

**Photochemistry**

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# Reductive Cyclization of Unactivated Alkyl Chlorides with Tethered Alkenes under Visible-Light Photoredox Catalysis

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Dedicated to Professor Pablo Espinet on the occasion of his 70th birthday

**Abstract:** The chemical inertness of abundant and commercially available alkyl chlorides precludes their widespread use as reactants in chemical transformations. Presented in this work is a metallaphotoredox methodology to achieve the catalytic intramolecular reductive cyclization of unactivated alkyl chlorides with tethered alkenes. The cleavage of strong C(sp<sup>3</sup>)-Cl bonds is mediated by a highly nucleophilic low-valent cobalt or nickel intermediate generated by visible-light photoredox reduction employing a copper photosensitizer. The high basicity and multidentate nature of the ligands are key to obtaining efficient metal catalysts for the functionalization of unactivated alkyl chlorides.

Visible-light photoredox catalysis has opened novel and milder approaches for C-C and C-heteroatom (C-Het) bond-forming reactions through carbon-centered radicals.<sup>[1]</sup> In this regard, organic halides are widely used electrophiles that can be activated through reducing single-electron transfer (SET) reactions, and therefore serve as convenient coupling partners. The continuous development of photoredox catalysts (PCs) have significantly expanded the reduction potential window (beyond -3 V vs. SCE),<sup>[2]</sup> facilitating the cleavage of alkyl bromides,<sup>[3]</sup> activated alkyl chlorides and aryl chlorides<sup>[2c,4]</sup> by SET processes. Additionally, the synergistic merging of a photosensitizer and either a coordination metal complex or silane has enabled the efficient activation of alkyl bromides towards the generation of new C-C or C-Het

bonds. This concept was recently be expanded to the carboxylation of aryl chlorides.<sup>[5]</sup>


Although alkyl chlorides are available and bench-stable feedstocks, their chemical inertness hinders their use as electrophilic partners in transition metal catalyzed reactions.<sup>[6]</sup> Indeed, unactivated alkyl chlorides are beyond the scope of current state-of-the-art photocatalytic methodologies. A direct homolytic cleavage of unactivated C(sp<sup>3</sup>)-Cl bonds, triggered by outersphere SET from current photosensitizers, is not feasible because of its extremely negative redox potential values.<sup>[7,8]</sup> Biologically relevant B<sub>12</sub>-dependent enzymes (that bear a cobalt corrinoid cofactor) and methyl-coenzyme M reductase (MCR; containing a nickel porphyrinoid F<sub>430</sub> cofactor), and their synthetic models exhibit an extreme nucleophilic reactivity.<sup>[9]</sup> Their ability to reach oxidation state +1 in basic ligand environments renders them supernucleophiles. Mechanistic studies of catalytically activated alkyl chlorides, and stoichiometric dehalogenation reactions of alkyl chlorides and bromides, with B<sub>12</sub> and methyl-coenzyme M reductase revealed the formation of C-centered radical intermediates.<sup>[10]</sup> This finding set the foundation for the development of C-C bond-forming reactions by strong chemical reductants,<sup>[11]</sup> electrocatalysis,<sup>[12]</sup> and, more recently, photocatalysis.<sup>[6c,13]</sup>


Inspired by these precedents, we envision the in situ photogeneration of low-valent cobalt and nickel complexes that behave as supernucleophiles, capable of activating strong C(sp<sup>3</sup>)-Cl bonds under visible-light irradiation (Figure 1). Herein, we disclose a new approach for the reductive cyclization of unactivated alkyl chlorides, bearing tethered alkenes, to form five-membered carbocycles with broad functional-group tolerance at mild reaction conditions. The combination of the photoredox catalyst PC<sub>Cu</sub> and the coordination cobalt or nickel complex [L<sup>H</sup>M(OTf)](OTf) (**1<sup>H</sup>M**, M = Co, Ni) enables reductive transformations that operate via low-valent metal intermediates (see Table 1).<sup>[14]</sup>

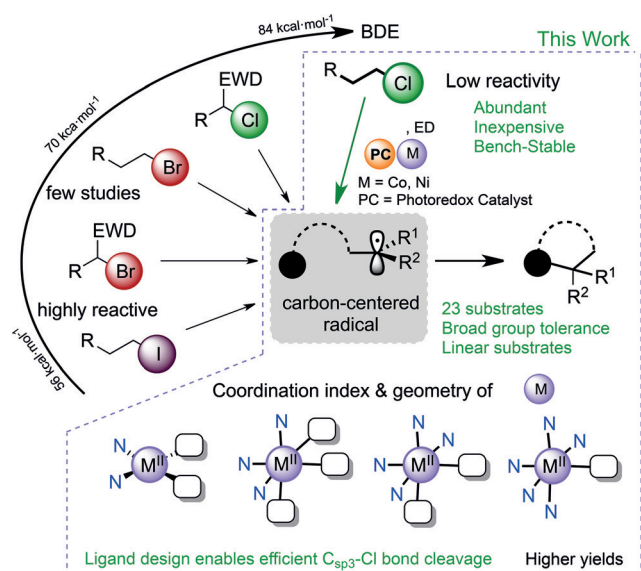
We chose the hex-5-enyl halide **2a** as a suitable model substrate for the desired transformation since the Thorpe-Ingold effect provided by the dimalonate unit facilitates the cyclization step (Table 1). After a systematic screening (see Table SI.EP-1 in the Supporting Information), optimal reaction conditions yielded 83% of the 5-exo-trig cyclic product **4a** when employing the PC<sub>Cu</sub>/**1<sup>H</sup>Co** catalyst system in combination with Et<sub>3</sub>N (14.4 equiv) in EtOH/MeCN (3:2) and irradiating with blue-light-emitting diodes (1 W, 447 nm) for 24 hours at 30 °C (Table 1, entry 1). The choice of EtOH as

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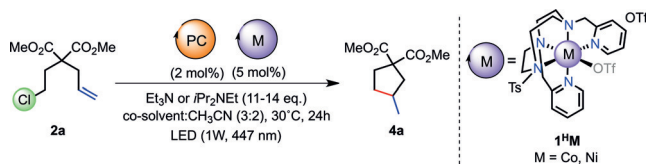
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**Figure 1.** Photocatalytic strategies towards reductive intramolecular cyclization reactions of alkyl halides. Best performance is obtained with the  $\text{PC}_{\text{Cu}}/\text{1}^{\text{H}}\text{Ni}$  catalyst system using  $i\text{Pr}_2\text{NEt}$  as an electron donor.

**Table 1:** Screening of conditions for the development of reductive cyclization of alkyl chlorides with tethered alkenes.



Catalyst	Cosolv.	ED	Yield (Conv.) [%] <sup>[a]</sup>
1	$\text{1}^{\text{H}}\text{Co}$	EtOH	Et <sub>3</sub> N 83 (96)
2	$\text{1}^{\text{H}}\text{Co}$	–	Et <sub>3</sub> N 17 (24)
3	$\text{1}^{\text{H}}\text{Co}$	H <sub>2</sub> O	Et <sub>3</sub> N 22 (67)
4	$\text{1}^{\text{H}}\text{Co}$	MeOH	Et <sub>3</sub> N 27 (39)
5	$\text{1}^{\text{H}}\text{Co}$	EtOH	$i\text{Pr}_2\text{NEt}$ 78 (93)
6	$\text{1}^{\text{H}}\text{Ni}$	EtOH	Et <sub>3</sub> N 74 (99)
7	$\text{1}^{\text{H}}\text{Ni}$	EtOH	$i\text{Pr}_2\text{NEt}$ 96 (99)
8	$\text{Co}(\text{OTf})_2(\text{MeCN})_2$	EtOH	Et <sub>3</sub> N 5 (7)
9	$\text{Ni}(\text{OTf})_2(\text{MeCN})_2$	EtOH	Et <sub>3</sub> N 1 (8)

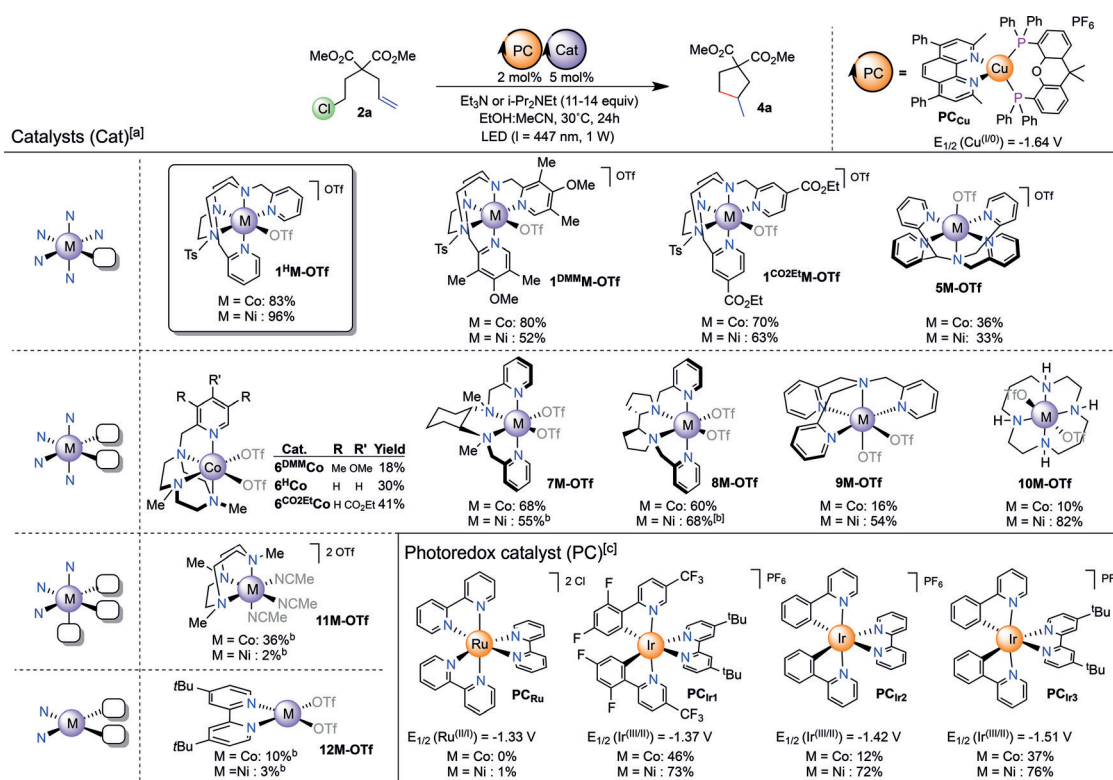
Reaction conditions: substrate (10 mM), PC ( $\text{PC}_{\text{Cu}}$ , 2 mol%), Co or Ni catalyst (5 mol%), electron donor (14.4 equiv. for Et<sub>3</sub>N or 11.4 equiv. for  $i\text{Pr}_2\text{NEt}$ ), cosolvent/MeCN (3:2), visible-light irradiation with blue LEDs (1 W, 447 nm) for 24 h at 30°C. [a] Conversion and yield were determined by GC using biphenyl as an internal standard. Reactions run in triplicate. ED = electron donor.

protic solvent was essential for achieving high yields of **4a**. For instance, **4a** was obtained in low yields when the reaction was performed in other solvent systems such as MeCN, H<sub>2</sub>O/MeCN, or MeOH/MeCN (entries 2–4). The use of  $i\text{Pr}_2\text{NEt}$  (11.4 equiv.) as an electron donor (ED) slightly decreased the yield of **4a** to 78% (entry 5). Strikingly, the analogous nickel complex  $[\text{L1}^{\text{H}}\text{Ni}(\text{OTf})](\text{OTf})$  ( $\text{1}^{\text{H}}\text{Ni}$ ) in combination with  $i\text{Pr}_2\text{NEt}$  yielded the desired product **4a** in 96% yield (entries 6 and 7). These observations are supported by the fact that  $\text{1}^{\text{H}}\text{Ni}$  shows faster kinetics for the formation of **4a** than its cobalt analogue  $\text{1}^{\text{H}}\text{Co}$  (see Figure SI.EP-3). Single-point monitoring experiments of the catalytic reduction of **2a**

throughout light-dark cycles show that the transformation is light-mediated (see Figure SI.EP-4). Likewise, control experiments indicate that all reaction components are required for its progression (see Table SI.EP-4). Furthermore, the role of the photosensitizer was investigated in greater detail, and it is particularly noteworthy that the combination of either  $\text{1}^{\text{H}}\text{Co}$  or  $\text{1}^{\text{H}}\text{Ni}$  with other PCs based on heavier transition metals, such as Ir and Ru, afforded lower yields of **4a** (Figure 2). Reactivity through Ni nanoparticles is discarded since mercury poisoning tests did not change the catalytic activity. Single-point monitoring experiments of competition between alkyl chlorides and bromides reveal that the activation of the alkyl chlorides starts just after the complete consumption of bromide substrate (see Figure SI.EP-6–8).

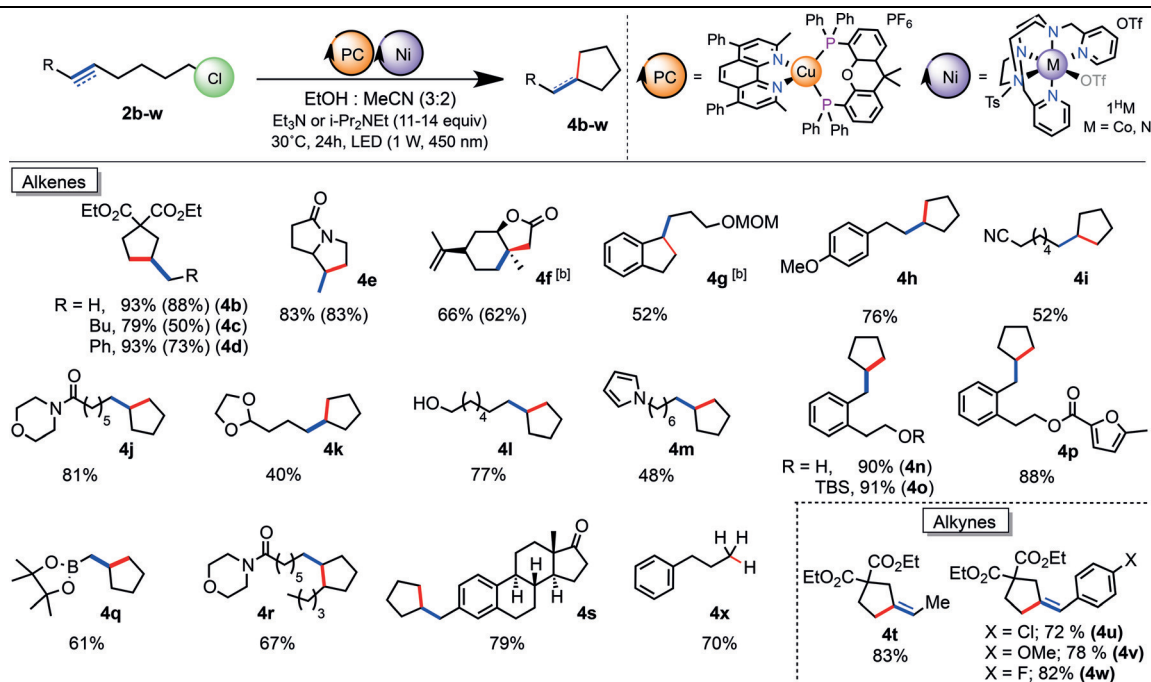
The use of the metallic precursor salts gave only trace amounts of **4a** (Table 1, entries 8 and 9), highlighting the importance of the  $\text{L1}^{\text{H}}$  ligand for the cleavage of strong  $\text{C}(\text{sp}^3)\text{--Cl}$  bonds. In this regard, we examined a variety of cobalt and nickel complexes bearing different coordination motifs for the reductive cyclization of **2a** under visible-light irradiation (Figure 2). In general terms, pentacoordinate Co complexes based on the triazacyclononane scaffold  $\text{1}^{\text{H}}\text{Co}$  ( $x = \text{H}, \text{MeOMe}, \text{CO}_2\text{Et}$ ) showed higher catalytic activity than the corresponding tetracoordinate  $\text{6}^{\text{H}}\text{Co}$  (70–83% yield vs. 18–41%, respectively). Tuning the electronic effects on the ligand has a greater impact on the reactivity of  $\text{1}^{\text{H}}\text{Ni}$  (varying from 52 to 96%) than for  $\text{1}^{\text{H}}\text{Co}$ . Other penta- and tetracoordinate Co and Ni complexes explored during this screening, including complexes **5M**, **7M**, **8M**, and **9M** showed low to moderate reactivity (16–68%). We also explored a variety of square-planar Co and Ni complexes that have been previously employed towards the reduction of alkyl halides (see Table SI.EP-3).<sup>[11,16]</sup> Among the tested complexes, only cobalt porphyrin (**18Co**) and Ni cyclam (**10Ni**) afforded **4a** in good yields (Figure 2; see Table SI.EP-3). Finally, metal catalysts based on commercially available ligands such as 4,4'-di-tert-butyl-2,2'-dipyridyl (dtbbpy), terpyridine, and 1,4,7-trimethyl-1,4,7-triazacyclononane afforded **4a** only in low yields (2–42%, see Table SI.EP-3). This study identifies that the Co and Ni complexes with high coordination numbers, 4 and 5, bearing basic N-based ligands are remarkably active for the activation of  $\text{C}(\text{sp}^3)\text{--Cl}$  bonds, showing moderate to high catalytic activity. The importance of the catalytic system is evidenced in the observation of the following unproductive conditions: 1)  $\text{Ni}(\text{COD})_2$  in combination with or without stoichiometric amount of ligand  $\text{L1}^{\text{H}}$  under photocatalytic conditions and 2)  $\text{1}^{\text{H}}\text{Ni}$  in combination with Zn or Mn as reductants instead of the PC and electron donor (see Table SI.EP-3).

The scope of the methodology was explored with the dual catalytic system  $\text{PC}_{\text{Cu}}/\text{1}^{\text{H}}\text{M}$  ( $\text{M} = \text{Co}, \text{Ni}$ ) owing to its excellent catalytic performance for the cyclization of the model substrate **2a** (Table 2). The bimetallic catalyst  $\text{PC}_{\text{Cu}}/\text{1}^{\text{H}}\text{Co}$  enabled the formation of five-membered carbocyclic products of different diethyl malonates (**4b–d**) in 50–88% yields as well as fused bicyclic structures such as the [5,5] pyrrolizidinone **4e** (83% yield)<sup>[5,6]</sup> and (*R*)-carveol derivative **4f** (62% yield, over 2 steps). The preparation of carbocycles starting from more challenging linear alkyl chlorides with  $\text{PC}_{\text{Cu}}/\text{1}^{\text{H}}\text{Co}$



**Figure 2.** Catalysts studied for the cyclization of unactivated alkyl chlorides. [a] Conversion and yield were determined by GC using biphenyl as an internal standard. Reactions run in triplicate. [b] Complex formed in situ in the reaction vessel. [c] Redox potentials are given vs. SCE.

**Table 2:** Substrate scope of the cyclization of unactivated alkyl chlorides.



Standard reaction conditions: substrate (10 mM), PC<sub>Cu</sub> (2 mol%), 1<sup>H</sup>Ni or 1<sup>H</sup>Co (5 mol%), ED [Et<sub>3</sub>N (14.4 equiv) or *i*-Pr<sub>2</sub>NEt (11.4 equiv.)], EtOH/MeCN (3:2), visible-light irradiation with blue LEDs (λ = 447 nm) at 30°C for 24 h. All are those of isolated products and averages of at least three reactions. Within parentheses are given the yield for 1<sup>H</sup>Co. [b] Yield of product isolated after two steps.

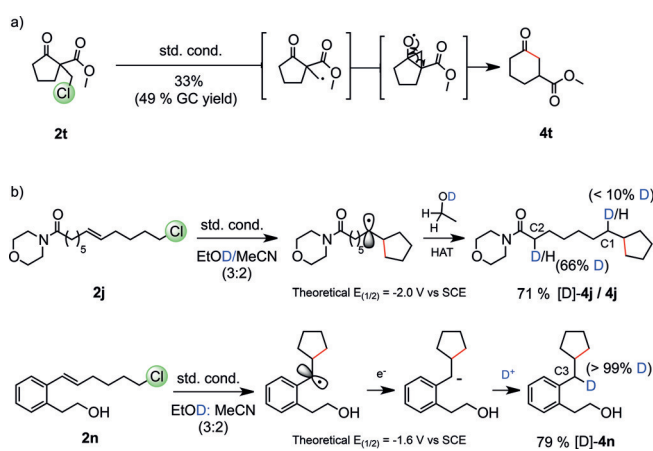
was troublesome, with the desired product obtained only in low yields. Likewise, the potential catalyst **18Co** also gave low

yields for the cyclization reaction of linear substrates (see Table SI.EP-4). Our group previously showed that 1<sup>H</sup>Co



catalyzes dihydrogen formation when protic solvents are used,<sup>[15a]</sup> and competes with the reductive cyclization (see Figure SI.EP-4). In contrast, **1<sup>H</sup>Ni** and **10Ni** catalysts are not active towards proton reduction under photocatalytic conditions,<sup>[15a]</sup> and might contribute to the improved reactivity towards C(sp<sup>3</sup>)-Cl bond cleavage.<sup>[17]</sup> We focused on **1<sup>H</sup>Ni** complex because it is slightly more efficient in comparison to **10Ni** (see Table SI.EP-4). Starting from diethyl malonate derivatives the corresponding carbocycles could be obtained in yields ranging from 79–93%. We also synthesized **4e** and **4f** in 83% and 66% (over two steps) yields, respectively, and the preparation of indane structure **4g** in 52% yield. Remarkably, the bimetallic **PC<sub>Cu</sub>/1<sup>H</sup>Ni** catalyst allowed the cyclization of several linear hex-5-enyl chlorides with synthetically useful yields and exhibiting various degrees of complexity as well as different functional groups. Owing to the mildness of the reaction conditions, our photocatalytic protocol is compatible with esters (**4b–d**, **4f**, **4p**, **4t–w**), alkenes (**4f**), nitriles (**4i**), carbamates (**4e**, **4j**, **4r**), ketones (**4s**), alcohol protecting groups (MOM (**4g**), TBS (**4o**), free alcohols (**4l**, **4o**), dioxolanes (**4k**), alkylboronates (**4q**), and heteroaromatics such as pyrrole (**4m**) and furan (**4p**).<sup>[17]</sup> Aromatic halides having either a chlorine (**4u**) and fluorine (**4w**) group are also compatible with this methodology. The secondary alkyl chloride **2r** yielded the corresponding cyclic product **4r** in 67% yield and the **2f** trisubstituted olefin forms a quaternary center in **4f** in 66% yield. The cyclization reaction can be expanded to internal alkynes which produces the desired cyclic products (**4t–w**) in a 1:1 mixture of *E/Z* isomers with synthetically useful yields (72–83% yield). In addition, we scaled up the reaction up to 5.1 mmol using **2a** (1.2 g) and obtained 81% yield of the desired product.

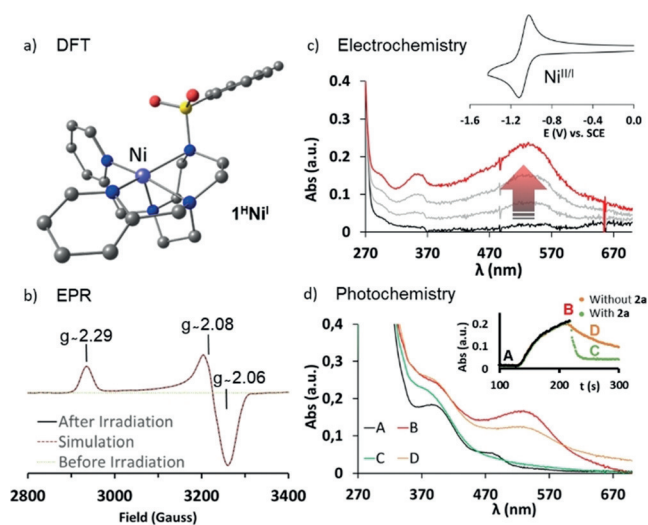
The proposal of radical intermediates during the reaction might explain the observed preference for the 5-*exo*-trig cyclic product with our photocatalytic protocol. In this regard, the Dowd–Beckwith ring-expansion reaction of the chloromethyl β-keto ester **2t** gave the corresponding one-carbon expanded product **4t** [49% yield (GC), 33% yield (isolated)], supporting the formation of alkyl radical intermediates (Figure 3a).<sup>[15]</sup> Labeling experiments using deuterated solvents are also in agreement with the formation of C-centered



**Figure 3.** a) Ring expansion test. b) Deuterium-labeling experiments.

radicals. The photocatalytic reductive cyclization of **2j** in EtOD/MeCN (3:2) gave **[D]-4j** in 71% yield with less than 10% of deuterium incorporation at C1.<sup>[16]</sup> This result endorses the formation of highly reactive alkyl radical intermediates that engage into hydrogen-atom transfer (HAT) from the solvent ([D]-ethanol, BDE(CH<sub>3</sub>CH<sub>2</sub>OD)–BDE(**4j**) = -3.1 kcal mol<sup>-1</sup>; see S.I.TS Section 1.1–1.2). Under the same reaction conditions, **2n** gave 79% yield of **[D]-4n** with complete incorporation of the deuterium atom at C3 (Figure 3b, BDE(CH<sub>3</sub>CH<sub>2</sub>OD)–BDE(**4n**) = 9.8 kcal mol<sup>-1</sup>).<sup>[17]</sup> In this case, the benzylic radical formed can be reduced during catalysis to the corresponding radical anion ( $E_{1/2} = -1.6$  V vs. SCE calculated by DFT, see S.I.TS Section 1.1–1.2), which is then protonated by the [D]-ethanol to give **[D]-4n**.

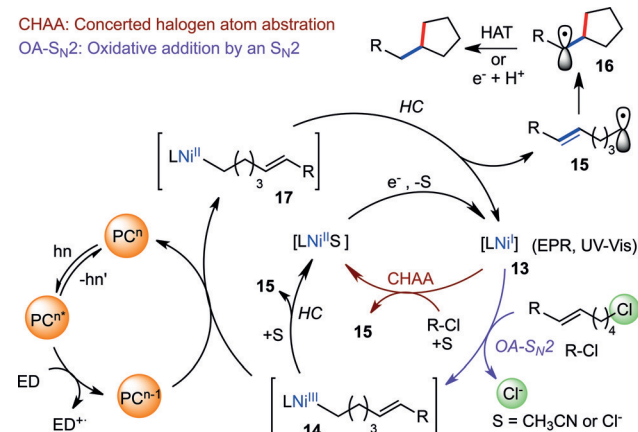
More insight into the reaction mechanism was obtained by monitoring (UV/Vis and EPR) the reaction under relevant catalytic conditions, electrochemical studies, and DFT modelling (Figure 4; see SI.EP and SI.TS for details). Under light irradiation, only significant changes in the UV/Vis and EPR signals are observed in the presence of **1<sup>H</sup>Ni**, **PC<sub>Cu</sub>**, and *i*Pr<sub>2</sub>NEt. A clear EPR signal with virtually axial symmetry is formed (*g*-values 2.06, 2.08 and 2.29). The obtained *g*-values combined with the appearance of an absorption band at 535 nm in the UV/Vis is consistent with the photogeneration of a Ni<sup>I</sup> spin 1/2 species. Equivalent features are reported for related Ni<sup>I</sup> complexes.<sup>[18a]</sup> Spectroelectrochemical (SEC) experiments further corroborate the formation of Ni<sup>I</sup> species. The same absorption band at 535 nm is obtained at the Ni<sup>II/I</sup> reduction wave (SI.EP Section 13).



**Figure 4.** a) Calculated structure for the proposed Ni<sup>I</sup> intermediate **13**. b) EPR spectra of Ni<sup>I</sup> spin 1/2 species formed by irradiation. c) UV/Vis SEC of **1<sup>H</sup>Ni** (4 mM in 0.2 M TBAH/CH<sub>3</sub>CN:EtOH (2:3)). Applied potential from the 0 V (black line) to the Ni<sup>II/I</sup> redox wave (ca. -1.1 V vs. SCE, red line). Inset CV of **1<sup>H</sup>Ni**; d) Changes in UV/Vis spectrum of a reaction mixture containing **PC<sub>Cu</sub>** (20 μM) in CH<sub>3</sub>CN:EtOH: *i*-Pr<sub>2</sub>NEt (2:3:0.1) by addition of **1<sup>H</sup>Ni** and **2a** at 140 and 220 s after the irradiation started (447 nm), respectively; A (black line) just before **1<sup>H</sup>Ni** addition (final concentration 50 μM). B (Red Line) 80 s after A (**1<sup>H</sup>Ni** addition) the light is switched off. C and D) 50 s after B with (C, green line) and without (D, orange line) **2a** (final concentration 1 mM) added at B time (220 s). The green trace decay is mainly due to the reaction of **2a** with **1<sup>H</sup>Ni**. Inset) UV/Vis traces at λ 535 nm.

In the absence of a substrate, cyclic voltammetry (CV) of  $1^{\text{H}}\text{Ni}$  shows a reversible  $\text{Ni}^{\text{III}}$  wave at  $-1.08$  V vs. SCE ( $\Delta E_{\text{p}} = 91$  mV; Figure 4). Notably, the addition of varying amounts of **2a** to the same solution leads to a progressive loss of reversibility of the  $\text{Ni}^{\text{III}}$  feature. Moreover, the peak current of the forward peak slightly increases, whereas a new anodic peak appears at  $-0.28$  V vs. SCE which is consistent with a reaction between the generated  $\text{Ni}^{\text{I}}$  species and **2a** within the CV timescale (see Figures S1.EP-27–31). In agreement with CV data, UV/Vis-SEC experiments reveal that the formation of  $\text{Ni}^{\text{I}}$  species ( $\lambda_{\text{max}}$  535 nm) in the presence of **2a** (20 equiv) is inhibited (see Figures S1.EP-35–41). The concomitant growth of absorption bands at  $\lambda_{\text{max}}$  290 and 359 nm further supports the formation of new species. Additionally, the in situ photochemical-generated  $\text{Ni}^{\text{I}}$  showed a fast decay of the  $\text{Ni}^{\text{I}}$  signal upon addition of **2a**.

Based on these results, we have proposed a plausible catalytic cycle for the visible-light reductive cyclization of alkyl chlorides with the  $\text{PC}_{\text{Cu}}/1^{\text{H}}\text{Ni}$  catalytic system (Figure 5).



**Figure 5.** Hypothetical catalytic cycle for the visible-light reductive cyclization of unactivated alkyl chlorides with tethered alkenes. HAT = hydrogen atom abstraction, HC = homolytic cleavage.

Under catalytic conditions, the photoreduced copper complex ( $E_{1/2}(\text{PC}_{\text{Cu}}^{\text{I/0}}) = -1.69$  V vs. SCE see S1.EP-32)<sup>[14b]</sup> reduces  $1^{\text{H}}\text{Ni}$  by one electron, forming new  $\text{Ni}^{\text{I}}$  species ( $\text{Ni}^{\text{III}}$   $-1.08$  V and  $-1.51$  V vs. SCE, for  $\text{TiO}_2^-$  and  $\text{Cl}^-$  complexes, respectively).<sup>[14b]</sup> Thermodynamics discard a potential outersphere SET from  $\text{PC}_{\text{Cu}}^{\text{0}}$  or its excited state ( $-1.02$  V)<sup>[3c]</sup> to a  $\text{C}(\text{sp}^3)\text{-Cl}$  bond ( $< -3$  V vs. SCE).<sup>[8]</sup> EPR, UV/Vis, and CV experiments suggest that the photogenerated  $\text{Ni}^{\text{I}}$  species can react with alkyl chlorides. In agreement is the low-energy barriers ( $12.9$  and  $19.3$  kcal mol<sup>-1</sup>) calculated by DFT for the reaction of  $1^{\text{H}}\text{Ni}^{\text{I}}$  (**13**) with **2x** (3-chloropropyl)benzene as a challenging unactivated model substrate). Based on DFT studies, we hypothesize two different scenarios for the  $\text{C}(\text{sp}^3)\text{-Cl}$  bond cleavage. First, the activation of the  $\text{C}(\text{sp}^3)\text{-Cl}$  bond by an oxidative addition through an S<sub>N</sub>2 mechanism (OA-S<sub>N</sub>2) that generates the organometallic intermediate **14** (Figure 5,  $\Delta G^\ddagger = 12.9$  kcal mol<sup>-1</sup> and  $\Delta G = -3.0$  kcal mol<sup>-1</sup>; see S1.TS section 1.3).<sup>[10,18]</sup> Then, homolytic cleavage of the relatively weak M–C bond ( $-0.5$  kcal mol<sup>-1</sup> for **2x**) could regenerate

the divalent metal catalyst while forming C-centered radical intermediates (**15**).<sup>[19]</sup> A single-electron reduction of complex alkyl-M<sup>III</sup> to form **17** is favorable ( $\Delta G = -30.7$  kcal mol<sup>-1</sup>), for which homolytic cleavage of the M–C bond at room temperature is also accessible ( $\Delta G = 22.1$  kcal mol<sup>-1</sup> for **2x**).<sup>[12a]</sup> Finally, the radical generated can be trapped by the tethered alkene to form the kinetically favored 5-*exo-trig* carbocyclic compound (**16**). Alternatively, the activation of the  $\text{C}(\text{sp}^3)\text{-Cl}$  bond can occur by concerted halogen atom abstraction (CHAA) to generate directly M<sup>II</sup> chloride complex and the corresponding organic radical **15** (Figure 5,  $\Delta G^\ddagger = 19.3$  and  $\Delta G = -1.4$  kcal mol<sup>-1</sup> for **2x**; see S1.TS section 1.3).<sup>[20]</sup>

In conclusion we have developed a robust and efficient visible-light metallaphotoredox methodology for the cleavage of unactivated  $\text{C}(\text{sp}^3)\text{-Cl}$  bonds under mild reaction conditions. The in situ photogeneration of low-valent cobalt and nickel complexes bearing pentacoordinate N-based ligands was key to the observed photocatalytic activity for the cleavage of strong  $\text{C}(\text{sp}^3)\text{-Cl}$  bonds studied. The catalytic system was used for the visible-light reductive cyclization, allowing the construction of five-membered carbocycles employing alkyl chlorides as convenient starting materials with a broad functional-group tolerance. We envision that the catalyst design principles found herein will trigger the development of novel visible-light synthetic protocols that exploit the use of currently considered unreactive molecules, as available feedstocks and biologically active molecules containing alkyl chlorides.

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## Conflict of interest

The authors declare no conflict of interest.

**Keywords:** cyclizations · haloalkanes · photochemistry · reaction mechanisms · synthetic methods

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