

“Naked Nickel”-Catalyzed Amination of Heteroaryl Bromides

Rakan Saeb,^a Bryan Boulenger^a and Josep Cornella^{a*}

^aMax-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, 45470, Mülheim an der Ruhr, Germany

In this article we report that the air-stable “naked nickel” $[\text{Ni}^{(4\text{-}t\text{Bu}^{\text{stb}})_3}]$ is a competent catalyst in thermal C–N bond formation between (hetero)aryl bromides and *N*-based nucleophiles. The catalytic system is characterized by a “naked nickel” complex and Zn, the absence of external light sources, photocatalysts, exogenous ligands, as well as electrical setups. By applying this method, various heteroaryls bearing Lewis-basic heteroatoms can be accommodated and directly aminated with a set of primary and secondary amines.

Introduction

The catalytic formation of C–N bonds between aromatic (pseudo)halides and amines (Buchwald–Hartwig amination) is one of the cornerstone reactions in modern homogeneous catalysis (Fig. 1).¹ This simple but challenging disconnection has dramatically impacted our society: from the synthesis of medicines and crop-protection agents to polymers and functional materials.^{1–2} Mechanistic studies over the years in the initial Pd-catalyzed C–N cross-coupling reaction have established the canonical $\text{Pd}^0/\text{Pd}^{\text{II}}$ catalytic redox cycle (Fig. 1A).^{1b} In the >50 years since its discovery, many iterations of ligands — mainly P-based — have appeared, which improved the reactivity for more challenging amines and aryl halides.^{1b} In recent years, alternatives to canonical Pd catalysis have appeared in the literature, identifying Cu and Ni as one of the most promising alternatives.³ Yet, the mechanistic framework of $\text{M}^0/\text{M}^{\text{II}}$ catalytic cycles based on complex phosphine or NHC ligands still dominated (Fig. 1A).⁴ In 2016, Buchwald and MacMillan provided a new platform that permitted facile C–N bond formation merging photoredox and nickel catalysis (Fig. 1B),⁵ avoiding the design and multi-step synthesis of supporting ligands. Whereas in conventional metal-catalyzed C–N coupling reactions the reductive elimination generally occurs from a M^{II} species,^{4d, 6} in this metallaphotoredox approach the C–N bond is presumably forged from a Ni^{III} intermediate, accessible *via* photocatalysis.^{5,7} Ni-catalyzed electrochemical approaches were also reported, pioneered by Baran, which complemented and even expanded the scope of opportunities for C–N bond formation with Ni (Fig. 1B).⁸ Many subsequent variants followed, and examples refining and improving the conditions with,⁹ or without the use of donating ligands are still at the forefront of the catalysis landscape.^{10, 11} Building up on this new mechanistic paradigm, in 2020, Nocera and co-workers reported a Ni-catalyzed protocol that allowed the formation of C–N bonds between electron-deficient aryl bromides and amines through a proposed $\text{Ni}^{\text{I}}/\text{Ni}^{\text{III}}$ redox process, without the need of light or a photocatalyst (Fig. 1C). Similar to the photoredox processes, no additional ligands on the Ni catalyst were required.¹² However, the proof-of-concept study reported by Nocera and co-workers was applied to simple bromoarenes. Importantly, no examples of heterocycles were reported;¹² this is not surprising, as heteroaryl coordination to the metal center could result in poisoning of the catalyst when no exogenous ligands are present.¹³ We hypothesized that this latter approach could be attractive to practitioners if expanded to accommodate heterocycles and various amines. In 1963, Wilke described Ni^0 -olefin complexes such as the air-sensitive $\text{Ni}(\text{COD})_2$ as “naked nickel” due to the lability of the coordinated olefins.¹⁴ Herein, we report that a robust, air-stable and commercially available “naked nickel” complex $[\text{Ni}^{(4\text{-}t\text{Bu}^{\text{stb}})_3}]$, CAS: 2468315-70-8,¹⁵ developed by our group, is able to catalyze the coupling of heteroaryl bromides with various *N*-based nucleophiles. Interestingly, C–N bonds can be forged without requiring P-, N-, or NHC-based ligands, and without the use of electro- or photochemical setups.

nickel” complex $[\text{Ni}^{(4\text{-}t\text{Bu}^{\text{stb}})_3}]$, CAS: 2468315-70-8,¹⁵ developed by our group, is able to catalyze the coupling of heteroaryl bromides with various *N*-based nucleophiles. Interestingly, C–N bonds can be forged without requiring P-, N-, or NHC-based ligands, and without the use of electro- or photochemical setups.

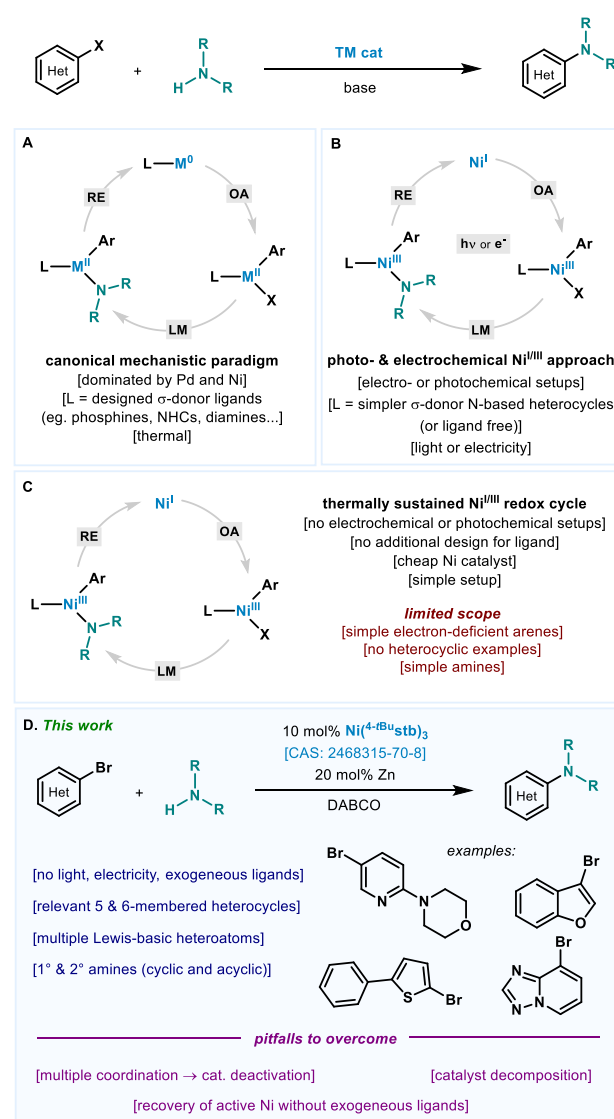
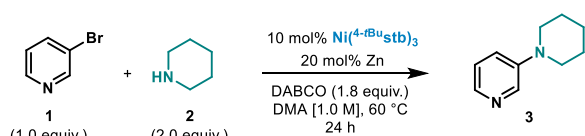


Fig. 1 Transition metal-catalyzed C–N cross-coupling reaction (Buchwald–Hartwig amination). A. Traditional $\text{M}^0/\text{M}^{\text{II}}$ redox cycle; B. emerging Ni-catalyzed photo- and electrochemical strategies via SET; C. Ligand-free, thermal Ni-catalyzed amination; D. This work: a “naked-nickel”-catalyzed amination of heteroaryl bromides.

Results and Discussion

We began to explore the process using 3-bromopyridine (**1**) due to its recalcitrance toward S_NAr reactivity with amines. The reaction of **1** with 2.0 equiv. of piperidine (**2**) in the presence of DABCO (1.8 equiv.), Ni(⁴-^tBu₃stb)₃ (10 mol%), and Zn (20 mol%) in DMA (1 M) at 60 °C resulted in 76% isolated yield of coupling product **3** (Table 1, entry 1). While the yield of **3** was only slightly reduced at 40 °C (Table 1, entry 2), only trace amounts of product were observed at 25 °C (entry 3). Importantly, an aged batch of Ni(⁴-^tBu₃stb)₃ stored in the freezer (−18 °C) under air for ca. 6 months resulted in similar reactivity, highlighting the robustness of the protocol (Table 1, entry 4). High yields could also be obtained with NiBr₂(dme) when handled inside the glovebox (Table 1, entry 5). NiBr₂(bipy)₃, a complex successfully employed in electrocatalytic amination,^{8b} led to no reactivity in our system (Table 1, entry 6). Expectedly, Ni(COD)₂ also afforded **3** in good yields when handling the pre-catalyst under inert atmosphere (Table 1, entry 7). Ni(⁴-CF₃stb)₃ as an alternative air-stable Ni⁰ source, also performed well (Table 1, entry 8). Yet, the utilization of Ni(COD)(DQ) did not result in formation of **3** (Table 1, entry 9).¹⁶ Furthermore, the reaction could be carried out in DMA, which was stored on the benchtop without special precautions (Table 1, entry 10). Control experiments (entry 11 and 12) confirmed the requirement of both Ni and Zn for the C–N coupling to proceed.

Table 1. Optimization of the “naked nickel”-catalyzed coupling of 3-bromopyridine with piperidine.



| entry | deviations from above | yield ^a in % of 3 | entry | deviations from above | yield ^a in % of 3 |
|-------|---|-------------------------------------|-------|---|-------------------------------------|
| 1 | none | 76, (76) ^b | 7 | Ni(COD) ₂ (glovebox) | 73 |
| 2 | 40 °C | 62 | 8 | Ni(⁴ -CF ₃ stb) ₃ | 76 |
| 3 | 25 °C | <5 | 9 | Ni(COD)(DQ) | <1 |
| 4 | old batch of Ni(⁴ - ^t Bu ₃ stb) ₃ ^c | 76 | 10 | DMA stored on benchtop | 77 |
| 5 | NiBr ₂ (dme) (glovebox) | 84 | 11 | No [Ni] | <1 |
| 6 | NiBr ₂ (bipy) ₃ | <1 | 12 | No Zn | 17 |

^a ¹H NMR yield as determined by using 1,3,5-trimethoxybenzene as internal standard.

^b Isolated yield (0.3 mmol scale), ^c 6 months old batch stored at −18 °C under air. ⁴-^tBu₃stb = (*E*)-1,2-bis(4-(*tert*-butyl)phenyl)ethene, dme = dimethoxyethane, bipy = 2,2'-bipyridine, COD = 1,5-cyclooctadiene, ⁴-CF₃stb = (*E*)-1,2-bis(4-(trifluoromethyl)phenyl)ethene, DQ = duroquinone.

With the optimized conditions in hand, we explored the scope of the protocol regarding heteroaryl bromides using piperidine as model nucleophile (Fig. 2). Besides electronically unbiased 3-bromopyridine (**3**), derivatives bearing electron-withdrawing groups (**4** and **5**) or electron-donating substituents (**6**) could be coupled in good yields. Ester functionalities in **4** and **16** remained intact under the reaction conditions. The coupling of 5-bromo-pyrimidine with piperidine delivered product **7** in moderate yield. We could demonstrate that both 3- and 7-bromoquinolines could satisfactorily deliver the desired product in high yields (**8** and **9**). Besides quinolines, fused heteroaromatics such as 3-bromo-1,5-naphthyridine could also be successfully coupled in high yield (**10**). A [5,6] fused heterocycle such as 8-bromo-[1,2,4]triazolo[1,5-*a*]pyridine (**11**) was also amenable for coupling. Electron-rich 5-membered heterocycles such as *N*-Boc

protected 3-bromoindole resulted in the formation of the desired product (**12**) in excellent yield. 3-Bromo-1-tosyl-1*H*-pyrrolo[2,3-*b*]pyridine containing an additional Lewis-basic N-atom could also be efficiently coupled (**13**). Furthermore, benzofuran with bromides at C-3 (**14**) and C-2 (**15**) positions smoothly underwent coupling to form the desired products in good yields. Ethyl 5-bromofuran-2-carboxylate underwent smooth coupling resulting in the formation of **16** in good yield. Finally, 2-bromo-5-phenylthiophene could be coupled with piperidine, giving the desired product (**17**) in moderate yield. Additionally, we were interested in benchmarking our protocol in the coupling of common aryl bromides employed in Ni^I/Ni^{III} catalytic systems.^{5, 8, 10a, c, f, h, j, k, 12} Indeed, aryl bromides containing electron withdrawing substituents such as CF₃, methylsulfone, CN and unprotected carboxamide (**18** – **21**) could be coupled in good to excellent yields thus comparing favorably to state-of-the-art protocols.^{5, 12} Although coupling was observed for 4-bromotoluene, using quinuclidine as base, the yield of **22** remained low; this has also been observed by Nocera and others in the coupling of electron-rich aryl halides.¹⁷

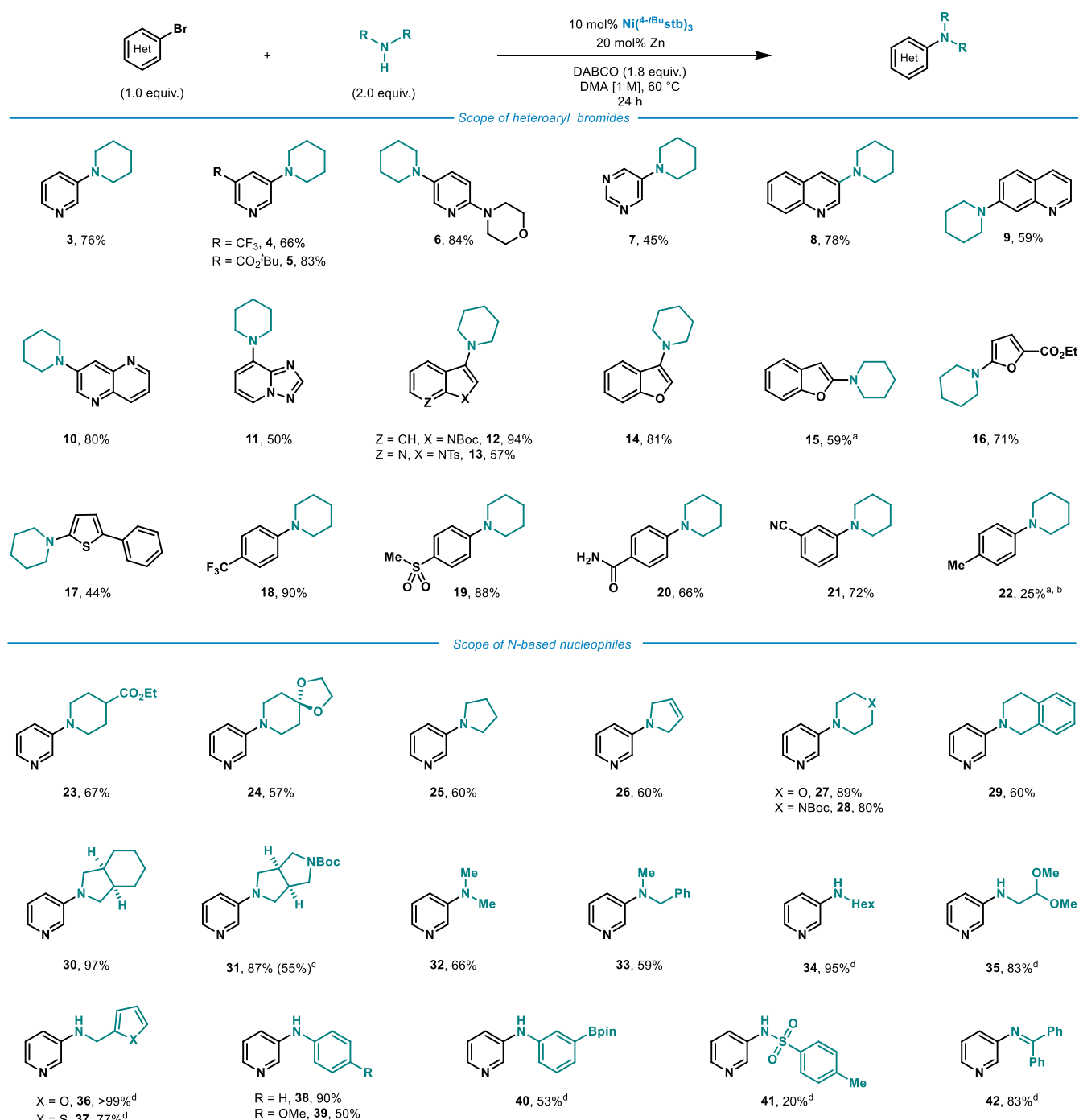


Fig. 2 Scope of the amination protocol. Reaction conditions: (hetero)aryl bromide (1.0 equiv.), amine (2.0 equiv.), DABCO (1.8 equiv.), Ni(⁴-tBu-stb)₃ (10 mol%), Zn dust (<60 μm particle size, 20 mol%), DMA (1 M), 60 °C, 24 h, 0.3 mmol scale. Yields represent isolated yields. ^a ¹H NMR yield, as determined by using 1,3,5-trimethoxybenzene as internal standard; ^b quinuclidine (1.8 equiv.) instead of DABCO; ^c 5.0 mmol scale; ^d deviations from reaction conditions: ^tBu-TMG (1.8 equiv.), Ni(⁴-tBu-stb)₃ (5 mol%), Zn dust (<60 μm particle size, 10 mol%), 100 °C

Next, we were interested in the scope of amines that could be utilized in our protocol (Fig. 2). Piperidine derivatives bearing ester (**23**) or cyclic acetal (**24**) functionalities could be both coupled in good yields. Furthermore, the coupling of pyrrolidine (**25**) and 3-pyrroline (**26**) was also performed with high efficiency. It is important to mention that the absence of electron-rich ligands for the Ni catalyst permits the coupling of 3-pyrroline without undesired Heck or isomerization side-reactivity.¹⁸ Amines with additional heteroatoms such as morpholine (**28**) and *N*-

Boc-piperazine (**29**) also delivered high yields of C–N coupling product. More sterically hindered bicyclic secondary amines were smoothly coupled with 3-bromopyridine, resulting in the formation of products **29** – **31**, with the latter being a synthetic precursor of a ligand to nicotinic acetylcholine receptors (nAChR).¹⁹ As exemplified by **31**, the reaction can also be scaled to 5 mmol, albeit in lower yield. Furthermore, dimethylamine and *N*-methyl benzylamine could be successfully coupled in good yield (**32** and **33**). Next we turned our

attention to primary amines, which required slight modifications, involving the use of ^tBu-TMG (2-*tert*-butyl-1,1,3,3-tetramethylguanidine)^{9c, 9} at 100 °C (see SI for details). Under these reaction conditions, hexylamine and 2,2-dimethoxyethylamine bearing an acyclic acetal moiety underwent efficient coupling (**34** and **35**). Furthermore aliphatic amines bearing pendant heteroaromatic substituents underwent efficient coupling with 3-bromopyridine (**36** and **37**). Different anilines also engaged smoothly in the desired reactivity (**38** and **39**) when using DABCO and 10 mol% of the Ni catalyst at 60 °C. An aniline bearing a *meta*-Bpin functionality (which can act as handle for further functionalization) was amenable under the re-adjusted reaction conditions affording product **40** in moderate yield. Finally, other *N*-based nucleophiles could also be applied; while the coupling with tosylamide afforded **41** in low yields (20%), the coupling of benzophenone imine resulted in formation of **42** in 83% isolated yield.

In 2020, Nocera stated that the coupling of heteroaryl bromides was not feasible as a result of the unproductive substrate coordination, resulting in coordinatively saturated Ni^I species.¹² In contrast to these precedent, the use of NiBr₂(dme) seemed feasible under our optimized conditions when using **1** (Table 1, entry 5). For this reason, we decided to benchmark the use of NiBr₂(dme) and Ni(^{4-t}Bu^ustb)₃ with other heteroaryl bromides. In agreement with Nocera,¹² the yields were substantially decreased when using NiBr₂(dme). For example, in the case of **6** the yield with Ni^{II} plummeted from 84% to 45% (Fig. 3). Furthermore, in the case of **7** the yield decreased to 18%. Addition of 30 mol% of ^{4-t}Bu^ustb did not help and further reduced the yield to 12%, showcasing the importance of applying Ni(^{4-t}Bu^ustb)₃ over ill-defined low-valent Ni species formed *in situ* from Ni^{II}.^{10b, 20} Finally, in the cases of **15** the yield got reduced to 45% and for **17** to 22%.

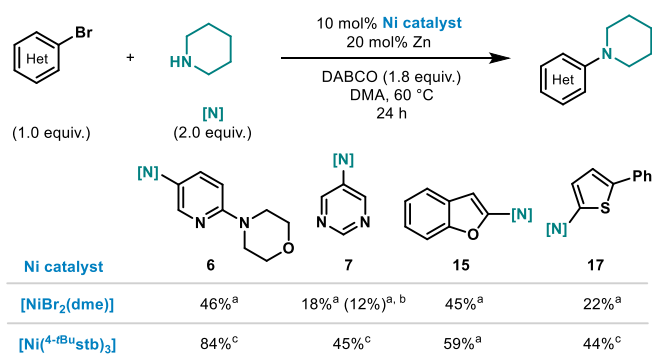


Fig. 3 Direct comparison between NiBr₂(dme) and Ni(^{4-t}Bu^ustb)₃ as catalysts. ^a ¹H NMR yields using 1,3,5-trimethoxy-benzene as internal standard. ^b 30 mol% of ^{4-t}Bu^ustb was added. ^c Isolated yields.

Based on Fig. 3, the presence of stilbene ligands seemed to result in a superior reactivity over the use of NiBr₂(dme).¹⁵ Pörschke reported on the displacement of olefin ligands by amines in Ni⁰ complexes, resulting in the formation of bis-(olefin)Ni⁰-amine species.²¹ Analyzing the reaction mixture and based on the work by Mizoroki, secondary amines should readily coordinate to the Ni-center in preference of tertiary amines.²² Slowly cooling a solution of Ni(^{4-t}Bu^ustb)₃ with excess amounts of piperidine in toluene resulted in formation of crystals of Ni(^{4-t}Bu^ustb)₂(piperidine) (**43**) suitable for XRD analysis (Fig. 4).²³

Coordination of the N atom to the Ni⁰ center has a relatively minor effect on the elongation of the C(sp²)=C(sp²) bond, suggesting minimal π back-donation [average of 1.40 Å in **43** vs. 1.39 Å in Ni(^{4-t}Bu^ustb)₃],¹⁵ which is in accordance with a THF derivative derived from Ni(^{4-t}CF₃stb)₃ (average of 1.41 Å in Ni(^{4-t}CF₃stb)₂(THF) vs. 1.39 Å in Ni(^{4-t}CF₃stb)₃).²⁴

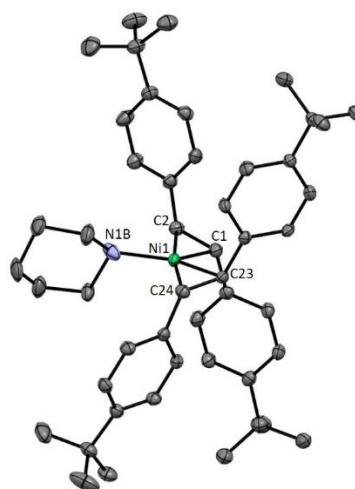


Fig. 4 XRD structure of Ni(^{4-t}Bu^ustb)₂(piperidine) (**43**). Color code: green, Ni; black, C; purple, N. Disordered piperidine and hydrogen atoms are omitted for clarity. C(sp²)=C(sp²) bond distances of the olefinic bonds: 1.405(3) Å, 1.403(3) Å.

By analogy to the thermally sustained Ni^I/Ni^{III} protocol reported by Nocera et al., we are inclined to propose that a similar pathway might be operative in our system, and species similar to **43** might prevent catalyst deactivation in our system. However, this hypothesis remains purely speculative at this point.

Conclusions

In conclusion, we have developed a catalytic protocol based on a “naked nickel” complex, which permits the coupling of various heteroaryl bromides bearing Lewis-basic heteroatoms with a variety of primary and secondary alkyl and arylamines. The catalytic protocol proceeds under thermal conditions without the need of light or electrochemical setups. The protocol also allows the coupling to proceed in the absence of fine-tuned exogenous ligands. These results do not aim at replacing current catalytic strategies for C–N bond formation, but serve as a proof-of-concept protocol for C–N cross-couplings, where certain heteroaryl bromides can be coupled to amines using a catalytic system with Ni and olefins.

Author Contributions

R.S. and J.C. conceived the project. All experimental work was carried out by R.S. Some substrates of the scope table were synthesized by B.B. R.S. and J.C. wrote the manuscript. J.C. directed the project.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Financial support for this work was provided by Max-Planck-Gesellschaft, Max-Planck-Institut für Kohlenforschung, Fonds der Chemischen Industrie (FCI-VCI). R.S. thanks the Fonds der Chemischen Industrie for financial support through a Kekulé PhD fellowship. B.B. thanks Département d'Enseignement et de Recherche de Chimie, École Normale Supérieure Paris-Saclay for financial support. We thank the analytical departments of the Max-Planck-Institut für Kohlenforschung for their support. We specially thank Prof. Dr. A. Fürstner for generous support.

Notes and references

1. a) P. Ruiz-Castillo and S. L. Buchwald, Applications of Palladium-Catalyzed C–N Cross-Coupling Reactions, *Chem. Rev.*, 2016, **116**, 12564–12649; b) R. Dorel, C. P. Grugel and A. M. Haydl, The Buchwald–Hartwig Amination After 25 Years, *Angew. Chem. Int. Ed.*, 2019, **58**, 17118–17129.
2. Y. Zhu, W. Dong and W. Tang, Palladium-catalyzed cross-couplings in the synthesis of agrochemicals, *Adv. Agrochem.*, 2022, **1**, 125–138.
3. a) D. Ma and Q. Cai, Copper/Amino Acid Catalyzed Cross-Couplings of Aryl and Vinyl Halides with Nucleophiles, *Acc. Chem. Res.*, 2008, **41**, 1450–1460; b) F.-S. Han, Transition-metal-catalyzed Suzuki–Miyaura cross-coupling reactions: a remarkable advance from palladium to nickel catalysts, *Chem. Soc. Rev.*, 2013, **42**, 5270–5298; c) S. Z. Tasker, E. A. Standley and T. F. Jamison, Recent advances in homogeneous nickel catalysis, *Nature*, 2014, **509**, 299–309; d) M. Marin, R. J. Rama and M. C. Nicasio, Ni-Catalyzed Amination Reactions: An Overview, *Chem. Rev.*, 2016, **16**, 1819–1832; e) B. Seifinoferest, A. Tanbakouchian, B. Larijani and M. Mahdavi, Ullmann-Goldberg and Buchwald–Hartwig C–N Cross Couplings: Synthetic Methods to Pharmaceutically Potential N-Heterocycles, *Asian J. Org. Chem.*, 2021, **10**, 1319–1344; f) V. M. Chernyshev and V. P. Ananikov, Nickel and Palladium Catalysis: Stronger Demand than Ever, *ACS Catal.*, 2022, **12**, 1180–1200; g) S.-T. Kim, M. J. Strauss, A. Cabré and S. L. Buchwald, Room-Temperature Cu-Catalyzed Amination of Aryl Bromides Enabled by DFT-Guided Ligand Design, *J. Am. Chem. Soc.*, 2023, **145**, 6966–6975.
4. a) J. P. Wolfe and S. L. Buchwald, Nickel-Catalyzed Amination of Aryl Chlorides, *J. Am. Chem. Soc.*, 1997, **119**, 6054–6058; b) B. t. Gradel, E. Brenner, R. Schneider and Y. Fort, Nickel-catalysed amination of aryl chlorides using a dihydroimidazole carbene ligand, *Tetrahedron Lett.*, 2001, **42**, 5689–5692; c) C. Desmarests, R. Schneider and Y. Fort, Nickel(0)/Dihydroimidazol-2-ylidene Complex Catalyzed Coupling of Aryl Chlorides and Amines, *J. Org. Chem.*, 2002, **67**, 3029–3036; d) S. Ge, R. A. Green and J. F. Hartwig, Controlling First-Row Catalysts: Amination of Aryl and Heteroaryl Chlorides and Bromides with Primary Aliphatic Amines Catalyzed by a BINAP-Ligated Single-Component Ni(0) Complex, *J. Am. Chem. Soc.*, 2014, **136**, 1617–1627; e) N. H. Park, G. Teverovskiy and S. L. Buchwald, Development of an Air-Stable Nickel Precatalyst for the Amination of Aryl Chlorides, Sulfamates, Mesylates, and Triflates, *Org. Lett.*, 2014, **16**, 220–223; f) C. M. Lavoie, P. M. MacQueen, N. L. Rottaloria, R. S. Sawatzky, A. Borzenko, A. J. Chisholm, B. K. V. Hargreaves, R. McDonald, M. J. Ferguson and M. Stradiotto, Challenging nickel-catalysed amine arylations enabled by tailored ancillary ligand design, *Nat. Commun.*, 2016, **7**, 11073; g) V. Rittig, M. Henrion and M. J. Chetcuti, Nickel N-Heterocyclic Carbene-Catalyzed C–Heteroatom Bond Formation, Reduction, and Oxidation: Reactions and Mechanistic Aspects, *ACS Catal.*, 2016, **6**, 890–906; h) A. V. Gatién, C. M. Lavoie, R. N. Bennett, M. J. Ferguson, R. McDonald, E. R. Johnson, A. W. H. Speed and M. Stradiotto, Application of Diazaphospholidine/Diazaphospholene-Based Bisphosphines in Room-Temperature Nickel-Catalyzed C(sp²)–N Cross-Couplings of Primary Alkylamines with (Hetero)aryl Chlorides and Bromides, *ACS Catal.*, 2018, **8**, 5328–5339; i) C. M. Lavoie and M. Stradiotto, Bisphosphines: A Prominent Ancillary Ligand Class for Application in Nickel-Catalyzed C–N Cross-Coupling, *ACS Catal.*, 2018, **8**, 7228–7250; j) C. M. Lavoie, J. P. Tassone, M. J. Ferguson, Y. Zhou, E. R. Johnson and M. Stradiotto, Probing the Influence of PAd-DalPhos Ancillary Ligand Structure on Nickel-Catalyzed Ammonia Cross-Coupling, *Organometallics*, 2018, **37**, 4015–4023; k) R. T. McGuire, J. F. J. Paffile, Y. Zhou and M. Stradiotto, Nickel-Catalyzed C–N Cross-Coupling of Ammonia, (Hetero)anilines, and Indoles with Activated (Hetero)aryl Chlorides Enabled by Ligand Design, *ACS Catal.*, 2019, **9**, 9292–9297; l) J. P. Tassone, E. V. England, P. M. MacQueen, M. J. Ferguson and M. Stradiotto, PhPAd-DalPhos: Ligand-Enabled, Nickel-Catalyzed Cross-Coupling of (Hetero)aryl Electrophiles with Bulky Primary Alkylamines, *Angew. Chem. Int. Ed.*, 2019, **58**, 2485–2489; m) R. Y. Liu, J. M. Dennis and S. L. Buchwald, The Quest for the Ideal Base: Rational Design of a Nickel Precatalyst Enables Mild, Homogeneous C–N Cross-Coupling, *J. Am. Chem. Soc.*, 2020, **142**, 4500–4507; n) S. H. Newman-Stonebraker, J. Y. Wang, P. D. Jeffrey and A. G. Doyle, Structure–Reactivity Relationships of Buchwald-Type Phosphines in Nickel-Catalyzed Cross-Couplings, *J. Am. Chem. Soc.*, 2022, **144**, 19635–19648.
5. E. B. Corcoran, M. T. Pirnot, S. Lin, S. D. Dreher, D. A. DiRocco, I. W. Davies, S. L. Buchwald and D. W. C. MacMillan, Aryl amination using ligand-free Ni(II) salts and photoredox catalysis, *Science*, 2016, **353**, 279–283.
6. a) 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, *Eur. J. Org. Chem.*, 2015, **2015**, 5995–6004; b) S. G. Rull, I. Funes-Ardoiz, C. Maya, F. Maseras, M. R. Fructos, T. R. Belderrain and M. C. Nicasio, Elucidating the Mechanism of Aryl Aminations Mediated by NHC-Supported Nickel Complexes: Evidence for a Nonradical Ni(0)/Ni(II) Pathway, *ACS Catal.*, 2018, **8**, 3733–3742.
7. N. A. Till, L. Tian, Z. Dong, G. D. Scholes and D. W. C. Macmillan, Mechanistic Analysis of Metallaphotoredox C–N Coupling: Photocatalysis Initiates and Perpetuates Ni(I)/Ni(III) Coupling Activity, *J. Am. Chem. Soc.*, 2020, **142**, 15830–15841.
8. a) C. Li, Y. Kawamata, H. Nakamura, J. C. Vantourout, Z. Liu, Q. Hou, D. Bao, J. T. Starr, J. Chen, M. Yan and P. S. Baran, Electrochemically Enabled, Nickel-Catalyzed Amination, *Angew. Chem. Int. Ed.*, 2017, **56**, 13088–13093; b) Y. Kawamata, J. C. Vantourout, D. P. Hickey, P. Bai, L. Chen, Q. Hou, W. Qiao, K. Barman, M. A. Edwards, A. F. Garrido-Castro, J. N. Degruyter, H. Nakamura, K. Knouse, C. Qin, K. J. Clay, D. Bao, C. Li, J. T. Starr, C. Garcia-Irizarry, N. Sach, H. S. White, M. Neurock, S. D. Minter and P. S. Baran, Electrochemically Driven, Ni-Catalyzed Aryl Amination: Scope, Mechanism, and Applications, *J. Am. Chem. Soc.*, 2019, **141**, 6392–6402.
9. a) M. S. Oderinde, N. H. Jones, A. Juneau, M. Frenette, B. Aquila, S. Tentarelli, D. W. Robbins and J. W. Johannes, Highly Chemoselective Iridium Photoredox and Nickel Catalysis for the Cross-Coupling of Primary Aryl Amines with Aryl Halides, *Angew. Chem. Int. Ed.*, 2016, **55**, 13219–13223; b) R. J. Key and A. K. Vannucci, Nickel Dual Photoredox Catalysis for the Synthesis of Aryl Amines, *Organometallics*, 2018, **37**, 1468–1472; c) D. Han, S. Li, S. Xia, M. Su and J. Jin, Nickel-Catalyzed Amination of (Hetero)aryl Halides Facilitated by a Catalytic Pyridinium Additive, *Chem. – Eur. J.*, 2020, **26**, 12349–12354; d) Y. Qin, B. C. M. Martindale, R. Sun, A. J. Rieth and D. G. Nocera, Solar-driven tandem photoredox nickel-catalysed cross-coupling using modified carbon nitride, *Chem. Sci.*, 2020, **11**, 7456–7461; e) S. Reischauer, V. Strauss and B. Pieber, Modular, Self-Assembling Metallaphotocatalyst for Cross-Couplings Using the Full Visible-Light Spectrum, *ACS Catal.*, 2020, **10**, 13269–13274; f) E. O. Bortnikov and S. N. Semenov, Coupling of Alternating Current to Transition-Metal Catalysis: Examples of Nickel-Catalyzed Cross-Coupling, *J. Org. Chem.*, 2021, **86**, 782–793; g) C. Zhu, A. P. Kale, H. Yue and M. Rueping, Redox-Neutral Cross-Coupling Amination with Weak N-Nucleophiles: Arylation of Anilines, Sulfonamides, Sulfoximines, Carbamates, and Imines via Nickelaelectrocatalysis, *JACS Au*, 2021, **1**, 1057–1065; h) Z. Zhao, S. Reischauer, B. Pieber and M. Delbianco, Carbon dot/TiO₂ nanocomposites as photocatalysts for metallaphotocatalytic carbon–heteroatom cross-couplings, *Green Chem.*, 2021, **23**, 4524–4530; i) Z. Zhao, B. Pieber and M. Delbianco, Modulating the Surface and Photophysical Properties of Carbon Dots to Access Colloidal Photocatalysts for Cross-Couplings, *ACS Catal.*, 2022, **12**, 13831–13837; j) G. Song, D.-Z. Nong, J.-S. Li, G. Li, W. Zhang, R. Cao, C. Wang, J. Xiao and D. Xue, General Method for the Amination of Aryl Halides with Primary and Secondary Alkyl Amines via Nickel Photocatalysis, *J. Org. Chem.*, 2022, **87**, 10285–10297; k) R. Li, C.-X. Yang, B.-H. Niu, L.-J. Li, J.-M. Ma, Z.-L. Li, H. Jiang and W.-M. Cheng, Visible light-induced Ni-catalyzed C–heteroatom cross-coupling of aryl halides via LMCT with DBU to access a Ni(0)/Ni(II) cycle, *Org. Chem. Front.*, 2022, **9**, 3847–3853; l) M. Traxler, S. Reischauer, S. Vogl, J. Roeser, J. Rabeah, C. Penschke, P. Saalfrank, B. Pieber and A. Thomas, Programmable Photocatalytic Activity of Multicomponent Covalent Organic Frameworks Used as Metallaphotocatalysts, *Chem. – Eur. J.*, 2023, **29**, e202202967; m) H. Luo, G. Wang, Y. Feng, W. Zheng, L. Kong, Y. Ma, S. Matsunaga and L. Lin, Photoinduced Nickel-Catalyzed Carbon–Heteroatom Coupling**, *Chem. – Eur. J.*, 2023, **29**, e202202385.
10. a) C.-H. Lim, M. Kudisch, B. Liu and G. M. Miyake, C–N Cross-Coupling via Photoexcitation of Nickel–Amine Complexes, *J. Am. Chem. Soc.*, 2018, **140**, 7667–7673; b) M. Kudisch, C.-H. Lim, P. Thordarson and G. M. Miyake, Energy Transfer to Ni–Amine Complexes in Dual Catalytic, Light-Driven C–N Cross-Coupling Reactions, *J. Am. Chem. Soc.*, 2019, **141**, 19479–19486; c) Y.-Y. Liu, D. Liang, L.-Q. Lu and W.-J. Xiao, Practical heterogeneous photoredox/nickel dual catalysis for C–N and C–O coupling reactions, *Chem. Commun.*, 2019, **55**, 4853–4856; d) E. B. Corcoran, J. P. McMullen, F. Lévesque, M. K. Wismer and J. R. Naber, Photon Equivalents as a Parameter for Scaling Photoredox Reactions in Flow: Translation of Photocatalytic C–N Cross-Coupling from Lab Scale to Multikilogram Scale, *Angew. Chem. Int. Ed.*, 2020, **59**, 11964–11968; e) B. Y. Park, M. T. Pirnot and S. L. Buchwald, Visible Light-Mediated (Hetero)aryl Amination Using Ni(II) Salts and Photoredox Catalysis in Flow: A Synthesis of Tetracaine, *J. Org. Chem.*, 2020, **85**, 3234–3244; f) S. Gisbertz, S. Reischauer and B. Pieber, Overcoming limitations in dual photoredox/nickel-catalysed C–N cross-couplings due to catalyst deactivation, *Nat. Catal.*, 2020, **3**, 611–620; g) C. Rosso, S. Gisbertz, J. D. Williams, H. P. L. Gemoets, W. Debrouwer, B. Pieber and C. O. Kappe, An oscillatory plug flow photoreactor facilitates semi-heterogeneous dual nickel/carbon nitride photocatalytic C–N couplings, *React. Chem. Eng.*, 2020, **5**, 597–604; h) S. L. Goldschmid, N. E. Soon Tay, C. L. Joe, B. C. Lainhart, T. C. Sherwood, E. M. Simmons, M. Sezen-Edmonds and T. Ravis, Overcoming Photochemical Limitations in Metallaphotoredox Catalysis: Red-Light-Driven C–N Cross-Coupling, *J. Am. Chem. Soc.*, 2022, **144**, 22409–22415; i) M. Traxler, S. Gisbertz, P. Pachfule, J. Schmidt, J. Roeser, S. Reischauer, J. Rabeah, B. Pieber and

- A. Thomas, Acridine-Functionalized Covalent Organic Frameworks (COFs) as Photocatalysts for Metallaphotocatalytic C–N Cross-Coupling, *Angew. Chem. Int. Ed.*, 2022, **61**, e202117738; j) I. Ghosh, N. Shlapakov, T. A. Karl, J. Düker, M. Nikitin, J. V. Burykina, V. P. Ananikov and B. König, General cross-coupling reactions with adaptive dynamic homogeneous catalysis, *Nature*, 2023, **619**, 87–93; k) T. Seo, K. Kubota and H. Ito, Dual Nickel(II)/Mechanoredox Catalysis: Mechanical-Force-Driven Aryl-Amination Reactions Using Ball Milling and Piezoelectric Materials, *Angew. Chem. Int. Ed.*, 2023, **62**, e202311531.
11. For a review on C–X bond formation via Facilitated reductive elimination see: C. Zhu, H. Yue, J. Jia, M. Rueping, *Angew. Chem. Int. Ed.*, 2021, **60**, 17810–17831.
 12. R. Sun, Y. Qin and D. G. Nocera, General Paradigm in Photoredox Nickel-Catalyzed Cross-Coupling Allows for Light-Free Access to Reactivity, *Angew. Chem. Int. Ed.*, 2020, **59**, 9527–9533.
 13. S. Ge and J. F. Hartwig, Highly Reactive, Single-Component Nickel Catalyst Precursor for Suzuki–Miyaura Cross-Coupling of Heteroaryl Boronic Acids with Heteroaryl Halides, *Angew. Chem. Int. Ed.*, 2012, **51**, 12837–12841.
 14. G. Wilke, B. Bogdanović, P. Borner, H. Breil, P. Hardt, P. Heimbach, G. Herrmann, H. J. Kaminsky, W. Keim, M. Kröner, H. Müller, E. W. Müller, W. Oberkirch, J. Schneider, J. Stedefeder, K. Tanaka, K. Weyer and G. Wilke, Cyclooligomerization of Butadiene and Transition Metal π -Complexes, *Angew. Chem. Int. Ed. Engl.*, 1963, **2**, 105–115.
 15. L. Nattmann and J. Cornella, Ni(^{4-*trans*}stb)₂: A Robust 16-Electron Ni(0) Olefin Complex for Catalysis, *Organometallics*, 2020, **39**, 3295–3300.
 16. a) G. N. Schrauzer and H. Thyret, Neuartige „Sandwich“-Verbindungen des Nickel(0). Zur Kenntnis von Durodihon-Nickel(0)-Komplexen mit cyclischen Dienen, *Z. Naturforsch., B: J. Chem. Sci.*, 1962, **17**, 73–76; b) V. T. Tran, Z.-Q. Li, O. Apolinar, J. Derosa, M. V. Joannou, S. R. Wisniewski, M. D. Eastgate and K. M. Engle, Ni(COD)(DQ): An Air-Stable 18-Electron Nickel(0)–Olefin Precatalyst, *Angew. Chem. Int. Ed.*, 2020, **59**, 7409–7413.
 17. In other systems, the amination of electron-rich aryl bromides has been shown to be challenging: a) E. B. Corcoran, M. T. Pirnot, S. Lin, S. D. Dreher, D. A. DiRocco, I. W. Davies, S. L. Buchwald, D. W. C. MacMillan, *Science*, 2016, **353**, 279–283; b) C. Li, Y. Kawamata, H. Nakamura, J. C. Vantourout, Z. Liu, Q. Hou, D. Bao, J. T. Starr, J. Chen, M. Yan, P. S. Baran, *Angew. Chem. Int. Ed.*, 2017, **56**, 13088–13093; c) C.-H. Lim, M. Kudisch, B. Liu, G. M. Miyake, *J. Am. Chem. Soc.*, 2018, **140**, 7667–7673; d) Y. Kawamata, J. C. Vantourout, D. P. Hickey, P. Bai, L. Chen, Q. Hou, W. Qiao, K. Barman, M. A. Edwards, A. F. Garrido-Castro, J. N. Degruyter, H. Nakamura, K. Knouse, C. Qin, K. J. Clay, D. Bao, C. Li, J. T. Starr, C. Garcia-Irizarry, N. Sach, H. S. White, M. Neurock, S. D. Minter, P. S. Baran, *J. Am. Chem. Soc.*, 2019, **141**, 6392–6402; e) R. Sun, Y. Qin, D. G. Nocera, *Angew. Chem. Int. Ed.*, 2020, **59**, 9527–9533; f) Goldschmid, N. E. Soon Tay, C. L. Joe, B. C. Lainhart, T. C. Sherwood, E. M. Simmons, M. Sezen-Edmonds, T. Rovis, *J. Am. Chem. Soc.*, 2022, **144**, 22409–22415; g) I. Ghosh, N. Shlapakov, T. A. Karl, J. Düker, M. Nikitin, J. V. Burykina, V. P. Ananikov, B. König, *Nature*, 2023, **619**, 87–93.
 18. a) S.-Z. Sun, M. Börjesson, R. Martin-Montero and R. Martin, Site-Selective Ni-Catalyzed Reductive Coupling of α -Haloboranes with Unactivated Olefins, *J. Am. Chem. Soc.*, 2018, **140**, 12765–12769; b) S.-Z. Sun, C. Romano and R. Martin, Site-Selective Catalytic Deaminative Alkylation of Unactivated Olefins, *J. Am. Chem. Soc.*, 2019, **141**, 16197–16201; c) X. Chen, J. Lin, B. Wang and X. Tian, Nickel-Catalyzed Mizoroki–Heck/Amination Cascade Reactions of *o*-Dihaloarenes with Allylamines: Synthesis of Indoles, *Org. Lett.*, 2020, **22**, 7704–7708.
 19. W. H. Bunnelle, K. R. Tietje, J. M. Frost, D. Peters, J. Ji, T. Li, M. J. C. Scanio, L. Shi, D. J. Anderson, T. Dyhring, J. H. Grønlien, H. Ween, K. Thorin-Hagene and M. D. Meyer, Octahydropyrrolo[3,4-*c*]pyrrole: A Diamine Scaffold for Construction of Either $\alpha\beta$ 2 or $\alpha\gamma$ -Selective Nicotinic Acetylcholine Receptor (nAChR) Ligands. Substitutions that Switch Subtype Selectivity, *J. Med. Chem.*, 2009, **52**, 4126–4141.
 20. M. Mohadjer Beromi, A. Nova, D. Balcells, A. M. Brasacchio, G. W. Brudvig, L. M. Guard, N. Hazari and D. J. Vinyard, Mechanistic Study of an Improved Ni Precatalyst for Suzuki–Miyaura Reactions of Aryl Sulfamates: Understanding the Role of Ni(I) Species, *J. Am. Chem. Soc.*, 2017, **139**, 922–936.
 21. a) W. Kaschube, K. R. Pörschke, W. Bonrath, C. Krüger and G. Wilke, Amine-Bis(ethene)nickel(0) Complexes; Structure of 1-Azabicyclo[2.2.2]octanebis(ethene)nickel(0), *Angew. Chem. Int. Ed. Engl.*, 1989, **28**, 772–773; b) B. Proft, K. R. Pörschke, F. Lutz and C. Krüger, 1,6-Heptadiene Nickel(0) Complexes: *rac*/meso-(μ - η^2 - η^2 -C₇{Ni(η^2 , η^2 -C₇H₁₂)₂} und L-Ni(η^2 , η^2 -C₇H₁₂), *Chem. Ber.*, 1991, **124**, 2667–2675.
 22. Y. Nakamura, K.-i. Maruya and T. Mizoroki, A Study of the Ligand Exchange of Bromo(*o*-tolyl)bis(triphenylphosphine)nickel(II) with Amine by Means of ³¹P- and ¹³C-NMR Spectroscopy, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 3089–3092.
 23. Deposition number **2312434** contains the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.
 24. L. Nattmann, R. Saeb, N. Nöthling and J. Cornella, An air-stable binary Ni(0)–olefin catalyst, *Nat. Catal.*, 2020, **3**, 6–13.