Reactivities of Photoredox Generated Nickel-Nucleophilic Reactive Organometallic Species

Reactivities of Photoredox Generated Nickel-Nucleophilic Reactive Organometallic Species

Andrea Gualandi, Francesco Calogero, Dario Corbisiero, Emanuele Pinosa and Pier Giorgio Cozzi

DOI: 10.1002/ajoc.202300574

Abstract: Dual photoredox catalysis has revolutionized the field of cross-coupling reactions, enabling the discovery of numerous highly efficient reactions. This breakthrough is attributed to the exceptional combination of nickel catalysis with photoredox catalysis. Nickel exhibits both oxidative addition and reductive elimination processes. In addition, nickel exhibits a wide range of oxidation states (ranging from I to IV) accessible within a single catalytic cycle. Furthermore, nickel complexes are capable of catalyzing various processes through radical mechanisms. The latest feature has proven to be incredibly potent in facilitating the formation of new C–C and C–X bonds (X = H, O, S, N). The powerful combination of photoredox and nickel catalysis reveals an expansive domain of unexplored possibilities. It offers unparalleled opportunities for improving reactions and exploring innovative pathways. Moreover, this powerful combination enables the realization of enantioselective processes, heralding a new era of precision in chemical synthesis. Under photoredox conditions, it is possible to form nucleophilic reactive organometallic intermediates, useful in reaction with electrophiles. We have devoted a research program towards the rediscovery and use of organometallic reagents, introduced by Corey, Hegedus, and Semmelack many years ago. Our group's contribution in this field is reported, as well as significant reports from other groups. The results unveiled the extraordinary capabilities of photoredox catalysis, enabling the creation and efficient utilization of potent nucleophilic organometallic reagents under mild conditions, free from the need for strong bases or stoichiometric metal reductants.

1. Introduction

The development of modern cross coupling reactions has considerably impacted the design and synthesis of active molecules.[1] Taking advantage of the unique characteristics of transition metal to interact with organic molecules, the formation of C–C and C–heteroatom bonds are now a common practice among the Academia and industry. Palladium have found many applications, with a successful development of tailored and powerful achiral and chiral ligands. Despite some health hazards,[2] nickel is increasingly playing a vital role in this field, positioned just above the Periodic Table. Nickel displays its own distinct behavior and properties, despite sharing some chemical properties and the ability to undergo oxidative addition and reductive elimination processes like palladium. Nickel, in contrast to palladium, is not only more naturally abundant but also less expensive. However, given its increasing demand for batteries, prices are poised to rise in the future. Moreover, although the chemistry of palladium was developed with careful design of new and effective ligands, a similar development is still far to be actuated in the case of nickel.[3] Nickel is more electropositive, favoring oxidative addition also in the presence of substrates that are hardly reactive with palladium. On the other hand, reductive elimination events are not as favored.[4] Both metals exhibit a variety of oxidation states, ranging from I to IV. However, generally, palladium cross-coupling reactions are believed to follow a Pd(0)/Pd(II) catalytic cycle, operating through a non-radical mechanism. Noteworthy, in recent years, through the utilization of photoredox conditions, there has been a growing interest in the exploration of expanding the repertoire of palladium oxidation states by leveraging radical cycles.[5] However, the relatively easy accessibility and stability of Ni(I) and Ni(III) oxidation states are particularly well-suited to be combined with radical cycles.[6]
Photoredox catalysis was re-invented as a powerful methodology to achieve the formation of radical species in mild conditions.[7] Connecting the SOMO (A Singly Occupied Molecular Orbital) chemistry developed for enamine catalysis[8] with some relevant contribution of the generation of radical species using $[Ru(bpy)_3]Cl_2$ as photocatalyst,[9] MacMillan and Nicewicz[10] opened the field of photoredox catalysis to practical use in Organic Chemistry. Some years after, Sanford,[11] MacMillan and Doyle,[12] and Molander[13] have reported the possibility to realize the dual photoredox catalysis[14] with nickel, in interesting cross coupling reactions. The combined use of photoredox and nickel catalysis has proven to be extremely captivating, bewitching the utmost attention. The alteration of the oxidation state is largely attributed to the transition metal's remarkable capacity to efficiently capture the photogenerated organic radicals.[15] Through a process called single-electron transfer, a wide range of radicals (including C-, O-, N-, S-, and P-centered radicals) can be produced through reductive quenching interactions with excited photocatalysts.[16]
Nickel complexes in low oxidation state can capture a radical formed alongside the photocatalytic cycle. The generation of the radical can occur either by direct interaction of the photocatalyst in its excited state with a stable radical precursor or by an indirect event. In the first case the radical precursor acts as an effective single electron quencher of the excited state of the photocatalyst, alternatively a consecutive electron transfer occurs to maintain the catalytic cycle.[17] An alternative possibility considers the oxidative addition aryl/alkyl/vinyl halides on Ni(0), with the concomitant formation of Ni(II) intermediates. Intercepting the generated radical, this last evolves in the corresponding Ni(III) intermediate. Both proposed mechanistic models came together to indicate the formation of the highly reactive Ni(III) species, which ultimately leads to the desired cross-coupled products through reductive elimination (Figure 1). The first use of photoredox reactions in reductive nickel-mediated cross coupling reactions were developed by Weix,[18] eliminating the need for

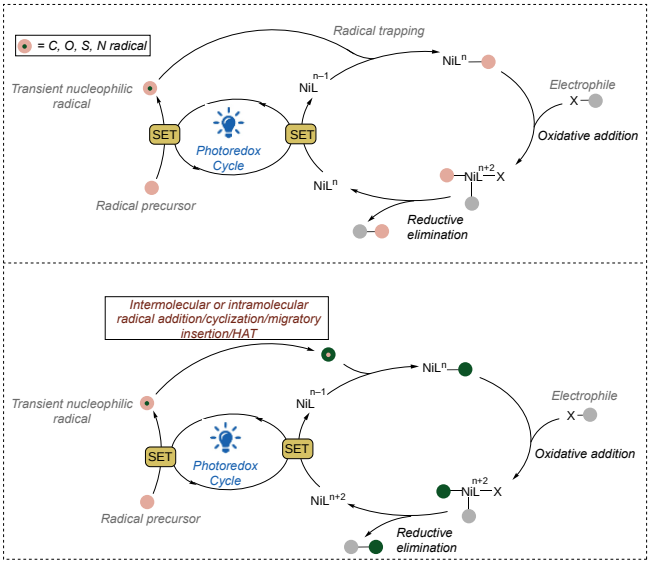


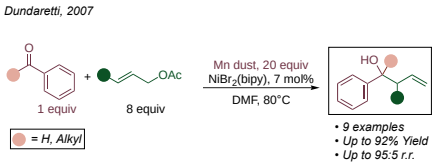
Figure 1. General model in dual nickel and photoredox catalytic approach.

stoichiometric amounts of metal reductant. These methodologies opened up various possibilities for the formation of C-C and C-heteroatom bonds.[19] In addition, the generation of radical species by hydrogen atom transfer (HAT) events further offers effective and gentle methods to generate radicals from inexpensive and non-functionalized starting materials.[20] These radicals can undergo towards various unimolecular processes, such as cyclization, radical addition, migratory insertion, β-scission, or 1,5-HAT, leading to the formation of new radical species. These last can then react with nickel, forming reactive intermediates following the above introduced pathways.

Finally, taking advantage of the fundamental work done by Fu in nickel stereoselective cross coupling reactions,[21] the enantioselective photoredox nickel promoted reactions were recently applied to a series of interesting and highly selective cross coupling reactions.[22] Although the realization of cross-coupling products through dual nickel and photoredox catalysis represents a major asset in the toolbox of synthetic chemistry, only in a few examples this knowledge has been used for generating nucleophilic organonickel reagents. By the employment of photoredox conditions is it possible to overcome limitations and enhance the possibility offered in the formation of nucleophilic organometallic reagents avoiding the use of stoichiometric metal reductant and using available and stable organic precursors for the direct access to the nucleophiles. This account aims to highlight the remarkable results achieved from our investigations, as well as the valuable contributions made by other groups in this rapidly progressing field. We will emphasize the practical and potent solutions that can be provided to a wide range of synthetic approaches.

2. Formation of Nucleophilic Reagents with Nickel: Allylation

(π-Allyl) nickel complexes were reported to react with organic halides by Corey and Semmelack.[23] In this approach, the organometallic allylating reagents were prepared *in situ* by using the toxic $[Ni(CO)_4]$ or with the highly sensitive $[Ni(COD)_2]$ (COD = 1,5-cyclooctadiene). This groundbreaking paper presents the remarkable reactivity displayed by carbonyl compounds. However, the authors observed that these reactions occurred at a noticeably slower rate compared to alkyl iodides. To achieve complete reaction, the assistance of heating at 50 °C was required. The use of toxic or quite sensitive material, in stoichiometric amount, and the low reactivity have probably hampered a careful reexamination of these reagents, until Durandetti and Périchon[24] reported the catalytic use of Ni(II) in the presence of bipyridine (bpy) ligands in combination with a stoichiometric metal as terminal reductants for allylation and Reformatsky reactions. Furthermore, it noteworthy that after several years, a previously underestimated electrophile, namely CO_2, was discovered to exhibit reactivity in the presence of nickel in low oxidation state. Martin and co-workers described a nickel-catalyzed carboxylation of allylic alcohols with CO_2, in the presence of a phenanthroline derivative as ligand, and zinc as stoichiometric reductant.[25] In addition, Durandetti described an electrochemical procedure[26] combining a nickel catalyst and a sacrificial zinc anode to form a reactive allylating nickel species,[27] able to react with aldehydes and ketones (Scheme 1).

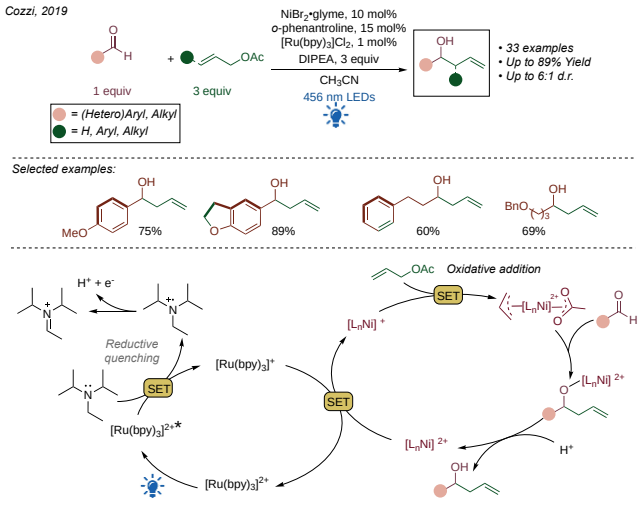


Scheme 1. Nickel promoted allylation of carbonyls with stoichiometric metal reductants.

Not only allylnickel formed by convenient methodologies in the presence of a stoichiometric reductant was founded effective, but an enantioselective Ni-catalyzed methodology of a reductive coupling of allylic carbonates with aldehydes was reported.[28] The procedure utilized zinc as the terminal reductant, in the presence of pyBOX [pyBOX = (oxazol-2-yl)pyridine ligand]·ligand and a substoichiomentric (50 mol%) amount of copper iodide as additive. The reaction conditions resulted quite effective for the 2-aryl-allylic carbonates, which generate the homo-allylic alcohols in good to excellent enantiomeric excesses (ees) for both aromatic and aliphatic aldehydes. At the same time, the employment of the simple allyl system gave moderate ees. In our laboratories, we want to explore if the nucleophilic allyl nickel complex could also be accessible through the reduction of nickel under photoredox conditions.

2.1. Photoredox Allylation Of Aldehydes with Nickel

During our studies remarkable examples of diastereoselective allylation of aldehydes through a combination of photoredox and chromium(II) catalysis was reported by Glorius[29] and Kanai,[30] publishing the first examples of formation nucleophilic organometallic reagents based on dual transition metal and photoredox catalysis. Both groups presented the formation of allylating organochromium reagents from allyl electron-rich arenes (indole, carbazole), electron-rich alkenes, or allylic anilines with aliphatic and aromatic aldehydes. The key element of both reports is the use a photocatalyst capable of behaving as a strong oxidant in its excited state allowing the generation of the allyl radical from the electron-rich organic substrate. This last is intercepted by the by Cr complexes in low oxidation state. In both cases, a redox-neutral cycle, without the need of a stoichiometric reductant, was developed thanks to the utilization of highly reactive and hardly to handle chromium(II) species. Through the radical polar cross over approach,[31] the allylic radical was intercepted by Cr(II) giving the reactive allylchromium nucleophile.[32] In our chemistry we have not used alkenes as precursors but we considered allyl acetate and carbonates as potential pronucleophiles. The basic idea was to reduce the nickel with the suited photocatalyst and, through oxidative addition and successive SET, generate the reactive allylnickel (Scheme 2).[33]



Scheme 2. Photoredox allylation of aldehyde promoted by nickel complex.

Our innovative dual photoredox method, using nickel as a catalyst, revolutionizes cross-electrophile coupling.[34] This technique offers several advantages: (i) the use of readily available and simple not-substituted allylating reagents such as allyl acetates or simple allyl esters; (ii) the *in situ* formation of a nickel allyl organometallic species, a highly valuable nucleophilic organometallic reagent obtained

through reductive photoredox processes; (iii) the elimination of the need for an argon filled glovebox to handle unstable or air-sensitive Ni(0) or Cr(II); (iv) the breakthrough ability to incorporate a unbiased propene moiety.[35] Through a meticulous evaluation of reaction parameters, we achieved optimal conditions employing [$NiBr_2$(glyme)] (glyme = dimethoxyethane) catalyst (10 mol%), allyl acetate (3 equiv.), diisopropylethylamine (DIPEA, 3 equiv.), (DIPEA = *N*,*N*-diisopropylethylamine) *o*-phenanthroline (15 mol%) as the nickel ligand, and $[Ru(bpy)_3]Cl_2$ (bpy = 2,2'-bypiridine ligand) as the photocatalyst (1 mol%), with blue LED irradiation at 450 nm. In the Scheme 2 a selected example of the reaction scope obtained after the investigation of a variety of aromatic and aliphatic aldehydes is reported. Since allyl nickel complex to respect other organometallic analogues presents a limited nucleophilicity, the reaction was found selective towards aldehydes. After successfully completing a comprehensive study enabling the realization of a wide library of homoallyl alcohols in a non-stereocontrolled fashion we promptly moved our attention towards an enantioselective variant. After a preliminary optimization, based on the screening of different chiral ligands without modifying other reaction parameters, we discover that a low enantiomeric excess was obtained performing the reaction in the presence of chiral bisoxazoline derived from *D*-phenylalaninol (see section 2.4). However, to acquire valuable insights into the process, it was crucial to thoroughly examine the reaction mechanism and strive towards advancing additional nucleophilic reactions. The photochemical mechanism was meticulously investigated by analyzing the quenching of the photocatalyst's luminescence caused by each component involved in the reaction. In particular, no change in the decay of the emission intensity of $[Ru(bpy)_3]Cl_2$ was observed upon addition of allyl acetate, *o*-phenanthroline, or the model aldehyde in the concentration used for the reaction. DIPEA was the effective quencher supporting the catalytic cycle illustrated in Scheme 2. The possibility to prepare effective nickel nucleophiles rely on the reduction of nickel complexes. The quenching of $[Ru(bpy)_3]^{2+}$ photocatalyst by DIPEA, produces the reduced $[Ru(bpy)_3]^{+}$ complex ($E_{½}$ = -1.33 V vs SCE) (SCE = standard calomel electrode),[36] a suitable reductant for phenanthroline Ni(II) complexes to Ni(I). By electrochemical investigation a reversible reduction process for $[Ni(phen)_3]^{2+}$ at -1.31 V (phen = phenanthroline ligand) was measured. When allyl acetate was added, the cyclic voltammogram displays a chemically irreversible reduction process. Our interpretation for this result was a rapid oxidative addition of allyl acetate followed by a fast SET able to generate the reactive [$L_nNi(\eta^3$-allyl)(OAc)] (OAc = acetate anion).[37] The process is quite different from many catalytic cycles suggested in cross coupling reactions when the photoredox catalysis was introduced, but calculations from other leading group in the field,[38] carefully spectroscopic and mechanistic investigations[39] are now reconsidering the effective role of Ni(I) as a key valence oxidation state in photoredox chemistry. Another discussion point regards the restoration of nickel complex in its pristine state. In this chemistry it is assumed that a protonation step liberates the nickel complex. The proton sources in the protocol are the intermediates formed because of the subsequent steps that the radical of DIPEA undergoes after quenching. Figure 2 illustrates the intricacy of the events, showing that various SET (SET = single electron transfer) events within a catalytic cycle can also be facilitated through the redox chemistry of the amine.

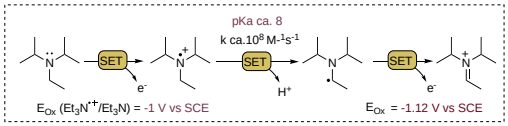
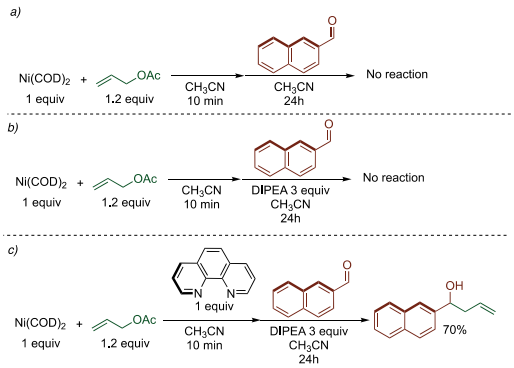


Figure 2. Oxidative pathway of triethylamine.

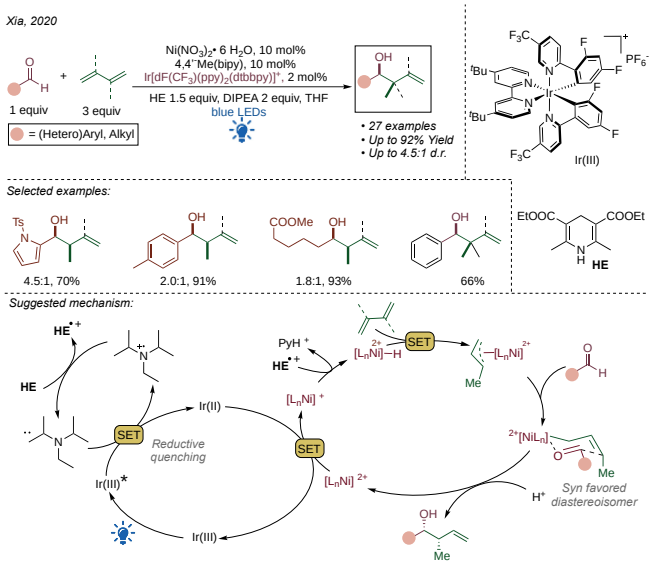
The modest reactivity of allyl nickel intermediates highlighted in the above presented pioneering reports was probably due to the absence of ligands. As a consequence, we have performed the allylation reaction of model aldehyde in dark conditions with allyl acetate using a stoichiometric amount of $[Ni(COD)_2]$ both with or without *o*-phenanthroline ligand and DIPEA, and we have observed that the reaction only occurred in the presence of o-phenanthroline (Scheme 3).



Scheme 3. Dark reaction to probe the reaction mechanism of photoredox allylation of aldehydes.

2.2. Allylation via dienes

1,3-butadiene, an abundant petrochemical feedstock, was employed as pro-nucleophile in allylation reaction promoted by ruthenium or iridium catalysts.[40] In addition, chromium-[41] and titanium-based[42] photoredox methodologies have employed butadiene as radical acceptor to produce allylic radicals suitable for radical to polar cross over coupling with organometallic complexes in low oxidation states.[43] Interestingly, it was reported that nickel can be used in the coupling of 1,3-dienes with aldehydes. it is possible to achieve this by using reducing agents such as Et_2Zn[44] or BEt_3.[45] Inspired by a König's group, that reported a photoredox Ni-catalyzed hydrocarboxylation of styrenes in presence of Hantzsch ester (HE) to produce a nickel hydride intermediate,[46] Xia employed butadiene in the allylation of aldehydes.[47] Using HE as the hydrogen source, the group employed $NiCl_2 \cdot 6H_2O$ (5 mol%) with 5,5′ -dimethyl-2,2′ -bipyridine (5 mol%) as ligand, and $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ ($dF(CF_3)ppy_2$ = cyclometalated iridium(III) complex; dtbbpy = ditertbutyl-2,2'-bipyridine) as photocatalyst under blue LED irradiation. Substate scope highlighted that aromatic, heterocyclic, and aliphatic aldehydes were suitable for the reaction, giving high yields of the desired product. It is worth noting that the presence of a catalytic amount of Hünig's base (DIPEA, 12 mol%) gave better results. To understand these outcomes, several experiments clarified that DIPEA acts as an electron shuttle between Hantzsch ester and photocatalyst.



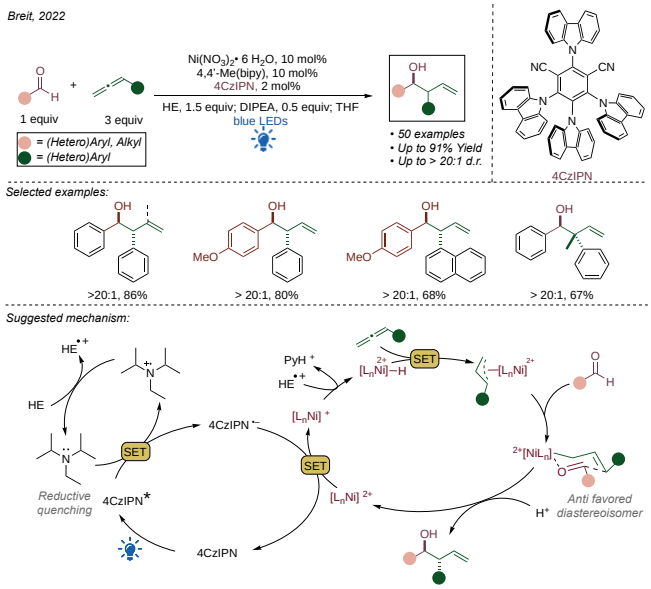
Scheme 4. Photoredox allylation of aldehyde starting from 1,3-dienes.

As illustrated in the Scheme 4, the proposed mechanism envisages a catalytic cycle in which the photocatalyst behaves as a good oxidant in its excited state ($E_{1/2red}$ [*Ir(III)/Ir(II)] = +1.21 V vs SCE)[48] and, via reductive quenching, it is able to oxides the DIPEA (E_{ox} (DIPEA) = +0.65 V vs SCE)[49] producing Ir(II) and $[DIPEA]^{\bullet+}$. The authors suppose that the Hantzsch ester is responsible for the reduction of $[DIPEA]^{\bullet+}$ forming the ($HE^{\bullet+}$), whereas the reduction of Ni(II) to the active Ni(I) ($E_{1/2red}$[Ni(II)/Ni(I)] = −0.68 V vs SCE in DMSO (DMSO = dimethylsulfoxide))[50] is determined by Ir(II) ($E_{1/2red}$[Ir(III)/Ir(II)] = −1.37 V vs SCE in CH_3CN),[51] and the interaction of $L_nNi(I)$ with $HE^{\bullet+}$ give the hydride (Ni−H) species and pyridinium ion Py-H^+ (Py-H^+ = protonated oxidized HE to the corresponding pyridine). Subsequently, diene is converted into the allylic nucleophile via migratory insertion. The observed product is determined by the coordination of the Ni(II)-allyl specie with aldehydes through a Zimmerman-Traxler transition state, in which the methyl group of the allylic reagent placed in pseudo-axial position.

2.3. Allylation via allenes

The employment of Hantzsch ester as reductant in the photoredox-mediated formation of the nucleophile could be extended towards the formation of the π-allylNi by using insertion of nickel hydride intermediate with suitable precursors. For example, Jamison and coworkers reported the reaction of allenes with nickel in low oxidation state through a nickel hydride intermediate.[52] Differently from

these pioneering investigations but using the same concept, Breit and coworkers reported[53] the generation of π-allylNi complexes by merging photoredox and nickel catalysis for the coupling with aldehydes to form homoallylic alcohols (Scheme 5).

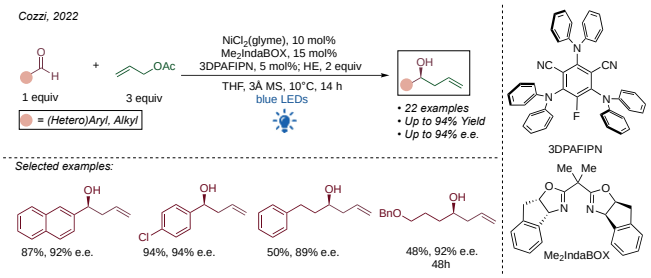


Scheme 5. Use of allenes for the nickel promoted photoredox allylation of aldehydes.

The reaction was carried out employing 4CzIPN (4CzIPN = 1,2,3,5-Tetrakis(carbazol-9-yl)-4,6-dicyanobenzene) as the active photocatalyst, in the presence of $Ni(NO_3)_2 \cdot 6H_2O$ and 4,4′ -dimethoxyl-2,2′ -bipyridine as the ligand, Hantzsch ester, and DIPEA under blue LED irradiation. The reaction tolerated a variety of differently functionalized aliphatic and aromatic aldehydes. Quite interestingly, the procedure can be extended to the formation of quaternary stereogenic centers with good diastereo control, that derived by a Zimmerman-Traxler transition state. Moreover, also in this case the addition of the base was motivated by the better results obtained and these outcomes were explained by the proton shuttle facilitation. The main hypothesis in the proposed mechanistic model is that the generation of $L_nNi(I)$ leads to a reaction with $HE\text{-}H^{\bullet+}$ resulting in the formation of $L_nNi(II)\text{-}H$. The potential referred to $HE\text{-}H^{\bullet+}$ ($E_{1/2red}$ [$HE\text{-}H^{\bullet+}$/$Py\text{-}H^{+}$]= − 0.76 V vs SCE)[54] makes this reaction possible.[55] Subsequently, the reaction between the $L_nNi\text{-}H$ and the allene generates the π-allylNi specie,[53] which after coordination with the aldehydes give the desired product via cyclic transition state.

2.4. Enantioselective photoredox allylation

As previously mentioned, once we introduced a powerful non-stereoselective for the allylation of aldehydes through dual nickelaphotoredox catalysis, we immediately looked for an enantioselective variant. Maintaining untouched the other reaction parameters, the best enantioselective result was obtained using the chiral bisoxazoline derived from D-phenylalaninol, with a conversion of 50% and an unsatisfactory enantiomeric excess of 44%. However, despite the use of many BOX (BOX = bisoxazolines) or *N*,*N*-type ligands we were not able to improve yields/ees. Rationalizing these results, we hypothesized that the presence of DIPEA, used as the sacrificial reductant, probably interfered with the coordination of nickel with BOX ligand. Therefore, we completely reassessed our catalytic system. Firstly, taking inspiration from our previous work of dual titanium and photoredox catalysis,[56] we moved through substituting the photocatalyst with organic dyes,[57] and employing TADF (TADF = thermally activated delayed fluorescence)[58] organic molecules. These systems were introduced in dual photoredox catalysis in 2016,[59] and although the stability under the reaction conditions needs to be carefully controlled,[60] their peculiar, delayed fluorescence enhance the lifetime of excited state, normally not very long for organic dyes.[61] By employing 3DPAFIPN (3DPAFIPN = 2,4,6-tris(diphenylamino)-5-fluoroisophthalonitrile) as a photocatalyst and Hantzsch's ester as an organic reductant,[62] in the presence of catalytic amounts of $NiBr_2$(glyme) and a chiral ligand described in chromium photoredox reactions promoted by Kanai,[30] we increased the yield and ees compared to the previous ones. Finally, by a careful optimization of these preliminary results and selecting the suitable BOX ligand, we developed a robust and highly enantioselective allylation of aldehydes (Scheme 6).[63]



Scheme 6. Enantioselective allylation of aldehydes under photoredox conditions.

The reaction was performed on aliphatic and aromatic aldehydes and the presence of functional groups was well tolerated. It is noteworthy that a careful control of the temperature was necessary to ensure the highest enantiomeric in a range between 89 and 95% e.e.. However, we observed that aromatic aldehydes capable to chelate the nickel (e.g., thiophene) were not reactive substrates. Moreover, homoallylic alcohols deriving from pyrrole or indole aldehydes are relatively sensitive to strong Brønsted acid and, therefore, they were obtained with unsatisfactory results due to decomposition pathways promoted by the presence pyridinium salts.

The study to elucidate the entire mechanism was quite challenging due to several reasons. Primarily, the complexity of the reaction did not allow the use of electrochemical studies to explain the mechanism; therefore, we settled a collaboration with the group of Prof. Cavallo to obtain DFT details. At the same time, photophysical studies were also quite demanding, since the use of TADF dyes, with the prompt and delayed fluorescence both able to interact with a possible quencher, complicated the Stern-Vomer studies. We observed the formation of a complex between 3DPAFIPN and the Hantzsch ester (HE), which can be considered in a static quenching.[64] The role of this complex is essential as the active species in photoredox reactions. Nevertheless, there is another way to understand the intricate quenching phenomenon.[65] Recent research suggests that the complex was quenched by both the Hantzsch ester and the chiral nickel complex. However, due to its higher concentration, the Hantzsch ester emerged as the more efficient quencher. As mentioned earlier, we carefully analyzed the reaction mechanism through DFT calculations.[66] The calculations have precisely forecasted that the 3DPAFIPN·HE complex forms with an exceptionally minimal activation barrier. Furthermore, the new complex was not altering the UV absorption of both reaction partners. Furthermore, the oxidative and reductive quenching events were evaluated by DFT and both cycles were possible; however, due to the experimental setup the reductive quenching resulted the most probable. It is noteworthy that our study can also be relevant for many similar processes promoted by TADF dyes in the presence of Hantzsch ester.

Although in our non-stereoselective version of the reaction the experimental electrochemical data suggested that Ni(0) was not involved, DFT calculation performed for the enantioselective version established that the starting point of the catalytic cycle is the Ni(0)-BOX complex coordinated to allyl-acetate, which evolve towards a Ni(II)-intermediate (Figure 3). This intermediate is then reduced to Ni(I)-allyl complex by a SET event and the subsequent allylation reaction takes place by insertion of aldehyde on the NI(I)-complex. This corresponds to the enantiodetermining step with formation of the stereocenter. Even though in many reactions performed in the presence of Hantzsch ester in dual nucleophilic photoredox reactions,[67] this last is believed to act as a "protonating agent" by liberating a proton upon oxidation, our DFT calculations illustrate a more complex mechanism. In fact, the interaction of Hantzsch derivative $HE^{\bullet+}/AcO^{-}$ onto the metal center of Ni(I)-complex after the aldehyde insertion breaks the O–Ni bond by a proton-coupled electron transfer (PCET). This step also recycles the Ni(I) to Ni(0), restarting the catalytic cycle. Finally, we have also rationalized the origin of the enantioselectivity of the reaction by a theoretical calculation of the hindrance of the transition state by minimization of the steric interactions.[66]

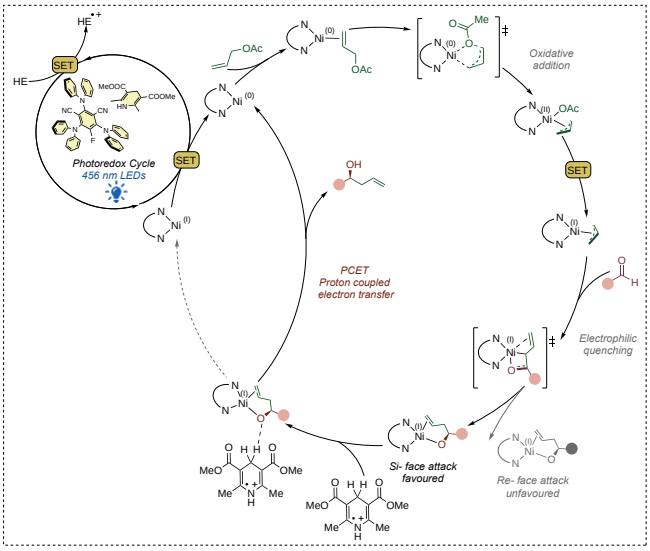


Figure 3. Proposed mechanism for the enantioselective allylation of aldehydes under photoredox conditions.

3. Vinyl Nickel as Nucleophiles with Carbonyl Compounds

η^2-Coordination of transition metals onto aldehydes can induce a nucleophilic behavior to the formyl group.[68] Ni(0) combined with electron donor ligand is an ideal combination for this type of the η^2 coordination.[69]

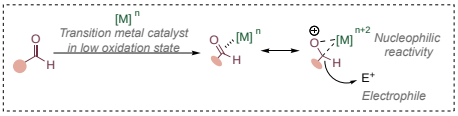


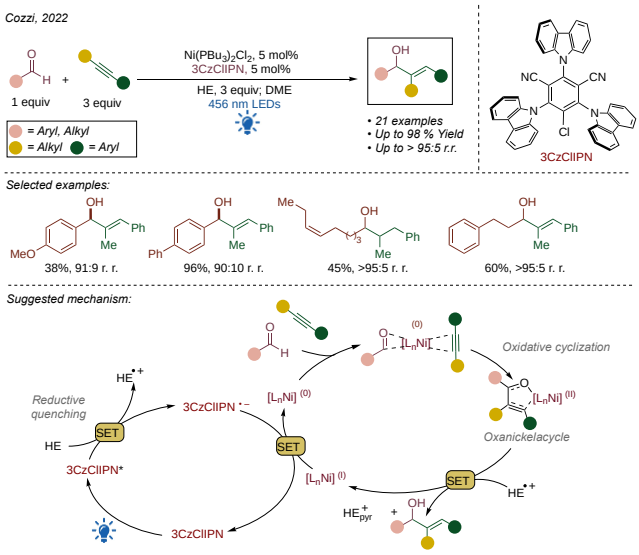
Figure 4. Activation of carbonyl by low oxidation state metal complexes.

The stoichiometric reaction for the η^2-coordination of aldehydes in the presence of alkynes, 1,3-dienes, allenes, and alkenes evolves upon oxidative cyclization into a five-membered oxanickelacycle complexes.[70] Formation of oxanickelacycle in catalytic conditions allowed to recycle nickel, with a stoichiometric amount of a reducing agent. As reducing agents, Et_2Zn,[71] alkyl silanes R_3SiH (R = Et, alkyl),[72] BEt_3,[73] were introduced by Montgomery and Jamison. To induce the formation of the nickelacycle, the employment of stoichiometric reductant is mandatory. Additionally, in most of the cases the use of extremely sensitive $Ni(COD)_2$ is necessary to start the catalytic cycle. Formation of nickel in low oxidation state, by using metallaphotoredox catalysis can be an advantage for this chemistry. By formation of nickel in low oxidation state in photoredox conditions, the need of stoichiometric air sensitive precursors (i.e., Et_2Zn or Et_3B) will be avoided. With this aim we have explored the use of organic dyes with nickel, in the presence of alkyne and aldehydes to introduce this rich chemistry, also explored in enantioselective transformations,[74] in the dual metallaphotoredox world.

3.1. Photoredox vinylation

We have selected 3CzClIPN (3CzClIPN = 2,4,6-tri(9H-carbazol-9-yl)-5-chloroisophthalonitrile) as photocatalyst in combination with the Hantzsch ester (HE) as organic reductant.[75] This organic dye was evaluated in function of the values of the available reduction potential both for the ground and for the excited state, that are lower than other cianoarene-based photocatalysts commonly employed, i. e. 4CzIPN, or 3DPAFIPN [values are referred to SCE: $E(4CzIPN^{\bullet+}/^*4CzIPN) = –1.18$ V; $E(3DPAFIPN^{\bullet+}/^*3DPAFIPN) = –1.38$ V; $E(3CzClIPN^{\bullet+}/^*3CzClIPN) = –0.93$ V. The lower reduction potential, both in excited that in the ground state is relevant when aromatic aldehydes are employed in conditions set to form Ni(0). To prevent any unwanted occurrence of parasitic pinacol coupling of the aromatic aldehyde in the presence of potent reducing photocatalysts[76] and a Brønsted acid, such as the oxidized Hantzsch ester, the photocatalyst was carefully chosen. The nickel catalyst for the transformation was selected by the fundamental work reported by

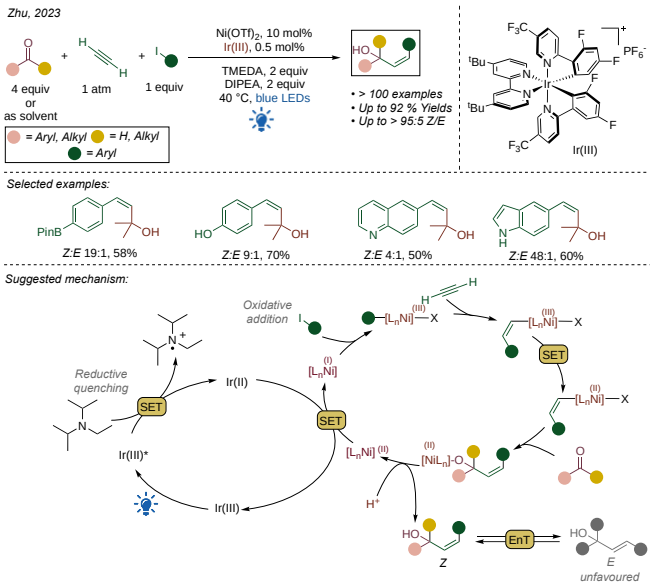
Jamison and Montgomery.[77] As we expected, active *N,N*-ligands (phenanthroline, bipyridine, BOX) previously employed in our allylation reaction were completely ineffective for this transformation. By selecting commercially available nickel complexes and investigate in detail all variables for these reactions, finally we found that the reaction was promoted employing [$NiCl_2$(*n*Bu_3P)$_2$] (5 mol%), 3CZClIPN (5 mol%), alkyne and Hantzsch' ester (3 equiv. each) under irradiation of blue LED (Scheme 7). We tested the optimized protocol on a wide range of substituted aromatic aldehydes and were thrilled to discover its exceptional tolerance towards different functional groups. The reactivity of the protocol ranged from discrete to excellent, showcasing its versatility and potential for numerous applications. On the other hand, the reactivity of aliphatic aldehydes was insufficient under the given circumstances. Therefore, Lewis acid, such as $MgBr_2$·Et_2O as additive, was required to activate the carbonyl group. Remarkably, this Lewis acid was specifically chosen due to its resistance to the reducing conditions of the system.



Scheme 7. Photoredox vinylation of aldehydes with alkynes.

The scope of the reaction with alkynes is limited by the fact that $L_nNi(0)$ is an active catalyst for cyclotrimerization of alkynes, and the presence of this byproduct is always revealed. Some differently 2-substituted 1-phenylacetylenes were found reactive. The Stern-Volmer analysis ruled out that Hantzsch ester is the quencher [E_{ox}(HE$^{\bullet+}$/HE) = 1.0 V vs. SCE].[78] The event produces the reduced form of the photocatalyst 3CzClIPN$^{\bullet-}$ able to reduce the Ni(II) to Ni(I) and to Ni(0) by a successive SET. Investigation of a possible enantioselective variant of this reaction is in progress. In our example the use of phenylacetylene was not possible, as in many other similar reactions previously described using Et_2Zn or BEt_3. In the case of photoredox conditions, unhindered phenylacetylene is quickly trimerized by the $L_nNi(0)$ complexes generated *in situ*. However, quite recently Zhu and co-workers[79] reported a photoredox/nickel dual-catalyzed three-component cross-coupling reaction, with acetylene gas (1 atm) as a two-carbon (C2) synthon (Scheme 8). They were able to solve the previous limitation of the reaction allowing to use a commodity available in large scale. Additionally, differently substituted alkenes were obtained by the cross coupling, allowing a fine tuning of the desired product. The reaction was optimized using $Ni(OTf)_2$ (10 mol%) as the catalyst, in the presence of 0.5 mol% of iridium-based photocatalyst under irradiation of blue LED. The presence of 2 equiv. of tetramethylethylenediamine (TMEDA) and DIPEA as sacrificial reductant was found necessary. The reaction worked with a broad number of aryl iodides, while bromide or chlorides were found unreactive. Intramolecular variant of the reaction was developed using bromoaryl ketones. Several substituents in the aryl moiety such as chloro-, bromo-, methylthio-, diphenylamino-, boronic ester, and ester were well tolerated. Moreover, the employment of nitrogen-, oxygen-, and sulfur- containing heterocycles was possible. Finally, aliphatic ketones, and aromatic and aliphatic aldehydes were found to be reactive. In many examples the authors observed a high diastereomeric control in favor of the *Z* isomer (> 9:1 *Z*/*E*). It was possible to use alkyl-substituted alkynes, although the yields were considerably reduced. As the TMEDA was used in more than stoichiometric amount, it is presumably the effective ligand for the nickel. Consequently, the authors investigated the cyclic voltammetry of $Ni(OTf)_2$·TMEDA complex (OTf = OSO_2CF_3) discovering two favored reduction events [E_p(Ni(II)/Ni(I)) = −0.55 V and E_p(Ni(I)/Ni(0)) = −0.86 V versus SCE in acetone]. The Stern Volmer experiment successfully indicated that DIPEA effectively extinguishes the excited state of iridium(III), resulting in the formation of the Ir(II) species [$E_{1/2}$(Ir(III)/Ir(II)) = −0.71 V versus SCE in acetone].The author suggested that the Ni(II) reduction was slightly difficult and therefore, a cycle in which Ni(I) plays a key role was suggested. The catalytic cycle is depicted in Scheme 8. In its reduced state, the photocatalyst has the remarkable ability to convert Ni(II) to Ni(I), paving the way for

the subsequent oxidative addition with the aryliodide. To this event a migratory insertion of acetylene and another SET event gave the $L_nNi(II)$ alkene complex, that, upon coordination of aldehyde and addition reaction gave the *E*-product. The final *Z*- product is observed because the Ir(III) complex is able to isomerize the trans alkene via energy transfer (EnT).[80]



Scheme 8. Three component allylation of aldehydes.

4. Summary and Outlook

In summary, the chosen example presented in this account has effectively illustrated the application of nickel complexes in metallaphotoredox catalysis. Different organometallic nucleophilic nickel species such as aryl[81] and Reformatsky reagents[82] have been reported using metal reductants, such as Mn or Zn in stoichiometric amounts, and the translation of these conditions in photoredox protocols seems suitable. Moreover, using new organic dyes operating in green[83] or red lights,[84] will be possible to solve the low penetration of the blue light used in many photoredox processes. This represents one of the major problems that concerns photoredox catalysis which hinders the scale-up and the application of photoredox conditions in larger scale, and that only occasionally with found solution the use of expensive technological protocols.[85] With the appropriate photoredox methodology,[86] translate these reactions in efficient enantioselective procedures, and enhancing the scope of the reactive electrophiles, including ketones and imines, will be our future goals and research in our laboratory.

Acknowledgements

P. G. C. acknowledges Italian National project (PRIN2017 ID: 20174SYJAF; SURSUMCAT “Raising up Catalysis for Innovative Developments”) for financial support of this research. A.G. and P.C. acknowledges the University of Bologna and for financial support. This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No. 951996. Jacopo Monaldi is aknowledged for the initial screening of ligands in the enantioselective photoredox allylation reaction.

Keywords: Nickel • catalysis • photoredox catalysis• aldehyde • ligands

References.

[1] J. P. Sestelo, L. A. Sarandeses, *Molecules* **2020**, *25*, 4500-4503.

[2] K. S. Egorova, V. P. Ananikov, *Organometallics* **2017**, *36*, 4071–4090.

[3] a) K. Wu, A. G. Doyle, *Nature Chem*. **2017**, *9*, 779-784; b) S. H. Newman-Stonebraker, S. R. Smith, J. B. Borowski, E. Peters, T. Gensch, H. C. Johnson, M.S. Sigman. A. G. Doyle, *Science*, **2021**, *374*, 301-308.

[4] S. Z. Tasker, E. A. Standley, T. F. Jamison, *Nature* **2014**, *509*, 299–309.

[5] P. Chuentragool, D. Kurandina, V. Gevorgyan, *Angew. Chem. Int. Ed.* **2019**, *58*, 11586–11598; *Angew. Chem.* **2019**, *131*, 11710-11722.

[6] C. Zhu, H. Yue, L. Chu, M. Rueping, *Chem. Sci.* **2020**, *11*, 4051–4064.

[7] For a few selected reviews: a) M. H. Shaw, J. Twilton, D. W. C. MacMillan, *J. Org. Chem.* **2016**, *81*, 6898–6926; b) L. Marzo, S. K. Pagire, O. Reiser, B. König, *Angew. Chem. Int. Ed.* **2018**, *57*, 10034–10072; *Angew. Chem.* **2018**, *130*, 10188-10228; c) D. M. Schultz, T. P. Yoon, *Science* **2014**, *343*, 985-993; d) J. D. Bell, J. A. Murphy, *Chem. Soc. Rev.* **2021**, *50*, 9540-9685.

[8] For a Review, see: M. Mečiarová, P. Tisovský, R. Šebesta, *New. J. Chem.* **2016**, *40*, 4855-4864.

[9] Okada and Oda first described the use of $[Ru(bpy)_3]^{2+}$ under photoredox conditions, see: a) K. Okada, K. Okamoto, M. Oda, *J. Chem. Soc., Chem. Commun.* **1989**, 1636; b) K. Okada, K. Okamoto, N. Morita, K. Okubo, M. Oda, *J. Am. Chem. Soc.* **1991**, *113*, 9401-9402.

[10] D. A. Nicewicz, D. W. C. MacMillan, *Science* **2008**, *322*, 77-80.

[11] D. Kalyani, K. B. McMurtrey, S. R. Neufeldt, M. S. Sanford, J. *Am. Chem. Soc.* **2011**, *133*, 18566-18569.

[12] Z. Zuo, D. T. Ahneman, L. Chu, J. A. Terrett, A. G. Doyle, D. W. C. MacMillan, *Science* **2014**, *345*, 437-440.

[13] J. C. Tellis, D. N. Primer, G. A. Molander, *Science* **2014**, *345*, 433-436.

[14] A. E. Allen, D. W. C. MacMillan, *Chem. Sci.* **2012**, *3*, 633-658.

[15] O. Gutierrez, J. C. Tellis, D. N. Primer, G. A. Molander, M. C. Kozlowski, *J. Am. Chem. Soc.* **2015**, *137*, 4896-4899.

[16] L. Buzzetti, G. E. M. Crisenza, P. Melchiorre, *Angew. Chem. Int. Ed.* **2019**, *58*, 3730-3747; *Angew. Chem.* **2019**, *131*, 3768-3786.

[17] N. A. Till, S. Oh, D. W. C. MacMillan, M. J. Bird, *J. Am. Chem. Soc.* **2021**, *143*, 9332-9337.

[18] D. A. Everson, D. J. Weix, *J. Org. Chem.* **2014**, *79*, 4793-4798.

[19] A. Y. Chan, I. B. Perry, N. B. Bissonnette, B. F. Buksh, G. A. Edwards, L. I. Frye, O. L. Garry, M. N. Lavagnino, B. X. Li, Y. Liang, E. Mao, A. Millet, J. V. Oakley, N. L. Reed, H. A. Sakai, C. P. Seath, D. W. C. MacMillan, *Chem. Rev.* **2022**, *122*, 1485-1542.

[20] L. Capaldo, D. Ravelli, M. Fagnoni, *Chem. Rev.* **2022**, *122*, 1875-1924.

[21] G. C. Fu, *ACS Cent. Sci.* **2017**, *3*, 692-700.

[22] A. H. Cherney, N. T. Kadunce, S. E. Reisman, *Chem. Rev.* **2015**, *115*, 9587-9652.

[23] E. J. Corey, M. F. Semmelhack, *J. Am. Chem. Soc.* **1967**, *89*, 2755-2757; for a mechanistic studies, see: L. S. Hegedus, D. H. P. Thompson, *J. Am. Chem. Soc.* **1985**, *107*, 5663-5669.

[24] a) M. Durandetti, J. Périchon, *Synthesis* **2006**, *9*, 1542-1548; b) M. Durandetti, C. Gosmini, J. Périchon, *Tetrahedron* **2007**, *63*, 1146-1153.

[25] M. van Gemmeren, M. Börjesson, A. Tortajada, S.-Z. Sun, K. Okura, R. Martin, *Angew. Chem. Int. Ed.* **2017**, *56*, 6558-6562; *Angew. Chem.* **2017**, *129*, 6658-6662.

[26] Nowadays, electrochemical processes are assisting to a renaissance; for a relevant review, see: M. Yan, Y. Kawamata, P. S. Baran, *Chem. Rev.* **2017**, *117*, 13230-13319.

[27] S. Durandetti, S. Sibille, J. Périchon, *J. Org. Chem.* **1989**, *54*, 2198-2204.

[28] Z. Tan, X. Wan, Z. Zang, Q. Qian, W. Deng, H. Gong, *Chem. Commun.* **2014**, *50*, 3827-3830.

[29] J. L. Schwarz, F. Schäfers, A. Tlahuext-Aca, L. Lückemeier, F. Glorius, *J. Am. Chem. Soc.* **2018**, *140*, 12705-12709.

[30] H. Mitsunuma, S. Tanabe, H. Fuse, K. Ohkubo, M. Kanai, *Chem. Sci.* **2019**, *10*, 3459-3465.

[31] L. Pitzer, J. L. Schwarz, F. Glorius, *Chem. Sci.* **2019**, *10*, 8285-8291.

[32] Y. Katayama, H. Mitsunuma, M. Kanai, *Synthesis* **2022**, *54*, 1684-1694.

[33] A. Gualandi, G. Rodeghiero, A. Faraone, F. Patuzzo, M. Marchini, F. Calogero, R. Perciaccante, T. P. Jansen, P. Ceroni, P. G. Cozzi, *Chem. Commun.* **2019**, *55*, 6838–6841.

[34] D. A. Everson, D. J. Weix, *J. Org. Chem.* **2014**, *79*, 4793-4798.

[35] Recently, Glorius reported a keen solution for this problem, by the employment of more oxidable allylsilanes, see: F. Schäfers, S. Dutta, R. Kleinmans, C. Mück-Lichtenfeld, F. Glorius, *ACS Catal.* **2022**, *12*, 12281-12290.

[36] N. E. Tokel-Takvoryan, R. E. Hemingway, A. Bard, *J. Am. Chem. Soc.* **1973**, *95*, 6582-6589.

[37] P. B. Kraikivskii, H.-F. Klein, V. V. Saraev, R. Meusinger, I. Svoboda, M. Pashchanka, *J. Organomet. Chem.* **2009**, *694*, 3912-3917.

[38] B. Maity, C. Zhu, M. Rueping, L. Cavallo, *ACS. Catal.* **2021**, *11*, 13973-13982.

[39] N. A. Till, L. Tian, Z. Dong, G. D. Scholes, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2020**, *142*, 15830-15841.

[40] a) S. W. Kim, W. Zhang, M. J. Krische, *Acc. Chem. Res.* **2017**, *50*, 2371-2380; b) K. D. Nguyen, B. Y. Park, T. Luong, H. Sato, V. J. Garza, M. J. Krische, *Science* **2016**, *354*, 300-305.

[41] J. L. Schwarz, H.-M. Huang, T. O. Paulisch, F. Glorius, *ACS Catal.* **2020**, *10*, 1621-1627.

[42] F. Li, S. Lin, Y. Chen, C. Shi, H. Yan, C. Li, C. Wu, L. Lin, C. Duan, L. Shi, *Angew. Chem. Int. Ed.* **2021**, *60*, 1561-1566; *Angew. Chem.* **2021**, *133*, 1585-1590.

[43] a) Y. Sato, M. Takimoto, K. Hayashi, T. Katsuhara, K. Takagi, M. Mori, *J. Am. Chem. Soc.* **1994**, *116*, 9771-9772; b) M. Takimoto, Y. Hiraga, Y. Sato, M. Mori, *Tetrahedron Lett.* **1998**, *39*, 4543-4546; c) Y. Sato, M. Takimoto, M. Mori, *J. Am. Chem. Soc.* **2000**, *122*, 1624-1634.

[44] M. Kimura, H. Fujimatsu, A. Ezoe, K. Shibata, M. Shimizu, S. Matsumoto, Y. Tamaru, *Angew. Chem. Int. Ed.* **1999**, *38*, 397-400; *Angew. Chem.* **1999**, *111*, 410-413.
[45] M. Kimura, A. Ezoe, K. Shibata, Y. Tamaru, *J. Am. Chem. Soc.* **1998**, *120*, 4033-4034.
[46] Q.-Y. Meng, S. Wang, G. S. Huff, B. König, *J. Am. Chem. Soc.* **2018**, *140*, 3198-3201.
[47] Y.-L. Li, W.-D. Li, Z.-Y. Gu, J. Chen, J.-B. Xia, *ACS Catal.* **2020**, *10*, 1528-1534.
[48] J. A. Terrett, J. D. Cuthbertson, V. W. Shurtleff, D. W. MacMillan, *Nature* **2015**, *524*, 330-334.
[49] T. Chatterjee, N. Iqbal, Y. You, E. J. Cho, *Acc. Chem. Res.* **2016**, *49*, 2284-2294.
[50] J. Li, Y. Luo, H. W. Cheo, Y. Lan, J. Wu, *Chem.* **2019**, *5*, 192-203.
[51] M. S. Lowry, J. I. Goldsmith, J. D. Slinker, R. Rohl, R. A. Jr. Pascal, G. G. Malliaras, S. Bernhard, *Chem. Mat.* **2005**, *17*, 5712-5719.
[52] S. S. Ng, T. F. Jamison, *Tetrahedron* **2005**, *61*, 11405-11417.
[53] H. Xie, B. Breit, *ACS Catal.* **2022**, *12*, 3249-3255.
[54] K. N. Lee, Z. Lei, M.-Y. Ngai, *J. Am. Chem. Soc.* **2017**, *139*, 5003-5006.
[55] Q. Lin, G. Dawson, T. Diao, *Synlett* **2021**, *32*, 1606-1620.
[56] A. Gualandi, F. Calogero, M. Mazzarini, S. Guazzi, A. Fermi, G. Bergamini, P. G. Cozzi, *ACS Catal.* **2020**, *10*, 3857-3863.
[57] A. Gualandi, M. Anselmi, F. Calogero, S. Potenti, E. Bassan, P. Ceroni, P. G. Cozzi, *Org. Biomol. Chem.* **2021**, *19*, 3527-3550.
[58] A. Tlili, S. Lakhdar, *Angew. Chem. Int. Ed.* **2021**, *60*, 19526-19549; *Angew. Chem.* **2021**, *133*, 19678-19701.
[59] J. Luo, J. Zhang, *ACS Catal.* **2016**, *6*, 873-877.
[60] Y. Kwon, J. Lee, Y. Noh, D. Kim, Y. Lee, C. Yu, J. C. Roldao, S. Feng, J. Gierschner, R. Wannemacher, M. S. Kwon, *Nat. Commun.* **2023**, *14*, 92-106.
[61] N. A. Romero, D. A. Nicewicz, *Chem. Rev.* **2016**, *116*, 10075-10166.
[62] P.-Z Wang, J.-R. Chen, W.-J. Xiao, *Org. Biomol. Chem.* **2019**, *17*, 6936-6951.
[63] F. Calogero, S. Potenti, E. Bassan, A. Fermi, A. Gualandi, J. Monaldi, B. Dereli, B. Maity, L. Cavallo, P. Ceroni, P. G. Cozzi, *Angew. Chemie Int. Ed.* 2022, 61, e202114981; *Angew. Chem.* **2021**, *134* ,e202114981.
[64] G. E. M. Crisenza, D. Mazzarella, P. Melchiorre, *J. Am. Chem. Soc.* **2020**, *142*, 5461-5476
[65] B. Limburg, A. Cristòfol, A. W. Kleij, *J. Am. Chem. Soc.* **2022**, *144*, 10912-10920.
[66] For other DFT investigation in photoredox catalysis, see: a) D. A. Cagan, D. Bím, B. Silva, N. P. Kazmierczak, B. J. McNicholas, R. G. Hadt, J. Am. Chem. Soc. 2022, 144, 6516-6531; b) J. Majhi, R. K. Dhungana, À. Rentería-Gómez, M. Sharique, L. Li, W. Dong, O. Gutierrez, G. A. Molander, *J. Am. Chem. Soc.* **2022**, *144*, 15871-15878. For a Review: c) M. Yuan, O. Gutierrez, *WIREs Comput Mol Sci.* **2022**, *12*, e1573.
[67] A. Gualandi, F. Calogero, E. Pinosa, D. Corbisiero, P. G. Cozzi, *Synthesis*, **2023**, *55*, 3737-3758.
[68] B. Thiyagarajan, M. E. Kerr, J. C. Bollinger, V. G. Jr. Young, J. W. Bruno, *Organometallics* **1997**, *16*, 1331-1334.
[69] For selected papers about η_2-aldehyde nickel(0) complexes, see: a) S. Ogoshi, M.-A. Oka, H. Kurosawa, *J. Am. Chem. Soc.* **2004**, *126*, 11802-11803; b) S. Ogoshi, H. Kamada, H. Kurosawa, *Tetrahedron* **2006**, *62*, 7583-7588; c) S. Ogoshi,T. Arai, M. Ohashi, H. Kurosawa, *Chem. Commun.* **2008**, 1347-1349; d) m. Ohashi, H. Saijo, T. Arai, S. Ogoshi, *Organometallics* **2010**, *29*, 6534-6540; e) S. Sakaki, K. Kitaura, K. Morokuma, K. Ohkubo, *Inorg. Chem.* **1983**, *22*, 104-108.
[70] a) J. Montgomery, *Angew. Chem. Int. Ed.* **2004**, *43*, 3890-3908; b) S. Z. Tasker, E. A. Standley, T. F. Jamison, *Nature* **2014**, *509*, 299-309; c) E. P. Jackson, H. A. Malik, G. J. Sormunen, R. D. Baxter, P. Liu, H. Wang, A.-R. Shareef, J. Montgomery, *Acc. Chem. Res.* **2015**, *48*, 1736-1745; d) Y. Cai, F. Li, Y.-Q. Li, W.-B. Zhang, F.-H. Liu, S.-L. Shi, *Tetrahedron Lett.* **2018**, *59*, 1073-1079.
[71] Montgomery, J., *Acc. Chem. Res.* **2000**, *33*, 467-473.
[72] S.-S. Ng, T. F. Jamison, *J. Am. Chem. Soc.* **2005**, *127*, 7320-7321.
[73] a) K. M. Miller, W.-S. Huang, T. F. Jamison, *J. Am. Chem. Soc.* **2003**, *125*, 3442-3443; b) K. M. Miller, T. F. Jamison, *J. Am. Chem. Soc.* **2004**, *126*, 15342-15343; c) K. M. Miller, T. Luanphaisarnnont, C. Molinaro, T. F. Jamison, *J. Am. Chem. Soc.* **2004**, *126*, 4130-4131; d) A. D. Jenkins, A. Herath, M. Song, J. Montgomery, *J. Am. Chem. Soc.* **2011**, *133*, 14460-14466.
[74] H.-H. Zhang, H. Chen, C. Zhu, S. Yu, *Sci. China Chem.* **2020**, *63*, 637-647.
[75] F. Calogero, G. Magagnano, S. Potenti, A. Gualandi, A. Fermi, P. Ceroni, P. Giorgio Cozzi, *Adv. Synth. Catal.* **2022**, *364*, 3410–3419.
[76] M. Nakajima, E. Fava, S. Loescher, Z. Jiang, M. Rueping, *Angew. Chem. Int. Ed.* **2015**, 54, 8828-8832; *Angew. Chem.* **2015**, 127, 8952-8956.
[77] W.-S. Huang, J. Chan, T. F. Jamison, *Org. Lett.* **2000**, *2*, 4221−4223
[78] P.-Z. Wang, J.-R. Chen, W.-J. Xiao, *Org. Biomol. Chem.* **2019**, *17*, 6936-6951.
[79] K. Li, X. Long, S. Zhu, *ACS Catal.* **2023**, *13*, 2422-2431.
[80] Y. Neveselý, M. Wienhold, J. J. Molloy, R. Gilmour, *Chem. Rev.* **2022**, *122*, 2650-2694.
[81] J. K. Garcia, J. M. Gilbert, D. J. Weix, *J. Am. Chem. Soc.* **2019**, *141*, 1823-1827.
[82] J. C. Adrian, M. Snapper, *J. Org. Chem.* **2003**, *68*, 2143-2150.
[83] M. Md. Hossain, T. L. Gianetti, *Trends in Chemistry* **2022**, *4*, 962-963.
[84] F. Calogero, G. Magagnano, S. Potenti, F. Pasca, A. Fermi, A. Gualandi, P. Ceroni, G. Bergamini, P. G. Cozzi, *Chem. Sci.* **2022**, *13*, 5973-5981.
[85] F. Lévesque, M. J. Di Maso, K. Narsimhan, M. K. Wismer, J. R. Naber, *Org. Proc. Res. Devel.* **2020**, *24*, 2935-2940.

[86] We have recently found suitable conditions for a metallaphotoredox Reformatsky reaction in which the reactive species is a nucleophilic nickel enolate.