Abstract: Ni catalysis constitutes an active research arena with notable applications in diverse fields. By analogy with its parent element palladium, Ni catalysts provide an appealing entry to build molecular complexity via cross-coupling reactions. While Pd catalysts typically involve a M⁰/MII redox scenario, in the case of Ni congeners the mechanistic elucidation becomes more challenging due to their innate properties (like enhanced reactivity, propensity to undergo single electron transformations vs. 2e⁻ redox sequences or weaker M–Ligand interaction). In recent years, mechanistic studies have demonstrated the participation of high-valent NiIII and NiIV species in a plethora of cross-coupling events, thus accessing novel synthetic schemes and unprecedented transformations. This comprehensive review collects the main contributions effected within this topic, and focuses on the key role of isolated and/or spectroscopically identified NiIII and NiIV complexes. Amongst other transformations, the resulting NiIII and NiIV compounds have efficiently accomplished: i) C–C and C–heteroatom bond formation; ii) C–H bond functionalization; and iii) N–N and C–N cyclizative couplings to forge heterocycles.

Keywords: NiIII and NiIV chemistry; cross-coupling reactions; C–H bond functionalization; trifluoromethylation; fluorination

1. Introduction

Cross-coupling reactions mediated by organometallics represent a cornerstone in the daily synthetic Chemist’s toolbox leading to complex organic scaffolds [1,2]. Since the pioneering approaches to C–C coupling in the 1960s [3], the field has experimented tremendous advances with plenty of applications in material science, drug discovery and manufacturing, or natural product synthesis [1,2]. While Pd catalysts are commonly the candidates of choice, nickel is attracting growing attention owed to its higher abundance and economic issues [4–6]. On the other hand, and what is considerably more relevant, the enhanced reactivity and diversity in terms of redox properties of nickel (compared to palladium) offers broad room for reaction discovery [7,8]. Since the late 1970s, Ni catalysts have been employed with success in cross-coupling reactions [9,10], with the classical Ni⁰/NiII vs. NiII/NiIII pathways and single electron transfer (SET) processes being commonly proposed as the most plausible redox scenarios [11–13]. High-valent NiIII and NiIV key intermediates were recently invoked in C–C and C–heteroatom bond forming reactions, albeit their isolation or detection/characterization are typically out of reach [14–19]. First, spectroscopical identification of a NiIIII mediating cross-coupling reactions was performed by Kochi and co-worker as early as 1978 [20]. In this seminal work, electron paramagnetic resonance spectroscopy (EPR) and UV-Vis spectroscopy allowed one to identify the trans-[PEt₃]₂Ni[Br]₂(2-MeOC₆H₄)(Br)⁺ species that underwent C(sp²)–Br coupling. While additional NiIII and NiIV complexes were isolated and characterized in the following decades [21–36],
investigations dealing with the isolation and characterization of Ni species in high oxidation states (+3 and +4) that are efficient in cross-coupling reactions remained latent until this century. Built on the growing interest on high-valent samples, this review compiles the most remarkable pieces of work addressing the long-time elusive NiIII and NiIV compounds (or analogous entities lacking Ni–C bonds) that are engaged in cross-coupling events or related transformations.

2. C–C Bond Forming Reactions Mediated by High-Valent NiIII and NiIV

Unlike Pt and Pd, the chemistry of organonickel species in the oxidation state +4 is underdeveloped. Nowadays, Pt-chemistry is mainly dominated by PtIII and PtIV complexes and a plethora of stable R-PtIV species are known since the origins of organometallic chemistry. Routes to access aryl- and alkyl-PdIV complexes have appeared over the last 40 years displaying very distinct and complementary reactivity patterns to the ones observed for Pd-analogs in low oxidation states. It seems obvious that going up in the group makes the study of organometallic MIV species more challenging. On the other hand, NiIV intermediates are often depicted in catalytic cycles [10–14]. Thus, the isolation, characterization and study of Ni species in oxidation states +3 and +4 represents a major challenge in modern organonickel chemistry.

Literature dealing with authenticated NiIII and NiIV samples and their use in cross coupling reactions was absent until the 2000s, when the pseudotetrahedral alkyl-NiIV species 2 was reported by Dimitrov and Linden (Scheme 1) [37]. The triorganyl-NiIV complex 2 was prepared through a 2e– oxidation step of the tris(1-norbornyl) precursor 1 with O2, and was fully characterized using nuclear magnetic resonance spectroscopy (NMR), X-ray diffraction (XRD), and elemental analysis (EA). The stability of 2 is probably given by the strong σ-donicity of the 1-norbornyl ligands. Remarkably, 2 resulted unstable at room temperature (r.t.) in solution and underwent elimination of dinorbornane (3). Alternatively, 3 was prepared upon addition of (1-norbornyl)lithium without the identification of the homolectic tetraorganyl-NiIV intermediate.

![Scheme 1](image_url)

**Scheme 1.** Isolation of the first NiIV complex 2 that proved active in C–C bond forming reactions. Adapted from reference [37].

The first homolectic NiIV complex 5 was made via two oxidative couplings of 4 with [NiII(COD)2] (COD = 1,5-cyclooctadiene) allowing to build the spirocyclic motif in 5 (Scheme 2) [38,39]. 5 was characterized using NMR and XRD, and proved stable upon heating or exposure to air. The enhanced stability of 5 was provided by the high shielded geometry around the NiIV-center imposed by the rigidity and bulkiness of the alkyl-based chelating ligands. Interestingly, 5 comes along with the trans,trans,trans-cyclobutane 6 that was formed in 36% yield. In contrast, the remarkable stability of 5 pointed to the reductive elimination (R.E.) of 6 from a low-valent nickelacycle. Alternatively, 6 was eliminated in ca. 40% yield upon mild heating of the tris(5Z,11E)-dibenzot[a,e]cyclooctatetraene)nickel(0) species 7, which was prepared from [NiII(tert-Bu3P)(COD)] and 4.
A couple of papers detailing the isolation, characterization (XRD, \(^1\)H NMR, magnetic data, and EA), and reactivity of the T-shaped Ni\(III\)-CH\(_3\) complex 10 were reported by Tilley (Scheme 3) \([40,41]\). 10 was prepared through oxidative addition of Mel to a Ni\(^1\) species generated through reduction of the stable [Ni\(^{II}\)(N(DIPP)SiMe\(_3\))\(_2\)] precursor 8 using KC\(_8\). 10 is conveniently stabilized by the two rigid and bulky bis(amido) ligands, but slowly decomposes to 8 with concomitant ethane production. In addition, 8 catalyzed the coupling of aryl halides and Grignard reagents.

Mirica has isolated the high-valent aryl-Ni\(^{III}\) compounds 14-Cl and 14-Br that underwent C–C coupling with alkyl Grignard reagents (Scheme 4) \([42]\). 14-Cl and 14-Br are stabilized by the \(N,N\)-di-tert-butyl-2,11-diaz[a3.3][2,6]pyridinophane \(^{15}\text{N}_2\text{N}_4\) ligand and were achieved in a two-step fashion through: \(i\) an initial coordination of the \(^{15}\text{N}_2\text{N}_4\) ligand to Ni\(^0\), followed by insertion into the C–X bond and \(ii\) 1e\(^–\) oxidation using ferrocenium hexafluorophosphate [Fc\(^+\)]\([PF_6]\). XRD, EPR, paramagnetic NMR, and magnetic data for 14-Cl and 14-Br confirmed the octahedral coordination of Ni and pointed to the presence of a mostly Ni\(^{III}\) located unpaired electron. 14-Cl and 14-Br reacted with MeMgI at \(-50^\circ\text{C}\) to afford 15. Notably, 15 constitutes the first di(hydrocarbyl)-Ni\(^{III}\) intermediate (identified using ESI-MS and EPR), and underwent the R.E. of 4-fluorotoluene (13) in moderate yield (48%). An improved yield (63%) was reached in a one-pot reaction of the aryl-Ni\(^{III}\)-Br complex 11-Br with MeMgBr and [Fc\(^+\)]\([PF_6]\). The addition of 2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) as a radical trap did not affect the coupling reaction and ruled out the involvement of organic radicals. In addition, the Ni\(^0\) and Ni\(^{III}\) complexes 11-Cl, 11-Br, 14-Cl, and 14-Br proved suitable in Negishi and Kumada couplings.
The lack of selective methods for aromatic trifluoromethylation represents a major concern [43–45]. This is mainly due to: i) the steadily increasing demand of organofluorine materials in pharmaceutical, agrochemical, and medical applications, or in material science [46–48] and ii) the disfavored transition metal mediated aryl–CF₃ bond formation due to the strong M–CF₃ bonds. It is believed that the current lack of environmentally-benign [49–51] and industrially-suitable routes to benzotrifluorides impedes faster advance in drug discovery. The impossibility to achieve aryl–CF₃ R.E. from a well-defined, low-valent aryl-Niᴵᴵ–CF₃ fragment was soon noticed independently by the groups of Vicic [52] and Grushin [53]. An elegant and certainly underexplored approach to enable the decisive R.E. step consists in the preparation of highly reactive Niᴵᴵ and Niᴵ_IV complexes, which are commonly inaccessible. Taken altogether, the use of CF₃-groups in organometallic chemistry offers a unique balance between stability and reactivity that allows for the isolation of high-valent compounds with strong M–CF₃ bonds, yet enables CF₃-group transfer into strategically designed organic scaffolds. While high-valent Ni species were unidentified, Ph–CF₃ bond formation was achieved by Sanford’s team upon 1e⁻ oxidation of well-defined [[P₂]Niᴵᴵ(Ph)(CF₃)] platforms using the outer-sphere oxidant [Fe⁺][PF₆⁻] [54]. These studies have shown the crucial role of the ancillary diphosphine ligand on the R.E. of benzotrifluorides [54]. As might be expected, small bite angles (β < 92°) conducted to insignificant amounts of benzotrifluoride (<10% yield), whereas bite angles ranging from 95° to 102° favored the aryl–CF₃ coupling (up to 77% yield).

The first approach to high-valent NiCF₃ species was reported by Vicic and co-workers [55]. They prepared and characterized in situ the cationic [([But]terpy)Niᴵᴵ(CF₃)₂][PF₆] species 16 using low-temperature EPR (Scheme 5). Unfortunately, 16 turned out to be unstable at r.t. and yielded complex [([But]terpy)Niᴵ_IV(CF₃)]⁺ via *CF₃ radical elimination. The use of a perfluorinated nickelacycle motif in 17 warranted the Niᴵᴵ stabilization and permitted its characterization using XRD and EPR [56]. Cyclic voltammetry of 17 displayed a low redox potential attributable to the reversible Niᴵᴵ/Niᴵ_IV couple, whereas elevated redox potentials are required to overcome the Niᴵᴵ/Niᴵ_IV oxidation potentials. The first isolable Niᴵᴵ,CF₃ compounds Ṁe₁₈ and ṀBr₁₈ were obtained in reasonable yields by Mirica’s group using highly donating tetradentate pyridinophane ligands Ṁe₂N₄ and ṀBr₂N₄ [57]. Ṁe₁₈ and ṀBr₁₈ were characterized using XRD, EPR, and computed by DFT (density functional theory). Besides the trifluoromethylation of the radical scavenger PBN (phenyl N-t-butyl nitronate), no evidence was provided for the participation of Ṁe₁₈,C₃ in trifluoromethylation reactions. Instead, a ligand modification strategy was highlighted to be key in order to lower the redox potential of the Niᴵᴵ/Ni_IV couple [56].
In spite of the significant number of NiIV coordination compounds that have been known since ca. 40 years ago [27–36], whether NiIV species are engaged in cross-coupling reactions or not has remained unclear until very recently. In 2015, Camasso and Sanford made a cutting-edge discovery: the isolation and complete characterization of the first NiIV compounds able to promote cross-coupling events [58–60]. Based on previous knowledge on related PdIV-chemistry [61–68], an isolable NiIV platform was designed through the combination of three distinct strategies: i) the use of strongly N-donor, tridentate scorpionate-type ligands [i.e., tris(pyrazolyl)borate (Tp) and tris(2-pyridil)methane (Py3CH)]; ii) the presence of the Ni(cyclo-neophyl) core known to improve stability vs. R.E. and H5-elimination elementary steps; and iii) the employment of a σ-donating CF3-ligand (Scheme 6) [58]. Following these premises, the Umemoto reagent S-trifluoromethyl)dibenzothiophenium triflate (TTDT) was added to 19, and the diamagnetic NiIV complex 20 was obtained in 92% yield. The high stability of nickelacycle 20 allowed its full characterization, including XRD that confirmed the facial coordination of the Py3CH ligand to the octahedral NiIV center. Heated to 95 °C, 20 underwent C(sp2)–C(sp3) reductive elimination to afford quantitatively the 1,1-dimethylbenzocyclobutene 21. This work represents the first spectroscopic support for the participation of NiIV species in cross-coupling reactions.

Scheme 5. Stable NiIII-CF3 complexes 16, Me18, and HBu18 and perfluorinated nickelacycle 17 [55–57].

In a following report, they performed the trifluoromethylation of aromatics from a well-defined arylniIV-CF3 fragment [69]. On this occasion, the high-valent NiIV-CF3 complexes 24a–e were stabilized by the tris(pyrazolyl)borate (Tp) ligand and two CF3-groups. 24a–e were obtained through a 2e− oxidation step of the NiII-CF3 precursor 22 with arylidonium salts at ~35 °C in acetonitrile (Scheme 7; top left) [69]. Alternatively, the NiII to NiIV conversion can be reached using the Umemoto reagent (TTDT) as demonstrated by the high-yielding isolation of 24a from [(Tp)NiIII(Ph)(CF3)] (25a; bottom left in Scheme 7) [69]. Once isolated and fully characterized, 24a–e were heated to 55 °C undergoing the elimination of the corresponding benzotrifluorides 26a–e accompanied by [NiII(Tp)2] and [NiII(CH3CN)2(CF3)2].

Kinetic studies and Hammett plot analysis for the R.E. step enabling benzotrifluoride formation provided a ρ value of −0.91 indicating faster reaction rates with electron-enriched arenes [69]. This beneficial effect was attributed to the larger trans-effect of electron rich arenes, along with the lower kinetic barriers associated with the nucleophilic attack of the electron rich σ-aryl ligand to the electrophilic CF3-group [69]. However, the bonding analysis of complex 24a pointed to an inverted ligand field situation [70] and the NiIV complexes 24a–e are better described as NiII species. This effect was called the σ-noninnocence of the cationic aryl ring [70] and the release of PhCF3 through a redox neutral R.E. step via “σ-noninnocence-induced masked aryl-cation transfer”, accordingly [70].
Scheme 7. Distinct oxidation strategies to reach the Ni IV species [Ni IV(Tp)(aryl)(CF3)2] 24a–e from [NMe4][Ni III(Tp)(CF3)2] (22) and arylidonium salts (top left) or [NBu4][Ni III(Tp)(Ph)(CF3)] (25a) and TTDT (bottom left), and R.E. of benzo trifluorides 26a–e from 24a–e. Adapted from reference [69].

The use of Py3CH or Tp ligands is necessary for accessing the Ni IV species 20 and 24a–e as shown by the reduced stability of analogous platforms bearing less donating bipyridine ligands (bpy or dtbpy; Scheme 8) [58,69]. As a result, the presumable Ni IV–CF3 intermediates 28 and 31a were exclusively identified using low-temperature NMR analysis, and rapidly released 1,1-dimethylbenzocyclobutene 21 or benzo trifluoride 26a at r.t., respectively. Replacement of the CF3-group by a distinct X-type ligand (i.e., halides, tosylate, or acetate) reduced the stability of Ni IV, thus favoring the C(sp2)–C(sp3) R.E. and hampering the detection of Ni IV species.

Scheme 8. Identification of the Ni IV–CF3 key intermediates 28 and 31a bearing bpy (a) or dtbpy (b) ligands, and subsequent R.E. steps upon warming up to r.t. Adapted from references [58,69].

Shortly after, they evaluated the capacity of similar Ni III complexes 33a–d to forge diverse C–C bonds (Scheme 9) [71]. The Ni III 33a–d were achieved in variable yields from 22 and 32a,c,d through a 1e− oxidation process with AgBF4. The isolated Ni III materials were characterized using EPR and XRD. Heated in acetonitrile, 33a,c,d decomposed into [Ni III(Tp)2] and Ni III with concomitant formation of the C–C coupled products in 33–69% yield. Remarkably, 33b merely produced 1% of hexafluoroethane. For complex 33a displaying the Ph-Ni III–CF3 fragment, enhanced rate and yield of benzo trifluoride 26a was reached in the presence of oxidants, such as [(Cp*)2Fe][BF4]. This observation was attributed to the efficient quenching of the resulting Ni I species generated in situ during Ph–CF3 formation. Detailed mechanistic investigations have demonstrated the direct R.E. from the Ni III species 33a,c,d (instead of the assumed Ni IV derivatives).
More recently, Mirica’s group has reported the synthesis and complete characterization of the high-valent Ni$^{III}$ and Ni$^{IV}$ compounds 36 and 37 enabled by: i) facial coordination of the tridentate ligand 1,4,7-trimethyl-1,4,7-triazacyclononane (Me$_3$tacn) and ii) the Ni(cyclo-neophyl) skeleton (Scheme 10) [72]. Complexes 36 and 37 were prepared in high yield from the Ni$^{IV}$-precursor 35 through two successive 1e$^-$ oxidation steps with ferrocenium tetrafluoroborate ([Fc$^+$][BF$_4$]) and acetylferrrocenium tetrafluoroborate ([AcFc$^+$][BF$_4$]). XRD studies confirmed the atom connectivity in 36 and 37 along with their square pyramidal and octahedral geometry, respectively. Heated to 80 °C, the Ni$^{IV}$ complex 37 underwent C(sp$^2$)-C(sp$^3$) R.E. in modest yield while blue LED irradiation drove to almost quantitative formation of 1,1-dimethylbenzocyclobutene 21. Interestingly, exposure of the Ni$^{III}$ species 36 to blue LED did not improve the reaction yield. This work argues in favor of Ni$^{IV}$ being most likely the coupling active species when dealing with dual Ni/photocatalytic approaches (instead of the commonly invoked Ni$^{III}$ intermediates) [73–76].

The tetradeionate $N,N$-dimethyl-2,11-diaza[3,3][2,6]pyridinophane ligand (Me$_3$N$_4$) enabled the isolation and full characterization of the first Ni$^{III}$-dialkyl complex 41. It was achieved from the square planar Ni$^{II}$ precursor 38 and [Fc$^+$][PF$_6$] (Scheme 11a) [77], and its octahedral geometry was confirmed using XRD and EPR. 41 in acetonitrile produced ethane and methane in ca. 55% and 30%, respectively. Ethane production was improved upon addition of [AcFc$^+$][PF$_6$] pointing to the formation of an elusive

Scheme 9. Syntheses of Ni$^{III}$ species 33a–d (a), and R.E. studies enabling Ph–CF$_3$ coupling (b). Adapted from reference [71].
Ni\textsuperscript{IV}-dialkyl intermediate 42 that decomposes rapidly to Ni\textsuperscript{II} material and ethane via a R.E. step. In order to stabilize the high-valent species, the cyclo-neophyl group was incorporated to the Ni\textsuperscript{II} platform (Scheme 11b) [77]. The two-step oxidation of 45 with [Fe\textsuperscript{+}][PF\textsubscript{6}\textsuperscript{-}] to give the Ni\textsuperscript{III} intermediate 46, followed by addition of NOPF\textsubscript{6} permitted the identification of the Ni\textsuperscript{IV} compound 47, which was characterized using NMR and X-ray photoelectron spectrometry (XPS). The enhanced stability of the Ni\textsuperscript{III} and Ni\textsuperscript{IV} compounds 46 and 47 (vs. 43 and 44) inhibited the R.E. and led to 21 in low yields (10% and 38%, respectively).

![Scheme 11](image)

Scheme 11. Syntheses of Ni\textsuperscript{III} and Ni\textsuperscript{IV} dialkyl complexes 41–44 and R.E. of ethane (a). Syntheses of stable Ni\textsuperscript{III} and Ni\textsuperscript{IV} cyclo-neophyl complexes 46 and 47 (b). Adapted from references [77,78].

In a subsequent article, the same group reported the synthesis and characterization of analogous Ni\textsuperscript{III}-dialkyl complexes 43 and 44 incorporating NMe/NTs or NTs/NTs donating groups [78]. The low denticity of the TsN-amino groups favored the formation of transient penta- or tetra-coordinated Ni\textsuperscript{III}-dialkyl species that are more prone to eliminate ethane (Scheme 11a) [78]. Compounds 43 and 44 are easily accessible in presence of O\textsubscript{2} or H\textsubscript{2}O\textsubscript{2} and underwent selective C–C bond formation. In addition, the quantitative formation of 21 was accomplished from an elusive Ni\textsuperscript{IV}-complex 48, very similar to 47 but with TsN-amino groups [79].

As shown earlier, Ni\textsuperscript{III} and Ni\textsuperscript{IV} complexes are engaged in C–C bond forming reactions, although limited knowledge is available concerning their comparative efficiency upon similar environments such as identical geometry, type of ligands or ligand set, and global charge. In this sense, Sanford’s group has evaluated the feasibility of C–C and C–heteroatom bond formation depending on: i) the nature of the transition metal (Ni vs. Pd) [80]; ii) the nature of the surrounding ligands (MeCN vs. CF\textsubscript{3}) [80]; and iii) the oxidation state at Ni (+3 vs. +4; see Scheme 12) [81].

Organometallic compounds 50–52 bearing a tris(pyrazolyl)borate ligand (Tp) were prepared from the corresponding salts [Q\textsuperscript{+}][(Tp)M\textsubscript{II}(cyclo-neophyl)] (Q\textsuperscript{-} = K\textsuperscript{+}, NMe\textsubscript{3}\textsuperscript{+}; M = Ni, Pd) through selective 1e\textsuperscript{-} or 2e\textsuperscript{-} oxidation processes. Kinetic studies performed for the elimination of 21 from the M\textsuperscript{IV} species 50, 51, and 52 proved the higher stability of 50 vs. 52, most likely due to the strong σ-donation of the CF\textsubscript{3}-group. The nature of the cationic species (Tp)-Ni\textsuperscript{IV} 52 and (Py\textsubscript{3}CH)-Ni\textsuperscript{III} 53 was authenticated using XRD, EPR (53) or NMR (52), and cyclic voltammetry [80,81]. Their ability to release 21 was then compared at r.t. in the dark or when exposed to daylight (Scheme 12), thus reflecting the higher activity of the (Py\textsubscript{3}CH)-Ni\textsuperscript{III} complex 53. It provided the coupled product in 87% yield after 12 h in the dark, whereas the Ni\textsuperscript{IV} released negligible amounts of 21 (<10%; 300-fold slower than 53). Exposure to
daylight improved the efficiency of the Ni\(^{IV}\) complex 52 to form the C–C bond (65% in 12 h), while no remarkable effect was accounted for the Ni\(^{III}\) 53.

![Scheme 12](image)

**Scheme 12.** C–C bond formation as a function of the metal (Ni vs. Pd; a), ancillary ligand (Tp vs. Py3CH and CF\(_3\) vs. MeCN; b and a, respectively) or oxidation state at the Ni-center (+3 vs. +4; a). Adapted from references [80,81].

In 2017, the group of Sanford reported the transmetallation reaction between the Ni\(^{IV}\)-O\(_2\)CF\(_3\) complex 54 and Ruppert’s silane in presence of [Me\(_2\)N][F] leading to Ni\(^{IV}\)-CF\(_3\) complex 55 (Scheme 13; the synthesis, characterization and reactivity of 54 is depicted below in Scheme 30) [82]. The Ni\(^{IV}\)-CF\(_3\) compound 55 was conveniently characterized using NMR methods and XRD and underwent aromatic trifluoromethylation leading to 56 in ca. 90% yield upon warming at 70 °C overnight. The addition of the electron rich PMe\(_3\) ligand improved kinetics and yield of aryl–CF\(_3\) production.

![Scheme 13](image)

**Scheme 13.** Transmetallation reaction between the Ni\(^{IV}\)-O\(_2\)CF\(_3\) complex 54 and CF\(_3\)TMS/NMe\(_4\)F to reach 55, and synthesis of the Ni\(^{III}\) species 56 via R.E. of aryl–CF\(_3\). Adapted from reference [82].

The same year, Ribas and co-workers reported the quantitative trifluoromethylation of triaza-macrocycles bearing an aromatic ring [83]. The reaction involves two independent steps namely: i) an aryl-Ni\(^{II}\) bond formation to reach 57a,b via aryl–Br oxidative addition to [Ni\(^{II}\)(COD)]\(_2\), or alternatively, C–H bond nickelation using [Ni\(^{II}\)(NO\(_3\))\(_2\)]\(_6\)(H\(_2\)O); and ii) the oxidative trifluoromethylation of the macrocyclic scaffold upon addition of the Umemoto or Togni reagents (Scheme 14) [83]. The authors proposed a Ni\(^{II}\) to Ni\(^{IV}\) oxidation step prior to R.E. of the coupled products 58a,b through an initial SET process to form a (N\(_3\)C\(_{arom}\))[Ni\(^{III}\)] intermediate and a *CF\(_3\) radical that subsequently recombine with each other to build the (N\(_3\)C\(_{arom}\))Ni\(^{IV}\) species 59a,b.
Scheme 14. Oxidative trifluoromethylation of N3Carom ligands mediated by Ni. C-CF3 bond formation from the elusive (N3Carom)NiIV intermediates 59a,b. Adapted from reference [83].

Klein, van der Vlugt and co-workers performed the 1e⁻ oxidation of the NiII-CH3 complex 60 upon addition of [1⁹Fc⁺][BF₄] to yield the transient NiIII-CH3 species 61 bearing an aryl-pyridine-phosphine (PNCarom) pincer ligand (Scheme 15) [84]. Reaction monitoring using ¹H NMR indicated the formation of the tolyl fragment and the release of the NiI complex 62, which was identified using EPR.

Scheme 15. Aryl-CH₃ coupling from an assumed cationic [(PNCarom)NiIII(CH₃)]⁺ pincer complex 61. Adapted from reference [84].

A ligand design strategy allowed the development of the oxidative cyation of aromatic rings enabled by a NiIII-CN key intermediate 65 (Scheme 16) [85]. Insertion of [NiII(COD)₂] into the triazamacrocycle ᵄBuN₃CB₉ provides [NiII(N₃C)NiII(Br)] (63). 63 further reacts with TIPF₆ and ᵄBuNC affording the highly stable bis(isocyanide) compound [(ᵗBuN₃)NiII(tBuNC)₂][PF₆] (64). In contrast, oxidative treatment of 64 with [Fc⁺][PF₆] or NOBF₄ yielded the cyanide-containing macrocycle ᵄBuN₃CCN instantaneously. The NiIII-mediated N-Bu heterolytic bond scission to give the NiIII-CN species and isobutylene was proposed in line with: i) the high stability of the NiIII-CN'Bu species 64; and ii) the quantitative yield of ᵄBuN₃CCN attained upon addition of AgCN to [(ᵗBuN₃)NiII(Br)] (63) [86]. The bis(acetonitrile) NiIII complex 66 was conveniently characterized using XRD and EPR, and was reacted with ᵄBuNC resulting in the liberation of ᵄBuN₃CCN. Monitoring the coupling reaction illustrated the simultaneous consumption of 66 and the formation of ᵄBuN₃CCN, thus suggesting the participation of NiIII species in the N-Bu bond breaking/aryl-CN bond forming sequence.

Scheme 16. NiIII-mediated aromatic cyation using ᵄBuN-containing pyridinophane scaffolds. Adapted from reference [85].
The nature of the pending RN-amino groups located at the apical positions drastically affects the stability and reactivity of the NiIII species, whereas modification of the aryl moiety does not impact reactivity significantly [87]. Complex 67 undergoes the full cyanation of the aromatic ring upon addition of 1BuNC in air (Scheme 17) [87]. Alternatively, 1BuN3CCN can be forged through initial bromide abstraction and exposure to air. These aerobic cyanations occur at r.t. within 5 min and imply the transient formation of NiII intermediates, as convincingly proved through the reactivity of the isolated NiIII 68 towards 1BuNC that afforded 1BuN3CCN in quantitative yield. High-yielding syntheses of NiIII species 69 and 68 were accomplished via 1e− oxidation either with [Fc+][PF6] or AgBF4 [88]. A distorted octahedral coordination of Ni and the presence of an unpaired electron in 68 and 69 was confirmed using XRD, EPR, and magnetic measurements [88].

Scheme 17. NiIII-mediated aromatic cyanation using NpN-containing pyridinophane scaffolds. Adapted from references [87,88].

The viability of NiII/NiIII/NiIV oxidation sequences involving successive SET processes has been investigated recently (Scheme 18) [89]. The isolation and characterization of NiIV metallacycles 74a,b was accomplished by controlled release of alkyl and aryl radicals upon heating of the NiII precursor 72 in presence of the corresponding diacyl peroxide 73a,b (Scheme 18a) [89]. An appropriate choice of perfluorinated ligand is necessary in order to enhance the NiIV stability, and negligible amount of NiIV-CF3 material was formed when starting from the parent compound 33b. In-depth mechanistic studies proved the release of free *R radicals and their subsequent recombination with 72 to build the NiIV. In contrast, 74a can be synthesized in high yield from 72 and aryl radicals (aryldiazonium salts combined with ferrocene; Scheme 18a) [89].

On the other hand, the diamagnetic NiIV-CH3 species 75 was prepared in moderate yield from the NiII-CF3 complex 22 and Mel, and was characterized using multinuclear NMR and EA. Most remarkably, 75 reacted with carbon-based *R radicals (generated from diacyl peroxides 73a–c) and underwent R–CH3 bond formation (65–78% yield; Scheme 18b) [89]. The operative radical substitution (S12) pathway and the absence of free *CH3 radicals were concluded according to: i) the observed product distribution; ii) the lack of ethane formation; and iii) the marginal influence of β-nitrostyrene.
with concomitant reduction of participation of cyclometallated Ni is diamagnetic due to antiferromagnetic coupling between the two low-spin Ni centers. This step that typically hampers catalytic turnover.

In this sense, seminal work by the group of Hillhouse has provided additional insights for the participation of cyclometallated Ni derivatives such as phenols or anilines. A useful and reliable tool in organic synthesis leading to relevant heterocyclic scaffolds and ary

Thorough mechanistic studies including one- and two-dimensional $^1$H NMR experiments, deuterium labelling, kinetic and crossover experiments, and EPR monitoring was performed by Diao and co-workers to prove the involvement of the [(py-pyrr)Ni$^{III}$](I(CH$_3$)$_2$]$_2$ species 79 in C(sp$^3$)–C(sp$^3$) bond formation (Scheme 19) [90]. The mixture of high-valent isomers 79 was achieved upon 1e$^-$ oxidation of the Ni$^{II}$-precursor 77 with I$_2$ at low temperature. The I-bridged binuclear complex 79 is diamagnetic due to antiferromagnetic coupling between the two low-spin Ni$^{III}$ centers. 79 was characterized using $^1$H and $^{13}$C NMR at low temperature and its structure was attributed according to DFT calculations and experimental observations. The capacity of 79 to mediate C(sp$^3$)–C(sp$^3$) couplings was demonstrated by simultaneous ethane formation and consumption of the Ni$^{III}$-CH$_3$ 79 (Scheme 19) [90]. The bimolecular pathway was evidenced by crossover experiments, the observed dependence of the [CH$_3$–CH$_3$]/[CH$_3$–I] ratio on [77], and the first order dependence in [79]. The synthesis of the Ni$^{III}$-CH$_3$ isomers in 79 and subsequent ethane formation involves: i) 1e$^-$ oxidation from Ni$^{II}$-CH$_3$ 77 to the square pyramidal Ni$^{III}$-CH$_3$ monomer 78 (EPR-identified); ii) dimerization of 78 leading to diamagnetic Ni$^{III}$ material 79 upon lutidine dissociation; and iii) C–C bond formation with concomitant reduction of 79 to Ni$^{II}$.

3. C–Heteroatom Bond Formation Mediated by High-Valent Ni$^{III}$ and Ni$^{IV}$

Amongst all types of cross-coupling reactions, C–heteroatom bond forming reactions constitute a useful and reliable tool in organic synthesis leading to relevant heterocyclic scaffolds and aryl derivatives such as phenols or anilines. In marked contrast to Pd-catalyzed cross-coupling reactions that operate through a M$^0$/M$^+$ catalytic loop, Ni$^{III}$ species are commonly accepted as key intermediates in C–heteroatom couplings since the early discoveries made by Kochi and co-worker in 1978 [20]. In this sense, seminal work by the group of Hillhouse has provided additional insights for the participation of cyclometallated Ni$^{III}$ compounds in the challenging C–heteroatom bond formation step that typically hampers catalytic turnover. Even though the authors failed to characterize
the high-valent Ni\textsuperscript{III}-intermediates, they have illustrated the potential utility of high-valent Ni\textsuperscript{III} species in C–heteroatom couplings giving rise to pyrrolidine [91,92], 3,4-dihydrocoumarin [92,93], or aziridine [94] scaffolds.

The reactivity of the aryl-Ni\textsuperscript{III}-X complexes 14-Cl and 14-Br towards alkyl Grignard and alkyl Zn derivatives was reported in 2014 (Scheme 4) [42]. In absence of an alkyl-type organometallic partner, the high-valent species 14-Cl and 14-Br underwent C(sp\textsuperscript{2})–Cl and C(sp\textsuperscript{2})–Br bond forming reactions upon warming up to r.t. (Scheme 20) [42]. Alternatively, the addition of [Fc\textsuperscript{+}[FPF\textsubscript{6}] to the aryl-Ni\textsuperscript{II} complexes 11-Cl and 11-Br in acetonitrile at −50 °C and ensuing exposure to r.t. leads to the corresponding aryl halides in up to 72% yield. The stirring of Ni\textsuperscript{III} complexes 14-Br and 81 in equimolar amounts at r.t. yielded the C(sp\textsuperscript{2})–X coupled products 80, 82–84 due to Ni\textsuperscript{III}-X bond dissociation and subsequent C–halide bond formation. This work has provided the first spectroscopic evidence for the Ni\textsuperscript{IV}-involvement in C–heteroatom coupling.

![Scheme 20](image)

**Scheme 20.** Proof of concept for the participation of well-defined aryl-Ni\textsuperscript{III}-X intermediates 14-Br and 81 in C(sp\textsuperscript{2})–X bond forming reactions. Adapted from reference [42].

The addition of bromine (Br\textsubscript{2}) or its safer substitute [BnNMe\textsubscript{3}][Br\textsubscript{3}] to 85 led to the nearly quantitative isolation of the Ni\textsuperscript{IV} Br\textsubscript{3} compound 86 bearing a bis-carbene pincer platform (\textsuperscript{3}HPP\textsubscript{CCC}; Scheme 21) [95]. XRD and \textsuperscript{1}H NMR confirmed the atom connectivity and the octahedral coordination in 86. The 2e\textsuperscript{−} reduction process in presence of organic substrates such as olefins or (mesityl)MgBr restores the Ni\textsuperscript{II}-Br 85 and yields the brominated products (Scheme 21).

![Scheme 21](image)

**Scheme 21.** C–Br couplings enabled by Ni\textsuperscript{IV}Br\textsubscript{3} species 86. Adapted from reference [95].

In analogy to Pd\textsuperscript{III}-chemistry [96–98], the role of intermetallic interactions when dealing with cross-coupling reactions and high-valent Ni homobimetals has been investigated (Scheme 22) [99]. Thus, the unprecedented Ni platforms 89 and 92 containing the benzo[\textit{h}]quinoline ligands were isolated and characterized. XRD, EPR, and DFT analyses on the homobimetallic complex 89 pointed to: \textit{i}) the presence of a binuclear Ni complex with a Ni–Ni bond order of \( \frac{1}{2} \); \textit{ii}) an average oxidation state of +2.5 for each Ni-center; and \textit{iii}) the stabilization of the electrodeficient [Ni\textsubscript{2}]\textsuperscript{5+} core by apical coordination of THF ligands. Addition of TDIT or PhICl\textsubscript{2} to 89 afforded the coupled products in 90% and 75% yield, respectively. In contrast, the addition of bromide anions to 89 resulted unfruitful. The 2e\textsuperscript{−} oxidation of the binuclear Ni\textsuperscript{II} complex 91 with [PhNMe\textsubscript{3}][Br\textsubscript{3}] gave rise to the Ni\textsuperscript{II}-Br–Ni\textsuperscript{III} species 92, which was characterized using XRD thereby proving the lack of a Ni–Ni bond. Warming up to r.t., the binuclear...
Ni\textsuperscript{III}–Br–Ni\textsuperscript{III} complex 92 underwent C(sp\textsuperscript{2})–Br bond formation and yielded 90-Br (Scheme 22) \[99\]. The high activity of the assumed Ni\textsuperscript{III}–X–Ni\textsuperscript{III} species coupled to the inactivity of the mixed-valence complex 89 seems to indicate that the C(sp\textsuperscript{2})–X coupling occurs at each Ni\textsuperscript{III}-center only in absence of any Ni–Ni interaction.

**Scheme 22.** C(sp\textsuperscript{2})–X couplings enabled by high-valent Ni\textsuperscript{III}–X–Ni\textsuperscript{III} homobimetallic complexes. Adapted from reference [99].

The selective incorporation of fluorine atoms to organic scaffolds is highly desirable due to: i) the unfavored R–F coupling from a well-defined R–M–F fragment; and ii) the importance of organofluorine chemistry in industry [44,46–48]. An impressive strategy to build C(sp\textsuperscript{2})–\textsuperscript{18}F bonds mediated by aryl-Ni\textsuperscript{III} precursors 93a–u, the iodine(III)-based oxidant 94 and aqueous \textsuperscript{18}F\textsuperscript{−} has been recently developed by Ritter and colleagues (Scheme 23) [100,101].

**Scheme 23.** C(sp\textsuperscript{2})–\textsuperscript{18}F coupling enabled by the Ni\textsuperscript{II}-platform 93a–u, aqueous \textsuperscript{18}F\textsuperscript{−} and 94. Adapted from references [100,101].

A common hallmark in the Ni\textsuperscript{II}-platform 93a–u resides in the sulfonamide moiety included in the bidentate ancillary ligand, a mandatory requirement for the C(sp\textsuperscript{2})–\textsuperscript{18}F bond forming reaction to proceed. While no high-valent Ni-species were initially detected, in situ EPR characterization of the key aryl-Ni\textsuperscript{III} species 96s,t-MeCN, and 96s,t-F was carried out in a subsequent article (Scheme 24) [102]. Enhanced stability of Ni\textsuperscript{III} was achieved upon the use of the more rigid Ni\textsuperscript{II} platforms 93s,t bearing the chelating \(\sigma\)-aryl-pyridine ligands. This strategy proved right, and the sulfonamide-stabilized key intermediates 96s-MeCN and 96s-F underwent C(sp\textsuperscript{2})–\textsuperscript{18}F coupling upon mild heating. In sharp contrast, the constrained geometry displayed by the parent aryl-Ni\textsuperscript{III} complexes 96t-MeCN and 96t-F prevented the aromatic fluorination.
displays a similar EPR pattern to (Scheme 26) [104]. The addition of an exogenous oxidant (PhI(PyOMe)) to their high instability. Nevertheless, the structure of analogous Ni ligand (Tp) was reacted with selectfluor to a yield. The Ni to their participation of Ni intermediates. The salts 103 and 104 were obtained by adding metallic alkoxides or hydroxides to 66 in alcoholic or aqueous media, respectively. Attempts to isolate 103 and 104 resulted unfruitful due to their high instability. Nevertheless, the structure of 103 was corroborated by: i) low-resolution XRD that confirmed its octahedral geometry; and ii) the large gave value of 2.192 obtained by EPR (vs. 2.145 and 2.125 for 101 and 66, respectively) that substantiated the coordination of the stronger σ- and π-donating methoxide ligands.

The NiOMe 103 decomposes in THF at r.t. to \(^{11}Bu\)N\(_3\)OCOMe and \(^{11}Bu\)N\(_3\)CH in ca. 1:1 ratio (Scheme 26) [104]. The addition of an exogenous oxidant (PhI(PyOMe))OTf\(_2\)) and additional KOMe improved the selectivity towards \(^{11}Bu\)N\(_3\)C–OMe bond formation. The parent NiOMe 106 displays a similar EPR pattern to 103 and decomposes rapidly to afford \(^{11}Bu\)N\(_3\)OCOMe (32%) and...
$^t$BuN$_3$CH (51%). The aryl–OR coupling takes place via a disproportionation reaction of 103 and 104 to generate an elusive [(BuN$_3$C)NiIV(OR)$_3$] species and subsequent R.E step.

Scheme 26. Ni$^{III}$-OR complexes 103 and 104, and their decomposition to build C(sp$^3$)–OR bonds. Adapted from reference [104].

Using the fully characterized Ni$^{III}$Br$_2$ complex 105 (Scheme 27) [105,106], C$_{ipso}$–heteroatom bond formation with several nucleophiles (water, methanol, ammonia, or hydrobromic acid) has been studied [107]. Metal–Ligand cooperation was invoked to cleave the H–Nu bond. Thus, a Me$_2$N-sidearm decoordinates and attacks the proton to create the aryl-Ni$_{III}$Nu moiety that is required to make possible the C(sp$^3$)–Nu coupling. Nevertheless, the coupled products are reached at best in ca. 50%. The structures of Ni$^{III}$ derivatives 109 and 108, prepared through halogen abstraction with AgSbF$_6$, were elucidated using XRD and EPR (Scheme 27) [108]. Both Ni$^{III}$ species 108 and 109 underwent C(sp$^3$)–O and C(sp$^3$)–N couplings at r.t. with concomitant formation of 110. The low yields were attributed in part to unwanted side-reactions namely: i) the generation of Ni$^{II}$ species 107 and 110; ii) protodemetallation; or iii) C(sp$^3$)–OH coupling with adventitious water.

Scheme 27. Ni$^{III}$-mediated C–O and C–N bond formation assisted by an NC$_{arom}$-N-pincer ligand. Adapted from references [107,108].

As mentioned before, the Ni$^{IV}$-CF$_3$ compounds 20 and 50 bearing tridentate scorpionate-type ligands (Py$_3$CH or Tp) underwent C(sp$^3$)–C(sp$^3$) cyclization (Schemes 6 and 12, respectively) [58].
Addition of heteroatom-based nucleophiles (i.e., alkoxides or amides) afforded the C(sp^3)–heteroatom coupled complexes 111a-d (78–94% yield; Scheme 28) [58,80]. Swain–Scott nucleophilicity parameters and kinetic studies pointed to a S_N2-type mechanistic pathway proceeding through nucleophilic attack of the exogenous heteroatom-based nucleophile into the Ni^{IV}–C(sp^3) bond. Comparative kinetic studies with analogous (Tp)Pd–F complexes proved the higher propensity of the Ni^{IV}–platform towards C(sp^3)–OAc coupling [80]. Intriguingly, the addition of [NBu_4][N_3] to 50 produced 3,3′-dimethylindoline (114) via double C–N bond forming reaction [58,80]. The formation of 114 occurs as follow: i) first C(sp^3)–N coupling giving rise to the diamagnetic Ni^{II}–CF_3 complex 111e; followed by ii) N_2-elimination and indoline-ring formation leading to the Ni^{II}–CF_3 113e; and iii) protodemetallation step with adventitious water.

Scheme 28. Proof of concept for the involvement of Ni^{IV} in C–heteroatom bond formation via R.E. Adapted from references [58,80].

The reactivity of closely related high-valent species 52 and 53 towards tetramethylammonium acetate was recently addressed as well (Scheme 29) [80,81]. As depicted in Scheme 12, the C(sp^3)–C(sp^3) cyclization to yield 21 proceeds more easily from the Ni^{II} 53 in dark conditions or exposed to daylight. Accordingly, addition of acetate as an exogenous nucleophile preferentially led to 21 in ca. 40% yield. In sharp contrast, the Ni^{IV} complex 52 underwent selective C(sp^3)–OAc bond formation. Protonolysis with trifluoroacetic acid (TFA) delivered 116a. The very distinct reactivity of 52 vs. 53 was attributed to the significantly enhanced electrophilicity of the Ni–C(sp^3) bond in the Ni^{IV} platform 52 vs. 53, thus favoring the nucleophilic attack via outer-sphere S_N2 pathway.

Scheme 29. Reactivity of cationic Ni^{III} and Ni^{IV} platforms 52 and 53 vs. [NBu_4][OAc]. Adapted from references [80,81].

The Ni^{IV}–O_2CCF_3 species 54 was synthesized through 2e^− oxidation of the anionic Ni^{II} complex 117 using bis(trifluoroacetoxy)iodobenzene (PhI(OTFA)_2; Scheme 30) [82]. 54 was fully characterized (NMR, XRD, and EA) and proved stable in solution at −35 °C. In contrast, it slowly underwent C(sp^3)–O bond formation in 2,5-dimethyltetrahydrofuran at r.t. Warming 54 up to 70 °C for 6 h led to heterocycle 119 through initial C–O bond formation giving rise to 118 followed by cyclization reaction and hydrolysis with moisture.
and the hydroxylated Ni species participating in C–H bond functionalization are very rare [120].

Electrophilic substitution, which works pretty smart when using Pt complexes, is preferred over the use of pre-functionalized substrates in view of reduced-waste production, at the same time the less activated C–H bonds makes these reactions more challenging [109–111]. Electrophilic substitution, which works pretty smart when using Pt and Pd catalysts fails for Ni and new approaches have focused on either Ni or high-valent Ni or Ni IV for this C–H activation. Remarkable efforts have been made in recent years on Ni-catalyzed C–H bond activation and functionalization enabled by directing groups, commonly requiring the use of sacrificial oxidants [112,113]. From a mechanistic point of view, most recent work by Chatani [14,15] and Ackermann [16,17] suggested a first C–H bond activation step enabling the formation of stable cyclometallated Ni species followed by a C–C or C–heteroatom coupling step from an in situ generated high-valent Ni species. Thus, there is current mechanistic debate dealing with the involvement of either Ni/Ni or Ni/Ni IV redox scenarios; different pathways were found viable by both computational and experimental methods [114–119]. However, reports elaborating on the isolation/identification of high-valent Ni species participating in C–H bond functionalization are very rare [120].

In 2016, the involvement of Ni species in oxidative C–H bond activation and functionalization was demonstrated (Scheme 32) [88]. A family of stable Ni III complexes bearing the tetradebate pyridinophane ligand (N3N3C) were prepared and characterized. The Ni III complexes 130 and 68 underwent aromatic cyanoalkylation assisted by an intramolecular (CF3 ligand in 130) or external

Mirica and colleagues have explored C–O bond formations using O2 or H2O2 as additives. These green and environmentally friendly oxidants allow to convert the nickelacycle 120 to high-valent Ni complexes, eventually acting as coupling partners (Scheme 31) [79]. NMR and GC-MS monitoring for the oxidation of 120 with O2 permitted the quantification of the reaction products 121 (protonolysis), 21 and 122-124 (C–C and C–O couplings, respectively). The Ni IV-hydroperoxo 125, the Ni IV-hydroxo 126 and the hydroxylated Ni III(cyclo-neophyl) species 128 were identified using cryo-ESI-MS that suggested their participation in the C–O bond forming reactions.

C–H Bond Activation and/or Functionalization Enabled by High-Valent Ni III and Ni IV

Direct C–H functionalization is preferred over the use of pre-functionalized substrates in view of reduced-waste production, at the same time the less activated C–H bonds makes these reactions more challenging [109–111].

Scheme 30. Synthesis of Ni IV–O2CCF3 complex 54 and C–O coupling to build the hemiketal 119. Adapted from reference [82].

Scheme 31. C–O bond formation enabled by high-valent Ni species 125, 126, and 128 generated from the Ni III precursor 120 and O2 or H2O2 as oxidants. Adapted from reference [79].

4. C–H Bond Activation and/or Functionalization Enabled by High-Valent Ni III and Ni IV

Direct C–H functionalization is preferred over the use of pre-functionalized substrates in view of reduced-waste production, at the same time the less activated C–H bonds makes these reactions more challenging [109–111]. Electrophilic substitution, which works pretty smart when using Pt II and Pd II catalysts fails for Ni II and new approaches have focused on either Ni II or high-valent Ni III or Ni IV for this C–H activation. Remarkable efforts have been made in recent years on Ni-catalyzed C–H bond activation and functionalization enabled by directing groups, commonly requiring the use of sacrificial oxidants [112,113]. From a mechanistic point of view, most recent work by Chatani [14,15] and Ackermann [16,17] suggested a first C–H bond activation step enabling the formation of stable cyclometallated Ni species followed by a C–C or C–heteroatom coupling step from an in situ generated high-valent Ni species. Thus, there is current mechanistic debate dealing with the involvement of either Ni II/Ni III or Ni II/Ni IV redox scenarios; different pathways were found viable by both computational and experimental methods [114–119]. However, reports elaborating on the isolation/identification of high-valent Ni species participating in C–H bond functionalization are very rare [120].

In 2016, the involvement of Ni III species in oxidative C–H bond activation and functionalization was demonstrated (Scheme 32) [88]. A family of stable Ni III complexes bearing the tetradebate pyridinophane ligand (N3N3C) were prepared and characterized. The Ni III complexes 130 and 68 underwent aromatic cyanoalkylation assisted by an intramolecular (CF3 ligand in 130) or external...
(KO\(^{137}\)Bu in 68) base that cleaves the C(sp\(^3\))–H bond. EPR monitoring and radical trap experiments pointed to the intermediacy of Ni\(^{III}\) species 131 and 132. These transient Ni\(^{III}\) species are formed through: i) deprotonation of MeCN to afford the ketenimine moiety in 131; and ii) ketenimine redistribution giving access to 132. The cyanoalkylated product \(\text{NP}_3\text{CCH}_2\text{CN}\) is finally released via reductive elimination from 132.

**Scheme 32.** C–H bond cyanomethylation promoted by Ni\(^{III}\). Adapted from reference [88].

Chatani carried out oxidative C-heteroatom couplings of quinoline-substituted amides catalyzed by Ni and suggested the participation of either Ni\(^{III}\) or Ni\(^{IV}\) intermediates [121]. Shortly after, Sanford and co-workers successfully prepared cyclometallated \(\sigma\)-alkyl and \(\sigma\)-aryl Ni\(^{II}\) complexes that were evaluated in C(sp\(^3\))–N or C(sp\(^3\))–I couplings upon oxidation with molecular I\(_2\) [122]. High-valent \(\sigma\)-aryl-Ni\(^{III}\) species are reachable upon 1e\(^-\) oxidation with silver salts, but failed to achieve the C(sp\(^3\))–I coupling. On the contrary, the \(\sigma\)-alkyl Ni\(^{III}\) complex 136 was isolated in 91% yield, was fully characterized using NMR and XRD, and gave rise to the \(\beta\)-lactam 135 via C(sp\(^3\))–N cyclizative coupling (Scheme 33) [122]. Nevertheless, harsh conditions were required and 136 resulted inactive under catalytic conditions.

**Scheme 33.** Access to cyclometallated \(\sigma\)-alkyl Ni\(^{III}\) complex 136 and synthesis of the \(\beta\)-lactam 135. Adapted from reference [122].

C(sp\(^3\))–H functionalization enabled by high-valent Ni compounds has been reported by Ackermann (Scheme 34) [123]. They carried out a nickellaelectro-catalyzed C(sp\(^3\))–H bond alkoxylation of aminooquinoline-based substrates such as 137, and provided support for: i) the Ni\(^{III}\)-mediated C(sp\(^3\))–OR coupling in presence or absence of electricity; and ii) the catalytic performance of the cyclometallated \(\sigma\)-aryl Ni\(^{III}\) 138. This Ni\(^{III}\) 138 was obtained in 39% yield upon electrolytic oxidation from [Ni\(^{II}\]COD\(_2\)] and 137, and was characterized using XRD and cyclic voltammetry (easy over-oxidation at 0.50 V vs. Fe\(^{0+/+}\)).
when the triflate was replaced by tetrafluoroborate. A Ni
constitutes the first isolated high-valent Ni species enabling C(sp
with excellent yields (up to 94%) and intriguing selectivity.

Mechanistic studies consisting of radical trap and competition experiments, evaluation of kinetic
isotope effects and DFT-analysis pointed to: i) facile C(sp²)–H bond scission; ii) involvement of
radicals; and iii) C(sp²)–OR coupling occurring from a transient formally σ-aryl NiIV key intermediate,
which is better described as a ligand centered radical NiIII species [123]. In short, the NiIII complex
138 constitutes the first isolated high-valent Ni species enabling C(sp²)–H functionalization under
stoichiometric and catalytic conditions [14–19,114–119].

An original ligand design strategy was employed to accomplish the C–H bond nickelation of arenes
and alkanes induced by N-fluoro-2,4,6-trimethylpyridinium triflate (NFTPT; Scheme 35) [124,125]. The
identity of the NiIV platforms 142a–c and 144-X was corroborated using NMR and XRD. The decisive
role of triflate to assist the C–H to C–Ni bond conversion was demonstrated through the isolation of
143a when the triflate was replaced by tetrafluoroborate. A NiIV-driven C–H bond nickelation was
found to be the preferred pathway by computational means (vs. the competing NiIII-mediated path).
Reaction of isolated 144-OTf with external nucleophiles 146a–h led to the C–Nu coupled products
146a–h, thereby ascertaining its capacity to promote C–C and C–heteroatom bond forming processes.

Scheme 34. Synthesis of the σ-aryl-NiIII intermediate 138, and 138-enabled C(sp²)–OPr bond formation
in the presence or absence of electricity. Adapted from reference [123].

Scheme 35. C–H bond breaking/C–NiIV bond forming sequence via NiIII/NiIV redox manifold and C–C
and C–heteroatom couplings mediated by 144-OTf. Adapted from references [124,125].

Our group has contributed to the field of C(sp²)–H bond functionalization and performed
aromatic trifluoromethylations enabled by high-valent NiIII-CF₃ and NiIV-CF₃ compounds named
149, 149-py, and 148, respectively (Scheme 36) [126]. These high-valent species are: i) stabilized
by simple, monodentate ligands (py, CF₃, and F-itself); ii) easily accessible from identical sources
(i.e., [(py)₂NiIII(CF₃)] (147) and XeF₂); iii) remarkably stable (isolable); and iv) authenticated using
XRD and EPR (149, 149-py) or XRD and NMR (148). Both NiIII-CF₃ and NiIV-CF₃ species underwent
the C–H bond breaking/C–CF₃ bond forming sequence of arenes (1,2-dichlorobenzene or pyridine)
with excellent yields (up to 94%) and intriguing selectivity.
The structures of compounds Ni$^{II}$-CF$_3$, Ni$^{III}$-CF$_3$, Ni$_{\text{tetraaza}}$-CF$_3$ and Ni$^{IV}$-CF$_3$ were ascertained by exhaustive spectroscopic characterization and DFT-calculations. This work has demonstrated the ability of the Ni$^{III}$-oxyl 152 and the Ni$^{III}$-OCI 154 to promote C(sp$^3$)–H bond oxidation of organic substrates.

Company and co-workers have synthesized the Ni$^{III}$-oxyl complex 152 [128] and the high-valent compounds Ni$^{IV}$-Cl 153 and Ni$^{III}$-OCI 154 by reaction of the tetraaza-Ni$^{II}$ precursor 151 and meta-chloroperbenzoic acid (H$m$CPBA) and CaOCl + acetic acid [129], respectively (Scheme 38). The structures of 152–154 were ascertained by exhaustive spectroscopic characterization and DFT-calculations. This work has demonstrated the ability of the Ni$^{III}$-oxyl 152 and the Ni$^{III}$-OCI 154 to promote C(sp$^3$)–H bond oxidation of organic substrates.
A dinuclear NiIII complex participating in C–H bond activation and the ensuing C–C or C=O bond forming reactions were published by Morimoto, Itoh and co-workers [130]. The NiIII species 156 bearing the triazadentate ligand dpema was synthesized by treatment of the NiII precursor 155 with H2O2 in acetone at −90 °C (Scheme 39) [130]. Anion exchange with NaBPh4 permitted the selective crystallization of 156 that was appropriately characterized (XRD, EPR, magnetic measurements (Superconducting Quantum Interference Device (SQUID)), Raman, and ESI-MS). The keen analysis of 156 demonstrated the unprecedented triplet ground state for a high-valent [M2(μ-O)2] core, along with the ferromagnetic coupling of the NiIII centers. In addition, 156 mediated the selective C–H bond functionalization of 2,4-di(tert-butyl)phenol (157) or xanthene (158) yielding 159 and 160, respectively.

A dinuclear NiIV that mediates C–H bond functionalization was synthesized and characterized by Swart and Browne (Scheme 40) [131]. The complex [(Me3tacn)NiIV(μ-O)2]2+ (162), attained from the dinuclear NiII complexes 161a,b and NaOCl, represents a rare example of an isolated dinuclear NiIV complex. Its structure was determined by NMR, Raman spectroscopy (labelling experiments), XANES, XES, ESI-MS, and computational data. The C–H functionalization mediated by 162 proved viable for several substrates (methanol, xanthene, 9,10-dihydroanthracene, and fluorene).

5. Miscellaneous

Other interesting transformations dealing with high-valent Ni complexes that are involved in cross-coupling events and bond forming reactions are disclosed in this section. Hereafter,
a short selection of cyclization reactions, C–heteroatom or N–N bond forging reactions, and olefin functionalization mediated by Ni[III] or Ni[IV] are collected.

A first example is constituted by the 141-catalyzed synthesis of heterocyclic salt [164][Cl] (Scheme 41) [125]. In this work, the functionalized bipyridine 163 was converted to [164][Cl] in 76% yield upon mild heating in presence of [NMe₂][Cl], NFTPT (excess) and 20 mol% of Ni[II]-CF₃ catalyst 141 (TON ca. 4). The viability of a Ni[II]/Ni[IV] redox scenario was strongly supported by the stoichiometric reaction of 144-O Tf with chloride anions that provided the heterocyclic salt [164][X] (X = Cl, OTf) in nearly quantitative yield.

**Scheme 41.** C(sp³)-H bond breaking/C(sp³)–N bond forming sequence via Ni[II]/Ni[IV] catalysis. Synthesis of the heterocyclic salt [164][X]. Adapted from reference [125].

Diao and co-workers discovered the N–N coupling of the guanidine derivative triazabicyclocedene (TBD) starting from the Ni[II] complex 165 and PhICl₂ (Scheme 42) [132]. Addition of PhICl₂ (0.5 equivalents) to 165 at low temperature allowed the isolation and characterization of the Ni[II]-Ni[III]-Cl mixed valence compound 167. The trans-influence of the chloride ligand in 167 prevented Ni–Ni bond interactions giving rise to a rare Ni[II]-Ni[III]-Cl homobimetallic complex with a zero order Ni–Ni bond. The isolated material 167 resulted to be coupling inactive. In the presence of PhICl₂, 167 underwent instantaneous N–N bond formation involving an elusive Cl-Ni[III]-Ni[III]-Cl species 168, which is reminiscent of Ritter’s Pd[III] chemistry [98].

**Scheme 42.** N–N bond formation from an assumed Ni[III]-Ni[III] species 168, generated from the mixed valence compound 167 and PhICl₂. Adapted from reference [132].

An indazole scaffold was synthesized in high yield by Vicic and co-workers from the perfluorinated metallacycle 169 in presence of mild oxidant, base and a fluoride source (Scheme 43) [133]. Once isolated and conveniently characterized (NMR and EA), the isolated Ni[IV]F₂ 172 underwent N–N cyclizative coupling upon addition of 173 and pyridine to build 170. The formation of 170 requires: i) coordination of 173 to 172; ii) deprotonation of the N–H moiety ligated to Ni[IV]; and iii) R.E. step and recovery of the Ni[II]C₄F₈ fragment.

**Scheme 43.** Isolable Ni[IV]F₂ 172 and its capacity to promote N–N bond forming processes. Adapted from reference [133].
The imido transfer reaction from M=NR fragments to organic substrates represents an innovative approach to build C–N bonds. In this sense, Warren disclosed the synthesis of the Ni\textsuperscript{III}–imido complex 174 by reacting the Ni\textsuperscript{II} precursor 173 with adamantylazide (AdN\textsubscript{3} in Scheme 44) [134]. The Ni\textsuperscript{III}=NAd complex was isolated in 52% yield and studied using XRD, EPR, and DFT-calculations. The imido-group transfer from 174 proved viable towards CO and CN\textsuperscript{+}Bu yielding cumulenes 175 and 176 in high yields.

\begin{center}
\textbf{Scheme 44.} Imido-group transfer reactions mediated by the Ni\textsuperscript{III}=NAd complex 174. Adapted from reference [134].
\end{center}

van Koten performed Kharasch additions involving aryl-Ni\textsuperscript{III} pincer complexes allowing for the double functionalization of olefins [135–141]. Mechanistic studies (IR, EPR, and NMR) using the aryl-Ni\textsuperscript{II} 177 pointed to the participation of mononuclear aryl-Ni\textsuperscript{II} intermediates (Scheme 45) [135–140]. The C–halogen bond scission and concomitant Ni\textsuperscript{II} to Ni\textsuperscript{III} oxidation was found to be the rate determining step of the catalytic cycle [138]. Later, the same group isolated and characterized (XRD, EPR, and EA) the aryl-Ni\textsuperscript{II}Cl\textsubscript{2} species 178 by reacting the corresponding aryl-Ni\textsuperscript{II}–Cl complex and CCl\textsubscript{4}, thus proving right their initial hypothesis [140]. Zargarian isolated the catalytically active Ni\textsuperscript{III}X\textsubscript{2} complexes 179 and 180a–c bearing bis(phosphinite) (POCOP) or phosphinite-amine (POCN) based pincer-type ligands (Scheme 45) [141–143]. The novel Ni\textsuperscript{III} platforms were authenticated using diverse techniques (including XRD), and mediated catalytic Kharasch additions.

\begin{center}
\textbf{Scheme 45.} Ni-pincer complexes involved in Kharasch addition reactions [135–143].
\end{center}

6. Summary and Conclusions

The study of fundamental organonickel chemistry and the use of nickel complexes in organometallic catalysis represent a jointly emerging research field. The main reasons are: i) the higher abundance and lower price of Ni compared with 4d and 5d metals; ii) the very rich and diverse redox reactivity of organonickel compounds; and iii) its enhanced reactivity that provides more room for reaction discovery. However, the air and moisture sensitivity of Ni-compounds and their propensity to undergo single electron transfer (SET) processes makes the mechanistic elucidation more challenging. This is particularly true for the commonly invoked, yet rarely proved, involvement of high-valent organonickel species in catalytic reaction mechanisms, including the highly demanded cross-coupling reactions. Here, the appropriate design of the ancillary ligand plays a pivotal role in improving the stability of Ni\textsuperscript{III} and Ni\textsuperscript{IV} complexes, thus allowing for their characterization and the discovery of their unprecedented reactivity. In this sense, this review aims to provide a general overview of most common strategies to successfully stabilize coupling active high-valent Ni species, namely: i) the coordination of polydentate N-donor ligands (Tp, Py\textsubscript{3}CH, pyridinophane derivatives ...); ii) the incorporation of nickelacyclic cores; or iii) the use of strong \(\sigma\)-donating perfluorinated ligands (CF\textsubscript{3} or the C\textsubscript{4}F\textsubscript{8} fragment).
On the other hand, most representative work enclosed in the field of cross-coupling reactions enabled by spectroscopically characterized Ni^{III} and Ni^{IV} compounds are herein disclosed [144,145]. As a representative example, while low-valent Ni catalysts perform well for classical cross-coupling events, the intermediacy of high-valent Ni compounds becomes necessary in order to achieve more challenging transformations such as the C–F or C–CF_{3} bond-forming reactions. In addition to their enhanced activity, distinct reactivity patterns are displayed quite frequently by high-valent organometallic compounds. This was perfectly illustrated by the efficient C(sp^{3})–heteroatom coupling found for the Ni^{IV} platforms 50 and 52 instead the more favorable C(sp^{2})–heteroatom bond formation, commonly mediated by low-valent Ni compounds.

The study and deep understanding of the elementary reactions occurring for the high oxidation states of Ni^{III} or Ni^{IV} permitted to broaden the scope of transformations enabled by Ni^{III} and Ni^{IV} species. The current State of the Art for Ni^{III} and Ni^{IV} mediated bond forming reactions includes: i) C–C and C–heteroatom bond formation; ii) C–H bond functionalization; and iii) alternative N–N and C–heteroatom couplings. Most remarkably, the first two approaches to Ni^{II}/Ni^{IV} catalysis have been reported recently and allowed for the C–H bond trifluoromethylation of industrially-relevant (hetero)arenes and C–N cyclization reactions. With no doubt, future work will expand the array of transformations mediated by Ni^{III} and Ni^{IV} species, and more catalytic applications mediated by a Ni^{II}/Ni^{IV} redox scenario will appear soon.

Acknowledgments: CNRS and UPS are acknowledged for continuous support. Ana M. Geer is acknowledged for valuable comments and proofreading of this manuscript. N.N. thanks the Institut de Chimie de Toulouse for the attribution of the ICT Young Investigator Award 2020.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Gildner, P.G.; Colacot, T.J. Reactions of the 21st Century: Two Decades of Innovative Catalyst Design for Palladium-Catalyzed Cross-Couplings. Organometallics 2015, 34, 5497–5508. [CrossRef]
2. Li, H.; Johansson Seechurn, C.C.C.; Colacot, T.J. Development of Preformed Pd Catalysts for Cross-Coupling Reactions, Beyond the 2010 Nobel Prize. ACS Catal. 2012, 2, 1147–1164. [CrossRef]
3. Johansson Seechurn, C.C.C.; Kitching, M.O.; Colacot, T.J.; Snieckus, V. Palladium-Catalyzed Cross-Coupling: A Historical Contextual Perspective to the 2010 Nobel Prize. Angew. Chem. Int. Ed. 2012, 51, 5062–5085. [CrossRef] [PubMed]
4. Lavoie, C.M.; Stradiotto, M. Bisphosphines: A Prominent Ancillary Ligand Class for Application in Nickel-Catalyzed C–N Cross-Coupling. ACS Catal. 2018, 8, 7228–7250. [CrossRef]
5. Budnikova, Y.H.; Vicic, D.A.; Klein, A. Exploring Mechanisms in Ni Terpyridine Catalyzed C–C Cross-Coupling Reactions—A Review. Inorganics 2018, 6, 18. [CrossRef]
6. Shi, R.; Zhang, Z.; Hu, X. Nickamine and Analogous Nickel Pincer Catalysts for Cross-Coupling of Alkyl Halides and Hydroisilylation of Alkenes. Acc. Chem. Res. 2019, 52, 1471–1483. [CrossRef]
7. Cornella, J.; Zarate, C.; Martin, R. Metal-Catalyzed Activation of Ethers via C–O Bond Cleavage: A New Strategy for Molecular Diversity. Chem. Soc. Rev. 2014, 43, 8081–8097. [CrossRef]
8. Borjesson, M.; Moragas, T.; Gallego, D.; Martin, R. Metal-Catalyzed Carboxylation of Organic (Pseudo)halides with CO_{2}. ACS Catal. 2016, 6, 6739–6749. [CrossRef]
9. Baba, S.; Negishi, E. A Novel Stereospecific Alkenyl–Alkenyl Cross-Coupling by a Palladium- or Nickel-Catalyzed Reaction of Alkenylalanes with Alkenyl Halides. J. Am. Chem. Soc. 1976, 98, 6729–6731. [CrossRef]
10. Negishi, E.-I.; King, A.O.; Okukado, N. Selective Carbon–Carbon Bond Formation via Transition Metal Catalysis. A Highly Selective Synthesis of Unsymmetrical Biaryls and Diarylmethanes by the Nickel- or Palladium-Catalyzed Reaction of Aryl- and Benzylzinc Derivatives with Aryl Halides. J. Org. Chem. 1977, 42, 1821–1823. [CrossRef]
11. Hu, X. Nickel-Catalyzed Cross Coupling of Non-Activated Alkyl Halides: A Mechanistic Perspective. Chem. Sci. 2011, 2, 1867–1886. [CrossRef]
12. Tasker, S.Z.; Standley, E.A.; Jamison, T.F. Recent Advances in Homogeneous Nickel Catalysis. Nature 2014, 509, 299–309. [CrossRef] [PubMed]

13. Ananikov, V.P. Nickel: The “Spirited Horse” of Transition Metal Catalysis. ACS Catal. 2015, 5, 1964–1971. [CrossRef]

14. Aihara, Y.; Chatani, N. Nickel-Catalyzed Direct Arylation of C(sp3)–H Bonds in Aliphatic Amides via Bidentate-Chelation Assistance. J. Am. Chem. Soc. 2014, 136, 898–901. [CrossRef] [PubMed]

15. Uemura, T.; Yamaguchi, M.; Chatani, N. Phenyllithiummethylammonium Salts as Methylation Reagents in the Nickel-Catalyzed Methylation of C–H Bonds. Angew. Chem. Int. Ed. 2016, 55, 3162–3165. [CrossRef]

16. Ruan, Z.; Lackner, S.; Ackermann, L. A General Strategy for the Nickel-Catalyzed C–H Alkylation of Anilines. Angew. Chem. Int. Ed. 2016, 55, 3153–3157. [CrossRef]

17. Zhang, S.-K.; Samanta, R.C.; Sauermann, N.; Ackermann, L. Nickel-Catalyzed Electrooxidative C–H Amination: Support for Nickel(IV). Chem. Eur. J. 2018, 24, 19166–19170. [CrossRef]

18. Xu, J.; Qiao, L.; Shen, J.; Chai, K.; Shen, C.; Zhang, P. Nickel(II)-Catalyzed Site-Selective C–H Bond Trifluoromethylation of Arylamine in Water through a Coordinating Activation Strategy. Org. Lett. 2017, 19, 5661–5664. [CrossRef]

19. Liu, X.; Mao, G.; Qiao, J.; Xu, C.; Liu, H.; Ma, J.; Sun, Z.; Chu, W. Nickel-catalyzed C–H Bond Trifluoromethylation of 8-Aminoquinoline Derivatives by Acyl-directed Functionalization. Org. Chem. Front. 2019, 6, 1189–1193. [CrossRef]

20. Tsou, T.T.; Kochi, J.K. Reductive Coupling of Organometals Induced by Oxidation-Detection of Metastable Paramagnetic Intermediates. J. Am. Chem. Soc. 1978, 100, 1634–1635. [CrossRef]

21. Lee, C.M.; Chuang, Y.L.; Chiang, C.Y.; Lee, G.-H.; Liaw, W.-F. Mononuclear Ni(II) Complexes [Ni(II)(L)(PC6H5-CN)](PF6): Relevance to the Nickel Site of [NiFe] Hydrogenases. Inorg. Chem. 2006, 45, 10895–10904. [CrossRef] [PubMed]

22. Chou, T.W.; Liaw, W.F. Mononuclear Nickel(III) Complexes [Ni(III)(OR)(PC6H5-CN2)](L)–(R = Me, Ph) Containing the Terminal Alkoxide Ligand: Relevance to the Nickel Site of Oxidized-Form [NiFe] Hydrogenases. Inorg. Chem. 2008, 47, 7908–7913. [CrossRef] [PubMed]

23. Lee, C.M.; Chen, C.H.; Liao, F.X.; Hu, C.-H.; Lee, G.-H. Mononuclear Ni(III)-Alkyl Complexes (Alkyl = Me and Et): Relevance to the Acetyl-CoA Synthase and Methyl-CoM Reductase. J. Am. Chem. Soc. 2010, 132, 9256–9258. [CrossRef] [PubMed]

24. Kuwamura, N.; Kitano, K.; Hirotsu, M.; Nishioka, T.; Teki, Y.; Santo, R.; Ichimura, A.; Hashimoto, H.; Wright, J.; Kinoshiba, I. Redox-Controlled, Reversible Rearrangement of a Tris(2-pyridylthio)methyl Ligand on Nickel to an Isomer with an “N,S-confused” 2-Pyridylthiolato Arm. Chem. Eur. J. 2011, 17, 10708–10715. [CrossRef] [PubMed]

25. Pfaeff, F.F.; Heims, F.; Kundu, S.; Mebs, S.; Ray, K. Spectroscopic Capture and Reactivity of S = 1/2 Nickel(III)–Oxygen Intermediates in the Reaction of a Ni(II) Salt with mCPBA. Chem. Commun. 2012, 48, 3730–3732. [CrossRef] [PubMed]

26. Chatterjee, S.K.; Roy, S.; Barman, S.K.; Maji, R.C.; Olmstead, M.M.; Patra, A.K. Shuttling of Nickel Oxidation States in N2S Coordination Geometry versus Donor Strength of Tridentate N2S Donor Ligands. Inorg. Chem. 2012, 51, 7625–7635. [CrossRef]

27. Baucam, E.L.; Drago, R.S. Nickel(II) and Nickel(IV) Complexes of 2,6-Diacetylpyridine Dioxide. J. Am. Chem. Soc. 1971, 93, 6469–6475. [CrossRef]

28. Robbins, J.L.; Edelstein, N.; Spencer, B.; Smart, J.C. Syntheses and Electronic-Structures of Decamethylmetalallocenes. J. Am. Chem. Soc. 1982, 104, 1882–1893. [CrossRef]

29. Kolle, U.; Khouzami, F.; Lueken, H. Permethylnickelocenes III. Decamethylnickelocene: The Neutral Sandwich Complex, the Monocation, the Dication, and Their Addition Reactions. Chem. Ber. 1982, 115, 1178–1196. [CrossRef]

30. Klein, H.-F.; Bickelhaupt, A.; Jung, T.; Cordier, G. Syntheses and Properties of the First Octahedral Dioorganonickel(IV) Compounds. Organometallics 1994, 13, 2557–2559. [CrossRef]

31. Klein, H.F.; Bickelhaupt, A.; Hammerschmitt, B. Ligand-Induced Fragmentation of MethylNickel Phenolates Containing a 2-Aldehyde Function-Structure of (3-Tert-butyl-5-methyl-2-oxobenzoyl)-tris(trimethylphosphine)nickel. Organometallics 1994, 13, 2944–2950. [CrossRef]
32. Klein, H.-F.; Bickelhaupt, A.; Lemke, M.; Jung, T.; Röhr, C. Synthesis and Structure of Octahedral Nickel(IV) Complexes Containing Two Chelating Acylphenolato Ligands. *Chem. Lett.* 1995, 24, 467–468. [CrossRef]
33. Klein, H.-F.; Bickelhaupt, A.; Lemke, M.; Sun, H.; Brand, A.; Jung, T.; Röhr, C.; Flörke, U.; Haupt, H.-J. Trimethylphosphine Complexes of Dihorganonickel(IV) Molecules. *Organometallics* 1997, 16, 668–676. [CrossRef]
34. Chen, W.Z.; Shimada, S.; Tanaka, M.; Kobayashi, Y.; Saigo, K. Reaction of \([2-(SiH_2)C_6H_4]_2SiH_2\) with \(Ni(ET_2PCH_2CH_2Pt_2)(PEt_3)_2\): Characterization of \(\eta^2-(Si–H)Ni\) and \(Ni^{IV}–H\) Complexes. *J. Am. Chem. Soc.* 2004, 126, 8072–8073. [CrossRef]
35. Dimitrov, V.; Linden, A. A Pseudotetrahedral, High-Oxidation-State Organonickel Compound: Synthesis and Structure of Bromotris(1-norbornyl)nickel(IV). *Angew. Chem. Int. Ed.* 2003, 42, 2631–2633. [CrossRef]
36. Klein, H.-F.; Kraikivskii, P. Unexpected Formation of a Molecular Tetraalkyl Nickel Complex from an Olefin(Nickel(0) System. *Angew. Chem. Int. Ed.* 2009, 48, 260–261. [CrossRef]
37. Carnes, M.; Buccella, D.; Chen, J.Y.-C.; Ramirez, A.P.; Turro, N.J.; Nuckolls, C.; Steigerwald, M. A Stable Diphosphine Nickel Complex. *Chem. Soc. Rev.* 2011, 41, 4475–4521. [CrossRef]
38. Liang, T.; Neumann, C.N.; Ritter, T. Introduction of Fluorine and Fluorine-Containing Functional Groups. Angew. Chem. Int. Ed. 2013, 52, 8214–8264. [CrossRef] [PubMed]
39. Alonso, C.; Martinez de Marigorta, E.; Rubiales, G.; Palacios, F. Carbon Trifluoromethylation Reactions of Hydrocarbon Derivatives and Heteroarenes. *Chem. Rev.* 2015, 115, 1847–1935. [CrossRef] [PubMed]
40. Müller, K.; Faeh, C.; Diederich, F. Fluorine in Pharmaceuticals: Looking Beyond Intuition. *Science* 2014, 317, 1881–1886. [CrossRef] [PubMed]
41. Purser, S.; Moore, P.R.; Swallow, S.; Gouverneur, V. Fluorine in Medicinal Chemistry. *Chem. Soc. Rev.* 2008, 37, 320–330. [CrossRef] [PubMed]
42. Anastas, P.T.; Warner, J.C. *Green Chemistry Theory and Practice*; Oxford University Press: Oxford, UK, 1998.
43. Sheldon, R.A.; Arends, I.W.C.E.; Henefeld, U. *Green Chemistry and Catalysis*; Wiley-VCH: Weinheim, Germany, 2007.
44. Poliakoff, M.; Fitzpatrick, J.M.; Farren, T.R.; Anastas, P.T. Green Chemistry: Science and Politics of Change. *Science* 2002, 297, 807–810. [CrossRef]
45. Dubinina, G.G.; Brennessel, W.W.; Miller, J.L.; Vicic, D.A. Exploring Trifluoromethylation Reactions at Nickel: A Structural and Reactivity Study. *Organometallics* 2008, 27, 3933–3938. [CrossRef]
46. Jover, J.; Miloserdov, F.M.; Benet-Buchholz, J.; Grushin, V.V.; Maseras, F. On the Feasibility of Nickel-Catalyzed Trifluoromethylation of Aryl Halides. *Organometallics* 2014, 33, 6531–6543. [CrossRef]
47. Bour, J.R.; Roy, P.; Canty, A.J.; Kampf, J.W.; Sanford, M.S. Oxidatively Induced Aryl–CF₃ Coupling at Diphosphine Nickel Complexes. *Organometallics* 2020, 39, 3–7. [CrossRef]
55. Zhang, C.-P.; Wang, H.; Klein, A.; Biewer, C.; Stirnat, K.; Yamaguchi, Y.; Xu, L.; Gomez-Benitez, V.; Vicic, D.A. A Five-Coordinate Nickel(II) Fluoroalkyl Complex as a Precursor to a Spectroscopically Detectable Ni(III) Species. J. Am. Chem. Soc. 2013, 135, 8141–8144. [CrossRef] [PubMed]

56. Yu, S.; Dudkina, Y.; Wang, H.; Kholin, K.V.; Kadirov, M.K.; Budnikova, Y.H.; Vicic, D.A. Accessing Perfluoroalkyl Nickel(II), (III), and (IV) Complexes Bearing a Readily Attached [C₄F₄] ligand. Dalton Trans. 2015, 44, 19443–19446. [CrossRef]

57. Tang, F.; Ritter, T. Mechanism of Electrophilic Fluorination with Pd II-Aryl–CF₃ Coupling. J. Am. Chem. Soc. 2012, 134, 12002–12009. [CrossRef] [PubMed]

58. Bour, J.R.; Camasso, N.M.; Sanford, M.S. Oxidation of NiII to NiIV with Aryl Electrophiles Enables Ni-Mediated Aryl–CF₃ Coupling. J. Am. Chem. Soc. 2015, 137, 8034–8037. [CrossRef]

59. Watson, M.B.; Rath, N.P.; Mirica, L.M. Oxidative C–C Bond Formation Reactivity of Organometallic NiII, NiIII, and NiIV Complexes. J. Am. Chem. Soc. 2017, 139, 35–38. [CrossRef]

60. Tellis, J.C.; Primer, D.N.; Molander, G.A. Single-Electron Transmetalation in Organoboron Cross-Coupling by Photoredox/Nickel Dual Catalysis. Science 2014, 345, 433–436. [CrossRef] [PubMed]

61. Zuo, Z.W.; Ahneman, D.T.; Chu, L.L.; Terrett, J.A.; Doyle, A.G.; MacMillan, D.W.C. Merging Photoredox with Nickel Catalysis: Coupling of α-Carboxyl sp²-Carbons with Aryl Halides. Science 2014, 345, 437–440. [CrossRef] [PubMed]

62. Tasker, S.Z.; Jamison, T.F. Highly Regioselective Indoline Synthesis under Nickel/Photoredox Dual Catalysis. J. Am. Chem. Soc. 2015, 137, 9531–9534. [CrossRef] [PubMed]
77. Schultz, J.W.; Fuchigami, K.; Zheng, B.; Rath, N.P.; Mirica, L.M. Oxidatively-Induced Aromatic Cyanation Mediated by Ni

78. Smith, S.M.; Rath, N.P.; Mirica, L.M. Axial Donor Effects on Oxidatively Induced Ethane Formation from Nickel-Dimethyl Complexes. Organometallics 2019, 38, 3602–3609. [CrossRef]

79. Smith, S.M.; Planas, O.; Gomez, L.; Rath, N.P.; Ribas, X.; Mirica, L.M. Aerobic C–C and C–O Bond Formation Reactions Mediated by High-Valent Nickel Species. Chem. Sci. 2019, 10, 10366–10372. [CrossRef]

80. Camasso, N.M.; Canty, A.J.; Ariaфard, A.; Sanford, M.S. Experimental and Computational Studies of High-Valent Nickel and Palladium Complexes. Organometallics 2017, 36, 4382–4393. [CrossRef]

81. Roberts, C.C.; Camasso, N.M.; Bowes, E.G.; Sanford, M.S. Impact of Oxidation State on Reactivity and Selectivity Differences between Nickel(III) and Nickel(IV) Alkyl Complexes. Angew. Chem. Int. Ed. 2019, 58, 9104–9108. [CrossRef]

82. Meucci, E.A.; Camasso, N.M.; Sanford, M.S. An Organometallic Ni^{IV} Complex That Participates in Competing Transmetalation and C(sp^2)–O Bond-Forming Reductive Elimination Reactions. Organometallics 2017, 36, 247–250. [CrossRef]

83. Rovira, M.; Roldan-Gomez, S.; Martin-Diaconescu, V.; Whiteoak, C.J.; Company, A.; Luis, J.M.; Ribas, X. Trifluoromethylation of a Well-Defined Square-Planar Aryl-Ni^{III} Complex involving Ni^{III}/CF_{3}^{*} and Ni^{IV}/CF_{3} Intermediate Species. Chem. Eur. J. 2017, 23, 11662–11668. [CrossRef] [PubMed]

84. Jongbloed, L.S.; Vogt, N.; Sandleben, A.; de Bruin, B.; Klein, A.; van der Vlugt, J.I. Nickel–Alkyl Complexes with a Reactive PNC-Pincer Ligand. Eur. J. Inorg. Chem. 2018, 2018, 2408–2418. [CrossRef] [PubMed]

85. Powers, D.C.; Ritter, T. Bimetallic Pd^{II} Complexes in Palladium-Catalysed Carbon–Heteroatom Bond Activation Mediated by Ni^{III}. J. Am. Chem. Soc. 2016, 138, 5777–5780. [CrossRef]

86. Bour, J.R.; Ferguson, D.M.; McClain, E.J.; Kampf, J.W.; Sanford, M.S. Connecting Organometallic Ni^{III} and Ni^{IV}: Reactions of Carbon-Centered Radicals with High-Valent Organonickel Complexes. J. Am. Chem. Soc. 2019, 141, 8914–8920. [CrossRef]

87. Xu, H.; Diccianni, J.B.; Katigbak, J.; Hu, C.; Zhang, Y.; Diao, T. Bimetallic C–C Bond-Forming Reductive Elimination from Nickel. J. Am. Chem. Soc. 2016, 138, 4779–4786. [CrossRef]

88. Han, R.; Hillhouse, G.L. Carbon–Oxygen Reductive-Elimination from Nickel(II) Oxametallacycles and Factors That Control Formation of Ether, Aldehyde, Alcohol, or Ester Products. J. Am. Chem. Soc. 1997, 119, 8135–8136. [CrossRef]

89. Lin, B.L.; Clough, C.R.; Hillhouse, G.L. Interactions of Aziridines with Nickel Complexes: Oxidative-Addition and Reductive-Elimination Reactions that Break and Make C–N Bonds. J. Am. Chem. Soc. 2002, 124, 2890–2891. [CrossRef] [PubMed]

90. Koo, K.; Hillhouse, G.L. Carbon–Nitrogen Bond Formation by Reductive Elimination from Nickel(II) Amido Alkyl Complexes. Organometallics 1995, 14, 4421–4423. [CrossRef]

91. Espinosa Martinez, G.; Ocampo, C.; Park, Y.J.; Fout, A.R. Accessing Pincer Bis(carbene) Ni^{IV} Complexes from Ni^{II} via Halogen and Halogen Surrogates. J. Am. Chem. Soc. 2016, 138, 4290–4293. [CrossRef] [PubMed]

92. Powers, D.C.; Ritter, T. Bimetallic Pd^{III} Complexes in Palladium-Catalysed Carbon–Heteroatom Bond Formation. Nat. Chem. 2009, 1, 302–309. [CrossRef]

93. Powers, D.C.; Benitez, D.; Tkatchouk, E.; Goddard, W.A.; Ritter, T. Bimetallic Reductive Elimination from Dinuclear Pd^{III} Complexes. J. Am. Chem. Soc. 2010, 132, 14092–14103. [CrossRef]
120. Khrizanforov, M.K.; Fedorenko, S.V.; Strekalova, S.O.; Kholin, K.V.; Mustafina, A.R.; Zhilkin, M.Y.; Khrizanforova, V.K.; Osin, Y.N.; Salnikov, V.V.; Gryaznova, T.V.; et al. A NiIII Complex Stabilized by Silica Nanoparticles as an Efficient Nanoheterogeneous Catalyst for Oxidative C–H Fluoroalkylation. 

Dalton Trans. 2016, 45, 11976–11982. [CrossRef]

121. Aihara, Y.; Chatani, N. Nickel-Catalyzed Reaction of C–H Bonds in Amides with I2: Ortho-Iodination via the Cleavage of C(sp2)-H Bonds and Oxidative Cyclization to β-lactams via the Cleavage of C(sp3)-H Bonds. ACS Catal. 2016, 6, 4323–4329. [CrossRef]

122. Roy, P.; Bour, J.R.; Kampf, J.W.; Sanford, M.S. Catalytically Relevant Intermediates in the Ni-Catalyzed C(sp2)-H and C(sp3)-H Functionalization of Aminoquinoline Substrates. J. Am. Chem. Soc. 2019, 141, 17382–17387. [CrossRef]

123. Zhang, S.-K.; Struwe, J.; Hu, L.; Ackermann, L. Nickellalectro-Catalyzed C–H Alkylation with Secondary Alcohols: Oxidation-Induced Reductive Elimination at Nickel(III). Angew. Chem. Int. Ed. 2020, 59, 3178–3183. [CrossRef] [PubMed]

124. Roberts, C.C.; Chong, E.; Kampf, J.W.; Ariafard, A.; Sanford, M.S. Oxidatively Induced C–H Activation at High Valent Nickel. J. Am. Chem. Soc. 2017, 139, 6058–6061. [CrossRef] [PubMed]

125. D’Accriscio, F.; Borja, P.; Saño, M.; Meucci, E.A.; Nguyen, S.N.; Camasso, N.M.; Chong, E.; Ariafard, A.; Canty, A.J.; Sanford, M.S. Nickel(II)-Catalyzed C–H Trifluoromethylation of Arenes Enabled by a Robust, High-Valent Nickel(IV) Complex. Angew. Chem. Int. Ed. 2017, 56, 12898–12902. [CrossRef] [PubMed]

126. Meucci, E.A.; Nguyen, S.N.; Camasso, N.M.; Chong, E.; Ariafard, A.; Canty, A.J.; Sanford, M.S. Nickel(IV)-Catalyzed C–H Trifluoromethylation of (Hetero)arenes. Chem. Eur. J. 2015, 21, 15029–15038. [CrossRef]

127. Corona, T.; Pfaff, F.F.; Acuña-Parés, F.; Draksharapu, A.; Whiteoak, C.J.; Martin-Diaconescu, V.; Lloret-Fillol, J.; Browne, W.R.; Ray, K.; Company, A. Reactivity of a Nickel(II) Bis(amidate) Complex with meta-Chloroperbenzoic Acid: Formation of a Potent Oxidizing Species. Chem. Eur. J. 2015, 21, 15029–15038. [CrossRef]

128. Corona, T.; Draksharapu, A.; Padamati, S.K.; Gamba, I.; Martin-Diaconescu, V.; Acuña-Parés, F.; Browne, W.; Company, A. Rapid Hydrogen and Oxygen Atom Transfer by a High-Valent Nickel–Oxygen Species. J. Am. Chem. Soc. 2016, 138, 12987–12996. [CrossRef]

129. Morimoto, Y.; Takagi, Y.; Saito, T.; Ogura, T.; Tohnai, N.; Nakano, M.; Itoh, S. A Bis(μ-oxo)dinickel(III) Complex with a Triplet Ground State. Angew. Chem. Int. Ed. 2018, 57, 7640–7643. [CrossRef]

130. Padamati, S.K.; Angelone, D.; Draksharapu, A.; Primig, G.; Martin, D.J.; Tromp, M.; Swart, M.; Browne, W.R. Transient Formation and Reactivity of a High-Valent Nickel(IV) Oxido Complex. J. Am. Chem. Soc. 2017, 139, 8718–8724. [CrossRef]

131. Diccianni, J.B.; Hu, C.; Diao, T. N–N Bond Forming Reductive Elimination via a Mixed-Valent Nickel(II)–Ni(III) Intermediate. Angew. Chem. Int. Ed. 2016, 55, 7534–7538. [CrossRef]

132. Kosobokov, M.D.; Sandleben, A.; Vogt, N.; Klein, A.; Vicic, D.A. Nitrogen–Nitrogen Bond Formation via a Substrate-Bound Anion at a Mononuclear Nickel Platform. Organometallics 2018, 37, 521–525. [CrossRef]

133. Kogut, E.; Wiencko, H.L.; Zhang, L.; Cordeau, F.F.; Acuña-Parés, F.; Draksharapu, A.; Whiteoak, C.J.; Martin-Diaconescu, V.; Browne, W.R.; Cordeau, D.E.; Warren, T.H. A Terminal NiIII-Imide with Diverse Reactivity Pathways. J. Am. Chem. Soc. 2005, 127, 11248–11249. [CrossRef] [PubMed]

134. Grove, D.M.; van Koten, G.; Verschuuren, A.H.M. New Homogeneous Catalysts in the Addition of Polyhalogenoalkanes to Olefins; Organonickel(II) Complexes [Ni(C6H5(CH2NMe2)2-O,0)][X] (X = Cl, Br, I). J. Mol. Catal. 1988, 45, 169–174. [CrossRef]

135. Grove, D.M.; Verschuuren, A.H.M.; van Koten, G.; van Beek, J.A.M. The Homogeneously Catalysed Addition Reaction of Polyhalogenoalkanes to Olefins by Divalent Arylnickel Complexes: Comparative Reactivity and Some Important Mechanistic Leads. J. Organomet. Chem. 1989, 372, C1–C6. [CrossRef]

136. Van de Kuil, L.A.; Grove, D.M.; Zwikker, J.W.; Jenneneskens, L.W.; Drenth, W.; van Koten, G. New Soluble Polysiloxane Polymers Containing a Pendant Terdentate Aryldiamine Ligand Substituent Holding a Highly Catalytically Active Organometallic Nickel(II) Center. Chem. Mater. 1994, 6, 1675–1683. [CrossRef]
138. Van de Kuil, L.A.; Grove, D.M.; Gossage, R.A.; Zwikker, J.W.; Jenneskens, L.W.; Drenth, W.; van Koten, G. Mechanistic Aspects of the Kharasch Addition Reaction Catalyzed by Organonickel(II) Complexes Containing the Monoanionic Terdentate Aryldiamine Ligand System \([C_6H_2(CH_2NMe_2)_2-2,6-R-4]^-\). *Organometallics* 1997, 16, 4985–4994. [CrossRef]

139. Knapen, J.W.J.; van der Made, A.W.; de Wilde, J.C.; van Leeuwen, P.W.N.M.; Wijkens, P.; Grove, D.M.; van Koten, G. Homogeneous Catalysts Based on Silane Dendrimers Functionalized with Arylnickel(II) Complexes. *Nature* 1994, 372, 659–663. [CrossRef]

140. Kleij, A.W.; Gossage, R.A.; Gebbink, R.J.M.K.; Brinkmann, N.; Reijerse, E.J.; Kragl, U.; Lutz, M.; Spek, A.L.; van Koten, G. A “Dendritic Effect” in Homogeneous Catalysis with Carboxilane-Supported Arylnickel(II) Catalysts: Observation of Active-Site Proximity Effects in Atom-Transfer Radical Addition. *J. Am. Chem. Soc.* 2000, 122, 12112–12124. [CrossRef]

141. Pandarus, V.; Zargarian, D. New Pincer-Type Diphosphinito (POCOP) Complexes of Ni^II^ and Ni^III^.* Chem. Commun.* 2007, 978–980. [CrossRef]

142. Pandarus, V.; Zargarian, D. New Pincer-Type Diphosphinito (POCOP) Complexes of Nickel. *Organometallics* 2007, 26, 4321–4334. [CrossRef]

143. Spasyuk, D.M.; Zargarian, D.; van der Est, A. New POCN-Type Pincer Complexes of Nickel(II) and Nickel(III). *Organometallics* 2009, 28, 6531–6540. [CrossRef]

144. Mirica, L.M.; Smith, S.M.; Griego, L. Organometallic Chemistry of High-Valent Ni^III^ and Ni^IV^ Complexes. In *Nickel Catalysis in Organic Synthesis: Methods and Reactions*; Ogoshi, S., Ed.; Wiley-VCH: Weinheim, Germany, 2009; pp. 223–248.

145. Diccianni, J.B.; Diao, T. Mechanisms of Nickel-Catalyzed Cross-Coupling Reactions. *Trends Chem.* 2019, 1, 830–844. [CrossRef]

© 2020 by the author. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).