European Journal of Inorganic Chemistry

EurJIC
European Journal of Inorganic Chemistry

Chemistry Europe
European Chemical Societies Publishing

CONCEPT OPEN ACCESS

Recent Developments in the Field of Air-Stable Nickel(0) Precatalysts for Cross-Coupling Reactions

Franziska Flecken | Schirin Hanf

Karlsruhe Institute of Technology, Institute for Inorganic Chemistry, Karlsruhe, Germany

Correspondence: Schirin Hanf (schirin.hanf@kit.edu)

Received: 29 October 2025 | **Revised:** 18 December 2025 | **Accepted:** 19 December 2025

Keywords: cross-coupling reactions | nickel catalyst | nickel(0) precatalysts | palladium alternatives

ABSTRACT

The development of bench-stable Ni(0) precatalysts marks a significant turning point in nickel catalysis, offering a practical path beyond the long-standing dependence on air-sensitive Ni sources, such as [Ni(COD)$_2$] (COD = cycloocta-1,5-diene). These next-generation complexes provide direct access to the catalytically active Ni(0) oxidation state, while remaining stable to air and moisture. This simplifies their handling and expands their potential for both academic and industrial applications. In this context, two main synthetic strategies dominate: ligand exchange from [Ni(COD)$_2$] and reduction of Ni(II) salts using chemical or electrochemical methods. The success of bench-stable Ni(0) complexes relies on a targeted ligand design, employing strong π-acceptors and donors, such as electron-deficient dienes, carbenes, and fluorophosphines, to balance catalyst stability with a high catalytic activity. At the same time, the ligand environment must allow a facile exchange, without the released ligand inhibiting the metal centre through re-coordination. Beyond their practical advantages, these systems are compatible with high-throughput and data-driven discoveries, accelerating the development of C–C and C–heteroatom cross-coupling reactions. As nickel catalysis continues, bench-stable Ni(0) systems are thought to open up a new generation of sustainable and scalable homogeneous catalysts for many organic transformations.

1 | Introduction

Nickel catalysis has gained significant attention in recent decades as a cost-effective and mechanistically versatile alternative to palladium-based systems [1]. While palladium has long dominated cross-coupling chemistry, due to its exceptional activity, selectivity, and well-understood two-electron redox behaviour [2, 3], the growing demand for sustainable and earth-abundant catalysts has shifted focus towards first-row transition metals, particularly nickel. Despite remarkable progress, Ni-based catalysts still lag behind Pd in terms of reliability and operational robustness [4]. Comparable yields and selectivities across certain substrate classes often require higher reaction temperatures, increased catalyst loadings, expensive additives, or extended reaction times [5]. Also many nickel salts and compounds exhibit significant toxicity, and certain species are recognized as carcinogenic when inhaled. Nevertheless, nickel's high natural abundance, roughly 100-fold greater than that of palladium [6], and its substantially lower cost make it an attractive choice for large-scale and industrial applications, where economic considerations are critical.

In contrast to palladium, which is typically encountered as low-spin, diamagnetic Pd(0), Pd(II), or Pd(IV) species during catalysis, nickel accesses a broader range of oxidation states from Ni(0) to Ni(IV) [7] and more frequently adopts open-shell electronic configurations, such as Ni(I) and Ni(III). This tendency is commonly linked to nickel's higher d-electron pairing energy relative to palladium, which makes unpaired-electron configurations comparatively favourable. This finding is consistent with nickel's more compact valence orbitals and the increased repulsion associated with electron pairing [8]. For instance, the one electron reduction of tetrahedral Ni(II) can be comparatively facile relative to square-planar Pd(II), thereby enabling pathways that proceed via radical intermediates alongside the conventional two-electron oxidative addition [9]. In general, nickel undergoes oxidative addition more readily, due to its lower reduction potential, smaller size, and lower electronegativity [10] in comparison to Pd, and shows a lower tendency for β-hydride elimination in alkyl–nickel intermediates. These features allow the activation of challenging or inert substrates, such as aryl chlorides and alkyl halides, which often resist oxidative addition to Pd(0) [11–17].

However, the high oxidative sensitivity of Ni(0) species, which typically serve as entry points and key intermediates in catalytic Ni(II)/Ni(0) cycles, remains a major challenge. Ni(0) complexes are readily oxidised by common oxidants, such as molecular oxygen [18], prompting the widespread use of air-stable Ni(II) precatalysts. These are typically reduced in situ by strong reductants, including Zn [19], KC_8 [20], or $NaBH_4$ [21], to generate the active Ni(0) species (Figure 1). Also the in situ electroreductive synthesis of nickel(0) complexes starting from $[Ni(acac)_2]$ (acac = acetylacetonate) has been reported [22]. While the reduction is an effective approach in many cases, such reductive reaction conditions can induce catalyst degradation and undesired side reactions, which limits the scope, controllability and reproducibility of the catalytic reaction [23]. To address this, modular Ni(II) precatalysts, such as [(TMEDA)Ni(*o*-tolyl)Cl], (TMEDA = tetramethylethylenediamine) have been developed. The lability of TMEDA in such complexes facilitates substitution by diverse ligands, including mono- and bidentate phosphines, diimines, and *N*-heterocyclic carbenes [24].

To circumvent the complexities of an in situ reduction, direct Ni(0) sources are highly desirable. A key milestone was Wilke's 1960 discovery of the 18-electron olefin complex $[Ni(COD)_2]$ (COD = cycloocta-1,5-diene, Figure 1), first reported at the Hauptversammlung der Gesellschaft Deutscher Chemiker in Stuttgart [25]. This compound became a cornerstone reagent in organonickel chemistry [26, 27] and remains the standard Ni(0) source, serving as an effective precatalyst with a wide range of ligands, including phosphines [28, 29] and *N*-heterocyclic carbenes (NHCs) [30, 31]. However, $[Ni(COD)_2]$ remains highly sensitive to air, light, and temperature, and the liberated COD ligands can inhibit catalysis, complicating handling and scale-up [18, 32]. These limitations, together with its relatively high cost, have motivated the search for new Ni(0) precursors and ligand frameworks that combine stability, activity, and controlled activation, while unlocking previously inaccessible reactivity.

An innovative approach by Garg and coworkers encapsulated $[Ni(COD)_2]$ in paraffin capsules containing auxiliary ligands, which melt under reaction conditions to release the active $[Ni(COD)_2]$/L (L = ligand) species. This strategy enables diverse coupling reactions, including esterification, Suzuki–Miyaura and Negishi couplings, under ambient conditions without the need for stringent air- and moisture-free synthesis techniques [33, 34]. Beyond such encapsulation, the targeted ligand design has emerged as a central concept to enhance the stability of Ni(0) complexes by replacing either one or both cyclooctadiene ligands. Hereby, the tailoring of the electronic and steric properties enables the stabilisation of reactive intermediates, modulation of catalytic pathways, and suppression of undesired side reactions. Advances in this field have allowed nickel catalysts to rival or even surpass palladium systems in several (novel) catalytic transformations, providing more sustainable and economically viable catalytic alternatives. The resulting methodologies now span polymerisation, cross-coupling, carbonylation, reductive coupling, C—H activation, and hydrogenation reactions [11].

Ultimately, the development of accessible and well-defined Ni(0) sources that balance stability, cost, and reactivity, while ensuring precise reaction control, remains a central challenge in advancing nickel catalysis. Effective systems must not only be air-stable and easy to handle but also enable the controlled ligand dissociation under catalytic reaction conditions to provide open sites for substrate binding, while avoiding re-coordination of the displaced ligand, a well-documented issue for $[Ni(COD)_2]$. Key developments in this area, particularly those focused on cross-coupling applications, will be discussed in this Concept Article.

2 | Design Principles of Air-Stable Ni(0) Precatalysts

Air-stable Ni(0) complexes are stabilised by carefully designed ligands that combine kinetic protection with sufficient lability to enable catalytic turnover in cross-coupling reactions. Common ligand classes include electron-deficient olefins, quinones, phosphines, and *N*-heterocyclic carbenes, alongside more recently developed or 'exotic' ligand systems. These ligands fulfil several critical functions:

- Shielding the Ni(0) centre from oxygen and moisture: bulky or electron-deficient ligands provide steric and/or electronic protection, allowing complexes to be handled under ambient conditions.
- Modulating the electronic properties of nickel: ligands, such as NHCs, phosphines, and electron-deficient olefins fine-tune the electron density at the metal centre, thereby controlling reactivity and selectivity.

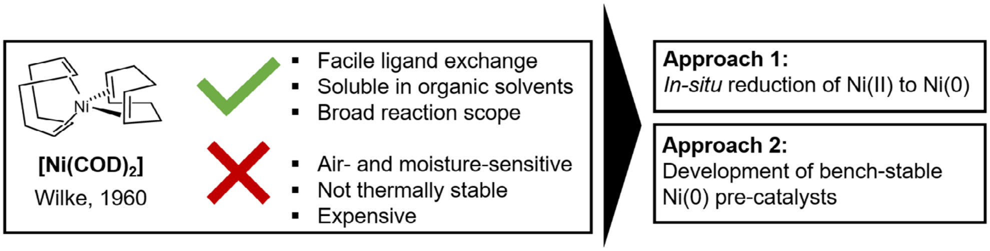


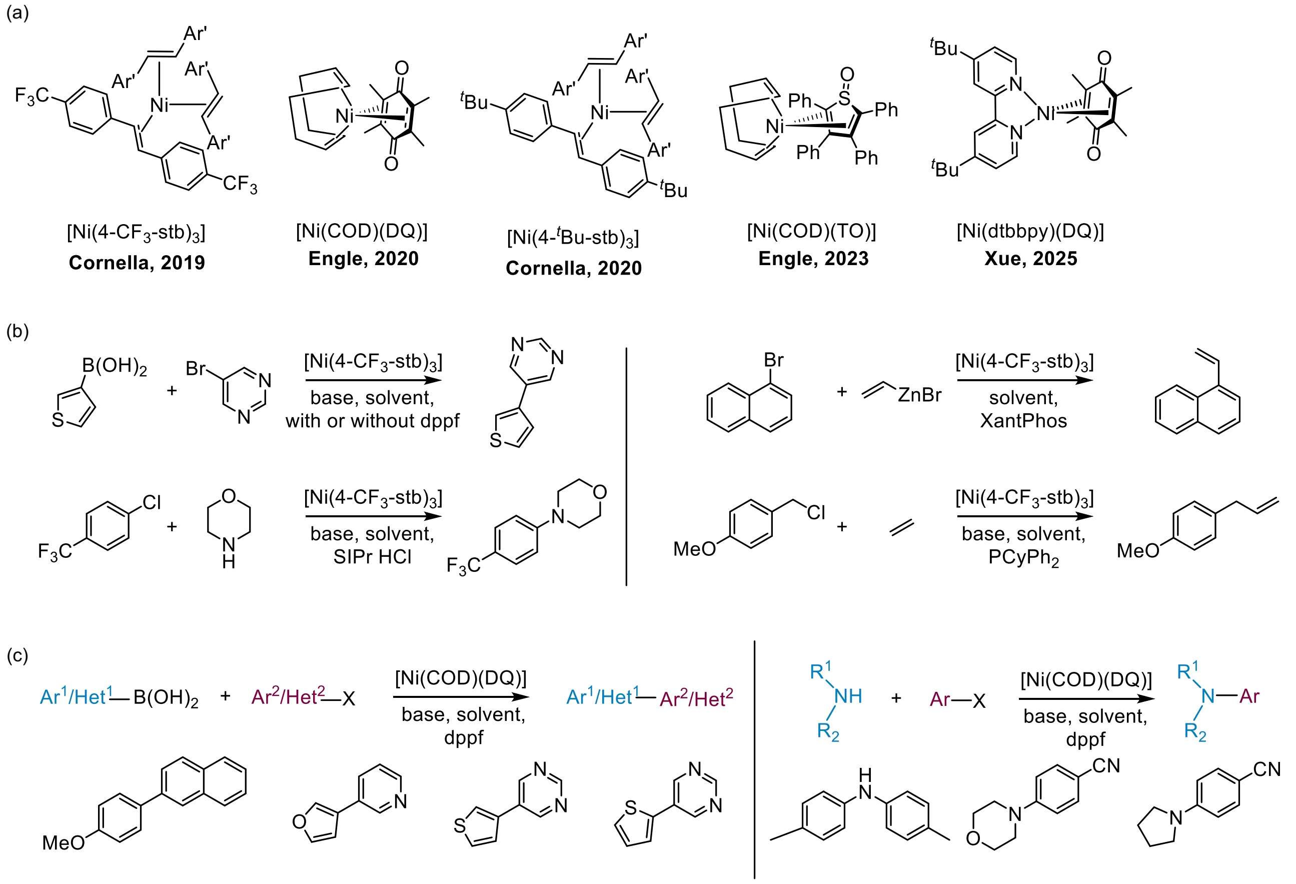
FIGURE 1 | To circumvent the use of air-sensitive $[Ni(COD)_2]$ as a precatalyst in catalytic cross-coupling reactions, alternative strategies have been developed. These include the in situ reduction of Ni(II) complexes or salts in the presence of suitable ligands, as well as the application of bench-stable Ni(0) precatalysts. This concept article focuses on the latter approach, whereby a targeted ligand design is central for tuning catalyst stability and catalytic selectivity as well as activity.

- Facilitating ligand exchange to generate the active catalyst: the appropriate lability of stabilising ligands is essential for the efficient catalyst activation. For instance, electron-deficient alkenes or TMEDA can be readily displaced to allow coordination of catalytically relevant donor ligands or substrates.
- Preventing inhibition by liberated ligands: once displaced, the original stabilising ligand must not re-coordinate or block the active site, as strongly binding or nonlabile liberated ligands can inhibit catalysis by occupying active sites and reducing turnover frequencies
- Enabling modular optimisation of precatalyst performance: the modularity of these ligand frameworks, for example through a systematic exchange of functional groups within the ligand, allows the tuning of stability, activity, and substrate scope across different catalytic transformations.
- Ensure sufficient stability of the molecular species: the agglomeration of the Ni(0) species leading to the formation of metal nanoparticles has to be avoided.

Recent advances have delivered air-stable Ni(0) complexes that are both robust and tuneable, designed to minimise ligand or product inhibition, while supporting a broad range of cross-coupling and other catalytic transformations under operationally simple reaction conditions.

3 | Nickel(0) Complexes with Electron-Deficient Olefins

Remarkable efforts in the field of air stable Ni(0) precatalysts come from Cornella and coworkers, who developed a family of 16-electron, stilbene-based complexes [Ni(4-R-stb)$_3$] (stb = tris(stilbene)), which can be handled under ambient conditions. In 2019 Cornella first reported the synthesis and catalytic activity of a unique 16-electron Ni(0)–olefin complex, namely [Ni(4-CF$_3$-stb)$_3$] (Scheme 1) [35]. The *p*-CF$_3$-stilbene ligands of the complex render the nickel centre remarkably stable under aerobic conditions and contribute to the bench stability. In contrast, the use of unsubstituted stilbene ligands resulted in complex decomposition, due to insufficient steric protection and weaker π* backbonding. [Ni(4-CF$_3$-stb)$_3$] was found to undergo ligand exchange with common donors, such as diamines, phosphines, and NHCs to afford well-defined Ni(0)–L species. When combined with auxiliary ligands, [Ni(4-CF$_3$-stb)$_3$] showed superior catalytic performance relative to [Ni(COD)$_2$] in heteroaryl Suzuki couplings, C—H activation, Buchwald–Hartwig C—N coupling, C—O arylation of acetals, hydroarylations, and C–SMe reduction with silanes (Scheme 1b) [35]. Only recently, Cornella et al. have applied [Ni(4-CF$_3$-stb)$_3$] as catalyst without the addition of any ligands for the heteroaryl–heteroaryl Suzuki Miyaura cross-coupling reaction under mild reaction conditions. This ‘naked nickel’ catalysed transformation gives access to a broad scope of heterobiaryl compounds with multiple Lewis basic heteroatoms [36]. In 2020, the Cornella group reported



SCHEME 1 | (a) Development of air-stable Ni(0) complexes with electron-deficient olefins. DQ = duroquinone, stb = *trans*-stilbene, TO = thiophene oxide. (b) Selected catalytic reactions reported by Cornella [35] and (c) selected catalytic reactions reported by Engle [39].

$[Ni(4\text{-}^tBu\text{-}stb)_3]$ as second-generation catalyst, which exhibited faster reaction kinetics and broader substrate scope, outperforming its CF_3 analogue in multiple Ni-catalysed transformations (Scheme 1). This work underlined the remarkable influence of the substituents at the *para* position of the stilbene unit on the compound's thermal stability, oxidation behaviour, and degradation in solution [37]. $[Ni(4\text{-}^tBustb)_3]$ can also be employed as 'naked nickel' catalyst, without any additional ligands, for C—N bond formation reactions between (hetero) aryl bromides and N-based nucleophiles [38].

Contributions to the development of novel and stable Ni(0) sources have also come from Engle and coworkers, who investigated the replacement of COD ligands in $[Ni(COD)_2]$ with olefins or cyclic dienes bearing electron-withdrawing groups in early 2020 (Scheme 1) [39]. The role of the electron-deficient olefin is hereby twofold. First, during the reductive elimination transition state, the negative charge that forms on the metal centre can be delocalised into the low-lying LUMO (lowest unoccupied molecular orbital) of the olefin. Second, such ligands alter the coordination environment of nickel, allowing access to five-coordinate intermediates that facilitate a facile reductive elimination [40]. Many of these electron-deficient olefins are intentionally sterically encumbered to promote their dissociation and generate vacant coordination sites on the metal centre. In this context, a notable example is [Ni(COD)(DQ)] (DQ = duroquinone), originally reported by Schrauzer in 1962 [41], and later revisited by Engle and coworkers as a robust, air-, moisture-, and bench-stable 18-electron Ni(0) precatalyst. The complex features a tetrahedral coordination geometry with orthogonal COD and DQ ligands and exhibits remarkable thermal stability both in the solid state and in solution. [Ni(COD)(DQ)] can undergo facile in situ ligand exchange with phosphines, diamines, or *N*-heterocyclic carbenes, and has demonstrated broad catalytic utility in catalytic reactions, such as aryl halide borylation, C—H activation/alkyne annulation, directed hydroarylation of unactivated alkenes, and decarboxylative cycloaddition to quinazolinediones (Scheme 1c) [39]. Engle and coworkers expanded this concept into a modular ligand toolkit, introducing quinones, cyclopentadienones, thiophene-S-oxides, and fulvenes as stabilising ligands, which all resulted in bench-stable Ni(0) complexes [42]. A comprehensive review of these developments was published by Engle in 2024 [43].

Xue and coworkers further advanced this field by replacing COD with 4,4′-di-tert-butyl-2,2′-bipyridine (dtbbpy) to afford [Ni(dtbbpy)(DQ)], which was found to exhibit distinctive photophysical properties. Under 620–630 nm light irradiation, it efficiently catalysed the etherification and amination of aryl bromides, acting simultaneously as a photocatalyst and as active metal-based catalyst [44].

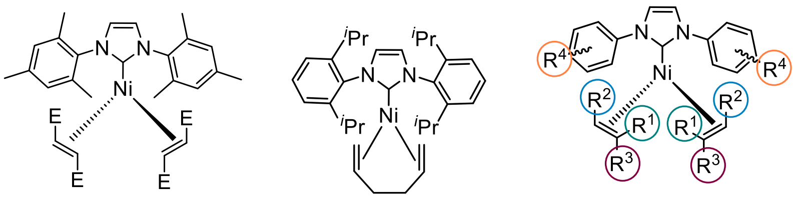
4 | Ni(0) Complexes with *N*-Heterocyclic Carbenes

Beyond the extensive development of Ni(0) precatalysts stabilised by electron-deficient olefins, *N*-heterocyclic carbenes have emerged as another important class of stabilising ligands (Scheme 2). Whereas Ni(0)–NHC catalysts were traditionally generated in situ from $[Ni(COD)_2]$, recent efforts have focused on the isolation of discrete, well-defined Ni(0)-NHC complexes. Early attempts to synthesise bis(NHC) complexes of the type $[Ni(NHC)_2]$ revealed that these species were often too stable for efficient catalytic turnover in cross-coupling reactions, as the strongly donating NHC ligands occupied all available coordination sites, therefore preventing substrate binding [7]. To address this limitation, mixed-ligand complexes of the general form $[Ni(NHC)L_n]$, featuring a labile coligand (L = phosphine, olefin, isonitrile, or CO) were developed. These auxiliary ligands provide kinetic stabilisation under ambient conditions, while allowing facile ligand dissociation during catalysis under reaction conditions [45].

For example, Ni(0)–NHC–(1,5-hexadiene) complexes were shown to undergo oxidative addition with allyl chloride derivatives to form (η^3-allyl)Ni–NHC intermediates, potentially serving as entry points to Ni(0)/Ni(II) catalytic cycles [46]. The concept of NHC–olefin-stabilised Ni(0) species was subsequently expanded to systems bearing a single NHC and two dimethyl fumarate (DMFU) ligands by Cavell and coworkers. These complexes exhibited exceptional long-term stability, showing negligible degradation even after several months [47].

In 2018, Montgomery and coworkers advanced this area by introducing a family of Ni(0)–NHC precatalysts stabilised by electron-withdrawing alkenes. Through careful pairing of the carbene ligand with fumarate or acrylate coligands, they achieved air-stable Ni(0) complexes whose catalytic activity could be tuned via modification of the olefin component. These systems demonstrated excellent performance in reductive couplings of aldehydes and alkynes, as well as *N*-arylation reactions of amines, underscoring the importance of ligand cooperativity in controlling both stability and reactivity [48].

Beside NHC-based Ni(0) complexes, also cyclic (alkyl)(amino) carbenes (CAACs) have been considered as ligands for homogeneous



Cavell, 2006
E = COOMe

Hazari, 2012

Montgomery, 2018
R^1 = H, CH_3; R^2 = H; R^3 = CO_2Me, CO_2Et, $CO_2{}^iPr$, $CO_2{}^iBu$, $CO_2{}^tBu$;
R^4 = Me, Ar

SCHEME 2 | Air-stable Ni(0) precatalysts incorporating *N*-heterocyclic carbene ligands. The systems developed my Montgomery show a highly modular character and can be tuned not only via the NHC ligand but also via the coordinating olefins.

transition metal catalysts [49]. In the field of nickel, [Ni(CAAC)$_2$Cl$_2$] was for example reduced to [Ni(CAAC)$_2$] and employed as catalysts for the homocoupling of various unactivated aryl chlorides/fluorides. Although this is a robust catalyst, the complex had to be handled under inert conditions [50]. Also, [Ni(MeBICAAC)$_2$] (BICAAC = bicyclic (alkyl)(amino)carbenes) has been reported as catalyst for Negishi cross-coupling reactions, but again the complex had to be handled under inert conditions [51].

5 | Ni(0) Complexes with Phosphites

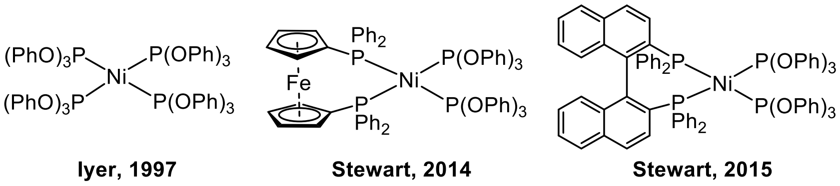
In the search for air-stable Ni(0) catalysts, nickel phosphite complexes have emerged as an important class of systems over the past two or three decades (Scheme 3). As early as 1997, complexes such as [Ni(P(OPh)$_3$)$_4$] and [Ni(P(OEt)$_3$)$_4$] were shown to catalyse the Heck-type coupling of aryl and vinyl halides with olefins and alkynes [52]. Building on these pioneering studies, Stewart and coworkers reported the synthesis of [Ni(dppf)(P(OPh)$_3$)$_2$] (dppf = (ferrocene-1,1′-diyl)bis(diphenylphosphine)) via the reaction of nickel tetrakis(triphenyl phosphite) with dppf. This complex exhibited excellent catalytic activity in C—N bond-forming amination reactions between aryl chlorides and various anilines or alkylamines [53].

To overcome the low yields typically obtained with less reactive primary alkylamines, the group later developed [Ni(BINAP)(P(OPh)$_3$)$_2$] (BINAP = ([1,1′-binaphthalene]−2,2-diyl)bis(diphenylphosphine)) a complex notable for both, its exceptional air stability and its ability to couple primary alkylamines in good to excellent yields. The enhanced reactivity of this BINAP-based system was attributed to its P–Ni–P bite angle of ≈94.5°, which induces geometric strain and thereby promotes the partial dissociation of the BINAP ligand, generating the catalytically active bisphosphite Ni(0) species. Despite these advantages, a key limitation of this system lies in its dependence on strong bases, which constrains its applicability to substrates lacking base-sensitive functional groups [54].

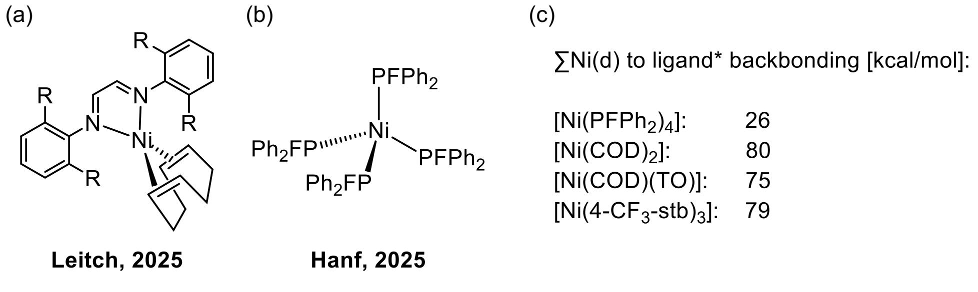
6 | Nickel(0) Complexes Stabilised by Other Ligands

Recent developments in nickel catalysis have expanded beyond traditional olefins, *N*-heterocyclic carbenes, and phosphite ligand systems to explore a broader range of ligand frameworks (Scheme 4). Notably, the successful stabilisation of Pd(0) catalysts with diazabutadiene (DAB) ligands [55] has inspired parallel innovations in Ni(0) chemistry. Building on this concept, *N,N'*-bis(2,6-dimethylphenyl)diazabutadiene (DMPDAB) and its bulkier analogue *N,N'*-bis(2,6-diisopropylphenyl)diazabutadiene (DIPPDAB) were combined with [Ni(COD)$_2$] to afford the complexes [Ni(DMPDAB)(COD)] and [Ni(DIPPDAB)(COD)]. The primary motivation behind these studies was to generate soluble, air-stable Ni(0) precursors that can be readily deployed in in situ catalyst formation under high-throughput experimentation (HTE) conditions. These complexes excel in this role: when paired with phosphine coligands such as dppf, CyJohnPhos ((2-biphenylyl)-dicyclohexylphosphine), PCy$_3$, or DPEPhos (bis[(2-diphenylphosphino)phenyl] ether), they deliver robust catalytic performance in Suzuki–Miyaura and C—N coupling reactions. Their combination of air-stability, solubility, and compatibility across solvent systems has made them powerful tools for accelerating HTE workflows and catalyst discovery pipelines [56].

A conceptually distinct yet equally impactful innovation involves Ni(0) fluorophosphine complexes, exemplified by [Ni(PFPh$_2$)$_4$] [57]. This complex presents a new candidate of air- and moisture-stable precatalysts, synthesised through a one-pot in situ reduction-fluorination process [58] that stabilises the otherwise labile fluorophosphine ligands. Thus far, only a handful of fluorophosphine complexes have demonstrated sustained stability in solution, typically achieved through sterically demanding or strongly electron-withdrawing substituents at the phosphorus centre, like ^{t}Bu or CF$_3$ [59–61]. The unique balance of strong π-acceptor and σ-donor properties imparts exceptional electronic stabilisation to the Ni(0) centre in [Ni(PFPh$_2$)$_4$], resulting in unprecedented bench-stability without compromising catalytic activity. This



SCHEME 3 | Development of air-stable phosphite-based nickel(0) precatalysts applied in C—C and C—N cross coupling reactions.



∑Ni(d) to ligand* backbonding [kcal/mol]:

[Ni(PFPh$_2$)$_4$]:	26
[Ni(COD)$_2$]:	80
[Ni(COD)(TO)]:	75
[Ni(4-CF$_3$-stb)$_3$]:	79

SCHEME 4 | Recent developments have focused on other ligand sets beyond electron-deficient olefins, *N*-heterocyclic carbenes and phosphites, for example (a) diazabutadienes (R = CH$_3$, ^{i}Pr) and (b) fluorophosphines. (c) The sum of the Ni(d) to ligand* backbonding, obtained from second order perturbation analysis, is shown. Numbers adapted from [57]. TO = 2,3,4,5-tetraphenylthiophene-1-oxide.

becomes also obvious from the electron back-donation from the Ni d-orbitals to the ligand* orbitals and underlines the unique role also in comparison with complexes with electron-deficient olefins (Scheme 4) [57]. When combined with ancillary ligands, such as dppf, [Ni(PFPh$_2$)$_4$] exhibits remarkable efficiency across diverse cross-coupling reactions, including Suzuki–Miyaura, Kumada–Tamao–Corriu, and Buchwald–Hartwig aminations, often outperforming the conventional Ni(0) source [Ni(COD)$_2$]. This superior reactivity is further enhanced by the photolabile nature of the fluorophosphine ligands, whose UV-induced decomposition mitigates catalyst inhibition.

7 | Bonding and Stability

To enable the rational design of Ni(0) (pre)catalysts in organic and organometallic chemistry, it is essential to understand how the bonding situation controls both reactivity and stability. This is particularly evident because many Ni(0) complexes undergo rapid ligand exchange reactions in solution, however, their robustness towards air and moisture differs dramatically. For example, both [Ni(COD)$_2$] and [Ni(4-CF$_3$-stb)$_3$] complexes show facile olefin exchange, or more precisely partial olefin dissociation, in solution, however, [Ni(COD) $_2$] is highly air- and moisture-sensitive, whereas [Ni(4-CF$_3$-stb)$_3$] can be handled under ambient conditions.

These contrasting properties and their underlying origins were analysed indetail by Mondal et al. in 2022 using (EDA-NOCV) energy decomposition analysis-natural orbitals for chemical valence calculations [62]. EDA-NOCV is particularly well suited for this purpose because it provides a chemically intuitive bonding model at the equilibrium geometry [63, 64]. Their calculations indicate that the Ni–olefin interaction in [Ni(COD)$_2$] is largely electrostatic, whereas the replacement of one COD by one DQ ligand in [Ni(COD)(DQ)] increases the covalency of the interaction. For [Ni(stb)$_3$], the electrostatic and orbital terms contribute equally, and importantly, the *para*-CF$_3$ substitution on the stilbene ligands does not substantially change the intrinsic nature of the Ni(0)–olefin interaction [62]. Notably, Mondal et al. also found that the Ni–COD dissociation energy in [Ni(COD)$_2$] is lower than the Ni–DQ dissociation energy in [Ni(COD)(DQ)]. In line with this, the π-backdonation is predicted to be ~16% higher in [Ni(COD)(DQ)] than in [Ni(COD)$_2$], which reflects the electron-withdrawing, π-accepting character of DQ [62]. Closely related conclusions were reported by Hanf et al. for Engle's [Ni(COD)L] complex (L = 2,3,4,5-tetraphenylthiophene-1-oxide) [57].

Beyond bond metrics, Mondal et al. highlighted that the highest occupied molecular orbital electron density in [Ni(COD)(DQ)] is largely ligand-centred, whereas in [Ni(COD)$_2$] it is more metal-centred, which may increase the susceptibility of the latter towards reactions with air and water [62]. Overall, these studies highlight that the nature of the metal–ligand interaction, the localisation of the frontier orbitals, and the extent of π-backdonation are key parameters that govern not only the reactivity of Ni(0) complexes, but also their stability under ambient conditions.

8 | Summary and Outlook

The development of bench-stable Ni(0) precatalysts has advanced significantly towards systems that are both operationally simple and highly reactive under ambient reaction conditions. While traditional nickel sources, like [Ni(COD)$_2$], remain widely used, their sensitivity to air and moisture requires specialised handling under inert reaction conditions, and high costs, which challenges the industrial adoption. Recent progress has therefore focused on air-stable Ni(0) complexes that maintain catalytic efficiency across a wide range of organic transformations. Current research reveals that no single Ni(0) system is universally applicable and ligand-substrate matching and activation conditions remain crucial. Mechanistic challenges, such as off-cycle Ni(I) species and competing pathways, complicate the catalyst optimisation but also highlight opportunities for the design of novel Ni(0) sources and their reactivities. Promising ligand frameworks include electron-deficient dienes, simple olefins, *N*-heterocyclic carbenes, phosphites, diazabutadienes and fluorophosphines, which balance the stability of the Ni(0) complex with its reactivity in cross-coupling reactions (Table 1).

TABLE 1 | Representative examples of air stable Ni(0)-based precatalysts for cross-coupling reactions.

Ni,0 source	Ligand	Representative cross-coupling application	References
[Ni(4-CF$_3$-stb)$_3$]	Electron-deficient olefin	C—C and C—N cross coupling, oxidative cyclisation, C—H activation	[35, 36]
[Ni(4-^{t}Bu-stb)$_3$]	Electron-deficient olefin	C—C and C—N cross coupling	[37, 38]
[Ni(COD)(DQ)]	Electron-deficient olefin	C—C and C—N cross coupling, borylation, C—H activation	[39, 42]
[Ni(NHC)(bis(acrylate/fumarate))]	*N*-heterocyclic carbene	C—N cross coupling, reductive coupling of aldehydes and alkenes	[48]
[Ni(dppf)(P(OPh)$_3$)$_2$]	Phosphite	C—N cross coupling	[53]
[Ni(BINAP)(P(OPh)$_3$)$_2$]	Phosphite	C—N cross coupling	[54]
[Ni(DMPDAB)(COD)]	Diazabutadiene	C—C and C—N cross coupling	[56]
[Ni(PFPh$_2$)$_4$]	Fluorophosphine	C—C and C—N cross coupling	[57]

Abbreviations: BINAP = ([1,1′-binaphthalene]–2,2-diyl)bis(diphenylphosphine), COD = cycloocta-1,5-diene, DMPDAB = *N*,*N*′-bis(2,6-dimethylphenyl)diazabutadiene, dppf = (ferrocene-1,1′-diyl)bis(diphenylphosphine), DQ = duroquinone, NHC = *N*-heterocyclic carbene.

The future development of bench-stable Ni(0) precatalysts will increasingly focus on creating universal, robust, and tuneable systems that operate under ambient conditions without the need for glovebox handling. One major direction is the rational expansion of ligand architectures to fine-tune reactivity, selectivity, and activation profiles. Hereby, a special focus will be on the modular design of ligands to enable a facile modification potential. Another particularly promising avenue is the integration of high-throughput experimentation and machine learning to accelerate the (pre)catalyst discovery. By systematically screening combinations of Ni(0) sources, ancillary ligands, substrates, and reaction conditions, HTE platforms can rapidly generate large datasets that capture structure–activity relationships. Machine learning algorithms can then analyse these datasets to identify predictive patterns and optimal parameter spaces, guiding the rational design of new Ni(0) systems. Such data-driven approaches will not only enhance catalyst performances but also improve reproducibility and scalability. Through these strategies Ni(0) precatalysts that are cost-effective, recyclable, and compatible with sustainable synthesis paradigms, will be developed. These efforts will help to integrate nickel catalysis seamlessly into industrial and automated synthesis workflows, ensuring that nickel continues to evolve as a complementary and essential element of modern catalysis, rather than merely a palladium substitute.

Acknowledgments

The authors thank the Stiftung der Deutschen Wirtschaft for a doctoral scholarship for F. F.

Open Access funding enabled and organized by Projekt DEAL.

Funding

The authors has nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. V. M. Chernyshev and V. P. Ananikov, “Nickel and Palladium Catalysis: Stronger Demand than Ever,” *ACS Catalysis* 12 (2022): 1180–1200.

2. C. C. C. Johansson Seechurn, M. O. Kitching, T. J. Colacot, and V. Snieckus, “Palladium-Catalyzed Cross-Coupling: A Historical Contextual Perspective to the 2010 Nobel Prize,” *Angewandte Chemie, International Edition* 51 (2012): 5062–5085.

3. A. Biffis, P. Centomo, A. Del Zotto, and M. Zecca, “Pd Metal Catalysts for Cross-Couplings and Related Reactions in the 21st Century: A Critical Review,” *Chemical Reviews* 118 (2018): 2249–2295.

4. Y. Tamaru, ed. Modern Organonickel Chemistry (WILEY-VCH, 2005).

5. N. Hazari, P. R. Melvin, and M. M. Beromi, “Well-Defined Nickel and Palladium Precatalysts for Cross-Coupling,” *Nature Reviews Chemistry* 1 (2017): 1–16.

6. S. Teng, P. Liang, and J. S. Zhou, “New Reactivity of Late 3d Transition Metal Complexes in Catalytic Reactions of Alkynes,” *Chemical Society Reviews* 54 (2025): 2664–2692.

7. A. Khamrai, S. Ghosh, and V. Ganesh, “Advances in Accessing Rare Oxidation States of Nickel for Catalytic Innovation,” *Chemical Communications* 61 (2025): 3037–3060.

8. J. Diccianni, Q. Lin, and T. Diao, “Mechanisms of Nickel-Catalyzed Coupling Reactions and Applications in Alkene Functionalization,” *Accounts of Chemical Research* 53 (2020): 906–919.

9. J. B. Diccianni, J. Katigbak, C. Hu, and T. Diao, “Mechanistic Characterization of (Xantphos)Ni(I)-Mediated Alkyl Bromide Activation: Oxidative Addition, Electron Transfer, or Halogen-Atom Abstraction,” *Journal of the American Chemical Society* 141 (2019): 1788–1796.

10. J. B. Mann, T. L. Meek, E. T. Knight, J. F. Capitani, and L. C. Allen, “Configuration Energies of the d-Block Elements,” *Journal of the American Chemical Society* 122 (2000): 5132–5137.

11. S. Z. Tasker, E. A. Standley, and T. F. Jamison, “Recent Advances in Homogeneous Nickel Catalysis,” *Nature* 509 (2014): 299–309.

12. B. Su, Z. C. Cao, and Z. J. Shi, “Exploration of Earth-Abundant Transition Metals (Fe, Co, and Ni) as Catalysts in Unreactive Chemical Bond Activations,” *Accounts of Chemical Research* 48 (2015): 886–896.

13. V. Ritleng, M. Henrion, and M. J. Chetcuti, “Nickel N-Heterocyclic Carbene-Catalyzed C-Heteroatom Bond Formation, Reduction, and Oxidation: Reactions and Mechanistic Aspects,” *ACS Catalysis* 6 (2016): 890–906.

14. T. B. Boit, A. S. Bulger, J. E. Dander, and N. K. Garg, “Activation of C—O and C—N Bonds Using Non-Precious-Metal Catalysis,” *ACS Catalysis* 10 (2020): 12109–12126.

15. X. Hu, “Nickel-Catalyzed Cross Coupling of Non-Activated Alkyl Halides: A Mechanistic Perspective,” *Chemical Science* 2 (2011): 1867–1886.

16. C. Zhu, H. Yue, J. Jia, and M. Rueping, “Nickel-Catalyzed C-Heteroatom Cross-Coupling Reactions under Mild Conditions via Facilitated Reductive Elimination,” *Angewandte Chemie, International Edition* 60 (2021): 17810–17831.

17. S. Kim, M. J. Goldfogel, M. M. Gilbert, and D. J. Weix, “Nickel-Catalyzed Cross-Electrophile Coupling of Aryl Chlorides with Primary Alkyl Chlorides,” *Journal of the American Chemical Society* 142 (2020): 9902–9907.

18. A. L. Clevenger, R. M. Stolley, J. Aderibigbe, and J. Louie, “Trends in the usage of Bidentate Phosphines as Ligands in Nickel Catalysis,” *Chemical Reviews* 120 (2020): 6124–6196.

19. O. Kühl, P. C. Junk, and E. Hey-Hawkins, “Facile Synthesis and Molecular Structure of [Ni(PPh2NHPh)4],” *Zeitschrift Fur Anorganische Und Allgemeine Chemie* 626 (2000): 1591–1594.

20. J. Mautz and G. Huttner, “Reductive Activation of Tripod Metal Compounds: Preparative Application,” *European Journal of Inorganic Chemistry* 2008 (2008): 1423–1434.

21. T. Tanase, H. Takahata, and Y. Yamamoto, “Zero-Valent group 10 Metal Complexes with a Triphosphine Ligand, [M(dpmp)2], where M=Pt, Pd, Ni, and dpmp = bis(diphenylphosphinomethyl)phenylphosphine,” *Inorganica Chimica Acta* 264 (1997): 5–9.

22. C. Z. Rubel, Y. Cao, T. El-Hayek Ewing, et al., “Electroreductive Synthesis of Nickel(0) Complexes,” *Angewandte Chemie, International Edition* 63 (2024): e202311557.

23. E. Richmond, J. Moran, E. Richmond, and J. Moran, “Recent Advances in Nickel Catalysis Enabled by Stoichiometric Metallic Reducing Agents”*Synthesis (Stuttg)* 50 (2018): 499–513.

24. J. D. Shields, E. E. Gray, and A. G. Doyle, “A Modular, Air-Stable Nickel Precatalyst,” *Organic Letters* 17 (2015): 2166–2169.

25. G. Wilke, “Hauptversammlung der Gesellschaft Deutscher Chemiker,” *Angewandte Chemie* 72 (1960): 565–593.

26. B. Bogdanović, M. Kröner, and G. Wilke, “Übergangsmetallkomplexe, I. Olefin-Komplexe Des Nickels(0,” *Justus Liebigs Annalen Der Chemie* 699 (1966): 1–23.

27. G. Wilke, “Contributions to Organo-Nickel Chemistry,” *Angewandte Chemie, International Edition* 27 (1988): 185–206.

28. D. K. Nielsen and A. G. Doyle, “Cross-Coupling Nickel-Catalyzed Cross-Coupling of Styrenyl Epoxides with Boronic Acids,” *Angewandte Chemie, International Edition* 50 (2011): 6056–6059.

29. S. Ge and J. F. Hartwig, “Nickel-Catalyzed Asymmetric α-Arylation and Heteroarylation of Ketones with Chloroarenes: Effect of Halide on Selectivity, Oxidation State, and Room-Temperature Reactions,” *Journal of the American Chemical Society* 133 (2011): 16330–16333.

30. R. Omar-Amrani, A. Thomas, E. Brenner, R. Schneider, and Y. Fort, “Efficient Nickel-Mediated Intramolecular Amination of Aryl Chlorides,” *Organic Letters* 5 (2003): 2311–2314.

31. T. Shimasaki, M. Tobisu, and N. Chatani, “Nickel-Catalyzed Amination of Aryl Pivalates by the Cleavage of Aryl C—O Bonds,” *Angewandte Chemie, International Edition* 49 (2010): 2929–2932.

32. E. A. Standley and T. F. Jamison, “Simplifying Nickel(0) Catalysis: An Air-Stable Nickel Precatalyst for the Internally Selective Benzylation of Terminal Alkenes,” *Journal of the American Chemical Society* 135 (2013): 1585–1592.

33. J. E. Dander, N. A. Weires, N. K. Garg, and O. Lett, “Benchtop Delivery of Ni(cod)2 using Paraffin Capsules,” *Organic Letters* 18 (2016): 3934–3936.

34. M. M. Mehta, T. B. Boit, J. E. Dander, and N. K. Garg, “Ni-Catalyzed Suzuki-Miyaura Cross-Coupling of Aliphatic Amides on the Benchtop,” *Organic Letters* 22 (2020): 1–5.

35. L. Nattmann, R. Saeb, N. Nöthling, and J. Cornella, “An Air-Stable Binary Ni(0)–olefin Catalyst,” *Nature Catalysis* 3 (2020): 6–13.

36. R. Saeb, B. Roh, and J. Cornella, ““Naked Nickel”-Catalyzed Heteroaryl–Heteroaryl Suzuki–Miyaura Coupling,” *Angewandte Chemie, International Edition* 64 (2025): e202424051.

37. L. Nattmann and J. Cornella, “Ni(4-TBu-Stb)3: A Robust 16-Electron Ni(0) Olefin Complex for Catalysis,” *Organometallics* 39 (2020): 3295–3300.

38. R. Saeb, B. Boulenger, and J. Cornella, ““Naked Nickel”-Catalyzed Amination of Heteroaryl Bromides,” *Organic Letters* 26 (2024): 5933.

39. V. T. Tran, Z. Q. Li, O. Apolinar, et al., “Ni(COD)(DQ): An Air-Stable 18-Electron Nickel(0)–Olefin Precatalyst,” *Angewandte Chemie, International Edition* 59 (2020): 7409–7413.

40. J. B. Johnson, T. Rovis, T. Rovis, and J. B. Johnson, “More than Bystanders: The Effect of Olefins on Transition-Metal-Catalyzed Cross-Coupling Reactions,” *Angewandte Chemie, International Edition* 47 (2008): 840–871.

41. G. N. Schrauzer and H. Thyret, “Neuartige” Sandwich“-Verbindungen Des Nickel(0). Zur Kenntnis von Durochinon-Nickel(0)-Komplexen Mit Cyclisdien Dienen,” *Zeitschrift für Naturforschung B* 17 (1962): 73–76.

42. V. T. Tran, N. Kim, C. Z. Rubel, et al., “Structurally Diverse Bench-Stable Nickel(0) Pre-Catalysts: A Practical Toolkit for In Situ Ligation Protocols,” *Angewandte Chemie, International Edition* 62 (2023): e202211794.

43. C. Z. Rubel, W. J. He, S. R. Wisniewski, and K. M. Engle, “Benchtop Nickel Catalysis Invigorated by Electron-Deficient Diene Ligands,” *Accounts of Chemical Research* 57 (2024): 312–326.

44. J. Li, P. Wang, B. Bai, et al., “Synthesis, Characterization, and Catalytic Activity of Ni(0) (DQ)dtbbpy, an Air-Stable, Bifunctional Red-Light-Sensitive Precatalyst,” *Journal of the American Chemical Society* 147 (2025): 5851–5859.

45. K. Matsubara, Y. Fukahori, T. Inatomi, et al., “Monomeric Three-Coordinate N-Heterocyclic Carbene Nickel(I) Complexes: Synthesis, Structures, and Catalytic Applications in Cross-Coupling Reactions,” *Organometallics* 35 (2016): 3281–3287.

46. J. Wu, J. W. Faller, N. Hazari, and T. J. Schmeier, “Stoichiometric and Catalytic Reactions of Thermally Stable Nickel(0) NHC Complexes,” *Organometallics* 31 (2012): 58.

47. N. D. Clement, K. J. Cavell, and L. L. Ooi, “Zerovalent N-Heterocyclic Carbene Complexes of Palladium and Nickel Dimethyl Fumarate: Synthesis, Structure, and Dynamic Behavior,” *Organometallics* 25 (2006): 4155–4165.

48. A. J. Nett, S. Cañ, Y. Higuchi, et al., “Stable, Well-Defined Nickel(0) Catalysts for Catalytic C–C and C–N Bond Formation,” *ACS Catalysis* 15 (2025): 41.

49. R. K. Singh, T. K. Khan, S. Misra, and A. K. Singh, “CAACs as Efficient Ancillary Ligands for the Synthesis of Robust Catalysts,” *Journal of Organometallic Chemistry* 956 (2021): 122133.

50. K. C. Mondal, P. P. Samuel, Y. Li, et al., “A Catalyst with Two-Coordinate Nickel: Theoretical and Catalytic Studies,” *European Journal of Inorganic Chemistry* 2014 (2014): 818–823.

51. S. K. Thakur, M. Kaur, K. K. Manar, M. Adhikari, A. R. Choudhury, and S. Singh, “Well-Defined Ni(0) and Ni(II) Complexes of Bicyclic (Alkyl)(Amino)Carbene (MeBICAAC): Catalytic Activity and Mechanistic Insights in Negishi Cross-Coupling Reaction,” *Chemistry – A European Journal* 28 (2022): e202202237.

52. S. Iyer, C. Ramesh, and A. Ramani, “Ni(0) Catalyzed Reactions of Aryl and Vinyl Halides with Alkenes and Alkynes,” *Tetrahedron Letters* 38 (1997): 8533–8536.

53. S. S. Kampmann, A. N. Sobolev, G. A. Koutsantonis, and S. G. Stewart, “Stable Nickel(0) Phosphites as Catalysts for C-N Cross-Coupling Reactions,” *Advanced Synthesis & Catalysis* 356 (2014): 1967–1973.

54. S. S. Kampmann, B. W. Skelton, D. A. Wild, G. A. Koutsantonis, and S. G. Stewart, “An Air-Stable Nickel(0) Phosphite Precatalyst for Primary Alkylamine C-N Cross-Coupling Reactions,” *European Journal of Organic Chemistry* 2015 (2015): 5995–6004.

55. J. Huang, M. Isaac, R. Watt, et al., “DMPDAB–Pd–MAH: A Versatile Pd(0) Source for Precatalyst Formation, Reaction Screening, and Preparative-Scale Synthesis,” *ACS Catalysis* 11 (2021): 5636–5646.

56. G. T. Thomas, O. D. Cruise, D. Peel-Smith, N. P. Fernández, C. Killeen, and D. C. Leitch, “Easily Accessible and Solution-Stable Ni(0) Precatalysts for High-Throughput Experimentation,” *Chemistry - A European Journal* 31 (2025): e202403960.

57. F. Flecken, A. Neyyathala, T. Grell, and S. Hanf, “A Bench-Stable Fluorophosphine Nickel(0) Complex and Its Catalytic Application,” *Angewandte Chemie* 64 (2025): e202506271.

58. S. Hanf, T. Grell, J. E. Waters, R. García-Rodríguez, E. Hey-Hawkins, and D. S. Wright, “Facile Synthesis of a Nickel(0) Phosphine Complex at Ambient Temperature,” *Chemical Communications* 56 (2020): 7893–7896.

59. A. M. Miles-Hobbs, P. G. Pringle, J. D. Woollins, and D. Good, “Monofluorophos–Metal Complexes: Ripe for Future Discoveries in Homogeneous Catalysis,” *Molecules* 29 (2024): 2368.

60. N. Fey, M. Garland, J. P. Hopewell, et al., “Stable Fluorophosphines: Predicted and Realized Ligands for Catalysis,” *Angewandte Chemie, International Edition* 51 (2012): 118–122.

61. V. V. Grushin and W. J. Marshall, “The Fluoro Analogue of Wilkinson’s Catalyst and Unexpected Ph-Cl Activation,” *Journal of the American Chemical Society* 126 (2004): 3068–3069.

62. S. M. N. V. T. Gorantla and K. C. Mondal, “The Labile Nature of Air Stable Ni(II)/Ni(0)-Phosphine/Olefin Catalysts/Intermediates: EDA-NOCV Analysis,” *Chemistry – an Asian Journal* 17 (2022): e202200572.

63. M. P. Mitoraj, A. Michalak, and T. Ziegler, “A Combined Charge and Energy Decomposition Scheme for Bond Analysis,” *Journal of Chemical Theory and Computation* 5 (2009): 962–975.

64. L. Zhao, M. Hermann, W. H. E. Schwarz, and G. Frenking, “The Lewis Electron-Pair Bonding Model: Modern Energy Decomposition Analysis,” *Nature Reviews Chemistry* 3 (2019): 48–63.

Biographies

Franziska Flecken studied chemistry at RWTH Aachen University before joining the group of Schirin Hanf at the Karlsruhe Institute of Technology for her doctoral research. She completed her Ph.D. in 2024, focusing on ligand design and 3d-metal-based homogeneous catalysis. Following a short postdoctoral stay at KIT, where she worked on the digitalisation of catalysis as part of the NFDI4Cat, she recently began her industrial career at Wacker.

Schirin Hanf completed her Ph.D. at the University of Cambridge in 2019 in the field of coordination chemistry and homogeneous catalysis. She then joined the high-throughput experimentation company (hte GmbH, BASF SE) in Heidelberg as a postdoctoral researcher in chemical engineering and heterogeneous catalysis. Since 2021, she has been a tenure-track professor at KIT, where she now focuses on the interface of molecular and solid-state catalysis and the digitalisation of catalysis-related research.