Review article

Recent Advances in Aldol Condensation: Mechanistic Insights, Catalytic Strategies, and Sustainable Applications

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ABSTRACT

Aldol condensation is one of the most versatile carbon–carbon bond-forming reactions in organic chemistry and plays a pivotal role in the synthesis of pharmaceuticals, fine chemicals, polymers, fragrances, and biomass-derived chemicals. Recent advances in catalyst design, mechanistic understanding, and sustainable reaction strategies have significantly enhanced the efficiency, selectivity, and industrial applicability of this transformation. This systematic review critically evaluates recent developments in aldol condensation by analysing peer-reviewed studies retrieved from major scientific databases, including Scopus, Web of Science, PubMed, ScienceDirect, and Google Scholar. The review comprehensively discusses reaction mechanisms, heterogeneous and homogeneous catalysts, bifunctional acid–base catalysts, metal–organic frameworks (MOFs), organocatalysts, computational investigations, and green chemistry approaches. Comparative analysis demonstrates that heterogeneous catalysts offer excellent recyclability and operational stability, bifunctional catalysts improve catalytic activity through cooperative activation of reactants, and MOFs provide enhanced selectivity owing to their tunable pore architecture and well-defined active sites. Organocatalysts, particularly proline-based systems, enable highly stereoselective transformations under mild and environmentally benign conditions. Sustainable methodologies, including solvent-free reactions, aqueous media, recyclable catalysts, tandem catalytic processes, and biomass-derived feedstocks, further improve the environmental performance of aldol condensation. Despite substantial progress, catalyst deactivation, hydrothermal instability, diffusion limitations, and challenges in large-scale implementation remain significant barriers.

Overall, this review integrates mechanistic insights, catalyst engineering, computational studies, and sustainability concepts to provide a comprehensive perspective on current advances and future opportunities for developing efficient, scalable, and environmentally sustainable aldol condensation processes for synthetic and industrial applications.

Keywords: Aldol condensation; Carbon–carbon bond formation; Heterogeneous catalysis; Organocatalysis; Green chemistry; Sustainable synthesis.

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1. INTRODUCTION

The aldol condensation reaction is one of the most fundamental but versatile carbon-carbon bond-forming reactions in organic chemistry, enabling the synthesis of complex structures from simple carbonyl building blocks (Perrin & Kim, 2022; Weinfeld et al., 2022). Since its discovery in the nineteenth century, the aldol reaction has progressed from traditional base-catalysed reactions to extremely complicated catalytic techniques that provide precise stereocontrol and functional group tolerance (Biesemans et al., 2024; Wang et al., 2022; Zhang et al., 2022; Zhang et al., 2023). The reaction comprises enolate or enol formation, nucleophilic addition to an electrophilic carbonyl, and subsequent dehydration to produce α,β-unsaturated carbonyl compounds (Figure 1) (Bargujar & Ratnani, 2022; Shibasaki & Kanai, 2008; Spieß et al., 2023; Zhu et al., 2024).

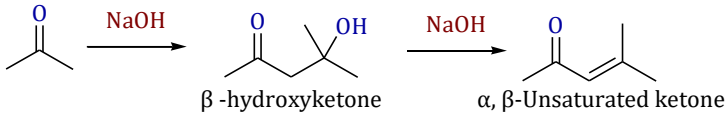

Figure 1: Schematic representation of the base-catalysed aldol reaction of acetone, illustrating formation of the β-hydroxyketone (aldol addition product) followed by dehydration to generate the α,β-unsaturated ketone (aldol condensation product).

Current research activities in aldol condensation include basic studies on reaction mechanisms, with a focus on elementary steps and transition states; the development of new heterogeneous and homogeneous catalysts with higher activity, selectivity, and recyclability; enantioselective reactions for asymmetric synthesis; and applications in biomass conversion and sustainable fuel synthesis (Bhasker-Ranganath et al., 2021; Choi et al., 2023; Hernández-Soto et al., 2022; Shao et al., 2021; Vanlaldinpuia et al., 2017; Yun et al., 2021; Zhang et al., 2023). The significance of aldol condensation extends beyond laboratory-scale organic synthesis to commercial applications such as fragrance synthesis, polymerisation, and biorefineries (Raguindin et al., 2025).

This systematic review synthesises existing knowledge on aldol condensation processes, mechanisms, and catalysts and conducts a thorough evaluation of peer-reviewed literature. The systematic review addresses key topics about catalyst design principles, processes, reaction scope, and novel applications, particularly in the context of sustainable chemistry (Li et al., 2021; Madriaga et al., 2025; Oliphant et al., 2024).

2. METHODS

This review was conducted following a systematic literature collection and screening approach to ensure transparency, reproducibility, and comprehensive coverage of recent advances in aldol condensation catalysis. Relevant scientific literature was retrieved from major electronic databases, including Scopus, Web of Science, PubMed, Google Scholar, and ScienceDirect. The literature search covered publications published between 2000 and 2025 to capture both foundational and recent developments in aldol condensation chemistry.

The search strategy employed combinations of keywords and Boolean operators such as “aldol condensation,” “heterogeneous catalysts,” “metal–organic frameworks,” “MOFs,” “organocatalysts,” “bifunctional catalysts,” “green catalysis,” “acid–base catalysis,” and “asymmetric aldol reaction.” Reference lists of relevant review articles and research papers were also manually screened to identify additional eligible studies.

Articles were included if they: (i) focused on catalytic aldol condensation reactions; (ii) investigated heterogeneous, homogeneous, organocatalytic, MOF-based, or bifunctional catalytic systems; (iii) reported catalytic activity, selectivity, mechanistic insights, recyclability, or sustainability aspects; and (iv) were published in peer-reviewed journals in the English language. Studies lacking experimental validation, duplicate publications, conference abstracts, patents, editorials, or articles with insufficient catalytic or mechanistic information were excluded from the review.

The collected records were screened through a multi-step selection process based on title review, abstract evaluation, and full-text assessment according to PRISMA-based systematic review principles. Duplicate records were removed before eligibility assessment. A total of 1110 articles were initially identified through database searching, of which 862 studies remained after duplicate removal. Following title and abstract screening, 248 articles were selected for full-text evaluation, and finally 82 studies meeting all inclusion criteria were incorporated into the present review. The complete article selection procedure is illustrated in the PRISMA workflow diagram presented in Figure 2.

Data extracted from the selected studies included catalyst type, catalyst composition, reaction conditions, substrate scope, catalytic efficiency, selectivity, mechanistic behaviour, catalyst stability, recyclability, and sustainability-related parameters. Comparative analysis was subsequently performed to critically evaluate the advantages, limitations, and structure–performance relationships of different catalytic systems employed in aldol condensation reactions (Booth, 2016; Higgins & Green, 2008; Page et al., 2021).

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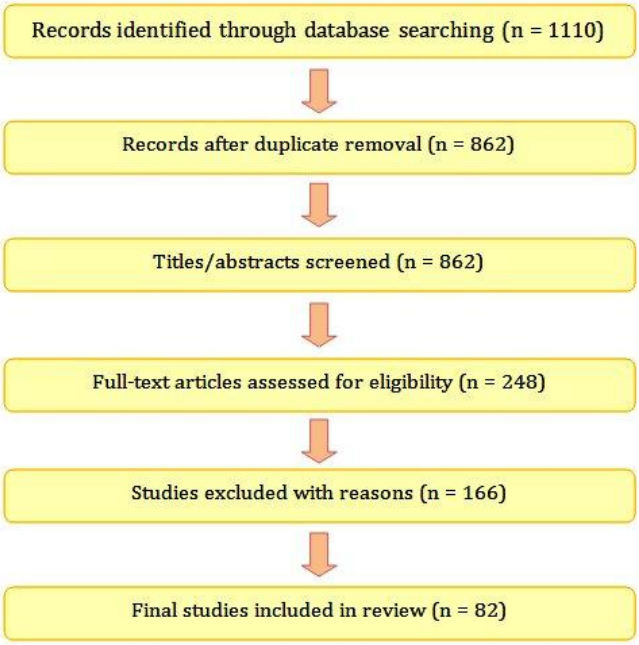

Figure 2: PRISMA flow diagram illustrating the systematic literature selection process for the present review. A total of 1110 records were identified through database searching, of which 248 duplicate records were removed. After title and abstract screening of 862 records, 638 articles were excluded. Subsequently, 224 full-text articles were assessed for eligibility, resulting in the exclusion of 142 studies due to insufficient catalytic, mechanistic, or experimental information. Finally, 82 studies meeting all inclusion criteria were incorporated into the review on catalytic aldol condensation reactions.

3. THE ALDOL REACTION

The aldol reaction is one of the oldest and most extensively studied carbon-carbon bond formation reactions in organic chemistry. The term "aldol" comes from the original discovery of the reaction, which is the base-catalysed self-condensation of acetaldehyde to produce 3-hydroxybutanal (aldol), which contains both aldehyde and alcohol functional groups (Erdmann et al., 2024; Machajewski & Wong, 2000; Miller et al., 2022; Tampieri et al., 2022). Over the past century, the aldol reaction has evolved from simple self-condensations to crossing aldol reactions, enantioselective reactions, and very complex catalytic processes (Shao et al., 2022; Verma et al., 2022).

Aldol condensation is a two-step process that dehydrates the aldol addition product to produce α,β-unsaturated carbonyl molecules. This process differs from the aldol addition reaction, which solely produces β-hydroxy carbonyl compounds. The condensation reaction is crucial in organic synthesis because it creates conjugated complexes with prolonged π-electron delocalisation, which can serve as flexible intermediates for subsequent functionalization reactions (Denmark et al., 2005; Machajewski & Wong, 2000; Verma et al., 2022; Zhao et al., 2023).

The aldol reaction has evolved through numerous stages, including conventional base- and acid-catalysed reactions, metal-mediated enolate chemistry, organocatalysis pioneered by List and other researchers, and contemporary heterogeneous catalysis for sustainable aldol processes. These steps can be seen as an overall trend in organic synthesis to provide softer reaction conditions, improved selectivity, recyclable catalysts, and environmentally sustainable procedures (Bargujar & Ratnani, 2022; Dutta, 2025; Patil et al., 2025; Reif et al., 2020; Valapil et al., 2021; Yamashita et al., 2018).

3.1. Reaction Mechanism

The aldol condensation reaction mechanism consists of multiple steps, each of which can determine the rate based on the catalyst and reaction circumstances. Perrin et al. conducted rigorous mechanistic research to demonstrate the chemical pathway from carbonyl to α,β-unsaturated molecules.

General Mechanism:

Enolate/Enol Formation: A base removes an α-proton from the carbonyl molecule (donor) to generate an enolate ion or enol. A Lewis acid catalyst increases the acidity of α-protons by binding carbonyl oxygen to the metal centre.

Nucleophilic Addition: The enolate or enol reacts with the electrophilic carbonyl carbon of the aldehyde or ketone, forming a new C-C bond and a β-alkoxide or β-hydroxy intermediate.

Protonation: The alkoxide intermediate undergoes protonation to produce the β-hydroxy carbonyl (aldol) product.

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Dehydration: In the presence of heat and/or acidic or basic catalysts, the β-hydroxy carbonyl molecule removes water, resulting in the α,β-unsaturated carbonyl compound. Dehydration can occur by E1 or E2 processes, depending on the catalyst and circumstances (Figure 3 and 4) (Bargujar & Ratnani, 2022; Climent et al., 2002; Dutta, 2025; Verma et al., 2022).

Base-catalysed aldol condensation

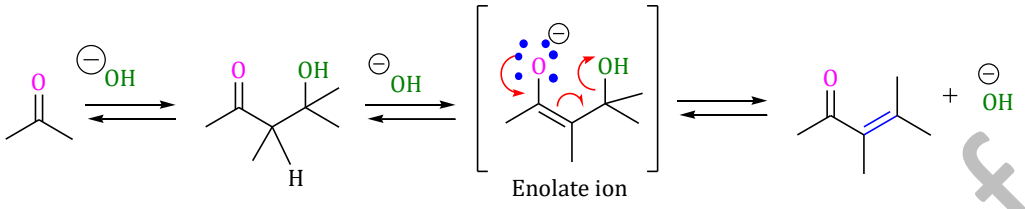

Figure 3: Mechanistic pathway of base-catalysed aldol condensation showing enolate ion formation, nucleophilic carbon–carbon bond formation with the carbonyl acceptor, protonation of the alkoxide intermediate, and dehydration to yield the conjugated α,β-unsaturated ketone.

Acid-catalysed aldol condensation

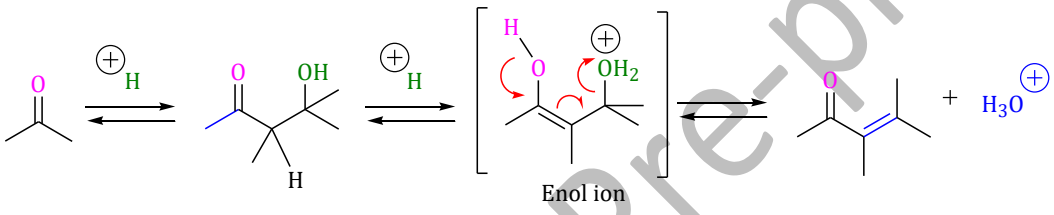

Figure 4: Proposed mechanism for acid-catalysed dehydration of β-hydroxyketone intermediates involving protonation of the hydroxyl group, water elimination, and formation of the α,β-unsaturated carbonyl compound.

Mechanistic Variations:
Bifunctional Catalysis: Climent et al. (2002) demonstrated that the cooperative action of acid-base pairs in solid catalysts accelerates aldol condensation processes by activating acceptor and donor carbonyls via base and acid sites. The bifunctional catalysis notion is fundamental to the design of heterogeneous catalysts (Climent et al., 2002).

Metal-Organic Frameworks: Hajek et al. (2015) refined the aldol reaction mechanism in UiO-66 and UiO-66-NH2 MOFs, indicating that the Zr Lewis acid sites regulate enolate production and dehydration reactions. The reaction conditions in the restricted micropores, as well as the distribution of active sites, influence selectivity and reaction routes (Hajek et al., 2015).

Organocatalytic Pathways: In proline-catalysed aldol reactions, enamine intermediates replace enolates. The proline carboxylic acid activates the acceptor carbonyl via hydrogen bonding, while the secondary amine enables the synthesis of an enamine with the donor ketone, allowing for stereoselective C-C bond formation (Al-Momani et al., 2023).

3.2. Thermodynamic and Kinetic Considerations

The aldol condensation reaction is typically thermodynamically advantageous due to the existence of a conjugated π-system in the result, which enhances the molecule's stability. However, the reaction kinetics and ultimate product composition are highly dependent on the catalyst, temperature, solvent, and reactant structure.
Herrmann et al. (2017) found that adding H_2 and Pt to acetone aldol condensation over aluminosilicates (FER, MFI, BEA, FAU) stabilises intermediates and inhibits catalyst deactivation. The reaction rate in acetone was first-order, with no kinetic isotope effect, showing that C-C bond formation is the rate-limiting step for H-bonded acetone. They also discovered that turnover rates depend substantially on pore size and structure, with optimum van der Waals contacts enhancing reactivity, as indicated by DFT and Lennard-Jones energy estimates (Herrmann & Iglesia, 2017).
Comisar et al. (2004) explored crossover aldol condensations in high-temperature water (250-350 °C) and discovered that water can function as both an acid and base catalyst without the use of additional chemicals. At 250 °C, they obtained maximum yields of 24% for benzalacetone and 21% for chalcone, while higher temperatures resulted in lower yields due to side-product production and subsequent reactions. Their research emphasises the importance of high-temperature water in stimulating aldol reactions and regulating product dispersion (Comisar & Savage, 2004).

Young et al. (2016) studied acetaldehyde aldol condensation on TiO_2, HAP, and MgO at 533-633 K and 220 kPa. Crotonaldehyde was the only product that exhibited substantial catalyst deactivation over 5 kPa acetaldehyde pressure. The process exhibited first-order kinetics at low pressure (0.05-5 kPa) and approached zero-order at higher

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pressures, with no kinetic isotope effect seen. These findings show that adsorption-desorption phases regulate the reaction process (Young et al., 2016).

4. CATALYST SYSTEMS FOR ALDOL CONDENSATION

4.1. Heterogeneous Base Catalysts

Heterogeneous base catalysts are chosen in aldol condensation reactions because they are easily separated and recyclable, as well as suitable for continuous flow processes. Base catalysts for aldol condensation processes include metal oxides, hydrotalcites, and modified alkaline earth minerals.

Metal Oxides:

Tang et al. (2013) used benzyl bromide to create a modified CaO solid-base catalyst for the aldol condensation of cyclohexanone and benzaldehyde. The catalyst had a high yield of 95.8% in 3 hours, compared to 92.1% in 12 hours with unmodified CaO, showing increased efficiency. The catalyst showed high selectivity, stability against CO_2 and moisture, and consistent performance across several aldehydes, as validated by FT-IR and TG analysis (Tang et al., 2013).

Mäki-Arvela et al. (2019) investigated the cross-aldol condensation of valeraldehyde and cyclopentanone at 130°C (atmospheric pressure) using metal-modified oxides. FeO-MgO (deposition precipitation) outperformed the other catalysts, yielding a maximum of 66% for 2-pentylidenecyclopentanone. The study discovered that having an ideal amount of strong basic sites is critical for enhancing cross-condensation over self-condensation (Mäki-Arvela et al., 2019).

Hydrotalcites and Layered Double Hydroxides (LDHs):

Hydrotalcites (Mg-Al LDHs) are among the most extensively researched base catalysts for aldol condensation due to their tunable basicity, large surface area, and structural stability. Abelló et al. (2008) investigated hydrotalcite catalysts for the aldol condensation of citral with acetone and discovered greater yields of pseudoionone than NaOH. However, they discovered substantial limitations, such as quick deactivation (about 50% activity loss after 1 hour owing to CO_2 exposure) and limited reusability, since the catalyst remained inactive after one cycle and required sophisticated regeneration. Despite its scalability, these drawbacks explain why the industry still chooses traditional liquid bases (Abelló et al., 2008).

Faba et al. (2012) investigated the aqueous-phase aldol condensation of acetone and furfural with mixed oxides (Mg-Zr, Mg-Al, Ca-Zr). At a 1:1 reactant ratio, the Mg-Zr catalyst demonstrated the best selectivity (>60% C13 yield), with activity being significantly dependent on medium-strength basic sites. In acetone, the reaction followed first-order kinetics, moving from C8 intermediates to C13 products, with enolate formation serving as the rate-determining step. Catalyst deactivation was primarily caused by interactions with water (Faba et al., 2012).

Tichit et al. (2003) investigated the liquid-phase aldol condensation of acetaldehyde and heptanal at 353-413 K, employing MgO and Mg(Al)O catalysts. Under ideal conditions (373 K, 2:1 acetaldehyde/heptanal ratio), Mg(Al)O demonstrated the maximum selectivity for 2-nonenal, the intended cross-condensation product. The study discovered that moderate Lewis acid-base sites support cross-condensation, whereas strong basic sites promote side products from self-condensation (Tichit et al., 2003).

Hernández et al. (2017) produced Mg-Zn-Al hydrotalcites and mixed oxides (calcined at 500 °C) for octanal self-condensation. Catalysts with a Zn/Mg ratio ≤1 demonstrated superior performance due to an appropriate balance of acidic and basic sites. Zn^{2+} increased surface acidity, while catalyst rebuilding increased OH^- groups, affecting selectivity towards α,β-unsaturated aldehydes (Hernández et al., 2017).

Dolomite and Natural Minerals:

O'Neill et al. (2014) studied the aldol condensation of furfural with acetone on activated dolomite at 306-413 K. The process proceeded via a C8 intermediate, which then produced a C13 dimer with excellent selectivity using first-order kinetics. The catalyst had good activity due to improved basicity; however, deactivation occurred at higher temperatures due to carbon deposition (O'Neill et al., 2014).

Meng et al. (2023) investigated cyclopentanone aldol condensation employing a SO_3H-modified catalyst (4 mmol/g) in solvent-free conditions. They achieved 85.53% conversion at 150 °C in 4 hours, with 69.04% dimer and 28.41% trimer selectivity. The study found that acid-base bifunctional sites are critical for improving catalytic efficiency and promoting sustainable biomass conversion (Meng et al., 2023).

Caesium-Exchanged Zeolites:

Ghosh et al. (2022) showed effective self- and cross-aldol condensations employing 1 wt% Cs^+ single sites in β-zeolite, demonstrating great activity and reusability. Despite lacking significant acid-base characteristics, the catalyst demonstrated great selectivity, a wide substrate range, and environmentally benign performance. DFT experiments revealed a non-traditional concerted process for C-C bond synthesis within zeolite channels (Ghosh et al., 2022).

4.2. Bifunctional Acid-Base Catalysts

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Bifunctional catalysts, which have both acid and base sites, perform better in aldol condensation reactions because they can activate the donor and acceptor carbonyls simultaneously.

Cooperative Acid-Base Mechanisms:
Wang et al. (2016) found that adding H_2 and Cu to TiO_2-catalyzed condensation of C_3 oxygenates enhances rate, selectivity, and stability by avoiding deactivation. The reaction is limited by enolate production (α-C-H cleavage), which requires moderately strong acid-base Ti-O site pairings. The researchers discovered that optimum Ti-O distances and site structure (anatase TiO_2) improve catalytic activity and govern condensation and esterification processes (Wang et al., 2016).

Amine-Functionalized Catalysts:
Shylesh et al. (2014) created a silica-supported amine catalyst for the gas-phase aldol condensation of n-butanal. They discovered that secondary amines (by enamine production) had higher activity, whereas primary amines were less active due to stable imine creation (up to 473 K). The work further showed that cooperation between amine and silanol groups is required, and DFT studies revealed that the rate-limiting phase involves C-C bond formation (Shylesh et al., 2014).

Barium-Lanthanum Catalysts:
Bao et al. (2017) investigated vapour-phase aldol condensation of methyl acetate and formaldehyde using Ba-La/Al_2O_3 catalysts. The 5Ba-0.5La/Al_2O_3 catalyst demonstrated great stability over 300 h and minimised carbon deposition due to the presence of La_2O_3. While Ba improved activity and selectivity, La increased catalytic stability by eliminating strong acid sites, which prevented deactivation (Bao et al., 2017).

4.3. Metal-Organic Frameworks (MOFs)
Metal-organic frameworks have been investigated as potential catalyst supports for aldol condensation processes because of their large surface area, tunable pore size, and controllable active sites.

UiO-66 and Amino-Functionalized Variants:
Vermoortele et al. (2011) found that Zr-based MOFs, such as UiO-66(NH_2), may effectively catalyse the cross-aldol condensation of benzaldehyde and heptanal. The closeness of Lewis acid-base sites inside the framework improves the reaction's selectivity and yield (Vermoortele et al., 2011).

Advantages of MOF Catalysts:
MOFs have various advantages in aldol condensation reactions, including a large surface area that provides plentiful active sites, variable pore diameters that allow for shape selectivity, and well-defined crystallinity that facilitates mechanistic research. They can also be changed after synthesis to add functional groups, and many, particularly Zr-based MOFs, have exceptional thermal and chemical stability, allowing them to operate under harsh reaction conditions. However, issues such as large-scale synthesis, cost, and stability in aqueous, highly acidic, or basic conditions must be addressed (Vermoortele et al., 2011).

4.4. Organocatalysts
Organocatalysis has revolutionised the study of asymmetric aldol reactions, enabling extremely enantioselective reactions under mild circumstances without the use of metal catalysts.

Proline and Proline Derivatives:
Benaglia et al. (2001), immobilising catalysts on polymer supports, combine homogeneous catalysis's excellent selectivity with heterogeneous systems' ease of recovery and recyclability. They underlined that optimal polymer supports should be soluble during reaction and insoluble during recovery for effective reuse (Benaglia et al., 2001).

Recent Advances in Organocatalytic Aldol Reactions:
Heravi et al. (2012), asymmetric aldol reactions can effectively generate C-C bonds, allowing for the production of chiral β-hydroxy carbonyl compounds. These compounds are important intermediates in natural products and medicines, and organocatalysis has played a significant role in recent improvements (Heravi & Asadi, 2012).

Vinylogous Aldol Reactions:
Pansare et al. (2011) reviewed the development of organocatalytic vinylogous aldol reactions, which can produce C-C bonds under moderate, metal-free conditions. They presented both the vinylogous Mukaiyama aldol reaction and direct vinylogous aldol reactions, emphasising their rising uses as well as current obstacles (Pansare & Paul, 2011).

Bisai (2012), the vinylogous aldol reaction extends the classical aldol process by efficiently forming C-C bonds to access δ-hydroxy-β-keto esters and α,β-unsaturated δ-hydroxy carbonyl compounds. These compounds can then be further transformed with good diastereoselectivity into polyol motifs commonly found in bioactive natural products (Bisai, 2012).

4.5. Metal Complex Catalysts

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Metal complexes catalyse the aldol reaction by a variety of processes, including Lewis acid activation, metal enolate production, and transition metal-mediated C-C bond formation.

Copper Peptide Catalysts:
Zaithun et al. (2018) found that Cu(II)-coordinated histidine-based tetrapeptides, CuP1 and CuP3, exhibit high enantioselectivity in asymmetric aldol reactions, such as p-nitrobenzaldehyde with cyclohexanone (87.3% ee and 80.3% ee) and p-anisaldehyde with cyclohexanone (95.5% ee and 90.9% ee), respectively (Zaithun et al., 2018).

Mukaiyama Aldol Reactions:
The Mukaiyama aldol reaction, which involves the reaction of silyl enol ethers with aldehydes in the presence of Lewis acid catalysts, is a significant variation in aldol chemistry. Hollis et al. (1995) discovered that in Mukaiyama aldol and Sakurai allylation processes, the active catalysts are silyl species (Me_3SiOTf or Me_3SiClO_4) generated in situ through Lewis acid hydrolysis, rather than the Lewis acids themselves. For example, $[Ti(Cp)_2(OTf)_2]$ works only as an initiator creating Me_3SiOTf, whereas reaction rate and stereoselectivity were shown to be substantially dependent on triflate ion concentration, with greater amounts decreasing the pace and modifying selectivity (Hollis & Bosnich, 1995).

Cordes et al. (2019) emphasised that the vinylogous Mukaiyama aldol reaction is a key transformation for constructing β-hydroxy ketone frameworks. It allows for the formation of extended structures with 1,5-relationships while simultaneously generating two stereocenters and a double bond with high selectivity (Cordes & Kalesse, 2019).

Metal Enolate Chemistry:
Adachi et al. (2009) found that catalytic enantioselective aldol additions to ketones can efficiently form tertiary aldols by activating acceptor ketones and enolate nucleophiles, overcoming the lower reactivity and steric challenges of ketones (Adachi & Harada, 2009).

Heterogeneous base catalysts are a popular choice for aldol condensation reactions due to their low cost, ease of separation, and recyclability. However, they are often deactivated due to coking, CO_2 poisoning, moisture sensitivity, and limited selectivity for cross-aldol products. Hydrotalcites and mixed oxides have tunable acid-base characteristics, but striking the right balance between catalytic activity and suppression of unwanted self-condensation processes remains difficult. Bifunctional acid-base catalysts, on the other hand, have superior cooperative activation of donor and acceptor carbonyl compounds, which frequently results in faster reaction rates and higher selectivity. Nonetheless, the precise spatial arrangement and strength of acid-base sites have a significant impact on catalytic efficiency, making rational catalyst design challenging.

Metal-organic frameworks (MOFs) offer particular advantages due to their large surface area, variable pore architecture, and well-defined active sites, allowing for better substrate accessibility and mechanistic control. Functionalized MOFs, such as UiO-66-NH_2, improve catalytic performance through synergistic Lewis acid-base interactions. However, their large-scale use is limited by synthesis expense, hydrothermal stability, and sensitivity under strong acidic or basic conditions. Organocatalysts, particularly proline-based systems, provide good stereoselectivity and environmentally friendly reaction conditions without the need for transition metals, making them extremely useful for asymmetric aldol synthesis. Despite these benefits, organocatalytic systems frequently necessitate longer reaction durations, increased catalyst loading, and substrate-specific tuning, which can limit industrial scalability.

In comparison, no single catalytic system currently meets all of the following requirements: high activity, broad substrate tolerance, stereoselectivity, catalyst stability, recyclability, and economic feasibility. As a result, recent research trends have increasingly focused on multifunctional and hybrid catalytic systems that combine the benefits of heterogeneous catalysis, organocatalysis, and bifunctional activation strategies to improve catalytic efficiency and sustainability in aldol condensation processes.

5. MECHANISTIC STUDIES AND COMPUTATIONAL INSIGHTS

Mechanistic knowledge is essential for rational catalyst design and reaction optimisation.

Complete Mechanistic Pathways:
The study discovered that the rate-determining step is affected by reaction circumstances: while basic conditions favour rate-determination by enolate production, acidic conditions make dehydration the rate-determining step. The study underlined the need to analyse the entire reaction pathway rather than individual phases in isolation.

Elementary Steps in Heterogeneous Catalysis:
Wang et al. (2016) discovered that enolate-mediated elementary stages are responsible for condensation and esterification over TiO_2. The rate-determining step is α-C-H bond cleavage of carbonyl compounds. The generated enolates undergo C-C bond formation with aldehydes/ketones or C-O bond formation with alcohols, whilst bifunctional Ti-O acid-base site pairs of moderate strength and proper spacing are critical for improving rate, selectivity, and catalyst stability (Wang et al., 2016).

MOF Mechanistic Studies:

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Hajek et al. (2015) found that aldol condensation over UiO-66 and UiO-66-NH_2 follows a similar pathway, with oxo-oxygen sites serving as the key fundamental centres for α-C-H deprotonation rather than the -NH_2 groups. The amino functionalization somewhat lowers activation barriers and boosts initial activity, but it can also promote side reactions such as imine production, emphasising the nuanced significance of bifunctional acid-base sites in MOF-catalysed aldol processes (Hajek et al., 2015).

Computational Modelling:
Migues et al. (2014) used DFT to demonstrate that mixed aldol condensation in acid zeolites (HZSM-5 and HY) occurs via keto-enol tautomerization followed by C-C bond formation. The tautomerization phase is rate-determining (activation energy ≈20 kcal/mol). They also proved that accurate energetics rely on proper modelling of the zeolite environment, as greater cluster sizes are necessary to reach convergence, particularly in HZSM-5 (Migues et al., 2014).

6. APPLICATIONS AND SYNTHETIC SCOPE

6.1. Enantioselective Aldol Reactions

Enantioselective aldol reactions are an essential part of asymmetric synthesis. They can be utilised to create chiral building blocks for application in the production of medicines, natural products, and high-performance materials.

Organocatalytic Enantioselective Aldol Reactions:
Mlynarski et al. (2014) emphasised the importance of aqueous asymmetric aldol reactions in producing enantiopure compounds, citing water as a sustainable and biologically relevant medium. Water-compatible chiral Lewis acids and amine-based organocatalysts have been developed to facilitate these reactions (Mlynarski & Baś, 2014).

Metal-Catalysed Enantioselective Aldol Reactions:
Carreira et al. (2006) emphasised that the aldol reaction is a key transformation in asymmetric synthesis, widely used to access polyketide fragments and other bioactive compounds, with two main approaches—diastereoselective methods using chiral auxiliaries and emerging enantioselective catalytic strategies—driving advances in complex molecule construction (Carreira et al., 2006).

Vinylogous and Extended Aldol Reactions:
Denmark et al. (2005) used vinylogy to extend nucleophilic or electrophilic reactivity through conjugated π-systems. They applied this principle to aldol reactions using dienol ethers, resulting in catalytic enantioselective vinylogous aldol methods with control over regio-,enantio-, and diastereoselectivity (Denmark et al., 2005).

Design Principles for Asymmetric Aldol Catalysts:
Saito et al. (2004) found that bifunctional acid-base catalysts, specifically diamine-Brønsted acid systems, improve asymmetric direct aldol reactions by combining strong acidic sites with cooperative hydrogen-bond networks that stabilise transition states, resulting in improved reactivity and selectivity (Saito & Yamamoto, 2004).

6.2. Biomass Conversion and Renewable Fuels

Aldol condensation processes are critical for the conversion of platform molecules (furfural, hydroxymethylfurfural, and levulinic acid) into sustainable fuels and chemicals.

Furfural-Based Aldol Condensations:
C8–C15 fuel intermediates are produced when furfural, a chemical originating from lignocellulosic biomass, combines with ketones via aldol condensation.

Ao et al. (2019), KF/γ-Al_2O_3 is a very effective solid-base catalyst for the aldol condensation of furfural with cyclopentanone, yielding up to 95.4% of the C_1ß fuel precursor F2C at 333 K in 2 hours with almost 100% product purity under ideal circumstances (Ao et al., 2019).

Li et al. (2019), cerous phosphate catalysts perform differently in the aldol condensation of furfural with acetone. The hexagonal phase achieved 89.1% furfural conversion with 42% and 17.5% yields of FAc and F_2Ac, respectively, while calcined monoclinic CP improved conversion up to 96% and total aldol product yield to 68.4% due to increased acidity. This highlights the strong influence of catalyst structure and calcination on activity and yield (Li et al., 2019).

Tišler et al. (2023) found that MgAl mixed oxide catalysts enable aldol condensation of furfural and acetone with total furfural conversion (100%) up to 28 h, but activity decreases to ~40% after 94 h. Adding 5 wt.% water boosted FAc selectivity by ~10% but accelerated catalyst deactivation. Increasing the furfural-to-acetone ratio (1:2.5 → 1:5) extended catalyst lifetime and enhanced FAc selectivity while reducing F_2Ac production by ~8% (Tišler et al., 2023).

Renewable Jet Fuel and Diesel Precursors:
Liu et al. (2018) showed that aldol condensation of biomass-derived furfural species with cyclic ketones, catalysed by NaOH, yields important intermediates in >90% yield at 30 °C within 40 min. These intermediates can then be hydrogenated and hydrodeoxygenated to produce C13–C18 cycloalkanes (76% yield), indicating an effective path toward renewable diesel and jet fuel components (Liu et al., 2018).

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6.3. Industrial Applications

Aldol condensation processes have been used in numerous commercial applications, including fragrance synthesis, polymer synthesis, and fine chemical synthesis.

Jasminaldehyde Synthesis:

Hajek et al. (2015) found that jasminaldehyde is synthesised through cross-aldol condensation of heptanal and benzaldehyde over UiO-66 and UiO-66-NH_2 catalysts. Oxo-oxygen sites drive α-C-H deprotonation. The amino-functionalized UiO-66-NH_2 shows somewhat higher initial activity due to stronger adsorption and lower activation barriers. However, both catalysts approach equivalent activity after ~40 min. The -NH_2 groups may also increase side reactions such as imine production (Hajek et al., 2015).

Methyl Methacrylate Precursors:

Wang et al. (2015) found that catalyst performance in the aldol condensation of methyl acetate with formaldehyde for methyl acrylate synthesis is substantially dependent on support characteristics, with increased basicity enhancing methyl acrylate selectivity and acidity promoting acetone production. Mesoporous SiO_2-supported Cs catalysts showed high activity due to enhanced diffusion and reduced ester hydrolysis. This highlights the impact of acid-base characteristics and mass transfer on catalytic efficiency (Wang et al., 2015).

Ethanol-to-Butadiene Process:

Pomalaza et al. (2020) stated that the ethanol-to-butadiene process is a promising sustainable route for butadiene production, involving complex catalytic steps such as dehydrogenation, aldol condensation, and dehydration, but challenges in catalyst design and process efficiency must be addressed for industrial viability (Pomalaza et al., 2020).

Higher Alcohol Synthesis:

Slaa et al. (1992) proposed that higher alcohol synthesis over $Cu/ZnO/Al_2O_3$ catalysts occurs through an extended aldol condensation mechanism, with catalyst additives (e.g., alkali or Mn compounds) and reaction conditions influencing product distribution and selectivity (Slaa et al., 1992).

6.4. Vinylogous and Mukaiyama Aldol Reactions

Vinylogous and Mukaiyama aldol reactions are notable variants that expand the aldol reaction domain.

Stereoselective Acetate Aldol Reactions:

Ariza et al. (2011) demonstrated that stereoselective acetate aldol reactions using metal enolates allow for the efficient and controlled formation of complex molecules, with strategies involving chiral auxiliaries, Lewis acids/bases, and substrate-controlled approaches to achieve high stereoselectivity in natural product synthesis (Ariza et al., 2011).

Vinylogous Aldol Reactions:

Vinylogous aldol reactions position the nucleophilic centre γ to the carbonyl group, resulting in the synthesis of δ-hydroxy-α,β-unsaturated carbonyl compounds.

Denmark et al. (2005), the vinylogous principle underpins vinylogous aldol reactions. Conjugated π-systems extend reactivity to enable dienol ether-based transformations, allowing catalytic enantioselective synthesis with control over regio-,enantio-, and diastereoselectivity in complex molecule construction (Denmark et al., 2005).

Mukaiyama Aldol Reactions:

The Mukaiyama aldol reaction is a Lewis acid-catalysed addition of silyl enol ethers to aldehydes that has complementary reactivity and selectivity to classic aldol reactions.

Matsuo et al. (2013) stated that the Mukaiyama aldol reaction, a Lewis acid-promoted cross-aldol reaction of silyl enol ethers with carbonyl compounds, is a powerful method for constructing stereochemically complex molecules, with related boron and tin enolate strategies further expanding its synthetic utility (Matsuo & Murakami, 2013).

7. GREEN CHEMISTRY AND SUSTAINABILITY

Sustainability challenges are becoming more significant in aldol condensation chemistry, with an emphasis on green solvents, recyclable catalysts, renewable materials, and energy-saving procedures.

Green Solvents:

Sharma et al. (2007), activated hydrotalcite (Mg/Al = 3.5) is a highly effective base catalyst for propanal aldol condensation. It achieves 97% conversion with 99% selectivity to 2-methylpentenal at 100 °C in 10 h, with an activation energy of 58 kJ and good recyclability over six cycles with no significant loss of performance (Sharma et al., 2007).

Mestres (2004) emphasised that aldol reactions are cost-effective for producing β-hydroxy and α,β-unsaturated carbonyl compounds. However, achieving greener processes requires balancing selectivity with waste and hazard. Advancements include solvent-free conditions, aqueous media, ionic liquids, heterogeneous and biocatalysis, and alternative activation methods like microwaves (Mestres, 2004).

Tandem and Cascade Reactions:

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Chi et al. (2008) found that an enzyme-like polymer catalyst based on hyperbranched polyethyleneimine-proline can suppress unwanted self-aldol reactions of enolizable aldehydes, allowing for highly selective cross-aldol reactions in water without excess reactants and achieving near-quantitative yields of α,β-unsaturated ketones through a controlled dynamic catalytic environment (Chi et al., 2008).

Strohmann et al. (2020) found that a multiphase tandem hydroformylation-aldol system with a Rh/sulfoXantphos catalyst and NaOH can efficiently convert 1-pentene to aldol products, with excellent recyclability over nine runs (TON ≈ 8700) and minimal rhodium leaching (~0.07% per run), highlighting the robustness of integrated catalytic processes (Strohmann et al., 2020).

Evans et al. (2018) stated that organocatalysis has evolved into a powerful and ecologically benign method for C-C bond production, including aldol reactions, with advancements enabling cascade and domino processes for the efficient synthesis of biologically relevant chemicals (Evans & Davis, 2018).

Schober et al. (2022) report that stereoselective synthesis of 1,3-diols is made possible by chemoenzymatic flow cascades that combine organocatalytic aldol reactions with biocatalytic reduction. In tandem systems, this results in 51% conversion with >99% ee and 8:1 d.r. and up to 76% conversion and 64% yield in sequential processes with >99% ee (Schober et al., 2022).

To provide a clearer comparative understanding of the catalytic systems employed in aldol condensation reactions, Table 1 summarises the catalytic performance, mechanistic characteristics, sustainability parameters, and industrial applicability of major catalyst classes reported in recent literature. In addition to conventional catalytic activity and selectivity data, the table incorporates important practical and green chemistry parameters such as catalyst recyclability, turnover number/turnover frequency (TON/TOF), catalyst stability, atom economy, E-factor considerations, energy efficiency, and scalability potential. This comparative presentation enables more critical evaluation of the advantages and limitations associated with heterogeneous catalysts, bifunctional acid–base systems, MOFs, organocatalysts, and hybrid multifunctional catalysts.

Table 1: Comparative analysis of major catalytic systems employed in aldol condensation reactions, highlighting catalytic activity, selectivity, turnover number/turnover frequency (TON/TOF), catalyst recyclability, operational stability, green chemistry metrics, industrial scalability, mechanistic advantages, and key limitations associated with heterogeneous catalysts, bifunctional acid–base systems, metal–organic frameworks (MOFs), organocatalysts, and hybrid catalytic platforms.

Catalyst System	Representative Catalyst	Catalytic Activity / Yield	Selectivity	TON / TOF	Recyclability	Catalyst Stability	Green Chemistry Metrics	Industrial Scalability	Major Advantages	Key Limitations	Ref.
Heterogeneous Base Catalysts	Modified CaO	~95.8% yield in cyclohexanone–benzaldehyde condensation within 3 h	High selectivity toward cross-aldol products	Moderate to high TOF	Reusable for multiple cycles	Good resistance to CO_2 and moisture after surface modification	Reduced solvent usage; low waste generation; improved atom economy	High	Low cost, easy separation, continuous-flow compatibility	Catalyst deactivation by coking and excessive basicity-induced side reactions	(Tang et al., 2013)
Metal Oxide Catalysts	FeO–MgO mixed oxide	Up to 66% yield for 2-pentylidene cyclopentanone	Good cross-condensation selectivity	Moderate	Moderate recyclability	Stable under atmospheric conditions	Lower E-factor than homogeneous bases	Moderate to high	Tunable acid–base properties	Limited selectivity at excessive basicity	(Mäki-Arvela et al., 2019)
Hydrotalcite / LDH Catalysts	Mg–Al hydrotalcite	Higher pseudoionone yield than NaOH systems	Moderate to high	Moderate	Limited; regeneration often	Rapid deactivation by CO_2 exposure	Reduced hazardous waste; recyclable solid catalyst	Moderate	Tunable basicity and large surface area	Loss of activity after repeated cycles	(Abelló et al., 2008)

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Mixed Oxide Catalysts	Mg–Zr mixed oxide	>60% selectivity toward C13 aldol product	High for cross-condensation	Moderate	Reusable under aqueous conditions	Water-sensitive deactivation observed	Water-compatible catalytic system	Moderate	Balanced medium-strength basic sites	Activity decreases in presence of excess water	(Faba et al., 2012)
Bifunctional Acid–Base Catalysts	TiO_2 acid–base pair catalyst	High condensation rates for oxygenates	Improved regioselectivity	High TOF	Good	Excellent resistance to catalyst poisoning under optimised conditions	Lower energy demand due to mild reaction conditions	High	Cooperative donor–acceptor activation; enhanced efficiency	Precise site arrangement required	(Wang et al., 2016)
Amine-Functionalized Catalysts	Silica-supported secondary amines	Efficient gas-phase n-butanal condensation	High selectivity toward desired enamine pathway	Moderate to high	Good catalyst recovery	Stable up to ~473 K	Reduced solvent demand and milder conditions	Moderate	Synergistic amine–silanol interactions	Imine formation with primary amines	(Shylesh et al., 2014)
Barium–Lanthanum Catalysts	Ba–La/Al_2O_3	Stable vapour-phase methyl acetate condensation over 300 h	High methyl acrylate selectivity	High TON	Good long-term reuse	Excellent resistance to carbon deposition	Long catalyst lifetime reduces process waste	High	Enhanced operational durability	Preparation complexity	(Bao et al., 2017)
MOF Catalysts	UiO-66 and UiO-66-NH_2	Efficient cross-aldol condensation of aldehydes and ketones	High due to pore confinement effects	Moderate to high	Moderate	Sensitive under strongly acidic/basic conditions	Mild reaction conditions; reduced solvent consumption	Moderate	Tunable pore architecture and Lewis acid–base sites	High synthesis cost and hydrothermal instability	(Hajek et al., 2015; Vermoortele et al., 2011)
Organocatalysts	L-proline	High enantioselective aldol efficiency under mild conditions	Excellent stereoselectivity and enantioselectivity	Moderate	Limited in homogeneous systems	Generally stable under mild conditions	Metal-free catalysis; environmentally benign	Moderate	Exceptional asymmetric induction	Higher catalyst loading and longer reaction times	(Heravi & Asadi, 2012; Valapil et al., 2021)

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Polymer-Supported Organocatalysts	PEG-supported proline	Good catalytic conversion with retained stereoselectivity	High enantiomeric excess	Moderate	Improved recyclability compared with homogeneous organocatalysts	Good under mild conditions	Reduced catalyst waste and easier separation	Moderate	Combines stereoselectivity with catalyst recovery	Lower activity than homogeneous analogues	(Benaglia et al., 2001)
Copper Peptide Catalysts	Cu(II)-histidine tetrapeptides	High asymmetric aldol activity	Up to 95.5% ee	Moderate	Moderate	Stable coordination framework	Reduced transition-metal usage	Low to moderate	Excellent asymmetric catalysis	Complex synthesis and cost	(Zaithun et al., 2018)
Zeolite-Based Catalysts	Cs^+/β-zeolite	Efficient self- and cross-aldol condensation	Excellent selectivity	High TOF	Highly reusable	Good thermal stability	Environmentally benign heterogeneous catalysis	High	Unique confined-channel mechanism	Diffusion limitations in microporous systems	(Ghosh et al., 2022)
Biomass Conversion Catalysts	KF/γ-Al_2O_3	Up to 95.4% yield of C15 fuel precursor	Near-complete product purity	High	Good	Stable under optimised conditions	Supports renewable fuel synthesis and biomass valorisation	High	Excellent for sustainable fuel intermediates	Catalyst deactivation under prolonged aqueous exposure	(Ao et al., 2019)
Hybrid Multifunctional Catalysts	Organosiliceous bifunctional catalysts	High tandem aldol–hydrogenation efficiency	High product selectivity	High TON	Reusable in continuous-flow systems	Good long-term stability	Integrated cascade reactions reduce waste and energy use	High potential	Combines multiple catalytic functions in one system	Synthetic complexity and optimization challenges	(Strohmann et al., 2020)

Abbreviations: TON = turnover number; TOF = turnover frequency; MOF = metal–organic framework; LDH = layered double hydroxide.

The comparative analysis presented in Table 1 demonstrates that each catalytic platform possesses distinct mechanistic and operational advantages, but also exhibits specific limitations that influence practical applicability. Heterogeneous catalysts and bifunctional systems provide superior catalyst recoverability, operational stability, and industrial scalability, whereas organocatalysts offer exceptional stereoselectivity under environmentally benign conditions. MOF-based catalysts exhibit remarkable mechanistic control and shape-selective catalysis due to their tunable pore architecture and well-defined active sites; however, their industrial implementation remains limited by synthesis cost and stability concerns. Overall, the comparison highlights that future development of aldol condensation catalysts should focus on multifunctional and hybrid catalytic systems capable of integrating high catalytic efficiency, stereoselectivity, recyclability, low energy consumption, and improved sustainability metrics to achieve industrially viable green catalytic processes.

8. DISCUSSION

Recent advances in aldol condensation catalysis show a distinct shift from traditional stoichiometric approaches to highly designed catalytic platforms that combine mechanistic precision, sustainability, and industrial applicability. Contemporary catalyst development is increasingly driven by the need to achieve high catalytic activity, substrate

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versatility, stereoselectivity, operational stability, catalyst recyclability, and low environmental impact, especially in the context of biomass valorisation and green synthetic chemistry (Biesemans et al., 2024; Perrin & Kim, 2022; Zhang et al., 2023). A comparative analysis of the catalytic systems discussed in this review reveals that catalytic performance is determined not only by intrinsic catalyst composition, but also by the cooperative interaction of active-site architecture, pore confinement effects, substrate diffusion, and transition-state stabilisation mechanisms (Oliphant et al., 2024; Tampieri et al., 2022).

Heterogeneous catalysts, among the catalytic systems used in aldol condensation reactions, remain particularly appealing for commercial implementation due to their operational simplicity, ease of catalyst separation, recyclability, and compatibility with continuous flow processing (Climent et al., 2002; Tang et al., 2013). Metal oxides, hydrotalcites, zeolites, and mixed oxide catalysts have strong catalytic activity and moderate-to-high selectivity, particularly in biomass-derived aldol conversions with furfural, acetone, and cyclic ketones (Faba et al., 2012; Mäki-Arvela et al., 2019; Patil et al., 2025). These catalysts accelerate aldol condensation by facilitating α-hydrogen abstraction and enolate production on basic sites, followed by nucleophilic assault on carbonyl substrates stimulated by neighbouring acidic centres (Climent et al., 2002; Wang et al., 2016). As a result, the density, strength, and spatial arrangement of active acid-base sites, as well as pore structure and catalyst microenvironment, all have a significant impact on catalytic performance (Herrmann & Iglesia, 2017; Wang et al., 2016). Modified CaO catalysts improve catalytic activity, stability, and resistance to moisture and CO_2 poisoning by stabilising active basic centres (Tang et al., 2013). Hydrotalcite-derived catalysts have superior conversion efficiency and recyclability due to their tunable layered structures and balanced acid-base properties (Abelló et al., 2008; Faba et al., 2012; Hernández et al., 2017; Tichit et al., 2003). In terms of sustainability, heterogeneous catalytic systems offer significant advantages over homogeneous catalytic processes, such as increased atom economy, reduced solvent requirements, enhanced catalyst reuse, and lower process E-factor values (Bargujar & Ratnani, 2022; Mestres, 2004). However, excessive basicity typically promotes uncontrolled self-condensation, side-product production, and oligomerisation processes, lowering selectivity for desired cross-aldol products (Tichit et al., 2003). Catalyst deactivation due to coking, pore obstruction, and active-site leaching remains a significant restriction during long-term industrial operation (Herrmann & Iglesia, 2017; O'Neill et al., 2014).

Bifunctional acid-base catalysts are a mechanistically advanced catalytic platform because they concurrently activate nucleophilic donor and electrophilic acceptor molecules via cooperative catalytic interactions (Climent et al., 2002; Wang et al., 2016). Catalysts with properly distributed acidic and basic sites enhance catalytic activity, regioselectivity, and operational stability by enabling synchronised enolate formation and carbonyl activation (Saito & Yamamoto, 2004; Shylesh et al., 2014). Mechanistically, adjacent acid-base centres stabilise transition-state intermediates and lower activation energy barriers for C-C bond formation, improving catalytic efficiency and product selectivity (Wang et al., 2016). Amine-functionalized silica catalysts, for example, have increased aldol activity because secondary amine groups produce reactive enamine intermediates, whereas neighbouring silanol groups stabilise electrophilic carbonyl substrates via hydrogen bonding interactions (Shylesh et al., 2014). Such cooperative activation routes enhance substrate compatibility and catalytic effectiveness at very mild reaction conditions, lowering energy consumption and increasing process sustainability. Furthermore, inhibition of extremely strong acidic sites has been demonstrated to minimise coke production and increase catalyst durability over multiple catalytic cycles(Bao et al., 2017). Despite these improvements, catalytic effectiveness is nevertheless heavily reliant on the precise spatial arrangement, closeness, and relative strength of acid-base sites, making rational catalyst design and tuning especially difficult (Climent et al., 2002; Wang et al., 2016). This emphasises the growing significance of modern computational modelling and operando characterisation techniques for comprehending active-site cooperativity and catalyst structure-performance correlations (Migues et al., 2014).

Metal-organic frameworks (MOFs) have developed as very complex catalytic materials due to their extremely large surface area, adjustable pore topologies, and structurally defined active sites. MOF catalysts like UiO-66 and UiO-66-NH_2 promote aldol condensation through synergistic Lewis acid-base interactions in restricted pore settings. The catalytic mechanism activates carbonyl substrates at unsaturated metal centres. Oxo-oxygen atoms enable α-C-H abstraction and enolate synthesis. Amino functionalization improves catalytic efficacy by lowering activation barriers, optimising substrate orientation, and stabilising transition-state intermediates within the porous framework. The constricted pore environment also influences substrate transport, shape selectivity, and catalytic microenvironment effects, which all contribute to enhanced selectivity and mechanistic control. Nonetheless, amino-functionalized MOFs may promote undesired side reactions such as imine production under certain reaction circumstances. MOFs also have significant sustainability benefits, such as improved catalyst recoverability, fewer solvent requirements, and efficient catalytic performance under relatively mild settings, resulting in lower process energy demand. However, larger industrial deployment is hampered by relatively high synthesis costs, hydrothermal instability, and low durability in strongly acidic or basic environments (Hajek et al., 2015; Vermoortele et al., 2011). Framework deterioration following numerous catalytic cycles may harm long-term catalyst reuse efficiency and overall process sustainability, underlining the importance of developing more durable MOF designs and scalable synthetic techniques (Tampieri et al., 2022).

Organocatalysts, particularly proline-based catalytic systems, have revolutionised asymmetric aldol chemistry by allowing for extremely stereoselective carbon-carbon bond synthesis under moderate and ecologically friendly conditions. Organocatalytic aldol reactions often follow enamine-mediated activation routes, in which the catalyst combines with the donor carbonyl molecule to produce a chiral enamine intermediate (Al-Momani et al., 2023). This enamine then assaults the electrophilic carbonyl substrate via a highly organised cyclic transition state, which

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determines the stereochemical result and enantioselective control (Valapil et al., 2021; Yamashita et al., 2018). The stereoselectivity of proline-catalysed aldol processes is principally due to hydrogen bonding interactions, steric shielding, and preferred transition-state stabilisation (Heravi & Asadi, 2012; Valapil et al., 2021). Polymer-supported and recyclable organocatalysts enhance catalyst recoverability and operational sustainability while retaining strong stereoselectivity. Furthermore, aqueous and solvent-free organocatalytic systems greatly improve green chemistry metrics by reducing reliance on toxic solvents and transition metals, resulting in less waste and better atom economy (Mestres, 2004; Mlynarski & Baś, 2014; Sharma et al., 2007). These systems usually run at ambient or low temperatures, helping to reduce energy consumption and increase environmental compatibility. However, when compared to heterogeneous and bifunctional catalytic systems, organocatalysts frequently necessitate high catalyst loading, longer reaction durations, and substantial substrate-specific tuning (Heravi & Asadi, 2012; Pansare & Paul, 2011). Catalyst recovery and recyclability remain challenges for several homogeneous organocatalytic systems, restricting their large-scale commercial applicability and increasing process E-factor values (Benaglia et al., 2001).

Mechanistic and computational studies have made significant contributions to understanding catalytic behaviour and directing rational catalyst design in aldol condensation chemistry. DFT studies found that elementary reaction steps, transition-state stability, and catalyst microenvironment effects all have a significant impact on catalytic efficiency and selectivity. Computational studies on zeolites and MOFs demonstrated that pore geometry and active-site confinement have a significant impact on adsorption energies, enolate stabilisation, and activation barriers (Hajek et al., 2015; Migues et al., 2014). Mechanistic investigations on TiO_2 and bifunctional catalysts show that α-C-H bond cleavage and enolate production are key rate-determining events in heterogeneous aldol condensation reactions (Wang et al., 2016; Young et al., 2016). Such insights are especially useful for developing next-generation catalysts with better active-site shape, increased stability, and higher selectivity.
The rapid incorporation of aldol condensation chemistry into biomass valorisation and renewable fuel generation emphasises the industrial and environmental relevance of this change. Aldol condensation of biomass-derived platform molecules, such as furfural, hydroxymethylfurfural, levulinic acid derivatives, and cyclic ketones, allows for efficient generation of C_8-C_{15} fuel intermediates and sustainable diesel or aviation fuel precursors (Ao et al., 2019; Liu et al., 2018). In this context, catalyst stability, resistance to water-induced deactivation, and selective suppression of side reactions are especially relevant because biomass-derived feedstocks frequently contain oxygenated contaminants and a high water content. Future catalyst development must emphasise hydrothermal stability, multifunctionality, and compatibility with continuous-flow biomass conversion systems.

Overall, comparative analysis shows that no single catalytic platform meets all of the requirements for ideal aldol condensation processes, such as high catalytic activity, substrate versatility, stereoselectivity, operational stability, catalyst recyclability, environmental sustainability, low energy consumption, favourable atom economy, and industrial feasibility. As a result, current research is increasingly focused on multifunctional and hybrid catalytic systems that combine the benefits of heterogeneous catalysis, bifunctional activation, MOF confinement effects, and organocatalytic stereoselectivity to achieve better catalytic performance and sustainable process development. Future advances in aldol condensation chemistry will most likely rely on a better mechanistic understanding of active-site cooperativity, advanced computational catalyst design, operando spectroscopic investigations, quantitative sustainability assessment, and scalable catalyst engineering capable of bridging the gap between laboratory-scale efficiency and industrial implementation.

9. CONCLUSION

This review critically reveals that aldol condensation chemistry has advanced far beyond traditional carbon-carbon bond formation technology to become a highly complex and environmentally friendly catalytic platform. Unlike previous reviews, which focused primarily on isolated catalytic systems or asymmetric aldol methodologies, the current work provides a comprehensive and comparative evaluation of heterogeneous catalysts, bifunctional acid-base systems, metal-organic frameworks, organocatalysts, hybrid multifunctional catalysts, mechanistic investigations, computational modelling, and biomass-based applications within a single systematic framework. Correlating catalyst structure, active-site cooperativity, mechanistic pathways, sustainability measures, and industrial applicability has received special attention, resulting in a broader and more critical viewpoint on current achievements in aldol condensation research.

According to the findings, synergistic acid-base interactions, pore-confinement effects, catalyst microenvironment, and transition-state stabilisation all have a significant impact on catalytic efficiency and selectivity. Despite significant progress in stereoselective synthesis, catalyst recyclability, and biomass valorisation, practical implementation is still hampered by some limitations, including catalyst deactivation, hydrothermal instability, diffusion constraints, and industrial scalability challenges. Importantly, no single catalytic system currently meets all of the criteria for optimum aldol processes, emphasising the need for next-generation multifunctional and hybrid catalysts.

Future advancements in aldol condensation chemistry will be dependent on the combination of sophisticated catalyst engineering, operando mechanistic research, computationally guided catalyst design, and green process intensification technologies. Given its growing importance in pharmaceutical synthesis, fine chemicals, renewable fuels, and sustainable manufacturing, aldol condensation is predicted to remain a key transition in modern synthetic and industrial chemistry.

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DATA AVAILABILITY

All data supporting the findings of this study are derived from previously published articles, which are cited appropriately within the manuscript and listed in the reference section. As this work is a review article, no new experimental data were generated or analysed. Any additional information related to the literature selection and analysis process is available from the corresponding author upon reasonable request.

CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation.

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STATEMENT OF AI INVOLVEMENT

QuillBot and Grammarly were used solely to improve the language, grammar, spelling, punctuation, and readability of the manuscript. These tools were not used for literature searching, data collection, data analysis, interpretation of results, or generation of scientific content. All scientific concepts, critical analysis, interpretations, and conclusions were developed and verified by the authors, who take full responsibility for the accuracy and integrity of the manuscript.

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