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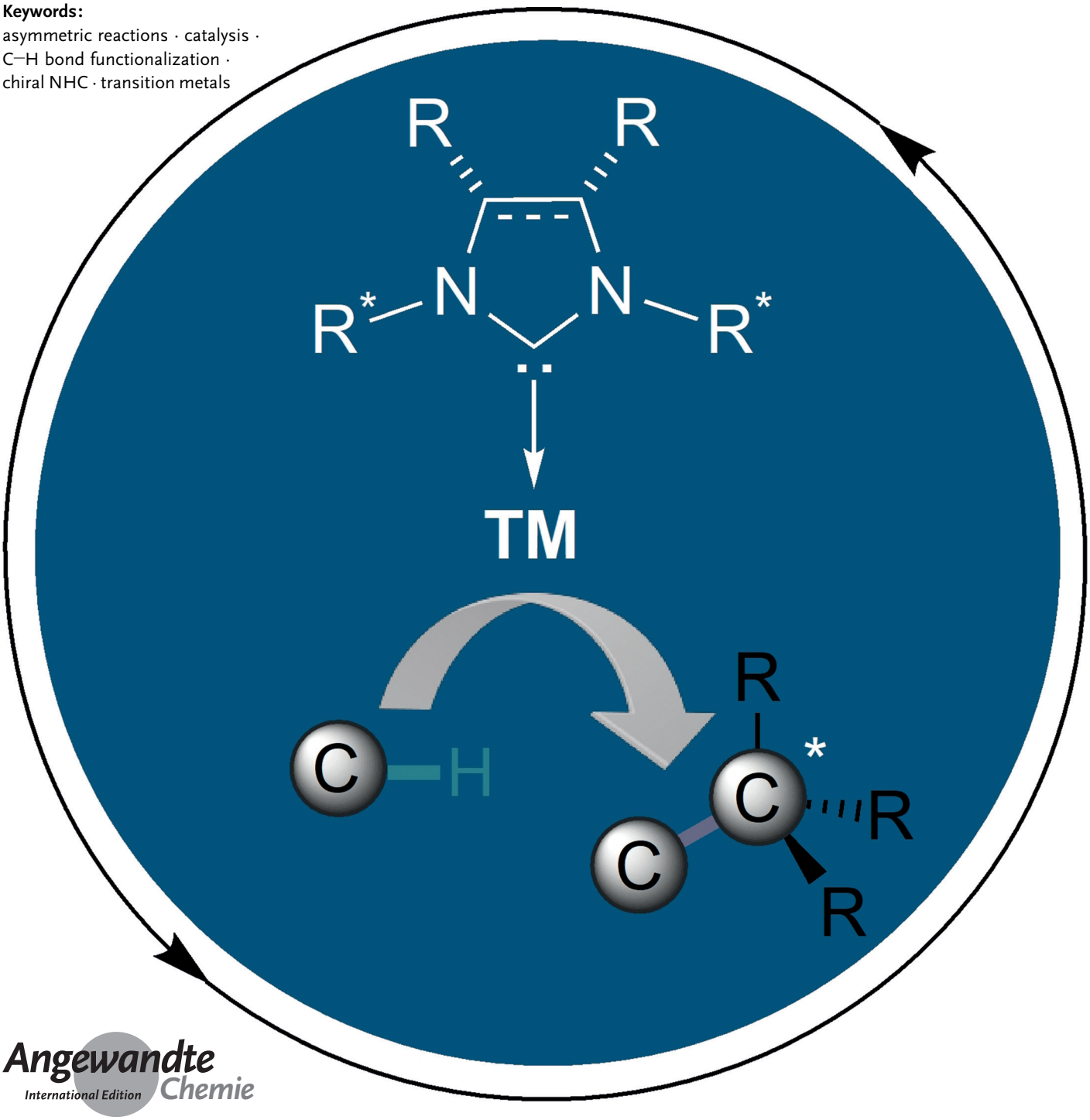
Asymmetric Catalysis

Chiral N-Heterocyclic Carbene Ligands Enable Asymmetric C–H Bond Functionalization

*Jompol Thongpaen, Romane Manguin, and Olivier Baslé**

Keywords:
asymmetric reactions · catalysis · C–H bond functionalization · chiral NHC · transition metals



The asymmetric functionalization of C–H bond is a particularly valuable approach for the production of enantioenriched chiral organic compounds. Chiral N-heterocyclic carbene (NHC) ligands have become ubiquitous in enantioselective transition-metal catalysis. Conversely, the use of chiral NHC ligands in metal-catalyzed asymmetric C–H bond functionalization is still at an early stage. This minireview highlights all the developments and the new advances in this rapidly evolving research area.

1. Introduction

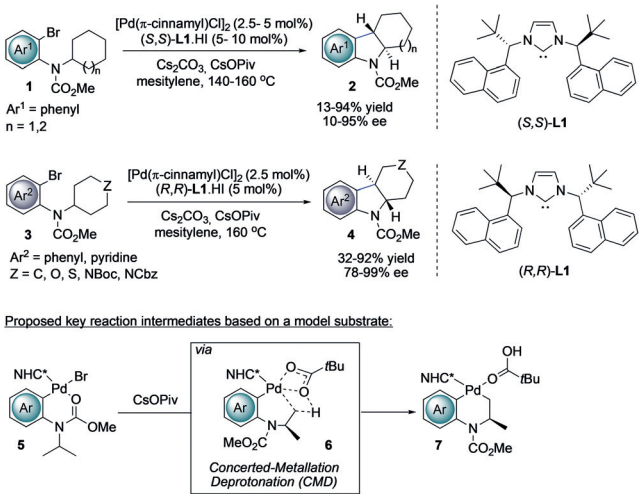
Chiral molecules play an important role in the chemistry of life, medicine, and material science. Pioneered by H. B. Kagan,[1] W. S. Knowles,[2] R. Noyori[3] and K. B. Sharpless,[4] the field of catalytic asymmetric synthesis has grown exponentially, resulting in innovative methods and processes for the efficient production of enantiomerically pure substances.[5] Among those contemporary methodologies, transition-metal-catalyzed asymmetric cross-coupling reaction has appeared in the past decades as one of the most powerful synthetic tools to construct C–C and C-heteroatom bonds.[6] Despite the tremendous success of these transformations, cross-coupling reactions require the use of prefunctionalized substrates such as organohalides and organometallic reagents, forcing synthetic chemists to pursue multistep manipulations. On the other hand, the transition-metal-catalyzed direct functionalization of inert C–H bonds has emerged over the past two decades as an increasingly important synthetic tool opening new avenues in the construction of chiral molecules from readily available materials.[7] As for other asymmetric catalytic processes, chiral ligand engineering has been the key to the success of TM-catalyzed C–H functionalization. Thanks to their manifold application possibilities, phosphorus-based chiral ligands have been central to numerous breakthroughs in asymmetric C–H functionalization.[7c,8] On the other hand, in 2009 Yu and co-workers demonstrated that monoprotected α-amino acids are effective chiral ligands for Pd^{II}-catalyzed enantioselective alkylation of $C(sp^2)$–H and $C(sp^3)$–H bonds.[9] This discovery has led in the past decade to significant advances in the development of efficient asymmetric C–H transformations.[10] Meanwhile, Cramer and co-workers developed a new class of chiral ligands based on C_2-symmetrical cyclopentadienyl derivatives that have proven to be efficient in asymmetric C–H functionalization catalyzed by rhodium,[11] while offering promising potential in a variety of other catalytic processes using TM-based Cp* complexes.[12]

Amongst alternative chiral ligands,[13] N-heterocyclic carbenes (NHCs) are unambiguously those offering the greatest perspectives in TM-catalyzed asymmetric C–H functionalization.[14] During the past two decades, NHCs have become ubiquitous ligands in coordination chemistry and catalysis. Their unique properties, including strong σ-donation, are responsible for forming robust TM catalysts that allow for the development of more efficient synthetic procedures.[15] Moreover, straightforward synthetic methods give access to a large variety of NHC structures with diverse chiral architectures.[16] Nevertheless, and despite the recent success of chiral NHC ligands in asymmetric homogeneous catalysis,[17] including intramolecular α-arylation of amides,[18–24] the use of such ligands in TM-catalyzed asymmetric C–H bond functionalization is still in its infancy. This minireview highlights all the developments and the new advances in this burgeoning and promising field of research.

2. Functionalization of $C(sp^3)$–H Bonds

2.1. Intramolecular Arylation of Unactivated $C(sp^3)$–H Bonds

In 2011, Kündig and co-workers reported the first example of the use of chiral NHC ligands in enantioselective functionalization of unactivated C–H bonds (Scheme 1).[25] In a continuing effort to demonstrate the potential of their unsaturated C_2-symmetrical NHC ligands based on *ortho*-substituted α-tert-butylbenzylamines,[23] high efficiency could be achieved using the naphthyl-based **L1** ligand in palladium-catalyzed intramolecular arylation of unactivated $C(sp^3)$–H bonds at high temperature (140–160 °C). The great robustness of the catalytic system allowed the synthesis of a variety of



Scheme 1. Asymmetric intramolecular arylation of unactivated $C(sp^3)$–H bonds for the synthesis of fused-indolines.

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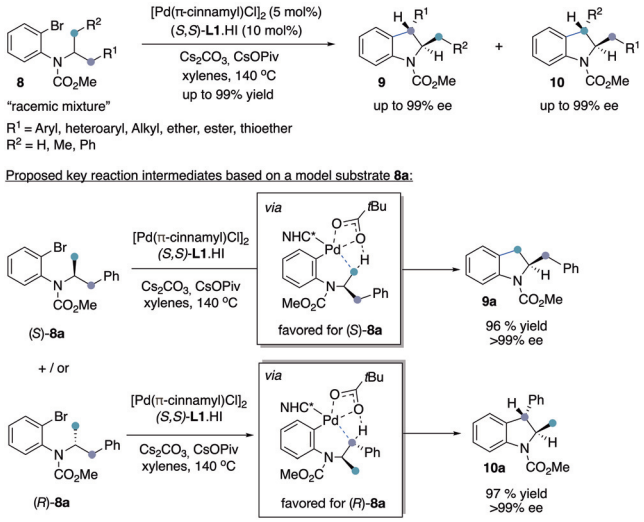
fused indolines (**2** and **4**) with very high enantioselectivity (up to 99% *ee*).[26] Mechanistic studies revealed that the reaction proceeds first through oxidative addition of the C–Br bond giving palladium(II) complex **5**, followed by the enantiodetermining C–H bond cleavage by means of a concerted-metalation deprotonation (CMD) process (see transition state **6**).[27] When the (*S*,*S*)-**L1** is employed, reductive elimination from the chiral cyclopalladated intermediate **7** affords preferentially the enantioenriched product with (*R*) configuration.

Later, the same group reported a regiodivergent synthetic approach to indolines using a similar catalytic system (Scheme 2).[28,29] The asymmetric C–H annulation of racemic carbamate substrates led to the formation of two different indolines with high enantio-induction. Enantiomers interact-

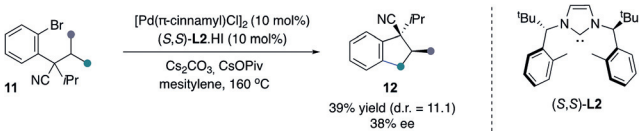


Scheme 2. Regiodivergent synthesis of indolines.

ed with the chiral catalyst differently, providing for each a regioselective product accordingly (Scheme 2). The observed behavior of this parallel kinetic resolution method was in a good agreement with computational studies based on calculated activation barriers of the CMD enantiopic-determining step. In the case of substrate (*S*)-**8a**, the C–H bond cleavage of CH_3 is more favored than that of CH_2 (with a large $\Delta\Delta G^{\neq} = 14.0\ kJ\,mol^{-1}$) affording the 2-substituted indoline **9a** exclusively. On the other hand, CH_2 bond cleavage of *(R)*-**8a** is more favored ($\Delta\Delta G^{\neq} = 19.2\ kJ\,mol^{-1}$) leading selectively to the 2,3-substituted product **10a**.

Baudoin and co-workers described in 2012 the Pd-catalyzed intramolecular asymmetric annulation of aryl bromides bearing unactivated C(sp^3)–H bonds.[30] While the highest enantioselectivity in the synthesis of indanes **12** was achieved with chiral phosphines, interesting enantio-discrimination could also be obtained applying the conditions previously described by Kündig and co-workers using the NHC ligand (*S*,*S*)-**L2** (Scheme 3).

Very recently, the same group extended this method towards the enantioselective synthesis of indane **17**, precursors of (nor)illudalane sesquiterpenes.[31] The strategy involved the intramolecular enantioselective arylation of a C-(sp^3)–H bond to generate a quaternary stereocenter at the adjacent position (Scheme 4). Among several NHC ligands that were surveyed, the (*S*,*S*)-**L1**, developed by Kündig and co-workers afforded the highest enantioinduction (80:20 e.r.) in the desymmetrization of the *gem*-dimethyl group of the morpholinamide substrate **13**. By employing (*L*)-proline-derived substrate **15**, the desired product **16** could be obtained with good 87% isolated yield and satisfactory 85:15 d.r. (matched case). The sequential treatments including hydrolysis of the amide group and recrystallization furnished the highly enantioenriched compound **17**, the parent substance of

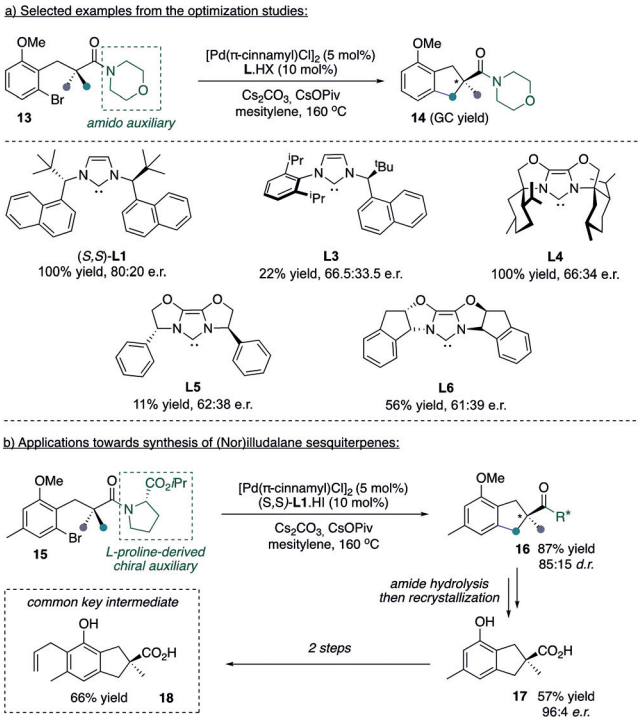


Scheme 3. Enantioselectivity in the synthesis of indanes.

Jompol Thongpaen received his bachelor's degree in chemistry in 2014 from Mahidol University, Thailand. He was granted a Franco-Thai scholarship from the French Embassy to pursue and complete his international master's degree at the University of Rennes 1, France. He performed his master's research in the group of Dr. M. Mauduit at ENSC-Rennes, France. He is currently pursuing his PhD work under the supervision of Dr. Olivier Baslé at Laboratoire de Chimie de Coordination (LCC), Toulouse. His research mainly focuses on C–H bond functionalization catalyzed by NHC–metal complexes.

Romane Manguin completed her bachelor's degree in Brest under the supervision of Prof. M. Berchel. Then she received her master's degree from the University of Rennes 1, where she performed research on diyne metathesis in the group of Dr. M. Mauduit. Currently, she is a PhD student in the same group under the supervision of Dr. Olivier Baslé and works on the design of new NHC–metal catalysts for asymmetric C–H functionalization.

Olivier Baslé completed his master's degree under the supervision of Prof. P. H. Dixneuf at the University of Rennes in 2006 and obtained his PhD degree in 2009 at McGill University under the guidance of Prof. C.-J. Li. After postdoctoral studies with Prof. J. Rodriguez and T. Constantieux in Marseille and Dr. D. Bourissou in Toulouse, he was appointed CNRS researcher in 2011 at ENSC-Rennes. In 2018, he joined the CNRS Laboratory of Coordination Chemistry in Toulouse. His research program focuses on the development of selective catalytic transformations using NHC–metal complexes.

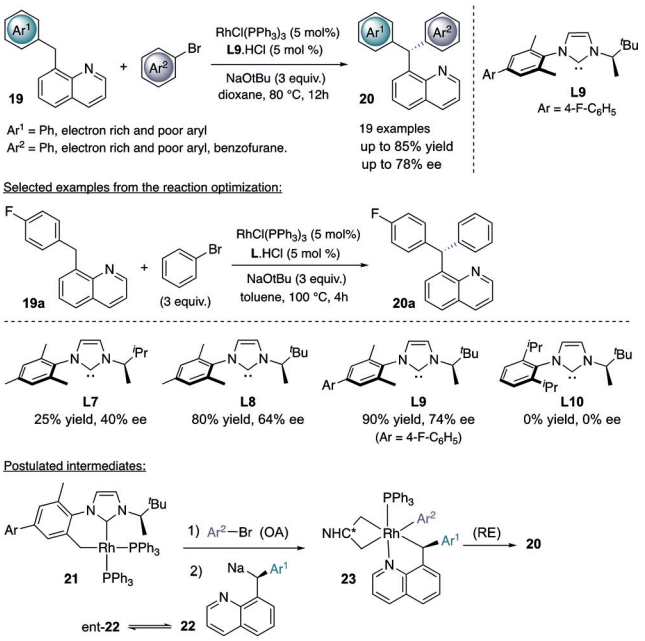


Scheme 4. Regiodivergent synthesis of indolines.

the key intermediate **18** in the synthesis of (nor)illudalane sesquiterpenes.

2.2. Intermolecular Arylation of Benzylic C–H Bonds.

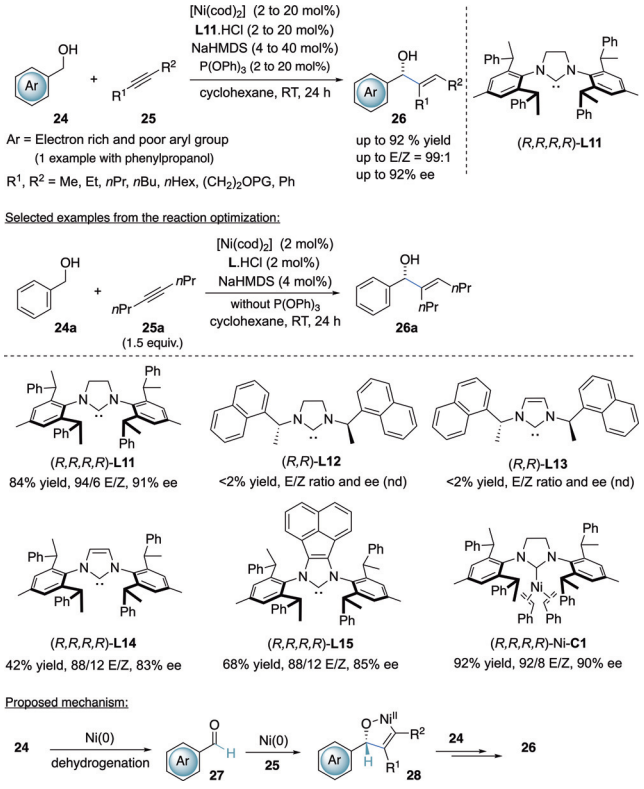
In 2016, Glorius and co-workers reported the first example of rhodium(I)-catalyzed intermolecular functionalization of C(sp^3)–H bonds (Scheme 5).[32] The use of NHC ligands afforded high selectivity in favor of the benzylic C–H arylation and the mesityl substituent on the NHC appeared crucial for the activity (no catalytic activity with Dipp-based ligand such as **L10**). The authors postulated that cyclometalation at the *o*-tolyl substituent of the NHC enabled the generation of the catalytically active species (**21**). Thanks to a multicomponent procedure affording a simple and rapid access to unsymmetrical imidazolium salts,[33] a large variety of chiral NHC precursors was screened and the best results were obtained with **L9** that afforded in a model reaction the desired product **20a** in high 85% isolated yield and 78% enantiomeric excess. The direct arylation reaction of 8-benzyl quinolones **19** with aryl bromides was only slightly influenced by the electronic and steric nature of the substituents on both substrates, affording the desired products **20** in high yields and good enantiomeric ratios. In the proposed mechanism, the authors postulated that the catalytically active cyclometalated species **21** undergoes successive oxidative addition of the aryl bromide and diastereoselective transmetalation with the deprotonated 8-benzyl quinolone substrate **22** to form the Rh^{III}-intermediate **23**.



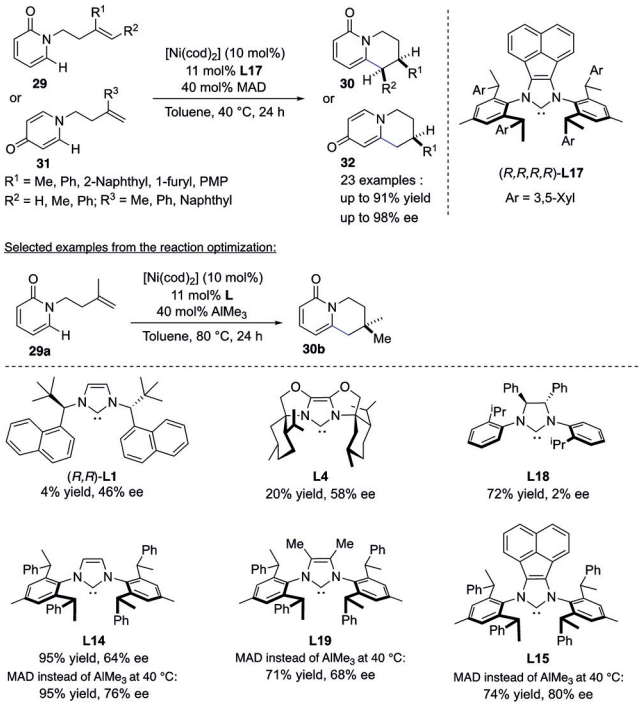
Scheme 5. Rhodium-catalyzed intermolecular enantioselective C(sp^3)–H bond arylation.

2.3. Intermolecular C–H Alkenylation of Alcohols

Very recently, Shi and co-workers described the first example of enantioselective C–H alkenylation of alcohols with alkynes (Scheme 6).[34] In order to achieve high stereoselectivity in this redox-neutral coupling catalyzed by nickel-(0)-system, the authors investigated a new class of bulky chiral NHCs, that was initially introduced by Gawley in 2011,[35] and concomitantly developed by the Shi[36] and the Cramer[37] groups (see below, section 3.1). The catalytic system made in situ from the deprotonation of the imidazolinium salt (**L11**·HCl; analogue of SiPr) by NaHMDS in the presence of $Ni(cod)_2$ and in combination with the electron deficient phosphite ligand $P(OPh)_3$ delivered the desired chiral allylic alcohols with high *E*/*Z* ratios (up to 99:1) and high enantioselectivities (up to 92% *ee*). Similar result could be obtained with the isolated Ni^0-NHC complex **C1** and control experiment in the absence of $P(OPh)_3$ evidenced only an erosion in *E*/*Z* ratio confirming the important role of the additive to suppress the product isomerization. It is also important to note that a range of chiral NHC ligands was tested during the optimization of the model reaction between benzyl alcohol (**24a**) and 4-octyne (**25a**) showing the strong impact of NHC structure on the reaction outcome. In fact, the commonly used C_2 symmetrical NHC ligands **L12** and **L13** proved to be inoperative. On the other hand, a noticeable decrease of the catalytic efficiency was observed in the presence of ligands **L14** and **L15,** unsaturated analogues of **L11**. The proposed mechanism involves dehydrogenation of alcohol **24** to generate the corresponding aldehyde **27**, which undergoes oxidative cyclization with alkyne **25** and Ni^0 to produce the enantioenriched oxanickelacycle **28** as a key intermediate.



Scheme 6. Nickel-catalyzed enantioselective C–H alkenylation of alcohols with alkynes.

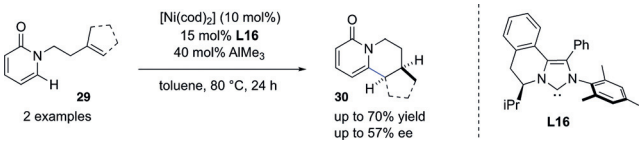


Scheme 8. Nickel-catalyzed enantioselective pyridone C–H functionalizations. MAD = methylaluminium bis(2,6-di-tert-butyl-4-methylphenoxide).

3. Functionalization of C(sp²)–H Bonds

3.1. Intramolecular Hydroarylation of Olefins

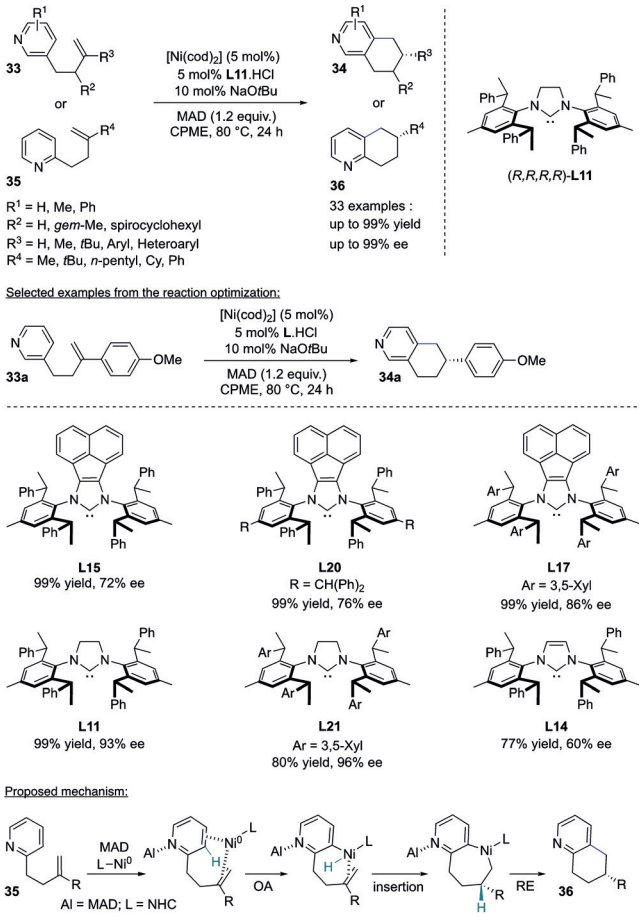
In 2014, Cramer and co-workers reported a nickel-catalyzed C–H functionalization of 2-pyridones by selective intramolecular olefin hydroarylation (Scheme 7).[38] The regioselectivity of the cyclization was fully controlled by the ligand and unsymmetrical chiral NHC **L16** based on the isoquinoline framework delivered selectively the *endo*-cyclization product with promising enantioselectivity.



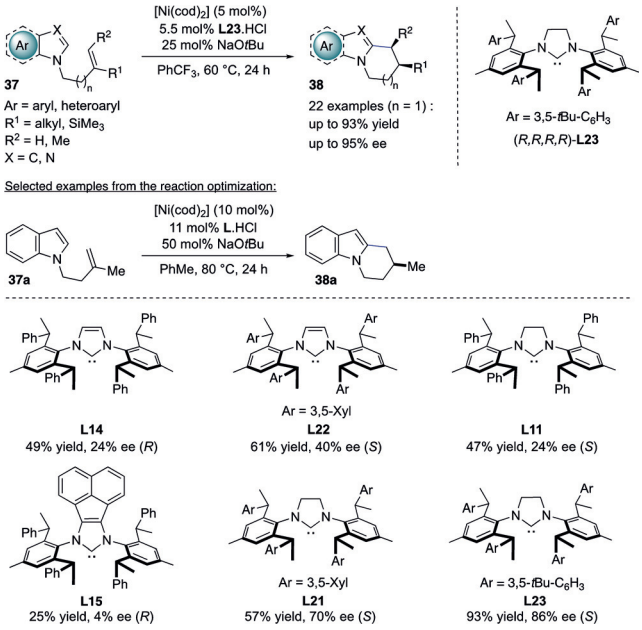
Scheme 7. Ligand controlled nickel-catalyzed annulation of pyridones.

More recently, the same group further investigated this transformation and among the chiral NHCs that were surveyed, the sterically demanding monodentate ligand **L17** allowed for highly enantioselective C–H functionalization of 2- and 4-pyridones (Scheme 8).[37] While unsatisfactory results were obtained with common chiral carbene ligands (**L4**, **L1**, **L18**), interesting catalytic activities could be obtained using **L14**.[35,36] Introduction of the acenaphthene fragment on the backbone of **L15** improved the selectivity and authors evidenced that this flexible ligand displays an improved C_2-symmetric binding pocket. The enantioselectivity could be further increased with the introduction of bulky aromatic side arms, that is, 3,5-di-methyl phenyl groups (**L17**). Then, in the presence of MAD (methylaluminium bis(2,6-di-tert-butyl-4-methylphenolate), the desired *endo*-cyclized annulated pyridines were obtained with high yields (up to 91 % yield) and enantioselectivities (up to 98 % *ee*) under mild reaction conditions. The *endo*-cyclization selectivity is in accordance with theoretical and mechanistic studies of Ni-catalyzed hydroarylations, in which a mechanism involving direct ligand-to-ligand hydrogen transfer (LLHT) is proposed.[39]

The intramolecular regio- and enantioseletive C–H cyclization of pyridines with olefins was very recently reported by Shi and co-workers (Scheme 9).[40] Among several chiral NHC ligands that were investigated, the bulky chiral saturated **L11**,[34] the analogue of SiPr, provided excellent catalytic activities and furnished the targeted tetrahydroquinolines and tetrahydroisoquinolines with excellent enantioinduction (up to 99 % *ee*). During the optimization of the reaction conditions, a pronounced ligand effect could be observed in the cyclization of substrate **33a**. Notably, while **L11** performed with high reactivity and selectivity (99 % yield and 93 % *ee*), its replacement by the unsaturated analogue **L14** dramatically decreased the yield and enantioselectivity (77 % yield and 60 % *ee*). It should be noted that **34a** could be obtained with up to 96 % *ee* using the bulkier ligand **L21**, but with slightly lower reactivity. The proposed mechanism involves coordination of the bulky MAD to the pyridine nitrogen, which favors the regioselective oxidative



Scheme 9. Nickel-catalyzed enantioselective C–H functionalization of pyridines.

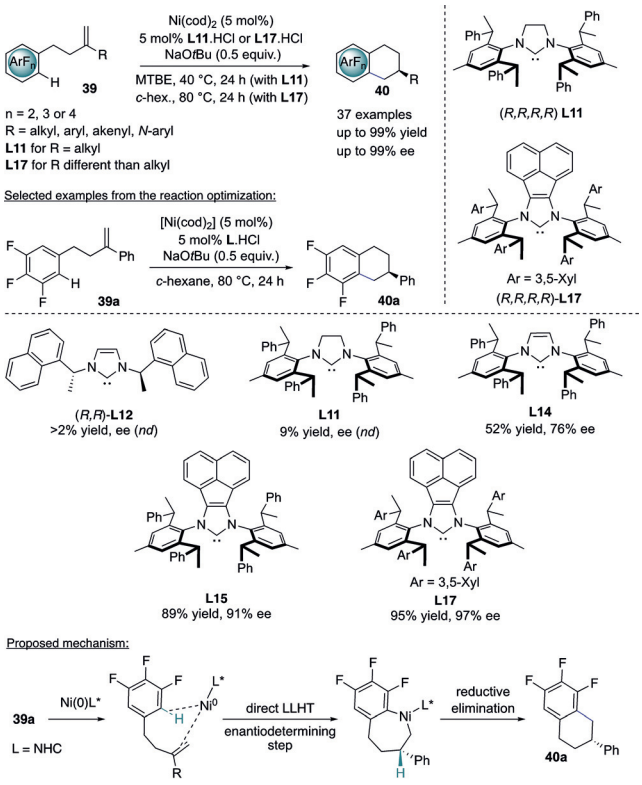


Scheme 10. Nickel-catalyzed enantioselective C–H functionalization of indoles and pyrroles.

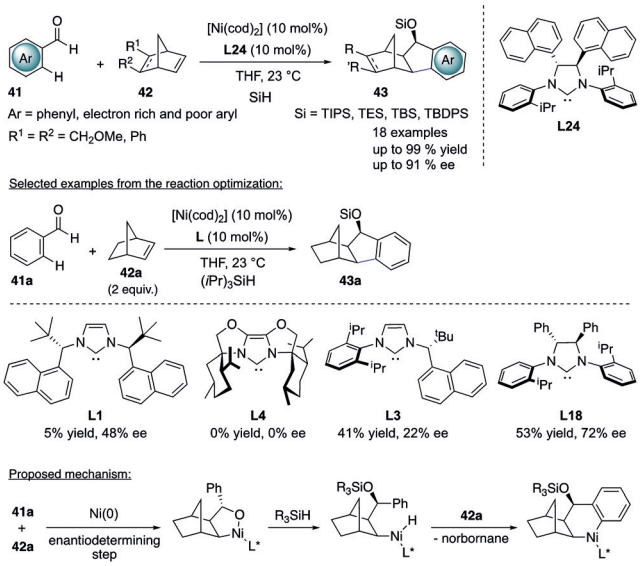
C–H bond addition on Ni^0, which is potentially the rate determining step (KIE = 2.5). The following anti-Markovnikov hydronickelation of the alkene and subsequent reductive elimination afford the desired *endo*-annulation product **36**. The electronic and steric properties of the NHC ligands are apparently critical to every elementary step of this catalytic cycle.

In 2019, Cramer and co-workers introduced new members of this ligands family to achieve high enantioselectivity in Ni-catalyzed C–H functionalization of indoles and pyrroles (Scheme 10).[41] The authors demonstrated that both the reactivity and selectivity of the cyclization reaction was impacted by the NHC ligand structure. While poor yield and enantiocontrol could be obtained using the imidazole-2-ylidene **L14,** an increase of the bulk on the aryl side-arms (**L22**) improved the catalytic activity and reversed the enantioselectivity to afford 61 % yield of the cyclized product **38 a** with 40 % *ee* in favor of the (*S*)-enantiomer. Pleasantly, the use of a dihydroimidazole-2-ylidene ligand with sterically more demanding 3,5-di-tert-butyl phenyl groups on the side arms (**L23**)[42] resulted in complete conversion of **37 a**, 93 % yield of **38 a** with 88 % *ee*. Finally, decreasing the reaction temperature to 60 °C and replacing the solvent to trifluorotoluene improved the enantiocontrol of the *endo*-cyclisation to obtain **38 a** with 90 % *ee*. The optimized conditions were then applied with high efficiency to the enantioselective cyclization of pyrroles, indoles and related aza-heterocycles with a variety of substituted alkenes. The regioselectivity of the cyclization and results obtained from deuterium transfer experiments support a mechanism involving direct ligand-to-ligand hydrogen transfer.[39]

In their continuing effort to develop asymmetric C–H cyclization reactions with alkenes, Shi and co-workers recently reported the first example of catalytic enantioselective functionalization of polyfluoroarenes.[43] The reaction achieved by the use of bulky NHC ligands (**L11** or **L17**) for Ni^0-based catalysts afforded a large variety of cyclized products in high efficiency and excellent levels of chemo-, regio-, and enantioselectivity (Scheme 11). Initial attempts to cyclize the styrene-based substrate **39 a** with a catalytic system generated in situ involving commonly used C_2-symmetrical chiral NHC ligands such as **L12** were unsuccessful. Under the same reaction conditions, the saturated ligand **L11** was inapplicable as predominant alkene isomerization occurred. On the other hand, its unsaturated ligand analogue **L14** could prevent alkene isomerization[44] and afforded the desired product **40 a** in good 52 % yield and enantioselectivity (76 % *ee*). Further ligand screening evidenced the bulky acenaphthene-based NHC **L17** as the most efficient ligand affording **40 a** in nearly quantitative yield and high 97 % enantiomeric excess. While the catalytic system based on **L17** was also applicable to 1,1-dialkyl alkene substrates, **L11** demonstrated higher efficiency with such substrates that are less prone to isomerize under the reaction conditions. With the optimized conditions in hand, a variety of chiral fluorotetralins **40** were synthesized with excellent enantiocontrol from tetrafluoro, trifluoro and difluorobenzenes tethered alkenes **39**. Importantly no competitive C–F bond cleavage was observed with the catalytic systems based on **L11** and **L17**. The authors reasoned that the



Scheme 11. Nickel-catalyzed enantioselective C–H alkylation of fluoroarenes with alkenes.



Scheme 12. Nickel-catalyzed enantioselective three-component coupling to access indanol derivatives.

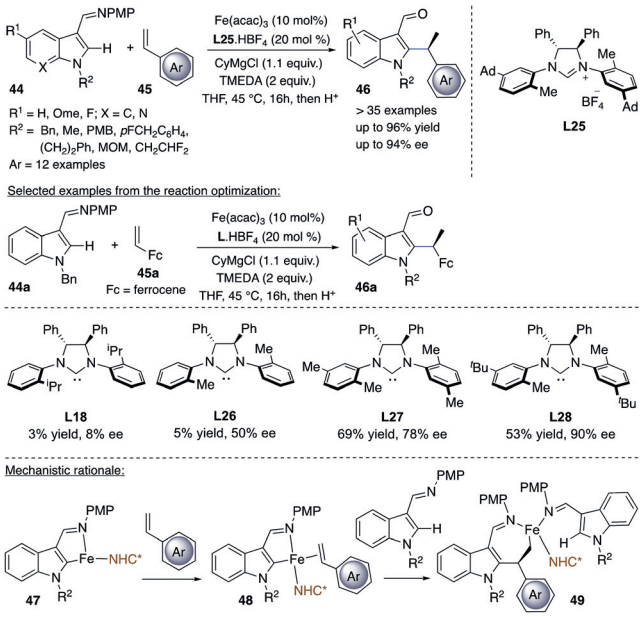
bulky NHCs favor the formation of monomeric active Ni-NHC catalysts which favor C–H activation. In the same way as for the C–H cyclization of pyridines with olefins (see above, Scheme 9), the electron-donating and sterically demanding properties of the NHC ligands are apparently critical to every elementary steps of the catalytic cycle. However, while a mechanism involving C–H oxidative addition of Ni^0 and alkene insertion is not excluded, deuterium transfer experiments indicate that direct ligand-to-ligand hydrogen transfer (LLHT) is likely the favored pathway.[39]

3.2. Intermolecular Hydroarylation of Olefins

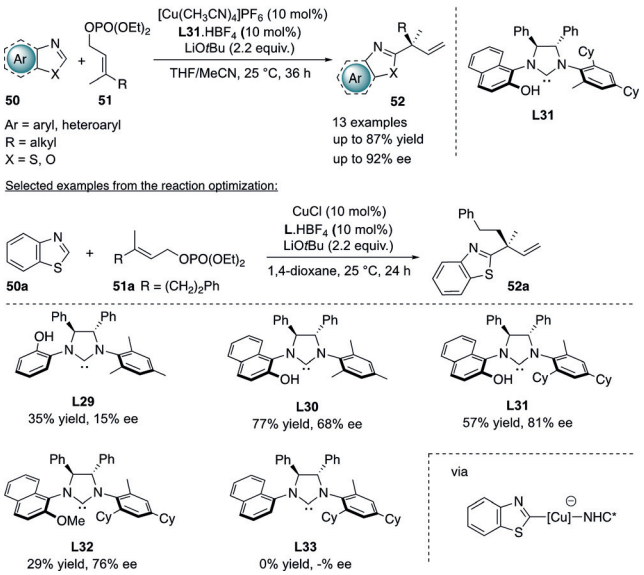
Catalytic systems based on chiral NHC ligand and Ni^0 have also demonstrated high potential in the asymmetric synthesis of indanol derivatives with the direct generation of four stereocenters (Scheme 12). The reductive three components coupling involving *ortho*-C–H functionalization of an aromatic aldehyde in the presence of a silane and a norbornene substrate was achieved by a Ni^0 catalyst bearing the chiral C_2-symmetric NHC ligand **L24**.[45] The originality of ligand **L24** resided in the 1,2-di(naphthalene-1-yl)ethylene diamine backbone that strongly influenced the reaction outcome to allow accessing the desired annulated products **43** as single diastereoisomer in high enantioselectivity. In the proposed mechanism, the enantiodetermining step is the formation of the oxanickelacycle, which subsequently reacts with silane leading to a nickel-hydride intermediate able to perform C(sp^2)–H activation in the presence of another equivalent of norbonene.

In a program to develop first-row transition metal-based systems for C–H functionalization, [46] Ackermann and co-workers described in 2017 the first enantioselective iron-catalyzed C–H alkylation using NHC ligand (Scheme 13).[47] In this study, the authors clearly demonstrated the critical role of the newly designed *meta*-decorated NHC ligands in the stereoinduction. Detailed mechanistic insights and additional experiments with isotopically labelled substrates strongly support an inner-sphere C–H activation mechanism.[48] The reaction is initiated by the formation of active species iron complex **47**, followed by the coordination of olefin. Then the enantio-determining step is believed to proceed during migratory insertion induced by secondary interaction in the transition state, which is promoted by the addition of the second molecule of substrate to form the key intermediate **49** involved in the C–H activation step.

In 2016, Ohmiya, Sawamura, and co-workers reported a copper-catalyzed enantioselective alkylations of electron-deficient azoles with γ,γ-disubstituted allylic phosphates (Scheme 14).[49] The reaction is believed to proceed through an inner-sphere mechanism involving the base assisted C–H cupration of heterocycles to form [ArCuL(O*t*Bu)$^-$] active species.[50] The structure of NHC ligand was found critical to form a controlled all-carbon quaternary stereogenic center. In the model reaction between benzothiazole (**50a**) and the *E*-allylic phosphate (**51a**), the unsymmetrical chiral NHC ligand **L29** bearing a phenoxy group at the *ortho* position afforded low catalytic activity and low enantioselectivity. However, by changing the phenol group to a naphtol group, dramatic increases in product yield and enantioselectivity were obtained using **L30**. The enantioselectivity could be further increased to 81% *ee* using ligand **L31** bearing the *N*-2,4-dicyclohexyl-6-methylphenylgroup, but at the expense of product yield. Under the optimized conditions using **L31** in



Scheme 13. Iron-catalyzed intermolecular asymmetric C–H Alkylation of indoles.

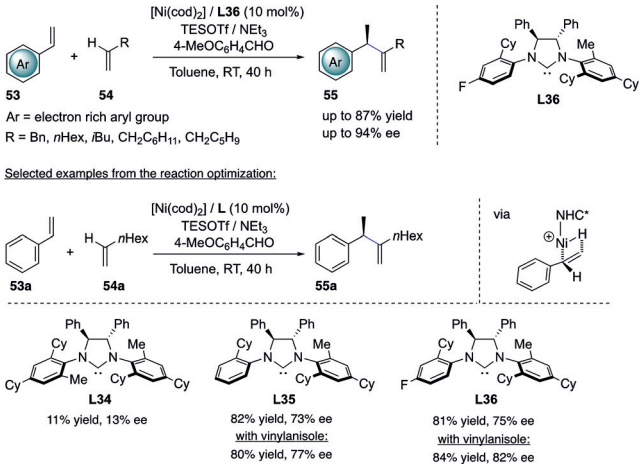


Scheme 14. Copper-catalyzed enantioselective C–H alkylation of azoles.

the presence of $[Cu(CH_3CN)_4]PF_6$ in a solvent mixture of THF/CH_3CN, the reaction between various azoles **50** and allylic phosphates **51** afforded a variety of quaternary stereogenic carbon centers with high enantioselectivity.

3.3. Intermolecular Hydroalkenylation of Olefins

Transition metal-catalyzed 1,2-hydrovinylation of two terminal alkenes via C–H functionalization can lead to a number of products with high degree of functional density.[51] The use of chiral NHC ligand in asymmetric nickel-catalyzed cross-hydrovinylation was reported by Ho and co-workers in 2015 (Scheme 15).[52] The intermolecular tail-to-tail hydroalkenylation of vinylarenes **53** with terminal olefins **54** was catalyzed by in situ generated NiH[53] complexes bearing C_1-symmetrical NHC **L36** and afforded the chiral gem-disubstituted olefin products **55** with high enantioselectivity. While both *N*-aryl groups of the NHC were substituted with a bulky cyclohexyl substituent at position 2, a steric discrimination at the *ortho*-positions was beneficial to the enantioselectivity of the reaction. Moreover, the reaction involving electron rich styrene substrates was found to be optimal when the electronics of one *N*-aryl group was modified by a fluoro substituent in the *para*-position.



Scheme 15. Nickel-catalyzed asymmetric cross-hydrovinylation.

4. Summary and Outlook

In this minireview, we highlighted the development and the recent advances in the field of TM-catalyzed enantioselective C–H functionalization using chiral NHC ligands. During the past two decades, NHCs have become ubiquitous ligands in coordination chemistry and catalysis. Concomitantly, enantioselective C–H functionalization has experienced an exponential growth. Nevertheless, and despite the success of chiral NHC ligands in asymmetric homogeneous catalysis, the use of such ligands in TM-catalyzed asymmetric C–H bond functionalization has remained, until recently, relatively limited. The unique properties of NHC ligands, including their strong σ-donation, allow for the development of highly stable TM-catalysts that can efficiently prevent undesired background reactions. This advantage was evidenced in the seminal work published by Kündig in 2011, which described the spectacular highly enantioselective functionalization of unactivated $C(sp^3)$–H bonds at up to 160 °C. Moreover, the numerous existing synthetic methodologies to construct NHCs offer a large diversity of chiral structures to be surveyed in a given asymmetric C–H transformation. This approach has played a significant role in the multiple recent successes encountered in enantioselective C–H functionalization with nickel-based catalysts and will certainly contribute to the exponential use of abundant 3d

TM-catalysts in this rapidly evolving research area.[54] Overall, chiral NHCs, including yet underexplored multifunctional NHCs,[55] are promising ligands for a variety of TM-catalyzed C–H functionalization reactions and we expect that the recent enthusiasm for their use in fine catalyst engineering will lead to an increasing pace of discovery in this exciting research field.

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Conflict of interest

The authors declare no conflict of interest.

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