

the formation of specific C<sub>2+</sub> products in CO<sub>2</sub>RR. The previous study on the formation of acetamide from co-electrolysis of CO and NH<sub>3</sub> demonstrated that acetate production might undergo a pathway involving the nucleophilic attack of OH<sup>-</sup> on the ketene-like intermediate (\*CCO).<sup>10</sup> Substituting other carbon precursors for FA will offer opportunities to comprehend C–C coupling steps and bifurcation toward ethylene versus ethanol in CO<sub>2</sub>RR. In summary, by taking co-electrolysis of CO<sub>2</sub> and FA as a showcase, Han and co-workers<sup>6</sup> have provided us with new inspiration for constructing C–C bonds and expanding the scopes of CO<sub>2</sub> utilization.

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### DECLARATION OF INTERESTS

The authors declare no competing interests.

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## Differentiation of enynes and alkynes in asymmetric multicomponent reactions by Pd catalysis

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In this issue of *Chem Catalysis*, Chen and co-workers describe a chemo- and stereodivergent asymmetric multicomponent reaction (AMCR) involving two different alkynes under palladium catalysis. Through the elaborate manipulation of catalytic conditions, the reactions selectively afford chiral tetra-substituted alkenes or *N*-heterocycles bearing an exocyclic double bond in either *E*- or *Z*-configuration.

The preparation of chiral compounds plays a vital role among synthetic community owing to the disparate physiological or pharmacological properties of both enantiomers.<sup>1</sup> To this end, the catalytic asymmetric multicomponent reac-

tions (AMCRs), which allow chemists to obtain chiral compounds from three or more reactants in a one-pot vessel, have exhibited a remarkable impact on the rapid assembly of complex products with the maximization of synthetic effi-

ciency and molecular diversity.<sup>2,3</sup> As a fundamental building block, alkyne is one of the most accessible synthons that has been widely employed in AMCRs.<sup>4</sup> In this regard, the transition-metal-catalyzed enantioselective difunctionalization of alkynes, specifically the simultaneous installation of one carbon nucleophile and one carbon electrophile across the internal alkyne bonds, is an extremely appealing protocol for the construction of valuable tetra-substituted alkenes. During the past decades, many

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elaborated methods have been exploited for this conversion.<sup>5</sup> However, the asymmetric difunctionalization reaction involving two different alkynes has still rarely been explored to date. The competitive reactivity between the two distinct triple bonds engaged in this reaction may pose substantial obstacles in chemo-, regio-, and stereoselective control and thus calls for high demands of suitable chiral catalytic systems.

Recently, the Chen group has revealed an elegant work on palladium-catalyzed asymmetric difunctionalization of 1,3-enynes with imines and boronic reagents.<sup>6</sup> It afforded the enantioenriched tetra-substituted alkene derivatives efficiently with high *cis*-selectivity. In this issue of *Chem Catalysis*, a remarkable contribution is continuously devoted by Chen and co-workers on the asymmetric multicomponent cascade reactions between 1,3-enynes **1**, *N*-sulfonylimines **2**, and terminal alkynes **3**.<sup>7</sup> Notably, several significant challenges should be expected in realizing the above transformation with two distinct alkynes: (1) chemoselectivity issues caused by side-reactions, such as the self-cyclotrimerization of alkynes, competitive reactivity between the two different alkynes, as well as the products distribution between tetra-substituted alkenes **4** and five-membered *N*-heterocycles **5** and **6**; (2) the regioselectivity control during alkynes addition process; and (3) the stereoselectivity issues, including enantioselective control and the configuration regulation of the exocyclic C=C bonds (Figure 1A). To address these obstacles, the reactivity controllable palladium catalysis is successfully exploited by Chen's team. In the presence of Pd<sub>2</sub>(dba)<sub>3</sub> with a BINOL-derived phosphoramidite (L1) as the ligand and triethylamine (Et<sub>3</sub>N) as the base, the reactions deliver all-carbon tetra-substituted alkenes **4** bearing an adjacent chiral center efficiently with good control of regio- and stereoselectivity (Figure 1B). A range of 1,3-enyne,

*N*-sulfonylimine, and terminal alkyne substrates with various functionalized groups are well tolerated with high levels of reactivity and enantioselectivity. Moreover, this asymmetric multicomponent strategy is also suitable for many drug-molecule-derived terminal alkynes, showcasing the application potential of current catalysis.

Interestingly, by a slight adjustment of base and additive, the reaction products can be totally switched from the tetra-substituted alkenes **4** to chiral five-membered *N*-heterocycles **5** with a (*Z*)-exocyclic double bond (Figure 1B). The synthetic utilization of this tandem procedure is demonstrated in a broad scope of over 20 substrates, where up to 85% yield and 99% ee are achieved in stereospecific (*Z*)-configuration. Control experiments show that the intramolecular hydroamination of tetra-substituted alkene products **4** should be responsible for formation of *N*-heterocycles, and the presence of extra terminal alkyne and MeOH are both indispensable in this hydroamination process.

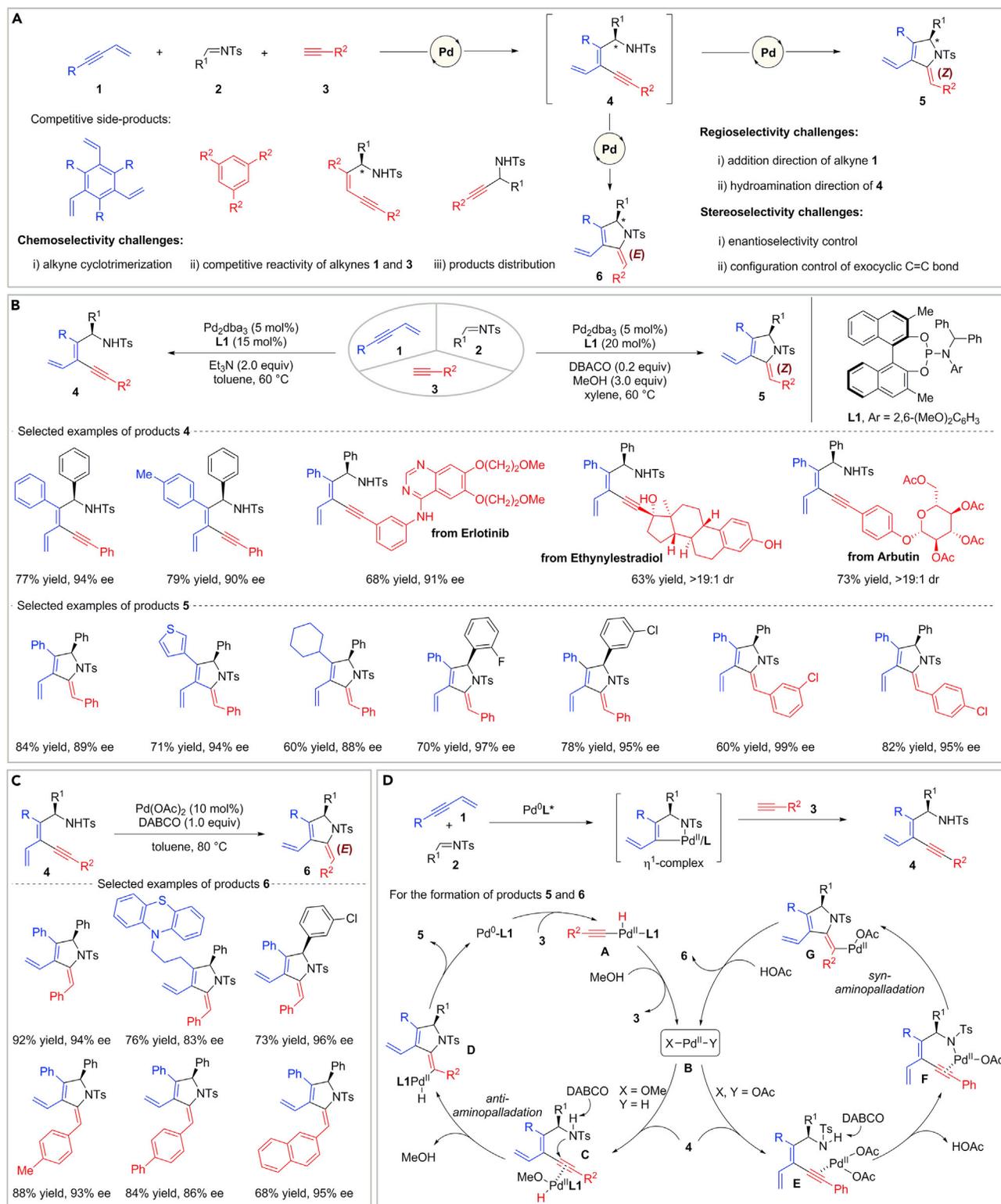
The stereodivergent construction of both *Z*- and *E*-configured double bonds from one set of substrates through the catalytic manipulation is an attractive yet challenging strategy in organic synthesis.<sup>8–10</sup> The investigations carried out by Chen and co-workers show that the stereoselectivity of exocyclic double bond in *N*-heterocyclic products can be governed by the choice of palladium precursor. With Pd(OAc)<sub>2</sub> as the catalyst, *N*-heterocycles **6** with an (*E*)-exocyclic double bond can be smoothly obtained in the intramolecular hydroamination reaction of tetra-substituted alkene products **4** (Figure 1C).

Based on the mechanism proposal, the reaction should be initiated by the reaction between 1,3-enyne **1** and imine **2** via  $\pi$ -Lewis base catalysis of Pd(0)/L to generate a  $\eta^1$ -complex, followed by the Sonogashira coupling reaction

with terminal alkyne **3** to give product **4** (Figure 1D). Under the one-pot Pd(0)-MeOH catalysis, the oxidative addition between alkyne **3** and Pd(0) catalyst produces alkynyl Pd<sup>II</sup>-hydride **A**, and then the ligand exchange occurs to give palladium alkoxide complex **B**. Subsequently, the obtained MeO-Pd<sup>II</sup>-H species **B** may coordinate with **4** and undergoes *anti*-aminopalladation to afford the alkenyl-Pd<sup>II</sup>-H intermediate **D**. After a reductive elimination, *N*-heterocycle **5** in (*Z*)-configuration is successfully delivered, and the reaction regenerates Pd(0) species.

On the other hand, when the reaction is conducted under Pd(OAc)<sub>2</sub>, the initially formed complex **E** may undergo ligand exchange to furnish intermediate **F** and AcOH. In this case, *syn*-aminopalladation may happen favorably, and intermediate **G** will be generated. Finally, the protolysis of intermediate **G** with AcOH produces *N*-heterocycle **6** with an (*E*)-exocyclic double bond and gives Pd(OAc)<sub>2</sub> for next catalytic cycle. The current studies highlight the art of accessing different stereoisomers by manipulating catalytic intermediates with metal catalysts bearing different valence.

In conclusion, the results from this *Chem Catalysis* paper provide a remarkable AMCR involving two different alkynes and *N*-sulfonylimines. With  $\pi$ -Lewis base catalysis of Pd(0)/L1, this cascade reaction proceeds through vinylogous addition and Sonogashira reaction successively to deliver enantioenriched all-carbon tetra-substituted alkene derivatives. Moreover, the chemoselectivity of this conversion is illustrated to be switchable by a MeOH and terminal alkyne promoted hydroamination to give five-membered *N*-heterocycles with a regioselective (*Z*)-exocyclic double bond. Of particular importance is that the configuration of this exocyclic double bond can also be turned into (*E*)-configuration by Pd(II) catalyst in a stepwise



**Figure 1. Palladium-catalyzed AMCRs between 1,3-enynes, imines, and terminal alkynes**

(A) Potential challenges in chemo-, regio-, and stereoselectivity control.

(B) The synthesis of tetra-substituted alkenes 4 and *N*-heterocycles 5 with an (*Z*)-exocyclic double bond.

(C) The synthesis of *N*-heterocycles 6 with an (*E*)-exocyclic double bond.

(D) The mechanism proposal.

manner. This chemo- and stereodivergent strategy will contribute insights in both alkyne chemistry and AMCRs.

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# Nickel-catalyzed asymmetric dicarbofunctionalization of alkynes to access axially chiral styrenes

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**In this issue of *Chem Catalysis*, Zhang and co-workers report a nickel-catalyzed asymmetric dicarbofunctionalization of alkynes, providing rapid access to axially chiral styrenes. This process features a broad substrate scope and useful product application. Density functional theory (DFT) calculations provided useful insights into the mechanism.**

Transition-metal-catalyzed dicarbofunctionalization of unsaturated C–C bond represents one of the most efficient approaches to access complex molecules.<sup>1</sup> Generally, this process can be classified as two-component and three-component fashions. The latter typically requires less substrate complexity and can deliver diversified products, but it requires powerful reaction conditions to achieve high selectivity and efficiency.<sup>2,3</sup> Among the various transition-metal catalysts, nickel complexes exhibit particularly

unique and intriguing features, such as multi-oxidation states, less propensity toward β-hydride elimination, and low cost.<sup>4</sup> As a result, nickel-catalyzed dicarbofunctionalization reactions have been extensively studied, especially in the realm of radical-involving conjugate cross-couplings.

Alkenes are widely employed as substrates in nickel-catalyzed dicarbofunctionalizations. Recently, the Nevado and Chu laboratories have also

achieved elegant enantioselective variants of these processes.<sup>5,6</sup> However, dicarbofunctionalizations of alkynes have been rarely known. In 2018, the Chu laboratory reported an important precedent—a three-component, regioselective, and *syn*-stereoselective alkylation of terminal alkynes via photoredox and nickel dual catalysis.<sup>7</sup>

Axially chiral styrenes have been a topic of great synthetic interests.<sup>8</sup> However, the majority of current syntheses of these compounds typically employ special substrates, thus limiting their applications. In this context, the development of concise and straightforward methods is highly desirable.

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