

Ferrocene-Based Planar Chiral Imidazopyridinium Salts for Catalysis**

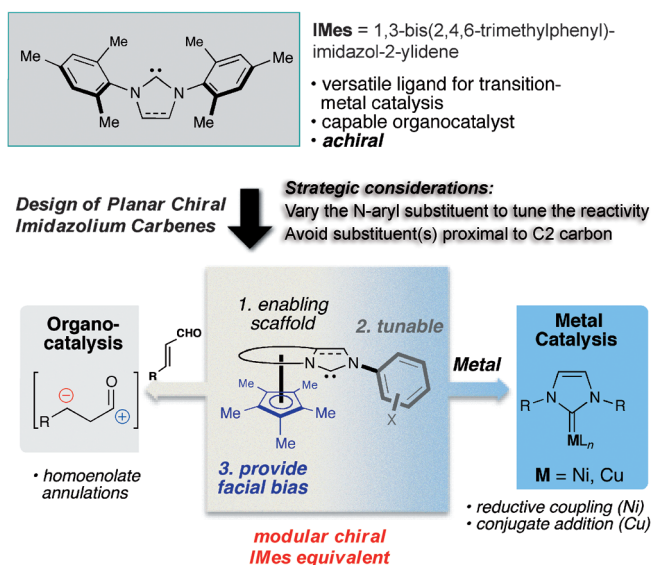
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Abstract: Planar chirality remains an underutilized control element in asymmetric catalysis. Factors that have limited its broader application in catalysis include poor catalyst performance and difficulties associated with the economical production of enantiopure planar chiral compounds. The construction of planar chiral azolium salts that incorporate a sterically demanding iron sandwich complex is now reported. Applications of this new *N*-heterocyclic carbene as both an organo-catalyst and a ligand for transition-metal catalysis demonstrate its unprecedented versatility and potential broad utility in asymmetric catalysis.

N-Heterocyclic carbenes (NHCs) are unique and enabling ligands for transition metal (TM) catalysis and have emerged as highly selective organocatalysts for a remarkably diverse array of transformations.^[1–3] Given the importance of these strongly nucleophilic Lewis bases in chemistry, major efforts by many laboratories have produced numerous classes of structurally and electronically diverse NHC structures.^[4] Within this truly broad family of heteroatom-stabilized divalent carbon species, two major classes of NHCs derived from triazolium and imidazolium salts have demonstrated applicability as Lewis base catalysts and TM ligands. Although triazolium salts have seen broad application in asymmetric organocatalysis, their success in metal-based transformations has been limited.^[2e] In contrast, imidazolium-derived NHCs (imidazol-2-ylidenes) have been widely deployed as successful ligands for TM catalysis and are unique platforms for organocatalytic transformations. The archetype imidazol-2-ylidene, IMes [1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene], was introduced by Arduengo in 1992.^[5] Surprisingly, in over two decades since the disclosure of IMes, only few chiral scaffolds based on this important species have been reported.^[6] As one notable example, the saturated analog of IMes, SIMes (4,5-dihydro-1,3-dimesityl-1*H*-imidazolium) has been translated into multiple chiral ligands for TM catalysis,^[7] but their reactivity in organocatalysis signifi-

cantly differs from that of IMes, and they have only recently been employed in asymmetric transformations.^[8]

A major challenge in carbene catalysis is the design and implementation of a chiral IMes analogue with competent ligand and/or catalyst characteristics. Whereas *C*₂-symmetric chiral imidazolium salts are rapidly accessible through the condensation of stereodefined amines with glyoxal,^[9] these NHCs rarely deliver high levels of selectivity as ligands in TM catalysis and are typically unsuitable as organocatalysts.^[10] Most notably, structurally rigid NHCs that invoke planar chirality are scarce in the literature, with most contemporary examples featuring pendant planar chiral motifs with various degrees of free rotation.^[6a,b] Encouraged by the potential opportunity to develop a versatile chiral IMes equivalent and the documented successes of chiral ferrocenyl-based ligands and catalysts as control elements in asymmetric transformations,^[11,12] we set out to create imidazolium-inspired NHCs featuring the fusion of a metal sandwich complex with the core structure of an NHC framework (Figure 1).^[13]



Examples of Chiral Imidazolium Salts

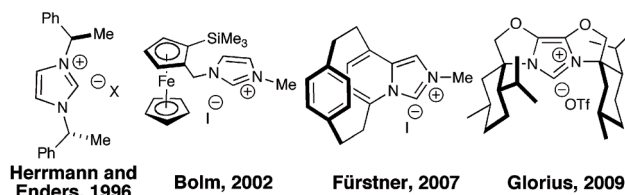


Figure 1. Chiral imidazolium strategy.

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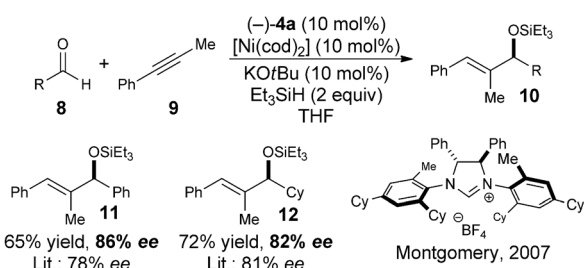
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aryl substituent as well as other structural factors is ongoing with the aim of imparting higher levels of selectivity and reactivity in umpolung transformations.

The use of NHCs as ligands in metal-catalyzed transformations has dramatically increased over the last two decades.^[1] In particular, IMes and related structures have been found to be successful ligands for a variety of important transformations, including olefin metathesis,^[20] cross-coupling,^[21] and hydrogenation^[22] as well as many others.^[23] A recent report by Montgomery et al. demonstrated the ability of saturated imidazolium NHCs to impart high levels of enantioselectivity in nickel-catalyzed reductive couplings, whereby the *C*₂-symmetric NHCs first reported by Grubbs and co-workers proved to be efficient ligands for the coupling of simple alkynes and aldehydes.^[7a,24] Although moderate to high selectivity has been reported for reductive couplings of alkynes and aldehydes, there remains room for further enhancement of the enantioselectivity and scope of these reactions.^[25,26] Inspired by this report and others (see below), we viewed this particular transformation as an excellent opportunity to evaluate the chiral environment engendered by **4** when bound to a transition metal such as nickel. Under reaction conditions developed by Montgomery, NHC **4a** proved to be a capable ligand for the Ni-catalyzed reductive coupling of 1-phenyl-1-propyne with benzaldehyde and cyclohexanecarboxaldehyde using triethylsilane as the reducing agent (Scheme 3). In both cases, the allylic alcohol product

Ni/NHC-catalyzed reductive coupling

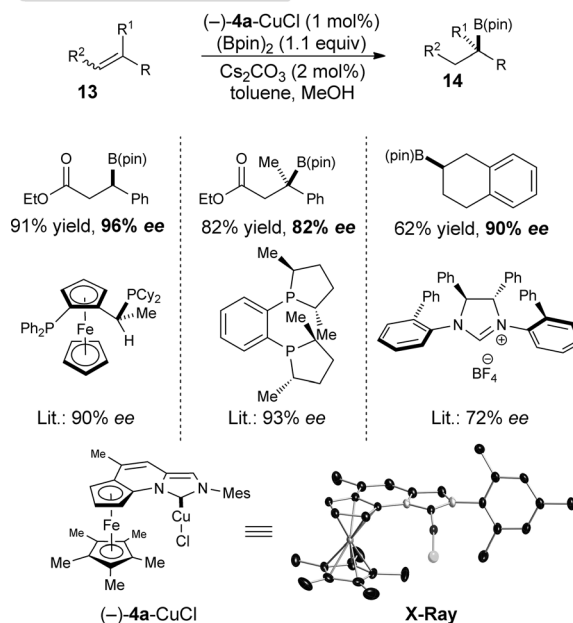


Scheme 3. Nickel catalysis. cod = cyclooctadiene, Cy = cyclohexyl.

was formed with excellent regioselectivity (>20:1 and 10:1) and enantiomeric excess (86% and 82% *ee*). To the best of our knowledge, these reactions provide some of the highest selectivities for this transformation to date and highlight the opportunity to explore both known and unreported Ni⁰-catalyzed transformations with these NHC ligands.

To further investigate the potential versatility of **4** in additional metal-catalyzed processes, we explored the copper-catalyzed borylation of olefins.^[27] The preparation of the enantiopure Cu/NHC complex (–)-**4a**-CuCl was accomplished following a literature procedure, and a crystal structure was obtained (Scheme 4).^[28] Gratifyingly, the isolated Cu/NHC complex catalyzed the borylation of a variety of substrates without the need for any reaction optimization and provided the products in good yields with high stereoselectivities (Scheme 4).

Cu/NHC-catalyzed borylation



Scheme 4. Copper catalysis.

To further our understanding of this new class of NHCs, we examined the electronic properties of the various aryl-substituted planar chiral ferrocenyl azolium salts through the use of the Tolman electronic parameter (TEP).^[4,29] Synthesis of the corresponding [(NHC)Rh(CO)₂Cl] complexes allowed for a comparison of the electron-donating properties of the planar chiral NHCs **15a–15d** with those of selected known NHCs (Figure 2).^[30] These new ferrocenyl-imidazo[1,5-*a*]pyridine NHCs have distinctive degrees of donating abilities depending on the N-aryl substituent. Surprisingly, the mesityl-substituted NHC (**15a**) possesses similar electronic properties to the parent IMes, which is fortuitous in light of our initial goal of creating a new chiral IMes equivalent for catalysis. The 2,6-dimethoxyphenyl-substituted carbene **15c** provided the largest donor capacity (TEP = 2047 cm^{–1}), which exceeds that of most common imidazolium and dihydroimidazolium carbenes. In contrast, the complex bearing a bis(trifluoromethyl)phenyl substituent (**15d**) demonstrated the smallest donor capacity (TEP = 2054 cm^{–1}), which is comparable to that of dihydroimidazolium complexes. The current range of modulation in the donating capability of our NHCs demonstrates that these NHCs are versatile in their steric environments as well as electronic properties.

In conclusion, a novel NHC scaffold that incorporates an iron sandwich complex into the azolium framework has been developed. This new class of planar chiral imidazopyridinium-based NHCs has proven to be highly competent as both Lewis base catalysts and as ligands for transition-metal complexes. Significantly, these new planar chiral NHCs impart high levels of stereoselectivity across three challenging platforms with distinct requirements for asymmetric induction (organocatalysis, nickel(I) and copper(I) catalysis), underscoring the potential generality of these systems.^[7a,18b,27b–e] The late-stage formation of the key azolium core allows for a modular

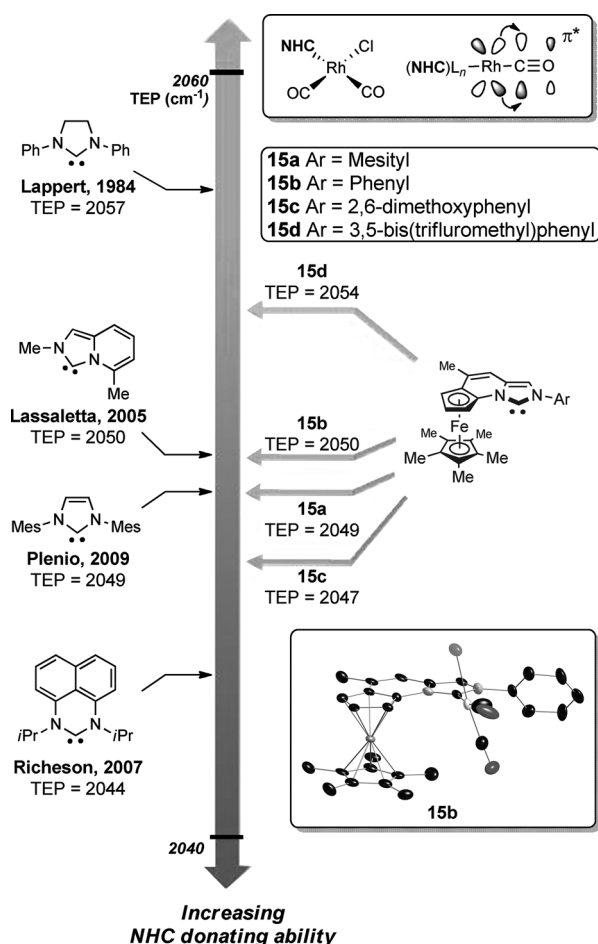


Figure 2. Donating abilities of various classes of NHCs. See the Supporting Information for details on the preparation of the rhodium complexes and on the calculation of the TEP values.

synthesis of related structures, thus providing a flexible platform for tuning the Lewis base donor capacity (as presently measured by TEP values). These NHCs represent a class of versatile and selective chiral azolium salts, and their wide range of steric and electronic properties should enable new directions and opportunities for catalysis with N-heterocyclic carbenes.

Keywords: asymmetric synthesis · N-heterocyclic carbenes · organocatalysis · transition-metal catalysis

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