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Visible Light-Induced Palladium-Catalyzed Carbocyclization of Unactivated Alkyl Bromides with Alkenes Involving C−I or C−B Coupling

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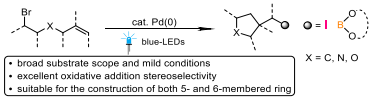


Abstract

A palladium-catalyzed, photochemical tandem cyclization/dicarbofunctionalization of unactivated alkyl halides containing an alkene moiety offers an appealing route to produce five- or six-membered rings in a redox-neutral fashion. Multisubstituted carbo- and heterocyclic compounds were prepared through the formation of new C–B or C–O bonds, which provides a convenient synthetic route for further transformations. This protocol is characterized by the reaction of alkene regio- and stereoselectivities, good functional group compatibility, wide substrate scope, and mild reaction conditions.

Increased attention is being paid to the development of pharmacophore-, biological molecule- and organic material-relevant heterocycles (e.g., pyrrolidines, tetrahydrofurans, and piperidine) or carbocycles.[1] Over the last few years, continuous research has successfully extended the scope of manifold cyclic products with numerous elegant versions. The functionalized cyclic motifs (iodine-functionalized or boron-functionalized compounds), premanufactured alkyl electrophiles, can serve as versatile building blocks for further structural elaboration by the derivatization of their self-contained carbon-iodine or carbon-boron bonds.[2] The ability to increase cyclic framework complexity captured our interest in this type of synthesis.

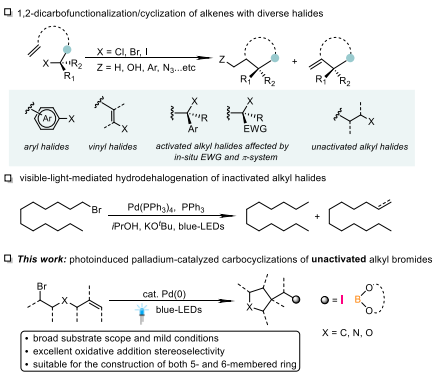
The 1,2-dicarbofunctionalization/cyclization of substituted alkenes with organic electrophiles and organometallic reagents is an appealing method for the stereoselective synthesis of valuable (hetero)cyclic compounds amenable to a single operational fashion.[3] Typically, previous studies have focused on aryl/vinyl halides, unactivated alkyl iodine, and activated alkyl halides (bearing a C(sp3)−X affected by the in situ activation of an electron-withdrawing group, π-system, or heteroatom) for application in intramolecular cross coupling with alkenes (Scheme 1).[4] The extension to widely unactivated alkyl bromides remains a long-standing challenge owing to the inherent energetic barrier of high redox potentials for the activation.[5] Fortunately, there are still numbers of strategies[6] available to achieve the abovementioned objective, in which the unactivated alkyl halides commonly act as electrophilic alkyl sources[7] participate in 1,2-dicarbofunctionalization of diverse substituted alkenes. A successful example is that a breakthrough has been realized by the Ito group for the copper(I)-catalyzed borylative radical cyclization of unactivated alkyl halides with bis(pinacolato)diboron[6a], which facile access to organoboron compounds with high stereoselectivity. However, the visible-light-mediated photoredox processes of unactivated carbon–halogen bonds via single-electron transfer (SET) scission are less explored, which presents us with practical demands.[2e, 8]

Visible light photocatalysis, an efficient and waste-minimizing process, is a powerful approach that is used in modern radical chemistry;[9] this method allows the rapid generation of carbon-centered radicals to access new reactivity.[4c, 4e, 10] The abovementioned advantages exist because the relatively narrow redox potential window and limited photosensitizers of typical photocatalysis hinder the potential applications of unactivated alkyl bromides. These

questions provide a considerable motivation to study the potential of photoinduced palladium catalysis in reaction development. Based on a previous study, which demonstrated the palladium-catalyzed hydrodehalogenation and Br/D exchange of inactivated aryl and alkyl halides in photocatalytic reaction (Scheme 1),[11] we questioned whether palladium catalyst-mediated radical initiation/tandem cyclization could be used to enable the construction of functionalized (hetero)cyclic organic compounds under visible light irradiation.

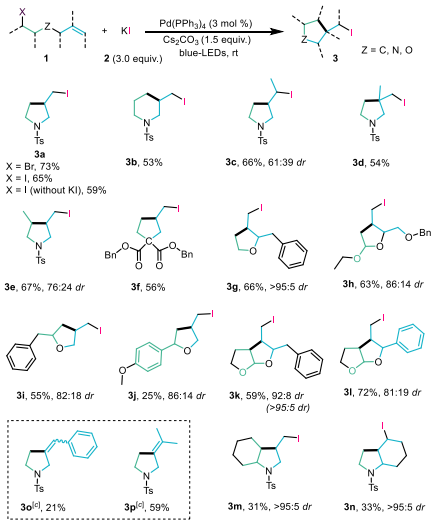
We discovered that the optimized conditions were suitable for photoinduced palladium and allowed to avoid potential pitfalls including: i) fast protodehalogenation or premature β-hydride elimination before radical oxidative addition to substituted olefins,[12, 13] and ii) unwanted sp2-hybridized or sp3-hydrogenated processes of a cyclized intermediate rather than trapped by an iodine/boron source.[14] However, currently, there are no practical intramolecular cyclization versions available to access valuable cyclic motifs involving the concomitant introduction of carbon–iodine, and previous borylative radical cyclization methods for the transition metal-catalyzed borylation products are restricted to the formation of 5-membered rings.

Scheme 1: Strategies for the Carbofunctionalization of Alkyl Halides.



This approach is an ideal entry to provide both five- and six-membered carbo- and heterocyclic products containing a functionalized alkyl iodide (boride) moiety, which is characterized by good to excellent diastereoselectivities and wide substrate scope of polysubstituted cyclic compounds (Scheme 1). We initiated our investigation by probing suitable conditions for the palladium-based systems that employed inexpensive potassium iodide as an iodine atom donor or accessible bis(pinacolato)diboron as an applicable boron reagent with challenging catalyzers, solvents, and bases (See ESI† for details).

Scheme 2: Reaction Scope for the Synthesis of Iodine-substituted Ring Compounds.[a, b]



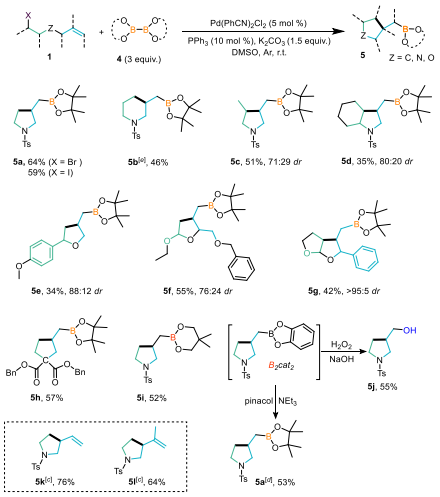
[a] Reaction conditions: **1** (0.2 mmol), **2** (0.6 mmol), [Pd] (3 mol %), Cs_2CO_3 (0.3 mmol), THF (1.0 mL), blue LED, rt, 24 h, and under argon atmosphere, yields of isolated products, X is equal to bromine unless otherwise noted. [b] Diastereoselectivity was determined by ^1H NMR analysis, see the Supporting Information for details. [c] This reaction was performed in 12 h.

First, we screened the iodization of unactivated alkyl bromides under optimized conditions. An assortment of primary and secondary alkyl bromide substrates containing internal or terminal alkenes were prepared according to Scheme 2; these compounds were amenable to an effective synthetic route with high regio- and stereoselectivities. Functionalized acyclic starting primary and secondary bromides allow to access important monocyclic products

3a-**3j** (e.g., pyrrolidines, tetrahydrofurans, and carbocycles) with a broad range of functional groups (e.g., alkanes, aromatics, esters, ethers, esters, acetals, and sulfonamides). The steric hindrance of **3d** negatively affects the transformation with a moderate yield (54%). The 5-exo carbocyclization of primary alkyl bromides was successful with disubstituted alkenes (entries **3c**-**3d**) and terminal alkene. However, neither styrenes nor tetrasubstituted alkenes were suitable for this strategy. Instead, **3o** and **3p** were rapidly converted to alkyl-Mizoroki-Heck-type products[15] in excellent yields. The efficient construction of bicyclic frameworks **3k**-**3n** can be built in reasonable yields using this protocol. Alkyl bromides bearing β-substituents **3h**-**3n** provided the corresponding products with good to reduced reactivity, albeit with a favourable stereoselectivity. We attribute the reduced yields to the relative feasibility of both possible reductive eliminations and hydrodehalogenation of the initially generated alkyl radical.

By comparing reactions with similar structures, it is determined that in general, the primary bromides **3a** reacted more efficiently than the secondary bromides **3e**. This approach was successfully extended to unactivated alkyl iodine **3a**, and the iodization reaction occurred in the absence of additional potassium iodide without significantly affecting the reaction efficiency. As demonstrated by the 6-exo cyclization of *N*-heterocycles **3b**, this radical cyclization reaction is not limited to the five-membered ring synthesis.

Scheme 3: Reaction Scope for the Synthesis of Boron-substituted Ring Compounds.[a, b]



[a] Reaction conditions: **1** (0.2 mmol), **3** (0.4 mmol), [Pd] (5 mol %), ligand (10 mol %), K_2CO_3 (0.3 mmol), DMSO (1.0 mL), blue LED, rt, 24 h, and under argon atmosphere, yields of isolated products, X is equal to bromine unless otherwise noted. [b] Diastereoselectivity was determined by ^{1}H NMR analysis, see the Supporting Information for details. [c] This reaction was performed in 12 h. [d] A solution of pinacol (0.80 mmol) in triethylamine (0.70 mL) was added to the mixture, 2 h, rt. [e] $Pd(PPh_3)_4$ was employed instead of $Pd(PhCN)_2Cl_2$, without additional ligands.

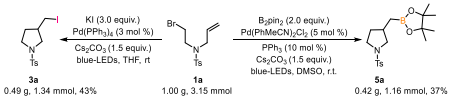
After assessing the scope of practicable route that afforded desired alkyl iodides, we continued to examine the use of the borylation system in intermolecular cross-coupling (Scheme 3). Both the six-membered alkylboration synthesis (**5b**) and the iodoalkyl group of tosylamide substrate cyclization (**5a**) underwent effective coupling under optimized conditions. In addition, the visible light-mediated alkylboration reaction tolerated modification on the primary and secondary bromoalkyl groups, as demonstrated by the formation of pyrrolidines (**5a**, **5c**), tetrahydrofurans (**5e**, **5f**), carbocycles (**5h**), and spiro-heterocycles (**5d**, **5g**) with similar or increased yields. The high diastereoselectivity of **5d** (and **3m**) is a response to the stabilization of the chair conformation by the anomeric effect. The byproduct **5l** was observed in the trisubstituted alkene example, which was attributed to the high propensity toward elimination to the terminal alkene product, and no reaction occurred in the absence of bis(pinacolato)diboron.

Meanwhile, we investigated the reactivity of other diboron reagents. Bis(catecholato)diborane (B_2cat_2) proved to be a competent boron source, and the reaction

proceeded smoothly to form an unstable the catecholboryl derivative. The boronic ester could be transformed into the corresponding alcohol **5j** after oxidative work up.[16] Furthermore, **5a** also could be obtained after transesterification with pinacol in a 53% yield.[17] Bis(neopentylglycolato)diboron (B_2neo_2) also reacted as anticipated to give boryl-containing *N*-heterocycle derivative **5i** in a moderate yield.

Two examples were conducted on a larger scale to demonstrate the practical utility of the above methods (Scheme 4). As representative examples, the iodization and the borylation of **1a** on a 3.15 mmol scale offered feasible gram scale synthesis of **2a** in 43% yield and **5a** in 37% yield, respectively.

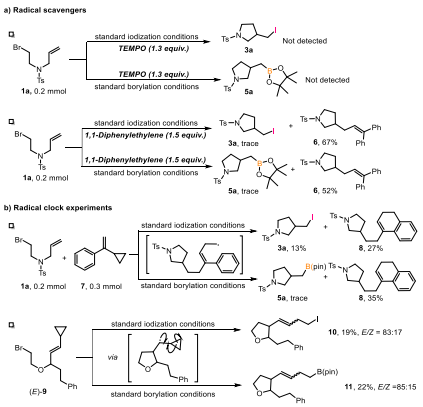
Scheme 4: Scale-up Experiment.



To obtain mechanistic insight into the current iodization and borylation reactions, mechanistic studies were carried out with radical trapping experiments and radical clock reactions (Scheme 5), which indicated that these photoinitiated reactions likely proceeded via a free-radical pathway and a 5-*exo*-*trig* radical intermediate was present in each catalytic cycle. The iodization or borylation experiments did not afford any detectable amount of product **3a** or **5a** when the reactions of **1a** were carried out in the presence of TEMPO (1.3 equiv.). The addition of 1,1-diphenylethylene (1.5 equiv.) to standard reaction mixture also displayed apparent inhibition effects by forming the adduct **6** with yields of 67% and 52%, respectively. Next, two radical clock experiments were performed by using the cyclopropyl moiety adjacent to olefin **7** as a radical scavenger. The ring-closure product **8** was obtained

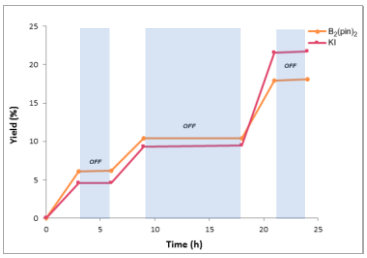
via radical rearrangements and the isolated yields in the respective catalysis were measured to be 27% and 35%, respectively. The cyclopropyl-bearing substrate **(*E*)-9** allow to access the corresponding ring-opened products **10** and **11** upon visible-light irradiation, providing additional supports to the radical nature of the transformation.

Scheme 5: Radical Process Experiments.

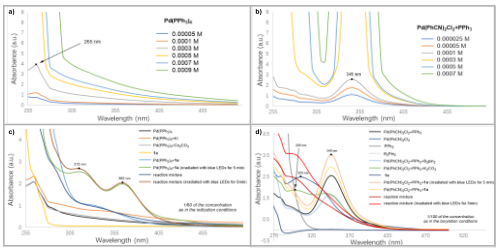


To further investigate the influence of light irradiation on reaction progresses and the photochemical behaviors of Pd species in these reactions, relevant experiments were performed including light on-off experiments, UV/Vis absorption spectra studies and Stern-Volmer luminescence quenching studies (See ESI† for details). The standard iodization and borylation reactions were intermittently exposed to blue-light while monitoring conversion (Scheme 6). It was found that the conversions ceased upon removal from irradiation and continued upon additional irradiation. We speculated that these systems may be amenable to photoinduced palladium catalyses which required constant irradiation, rather than just photoinitiated radical-chain processes.

Scheme 6: Influence of Light Irradiation.



Scheme 7: UV/Vis Absorption Spectra Studies.

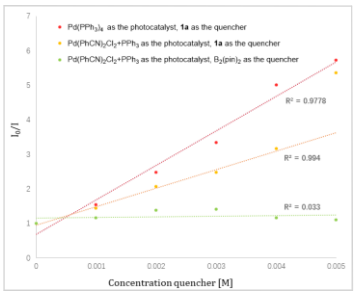


(a) $Pd(PPh_3)_4$ in THF with different concentrations. (b) $Pd(PhCN)_2Cl_2$+PPh_3 in DMSO with different concentrations. (c) **1a** and $Pd(PPh_3)_4$ in the presence of other reaction components. (d) Starting materials and $Pd(PhCN)_2Cl_2$+PPh_3 in the presence of other reaction components.

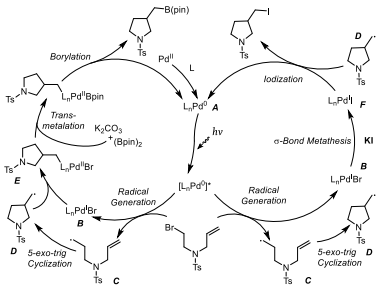
Next, we measured UV/Vis absorption spectra of the Pd catalysts in the absence and the presence of reaction components (Scheme 7 and Figure S1-S4). Broad absorbances were observed in the region 400-500 nm under the iodization and borylation reactions. Notably, two new peaks (λmax = 315 nm and 365 nm) were observed when $Pd(PPh_3)_4$ and **1a**, as well as the reaction mixture, were stirred under blue-light irradiation for 5min (Scheme 7c). This phenomenon is similar with results demonstrated by others.[9c] In addition, A new peaks (λmax = 295 nm) was observed, indicative of the possibility that K_2CO_3 may participate in the construction of a photoabsorbing Pd(0) species in the borylation system (Scheme 7d).

Furthermore, fluorescence quenching experiments and Stern–Volmer studies (Scheme 8) demonstrated that the alkyl bromides quenched the excited Pd species in line with the envisaged SET event to afford the alkyl radical.

Scheme 8: Stern-Volmer Luminescence Quenching Studies.



Scheme 9: Plausible Mechanism.



Based on the prior works and our observations, a plausible reaction mechanism is proposed in Scheme 9. Our design is based on the hypothesis that rather than as a simple initiator, palladium acts as a true catalyst in both catalytic cycles. The palladium complex, which is generated by the reduction of bis(benzonitrile)palladium(II) chloride with triphenylphosphine under the borylation conditions, exhibits blue light absorption and provides a photoexcited Pd(0)L species **A**. **A** transfers an electron to an oxidative quencher and produces a putative palladium(I) intermediate **B** and a carbon-centered radical **C**. Alkyl radical **C** attacks one unsaturated bond to deliver a 5-exo cyclization intermediate **D**. In the borylation catalyst cycle, the subsequent recombination with Pd(I)Br generates the key Pd(II) species **E** via the SET process. Base-promoted transmetalation[18] of **E** with bis(pinacolato)diboron provides a new intermediate, which leads to the observed final product during the regeneration of the Pd(0) catalyst. In addition, during the iodization stage, the coordination of KI to the palladium (I) center of **B** offers another palladium species **F**. This is followed by the iodization of **D** to generate the desired heterocyclic iodide formed by the

iodine atom transfer from the **F** catalyst. Simultaneously, oxidized palladium returns to its original oxidation state that can participate in the new Pd-catalyst turnover.

In summary, a palladium-catalyzed intramolecular version provides a straightforward route to access iodine- or boron-substituted cyclic frameworks (e.g., pyrrolidine, piperidine, cyclopentane, and tetrahydrofuran) by photocatalysis that are difficult to prepare by conventional methods. The optimized conditions form the kinetically favorable cyclization of electrophilic addition to alkene. Alkyl bromides and alkyl iodines can be developed, and a series of tests on boron reagents is devoted to extend the synthetic application. In addition, several reductive cyclization byproducts can be observed with photoinduced palladium catalysis, and some of them are absent from the literature. Further studies along the tandem cyclization/functionalization line are currently in progress.

Experimental Section

General Methods. For Column chromatography, 200-300 mesh silica gel was employed. Analytical TLC was performed with silica gel GF254 plates. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded in CDCl3 using TMS as internal standard. All products were further characterized by high resolution mass spectra (HRMS); copies of their ^{1}H NMR and ^{13}C NMR spectra are provided. The HRMS was obtained using a Q-TOF instrument equipped with ESI source. Commercially available reagents were used without further purification. All solvents were dried under standard method. Photochemical reactions were conducted in a reaction box (Kessil brand Blue LED Grow Light, 440 (± 15) nm, 75W, 5-7 cm away, with cooling fan to keep reaction temperature between 20 °C and 30 °C, and the irradiation vessels are Schlenk tubes of

borosilicate glass). Starting materials were prepared in analogy to several literature procedures; spectral data were in agreement with literature values.[3g, 6b, 6e, 19]

General Procedures for the Synthesis of the Products 3.

To a Schlenk tube were added unactivated alkyl bromides **1** (0.2 mmol, 1.0 equiv), potassium iodide **2** (0.6 mmol, 3.0 equiv), palladium catalyst (0.006 mmol, 3 mol %), and Cs_2CO_3 (0.3 mmol, 1.5 equiv). The reaction vessel was evacuated and backfilled with Argon for three times, and then injected 1.0 mL THF (0.2 M) into the tube. The reaction mixture was stirred under blue LED irradiation at room temperature for 24 hours. After full conversion, the reaction mixture was transferred into a separating funnel and 20.0 mL of distilled water and 5.0 mL of brine were added. The resulting mixture was extracted with Et_2O (20.0 mL *2) and combined organic layer were dried over $MgSO_4$, filtered and concentrated in vacuum. The product was purified by flash column chromatography on silica gel with *n*-pentane/ethyl acetate as eluent to give the corresponding product **3**.

General Procedures for the Synthesis of the Products 5.

To a Schlenk tube were added unactivated alkyl bromides **1** (0.2 mmol, 1.0 equiv), boron reagent **4** (0.4 mmol, 2.0 equiv), Bis(benzonitrile)palladium(II) chloride (0.01 mmol, 5 mol %), PPh_3 (0.02 mmol, 10 mol %) and K_2CO_3 (0.3 mmol, 1.5 equiv). The reaction vessel was evacuated and backfilled with Argon for three times, and then injected 1.0 mL DMSO (0.2 M) into the tube. The reaction mixture was stirred under blue LED irradiation at room temperature for 24 hours. Then the reaction mixture was quenched with water (25 mL) and extracted with Et_2O (20 mL × 3). The combined organic layers were washed twice with water (15 mL each time) and brine (15 mL),

dried over $MgSO_4$. After filtration, the solvents were evaporated under reduced pressure. The organic extracts was purified by flash column chromatography on silica gel with *n*-pentane/ethyl acetate as eluent (to facilitate separation, a small amount of acetic acid is added in the solvent) to give the corresponding product **5**.

Preparation of (1-tosylpyrrolidin-3-yl)methanol (5j).[16]

To a schlenk tube were added **1a** (63.4 mg, 0.2 mmol, 1.0 equiv), bis(catecholato)diborane (96.0 mg, 0.4 mmol, 2.0 equiv), Bis(benzonitrile)palladium(II) chloride (3.8 mg, 0.01 mmol, 5 mol %), PPh_3 (5.3 mg, 0.02 mmol, 10 mol %) and K_2CO_3 (41.4 mg, 0.3 mmol, 1.5 equiv). The reaction vessel was evacuated and backfilled with Argon for three times, and then injected 1.0 mL DMSO into the tube. The reaction mixture was stirred under blue LED irradiation at room temperature. The reaction progress was monitored by GC analysis. Then the reaction mixture was quenched with water (25 mL) and extracted with Et_2O (20 mL × 3). The combined organic layers were washed twice with water (15 mL each time) and brine (15 mL), dried over $MgSO_4$. After filtration, the solvents were evaporated under reduced pressure. Then 3.0 mL of MeOH, NaOH (aq, 3.0 mL, 3M) and H_2O_2 (2.0 mL, 33%) were added to the organic extract and it was cooled at 0 °C. After the schlenk tube was stirred at 0 °C to room temperature overnight, saturated solution of $Na_2S_2O_3$ was added to the mixture. The resulting mixture was extracted with dichloromethane (7.0 mL *2) and combined organic layer were dried over $MgSO_4$, filtered and concentrated in vacuum. The product was purified by flash column chromatography on silica gel to to afford the final product **5j**.

Scale-up Experiment

To a round-bottom flask were added unactivated alkyl bromides **1a** (1.0 g, 3.15 mmol, 1.0 equiv), potassium iodide **2** (9.45 mmol, 3.0 equiv), palladium catalyst (0.095 mmol, 3 mol %), and Cs_2CO_3 (4.73 mmol, 1.5 equiv). The reaction vessel was evacuated and backfilled with Argon for three times, and then injected 15.7 mL THF (0.2 M) into the tube. The reaction mixture was stirred under blue LED irradiation at room temperature for 24 hours. After full conversion, the reaction mixture was transferred into a separating funnel and 30.0 mL of distilled water and 30.0 mL of brine were added. The resulting mixture was extracted with Et_2O (50.0 mL *2) and combined organic layer were dried over $MgSO_4$, filtered and concentrated in vacuum. The product was purified by flash column chromatography on silica gel with *n*-pentane/ethyl acetate as eluent to give the product **3a** (0.49 g, 1.34 mmol, 43%).

To a round-bottom flask were added unactivated alkyl bromides **1a** (1.0 g, 3.15 mmol, 1.0 equiv), boron reagent **4** (6.30 mmol, 2.0 equiv), Bis(benzonitrile)palladium(II) chloride (0.157 mmol, 5 mol %), PPh_3 (0.315 mmol, 10 mol %) and K_2CO_3 (4.73 mmol, 1.5 equiv). The reaction vessel was evacuated and backfilled with Argon for three times, and then injected 15.7 mL DMSO (0.2 M) into the tube. The reaction mixture was stirred under blue LED irradiation at room temperature for 24 hours. Then the reaction mixture was quenched with water (30 mL) and extracted with Et_2O (50 mL × 3). The combined organic layers were washed twice with water (30 mL each time) and brine (30 mL), dried over $MgSO_4$. After filtration, the solvents were evaporated under reduced pressure. The organic extracts was purified by flash column chromatography on silica gel with *n*-pentane/ethyl acetate as eluent (to facilitate separation, a small amount of acetic acid is added in the solvent) to give corresponding product **5a** (0.42 g, 1.16 mmol, 37%).

Light On-off Experiment

12 samples were conducted under the standard iodization and borylation conditions (six samples for each of the transformations), except light on-off condition. The reactions were intermittently exposed to blue-light, and each example was removed at the start and after each interval. Yields of the **3a** and **5a** were determined by 1H NMR with 1,3,5-trimethoxybenzene as an internal standard. It was found that the conversions ceased upon removal from irradiation and continued upon additional irradiation. We speculated that these systems may be amenable to photoinduced palladium catalyses which required constant irradiation, rather than just photoinitiated radical-chain processes.

UV/Vis Absorption Spectra Studies

We measured UV/Vis absorption spectra to gain more insight into the photoabsorbing Pd species. To an oven-dried Schlenk tube were added a appropriate amount of samples and solvents according to the concentrations shown in the pictures. The solutions of the reaction mixtures were degassed thoroughly by bubbling argon- stream for 20 minutes, and then sealed in the tubes. Prior to the measurement, the mixtures were kept in the dark unless otherwise noted.

Stern-Volmer Luminescence Quenching Studies.

Stern-Volmer studies were conducted using $Pd(PPh_3)_4$ and $Pd(PhCN)_2Cl_2$+PPh_3 as the photocatalysts, respectively. **1a** and $B_2(pin)_2$ were measured to illustrate potential quenching of the excited Pd species. Prior to the measurement, the solutions of the reaction mixtures were degassed thoroughly by bubbling argon-stream for 20 minutes. $Pd(PPh_3)_4$ sample was irradiated at 345 nm and emission was measured at 467 nm. $Pd(PhCN)_2Cl_2$+PPh_3 samples were irradiated at 310 nm and emission was measured at 397 nm. First, the emission spectra of a 1.0×10^{-3} M

solution of $Pd(PPh_3)_4$ in THF and $Pd(PhCN)_2Cl_2$+PPh_3 in DMSO were collected, respectively. Then, the emission spectra of remaining samples was collected.

Characterization Data of Products 3a - 3p, 5a - 5l, 6, 8, 10 and 11.[20]

*3-(iodomethyl)-1-tosylpyrrolidine (**3a**).* The product **3a** was obtained in 73% yield (53.3 mg, 0.146 mmol, colorless oil); R_f = 0.40 (hexane:ethyl acetate 5:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 – 7.67 (m, 2H), 7.39 – 7.30 (m, 2H), 3.50 – 3.35 (m, 2H), 3.30 – 3.19 (m, 1H), 3.09 – 2.93 (m, 3H), 2.44 (s, 3H), 2.43 – 2.35 (m, 1H), 2.08 – 1.96 (m, 1H), 1.61 – 1.49 (m, 1H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.6, 133.3, 129.7, 127.5, 53.6, 47.4, 41.2, 32.0, 21.5, 7.2; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{12}H_{16}INO_2NaS$ 387.9836, Found 387.9839.

*3-(iodomethyl)-1-tosylpiperidine (**3b**).* The product **3b** was obtained in 53% yield (40.2 mg, 0.106 mmol, yellow oil); R_f = 0.40 (hexane:ethyl acetate 5:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.68 – 7.62 (m, 2H), 7.38 – 7.30 (m, 2H), 3.75 – 3.66 (m, 1H), 3.56 – 3.48 (m, 1H), 3.17 – 2.98 (m, 2H), 2.44 (s, 3H), 2.42 – 2.33 (m, 1H), 2.23 – 2.14 (m, 1H), 1.87 – 1.57 (m, 4H), 1.12 – 0.99 (m, 1H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.5, 133.2, 129.6, 127.6, 51.6, 46.4, 37.4, 30.4, 23.8, 21.5, 9.0; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{13}H_{18}INO_2NaS$ 401.9995, Found 401.9993.

*3-(1-iodoethyl)-1-tosylpyrrolidine (**3c**).* The product **3c** was obtained in 66% yield (50.0 mg, 0.132 mmol, yellow oil); The diastereomer ratio of **3c** around C_3 and C_6 on the pyrrolidine ring was determined by ^{1}H NMR analysis (61:39); R_f = 0.40 (hexane:ethyl acetate 5:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 – 7.65 (m, 2H), 7.39 – 7.30 (m, 2H), 4.08 – 3.90 (m, 1H), 3.62 – 3.33 (m, 2H), 3.32 – 3.14 (m, 1H), 2.99 – 2.83 (m, 1H), 2.44 (s, 3H), 2.23 – 1.94 (m, 2H), 1.89 – 1.80 (m, 3H), 1.67 – 1.38 (m, 1H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.5, 133.3, 129.6, 127.5, 54.6, 48.3, 48.2, 30.3, 29.6, 27.2, 21.5; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{13}H_{18}INO_2NaS$

401.9995, Found 401.9995.

*3-(iodomethyl)-3-methyl-1-tosylpyrrolidine (**3d**).* The product **3d** was obtained in 54% yield (40.9 mg, 0.108 mmol, yellow oil); R_f = 0.40 (hexane:ethyl acetate 5:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 – 7.67 (m, 2H), 7.38 – 7.30 (m, 2H), 3.40 – 3.27 (m, 2H), 3.23 – 3.18 (m, 1H), 3.11 – 3.02 (m, 3H), 2.44 (s, 3H), 1.87 – 1.65 (m, 2H), 1.05 (s, 3H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.5, 133.5, 129.6, 127.3, 58.1, 46.8, 42.4, 36.9, 24.6, 21.4, 17.4; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{13}H_{18}INO_2NaS$ 401.9995, Found 401.9995.

*3-(iodomethyl)-4-methyl-1-tosylpyrrolidine (**3e**).* The product **3e** was obtained in 67% yield (50.8 mg, 0.134 mmol, colorless oil); The diastereomer ratio of **3e** around C_3 and C_4 on the pyrrolidine ring was determined by ^{1}H NMR analysis (76:24); R_f = 0.40 (hexane:ethyl acetate 5:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75 – 7.69 (m, 2H), 7.37 – 7.31 (m, 2H), 3.63 – 3.35 (m, 2H), 3.23 – 2.81 (m, 4H), 2.50 – 1.77 (m, 5H), 1.06 – 0.70 (m, 3H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.5, 133.8, 129.7, 127.4, 54.4, 51.8, 45.2, 36.1, 21.5, 12.4, 2.7; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{13}H_{18}INO_2NaS$ 401.9995, Found 401.9994.

*Dibenzyl 3-(iodomethyl)cyclopentane-1,1-dicarboxylate (**3f**).* The product **3f** was obtained in 56% yield (53.5 mg, 0.112 mmol, colorless oil); R_f = 0.50 (hexane:ethyl acetate 15:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.20 (m, 10H), 5.14 – 5.06 (m, 4H), 3.22 – 3.08 (m, 2H), 2.61 – 2.49 (m, 1H), 2.45 – 2.17 (m, 3H), 2.02 – 1.83 (m, 2H), 1.48 – 1.32 (m, 1H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 171.7, 135.3, 128.5, 128.2, 127.9, 67.1, 60.3, 41.9, 40.8, 33.7, 32.6, 11.1; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{22}H_{23}IO_4Na$ 501.0533, Found 501.0530.

2-benzyl-3-(iodomethyl)tetrahydrofuran *(**3g**).* The product **3g** was obtained in 66% yield (39.9 mg, 0.132 mmol, colorless oil); The diastereomer ratio of **3g** around C_2 and C_3 on the

tetrahydrofuran ring was determined by ^{1}H NMR analysis (86:14); R_f = 0.40 (hexane:ethyl acetate 30:1);^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.14 (m, 5H), 3.95 – 3.69 (m, 3H), 3.12 – 2.78 (m, 4H), 2.30 – 2.01 (m, 2H), 1.71 (dt, *J* = 12.5, 6.6 Hz, 1H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 138.0, 129.2, 128.4, 126.4, 84.5, 66.5, 46.1, 40.8, 34.1, 9.2; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{12}H_{15}IONa$ 325.0060, Found 325.0056.

*2-((benzyloxy)methyl)-5-ethoxy-3-(iodomethyl)tetrahydrofuran (**3h**).* The product **3h** was obtained in 63% yield (47.4 mg, 0.126 mmol, colorless oil); The diastereomer ratio of **3h** around C_2 and C_3 on the tetrahydrofuran ring was determined by ^{1}H NMR analysis (86:14); R_f = 0.50 (hexane:ethyl acetate 20:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.23 (m, 5H), 5.25 – 5.03 (m, 1H), 4.65 – 4.55 (m, 2H), 4.04 – 2.93 (m, 7H), 2.55 – 1.72 (m, 3H), 1.24 – 1.09 (m, 3H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 138.06, 138.05, 128.34, 128.28, 127.63, 127.60, 127.59, 127.58, 103.4, 103.3, 82.9, 82.2, 73.6, 73.4, 73.3, 71.4, 62.8, 62.4, 43.0, 42.7, 41.1, 40.4, 15.2, 15.1, 9.8, 9.2; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{15}H_{21}IO_3Na$ 399.0428, Found 399.0422.

*2-benzyl-4-(iodomethyl)tetrahydrofuran (**3i**).* The product **3i** was obtained in 55% yield (33.2 mg, 0.110 mmol, colorless oil); The diastereomer ratio of **3i** around C_3 and C_5 on the tetrahydrofuran ring was determined by ^{1}H NMR analysis (82:18); R_f = 0.40 (hexane:ethyl acetate 30:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 – 7.13 (m, 5H), 4.28 – 4.10 (m, 1H), 4.09 – 3.83 (m, 1H), 3.64 – 3.40 (m, 1H), 3.30 – 3.09 (m, 2H), 3.01 – 2.85 (m, 1H), 2.83 – 2.69 (m, 1H), 2.68 – 2.55 (m, 1H), 2.23 – 1.67 (m, 2H), 1.58 – 0.84 (m, 1H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 138.3, 129.2, 128.4, 126.3, 79.6, 73.6, 41.9, 41.8, 38.4, 8.7; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{12}H_{15}IONa$ 325.0060, Found 325.0057.

*4-(iodomethyl)-2-(4-methoxyphenyl)tetrahydrofuran (**3j**).* The product **3j** was obtained in

25% yield (15.9 mg, 0.050 mmol, colorless oil); The diastereomer ratio of **3j** around C_3 and C_5 on the tetrahydrofuran ring was determined by ^{1}H NMR analysis (86:14); R_f = 0.50 (hexane:ethyl acetate 30:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.15 (m, 2H), 7.00 – 6.79 (m, 2H), 4.99 (t, *J* = 7.2 Hz, 1H), 4.35 – 4.16 (m, 1H), 3.79 (s, 3H), 3.63 – 3.51 (m, 1H), 3.38 – 3.15 (m, 2H), 2.89 – 2.66 (m, 1H), 2.17 – 1.98 (m, 2H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 158.9, 134.5, 126.8, 113.7, 79.9, 74.1, 55.3, 42.0, 41.6, 8.5; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{12}H_{15}IO_2Na$ 341.0009, Found 341.0004.

*2-benzyl-3-(iodomethyl)hexahydrofuro[2,3-b]furan (**3k**).* The product **3k** was obtained in 59% yield (40.6 mg, 0.118 mmol, colorless oil); The diastereomer ratio of **3k** around C_3 and C_4 on the tetrahydrofuran ring was determined by ^{1}H NMR analysis (92:8), and the diastereomer ratio of **3k** around C_2 and C_3 on the tetrahydrofuran ring was over 95:5; R_f = 0.40 (hexane:ethyl acetate 20:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.19 (m, 5H), 5.68 – 5.60 (m, 1H), 3.99 – 3.65 (m, 3H), 3.09 – 2.86 (m, 4H), 2.63 – 2.52 (m, 1H), 2.06 – 1.91 (m, 1H), 1.79 – 1.63 (m, 2H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 137.2, 129.4, 128.4, 126.6, 107.7, 84.1, 66.5, 51.0, 49.9, 40.3, 32.5, 7.8; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{14}H_{17}IO_2Na$ 367.0165, Found 367.0163.

*3-(iodomethyl)-2-phenylhexahydrofuro[2,3-b]furan (**3l**).* The product **3l** was obtained in 72% yield (47.5 mg, 0.144 mmol, colorless oil); The diastereomer ratio of **3l** around C_3 and C_4 on the tetrahydrofuran ring was determined by ^{1}H NMR analysis (81:19); R_f = 0.40 (hexane:ethyl acetate 25:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.27 (m, 5H), 5.97 – 5.87 (m, 1H), 4.60 – 4.41 (m, 1H), 4.10 – 3.91 (m, 2H), 3.22 – 2.49 (m, 4H), 2.17 – 1.84 (m, 2H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 138.8, 128.6, 128.5, 126.4, 107.6, 83.5, 68.9, 54.3, 47.9, 24.8, 0.1; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{13}H_{15}IO_2Na$ 353.0009, Found 353.0004.

*3-(iodomethyl)-1-tosyloctahydro-1H-indole (**3m**).* The product **3m** was obtained in 31% yield (26.0 mg, 0.062 mmol, colorless oil); The diastereomer ratio of **3m** around C_2 and C_3 on the pyrrolidine ring was determined by ^{1}H NMR analysis (>95:5); R_f = 0.40 (hexane:ethyl acetate 4:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 – 7.67 (m, 2H), 7.37 – 7.31 (m, 2H), 3.65 – 3.55 (m, 1H), 3.36 – 3.30 (m, 1H), 3.25 – 3.15 (m, 1H), 3.06 – 2.90 (m, 2H), 2.63 – 2.54 (m, 1H), 2.45 (s, 3H), 2.07 – 1.95 (m, 2H), 1.84 – 1.74 (m, 1H), 1.64 – 1.43 (m, 4H), 1.24 – 1.10 (m, 2H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.5, 133.5, 129.7, 127.6, 61.0, 52.9, 43.6, 42.0, 28.5, 24.1, 21.5, 21.3, 20.0, 1.9; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{16}H_{22}INO_2NaS$ 442.0308, Found 442.0305.

*4-iodo-1-tosyloctahydro-1H-indole (**3n**).* The product **3n** was obtained in 33% yield (26.7 mg, 0.066 mmol, yellow oil); The diastereomer ratio of **3n** around C_2 and C_3 on the pyrrolidine ring was determined by ^{1}H NMR analysis (> 95:5); R_f = 0.30 (hexane:ethyl acetate 4:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 – 7.67 (m, 2H), 7.37 – 7.28 (m, 2H), 4.42 – 4.32 (m, 1H), 3.71 – 3.62 (m, 1H), 3.62 – 3.50 (m, 1H), 3.32 – 3.21 (m, 1H), 2.44 (s, 3H), 2.35 – 2.22 (m, 1H), 2.15 – 1.74 (m, 5H), 1.73 – 1.56 (m, 3H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.4, 134.1, 129.7, 127.4, 58.9, 49.5, 47.1, 34.9, 32.3, 28.7, 28.6, 21.9, 21.5; HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{15}H_{20}INO_2NaS$ 428.0152, Found 428.0149.

*3-benzylidene-1-tosylpyrrolidine (**3o**).* The product **3o** was obtained in 21% yield (13.2 mg, 0.042 mmol, white solid); The crude product **3o** is a diastereomixture in term of the new formed double bond; R_f = 0.30 (hexane:ethyl acetate 25:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 – 7.66 (m, 2H), 7.43 – 7.27 (m, 4H), 7.25 – 7.09 (m, 3H), 6.40 – 6.23 (m, 1H), 4.14 – 3.92 (m, 2H), 3.45 – 3.23 (m, 2H), 2.80 – 2.63 (m, 2H), 2.47 – 2.37 (m, 3H). ^{13}C{1H} NMR (101 MHz,

Chloroform-*d*) δ 143.73, 143.65, 137.0, 136.77, 136.76, 136.5, 132.8, 132.4, 129.70, 129.69, 128.5, 128.4, 128.1, 127.92, 127.90, 127.7, 126.9, 126.8, 123.3, 122.6, 53.7, 50.4, 48.5, 46.7, 33.7, 29.8, 21.5, 21.5; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{18}H_{20}NO_2S$ 314.1209, Found 314.1204.

*3-(propan-2-ylidene)-1-tosylpyrrolidine (**3p**).* The product **3p** was obtained in 59% yield (31.3 mg, 0.118 mmol, colorless oil); R_f = 0.50 (hexane:ethyl acetate 20:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 – 7.69 (m, 2H), 7.38 – 7.30 (m, 2H), 3.76 – 3.66 (m, 2H), 3.26 – 3.22 (m, 2H), 2.43 (s, 3H), 2.42 – 2.37 (m, 2H), 1.60 - 1.55 (m, 6H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.5, 132.3, 129.5, 127.9, 127.6, 124.1, 50.5, 48.2, 28.9, 21.4, 20.8, 20.7; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{20}NO_2S$ 266.1209, Found 266.1204.

*3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-1-tosylpyrrolidine (**5a**).* The product **5a** was obtained in 64% yield (46.7 mg, 0.128 mmol, colorless oil); R_f = 0.30 (hexane:ethyl acetate 5:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75 – 7.67 (m, 2H), 7.35 – 7.29 (m, 2H), 3.57 – 3.45 (m, 1H), 3.39 – 3.30 (m, 1H), 3.25 – 3.15 (m, 1H), 2.77 – 2.69 (m, 1H), 2.43 (s, 3H), 2.23 – 2.10 (m, 1H), 2.00 – 1.89 (m, 1H), 1.40 – 1.29 (m, 1H), 1.21 (s, 12H), 0.77 – 0.75 (m, 2H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.1, 134.0, 129.5, 127.5, 83.2, 55.0, 47.7, 34.8, 33.5, 24.75, 24.71, 21.5 (The carbon directly attached to the boron atom was not detected); HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{28}BNO_4NaS$ 388.1724; Found 388.1721.

*3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-1-tosylpiperidine (**5b**).* The product **5b** was obtained in 46% yield (11.2 mg, 0.030 mmol, colorless oil); R_f = 0.30 (hexane:ethyl acetate 5:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 – 7.61 (m, 2H), 7.34 – 7.29 (m, 2H), 3.72 – 3.58 (m, 2H), 2.43 (s, 3H), 2.29 – 2.16 (m, 1H), 2.01 – 1.89 (m, 1H), 1.89 – 1.80 (m, 1H), 1.79 – 1.53 (m, 3H), 1.24 (s, 12H), 0.92 – 0.77 (m, 1H), 0.75 – 0.60 (m, 2H); ^{13}C{1H} NMR (101

MHz, Chloroform-*d*) δ 143.1, 133.7, 129.4, 127.6, 83.1, 53.4, 46.3, 32.3, 32.0, 24.73, 24.72, 21.4, 16.1; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{19}H_{30}BNO_4NaS$ 402.1881; Found 402.1883.

3-methyl-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-1-tosylpyrrolidine (***5c***).

The product **5c** was obtained in 51% yield (38.7 mg, 0.102 mmol, colorless oil); The diastereomer ratio of **5c** around C_3 and C_4 on the pyrrolidine ring was determined by ^1H NMR analysis (71:29); R_f = 0.30 (hexane:ethyl acetate 5:1); ^1H NMR (400 MHz, Chloroform-*d*) δ 7.74 – 7.66 (m, 2H), 7.35 – 7.28 (m, 2H), 3.65 – 3.31 (m, 2H), 3.02 – 2.74 (m, 2H), 2.43 (s, 3H), 2.24 – 2.12 (m, 1H), 1.71 – 1.55 (m, 1H), 1.22 (s, 12H), 0.91 – 0.87 (m, 1H), 0.72 – 0.66 (m, 3H), 0.60 – 0.50 (m, 1H); $^{13}C\{1H\}$ NMR (101 MHz, Chloroform-*d*) δ 143.1, 143.1, 134.2, 134.1, 129.5, 129.5, 127.4, 127.4, 83.3, 83.2, 54.8, 54.8, 54.4, 53.2, 41.8, 41.0, 37.7, 36.2, 24.8, 24.74 , 24.72 , 21.5, 15.5, 13.0 (The carbon directly attached to the boron atom was not detected); HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{19}H_{30}BNO_4NaS$ 402.1881; Found 402.1881.

3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-1-tosyloctahydro-1H-indole (***5d***).

The product **5d** was obtained in 35% yield (29.4 mg, 0.070 mmol, colorless oil); The diastereomer ratio of **5d** around C_3 on the pyrrolidine ring was determined by ^1H NMR analysis (80:20); R_f = 0.30 (hexane:ethyl acetate 4:1); ^1H NMR (400 MHz, Chloroform-*d*) δ 7.76 – 7.66 (m, 2H), 7.36 – 7.27 (m, 2H), 3.64 – 3.49 (m, 1H), 3.36 – 3.26 (m, 1H), 3.17 – 3.04 (m, 1H), 2.43 (s, 3H), 1.90 – 1.78 (m, 1H), 1.80 – 1.58 (m, 3H), 1.53 – 1.39 (m, 4H), 1.21 (s, 12H), 1.16 – 1.04 (m, 2H), 0.77 – 0.59 (m, 2H); $^{13}C\{1H\}$ NMR (101 MHz, Chloroform-*d*) δ 143.0, 134.0, 129.5, 127.7, 83.2, 61.1, 54.7, 42.3, 36.4, 28.6, 24.7, 24.5, 22.3, 21.5, 20.2 (The carbon directly attached to the boron atom was not detected); HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{22}H_{34}BNO_4NaS$ 442.2194; Found 442.2194.

*2-((5-(4-methoxyphenyl)tetrahydrofuran-3-yl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5e**).* The product **5e** was obtained in 34% yield (21.6 mg, 0.068 mmol, colorless oil); The diastereomer ratio of **5e** around C_3 and C_5 on the tetrahydrofuran ring was determined by ^{1}H NMR analysis (88:12); R_f = 0.30 (hexane:ethyl acetate 30:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 – 7.21 (m, 2H), 6.90 – 6.79 (m, 2H), 4.94 (t, *J* = 7.0 Hz, 1H), 4.27 – 4.18 (m, 1H), 3.79 (s, 3H), 3.46 – 3.38 (m, 1H), 2.57 – 2.48 (m, 1H), 2.08 – 1.98 (m, 1H), 1.96 – 1.89 (m, 1H), 1.24 (s, 12H), 0.96 – 0.94 (m, 2H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 158.7, 135.9, 127.0, 113.6, 83.1, 79.8, 75.9, 55.2, 42.7, 34.7, 24.8 (The carbon directly attached to the boron atom was not detected); HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{27}BO_4Na$ 341.1895; Found 341.1895.

*2-((2-((benzyloxy)methyl)-5-ethoxytetrahydrofuran-3-yl)methyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5f**).* The product **5f** was obtained in 55% yield (41.4 mg, 0.110 mmol, colorless oil); The diastereomer ratio of **5f** around C2 and C3 on the tetrahydrofuran ring was determined by ^{1}H NMR analysis (76:24); The product **5f** is a diastereomixture in term of the acetal moiety (C_5) due to the stereochemistry of the starting material; R_f = 0.40 (hexane:ethyl acetate 20:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.27 (m, 5H), 5.23 – 4.87 (m, 1H), 4.66 – 4.28 (m, 2H), 3.87 – 3.30 (m, 5H), 2.46 – 1.90 (m, 2H), 1.69 – 1.47 (m, 1H), 1.28 – 0.75 (m, 17H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 138.5, 138.4, 128.3, 128.0, 127.7, 127.6, 127.4, 127.4, 103.8, 103.6, 86.1, 83.9, 83.2, 83.1, 73.8, 73.3, 73.2, 71.2, 63.0, 62.2, 41.1, 40.9, 35.9, 35.2, 24.8, 24.7, 15.3, 15.2 (The carbon directly attached to the boron atom was not detected); HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{21}H_{33}BO_5Na$ 399.2313, Found 399.2309.

*4,4,5,5-tetramethyl-2-((2-phenylhexahydrofuro[2,3-b]furan-3-yl)methyl)-1,3,2-dioxaborolane (**5g**).* The product **5g** was obtained in 42% yield (27.7 mg, 0.084 mmol, colorless oil); The

diastereomer ratio of **5g** around C_3 on the tetrahydrofuran ring was determined by ^{1}H NMR analysis (>95:5); R_f = 0.40 (hexane:ethyl acetate 20:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.27 (m, 5H), 5.76 (d, *J* = 5.5 Hz, 1H), 4.35 (d, *J* = 9.4 Hz, 1H), 4.08 – 4.01 (m, 2H), 2.64 – 2.56 (m, 1H), 1.99 – 1.83 (m, 3H), 1.23 – 1.16 (m, 12H), 1.08 – 0.95 (m, 1H), 0.89 – 0.80 (m, 1H).; ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 140.2, 128.3, 127.8, 126.4, 108.4, 87.7, 83.3, 66.8, 51.2, 48.4, 32.1, 24.9 (The carbon directly attached to the boron atom was not detected); HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{19}H_{27}BO_4Na$ 353.1895; Found 353.1896.

*Dibenzyl 3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclopentane-1,1-dicarboxylate (**5h**).* The product **5h** was obtained in 57% yield (54.5 mg, 0.114 mmol, colorless oil); R_f = 0.50 (hexane:ethyl acetate 15:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.15 (m, 10H), 5.28 – 4.92 (m, 4H), 2.59 – 2.51 (m, 1H), 2.38 – 2.30 (m, 1H), 2.23 – 2.08 (m, 2H), 1.96 – 1.86 (m, 1H), 1.79 – 1.67 (m, 1H), 1.26 (s, 1H), 1.21 (s, 12H), 0.94 – 0.79 (m, 2H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 172.4, 135.7, 128.4, 128.1, 127.9, 83.0, 66.9, 60.3, 42.9, 35.9, 34.3, 34.0, 24.8 (The carbon directly attached to the boron atom was not detected); HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ Calcd for $C_{28}H_{35}BO_6Na$ 501.2420; Found 501.2419.

*3-((5,5-dimethyl-1,3,2-dioxaborinan-2-yl)methyl)-1-tosylpyrrolidine (**5i**).* The product **5i** was obtained in 52% yield (36.5 mg, 0.104 mmol, colorless oil); R_f = 0.30 (hexane:ethyl acetate 5:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75 – 7.66 (m, 2H), 7.35 – 7.28 (m, 2H), 3.55 (s, 4H), 3.53 – 3.47 (m, 1H), 3.37 – 3.29 (m, 1H), 3.22 – 3.14 (m, 1H), 2.76 – 2.68 (m, 1H), 2.43 (s, 3H), 2.20 – 2.09 (m, 1H), 1.97 – 1.88 (m, 1H), 1.37 – 1.25 (m, 1H), 0.93 (s, 6H), 0.72 – 0.65 (m, 2H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.0, 134.1, 129.5, 127.4, 71.9, 55.1, 47.7, 34.8, 33.7, 31.5,

21.7, 21.5 (The carbon directly attached to the boron atom was not detected); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{27}BNO_4S$ 352.1748, Found 352.1743.

*(1-tosylpyrrolidin-3-yl)methanol (**5j**).* The product **5j** was obtained in 55% yield (28.1 mg, 0.110 mmol, colorless oil); R_f = 0.30 (hexane:ethyl acetate 1:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 – 7.66 (m, 2H), 7.38 – 7.30 (m, 2H), 3.52 – 3.40 (m, 2H), 3.37 – 3.28 (m, 2H), 3.24 – 3.14 (m, 1H), 3.11 – 3.04 (m, 1H), 2.44 (s, 3H), 2.37 – 2.26 (m, 1H), 1.96 – 1.85 (m, 1H), 1.68 (s, 1H), 1.63 – 1.53 (m, 1H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.5, 133.4, 129.6, 127.6, 64.1, 50.3, 47.3, 40.7, 27.6, 21.5; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{12}H_{18}NO_3S$ 256.1002, Found 256.0996.

*1-tosyl-3-vinylpyrrolidine (**5k**).* The product **5k** was obtained in 76% yield (38.2 mg, 0.152 mmol, colorless oil); R_f = 0.50 (hexane:ethyl acetate 20:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 – 7.64 (m, 2H), 7.41 – 7.30 (m, 2H), 5.65 – 5.54 (m, 1H), 5.05 – 4.91 (m, 2H), 3.49 – 3.43 (m, 1H), 3.40 – 3.34 (m, 1H), 3.28 – 3.20 (m, 1H), 2.98 – 2.90 (m, 1H), 2.72 – 2.61 (m, 1H), 2.43 (s, 3H), 2.00 – 1.89 (m, 1H), 1.63 – 1.51 (m, 1H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.3, 137.4, 133.7, 129.5, 127.3, 115.7, 52.4 , 47.3, 42.3, 31.4, 21.4; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{13}H_{18}NO_2S$ 252.1053, Found 252.1050.

*3-(prop-1-en-2-yl)-1-tosylpyrrolidine (**5l**).* The product **5l** was obtained in 64% yield (33.9 mg, 0.128 mmol, colorless oil); R_f = 0.50 (hexane:ethyl acetate 20:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 – 7.67 (m, 2H), 7.43 – 7.30 (m, 2H), 4.79 – 4.59 (m, 2H), 3.53 – 3.35 (m, 2H), 3.28 – 3.19 (m, 1H), 3.06 – 2.97 (m, 1H), 2.68 – 2.54 (m, 1H), 2.43 (s, 3H), 1.98 – 1.89 (m, 1H), 1.71 – 1.58 (m, 4H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.6, 143.3, 133.8, 129.5, 127.3, 110.7, 51.4, 47.6, 45.0 , 29.8, 21.4, 20.9; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{20}NO_2S$ 266.1209, Found 266.1205.

*3-(3,3-diphenylallyl)-1-tosylpyrrolidine (**6**)*. The product **6** were obtained in 67% yield (55.9 mg, 0.134 mmol, colorless oil) and 52% yield (43.4 mg, 0.104 mmol, colorless oil), respectively; R_f = 0.50 (hexane:ethyl acetate 15:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.7 – 7.6 (m, 2H), 7.4 – 7.2 (m, 8H), 7.2 – 7.1 (m, 2H), 7.1 – 7.1 (m, 2H), 5.9 (t, *J* = 7.3 Hz, 1H), 3.5 – 3.4 (m, 1H), 3.3 – 3.1 (m, 2H), 2.8 – 2.7 (m, 1H), 2.4 (s, 3H), 2.2 – 2.0 (m, 3H), 2.0 – 1.8 (m, 1H), 1.5 – 1.3 (m, 1H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.3, 143.2, 142.2, 139.7, 133.9, 129.7, 129.6, 128.3, 128.1, 127.5, 127.13, 127.11, 127.08, 126.3, 52.9, 47.4, 39.2, 32.8, 30.9, 21.5; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{26}H_{28}NO_2S$ 418.1835, Found 418.1835.

*3-(2-(3,4-dihydronaphthalen-1-yl)ethyl)-1-tosylpyrrolidine (**8**)*. The product **8** were obtained in 27% yield (20.6 mg, 0.054 mmol, colorless oil) and 35% yield (26.7 mg, 0.070 mmol, colorless oil), respectively; R_f = 0.50 (hexane:ethyl acetate 10:1); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.8 – 7.7 (m, 2H), 7.4 – 7.3 (m, 2H), 7.2 – 7.1 (m, 4H), 5.8 (t, *J* = 4.6 Hz, 1H), 3.5 – 3.4 (m, 1H), 3.4 – 3.3 (m, 1H), 3.2 – 3.1 (m, 1H), 2.8 – 2.8 (m, 1H), 2.7 – 2.6 (m, 2H), 2.4 (s, 3H), 2.4 – 2.3 (m, 2H), 2.3 – 2.2 (m, 2H), 2.1 – 2.0 (m, 1H), 2.0 – 1.9 (m, 1H), 1.5 – 1.3 (m, 3H); ^{13}C{1H} NMR (101 MHz, Chloroform-*d*) δ 143.2, 136.8, 135.7, 134.4, 133.9, 129.6, 127.7, 127.5, 126.7, 126.3, 125.2, 122.4, 53.2, 47.5, 38.5, 31.8, 31.4, 31.2, 28.3, 23.0, 21.5; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{23}H_{28}NO_2S$ 382.1835, Found 382.1833.

*3-(4-iodobut-1-en-1-yl)-2-phenethyltetrahydrofuran (**10**).* The product **10** was obtained in 19% yield (13.5 mg, 0.038 mmol, colorless oil); The *E/Z* ratio of **10** was determined by ^{1}H NMR analysis (83:17); R_f = 0.40 (hexane:ethyl acetate 30:1); ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.3 – 7.2 (m, 2H), 7.2 – 7.1 (m, 3H), 5.5 – 5.4 (m, 2H), 4.0 – 3.8 (m, 2H), 3.5 – 3.4 (m, 1H), 3.2 – 3.1 (m, 2H), 2.9 – 2.8 (m, 1H), 2.7 – 2.3 (m, 4H), 2.2 – 2.1 (m, 1H), 2.0 – 1.8 (m, 1H), 1.8 – 1.7 (m, 2H);

$^{13}C\{1H\}$ NMR (151 MHz, Chloroform-*d*) δ 142.2, 133.4, 129.9, 128.4, 128.3, 125.7, 83.0, 67.0, 48.7, 36.3, 35.7, 33.4, 32.8, 5.9; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{16}H_{21}IONa$ 379.0529, Found 379.0527.

*4,4,5,5-tetramethyl-2-(4-(2-phenethyltetrahydrofuran-3-yl)but-3-en-1-yl)-1,3,2-dioxaborolane (**11**).* The product **11** was obtained in 22% yield (15.7 mg, 0.044 mmol, colorless oil); The *E/Z* ratio of **11** was determined by ^1H NMR analysis (85:15); R_f = 0.30 (hexane:ethyl acetate 15:1); ^1H NMR (600 MHz, Chloroform-*d*) δ 7.3 – 7.2 (m, 2H), 7.2 – 7.1 (m, 3H), 5.6 – 5.4 (m, 1H), 5.3 – 5.1 (m, 1H), 3.9 – 3.8 (m, 2H), 3.5 – 3.4 (m, 1H), 2.9 – 2.8 (m, 1H), 2.7 – 2.6 (m, 1H), 2.4 – 2.2 (m, 1H), 2.1 – 2.1 (m, 3H), 1.9 – 1.8 (m, 1H), 1.8 – 1.7 (m, 2H), 1.2 – 1.2 (m, 12H), 0.9 – 0.8 (m, 2H); $^{13}C\{1H\}$ NMR (151 MHz, Chloroform-*d*) δ 142.4, 133.8, 128.99, 128.98, 128.4, 128.2, 125.6, 83.2, 82.9, 67.0, 48.7, 35.7, 33.7, 32.8, 26.7, 24.8, 22.1; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{22}H_{33}BO_3Na$ 379.2415, Found 379.2412.

Supporting Information

Instrumentation, the graphics of carbon atom numbers in characterization data, optimization of reaction conditions. UV/Vis absorption spectra studies, Stern-Volmer luminescence quenching studies and NMR Spectra

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(20) The graphics of carbon atom numbers in the molecular framework (**3a-3p** and **5a-5l**) referred to following descriptions is placed in the supporting information.