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ARTICLE

Recent Progress in Catalytic Asymmetric Synthesis of Triarylmethanes

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Chiral triarylmethanes, with their unique three-dimensional spatial configuration, tunable electronic properties, and excellent functional group compatibility, have wide applications in fields such as the dye industry, materials science, and medicinal chemistry. Their catalytic asymmetric synthesis has become a research hotspot in the field of organic synthesis. This review provides a systematic summary of the research progress in the catalytic asymmetric synthesis of chiral triarylmethanes over the past two decades. The advancements are categorized into eight core strategies based on types of reaction and substrate, offering a comprehensive discussion on the evolution of synthetic methodologies for chiral triarylmethanes. Achievements for each strategy are elaborated on, with an elaboration focused particularly on the enantioselectivity, yield advantages, and potential for scale-up applications of reactions. The key features, catalytic systems, stereocontrol mechanisms, and synthetic merits of each strategy are highlighted and compared. The current challenges in this field are summarized, and the future development directions are prospected, providing a comprehensive reference for the development of new synthetic methods for chiral triarylmethanes and the design of function-oriented molecules.

1. Introduction

Triarylmethanes are a class of organic molecules with a core structure of "a central *sp*³ hybridized carbon atom connected to three aromatic rings (or heteroaromatic rings)". The structure of these compounds is highly malleable, and their physicochemical properties and functional activities can be regulated precisely by modifying the substituents on the aromatic rings (such as alkoxy, halogen, amino, etc.). So, owing to their unique three-dimensional spatial configuration, tunable electronic properties, and excellent functional group compatibility, triarylmethanes have emerged as highly valuable core scaffolds in the dye industry,[1] materials science[2] and medicinal chemistry.[3] Especially in medical science, they are considered as propitious contenders for pharmaceutical research (Figure 1a).[4]

However, numerous studies have witnessed that the biological activity of a molecule is dramatically influenced by its chirality. Therefore, the synthesis of chiral triarylmethanes has attracted much attention from the synthetic community, and catalytic asymmetric construction of chiral triarylmethanes has emerged as a vibrant research frontier in modern organic synthesis. Over the past two decades, diverse catalytic asymmetric strategies have been established for the efficient assembly of enantioenriched triarylmethanes. To provide an intuitive and clear overview of this field, the representative synthetic strategies are classified into eight categories and summarized in Figure 1b, including: (1) stereospecific cross-coupling reaction; (2) Friedel–Crafts type arylation of diarylmethanols and their derivatives; (3) organocatalytic asymmetric arylation of azadienes; (4) conjugate addition to quinonemethides (QMs); (5) desymmetrization reaction; (6) catalytic asymmetric hydrogenation; (7) asymmetric C–H arylation; and (8) other emerging methods.

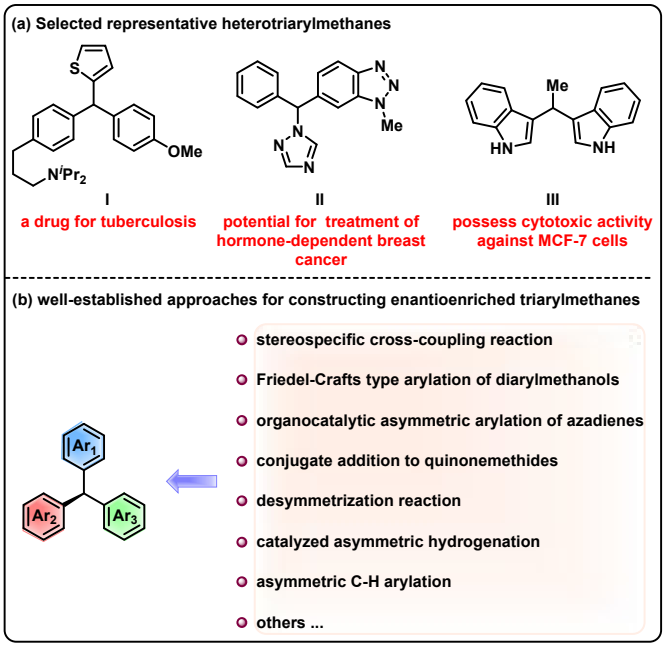

Figure 1. Selected representative triarylmethanes and summary of catalytic asymmetric strategies for chiral triarylmethanes.

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In addition, several reviews on the synthesis[5] and applications[6] of triarylmethanes have been documented. A 2017 review on the enantioselective synthesis of molecules containing dimethylmethylene stereocenters provided only a limited and incomplete overview of this topic. [7] Compared with existing reviews, which mainly focus on the general synthesis and applications of triarylmethanes or only provide limited coverage of asymmetric transformations, the present review is the first comprehensive, systematic, and critical overview dedicated to catalytic asymmetric synthesis of chiral triarylmethanes. This review not only classifies the strategies into eight categories by reaction types and substrate classes, with emphasis on synthetic efficiency, enantioselectivity, and scalability but also provides in-depth mechanistic discussion, critical evaluation of advantages and limitations, and integrated comparison of different methods. Furthermore, current challenges and future opportunities are also discussed, aiming to provide a valuable reference for developing novel asymmetric methods and function-oriented chiral triarylmethanes. Therefore, this review has distinctive novelty and will serve as a unique and valuable reference for researchers in this field.

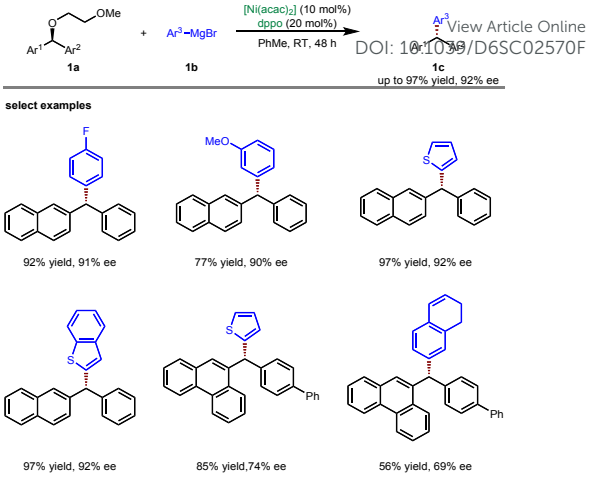
2. The Methods of catalytic asymmetric synthesis of triarylmethanes

2.1 Stereospecific cross-coupling reaction

The stereospecific cross-coupling reaction, a key strategy for constructing chiral triarylmethanes, operates via transition metal-catalyzed coupling of chiral benzyl electrophiles with aryl nucleophiles, efficiently building the triaryl stereocenter through C–C bond formation while rigorously retaining or selectively inverting the pre-existing chirality. Stereospecificity originates from stereospecific C–O bond cleavage and SN_2-type inversion or retention governed by ligand bite angle and metal coordination geometry. The chiral information is faithfully transferred via a closed-shell transition state without racemization.

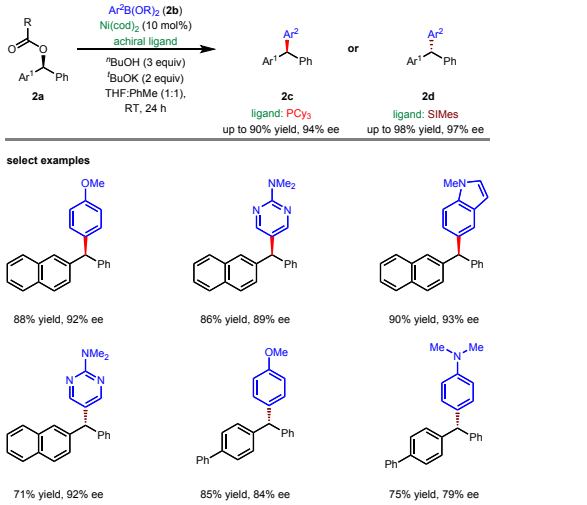
In 2012, Jarvo and co-workers achieved the synthesis of enantioenriched triarylmethanes by nickel-catalyzed stereospecific cross-coupling reaction (Scheme 1).[8] A variety of triarylmethanes **1c** were obtained in good yields (up to 97%) and high enantioselectivities (up to 92% ee) by nickel-catalyzed traceless directing C–O bond activation strategy. The substrates employed in this reaction were diarylmethanol derivatives **1a**, and such compounds can be readily synthesized via the asymmetric arylation of aldehydes. During the cross-coupling reaction, a wide variety of aryl Grignard reagents **1b** are applicable, and all these reactions proceed with high levels of enantiospecificity. This strategy provided a novel and powerful tool for the efficient construction of chiral triarylmethanes.

Then, in 2013, Jarvo and co-workers developed another nickel-catalyzed Suzuki-Miyaura cross-coupling method for the synthesis of enantioenriched triarylmethanes **2c** and **2d**, achieving good yields (up to 98% yield) and excellent enantioselectivities (up to 97% ee) (Scheme 2).[9] This method



Scheme 1. Synthesis of enantioenriched triarylmethanes by nickel-catalyzed stereospecific cross-coupling reaction.

was significant as it enabled stereodivergent synthesis from a single enantiomer of starting material through ligand control. In addition, because simple benzhydril pivalates **2a** and a variety of functionalized arylboronic esters **2b** (including ones containing heterocyclic groups) were all well-tolerated, this approach broadened the scope of enantioenriched triarylmethanes accessible via synthesis.



Scheme 2. Nickel-catalyzed Suzuki-Miyaura cross-coupling method for the synthesis of enantioenriched triarylmethanes.

In 2013, Watson and co-workers developed a stereospecific nickel-catalyzed cross-coupling of benzylic pivalates **3a** with arylboroxines **3b** for the synthesis of chiral triarylmethanes (Scheme 3).[10] This method provided the products **3c** in good to excellent yields (up to 96% yield) and enantiomeric excesses (up to 98% ee), with a broad scope for both coupling partners. The effective development of this reaction relied on the screening of $Ni(cod)_2$ as the optimal catalyst and NaOMe as an exclusively efficient base. The work provided a versatile strategy for accessing enantioenriched triarylmethanes that were key structural motifs in organic chemistry and highlighted the potential of nickel catalysis in stereospecific cross-couplings involving benzylic pivalates.

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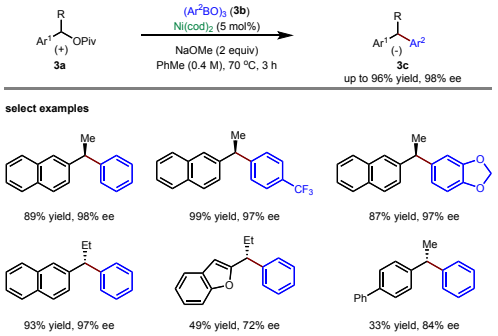
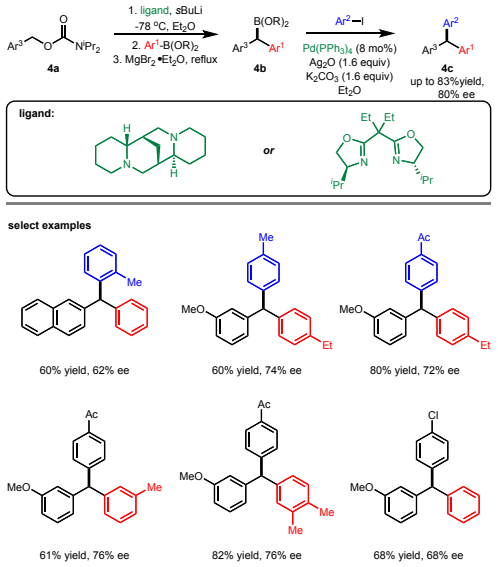


Scheme 3. Nickel-catalyzed cross-coupling of benzylic pivalates with arylboroxines.

In 2014, Crudden and co-workers developed the first enantioselective synthesis of dibenzylic boronic esters **4b** and the development of their palladium-catalyzed Suzuki-Miyaura cross-coupling with aryl iodides for synthesis of triarylmethanes (Scheme 4).[11] And the products **4c** were obtained with up to 100% enantiomeric retention (up to 80% ee) and yields of up to 83%.



Scheme 4. Pd-catalyzed Suzuki-Miyaura cross-coupling reaction for the synthesis of enantioenriched triarylmethanes.

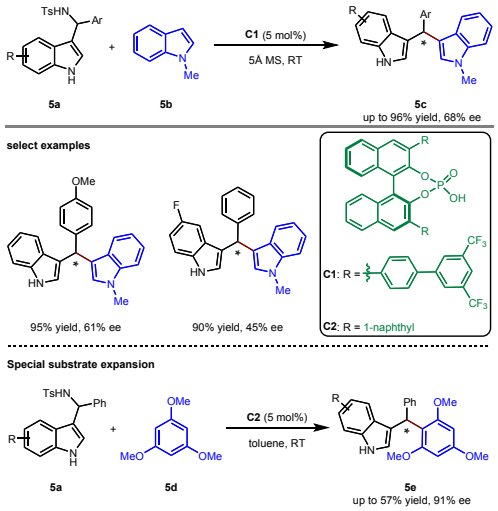
The stereospecific cross-coupling strategy offers high step economy and well-defined stereochemical logic, as chirality is pre-installed in the starting materials and faithfully transferred to the final products. Nevertheless, this approach still has several drawbacks, including its reliance on the pre-synthesis of enantiopure benzyl electrophiles, which increases synthetic steps and overall costs; its substrate scope is largely restricted to specific benzyl derivatives, thereby limiting the facile construction of triarylmethanes with three different aryl groups; additionally, most reactions require sensitive organometallic reagents such as Grignard reagents, which greatly restricts their scalability for industrial applications. In comparison to alternative strategies, this method is better suited for constructing specific chiral triarylmethane frameworks rather than serving as a general synthetic route.

2.2 Friedel–Crafts type arylation of diarylmethanols and their derivatives

The Friedel–Crafts arylation of diarylmethanols and their derivatives is one of the most well known strategies for synthesis of triarylmethanes. In recent years, there has been a substantial increase in research reports focusing on this approach. So far, a few protocols for the enantioselective synthesis of triarylmethanes have been developed via the Friedel–Crafts type reaction of diarylmethanols and their derivatives, where both the diversity and variety of catalytic systems have expanded significantly.

As documented in the literature, indolylmethanols and their derivatives represent the most widely utilized subclass of diarylmethanols[12] and derivatives in this strategy. Accordingly, impressive progress has been achieved in the catalytic asymmetric transformations of indolylmethanols.

The pioneering work in this field was reported by the You group in 2010. They developed an asymmetric synthesis method catalyzed by Chiral Brønsted acids **C1** and **C2** to provide enantioenriched unsymmetrical triarylmethanes (**5c** and **5e**) via Friedel–Crafts alkylation of electron-rich arenes (**5b** and **5d**) with (3-indolyl)methanamines (**5a**) (Scheme 5).[13] Excellent yields (up to 96%) and high enantioselectivities (up to 91% ee) were achieved for triarylmethanes with 5 mol% catalyst loading. Furthermore, this method had excellent compatibility with substrates of different electronic effects (donor electron, acceptor electron) and substitution positions, making up for the significant deficiency of the asymmetric triarylmethane catalytic synthesis methods at that time.



Scheme 5. Chiral Brønsted acid catalyzed Friedel–Crafts alkylation of electron-rich arenes with (3-indolyl)methanamines.

Subsequently, continuous advances have been made based on indolylmethanol-type substrates. In 2014, Han and co-workers developed the first chiral phosphoramide-catalyzed asymmetric reaction of indol-2-yl methanols with indole derivatives for the enantioselective synthesis of 2,3'-biindolylarylmethanes, a significant type of heterocyclic triarylmethane with potential anticancer activity (Scheme 6).[14] Employing the unsubstituted BINOL-derived chiral

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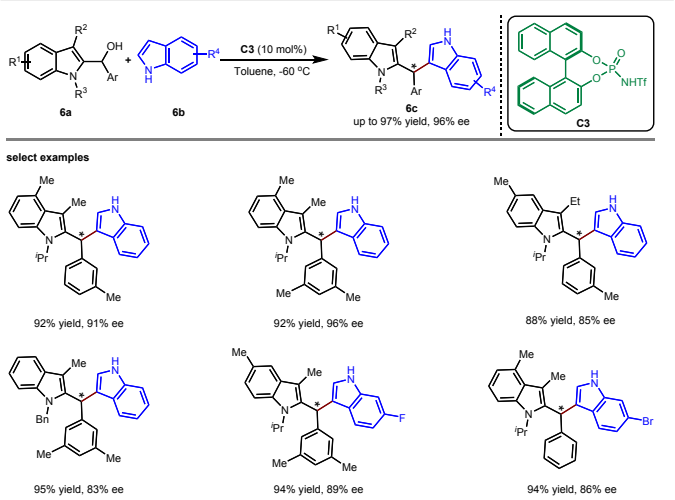
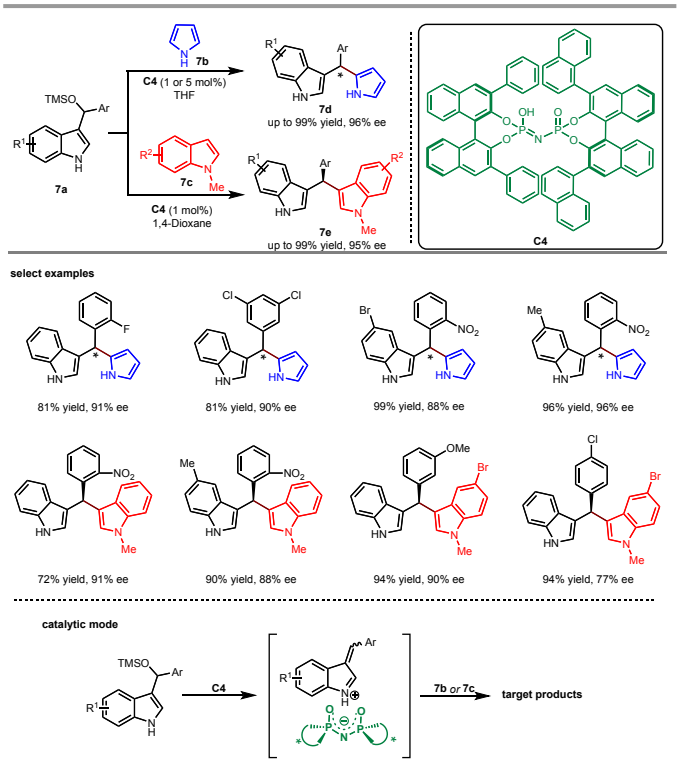
phosphoramide **C3** as the optimal catalyst (10 mol%) in toluene at –60 °C, the reaction achieved products up to 97% yield and 96% ee. The protocol featured a broad substrate scope, tolerating diverse substituents on both indol-2-yl methanol and indole nucleophile. Notably, water was generated as the sole byproduct, highlighting the atom economy and cleanliness of this transformation. Furthermore, the corresponding enantiomer could be readily accessed by employing the opposite catalyst configuration (*S*)-**C3**, thus providing a solid foundation for subsequent investigations into anticancer activity.



Scheme 6. Chiral phosphoramide-catalyzed enantioselective synthesis of chiral triarylmethanes.

In 2014, Zhang and co-workers reported, for the first time, the asymmetric Friedel–Crafts reaction catalyzed by chiral iminodiphosphoric acid, successfully achieving the efficient synthesis of two types of triarylmethanes: one being pyrrole-substituted triarylmethanes **7d** (before then lacking asymmetric synthetic methods) and the other being bisindole-substituted triarylmethanes **7e** (before then only obtainable with moderate ee values) (Scheme 7).[15] This reaction employed a novel iminodiphosphoric acid catalyst **C4**, derived from two (*R*)-BINOL skeletons (with different 3,3'-substituents), characterized by low catalyst loading (as low as 1 mol%) and broad functional group compatibility. The yield of the target products could reach up to 99%, the enantiomeric excess of the pyrrole-substituted type was up to 96%, and the enantiomeric excess of the diindolyl-substituted type was up to 95%. In the reaction, the chiral imidodiphosphoric acid catalyst promoted dehydration of the trimethylsilyl(TMS)-protected indolylmethanols **7a** to generate an alkylideneindolenine cation intermediates. These intermediates formed a tight chiral ion pairs with the catalyst's bisphosphate anion, which created a confined chiral microenvironment. The nucleophiles (pyrrole or indole) then attacked the less hindered face of the ion pairs, affording chiral triarylmethanes with high regio- and enantioselectivity. The asymmetric bis(BINOL) backbone of the catalyst enabled stronger hydrogen-bonding interactions and superior stereocontrol compared with conventional monophosphoric acid. Additionally, gram-scale synthesis was achieved, providing a practical pathway for the preparation of biologically active triarylmethanes.



Scheme 7. Chiral imidodiphosphoric acids catalyzed Friedel–Crafts reactions for synthesis of chiral triarylmethanes.

In 2015, Shi and co-workers established a chiral phosphoric acid (CPA) catalyzed asymmetric arylation reaction of 3-indolylmethanols (Scheme 8).[16] This reaction employed isatin-derived 3-indolylmethanols **8a** and 3-methylindoles **8b** to synthesize biologically active 3,3'-bisindolyloxindoles (containing stereocenter of quaternary carbon), a significant type of heterocyclic triarylmethane, via an atom-economical pathway. Under optimized conditions (10 mol% CPA **C5**, dichloromethane, –10 °C), the target products were obtained in excellent yields (up to 99%) with high enantioselectivities (up to 82% ee). Control experiments confirmed that the NH group of the indolyl ring of 3-indolylmethanol was crucial for improving the enantiomeric selectivity, while the NH group of 3-methylindole determined the reactivity through hydrogen bonding with the catalyst. And a plausible mechanism was proposed. CPA **C5** promoted dehydration of 3-indolylmethanols to form a vinyliminium intermediates, which were stabilized via ion-pairing and hydrogen bonding. At the same time, 3-methylindoles were activated by hydrogen bonding between their NH group and the P=O group of **C5**. The bifunctional CPA catalyst thus enabled dual activation of both reaction partners. Enantioselective 1,4-addition then taked place under stereocontrol from the chiral BINOL framework, generating the (*R*)-configured quaternary stereocenter. Proton transfer afforded the chiral 3,3′-bis(indolyl)oxindoles with water as the sole byproduct. This method exhibited a broad substrate scope and provided an efficient strategy for synthesizing

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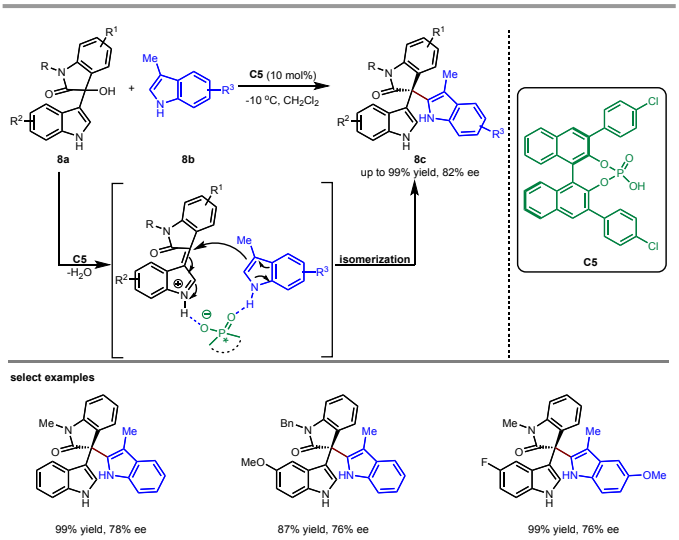
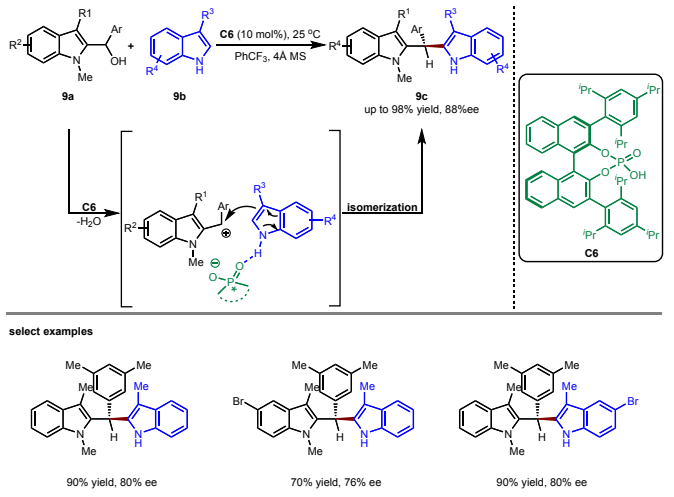
enantiomeriched 3,3'-bisindolyloxindoles, with potential applications in chemical biology and drug discovery.



Scheme 8. Catalytic asymmetric arylation of 3-indolylmethanols.

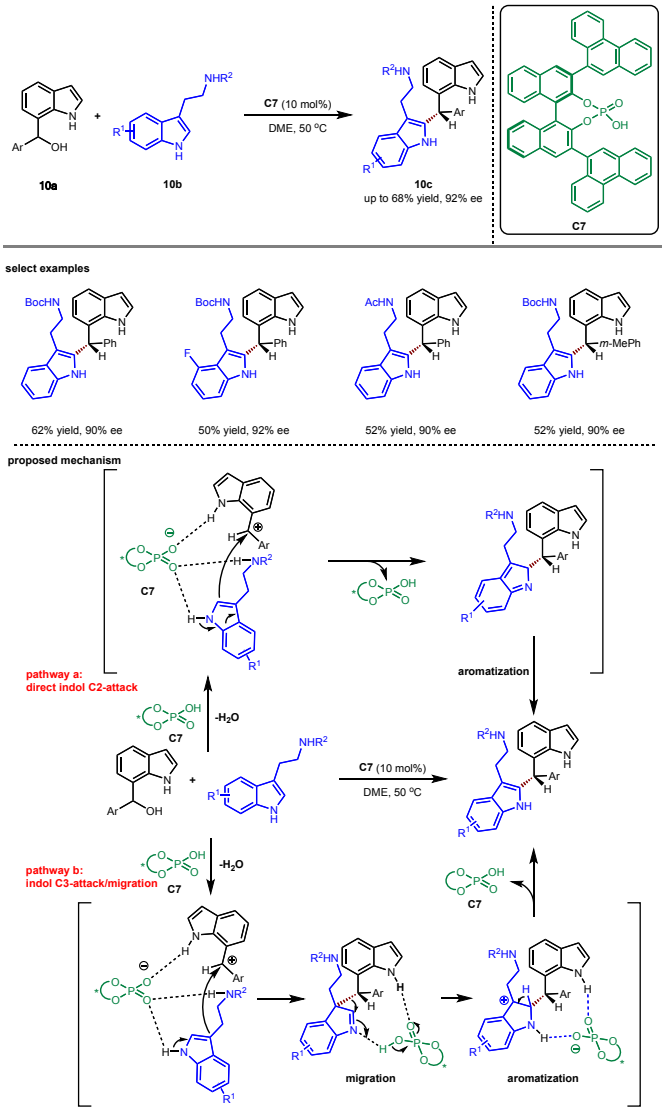
In 2015, Shi and co-workers established an asymmetric reaction between 2-indolylmethanols **9a** and 3-alkylindoles **9b** catalyzed by a CPA, enabling the efficient construction of biologically active 2,2'-biindolylmethane skeletons **9c** (Scheme 9).[17] The optimal catalyst was identified as BINOL-derived chiral phosphoric acid **C6** bearing a bulky 2,4,6-triisopropylphenyl (trip) group. Under mild conditions (10 mol% catalyst, trifluorotoluene as solvent, 25 °C, 4 Å molecular sieves), the reaction afforded the desired products in excellent yields (up to 98%) with high enantioselectivity (up to 88% ee). The process was successfully scaled up to gram-scale. Mechanistic studies revealed that activation occured via hydrogen bonding between the N–H group of the 3-alkylindole and the CPA catalyst. A plausible catalytic cycle was proposed wherein CPA **C6** promoted the dehydration of 2-indolylmethanols to generate 2-indolyl carbocation intermediates. These intermediates were stabilized via ion-pairing with the catalyst. Concurrently, CPA **C6**



Scheme 9. Chiral phosphoric acid-catalyzed asymmetric reactions of 2-indolylmethanols with 3-alkylindoles.

activated 3-alkylindole through N–H···O hydrogen bonding involving its P=O group. Under the stereocontrol dictated by the chiral BINOL–Trip framework, an enantioselective nucleophilic addition occured, followed by protonation to yield the (*S*)-2,2'-bisindolylmethane products. This work provided a key strategy for asymmetric transformations involving 2-indolylmethanols and addressed a significant gap at the time in the enantioselective synthesis of 2,2'-biindolylmethanes.

In 2018, a novel catalytic asymmetric arylation reaction for construction of triarylmethanes **10c** were developed by Shi, Mei and co-workers.[18] Under the optimized conditions (10 mol% CPA **C7**, which featured a 9-phenanthryl group at the 3,3'-positions, in DME at 50 °C), the target products were obtained in moderate yields (up to 68%) with excellent enantioselectivities (up to 92% ee) (Scheme 10). The control experiments confirmed that the NH groups of 7-indolylmethanol and tryptamine form hydrogen bonds with the catalyst, determining the reactivity and enantiomeric selectivity of the reaction. The reaction also involved a kinetic resolution



Scheme 10. Chiral phosphoric acid-catalyzed enantioselective arylation reaction between 7-indolylmethanols with tryptamines.

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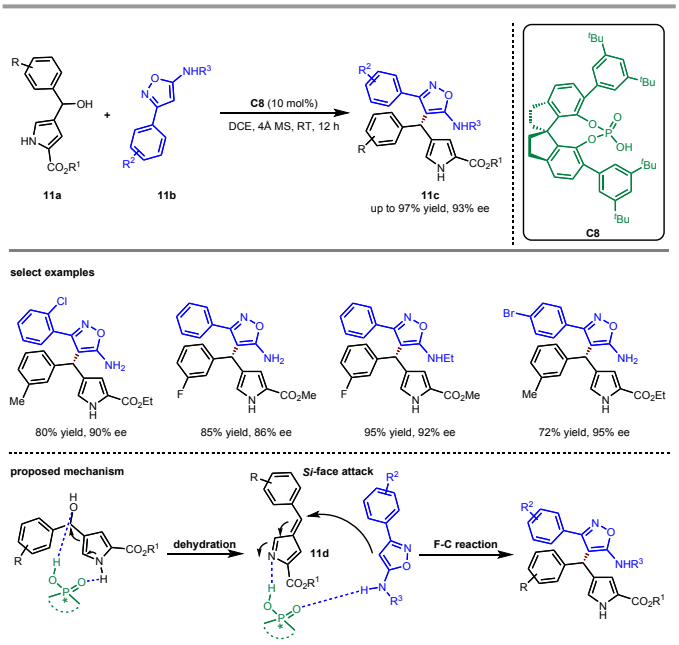
of the 7-indolylmethanol (the recovered starting material had 94% ee) and was scalable to a 1 mmol reaction. In detail, CPA **C7** catalyzed the dehydration of 7-indolylmethanols to form stabilized carbocation intermediates via ion-pairing and hydrogen-bonding. Simultaneously, the catalyst activated tryptamines through N–H···O hydrogen bonding to enable enantioselective addition. The reaction proceeded via either direct C2-attack or tandem C3-attack/migration, followed by aromatization to afford enantioenriched (*S*)-7-indolylmethanes. This work provided a novel strategy for the chiral synthesis of triarylmethanes and enriched the application of indolylmethanols.

Besides indolylmethanols, 1*H*-pyrrol-3-ylmethanols (which can dehydrate to form 3-methylene-3*H*-pyrroles) have also emerged as another highly valuable and frequently employed substrate class in this strategy. These reactive intermediates exhibit excellent reactivity toward various electron-rich arenes, enabling the efficient construction of structurally diverse chiral hetero-triarylmethanes.

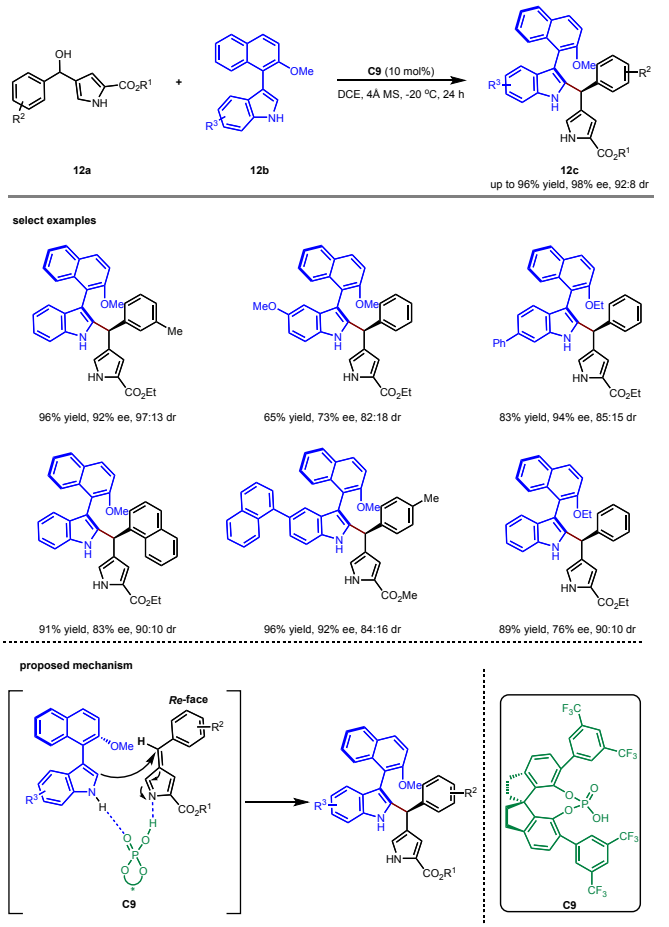
In 2023, Lin and co-workers developed a asymmetric Friedel–Crafts reaction to synthesize hetero-triarylmethanes catalyzed by a chiral spiro phosphoric acid (Scheme 11).[19] In this work, the efficient synthesis of chiral hetero-triarylmethanes containing an amino acid motif **11c** via the reactions of 3-aryl-isoxazol-5-amines **11b** with *in situ* generated 3-methylene-3*H*-pyrroles (formed by dehydration of 1*H*-pyrrol-3-ylmethanols **11a**). The optimal conditions were established as follows: 10 mol% of **C8** as the catalyst, dichloroethane (DCE) as the solvent, 4Å molecular sieves as additive, and a reaction time of 12 hours at room temperature. Under these conditions, the target products were obtained in excellent yields (up to 97%) with high enantioselectivities (up to 93% ee). Furthermore, the reaction was scalable (1 mmol) and the enantioselectivity was retained after hydrolysis of product. Mechanistic studies confirmed that



Scheme 11. Asymmetric Friedel–Crafts reaction for synthesis of hetero-triarylmethanes catalyzed by chiral spiro phosphoric acid.

the NH group of the 3-aryl-isoxazol-5-amine regulated both reactivity and enantioselectivity by forming a hydrogen bond with the catalyst, whereas 4 Å MS improved enantiocontrol by trapping water. Firstly, CPA **C8** promoted the dehydration of 1*H*-pyrrol-3-yl carbinols to form reactive 3-methide-3*H*-pyrrole intermediates. The **C8** also activated 3-arylisoxazol-5-amines via dual hydrogen bonding, enabling enantioselective Friedel–Crafts addition to the *Si*-face of the pyrrole methides. The resulting stereocontrol afforded (*S*)-heterotriarylmethanes with an amino acid moiety. This work provided an efficient and scalable route for synthesizing chiral hetero-triarylmethanes bearing isoxazole and pyrrole skeletons.

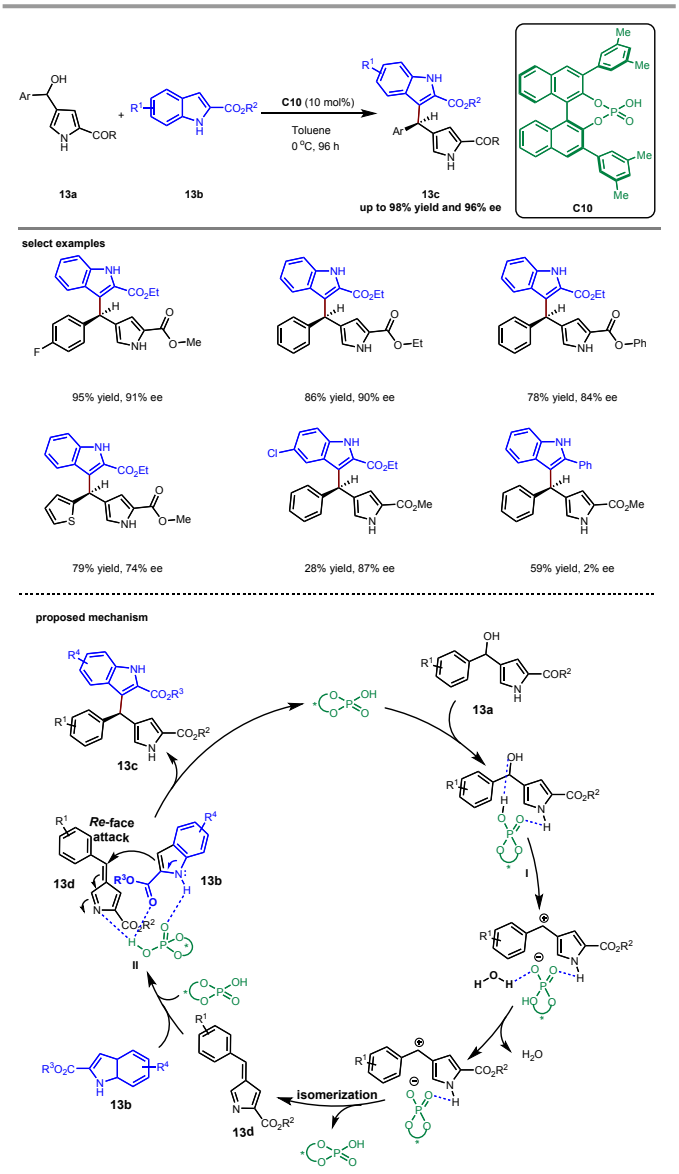
In 2025, Lin and co-workers reported a CPA-catalyzed enantioselective Friedel–Crafts reaction between C2-unsubstituted naphthyl-indoles **12b** and racemic *in situ* generated 3-methylene-3*H*-pyrroles from 1*H*-pyrrol-3-yl carbinols **12a** for construction of hetero-triarylmethanes containing axially chiral naphthyl-indole and centrally chiral pyrrole moieties **12c** (Scheme 12).[20] The target products were provided in good to excellent yields (62–96%), enantioselectivities (53–98% ee) and diastereoselectivities (82:18 to 92:8 dr) with **C9** as catalyst, 4 Å molecular sieves as additive in DCE at −20 °C for 24 hours. And a plausible mechanism was proposed. Firstly, the reactive 3-methide-3*H*-pyrrole intermediates were obtained by dehydration of 1*H*-



Scheme 12. Organocatalytic asymmetric synthesis of axially and centrally chiral heterotriarylmethanes by a Friedel–Crafts reaction.

pyrrol-3-yl carbinols with the catalysis of CPA **C9**. The catalyst simultaneously activated naphthyl-indoles via dual N–H···O hydrogen bonding, enabling enantioselective Friedel–Crafts addition to the *Re*-face of the pyrrole methides. This convergent process constructed both axial (naphthyl-indole) and central (pyrrole-bound carbon) chirality in a single step, affording (S_a, *S*)-heterotriarylmethanes. Free NH group was critical for activation and stereocontrol, and 4 Å MS enhanced enantioselectivity by trapping water. Notably, the efficiency was maintained even on a gram scale. Biological evaluation revealed that one of the products exhibited significant anti-proliferative activity against PC-3 prostate cancer cells, highlighting its potential as a lead compound in medicinal chemistry. Mechanistic studies confirmed that the free NH group in the substrate was crucial for the reaction.

In 2026, Our group developed an asymmetric Friedel–Crafts reaction catalyzed by chiral phosphoric acid **C10** (Scheme 13).[21] The reaction employed 1*H*-pyrrol-3-ylmethanols **13a** as substrates, which underwent *in situ* dehydration to generate 3-methylene-3*H*-pyrrole intermediates, followed by coupling with indoles **13b**. This protocol enabled the efficient construction of chiral triarylmethanes bearing three distinct aryl/heteroaryl moieties. The products were obtained in 14%–98% yields with up to 96% ee. Notably, triarylmethanes containing three different heteroaryl groups were synthesized for the first time using this strategy. The reaction may proceeded through a CPA-catalyzed dehydration of pyrrole carbinols to form 3-methide-3*H*-pyrrole intermediates. Simultaneously the catalyst activated both intermediates and indoles through a dual hydrogen-bonding. This arrangement directed the stereoselective nucleophilic attack of indoles at the *Re*-face of the intermediates. Following proton transfer, chiral heterotriarylmethanes were obtained with high ee values. Mechanistic studies reveal that free NH groups in both substrates were indispensable for catalysis; their absence completely inhibited the reaction. Furthermore, the reaction could be performed on a gram scale with retained stereoselectivity, providing a straightforward and versatile approach toward structurally diverse chiral hetero-triarylmethanes.



Scheme 13. Chiral Brønsted acid-catalyzed conjugate addition of indoles to azadienes.

This strategy features mild reaction conditions, excellent functional group compatibility, and high atom economy, making it the most widely adopted approach for constructing heteroaryl-substituted triarylmethanes. The chiral Brønsted acid catalysts enable efficient stereocontrol through hydrogen-bonding interactions, representing a green and cost-effective catalytic pathway. Nevertheless, several notable limitations remain: the substrate scope is largely restricted to electron-rich arenes such as indoles and pyrroles, with limited reactivity toward electron-deficient aryl nucleophiles; most reactions are confined to indolylmethanol or pyrrolylmethanol substrates, showing poor applicability to common diarylmethanols; and stereocontrol remains challenging for triarylmethanes bearing three similar aryl groups.

2.3 Organocatalytic asymmetric arylation of azadienes

Organocatalytic asymmetric arylation of aza-dienes is an efficient strategy for constructing chiral triarylmethanes. In this reaction, aryl-substituted aza-dienes serve as electrophiles and undergo enantioselective arylation with aryl nucleophiles (such as indoles, naphthols, and arylboronic acids) under the regulation of chiral organocatalysts. By precisely controlling the stereoconfiguration of C–C bond formation, the key chiral benzylic carbon center in triarylmethanes (i.e., the triaryl-substituted stereocenter) can be directly constructed. Among them, the chiral Brønsted acid catalytic system, which protonates the nitrogen atom of aza-dienes to generate stable chiral ion pair intermediates and further guides the enantioselective attack of nucleophiles, has become the most widely used catalytic mode in this field.

In 2019, Zhou and co-workers developed a chiral Brønsted acid-catalyzed conjugate addition of indoles **14b** to aza-dienes **14a** for synthesis of hetero-triarylmethanes **14c** (Scheme 14).[22] This transformation exhibited a broad substrate scope, tolerating various substituents at the 2-, 5-, and 7-positions of indoles as well as on the aryl ring of the aza-dienes. In the reaction, using (*R*)-TRIP CPA **C6** as the optimal catalyst,

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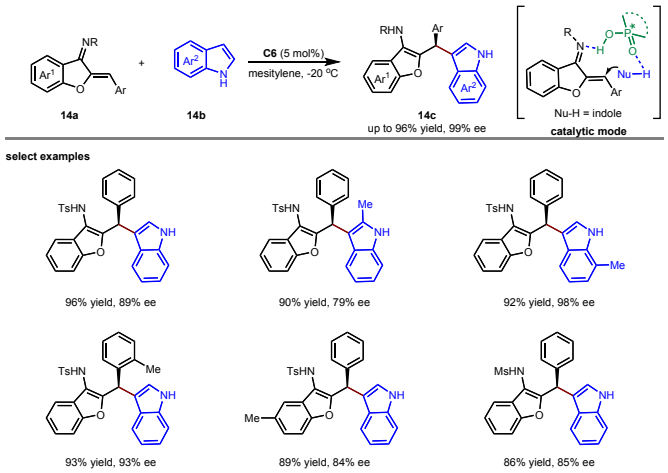
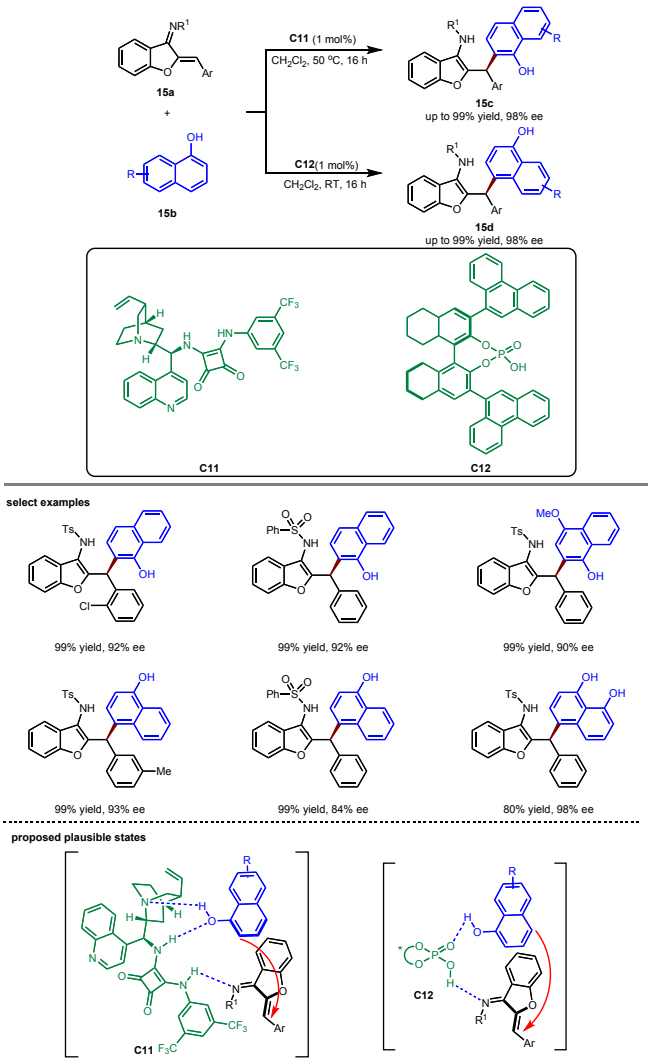
mesitylene as the solvent, and −20°C as the reaction temperature, 24 examples of chiral triarylmethanes were efficiently synthesized through a dual hydrogen bond activation mechanism. The target products were isolated in good to excellent yields (up to 96%) with high enantioselectivities (up to 99% ee). And the reaction could also be scaled up to gram scale. Furthermore, the products could be readily derivatized with excellent enantioselectivity retention. A plausible reaction mechanism was as follows: CPA **C6** simultaneously activated both azadienes and indoles through dual hydrogen-bonding interactions. The bulky substituents shield the *Si*-face of the azadienes, enabling the selective addition of indoles to the *Re*-face of the azadienes, finally affording the *S*-configured heterotriarylmethane products with high ee values. The free N–H group of indole was crucial for hydrogen-bond formation, as well as for maintaining the reactivity and enantioselectivity of the reaction. This work not only provided a novel strategy for synthesizing chiral hetero-triarylmethanes but also expanded the application of chiral Brønsted acid catalysis to asymmetric reactions of aza-dienes.



Scheme 14. Chiral Brønsted acid-catalyzed conjugate addition of indoles to azadienes.

In 2020, Li and co-workers established an organocatalyst-controlled site-selectivity switchable enantioselective Friedel–Crafts reaction of unprotected 1-naphthols **15b** via the conjugate addition of 1-azadienes **15a** to obtain triarylmethanes **15c** and **15d** (Scheme 15).[23] The reaction achieved selective alkylations at either the *ortho* (*o*-) or *para* (*p*-) position of 1-naphthols with 1-azadienes by employing two complementary catalysts (a chiral squaramide **C11** and a CPA **C12**). Under the squaramide-catalyzed system (dichloromethane, 50 °C), the **15c** were obtained in 66%–99% yields with excellent enantioselectivities (up to 98% ee). When using the chiral phosphoric acid system (dichloromethane, room temperature), the products **15d** were furnished in 73%–99% yields with up to 93% ee. This transformation was amenable to scale-up, successfully proceeding on a 2 mmol scale. Crucially, control experiments confirmed that the free hydroxyl group of 1-naphthol was essential for the regioselectivity switching. Mechanistic studies revealed that regioselectivity was governed by the nature of the chiral catalyst. Chiral squaramide activated substrates by a dual hydrogen-bonding between the hydroxyl group of 1-naphthols and the sulfonamide group of the azadienes. This interaction stabilized a transition state that enforced exclusive *ortho*-selectivity and through a chiral cavity effect, delivered the products with high enantioselectivity. Conversely, CPA operated via a combined protonation-hydrogen-bonding mode: protonating the azadienes while hydrogen-bonding to the naphthol hydroxyl. This switch in activation strategy redirected the nucleophilic attack to the *para*-position, achieving exclusive *para*-selectivity. This strategy provided an efficient and divergent route to chiral triarylmethanes, significantly expanding the application of organocatalytic regiodivergent asymmetric synthesis.



Scheme 15. Organocatalytic enantioselective regiodivergent C–H bond functionalization of 1-naphthols with 1-azadienes.

In 2020, Shi group demonstrated an asymmetric 1,4-addition reaction of benzofuran-derived aza-dienes **16a** with 3-substituted indoles **16b** catalyzed by a CPA **C13** (Scheme 16).[24] This reaction afforded enantioenriched tri(hetero)arylmethane products **16c** in high yields (up to 98%) and with excellent enantioselectivities (up to 98% ee). Through extensive

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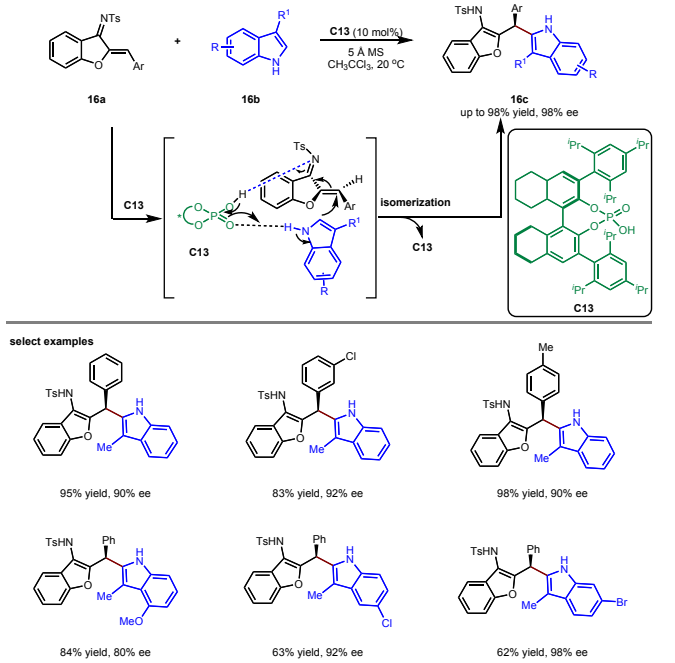
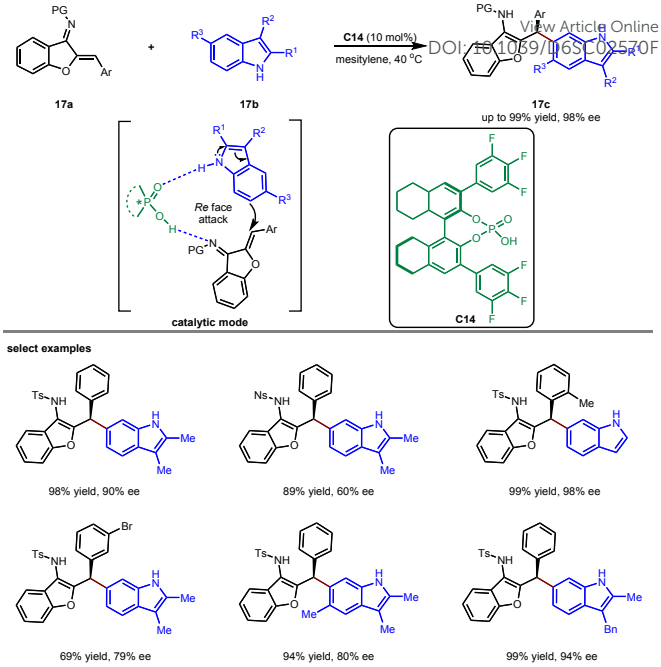
screening, the optimal conditions of this work were identified as follows: the H_8-BINOL-derived CPA **C13** as the optimal catalyst, 1,1,1-trichloroethane as the solvent, a reaction temperature of 20 °C, and 5Å molecular sieves as additive. Moreover, the reaction was successfully scaled up to 1 mmol while maintaining excellent performance. In the reaction, CPA **C13** activated both substrates via dual hydrogen-bonding to promote enantioselective 1,4-addition. Isomerization afforded the *S*-configured products, and the indole N–H was essential. This work established the application of CPA in the asymmetric transformation of benzofuran-derived aza-dienes, offering an efficient route to chiral triarylmethanes.



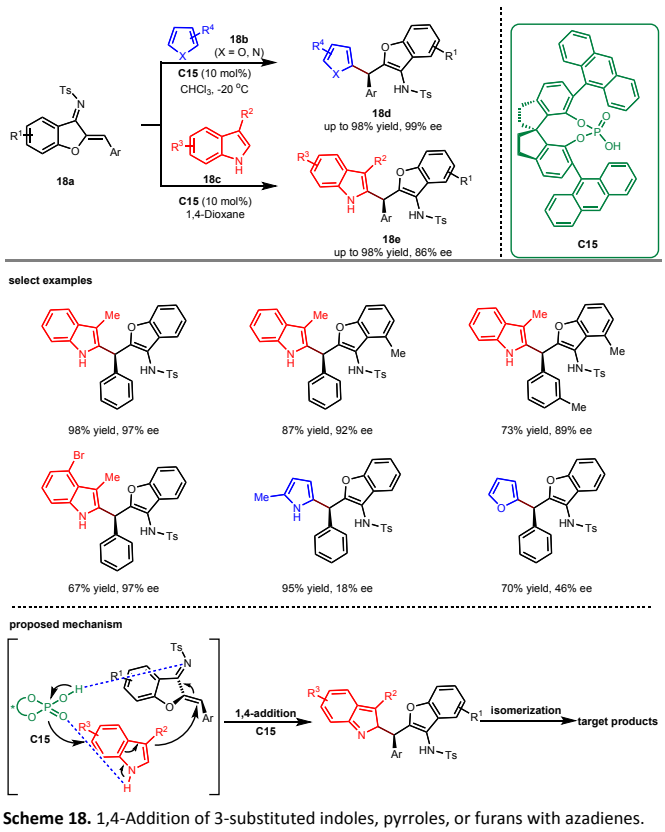
Scheme 16. Asymmetric 1,4-addition of benzofuran-derived azadienes with 3-substituted indoles.

In 2021, Zhou, Jiang and and co-workers provided a convenient approach to synthesize the optically active heterotriarylmethanes by a CPA-catalyzed direct regio- and enantioselective C6-functionalization of 2,3-disubstituted indoles **17b** with azadienes **17a** (Scheme 17).[25] Under the optimized conditions (H_8-BINOL-derived fluorinated CPA **C14** as the catalyst, mesitylene as the solvent, and a reaction temperature of 40 °C), a series of heterotriarylmethanes were obtained in excellent yields (up to 99%), broad substrate scope and with high enantioselectivities (up to 98% ee). Notably, the reaction could be scaled up to a gram-scale while maintaining a excellent yield and enantioselectivity. Mechanistic studies revealed that a hydrogen-bonding interaction between the free N–H group of the indole and the phosphoryl oxygen of the catalyst was crucial for enantiocontrol. In detail, CPA **C14** activated azadienes and indoles through dual hydrogen-bonding interactions. By steric shielding of the *Si*-face, it enabled reversible N-alkylation of indoles and highly selective C6-functionalization, affording the chiral heterotriarylmethane products with *S*-configuration.



Scheme 17. Direct regio- and enantioselective C6 functionalization of 2,3-disubstituted indoles with azadienes.

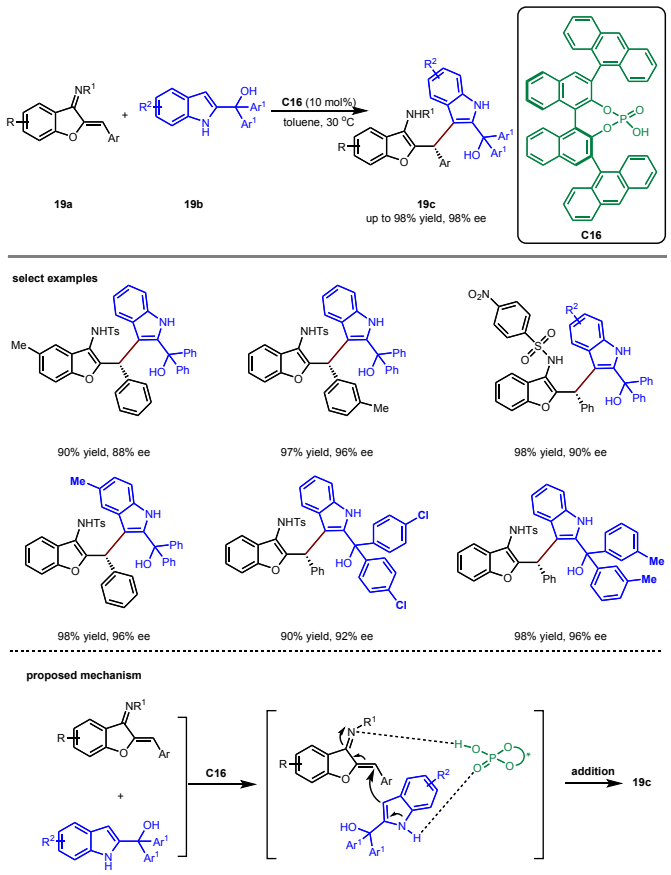
In 2021, Liao group developed a protocol for synthesis of C2-substituted heterotriarylmethane derivatives **18d** and **18e** via a asymmetric 1,4-addition of 3-substituted indoles **18c**, **18b** (pyrroles, and furans) to azadienes **18a** catalyzed by CPA (Scheme 18).[26] Optimal performance was achieved using the chiral spiro phosphoric acid **C15**, bearing a bulky 9-anthryl group,



Scheme 18. 1,4-Addition of 3-substituted indoles, pyrroles, or furans with azadienes.

in $CHCl_3$ or 1,4-dioxane at –20 °C. Under the optimal conditions, the reaction afforded the target products in moderate to excellent yields (up to 98%) with outstanding enantioselectivities (up to 99% ee). In the reaction, CPA **C15** acted as a bifunctional hydrogen-bonding catalyst to simultaneously activate 3-substituted indoles and azadienes via dual hydrogen-bonding interactions. Enantioselective 1,4-addition followed by rapid isomerization afforded the *S*-configured C2-substituted heterotriarylmethane products. This work provided a important strategy for asymmetric construction of the heterotriarylmethane scaffolds, which is significant for medicinal chemistry and materials science.

In 2026, Shi group established a condition-controlled catalytic asymmetric chemodivergent reaction for three divergent transformations of benzofuran-derived azadienes with 2-indolylmethanols (Scheme 19).[27] Among them, a series of triarylmethane derivatives could be obtained in up to 98% yield and 98% ee with CPA **C16** as catalyst in toluene at 30 °C by ctalytic asymmetric addition reaction of benzofuran-derived zadienes **19a** and 2-indolylmethanols **19b**. This protocol exhibited excellent substrate compatibility toward a wide range of substituted benzofuran-derived azadienes and 2-indolylmethanols. The catalytic system was simple and efficient, requiring only 10 mol% chiral phosphoric acid **C16** without any metal catalysts or additional additives, thus being environmentally benign and economically sustainable.



Scheme 19 Ctalytic asymmetric addition of benzofuran-derived zadienes and 2-indolylmethanols.

Meanwhile, the reaction proceeded rapidly and efficiently with completion within just 3 hours. The reaction mechanism was as follows: CPA **C16** simultaneously activated benzofuran-derived azadienes and 2-indolylmethanols via hydrogen bonding, promoting a highly enantioselective 1,4-addition to directly afford the chiral products **19c**. Furthermore, the reaction could be readily scaled up to 1 mmol scale with nearly unchanged yield and enantioselectivity, demonstrating promising synthetic applicability. The resulting chiral triarylmethanes readily underwent phosphorylation with complete retention of chirality.

This strategy enables direct construction of chiral centers with high catalytic efficiency under metal-free conditions, aligning well with the principles of green chemistry. The regiodivergent and chemodivergent nature of these reactions significantly enhances the structural diversity of the products. However, several limitations should be noted: the synthesis of azadiene substrates remains relatively complex, and some derivatives exhibit poor stability; the nucleophile scope is currently restricted to electron-rich heteroarenes and naphthols; and stereocontrol relies heavily on hydrogen-bonding interactions, making it challenging to extend to substrates lacking NH/OH functional groups.

2.4 Conjugate additions to quinonemethides

The organocatalytic conjugate addition of quinone methides also has been the most common method for synthesis of unsymmetric triarylmethanes. It mainly activates quinone methides via chiral Brønsted acids, squaramides, phase-transfer catalysts, etc., followed by reactions with nucleophiles such as indoles, naphthols, and pyrroles.

In 2015, Sun group developed an efficient catalytic asymmetric intermolecular C–C bond forming reaction for construction of heterotriarylmethanes (Scheme 20).[28] This methodology employed racemic tertiary alcohols containing a directing group **20a** as electrophiles and indoles **20b** as carbon nucleophiles. The reaction started with protonation of alcohol **20a**, followed by C–O bond cleavage to generate a tertiary carbocation whose resonance form is *ortho*-quinone methide (*o*-QM), which was ion-paired with the chiral phosphate anion. Subsequent indole nucleophilic attack afforded the observed heterotriarylmethane. The optimal conditions were identified as follows: using the spiro-skeleton-based CPA **C17** as the catalyst, DCE as the solvent, a reaction temperature of 0 °C, and a concentration of 0.05 M. Under these conditions, the desired heterotriarylmethanes **20c** were obtained in excellent yields (up to 99%) with high enantioselectivities (up to 95% ee). In the reaction, CPA **C17** protonated the tertiary alcohols and promoted dehydration to form tertiary carbocations, which generated ion pairs with the chiral phosphate anion. Meanwhile, indoles were activated via hydrogen bonding, enabling highly enantioselective nucleophilic attack to construct an all-carbon quaternary stereocenter in one step. The *ortho*-hydroxy group of the substrate served as an essential directing group and determined the reactivity and stereoselectivity. This work provided a key method for the synthesis of heterotriarylmethane derivatives featuring challenging all-

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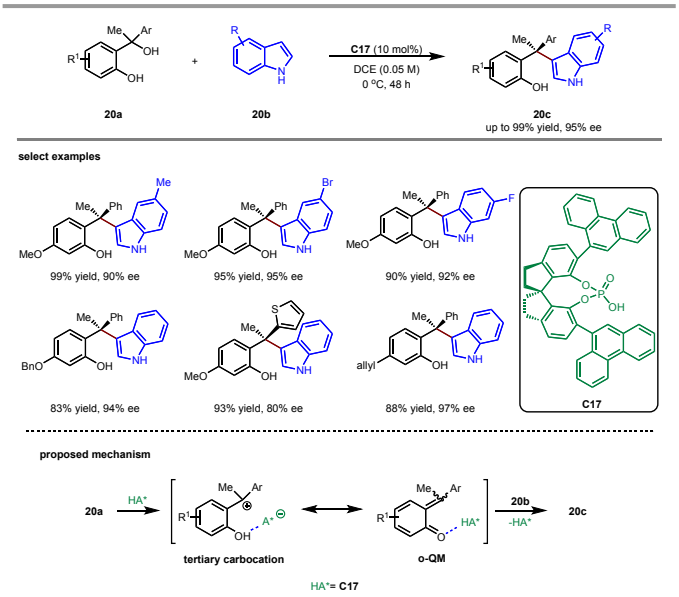
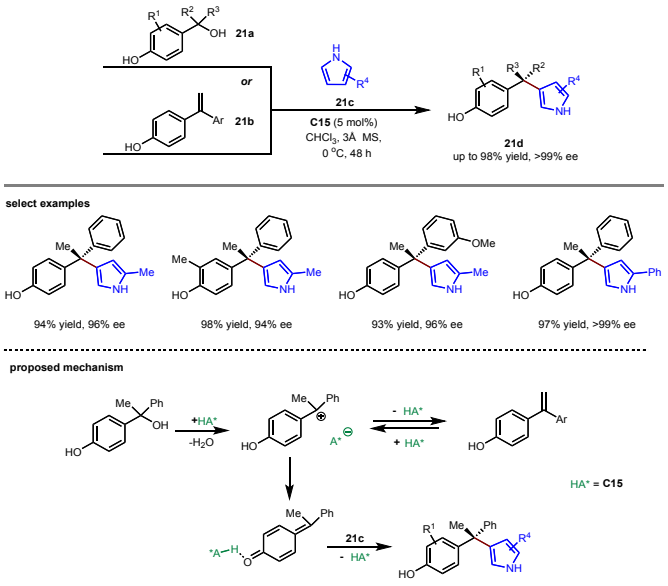
carbon quaternary stereocenters, which are valuable scaffolds in natural products and bioactive molecules.



Scheme 20. Catalytic asymmetric intermolecular C–C bond forming reaction for construction of heterotriarylmethanes.

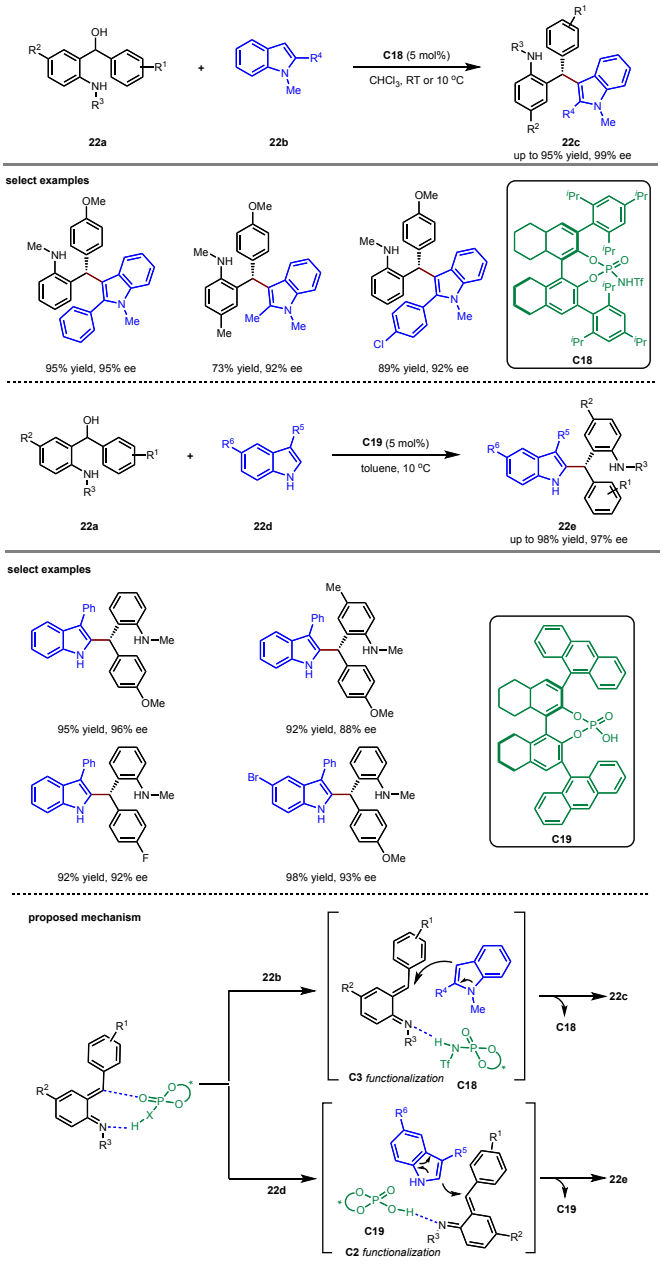
In 2015, Sun group afforded triarylmethanes by an asymmetric CPA catalyzed 1,6-conjugate addition reaction of *para*-quinone methides (*p*-QMs) *in situ* generated from stable phydroxybenzyl alcohol **21a** or styrenes **21c** precursors (Scheme 21).[29] Optimal results were achieved using the CPA **C15** bearing a 9-anthryl substituent as the catalyst in $CHCl_3$ at 0 °C with the addition of 3Å molecular sieves. Under these conditions, affording triarylmethane products were afforded in excellent yields (up to 98%) and enantioselectivities (up to >99% ee). In the reaction, CPA **C15** protonated and dehydrated *para*-hydroxybenzyl alcohols to *in situ* generate *p*-QM intermediates, which form ion pairs with phosphate anion. Meanwhile, it activated nucleophiles such as pyrroles via hydrogen bonding,



Scheme 21. Catalytic asymmetric 1,6-conjugate addition of *p*-QMs.

enabling highly enantioselective 1,6-conjugate addition to efficiently construct all-carbon quaternary stereocenters in one step. The phenolic hydroxyl group in the substrate was essential for the formation of *p*-QMs, and the catalyst achieved precise remote stereocontrol through hydrogen bonding and steric hindrance.

In 2015, Rueping and co-workers provided triarylmethane derivatives via a regiodivergent reaction catalyzed by a chiral Brønsted acid (Scheme 22).[30] In this reaction, target products **22c** and **22e** were obtained in high yields (up to 98%) and with excellent enantioselectivities (up to 99% ee) by asymmetric Brønsted acid catalyzed addition of 2- and 3-substituted indoles (**22b** and **22d**) to the *in situ* generation of aza-*ortho*-quinone methides (aza-*o*-QMs) from *ortho*-amino benzyl alcohol **22a**. Remarkably, regioselectivity was governed by substrate. Indoles



Scheme 22. Synthesis of triarylmethanes by regiodivergent reaction catalyzed by a chiral Brønsted acid.

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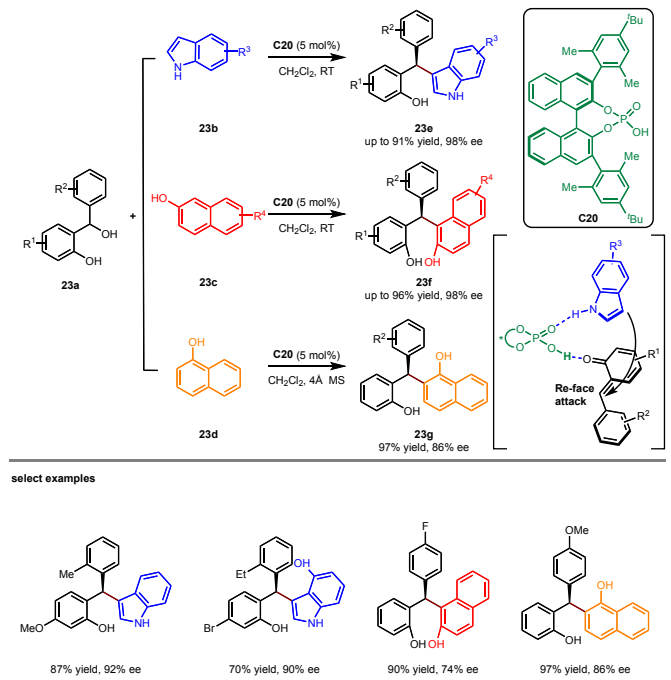
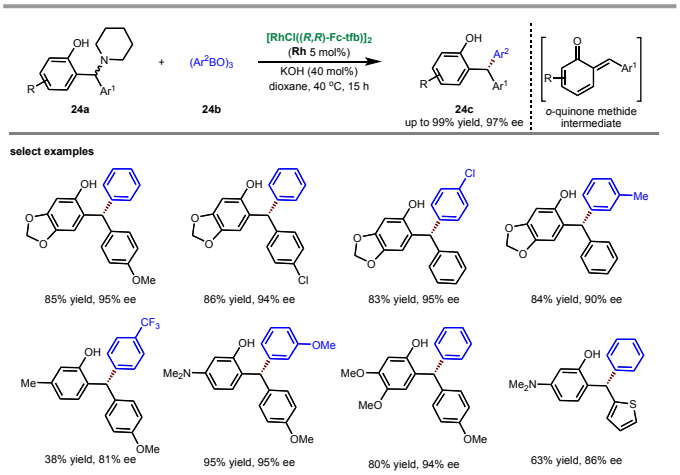
with an unprotected C3-position (**22b**) yield C3-functionalized products (**22c**), whereas indoles with a sterically hindered C3-position (**22d**) underwent C2-functionalization. The reaction mechanism was as follows: **C18/C19** acted as a bifunctional Brønsted acid catalysts to protonate and dehydrate *ortho*-aminobenzyl alcohols for the *in situ* generation of aza-*o*-QM intermediates. These intermediates were stabilized via hydrogen bonding to form a chiral environment, enabling regioselective C3/C2 functionalization with indoles and realizing highly enantioselective chemodivergent synthesis.

In 2015, Schneider group obtained chiral triarylmethanes successfully by the reaction of *in situ* generation of *o*-QM intermediates from stable *ortho*-hydroxybenzhydrols (**23a**) with electron-rich arenes such as indoles (**23b**) and naphthols (**23c** and **23d**) (Scheme 23).[31] Employing only 5 mol% of CPA **C20** (Ar = 2,6-Me_2-4-$^tBuC_6H_2$) as the optimal catalyst in dichloromethane at room temperature, the reaction afforded diaryl(indolyl)methanes and triarylmethanes in excellent yields (up to 97%) and with high enantioselectivities (ee up to 98%). Furthermore, the reaction demonstrated good tolerance and a broad set of heteroaryl-substituted triarylmethanes was obtained in good yields and enantioselectivities. The reaction mechanism was as follows: Firstly, *o*-QM intermediates were generated *in situ* from *ortho*-hydroxybenzhydryl alcohols via protonation and dehydration mediated by CPA. The catalyst simultaneously activated both *o*-QMs and indoles (or naphthols) nucleophiles through dual hydrogen-bonding interactions, precisely controlling the stereochemical environment and directing nucleophiles to selectively attack the *Re*-face of the intermediates. This enabled highly enantioselective Friedel–Crafts alkylation, efficiently affording chiral diarylindolylmethanes and triarylmethanes. The NH group of indole significantly enhanced enantioselectivity via hydrogen bonding and served as a key site. This work provided an efficient strategy for the synthesis of important active molecules in medicinal chemistry.



Scheme 23. Enantioselective synthesis of triarylmethanes by the reaction of electron-rich arenes with *in situ* generated *o*-QMs.

In 2015, Hayashi and co-workers reported a novel rhodium-catalyzed asymmetric synthesis of triarylmethanes **24c** (Scheme 24).[32] This methodology employed racemic 2-hydroxy-substituted diarylmethylamines (**24a**) and arylboroxines (**24b**) as starting materials. Under the catalysis of a chiral diene-rhodium complex, with [RhCl((*R,R*)-Fc-tfb)]$_2$ identified as the optimal catalyst, the reaction proceeded via *o*-QM intermediates to achieve rhodium-catalyzed asymmetric 1,4-addition of the arylboron reagents. This transformation afforded chiral triarylmethanes in high yields (up to 99%) with excellent enantioselectivities (up to 97% ee). Furthermore, the resulting products could be further transformed through reactions such as palladium-catalyzed reduction without racemization.



Scheme 24. Asymmetric synthesis of triarylmethanes by rhodium-catalyzed arylation of diarylmethylamines with arylboroxines.

In 2016, Sun group reported a novel CPA-catalyzed asymmetric synthesis of triarylmethanes (Scheme 25).[33] This method used racemic secondary *para*-hydroxybenzyl alcohols **25a** as precursors, under optimized conditions (**C15** as the chiral phosphoric acid catalyst, cyclopentyl methyl ether (CPME) as the solvent, 80 mg of 4 Å molecular sieves as additive, and a reaction time of 72 hours at room temperature), *p*-QMs were generated *in situ*. These intermediates subsequently underwent an asymmetric 1,6-addition with naphthols **25b** (primarily 2-naphthol, although 1-naphthol was also applicable), yielding triarylmethanes bearing a chiral tertiary carbon center in high yields (up to 99%) and with high enantioselectivities (up to 93% ee). In the reaction, CPA protonated and dehydrated *p*-hydroxybenzyl alcohols to generate *p*-QM intermediates *in situ*. It simultaneously activated both *p*-QMs and naphthol nucleophiles via hydrogen-bonding cooperation to form a compact transition state, enabling highly enantioselective 1,6-conjugate addition and efficiently constructing triarylmethane products bearing tertiary chiral stereocenters. Molecular sieves promoted the formation of intermediates and improved reaction efficiency and selectivity by removing water generated during the reaction. This strategy overcomed the limitations of

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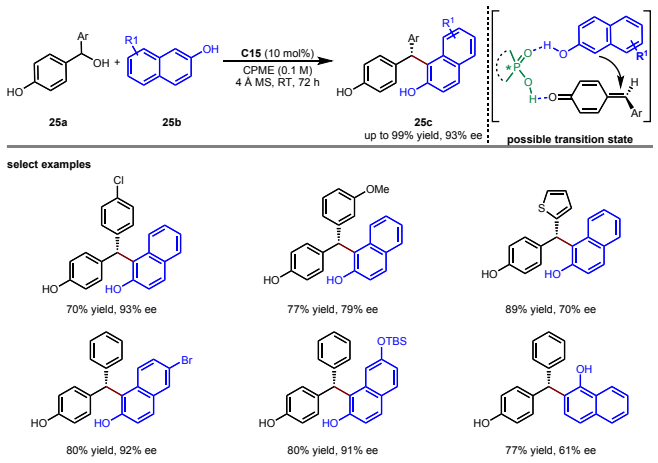
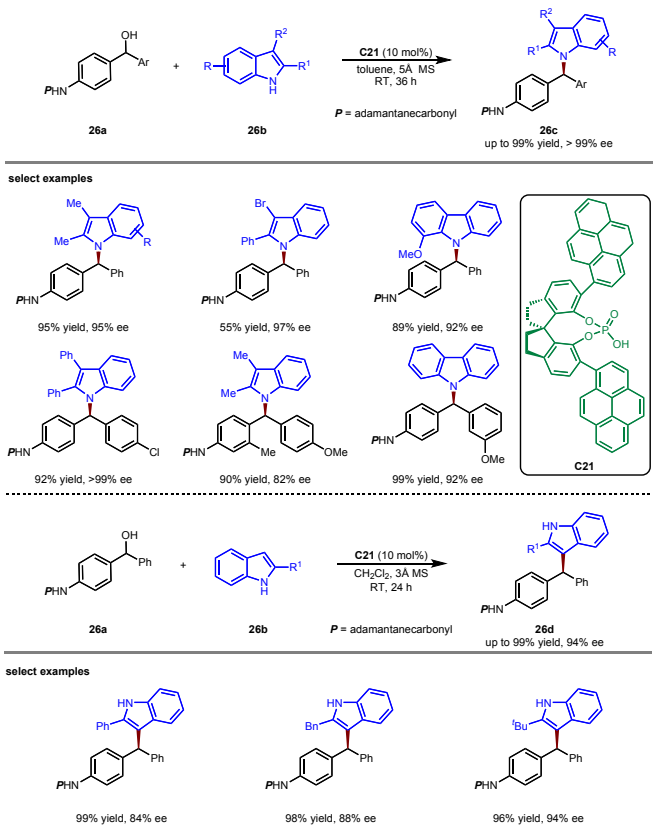
conventional *p*-QM reactions, which often require the *pre*-synthesis of unstable substrates or rely on bulky α-substituents for stabilization. Furthermore, the products could be further derivatized via oxidative cyclization without loss of enantiomeric excess, providing an efficient route to triarylmethane-based functional molecules, such as natural products and bioactive compounds.



Scheme 25. Asymmetric addition of naphthols to *p*-QMs.

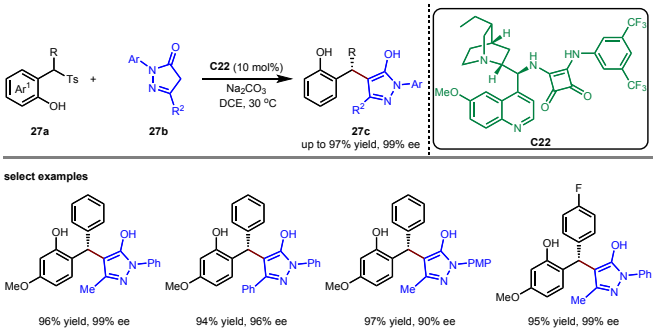
In 2017, Sun group, established a novel CPA **C21**-catalyzed asymmetric *N*-alkylation of indoles **26b** and carbazoles **26a** for construction of triarylmethanes (Scheme 26).[34] This method produced a series of triarylmethanes **26c** in high yields (up to 99%) with high enantioselectivities (up to >99% ee) by



Scheme 26. Catalytic asymmetric *N*-alkylation of indoles and carbazoles.

asymmetric 1,6-conjugate addition between 2,3-substituted indoles and aza-*para*-quinone methides (aza-*p*-QMs) *in situ* generated from *N*-protected *para*-aminobenzyl alcohols. It was worth noting that 1,6-conjugate addition between indoles with an unprotected C3-position and aza-*p*-QMs generated another triarylmethanes **26d** in high yields (up to 99%) with high enantioselectivities (up to 94% ee). This strategy effectively addressed the limitations of poor regioselectivity and narrow substrate scope associated with traditional *N*-alkylation methods for indoles and carbazoles. Moreover, the role of the aza-*p*-QM intermediates was verified through control experiments.

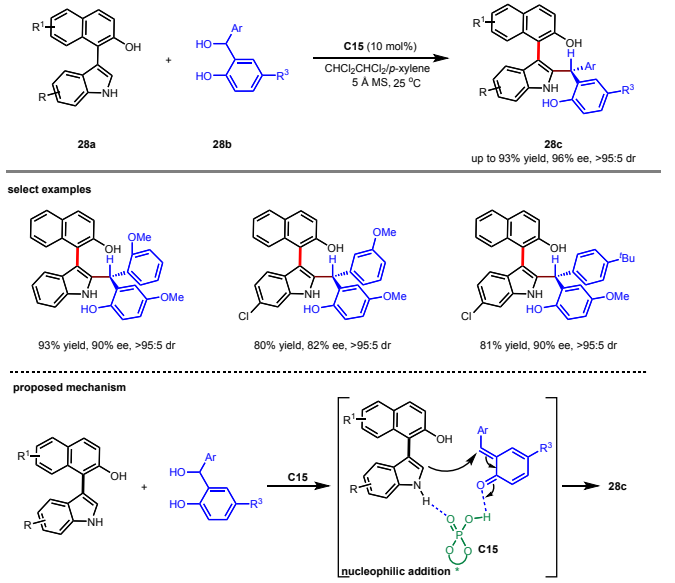
In 2018, Jiang an co-workers reported a bifunctional squaramide-catalyzed method for the synthesis of chiral triarylmethanes (Scheme 27).[35] In this reaction, a series of chiral triarylmethanes **27c** were provided in high yields (up to 97%) with high enantioselectivities (up to 99% ee) by Michael addition of pyrazolin-5-ones **27b** with *o*-QMs *in situ* generated from 2-(1-tosylalkyl)phenols **27a**. The practicality of this methodology was demonstrated in a 1.2 mmol scale-up experiment, where the target product was obtained with enantiomeric excess maintained. This work provided an efficient strategy for constructing triarylmethanes containing a pyrazolinone scaffold.



Scheme 27. Squaramide-catalyzed reaction of pyrazolin-5-ones with *o*-QMs.

In 2019, Shi and co-workers reported a dynamic kinetic resolution (DKR) strategy for the synthesis of triarylmethanes containing both axial chirality and central chirality (Scheme 28).[36] Using racemic naphthyl-indoles **28a** as substrates, the reaction proceeded with *in situ* generated *o*-QMs from *ortho*-hydroxybenzyl alcohols **28b** under catalysis of CPA **C15**. This method afforded naphthyl-indole-based triarylmethanes **28c** with both axial chirality and central chirality in high yields (up to 93%) with high stereoselectivitites (>95:5 dr, up to 96% ee). In detail, the racemic naphthyl-indoles underwent rapid racemization via free rotation around the chiral axis. The catalyst simultaneously activated the substrates and sterically bulky electrophiles (*o*-QM intermediates generated *in situ* from *ortho*-hydroxybenzyl alcohols) through hydrogen-bonding interactions, enabling highly stereoselective nucleophilic addition. The resulting adducts featured stabilized axial chirality because the steric congestion imposed by bulky *ortho*-substituents restricts the free rotation of the aromatic rings. Furthermore, this approach not only served as a notable

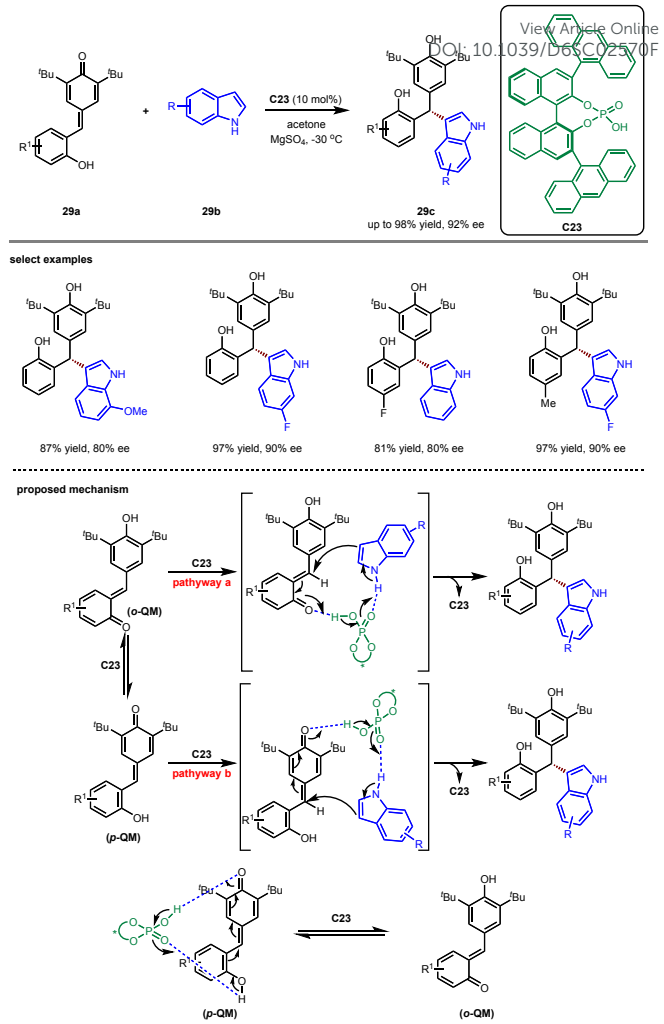
example of catalytic asymmetric synthesis of axially chiral molecules via DKR of racemic substrates but also enabled simultaneous control of axial chirality and central chirality of the naphthyl-indole-based triarylmethanes.



Scheme 28. A DKR strategy for the synthesis of triarylmethanes containing both axial chirality and central chirality.

In 2019, Shi, Mei and co-workers reported an asymmetric conjugate addition of indoles **29b** to *ortho*-hydroxyphenyl-substituted *p*-QMs **29a** catalyzed by CPA **C21** to afford chiral indole-containing triarylmethanes **29c** (Scheme 29).[37] In this reaction, the target products were obtained in yields of 54–98% with 80–92% ee with bis(9-anthryl)-substituted CPA **C23** as catalyst, acetone as the solvent and $MgSO_4$ as an additive at −30 °C. In addition, two possible mechanistic pathways were proposed for this reaction. In pathway A, CPA catalyzed the proton-transfer-induced *in situ* isomerization of *ortho*-hydroxyphenyl-substituted *p*-QMs into *o*-QM intermediates, which then undergo highly enantioselective 1,4-addition via dual hydrogen-bonding activation of both intermediates and indoles. In Pathway B, *para*-quinone methides were directly attacked by indoles to undergo 1,6-conjugate addition without isomerization. Control experiments indicated that the *o*-QMs was essential for the reaction, supporting pathway A as the major process, although pathway B cannot be completely ruled out. Furthermore, a gram-scale experiment and successful derivatization of products demonstrated the practicality of the method and the synthetic utility of the products. This methodology not only advanced the field of catalytic asymmetric transformations of *para*- and *ortho*-quinone methides but also offered a practical route to enantioenriched triarylmethane.

In 2019, Pengfei Li, Wenjun Li and co-workers provided chiral triarylmethanes by an asymmetric conjugate addition of 2-naphthols **30b** to *ortho*-hydroxyphenyl-substituted *p*-QMs **30a** catalyzed by CPA (Scheme 30).[38] Under optimized conditions (employing 1 mol% **C24** as the optimal catalyst, dichloromethane as the solvent at room temperature for 24 h),



Scheme 29. Catalytic asymmetric conjugate addition of indoles to *para*-quinone methide derivatives.

the reaction proceeded efficiently between 2-naphthols and *ortho*-hydroxyphenyl *p*-QMs yielding chiral triarylmethanes in 58–95% yields with enantioselectivities of 83–96% ee. Furthermore, the reaction demonstrated good tolerance. And a scale-up experiment (4.5 mmol) confirmed the practical utility of the method. Control experiments revealed that the free hydroxyl group of the *p*-QMs was essential for both reaction efficiency and selectivity. In detail, *p*-QMs were initially protonated and activated with the catalysis of CPA **C24**. Then the catalyst precisely orientated *p*-QMs and 2-naphthols through hydrogen-bonding interactions, thereby enabling highly enantioselective conjugate addition. Meanwhile, since the isomerization energy barrier for the conversion of *p*-QMs into o-QMs was only 6.7 kcal·mol^{-1}, the reaction may also preferentially underwent *p*-QM to *o*-QM isomerization, followed by **C24**-mediated activation of *o*-QMs and naphthols to accomplish the highly selective addition. This strategy offered an efficient route for the synthesis of chiral triarylmethanes containing naphthol scaffolds.

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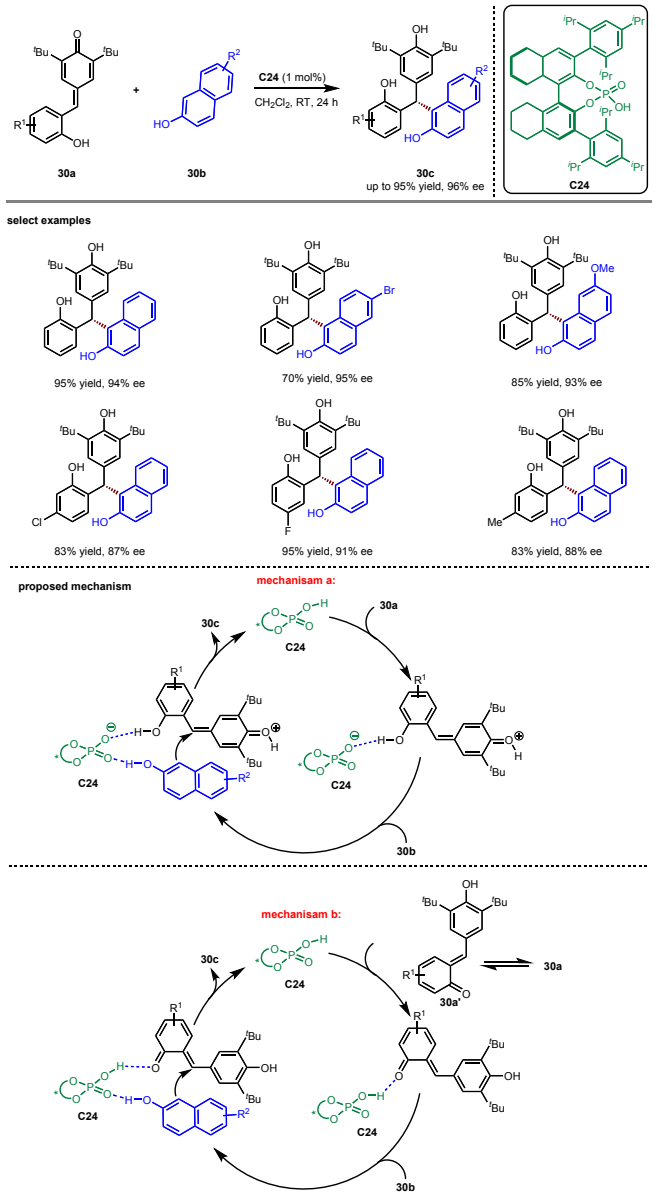
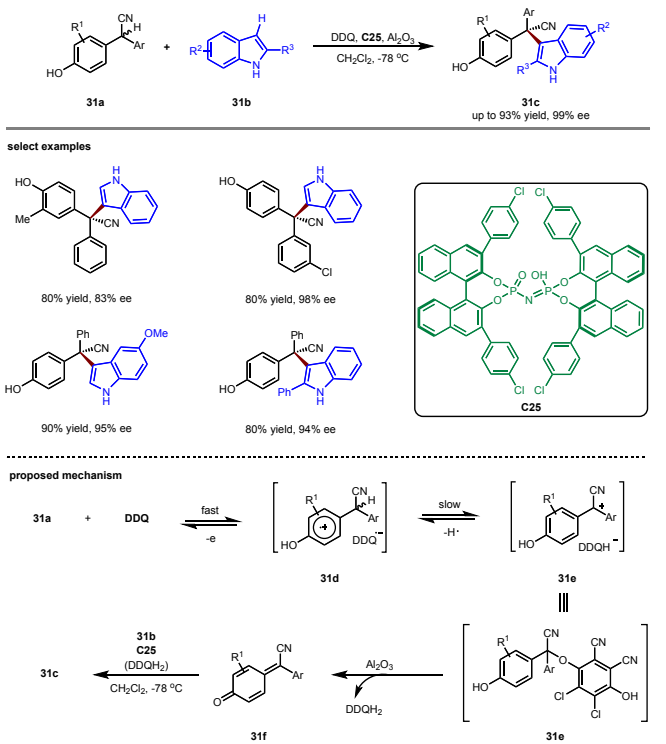


Scheme 30. Organocatalytic enantioselective conjugate addition of 2-naphthols to *ortho*-hydroxyphenyl substituted *para*-quinone methides.

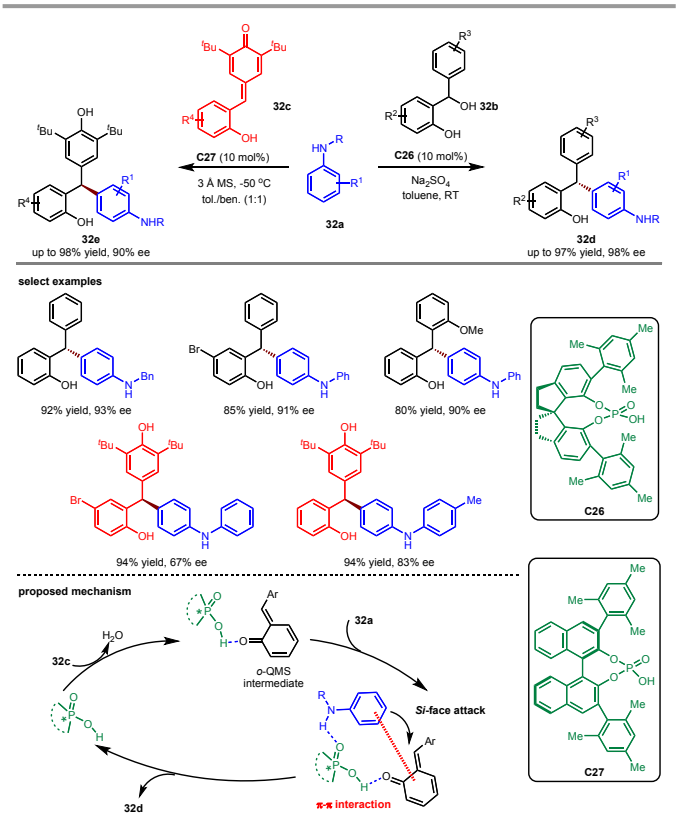
In 2020, Liu and co-workers reported an asymmetric oxidative cross-coupling reaction catalyzed by a CPA to efficiently construct triarylmethanes featuring an all-carbon quaternary stereogenic center (Scheme 31).[39] This transformation employed racemic 2,2-diarylacetonitriles **31a** and indoles **31b** as substrates with **C25** as catalyst, dichloromethane as the solvent, DDQ as oxidant and Al_2O_3 as additive at –78°C for 12 h. This reaction proceeded via the *in situ* generation of *p*-QM intermediates **31f** to efficiently construct triarylmethanes in good to excellent yields (72%–93%) with high enantioselectivitites (92%–99%ee). Moreover, the method exhibited extensive applicability and was applied to other electron-rich (hetero)arenes such as 1-naphthols, and pyrroles with other appropriate CPAs. The reaction mechanism was as follows: racemic 2,2-diarylacetonitriles were reversibly oxidized by DDQ to generate *p*-QM intermediates, and basic alumina promoted the irreversible formation of these intermediates. CPA **C25** acted as a bifunctional catalyst to synergistically activate the *p*-QM intermediates and electron-rich (hetero)arenes via hydrogen bonding, enabling highly enantioselective 1,6-conjugate addition in a compact transition state to directly construct chiral triarylmethanes bearing all-carbon quaternary stereocenters, where the N–H bond of indole was crucial for stereocontrol. Furthermore, the cyano (–CN) group in the products could be further derivatized into other functional groups through transformations such as reduction and hydrolysis, providing an efficient strategy for synthesizing challenging chiral triarylmethane molecules.



Scheme 31. Catalytic asymmetric oxidative cross-coupling of 2,2-diarylacetonitriles and (hetero)arenes.

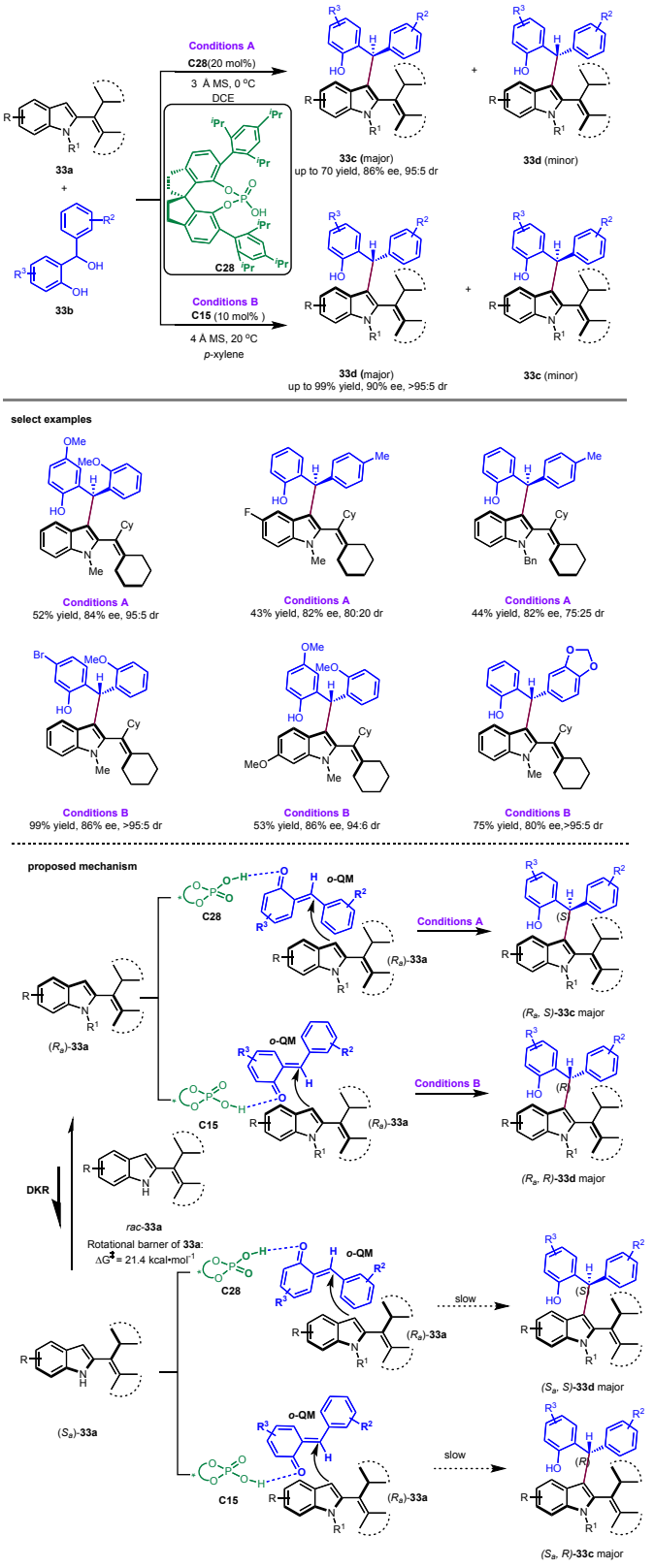
In 2023, Sun, Shen and co-workers established a CPA-catalyzed asymmetric alkylation of aniline derivatives **32a**, utilizing the high reactivity of *in situ*-generated *o*-QMs to afford chiral triarylmethanes with high regioselectivity and enantioselectivity (Scheme 32).[40] This reaction employed *ortho*-hydroxybenzyl alcohols **32b** as *o*-QM precursors with **C26** as the optimal catalyst, toluene as the solvent, and Na_2SO_4 as an additive at room temperature, affording chiral triarylmethanes bearing three substituted aryl groups in up to 97% yield and 98% ee. What's more, this method was also applicable to *ortho*-hydroxyphenyl-substituted *p*-QMs **32c**. Chiral triarylmethanes could be obtained in high yields and enantioselectivities (up to 98% yield and 90% ee) catalyzed by **C27**. And its practicality was demonstrated through a 5 mmol-scale reaction and diverse derivatizations without significant loss in yield or enantioselectivity. The reaction mechanism was as follows: as a bifunctional hydrogen-bonding catalyst, CPA promoted the *in situ* dehydration of *ortho*-hydroxybenzyl alcohols to form *o*-QM

intermediates. It simultaneously activated both the intermediates and aniline derivatives through dual hydrogen-bonding interactions, precisely directing the anilines to selectively attack the *Si*-face of *o*-QMs, thus achieving Friedel–Crafts alkylation with high regio- and enantioselectivity. Density functional theory (DFT) calculations revealed that π–π interactions and steric effects were identified as key factors responsible for the high enantioselectivity.



Scheme 32. Asymmetric synthesis of triphenylmethanes.

In 2024, Shi, Zhang, Ni and co-workers achieved the chiral phosphoric acid-catalyzed diastereodivergent synthesis of triarylmethanes **33c** and **33d** bearing both axial and central chirality via chiral phosphoric acid-catalyzed addition reactions of C3-unsubstituted 2-alkenylindoles **33a** with *ortho*-hydroxybenzyl alcohols **33b** (Scheme 33).[41] By simply tuning reaction conditions, two sets of diastereoisomers could be obtained selectively, affording products in up to 99% yield, 95:5 er, and >95:5 dr. The products exhibited excellent configurational stability and could serve as chiral phosphine ligands for asymmetric catalysis, and some products display remarkable cytotoxicity against HepG2 and PC-3 cancer cells. The reaction mechanism was as follows: CPA first promoted the *in situ* dehydration of *ortho*-hydroxybenzyl alcohols to generate o-QM intermediates. Racemic C3-unsubstituted 2-alkenylindoles underwent rapid tautomerization and racemization; during dynamic kinetic resolution, the catalyst synergistically activated *o*-QMs and the favorable conformer of indoles via hydrogen bonding, and precisely controled both axial and central chirality under different catalytic systems and reaction conditions, thereby achieving diastereodivergent addition. DFT calculations revealed the origin of stereoselectivity and diastereodivergence, offering a novel strategy for the precise synthesis of indole scaffolds bearing dual chiral elements.



Scheme 33. Catalytic asymmetric diastereodivergent synthesis of triarylmethanes bearing both axial and central chirality.

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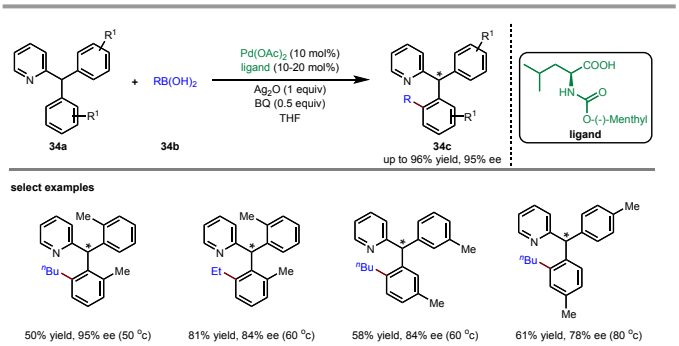
This strategy features a broad substrate scope, mild reaction conditions, and excellent scalability, rendering it one of the most practical approaches for the industrial-scale synthesis of chiral triarylmethanes. The *in situ* generation of QMs circumvents the isolation of unstable intermediates, thereby enhancing overall reaction efficiency. Nevertheless, several critical limitations remain: QMs readily undergo side reactions such as dimerization and polymerization, which compromise reaction selectivity; stereocontrol remains challenging for QMs with minimal steric differentiation; and most protocols require molecular sieves as additives, increasing the complexity of post-reaction processing.

2.5 Desymmetrization reaction

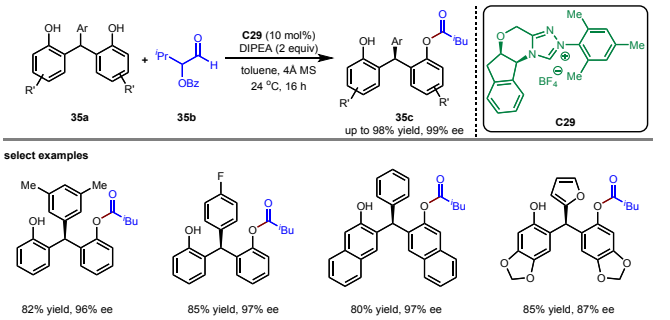
Desymmetrization reaction represent an efficient strategy for constructing chiral triarylmethanes. Such reaction used symmetric triarylmethane precursors (such as symmetric diols, diarylpyridylmethanes, triaryl-substituted prochiral compounds, etc.) as substrates, which undergo selective activation and transformation of symmetric functional groups (e.g., C–H bond functionalization, acylation, borylation, etc.) under chiral catalysis. And chiral triarylmethanes framework containing a chiral center are constructed after breakage of molecular symmetry.

In 2008, Yu and co-workers reported a desymmetrization reaction for synthesis of triarylmethanes by Pd^{II}-catalyzed enantioselective activation of both C(sp^2)–H and C(sp^3)–H bonds/C–C coupling pathway (Scheme 34).[42] Using a monoprotected amino acid as the chiral ligand, the reaction proceeded by the coupling of **34a** with **34b** to afford product **34c**. Under optimized conditions, the transformation achieved high enantioselectivities of up to 95% ee, which was retained even when the ligand loading was reduced to 10 mol%. This strategy offerd a novel approach for the efficient synthesis of chiral triarylmethanes relevant to organic synthesis and medicinal chemistry.



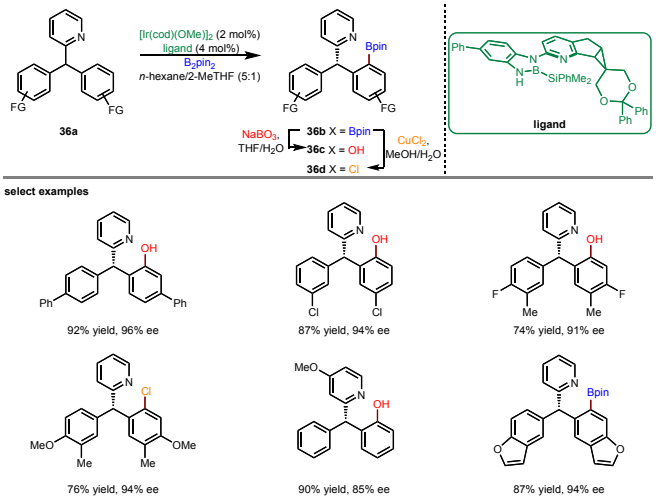
Scheme 34. Desymmetrization reaction for synthesis of triarylmethanes by Pd^{II}-catalyzed enantioselective activation.

In 2016, Zhao, Wong and co-workers reported an efficient and enantioselective synthesis of triarylmethanes through *N*-heterocyclic carbene (NHC)-catalyzed desymmetric acylation of bisphenols **35a** (Scheme 35).[43] The reaction efficiently afforded enantioenriched triarylmethanes **35c** in excellent enantioselectivities (up to 99% ee) and yields (up to 98%) with bis-phenols derived from triarylmethanes as substrates, aldehyde **35b** as the acylating agent, and a chiral triazolium salt **C29** as a precatalyst in toluene. Furthermore, the products could be further derivatized (such as conversion to triflates and Suzuki coupling), confirming the utility of this method which offerd a versatile approach to valuable chiral scaffolds for drug and material applications.



Scheme 35. Synthesis of enantiopure triarylmethanes by NHC-catalyzed acylative desymmetrization.

In 2021, Li, Xu and co-workers developed an enantioselective iridium-catalyzed desymmetrizing C–H borylation reaction of diaryl(2-pyridyl)methane compounds **36a**, a significant type of heterocyclic triarylmethane, with up to 96% ee and 93% yield (Scheme 36).[44] Moreover, the borylated products **36b** could be readily transformed into various chiral tri(hetero)arylmethane compounds, such as phenols **36c** and chlorides **36d**. A tunable chiral pyridine framework used as ligand in this reaction, which was incorporated into an N,B-bidentate ligand, were new designed and synthesized. This chiral pyridine ligand addressed limitations of conventional pyridine ligands, such as difficulties in structural modification and high local steric hindrance, offering a new strategy for asymmetric catalysis and the synthesis of chiral triarylmethanes which are important scaffolds in pharmaceutical and materials science.



Scheme 36. Enantioselective iridium-catalyzed desymmetrizing C–H borylation reaction of diaryl(2-pyridyl)methane compounds.

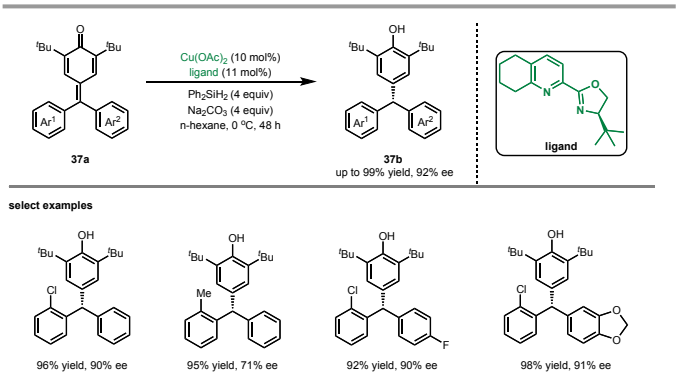
The desymmetrization strategy features short synthetic steps and high structural economy, as it directly converts symmetric precursors into chiral products. The combination with C–H activation further improves the reaction efficiency. However,

this strategy has obvious bottlenecks: the types of symmetric precursors are very limited, making it difficult to design and synthesize diverse prochiral triarylmethane substrates; the catalytic systems are mostly transition metal-based, resulting in high cost and poor environmental friendliness; and the substrate scope is narrow, only suitable for specific symmetric skeletons.

2.6 Catalyzed asymmetric hydrogenation

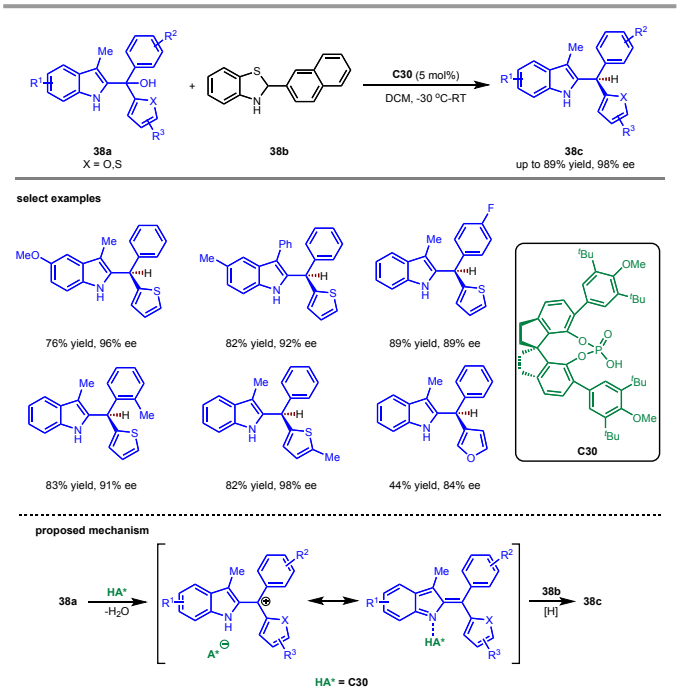
Catalyzed asymmetric hydrogenation, in the synthesis of triarylmethanes, mainly constructs central chiral carbons (triaryl-substituted stereocenters) through stereoselective hydrogenation of unsaturated bonds containing the triarylmethane precursor skeleton. This synthetic strategy involves two key steps: first, preparing a prochiral unsaturated intermediate containing the basic skeleton of triarylmethane; subsequently, activating hydrogen gas (or other hydrogen sources) using a chiral metal catalyst or organocatalyst to selectively attack one side of the unsaturated bond, thereby generating the chiral triarylmethane product.

In 2019, Fan, Liu, Chu and co-workers reported a catalytic asymmetric method for synthesizing triarylmethane by CuH-catalyzed asymmetric 1,6-conjugate reduction of *p*-QMs **37a** (Scheme 37).[45] This approach efficiently synthesized chiral triarylmethanes **37b** in up to 99% yield and 92% ee and broad functional group tolerance with $Cu(OAc)_2$ and tetrahydroquinoline ligand as catalyst, Ph_2SiH_2 as the hydride source, K_2CO_3 as the base and *n*-hexane as solvent at 0 °C. The work proposed a stereocontrol model based on "π-stacking interactions and steric repulsion" to explain enantioselectivity. Moreover, the product could be stably prepared via gram-scale reaction (2.0 mmol) and underwent derivative transformations such as de-*tert*-butylation and Pd-catalyzed reaction without ee loss. This strategy provided a new C–H bond-based synthetic route for key chiral triarylmethanes in pharmaceuticals and materials.



Scheme 37. Enantioselective synthesis of triarylmethanes by CuH-catalyzed asymmetric 1,6-conjugate reduction of *p*-QMs.

In 2022, Sun group developed a enantioselective synthesis of bioactive indole-containing triarylmethanes (Scheme 38).[46] In the presence of a CPA catalyst **C30**, 2-indole imine methides could be obtained *in situ* from indole-derived tertiary alcohols **38a**. Coupled with benzothiazoline **38b** as the hydrogen source, this reaction efficiently synthesized chiral triarylmethanes containing indole moieties in up to 89% yield and 98% ee by dehydration (rate-determining step) and transfer hydrogenation. In the reaction, CPA **C30** catalyzed the dehydration of racemic tertiary alcohols to generate indole imine methide ion-pair intermediates; this step was rate-determining and accompanied by kinetic resolution of the substrate. Benzothiazolines then acted as the hydride source to underwent enantioselective nucleophilic addition to the intermediates, affording chiral triarylmethanes. DFT calculations confirmed that the enantioselectivity originated from π-π stacking interactions (electron-complementary stacking between thiophene/furan and benzothiazoline) rather than hydrogen bonding. Preliminary biological experiments showed that the products exhibited activity against both A549 lung cancer cells and EV-A71 virus. This work contributed new molecular scaffolds for developing anticancer and antiviral drug candidates.



Scheme 38. Enantioselective synthesis of bioactive indole-containing triarylmethanes.

The same year, a new organocatalytic asymmetric method for the synthesis of enantioenriched triarylmethanes via organocatalytic transfer hydrogenation of *p*-QMs was developed by Sun group (Scheme 39).[47] The approach avoided using heteroaryl rings and bypasses the presynthesis of unstable *p*-QMs. Instead, the stable racemic triarylmethanols **39a** were used as substrates for the *in situ* generation of the *p*-QMs with CPA catalyst **C31**. And the asymmetric hydrogenation of *p*-QMs was achieved by employing benzothiazolin **39b** as hydrogen source. Under optimized conditions (DCE as solvent, 1 mol% catalyst loading, room temperature), chiral triarylmethanes containing three sterically and electronically similar benzene rings **39c** were efficiently synthesized in up to 99% yield with up to 97% ee. Control experiments and kinetic studies revealed that hydrogen bonding served as the key interaction for stereocontrol. The reaction mechanism was as follows: CPA **C31** catalyzed the *in situ* dehydration of racemic

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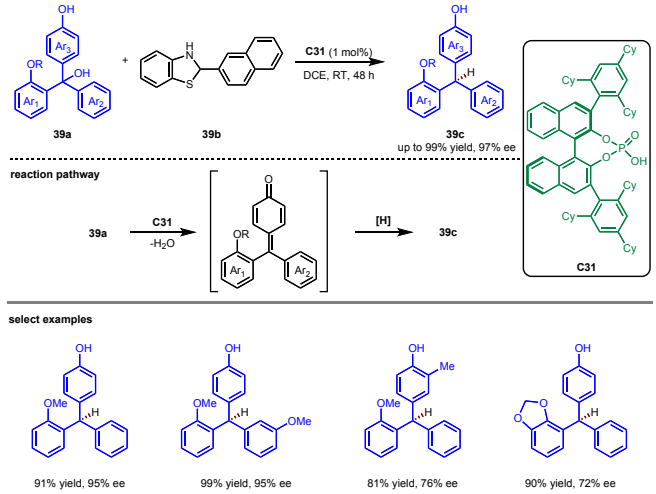
triarylmethanols to form *p*-QM intermediates, and this dehydration step was rate-determining. Subsequently, benzothiazoline acted as the hydride source and underwent highly enantioselective transfer hydrogenation with the *p*-QM intermediates under the hydrogen-bonding-directed activation of CPA, finally enabling the synthesis of chiral triarylmethanes.This approach provided an efficient, versatile organic catalytic strategy for synthesizing chiral triarylmethanes containing three sterically and electronically similar benzene rings.



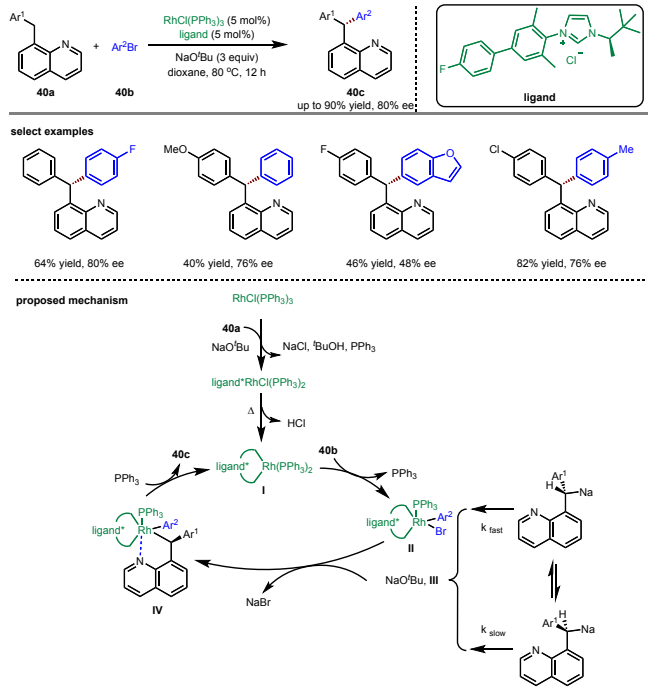
Scheme 39. Organocatalytic transfer hydrogenation of *p*-QMs.

This strategy has high atom economy and mild reaction conditions, and the organocatalytic transfer hydrogenation avoids the use of high-pressure hydrogen gas, which is safer and more practical. However, its limitations lie in the difficult design and synthesis of prochiral unsaturated precursors, low enantioselectivity toward triarylmethanes bearing three similar aryl groups, and a substrate scope restricted to QM and imine methide derivatives.

2.7 Asymmetric C–H arylation

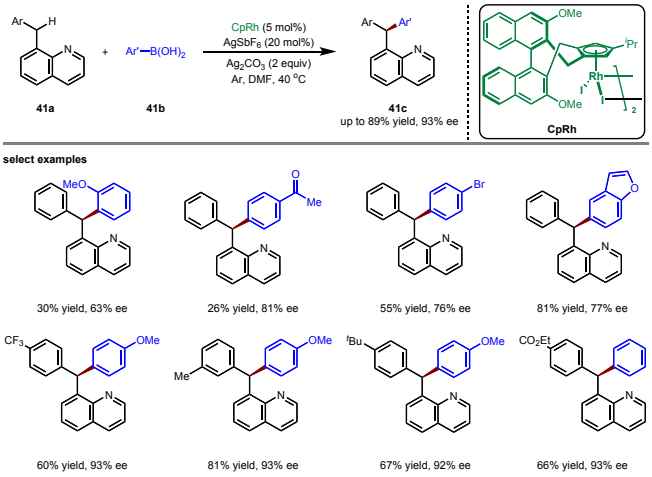
Undoubtedly, the direct C–H bond arylation reaction possesses distinct advantages over the conventional methods in terms of reaction efficiency and atom economy. So, the development of efficient synthesis of diverse chiral triarylmethanes by asymmetric C–H bond functionalization is highly desirable.

In 2016, Glorius and co-workers developed a method for enantioselective synthesis of triarylmethanes by Rh(I)/chiral NHC-catalyzed intermolecular asymmetric arylation of C(sp^3)–H bonds (Scheme 40).[48] The reaction achieved site- and enantioselective functionalization of benzylic C(sp^3)–H bonds by employing 8-benzylquinoline derivatives **40a** as substrates and aryl bromides **40b** as the aryl source. And a series of chiral triarylmethanes **40c** were synthesized in up to 90% yield and 80% ee with $RhCl(PPh_3)_3$ as catalyst precursor, NHC·HCl (5 mol%) as a carbene precursor, NaO^tBu as base, 1,4-dioxane as solvent at 80 °C for 12 h. Mechanistic studies confirmed a pathway involving oxidative addition, deprotonation, transmetalation, and reductive elimination. In detail, Rh(I) coordinates with chiral NHC ligands to form an active rhodium complexs *in situ*, followed by intramolecular C–H bond activation to generate a rigid chiral Rh(I)-complexs **I**. Aryl halides then underwent oxidative addition to afford Rh(III)-complexs **II**; after deprotonation of substrate **III** assisted by a base, transmetalation occured to yield benzyl Rh(III)-complexes **IV**. Finally, reductive elimination delivered chiral triarylmethanes. The cleavage of the C(sp^3)–H bond was identified as the rate-determining step. In intramolecular C–H activation, the NHC ligand constructs a rigid chiral environment, which was crucial for achieving high selectivity.



Scheme 40. Synthesis of triarylmethanes via Rh(I)/NHC-catalyzed site- and enantioselective functionalization of C(sp^3)–H bonds.

In 2024, You, Gu and co-workers developed an asymmetric C(sp^3)–H arylation of 8-benzylquinolines **41a** with arylboronic acids **41b** catalyzed by BINOL derived chiral cyclopentadienyl (Cp) rhodium complex (CpRh) (Scheme 41).[49] This reaction



Scheme 41. Rh-catalyzed asymmetric C(sp^3)–H arylation of 8-benzylquinolines with arylboronic acids.

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efficiently afforded chiral triarylmethanes by CpRh as the catalyst, Ag_2CO_3 as the oxidant, and $AgSbF_6$ as an additive in *N,N*-Dimethylformamide (DMF) solvent at 40 °C. This method displayed a broad substrate scope, tolerating both electron-withdrawing and electron-donating groups on 8-benzylquinolines, as well as heteroaryl boronic acids, affording products in up to 89% yield and 93% ee. Furthermore, a gram-scale reaction (1 mmol) could proceed smoothly, retaining desired yield and enantioselectivity. This work provided a mild and efficient method for synthesizing triarylmethanes.

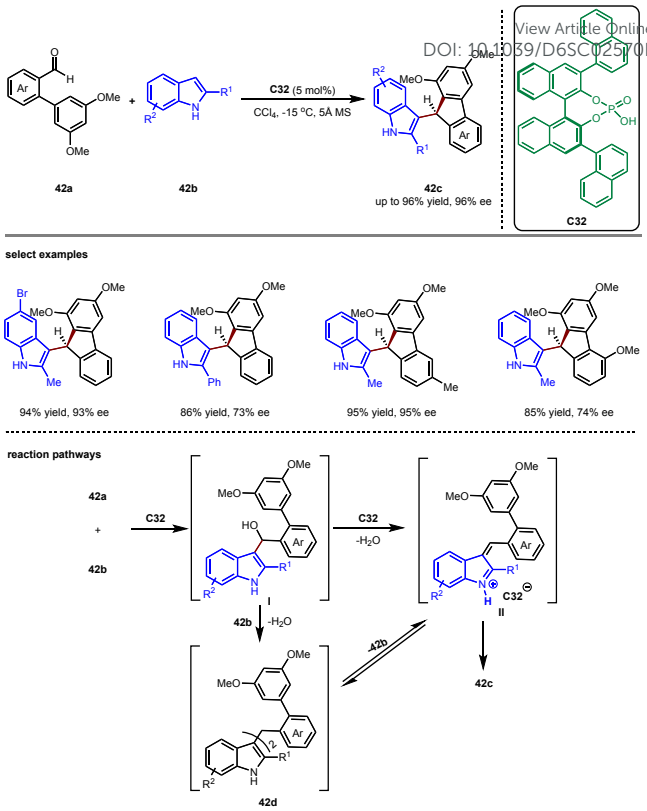
This strategy represents the development direction of green and efficient organic synthesis due to the avoidance of pre-functionalization. However, it is still in the initial stage of development, with obvious shortcomings: the substrate scope is extremely narrow, only limited to 8-benzylquinoline derivatives with directing groups; the enantioselectivity is generally lower than that of other strategies; and the catalytic system relies on expensive rhodium catalysts, which is not conducive to large-scale application.

2.8 Others

In addition to the aforementioned mainstream strategies for the catalytic asymmetric synthesis of triarylmethanes, a variety of emerging and alternative synthetic paradigms have emerged in recent years, including photocatalysis, radical asymmetric catalysis, metal–organo cooperative catalysis, one-pot modular cascade reactions, and phase-transfer catalysis. These approaches overcome inherent limitations of conventional methods and open new avenues toward structurally diverse chiral triarylmethanes that were previously inaccessible.

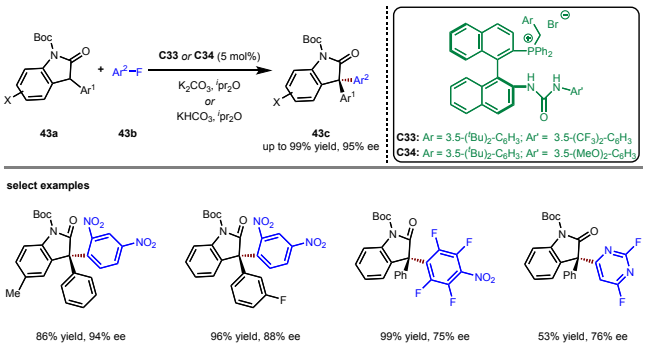
In 2009, You and co-workers presented a development of a chiral phosphoric acid-catalyzed tandem double Friedel–Crafts reaction between indoles **42b** and 2-formylbiphenyl **42a** (Scheme 42).[50] The method exhibited broad substrate scope, accommodating both electron-withdrawing and electron-donating substituents on indoles and biphenyls. A series of 9-(3-indolyl)fluorene derivatives, a type of triarylmethanes, were obtained in up to 96% yield and 96% ee with CPA **C29** (5 mol%) as the catalyst, CCl_4 as the solvent, and 5 Å molecular sieves as an additive at –15 °C. In this reaction, the secondary alcohols **I** were obtained by the first Friedel–Crafts reaction between **42a** and **42b** catalyzed by **C32**. Then alcohols **I** could come into being the close counterions **II** with CPA. A key enantiocontrol was the creation of a chiral microenvironment by the phosphate anion, which dictated the stereochemical outcome of the ensuing second Friedel–Crafts reaction. This work addressed a gap at that time in the asymmetric synthesis of fluorene derivatives and offers a novel reaction model for chiral Brønsted acid catalysis.

In 2014, Maruoka and co-workers described the first chiral bifunctional quaternary phosphonium salt-catalyzed phase-transfer S_NAr reaction (Scheme 43).[51] The 3,3'-diaryloxyindoles **43c** bearing an all-carbon quaternary stereocenter, a type of triarylmethanes, were obtained by asymmetric arylation of 3-aryloxyindoles **43a** with electron-deficient aryl fluorides **43b** with ureidyl-functionalized chiral quaternary phosphonium bromide (**C33** or **C34**) as the catalyst in diisopropyl ether at 20 °C. The method exhibited a broad substrate scope, accommodating



Scheme 42. Chiral phosphoric acid catalyzed tandem double Friedel–Crafts reaction.

both electron-rich and electron-deficient oxindoles as well as heteroaryl fluorides, delivering products in up to 99% yield and 95% ee. Futhermore, this reaction proceeded smoothly on a gram scale, and the nitro group in the products could be readily converted into other functionalities, offering an efficient and mild strategy for synthesizing key chiral scaffolds relevant to pharmaceutical applications.



Scheme 43. Catalytic asymmetric synthesis of 3,3'-diaryloxindoles.

In 2016, Nishibayashi and co-workers reported a one-pot method for the enantioselective synthesis of triarylmethanes (Scheme 44).[52] In this reaction, firstly, indole derivatives bearing a terminal alkyne group were obtained by asymmetric propargylation of indoles **44b** and propargylic esters **44a** with CuOTf·1/2C_6H_6 as the catalyst precursor, (4*S*,5*R*)-diPh-Pybox as the chiral ligand, and 4-methylmorpholine as the base in methanol at 0 °C. And subsequent one-pot Huisgen

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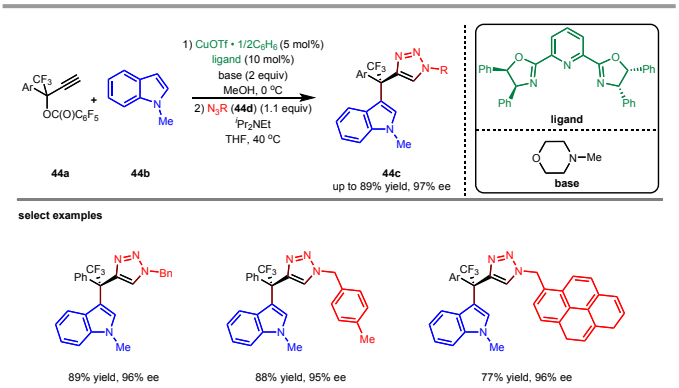
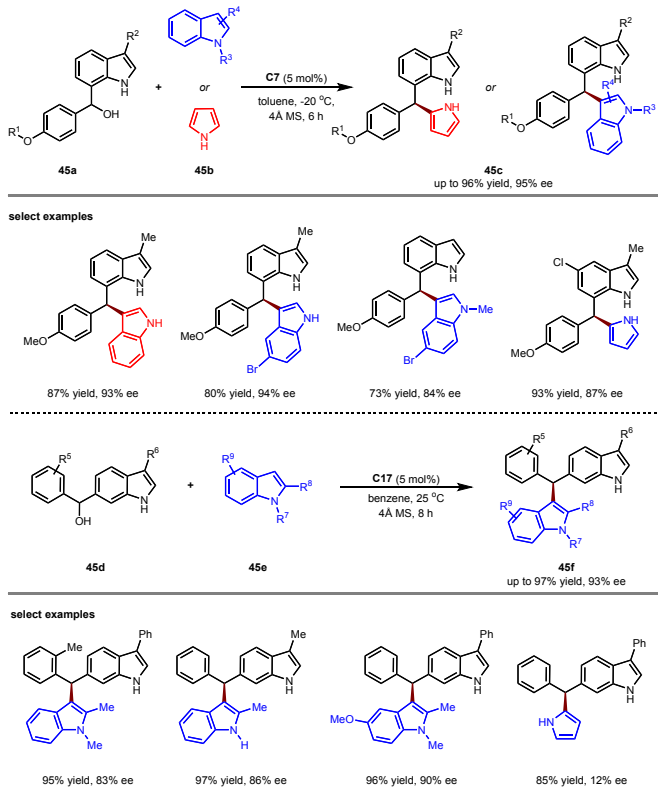
cycloaddition with azides **44d** afforded chiral triarylmethanes **44c** in up to 89% yield and 97% ee. Moreover, this method achieved the asymmetric synthesis of a chiral tetraarylmethanes by using a tertiary propargylic esters, bearing two different aromatic moieties at the propargylic position, as substrates. Mechanistic studies identified a dinuclear copper complex as the key active species, providing an efficient new strategy for synthesizing arylmethane molecules with quaternary stereocenters relevant to pharmaceutical and materials science.



Scheme 44. One-pot method for enantioselective synthesis of triarylmethanes.

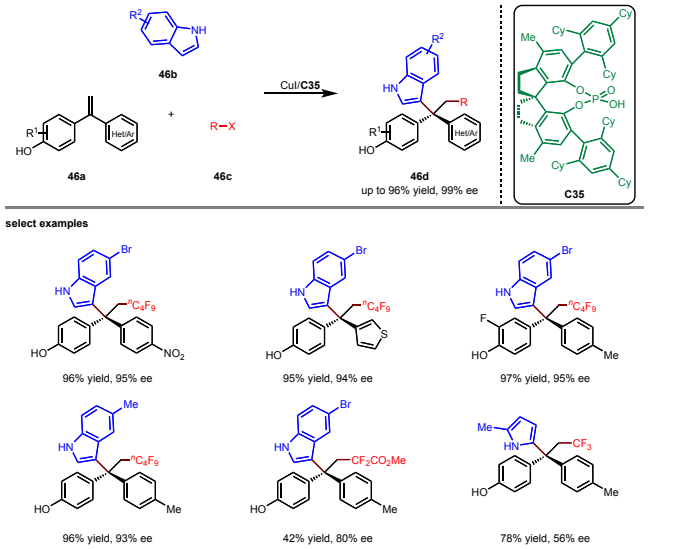
In 2018, Antilla and co-workers developed the CPA-catalyzed remote asymmetric activation strategy via two distinct pathways for the efficient synthesis of chiral heterocyclic triarylmethanes (Scheme 45).[53] Two efficient reaction mode were achieved by tuning the substrate structure and catalytic



Scheme 45. Asymmetric synthesis of heterotriarylmethanes from racemic indolyl alcohols.

system in this method. When using racemic indolyl alcohols (**45a** or **45d**) as substrates, CPA catalysis enabled *in situ* generation of either 7-methylene-7*H*-indole or 6-methylene-6*H*-indole intermediates, leading to 1,4- or 1,8-conjugate addition reactions with indoles or pyrroles (**45b** or **45e**), respectively, for the efficient synthesis of chiral heterocyclic triarylmethanes. The 1,4-addition products **45c** were obtained in up to 96% yield and 95% ee with **C7** as catalyst and 4 Å molecular sieves as an additive in toluene at –20 °C for 6 hours. Meanwhile, employing **C17** as catalyst and 4 Å molecular sieves as an additive in benzene at room temperature for 8 hours provided the 1,8-addition products (**45f**) in up to 97% yield and 93% ee. The method exhibited broad substrate scope and scalability to gram-level synthesis with maintaining enantioselectivity. This method offered an efficient and flexible approach to asymmetric synthesis of heterocyclic triarylmethanes.

In 2019, Liu, Hong and co-workers provided a straightforward access to chiral triarylmethanes bearing quaternary all-carbon stereocenters by Cu(I)/CPA cooperative catalyzed the asymmetric intermolecular three-component radical-initiated 1,2-dicarbofunctionalization of alkenes (Scheme 46).[54] A series of chiral triarylmethanes bearing an all-carbon quaternary stereogenic center **46d** were efficiently constructed in up to 96% yield with up to 99% ee, employing 1,1-diarylalkenes **46a**, diverse carbon-centered radical precursors **46c**, and electron-rich heteroarenes **46b** as substrates. This strategy utilized a sterically hindered of CPA to suppress side reactions. Chiral induction was achieved through the synergistic interplay between a removable hydroxy directing group and the CPA (via hydrogen bonding and ion-pair interactions). In addition, the efficiency was maintained on a gram scale.



Scheme 46. Asymmetric synthesis of heterotriarylmethanes by Cu/CPA-catalyzed asymmetric three-component reaction.

In 2023, Davies and co-workers developed a two-step protocol involving rhodium-catalyzed C–H functionalization of diaryldiazomethanes **47a** with cyclohexadiene derivatives **47b** followed byoxidation with DDQ, achieving the synthesis of chiral

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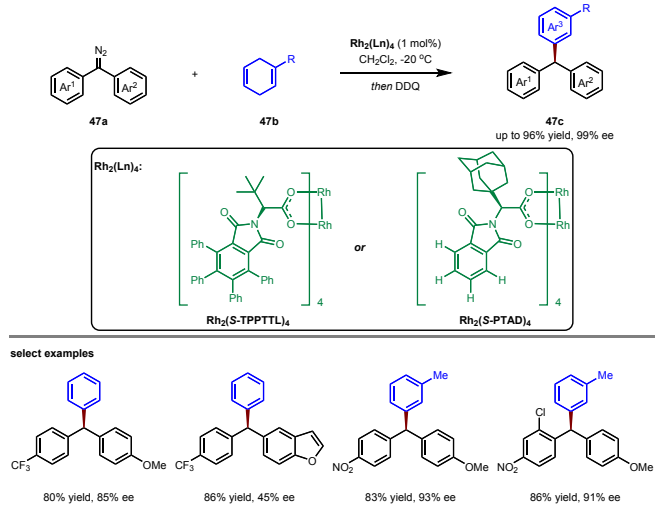
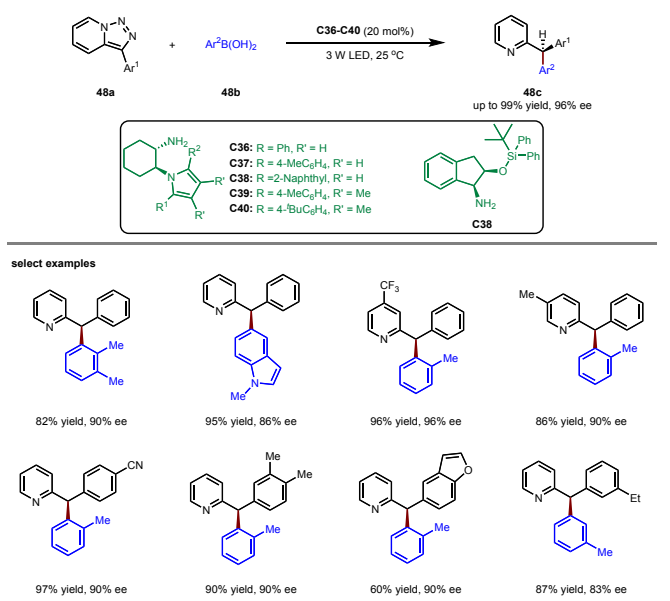
triarylmethanes **47c** (Scheme 47).[55] The target products were provided in up to 96% yield and 99% ee with Rh_2(S-PTAD)$_4$ and Rh_2(S-TPPTTL)$_4$ as optimal chiral catalysts in CH_2Cl_2 at –20 °C. The reaction tolerated both electron-rich and electron-deficient aryl groups, heterocycles (e.g., benzofuran, pyridine), and *ortho*-chloro substituents. Gram-scale synthesis (1 mmol) maintained excellent yield and enantioselectivity, with no racemization observed during the oxidation step.



Scheme 47. Intermolecular C–H functionalization of cyclohexadienes with diaryldiazomethanes.

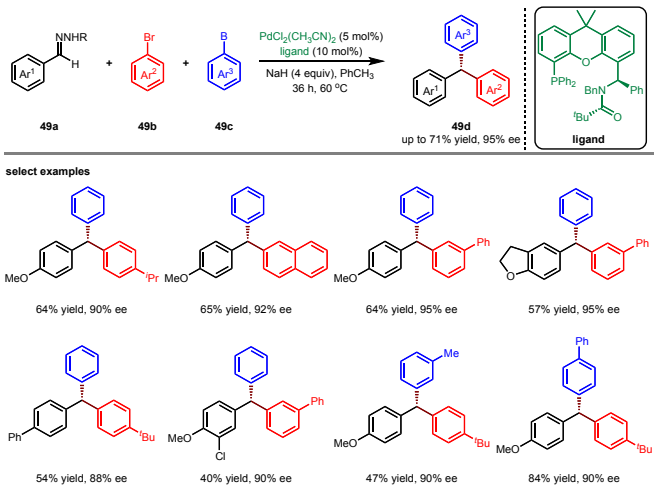
In 2025, Jiang, Cao and co-workers efficiently constructed imine-containing azaarene-based triarylmethanes by a chiral primary amine-catalyzed photochemical asymmetric reaction between pyridotriazoles **48a** and arylboronic acids **48b** (Scheme 48).[56] In this reaction, chiral triarylmethanes containing imine-functionalized heteroaromatic structures **48c** were constructed efficiently by utilizing a novel chiral diamine-derived pyrrole-primary amine catalyst **C36**-**C40** to generate a boron-containing



Scheme 48. Synthesis of chiral triarylmethanes by asymmetric photochemical reactions of pyridotriazoles with boronic acids.

enamine intermediate via 1,4-boron shift and subsequent enantioselective protonation. The target products were afforded in 71–99% yields with 70–96% ee. Futhermore, this work had a broad functional group tolerance including alkenes, alkynes, and silyl groups. This work addressed a significant gap in the asymmetric synthesis of triarylmethanes derived from electron-deficient heteroaromatics.

In 2025, Zhang, Wu, Yang and co-workers reportd a Pd/SadPhos catalytic system that enabled the modular asymmetric assembly of aldehyde-derived hydrazones **49a**, aryl halides **49b**, and aryl nucleophiles **49c** via a one-pot cascade reaction, efficiently constructing chiral triarylmethanes **49d** (Scheme 49).[57] The reaction concurrently formed two C–C bonds with excellent step- and atom-economy. The enantioselectivity-determining step was identified as the transition metal-carbene migratory insertion, overcoming limitations of traditional methods. The products were obtained in up to 71% yield and 95% ee with $Pd(CH_3CN)_2Cl_2$ as the precatalyst, sulfinamide phosphine ligand (SadPhos) as the ligand and NaH as the base in toluene at 60 °C. Notably, both enantiomers could be readily accessed by simply switching the aromatic rings. Density functional theory (DFT) calculations verified that the transmetalation step was rate-determining, while the carbene formation step governed enantioselectivity. Futhermore, this methodology was successfully applied to gram-scale synthesis and the preparation of an anti-tuberculosis active molecule.



Scheme 49. Modular and enantioselective assembly of triarylmethanes.

Compared with conventional strategies, these emerging alternative approaches possess unique and irreplaceable advantages, as they can construct novel skeletons including electron-deficient azaarene-type triarylmethanes, fluorene derivatives and quaternary-carbon-containing molecules that are inaccessible through traditional methods; meanwhile, photocatalysis, radical catalysis and one-pot cascade reactions greatly improve step economy, reduce waste generation and enhance sustainability, which is well in line with the development trend of modern green chemistry, and metal–organo cooperative catalysis as well as phase-transfer catalysis also further expand the catalytic scope beyond conventional

CPA and transition-metal catalysis. Nevertheless, multiple challenges still exist: most emerging strategies are still in the initial research stage with narrow substrate adaptability and insufficient generality, photocatalytic and radical catalytic systems usually rely on scarce specific catalysts or ligands, and the mechanistic basis, especially the stereocontrol mechanism of photochemical and radical reaction pathways, still remains poorly understood.

Despite these challenges, emerging approaches represent the future direction of this field, and further exploration will undoubtedly enable more efficient, versatile, and sustainable synthesis of chiral triarylmethanes.

3. Summary and Outlook

From classic organic dyes to modern anti-cancer drugs, from fluorescent probes to nonlinear optical materials, the applications of triarylmethanes have been continuously expanding. Their synthetic methodologies have also been constantly breaking through with the innovation of catalytic technologies, becoming a key molecular framework that connects fundamental chemistry with practical applications. Chiral triarylmethanes have witnessed a leapfrog development in their asymmetric synthesis methodologies over the past 20 years, evolving from "specific skeleton construction" to "modular and universal preparation". Relying on technological innovations such as transition metal catalysis and organocatalysis, this field has gradually overcome the bottlenecks of traditional methods, including limited substrate scope, difficult control of stereoselectivity, and low step economy, forming a research landscape where multiple strategies coexist and various catalytic systems complement each other. In addition, although mainstream strategies have been well-established, the development of emerging and alternative approaches, such as photocatalysis, electrocatalysis, radical asymmetric catalysis, and multicomponent cooperative catalysis, is still in the early stage. These new strategies show unique advantages in expanding structural diversity, improving step economy, and achieving green synthesis, yet their substrate scope, catalytic efficiency, and mechanistic foundation require further improvement.

However, despite these impressive achievements, substantial challenges remain, and the future development of this field requires focused innovation in fundamental science and practical application.

Core current challenges:

(1) Insufficient stereocontrol toward triarylmethanes bearing three electronically and sterically similar aryl groups;

(2) Lack of general and substrate-independent synthetic platforms applicable to diverse aromatic substituents;

(3) Unresolved limitations in scalability, cost-effectiveness, and industrial practicality;

(4) Insufficient mechanistic insights that hinder rational design of highly selective catalysts;

(5) Underdeveloped green and unconventional synthetic manifolds with sustainable energy inputs.

Future directions and opportunities

(1) Design and synthesis of highly stereodiscriminative chiral catalysts;

(2) Development of universal, modular, and substrate-compatible synthetic strategies;

(3) Advancement of scalable, sustainable, and industrially viable synthetic protocols;

(4) Mechanism-guided catalyst optimization combined with computational rational design;

(5) Expansion and maturation of emerging asymmetric platforms including photochemistry, electrochemistry, and radical catalysis.

In summary, the catalytic asymmetric synthesis of chiral triarylmethanes is transitioning from exploratory method development to a phase of rational design, scalability, and functional application. By addressing the current challenges and pursuing the proposed directions, this field will continue to expand rapidly and deliver innovative molecules for pharmaceuticals, materials science, and synthetic chemistry.

Author contributions

Y. H., L. L. and T.-P. Loh co-wrote the manuscript.

Conflicts of interest

There are no conflicts to declare.

Data availability

No datasets were generated or analyzed during the current study.

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