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(NHC)NiCp$_2$ complexes: new air-stable thermally activated precatalysts for olefin hydroheteroarylation

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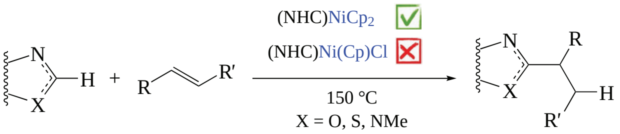
Readily available air-stable (NHC)NiCp$_2$ complexes (NHC is N-heterocyclic carbene, Cp is cyclopentadienyl anion ligand) can be used as efficient thermally activated precatalysts for hydroheteroarylation of olefins with various heteroarenes. According to preliminary mechanistic studies, precatalyst activation may involve reductive elimination of two Cp ligands to give 1,1′-bi(cyclopenta-2,4-diene) and (NHC)Ni^0 active species under elevated temperature.

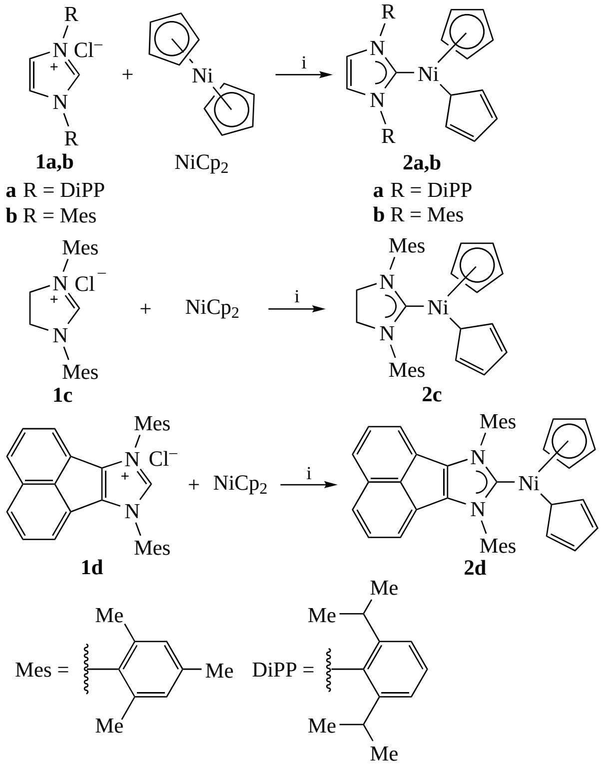


Keywords: nickel complexes, N-heterocyclic carbenes, cyclopentadienyl anion ligand, C–H activation.

Transition metal-catalyzed hydroheteroarylation of olefins with electron-deficient heteroarenes provides a direct access to substituted medicinally-oriented heteroaromatic compounds inaccessible *via* classical acid or Friedel–Crafts types of catalysis.[1,2] Catalytic systems relied on Ni complexes with N-heterocyclic carbene (NHC) ligands (Ni/NHC) have received much attention as promising catalysts for hydroheteroarylation.[3] The reaction mechanisms typically involve participation of Ni^0/NHC active species.[3] Therefore, well-defined Ni^0/NHC complexes,[4,5] or NHCs in combination with Ni^0 source, usually Ni(COD)$_2$ (COD is cycloocta-1,5-diene),[3] are mostly used as precatalysts. However, most of well-defined Ni^0/NHC complexes, as well as free NHCs and Ni(COD)$_2$, are extremely air sensitive, which requires the use of a glovebox. Bench-stable air-tolerant Ni^{II}/NHC complexes in the presence of appropriate Ni^{II} to Ni^0 reductants can also be applied as precatalysts, although formation of inorganic wastes from a reductant used in a large excess is a main drawback of this approach.[6,7]

An alternative route to overcome the above limitations involves the use of air-stable Ni^{II} complexes with sacrificial ligands which can serve as internal reductants.[8–15] For example, well defined Ni^{II}/NHC complexes with a specially designed C,N-donor bidentate aryl ligands containing an appended olefin moiety which facilitate the reduction of Ni^{II} to Ni^0 by an intramolecular Heck reaction were successfully applied in the catalysis of several C–H and C–C bond-forming reactions.[13] In searching for Ni complexes with more accessible potential sacrificial ligands for catalysis of alkene hydroheteroarylation, we turned our attention to readily available air-stable (NHC)NiCp$_2$ complexes (Cp is cyclopentadienyl anion).[16–18] We proposed that two Cp ligands can suffer reductive elimination (C–C coupling) thus providing Ni^{II} to Ni^0 reduction. Unlike catalytic properties of widely used (NHC)NiCpHal complexes,[19] those of (NHC)NiCp$_2$ complexes are still almost unexplored.[18] Herein, we introduced a new type of readily available thermally activated (NHC)NiCp$_2$ precatalysts for alkene hydroheteroarylation.

Complexes (NHC)NiCp$_2$ used in this study were prepared by the reaction of NHC-proligands **1a–d** with nickelocene and Bu^{t}ONa according to modified procedure[18] (Scheme 1). The application of strong base such as Bu^{t}ONa was crucial to prevent formation of (NHC)Ni(Cl)Cp byproducts (see Online Supplementary Materials, Table S1). Apparently, this may be explained by higher basicity of Cp ligands and their predominant protonation in the presence of weaker bases such as Cs$_2$CO$_3$,



Scheme 1 *Reagents and conditions*: i, **1a–d** (0.55 mmol), NiCp$_2$ (0.5 mmol), Bu^{t}ONa (0.58 mmol), toluene (4 ml), 25 °C, 2 h.

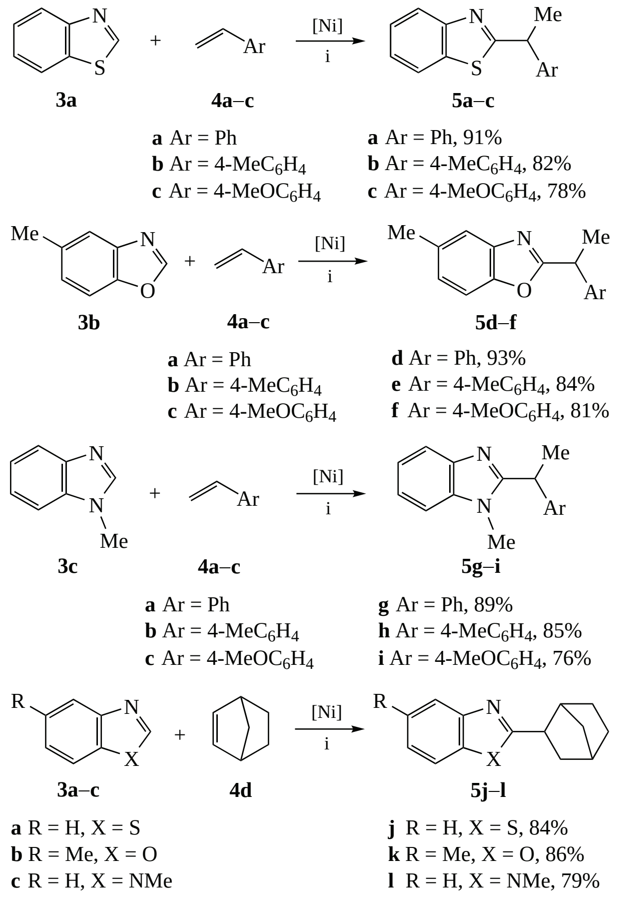
Table 1 Optimization of the reaction conditions.[a]

Entry	Precatalyst (mol%)	T/°C	Yield of **5a** (%)[b]
1	**2a** (10)	150	2
2	**2b** (10)	110	31
3	**2b** (10)	140	78
4	**2b** (10)	150	96
5	**2b** (10)	160	95
6	**2b** (5)	150	58
7	**2b** (15)	150	97
8	**2b** (10)	150	73[c]
9	**2c** (10)	150	46
10	**2d** (10)	150	38
11	**6** (10)	150	0

[a] *Reagents and conditions*: **3a** (0.25 mmol), **4a** (0.3 mmol), precatalyst **2a**–**d** or (IMes)Ni(Cp)Cl **6**, *o*-xylene (1 ml), 5 h. [b] Yields were determined by GC-MS using 1,3-diisopropylbenzene as an internal standard. [c] Reaction time 2 h.

K_3PO_4 or NaOAc. Complexes **2a**–**d** were obtained as red-colored air-stable microcrystalline compounds. Complex **2a** was previously described,[18] structures of novel complexes **2b**–**d** were confirmed by ^{1}H and ^{13}C NMR spectra and elemental analyses. NMR spectra of complexes **2a**–**d** are analogous to those of compound **2a** and similar complexes reported in literature[16–18] and contain characteristic singlets for one η^1-bonded Cp ring (~5.3–5.5 ppm in ^{1}H NMR, ~108.0–108.5 ppm in ^{13}C NMR) and one η^5-bonded Cp ring (~3.8–4.0 ppm in ^{1}H NMR, ~92.0–92.6 ppm in ^{13}C NMR).

Catalytic activity of complexes **2a**–**d** was evaluated in the reaction between benzo[*d*]thiazole **3a** and styrene **4a** affording product **5a** (Tables 1 and S2, Scheme 2). Complex (IMes)Ni(Cp)Cl **6** (IMes is 1,3-bis(2,4,6-trimethylphenyl)-1,3-dihydro-2*H*-imidazol-2-ylidene) which demonstrated excellent activity in this reaction conducted in the presence of HCO_2Na (Ni^{II} to Ni^0 reductant)[7] was tested for comparison. Significant dependence of catalytic activity on reaction temperature and NHC structure was observed. Complex **2a** containing bulkiest NHC ligand with DiPP N-aryl groups was almost inactive at 110 °C and provided only 2% yield of **5a** at 150 °C (see Table 1, entry 1, and Table S2). In contrast, complexes **2b**–**d** containing less bulky NHC ligands with Mes N-aryl groups provided reasonable yields of **5a** at temperatures 110–160 °C (see Table 1, entries 2–10). Complex **2b** exhibited highest catalytic activity among complexes **2a**–**d** (compare entry 4 with entries 1, 9, 10). Apparently, lower activity of other studied complexes may be explained by higher steric bulkiness of NHC ligands in these complexes. Nickelocene ($NiCp_2$) in the absence of NHC ligands was also completely inactive under the studied conditions (see Table S2, entry 20). Highest efficiency of IMes ligand for Ni/NHC-catalyzed hydroheteroarylation reactions involving similar substrates and reagents was mentioned in the literature.[7] Best yield of **5a** was observed under conditions of entry 4 (150 °C, 10 mol% **2b** loading). The yield decreased significantly at lower temperatures and precatalyst loadings (entries 2, 3 and 6) and was almost not affected at higher temperature (entry 5) and precatalyst loading (entry 7). Other solvents (DMF, toluene, dioxane, THF, MeCN) were also less efficient than *o*-xylene (see Table S2). Therefore, conditions of entry 4 (see Table 1) were accepted as optimal. Remarkably, complex **6** used for comparison was completely inactive under studied conditions (entry 11).

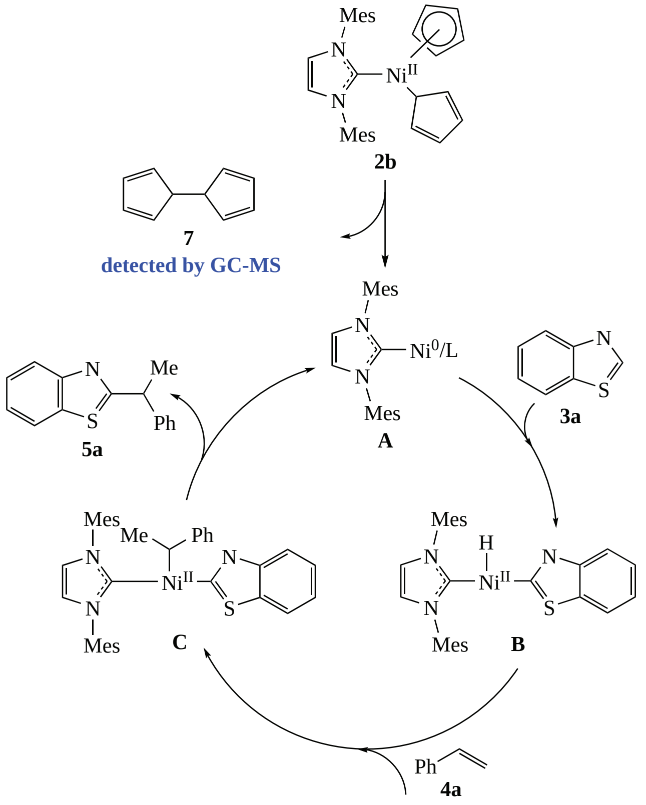


Scheme 2 *Reagents and conditions*: i, **3a**–**c** (0.25 mmol), **4a**–**d** (0.3 mmol), precatalyst **2b** (10 mol%), *o*-xylene (1 ml), 150 °C, 5 h.

With the optimal conditions in hand, we evaluated the **2b** catalytic efficiency in the alkylation of a broader scope of heteroarenes **3a**–**c** with alkenes **4a**–**d** (Scheme 2). Desired alkylated products **5** were obtained in 76–93% isolated yields. Attempts to use unactivated olefins such as hex-1-ene, hept-1-ene and oct-1-ene as alkylating agents were unsuccessful, only trace yields of alkylated products were detected by GC-MS, that is in agreement with our previous data.[7]

Essentially different catalytic activity of complexes **2b** and **6** containing the same NHC ligand (see Table 1, entries 4 and 11) indicate the critical importance of the presence of two Ni-coordinated Cp ligands for providing catalytic activity of studied complexes in the absence of external Ni^{II} to Ni^0 reductants. Plausible reaction mechanism taking into account previous literature data[7,20] is presented in Scheme 3. Precatalyst activation proceeds through the reductive elimination of two Cp ligands affording bicyclopentadiene **7** and (NHC)Ni^0 **A** active species. Active complex **A** further enters in the oxidative addition of C–H acidic heteroaromatic substrate to give hydride complex **B** which undergoes the subsequent alkene coordination, insertion into a Ni–H bond to form organonickel intermediate **C**. Intermediate **C** then suffers a reductive elimination to result in the corresponding alkylation product **5**. The observed regioselectivity and formation of 1,1-disubstituted ethanes from styrenes under catalysis with NHC/Ni complexes containing IMes and other NHC ligands of moderate steric bulkiness is explained by higher thermodynamic stability of intermediate **C** with phenylethyl ligand connected to Ni by C^1 atom of ethane chain over isomeric complex with ligand connected to Ni by C^2 atom of ethane chain.[6,20–22] The proposed route of **2b** activation agrees well with the formation of dimer **7** (detected by GC-MS) upon heating **2b** in xylene at 150 °C. Attempts to isolate compound **7** were unsuccessful due to its low stability.[23]

In conclusion, high efficiency of readily available complexes (NHC)$NiCp_2$ as a new class of thermally activated Ni/NHC precatalysts for alkene hydroheteroarylation was demonstrated.



Scheme 3

The main benefits of these precatalysts over previously reported Ni^{II} and Ni^0 ones are the needlessness of using special Ni^{II} to Ni^0 reductants for precatalyst activation, easy handling and storage, and simplification of synthetic procedures.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2024.01.020.

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