolution. The key to this transformation lies in the reversible covalent bonding between the catalyst and substrate, which plays a pivotal role in directing regio- and enantioselectivity. Initially, the primary alcohol reacts more rapidly due to its higher intrinsic reactivity, leading to preferential formation of the silylated product from one enantiomer. As the reaction proceeds, acid byproducts promote dynamic exchange between catalyst and substrate, which accelerates the silylation of the less reactive enantiomer. By fine-tuning the reaction parameters, such as the rate of silyl chloride addition and reaction temperature, the authors achieved high enantioselectivity and synthetically useful yields. This regiodivergent resolution offers an efficient approach to access enantiopure, mono-protected diols.



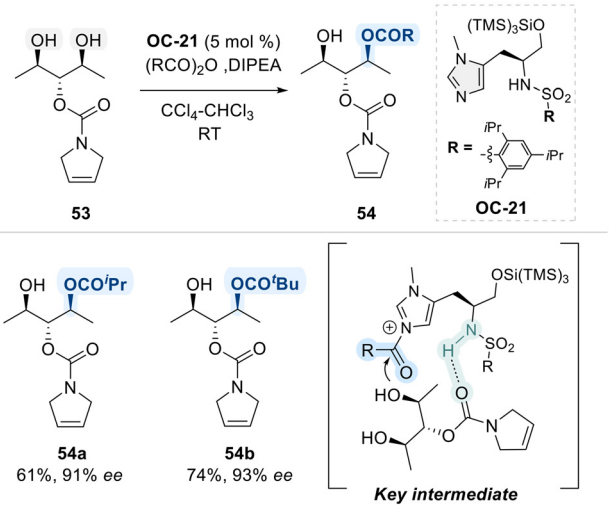
Scheme 29 Enantioselective silylation of *meso*-1,2-diols employing bifunctional imidazole catalyst (**OC-20**).



Scheme 30 Regiodivergent kinetic resolution of terminal 1,2-diols.

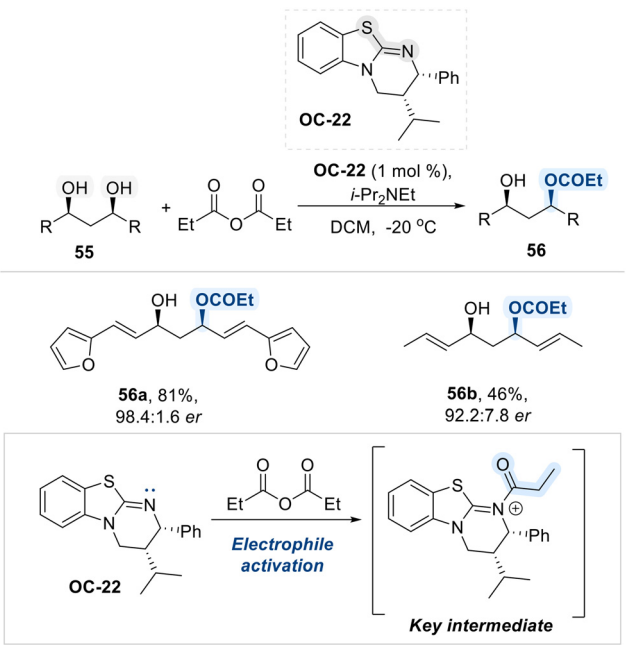
Subsequently, the Ishihara group developed a novel bifunctional organocatalyst (**OC-21**), which integrates a chiral sulfonamide moiety as a hydrogen-bond donor and an imidazole unit as an electrophilic acceptor (Scheme 31).[99] Leveraging its potent hydrogen-bond donating capability, catalyst **OC-21** effectively promoted the enantioselective acylation of *meso*-1,3-diols bearing a hydrogen-bond-accepting 3-pyrroline-1-carbonyl (Pyroc) group. The established hydrogen-bond network between sulfonamide and Pyroc group creates a chiral environment that facilitates acyl transfer from the acyl ammonium intermediate to the diol substrate, achieving enantioselectivity.

Moreover, like pyridine and imidazole, isothioureas are widely recognized as highly effective nucleophilic organocatalysts, owing to the presence of an electron-rich nitrogen



Scheme 31 Enantioselective acylation of *meso*-1,3-diols using **OC-21**.

atom adjacent to a thiocarbonyl group. This structural feature endows isothioureas with strong nucleophilic character, enabling them to efficiently activate electrophilic centers, particularly carbonyl-containing compounds. Considering this intrinsic nucleophilic reactivity of isothioureas, Bressy group developed a highly enantioselective method for the desymmetrization of acyclic *meso*-1,3-diols *via* acylation, utilizing a chiral isothiourea-based organocatalyst (**OC-22**) (Scheme 32).[100] Mechanistically, the reaction proceeds *via* a nucleophilic attack by the electron-rich nitrogen atom of the catalyst (**OC-22**) on the anhydride electrophile, generating a chiral *N*-acyl isothiouronium intermediate. This intermediate

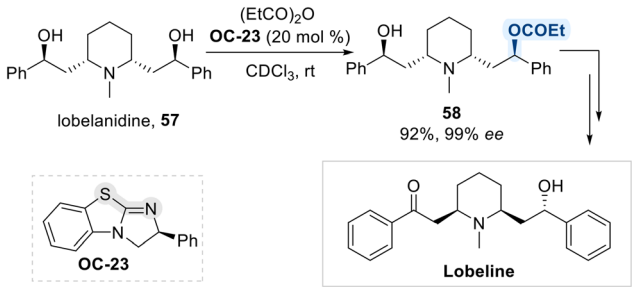


Scheme 32 Isothiourea catalyzed desymmetrization of *meso* 1,3-diols.

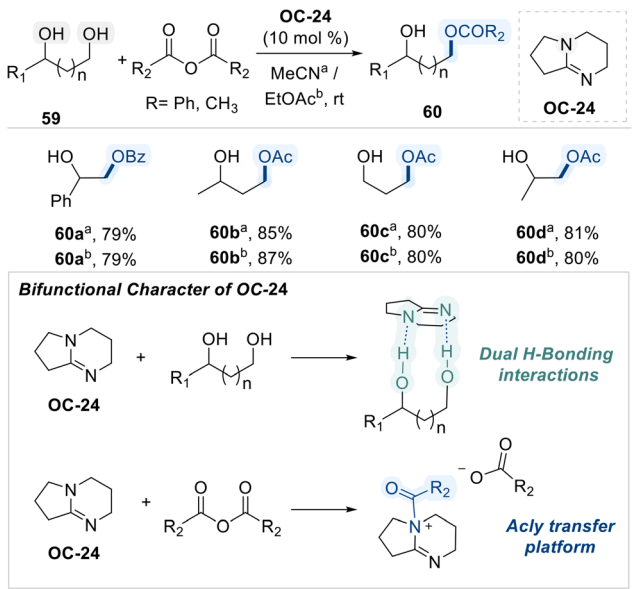
acts as an efficient acyl transfer agent, enabling the enantioselective acylation of the *meso*-diol with high stereocontrol.

Expanding upon this strategy, Birman *et al.* employed an isothiourea-based organocatalyst (**OC-23**) for the enantio-selective acylation of lobelanidine (**57**), enabling the asymmetric synthesis of lobeline under ambient conditions using propionic anhydride as the acyl donor (Scheme 33).[101] The reaction proceeds *via* formation of a chiral *N*-isopropanoyl isothiouronium intermediate, which acts as an electrophilic acyl transfer agent, delivering the acyl group with high regio- and enantioselectivity.

Building on the nucleophilic character of N-heterocycles in facilitating selective diol functionalization, Ren and co-workers subsequently reported a cost-effective and highly efficient method for the regioselective acylation of diols using 1,5-diazabicyclo[4.3.0]non-5-ene (DBN, **OC-24**) as an organo-catalyst (Scheme 34).[102] The authors propose that the bifunctional character of DBN arises from its ability to simultaneously engage in dual hydrogen-bonding interactions with the diol



Scheme 33 Synthesis of lobeline *via* regioselective acylation of lobelanidine (**57**).



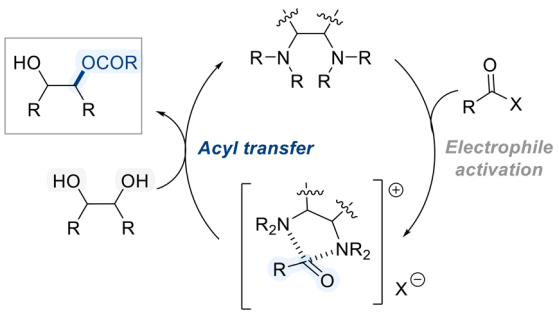
Scheme 34 DBN (**OC-24**) catalyzed regioselective acylation of diols.

substrate and promote acyl transfer through the formation of a reactive acyl–ammonium electrophilic intermediate. This dual activation mode facilitates regioselective acylation at the sterically less hindered hydroxyl group, ultimately affording the monoacylated product **60**.

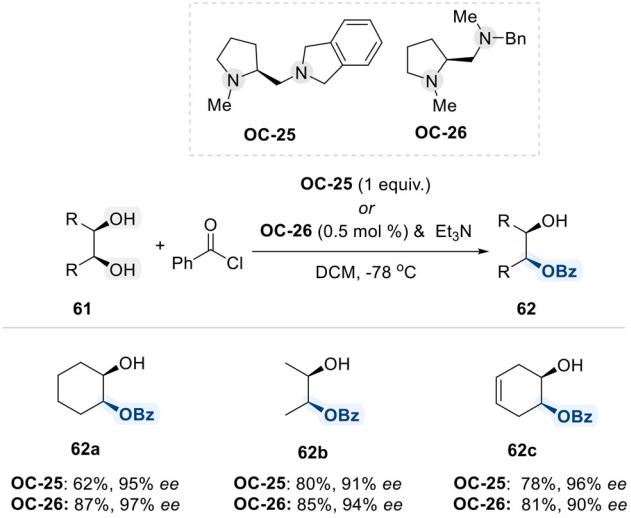
3.2. Diamine catalysis

Diamine catalytic system features two nitrogen atoms whose electron-rich character imparts strong nucleophilic and Brønsted basic properties, enabling activation of electrophilic substrates or acidic protons.[103] Leveraging their inherent nucleophilic character, diamines have been employed as effective catalysts in acyl transfer reactions. Notably, chiral ethylenediamine frameworks have attracted considerable attention as asymmetric catalysts in the enantioselective acylation of diol substrates. A plausible mechanistic pathway involves the bidentate coordination of the diamine catalyst to the carbonyl carbon of the acylating agent, thereby enhancing the electrophilicity of the acyl donor and facilitating regioselective acylation at a specific hydroxyl group of the diol substrate (Scheme 35).[104] The resulting regioselectivity is governed by the steric and electronic properties of the diamine catalyst, providing a strategic platform for the rational design of highly selective diamine-based catalytic systems for diol functionalization.

A study conducted by Oriyama and colleagues demonstrated the enantioselective benzoylation of *meso*-diols utilizing the chiral 1,2-diamine reagent **OC-25**, which was synthesized from (*S*)-proline (Scheme 36).[105] Although this method requires a stoichiometric amount (1.0 equivalent) of **OC-25**, it illustrates that diamine-based systems serve as effective platforms for the acylation of diol substrates, and that high enatioselectivity can be achieved through the rational design of the diamine catalyst. To enhance economic feasibility, the same research group subsequently developed a structurally optimized chiral 1,2-diamine catalyst (**OC-26**), which exhibited significantly enhanced catalytic efficiency in the enantioselective benzoylation reaction when employed alongside triethylamine as a base.[106] Remarkably, utilizing only 0.5 mol% of **OC-26** resulted in benzoylation of *meso*-diols with selectivity comparable to the stoichiometric **OC-25** system, while simultaneously increasing reaction efficiency and sustainability through substantial catalyst load reduction.



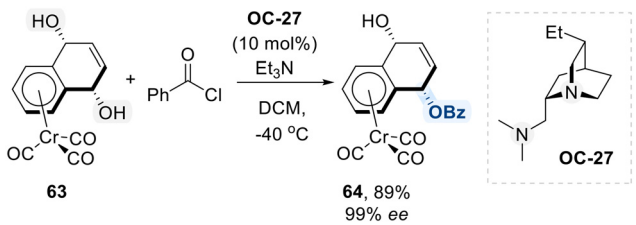
Scheme 35 General mechanism of 1,2-diamine-catalyzed regioselective acylation of diols.



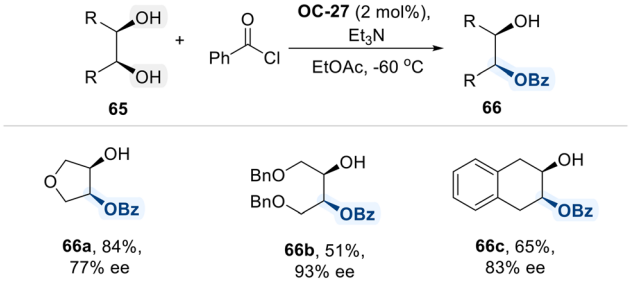
Scheme 36 Enantioselective benzoylation of *meso*-diol using chiral diamines (**OC-25** and **OC-26**).

Next, Kundig group explored their application in the desymmetrization of *meso*-1,4-diol complexes derived from [Cr(CO)$_3$(naphthoquinone)] while preserving metal coordination (Scheme 37).[107] This transformation was achieved through enantioselective monobenzoylation, facilitated by a new quinidine-derived chiral diamine catalyst (**OC-27**). As illustrated in the proposed mechanism in Scheme 35, **OC-27** interacts with the carbonyl carbon of benzoyl chloride, increasing its electrophilicity and enabling transfer of the benzoyl group to *meso*-1,4-diol complexes in an enantioselective manner. This strategy enables access to highly enantioenriched planar chiral chromium complexes **64**, which serve as valuable chiral building blocks for highly diastereoselective transformations, such as chromium-mediated dearomatization reactions.[108]

To further explore the applicability of the chiral diamine catalyst **OC-27**, the same group extended its use to commonly encountered *meso*-1,2-diols (Scheme 38).[109] Employing **OC-27**, they successfully achieved the desymmetrization of various cyclic and acyclic *meso*-diols through benzoylation, obtaining monobenzoylated products with good to excellent yields and high enantioselectivities. This group study underscored the versatility of quinidine-derived organocatalyst (**OC-27**) in enantioselective benzoylation of *meso* diols.



Scheme 37 Desymmetrization of *meso*-1,4-diol chromium complex.



Scheme 38 Enantioselective benzoylation of *meso*-1,2-diols using cinchona alkaloid-derived catalyst (**OC-27**).

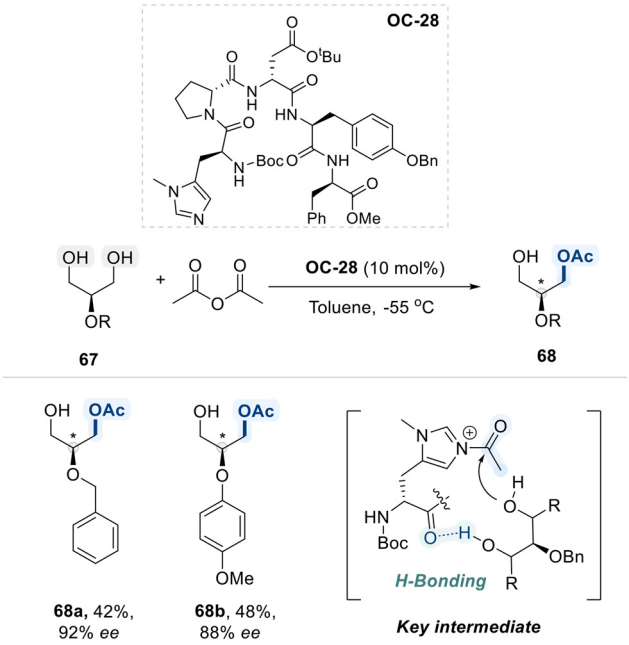
3.3. Peptide catalysis

Peptides have emerged as powerful catalysts in regioselective transformation of organic compounds due to their inherent structural flexibility, precise molecular recognition, and ability to engage in non-covalent interactions, such as hydrogen bonding and electrostatic forces.[110] In the context of selective functionalization of diols, these properties enable peptide-based catalysts to distinguish between two hydroxyl groups, thereby facilitating regio- and enantioselective transformations, including acylation and silylation reactions.

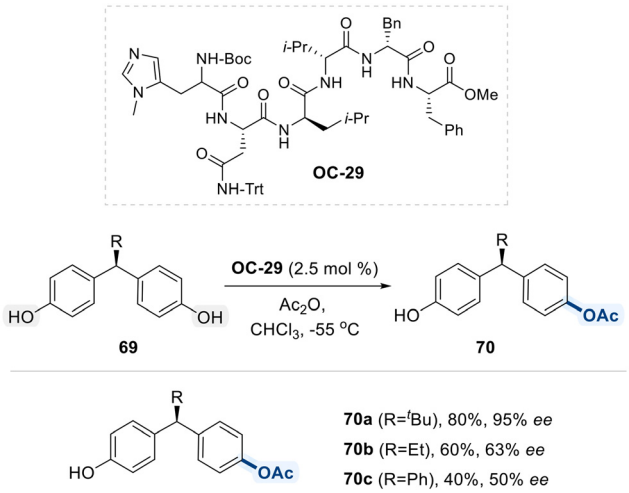
Particularly, short peptide sequences containing proline, histidine, or other nucleophilic residues have been employed to catalyze diol desymmetrization, yielding regioselectively modified products with high enantiocontrol. Their catalytic activity primarily stems from functional groups, bearing amines, carboxylates, and hydroxyls, which participate in hydrogen bonding, Brønsted acid–base interactions, and steric control.[111] These interactions play a crucial role in stabilizing key transition states and reactive intermediates, thereby minimizing activation energy barriers and precisely directing selective transformations at a single hydroxyl site. Such cooperative effects not only enhance reaction efficiency but also expand the scope of peptide catalysis in asymmetric diol transformation.

In 2005, Lewis *et al.* disclosed desymmetrizative acylation of *meso*-glycerol derivatives **67**, employing a chiral histidine-derived peptide-based organocatalyst (**OC-28**) (Scheme 39).[112] The catalyst combines an imidazole moiety, which activates the acyl group, with a peptide chain that accepts a hydrogen bond from one hydroxyl group of the diol substrate. This interaction spatially orients the second hydroxyl group, guiding highly enantioselective acylation. Collectively, this approach enables access to enantioenriched products with excellent selectivity.

Building on their earlier work, the same research group developed **OC-29**, a synthetic, miniaturized peptide-based organocatalyst that mimics enzyme function, for the desymmetrization of sterically and structurally challenging remote *meso*-diols **69** (Scheme 40).[113] This transformation proceeds *via* an enantioselective desymmetrizing acylation reaction. Although the precise mode of asymmetric induction remains ambiguous, the authors propose that undefined, yet functionally significant, non-covalent interactions between the catalyst and substrate contribute to the observed enantioselectivity. Notably, reducing the steric bulk of the alkyl substituents on diol substrate **69** led to a marked decrease in enantioselectivity, underscoring the reaction's sensitivity to substrate sterics.

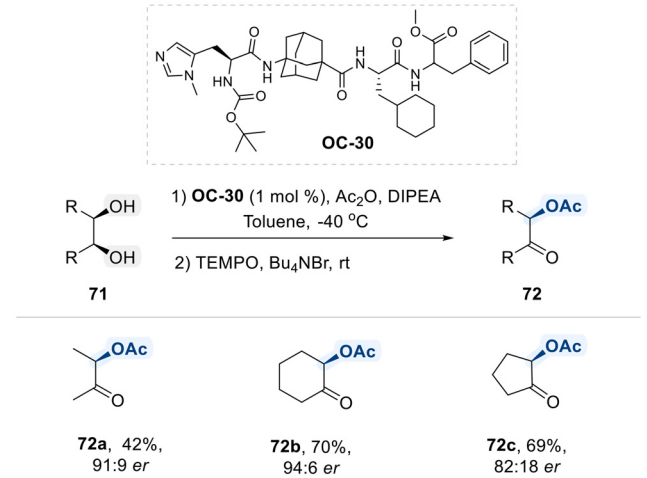


Scheme 39 Selective acylation of glycerol derivatives.



Scheme 40 Desymmetrization of remote *meso*-diol *via* enantioselective acylation.

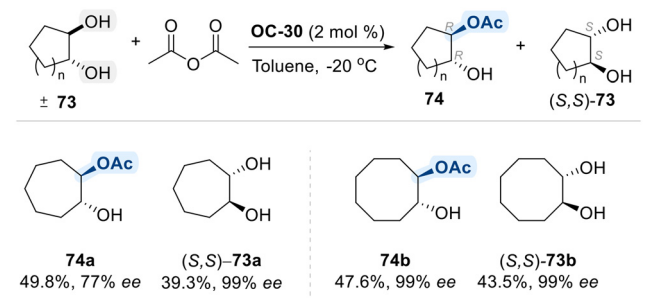
Schreiner *et al.* have introduced a novel approach for desymmetrizing *meso*-diols through enantioselective acylation, coupled with an *in situ* oxidation step to protect the valuable product from racemization (Scheme 41).[114] This strategy employs a highly lipophilic, histidine-derived peptide catalyst (**OC-30**), incorporating an adamantane-based amino acid



Scheme 41 Enantioselective acylation of *meso*-1,2-diols using **OC-30**.

motif. Their study demonstrated that the lipophilic peptide catalyst **OC-30** effectively facilitates the desymmetrization of *vicinal meso*-diols *via* enatioselective acyl transfer from a chiral imidazolium intermediate. Furthermore, the subsequent TEMPO-mediated oxidation of the monoacylated product provided the corresponding α-acetoxy ketones in high isolated yields, with no loss of enantioselectivity.

Building on their earlier work, the same group further advanced the field by reporting an enantioselective kinetic resolution of *trans*-cycloalkane-1,2-diols through a monoacylation process, employing their previously developed peptide-based organocatalyst **OC-30** (Scheme 42).[115] The reaction proceeds *via* a selective acyl transfer from a chiral imidazolium intermediate, wherein one hydroxyl group of the diol undergoes acylation while the other engages in hydrogen bonding with the peptide backbone, an interaction essential for precise chiral recognition. Notably, when the reaction was performed in more polar solvents such as acetonitrile, dichloromethane (DCM), or trifluoromethylbenzene, both enantioselectivity and reaction rate declined significantly. These findings highlight the pivotal role of solvent polarity in maintaining the non-covalent interactions necessary for effective substrate orientation and high stereocontrol within the catalytic system.

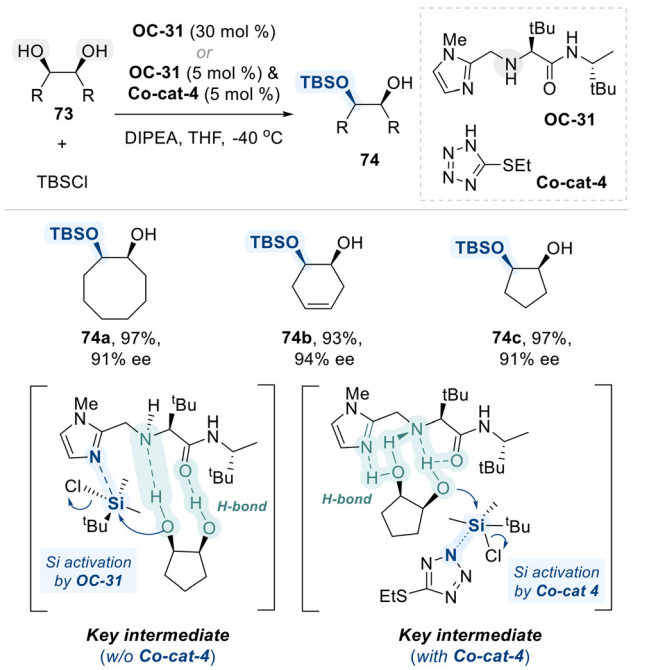


Scheme 42 Kinetic resolution of *trans*-cycloalkane-1,2-diols employing **OC-30**.

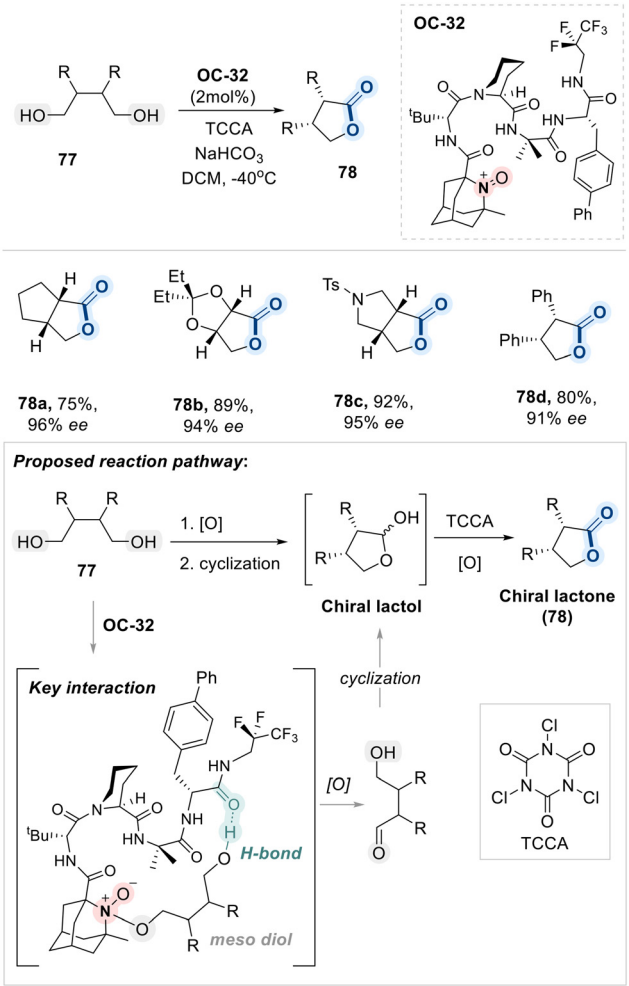
Subsequently, the Snapper group designed a simple, amino-acid-based small molecule as a chiral organocatalyst (**OC-31**) for the enantioselective silylation of *meso*-diols (Scheme 43).[116,117] Structurally, **OC-31** incorporates a Lewis basic imidazole group, which enhances the electrophilicity of the silyl halide reagent, along with a chiral amino acid moiety that engages in hydrogen bonding interactions with the diol substrate. These interactions facilitate the selective activation of one hydroxyl group, thereby enabling enantioselective silylation. In their initial investigation of *meso*-diol desymmetrization *via* silyl group transfer, the reaction required a high catalyst loading (30 mol%) and prolonged reaction times of several days.[116] To enhance the efficiency of this catalytic system, the authors utilzed an achiral co-catalyst (**Co-cat-4**) as a nucleophilic promotor alongside a chiral catalyst (**OC-31**) as Brønsted base.[117] This dual-catalyst system effectively accelerated the reaction, enabling completion within one hour while delivering the desired products in high yields and enantiomeric ratios with a reduced catalyst loading of just 5 mol% catalyst (**OC-31**).

A landmark contribution from the Miller group introduced a pioneering strategy for the oxidative desymmetrization of *meso*-1,4-diols using a novel aminoxyl-functionalized, peptide-based organocatalyst (**OC-32**). This elegant approach enables the enantioselective synthesis of enantioenriched lactones with remarkable efficiency and selectivity (Scheme 44).[118]

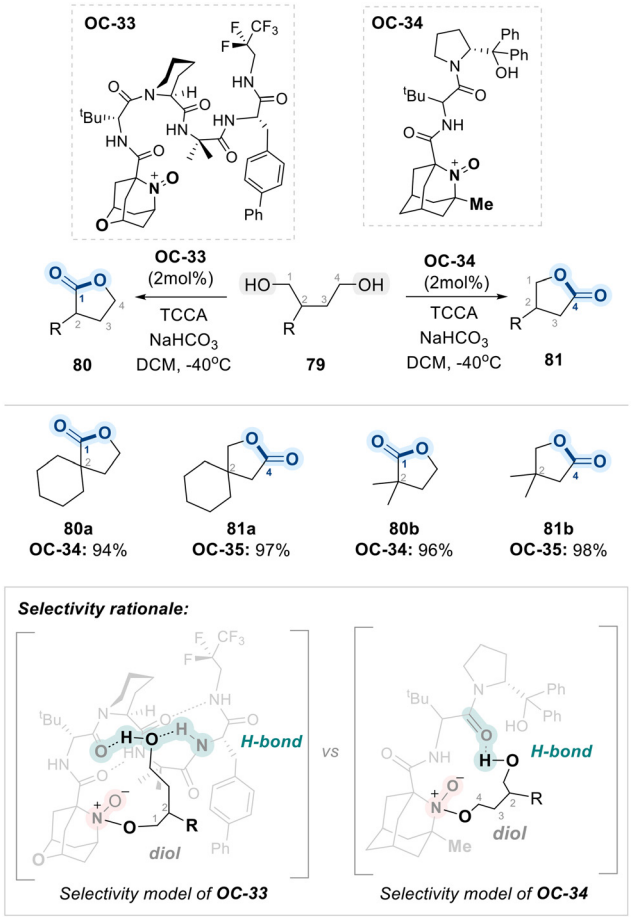
Central to this transformation is **OC-32**, a bifunctional catalyst that integrates an oxidizing oxoammonium species with a chiral peptide backbone. The oxoammonium group serves as an oxidizing agent, while the peptide framework provides a



Scheme 43 Enantioselective silylation of *meso*-1,2-diols utilizing amino-acid-based organocatalyst (**OC-31**).



Scheme 44 Oxidative desymmetrization of *meso*-1,4-diols using **OC-32**.

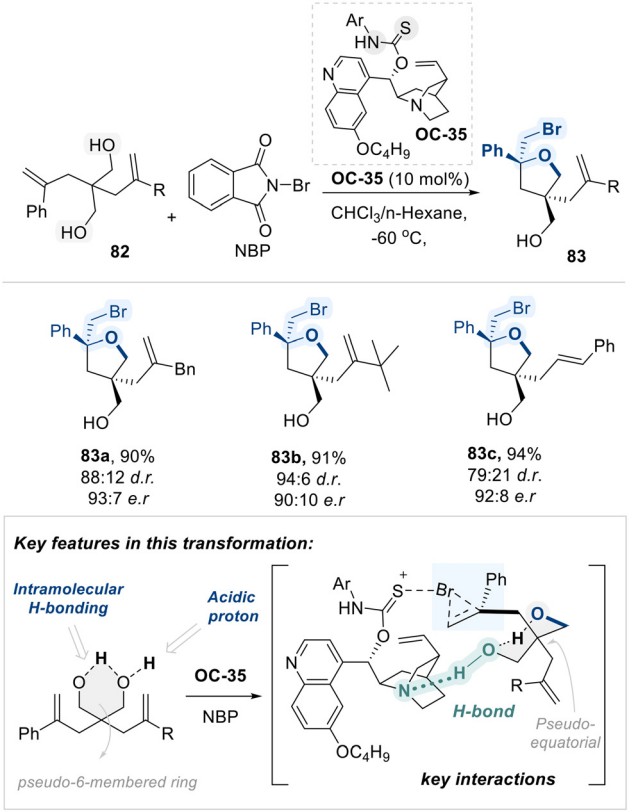


Scheme 45 Regiodivergent oxidation of unsymmetrical-1,4-enabled by **OC-33** and **OC-34**.

well-organized hydrogen-bonding network that reinforces chiral induction. Mechanistically, the reaction begins by forming a stabalized hydrogen bond of one of the hydroxyl groups of *meso* diol with the peptide backbone, anchoring the substrate within a chiral environment followed by the site-selective oxidation of free hydroxyl group of *meso*-diol substrate, generating a transient aldehyde intermediate. Following initial oxidation, intramolecular cyclization occurs *via* nucleophilic attack of the unoxidized hydroxyl group on the newly formed aldehyde, resulting in the formation of a chiral lactol. This intermediate is then subjected to a second oxidation step, typically mediated by trichloroisocyanuric acid (TCCA), to furnish the corresponding enantioenriched lactone product.

Recently, the same research group reported a regiodivergent oxidation of unsymmetrical diols (**79**) using structurally tailored, aminoxyl-containing peptide-based organocatalysts (**OC-33** and **OC-34**) (Scheme 45).[119] This approach enabled catalyst-controlled selective oxidation of either the less hindered or the more hindered hydroxyl group with high levels of regioselectivity. According to their findings, **OC-34** favors oxidation at the less hindered hydroxyl group. This preference arises because a nearby methyl group at the aminoxyl-core in the catalyst (**OC-34**) structure sterically blocks access to the more hindered hydroxyl group, making the less hindered site more accessible for oxidation. In contrast, **OC-33** features a bulkier, more sterically crowded peptide core. This design encourages binding of the less hindered hydroxyl group within a confined "pocket" of the peptide, thereby positioning the more hindered hydroxyl group near the reactive oxoammonium center. As a result, oxidation occurs preferentially at the more hindered site. As outlined in Scheme 45, initial oxidation leads to the formation of a chiral lactol *via* intramolecular cyclization, which undergoes further oxidation with TCCA to afford the final chiral lactone products.

Inspired by the participation of the peptide's carbonyl group in hydrogen bonding and secondary interactions, the Yeung group utilized a chiral amino-thiocarbamate catalyst (**OC-35**), featuring a thiocarbamate moiety analogous to the amide functional group, to promote an intriguing bromocyclization of diolefinic diols (**82**) with high diastereo- and enantioselectivity (Scheme 46).[120] The selectivity observed in this transformation is governed by a combination of structural fea-



Scheme 46 Amino thiocarbamate (**OC-35**)-catalyzed bromocyclization of diolefinic diols.

tures of the 1,3-diol substrate and noncovalent interactions induced by the catalyst. Specifically, an internal hydrogen-bonding network within the 1,3-diol enforces a pseudo-chair conformation resembling a six-membered ring. This conformation is further stabilized by a bulky substituent adopting a pseudo-equatorial orientation, thereby minimizing steric repulsion.

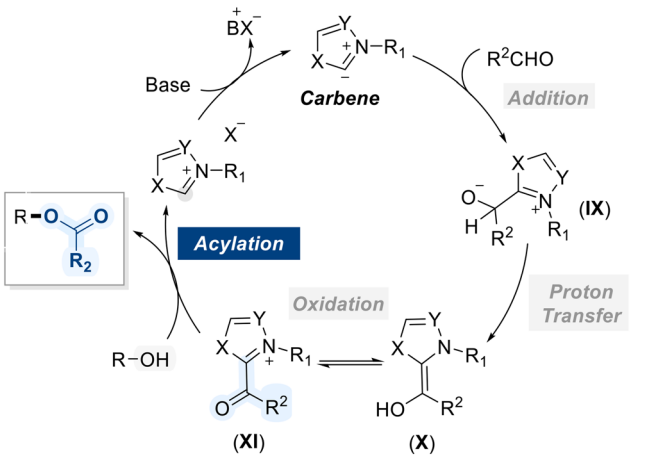
Concurrently, the amino-thiocarbamate catalyst (**OC-35**) forms a bifunctional catalytic pocket. First, the quinuclidine moiety acts as a hydrogen bond acceptor, interacting with the acidic proton of the 1,3-diol. Second, it serves as a bromine transfer platform: the catalyst abstracts bromine from *N*-bromophthalimide (NBP) and delivers it to the alkene substrate. This controlled delivery imposes a geometrical constraint that promotes selective bromonium ion formation. Subsequent intramolecular nucleophilic attack by the free hydroxyl group of the 1,3-diol onto the bromonium intermediate affords the cyclic ether product with high diastereo- and stereoselectivity.

3.4. N-Heterocyclic carbenes (NHCs) catalysis

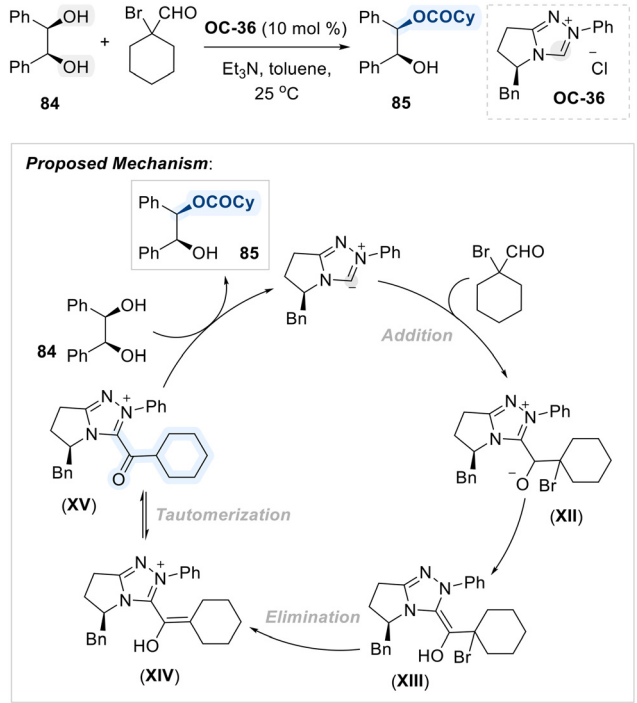
N-Heterocyclic carbenes (NHCs) represent a distinct class of stable carbenes, characterized by a divalent carbon atom embedded within a nitrogen-containing heterocyclic ring.[121] Unlike conventional carbenes, which are typically highly reactive and short-lived, NHCs exhibit remarkable stability due to electron donation from adjacent nitrogen atoms and steric protection provided by the ring system. Owing to their strong electron-donating properties, NHCs play a pivotal role in catalyzing the acylation of alcohols by facilitating the activation of aldehydes as acyl anion equivalents. Mechanistically, the reaction commences with the generation of an NHC carbene from the deprotonation of its corresponding azolium salt using base (Scheme 47).[122] The carbene, functioning as a strong nucleophile, attacks the electrophilic carbonyl carbon of the aldehyde to generate a tetrahedral intermediate (**IX**), which undergoes proton transfer to yield the corresponding enaminol (**X**). This is followed by an internal redox process that generates the NHC–acyl intermediate (**XI**), which exhibits enhanced electrophilicity at the carbonyl center. This activation facilitates nucleophilic attack by the alcohol, leading to the formation of the ester product while simultaneously regenerating the NHC catalyst.

Considering these mechanistic insights, the Rovis group investigated the enantioselective acylation of *meso*-hydrobenzoin **84** using a chiral nucleophilic carbene catalyst (**OC-36**) and α-bromo-cyclohexane carboxaldehyde as an acylating source (Scheme 48).[123] The catalytic cycle begins with the nucleophilic attack of the carbene on the aldehyde, followed by hydrogen transfer to generate an α-bromo enol intermediate (**XIII**) which undergoes leaving group elimination to form an enol intermediate (**XIV**), which tautomerizes to yield an active acylating species (**XV**) for the selective acylation of the diol. This approach offers a unique and efficient strategy for the enantioselective functionalization of diols, thereby expanding the scope of chiral carbene-catalyzed transformations in asymmetric synthesis.

In the following year, Scheidt *et al.* developed the enantioselective monoacylation of *cis*-cyclohexane-1,2-diol with cinnamaldehyde using a chiral triazolium salt (**OC-37**) as an N-heterocyclic carbene (NHC) catalyst (Scheme 49).[124] The



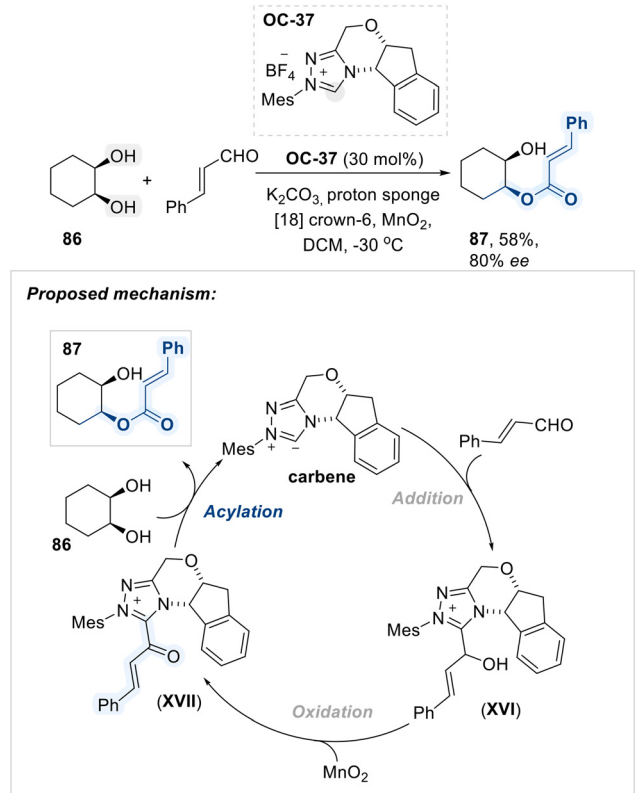
Scheme 47 General mechanism of NHC-catalyzed acylation of alcohols.



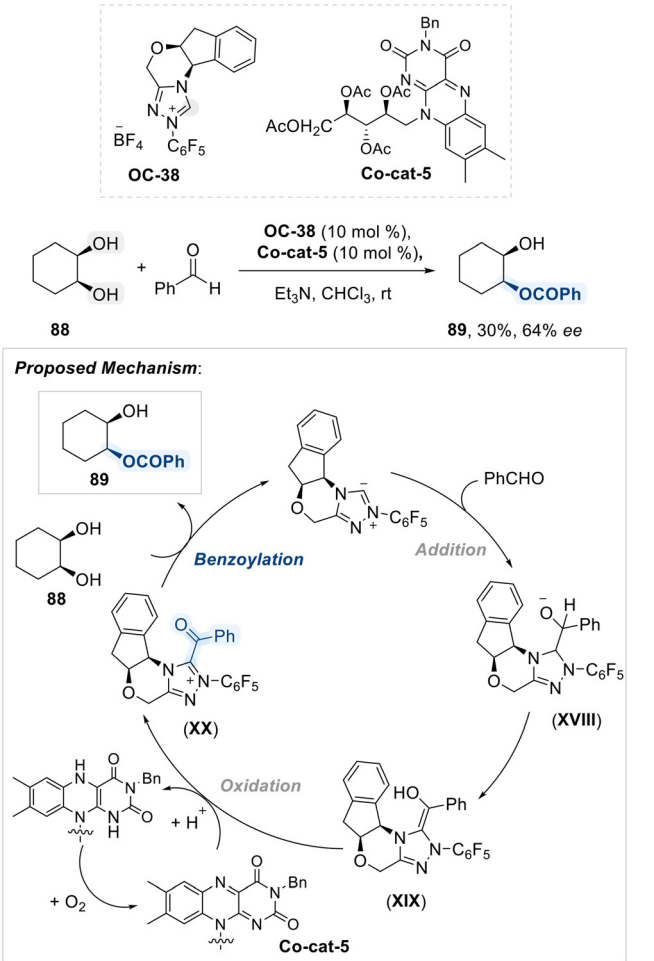
Scheme 48 Enantioselective acylation of *meso*-hydrobenzoin using chiral carbene catalyst (**OC-36**).

transformation initiates with NHC-catalyzed activation of cinnamaldehyde, yielding addition intermediate **XVI**, which undergoes oxidation to furnish the key α,β-unsaturated carbonyl–NHC species **XVII**. This chiral acyl transfer platform subsequently facilitates the enantioselective acylation of diol substrates.

Subsequent study by Iwahana and his team disclosed a combination of a chiral N-heterocyclic carbene (**OC-38**) and a redox-active flavin (**Co-cat-5**) as an effective system for promoting the enantioselective benzoylation of *cis*-cyclohexane-1,2-diol with benzaldehyde under ambient air conditions (Scheme 50).[125] The reaction mechanism involves the generation of enol intermediate (**XIX**) by the nucleophilic addition of carbene to benzaldehyde. The riboflavin derivative (**Co-cat-5**) serves as the oxidant, facilitating the oxidation of the enol intermediate (**XIX**) to an NHC-acyl intermediate (**XX**), thereby directing enantioselective benzoylation of diol. This approach provides a straightforward and effective method for asymmetric functionalization under mild, air-tolerant conditions.



Scheme 49 Asymmetric monoacylation of *cis*-cyclohexane-1,2-diol using **OC-37**.



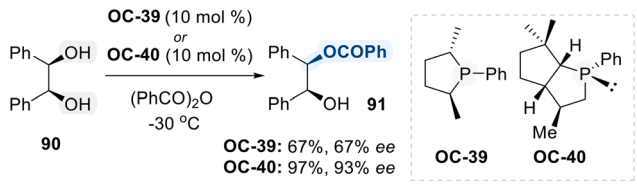
Scheme 50 Desymmetrization of 1,2-diol using chiral N-heterocyclic carbene (**OC-38**) and a redox-active flavin (**Co-cat-5**).

4. Phosphorus-based organocatalytic systems

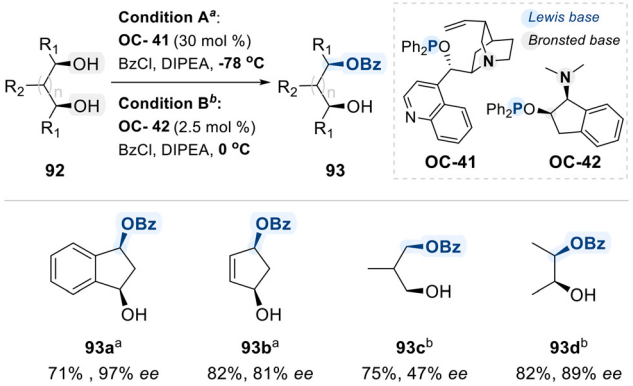
Phosphorus-based organocatalysts play a crucial role in modern organic synthesis, owing to their versatile reactivity profiles that encompass nucleophilic activation, Brønsted acid catalysis, and Lewis's base interactions.[126] This intrinsic tunability renders them particularly valuable in the selective functionalization of diols. Among the commonly employed phosphorus-containing catalysts are chiral phosphines, chiral phosphoric acids (CPAs), and phosphonium salts, each leveraging distinct mechanistic pathways to promote selective transformations of diols.[127] Like chiral phosphines act as nucleophilic catalysts, enabling the activation of electrophiles for regioselective modifications of diol substrates. On the other hand, CPAs, typically derived from BINOL or SPINOL frameworks, serve as Brønsted acid catalysts, promoting transformations through hydrogen bonding and ion-pair interactions.[128] The versatility of phosphorus-based catalysts underscores their pivotal role in the development of selective diol functionalization strategies.

In this contribution, Vedejs and co-workers initially developed a chiral phosphine organocatalyst (**OC-39**) catalyzed monobenzoylation of *meso*-hydrobenzoin (**90**), achieving moderate levels of conversion and enantioselectivity (Scheme 51).[129] To improve these outcomes, the same group subsequently developed a structurally refined phosphine catalyst (**OC-40**), which exhibited markedly enhanced reactivity and enantioselectivity in the functionalization of diol (**90**).[130] It is assumed that chiral phosphines promote acylation through nucleophilic activation of the acyl donor, generating a reactive chiral *P*-acyl phosphonium intermediate. This intermediate facilitates enantioselective acyl transfer to the hydroxyl group, enabling high levels of stereocontrol during the transformation.

As a further advancement, the Fujimoto group developed a bifunctional phosphinite catalyst (**OC-41**), derived from cinchona alkaloids, which integrates a Lewis-basic phosphinite moiety with a Brønsted-basic tertiary amine to achieve the enantioselective desymmetrization of *meso*-1,2-diols *via* benzoylation (Scheme 52).[131] Despite its effectiveness, this system required over 30 mol% catalyst loading. To make it more economical, subsequently the same group introduced a more practical and readily accessible amino-phosphinite catalyst (**OC-42**), synthesized from *cis*-aminoindanol.[132] This improved catalyst enabled the enantioselective benzoylation of *meso*-1,2-



Scheme 51 Phosphines catalyzed regioselective reaction of *cis*-cyclohexane-1,2-diol.



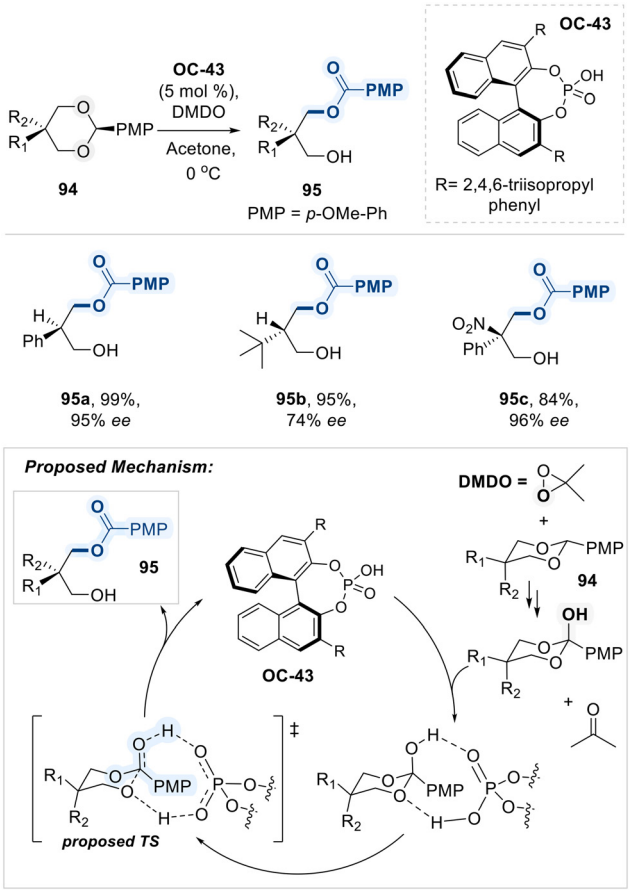
Scheme 52 Enantioselective monobenzoylation of *meso*-diols *via* phosphinite derivatives (**OC-41** or **OC-42**).

diols using substantially lower loadings (2.5 mol%). Although the detailed reaction mechanism remains unelucidated, the authors propose that benzoyl chloride activation likely proceeds through coordination to the phosphinite Lewis base.

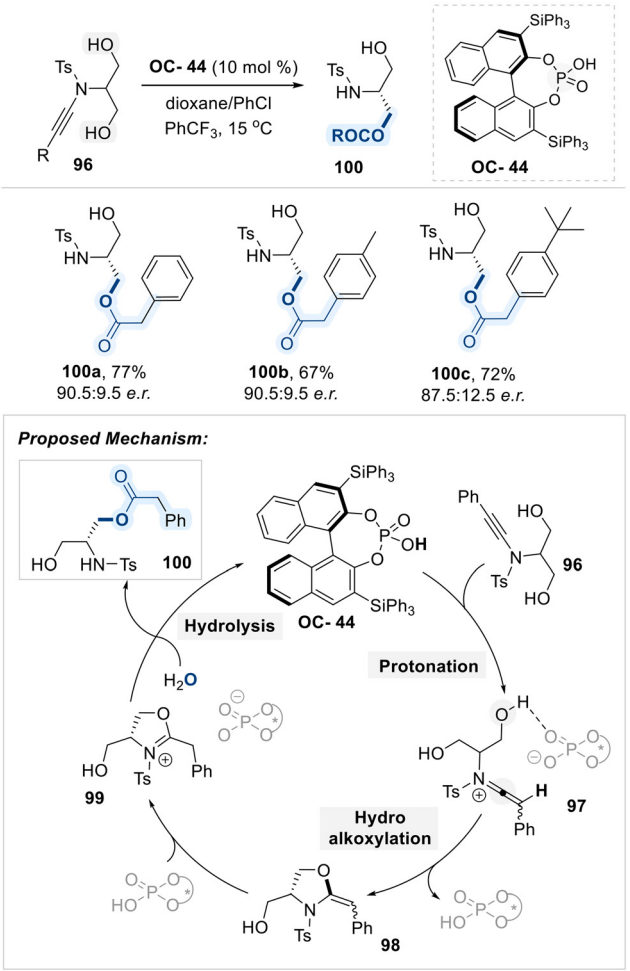
In 2014, Zheng and co-workers reported a noteworthy application of a BINOL-based chiral phosphoric acid catalyst (**OC-43**) for the highly enantioselective desymmetrization of 2-substituted 1,3-diols (Scheme 53).[133] The reaction begins with dimethyldioxirane (DMDO)-promoted oxidation of a 1,3-diol benzylidene acetal **94**, generating acetone and an *ortho*-ester intermediate. This intermediate subsequently undergoes chiral phosphoric acid (**OC-43**) mediated proton transfer reaction, delivering the final product **95** with efficient yield and selectivities. DFT calculations reveal that the oxidation of the acetal by DMDO is the rate-determining step, while the exceptional enantioselectivity arises from favorable aryl–aryl interactions between the substrate and catalyst. In subsequent studies, the authors demonstrated that this asymmetric desymmetrization strategy could be further utilized for the highly enantioselective synthesis of acyclic α-tertiary amines.[134]

Recognizing the potential of chiral phosphoric acids as Brønsted acids, Cui and co-workers developed a highly enantioselective desymmetrization of *meso*-1,3-diol bearing ynamide scaffold **96**, employing a BINOL-derived CPA catalyst (**OC-44**) (Scheme 54).[135] The reaction begins with protonation of the ynamide **96** by the catalyst **OC-44**, generating a keteniminium intermediate **97**. This intermediate then undergoes intramolecular hydroalkoxylation to afford a chiral oxazolidine intermediate **98**, which serves as the enantio-determining step. A subsequent proton transfer from the CPA (**OC-44**) to intermediate **98** generates a cyclic iminium species (**98**), which undergoes hydrolysis to deliver the chiral β-amino alcohol **100** with regeneration of the catalyst. The observed enantioselectivity arises from well-defined hydrogen-bonding and ion-pairing interactions between the keteniminium intermediate **97** and the chiral Brønsted acid catalyst.

Notably, Suga group employed a novel carbonyl-stabilized phosphonium ylide (**OC-45**) as an ionic nucleophilic catalyst for the selective acylation of primary alcohols in terminal diols



Scheme 53 Desymmetrization of 1,3-diols employing chiral phosphoric acid (**OC-43**).



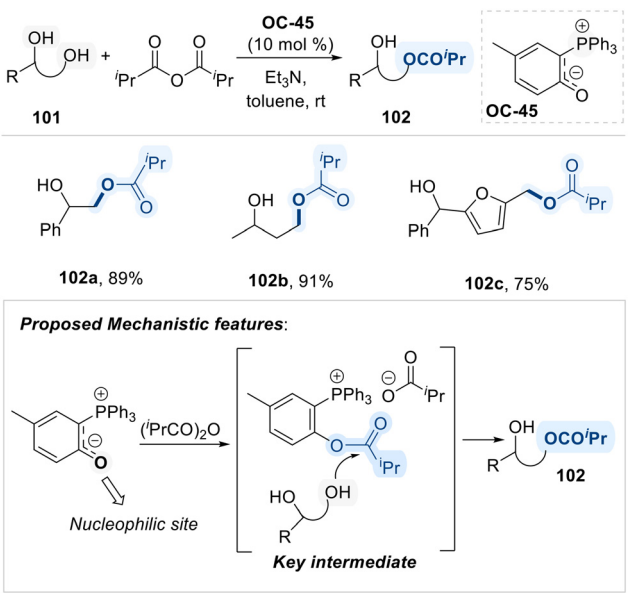
Scheme 54 Desymmetrization of serinol-derived ynamides using chiral phosphoric acid catalyst (**OC-44**).

(Scheme 55).[136] The proposed mechanism initiates with the nucleophilic attack of the phosphonium ylide (**OC-45**) on the electrophilic carbon of isopropyl anhydride, resulting in the formation of an *O*-isopropylated intermediate is activated species subsequently undergoes acyl transfer to the diol substrate, selectively targeting the primary hydroxyl group. The observed regioselectivity is attributed to steric hindrance imposed by the bulky triphenylphosphine moiety, which disfavors nucleophilic attack at the more hindered secondary alcohol, thereby favoring acylation at the less hindered primary site.

5. Organophoto-catalytic systems

Traditional approaches to site-selective diol functionalization have primarily relied on two-electron pathways. In these systems, selectivity is often induced by the structural features of the catalyst, particularly in enantioselective transformations where chiral architectures play a central role. Alternatively, selectivity may result from the intrinsic steric or electronic properties of the substrate.

More recently, organophotocatalysis has emerged as a mechanistically distinct strategy, enabling site-selective modifi-

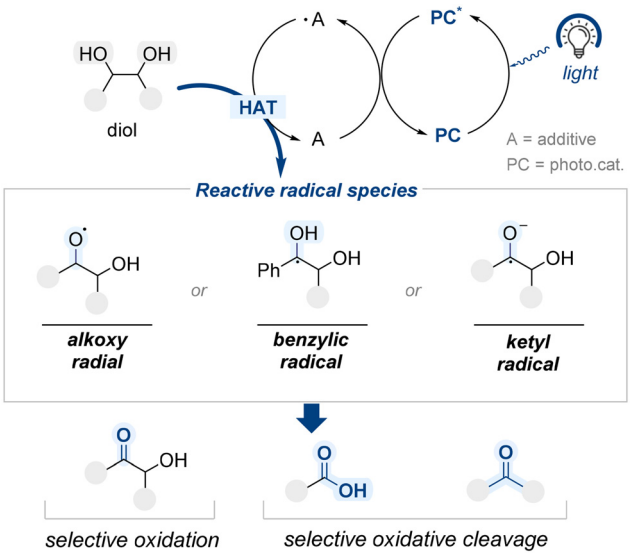


Scheme 55 Phosphonium ylide (**OC-45**) catalyzed regioselective acylation of diol.

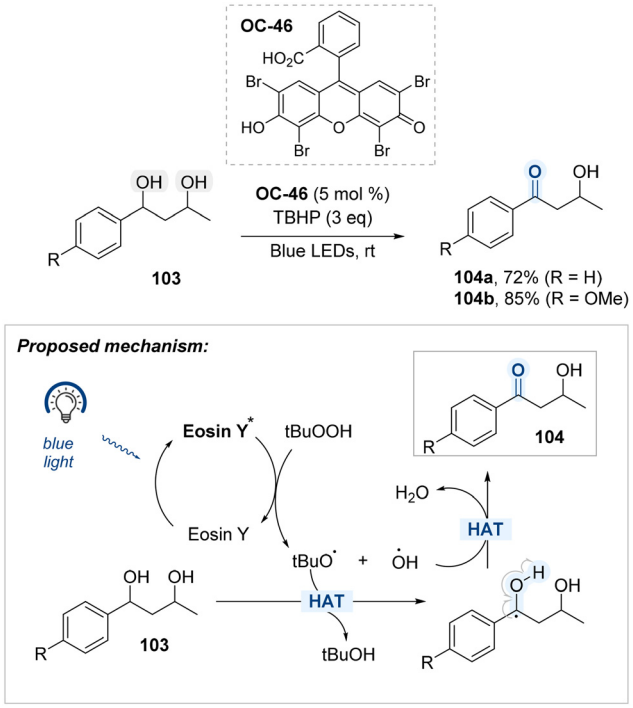
cation of diol substrates through single-electron processes initiated by visible light. Upon photoexcitation, the excited photocatalyst (PC*) engages in a single-electron transfer with a redox-active additive (A), generating a radical species (•A) (Scheme 56). This additive radical species subsequently reacts with the diol substrate through hydrogen atom transfer (HAT), forming reactive intermediates, such as alkoxy, benzylic, or ketyl radical species. These reactive intermediates serve as branching points for various downstream reactions, including selective oxidation at specific hydroxyl groups and oxidative cleavage of *vicinal* C–C bonds. This section examines how such photochemical radical-based strategies have been harnessed to achieve site-selective transformations of diols through well-controlled single-electron pathways.

A regioselective oxidation protocol targeting benzylic hydroxyl groups within diol substrates was developed by Rizvi, and Shah, employing Eosin Y (**OC-46**) as an organophotocatalyst and *tert*-butyl hydroperoxide (TBHP) as the oxidant under blue light irradiation (Scheme 57).[137] Underlying this transformation is a mechanism in which photoexcited Eosin Y initiates homolytic cleavage of TBHP to generate *tert*-butoxy and hydroxyl radicals. The former abstracts a hydrogen atom adjacent to the aromatic ring, forming a stabilized benzylic radical, which is subsequently oxidized by the latter to yield the carbonyl product. The observed selectivity stems from the lower bond dissociation energy and enhanced stability of the benzylic radical. In substrates such as 1,3-diol, oxidation occurs exclusively at the benzylic hydroxyl group, leaving the primary alcohol unmodified.

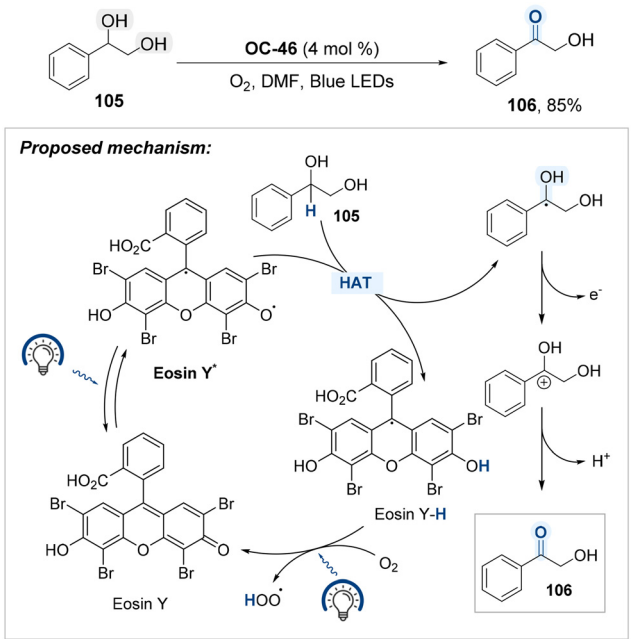
Building on the utility of Eosin Y (**OC-46**) as an organophotocatalyst, Song, Xu, and Gao developed a blue-light-mediated protocol for the selective oxidation of hydroxyl groups located at benzylic positions, employing molecular oxygen as the terminal oxidant (Scheme 58).[138] **OC-46** has been shown to promote aerobic oxidation at benzylic positions *via* a hydrogen atom transfer (HAT) mechanism under visible light irradiation. Upon photoexcitation, the Eosin Y catalyst reaches its excited state and abstracts a hydrogen atom from the benzylic C–H bond, generating a benzylic radical and the reduced form of the catalyst (Eosin Y–H). The benzylic radical



Scheme 56 General mechanism of selective oxidation of diol *via* photocatalysis.



Scheme 57 Blue light-mediated chemoselective oxidation of 1,3-diol.

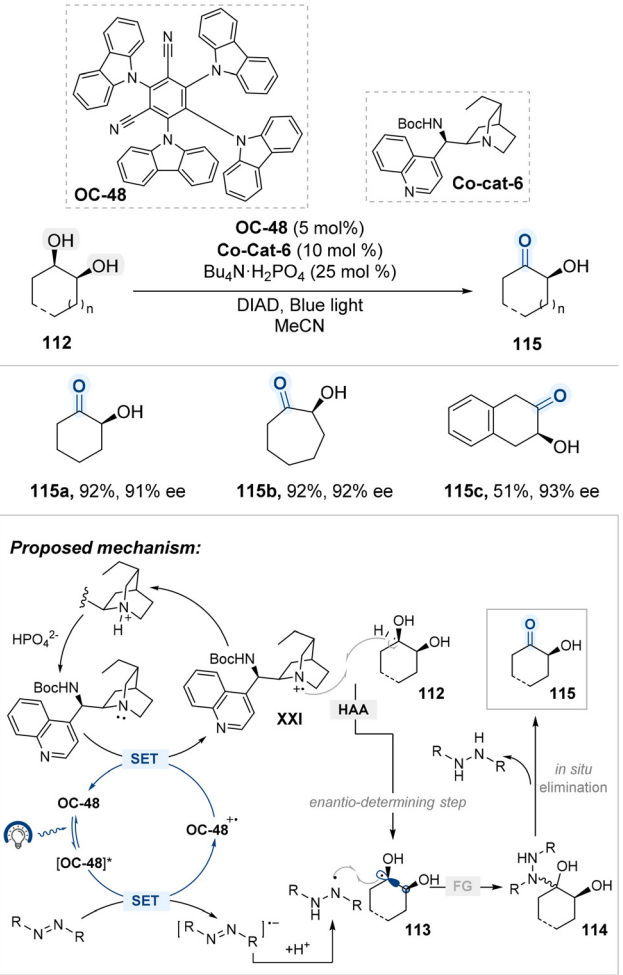


Scheme 58 Photocatalyzed selective oxidation of 1,2-diols.

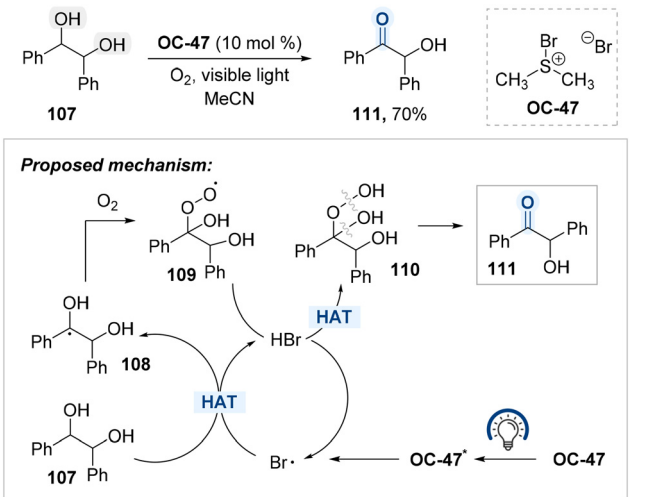
is subsequently oxidized to furnish a benzyl carbocation, which undergoes deprotonation to yield the corresponding carbonyl product **106**. Under blue light irradiation, the reduced photocatalyst (Eosin Y–H) is reoxidized by molecular oxygen, thereby regenerating Eosin Y and closing the catalytic cycle.

Ananthakrishnan and co-workers also developed a photo-induced oxidation protocol for benzylic hydroxyl groups using bromodimethylsulfonium bromide (BDMS, **OC-47**) and molecular oxygen, enabling the site-selective conversion of secondary alcohols to ketones (Scheme 59).[139] In the proposed mechanism, **OC-47** undergoes photoactivation to generate bromine radicals, which initiate hydrogen atom abstraction from the benzylic C–H bond of diol **107**, forming benzylic radical intermediates **108**. These radicals subsequently react with molecular oxygen to produce a diol–peroxy radical adduct **109**. The resulting peroxy radicals abstract hydrogen atoms from *in situ* generated HBr, thereby regenerating bromine radicals and forming hydroperoxide species **110**,[140] which are believed to be intermediates *en route* to the formation of ketone **111**. Notably, overoxidation beyond the ketone stage is not observed under the reaction conditions.

Phipps and colleagues reported a catalytic system for the enantioselective oxidation of *meso*-diols *via* visible-light-driven radical generation (Scheme 60).[141] This transformation utilizes 4CzIPN (**OC-48**) as an organophotocatalyst in combination with a cinchona alkaloid-derived co-catalyst (**Co-cat-6**), which collectively enable the stereocontrolled formation of radical intermediates under mild conditions. Upon photoexcitation, **OC-48** undergoes oxidative quenching with diisopropyl azodicarboxylate (DIAD), a sacrificial oxidant that generates the radical ion pair $[\mathbf{OC\text{-}48}]^{\bullet+}$ and $DIAD^{\bullet-}$. The latter is protonated to afford a persistent $DIAD^{\bullet}$ species capable of participating in downstream radical coupling. Meanwhile, the oxidized photocatalyst facilitates single-electron oxidation of quinuclidine



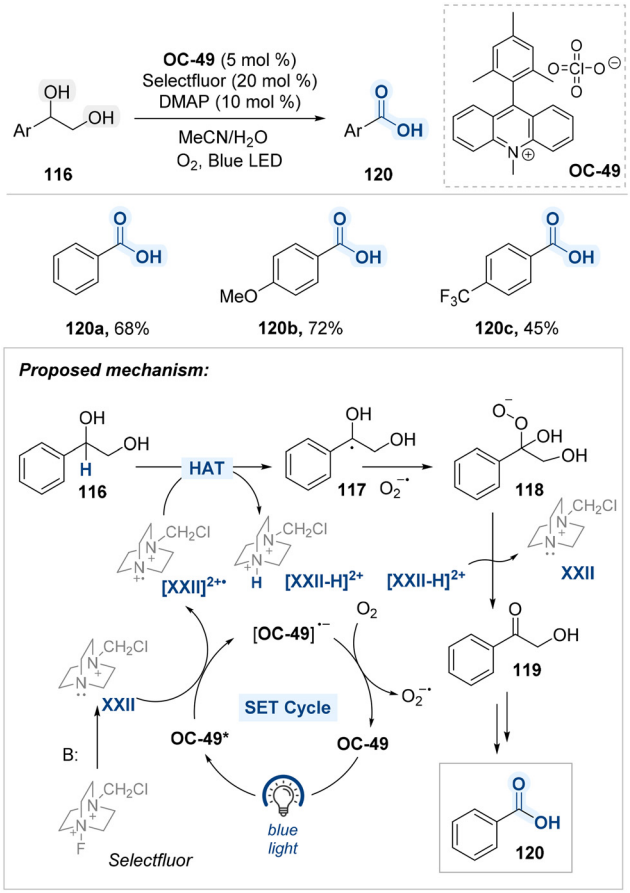
Scheme 60 Photocatalyzed oxidative desymmetrization of *meso*-1,2-diols.



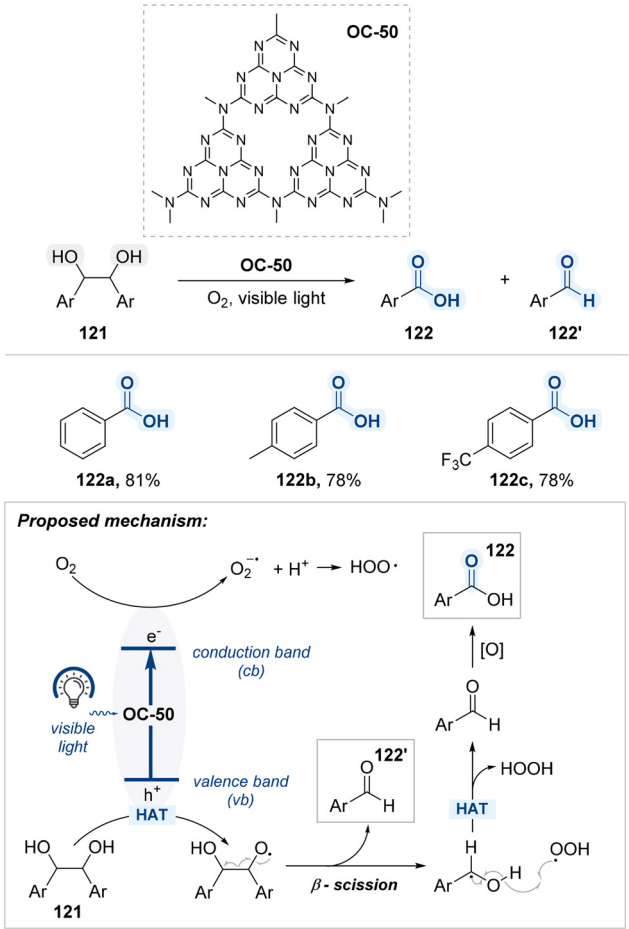
Scheme 59 OC-47-catalyzed selective benzylic oxidation under visible light.

moiety of **Co-cat-6**, producing a chiral quinuclidinium radical cation **XXI** that selectively abstracts a hydrogen atom from the *meso*-diol substrate **112**. This enantio-determining step breaks molecular symmetry to yield a stereodefined ketyl radical intermediate **113**, which subsequently undergoes radical–radical coupling with $DIAD^{\bullet}$ to form intermediate **114**. Elimination of this adduct furnishes the enantioenriched hydroxyketone product **115**. This strategy represents a mechanistically distinct approach for the de-symmetrization of *meso*-diols, achieving high enantioselectivity through controlled generation and selective capture of ketyl radical intermediates.

Kundu and co-workers reported a site-selective oxidative C–C bond cleavage of diol substrates under blue light irradiation, employing an acridinium-based photocatalyst (**OC-50**), Selectfluor as a HAT agent, and DMAP as a base (Scheme 61).[142] This transformation operates through a radical mechanism involving sequential single-electron transfer (SET) and hydrogen atom transfer (HAT) steps. In this system, photo-excited photocatalyst (**OC-50***) facilitate a SET to oxidize the base-activated form of Selectfluor (**XXII**), generating the elec-



Scheme 61 Blue light-mediated oxidative cleavage of terminal 1,2-diols.

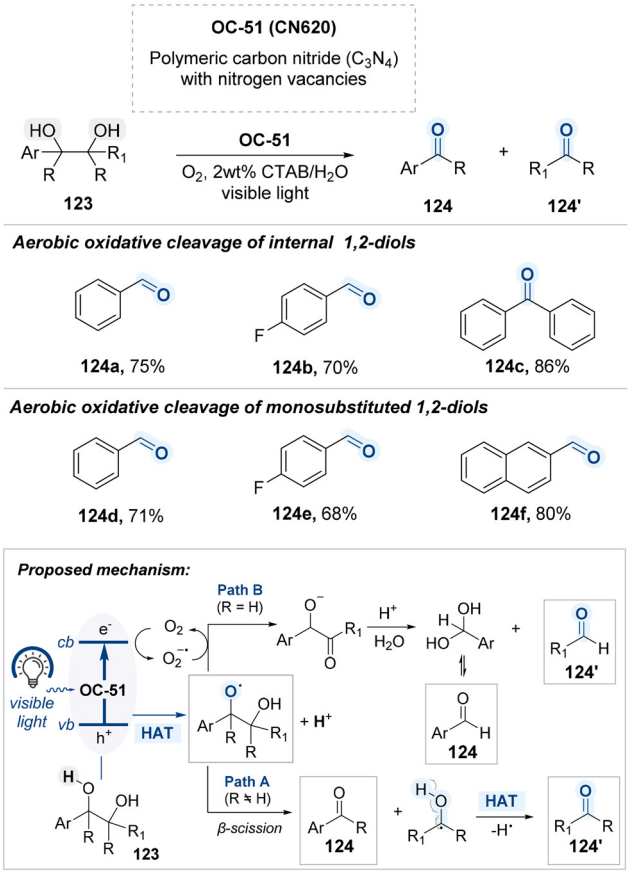


Scheme 62 Photocatalyzed oxidative cleavage of C–C bonds in *vicinal* diol substrates.

trophilic radical cation species *N*-(chloromethyl)triethylenediamine (TED$^{\bullet 2+}$, **[XXII]**$^{\bullet 2+}$). This radical cation serves as an effective hydrogen atom abstractor, selectively removing a hydrogen atom from the benzylic position of the diol **116** to form a resonance-stabilized benzylic radical intermediate **117**. The benzylic radical species goes through oxidation by superoxide radical ($O_2^{\bullet -}$), forming a hydroperoxide intermediate **118**. This species is subsequently converted into an α-hydroxy ketone intermediate **119**, which is further transformed into the corresponding benzoic acid **120** *via* a well-established oxidative pathway[143,144] The reaction showcases the role of **[XXII]**$^{\bullet 2+}$ as a potent photogenerated HAT species, driving selective benzylic oxidation through a multi-step cascade involving radical formation, oxygenation, and hydrolysis.

Fu and co-workers demonstrated that mesoporous graphitic carbon nitride (mpg-C_3N_4, **OC-50**), a visible-light-responsive organic semiconductor with a high surface area and tunable nitrogen-rich structure, can efficiently promote the aerobic oxidative cleavage of 1,2-diols under mild conditions (Scheme 62).[145] Under the visible light, the **OC-50** promotes a photoredox-mediated activation of molecular oxygen. During this process, charge separation occurs to generate holes (h^+) in the valence band and electrons (e^-) in the conduction band. The photoexcited electron in conduction band reduces molecular oxygen to produce reactive oxygen species, such as superoxide radicals ($O_2^{\bullet -}$ or HOO$^{\bullet}$). Concurrently, the photogenerated hole facilitates hydrogen atom transfer from benzylic alcohol moiety of the diol substrate **121**, furnishing an alkoxy radical intermediate. This radical undergoes β-scission,[146] yielding a benzaldehyde **122′** with benzylic radical. The resulting benzylic radical can go through a second hydrogen atom transfer or couple with reactive oxygen species, ultimately forming an additional equivalent of aldehyde. In subsequent steps, aldehydes are proposed to be oxidized to carboxylic acids **122** through a well-established radical-mediated pathway.

As part of ongoing efforts to design photocatalytic systems operable in aqueous media, a method employing nitrogen-deficient carbon nitride (CN620, **OC-51**) was reported by Niu and Ni for the oxidative cleavage of 1,2-diols under visible light (Scheme 63).[147] Photoexcitation of **OC-51** generates electron–hole pairs, initiating redox processes in which the photogenerated electrons reduce molecular oxygen to superoxide radicals ($O_2^{\bullet -}$), while the holes oxidize 1,2-diols to form alkoxy radical intermediates. From this point, two distinct mechanistic pathways are proposed, depending on the nature of the sub-



Scheme 63 Photocatalytic aerobic oxidative cleavage of C–C bonds in 1,2-diols.

stituent (R) on the diol substrate **123**: pathway A operates when R is a non-hydrogen substituent, while pathway B proceeds when R is a hydrogen atom. In pathway A, the alkoxy radical undergoes β-scission to cleave the adjacent C–C bond, generating a α-hydroxy radical and a carbonyl compound **124**. The resulting carbon-centered radical is then oxidized *via* hydrogen atom transfer (HAT) from either the solvent or another alkoxy radical, affording a second aldehyde or ketone product **124′**.[148] In contrast, pathway B involves direct oxidation of the alkoxy radical by a putative superoxide radical species, generating a peroxy anion intermediate and water. This intermediate undergoes hydrolysis to form a *gem*-diol and desired aldehyde **124** which subsequently dehydrates to afford the carbonyl product **124′**.

6. Conclusions and future outlook

This review provides a comprehensive overview of recent advances in the organocatalytic functionalization of diols, with particular emphasis on methodologies that enable precise regio- and stereochemical control. The literature is categorized based on the nature of the organocatalyst, with particular attention to boron, nitrogen, and phosphorus-based systems, alongside emerging photoredox-catalyzed methodologies. Throughout, key mechanistic insights were highlighted, emphasizing their impact on reactivity and regio- and stereoselective outcomes.

In the domain of boron-based organocatalysis, representative classes such as boranes, borinic acids, boronic acids, and their heterocyclic derivatives (*e.g.*, benzoxazaborine, benzazaborole and benzoxaborole) were introduced, with a focus on their characteristic activation modes in diol functionalization. For borane catalysts, the selective deoxygenation of diols using the BCF/hydrosilane system has been discussed, proceeding *via* either cyclic or acyclic intermediates. The nature of the intermediate is highly dependent on both substrate structure and reaction conditions, thereby influencing the transformation's efficiency and selectivity. In the case of borinic acids, boronic acids, and their derivatives, the electrophilic boron center engages in reversible interactions with the hydroxyl groups of diols, forming cyclic borinate or boronate ester intermediates. In this scenario, the selective transformation of the diol was achieved through careful tuning of the catalyst's steric and electronic environment.

In the context of nitrogen-based organocatalytic functionalization of diols, this review encompassed a diverse range of catalytic systems, including N-heterocycles, diamines, peptides, and N-heterocyclic carbenes (NHCs). These catalysts operate *via* diverse mechanistic pathways, such as electrophile activation, hydrogen bonding, Brønsted acid–base interactions, and steric modulation. Such interactions facilitate differentiation between hydroxyl groups and stabilize key transition states, ultimately enabling high levels of regioselectivity.

For phosphorus-containing organocatalysts, systems such as chiral phosphines, chiral phosphoric acids, and phosphonium salts have been reviewed for their ability to promote the selective transformation of diols *via* mechanisms involving nucleophilic activation, Brønsted acidity, or Lewis base catalysis.

The last section highlighted recent advances in diol-selective organophotocatalytic oxidation, which typically proceed *via* redox-additive mediated photoinduced single-electron transfer (SET) process that generates radical species. These radical species react with diol through hydrogen atom transfer (HAT), forming reactive intermediates that drive site-selective oxidation. Crucially, the selective generation of these intermediates is governed by differences in C–H bond dissociation energies, radical stability, and steric accessibility factors.

Although selective transformations of hydroxyl groups in diols have been pursued for more than a century, several key challenges persist, offering compelling avenues for future research. A major limitation lies in the relatively narrow substrate generality, as most strategies discussed in this review have predominantly been developed for *meso*-diols or secondary-primary diols, underscoring a constrained chemical space. In contrast, the regioselective functionalization of more challenging motifs, such as unsymmetrical secondary–secondary diols, remote diols, and tertiary–secondary diols, remains particularly demanding due to their comparable reactivity profiles and lack of inherent differentiation.

Another significant challenge is the development of more economical and finely tunable catalytic platforms that minimize the use of sacrificial reagents, override steric biases, and enable reversals of inherent selectivity trend. The design of such catalysts may benefit from leveraging novel synergistic non-covalent interactions, which can provide the level of control required for broad substrate applicability and enhanced selectivity. Given that diols represent a valuable model system for developing functionalization strategies applicable to more complex polyol frameworks, advances in catalyst design for diol substrates are likely to translate effectively to polyols, governed by similar selectivity-controlling principles. Ultimately, such developments will open new avenues for the regioselective transformation of complex polyol architectures, thereby accelerating innovation in polyol building block synthesis.

We believe that the organocatalyzed methods for selective transformation of diol discussed in this review will serve as an attractive catalytic platform to achieve further exciting breakthroughs. We hope this contribution provides a succinct summary of the field and encourages exploration of related synthetic methodologies.

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this review.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Acknowledgements

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