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Review

C_2-Symmetric *N*-Heterocyclic Carbenes in Asymmetric Transition-Metal Catalysis

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Abstract: The last decades have witnessed a rapid growth of applications of *N*-heterocyclic carbenes (NHCs) in different chemistry fields. Due to their unique steric and electronic properties, NHCs have become a powerful tool in coordination chemistry, allowing the preparation of stable metal-ligand frameworks with both main group metals and transition metals. An overview on the use of five membered monodentate C_2-symmetric *N*-heterocyclic carbenes (NHCs) as ligands for transition-metal complexes and their most relevant applications in asymmetric catalysis is offered.

Keywords: NHC; asymmetric catalysis; transition metals

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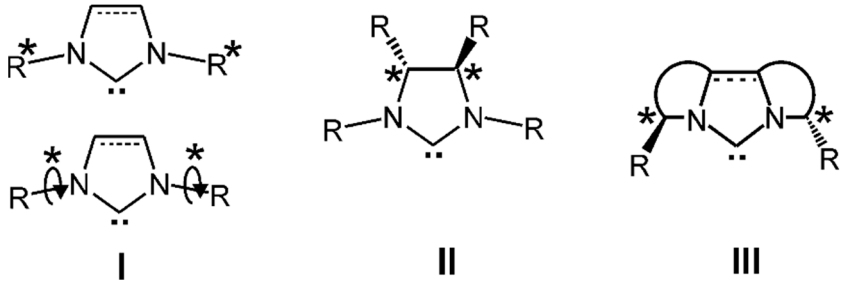
1. Introduction

N-heterocyclic carbenes (NHCs) are nowadays considered privileged ligands for transition metal complexes [1–3]. The strong σ-donating properties of NHCs are crucial in determining their interaction with metal centers and, consequently, along with their steric features, in influencing the selectivity and reactivity in transition-metal catalysis [4,5]. The easy synthetic access to different NHC architectures in which stereo electronic properties of the ligand scaffold can be modulated by varying the nature of the backbone (saturated or unsaturated), the substitution at the nitrogen and/or carbon atoms, and the ring size has led to the development of a huge number of NHC transition-metal complexes for various catalytic applications [6–12]. The further possibility of introducing chirality into the NHC framework has paved the way to the design of chiral NHC ligands for applications in asymmetric transition-metal catalysis. Among them, several chiral monodentate NHCs have been developed and used as stereo directing ancillary ligands in a wide range of catalytic transformations [13–16]. There are three strategies commonly employed to create a chiral environment around the carbenic carbon of the NHC scaffold that can lead to effective chiral induction in catalysis. The resulting basic structures are illustrated in Scheme 1. The first strategy implies the introduction of chirality on one or two of the substituents on the nitrogen atoms of the NHC. This can be achieved by introducing stereogenic centers on the *N*-substituents or even by exploiting the presence of planar chiral groups bound to nitrogen atoms as well as the axial chirality due to unsymmetrically substituted aromatic groups as the *N*-substituents (**I**). The second strategy is based on the direct installation of chirality on the backbone of a saturated NHC framework, which can be transferred to the metal through suitable *N*-substituents (**II**).

The third strategy in the design of chiral NHC ligands involves the development of structures where a central NHC ring is fused with one or two cyclic units to form rigid NHC architectures containing the necessary chiral information (**III**).

This review provides an overview on chiral monodentate C_2-symmetric NHC ligands, which have allowed to reach high levels of enantioselectivity (≥90% *ee*) in various applications of asymmetric catalysis mediated by transition-metal complexes. Relevant literature data since 1996 (the year of the first report on a chiral NHC ligand) through March 2022 are discussed

according to the different types of chiral NHCs, highlighting the crucial role of suitable NHC design in the development of transition-metal catalysts with improved enantioselectivities.



Scheme 1. Common frameworks (**I**, **II**, **III**) of chiral monodentate C_2-symmetric *N*-heterocyclic carbene (NHC) ligands.

2. Discussion

The C_2-symmetric NHC structures described in this review are depicted in Figures 1–3, along with the corresponding Noyori's quadrant model. Noyori's quadrant model represents the expected occupancy of the ligand and is an easy way to visualize how the symmetry of the ligand affects the symmetry of the catalytic pocket. The color of the quadrants indicates the level of occupancy (darker colors indicates higher occupancy).

2.1. NHCs with Chiral N-Substituents

C_2-symmetric NHC ligands with chiral *N*-substituents are commonly obtained starting from chiral primary amines, which become the *N*-substituents of the resulting NHC scaffolds. This approach allows for creating a chiral environment in close proximity to the metal center, which is essential to ensure an efficient enantioinduction. However, the possible rotation of chiral *N*-substituents around the C-N bond can lead to an ill-defined active chiral space at the metal center, compromising enantioselectivity.

The first examples of C_2-symmetric monodentate NHC ligand containing chiral *N*-substituents (1-phenylethyl (**1**) or 1-naphthylethyl (**2**), Figure 1) were reported by Hermann [17] and Enders [18] in 1996. However, low enantiomeric excesses in asymmetric catalytic applications such as a palladium-catalyzed Heck reaction and a rhodium-catalyzed hydrogenation were observed. Later, Alexakis observed higher enantioselectivities (up to 93%) in the copper-catalyzed conjugate addition of diethyl zinc to cycloheptenone [19]. Starting from 2011, the saturated version of chiral NHC ligand with 1-naphthylethyl *N*-substituents (**2**) was successfully applied by Glorius in several ruthenium-catalyzed asymmetric hydrogenations of various heterocyclic compounds, providing in all cases the desired products with high enantioselectivities [20–26]. Very recently, Glorius utilized the ligand cooperation concept as an alternative strategy to optimize enantioselective processes, reporting on a new combination of chiral NHC ligand **2** and chiral diamine ligands for the ruthenium-catalyzed enantioselective hydrogenation of isocoumarins, benzothiophene 1,1-dioxides, and ketones [27,28]. With respect to Hermann/Enders-type NHC ligands, a more sterically encumbered chiral NHC having 1-(2,4,6-trimethylphenyl)propyl groups on the nitrogen (**3**) was introduced in 2007 by Sato in the nickel-catalyzed asymmetric three-component coupling of 1,3-dienes, aldehydes, and silanes. Various coupling products were produced in good yields with high optical purities (up to 97% *ee*) [29].

In the same year Kündig introduced bulkier chiral *N*-substituents in which the methyl group of the stereogenic center in the Hermann-type scaffolds was replaced by a tert-butyl group (**4**–**6**). High enantioselectivities were obtained in the palladium-catalyzed asymmetric intramolecular α-arylation of amides to furnish oxindoles (94–97% *ee*) [30,31] and in the synthesis of highly enantioenriched indolines by palladium-catalyzed asymmetric C(sp^3)-H/C(Ar) coupling reactions (up to 99% *ee*) [32–34].

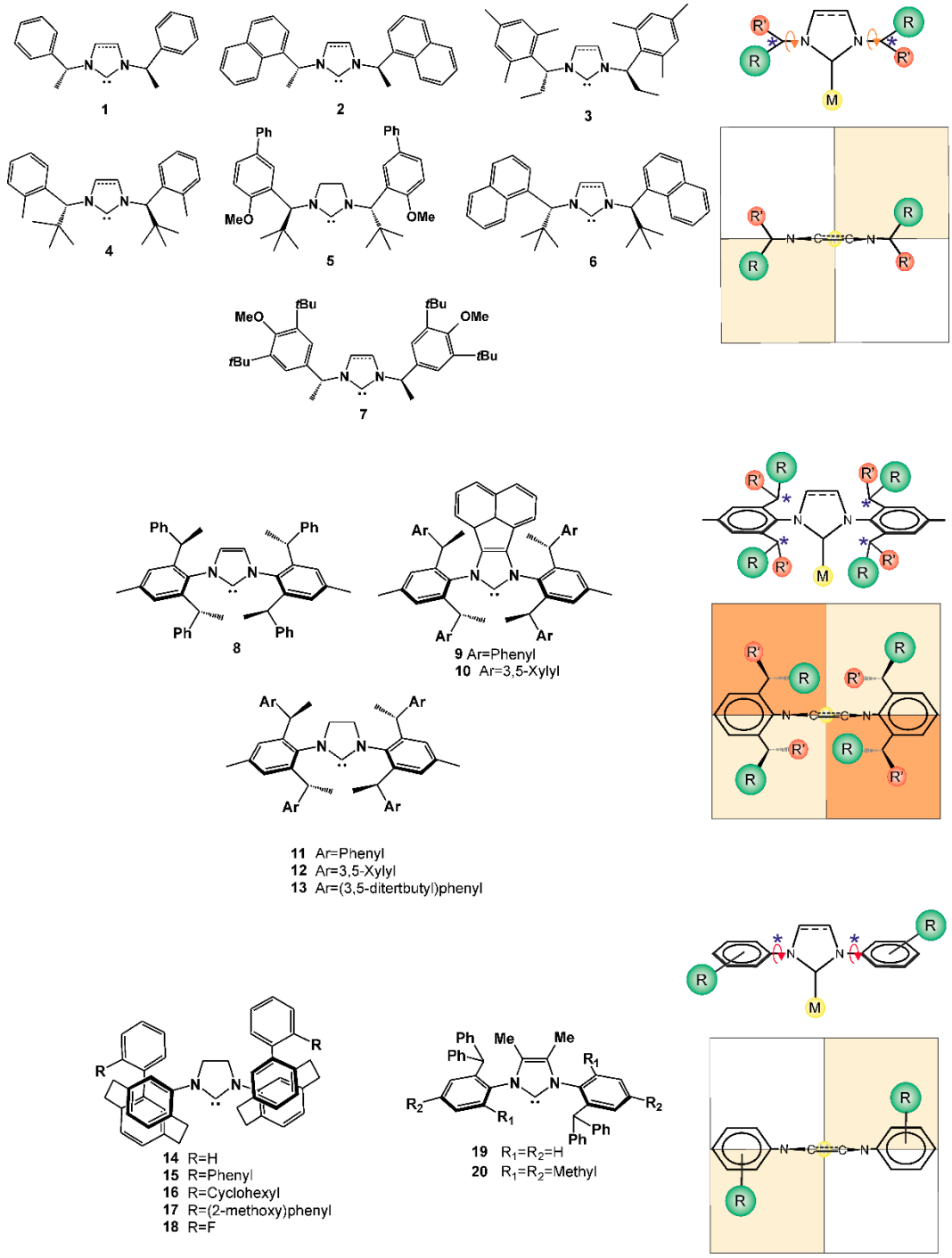


Figure 1. C_2-symmetric NHC ligands containing chiral *N*-substituents (**A**). On the right quadrant, maps of the depicted ligands from a top view are reported. The asterisk denotes the stereogenic elements (center, axis or plane).

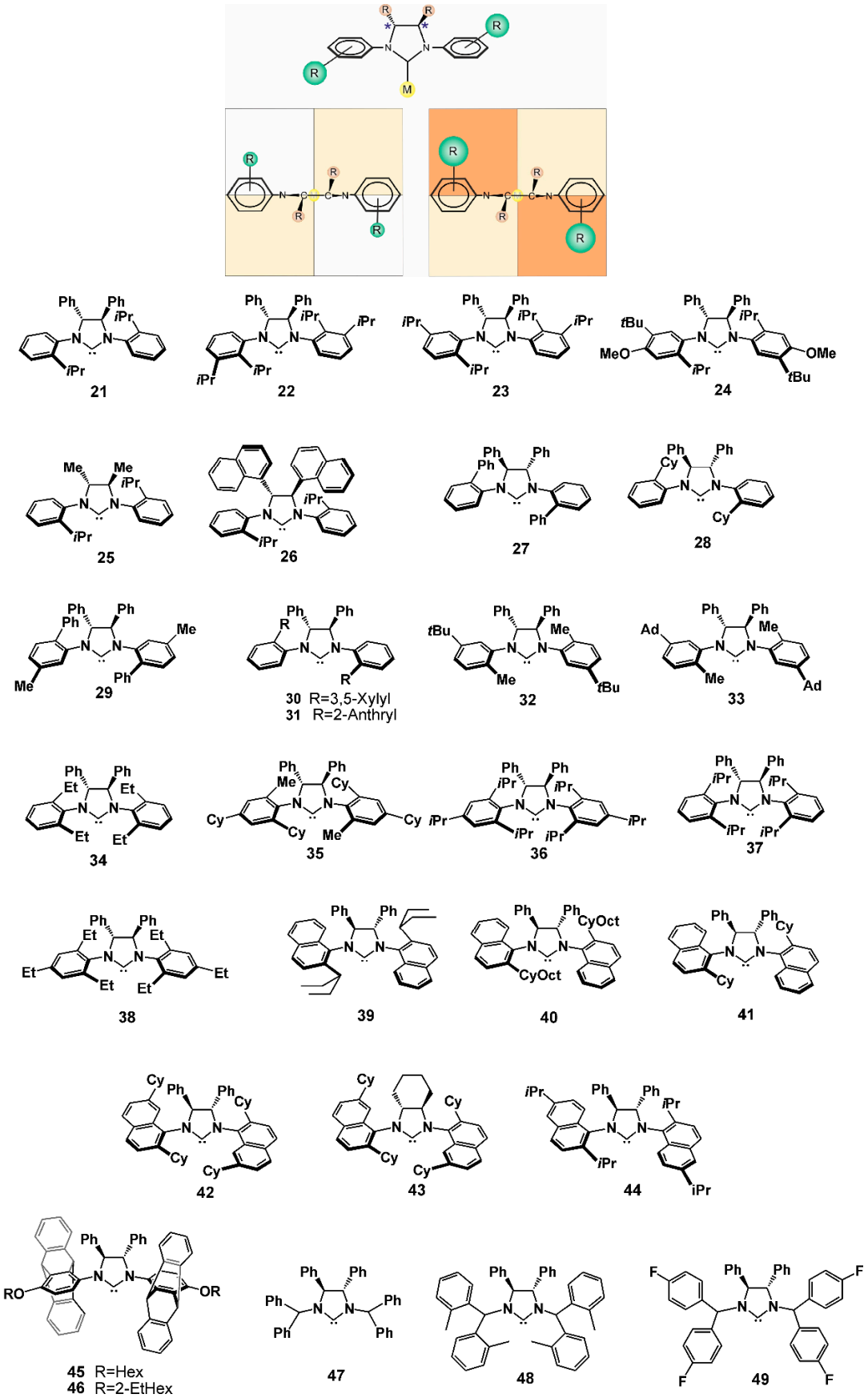


Figure 2. C_2-symmetric NHC ligands containing chiral backbone (**B**). On the top quadrant, maps of the depicted ligands from a top view are reported. The asterisks denote the stereogenic centers.

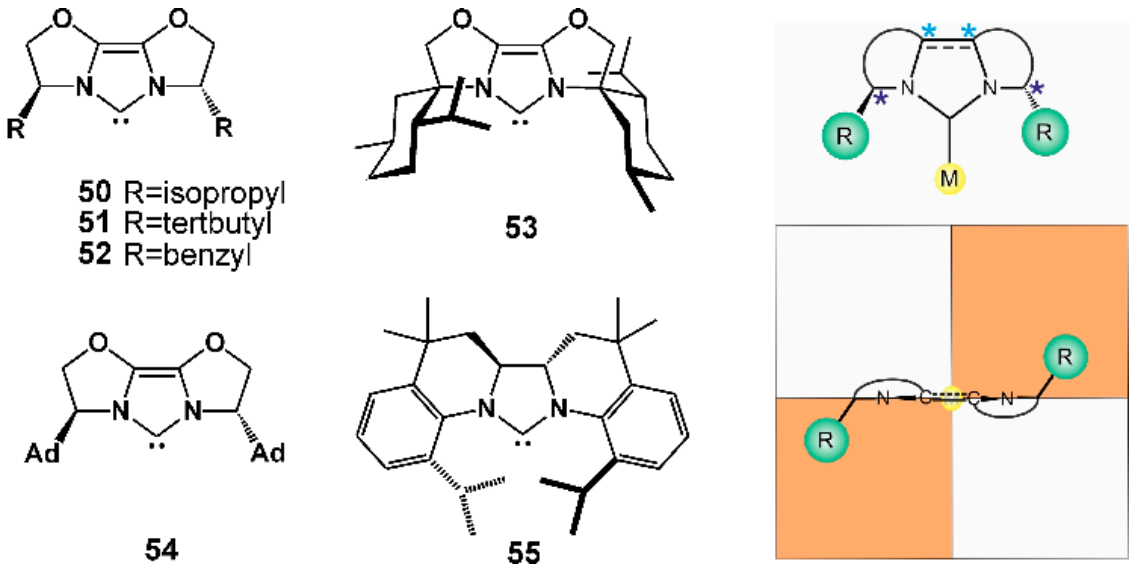


Figure 3. C_2-symmetric NHC ligands with tricyclic structures (**C**). On the right quadrant, maps of the depicted ligands from a top view are reported. The asterisks denote the stereogenic centers.

NHC ligand (**6**) was used later by Procter in the enantioselective copper-catalyzed three-component coupling of imines, allenes, and diboranes affording the desired products with adjacent stereocenters in high enantioselectivities [35]. A new NHC ligand, in which steric encumbered substituents are located on the aryl groups, rather distant from the stereogenic center (**7**), was reported, in combination with a copper catalyst, by Ohmiya and Sawamura in the first catalyzed enantioselective conjugate addition of alkylboron derivatives [36].

A new concept to develop chiral, C_2-symmetric unsaturated and saturated NHC ligands was proposed by Gawley in 2011 [37,38]. He modified the structural motif of classical achiral *N*,*N*′-diaryl-substituted NHCs, introducing *ortho*-substituted *N*-aryl groups having stereogenic center(s) γ to the annular nitrogen(s). This new class of NHCs coordinated to copper chloride was tested in the enantioselective hydrosilylation of prochiral ketones, which provides access to enantioenriched alcohols, and the system **8**/CuCl led to the isolation of nearly enantiopurecorresponding silylethers (95–99% *ee*) [38]. In more recent years, steric and electronic modifications of Gawley's NHC scaffold were introduced by Cramer and Shi to expand the scope of this kind of ligands in metal-catalyzed asymmetric applications (e.g., **9**–**13**). Cramer first developed sterically demanding chiral NHCs by introducing substituents on the backbone of the imidazolylidene ring (Cl, Me) or exploiting the acenaphthoimidazolylidene framework, hypothesizing that such steric constraints could slightly push the flanking groups toward the metal-center, improving selectivity. The new NHCs were tested in the enantioselective nickel-catalyzed C-H functionalizations of (**2**), (**4**)-pyridones, and ligand (**10**) was found to give excellent enantioselectivities [39]. One year later, Cramer reported a saturated version of Gawley's NHC ligand with very bulky (**3**,**5**-ditertbutyl)phenyl flanking groups (**13**) that enables enantioselective nickel-catalyzed C-H functionalizations of indoles and pyrroles [40].

As of 2018, Shi and coworkers also focused on the development and application in different asymmetric metal-catalyzed reactions of Gawley-type NHC ligands. The first report described a highly enantioselective copper-catalyzed Markovnikov protoboration of unactivated terminal alkenes in which the sterically hindered *N*-heterocyclic carbene **9** based on the acenaphthoimidazolylidene framework was employed [41].

Then, they investigated the chiral NHCs **9**, **10**, **11**, and **12** in a series of nickel-catalyzed transformations. The chiral *N*-heterocyclic carbene ligand **11** led to success in the enantioselective redox-neutral coupling of alcohols and alkynes to form allylic alcohols promoted by nickel catalyst $Ni(COD)_2$ [42] (COD = cyclooctadiene) as well as in the enantioselective endo-selective C-H cyclization of pyridines, pyridines, and pyrimidones with alkenes

to give chiral annulated products [43,44]. In 2019, Shi reported the first enantioselective C-H alkylation of polyfluoroarenes with alkenes to furnish valuable chiral fluorotetralins. Excellent levels of enantiocontrol were observed using **10**/Ni(COD)$_2$ [45]. Meanwhile, the potential of this class of sterically bulky NHC ligands was investigated by Ye in the Ni-catalyzed reductive coupling of alkynes and imines for the synthesis of allylic amines using readily available isopropanol as a reductant. Enantiomeric excess of 95% was reached using **10** as the nickel ligand [46].

Most recently, Shi described an asymmetric NHC/Ni-catalyzed addition of readily available and stable arylboronic esters to ketones providing various optically enriched tertiary alcohols. An excellent enantiocontrol (up to 98% *ee*) was observed with the employment of the bulky C_2-symmetric chiral NHC ligand **10** [47]. The system based on the complex **9**/Ni(COD)$_2$ was instead identified as the most efficient in the arylation of racemic secondary alcohols to give enantioenriched tertiary alcohols with various functional groups and heterocycles [48].

The key to success of this class of C_2-symmetric chiral NHCs in asymmetric catalysis is mainly related to their steric properties. Their bulkiness, associated to the conformational flexibility deriving from the multiple rotations of the single C-C and C-N bonds, enabled an unprecedented low-temperature, highly enantioselective nickel-catalyzed amination of aryl halides with sterically encumbered secondary amines affording chiral amine products through a kinetic resolution process (up to 99.5% *ee* with **9**) [49].

In 2022, the Shi group developed a protocol that allowed for the highly enantioselective arylation and alkenylation of simple aldehydes using readily available and stable organoboronic esters. Through this approach, a wide range of chiral secondary alcohols was obtained in high enantiomeric excesses (up to 97%) employing the NHC ligand **10** in combination with Ni(COD)$_2$ [50].

Apart from asymmetric nickel-catalyzed transformations, Shi and coworkers also investigated the behavior of sterically demanding C_2-symmetric chiral NHCs in the palladium-catalyzed Suzuki−Miyaura cross-coupling reactions for constructing biaryl atropisomers, reaching high enantioselectivities (>90% ee) using the extremely bulky NHC **13** coordinated to Pd(η^3cinnamyl)chloride [51].

More exotic chiral C_2-symmetric NHC ligands, adorned with two planar-chiral cyclophane units bound to the nitrogen atoms, were developed by Andrus and coworkers in 2003 [52]. These NHCs were able to promote highly enantioselective Rh-catalyzed conjugate additions (**14**–**17**) [52], asymmetric Ru-catalyzed hydrosilylation of ketones (**14**, **15** and **17**) [53], and asymmetric copper-catalyzed β-boration of α, β-unsaturated esters (**18**) [54]. Recently, Clavier and Mauduit described optically pure transition metal complexes bearing C_2-symmetric NHC ligands prepared from prochiral NHC precursors. The formation of the metal-carbene bond induces an axis of chirality. Enantiomeric excesses $\geq$ 90% were achieved with **19** and **20** in the Cu-catalyzed asymmetric allylic alkylation of diethylzinc to allyl phosphates and Pd-catalyzed asymmetric intramolecular α-arylation of amides, respectively [55].

Table 1 summarizes the most relevant transition-metal catalyzed enantioselective transformations ($\geq$90% *ee*) performed with NHCs containing chiral *N*-substituents (**A**).

Table 1. Highly enantioselective NHC (**A**)/metal-catalyzed transformations.

Metal	NHC	Reactions	References
Cu	**2,7**	Conjugate addition	[19,37]
	6	Three-component coupling	[35]
	8	Hydrosylilation	[37,38]
	9	Protoboration	[41]
	18	Boration of α, β-unsaturated esters	[44]
	19	Allylic alkylation	[55]
Ni	**3**	Three-component coupling	[29]
	9	Arylation of secondary alcohols	[48]
	9	C-N cross-coupling	[49]
	10	C-H alkylation of polyfluoroarenes	[45]
	10	Reductive coupling of alkynes and imines	[46]
	10	Arylboration of ketones	[47]
	10	Arylboration and alkenylboration of aldehydes	[50]
	11	Reductive coupling of alcohols and alkynes	[42]
	11	C-H cyclization of pyridines, pyridones and pyrimidines	[43,44]
	13	C-H functionalization of indoles and pyrroles	[40]
Pd	**4,5,20**	Intramolecular α-arylation of amides	[30,31,55]
	4,6	$C(sp^3)$-H/C(Ar) coupling	[32–34]
	13	Suzuki-Miyaura cross-coupling	[51]
Rh	**15–18**	Conjugate addition	[52]
Ru	**2**	Hydrogenation	[19–26]
	14, 15, 17	Hydrosilylation of ketones	[53]

2.2. NHCs with Chiral Backbones

The second common strategy to prepare chiral NHC ligands involves the incorporation of chiral 1,2-diamines into the NHC framework. The substituents so introduced on the backbone of the saturated NHC ring exert a conformational control on the *N*-substituents restricting their rotation and influencing their orientation. In this way, the chiral information on the NHC backbone is transferred to the metal center. In 2001, Grubbs reported the first study on the employment of a NHC motif based on the commercially available enantiopure chiral 1,2-diphenylethylendiamine in the asymmetric ruthenium-catalyzed ring-closing metathesis of prochiral trienes, in which high enantiomeric excesses (up to 90% *ee*) were reached using ligand **21** [56]. Crucial to create a C_2-symmetric environment through a chiral relay mechanism was the presence of mono-*ortho* substituted *N*-phenyl groups [57]. To expand the substrate scope and enhance the enantioselectivity, in 2006, Grubbs and coworkers reported NHCs **22–24** differing for the number of substituents and/or for their relative arrangement on the *N*-aryl rings. Improved enantioselectivities were registered with **22** [58]. The nature of the substituents on the NHC skeleton in the same asymmetric ruthenium catalyzed ring-closing metathesis reaction was investigated by our group in 2011 [59]. Installing methyl instead of phenyl substituents on the NHC backbone (**25**), no major impact on the stereochemical outcome was observed, as the same *ee* values were obtained. On the contrary, the effect of backbone substitution was found to influence the reaction selectivity in another metal-catalyzed transformation.

Cramer, indeed, in 2016 observed that the replacement of the 1,2-diphenylethylene diamine backbone with the 1,2-di(napthalen-1-yl)ethylene diamine backbone to give the new bulky NHC ligand **26** led to increased enantioselectivity in the nickel-catalyzed reductive three-component coupling between aromatic aldehydes, norbornenes, and silanes affording silyl-protected indanol derivatives [60]. The NHC design principle based on the 1,2-diphenylethylene diamine backbone has been largely exploited to successfully accomplish numerous asymmetric metal-catalyzed reactions. In the ambit of copper-catalyzed transformations, at the beginning of the last decade, Hoveyda's group reported

ligands **27** and **28** in the enantioselective conjugate silyl additions to unsaturated carbonyls [61] and to dienones and dienoates [62], respectively, while in 2019 Shen and Xu identified ligands **29**–**31** as highly efficient in the enantioselective conjugate silyl addition to indol-1-ylacrylate derivatives (up to 98% *ee*) [63]. As for nickel-catalyzed reactions, a highly enantioselective synthesis of benzoxasiloles (up to 99.9% *ee*), reported by Ogoshi and coworkers, was achieved via the sequential activation of an aldehyde and a silane by $Ni(COD)_2$ in the presence of ligand **21** [64]. The same group employed the catalytic system **27**/$Ni(COD)_2$ to successfully accomplish an intermolecular, enantioselective [2 + 2 + 2] cycloaddition of two enones and an alkyne leading to the formation of cyclohexenes with four adjacent stereogenic centers [65].

In 2017, NHCs **32** and **33** with sterically encumbered *N*-aryl groups were exploited by Ackermann's group to develop the first enantioselective iron-catalyzed indole C-H alkylation by inner sphere C-H activation [66]. In the following years, a series of C_2-symmetric NHCs with di-*ortho*-substituted *N*-aryl rings were reported. Ogoshi et al. described a nickel-catalyzed highly enantioselective synthesis of chiral fused tricyclic scaffolds with five contiguous chiral centers in the presence of NHCs **34** and **35** [67], whereas Montgomery and coworkers reported on the nickel-catalyzed asymmetric reductive coupling reactions of aldehydes and alkynes using novel enantiopure NHC ligands with exceptional steric demand, such as **36** [68]. Ding and Hou reported a similar bulky NHC (**37**) in the palladium-catalyzed asymmetric [3 + 2] cycloaddition of vinyl epoxides with allenic amides [69], while Dang and Ho investigated the bulky rigid NHC **38** in the nickel-catalyzed enantioselective synthesis of 1,4-dienes by the cross-hydroalkenylation of cyclic 1,3-dienes and heterosubstituted terminal olefins. However, in this reaction, **38** was found to be less efficient than the less bulky and more flexible C_2 chiral NHC **28** [70]. It should be noted that, with respect to chiral NHCs containing mono-*ortho*-substituted *N*-aryl groups, for symmetrically di-*ortho*-aryl substituted NHC ligands (**34**, **36**, **37** and **38**), the origin of chiral induction is associable only to the C_2-symmetry of the NHC backbone.

Table 2 summarizes the most relevant transition-metal catalyzed enantioselective transformations ($\geq$90% *ee*) performed with NHCs containing a chiral backbone (**B**).

A family of NHC ligands bearing mono- and di-*ortho*-substituted 1-naphthyl groups as the *N*-substituents was developed by Dorta and coworkers (e.g., **39**–**43**). These NHCs are characterized, in addition to backbone chirality, by axial chirality due to the dissymmetric aromatic *ortho*-substitution. Ligands **39** and **40** were successfully employed in the palladium-catalyzed asymmetric α-arylation of amides to provide allylated oxindoles with quaternary carbon centers [71] and 3-fluoro-3-aryl oxindoles [72] with excellent enantioselectivities (up to 99% ee). In more recent years, Dorta et al. used NHCs **41**–**43** in the iridium-catalyzed asymmetric intramolecular hydroamination reaction of unactivated aminoalkenes [73–75], in which high levels of enantioselectivity were obtained. Moreover, in 2020, they evaluated the behavior of various NHCs with 1-naphthyl side chains in the iridium-catalyzed enantioselective ring-opening amination of oxabicycles, identifying ligand **42**, with overall less sterically demanding and more flexible wingtips on the NHC core, as the most efficient (up to 96% *ee*) [76]. In the same year, Zhang, Luo, and Hou developed a highly enantioselective copper-catalyzed cyanoborylation of allenes by using a new chiral NHC ligands, having isopropyl substituents at the C2 and C6 positions of the naphthyl groups (**44**) [77]. More complex NHC architectures containing sterically demanding trypticene substituents as the flanking aryl substituents on the nitrogen atoms, in combination with a chiral backbone, were developed by Plenio, who evaluated ligand **45** and **46** in the copper-catalyzed enantioselective borylation of α, β-unsaturated esters, reaching *ee* values close to 90% [78].

Another design approach to C_2-symmetric NHC ligands was introduced in 2001 by Alexakis, which reported some encouraging results in the asymmetric copper-catalyzed 1,4-conjugate addition of diethylzinc to enones using NHCs possessing a chiral backbone (1,2-diphenylethylenediamine) and chiral nitrogen substituents (1-phenylethyl groups) [79]. A similar NHC ligand structure differing only in the nature of substituents on the back-

bone (methyl instead of phenyl) was reported by our group in asymmetric ring-closing metathesis performed by ruthenium catalysts, where only modest enantioselectivities were registered [80]. Some years later, chiral copper-complexes bearing NHCs **47**–**49** were reported by Tomioka and coworkers as efficient catalysts in the asymmetric allylic arylation of cinnamyl-type substrates [81] and aliphatic allylic bromides [82] with aryl Grignard reagents (up to 98% *ee*). In 2016, NHCs **47** and **48** were employed by Hornillos and Feringa in the first enantioselective copper-catalyzed allylic arylation with organolithium compounds to afford optically active diarylvinylmethanes with excellent enantioselectivities (up to 97%) [83].

Table 2. Highly enantioselective NHC(**B**)/metal-catalyzed transformations.

Metal	NHC	Reactions	References
Cu	**28–31,34**	Conjugate sylil addition	[61–63]
	44	Cyanoborylation of allenes	[77]
	45,46	Borylation of α, β-unsaturated esters	[78]
	47–49	Allylic arylation	[81–83]
Fe	**32,33**	C-H alkylation	[66]
Ir	**41–43**	Intramolecular hydroamination	[73–75]
	42	Ring-opening amination	[76]
Ni	**21**	Synthesis of benzoxasiloles	[64]
	26	Three-component coupling	[60]
	27	Intermolecular [2 + 2 + 2] cycloaddition of enones with alkynes	[65]
	28,38	Cross-hydroalkenylation	[70]
	34,35	Desymmetrization and following [4 + 2] cycloaddition	[67]
	36	Reductive coupling of aldehydes and alkynes	[68]
Pd	**37**	[3 + 2] cycloaddition of vinyl epoxides with allenic amides	[69]
	39,40	α-arylation of amides	[71,72]
Ru	**21–25**	Ring-closing metathesis	[56,58,59]

2.3. NHCs with Fused Cycles

The third approach to build up chiral C_2-symmetric NHC ligands implies the use of NHC architectures featuring a fused tricyclic skeleton. The first example exploiting oxazolines as chiral building blocks for NHCs was introduced in 2002 by Glorius and coworkers, who employed the new ligands **50**–**52** in the palladium-catalyzed intramolecular α-arylation of amides reaching a 43%*ee* in the presence of **51** [84]. Some years later, Glorius modified the original design by developing an extraordinarily sterically demanding, rigid, C_2-symmetric NHC ligand, IBiox[(−)-menthyl] NHC **53**, which was successfully applied in palladium-catalyzed α-intramolecular arylations giving high levels of enantioselectivity (up to 99%) [85]. The same ligand coordinated to a rhodium(I) complex was used by Bexrud and Lautens for the asymmetric hydroarylation of azabicyles, affording high enantiomeric excesses (93–99%) [86]. In 2021, Baudoin et al. employed chiral C_2-symmetric IBiox ligands **51** and **54** in the palladium-catalyzed intramolecular arylation of nonactivated secondary C-H bonds, affording high enantioselectivities for a broad range of valuable indane products [87]. Chiral NHCs having a 2,2′-bisquinoline-based C_2 symmetric skeleton such as **55** were developed by Murakami and coworkers and applied to the palladium-catalyzed intramolecular arylation reaction of amides to give 3,3-disubsituted oxindoles in high enantioselectivities (up to 97% *ee*) [88].

Table 3 summarizes the most relevant transition-metal catalyzed enantioselective transformations (≥90% *ee*) performed with NHCs possessing tricyclic structures (**C**).

Table 3. Highly enantioselective NHC(**C**)/metal-catalyzed transformations.

Metal	NHC	Reactions	References
Pd	**53,55**	α-arylation of amides	[85,88]
	51,54	C-H arylation	[87]
Rh	**53**	Hydroarylation	[86]

3. Conclusions

Asymmetric catalysis is an indispensable tool for the preparation of optically active compounds and has become one of the most prominent areas of organo-transition metal chemistry. The fast development of suitable catalytic systems has now reached a stage where some of them are stereoselective enough to find industrial application. The introduction of chiral NHCs as ligands for transition metal catalysis has offered new opportunities in asymmetric organic synthesis. Chiral monodentate C_2-symmetric NHC ligands can be essentially synthesized through three different approaches, based on the use of chiral *N*-substituents, the use of chiral NHC backbones, and the synthesis of rigid tricyclic NHCs. This review focuses on those NHC architectures, which have allowed tremendous advances in reaching high levels of enantioselectivity in transition-metal catalysis, highlighting the key role played by the appropriate NHC substitution pattern.

The possibility of further modifying C_2-symmetric NHC ligand designs to improve enantioselectivities and to expand the range of applications of transition metal complexes is the next challenge in the field of asymmetric catalysis research.

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