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INVESTIGATION OF REACTIONS OF ARYL TRIAZENE/DIAZENE AND THEIR APPLICATION FOR SYNTHESIS OF ARYLBORONIC ESTERS AND DIAZAHETEROCYCLES

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SCHOOL OF PHYSICAL & MATHEMATICAL SCIENCES

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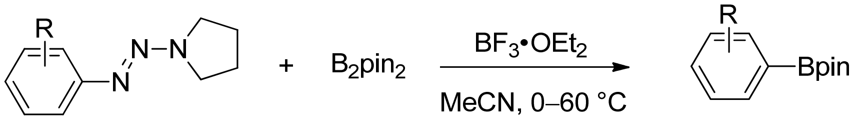
ABSTRACT

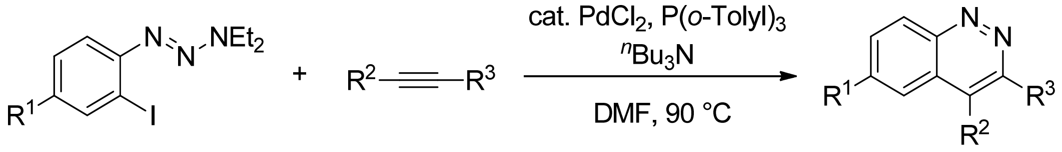
1-Aryltriazene and 1,2-diaryldiazene are important organic compounds not only for their biological or physical activities, but also for their synthetic applications. They are widely used as building block in heterocycle synthesis and coupling reactions for containing the unique N=N double bond. Thus the author started a research on these two kind of interesting compounds. In this Ph.D thesis, an investigation of the reaction of 1-aryltriazenes and 1,2-diaryldiazenes and their applications in organic synthesis is described.

1-Aryltriazenes are traditionally used as an equiverlant of aryldiazonium salt in the presence of a Brønsted or Lewis acid and could be applied to various nucleophilic substitution reactions, such as halogenation, hydroxylation and hydrogenation. However, there are no known reports about the carbon−metal bond formation in this kind of transformation, for example, creating a carbon−boron bond. At first the author focused on the reactivity of 1-aryltriazenes toward boron reagents. The author found 1-aryltriazene could be converted into the corresponding arylboronic ester via the deaminoborylation with B_2pin_2 mediated by BF_3•OEt_2.

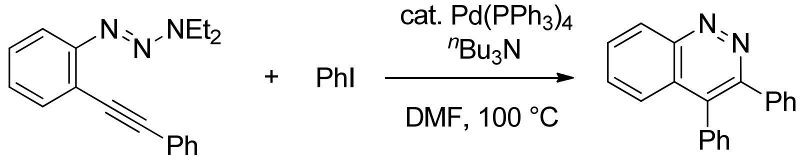


This method provides a facile transition-metal-free access to a variety of arylboronic esters, especially the electron-rich ones in moderate to good yield. 1-Aryltriazenes could be readily prepared from the corresponding arylamine in high yield and well tolerated under various conditions. Moreover, polymer-bonded 1-aryltriazenes have been extensively used in solid-supported synthesis. Thus this method is potentially useful in multistep synthesis and combinatorial chemistry.

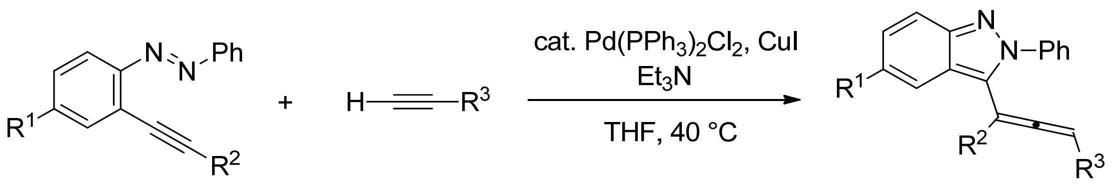
Next, the author investigated the reaction of 1-aryltriazenes with a transition-metal catalyst instead of Lewis acid. It was found that cinnolines could be achieved by palladium-catalyzed annulation of 1-(2-iodoaryl)triazene with internal alkynes. That is, 1-(2-iodoaryl)triazene react with internal alkyne in the presence of a palladium catalyst under basic condition to furnish 3,4-disubstituted cinnolines in moderate to good yields. Several internal alkynes are applicable for this reaction and it is compatible with a number of functional groups. By this method, not only a series of potentially useful cinnolines could synthesized, but also a new reactivity of the triazene group was shown.



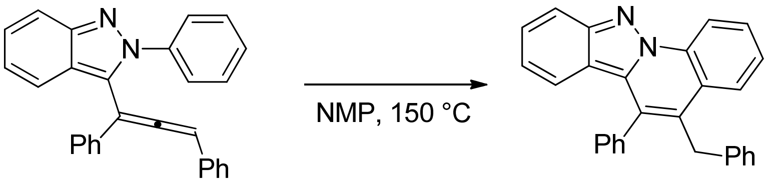
As a complement of the above cinnoline synthsis, the author found that the same 3,4-disubstituted cinnolines could be synthesized by palladium-catalyzed annulation of 1-(2-alkynylaryl)triazenes with arylhalides. This method provides a possibility to introduce different substitutions into the 3 and 4 position of cinnolines selectively although the yield was only about 40%.



1,2-Diazryldiazenes showed different reactivity from that of 1-aryltriazenes although they both contain the N=N double bond. Since the palladium-catalyzed annulation of 1-(2-phenylethynyl)phenyltriazenes afforded the 3,4-diphenylcinnolines, the author continued to study the corresponding the annulation of 1-(2-(phenylethynyl)phenyl)-2-phenyldiazenes. Finally, the author developed a $Pd(PPh_3)_2Cl_2/CuI$-catalyzed sequential cyclization/coupling of 1-(2-alkynylaryl)-2-phenyldiazene and the corresponding derivatives with a wide range of terminal alkynes provides 3-allenyl-2*H*-indazoles in good to excellent yields.



The reaction is quite general in which aryl, alkyl, silyl acetylene can be utilized. Under the optimized conditions a variety of substituents can be accommodated on the 1-(2-alkynylaryl)-2-phenyldiazene. Also, this method gives a hint as to how to introduce an alleny substitution into a heterocyclic system in an efficient and simple manner. Furthermore, indazolo[2,3-*a*]quinoline has been synthesized by thermal cyclization of 3-allenyl-2*H*-indazole. This aza-ene-ene-allene cyclization is very rare and represents a new stragety to synthesize the complex heterocycles.



Keywords: 1-aryltriazene, arylboronic ester, cinnoline, 1,2-diaryldiazene, carbene, 3-allenyl-2*H*-indazole.

INDEX OF ABBREVIATION

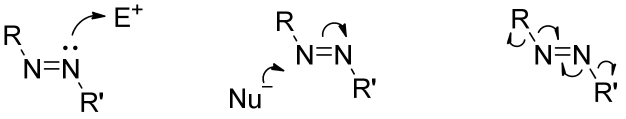
δ	chemical shift
ºC	degree centigrade
Ac	acetyl
AcOH	acetic acid
atm	standard atmosphere
B_2pin_2	bis(pinacolato)diboron
$CDCl_3$	deuterated chloroform
dba	dibenzylideneacetone
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
dppp	1,2-bis(diphenylphosphino)propane
DPSO	diphenyl sulfoxide
DME	1,2-dimethoxyethane
dppf	1, 1'-bis(diphenylphosphino)ferrocene
equiv	equivalent
FT-IR	Fourier transform infrared spectroscopy
Hz	hertz
h	hour
HRMS	high resolution mass spectroscopy
J	coupling constant
M^+	parent ion peak (mass spectrometry)
MHz	megahertz
min	minute
NMP	N-methyl-2-pyrrolidone

NMR	nuclear magnetic resonance
rt	room temperature
TBAF	tetra-*n*-butylammonium fluoride
THF	tetrahydrofuran
Temp	temperature
TESOH	triethylsilanol
TLC	thin layer chromatography

CHAPTER I Introduction

1. Overview

N=N bonds are present in many kinds of compounds, such as 1-aryltriazenes, 1,2-diaryldiazenes and diazaheterocycles. These compounds usually exhibit biological and physical activities due to the special structure. Furthermore, these compounds, especially the acyclic compounds, possess versatile reactivity in organic synthesis. First, the two nitrogen atoms both can act as a nucleophile to react with an electrophile. Second, the presence of the double bond makes it accessible to nucleophilic attack in particular it is activated by an adjacent electron-withdrawing group. In addition, the two bonded nitrogen atoms have the potential to form nitrogen gas and lead to other radical or ionic intermediates, which can subsequently undergo diverse transformations. Given their various useful applications in organic synthesis, they have attracted great attention for decades. Usually, the N=N bond can be stabilized by aryl groups and this makes the compounds easy to prepare and handled in the laboratory. Among the various compounds with a N=N bond substituted by aryl groups, 1-aryltriazenes and 1,2-diaryldiazenes have been extensively studied. Herein, the author would like to introduce these two kinds of compounds and related reactions.

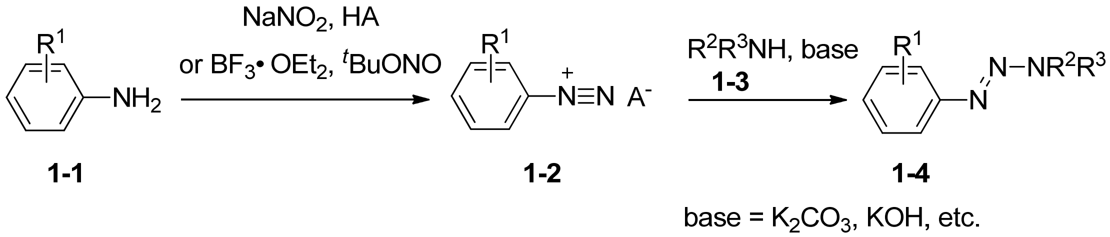


Scheme 1–1. Potential reactivities of N=N bonds

2. 1-Aryltriazene and related reactions

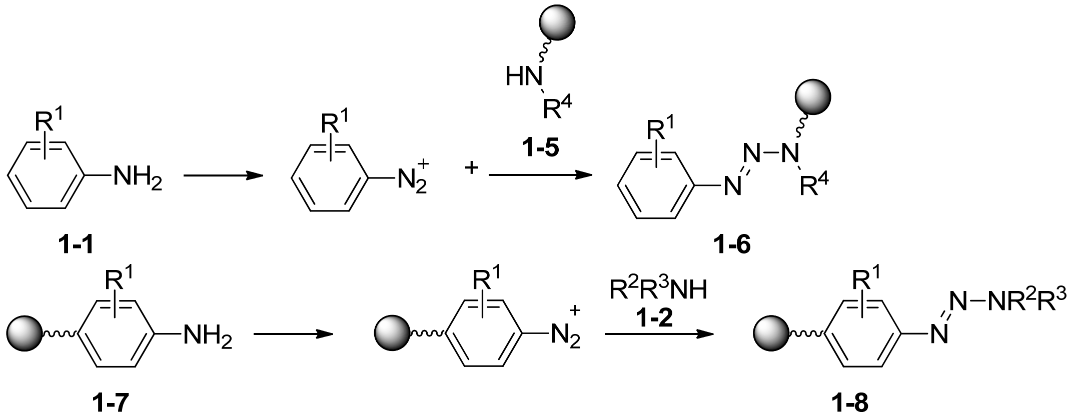
1-Aryltriazene refers to compounds bearing the functional group Ar-N=N-N-R^1R^2, in which R^1 and R^2 can be an alkyl, aryl or hydrogen group. 1-Aryltriazenes have been proved to be useful reagents since their discovery. The synthetic applications of 1-aryltriazene were developed mainly on the basis of dediazoniation transformations before 1950s. Recently, 1-aryltriazenes were recognized as a versatile tool which was widely used in organic synthesis, combinatorial chemistry, organometallic chemistry, polymer synthesis, etc.[1]

1-Aryltriazenes **1-4** can be easily prepared from readily available arylamines **1-1** which was diazotized with $NaNO_2$ and acid (e.g. HBF_4, HCl) to form the diazonium salt **1-2**, and then treated with primary or secondary amines in presence of base at -15–0 °C to afford corresponding 1-aryltirazene in high yield (Scheme 1–2). Alternatively the diazonium salt intermediate could also be prepared by treating arylamines with *ᵗ*BuONO and a strong Lewis acid like $BF_3 \bullet OEt_2$.



Scheme 1–2. Preparation of 1-aryltriazene

In addition to their use as synthetic building block, 1-aryltriazenes can be used as linker in solid-phase organic synthesis which is an important tool in combinatorial chemistry.[2] The synthesis of the solid-supported 1-aryltriazene **1-6** and **1-8** usually includes two approaches: reaction of a solid-supported amine with free diazonium ion[3] or a solid-supported diazonium ion with free amines[4] (Scheme 1–3).



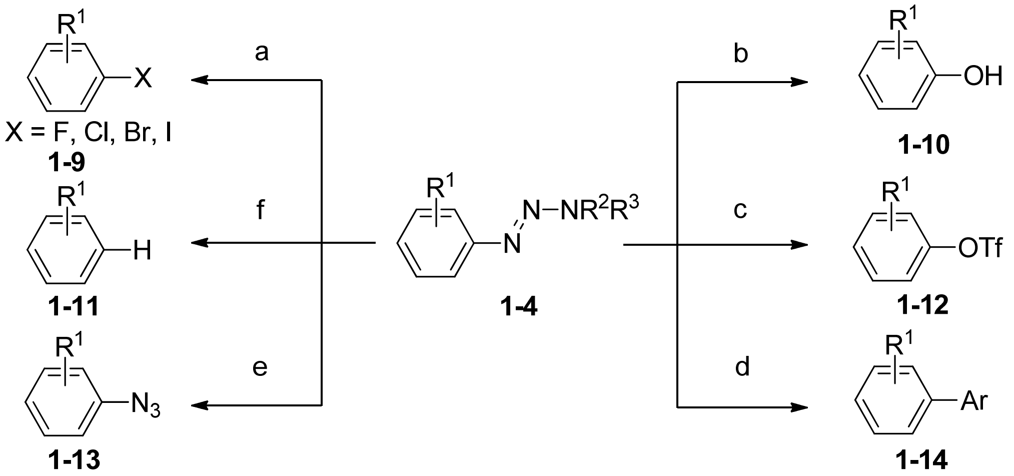
Scheme 1–3. Preparation of solid-support 1-aryltriazene

Normally, 1-aryltriazenes adopt *trans* conformation and could isomerize to *cis* conformation upon irradiation.[5] Also, the *cis*-triazenes could be converted into *trans*-triazene by thermally induced (for 1-aryltriazene derived from secondary amines)[6] or acid/base promoted (for 1,3-diaryltriazene)[7] isomerization.

Biological activities of 1-aryltriazenes have been thoroughly investigated by several groups.[8] It was shown that 3,3-dimethyl-1-phenyltriaz-1-ene could generate the methyldiazonium ion which may alkylate DNA. Thus 1-aryltriazene was considered to be carcinogenic and a potential antitumor reagent. *Thus considering its toxicity effect 1-aryltriazene should be handled cautiously and strictly avoided contact with skin.*

2.1. Aromatic nucleophilic substitution reactions of 1-aryltriazene

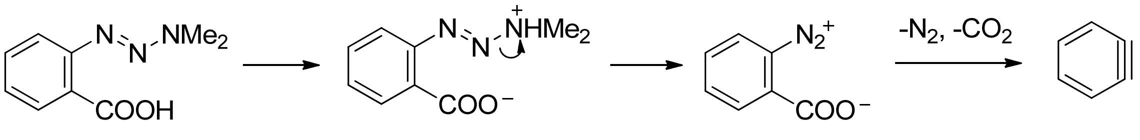
The development of efficient and reliable methods for the functionalization of arenes continues to attract considerable attention in organic chemistry. It has been known for many years that arylamines can undergo diazoniation and subsequent replacement by various nucleophiles to afford halo-, cyano-, hydroxyl-, vinyl-, aryl-, azido- arenes via either radical or ionic mechanism. These reactions have been widely used in the preparation of functionalized arenes because they offer the distinctive advantage of the aryl amine being inexpensive, abundant and readily available from nitration and subsequent reduction of arenes. 1-Aryltriazenes in organic chemistry appear most frequently as an equivalent of diazonium salts because they could be converted into the corresponding diazonium salt by treating with a protic or Lewis acid. In this respect, their reactions with nucleophiles, such as halogen, hydrogen, hydroxyl and azido groups proceed in the similar way as diazonium salt (Scheme 1–4).



Scheme 1–4. a) $(CH_3)_3SiCl$, NaI or NaBr, MeCN, 60 °C; b) Bio-Rad AG 50W-X12 acid resin, H_2O, reflux; c) TfOH, 90 °C; d) CF_3COOH, Arene, rt; e) $BF_3{\bullet}OEt_2/CF_3COOH$, NaN_3, CH_2Cl_2, rt; f) $HSiCl_3$, CH_2Cl_2, rt.

1-Aryltriazene reacts with halogen anions (F^-, Cl^-, Br^-, I^-) in acidic medium to give aryl-halide **1-9** in moderate to good yield.[9] Additionally, aryliodides could also be prepared from aryltriazene by treating with I_2 or MeI at elevated temperature.[10] Likewise, phenol derivatives **1-10** can be synthesized from decomposition of aryltrizenes by treating with acid in water.[11] Also, 1-aryltriazenes have been used to react with TfOH for the synthesis of aryltriflates **1-12**.[12] A biaryl synthesis was achieved by treating 1-aryltriazene with CF_3COOH in the corresponding aromatic solvent.[13] Moreover, arylazides **1-13** were obtained by the treatment of 1-aryltriazenes with NaN_3 under acidic condition.[14] Triazene group was found to be removed with acid in H_2O at room temperature to furnish the corresponding arene **1-11** in good yield.[15] Similarly, the solid-support 1-aryltriazene could be applied into nuleophilic substitution reactions such as azidation,[16] halogenation, and hydrogenation.[17]

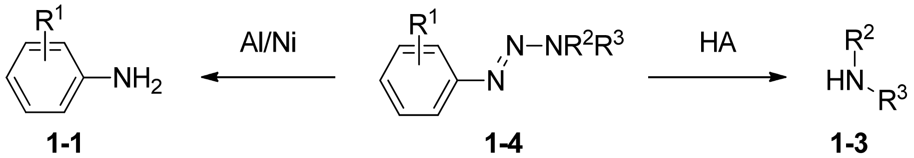
As a variant of nucleophilic substitution reactions, Heaney et al. demonstrated an application of 1-aryltriazene that bearing an *o*-carboxyl group as an aryne precursor. Upon heating, 2-(3,3-dimethyltriaz-1-en-1-yl)benzoic acid **1-15** and its derivatives afforded a variety of arynes which could be applied to subsequent cycloaddition reactions (Scheme 1–5).[18]



1-15 **1-16**

Scheme 1–5.

Not only the aryl intermediate derived from the decomposition of 1-aryltriazene but also the resultant amines can be used in organic synthesis. In this regard, 1-aryltriazene can be seen as protected primary/secondary amine which is tolerable under amine sensitive conditions.[19] In a few examples 1-aryltriazene were also used as protecting group of arylamines which were compatible with a series of organometallic reagents. The deprotection procedures include reduction of 1-aryltriazene by Al/Ni alloy to arylamine (Scheme 1–6).[20]

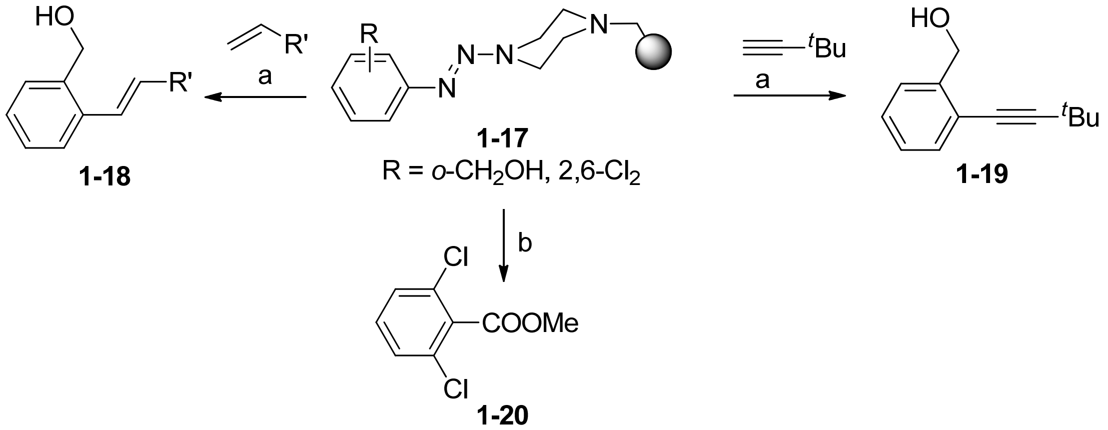


1-1 **1-4** **1-3**

Scheme 1–6. Deprotection of 1-aryltriazene

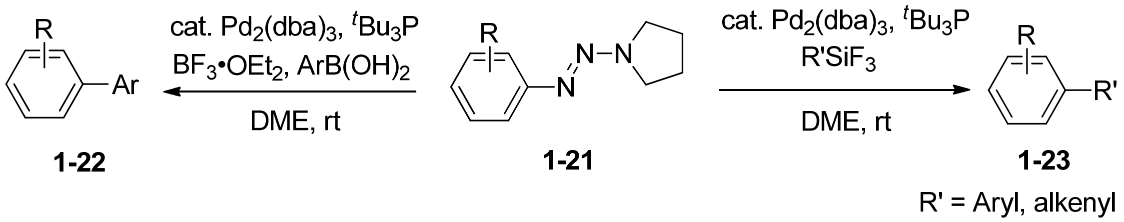
2.2. Palladium-catalyzed cross-coupling reactions with 1-aryltriazene

Dazonium salts have proven to be effective substrates for palladium-catalyzed cross-coupling reactions.[21] In presence of a palladium catalyst, diazonium salts served as equivalent of aryl halide and underwent oxidative addition to Pd(0) species, subsequent transmetallation and reductive elimination afforded desired coupling product. Despite the importance of diazonium salts and the high efficiency in a variety of transformation, poor stability and potential explosive hazard becomes a formidable problem. Recently, in view of 1-aryltriazenes which are used to generate diazonium salt by treating with protic or Lewis acid, significant efforts have been made to use aryltriazenes as a coupling partner. In 1999, Bräse and Schroen reported Mirozoki-Heck coupling and Sonogashira coupling reaction of solid-support 1-aryltriazenes. 1-Aryltriazene and alkene or alkyne were treated with TFA in presence of $Pd(OAc)_2$ or Pd/C to afford arylalkene **1-18** or arylalkyne **1-19** respectively.[3b] When CO was employed in the reaction, carbonylation was observed. Application of these transformations is particularly important to solid-support synthesis because they provide various modification of desired product from the resin after multicomponent or step synthesis by the cleavage of triazene linker.



Scheme 1–7. a) $Pd(OAc)_2$ or Pd/C, 2 equiv TFA, MeOH, 2 h, 40 °C; b) 1 bar CO, $Pd(OAc)_2$, 2 equiv TFA, MeOH, 2 h, 40 °C.

In 2002, Saeki and co-workers developed Suzuki-Miyaura coupling using 1-aryltriazene instead of aryl halides (Scheme 1–8).[22] 1-Aryltriazenes **1-21** were treated with $BF_3•OEt_2$, along with the arylboronic acid in the presence of $Pd_2(dba)_3/^tBu_3P$, biaryl **1-22** were obtained. Later, Saeki and co-workers reported the reaction between the 1-aryltriazene and aryl/alkenyltrifluorolsilane in the presence of Pd(0) catalyst delivered Hiyama cross-coupling products **1-23** (Scheme 1–8).[23] It was proposed that in the Suzuki-Miyaura coupling reaction, $BF_3•OEt_2$ palys dual roles: (1)acting as Lewis acid to generate diazonium salt intermediate; (2) providing F^- to assist the transmetallation of arylboronic acid by coordination to the boron atom. Whereas in the case of Hiyama coupling reaction, aryl/alkenyltrifluorosilane was used as Lewis acid to release the diazonium ion.

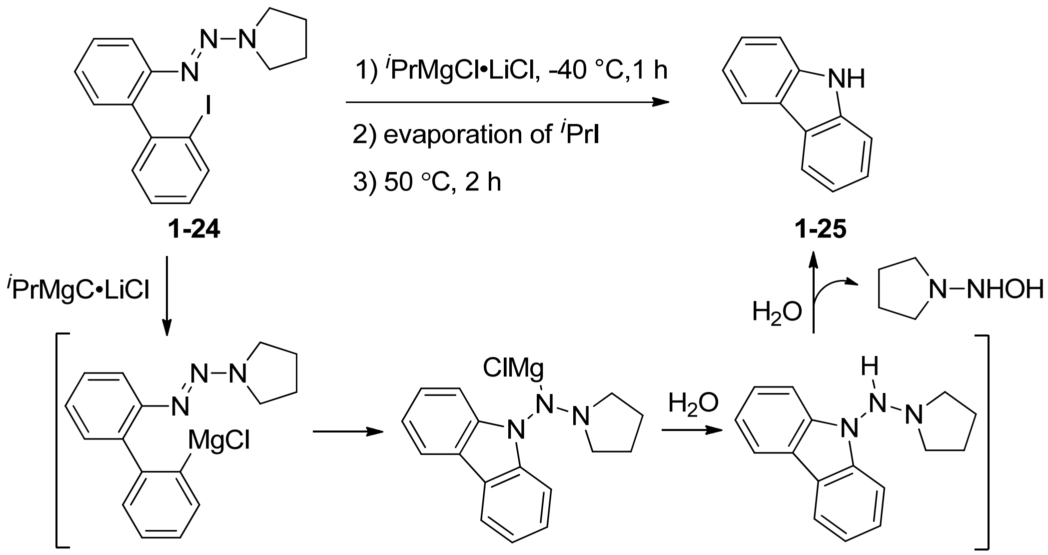


Scheme 1–8. Palladium-catalyzed Suzuki-Miyaura coupling and Hiyama coupling

2.3. Synthesis of aza-heterocycles with 1-aryltriazene

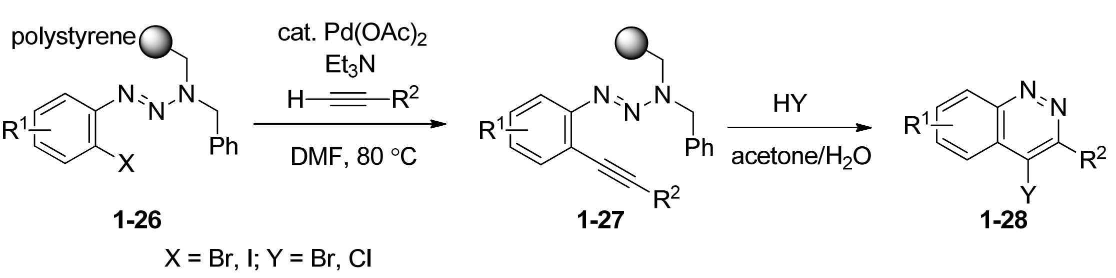
Aza-heterocycles are ubiquitous in natural products, pharmaceuticals, and as structural motifs in functional materials, as well as ligand in metal catalysis. As a result, strategies for the efficient and selective construction of various aza-heterocycles have been explored extensively. In addition to acting as a well-known leaving group, triazenes serve as a versatile building block which could be used as a one-nitrogen, two-nitrogen or three-nitrogen unit in different aza-heterocycles synthesis.

Liu et al. reported carbazole **1-25** synthesis from aryltriazene (Scheme 1–9). [24] In this protocol, 1-aryltriazenes could be regarded as masked arylamines. Accordingly, it undergoes intramolecular nucleophilic addition with the arylmagnesium reagent, forming a new C-N bond and releasing the hydroxylamine derivative after subsequent hydrolysis, finally providing the carbazole product.



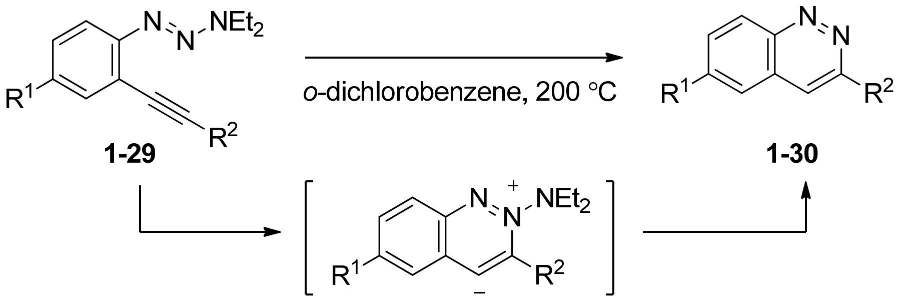
Scheme 1–9.

As a two-nitrogen synthon, 1-aryltriazenes were used to synthesize cinnoline derivatives. Bräse and co-workers developed an improved Richter-type[25] cinnoline synthesis from solid-support 1-aryltriazene **1-27** which involved the formation of the diazonium ion by protonation of the terminal nitrogen (**N3**) followed by 6-*endo* cyclization with an *o*-alkyne to form 3-halocinnolines **1-28** (Scheme 1–10).[26]



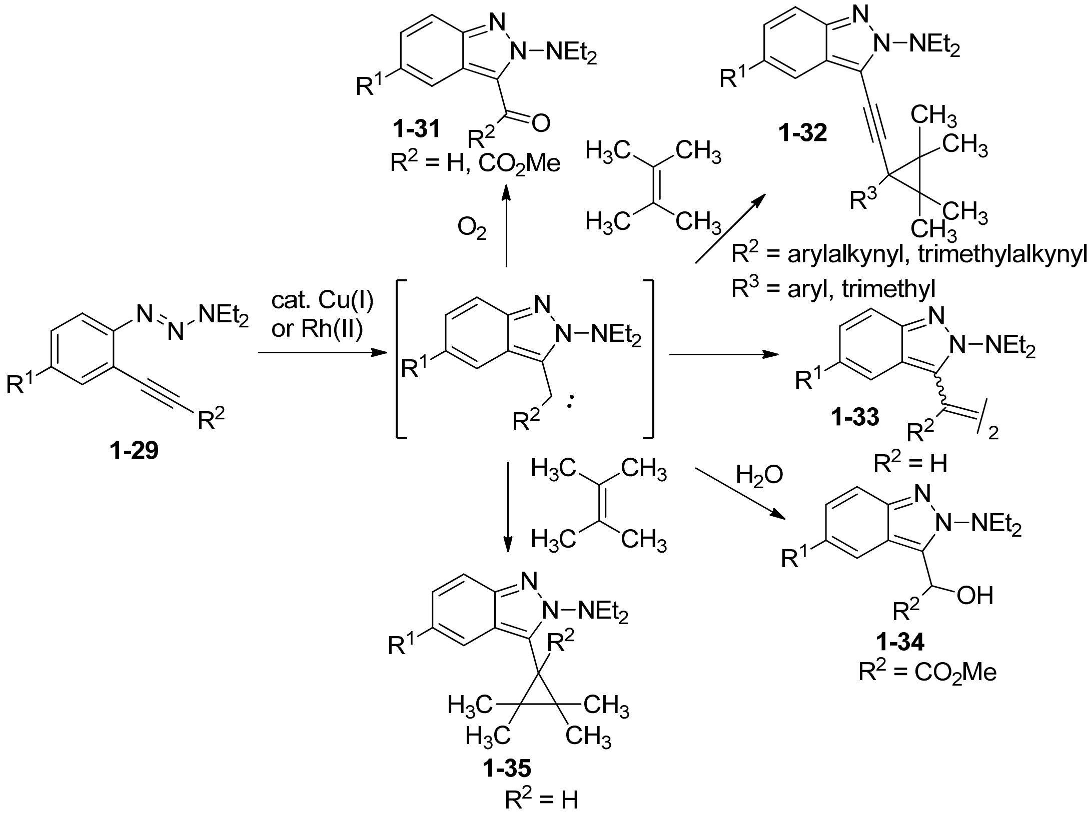
Scheme 1–10.

Haley and co-workers first achieved thermal cyclization of 1-(2-alkynylaryl)triazene, which entails ring closure of an azo-ene-yne system. When 1-(2-alkynylaryl)triazene was heated at 200 °C in *o*-dichlorobenzene, cinnoline **1-30** was obtained in excellent yield (Scheme 1–11).[27] The authors proposed a mechanism which involves formation of a zwitterion, abstraction of hydrogen from the methylene group attached to terminal N and finally production of cinnoline.[28]



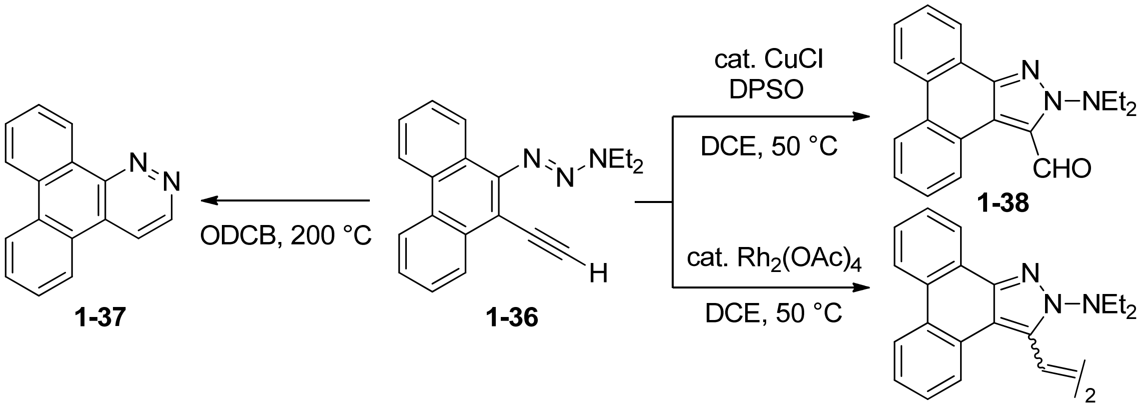
Scheme 1–11.

Furthermore, the use of 1-(2-alkynylaryl)triazenes were extended toward the preparation of various 2*H*-indazoles. When 3,3-diethyl-1-(2-alkynylphenyl)-triazene was subjected to the Cu(I) in the presence of O_2 at 60 °C, 1-(2-(diethylamino)-2*H*-indazol-3-yl)ketone or aldehyde was obtained in excellent yield.[27, 29] DFT calculation suggests a coarctate cyclization[30] pathway to form a carbene intermediate which reacts with O_2 to afford the ketone/aldehyde product. Moreover, use the carbene intermediate in other elaboration (e.g., C=C double bond insertion, dimerization, O-H bond insertion) (Scheme 1–12). Interestingly, when R^2 is alkynyl group the carbene intermediate is prone to undergo a 1,3-carbene shift and the rearranged carbene can be trapped by 2,3-dimethyl-2-butene.[31]



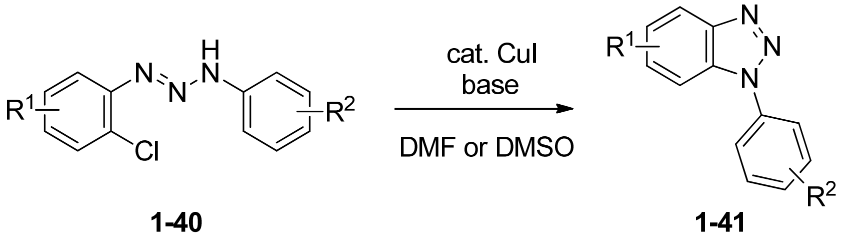
Scheme 1–12.

Recently, the Haley group successfully expanded this benzo-fused azo-ene-yne annulation to phenanthreno-fused azo-ene-yne systems(Scheme 1–13).[32]



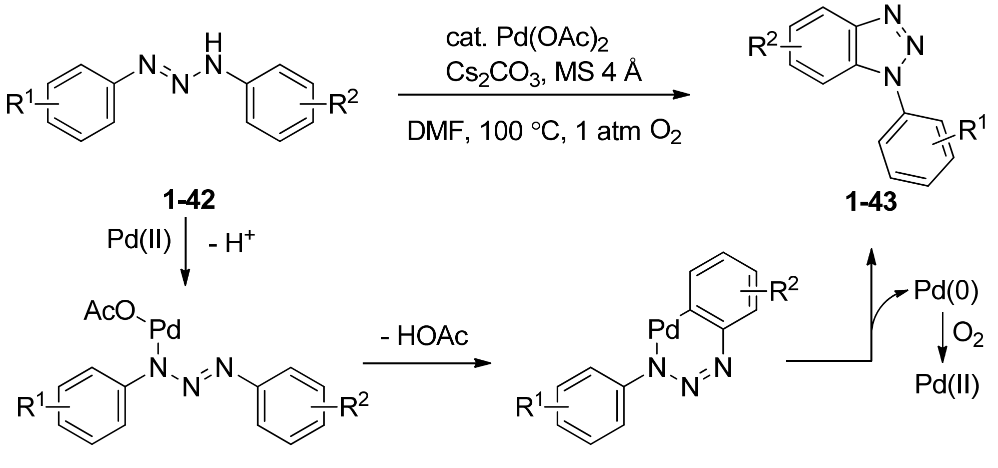
Scheme 1–13.

In addition, 1-aryltriazenes are valuable precursors for the preparation of benzotriazole and derivatives. It was reported that CuI-catalyzed intramolecular C-N bond formation of *o*-halo-1,2,3-benzotriazenes directly led to benzotriazoles **1-41** (Scheme 1–14).[33]



Scheme 1–14.

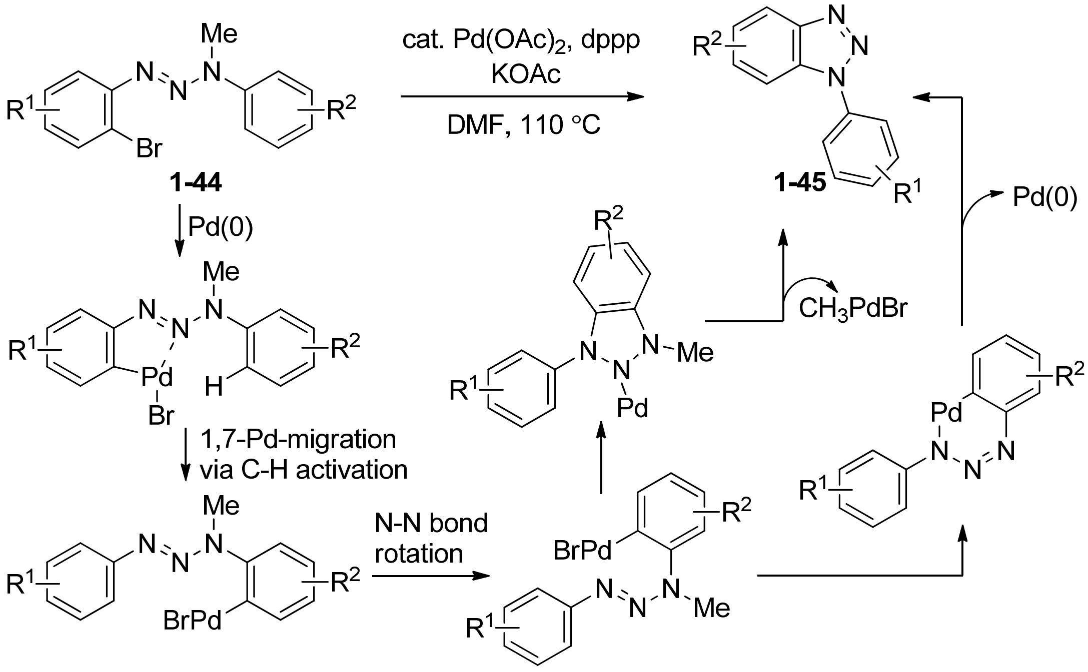
Benzotriazoles can also be accessed by the cyclization of 1,2,3-benzotriazenes **1-43** by means of oxidative C-N coupling. Kumar et al. made use of triazene group to direct palladium to activate aryl C-H bond towards amination. In this approach, the triazene group acts as both the directing group and amination reagent (Scheme 1–15).[34]



Scheme 1–15.

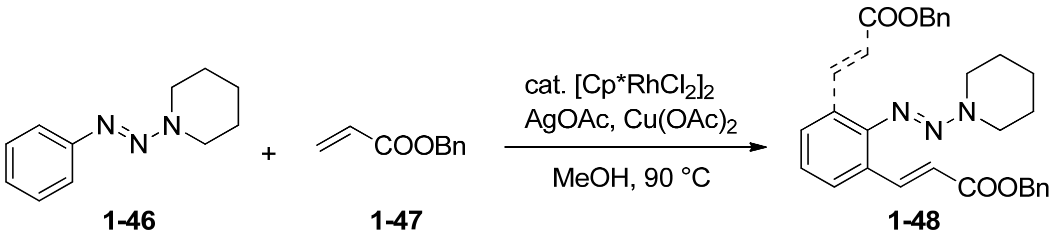
Although the aerobic oxidative cyclization of 1,2,3-benzotriazene provides quick access to benzotriazole, the regioselectivity of benzotriazole formation from asymmetric aryltriazene is difficult to control. A mixture of two regioisomers forms due to the 1,3-hydride shift induced isomerization of triazene.[35] With a closely related catalytic system, Ren and co-workers were able to synthesize benzotriazoles via a tandem oxidative addition, 1,7-palladium migration and followed by a C-N bond formation to afford a single product **1-**

45 selectively in good yields (Scheme 1–16).[36]



Scheme 1–16.

Regarding to the C-H activation reaction by using tirzene as directing group, there is an exciting development in 2012 (Scheme 1–17). In this reaction acrylate was introduced to the *ortho*-position of triazene by a Rh(III)-catalyzed Heck-type reaction.[37] As mentioned in section 2.1 and 2.2, the triazene moiety could be further transformed in to a variety of functional groups so as to afford a series of *ortho*-functionalized cinnamate.

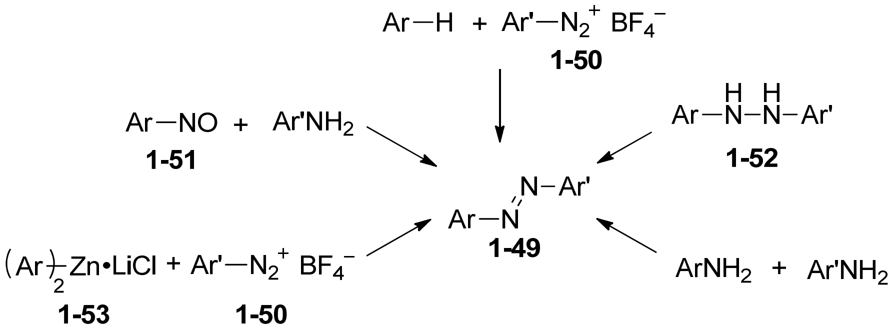


Scheme 1–17.

3. 1,2-Diaryldiazene and related reactions

1,2-Diaryldiazenes represented by the formula Ar-N=N-Ar’, in which the N=N bond could be stabilized by two aryl groups. 1,2-Diaryldiazene have attracted particular attention because of their photochromic isomerization between *trans* and *cis* conformation under thermal or irradiation conditions. This unique feature lead to the broad application of 1,2-diaryldiazenes in material and biological sciences, such as molecular machines, holographic recording devices and protein probes.[38] 1,2-Diaryldiazenes are also important to organic chemistry because they have been widely used as ligands in metal complexes, precursors of aza-heterocycles and substrates for transition-metal-catalyzed C-H activation reactions.

There are several methods available in the literature for the preparation of 1,2-diaryldiazene. The traditional method is oxidative condensation of arylamines with nitrosoarenes.[39] Also, 1,2-diaryldiazene could be prepared from simple azo coupling of diazonium salt and aromatic compounds especially the electron-rich aromatic compounds.[40] Additionally, 1,2-diaryldiazene have been prepared in good to excellent yields through the oxidation of 1,2-diarylhydrazine **1-52** (Scheme 1–18). [41]

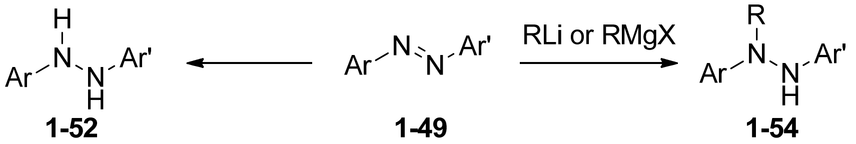


Scheme 1–18. Reported methods for the synthesis of 1,2-diaryldiazene

Recent advance of 1,2-diaryldiazene synthesis include the use of nano gold as catalyst and O_2 as oxidant to afford 1,2-diaryldiazenes from arylamines.[42] Later, Jiao and coworkersalso reporteda high yielding copper-catalyzed aerobic oxidative dehydrogenative coupling of arylamines to afford symmetric and asymmetric 1,2-diaryldiazene.[43] In these processes, dehydrogenative coupling of arylamine to 1,2-diarylhydrazine and further oxidation of 1,2-diarylhydrazine provides desired 1,2-diaryldiazene. Knochel and co-workers reported a novel synthesis of 1,2-diaryldiazenes from arylzinc reagents and arene diazounium salts.[44]

3.1. Hydrazine synthesis from 1,2-diaryldiazene

The reduction of aryldiazenes is a useful method for preparing syntheticcally useful biological active arylhydrazines **1-52**. A variety of reductants can be employed in this transformation, such as H_2, hydrazine,[45] organosilane and Zn/HCOOH.[46] Reaction of 1,2-diaryldiazenes with Grignard reagents or organolithium reagents have been reported to lead to trisubstituted hydrazine **1-54**. This reaction proceeds with addition of the organometallic reagent to the N=N bond and hydrolysis of the resulting intermediate to afford the desired hydrazine (Scheme 1–19).



Scheme 1–19.

3.2. *Ortho*-C−H bond functionalization reactions of 1,2-diaryldiazene

Owing to its coordinating property, 1,2-diaryldiazene has been widely used as a ligand in complex of main group metals (e.g. Sn,[47] B,[48] Se[49] and Te[50]) and transition metals (e.g. Pd,[51] Rh,[52] Ni,[53] Ru,[54] Pt,[55] Os,[56] Au,[57], Co[58] and Ir[59]). The metal atom is cooperatively stabilized by the phenyl, hydroxyl or amino groups while forming a chelate complex (Figure 1–1).

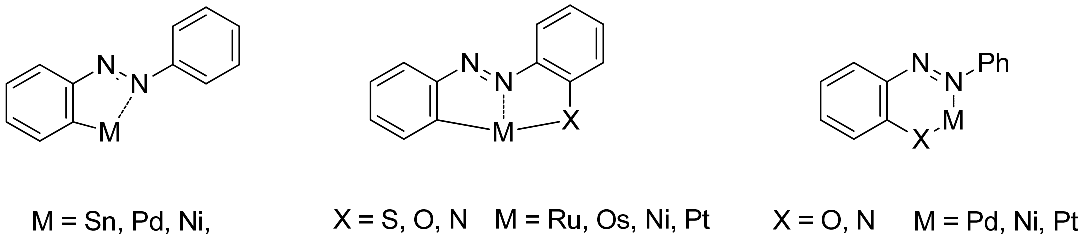
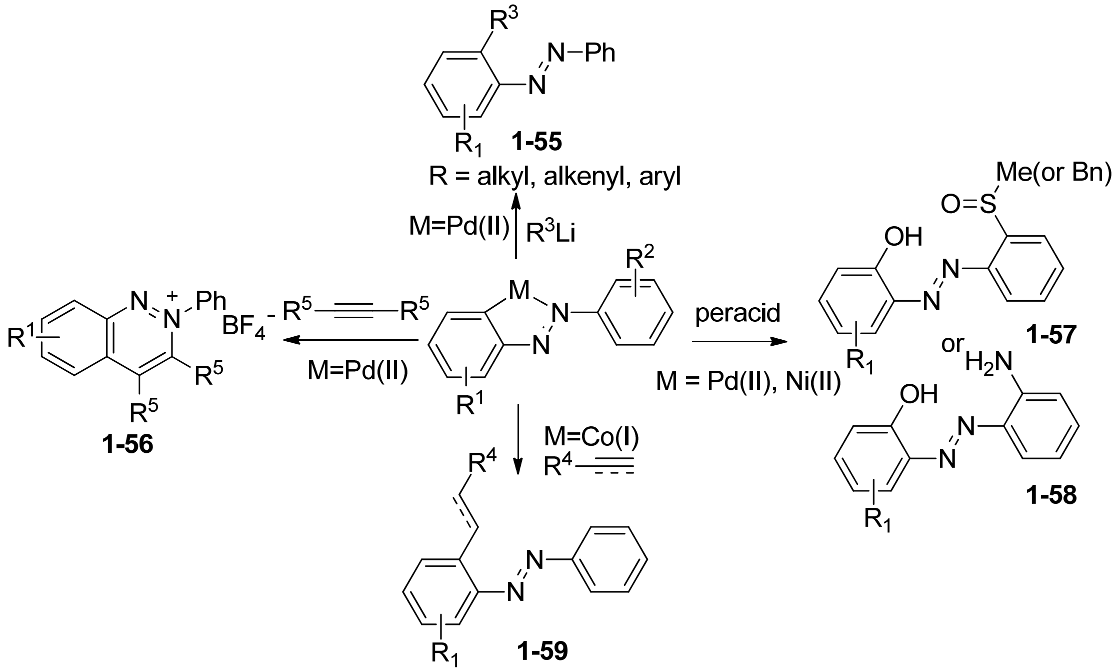


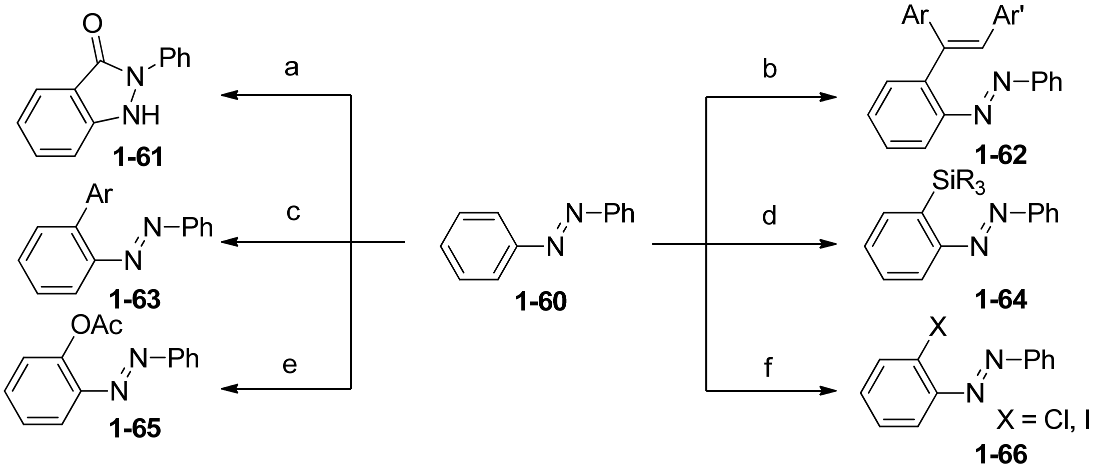
Figure 1–1.

From a synthetic point of view, various complexes of metals contains in 1,2-diaryldiazene as a ligand could be applied to prepare the *o*-functionalized 1,2-diaryldiazenes. For example, the available 1,2-diaryldiazene complexes of Pd(II) or Ni(II) could be oxidized by peracid to afford the 2’-hydroxyl-1,2-diaryldiazene **1-57** or **1-58**.[60] When the Pd(II) complex reacted with an alkyne an adduct cinnolinium salt was obtained.[61] Moreover, the reaction of Pd(II) complexes with organolithium led to 2’-alkyl, alkenyl and aryl-1,2-diaryldiazene respectively (Scheme 1–20).[62] It is noteworthy to mention that Kauffmann and co-workers reported direct *o*-methylation of 1,2-diaryldiazenes with MeLi in presence of $FeCl_3$ in which the $(CH_3)_3FeLi$ derived from MeLi and $FeCl_3$ was supposed to be the reactive alkylating reagent.[63] In another example, 1,2-diaryldiazene complexes of Co(II) provided 2’-alkenyl or alkyl-1,2-diaryldiazene via addition to alkyne or alkene.[64]



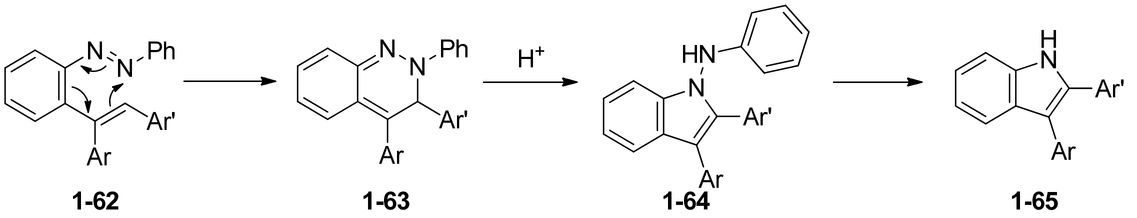
Scheme 1–20.

Consequently, considerable efforts have been directed toward the exploration of catalytic reactions, where the carbon-metal bond is not preformed, but via the chelation assisted C-H activation during the reaction (Scheme 1–21).



Scheme 1–21. a) $Co_2(CO)_8$, CO, 190 °C; b) $RhCl(PPh_3)_3$, ArC≡CAr', AcOH, 110 °C; c) $[Rh(OMe)(cod)]_2$, $ArB(OH)_2$; d) $Ru_3(CO)_{12}$, R_3SiH; e) $Pd(OAc)_2$, $PhI(OAc)_2$, AcOH; f) $Pd(OAc)_2$, NXS.

In 1956, Murahashi and Horiie firstly reported the $Co_2(CO)_8$ catalyzed *o*-carbonylation of 1,2-diphenyldiazene under 150 atm CO to afford 2-phenyl-1*H*-indazol-3(2*H*)-one **1-61**.[65] In 1990s, Kisch and co-workers studied the addition of 1,2-diaryldiazne to alkyne catalyzed by Ru, $RhCl(PPh_3)_3$[66] and $CoH_3(PPh_3)_3$[67] in presence of an acid. As expected 2'-alkenyl-1,2-diaryldiazene **1-62** was obtained via the insertion of the alkyne to the M-H bond derived from the *ortho*-metalation of 1,2-diaryldiazene. Interestingly, in the case of the $RhCl(PPh_3)_3$ catalyzed reaction, which was performed at 110 °C, 2'-alkenyl-1,2-diaryldiazene **1-62** was easily converted to 2,3-dihydrocinnoline **1-63** spontaneously by cyclization. Subsequent rearrangement under the acidic condition afforded *N*-aminoindole **1-64**, which finally gave the indole **1-65** as the isolated product by N-N bond cleavage (Scheme 1–22).



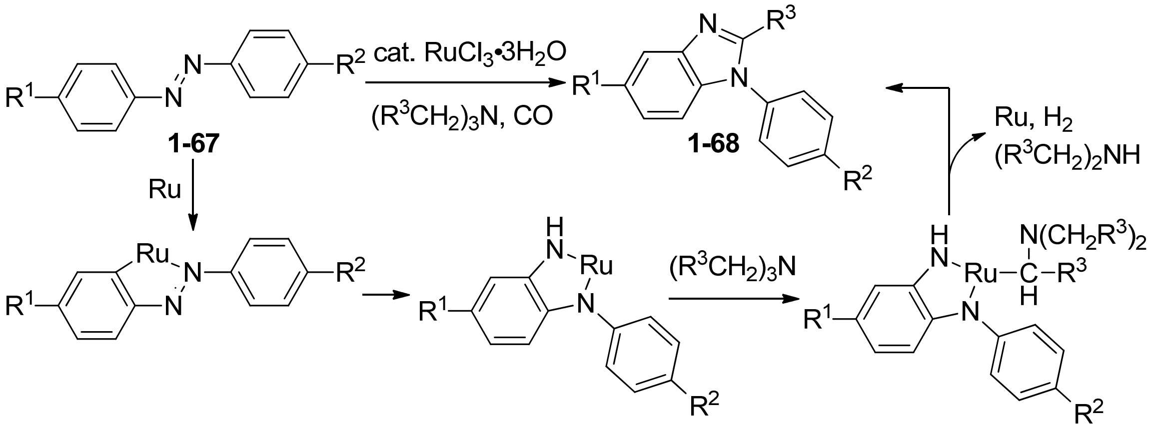
Scheme 1–22.

Along with the development of transition-metal-catalyzed C-H activation reactions, 1,2-diaryldiazenes were found to be versatile substrates in various transformations. In 2008, Miura et al. reported $[Rh(OMe)(cod)]_2$ catalyzed arylation of 1,2-diphenyldiazene with arylboronic acids.[68] Also, $Ru_3(CO)_{12}$ was used to activate the *o*-C-H bond of 1,2-diphenyldiazenes toward silylation with trialkylsilane.[69] The palladium-catalyzed acetyloxyation was achieved by Sanford and co-workers by treating 1,2-diaryldiazenes with $PhI(OAc)_2$ in acetic acid and in presence of $Pd(OAc)_2$.[70] Such C-H functionalization was further applied to halogenations by using NXS instead of $PhI(OAc)_2$.[71]

3.3. Aza-heterocycles synthesis from 1,2-diaryldiazene

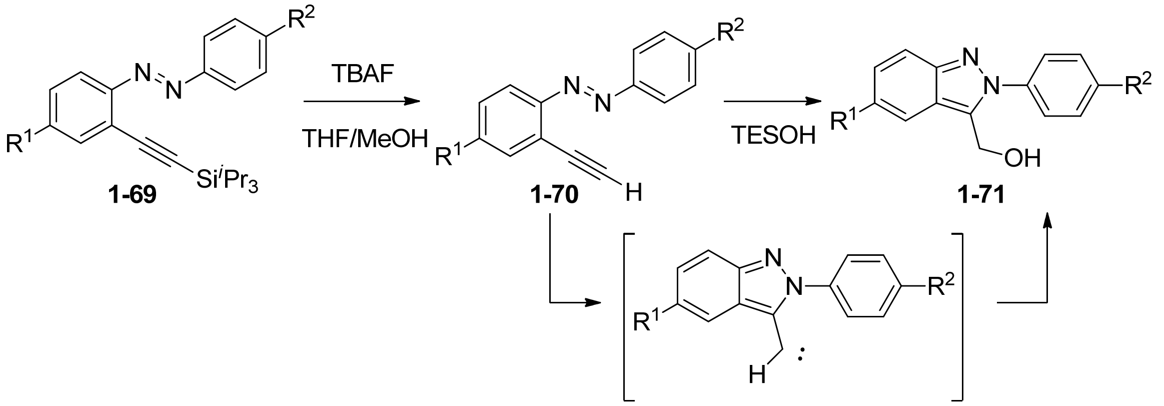
As shown above, cinnolinium salts, indazolone and indole were prepared by direct *o*-functionalization of 1,2-diaryldiazenes or derived from subsequent transformation. Other than this strategy, 1,2-diaryldiazenes can also be used in transition metal catalyzed aza-heterocyclic synthesis via rearrangement and annulation routes.

In 1985, Spencer reported a 1*H*-benzo[*d*]imidazole synthesis based on $RuCl_3•3H_2O$ catalyzed rearrangement of 1,2-diphenyldiazenes.[72] In this reaction, the 1,2-diphenyldiazene **1-67** form a metallacycle with Ru which underwent rearrangement to a *N*-phenyl-1,2-phenylene-diamine intermediate, followed by alkylation with an alkyl group from the tertiary amine, ring closure and aromatization to afford the desired product **1-68** (Scheme 1–23).



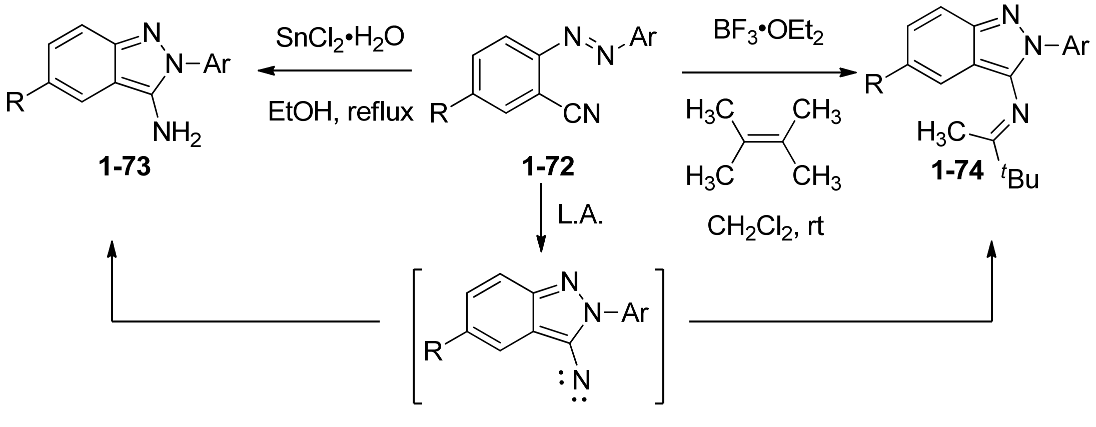
Scheme 1–23.

1-(2-alkynylaryl)-2-aryldiazenes can be viewed as an analogue of 1-(2-alkynyaryl)triazenes. When 1-aryl-2-(2-((triisopropylsilyl)ethynyl)aryl)diazene **1-69** was heated with TBAF at 60 °C in ethanol, (2-aryl-2*H*-indazol-3-yl)methanol **1-71** was furnished as the product (Scheme 1–24).[73] In this reaction, 1-aryl-2-(2-((triisopropylsilyl)ethynyl)aryl)diazene **1-69** underwent desilylation followed by cyclization to generate a carbene intermediate and O-H insertion, affording the desired alcohol products.



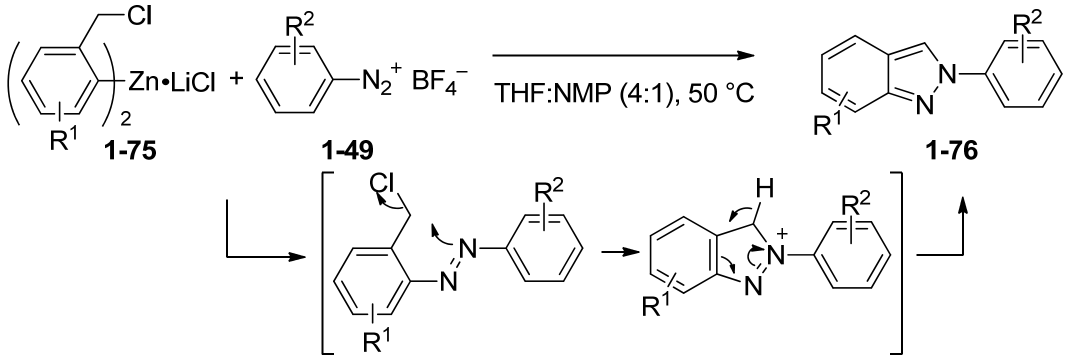
Scheme 1–24.

In an analogous reaction, the $SnCl_2•2H_2O$ promoted cyclization of 2-cyanoaryldiazenes **1-72** led to the formation of 3-amino-2*H*-indazoles **1-73**. When 2-cyanoaryldiazene was treated with 5.0 equiv. $BF_3•OEt_2$ in the presence of 2,3-dimethylbutene, iminylindazoles **1-74** were obtained (Scheme 1–25). The nitrene was proposed as the key intermediate which was converted into amine and imine by hydrolysis and C-H bond insertion respectively.[74]



Scheme 1–25.

2*H*-indazole can also be prepared from simple intramolecular nucleophilic substitution. Using 2’-chloromethyl-1,2-diaryldiazene as key intermediate, Knochel and co-workers established a one-pot synthesis of 2-aryl-2*H*-indazoles **1-76** from arylzinc reagents bearing a *o*-chloromethyl group and arene diazonium salts under similar reaction conditions (Scheme 1–26).[44]

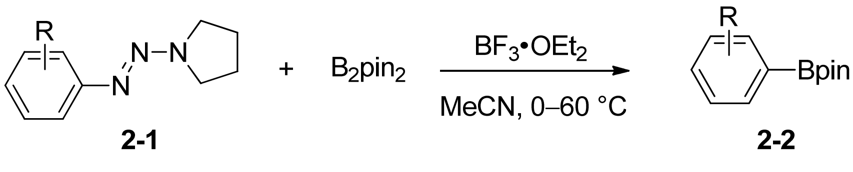


Scheme 1–26.

Here, we presented a concise review of literature of aryltriazene/diazene, demonstrating their applications as versatile reagents in organic synthesis. They provide a starting point for many studies in the field of organic chemistry as well as organometallic chemistry. Although numerous organic transformations have been applied to aryltriazenes/diazenes, it still attracts much interest to make effort to relatively unexplored field.

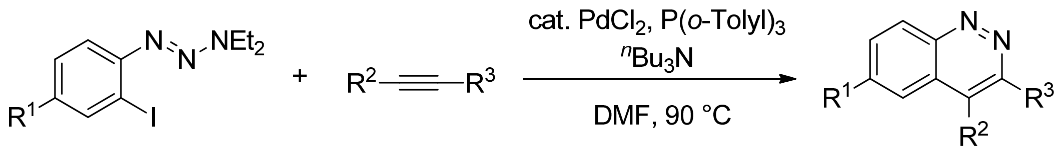
In the following 3 chapters the author would like to present his work about aryltriazenes/diazenes.

In chapter 2, the author studied the borylation of 1-aryltriazenes mediated by BF_3•OEt_2 (Scheme 1–27). This method not only provides a facile access to arylboronic esters but also becomes an important strategy complementary to the transformation of 1-aryltriazenes.



Scheme 1–27.

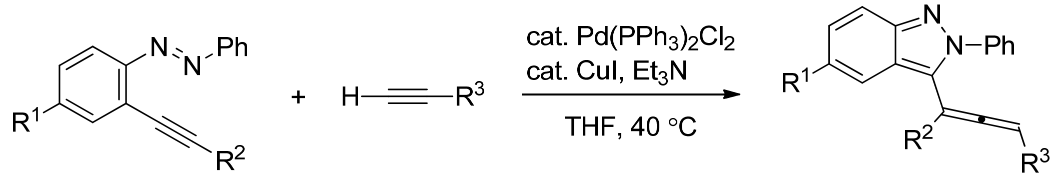
Subsequently, the author studied the synthesis of 3,4-disubstituted cinnolines via palladium-catalyzed annulation of 1-(2-iodoaryl)triazene with internal alkynes in chapter 3 (Scheme 1–28). This method provides a easy way to multi-substituted cinnolines, which are potentially useful heterocycles in bio- and physical chemistry.



3-1 **3-2** **3-3**

Scheme 1–28.

In chapter 4, the author found an unexpected reaction, the palladium/copper catalyzed sequential cyclization and coupling of 1-(2-alkynylaryl)-2-aryldiazene with terminal alkynes to affored 3-allenyl-2*H*-indazole (Scheme 1–29). This reaction represents a fast and efficient strategy to complex heterocycles.



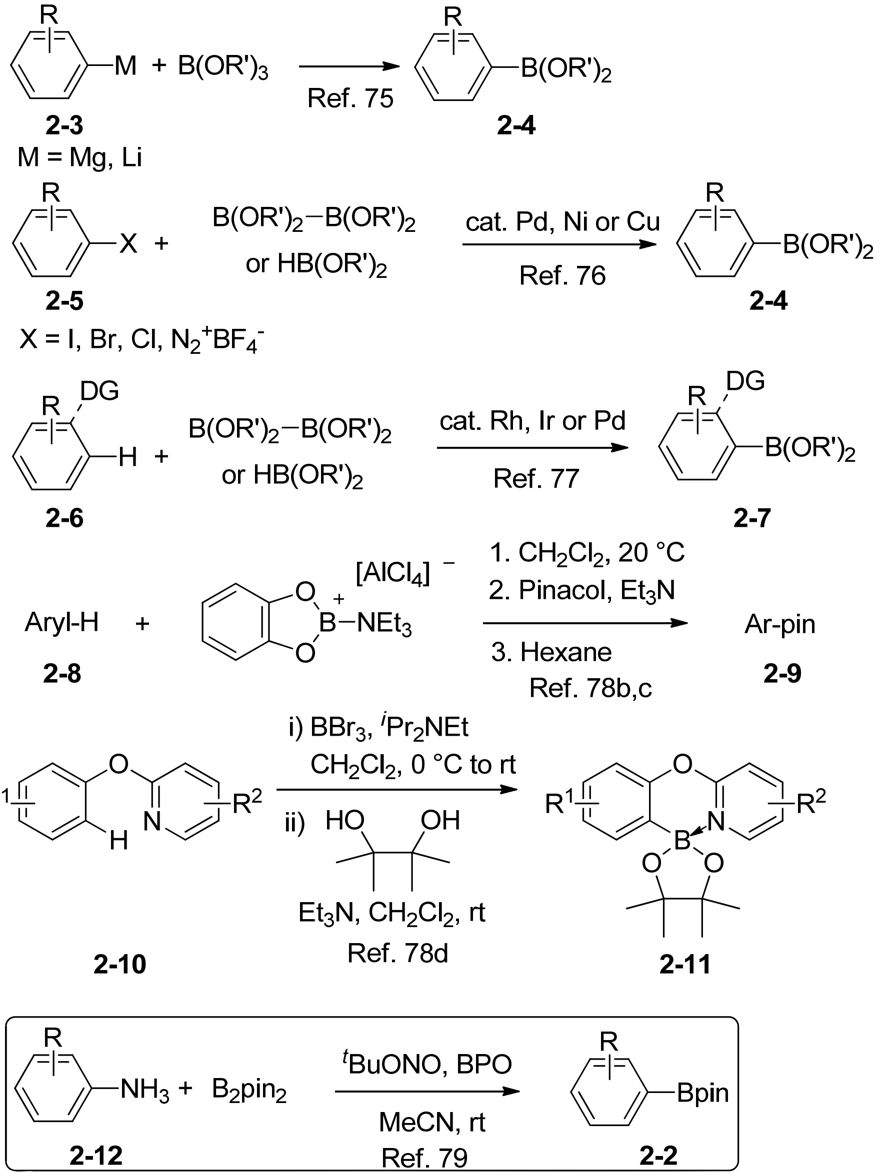
4-1 **4-2** **4-3**

Scheme 1–29.

CHAPTER II Transition-Metal-Free Borylation of 1-Aryltriazene Mediated by BF_3•OEt_2

1. Introduction

Arylboronic acids and esters have been widely used to create carbon−carbon and carbon−heteroatom bonds in organic synthsis over the past several decades.[75] As they are one of the most powerful synthetic tools, various methods for the synthesis of arylboronic acid derivatives have been developed. Conventional methods to prepare these boron compounds usually involve a stoichiometric amount of air and moisture sensitive aryl-metal reagents under harsh reaction conditions.[76] In this aspect, transition metal-catalyzed borylation of aryl halides which possess tremendous versatility and functional group compatibility is a more reliable route.[77] This methodology has been recently expanded to include C−H bond activation strategy and a significant progress was achieved.[78] As transition metal catalysts are expensive and can cause a problem of metal residue in the final pharmaceutical product, there has been focus on development of transition-metal-free processes in organic synthesis.[79] Recently, borylation of arylamines via oxidative deamination by *tert*-butyl nitrite has been reported.[80] It provides a direct conversion of arylamine to arylboronic ester under metal-free conditions which brought an innovative development to arylboronic ester synthesis. However, the substrate scope was still limited.



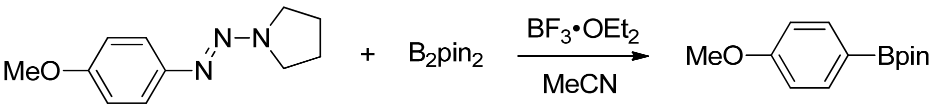
Scheme 2–1. Reported methods for preparation of arylboronic ester.

Herein, we report $BF_3{\bullet}OEt_2$-mediated deaminoborylation of a wide range of functionalized aryltriazenes. Aryltriazene could be readily prepared from corresponding arylamine in high yield and easy to handle. Moreover, polymer-bonded triazenes have been extensively used in solid-supported synthesis.[2] Thus this method may potentially have wide application in combinatorial chemistry. Besides, triazene moiety could be tolerated under various reaction conditions.[24, 81] Thus 1-aryltriazene was expected to be a useful precursor to arylboronic ester in a multistep synthesis.

2. Result and discussion

Inspired by the borylation of arylamine and Pd-catalyzed Suzuki-Miyaura coupling of 1-aryltriazene in presence of BF_3•OEt_2, we envisioned a borylation of 1-aryltriazene in presence of BF_3•OEt_2. Our initial study began with *p*-methoxyphenyltriazene **2-1a,** which was reacted with 1 equiv of bis(pinacolato)diboron (B_2pin_2) in the presence of 1.1 equiv of BF_3•OEt_2 in 1,2-dimethoxyethane (Table 2–1, entry 1). Gratifyingly, the reaction proceeded smoothly and the desired product, arylboronic ester **2-2a** was isolated in 41% yield after 10 min at room temperature. Next, the reaction solvents were screened under the same reaction conditions (entries 1−9), and acetonitrile gave the highest yield of 52% (entry 6). Only trace amount of product was observed when more polar solvents such as DMSO and DMF were used and aryltriazene **2-1a** was recovered in a significant amount (entries 3 and 4). When the amount of BF_3•OEt_2 was reduced to 1 equiv, the yield of product was not affected at all (compare entries 6 and 10). Then catalytic amount of BF_3•OEt_2 was tested but thus led to only trace amount of product (entry 11). This meant that BF_3•OEt_2 acted as a stoichiometric reagent rather than as a catalyst. The yields increased when the reaction was performed at lower temperatures (entries 12 and 13). The amount of B_2pin_2 was optimized in entries 14−17, and 1.5 equiv showed the highest efficiency (entry 15). The effect of the counter anion on the Lewis acid was investigated by using BCl_3 and BBr_3 in replace of BF_3•OEt_2 (entries 19 and 20). The desired product **2-2a** was obtained in both cases, however the yields dropped to a large extent. It is known that radical initiators such as benzoyl peroxide (BPO) enhance the borylation of aryl amine which was proposed a radical mechanism, however, adding BPO gave no improvement in both product yield and reaction time (entry 21).[80] Finally, we concluded that the optimized reaction conditions is: 1 equiv BF_3•OEt_2 added to a mixture of 1-aryltriazene and 1.5 equiv of B_2pin_2 in MeCN dropise at 0 °C and then the resulting mixture stirred at 0 °C.

Table 2–1. Reaction Conditions Optimization[a]



2-1a **2-2a**

Entry	Molar Ratio (**2-1a**/B_2pin_2/ BF_3•OEt_2)	Solvent	Time (min)	Temp (°C)	Yield[b] (%)
1	1/1/1.1	DME	90	rt	41
2	1/1/1.1	DCM	5	rt	27
3	1/1/1.1	DMF	120	rt	trace[c]
4	1/1/1.1	DMSO	120	rt	trace[c]
5	1/1/1.1	EtOH	90	rt	43
6	1/1/1.1	MeCN	5	rt	52
7	1/1/1.1	Benzene	5	rt	38[d]
8	1/1/1.1	Acetone	120	rt	trace
9	1/1/1.1	1,4-dioxane	120	rt	trace
10	1/1/1	MeCN	5	rt	52
11	1/1/0.2	MeCN	30	rt	trace[c]
12	1/1/1	MeCN	5	0	60
13	1/1/1.1	MeCN	15	−15	62
14	1/1.1/1	MeCN	5	0	62
15	1/1.5/1	MeCN	5	0	73
16	1/2/1	MeCN	5	0	75
17	1/0.5/1	MeCN	30	0	28
18	1/1.5/1	MeCN	5	0	73[e]

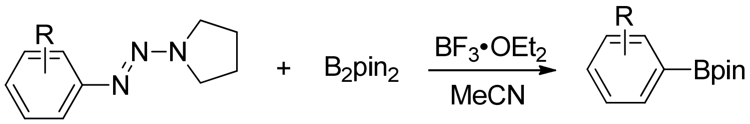
19	1/1.5/1	MeCN	5	0	30[e,f]
20	1/1.5/1	MeCN	5	0	5[e,g]
21	1/1.5/1	MeCN	5	0	73[e,h]

[a] Unless otherwise stated, reactions were carried out on a 0.5 mmol scale 5.0 mL solvent under N_2 atmosphere and monitored by TLC. [b] Isolated yield. [c] Starting material remained. [d] 6% 1-methoxy-4-phenylbenzene was obtained as a side product. [e] 2.0 mL MeCN was used. [f] 1.0 equiv of BCl_3 (1 mol/L hexane solution) was used in place of BF_3•OEt_2. [g] 1.0 equiv of BBr_3 (1 mol/L dichloromethane solution) was used in place of BF_3•OEt_2. [h] 2 mol% BPO in comparison with literature.

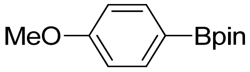
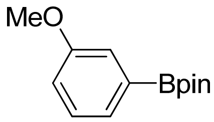
As shown in Table 2–2, a series of aryltriazene were then subjected to the above optimized reaction conditions. The reaction was successful for a variety of aryltriazenes and provided low to high yields of the corresponding arylboronic ester. The reactivity of substrates was found to be linked to the electronic effects of the substituent on the benzene ring. For example, 4-methoxyphenyltriazene gave **2-2a** in 73% yield within 5 min at 0 °C (Table 2–2, entry 2), however the less electron rich 3-methoxyphenyltriazene rendered the reaction more sluggish, afforded **2-2b** in 50% yield after 30 min at room temperature (Table 2–2, entry 3). Unsubstituted phenyltriazene displayed inferior reactivity and led to only 36% yield while napthyltriazene furnished **2-2k** in 65% yield (Table 2–2, entry 11). The substrates bearing 4-thionyl or 4-amino group is considered to be unstable towards an oxidant such as nitrite which was used in the borylation of arylamines. Even with such a substrate, the reaction proceeded and gave the desired boronic ester which has a sulfur or nitrogen functionality although the yields are modest, possibly due to the stronger coordination of sulfur and nitrogen atoms to BF_3 (Table 2–2, entries 4−5). The reactions of phenyltriazene with a simple alkyl substituent at para-, ortho-position also proceeded to afford **2-2g**, **2-2h** and **2-2i** in 75%, 83%, and 71% yield, respectively (Table 2–2, entries 7−9). The borylation of *ortho*-methyl substituted substrate (Table 2–2, entry 8) led to good yield in contrast with an *ortho*-methoxyl substituted one, which gave no product

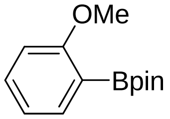
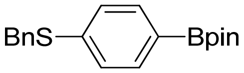
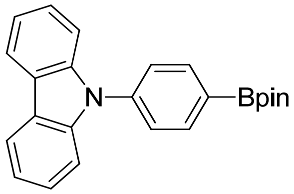
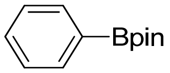
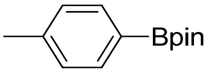
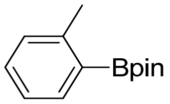
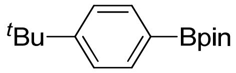
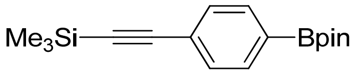
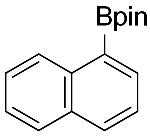
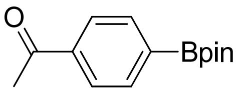
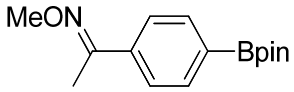
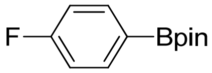
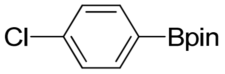
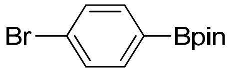
(Table 2–2, entry 3). The alkynyl moiety was found to be tolerated in the reaction conditions to give alkynylphenylboronic ester **2-2j** in 53% yield. As stated above, the reaction is suitable for rather electron rich aryltriazenes and it was revealed that strongly electron-deficient aryltriazenes such as acylphenyltriazene gave no desired product (entry 12). It is noteworthy that oxime derivative which is a synthetic equivalent to a ketone could be applied for this borylation, and boronic ester **2-2m** which has an oxime functionality was obtained in 70% yield (Table 2–2, entry 13). Development of the preparation of haloarylboronic esters, especially bromo- and iodo-substituted ones, is important because they are difficult to synthesize by the conventional transition metal-catalyzed borylation of arylhalides. It is notable that a variety of haloaryltriazenes are applicable for this borylation (entries 14–21). Although requiring a higher temperature (60 °C) and longer reaction times (1–2 h) for the complete consumption of the starting material, 4-fluoro-, 4-chloro-, 4-bromo-, and 4-iodophenyltriazenes were converted to the corresponding boronic esters **2-2n–p**, **2-2s** in 34–54% yields (entries 14–16, 19). The reactivity and yield were improved when electron-donating substituents were attached to the phenyl ring (entries 18, 20, 21).

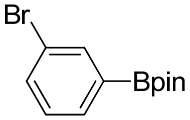
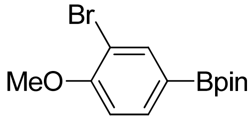
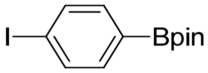
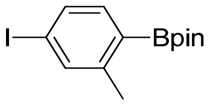
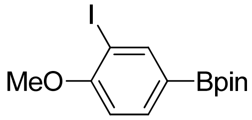
Table 2–2. Substrates scope for the borylation of 1-aryltriazene[a]



2-1a–u **2-2a–u**

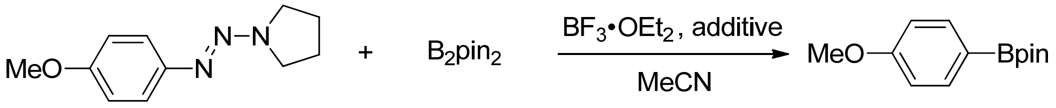
Entry	Product	Temp (°C)	Time (min)		Yield (%)^b
1		0	5	**2-2a**	73
2		rt	30	**2-2b**	50

3		60	30	**2-2c**	trace
4		rt	15	**2-2d**	$62^{c,d}$
5		rt	30	**2-2e**	$52^{c,d}$
6		0	60	**2-2f**	36
7		0	20	**2-2g**	75
8		0	20	**2-2h**	83
9		0	20	**2-2i**	71
10		rt	90	**2-2j**	53
11		0	30	**2-2k**	65
12		rt	60	**2-2l**	trace
13		0	60	**2-2m**	$70^{c,d}$
14		60	60	**2-2n**	54
15		60	60	**2-2o**	44
16		60	60	**2-2p**	44

17		60	120	**2-2q**	30
18		0	90	**2-2r**	72
19		60	60	**2-2s**	34
20		0	120	**2-2t**	64[c]
21		0	90	**2-2u**	62

[a] Unless otherwise stated, all the reactions were carried out by adding 0.5 mmol BF$_3$•OEt$_2$ to a solution of 0.5 mmol **2-1** and 0.75 mmol B$_2$pin$_2$ in 2 mL MeCN under N$_2$ atmosphere and monitored by TLC. [b] Isolated yield. [c] 5 mL solvent was used. [d] BF$_3$•OEt$_2$ was added at 0 °C and the reaction mixture was warm to rt gradually.

To understand the mechanism of this transformation we performed a series of control reactions and obtained a number of valuable insights (Scheme 2–2). A radical mechanism was proposed for the direct conversion of arylamines to arylboronic esters via an arenediazonium salt intermediate.[80] Accordingly, we tested the parent reaction described above in presence of some radical trapping reagents (Scheme 2–2). Product **2-2a** arising from the borylation in presence of 1.0 equiv BHT was isolated in 72% yield. Repeating the reaction in the presence of 1.0 equiv of ^{n}Bu$_3$SnH gave **2-2a** in 70% yield. Although a longer reaction time and room temperature was required the desired product was obtained with no significant loss. Given the effect of radical trapping reagents and radical initiator (Table 2–1, entry 21) observed for the borylation of aryltriazene, radical intermediate seems not involved in this reaction.



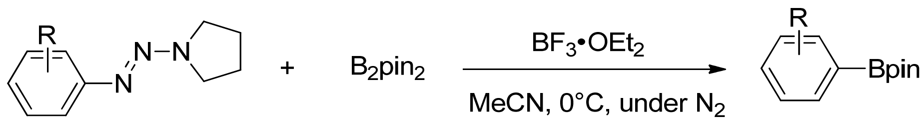
2-1a **2-2a**

additive:	BHT	0 °C	5 min	72%
	$^nBu_3SnH$	0 °C–rt	30 min	70%

Scheme 2–2 All the reactions were carried out by adding 0.5 mmol BF_3•OEt_2 to a solution of 0.5 mmol **2-1a**, 0.75 mmol B_2pin_2 and 0.5 mmol additive in 2 mL MeCN under N_2 atmosphere and monitored by TLC.

Hammett study

To investigate the reaction kinetics, 4-methyl, 3-methyl, 4-methoxy, 3-methoxy, 4-tert-butyl phenyltriazene were subjected to a simple Hammett study.[82]



R = 4-H (**2-1f**), 4-Me (**2-1g**), 3-Me (**2-1v**), 4-OMe (**2-1a**), 3-OMe (**2-1b**), 4-^{t}Bu (**2-1i**)

Scheme 2–3.

At first, initial kinetic data of borylation of 1-(phenyldiazenyl)pyrrolidine **3-3f** showed the apparent first-order kinetics of this reaction (Figure 2–1). Then, the reaction constants *k* of **2-1g**, **2-1a**, **2-1b**, **2-1g**, **2-1i**, **2-1v** were determined based on first order kinetics (Figure 2–2). At last, Hammett plot of logarithm of *k*rel vs. σ was shown in Figure 2–3. Negative slope (ρ) indicating positive charge buildup on rate-determining step.

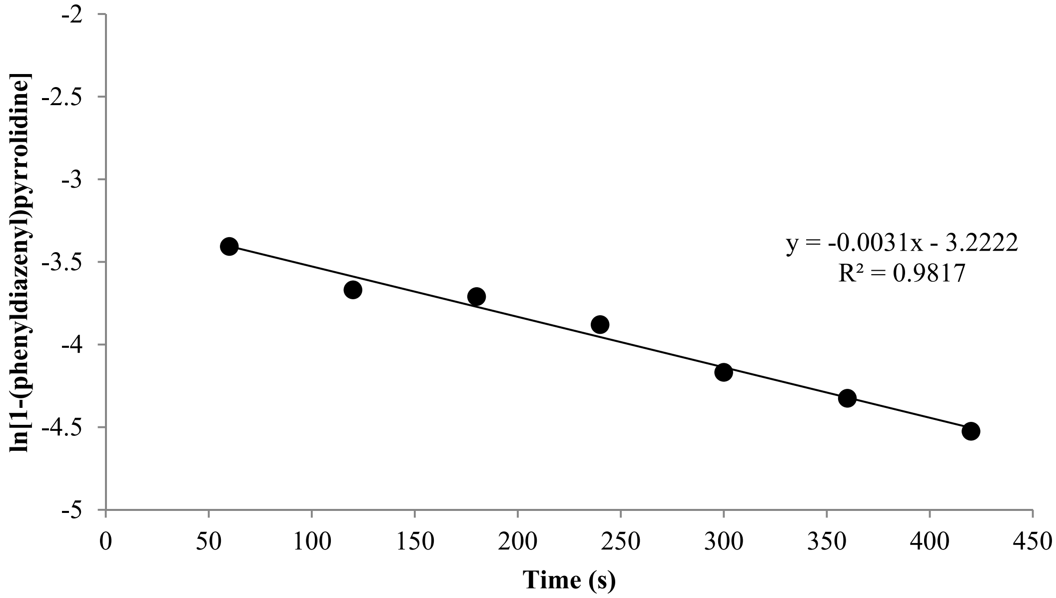


Figure 2–1. Initial kinetic data of borylation of 1-(phenyldiazenyl)pyrrolidine showed the apparent first-order kinetics

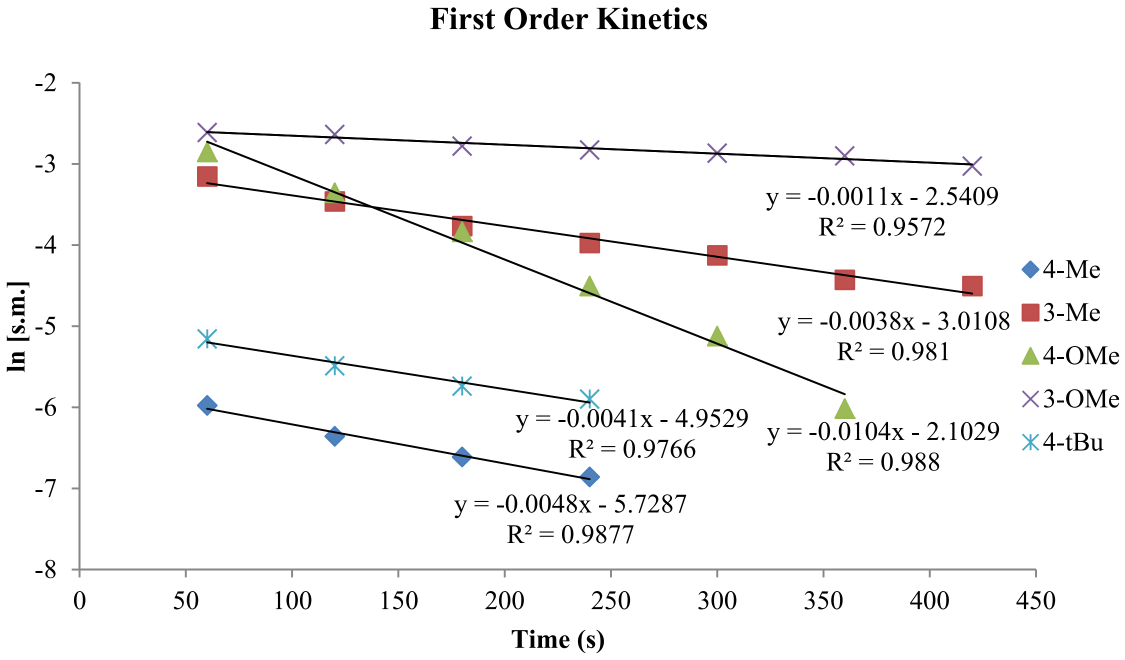


Figure 2–2. Reaction rate constant plot

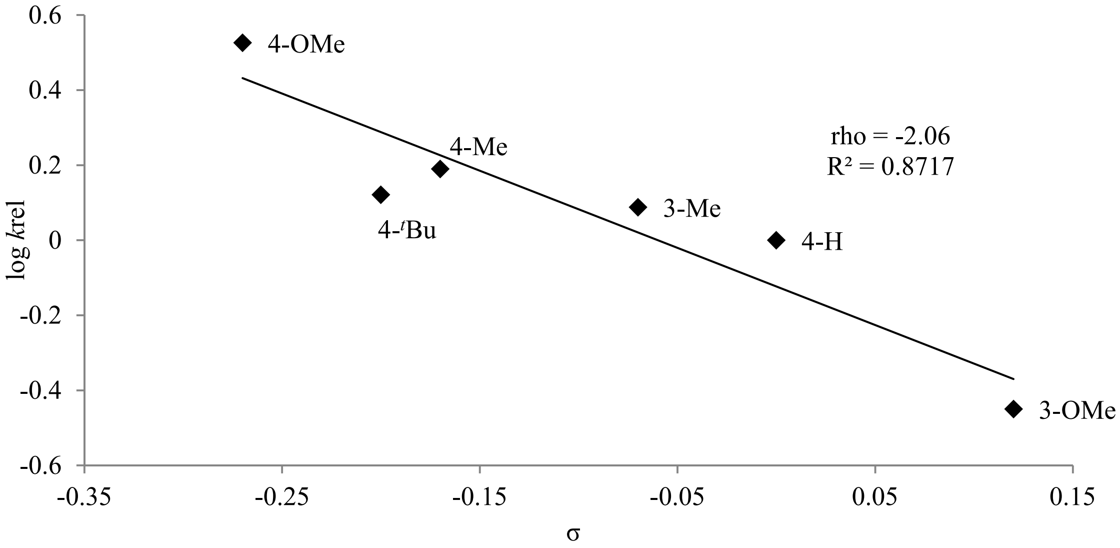
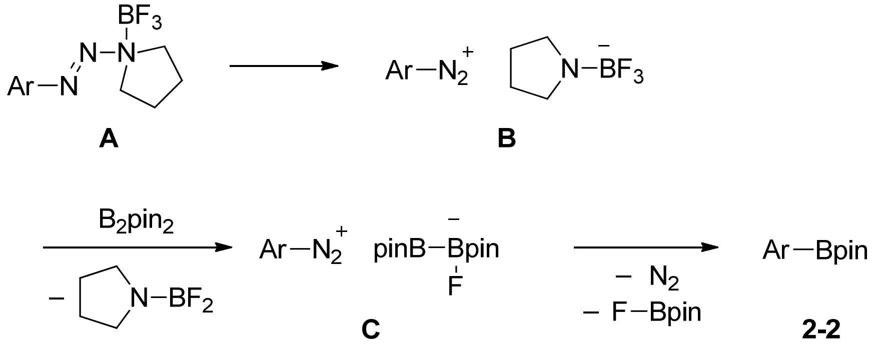


Figure 2–3. Hammett plot with negative slope (ρ) indicating positive charge buildup on rate-determining step.

Based on the evidence of the mechanistic study described above, a plausible mechanism was proposed for the BF_3•OEt_2 mediated borylation of 1-aryltriazenes. The formation of triazene-BF_3 complex **A** is followed by the generation of arenediazonium salt **B**. This step is supported by the observed electronic effect of the substituent on the phenyl group of aryltriazenes which affect the reactivity of aryltriazenes. The formation of diazoniumsalt **B** is also supported by a preliminary investigation of a simple Hammett plot which gave a negative ρ value (-2.06). The fluoride anion transfers from the trifluoroborate anion onto B_2pin_2 to give diboronate **C**.[83] Then, nucleophilic substitution of N_2 in arenediazonium part takes place to give the desired product, arylboronic ester **2-2** together with F-Bpin.



Scheme 2–4. Plausible mechanism for BF_3•OEt_2 mediated borylation of 1-aryltriazene·

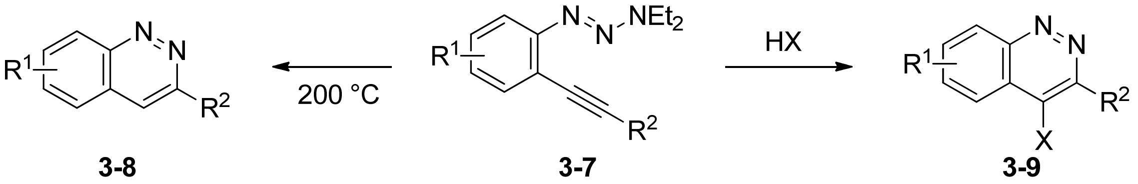
3. Conclusion

In summary, we have demonstrated a novel synthesis of arylboronic esters via direct borylation of 1-aryltriazenes mediated by BF_3•OEt_2. Under a nitrogen atmosphere, the reaction completed within 5-120 min at 0 to 60 °C. The absence of metal reagents, a transition metal catalyst or radical initiator makes this approach very easy to handle. This method is complementary to the existing arylboronic ester synthesis with the advantage of high efficiency, unique selectivity, and an environmental friendly nature. Moreover, the reaction conditions are very mild and can tolerate many functional groups, particularrly halides. Further efforts to expand the scope of this transformation are still under investigation.

CHAPTER III Synthesis of 3,4-Disubstituted Cinnolines by the Pd-catalyzed Annulation of 1-(2-Iodoaryl)triazenes with an Internal Alkyne

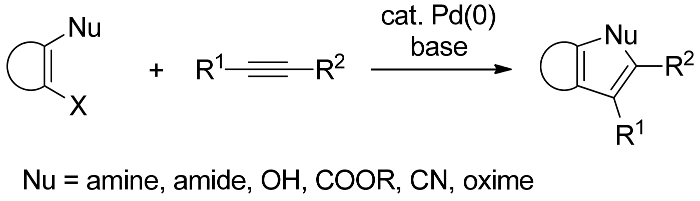
1. Introduction

Cinnolines and their derivatives exhibit a broad range of biological activity, such as: anticancer, fungicidal, bactericidal, and anti-inflammatory properties.[84] Additionally, compounds containing a cinnoline fragment demonstrate a series of interesting physical characteristics, such as luminescent and nonlinear optical properties.[85] Hence, the synthesis of cinnolines has been studied for many years.[86] Most syntheses of cinnolines involve arenediazonium salts,[87] arylhydrazones,[88] arylhydrazines,[89] and nitriles[90] as their starting materials. These procedures often suffer from certain drawbacks, such as multi-step reactions and harsh reaction conditions. Recently, alkynyl-substituted 1-aryltriazene **3-7** was used as the precursor to prepare cinnolines, however, high temperatures or strong acidic conditions were still required (Scheme 3–1).[1, 26, 91]



Scheme 3–1. Reported synthesis of cinnoline from 1-(2-alkynylaryl)triazene

These reported annulation reactions prompted us to investigate a single catalytic reaction to prepare cinnolines and their derivatives. Transition-metal catalyzed annulation of alkynes by functionally substituted aryl halides has been demonstrated to be a versatile methodology to construct a wide variety of complicated hetero- and carbocycles, such as amine, amide, imine, oxime, alcohol, ester, cyano and so forth.[92]



Scheme 3–2.

Although many nucleophiles were subjected to this annulation protocol triazene has not been used. As a nucleophile, triazene is a special functional group because there are three potentially reactive nitrogen atom centers. As mentioned in the Chapter I, **N3** could act as a nucleophile to react with protic or Lewis acid to generate the diazonium salt (Figure 3–1). However, reactions which involve **N1** and **N2**, especially **N2** as the nucleophile, are rare. Herein, we report a novel and efficient protocol to synthesize various 3,4-disubstituted cinnolines by the reaction of 1-(2-iodoaryl)triazenes with internal alkynes with a palladium catalyst.

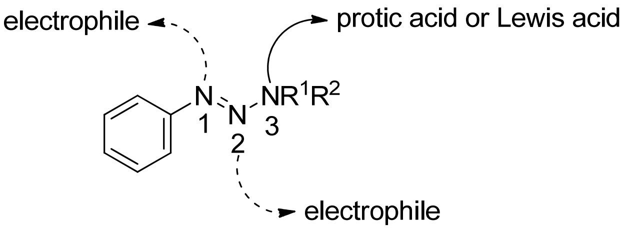
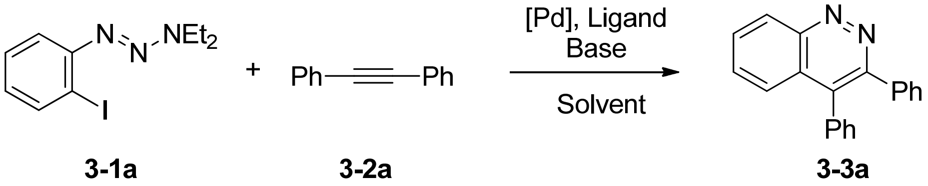


Figure 3–1.

2. Result and Discussion

The palladium-catalyzed reactions of 1-(2-iodoaryl)triazene with diphenylacetylene are summarized in Table 3–1. 1-(2-Iodoaryl)triazene **3-1a** was treated with diphenylacetylene (3 equiv) and Et_3N (2 equiv) in the presence of 10 mol % $Pd(dba)_2$ in DMF and the reaction mixture was heated at 100 °C for 24 h. As expected, 3,4-diphenylcinnoline **3-3a** was obtained in 40% yield (Table 3–1, entry 1). Polar solvents gave better yields and DMF was found as the best solvent amongst the four solvents examined (Table 3–1, entries 1-4). $PdCl_2/PPh_3$ gave a similar result with 42% yield of **3-3a** (Table 3–1, entry 5). Various phosphine ligands were tested and P(*o*-Tolyl)$_3$ gave the highest yield (Table 3–1, entries 6-9). Furthermore, different bases, such as Et_3N, $^i Pr_2NEt$, $^n Bu_3N$, and K_2CO_3 were tested in the reaction, it was revealed that $^n Bu_3N$ is superior to the others (Table 3–1, entries 10-13). When lower catalyst loadings were tested with 7.5 mol % and 5 mol % of $PdCl_2$, cinnoline **3-3a** was still obtained in 71% and 69% yields, although longer reaction times of 15 h and 36 h were required, respectively (Table 3–1, entries 13 and 14). We therefore concluded that the optimal reaction conditions for this annulation reaction is as follows: a mixture of 2-iodophenyltriazene and 3 equiv of alkyne in DMF in the presence of 7.5 mol % of $PdCl_2$, 15 mol % P(*o*-Tolyl)$_3$ and 2 equiv of $^n Bu_3N$ stirred at 90 °C.

Table 3–1. Palladium-Catalyzed Reaction of 1-(2-Iodoaryl)triazene **3-1a** with Diphenylacetylene **3-2a**^{a}



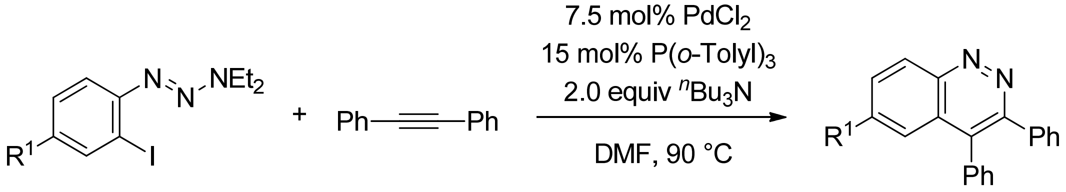
Entry	Catalyst	Solvent	Base	Ligand	Temp. (°C)	Time (h)	Yield (%)
1	Pd(dba)$_2$	DMF	Et_3N	None	100	24	40
2	Pd(dba)$_2$	CH_3CN	Et_3N	None	reflux	24	30
3	Pd(dba)$_2$	Toluene	Et_3N	None	100	24	7
4	Pd(dba)$_2$	1,4-Dioxane	Et_3N	None	100	24	8
5	$PdCl_2$	DMF	Et_3N	PPh_3	90	24	42
6	$PdCl_2$	DMF	Et_3N	P(*o*-Tolyl)$_3$	90	12	62

7	PdCl$_2$	DMF	Et$_3$N	dppe	90	24	trace
8	PdCl$_2$	DMF	Et$_3$N	dppf	90	24	45
9	PdCl$_2$	DMF	Et$_3$N	P(2-Furyl)$_3$	90	24	30
10	PdCl$_2$	DMF	^{i}Pr$_2$NEt	P(*o*-Tolyl)$_3$	90	24	65
11	PdCl$_2$	DMF	^{n}Bu$_3$N	P(*o*-Tolyl)$_3$	90	12	67
12	PdCl$_2$	DMF	K$_2$CO$_3$	P(*o*-Tolyl)$_3$	100	12	65
13	PdCl$_2$	DMF	^{n}Bu$_3$N	P(*o*-Tolyl)$_3$	90	15	71[b]
14	PdCl$_2$	DMF	^{n}Bu$_3$N	P(*o*-Tolyl)$_3$	90	24	69[c]

[a] Unless otherwise stated, all reactions were carried out with 0.25 mmol **3-1a**, 0.75 mmol **3-2a**, 10 mol% Pd catalyst (10 mol %), 20 mol% ligand and 0.05 mmol base in 5 mL solvent under N$_2$ atomsphere and monitored by TLC. [b] 7.5 mol% PdCl$_2$ and 15 mol % P(*o*-Tolyl)$_3$ were employed. [c] 5 mol % PdCl$_2$ and 10 mol % P(*o*-Tolyl)$_3$ were employed.

We proceeded to examine the scope and generality of this reaction. A series of 4-substituted phenyltriazenes were employed in this reaction (Table 3–2).We found that the reaction can tolerate a variety of functional groups, such as alkyl, methoxy, cyano, nitro, trifluoromethyl, acetyl, and methoxycarbonyl groups. The triazenes gave the corresponding annulation products in moderate to good yields. Amongst these substrates triazenes bearing alkyl substitutions lead to the highest yields (Table 3–2, entries 2 and 3).

Table 3–2. Palladium-catalyzed reaction of 1-(2-iodoaryl)triazene **3-1a–i** with diphenylacetylene **3-2a**[a]

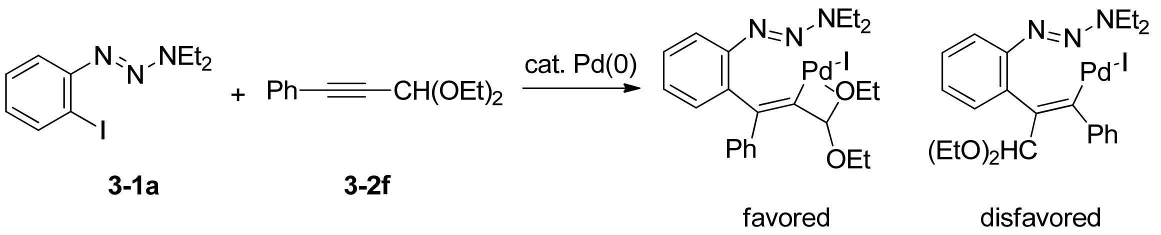


3-1a–i **3-2a** **3-3a–i**

Entry	R^1	Time (h)	Product	Yield (%)[b]
1	H (**3-1a**)	15	**3-3a**	71
2	Me (**3-1b**)	15	**3-3b**	73
3	^{t}Bu (**3-1c**)	12	**3-3c**	84
4	OMe (**3-1d**)	15	**3-3d**	50[b]
5	CN (**3-1e**)	24	**3-3e**	42
6	NO_2 (**3-1f**)	36	**3-3f**	46[c]
7	CF_3 (**3-1g**)	24	**3-3g**	52
8	COMe (**3-1h**)	18	**3-3h**	64
9	COOMe (**3-1i**)	24	**3-3i**	60

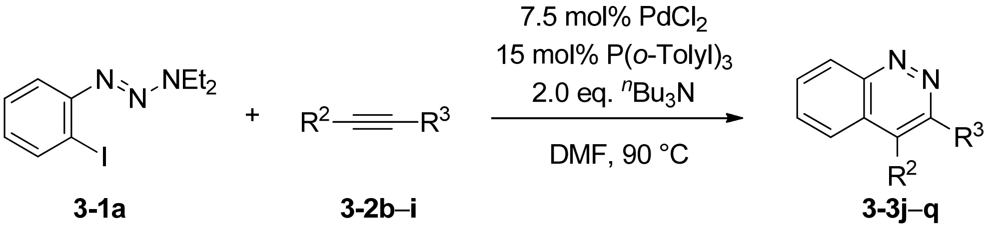
[a] Unless otherwise stated, all reactions were carried out with 0.25 mmol **3-1**, 0.75 mmol **3-2a**, 7.5 mol% $PdCl_2$, 15 mol% P(*o*-Tolyl)$_3$ and 0.5 mmol ^{n}Bu$_3$N in 5 mL DMF under N_2 atmosphere at 90 °C and monitored by TLC. [b] Isolated yield. [c] 2.0 equiv of K_2CO_3 was used as base and stirred at 100 ºC for 24 h. [d] 5 equiv of ^{n}Bu$_3$N was employed.

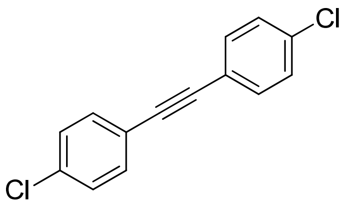
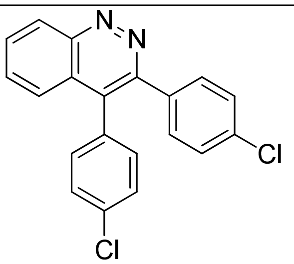
Next, we examined the applicability of internal alkynes for this reaction (Table 3–3). Symmetrical alkynes were tested first to check functional group tolerance. When 4,4’-substituted diphenylacetylenes **3-2b−e** were used in the reaction with 3,3-diethyl-(2-iodophenyl)triazene (**3-1a**), the corresponding 3,4-disubstituted cinnolines **3-3j−m** were obtained in good yields (Table 3–3, entries 1−4). Thus, carbonyl and chloro groups on the phenyl ring of the internal alkyne were found to be tolerated. The chemoselectivity of this annulation process is apparently very low, because when we used unsymmetrical alkynes, such as ethyl phenylpropiolate (**3-2g**),1-phenylpropyne (**3-2h**), and 1-phenylhexyne (**3-2i**), two regioisomers of cinnolines were obtained in moderate yields in 56:44, 59:41, and 33:67 ratios, respectively (Table 3–3, entries 6−8). Although the consumption of the iodophenyltriazene **3-1a** was faster in the reaction with electron deficient alkyne such as ethyl phenylpropiolate, the reaction gave cinnoline and unidentified byproducts. It should be noted, (3,3-diethoxyprop-1-ynyl) benzene (**3-2f**) gave a mixture of regioselective products, 3-phenylcinnolines having an acetal or aldehyde moiety, albeit in only 50% overall yield. Coordination of the ethoxy group of the alkyne may facilitate the regioselective addition of organopalladium intermediate although we are not sure because the yield of the regioselective product is not high enough to discuss the regioselectivity (Scheme 3–3).

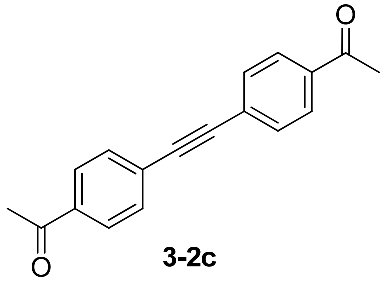
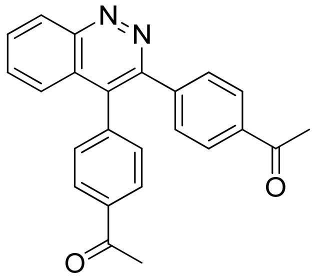
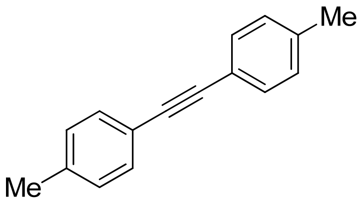
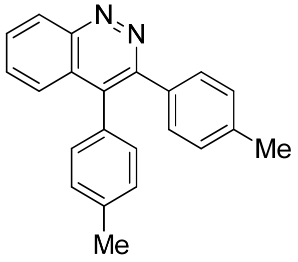
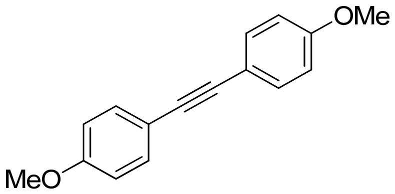
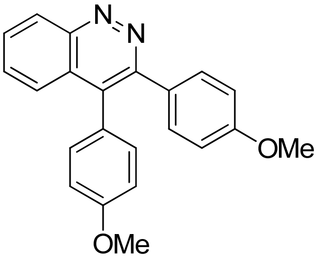
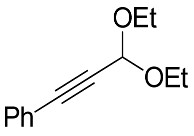
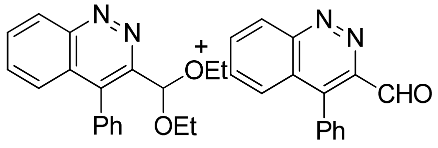
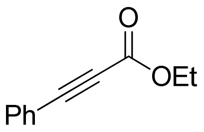
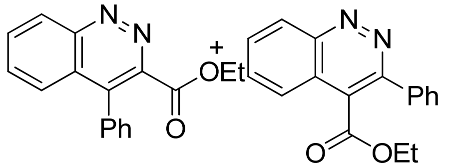
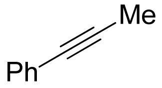
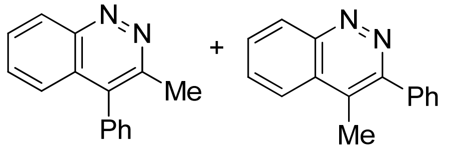


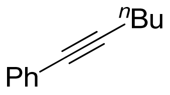
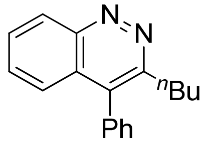
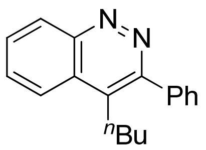
Scheme 3–3.

Table 3–3. Synthesis of 3,4-disubstituted cinnoline of **3-1a** with **3-2b–h**^{a}



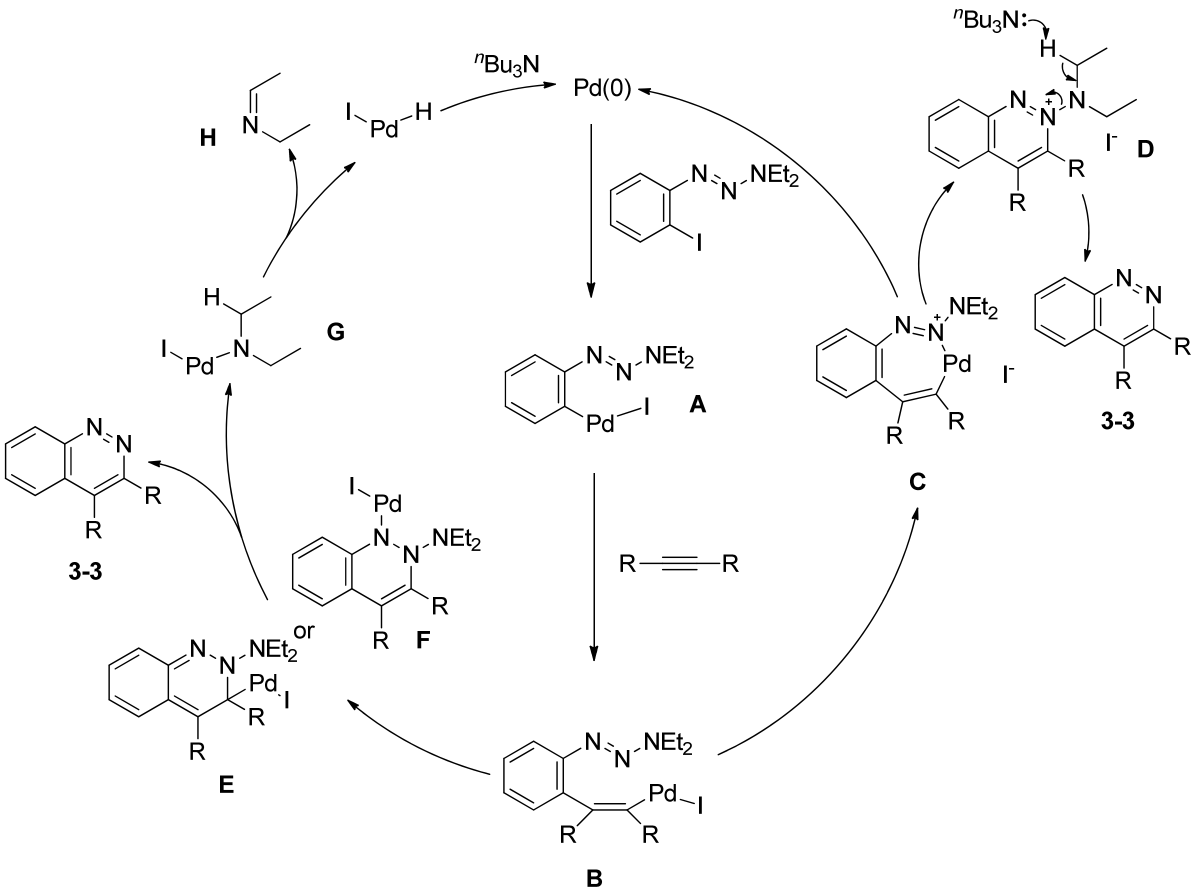
Entry	Alkyne	Time (h)	Product	Yield (%)
1	 **3-2b**	18	 **3-3j**	75

2	 **3-2c**	18	 **3-3k**	82
3	 **3-2d**	15	 **3-3l**	73
4	 **3-2e**	15	 **3-3m**	78
5	 **3-2f**	15	 **3-3n** **3-3n'** (1 : 0.1)	50
6	 **3-2g**	15	 **3-3o** **3-3o'** (0.8 : 1)	35
7	 **3-2h**	15	 **3-3p** **3-3p'** (0.7 : 1)	81[c]

8	 **3-2i**	15	 +  **3-3q** **3-3q'** (0.5 : 1)	80

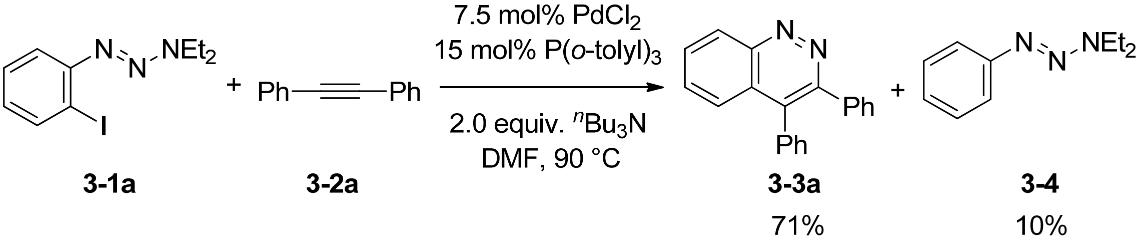
[a] Unless otherwise stated, all reactions were carried out with 0.25 mmol **3-1a,** 0.75 mmol **3-2**, 7.5 mol% $PdCl_2$, 15 mol% P(*o*-Tolyl)$_3$, and 0.5 mmol ^{n}Bu$_3$N in 5 mL DMF under N_2 atmosphere at 90 °C and monitored by TLC. [b] Isolated yield. [c] The two regioisomers were obtained as an inseparable mixture and their regiostructures were not assigned.

Plausible mechanisms for the annulation reaction of **3-1** with internal alkyne **3-2** are illustrated in Scheme 3–4. Oxidative addition of the 2-iodoaryltriazene to the in situ generated palladium(0) species leads to arylpalladium intermediate **A**, which is followed by the formation of vinylpalladium iodide complex **B** via addition to the alkyne. One pathway is intermediate **B** undergoes a 6-*endo* addition[93] of the vinylpalladium intermediate to the nitrogen-nitrogen double bond to form an aminopalladium intermediate **F**[94] or a 6π electrocyclization[91b-e] occurs to give another aminopalladium intermediate **E**. Then β-amino elimination from **E** or **F** forms the desired cinnoline as well as a diethylaminopalladium species, which undergoes a β-hydride elimination and subsequent elimination of HI by base to regenerate the Pd(0) catalyst. An alternative pathway is that coordination of the pendent triazene to vinylic palladium to form a seven-membered palladacyle **C**, which subsequently generates a diethyliminoimmonium salt **D** as well as Pd(0) via reductive elimination.[61] As previously suggested by Haley, the diethyliminommounium salt **D** would afford cinnoline in the presence of base.



Scheme 3–4. Proposed mechanism for Pd-catalyzed annulation of 1-(2-iodoaryl)triazene with internal alkyne

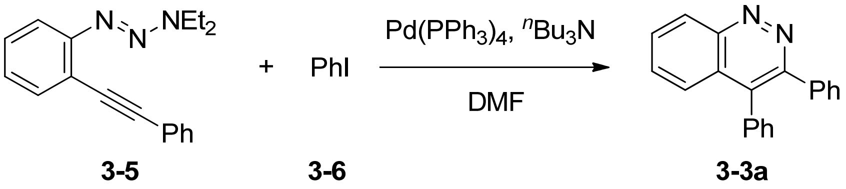
Hydrodehalogenation, a common side reaction involved in the palladium-catalyzed reactions with arylhalide[95] was also observed in the reaction of **3-1a** and **3-2a** (Scheme 3–5). 10% of the reduced product **3-4** was isolated as the main side product. DMF has been proved to be a reductant for the formation of hydrodehalogenated products.[96]



Scheme 3–5.

Although we successfully achieved the synthesis of cinnoline by palladium-catalyzed annulation of 1-(2-iodoaryl)triazene and internal alkynes, problems still exist, such as limited substates scope, unsatisfying regioselectivity and unavoidable side reactions. In order to overcome the limitations of the methodology, we also studied the reaction between 3,3-diethyl-1-(2-(phenylethynyl)phenyl)triaz-1-ene (**3-5**) and iodobenzene.[97] When **3-5** reacts with 5.0 equiv. of iodobenzene in DMF in presence of 3.0 equiv. of $^{n}Bu_3N$ and catalytic amount of $PdCl_2$/P(*o*-tolyl)$_3$ at 100 °C, the desired cinnoline product (**3-3a**) was observed to form in 29% yield at 100 °C (Table 3–4, entry 1). This result suggested that the annulation pathway would indeed be possible and lead to the regioselective product in the present case. Next we tried to improve the yield of the desired product. Initially, $Pd(dba)_2$ was used as catalyst instead of $PdCl_2$ and this resulted in an increased product yield (Table 3–4, entry 2). Then, inorganic base K_2CO_3 and KOAc were employed in the reaction, only trace amout of cinnoline **3-3a** was isolated, along with a mixture of unidentified side products (Table 3–4, entries 3 and 4). This suggested organic base is better than inorganic base for this cinnoline arylation process. From entries 5 and 6, other ligands, dppp and P(2-Furyl)$_3$ have been used. By employing dppp as the ligand, the reaction became sluggish and the product yield was not improved. Also, P(2-Furyl)$_3$ resulted in only a slightly increased yield. $Pd(PPh_3)_4$ has be proven to be an effective catalyst in similar palladium-catalyzed annulation reactions. When $Pd(PPh_3)_4$ was used instead of $Pd(dba)_2$/P(2-Furyl)$_3$, the desired product was isolated in 39% yield as the best result (Table 3–4, entry 9). Finally, despite much effort has been put in to optimize the reaction conditions only 39% yield was obtained due to a series of byproducts.

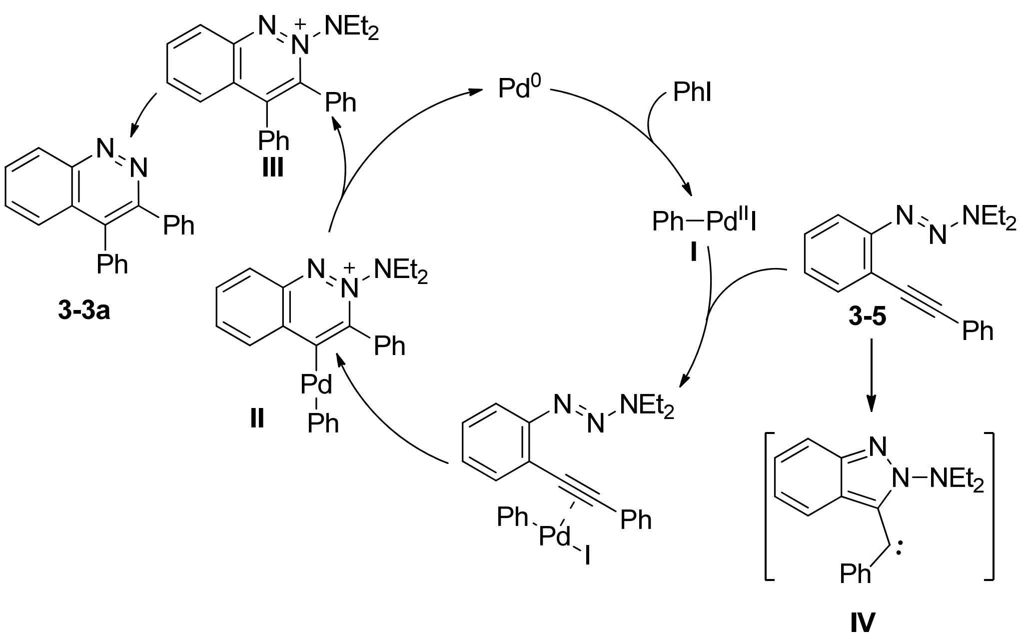
Table 3–4. Palladium-Catalyzed Reaction of 3,3-diethyl-1-(2-(phenylethynyl)phenyl)triaz-1-ene **3-5** with iodobenzene[a]



Entry	Catalyst	Base	Ligand	Temp. (°C)	Time (h)	Yield (%)[b]
1	$PdCl_2$	^{n}Bu_3N	P(*o*-Tolyl)$_3$	100	5	25
2	$Pd(dba)_2$	^{n}Bu_3N	P(*o*-Tolyl)$_3$	100	9	34
3	$Pd(dba)_2$	K_2CO_3	P(*o*-Tolyl)$_3$	100	9	trace[c]
4	$Pd(dba)_2$	KOAc	P(*o*-Tolyl)$_3$	100	9	trace[c]
5	$Pd(dba)_2$	^{n}Bu_3N	dppp	100	23	34[d]
6	$Pd(dba)_2$	^{n}Bu_3N	P(2-Furyl)$_3$	100	10	35
7	$Pd(PPh_3)_4$	^{n}Bu_3N	None	100	9	39

[a] Unless otherwise stated, all reactions were carried out with 0.25 mmol **3-5**, 1.25 mmol **3-6**, 10 mol% Pd catalyst, 20 mol% ligand and 0.75 mmol ^{n}Bu_3N in 5 mL solvent under N_2 atmosphere at 100 °C and monitored by TLC. [b] Isolated yield. [c] **3-4** was consumed completely monitored by TLC. [d] 10 mol% dppp was used.

According to the literature, a possible mechanism for this cinnoline synthesis was proposed as shown in Scheme 3–6. The reaction presumably proceeds via (1) oxidative addition of the Pd(0) to iodobenzene, (2) coordination of the alkyne to the palladium atom of the resulting arylpalladium intermediate **I**, (3) nucleophilic attack of triazene to the activated C≡C triple bond to form a six-membered 4-palladated heterocycle **II**, (4) reductive elimination of intermediate **II** to form the cinnolinium salt **III** and regenerate Pd(0) and (5) decomposition of **III** to afford cinnoline **3-3a**.[97a] Besides the cinnoline formation route, another possible way from **3-5** is generating the indazoyl carbene intermediate **IV** as demonstrated by Haley and co-workers which could undergo complex transformation to give byproducts involving 2*H*-indazole motif.



Scheme 3–6. Proposed mechanism for Pd-catalyzed annulation of 1-(2-phenylethynylphenyl)triazene with iodobenzene

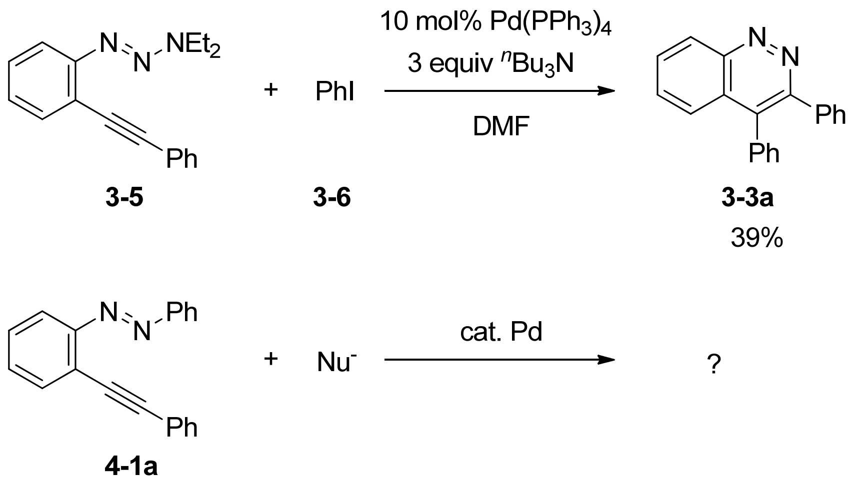
3. Conclusion

In summary, we have demonstrated a simple and efficient strategy for the synthesis of potentially important 3,4-disubstituted cinnoline derivatives by palladium-catalyzed annulation of 1-(2-iodophenyl)triazenes and internal alkynes. A wide range of functionalized 1-(2-iodophenyl)triazenes as well as symmetric and asymmetric internal alkynes can be utilized. In order to overcome the inherent problems encountered in the methodology, we investigated the palladium catalyzed annulation of 1-(2-alkynylphenyl)triazene with iodobenzene. Unfortunately, although the desired cinnoline product was obtained, the yield was only 39% even after much effort due to the parallel coarctate cyclization.[30]

CHAPTER IV Preparation of 3-Allenyl-2*H*-indazoles from 1-(2-Alkynylaryl)-2-aryldiazenes and Terminal Alkynes and A Novel Synthesis of Indazolo[2,3-*a*]quinoline

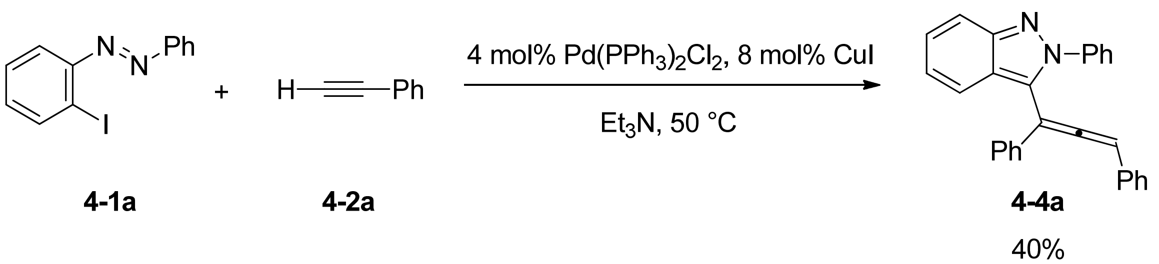
1. Introduction

Inspired by the palladium-catalyzed annulation of 1-(2-phenylethynylphenyl)triazene affording 3,3-diphenylcinnoline as product, we continued to investigate the similar reaction of palladium-catalyzed annulation of 1-(2-phenylethynylphenyl)-2-phenyldiazene (Scheme 4–1).



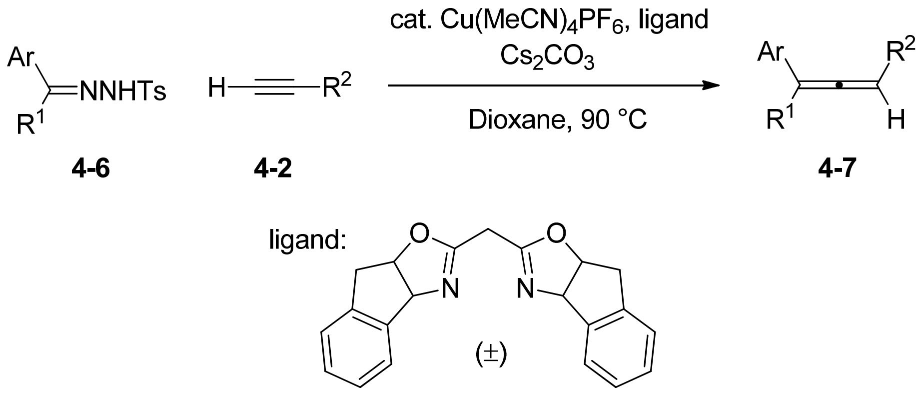
Scheme 4–1.

Inserestingly, during the preparation of 1-(2-phenylethynyl)-2-phenyldiazene we found 3-allenyl-2*H*-indazole was obtained as a major product in 40% yield from Sonogashira coupling of 1-(2-iodophenyl)-2-phenyldiazene with phenylacetylene (Scheme 4–2). By using this approach, we envisioned that 3-allenyl-2*H*-indazole could be readily prepared from 1-(2-alkynylaryl)-2-aryldiazene.



Scheme 4–2. Unexpected product of Sonogashira reaction of 1-(2-iodophenyl)-2-phenyldiazene with phenylacetylene

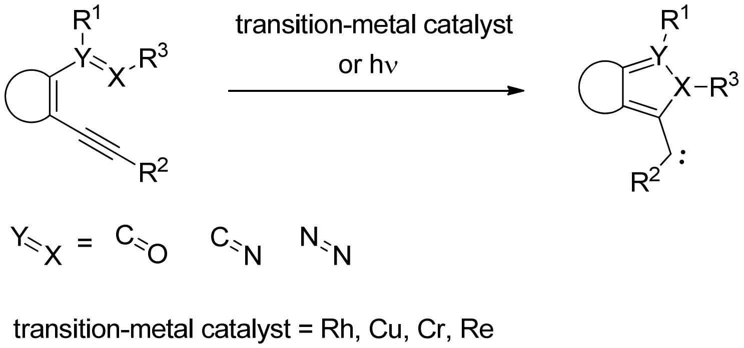
Allene moieties are extensively present in natural products as well as pharmaceutically related compounds.[98] The utility of allenes as building blocks in organic synthesis has also demonstrated their versatile reactivity and unique selectivity.[99] As a result, a variety of methods have been developed for the preparation of allenes.[100] In general, stoichiometric amount of organometallic reagents were involved in these methods such as S_N2' type[101] and rearrangement type[102] allene synthesis. Hence there has been considerable interest in catalytic synthesis of allenes.[103] Very recently, it has been reported that allenes can be readily prepared from terminal alkynes and tosylhydrazone.[104] The reaction presumably involves copper carbenoid complexes as intermediates (Scheme 4–3).



Scheme 4–3.

It isknown, tosylhydrazone is a useful carbene precursor which can generate diazoalkane under basic condition and then decomposed by transition metal complexes to generate

Fischer-type metal carbene intermediates.[105] Besides diazoalkane/tosylhydrazone, an alternative strategy to generate carbene intermediates is from a conjugated 'ene-ene-yne' manifold,[106] such as ketone (aldehyde),[107] imine,[108] triazene, diazene with ene-yne, attracted particular interest because they provide the carbene intermediate together with the formation of heterocycle which make it possible to construct various functionalized heterocycle in a rapid and convenient way (Scheme 4–4).



Scheme 4–4.

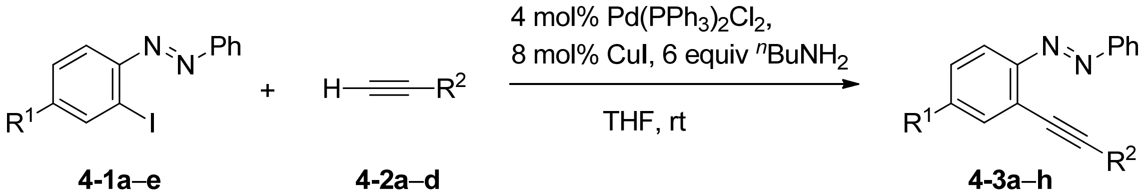
As mentioned in chapter 1, investigations over the past few years have demonstrated that the cyclization of 2-alkynylaryltriazene or (2-ethynylaryl)aryldiazene could generate 3-indazoylcarbenoid which was further trapped by alkene, O_2, alcohol and water to give the corresponding cyclopropyl, carbonyl, alkoxyl and hydroxyl substituted 2*H*-indazole.[27-28, 31-32, 73-74, 109] Thus, in spite of the importance and biological activities of indazole deviratives,[110] a practical synthesis of 3-allenyl-2*H*-indazoles has not been reported yet.

Herein a study of $Pd(PPh_3)_2Cl_2$/CuI catalyzed 3-allenyl-2*H*-indazole synthesis by using 1-(2-alkynylaryl)-2-aryldiazene as carbenoid precursor without involving the corresponding tosylhydrazone was undertaken. Moreover, 3-allenyl-2*H*-indazole could be transformed to polycyclic heterocycles.

2. Result and Discussion

We began our investigation with the preparation of 1-(2-alkynylaryl)-2-aryldiazene. 1-(2-iodoaryl)-2-phenyldiazenes **4-1a–h** were easily prepared from the corresponding anilines according to the reported procedure.[73] $Pd(PPh_3)_2Cl_2$/CuI catalyzed crosseoupling of 1-(2-iodoaryl)-2-aryldiazene with phenylacetylene in presence of Et_3N only afforded a poor yield of 1-(2-alkynylaryl)-2-aryldiazene due to the over-reaction. To overcome this problem, we tried to use weak base $^nBuNH_2$ instead of Et_3N. Fortunately, 6.0 equiv of $^nBuNH_2$ furnished the 1-(2-alkynylaryl)-2-aryldiazenes in up to 80% yield.

Table 4–1. Preparation of 1-(2-Alkynylaryl)-2-aryldiazenes from 1-(2-iodoaryl)-2-aryldiazene and terminal alkyne.[a]



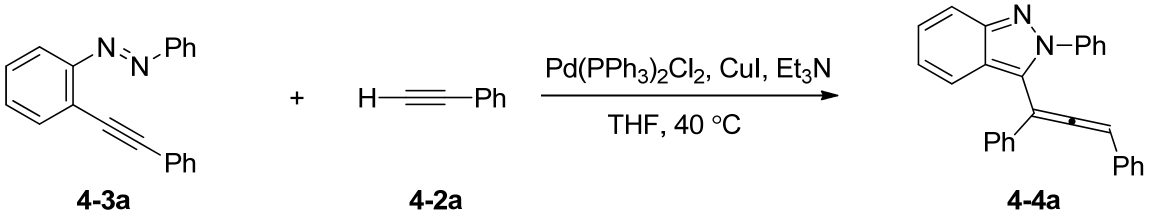
Entry	R^1	R^2		Time (h)	Yield (%)[b]
1	H	Ph	**4-3a**	2	80
2	Me	Ph	**4-3b**	2	78
3	^{t}Bu	Ph	**4-3c**	2	75
4	F	Ph	**4-3d**	2	65
5	Cl	Ph	**4-3e**	2	69
6	H	4-$MeOC_6H_4$	**4-3f**	2	55
7	H	4-ClC_6H_4	**4-3g**	2	60
8	H	^{n}Pr	**4-3h**	7	50

[a] Unless otherwise stated, all reactions were carried out with 1.0 mmol **4-1a–e**, 2.0 mmol **4-2a–d**, 4 mol% $Pd(PPh_3)_2Cl_2$, 8 mol% CuI, 6.0 mmol $^nBuNH_2$ in 5 mL anhydrous THF under N_2 atomsphere at rt and moni-

tored by TLC. [b] Isolated yield.

Synthesis of 3-allenyl-2*H*-indazole

Table 4–2. Optimization of reaction condition of 3-allenyl-2*H*-indazole synthesis[a]



Entry	Catalyst	Solvent	Time (h)	Yield (%)[b]
1	$CuI/Pd(PPh_3)_2Cl_2$	THF	20	80
2	$Pd(PPh_3)_2Cl_2$	THF	24	0[c]
3	CuI	THF	24	49
4	CuI/PPh_3	THF	24	30
5	$CuI/Pd(PPh_3)_2Cl_2$	THF	20	81[d]
6	$CuI/ Pd(PPh_3)_2Cl_2$	THF	20	68[d,e]
7	$CuI/ Pd(PPh_3)_2Cl_2$	THF	20	71[f]
8	$CuI/ Pd(PPh_3)_2Cl_2$	DCE	20	63[d]
9	$CuI/ Pd(PPh_3)_2Cl_2$	MeCN	20	72[d]
10	$CuI/Pd(PPh_3)_2Cl_2$	THF	15	84[d,g]

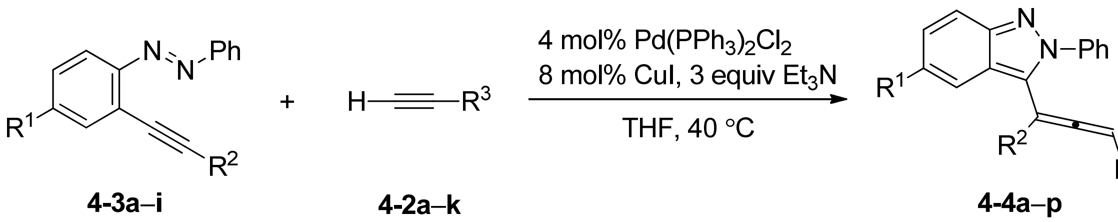
[a] Unless otherwise stated, reactions were carried out with 0.25 mmol **4-3a**, 0.50 mmol **4-2a,** 4 mol% $Pd(PPh_3)_2Cl_2$, 8 mol% CuI and 2.5 mmol Et_3N in 2.5 mL of anhydrous THF under N_2 atmosphere at 40 °C and monitored by TLC. [b] Isolated yield. [c] 80% starting material was recovered. [d] 3.0 equiv of Et_3N was employed. [e] 4 mol% CuI was employed. [f] 2.0 equiv of Et_3N was employed. [g] 3.0 equiv of **4-2a** was employed.

In an initial attempt, 1-(2-phenylethynyl)-2-phenyldiazene **4-3a** was treated with 2.0 equiv phenylacetylene in THF in presence of $Pd(PPh_3)_3Cl_2$/CuI and 10.0 equiv of Et_3N at 40 °C. To our delight, the desired 3-allenyl-2*H*-indazole was formed in 80% yield (Table

4–2, entry 1). However, it was found that the desired product was not observed when $Pd(PPh_3)_2Cl_2$ was used (Table 4–2, entry 2). On the other hand, the yield dramatically decreased when CuI was used or together with PPh_3 (Table 4–2, entries 3−4). It is noteworthy that 3-(1,2-diphenylcycloprop-2-en-1-yl)-2-phenyl-2*H*-indazole **4-4a’** was isolated in 30% yield (Table 4–2, entry 3).[111] Then we turned our attention to the use of the combined system of palladium and copper. The reaction could also be performed in DCE or MeCN, but leading to 3-allenylindazole **4-4a** in 63–72% yields (Table 4–2, entries 8 and 9). Upon decreasing the amount of Et_3N from 10 equiv to 3 equiv the yield was not affected (Table 4–2, entry 6). A low catalyst loading of 4 mol % of CuI led to a lower yield (Table 4–2, entry 6). Increasing the amounts of phenylacetylene from 2 equiv to 3 equiv resulted in a slightly higher yield (Table 4–2, entry 10).

Next, the scope of terminal alkyne and 2-alkynyldiazenes were examined in reactions under the optimized conditions. First we found that treatment of 1-(2-phenylethynyl)-2-phenyldiazene with a variety of terminal alkynes provided the corresponding 3-allenyl-2*H*-indazoles in good yield (Table 4–3, entries 1−10). The structure of the product **4-4f** was confirmed by X-ray crystal structure analysis (Figure 4–1). In the case of R^3 as aryl groups, the nature of the substituents on the aromatic ring does not significantly influence the reactions. Moreover, the reaction system is tolerant of many functional groups, such as alkyl, alkyloxyl, ester and nitro group. Notably, arylacetylene with *ortho*-substitution led to a lower yield (Table 4–3, entry 3). In addition, alkyl and silyl acetylene could be applied in this reaction although a low yield was achieved with alkylacetylene. Next, a variety of substituents were employed on the 1-(2-alkynylaryl)-2-aryldiazene coupling partner, including alkyl, alkoxyl, halide and trimethylsilyl (Table 4–3, entries 11−16). Electron-donating R^1 groups were superior to electron-withdrawing ones in this reaction (Table 4–3, entries 11−14). When R^2 was aromatic functional group, good yields were obtained. However, 1-(2-alkylethynylphenyl)-2-phenyldiazene and 1-(2-trimethylsilylethynyl-phenyl)-2-phenyldiazene failed to afford the desired product (Table 4–3, entries 17 and 18). These two substrates **4-3h** and **4-3i** revealed the limitations of the method. It is apparent that an aryl substituent at the R^2 position of the alkyne was crucial. In its absence, no allene was formed.

Table 4–3. $Pd(PPh_3)_2Cl_2$/CuI catalyzed 3-allenyl isoindazole synthesis[a]



Entry	**4-3**, R^1, R^2	**4-2**, R^3	Time/h	**4-4**, Yield/%[b]
1	**4-3a**, H, Ph	**4-2a**, Ph	20	**4-4a**, 81
2	**4-3a**, H, Ph	**4-2e**, *p*-MeC_6H_5	20	**4-4b**, 82
3	**4-3a**, H, Ph	**4-2f**, *o*-MeC_6H_5	20	**4-4c**, 62
4	**4-3a**, H, Ph	**4-2b**, *p*-$MeOC_6H_5$	18	**4-4d**, 73
5	**4-3a**, H, Ph	**4-2g**, *p*-$EtOCOC_6H_5$	18	**4-4e**, 66
6	**4-3a**, H, Ph	**4-2h**, *p*-$O_2NC_6H_5$	18	**4-4f**, 70
7	**4-3a**, H, Ph	**4-2i**, 2-naphthyl	20	**4-4g**, 82
8	**4-3a**, H, Ph	**4-2j**, 2-thienyl	15	**4-4h**, 79
9	**4-3a**, H, Ph	**4-2d**, $^nC_3H_7$	15	**4-4i**, 50
10	**4-3a**, H, Ph	**4-2k**, $SiMe_3$	14	**4-4j**, 80
11	**4-3b**, Me, Ph	**4-2a**, Ph	20	**4-4k**, 85
12	**4-3c**, ^{t}Bu, Ph	**4-2a**, Ph	20	**4-4l**, 85
13	**4-3d**, F, Ph	**4-2a**, Ph	20	**4-4m**, 74
14	**4-3e**, Cl, Ph	**4-2a**, Ph	20	**4-4n**, 75

15	**4-3f**, H, p-MeOC$_6$H$_5$	**4-2a**, Ph	18	**4-4o**, 72
16	**4-3g**, H, p-ClC$_6$H$_5$	**4-2a**, Ph	15	**4-4p**, 73
17	**4-3h**, H, ^{n}C$_3$H$_7$	**4-2a**, Ph	20	-[c]
18	**4-3i**, H, SiMe$_3$	**4-2a**, Ph	20	-[c]

[a] Unless otherwise stated, reactions were carried out with 0.25 mmol **4-3**, 0.50 mmol **4-2,** 4 mol% Pd(PPh$_3$)$_2$Cl$_2$, 8 mol% CuI and 0.75 mmol Et$_3$N in 2.5 mL of anhydrous THF under N$_2$ atmosphere at 40 °C and monitored by TLC. [b] Isolated yield. [c] The reaction was performed at 70 °C but no desired product was obtained upon complete consumption of **4-3**.

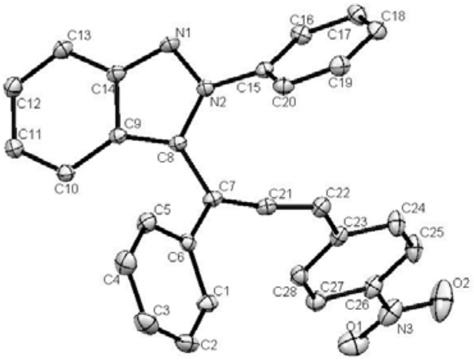
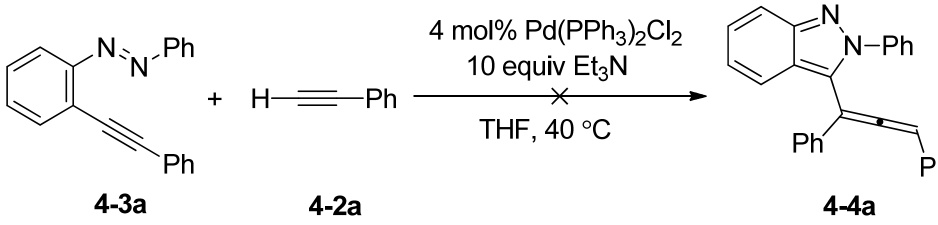


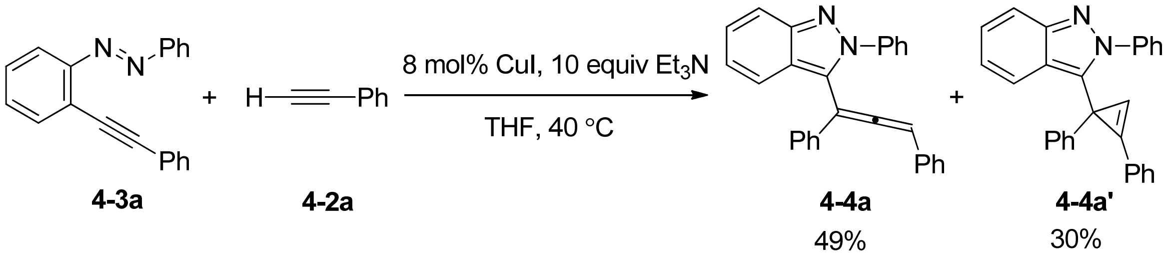
Figure 4–1 ORTEP drawing of 3-(3-(4-nitrophenyl)-1-phenylpropa-1,2-dien-1-yl)-2-phenyl-2*H*-indazole **4-4f**.

To understand the mechanism of this reaction we performed some control reactions. Firstly, the reaction was performed by using only Pd(PPh$_3$)$_2$Cl$_2$ as catalyst. In this reaction no desired product was obtained and starting material was recovered after 24 h (Scheme 4–5). This is in accordance with literature that copper catalyze the cyclization of azo-ene-yne manifold.



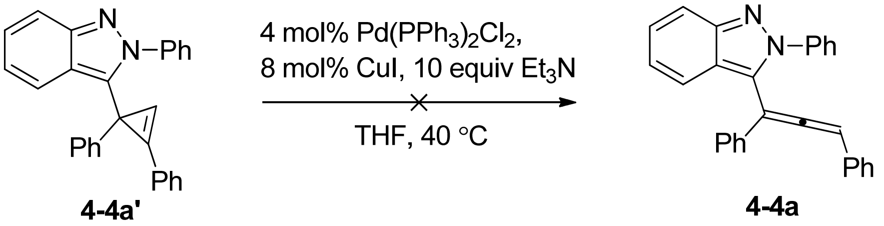
Scheme 4–5.

Secondly, the reaction was performed with only CuI as the catalyst. We found that 30% yield of the cyclopropene was produced together with 49% yield of the allene in presence of only CuI (Scheme 4–6).



Scheme 4–6.

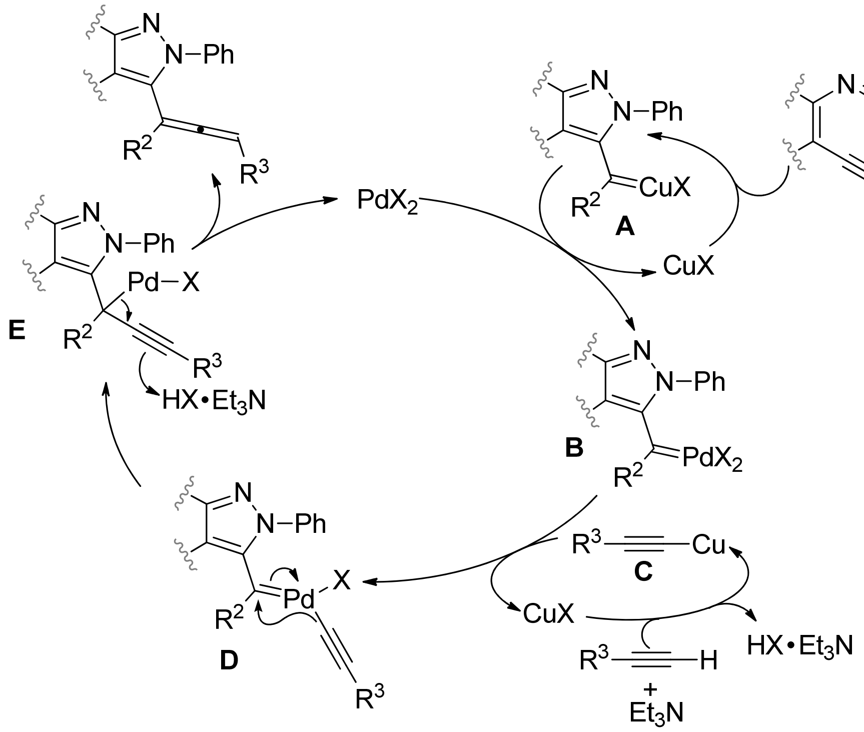
It is obvious that CuI is an effective catalyst to this transformation and cyclopropene is possible intermediate to the allene.[112] Therefore, we explored the possibility of cyclopropene rearrangement to the allene. Cyclopropene **4-4a'** was treated in the optimized conditions 4 mol% $Pd(PPh_3)_2Cl_2$, 8 mol% CuI and 3 equiv of Et_3N, however no allene was formed and 80% cyclopropene was recovered after 24 h (Scheme 4–7).



Scheme 4–7.

From this obsvervation we conclude that cyclopropene formation is a competing pathway to allene formation. Thus, we believe that $Pd(PPh_3)_2Cl_2$ is essential and efficient to suppress the cyclopropene byproduct since the combination of $Pd(PPh_3)_2Cl_2$ and CuI afford a single allene product.

Based on the above studies and the established mechanism for cyclization of azo-ene-yne system and allene synthesis from tosylhydrazone and terminal alkyne, a plausible mechanism of the present 3-allenyl-2*H*-indazole formation is depicted in Scheme 4–8. It can be assumed copper carbenoid **A** formed via CuI-catalyzed intramolecular cyclization of 1-(2-alkynylaryl)-2-aryldiazene. Then Pd(II) replaces of Cu(I) in carbenoid **A** to form complex **B**.[105, 113] Meanwhile, CuI and terminal alkyne form copper acetylide **C** in presence of Et_3N. Transmetallation of acetylenyl from copper to palladium lead to the alkynyl palladium carbene complex **D**. Subsequent migration of alkynyl group to carbenoic carbon afford intermediate **E**.[114] The following protonation gives the 3-allenyl-2*H*-indazole and regenerate Pd(II) species.[113b]

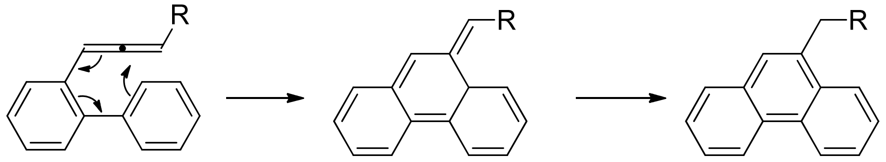


Scheme 4–8. Proposed mechanism of 3-allenyl-2*H*-indazole synthesis from

$Pd(PPh_3)_2Cl_2/CuI$ catalyzed reaction of 1-(2-alkynylaryl)-2-aryldiazene with terminal alkyne.

Synthesis of indazolo[2,3-*a*]quinolone

Since allenes possess numerous possibilities for further modification, we subsequently explored the applications of 3-allenyl-2*H*-indazole. Diels-Alder reaction is one of the most efficient methods to access to polycyclic ring systems. Allenes have been proven to be extremely useful in the various pericyclic reactions,[115] for example the cyclization of the allenyl-biphenyl system (Scheme 4–9).[104c, 116] However, the cyclization with allene involving a heteroatom is still very rare and stimulates development of novel cyclization reactions.

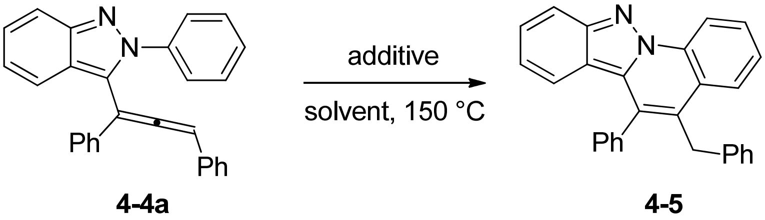


Scheme 4–9.

We embarked on our studies with the simple cyclization of **4-4a** under thermal conditions. When **4-4a** was heated in NMP in a sealed tube at 150 °C, the desired 5-benzyl-6-phenylindazolo[2,3-*a*]quinoline **4-5** was obtained in 53% yield (Table 4–4, entry 1). Notably, the indazolo[2,3-*a*]quinoline derivatives have been shown to exhibit antitumor activity[117] and interesting optical properities.[118] In order to improve the yield of **4-5** we tested the reaction with several metal species in different solvents. The results of selected experiments are shown in Table 4–4. A key requirement for the success of the cyclization is high temperature. The reactions in DMSO, diglyme, *o*-xylene were found also proceed at 150 °C, but affording rather complex product mixtures (Table 4–4, entries 2−4). In an attempt to enhance the reactivity of **4-4a**, a series of metal species was tested in *o*-xylene.

While $SnCl_4$, $ZnCl_2$, $Zn(OTf)_2$, and $AuCl_3$ resulted in discouraging yields (Table 4–4, entries 5−8), $In(OTf)_3$ was found to effect the desired transformation in 48% yield (Table 4–4, entry 9) despite lower than only heating in NMP. Finally, we concluded the optimal conditions for the cyclization of **4-4a** is heating at 150 °C in NMP.

Table 4–4. Synthesis of 5-benzyl-6-phenylindazolo[2,3-*a*]quinolone[a]



Entry	Solvent	Additive	Time (h)	Yield (%)[b]
1	NMP	None	7	53
2	DMSO	None	7	38
3	Diglyme	None	7	trace
4	*o*-Xylene	None	7	trace
5	*o*-Xylene	1.2 equiv $SnCl_4$	7	trace
6	*o*-Xylene	1.2 equiv $ZnCl_2$	7	32
7	*o*-Xylene	1.2 equiv $Zn(OTf)_2$	7	33
8	*o*-Xylene	1.2 equiv $AuCl_3$	10	trace
9	*o*-Xylene	1.2 equiv $In(OTf)_3$	7	48

[a] All reactions were carried out with 0.25 mmol **4-4a**, 0.3 mmol additive in 1 mL solvent at 150 °C. [b] Isolated yield.

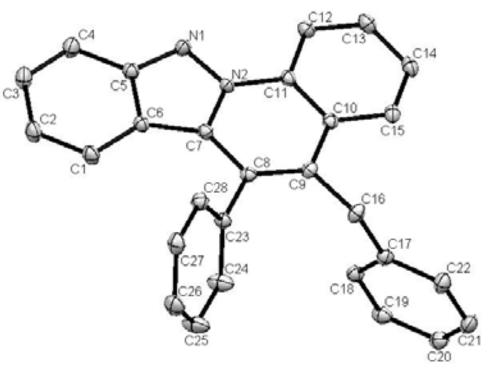
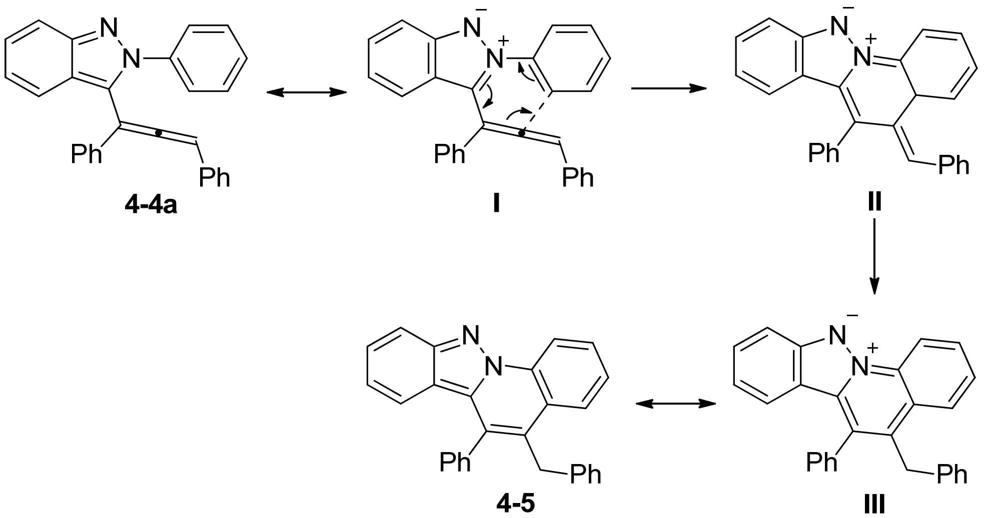


Figure 4–2. ORTEP drawing of 5-benzyl-6-phenylindazolo[2,3-*a*]quinolone **4-5**.

As shown in Scheme 4–10, a plausible mechanism was proposed for the cyclization. At first, **4-4a** undergoes 6π electrocyclization to give intermediate **II** as suggested by Wang[116] and Ye[104c]. Then isomerization occurs to afford the desired product **4-5**.



Scheme 4–10. Proposed mechanism of thermal cyclization of **4-4a**.

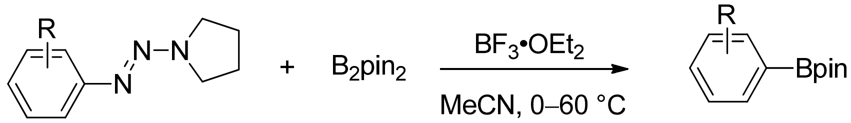
3. Conclusion

In summary, an efficient $Pd(PPh_3)_2Cl_2$/CuI catalyzed 3-allenyl-2*H*-indazole synthesis from 1-(2-alkynylaryl)-2-phenyldiazene and terminal alkynes was successfully developed. The carbene formed via intermolecular cyclization followed by coupling with terminal alkyne to afford 3-allenyl-2*H*-indazoles. This protocol features very mild conditions and high efficency. The obtained 3-allenyl-2*H*-indazole has also been used to the synthesis of indazolo[2,3-*a*]quinoline compounds by thermal cyclization. This aza-ene-ene-allene cyclization not only provides a concise synthesis to potentially useful molecules, but also shed light on a novel strategy to construct polycyclic skeleton of heterocycles.

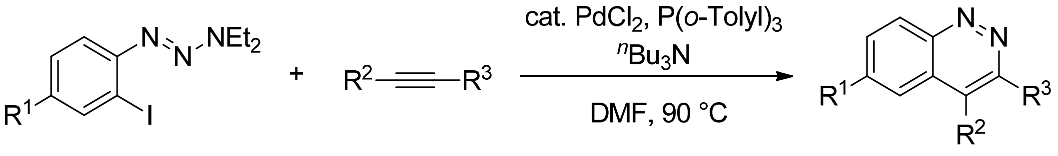
CHAPTER V Summary and Perspective

1-Aryltriazenes and 1,2-diaryldiazenes are important organic compounds because they exhibit interesting chemical, biological, pharmaceutical, and material functions. In particular, they have already revealed many applications in organic synthesis. This thesis has presented several new applications of 1-aryltriazene, 1,2-diaryldiazene and their derivatives in arylboronic ester and diaza-heterocycle synthesis.

It has been shown that 1-aryltriazene is a useful reagent to cross-coupling reaction either with Pd catalyst or metal-free condition. However, no example of arylboronic ester was found in these reports. In Chapter II, an expeditious, experimentally simple, and economical borylation method with 1-aryltriazene mediated by BF_3•OEt_2 was described (Scheme 5–1). While electron-rich 1-aryltriazene is especially effective in this reaction, borylation of electron-deficient substrates remains a challenging task. Notably, conversion of 1-aryltriazene bearing halide substitution to the corresponding boronic ester has been achieved exclusively. Experimental and kinetic studies were performed to get some information on the reaction mechanism. It was concluded that diazonium ion generated from coordination of BF_3•OEt_2 to 1-aryltriazene was the key intermediated. For decomposition of the aryldiazonium ion, the experimental results suggested an ionic pathway and the kinetic study was consistent with this conclusion. However, the radical pathway can not be completely ruled out at this stage.

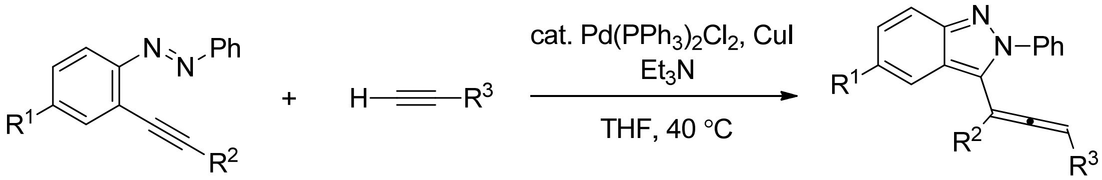


Scheme 5–1. BF_3•OEt_2 mediated deaminoborylation of 1-aryltriazene with B_2pin_2



Scheme 5–2. Pd-catalyzed cinnoline synthesis from 1-(2-iodoaryl)traizene and internal alkyne

1-(2-Alkynylaryl)triazene was applied to prepare cinnoline derivatives, however harsh conditions were required to furnish the desired products in good yield. In Chapter III a rapid and mild method for the synthesis of cinnoline from 1-(2-iodoaryl)triazene was described. The reaction was applicable to the syntheses of various 3,4-disubstituted cinnolines by Pd-catalyzed intermolecular annulation of 1-(2-iodoaryl)triazene with internal alkyne. A wide variety of 1-(2-iodoaryl)triazenes and internal alkynes have been successfully employed in this synthetic protocol. A number of functional groups, including ether, nitrile, nitro, trifluoromethyl, ketone, and ester groups, are compatible with the reaction conditions. However, only poor regioselectivity was observed in case of asymmetric alkynes were applied in the reaction. In addition, the undesired hydrodehalogenated product was obtained despite a very low yield.

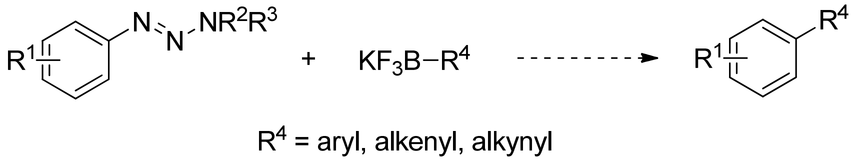


Scheme 5–3. Pd/Cu catalyzed 3-allenyl-2*H*-indazole from 2-(2-alkynylaryl)-1-phneyldiazene and terminal alkyne

In Chapter IV the author disclosed a concise approach to 3-allenyl-2*H*-indazole by Pd(PPh$_3$)$_2$Cl$_2$/CuI catalyzed sequential cyclization/coupling of 2-alkynylaryldiazene and the corresponding derivatives with a wide variety of terminal alkynes (Scheme 5–3). Various substrates could be employed in this transformation, and the desired 3-allenyl-2*H*-indazole derivatives were obtained in good to excellent chemical yields. The key feature of this transformation is the coarctate cyclization[30] of 1-(2-alkynylaryl)-2-phenyldiazene to form carbenoid intermediate. Subsequent insertion to carbenoid species and rearrangement affords 3-allenyl-2*H*-indazole. Moreover, one example of synthesis of indazolo[2,3-*a*]quinoline via thermal cyclization of 3-allenyl-2*H*-indazole was also demonstrated.

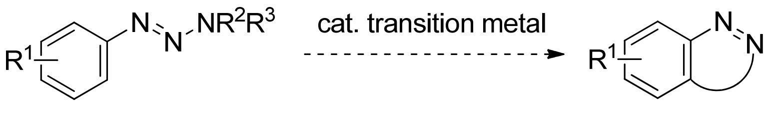
On the whole, three new synthetic methods have been made in Chapters 2, 3 and 4 of this thesis, however some insufficiency exist, such as relatively limited substrates scope and dissatisfatory regioselectivity. Thus, some efforts should be done in the future to improve the scope and selectivity.

For the future work, $BF_3•OEt_2$ mediated borylation of 1-aryltriazene points out a possibility to creat carbon−carbon bond under transition-metal-free condition (Scheme 5–4).



Scheme 5–4. Proposed transition-metal-free C−C coupling reaction of 1-aryltriazene

Furthermore, as already mentioned in Chapter 1, the C-H activation strategy has been applied to synthesize benzotriazole from 1,3-diaryltriazene, however the examples involved triazene are still rare. Meanwhile, these reports indicate the triazene can play a role of directing group like diazene. For the future research, the author proposes to extend the similar strategy to other heterocycle synthesis or C-H functionalization (Scheme 5–5).



Scheme 5–5. Proposed C-H activation reaction of 1-aryltriazene

At last, because trisbustituted allene is a chiral molecule, with some chiral ligands probably an asymmetric synthesis of 3-allenyl-2*H*-indazole could be achieved. For the continuing work, the author proposed to expand this catalytic synthetic strategy of allene to asymmentric method.

EXPERIMENTAL

^{1}H NMR (400 MHz) spectra were recorded on Bruker AVANCE 400 spectrometers in $CDCl_3$ [using tetramethylsilane (for 1H, $\delta = 0$) as internal standard] unless otherwise mentioned. ^{13}C NMR (100 MHz) spectra were recorded on Bruker AVANCE 400 spectrometers in CDCl3 [using CDCl3 (for ^{13}C, $\delta = 77.00$) as internal standard] unless other mentioned. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad. IR spectra were recorded on Horiba FT 300-S by the ATR method and Shimazu IR Prestige-21 FT-IR Spectrometer. High-resolution mass spectra were obtained with JEOL MS-700P mass spectrometer and Finnigan MAT 95 XP mass spectrometer (Thermo Electron Corporation) and Q-Tof Premier. Melting points were recorded on Buchi B-54 melting point apparatus and are uncorrected. HPLC was performed using a Shimadzu LC-20AD series HPLC system fitted with a Chiralpak IB column, eluting with hexane/isopropylalcohol (98 : 2). Flash column chromatography was performed using Merck silica gel 60 with distilled solvents. Unless otherwise specified, materials were purchased from commercial suppliers and used without further purification. Dry tetrahydrofuran (THF), acetonitrile (MeCN), toluene and dichloromethane (CH_2Cl_2) were taken from a solvent purification system (PS-400-5, innovative technology Inc.). *N*,*N*-dimethylformamide (DMF) were distilled from calcium hydride (CaH_2) and stored over Molecular Sieves 4Å (MS 4Å). Tributylamine ($^{n}Bu_3N$) and pyridine were distilled from CaH_2 and stored over KOH.

CHAPTER II BF_3•OEt_2 Mediated Metal-free Borylation of 1-Aryltriazene under Mild Reaction Condition

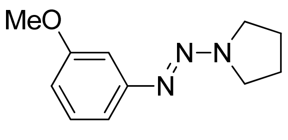
4-(benzylsulfanyl)aniline,[119] 4-(9*H*-carbazol-9-yl)aniline,[120] 3-bromo-4-methoxyaniline, 3-iodo-4-methoxyaniline,[121] 4-iodo-2-methylaniline,[122] 1-[2-(4-methoxyphenyl)diazen-1-

yl]pyrrolidine **2-1a,**[123] 1-[2-(4-methylphenyl)diazen-1-yl]pyrrolidine **2-1f**,[123] 1-[2-(4-methylphenyl)diazen-1-yl]pyrrolidine **2-1g,**[123] 1-[2-{4-[2-(trimethylsilyl)ethynyl]phenyl}-diazen-1-yl]pyrrolidine **2-1j**,[124] 1-[2-(naphthalen-1-yl)diazen-1-yl]pyrrolidine **2-1k**,[123] 1-[2-(4-fluorophenyl)diazen-1-yl]pyrrolidine **2-1n**,[125] 1-[2-(4-chlorophenyl)diazen-1-yl]pyrrolidine **2-1o**,[126] 1-[2-(4-bromophenyl)diazen-1-yl]pyrrolidine **2-1p**,[123] 1-[2-(3-bromophenyl)diazen-1-yl]pyrrolidine **2-1q**,[20] 1-[2-(4-iodophenyl)diazen-1-yl]pyrrolidine **2-1r**[123] were prepared from corresponding aniline by the literature method.

General procedure to synthesis 1-aryltriazene 2-1b, 2-1c, 2-1d, 2-1e, 2-1h, 2-1i, 2-1l, 2-1r, 2-1t, 2-1u and 2-1v.

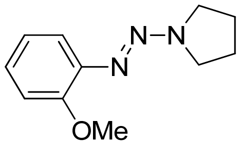
A solution of corresponding aniline (5.0 mmol) in 2.0 mL of conc. HCl was cooled in an ice bath while a solution of $NaNO_2$ (362 mg, 5.3 mmol) in cold water (10 mL) was added dropwise. The resulting solution of the diazonium salt was stirred at 0 °C for 30 min and then added to a solution of pyrrolidine (2.6 g, 36.2 mmol) and K_2CO_3 (12.5 g, 90.5 mmol) in 1:2 acetonitrile/water (25 mL) by one portion. The reaction mixture was allowed to warm to room temperature and stirred for 30 min. The aqueous phase was extracted with EtOAc (3 × 15 mL). The organic layer was washed twice with brine, dried ($MgSO_4$), filtered, and concentrated by evaporation. The crude product was purified by flash chromatography over silica gel giving the pure product.

1-[2-(3-methoxyphenyl)diazen-1-yl]pyrrolidine (2-1b)



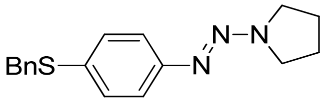
Orange solid; mp 48-49 °C; Yield: 74%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.19 (m, 1H), 7.02-6.99 (m, 2H), 6.69 (dd, J = 8.0, 2.4 Hz, 1H), 3.82 (s, 3H), 3.79 (br, 4H), 2.02 (t, J = 6.8 Hz, 4H); ^{13}C NMR (100MHz, $CDCl_3$) δ 160.2, 152.8, 129.4, 113.2, 111.5, 105.1, 55.2, 23.8; IR (neat) cm^{-1} 3053, 2982, 2876, 1597, 1410, 1315, 1265; ESI-HRMS: Found: m/z 206.1293. Calcd for $C_{11}H_{15}N_3O$: $(M+H)^+$ 206.1289.

1-[2-(2-methoxyphenyl)diazen-1-yl]pyrrolidine (2-1c)



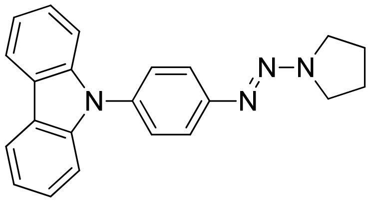
Pale yellow solid; mp 39-40 °C; Yield: 97%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 8.0 Hz, 1H), 7.11 (dd, J = 8.0, 8.0 Hz, 1H), 6.93-6.89 (m, 2H), 3.90 (s, 3H), 3.83 (br, 4H), 2.01 (br, 4H); ^{13}C NMR (100MHz, $CDCl_3$) δ 152.8, 140.9, 126.0, 120.9, 118.6, 111.7, 56.0, 23.8; IR (neat) cm^{-1} 3051, 2980, 2874, 1587, 1491, 1412, 1317, 1265; ESI-HRMS: Found: m/z 206.1296. Calcd for $C_{11}H_{16}N_3O$: $(M+H)^+$ 206.1293.

1-[2-[4-(benzylsulfanyl)phenyl]diazen-1-yl]pyrrolidine (2-1d)



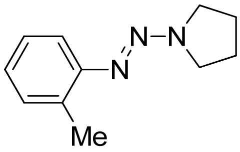
Pale yellow solid; mp 113-114 °C; Yield: 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.18 (m, 9H), 4.05 (s, 2H), 3.76 (br, 4H), 1.99 (t, J = 6.8 Hz, 4H); ^{13}C NMR (100MHz, $CDCl_3$) δ 150.3, 137.8, 131.7, 131.6, 128.8, 128.3, 127.0, 120.7, 40.0, 23.7; IR (neat) cm^{-1} 3053, 2984, 2831, 1422, 1339, 1265; ESI-HRMS: Found: m/z 298.1376. Calcd for $C_{17}H_{20}N_3S$: $(M+H)^+$ 298.1378.

9-{4-[2-(pyrrolidin-1-yl)diazen-1-yl]phenyl}-9*H*-carbazole (2-1e)



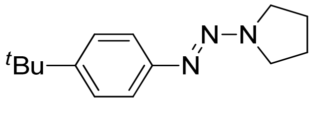
Pale yellow solid; mp 143-144 °C; Yield: 77%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 7.6 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.41-7.39 (m, 4H), 7.29-7.23 (m, 2H), 3.84 (br, 4H), 2.07 (br, 4H); ^{13}C NMR (100MHz, $CDCl_3$) δ 150.6, 141.1, 134.3, 127.6, 125.8, 123.2, 121.5, 120.2, 119.7, 109.8, 23.8; IR (neat) cm^{-1} 3053, 2982, 2876, 1506, 1427, 1404, 1315, 1265; ESI-HRMS: Found: m/z 341.1769. Calcd for $C_{22}H_{21}N_4$: $(M+H)^+$ 341.1766.

1-[2-(2-methylphenyl)diazen-1-yl]pyrrolidine (2-1h)



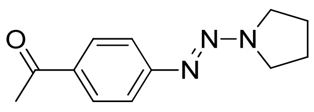
Red oil; Yield: 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 7.8 Hz, 1H), 7.20-7.14 (m, 2H), 7.05 (dd, J = 7.8, 7.2 Hz, 1H), 3.80 (br, 4H), 2.43 (s, 3H), 2.03 (t, J = 6.8 Hz, 4H); ^{13}C NMR (100MHz, $CDCl_3$) δ 149.2, 132.3, 130.5, 126.2, 116.5, 23.8, 17.6; IR (neat) cm^{-1} 3065, 3020, 2972, 2868, 1483, 1415, 1319, 1223; ESI-HRMS: Found: m/z 190.1343. Calcd for $C_{11}H_{16}N_3$: $(M+H)^+$ 190.1344.

1-[2-(4-*tert*-butylphenyl)diazen-1-yl]pyrrolidine (2-1i)



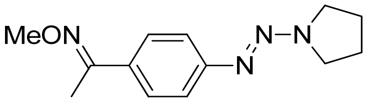
Pale yellow solid; mp 74-75 °C; Yield: 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 4H), 3.78 (br, 4H), 2.01 (m, 4H), 1.33 (s, 9H); ^{13}C NMR (100MHz, $CDCl_3$) δ 149.0, 148.0, 125.6, 119.8, 34.4, 31.4, 23.8; IR (neat) cm^{-1} 3053, 2964, 2872, 1246, 1319, 1265; ESI-HRMS: Found: m/z 232.1816. Calcd for $C_{14}H_{22}N_3$: $(M+H)^+$ 232.1814.

1-{4-[2-(pyrrolidin-1-yl)diazen-1-l]phenyl}ethan-1-one (2-1l)



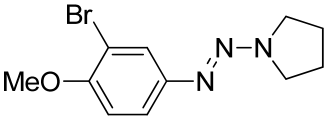
Pale yellow solid; mp 115-116 °C; Yield 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 3.83 (d, J = 102.8 Hz, 4H), 2.58 (s, 3H), 2.05 (br, 4H); ^{13}C NMR (100MHz, $CDCl_3$) δ 197.4, 155.2, 133.7, 129.6, 120.2, 51.3, 46.5, 26.5, 23.7; IR (neat) cm^{-1} 3053, 2982, 2876, 1672, 1595, 1420, 1355, 1224; ESI-HRMS: Found: m/z 218.1289. Calcd for $C_{12}H_{16}N_3O$: $(M+H)^+$ 218.1293.

(*E*)-methoxy(1-{4-[2-(pyrrolidin-1-yl)diazen-1-yl]phenyl}ethylidene)amine (2-1m)



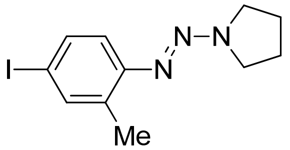
To a solution of **2-1l** (5.0 mmol, 1 equiv) in H_2O/EtOH (15 mL, 3/1) $MeONH_2$•HCl (1.1 g, 13.5 mmol) and NaOAc (1.8 g, 22.0 mmol) were added. The resulting mixture was heated at 70°C for 2 h. After cooling to room temperature, the mixture was extracted with EtOAc (3 x 25 mL). The combined organic phase was dried with $MgSO_4$ and concentrated under reduced pressure. The crude residue was purified by flash column chromtography over silica gel to afford **2-1m** as pale yellow solid; mp 99-100 °C; Yield: 15%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 3.99 (s, 3H), 3.79 (br, 4H), 2.22 (s, 3H), 2.00 (br, 4H); ^{13}C NMR (100MHz, $CDCl_3$) δ 154.4, 151.9, 133.0, 126.5, 120.2, 61.7, 23.7, 12.4; IR (neat) cm^{-1} 3053, 2984, 2876, 1205, 1422, 1400, 1315, 1265; ESI-HRMS: Found: m/z 247.1557. Calcd for $C_{13}H_{19}N_4O$: $(M+H)^+$ 247.1559.

1-[2-(3-bromo-4-methoxyphenyl)diazen-1-yl]pyrrolidine (2-1s)



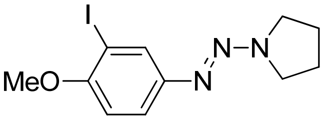
Pale yellow solid; mp 82-83 °C; Yield: 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 2.4 Hz, 1H), 7.32 (dd, J = 8.4, 2.4 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 3.88 (s, 3H), 3.76 (br, 4H), 2.03-1.99 (m, 4H); ^{13}C NMR (100MHz, $CDCl_3$) δ 153.4, 145.9, 124.3, 120.8, 111.9, 111.8, 56.4, 23.7; IR (neat) cm^{-1} 3053, 2984, 2876, 1423, 1339, 1265; ESI-HRMS: Found: m/z 284.0402. Calcd for $C_{11}H_{15}BrN_3O$: $(M+H)^+$ 284.0398.

1-[2-(4-iodo-2-methylphenyl)diazen-1-yl]pyrrolidine (2-1t)



Pale orange oil; Yield: 86%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.09 (d, J = 8.4 Hz, 1H), 3.78 (br, 4H), 2.35 (s, 3H), 2.02 (t, J = 7.6 Hz, 4H); ^{13}C NMR (100MHz, $CDCl_3$) δ 148.9, 139.0, 135.1, 134.8, 118.3, 89.1, 23.8, 17.2; IR (neat) cm^{-1} 2970, 2920, 2868, 1470, 1415, 1315, 1267, 1225; ESI-HRMS: Found: m/z 316.0311. Calcd for $C_{11}H_{15}IN_3$: $(M+H)^+$ 316.0311.

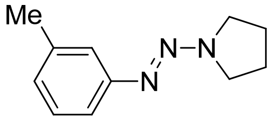
1-[2-(3-iodo-4-methoxyphenyl)diazen-1-yl]pyrrolidine (2-1u)



Pale yellow solid; mp 69-70 °C; Yield: 100%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J =

2.4 Hz, 1H), 7.35 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 3.86 (s, 3H), 3.75 (br, 4H), 2.00 (t, *J* = 7.6 Hz, 4H); ^{13}C NMR (100MHz, $CDCl_3$) δ 155.6, 146.3, 130.4, 121.8, 110.7, 86.1, 56.6, 23.7; IR (neat) cm^{-1} 3051, 2978, 2874, 1485, 1422, 1391, 1337, 1265; ESI-HRMS: Found: m/z 332.0263. Calcd for $C_{11}H_{15}IN_3O$: $(M+H)^+$ 332.0260.

1-[2-(3-methylphenyl)diazen-1-yl]pyrrolidine (2-1v)

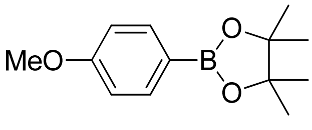


Pale yellow slid; mp 34-35 °C; Yield: 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.20 (m, 3H), 6.95 (dd, *J* = 4.0, 4.0 Hz), 3.79 (br, 4H), 2.35 (s, 3H), 2.04-2.00 (m, 4H); ^{13}C NMR (100MHz, $CDCl_3$) δ 151.4, 138.5, 128.6, 126.0, 120.9, 117.5, 23.8, 21.4; IR (neat) cm^{-1} 3051, 2978, 2874, 1410, 1319, 1265; ESI-HRMS: Found: m/z 190.1349. Calcd for $C_{11}H_{16}N_3$: $(M+H)^+$ 190.1344.

General procedure to synthesis Arylboronic ester 2-2

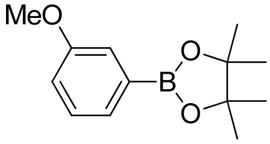
4,4,5,5-tetramethyl-2-(tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (0.75 mmol), 1-aryltriazene **2-1** (0.5 mmol) were added to a 25 mL two-neck round bottom flask which was purged thoroughly with N_2. Anhydrous MeCN (2 mL) was added via syringe and the reaction mixture was cooled to 0 °C in an ice-water bath. Then $BF_3 \bullet OEt_2$ (0.5 mmol) was added dropwies. The resulting reaction mixture was allowed to stir for 5−120 min at 0−60 °C until **2-1** was consumed as monitored by TLC. The solution was then concentrated under reduced pressure and the crude residue was purified by flash column chromatography on silica gel (hexane/ethyl acetate 50:1 to 20:1) to afford corresponding arylboronic ester.

2-(4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2-2a)[77c]



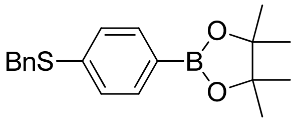
Pale yellow oil; Yield: 73%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.76 (d, J = 8.4 Hz, 2H), 6.90 (d, J = 8.4 Hz, 2H), 3.83 (s, 3H), 1.34 (s, 12H); ^{13}C NMR (100MHz, CDCl$_3$) δ 162.1, 136.5, 113.3, 85.5, 55.1, 24.8; ^{11}B (96 MHz, CDCl$_3$) δ 30.2.

2-(3-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2-2b)[77d]



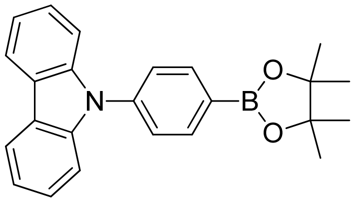
Pale orange oil; Yield: 50%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.42 (m, 1H), 7.35 (m, 1H), 7.31 (m, 1H), 7.02 (m, 1H), 3.84 (s, 3H), 1.36 (s, 12H); ^{13}C NMR (100MHz, CDCl$_3$) δ 159.0, 128.9, 127.2, 118.7, 117.9, 83.8, 55.2, 24.8; ^{11}B (96 MHz, CDCl$_3$) δ 30.7.

2-[4-(benzylsulfanyl)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2-2d)



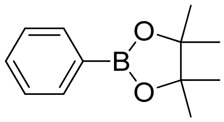
Pale yellow solid; mp 48-49 °C; Yield: 62%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.68 (d, J = 8.0 Hz, 2H), 7.34-7.22 (m, 7H), 4.16 (s, 2H), 1.33 (s, 12H); ^{13}C NMR (100MHz, CDCl$_3$) δ 140.7, 137.0, 135.1, 128.8, 128.5, 127.4, 127.2, 83.8, 37.8, 24.8; ^{11}B (96 MHz, CDCl$_3$) δ 30.6; IR (neat) cm^{-1} 3053, 2982, 1597, 1393, 1360, 1265, 1144, 1101; ESI-HRMS: Found: m/z 327.1592. Calcd for $C_{19}H_{24}BO_2S$: $(M+H)^+$ 327.1590.

9-[4-(tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]-9*H*-carbazole (2-2e)



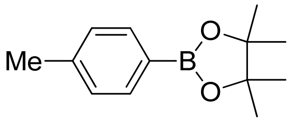
Orange solid; mp 167-168 °C; Yield: 52%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.17 (d, J = 7.6 Hz, 2H), 8.10 (d, J = 8.0 Hz, 2H), 7.64 (d, J = 8.4 Hz, 2H), 7.50-7.42 (m, 4H), 7.34-7.30 (m, 2H), 1.44 (s, 12H); ^{13}C NMR (100MHz, CDCl$_3$) δ 140.6, 140.4, 136.4, 126.0, 125.9, 123.5, 120.3, 120.0, 109.8, 84.0, 24.9; ^{11}B (96 MHz, CDCl$_3$) δ 30.4; IR (neat) cm^{-1} 3051, 2982, 2682, 1605, 1452, 1362, 1265, 1144, 1088; ESI-HRMS: Found: m/z 370.1979. Calcd for $C_{24}H_{25}BNO_2$: (M+H)$^+$ 370.1978.

4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (2-2f)



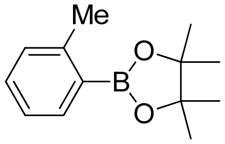
Orange oil; Yield: 36%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.83 (d, J = 6.8 Hz, 2H), 7.47 (t, J = 8.4 Hz, 1H), 7.38 (dd, J = 6.8, 7.6 Hz, 2H), 1.36 (s, 12H); ^{13}C NMR (100MHz, CDCl$_3$) δ 134.7, 131.2, 127.7, 83.7, 24.8; ^{11}B (96 MHz, CDCl$_3$) δ 30.9.

4,4,5,5-tetramethyl-2-(4-methylphenyl)-1,3,2-dioxaborolane (2-2g)[80]



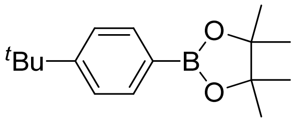
Pale orange oil; Yield: 75%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.70 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 2.37 (s, 3H), 1.34 (s, 12H); ^{13}C NMR (100MHz, CDCl$_3$) δ 141.3, 134.8, 128.5, 83.6, 24.8, 21.7; ^{11}B (96 MHz, CDCl$_3$) δ 31.0.

4,4,5,5-tetramethyl-2-(2-methylphenyl)-1,3,2-dioxaborolane (2-2h)[77d]



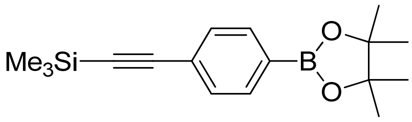
Orange oil; Yield: 83%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.76 (d, J = 6.8 Hz, 1H), 7.32 (dd, J = 7.6, 7.2 Hz, 1H), 7.17-7.14 (m, 2H), 2.54 (s, 3H), 1.34 (s, 12H); ^{13}C NMR (100MHz, CDCl$_3$) δ 144.8, 135.8, 130.8, 129.8, 124.7, 83.4, 24.9, 22.2; ^{11}B (96 MHz, CDCl$_3$) δ 30.2.

2-(4-*tert*-butylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2-2i)[77c]



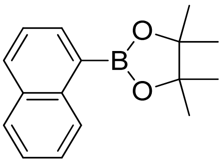
Pale orange solid; mp 134-135 °C; Yield: 71%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.78 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 1.35 (s, 12H), 1.34 (s, 9H); ^{13}C NMR (100MHz, CDCl$_3$) δ 154.5, 134.7, 124.7, 83.6, 34.9, 31.2, 24.8; ^{11}B (96 MHz, CDCl$_3$) δ 30.7.

trimethyl({2-[4-(tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]ethynyl})silane (2-2j)[76b]



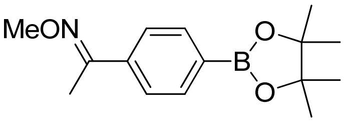
Pale yellow solid; mp 152-153 °C; Yield: 53%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.72 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 8.0 Hz, 2H), 1.34 (s, 12H), 0.25 (s, 9H); ^{13}C NMR (100MHz, CDCl$_3$) δ 134.4, 131.1, 125.7, 105.2, 95.5, 83.9, 24.9, -0.1; ^{11}B (96 MHz, CDCl$_3$) δ 30.4.

4,4,5,5-tetramethyl-2-(naphthalen-1-yl)-1,3,2-dioxaborolane (2-2k)[77d]



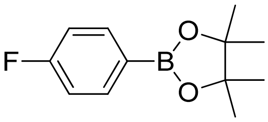
Red solid; mp 54-55 °C; Yield: 65%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J = 8.0 Hz, 1H), 8.14 (d, J = 6.8 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.59 (dd, J = 8.0, 6.8 Hz), 7.52 (dd, J = 8.0, 6.8 Hz, 1H), 1.47 (s, 12H); ^{13}C NMR (100MHz, $CDCl_3$) δ 136.9, 135.6, 133.2, 131.6128.4, 128.3, 126.3, 125.4, 124.9, 83.7, 24.9; ^{11}B (96 MHz, $CDCl_3$) δ 31.5.

methoxy({1-[4-(tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]ethylidene})amine (2-2m)



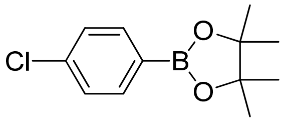
Orange solid; mp 40-41 °C; Yield: 70%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.0 Hz, 2H), 4.01 (s, 3H), 2.23 (s, 3H), 1.35 (s, 12H); ^{13}C NMR (100MHz, $CDCl_3$) δ 154.5, 139.1, 134.8, 125.2, 83.8, 61.9, 24.8, 12.5; ^{11}B (96 MHz, $CDCl_3$) δ 30.2; IR (neat) cm^{-1} 3051, 2982, 2818, 1601, 1396, 1265, 1144, 1049; ESI-HRMS: Found: m/z 276.1775. Calcd for $C_{15}H_{23}BNO_3$: $(M+H)^+$ 276.1771.

2-(4-fluorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2-2n)[76b]



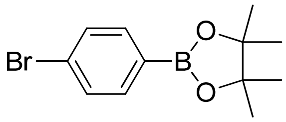
Brown oil; Yield: 54%; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.81-7.79 (m, 2H), 7.05 (t, J = 8.8 Hz, 2H), 1.34 (s, 12H); ^{13}C NMR (100MHz, $CDCl_3$) δ 166.3, 163.8, 137.0, 136.9, 114.9, 114.7, 83.9, 24.8; ^{11}B (96 MHz, $CDCl_3$) δ 30.5.

2-(4-chlorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2-2o)[80]



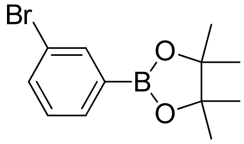
Orange solid; mp 52-53 °C; Yield: 44%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.4, Hz, 2H), 7.34 (d, *J* = 8.4Hz, 2H), 1.34 (s, 12H); ^{13}C NMR (100MHz, $CDCl_3$) δ 137.5, 136.1, 128.0, 84.0, 24.8; ^{11}B (96 MHz, $CDCl_3$) δ 30.7.

2-(4-bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2-2p)[77d]



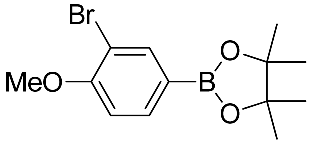
Orange solid; mp 68-69 °C; Yield: 44%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.0 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 1.34 (s, 12H); ^{13}C NMR (100MHz, $CDCl_3$) δ 136.3, 130.9, 126.2, 84.0, 24.8; ^{11}B (96 MHz, $CDCl_3$) δ 30.6.

2-(3-bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2-2q)[127]



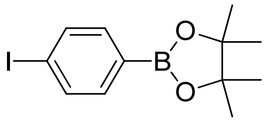
Red oil; Yield: 30%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 1.2 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.59-7.56 (m, 1H), 7.24 (dd, *J* = 7.6, 8.0 Hz, 1H), 1.34 (s, 12H); ^{13}C NMR (100MHz, $CDCl_3$) δ 137.5, 134.2, 133.1, 129.5, 122.4, 84.1, 24.8; ^{11}B (96 MHz, $CDCl_3$) δ 30.3.

2-(3-bromo-4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2-2r)



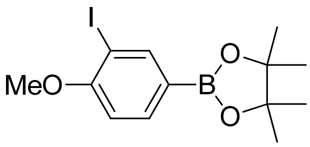
White solid; mp 75-76 °C; Yield: 72%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.98 (s, 1H), 7.71 (d, J = 8.0 Hz, 1H), 6.88 (d, J = 8.0 Hz, 1H), 1.33 (s, 12H); ^{13}C NMR (100MHz, CDCl$_3$) δ 158.2, 139.7, 135.5, 111.5, 111.2, 83.9, 56.1, 24.8; ^{11}B (96 MHz, CDCl$_3$) δ 30.1; IR (neat) cm^{-1} 3051, 2980, 2843, 1597, 1389, 1265, 1142, 1098; ESI-HRMS: Found: m/z 335.0430. Calcd for: (M+Na)$^+$ 335.0430.

2-(4-iodophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2-2s)[77d]



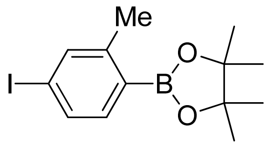
Orange solid; mp 90-91 °C; Yield: 34%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.72 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.0 Hz, 2H), 1.33 (s, 12H); ^{13}C NMR (100MHz, CDCl$_3$) δ 136.9, 136.3, 98.8, 84.0, 24.8; ^{11}B (96 MHz, CDCl$_3$) δ 30.8.

2-(3-iodo-4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2-2t)



White solid; mp 110-111 °C; Yield: 64%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.21 (s, 1H), 7.73 (d, J = 8.0 Hz, 1H), 6.80 (d, J = 8.0 Hz, 1H), 3.90 (s, 3H), 1.33 (s, 12H); ^{13}C NMR (100MHz, CDCl$_3$) δ 160.3, 145.9, 136.5, 110.3, 85.9, 83.9, 56.2, 24.8; ^{11}B (96 MHz, CDCl$_3$) δ 30.3; IR (neat) cm^{-1} 3053, 2984, 1591, 1352, 1265, 1142; ESI-HRMS: Found: m/z 361.0471. Calcd for $C_{13}H_{19}BIO_3$: (M+H)$^+$ 361.0472.

2-(4-iodo-2-methylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2-2u)



Orange oil; Yield: 62%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.56 (s, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 2.48 (s, 3H), 1.33 (s, 12H); ^{13}C NMR (100MHz, CDCl$_3$) δ 146.9, 138.6, 137.2, 133.9, 98.4, 83.6, 24.9, 21.8; ^{11}B (96 MHz, CDCl$_3$) δ 31.3; IR (neat) cm^{-1} 3051, 2980, 1578, 1344, 1265, 1145, 1063; ESI-HRMS: Found: m/z 345.0531. Calcd for $C_{13}H_{19}BIO_2$: $(M+H)^+$ 345.0528.

Hammett study

4,4,5,5-Tetramethyl-2-(tetra--methyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (0.75 mmol), hexafluorobenzene (internal standard, 0.35 mmol, 40 μL), aryltriazene (0.5 mmol) were added to a 25 mL two-neck round bottom flask which was purged thoroughly with N_2. Anhydrous acetonitrile (2 mL) was added via syringe and the reaction mixture was cooled to 0 °C in an ice-water bath. Then, BF_3•OEt_2 (0.5 mmol) was added by one portion. About 2 μL of reaction mixture was taken via capillary tube, then quenched by 1500 μL of 0.05 mol/L acetonitrile solution of triethylamine and analyzed by HPLC analysis (UV detector 230 nm). Substrate area/internal standard area was converted to absolute concentration by a calibration curve.

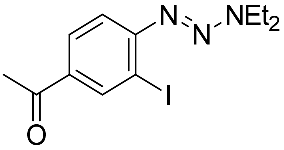
CHAPTER III Synthesis of 3,4-disubstituted cinnolines by the Pd-catalyzed annulation of 2-iodophenyltriazeneswith an internal alkyne

3,3-diethyl-1-(2-iodophenyl)triaz-1-ene **3-1a**, 3,3-diethyl-1-(2-iodo-4-methylphenyl)triaz-1-ene **3-1b**, 1-(4-*tert*-butyl-2-iodophenyl)-3,3-diethyltriaz-1-ene **3-1c**, 3,3-diethyl-1-(2-iodo-4-methoxyphenyl)triaz-1-ene **3-1d**, 3,3-diethyltriaz-1-en-1-yl]-3-

iodobenzonitrile **3-1e**, 3,3-diethyl-1-(2-iodo-4- nitro-phenyl)triaz-1-ene **3-1f**, 3,3-diethyl-1-[2-iodo-4- (trifluoro-methyl)phenyl]triaz-1-ene **3-1g**, methyl 4-(3,3-diethyltriaz-1-en-1-yl)- 3-iodo-benzoate **3-1i** were prepared from corresponding 4-substitueted-2-iodoaniline by the literature method.[128] The corresponding 2-iodo-4-methylaniline,[129] 2-iodo-4-*tert*-butylaniline,[130] 2-iodo-4-methoxyaniline,[131] 4-amino-3-iodobenzonitrile,[132] 2-iodo-4-nitroaniline,[130] 2-iodo-4-(trifluoromethyl)aniline,[130] 1-(4-amino-3-iodophenyl)ethanone[133] and methyl 4-amino-3-iodobenzoate[132] were prepared by iodination of 4-substituted aniline. 1-chloro-4-[2-(4-chlorophenyl)-ethynyl]benzene **3-2b**, 1,1'-(4,4'-(ethyne-1,2-diyl)bis(4,1-phenylene))diethanone **3-2c**, 1-methyl-4-[2-(4-methylphenyl)-ethynyl]benzene **3-2d** and 1-methoxy-4-[2-(4-methoxyphenyl)-ethynyl]benzene **3-2e** were prepared by the reported method.[134]

Procedure for preparation of 1-[4-(3,3-diethyltriaz-1-en-1-yl)-3-iodophenyl]ethan-1-one (3-1h)

To a solution of 1-(4-amino-3-iodophenyl)ethanone (8.6 mmol) in 1:3 acetonitrile/water (2 mL) was added 5.7 mL of conc. HCl and then cooled in an ice bath. To the mixture a solution of $NaNO_2$ (1.31 g, 19.0 mmol) in 1:3 acetonitrile/water (10 mL) was added dropwise. The resulting solution of the diazonium salt was stirred at 0 °C for 30 min and then added to a solution of diethylamine (6.3 g, 86.2 mmol) and K_2CO_3 (6.0 g, 43.1 mmol) in 1:3 acetonitrile/water (860 mL) at 0 °C by one portion. The reaction mixture was allowed to warm to room temperature and stirred for 30 min. The aqueous phase was extracted with EtOAc (3 × 100 mL). The organic layer was washed twice with brine, dried ($MgSO_4$), filtered, and concentrated by evaporation. The crude product was purified by flash chromatography (hexane/ethyl acetate 20:1) on silica gel to afford 1-[4-(3,3-diethyltriaz-1-en-1-yl)-3-iodophenyl]ethan-1-one.

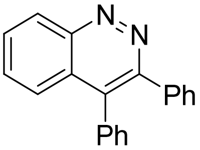


Yellow oil; Yield: 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (dt, J = 19.6, 7.0 Hz, 6H), 3.84 (q, J = 7.0 Hz, 4H), 7.40 (d, 1H, J = 8.4 Hz), 7.87 (dd, J = 8.4, 1.6 Hz, 1H), 8.42 (d, J = 1.6 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 10.9, 14.4, 26.5, 42.7, 49.7, 96.2, 116.8, 128.9, 134.8, 139.8, 153.9, 196.1; IR (neat) 2974, 2934, 2872, 1674, 1581, 1542 cm^{-1}; ESI-HRMS calcd for $C_{12}H_{17}N_3OI$ 346.0416, found 346.0416.

General procedure for annulation of 2-iodoaryltriazene with internal alkyne.

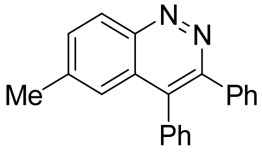
The solution of **3-1** (0.25 mmol), **3-2** (0.75 mmol), $PdCl_2$ (3.3 mg, 0.02 mmol), P(*o*-Tolyl)$_3$ (11.4 mg, 0.04 mmol) and ^{n}Bu$_3$N (119 µL, 0.50 mmol) in DMF (5 mL) was stirred under N_2 at 90 ºC until **3-1** was consumed as monitored by TLC. The reaction mixture was allowed to cool to room temperature. The solvent was evaporated and the residue was purified by column chromatography on silica gel (hexanes/ethyl acetate/dichloromethane 10:1:1 to 5:1:1) to afford corresponding cinnoline.

3,4-Diphenylcinnoline (3-3a)[135]



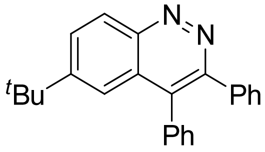
Pale yellow solid; mp 150-151 °C; Yield: 71%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.28 (m, 5H), 7.40-7.42 (m, 3H), 7.47-7.49 (m, 2H), 7.64-7.68 (m, 1H), 7.72-7.75 (m, 1H), 7.80-7.84 (m, 1H), 8.61-8.8.64 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 125.3, 125.5, 127.87, 127.9, 128.3, 128.5, 129.8, 129.9, 130.4, 130.5, 131.2, 132.9, 134.1, 137.6, 149.4, 153.0; IR (neat) 3105, 3061, 2980, 2930, 2245, 1636 cm^{-1}; ESI-HRMS: Found: m/z 283.1236. Calcd for $C_{20}H_{15}N_2$: $(M+H)^+$ 283.1235.

6-methyl-3,4-diphenylcinnoline (3-3b)



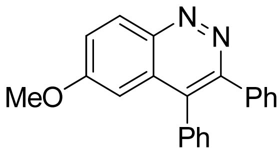
Pale yellow solid; mp 211-212 °C; Yield: 73%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (s, 3H), 7.22-7.26 (m, 5H), 7.39-7.41 (m, 3H), 7.45-7.47 (m, 3H), 7.63 (dd, J = 8.4, 1.2 Hz, 1H), 8.49 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 22.2, 123.5, 125.6, 127.8, 128.2, 128.5, 129.6, 130.4, 130.5, 132.3, 134.3, 137.8, 141.9, 148.4, 153.0. IR (neat) 3055, 2982, 2951, 2305, 1622 cm^{-1};ESI-HRMS: Found: m/z 297.1398. Calcd for $C_{21}H_{17}N_2$: $(M+H)^+$ 297.1392.

6-*tert*-butyl-3,4-diphenylcinnoline (3-3c)



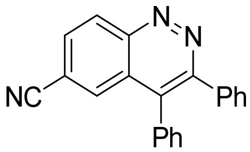
Pale yellow solid; mp 147-148 °C; Yield: 84%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (s, 9H), 7.25-7.27 (m, 5H), 7.40-7.41 (m, 3H), 7.46-7.48 (m, 2H), 7.65 (d, J = 2.0 Hz, 1H), 7.92 (dd, J = 8.8, 2.0 Hz, 1H), 8.55 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 30.7, 35.5, 119.6, 125.3, 127.7, 127.8, 128.2, 128.4, 129.1, 129.4, 130.4, 130.5, 133.0, 134.3, 137.9, 148.4, 153.1, 154.4; IR (neat) 3051, 2966, 2909, 2870, 1620, 1554 cm^{-1}; ESI-HRMS: Found: m/z 339.1861. Calcd for $C_{24}H_{23}N_2$: $(M+H)^+$ 339.1869.

6-methoxy-3,4-diphenylcinnoline (3-3d)



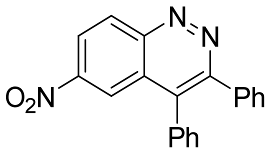
Pale brown solid; mp 161-162 °C; Yield: 50%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.77 (s, 3H), 6.87 (d, J = 2.8 Hz, 1H), 7.23-7.26 (m, 5H), 7.39-7.46 (m, 5H), 8.48 (d, J = 9.2 Hz, 1H); ^{13}C NMR (100MHz, CDCl$_3$) δ 55.6, 101.3, 123.6, 127.6, 127.8, 128.2, 128.6,130.2, 130.5, 131.7, 131.9, 134.6, 137.8, 146.8, 153.0, 161.2; IR (neat) 3084, 3055, 2980, 2964, 2253, 1620 cm^{-1}; ESI-HRMS: Found: m/z 313.1347. Calcd for $C_{21}H_{17}N_2O$: $(M+H)^+$ 313.1341.

3,4-diphenylcinnoline-6-carbonitrile (3-3e)



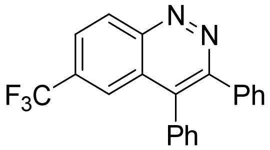
Yellow solid; mp 171-172 °C; Yield: 42%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.24-7.26 (m, 2H), 7.31-7.32 (m, 3H), 7.48-7.49 (m, 5H), 7.95 (dd, J = 8.8, 1.6 Hz, 1H), 8.16 (d, J = 1.6 Hz, 1H), 8.75 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100MHz, CDCl$_3$) δ 114.9, 117.8, 125.0, 128.1, 128.6, 129.0, 129.2, 130.0, 130.2, 130.5, 131.6, 132.7, 132.8, 136.7, 148.4, 154.5; IR (neat) 3103, 3055, 2984, 2253, 2231, 1645, 1616 cm^{-1}; ESI-HRMS: Found: m/z 308.1198. Calcd for $C_{21}H_{14}N_3$: $(M+H)^+$ 308.1188.

6-nitro-3,4-diphenylcinnoline (3-3f)



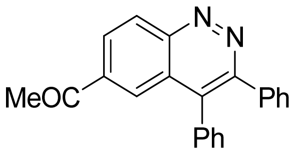
Yellow solid; mp 192-193 °C; Yield: 46%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.33 (m, 5H), 7.48-7.50 (m, 5H), 8.53-8.56 (m, 1H), 8.69 (d, J = 2.0 Hz, 1H), 8.81 (d, J = 9.2 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 123.0, 123.2, 125.0, 128.1, 128.6, 129.1, 129.3, 130.3, 130.5, 132.4, 132.6, 134.2, 136.5, 148.4, 149.1, 154.5; IR (neat) 3090, 3049, 2986, 2305, 1624 cm^{-1}; ESI-HRMS: Found: m/z 328.1092. Calcd for $C_{20}H_{14}N_3O_2$: $(M+H)^+$ 328.1086.

3,4-diphenyl-6-(trifluoromethyl)cinnoline (3-3g)



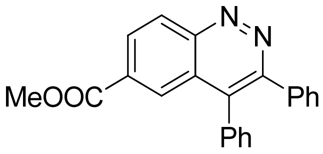
Yellow solid; mp 164-165 °C; Yield: 52%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.31 (m, 5H), 7.45-7.49 (m, 5H), 7.97-8.00 (m, 1H), 8.07 (s, 1H), 8.77 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 122.0, 123.3 (q, J = 272.0 Hz), 123.7 (q, J = 5.0 Hz), 124.8, 125.5 (q, J = 3.0 Hz), 128.0, 128.4, 128.89, 128.94, 130.3, 130.5, 131.6, 132.5 (q, J = 22.0 Hz), 133.1, 133.6, 137.0, 149.2, 154.2; IR (neat) 3084, 3053, 2984, 2253, 1634 cm^{-1}; ESI-HRMS: Found: m/z 351.1119. Calcd for $C_{21}H_{14}F_3N_2$: $(M+H)^+$ 351.1109.

1-(3,4-diphenylcinnolin-6-yl)ethan-1-one (3-3h)



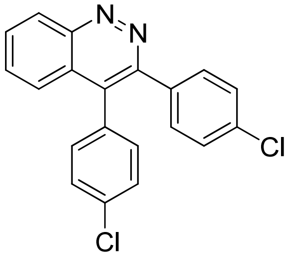
Yellow solid; mp 170-171 °C; Yield: 64%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.60 (s, 3H), 7.27-7.31 (m, 5H), 7.44-7.49 (m, 5H), 8.32-8.34 (m, 2H), 8.69 (d, J = 9.2 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 26.7, 125.0, 127.5, 127.8, 128.0, 128.2, 128.79, 128.85, 130.4, 130.5, 130.6, 133.4, 134.0, 137.1, 138.3, 149.7, 154.0, 197.0; IR (neat) 3053, 2984, 2304, 2252, 1687 cm^{-1}; ESI-HRMS: Found: m/z 325.1335. Calcd for $C_{22}H_{17}N_2O$: $(M+H)^+$ 325.1341.

methyl 3,4-diphenylcinnoline-6-carboxylate (3-3i)



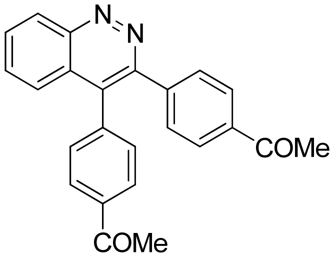
Yellow solid; mp 199-200 °C; Yield: 60%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.94 (s, 3H), 7.26-7.30 (m, 5H), 7.44-7.49 (m, 5H), 8.37-8.40(m, 1H), 8.49-8.50 (m, 1H), 8.66-8.69 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 52.7, 124.8, 128.0, 128.2, 128.8, 129.2, 130.4, 130.5, 132.1, 133.4, 133.9, 137.2, 149.7, 153.9, 165.8; IR (neat) 3053, 2986, 2955, 2305, 1724 cm^{-1}; ESI-HRMS: Found: m/z 341.1294. Calcd for $C_{22}H_{17}N_2O_2$: $(M+H)^+$ 341.1290.

3,4-bis(4-chlorophenyl)cinnoline (3-3j)



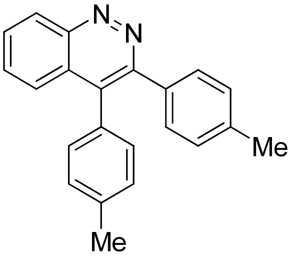
Pale yellow solid; mp 164-165 °C; Yield: 75%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 7.70 (m, 2H), 7.84 (m, 1H), 8.61 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 124.8, 125.1, 128.3, 129.1, 130.0, 130.2, 131.61, 131.65, 131.7, 131.8, 132.3, 134.4, 134.8, 135.8, 149.3, 151.7; IR (neat) 3053, 2984, 2305, 1645, 1636, 1597 cm^{-1}; ESI-HRMS: Found: m/z 351.0453. Calcd for $C_{20}H_{13}Cl_2N_2$: $(M+H)^+$ 351.0456.

1-{4-[3-(4-acetylphenyl)cinnolin-4-yl]phenyl}ethan-1-one (3-3k)



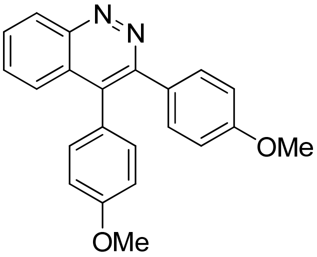
Pale yellow solid; mp 182-183 °C; Yield: 82%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.60 (s, 3H), 2.66 (s, 3H), 7.40 (d, J = 8.4 Hz, 2H), 7.58 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 8.4 Hz, 1H), 7.75 (dd, J = 8.4, 6.8 Hz, 1H), 7.88-7.93 (m, 3H), 8.03 (d, J = 8.4 Hz, 2H), 8.68 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 26.6, 124.8, 124.9, 128.0, 130.2, 130.6, 130.71, 130.74, 131.9, 132.3, 136.4, 137.0, 138.7, 141.9, 149.4, 151.6, 197.3, 197.7; IR (neat) 3053, 3003, 2984, 1684, 1606 cm^{-1}; ESI-HRMS: Found: m/z 367.1448. Calcd for $C_{24}H_{19}N_2O_2$: $(M+H)^+$ 367.1447.

3,4-bis(4-methylphenyl)cinnoline (3-3l)



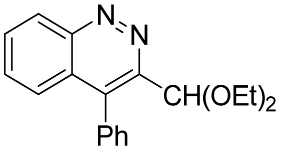
Pale yellow solid; mp 136-137 °C; Yield: 73%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.32 (s, 3H), 2.40 (s, 3H), 7.08 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.60-7.7.64 (m, 1H), 7.71-7.74 (m, 1H), 7.75-7.79 (m, 1H), 8.57-8.60 (m, 1H); ^{13}C NMR (100MHz, CDCl$_3$) δ 21.2, 21.3, 125.4, 125.7, 128.6, 129.2, 129.6, 129.8, 130.2, 130.4, 130.9, 131.2, 132.7, 134.8, 137.6, 138.0, 149.2, 153.0; IR (neat) 3049, 3030, 2982, 2922, 2243, 1612 cm^{-1}; ESI-HRMS: Found: m/z 311.1542. Calcd for $C_{22}H_{19}N_2$: (M+H)$^+$ 311.1548.

3,4-bis(4-methoxyphenyl)cinnoline (3-3m)



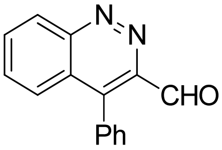
Pale yellow solid; mp 137-138 °C; Yield: 78%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.79 (d, J = 1.2 Hz, 3H), 3.85 (d, J = 0.8 Hz, 3H), 6.82 (d, J = 8.4 Hz, 2H), 6.96 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.61-7.65 (m, 1H), 7.75-7.79 (m, 2H), 8.56-8.58 (m, 1H); ^{13}C NMR (100MHz, CDCl$_3$) δ 55.1, 55.2, 113.4, 114.1, 125.3, 125.9, 126.3, 129.5, 129.8, 130.2, 130.9, 131.6, 131.8, 132.1, 149.2, 152.8, 159.3, 159.5; IR (neat) 3051, 3005, 2960, 2936, 2837, 2250, 1609 cm^{-1}; ESI-HRMS: Found: m/z 343.1454. Calcd for $C_{22}H_{19}N_2O_2$: (M+H)$^+$ 343.1447.

4-(diethoxymethyl)-3-phenylcinnoline (3-3n)



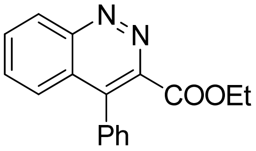
Pale brown oil; Yield: 46%. The regiostructure of **3-3n** was confirmed by NOESY analysis which shows no correlation between the hydrogen next to ethoxy groups and the hydrogen on 5-cabon of cinnoline; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15 (t, *J* = 7.2 Hz, 6H), 3.36 (m, 2H), 3.68 (m, 2H), 5.60 (s, 1H), 7.52-7.58 (m, 3H), 7.69-7.71 (m, 2H), 7.77 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.83 (dd, *J* = 8.4, 8.4 Hz, 1H), 8.58 (d, *J* = 8.4 Hz, 1H), 8.81 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 15.2, 64.0, 102.3, 123.5, 126.8, 128.0, 128.4, 128.8, 129.9, 130.0, 130.2, 130.7, 137.2, 150.6, 153.5; IR (neat) 3061, 2957, 2930, 2870, 1738, 1657 cm^{-1}; ESI-HRMS: Found: m/z 309.1599. Calcd for $C_{19}H_{21}N_2O_2$: $(M+H)^+$ 309.1603.

4-phenylcinnoline-3-carbaldehyde (3-3n')



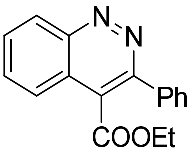
Pale yellow solid; mp 245-246 °C; Yield: 5%. The regiostructure of **3-3n'** was confirmed by NOESY analysis which shows no correlation between the hydrogen on the formyl group and the hydrogen on 5-cabon of cinnoline. ^{1}H NMR (400 MHz, DMSO-d_6, using residual DMSO as the internal standard; δ 2.50) δ 7.23-7.31 (m, 2H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.56-7.63 (m, 3H), 7.77-7.79 (m, 2H), 8.21 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100MHz, DMSO-d_6, using DMSO-d_6 as the internal standard; δ 39.5) δ 112.0, 113.5, 121.0, 122.4, 123.7, 125.8, 129.0, 129.77, 129.84, 129.9, 135.9, 149.1, 185.5; IR (neat) 3163, 3001, 2943, 2291, 2253, 1634 cm^{-1}; ESI-HRMS: Found: m/z 257.0700. Calcd for $C_{15}H_{10}NaN_2O$: $(M+Na)^+$ 257.0691.

ethyl 4-phenylcinnoline-3-carboxylate (3-3o)



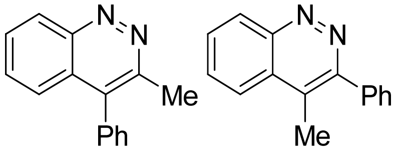
Pale yellow viscous oil; Yield: 19%. The regiostructure of **3-3o** was assumed according to the assignment of the regiostructure of **3-3o'**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (t, J = 7.2 Hz, 3H), 4.27 (q, J = 7.2 Hz, 2H), 7.38-7.40 (m, 2H), 7.52-7.55 (m, 3H), 7.75 (d, J = 3.6 Hz, 1H), 7.91-7.95 (m, 1H), 8.68 (d, J = 8.4 Hz, 1H), 8.65 (dd, J = 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 13.8, 62.0, 125.1, 125.8, 128.5, 129.0, 129.2, 130.2, 131.5, 131.8, 133.1, 135.6, 145.9, 150.5, 165.9; IR (neat) 3055, 2984, 2936, 1722, 1626 cm^{-1}; ESI-HRMS: Found: m/z 279.1129. Calcd for $C_{17}H_{15}N_2O_2$: $(M+H)^+$ 279.1134.

ethyl 3-phenylcinnoline-4-carboxylate (3-3o')[136]



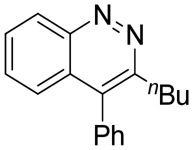
Pale yellow solid; Yield: 16%. The structure of **3-3o'** was confirmed by comparing the spectral data of the authentic compound which was synthesized according to the reference;[14] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (t, J = 7.2 Hz, 3H), 4.32 (q, J = 7.2 Hz, 2H), 7.51-7.56 (m, 3H), 7.82-7.92 (m, 4H), 8.03 (d, J = 8.0 Hz, 1H), 8.65 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 13.7, 62.4, 122.3, 124.0, 124.6, 128.6, 129.27, 129.29, 130.4, 132.5, 137.2, 149.3, 151.1, 166.6.

3-methyl-4-phenylcinnoline and 4-methyl-3-phenylcinnoline (3-3p + 3-3p')



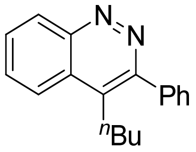
An inseparable 59 : 41 mixture of two isomers **3-3p** and **3-3p'** were obtained in 81% yield (44.6 mg, 20.2 mmol) as a pale yellow solid. Their regiostructures were not assigned. ^{1}H NMR (400 MHz, $CDCl_3$) for minor isomer: δ 2.76 (s, 3H), 7.30-7.32 (m, 2H), 7.47-7.62 (m, 5H), 7.73-7.77 (m, 1H), 8.53 (d, J = 8.4 Hz, 1H). ^{1}H NMR (400 MHz, $CDCl_3$) for major isomer: δ 2.71 (s, 3H), 7.47-7.62 (m, 3H), 7.67-7.70 (m, 2H), 7.78-7.86 (m, 2H), 8.07-8.09 (m, 1H), 8.56-8.58 (m, 1H). ^{13}C NMR (100MHz, $CDCl_3$) for mixture: δ 14.6, 20.9, 123.3, 124.7, 125.4, 126.4, 128.3, 128.46, 128.52, 128.8, 129.1, 129.2, 129.6, 129.7, 130.2, 130.4, 130.8, 130.9, 133.5, 134.3, 138.0, 148.5, 149.3, 151.5, 155.3; IR (neat) 3051, 2980, 2930, 2304, 1616 cm^{-1}; ESI-HRMS: Found: m/z 221.1081. Calcd for $C_{15}H_{13}N_2$: $(M+H)^+$ 221.1079.

3-butyl-4-phenylcinnoline (3-3q)



Pale yellow viscous oil; Yield: 27%. The regiostructure of **3-3q** was confirmed by NOE-SY analysis which showed no correlation between butyl hydrogen and the hydrogen on 5-carbon of the cinnoline ring. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (t, J = 7.4 Hz, 3H), 1.24-1.32 (m, 2H), 1.70-1.76 (m, 2H), 3.00-3.04 (m, 2H), 7.29-7.31 (m, 2H), 7.44 (d, J = 8.4 Hz, 1H), 7.51-7.60 (m, 4H), 7.72-7.76 (m, 1H), 8.54 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 13.8, 22.5, 32.5, 33.4, 125.0, 125.7, 128.4, 128.6, 129.1, 129.4, 129.8, 130.7, 133.2, 134.3, 149.0, 155.3; IR (neat) 3061, 2959, 2930, 2870, 1634, 1614 cm^{-1}; ESI-HRMS: Found: m/z 263.1541. Calcd for $C_{18}H_{19}N_2$: $(M+H)^+$ 263.1548.

4-butyl-3-phenylcinnoline (3-3q')



Pale yellow solid; mp 68-69 °C; Yield: 53%. The regiostructure of **3-3q'** was confirmed by NOESY analysis which showed a correlation between butyl hydrogen and the hydrogen on 5-carbon of the cinnoline ring. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, J = 7.4 Hz, 3H), 1.32-1.38 (m, 2H), 1.60-1.66 (m, 2H), 3.05-3.09 (m, 2H), 7.49-7.56 (m, 3H), 7.60-7.63 (m, 2H), 7.77-7.84 (m, 2H), 8.09 (dd, J = 7.8, 1.8 Hz, 1H), 8.58 (dd, J = 7.8, 1.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 13.6, 22.9, 27.5, 33.0, 123.4, 125.7, 128.3, 129.6, 129.8, 130.7, 130.8, 133.2, 138.4, 149.2, 155.5; IR (neat) 3061, 2959, 2930, 2870, 1638, 1614 cm^{-1}; ESI-HRMS: Found: m/z 263.1539. Calcd for $C_{18}H_{19}N_2$: $(M+H)^+$ 263.1548.

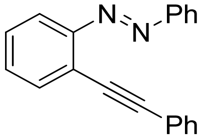
CHAPTER III Preparation of 3-Allenylindazole from 2-Alkynyldiazene and Terminal alkyne and A Novel Synthesis of Indazolo[2,3-*a*]quinolone

1-(2-iodophenyl)-2-phenyldiazene **4-1a**, 1-(2-iodo-4-methylphenyl)-2-phenyldiazene **4-1b**, 1-(4-(*tert*-butyl)-2-iodophenyl)-2-phenyldiazene **4-1c**, 1-(4-fluoro-2-iodophenyl)-2-phenyldiazene **4-1d**, 1-(4-chloro-2-iodophenyl)-2-phenyldiazene **4-1e**, 1-phenyl-2-(2-((trimethylsilyl)ethynyl)phenyl)-diazene **4-3i** were prepared according to known procedures.[73]

General procedure for preparation of 1-phenyl-2-(2-alkynylaryl)diazene

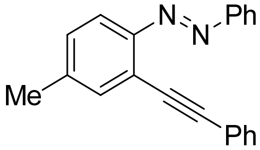
4-1 (1.0 mmol), $Pd(PPh_3)_2Cl_2$ (28.1 mg, 0.04 mmol), CuI (15.2 mg, 0.08 mmol) and $^nBuNH_2$ (497 μL, 6.0 mmol) were dissolved in 10 mL anhydrous THF under N_2. The mixture was immediately purged by N_2 three times. To resulting solution alkyne was added dropwise. The mixture was stirred at room temperature. After the reaction was completed according to TLC reaction control (2-7 h), NH_4Cl saturated aqueous solution (15 mL) was added. The organic layer was separated, and the aqueous layer was extracted twice with ethyl acetate (5 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude residue was purified by column chromatography (hexane/ethyl acetate 50:1 to 20:1) on silica gel to afford desire product.

1-phenyl-2-(2-(phenylethynyl)phenyl)diazene (4-3a)



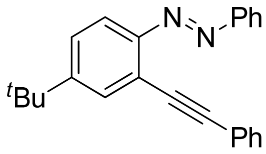
Red solid; mp 53-55 °C; Yield: 80%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.39 (m, 3H), 7.42-7.47 (m, 2H), 7.49-7.56 (m, 3H), 7.58-7.61 (m, 2H), 7.71-7.77 (m, 2H), 8.03 (d, J = 7.1 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 86.8, 95.6, 116.2, 123.3, 123.4, 123.7, 128.36, 128.44, 129.1, 130.5, 131.3, 131.6, 133.3, 152.9, 153.1; IR (neat) cm^{-1} 3053, 2986, 2305, 1422, 1265, 895, 741, 704; ESI-HRMS: Found: m/z 283.1240. Calcd for: $(M+H)^+$ 283.1245.

1-(4-methyl-2-(phenylethynyl)phenyl)-2-phenyldiazene (4-3b)



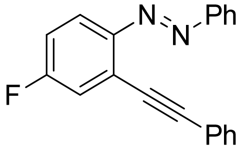
Red solid; mp 83-85 °C; Yield: 78%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 7.23 (d, 1H, J = 8.4 Hz), 7.35-7.39 (m, 3H), 7.47-7.54 (m, 4H), 7.58-7.60 (m, 2H), 7.69 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 7.2 Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 21.2, 87.0, 95.3, 116.0, 123.2, 123.5, 123.9, 128.4, 129.1, 129.9, 131.0, 131.7, 133.6, 141.1, 151.1, 152.9; IR (neat) cm^{-1} 3053, 2986, 1599, 1422, 1265, 746, 706; ESI-HRMS: Found: m/z 297.1399. Calcd for $C_{21}H_{16}N_2$: $(M+H)^+$ 297.1392.

1-(4-(*tert*-butyl)-2-(phenylethynyl)phenyl)-2-phenyldiazene (4-3c)



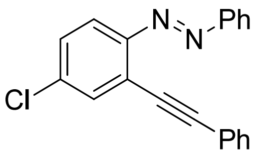
Red solid; mp 83-85 °C; Yield: 75%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (s, 9H), 7.34-7.37 (m, 3H), 7.43-7.53 (m, 4H), 7.59-7.62 (m, 2H), 7.69-7.72 (m, 2H), 8.00-8.02 (m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 31.1, 35.0, 87.5, 94.9, 115.8, 122.8, 123.2, 123.4, 123.6, 126.4, 128.4, 129.1, 130.1, 131.0, 131.7, 151.0, 153.0, 154.1; IR (neat) cm^{-1} 3051, 2966, 1599, 1265, 739, 690; ESI-HRMS: Found: m/z 339.1868. Calcd for $C_{24}H_{22}N_2$: $(M+H)^+$ 339.1861.

1-(4-fluoro-2-(phenylethynyl)phenyl)-2-phenyldiazene (4-3d)



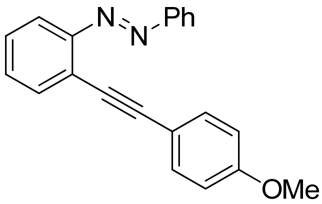
Red solid; mp 79-81 °C; Yield: 65%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10-7.15 (m, 1H), 7.37-7.41 (m, 4H), 7.47-7.56 (m, 3H), 7.57-7.61 (m, 2H), 7.80 (dd, J = 3.4, 9.0 Hz, 1H), 7.99-8.02 (m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 85.7 (d, J = 3.0 Hz), 96.7, 116.4 (d, J = 23.0 Hz), 118.1 (d, J = 9.0 Hz), 119.4 (d, J = 24.0 Hz), 123.0, 123.2, 125.9 (d, J = 10.2 Hz), 128.4, 128.8, 129.1, 131.3, 131.7, 149.6 (d, J = 3.2 Hz), 152.7, 164.9; IR (neat) cm^{-1} 3051, 2984, 1602, 1578, 1265, 739; ESI-HRMS: Found: m/z 301.1151. Calcd for $C_{20}H_{13}FN_2$: $(M+H)^+$ 301.1141.

1-(4-chloro-2-(phenylethynyl)phenyl)-2-phenyldiazene (4-3e)



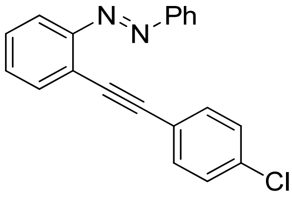
Red solid; mp 88-90 °C; Yield: 69%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.37-7.39 (m, 4H), 7.50-7.60 (m, 5H), 7.70-7.74 (m, 2H), 8.00-8.02 (m, 2H); ^{13}C NMR (100MHz, CDCl$_3$) δ 85.5, 96.8, 117.4, 123.0, 125.3, 128.4, 128.8, 129.2, 131.6, 131.7, 132.8, 136.4, 151.4, 152.7; IR (neat) cm^{-1} 3053, 2986, 1422, 1265, 896, 739, 704; ESI-HRMS: Found: m/z 317.0847. Calcd for $C_{20}H_{13}ClN_2$: $(M+H)^+$ 317.0846.

1-(2-((4-methoxyphenyl)ethynyl)phenyl)-2-phenyldiazene (4-3f)



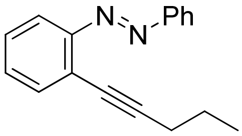
Red solid; mp 73-75 °C; Yield: 55%; ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.84 (s, 3H), 6.89-6.91 (m, 2H), 7.39-7.56 (m, 7H), 7.68-7.75 (m, 2H), 8.01-8.04 (m, 2H); ^{13}C NMR (100MHz, CDCl$_3$) δ 55.3, 85.6, 95.8, 114.0, 114.1, 115.6, 116.1, 123.2, 133.1, 133.2, 152.90, 152.92, 159.8; IR (neat) cm^{-1} 3051, 2986, 2253, 1512, 1265, 906, 741, 733; ESI-HRMS: Found: m/z 313.1343. Calcd for $C_{21}H_{16}N_2O$: $(M+H)^+$ 313.1341.

1-(2-((4-chlorophenyl)ethynyl)phenyl)-2-phenyldiazene (4-3g)



Red solid; mp 80-82 °C; Yield: 60%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.36 (m, 2H), 7.43-7.46 (m, 2H), 7.49-7.56 (m, 5H), 7.69-7.71 (m, 1H), 7.74-7.76 (m, 1H), 7.99-8.02 (m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 87.8, 94.4, 116.3, 121.9, 123.2, 123.3, 128.7, 129.1, 130.5, 131.4, 132.8, 133.3, 134.5, 152.8, 153.1; IR (neat) cm^{-1} 3053 2986, 1422, 1263, 895, 733, 706; ESI-HRMS: Found: m/z 317.0836. Calcd for $C_{20}H_{13}ClN_2$: $(M+H)^+$ 317.0846.

1-(2-(pent-1-yn-1-yl)phenyl)-2-phenyldiazene (4-3h)

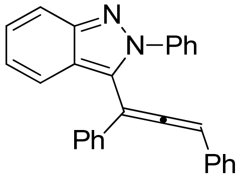


Red oil; Yield 50%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09 (t, J = 7.3 Hz, 3H), 1.69 (m, 2H), 2.50 (t, J = 6.8 Hz, 2H), 7.33-7.40 (m, 2H), 7.46-7.53 (m, 3H), 7.58 (d, J = 6.8 Hz, 1H), 7.67 (d, J = 7.4 Hz, 1H), 7.97 (d, J = 6.9 Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 13.5, 21.8, 22.2, 97.0, 115.9, 123.2, 124.6, 128.1, 129.0, 130.4, 131.1, 133.5, 152.9, 153.2; IR (neat) cm^{-1} 3053, 2961, 2158, 1422, 1265, 868, 735; ESI-HRMS: Found: m/z 249.1387. Calcd for $C_{28}H_{20}N_2$: $(M+H)^+$ 249.1392.

General procedure for preparation of 3-allenyl-2-phenyl-2*H*-indazole

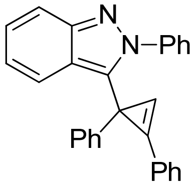
Compound **4-3** (0.25 mmol), **4-2** (0.50 mmol), $Pd(PPh_3)_2Cl_2$ (7.0 mg, 0.01 mmol), CuI (3.8 mg, 0.02 mmol) and Et_3N (108 μL, 0.75 mmol) were dissolved in 2.5 mL anhydrous THF under N_2. The mixture was immediately purged by N_2 three times. To resulting solution phenylacetylene was added. The mixture was stirred at 40 °C. After the reaction was completed according to TLC reaction control (14-24 h). The solvent was removed in vacuo. The crude residue was purified by column chromatography (hexane/ethyl acetate 50:1 to 20:1) on silica gel to afford desire product.

3-(1,3-diphenylpropa-1,2-dien-1-yl)-2-phenyl-2*H*-indazole (4-4a)



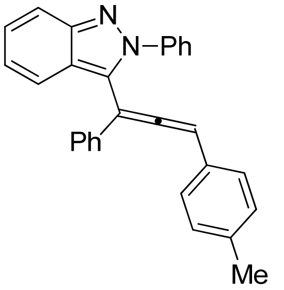
Pale yellow solid; mp 138-140 °C; Yield: 81%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.40 (s, 1H), 7.03-7.08 (m, 3H), 7.17-7.22 (m, 3H), 7.23-7.30 (m, 3H), 7.32-7.39 (m, 6H), 7.56-7.58 (m, 2H), 7.80 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 98.6, 103.0, 117.9, 120.6, 122.2, 122.6, 125.5, 126.8, 127.2, 127.7, 127.9, 128.3, 128.7, 128.8, 129.0, 129.3, 132.4, 134.5, 140.2, 149.0, 209.5; IR (neat) cm^{-1} 3053, 2986, 2305, 1422, 1265, 895, 739, 704; ESI-HRMS: Found: m/z 385.1711. Calcd for $C_{28}H_{20}N_2$: $(M+H)^+$ 385.1705.

3-(1,2-diphenylcycloprop-2-en-1-yl)-2-phenyl-2*H*-indazole (4-4a')



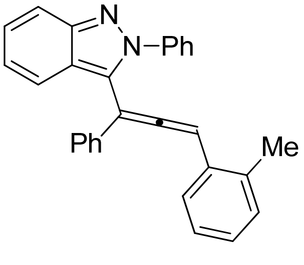
Pale yellow viscous oil; Yield: 30%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (s, 1H), 7.00-7.04 (m, 1H), 7.16-7.22 (m, 3H), 7.24-7.31 (m, 5H), 7.38-7.44 (m, 5H), 7.48-7.51 (m, 2H), 7.66 (d, J = 8.5 Hz, 1H), 7.75 (d, J = 8.7 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 27.7, 103.8, 117.8, 120.7, 121.1, 121.4, 126.0, 126.1, 126.3, 126.4, 126.5, 128.4, 128.7, 128.75, 128.82, 129.3, 129.6, 139.0, 140.5, 145.4, 148.8; IR (neat) cm^{-1} 3059, 2961, 2234, 1476, 1153, 771, 687; ESI-HRMS: Found: m/z 385.1712. Calcd for $C_{28}H_{20}N_2$: $(M+H)^+$ 385.1705.

2-phenyl-3-(1-phenyl-3-(*p*-tolyl)propa-1,2-dien-1-yl)-2*H*-indazole (4-4b)



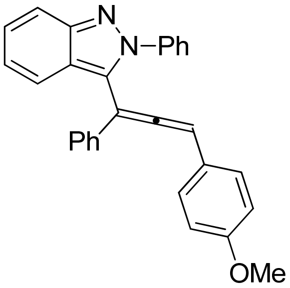
Pale yellow solid; mp 119-121 °C; Yield: 82%; ^{1}H NMR (400 MHz, $CDCl_3$) δ2.29 (s, 3H), 6.38 (s, 1H), 6.94 (d, J = 8.1 Hz, 2H), 7.02 (d, J = 8.0 Hz), 7.03-7.08 (m, 1H), 7.22-7.39 (m, 9H), 7.45-7.48 (m ,1H), 7.56-7.59 (m, 2H), 7.80 (d, J = 8.7 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 21.2, 98.4, 102.8, 117.9, 120.6, 122.2, 122.6, 125.5, 126.8, 127.2, 127.8, 128.3, 128.7, 129.0, 129.3, 129.4, 129.5, 134.7, 137.7, 140.3, 149.0, 209.4; IR (neat) cm^{-1} 3053, 2984, 1734, 1420, 1265, 895, 739, 704; ESI-HRMS: Found: m/z 399.1867. Calcd for $C_{29}H_{22}N_2$: $(M+H)^+$ 399.1861.

2-phenyl-3-(1-phenyl-3-(*o*-tolyl)propa-1,2-dien-1-yl)-2*H*-indazole (4-4c)



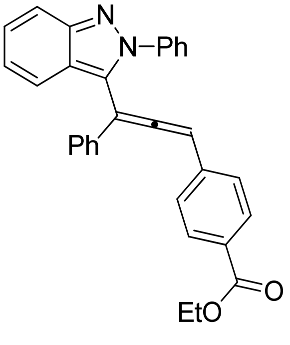
Pale yellow viscous oil; Yield: 62%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.22 (s, 3H), 6.52 (s, 1H), 6.99-7.08 (m, 5H), 7.21-7.43 (m, 10H), 7.55-7.58 (m, 2H), 7.80 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 19.8, 96.0, 102.1, 117.9, 120.7, 122.1, 122.4, 125.5, 126.2, 126.8, 127.7, 127.8, 127.9, 128.2, 128.8, 128.9, 129.4, 130.6, 130.7, 134.6, 135.4, 140.2, 149.0, 210.0; IR (neat) cm^{-1} 3053, 2984, 2305, 1734, 1420, 1265, 895, 739, 704; ESI-HRMS: Found: m/z 279.1862. Calcd for $C_{19}H_{22}N_2$: $(M+H)^+$ 279.1861.

3-(3-(4-methoxyphenyl)-1-phenylpropa-1,2-dien-1-yl)-2-phenyl-2*H*-indazole (4-4d)



Pale yellow viscous oil; Yield: 73%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 3H), 6.38 (s, 1H), 6.74 (d, J = 8.7 Hz, 2H), 6.97 (d, J = 8.7 Hz, 2H), 7.04-7.08 (m ,1H), 7.23-7.39 (m, 9H), 7.46 (d, J = 8.5 Hz, 1H), 7.56-7.58 (m, 2H), 7.80 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 55.3, 98.1, 102.8, 114.2, 117.9, 120.7, 122.2, 122.5, 124.5, 125.6, 126.8, 126.9, 127.8, 128.3, 128.5, 128.7, 129.0, 129.7, 134.8, 140.3, 149.0, 159.3, 209.2; IR (neat) cm^{-1} 3051, 2982, 1734, 1508, 1265, 1250, 1032, 737, 702; ESI-HRMS: Found: m/z 415.1816. Calcd for $C_{29}H_{22}N_2O$: $(M+H)^+$ 415.1810.

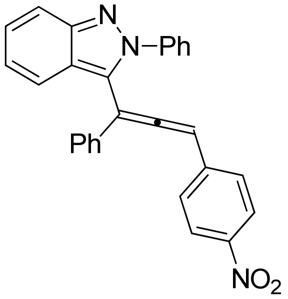
ethyl 3-(1,3-diphenylpropa-1,2-dien-1-yl)-2-phenyl-2*H*-indazole-5-carboxylate (4-4e)



Pale yellow viscous oil; Yield: 66%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (t, J = 7.1 Hz, 3H), 4.36 (q, J = 7.1 Hz, 2H), 6.44 (s, 1H), 7.05-7.09 (m, 3H), 7.24-7.39 (m, 9H), 7.44 (d, J = 8.5 H, 1H), 7.55-7.57 (m, 2H), 7.81 (d, J = 8.8 Hz, 1H), 7.88 (d, J = 8.4 Hz,1 H); ^{13}C

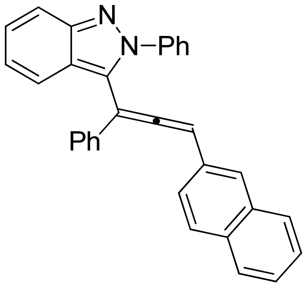
NMR (100MHz, $CDCl_3$) δ 14.3, 60.9, 98.1, 103.5, 118.0, 120.4, 122.4, 122.6, 125.5, 126.9, 127.0, 128.2, 128.5, 128.7, 128.9, 129.0, 129.5, 130.0, 134.0, 137.2, 140.2, 149.0, 166.1, 210.2; IR (neat) cm^{-1} 3051, 2984, 2305, 1709, 1265, 1107, 739, 704; ESI-HRMS: Found: m/z 457.1908. Calcd for $C_{31}H_{24}N_2O_2$: $(M+H)^+$ 457.1916.

3-(3-(4-nitrophenyl)-1-phenylpropa-1,2-dien-1-yl)-2-phenyl-2*H*-indazole (4-4f)



Pale yellow solid; mp 179-181 °C; Yield: 70%; ^1H NMR (400 MHz, $CDCl_3$) δ 6.46 (s, 1H), 7.07-7.12 (m, 3H), 7.33-7.38 (m, 6H), 7.39-7.42 (m, 4H), 7.53-7.56 (m, 2H), 7.82 (d, J = 8.8 Hz, 1H), 8.02-8.05 (m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 97.4, 104.2, 118.1, 120.3, 122.7, 124.1, 125.6, 127.00, 127.04, 127.7, 128.1, 129.1, 129.2, 133.4, 139.7, 140.2, 147.0, 149.1, 210.8; IR (neat) cm^{-1} 3053, 2984, 1520, 1344, 1265, 908, 737, 704; ESI-HRMS: Found: m/z 430.1564. Calcd for $C_{28}H_{19}N_3O_2$: $(M+H)^+$ 430.1556.

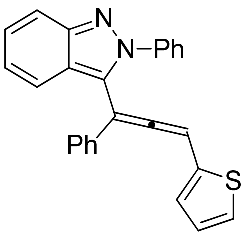
3-(3-(naphthalen-2-yl)-1-phenylpropa-1,2-dien-1-yl)-2-phenyl-2*H*-indazole (4-4g)



Pale yellow solid; mp 95-97 °C; Yield: 82%; ^1H NMR (400 MHz, $CDCl_3$) δ 6.63 (s, 1H), 7.11-7.19 (m, 2H), 7.28-7.50 (m, 11H), 7.56-7.57 (m, 2H), 7.63-7.69 (m, 3H), 7.74-7.77

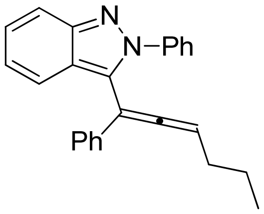
(m, 1H), 7.79-7.82 (m, 1H), 7.87 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 99.0, 103.2, 117.9, 120.6, 122.3, 122.6, 124.7, 125.6, 126.1, 126.3, 126.5, 126.9, 127.7, 127.8, 128.0, 128.4, 128.8, 129.0, 129.3, 129.9, 132.9, 133.5, 134.5, 140.3, 149.0, 210.1; IR (neat) cm^{-1} 3051, 2984, 2303, 1734, 1597, 1265, 895, 739, 704; ESI-HRMS: Found: m/z 435.1858. Calcd for $C_{32}H_{22}N_2$: $(M+H)^+$ 435.1861.

2-phenyl-3-(1-phenyl-3-(thiophen-2-yl)propa-1,2-dien-1-yl)-2*H*-indazole (4-4h)



Pale yellow viscous oil; Yield: 79%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (s, 1H), 6.83-6.85 (m, 1H), 6.91-6.93 (m, 1H), 7.06-7.10 (m, 1H), 7.21-7.30 (m, 5H), 7.31-7.39 (m, 4H), 7.52 (d, *J* = 8.5 Hz, 1H), 7.59-7.62 (m, 2H), 7.80 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 92.6, 103.3, 117.9, 120.6, 122.3, 122.7, 125.4, 125.6, 126.4, 126.9, 127.1, 127.6, 128.0, 128.3, 128.7, 128.9, 129.0, 134.4, 136.0, 140.2, 149.0, 209.3; IR (neat) cm^{-1} 3053, 2986, 2305, 1422, 1265, 895, 739, 704; ESI-HRMS: Found: m/z 391.1272. Calcd for $C_{26}H_{18}N_2S$: $(M+H)^+$ 391.1269.

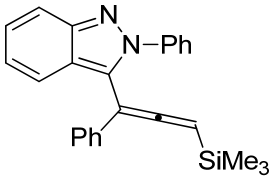
2-phenyl-3-(1-phenylhexa-1,2-dien-1-yl)-2*H*-indazole (4-4i)



Pale yellow viscous oil; Yield: 50%; 1H NMR (400 MHz, $CDCl_3$) δ 0.80 (t, *J* = 7.4 Hz, 3H), 1.24-1.30 (m, 2H), 1.73-1.80 (m, 2H), 5.40 (t, *J* = 7.0 Hz), 7.00-7.04 (m, 1H), 7.19-

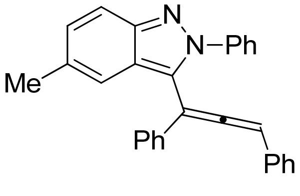
7.40 (m, 10H), 7.56-7.59 (m, 2H), 7.79 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) *δ* 13.6, 22.4, 30.0, 95.3, 98.8, 117.8, 120.8, 121.8, 122.3, 125.4, 126.7, 126.8, 127.3, 128.1, 128.6, 128.8, 130.4, 135.4, 140.4, 149.0, 206.9; IR (neat) cm^{-1} 3051, 2984, 1499, 1420, 1265, 739, 704; ESI-HRMS: Found: m/z 351.1853. Calcd for $C_{25}H_{22}N_2$: $(M+H)^+$ 351.1861.

2-phenyl-3-(1-phenyl-3-(trimethylsilyl)propa-1,2-dien-1-yl)-2*H*-indazole (4-4j)



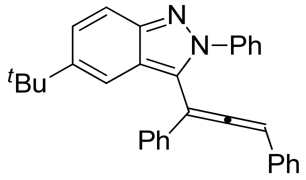
Pale yellow viscous oil; Yield: 80%; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 0.15 (s, 9H), 5.36 (s, 1H), 7.10-7.14 (m, 1H), 7.23-7.26 (m, 3H), 7.30-7.34 (m, 2H), 7.38-7.46 (m, 4H), 7.52 (d, *J* = 8.6 Hz, 1H), 7.65-7.67 (m, 2H), 7.87 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) *δ*-0.8, 87.1, 92.5, 117.8, 120.8, 121.8, 122.6, 125.2, 125.9, 126.6, 128.1, 128.6, 128.8, 130.0, 135.2, 140.4, 149.0, 209.8; IR (neat) cm^{-1} 3051, 2984, 1919, 1265, 845, 739, 704; ESI-HRMS: Found: m/z 381.1795. Calcd for $C_{25}H_{24}N_2Si$: $(M+H)^+$.381.1787.

3-(1,3-diphenylpropa-1,2-dien-1-yl)-5-methyl-2-phenyl-2*H*-indazole (4-4k)



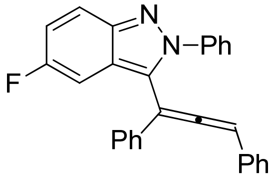
Pale yellow solid; mp 151-153 °C; Yield: 85%; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 2.35 (s, 3H), 6.40 (s, 1H), 7.02-7.04 (m, 2H), 7.17-7.29 (m, 8H), 7.31-7.33 (m, 5H), 7,55-7.57 (m, 2H), 7.70 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) *δ* 21.8, 98.4, 103.0, 117.6, 118.5, 122.9, 125.4, 126.8, 127.2, 127.8, 128.2, 128.67, 128.75, 128.9, 129.8, 131.7, 132.4, 134.5, 140.3, 148.0, 209.4; IR (neat) cm^{-1} 3053, 2986, 2305, 1501, 1263, 895, 737, 704; ESI-HRMS: Found: m/z 399.1859. Calcd for $C_{29}H_{22}N_2$: $(M+H)^+$ 399.1861.

5-(*tert*-butyl)-3-(1,3-diphenylpropa-1,2-dien-1-yl)-2-phenyl-2*H*-indazole (4-4l)



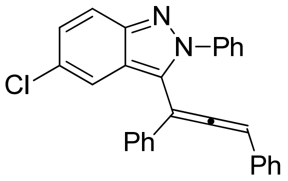
Pale yellow solid; mp 155-157 °C; Yield: 78%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (s, 9H), 6.51 (s, 1H), 7.13-7.15 (m, 2H), 7.19-7.26 (m, 6H), 7.28-7.53 (m, 6H), 7.44-7.48 (m, 1H), 7.54-7.57 (m, 2H), 7.74 (d, J = 9.2 hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 31.1, 34.8, 98.5, 103.2, 114.7, 117.4, 122.5, 125.4, 126.7, 127.4, 127.7, 127.8, 128.1, 128.6, 128.8, 128.9, 129.0, 132.6, 134.4, 140.5, 145.0, 147.8, 209.4; IR (neat) cm^{-1} 3053, 2986, 2305, 1422, 1263, 895, 739, 706; ESI-HRMS: Found: m/z 441.2333. Calcd for $C_{32}H_{28}N_2$: $(M+H)^+$ 441.2331.

3-(1,3-diphenylpropa-1,2-dien-1-yl)-5-fluoro-2-phenyl-2*H*-indazole (4-4m)



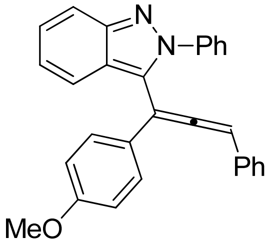
Pale yellow viscous oil; Yield: 74%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.40 (s, 1H), 7.01-7.05 (m, 3H), 7.11-7.22 (m, 4H), 7.24-7.32 (m, 5H), 7.36-7.40 (m, 3H), 7.54-7.57 (m, 2H), 7.77 (dd, J = 4.7, 9.3 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 98.7, 103 (d, J = 45.6 Hz), 102.9, 118.5 (d, J = 28.8 Hz), 120.1 (d, J = 9.6 Hz), 121.9 (d, J = 11.4 Hz), 125.4, 126.8, 127.8, 128.0, 128.5, 128.76, 128.86, 129.0, 129.5 (d, J = 8. Hz), 132.2, 134.2, 140.1, 146.4, 157.2, 159.6, 209.5; IR (neat) cm^{-1} 3051, 2984, 1265, 739, 702; ESI-HRMS: Found: m/z 403.1618. Calcd for $C_{28}H_{19}FN_2$: $(M+H)^+$ 403.1611.

5-chloro-3-(1,3-diphenylpropa-1,2-dien-1-yl)-2-phenyl-2*H*-indazole (4-4n)



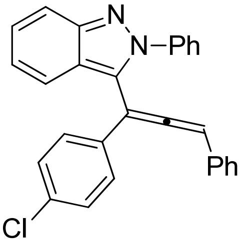
Pale yellow solid; mp 142-144 °C; Yield: 75%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.64 (s, 1H), 7.03 (d, J = 7.5 Hz, 2H), 7.19-7.21 (m, 3H), 7.25-7.30 (m, 6H), 7.36-7.38 (m, 3H), 7.45 (s, 1H), 7.54-7.57 (m, 2H), 7.73 (d, J = 9.1 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 98.8, 102.5, 119.2, 122.9, 125.4, 126.7, 127.2, 127.8, 128.1, 128.3, 128.6, 128.8, 128.9, 129.0, 129.2, 132.1, 134.1, 140.0, 147.3, 209.5; IR (neat) cm^{-1} 3053, 2980, 1265, 740, 704; ESI-HRMS: Found: m/z 419.1310. Calcd for $C_{28}H_{19}ClN_2$: $(M+H)^+$ 419.1315.

3-(1-(4-methoxyphenyl)-3-phenylpropa-1,2-dien-1-yl)-2-phenyl-2*H*-indazole (4-4o)



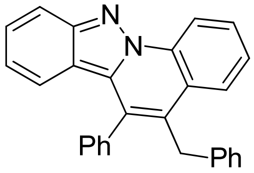
Pale yellow viscous oil; Yield: 72%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (s, 3H), 6.36 (s, 1H), 6.84-6.80 (m, 2H), 7.02-7.08 (m, 3H), 7.16-7.26 (m, 5H), 7.32-7.40 (m, 4H), 7.48 (d, J = 7.0 Hz, 1H), 7.56-7.59 (m, 2H), 7.70 (d, J = 8.7 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 55.3, 98.6, 102.5, 114.3, 117.9, 120.7, 122.2, 122.5, 126.7, 126.8, 127.2, 127.6, 128.1, 128.4, 128.7, 129.0, 129.6, 132.7, 140.3, 149.0, 159.5, 208.9; IR (neat) cm^{-1} 3053, 2984, 1734, 1508, 1265, 739, 704; ESI-HRMS: Found: m/z 415.1801. Calcd for $C_{29}H_{22}N_2O$: $(M+H)^+$ 415.1810.

3-(1-(4-chlorophenyl)-3-phenylpropa-1,2-dien-1-yl)-2-phenyl-2*H*-indazole (4-4p)



Pale yellow viscous oil; Yield: 73%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.42 (s, 1H), 7.02-7.10 (m, 3H), 7.32-7.41 (m, 4H), 7.45 (d, J = 8.5 Hz, 1H), 7.52-7.56 (m, 2H), 7.80 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 99.0, 102.2, 118.0, 120.4, 122.5, 125.5, 126.9, 127.3, 127.9, 128.0, 128.5, 128.75, 128.79, 128.97, 129.05, 133.0, 133.8, 140.1, 149.0, 209.5; IR (neat) cm^{-1} 3053, 2982, 1734, 1579, 1373, 1265, 1045, 739; ESI-HRMS: Found: m/z 419.1313. Calcd for $C_{28}H_{19}ClN_2$: $(M+H)^+$ 419.1315.

Procedure for preparation of 5-benzyl-6-phenylindazolo[2,3-*a*]quinoline (4-5)



3-(1,3-diphenylpropa-1,2-dien-1-yl)-2-phenyl-2*H*-indazole **4-4a** (0.25 mmol) was dissolved in 2.5 mL anhydrous NMP under N_2. The mixture was immediately purged by N_2 three times and then sitrred at 150 °C for 2 h. After the reaction was completed, the solvent was evaporated under vacuum. The crude residue was purified by column chromatography (hexane/ethyl acetate 20:1) on silica gel to afford 5-benzyl-6-phenylindazolo[2,3-*a*]quinolone **4-5** as a white solid; mp 197-199 °C; Yield: 53%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.33 (s, 2H), 6.51 (d, J = 8.5 Hz, 1H), 6.88 (t, J = 7.6 Hz, 1H), 7.08 (d, J = 7.2 Hz, 1H), 7.12-7.16 (m, 1H), 7.18-7.24 (m, 2H), 7.40-7.44 (m, 3H), 7.46-7.56 (m, 4H), 7.72-7.77 (m, 1H), 7.90-7.93 (m, 2H), 9.06 (d, J = 8.4 Hz, 1H); ^{13}C NMR

(100MHz, $CDCl_3$) δ 34.5, 116.3, 117.4, 117.6, 120.4, 121.5, 124.8, 126.1, 126.2, 126.5, 127.6, 128.0, 128.5, 128.6, 128.9, 129.0, 129.1, 129.4, 131.7, 131.9, 133.9, 136.6, 140.3, 149.4; IR (neat) cm^{-1} 3942, 3684, 3053, 2986, 2304, 1422, 1265, 895, 739; ESI-HRMS: Found: m/z 385.1709. Calcd for $C_{28}H_{20}N_2$: $(M+H)^+$ 385.1705.

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