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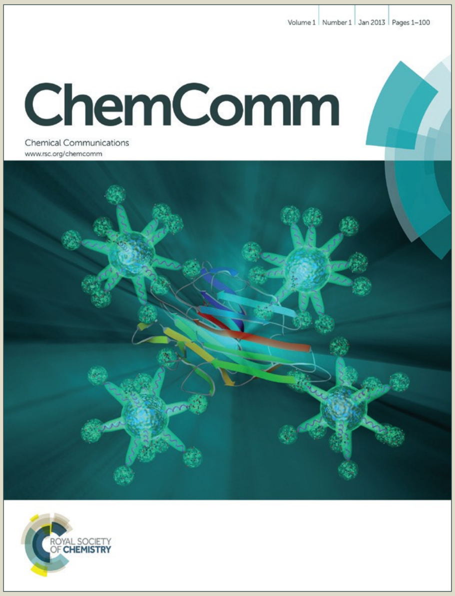

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Communication

Visible-light photoredox synthesis of internal alkynes containing quaternary carbons

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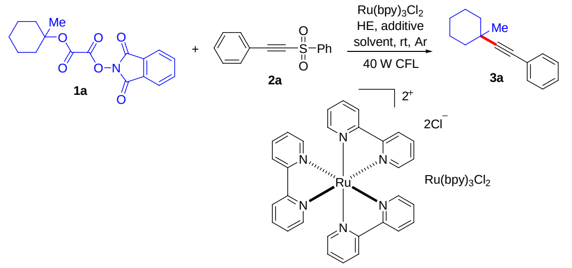
A novel and efficient visible-light photoredox method for synthesis of internal alkynes containing quaternary carbons has been developed via couplings of *N*-phthalimidoyl oxalates of *tert*-alcohols with 1-(2-(arylsulfonyl)ethynyl)benzenes. The reactions were performed well at room temperature with good functional group tolerability.

Internal alkyne intermediates are important building blocks, and they are widely used in synthesis of antibiotics,[1] antimycotics,[2] polymers, optical or electronic materials, and liquid crystals.[3] The traditional method for synthesis of internal alkynes is through palladium/copper co-catalyzed Sonogashira couplings of terminal alkynes with aryl halides,[4] and the corresponding C(sp^2)–C(sp) bonds are constructed.[5] The protocol shows high efficiency with tolerance of functional groups. However, diversity of the synthesized products is limited by using this strategy. Recently, other transition-metal catalysts[6] such as ruthenium,[7] indium,[8] gold,[9] silver,[10] cobalt,[11] nickel,[12] copper,[13] and iron[14] have been developed. Unfortunately, the higher temperatures (80 ~ 135 °C) and appropriate ligands are usually necessary, which leads to higher cost and is not favor for construction of some functional molecules. It is a long-term goal to develop less expensive, more highly efficient catalyst systems to make diverse internal alkynes under mild conditions. Recently, visible-light photoredox catalysis has emerged as a powerful activation protocol in new chemical transformations,[15] and great achievements have been made on photoredox decarboxylative couplings of carboxylic acids and their derivatives.[16] Alcohols widely occur in organic molecules, natural products and biomasses, and their chemical transformations provide diverse compounds. Interestingly, Overman and co-workers have developed visible-light photoredox coupling of electron-deficient alkenes with *tert*-alkyl *N*-phthalimidoyl oxalate intermediates that were easily prepared from reaction of tertiary alcohols with chloro *N*-phthalimidoyl oxalate.[17] However, development of *tert*-alkyl *N*-phthalimidoyl oxalate derivatives is limited. Chen and co-workers reported that 1-(2-(arylsulfonyl)ethynyl)benzenes were useful radical acceptors.[18] To the best of our knowledge, it is difficult to make internal alkynes containing quaternary carbons with terminal alkynes and alkyl halides. Herein, we report visible-light photoredox decarboxylative coupling of *tert*-alkyl *N*-phthalimidoyl oxalate derivatives with 1-(2-(arylsulfonyl)ethynyl)benzenes leading to internal alkynes containing quaternary carbons.

Table 1 Optimization of conditions on visible-light photoredox coupling of *N*-phthalimidoyl oxalate **1a** with 1-(2-(phenylsulfonyl)ethynyl)benzene (**2a**)[a]

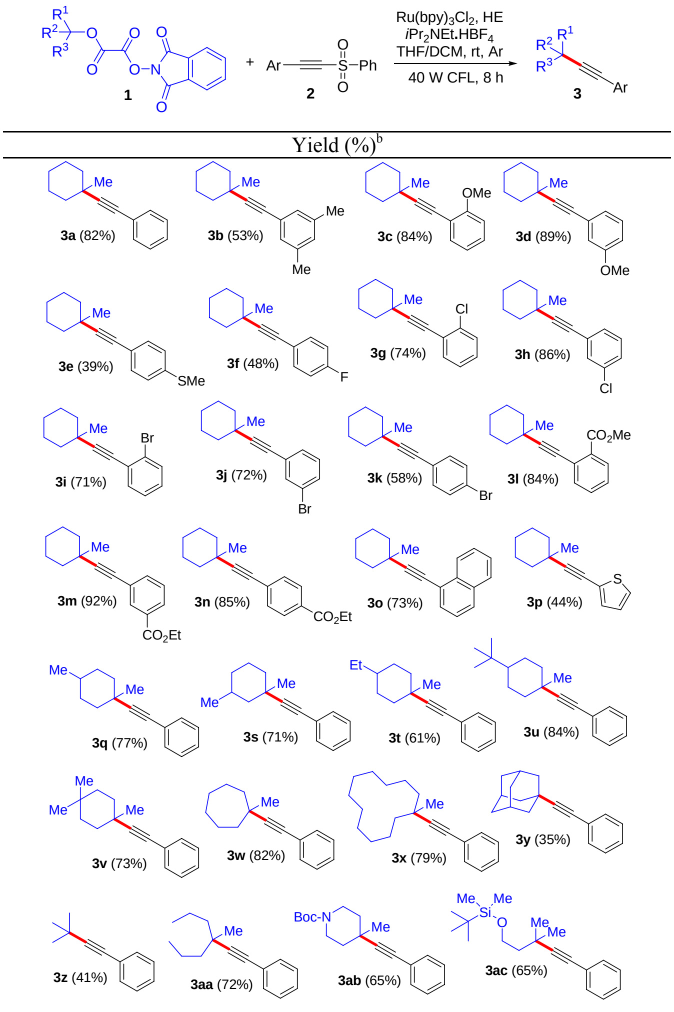


Entry	**1a** (equiv)	**2a** (equiv)	Additive	Solvent	Yield (%)[b]
1	1	1.5	*i*Pr$_2$NEt	DCM	16
2	1	1.5	*i*Pr$_2$NEt·HBF$_4$	DCM	42
3	1	1.5	*i*Pr$_2$NEt·HBF$_4$	MeCN	15
4	1	1.5	*i*Pr$_2$NEt·HBF$_4$	DMF	53
5	1	1.5	*i*Pr$_2$NEt·HBF$_4$	THF	55
6	1	1.5	*i*Pr$_2$NEt·HBF$_4$	THF/DCM	78[c]
7	**1.5**	**1**	***i*Pr$_2$NEt·HBF$_4$**	**THF/DCM**	**82**[c]
8	1.5	1	*i*Pr$_2$NEt	THF/DCM	38[c]
9	1.5	1	*i*Pr$_2$NEt·HBF$_4$	THF/DCM	80[c,d]
10	1.5	1	*i*Pr$_2$NEt·HBF$_4$	THF/DCM	79[c,e]
11	1.5	1	-	THF/DCM	35[c]
12	1.5	1	*i*Pr$_2$NEt·HBF$_4$	THF/DCM	NR[c,f]
13	1.5	1	*i*Pr$_2$NEt·HBF$_4$	THF/DCM	NR[c,g]

[a] Reaction conditions: under argon atmosphere and irradiation of visible light, Ru(bpy)$_3$Cl$_2$ (1 μmol), **1a** (0.1 mmol for entries 1-6; 0.15 mmol for entries 7-12), **2a** (0.15 mmol for entries 1-6; 0.1 mmol for entries 7-12), Hantzsch ester (HE) (0.15 mmol), additive (0.12 mmol), solvent (2 mL), time (8 h) in a sealed Schlenk tube. [b] Isolated yield. [c] Using a mixed solvent of THF (1 mL) and DCM (1 mL). [d] Using *i*Pr$_2$NEt·HBF$_4$ (0.1 mmol) as the additive. [e] Using *i*Pr$_2$NEt·HBF$_4$ (0.25 mmol) as the additive. [f] In the absence of photocatalyst. [g] No light. DCM = dichloromethane. CFL = compact fluorescent light.

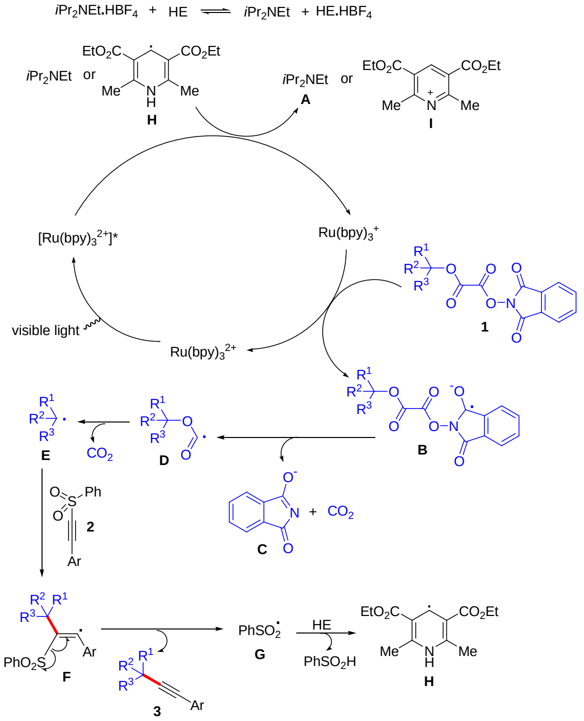
Initially, coupling of *N*-phthalimidoyl oxalate **1a** with 1-(2-(phenylsulfonyl)ethynyl)benzene (**2a**) was used as the model reaction to optimize conditions including ratio of **1a** and **2a**, additives and solvents in 8 h under atmosphere of argon and irradiation of visible-light with 40 W compact fluorescent light (CFL). As shown in Table 1, six solvents were tested using 1.0 mol% [Ru(bpy)$_3$]Cl$_2$ as the photoredox catalyst, one equiv of **1a** and 1.5 equiv of **2a** as the substrates, 1.2 equiv of *i*Pr$_2$NEt·HBF$_4$ as the additive in the presence of Hantzsch ester (HE) (entries 1-6), and mixed solvent of THF and dichloromethane (DCM) provided the highest yield (entry 6). When ratio of **1a** and **2a** was changed into 1.5 equiv of **1a** and one equiv of **2a** as the substrates, yield increased (entry 7). The reactivity greatly decreased using *i*Pr$_2$NEt as the additive (entry 8). When amount of *i*Pr$_2$NEt·HBF$_4$ was changed, yield slightly decreased (entries 9 and 10). Only 35% yield was afforded in the absence of additive (entry 11). The reaction did not work without photocatalyst (entry 12) or light (entry 13).

Table 2 Substrate scope on the visible-light photoredox synthesis of internal alkynes containing quaternary carbons[a]



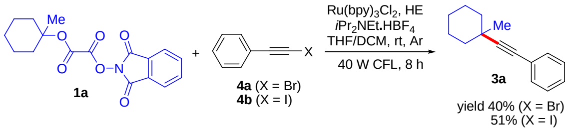
[a] Reaction conditions: under argon atmosphere and irradiation of visible light, Ru(bpy)$_3$Cl$_2$ (1 μmol), **1** (0.15 mmol), **2** (0.1 mmol), Hantzsch ester (HE) (0.15 mmol), *i*Pr$_2$NEt·HBF$_4$ (0.12 mmol), THF (1 mL), DCM (1 mL), time (8 h) in a sealed Schlenk tube. [b] Isolated yield.

After the optimized process above, substrate scope on the visible-light photoredox synthesis of internal alkynes containing quaternary carbons was investigated. As shown in Table 2, reactivity of different 1-(2-(arylsulfonyl)ethynyl)benzenes (**2**) was explored using **1a** as the partner. The substrates containing electron-withdrawing groups on the aromatic rings (see **3l-n**) displayed higher reactivity than those containing electron-donating groups, and the substrates with electron-donating substituents at *para*-site of aryl rings gave lower yields than those at *ortho*- and *meta*-sites. The coupling reactions could tolerate various functional groups including ether (**3c** and **3d**), thioether (**3e**), carbon-halogen bonds (**3f-k**), ester groups (**3l-n**), naphthyl (**3o**) and *S*-heterocycle (**3p**) on the aryl rings, and but the substrates with thioether (**3e**), C-F bond (**3f**) and *S*-heterocycle (**3p**) provided lower yields. Furthermore, *N*-phthalimidoyl oxalates of various *tert*-alcohols were surveyed. First, different-sized cyclic *N*-phthalimidoyl oxalates were tested (**3q-x**), and they showed high reactivity. Unfortunately, product **3y** containing adamantane was obtained in only 35% yield for occurrence of unknown by-products. Subsequently, we determined non-cyclic *N*-phthalimidoyl oxalates, and they afforded reasonable yields (**3z-ac**). Interestingly, the substrates containing amide (**3ab**) and silylether (**3ac**) were also acceptable substrates. We attempted visible-light photoredox coupling of *N*-phthalimidoyl oxalate (**1a**) (1.5 mmol) with 1-(2-(phenylsulfonyl)ethynyl)benzene (**2a**) (1.0 mmol), and the target product **3a** was obtained in 58% (114 mg) yield.



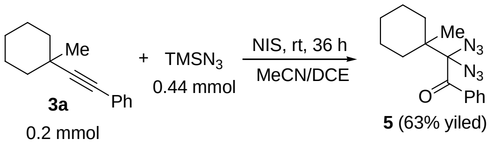
Scheme 1 A plausible mechanism on the visible-light photoredox synthesis of internal alkynes

We investigated mechanism on the visible-light photoredox synthesis of internal alkynes. A plausible mechanism is suggested in Scheme 1. Reversible treatment of *i*Pr$_2$NEt·HBF$_4$ and HE leads to *i*Pr$_2$NEt (DIPEA) and HE·HBF$_4$. Irradiation of Ru(bpy)$_3^{2+}$ with visible light gives the oxidizing excited-state [Ru(bpy)$_3^{2+}$]* ($E_{1/2}{}^{*II/I}$ = +0.77 V vs SCE in MeCN[15a]), and [Ru(bpy)$_3^{2+}$]* accepts an electron from DIPEA ($E_{1/2}{}^{red}$ = +0.65 V vs SCE in MeCN) to provide Ru(bpy)$_3^+$ leaving **A**. One electron in Ru(bpy)$_3^+$ transfers to oxygen of phthalimide in **1** provides radical **B** regenerating catalyst Ru(bpy)$_3^{2+}$, and leaving of phthalimide anion (**C**) and the first carbon dioxide from **B** donates carbonyl radical **D**, and subsequent desorption of the second carbon dioxide from **D** gives **E**.[17] Addition of **E** to alkyne sulfone (**2**) forms radical **F**,[18] and homolytic cleavage C-S bond in **F** affords the desired internal akyne (**3**) freeing radical $PhSO_2^{\cdot}$ (**G**). The similar radical C(sp^3)-C(sp) couplings were reported in the previous researches.[19] Treatment of **G** with HE provides $PhSO_2H$ freeing radical **H**, and reduction of $[Ru(bpy)_3^{2+}]^*$ by **H** gives $Ru(bpy)_3^+$ releasing **I**.



Scheme 2 Coupling of **1a** with 1-(2-bromoethynyl)benzene (**4a**) or 1-(2-iodoethynyl)benzene (**4b**) under the standard photoredox conditions

Coupling of **1a** with 1-(2-bromoethynyl)benzene (**4a**) or 1-(2-iodoethynyl)benzene (**4b**)[20] leading to **3a** was performed under the standard photoredox conditions, and the reasonable yields were afforded (Scheme 2). We investigated application of the synthesized products. Reaction of **3a** with trimethylsilyl azide ($TMSN_3$) in the presence of *N*-iodosuccinimide (NIS) gave **5** containing azido in 63% yield (Scheme 3), which is useful for further structural modification.



Scheme 3 Reaction of **3a** with $TMSN_3$ in the presence NIS

In summary, we have developed a novel and efficient method for visible-light photoredox synthesis of internal alkynes containing quaternary carbons. The protocol used readily available *N*-phthalimidoyl oxalates of *tert*-alcohols and 1-(2-(arylsulfonyl)ethynyl)benzenes as the starting materials, and the reactions were performed well at room temperature with good tolerance of functional groups. Various novel internal alkynes were prepared by using the present method, but it is difficult to make them in the previous methods. Therefore, the development of this method enriches synthesis of internal alkynes, and we believe that it will be of wide applications.

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Notes and references

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† Electronic supplementary information (ESI) available: General procedure for visible-light photoredox synthesis of internal alkynes, characterization data for compounds **3a-ac**, references, and ^{1}H and ^{13}C NMR spectra of compounds **3a-ac**. See http://dx.doi.org/10.1039/b000000x/

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