



Recent advances in catalytic asymmetric synthesis of chiral organogermanes

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Abstract

Chiral organogermanes hold great potential as bioisosteres in medicinal chemistry and functional materials, yet their development has long been hindered by a scarcity of efficient synthetic strategies. This review offers a comprehensive overview of recent advances in the catalytic asymmetric synthesis of chiral organogermanes, highlighting a shift from traditional resolution methods toward asymmetric catalytic approaches. The content is organized into three main categories: (i) synthesis of C-stereogenic germanes, (ii) synthesis of Ge-stereogenic germanes, and (iii) synthesis of other chiral germanes, including planar, inherent, and axially chiral types. Key synthetic methodologies are systematically examined, such as enantioselective alkene hydrofunctionalization, carbene insertion, coupling reactions, and [2+2+2] cycloaddition, utilizing a variety of catalytic systems ranging from transition metals (Rh, Cu, Ni, Co) and Lewis acids to engineered metalloenzymes. Particular emphasis is placed on the mechanistic insights and ligand design principles that enable stereochemical control in these transformations. We hope this review will inspire chemists working in related areas and contribute to the future advancement of this field.

Keywords: Asymmetric catalysis, chiral organogermanes, C-stereogenic germanes, Ge-stereogenic germanes

1. Introduction

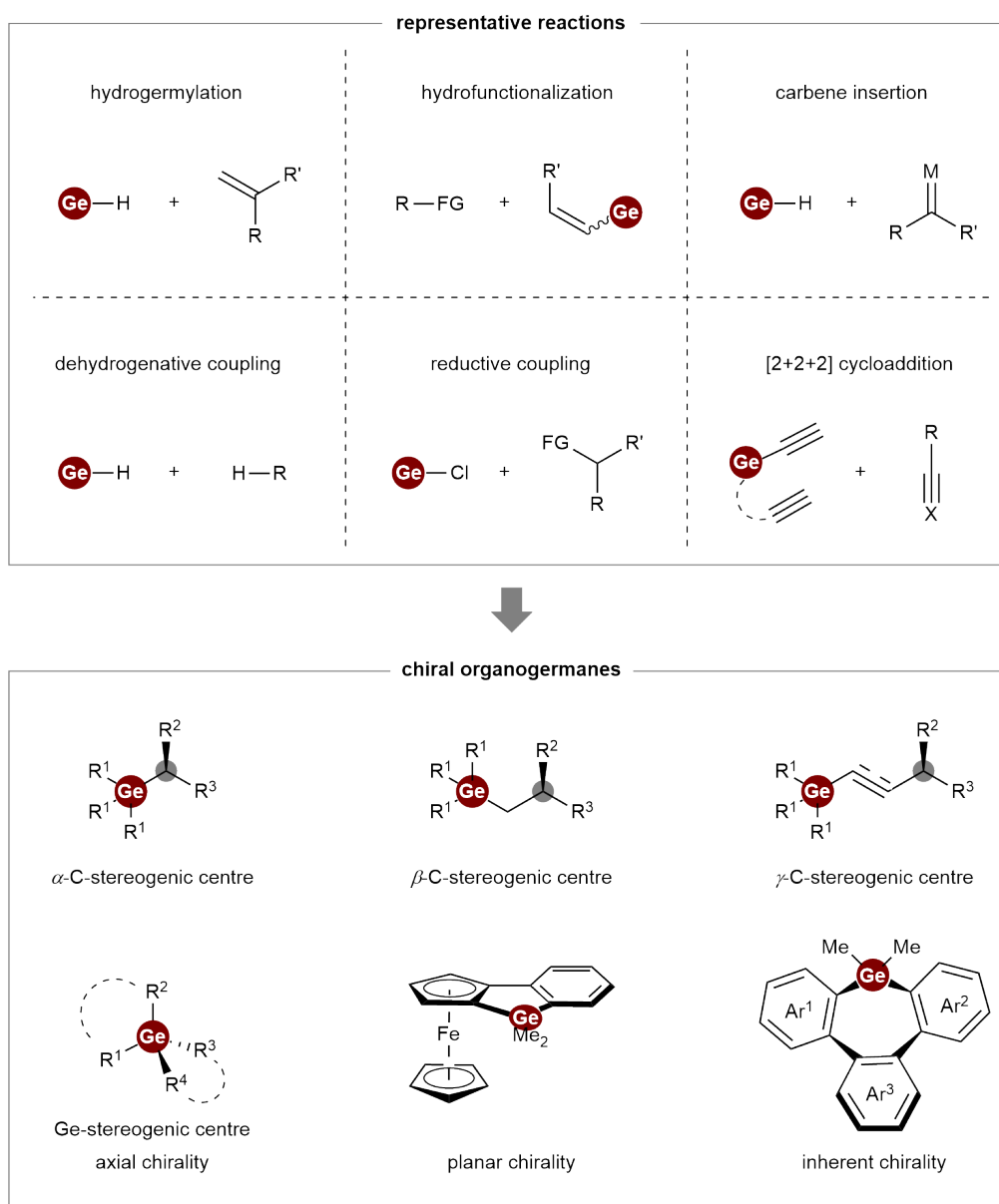
Chiral molecules play a significant role in the areas of pharmaceuticals, agrochemicals, and functional materials. While asymmetric synthetic methodologies for carbon stereogenic centers have matured, the catalytic, enantioselective creation of architectures centered on heavier Group 14 elements, particularly germanium, remains an underexplored frontier. Germanium possesses unique physical and chemical attributes, including a larger atomic radius (122 pm) and lower electronegativity ($\chi^p = 2.01$) compared to carbon, coupled with enhanced stability and lipophilicity relative to silicon. These attributes make organogermanes promising candidates as bioisosteres of carbon and silicon in biological studies^[1-3] and as functional components in materials science^[4-7]. Despite many studies on organo-germanium compounds in recent years^[8-10], the known methods toward optically active organogermanes remain limited^[11].

Traditional access to enantiopure organogermanes relied on resolution techniques or stoichiometric chiral auxiliaries, approaches that are inefficient and limited in scope^[12,13]. Recent years have witnessed a transformative shift with the emergence of catalytic strategies. Notable advances include transition-metal-catalyzed asymmetric hydrogermylation of alkenes, hydrofunctionalization of vinylgermanes, carbene insertion into Ge-H bonds, dehydrogenative and reductive couplings, and [2+2+2] cycloadditions, all of which collectively enable efficient construction of chiral organogermanes. These catalytic breakthroughs have unlocked access to a full spectrum of chiral germanes, ranging from C- and Ge-stereocentric to planar, inherent, and axially chiral systems (Scheme 1).

This review provides a comprehensive survey of recent advances in the catalytic asymmetric synthesis of chiral organogermanes, systematically organized into three sections based on the nature of the stereogenic element: (i) synthesis of C-stereogenic germanes, (ii) synthesis of Ge-stereogenic germanes, and (iii) synthesis of other chiral germane types—including planar, inherent, and axially



chiral systems. The article concludes with an outlook on persisting challenges and promising future directions, offering perspectives on potential trends in this rapidly evolving research field.



Scheme 1. Representative reactions for the catalytic asymmetric synthesis of chiral organogermanes.

2. Catalytic Asymmetric Synthesis of C-Stereogenic Germanes

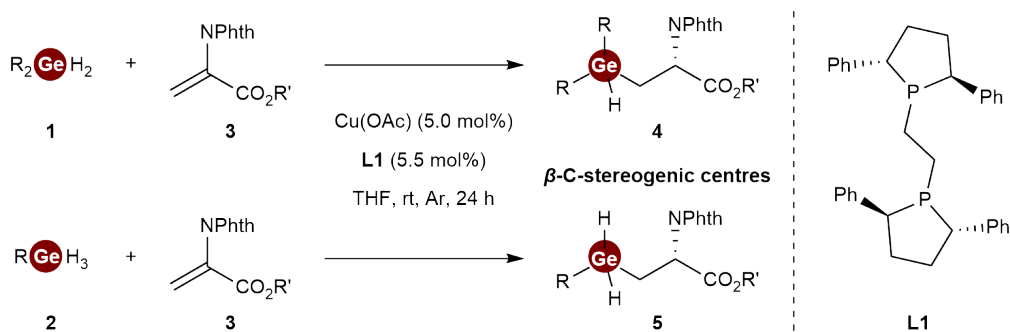
The catalytic asymmetric synthesis of chiral organogermanes has to date primarily focused on the stereocontrol at carbon centers. To provide a clear and systematic overview of this progress, the following sections are organized according to key reaction types: alkene hydrofunctionalization, carbene insertion, and coupling reactions.

2.1 Alkene hydrofunctionalization

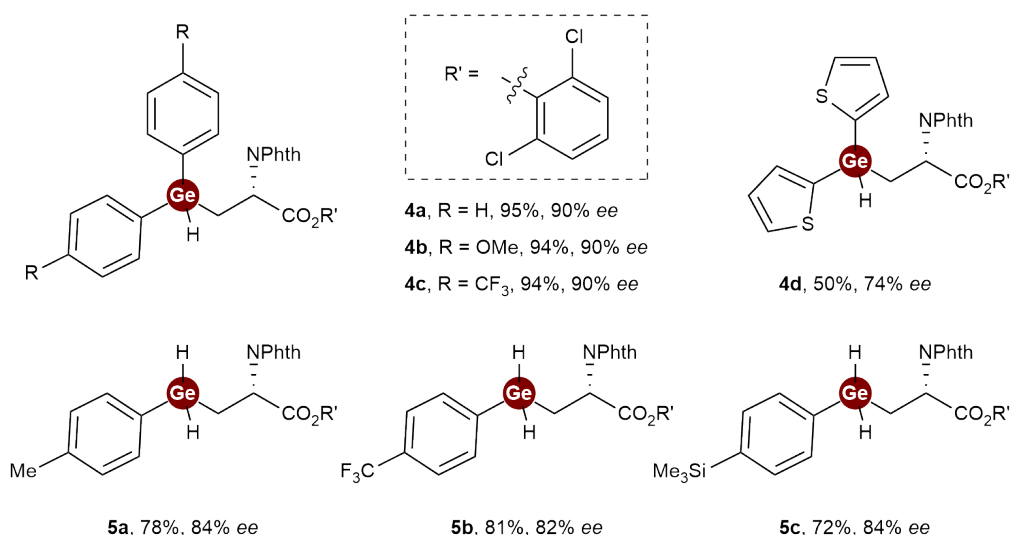
Hydrogermylation of alkenes represents one of the most straightforward and atom-economic approaches for the construction of organogermanium compounds^[14]. Despite considerable progress in hydrogermylation methodologies over the past decades, achieving an enantioselective variant has remained a formidable challenge. In 2022, He and co-workers achieved a breakthrough by reporting a copper-catalyzed enantioselective intermolecular hydrogermylation of dehydroalanines **3** with dihydrogermanes **1** and trihydrogermanes **2**^[15]. By employing a catalytic system consisting of Cu(OAc) and the chiral bisphosphine ligand (S,S)-Ph-BPE **L1**, this process gave access to a variety of chiral β -germyl α -amino acid derivatives **4** and **5** in decent yields with good to excellent enantioselectivities (Scheme 2). This work represents the first example of a catalytic enantioselective hydrogermylation of alkenes. To

underscore the synthetic utility of the method, the authors demonstrated that hydrazine mediated deprotection of product **4e** yielded the fully deprotected β -germyl α -amino acid **6** without erosion of enantiopurity, highlighting the robustness of the stereocenter under the reaction conditions.

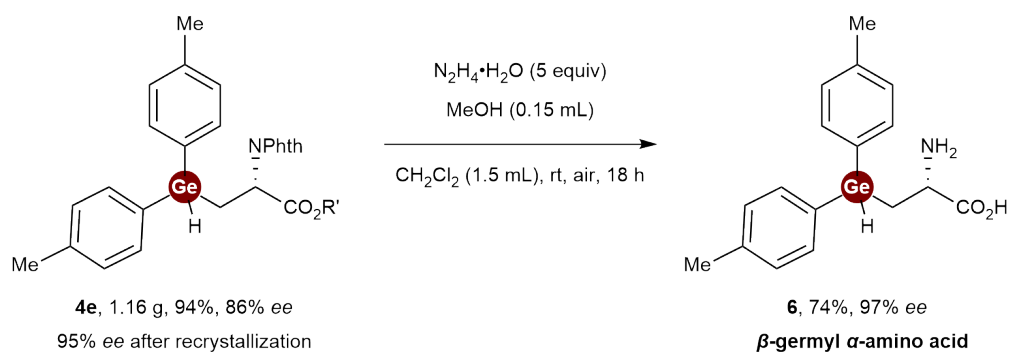
C. He, 2022



selected examples



synthetic application

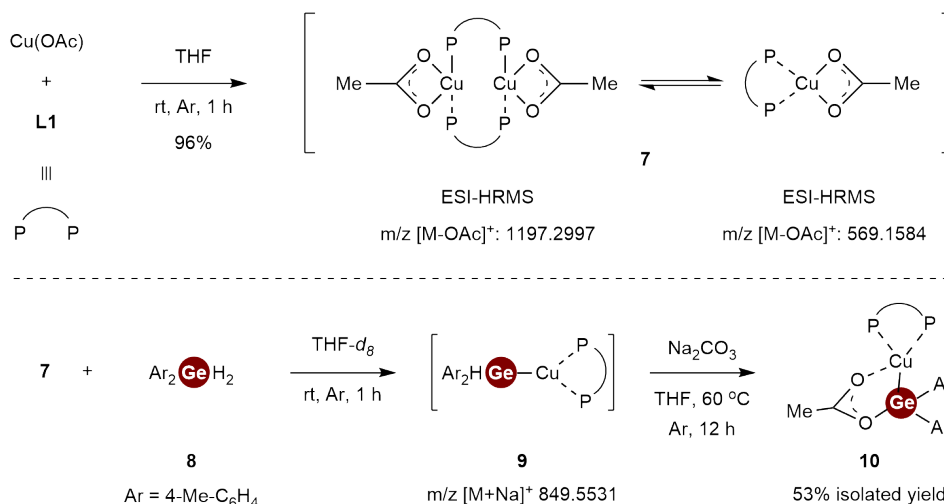


Scheme 2. Copper-catalyzed enantioselective hydrogermylation of dehydroalanines with dihydrogermanes and trihydrogermanes.

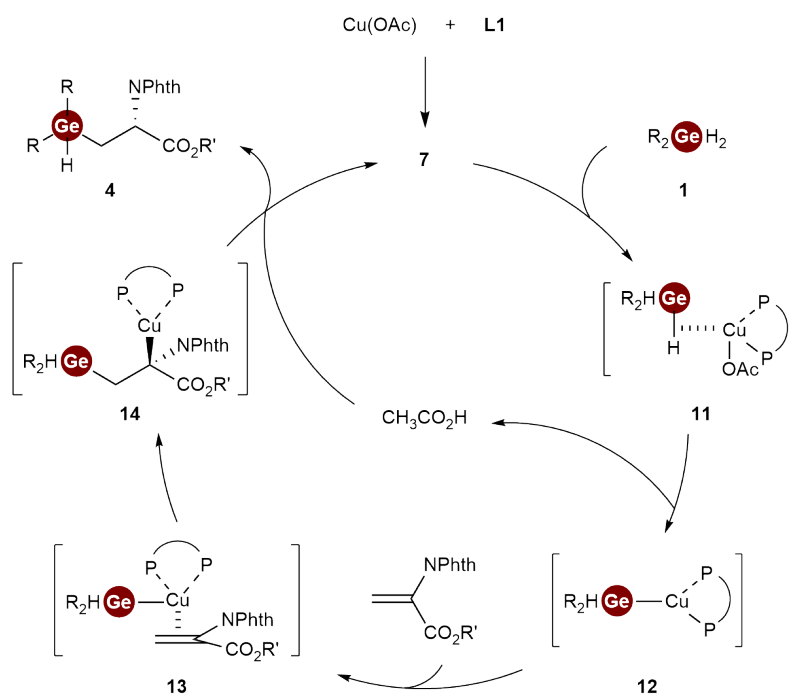
To investigate the reaction mechanism of this hydrogermylation process, a series of experimental studies were conducted (Scheme 3). Initially, the stoichiometric reaction of Cu(OAc) with **L1** yielded complex **7** in 96% isolated yield. Analysis by ^1H NMR, ^{31}P NMR, X-ray crystallography, and ESI-HRMS revealed that there were two components (dimer and monomer) in complex **7**. Subsequent ESI-HRMS monitoring of the reaction between complex **7** and dihydrogermane **8** indicated the formation of a $[\text{Cu-Ge}]$ species **9**, which was subsequently trapped and structurally characterized by X-ray crystallography as the stabilized complex **10**. Notably, this behavior contrasts with previously reported reactions of Cu complexes with hydrosilanes, which typically lead to the formation of $[\text{Cu-H}]$ species^[16]. On the basis of these findings, a plausible catalytic cycle was proposed: First, the reaction between Cu(OAc) and **L1**

generated the active catalytic species complex **7**. Then, coordination between dihydrogermanes **1** and complex **7** formed complex **11**, followed by the formation of [Cu–Ge] species **12** with the release of $\text{CH}_3\text{CO}_2\text{H}$. Next, the coordination and nucleophilic addition of complex **12** to dehydroalanine occurred, producing complexes **13** and **14** subsequently. Finally, the protonation of intermediate **14** by $\text{CH}_3\text{CO}_2\text{H}$ afforded the desired product **4** and regenerates complex **7**, thereby completing the catalytic cycle.

mechanistic studies



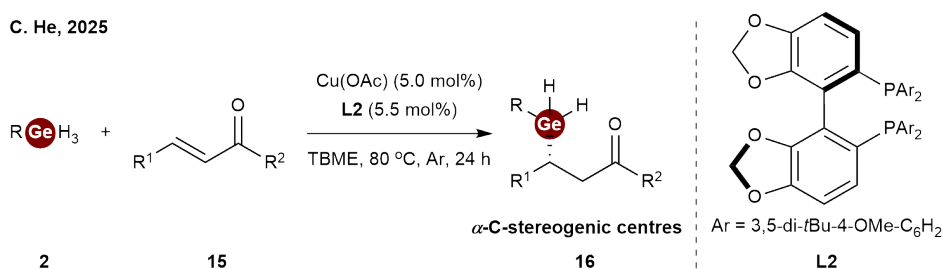
proposed mechanism



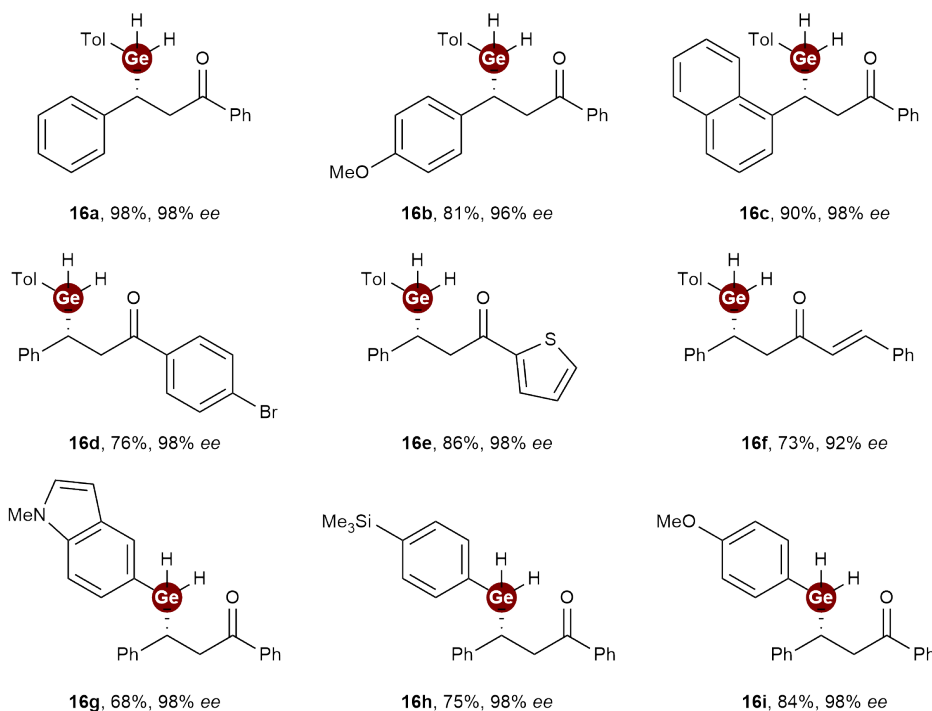
Scheme 3. Mechanistic studies and proposed mechanism for the hydrogermylation of dehydroalanines with dihydrogermanes.

Based on their previous success in the asymmetric hydrogermylation for the synthesis of β -C-stereogenic germanes, in 2025, He and co-workers expanded this strategy to the synthesis of α -C-stereogenic germanes^[17]. Utilizing $\text{Cu}(\text{OAc})$ as the catalyst and DTBM-Segphos **L2** as ligand, the enantioselective hydrogermylation reaction converted various α,β -unsaturated compounds **15** and trihydrogermanes **2** into the corresponding α -C-stereogenic germanes **16** in good yields with excellent enantioselectivities (up to 98% ee). The synthetic utility of this protocol was further demonstrated by the stereospecific derivatization of **16a** into functionalized chiral germanes **17–20** via nucleophilic addition with PhMgBr , condensation with 2,4-dinitrophenylhydrazine, hydrogermylation with methyl acrylate, and cross-coupling with methyl iodobenzene, respectively (Scheme 4).

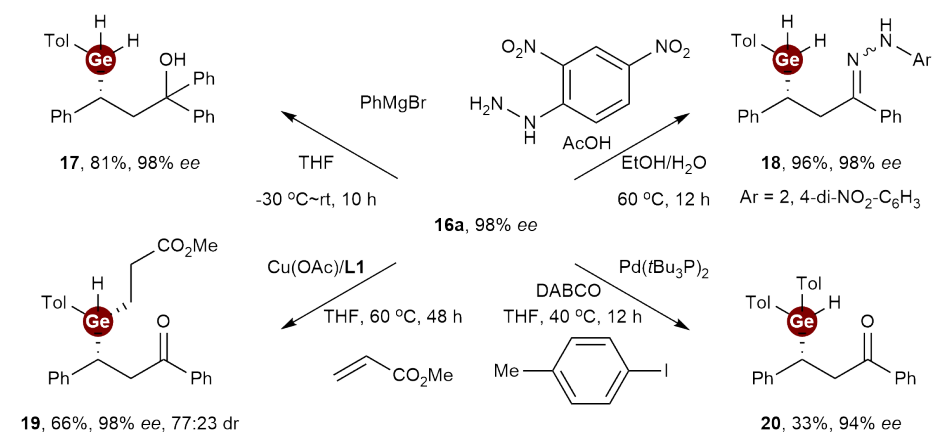
C. He, 2025



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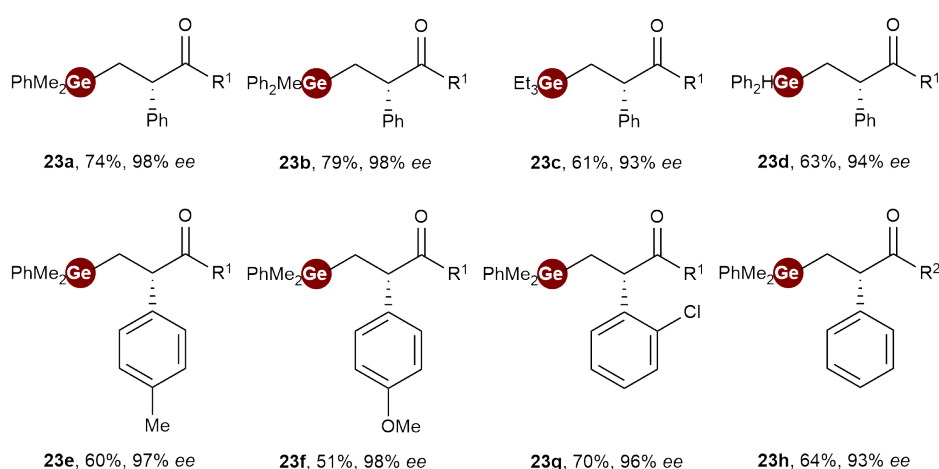
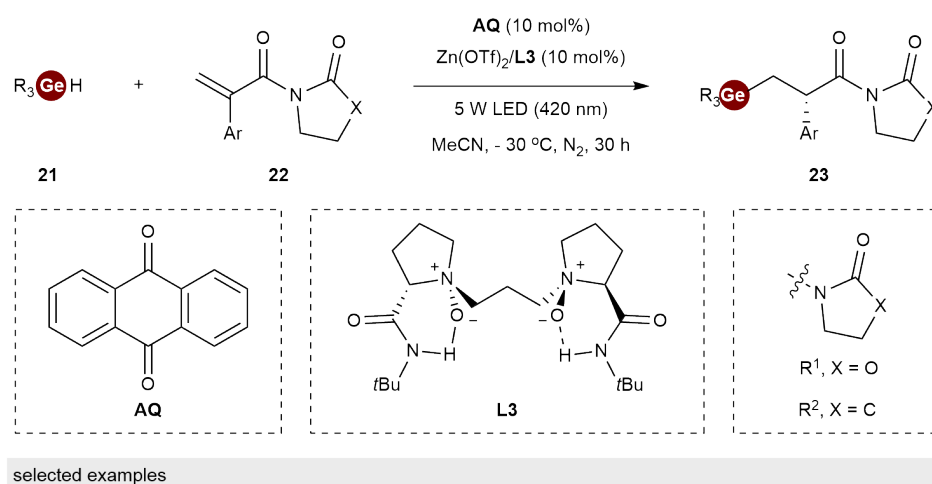


synthetic application

**Scheme 4.** Copper-catalyzed enantioselective hydrogermylation of α,β -unsaturated compounds with trihydrogermanes.

In addition to transition-metal catalysis, chiral Lewis acid catalysis also serves as an effective approach for asymmetric hydrogermylation reactions. Taking advantage of the unique chiral N,N' -dioxide ligand^[18], in 2025, Chen and co-workers reported a synergistic catalytic strategy for enantioselective hydrogermylation of α,β -unsaturated amides **22** with germanes **21**^[19]. This system integrates anthraquinone (AQ) as a dual-functional photocatalyst with a chiral Lewis acid catalyst derived from $\text{Zn}(\text{OTf})_2$ and ligand **L3**. This approach demonstrates broad substrate scope. A variety of chiral organogermanes **23** bearing α -C-stereogenic centers were afforded in high yields with good chemo-, regio and enantioselectivities (Scheme 5).

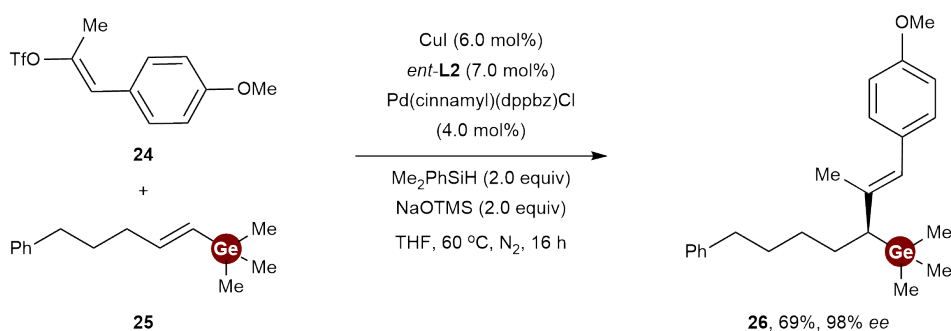
Feng and Cao, 2025



Scheme 5. Enantioselective hydrogermylation of α,β -unsaturated amides mediated by synergistic HAT photocatalyst and chiral Lewis acid. HAT: hydrogen atom transfer.

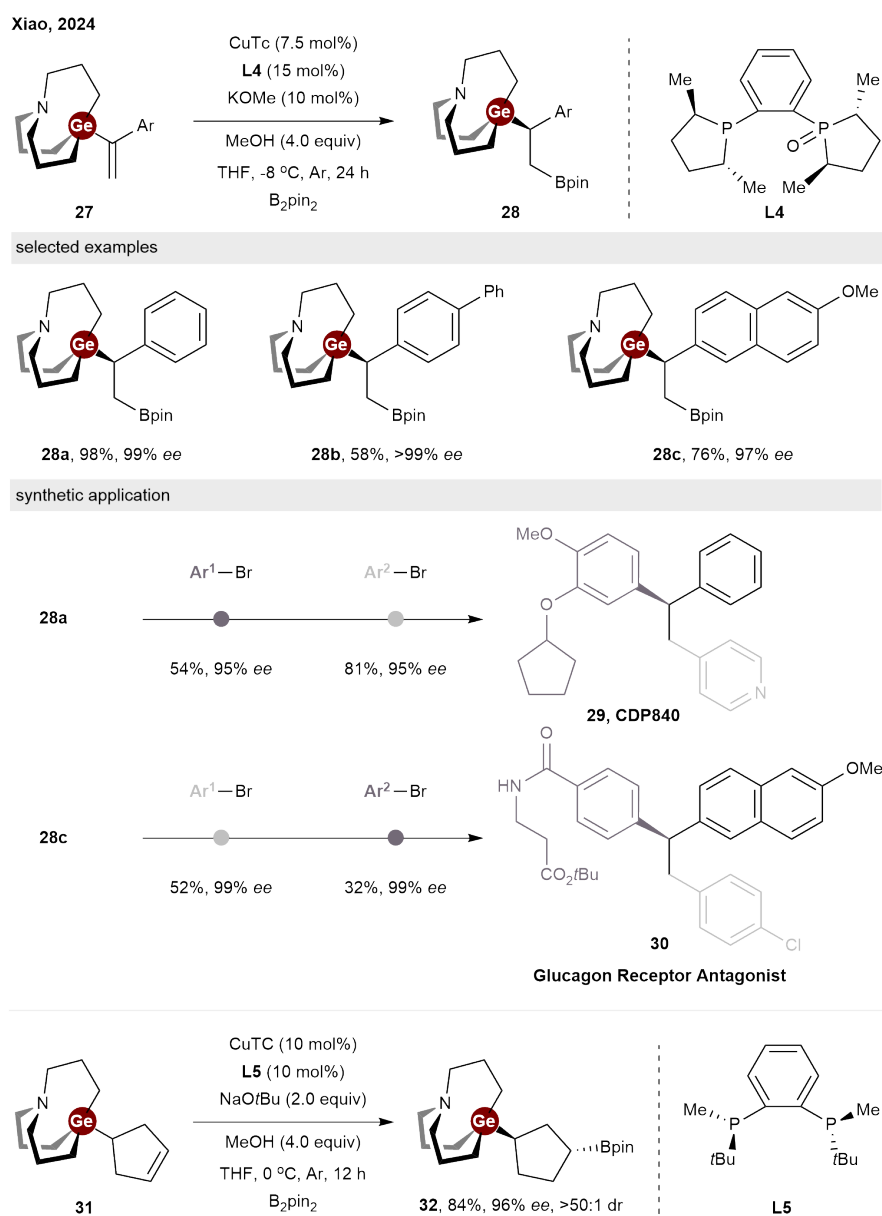
Diverging from the aforementioned hydrogermylation strategies centered on Ge-H bond activation, alternative hydrofunctionalization of vinylgermanes has also been developed. In these transformations, the germanium moiety does not participate in bond cleavage, remaining intact throughout the bond-forming process. In 2022, Buchwald and co-workers disclosed a protocol for the asymmetric synthesis of α -stereogenic allyl metalloids via dual CuH- and Pd-catalyzed hydroalkenylation^[20]. Although the study primarily focused on silicon and boron substrates, its applicability was successfully extended to organogermanium chemistry. Under optimized conditions employing CuI/*ent*-L2 and Pd(cinnamyl)(dppbz)Cl as dual catalysts, the enantioselective hydroalkenylation of vinylgermane 25 with enol triflate 24 afforded the chiral organogermane 26 in 69% yield with 98% ee (Scheme 6).

Buchwald, 2022



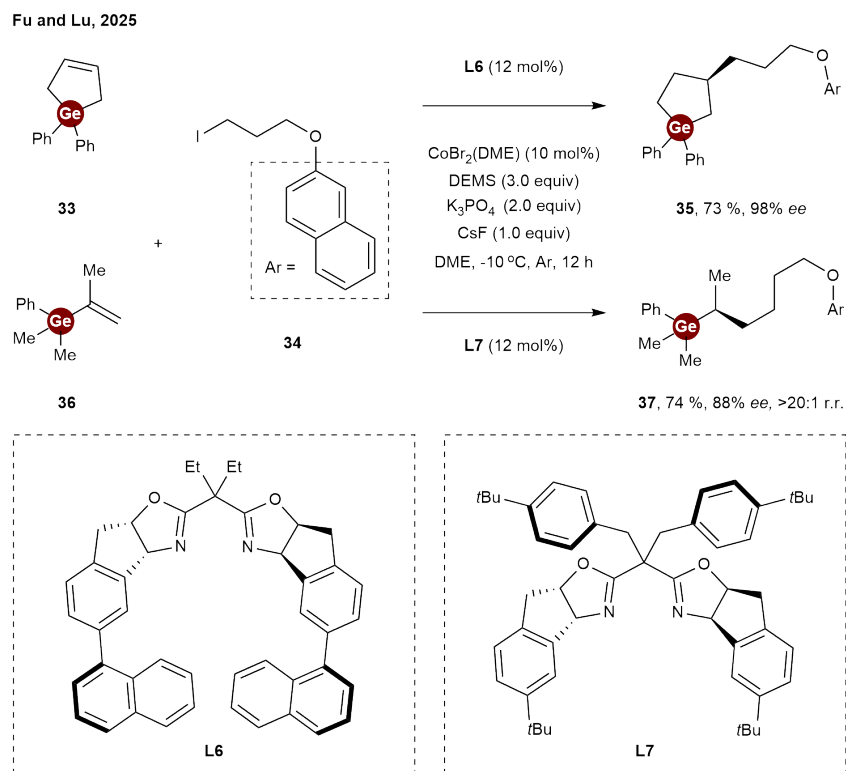
Scheme 6. Enantioselective hydroalkenylation of vinyl germane with enol sulfonate via dual copper hydride- and palladium-catalysis.

In 2024, Xiao and co-workers reported a copper-catalyzed enantioselective hydroboration of vinylgermanes^[21]. In this study, carbagermatrane-containing alkenes **27** underwent hydroboration in the presence of the CuTc/L4 catalyst, yielding target products **28** in moderate to good yields and excellent enantioselectivities (Scheme 7). These sp^3 -Ge/B bimetallic modules demonstrated remarkable orthogonal cross-coupling selectivity under different Pd-catalyzed conditions. For example, enantioenriched **29** and **30** can be readily prepared via -Ge/-B iterative cross-coupling sequence or -B/-Ge iterative cross-coupling sequence from **28a** and **28c**. They also expanded this asymmetric hydroborylation strategy to cyclopent-3-ene-1-carbagermatrane **31**. This allowed rapid access to highly enantioenriched cyclopentyl-Ge/B module **32**, which may serve as a useful building block for the construction of valuable 3D cyclopentyl molecules.



Scheme 7. Copper-catalyzed enantioselective hydroboration.

In 2025, Fu and Lu achieved the extension of their well-established cobalt-catalyzed alkene hydroalkylation strategies^[22] to the synthesis of chiral organogermanium compounds^[23]. They showcased the versatility of their catalytic platform by successfully extending it to germanium-containing alkenes. Employing the chiral bisoxazoline ligand **L6**, the hydroalkylation of germacyclopent-3-ene **33** with alkyl iodide **34** proceeded smoothly, affording the β -C-stereogenic germane **35** in 73% yield with 98% ee (Scheme 8). By changing the chiral ligand to **L7**, this methodology was also applicable to acyclic vinylgermanes. The α -C-stereogenic organogermane **37** could be obtained via the hydroalkylation of 1,1-disubstituted vinylgermane **36** with alkyl iodide **34** in high regioselectivity (>20:1 r.r.) and good enantiocontrol (88% ee). Together, this work establishes a general and modular platform for the stereodefined synthesis of both α - and β -stereogenic organogermanes via cobalt-catalyzed hydroalkylation.

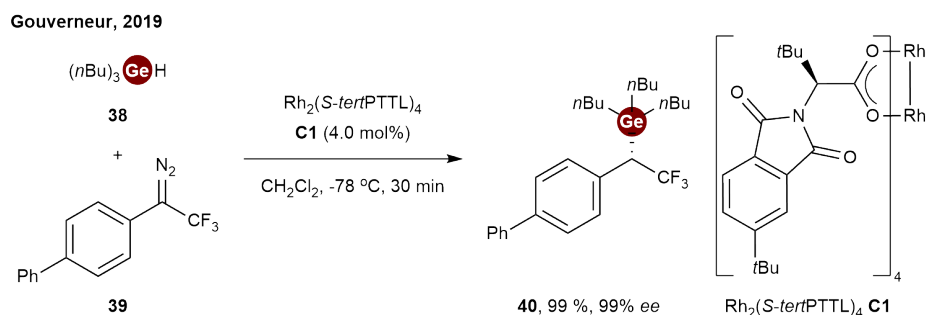


Scheme 8. Cobalt-catalyzed enantioselective hydroalkylation of germacyclopent-3-enes and vinylgermaniums.

In summary, the catalytic strategies for asymmetric alkene hydrofunctionalization differ in mechanism and scope. For hydrogermylation, the copper-catalyzed system proceeds via a key Cu–Ge intermediate, while the photocatalytic/chiral Lewis acid system likely involves a germyl radical pathway. However, both catalytic systems are currently effective only for electron-deficient alkenes, and extending these methodologies to unactivated alkenes represents an important future direction. On the other hand, for the hydrofunctionalization of vinylgermanes, reported methods have so far been limited to hydroalkenylation, hydroboration, and hydroalkylation. Other potentially valuable transformations such as hydrosilylation and hydroamination remain undeveloped and warrant further investigation.

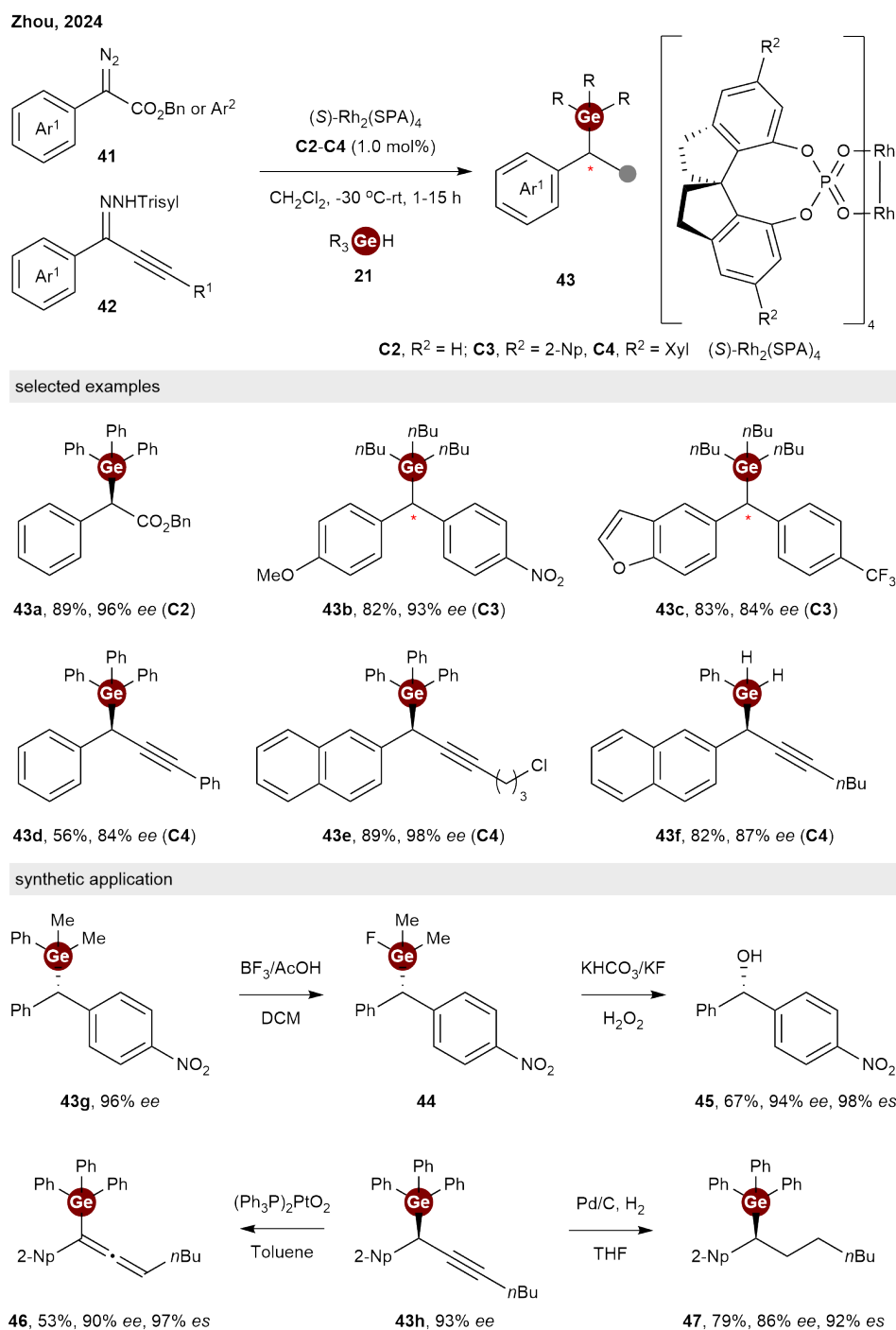
2.2 Carbene insertion

Carbene insertion into heteroatom–hydrogen (X–H) bonds is a powerful method for constructing carbon–heteroatom bonds^[24,25]. While asymmetric insertions into Si–H and B–H bonds are well-established^[26,27], the corresponding transformation with Ge–H bonds had remained unexplored. To bridge this gap, in 2019, Gouverneur and co-workers disclosed a rhodium-catalyzed asymmetric carbene insertion strategy, primarily focusing on tin hydrides (Sn–H) while successfully extending it to germanium substrates^[28]. To access bench-stable chiral α -trifluoromethylated derivatives, the authors employed the sterically demanding dirhodium catalyst **C1** to mediate the reaction between aryl-substituted 2,2,2-trifluorodiazaoethane **39** and tributylgermane **38**. Notably, when conducted at $-78\text{ }^{\circ}\text{C}$, the carbene insertion proceeded with exceptional efficiency, furnishing the chiral α -trifluoromethyl alkylgermane **40** in 99% yield with 99% ee (Scheme 9).



Scheme 9. Rhodium-catalyzed enantioselective insertion of trifluorodiazaoethanes into germanium hydrides.

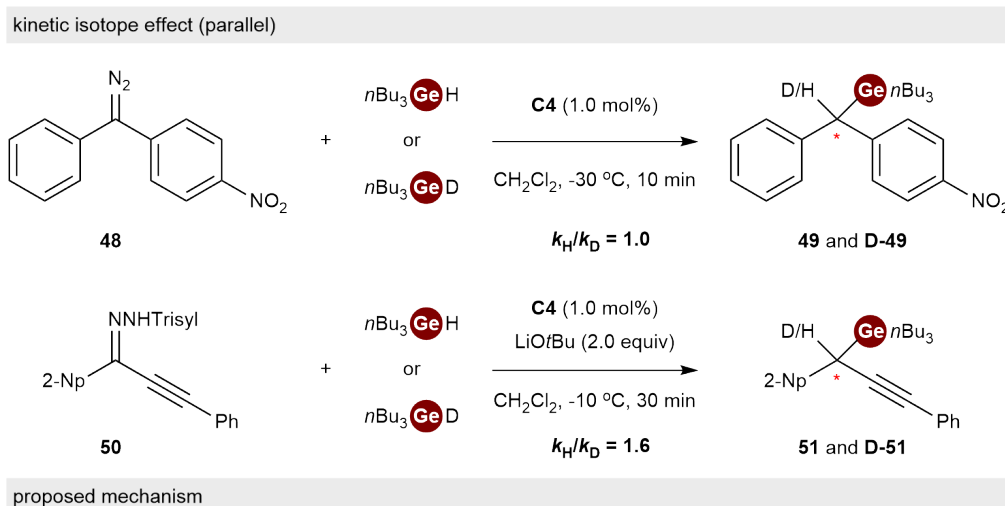
In 2024, Zhou and co-workers established a general and highly enantioselective strategy for carbene insertion into Ge–H bonds^[29], leveraging their expertise in asymmetric Si–H and B–H insertions^[30–31]. Utilizing the rigid chiral spiro dirhodium phosphate catalysts (S)-Rh₂(SPA)₄ (C2–C4), they achieved the efficient insertion of carbenes derived from α -diazo esters and diaryldiazomethanes **41**, as well as propargyl *N*-trisylhydrazones **42**, into various hydrogermanes **21** (Scheme 10). This protocol afforded a diverse library of chiral α -C-stereogenic organogermanes **43** in high yields with excellent enantioselectivities (up to 99% ee), demonstrating remarkable tolerance toward a wide range of functional groups including halides, ethers, and nitro groups. The synthetic utility of this protocol was further highlighted by the stereospecific transformations of the products, such as **43g** was oxidized to chiral alcohol **45**, and **43h** was converted into allenylgermane **46** and alkylgermane **47**, all with preservation of enantiopurity.



Scheme 10. Rhodium-catalyzed enantioselective C–Ge bond formation by carbene insertion.

To elucidate the reaction mechanism, they studied the kinetic isotope effect (KIE) in the reactions of carbene precursor **48** and **50** with *n*Bu₃GeH or *n*Bu₃GeD (Scheme 11). The KIEs of the reactions were 1.0 and 1.6, respectively, suggesting that C–Ge bond formation

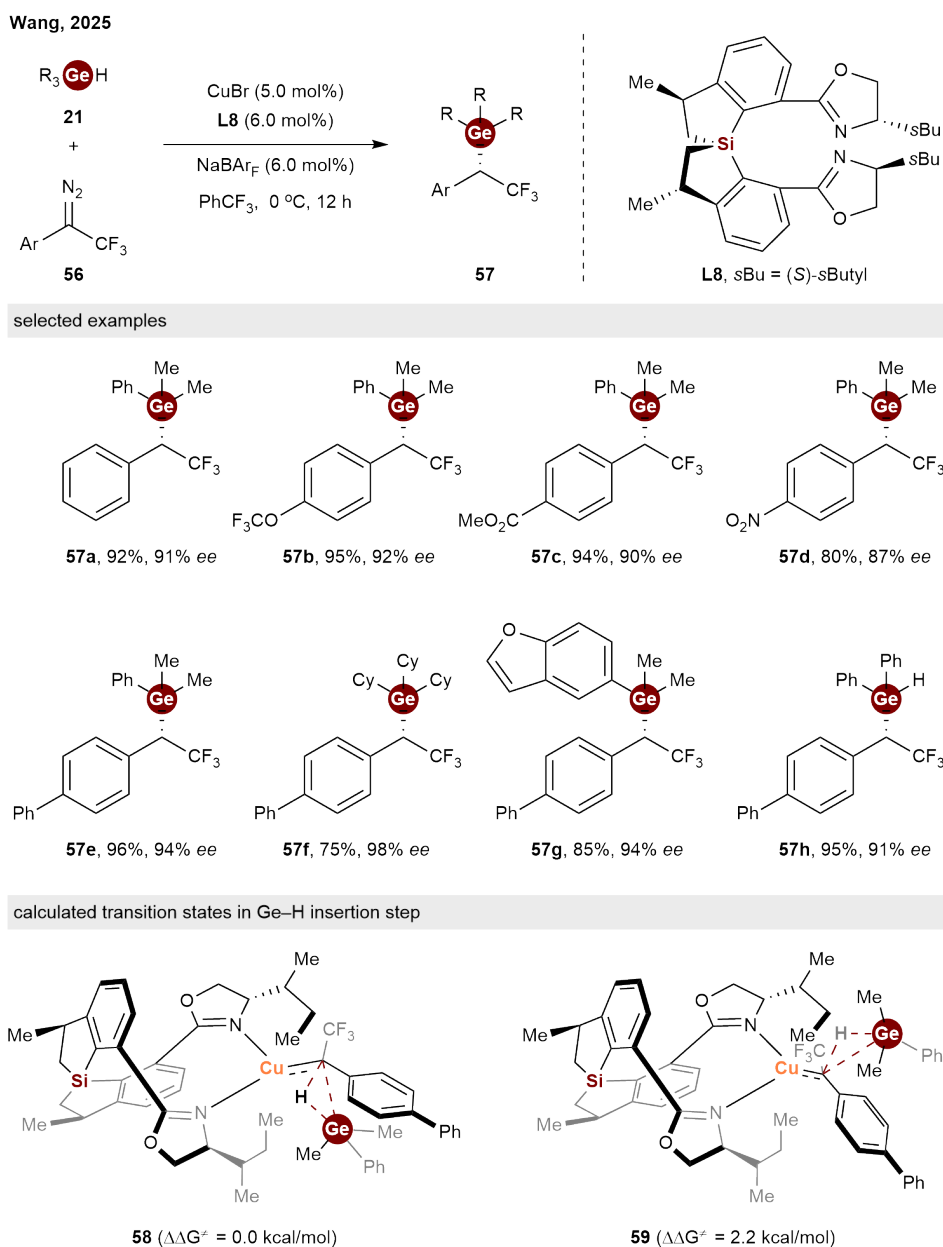
may not be the rate-limiting step. Based on the results, they proposed a mechanism for the Ge–H bond insertion. The catalytic cycle commences with the coordination of the diazo substrate **41** or **42** to the chiral dirhodium catalyst, forming adduct **52**. Subsequent nitrogen extrusion via transition state **53** generates the reactive rhodium-carbene species **54**. The electrophilic carbene intermediate **54** undergoes a concerted, irreversible insertion into the Ge–H bond via a three-center transition state **55**. DFT calculations further elucidated the origin of stereocontrol, revealing that the excellent enantioselectivity stems from destabilizing steric repulsion between the catalyst ligand and the substrate in the unfavorable transition state, thereby energetically favoring the formation of the chiral organogermane **43**.



Scheme 11. Mechanistic studies and proposed mechanism for the Ge–H bond insertion reaction.

In 2025, Wang and co-workers demonstrated the good performance of chiral spiroisilacycle ligands in the Cu-catalyzed asymmetric carbene insertion into Ge–H bonds^[32]. Enabled by newly developed C_2 -symmetrical bisoxazoline ligands **L8**, the reaction of various α -trifluoromethyl diazo compounds **56** with hydrogermanes **21** proceeded smoothly to afford a diverse array of chiral α -trifluoromethyl organogermanes **57** in high yields with excellent enantioselectivities (Scheme 12). Combined mechanistic studies and DFT calculations elucidated that the reaction proceeds via a concerted insertion pathway. Specifically, the calculations identified that the excellent stereocontrol originates from the steric repulsion between the sBu group of the oxazoline unit and the substituents on the germanium center, which effectively destabilizes the disfavored transition state, resulting in a calculated activation free energy difference of 2.2 kcal/mol.

A comparison of the mechanistic studies by Zhou's and Wang's groups reveals a unified stereocontrol model for asymmetric carbene insertion into Ge–H bonds, despite their distinct catalytic systems. Both works identify steric repulsion as the decisive factor governing enantioselectivity, as confirmed by DFT calculations. The key difference lies in the source of this repulsion. In Zhou's chiral dirhodium system, enantiocontrol arises primarily from repulsion between the bulky chiral ligand scaffold and the substituents on the carbene precursor. In contrast, Wang's copper/SPSiBox system relies on a more localized clash between a specific ligand alkyl group and the substituents on the germanium center. These findings collectively demonstrate that constructing a tailored chiral pocket to differentially destabilize one transition state through steric interactions is a general strategy across diverse catalyst platforms.



Scheme 12. Copper-catalyzed enantioselective carbene insertion into Ge–H bonds enabled by SPsiBox ligand.

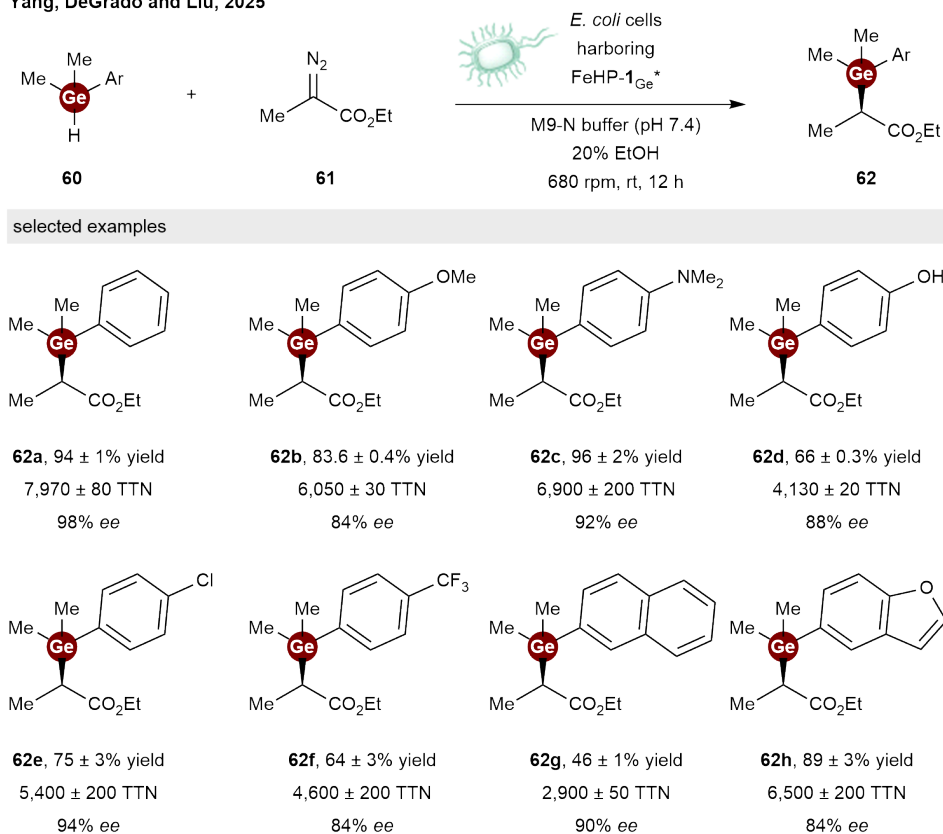
Over the past decade, *de novo* designed protein catalysts have shown considerable potential to advance the field of biological catalysis, attracting increasing attention toward enzyme engineering. Notably, a range of stereoselective catalytic reactions that are not found in nature have been developed. The representative examples are the pioneering work by Arnold, which demonstrated that engineered natural hemoproteins can catalyze Si–H and B–H insertion reactions^[33,34]. Recently, Huang and co-workers reported the *de novo* design and directed evolution of helical bundle proteins as enantioselective catalysts for germylation via Ge–H insertion^[35]. Addressing the specific challenge of controlling the earlier and more flexible transition state inherent to this transformation, the authors synergized *de novo* protein design with directed evolution to engineer a heme-binding helical bundle protein catalyst,

FeHP-1_{Ge}*. This biocatalyst was specifically tailored to accommodate distinct steric demands and the larger transition state associated with the germanium center, efficiently promoting the insertion of α -alkyl diazoesters **61** into various dimethylarylgermanes **60** under mild conditions (Scheme 13). The protocol exhibited a broad substrate scope and high catalytic efficiency (up to 8,000 total turnover numbers, TTN), furnishing a series of chiral aryl-substituted germane derivatives **62** with excellent yields and enantioselectivities (up to 98% ee).

2.3 Coupling reactions

Enantioconvergent cross-electrophile coupling has emerged as a powerful technique for constructing chiral molecules and has witnessed rapid advancement in recent years^[36–39]. Current approaches to stereochemical control predominantly rely on redox-active substrates, such as alkyl halides, which can be readily activated into carbon radicals for subsequent interaction with coordinated metals. Achieving stereoconvergent coupling with non-redox-active and stable alcohol derivatives is synthetically attractive but has remained largely underdeveloped. In 2024, Shu and co-workers explored a nickel-catalyzed stereoconvergent coupling of non-redox-active propargylic esters **64** with chlorogermanes **63**^[40]. This transformation provides an efficient route to chiral propargyl germanes **65** with excellent regio- and enantioselectivity across a broad range of functional groups (Scheme 14). Derivatization offers opportunities for expansion of the molecular diversity of germanium compounds. For example, the hydroboration and semihydrogenation of **65a** afforded alkenyl boronate **66** and (Z)-allylgermane **67**, respectively. The propargylic addition of germane to aldehyde yielded compound **68** without affecting the enantiopurity. Furthermore, this regiocontrolled addition process could be directed to furnish the allenic addition product **69** at high stereospecificity.

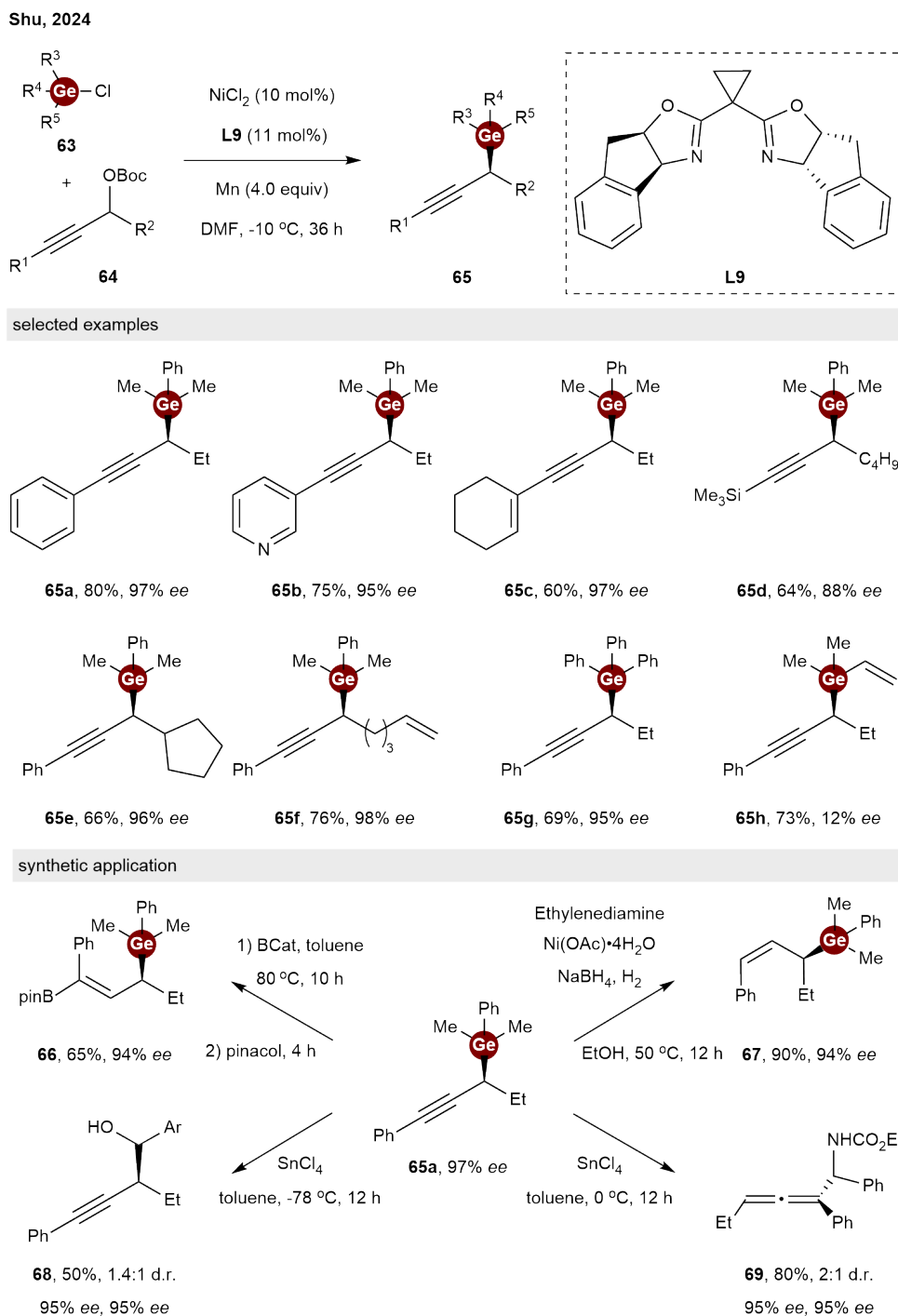
Yang, DeGrado and Liu, 2025



Scheme 13. Biocatalytic enantioselective carbene insertion into Ge–H bonds.

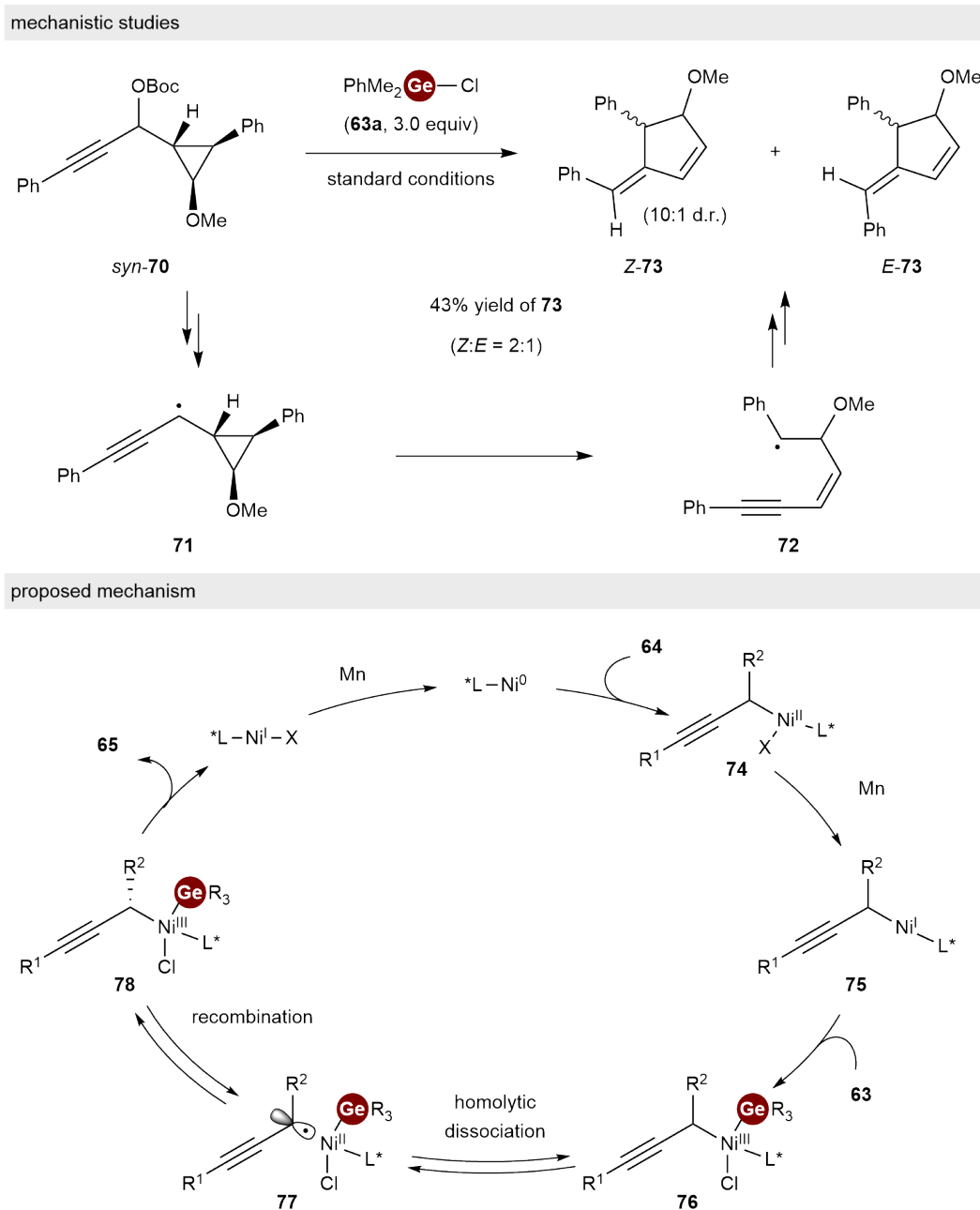
To gain insight into the mechanism of this process, a radical clock experiment was conducted (Scheme 15, top). Under standard conditions, the reaction of cyclopropyl substrate *syn*-**70** with **63a** resulted in the ring expanded product **73** at 43% yield with a *Z*:*E* ratio of 2:1. This result is consistent with a radical ring-opening/closing process via intermediates **71** and **72**. Based on these experimental results and relevant literature precedents, a catalytic cycle was proposed (Scheme 15, bottom). Initially, propargylic ester **64** reacts with Ni(0), followed by reduction with Mn, to generate propargylic Ni(I) species **75**. Subsequent oxidative addition of **75** to chlorogermane **63** yields Ni(III) complex **76**. Reversible homolytic cleavage of the Ni–C bond in **76**, followed by recombination between the resulting Ge–Ni(II)X species and the propargyl radical via intermediate **77**, produces enantioenriched complex **78**. Finally, stereospecific reductive elimination from **78** delivers the desired chiral product **65**.

In addition to the aforementioned asymmetric C–Ge coupling approach for synthesizing C-stereogenic germanes, an alternative strategy involves the asymmetric C–C coupling between germylated allylic electrophiles and alkyl nucleophiles. In 2023, Oestreich and co-workers developed a nickel-catalyzed enantio- and regioconvergent cross-coupling of regioisomeric mixtures of racemic germylated allylic electrophiles **79** with alkylzinc reagents^[41]. The success of this method relies on a newly designed hept-4-yl-substituted Pybox ligand **L10**, which facilitates access to a range of γ -C-stereogenic germanes **80** as a single regioisomer in excellent yields and enantioselectivities (Scheme 16). The observed regioconvergence is attributed to the directing effect exerted by the sterically demanding germyl group. To further demonstrate the potential synthetic utility of the generated γ -chiral vinyl germanes, a halodegermylation of **80h** was conducted to obtain the desired vinyl bromide **81** in 72% yield with an *E/Z* ratio of 20:1. These motifs can easily undergo a Negishi cross-coupling reaction to access arylated product **82** without the loss of enantiopurity.



Scheme 14. Nickel-catalyzed enantioconvergent and regioselective reductive coupling of propargylic esters with chlorogermane.

The nickel-catalyzed asymmetric coupling methods discussed herein, including stereoconvergent reductive cross-coupling and enantio- and regioconvergent C–C coupling, provide efficient routes to chiral germanes. Despite these advances, significant challenges and opportunities remain in this field. Currently, the substrate scope is largely confined to activated electrophiles, such as propargylic and allylic derivatives. Expanding these methodologies to encompass less activated or simpler electrophiles would substantially broaden their synthetic leverage and practical utility. Furthermore, the development of catalytic asymmetric intermolecular dehydrogenative Ge–H/X–H couplings remains an underexplored yet promising avenue for the direct construction of Ge–stereogenic centers.

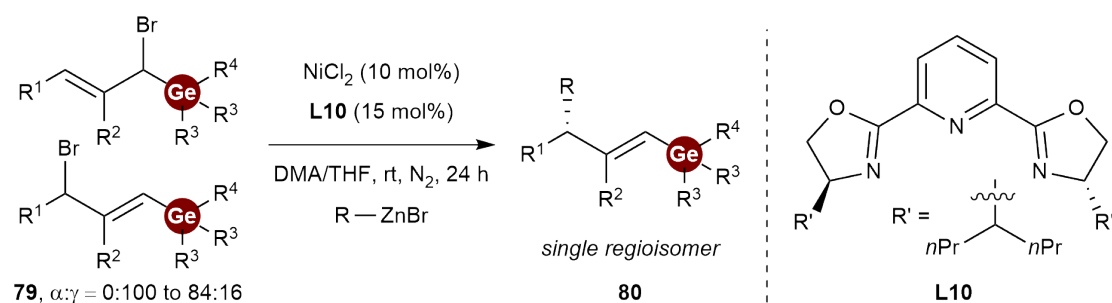


Scheme 15. Mechanistic studies and proposed mechanism for the reductive C–Ge coupling.

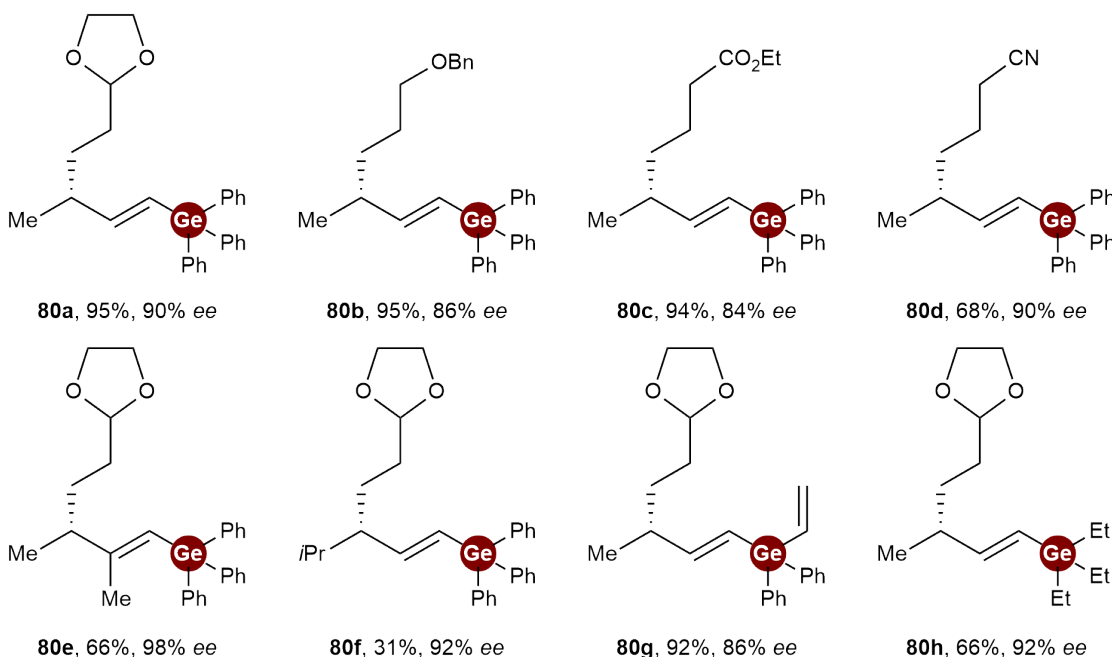
3. Catalytic Asymmetric Synthesis of Ge-Stereogenic Germanes

The construction of germanium-stereogenic centers represents a frontier in main-group stereochemistry. Unlike carbon chirality, where precursors are abundant, accessing Ge-stereogenic compounds typically requires the desymmetrization of prochiral substrates or complex resolution steps. Recent years have seen the development of elegant catalytic strategies to address this challenge, focusing on the desymmetrization of dihydrogermanes and tetraorganogermanes.

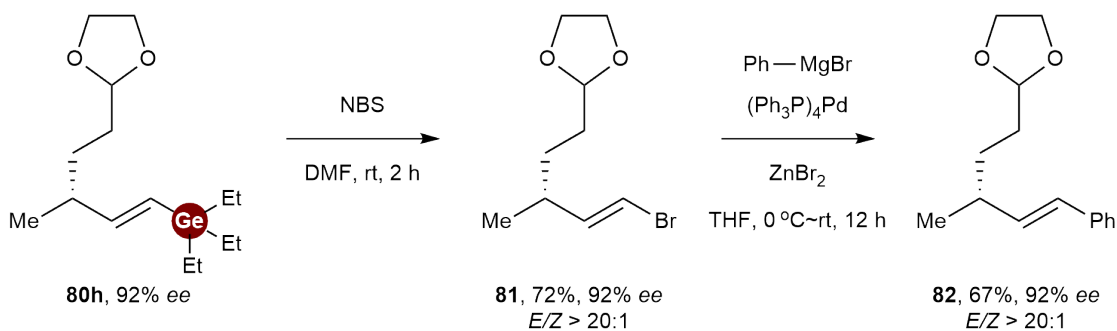
Oestreich, 2023



selected examples



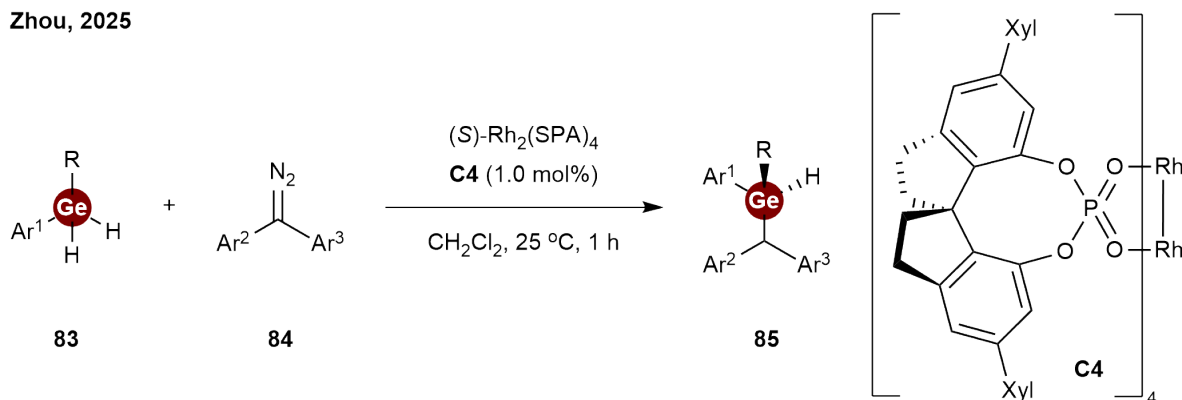
synthetic application

Scheme 16. Nickel-catalyzed enantio- and regioconvergent $C(sp^3)$ – $C(sp^3)$ cross-coupling of germylated allylic electrophiles.

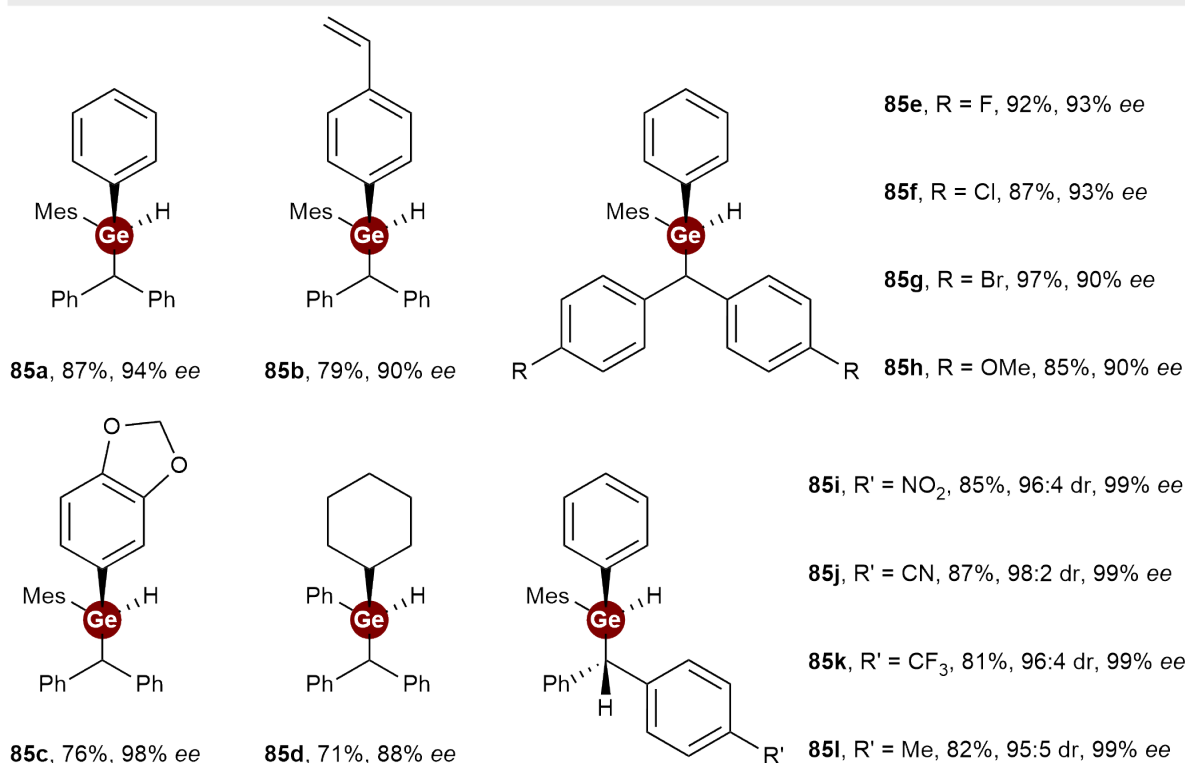
3.1 Desymmetrization of dihydrogermanes

Building upon their earlier success with C-stereogenic germanes, Zhou and co-workers recently achieved the construction of Ge-stereogenic centers via rhodium-catalyzed desymmetric Ge–H bond insertion of dihydrogermanes^[42]. In this process, the chiral rhodium phosphate catalyst (S)-Rh₂(SPA)₄ C4 decomposes diaryldiazomethanes **84** to generate rhodium carbenes that insert enantioselectively into one of the two Ge–H bonds of dihydrogermanes **83** to form Ge-stereogenic germanes **85** in high yield with excellent enantioselectivities under mild conditions (Scheme 17). Furthermore, this protocol was readily applied to unsymmetrical diaryldiazomethanes, affording germanes **85i–85l** with dual (Ge and C) stereogenic centers with excellent diastereo- and enantioselectivity.

Zhou, 2025



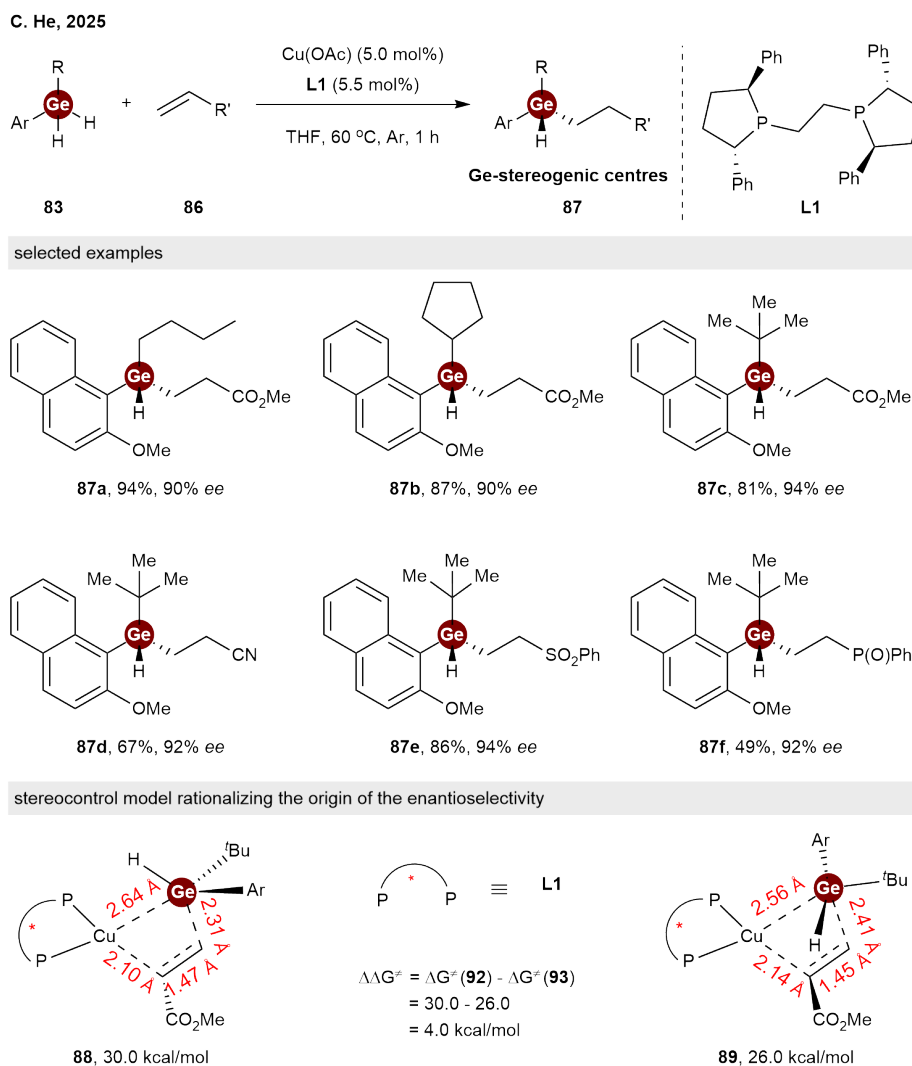
selected examples

**Scheme 17.** Rhodium-catalyzed desymmetric Ge–H bond insertion of dihydrogermanes.

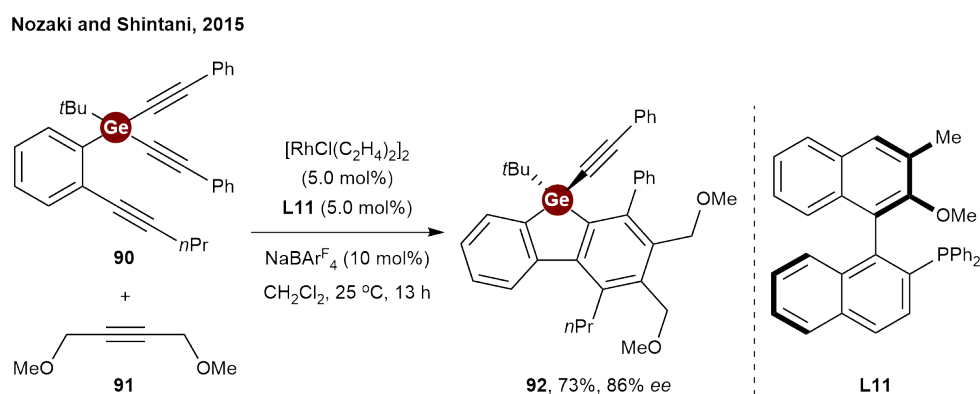
Following the development of synthetic routes to α - and β -C-stereogenic germanes, C. He and co-workers have successfully extended the asymmetric hydrogermylation strategy to the construction of Ge-stereogenic germanes^[17]. Employing a catalytic system of $\text{Cu}(\text{OAc})$ and the chiral ligand (*S,S*)-Ph-BPE **L1**, they achieved the desymmetric hydrogermylation of activated alkenes **86** with prochiral dihydrogermanes **83** in THF at 60°C (**Scheme 18**). This protocol featured a broad substrate scope, furnishing the desired chiral germanes **87** in high yields with good to excellent enantioselectivities. DFT calculations elucidated the origin of the enantioselectivity, indicating that the reaction proceeds via the nucleophilic addition of an *in situ* generated $[\text{Cu}\text{-Ge}]$ intermediate to the alkene. As illustrated in the stereocontrol model, the transition state leading to the major enantiomer **89** (26.0 kcal/mol) is energetically favored by 4.0 kcal/mol over the minor pathway **88** (30.0 kcal/mol). This preference is ascribed to the minimized steric repulsion between the ligand framework and the substituents on the germanium atom in the favored transition state.

3.2 Desymmetrization of tetraorganogermanes

The pioneering example of transition-metal-catalyzed desymmetrization of tetraorganogermanes was reported by Nozaki and Shintani in 2015^[43]. By extending the rhodium-catalyzed [2+2+2] cycloaddition strategy to heavier group 14 elements, they achieved the desymmetrization of germanium-containing triyne **90** with alkyne **91** by using the axially chiral monophosphine ligand **L11** (**Scheme 19**). This reaction afforded dibenzogermole **92** bearing a Ge-stereogenic center in 73% yield with 86% ee.



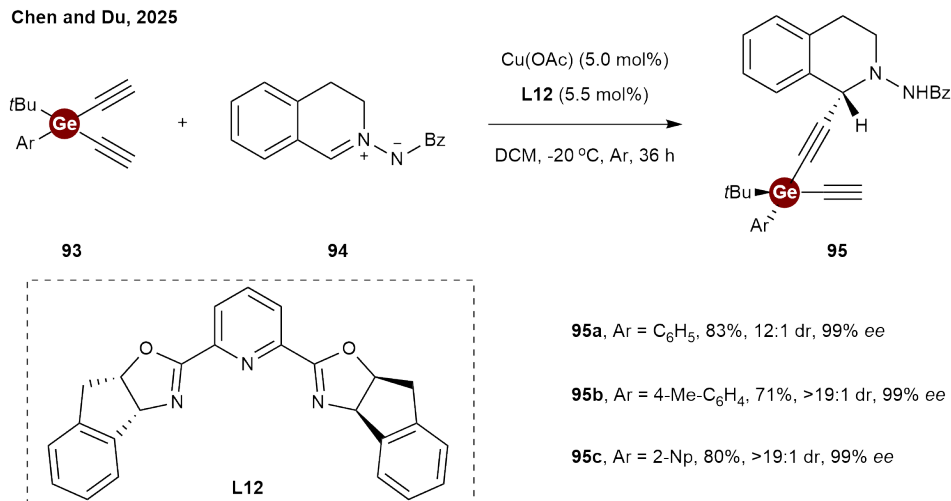
Scheme 18. Copper-catalyzed enantioselective hydrogermylation of activated alkenes with dihydrogermanes.



Scheme 19. Rhodium-catalyzed enantioselective [2+2+2] cycloaddition of germanium-containing prochiral trienes.

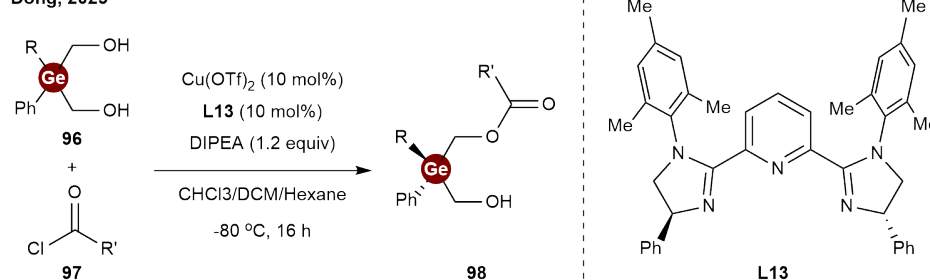
The installation of distant stereogenic centers (such as 1,4-positioned centers) in acyclic systems remains a formidable challenge. In 2025, Chen and Du reported a copper-catalyzed asymmetric alkynylation of *C*, *N*-cyclic azomethine imine **94** with dialkynylgermanes **93** (Scheme 20)^[44]. This methodology afforded enantioenriched propargylic germanes **95** with high diastereo- and enantioselectivities. This sequential asymmetric deprotonation-alkynylation approach, mediated by a single chiral catalyst, offers a reliable and efficient method for the diastereo- and enantioselective synthesis of products featuring conventionally difficult-to-access rectilinear 1,4-central chirality.

Chen and Du, 2025

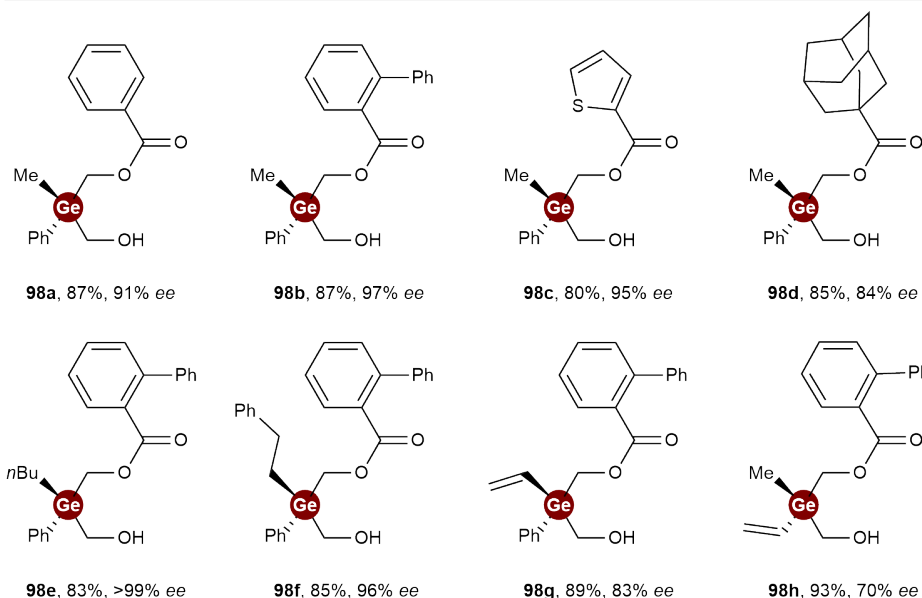
**Scheme 20.** Copper-catalyzed asymmetric alkynylation of *C,N*-cyclic azomethine imine with dialkynylgermanes.

In addition to constructing Ge-stereogenic centers through the desymmetrization of germanium-containing bis-alkynes, germanium-based 1,3-diols have also been demonstrated to serve as viable prochiral substrates. In 2025, Dong and co-workers reported a copper-catalyzed desymmetrization of diols to access chiral germanium centers^[45]. Employing a pyridine-bisimidazoline **L13** as the chiral ligand and acyl chlorides **97** as acylating agents, the hydroxyl groups of diol substrate **96** were selectively mono-acylated, affording mono-benzoyl-protected chiral germanium products **98** in high yields and enantioselectivity (Scheme 21).

Dong, 2025



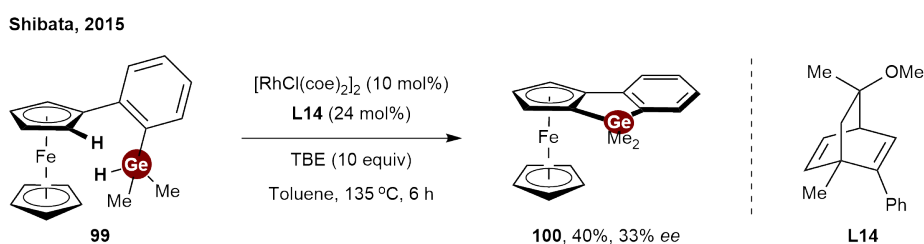
selected examples

**Scheme 21.** Copper-catalyzed desymmetrization of germanium containing 1,3-diols.

As noted in Section 3, the current catalytic desymmetrization strategies for constructing Ge-stereocenters largely rely on germanes bearing bulky substituents. The development of methods applicable to simpler dihydrogermanes and tetraorganogermanes remains a challenging but highly desirable goal. Addressing this limitation will likely require the design of new chiral ligands and catalytic systems.

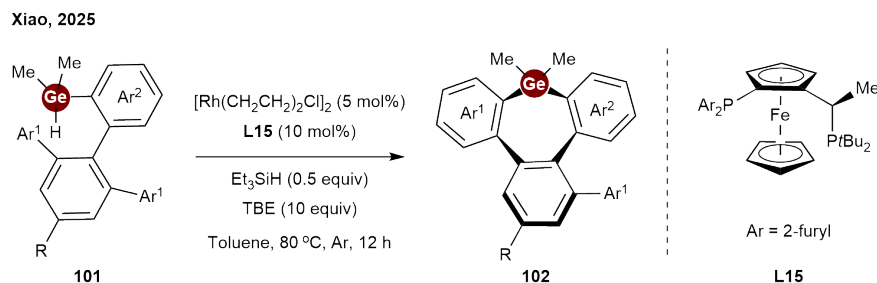
4. Catalytic Asymmetric Synthesis of Other Chiral Germanes

In recent years, the asymmetric catalytic synthesis of other chiral germanes has also been reported. Parallel to the reports by Takai and He on the enantioselective synthesis of silicon-bridged planar-chiral ferrocenes in 2015^[46,47], Shibata and co-workers independently disclosed a similar rhodium-catalyzed intramolecular dehydrogenative coupling strategy^[48]. Notably, while concurrent studies focused predominantly on silylation, they successfully expanded the scope of this methodology to the heavier congener, germanium. By using a Rh/chiral diene **L14** catalyst with *tert*-butyl ethylene (TBE) as a hydrogen acceptor, the intramolecular C–H/Ge–H dehydrogenative coupling of 2-(dimethylhydrogermyl) phenylferrocene **99** proceeded to afford benzogermoloferrrocene **100** in 40% yield with 33% ee (Scheme 22).

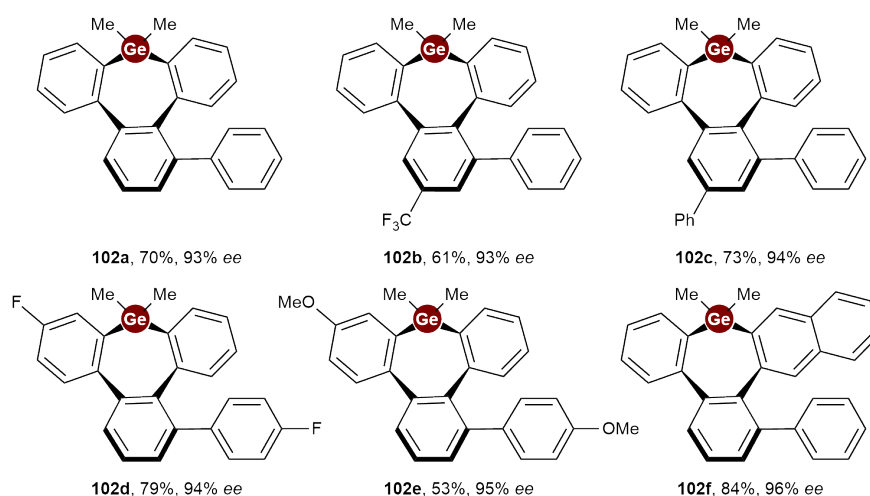


Scheme 22. Rhodium-catalyzed enantioselective intramolecular C–H germylation toward planar-chiral benzogermoloferrrocene.

Recently, Xiao and co-workers extended the rhodium-catalyzed enantioselective intramolecular C–H/Ge–H dehydrogenative coupling strategy to the synthesis of inherently chiral germanes^[49]. Employing the chiral Josiphos-type ligand **L15**, a series of inherently chiral tribenzogermepins **102** were successfully synthesized via this intramolecular asymmetric C–H germylation of hydrogermane precursors **101** in moderate to high yields with excellent stereoselectivity (Scheme 23).

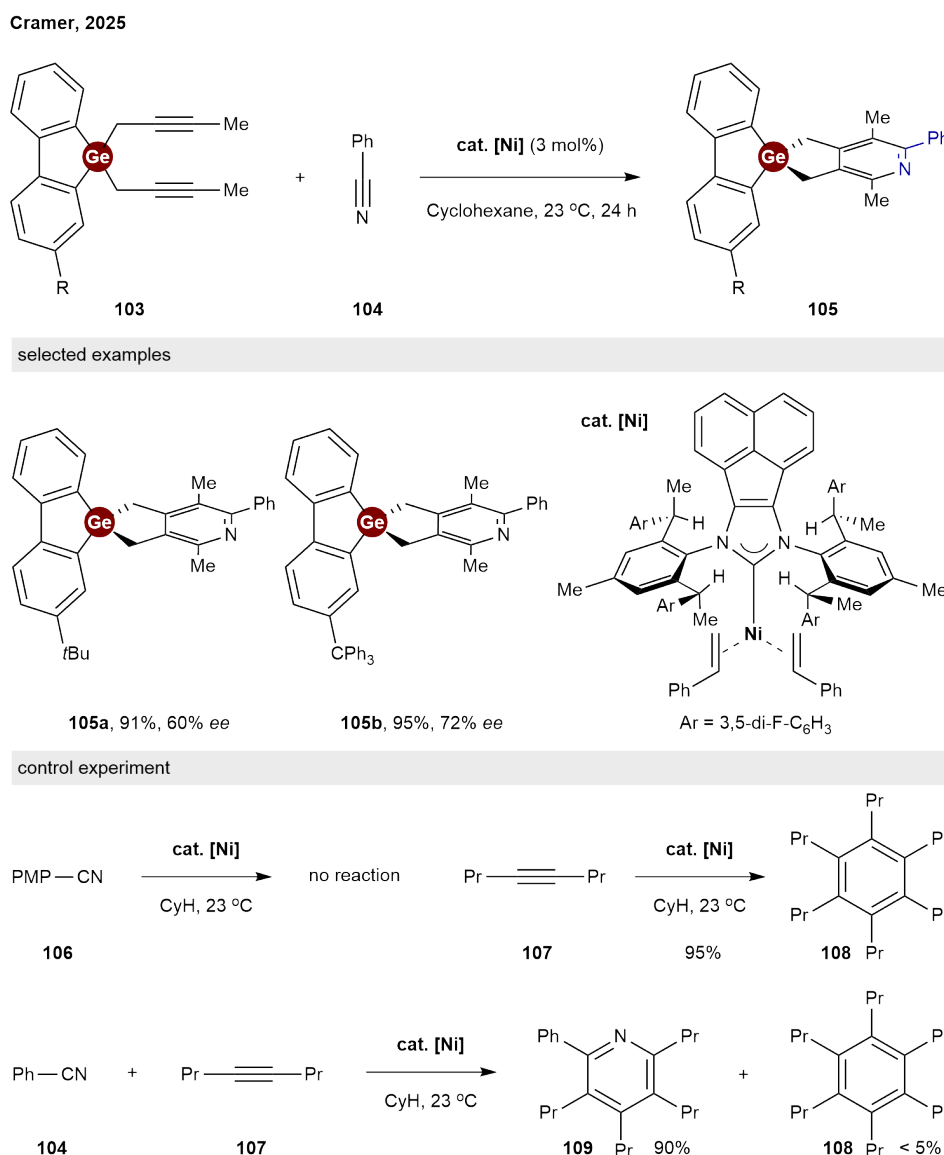


selected examples



Scheme 23. Rhodium-catalyzed enantioselective intramolecular C–H germylation toward inherently chiral germepins.

In 2025, Cramer and co-workers reported a unified strategy for the construction of chiral spirocyclic skeletons via nickel-catalyzed enantioselective hetero [2+2+2] cycloaddition^[50]. A chiral designer Ni(0) N-heterocyclic carbene complex **cat. [Ni]** enables the required long-range enantioinduction. After demonstrating its broad utility for synthesizing carbon- and boron-centered spirocycles, they successfully extended this protocol to the chiral spirogermanium center. When dialkynylgermanes **103** and benzonitrile **104** were selected as substrates for this hetero [2+2+2] cycloaddition, the target spiro germafluorene **105a** and **105b** were obtained in 91% and 93% yields with 60% and 72% ee, respectively (Scheme 24). To shed some light on the reaction mechanism, some control experiments were conducted. No reaction occurred between precatalyst **cat. [Ni]** and *p*-methoxybenzonitrile **106**, indicating that nickel has a stronger affinity for styrene than nitrile and that coordination of the nitrile is contingent following ligand exchange of styrene with alkyne substrate. In the absence of a nitrile, **cat. [Ni]** cleanly catalyzed trimerization of alkyne **107** to afford **108** in 95% yield; however, the formation of pyridine **109** is largely favored in its presence. This indicates that pyridine formation proceeds much faster than cyclotrimerization of alkyne. These experimental results support that the reaction proceeds by a heterocoupling mechanism in which one of the alkynes and the nitrile link together first.



Scheme 24. Nickel-catalyzed enantioselective hetero [2+2+2] cycloaddition for construction of spiro germafluorene.

5. Conclusion and Perspective

This review has summarized recent advances in the catalytic asymmetric synthesis of chiral organogermanes, including the construction of C-stereogenic and Ge-stereogenic centers, as well as planar, inherent, and axial chiral organogermanes. Despite these achievements, several challenges and opportunities for improvement remain. First, the range of methodologies for constructing Ge-stereogenic centers is still relatively narrow, and the substrates are also largely limited to germanes bearing bulky

substituents. The development of novel approaches would significantly expand structural diversity and enhance synthetic practicality, such as in intermolecular asymmetric Ge–H/X–H dehydrogenative coupling reactions. Second, achieving the synthesis of complex architectures bearing multiple stereogenic centers represents a formidable next frontier, demanding innovative catalytic strategies to control both enantioselectivity and diastereoselectivity simultaneously. Third, in-depth mechanistic studies are essential to understand the stereocontrol processes, thereby guiding the rational design of chiral catalysts. Fourth, the practical utility of these chiral organogermanes, for example, as chiral ligands or functional materials, requires more systematic investigation to fully demonstrate their unique value.

In conclusion, while established methods provide access to certain chiral organogermanes, the field presents clear opportunities for future development. Addressing the current limitations in reaction methodology, mechanistic understanding, and functional exploration will be key to advancing the chemistry and utility of chiral organogermanium compounds.

Declarations

Authors contribution

Liu S: Investigation, writing-original draft, visualization.

Ke J: Project administration, methodology, writing-review & editing.

He C: Conceptualization, funding acquisition, supervision, writing-review & editing.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

Not applicable.

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