Master's Thesis

Visible light photocatalysis alkene-alkyne [2+2] cycloaddition by energy transfer

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Approved by

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Abstract

The alkyne-alkene [2+2] cycloaddition is straightforward approach to cyclobutene derivatives. Cyclobutenes are widely present in numerous natural products and pharmacological compounds with various biological properties. In addition, Structural characteristics of cyclobutene such as the high ring strain and unsaturation give the ability for many useful synthetic transformations. because the [2+2] cycloaddition is thermally forbidden, it can be achieved by photochemically. But this process has mostly been developed under UV light irradiation condition.

The excited state of molecules has different reactivity from ground state. straightforward way to access the excited state of molecules is through a direct photoexcitation approach. Most organic molecules need high energy source for direct excitation such as UV light. But using high energy source like UV light has disadvantage for selectivity of the reaction, functional group resistance and general applicability.

Recently, Visible light photocatalysis has attracted much attention from organic synthetic society because of its environmentally friendly and mild condition. Visible light mediated energy transfer process is a method to access excited (triplet) state in mild condition.

Herein, we develop visible light photocatalysis [2+2] cycloadditions of alkene-alkyne by energy transfer mechanism. Under Blue LED light by using Iridium catalysts as photocatalyst, diverse cyclobutenes can be accessed in mild condition in moderated to excellent yields. Also, in intramolecular reaction, highly substituted 1,3-Dienes are observed by tandem intramolecular [2+2] cycloaddition - ring opening reaction. Moreover, further synthetic transformations to valuable structure like extended π-systems were explored based on our synthesis method.

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Abbreviations

Ac Acetyl

acac Acetylacetone

Ar Aryl

Bn Benzyl

bpy 2,2′-Bipyridine

CFL Compact fluorescent lamp

COD 1,5-Cyclooctadiene

DBU 1,8-Diazabicyclo(5.4.0)undec-7-ene

DCC *N,N′*-Dicyclohexylcarbodiimide

DCE 1,2-Dichloroethene

diglyme bis(2-methoxyethyl) ether

DMAP 4-Dimethylaminopyridine

DMBP 4,4'-Dimethoxybenzophenone

DMF Dimethylformamide

DMSO Dimethyl sulfoxide

dppe 1,2-Bis(diphenylphosphino)ethane

dppp 1,3-Bis(diphenylphosphino)propane

dtbbpy 4,4′-Di-tert-butyl-2,2′-dipyridyl

dtbpy Di-tert-butyl-2,2'-bipyridine

EWG electron withdrawing group

iPr isopropyl

ISC Intersystem crossing

LED Light Emitting Diode

Mbs m-maleimidobenzoyl-*N*-hydroxysuccinimide ester

Me	Methyl
MS	Molecular sieve
n.r.	no reaction
nBu	nButyl
NOE	nuclear Overhauser effect
PC	photocatalyst
PE	Petroleum ether
Ph	phenyl
Piv	Pivalic acid
PyBox	bis(oxazoline) ligand
tBu	tert butyl
Tf	trifluoromethanesulfonate
TFA	Trifluoroacetic acid
tfacac	1,1,1-trifluoroacetylacetone
THF	Tetrahydrofuran
TIPS	Triisopropylsilyl ether
TMS	Tetramethylsilane
Ts	Tosyl
TSA	Toluenesulfonic acid
UV	ultraviolet

I. INTRODUCTION

1.1. Cyclobutene

Cyclobutene is All-carbon four-membered ring which widely presents in numerous natural products and pharmacological compounds with various biological properties (figure 1).[1-4]

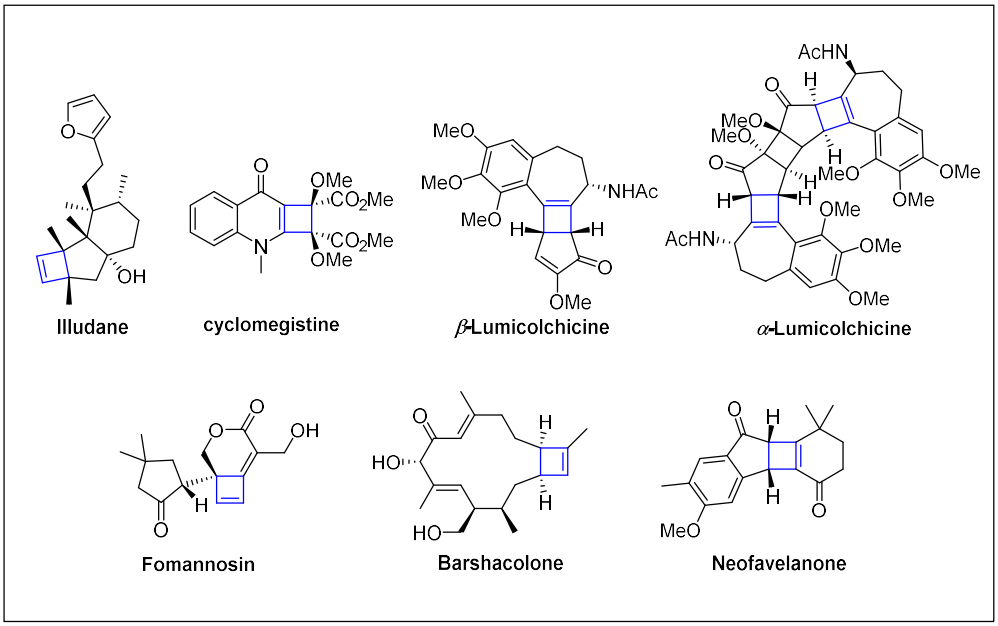


Figure 1. Natural products containing a cyclobutene scaffold

In addition, Cyclobutenes are versatile synthetic intermediates that have unique reactivity due to its ring strain and unsaturation. By hydrogenation[5-6] and conjugate addition[7], cyclobutenes can be converted to cyclobutanes, common core structures of important biologically active natural products (Figure 2a).[8-9] Because of the ring strain, the ring opening is caused by simple heating.[10] This allows easy access to the conjugated dienes by electrocyclic ring-opening reaction. Conjugated dienes are valuable structural motif because can be reacted with dienophiles for a Diels-Alder reaction[11], which form a compound that contains a cyclohexene ring (Figure 2b).

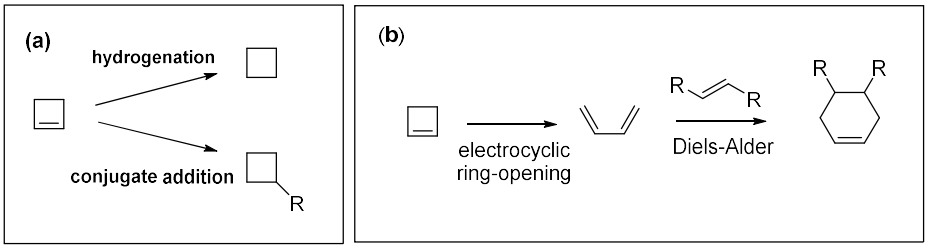


Figure 2. The transformations of cyclobutene

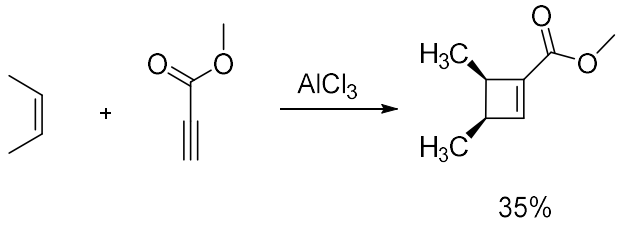
1.2. Alkyne-alkene [2+2] cycloaddition

Cycloaddition reaction is one of powerful tool to access cyclic structures. Among them, alkyne-alkene [2+2] cycloaddition is straightforward approaches to access cyclobutene derivatives.[12] Because [2+2] cycloaddition reactions are thermally forbidden process by the Woodward-Hoffmann rule[13], can be induced photochemically**,** or under transition metal catalyzed condition or Lewis acid catalyzed condition.[14]

1.2.1. Lewis acid catalyzed alkyne-alkene [2+2] cycloaddition

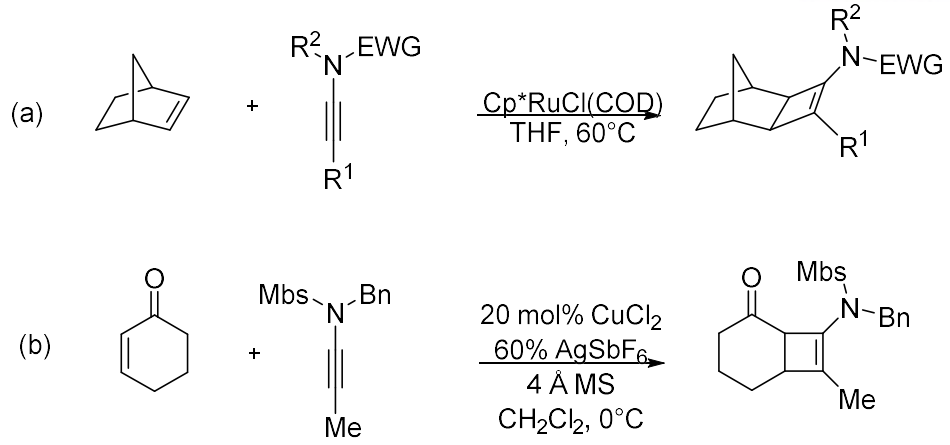
There are several approaches at alkyne-alkene [2+2] cycloadditions catalyzed by Lewis acids.[15-19] Lewis acid-catalyzed reactions are generally derived due to the imbalance between electrons. Therefore, the substrates need to be electron-rich on one side electron deficient on the other.

Initial investigations include an $AlCl_3$-catalyzed reaction of methyl propiolate with cis-2-butene studied by snider group in 1979 (Scheme 1).[16-17]



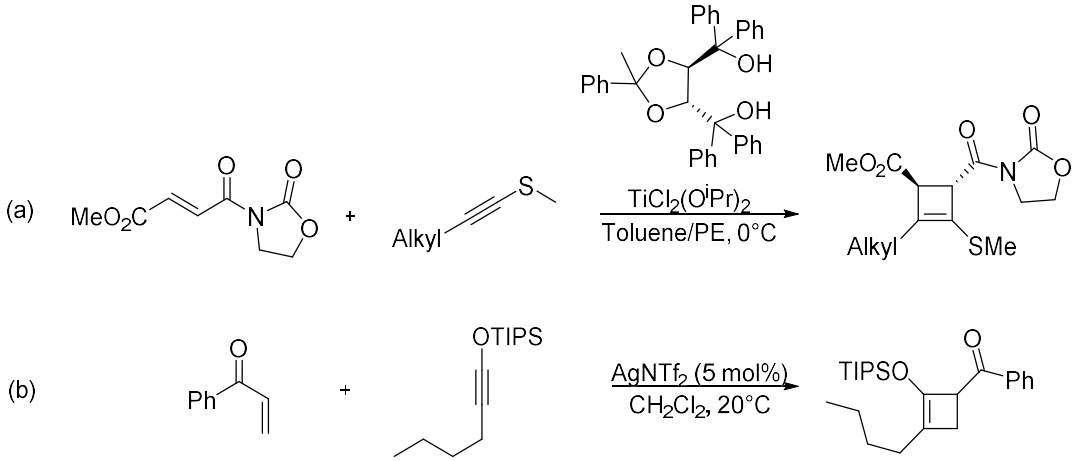
Scheme 1. AlCl3-catalyzed reactions of methyl propiolate with cis-2-butene

Recently, Several cases of Ficini Reactions, which were Lewis acid Catalyzed Ynamide-alkene [2+2] Cycloaddition, are reported.[20-22] Ficini reaction was original designed cycloaddition of an ynamine with a cyclic enone without catalyst.[23] But recently reactions with more stable yamide using Lewis aicd have been developed. Ruthenium catalyzed [2+2] cycloaddition of norbornene with ynamide was reported by Tam group (Scheme 2a).[21] And Hsung reported Ficini [2+2] Cycloaddition using ynamides with *N*-sulfonyl group using copper chloride (Scheme 2b).[22]



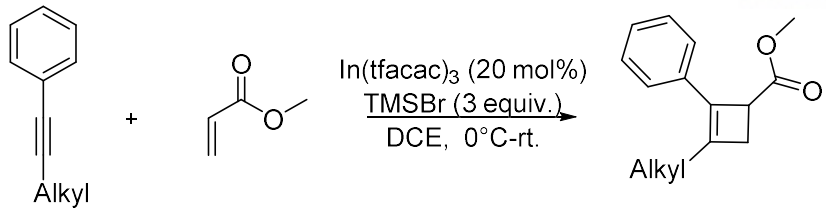
Scheme 2. examples of Ficini Reactions

In addition to ynamide, reactions with other heteroatoms, such as siloxy alkyne or alkynyl sulfide, were reported. Narasaka group developed asymmetric reaction by a chiral titanium catalyst using alkynyl sulfides (Scheme 3a).[18] And Kozmin group reported silver-catalyzed reaction using Siloxy alkynes (Scheme 3b).[15]



Scheme 3. Lewis acid catalyzed alkyne-alkene [2+2] cycloaddition

Most of these approaches have limitation to need reactive alkynes such as heteroatom substituent. Loh group investigated direct [2+2] cycloaddition of unactivated aryl alkyne with acrylate using In(tfacac)3-TMSBr as catalyst system (Scheme 4).[24]



Scheme 4. [2+2] cycloaddition of aryl alkyne with acrylate using In(tfacac)3-TMSBr

Despite these recent developments, Lewis acid catalyzed [2+2] cycloadditions have limitations that require activated alkyne and are sensitive to water because of Lewis acid.

1.2.2. Transition Metal-Catalyzed [2+2] Cycloadditions of alkyne with alkene

There were several reports about transition Metal-catalyzed [2+2] cycloadditions with alkynes and alkenes. But scope of transition metal-catalyzed reaction is restricted, because most of reactions need strained alkenes. These reactions generally process by oxidative cyclometallation step to form metallacyclopentene intermediate and followed by reductive elimination step to give cyclobutene. (Figure 3).[14]

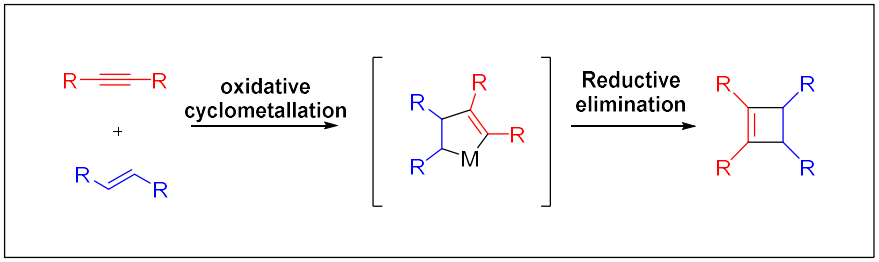
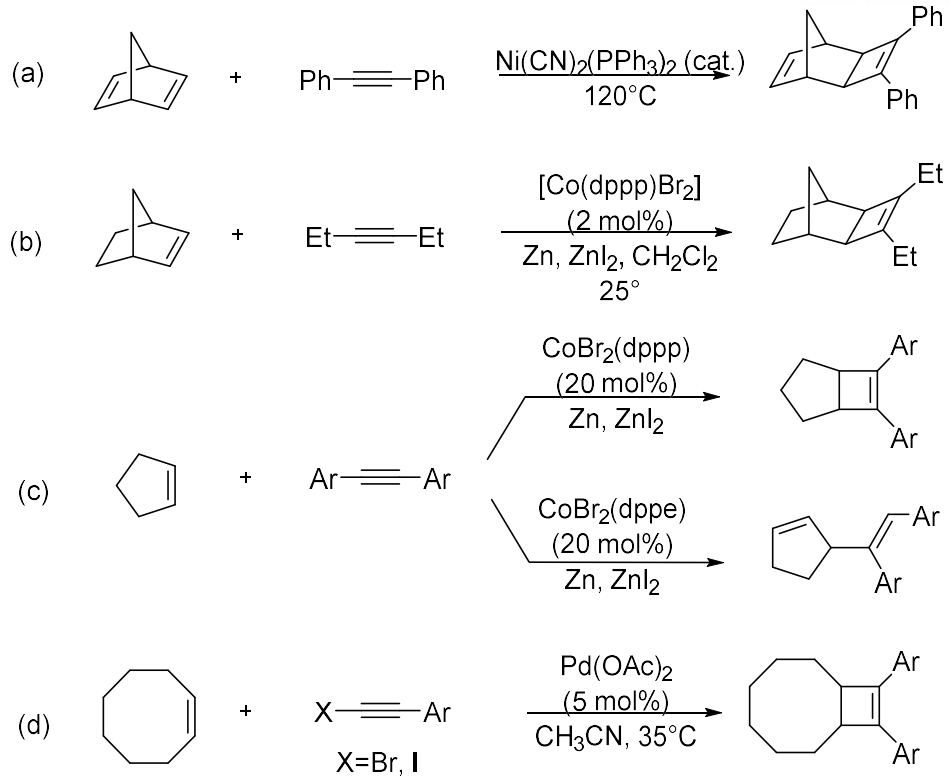


Figure 3. General mechanism of transition metal-catalyzed alkyne-alkene [2+2] cycloaddition

The first reaction of transition-metal catalyzed alkene-alkyne [2+2] cycloaddition to form cyclobutene is reaction that Schrauzer group reported nickel-catalyzed [2+2] cycloaddition of norbornadiene with diphenylacetylene in 1964 (Scheme 5a).[25] The reaction of norbornene and norbornadiene with various metal catalysts has been studied such as cobalt, palladium, Ruthenium. In 2008, Hilt group reported cobalt catalyzed reactions with norbornenes and internal alkynes, under mild condition and wide scopes (Scheme 5b).[26] Few years after same group reported cobalt-catalyzed [2+2] Alder−Ene Reaction and cycloaddition reaction with cyclopentenes and internal alkynes. In this report, the chemo selectivity toward the Alder−ene or the [2+2] cycloaddition products are controlled alkyne substituents and diphosphine ligand used (Scheme 5c).[27] Jiang group reported palladium catalyzed reaction with cyclooctene under mild condition (Scheme 5d).[28]



Scheme 5. transition metal-catalyzed alkyne-alkene [2+2] cycloaddition

1.2.3. Photochemical [2+2] Cycloadditions of alkyne with alkene

Photochemical [2+2] cycloaddition reactions have been extensively studied for decades. However, [2+2] cycloaddition with alkenes and alkynes have been reported to be relatively less compared to other combinations.[29-31] Generally, excitation of molecules proceeds in two ways, direct excitation and sensitization. The direct excitation is the most straightforward method for access to an excited state (Figure 4). By irradiation, Alkenes are excited to excited singlet state from the ground state and proceed cycloaddition reaction with alkyne. Or another way, after substrates are excited to singlet state and can undergo to a triplet state by intersystem crossing (ISC).[30]

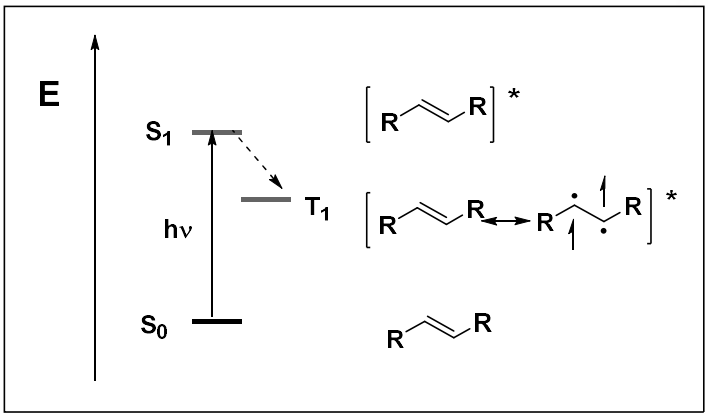


Figure 4. The direct excitation of alkene

Also, Triplet state can be induced by energy transfer (EnT) from triplet excited sensitizer (Figure 5). Sensitizer excites to singlet excited by irritation state and undergo to a triplet state by intersystem crossing (ISC). Once in the triplet state, the sensitizer can transfer its energy to a substrate by Dexter energy transfer. For energy transfer to occur effectively, the triplet energy of the substrate must be lower than the triplet energy of the sensitizer. This process has advantages because it requires a longer wavelength than a direct process. Also, triplet state lasts longer than singlet state, which enables intermolecular reaction.[30]

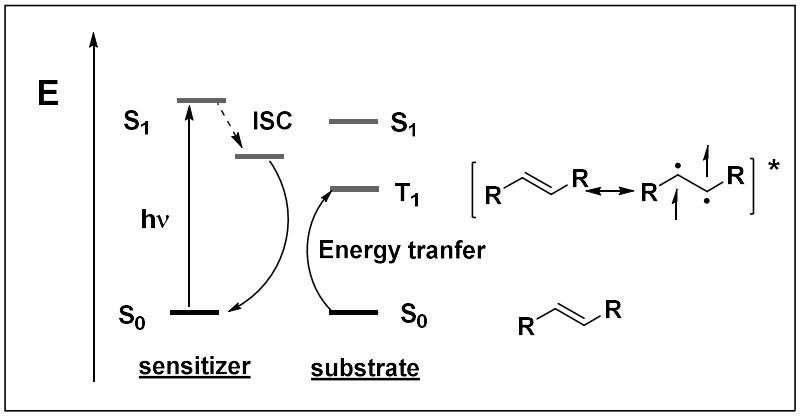
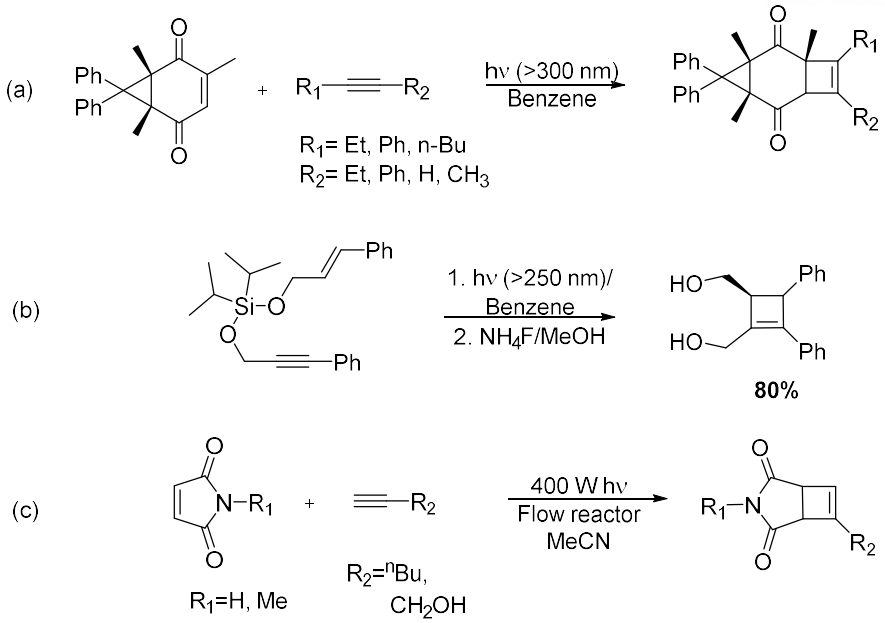


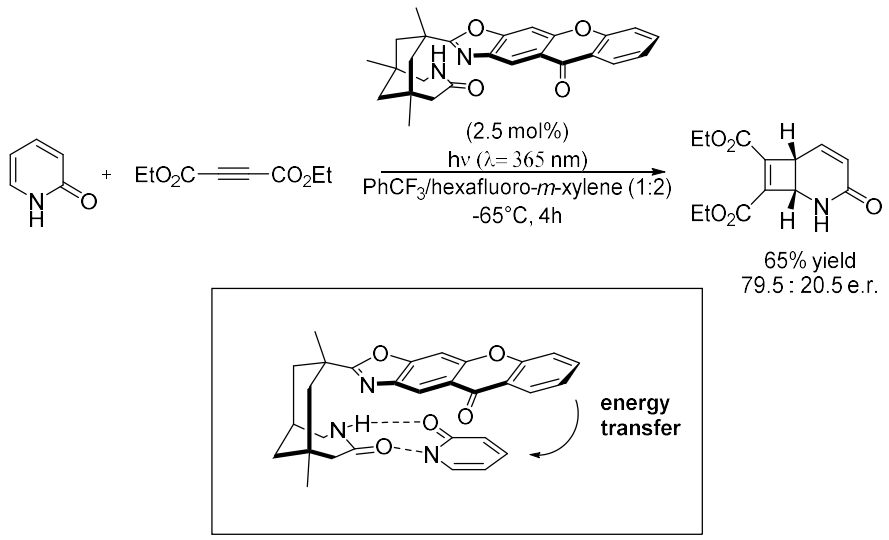
Figure 5. Sensitization via EnT from a Sensitizer to a substrate

Oshima group reported [2+2] cycloaddition reaction using homobenzoquinone derivatives with alkyne under UV light. In this reaction, the homobenzoquinone activates by direct excitation (Scheme 6a).[32] Fleming group investigated intramolecular [2+2] cycloaddition of silyl-tethered enyne by directed excitation of UV light. The tethered intermediates were desilylated with ammonium fluoride thereby substituted cyclobutene is obtained (Scheme 6b).[33] Booker-Milburn group reported the [2+2] cycloaddition of maleimides and terminal alkynes using UV flow reactor (Scheme 6c).[33]



Scheme 6. Photochemical [2+2] Cycloadditions by direct excitation.

Bach group reported cycloadditions of 2-pyridones with Acetylene dicarboxylates using a chiral triplet sensitizer by energy transfer (Scheme 7).[34] In this report, the chiral triplet sensitizer is bound with 2-pyridone through two-point binding. These bindings give enantioselectivity to the reaction.



Scheme 7. Intermolecular [2+2] cycloaddition with chiral photocatalyst

These approaches have a limitation of requiring high energy source for direct excitation such as UV light. But using high energy source like UV light has disadvantage for selectivity of the reaction, functional group resistance and general applicability.

1.3. Energy transfer catalysis reactions by visible light

Finding environmentally and atomically efficient synthetic methods to synthesis useful molecules has been one of the major challenges for organic chemists. In this respect, Visible light is easily accessible to the surroundings and an environmentally friendly energy source, and development of synthetic methods using visible light has been widely attempted. However, since most organic molecules show low absorbance of visible light, the method of using photocatalyst would serve as a valuable tool for overcoming this barrier.[35-39]

In past decade, visible light photocatalysis has been gaining huge attention in a way that can easily synthesize complex organic molecules. These photochemical reactions generally proceed by two mechanisms, a single-electron transfer (SET) mechanism or energy transfer mechanism (Figure 6).

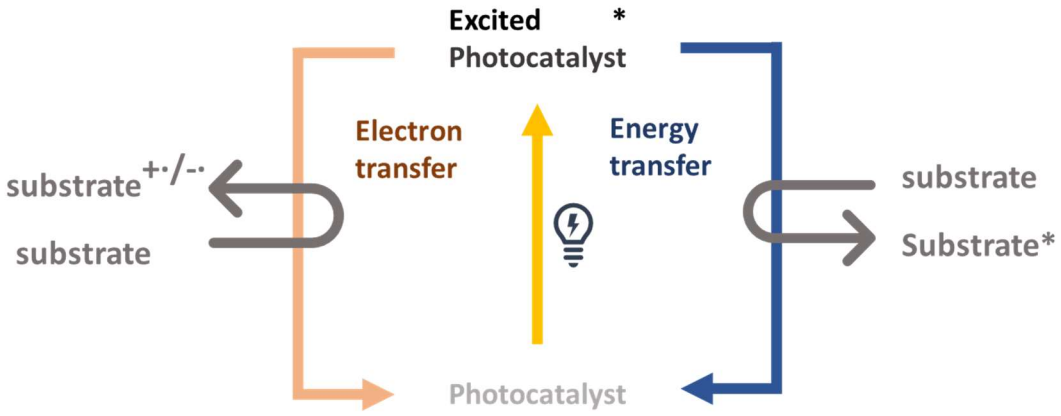


Figure 6. Visible-light-induced photocatalysis.

Most of visible light photocatalysis reactions process via a single-electron transfer (SET) process (Figure 7a). SET proceed that single electron oxidation/reduction occurs by excited photocatalyst via irradiation of visible light. when the catalyst is reduced, it is called a reductive quenching, and when catalyst is oxidized, it is called an oxidative quenching. Since the catalyst should be returned to the original oxidation state for the catalytic cycle, reagent or substrate are required to be used as the oxidant/reductant. Single-electron transfer processes are highly dependent on the redox potential energy of the catalyst or substrate.

In the other hand, at energy transfer process, the triplet state energy of the catalyst and substrate is a major factor in the reaction. Energy transfer (EnT) proceeds differently with electron transfer process

(Figure 7b). First, ground singlet state photocatalyst excited to singlet state (S_1) by visible light irradiation. And photocatalyst undergo to a triplet state by intersystem crossing (ISC). When photocatalyst is excited in a triplet state, energy transfer to the substrate can occur by Dexter type energy transfer. For an effective energy transfer method, it is important that the photocatalyst has higher energy than the energy acceptor.

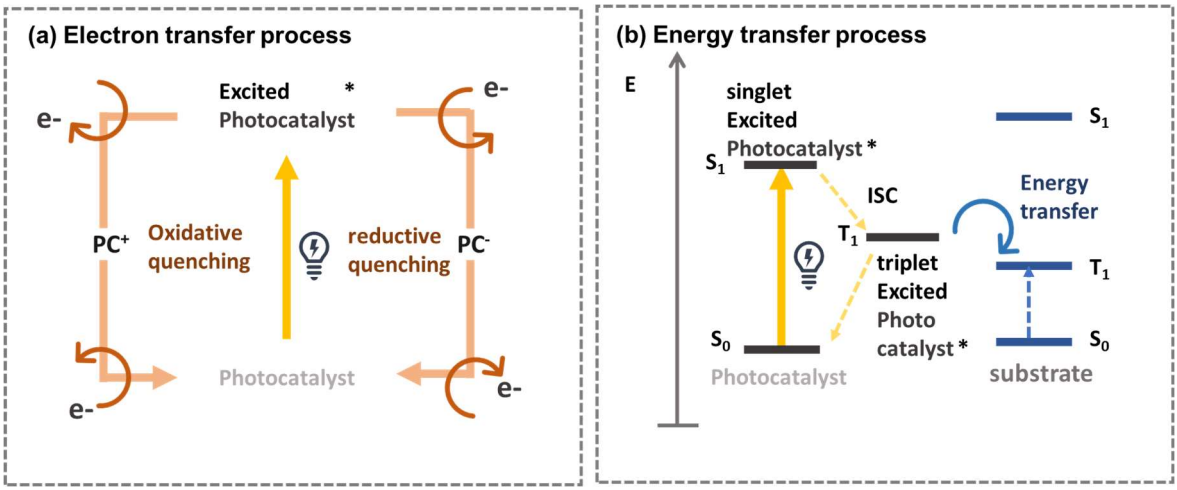


Figure 7. General mechanisms of Visible-light-induced photocatalysis.

Since the energy transfer method can easily approach the excited state of the molecule, the energy transfer strategy using visible light is attracted great attention. Recently, synthetic methods using the energy transfer method have been widely investigated for accessing complex organic molecular.[40-41]

1.3.1. Generation of Singlet Oxygen

Oxygen is an abundant substance in nature and is used in various fields. Reactivity of oxygen increase when triplet state oxygen converted to singlet state oxygen. singlet oxygen is widely used in chemistry as well as biological and medical fields.[42-43] Production of singlet oxygen is diversified, but a convenient method is energy transfer from excited state of a photocatalyst. triplet oxygen ($^1O_2$) turn into singlet oxygen ($^3O_2$) by EnT for catalyst.

Synthetic methods using singlet oxygen have also been studied in various ways to generate oxygenated compounds such as endoperoxide by Diels-alder reactions, dioxanes by [2+2] cycloadditions, hydroperoxides, sulfoxide and phosphine oxides. In addition to these general reactions, various reactions for transformations have been developed (Figure 8).[42-43]

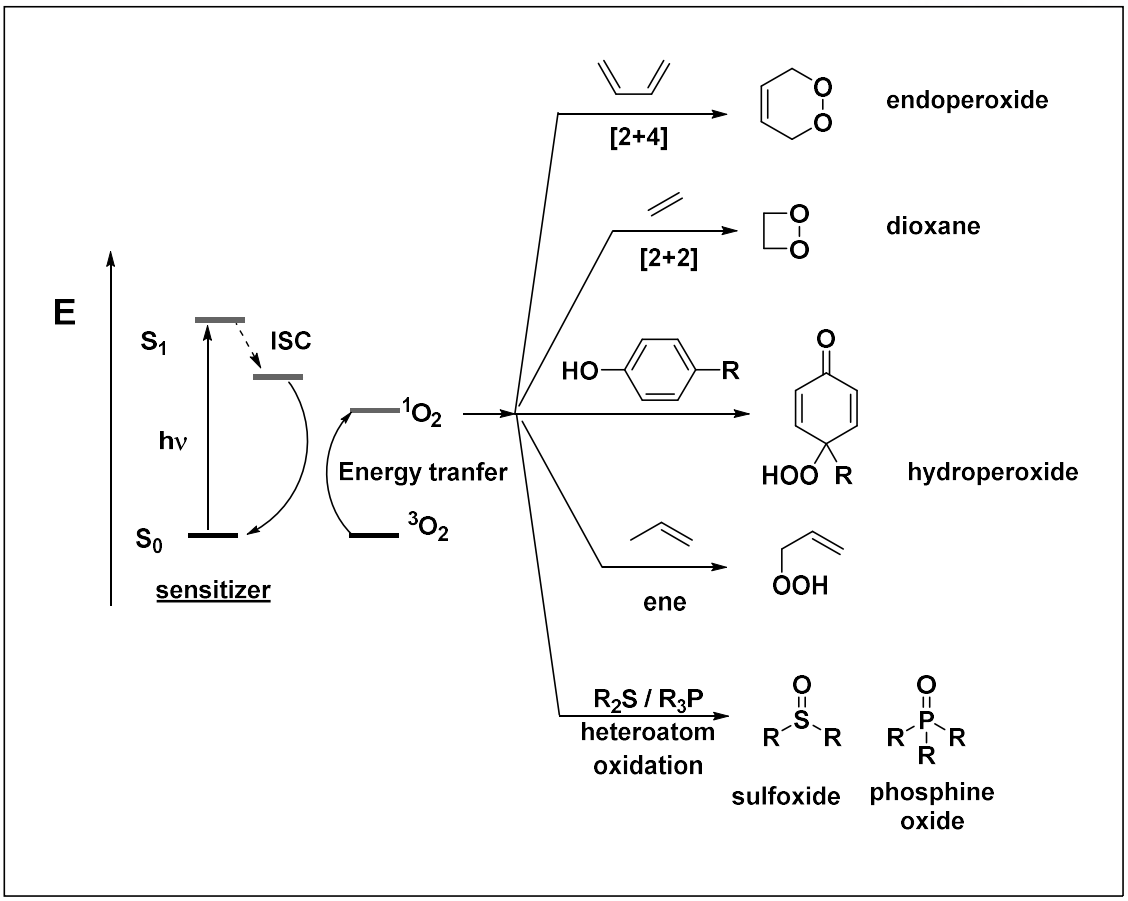
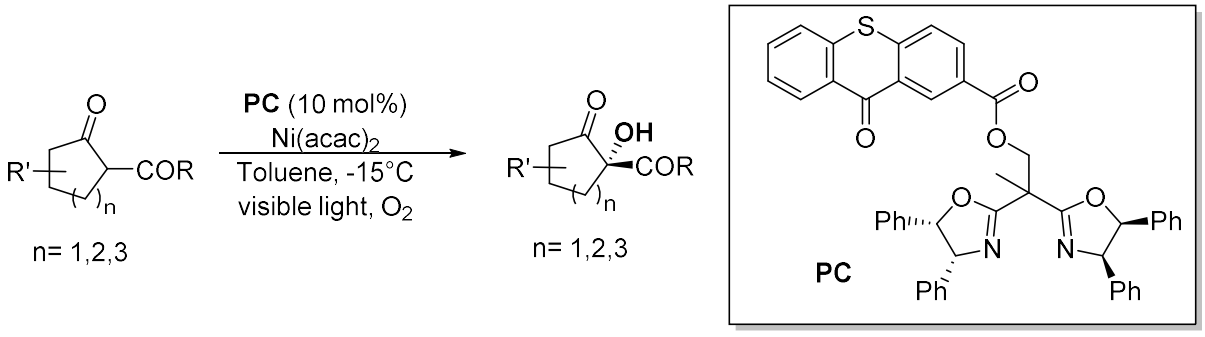


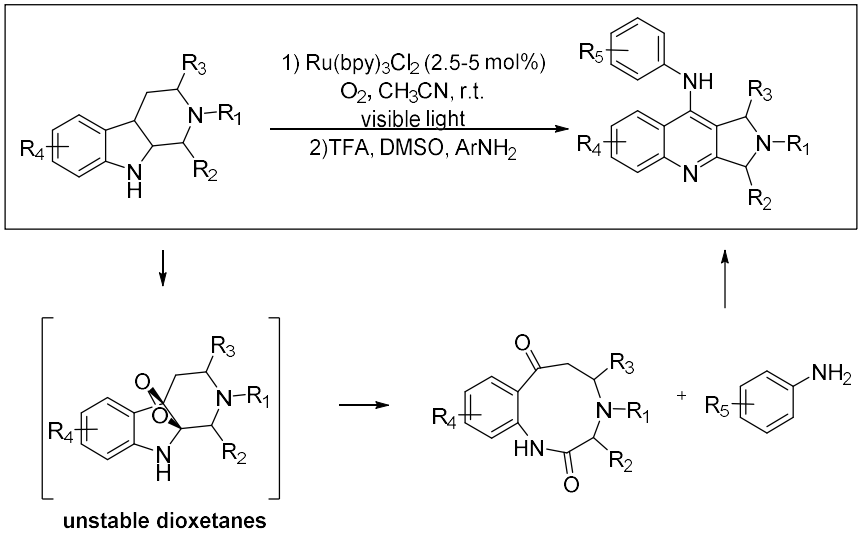
Figure 8. Synthetic Utility of singlet Oxygen ($^1O_2$).

In 2017, Xiao group developed the enantioselective aerobic oxidation of β-ketoesters using triplet state photosensitizer to chiral bisoxazoline ligands.[44] By making a complex with Ni(acac)2, this ligand allows for asymmetric oxidation of β-ketoesters. The thioxanthone component of the catalyst acts an efficient energy transfer catalyst to produce oxygen ($^1O_2$).



Scheme 8. Enantioselective Aerobic Oxidation of β-Ketoesters

In 2018, Chen group reported unexpected oxidative rearrangement/coupling reaction. tetrahydro-b-carbolines transformed to pyrrolo[3,4-b]quinolin-9-amines through unstable dioxetane (Scheme 9).[45] Dioxetane is produced by [2+2] cycloaddition with single oxygen ($^1O_2$). The unstable dioxetane is converted into ring opening 9-membered ring intermediate through cleavage of O−O/C−C bond. By protonation by TFA, the 9-membered ring intermediate underwent intramolecular rearrangement and react with aromatic amine to form final product.



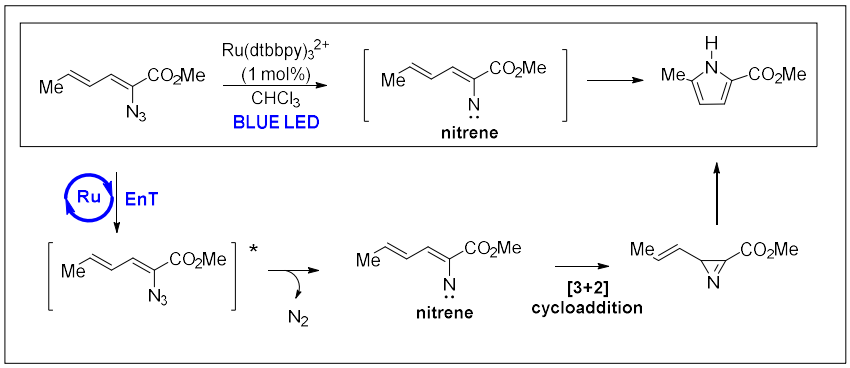
Scheme 9. [2+2] cycloaddition/rearrangement reaction via singlet oxygen ($^1O_2$).

1.3.2. Sensitization of Azide

Organic azides are widely used in synthetic organic chemistry, to transform to a wide range of nitrogenous compounds.[46-48] However, harsh condition such as UV light or high temperatures have been required to transform azide. Therefore, the transformation of azide into other nitrogen-containing compounds by energy transfer has been useful and widely studied.[49-54]

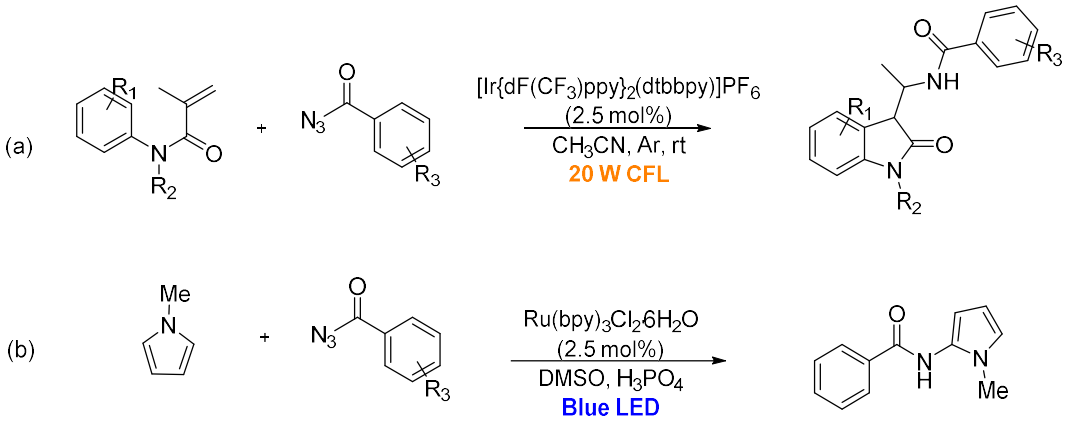
In 2014, Yoon group achieved sensitization of aryl vinyl and aryl azide to access nitrene, which form C-N bond in various ways, using Ruthenium photocatalyst (Scheme 10).[55] In this way, highly substituted pyrrole and indole can be synthesized. The reaction proceeds by nitrene intermediate pathway. First, the Ruthenium catalyst excited by blue LED light delivers energy to the azide. The triplet excited azide releases nitrogen and is converted to reactive nitrene intermediate. this intermediate

becomes azirine by cyclization. Finally, the azirine transforms to the final pyrrole product by intramolecular [3+2] cycloaddition.



Scheme 10. Intramolecular cycloaddition of vinyl azides via nitrene

Chang group reported the reaction using benzoyl azides for intermolecular reaction with *N*-aryl methacryl amides (Scheme 11a).[49] By mechanistic studies, it suggested that triplet benzoyl azide was the intermediate in this reaction processes by non-nitrene pathway. Benzoyl Azide also used for C-H Amidation of heteroarenes. König group demonstrated C-H amidation of heteroarenes with phosphoric acid using Ru-photocatalyst under blue LED light (Scheme 11b).[50]



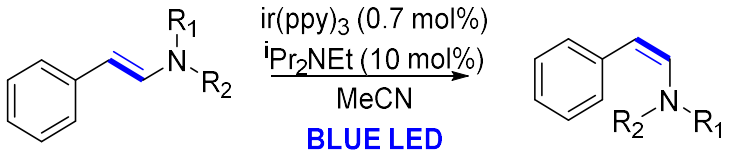
Scheme 11. Azide sensitization via an EnT process

1.3.3. Catalytic Alkene Isomerization

Alkenes are a basic structure for many organic molecules and served as versatile starting materials for various transformations. Alkenes are available in a variety of synthetic methods but are difficult to access in the case of *(Z)*-alkenes because of thermodynamic instability. Various methods are developed

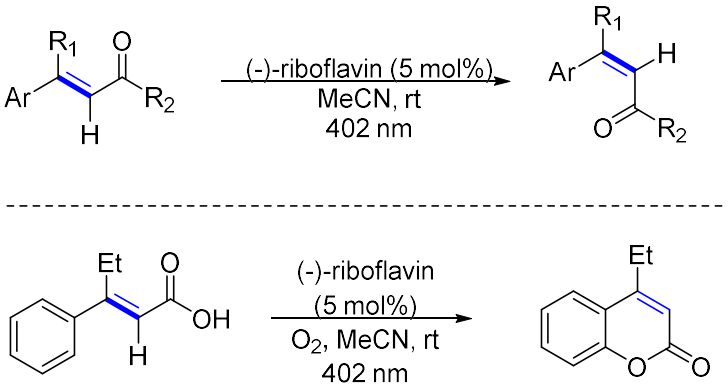
to access (Z)-Alkene such as Wittig reaction, hydrogenation of alkyne and cross-coupling.[56] Recently, (E)/(Z) isomerization of alkene using visible light was recently developed.[57-61]

In 2014, Weaver group investigated *E/Z* isomerizations of allylamines from (E)-alkene to thermodynamically less stable alkenes by $Ir(ppy)_3$ as the photocatalyst (Scheme 12).[61]



Scheme 12. *E/Z* isomerization of allylamine

Gilmour group investigated (*Z*)-isomerization of activated olefins using (−)-riboflavin.[59] And, they discovered that coumarin scaffold could be approached by one pot isomerization/cyclization strategy in the same time by energy transfer and singlet electron transfer.



Scheme 13. E/Z alkene isomerization using (−)-riboflavin as photocatalyst.

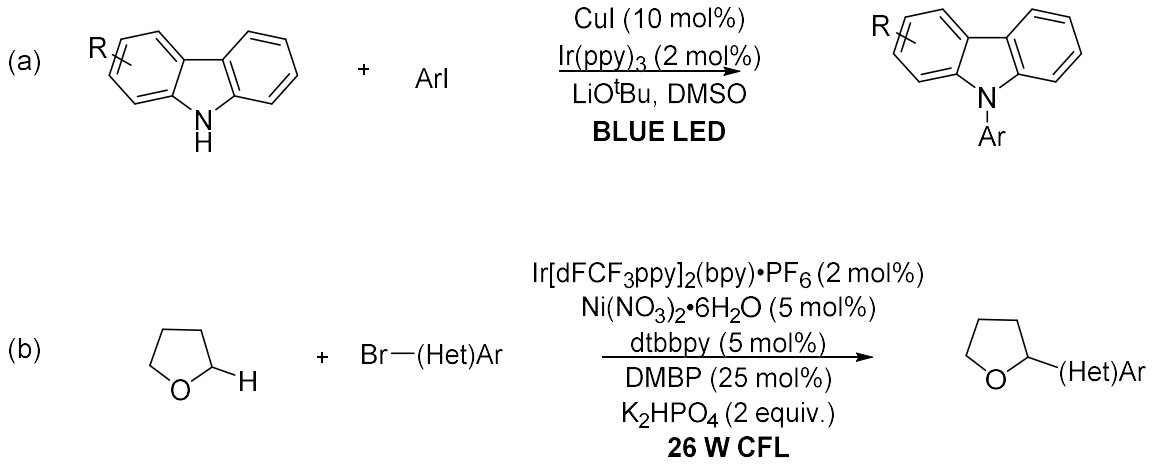
1.3.4. Sensitization of Metal Complexes

Transition-metal catalysis has been occupied an important role in organic chemistry.[62-64] Reactions using transition-metal catalysis have been widely used in various organic transformations that can't achieved non-metal chemistry.

In general, the traditional transition metal catalyst method requires strong heat or stoichiometric agent. In order to overcome these shortcomings, recently, dual catalyst systems are being developed that uses the combination of transition metal catalyst and photocatalyst, which usually proceed through SET process.[65-67] Also, the direct excitation of transition metals with visible light have been

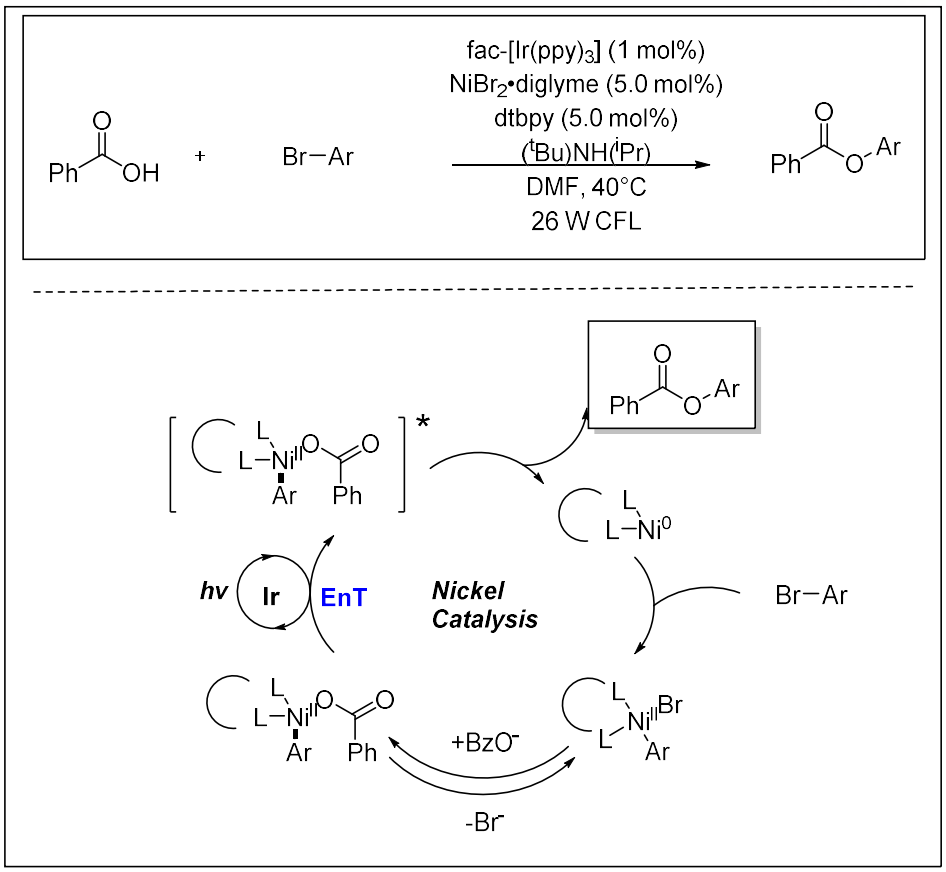
investigated.[68] However, most transition metal complexes do not absorb visible light directly, which is significantly limitation of this method. To overcome this limitation, Transition-metal complexes can be converted to excited states through energy transfer using sensitizer.[69] This approach makes transition metal catalysis accessible in an environmentally friendly manner under mild conditions.

In 2015, Kobayashi group reported Ullmann-type C−N cross-coupling reaction between carbazole derivatives and aryl iodides by dual catalyst system of an Ir-photocatalyst and a copper iodide under blue LED light (Scheme 14a.).[70] Molander group achieved Ni-catalyzed C(sp^3)−H arylation using Ir photocatalyst under blue LED light (Scheme 14b.).[71] Various aryl bromides show tolerance that coupled with activated α-hetero substituted or benzylic C(sp^3)−H bonds. Through mechanism studies, they propose a mechanism in which the excited nickel complex generated by an energy transfer pathway initiates C–H functionalization through homolysis of a Ni–halide bond.



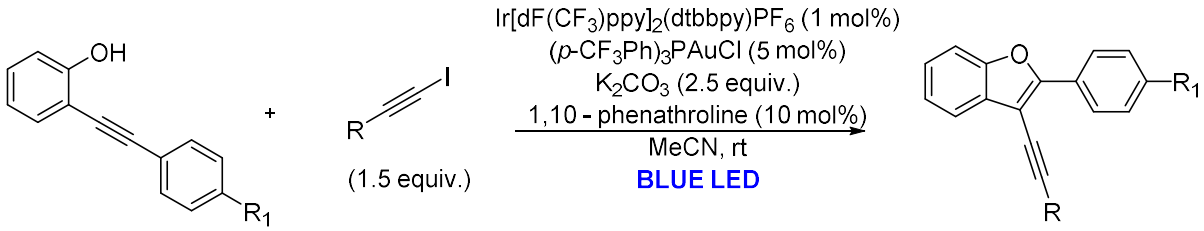
Scheme 14. Transition-metal-catalysis via EnT process

MacMillan group demonstrated Ni-catalyzed C-O cross-coupling reaction with carboxylic acids and aryl halides used Ir photocatalyst (Scheme 15).[72] This reaction starts with an oxidative addition of the aryl halide, generated nickel complex. Then a carboxylate nucleophile coordinated with this nickel complex to form aryl-Ni^{II} complex. The resulting aryl-Ni^{II} complex turned into excited state by energy transfer from by the excited photocatalyst. At the end, reductive elimination occurred from the excited-state nickel complex to give the final C-O coupling product.



Scheme 15. Ni-catalyzed C(sp^2)-O cross-coupling reaction with carboxylic acids and aryl halides.

Fensterbank group investigated a dual catalysis transformation, involving electrophilic gold catalysis and Ir-photocatalyst to allow a cross-coupling reaction for the alkynylation of benzofurans.[73] Excited Ir-photocatalyst made vinyl gold(I) intermediate to excited state via energy transfer. The triplet excited state of the vinyl gold(I) intermediate and the alkynyl iodide readily engage in an oxidative addition–trans/cis isomerization that forges the desired C(sp^2)-C(sp) bond, followed by reductive elimination that delivers the benzofuran product.

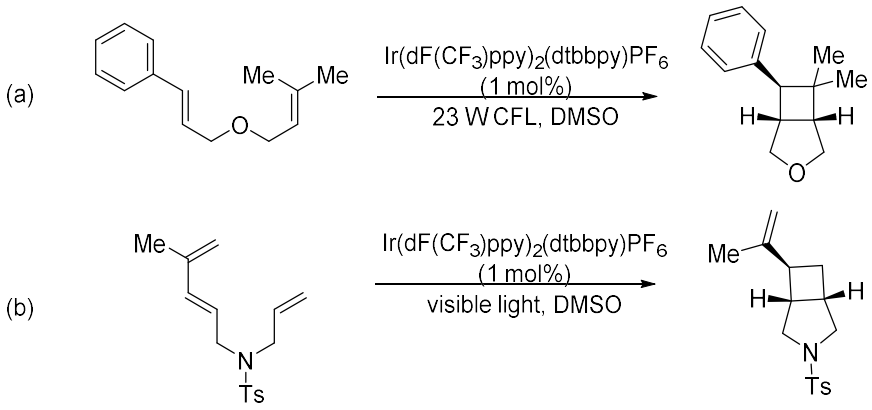


Scheme 16. oxidative addition of an alkynyl iodide onto a vinyl gold(I) intermediate to deliver C(sp^2)–C(sp) coupling via EnT

1.3.5. [2+2] cycloaddition reaction

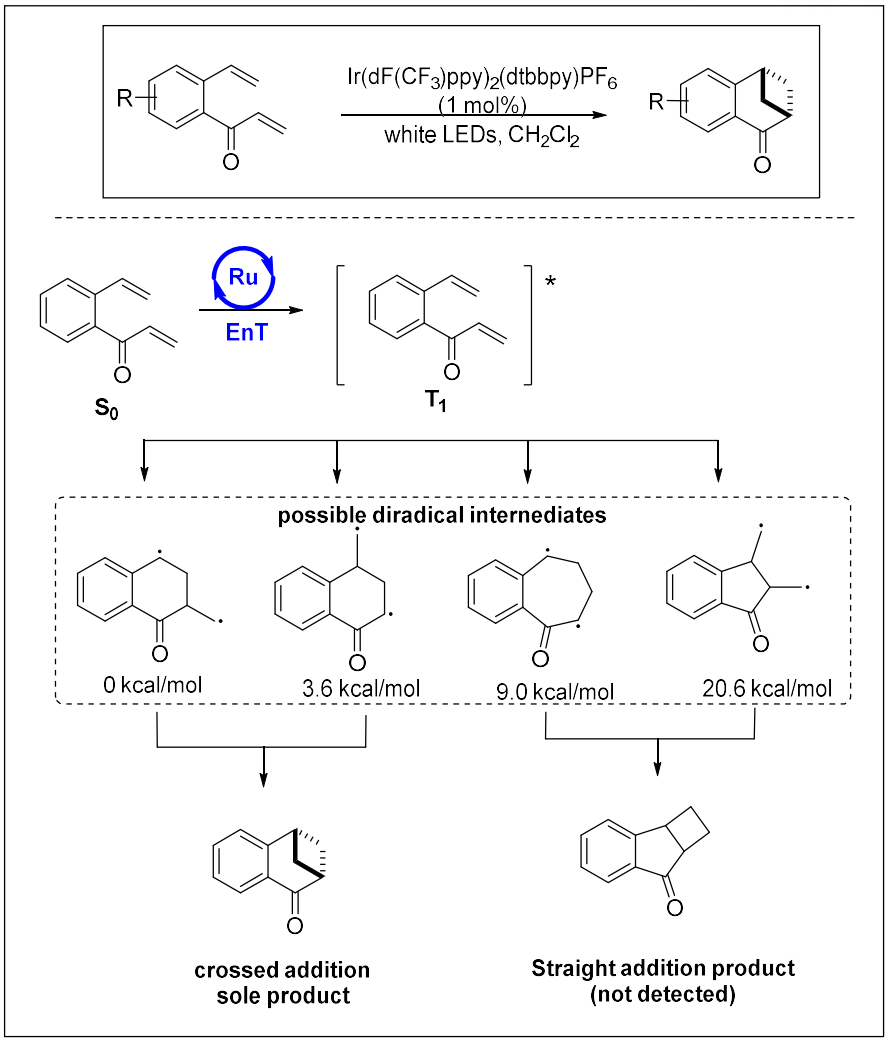
The [2+2] cycloaddition is straightforward approach to four membered ring derivatives. [2+2] cycloaddition is thermally forbidden, it can be achieved by photochemically. this process has mostly been developed under UV light irradiation condition.[29-31, 74-75] But these approaches have a limitation that need UV light irradiation, need high energy source for direct excitation such as UV light, which has disadvantage for selectivity of the reaction, functional group resistance and general applicability.

Because of these limitations, in recent years, [2+2] photocycloaddition via EnT was extensively studied. In 2012, Yoon group reported intramolecular [2+2] cycloadditions of Styrenes through energy transfer mechanism (Scheme 17a).[76] In this method, a variety of substituted cyclobutanes obtained by using $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ as a photocatalyst under visible light. After this work, they extended their chemistry to intramolecular [2+2] photocycloaddition of 1,3-diene (Scheme 17b).[77]



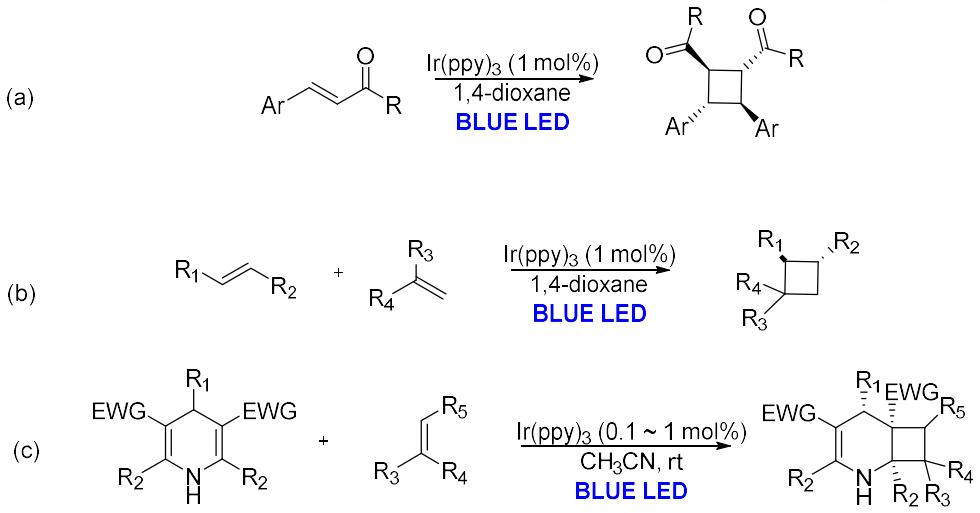
Scheme 17. Intramolecular [2+2] cycloaddition via EnT

At 2017, kwon group presented the intramolecular [2+2] cycloadditions of dienone to form bridged cyclobutanes through energy transfer using $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ as photocatalyst (Scheme 18).[78] Unlikely to previous examples of straight [2+2] cycloadditions, in this reaction crossed additions occur delivered desired bridged benzobicycloheptanone products with excellent regioselectivity in high yields. triplet state Dienone formed a radical intermediate through intramolecular cyclization. The DFT results suggest that benzyl radicals are thermodynamically favored intermediates among the four types of diradicals.



Scheme 18. The intramolecular [2+2] cycloadditions of dienone

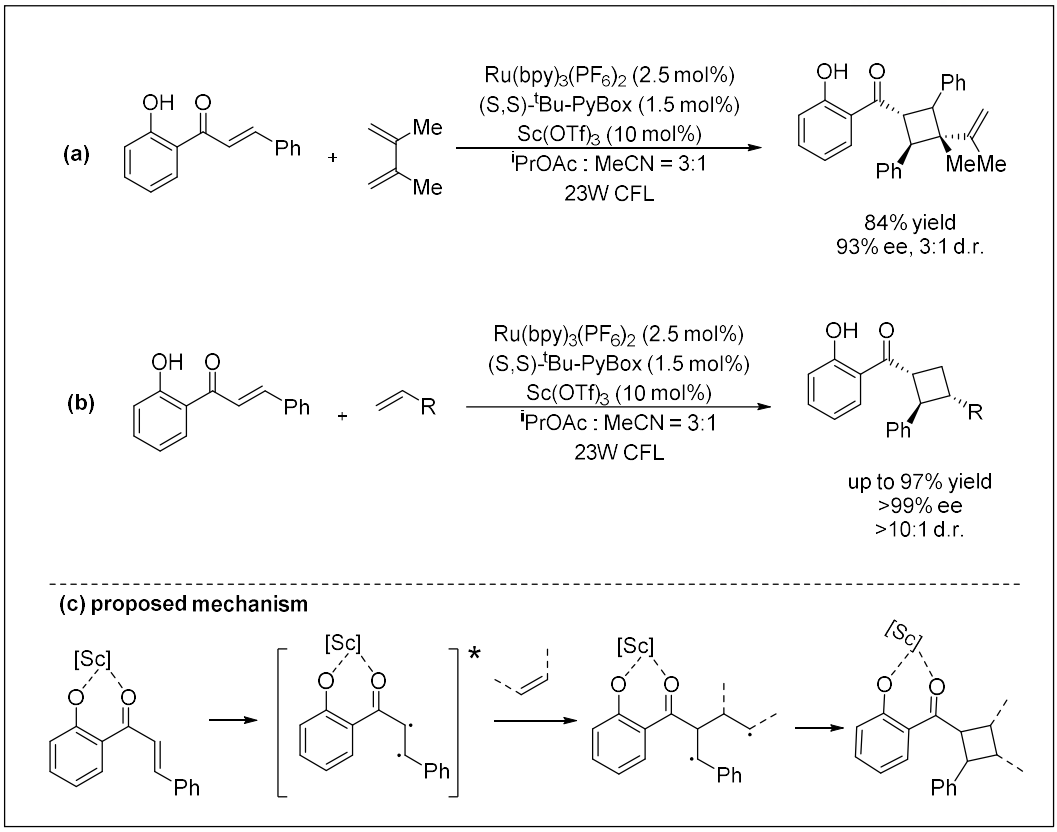
Intermolecular [2+2] cycloaddition is more challenging than intramolecular [2+2] cycloaddition. At 2017, Wu group reported intermolecular [2+2] dimerization reactions and intermolecular [2+2] cycloaddition of 1,1-diarylethylene with various alkenes, yielding unsymmetrical cyclobutanes with high stereospecificity using $Ir(ppy)_3$ as photocatalyst (Scheme 19a, b).[79] And Lu group developed visible light-promoted [2 + 2] cycloaddition 1,4-dihydropyridines and olefins by using Ir-photocatalyst (Scheme 19c).[80]



Scheme 19. Intermolecular [2+2] cycloaddition reaction via EnT

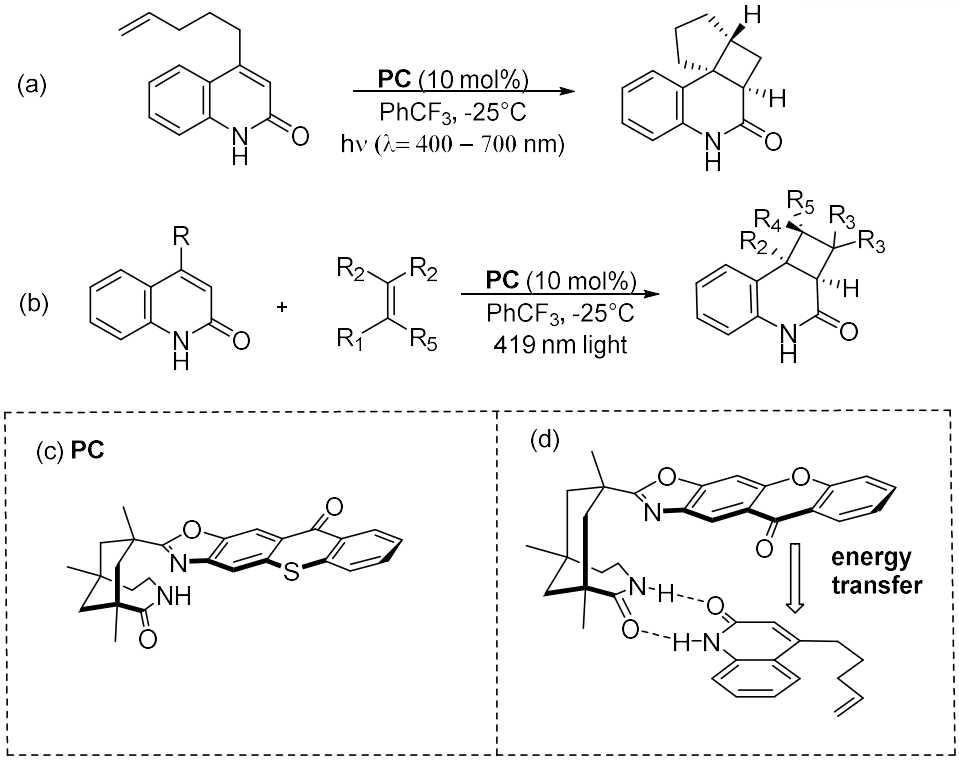
Controlling enantioselectivity in reactions involving excited organic intermediates is a significant challenge. In case of [2+2] cycloadditions, a variety of enantioselective catalysis method were developed by using chiral catalyst or Lewis acid.

In 2016, Yoon group achieved Enantioselective [2 + 2] photocycloadditions by using Lewis acid and EnT catalyst (Scheme 20a).[81] They suggest the complex of Lewis acid and 2'-hydroxychalcones (E_T = 33 kcal mol^{-1}) has lower triplet energy than 2'-hydroxychalcones (E_T = 54 kcal mol^{-1}), offering the enantioselectivity to reaction. When 2'-hydroxychalcones coordinates with $Sc(OTf)_3$ to form Sc(III)-complex, Ru(bpy)3(PF6)2 (E_T = 45 kcal mol^{-1}) are enable to transform Sc(III)-complex to excited diradical intermediate, which undergoes a stepwise addition with alkene to generate benzylic 1,4-diradical (Scheme 20c). And final cyclization occurs to form the desired cyclobutane product. After, they expended their chemistry to enantioselective [2+2] photocycloadditions of 2'-hydroxychalcones with styrenes (Scheme 20b).[81] In this process, 1,2-diarylcyclobutanes are enable to synthesis under a controlled enantioselective method.



Scheme 20. Enantioselective intermolecular [2 + 2] photocycloadditions.

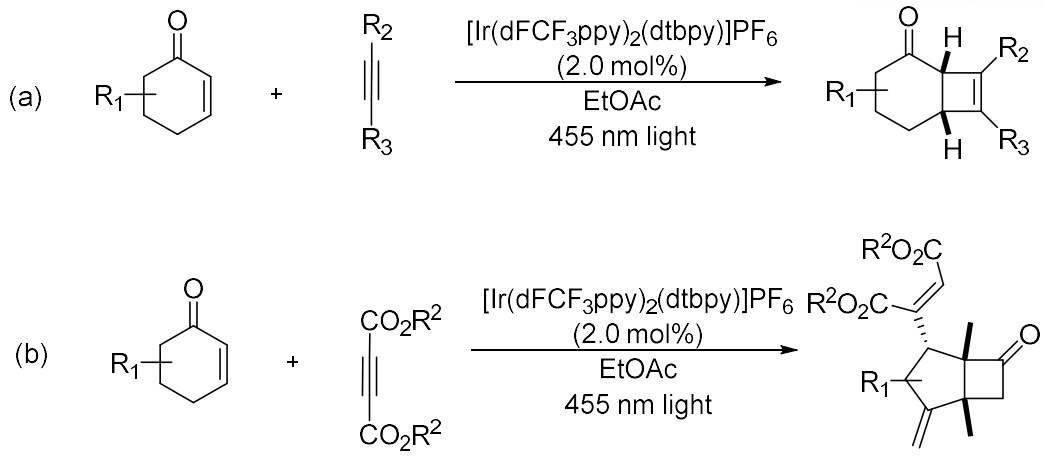
Bach group developed chiral Thioxanthone as a photocatalyst for enantioselective [2+2] cycloaddition reaction (Scheme 21a).[82] They demonstrated intramolecular [2+2] cycloaddition of quinoline that applied chiral thioxanthone as a photocatalyst. There is a hydrogen bonding interaction between thioxanthone catalyst and quinoline, which achieves very high enantioselectivity. After hydrogen bonding is achieved, the catalyst transfers energy to the quinoline, which reaches the triplet extended state. A few years later, they reported enantioselective intermolecular [2+2] cycloaddition reaction of quinolones with alkenes by adopting same photocatalyst system (Scheme 21b).[83]



Scheme 21. Enantioselective [2+2] cycloaddition Reactions with A Chiral Thioxanthone.

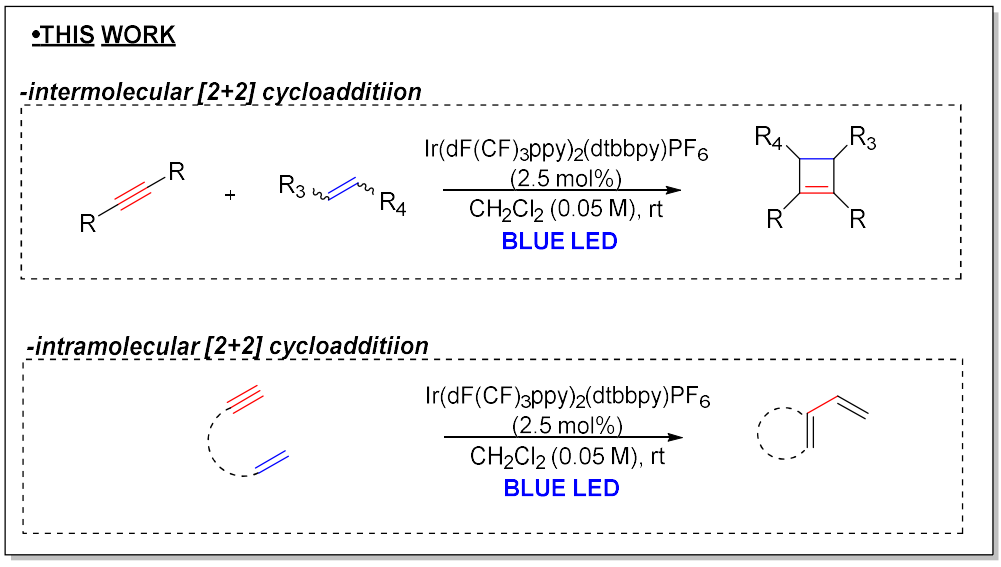
While alkene-alkene [2 + 2] cycloaddition has been extensively studied under visible light, alkyne-alkene [2+2] cycloaddition have been relatively rarely reported.

Recently, Glorius group reported [2+2] Cycloaddition of Enones with alkynes using $[Ir(dFCF_3ppy)_2(dtbpy)]PF_6$ as photosensitizer under 455 nm LED light (Scheme 22).[84] When [2+2] cycloaddition was carried out with an alkyne rich electron the expected cyclobutenes was obtained, but the rearrangement was observed when the reaction was carried out with electron deficient alkynes. This method has the disadvantage that alkene source is limited to enone structure and also alkynes has limited scope.



Scheme 22. [2+2]-Cycloaddition/Rearrangement of Enones with Alkynes.

Herein, we develop visible light photocatalysis [2+2] cycloadditions of alkene-alkyne by energy transfer mechanism (Scheme 23). $Ir(dF(CF)_3ppy)_2(dtbbpy)PF_6$ are used as photocatalyst and blue LED light is used for irradiation. Both Inter/intramolecular reactions are investigated and in case of intermolecular [2+2] cycloaddition shows board scope with a variety of alkyne. in the other hand, at intramolecular [2+2] cycloaddition, 1,3-diene are produced by tandem intramolecular [2+2] cycloaddition – ring opening reaction. This approach is significant in that developed the [2 + 2] cycloaddition reaction under visible light and provided access to various cyclobutene and conjugated diene structures.

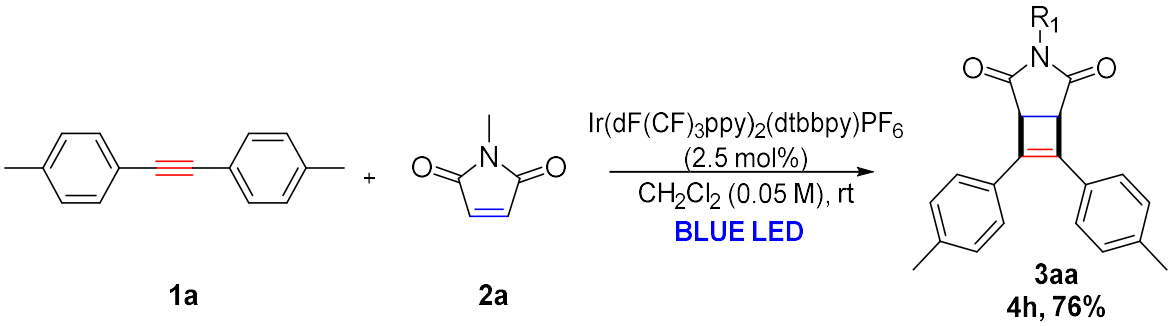


Scheme 23. THIS WORK: visible light photocatalysis [2+2] cycloadditions of alkene-alkyne by energy transfer.

II. RESULTS AND DISSCUSION

Based on our investigations, we designed the reaction of alkene with alkyne using photocatalyst under visible light. In the early study, It turned out when di(p-tolyl)acetylene (**1a**) and N-methylmaleimide (**2a**) were employed as coupling partners using a blue LED as a light source and an Ir(dF(CF)3ppy)2(dtbbpy)PF6 as a photosensitizer, the desired cyclobutene product was obtained with 76% yield (Scheme 24).

2.1. substrate scope



Scheme 24. Initial research: visible light photocatalysis [2+2] cycloadditions of di(*p*-tolyl)acetylene (**1a**) with *N*-methylmaleimide (**2a**).

Intermolecular substrate scope

Based on the initial research, various coupling partners were applied to demonstrate the utility of the reactions. First, we investigated the reactivity of alkyne part by reacting with N-methylmaleimide (**2a**) (Figure 9). Tolerance of alkynes substituted with aryl groups are investigated. It was found a TFA protected aniline (**1b**) reacted smoothly in 88% yield (**3ba**). In order to examine what not only alkynes substituted with aryl groups but also with alkyl groups apply to this system, several kinds of alkynes substituted with alkyl groups (**1c-1e**) have been tested. As a result, highly steric substitutions like adamantane group (**1c**) and cyclohexanol group (**1d**) well processed in good yield (**3ca, 3da**). Also, reaction with silyl substituted alkyne (**1d**) processed with excellent yield (**3da**). And reaction showed tolerance with hydroxy group without any protection (**3da, 3ea**).

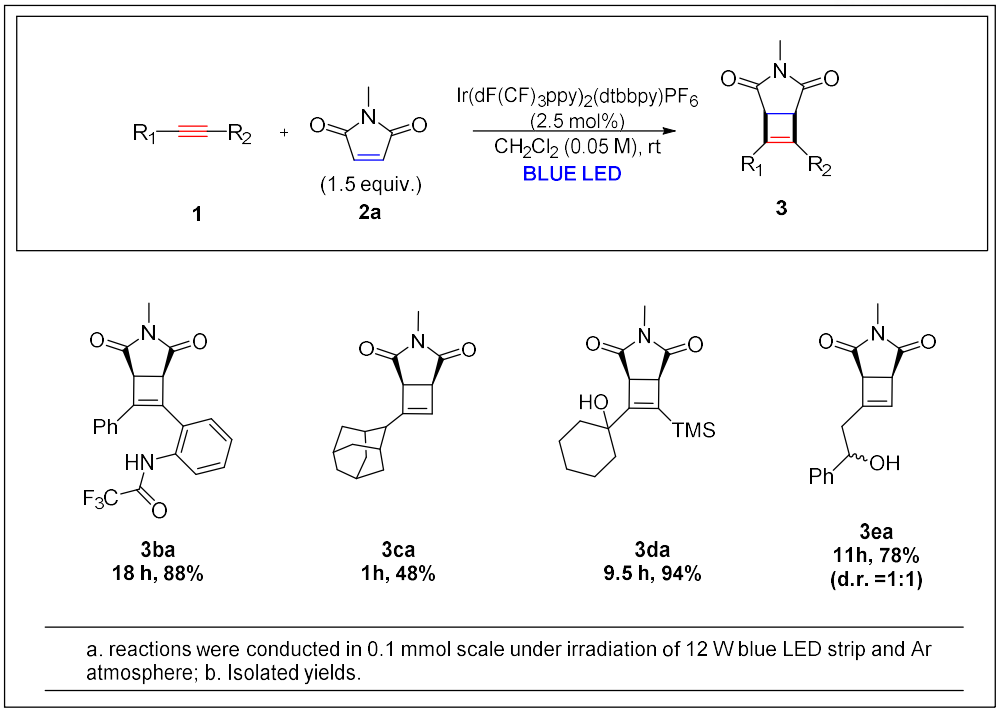


Figure 9. Substrate scope of alkynes with N-methylmaleimide (2a)[a,b].

Next, we tested with various maleimide derivatives (Figure 10). Substituted maleimides (**2b, 2c**) gave cyclobutenes (**3ab, 3ac**) with excellent yield. Also, not only N-methyl substituted maleimide but also N-phenyl substituted maleimide (**2c**) processed well (**3ac**).

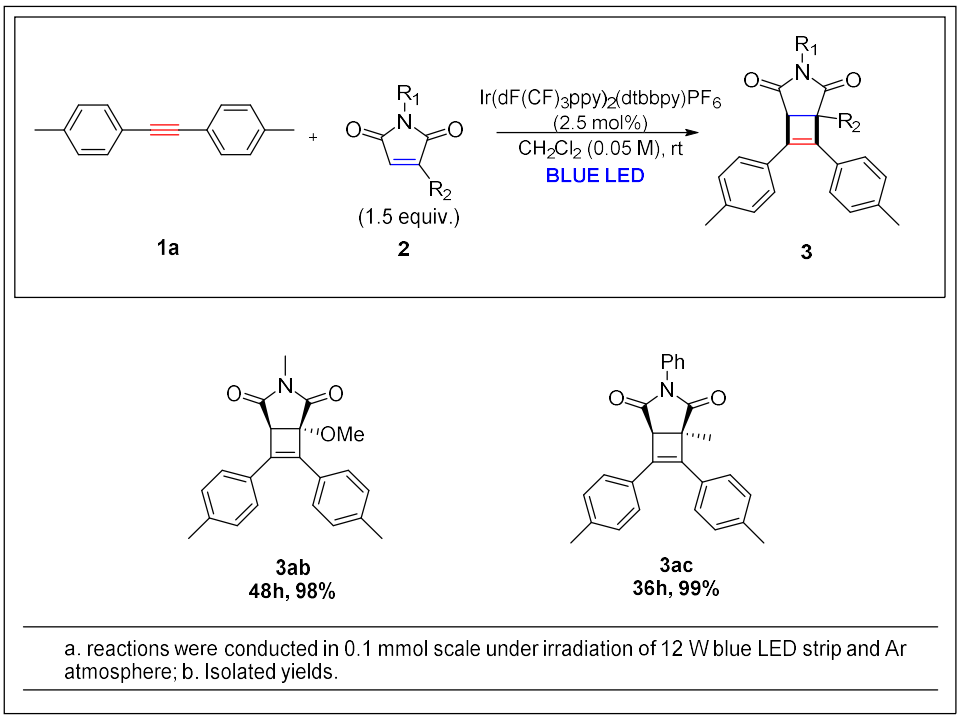
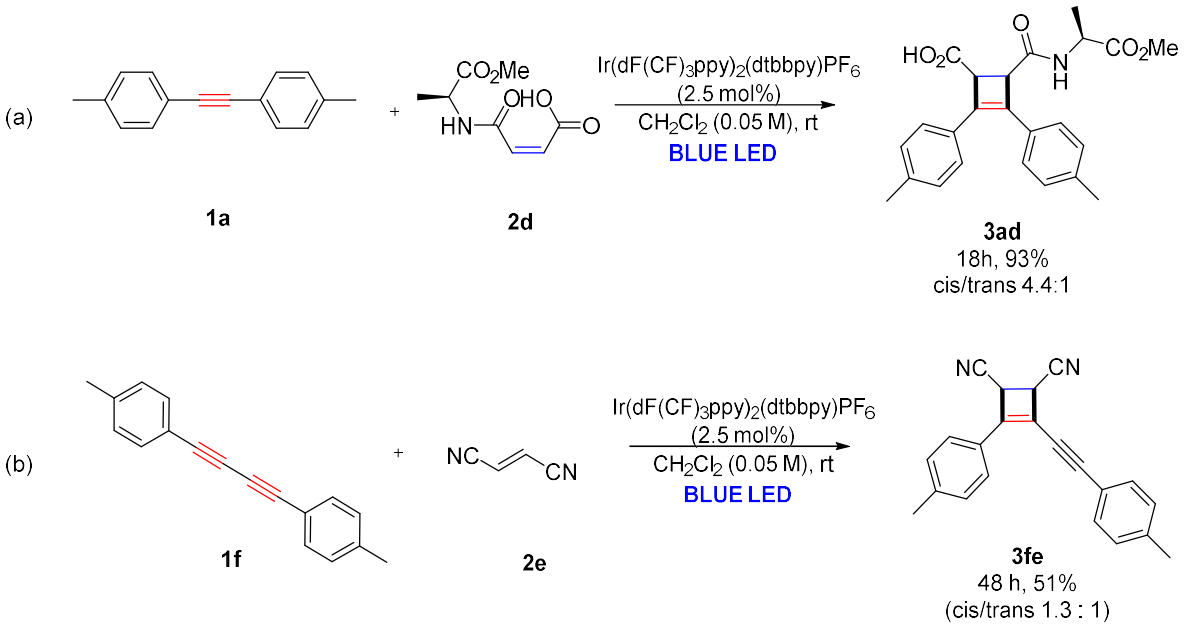


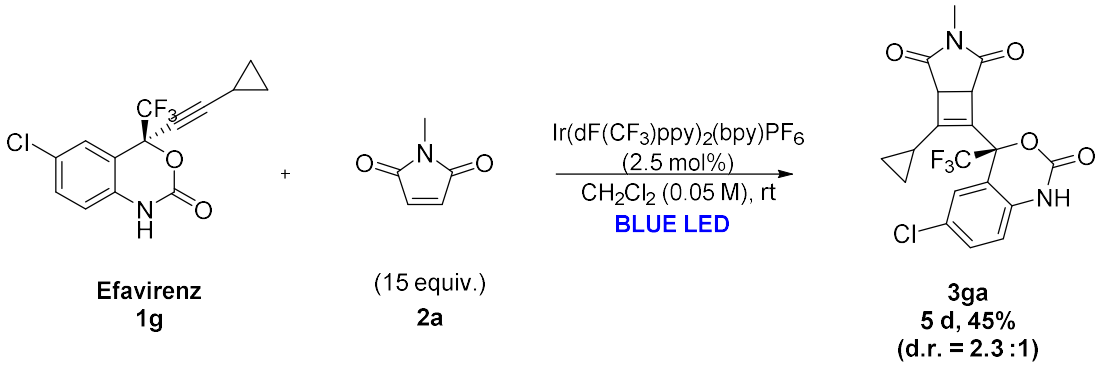
Figure 10. Substrate scope of maleimide derivatives with di(p-tolyl)acetylene (1a) [a,b]

In order to expand the scope of alkenes, alkenes other than maleimide was investigated (Scheme 25). Unsymmetrical alkene substituted carboxylic acid and amide (**2d**) was smoothly reacted with di(*p*-tolyl)acetylene (**1a**). It showed the reaction had tolerance with carboxylic acid without protection. 1,3-diyne (**1f**) was reacted with fumaronitrile (**2e**) with nitrile group which was versatile functional groups.



Scheme 25. Substrate scope of alkynes with alkenes

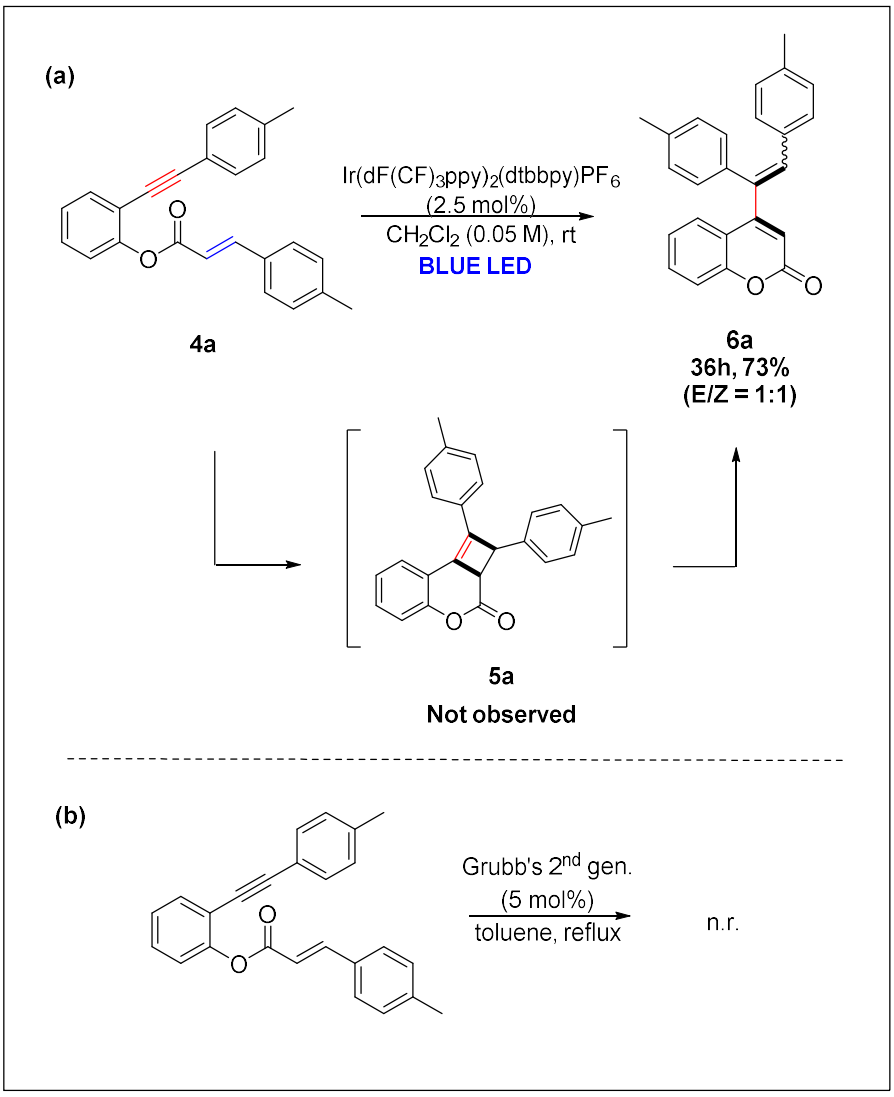
In order to verify utility of the reaction, last stage functionalization was attempted with a commercial drug, Efavirenz (Scheme 26). Alkyne part of Efavirenz (**1g**) was reacted with N-methyl maleimide **(2a)** smoothly using Ir(dF(CF$_3$)ppy)$_2$(bpy)PF$_6$ as catalyst and gave desired cyclobutene product (**3ga**) with 45% yield.



Scheme 26. last stage functionalization with a commercial drug.

Intramolecular substrate scope

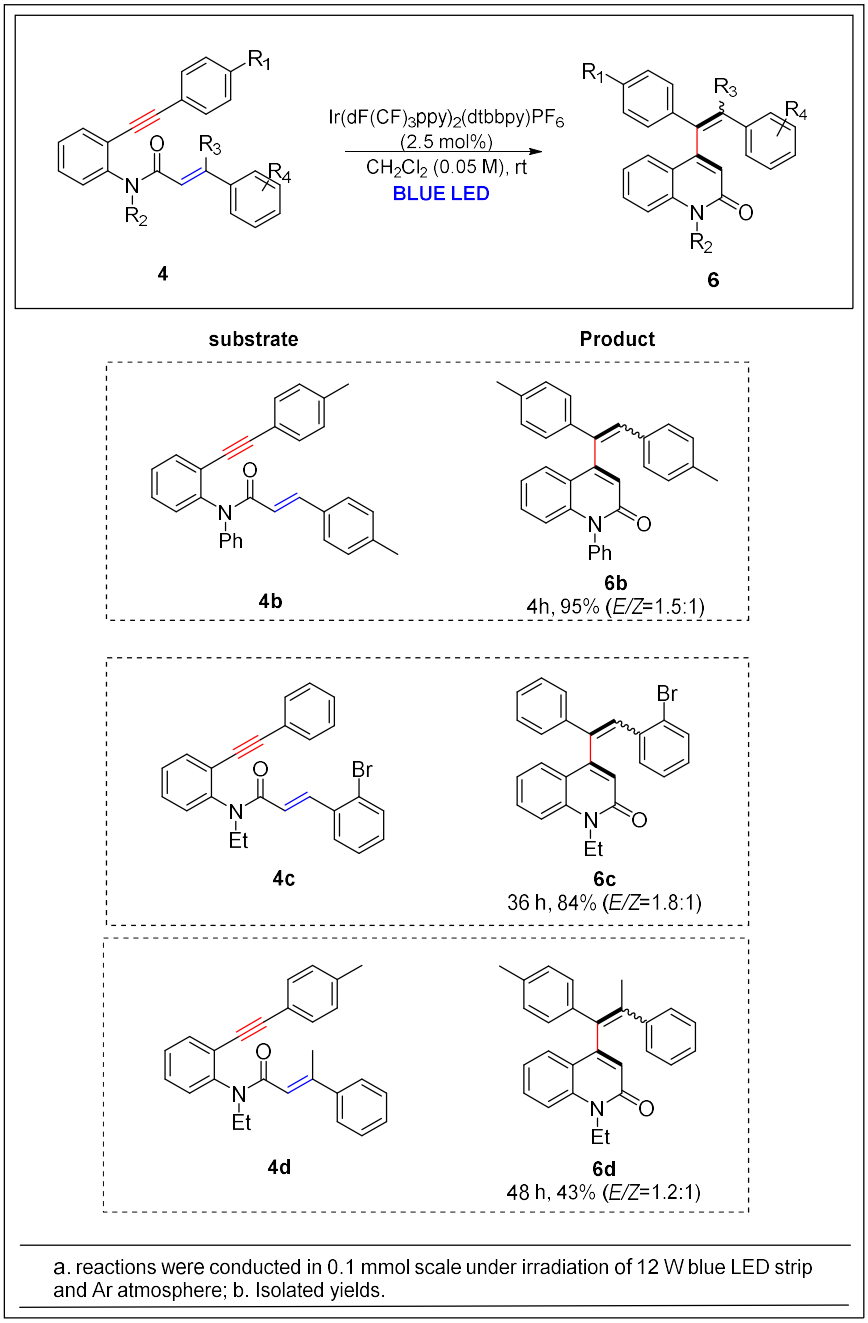
To expend a range of our chemistry, we designed intramolecular reactions with enynes (Scheme 27a). First, ester-tethered enyne (**4a**) was subjected to the optimized condition of intermolecular reactions. Surprisingly, 1,3-Diene (**6a**) was obtained in 73% yield and expected cyclobutene (**5a**) wasn't observed. We assumed that these 1,3-dienes were formed by ring openings of cyclobutenes. These kinds of 1,3-diene moiety have generally been synthesized by enyne metathesis.[85-87] However, in case of traditional enyne metathesis, it is hard to find a case of synthesis of highly substituted 1,3-dienes.[85-87] When we tried traditional enyne metathesis with ester-tethered enyne (**4a**) using Grubb's 2nd generation catalyst, couldn't observed desired product (**6a**), whereas the intramolecular [2+2] photocycloaddition gave in 73% yield (Scheme 27b).



Scheme 27. (a) intramolecular reactions with enynes (b) Enyne metathesis with Grubb's catalyst.

In addition to ester-tethered enyne, amide-tethered enyne were examined and gave 2-quiolones, which were core structures of pharmacological compounds with various biological properties (Table 1).[88-89] To investigate the tolerance of amino-tethered enyne, various enynes were examined. substitution in N-position with alkyl and aryl group (**4b - 4d**) both smoothly reacted in good and excellent yield. an enyne with trisubstituted alkene part (**4d**) gave **6d** moderate yield. Also, reaction with 2-bromo phenyl group at alkene moiety was processed smoothly to afford **6c** in 43% yield.

Table 1. Scope of the Intramolecular Reaction[a, b]



a. reactions were conducted in 0.1 mmol scale under irradiation of 12 W blue LED strip and Ar atmosphere; b. Isolated yields.

Configurations of *(Z)*- and *(E)*-1,3-dienes were confirmed by 1D-selective 1H NOE spectroscopy (Figure 11). In case of ***(Z)*-6a**, we selectively irradiated vinyl proton (H_b) and NOE signals of *o*-position proton of tolyl group were detected (Ha, Hc) in comparison with the 1H NMR spectrum. And when allylic methyl proton (H_d) of **(*Z*)-6d** was selectively irradiated, NOE single of o-position proton (He) of tolyl group were detected. Based on these results, configurations of (Z)/(E)-1,3-dienes were confirmed.

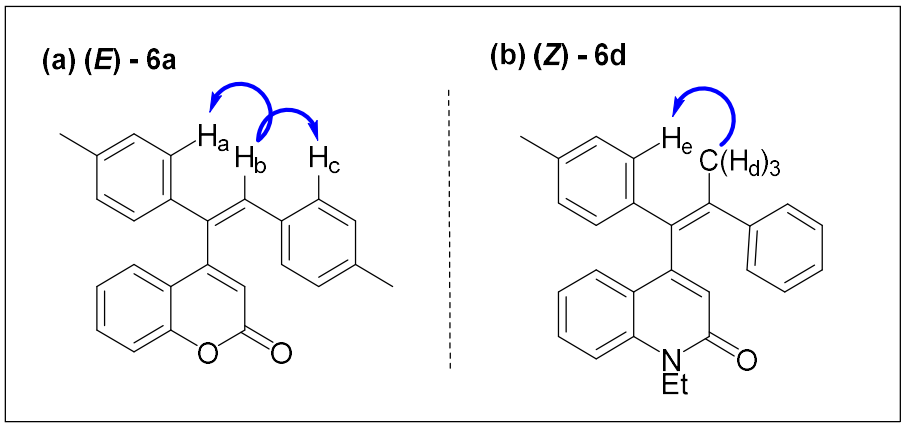
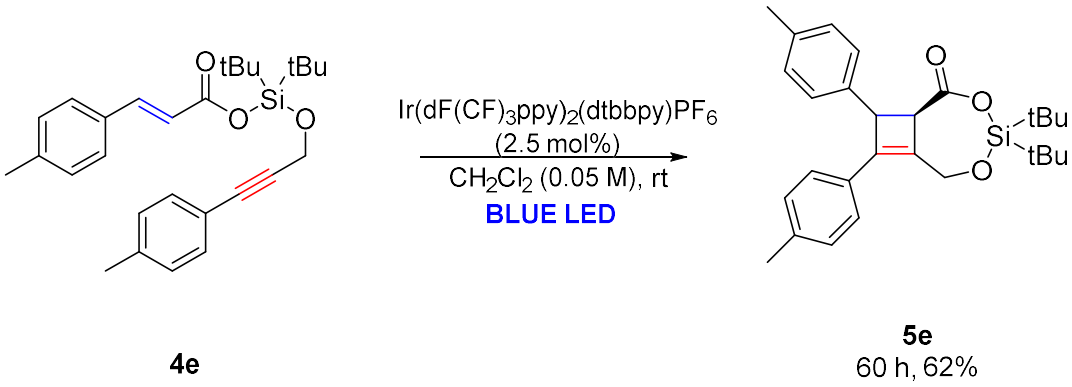


Figure 11. Stereochemical Assignments by 1D NOE Experiments

When silyl-tethered enyne (**4e**) was subjected to the reaction conditions, cyclobutene with 7-membered ring **5e** was obtained in 62% yield instead of 1,3-diene. This result suggests that cyclobutene is an intermediate of 1,3-diene.



4e

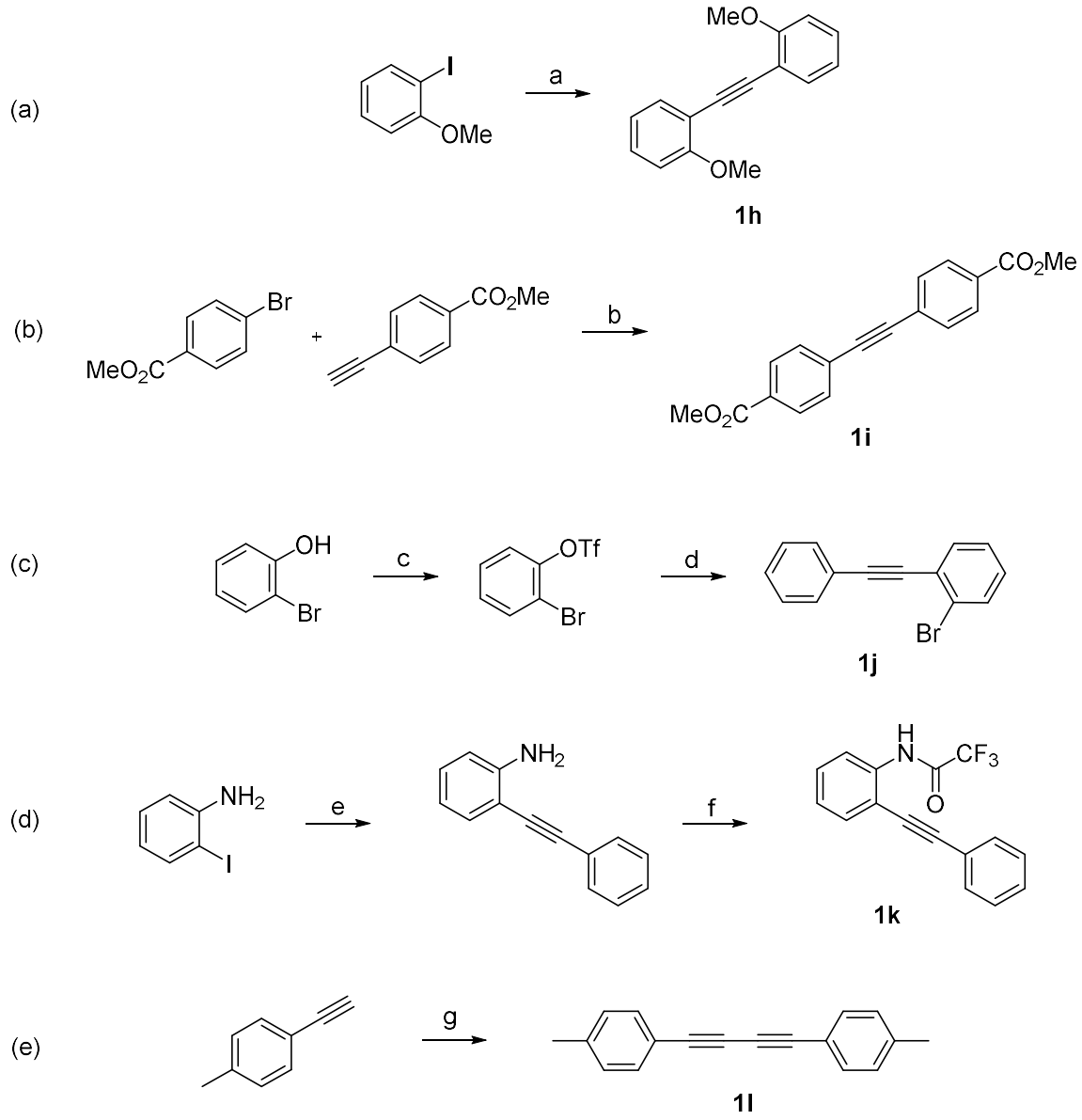
5e
60 h, 62%

Scheme 28. intramolecular [2 + 2] photocycloaddition of silyl-tethered enyne

Synthesis of substrates

In order to expend the scope, various kinds of alkyne and alkene were synthesized. First, we verified the utility of our reaction by trying various aryl alkynes, which are synthesized through Sonogashira

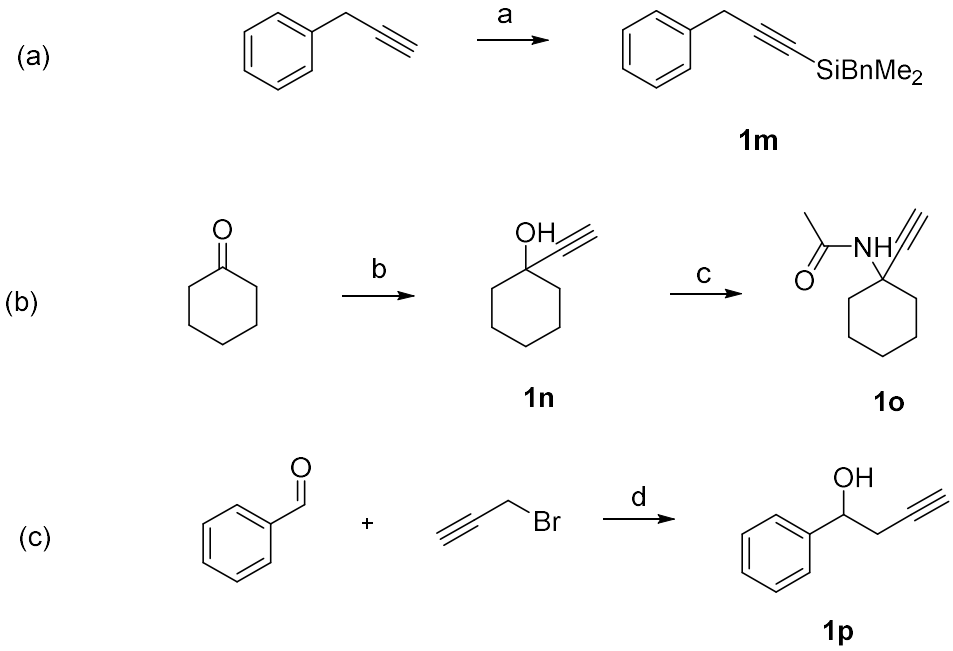
coupling reactions. Alkyne (**1h**) was synthesized by calcium carbide as the alkyne source for Sonogashira cross coupling reaction (Scheme 30a). Methyl 4-ethynylbenzoate reacted with methyl 4-bromobenzoate to form alkyne (**1i)** using copper-free Sonogashira coupling reaction (Scheme 30b). 2-bromophenyl trifluoromethanesulfonate was prepared by reaction of 2-bromophenol with Trifluoromethanesulfonic anhydride. And Sonogashira coupling reaction of 2-bromophenyl trifluoromethanesulfonate gaves 1-bromo-2-(phenylethynyl)benzene (**1j**) (Scheme 30c). TFA-protected aniline (**1k**) was prepared by Sonogashira coupling reaction following by amine protection (Scheme 30c). And Glaser coupling with p-tolylacetylene generated dialkyne (**1l)** (Scheme 30d).



Scheme 29. Synthesis of aryl alkynes: Reagents and conditions: : a) CaC_2, $Pd(OAc)_2$, CuI, PPh_3, Et3N, MeCN, r.t., 97%, b) piperidine, MeCN, 85°C, 84%, c) Tf_2O, pyridine, CH_2Cl_2, 0°C to r.t., 98%, d)

phenylacetylene, Pd(OAc)2, dppf, CuI, Et_3N, DMF, r.t.,70%, e) $Pd(PPh_3)_2Cl_2$, CuI, 2-iodoaniline, and phenylacetylene, Et3N, 70°C, 88%, f) Tf_2O, pyridine, CH_2Cl_2, 0°C to r.t., 86%, g) Cu(I)Cl, piperidine, CH_2Cl_2, r.t., 99%

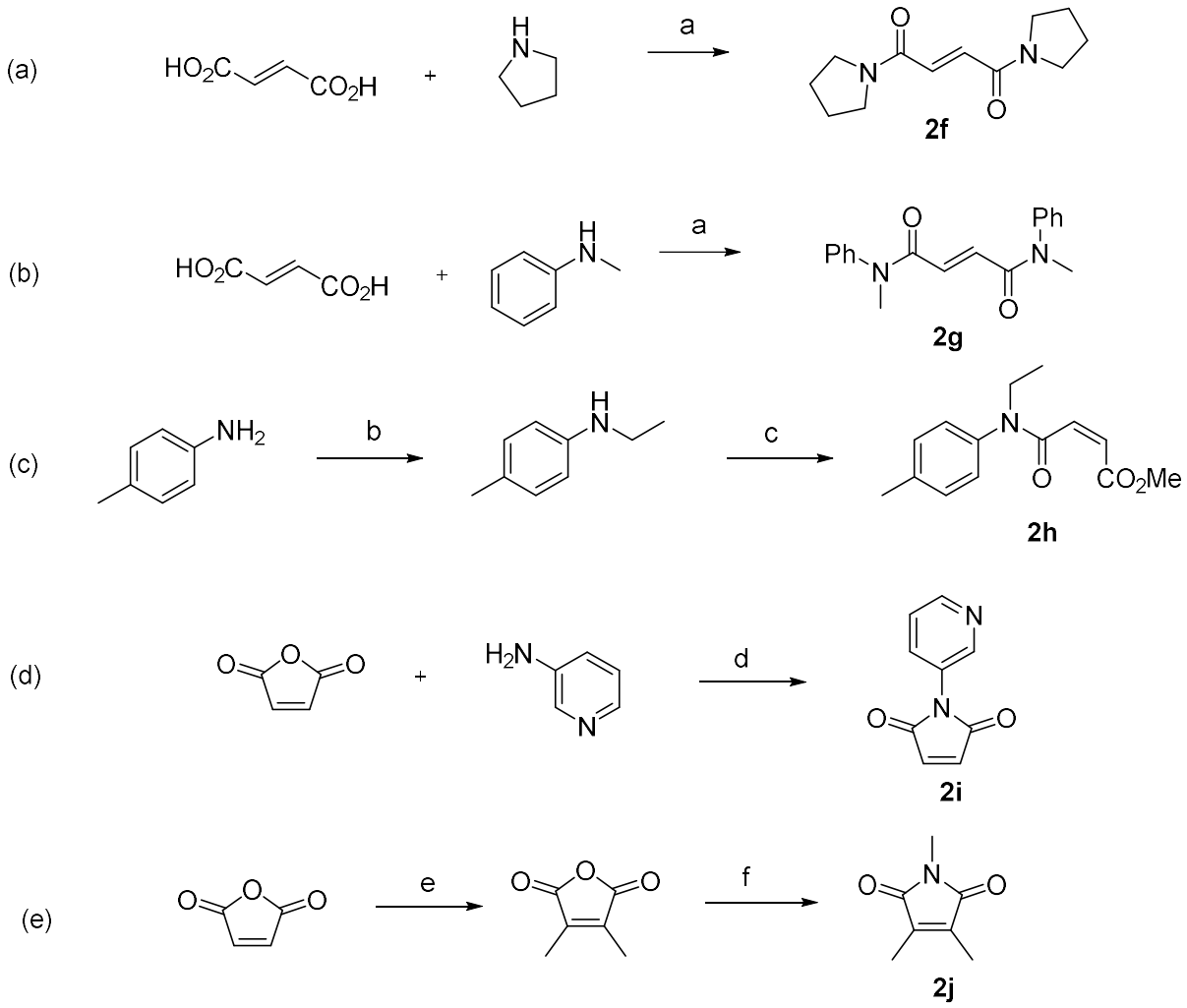
Following aryl alkyne, various aliphatic alkyne was also synthesized (Scheme 30). Silyl alkyne (**1m**) was produced by using prop-2-yn-1-ylbenzene as staring material, which reacted with benzyl(chloro)dimethylsilane. And alkynes with alcohol moiety are prepared. In case of **1n**, cyclohexanone transformed to propargyl alcohol (**1n**) with calcium carbide as the acetylene source. And **1p** was prepared by Barbier reaction. Ritter reaction of **1n** with acetonitrile afforded alkyne with amide moiety (**1o**).



Scheme 30. Synthesis of aliphatic alkyne: Reagents and conditions: a) n-BuLi., benzyl(chloro)dimethylsilane, THF, -78°C to r.t,, 78%, b) Cs_2CO_3, CaH_2, DMSO/H_2O (50 : 1), 60°C, 77%, c)H_2SO_4, CH_2Cl_2/MeCN, 0°C to r.t., 44%, d) propargyl bromide, $FeCl_3$, Zinc dust , 0°C to r.t., 67%

Various alkenes have also been prepared for investigating to utility of the reaction (Scheme 31). Acyl chloride, which was transformed to bis-amides (**2f, 2g**) by amine, were produced from fumaric acid using thionyl chloride. Ethylation of *p*-toluidine at microwave condition, followed by acyl chloride mediated amide formation afforded asymmetric alkene (**2h**). Also, reaction of maleic anhydride with 3-aminopyridine gave N-pyridine group of maleimide (**2i**) at one pot. Maleic anhydride reacted with 2-

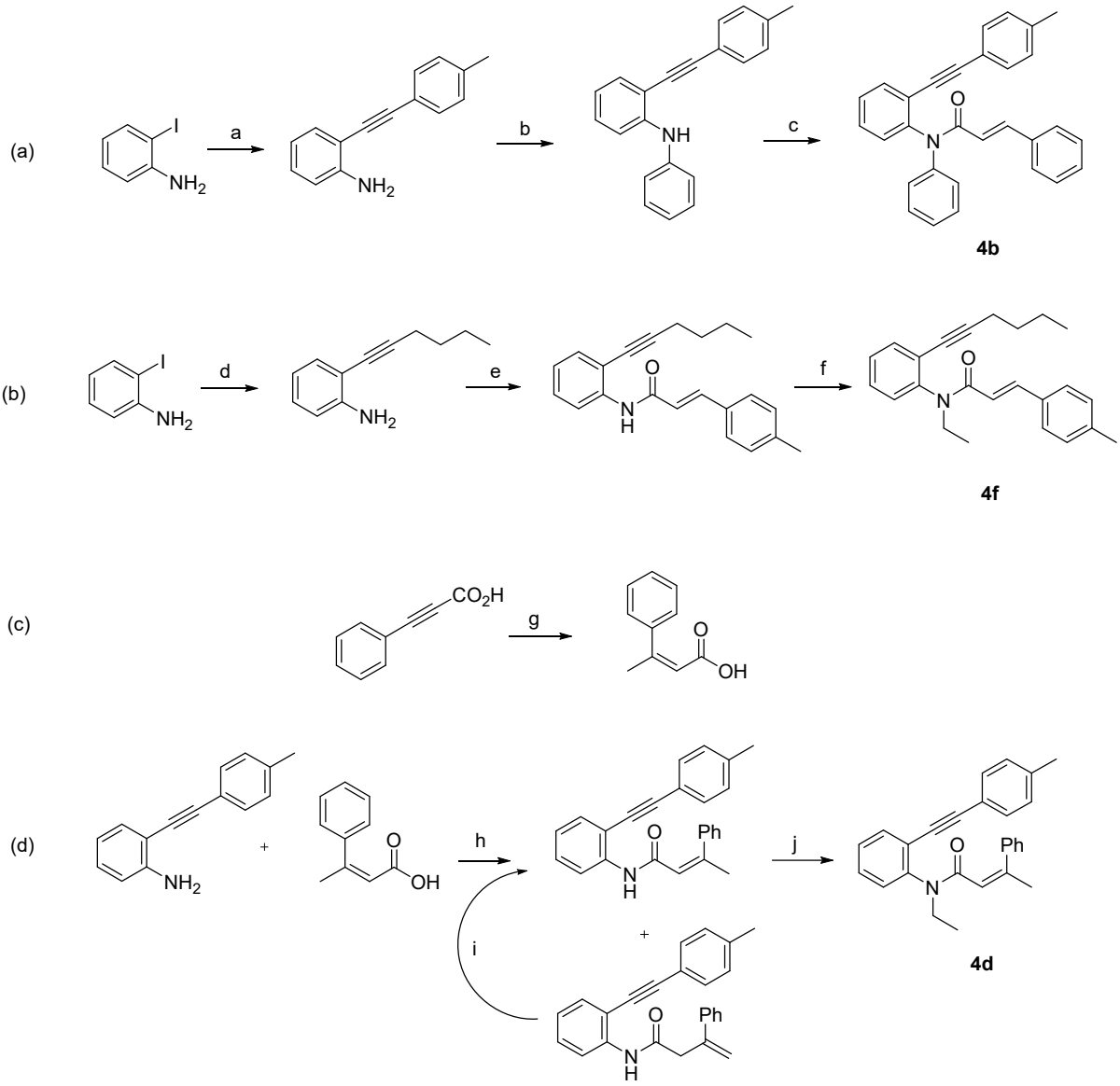
aminopyridine afforded 2,3-Dimethylmaleic anhydride, which was subjected to 2,3-Dimethyl-N-methyl maleimide (**2j**) by reaction with methylamine and sodium acetate.



Scheme 31. synthesis of alkenes: a) DMF (cat.), oxalyl chloride, CH_2Cl_2, 0°C to r.t., b)EtI, H_2O, µW 150°C, 44%, c)(i)maleic anhydride, CH_2Cl_2, r.t., (ii) $SOCl_2$, MeOH, 0°C to r.t., 67% d) (i)THF, r,t., (ii)NaOAc, Ac_2O, 80°, 50%, e)2-aminopyridine, AcOH, H_2SO_4, reflux, 60%, f) CH_3NH_2·HCl, NaOAc, AcOH, 100°C, 72%

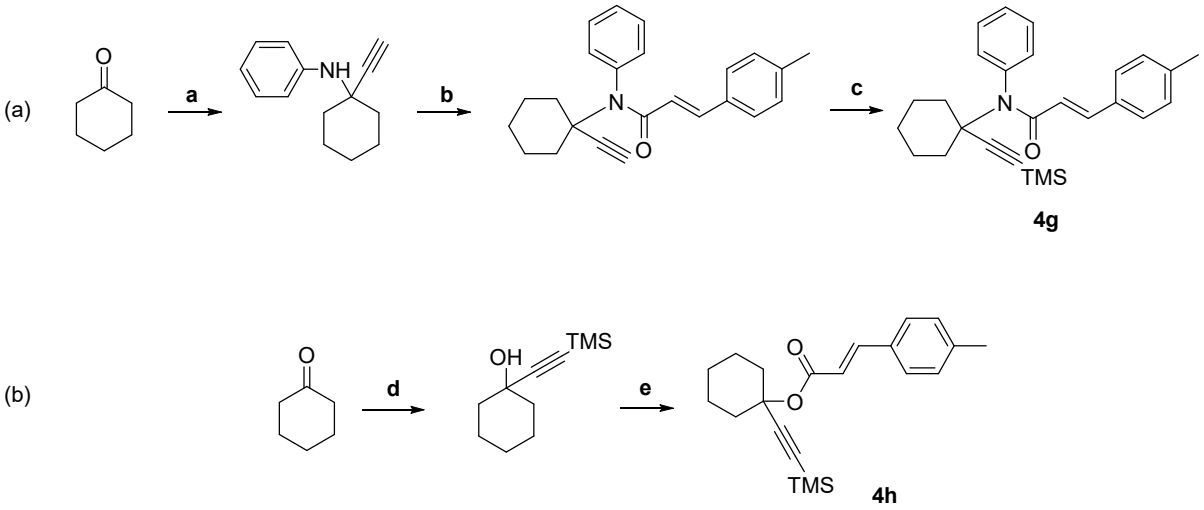
For intramolecular [2+2] cycloaddition reaction, enyne substrate with cinnamamide moiety were prepared through acyl chloride, which produced from carboxylic acid using oxalic acid (Scheme 32). Sonogashira reactions of 2-iodoaniline with alkynes produced o-alkynylaniline derivative. Enyne **4b** prepared by Chan-Lam Coupling from o-alkynylaniline with boronic acid, followed by amide coupling via acyl chloride (scheme 32a). And alkyl alkyne tethered enyne (**4f**) prepared amide coupling first and followed by ethylation. In case of synthesis of **4d**, both the desired product and isomerized products

were produced from amide coupling reaction (scheme (b). b). this isomerized product could convert under DBU condition to desired product, which was subjected to ethylation to afford to finally product **4d** (Scheme 32b). (*Z*)-3-phenylbut-2-enoic acid, which is carboxylic acid for 4d, was prepared from 3-phenylpropynoic acid by Gilman reagent through copper iodide and methyllithium (scheme 32a).



Scheme 32. Synthesis of Enyne substrates with cinnamamide moiety: a) Pd(PPh3)2Cl2, CuI, phenylacetylene, Et3N, 70°C, 88%, b) Phenylboronic acid, pyridine, Cu(OAc)2, O_2 (balloon), r.t., 81%, c) $(COCl)_2$, DMF (cat.), 4-methylcinnamic acid, K_2CO_3, CH_2Cl_2, d) Pd(PPh3)2Cl2, CuI, 1-Hexyne, Et3N, r.t., 83%, e) 4-methylcinnamic acid, $(COCl)_2$, DMAP, CH2Cl2, r.t., 50%, f) NaH, EtI, THF, 0°C to r.t., 99%, g) CuI, MeLi, Et_2O, -78°C to -20°C, 92%, h) $(COCl)_2$, DMAP, CH2Cl2, r.t., 50%, r.t., 75%, i) DBU, THF, reflux, 63%, j)) NaH, EtI, THF, 0°C to r.t., 67%

Enyne substrates with cinnamamide moiety followed by cyclohexyl derivatives were also synthesized to access the spirocyclic compounds (Scheme 33). cyclohexyl derivatives with cinnamamide moiety was prepared from cyclohexanone. The alkyne moiety was introduced by reacting trimethylsilylacetlyene with imine, which was formed by reaction with cyclohexanone and aniline with p-TSA as acid catalyst. Next, amide coupling with 4-methylcinnamic acid via acyl chloride, followed by silylation of terminal alkyne afforded desired product **4g**. In the other hand, cinnamyl etser moiety of cyclohexyl derivatives **4h** are introduced by ester coupling with DCC/DMAP condition from cyclohexyl alcohol, which prepared by addition of TMS alkyne to cyclohexanone.



Scheme 33. Synthesis of cyclohexyl derivatives : a) (i) aniline, p-TSA, toluene, 110°C, (ii) trimethylsilylacetlyene, ^{t}BuOK, DMSO, 40°C, 45%, b) (i) 4-methylcinnamic acid, DMF (cat.), CH2Cl2, 0°C to r.t., (ii)Et_3N, DMAP, 0°C, 83%, c) LiHMDS, chlorotrimethylsilane, THF, -78°C, 83%, d) Trimethylsilyacetylene, ^{n}BuLi, THF, -78°C to r.t., 94%, e) 4-methylcinnamic acid, DCC, DMAP, CH_2Cl_2, reflux, 65%

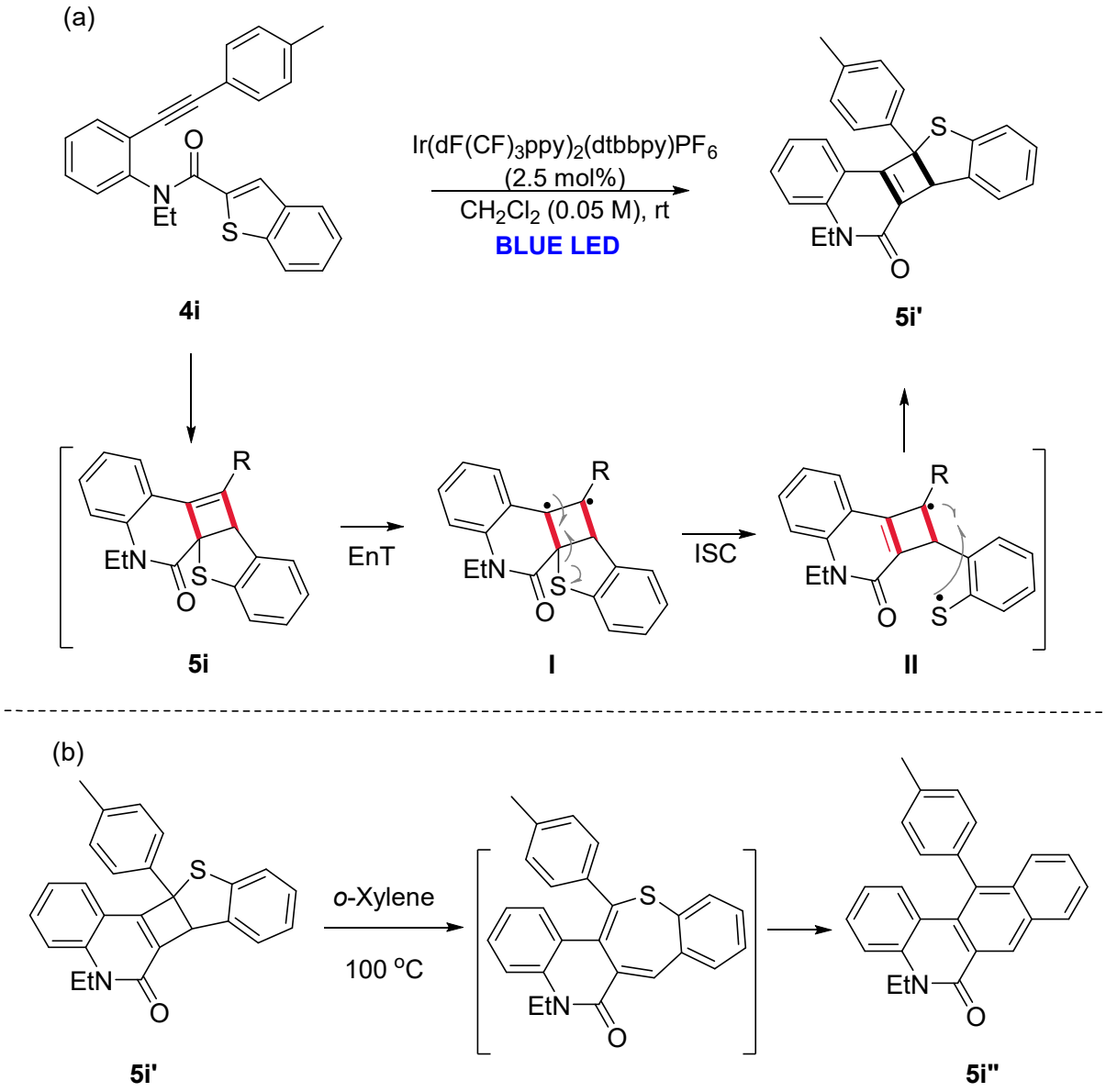
2.2. Application

Based on our synthesis method, further synthetic transformations to valuable structure were explored.

Extended π-systems

When enyne containing benzo[b]thiophene (**4i**) as an alkene counterpart was subjected to the reaction conditions, rearranged cyclobutene (**5i'**) was obtained in 99% yield instead of 1,3-diene. **5i'** is a polycyclic heteroaromatic compound, a valuable structure that can be used for various applications.[90] Mechanism of the rearrangement was assumed that excitation of the cyclobutene intermediate **5i** leads

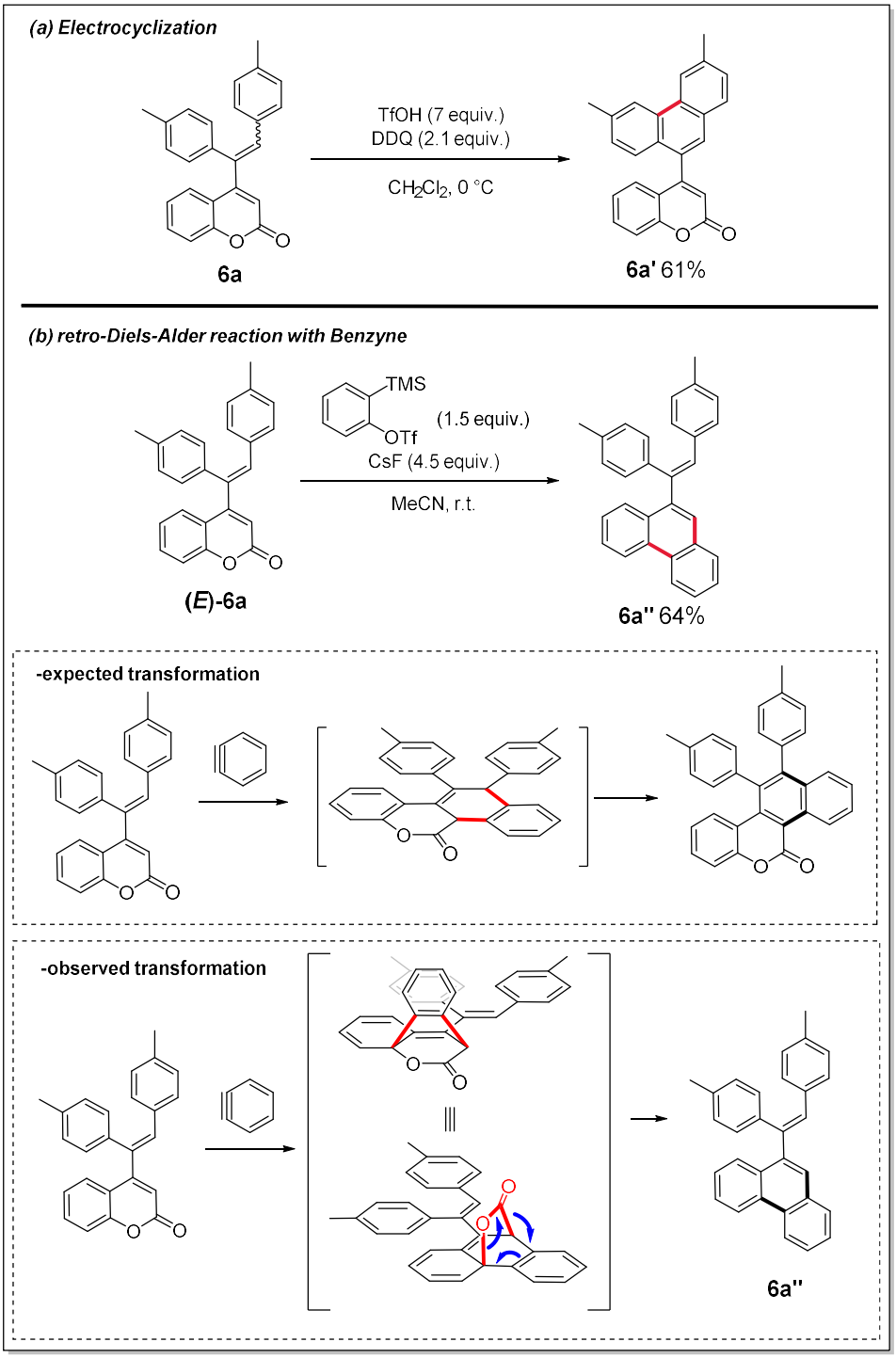
to the formation of 1,2-diradical **I**, which undergoes fragmentation to give 1,5-diradical **II** followed by recombination to give **5i'**. For further transformation, we heated up **5i'** in anticipation of ring expansion. When **5i'** was heated up at 100°C, thermal electrocyclic ring opening followed by sulfur extrusion occurred to give **5i''**, which was tetracyclic heteroaromatic hydrocarbon containing 2-quiolone core structure.



Scheme 34. Tandem cycloaddition followed by rearrangement of benzothiophenes

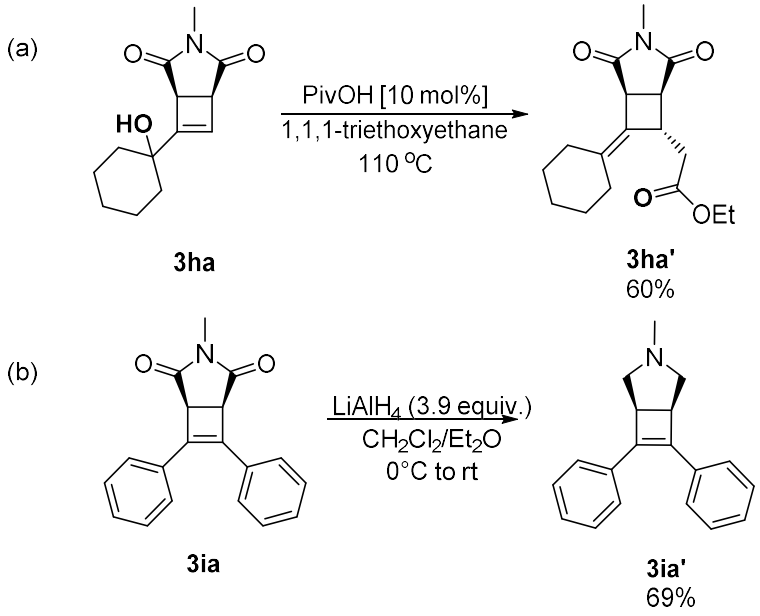
In order to access more various Extended π-systems, we tried various transformations to coumarin **6a** (Scheme 35). Electrocyclization was attempted under a number of conditions, and the reaction occurred when TfOH and DDQ were used, coumarin substituted with phenanthrene (**6a'**) was obtained

61% yield. And when Diels-Alder reaction was attempted to coumarin as diene with benzyne as dienophile. Initially expected, a diels-Alder reaction underwent the diene part of **6a** to yield tetracyclic heteroaromatic hydrocarbons. As a result of the reaction, it was confirmed that the retro-dies alder proceeded in diene part of coumarin to form the phenanthrene structure (**6a"**).



Scheme 35. Derivatization of coumarin

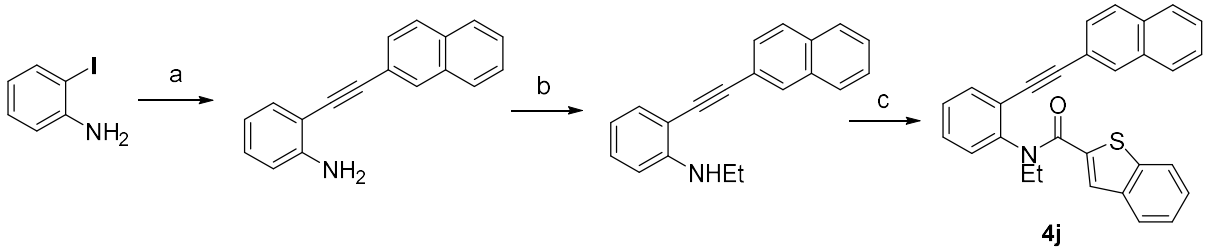
Also, Transformations from cyclobutenes were explored (Scheme 36). Exomethylene cyclobutane could be synthesized with allylic alcohol **3ha** by Johnson-Claisen rearrangement. In addition, pyrrolidine (**3ia'**) was prepared by reduction of succinimide moiety of cyclobutene.



Scheme 36. (a) Synthesis of exomethylene cyclobutane (b) Synthesis of pyrrolidine derivative

Substrate synthesis for application

To broaden the scope of Tandem cycloaddition followed by rearrangement of benzothiophenes (scheme 37), benzo[b]thiophene derivative with alkyne moiety having naphthyl group was prepared similar way to synthesis of **4g** except that the ethylation step was processed to aniline with ^{n}BuLi before amide coupling step.

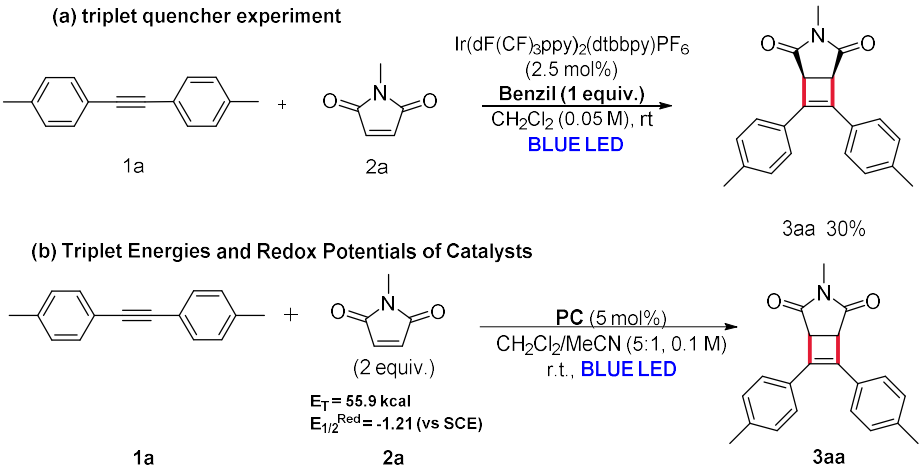


Scheme 37. synthesis of benzo[b]thiophene derivative: a) Pd(PPh3)2Cl2, CuI, 2-ethynylnaphthalene, Et3N, r.t.,b)EtI, ^{n}BuLi, THF, -78°C to r.t., 84%, c) benzo[b]thiophene-2-carboxylic acid, (COCl)2, DMAP, DCE, r.t., 65%,

2.3. Mechanism study

To get further insight into the mechanism of our chemistry, various mechanism study was conducted. First, in order to determine if the reaction proceeds with an energy transfer process, mechanism studies were conducted using the triplet quencher (Table 2a). we performed an experiment in the presence of triplet quencher benzil (53.4 kcal/mol) and found that the yield significantly decreased to 30%. To be more certain, the reaction proceeded with various photocatalysts (Table 2b). As a result, the yield of the reaction was shown to be related to the triplet energy of catalysts. On the other hand, there was no correlation with reduction potential. These results show our [2+2] cycloaddition of alkynes with alkene proceeds by energy transfer process.

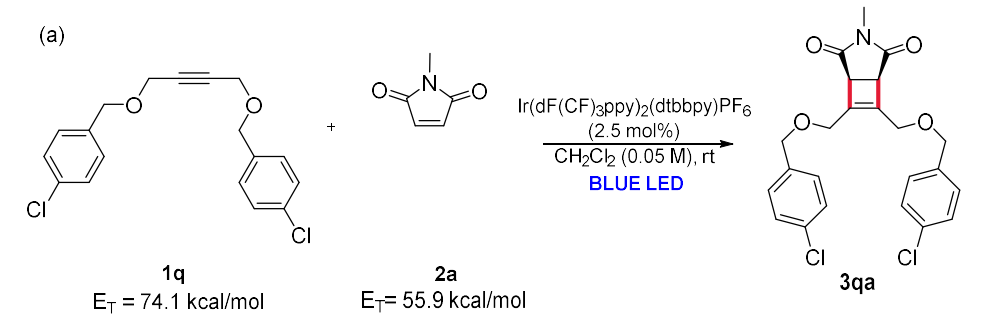
Table 2. (a) triplet quencher experminet (b) Triplet Energies and Redox Potentials of Catalysts[a]



Entry	Photocatalyst	$E_{1/2}^{red}$ / $E_{1/2}^{ox}$ (V)	E_T (kcal/mol)	Yield[b]
1	**Ir[dF(CF3)ppy]2(dtbbpy)PF6**	-0.89 / 1.21	60.8	76%
2	**Ir(dFppy)$_2$pic**	-1.23 / 1.40	60.5	74%
3	**Ir[dF(CF3)ppy]2(bpy)PF6**	-0.97 / 0.97	60.4	74%
4	**Ir[dFppy]2(dtbbpy)PF6**	-0.93 / 1.14	55.4	62%
5	**Ir(Fppy)2(dtbbpy)PF6**	-1.04 / 1.07	53.0	35%
6	**Ir(ppy)2(dtbbpy)PF6**	-0.96 / 0.66	49.2	trace
7	**Ru(bpy)$_3$(PF$_6$)$_2$**	-0.81 / 0.77	46.5	n.r.
8	**Rose Bengal**	-0.68 / 0.99	40.9	n.r.

[a] Reactions were performed with 0.05 mmol scale under Ar. [b] Yields determined by ^{1}H NMR spectroscopic analysis against an internal standard. (1,1,2-trichloroethene). *bpy = 2,2'-bipyridine; ppy = 2-phenylpyridine; n.r. = no reaction.

After confirming that the reaction is conducted with an energy transfer process, we explored which of activated part take part in reaction between alkene and alkyne by energy transfer process (Figure 12). When the reaction proceeded with **1q** as alkyne part which has triplet energy higher than photocatalyst, it was confirmed that the reaction proceeded smoothly. Also by the analysis of the Stern-Volmer experiments, no quenching of $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ by alkyne **1q** was observed, in the other hand, **2a** act as a quencher of $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$. This result suggests that the reaction proceeds as the alkene moiety is activated.



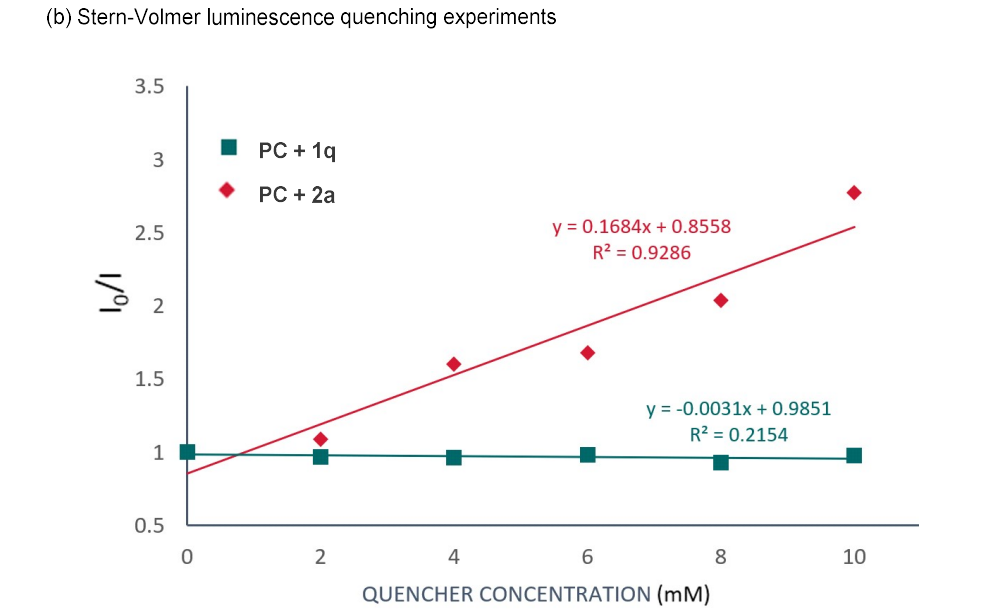
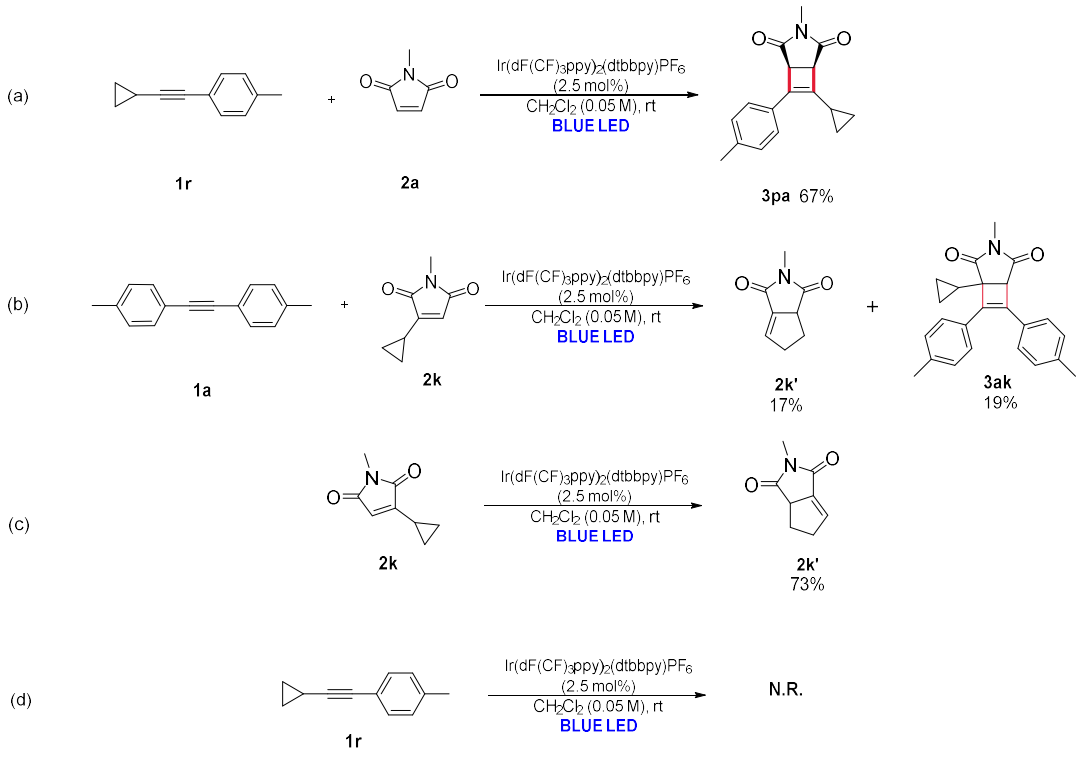


Figure 12. Mechanistic studies: (a) [2+2] cycloaddition of **1q** with **2a** (b) Stern-Volmer luminescence quenching experiments using a 0.1 mM solution of $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ and variable concentrations of substrate **1q** and **2a** in CH_2Cl_2**.**

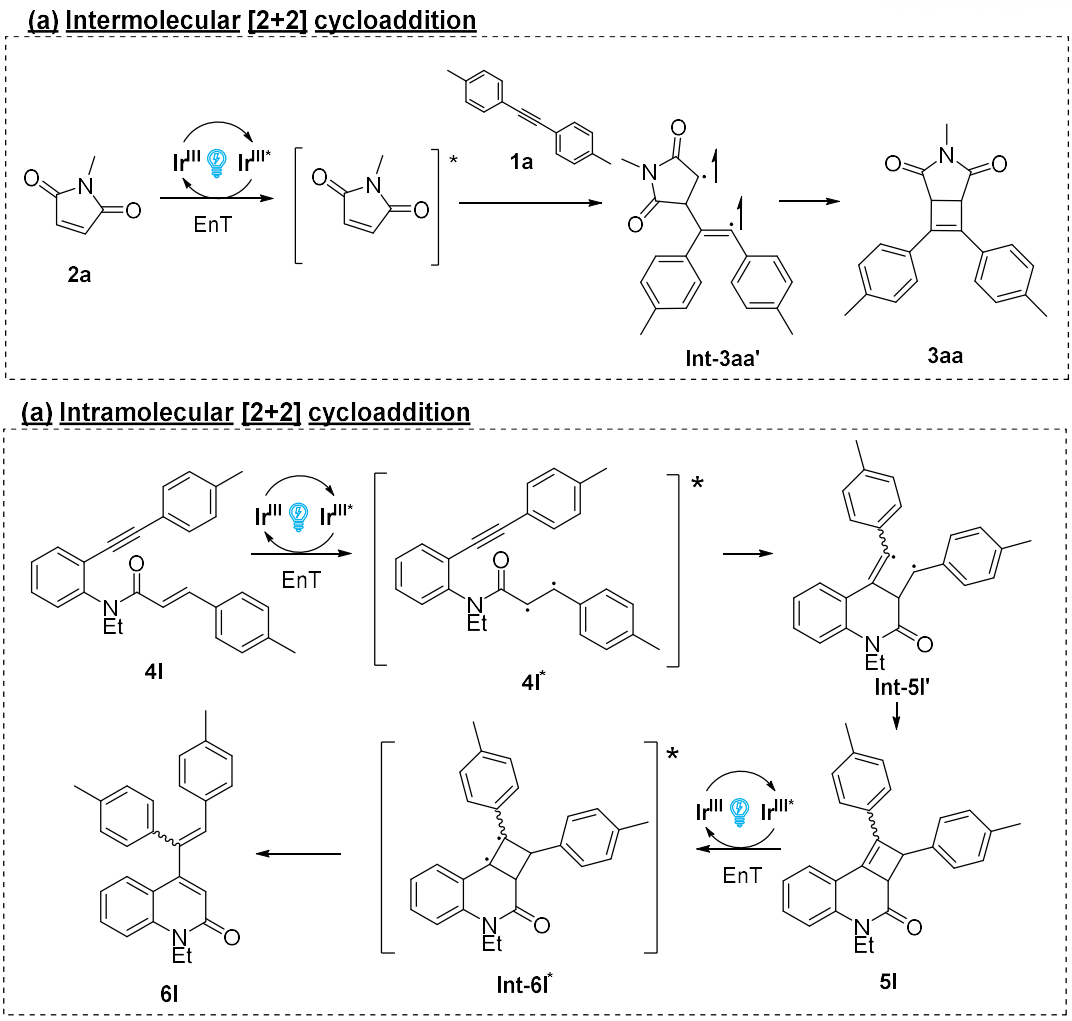
A radical clock study was conducted to find more convincing evidence (Scheme 38). When cyclopropyl alkyne (**1r**) was reacted with N-methyl maleimide (**2a**), cyclobutene with cyclopropyl group (**3ra**) was obtained not a ring opening form. but the reaction of cyclopropyl maleimide (**2k**) with

alkyne (**2a**) proceeded to give isomerization product (**2k'**) along with cycloadduct (**3ak**) was obtained in low yields. And when cyclopropyl maleimide (**2k**) alone was subjected to the optimized condition, cycloadduct (**2k'**) was obtained 73% yield. On the other hand, there was no reaction when cyclopropyl alkyne (**1r**) was subjected to the optimized condition. These results indicate reaction process by excited alkene between alkene and alkyne by energy transfer process



Scheme 38. Radical clock experiments.

Based on mechanism studies, proposed mechanism is demonstrated in scheme 39. First, Iridium photocatalyst excited to triplet state by irradiation of blue LED light. Excitation of 2a to its triplet excited state by the catalyst followed by the reaction with alkyne 1a leads to the formation of the triplet intermediate (**Int-3aa'**). And then cyclization of **Int-3aa'** produce the final cyclobutene product (**3aa**). The intramolecular [2+2] cycloaddition proceeds similarly to the intermolecular [2+2] cycloaddition. Cinnamyl moiety of **4l** are excited to triplet via energy transfer and reacts with alkyne moiety of **4l** to afford the triplet intermediate (**Int-5l'**), which cyclize to afford the cyclobutene intermediate (**5l**). Immediately this intermediate transform to triplet diradical state (**Int-6l***) through the photocatalyst. Rearrangement of the triplet diradical yields the final diene product (**6l**).



Scheme 39. Proposed mechanism

III. CONCULSION

In conclusion, we have developed alkyne-alkene [2+2] cycloaddition cycloaddition based on visible light EnT photocatalysis. Intermolecular/intramolecular [2+2] cycloadditions were performed by using Ir-catalyst as photocatalyst and blue LED light as irradiation source. In case of the intermolecular [2+2] cycloaddition, a broad range of alkynes reacted smoothly with electron-deficient alkenes to afford the corresponding cyclobutenes. In the other hand, in the intramolecular reaction, 1,3-diene structure was formed through the ring opening of cyclobutene intermediates via tandem triplet excitation. Various mechanism studies and computational studies were performed to investigate the mechanism of the reaction. In addition, the utility of the [2+2] cycloaddition has been demonstrated by the several synthetic transformations including synthesis of various extended π-systems.

IV. EXPERIMENTAL

4.1. General Information

All reactions were conducted under a nitrogen atmosphere with oven-dried glassware and standard Schlenk or vacuum line techniques. All solutions were handled under nitrogen or argon and transferred via syringe. Anhydrous solvents were purchased and stored over activated 4 Å molecular sieves. Unless otherwise stated, reagents were commercially available and used as purchased without further purification. Chemicals were purchased from Sigma-Aldrich, Acros, Alfa Aesar or TCI. Progress of reactions was monitored by thin-layer chromatography (TLC) using Merck 60 F254 precoated silica gel plate and visualized by short-wave ultraviolet light as well as by treatment with basic solution of potassium permanganate or acidic solution of ceric molybdate. Flash chromatography was performed with Silica Flash P60 silica gel (230 – 400 mesh). ^{1}H and ^{13}C NMR spectra were obtained using an Agilent 400-MR DD2 Fourier-transform NMR spectrometer at 400 and 100 MHz, respectively. Chemical shifts were reported in units of parts per million (ppm) downfield from tetramethylsilane (TMS), and all coupling constants were reported in hertz. The residual solvent signals were taken as the reference ($CDCl_3$ 7.26 ppm, DMSO-d_6 2.50 ppm and CD_3OD 3.31 ppm for ^{1}H NMR spectra and $CDCl_3$ 77.0 ppm, DMSO-d_6, 39.52 ppm, CD_3OD 49.00 ppm and CD_2Cl_2 53.84 ppm for ^{13}C NMR spectra). The signals observed are described as: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad signal). Mass analysis were carried out using Advion Expression CMS mass spectrometer and LC-ELSD analysis was carried out using Agilent 1260 Infinity ELSD coupled with Agilent 1220 HPLC. High resolution mass analysis was performed with JOEL AccuTOF 4G+ DART-HRMS and on Bruker, 1200 Series & HCT Basic System. Voltammetric measurements were proceeded using a Potentiostat (WizECM – 1200 Premium). Luminescence quenching studies were performed with Varian Cary Eclipse.

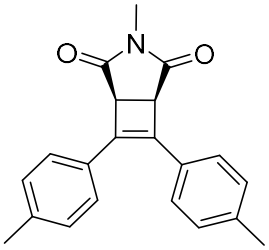
4.2. General procedure and characterization of Alkyne-Alkene [2+2] Cycloaddition

intermolecular Alkyne-Alkene [2+2] Cycloaddition

General procedure A **(for the synthesis of cyclobutenes)**

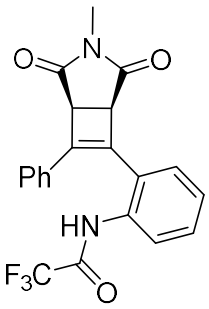
Alkyne (0.1 mmol, 1.0 equiv.), alkene (1.5 equiv.), and photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5 mol%) were added to an oven-dried 4 mL vial equipped with a stir bar. The combined materials were dissolved in CH_2Cl_2 (2 mL) under argon atmosphere in glovebox. The reaction mixture was then irradiated by 12 W blue LED strip 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 column chromatography on silica gel to give the desired product.

3-methyl-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (3aa)



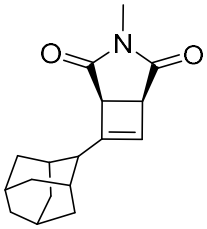
Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **1a** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **2a** (1.5 equiv.), 24 mg, 76% yield; white solid; m.p. 134 – 135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.2 Hz, 4H), 7.18 (d, *J* = 7.9 Hz, 4H), 4.06 (s, 2H), 2.97 (s, 3H), 2.37 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 139.2, 138.3, 130.3, 129.3, 126.8, 44.9, 24.8, 21.4; HRMS *m/z* calculated for $[C_{21}H_{20}NO_2]^+$ ($[M+H]^+$): 318.1489, observed : 318.1490

3-methyl-6-phenyl-7-(2-((trifluoromethoxy)amino)phenyl)-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (3ba)



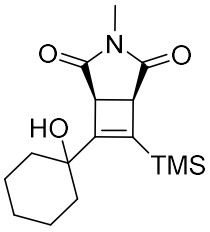
Prepared according to the ***General Procedure A*** using 2,2,2-trifluoro-*N*-(2-(phenylethynyl)phenyl)acetamide **1b** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **2a** (1.5 equiv.), 35 mg, 88% yield; yellow viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) 8.38 (s, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.51 – 7.41 (m, 3H), 7.40 – 7.35 (m, 3H), 7.32 (t, *J* = 7.6 Hz, 1H), 4.21 (d, *J* = 3.5 Hz, 1H), 4.15 (d, *J* = 3.5 Hz, 1H), 3.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ175.3, 174.0, 143.0, 134.6, 131.7, 131.5, 130.31, 130.26, 129.0, 128.7, 127.0, 125.91, 125.90, 124.2, 46.2, 45.6, 25.1; HRMS *m/z* calculated for $[C_{21}H_{15}F_3N_2NaO_3]^+$ ($[M+Na]^+$): 423.0927, observed : 423.0932.

6-((1*r*,3*r*,5*r*,7*r*)-adamantan-2-yl)-3-methyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (3ca)



Prepared according to the ***General Procedure A*** using (3*r*,5*r*,7*r*)-1-ethynyladamantane **1c** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **2a** (1.5 equiv.), 13 mg, 48% yield; white solid; m.p. 138-139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97 (d, *J* = 0.9 Hz, 1H), 3.76 (d, *J* = 3.2 Hz, 1H), 3.55 (dd, *J* = 3.2, 1.1 Hz, 1H), 2.95 (s, 3H), 2.00 (s, 3H), 1.77 – 1.62 (m, 12H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 175.4, 162.1, 125.8, 46.2, 43.1, 39.6, 36.5, 36.1, 27.8, 24.8; HRMS *m/z* calculated for $[C_{17}H_{22}NO_2]^+$ ($[M+H]^+$): 272.1645, observed 272.1645.

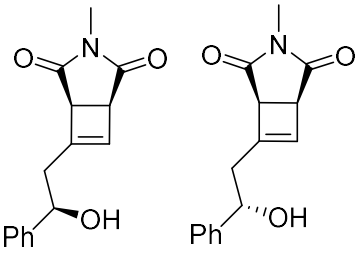
6-(1-hydroxycyclohexyl)-3-methyl-7-(trimethylsilyl)-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (3da)



Prepared according to the ***General Procedure A*** using 1-((trimethylsilyl)ethynyl)cyclohexan-1-ol **1d** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **2a** (1.5 equiv.), 29 mg, 94% yield; white solid; m.p. 89 – 91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (d, *J* = 3.2 Hz, 1H), 3.48 (d, *J* = 3.2 Hz, 1H), 2.95 (s, 3H), 1.72 – 1.49 (m, 9H), 1.30 – 1.16 (m, 1H), 0.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 175.8,

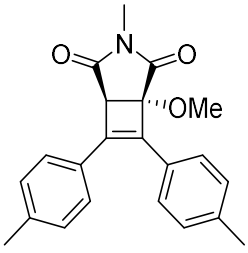
168.0, 146.2, 72.7, 47.1, 43.8, 36.4, 36.0, 25.2, 25.0, 21.24, 21.18, -0.4; HRMS *m/z* calculated for $[C_{16}H_{26}NO_3Si]^+$ ($[M+H]^+$): 308.1676, observed 308.1679.

6-(2-hydroxy-2-phenylethyl)-3-methyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (3ea)



Prepared according to the ***General Procedure A*** using 1-phenylbut-3-yn-1-ol **1e** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **2a** (1.5 equiv.), 20 mg, 78% yield (d.r. = 1:1); pale yellow solid; m.p. 104 – 106 °C; The NMR spectrum was obtained on a partially purified material as a mixture of diastereomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.34 (m, 6.13H), 7.31 – 7.28 (m, 1.28H), 6.17 (d, *J* = 1.4 Hz, 1H), 6.14 (d, *J* = 1.4 Hz, 0.5H), 4.98 (dt, *J* = 7.9, 3.7 Hz, 1H), 4.89 (dt, *J* = 8.1, 3.9 Hz, 0.5H), 3.78 (d, *J* = 3.0 Hz, 0.5H), 3.74 (d, *J* = 2.8 Hz, 1H), 3.64 (m, 1.5H), 3.01 (d, *J* = 3.7 Hz, 0.5H), 2.96 (s, 1.5H), 2.91 (s, 3H), 2.73 – 2.57 (m, 3.4H), 2.39 (d, *J* = 4.1 Hz, 1H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 175.8, 175.5, 175.4, 150.5, 150.5, 143.5, 143.5, 132.4, 132.2, 128.7, 128.7, 128.0, 128.0, 125.8, 125.8, 71.8, 71.7, 49.2, 48.9, 44.7, 44.6, 39.9, 39.5, 25.0, 24.9; HRMS *m/z* calculated for $[C_{15}H_{15}NNaO_3]^+$ ($[M+Na]^+$): 280.0944, observed : 280.0944

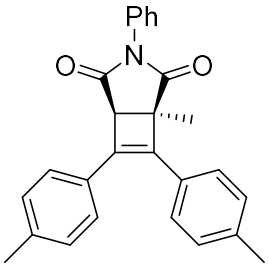
1-methoxy-3-methyl-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (3ab)



Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **1a** (0.1 mmol, 1.0 equiv.) and 3-methoxy-1-methyl-1*H*-pyrrole-2,5-dione **2b** (1.5 equiv.), 34 mg, 98% yield; white solid; m.p. 152 – 154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 8.2 Hz, 4H), 4.11 (s, 1H), 3.42 (s, 3H), 2.99 (s, 3H), 2.37 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

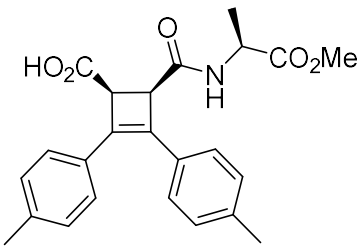
174.0, 173.5, 140.1, 139.4, 139.3, 138.7, 129.4, 129.4, 129.3, 128.9, 127.3, 127.1, 81.7, 53.4, 49.1, 24.7, 21.49, 21.48; HRMS *m/z* calculated for $[C_{22}H_{22}NO_3]^+$ ($[M+H]^+$): 348.1594, observed 348.1595.

1-methyl-3-phenyl-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (3ac)

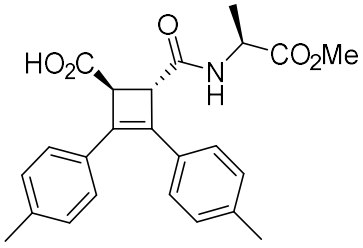


Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **1a** (0.1 mmol, 1.0 equiv.) and 3-methyl-1-phenyl-1*H*-pyrrole-2,5-dione **2c** (1.5 equiv.), 39 mg, 99% yield; white solid; m.p. 210 – 211 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (t, *J* = 8.0 Hz, 4H), 7.47 – 7.31 (m, 3H), 7.27 (d, *J* = 8.6 Hz, 2H), 7.23 – 7.14 (m, 4H), 3.94 (s, 1H), 2.39 (s, 3H), 2.37 (s, 3H), 1.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 173.6, 142.1, 139.3, 139.0, 137.2, 132.1, 129.8, 129.7, 129.4, 129.3, 128.9, 128.3, 127.3, 126.9, 126.6, 51.3, 50.6, 21.48, 21.47, 15.8; HRMS *m/z* calculated for $[C_{27}H_{24}NO_2]^+$ ($[M+H]^+$): 394.1802, observed 394.1807.

4-(((*S*)-1-methoxy-1-oxopropan-2-yl)carbamoyl)-2,3-di-*p*-tolylcyclobut-2-ene-1-carboxylic acid (3ad)



***cis*-3au**

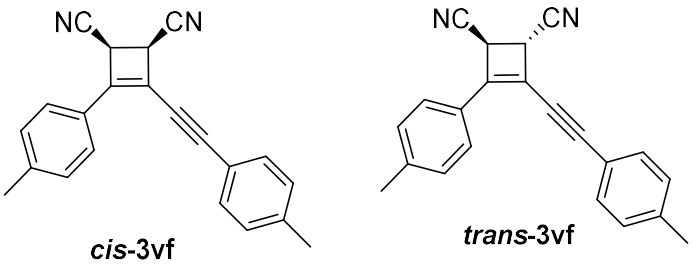


***trans*-3au**

Prepared according to the ***General Procedure A*** using di(*p*-tolyl)acetylene **1a** (0.1 mmol, 1.0 equiv.) and (*S,Z*)-4-((1-methoxy-1-oxopropan-2-yl)amino)-4-oxobut-2-enoic acid **2d** (1.5 equiv.), 38 mg, 93% yield (*cis*/*trans* 4.4:1); The NMR spectrum was obtained on a partially purified material as a mixture of diastereomers; **(*cis*-3ad) (d.r. 1:1) :** white solid; m.p. 168 – 169 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ

8.63 (d, *J* = 6.9 Hz, 0.5H), 8.50 (d, *J* = 7.7 Hz, 0.5H), 7.44 – 7.27 (m, 4H), 7.19 – 7.10 (m, 4H), 4.29 (td, *J* = 7.3, 5.4 Hz, 1H), 4.11 – 4.01 (m, 2H), 3.61 (s, 1.5H), 3.59 (s, 1.5H), 2.29 (s, 3H), 2.28 (s, 3H), 1.29 (d, *J* = 7.3 Hz, 1.5H), 1.25 (d, *J* = 7.1 Hz, 1.5H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.5, 173.1, 171.8, 171.7, 170.1, 169.7, 138.4, 138.2, 138.12, 138.07, 137.8, 137.7, 137.6, 137.4, 131.92, 131.86, 131.60, 131.57, 129.5, 129.4, 129.22, 129.20, 127.2, 127.1, 126.48, 126.45, 52.3, 52.2, 48.11, 48.02, 47.97, 47.9, 45.5, 45.4, 21.4, 21.3, 17.8, 17.5.; HRMS m/z calculated for $[C_{24}H_{25}NNaO_5]^+$ ([M+Na]$^+$) : 430.1625, observed 430.1626; **(*trans*-3ad) (d.r. 1.5:1)** : white solid; m.p. 190 – 192 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.75 (t, *J* = 8.7 Hz, 1H), 7.42-7.36 (m, 4H), 7.19 (t, *J* = 7.5 Hz, 4H), 4.29 (dp, *J* = 14.5, 7.2 Hz, 1H), 3.98 (d, *J* = 1.9 Hz, 0.6H), 3.91 (d, *J* = 1.8 Hz, 0.4H), 3.77 (d, *J* = 1.8 Hz, 0.6H), 3.72 (d, *J* = 1.8 Hz, 0.4H), 3.61 (s, 1.8H), 3.52 (s, 1.2H), 2.31 (s, 3.6H), 2.30 (s, 2.4H), 1.31 (d, *J* = 7.3 Hz, 1.2H), 1.24 (d, *J* = 7.2 Hz, 1.8H) ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.5, 173.4, 173.35, 173.26, 170.4, 170.3, 138.83, 138.80, 138.4, 138.33, 138.33, 138.30, 138.0, 137.9, 131.3, 131.15, 131.13, 131.13, 129.6, 129.6, 129.5, 129.4, 126.53, 126.49, 126.46, 126.4, 52.3, 52.2, 48.2, 48.0, 46.8, 46.7, 46.0, 45.6, 40.6, 21.39, 21.38, 17.6, 17.4; HRMS m/z calculated for $[C_{24}H_{25}NNaO_5]^+$ ([M+Na]$^+$) : 430.1625, observed 430.1625.

3-(*p*-tolyl)-4-(*p*-tolylethynyl)cyclobut-3-ene-1,2-dicarbonitrile (3fe)

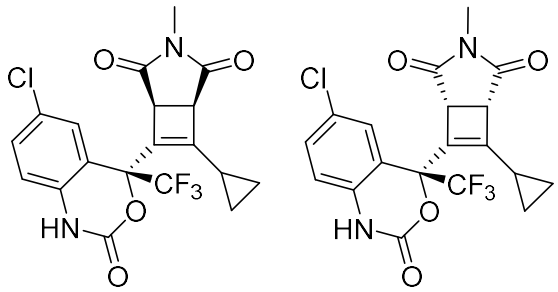


cis-3vf *trans*-3vf

Prepared according to the ***General Procedure A*** using 1,4-di-*p*-tolylbuta-1,3-diyne **1f** (0.1 mmol, 1.0 equiv.) and fumaronitrile (1.5 equiv.), 16 mg, 51% yield, (*cis*/*trans* 1.3:1); **(*cis*-3fe)**: yellow solid; m.p. 163 – 164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.1 Hz, 2H), 7.45 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.21 (d, *J* = 7.9 Hz, 2H), 4.23 (d, *J* = 5.1 Hz, 1H), 4.17 (d, *J* = 5.1 Hz, 1H), 2.41 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 141.5, 140.3, 131.9, 129.7, 129.4, 127.8, 125.9, 118.2, 115.2, 115.1, 114.7, 99.8, 81.0, 33.9, 31.3, 21.71, 21.67; HRMS *m/z* calculated for $[C_{22}H_{16}N_2Na]^+$ ([M+Na]$^+$): 331.1206, observed 331.1206; **(*trans*-3fe)**: yellow solid; m.p. 57 – 58 °C; ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.61 (d, *J* = 8.1 Hz, 2H), 7.45 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 7.9 Hz, 2H), 4.11 (d, *J* = 2.4 Hz, 1H), 4.07 (d, *J* = 2.3 Hz, 1H), 2.41 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 141.6, 140.4, 131.9, 129.8, 129.4, 127.7, 125.9, 118.2, 115.92,

115.90, 114.7, 99.9, 80.9, 34.1, 31.4, 21.71, 21.67; HRMS *m/z* calculated for $[C_{22}H_{16}N_2Na]^+$ ($[M+Na]^+$): 331.1206, observed 331.1206.

6-(6-chloro-2-oxo-4-(trifluoromethyl)-1,4-dihydro-2*H*-benzo[*d*][1,3]oxazin-4-yl)-7-cyclopropyl-3-methyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (3ga)



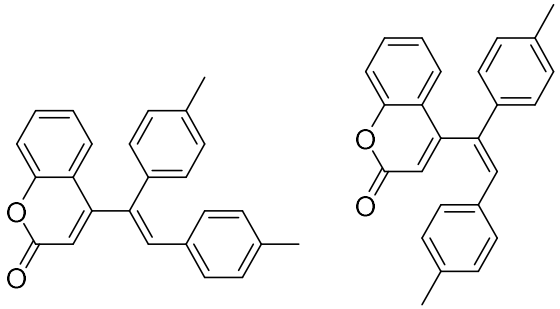
Prepared according to the ***General Procedure A*** using Efavirenz **1g** (0.1 mmol, 1.0 equiv.) and *N*-methylmaleimide **2a** (15.0 equiv.), 19 mg, 45% yield (d.r. = 2.3:1); yellow viscous oil; The NMR spectrum was obtained on a partially purified material as a mixture of diastereomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (s, 1H), 7.39 – 7.35 (m, 1.3H), 7.34 (d, *J* = 2.2 Hz, 0.3H), 7.29 (s, 0.3H), 6.89 (dd, *J* = 8.5, 1.3 Hz, 0.3H), 6.85 (d, *J* = 8.4 Hz, 0.7H), 3.69 (d, *J* = 3.4 Hz, 0.7H), 3.56 (d, *J* = 3.5 Hz, 0.3H), 3.48 (d, *J* = 3.4 Hz, 0.3H), 3.45 (d, *J* = 3.4 Hz, 0.7H), 2.92 (s, 0.9H), 2.90 (s, 2.1H), 1.82 – 1.66 (m, 2H), 1.34 – 1.20 (m, 1H), 1.05 – 0.80 (m, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) 173.6, 173.2, 173.2, 173.0, 155.3, 154.3, 148.5, 148.3, 134.1, 133.9, 131.6, 131.5, 130.9, 130.4, 129.2, 128.9, 126.8, 126.6, 116.7, 116.6, 114.1, 114.0, 77.3, 77.2, 43.7, 43.6, 43.0, 42.9, 25.1, 24.9, 10.8, 10.6, 7.9, 7.6, 7.0, 6.9.; HRMS *m/z* calculated for $[C_{19}H_{14}ClF_3N_2NaO_4]^+$ ($[M+Na]^+$): 449.0486, observed 449.0485.

Intermolecular Alkyne-Alkene [2+2] Cycloaddition

General Procedure B (for the synthesis of 1,3-diene)

Enyne (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 4 mL vial equipped with a stir bar. The combined materials were dissolved in CH_2Cl_2 (2 mL) under argon atmosphere in glovebox. The reaction mixture was then irradiated by 12 W blue LED strip 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 column chromatography on silica gel to give the desired product.

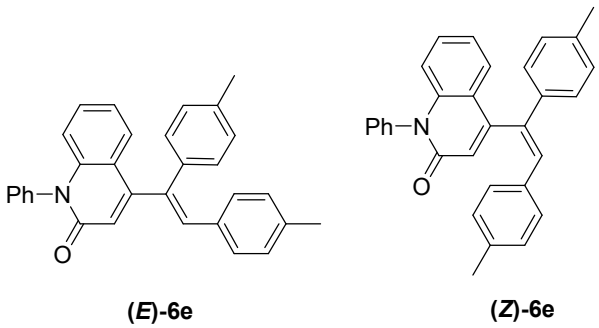
4-(1,2-di-*p*-tolylvinyl)-2*H*-chromen-2-one (6a)



(*E*)-6a (*Z*)-6a

Prepared according to the ***General Procedure B*** using 2-(*p*-tolylethynyl)phenyl *(E)*-3-(*p*-tolyl)acrylate **4a** (0.1 mmol, 1.0 equiv.), 26 mg, 73% yield, (*E/Z* 1:1); ***(E)*-6a**: pale yellow solid; m.p. 144 – 146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.45 (ddd, *J* = 8.7, 7.3, 1.6 Hz, 1H), 7.34 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.16 – 7.06 (m, 7H), 7.03 (d, *J* = 8.2 Hz, 2H), 6.83 (s, 1H), 6.41 (s, 1H), 2.33 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 157.8, 154.2, 138.3, 138.2, 136.2, 135.0, 133.0, 132.8, 131.6, 129.8, 129.8, 129.4, 129.1, 127.3, 124.1, 119.2, 117.3, 115.7, 21.45, 21.45; HRMS m/z calculated for $[C_{25}H_{21}O_2]$+ ($[M+H]^+$): 353.1536, observed : 353.1536; **(*Z*)-6a** : pale yellow solid; m.p. 76 – 77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (t, *J* = 7.8 Hz, 1H), 7.47 – 7.36 (m, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.23 (s, 1H), 7.15 (d, *J* = 8.4 Hz, 2H), 7.14 – 7.09 (m, 1H), 7.05 (d, *J* = 8.1 Hz, 2H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.35 (s, 1H), 2.35 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 160.9, 155.5, 154.3, 138.4, 138.1, 137.2, 134.6, 133.0, 132.1, 130.9, 129.7, 129.4, 128.9, 127.1, 126.3, 124.7, 119.2, 117.4, 117.2, 21.32, 21.28; HRMS m/z calculated for $[C_{25}H_{21}O_2]^+$ ($[M+H]^+$): 353.1536, observed : 353.1536

4-(1,2-di-*p*-tolylvinyl)-1-phenylquinolin-2(1*H*)-one (6b)

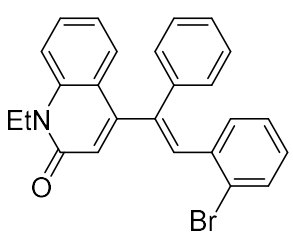


(*E*)-6e (*Z*)-6e

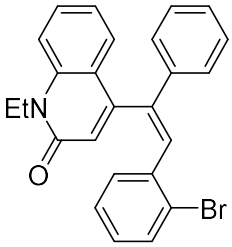
Prepared according to the ***General Procedure B*** using *(E)*-*N*-phenyl-3-(*p*-tolyl)-*N*-(2-(*p*-tolylethynyl)phenyl)acrylamide **4b** (0.1 mmol, 1.0 equiv.), 40 mg, 94% yield (*E/Z* 1.5:1); ***(E)*-6e** : white

solid; m.p. 142 – 144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 1H), 7.62 (m, 2H), 7.53 (m, 1H), 7.33 (d, *J* = 7.6 Hz, 2H), 7.29 – 7.21 (m, 3H), 7.10 (t, *J* = 7.4 Hz, 4H), 7.05 (t, *J* = 8.1 Hz, 3H), 6.83 (s, 2H), 6.67 (d, *J* = 8.5 Hz, 1H), 2.34 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 153.8, 141.4, 137.8, 137.7, 137.5, 137.5, 135.8, 133.4, 131.7, 130.2, 129.9, 129.5, 129.5, 129.3, 128.9, 128.9, 128.9, 127.4, 122.0, 122.0, 120.1, 116.3, 21.3, 21.3; HRMS *m/z* calculated for $[C_{31}H_{26}NO]^+$ ([M+H]$^+$): 428.2009, observed 428.2009; **(*Z*)-6e** : white solid; m.p. 144 – 146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.51 (m, 4H), 7.40 – 7.34 (m, 4H), 7.28 (ddd, *J* = 8.7, 7.1, 1.5 Hz, 1H), 7.24 (s, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.1 Hz, 2H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.71 (m, 2H), 2.36 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 150.8, 141.4, 137.9, 137.9, 137.7, 137.5, 136.0, 133.3, 130.2, 130.2, 130.2, 130.1, 129.4, 129.1, 129.1, 129.0, 128.9, 128.8, 127.2, 126.2, 123.0, 122.5, 120.1, 116.3, 21.2, 21.1.; HRMS *m/z* calculated for $[C_{31}H_{26}NO]^+$ ([M+H]$^+$): 428.2009, observed 428.2009.

4-(2-(2-bromophenyl)-1-phenylvinyl)-1-ethylquinolin-2(1*H*)-one (6c)



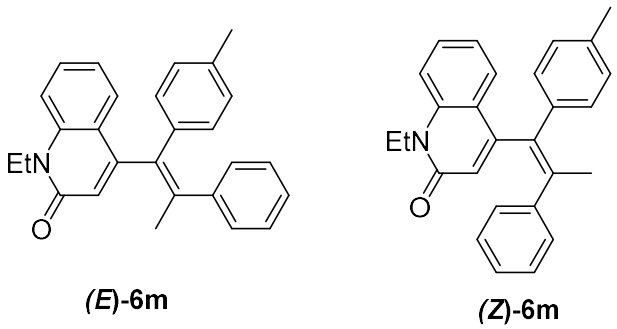
(*E*)-6d



(*Z*)-6d

Prepared according to the ***General Procedure B*** using *(E)*-3-(2-bromophenyl)-*N*-ethyl-*N*-(2-(phenylethynyl)phenyl)acrylamide **4c** (0.1 mmol, 1.0 equiv.). 32 mg, 74% yield (*E/Z* 1.8:1); yellow solid; The NMR spectrum was obtained on a partially purified material as a mixture of *E/Z* isomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 8.1, 1.3 Hz, 0.35H), 7.59 (t, *J* = 7.1 Hz, 1H), 7.54 – 7.48 (m, 1.35H), 7.46 – 7.30 (m, 3.35H), 7.20 – 7.13 (m, 3H), 7.11 – 7.00 (m, 3H), 7.01 – 6.92 (m, 0.65H), 6.93 – 6.87 (m, 0.35H), 6.87 (s, 0.65H), 6.83 (s, 0.65H), 6.63 (s, 0.35H), 4.50 – 4.25 (m, 2H), 1.40 (m, 1.45 –1.35, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 161.4, 151.7, 148.5, 140.1, 140.0, 139.3, 139.1, 139.0, 137.7, 137.2, 136.6, 132.59, 132.55, 131.4, 131.3, 130.6, 130.4, 130.3, 129.6, 129.3, 129.0, 128.9, 128.7, 128.5, 128.4, 127.99, 127.98, 127.8, 126.94, 126.93, 126.7, 124.7, 124.6, 123.2, 122.1, 122.0, 121.8, 120.7, 120.5, 114.4, 114.3, 37.4, 37.4, 12.9, 12.8; HRMS m/z calculated for $[C_{25}H_{21}BrNO]^+$ ([M+H]$^+$): 430.0801, observed 430.0799.

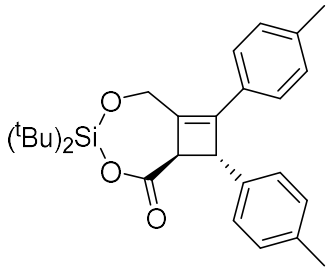
1-ethyl-4-(2-phenyl-1-(*p*-tolyl)prop-1-en-1-yl)quinolin-2(1*H*)-one (6d)



(*E*)-6m (*Z*)-6m

Prepared according to the ***General Procedure B*** using (*E*)-*N*-ethyl-3-(*p*-tolyl)-*N*-(2-(*p*-tolylethynyl)phenyl)but-2-enamide **4d** (0.1 mmol, 1.0 equiv.), 16 mg, 43% yield (*E/Z* = 1.2:1); yellow solid; m.p. 86 – 88 °C; The NMR spectrum was obtained on a partially purified material as a mixture of *E/Z* isomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.9 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 0.6H), 7.46 – 7.37 (m, 1H), 7.34 – 7.02 (m, 8H), 6.92 (d, *J* = 8.0 Hz, 1.2H), 6.84 (d, *J* = 8.0 Hz, 1.2H), 6.75 (s, 0.6H), 6.49 (s, 0.4H), 4.50 – 4.29 (m, 1.6H), 4.14 (dq, *J* = 14.1, 7.1 Hz, 0.4H), 2.32 (s, 1.2H), 2.27 (s, 1.2H), 2.17 (s, 1.8H), 2.02 (s, 1.8H), 1.41 (t, *J* = 7.1 Hz, 1.8H), 1.26 (t, *J* = 7.1 Hz, 1.2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 161.6, 152.0, 151.8, 143.1, 142.6, 139.4, 139.1, 138.9, 137.8, 137.4, 137.00, 136.97, 136.2, 134.4, 133.7, 130.5, 130.0, 129.6, 129.1, 129.05, 129.01, 128.6, 128.1, 128.08, 128.04, 127.6, 127.4, 126.8, 126.8, 122.9, 122.0, 121.6, 121.5, 121.2, 120.5, 114.4, 114.1, 37.4, 37.0, 23.4, 22.8, 21.2, 21.0, 12.9, 12.8; HRMS m/z calculated for $[C_{27}H_{26}NO]^+$ ($[M+H]^+$): 380.2009, observed

4,4-di-*tert*-butyl-8,9-di-*p*-tolyl-3,5-dioxa-4-silabicyclo[5.2.0]no*N*-7-en-2-one (5e)



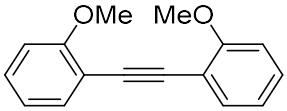
Prepared according to the ***General Procedure B*** using di-*tert*-butyl((3-(*p*-tolyl)prop-2-yn-1-yl)oxy)silyl (*E*)-3-(*p*-tolyl)acrylate **4e** (0.1 mmol, 1.0 equiv.), 28 mg, 62% yield; white solid; m.p. 68 – 70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.0 Hz, 2H), 7.14 – 7.05 (m, 4H), 7.02 (d, *J* = 8.1 Hz, 2H), 5.22 (dt, *J* = 15.8, 1.8 Hz, 1H), 4.95 (dt, *J* = 15.9, 2.3 Hz, 1H), 4.45 (d, *J* = 2.1 Hz, 1H), 3.61 (d, *J* = 1.7 Hz,

2H), 2.32 (s, 3H), 2.31 (s, 3H), 1.07 (s, 9H), 1.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 69.0, 142.2, 138.2, 137.0, 136.5, 133.9, 130.1, 129.3, 129.3, 127.1, 127.0, 62.5, 56.1, 48.7, 27.3, 27.0, 21.3, 21.1, 21.0.. HRMS *m/z* calculated for $[C_{28}H_{37}O_3Si]^+$ ($[M+H]^+$): 449.2506, observed 449.2506.

4.3. Synthesis of substrates

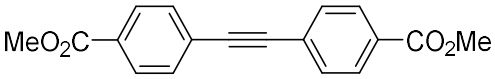
Preparation and characterization of substrates for intermolecular reaction

1,2-bis(2-methoxyphenyl)ethyne (1h)



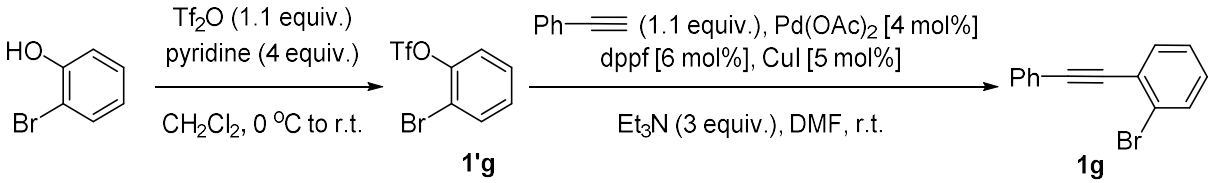
To a suspension of Pd(OAc)2 (5 mol%), CuI (10 mol%), and triphenylphosphine (10 mol%) in degassed MeCN (2.5 mL, 0.4 M) was added Et3N (3.0 equiv.), 1-iodo-2-methoxybenzene (1.0 mmol, 1.0 equiv.), and calcium carbide (3.0 equiv.) under nitrogen atmosphere. The reaction mixture was stirred at r.t. for overnight. The reaction mixture was filtered through a pad of Celite®, and concentrated. The crude material was purified by flash chromatography. 97% yield; white solid; 1H NMR (400 MHz, CDCl3) δ 7.52 (dd, J = 7.6, 1.7 Hz, 2H), 7.29 (ddd, J = 8.4, 7.4, 1.8 Hz, 2H), 6.93 (td, J = 7.5, 0.9 Hz, 2H), 6.91 (d, J= 8.4 Hz, 2H), 3.93 (s, 6H); The compound was identified by spectral comparison with literature data.

Dimethyl 4,4'-(ethyne-1,2-diyl)dibenzoate (1i)

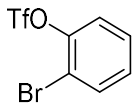


To solution of methyl 4-bromobenzoate (0.5 mmol, 1.0 equiv.), methyl 4-ethynylbenzonate (1.0 equiv.) and piperidine (5.0 equiv.) in degassed acetonitrile (1.4 mL, 0.35 M) was added $Ph(PPh_3)_4$ (2 mol%) under nitrogen atmosphere. The reaction mixture was stirred at 85 °C for 3 hours. The reaction mixture was filtered through a pad of Celite®, and concentrated. The crude material was purified by flash chromatography. 84% yield; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.6 Hz, 4H), 7.61 (d, *J* = 8.5 Hz, 4H), 3.94 (s, 6H); The compound was identified by spectral comparison with literature data.[91]

Synthesis of 1-bromo-2-(phenylethynyl)benzene (1j)

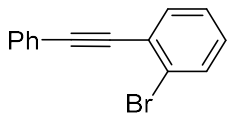


2-bromophenyl trifluoromethanesulfonate (1′j)



To a suspension of 2-bromophenol (1.0 mmol, 1.0 equiv.) in CH_2Cl_2 (3 mL, 0.3 M) was added pyridine (4.0 equiv.). Then the reaction mixture was cooled to 0 ºC and Trifluoromethanesulfonic anhydride (1.1 equiv.) was added dropwise. The reaction mixture was slowly warmed up to room temperature. and stirred at room temperature for 4 hours. The reaction mixture was washed 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. 98% yield; colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, J = 8.0, 1.6 Hz, 1H), 7.44 – 7.33 (m, 2H), 7.30 – 7.23 (m, 1H); The compound was identified by spectral comparison with literature data.[92]

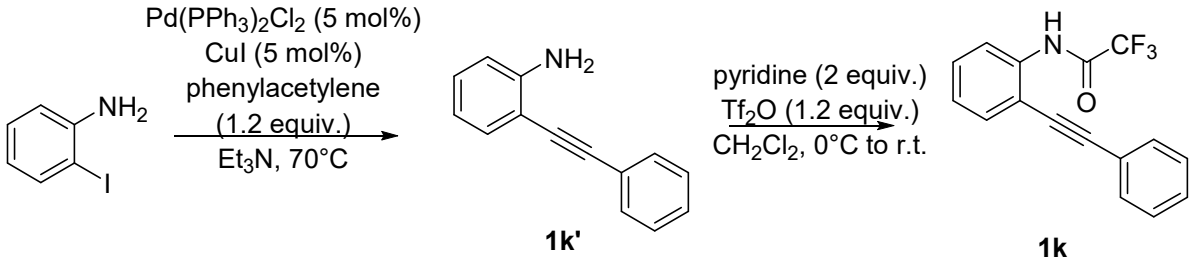
1-bromo-2-(phenylethynyl)benzene (1j)



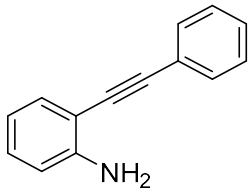
To a suspension of $Pd(OAc)_2$ (4 mol%), dppf (6 mol%), CuI (5 mol%), 2-bromophenyl trifluoromethanesulfonate **1′g** (1.0 mmol, 1.0 equiv.) and Et_3N (3.0 equiv.). in degassed DMF (10 mL, 0.1 M) were added dropwise phenylacetylene (1.1 equiv.). The reaction mixture was stirred at room temperature for 6 hours. The reaction mixture was washed 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. 70% yield; colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 –

7.48 (m, 4H), 7.39 – 7.33 (m, 3H), 7.29 (td, *J* = 7.6, 1.2 Hz, 1H), 7.18 (td, *J* = 7.8, 1.7 Hz, 1H); The compound was identified by spectral comparison with literature data.[93]

Synthesis of 2,2,2-trifluoro-*N*-(2-(phenylethynyl)phenyl)acetamide (1k)

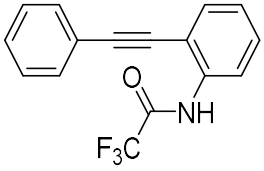


2-(phenylethynyl)aniline (1k')



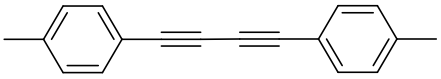
To a suspension of $Pd(PPh_3)_2Cl_2$ (5 mol%), CuI (5 mol%), 2-iodoaniline (1.5 mmol, 1.0 equiv.) in degassed Et_3N (0.5 M, 5 mL) was added dropwise phenylacetylene (1.2 equiv.) under nitrogen atmosphere. The reaction mixture was stirred until TLC indicated complete consumption of the starting material at 70°C. 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. 88% yield; brown solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.52 (m, 2H), 7.43 – 7.31 (m, 4H), 7.19 – 7.12 (m, 1H), 6.77 – 6.71 (m, 2H), 4.28 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 132.2, 131.5, 129.7, 128.4, 128.2, 123.3, 118.0, 114.3, 107.9, 94.7, 85.9; MS (APCI): *m/z* 194.1 $[M+H]^+$

2,2,2-trifluoro-*N*-(2-(phenylethynyl)phenyl)acetamide (1k)



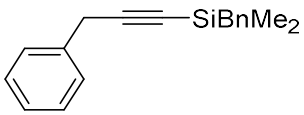
To solution of 2-(phenylethynyl)aniline **1k'** (0.2 mmol, 1.0 equiv.) in CH_2Cl_2 (1.3 mL, 0.15 M) was added pyridine (2.0 equiv.) and trifluoroacetic anhydride (1.2 equiv.) at 0 °C. The reaction mixture was slowly warmed up to room temperature and stirred at room temperature for 3 hours. The reaction mixture was washed 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. 86% yield; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.38 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.59 – 7.51 (m, 3H), 7.46 – 7.38 (m, 4H), 7.22 (td, *J* = 7.6, 1.2 Hz, 1H); The compound was identified by spectral comparison with literature data.[94]

1,4-di-*p*-tolylbuta-1,3-diyne (1l)



To a suspension of Cu(I)Cl (10 mol%) and piperidine (1.2 equiv.) in CH_2Cl_2 (2 mL, 0.1 M) with freshly activated molecular sieve (3Å) was added *p*-tolylacetylene (0.2 mmol, 1.0 equiv.). The reaction mixture was stirred at room temperature under air for 1 hour. The reaction mixture was filtered to remove the solids, washed 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. 99% yield; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.1 Hz, 4H), 7.14 (d, *J* = 8.2 Hz, 4H), 2.36 (s, 6H); The compound was identified by spectral comparison with literature data.[95]

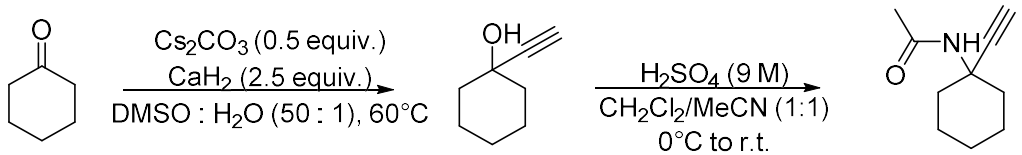
Benzyldimethyl(3-phenylprop-1-yn-1-yl)silane (1m)



To a solution of prop-2-yn-1-ylbenzene (1 mmol, 1.0 equiv.) in THF (2 mL, 0.5 M) was added dropwise *n*-BuLi (2.5 M in hexane, 1.1 equiv.) at -78 °C. After 1 h, benzyl(chloro)dimethylsilane (1.1 equiv.) was added to the solution. The reaction mixture was slowly warmed up to room temperature and stirred at room temperature for overnight. The reaction mixture was quenched with water and extracted with Et_2O.

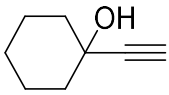
The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography. 78%; colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 4H), 7.28 – 7.17 (m, 3H), 7.13 – 7.03 (m, 3H), 3.65 (s, 2H), 2.21 (s, 2H), 0.15 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 136.3, 128.6, 128.5, 128.3, 128.1, 126.7, 124.4, 105.8, 85.5, 26.6, 26.4, -1.8; MS (APCI): *m/z* 265.6 $[M+H]^+$

Synthesis of alkyne derivatives with cyclohexyl group (1n, 1o)



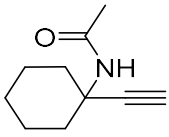
1n **1o**

1-ethynylcyclohexan-1-ol (1n)



A suspension of cesium carbonate (0.5 equiv.), calcium carbide (2.5 equiv.) in DMSO/H_2O (33.6 mL, 50:1, 0.3 M) was bubbled with nitrogen for 20 min, and cyclohexanone (10 mmol, 1.0 equiv.) was added. The reaction mixture was stirred at 60 °C for overnight. 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. 77% yield; colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (s, 1H), 1.96 – 1.89 (m, 2H), 1.80 – 1.65 (m, 2H), 1.64 – 1.44 (m, 5H), 1.33 – 1.17 (m, 1H); The compound was identified by spectral comparison with literature data.[96]

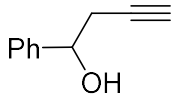
***N*-(1-ethynylcyclohexyl)acetamide (1o)**



To a solution of 1-ethynylcyclohexa-1-ol **1q** (0.5 mmol, 1.0 equiv.) in CH_2Cl_2/MeCN (0.8 mL, 1:1, 0.5 M) was added dropwise concentrated Sulfuric acid (55 μL, 9 M) at 0 °C. The reaction mixture was

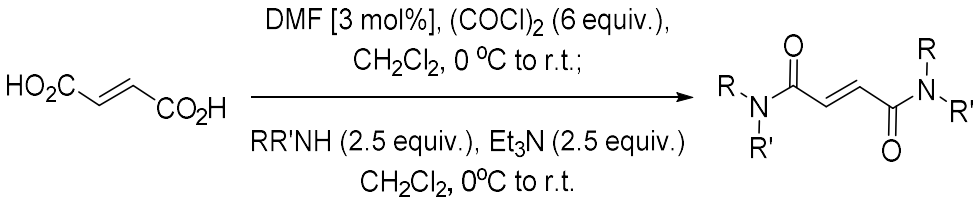
slowly warmed up to room temperature and stirred at room temperature for 4 hours. The reaction mixture was washed with saturated aqueous sodium bicarbonate and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography. 44% yield; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.56 (br s, 1H), 2.39 (s, 1H), 2.12 (d, *J* = 12.1 Hz, 2H), 1.96 (s, 3H), 1.86 – 1.50 (m, 7H), 1.35 – 1.16 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 85.5, 71.3, 51.7, 36.8, 25.2, 24.2, 22.4; MS (APCI): *m/z* 166.2 $[M+H]^+$

1-phenylbut-3-yn-1-ol (1p)



To a suspension of benzaldehyde (5 mmol, 1.0 equiv.) and propargyl bromide (3.0 equiv.) in THF (17 mL, 0.3 M) was added iron chloride (3.0 equiv.) at 0 °C. After stirring the mixture for 10 min, zinc dust (3.0 equiv.) was added in a few portions over a period. The reaction mixture was slowly warmed up to room temperature and stirred at room temperature for overnight. The reaction mixture was washed with 1 N aqueous HCl solution 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. 67% yield; colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.30 (m, 4H), 7.33 – 7.27 (m, 1H), 4.89 (t, *J* = 6.4 Hz, 1H), 2.65 (dd, *J* = 6.1, 2.6 Hz, 2H), 2.35 (s, 1H), 2.08 (t, *J* = 2.5 Hz, 1H); The compound was identified by spectral comparison with literature data.[96]

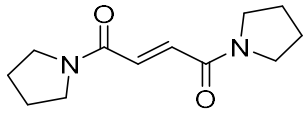
Synthesis of *N*, *N*'-difumaramide (2f, 2g)



To a suspension of fumaric acid (1.0 equiv., 5.0 mmol), DMF (3 mol%) in dry CH_2Cl_2 (20 mL, 0.25 M) was added dropwise oxalyl chloride (6.0 equiv.) at 0 °C. The reaction mixture was stirred at room temperature for 8 hours. Then, the solvent was removed under reduced pressure. The residue was dissolved in dry CH_2Cl_2 and slowly added dropwise to a solution of amine (2.5 equiv.) and Et_3N (2.5 equiv.) in dry CH_2Cl_2 (25 mL, 0.2 M) at 0°C. The mixture was stirred at room temperature for 2 hours.

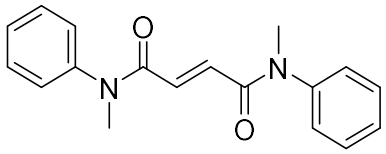
The reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel.

(*E*)-1,4-di(pyrrolidin-1-yl)but-2-ene-1,4-dione (2f)



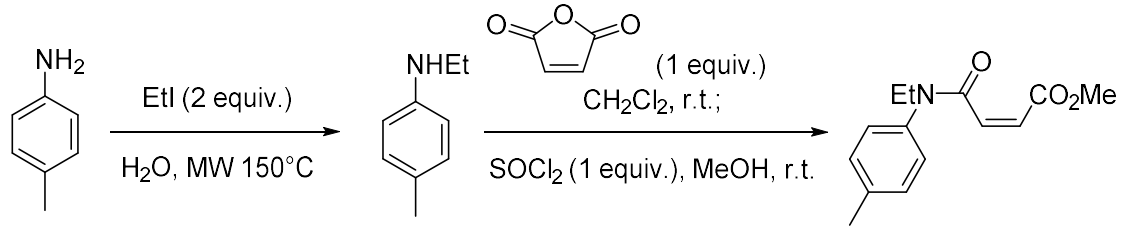
Prepared according to the above procedure using pyrrolidine (2.5 equiv.). 43% yield; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (s, 2H), 3.60 (t, *J* = 6.8 Hz, 4H), 3.53 (t, *J* = 6.9 Hz, 4H), 1.97 (p, *J* = 6.7 Hz, 4H), 1.87 (p, *J* = 6.7 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 131.6, 46.7, 46.1, 26.0, 24.2.; MS (APCI): *m/z* 223.5 $[M+H]^+$

N^1,N^4-dimethyl-N^1,N^4-diphenylfumaramide (2g)

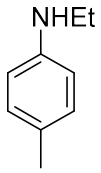


Prepared according to the above procedure using *N*-methyl aniline (2.5 equiv.). 90% yield; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (t, *J* = 7.7 Hz, 4H), 7.32 (t, *J* = 7.3 Hz, 2H), 7.12 (d, *J* = 7.7 Hz, 4H), 6.84 (s, 2H), 3.29 (s, 6H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 142.8, 131.5, 129.8, 127.9, 127.0, 37.6.; MS (APCI): *m/z* 295.7 $[M+H]^+$

Synthesis of methyl (*Z*)-4-(ethyl(*p*-tolyl)amino)-4-oxobut-2-enoate (2h)

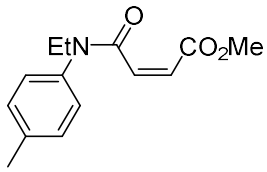


_N_-ethyl-4-methylaniline (2′h)



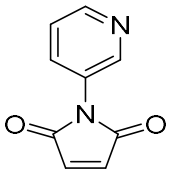
A mixture of *p*-toluidine (0.5 mmol, 1.0 equiv.) and ethyl iodide (2.0 equiv.) in water (0.17mL, 3 M) was microwave irradiated at 150°C for 20 minutes. The reaction mixture was washed with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography. 44% yield; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (d, *J* = 8.4 Hz, 2H), 6.54 (d, *J* = 8.4 Hz, 2H), 3.41 (s, 1H), 3.14 (q, *J* = 7.1 Hz, 2H), 2.24 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); The compound was identified by spectral comparison with literature data.[97]

Methyl (*Z*)-4-(ethyl(*p*-tolyl)amino)-4-oxobut-2-enoate (2h)



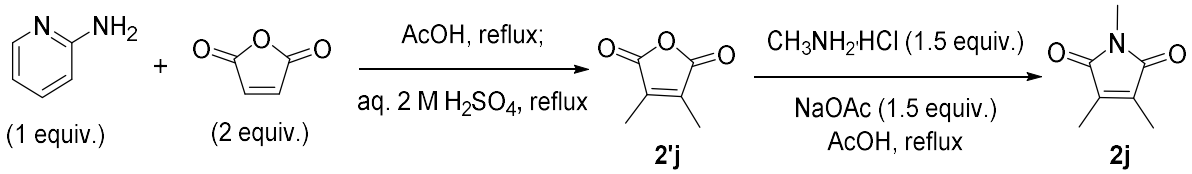
To the solution of *N*-ethyl-4-methylaniline **2′g** (0.18 mmol, 1.0 equiv.) in CH_2Cl_2 (0.9 mL, 0.2 M) was added maleic anhydride (1.0 equiv.). The reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was stirred at room temperature for 1 h. The solvent was evaporated under reduced pressure, the reaction mixture was dissolved in the methanol (0.9 mL, 0.2 M) and added thionyl chloride (1.0 equiv.) at 0 °C. The reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was washed 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. 67% yield; colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.3 Hz, 2H), 6.24 (d, *J* = 11.9 Hz, 1H), 5.74 (d, *J* = 11.9 Hz, 1H), 3.82 (q, *J* = 7.2 Hz, 2H), 3.78 (s, 3H), 2.36 (s, 3H), 1.17 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 165.5, 138.5, 138.2, 137.1, 130.0, 127.9, 123.8, 51.8, 43.5, 21.1, 12.8; MS (APCI): *m/z* 248.5 $[M+H]^+$

1-(pyridin-3-yl)-1*H*-pyrrole-2,5-dione (2i)

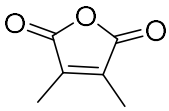


To a solution of maleic anhydride (1.1 equiv.) in THF (0.25 M) was added dropwise 3-aminopyridine (0.5 mmol, 1.0 equiv.). After the reaction mixture was stirred at room temperature for 0.5 h, the precipitate was filtered and washed with diethyl ether several time. The collected precipitate was dried under reduced pressure and used without further purification. To a solution of maleic acid (1.0 equiv.) in acetic anhydride (0.2 M) was added sodium acetate (1.2 equiv.) and the solution was heated at 80 °C for 1 hour. The mixture was concentrated under reduced pressure and purified by flash chromatography on silica gel. 50% yield; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 2.3 Hz, 1H), 8.58 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.71 (ddd, *J* = 8.2, 2.5, 1.6 Hz, 1H), 7.39 (dd, *J* = 8.2, 4.8 Hz, 1H), 6.88 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 148.6, 146.7, 134.5, 133.0, 128.3, 123.6; MS (APCI): *m/z* 175.4 $[M+H]^+$

Synthesis of 1,3,4-trimethyl-1*H*-pyrrole-2,5-dione (2j)



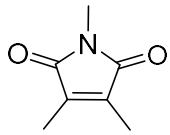
3,4-dimethylfuran-2,5-dione (2′j)



A solution of 2-aminopyridine (12.0 mmol, 1.0 equiv.) in acetic acid (3 mL, 4 M) was refluxed for 1 h, then a solution of maleic anhydride (2.0 equiv.) in acetic acid (3 mL, 4 M) was added. The reaction mixture was refluxed for 3 hours. The solvent was evaporated under reduced pressure, aqueous 2 M sulfuric acid was added. Reaction mixture was refluxed for 2 hours. The reaction mixture was washed with 1 N aqueous HCl solution and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude is used without further purification. 60% yield; white solid;

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.08 (s, 6H); The compound was identified by spectral comparison with literature data.[98]

1,3,4-trimethyl-1*H*-pyrrole-2,5-dione (2j)



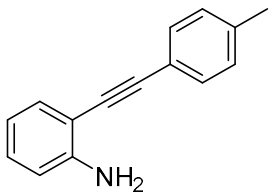
To a solution of 3,4-dimethylfuran-2,5-dione **2′t** (2.4 mmol, 1.0 equiv.) in AcOH (8 mL, 0.3 M) was added methylamine hydrochloride (1.5 equiv.) and sodium Acetate (1.5 equiv.). The reaction mixture was stirred at 100°C for 6 hours. The mixture was concentrated *in vacuo* and, washed with saturated aqueous $NaHCO_3$ and extracted with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography. 72% yield; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.99 (s, 3H), 1.96 (s, 6H); The compound was identified by spectral comparison with literature data.[99]

Preparation and characterization of substrates for intermolecular reaction

***General procedure C* (for Sonogashira coupling)**

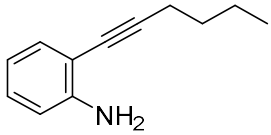
To a suspension of $Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (4 mol%), and 2-iodophenol or 2-iodoaniline (1.0 equiv.) in degassed Et_3N (0.5 M) was added dropwise the corresponding alkyne (2.0 equiv.) under nitrogen atmosphere. The reaction mixture was stirred until TLC indicated complete consumption of the starting 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)aniline (S1)



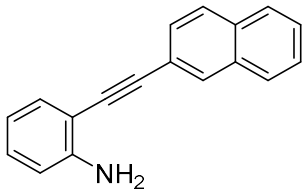
Prepared according to the ***General Procedure C*** using $Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (2 mol%), 2-iodoaniline (3.0 mmol, 1.0 equiv.), and *p*-tolylacetylene (1.2 equiv.) in Et_3N (0.2 M) at room temperature, 99% yield; yellow solid; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.16 (d, *J* = 7.9 Hz, 2H), 7.12 (dd, *J* = 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.[100]

2-(hex-1-yn-1-yl)aniline (S2)



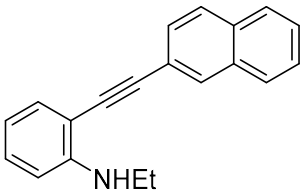
Prepared according to the ***General Procedure C*** using $Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (1 mol%), 2-iodoaniline (0.5 mmol, 1.0 equiv.), and 1-Hexyne (1.2 equiv.) in Et_3N (1 mL, 0.5 M) at room temperature, 83% yield; brown liquid; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.10 – 7.04 (m, 1H), 6.70 – 6.61 (m, 2H), 4.15 (s, 1H), 2.47 (t, *J* = 7.0 Hz, 2H), 1.66 – 1.56 (m, 2H), 1.55 – 1.41 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H); The compound was identified by spectral comparison with literature data.[101]

2-(naphthalen-2-ylethynyl)aniline (S3′)



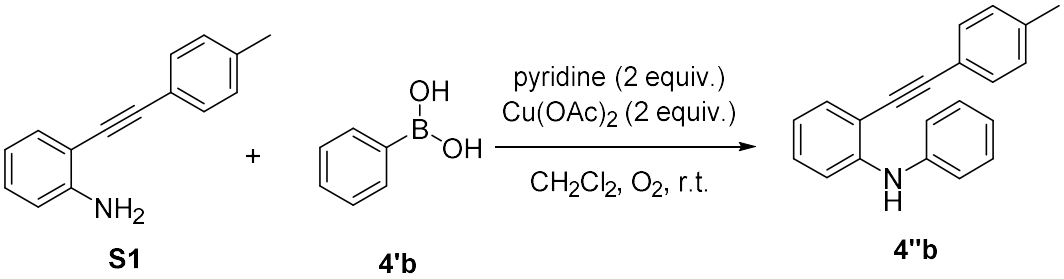
Prepared according to the ***General Procedure C*** using $Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (4 mol%), 2-iodoaniline (0.27 mmol, 1.0 equiv.), and 2-ethynylnaphthalene (1.2 equiv.) in Et_3N (0.68 mL,0.4 M) at room temperature, 96% yield; white solid; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.85 –7.80 (m, 3H), 7.58 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.53 – 7.48 (m, 2H), 7.45 – 7.38 (m, 1H), 7.16 (ddd, *J* = 8.2, 7.4, 1.6 Hz, 1H), 6.79 – 6.70 (m, 2H), 4.33 (s, 2H); The compound was identified by spectral comparison with literature data.[102]

***N*-ethyl-2-(naphthalen-2-ylethynyl)aniline (S3)**

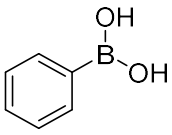


Corresponding 2-(naphthalen-2-ylethynyl)aniline **S3′** (0.25 mmol, 1.0 equiv.) was dissolved in THF (0.2 M) under nitrogen atmosphere and cooled to -78°C. *n*-BuLi solution (2.5 M in hexane, 1.1 equiv.) was added dropwise, and the mixture was stirred for 1h. Iodoethane (1.0 equiv.) was added dropwise 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. 84% Yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.84 – 7.74 (m, 3H), 7.56 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.41 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.27 – 7.18 (m, 1H), 6.70 – 6.60 (m, 2H), 4.63 (s, 1H), 3.32 – 3.20 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 133.0, 132.7, 132.2, 131.0, 130.1, 128.3, 128.0, 127.8, 127.7, 126.6, 126.6, 120.7, 116.2, 109.5, 107.2, 95.4, 86.5, 38.1, 14.8; MS (APCI): *m/z* 272.0 $[M+H]^+$

Synthesis of *N*-phenyl-2-(*p*-tolylethynyl)aniline (4″b)



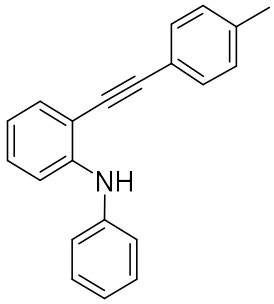
Phenylboronic acid (4′b)



To make Grignard reagent first, put oven dried magnesium (1.2 equiv.) into flask, and dissolved in at least amount of THF (1 M). Using heat-gun, heated up the solution until it was boiling. Quickly added 1 drop of 1,2-dibromoethane and watch if the bubble is shown on surface of magnesium. Then, slowly added about 20% of solution of bromobenzene dissolved in THF then, slowly added rest of the solution and then warmed to 50 ºC until nearly all magnesium was dissolved. The Grignard solution was added

to another solution of trimethylbormate in Et_2O at -78 ºC under inert atmosphere. The mixture was stirred for 30 min. and cool bath was removed then stirred overnight at room temperature. Then, the boronic ester was hydrolyzed by 1 N HCl solution, followed by 1 h stirring. The reaction mixture was extracted with Et_2O, the combined organic layers dried over Na_2SO_4 and evaporated to dryness *in vacuo*, and without purification, use crude residue can be converted directly into next step. 92% yield; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.24 (m, 2H), 7.63 – 7.59 (m, 1H), 7.54 – 7.50 (m, 2H); The compound was identified by spectral comparison with literature data.[103]

***N*-phenyl-2-(*p*-tolylethynyl)aniline (4″b)**



2-(*p*-tolylethynyl)aniline **S1** was dissolved in CH_2Cl_2 at room temperature. Phenylboronic acid **4′b** (2.0 equiv.), pyridine (2.0 equiv.) and copper diacetate (2.0 equiv.) were added and the reaction mixture was stirred at room temperature under O_2 atmosphere (balloon) for overnight. The reaction mixture was partitioned between aqueous copper sulfate and CH_2Cl_2, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by flash chromatography on silica gel. 81% yield; yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.41 (m, 3H), 7.35 – 7.31 (m, 2H), 7.26 – 7.16 (m, 6H), 7.05 – 7.00 (m, 1H), 6.83 – 6.80 (m, 1H), 6.52 (s, 1H), 2.37 (s, 3H); The compound was identified by spectral comparison with literature data.[104]

***General Procedure* D (for ester and amide synthesis via acid chloride)**

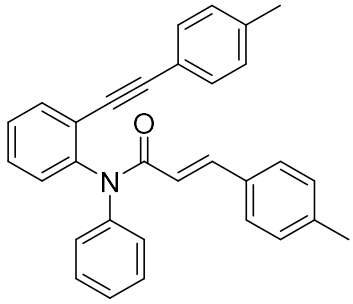
To a suspension of the corresponding acid (1.2 equiv.), DMF (3 mol%) in dry CH_2Cl_2 (0.5 M) was added dropwise oxalyl chloride (1.1 equiv., per acid) at 0°C. The reaction mixture was stirred at room temperature for 1h. Then, the solvent was removed under reduced pressure. The residue was dissolved in dry THF (0.3 M) and slowly added dropwise to a solution of the appropriate phenol or aniline (1.0 equiv.) and Et_3N (1.2 equiv.) 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.

***General Procedure* E (for ethylation of amide)**

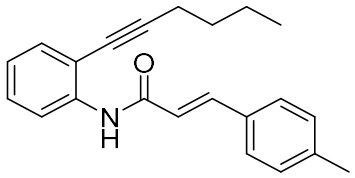
To solution of the corresponding amide (1.0 equiv.) in THF (0.3 M) was added sodium hydride (1.5 equiv.) at 0°C. The reaction mixture was stirred at room temperature for 1 hour. Then iodoethane (2.9 equiv.) was added dropwise. The reaction mixture was monitored by TLC. The reaction mixture was washed with a saturated solution of NH_4Cl and extracted with EtOAc. 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*)-*N*-phenyl-3-(*p*-tolyl)-*N*-(2-(*p*-tolylethynyl)phenyl)acrylamide (4b)



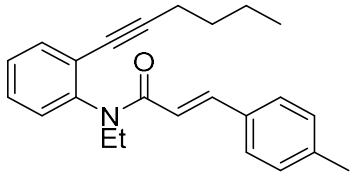
Prepared according to the ***General Procedure D*** using 4-methylcinnamic acid (1.5 equiv.), *N*-phenyl-2-(*p*-tolylethynyl)aniline **4″b** (1.5 mmol, 1.0 equiv.) and K_2CO_3 (3.0 equiv.) instead of Et_3N in CH_2Cl_2 (3 mL, 0.5 M) and additional DMAP (0.6 equiv.). 69% yield; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 15.5 Hz, 1H), 7.64 – 7.57 (m, 1H), 7.40 – 7.26 (m, 9H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 7.4 Hz, 1H), 7.07 (d, *J* = 7.9 Hz, 2H), 7.04 (d, *J* = 7.9 Hz, 2H), 6.45 (d, *J* = 15.5 Hz, 1H), 2.30 (s, 3H), 2.29 (s, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 144.1, 142.7, 142.6, 139.8, 138.6, 133.1, 132.7, 131.5, 129.5, 129.3, 129.1, 129.0, 128.8, 127.9, 127.6, 126.8, 126.2, 123.9, 119.8, 118.9, 85.6, 77.2, 21.4, 21.2.; MS (APCI): *m/z* 428.9 $[M+H]^+$

(*E*)-*N*-(2-(hex-1-yn-1-yl)phenyl)-3-(*p*-tolyl)acrylamide (4′f)



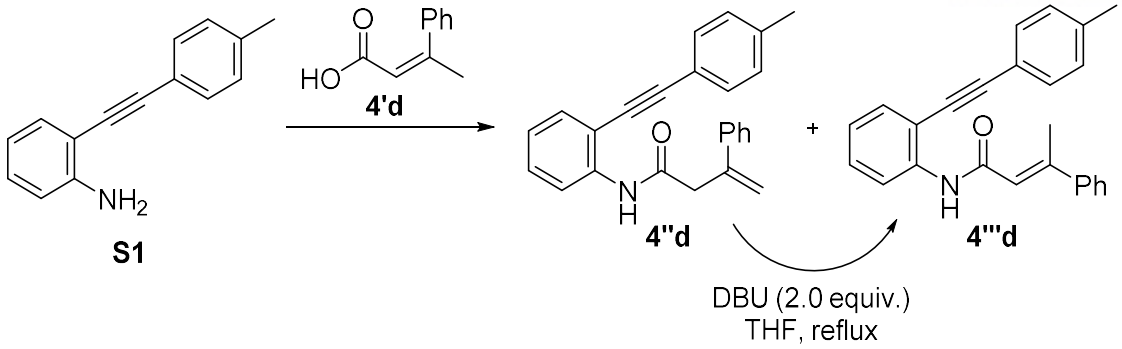
Prepared according to the ***General Procedure D*** using 4-methylcinnamic acid (1.5 equiv.), and 2-(hex-1-yn-1-yl)aniline **S2** (0.4 mmol, 1.0 equiv.) and additional DMAP (0.2 equiv.) in CH_2Cl_2 (2 mL, 0.2 M). 50% yield; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.4 Hz, 1H), 8.12 (s, 1H), 7.73 (d, *J* = 15.5 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 2H), 7.38 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.32 (ddd, *J* = 8.7, 7.6, 1.6 Hz, 1H), 7.21 (d, *J* = 7.9 Hz, 2H), 7.02 (td, *J* = 7.6, 1.1 Hz, 1H), 6.49 (d, *J* = 15.5 Hz, 1H), 2.56 (t, *J* = 7.0 Hz, 2H), 2.39 (s, 3H), 1.74 – 1.64 (m, 2H), 1.63 – 1.54 (m, 2H), 1.00 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 142.3, 140.4, 139.0, 131.8, 131.5, 129.6, 128.9, 127.9, 123.2, 119.9, 119.2, 112.7, 98.0, 76.1, 30.8, 22.2, 21.4, 19.3, 13.7; MS (APCI): *m/z* 318.5 $[M+H]^+$

(*E*)-*N*-ethyl-*N*-(2-(hex-1-yn-1-yl)phenyl)-3-(*p*-tolyl)acrylamide (4f)

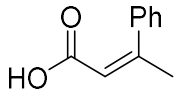


Prepared according to the ***General Procedure E*** using (*E*)-*N*-(2-(hex-1-yn-1-yl)phenyl)-3-(*p*-tolyl)acrylamide **4′f** (0.19 mmol, 1.0 equiv.). 99% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 15.4 Hz, 1H), 7.54 – 7.47 (m, 1H), 7.36 – 7.28 (m, 2H), 7.23 – 7.14 (m, 3H), 7.06 (d, *J* = 7.9 Hz, 2H), 6.13 (d, *J* = 15.6 Hz, 1H), 4.10 – 3.99 (dq, *J* = 14.1, 7.1 Hz, 1H), 3.73 (dq, *J* = 14.1, 7.1 Hz, 1H), 2.34 (t, *J* = 7.0 Hz, 2H), 2.30 (s, 3H), 1.56 – 1.45 (m, 2H), 1.44 – 1.33 (m, 2H), 1.16 (t, *J* = 7.2 Hz, 3H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 143.1, 141.2, 139.4, 133.2, 132.7, 129.6, 129.3, 128.4, 127.8, 127.7, 124.3, 118.3, 96.5, 76.9, 43.7, 30.5, 21.9, 21.3, 19.2, 13.5, 13.0; MS (APCI): *m/z* 346.5 [M+H]+

Synthesis of 3-phenyl-*N*-(2-(*p*-tolylethynyl)phenyl)but-2-enamide (4‴d)

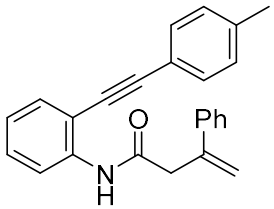


(*Z*)-3-phenylbut-2-enoic acid (4′d)



To suspension of CuI (2.0 equiv.) of dry diethyl ether (1.7 mL, 0.3 M) was added dropwise methyllithium solution (3.1 M in diethoxymethane, 4.0 equiv.) at -20°C. The suspension was stirred at -20°C while the solid dissolved. To the solution, 3-phenylpropynoic acid (0.5 mmol, 1.0 equiv.) was added at -78°C. The reaction mixture was stirred at -20°C for 3 hours. The reaction mixture was poured into 1 N aqueous HCl solution 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. 92%; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 3H), 7.22 – 7.18 (m, 2 H), 5.90 (d, *J* = 1.4 Hz, 1H), 2.19 (d, *J* = 1.4 Hz, 3H); The compound was identified by spectral comparison with literature data.[105]

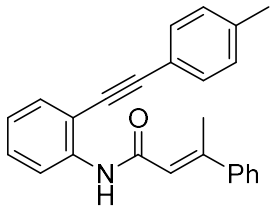
3-phenyl-*N*-(2-(*p*-tolylethynyl)phenyl)but-3-enamide (4″d)



Prepared according to the ***General Procedure E*** using (*Z*)-3-phenylbut-2-enoic acid **4′d** (1.5 equiv.), and 2-(*p*-tolylethynyl)aniline **S1** (0.1 mmol, 1.0 equiv.) in CH_2Cl_2 (0.2 mL, 0.5 M) and additional DMAP (0.2 equiv.). 75% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.46 (d, *J* = 8.3 Hz, 1H), 7.45 – 7.38 (m, 3H), 7.35 – 7.24 (m, 5H), 7.21 – 7.12 (m, 2H), 7.03 (td, *J* = 7.6, 1.2 Hz, 1H), 5.58 (d, *J* = 0.9 Hz, 1H), 5.37 (d, *J* = 0.9 Hz, 1H), 3.67 (d, *J* = 0.9 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz,

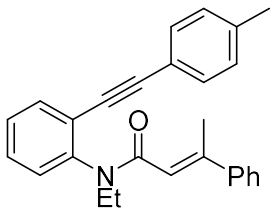
$CDCl_3$) δ 168.4, 141.9, 139.1, 138.7, 138.5, 131.6, 131.4, 129.5, 129.2, 128.6, 128.3, 125.7, 123.4, 119.3, 118.9, 117.9, 112.1, 96.3, 83.3, 45.8, 21.6; MS (APCI): *m/z* 352.8 $[M+H]^+$

3-phenyl-*N*-(2-(*p*-tolylethynyl)phenyl)but-2-enamide (4‴d)



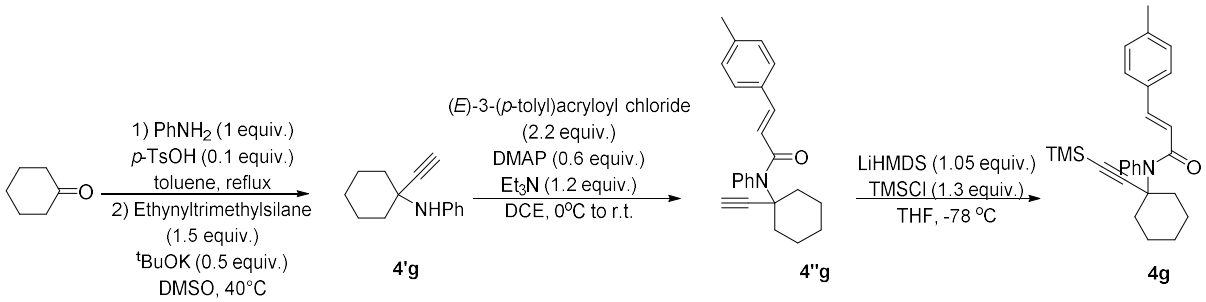
To a solution of 3-phenyl-*N*-(2-(*p*-tolylethynyl)phenyl)but-3-enamide **4″d** (0.11 mmol, 1.0 equiv.) in THF (0.28 mL, 0.4 M) was added DBU (2.0 equiv.). The reaction mixture was refluxed for 2 hours. The reaction mixture was washed with a saturated solution of NH_4Cl and extracted with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel. 63% yield; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 8.4 Hz, 1H), 8.11 (s, 1H), 7.53 – 7.44 (m, 3H), 7.44 – 7.33 (m, 5H), 7.17 (d, *J* = 7.8 Hz, 2H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.19 (s, 1H), 2.65 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 153.4, 142.6, 139.2, 139.1, 131.7, 131.4, 129.5, 129.3, 128.8, 128.6, 126.3, 123.3, 120.1, 119.3, 119.3, 112.2, 96.8, 83.9, 21.5, 18.1; MS (APCI): *m/z* 352.8 $[M+H]^+$

(*E*)-*N*-ethyl-3-phenyl-*N*-(2-(*p*-tolylethynyl)phenyl)but-2-enamide (4d)

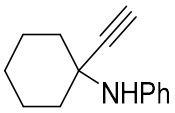


Prepared according to the ***General Procedure E*** using 3-phenyl-*N*-(2-(*p*-tolylethynyl)phenyl)but-2-enamide **4‴d** (0.06 mmol, 1.0 equiv.). 67% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 7.3, 1.9 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.37 – 7.30 (m, 2H), 7.25 – 7.19 (m, 4H), 7.14 (d, *J* = 7.9 Hz, 2H), 7.11 – 7.08 (m ,2H), 5.85 (d, *J* = 1.2 Hz, 1H), 4.04 – 3.83 (m, 2H), 2.42 (d, *J* = 1.1 Hz, 3H), 2.35 (s, 3H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 148.7, 143.6, 143.0, 138.8, 132.8, 131.6, 129.1, 129.1, 129.0, 128.2, 127.9, 127.7, 126.1, 123.9, 120.3, 119.7, 94.8, 85.4, 43.6, 21.5, 18.1, 13.2; MS (APCI): *m/z* 380.9 $[M+H]^+$

Synthesis of (*E*)-*N*-phenyl-3-(*p*-tolyl)-*N*-(1-((trimethylsilyl)ethynyl)cyclohexyl)acrylamide (4g)

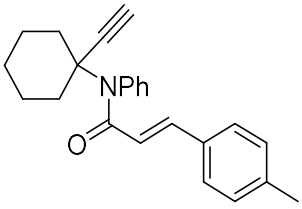


***N*-(1-ethynylcyclohexyl)aniline (4′g)**



A solution of aniline (0.5 mmol, 1.0 equiv.) and cyclohexanone (1.5 equiv.) in dry toluene (0.5 mL, 1 M) was added *p*-toluenesulfonic acid (0.1 equiv.). The reaction mixture was stirred at 110°C for 24 hours. The mixture was taken up in hexane and filtered through a pad of Celite®. The solvent was then removed under vacuum to obtain *N*-phenyl cyclohexanimine, which was used in the next step without purification. To mixture of *N*-phenyl cyclohexanimine (1.0 equiv.) and Ethynyltrimethylsilane (1.5 equiv.) in DMSO (1.7 mL, 0.3 M) was added potassium tert-butoxide (0.5 equiv.). The reaction mixture was stirred at 40°C to 20 min. The mixture was washed with saturated aqueous Na_2CO_3 and extracted with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography. 45% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 8.6, 7.3 Hz, 2H), 6.95 (dd, *J* = 8.6, 1.1 Hz, 2H), 6.77 (tt, *J* = 7.4, 1.1 Hz, 1H), 3.64 (s, 1H), 2.45 (s, 1H), 2.19 (d, *J* = 12.1 Hz, 2H), 1.77 – 1.49 (m, 7H), 1.35 – 1.21 (m, 1H); The compound was identified by spectral comparison with literature data.[106]

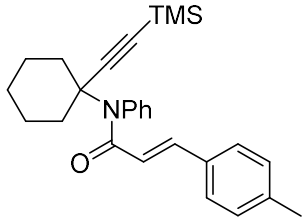
(*E*)-*N*-(1-ethynylcyclohexyl)-*N*-phenyl-3-(*p*-tolyl)acrylamide (4″g)



To a suspension of 4-methylcinnamic acid (2.2 equiv.), DMF (3 mol%) in dry CH_2Cl_2 (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 DCE and slowly added dropwise to a solution of *N*-(1-ethynylcyclohexyl) aniline **4′g** (0.21 mmol, 1.0 equiv.), Et_3N (1.2 equiv.) and DMAP (0.6 equiv.) 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 EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by flash chromatography on silica gel. 83% yield; yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 15.5 Hz, 1H), 7.45 – 7.37 (m, 3H), 7.29 – 7.21 (m, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 5.96 (d, *J* = 15.5 Hz, 1H), 2.56 (s, 1H), 2.43 – 2.30 (m, 2H), 2.29 (s, 3H), 1.77 (q, *J* = 13.3 Hz, 2H), 1.66 – 1.61 (m, 3 H), 1.56 – 1.44 (m, 2 H), 1.16 – 1.02 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 141.3, 140.1, 139.5, 132.5, 131.0, 129.3, 129.1, 128.5, 127.7, 120.1, 85.1, 73.4, 59.0, 36.9, 25.3, 23.3, 21.3; MS (APCI): *m/z* 344.1 $[M+H]^+$

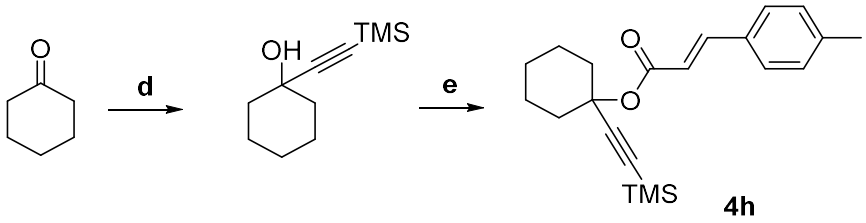
(*E*)-*N*-phenyl-3-(*p*-tolyl)-*N*-(1-((trimethylsilyl)ethynyl)cyclohexyl)acrylamide (4g)



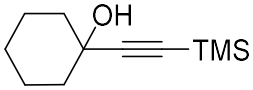
To a solution of ((*E*)-*N*-(1-ethynylcyclohexyl)-*N*-phenyl-3-(*p*-tolyl)acrylamide **4″g** (0.15 mmol, 1.0 equiv.) in THF (0.2 mL, 0.8 M) was add lithium bis(trimethylsilyl)amide solution (1 M in THF, 1.05.0 equiv.) at -78°C under nitrogen. The reaction mixture was stirred at -78°C for 1 hour. then Chlorotrimethylsilane (1.3 equiv.) was added dropwise, and the solution stirred for 3 hours at -78°C. 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. 83% yield; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 15.5 Hz, 1H), 7.42 – 7.35 (m, 3H), 7.25 – 7.18 (m, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.01 (d, *J* = 15.4 Hz, 1H), 2.29 (s, 3H), 2.24 – 2.09 (m, 4H), 1.82 – 1.52 (m, 5H), 1.27 – 1.10 (m, 1H), 0.06 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 141.4, 140.7, 139.6, 132.8, 131.1,

129.4, 128.9, 128.3, 127.8, 121.0, 106.8, 92.3, 62.0, 36.0, 25.3, 23.9, 21.5, 0.1; MS (APCI): *m/z* 416.3 $[M+H]^+$

Synthesis of 1-((trimethylsilyl)ethynyl)cyclohexyl (*E*)-3-(*p*-tolyl)acrylate (4h)

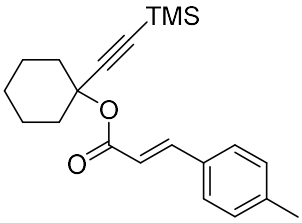


1-((trimethylsilyl)ethynyl)cyclohexan-1-ol (1d)



A flame-dried round-bottom flask was charged with *n*-BuLi (2.5 M in hexane, 1.3 equiv.) under an argon atmosphere. Anhydrous THF (6 mL, 0.5 M) was added, and the flask was cooled to -78 °C. Trimethylsilylacetylene (1.3 equiv.) was then added dropwise. After 30 minutes at -78 °C, cyclohexanone (3.05 mmol, 1.0 equiv.) was added dropwise. The reaction mixture was warmed to r.t. and stirred overnight. After completion, saturated NH_4Cl solution was added. The mixture was extracted with Et_2O, and the organic phases were combined and washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated to yield crude product. The crude product was purified by flash chromatography. 94% yield; white solid; ^1H NMR (400 MHz, $CDCl_3$) δ 1.95 – 1.83 (m, 3H), 1.73 – 1.64 (m, 2H), 1.59 – 1.50 (m, 5H), 0.17 (d, *J* = 0.6 Hz, 9H); The compound was identified by spectral comparison with literature data.[107]

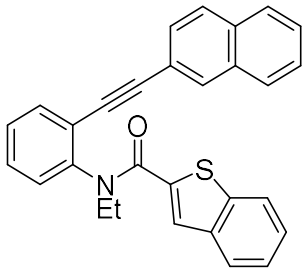
1-((trimethylsilyl)ethynyl)cyclohexyl (*E*)-3-(*p*-tolyl)acrylate (4h)



To a suspension of 4-methylcinnamic acid (1.2 equiv.) and the 1-((trimethylsilyl)ethynyl)cyclohexan-1-ol **1d** (0.3 mmol, 1.0 equiv.) in dry CH_2Cl_2 (0.2 M) was added 4-(dimethylamino)pyridine (0.6 equiv.).

The solution was cooled to 0 °C and *N*,*N*'-dicyclohexyl carbodiimide (1.5 equiv.) was added. The reaction mixture was refluxed 24 hours. The precipitated *N*,*N*-dicyclohexylurea was separated by filtration, and the filtrate was concentrated. The crude material was purified by flash chromatography. 65% yield; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 16.0 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 2H), 7.18 (d, *J* = 7.7 Hz, 2H), 6.36 (d, *J* = 16.0 Hz, 1H), 2.37 (s, 3H), 2.24 – 2.10 (m, 2H), 2.00 – 1.86 (m, 2H), 1.72 – 1.47 (m, 5H), 1.34 (dp, *J* = 14.0, 7.3, 6.9 Hz, 1H), 0.17 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 144.2, 140.4, 131.8, 129.5, 128.0, 118.2, 105.4, 90.8, 75.7, 37.2, 25.2, 22.7, 21.4, -0.0; MS (APCI): *m/z* 341.8 $[M+H]^+$

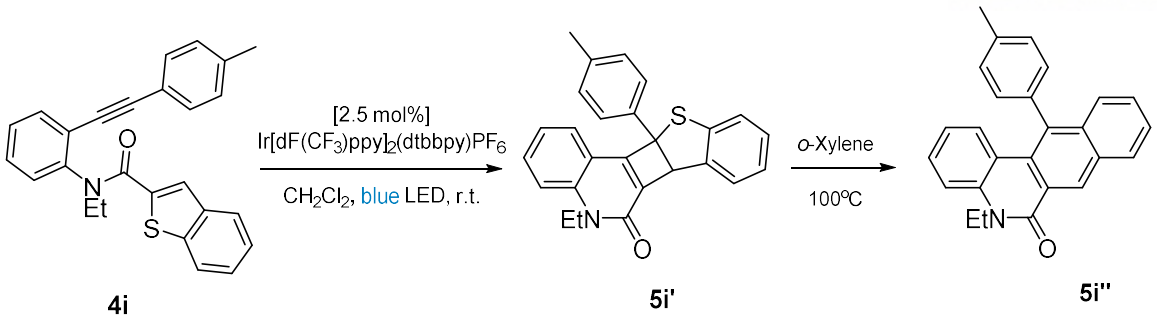
_N_-ethyl-_N_-(2-(naphthalen-2-ylethynyl)phenyl)benzo[b]thiophene-2-carboxamide (4j)



Prepared according to the ***General Procedure D*** using benzo[*b*]thiophene-2-carboxylic acid (1.5 equiv.), and *N*-ethyl-2-(naphthalen-2-ylethynyl)aniline **S3** (0.22 mmol, 1.0 equiv.) in DCE (1.1 mL, 0.2 M) and additional DMAP (0.2 equiv.). 65% yield; white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.89 – 7.75 (m, 3H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.64 – 7.54 (m, 3H), 7.53 – 7.46 (m, 2H), 7.46 – 7.35 (m, 3H), 7.25 (m, 2H), 7.10 (s, 1H), 4.12 (qt, *J* = 13.0, 7.3 Hz, 1H), 1.35 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 143.8, 141.3, 138.7, 138.5, 133.1, 133.0, 132.9, 131.7, 129.5, 129.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.8, 126.9, 126.6, 125.8, 124.9, 124.2, 124.2, 122.1, 119.9, 95.6, 86.1, 46.1, 12.7; MS (APCI): *m/z* 432.0 $[M+H]^+$

4.4. Synthesis of Extended π-Systems and synthetic applications

4.4.1 Rearrangement & Desulfurization of Benzothiophene

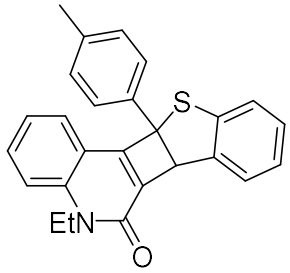


4i **5i'** **5i''**

Step 1 : Enyne **4i** (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 CH_2Cl_2 (2 mL) under argon atmosphere in glovebox. The reaction mixture was then irradiated by 12 W 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 **5i′**.

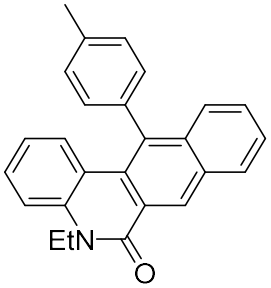
Step 2 : Solution of **5i′** in *o*-xylene was stirred at 100 °C. After completion of the reaction as indicated by TLC, the solution was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to give the desired product **5i′′**.

5-ethyl-11a-(*p*-tolyl)-6b,11a-dihydrobenzo[4',5']thieno[2',3':3,4]cyclobuta[1,2-c]quinolin-6(5*H*)-one (5i′)



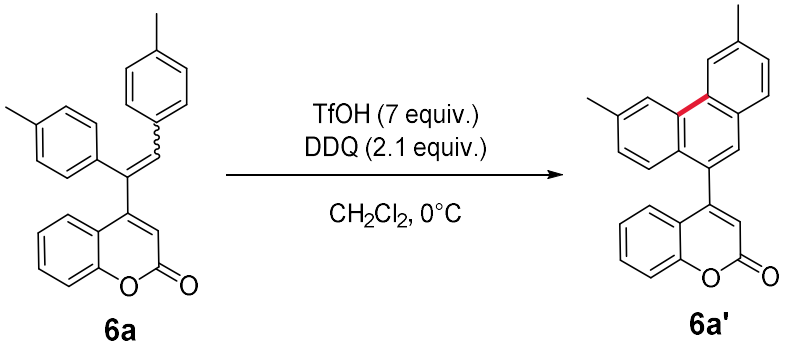
40 mg, >99% yield; white solid; m.p. 146 – 147 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.61 – 7.55 (m, 2H), 7.46 (d, *J* = 8.2 Hz, 3H), 7.27 – 7.18 (m, 2H), 7.18 – 7.12 (m, 4H), 5.09 (s, 1H), 4.35 (qd, *J* = 7.0, 2.6 Hz, 2H), 2.35 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 152.8, 142.1, 141.9, 138.0, 136.6, 134.2, 131.7, 130.4, 129.4, 128.4, 127.2, 126.1, 125.2, 125.0, 122.6, 122.1, 116.9, 115.7, 68.6, 66.9, 37.5, 21.1, 13.1.; HRMS *m/z* calculated for $[C_{26}H_{22}NOS]^+$ ($[M+H]^+$): 396.1417, observed 396.1421.

5-ethyl-12-(*p*-tolyl)benzo[*j*]phenanthridin-6(5*H*)-one (5i′′)



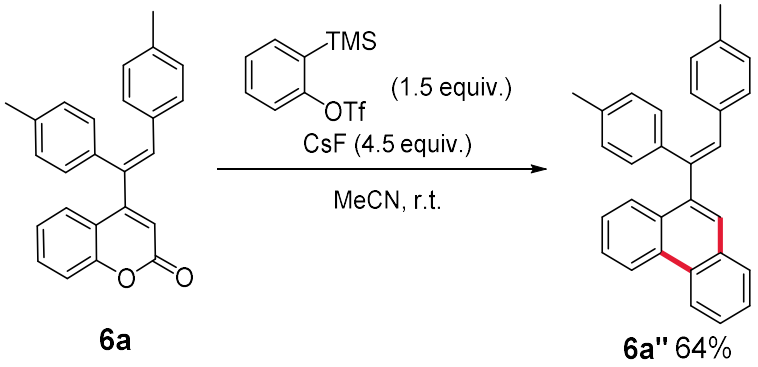
65% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (s, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 1H), 7.54 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H), 7.47 (ddd, *J* = 8.3, 6.7, 1.3 Hz, 1H), 7.41 (d, *J* = 7.9 Hz, 2H), 7.39 – 7.30 (m, 3H), 7.25 (d, *J* = 9.1 Hz, 2H), 6.78 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 4.48 (q, *J* = 7.1 Hz, 2H), 2.55 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 137.8, 137.5, 137.3, 136.5, 135.7, 131.8, 130.31, 130.26, 130.1, 129.4, 129.3, 128.4, 128.0, 127.6, 126.9, 126.2, 124.5, 121.1, 120.9, 114.7, 38.2, 21.5, 12.7.; HRMS *m/z* calculated for $[C_{26}H_{22}NO]^+$ ($[M+H]^+$): 364.1696, observed 364.1697.

4.4.2. Derivatization of Coumarin



6a **6a'**

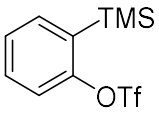
To a mixture of diene **6a** (0.2 mmol, 1.0 equiv.) and DDQ (2.1 equiv.) in dry CH_2Cl_2 (7 mL, 0.03 M) at 0°C was added trifluoromethanesulfonic acid (7.0 equiv.) dropwise. The reaction mixture was stirred at 0 °C for 3 hours. The mixture was quenched by saturated $NaHCO_3$ solution and extracted by CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica gel to give the desired product **6a′**. 43 mg, 61% yield; white solid; m.p. 199 – 200 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.54 (s, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.64 (s, 1H), 7.55 – 7.42 (m, 4H), 7.32 (d, *J* = 8.3 Hz, 1H), 7.08 – 7.00 (m, 2H), 6.57 (s, 1H), 2.67 (s, 3H), 2.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 155.6, 153.7, 137.5, 136.9, 131.9, 130.6, 130.5, 130.2, 129.0, 128.9, 128.8, 128.7, 127.8, 127.6, 126.5, 126.2, 124.2, 122.9, 122.4, 120.1, 117.1, 116.7, 22.2, 22.0; HRMS *m/z* calculated for $[C_{25}H_{19}O_2]^+$ ($[M+H]^+$): 351.1380, observed 351.1380.



6a **6a"** 64%

To a solution of diene **(*E*)-6a** (0.045 mmol, 1.0 equiv.) and 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (1.5 equiv.) in THF (0.45 mL, 0.1 M) was added cesium fluoride (4.5 equiv.). The reaction mixture was stirred at room temperature for 18 hours. The reaction mixture was concentrated under vacuum. The residue was purified by flash chromatography on silica gel. 11 mg, 64% yield of **6a"**; White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (t, *J* = 8.4 Hz, 2H), 8.08 (d, *J* = 8.3 Hz, 1H), 7.89 (d, *J* = 7.7 Hz, 1H), 7.69 – 7.55 (m, 3H), 7.46 (ddq, *J* = 8.1, 6.9, 1.3 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 7.7 Hz, 2H), 7.00 (d, *J* = 7.8 Hz, 2H), 6.83 (s, 1H), 2.34 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.9, 140.8, 137.5, 137.0, 136.7, 134.6, 131.6, 131.2, 130.8, 130.7, 130.1, 129.5, 129.4, 129.0, 128.8, 128.6, 127.9, 127.2, 126.7, 126.5, 126.4, 126.2, 122.8, 122.5, 76.7, 21.3; HRMS *m/z* calculated for $[C_{30}H_{24}Na]^+$ ($[M+Na]^+$): 407.1770, observed 407.1770.

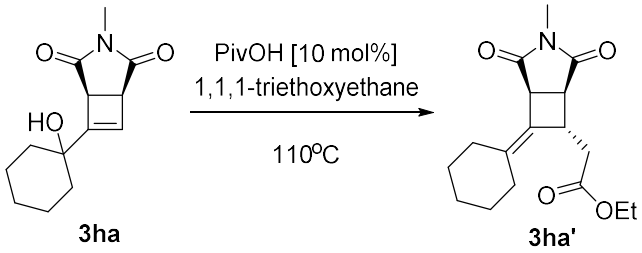
2-(trimethylsilyl)phenyl trifluoromethanesulfonate



To a solution of 2-bromophenol (1.5 mmol, 1.0 equiv.) in THF (3 mL, 0.5 M) was added HMDS (2.0 equiv.) at room temperature. The reaction mixture was reflux for 3 hours. Then the solvent and remained HMDS was removed under vacuum to obtain 2-bromophenyl trimethylsilyl ether, which was used in the next step without purification. To a solution of 2-bromophenyl trimethylsilyl ether in THF (2.1 mL, 0.7 M) was added n-BuLi (2.0 equiv., 2.5 M in hexane) dropwise at -78 °C. After 20 min, Trifluoromethanesulfonic anhydride (2.0 equiv.) was added to the mixture, and stirred 1 hour at -78 °C. The mixture was quenched by saturated $NaHCO_3$ solution and extracted by EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash

chromatography on silica gel. 39% yield; colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, J = 7.5, 1.9 Hz, 1H), 7.47 – 7.39 (m, 1H), 7.37 – 7.31 (m, 2H), 0.37 (s, 9H); The compound was identified by spectral comparison with literature data.[108]

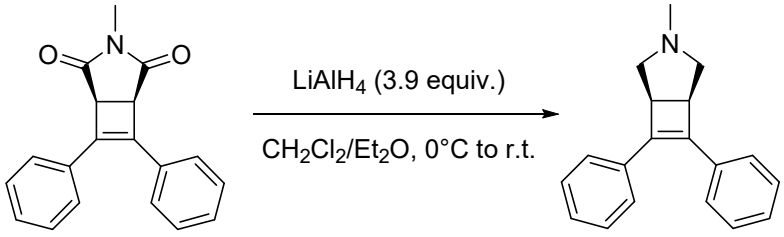
4.4.3. Synthesis of exomethylene cyclobutane



3ha 3ha'

To a solution of cyclobutene **3ha** (0.1 mmol, 1.0 equiv.) in triethyl orthoacetate (0.5 mL, 0.2 M) was added a catalytic quantity of trimethylacetic acid (0.1 equiv.) at room temperature. The reaction mixture was stirred at 110 °C for 24 hours. The reaction mixture was washed with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica gel to give the desired product **3ha′**. 18 mg, 60% yield; colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.16 (q, *J* = 7.1 Hz, 2H), 3.90 (d, *J* = 6.1 Hz, 1H), 3.34 (d, *J* = 3.5 Hz, 1H), 3.14 (dd, *J* = 6.1, 3.0 Hz, 1H), 2.97 (s, 3H), 2.74 (dd, *J* = 15.5, 4.2 Hz, 1H), 2.60 (dd, *J* = 15.5, 9.3 Hz, 1H), 2.21 (s, 2H), 2.00 – 1.85 (m, 2H), 1.49 (s, 6H), 1.27 (t, *J* = 7.5 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 176.3, 170.9, 141.8, 121.9, 60.7, 45.4, 41.5, 41.0, 38.5, 30.0, 29.6, 27.5, 27.4, 26.0, 25.1, 14.2; HRMS *m/z* calculated for $[C_{17}H_{24}NO_4]^+$ ($[M+H]^+$): 306.1700, observed 306.1701.

4.4.4. Synthesis of 3-methyl-6,7-diphenyl-3-azabicyclo[3.2.0]hept-6-ene (9)



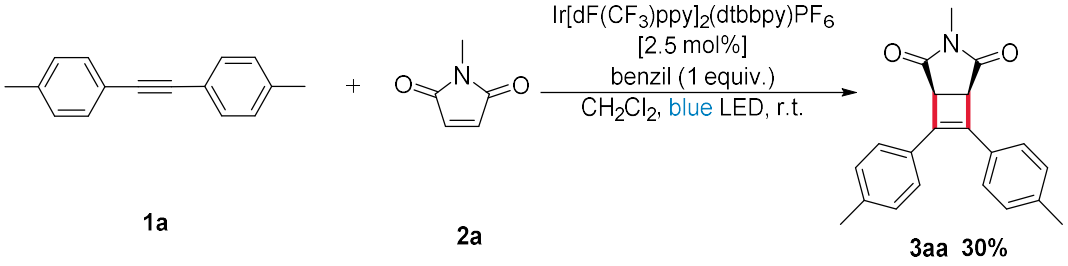
3ia 3ia'

To a slurry of $LiAlH_4$ (3.9 equiv.) in Et_2O (0.25 mL, 0.2 M) was added solution of cyclobutene **3ia** (0.05 mmol, 1.0 equiv.) in CH_2Cl_2 (0.5 mL, 0.1 M) at 0°C under nitrogen. The mixture was stirred at room

temperature for 1 hour, and H_2O was carefully added at 0 °C. To reaction suspension was dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on silica gel to give the desired product **3ia′**. 9 mg, 69% yield; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.54 (m, 4H), 7.34 – 7.28 (m, 4H), 7.27 – 7.21 (m, 2H), 3.54 (d, J = 6.0 Hz, 2H), 3.14 (d, J = 9.9 Hz, 2H), 2.36 (s, 3H), 2.08 – 1.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 134.4, 128.4, 128.0, 126.5, 55.5, 44.1, 42.2.; HRMS *m/z* calculated for $[C_{19}H_{20}N]^+$ ($[M+H]^+$): 262.1590, observed 262.1592.

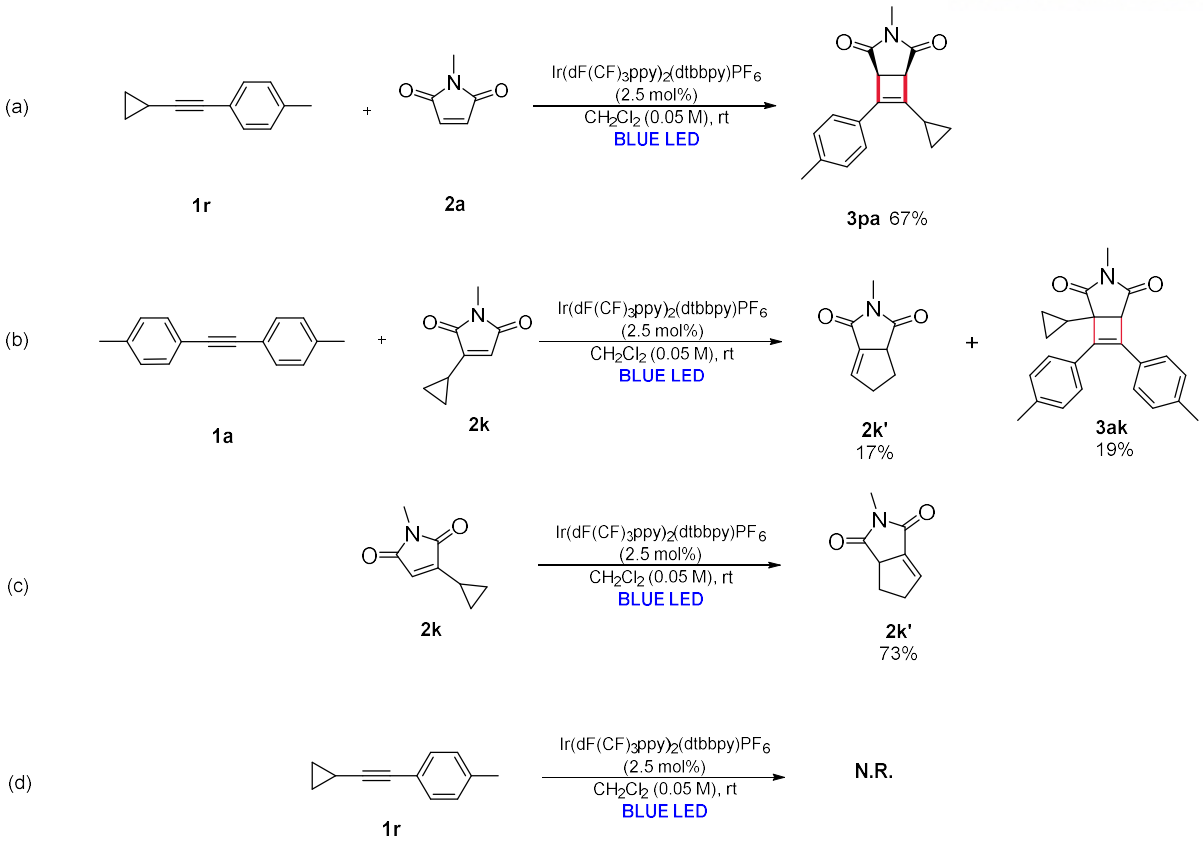
4.5. Mechanistic studies

4.5.1. Effect of Triplet Quencher



di(*p*-tolyl)acetylene **1a** (0.05 mmol, 1.0 equiv.), *N*-methylmaleimide **2a** (1.5 equiv.), photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5 mol%) and triplet quencher benzil (1.0 equiv.) were added to an oven-dried 4mL vial equipped with a stir bar. The combined materials were dissolved in CH_2Cl_2 (2 mL) under argon atmosphere in glovebox. The reaction mixture was then irradiated by 12 W blue LED lamp at room temperature (maintained with a cooling fan) for 4 hours. the solution was concentrated under reduced pressure. The yield was determined by ^{1}H NMR analysis ($CDCl_3$) of the crude reaction mixture using trichloroethylene as the internal standard; 30% yield.

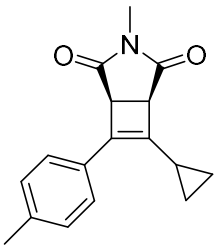
4.5.2. Radical Clock Experiments



a)

1-(cyclopropylethynyl)-4-methylbenzene **1r** (0.1 mmol, 1.0 equiv.), *N*-methylmaleimide **2a** (1.5 equiv.), (1.5 equiv.), and photocatalyst Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (2.5 mol%) were added to an oven-dried 4 mL vial equipped with a stir bar. The combined materials were dissolved in CH_2Cl_2 (2 mL) under argon atmosphere in glovebox. The reaction mixture was then irradiated by 12 W blue LED lamp at room temperature (maintained with a cooling fan). the solution was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to give **3ra**.

6-cyclopropyl-3-methyl-7-(*p*-tolyl)-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (3ra)

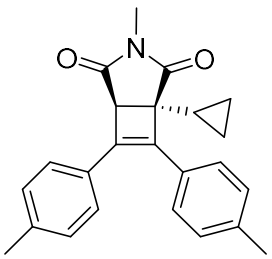


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.3 Hz, 2H), 3.89 (d, *J* = 3.5, 1H), 3.50 (d, *J* = 3.5 Hz, 1H), 2.94 (s, 3H), 2.35 (s, 3H), 1.96 – 1.89 (m, 1H), 1.16 – 1.10 (m, 1H), 1.00 – 0.80 (m, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 175.5, 143.1, 138.8, 138.2, 130.5, 129.5, 126.3, 43.8, 24.9, 21.5, 11.4, 6.8, 6.5; HRMS *m/z* calculated for $[C_{17}H_{18}NO_2]^+$ ($[M+H]^+$): 268.1332, observed : 268.1334

b)

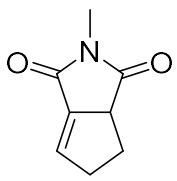
Di(*p*-tolyl)acetylene **1a** (0.1 mmol, 1.0 equiv.), 3-cyclopropyl-1-methyl-1H-pyrrole-2,5-dione **2k** (1.5 equiv.), and photocatalyst $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.5 mol%) were added to an oven-dried 4 mL vial equipped with a stir bar. The combined materials were dissolved in CH_2Cl_2 (2 mL) under argon atmosphere in glovebox. The reaction mixture was then irradiated by 12 W blue LED lamp at room temperature (maintained with a cooling fan) for 48 hours. the solution was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to give **3ak** (19% yield) and **2k′** (17% yield).

1-cyclopropyl-3-methyl-6,7-di-*p*-tolyl-3-azabicyclo[3.2.0]hept-6-ene-2,4-dione (3ak)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.2 Hz, 2H), 7.56 (d, *J* = 8.3 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 1H), 3.49 (s, 1H), 2.97 (s, 3H), 2.37 (s, 3H), 2.34 (s, 3H), 1.59 – 1.51 (m, 1H), 0.68 – 0.60 (m, 1H), 0.59 – 0.50 (m, 2H), 0.37 – 0.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 175.0, 141.7, 139.3, 139.0, 137.7, 130.3, 129.9, 129.4, 129.4, 127.5, 126.8, 55.7, 47.3, 25.0, 21.63, 21.60, 10.6, 2.5, 1.5; HRMS *m/z* calculated for $[C_{24}H_{24}NO_2^+]^+$ ($[M+H]^+$): 358.1802, observed 358.1802.

2-methyl-4,5-dihydrocyclopenta[*c*]pyrrole-1,3(2*H*,3a*H*)-dione (2k′)



^{1}H NMR (400 MHz, $CDCl_3$) δ 6.66 (dt, *J* = 3.7, 2.5 Hz, 1H), 3.80 (td, *J* = 7.9, 3.8 Hz, 1H), 3.00 (s, 3H), 2.98 – 2.83 (m, 1H), 2.74 (ddd, *J* = 17.6, 8.6, 3.8 Hz, 1H), 2.46 (dt, *J* = 13.8, 7.0 Hz, 1H), 2.03 (dtd, *J* = 12.5, 10.8, 8.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 165.1, 138.4, 136.3, 51.1, 37.4, 28.8, 24.6; HRMS *m/z* calculated for $[C_8H_{10}NO_2^+]^+$ ($[M+H]^+$): 152.0706, observed 152.0708.

c)

3-cyclopropyl-1-methyl-1H-pyrrole-2,5-dione **2k** (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 CH_2Cl_2 (2 mL) under argon atmosphere in glovebox. The reaction mixture was then irradiated by 12 W blue LED lamp at room temperature (maintained with a cooling fan) for 4 hours. the solution was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to give **2k′** (73% yield).

d)

1-(cyclopropylethynyl)-4-methylbenzene **1r** (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 CH_2Cl_2 (2 mL) under argon atmosphere in glovebox. The reaction mixture was then irradiated by 12 W blue LED lamp at room temperature (maintained with a cooling fan) for 48 hours. the solution was concentrated under reduced pressure. The reaction wasn't processed. (determined by ^{1}H NMR analysis ($CDCl_3$) of the crude reaction mixture.)

4.5.3. Stern-Volmer luminescence quenching experiments

Stern-Volmer luminescence quenching studies were carried out using a 0.1 mM solution of photocatalyst and variable concentrations of substrate in dry CH_2Cl_2 at room temperature under an argon atmosphere. The samples were prepared in 0.5 mL quartz cuvettes inside an argon filled glove-box and sealed with parafilm. The solutions were irradiated at 420 nm and the luminescence was measured at maximum emission wavelength of each photocatalyst. (I_0 = emission intensity of the photocatalyst in isolation at the specified wavelength; I = observed intensity as a function of the quencher concentration)

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