A general visible-light-induced single nickel-catalyzed cross-coupling method with alkylzirconocenes has been developed. Alkylzirconocenes are generated in situ from terminal or internal alkenes through hydrozirconation and chain walking. This method is suitable for a wide range of organic halides and alkenes with excellent functional group tolerance, suggesting great potential for construction of carbon–carbon bonds. This method represents the first visible-light-induced cross-coupling of alkylzirconocenes.
Visible-Light-Induced Nickel-Catalyzed Cross-Coupling with Alkylzirconocenes from Unactivated Alkenes

Yadong Gao,1,2 Chao Yang,1,2 Songlin Bai,2 Xiaolei Liu,2,3 Qingcui Wu,2 Jing Wang,4 Chao Jiang,1,* and Xiangbing Qi2,5,6,*

SUMMARY
Transition-metal-catalyzed cross-coupling reactions between naturally abundant sp3-hybridized carbon centers facilitate access to diverse molecules with complex three-dimensional structures. Organometallic compounds are among one of the most powerful reagents that are broadly used in carbon–carbon bond formations. Although sp2-hybridized organometallic compounds are widely employed in cross-couplings, sp3-hybridized organometallic coupling partners are less developed. Herein, we report visible-light-induced single nickel-catalyzed C(sp3)–C(sp3), C(sp3)–C(sp2), and C(sp3)–C(sp) cross-coupling reactions using alkylzirconocenes, which are easily generated in situ from terminal or internal unactivated alkenes through hydrozirconation and chain walking. This method is mild and applicable for a large range of substrates including primary, secondary, tertiary alkyl, aryl, alkenyl, alkynyl halides, and a variety of alkenes. Mechanistic studies suggest a novel nickel-catalyzed radical cross-coupling pathway, which represents the first visible-light-induced transformation of alkylzirconocenes.

INTRODUCTION
Transition-metal-catalyzed cross-coupling reactions have become one of the most versatile synthetic methods for constructing carbon–carbon bonds.1 During the last several decades, tremendous progress has been made in the formation of bonds between sp2-hybridized carbons with cross-coupling strategies,2,3,4 distinguished examples including Heck, Negishi, and Suzuki-Miyaura cross-couplings, which have been widely applied in organic synthesis.5 In the past years, multiple new methods have been developed that enable cross-couplings of more challenging sp3-hybridized carbons, thereby greatly expanding its capacity to rapidly access carbon–carbon bonds that are embedded in three-dimensional architectures.6–9 The Fu,10 MacMillan,11,12 Baran,13–15 Knochel,16,17 Molander,16,18 and other research groups19–21 have made tremendous contributions in this field. Although sp2-hybridized organometallic compounds are widely used in cross-couplings, such as aryl or alkenyl magnesium, zinc, tin, boron, silicon, and so on,1,22 sp3-hybridized organometallic partners in cross-couplings are at present mainly limited to alkylmagnesiums, alkylzincs, and alkylborons.1 Alkylmagnesiums23–25 and alkylzincs24 are usually formed through deprotonation, metal-halogen exchange or transmetalation processes, and harsh reaction conditions and/or low functional group compatibility has limited their application scope (Figure 1A). Alkylborons represent an outstanding choice for cross-coupling reactions of sp3-hybridized carbons,18,25 which can be generated through alkene hydroboration (Figure 1A). However, as
far as we know, hydroboration/cross-coupling strategy is only known for the 9-BBN (9-Borabicyclo[3.3.1]nonane) reagent, the narrow reaction scope and lack of chain-walking property of alkylboron limited its potential application.

Organozirconocenes have emerged as very practical organometallic reagents, such as the homogeneous zirconium type Ziegle r-Natta catalysts that are used in the synthesis of polymers of alkenes. 26 Alkylzirconocene reagents, easily prepared from hydrozirconation of alkenes with bis(cyclopentadienyl)zirconium chloride hydride (Schwartz reagent), are capable of reacting with electrophiles to form various C–C (or X) bonds, 27–32 which represents one of the most attractive methods for value-added synthetic applications of unactivated alkenes. Compared with other alkylmetallic reagents, alkylzirconocenes offer several advantages, including mild generation conditions, excellent functional group tolerance, potential photoactivity, 33,34 and remote functionalization through rapid “chain walking,” 27 which provides an additional advantage compared with hydroboration. Therefore, we envisioned that alkylzirconocenes could be used as potential nucleophilic partners in cross-coupling reactions. Although sp²-hybridized alkynylzirconocenes have gained increasing application in cross-coupling reactions, 35–38 sp³-hybridized alkylzirconocenes have been far less explored: only copper-catalyzed couplings with allyl, alkynyl halides, and Michael acceptors have been reported 39–42 —likely due to the lack of σ-systems to stabilize the binding capability of zirconium to achieve suitable transmetalation. 27 It is worth noting that hydroalkylation and hydroarylation of alkenes mediated by metal-hydride chemistry has attracted significant attention 43–49 and represents a practical strategy for the construction of carbon–carbon bonds.

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**Figure 1. Transition-Metal-Catalyzed Cross-Coupling Strategy**

(A) Transition-metal-catalyzed cross-coupling with organometallic reagents.

(B) Metal-hydride-catalyzed hydrocarbonation of alkenes.

(C) Visible-light-induced transition-metal-catalyzed cross-coupling with organometallic reagents.

(D) This work: visible-light-induced nickel-catalyzed cross-coupling with alkylzirconocenes.

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1School of Chemical Engineering, Nanjing University of Science and Technology, Nanjing, Jiangsu 210094, China

2National Institute of Biological Sciences, 7 Science Park Road, Zhongguancun Life Science Park, Beijing 102206, China

3Institute for Smart Materials & Engineering, School of Chemistry and Chemical Engineering, University of Jinan, Ji-nan, Shandong 250022, China

4State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, 38 Xueyuan Road, Beijing 100191, China

5Tsinghua Institute of Multidisciplinary Biomedical Research, Tsinghua University, Beijing 100084, China

6Lead Contact

*Correspondence: chaojiang@njust.edu.cn (C.J.), qixiangbing@nibs.ac.cn (X.Q.)

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bonds without using any organometallic reagents and can even be used for remote functionalizations\(^{50-52}\) and asymmetric synthesis (Figure 1B).\(^ {53,54}\) However, the notable limitation of these methods is their typical need for excess equivalents of silanes\(^ {47-54}\) as reducing agents or high loading of multi-transition-metal catalysts.\(^ {48,49}\) Therefore, the hydrozirconation and cross-coupling strategy will offer an alternative attractive method for synthetic applications with alkenes.

The combination of transition-metal and photocatalysis has become an attractive strategy for carbon–carbon bond formation.\(^ {55}\) A more desirable approach is to utilize the transition-metal to play “double duty” roles by both harvesting light and catalyzing cross-coupling.\(^ {56-58}\) Very recently, visible-light-induced nickel or palladium-catalyzed alkylzincs coupling with aryl halides,\(^ {59,60}\) gold-catalyzed arylsilicons, arylborons, and alkynylsilicons coupling with aryl halides\(^ {61,62}\) were reported (Figure 1C), indicating that organometallic reagents are capable of engaging in the light-induced single transition-metal-catalyzed transformations. However, to the best of our knowledge, the visible-light-induced single transition-metal-catalyzed C(sp\(^3\))–C(sp\(^3\)) cross-coupling of alkylmetallic reagents is barely studied. We speculated that the intrinsic low reactivity of sp\(^3\)-hybridized alkylzirconocenes might be enhanced through a radical-mediated pathway by identifying a synergistic effect between alkylzirconocenes and photocatalysis. Herein, we present a convenient visible-light-induced single nickel-catalyzed cross-coupling method with alkylzirconocenes that are generated in situ from unactivated terminal or internal alkenes. A series of C(sp\(^3\))–C(sp\(^3\)), C(sp\(^3\))–C(sp\(^2\)), and C(sp\(^3\))–C(sp) bonds were formed via a blue-light-induced nickel-catalyzed transformation (Figure 1D). This method is mild and applicable for substrates including primary, secondary, tertiary alkyl, (het)aryl, alkenyl, and alkynyl halides.

**RESULTS AND DISCUSSION**

**Reaction Development**

Our initial study of this visible-light-induced cross-coupling method was focused on the C(sp\(^3\))–C(sp\(^3\)) coupling between (2-iodoethyl)benzene and hexylzirconocene, which was prepared from 1-hexene and Schwartz reagent. After examining a range of transition-metal catalysts, ligands, additives, and solvents (more than 2,000 variations of reaction conditions were tested), the desired C(sp\(^3\))–C(sp\(^3\)) cross-coupling product octylbenzene could be achieved in 63% yield with a novel nickel precatalyst containing 4,4‘-di-adamantane-2,2‘-bipyridine ligand (Ni-1) (Figure S1 in the presence of tetrabutylammonium 4-toluenesulfonate in THF under irradiation from blue-light-emitting diodes (LEDs) at room temperature, the nickel precatalyst exhibited high efficiency and the loading was reduced to only 1 mol % (for detailed optimization studies, see Tables S1–S12). The single crystal structure of Ni-1 shows an octahedral-coordinate nickel complex with two bipyridine ligands (Figure S1). The structure of Ni-1 was then drawn based on its crystal structure. As far as we know, this is the first example that shows the concrete structure of a nickel precatalyst with two bipyridine ligands.

**Reaction Scope**

With the optimal reaction conditions in hand, we next explored the substrate scope of this visible-light-induced cross-coupling process (Figure 2A). A series of primary alkyl iodides with varying chain length (1-3) and different functional groups, such as alkyl chlorides (4), ethers (5-7), esters (8), phthalimides (9), indoles (10), acetics (11), amides (12, 13), alcohols (28), and alkenes (29), were well-tolerated, and both benzyl chloride derivatives (14–16) and allyl bromide (24) were suitable substrates. Secondary alkyl iodides bearing phenyl groups (17, 18, 21), ethers (19), and
**Figure 2. Substrate Scope of the Visible-Light-Induced Nickel-Catalyzed Cross-Coupling**

(A) Scope of C(sp<sup>2</sup>)<sub>-</sub>C(sp<sup>3</sup>) cross-coupling

(B) Scope of C(sp<sup>3</sup>)<sub>-</sub>C(sp<sup>3</sup>) cross-coupling

(C) Scope of C(sp<sup>3</sup>)<sub>-</sub>C(sp<sup>3</sup>) cross-coupling

Unless otherwise noted, all yields are isolated yields at a 0.5 mmol scale. TBDPS, tert-butylidiphenylsilyl; Phth, 1,2-phenylenedicarbonyl; DMT, 4,4-dimethoxytrityl; Ts, p-toluenesulfonate; TIPS, triisopropylsilyl. *4 equiv alkylzirconocene was used. **Organic chloride as the substrate. ***Organic bromide as the substrate. ****Isolated yields on 10 mmol scale in a flow system for 7 h. ******Isolated yields on 10 mmol scale. ******Alkene: ZrCp₂HCl = 1:2 in hydrozirconation process. See the Supplemental Information for detailed reaction conditions.
sulfonamides (20) also coupled with the alkylzirconocenes in moderate yields. A secondary alkyl iodide substrate based on cholesterol delivered corresponding product 31, further highlighting the utility of this new process for the late-stage modification of complex natural products. For the most challenging tertiary alkyl halides, triarylchloromethane (22, 23) and ethyl 2,2-difluoro-2-iodoacetate (30) were found to be productive substrates for this cross-coupling method. With respect to the alkene as the starting material for hydrozirconation and cross-coupling, unactivated alkenes and substituted alkenes were amenable to this method: sulfonamides (28–31), silanes (26), and ethers (27) were tolerated.

After establishing the visible-light-induced nickel-catalyzed C(sp^3)–C(sp^3) cross-coupling reaction, we then expanded the protocol to C(sp^2)–C(sp^3) cross-coupling between aryl iodides and alkylzirconocenes employing a more easily accessible catalyst: Ni(dtbbpy)Br_2 (Ni-2). As shown in Figure 2B, this method displayed excellent functional group tolerance for the aryl iodides bearing fluoro (33), chloro (34, 50), methyl (35, 45, 48), trifluoromethyl (37, 47), and methoxy (38, 46, 49) groups, as well as more reactive functional groups such as nitriles (36), ketones (39), esters (40), amides (41), anilines (42), phenols (43), and primary alcohols (44). Notably, the substitution pattern and electronic properties had a negligible effect on the yield, and the corresponding cross-coupling products were obtained in good to excellent yields. Furthermore, the potential application of this visible-light-induced cross-coupling in modern synthesis was demonstrated by carrying out at a gram scale process using flow chemistry (32, 70% yield) and a batch system (38, 72% yield).

Heteroaromatic iodides, including pyridines (52), pyrazines (53), thiophenes (54), indoles (55), and even the cholesterol derivatives (56) were confirmed as effective coupling partners. Additionally, we observed that alkenyl bromide substrates could also undergo coupling to generate alkenes 68 and 69, providing an alternative regioselective approach to Heck coupling. Regarding the scope of alkenes, a series of simple (57) and substituted alkenes (58–67) were viable coupling partners for this method; and thioethers (59), silanes (60), ethers (62), chloro groups (63), sulfonamides (64), and even hydroxyl groups (67) were all tolerated. Notably, alkene derivatives from natural products, including estrone (70) and quinine (71), were compatible with both hydrozirconation and subsequent cross-coupling.

The visible-light-induced nickel-catalyzed cross-coupling method was also efficient for C(sp)–C(sp^3) cross-coupling reactions with Ni(dtbbpy)Br_2 (Ni-2), as outlined in Figure 2C. The electronic properties of the alkynes did not have dramatic impact on the coupling outcome. The unactivated alkynes (72, 73, 75), electron-deficient alkyne (74) and conjugated alkyne (76–81) all gave moderate to good yields. Notably, 1-(bromoethyl)-4-chlorobenzene and 1-bromo-4-(bromoethynyl)benzene gave corresponding products 77 and 78 in 65% and 56% yields, respectively, demonstrating a high chemoselectivity between C(sp)–C(sp^3) and C(sp^3)–C(sp^3) cross-couplings. Moreover, variation of the alkenes was also feasible: simple alkenes and alkenes possessing a hetero atom (Cl, Br, N, S, Si, or O) all gave the desired cross-coupling products in good yields (83–95), and alkylzirconocenes derived from the natural products (e.g., estrone (96) and quinine (97)), could also couple with alkyne halides, further showcasing the versatility of this protocol.

**Reaction Utilities**

Under thermodynamic control, terminal or internal alkenes, all generate terminal alkylzirconocenes through hydrozirconation and subsequent rapid “chain walking” for
the latter case that occurs to relieve steric crowding. Such “chain walking” after initial hydrometalation is now understood as a powerful means of activating otherwise inert C-H bonds in an aliphatic chain, and represents a new strategic approach for preparing useful building blocks from simple internal alkenes. In the past few years, seminal works from the research groups of Marek, Martin, Zhu, and others have spurred intense efforts to this field. With our visible-light-induced nickel-catalyzed cross-coupling method, a range of internal alkenes with different chain length and geometric isomers of the double bonds can be efficiently functionalized via a “chain walking” and cross-coupling relay strategy (Figure 3A). The trans-anethole could give three corresponding products with C(sp<sup>3</sup>)–C(sp<sup>3</sup>) (98), C(sp<sup>3</sup>)–C(sp<sup>2</sup>) (99), and C(sp<sup>3</sup>)–C(sp) (100) bond formation at terminal sites in decent yields. Furthermore, the “chain walking” length of different internal alkenes could be varied from one to eleven methylene units without drastic changes in yields (101–112), showcasing a highly efficient “chain walking” process. Given that isomeric mixtures of alkenes are available at an enormous scale (as industrial feedstocks derived directly from petrochemical sources), alkylzirconocenes derived from regio- and stereo-isomeric mixtures of hexene and octene were reacted with various coupling partners, leading to corresponding single products in moderate to good yields (113–120) (Figure 3B).

Figure 3. Chain Walking Strategy
(A) Chain walking and cross-coupling.
(B) Regioconvergent events.
Unless otherwise noted, all yields are isolated yields at a 0.5 mmol scale, hydrozirconation was run at 50 °C for 5 h. Phth, 1,2-phenylenedicarbonyl; TIPS, triisopropylsilyle. A equiv alkylzirconocene was used. Hydrozirconation was run at 50 °C for 24 h. 3 equiv alkylzirconocene was used. See the Supplemental Information for detailed reaction conditions.
To further demonstrate the synthetic utility of this visible-light-induced nickel-catalyzed cross-coupling protocol, we applied it in combination with olefin metathesis. Olefin metathesis has proved to be a powerful synthetic tool in organic synthesis, though alkene isomerization has been recognized as a side reaction in olefin metathesis. The alkene mixtures generated from olefin metathesis are so complex that separating them or further generating value-added products directly is considered to be prohibitively difficult. However, these alkene mixtures are sustainable and economic raw materials for our cross-coupling method. A large number of cross-coupling analogs containing different alkyl chains were obtained efficiently in a one-pot reaction (121–131, Figure S3). The synthetic advance of this strategy was additionally illustrated via the rapid synthesis of the Novartis’ drug Gilenya (Fingolimod) and its derivatives in a one-pot reaction (132–137, Figure S4). Thus, this synergistic combination of olefin metathesis and cross-coupling represents an attractive strategy for rapidly characterizing the structure-activity-relationship (SAR) of drug candidates that contain aliphatic chains.

**Mechanism Studies**

The data summarized above provide compelling evidence that alkylzirconocenes exploit an unrecognized opportunity in the field of visible-light-induced nickel-catalyzed cross-coupling reactions. A series of designed substrates were reacted under standard conditions. The racemic product 139 was obtained from a chiral alkyl iodide substrate, whereas the cyclopropane ring-opening 140 and 5-exo-trig cyclization product 141 were generated from the corresponding radical probe substrates (Figure 4A, equations 1–3), suggesting that an alkyl radical was generated from the alkyl iodide substrates. Using an aryl iodide radical probe substrate, a 5-exo-trig cyclization product 142 was detected (Figure 4A, equation 4), presumably through a radical pathway or a migratory insertion after the oxidative addition. A single diastereomer 144 was obtained from the deuterated substrate S144 (Figure 4A, equation 5), favoring a migratory insertion pathway over an aryl radical mechanism (See also Figure S5).

It was notable that when we developed the C(sp³)–C(sp³) cross-coupling, in addition to the desired cross-coupling product, we invariably obtained the homo-coupling byproducts of both alkyl iodide and alkylzirconocene (145 and 146; Figure 4B, equation 1). Controlled experiments showed that a trace amount of homo-coupling product could be observed from single alkylzirconocene under blue-light excitation, whereas alkyl iodide substrate could not undergo any transformation under conditions without alkylzirconocene (Figure 4B, equations 2 and 3; Figure S6). The deiodination product 147 from the alkyl iodide substrate could be obtained in the presence of alkylzirconocene even without the nickel catalyst (Figure 4B, equation 4). Furthermore, conducting the identical reaction in the presence of the radical scavenger compound 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) resulted in both hexanyland phenylethyl trapped TEMPO adducts 148 and 149, whereas only adduct 148 was obtained under dark conditions (Figure S7), which could be generated from the direct reaction of the alkylzirconocene with TEMPO. We thus propose that a hexanyl radical is generated from hexanylzirconocene under visible-light excitation and subsequently a phenylethyl radical is initiated from the alkyl iodide.

Ultraviolet–visible spectra were recorded to facilitate evaluation of the light absorption characteristics of each component of the reaction. Only nickel precatalysts and alkylzirconocene exhibited absorption around the blue-light region (Figures S8 and S9), indicating that both nickel and zirconium species could potentially serve as photosensitizers. A 1:1 mixture of alkylzirconocene and a nickel catalyst exhibited
significant changes in absorption between 450–550 nm (Figures S10 and S11). This can possibly be ascribed to a reduced Ni$_0$ or Ni$_I$ species, which are common active nickel catalysts that participate in the catalytic cycles via Ni$_0$/Ni$_{II}$ or Ni$_I$/Ni$_{III}$, respectively. In order to determine which of these was the most likely active nickel species, pre-prepared Ni$_0$, Ni$_I$, and Ni$_{II}$ catalysts were used in the typical coupling reactions. Unexpectedly, all of the reactions occurred successfully under Ni$_0$, Ni$_I$, and Ni$_{II}$ catalysts (Figures 4C and S12), and we thus speculate a possible radical mechanism involving Ni$_0$, Ni$_I$, or Ni$_{II}$ species.

The kinetic studies and the reaction rate order of each component employed in the coupling reaction was determined by the initial-rate method (Figures S13–S20; Tables S14–S17). The dependence of the coupling rate on alkyl and aryl halide substrates were found to be zero order, whereas the dependence of the alkylzirconocene was found to be approximately first-order. Taken together with previous findings, it suggests that radical generation from alkylzirconocenes might be the

Figure 4. Mechanism Studies
(A) Evidence for radicals from organic halide substrates.
(B) Evidence for radicals from alkylzirconocenes.
(C) Ni$_{II}$, Ni$_0$, and Ni$_I$ catalyzed cross-coupling.
See the Supplemental Information for detailed reaction conditions.
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rate-determining step in the catalytic cycle. In addition, an obvious halogen exchange product at the beginning of the reaction was observed when high loading of a nickel catalyst was applied (Figures S21 and S22). We proposed that this halogen exchange might be related to the formation of an active nickel species, and controlled experiments showed that this reaction depended on a nickel catalyst and alkylzirconocene and promoted by a phase transfer reagent and blue-light excitation (Figure S23). Therefore, we proposed a visible-light-induced initiation process with the aid of alkylzirconocene and a phase transfer reagent.

Density functional theory (DFT) calculations were carried out to gain a more detailed understanding of the initiation process (Figures S30 and S31). The HOMO orbital of butylzirconocene is mainly distributed between the C and Zr atom, forming the C-Zr sigma bond, whereas the LUMO orbital is mainly distributed on the 4d orbital of Zr atom (Figure 5A). We thus speculate that the excitation of butylzirconocene under blue light could be identified as electron transfer from the C-Zr bonding orbital to 4d orbital of Zr, leading to the homolysis of butylzirconocene to form a butyl radical and a ZrIII species. The reductive ZrIII species could reduce LNiIBr2 to LNiIBr or LNi0THF (LNi0THF complex is more stable than LNi0, Figure S32) undergoing an exergonic process of 29.3 and 14.6 kcal/mol, respectively, whereas reduction by butyl radical is more difficult. Homocoupling of butyl radical is exergonic by 74.5 kcal/mol, which could indicate the presence of a homo-coupling byproduct of alkylzirconocene. It is noteworthy that the ZrIII species could also reduce hexyl iodide to form the hexyl radical (an exergonic process of 9.7 kcal/mol), which represents a more favored process than butyl radical reduction (an endergonic process of 0.2 kcal/mol). These results are consistent with the controlled experiments in Figure 4B. In addition, the oxidative addition of iodobenzene to LNiIBr and the subsequent reductive elimination of the LNiIII species to form bromobenzene are favorable (an overall exergonic process of 1.1 kcal/mol), which is consistent with the halide exchange of iodobenzene.

The Hammett plot for C(sp3)-C(sp2) cross-coupling reveals a line with a slope close to zero ($\rho = 0.05$, Figures S24 and S25; Table S18), which indicates a neutral intermediate such as the aryl radical or a 3-centered nickel transition state if it is involved in the rate-determining step. However, the competition experiments for the Hammett plot showed an absolute superiority of iodobenzene with electron-withdrawing substituents (Figures 5B and S26-S29). We speculate that there could be a fast concerted but irreversible oxidative addition step in this C(sp3)-C(sp3) cross-couplings. The DFT calculations showed the oxidative addition of iodobenzene to LNi0THF complex was an exergonic process via TS1 with a barrier of 7.9 kcal/mol, whereas OMe and CF3 substituted iodobenzene via TS2 and TS3 with a barrier of 2.4 and −1.0 kcal/mol relative to TS1, respectively (Figure 5B). The oxidative addition of iodobenzene to LNi-alkyl complex was an exergonic process via TS4 with a barrier of 12.8 kcal/mol, whereas the OMe and CF3 substituted iodobenzene via TS5 and TS6 with a barrier of 1.9 and −4.2 kcal/mol relative to TS4, respectively (Figure 5B), which was more applicable with the experimental results. Additional kinetic studies disclosed that the reaction rate of aryl iodide substrates is zero order
The detailed DFT calculations of C(sp^3)–C(sp^3) coupling were shown in Figure 5C (Figure S32). The homolysis of butylzirconocene generate butyl radical and Zr^{III} species under blue-light excitation, which might be the rate-determining step in the catalytic cycle. The butyl radical capture of LNi^{0}THF complex to form LNi^{I}Bu species is exergonic by 35.5 kcal/mol. Then oxidative addition of iodobenzene gives LNi^{II} complex via TS4 with a barrier of 12.8 kcal/mol, and subsequent reductive elimination forms the LNi^{II} complex via TS9 with a barrier of 3.9 kcal/mol, which could be reduced by the Zr^{III} species to LNi^{0}THF. Similar DFT calculations of C(sp^3)–C(sp^3) coupling were shown in Figure 5D (Figure S33) and the successive radical oxidative addition of hexyl iodide substrate via TS10 with a barrier of 14.4 kcal/mol. Subsequent reductive elimination via TS11 with a barrier of 6.3 kcal/mol forms the LNi^{II} complex. The butyl radical capture of LNi^{0}THF is more favorable than hexyl iodide oxidative addition of LNi^{0}THF (Figures S33 and S34), therefore favoring the sequence of alkylzirconocene radical capture and alkyl halide oxidative addition, although we cannot exclude another pathway (Figure S34).

On the basis of our mechanistic investigations and thorough DFT calculations of each single step, we tentatively propose a plausible reaction mechanism as depicted in Figure 5E (Figure S38). The octahedral-coordinate nickel complex could dissociate to the active Ni^{II} species in THF solution (Figure S2). The homolysis of alkylzirconocenes generates the alkyl radical and the Zr^{III} species under blue-light excitation, and the Ni^{0} complex is generated from the Ni^{II} species via reduction by Zr^{III}, which undergoes alkyl radical capture to provide the Ni^{I}-alkyl complex. A subsequent radical oxidative addition of the alkyl halide or a concerted oxidative addition of the aryl or alkynyl halide forms a Ni^{III} complex. Finally, reductive elimination affords the desired cross-coupled products and simultaneously regenerates the Ni^{I} halide catalyst. The reductive Zr^{III} species could reduce Ni^{I} halide to Ni^{0}, which could participate in the next catalytic cycle. Light-dark interval experiments have revealed that continuous irradiation with visible light is essential for the reaction (Figure S37), which is in accordance with the continuous homolysis process of alkylzirconocenes. DFT calculations showed that the anion exchange of alkylzirconocenes was unfavorable (Figure S36), and we then tentatively propose that the phase transfer reagent might help to increase the ionization tendency of the coupling system. Clearly, considering the difficulty of identifying the particular species involved in each single step, we cannot yet fully illustrate the unbiased details of this new chemistry, and further work will be required to fully elucidate the relevant mechanism.

In summary, we have disclosed the first visible-light-induced single nickel-catalyzed cross-coupling method with alkylzirconocenes. A series of C(sp^3)–C(sp^3), C(sp^3)–C(sp^3), and C(sp^3)–C(sp) bonds were formed from the corresponding alkyl, aryl, alkenyl, and alkynyl halides. Employing a one-pot chain walking and cross-coupling relay strategy, a range of internal alkenes and isomeric mixture of alkenes could be efficiently functionalized to give terminal coupled products. Given its mild conditions, scalability, and extremely general scope across a large range of organic halides, and considered alongside its excellent functional group compatibility, we anticipate that this strategy will serve as an innovative cross-coupling paradigm and will inspire researchers to revisit the synthetic potential of organozirconium chemistry. Mechanistic experiments suggest a nickel-catalyzed radical type reaction.
pathway, and ongoing work in our lab is focused on the details for the mechanism of this novel reaction.

**EXPERIMENTAL PROCEDURES**
Full experimental procedures are provided in the Supplemental Information.

**SUPPLEMENTAL INFORMATION**
Supplemental Information can be found online at [https://doi.org/10.1016/j.chempr.2019.12.010](https://doi.org/10.1016/j.chempr.2019.12.010).

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**AUTHOR CONTRIBUTIONS**
C.J. and X.Q. conceived the study; Y.G. and C.Y. carried out most of the reaction and prepared the manuscript and Supplemental Information; S.B. and Y.G. performed the theoretical study; J.W. provided technical assistance of UV-visible experiments; Y.G., C.Y., X.L., Q.W., C.J., and X.Q. analyzed the data. All authors discussed the results and commented on the manuscript.

**DECLARATION OF INTERESTS**
The authors declare no competing interests.

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