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Study on New Methodology for Radical Functionalization of Olefins by Photoredox Catalysis

（フォトレドックス触媒によるオレフィン類の新規なラジカル的官能基化法に関する研究）

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Chapter 1

General Introduction

In the field of synthetic organic chemistry, radical chemistry has been recognized as a unique area because radical species behave in a different manner from ionic species, i.e., cation and anion species.[1] Thus, the author expects radical reactions to be feasible for elusive transformation which ionic species cannot induce. In general, radical species are known as reactive and unstable chemical species. Their properties are strongly influenced by their structure. As a matter of course, the methodologies for generation of such reactive radical species are important to design highly efficient and selective reactions.

Firstly, in this Chapter, the author describes general properties of carbon-centered radicals and characteristic reactivities of radical species. Secondly, the section will be dealt with strategies for generation of organic radicals. Conventional methods are referred to, preceding explanation of new protocol related to this thesis, i.e., *visible-light-driven photoredox catalysis*. In addition, the author will introduce seminal works based on photoredox catalysis. In the third section, the author will refer to trifluoromethylation, which will be discussed in Chapters 4−7. In particular, significance and outline of previous trifluoromethylation will be given. Finally, the author will present survey of this thesis.

1.1 Properties and Reactivities of Carbon-Centered Radicals

1.1.1 π–Radicals and σ–Radicals

The carbon-centered radicals can be classified into two types from their hybridization, that is, (1) π–radical and (2) σ–radical.[2] Unpaired electron of the former is located at only p-orbital, in contrast, that of the latter is located at both s-orbital and p-orbital. Examples of these radicals are shown in Figure 1.1.

Various alkyl radicals such as a methyl- (CH_3), a *tert*-butyl- (^{t}Bu), an allyl-, and a benzyl radical belong to π–radicals (Figure 1.1a). Among them, ^{t}Bu-, allyl, and benzyl radicals undergo hyperconjugation or π–conjugation, thus they are stabilized. Such radicals often induce homocoupling to afford dimerized products.

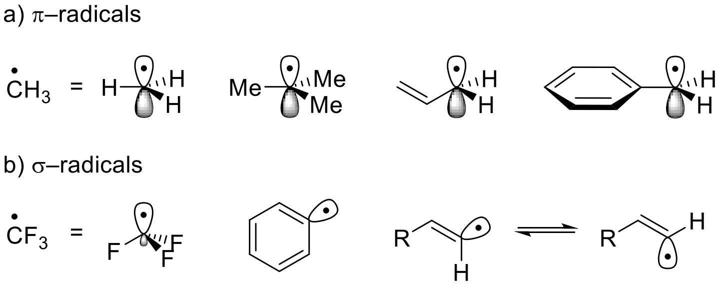
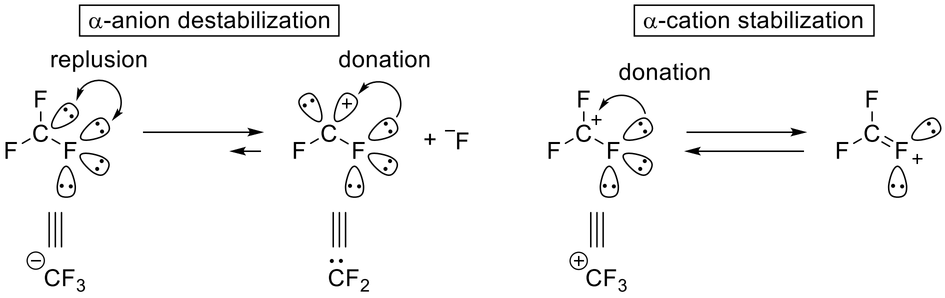


Figure 1.1. Examples of Typical π–Radicals (a) and σ–Radicals (b).

On the other hand, pyramidal structure of a trifluoromethyl (CF_3) radical belongs to a σ–radical. High electronegativity of the fluorine atom exerts a strong σ-inductive effect on carbon radical. At the same time, the F atom behaves as a weak π–donor, because the lone pairs of the F atoms show good overlap with the singly occupied molecular orbital (SOMO) at the carbon. These two effects induce its non-planar structure.[3] In addition, phenyl and vinyl radicals are also typical σ–radicals. The vinyl radical exhibits a rapid *cis*/*trans* isomerization shown in Figure 1.1b, which often influences in stereoselective reactions.

1.1.2 Carbon-Centered Radicals and Ionic Species

Carbon-centered radicals enable efficient and selective C−C bond formation under mild conditions. For example, the ^{t}Bu radical is insusceptible to steric environment compared with the corresponding ionic species. In fact, the reactions of the bulky ^{t}Bu radical proceed smoothly. Furthermore, the CF_3 radical, which have been proved to be accessed by several methods, can achieve an efficient trifluoromethylation. In contrast, reactions with the corresponding ionic species, i.e., CF_3 anion and cation, are elusive because ionic species are hard to handle. The CF_3 anion undergoes the n–p repulsion between a negatively-charged anion and the lone pairs of the F atom to rapidly convert to the difluorocarbene, which are stabilized by a donation from lone pairs on the F atom into unoccupied orbital on the carbon atom. On the other hand, the CF_3 cation is stabilized by the donation of lone pairs on the F atom. Therefore, the reactivity of the CF_3 cation is lower than that of the CF_3 radical.[4]

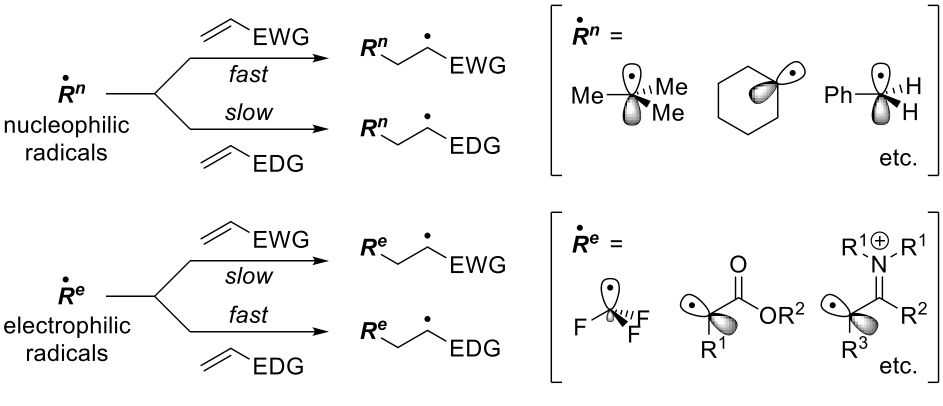


Scheme 1.1. The CF_3 anion and cation.

Next, the author describes peculiar reactions of radical species with olefins.

1.1.3 Addition Reactions of Carbon-Centered Radicals to Olefins

In the case of radical addition to olefins, alkyl radicals such as the ^{t}Bu radical react with electron-deficient olefins rapidly (Scheme 1.2). But, reactions with electron-rich olefins slowly proceed. This reactivity is based on nucleophilic properties of alkyl radicals.



Scheme 1.2. Radical Addition Reactions. EWG = Electron-Withdrawing Group, EDG = Electron-Donating Group.

As shown in Figure 1.2, singly occupied molecular orbital (SOMO) of nucleophilic radicals is located in high energy level, which can strongly interact with LUMO of electron-deficient alkenes (Figure 1.2a) due to close energy level between the both orbitals.

On the other hand, the carbon-centered radicals bearing electron-withdrawing functionalities such as carbonyl groups, halogen atoms, and inimium ions show electrophilic properties, thus they are compatible with electron-rich alkenes. The SOMO is located in low energy level, which can interact with HOMO of electron-rich alkenes (Figure 1.2b).

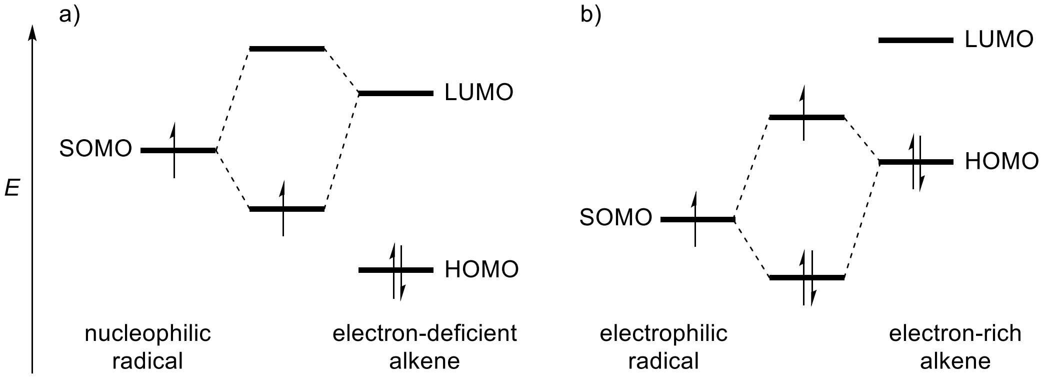
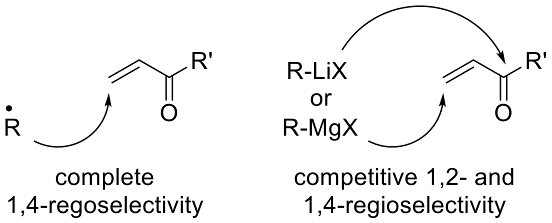


Figure 1.2. SOMO–LUMO and SOMO–HOMO Interactions in Radical Addition Reactions.

Radical addition reactions with electron-deficient alkenes show highly regioselectivity even if substrates are containing ketone and ester functionalities. In contrast, addition reactions of organolithium or Grignard reagents, which are strong nucleophiles, exhibit competitive 1,2- and 1,4-additions (Scheme 1.3).



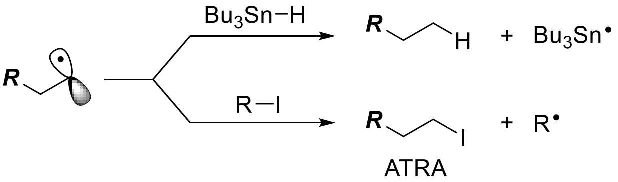
Scheme 1.3. Regioselectivities in Addition Reactions with Enones.

The use of radicals in organic synthesis can provide characteristic transformation, that it is difficult to be accessed by ionic reactions.

Next, peculiar reactivities of generated radical intermediates after radical addition reactions are given.

1.1.4 S_H2 Reaction (Substitution Homolytic Bimolecular)

Radical intermediates generated by radical addition reactions can easily abstract a hydrogen atom and a halogen atom from tributyltin hydride (Bu_3SnH) and alkyl iodides, respectively. These reactions are called S_H2 reaction (substitution homolytic bimolecular) (Scheme 1.4). In particular, the latter reaction is well-known as atom transfer radical addition (ATRA).



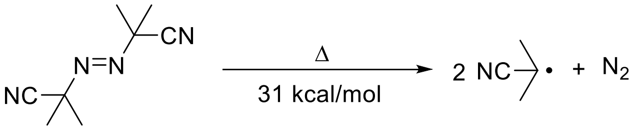
Scheme 1.4. S_H2 Reactions.

1.2 Methods for Generation of Carbon-Centered Radicals

Many methods for generation of radicals have been developed so far. Typical protocols are briefly described.[5]

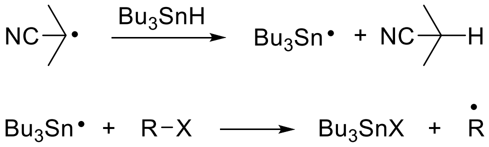
1.2.1 Radical Generation by Thermolysis

A covalent bond is generally cleaved to its radical fragments at temperatures higher than 800 ^{o}C. Organic molecules with weak bonds (dissociation energies = 30−40 kcal/mol) can be cleaved at <150 ^{o}C. Azo compounds, peroxides, ester of *N*-hydroxy-2-thiopyridine (Barton ester) etc. fit into this class of compounds. An example of generation of radicals from 2,2’-Azobisisobutyronitrile (AIBN) is shown in Scheme 1.5.



Scheme 1.5. Thermal Decomposition of AIBN.

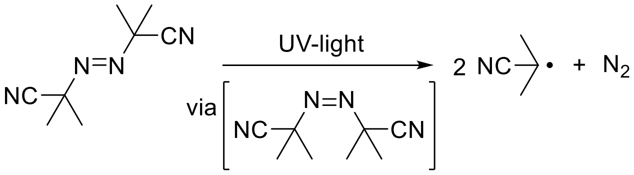
In addition, Bu_3SnH has been used in combination with the above reagents because it shows two properties, that is, (1) it can easily generate $Bu_3Sn^\bullet$ *via* an abstraction of H atom from the weak Sn−H bond to and (2) the generated $Bu_3Sn^\bullet$ can abstract halogen atoms from alkyl, vinyl and aryl halides (Scheme 1.6). Thus, Bu_3SnH has been well-known as radical initiator.



Scheme 1.6. Radical Initiating System with AIBN and Bu_3SnH.

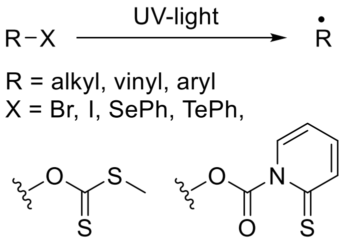
1.2.2 Radical Generation by Photolysis

Photolysis can be used to achieve homolytic fission. For example, azo compounds produce radicals by decomposition through *cis*-isomerization triggered by UV-light irradiation (Scheme 1.7). Peroxides also produce alkoxy radicals and acyloxy radicals as cleaved products by UV-light.



Scheme 1.7. Photochemical Decomposition of AIBN.

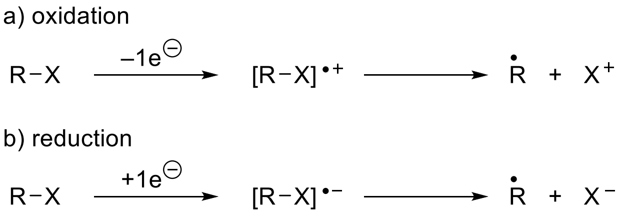
Alkyl, vinyl, and aryl halides bearing a relatively weak C−X bond can undergo same homolysis, generating carbon-centered radicals (Scheme 1.8). Chalcogen compounds, Barton esters and xanthate derivatives can also produce radical species under similar conditions.



Scheme 1.8. Generation of Radicals by Photolysis.

1.2.3 Radical Generation by Redox

Oxidation or reduction reactions (redox reactions, Scheme 1.9) generate radicals through an intermolecular single-electron transfer (SET). In most case of these redox reactions, excess amount of metal oxidants and reductants as well as electrochemical methods are used.



Scheme 1.9. Radical Generation by Redox Reactions.

As described above, there are various protocols for generation of radicals. However, most radical initiating methods show several disadvantages, that is, (1) requirement of toxic tin reagent and explosive azo compounds and peroxides, (2) the need for inconvenient high-energy UV-light with expensive equipment and (3) formation of a large amount of metallic wastes derived from oxidants or reductants. In modern synthetic organic chemistry, protocols need to be easy and safe to use, and efficient and selective outcomes should be provided.

1.2.4 Radical Generation by Visible-Light-Induced Photoredox Catalysis

Visible-light-triggered radical reactions are considered as an attractive approach for green organic synthesis because visible light is non-toxic and a main component of the most abundant energy source, *sunlight*. But, most organic molecules are colorless, resulting inactivity under visible light irradiation. In contrast, various inorganic and organometallic compounds can absorb strongly visible light. The author paid the attention to tris(bipyridyl)ruthenium(II) ($[Ru(bpy)_3]^{2+}$) because it has some outstanding properties (*vide infra*).[6]

Its absorption maximum (around 450 nm) is in visible-light region, indicating that it can be easily excited by visible light. The luminescent triplet excited state (lifetime τ = approximated 1 μs), $^*[Ru(bpy)_3]^{2+}$, which is resulting from electron transfer from dπ orbital of the Ru center to the π* orbital of the 2,2'-bipyridine ligand, i.e., MLCT (metal-to-ligand charge transfer transition), is sufficiently long enough for chemical transformations to proceed. The triplet excited state, $^*[Ru(bpy)_3]^{2+}$, undergoes SET to/from organic molecules, i.e., this triplet state can serve either as a 1e-oxidant or a 1e-reductant before returning to the initial ground state $[Ru(bpy)_3]^{2+}$ (Figure 1.3).

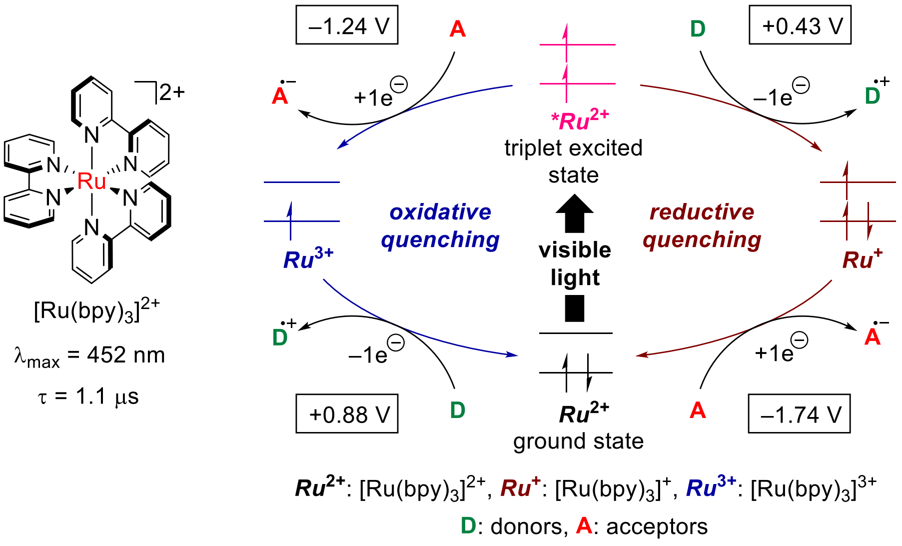


Figure 1.3. Photoredox Cycle of $[Ru(bpy)_3]^{2+}$(Redox Potential = $E_{1/2}$ (vs. Cp_2Fe)).

Therefore, photoredox processes catalyzed by this complex should be useful and powerful tools for redox reactions of organic molecules. The cycle consisting of sequence of (i) electron transfer from an electron donor **D** to *$[Ru(bpy)_3]^{2+}$ (****Ru*$^{2+}$) associated with formation reduced $[Ru(bpy)_3]^{+}$ (***Ru***$^{+}$), and (ii) reduction of an electron acceptor **A** associated with regeneration of ground state of the catalyst is called *reductive quenching cycle*. On the other hand, the cycle consisting of a sequence of (iii) electron transfer from *$[Ru(bpy)_3]^{2+}$ (****Ru*$^{2+}$) to an electron acceptor **A** associated with formation of high-oxidation-state $[Ru(bpy)_3]^{3+}$ (***Ru***$^{3+}$), and (iv) oxidation of an electron donor **D** associated with regeneration of the ground state of the catalyst is called the *oxidative quenching cycle*. Both these cycles produce $\mathbf{D}^{\bullet+}$ and $\mathbf{A}^{\bullet-}$ radicals in a single reactor through SET processes to make, overall, the transformation *redox neutral*.

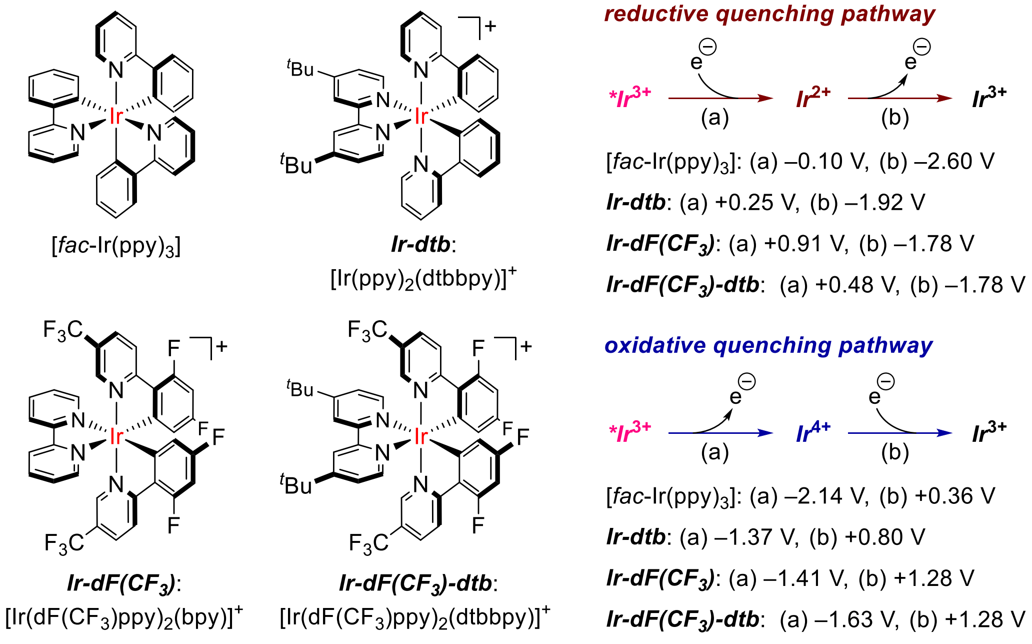


Figure 1.4. Redox Potentials of Cyclometalated Ir Complexes.

The terms *reductive* and *oxidative* are confusing and require explanation. *Reductive* refers to reduction of the photoexcited species, whereas the external electron donor **D** is oxidized in same process. *Oxidative* means oxidation of the photoexcited species concomitant with reduction of the external electron acceptor **A**.

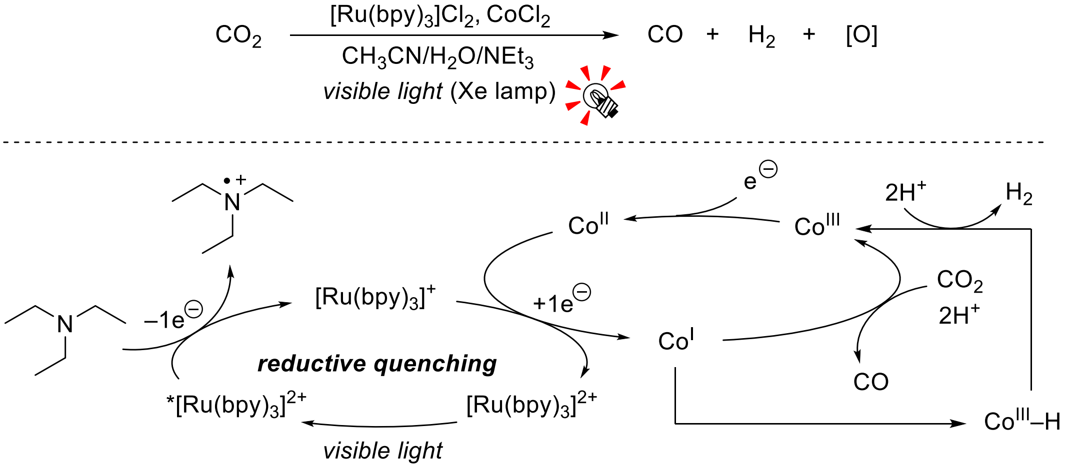
Redox potential of each catalytic species is one of the most important factors to design visible-light-induced redox reactions by photoredox catalyst. The redox potentials of the catalytic species can be modified by ligands and changing central metal. In particular, relevant cyclometalated Ir complexes have been often used as alternative photoredox catalysts. Redox potentials of representative Ir species are shown in Figure 1.4.[7]

1.2.4.1 Activation of Small Inorganic Molecules Using $[Ru(bpy)_3]^{2+}$ Derivatives

Photoredox properties of $[Ru(bpy)_3]^{2+}$ has been especially well used to studies on artificial photosynthesis and dye-sensitized solar cell as well as photofunctional materials.[8–11] In particular, there are many studies on photoinduced activation of small inorganic molecules. Representative examples are shown below.

1.2.4.1.1 Reduction of Carbon Dioxide (CO_2) by $[Ru(bpy)_3]^{2+}/CoCl_2$ System

Photoinduced splitting of water and reduction of carbon dioxide (CO_2) are the basic reactions of natural photosynthesis. Lehn et al. reported that a multicomponent catalytic system, $[Ru(bpy)_3]^{2+}$ and $CoCl_2$, effects on reduction of CO_2 under visible light irradiation (Scheme 1.10).[12]

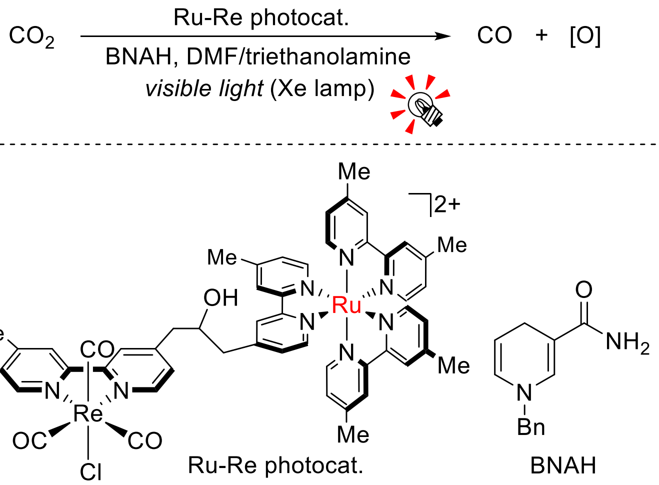


Scheme 1.10. Photocatalytic Reduction of CO_2 by $[Ru(bpy)_3]^{2+}/CoCl_2$ System.

Plausible mechanism based on reductive quenching is shown in Scheme 1.10. Initially, NEt_3 acts as an electron donor to reduce the photoexcited $[Ru(bpy)_3]^{2+}$, providing a radical cation ($^{+\bullet}NEt_3$) and $[Ru(bpy)_3]^{+}$. The $[Ru(bpy)_3]^{+}$ gives an electron into a Co^{II} species to generate a strong reductant Co^{I}. CO_2 is reduced by the Co^{I} species to provide CO (Scheme 1.10). It is also proposed that Co^{III}-H species involve in generation of H_2.

1.2.4.1.2 Reduction of CO_2 by Ru−Re Dinuclear Complex

Recently, photoinduced reduction of CO_2 was achieved by single-component system, i.e., Ru–Re dinuclear complex. Ishitani et al. reported the Ru−Re dinuclear complex enables reduction of CO_2 in the presence of sacrificial electron donor, 1-benzyl-1,4-dihydronicotinamide (BNAH) under visible light irradiation (Scheme 1.11).[13] In this reaction, an efficient SET process between the reduced ***Ru***$^{+}$ center generated from 1e-reduction of the photoexcited ****Ru***$^{2+}$ by BNAH and the Re fragment is a key to success. The CO_2 reduction activity of this single component system is higher than that of multicomponent system.



Scheme 1.11. Photocatalytic Reduction of CO_2 by Ru−Re Dinuclear Complex.

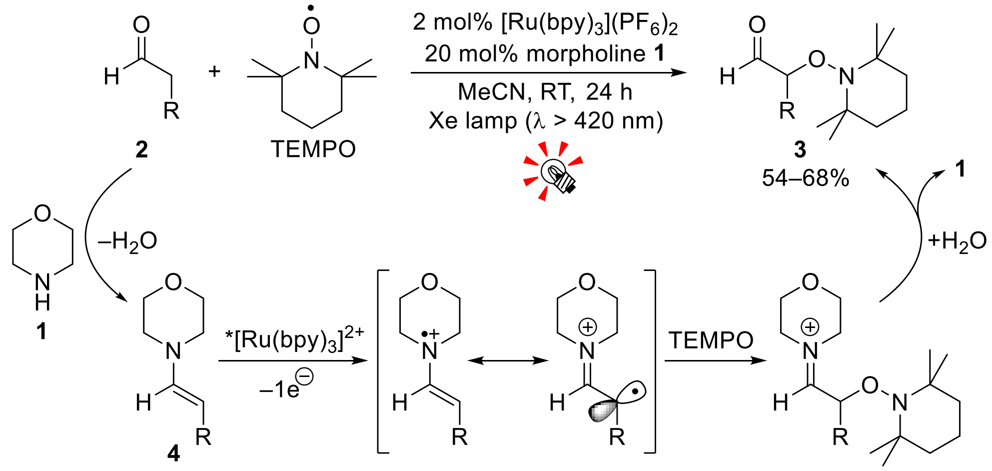
1.2.4.2 Synthetic Application of Photoredox Catalysis

So far, application of photoredox catalysts in organic synthesis has not been sufficiently investigated compared with above-mentioned studies on artificial photosynthesis.

Since 2008, photoredox catalysis with $[Ru(bpy)_3]^{2+}$ and relevant cyclometalated Ir complexes in the synthetic organic chemistry has become an active research area.[14,15] The author presents seminal works based on photoredox catalysis below.

1.2.4.2.1 Oxyamination of Aldehydes (Our Group)

The photoexcited state $*[Ru(bpy)_3]^{2+}$ is converted into the reduced species $[Ru(bpy)_3]^{+}$ by a SET process in the presence of a sacrificial electron donor such as triethanolamine or NEt_3. This suggested that $*[Ru(bpy)_3]^{2+}$ might be capable of one-electron oxidation of electron-rich tertiary amines. Thus, our group first attempted photocatalytic transformation of an enamine of a tertiary amine through a 1e-oxidation process. In general, oxidative transformation of enamines has been conducted in the presence of an excess amount of metal oxidants such as ceric ammonium nitrate (CAN) and $FeCl_3$.[5] Catalytic oxidative transformation of enamines is attractive from the viewpoint of green chemistry.

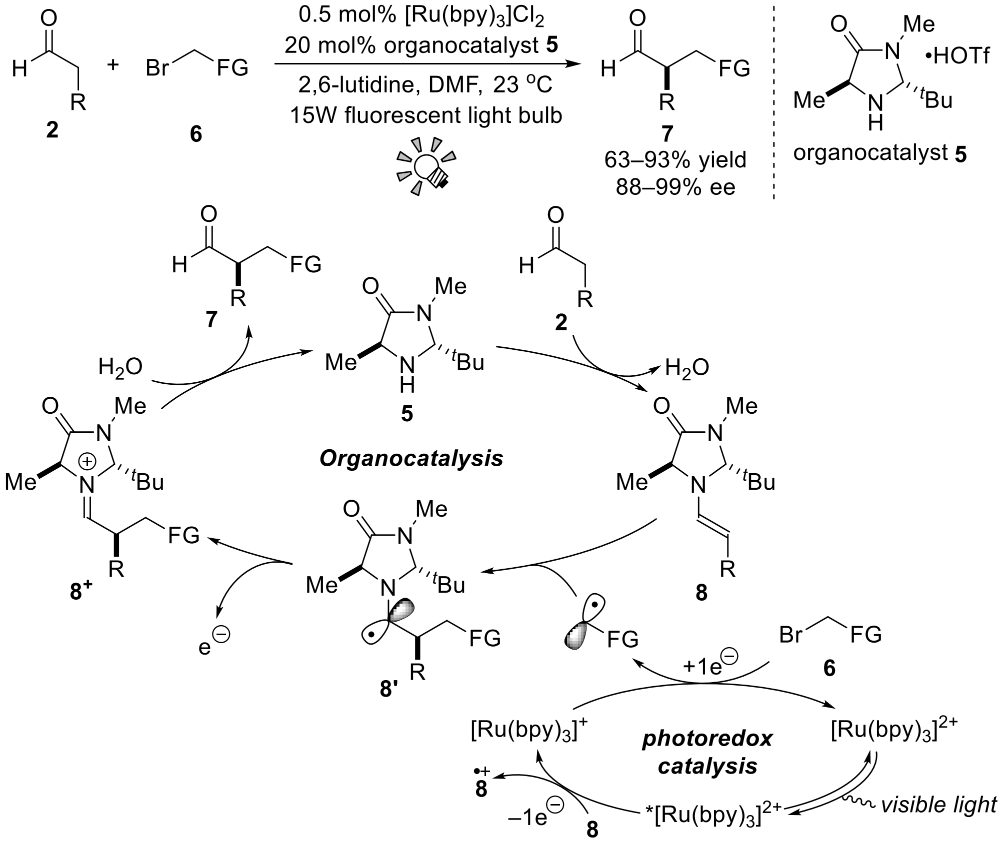


Scheme 1.12. Photocatalytic α-Oxyamination of Aldehydes.

Our group found that the reaction mixture of aldehyde **2**, 2 mol% of $[Ru(bpy)_3](PF_6)_2$, 20 mol% of morpholine **1** as a secondary amine, and radical trapping reagent, (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO), in CH_3CN under irradiation of visible light (λ > 420 nm, xenon lamp) gave the α-oxyaminated aldehyde **3** in 54–68% yields (Scheme 1.12).[15] In this reaction, morpholine **1** initially reacts with **2** to give enamine **4**, which then undergoes 1e-oxidation by $*[Ru(bpy)_3]^{2+}$. Final radical coupling of cationic radical intermediates with TEMPO, followed by hydrolysis, affords the α-oxyaminated product **3** and morpholine **1**.

1.2.4.2.2 Asymmetric α-Alkylation of Aldehydes (MacMillan)

While our group was conducting above-mentioned studies, MacMillan and Nicewicz published an elusive asymmetric intermolecular α-alkylation of aldehydes by elegantly merging Ru photoredox catalysis with chiral amine organocatalysis.[16] The reaction mechanism proposed for the synergistic catalysis is illustrated in Scheme 1.13.

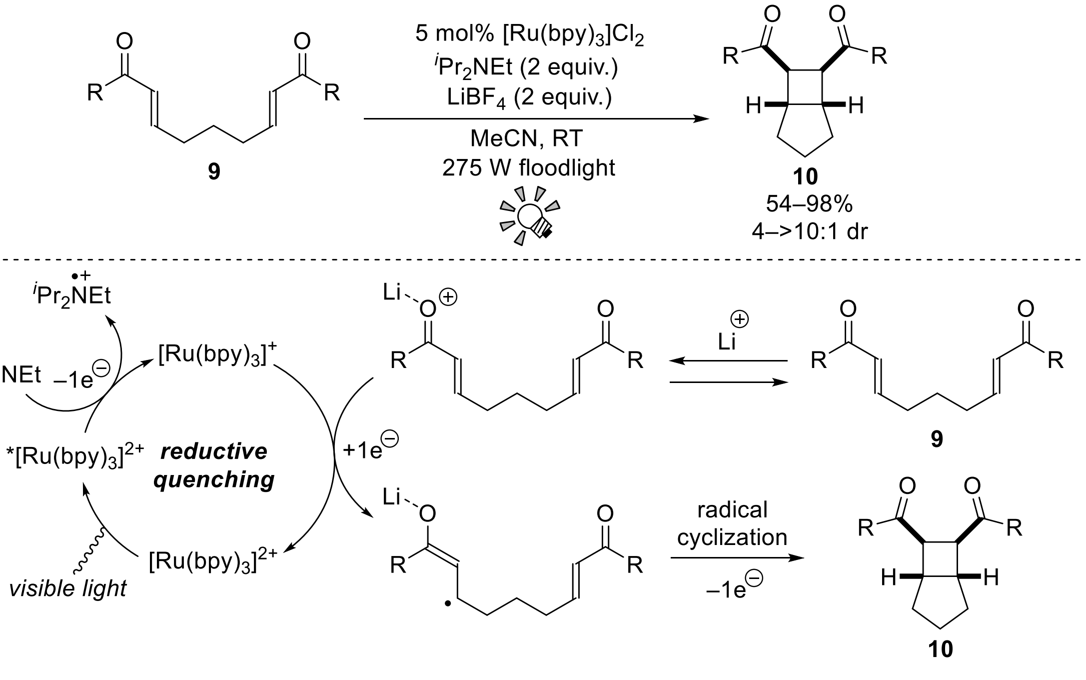


Scheme 1.13. Asymmetric α-Alkylation of Aldehydes with alkylhalides.

At the initial stage, the Ru catalyst, $[Ru(bpy)_3]^{2+}$, is excited by irradiation with a 15 W fluorescent light bulb to form the excited species, $*[Ru(bpy)_3]^{2+}$, which is reduced by enamine **8** derived from the reaction of the secondary chiral amine catalyst **5** with aldehyde **2**. The resulting strong reductant, $[Ru(bpy)_3]^{+}$,undergoes SET to alkyl halides **6**, leading to formation of alkyl radical and regeneration of the ground state, $[Ru(bpy)_3]^{2+}$. The alkyl radical reacts with preformed enamine **8** to give the C–C coupled radical intermediate **8'**. The 1e-oxidation of radical intermediate **8'** by the photoexcited Ru species affords the inimium intermediate **8**$^{+}$. Subsequent hydrolysis produces the enantioenriched α-alkylated aldehyde product **7** and regenerates the organocatalyst **5**. It is noteworthy that the present catalytic system can allow us an easy access to various optically active α-alkylated aldehydes **7** in high yields with excellent enantioselectivity.

1.2.4.2.3 [2+2] Photocycloaddition Reaction (Yoon)

In 2008, Yoon and co-workers reported photoredox-catalyzed intramolecular [2+2] cycloaddition of bisenones **9** (Scheme 1.14).[17a]



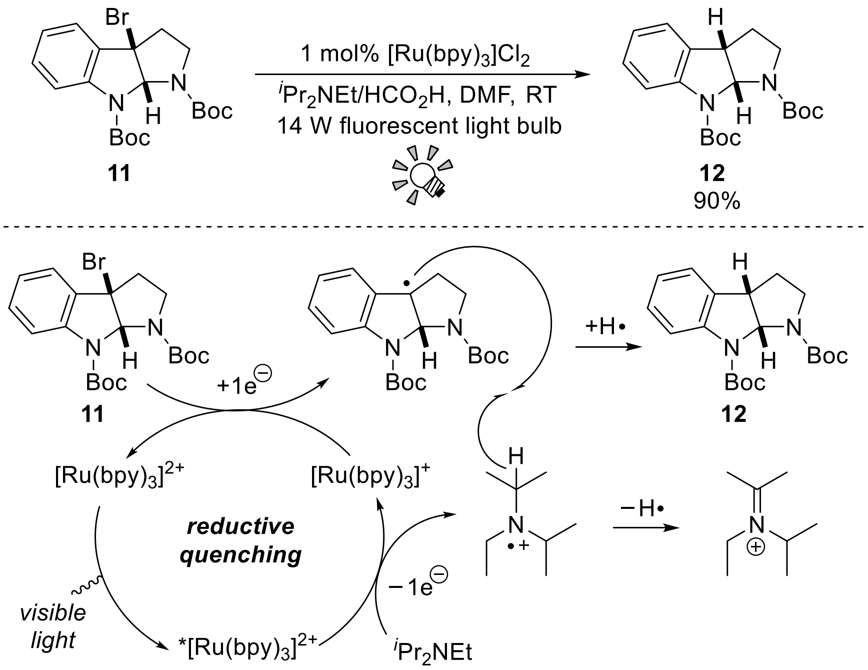
Scheme 1.14. Photocatalytic [2+2] Cycloaddition of Bisenones.

Irradiation of bisenones **9** with visible light in the presence of 5 mol% of [Ru(bpy)$_3$]Cl$_2$, ^{i}Pr$_2$NEt as an electron donor, and LiBF$_4$ as a Lewis acid gave the [2+2] cycloaddition adducts **10** in high yield with excellent diastereoselectivity.

In this reaction, addition of ^{i}Pr$_2$NEt and LiBF$_4$ is essential to produce a strong reductant, [Ru(bpy)$_3$]$^+$, from the photoactivated species, *[Ru(bpy)$_3$]$^{2+}$, and lower the LUMO level of **9**, respectively. Analogous [2+2] cyclizations by high-energy UV photolysis and electrochemical methods were reported, but these systems usually require special reactors. In contrast, the present photocatalytic protocol allows us to conduct the reaction by the use of usual glassware and easily available visible light. Moreover, the group of Yoon extended the present reaction to crossed intermolecular [2+2] cycloadditions of enones.[17b]

1.2.4.2.4 Tin-Free Reductive Dehalogenation of Alkylhalides (Stephenson)

In 2009, Stephenson and co-workers reported tin-free reductive dehalogenation of activated alkylhalides by photoredox catalysis (Scheme 1.15).[18a]



Scheme 1.15. Radical Reductive Dehalogenation by Photoredox Catalysis.

They found that the reaction mixture of alkyl halides **11**, 2.5 mol% of $[Ru(bpy)_3]Cl_2$, $^iPr_2NEt$ as a hydrogen donor, and HCO_2H in DMF under visible light irradiation (14W fluorescent light bulb) provided the corresponding dehalogenated product **12**. It is proposed that alkyl radicals are formed *via* 1e-reduction of alkyl halides **11** by the action of photoredox catalyst. Furthermore, related photocatalytic cyclization reactions though a tin-free generation of organic radicals were also developed.[18b]

As mentioned above, photoredox catalysts, $[Ru(bpy)_3]^{2+}$ and the relevant cyclometalated Ir complexes, can induce single-electron-transfer (SET) under visible light irradiation, generating radical species from organic electron donors and electron acceptors. This radical generation method can provide synthetically useful advantages, that is, (1) experimentation under mild conditions, and (2) operationally easy protocol. As a result, this strategy can provide a chance to explore new radical species and radical reactions. The author has been intensively working on the development of radical trifluoromethylation by photoredox catalysis. In the next section, significance of trifluoromethylation and research background will be shown.

1.3 Trifluoromethylation

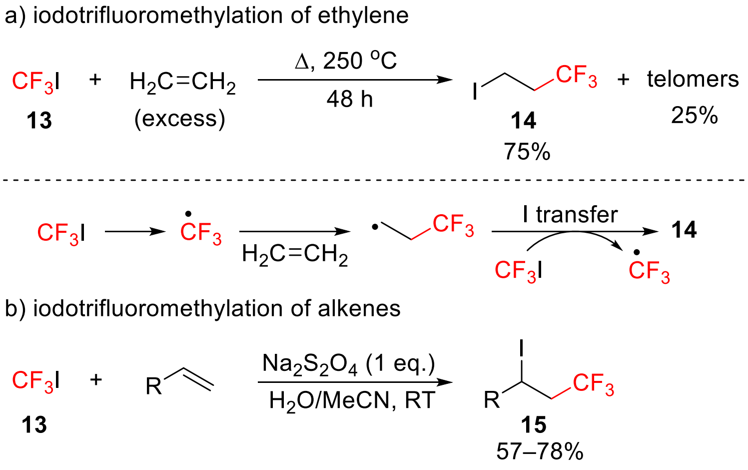
Organofluorine compounds continue to increase in importance in the pharmaceutical and agrochemical fields as well as in the materials science field.[19] In particular, trifluoromethyl (CF_3) group is considered to be a useful structural motif in many biologically active molecules because it can often influence chemical and metabolic stability, lipophilicity, and binding selectivity.[20] Thus, the development of new methodologies for highly efficient and selective incorporation of a CF_3 group into diverse skeletal structures has attracted great interest of synthetic chemists.[21] The strategies for trifluoromethylation can be classified into three types, that is, radical, nucleophilic, and electrophilic trifluoromethylation. Examples of these reactions are shown below.

1.3.1 Radical Trifluoromethylation

The CF_3 radical can be generated under oxidative, reductive, photochemical, thermal, and electrochemical conditions.[3] Thus, a wide variety of molecules has been used as precursors of the CF_3 radical. Typical radical trifluoromethylating reagents are given.

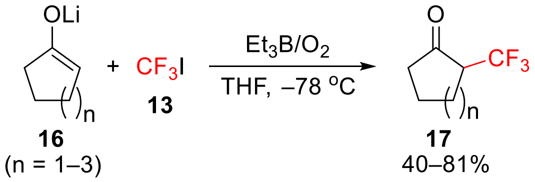
Trifluoromethyl Iodide (CF_3I)

Haszeldine reported in the late 1940s that CF_3 radical are generated from gaseous CF_3I **13** through C−I bond homolysis upon irradiation or heating.[22] In the presence of ethylene he observed the formation of 3-iodo-1,1,1-trifluoropropane (**14**) as the major product resulting from ATRA (Scheme 1.16a). Since this report, same type ATRA reaction with various radical initiating methods has been reported.[3] For example, sodium dithionate ($Na_2S_2O_4$) mediated iodotrifluoromethylation of alkenes (Scheme 1.16b).[23]



Scheme 1.16. Iodotrifluoromethylation of Alkenes with CF_3I.

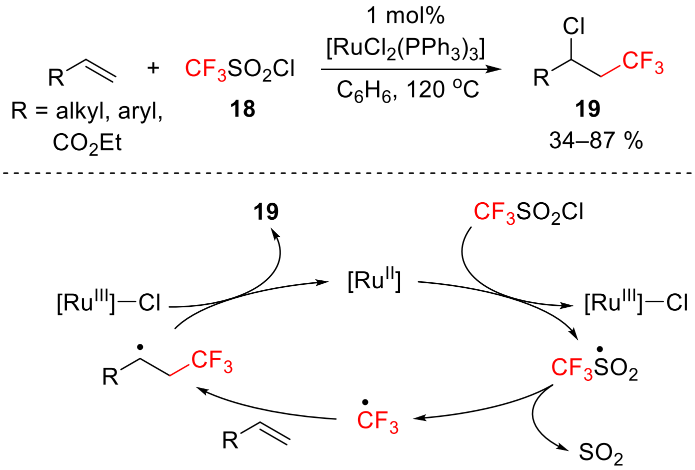
Due to electrophilic nature of the CF_3 radical, reactions with electron-rich alkenes such as enamines and silyl enol ethers have been well investigated.[24] Mikami and Itoh reported that Li enolates **16** derived from cyclic ketones undergo α-trifluoromethylation at −78 °C under Et_3B/O_2 system to give the CF_3-substituted ketones **17** (Scheme 1.17).[24c]



Scheme 1.17. Trifluoromethylation of Lithium Enolate with CF_3I.

Trifluoromethanesulfonyl Chloride (CF_3SO_2Cl)

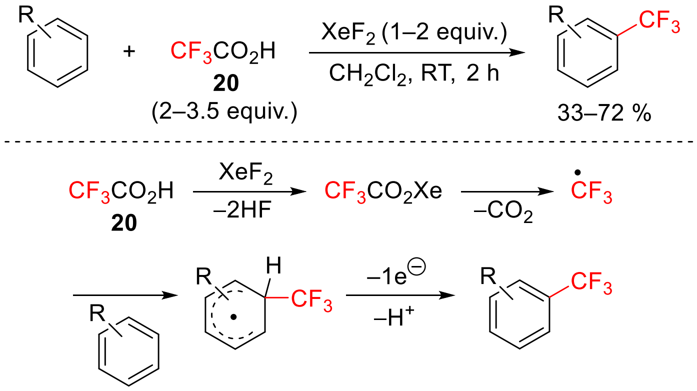
In 1991, Kamigata et al. reported ATRA reactions of alkenes with moisture sensitive trifluoromethanesulfonyl chloride (CF_3SO_2Cl, **18**) by $[RuCl_2(PPh_3)_3]$ catalyst (Scheme 1.18).[25] In these reactions, Cl atom of CF_3SO_2Cl **18** is first abstracted by $[Ru^{II}]$ complex to give CF_3SO_2 radical and $[Ru^{III}]$−Cl complex. Then, CF_3SO_2 radical undergoes elimination of SO_2 to give the CF_3 radical. Radical addition to the alkene provides radical intermediate, which abstracts Cl atom from the $[Ru^{III}]$−Cl complex to afford the product **19** and the $[Ru^{II}]$ complex.



Scheme 1.18. ATRA Reactions of Alkenes with CF_3SO_2Cl.

Trifluoroacetic Acid (CF_3CO_2H)

Oxidation of trifluoroacetic acid (CF_3CO_2H, **20**) produces the CF_3 radical. For example, xenon difluoride (XeF_2) was successfully used as a strong oxidant for generation of the radical.[26]

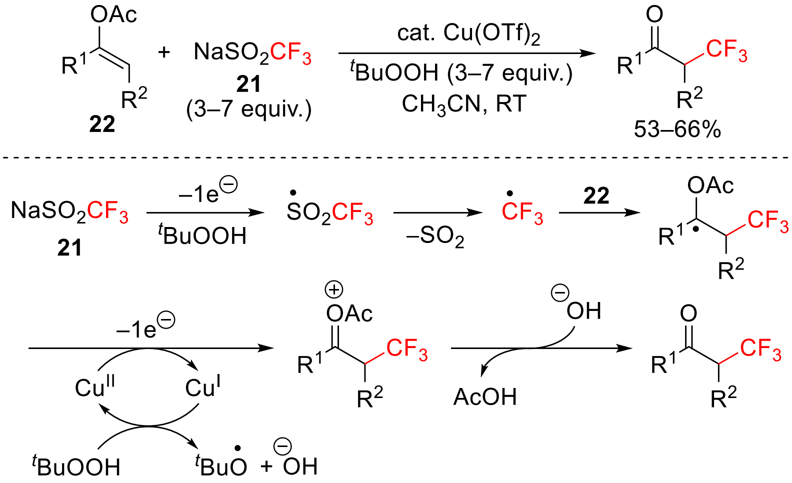


Scheme 1.19. Radical Trifluoromethylation of Arenes with CF_3CO_2H.

Various multisubstituted arenes were trifluoromethylated in moderate to good yields (Scheme 1.19). The reactions were proposed to occur *via* xenon(II) trifluoroacetate as an intermediate, which acts as precursor of the CF_3 radical.

Sodium Trifluoromethanesulfinate ($NaSO_2CF_3$, Langlois Reagent)

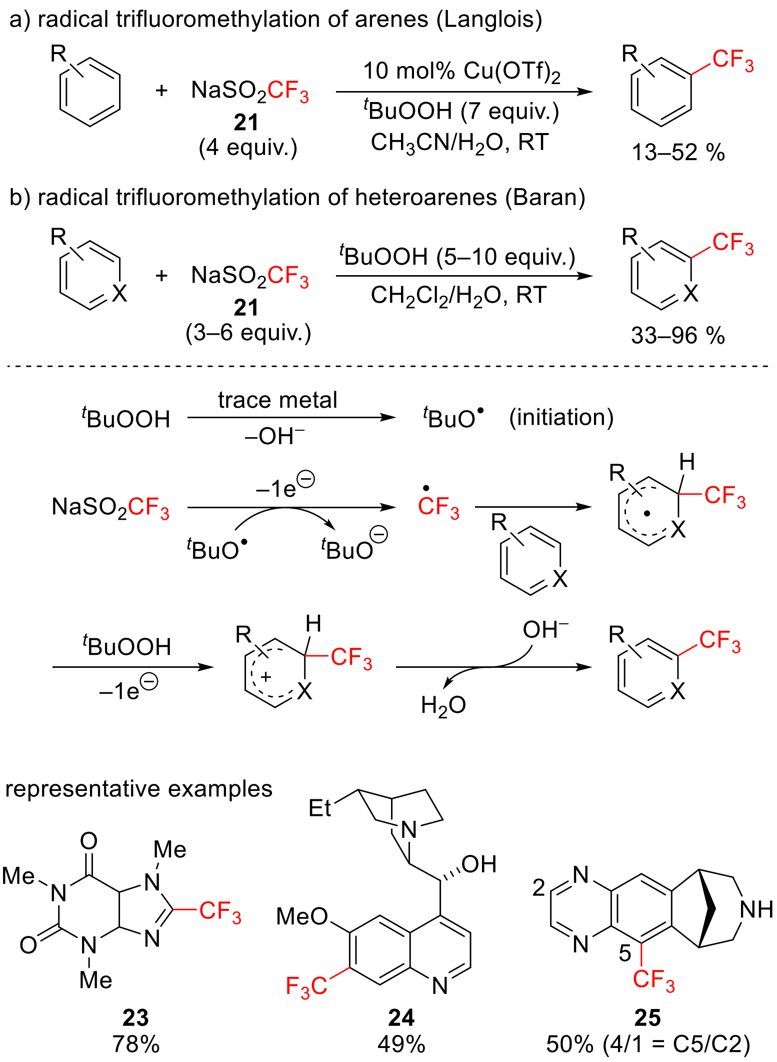
In 1992, Langlois and co-workers reported that radical trifluoromethylation of enol acetates **22** using air and moisture stable sodium trifluoromethanesulfinate ($NaSO_2CF_3$, **21**) as the CF_3 radical source (Scheme 1.20).[27a]



Scheme 1.20. Radical Trifluoromethylation of Enol Acetates with $NaSO_2CF_3$.

The CF_3 radical is generated by oxidation reaction of $NaSO_2CF_3$ **21** with a catalytic amount of $Cu(OTf)_2$ (Tf = SO_2CF_3) in the presence of an excess amount of ^{t}BuOOH as a stoichiometric oxidant. Next, the CF_3 radical adds to the enol acetate **22** to provide radical intermediate. Cu^{II} species further oxidize the radical intermediate to give the oxonium, which undergoes hydrolysis to afford the CF_3-substituted ketone.

This oxidative radical trifluoromethylation methodology can also be applicable to aromatic compounds. CF_3-substituted arenes were obtained in 13−52% yields (Scheme 1.21a).[27b]



Scheme 1.21. Radical Trifluoromethylation of Arenes and Heteroarenes with CF_3SO_2Na.

Baran et al. recently established similar type of radical trifluoromethylation of heteroarenes (Scheme 1.21b).[28a] These reactions proceeded in the absence of any transition metal. The radical reactions were proposed to initiate by the reaction of trace amount of metal in $NaSO_2CF_3$ **21** and ^{t}BuOOH. Various pyridines, pyrimidines, thiazols, and uracils were successfully trifluoromethylated in moderate to good yields (33−96%). Notably, Baran proved this protocol can provide a *late-stage trifluoromethylation* of biologically active molecules and drugs. Representative examples are given in Scheme 1.21. The CF_3-substituted caffein **23**, quinine **24**, and varenicline **25** are isolated in moderate to good yields. Based on these results, the present radical functionalization can be applicable to the rapid synthesis of candidate drugs and agrochemicals.

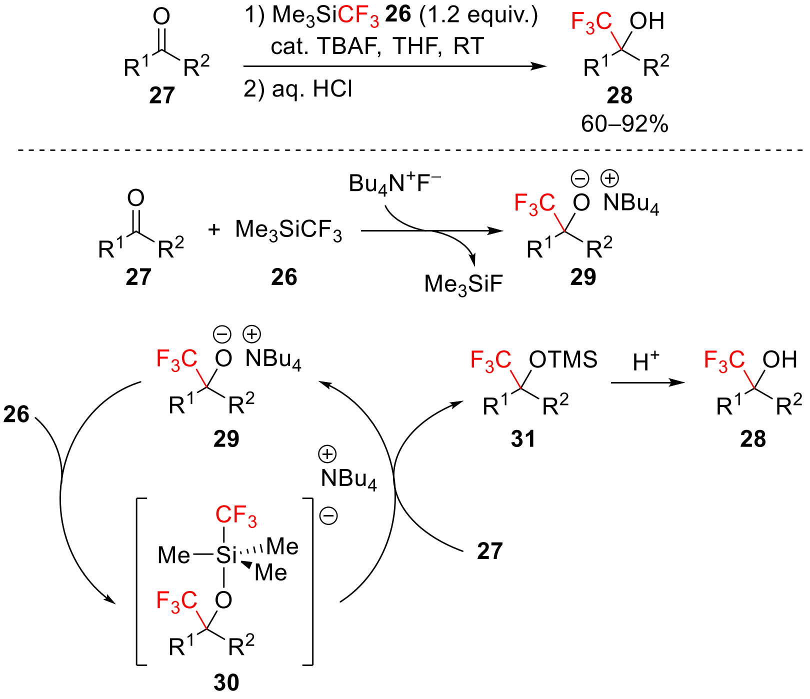
More recently, Baran and co-workers reported related radical fluoroalkylation of heteroarenes with zinc fluoroalkylmethanesufinate ($(RfSO_2)_2Zn$, Baran's reagents).[28b,c] Further development of new fluoroalkylating reagents and its radical reactions are continuing.

1.3.2 Nucleophilic Trifluoromethylation

As shown in Scheme 1.1 of the section 1.1, the liberated CF_3 anion is unstable and easily decomposes to the corresponding difluorocarbene. In 1984, Ruppert et al. found that trifluoromethylorganosilane compounds become useful nucleophilic trifluoromethylating reagents.[29] Trifluoromethyltrimethylsilane, Me_3SiCF_3 (Ruppert's reagent, **26**), is currently the most commonly used as a nucleophilic trifluoromethylating reagent in addition reactions and cross-coupling reactions. Typical examples are shown below.

Trifluoromethyloganosilane (R_3SiCF_3, Ruppert's reagents)

In 1989, Prakash et al. reported 1,2-addition reactions of carbonyl compounds with Me_3SiCF_3 **26** in the presence of tetra-*n*-butylammonium fluoride (TBAF) (Scheme 1.22).[30] Addition of catalytic amount of TBAF to the reaction mixture of a carbonyl compound **27** and Me_3SiCF_3 **26** induces the formation of Me_3SiF and alkoxide adduct **29**, stabilized by the tetrabutylammonium cation. The alkoxide **29** reacts with Me_3SiCF_3 **26** to afford the pentavalent Si complex **30** followed by the transfer of the CF_3 group to another carbonyl compounds **27**, generating the CF_3-substituted ether **31**.



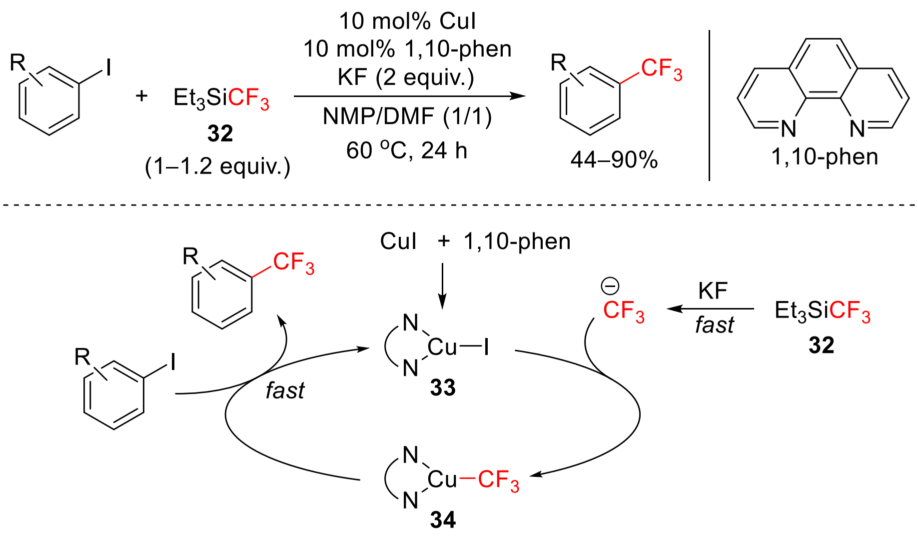
Scheme 1.22. Nucleophilic Trifluoromethylation of Ketones with Me_3SiCF_3.

This method can be applied to asymmetric version. Indeed, a variety of enantioselective nucleophilic trifluoromethylation using various chiral ammonium salts have been developed.[31]

Copper–Trifluoromethyl (Cu–CF_3) Species

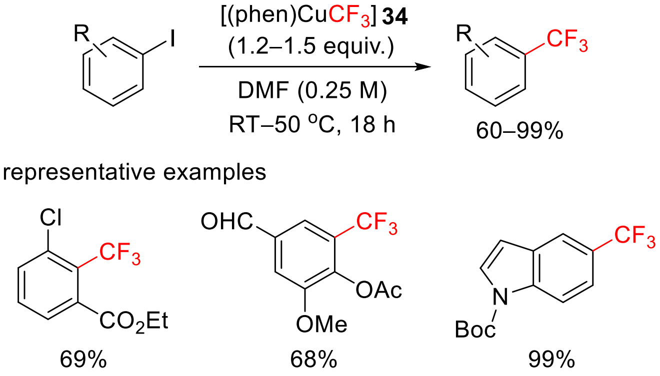
Amii et al. reported copper-catalyzed nucleophilic trifluoromethylation of aryl iodides with trifluoromethyltriethylsilane (Et_3SiCF_3, **32**) (Scheme 1.23).[32] In this reaction, the use of 1,10-phenanthroline (phen) ligand is a key because the diimine ligand can provide following effects, (1) stabilization of the copper complex **33** and (2) enhancement of nucleophilicity of [(phen)$CuCF_3$] **34**. These effects support the reaction with the unstable

CF_3 anion.



Scheme 1.23. Copper-Catalyzed Trifluoromethylation of Aryl Iodides.

Since this report, many studies for regioselective metal-mediated and -catalyzed C_{aryl}-CF_3 bonds formation have been developed.[21] For example, Hartwig and co-workers reported isolation of [(phen)$CuCF_3$] **34** and its trifluoromethylation of aryl iodides (Scheme 1.24).[33]



Scheme 1.24. Trifluoromethylation of Aryl Iodides Using [(phen)$CuCF_3$].

The method of Hartwig and co-workers is the most functional group tolerant and allows the trifluoromethylation of electron-poor, electron-rich, and even *ortho*, *ortho*-disubstituted arenes, which were not shown in Amii's report. Now, this copper salt **34** is commercially available from Aldrich.

At the same time, Grushin et al. reported that similar nucleophilic Cu–CF_3 complex is generated from the reaction of CuCl with cheap CF_3H in the presence of a base.[34]

As mentioned above, there are a great number of reports on radical and nucleophilic trifluoromethylation reactions with a various trifluoromethylating reagents. In the case of radical trifluoromethylation, most reactions are conducted with operationally careful gaseous CF_3I **13** and toxic and moisture sensitive CF_3SO_2Cl **18** under harsh reaction conditions. Langlois salt, $NaSO_2CF_3$ **21**, is an ideal CF_3 source, but the reagent shows high oxidation potential ($E_{1/2}$ = +1.46 V vs. Cp_2Fe)[35] and poor solubility into organic solvents. Thus, hazardous peroxides were generally used as shown in Scheme 1.20 and 1.21. Ruppert's reagent **26** is commercially available and air-stable nucleophilic CF_3 reagents, but a fluoride anion source is required.

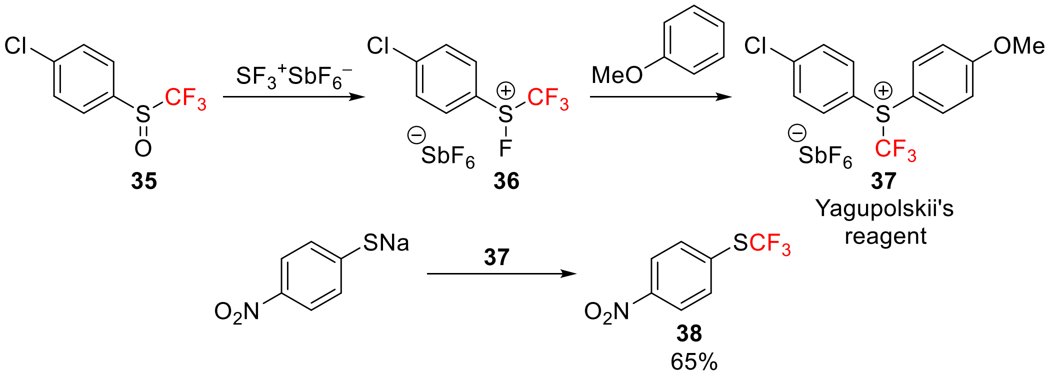
In contrast, electrophilic trifluoromethylating reagents, which will be referred to in the next section, have attracted attention because the reagents are easy to handle in terms of shelf-stable solid chemicals at room temperature.

1.3.3 Electrophilic Trifluoromethylation

The CF_3 cation ($^+CF_3$) is very stable species but their production from trifluromethylated compounds is difficult. Thus, synthesis of an equivalent of the $^+CF_3$ has been studied. Yagupolskii first reported that new electrophilic trifluoromethylating reagents through the introduction of the CF_3 group on the sulfur atom. Since of this report, Umemoto et al., Togni et al., and Shibata et al. independently developed new electrophilic trifluoromethylating reagents. Their seminal reports on synthesis of their $^+CF_3$ reagents and reactions using their reagents are given below.

S-(Trifluoromethyl)diarylsulfonium Salt (Yagupolskii's Reagent)

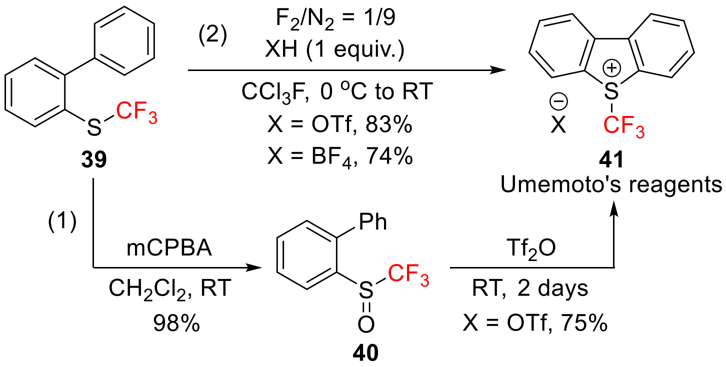
In 1984, Yagupolskii and co-workers successfully achieved development of first electrophilic trifluoromethylating reagent (Yagupolskii's reagent, **37**).[36] This reagent was obtained by treatment of aryltrifluoromethyl sulfoxide **35** with $SF_3^+SbF_6^-$ and subsequent reaction of the fluoro(trifluoromethyl)arylsulfonium salt **36** with *p*-methoxybenzene. The reagent **37** reacted with sodium *p*-nitro-thiophenolate to give the corresponding trifluoromethyl sulfide **38** in 65% yield (Scheme 1.25).



Scheme 1.25. Preparation of Yagupolskii's Reagent and Its Reaction with a Thiophenolate.

S-(Trifluoromethyl)dibenzothiophenium Salts (Umemoto's Reagents)

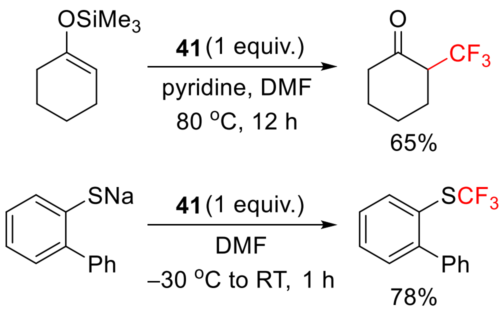
In 1990, Umemoto et al. developed new electrophilic trifluoromethylating reagents i.e., *S*-(trifluoromethyl)dibenzothiophenium salts (Umemoto's reagents, **41**).[37]



Scheme 1.26. Preparation of Umemoto's Reagents.

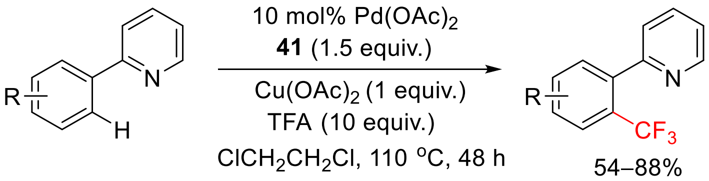
The reagents were synthesized by two routes, that is, (1) oxidation of starting sulfide **39** with *m*-chloroperbenzoic acid (mCPBA) followed by cyclization of the corresponding sulfoxide **40** with triflic anhydride and (2) direct fluorination with 10% F_2/N_2 in the presence of one equivalent of triflic acid or HBF_4 (Scheme 1.26). Umemoto's reagents **41** are air and moisture stable under ambient conditions.

Various nucleophiles such as carboanions, enamines, silyl enol ethers, phenols, anilines, and thiolates react with Umemoto's reagent **41** to afford the corresponding CF_3-substituted products. Selected examples are shown in Scheme 1.27.



Scheme 1.27. Electrophilic Trifluoromethylation with Umemoto's Reagent.

In 2009, Yu and co-workers reported palladium-catalyzed *ortho*-selective trifluoromethylation of heterocycle-substituted arenes with Umemoto's reagent **41** (Scheme 1.28).[38a] Various *ortho*-trifluoromethylated heteroaromatic compounds were obtained in good yields. The C−H trifluoromethylation reactions were proposed to occur through Pd(II)/Pd(IV) pathway. More recently, Yu et al. published related *ortho*-selective trifluoromethylation of arylamides with **41**.[38b]



Scheme 1.28. Pd-Catalyzed *Ortho*-Selective Trifluoromethylation.

Hypervalent Iodine(III)−CF_3 Reagents

Initial attempts by Yagupolskii and Umemoto to synthesize iodonium salts with the CF_3

group were unsuccessful. Iodonium salts including *p*-tolylperfluoroalkyliodonium chloride and perfluoroalkylphenyliodonium triflates (FITS) (Figure 1.5) have been reported as perfluoroalkylating agents, however, the corresponding trifluoromethylating reagents are unstable.[39]

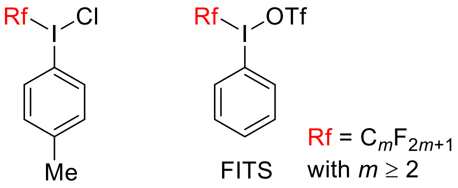
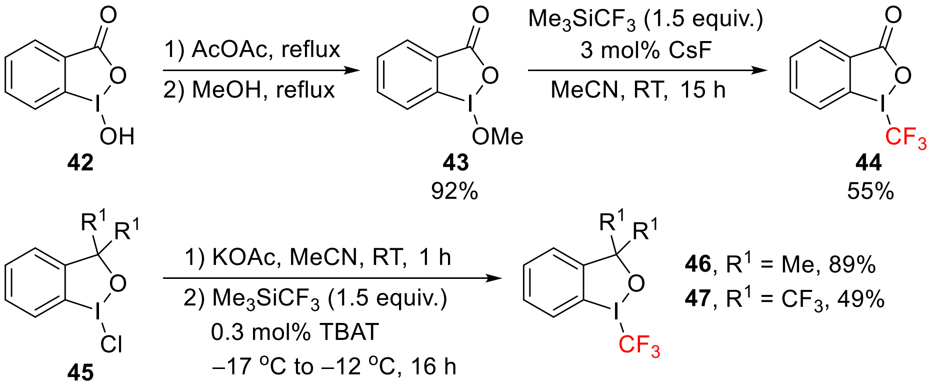


Figure 1.5. Perfluoroalkyliodonium Salts.

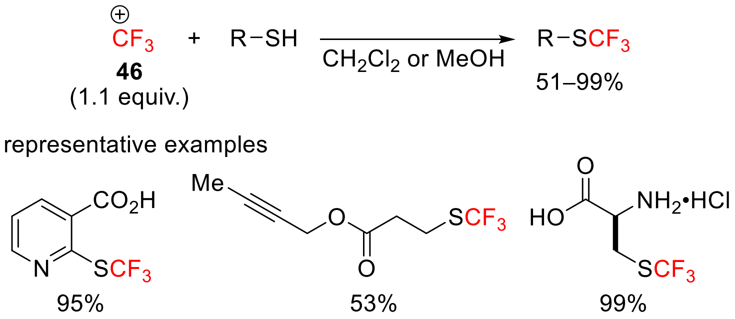
In 2006, Togni and co-workers reported a new family of hypervalent iodine compounds in which the CF_3 group is bonded to the iodine atom.[40]



Scheme 1.29. Preparation of Togni's Reagents.

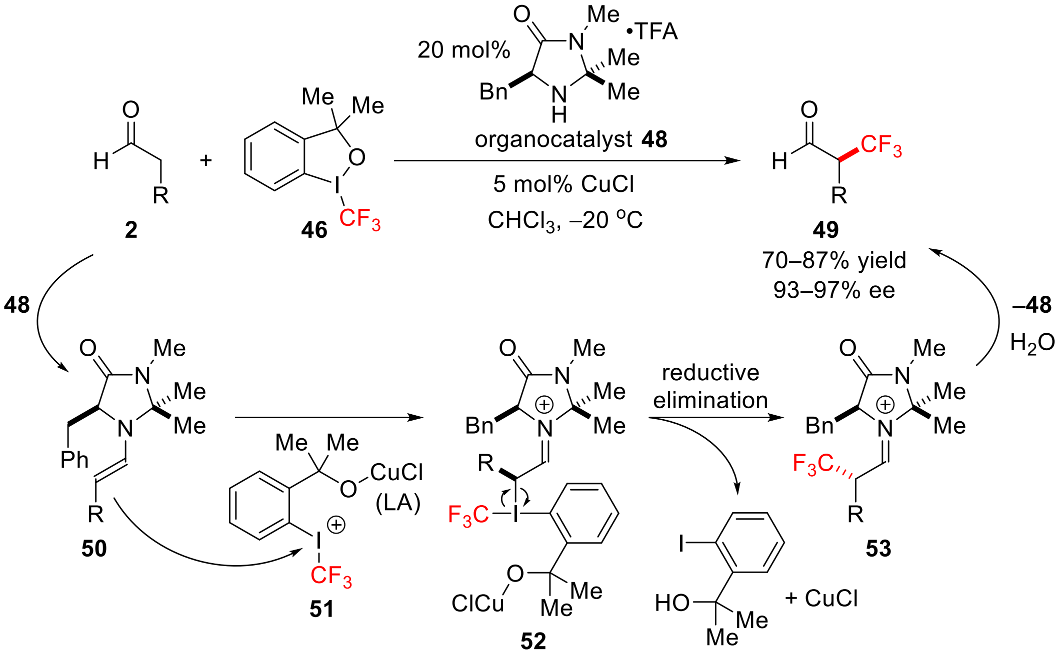
The reaction of 1-methoxy-1,2-benziodoxol-3-(*1H*)-one **43** with Me_3SiCF_3 (Ruppert's reagent) in the presence of a catalytic amount of CsF in CH_3CN at room temperature gave 1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one **44** (Togni's reagent) in 55% yield (Scheme 1.29).[40a] Related reagents **46** and **47** were preferentially obtained in one-pot procedure.[40b] These reagents are shelf-stable, non-explosive under ambient conditions.

Togni and co-workers also showed that the Togni's reagent **46** reacts with both aromatic and aliphatic thiols to produce the corresponding S trifluoromethylated products in good yields without loss of functional groups (Scheme 1.30).



Scheme 1.30. Electrophilic Trifluoromethylation of Thiols Using Togni’s Reagent.

In 2010, MacMillan et al. established that asymmetric electrophilic α-trifluoromethylation of aldehydes by a combination of organocatalyst **48** and Togni’s reagent **46** (Scheme 1.31).[41]

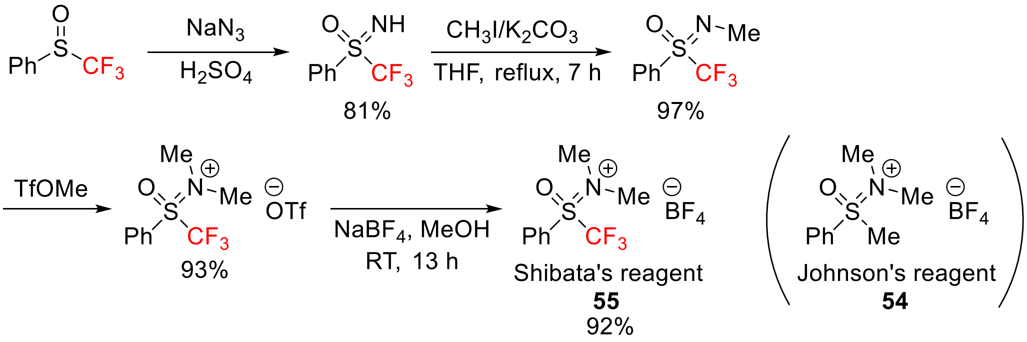


Scheme 1.31. Organocatalytic α-Trifluoromethylation of Aldehydes.

A catalytic amount of CuCl acts as a Lewis acid to activate **46**. Initially, reaction of organocatalyst **48** with an aldehyde **2** generates a chiral enamine **50**, which reacts with an activated electrophilic iodonium reagent **51** to produce λ^3-iodane species **52**. Finally, reductive elimination with stereoretentive alkyl transfer and followed by hydrolysis afford the enantioenriched α-trifluoromethylated aldehyde **49**.

Fluorinated Johnson's Type Reagent (Shibata's Reagent)

In 2008, a novel type of electrophilic trifluoromethylating agent, a trifluoro analog of Johnson's methyl-transfer reagent **54**, was synthesized by Shibata and co-workers.[42] The synthetic route to the sulfoximinium salt **55** starts from phenyl trifluoromethyl sulfoxide as illustrated in Scheme 1.32. The reagent **55** can react with many nucleophiles with similar to above-mentioned electrophilic CF_3 sources.



Scheme 1.32. Preparation of Shibata's Reagent.

As explained above, useful electrophilic trifluoromethylating reagents were successfully synthesized by Yagpolskii, Umemoto, Togni, and Shibata. Their reagents are air and moisture stable under ambient conditions. Umemoto's reagents and Togni's reagents are most popular reagents because they are commercially available from Aldrich and TCI. The chemistry of the $^+CF_3$ reagents is still new. In addition, trifluoromethylation of diverse molecular architectures using these reagents have not been studied sufficiently. In particular, trifluoromethylation of simple alkenes was an unexplored research field.

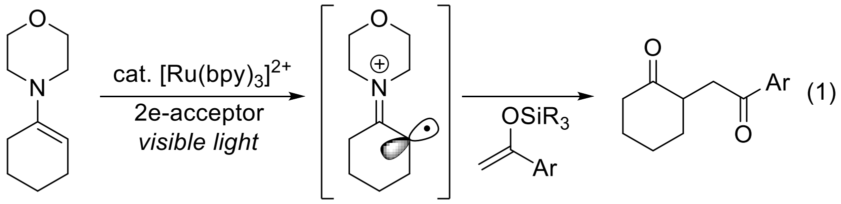
1.4 Survey of This Thesis

Both radical reaction and photoreaction are attractive synthetic tools in terms of different transformation from ionic and thermal reactions. But, people usually hesitate to use them because of their difficulties which have been described in this chapter. The author believes that development of efficient synthetic protocol under mild conditions allows us to access new reactions and molecules. Thus, the author paid the attention to develop photoredox-catalyzed radical reaction driven by visible light as a mild stimulus.

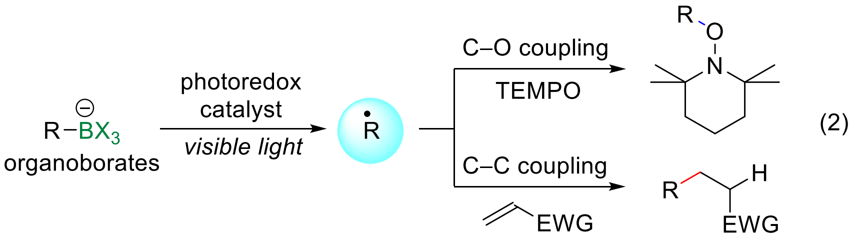
So far, several photoredox catalyzed reactions have been developed by above-mentioned chemists and our group. However, when the author started the study, carbon-centered radical sources of photoredox catalysts were very limited. Therefore, the author focused on exploring of useful radical precursors and their reactions. In particular, the author aspired for *redox neutral* reactions using olefins.

In this thesis, the author has developed various photocatalytic reactions with enamines, organoborates, and electrophilic trifluoromethylating reagents as carbon-centered radical precursors. The experimental details are given in the following seven Chapters.

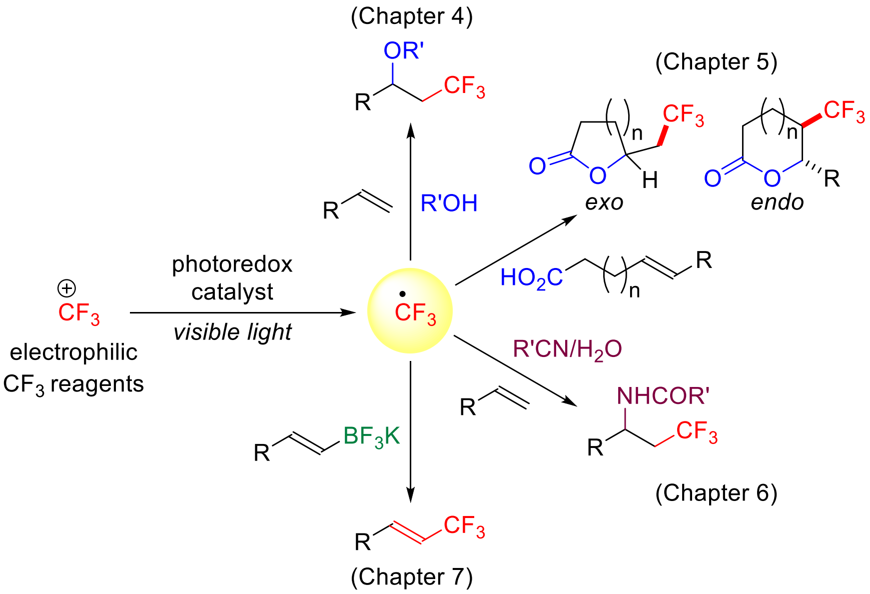
In Chapter 2, the author shows oxidative coupling of enamines with silyl enol ethers *via* a two-electron oxidation process (eq. 1).



In chapter 3, results of radical C−O and C−C bond formation reactions with organoborates are summarized (eq. 2).



In Chapters 4–7, radical trifluoromethylation reactions of alkenes with electrophilic trifluoromethylating reagents are described (Scheme 1.33).



Scheme 1.33. Photoredox-Catalyzed Radical Trifluoromethylation with $^{+}CF_3$ Reagents.

Finally, summary and outlook are shown in Chapter 8.

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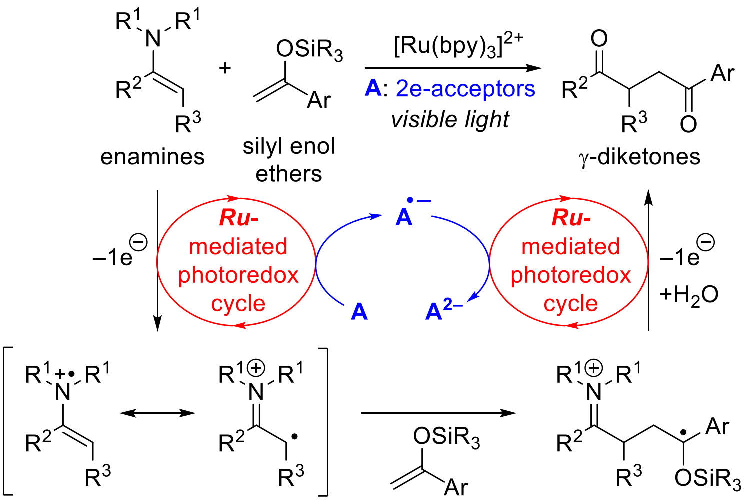
Chapter 2

Visible-Light-Driven Synthesis of γ-Diketones *via* Oxidative Coupling of Enamines with Silyl Enol Ethers Catalyzed by $[Ru(bpy)_3]^{2+}$

ABSTRACT: A photosensitizer $[Ru(bpy)_3]^{2+}$ catalyzes oxidative coupling reaction of enamines with silyl enol ethers under visible light irradiation by a Xe lamp or sunlight to produce γ-diketones. A 2e-oxidation process involved in this reaction is achieved by a combination of the photoexcited $[Ru(bpy)_3]^{2+}$ species and duroquinone, a 2e-acceptor.

2.1 Introduction

Photoexcited state of photoredox catalyst, e.g. *$[Ru(bpy)_3]^{2+}$, can oxidize electron-rich tertiary amines under visible light irradiation.[1,2] Thus, several useful works of photoredox-catalyzed functionalization of amines have been developed.[2] On the other hand, our group also previously reported photocatalytic oxyamination of enamines using the $[Ru(bpy)_3]^{2+}$ catalyst and proposed that photoactivated $[Ru(bpy)_3]^{2+}$ species can serve as a 1e-oxidant to produce the corresponding cationic radical intermediates *via* the oxidation of enamines.[3] As an extension of this single electron transfer (SET) catalysis, the author expects that $[Ru(bpy)_3]^{2+}$ may catalyze multielectron transfer processes including 2e-oxidation reactions such as oxidative coupling of enamines with silyl enol ethers[4] in the presence of a suitable electron acceptor **A** as shown in Scheme 2.1. A conceptional 2e-redox system, which is based on the SET photoredox cycles mediated by $[Ru(bpy)_3]^{2+}$, involves the consecutive electron relays from enamines and radical intermediates to 2e-acceptor **A**.



Scheme 2.1. Concept of a Photocatalytic 2e-Redox Process.

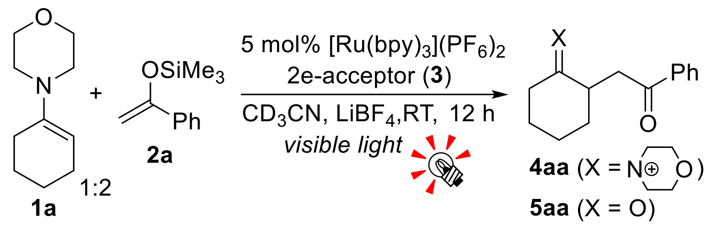
In this chapter, the author describes that the photochemical 2e-redox process is achieved by a combination of the Ru photocatalyst and a 2e-acceptor under visible light irradiation.

Notably, this protocol allows sunlight-driven catalytic C–C bond formation *via* the oxidation of enamines.

2.2 Optimization of Coupling Reaction of Enamine with Silyl Enol Ether

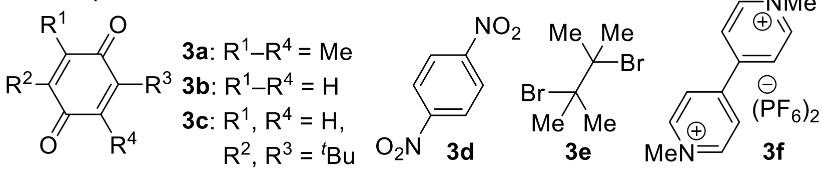
The author examined a variety of organic 2e-acceptors (**3a**–**f**) for the oxidative coupling of enamine **1a** with an excess amount of silyl enol ether **2a** (2 equiv.) in the presence of [Ru(bpy)$_3$](PF$_6$)$_2$ (5 mol%) under visible light irradiation (a Xe lamp: λ > 420 nm) (Table 2.1).

Table 2.1. Optimization Studies.



Entry	2e-acceptor **3** (molar ratio: **3**/**1a**)	LiBF$_4$/mol%	Yield of **4aa**/%[a]
1	**3a** (1.0)	—	22
2	**3b** (1.0)	—	0
3	**3c** (1.0)	—	0
4	**3d** (1.0)	—	8
5	**3e** (1.0)	—	trace
6	**3f** (1.0)	—	trace
7	**3a** (1.0)	30	67
8	**3a (1.2)**	**30**	**77(67[b])**
9	**3a** (1.2)	15	48
10	**3a** (1.2)	50	38
11[c]	**3a** (1.2)	30	0
12[d]	**3a** (1.2)	30	0

2e-acceptor **3**:



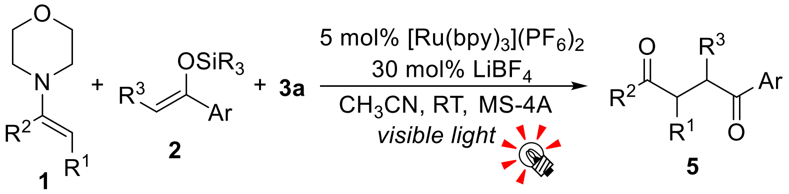
Reactions were conducted in degassed CD$_3$CN (0.1 M) solutions at room temperature for 12 h under visible light irradiation by a Xe lamp with a cut-off filter (λ > 420 nm). [a] Determined by ^{1}H NMR using 1,4-dimethoxybenzene as an internal standard. [b] Isolated yield for **5aa**. [c] In the absence of [Ru(bpy)$_3$]$^{2+}$. [d] In the dark.

As a result, the photoreaction in the presence of duroquinone **3a** gave the corresponding C–C coupled iminium ion **4aa** in 22% NMR yield (entry 1 in Table 2.1).[5] Other typical 2e-acceptors turned out to be ineffective (entries 2–6). Furthermore, addition of $LiBF_4$ (30 mol%) improved the yield of **4aa** dramatically (entry 7). Under these conditions, all signals of enamine **1a** disappeared in a ^{1}H NMR experiment (see Figure S2.1 in Experimental Section). Addition of a slight excess of **3a** to **1a** afforded **4aa** in the highest yield (entry 8).[6] Then, γ-diketone **5aa** was isolated after hydrolytic workup of the reaction mixture. Addition of MS-4A provided the product in a slightly higher isolated yield in a preparative Schlenk-tube experiment. $LiBF_4$ should act as a Lewis acid to activate acceptor **3a**, accelerating the electron transfer.[7] In this reaction, it was found that the amount of $LiBF_4$ is important for the efficiency and selectivity. A smaller amount of $LiBF_4$ was not enough to convert all **1a** (entry 9). A larger amount of $LiBF_4$ gave unidentified products (entry 10). The reaction didn't proceed at all either in the absence of Ru photocatalyst or in the dark (entries 11 and 12), suggesting that a photoexcited species of $[Ru(bpy)_3]^{2+}$ is involved in this reaction.

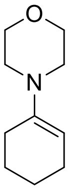
2.3 Exploration of Reaction Scope

The scope and limitations of the reaction are summarized in Table 2.2. First of all, we investigated the reaction of enamines (**1a**−**1f**) with silyl enol ether **2a**. As a result, the structure of enamines turned out to be crucial. 1-Morpholino-1-cyclopentene **1b**, 1-morpholino-1-cycloheptene **1c** and 2-morpholino-3,3-dimethylbutene **1d** gave complicated mixtures of products (entries 2−4 in Table 2.2). In contrast, 1-morpholino-1-cyclohexene derivatives **1d** and **1e** afforded the corresponding γ-diketones **5ea** and **5fa** in 54% and 50% yields, respectively (entries 5 and 6). Next, the coupling reactions of enamine **1a** with olefins **2** bearing various functional groups were investigated.

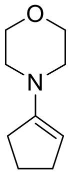
Table 2.2. Ru-Catalyzed Coupling Reaction of **1** with **2**.



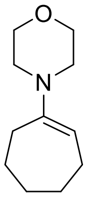
enamine **1**:



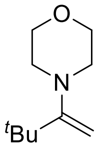
1a



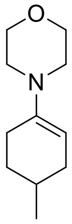
1b



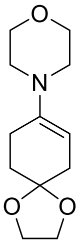
1c



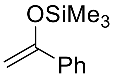
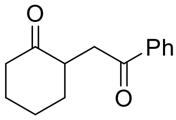
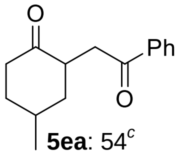
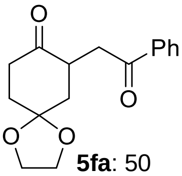
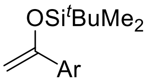
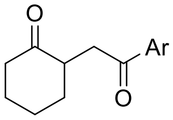
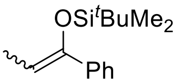
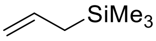
1d



1e



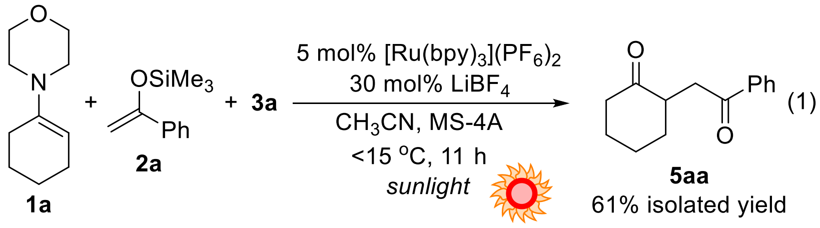
1f

Entry	Enamine **1**	Olefin **2**	Isolated yield for γ-diketone **5**/%
1	**1a**	 **2a**	 **5aa**: 67
2	**1b**	**2a**	—[a]
3	**1c**	**2a**	—[a]
4	**1d**	**2a**	—[a]
5[b]	**1e**	**2a**	 **5ea**: 54[c]
6[b]	**1f**	**2a**	 **5fa**: 50
7	**1a**	 **2b**: Ar = 4-$CH_3C_6H_4$	 **5ab**: 69
8	**1a**	**2c**: Ar = 4-$CH_3OC_6H_4$	**5ac**: 63
9	**1a**	**2d**: Ar = 4-FC_6H_4	**5ad**: 19
10	**1a**	**2e**: Ar = 4-BrC_6H_4	**5ae**: 33
11	**1a**	**2f**: Ar = 4-$NO_2C_6H_4$	**5af**: 0
12	**1a**	**2g**: Ar = 2-Furyl	**5ag**: 55
13	**1a**	**2h**: Ar = 2-Thienyl	**5ah**: 58
14	**1a**	**2i**: Ar = 4-PMBOC_6H_4	**5ai**: 52
15	**1a**	 **2j**	**5aj**: 0
16	**1a**	 **2k**	**5ak**: 0

Reactions were conducted in degassed CH_3CN (0.1 M) solutions at room temperature for 12 h under visible light irradiation. Yield of isolated product after hydrolysis. [a] Complicated product mixture. [b] Reaction mixture was irradiated by visible light for 5 h. [c] dr = 2.5:1. PMB = *p*-methoxybenzyl.

Reactions of the silyl enol ethers with electron-donating substituents on the benzene ring (**2b**,**c**) (entries 7 and 8) and heterocyclic aromatics (**2g**,**h**) smoothly proceeded (entries 12 and 13). However, substrates with electron-withdrawing groups on the benzene ring (**2d**,**e**) resulted in low yields (entries 9 and 10). In the case of the nitro derivative **2f**, the reaction didn't proceed at all (entry 11). These results are consistent with the assumption that the cationic radical formed from enamine **1** reacts with electron-rich silyl enol ethers. In addition, 1-siloxy-1-phenylpropene **2j** with the methyl group at the reaction site and allyltrimethylsilane **2k** didn't react at all (entries 15 and 16). Interestingly, silyl enol ether bearing a *p*-methoxybenzyl (PMB) ether protecting group (**2i**), which could be removed by oxidation, gave the desired oxidative coupling product **5ai** in 52% isolated yield (entry 14).

The author attempted this photoredox catalysis under sunlight.[8] It is remarkable that sunlight efficiently induced the reaction in a manner similar to the result obtained by using a Xe lamp as the light source, even though the experiment was carried out in winter in Japan (in February 21st, 22nd, and 24th, 2012) (eq. 1).



2.4 Mechanism Studies

To gain insight into the reaction mechanism, Stern–Volmer studies on the Ru catalyst and electrochemical studies on **1a**, **2a**, and **3a** were performed (Figure 2.1 and 2.2). Notably, fluorescence from photoexcited Ru catalyst (*$[Ru(bpy)_3]^{2+}$) was not quenched by silyl enol ether **2a**. On the other hand, the ratio of fluorescence intensity (I_0/I) turned out to show first-order dependence on the concentration of enamine **1a** and duroquinone **3a**, respectively.

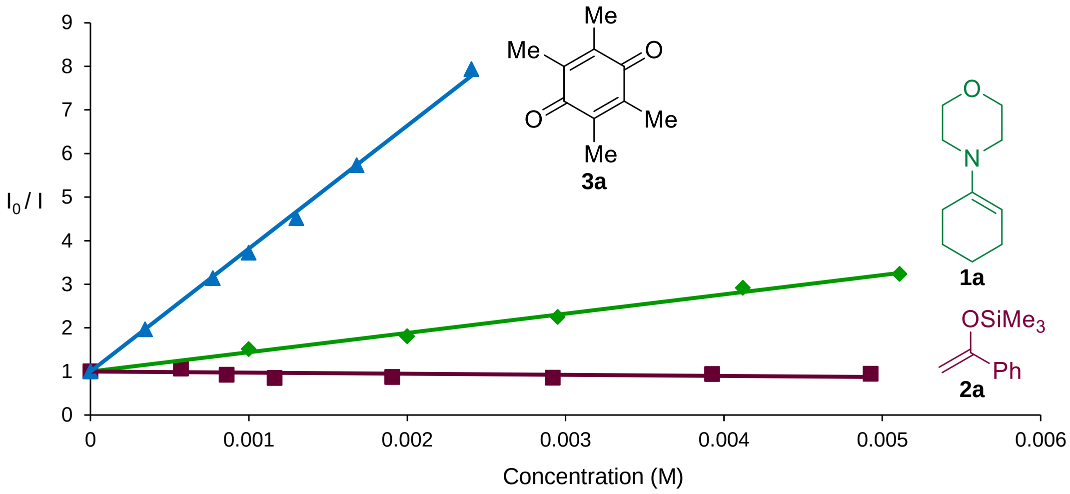


Figure 2.1. Stern-Volmer Studies.

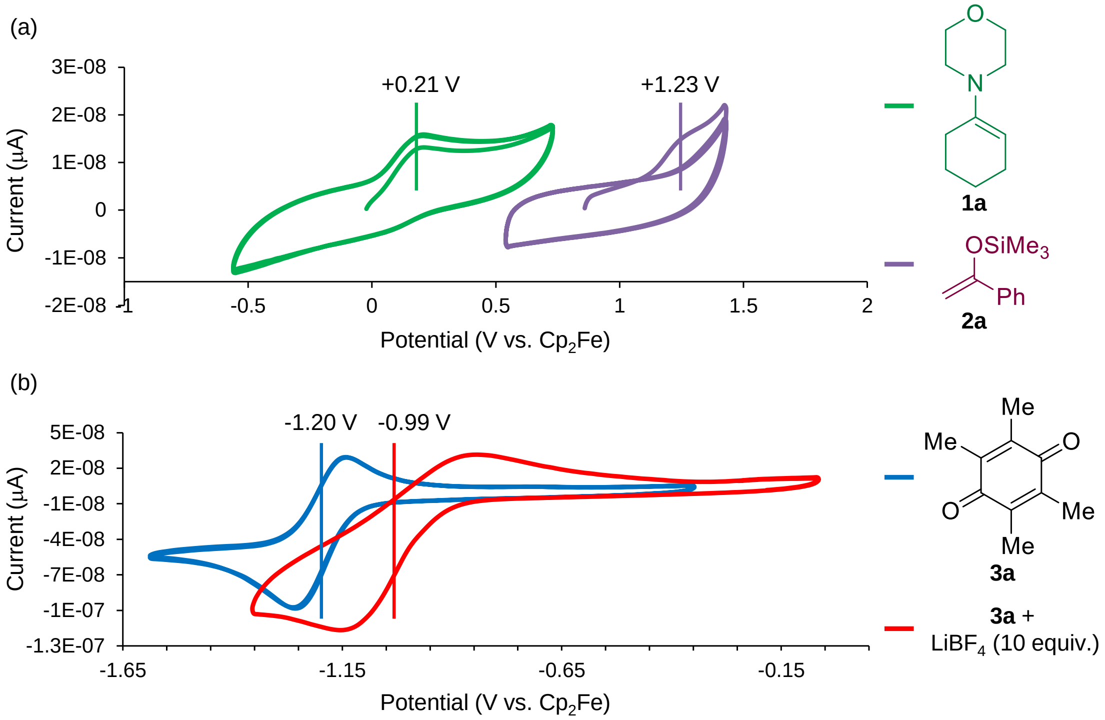
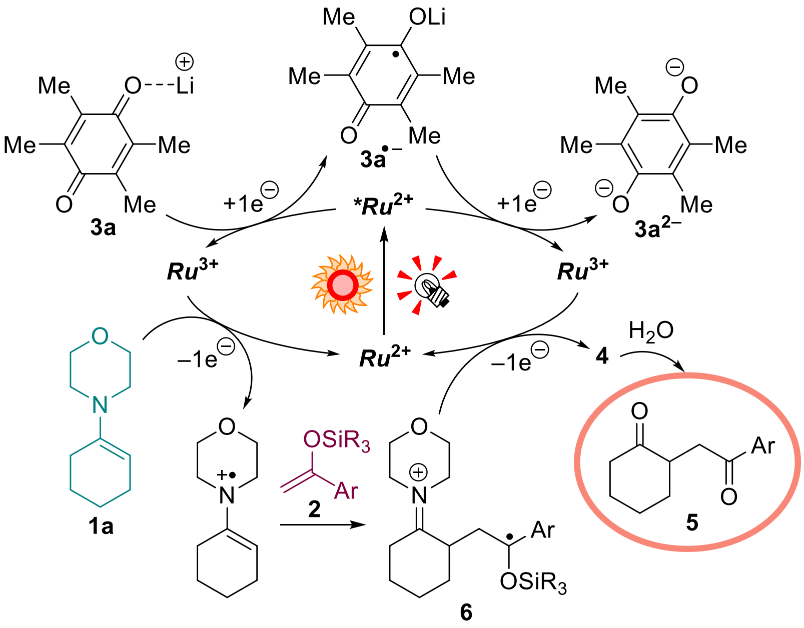


Figure 2.2. Cyclic Voltammograms.

Besides it was found that **3a** quenched the fluorescence more efficiently than **1a** did. These results suggest that electron transfer occurs from $*[Ru(bpy)_3]^{2+}$ to duroquinone **3a** first. A cyclic voltammogram for **3a** exhibited a broad reversible redox wave at –1.20 V (vs. Cp_2Fe). Addition of $LiBF_4$ (10 equiv.) caused an anodic shift of the redox potential by –0.99 V, indicating lowering of the LUMO level of **3a**. The irreversible oxidation wave for

1a (+0.21 V) was observed at a potential lower than that for **2a** (+1.23 V).

On the basis of these experimental results, a possible reaction mechanism is presented in Scheme 2.2. First, visible-light irradiation of $[Ru(bpy)_3]^{2+}$ (abbreviated as ***Ru***$^{2+}$) by either a Xe lamp or the sun causes excitation to ****Ru***$^{2+}$. Then, ****Ru***$^{2+}$ undergoes 1e-transfer to **3a** activated by Li^+ and converts into ***Ru***$^{3+}$ demanding an electron. Oxidation of enamine **1** by the resultant ***Ru***$^{3+}$ followed by addition to **2** gives radical intermediate **6**, and subsequent 1e-oxidation[9] furnishes the coupling product **4**, which is converted to γ-diketone product **5** by hydrolysis.



Ru^{2+}: $Ru(bpy)_3{}^{2+}$, ***Ru***$^{3+}$: $Ru(bpy)_3{}^{3+}$

Scheme 2.2. A Possible Reaction Mechanism.

2.5 Conclusion

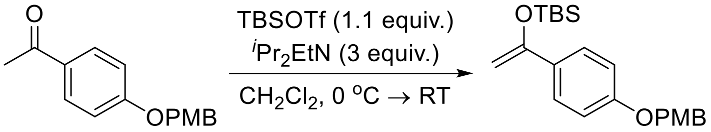
In conclusion, the author has developed photocatalytic synthesis of γ-diketones *via* oxidative coupling of enamines with silyl enol ethers using the $[Ru(bpy)_3]^{2+}$ catalyst under visible light irradiation. Sunlight can be successfully used for this photoreaction. A 2e-oxidation process involved in this transformation is achieved by the electron relay system composed of the SET photoredox catalyst and the suitable electron acceptor, duroquinone **3a**.

2.6 Experimental

Materials and Methods

$[Ru(bpy)_3](PF_6)_2$ was prepared according to the literature procedures.[10] Enamine **1a** was purchased from TCI. Other enamines were prepared according to the literature procedures.[111] Silyl enol ether **2a** was purchased from TCI. Other silyl enol ethers were prepared according to the literature procedures.[12] Ketone bearing PMB group was prepared according to the literature procedures.[13] Catalytic reactions were performed under an atmosphere of nitrogen using standard Schlenk techniques unless otherwise noted. Solvents were dried by standard procedures (CH_3CN, CH_2Cl_2 (P_2O_5), DMF (CaH_2)), distilled, and stored under nitrogen. NMR solvents were dried over molecular sieves, degassed and stored under N_2. Thin-layer chromatography was performed on Merck TLC plate with 60 F_{254}. Visible light irradiations were performed with a Soma Kogaku Xe lamp (150 W; $\lambda > 420$ nm with L42 cut-off filter). The ^{1}H NMR was acquired on Bruker AVANCE-400 (400 MHz). NMR chemical shifts were referenced to residual protio impurities in the deuterated solvent. HRMS (ESI-TOF Mass spectra) were obtained with a Bruker micrOTOF II. Single-crystal X-ray measurement was made on a Bruker SMART APEX II ULTRA. The crystallographic data for **5ai** are summarized in Table S2.1. The crystallographic data were deposited at the Cambridge Crystallographic Data Centre: CCDC 869541(**5ai**). Sunlight spectra were measured with EKO portable spectroradiometer MS-720.

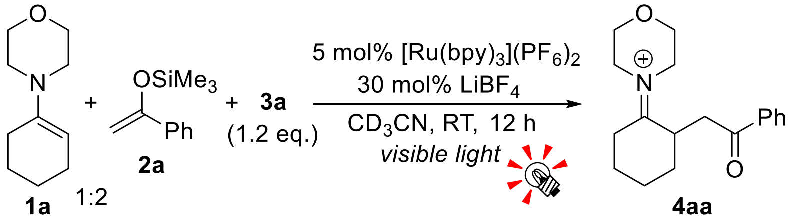
Synthesis of Silyl Enol Ether Bearing PMB-group (2i)



50 mL-Schlenk tube was charged with ketone (1.9 g, 7.4 mmol) and dry CH_2Cl_2 (18 mL) under N_2 atmosphere at room temperature. Then, ^{i}Pr$_2$NEt (2.70 g, 21.0 mmol, 3.0 equiv.) was added and the reaction mixture was cooled to 0 °C. *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (2.5 g, 8.2 mmol, 1.1 equiv.) was added to the reaction solution during 10 min under N_2. The resulting mixtures were stirred at room temperature for overnight. Saturated NH_4Cl aq. (100 mL) was added to the pale pink solution, and organic layer was washed with NH_4Cl aq. (200 mL) and dried over Na_2SO_4. The residue was concentrated in *vacuo* to afford **2i** as a white solid (2.9 g, 99% yield).

^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.53 (d, J = 8.8 Hz, 2 H), 7.35 (d, J = 8.8 Hz, 2 H), 6.95-6.90 (m, 4 H), 5.00 (s, 2 H), 4.77 (s, 1 H), 4.32 (s, 1 H), 3.82 (s, 3 H), 1.00 (s, 9H), 0.21 (s, 6 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 159.6, 159.1, 155.9, 130.8, 129.4, 129.1, 126.7, 114.5 114.2, 89.4, 69.9, 55.4, 26.0, 25.8, 18.5, −4.46. **HRMS** (ESI-TOF): calculated for $[C_{22}H_{30}O_3Si+Na]^+$ requires 393.1856, found 393.1859.

Typical NMR Experimental Procedure and NMR Spectra of Entry 8 in Table 2.1



$LiBF_4$ (1.4 mg, 15 μmol) was weighted in an NMR tube under N_2, and $[Ru(bpy)_3](PF_6)_2$ (2.2 mg, 2.5 μmol), duroquinone (9.8 mg, 60 μmol), 1,4-dimethoxybenzene (2.0 mg) as an internal standard, and CD_3CN (0.50 mL) were added to the NMR tube. After enamine **1a** (8.4 mg, 50 μmol) and silyl enol ether **2a** (19.2 mg, 100 μmol) were introduced, the reaction mixture was degassed by freeze-pump-thaw cycle. Then tube was closed. The reaction was carried out at room temperature (water bath) under irradiation of visible light (placed at a distance of 6–7 cm from Xe lamp with cut-off filter: hν > 420 nm).

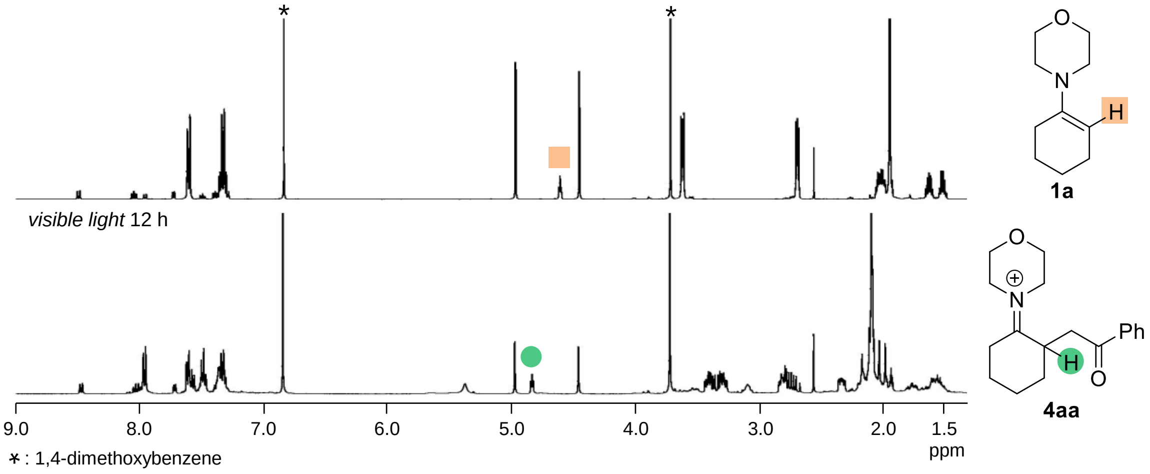


Figure S2.1. ^{1}H NMR Spectra (400 MHz, CD_3CN, RT).

In ^{1}H NMR spectrum of the reaction mixture under visible light for 12 h, complete conversion of enamine (**1a**) and appearance of new signal at 4.84 ppm were observed (Figure S2.1). In addition, HMBC spectrum gave a correlation between characteristic ^{1}H peak at 4.84 ppm and ^{13}C signal at 150.7 ppm assignable to iminium carbon (Figure S2.2). These results suggest formation of iminium ion **4aa** under these reaction conditions.

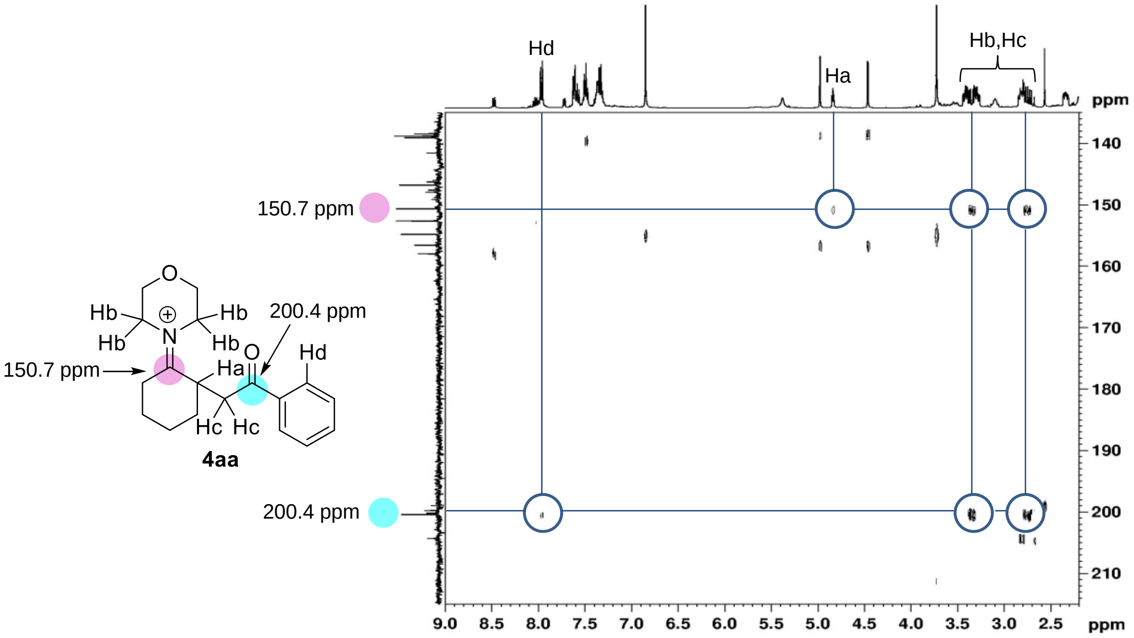
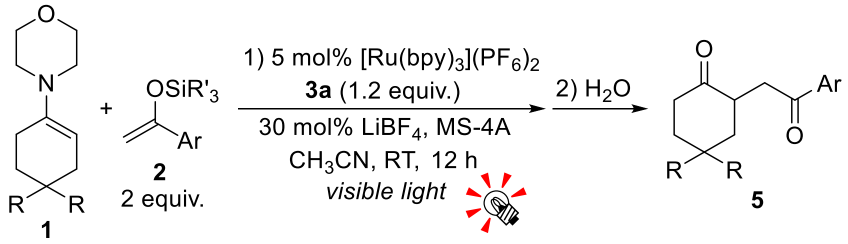


Figure S2.2. HMBC Spectrum (400 MHz, CD_3CN, RT).

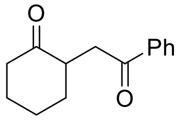
General Procedure for the Preparation of γ-Diketones



20 mL-Schlenk tube was charged activated MS-4A pellet (100 mg), duroquinone **3a** (49 mg, 0.30 mmol, 1.2 equiv.), $[Ru(bpy)_3](PF_6)_2$ (11 mg, 13 μmol) and CH_3CN (2.0 mL) under N_2. Silyl enol ether **2** (0.50 mmol, 2.0 eq.), enamine **1** (0.25 mmol, 1.0 equiv.) and solution of $LiBF_4$ in CH_3CN (7.0 mg, 0.075 mmol, 0.5 mL) were added to the reaction mixture, and the solution was degassed by the freeze-pump-thaw method with three times. The tube was placed at a distance of 5–6 cm from Xe lamp with cut-off filter: hν > 420 nm. The orange solution was stirred at room temperature under visible light irradiation for 12 h. After, the reaction mixture was poured into saturated aqueous NH_4Cl and stirred for another 1 h. The resulting mixture was extracted with CH_2Cl_2. Combined organic layers were dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified

by preparative TLC (PTLC) to afford γ-diketones **5**.

2-Phenacylcyclohexanone (5aa)

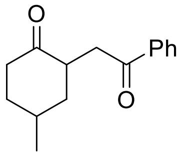


According to general procedure, **3a** (50 mg, 0.31 mmol), $[Ru(bpy)_3](PF_6)_2$ (11 mg, 13 μmol), enamine **1a** (42 mg, 0.25 mmol) and silyl enol ether **2a** (100 mg, 0.52 mmol) afforded **5aa** as a colorless oil (36 mg, 67% yield) after purification with silica PTLC (hexane/EtOAc = 4:1). Spectral data are in agreement with the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.98 (dd, J = 6.8, 1.4 Hz, 2 H), 7.54 (dd, J = 6.8, 1.4 Hz, 1 H), 7.45 (dd, J = 6.8, 1.4 Hz, 2 H), 3.57 (dd, J = 17.6, 6.4 Hz, 1 H), 3.18-3.13 (m, 1 H), 2.67 (dd, J = 17.6, 5.6 Hz, 1 H), 2.46-2.40 (m, 2 H), 2.41(s, 3H), 2.23-2.11 (m, 2 H), 1.91-1.61 (m, 4 H), 1.47-1.38 (m, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 211.6, 198.8, 137.2, 133.1, 128.6, 128.2, 46.6, 42.1, 38.5, 34.5, 28.1, 25.5. **HRMS** (ESI-TOF): calculated for $[C_{14}H_{16}O_2+Na]^+$ requires 239.1045, found 239.1043.

Ref.: J. Xie, Z-Z. Huang, *Chem. Commun.* **2010**, *46*, 1947.

2-Phenacyl-4-methylcyclohexanone (5ea)

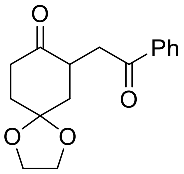


According to general procedure, **3a** (50.0 mg, 0.31 mmol), $[Ru(bpy)_3](PF_6)_2$ (11 mg, 13 μmol), enamine **1e** (43 mg, 0.24 mmol) and silyl enol ether **2a** (93 mg, 0.48 mmol) afforded **5ea** as a colorless oil (29 mg, 54% yield, 2.5:1 dr) after purification with silica PTLC (hexane/EtOAc = 4:1). Spectral data are in agreement with the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt) of diastereomer mixture: δ 7.98 (dd, J = 7.2, 1.4 Hz, 2 H), 7.54 (dd, J = 6.4, 1.4 Hz, 1 H), 7.45 (m, 2 H), 3.58-3.50 (m, 1 H), 3.18-3.13 (m, 1 H), 3.34-3.32 (m, 1 H), 2.73-2.12 (m, 5 H), 1.96-1.86 (m, 2H), 1.77-1.31 (m, 1 H), 1.28-0.98 (m, 3 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt) of diastereomer mixture: δ 212.4, 211.9, 198.7, 137.2, 133.2, 128.7, 128.2, 45.6, 42.5, 41.8, 41.3, 39.6, 38.6, 38.4, 37.6, 36.0, 33.3, 32.2, 27.3, 21.4, 18.2. **HRMS** (ESI-TOF): calculated for $[C_{15}H_{18}O_2+Na]^+$ requires 253.1210, found 253.1199.

Ref.: V. B. Anderson, M. N. Agnew, R. C. Allen, J. C. Wilker, H. B. Lassman, W. J. Novick, Jr., *J. Med. Chem.* **1976**, *19*, 318.

2-Phenacyl-1,4-dioxaspiro[4.5]decan-8-one (5fa)

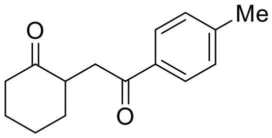


According to general procedure, enamine **1f** (62 mg, 0.25 mmol), **3a** (54.0 mg, 0.33 mmol), $[Ru(bpy)_3](PF_6)_2$ (12 mg, 14 μmol) and silyl enol ether **2a** (96 mg, 0.50 mmol) afforded **5fa** as a pale yellow solid (34 mg, 50% yield) after purification with silica PTLC (hexane/EtOAc = 7:3). Spectral data are in agreement with the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.97 (dd, J = 8.4, 1.2 Hz, 2 H), 7.54 (dd, J = 8.8, 1.2 Hz, 1 H), 7.45 (dd, J = 8.8, 1.2 Hz, 2 H), 4.12-3.99 (m, 4 H), 3.59-3.48 (m, 2 H), 2.80-2.72 (m, 2 H), 2.46-2.40 (m, 2 H), 2.46-2.41 (m, 1 H), 2.20-2.02 (m, 2 H), 1.88-1.80 (m, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 210.4, 198.0, 137.0, 133.1, 128.6, 128.1, 107.3, 64.9, 64.7, 42.5, 40.5, 38.0, 34.8. **HRMS** (ESI-TOF): calculated for $[C_{16}H_{18}O_4+Na]^+$ requires 297.1097, found 297.1097.

Ref.: P. W. Groundwater, M. A. Munawar, *Journal of Chemical Research, Synopses*, **1996**, *5*, 256.

2-(4-Methylphenacyl)cyclohexanone (5ab)



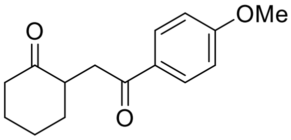
According to general procedure, **3a** (49 mg, 0.30 mmol), $[Ru(bpy)_3](PF_6)_2$ (12 mg, 14 μmol), enamine **1a** (42 mg, 0.25 mmol) and silyl enol ether **2b** (124 mg, 0.50 mmol) afforded **5ab** as a white solid (40 mg, 69% yield) after purification with silica PTLC (hexane/EtOAc = 4:1). Spectral data are in agreement with the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.88 (d, J = 8.0 Hz, 2 H), 7.25 (d, J = 8.0 Hz, 2 H), 3.60 (dd, J = 17.6, 6.8 Hz, 1 H), 3.19-3.14 (m, 1 H), 2.67 (dd, J = 17.6, 5.6 Hz, 1 H), 2.46-2.41 (m, 2 H), 2.23-2.12 (m, 2 H), 1.90-1.66 (m, 4 H), 1.48-1.32 (m, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 211.7, 198.4, 143.9, 134.8, 129.3, 128.3, 46.6, 42.1, 38.3, 34.5, 28.1, 25.5, 21.7. **HRMS** (ESI-TOF): calculated for $[C_{15}H_{18}O_2+Na]^+$ requires 253.1210, found

253.1199.

Ref.: T. Fujimura, S. Aoki, E. Nakamura, *J. Org. Chem.* **1991**, *56*, 2809.

2-(4-Methoxylphenacyl)cyclohexanone (5ac)

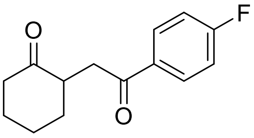


According to general procedure, **3a** (49.0 mg, 0.30 mmol), $[Ru(bpy)_3](PF_6)_2$ (10 mg, 12 μmol), enamine **1a** (40 mg, 0.24 mmol) and silyl enol ether **2c** (130 mg, 0.49 mmol) afforded **5ac** as a pale yellow solid (37 mg, 63% yield) after purification with silica PTLC (hexane/EtOAc = 4:1). Spectral data are in agreement with the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.97 (d, J = 8.8 Hz, 2 H), 6.93 (d, J = 8.8 Hz, 2 H), 3.87 (s, 3 H), 3.59 (dd, J = 17.2, 6.0 Hz, 1 H), 3.18-3.12 (m, 1 H), 2.67 (dd, J = 17.6, 6.0 Hz, 1 H), 2.46-2.41 (m, 2 H), 2.22-2.11 (m, 2 H), 1.91-1.55 (m, 4 H), 1.46-1.38 (m, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 211.8, 197.3, 163.6, 130.5, 130.4, 113.8, 55.6, 46.7, 42.2, 38.1, 34.6, 28.2, 25.6. **HRMS** (ESI-TOF): calculated for $[C_{15}H_{18}O_3+Na]^+$ requires 269.1149, found 269.1148.

Ref: J. Xie, Z-Z. Huang, *Chem. Commun.* **2010**, *46*, 1947.

2-(4-Fluorophenacyl)cyclohexanone (5ad)

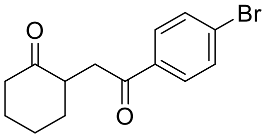


According to general procedure, **3a** (49 mg, 0.30 mmol), $[Ru(bpy)_3](PF_6)_2$ (11 mg, 13 μmol), enamine **1a** (44 mg, 0.26 mmol) and silyl enol ether **2d** (126 mg, 0.54 mmol) afforded **5ad** as a pale yellow oil (12 mg, 19% yield) after purification with silica PTLC (hexane/EtOAc = 4:1). Spectral data are in agreement with the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 8.01 (dd, J = 9.2, 5.2 Hz, 2 H), 6.93 (dd, J = 7.2, 5.2 Hz, 2 H), 3.56 (dd, J = 17.6, 6.2 Hz, 1 H), 3.19-3.13 (m, 1 H), 2.66 (dd, J = 17.6, 5.6 Hz, 1 H), 2.46-2.41 (m, 2 H), 2.22-2.13 (m, 2 H), 1.93-1.52 (m, 4 H), 1.51-1.38 (m, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 211.6, 197.2, 166.5 (d, J = 252.9 Hz), 133.6, 130.8 (d, J = 9.3 Hz), 115.7 (d, J = 21.8 Hz), 46.6, 42.1, 38.4, 34.5, 28.1, 25.5. **HRMS** (ESI-TOF): calculated for $[C_{14}H_{15}O_2F+Na]^+$ requires 257.0948, found 257.0951.

Ref.: V. B. Anderson, M. N. Agnew, R. C. Allen, J. C. Wilker, H. B. Lassman, W. J. Novick, Jr., *J. Med. Chem.* **1976**, *19*, 318.

2-(4-Bromophenacyl)cyclohexanone (5ae)

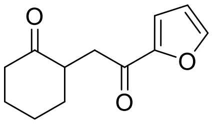


According to general procedure, **3a** (50.0 mg, 0.31 mmol), [Ru(bpy)$_3$](PF$_6$)$_2$ (10 mg, 12 μmol), enamine **1a** (42 mg, 0.25 mmol) and silyl enol ether **2e** (150 mg, 0.48 mmol) afforded **5ae** as a pale brown solid (24 mg, 33% yield) after purification with silica PTLC (hexane/EtOAc = 4:1). Spectral data are in agreement with the literature.

^{1}H NMR (400 MHz, CDCl$_3$, rt): δ 7.85 (dd, *J* = 9.0, 1.8 Hz, 2 H), 7.61 (dd, *J* = 9.0, 1.8 Hz, 2 H), 3.55 (dd, *J* = 17.6, 6.8 Hz, 1 H), 3.19-3.13 (m, 1 H), 2.61 (dd, *J* = 17.6, 5.6 Hz, 1 H), 2.46-2.41 (m, 2 H), 2.22-2.03 (m, 2 H), 1.93-1.66 (m, 4 H), 1.51-1.38 (m, 1 H). **^{13}C NMR** (100 MHz, CDCl$_3$, rt): δ 211.5, 197.8, 136.0, 132.0, 129.8, 128.3, 46.7, 42.1, 38.5, 34.4, 28.1, 25.5. **HRMS** (ESI-TOF): calculated for [C$_{14}$H$_{15}$O$_2$Br+Na]$^+$ requires 317.0148, found 317.0140.

Ref.: J. Xie, Z-Z. Huang, *Chem. Commun.* **2010**, *46*, 1947.

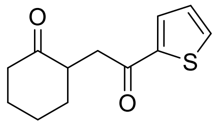
2-[2-Oxo-2-(2-furyl)ethyl]cyclohexanone (5ag)



According to general procedure, **3a** (53.0 mg, 0.32 mmol), [Ru(bpy)$_3$](PF$_6$)$_2$ (11 mg, 13 μmol), enamine **1a** (48 mg, 0.29 mmol) and silyl enol ether **2g** (119 mg, 0.53 mmol) afforded **5ag** as a white solid (32 mg, 55% yield) after purification with silica PTLC (hexane/EtOAc = 4:1).

^{1}H NMR (400 MHz, CDCl$_3$, rt): δ 7.85 (dd, *J* = 1.6, 0.8 Hz, 1 H), 7.21 (dd, *J* = 3.6, 0.8 Hz, 1 H), 6.53 (dd, *J* = 3.6, 1.6 Hz, 1 H), 3.45 (dd, *J* = 17.2, 6.8 Hz, 1 H), 3.15-3.10 (m, 1 H), 2.58 (dd, *J* = 17.6, 6.0 Hz, 1 H), 2.44-2.39 (m, 2 H), 2.21-2.10 (m, 2 H), 1.91-1.54 (m, 4 H), 1.50-1.40 (m, 1 H). **^{13}C NMR** (100 MHz, CDCl$_3$, rt): δ 211.3, 187.9, 152.9, 146.4, 117.1, 112.3, 46.4, 42.0, 38.3, 34.3, 28.0, 25.4. **HRMS** (ESI-TOF): calculated for [C$_{12}$H$_{14}$O$_3$+Na]$^+$ requires 229.0835, found 229.0835.

2-[2-Oxo-2-(2-thienyl)ethyl]cyclohexanone (5ah)

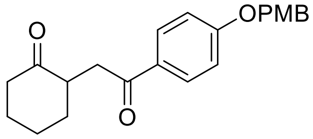


According to general procedure, **3a** (50.0 mg, 0.31 mmol), [Ru(bpy)$_3$](PF$_6$)$_2$ (12 mg, 14 μmol), enamine **1a** (42 mg, 0.25 mmol) and silyl enol ether **2h** (122 mg, 0.51 mmol) afforded **5ah** as a pale yellow oil (32 mg, 58% yield) after purification with silica PTLC (hexane/EtOAc = 4:1). Spectral data are in agreement with the literature.[6,7]

^{1}H NMR (400 MHz, CDCl$_3$, rt): δ 7.77 (dd, *J* = 4.0, 1.2 Hz, 1 H), 7.63 (dd, *J* = 5.2, 1.2 Hz, 1 H), 7.12 (dd, *J* = 5.2, 4.0 Hz, 1 H), 3.51 (dd, *J* = 17.2, 6.4 Hz, 1 H), 3.16-3.11 (m, 1 H), 2.66 (dd, *J* = 17.2, 6.0 Hz, 1 H), 2.45-2.40 (m, 2 H), 2.23-2.15 (m, 2 H), 1.89-1.55 (m, 4 H), 1.50-1.42 (m, 1 H). **^{13}C NMR** (100 MHz, CDCl$_3$, rt): δ 211.4, 191.7, 144.4, 133.5, 132.0, 128.1, 46.6, 42.0, 39.1, 34.3, 28.0, 25.4. **HRMS** (ESI-TOF): calculated for [$C_{12}H_{14}O_2S$+Na]$^+$ requires 245.0607, found 245.0602.

Ref.: V. B. Anderson, M. N. Agnew, R. C. Allen, J. C. Wilker, H. B. Lassman, W. J. Novick, Jr., *J. Med. Chem.* **1976**, *19*, 318.

2-(4-*p*-Methoxybenzyloxyphenacyl)cyclohexanone (5ai)



According to general procedure, **3a** (36 mg, 0.22 mmol), [Ru(bpy)$_3$](PF$_6$)$_2$ (8.6 mg, 10 μmol), enamine **1a** (30 mg, 0.18 mmol) and silyl enol ether **2i** (136 mg, 0.37 mmol) afforded **5ai** as a pale yellow solid (33 mg, 52% yield) after purification with silica PTLC (hexane/EtOAc = 7:3).

^{1}H NMR (400 MHz, CDCl$_3$, rt): δ 7.96 (dd, *J* = 7.0, 2.4 Hz, 2 H), 7.35 (dd, *J* = 7.0, 1.6 Hz, 2 H), 7.00 (dd, *J* = 6.8, 2.4 Hz, 2 H), 6.92 (dd, *J* = 6.8, 2.0 Hz, 2 H), 5.05 (s, 2 H), 3.82 (s, 3 H), 3.55 (dd, *J* = 17.6, 6.4 Hz, 1 H), 3.18-3.12 (m, 1 H), 2.64 (dd, *J* = 17.6, 6.0 Hz, 1 H), 2.45-2.41 (m, 2 H), 2.22-2.12 (m, 2 H), 1.88-1.55 (m, 4 H), 1.46-1.41 (m, 1 H). **^{13}C NMR** (100 MHz, CDCl$_3$, rt): δ 211.8, 197.3, 162.8, 159.7, 130.5, 130.4, 129.4, 128.3, 114.6, 114.2, 70.1, 55.4, 46.6, 42.1, 38.1, 34.5, 28.1, 25.5. **HRMS** (ESI-TOF): calculated for [$C_{22}H_{24}O_4$+Na]$^+$ requires 375.1567, found 375.1563.

Sunlight-Driven Reaction

Cylindrical vessel was used for photoreaction under sunlight (right). The vessel was charged activated MS-4A pellet (100 mg), duroquinone **3a** (50 mg, 0.31 mmol), $[Ru(bpy)_3](PF_6)_2$ (11 mg, 13 μmol), then **1a** (42 mg, 0.25 mmol), **2a** (103 mg, 0.54 mmol), $LiBF_4$ in CH_3CN (7.0 mg, 0.075 mmol, 0.5 mL) and CH_3CN (2.0 mL) were added. The reaction mixture was exposed to sunlight for 11 h (in February 21st, 22nd, and 24th, 2012) below 15 ^{o}C. After workup, **5aa** was obtained as oil (33 mg, 61% yield).

Sunlight spectrum was measured in the 300−1150 nm region as shown in Figure S2.3.

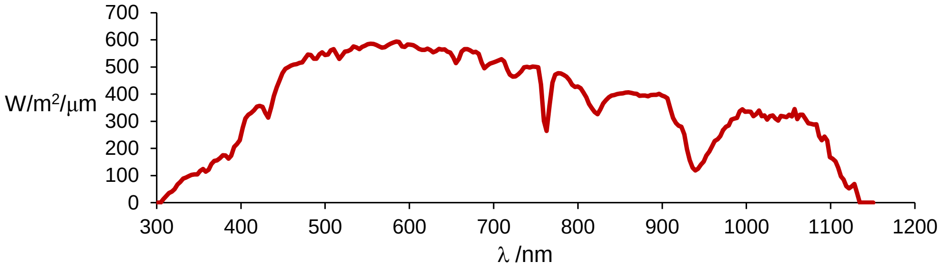


Figure S2.3. Typical Solar Spectrum (14:07, 21st, February, 2012).

Cyclic Voltammograms

Cyclic voltammetry experiments were performed using Hokutodenkou HZ-5000 analyzer (observed in 0.001 M CH_3CN; $[NBu_4PF_6]$= 0.1 M; Ag/AgCl = electrode; reported with respect to the $[FeCp_2]/[FeCp_2]^+$ couple) under N_2 at room temperature.

Stern-Volmer Studies

Emission spectra for the Ru catalyst in a deaerated solution whose concentration was adjusted so as to show the absorbance 0.1 at excitation wavelength were recorded at room temperature by SHIMADZU RF-5300PC spectrometer. ($[Ru(bpy)_3](PF_6)_2$ excited at 450 nm in CH_3CN exhibited emission band at 610 nm.)

General experimental procedure: A solution of the Ru catalyst was prepared and degassed three times via freeze-pump-thaw cycle in a 1 cm quartz cell equipped with a sphere moiety for freeze. The solution of quencher was added to the solution of the Ru catalyst before measurement of emission intensities.

Crystallographic Data for 5ai

Diffraction measurements were made on a Bruker SMART APEX II ULTRA/CCD. Intensity measurements were performed using monochromated (doubly curved silicon crystal) Mo-Kα-radiation (0.71073 Å) from a sealed microfocus tube. Data collection temperature was –183 °C for **5ai**. Data were acquired using three sets of Omega scans at different Phi settings. The frame width was 0.5 °. The crystallographic data are summarized in Table S2.1.

The structural analysis was performed on an APEX2 software for preliminary determination of the unit cell. Determination of integrated intensities and unit cell refinement were performed using SAINT. Unless otherwise stated, all non-hydrogen atoms were refined anisotropically by full-matrix least-square techniques based on F^2. All hydrogen atoms were fixed at the calculated positions.

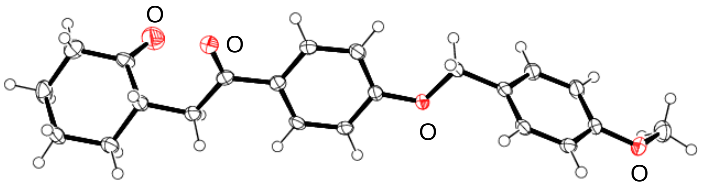


Figure S2.4. ORTEP Drawing of **5ai**.

Table S2.1. Crystal Data and Structure Refinement for **5ai**.

Empirical formula	C22 H24 O4	
Formula weight	352.41	
Temperature	93(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 6.9714(17) Å	α = 75.680(4)°
	b = 9.360(3) Å	β = 82.150(3)°
	c = 15.546(4) Å	γ = 68.441(3)°
Volume	913.0(4) $Å^3$	
Z	2	
Density (calculated)	1.282 Mg/cm^3	
Absorption coefficient	0.087 mm^{-1}	
F(000)	376	
Theta range for data collection	2.40 to 28.71°	

Index ranges	-9<=h<=7, -11<=k<=12, -19<=l<=20
Reflections collected	5292
Independent reflections	4074 [R(int) = 0.1356]
Completeness to theta = 28.71°	86.10%
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4074 / 0 / 237
Goodness-of-fit on F^2	0.992
Final R indices [I>2sigma(I)]	R1 = 0.0826, wR2 = 0.2177
R indices (all data)	R1 = 0.1130, wR2 = 0.2402
Largest diff. peak and hole	1.346 and -0.508

2.7 References

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5 A ^{1}H NMR spectrum for **4aa** shows a characteristic multiplet signal at 4.84 ppm, assignable to the α-methine proton (see Experimental Section).

6 Identified byproducts are the photoinduced coupling product of **2a** with **3a**. Homocoupling products of **1a** and **2a** were not observed.

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9 We cannot exclude the pathway that **3a**$^{\bullet-}$ directly oxidizes **6**.

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Chapter 3

Visible-Light-Induced Selective Generation of Radicals from Organoborates by Photoredox Catalysis

ABSTRACT: A new strategy for the generation of carbon-centered radicals *via* oxidation of alkyl-, allyl-, benzyl- and arylborates by visible-light-driven single electron transfer (SET) photoredox catalysis has been established. The generated radicals smoothly react with TEMPO and electron-deficient alkenes to afford C–O and C–C coupling products, respectively. In this radical initiating system, cyclic organo(triol)borates turn out to be useful radical precursors.

Chapter 4

Three-Component Oxytrifluoromethylation of Alkenes: Highly Efficient and Regioselective Difunctionalization of C=C Bonds Mediated by Photoredox Catalysts

ABSTRACT: A facile vicinal difunctionalization of alkenes, oxytrifluoromethylation, was established by visible-light-driven photoredox catalysis. Judicious choice of the CF_3 source is key. Nucleophiles such as water, alcohols, and carboxylic acids can be used in this highly efficient (2–4 h) and regioselective (100%) transformation using blue LED lamps and natural sunlight.

Chapter 5

Highly Regio- and Diastereo-Selective Synthesis of CF_3-Substituted Lactones *via* Photoredox-Catalyzed Carbolactonization of Alkenoic Acids

ABSTRACT: Trifluoromethylative lactonization of both terminal and internal alkenoic acids by photoredox catalysis has been developed. The strategy of Ru photocatalyst and Umemoto's reagent as a CF_3 source is a key in the present carbolactonization. Highly *endo*- and diastereoselective synthesis of CF_3-substituted five-, six- and seven-membered ring lactones from internal alkenoic acids is the first example.

Chapter 6

Intermolecular Aminotrifluoromethylation of Alkenes by Visible-Light-Driven Photoredox Catalysis

ABSTRACT: Intermolecular aminotrifluoromethylation of alkenes catalyzed by $[Ru(bpy)_3]^{2+}$ under visible light irradiation has been explored. The present photocatalytic protocol achieves highly efficient and regioselective difunctionalization of C=C bonds, leading to a variety of β-trifluoromethylamines. The reaction is applied to “late-stage aminotrifluoromethylation” of steroid and amino acid scaffolds.

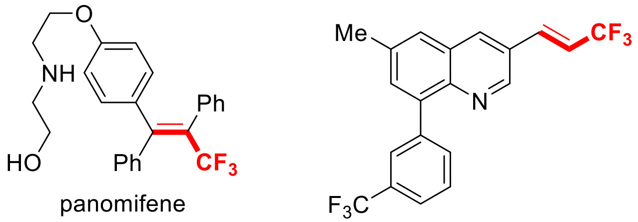
Chapter 7

Visible-Light-Induced Synthesis of a Variety of (*E*)-Trifluoromethylated Alkenes from Potassium Alkenyltrifluoroborates by Photoredox Catalysis

ABSTRACT: A facile and efficient radical trifluoromethylation of alkenyltrifluoroborates has been developed. Togni's reagent (1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one) can serve as a CF_3 radical precursor in the presence of the photoredox catalyst, $[Ru(bpy)_3](PF_6)_2$, under visible light irradiation. This new photocatalytic protocol can be applicable to a wide variety of vinylborates containing electronically diverse substituents and hetero-arenes leading to (*E*)-trifluoromethylated alkenes in good yields with a regio- and stereoselective fashion.

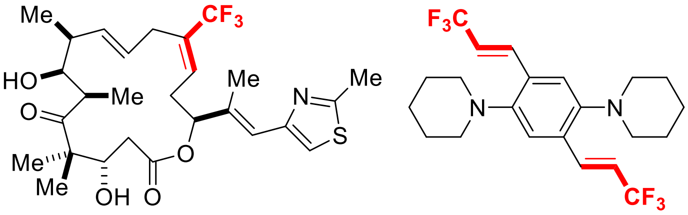
7.1 Introduction

Over the past few years, a variety of transition-metal-catalyzed trifluoromethylation of aryl halides, aryl boronic acids, and aromatic C–H bonds for construction of C_{aryl}–CF_3 bonds have been well developed.[1] On the other hand, stereoselective construction of $C_{alkenyl}$–CF_3 bonds is significantly more limited although trifluoromethylated alkenes are a promising building block for pharmaceuticals, agrochemicals, functional materials, and further conversion into CF_3-containing substances.[2–6]



panomifene (anti-estrogen drug)

herbicide



fludelone (antitumor)

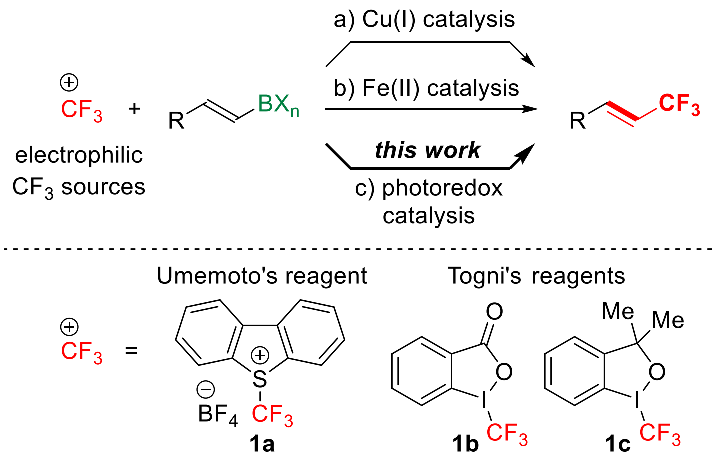
fluorescent material

Figure 7.1. $C_{alkenyl}$–CF_3 Bond Moiety-Containing Molecules.

As described in Chapters 1 and 4–6, the strategies for trifluoromethylation using electrophilic trifluoromethylating ($^+CF_3$) reagents such as Umemoto's reagent **1a** and Togni's reagent **1b,c** have attracted great attention.[7–9] Over the past few years, several catalytic synthetic methods for construction of $C_{alkenyl}$–CF_3 bonds with "$^+CF_3$" reagents have been reported.[12] The groups of Shen and Liu have shown non-stereoselective trifluoromethylation of alkenylboronic acids by Cu(I) catalysis (Scheme 7.1a).[110a,b] Furthermore, Buchwald and co-workers reported an Fe(II)-catalyzed stereoselective trifluoromethylation of alkenyltrifluoroborates (Scheme 7.1b).[10c] In addition, there are a few reports on copper-mediated trifluoromethylation of α,β-unsaturated carboxylic acids,[10d] alkynes[10e] and enamides.[10f] These methods, however, exhibit limited substrate scopes with respect to hetero-aromatics and functional groups. Therefore, a new general protocol for construction of $C_{alkenyl}$–CF_3 bonds with an efficient and stereoselective manner is highly desirable.

As described in Chapters 4–6, the author have found oxy- and aminotrifluoromethylation of alkenes with "$^{+}CF_3$" reagents and *O*- and *N*-nucleophiles besed on SET photoredox process.[11,12] Importantly, easy-handling "$^{+}CF_3$" reagents can serve as the CF_3 radical precursor in the presence of photoredox catalysts under visible light irradiation.

Herein the author discloses highly regio- and stereoselective deboronated trifluoromethylation of alkenyltrifluoroborates with commercially available and air-stable Togni's reagent **1b** by visible-light-driven photoredox catalysis (Scheme 7.1c). In particular, this new photocatalytic protocol is effective in the selective and large-scale synthesis of (*E*)-trifluoromethylated alkenes bearing a hetero-aromatic moiety, which are difficult to access by previous catalytic systems.

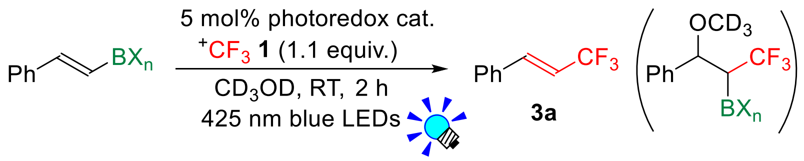


Scheme 7.1. Trifluoromethylation of Alkenylboronic Acid Derivatives.

7.2 Photocatalytic Trifluoromethylation of (*E*)-Styrylboronic Acid Derivatives

The author initially examined the photocatalytic trifluoromethylation of (*E*)-styrylboronic acid derivatives **2** with 1.1 equivalent of Togni's reagent **1b**[17] as a CF_3 source in the presence of 5 mol% photoredox catalyst, [*fac*-Ir(ppy)$_3$], in MeOH under blue LED irradiation for 2 h.

Table 7.1. Optimization Studies.[a]



Entry	CF_3 reagent	BX$_n$	Photocatalyst	*E*/*Z*[b]	Yield of **3a**/%[b]
1	**1b**	B(OH)$_2$	[*fac*-Ir(ppy)$_3$]	57/43	53
2	**1b**	Bpin	[*fac*-Ir(ppy)$_3$]	54/46	36
3	**1b**	BF_3K **2a**	[*fac*-Ir(ppy)$_3$]	94/6	85
4	**1a**	**2a**	[*fac*-Ir(ppy)$_3$]	90/10	83
5	**1c**	**2a**	[*fac*-Ir(ppy)$_3$]	85/15	79
6[c]	CF_3SO_2Cl **1d**	**2a**	[*fac*-Ir(ppy)$_3$]	99/1	27
7[d]	**1b**	**2a**	**[Ru(bpy)$_3$](PF$_6$)$_2$**	**98/2**	**81**
8	**1b**	**2a**	none	–	0
9[e]	**1b**	**2a**	[Ru(bpy)$_3$](PF$_6$)$_2$	–	0

[a] Reaction conditions: A mixture of photocatalyst (1.25 μmol, 0.05 M in solvent), **1** (0.0275 mmol), **2a** (5.4 mg, 0.025 mmol), was irradiated by 3W blue LEDs (λ = 425 ± 15 nm) at room temperature. [b] Yields and *E*/*Z* ratios were determined by ^1H and ^{19}F NMR spectroscopies. [c] CD_3CN was used as solvent. [d] Reaction time = 5 h. [e] In the dark.

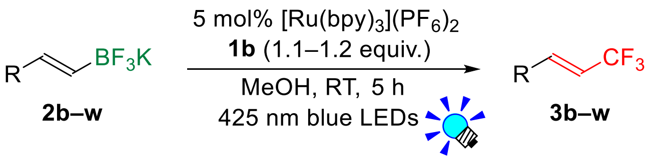
Every entry resulted in formation of β-trifluoromethylstyrene **3a** (Table 7.1, entries 1–3). As a result, a choice of the boron auxiliary turned out to be crucial for yield and selectivity. The reaction of potassium (*E*)-styryltrifluoroborate **2a** afforded the product **3a** with *E*/*Z* ratio of 94/6 in 85% yield (entry 3). In contrast, the substrates with B(OH)$_2$ and Bpin groups gave the mixture of **3a** and methoxytrifluoromethylated by-product. Next, examination of CF_3 reagents has revealed that Togni's reagent **1b** is the best choice in terms of yield and selectivity. The use of **1c** and Umemoto's reagent **1a** provided product **3a** in good yields, but did not improve selectivity (entries 4 and 5). A typical CF_3 radical source, CF_3SO_2Cl **1d**, gave a mixture of product **3a**, styrene and unidentified by-products (entry 6). Finally, the Ru photocatalyst, $[Ru(bpy)_3](PF_6)_2$, also promoted the present reaction, providing the product **3a** with excellent *E*/*Z* selectivity (98/2) in 81% yield upon 5 h irradiation (entry 7). Notably, the product **3a** was not obtained at all either in the dark or in the absence of the photoredox catalyst (entries 8 and 9), strongly supporting that the photoexcited species of the photoredox catalyst play key roles in the reaction.

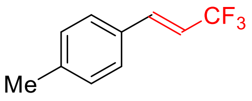
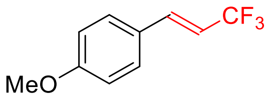
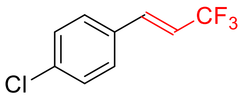
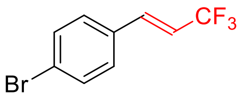
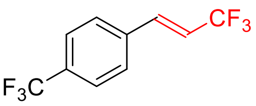
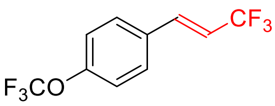
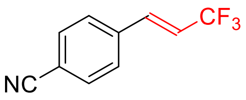
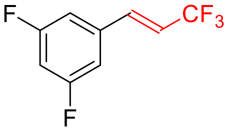
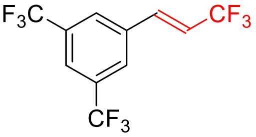
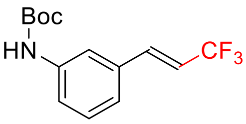
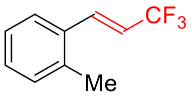
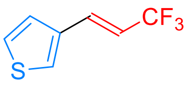
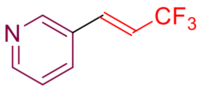
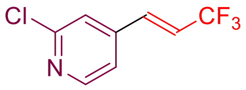
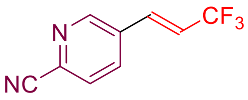
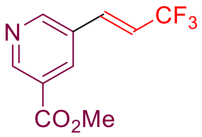
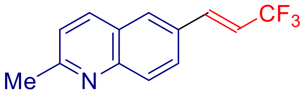
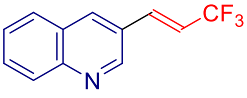
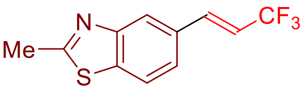
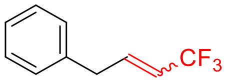
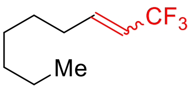
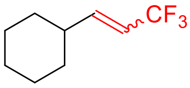
7.3 Photocatalytic Trifluoromethylation of (*E*)-Alkenyltrifluoroborates

The scope and limitations of the present photocatalytic trifluoromethylation of vinyltrifluoroborates are summarized in Table 7.2. (*E*)-Styrylborates with an electron-donating substituent, Me (**2b**, **l**) and MeO (**2c**), smoothly produced the corresponding β-CF_3-styrene products with high *E*/*Z* selectivities in good yields (**3b**, **c**, **l**). In addition, this reaction can be applied to vinylborates bearing a variety of electron-withdrawing functional groups, F (**2i**), Cl (**2d**), Br (**2e**), CF_3 (**2f**, **j**), OCF_3 (**2g**), CN (**2h**), and NHBoc (**2k**). The corresponding trifluoromethylated alkene products (**3d**–**k**) were obtained without any loss of the functional groups with excellent *E*/*Z* selectivities (>94/<6) in high yields (68–93%). This broad application to vinylborates should be remarkable. The above-mentioned Buchwald's catalytic system with vinyltrifluoroborates, Togni's reagent **1b**, and Fe(II) salt is ineffective for electron-deficient substrates.[10c] In contrast, the present photocatalytic system does not have such a limitation.

Next, to expand the scope, alkenylborates containing heteroaryl groups such as thiophene, pyridine, quinoline and benzothiazole were examined. Hetero-aromatic substrates are relevant to the pharmaceuticals and agrochemicals because hetero-arenes are ubiquitous structure in biologically active compounds.[14]

Table 7.2. Scope and Limitation of the Present Trifluoromethylation of **2**.[a,b,c]



 **3b**: 81%, *E*/*Z* = 92/8	 **3c**: 88%, *E*/*Z* = 99/1	 **3d**: 72%, *E*/*Z* = 95/5	 **3e**: 81%, *E*/*Z* = 95/5
 **3f**: 79%,[d,e] *E*/*Z* = 98/2	 **3g**: 69%, *E*/*Z* = 95/5	 **3h**: 78%, *E*/*Z* = 96/4	 **3i**: 68%, *E*/*Z* = 96/4
 **3j**: 81%,[d,e] *E*/*Z* = 97/3	 **3k**: 93%, *E*/*Z* = 94/6	 **3l**: 70%, *E*/*Z* = 95/5	 **3m**: 63%,[f,g] *E*/*Z* = 96/4
 **3n**: 68%, *E*/*Z* = 97/3	 **3o**: 56%, *E*/*Z* = 98/2	 **3p**: 66%, *E*/*Z* = 98/2	 **3q**: 70%, *E*/*Z* = 98/2
 **3r**: 69%, *E*/*Z* = 97/3	 **3s**: 71%, *E*/*Z* = 98/2	 **3t**: 82%, *E*/*Z* = 97/3	
 **3u**: 60%, *E*/*Z* = 63/37	 **3v**: 41% (67%[h]), *E*/*Z* = 67/33	 **3w**: 79%,[h] *E*/*Z* = 73/27	

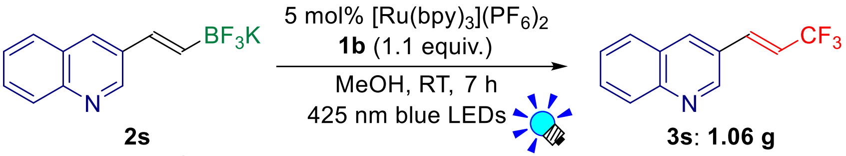
[a] Reaction conditions: A mixture of [Ru(bpy)$_3$](PF$_6$)$_2$ (12.5 μmol, 0.05 M in MeOH), **1b** (0.275–0.30 mmol), **2** (0.25 mmol) was irradiated by 3W blue LEDs (λ = 425 ±15 nm) at room temperature. [b] Isolated yields. [c] *E*/*Z* ratios were determined by ^{1}H and ^{19}F NMR spectroscopies of the crude product mixture. [d] [*fac*-Ir(ppy)$_3$] (0.5 mol%) was used as the photocatalyst. [e] Reaction time = 2 h. [f] 1.1 equiv. of vinylborate with respect to **1b** was used. [g] Protodeboronated by-product was contained with 2%. [h] NMR yield.

The photocatalytic reactions of **2m**–**t** gave the corresponding CF$_3$-substituted alkenes **3m**–**t**[15] with excellent *E*/*Z* selectivities (>96/<4) in moderate to good yields (56–82%).

Formation of $C_{alkenyl}$–CF_3 bonds with π electron-deficient hetero-aromatics have not been so far reported,[10] thus present photocatalytic protocol might be attractive from the viewpoint of regio- and stereoselective introduction of a CF_3 group into these scaffolds.In addition, no C–H trifluoromethylation of hetero-arene with CF_3 radical was observed under these reaction conditions.[12a,16] Furthermore, alkylalkenylborates (**2u**–**w**) can be applicable to this photocatalytic system with moderate selectivities and good yields (**3u**–**w**).

7.4 Gram Scale Reaction

As a demonstration of scalability of this transformation, the trifluoromethylation of **2s** was carried out on a gram scale (Scheme 7.2). As a result, the trifluoromethylated alkene with quinoline moiety **3s**, which is a herbicide-related molecule as mentioned above, was obtained in good yield (64%, 1.06 g) with excellent *E*/*Z* selectivity (>99/<1).



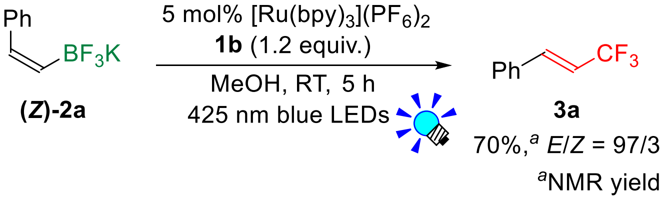
2s
7.5 mmol

3s: **1.06 g**
(64%, *E*/*Z* = >99/<1)

Scheme 7.2. Gram-Scale Synthesis of **3s**.

7.5 Plausible Reaction Mechanism

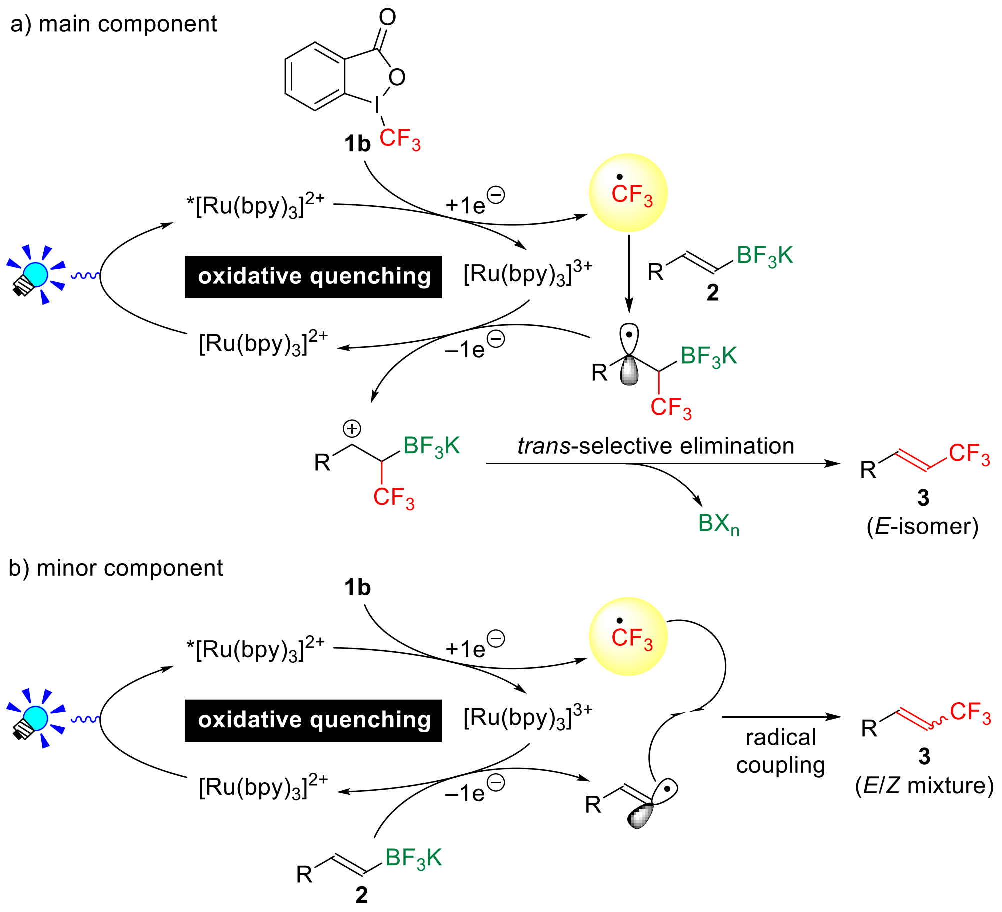
To gain insight into the reaction mechanism, the author examined the trifluoromethylation of (*Z*)-styryltrifluoroborate (**(*Z*)-2a**) (eq. 1). As a results, the reaction provided (*E*)-trifluoromethylstyrene (**3a**) as a major isomer (*E*/*Z* = 97/3). This result suggests same intermediate can be involved in the reaction with both (*E*)- and (*Z*)-alkenylbotares.



(1)

Based on above-mentioned result, a plausible reaction mechanism is shown in Scheme 7.3a. First, $^{\bullet}CF_3$ can be generated from 1e-reduction of electrophilic Togni's reagent **1b**. Cyclic voltammograms for alkenylborate **2a** showed a broad irreversible oxidation wave around $E_{1/2}$ = +1.01 V vs Cp_2Fe (see Figure S7.1 in Experimental Section). Thus, generation of radicals from oxidation of alkenylborates by photoexcited state of $[Ru(bpy)_3]^{2+}$ ($E_{1/2}$ = +0.43 V vs Cp_2Fe) is excluded. Generated $^{\bullet}CF_3$ reacts with a C=C bond of alkenylborates **2** to give β-borato-stabilized radical intermediates[17] in a regioselective manner. Subsequent 1e-oxidation by the high-oxidation state photocatalyst, $[Ru(bpy)_3]^{3+}$, produces β-borato cation intermediates.[18] Finally predominant Peterson elimination of the boron-based group with *trans*-selectivity provides (*E*)-trifluoromethylated alkenes **3**.[19]

However, production of (*Z*)-trifluoromethylated alkene as a minor product in this photocatalytic system indicates that other reaction mechanism is involved in the present reaction. Putative reaction mechanism is shown in Scheme 7.3b. As mentioned above, first step of the present trifluoromethylation is 1e-reduction of Togni's reagent **1b** by $^*[Ru(bpy)_3]^{2+}$. Generated $[Ru(bpy)_3]^{3+}$ species exhibit high oxidation potential ($E_{1/2}$ = +0.88 V vs Cp_2Fe). Thus, alkenylborate **2** can be oxidized by $[Ru(bpy)_3]^{3+}$ to give the vinyl radical intermediate, which easily undergoes *cis*/*trans* isomerization. Finally, radical coupling produces *E*/*Z* mixture of trifluoromethylated alkenes **3**.



Scheme 7.3. A Plausible Reaction Mechanism.

7.6 Conclusion

In conclusion, the author has developed the new and facile visible-light-induced trifluoromethylation of alkenyltrifluoroborates using photoredox catalyst, $[Ru(bpy)_3](PF_6)_2$.[20] This highly efficient and regio- and stereoselective reaction can be applicable to a wide variety of alkenylborates containing electronically diverse substituents and hetero-arenes, indicating that it can be a highly versatile protocol. In addition, this method is operationally easy. Importantly, Togni's reagent **1b** turns out to be crucial for efficient and selective trifluoromethylation. Furthermore, the present photocatalytic trifluoromethylation allows large-scale synthesis of (*E*)-trifluoromethylated alkenes.

7.7 Experimental

Materials and Methods

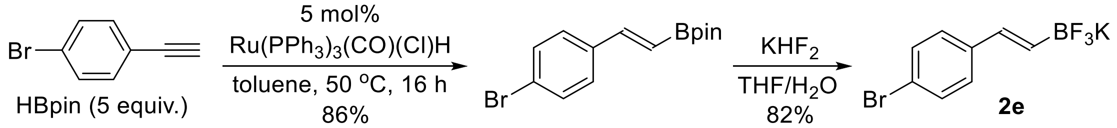
Togni's reagent (**1a**) was purchased from TCI. Potassium (*E*)-vinyltrifluoroborate, **2b**,[21a] **2c**,[21b] **2d**,[21c] **2f**[21b] and **2w**[21b] were prepared according to the literature procedures. Trifluoromethylated alkene **3w** was assigned by ^1H NMR spectroscopy based on the previous report.[22d] Catalytic reactions were performed under an atmosphere of nitrogen using standard Schlenk techniques unless otherwise noted. Methanol (dehydrated solvent, KANTO CHEMICAL CO., INC.) was degassed with ultrasonic bath, and stored under N_2 atmosphere. NMR solvents (CD_3OD) was dried over molecular sieves 3Å, degassed and stored under N_2. Visible light irradiations were performed with a Relyon LED lamp (3 W x 2; λ_{max} = 425 nm). HRMS (ESI-TOF Mass spectra) were obtained with a Bruker micrOTOF II. HRMS (EI Mass spectra) were recorded on a JEOL JMS-700 mass spectrometers. The crystallographic data for **3q** are summarized in Table S7.1. The crystallographic data were deposited at the Cambridge Crystallographic Data Centre: CCDC 900630 (**3q**).

Reaction Apparatus

Irradiation of visible light was performed with a Relyon LED lamp (3 W x 2; λ_{max} = 425 nm).

Synthesis of Potassium (*E*)-Alkenyltrifluoroborate (2)

Potassium (*E*)-2-(4-Bromophenyl)ethenyltrifluoroborate (2e)



A 2-neck 100 mL round-bottom flask was charged with alkyne (1.15 g, 6.35 mmol), $Ru(PPh_3)_3(CO)(Cl)H$ (303 mg, 0.32 mmol) and dry toluene (26 mL), then 4,4,5,5-tetramethyl-1,3,2-dioxaborane (HBpin) (4.62 mL, 31.8 mmol, 5 equiv.) was added to the mixture under N_2. The reaction mixture was stirred at 50 °C for 16 h. After cooling to room temperature, the solvent was removed under vaccum. Resulting reaction mixture was diluted with Et_2O, washed with sat. aq. $NaHCO_3$, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1) to afford the (*E*)-2-(4-bromostyryl)ethenylboronic acid pinacol ester as a white solid (1.69 g, 86% yield). The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 7.46 (dd, J = 6.8, 1.6 Hz, 2 H), 7.35-7.29 (m, 3 H), 6.14 (d, J = 18.4 Hz, 1 H), 1.30 (s, 12 H). **^{11}B NMR** (125.7 MHz, $CDCl_3$, rt) δ 29.6.

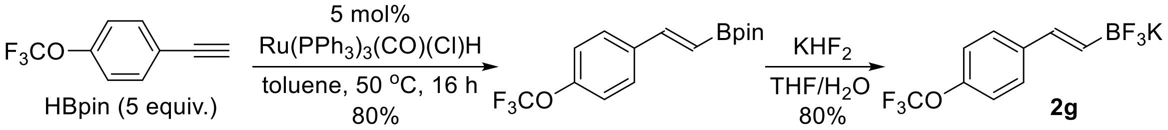
Ref.: H. Jang, A. R. Zhugralin, Y. Lee, A. H. Hoveyda, *J. Am. Chem. Soc.* **2011**, *133*, 7859.

To a solution of (*E*)-2-(4-bromophenyl)ethenylboronic acid pinacol ester (1.69 g, 5.47 mmol) in dry THF (30 mL) was added a solution of KHF_2 (2.56 g, 32.8 mmol) in water (10 mL). The raction mixture was stirred at room temperature for overnight. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum, and the crude product was washed with ether and pentane to afford **2e** as a white solid (1.3 g, 82% yield). The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, DMSO, rt) δ 7.41 (d, J = 8.4 Hz, 2 H), 7.26 (d, J = 8.4 Hz, 2 H), 6.42 (d, J = 18.4 Hz, 1 H), 6.20 (dq, J = 18.0, 3.2 Hz, 1 H). **^{11}B NMR** (128.4 MHz, DMSO, rt) δ 2.36. **^{19}F NMR** (376.5 MHz, DMSO, rt) δ -138.0.

Ref.: A. T. Parsons, T. D. Senecal, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2012**, *51*, 2947.

Potassium (*E*)-2-(4-Trifluoromethoxyphenyl)ethenyltrifluoroborate (2g)



A 2-neck 100 mL round-bottom flask was charged with alkyne (1.0 g, 5.37 mmol), $Ru(PPh_3)_3(CO)(Cl)H$ (256 mg, 0.27 mmol) and dry toluene (21 mL), then HBpin (3.91 mL, 26.9 mmol) was added to the mixture under N_2. The reaction mixture was stirred at 50 °C for 16 h. After cooling to room temperature, the solvent was removed under vaccum. Resulting reaction mixture was diluted with Et_2O, washed with sat. aq. $NaHCO_3$, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1→4/1) to afford the (*E*)-2-(4-trifluoromethoxyphenyl)ethenylboronic acid pinacol ester as a pale yellow oil (1.35 g, 80% yield).

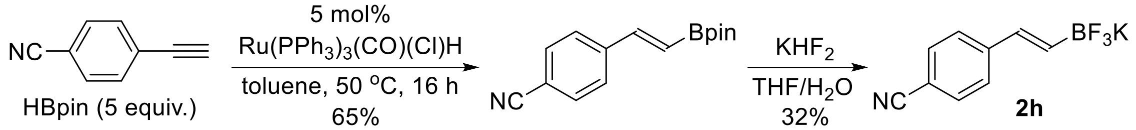
^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 7.49 (dd, J = 6.8, 2.0 Hz, 2 H), 7.35 (d, J = 18.4 Hz, 1 H), 7.17 (d, J = 8.8 Hz, 2 H), 6.13 (d, J = 18.4 Hz, 1 H), 1.31 (s, 12 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt) δ 149.6, 147.8, 136.4, 128.4, 121.0, 120.6 (q, J = 256 Hz), 83.6, 24.9. **^{11}B NMR**

(125.7 MHz, $CDCl_3$, rt) δ 30.0. **HRMS** (ESI-TOF): calculated for $[C_{15}H_{18}BF_3O_3\text{-}H]^-$ requires 313.1231, found 313.1230.

To a solution of (*E*)-2-(4-trifluoromethoxyphenyl)ethenylboronic acid pinacol ester (1.1 g, 3.5 mmol) in dry THF (20 mL) was added a solution of KHF_2 (1.64 g, 21 mmol) in water (10 mL). The raction mixture was stirred at room temperature for overnight. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum, and the crude product was diluted acetone, and excess amount of ether was added. The precipitate was filtered, washed with pentane, and dried *in vacuo*. Resulting solid was wash with CH_2Cl_2 to afford **2g** as a white solid (0.82 g, 80% yield).

^{1}H NMR (400 MHz, acetone, rt) δ 7.41 (d, J = 8.0 Hz, 2 H), 7.17 (d, J = 8.0 Hz, 2 H), 6.68 (d, J = 18.4 Hz, 1 H), 6.20 (dq, J = 18.4, 3.6 Hz, 1 H). **^{13}C NMR** (100 MHz, acetone, rt) δ 148.1, 141.1, 133.5, 127.8, 121.6, 121.5 (q, J = 253 Hz). **^{11}B NMR** (128.4 MHz, acetone, rt) δ 3.06. **^{19}F NMR** (376.5 MHz, acetone, rt) δ -58.6, -141.8. **HRMS** (ESI-TOF): calculated for $[C_9H_6BF_6O]^-$ requires 255.0423, found 255.0442.

Potassium (*E*)-2-(4-Cyanophenyl)ethenyltrifluoroborate (2h)



A 2-neck 100 mL round-bottom flask was charged with alkyne (1.0 g, 7.87 mmol), $Ru(PPh_3)_3(CO)(Cl)H$ (373 mg, 0.39 mmol) and dry toluene (31 mL), then HBpin (5.72 mL, 39.3 mmol) was added to the mixture under N_2. The reaction mixture was stirred at 50 ^{o}C for 16 h. After cooling to room temperature, the solvent was removed under vaccum. Resulting reaction mixture was diluted with Et_2O, washed with sat. aq. $NaHCO_3$, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1) to afford the (*E*)-2-(4-cyanophenyl)ethenylboronic acid pinacol ester as a yellow solid (1.3 g, 65% yield).

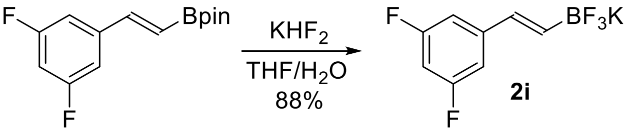
^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 7.62 (d, J = 8.4 Hz, 2 H), 7.54 (d, J = 8.4 Hz, 2 H), 7.36 (d, J = 18.4 Hz, 1 H), 6.27 (d, J = 18.4 Hz, 1 H), 1.31 (s, 12 H). **^{11}B NMR** (125.7 MHz, $CDCl_3$, rt) δ 29.3.

To a solution of (*E*)-2-(4-cyanophenyl)ethenylboronic acid pinacol ester (1.3 g, 5.1

mmol) in dry THF (20 mL) was added a solution of KHF_2 (2.39 g, 31 mmol) in water (10 mL). The raction mixture was stirred at room temperature for overnight. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum, and the crude product was washed with ether, pentane and CH_2Cl_2 to afford **2h** as a yellow solid (0.38 g, 32 % yield).

^{1}H NMR (400 MHz, DMSO, rt) δ 7.67 (d, J = 8.4 Hz, 2 H), 7.49 (d, J = 8.4 Hz, 2 H), 6.53 (d, J = 18.4 Hz, 1 H), 6.42 (dq, J = 18.4, 3.2 Hz, 1 H). **^{13}C NMR** (100 MHz, DMSO, rt) δ 144.9, 132.1, 131.8, 126.0, 119.2, 107.8. **^{11}B NMR** (128.4 MHz, DMSO, rt) δ 2.42. **^{19}F NMR** (376.5 MHz, DMSO, rt) δ -138.4. **HRMS** (ESI-TOF): calculated for $[C_9H_6BF_3N]^-$requires 196.0553, found 196.0560.

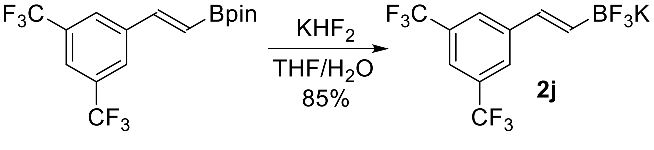
Potassium (*E*)-2-(3,5-Difluorophenyl)ethenyltrifluoroborate (2i)



To a solution of (*E*)-2-(3,5-difluorophenyl)ethenylboronic acid pinacol ester (1.0 g, 3.75 mmol) in dry THF (20 mL) was added a solution of KHF_2 (1.76 g, 23 mmol) in water (10 mL). The raction mixture was stirred at room temperature for 5 h. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum, and the crude product was washed with ether and pentane to afford **2i** as a white solid (0.81 g, 88% yield).

^{1}H NMR (400 MHz, DMSO, rt) δ 7.00 (d, J = 7.6 Hz, 2 H), 6.90 (dd, J = 9.2, 2.0 Hz, 1 H), 6.46 (d, J = 18.4 Hz, 1 H), 6.32 (dq, J = 18.4, 3.6 Hz, 1 H). **^{13}C NMR** (100 MHz, DMSO, rt) δ 162.6 (d, J = 293 Hz), 162.5 (d, J = 293 Hz), 144.5, 131.1, 107.9 (d, J = 18.2 Hz), 107.8 (d, J = 18.2 Hz), 100.8 (d, J = 26.0 Hz), 100.5 (d, J = 26.0 Hz). **^{11}B NMR** (128.4 MHz, DMSO, rt) δ 2.46. **^{19}F NMR** (376.5 MHz, DMSO, rt) δ -111.0 (d, J = 8.66 Hz), -138.2. **HRMS** (ESI-TOF): calculated for $[C_8H_5BF_5]^-$ requires 207.0411, found 207.0453.

Potassium (*E*)-2-[3,5-Bis(trifluoromethyl)phenyl]ethenyltrifluoroborate (2j)

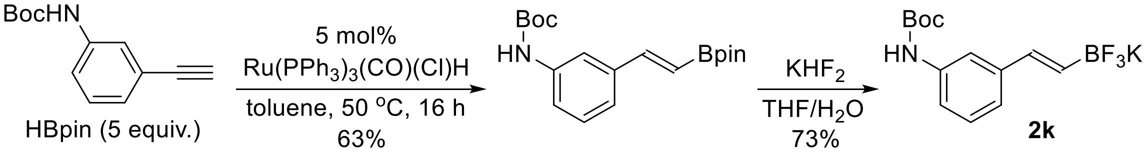


To a solution of (*E*)-2-[3,5-bis(trifluoromethyl)phenyl)ethenylboronic acid pinacol ester

(1.0 g, 2.73 mmol) in dry THF (20 mL) was added a solution of KHF_2 (1.3 g, 16 mmol) in water (10 mL). The raction mixture was stirred at room temperature for 5 h. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum to yield a pale yellow oil. The crude oil was diluted ether, and excess amount of pentane was added. The precipitate was filtered and washed with pentane. The resulting solid was dried *in vacuo* to afford **2j** as a white solid (0.80 g, 85% yield).

^{1}H NMR (400 MHz, DMSO, rt) δ 7.94 (s, 2 H), 7.76 (s, 1 H), 6.66 (d, J = 18.4 Hz, 1 H), 6.50 (dq, J = 18.4, 3.6 Hz, 1 H). **^{13}C NMR** (100 MHz, DMSO, rt) δ 142.9, 130.4, 130.3 (q, J = 32.2 Hz), 125.5, 123.5 (q, J = 271 Hz), 118.8. **^{11}B NMR** (128.4 MHz, DMSO, rt) δ 2.16. **^{19}F NMR** (376.5 MHz, DMSO, rt) δ -61.4, -138.5. **HRMS** (ESI-TOF): calculated for $[C_{10}H_5BF_9]^-$ requires 307.0348, found 307.0358.

Potassium (*E*)-2-(3-*tert*-Butoxycarbonylaminophenyl)ethenyltrifluoroborate (2k)



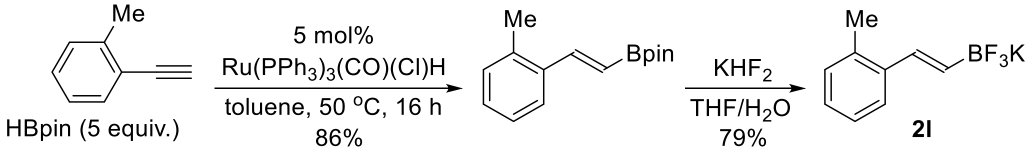
A 2-neck 100 mL round-bottom flask was charged with Boc-protected alkyne[22] (2.0 g, 9.2 mmol), $Ru(PPh_3)_3(CO)(Cl)H$ (447 mg, 0.47 mmol) and dry toluene (37 mL), then HBpin (6.8 mL, 46.8 mmol) was added to the mixture under N_2. The reaction mixture was stirred at 50 °C for 16 h. After cooling to room temperature, the solvent was removed under vaccum. Resulting reaction mixture was diluted with Et_2O, washed with sat. aq. $NaHCO_3$, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (pentane/Et_2O = 9/1→4/1) to afford the (*E*)-2-(3-*tert*-butoxycarbonylaminophenyl)ethenylboronic acid pinacol ester as a white solid (2.0 g, 63% yield).

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 7.45 (s, 1 H), 7.38-7.22 (m, 3 H), 7.16 (d, J = 7.6 Hz, 1 H), 6.46 (bs, 1 H), 6.15 (d, J = 18.4 Hz, 1 H), 1.51 (s, 9 H), 1.30 (s, 12 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt) δ 152.8, 149.3, 138.8, 138.6, 129.2, 121.9, 119.2, 117.2, 83.4, 80.7, 28.4, 24.9. **^{11}B NMR** (125.7 MHz, $CDCl_3$, rt) δ 30.5. **HRMS** (ESI-TOF): calculated for $[C_{19}H_{28}BNO_4+H]^-$ requires 344.2195, found 344.2196.

To a solution of (*E*)-2-(3-*tert*-butoxycarbonylaminophenyl)ethylenylboronic acid pinacol ester (1.2 g, 3.5 mmol) in dry THF (20 mL) was added a solution of KHF_2 (1.64 g, 21 mmol) in water (10 mL). The raction mixture was stirred at room temperature for overnight. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum, and the crude product was washed with ether, pentane and CH_2Cl_2 to afford **2k** as a white solid (0.82 g, 73 % yield).

^{1}**H NMR** (400 MHz, DMSO, rt) δ 7.37 (s, 1 H), 7.25 (d, J = 8.0 Hz, 1 H), 7.10 (dd, J = 8.0, 7.6 Hz, 1 H), 6.88 (d, J = 7.6 Hz, 1 H), 6.37 (d, J = 18.0 Hz, 1 H), 6.10 (dq, J = 18.0, 3.2 Hz, 1 H), 1.47 (s, 9 H). ^{13}**C NMR** (100 MHz, DMSO, rt) δ 152.7, 140.7, 139.4, 133.1, 133.0, 128.2, 119.4, 115.8, 115.1, 78.7, 39.5, 28.1. ^{11}**B NMR** (128.4 MHz, DMSO, rt) δ 2.70. ^{19}**F NMR** (376.5 MHz, DMSO, rt) δ -138.0. **HRMS** (ESI-TOF): calculated for $[C_{13}H_{16}BF_3NO_2]^-$ requires 286.1234, found 286.1233.

Potassium (*E*)-2-(2-Tolyl)ethenyltrifluoroborate (2l)



A 2-neck 100 mL round-bottom flask was charged with alkyne (1.0 g, 8.61 mmol), $Ru(PPh_3)_3(CO)(Cl)H$ (407 mg, 0.43 mmol) and dry toluene (35 mL), then HBpin (6.25 mL, 43 mmol) was added to the mixture under N_2. The reaction mixture was stirred at 50 °C for 16 h. After cooling to room temperature, the solvent was removed under vaccum. Resulting reaction mixture was diluted with Et_2O, washed with sat. aq. $NaHCO_3$, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 9/1→4/1) to afford the (*E*)-2-(2-tolyl)ethenylboronic acid pinacol ester as a pale yellow solid (1.8 g, 86% yield). The spectral data of the product were identical with those reported in the literature.

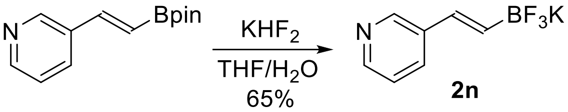
^{1}**H NMR** (400 MHz, $CDCl_3$, rt) δ 7.64 (d, J = 18.0 Hz, 1 H), 7.55 (d, J = 5.6 Hz, 1 H), 7.20-7.12 (m, 3 H), 6.08 (d, J = 18.0Hz, 1 H), 1.31 (s, 12 H). ^{11}**B NMR** (125.7 MHz, $CDCl_3$, rt) δ 29.8.

Ref.: H. Jang, A. R. Zhugralin, Y. Lee, A. H. Hoveyda, *J. Am. Chem. Soc.* **2011**, *133*, 7859.

To a solution of (*E*)-2-(2-tolyl)ethenylboronic acid pinacol ester (1.80 g, 7.37 mmol) in dry THF (30 mL) was added a solution of KHF_2 (3.46 g, 44.2 mmol) in water (10 mL). The raction mixture was stirred at room temperature for overnight. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum, and the crude product was washed with ether, pentane and CH_2Cl_2 to afford **2l** as a white solid (1.3 g, 79% yield).

^{1}H NMR (400 MHz, DMSO, rt) δ 7.38 (d, J = 7.6 Hz, 1 H), 7.11-6.99 (m, 3 H), 6.68 (d, J = 18.0 Hz, 1 H), 6.06 (dq, J = 18.0, 3.2 Hz, 1 H), 2.25 (s, 3 H). **^{13}C NMR** (100 MHz, DMSO, rt) δ 139.2, 133.5, 130.2 (d, J = 4.0 Hz), 129.7, 125.6, 125.4, 124.4, 19.3. **^{11}B NMR** (128.4 MHz, DMSO, rt) δ 2.55. **^{19}F NMR** (376.5 MHz, DMSO, rt) δ -137.7. **HRMS** (ESI-TOF): calculated for $[C_9H_9BF_3]^-$ requires 185.0757, found 185.0759.

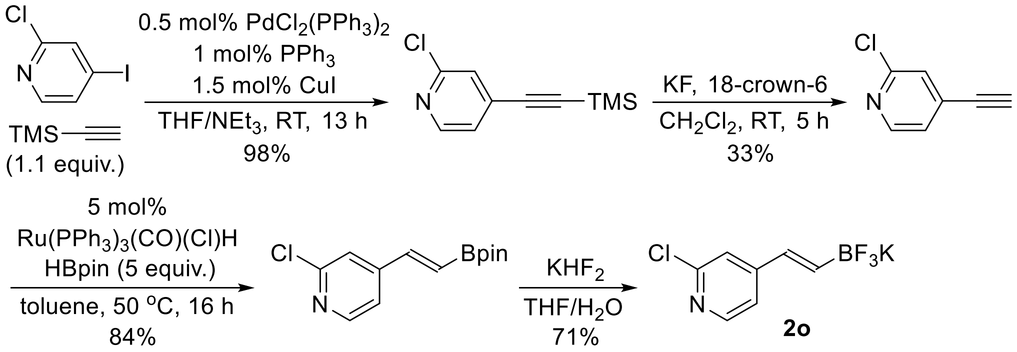
Potassium (*E*)-2-(3-Pyridine)ethenyltrifluoroborate (2n)



To a solution of (*E*)-3-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl]pyridine[23] (2.2 g, 9.5 mmol) in dry THF (35 mL) was added a solution of KHF_2 (4.5 g, 57 mmol) in water (10 mL). The raction mixture was stirred at room temperature for 5 h. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum, and the crude product was washed with ether, pentane and CH_2Cl_2 to afford **2n** as a pale yellow solid (1.3 g, 65 % yield).

^{1}H NMR (400 MHz, DMSO, rt) δ 8.47 (s, 1 H), 8.31 (dd, J = 4.8, 1.6 Hz, 1 H), 7.73 (dd, J = 8.0, 1.6 Hz, 1 H), 7.26 (dd, J = 8.0, 4.8 Hz, 1 H), 6.48 (d, J = 18.4 Hz, 1 H), 6.33 (dq, J = 18.0, 3.2 Hz, 1 H). **^{13}C NMR** (100 MHz, DMSO, rt) δ 147.4, 146.9, 135.4, 131.7, 129.7, 129.6, 123.5. **^{11}B NMR** (128.4 MHz, DMSO, rt) δ 2.38. **^{19}F NMR** (376.5 MHz, DMSO, rt) δ -138.2. **HRMS** (ESI-TOF): calculated for $[C_7H_6BF_3N]^-$ requires 172.0552, found 172.0560.

Potassium (*E*)-2-[4-(2-Chloropyridine)]ethenyltrifluoroborate (2o)



A 2-neck 300 mL round-bottom flask was charged with 4-iodo-2-chloropyridine (5.0 g, 20.9 mmol), $PdCl_2(PPh_3)_2$ (77 mg, 0.11 mmol), PPh_3 (55 mg, 0.22 mmol), dry THF (16 mL) and NEt_3 (25 mL) under N_2. After bubbling N_2 into the solution for 15 min, CuI (40 mg, 0.33 mmol) and trimethylsilylacetylene (3.3 mL, 23.0 mmol) were added sequentially. The reaction mixture was stirred at room temperature. After 13 h, the precipitate (NEt_3•HI) was filtered off and washed with EtOAc. The filtrate solution was concentrated and residue was diluted with ether/hexane. The crude product was purified by flash column chromatography on silica gel (hexane→hexane/AcOEt = 9/1) to afford the 2-chloro-4-((trimethylsilyl)ethynyl)pyridine as a pale yellow oil (4.30 g, 98% yield). The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 8.32 (dd, J = 5.2, 0.8 Hz, 1 H), 7.35 (dd, J = 1.2, 0.8 Hz, 1 H), 7.21 (dd, J = 5.2, 1.2 Hz, 1 H), 0.25 (s, 9 H).

Ref.: Y. Takayama, T. Hanazawa, T. Andou, K. Muraoka, H. Ohtani, M. Takahashi, F. Sato, *Org. Lett.* **2004**, *6*, 4253.

A 2-neck 100 mL round-bottom flask was charged with TMS-alkyne (4.3 g, 20.5 mmol), 18-crown-6-ether (5.42 g, 20.5 mmol) and dry CH_2Cl_2 (28 mL), then KF (2.38 g, 41 mmol) was added to the mixture under N_2. The reaction mixture was stirred at room temperature for 5 h. Resulting reaction mixture was extracted with CH_2Cl_2, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (pentane/Et_2O = 4/1) to afford the 2-chloro-4-ethynylpyridine as a colorless crystal (0.94 g, 33% yield). The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 8.37 (dd, J = 4.8, 0.4 Hz, 1 H), 7.39 (br s, 1 H), 7.27 (dd, J = 5.2, 1.6 Hz, 1 H), 3.35 (s, 1 H).

Ref.: A. Conte, H. Kuehne, T. Luebbers, P. Mattei, C. Maugeais, W. Mueller, P. Pflieger, Patent: US2007/185058 A1, **2007**, 12.

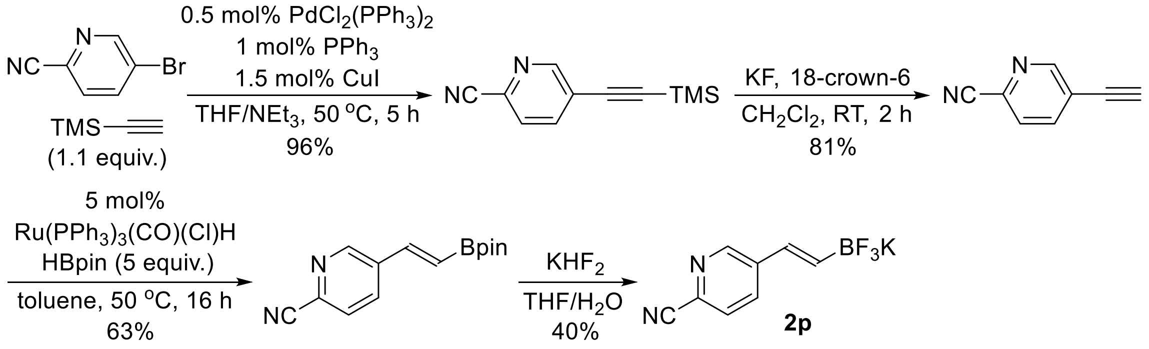
A 2-neck 100 mL round-bottom flask was charged with 2-chloro-4-ethynylpyridine (0.82 g, 8.96 mmol), $Ru(PPh_3)_3(CO)(Cl)H$ (281 mg, 0.30 mmol) and dry toluene (23 mL), then HBpin (4.3 mL, 29.8 mmol) was added to the mixture under N_2. The reaction mixture was stirred at 50 ^oC for 16 h. After cooling to room temperature, the solvent was removed under vaccum. Resulting reaction mixture was diluted with Et_2O, washed with sat. aq. $NaHCO_3$, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 9/1→4/1) to afford the (*E*)-2-chloro-4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)pyridine as a colorless oil (1.34 g, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 8.39 (d, *J* = 4.8 Hz, 1 H), 7.38 (d, *J* = 0.8 Hz, 1 H), 7.29 (dd, *J* = 5.6, 1.6 Hz, 1 H), 7.28 (d, *J* = 18.4 Hz, 1 H), 6.41 (d, *J* = 18.4, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt) δ 152.2, 150.0, 147.8, 144.9, 121.8, 119.8, 83.9, 24.8. **^{11}B NMR** (128.4 MHz, $CDCl_3$, rt) δ 29.5. **HRMS** (ESI-TOF): calculated for $[C_{13}H_{17}ClBNO_2]^-$ requires 266.1127, found 266.1198.

To a solution of (*E*)-2-chloro-4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)--vinyl)pyridine (1.2 g, 4.52 mmol) in dry THF (20 mL) was added a solution of KHF_2 (2.30 g, 29.4 mmol) in water (10 mL). The raction mixture was stirred at room temperature for overnight. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum, and the crude product was washed with ether, pentane and CH_2Cl_2 for several times to afford **2o** as a white solid (0.79 g, 71% yield).

^{1}H NMR (400 MHz, DMSO, rt) δ 8.21 (d, *J* = 5.2 Hz, 1 H), 7.35-7.33 (m, 2 H), 6.61 (dq, *J* = 18.0, 3.2 Hz, 1 H), 6.45 (q, *J* = 18.0 Hz, 2 H). **^{13}C NMR** (100 MHz, DMSO, rt) δ 151.1, 150.9, 149.6, 130.0, 120.3, 119.4. **^{11}B NMR** (128.4 MHz, DMSO, rt) δ 1.90. **^{19}F NMR** (376.5 MHz, DMSO, rt) δ -138.7. **HRMS** (ESI-TOF): calculated for $[C_7H_5ClBF_3N]^-$ requires 206.0162, found 206.0166.

Potassium (*E*)-2-[3-(2-Cyanopyridine)]ethenyltrifluoroborate (2p)



A 2-neck 300 mL round-bottom flask was charged with 5-bromo-2-cyanopyridine (5.0 g, 27.3 mmol), $PdCl_2(PPh_3)_2$ (111 mg, 0.158 mmol), PPh_3 (86 mg, 0.328 mmol), dry THF (25 mL) and NEt_3 (37 mL) under N_2. After bubbling N_2 into the solution for 15 min, CuI (64 mg, 0.33 mmol) and trimethylsilylacetylene (4.8 mL, 34 mmol) were added sequentially. The reaction mixture was stirred at 50 °C for 5 h. After cooling to room temperature, the precipitate (NEt_3•HBr) was filtered off and washed with EtOAc. The filtrate solution was concentrated and residue was diluted with ether/hexane. The crude product was purified by flash column chromatography on silica gel (hexane→hexane/AcOEt = 4/1) to afford the 5-((trimethylsilyl)ethynyl)picolinonitrile as a pale yellow solid (5.27 g, 96% yield). The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 8.73 (dd, J = 2.0, 0.8 Hz, 1 H), 7.84 (dd, J = 8.4, 2.0 Hz, 1 H), 7.62 (dd, J = 8.4, 0.8 Hz, 1 H), 0.27 (s, 9 H).

Ref.: A. A. Farahat, A. Kumar, M. Say, A. E.-D. M. Barghash, F. E. Goda, H. M. Eisa, T. Wenzler, R. Brun, Y. Liu, L. Mickelson, W. D. Wilson, D. W. Boykin, *Bioorganic & Medicinal Chemistry*, **2010**, *18*, 557.

A 2-neck 100 mL round-bottom flask was charged with TMS-alkyne (4.0 g, 20.0 mmol), 18-crown-6-ether (5.28 g, 20.0 mmol) and dry CH_2Cl_2 (30 mL), then KF (2.32 g, 40 mmol) was added to the mixture under N_2. The reaction mixture was stirred at room temperature for 2 h. Resulting reaction mixture was extracted with CH_2Cl_2, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (pentane/Et_2O = 4/1→2/1) to afford the 5-ethynylpicolinonitrile as an orange solid (2.08 g, 81% yield). The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 8.77 (dd, J = 2.0, 1.0 Hz, 1 H), 7.90 (dd, J = 8.0, 2.0 Hz, 1 H), 7.66 (dd, J = 8.0, 1.0 Hz, 1 H), 3.45 (s, 1 H).

Ref.: A. A. Farahat, A. Kumar, M. Say, A. E.-D. M. Barghash, F. E. Goda, H. M. Eisa, T.

Wenzler, R. Brun, Y. Liu, L. Mickelson, W. D. Wilson, D. W. Boykin, *Bioorganic & Medicinal Chemistry,* **2010**, *18*, 557–566.

A 2-neck 100 mL round-bottom flask was charged with 5-ethynylpicolinonitrile (1.2 g, 9.36 mmol), Ru(PPh$_3$)$_3$(CO)(Cl)H (447 mg, 0.47 mmol) and dry toluene (37 mL), then HBpin (6.8 mL, 46.8 mmol) was added to the mixture under N_2. The reaction mixture was stirred at 50 ^{o}C for 16 h. After cooling to room temperature, the solvent was removed under vaccum. Resulting reaction mixture was diluted with Et_2O, washed with sat. aq. $NaHCO_3$, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1→4/1) to afford the (*E*)-5-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)picolinonitrile as a white solid (1.50 g, 63% yield).

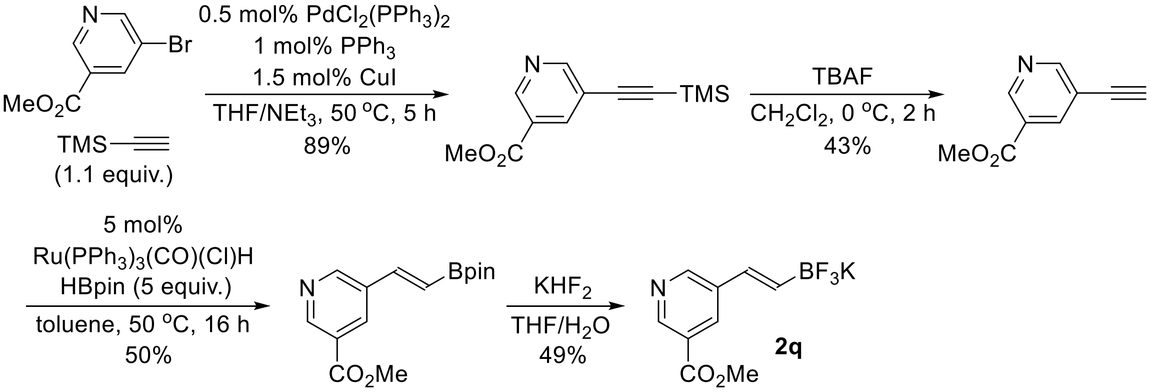
^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 8.76 (d, *J* = 2.0 Hz, 1 H), 7.87 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.66 (d, *J* = 8.4 Hz, 1 H), 7.36 (d, *J* = 18.4 Hz, 1 H), 6.38 (d, *J* = 18.4, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt) δ 150.1, 143.5, 136.2, 134.0, 133.2, 128.4, 117.3, 84.1, 24.9. **^{11}B NMR** (128.4 MHz, $CDCl_3$, rt) δ 29.3.

HRMS (ESI-TOF): calculated for $[C_{14}H_{17}BN_2O_2\text{-}H]^-$ requires 255.1313, found 255.1310.

To a solution of (E)-5-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)--vinyl)picolinonitrile (1.3 g, 5.47 mmol) in THF (20 mL) was added a solution of KHF_2 (2.38 g, 30.5 mmol) in water (10 mL). The raction mixture was stirred at room temperature for 5 h. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum, and the crude product was washed with ether, pentane and CH_2Cl_2 to afford **2p** as a white solid (0.48 g, 40% yield).

^{1}H NMR (400 MHz, DMSO, rt) δ 8.67 (d, *J* = 2.0 Hz, 1 H), 7.95 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.86 (d, *J* = 8.4 Hz, 1 H), 6.61-6.58 (m, 2 H). **^{13}C NMR** (100 MHz, DMSO, rt) δ 148.8, 139.0, 132.7, 129.1, 128.7, 128.5, 117.8. **^{11}B NMR** (128.4 MHz, DMSO, rt) δ 2.35. **^{19}F NMR** (376.5 MHz, DMSO, rt) δ -138.8. **HRMS** (ESI-TOF): calculated for $[C_8H_5BF_3N]^-$ requires 197.0505, found 197.0508.

Potassium (*E*)-2-[3-(3-Pyridinecarboxylic acid methyl ester)]ethenyltrifluoroborate (2q)



A 2-neck 300 mL round-bottom flask was charged with 5-bromo-3-pyridinecarboxylic acid methyl ester (2.5 g, 11.6 mmol), $PdCl_2(PPh_3)_2$ (39 mg, 0.056 mmol), PPh_3 (30 mg, 0.11 mmol), dry THF (25 mL) and NEt_3 (13 mL) under N_2. After bubbling N_2 into the solution for 15 min, CuI (22 mg, 0.11 mmol) and trimethylsilylacetylene (1.8 mL, 12.7 mmol) were added sequentially. The reaction mixture was stirred at 50 °C for 5 h. After cooling to room temperature, the precipitate (NEt_3•HBr) was filtered off and washed with EtOAc. The filtrate solution was concentrated and residue was diluted with ether/hexane. The crude product was purified by flash column chromatography on silica gel (hexane→hexane/AcOEt = 10/1→4/1) to afford the methyl 5-((trimethylsilyl)ethynyl)nicotinate as a pale yellow solid (2.42 g, 89% yield).

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 9.10 (d, J = 2.0 Hz, 1 H), 8.81 (d, J = 2.0 Hz, 1 H), 8.33 (dd, J = 2.0, 2.0 Hz, 1 H), 3.95 (s, 3 H), 0.27 (s, 9 H).

A 2-neck 100 mL round-bottom flask was charged with TMS-alkyne (1.86 g, 7.9 mmol), and dry THF (15 mL), then TBAF (1.0 M THF soln.) (13 mL, 13 mmol) was added to the solution at 0 °C under N_2. The reaction mixture was stirred at 0 °C for 1 h. The reaction mixture was extracted with CH_2Cl_2, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1→3/1) to afford the methyl 5-ethynylnicotinate as a white solid (0.72 g, 43% yield). The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 9.15 (d, J = 2.4 Hz, 1 H), 8.85 (d, J = 2.0 Hz, 1 H), 8.36 (dd, J = 2.4, 2.0 Hz, 1 H), 3.96 (s, 3 H), 3.27 (s, 1 H).

Ref.: S. L. Bender, D. Bhumralkar, M. R. Collins, S. J. Cripps, J. G. Deal, L. Jia, M. D. Nambu, C. L. Palmer, Z. Peng, M. D. Varney, Patent: US2002/103203 A1, **2002**.

A 2-neck 100 mL round-bottom flask was charged with methyl 5-ethynylnicotinate (1.22

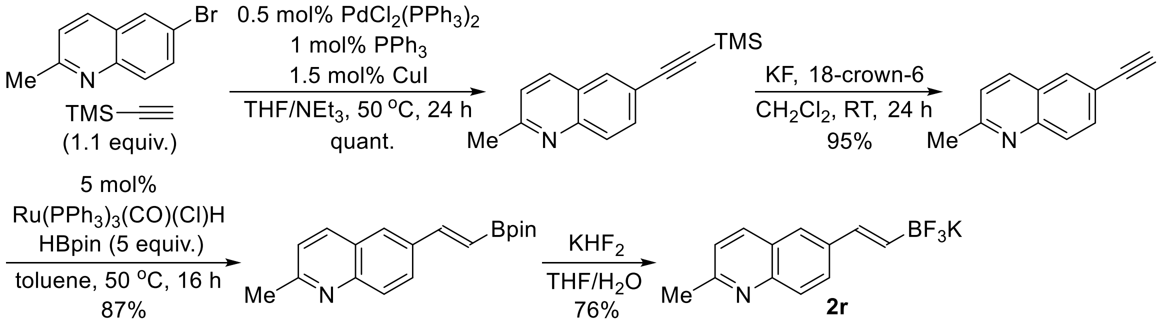
g, 7.57 mmol), $Ru(PPh_3)_3(CO)(Cl)H$ (358 mg, 0.38 mmol) and dry toluene (31 mL), then HBpin (5.5 mL, 37.9 mmol) was added to the mixture under N_2. The reaction mixture was stirred at 50 ^{o}C for 16 h. After cooling to room temperature, the solvent was removed under vaccum. Resulting reaction mixture was diluted with Et_2O, washed with sat. aq. $NaHCO_3$, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (hexane→hexane/AcOEt = 9/1→4/1) to afford the methyl (*E*)-5-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)nicotinate as a white solid (1.10 g, 50% yield).

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 9.11 (d, J = 2.0 Hz, 1 H), 8.82 (d, J = 2.4 Hz, 1 H), 8.39 (dd, J = 2.4, 2.0 Hz, 1 H), 7.40 (d, J = 18.8 Hz, 1 H), 6.34 (d, J = 18.8 Hz, 1 H), 3.96 (s, 3 H), 1.32 (s, 9 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt) δ 165.7, 152.4, 150.6, 144.5, 134.3, 133.0, 126.2, 83.8, 52.6, 24.9. **^{11}B NMR** (128.4 MHz, $CDCl_3$, rt) δ 28.5. **HRMS** (ESI-TOF): calculated for $[C_{15}H_{20}BNO_4\text{-}H]^-$ requires 288.1415, found 288.1463.

To a solution of methyl (*E*)-5-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)--vinyl)nicotinate (1.0 g, 3.45 mmol) in dry THF (20 mL) was added a solution of KHF_2 (1.62 g, 20.8 mmol) in water (10 mL). The raction mixture was stirred at room temperature for 5 h. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum, and the crude product was washed with ether, pentane and CH_2Cl_2 for several times to afford **2q** as a white solid (0.45 g, 49% yield).

^{1}H NMR (400 MHz, DMSO, rt) δ 8.82 (d, J = 1.6 Hz, 1 H), 8.72 (d, J = 2.0 Hz, 1 H), 8.15 (dd, J = 2.0, 1.6 Hz, 1 H), 6.56 (d, J = 18.4 Hz, 1 H), 6.42 (dq, J = 18.4, 3.6 Hz, 1 H), 3.88 (s, 3 H). **^{13}C NMR** (100 MHz, DMSO, rt) δ 165.4, 151.0, 146.9, 135.4, 131.8, 128.3, 125.3, 52.1. **^{11}B NMR** (128.4 MHz, DMSO, rt) δ 2.27. **^{19}F NMR** (376.5 MHz, DMSO, rt) δ -138.5. **HRMS** (ESI-TOF): calculated for $[C_9H_8BF_3NO_2]^-$ requires 230.0607, found 230.0610.

Potassium (*E*)-2-[6-(2-Methylquinoline)]ethenyltrifluoroborate (2r)



A 2-neck 300 mL round-bottom flask was charged with 6-bromo-2-methylquinoline (5.0 g, 22.5 mmol), $PdCl_2(PPh_3)_2$ (79 mg, 0.112 mmol), PPh_3 (59 mg, 0.225 mmol), dry THF (21 mL) and NEt_3 (30 mL) under N_2. After bubbling N_2 into the solution for 15 min, CuI (43 mg, 0.225 mmol) and trimethylsilylacetylene (3.5 mL, 24.8 mmol) were added sequentially. The reaction mixture was stirred at 50 °C for 24 h. After cooling to room temperature, the precipitate (NEt_3•HBr) was filtered off and washed with EtOAc. The filtrate solution was concentrated and residue was diluted with ether/hexane. The crude product was purified by flash column chromatography on silica gel (hexane→hexane/AcOEt = 4/1) to afford the 2-methyl-6-((trimethylsilyl)ethynyl)quinoline as a pale yellow solid (5.5 g, quant.). The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 7.96 (d, J = 8.4 Hz, 1 H), 7.92-7.90 (m, 2 H), 7.70 (d, J = 8.8 Hz, 1 H), 7.28 (d, J = 8.4 Hz, 1 H), 2.73 (s, 3 H), 0.27 (s, 9 H).

Ref.: CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE, P. Dalko, M. Petit, D. Ogden, F. Acher, WO2011/86469 A1, 40.

A 2-neck 100 mL round-bottom flask was charged with TMS-alkyne (3.0 g, 12.5 mmol), 18-crown-6-ether (3.3 g, 12.5 mmol) and dry CH_2Cl_2 (20 mL), then KF (1.45 g, 25 mmol) was added to the mixture under N_2. The reaction mixture was stirred at room temperature for 24 h. Resulting reaction mixture was extracted with CH_2Cl_2, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (pentane/Et_2O = 4/1 → 3/1) to afford the 6-ethynyl-2-methylquinoline as a white solid (1.99 g, 95% yield). The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 8.00-7.93 (m, 3 H), 7.71 (dd, J = 8.4, 2.0 Hz, 1 H), 7.29 (d, J = 8.8, Hz, 1 H), 3.15 (s, 1 H), 2.74 (s, 3 H).

Ref.: CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE, P. Dalko, M. Petit, D. Ogden, F. Acher, WO2011/86469 A1, 40.

A 2-neck 100 mL round-bottom flask was charged with 6-ethynyl-2-methylquinoline (1.5

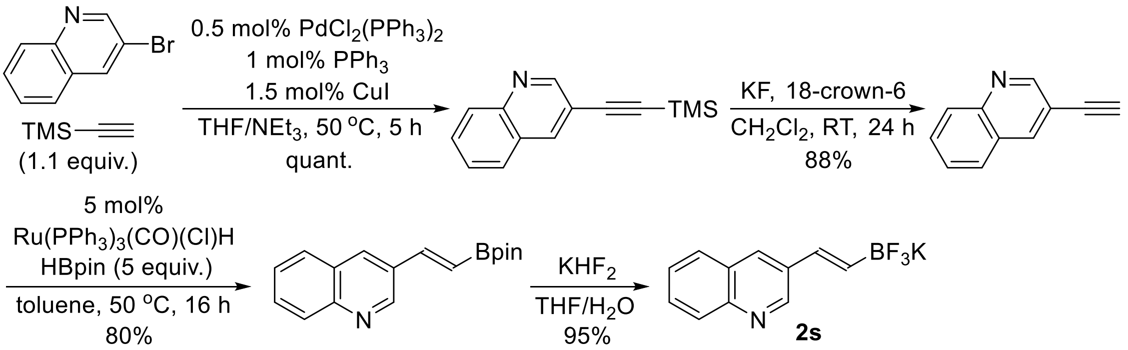
g, 8.97 mmol), Ru(PPh$_3$)$_3$(CO)(Cl)H (427 mg, 0.45 mmol) and dry toluene (36 mL), then HBpin (6.5 mL, 45 mmol) was added to the mixture under N$_2$. The reaction mixture was stirred at 50 ^{o}C for 16 h. After cooling to room temperature, the solvent was removed under vaccum. Resulting reaction mixture was diluted with Et$_2$O, washed with sat. aq. NaHCO$_3$, dried (Na$_2$SO$_4$), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1→4/1→2/1→ 1/1) to afford the (*E*)-2-methyl-6-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)quinoline as a white solid (2.3 g, 87% yield).

^{1}H NMR (400 MHz, CDCl$_3$, rt) δ 8.01 (dd, *J* = 8.4, 3.6 Hz, 1 H), 7.96 (d, *J* = 8.8 Hz, 1 H), 7.87 (dd, *J* = 8.8, 1.6 Hz, 1 H), 7.76 (s, 1 H), 7.54 (d, *J* = 18.4 Hz, 1 H), 7.29-7.25 (m, 1 H), 6.28 (d, *J* = 18.4, 1 H), 2.72 (s, 3 H), 1.32 (s, 12 H). **^{13}C NMR** (100 MHz, CDCl$_3$, rt) δ 159.4, 148.7, 148.3, 136.5, 135.0, 129.0, 127.3, 127.1, 126.5, 122.4, 83.5, 25.0, 24.9. **^{11}B NMR** (128.4 MHz, CDCl$_3$, rt) δ 29.8. **HRMS** (ESI-TOF): calculated for $[C_{18}H_{22}BNO_2\text{-}H]^-$ requires 294.1674, found 294.1643.

To a solution of (*E*)-2-methyl-6-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)- -vinyl)quinoline (1.3 g, 4.4 mmol) in dry THF (10 mL) was added a solution of KHF$_2$ (2.06 g, 26.4 mmol) in water (10 mL). The raction mixture was stirred at room temperature for 5 h. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum, and the crude product was washed with ether, pentane and CH$_2$Cl$_2$ to afford **2r** as a white solid (0.92 g, 76% yield).

^{1}H NMR (400 MHz, DMSO, rt) δ 8.14 (d, *J* = 8.4 Hz, 1 H), 7.82-7.76 (m, 2 H), 7.67 (s, 1 H), 7.33 (d, *J* = 8.4 Hz, 1 H), 6.64 (d, *J* = 18.0 Hz, 1 H), 6.35 (dq, *J* = 18.0, 3.6 Hz, 1 H). **^{13}C NMR** (100 MHz, DMSO, rt) δ 157.2, 146.5, 137.5, 135.7, 132.4, 127.9, 126.9, 126.4, 123.5, 121.9, 24.6. **^{11}B NMR** (128.4 MHz, DMSO, rt) δ 2.40. **^{19}F NMR** (376.5 MHz, DMSO, rt) δ -137.9. **HRMS** (ESI-TOF): calculated for $[C_{12}H_{10}BF_3N]^-$ requires 236.0866, found 236.0873.

Potassium (*E*)-2-(6-Quinoline)ethenyltrifluoroborate (2s)



2s

A 2-neck 300 mL round-bottom flask was charged with 3-bromoquinoline (6.0 g, 28.8 mmol), $PdCl_2(PPh_3)_2$ (82 mg, 0.117 mmol), PPh_3 (61 mg, 0.233 mmol), dry THF (18 mL) and NEt_3 (27 mL) under N_2. After bubbling N_2 into the solution for 15 min, CuI (44 mg, 0.233 mmol) and trimethylsilylacetylene (4.5 mL, 31.7 mmol) were added sequentially. The reaction mixture was stirred at 50 °C for 24 h. After cooling to room temperature, the precipitate (NEt_3•HBr) was filtered off and washed with EtOAc. The filtrate solution was concentrated and residue was diluted with ether/hexane. The crude product was purified by flash column chromatography on silica gel (hexane→hexane/AcOEt = 9/1) to afford the 3-((trimethylsilyl)ethynyl)quinoline as a brown oil (6.7 g, quant.). The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 8.91 (d, *J* = 2.0 Hz, 1 H), 8.24 (br s, 1 H), 8.07 (d, *J* = 8.4 Hz, 1 H), 7.75 (d, *J* = 8.0 Hz, 1 H), 7.70 (dd, *J* = 8.0, 8.4 Hz, 1 H), 7.54 (dd, *J* = 8.4, 8.0 Hz, 1 H), 0.29 (s, 9 H).

Ref.: T. Li, L. Guo, Y. Zhang, J. Wang, Z. Li, L. Lin, Z. Zhang, L. Li, J. Lin, W. Zhao, J. Li, P. G. Wang, Carbohydrate Research, **2011**, *346*, 1083.

A 2-neck 100 mL round-bottom flask was charged with TMS-alkyne (6.7 g, 29.7 mmol), 18-crown-6-ether (7.86 g, 29.7 mmol) and dry CH_2Cl_2 (40 mL), then KF (3.45 g, 59.4 mmol) was added to the mixture under N_2. The reaction mixture was stirred at room temperature for 24 h. Resulting reaction mixture was extracted with CH_2Cl_2, dried (Na_2SO_4), and filtered. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography on silica gel (pentane/Et_2O = 4/1→3/2) to afford the 3-ethynylquinoline as a pale yellow solid (4.0 g, 88% yield). The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 8.94 (d, *J* = 2.0 Hz, 1 H), 8.28 (br s, 1 H), 8.09 (d, *J* = 8.4 Hz, 1 H), 7.78 (d, *J* = 8.0 Hz, 1 H), 7.73 (dd, *J* = 7.6, 7.2 Hz, 1 H), 7.57 (dd, *J* = 7.6, 7.2 Hz, 1 H), 3.27 (s, 1 H).

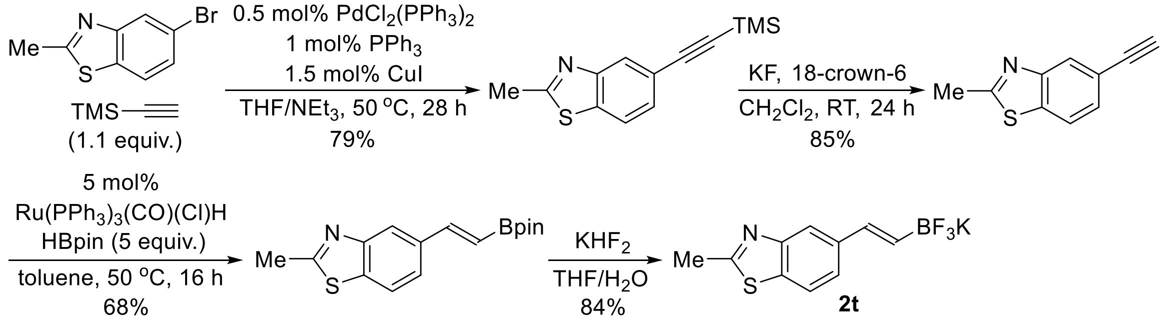
Ref.: N. S. Gulykina, T.M. Dolgina, G. N. Bondarenko, and I. P. Beletskaya, *Russian Journal of Organic Chemistry*, **2003**, *39*, 797.

A 2-neck 100 mL round-bottom flask was charged with 3-ethynylquinoline (1.5 g, 9.79 mmol), $Ru(PPh_3)_3(CO)(Cl)H$ (464 mg, 0.49 mmol) and dry toluene (39 mL), then HBpin (7.1 mL, 49 mmol) was added to the mixture under N_2. The mixture was stirred at 50 °C for 16 h. After cooling to room temperature, the solvent was removed under vaccum. Resulting reaction mixture was diluted with Et_2O, washed with sat. aq. $NaHCO_3$, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 9/1 → 4/1) to afford the corresponding (*E*)-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)quinoline as a yellow solid (2.2 g, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 9.08 (dd, *J* = 1.6 Hz, 1 H), 8.15 (br s, 1 H), 8.07 (d, *J* = 8.4 Hz, 1 H), 7.82 (d, *J* = 8.4 Hz, 1 H), 7.69 (dd, *J* = 7.6, 7.6 Hz, 1 H), 7.60-7.52 (m, 2 H), 6.41 (d, *J* = 18.8, 1 H), 1.33 (s, 12 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt) δ 149.6, 148.2, 146.0, 133.7, 130.4, 129.8, 129.4, 128.3, 128.0, 127.1, 83.7, 24.9. **^{11}B NMR** (128.4 MHz, $CDCl_3$, rt) δ 29.4. **HRMS (ESI-TOF)**: calculated for $[C_{17}H_{20}BNO_2\text{-}H]^-$ requires 280.1517, found 281.1541.

To a solution of (*E*)-3-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)quinoline (2.0 g, 7.1 mmol) in dry THF (28 mL) was added a solution of KHF_2 (3.33 g, 42.7 mmol) in water (10 mL). The raction mixture was stirred at room temperature for overnight. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum, and the crude product was washed with ether, pentane and CH_2Cl_2 for several times to afford **2r** as a white solid (1.77 g, 95% yield). **^{1}H NMR** (400 MHz, DMSO, rt) δ 8.97 (s, 1 H), 8.14 (s, 1 H), 7.94 (d, *J* = 8.4 Hz, 1 H), 7.91 (d, *J* = 8.0 Hz, 1 H), 7.64 (m, 1 H), 7.53 (dd, *J* = 8.0, 8.0 Hz, 1 H), 6.68 (d, *J* = 18.4 Hz, 1 H), 6.53 (dq, *J* = 18.4, 3.2 Hz, 1 H). **^{13}C NMR** (100 MHz, DMSO, rt) δ 149.4, 146.3, 132.9, 130.1, 129.8, 128.5, 128.1, 128.0, 127.8, 126.4. **^{11}B NMR** (128.4 MHz, DMSO, rt) δ 2.51. **^{19}F NMR** (376.5 MHz, DMSO, rt) δ -138.2. **HRMS** (ESI-TOF): calculated for $[C_{11}H_8BF_3N]^-$ requires 222.0709, found 222.0746.

Potassium (*E*)-2-[5-(2-Methylbenzothiazole)]ethenyltrifluoroborate (2t)



A 2-neck 300 mL round-bottom flask was charged with 5-bromo-2-methylbenzothiazole (5.0 g, 21.9 mmol), $PdCl_2(PPh_3)_2$ (294 mg, 0.42 mmol), PPh_3 (220 mg, 0.84 mmol), dry THF (17 mL) and NEt_3 (25 mL) under N_2. After bubbling N_2 into the solution for 15 min, CuI (160 mg, 0.84 mmol) and trimethylsilylacetylene (3.4 mL, 24.1 mmol) were added sequentially. The reaction mixture was stirred at 50 °C for 28 h. After cooling to room temperature, the precipitate (NEt_3•HBr) was filtered off and washed with EtOAc. The filtrate solution was concentrated and residue was precipitated with ether/pentane. The crude product was washed with ether/penrane (1/1) for several times to afford the 2-methyl-5-((trimethylsilyl)ethynyl)benzo[d]thiazole as a pale pink solid (4.2 g, 79% yield).

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 8.02 (d, J = 1.4 Hz, 1 H), 7.72 (dd, J = 8.0, 0.4 Hz, 1 H), 7.43 (dd, J = 8.0, 1.4 Hz, 1 H), 2.83 (s, 3 H), 0.27 (s, 9 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt) δ 168.0, 153.3, 136.1, 128.4, 125.9, 121.3, 121.0, 104.8, 94.5, 20.3, 0.11. **HRMS (ESI-TOF)**: calculated for $[C_{13}H_{15}NSSi+H]^+$ requires 246.0767, found 246.0768.

A 2-neck 100 mL round-bottom flask was charged with TMS-alkyne (2.5 g, 10.2 mmol), 18-crown-6-ether (2.7 g, 10.2 mmol) and dry CH_2Cl_2 (15 mL), then KF (1.2 g, 20.4 mmol) was added to the mixture under N_2. The reaction mixture was stirred at room temperature for 24 h. Resulting reaction mixture was extracted with CH_2Cl_2, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (pentane/Et_2O = 4/1→3/2) to afford the 5-ethynyl-2-methylbenzo[*d*]thiazole as a yellow solid (1.50 g, 85% yield).

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 8.05 (d, J = 1.2 Hz, 1 H), 7.74 (d, J = 8.4 Hz, 1 H), 7.44 (dd, J = 8.4, 1.2 Hz, 1 H), 3.11 (s, 1 H), 2.82 (s, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt) δ 168.3, 153.3, 136.5, 128.4, 126.2, 121.4, 119.9, 83.5, 77.4, 20.3. **HRMS** (ESI-TOF): calculated for $[C_{10}H_7NS+H]^+$ requires 174.0372, found 174.0356.

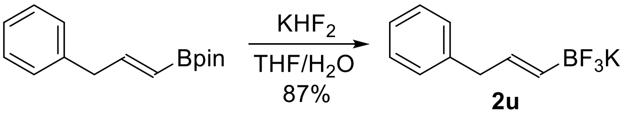
A 2-neck 100 mL round-bottom flask was charged with 5-ethynyl-2-methyl--benzo[*d*]thiazole (1.30 g, 7.5 mmol), $Ru(PPh_3)_3(CO)(Cl)H$ (356 mg, 0.375 mmol) and dry toluene (30 mL), then HBpin (5.4 mL, 37.5 mmol) was added to the mixture under N_2. The reaction mixture was stirred at 50 ^oC for 16 h. After cooling to room temperature, the solvent was removed under vaccum. Resulting reaction mixture was diluted with Et_2O, washed with sat. aq. $NaHCO_3$, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel (pentane→pentane/Et_2O = 4/1→3/2) to afford the (*E*)-2-methyl-5-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)benzo[*d*]thiazole as a yellow solid (1.54 g, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 8.01 (d, *J* = 1.2 Hz, 1 H), 7.75 (d, *J* = 8.4 Hz, 1 H), 7.53-7.47 (m, 2 H), 6.2 (d, *J* = 18.0 Hz, 1 H), 2.82 (s, 3 H), 1.32 (s, 9 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt) δ 167.7, 154.0, 149.1, 136.3, 136.1, 123.5, 121.4, 121.2, 83.5, 24.9, 20.2. **^{11}B NMR** (128.4 MHz, $CDCl_3$, rt) δ 29.5. **HRMS** (ESI-TOF): calculated for $[C_{16}H_{20}BNO_2S\text{-}H]^-$ requires 300.1238, found 300.1220.

To a solution of (*E*)-2-methyl-5-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)--vinyl)benzo[*d*]thiazole (1.2 g, 3.98 mmol) in dry THF (20 mL) was added a solution of KHF_2 (1.87 g, 23.9 mmol) in water (10 mL). The raction mixture was stirred at room temperature for overnight. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum, and the crude product was washed with ether, pentane and CH_2Cl_2 for several times to afford **2t** as a pale pink solid (0.94 g, 84% yield).

^{1}H NMR (400 MHz, DMSO, rt) δ 7.85 (d, *J* = 8.0 Hz, 1 H), 7.75 (d, *J* = 1.2 Hz, 1 H), 7.40 (dd, *J* = 8.4, 1.6 Hz, 1 H), 6.56 (d, *J* = 18.4 Hz, 1 H), 6.26 (dq, *J* = 18.4, 3.2 Hz, 1 H), 2.76 (s, 3 H). **^{13}C NMR** (100 MHz, DMSO, rt) δ 166.6, 153.6, 138.8, 132.6, 132.4, 122.4, 121.2, 118.3, 19.6. **^{11}B NMR** (128.4 MHz, DMSO, rt) δ 2.80. **^{19}F NMR** (376.5 MHz, DMSO, rt) δ -137.8. **HRMS** (ESI-TOF): calculated for $[C_{10}H_8BF_3NS]^-$ requires 242.0430, found 242.0436.

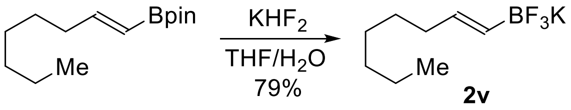
Potassium (*E*)-3-Phenyl-1-propen-1-yltrifluoroborate (2u)



To a solution of (*E*)-3-phenyl-1-propen-1-ylboronic acid (1.0 g, 6.17 mmol) in dry THF (30 mL) was added a solution of KHF_2 (2.9 g, 37 mmol) in water (15 mL). The raction mixture was stirred at room temperature for 4 h. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum to yield a mixture of **2u** and pinacol. The crude product was washed with ether, pentane and CH_2Cl_2 for several times to afford **2u** as a white solid (1.2 g, 87% yield).

^{1}H NMR (400 MHz, DMSO, rt) δ 7.28-7.23 (m, 2 H), 7.16-7.12 (m, 3 H), 5.66-5.58 (m, 1 H), 5.35-5.28 (m, 1 H), 3.21 (d, J = 6.4 Hz, 2 H). **^{13}C NMR** (100 MHz, DMSO, rt) δ 141.8, 132.4, 128.3, 127.9, 125.4, 41.9. **^{11}B NMR** (128.4 MHz, DMSO, rt) δ 2.41. **^{19}F NMR** (376.5 MHz, DMSO, rt) δ -137.4. **HRMS** (ESI-TOF): calculated for $[C_9H_9BF_3]^-$ requires 185.0757, found 185.0765.

Potassium (*E*)-1-Octen-1-yltrifluoroborate (2v)

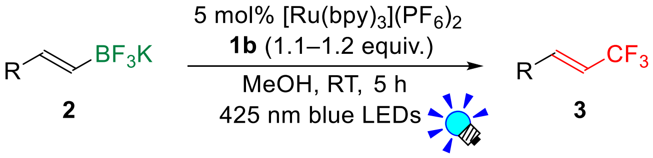


To a solution of (*E*)-1-octen-1-ylboronic acid (1.0 g, 6.4 mmol) in dry THF (30 mL) was added a solution of KHF_2 (3.0 g, 38 mmol) in water (15 mL). The raction mixture was stirred at room temperature for 5 h. The mixture was concentrated *in vacuo*. The residue was dissolved in hot acetone, and filtered. The filtrate was reduced under vacuum to yield a mixture of **2v** and pinacol. The crude product was washed with ether, pentane and CH_2Cl_2 to afford **2v** as a white solid (1.1 g, 79% yield).

^{1}H NMR (400 MHz, DMSO, rt) δ 5.47 (d, J = 18.0 Hz, 1 H), 5.20 (d, J = 18.0 Hz, 1 H), 1.87 (br s, 2 H), 1.24 (br s, 8 H), 0.85 (t, J = 6.0 Hz, 3 H). **^{13}C NMR** (100 MHz, DMSO, rt) δ 133.4, 35.2, 31.2, 29.1, 28.3, 22.0, 13.8. **^{11}B NMR** (128.4 MHz, DMSO, rt) δ 2.52. **^{19}F NMR** (376.5 MHz, DMSO, rt) δ -137.2. **HRMS** (ESI-TOF): calculated for $[C_8H_{15}BF_3]^-$ requires 179.1226, found 179.1240.

General Procedure for the Photocatalytic Synthesis of (*E*)-Trifluoromethylated Alkenes (Reaction Conditions in Table 7.2)

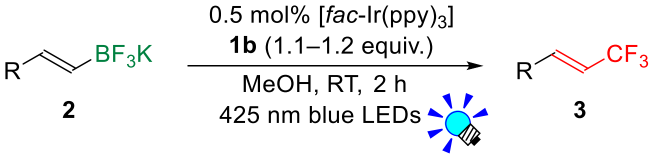
General Procedure A



20 mL-Schlenk tube was charged with Togni’s reagent (**1b**) (0.275–0.30 mmol, 1.1 eq–1.2

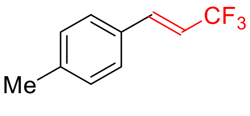
eq), [Ru(bpy)$_3$](PF$_6$)$_2$ (10.7 mg, 12.5 μmol, 5 mol%), alkenylborate (**2**) (0.25 mmol, 1.0 eq) and MeOH (5.0−10.0 mL) under N$_2$. **2** was dissolved with ultrasonic bath. The tube was placed at a distance of 2−3 cm from 3W blue LED lamp (hν = 425 ± 15 nm). The red solution was stirred at room temperature (water bath) under visible light irradiation. After 5 h, aqueous saturated NaHCO$_3$ solution was added. The resulting mixture was extracted with ether or pentane, dried (Na$_2$SO$_4$), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by chromatography on silica gel to afford trifluoromethylated alkene **3**.

General Procedure B



20 mL-Schlenk tube was charged with **1b** (0.275−0.30 mmol, 1.1 eq−1.2 eq), [*fac*-Ir(ppy)$_3$] (0.8 mg, 1.25 μmol, 0.5 mol%), **2** (0.25 mmol, 1.0 eq) and MeOH (5.0 mL) under N$_2$. **2** was dissolved with ultrasonic bath. The tube was placed at a distance of 2−3 cm from 3W blue LED lamp. The yellow solution was irradiated with visible light at room temperature (the stirring cause a lowering of *E*/*Z* selectivity). After 2 h, aqueous saturated NaHCO$_3$ solution was added. The resulting mixture was extracted with ether or pentane, dried (Na$_2$SO$_4$), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by chromatography on silica gel to afford trifluoromethylated alkene **3**.

(*E*)-1-(3,3,3-Trifluoroprop-1-enyl)-4-methylbenzene (3b)



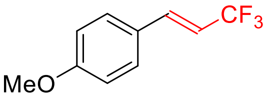
According to general procedure A, **1b** (348 mg, 1.1 mmol), [Ru(bpy)$_3$](PF$_6$)$_2$ (40 mg, 46.5 μmol), (*E*)-alkenylborate (**2b**) (224 mg, 1.0 mmol) and MeOH (20 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane) afforded **3b** (151.2 mg, 81% yield) as a white solid containing approximately 1% of (*Z*)-product. The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, CDCl$_3$, rt): δ 7.34 (d, J = 8.0 Hz, 2 H), 7.19 (d, J = 8.0 Hz, 2 H), 7.10

(dq, *J* = 16.4, 2.0 Hz, 1 H), 6.15 (dq, *J* = 16.4, 6.4 Hz, 1 H), 2.37 (s, 3 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 140.4, 137.7 (q, *J* = 6.6 Hz), 130.8, 129.7, 127.6, 123.9 (q, *J* = 267 Hz), 115.0 (q, *J* = 33.6 Hz), 21.4. **^{19}F NMR** (376.5 MHz, $CDCl_3$, rt): δ -63.11 (dd, *J* = 6.6, 2.2 Hz, 3 F).

Ref.: T. Liu, Q. Shen, *Org. Lett.* **2011**, *13*, 2342.

(*E*)-1-(3,3,3-Trifluoroprop-1-enyl)-4-methoxylbenzene (3c)

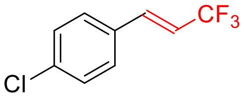


According to general procedure A, **1b** (84 mg, 0.266 mmol), $[Ru(bpy)_3](PF_6)_2$ (10.7 mg, 12.5 μmol), (*E*)-alkenylborate (**2c**) (56 mg, 0.233 mmol) and MeOH (10 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane/ether = 20/1) afforded **3c** (42 mg, 88% yield) as a white solid containing approximately 1% of (*Z*)-product. The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.39 (dd, *J* = 7.0, 2.0 Hz, 2 H), 7.07 (dq, *J* = 16.0, 2.0 Hz, 1 H), 7.91 (dd, *J* = 7.0, 2.0 Hz, 2 H), 6.06 (dq, *J* = 16.0, 6.8 Hz, 1 H), 3.83 (s, 3 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 161.2, 137.3 (q, *J* = 6.7 Hz), 129.1, 126.3, 124.1 (q, *J* = 262 Hz), 114.5, 113.6 (q, *J* = 33.7 Hz), 21.4. **^{19}F NMR** (376.5 MHz, $CDCl_3$, rt): δ -62.85 (d, *J* = 6.7 Hz, 3 F).

Ref.: T. Liu, Q. Shen, *Org. Lett.* **2011**, *13*, 2342.

(*E*)-1-(3,3,3-Trifluoroprop-1-enyl)-4-chlorobenzene (3d)

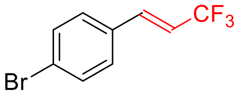


According to general procedure A, **1b** (87 mg, 0.275 mmol), $[Ru(bpy)_3](PF_6)_2$ (10.7 mg, 12.5 μmol), (*E*)-alkenylborate (**2d**) (87 mg, 0.25 mmol) and MeOH (5.0 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane) afforded **3d** (37 mg, 72% yield) as a colorless oil containing approximately 3% of (*Z*)-product. The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.41-7.35 (m, 4 H), 7.10 (dq, J = 16.4, 2.0 Hz, 1 H), 6.18 (dq, J = 16.4, 6.4 Hz, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 136.6 (q, J = 6.7 Hz), 136.1, 132.1, 129.3, 128.8, 123.5 (q, J = 267 Hz), 116.7 (q, J = 33.7 Hz). **^{19}F NMR** (376.5 MHz, $CDCl_3$, rt): δ -63.44 (d, J = 7.3 Hz, 3 F).

Ref.: T. Hanamoto, N. Morita, K. Shindo, *Eur. J. Org. Chem.* **2003**, *21*, 4279.

(*E*)-1-(3,3,3-Trifluoroprop-1-enyl)-4-bromobenzene (3e)

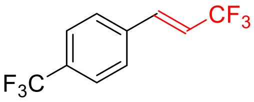


According to general procedure A, **1b** (90 mg, 0.284 mmol), $[Ru(bpy)_3](PF_6)_2$ (10.7 mg, 12.5 μmol), (*E*)-alkenylborate (**2e**) (72 mg, 0.25 mmol) and MeOH (5.0 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane) afforded **3e** (47 mg, 81% yield) as a colorless oil containing approximately 4% of (*Z*)-product. The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.53 (d, J = 8.4 Hz, 2 H), 7.31 (d, J = 8.4 Hz, 2 H), 7.09 (dq, J = 16.4, 2.0 Hz, 1 H), 6.20 (dq, J = 16.4, 6.8 Hz, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 136.6 (q, J = 6.6 Hz), 132.5, 132.3, 129.1, 124.4, 123.5 (q, J = 267 Hz), 116.9 (q, J = 33.8 Hz). **^{19}F NMR** (376.5 MHz, $CDCl_3$, rt): δ -63.49 (d, J = 6.9 Hz, 3 F).

Ref.: A. T. Parsons, T. D. Senecal, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2012**, *51*, 2947.

(*E*)-1-(3,3,3-Trifluoroprop-1-enyl)-4-trifluoromethylbenzene (3f)



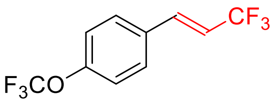
According to general procedure B, **1b** (87 mg, 0.275 mmol), [*fac*-$Ir(ppy)_3$] (0.8 mg, 1.25 μmol), (*E*)-alkenylborate (**2f**) (70 mg, 0.25 mmol) and MeOH (5.0 mL) were irrradiated with blue LEDs for 2 h. After workup, purification by column chromatography on silica gel (pentane) afford **3f** (47 mg, 79% yield) as a colorless oil containing approximately 4% of (*Z*)-product. The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.66 (d, J = 8.4 Hz, 2 H), 7.56 (d, J = 8.4 Hz, 2 H), 7.19

(dq, *J* = 16.0, 2.0 Hz, 1 H), 6.30 (dq, *J* = 16.0, 6.4 Hz, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): *δ* 137.0, 136.4 (q, *J* = 6.5 Hz), 131.2 (q, *J* = 32.7 Hz), 127.9, 126.1, 123.9 (q, *J* = 271 Hz), 123.3 (q, *J* = 268 Hz), 118.7 (q, *J* = 34.0 Hz). **^{19}F NMR** (376.5 MHz, $CDCl_3$, rt): *δ* -62.92 (s, 3 F), -63.80 (d, *J* = 5.1 Hz, 3 F).

Ref.: T. Hanamoto, N. Morita, K. Shindo, *Eur. J. Org. Chem.* **2003**, *21*, 4279.

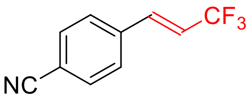
(*E*)-1-(3,3,3-Trifluoroprop-1-enyl)-4-trifluoromethoxybenzene (3g)



According to general procedure A, **1b** (90 mg, 0.284 mmol), $[Ru(bpy)_3](PF_6)_2$ (10.7 mg, 12.5 μmol), (*E*)-alkenylborate (**2g**) (70 mg, 0.238 mmol) and MeOH (5.0 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane/ether = 10/1) afforded **3g** (42 mg, 69% yield) as a colorless oil containing approximately 6% of (*Z*)-product.

^{1}H NMR (400 MHz, $CDCl_3$, rt): *δ* 7.49 (d, *J* = 8.8 Hz, 2 H), 7.24 (d, *J* = 8.8 Hz, 2 H), 7.13 (dq, *J* = 16.0, 2.0 Hz, 1 H), 6.19 (dq, *J* = 16.0, 6.4 Hz, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): *δ* 150.4, 136.3 (q, *J* = 6.8 Hz), 132.2, 129.1, 123.4 (q, *J* = 267 Hz), 121.4, 120.6 (q, *J* = 262 Hz), 117.0 (q, *J* = 34.0 Hz). **^{19}F NMR** (376.5 MHz, $CDCl_3$, rt): *δ* -57.84 (s, 3 F), -63.56 (d, *J* = 6.6 Hz, 3 F). **HRMS** (ESI-TOF): calculated for $[C_{10}H_6F_6O+Na]^+$ requires 279.0215, found 279.0210.

(*E*)-4-(3,3,3-Trifluoroprop-1-enyl)benzenecarbonitrile (3h)



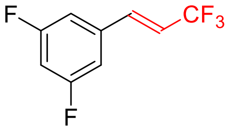
According to general procedure A, Togni's reagent (**1a**) (90 mg, 0.284 mmol), $[Ru(bpy)_3](PF_6)_2$ (8.9 mg, 10.3 μmol), (*E*)-vinylborate (**2h**) (52 mg, 0.221 mmol) and MeOH (10 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane/ether = 20/1) afforded **3h** (34 mg, 78% yield) as a white solid containing approximately 3% of (*Z*)-product. The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt): *δ* 7.69 (d, *J* = 8.4 Hz, 2 H), 7.55 (d, *J* = 8.4 Hz, 2 H), 7.17

(dq, *J* = 16.0, 2.4 Hz, 1 H), 6.31 (dq, *J* = 16.4, 6.4 Hz, 1 H). ^{13}**C NMR** (100 MHz, $CDCl_3$, rt): δ 137.8, 136.0 (q, *J* = 6.7Hz), 132.8, 128.1, 123.1 (q, *J* = 268 Hz), 119.6 (q, *J* = 34.2 Hz), 118.3, 113.6. ^{19}**F NMR** (376.5 MHz, $CDCl_3$, rt): δ -63.90 (d, *J* = 4.5 Hz, 3 F).

Ref.: T. Kobayashi, T. Eba, O. Tamura, H. Ishibashi, *J. Org. Chem.* **2002**, *67*, 3156.

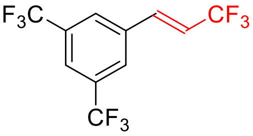
(*E*)-1-(3,3,3-Trifluoroprop-1-enyl)-3,5-difluorobenzene (3i)



According to general procedure A, **1b** (87 mg, 0.275 mmol), $[Ru(bpy)_3](PF_6)_2$ (10.7 mg, 12.5 µmol), (*E*)-alkenylborate (**2i**) (61 mg, 0.25 mmol) and MeOH (5.0 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane) afforded **3i** (35 mg, 68% yield) as a colorless oil containing approximately 5% of (*Z*)-product.

^{1}**H NMR** (400 MHz, $CDCl_3$, rt): δ 7.07 (dq, *J* = 16.0, 2.0 Hz, 1 H), 7.01-6.94 (m, 2 H), 6.88-6.81 (m, 1 H), 6.22 (dq, *J* = 16.0, 6.4 Hz, 1 H). ^{13}**C NMR** (100 MHz, $CDCl_3$, rt): δ 163.4 (d, *J* = 248 Hz), 136.9 (q, *J* = 9.4 Hz), 135.8, 123.1 (q, *J* = 267 Hz), 118.9 (q, *J* = 34.3 Hz), 110.5 (d, *J* = 26.0 Hz), 105.4 (t, *J* = 25.3 Hz). ^{19}**F NMR** (376.5 MHz, $CDCl_3$, rt): δ -63.84 (d, *J* = 7.5 Hz, 3 F), -108.75 (m, 2 F). **HRMS** (ESI-TOF): calculated for $[C_9H_5F_5+Na]^+$ requires 231.0204, found 231.0208.

(*E*)-1-(3,3,3-Trifluoroprop-1-enyl)-3,5-ditrifluoromethylbenzene (3j)

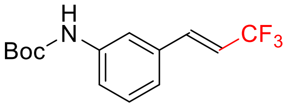


According to general procedure B, **1b** (94 mg, 0.30 mmol), [*fac*-$Ir(ppy)_3$] (0.8 mg, 1.25 µmol), (*E*)-alkenylborate (**2j**) (86.5 mg, 0.25 mmol) and MeOH (5.0 mL) were irrradiated with blue LEDs for 2 h. After workup, purification by column chromatography on silica gel (pentane) afforded **3j** (63 mg, 81% yield) as a colorless oil containing approximately 2% of (*Z*)-product.

^{1}**H NMR** (400 MHz, $CDCl_3$, rt): δ 7.89 (br s, 3 H), 7.24 (dq, *J* = 16.4, 2.0 Hz, 1 H), 6.39 (dq, *J* = 16.4, 6.0 Hz, 1 H). ^{13}**C NMR** (100 MHz, $CDCl_3$, rt): δ 135.7, 135.3 (q, *J* = 6.6 Hz), 132.8 (*J* = 33.6 Hz), 127.5, 123.5, 123.1 (q, *J* = 271 Hz), 122.9 (q, *J* = 268 Hz), 120.2 (q, *J*

= 34.5 Hz). **^{19}F NMR** (376.5 MHz, CDCl$_3$, rt): δ -63.13 (s, 3 F), -63.14 (s, 3 F), -64.06 (d, J = 6.4 Hz, 3 F). **HRMS** (ESI-TOF): calculated for [$C_{11}H_5F_9$+Na]$^+$ requires 331.0140, found 331.0145.

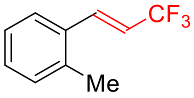
(*E*)-1-(3,3,3-Trifluoroprop-1-enyl)-3-*tert*-butoxycarbonylaminobenzene (3k)



According to general procedure A, **1b** (90 mg, 0.284 mmol), [Ru(bpy)$_3$](PF$_6$)$_2$ (9.0 mg, 10.5 µmol), (*E*)-alkenylborate (**2k**) (78 mg, 0.240 mmol) and MeOH (5.0 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane/ether = 10/1) afford **3k** (64 mg, 93% yield) as a white solid containing approximately 5% of (*Z*)-product.

^{1}H NMR (400 MHz, CDCl$_3$, rt): δ 7.64 (s, 1 H), 7.32-7.22 (m, 2 H), 7.13-7.09 (m, 2 H), 6.56 (br s, 1 H), 6.21 (dq, J = 16.0, 6.4 Hz, 1 H), 1.53 (s, 9 H). **^{13}C NMR** (100 MHz, CDCl$_3$, rt): δ 152.8, 139.2, 137.6 (q, J = 6.6 Hz), 134.5, 129.6, 124.0 (q, J = 267 Hz), 122.4, 120.1, 117.3, 116.5 (q, J = 33.8 Hz), 81.0, 28.4. **^{19}F NMR** (376.5 MHz, CDCl$_3$, rt): δ -63.37 (d, J = 3.8 Hz, 3 F). **HRMS** (ESI-TOF): calculated for [$C_{14}H_{16}F_3NO_2$+Na]$^+$ requires 310.1025, found 310.1025.

(*E*)-1-(3,3,3-Trifluoroprop-1-enyl)-2-methylbenzene (3l)

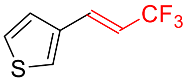


According to general procedure A, **1b** (90 mg, 0.284 mmol), [Ru(bpy)$_3$](PF$_6$)$_2$ (10.7 mg, 12.5 µmol), (*E*)-alkenylborate (**2k**) (56 mg, 0.25 mmol) and MeOH (5.0 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane) afforded **3k** (33 mg, 70% yield) as a colorless oil containing approximately 3% of (*Z*)-product.

^{1}H NMR (400 MHz, CDCl$_3$, rt): δ 7.48-7.40 (m, 2 H), 7.31-7.20 (m, 3 H), 6.12 (dq, J = 19.6, 6.4 Hz, 1 H). **^{13}C NMR** (100 MHz, CDCl$_3$, rt): δ 137.0, 135.7 (q, J = 6.7 Hz), 132.8, 130.0, 129.9, 126.5, 126.3, 123.7 (q, J = 267 Hz), 117.3 (q, J = 33.4 Hz),19.7. **^{19}F NMR** (376.5 MHz, CDCl$_3$, rt): δ -63.32 (dd, J = 6.7, 2.2 Hz, 3 F).

Ref.: G. K. S. Prakash, H. S. Krishnan, P. V. Jog, A. P. Lyer, G. A. Olah, *Org. Lett.* **2012**, *14*, 1146–1149.

(*E*)-1-(3,3,3-Trifluoroprop-1-enyl)-3-thiophene (3m)

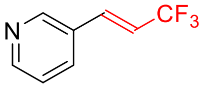


According to general procedure A, **1b** (79 mg, 0.25 mmol), [Ru(bpy)$_3$](PF$_6$)$_2$ (8.9 mg, 10.3 μmol), (*E*)-alkenylborate (**2m**) (60 mg, 0.275 mmol) and MeOH (10 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane/ether = 20/1) afforded **3m** (28 mg, 63% yield) as a pale yellow solid containing approximately 2% of (*Z*)-product and 2% of protodeboronated by-product. The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, CDCl$_3$, rt): δ 7.42 (d, J = 2.4 Hz, 1 H), 7.35 (dd, J = 5.2, 0.4 Hz, 1 H), 7.24 (dd, J = 5.2, 1.2 Hz, 1H), 7.14 (dq, J = 16.0, 2.0 Hz, 1 H), 6.05 (dq, J = 16.0, 6.4 Hz, 1 H). **^{13}C NMR** (100 MHz, CDCl$_3$, rt): δ 136.4, 131.6 (q, J = 6.8 Hz), 127.2, 127.0, 126.5 (q, J = 267 Hz), 125.0, 115.5 (q, J = 34.1 Hz). **^{19}F NMR** (376.5 MHz, CDCl$_3$, rt): δ -63.29 (dd, J = 6.7, 2.2 Hz, 3 F).

Ref.: A. T. Parsons, T. D. Senecal, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2012**, *51*, 2947.

(*E*)-3-(3,3,3-Trifluoroprop-1-enyl)pyridine (3n)

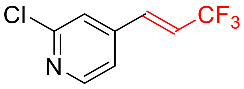


According to general procedure A, **1b** (90 mg, 0.284 mmol), [Ru(bpy)$_3$](PF$_6$)$_2$ (9.5 mg, 11.0 μmol), (*E*)-alkenylborate (**2n**) (52 mg, 0.246 mmol) and MeOH (5.0 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane/ether = 10/1→0/1) afforded **3n** (29 mg, 68% yield) as a pale yellow oil approximately 2% of (*Z*)-product. The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, CDCl$_3$, rt): δ 8.69 (d, J = 2.0 Hz, 1 H), 8.62 (dd, J = 4.8, 2.0 Hz, 1 H), 7.78 (dt, J = 8.0, 2.0 Hz, 1 H), 7.34 (dd, J = 8.0, 4.8 Hz, 1 H), 7.16 (dq, J = 16.4, 2.0 Hz, 1 H), 6.29 (dq, J = 16.4, 6.4 Hz, 1 H). **^{13}C NMR** (100 MHz, CDCl$_3$, rt): δ 151.1, 149.3, 134.6 (q, J = 6.8 Hz), 129.3, 123.8, 123.2 (q, J = 267 Hz), 118.4 (q, J = 34.3 Hz). **^{19}F NMR** (376.5 MHz, CDCl$_3$, rt): δ -63.82 (d, J = 7.2 Hz, 3 F).

Ref.: T. Kobayashi, T. Eba, O. Tamura, H. Ishibashi, *J. Org. Chem.* **2002**, *67*, 3156.

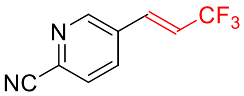
(*E*)-4-(3,3,3-Trifluoroprop-1-enyl)-2-chloropyridine (3o)



According to general procedure A, **1b** (87 mg, 0.275 mmol), $[Ru(bpy)_3](PF_6)_2$ (10.7 mg, 12.5 μmol), (*E*)-alkenylborate (**2o**) (61 mg, 0.25 mmol) and MeOH (8.0 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane/ether = 9/1→3/2) afforded **3o** (29 mg, 56% yield) as a colorless crystal.

^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 8.44 (d, J = 4.8 Hz, 1 H), 7.37 (s, 1 H), 7.25 (dd, J = 4.8, 1.6 Hz, 1 H), 7.07 (dq, J = 16.0, 2.0 Hz, 1 H), 6.41 (dq, J = 16.0, 6.4 Hz, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 152.8, 150.5, 143.9, 134.3 (q, J = 6.5 Hz), 122.6 (q, J = 268 Hz), 122.4, 121.9 (q, J = 34.6 Hz), 120.3. **^{19}F NMR** (376.5 MHz, $CDCl_3$, rt): δ -64.36 (d, J = 5.6 Hz, 3 F). **HRMS** (ESI-TOF): calculated for $[C_8H_5F_3NCl+Na]^+$ requires 229.9955, found 229.9956.

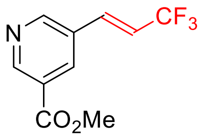
(*E*)-3-(3,3,3-Trifluoroprop-1-enyl)-2-cyanopyridine (3p)



According to general procedure A, **1b** (90 mg, 0.284 mmol), $[Ru(bpy)_3](PF_6)_2$ (8.6 mg, 10.0 μmol), (*E*)-alkenylborate (**2p**) (58 mg, 0.246 mmol) and MeOH (5.0 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane/ether = 10/1→0/1) afforded **3p** (32 mg, 66% yield) as a pale yellow solid containing approximately 1% of (*Z*)-product.

^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 8.79 (d, J = 2.0 Hz, 1 H), 7.91 (dd, J = 8.0, 2.4 Hz, 1 H), 7.74 (d, J = 8.0 Hz, 1 H), 7.19 (dq, J = 16.4, 2.0 Hz, 1 H), 6.41 (dq, J = 16.4, 6.0 Hz, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 150.2, 135.0, 134.6, 132.9 (q, J = 6.7 Hz), 132.4, 128.5, 122.6 (q, J = 268 Hz), 121.6 (q, J = 34.7 Hz), 116.8. **^{19}F NMR** (376.5 MHz, $CDCl_3$, rt): δ -64.26 (d, J = 7.1 Hz, 3 F). **HRMS** (ESI-TOF): calculated for $[C_9H_5F_3N_2+Na]^+$ requires 221.0297, found 221.0301.

(*E*)-3-(3,3,3-Trifluoroprop-1-enyl)-3-pyridinecarboxylic Acid Methy Ester (3q)

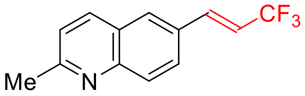


According to general procedure A, **1b** (90 mg, 0.284 mmol), $[Ru(bpy)_3](PF_6)_2$ (9.2 mg, 10.6 μmol), (*E*)-alkenylborate (**2q**) (63 mg, 0.234 mmol) and MeOH (10 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane/ether = 10/1→0/1) afforded **3q** (38 mg, 70% yield) as a colorless solid containing approximately 1% of (*Z*)-product.

^{1}**H NMR** (400 MHz, $CDCl_3$, rt): δ 9.20 (d, *J* = 2.0 Hz, 1 H), 8.83 (d, *J* = 2.0 Hz, 1 H), 8.39 (dd, *J* = 2.0, 2.0 Hz, 1 H), 7.20 (dq, *J* = 16.0, 2.0 Hz, 1 H), 6.41 (dq, *J* = 16.0, 6.4 Hz, 1 H), 3.98 (s, 3 H). ^{13}**C NMR** (100 MHz, $CDCl_3$, rt): δ 165.2, 152.6, 151.8, 134.9, 133.5 (q, *J* = 6.7 Hz), 129.3, 126.4, 123.0 (q, *J* = 268 Hz), 119.7 (q, *J* = 34.4 Hz), 52.7. ^{19}**F NMR** (376.5 MHz, $CDCl_3$, rt): δ -64.01 (d, *J* = 4.1 Hz, 3 F).

HRMS (ESI-TOF): calculated for $[C_{10}H_8F_3NO_2+Na]^+$ requires 254.0399, found 254.0399.

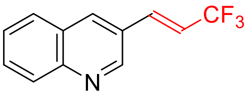
(*E*)-6-(3,3,3-Trifluoroprop-1-enyl)-2-methylquinoline (3r)



According to general procedure A, **1b** (95 mg, 0.30 mmol), $[Ru(bpy)_3](PF_6)_2$ (10.7 mg, 12.5 μmol), (*E*)-alkenylborate (**2r**) (66 mg, 0.24 mmol) and MeOH (5.0 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane/ether = 10/1) afforded **3r** (39 mg, 69% yield) as a colorless solid containing approximately 2% of (*Z*)-product.

^{1}**H NMR** (400 MHz, $CDCl_3$, rt): δ 8.07-8.01 (m, 2 H), 7.82-7.79 (m, 2 H), 7.35-7.27 (m, 2 H), 6.32 (dq, *J* = 16.4, 6.4 Hz, 1 H). ^{13}**C NMR** (100 MHz, $CDCl_3$, rt): δ 160.4, 148.7, 137.2 (q, *J* = 6.7 Hz), 136.4, 130.9, 129.7, 128.3, 127.0, 126.5, 123.7 (q, *J* = 267 Hz), 122.9, 116.8 (q, *J* = 33.9 Hz), 25.5. ^{19}**F NMR** (376.5 MHz, $CDCl_3$, rt): δ -63.28 (d, *J* = 6.7 Hz, 3 F). **HRMS** (ESI-TOF): calculated for $[C_{13}H_{10}F_3N+H]^+$ requires 238.0838, found 238.0839.

(*E*)-3-(3,3,3-Trifluoroprop-1-enyl)-quinoline (3s)

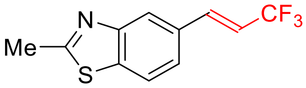


According to general procedure A, **1b** (87 mg, 0.275 mmol), $[Ru(bpy)_3](PF_6)_2$ (10.7 mg, 12.5 μmol), (*E*)-alkenylborate (**2s**) (63 mg, 0.241 mmol) and MeOH (5.0 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane/ether = 10/1 → 3/2) afforded **3s** (38 mg, 71% yield) as a pale yellow crystal.

^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 9.03 (s, 1 H), 8.20 (d, *J* = 2.0 Hz, 1 H), 8.12 (d, *J* = 8.0 Hz, 1 H), 7.85 (d, *J* = 8.0 Hz, 1 H), 7.77 (dt, *J* = 7.2, 1.6 Hz, 1 H), 7.60 (dt, *J* = 7.2, 1.6 Hz, 1 H), 7.33 (dq, *J* = 16.0, 2.0 Hz, 1 H), 6.45 (dq, *J* = 16.0, 6.4 Hz, 1 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 148.9, 148.7, 135.0, 134.8 (q, *J* = 6.6 Hz), 130.7, 129.6, 128.3, 127.6, 127.3, 126.5, 123.3 (q, *J* = 267 Hz), 118.0 (q, *J* = 34.1 Hz). **^{19}F NMR** (376.5 MHz, $CDCl_3$, rt): δ -63.63 (dd, *J* = 5.2, 2.2 Hz, 3 F).

HRMS (ESI-TOF): calculated for $[C_{12}H_8F_3N+H]^+$ requires 224.0682, found 224.0682.

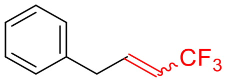
(*E*)-5-(3,3,3-Trifluoroprop-1-enyl)-2-methyl-1,3-benzothiazole (3t)



According to general procedure A, **1b** (87 mg, 0.275 mmol), $[Ru(bpy)_3](PF_6)_2$ (9.5 mg, 10.4 μmol), (*E*)-alkenylborate (**2t**) (70 mg, 0.25 mmol) and MeOH (5.0 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane/ether = 10/1) afforded **3t** (50 mg, 82% yield) as a white solid containing approximately 3% of (*Z*)-product.

^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.99 (s, 1 H), 7.83 (dd, *J* = 8.0, 4.4 Hz, 1 H), 7.45 (d, *J* = 8.4 Hz, 1 H), 7.26 (d, *J* = 16.0 Hz, 1 H), 6.28 (dq, *J* = 16.0, 6.4 Hz, 1 H), 2.85 (s, 3 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 168.5, 154.0, 137.5 (q, *J* = 6.7 Hz), 131.2, 123.7 (q, *J* = 267 Hz), 123.5, 121.8, 116.2 (q, *J* = 32.9 Hz), 20.2. **^{19}F NMR** (376.5 MHz, $CDCl_3$, rt): δ -63.21 (d, *J* = 6.4 Hz, 3 F). **HRMS** (ESI-TOF): calculated for $[C_{11}H_8F_3NS+H]^+$ requires 244.0402, found 244.0402.

(4,4,4-Trifluorobut-2-enyl)benzene (3u)

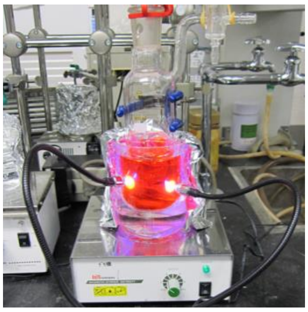


According to general procedure A, **1b** (87 mg, 0.275 mmol), $[Ru(bpy)_3](PF_6)_2$ (10.7 mg, 12.5 μmol), (*E*)-alkenylborate (**2u**) (56 mg, 0.25 mmol) and MeOH (5.0 mL) were stirred under blue LEDs. After workup, purification by column chromatography on silica gel (pentane) afforded **3u** (28 mg, 60% yield, *E*/*Z* = 65/35) as a colorless oil. The spectral data of the product were identical with those reported in the literature.

^{1}H NMR (400 MHz, $CDCl_3$, rt) of (*E*)-isomer: δ 7.36-7.18 (m, 5 H), 6.58-6.52 (m, 1 H), 5.68-5.57 (m, 1 H), 3.50-3.47 (m, 2 H). **^{1}H NMR** (400 MHz, $CDCl_3$, rt) of (*Z*)-isomer: δ 7.36-7.18 (m, 5 H), 6.17-6.10 (m, 1 H), 5.75-5.62 (m, 1 H), 3.64 (d, *J* = 8.0 Hz, 2 H). **^{13}C NMR** (100 MHz, $CDCl_3$, rt): δ 141.2 (q, *J* = 5.2 Hz, (*Z*)-isomer), 139.5 (q, *J* = 6.4 Hz, (*E*)-isomer), 138.3, 137.4, 128.9, 128.8, 128.6, 127.0, 126.8, 123.1 (q, *J* = 267 Hz), 119.7 (q, *J* = 33.3 Hz, (*E*)-isomer), 118.9 (q, *J* = 33.3 Hz, (*Z*)-isomer), 37.8, 34.7, 31.7, 29.8, 22.8, 14.2. **^{19}F NMR** (376.5 MHz, $CDCl_3$, rt): δ -57.66 (dd, *J* = 7.9, 3.0 Hz, 3 F, (*Z*)-isomer), -63.97 (dd, *J* = 6.0, 2.6Hz, 3 F, (*E*)-isomer).

Ref.: T. Chu, F.–L. Qing, *Org. Lett.* **2010**, *12*, 5060.

Gram-Scale Synthesis of 3s (Reaction Conditions in Scheme 7.2)



300 mL-Schlenk tube was charged with **1b** (2.6 g, 8.25 mmol), $[Ru(bpy)_3](PF_6)_2$ (320 mg, 0.372 mmol), **2s** (1.96 g, 7.5 mmol) and MeOH (145 mL) under N_2. **2s** was dissolved with ultrasonic bath. The tube was placed at a distance of 2–3 cm from 3W blue LED lamp. The red solution was stirred at room temperature (water bath) under visible light irradiation. After 7 h, aqueous saturated $NaHCO_3$ solution was added. The resulting mixture was extracted with pentane, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by chromatography on silica gel (pentane/ether = 10/1→3/2) to afford **3s** (1.06 g, *E*/*Z* = >99/<1, 64% yield) as a pale yellow solid.

Cyclic voltammograms

Cyclic voltammetry experiments were performed using Hokutodenkou HZ-5000 analyzer under N_2 at room temperature (observed in 0.002 M CH_3CN; $[(NBu_4)PF_6]$= 0.1 M; Ag/AgCl = electrode; reported with respect to the $[FeCp_2]/[FeCp_2]^+$couple). CV of **2a** was shown in Figure S7.1.

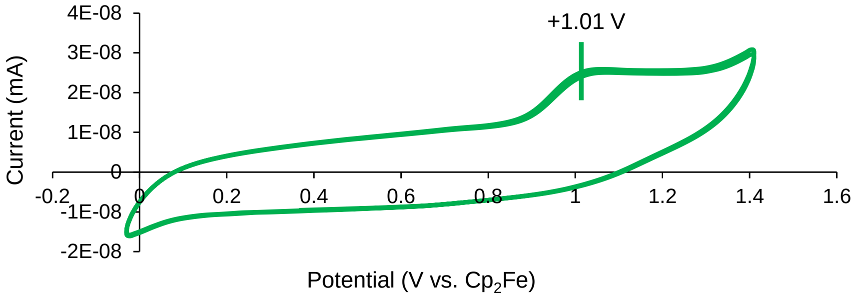


Figure S7.1. Cyclic Voltammogram of **2a**.

Crystallographic Data for 3q

Diffraction measurements were made on a Bruker SMART APEX II ULTRA/CCD. Intensity measurements were performed using monochromated (doubly curved silicon crystal) Mo-Kα-radiation (0.71073 Å) from a sealed microfocus tube. Data collection temperature was –183 °C for **3q**. Data were acquired using three sets of Omega scans at different Phi settings. The frame width was 0.5 °. The crystallographic data are summarized in Table S7.1.

The structural analysis was performed on an APEX2 software for preliminary determination of the unit cell. Determination of integrated intensities and unit cell refinement were performed using SAINT. Unless otherwise stated, all non-hydrogen atoms were refined anisotropically by full-matrix least-square techniques based on F^2. All hydrogen atoms were fixed at the calculated positions.

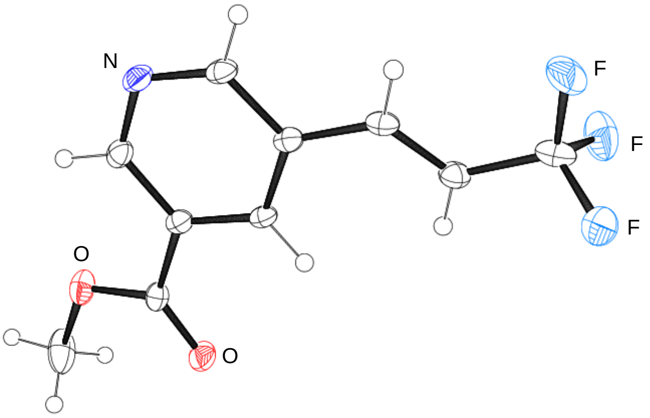


Figure S7.2. Crystal Structure of **3q.**

Table S7.1. Crystal Data and Structure Refinement for **3q**.

Empirical formula	C10 H8 F3 N O2

Formula weight	231.17	
Temperature	93(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	a = 13.040(2) Å	α = 90°
	b = 12.456(2) Å	β = 104.452(2)°
	c = 19.177(4) Å	γ = 90°
Volume	3016.3(10) $Å^3$	
Z	12	
Density (calculated)	1.527 g/cm^3	
Absorption coefficient	0.143 mm^{-1}	
F(000)	1416	
Crystal size	0.25 x 0.30 x 0.40 mm^3	
Theta range for data collection	1.61 to 28.76°	
Index ranges	-12<=h<=17, -16<=k<=12, -24<=l<=20	
Reflections collected	17047	
Independent reflections	7077 [R(int) = 0.0332]	
Completeness to theta = 28.76°	90.10%	
Absorption correction	Multiscan	
Max. and min. transmission	0.9652 and 0.9451	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7077 / 0 / 436	
Goodness-of-fit on F^2	1.084	
Final R indices [I>2sigma(I)]	R1 = 0.0534, wR2 = 0.1382	
R indices (all data)	R1 = 0.0982, wR2 = 0.1546	
Largest diff. peak and hole	0.668 and -0.296	

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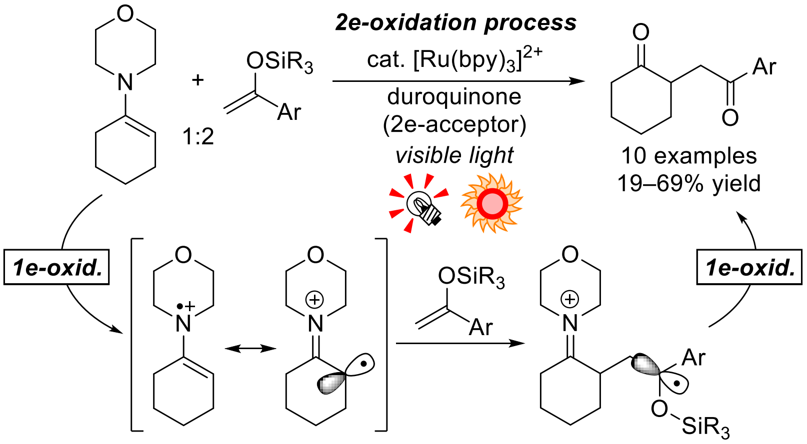
Chapter 8

Summary and Outlook

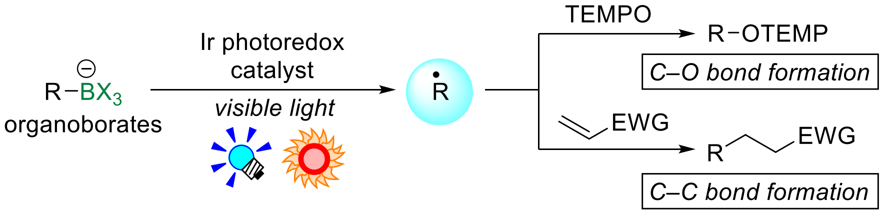
Through this thesis, the author developed novel photoredox-catalyzed radical functionalization of olefins under visible light irradiation. The overview is given below.

In Chapter 2, the author found that oxidative coupling reaction of enamines with silyl enol ethers using photoredox catalyst, $[Ru(bpy)_3]^{2+}$ (Scheme 8.1). In the presence of duroquinone as a 2e-acceptor, the C−C bond formation reaction proceeded efficiently under visible light irradiation to produce the corresponding γ-diketones. This protocol allows us to first catalytic oxidative C–C coupling of enamines with silyl enol ethers, resulting in decrease of metallic waste derived from oxidants, which are used in similar 2e-oxidation reactions.



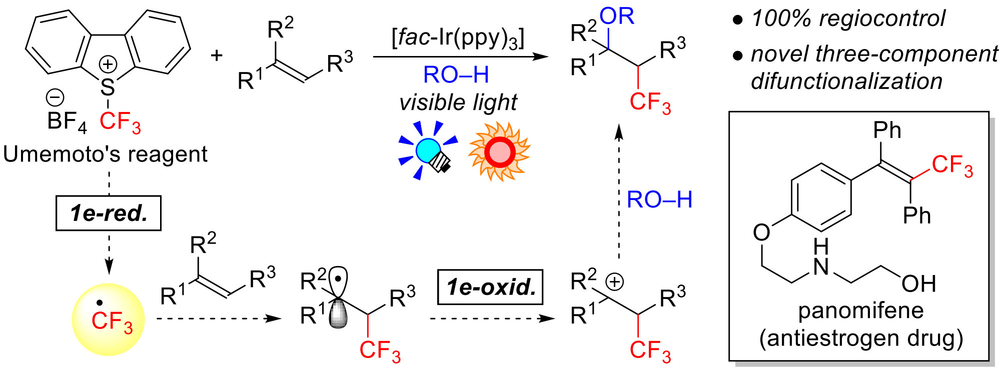
Scheme 8.1. Oxidative Coupling of Enamines with Silyl Enol Ethers.

In Chapter 3, the author developed that radical C–O and C–C coupling of organoborates with TEMPO and electron-deficient alkenes by photoredox catalysis (Scheme 8.2). The choice of organoborates is a key for efficient generation of radicals. Cyclic organo(triol)borates turn out to be useful precursors of primary and secondary alkyl radicals.



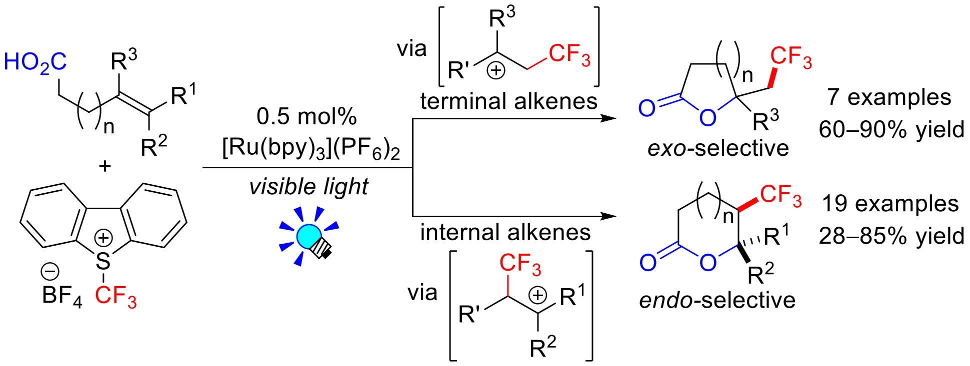
Scheme 8.2. Visible-Light-Induced Radical C−O and C−C Coupling with Organoborates.

In Chapter 4, the author found that electrophilic trifluoromethylating reagents can serve as precursors of the CF_3 radical in the presence of photoredox catalysts. The author also developed highly efficient (usually 2−4 h) and regioselective (100% in all cases) oxytrifluoromethylation of alkenes with catalytic amount of [*fac*-Ir(ppy)$_3$] (0.5 mol%) in the presence of a variety of oxygen nucleophiles such as water, alcohols, and carboxylic acids (Scheme 8.3). Various CF_3-substituted alcohols, ethers, and esters are obtained in good to excellent yields *via* a single step. Choice of electrophilic trifluoromethylating reagents is a key. Umemoto’s reagent is essential for selective reactions. This three-component reaction is achieved by consecutive generation of the CF_3 radical and the β-trifluoromethylated carbocation based on a SET process. Usefulness of this photocatalytic reaction was proven by the synthesis of the intermediate of antiestrogen drug panomifene. In addition, ambient sunlight induced this transformation.



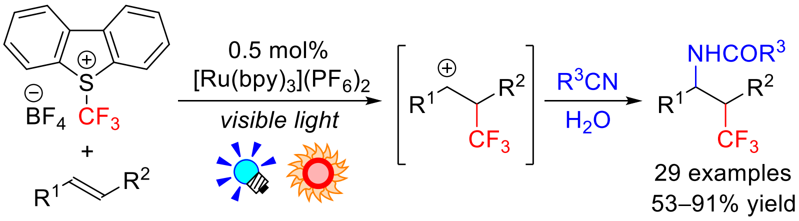
Scheme 8.3. Three-Component Oxytrifluoromethylation of Alkenes.

In Chapter 5, the author developed trifluoromethylative lactonization of both terminal and internal alkenoic acids by [Ru(bpy)$_3$](PF$_6$)$_2$ (Scheme 8.4). Regioselective trifluoromethylation of C=C bonds and intramolecular nucleophilic attack of a pendent carboxylate to β-CF$_3$ carbocation intermediate achieves regiospecific carbolactonizaton of alkenoic acids. In particular, this operationally easy trifluoromethylative cyclization protocol for internal alkenoic acids enables access to a variety of CF$_3$-substituted five-, six- and seven-membered ring *endo*-lactones bearing many functional groups with diastreoselective manner, which is the unprecedented transformation.



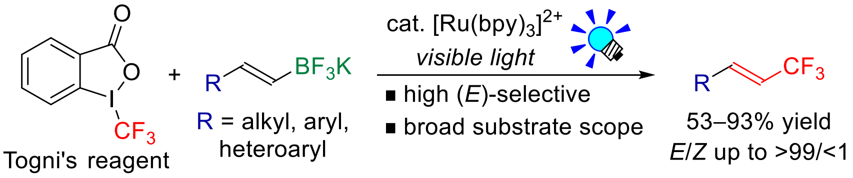
Scheme 8.4. Trifluoromethylative Lactonization of Alkenoic Acids.

In Chapter 6, the author found that easy change of *O*-nuleophiles in Scheme 8.3 to organic nitriles induces novel intermolecular aminotrifluoromethylation of alkenes (Scheme 8.5). This protocol achieves facile one-step access to a variety of 1,1,1-trifluoro-3-acetylaminopropane derivatives, which are important structural motifs in CF$_3$-containing biologically active compounds.



Scheme 8.5. Intermolecular Aminotrifluoromethylation of Alkenes.

In Chapter 7, the author developed a facile and stereoselective radical trifluoromethylation of alkenyltrifluoroborates (Scheme 8.6). The author found that reactions of alkenylborates with above-mentioned system can induce regio- and stereoselective deboronated trifluoromethylation. Togni's reagent can serve as a CF_3 radical precursor in the presence of the photoredox catalyst, $[Ru(bpy)_3](PF_6)_2$, under visible light irradiation (blue LED). This mean is applicable to a wide variety of alkenylborates containing electronically diverse substituents and hetero-aromatics leading to (*E*)-trifluoromethylated alkenes in good yields with a regio- and stereoselective fashion.

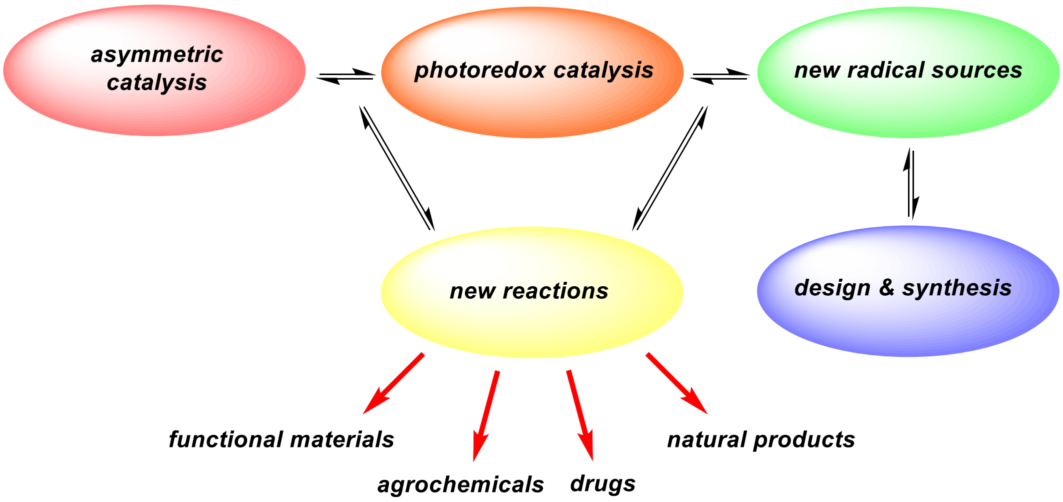


Scheme 8.6. (*E*)-Selective Trifluoromethylation of Alkenyltrifluoroborates.

As mentioned above, the author has opened up new area of visible-light-driven photoredox catalysis in synthetic organic chemistry. In particular, photocatalytic reactions using organoborates and electrophilic trifluoromethylating reagents as carbon-centered radical sources show high functional group tolerance and good chemo- and regio-selectivities under mild conditions. Thus, these methods would be applicable to a variety of synthetic valuable transformations.

In the trifluoromethylation of alkenes, enantioselective reaction is a challenging problem that remains to be addressed. In addition, related reactions with fluoroalkyl substituents such as a difluoromethyl (CF_2H) group and a monofluoromethyl (CH_2F) group, which are well found in bioactive molecules and pharmaceuticals, remains as a task. To solve these challenges, the author and co-workers are trying to (1) develop new asymmetric trifluoromethylation of alkenes by combination of photoredox catalysis and chiral organocatalysis and (2) make new fluoroalkylating reagents compatible with photoredox catalysts.

The author believes that further study of photoredox-catalyzed reactions developed in this thesis would contribute to efficient construction of candidate drugs and agrochemicals as well as functional materials in the future.



List of Publications

Chapter 2

Sunlight-Driven Synthesis of γ-Diketones *via* Oxidative Coupling of Enamines with Silyl Enol Ethers Catalyzed by $[Ru(bpy)_3]^{2+}$

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   特願 2013-029911, 2013 年 2 月 19 日

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