Visible-Light-Induced [2+2] cycloaddition of alkyne with alkene

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Approved by

Advisor
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Abstract

All-carbon four-membered rings are important structural motifs because they can be found in numerous natural products. Also, they are useful intermediates for chemical synthesis due to their ring strain. The [2+2] cycloadditions are straightforward route to make the four-membered ring scaffold. However, there are disadvantages in terms of environmental impact due to the requirement of harsh condition such as UV light irradiation.

Visible-light photocatalysis has emerged as a powerful tool for various organic synthesis because of its environmental strength. Visible-light irradiation is attractive because this reaction can tolerate sensitive functional groups that might be easily decomposed by UV irradiation. This strategy is mild and operationally simple reaction. Many variants using visible-light photocatalysis have been reported for significant transformations in organic synthesis. Visible-light-promoted [2+2] cycloadditions of alkene have also been vigorously developed. Nevertheless, the preparation of functionalized cyclobutenes still remains a challenge in contrast to cyclobutanes.

Herein, we developed visible-light-induced [2+2] cycloaddition between alkyne and alkene. The visible-light-induced [2+2] photocycloaddition of alkyne with alkene was achieved via energy transfer mechanism. Using a blue LED as a light source and an iridium photocatalyst as a photosensitizer, a variety of cyclobutenes products were constructed in moderated to excellent yields. Also, conjugated diene products were directly accessed through [2+2] cycloaddition of enyne followed by electrocyclic ring-opening reaction.

In contrast to previous examples of [2+2] photocycloadditions between alkyne and alkene, this strategy was achieved under visible-light irradiation. The resulting products are poised for various further modifications. Consequently, this method is expected to play an important role in the synthesis of complex organic molecules.

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Abbreviations

UV	Ultraviolet radiation
DCM	Dichloromethane
DCE	1,2-Dichloroethane
$In(tfacac)_3$	Indium(III) trifluoroacetylacetonate
Me	Methyl group
Et	Ethyl group
iPr	isopropyl group
tBu	tert-butyl group
TMS	Trimethylsilyl group
Ar	Aryl group
Ph	Phenyl group
2-py	2-Pyridyl group
ee	Enantiomeric excess
dppp	1,3-Bis(diphenylphosphino)propane
PPh_3	Triphenylphosphine
IPrAuCl	Chloro(1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene)gold(I)
NaBARF	Sodium tetrakis(3,5-bis(trifluoromethyl)phenyl)borate
HFX	Hexafluoro-*m*-xylene
TFT	Trifluorotoluene
bpy	2,2'-Bipyridine
ppy	2-Phenylpyridine
dtbbpy	4,4′-Di-tert-butyl-2,2′-bipyridine
SET	Single electron transfer
EnT	Energy transfer
PC	Photocatalyst

ISC	Intersystem crossing
A	Acceptor
S_0	Ground singlet state
S_1	Excited state
T_1	Triplet state
ATRA	Atom transfer radical addition reactions
MV^{2+}	Methyl viologen
***i*-PrOAc**	Isopropyl acetate
d.r.	Diastereomeric ratio
dF(CF_3)ppy	2-(2,4-Difluorophenyl)-5-(trifluoromethyl)pyridine
DMSO	Dimethyl sulfoxide
OTf	The triflate group
***t*-Bu-PyBox**	2,6-bis(4-tert-butyl-2-oxazolin-2-yl)pyridine
THF	Tetrahydrofuran
EWG	Electron withdrawing group
NR	No reaction
NaAsc	Sodium ascorbate
Acr-$Mes^+ClO_4^-$	9-mesityl-10-methylacridinium perchlorate
Fppy	2-(4-fluorophenyl)pyridine
dFppy	2-(2,4-Difluorophenyl)pyridine
pic	2-Picolylamine
SCE	Saturated calomel electrode
DFT	Discrete Fourier Transform
DMF	Dimethylformamide
NBS	N-bromosuccinimide
***p*-TsOH**	*p*-Toluenesulfonic acid
NaHMDS	Sodium bis(trimethylsilyl)amide

nBuLi	n-Butyllithium
MeI	Iodomethane
EtI	Iodoethane
LAH	Lithium aluminium hydride, $LiAlH_4$
DIPA	Diisopropylamine
IBCF	Isobutyl chloroformate

I. INTRODUCTION

1.1 Cyclobutene

Carbocyclic four-membered rings are important structures, mainly due to two reasons. First, they are found in a number of biologically active compounds. Also, they have high reactivity for versatile transformations originating from their inherent ring strain. Among them, we focus on cyclobutene structure.

Cyclobutene is one of the cycloalkenes with a four-membered ring and one double bond. There are a lot of natural products, bioactive molecules and organic dyes containing cyclobutene motifs.[1] Representative examples of natural products containing a cyclobutene scaffold are shown in the figure below (Figure 1).

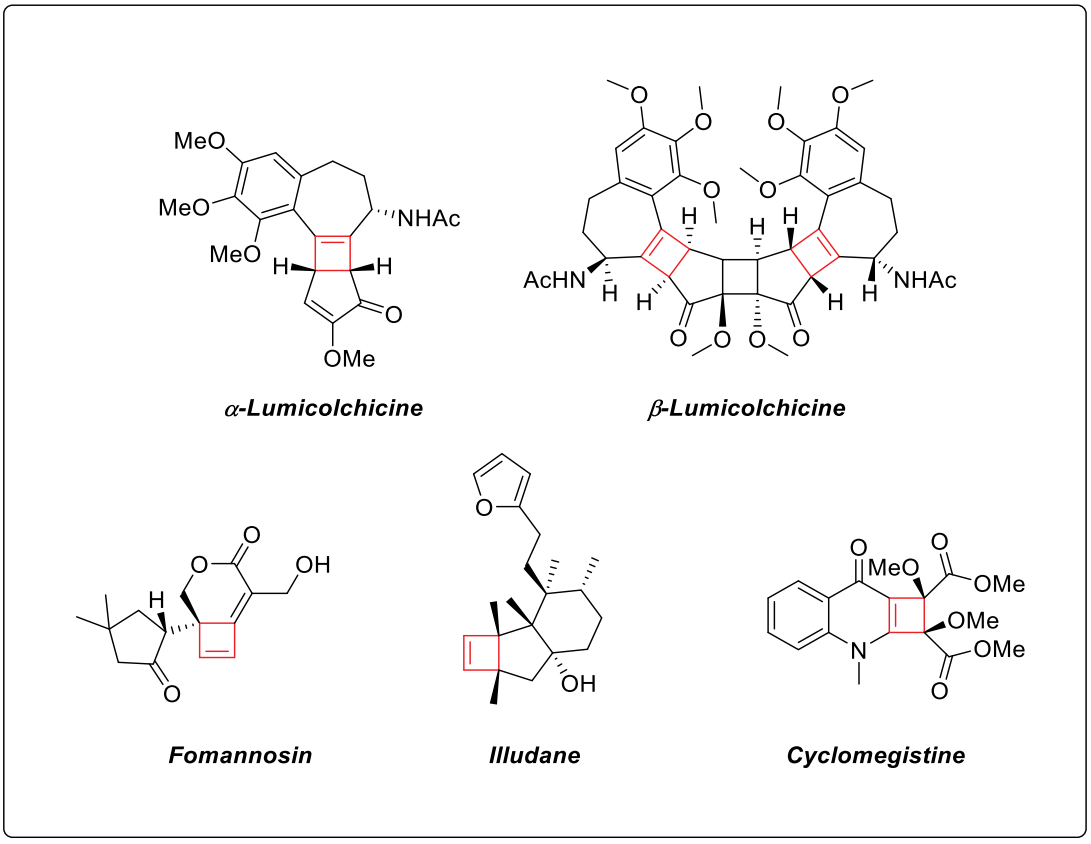


Figure 1. Natural products containing a cyclobutene scaffold.

Cyclobutene is one of the most fascinating structures in organic synthesis. Generally, cyclobutene is used as starting materials for the synthesis of a complex organic molecule (Figure 2).[2] Due to its ring-strain energy, ring cleavage of cyclobutene is facile. Conjugated diene derivatives are introduced via electrocyclic ring-opening reaction. The resulting diene products are important structural motifs because they can undergo a further transformation, such as Diels-Alder reaction. The subsequent Diels-Alder reaction of the resulting diene readily introduces cyclohexene derivatives. Additionally, other small-ring molecules, used as highly reactive intermediates, can be easily obtained from cyclobutene. Cyclobutane derivatives can be readily accessible by the hydrogenation of cyclobutene. Cyclobutene can be also converted to cyclopropane by epoxidation followed by ring contraction. Additionally, cyclopropane derivative can be made by oxidative ring contraction of cyclobutene derivative.[2c] In addition, a variety of heterocycles can be obtained from cyclobutene through further transformations. For example, pyrrole and furan motifs can be prepared by a simple two-step reaction starting from cyclobutene derivative. Cyclobutene is converted to 1,4-diketone via ozonolysis. The resulting 1,4-diketone undergo Paal-Knorr reaction, thus pyrrole and furan molecule can be synthesized. As you see, cyclobutene is an attractive scaffold because of its broad synthetic range of transformations.

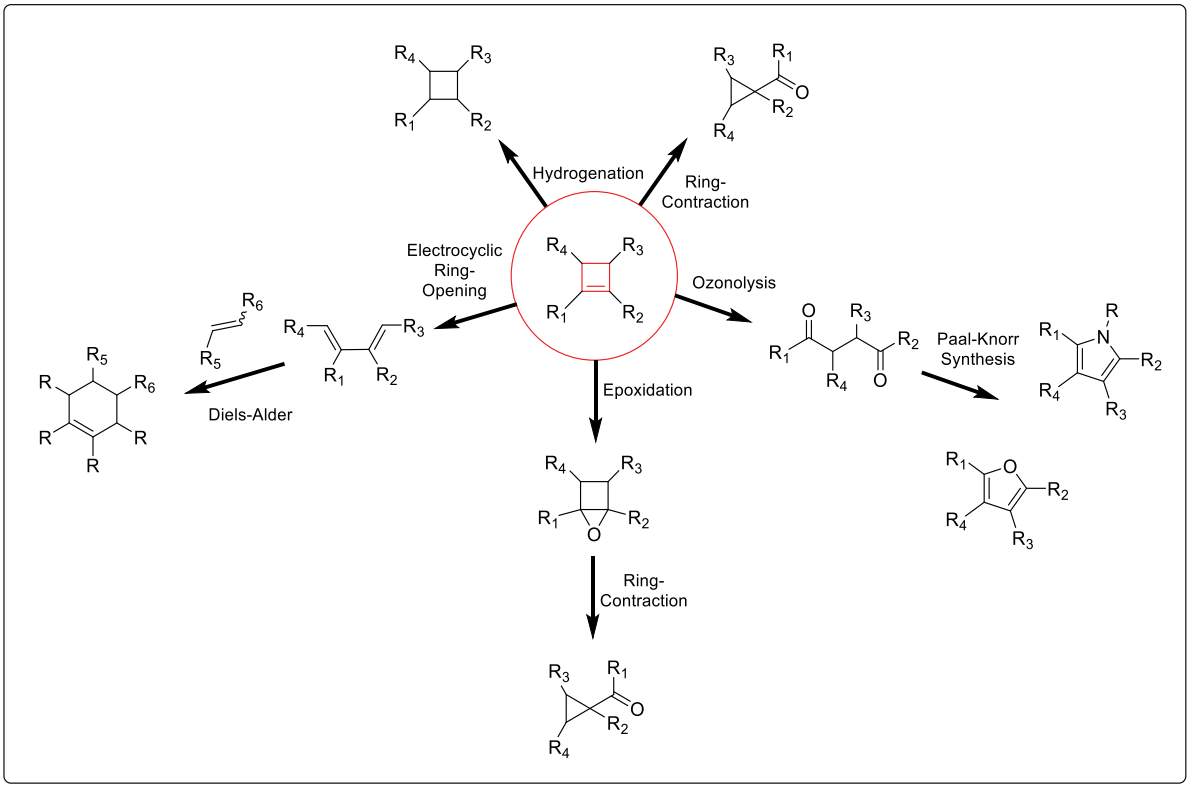


Figure 2. The application of cyclobutene in organic synthesis

1.2 [2+2] cycloaddition of alkyne with alkene

Cycloaddition is a reaction, in which more than two unsaturated molecules convert to a cyclic product in a single step. It is one of the most efficient transformations because it generates molecular complexity with a high atom economy. There are various cycloaddition family such as [2+2], [3+2], and [4+2] variants, but we focus on [2+2] cycloaddition. The [2+2] cycloaddition is a straightforward synthetic method to access the carbocyclic four-membered ring scaffold.[3]

The most efficient and direct route for the preparation of cyclobutene is [2+2] cycloaddition of alkyne with alkene.[3] The [2+2] cycloaddition of alkyne with an alkene is largely categorized as a photochemical reaction and catalyzed reaction.

1.2.1 Catalyzed [2+2] cycloaddition

According to the Woodward-Hoffmann rules, the [2+2] cycloaddition of alkyne with alkene is generally forbidden under thermal conditions. Alternatively, catalyzed [2+2] cycloaddition makes it possible to construct a cyclobutene ring under thermal conditions. The substrates are converted to reactive intermediates such as metallated C-C multiple bonds and cations which undergo cycloaddition more readily. Using this approach, a lot of methodologies have been reported using transition metal[4,5,6] and Lewis acid[7,8] as a catalyst.

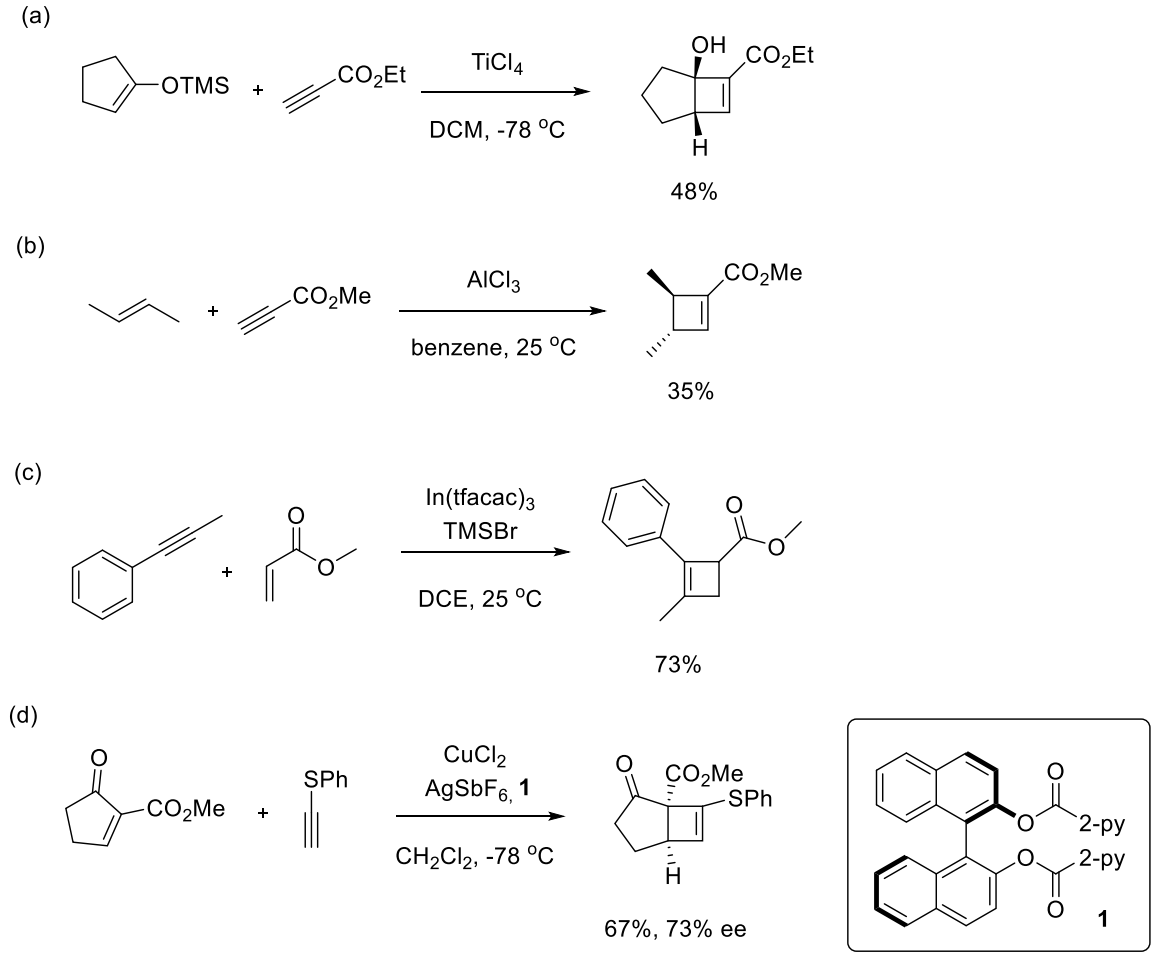
1.2.1.1 Lewis acid catalyzed [2+2] cycloaddition

Lewis acid catalysts have been developed for the [2+2] cycloaddition.[7,8] In this approach, Lewis acid catalyzed reaction usually requires a combination of electron-rich and electron-deficient substrates. Selected examples of Lewis acid catalyzed alkyne-alkene [2+2] cycloaddition are shown below (Scheme 1).

In 1976, the Snider group reported [2+2] cycloaddition using strong Lewis acids, $AlCl_3$.[7a] Additionally, the Snider[7b] and the Clark[7c] group reported methods for [2+2] cycloaddition using strong Lewis acids, $AlCl_3$, $TiCl_4$ (scheme 1a,b). However, these methods had several disadvantages. The use of strong Lewis acid resulted in the formation of cyclobutene derivatives with only low efficiency. Also, there was a requirement of stoichiometric Lewis acid. By continued effort, many methodologies have been reported using Lewis acid.[8] Shen and co-workers reported [2+2] cycloaddition of aryl alkyne with acrylate (Scheme 1c).[8f] To form cyclobutene derivatives, this method uses combined Lewis acid as a catalyst, $In(tfacac)_3$-TMSBr. Recently, enantioselective [2+2] cycloadditions using

Lewis acid have been investigated.[8] To utilize the total synthesis of (+)-tricycloclavulone, the Iguchi group developed enantioselective [2+2] cycloaddition of phenylthioacetylene and cyclopentenone derivative (Scheme 1d).[8b] They used chiral ligand **1** to provide enantioselectivity.

Unfortunately, Lewis acid catalyzed [2+2] cycloadditions require the presence of polar functional groups in the substrates. Also, substrate scope is limited because substrates require the absence of acid sensitive functional groups.

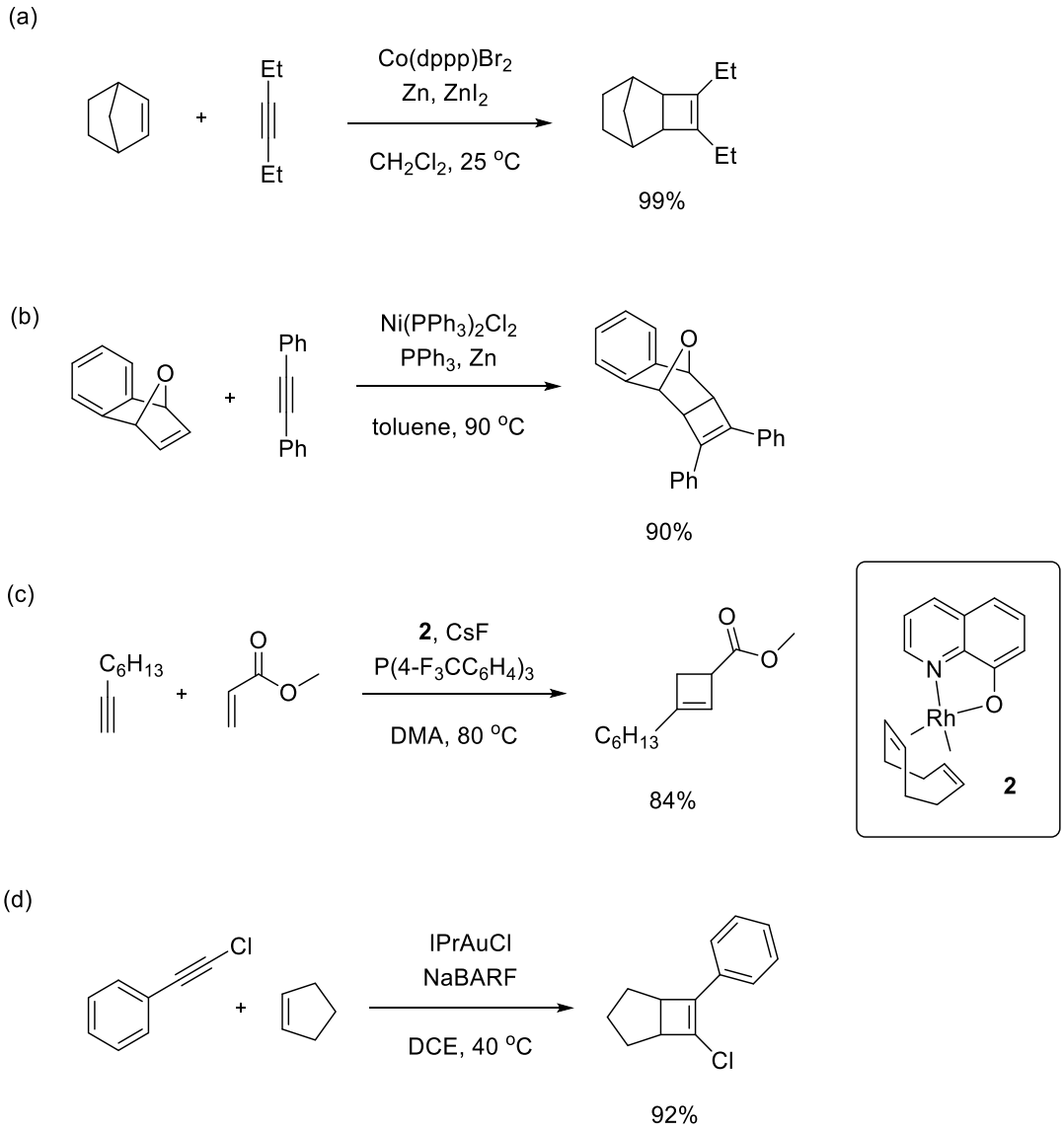


Scheme 1. Lewis acid catalyzed [2+2] cycloaddition of alkyne with alkene

1.2.1.2 Transition metal catalyzed [2+2] cycloaddition

Various transition metal catalysts have been well developed for [2+2] cycloaddition.[6] [2+2] cycloadditions using transition metal catalysts often require activated substrates, such as ynamide, phenylthioacetylene, siloxy alkyne or ring-strained alkene.[6] Transition metal catalyzed reactions of non-activated substrates undergo [2+2] cycloaddition under harsh conditions like high temperature. Various transition metals have been developed for [2+2] cycloaddition, such as gold, rhodium, cobalt, and nickel. (Scheme 2).[4,5,6]

Transition metal catalyzed [2+2] cycloadditions are usually carried out with gold[5b], rhodium[5a], or ruthenium[5d] complex. Recently, a lot of methodologies have been reported using a very efficient Co and Ni complex (Scheme 2a and b).[4] The Hilt group reported the cobalt-catalyzed [2+2] cycloaddition of highly strained norbornene derivatives with alkyne (Scheme 2a).[4d] The transformation proceeds via the coordination of the substrates to the cobalt, followed by oxidative addition. Then, reductive elimination gives the desired cyclobutene product. The [2+2] cycloaddition promoted by the nickel complex was developed in the same manner (Scheme 2b).[4a] Enantioselective [2+2] cycloadditions catalyzed by transition metal have also been developed.[6] For example, Kakiushi and co-workers reported enantioselective [2+2] cycloaddition of terminal alkynes with electron-deficient alkene (Scheme 2c).[5a] The chiral rhodium/phosphine catalyst promotes the formation of the desired cyclobutene. Recently, transition metal catalyzed [2+2] cycloadditions of non-activated substrates have been vigorously investigated. In 2018, the Zhang group reported gold-catalyzed [2+2] cycloaddition between chloroalkynes and unactivated alkenes (Scheme 2d).[5b] However, despite many efforts, only a few reported transition metal catalyzed [2+2] cycloaddition of unactivated substrates have been known.[5b, 5e, 5f] Usually, non-activated substrates undergo transition metal catalyzed [2+2] cycloaddition under harsh conditions like high temperature, or a requirement of expensive transition metal catalysts.



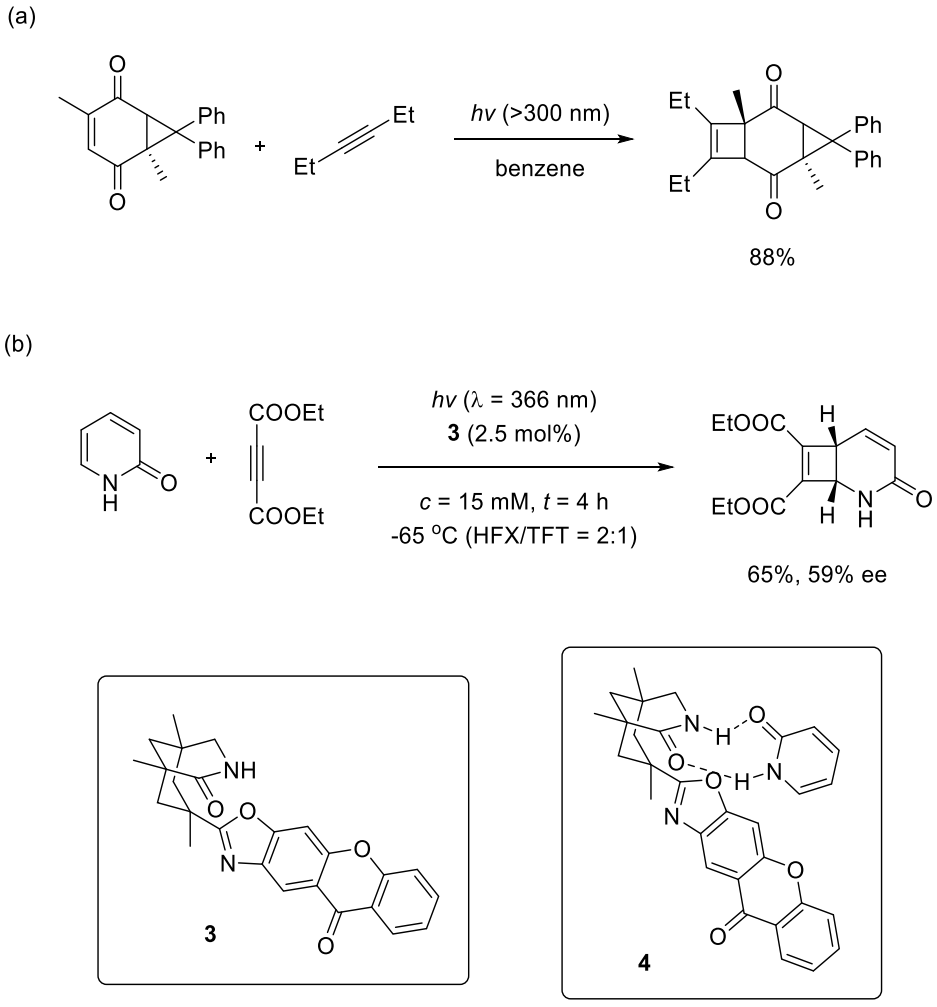
Scheme 2. Transition metal catalyzed [2+2] cycloaddition of alkyne with alkene

1.2.2 Photochemical [2+2] cycloaddition

Photochemical [2+2] cycloadditions promoted by UV irradiation are well-established methodologies for the construction of the carbocyclic four-membered ring.[9] The construction of cyclobutene ring via photochemical [2+2] cycloaddition has been reported until recently.[10] Generally, the [2+2] photocycloadditions proceed through the transfer of energy from an excited-state catalyst to substrates. The selected examples of the formation of cyclobutene derivatives via [2+2] photocycloaddition are shown below (Scheme 3).

In 2002, the Oshima group reported photochemical [2+2] cycloaddition of benzoquinone derivative with alkyne (Scheme 3a).[10a] UV irradiation activates benzoquinone derivative instead of the photosensitizer. However, the enantioselective [2+2] photocycloaddition has been significant difficult.[11] To overcome this disadvantage, enantioselective photochemical [2+2] cycloadditions have been vigorously investigated.[11] The Bach group developed the method for intermolecular cycloadditions of 2-pyridones with acetylene dicarboxylates (Scheme 3b).[10b] This method uses chiral photocatalyst **3** to give enantioselectivity. Catalyst **3** was designed to interact with pyridone substrates. The absolute configuration was assigned through a formation of complex **4**.

The formation of cyclobutene derivatives via photochemical [2+2] cycloaddition requires high-energy UV irradiation. Thus, the substrate scope is limited because the reaction cannot tolerate sensitive functional groups that could be readily decomposed by UV irradiation.



Scheme 3. Photochemical [2+2] cycloaddition of alkyne with alkene

1.3 Visible-Light Photocatalysis

Chemists have aspired to develop atom economical and environmentally friendly synthetic methods for making complex organic molecules. In this respect, the use of visible-light is attractive reagent because it is a safe, inexpensive, abundant, and renewable source. Over the last decade, visible-light photocatalysis has been proven to be an important tool in organic synthesis.[12]

Visible-light photocatalysis describes the synthetic method that required visible-light as an energy source to proceed reaction. Also, it usually requires the use of light-absorbing photocatalysts, such as organic dyes or transition metal complexes. A variety of iridium- and ruthenium- based polypyridyl complexes and organic dyes are typically used to photocatalyst (Figure 3). These photocatalysts have their own redox potential and photophysical properties.[12c,13] To fully understand this kind of reaction, general mechanisms of visible-light photocatalysis are described below.

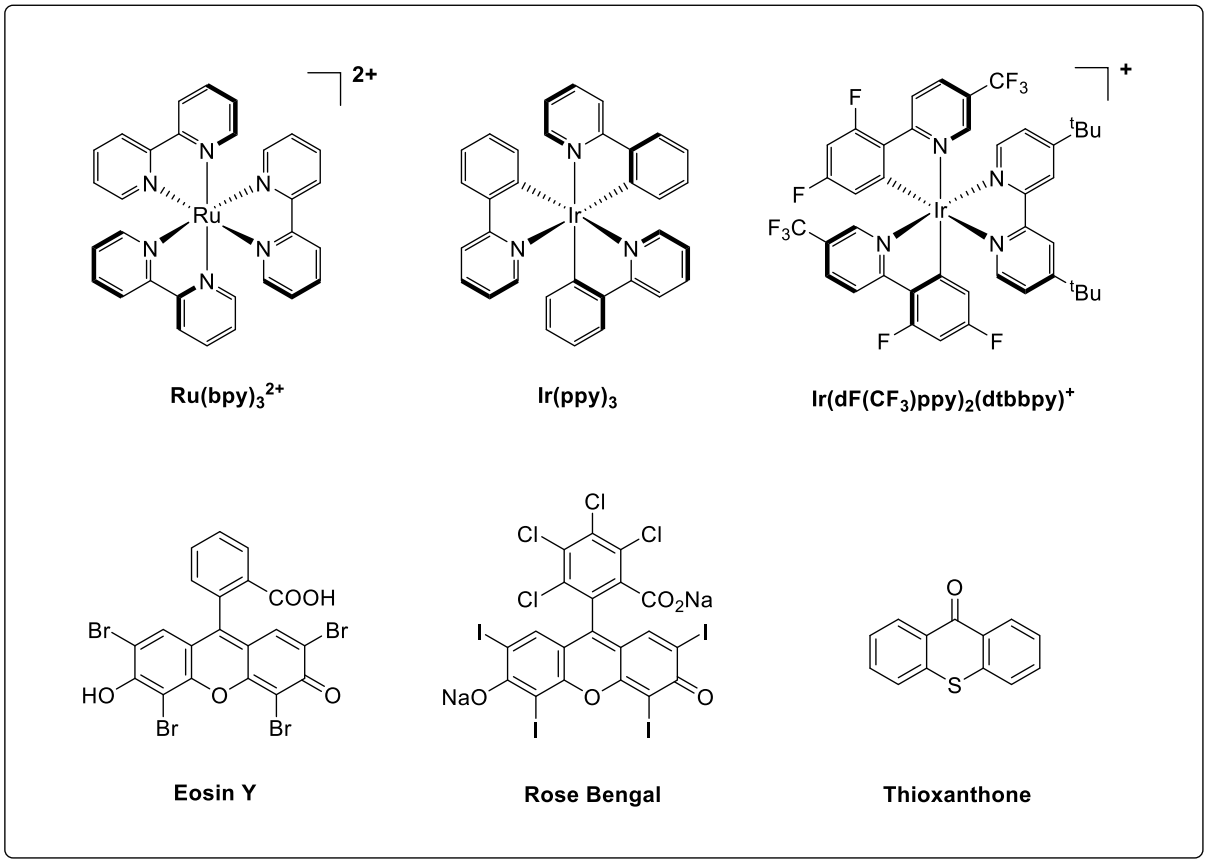


Figure 3. Typical photocatalysts

1.3.1 General mechanisms of visible-light photocatalysis

As illustrated in Figure 4a, visible-light photocatalysis was largely divided into two types: single electron transfer (**SET**) and energy transfer (**EnT**) pathways.[13]

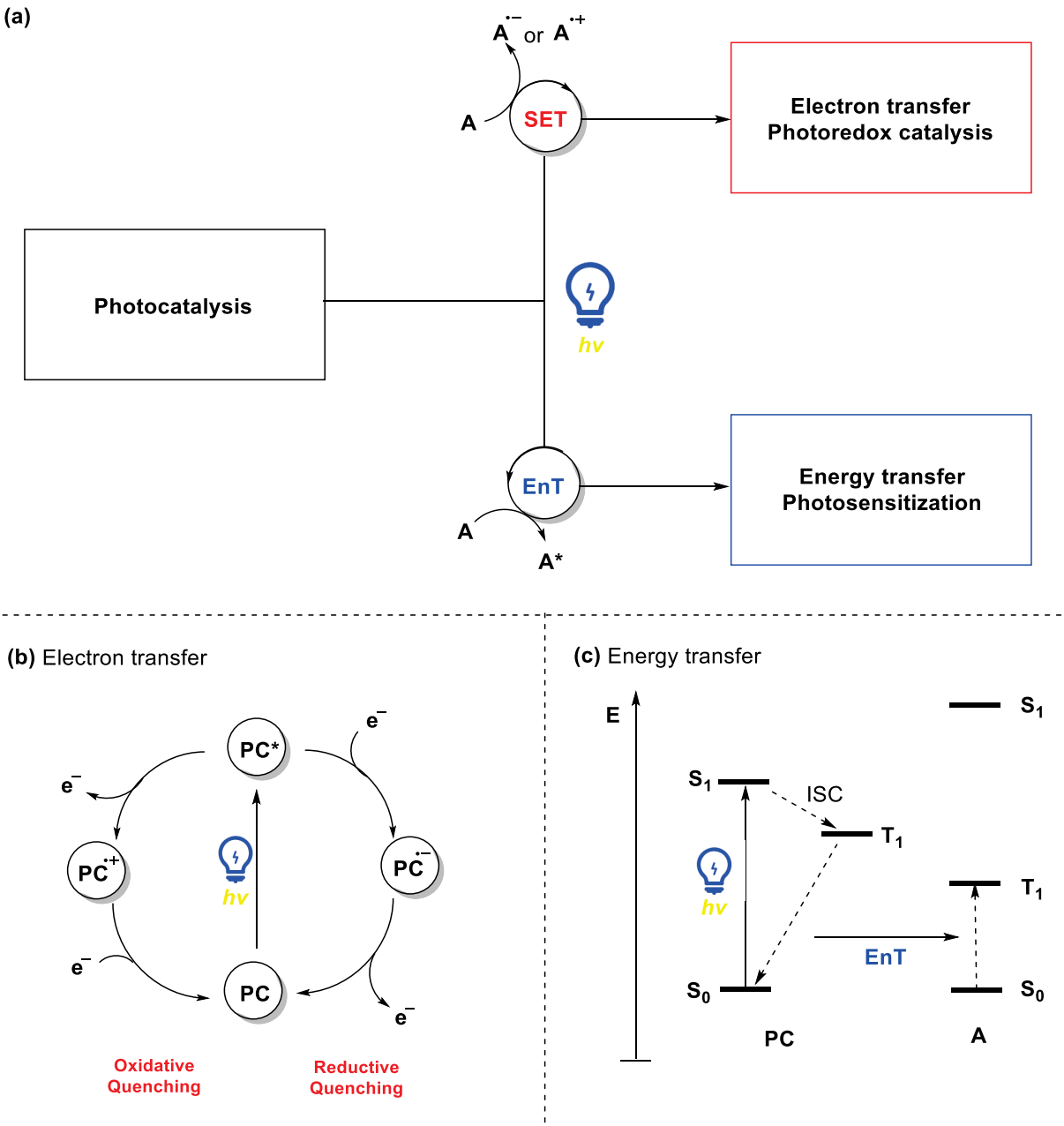


Figure 4. General mechanisms of photocatalysis

Most of the visible-light photocatalysis proceeds via a single electron transfer from the excited photocatalyst to the reagent or substrate (Figure 4b). Photocatalysis through the single electron transfer is called a photoredox catalysis. In this reaction, the photocatalyst (**PC**) is excited by irradiation of visible-light. Then, excited photocatalyst undergoes the single electron transfer with an acceptor (**A**), such as the substrate or a reagent, to generate radical ion. Two different mechanistic cycles are possible after excitation of the photocatalyst: One is the oxidative quenching cycle, the other is the reductive quenching cycle. The oxidative quenching cycle is the reaction that the excited photocatalyst is first oxidized and then reduced to regenerate photocatalyst. The reductive quenching cycle is the opposite. The success of the photoredox catalysis depends on the redox properties of the substrates, and photocatalyst.

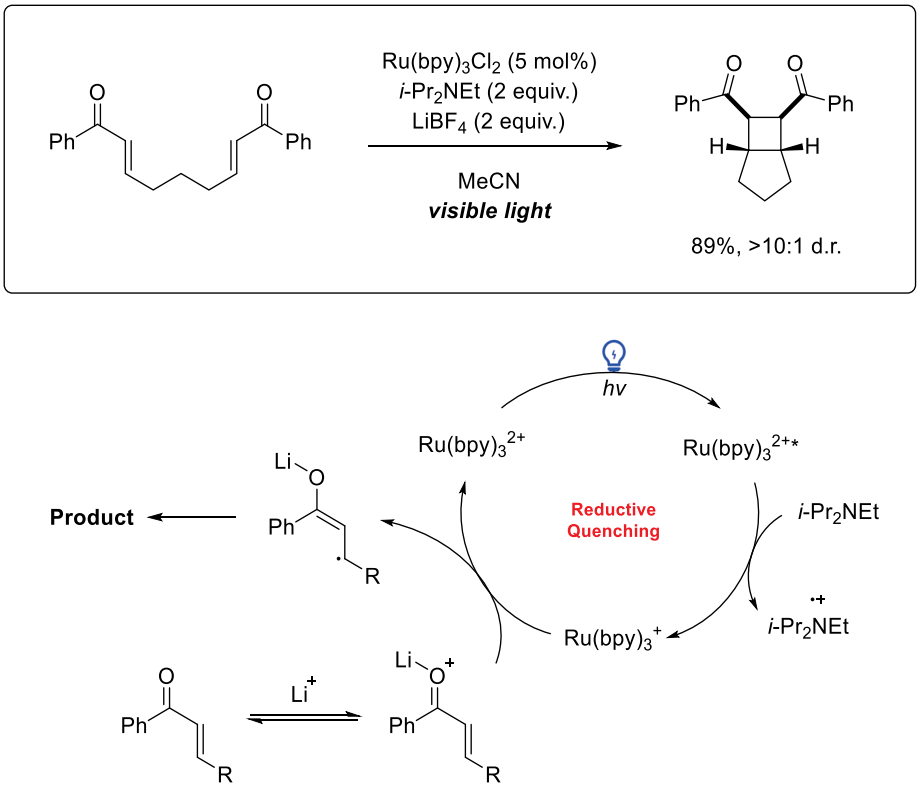
The other mechanistic process is photosensitization (Figure 4c). The reaction proceeds through energy transfer between an energy acceptor and an energy donor. The excited photocatalyst serves as an energy donor and the substrate uses as an energy acceptor (**A**). The energy transfer pathway is described in Figure 4c. First, the photocatalyst (**PC**) absorbs light source and is excited into the $\mathbf{S_1}$ state from its ground singlet state ($\mathbf{S_0}$). Next, the excited state of photocatalyst ($\mathbf{S_1}$) turns into its triplet state ($\mathbf{T_1}$) through an intersystem crossing (ISC). After then, facile energy transfer occurs from photocatalyst to the substrate. As a result, the substrate from its ground singlet state ($\mathbf{S_0}$) is excited to the active triplet state ($\mathbf{T_1}$). The resulting excited substrate will undergo in organic transformations. This strategy is not limited by redox properties, but depends on the triplet-state energies of the photocatalyst and substrate.

1.3.2 [2+2] cycloaddition by visible-light photocatalysis

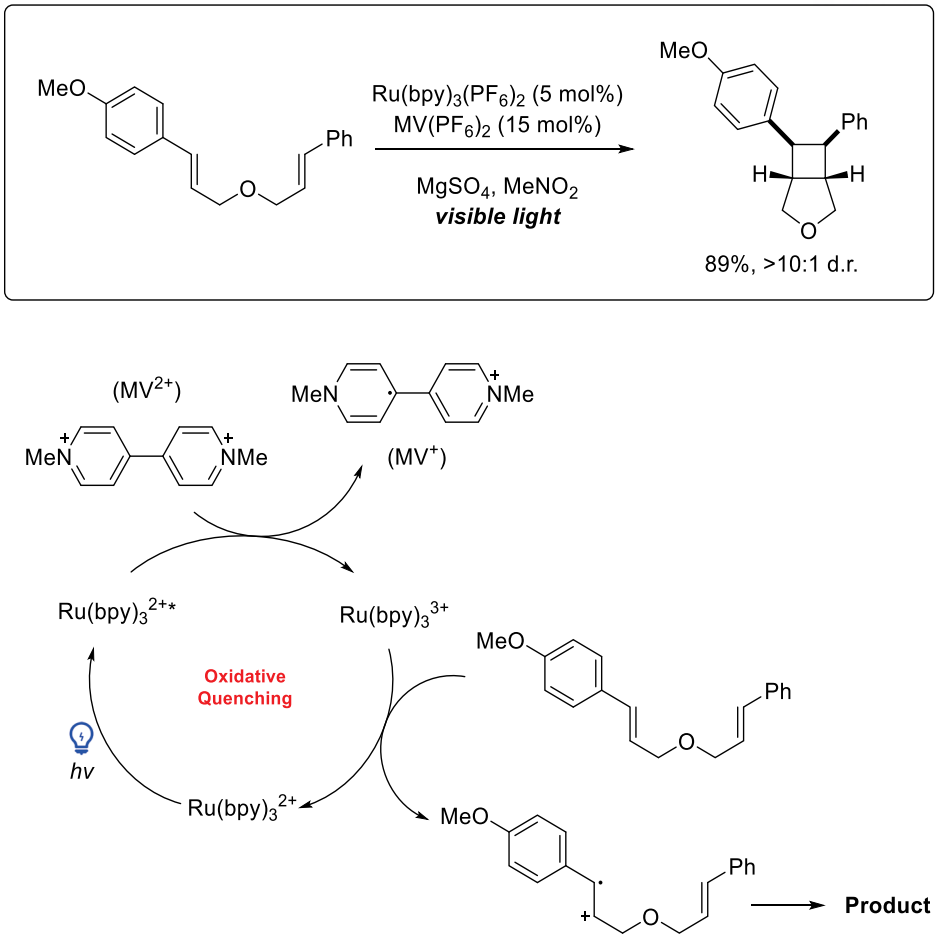
The new methodologies using visible-light photocatalysis have been reported for many important transformations, such as α-amino functionalization reactions, cross-coupling reactions, and atom transfer radical addition reactions (ATRA).[12] [2+2] photocycloadditions of alkene through visible-light have been also demonstrated by several research groups.[14,15] In 1986, the Kutal group first reported visible-light induced [2+2] photocycloaddition of norbornadienes.[16] This reaction undergoes via energy transfer process from excited photocatalyst, $Ru(bpy)_3Cl_2$, to substituted norbornadiene substrate.

In the last decade, the Yoon group has greatly contributed to the development of visible-light induced [2+2] photocycloaddtion.[14] Pioneering work was reported by the Yoon group that [2+2] cycloadditions between electron-deficient alkenes can be efficiently induced by visible light (Scheme 4).[14a] This reaction utilizes the reductive quenching cycle of visible-light photoredox catalysis. The amine serves as an electron donor to generate reduced photocatalyst, $Ru(bpy)_3^+$. The resulting $Ru(bpy)_3^+$ reduces the activated enone to the radical intermediate, while regenerating photocatalyst.

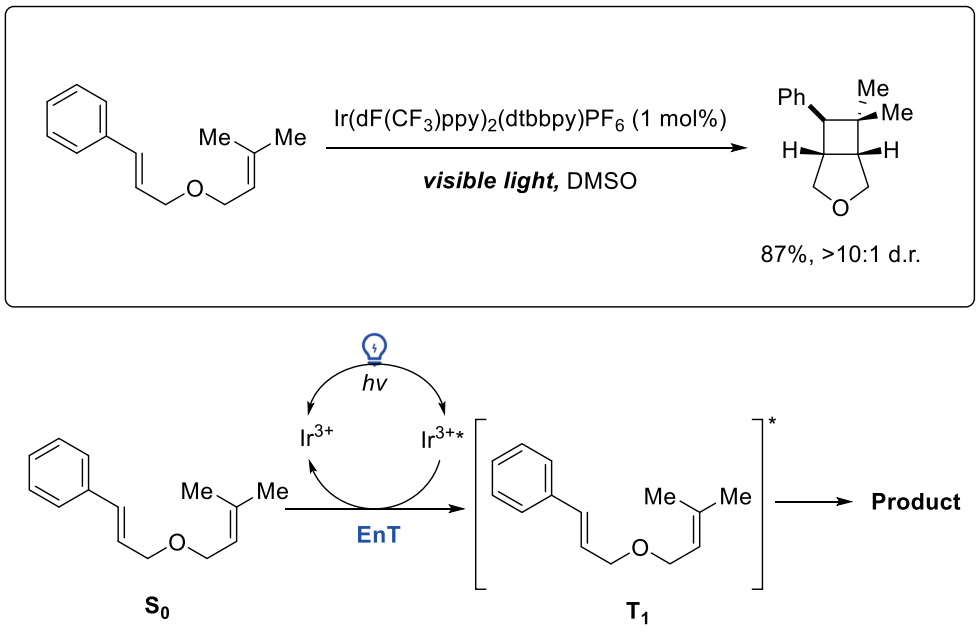
Then, the resulting intermediate undergoes cyclization to generate cyclobutane products. One year later, an intermolecular [2+2] photocycloaddition was reported in the same manner.[14b] In 2010, [2+2] cycloaddition via oxidative photocatalytic cycle was also developed (Scheme 5).[14c] Methyl viologen (MV^{2+}), an electron acceptor, oxidizes the excited photocatalyst, affording the reduced MV^{+} and the $Ru(bpy)_3^{3+}$. The resulting $Ru(bpy)_3^{3+}$ oxidizes the styrene to generate the radical cation, while regenerating photocatalyst. Then, radical cation undergoes cyclization to form desired products. These strategies are limited by the redox properties of substrates. Alternatively, [2+2] photocycloadditions can be achieved by an energy transfer pathway. Compare to the electron transfer mediated process, energy transfer process improves functional group tolerance. In 2012, visible-light induced intramolecular [2+2] cycloaddition of styrenes was developed via the energy transfer process (Scheme 6).[14d] Iridium complex is utilized as a photosensitizer under visible-light irradiation. Enantioselective [2+2] photocycloaddition with a chiral Lewis acid complex has also been reported via energy transfer (Scheme 7).[14e]



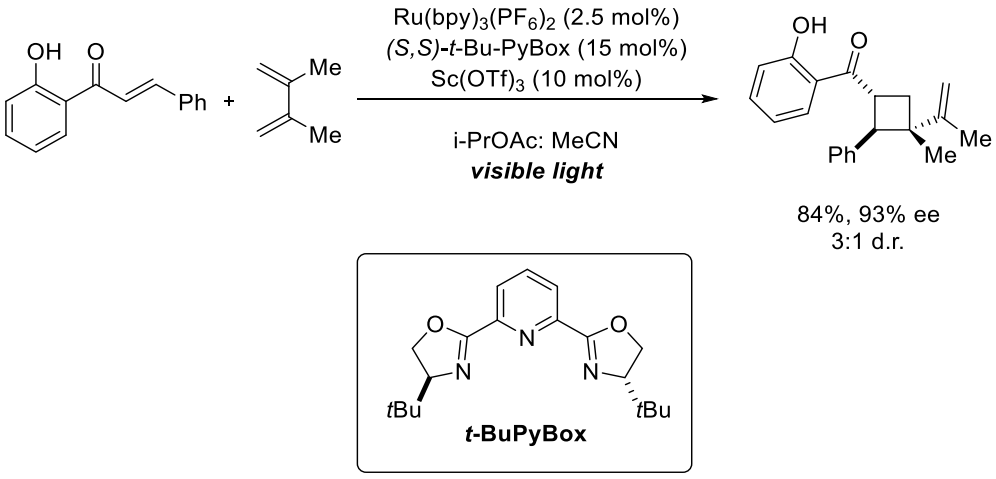
Scheme 4. Visible-light induced [2+2] photocycloaddition by reductive quenching process



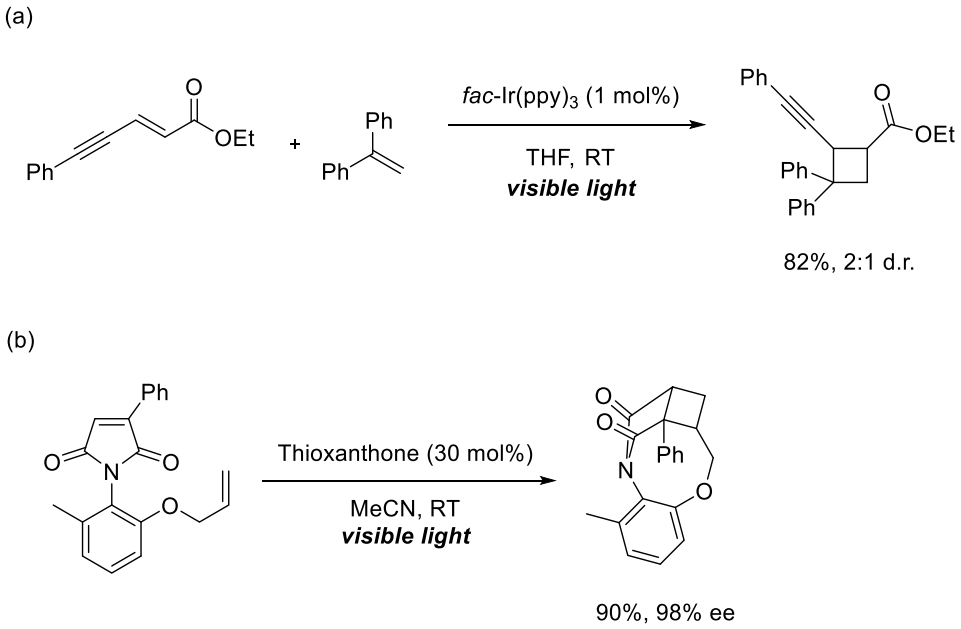
Scheme 5. Visible-light induced [2+2] photocycloaddition by oxidative quenching process



Scheme 6. Visible-light induced [2+2] photocycloaddition by energy transfer process

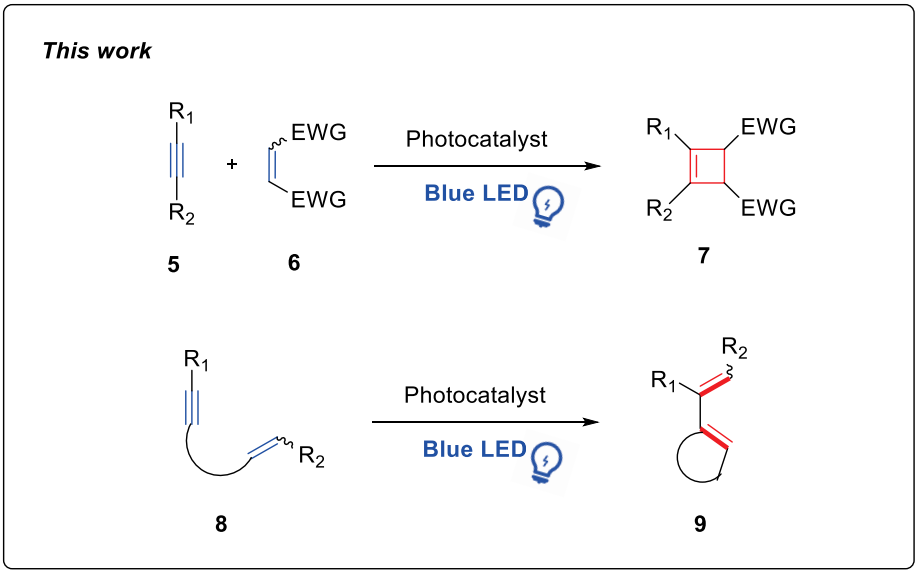


Scheme 7. Enantioselective [2+2] photocycloaddition



Scheme 8. Visible-light induced [2+2] photocycloaddition of alkene

In recent years, [2+2] cycloaddition between an enyne and olefin via visible-light photocatalysis was reported (Scheme 8a).[15c] Surprisingly, the alkyne part does not interact with olefin. Only cyclobutane products are formed with high selectivity. Additionally, the Sivaguru group reported [2+2] cycloaddition of atropisomeric maleimide (Scheme 8b).[15a]



Scheme 9. This work

As you see, visible-light-induced [2+2] photocycloadditions for making cyclobutanes are well-developed methods. Nevertheless, the formation of cyclobutene structures through visible-light photocatalysis has been met with significant challenges. Herein, we developed the first visible-light induced [2+2] cycloaddition of alkyne with electron-deficient alkene (Scheme 9). Also, unexpected conjugated diene products were directly synthesized through the use of enyne substrates.

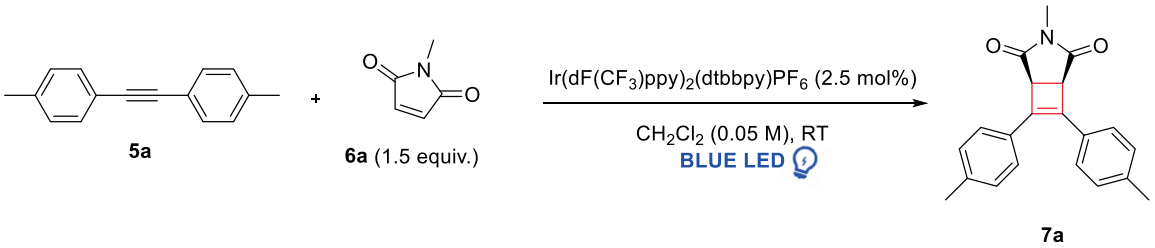
II. RESULTS AND DISSCUSION

2.1 Visible-Light-Induced intermolecular [2+2] cycloaddition of alkyne

Reaction design and development.

We envisioned a catalytic cycle for the direct synthesis of cyclobutene structures based on visible-light photocatalysis. First, we designed the reaction of alkyne **5a** with maleimide **6a** under visible-light photocatalytic conditions to form cyclobutene derivative (Table 1). Our endeavors commenced with the reaction of di-*p*-tolylacetylene **5a** with N-methylmaleimide **6a** under visible-light irradiation in the presence of a variety of photocatalysts (Table 1, entries 1-10). The use of various photocatalysts and organic dyes, such as *fac*-[$Ir(ppy)_3$], $Ir(ppy)_2(dtbbpy)PF_6$, $Ru(bpy)_3(PF_6)_2$, Eosin Y, Rose Bengal, and Acr-$Mes^+ClO_4^-$ was shown ineffective to form the desired product (entries 1-6). Pleasingly, numerous iridium-based photocatalysts were found to efficiently synthesize the desired cyclobutene **7a** (entries 7-10). Among them, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ was the most promising photocatalyst, delivering the desired product **7a** in 76% yield (entry 10). Next, with $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ as an optimal photocatalyst, we investigated the effects of a variety of solvent (entries 11-15). The results indicated that CH_2Cl_2 was superior to the others (entry 11). Further optimization of the equivalents of photocatalyst and reaction concentration caused an improved yield (entry 16). Finally, control experiments performed in the absence of either light or catalyst confirmed no product formation, which supports that the reaction was facilitated by visible-light photocatalysis (entries 17 and 18). Consequently, optimal conditions were established as follows: **5a** (1.0 equiv.) **6a** (1.5 equiv.), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5 mol%) in CH_2Cl_2 (0.05 M) under N_2 atmosphere at room temperature for 4h with the irradiation of blue LEDs.

Table 1. Optimization Table.[a]

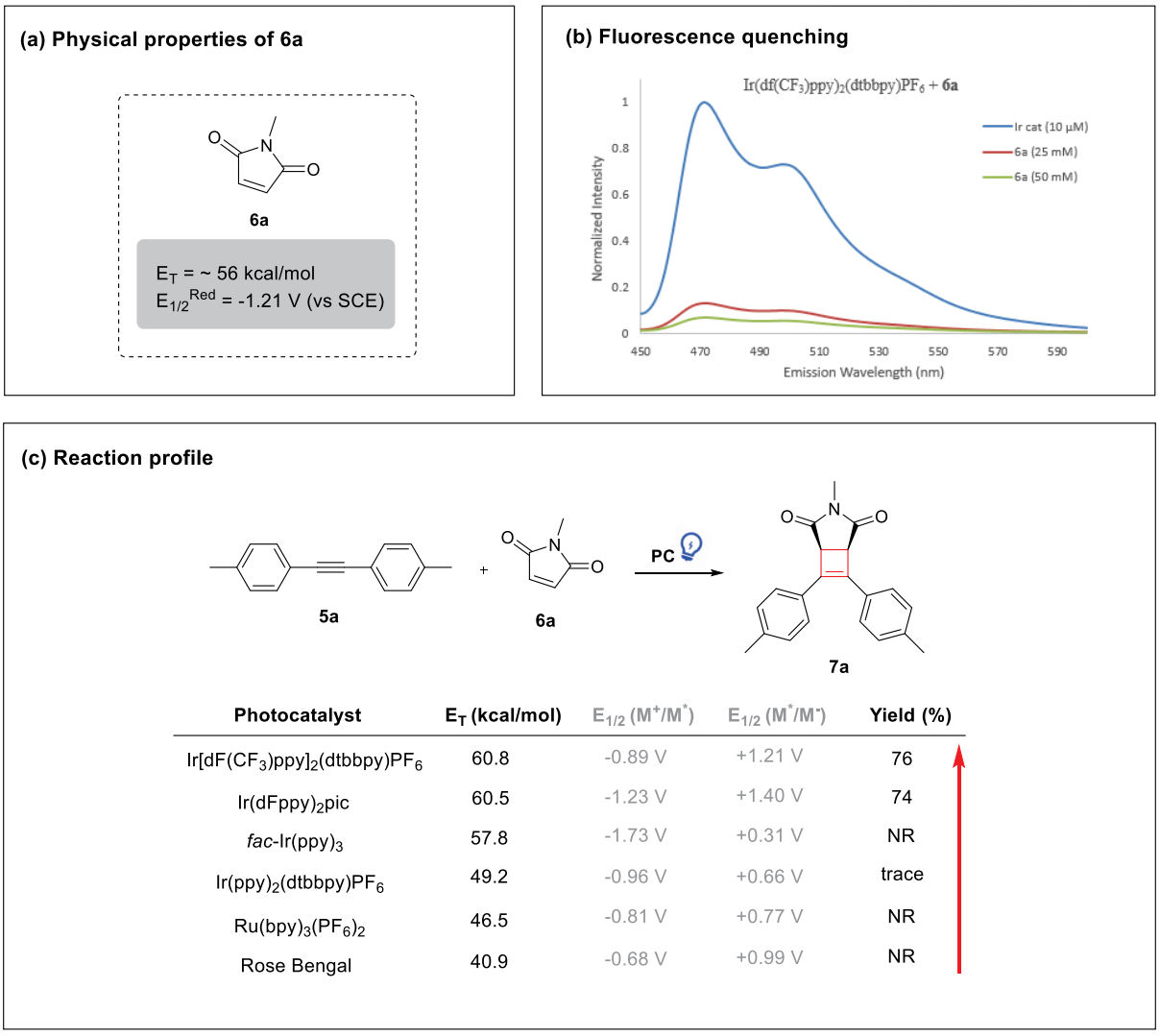


Entry	6a (equiv.)	Photocatalyst (mol%)	Solvent	Conc. [M]	Yield (%)[b]
1	2.0	Eosin Y (5)	$^{c}CH_2Cl_2$ / MeCN	0.1	NR
2	2.0	Rose Bengal (5)	$^{c}CH_2Cl_2$ / MeCN	0.1	NR
3	2.0	Acr-Mes$^{+}ClO_4^{-}$ (5)	$^{c}CH_2Cl_2$ / MeCN	0.1	NR
4	2.0	$Ru(bpy)_3(PF_6)_2$ (5)	$^{c}CH_2Cl_2$ / MeCN	0.1	NR
5	2.0	$Ir(ppy)_3$ (5)	$^{c}CH_2Cl_2$ / MeCN	0.1	NR
6	2.0	$Ir(ppy)_2(dtbbpy)PF_6$ (5)	$^{c}CH_2Cl_2$ / MeCN	0.1	trace
7	2.0	$Ir(Fppy)_2(dtbbpy)PF_6$ (5)	$^{c}CH_2Cl_2$ / MeCN	0.1	35
8	2.0	$Ir(dFppy)_2(dtbbpy)PF_6$ (5)	$^{c}CH_2Cl_2$ / MeCN	0.1	62
9	2.0	$Ir(dFppy)_2pic$ (5)	$^{c}CH_2Cl_2$ / MeCN	0.1	74
10	2.0	$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5)	$^{c}CH_2Cl_2$ / MeCN	0.1	76
11	1.5	$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5)	CH_2Cl_2	0.1	74
12	1.5	$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5)	$CHCl_3$	0.1	73
13	1.5	$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5)	THF	0.1	15
14	1.5	$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5)	DMF	0.1	53
15	1.5	$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5)	Acetone	0.1	58
16	***1.5***	***$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5)***	***CH_2Cl_2***	***0.05***	***83 (76[d])***
17	1.5	**X**	CH_2Cl_2	0.05	trace
[e]18	1.5	$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5)	CH_2Cl_2	0.05	NR

[a] Reactions conducted on a 0.05 mmol scale. NR = No reaction
[b] Yields were determined via ^1H NMR analysis versus an internal standard. $^{c}CH_2Cl_2$/MeCN (5:1)
[d] **5a** (0.1 mmol scale); Isolated yield; 4h. [e] Dark.

Plausible mechanism.

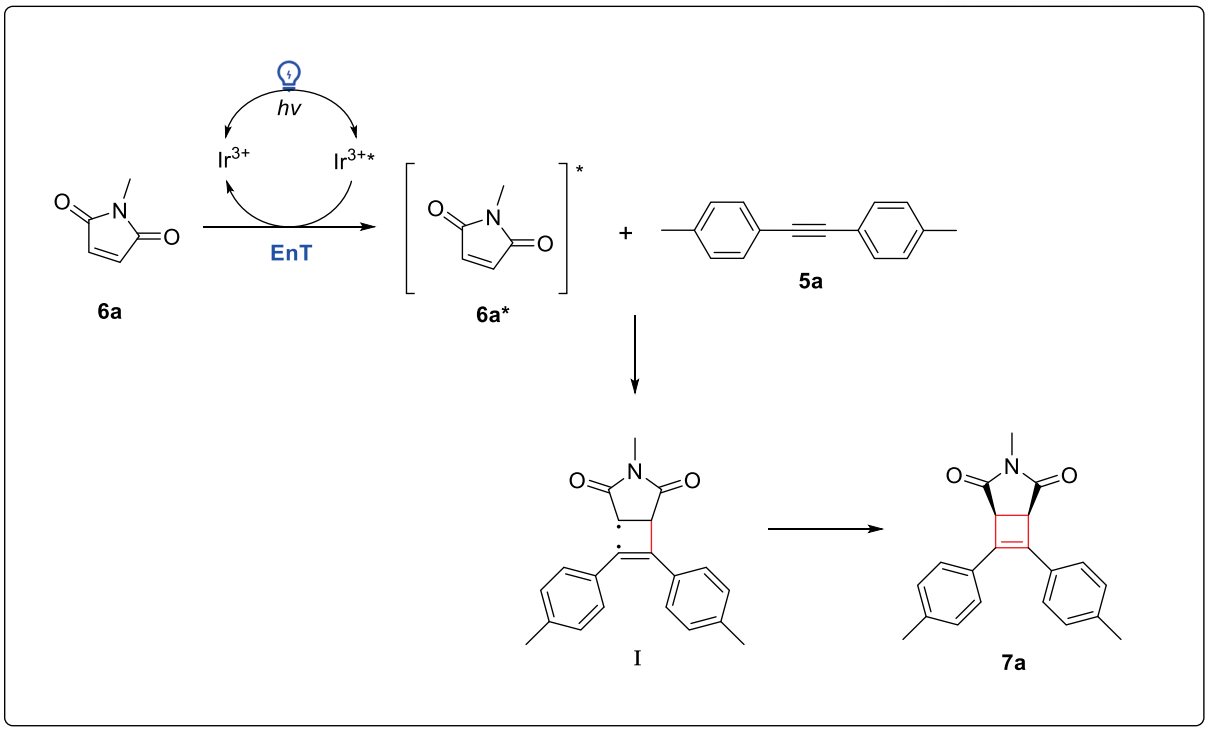
Then, we turned our attention to characterizing the reaction mechanism. In order to demonstrate the reaction pathways, we compared the physical properties of maleimide **6a** to the properties of photocatalyst, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (Figure 5a). The activation of N-methylmaleimide **6a** through electron transfer by $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (-0.89 V vs. SCE)[13a] was thermodynamically unfavorable due to their high reduction potential (-1.21 V vs. SCE for **6a**)[17]. On the other hand, the triplet energy of $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (60.8 kcal/mol)[13a] was higher than triplet energy of **6a** (estimated ~ 56 kcal/mol)[18], indicating that energy transfer from the catalyst to the substrate was feasible. Fluorescence quenching experiments also demonstrated the maleimide substrate **6a** efficiently quenches the excited state of iridium photocatalyst (Figure 5b). To support the energy transfer pathway, substrates **5a** and **6a** were reacted with various photocatalysts having different triplet energies and redox properties (Figure 5c). A correlation was not observed between the redox potential of the photocatalysts and the formation of **7a**. The results suggested that a single electron transfer process was not in operation. In contrast, there was a clear correlation between the triplet energy of photocatalyst and the formation of **7a**, except in the case of *fac*-$Ir(ppy)_3$. Considering these results, we speculated that the reaction proceeds via the energy transfer process rather than electron transfer. Further mechanistic studies and DFT calculations are ongoing in our laboratory.



Photocatalyst	E_T (kcal/mol)	$E_{1/2}$ (M^+/M^*)	$E_{1/2}$ (M^*/M^-)	Yield (%)
$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$	60.8	-0.89 V	+1.21 V	76
$Ir(dFppy)_2pic$	60.5	-1.23 V	+1.40 V	74
fac-$Ir(ppy)_3$	57.8	-1.73 V	+0.31 V	NR
$Ir(ppy)_2(dtbbpy)PF_6$	49.2	-0.96 V	+0.66 V	trace
$Ru(bpy)_3(PF_6)_2$	46.5	-0.81 V	+0.77 V	NR
Rose Bengal	40.9	-0.68 V	+0.99 V	NR

Figure 5. Mechanistic studies

On the basis of the mechanistic studies, we proposed a reaction mechanism illustrated in Scheme 10. First, visible-light irradiation of the iridium photosensitizer produces the long-lived excited state of iridium complex. The resulting excited iridium complex activates maleimide **6a** via energy transfer, which generates the triplet intermediate **6a***. Triplet maleimide species **6a*** react with the ground state alkyne **5a** to yield the diradical **I**. Diradical intermediates **I** then undergo ring closure to afford cyclobutene **7a**.

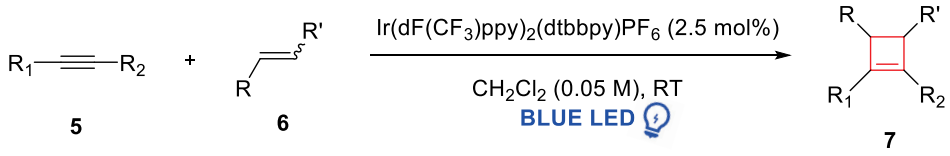


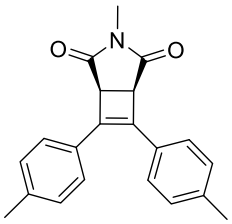
Scheme 10. Plausible mechanism.

Substrate synthesis

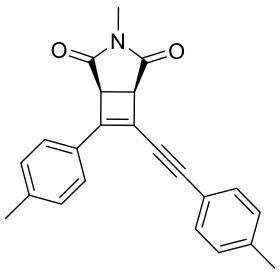
With the optimized conditions in hand, the substrate scope of the reaction was investigated. Initially, we examined the reactivity of several alkynes and alkenes to investigate the feasibility of introducing various substrates (Table 2). The reactions of N-methylmaleimide **6a** with aryl, heteroaryl, and alkyl alkynes were studied. Symmetrical diyne (**5b**) could be transformed into the corresponding cyclobutene (**7b**). As well as aryl containing substrates, heteroaryl- and alkyl- containing substrates provided the corresponding cyclobutene **7c** and **7d** in moderated yields. Accordingly, we expected that this reaction was not limited to aryl alkynes but heteroaryl and alkyl alkynes can also be used. Subsequently, we examined the effect of substituents on maleimide. The reaction of the di-substituted maleimide also proceeded smoothly to furnish the desired product **7e**, suggesting that steric hindrance was tolerated in the reaction. We examined the compatibility of N-aryl maleimide. In the case of N-aryl maleimide, electron-withdrawing substituent afforded the desired cyclobutene **7f** in moderate yields. Also, electron-deficient alkenes turned out to be a good coupling partner affording corresponding cyclobutene **7g**. Our preliminary results gave reasonable promise of having a broad range of substrates.

Table 2. Substrate scope of alkynes and alkenes[a,b]

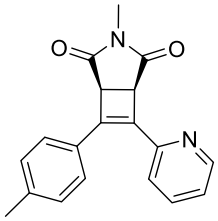




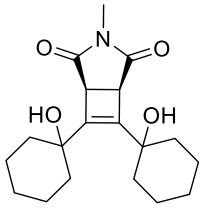
7a (76%)[c]



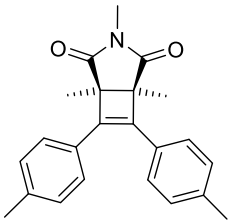
7b (70%)[d]



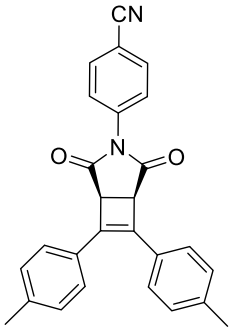
7c (53%)[d]



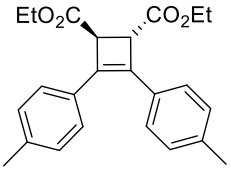
7d (58%)[d,e,f]



7e (55%)[d]



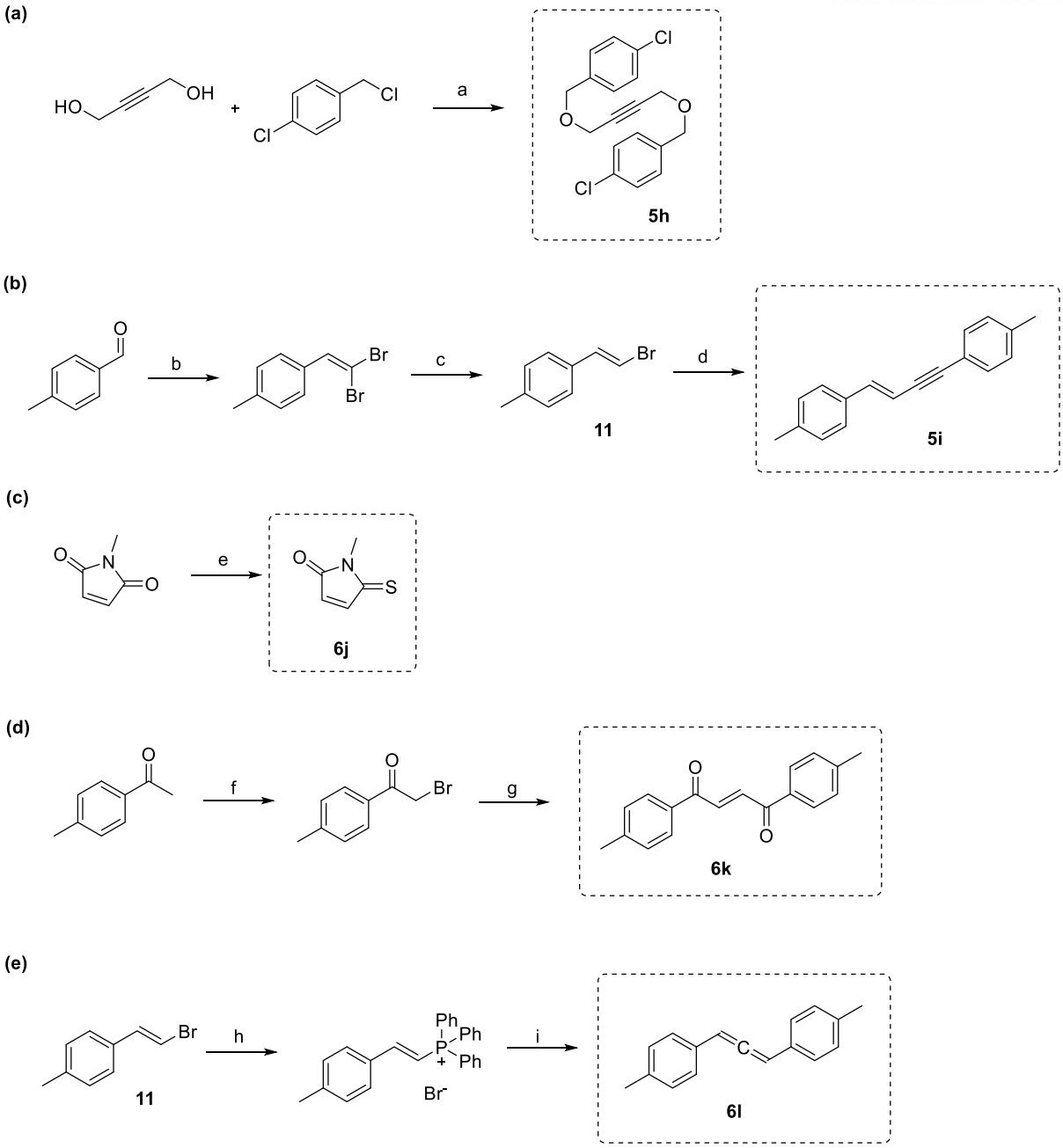
7f (59%)[c]



7g (51%)[d]

[a] Reaction conditions: Reactions were performed with **5** (0.10 mmol, 0.05 M), **6** (0.15 mmol), and $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ (2.5 mol%) in dry CH_2Cl_2 under N_2.
[b] Isolated yield. [c] Rxn time: 4 h ~ 18 h. [d] Rxn time: 24 h ~ 48 h. [e] **6** (2.0 equiv.). [f] catalyst (5.0 mol%).

To further broaden the substrate scope, we synthesized various compounds containing alkyne or alkene moiety (Scheme 11). First, we aimed to form alkyne **5h** in order to prove that substrates with other alkyl substituents, besides cyclohexanol, proceeded to furnish the desired product. The alkyne **5h** was readily synthesized by reacting with but-2-yne-1,4-diol on to the benzyl chloride. Conjugated enyne **5i** was also prepared to ascertain the reactivity with **5a** or **6a**. *p*-Tolualdehyde was converted to the vinyl bromide **11** via the Ramirez olefination followed by the reduction of the homologated dibromoolefin. The subsequent Sonogashira coupling with *p*-tolylacetylene gave enyne **5i**. Next, we tried to make various alkene structures **6j**, **6k**. The mono-thionation of N-methylmaleimide proceeded smoothly using Lawesson's reagent to furnish the desired product **6j**. The desired alkene **6k** was obtained through bromination of 4'-methylacetophenone followed by sodium sulfonate mediated reaction. Additionally, we hoped to afford allene derivatives, the structure having great importance in [2+2] cycloaddition reactions.[19] The desired allene **6l** was prepared starting from the vinyl bromide **11**. Treatment of $Pd(PPh_3)_4$ and PPh_3 with **11** led to the formation of phosphonium salt. The target product **6l** was obtained from the resulting phosphonium salt. Disappointingly, we proved that these substrates (**5i, 6j-l**) didn't provide the desired cyclobutene products except the alkyne **5h**.



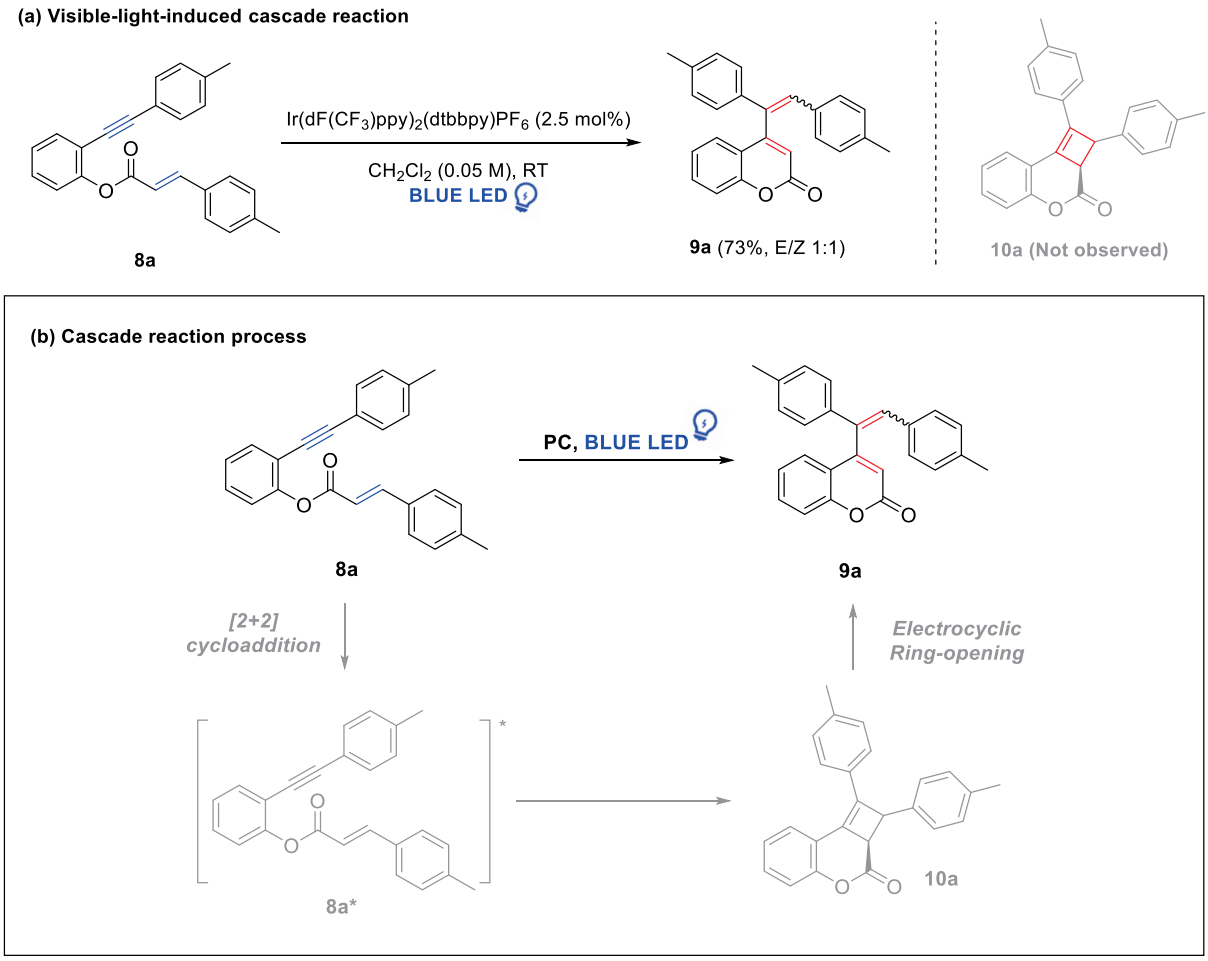
Scheme 11. Synthesis of alkyne and alkene structures - Reagents and conditions: a) NaH, DMF, 69%, b) CBr_4, PPh_3, DCM, 0°C, 94%, c) Dimethyl phosphite, Et_3N, DMF, 94%, d) *p*-Tolylacetylene, Cu_2O, Cs_2CO_3, DMF, 135°C, 82%, e) Lawesson's reagent, toluene, reflux, 96%, f) NBS, p-TsOH, MeCN, reflux, 96%, g) Sodium *p*-toluenesulfinate, K_2CO_3, DMF, 66%, h) $Pd(PPh_3)_4$, PPh_3, toluene, 100°C, 86%, i) NaHMDS, DCM, -78°C then *p*-tolualdehyde, THF, -78°C to 40°C, 82%

2.2 Visible-Light-Induced Synthesis of conjugated diene derivatives

Reaction design and development.

To examine the feasibility of broadening the substrate scope, we envisioned an intramolecular [2+2] cycloaddition of enyne via visible-light photocatalysis (Scheme 12).

Scheme 12. Design for intramolecular [2+2] cycloaddition of enyne

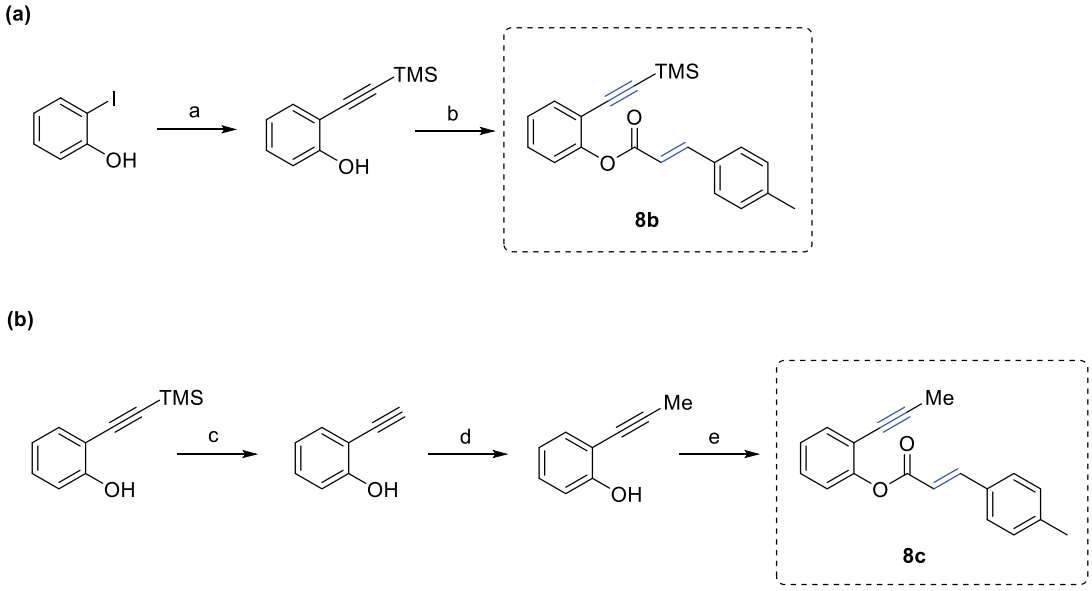


Scheme 13. Visible-light-induced cascade reaction of enyne

Initially, we tested a cinnamate derivative **8a** (Scheme 13). It was readily accessible through the Sonogashira reaction of the corresponding acetylene with 2-iodophenol and subsequent esterification via acid chloride. Surprisingly, we discovered an unexpected product when enyne **8a** was used as the intramolecular substrate (Scheme 13a). We were intrigued by this transformation as it represents a direct one-pot synthesis of conjugated diene derivatives from enyne derivatives. We expected that product **9a** was formed through visible-light induced photocatalytic cascade reaction (Scheme 13b). Enyne **8a** underwent visible-light promoted [2+2] photocycloaddition followed by electrocyclic ring-opening reaction, and the resulting product **9a** was afforded. Using DFT calculation, detailed mechanistic studies are ongoing in our laboratory.

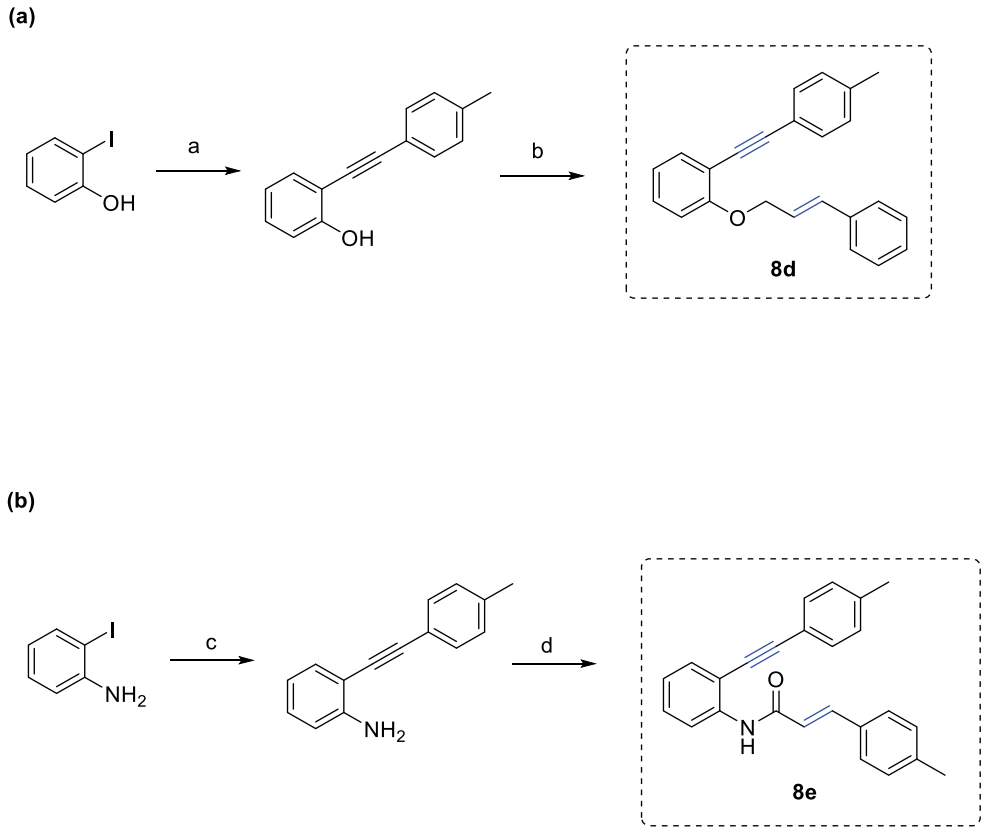
Substrate synthesis

In order to explore the scope, we devised a variety of enyne substrates. At first, we tried to make cinnamate derivatives to investigate the influence of various substituents on the yne part of the enyne (Scheme 14). Instead of aryl substituents, other substrates with alkyl and trimethylsilyl substituents were prepared. Substrate **8b** with trimethylsilyl substituent was synthesized by the same procedure for the synthesis of **8a**. The synthesis of another enyne compound **8c** was started from the appropriate phenol, which prepared by deprotection of the TMS group followed by methylation. The desired enyne was obtained by esterification from acid chloride.



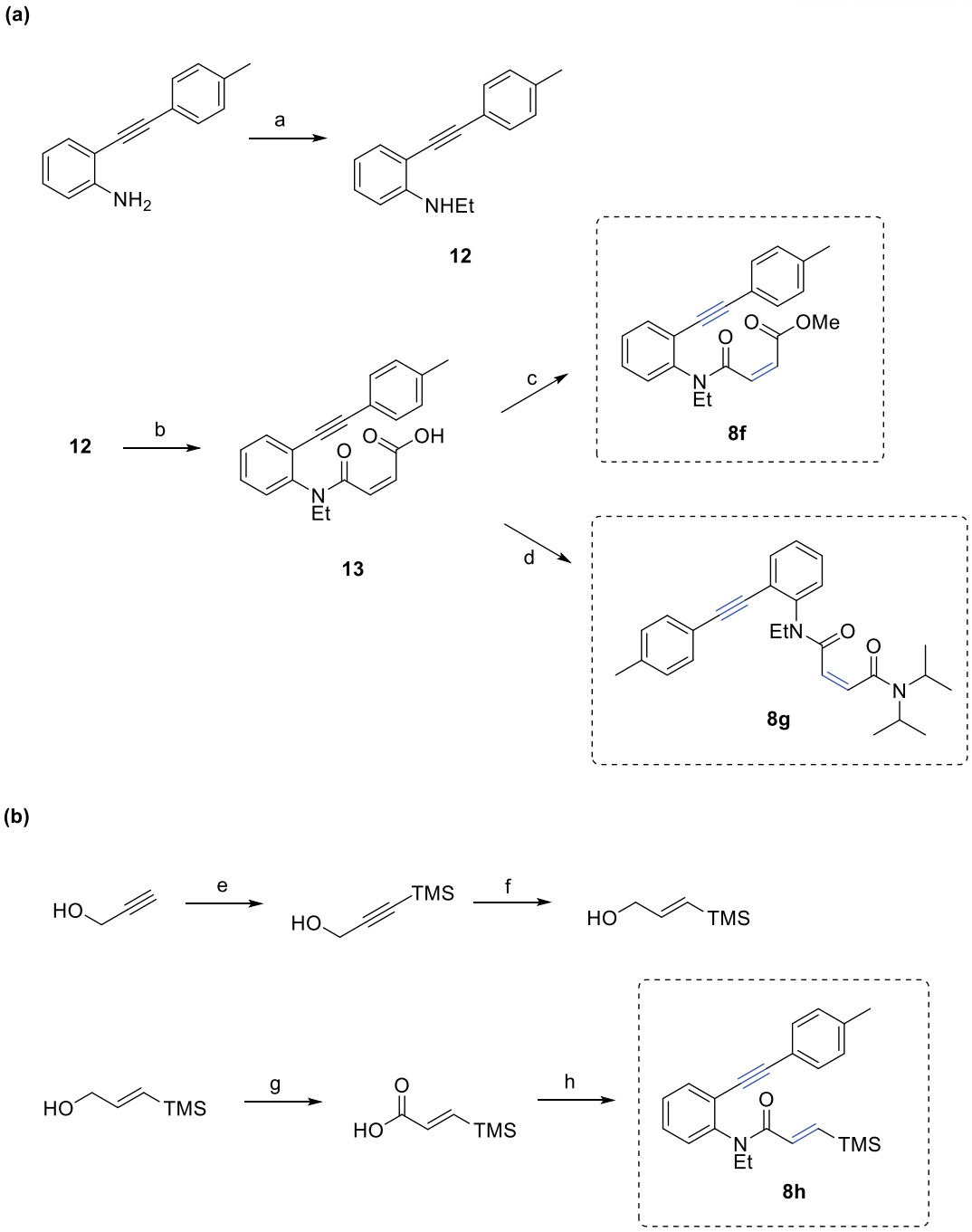
Scheme 14. Synthesis of cinnamate derivatives - Reagents and conditions: a) (Trimethylsilyl)acetylene, $Pd(PPh_3)_2Cl_2$, CuI, THF:Et_3N (4:1), 98%, b) 4-Methylcinnamic acid, $(COCl)_2$, DMF, DCM, 0°C, then corresponding phenol, Et_3N, 72% c) KF, MeOH, 76%, d) nBuLi, THF, -78°C, then MeI, 0°C, 85%, e) 4-Methylcinnamic acid, $(COCl)_2$, DMF, DCM, 0°C, then corresponding phenol, Et_3N, 86%

Besides cinnamate derivatives, we designed *o*-allyloxyl(ethynyl)benzene and cinnamamide derivatives to broaden the scope. They were readily accessible through the Sonogashira reaction of terminal acetylene with 2-iodophenol followed by O-alkylation with corresponding allyl bromide (Scheme 15a). Cinnamamide **8e** was also afforded by the Sonogashira reaction of *p*-tolylacetylene with 2-iodoaniline and subsequent amide formation via acid chloride (Scheme 15b).

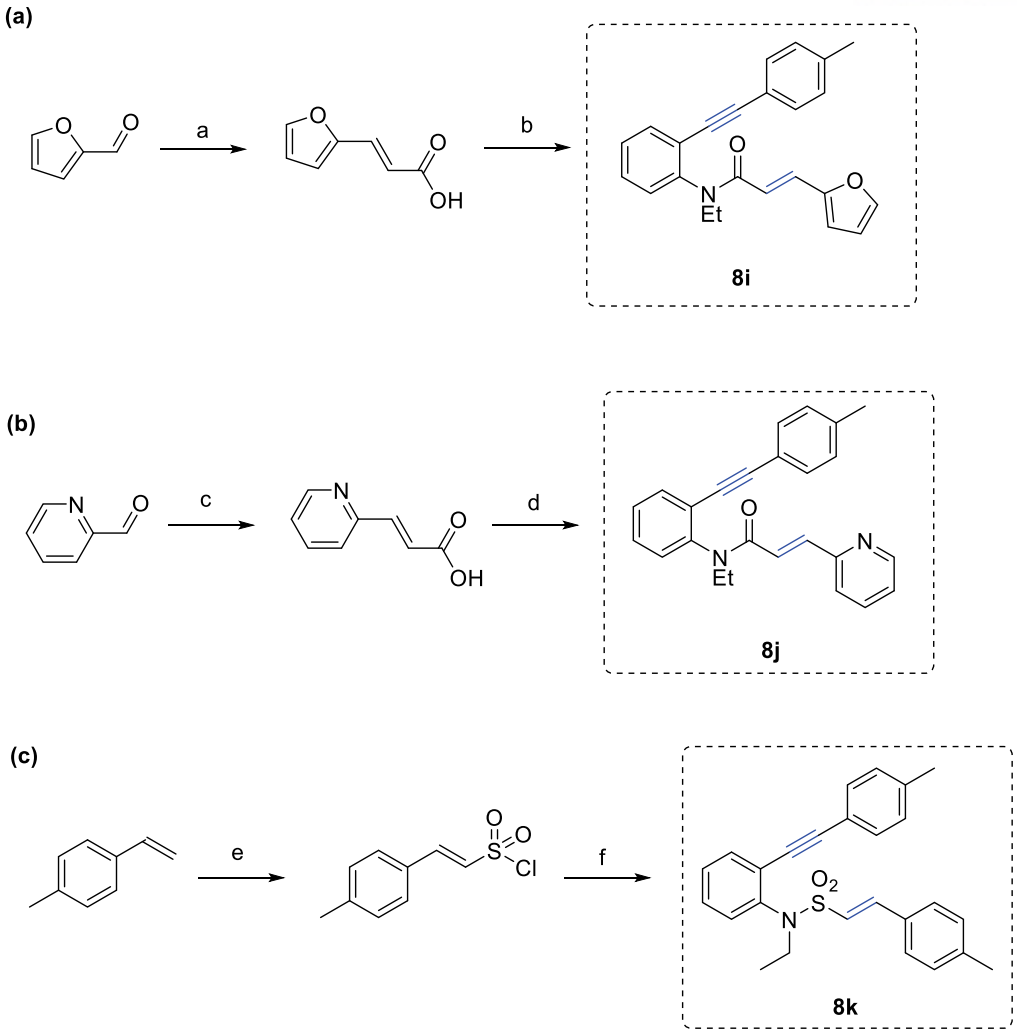


Scheme 15. Synthesis of *o*-allyloxyl(ethynyl)benzene and cinnamamide derivatives - Reagents and conditions: (a) *p*-Tolylacetylene, $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, 90%, (b) Cinnamyl bromide, K_2CO_3, MeCN, 84% (c) *p*-Tolylacetylene, $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, 96%, (d) 4-Methylcinnamic acid, $(COCl)_2$, DMF, DCM, 0°C, then corresponding aniline, Et_3N, 82%

Then, we aimed to synthesis various acrylamide derivatives to evaluate the feasibility of introducing various functional groups on the ene side of enynes. Accordingly, we desired to obtain maleamate **8f**, and maleamide **8g**, (trimethylsilyl)acrylamide **8h** (Scheme 16). First, we made maleic acid monomethyl ester and maleic acid monoamide derivatives derived from maleic anhydride to react with appropriate aniline to synthesize **8f** and **8g**. Unfortunately, the resulting maleic acid derivatives failed to react with N-ethyl-2-(*p*-tolylethynyl)aniline. Because of the difficulties encountered with the formation of **8f** and **8g**, we designed an alternative route to prepare desired products (Scheme 16a). N-ethyl-2-(*p*-tolylethynyl)aniline was directly reacted with maleic anhydride to prepare maleic acid **13**. Finally, maleamate **8f** was obtained by acid-catalyzed esterification with methanol. The desired maleamide **8g** was also afforded by amide formation via mixed anhydride with DIPA. Another acrylamide derivative **8h** was formed by a four-step sequence starting from commercially available propargyl alcohol (Scheme 16b). Propargyl alcohol was transformed into TMS substituted allylic alcohol by TMS protection with nBuLi followed by LAH reduction. The subsequent Jones oxidation and amide coupling using acid chloride gave the desired compound **8h**. Heterocyclic compounds including furan derivative (**8i**) as well as pyridine derivatives (**8j**) were also prepared (Scheme 17a and b). The synthesis of heterocyclic compound (**8i**, **8j**) was initiated from the corresponding acrylic acid, which obtained by Doebner modification of the Knoevenagel condensation. Amide synthesis with in the presence of oxalyl chloride and DMF as a catalyst gave the desired product **8i**. However, attempts to make the pyridine derivatives **8j**, through carbodiimide, and acid chloride, didn't afford the desired product. At last, the substrate **8j** was prepared by amide coupling using mixed anhydrides. Additionally, sulfonamide **8k** was formed by the reaction of the appropriate aniline with sulfonyl chlorides, which prepared from 4-methylstyrene (Scheme 17c).

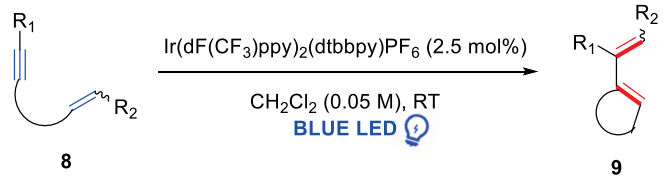


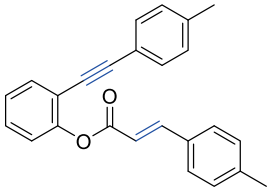
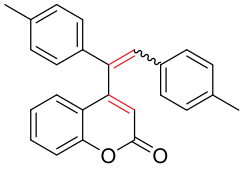
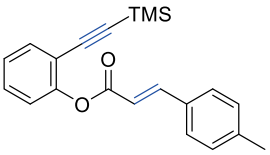
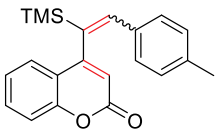
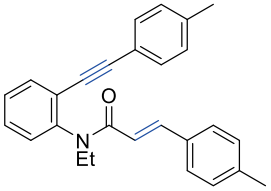
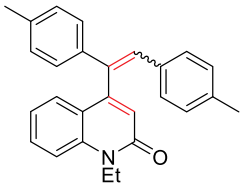
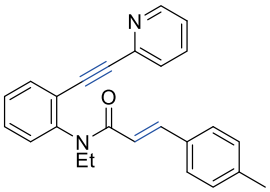
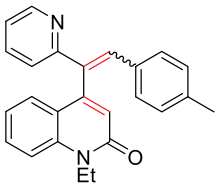
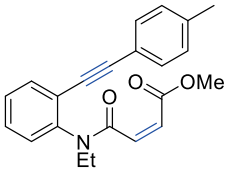
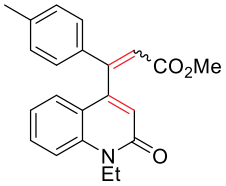
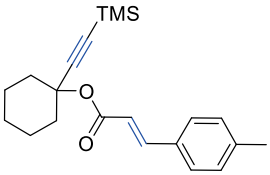
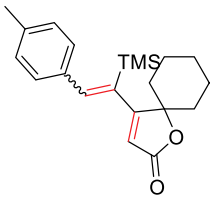
Scheme 16. Synthesis of acrylamide derivatives - Reagents and conditions: a) nBuLi, THF, -78°C, then EtI, 96%, b) Maleic anhydride, Et_2O, 73%, c) *p*-TsOH·H_2O, MeOH, reflux, 99%, d) IBCF, Et_3N, DCM, 0°C, then DIPA, 0°C to reflux, 78%, e) nBuLi, THF, -78°C, then TMSCl, 74%, f) $LiAlH_4$, THF, g) Jones reagent, Acetone, h) $(COCl)_2$, DMF, DCM, 0°C, then **12**, Et_3N, 70%,



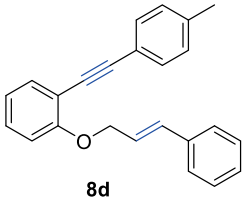
Scheme 17. Synthesis of acrylamide and sulfonamide derivatives - Reagents and conditions: a) malonic acid, pyridine, piperidine, reflux, 92%, b) $(COCl)_2$, DMF, DCM, 0°C, then **12**, Et_3N, 91%, c) malonic acid, pyridine, piperidine, reflux, 61%, d) *t*-BuOCOCl, Et_3N, DCM, 0°C, then **12**, 0°C to reflux, 58%, e) SO_2Cl_2, DMF, 0°C to 80°C, 68%, f) **12**, pyridine, DCM, 0°C, 73%

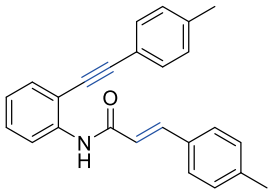
Table 3. Substrate scope of enynes[a,b]

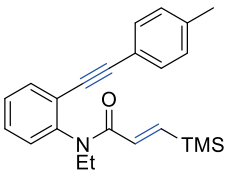


-Substrate-	-Product-	-Substrate-	-Product-
	 **9a** (73%, E/Z 1:1)[d]		 **9b** (60%, E/Z 1.2:1)[c]
	 **9l** (80%, E/Z 2:1)[c]		 **9m** (69%, E/Z 2.8:1)[d]
	 **9f** (60%, E/Z 1.5:1)[c]		 **9n** (41%, E/Z 1.3:1)[d]

-Unsuccessful substrate-


8d


8e


8h

[a] Reaction conditions: Reactions were performed with **8** (0.10 mmol, 0.05 M) and Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)PF$_6$ (2.5 mol%) in dry CH_2Cl_2 under N_2.
[b] Isolated yield. [c] Rxn time: 2 h ~ 18 h. [d] Rxn time: 24 h ~ 48 h.

We then evaluated the scope of enyne derivatives (Table 3). At first, various cinnamate derivatives have been investigated for their reactivity in this method. Instead of aryl substituents on the yne part of enyne, another substrate with trimethylsilyl substituent **8b** was proven successful for the present transformation. Then, the *o*-allyloxyl(ethynyl)benzene derivative **8d** was tested. Unfortunately, the desired cyclobutene product was not observed; only isomerization product of **8d** was detected by crude NMR. In addition to cinnamate derivatives, we evaluated the reaction of cinnamamide derivatives. Unlike secondary cinnamamide **8e**, tertiary cinnamamide **8l** was suitable for the present transformation. N-alkyl substituted conjugated diene **9l** could be prepared in improved yields. Heterocyclic compound including pyridine derivative (**9m**) was also successfully transformed. Besides cinnamamide derivatives, maleamate **8f** proceeded smoothly to furnish the desired product **9f** in moderate yields. Unfortunately, substrate **8h** proved to be unsuitable for this transformation. Interestingly, we could synthesize a unique spirocyclic butenolide derivative **9n**, which one of the important heterocyclic compounds widely used as a key structural moiety in natural products.[20] Further examination of the scope is ongoing in our laboratory.

III.CONCULSION

In conclusion, we have developed a new type of photochemical [2+2] cycloadditions between alkynes and electron-deficient alkenes under visible-light irradiation. This reaction would serve as an efficient method for the synthesis of cyclobutene derivatives via the energy transfer process. In addition, conjugated diene derivatives could be synthesized by simply transforming the substrates into enyne. Enyne derivatives undergo visible-light promoted [2+2] photocycloaddition followed by an electrocyclic ring-opening reaction. The reaction is mild conditions, simple operation compare to existing [2+2] photocycloadditions. We believe that this synthetic method will play an important role to construct an array of important molecules. Further studies on the detailed mechanism and synthetic applications are ongoing in our laboratory.

IV. EXPERIMENTAL

General methods

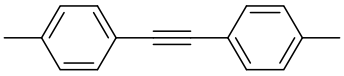
All the reactions were conducted in oven dried glassware under nitrogen atmosphere with freshly distilled dry solvents under anhydrous conditions unless otherwise indicated. All reagents were purchased from commercial sources, such as Alfa Aesar, Sigma-Aldrich, Acros, or TCI Chemicals, and were used without further purification. The progress of the reaction was monitored by thin layer chromatography (TLC) using Merck TLC Silica gel 60 F254 precoated plates (0.2 mm thickness). The plates were visualized by 254 nm of ultraviolet light. Also, further visualization is conducted by treatment with basic solution of potassium permanganate or acidic solution of ceric molybdate. Flash column chromatography was performed with Silica Flash P60 silica gel (230-400 mesh).

A systematic nomenclature for the compounds follows the numbering system as defined by IUPAC with assistance from CS Chemdraw® software. Proton (^{1}H) and carbon (^{13}C) NMR spectra were obtained using 400/100 MHz Bruker Advance III FT-NMR spectrometer or 400/100 MHz Agilent 400M FT-NMR spectrometer. NMR solvents were purchased from Cambridge Isotope Laboratories and the residue solvent signals were taken as the reference (0.0 ppm for ^{1}H NMR spectra and 77.0 ppm for ^{13}C NMR spectra in $CDCl_3$ and 2.50 ppm for ^{1}H NMR spectra and 39.52 ppm for ^{13}C NMR spectra in DMSO-d_6). Chemical shifts (δ) were reported in units of parts per million (ppm) and coupling constants (*J*) were given in hertz (Hz). The following abbreviations described the multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Mass analysis was conducted using Advion Expression CMS mass spectrometer. Luminescence quenching studies were performed with F-7000 FL Spectrophotometer.

Substrates synthesis:

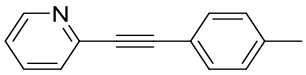
Preparation and characterization of alkyne compounds (5)

1,2-di-*p*-tolylethyne (5a)



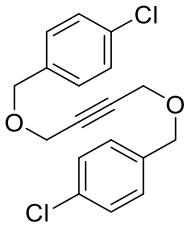
To a suspension of $Pd(PPh_3)_4$ (5 mol%), CuI (10 mol%), and 4-bromotoluene (1.0 equiv.) in degassed piperidine (0.2 M) was added dropwise *p*-tolylacetylene (1.0 equiv.) under nitrogen atmosphere. The reaction mixture was stirred at 80°C for overnight. The reaction mixture was washed with a saturated solution of NH_4Cl and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography. 77% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 8.0 Hz, 4H), 7.14 (d, 7.9 Hz, 4H), 2.36 (s, 6H); The compound was identified by spectral comparison with literature data.[S1]

2-(*p*-tolylethynyl)pyridine (5c)



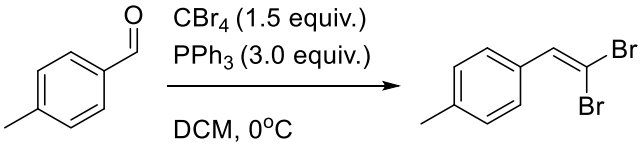
To a suspension of $Pd(PPh_3)_2Cl_2$ (3 mol%), CuI (6 mol%), and 2-bromopyridine (1.0 equiv.) in degassed Et_3N (0.4 M) was added dropwise *p*-tolylacetylene (1.5 equiv.) under nitrogen atmosphere. The reaction mixture was stirred at 80°C for overnight. The reaction mixture was washed with a saturated solution of NH_4Cl and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel. 90% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H), 7.67 (td, 7.7, 1.8 Hz, 1H), 7.53 – 7.48 (m, 3H), 7.23 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H), 7.17 (d, 7.8 Hz, 2H), 2.38 (s, 3H); The compound was identified by spectral comparison with literature data.[S2]

1,4-bis((4-chlorobenzyl)oxy)but-2-yne (5h)



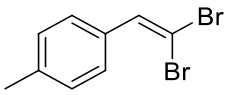
To a suspension of NaH (60% in mineral oil, 2.5 equiv.) in dry DMF was added slowly a solution of 2-butyne-1,4-diol (1.0 equiv., 0.3 M) in DMF at 0°C under nitrogen atmosphere. The reaction mixture was stirred at 0°C for 1h. 4-Chlorobenzyl chloride in dry DMF was added to the reaction mixture. Then, the reaction temperature was increased to room temperature and the mixture was stirred for 6h. The reaction mixture was washed with water and extracted with Et_2O. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel. 69% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 8H), 4.56 (s, 4H), 4.23 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.87, 133.65, 129.26, 128.59, 82.45, 70.84, 57.54; MS (APCI): *m/z* 335.3 $[M+H]^+$

(E)-4,4'-(but-1-en-3-yne-1,4-diyl)bis(methylbenzene) (5i)

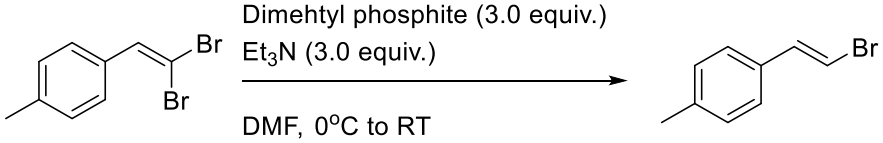


Step 1[S3]: *p*-Tolualdehyde (1.0 equiv., 0.15 M) and CBr_4 (1.5 equiv.) were dissolved in CH_2Cl_2 and cooled to 0°C. A solution of PPh_3 (3.0 equiv.) in CH_2Cl_2 was added dropwise keeping the temperature below to 0°C. The reaction mixture was stirred at 0°C for 1h under nitrogen atmosphere. Et_2O was added, and the mixture was filtered through a short pad of silica gel. The filtrate was concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel.

1-(2,2-dibromovinyl)-4-methylbenzene

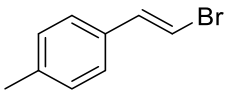


: 94% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.43 (m, 3H), 7.17 (d, 8.0 Hz, 2H), 2.34 (s, 3H); The compound was identified by spectral comparison with literature data.[S4]

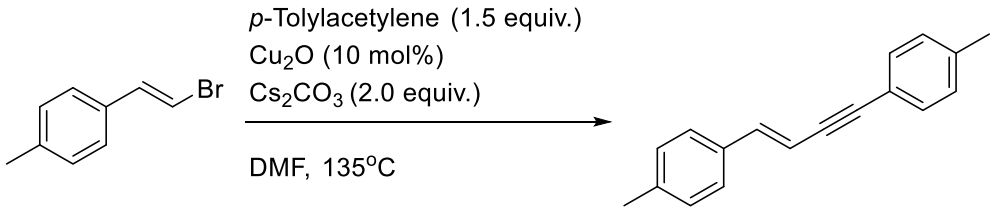


Step 2[S3]: To a solution of dibromide (1.0 equiv.), Et_3N (3.0 equiv.) in DMF (1.0 M) was added dimethyl phosphite (3.0 equiv.) at 0°C. The solution was stirred at room temperature for overnight. The reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layer was washed with a saturated solution of NH_4Cl and dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel.

(E)-1-(2-bromovinyl)-4-methylbenzene

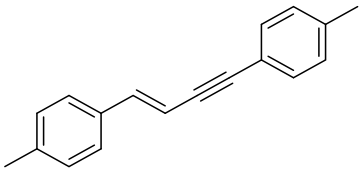


: 94% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, 8.2 Hz, 2H), 7.13 (d, 8.0 Hz, 2H), 7.07 (d, 14.0 Hz, 1H), 6.70 (d, 14.0 Hz, 1H), 2.32 (s, 3H); The compound was identified by spectral comparison with literature data.[S5]



Step 3[S6]: To a suspension of Cs_2CO_2 (2 equiv.), Cu_2O (10 mol%), vinyl bromide (1.0 equiv.) in DMF (1.0 M) was added dropwise *p*-tolylacetylene (1.5 equiv.) under nitrogen atmosphere. The reaction mixture was stirred at 135°C for overnight, and the heterogeneous mixture was cooled to room temperature. The resulting solution was filtered through a short pad of silica gel, then washed with ethyl acetate, and concentrated to give the crude material. The resulting crude was purified by flash chromatography on silica gel.

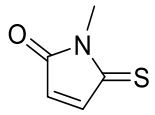
(E)-4,4'-(but-1-en-3-yne-1,4-diyl)bis(methylbenzene) (5i)



: 82% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, 8.1 Hz, 2H), 7.31 (d, 8.2 Hz, 2H), 7.17 – 7.11 (m, 3H), 6.99 (d, 16.2 Hz, 1H), 6.33 (d, 16.2 Hz, 1H), 2.35 (s, 6H); The compound was identified by spectral comparison with literature data.[S7]

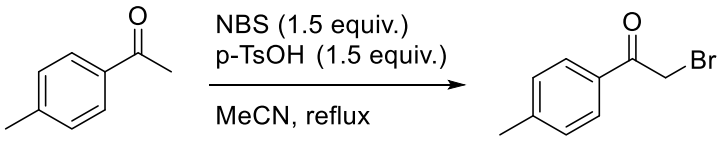
Preparation and characterization of alkene compounds (6)

1-methyl-5-thioxo-1,5-dihydro-2H-pyrrol-2-one (6j)



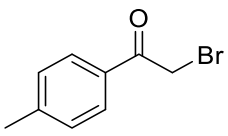
To a hot solution of N-methylmaleimide (2.0 equiv.) in dry toluene was added a boiling suspension of Lawesson's reagent (1.0 equiv., 0.12 M) in dry toluene. The reaction mixture was refluxed for 1h, and the mixture was cooled to room temperature. The resulting solution was filtered quickly through a short pad of silica gel, and concentrated to give the crude material. The resulting crude was purified by flash chromatography on silica gel. 45% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77 (d, 5.7 Hz, 1H), 6.68 (d, 5.7 Hz, 1H), 3.29 (s, 3H); The compound was identified by spectral comparison with literature data.[S8]

(E)-1,4-di-*p*-tolylbut-2-ene-1,4-dione (6k)

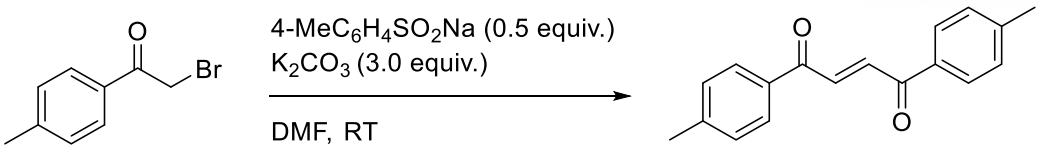


Step 1[S9]: To a solution of acetophenone (1.0 equiv.), NBS (1.2 equiv.), and *p*-TsOH (1.5 equiv.) in acetonitrile (0.2 M) was refluxed for 1h. The mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure. The reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel.

2-bromo-1-(*p*-tolyl)ethan-1-one (11)

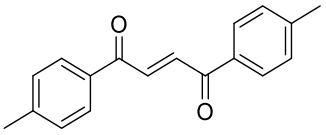


: 96% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, 8.2 Hz, 2H), 7.29 (d, 7.9 Hz, 2H), 4.43 (s, 2H), 2.43 (s, 3H); The compound was identified by spectral comparison with literature data.[S9]



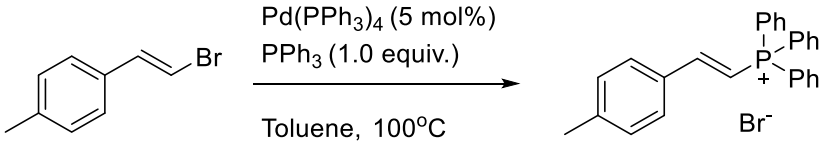
Step 2[S10]: To a suspension of 2-bromoacetophenone (1.0 equiv.), K2CO3 (1.5 equiv.), and sodium 4-toluenesulfinate (0.5 equiv.) in DMF (1.0 M) was stirred at room temperature for overnight. The mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure. The reaction mixture was diluted with water and extracted with CH_2Cl_2, and the combined organic layer was washed with brine. The resulting solution was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel.

(E)-1,4-di-p-tolylbut-2-ene-1,4-dione (6k)



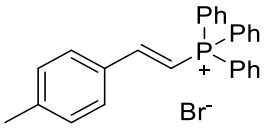
: 66% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 2H), 7.98 (d, 8.2 Hz, 4H), 7.33 (d, 7.9 Hz, 4H), 2.45 (s, 6H); The compound was identified by spectral comparison with literature data.[S10]

1,3-di-p-tolylpropa-1,2-diene (6l)

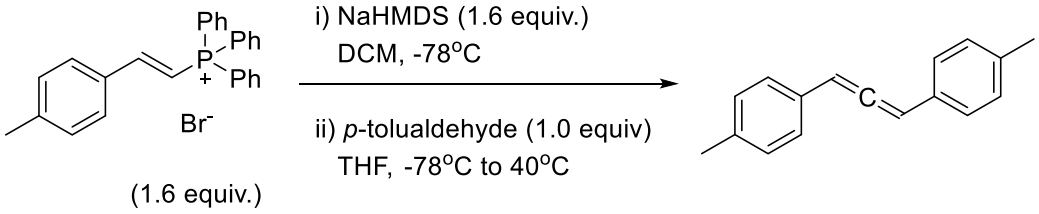


Step 1[S11]: To a suspension of $Pd(PPh_3)_4$ (5 mol%), 2-bromo-1-(*p*-tolyl)ethan-1-one (1.0 equiv.), and triphenylphosphine (1.0 equiv.) in toluene (0.2 M) was stirred at 100°C for 1h under nitrogen atmosphere. The reaction mixture was cooled to room temperature. The resulting solid was collected by filtration, and washed with toluene and Et_2O to afford pure white solid.

(E)-(4-methylstyryl)triphenylphosphonium bromide

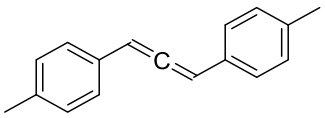


: 86% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (dd, 20.1, 17.1 Hz, 1H), 7.89 (d, 8.1 Hz, 2H), 7.85 – 7.68 (m, 15H), 7.27 (d, 8.0 Hz, 2H), 7.02 (dd, 23.1, 17.1 Hz, 1H), 2.38 (s, 3H);



Step 2[S12]: (E)-(4-methylstyryl)triphenylphosphonium bromide (1.0 equiv., 0.15 M) was dissolved in CH_2Cl_2 (0.3 M) and cooled to -78°C. NaHMDS solution (1.0 M in THF, 1.6 equiv.) was added dropwise, and the solution was stirred for 1h at -78°C. A solution of *p*-tolualdehyde (3.0 equiv.) in THF (0.6 M) was added dropwise at -78°C, and the reaction mixture was stirred for overnight at 40°C. The reaction mixture was diluted with water and extracted with Et_2O. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel.

1,3-di-p-tolylpropa-1,2-diene (6l)



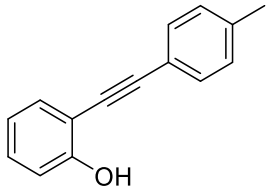
: 82% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, 8.1 Hz, 4H), 7.11 (d, 7.9 Hz, 4H), 6.55 (s, 2H), 2.33 (s, 6H); The compound was identified by spectral comparison with literature data.[S13]

Preparation and characterization of enynes 8

General procedure A (for Sonogashira coupling)

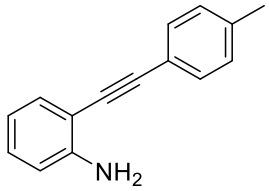
To a suspension of $Pd(PPh_3)_2Cl_2$ (x mol%), CuI (x mol%), and 2-iodophenol or 2-iodoaniline (1.0 equiv.) in degassed Et_3N (x M) was added dropwise the corresponding alkyne (x equiv.) under nitrogen atmosphere. The reaction mixture was stirred until TLC indicated complete consumption of the starting material. The reaction mixture was washed with a saturated solution of NH_4Cl and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel.

2-(p-tolylethynyl)phenol



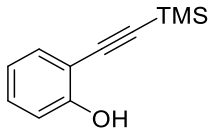
Prepared according to the *General Procedure A* using $Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (4 mol%), 2-iodophenol (1.0 equiv.), and *p*-tolylacetylene (2.0 equiv.) in Et_3N (0.5 M) at reflux, 90% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.39 (m, 3H), 7.29 – 7.23 (m, 1H), 7.18 (dt, 7.9, 0.7 Hz, 2H), 6.98 (dd, 8.3, 0.7 Hz, 1H), 6.90 (td, 7.5, 1.1 Hz, 1H), 5.85 (s, 1H), 2.38 (s, 3H); The compound was identified by spectral comparison with literature data.[S14]

2-(p-tolylethynyl)aniline



Prepared according to the *General Procedure A* using $Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (2 mol%), 2-iodoaniline (1.0 equiv.), and *p*-tolylacetylene (1.2 equiv.) in Et_3N (0.2 M) at room temperature, 99% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, 8.1 Hz, 2H), 7.35 (d, 8.2 Hz, 1H), 7.16 (d, 7.9 Hz, 2H), 7.12 (dd, 7.8, 1.2 Hz, 1H), 6.76 – 6.67 (m, 2H) 4.26 (s, 2H), 2.37 (s, 3H); The compound was identified by spectral comparison with literature data.[S15]

2-((trimethylsilyl)ethynyl)phenol

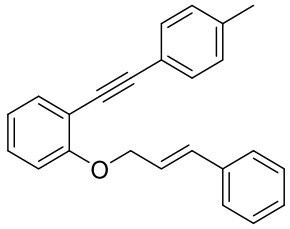


Prepared according to the *General Procedure A* using $Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (4 mol%), 2-iodophenol (1.0 equiv.), and trimethylsilylacetylene (1.5 equiv.) in Et_3N (0.5 M) at reflux, 98% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, 7.7, 1.6 Hz, 1H), 7.27 – 7.21 (m, 1H), 6.94 (dd, 8.3, 0.8 Hz, 1H), 6.85 (td, 7.6, 1.0 Hz, 1H), 7.11 (d, 7.9 Hz, 4H), 5.82 (s, 1H), 0.28 (s, 9H); The compound was identified by spectral comparison with literature data.[S15]

General procedure B (for O-alkylation)

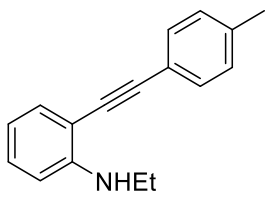
To a suspension of 2-(*p*-tolylethynyl)phenol (1.0 equiv.), the corresponding bromide (1.2 equiv) in solvent (0.6 M) was added K_2CO_3 (1.5 equiv.). The reaction mixture was stirred at room temperature until TLC indicated complete consumption of the starting material. The reaction mixture was diluted with water and extracted with Et_2O. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel.

1-(cinnamyloxy)-2-(*p*-tolylethynyl)benzene (8d)



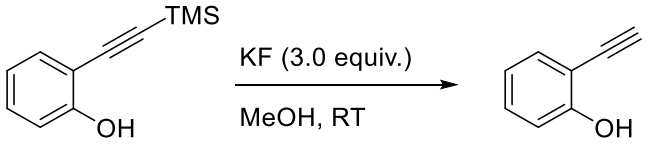
Prepared according to the *General Procedure B* using cinnamyl bromide in MeCN, 84% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (dd, 7.8, 1.6 Hz, 1H), 7.46 (d, 8.2 Hz, 2H), 7.39 (d, 7.4 Hz, 2H), 7.35 – 7.24 (m, 4H), 7.14 (d, 8.0 Hz, 2H), 6.98 – 6.92 (m, 2H), 6.86 (d, 16.2 Hz, 1H), 6.46 (dq, 16.3, 5.2 Hz, 1H), 4.82 (dd, 5.1, 1.7 Hz, 2H), 2.36 (s, 3H); The compound was identified by spectral comparison with literature data.[S16]

N-ethyl-2-(p-tolylethynyl)aniline (12)



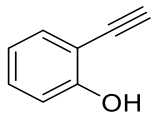
2-(p-tolylethynyl)aniline (1.0 equiv.) was dissolved in THF (0.2 M) under nitrogen atmosphere and cooled to -78°C. nBuLi solution (2.5 M in hexane, 1.1 equiv.) was added dropwise, and the mixture was stirred for 1h. Iodoethane (1.0 equiv.) was added dropwise at -78°C, and the reaction mixture was stirred for 1h at room temperature. The reaction mixture was quenched by addition of saturated solution of NH_4Cl and extracted with ethyl acetate. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel. 96% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, 8.0 Hz, 2H), 7.35 (dd, 7.4, 1.5 Hz, 1H), 7.20 (ddd, 8.9, 8.0, 1.6 Hz, 1H), 7.16 (d, 7.8 Hz, 2H), 6.66 – 6.60 (m, 2H), 4.56 (bs, 1H), 3.24 (qd, 7.2, 5.5 Hz, 1H), 2.37 (s, 3H), 1.32 (t, 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.04, 138.41, 132.18, 131.45, 129.97, 129.28, 120.47, 116.26, 109.60, 107.60, 95.28, 85.50, 38.19, 21.64, 14.95; MS (APCI): *m/z* 236.2 $[M+H]^+$

2-(prop-1-yn-1-yl)phenol

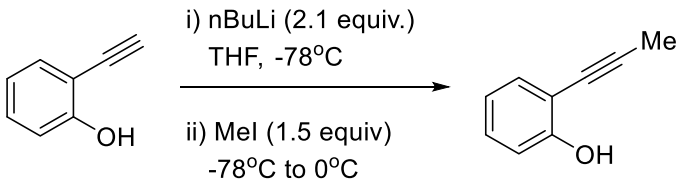


Step 1[S17]: To a solution of 2-((trimethylsilyl)ethynyl)phenol (1.0 equiv.) in MeOH (0.2 M) was added KF (3.0 equiv.). The mixture was stirred at room temperature for 3h, and the solvent was evaporated under reduced pressure. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel.

2-ethynylphenol

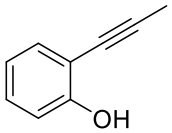


: 76% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, 7.5, 1.5 Hz, 1H) 7.31 – 7.26 (m, 1H), 6.95 (d, 8.3 Hz, 1H), 6.88 (td, 7.6, 1.0 Hz, 1H), 5.77 (bs, 1H), 3.47 (s, 1H); The compound was identified by spectral comparison with literature data.[S17]



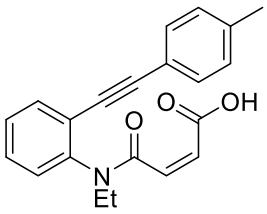
Step 2: 2-ethynylphenol (1.0 equiv.) was dissolved in THF (0.4 M) under nitrogen atmosphere and cooled to -78°C. nBuLi solution (2.5 M in hexane, 2.5 equiv.) was added dropwise, and the mixture was stirred for 1h. Iodomethane (1.5 equiv.) was added dropwise at -78°C, and the reaction mixture was stirred for 1h at 0°C. The reaction mixture was quenched by the addition of a saturated solution of NH_4Cl and extracted with Et_2O. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel.

2-(prop-1-yn-1-yl)phenol



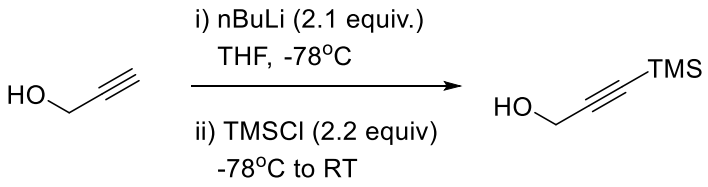
: 85% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (dd, 7.7, 1.4 Hz, 1H) 7.23 – 7.16 (m, 1H), 6.92 (d, 7.9 Hz, 1H), 6.84 (td, 7.6, 0.9 Hz, 1H), 5.79 (s, 1H), 2.13 (s, 3H); The compound was identified by spectral comparison with literature data.[S18]

(Z)-4-(ethyl(2-(p-tolylethynyl)phenyl)amino)-4-oxobut-2-enoic acid (13)



To a solution of maleic anhydride (1.0 equiv.) in Et_2O was added a solution of N-ethyl-2-(p-tolylethynyl)aniline (1.0 equiv, 0.8 M) in Et_2O. The reaction mixture was stirred at room temperature for 6h. The solvent was evaporated under reduced pressure. The crude material was purified by flash chromatography on silica gel. 73% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, 5.9, 3.4 Hz, 1H), 7.45 (dd, 5.8, 3.4 Hz, 2H), 7.34 (d, 8.1 Hz, 2H), 7.25 (dd, 5.7, 3.6 Hz, 1H), 7.17 (d, 7.9 Hz, 2H), 6.18 (d, 13.0 Hz, 1H), 6.11 (d, 13.2 Hz, 1H), 3.94 (q, 7.2 Hz, 1H), 2.37 (s, 3H), 1.25 (t, 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.28, 164.85, 140.91, 139.65, 136.21, 133.17, 131.43, 129.57, 129.37, 129.28, 128.53, 128.06, 123.41, 118.63, 96.64, 83.77, 45.66, 21.56, 12.34; MS (APCI): *m/z* 334.2 $[M+H]^+$

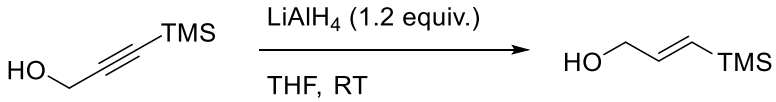
(E)-3-(trimethylsilyl)acrylic acid



Step 1: To a solution of propargyl alcohol (1.0 equiv) in THF (0.4 M) was cooled to -78°C, and nBuLi solution (2.5 M in hexane, 2.1 equiv.) was added dropwise under nitrogen atmosphere. After stirring for 30 min, trimethylsilyl chloride (2.2 equiv.) was added dropwise at -78°C, and the reaction mixture was stirred at room temperature for overnight. The reaction mixture was cooled to 0°C, quenched by water, and added 1 N HCl solution. The mixture was stirred at room temperature for 1h. The resulting solution was then carefully neutralized with a saturated solution of $NaHCO_3$ and extracted with Et_2O. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel.

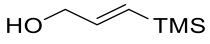
3-(trimethylsilyl)prop-2-yn-1-ol

: 74% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.27 (d, 5.9 Hz, 2H), 1.43 (bs, 1H), 0.18 (s, 9H); The compound was identified by spectral comparison with literature data.[S19]

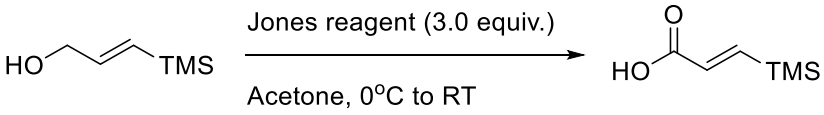


Step 2: To a suspension of $LiAlH_4$ (1.2 equiv.) in THF was added a solution of 3-(trimethylsilyl)prop-2-yn-1-ol (1.0 equiv, 0.4 M) in THF. The reaction mixture was stirred at room temperature for 1h. The reaction mixture was quenched by the addition of a saturated solution of NH_4Cl and extracted with Et_2O. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The resulting crude mixture was used for the next step without further purification.

(E)-3-(trimethylsilyl)prop-2-en-1-ol

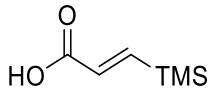


: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (dt, 18.8, 4.4 Hz, 1H), 5.92 (dt, 18.8, 1.8 Hz, 1H), 4.19 (d, 3.0 Hz, 2H), 0.08 (s, 9H); The compound was identified by spectral comparison with literature data.[S20]



Step 3: (E)-3-(trimethylsilyl)prop-2-en-1-ol was dissolved in acetone (0.35 M) and cooled to 0°C. Jones reagent (2.5 M in water, 3.0 equiv.) was added dropwise, and the mixture was stirred at room temperature for 1h. The reaction mixture was diluted with water and extracted with Et_2O. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The resulting crude mixture was used for the next step without further purification.

(E)-3-(trimethylsilyl)acrylic acid

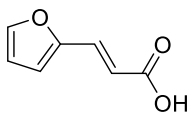


: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, 18.9 Hz, 1H), 6.25 (d, 18.9 Hz 1H), 0.16 (s, 9H); The compound was identified by spectral comparison with literature data.[S21]

General procedure C (for Knoevenagel condensation)

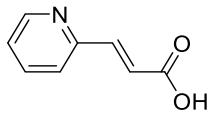
To a solution of the corresponding aldehyde (1.0 equiv.), malonic acid (1.5 equiv.), and piperidine (10.0 M) in pyridine (1.0 M) was refluxed for 1h. The reaction mixture was poured into ice and a solution of 1N HCl was added dropwise. The resulting solid was collected by filtration, and washed with water to afford pure white solid.

(E)-3-(furan-2-yl)acrylic acid



Prepared according to the *General Procedure C* using 2-furaldehyde, 92% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.36 (s, 1H), 7.83 (s, 1H), 7.39 (d, 15.8 Hz, 1H), 6.92 (d. 3.4 Hz, 1H), 6.62 (dd, 3.4, 1.8 Hz, 1H), 6.16 (d, 15.8 Hz, 1H); The compound was identified by spectral comparison with literature data.[S22]

(E)-3-(pyridin-2-yl)acrylic acid

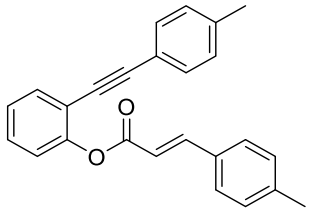


Prepared according to the *General Procedure C* using pyridine-2-carbaldehyde, 61% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.54 (s, 1H), 8.64 (dd, 4.8, 0.9 Hz, 1H), 7.86 (td, 7.7, 1.8 Hz, 1H), 7.72 (d, 7.8 Hz, 1H), 7.59 (d, 15.7 Hz, 1H), 7.40 (ddd, 7.6, 4.8, 1.1 Hz, 1H), 6.82 (d, 15.7 Hz, 1H); The compound was identified by spectral comparison with literature data.[S23]

General procedure D (for esterification via acid chloride)

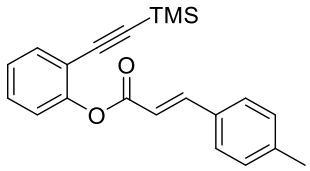
To a suspension of 4-methylcinnamic acid (1.2 equiv.), DMF (3 mol%) in dry DCM (0.5 M) was added dropwise oxalyl chloride (1.1 equiv., per acid) at 0°C. The reaction mixture was stirred at room temperature for 1h. Then, the solvent was removed under reduced pressure. The residue was dissolved in dry THF and slowly added dropwise to a solution of the appropriate phenol (1.0 equiv.) and Et_3N (1.2 equiv.) in dry THF (0.3 M) at 0°C. The mixture was stirred at room temperature until TLC indicated complete consumption of the starting material. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel.

2-(p-tolylethynyl)phenyl (E)-3-(p-tolyl)acrylate (8a)



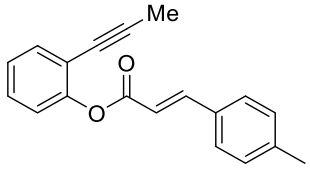
Prepared according to the *General Procedure D* using 2-(*p*-tolylethynyl)phenol, 94% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, 16.0 Hz, 1H), 7.59 (dd, 7.7, 1.6 Hz, 1H), 7.49 (d, 8.1 Hz, 2H), 7.37 (td, 7.8, 1.6 Hz, 1H), 7.32 (d, 8.2 Hz, 2H), 7.29 – 7.18 (m, 4H), 7.04 (d, 7.9 Hz, 2H), 6.67 (d, 16.0 Hz, 1H), 2.41 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.11, 151.80, 146.98, 141.33, 138.68, 132.94, 131.64, 131.62, 129.85, 129.33, 129.16, 128.48, 125.91, 122.51, 120.04, 117.82, 116.11, 94.81, 83.96, 21.67, 21.60 ; MS (APCI): *m/z* 353.3 $[M+H]^+$

2-((trimethylsilyl)ethynyl)phenyl (E)-3-(p-tolyl)acrylate (8b)



Prepared according to the *General Procedure D* using 2-((trimethylsilyl)ethynyl)phenol, 72% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, 16.0 Hz, 1H), 7.52 (dd, 7.7, 1.7 Hz, 1H), 7.49 (d, 8.1 Hz, 2H), 7.37 (td, 7.8, 1.7 Hz, 1H), 7.24 (d, 8.1 Hz, 2H), 7.21 (dd, 7.6, 1.1 Hz, 1H), 7.04 (d, 7.9 Hz, 2H), 7.17 (dd, 8.1, 1.1 Hz, 1H), 6.62 (d, 16.0 Hz, 1H), 2.40 (s, 3H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.74, 152.31, 146.67, 141.14, 133.03, 131.49, 129.72, 129.60, 128.24, 125.65, 122.31, 117.37, 115.96, 99.92, 99.69, 21.50, -0.18; MS (APCI): *m/z* 335.2 $[M+H]^+$

2-(prop-1-yn-1-yl)phenyl (E)-3-(p-tolyl)acrylate (8c)

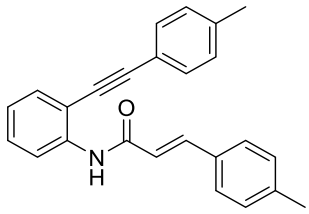


Prepared according to the *General Procedure D* using 2-(prop-1-yn-1-yl)phenol, 86% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, 16.0 Hz, 1H), 7.51 (d, 8.2 Hz, 2H), 7.46 (dd, 7.7, 1.6 Hz, 1H), 7.32 (td, 7.8, 1.6 Hz, 1H), 7.24 (d, 7.9 Hz, 2H), 7.18 (td, 7.6, 1.3 Hz, 1H), 7.14 (d, 8.1, 1.1 Hz, 1H), 6.64 (d, 16.0 Hz, 1H), 2.40 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.07, 151.70, 146.59, 141.16, 133.02, 131.48, 129.69, 128.59, 128.29, 125.66, 122.19, 118.07, 115.94, 91.10, 74.68, 21.49, 4.49; MS (APCI): *m/z* 277.2 $[M+H]^+$

General procedure E (for amide synthesis via acid chloride)

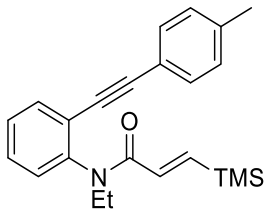
To a suspension of the corresponding acid (x equiv.), DMF (3 mol%) in dry DCM (0.5 M) was added dropwise oxalyl chloride (1.1 equiv., per acid) at 0°C. The reaction mixture was stirred at room temperature for 1h. Then, the solvent was removed under reduced pressure. The residue was dissolved in dry THF and slowly added dropwise to a solution of the appropriate aniline (1.0 equiv.) and Et_3N (1.2 equiv.) in dry THF (0.3 M) at 0°C. The mixture was stirred at room temperature until TLC indicated complete consumption of the starting material. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel.

(E)-3-(p-tolyl)-N-(2-(p-tolylethynyl)phenyl)acrylamide (8e)



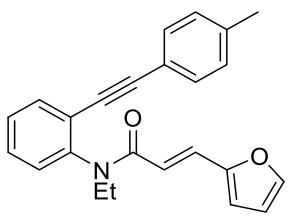
Prepared according to the *General Procedure E* using 4-methylcinnamic acid (1.2 equiv.), and 2-(*p*-tolylethynyl)aniline (1.0 equiv.), 82% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, 8.1 Hz, 1H), 8.18 (s, 1H), 7.73 (d, 15.6 Hz, 1H), 7.51 (d, 7.8 Hz, 1H), 7.48 (d, 7.9 Hz, 2H), 7.44 (d, 7.8 Hz, 2H), 7.38 (t, 7.7 Hz, 1H), 7.21 (t, 8.5 Hz, 4H), 7.08 (t, 7.5 Hz, 1H), 6.51 (d, 15.6 Hz, 1H), 2.43 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.98, 142.35, 140.44, 139.25, 131.73, 131.64, 131.46, 129.61, 129.59, 129.37, 127.99, 123.39, 119.93, 119.45, 119.45, 119.30, 96.82, 83.76, 21.56, 21.44; MS (APCI): *m/z* 352.3 $[M+H]^+$

(E)-N-ethyl-N-(2-(p-tolylethynyl)phenyl)-3-(trimethylsilyl)acrylamide (8h)



Prepared according to the *General Procedure E* using (E)-3-(trimethylsilyl)acrylic acid (1.2 equiv.), and N-ethyl-2-(p-tolylethynyl)aniline (1.0 equiv.), 70% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.51 (m, 1H), 7.40 – 7.32 (m, 4H), 7.21 – 7.18 (m, 1H), 7.17 – 7.10 (m, 3H), 6.06 (d, 18.4 Hz, 1H), 4.03 – 3.81 (m, 2H), 2.36 (s, 3H), 1.18 (t, 7.2 Hz, 3H), -0.08 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.34, 144.55, 143.01, 138.83, 134.82, 132.64, 131.45, 129.27, 129.10, 128.84, 127.76, 123.78, 119.58, 95.16, 85.19, 44.12, 21.52, 12.89, -1.92; MS (APCI): *m/z* 362.0 $[M+H]^+$

(E)-N-ethyl-3-(furan-2-yl)-N-(2-(p-tolylethynyl)phenyl)acrylamide (8i)



Prepared according to the *General Procedure E* using (E)-3-(furan-2-yl)acrylic acid (1.2 equiv.), and N-ethyl-2-(p-tolylethynyl)aniline (1.0 equiv.), 91% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.61 (m, 1H), 7.44 (d, 15.2 Hz, 1H), 7.41 – 7.34 (m, 4H), 7.29 – 7.21 (m, 2H), 7.12 (d, 7.8 Hz, 2H), 6.43 (d, 3.4 Hz, 1H), 6.34 (dd, 3.4, 1.8 Hz, 1H), 6.12 (d, 15.2 Hz, 1H), 4.14 – 4.00 (m, 1H), 3.88 – 3.78 (m, 1H), 2.34 (s, 3H), 1.20 (t, 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.83, 151.69, 143.62, 143.02, 138.83, 132.83, 131.50, 129.52, 129.10, 129.03, 128.36, 127.94, 123.85, 119.58, 116.87, 113.45, 111.88, 95.20, 85.15, 44.04, 21.50, 13.02; MS (APCI): *m/z* 356.3 $[M+H]^+$

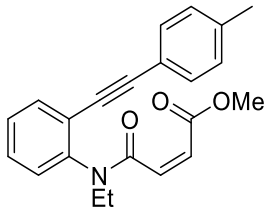
General procedure F (for Fischer esterification)

To a solution of the corresponding acid (1.0 equiv.), and p-toluenesulfonic acid monohydrate (0.2 equiv.) in MeOH (0.1 M) was refluxed for 3h. The solvent was evaporated under reduced pressure. The solvent was evaporated under reduced pressure. The crude material was purified by flash chromatography on silica gel.

General procedure G (for amide synthesis via mixed anhydride)

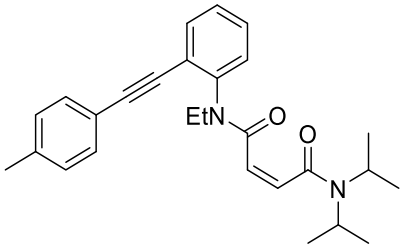
To a solution of the corresponding acid (1.0 equiv.), and Et_3N (1.2 equiv.) was dissolved in solvent (x M) under nitrogen atmosphere and cooled to 0°C. Isobutyl chloroformate (1.0 equiv.) was added dropwise, and the mixture was stirred for 30 min at 0°C. The appropriate amine (x equiv.) in solvent was added dropwise at 0°C, and the reaction mixture was stirred at room temperature. The solvent was evaporated under reduced pressure. The crude material was purified by flash chromatography on silica gel.

methyl (Z)-4-(ethyl(2-(p-tolylethynyl)phenyl)amino)-4-oxobut-2-enoate (8f)



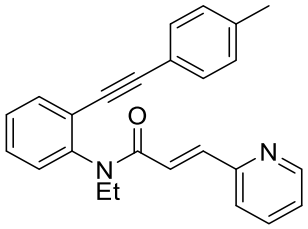
Prepared according to the *General Procedure F* using acid **13**, 99% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.52 (m, 1H), 7.41 (d, 8.1 Hz, 2H), 7.37 – 7.24 (m, 3H), 7.15 (d, 7.9 Hz, 2H), 6.39 (d, 11.9 Hz, 1H), 5.72 (d, 11.9 Hz, 1H), 4.03 – 3.84 (m, 2H), 3.74 (s, 3H), 2.37 (s, 3H), 1.23 (t, 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.72, 165.58, 142.37, 139.12, 137.24, 132.58, 131.60, 129.19, 128.99, 128.96, 128.24, 123.67, 123.55, 119.29, 95.19, 84.91, 51.75, 43.48, 21.53, 12.77; MS (APCI): *m/z* 348.3 $[M+H]^+$

N^1-ethyl-N^4,N^4-diisopropyl-N^1-(2-(p-tolylethynyl)phenyl)maleamide (8g)



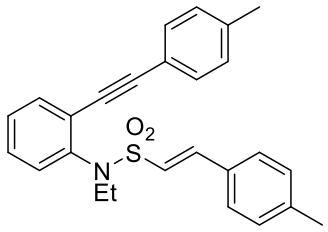
Prepared according to the *General Procedure G* using acid **13** (1.0 equiv.), and DIPA (1.2 equiv.), 78% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.56 (m, 1H), 7.38 (d, 8.0 Hz, 2H), 7.36 – 7.32 (m, 3H), 7.14 (d, 7.8 Hz, 2H), 6.09 (d, 11.9 Hz, 1H), 4.14 – 3.98 (m, 1H), 3.97 – 3.85 (m, 1H), 3.83 – 3.69 (m, 1H), 3.56 – 3.44 (m, 1H), 2.36 (s, 3H), 1.52 (d, 6.8 Hz, 3H), 1.45 (d, 6.9 Hz, 3H), 1.18 – 1.12 (m, 6H), 1.09 (d, 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.93, 164.66, 142.83, 138.98, 134.38, 132.78, 131.59, 130.33, 129.13, 129.09, 127.93, 124.94, 123.09, 119.53, 95.14, 85.16, 50.10, 45.39, 43.25, 21.55, 20.84, 20.51, 20.23, 12.87; MS (APCI): *m/z* 417.4 $[M+H]^+$

(E)-N-ethyl-3-(pyridin-2-yl)-N-(2-(p-tolylethynyl)phenyl)acrylamide (8j)



Prepared according to the *General Procedure G* using (E)-3-(pyridin-2-yl)acrylic acid (1.0 equiv.), and N-ethyl-2-(p-tolylethynyl)aniline (1.0 equiv.), 58% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 – 8.46 (m, 1H), 7.68 (d, 15.2 Hz, 1H), 7.64 – 7.55 (m, 2H), 7.42 – 7.34 (m, 4H), 7.29 – 7.20 (m, 2H), 7.16 – 7.08 (m, 3H), 6.78 (d, 15.2 Hz, 1H), 4.14 – 4.03 (m, 1H), 3.93 – 3.81 (m, 1H), 2.34 (s, 3H), 1.20 (t, 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.79, 153.91, 149.89, 143.02, 140.67, 138.97, 136.53, 133.03, 131.62, 129.60, 129.26, 129.25, 128.13, 124.18, 123.93, 123.48, 123.32, 119.73, 95.40, 85.35, 44.37, 21.64, 13.08; MS (APCI): *m/z* 367.2 $[M+H]^+$

(E)-N-ethyl-2-(p-tolyl)-N-(2-(p-tolylethynyl)phenyl)ethene-1-sulfonamide (8k)



Sulfuryl chloride (2.0 equiv., per styrene) was added dropwise to stirred anhydrous DMF (2.0 M) at 0°C under nitrogen atmosphere. The reaction mixture was heated to room temperature and stirred for 0.5h. 4-Methylstyrene (1.2 equiv.) was added dropwise, and the reaction mixture was stirred for 1h at 80°C. The mixture was filtered through a short pad of silica gel. The filtrate was concentrated under reduced pressure. The resulting sulfonyl chloride was dissolved in DCM and slowly added dropwise to a solution of N-ethyl-2-(p-tolylethynyl)aniline (1.0 equiv.) and pyridine (1.5 equiv.) in DCM (0.33 M) at 0°C. The reaction mixture was stirred at 0°C for overnight. The solvent was evaporated under reduced pressure. The crude material was purified by flash chromatography on silica gel. 73% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, 7.2, 2.0 Hz, 1H), 7.45 (dd, 7.7, 1.5 Hz, 1H), 7.39 – 7.30 (m, 3H), 7.26 – 7.24 (m, 2H), 7.15 (d, 8.1 Hz, 2H), 7.02 – 6.96 (m, 4H), 6.85 (d, 15.4 Hz, 1H), 3.86 (q, 7.1 Hz, 2H), 2.33 (s, 3H), 2.31 (s, 3H), 1.20 (t, 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.77, 140.58, 139.51, 138.80, 133.34, 133.12, 131.30, 130.06, 129.38, 129.05, 128.90, 128.26, 128.16, 124.41, 123.89, 119.38, 94.97, 86.16, 45.41, 21.50, 21.40, 14.90; MS (APCI): *m/z* 416.3 $[M+H]^+$

General procedures for visible-light photocatalysis

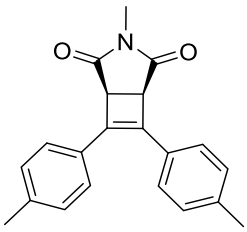
General procedure 1 (for the synthesis of cyclobutenes)

Alkyne **5** (0.1 mmol, 1.0 equiv.), alkene **6** (1.5 equiv.), and photocatalyst $Ir[df(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5 mol%) were added to an oven-dried 4mL vial equipped with a stir bar. The combined materials were dissolved in DCM (2 mL) under argon atmosphere in glovebox. The reaction mixture was then irradiated by 12W blue LED lamp at room temperature (maintained with a cooling fan). After completion of the reaction as indicated by TLC, the solution was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to give the desired product **7**.

General procedure 2 (for the synthesis of conjugated diene)

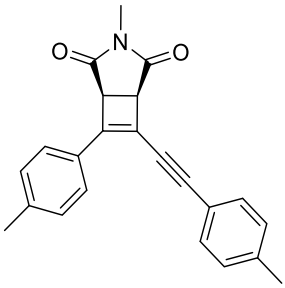
Enyne **8** (0.1 mmol, 1.0 equiv.), and photocatalyst $Ir[df(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5 mol%) were added to an oven-dried 4mL vial equipped with a stir bar. The combined materials were dissolved in DCM (2 mL) under argon atmosphere in glovebox. The reaction mixture was then irradiated by 12W blue LED lamp at room temperature (maintained with a cooling fan). After completion of the reaction as indicated by TLC, the solution was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to give the desired product **9**.

(1R,5S)-3-methyl-6,7-di-p-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (7a)



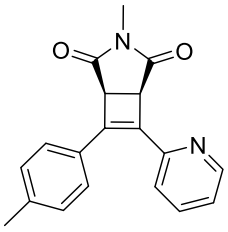
Prepared according to the ***General Procedure 1*** using 1,2-di-*p*-tolylethyne (0.1 mmol, 1.0 equiv.) and N-methylmaleimide (1.5 equiv.), 76% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, 8.2 Hz, 4H), 7.18 (d, 7.9 Hz, 4H), 4.06 (s, 2H), 2.97 (s, 3H), 2.37 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.24, 139.17, 138.25, 130.26, 129.28, 126.75, 44.94, 24.79, 21.44; MS (APCI): *m/z* 318.3 $[M+H]^+$

(1R,5S)-3-methyl-6-(p-tolyl)-7-(p-tolylethynyl)-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (7b)



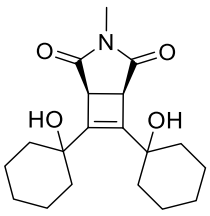
Prepared according to the ***General Procedure 1*** using 1,2-di-*p*-tolylbuta-1,3-diyne (0.1 mmol, 1.0 equiv.) and N-methylmaleimide (1.5 equiv.), 70% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, 8.2 Hz, 2H), 7.43 (d, 8.1 Hz, 2H), 7.23 (d, 7.9 Hz, 2H), 7.18 (d, 7.9 Hz, 2H), 4.08 (d, 3.6 Hz, 1H), 3.95 (d, 3.6 Hz, 1H), 2.98 (s, 3H), 2.38 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.15, 174.03, 148.58, 140.19, 139.48, 131.70, 129.60, 129.36, 129.20, 126.38, 119.16, 117.99, 99.33, 82.51, 46.62, 45.36, 24.89, 21.62, 21.59; MS (APCI): *m/z* 342.1 $[M+H]^+$

(1S,5R)-3-methyl-6-(pyridin-2-yl)-7-(p-tolyl)-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (7c)



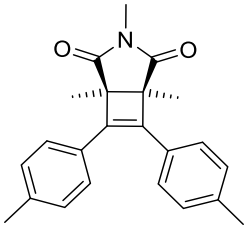
Prepared according to the ***General Procedure 1*** using 2-(*p*-tolylethynyl)pyridine (0.1 mmol, 1.0 equiv.) and N-methylmaleimide (1.5 equiv.), 53% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (ddd, 4.8, 1.8, 1.0 Hz, 1H), 8.42 (d, 8.3 Hz, 2H), 7.83 (dt, 7.9, 1.1 Hz, 1H), 7.80 – 7.75 (m, 1H), 7.26 (d, 8.0 Hz, 2H), 7.23 (ddd, 7.4, 4.8, 1.3 Hz, 1H), 4.19 (d, 3.7 Hz, 1H), 4.15 (d, 3.7 Hz, 1H), 2.97 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.20, 174.78, 151.69, 149.44, 143.73, 140.30, 136.57, 136.15, 129.66, 129.08, 122.88, 122.67, 44.57, 43.89, 24.80, 21.61; MS (APCI): *m/z* 305.3 $[M+H]^+$

(1R,5S)-6,7-bis(1-hydroxycyclohexyl)-3-methyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (7d)



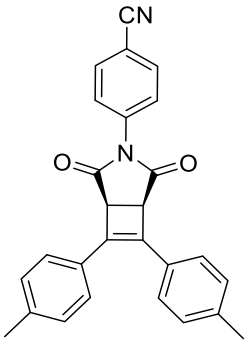
Prepared according to the ***General Procedure 1*** using 1,1'-(ethyne-1,2-diyl)bis(cyclohexan-1-ol) (0.1 mmol, 1.0 equiv.), N-methylmaleimide (2.0 equiv.), and $Ir[df(CF_3)ppy]_2(dtbbpy)PF_6$ (5 mol%), 58% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 3.66 (s, 2H), 3.58 (s, 2H), 2.95 (s, 3H), 1.83 – 1.51 (m, 18H), 1.33 – 1.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.12, 148.33, 71.58, 43.44, 36.53, 36.05, 25.04, 21.08; MS (APCI): *m/z* 316.4 $[M+H-H_2O]^+$ 298.4 $[M+H-2H_2O]^+$

(1R,5S)-1,3,5-trimethyl-6,7-di-p-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (7e)



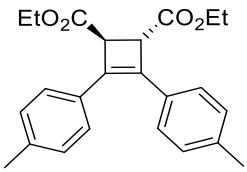
Prepared according to the ***General Procedure 1*** using 1,2-di-*p*-tolylethyne (0.1 mmol, 1.0 equiv.) and 1,3,4-trimethyl-1H-pyrrole-2,5-dione (1.5 equiv.), 55% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, 8.2 Hz, 4H), 7.14 (d, 7.9 Hz, 4H), 2.97 (s, 3H), 2.35 (s, 6H), 1.58 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.54, 142.06, 138.78, 129.74, 129.25, 127.15, 54.29, 24.77, 21.42, 13.33; MS (APCI): *m/z* 346.3 $[M+H]^+$

4-((1R,5S)-2,4-dioxo-6,7-di-p-tolyl-3-azabicyclo[3.2.0]hept-6-en-3-yl)benzonitrile (7f)



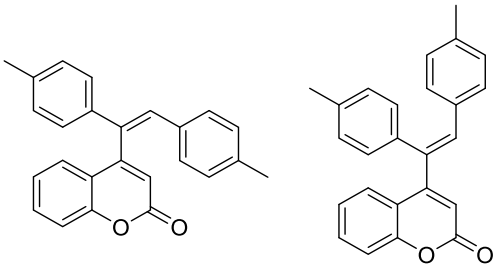
Prepared according to the ***General Procedure 1*** using 1,2-di-*p*-tolylethyne (0.1 mmol, 1.0 equiv.) and 4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzonitrile (1.5 equiv.), 59% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, 8.9 Hz, 2H), 7.67 (d, 8.2 Hz, 4H), 7.47 (d, 8.9 Hz, 2H), 7.20 (d, 7.9 Hz, 4H), 4.24 (s, 2H), 2.38 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.24, 139.57, 138.14, 135.94, 129.89, 129.40, 127.04, 126.79, 118.08, 111.87, 44.75, 21.47; MS (APCI): *m/z* 405.3 $[M+H]^+$

Diethyl (1S,2S)-3,4-di-p-tolylcyclobut-3-ene-1,2-dicarboxylate (7g)



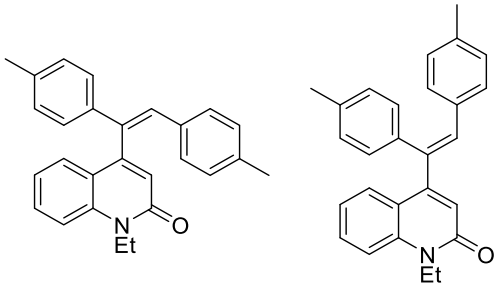
Prepared according to the ***General Procedure 1*** using 1,2-di-*p*-tolylethyne (0.1 mmol, 1.0 equiv.) and Diethyl fumarate (1.5 equiv.), 51% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, 8.2 Hz, 4H), 7.12 (d, 7.9 Hz, 4H), 4.18 – 4.08 (m, 6H), 2.35 (s, 6H), 1.19 (t, 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.47, 138.34, 138.04, 130.64, 128.97, 126.56, 60.85, 45.85, 21.38, 14.13; MS (APCI): *m/z* 379.4 $[M+H]^+$

4-(1,2-di-p-tolylvinyl)-2H-chromen-2-one (9a)



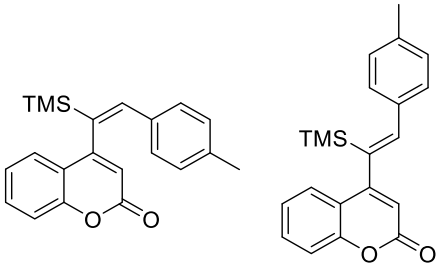
Prepared according to the ***General Procedure 2*** using 2-(p-tolylethynyl)phenyl (E)-3-(p-tolyl)acrylate (0.1 mmol, 1.0 equiv.), 73% total yield, (E/Z 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (ddd, 8.6, 7.2, 1.6 Hz, 1H), 7.40 (ddd, 9.8, 8.1, 1.3 Hz, 2H), 7.29 (d, 8.3 Hz, 2H), 7.22 (s, 1H), 7.14 (d, 8.0 Hz, 2H), 7.11 (ddd, 8.2, 7.4, 1.2 Hz, 1H), 7.04 (d, 8.2 Hz, 2H), 6.97 (d, 8.1 Hz, 2H), 6.33 (s, 1H), 2.34 (s, 3H), 2.26 (s, 3H); δ 7.53 (dd, 8.0, 1.5 Hz, 1H), 7.45 (ddd, 8.7, 7.3, 1.6 Hz, 1H), 7.34 (dd, 8.3, 1.2 Hz, 1H), 7.16 – 7.06 (m, 7H), 7.03 (d, 8.2 Hz, 2H), 6.83 (s, 1H), 6.41 (s, 1H), 2.34 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.77, 155.30, 154.15, 138.29, 137.93, 137.00, 134.42, 132.81, 131.90, 130.78, 129.53, 129.21, 128.76, 126.94, 126.12, 124.50, 119.06, 117.20, 117.01, 21.16, 21.12; δ 161.06, 157.64, 154.07, 138.16, 138.02, 136.09, 134.88, 132.63, 131.45, 129.64, 129.61, 129.28, 128.96, 127.11, 123.98, 119.05, 117.17, 115.55, 21.29, 21.29; MS (APCI): *m/z* 353.3 $[M+H]^+$

4-(1,2-di-p-tolylvinyl)-1-ethylquinolin-2(1H)-one (9l)



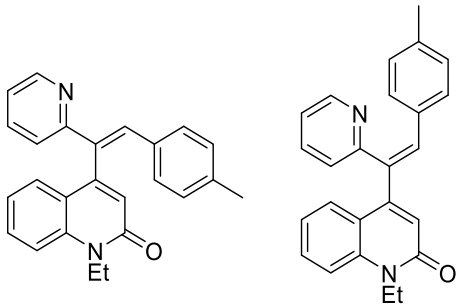
Prepared according to the ***General Procedure 2*** using (E)-N-ethyl-3-(p-tolyl)-N-(2-(p-tolylethynyl)phenyl)acrylamide (0.1 mmol, 1.0 equiv.), 80% total yield, (E/Z 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, 8.0, 1.4 Hz, 1H), 7.52 (ddd, 8.6, 7.1, 1.5 Hz, 1H), 7.44 (d, 8.4 Hz, 1H), 7.30 (d, 8.2 Hz, 2H), 7.19 (s, 1H), 7.11 (d, 8.0 Hz, 2H), 7.10 – 7.01 (m, 1H), 6.98 (d, 8.2 Hz, 2H), 6.91 (d, 8.2 Hz, 2H), 6.63 (s, 1H), 4.50 (dq, 14.3, 7.1 Hz, 1H), 4.36 (dq, 14.1, 7.1 Hz, 1H), 2.33 (s, 3H), 2.23 (s, 3H) 1.43 (t, 7.1 Hz, 3H); δ 7.74 (dd, 8.1, 1.5 Hz, 1H), 7.49 (ddd, 8.6, 7.1, 1.5 Hz, 1H), 7.39 (d, 8.6 Hz, 1H), 7.16 (d, 8.1 Hz, 2H), 7.10 – 7.00 (m, 7H), 6.74 (s, 1H), 6.73 (s, 1H), 4.39 (q, 7.1 Hz, 2H), 2.31 (s, 3H), 2.30 (s, 3H) 1.39 (t, 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.40, 149.76, 139.31, 138.01, 137.77, 137.35, 135.96, 133.30, 130.64, 129.92, 129.31, 129.01, 128.81, 127.79, 126.14, 122.62, 122.11, 120.65, 114.34, 37.36, 21.13, 21.11, 12.95; δ 161.73, 152.83, 139.26, 137.59, 137.54, 137.38, 135.77, 133.46, 131.47, 130.26, 129.43, 129.36, 129.20, 128.03, 121.69, 120.70, 114.22, 37.26, 21.25, 21.25, 12.80; MS (APCI): *m/z* 380.4 $[M+H]^+$

4-(2-(p-tolyl)-1-(trimethylsilyl)vinyl)-2H-chromen-2-one (9b)



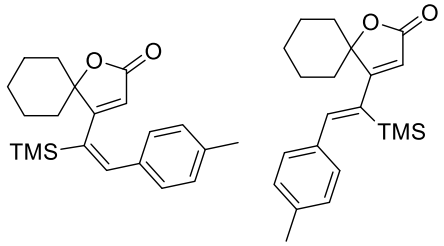
Prepared according to the ***General Procedure 2*** using 2-((trimethylsilyl)ethynyl)phenyl (E)-3-(p-tolyl)acrylate (0.1 mmol, 1.0 equiv.), 60% total yield, (E/Z 1.2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, 7.9, 1.6 Hz, 1H), 7.55 (ddd, 8.8, 7.3, 1.6 Hz, 1H), 7.49 (ddd, 8.6, 7.3, 1.6 Hz, 1H), 7.43 (dd, 7.9, 1.5 Hz, 1H), 7.36 (ddd, 8.3, 3.5, 1.0 Hz, 2H), 7.32 – 7.27 (m, 2H), 7.26 (s, 1H), 7.20 (d, 8.0 Hz, 2H), 7.13 (ddd, 8.3, 7.3, 1.2 Hz, 1H), 7.05 (d, 8.2 Hz, 2H), 7.00 (s, 1H), 6.94 (d, 8.1 Hz, 2H), 6.16 (s, 1H), 6.13 (s, 1H), 2.39 (s, 3H), 2.23 (s, 3H), 0.16 (s, 9H), 0.01 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.50, 161.03, 160.86, 158.89, 153.84, 153.75, 146.44, 140.12, 139.97, 138.39, 138.11, 138.00, 135.20, 133.27, 131.95, 131.79, 129.18, 128.87, 128.43, 126.90, 126.67, 124.14, 123.99, 120.11, 118.19, 117.21, 117.18, 112.08, 111.85, 21.29, 21.14, 0.30, -1.46; MS (APCI): *m/z* 335.3 $[M+H]^+$

1-ethyl-4-(1-(pyridin-2-yl)-2-(p-tolyl)vinyl)quinolin-2(1H)-one (9m)



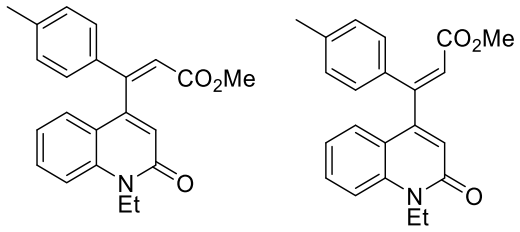
Prepared according to the ***General Procedure 2*** using (E)-N-ethyl-N-(2-(pyridin-2-ylethynyl)phenyl)-3-(p-tolyl)acrylamide (0.1 mmol, 1.0 equiv.), 69% total yield, (E/Z 2.8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (ddd, 4.8, 1.9, 0.9 Hz, 1H), 8.12 (s, 1H), 7.60 – 7.52 (m, 2H), 7.52 – 7.45 (m, 2H), 7.15 (ddd, 7.5, 4.8, 1.1 Hz, 1H), 7.11 – 7.02 (m, 3H), 6.97 (dt, 8.0, 1.0 Hz, 1H), 6.93 (d, 8.0 Hz, 2H), 6.70 (s, 1H), 4.53 (dq, 14.3, 7.2 Hz, 1H), 4.40 (dq, 14.0, 7.1 Hz, 1H), 2.24 (s, 3H) 1.46 (t, 7.1 Hz, 3H); δ 8.59 (ddd, 4.9, 1.7, 0.9 Hz, 1H), 7.81 (dd, 8.1, 1.4 Hz, 1H), 7.56 (td, 7.7, 1.8 Hz, 1H), 7.50 (ddd, 8.6, 7.1, 1.5 Hz, 1H), 7.39 (d, 8.4 Hz, 1H), 7.29 (d, 7.9 Hz, 1H), 7.15 (ddd, 7.5, 4.9, 1.1 Hz, 1H), 7.10 – 7.05 (m, 1H), 7.04 – 6.97 (m, 4H), 6.96 (s, 1H), 6.75 (s, 1H), 4.39 (q, 7.1 Hz, 2H), 2.31 (s, 3H), 1.39 (t, 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.71, 156.56, 149.46, 148.99, 139.35, 138.15, 136.69, 133.90, 132.67, 130.92, 129.52, 129.06, 127.53, 123.00, 122.26, 121.40, 120.59, 114.44, 37.46, 21.20, 12.96; δ 161.64, 157.99, 151.64, 150.03, 139.27, 138.00, 137.34, 136.34, 134.59, 132.75, 130.31, 129.45, 128.94, 128.07, 125.02, 122.41, 121.95, 121.65, 120.74, 114.22, 37.29, 21.24, 12.74; MS (APCI): *m/z* 367.3 $[M+H]^+$

4-(2-(p-tolyl)-1-(trimethylsilyl)vinyl)-1-oxaspiro[4.5]dec-3-en-2-one (9n)



Prepared according to the ***General Procedure 2*** using 1-((trimethylsilyl)ethynyl)cyclohexyl (E)-3-(p-tolyl)acrylate (0.1 mmol, 1.0 equiv.), 41% total yield, (E/Z 1.3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, 8.1 Hz, 2H), 7.06 (d, 8.0 Hz, 2H), 6.90 (s, 1H), 5.85 (s, 1H), 2.32 (s, 3H), 1.69 – 1.21 (m, 10H), 0.23 (s, 9H); δ 7.20 – 7.12 (m, 5H), 5.62 (s, 1H), 2.37 (s, 3H), 1.83 – 1.61 (m, 10H), 0.02 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.64, 172.08, 141.44, 138.57, 136.59, 135.56, 129.16, 129.13, 117.04, 91.75, 34.56, 24.48, 22.34, 21.45, 0.17; δ 179.45, 175.15, 145.97, 138.13, 137.21, 135.35, 128.82, 128.38, 114.68, 89.92, 33.85, 24.62, 22.14, 21.27, 1.30; MS (APCI): *m/z* 341.4 $[M+H]^+$

Methyl 3-(1-ethyl-2-oxo-1,2-dihydroquinolin-4-yl)-3-(p-tolyl)acrylate (9f)



Prepared according to the ***General Procedure 2*** using methyl (Z)-4-(ethyl(2-(p-tolylethynyl)phenyl)amino)-4-oxobut-2-enoate (0.1 mmol, 1.0 equiv.), 60% total yield, (E/Z 1.5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, 8.0 Hz, 1H), 7.51 (t, 7.8 Hz, 1H), 7.39 (d, 8.6 Hz, 1H), 7.27 (d, 8.7 Hz, 2H), 7.13 (d, 8.0 Hz, 2H), 7.08 (d, 7.8 Hz, 2H), 6.69 (s, 1H), 6.13 (s, 1H), 4.36 (q, 7.1 Hz, 2H), 3.71 (s, 3H), 2.23 (s, 3H), 1.39 (t, 7.1 Hz, 3H); δ 7.51 (ddd, 8.6, 7.1, 1.5 Hz, 1H), 7.43 (d, 8.9 Hz, 1H), 7.39 (dd, 8.0, 1.5 Hz, 1H), 7.34 (d, 8.3 Hz, 2H), 7.13 (d, 8.6 Hz, 2H), 7.07 (ddd, 8.1, 7.1, 1.1 Hz, 1H), 6.62 (s, 1H), 6.55 (s, 1H), 4.52 – 4.34 (m, 2H), 2.34 (s, 3H), 1.39 (t, 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.07, 161.20, 151.87, 150.43, 139.38, 139.21, 133.63, 130.70, 128.91, 128.56, 127.61, 121.91, 121.35, 120.61, 119.66, 114.36, 51.61, 37.43, 21.34, 12.73; δ 165.29, 161.39, 151.64, 148.62, 140.70, 138.89, 134.43, 130.51, 129.63, 127.08, 126.90, 121.97, 120.40, 120.30, 117.81, 114.39, 51.48, 37.52, 21.27, 12.89; MS (APCI): *m/z* 348.3 $[M+H]^+$

Luminescence quenching studies

Ir[df(CF_3)ppy]$_2$(dtbbpy)PF_6 and N-methylmaleimide (**6a**) dissolved in DCM were added to 10 mm quartz cuvette inside a glove box. Fluorescence emission spectra were collected on F-7000 FL Spectrophotometer. All samples were excited at 430 nm and the emission maximum was monitored at 471 nm. All measurements were conducted under the same conditions. For each quenching experiment, the emission intensity of photosensitizer (10 μM) with different concentration of quencher (N-methylmaleimide **6a**) was collected: 0, 25, 50 mM.

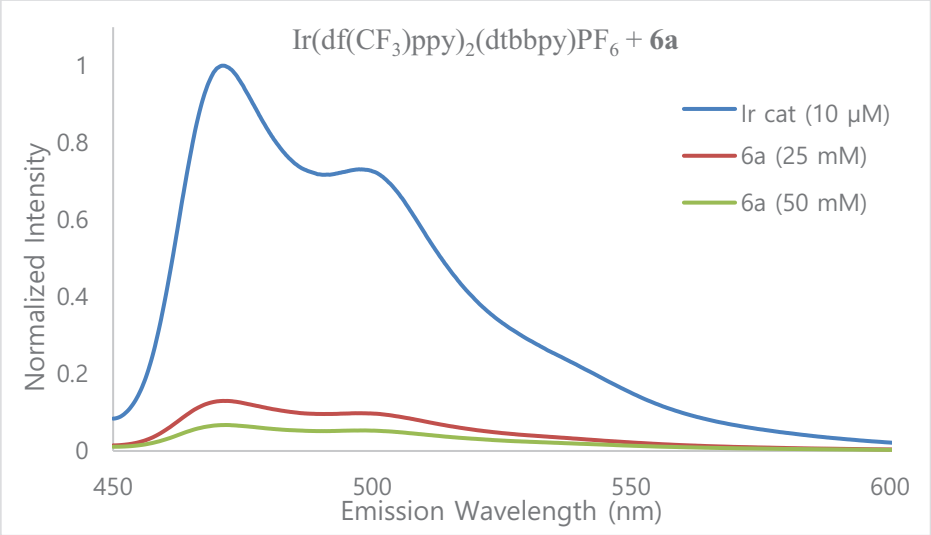


Figure S1. Luminescence quenching studies

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