Gold(I)-Catalyzed Construction of Nitrogen-Containing Medium-Sized Ring and Azaspirocyclic Systems

金(I)触媒による含窒素中員環ならびにアザスピロ環の構築

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Abstract

Gold complexes can increase the electrophilicity of alkynes by coordination and facilitate smooth nucleophilic addition to make a new bond. In general, the reaction of enyne-containing substrates with gold catalysts, called cycloisomerization, is well developed because it gives a cyclic structure by C-C bond formation in high atom efficiency under mild conditions. Among these reactions, there are many reports where part of an aromatic ring acts as an ene moiety, and this transformation is hydroarylation. In particular, 6-*endo-dig* type hydroarylation is most popular. However, examples of medium-sized ring construction by gold-catalyzed hydroarylation is rare. In addition, nitrogen-containing medium-sized ring compounds are known to exhibit interesting biological activities.

Another synthetic use of gold complexes is the preparation of gold carbenoid species, which undergo cyclopropanation, C-H insertion and Büchner reaction, etc. The gold carbenoid species is commonly prepared from gold(I) complexes and diazo compounds. New strategies for the generation of the gold carbenoid species without the use of diazo compounds were successively developed. The first example is gold-catalyzed rearrangement of propargylic esters. The second strategy is retro-Büchner reaction of 7-substituted 1,3,5-cycloheptatrienes. The third method is the generation from cyclopropenes. The fourth method is the reaction of alkynes with an oxidant. Against this background, the author paid attention to ynamides as attractive precursors of gold carbenoid species, because their reactivity can be tuned by the nitrogen-protecting group, and the highly polarized alkyne leads to regioselective transformations.

This thesis consists of four chapters.

In Chapter 1, general introduction was described.

In Chapter 2, the author explained the construction of nitrogen-containing medium-sized rings by gold(I)-catalyzed hydroarylation of alkynes. The hydroarylation of 2-alkynyldiphenylamine derivatives by cationic gold(I)-catalyst gave 7-*endo-dig* products selectively. The resonance effect of nitrogen was important for high reactivity, and hexacyclic compounds as well as simple *N*-methyldibenzazepine were synthesized by this protocol. On the other hand, the gold(I)-catalyzed reaction of 2-propargylaminotriphenylamine derivatives proceeded via 8-*exo-dig* cyclization to provide dibenzodiazocines selectively. The control experiment of *o*-aminophenol tethered substrates indicated that *o*-diaminobenzene tether was crucial for the 8-*exo-dig* selective hydroarylation. For the reaction of internal alkynes, the use of the IPr ligand was important to obtain high yields.

In Chapter 3, the author described dearomative spirocyclization of phenol derivatives via gold carbenoid species derived from ynamides. The reaction of ynamides derived from *p*-methoxybenzylamine in the presence of a gold catalyst and *N*-oxide proceeded to give azaspiro-

cyclic compounds. By-product formation was suppressed by using IPr as the ligand and water as the co-solvent. One of the products was efficiently transformed to a gabapentin lactam derivative.

In Chapter 4, summary of this thesis was presented.

Contents

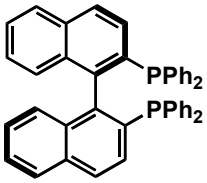
List of Abbreviations

Ac	acetyl
AcOH	acetic acid
aq	aqueous
Ar	aryl
Bn	benzyl
br	broad
BTMS	3,5-bis(trimethylsilyl)phenyl
Bu	butyl
ca.	circa
C-C	carbon-carbon
C-H	carbon-hydrogen
cod	1,5-cyclooctadiene
conc	concentrated
Cy	cyclohexyl group
d	doublet
DART	direct analysis in real time
dba	dibenzylideneacetone
DCE	1,2-dichloroethane
DCM	dichloromethane
dd	doublet of doublets
ddd	doublet of doublet of doublets
DDQ	2,3-dichloro-5,6-dicyano-*p*-benzoquinone
DG	directing group
dig	digonal
DMA	*N,N*-dimethylacetamide
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
DNBS	2,4-dinitrobenzenesulfonyl
dt	doublet of triplets
DTBM	3,5-di-*tert*-butyl-4-methoxyphenyl
ee	enantiomeric excess
eq.	equivalent
ESI	electro spray ionization

Et	ethyl
EtOAc	ethyl acetate
FAB	fast atom bombardment
fac-	facial
h	hour(s)
HIV	human immunodeficiency virus
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectra
i	iso
J	coupling constant
LED	light emitting diode
LG	leaving group
M	molar, mol/L
m	multiplet
m	meta
*m*CPBA	*m*-chloroperoxybenzoic acid
Me	methyl
Mes	mesityl
mp	melting point
MS	molecular sieve
Ms	methanesulfonyl
n	normal
N.D.	not detected
NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
NOESY	NOE correlated spectroscopy
N.R.	no reaction
Ns	2-nitrobenzenesulfonyl
o	ortho
OLED	organic light-emitting diodes
p	para
PG	protecting group
Ph	phenyl

PMP	*p*-methoxyphenyl
ppy	2-phenylpyridinato
Pr	propyl
PTLC	preparative thin layer chromatography
q	quartet
rac	racemic
ref	reference
r.t.	room temperature
s	singlet
sat.	saturated
t	triplet
t	tertiary
TADDOL	α,α,α',α'-tetraaryl-2,2-disubstituted 1,3-dioxolane-4,5-dimethanol
TBAF	tetrabutylammonium fluoride
TBS	*t*-butyldimethylsilyl
TEA	triethylamine
temp.	temperature
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMS	trimethylsilyl (as a functional group) tetramethylsilane (as a standard material)
tol	tolyl
Ts	*p*-toluenesulfonyl
UV	ultraviolet
xyl	3,5-xylyl

List of Ligands



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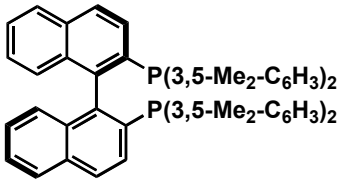
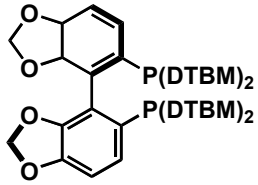
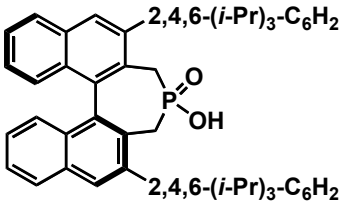


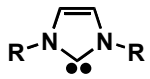
(*R*)-xyl-BINAP



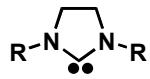
(*R*)-DTBM-SEGPHOS



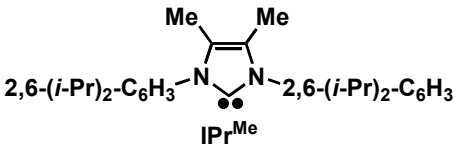
(*S*)-TRIP



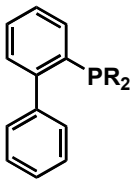
IPr: R = 2,6-(*i*-Pr)$_2$-C$_6$H$_3$
IMes: R = 2,4,6-Me$_3$-C$_6$H$_2$
ICy: R = Cy



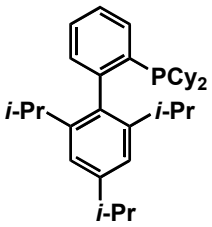
SIPr: R = 2,6-(*i*-Pr)$_2$-C$_6$H$_3$
SIMes: R = 2,4,6-Me$_3$-C$_6$H$_2$



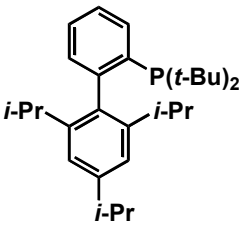
IPr^{Me}



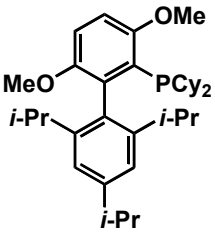
Johnphos: R = *t*-Bu
CyJohnphos: R = Cy



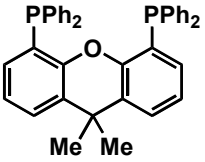
XPhos



^{t}BuXPhos



Brettphos



Xantphos

Chapter 1

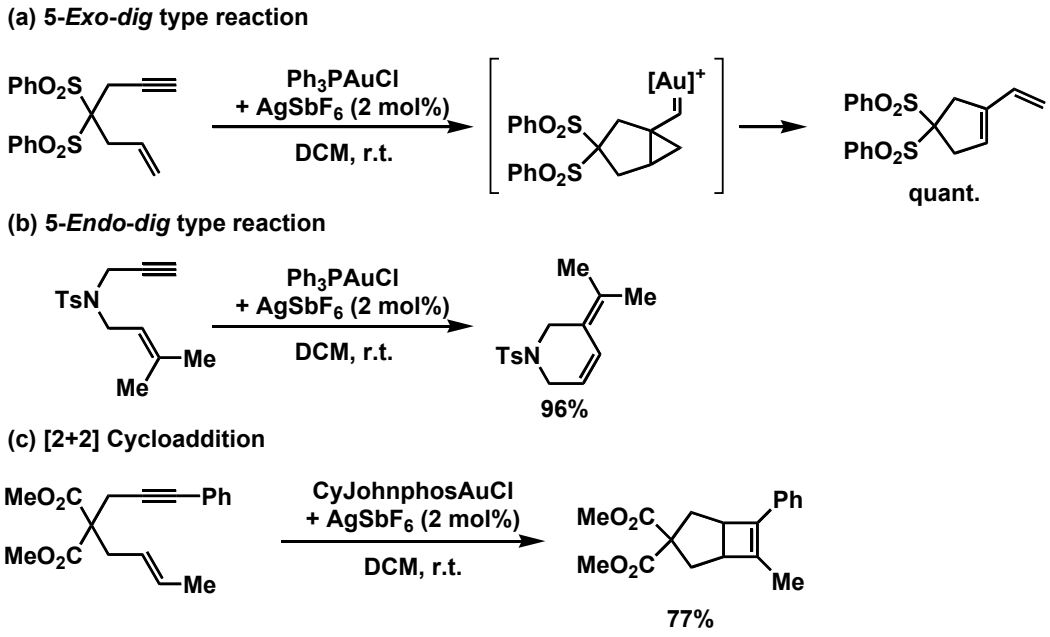
General Introduction

Backgrounds

Gold complexes can increase the electrophilicity of alkynes by coordination and nucleophilic addition proceeds smoothly to make a new bond.[1] In particular, the reaction of enyne-containing substrate with gold catalysts, called cycloisomerization, is well developed because it can give a cyclic structure by C-C bond formation in high atom efficiency under mild conditions.[2]

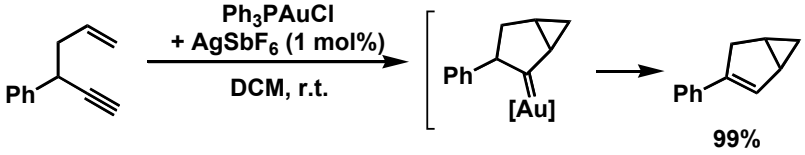
For the pioneering works, in 2004, Echavarren and co-workers reported a cationic gold(I)-catalyzed cycloisomerization of 1,6-enyne to give a 5-*exo-dig* type product (Scheme 1a).[3] This reaction was considered to provide conjugated dienes via gold carbenoid species. The reaction pathway was changed by the tether moiety and/or substituents on the alkene and alkyne. The reaction of dimethyl-substituted substrate gave a 6-*endo-dig* type product selectively under the same reaction conditions (Scheme 1b).[3] In contrast, the combination of internal alkyne and gold catalyst possessing a bulky ligand gave a cyclobutene derivative by formal [2+2] cycloaddition (Scheme 1c).[4]

Scheme 1. Examples of the reactions of 1,6-enynes



In 2004, Toste and co-workers reported cationic gold(I)-catalyzed cycloisomerization of 1,5-enynes (Scheme 2).[5] This reaction proceeded via gold carbenoid species to give bicyclo[3.1.0]hexenes under mild conditions.

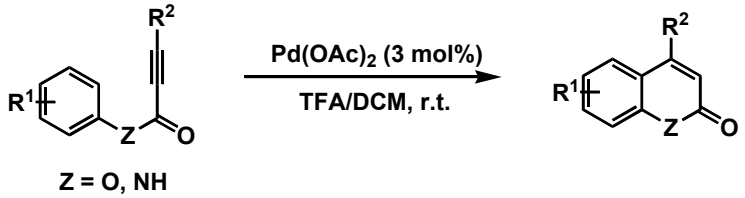
Scheme 2. Example of the reactions of 1,5-enynes



After these pioneering works, various 1,*n*-enynes were subjected to gold(I)-catalyzed cycloisomerization and a variety of ring structures were constructed under similar reaction conditions.[2] Gold-catalyzed cycloisomerization was also used as a key step in total synthesis.[1b] Among these reactions, there are many reports where part of an aromatic ring acts as an ene moiety, and this transformation is hydroarylation. In particular, 6-*endo-dig* type hydroarylation is most popular.[6] There are two types of substrates for 6-*endo-dig* hydroarylation; heteroatom-tethered and *ortho*-phenylene-tethered alkynes.

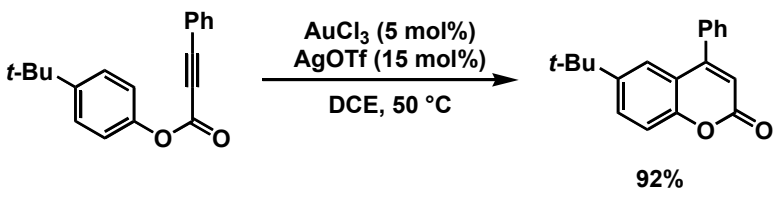
As for the heteroatom-tethered substrates, in 2000, Fujiwara and co-workers reported palladium-catalyzed 6-*endo-dig*-selective hydroarylation of phenyl phenylpropiolate, and coumarins (Z = O) and quinolinones (Z = NH) were obtained (Scheme 3).[6a,6b] This report was the first example of 6-*endo-dig*-selective hydroarylation. However, this transformation required the use of TFA as a co-solvent.

Scheme 3. Palladium-catalyzed 6-*endo-dig*-selective hydroarylation



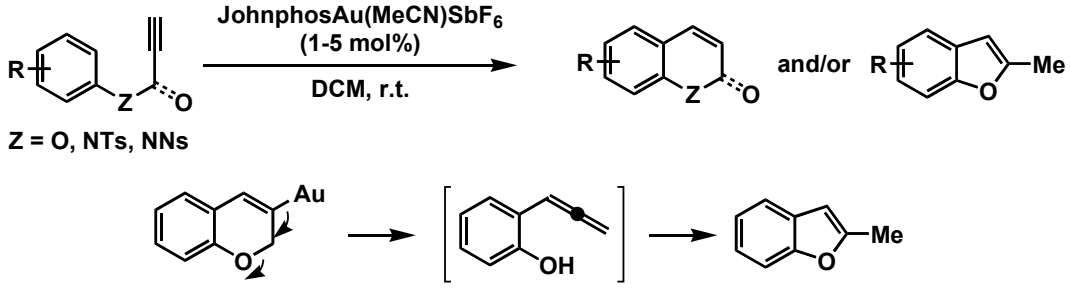
In 2004, He and co-workers reported cationic gold(III)-catalyzed 6-*endo-dig*-selective hydroarylation to provide coumarin derivatives (Scheme 4).[6c] This transformation was the first example of gold-catalyzed reaction, but heated conditions were required. The deuterium experiments indicated the presence of arylgold(III) species which was generated by the direct metalation of electron-rich arene, but the possibility of alkyne activation by gold(III) catalyst as a Lewis acid could not be excluded.

Scheme 4. Gold(III)-catalyzed 6-*endo-dig*-selective hydroarylation



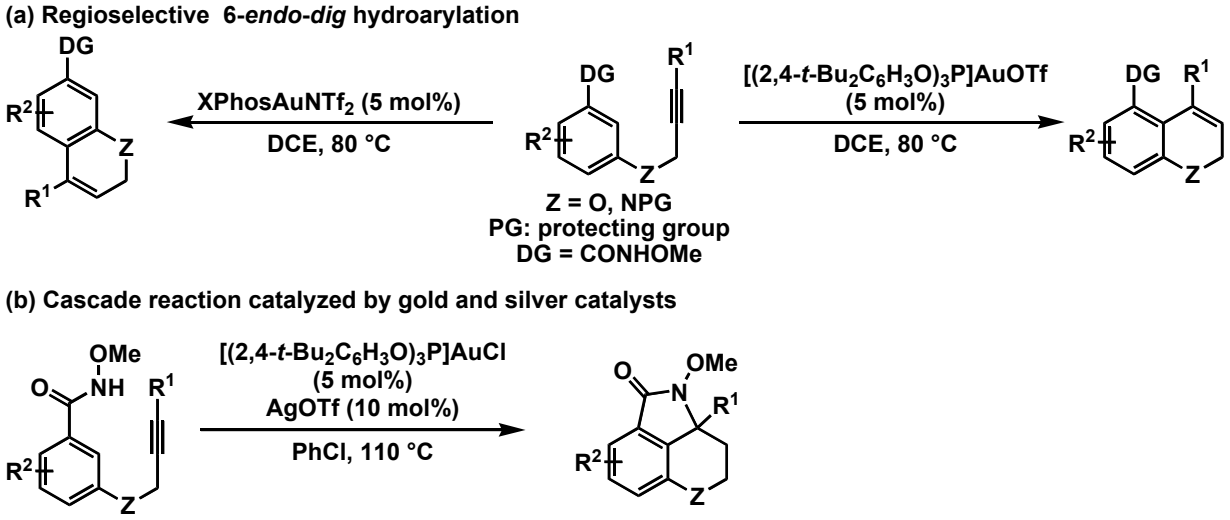
In 2009, Banwell and co-workers achieved gold(I)-catalyzed 6-*endo-dig*-selective hydroarylation of terminal alkynes (Scheme 5).[6d] The reaction was catalyzed by an isolated cationic gold(I)-monophosphine complex and proceeded under mild conditions to yield coumarins, chromenes, and dihydroquinolines. In the reactions of some propargyl ether-containing substrates, benzofurans were also obtained by the fragmentation of vinyl-gold species, which were formed by the 6-*endo-dig* hydroarylation.

Scheme 5. Gold(I)-catalyzed 6-*endo-dig*-selective hydroarylation of terminal alkynes



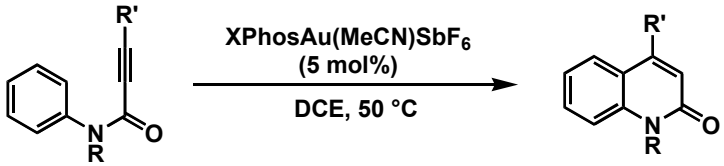
The main problems of hydroarylation are poor regioselectivity and tolerability of electron-deficient aromatic ring-containing substrates. In 2016, Jiang and co-workers overcame these problems by the ligand tuning of gold(I)-catalysts and the use of directing groups (DG) (Scheme 6).[6f] When they used an electron-deficient phosphite ligand, which enables the coordinations of both alkyne and DG to the metal center, the reaction at sterically hindered *ortho*-position with an alkyne moiety proceeded (Scheme 6a, right). In contrast, the use of rigid and bulky electron-rich phosphine ligand prevented the coordinations and generated steric repulsion with DG, and cyclization proceeded at sterically less hindered *para*-position (Scheme 6a, left). In addition, when the substrates were subjected to hydroarylation using an electron-deficient phosphite ligand, the use of both gold and silver catalysts enabled successive hydroarylation and hydroamination with DG to provide a tricyclic product selectively (Scheme 6b). The first hydroarylation was catalyzed by a cationic gold(I)-catalyst, then the second hydroamination to alkene was catalyzed by a silver catalyst. It is noteworthy that internal alkynes and electron-deficient substrates were also applicable for this reaction.

Scheme 6. Gold(I)-catalyzed regioselective 6-*endo-dig* hydroarylation and cascade reactions



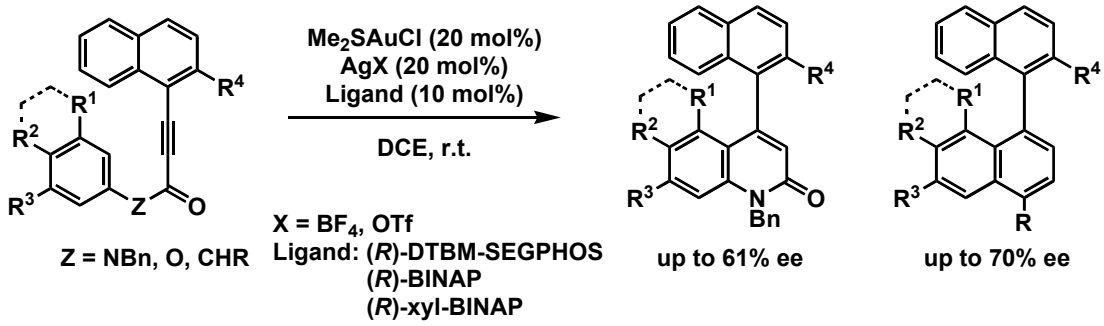
Another gold(I)-catalyzed hydroarylation of internal alkynes was achieved by Vadola and co-workers in 2017 (Scheme 7).[6g] They used a rigid and sterically hindered phosphine ligand to synthesize various quinolinone derivatives.

Scheme 7. Gold(I)-catalyzed 6-*endo-dig* hydroarylation of internal alkynes



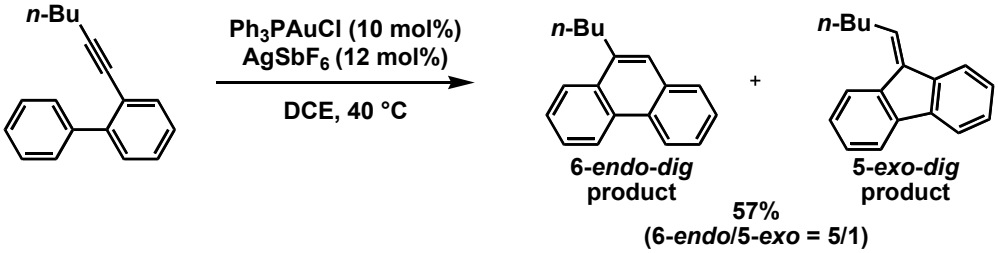
Some enantioselective hydroarylations were also reported. In 2011, Tanaka and coworkers achieved gold(I)-catalyzed enantioselective synthesis of axially chiral heterobiaryls using chiral biaryl bisphosphine as a chiral ligand (Scheme 8).[6e] They also reported atropselective synthesis of all-benzenoid biaryls by a gold(I)-catalyst.[7h,7j] However, the enantioselectivity was low to moderate in both reactions.

Scheme 8. Gold(I)-catalyzed enantioselective 6-*endo-dig* hydroarylation



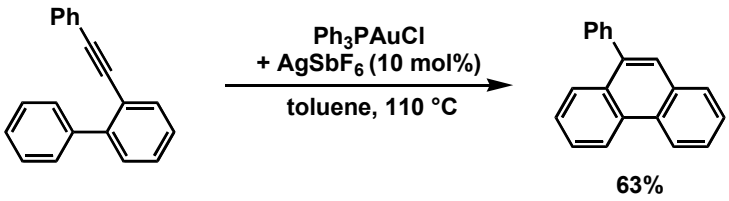
Next, the examples of *ortho*-phenylene-tethered alkynes, namely 2-alkynylbiphenyls are listed.[7] In 2006, our group reported that cationic gold(I)-catalyzed cycloisomerization of 2-(1-hexynyl)biphenyl gave a phenanthrene derivative as major product (Scheme 9).[7a] This report was the first example of gold(I)-catalyzed 6-*endo-dig* hydroarylation. However, the selectivity was not perfect and a 5-*exo-dig* product was also formed.

Scheme 9. Previous work by our group



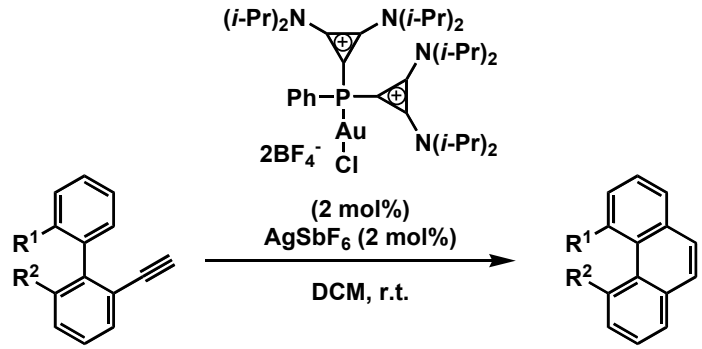
In 2008, Yang and coworkers reported that the gold(I)-catalyzed hydroarylation of phenyl-substituted 2-alkynylbiphenyl realized 6-*endo-dig*-selective transformation (Scheme 10).[7b] The catalytic systems were almost the same as Scheme 8, but the selectivity was perfect. These results imply that substituent on alkyne have a significant effect on the selectivity of cyclization fashion.

Scheme 10. Hydroarylation of phenyl-substituted 2-alkynylbiphenyl



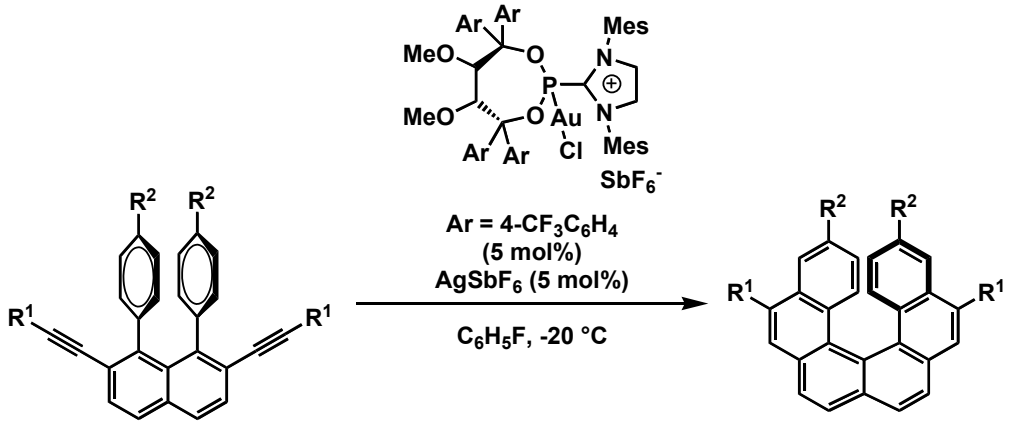
In 2013, Alcarazo and coworkers reported the 6-*endo-dig*-selective hydroarylation of sterically hindered 4 and/or 5-substituted 2-alkynylbiphenyls using an extremely π-acidic catalyst (Scheme 11).[7e] They developed new positively charged electron-poor phosphines, (dialkylamino)cyclopropenium-substituted phosphines, which are bench-stable crystalline solids. The new phosphine ligands have the same donor ability as $P(CF_3)_3$, which is a liquid with low boiling point and difficult to handle. They synthesized new extremely π-acidic gold catalysts with the new electron poor phosphines and subjected them to the hydroarylation of 4 and/or 5-substituted 2-alkynylbiphenyls, which were less reactive because of steric repulsion. As a result, 4,5-substituted non-planar phenanthrenes were obtained in high yields. They also used this transformation as a key step in total synthesis of calaquinone C and calahydroquinone A by modifying the structure of ligand.[7g]

Scheme 11. Synthesis of 4,5-substituted non-planar phenanthrene by extremely π-acidic gold catalyst



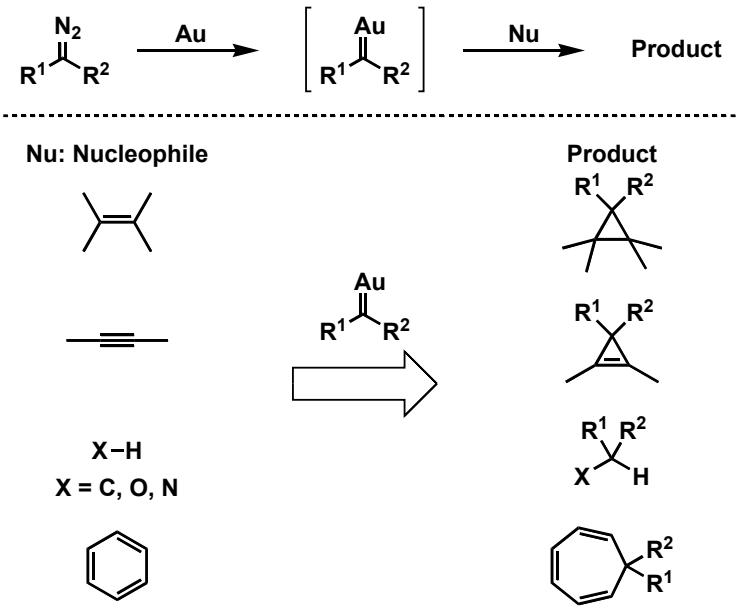
An extremely π-acidic phosphine was modified to a chiral ligand.[7h,7i] In 2017, Alcarazo and coworkers reported enantioselective synthesis of [6]carbohelicenes via 6-*endo*-*dig*-selective double hydroarylation using a Au(I)-TADDOL-derived cationic phosphonite catalyst (Scheme 12).[7i]

Scheme 12. Enantioselective synthesis of [6]carbohelicene via hydroarylation



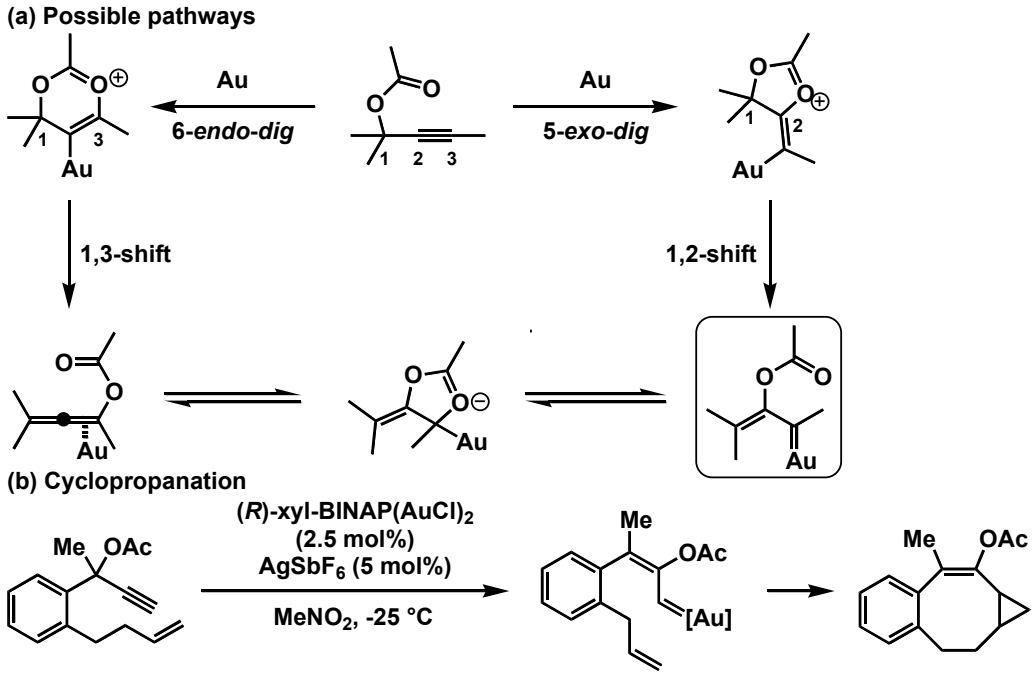
Another synthetic use of gold complexes is the preparation of gold carbenoid species which undergo cyclopropanation, C-H insertion, and Büchner reaction.[8,9] The gold carbenoid species is commonly prepared from Au(I) complexes and diazo compounds (Scheme 13).[8]

Scheme 13. Generation of gold carbenoid species from diazo compounds and their reactivity



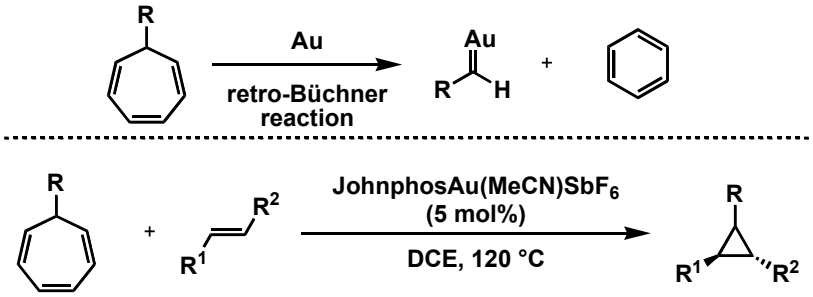
New strategies for the generation of gold carbenoid species without the use of diazo compounds were successively developed. The first example is gold-catalyzed rearrangement of propargylic esters (Scheme 14a).[9] 5-*Exo-dig* pathway gave the gold carbenoid species by 1,2-shift. On the other hand, 6-*endo-dig* pathway provided allene intermediates by 1,3-shift. Allene intermediates could be converted to gold-carbenoid species through cyclic intermediates. In 2009, Toste and co-workers reported cationic gold(I)-catalyzed enantioselective intramolecular cyclopropanation via *in-situ* generated gold carbenoid species with rearrangement of propargylic esters (Scheme 14b).[10]

Scheme 14. Generation of gold carbenoid species from propargylic esters



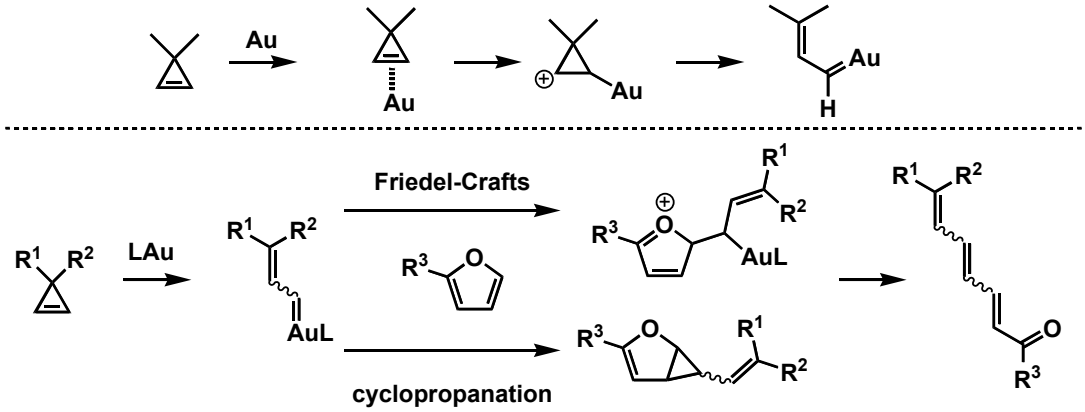
The second strategy is retro-Büchner reaction of 7-substituted 1,3,5-cycloheptatrienes (Scheme 15). In 2011, Echavarren and coworkers reported that the reaction of 7-substituted 1,3,5-cycloheptatriene with alkene in the presence of cationic gold(I)-catalysts gave cyclopropanes, which indicates the generation of gold carbenoid species by retro-Büchner reaction of 7-substituted 1,3,5-cycloheptatriene.[11] This method can provide new gold carbenoid species, which were difficult to prepare from diazo compounds.

Scheme 15. Generation of gold carbenoid species by retro-Büchner reaction



The third method is the generation from cyclopropenes (Scheme 16). The release of the ring strain of cyclopropene is the driving force for the generation of vinyl carbenoid species. In 2011, Hadfield and Lee demonstrated the reaction of cyclopropenes with furans in the presence of a gold catalyst to give conjugated trienones (Scheme 16).[12] The mechanism of this reaction was considered to be Friedel-Crafts type pathway or cyclopropanation.

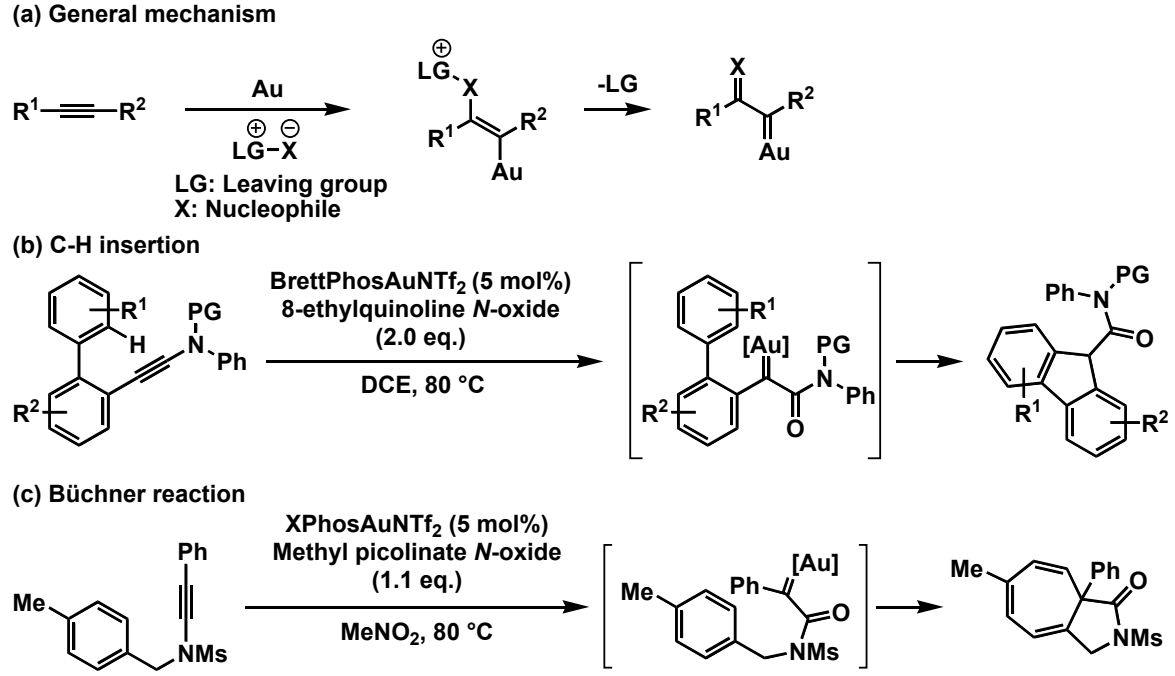
Scheme 16. Generation of gold carbenoid species from cyclopropenes



The forth method is the reaction of alkynes with oxidants (Scheme 17a).[13] The alkynes are attacked by nucleophiles to form a negatively charged vinyl-gold complex. This complex releases leaving group to form gold carbenoid species. There are many combinations of alkynes and nucleophiles. In particular, ynamides are attractive precursors of gold carbenoid species because their reactivity could be tuned by the protecting group, and the highly polarized alkyne leads to regioselective transformations.[13d] For example, Ye and co-workers achieved intramolecular C-H insertion

via α-oxo-gold carbenoid species derived from ynamide by using *N*-oxide as the oxidant (Scheme 17b).[14] Davies and co-workers used this ynamide strategy for intramolecular Büchner reaction (Scheme 17c).[15] In both examples, the reactivity could be changed by the ynamides and *N*-oxides.

Scheme 17. Generation of gold carbenoid species from alkyne and oxidant



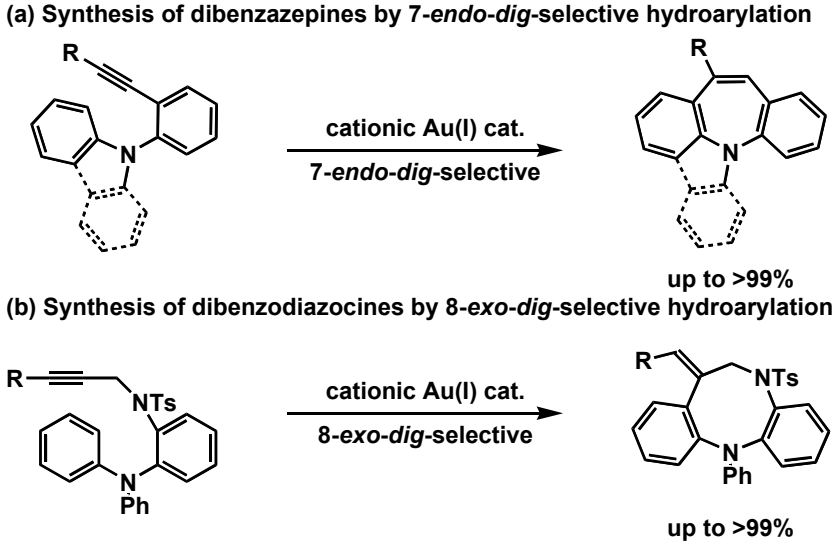
Purpose of this thesis

As mentioned above, there are many examples of 6-*endo*-*dig*-selective hydroarylation of alkynes. However, examples of medium-sized ring construction by gold-catalyzed hydroarylation are rare, which are shown in the introduction of Chapter 2. Therefore, the atom-economical construction of 7-membered dibenzazepines and 8-membered dibenzodiazocines by gold-catalyzed hydroarylation of alkynes is attractive.

In Chapter 2, the author explained the construction of nitrogen-containing medium-sized rings by gold(I)-catalyzed hydroarylation of alkynes (Scheme 18). The hydroarylation of 2-alkynyldiphenylamine derivatives by cationic gold(I)-catalysts gave a 7-*endo*-*dig* product selectively (Scheme 18a). The resonance effect of nitrogen was important for high reactivity, and hexacyclic compounds and simple *N*-methyldibenzazepine were synthesized by this protocol. On the other hand, the gold(I)-catalyzed reaction of 2-propargylaminotriphenylamine derivatives proceeded via 8-*exo*-*dig* selectivity to provide dibenzodiazocines (Scheme 18b). The control experiment of *o*-aminophenol tethered substrates indicated that *o*-diaminobenzene tether was crucial for the 8-*exo*-*dig*-selective hydroarylation. For the reaction of internal alkynes, the use of IPr ligand was

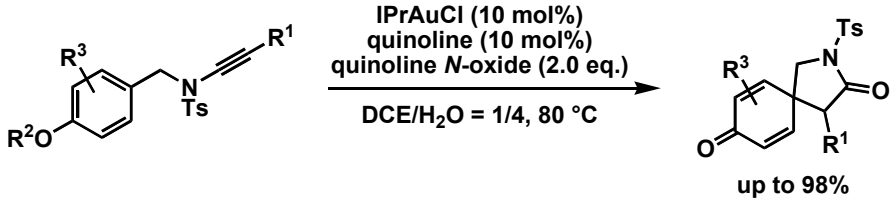
important for the high reactivity.

Scheme 18. Gold(I)-catalyzed construction of nitrogen-containing medium-sized ring



In Chapter 3, the author described dearomative spirocyclization of phenol derivatives via gold carbenoid species derived from ynamides (Scheme 19). The reaction of ynamide derived from *p*-methoxybenzylamine in the presence of a gold catalyst and *N*-oxide proceeded to give an azaspirocyclic compound. By-product formation was suppressed by using IPr as a ligand and water as a co-solvent. The product was efficiently transformed to a gabapentin lactam derivative.

Scheme 19. Dearomative spirocyclization of phenol derivatives via gold carbenoid species



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Chapter 2

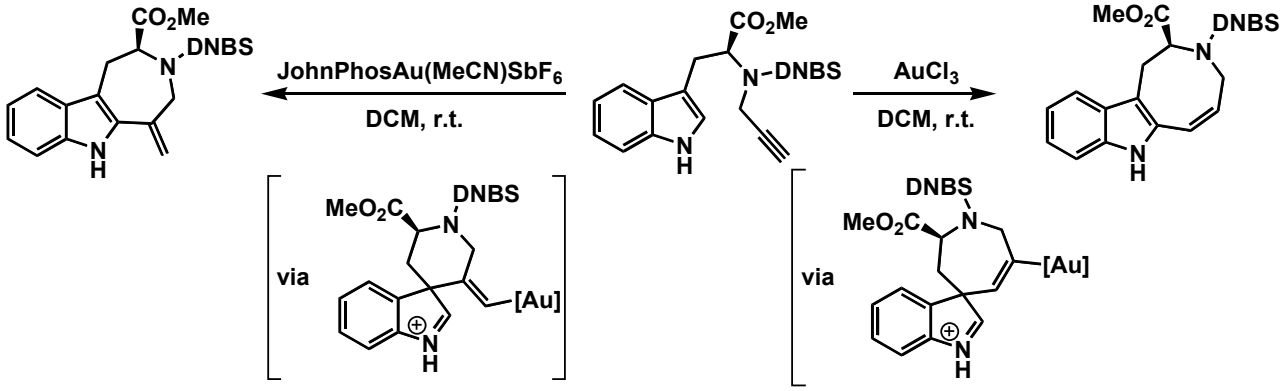
Construction of Nitrogen-Containing Medium-Sized Ring by Gold(I)-Catalyzed Cycloisomerization

Backgrounds

Nitrogen-containing heterocyclic structures are attractive for synthetic chemists because they are confirmed in many biologically active compounds and functional materials.[1] For an example of a medium-sized ring system, the dibenzazepine skeleton, which has one nitrogen atom in a seven-membered ring fused with two benzene rings, is a substructure of tricyclic antidepressants.[2] In addition, the diazocine skeleton, which has two nitrogen atoms in an eight-membered ring, is included in antibacterial agents and HIV-1 integrase inhibitors.[3]

As mentioned in Chapter 1, there are many reports of 6-*endo-dig*-selective hydroarylation, but only a few examples for construction of medium-sized rings by hydroarylation have been reported. In 2006, Echavarren and co-workers reported the 7-*exo-dig*- and 8-*endo-dig*-selective hydroarylation of alkynes using an indole moiety as a nucleophile (Scheme 1).[4] The use of a gold(I)-catalyst induced 7-*exo-dig*-selective hydroarylation. On the other hand, the use of a gold(III)-catalyst selectively provided an 8-*endo-dig* product. In both cases, the reaction initially proceeded at the C3-position of indole in a 6-*exo-dig* and 7-*endo-dig* fashions to give spirocyclic intermediates. These spirocyclic intermediates were readily rearranged to give the formal 7-*exo-dig* and 8-*endo-dig* products, respectively. This strategy was used for the total synthesis of various indole alkaloids.[4d]

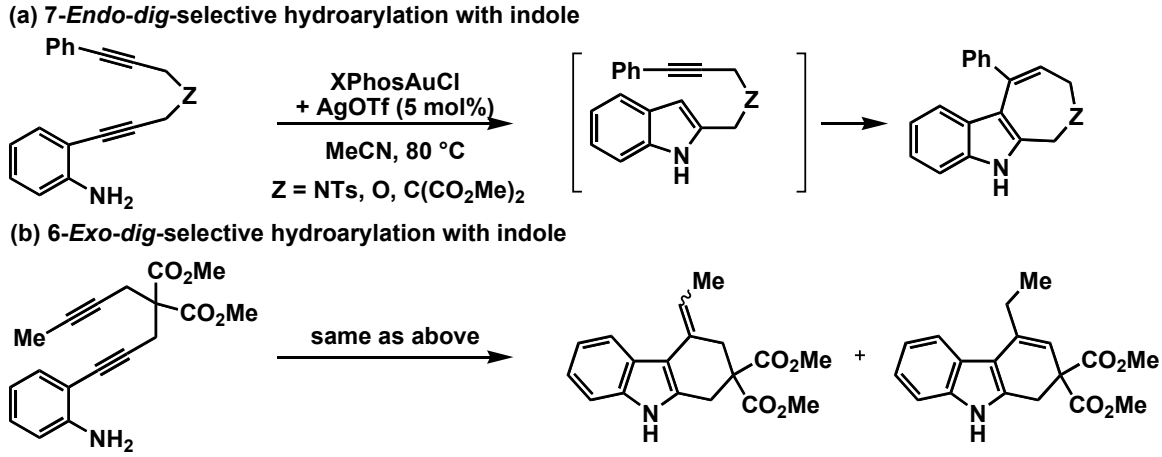
Scheme 1. 7-*Exo-dig*- and 8-*endo-dig*-selective hydroarylation of alkynes by using indoles



In 2011, Fujii, Ohno, and co-workers reported a cascade reaction of hydroamination and 7-*endo-dig*-selective hydroarylation (Scheme 2).[5] They synthesized various *ortho*-1,6-diyne-substituted anilines and subjected them to gold(I)-catalyzed reactions. The first reaction was hydroamination of alkyne to provide a C2-substituted indole intermediate. The C3-position of the indole was highly nucleophilic and successive reaction with the remaining alkyne moiety selectively gave 7-*endo-dig* products by hydroarylation (Scheme 2a). When methyl-substituted alkyne was subjected to the gold(I)-catalyzed cascade reaction, a

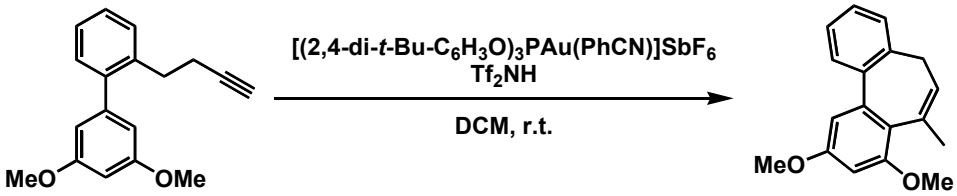
6-*exo-dig*-selective hydroarylation proceeded (Scheme 2b). These results indicated that the substituents on alkyne affected the selectivity of hydroarylation.

Scheme 2. Cascade reaction of hydroamination and hydroarylation



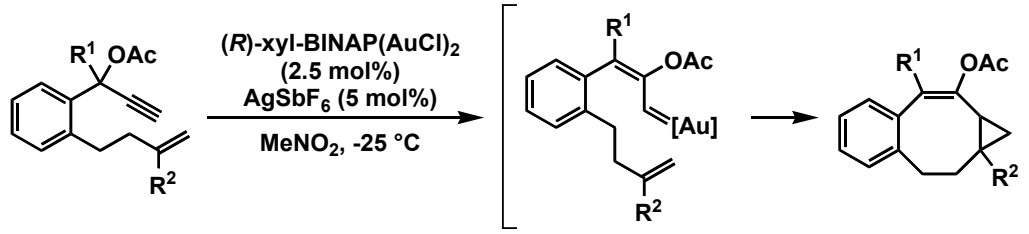
While indole moieties have been used as a nucleophile in hydroarylations, Hashmi and co-workers reported gold(I)-catalyzed 7-*exo-dig*-selective hydroarylation of alkynes by using a 3,5-dimethoxyphenyl group as a nucleophile. Dibenzocycloheptatriene was obtained after complete isomerization of *exo*-olefin using Tf_2NH as a strong acid (Scheme 3).[6] This reaction was promoted by an electron-deficient phosphite ligand.

Scheme 3. 7-*Exo-dig*-selective hydroarylation of alkyne



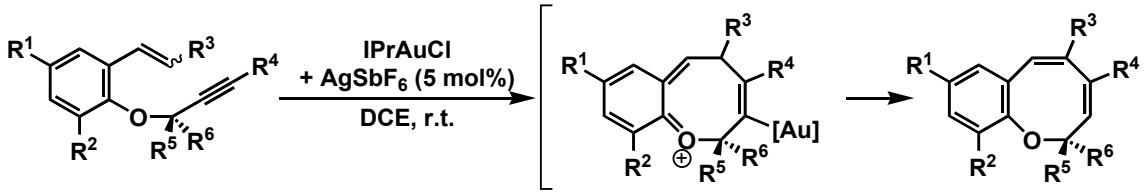
As for the construction of eight-membered rings, there are some examples of ene-yne cycloisomerization. In 2009, Toste and co-workers disclosed an intramolecular cyclopropanation of 1,8-enynes via *in situ* generated gold carbenoid species, which was prepared by the rearrangement of propargylic esters, and cyclopropane-fused eight-membered ring compounds were obtained (Scheme 4).[7] Enantioselective reaction was also achieved by using a chiral ligand.

Scheme 4. Construction of eight-membered ring by cyclopropanation



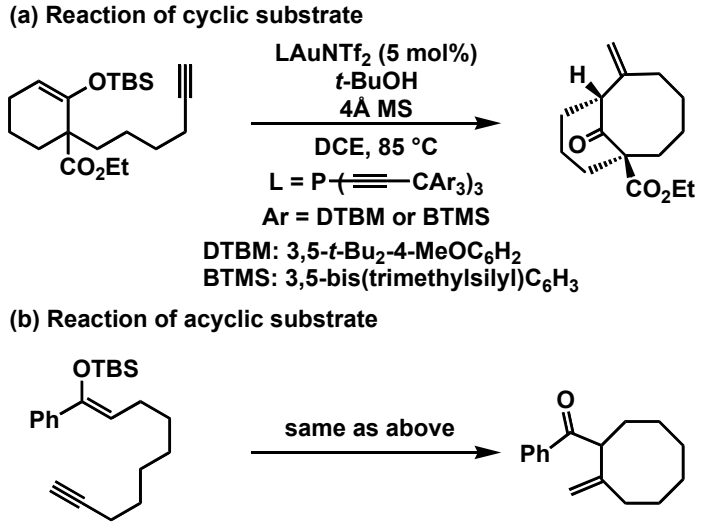
In 2011, Kumar, Waldmann and a co-worker reported 8-*endo-dig*-selective cycloisomerization of *o*-propargyloxy styrenes for the synthesis of benzoxocines (Scheme 5).[8] The reaction was considered to proceed via a cationic eight-membered ring intermediate which was initiated by an electron-donating resonance effect of the oxygen atom.

Scheme 5. 8-*Endo-dig*-selective cycloisomerization



In 2013, Sawamura and co-workers reported 8-*exo-dig*-selective cycloisomerization of silyl enol ethers possessing an alkynyl side chain, and a bridged bicyclic system containing an eight-membered ring was constructed (Scheme 6).[9] Their originally developed semihollow triethynylphosphane ligands enabled the cyclization of the highly flexible substrate. In particular, this methodology could also be used for acyclic substrates (Scheme 6b).

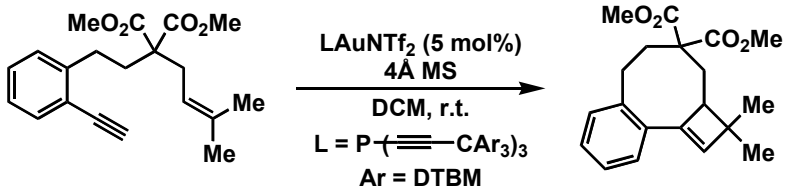
Scheme 6. 8-*Exo-dig*-selective cycloisomerization



While an intramolecular gold(I)-catalyzed [2+2] cycloaddition had been developed for the construction of seven-membered ring and macrocycles,[10] Sawamura and co-workers reported the con-

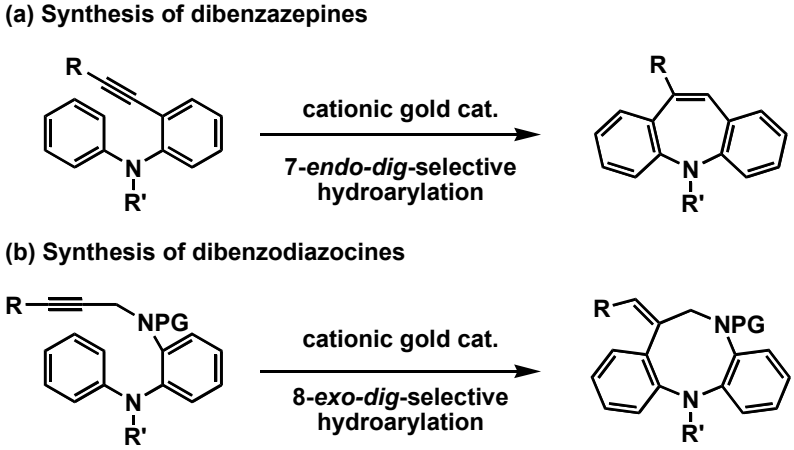
struction of cyclobutene-fused eight-membered ring by intramolecular gold(I)-catalyzed [2+2] cycloaddition (Scheme 7).[11] The dehydrated condition was important for high reactivity.[12]

Scheme 7. Construction of eight-membered ring by [2+2] cycloaddition



Against this background, the author considered that the construction of a nitrogen-containing medium-sized ring could be achieved by using diphenylamine possessing an alkyne moiety as a substrate of cationic gold(I)-catalyzed hydroarylation (Scheme 8). When the reaction of 2-(1-alkynyl)-*N*-phenylanilines proceeded in a 7-*endo*-*dig*-selective fashion, dibenzazepines would be obtained (Scheme 8a).[13] When the reaction of 2-propargylaminodiphenylamines proceeded in a 8-*exo*-*dig*-selective manner, dibenzodiazocines would be obtained (Scheme 8b).[14]

Scheme 8. Concept of this work



Results and Discussion

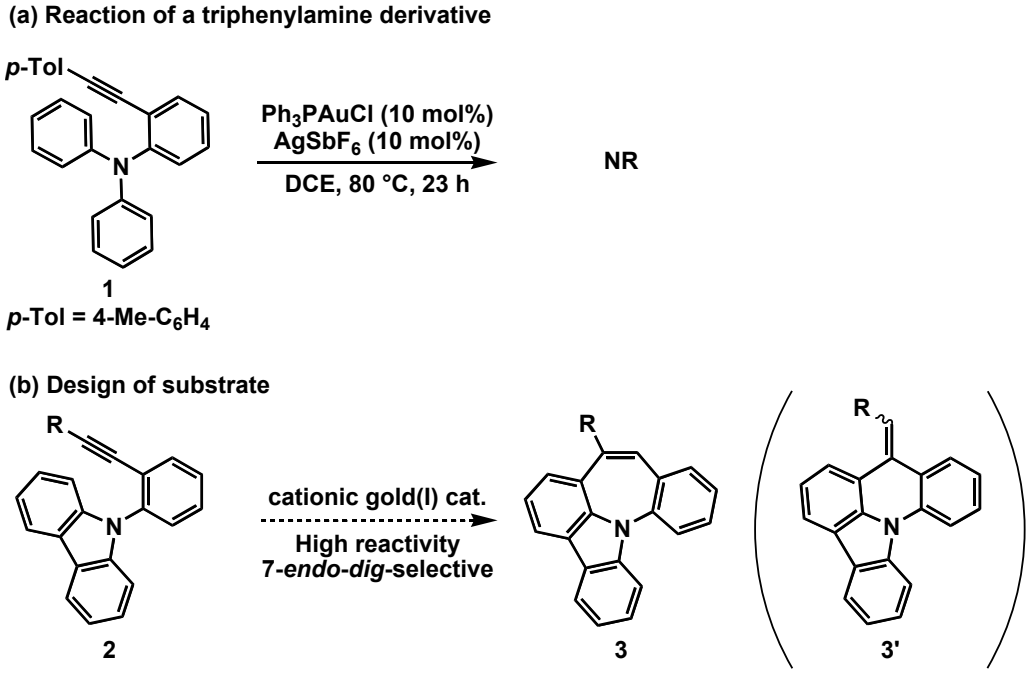
2.1. Synthesis of Dibenzazepines by 7-*endo*-*dig*-Selective Cycloisomerization

2.1.1. Reactions of Carbazole-Containing Substrates

First, the author subjected triphenylamine derivative **1** to gold(I)-catalyzed cycloisomerization, but no reaction proceeded (Scheme 9a). The author considered that the reactivity of the *ortho* position of amino group was too low to react due to free rotation of the phenyl ring. Therefore, the author designed carbazole-containing substrate **2** because the planarity of carbazole was expected to increase the nucleophilicity by the electron-donating resonance effect of nitrogen atom as well as

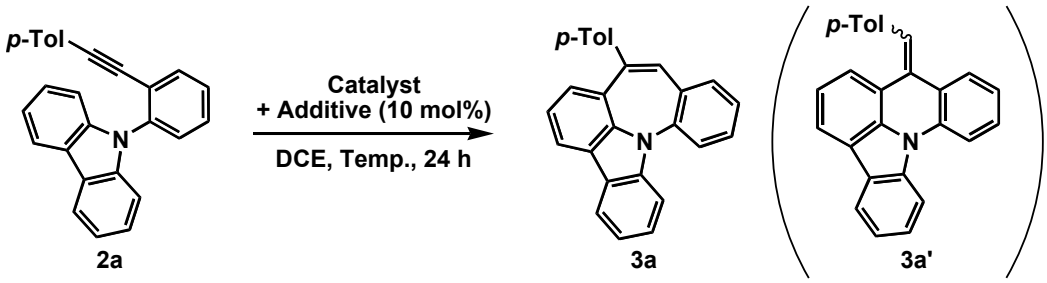
the accessibility to an alkyne moiety (Scheme 9b). Moreover, the formation of undesired 6-*exo-dig* product **3'** would be suppressed by the effect of substituents on alkyne.

Scheme 9. Preliminary result and design of substrate



p-Tolyl-substituted alkyne **2a** was used for the optimization of reaction conditions (Table 1). When the reaction of **2a** was conducted in the presence of chloro(triphenylphosphine)gold(I) and silver hexafluoroantimonate in DCE at 80 °C, the desired 7-*endo-dig* product **3a** was obtained selectively in high yield (Entry 1). Its structure was confirmed by single-crystal X-ray analysis (Figure 1) and the undesired 6-*exo-dig* product **3a'** was not obtained. Hexafluoroantimonate and trifluoromethanesulfonate exhibited almost the same reactivity, but the use of tetrafluoroborate gave a poor result and the yield of **3a** was low (Entries 1-3). In the absence of silver salt, only a trace amount of **3a** was obtained (Entry 4). This result indicated that the cationic character of gold catalysts was important for this reaction. Drastic decrease of yield was observed at lower reaction temperatures (Entries 5 and 6). When a more electrophilic gold(I) catalyst possessing an electron-deficient phosphine ligand was used, the reaction proceeded even at room temperature, albeit in moderate yield along with the remaining of the substrate (Entries 7-10). The author determined Entry 1 as the best conditions for **2a**.

Table 1. Screening of reaction conditions for **2a**



Entry	Catalyst	Additive	Temp. /°C	Yield /%
1	Ph_3PAuCl	$AgSbF_6$	80	90
2	Ph_3PAuCl	AgOTf	80	88
3	Ph_3PAuCl	$AgBF_4$	80	12
4	Ph_3PAuCl	None	80	Trace
5	Ph_3PAuCl	$AgSbF_6$	60	27
6	Ph_3PAuCl	$AgSbF_6$	40	14
7	$[(4\text{-}CF_3C_6H_4)_3P]AuCl$	$AgSbF_6$	r.t.	58
8	$[(4\text{-}CF_3C_6H_4)_3P]AuCl$	AgOTf	r.t.	65
9	$[(C_6F_5)_3P]AuCl$	$AgSbF_6$	r.t.	33
10	$[(C_6F_5)_3P]AuCl$	AgOTf	r.t.	42

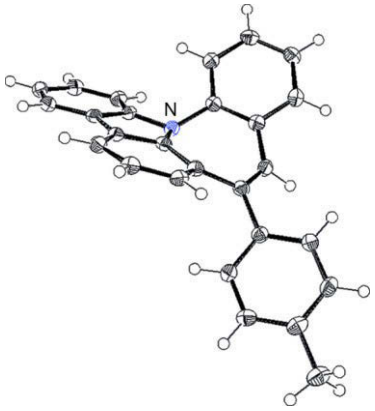
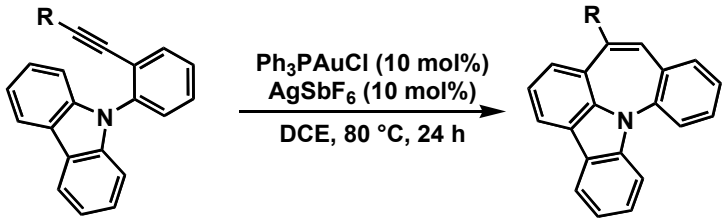


Figure 1. ORTEP diagram of **3a** (thermal ellipsoids shown at 50% probability)

Under the optimized conditions, the author subjected various alkynes to the cycloisomerization (Table 2). The reaction of sterically hindered *o*-tolyl-substituted alkyne **2b** proceeded to give **3b** in good yield (Entry 1). *p*-Anisyl-substituted alkyne **2c** showed high reactivity: the reaction concluded

within 6 h and product **3c** was obtained in excellent yield (Entry 2). Naphthyl- and thienyl-substituted alkynes **2d**-**2f** could also be used as substrates to provide cycloadducts **3d**-**3f** in high yields (Entries 3-5). Terminal alkyne **2g** was completely consumed within 2 h at room temperature and high yield was achieved (Entry 6). In contrast, the reactivity of phenyl-substituted alkyne **2h** was low under these conditions (Entry 7).

Table 2. Substrate scope of alkyne terminus

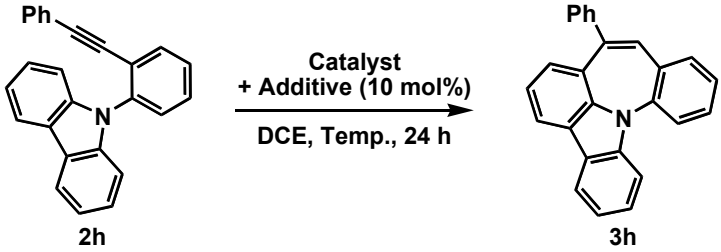


Entry	R	Yield /%
1	2-MeC_6H_4 (**2b**)	75 (**3b**)
2[a]	4-$MeOC_6H_4$ (**2c**)	98 (**3c**)
3	1-Naphthyl (**2d**)	92 (**3d**)
4	3-Thienyl (**2e**)	86 (**3e**)
5	2-Thienyl (**2f**)	91 (**3f**)
6[b]	H (**2g**)	82 (**3g**)
7	Ph (**2h**)	20 (**3h**)

[a] The reaction was conducted for 6 h. [b] AgOTf was used instead of $AgSbF_6$. The reaction was conducted at r.t. for 2 h.

To improve the yield of the reaction of **2h**, the author conducted condition screening again (Table 3). When more electrophilic gold(I) catalyst, chloro(tris(4-trifluoromethylphenyl)phosphine)-gold(I), was used at 80 °C, the desired product **3h** was obtained in low yield and most of the substrate **2h** remained (Entry 1). Since the author considered that the reason for the low conversion might be the instability of electrophilic gold(I) catalysts at high temperature, the reaction was conducted at room temperature (Entry 2). Gratifyingly, the yield improved to 45% as expected. After screening of various counteranions, trifluoromethanesulfonate was found to be best (Entry 3). When the more electrophilic chloro(tris(pentafluorophenyl)phosphine)gold(I) catalyst was used, the reaction proceeded quantitatively within 3 h (Entry 4).

Table 3. Screening of reaction conditions for **2h**



Entry	Catalyst	Additive	Temp. /°C	Yield /%
1	$[(4\text{-}CF_3C_6H_4)_3P]AuCl$	$AgSbF_6$	80	7
2	$[(4\text{-}CF_3C_6H_4)_3P]AuCl$	$AgSbF_6$	r.t.	45
3	$[(4\text{-}CF_3C_6H_4)_3P]AuCl$	AgOTf	r.t.	98
4[a]	$[(C_6F_5)_3P]AuCl$	AgOTf	r.t.	>99

[a] The reaction was conducted for 3 h.

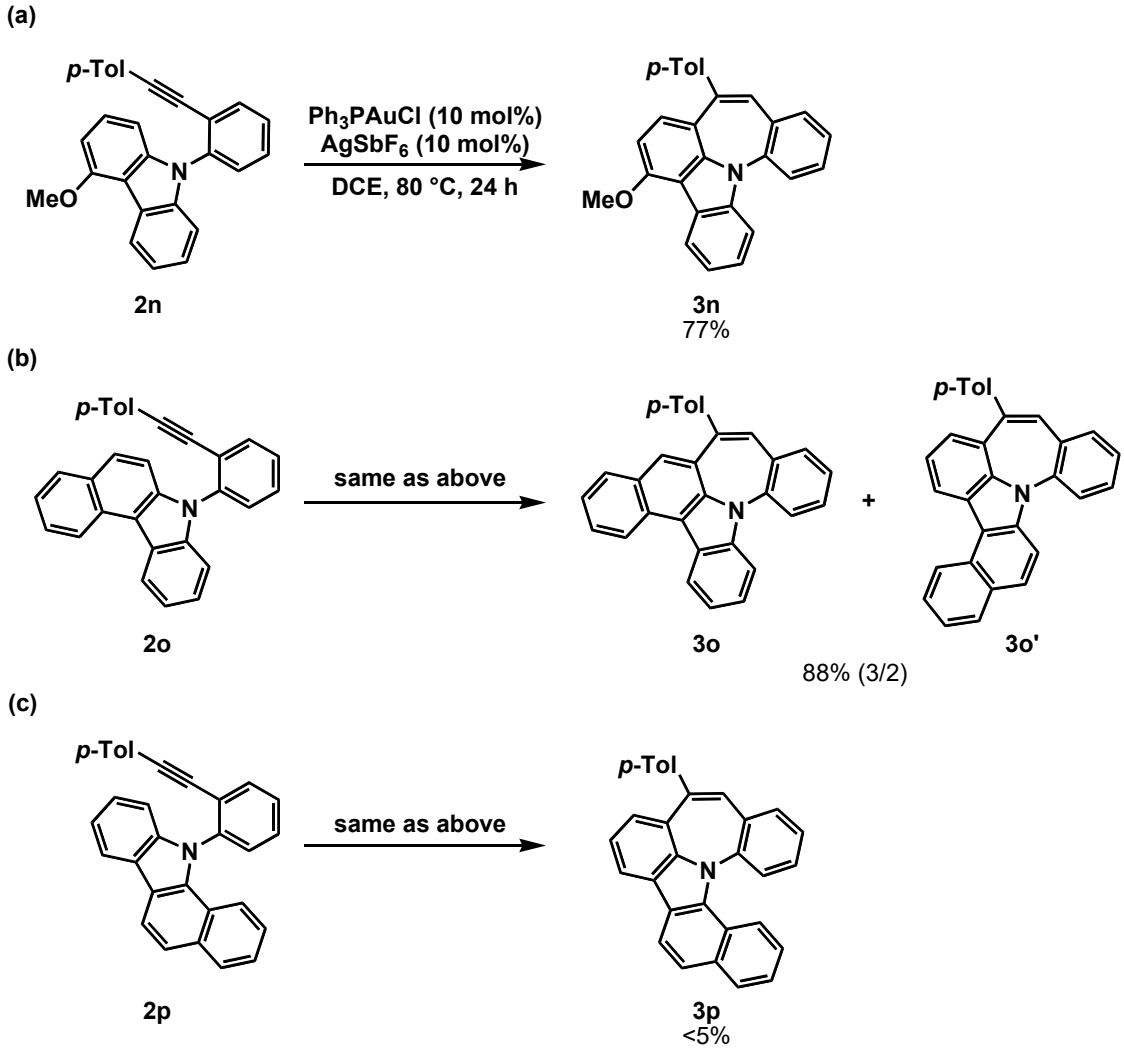
Under the optimized conditions in Entry 4 of Table 3, other alkynes were subjected to the cycloisomerization (Table 4). The reaction of *m*-tolyl, *m*-anisyl, and *p*-biphenyl-substituted alkynes **2i**, **2j**, **2k** proceeded smoothly to give the desired products **3i**, **3j**, and 3**k**, respectively in high to excellent yields (Entries 1-3). Alkynes possessing electron-withdrawing group-substituted aryl groups **2l** and **2m** could also be used as substrates to give **3l** and **3m** in high yields (Entries 4 and 5). The reaction of **2a** under these conditions gave **3a** in lower yield (42%, see entry 10 in Table 1).

Table 4. Substrate scope of alkyne terminus

Entry	R	Yield /%
1	$3\text{-}MeC_6H_4$ (**2i**)	86 (**3i**)
2	$3\text{-}MeOC_6H_4$ (**2j**)	93 (**3j**)
3	$4\text{-}PhC_6H_4$ (**2k**)	98 (**3k**)
4	$4\text{-}ClC_6H_4$ (**2l**)	85 (**3l**)
5	$4\text{-}CF_3C_6H_4$ (**2m**)	97 (**3m**)

Next, the author subjected substrates possessing a substituent on the carbazole ring to the cycloisomerization (Scheme 10). The reaction of 4-methoxycarbazole-containing substrate **2n** proceeded selectively at the methoxy-substituted aromatic ring with the slightly remaining of the substrate to provide **3n** in good yield, but it was lower than that of **3a** (Scheme 10a). The author considered that **2a** had two possible reactive carbons in its symmetrical structure, but **2n** had only one possible reactive carbon, which resulted in lower yield of **3n**. To synthesize π-extended polycyclic compounds, benzocarbazole-containing substrates were examined (Scheme 10b and 10c). The reaction of benzo[*c*]carbazole-based substrate **2o** gave cycloadducts **3o** and **3o'** as an inseparable mixture (Scheme 10b). The reactivity of substrate **2p** possessing a benzo[*a*]carbazole moiety was extremely low and only a trace amount of **3p** was obtained (Scheme 10c). The steric repulsion between naphthalene ring and 2-alkynylphenyl group of **3p** was responsible for the low reactivity.

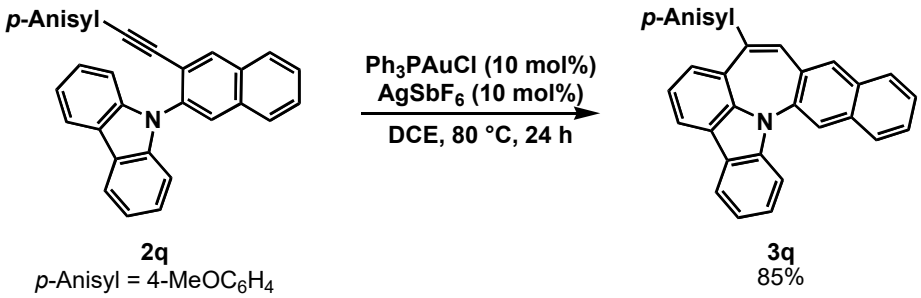
Scheme 10. Scope of substrates possessing substituent on carbazole moiety



In place of phenylene-tethered substrates, naphthylene-tethered substrate **2q** was subjected to the cycloisomerization to synthesize a hexacyclic compound (Scheme 11). The reaction of **2q** gave the

desired π-extended product **3q** in high yield.

Scheme 11. Synthesis of hexacyclic compound **3q**

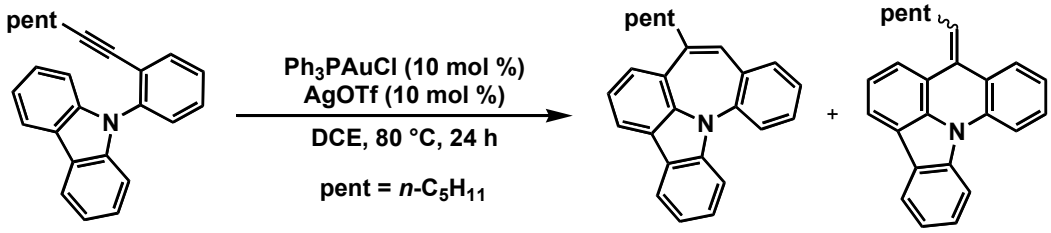


2q
p-Anisyl = 4-$MeOC_6H_4$

3q
85%

When the reaction of alkyl substituted alkyne **2r** was conducted, the cyclization proceeded, but the desired 7-*endo-dig* product **3r** was minor product while the undesired 6-*exo-dig* product **3r'** was major product (Scheme 12). In this reaction, the starting material remained and could not be separated from the product.

Scheme 12. Reaction of alkyl-substituted alkyne **2r**



2r **3r** **3r'**

ca. 37%
***endo*/*exo* = 1/12**

The author speculated the *endo*/*exo* selectivity as follows (Figure 2). In the case of aryl-substituted alkynes, the gold catalyst would be ligated to distal carbon because of the steric repulsion with bulky aryl group, which resulted in 7-*endo-dig* cyclization. In the case of alkyl-substituted alkyne, when the reaction proceeded in 6-*exo-dig* manner, the partial positive charge would be at distal carbon of alkyne from alkyl group and stabilized by resonance effect of aromatic ring.

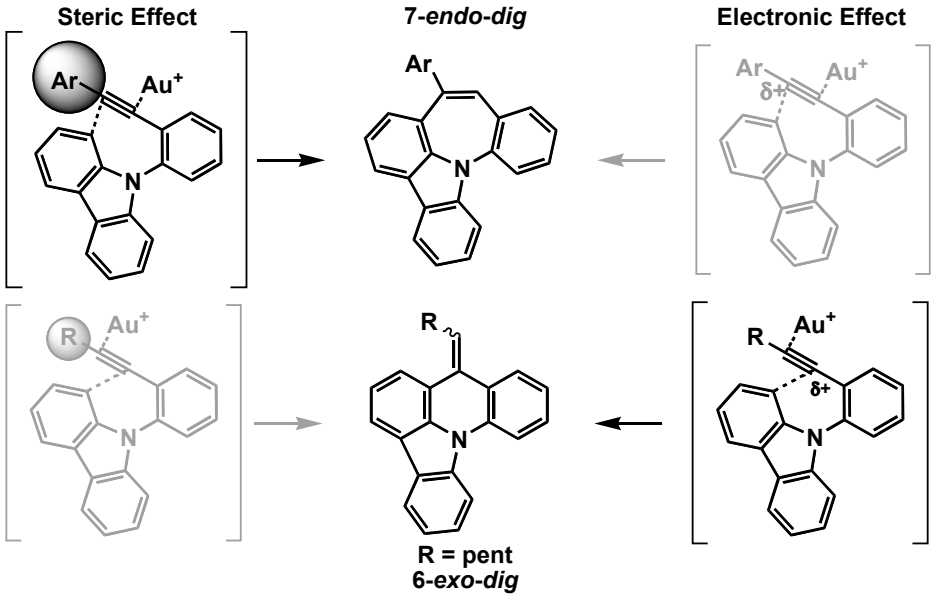
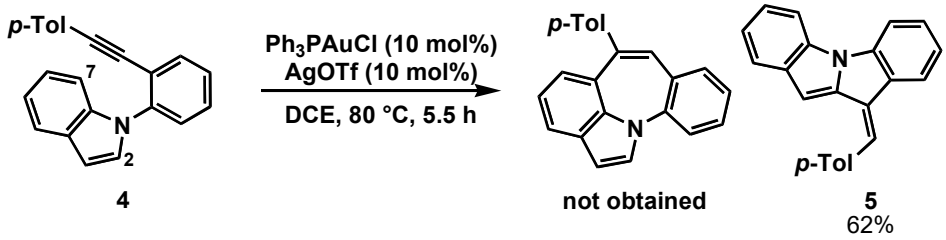


Figure 2. Explanation of *endo*/*exo* selectivity

2.1.2. Reactions of Indoline-Containing Substrates

To further investigate the substrate scope of this 7-*endo-dig*-selective cycloisomerization, the author subjected indole-containing substrate **4** to gold(I)-catalyzed reaction (Scheme 13). While the desired 7-*endo-dig* cyclization did not proceed, 5-*exo-dig* product **5** was obtained in moderate yield. This result indicated the reactivity of the C2 position of indole is higher than the C7 position.

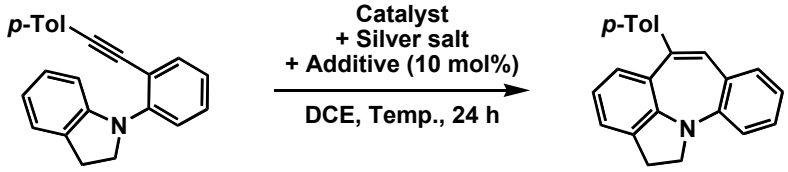
Scheme 13. Reaction of indole-containing substrate



To suppress the 5-*exo-dig* cycloisomerization, an indoline-containing substrate possessing a sp^3 carbon at the C2 position was examined. The author subjected *p*-tolyl-substituted alkyne **6a** to the cycloisomerization (Table 5). The desired product **7a** was obtained in good NMR yield under the conditions of Entry 2 in Table 1 and 5-*exo-dig* cycloadduct could not be detected as expected, but alkyne **6a** was not completely consumed after 24 h (Entry 1). The author considered that the cationic gold catalyst was deactivated during the progress of the reaction. To stabilize the catalyst, a catalytic amount of pyridine was added. As a result, alkyne **6a** was completely consumed and the NMR yield exceeded 90% (Entry 2). The reaction did not proceed without a gold catalyst or a silver salt (Entries 3 and 4). These results indicated that the cationic character of gold species was

important for high reactivity. After screening of various counteranions, trifluoromethanesulfonate gave the best result (Entries 2, 5, and 6). Unlike the reaction of carbazole-based substrates, tetrafluoroborate also realized a high yield. The reaction temperature could be decreased to room temperature without drastic decrease of yield and the reaction proceeded quantitatively at 40 °C, which was determined to be the best conditions (Entries 2, 7-9). To compare the reactivity of carbazole- and indoline-containing substrates, the reaction under the conditions of Entry 6 in Table 1 was examined (Entry 10). The starting material **6a** slightly remained, but the yield (79%) was higher than that of carbazole-containing substrate (14%). These results indicated that indoline-containing substrates had higher reactivity than the carbazole-containing ones.

Table 5. Screening of reaction conditions for **6a**



6a **7a**

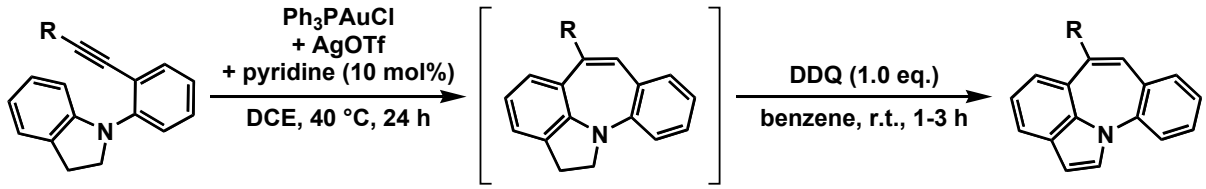
Entry	Catalyst	Silver salt	Additive	Temp. /°C	NMR yield /%[a]
1	Ph_3PAuCl	AgOTf	None	80	75
2	Ph_3PAuCl	AgOTf	Pyridine	80	93
3	None	AgOTf	Pyridine	80	N.R.
4	Ph_3PAuCl	None	Pyridine	80	N.R.
5	Ph_3PAuCl	$AgBF_4$	Pyridine	80	89
6	Ph_3PAuCl	$AgSbF_6$	Pyridine	80	92
7	Ph_3PAuCl	AgOTf	Pyridine	60	93
8	Ph_3PAuCl	AgOTf	Pyridine	40	>99
9	Ph_3PAuCl	AgOTf	Pyridine	r.t.	83
10	Ph_3PAuCl	$AgSbF_6$	None	40	79

[a] NMR yields was measured using 1,1,2,2-tetrachloroethane as an internal standard.

Under the optimized conditions of Entry 8 in Table 5, substituent scope of the alkyne moiety was examined (Table 6). Compounds **7** were generally unstable and part of the obtained compound was oxidized to indole **8** during purification by preparative TLC. Therefore, products were isolated and fully characterized as indole derivatives **8** after DDQ oxidation.[15] The oxidation of compound **7a** yielded the indole derivative **8a** and the two-step yield was high (Entry 1). Tolyl, anisyl, and phe-

nyl-substituted alkynes **6b**-**6g** gave indole-containing dibenzazepines **8b**-**8g** in high to excellent yields (Entries 2-7). In particular, sterically hindered alkynes **6c** and **6f** could also be used for this reaction. Electron-deficient chlorophenyl-substituted alkynes **6h** and **6i** provided cyclcoadducts **8h** and **8i** in high yields (Entries 8 and 9). The reaction of 4-(trifluoromethyl)phenyl-substituted alkyne **6j** yielded cyclcoadduct **8j** in moderate yield due to low conversion (Entry 10). The use of more electrophilic gold catalysts slightly improved the yield, but the substrate still remained after 24 h (Entry 11). 1-Naphthyl- and 4-biphenyl-substituted alkynes **6k** and **6l** were transformed into **8k** and **8l** in good to high yields (Entries 12 and 13). When terminal alkyne **6m** was subjected to the cycloisomerization, more electrophilic gold catalysts were effective and indoline-containing cycloadduct **7m** was obtained in 80% NMR yield. But the oxidation gave several unidentified products and the isolated yield of **8m** was moderate (Entry 14).

Table 6. Scope of substituents on alkyne for indoline-containing substrate



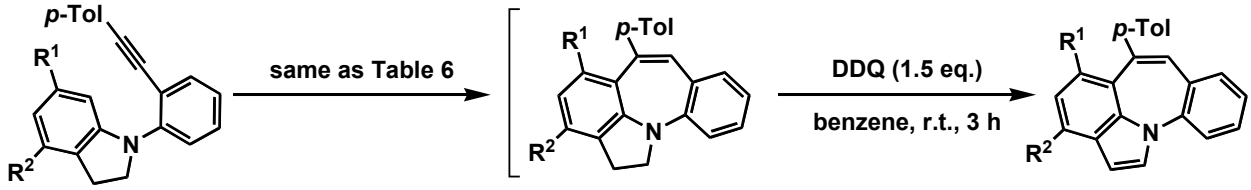
6 **7** **8**

Entry	R	Yield /%[a]	Entry	R	Yield /%[a]
1	4-MeC_6H_4 (**6a**)	93 (**8a**)	8	4-ClC_6H_4 (**6h**)	88 (**8h**)
2	3-MeC_6H_4 (**6b**)	98 (**8b**)	9	3-ClC_6H_4 (**6i**)	>99 (**8i**)
3	2-MeC_6H_4 (**6c**)	87 (**8c**)	10	4-$CF_3C_6H_4$ (**6j**)	51 (**8j**)
4	4-$MeOC_6H_4$ (**6d**)	86 (**8d**)	11[b]	4-$CF_3C_6H_4$ (**6j**)	64 (**8j**)
5	3-$MeOC_6H_4$ (**6e**)	96 (**8e**)	12	1-Naphthyl (**6k**)	98 (**8k**)
6	2-$MeOC_6H_4$ (**6f**)	88 (**8f**)	13	4-PhC_6H_4 (**6l**)	76 (**8l**)
7	Ph (**6g**)	>99 (**8g**)	14[b]	H (**6m**)	56 (**8m**)

[a] Isolated yield. [b] $[(C_6F_5)_3P]AuCl$ and $AgBF_4$ were used.

Next, the author examined the substituent on the indoline moiety (Scheme 14). Both electron-withdrawing and -donating groups could be used, and fluoro-substituted cycloadduct **8n** and methoxy-substituted cycloadduct **8o** were obtained in moderate yields.

Scheme 14. Reaction of substrates possessing a substituent on indoline moiety

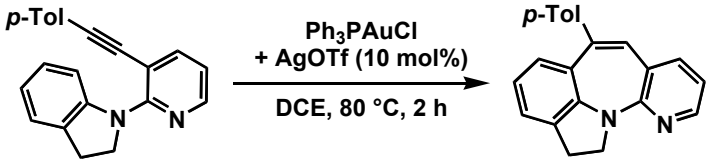


6n (R^1 = F, R^2 = H)
6o (R^1 = H, R^2 = OMe)

8n: 71%
8o: 63%

The cycloisomerization of pyridine-containing substrate **6p** proceeded smoothly at 80 °C without addition of external pyridine. Indoline-containing cycloadduct **8p** was isolated in high yield without further oxidation (Scheme 15).

Scheme 15. Reaction of pyridine-containing substrate

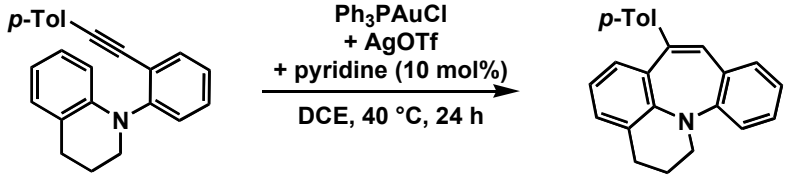


6p

8p
97%

To evaluate the effect of ring structure in the substrate, tetrahydroquinoline-based substrate **9** was subjected to the cycloisomerization (Scheme 16). As a result, the reaction proceeded at lower reaction temperature and tetracyclic product **10** was obtained in high yield. This result implies that the flexibility of nitrogen-containing ring in the substrate does not affect the reactivity.

Scheme 16. Reaction of tetrahydroquinoline-containing substrate

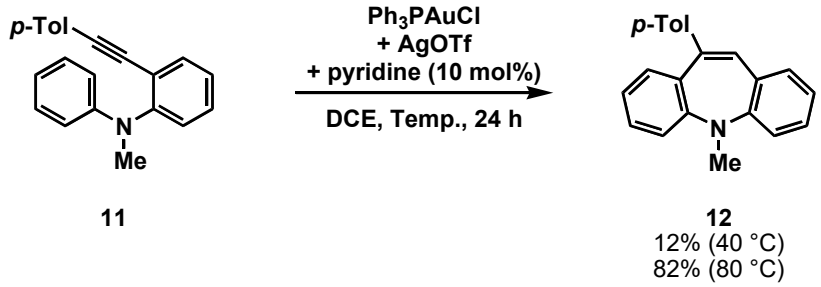


9

10
94%

Finally, the author examined more flexible substrate **11** without fused ring structure (Scheme 17). At 40 °C, the conversion was low but the desired dibenzazepine derivative **12** was obtained.[16,17] The yield was improved to 82% at higher reaction temperature of 80 °C.

Scheme 17. Reaction of acyclic substrate



The author speculated higher reactivity of indoline-containing substrates than carbazole-containing ones as follows (Figure 3). In the case of carbazole-containing substrate, there were two reactive carbons for cyclization. The lone pair of nitrogen atom delocalized to two aromatic rings of carbazole moiety. In contrast, indoline-containing substrate had only one reactive carbon and the lone pair delocalized to one aromatic ring of indoline moiety. As a result, the resonance effect of nitrogen atom of indoline-containing substrate would be stronger than that of carbazole-containing substrate. In addition, the alkyl moiety of indoline moiety acted as electron-donating group to increase the nucleophilicity.

Figure 3. Higher reactivity of indoline-containing substrates than carbazole-containing ones

While the reaction of triphenylamine derivative **1** did not proceed (Scheme 1a), the reaction of 2-alkynyl-*N*-methyldiphenylamine derivative **11** proceeded. The author speculated the strikingly different reactivity of phenyl and methyl groups as follows (Figure 4). In the case of triphenylamine derivative **1**, the steric repulsion of two phenyl groups made the phenyl group and the lone pair of nitrogen atom difficult to occupy the same plane. As a result, the resonanace effect of nitrogen atom was small, and phenyl group acted as an electron-withdrawing group. In contrast, in the case of less bulky methyl-substituted substrate **11**, phenyl group and the lone pair of nitrogen atom occupy the same plane and resonance effect of nitrogen was large, moreover, methyl group acted as an electron-donating group.

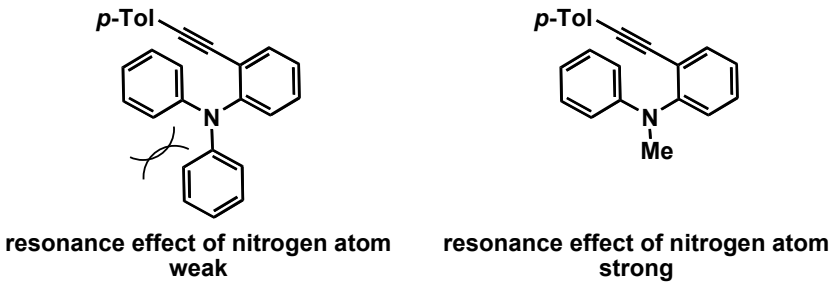


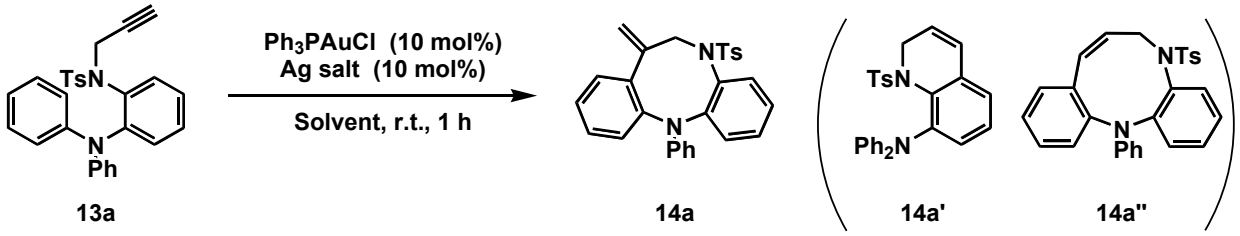
Figure 4. Effect of substituent for the reactivity

2.2. Synthesis of Dibenzodiazocines by 8-*exo*-*dig*-Selective Cycloisomerization

In the previous section, the 7-*endo-dig* cycloisomerization of 2-alkynyldiphenylamine was explained. In this section, the author describes the 8-*exo-dig*-selective cycloisomerization of 2-propargylaminotriphenylamines.

First, tosyl-protected 2-(propargylamino)triphenylamine **13a** was subjected to the gold(I)-catalyzed cycloisomerization (Table 7). The reaction of **13a** proceeded smoothly in the presence of chloro(triphenylphosphine)gold(I) and silver hexafluoroantimonate in DCM at room temperature, and the desired 8-*exo-dig* product **14a** was selectively obtained (Entry 1). Other cycloadducts, such as 6-*endo-dig* product **14a'** and 9-*endo-dig* product **14a"**, were not obtained. After screening of silver salts, silver hexafluoroantimonate was found to be the best (Entries 1-3). In the absence of a gold catalyst or a silver salt, the reaction was totally deterred (Entries 4 and 5). The use of toluene as a solvent improved the yield, and the reaction proceeded quantitatively in chlorobenzene (Entries 6 and 7). The amount of catalyst loading could be reduced to 5 mol% without drastic decrease of yield (Entry 8).

Table 7. Screening of reaction conditions for **13a**



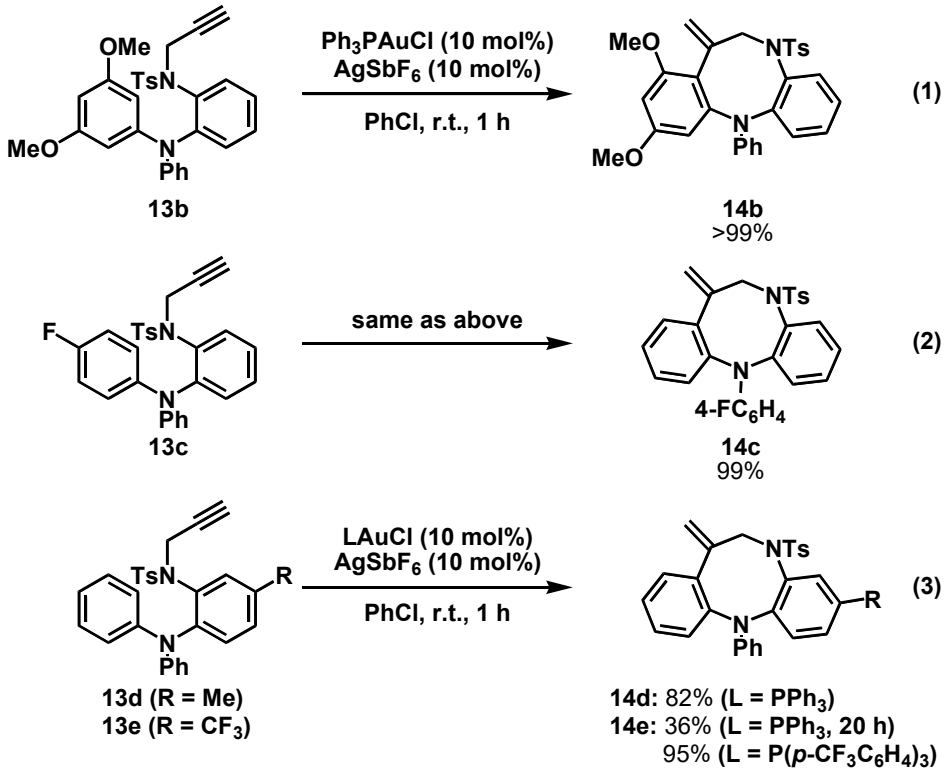
13a 14a 14a' 14a''

Entry	Ag salt	Solvent	Yield of **14a** /%[a]
1	$AgSbF_6$	DCM	90
2	AgOTf	DCM	(47)[b]
3	$AgBF_4$	DCM	(52)[b]
4	None	DCM	N.R.
5[c]	$AgSbF_6$	DCM	N.R.
6	$AgSbF_6$	toluene	97
7	$AgSbF_6$	PhCl	99
8[d]	$AgSbF_6$	PhCl	79

[a] Isolated yield. NMR yield was shown in parentheses. [b] NMR yields was measured using 1,1,2,2-tetrachloroethane as an internal standard. [c] The reaction was conducted without gold catalyst. [d] Gold complex and Ag salt (5 mol%) was used.

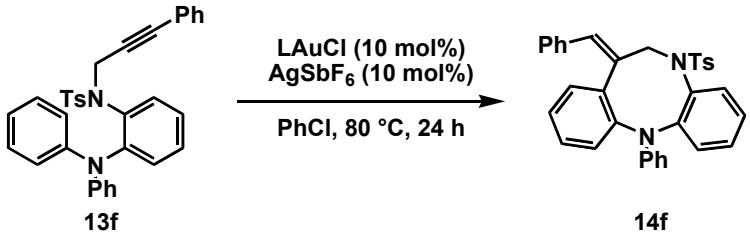
Under the reaction conditions of Entry 7 in Table 7, substrates possessing substituents on aromatic rings were subjected to the cycloisomerization (Scheme 18). The reaction of *N*-(3,5-dimethoxyphenyl)-substituted substrate **13b** proceeded quantitatively to give the product **14b**, where more electron-rich arene was selectivity involved in the transformation [Equation (1)]. In contrast, *N*-(4-fluorophenyl)-substituted substrate **13c** was selectively converted into **14c**, where the electron-poor arene was untouched [Equation (2)]. The substituents on the *o*-diaminobenzene moiety were also examined [Equation (3)]. While the reaction of methyl-substituted substrate **13d** gave the desired product **14d** in high yield, that of trifluoromethyl-substituted substrate **13e** afforded the corresponding cycloadduct **14e** in low yield, even after a longer reaction time. The reason for the low reactivity of **13e** could be explained by the strong electron-withdrawing effect of the trifluoromethyl group. Therefore, the author used the more electrophilic gold catalyst to make the alkyne moiety more electrophilic. As a result, the yield was dramatically improved to 95%.

Scheme 18. Reactions of substrates possessing substituents on the aromatic rings



Next, the author examined the reaction of internal alkyne **13f** (Table 8). Under the optimized conditions for terminal alkynes as above, the reaction sluggishly proceeded and only a trace amount of the desired product **14f** was detected even at high temperature (Entry 1). After screening of phosphine ligands, the more sterically hindered and electron-rich phosphine ligand, ^{t}BuXPhos, gave **14f** in low yield (Entry 2). Various ligands were examined and IPr type ligands were found more effective for this transformation (Entries 3, 6 and 7). IMes type ligands were ineffective in the present reaction and the formation of **14f** was not detected (Entries 3 and 4). These results suggested that the bulkiness around the gold catalyst and the strong σ-donation of the NHC ligand were crucial for this reaction of internal alkyne.[18] The olefin moiety of **14f** was confirmed to be *E* isomer by NOESY analysis.

Table 8. Screening of reaction conditions for internal alkyne **13f**

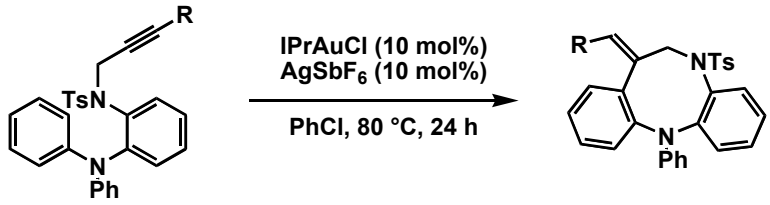


13f 14f

Entry	L	Isolated yield /%
1	PPh_3	trace
2	^{t}BuXPHOS	8
3	IPr	94
4	IMes	N.D.
5	SIMes	N.D.
6	SIPr	88
7	IPr^{Me}	71

Under the optimized conditions of Entry 3 in Table 8, various internal alkynes were subjected to the cycloisomerization (Table 9). Anisyl-substituted alkynes **13g-13i** were not completely consumed and the yields of cycloadducts **14g-14i** were moderate (Entries 1-3).[19] In contrast, electron-withdrawing group-substituted arylalkynes **13j-13l** were completely consumed and the desired products **14j-14l** were obtained in high yields (Entries 4-6). Ethoxycarbonyl-substituted alkyne **13m** was the best substrate and gave cycloadduct **14m** in 98% (Entry 7).

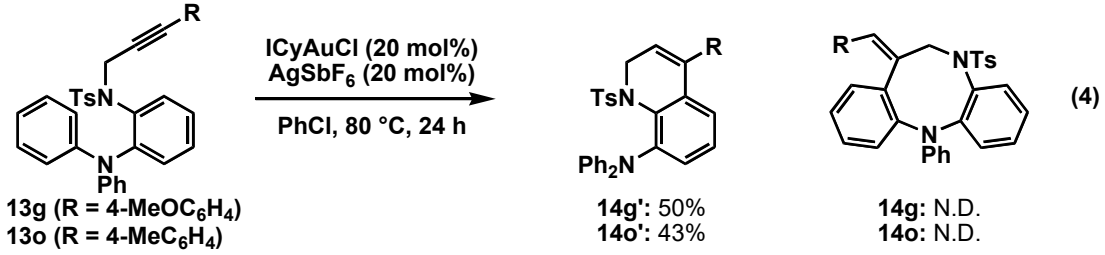
Table 9. Substrate scope for internal alkynes



Entry	R	Yield /%
1	4-$MeOC_6H_4$ (**13g**)	41 (**14g**)
2	3-$MeOC_6H_4$ (**13h**)	53 (**14h**)
3	2-$MeOC_6H_4$ (**13i**)	50 (**14i**)
4	4-$CF_3C_6H_4$ (**13j**)	85 (**14j**)
5	4-FC_6H_4 (**13k**)	87 (**14k**)
6	4-ClC_6H_4 (**13l**)	93 (**14l**)
7	CO_2Et (**13m**)	98 (**14m**)

During the screening of NHC ligands, ICy ligand showed different regioselectivity (Scheme 19). In the reactions of electron-donating group-substituted arylalkynes **13g** and **13o**, 6-*endo-dig* products **14g'** and **14o'** were selectively obtained in moderate yields and 8-*exo-dig* products **14g** and **14o** were not be detected. In Entry 1 of Table 9, 6-*endo-dig* product **14g'** was obtained as a by-product.[19] The author considered that the combination of electron-donating group-substituted arene and less bulky ligand changed the regioselectivity.

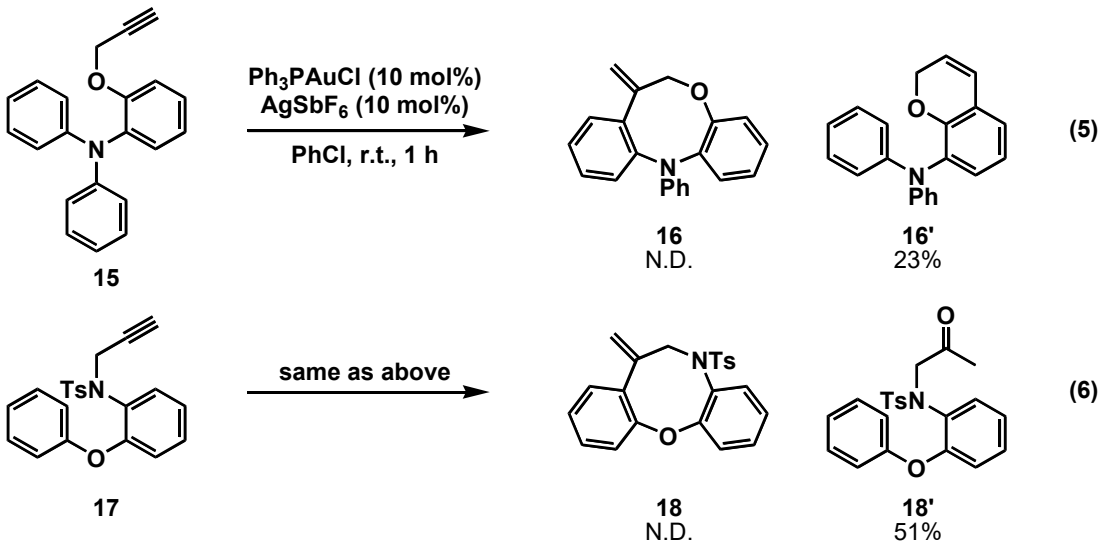
Scheme 19. Undesired 6-*endo-dig* cyclization for the internal alkynes



To investigate the effect of nitrogen atoms for this selective transformation, the author examined the reactions of *o*-aminophenol-tethered substrates **15** and **17** (Scheme 20). In the case of propargyl ether-containing substrate **15**, the reaction proceeded in selective 6-*endo-dig* fashion to give **16'** in low yield without formation of 8-*exo-dig* product **16** [Equation (5)]. These results indicated that the propargyl moiety and the diphenylamino group could be readily accessible because of the steric repulsion between the tosyl and diphenylamino groups (Figure 5). Moreover, the electron-withdrawing effect of the tosyl group decreased the nucleophilicity of its *ortho* position and

6-*endo-dig* cycloisomerization hardly proceeded. On the other hand, the reaction of phenoxy-substituted substrate **17** did not provide any cycloadducts, but gave hydration product **18'** [Equation (6)]. This result suggested that the arene moiety was hardly accessible to the alkyne moiety due to the flexible phenoxy group (Figure 6). In addition, tosyl and phenoxy groups acted as electron-withdrawing ones to lower the nucleophilicity for 6-*endo-dig* cycloisomerization.

Scheme 20. Effect of heteroatom-tether



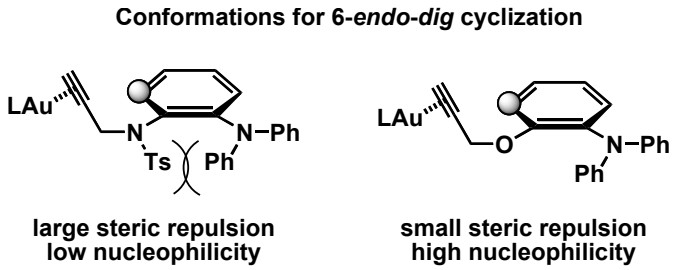


Figure 5. Effect of propargylamino group

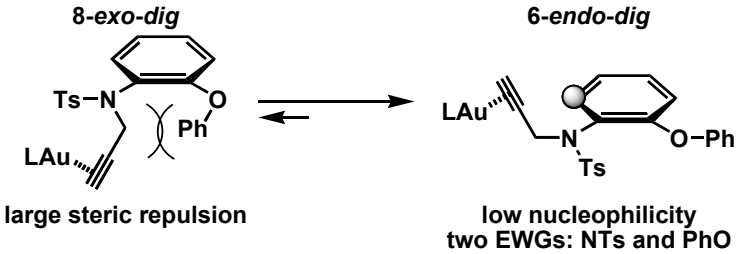


Figure 6. Explanation of low reactivity of phenoxy-containing substrate

6-*Endo-dig*-selective cycloisomerization was observed in the reaction of electron-donating group-substituted alkynes with less bulky NHC ligand (see, Scheme 18). The author speculated the

reason for this selectivity as follows (Figure 7). First, the electron-donating group at alkyne terminus stabilized more the proximal partial positive charge in the transition state for 6-*endo-dig* cycloisomerization than distal one in the transition state for 8-*exo-dig* cycloisomerization (Figure 7a). Second, the use of bulky NHC ligand (IPr) induced propargyl moiety to approach diphenylamine group by the steric repulsion between tosyl group and gold catalyst coordinated to alkyne (Figure 7b).

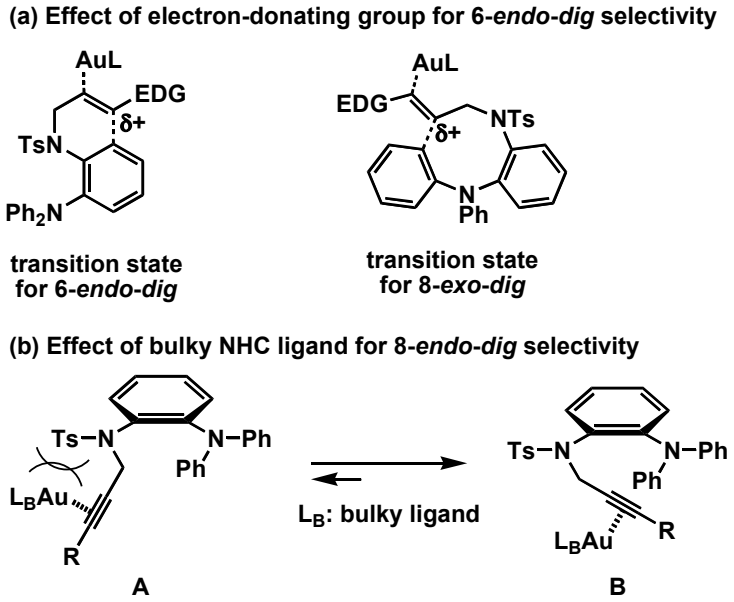


Figure 7. Explanation of selectivity of the reaction of internal alkyne

Conclusion

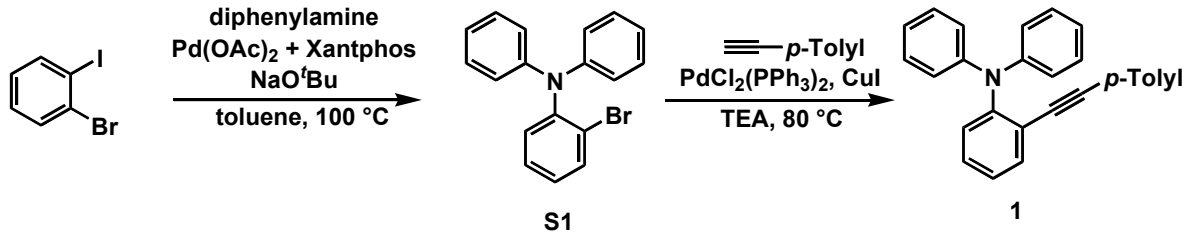
The author developed gold(I)-catalyzed 7-*endo-dig*- and 8-*exo-dig*-selective cycloisomerizations for the synthesis of dibenzazepines and dibenzodiazocines. The 7-*endo-dig*-selective cycloisomerization proceeded when 2-(1-alkynyl)diphenylamine derivatives were used as substrates. The flexibility around the nitrogen atom affected the reactivity, which meant more rigid structure exhibited higher reactivity. The author speculated the reason as follows. The fixed structure led to the lone pair of nitrogen atom and reactive aromatic ring aligned in the same plane and increased the nucleophilicity by resonance effect. In addition, the use of indoline moiety increased the nucleophilicity compared to carbazole-derived substrate by eletron-donating effect of alkyl group. The 8-*exo-dig*-selective cycloisomerization was achieved by using 2-propargylaminotriphenylamine derivatives as substrates. *ortho*-Diaminobenzene tether was important for the selective cycloisomerization. The steric repulsion between *N*-tosyl group and diphenylamine group might make the substrate conformation such that the propargyl moiety is only accessible from the reaction site 8-*exo-dig* cyclization. The electron-withdrawing effect of Ts group might also make the

6-*endo*-*dig*-selective reaction site less nucleophilic. For the reaction of internal alkynes, the use of IPr as a ligand and electron-withdrawing substituents on alkyne terminus were crucial for the 8-*exo*-*dig* selective cycloisomerization. The use of less bulky NHC ligand (ICy) and electron-donating group on alkyne terminus promoted 6-*endo*-*dig*-selective cycloisomerization. The author speculated that the bulky NHC ligand (IPr) caused steric repulsion with tosyl group to induce the propargyl moiety approaching diphenylamine group and electron-donating group on alkyne terminus made the transition state of 6-*endo*-*dig* cycloisomerization more stable than that of 8-*exo*-*dig*.

Experimental Section

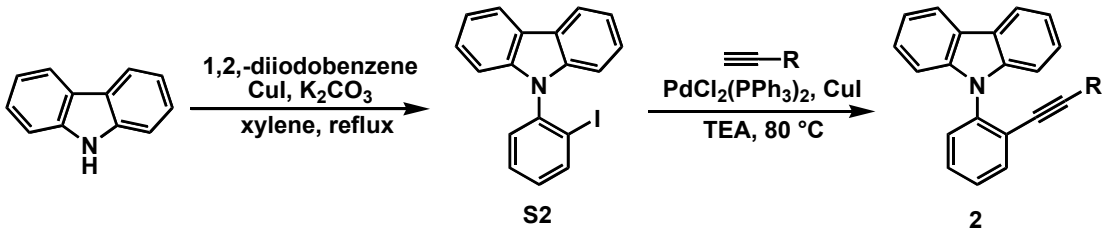
General information: ^{1}H NMR spectra were recorded on JEOL ECX-500 (500 MHz) spectrometers. The chemical shifts were reported in parts per million (δ) relative to internal standard TMS (0 ppm) for $CDCl_3$. The peak patterns are indicated as follows: s, singlet; d, doublet; dd, doublet of doublets; t, triplet; td, triplet of doublets; m, multiplet; q, quartet. The coupling constants, *J*, are reported in Hertz (Hz). ^{13}C NMR spectra were obtained by JEOL ECX-500 (125 MHz) spectrometers and referenced to the internal solvent signals (central peak is 77.16 ppm in $CDCl_3$). $CDCl_3$ was used as a NMR solvent. High-resolution mass spectra (HRMS) were measured on a JMS-T100CS with ESI (Electro Spray Ionization) method. Preparative thin-layer chromatography (PTLC) was performed with silica gel-precoated glass plates (Wakogel B-5F) prepared in our laboratory, Flash silica gel column chromatography was performed over silica gel 200-300. All reagents were weighed and handled in air and backfilled under argon at room temperature. Unless otherwise noted, all reactions were performed under an argon atmosphere. All reagents were purchased from Wako, Kanto, Aldrich, TCI and Strem and used without further purification. Compounds **2h**[20], **S1**[21] and **S2**[22] are known. 4-methoxy-9*H*-carbazole, 7*H*-benzo[*c*]carbazole, 11*H*-benzo[*a*]carbazole, and 1-bromo-2-[2-(4-methylphenyl)ethynyl]benzene were synthesized by reported protocol.[23-26]

Synthetic schemes of substrates in 2.1.1.



Preparation of 2-(4-methylphenyl)ethynyl-*N*,*N*,-diphenyl-benzenamine (1):

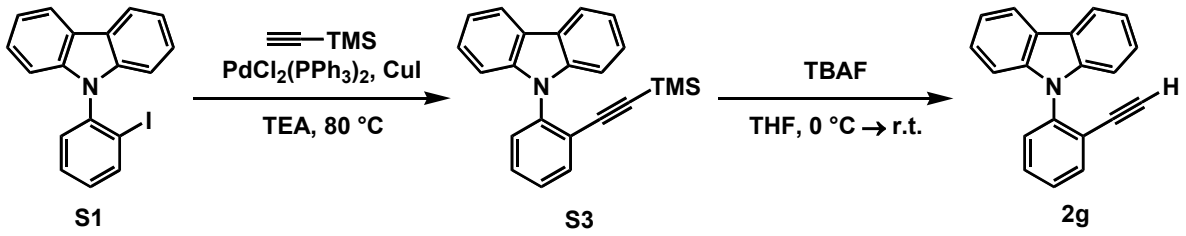
A dry Schlenk tube was charged 1-bromo-2-iodobenzene (1.0 mmol), $Pd(OAc)_2$ (0.030 mmol), Xantphos (0.050 mmol), NaO^{t}Bu (1.5 mmol), diphenylamine (1.2 mmol) and toluene (1.4 mL). The solution was stirred at 110 °C (bath temperature) for 1 h. After cooling, it was filtered by silica gel and the solvents were removed. Then the residue was purified by flash silica gel column chromatography on silica gel (hexane/EtOAc = 92/8) to give **S1**, 74%.[26] The next step was the same as the second step of following synthesis of **2**.



Preparation of 9-(2-alkynylphenyl)-9*H*-carbazole derivatives (2):

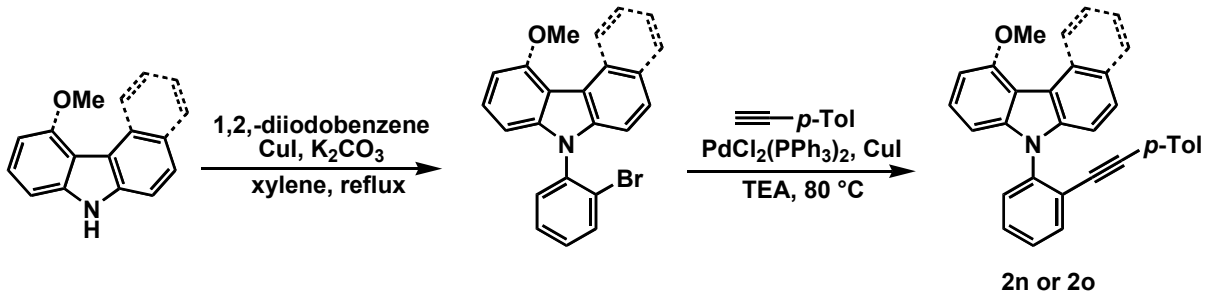
A 50 mL dry two-necked pear-shaped flask equipped with a rubber septum, Allihn condenser and argon balloon was charged with carbazole or derivatives (5.5 mmol), CuI (3.5 mmol), K_2CO_3 (9.0 mmol) and xylene (12.0 mL). The solution was stirred at room temperature, and 1,2,-diiodobenzene (6.0 mmol) was added. The reaction mixture was stirred at 150 °C for 72 h. The solution was cooled to room temperature, 1N HCl (10 mL) was added. The aqueous layer was extracted with DCM, and the organic extract was dried over Na_2SO_4, filtered, and evaporated under reduced pressure. After removal of solvent, it was purified by flash silica gel column chromatography (hexane/DCM = 9/1) and compound **S2** was obtained, 61%.[27]

A dry Schlenk tube was charged compound S1 (0.25 mmol), $PdCl_2(PPh_3)_2$ (0.020 mmol), CuI (**1** 0.023 mmol) and distilled Et_3N (TEA, 0.50 mL) and stirred at room temperature. Alkynes (0.50 mmol) was added to the reaction vessel. The solution was then stirred at 80 °C (bath temperature) for 16 h. After cooling, the solvents were removed, and the residue was purified by flash silica gel column chromatography on silica gel (hexane/DCM = 9/1) to give **2**.[28]



Preparation of 9-(2-((trimethylsilyl)ethynyl)phenyl)-9*H*-carbazole (2g):

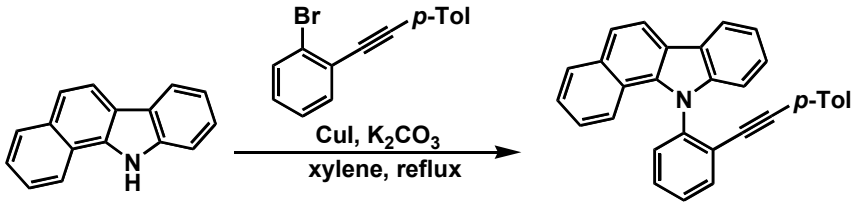
First step was the same as the synthesis protocol of **2**, to give **S2**, and the second step was examined without complete purification. A dry Schlenk tube was charged compound **S2** (0.40 mmol) and THF 1.5 mL and stirred at 0 ℃. 1 M TBAF in THF (0.8 mL) was added to the reaction mixture, and it was stirred at room temperature. After 1 h, sat.NH_4Cl 2.0 mL was added and extracted by EtOAc (5.0 mL×3). The organic layer was washed H_2O and brine, and dried over Na_2SO_4. After removal of solvent, it was purified by column chromatography on silica gel (hexane/DCM = 9/1) to give **2g**, 72%.[28]



2n or 2o

Preparation of 9-(2-iodophenyl)-9*H*-carbazole derivatives (2n, 2o):

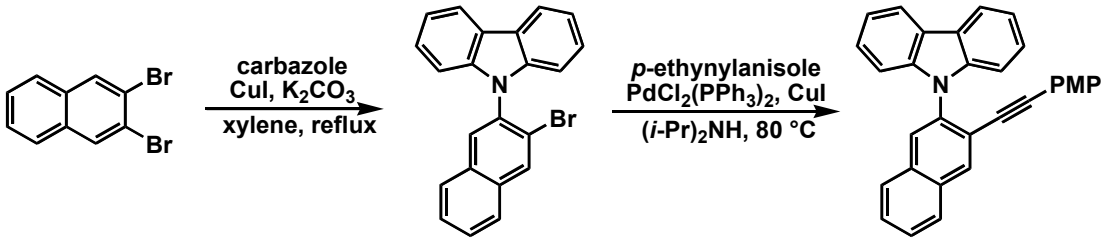
The reaction was the same as the synthesis protocol of **2** using 4-methoxy-9*H*-carbazole or 7*H*-benzo[*c*]carbazole instead of carbazole. The second step was examined without purification.



2p

Preparation of benzo[1,2]-9-(2-((4-methylphenyl)ethynyl)phenyl)-11*H*-carbazole (2p):

The reaction was the same as the first step of synthesis protocol of **2** using 11*H*-benzo[*a*]carbazole and 1-bromo-2-[2-(4-methylphenyl)ethynyl]-benzene.



2q

Preparation of 9-(2-(3-(4-methoxyphenyl)ethynyl)naphthalenyl)-9*H*-carbazole (2q):

The reaction was the same as the synthesis protocol of **2** by using 2,3,-dibromonaphthalene instead of 1,2,-diiodobenzene. The second step was examined without purification, and $(i\text{-Pr})_2NH$ was used as the solvent instead of TEA.

General procedure for cycloisomerization in Tables 2 and Table 4:

Table 2: Ph_3PAuCl (0.0050 mmol), $AgSbF_6$ (0.0050 mmol), and 9-(2-ethynylphenyl)-9*H*-carbazole derivatives **2** (0.050 mmol) were placed in a Schlenk tube, which was then evacuated and back-filled with argon (×3). To the reaction vessel was added anhydrous DCE (0.50 mL). The solution was then stirred at 80 °C (bath temperature). The reaction mixture was cooled to room temperature

and the solvent was evaporated. The obtained crude product was purified by PTLC to give products **3**.

Table 4: $(C_6F_5)_3PAuCl$ (0.0050 mmol), AgOTf (0.0050 mmol), and 9-(2-ethynylphenyl)-9*H*-carbazole derivatives **2** (0.050 mmol) were placed in a Schlenk tube, which was then evacuated and backfilled with argon (×3). To the reaction vessel was added anhydrous DCE (0.50 mL). The solution was then stirred at room temperature. After removal of solvent, the crude product was purified by PTLC to give products **3**.

Characterization data for new compounds in 2.1.1.

2-(4-Methylphenyl)ethynyl-*N*,*N*,-diphenylbenzenamine (1)

Isolated by PTLC (hexane/DCM = 8/1 x2). The title compound was obtained as a pale yellow solid, 20%; mp 79 °C; ^{1}H NMR δ 7.55-7.51 (m, 1H), 7.29-7.24 (m, 1H, overlapped with $CHCl_3$), 7.24-7.19 (m, 4H), 7.16-7.11 (m, 2H), 7.06-7.03 (m, 4H), 7.02-6.98 (m, 2H), 6.97-6.92 (m, 4H), 2.29 (s, 3H); ^{13}C NMR δ 148.5, 147.9, 138.2, 134.2, 131.6, 129.5, 129.1, 128.9, 128.9, 124.9, 123.0, 122.1, 122.1, 120.3, 95.4, 86.8, 21.6; HRMS (DART, positive): m/z calcd. for $C_{27}H_{22}N$ $[M + H]^+$ 360.1746, found 360.1747.

9-(2-((4-Methylphenyl)ethynyl)phenyl)-9*H*-carbazole (2a)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as a white solid, 77%; mp 107 °C; ^{1}H NMR δ 8.16 (dd, J = 7.4, 1.3 Hz, 2H), 7.76 (dd, J = 7.7, 1.6 Hz, 1H), 7.59-7.51 (m, 2H), 7.48 (ddd, J = 7.4, 7.4, 1.6 Hz, 1H), 7.40-7.35 (m, 2H), 7.27 (dd, J = 7.4, 7.4 Hz, 4H), 6.86 (d, J = 8.0 Hz, 2H), 6.49 (d, J = 8.3 Hz, 2H), 2.20 (s, 3H); ^{13}C NMR δ 140.9, 138.9, 138.4, 133.3, 131.2, 129.2, 129.0, 128.7, 128.0, 125.7, 123.3, 123.2, 120.1, 119.7, 119.4, 110.6, 95.7, 85.5, 21.4; HRMS (DART, positive): m/z calcd. for $C_{27}H_{20}N$ $[M + H]^+$ 358.1591, found 358.1590.

9-(2-((2-Methylphenyl)ethynyl)phenyl)-9*H*-carbazole (2b)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as a white solid, 86%; mp 125-126 °C; ^{1}H NMR δ 8.14 (d, J = 7.8 Hz, 2H), 7.83-7.79 (m, 1H), 7.56-7.48 (m, 3H), 7.39-7.35 (m, 2H), 7.28-7.21 (m, 4H, overlapped with $CHCl_3$), 7.02 (dd, J = 7.8, 7.8 Hz, 1H), 6.90 (dd, J = 7.5, 7.5 Hz, 2H), 6.73 (d, J = 7.7 Hz, 1H), 1.58 (s, 3H); ^{13}C NMR δ 141.1, 140.2, 138.6, 133.7, 131.9, 129.4, 129.2, 128.3, 128.2, 125.8, 125.2, 123.7, 123.4, 122.3, 120.1, 119.7, 110.4, 110.6, 93.8, 89.6, 19.5; HRMS (DART, positive): m/z calcd. for $C_{27}H_{20}N$ $[M + H]^+$ 358.1591, found 358.1590.

9-(2-((4-Methoxylphenyl)ethynyl)phenyl)-9*H*-carbazole (2c)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as a white solid, 88%; mp 82 °C; ^{1}H NMR δ 8.16 (dd, *J* = 7.5, 1.3 Hz, 2H), 7.74 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.59-7.50 (m, 2H), 7.50-7.46 (m, 1H), 7.38 (ddd, *J* = 7.6, 7.6, 1.3 Hz, 2H), 7.28 (dd, *J* = 7.6, 7.6 Hz, 4H), 6.58 (d, *J* = 9.0 Hz, 2H), 6.52 (d, *J* = 9.0 Hz, 2H), 3.69 (s, 3H); ^{13}C NMR δ 159.6, 140.9, 138.7, 133.1, 132.8, 128.9, 128.0, 125.7, 123.3, 123.3, 120.1, 119.7, 114.6, 114.2, 113.6, 110.6, 95.6, 84.9, 55.1; HRMS (DART, positive): m/z calcd. for $C_{27}H_{19}NNaO$ $[M + Na]^+$ 396.1360, found 396.1359.

9-(2-((1-naphthyl)ethynyl)phenyl)-9*H*-carbazole (2d)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as a white solid, 87%; mp 149 °C; ^{1}H NMR δ 8.21 (d, *J* = 7.8 Hz, 2H), 7.91 (d, *J* = 7.2 Hz, 1H), 7.63 (dd, *J* = 8.2, 2.6 Hz, 2H), 7.58-7.52 (m, 3H), 7.38 (dd, *J* = 7.1, 7.1 Hz, 2H), 7.34-7.26 (m, 5H), 7.21 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.12-7.05 (m, 2H), 6.95 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR δ 141.2, 138.7, 133.9, 132.8, 130.5, 129.6, 129.3, 128.8, 128.3, 127.8, 126.6, 126.1, 125.9, 125.8, 124.9, 123.6, 123.4, 120.2, 119.9, 110.4, 93.1, 90.6 (two pairs of peaks at the aromatic region were over-lapped); HRMS (DART, positive): m/z calcd. for $C_{30}H_{20}N$ $[M + H]^+$ 394.1591, found 394.1591.

9-(2-((3-Thienyl)ethynyl)phenyl)-9*H*-carbazole (2e)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as a brown solid, 77%; mp 109 °C; ^{1}H NMR δ 8.16 (d, *J* = 7.9 Hz, 2H), 7.74 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.61-7.52 (m, 2H), 7.49 (ddd, *J* = 7.5, 7.5, 1.4 Hz, 1H), 7.42-7.36 (m, 2H), 7.32-7.25 (m, 4H), 7.00 (dd, *J* = 4.9, 3.0 Hz, 1H), 6.63 (dd, *J* = 2.8, 1.1 Hz, 1H), 6.32 (dd, *J* = 4.9, 1.1 Hz, 1H); ^{13}C NMR δ 140.9, 139.0, 133.0, 129.3, 129.2, 129.0, 128.9, 128.0, 125.7, 124.9, 123.3, 123.0, 121.6, 120.1, 119.8, 110.6, 90.8, 85.7; HRMS (DART, positive): m/z calcd. for $C_{24}H_{16}NS$ $[M + H]^+$ 350.0999, found 350.0998.

9-(2-((2-Thienyl)ethynyl)phenyl)-9*H*-carbazole (2f)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as a brown solid, 75%; mp 123-124 °C; ^{1}H NMR δ 8.16 (d, *J* = 7.8 Hz, 2H), 7.74 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.60-7.52 (m, 2H), 7.48 (ddd, *J* = 7.5, 7.5, 1.5 Hz, 1H), 7.42-7.35 (m, 2H), 7.31-7.24 (m, 4H), 7.06 (dd, *J* = 5.1, 1.1 Hz, 1H), 6.73 (dd, *J* = 5.1, 3.8 Hz, 1H), 6.42 (dd, *J* = 3.8, 1.1 Hz, 1H); ^{13}C NMR δ 140.9, 138.8, 132.9, 132.1, 129.4, 129.0, 128.0, 127.7, 126.8, 125.7, 123.4, 122.7, 122.4, 120.2, 119.8, 110.5, 89.8, 88.8; HRMS (DART, positive): m/z calcd. for $C_{24}H_{16}NS$ $[M + H]^+$ 350.0999, found 350.0998.

9-(2-Ethynylphenyl)-9*H*-carbazole (2g)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as a white solid, 66% (2 steps); mp 64 °C; ^{1}H NMR δ 8.14 (d, *J* = 7.8 Hz, 2H), 7.78 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.56 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1H), 7.51-7.46 (m, 2H), 7.42-7.37 (m, 2H), 7.28 (dd, *J* = 7.4, 7.4 Hz, 2H), 7.19 (d, *J* = 8.2 Hz, 2H), 2.79 (s, 1H); ^{13}C NMR δ 141.2, 139.8, 134.6, 130.3, 129.3, 128.3, 125.8, 123.5, 122.4, 120.3, 120.0, 110.5, 82.8, 79.9; HRMS (DART, positive): m/z calcd. for $C_{20}H_{14}N$ $[M + H]^+$ 268.1121, found 268.1121.

9-(2-((3-Methylphenyl)ethynyl)phenyl)-9*H*-carbazole (2i)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as a white solid, 86%; mp 106 °C; ^{1}H NMR δ 8.17 (d, *J* = 7.8 Hz, 2H), 7.76 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.61-7.52 (m, 2H), 7.49 (ddd, *J* = 7.6, 7.6, 1.5 Hz, 1H), 7.41-7.35 (m, 2H), 7.31-7.25 (m, 4H), 6.97-6.91 (m, 2H), 6.49-6.44 (m, 1H), 6.28 (s, 1H), 3.69 (s, 3H); ^{13}C NMR δ 141.1, 139.2, 137.7, 133.4, 132.2, 129.4, 129.3, 129.1, 128.3, 128.2, 127.9, 125.9, 123.5, 123.3, 122.4, 120.3, 119.9, 110.7, 95.9, 85.9, 21.2; HRMS (DART, positive): m/z calcd. for $C_{27}H_{20}N$ $[M + H]^+$ 358.1590, found 358.1590.

9-(2-((3-Methoxylphenyl)ethynyl)phenyl)-9*H*-carbazole (2j)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as a white solid, 63%; mp 78 °C; ^{1}H NMR δ 8.15 (d, *J* = 7.5 Hz, 2H), 7.77 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.60-7.53 (m, 2H), 7.50 (ddd, *J* = 7.4, 7.4, 1.6 Hz, 1H), 7.42-7.36 (m, 2H), 7.30-7.25 (m, 4H), 6.97 (dd, *J* = 8.0, 8.0 Hz, 1H), 6.70-6.66 (m, 1H), 6.35 (d, *J* = 7.7 Hz, 1H), 5.99 (dd, *J* = 2.1, 1.1 Hz, 1H), 3.59 (s, 3H); ^{13}C NMR δ 159.1, 141.1, 139.2, 133.5, 129.6, 129.1, 128.2, 125.9, 125.9, 123.8, 123.6, 123.4, 123.1, 120.2, 119.9, 115.9, 115.4, 110.7, 95.5, 85.9, 55.4; HRMS (DART, positive): m/z calcd. for $C_{27}H_{20}NO$ $[M + H]^+$ 374.1540, found 374.1539.

9-(2-((4-Biphenyl)ethynyl)phenyl)-9*H*-carbazole (2k)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as a white solid, 65%; mp 133-134 °C; ^{1}H NMR δ 8.18 (d, *J* = 7.1 Hz, 2H), 7.79 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.62-7.54 (m, 2H), 7.50 (ddd, *J* = 7.4, 7.4, 1.6 Hz, 1H), 7.48-7.44 (m, 2H), 7.42-7.35 (m, 4H), 7.32-7.27 (m, 7H), 6.65 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR δ 141.1, 140.4, 139.2, 133.5, 131.8, 129.5, 129.2, 128.9, 128.2, 127.7, 127.1, 126.8, 125.9, 123.5, 123.2, 121.5, 120.3, 119.9, 110.7, 95.5, 86.9 (a pair of peaks at the aromatic region was overlapped); HRMS (DART, positive): m/z calcd. for $C_{32}H_{22}N$ $[M + H]^+$ 420.1745, found 420.1747.

9-(2-((4-Chlorophenyl)ethynyl)phenyl)-9*H*-carbazole (2l)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as yellow oil, 87%; ^{1}H NMR δ 8.17 (d, *J* = 7.8 Hz, 2H), 7.76 (d, *J* = 7.7 Hz, 1H), 7.63-7.55 (m, 2H), 7.51 (ddd, *J* = 7.3, 7.3, 1.6 Hz, 1H), 7.41-7.36 (m, 2H), 7.32-7.22 (m, 4H, overlapped with $CHCl_3$), 7.03 (dd, *J* = 8.4, 1.4 Hz, 2H), 6.52-6.44 (m, 2H); ^{13}C NMR δ 141.0, 139.3, 134.4 133.4, 132.6, 129.8, 129.2, 128.4, 128.2, 125.9, 123.5, 122.8, 121.1, 120.3, 120.0, 110.7, 94.4, 87.1; HRMS (DART, positive): m/z calcd. for $C_{26}H_{17}ClN$ $[M + H]^+$ 378.1045, found 378.1044.

9-(2-((4-Trifluoromethylphenyl)ethynyl)phenyl)-9*H*-carbazole (2m)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as yellow oil, 89%; ^{1}H NMR δ 8.17 (d, *J* = 7.7 Hz, 2H), 7.78 (d, *J* = 7.4 Hz, 1H), 7.64-7.57 (m, 2H), 7.52 (ddd, *J* = 7.6, 7.6, 2.0 Hz, 1H), 7.41-7.36 (m, 2H), 7.33-7.25 (m, 6H), 6.64 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR δ 141.0, 139.5, 133.6, 131.5, 130.2, 130.1, 129.8, 129.3, 128.3, 126.4, 125.9, 125.0 (q, $J_{C\text{-}F}$ = 3.8 Hz, 1C), 123.5, 122.5, 120.4, 120.1, 110.6, 94.0, 88.4; HRMS (DART, positive): m/z calcd. for $C_{27}H_{17}F_3N$ $[M + H]^+$ 412.1308, found 412.1308.

9-(2-((4-Methylphenyl)ethynyl)phenyl)-4-methoxy-9*H*-carbazole (2n)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as a brown solid, 58% (2 steps); mp 40 °C; ^{1}H NMR δ 8.41 (d, *J* = 7.7 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.56-7.43 (m, 3H), 7.36-7.21 (m, 4H), 6.90-6.84 (m, 3H), 6.72 (d, *J* = 7.9 Hz, 1H), 6.53 (d, *J* = 7.8 Hz, 2H), 4.11 (s, 3H), 2.20 (s, 3H); ^{13}C NMR δ 156.4, 142.5, 140.3 139.2, 138.5, 133.3, 131.3, 129.2, 129.2, 128.8, 128.1, 126.5, 124.9, 123.4, 123.1, 122.8, 120.0, 119.6, 112.7, 110.2, 103.6, 101.0, 95.7, 85.6, 55.7, 21.5; HRMS (DART, positive): m/z calcd. for $C_{28}H_{22}NO$ $[M + H]^+$ 388.1696, found 388.1696.

Benzo[3,4]-9-(2-((4-methylphenyl)ethynyl)phenyl)-7*H*-carbazole (2o)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as a white solid, 13% (2 steps); mp 74-75 °C; ^{1}H NMR δ 8.88 (d, *J* = 8.4 Hz, 1H), 8.68-8.63 (m, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.83-7.71 (m, 3H), 7.62-7.52 (m, 3H), 7.51-7.35 (m, 5H), 6.75 (d, *J* = 8.1 Hz, 2H), 6.42 (d, *J* = 8.1 Hz, 2H), 2.15 (s, 3H); ^{13}C NMR δ 140.3, 138.9, 138.8, 138.6, 133.4, 131.2, 130.1, 129.6, 129.5, 129.3, 129.3, 128.8, 128.5, 127.2, 126.9, 124.4, 124.1, 123.8, 123.5, 123.1, 122.1, 120.7, 119.3, 115.6, 112.5, 111.2, 95.7, 85.3, 21.5; HRMS (DART, positive): m/z calcd. for $C_{31}H_{22}N$ $[M + H]^+$ 408.1748, found 408.1747.

Benzo[1,2]-9-(2-((4-methylphenyl)ethynyl)phenyl)-11*H*-carbazole (2p)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as a white solid 12%; mp 125 °C; ^{1}H NMR δ 8.24 (d, *J* = 8.5 Hz, 1H), 8.19 (d, *J* = 7.7 Hz, 1H), 7.94 (d, *J* = 8.2 Hz, 1H), 7.80-7.75 (m, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.65-7.54 (m, 3H), 7.43 (d, *J* = 8.5 Hz, 1H), 7.40-7.28 (m, 3H), 7.23-7.15 (m, 2H), 6.77 (d, *J* = 8.0 Hz, 2H), 6.36 (d, *J* = 8.0 Hz, 2H), 2.13 (s, 3H); ^{13}C NMR δ 141.7, 141.7, 138.5, 135.9, 133.5, 133.2, 131.3, 130.0, 129.5, 129.2, 129.1, 128.8, 125.3, 125.1, 124.9, 124.8, 123.8, 122.6, 122.0, 121.3, 120.5, 119.7, 119.6, 119.4, 119.3, 110.8, 95.3, 84.7, 21.5; HRMS (DART, positive): m/z calcd. for $C_{31}H_{22}N$ $[M + H]^+$ 408.1748, found 408.1747.

9-(3-(4-Methoxyphenyl)ethynylnaphthalen-2-yl)-9*H*-carbazole (2q)

Isolated by flash silica gel column chromatography (hexane/DCM = 9/1). The title compound was obtained as a white solid, 27% (2 steps); mp 164 °C; ^{1}H NMR δ 8.25 (s, 1H), 8.19 (d, *J* = 7.6 Hz, 2H), 8.06 (s, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.63-7.56 (m, 2H), 7.40-7.38 (m, 2H), 7.31-7.27 (m, 4H), 6.59 (d, *J* = 9.0 Hz, 2H), 6.51 (d, *J* = 9.0 Hz, 2H), 3.70 (s, 3H); ^{13}C NMR δ 159.7, 141.7, 135.7, 133.2 133.1, 132.9, 132.8, 128.1, 128.0, 127.8, 127.4, 125.9, 123.4, 121.4, 120.3, 119.9, 114.8, 114.3, 113.8, 110.7, 95.1, 85.3, 55.3; HRMS (DART, positive): m/z calcd. for $C_{31}H_{22}NO$ $[M + H]^+$ 424.1695, found 424.1696.

9-(2-(Pentylethynyl)phenyl)-9*H*-carbazole (2r)

Isolated by flash silica gel column chromatography (hexane/DCM = 17/3). The title compound was obtained in 27% as a colorless oil; ^{1}H-NMR δ 8.12 (dd, *J* = 0.6, 7.7 Hz, 2H), 7.64 (d, *J* = 7.3 Hz, 1H), 7.52-7.32 (m, 5H), 7.30-7.15 (m, 4H, overlapped with $CHCl_3$), 1.87 (t, *J* = 6.8 Hz, 2H), 1.02-0.62 (m, 9H).

Benzo[6,7]-8-(4-methylphenyl)azepino[3,2,1-*jk*]-9*H*-carbazole (3a)

Isolated by PTLC (hexane/DCM = 15/1 x2). The title compound was obtained as a yellow solid, 90%; mp 202-203 °C; ^{1}H NMR δ 7.98 (d, *J* = 7.5 Hz, 1H), 7.80 (d, *J* = 8.3 Hz, 1H), 7.72 (dd, *J* = 7.7, 1.1 Hz 1H), 7.46-7.41 (m, 1H), 7.31 (dd, *J* = 7.2, 7.2 Hz, 2H), 7.21-7.17 (m, 4H), 7.16-7.10 (m, 2H), 7.06-7.02 (m, 2H), 6.75 (dd, *J* = 7.7, 0.8 Hz, 1H), 6.61 (s, 1H), 2.39 (s, 3H); ^{13}C NMR δ 151.4, 143.9, 142.5, 141.8, 140.8, 137.7, 132.1, 131.8, 131.5, 129.6, 129.2, 129.2, 128.3, 128.2, 127.6, 126.8, 125.8, 125.1, 122.8, 122.2, 120.9, 120.7, 119.2, 116.5, 21.5; HRMS (DART, positive): m/z calcd. for $C_{27}H_{20}N$ $[M + H]^+$ 358.1585, found 358.1590. Crystal data of **3a**; $C_{27}H_{19}N$, *M* = 357.45, monoclinic, Space Group $P2_1/n$ (#14), *a* = 9.10081(16) Å, *b* = 11.9738(2) Å, *c* = 16.5272(3) Å, β = 96.3113(10)°, *V* = 1790.07(6) Å^3, *T* = 123.2 K, *Z* = 4, μ(CuKα) = 5.841 cm^{-1}, Number of Reflec-

tions Measures: Total 19243, Unique: 3266 (R*int* = 0.0402), *R1* = 0.0418, *wR2* = 0.1321. CCDC 1495449.

Benzo[6,7]-8-(2-methylphenyl)azepino[3,2,1-*jk*]-9*H*-carbazole (3b)

Isolated by PTLC (hexane/DCM = 15/1). The title compound was obtained as a yellow solid, 75%; mp 172 °C; ^{1}H NMR δ 7.97 (d, *J* = 7.8 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 1H), 7.67 (d, *J* = 7.6 Hz 1H), 7.43 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.36 (d, *J* = 8.3 Hz, 1H), 7.32-7.25 (m, 2H), 7.24-7.19 (m, 3H), 7.18-7.13 (m, 1H), 7.08-7.01 (m, 2H), 6.95 (dd, *J* = 7.6. 7.6 Hz, 1H), 6.46-6.42 (m, 2H), 2.04 (s, 3H); ^{13}C NMR δ 150.3, 143.7, 142.9, 142.0, 141.5, 136.8, 132.1, 131.9, 131.8, 130.4, 130.0, 129.8, 128.1, 127.9, 127.4, 127.2, 126.5, 126.1, 125.8, 125.2, 123.1, 122.1, 121.3, 120.7, 119.2, 116.2, 19.8; HRMS (DART, positive): m/z calcd. for $C_{27}H_{19}N$ $[M]^+$ 357.1512, found 357.1512.

Benzo[6, 7]-8-(4-methoxylphenyl)azepino[3, 2, 1-*jk*]-9*H*-carbazole (3c)

Isolated by PTLC (hexane/DCM = 15/1). The title compound was obtained as a yellow solid, 98%; mp 151 °C; ^{1}H NMR δ 7.98 (d, *J* = 7.7 Hz, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.72 (dd, *J* = 7.7, 1.0 Hz 1H), 7.45-7.41 (m, 1H), 7.33-7.29 (m, 2H), 7.20 (d, *J* = 8.7, 2H), 7.16-7.09 (m, 2H), 7.07-7.02 (m, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 6.76 (d, *J* = 7.6 Hz, 1H), 6.60 (s, 1H), 3.84 (s, 3H) ; ^{13}C NMR δ 159.5, 151.3, 143.6, 142.6, 141.8, 136.1, 132.0, 131.8, 131.3, 130.5, 129.5, 128.3, 128.2, 127.6, 126.8, 125.8, 125.1, 122.8, 122.3, 120.9, 120.7, 119.2, 116.5, 113.9, 55.6; HRMS (DART, positive): m/z calcd. for $C_{27}H_{20}NO$ $[M + H]^+$ 374.1539, found 374.1539.

Benzo[6,7]-8-(1-naphthyl)azepino[3,2,1-*jk*]-9*H*-carbazole (3d)

Isolated by PTLC (hexane/DCM = 15/1). The title compound was obtained as a yellow solid, 92%); mp 204 °C; ^{1}H NMR δ 7.99 (d, *J* = 7.7 Hz, 1H), 7.90-7.82 (m, 3H), 7.78 (d, *J* = 8.3 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.51 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.48-7.37 (m, 4H), 7.36-7.26 (m, 2H), 7.22-7.16 (m, 1H), 7.09-7.01 (m, 1H), 6.82 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.62 (s, 1H), 6.38 (s, 1H); ^{13}C NMR δ 150.1, 142.4, 142.1, 141.6, 141.0, 134.0, 133.3, 132.3 (a pair of peaks was overlapped), 131.8, 130.0, 128.6, 128.4, 128.3, 127.9, 127.5, 127.2, 126.6, 126.4, 126.4, 126.1, 125.8, 125.8, 125.3, 123.1, 122.2, 121.3, 120.8, 119.3, 116.3; HRMS (DART, positive): m/z calcd. for $C_{30}H_{20}N$ $[M + H]^+$ 394.1588, found 394.1590.

Benzo[6,7]-8-(3-thienyl)azepino[3,2,1-*jk*]-9*H*-carbazole (3e)

Isolated by PTLC (hexane/DCM = 15/1). The title compound was obtained as a yellow solid, 86%; mp 73-74 °C; ^{1}H NMR δ 7.98 (d, *J* = 7.9 Hz, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.73 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.46-7.39 (m, 1H), 7.34-7.27 (m, 4H), 7.16-7.02 (m, 4H), 6.98 (dd, *J* = 5.0, 1.2 Hz, 1H),

6.90 (d, *J* = 7.3 Hz, 1H), 6.74 (s, 1H); ^{13}C NMR δ 150.9, 143.9, 142.5, 141.5, 138.6, 131.8, 131.3, 131.1, 129.4, 128.6, 127.5, 127.5, 127.3, 126.6, 125.7, 125.1, 124.9, 123.6, 122.6, 122.1, 120.7, 120.5, 119.2, 116.3; HRMS (DART, positive): m/z calcd. $C_{24}H_{16}NS$ $[M + H]^+$ 350.0999, found 350.0998.

Benzo[6,7]-8-(2-thienyl)azepino[3,2,1-*jk*]-9*H*-carbazole (3f)

Isolated by PTLC (hexane/DCM = 15/1). The title compound was obtained as a yellow solid, 91%; mp 54-55 °C; ^{1}H NMR δ 7.98 (d, *J* = 7.9 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.76 (dd, *J* = 6.5, 2.4 Hz, 1H), 7.45-7.40 (m, 1H), 7.34-7.26 (m, 3H), 7.17-7.08 (m, 4H), 7.07-6.98 (m, 3H), 6.86 (s, 1H); ^{13}C NMR δ151.2, 145.3, 142.9, 141.8, 136.8, 132.3, 132.1, 131.1, 129.8, 127.9, 127.6, 127.3, 127.1, 127.1, 127.0, 125.9, 125.2, 125.1, 122.8, 122.3, 120.7, 120.7, 119.6, 116.5; HRMS (DART, positive): m/z calcd. for $C_{24}H_{16}NS$ $[M + H]^+$ 350.0997, found 350.0998.

Benzo[6,7]azepino[3,2,1-*jk*]-9*H*-carbazole (3g)

Isolated by PTLC (hexane/DCM = 15/1). The title compound was obtained as a yellow solid, 81%; mp 109 °C; ^{1}H NMR δ 7.95-7.93 (m, 1H), 7.77 (dd, *J* = 8.3 Hz, 1H), 7.64 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.42-7.36 (m, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.26 (ddd, *J* = 7.4, 7.4, 1.3 Hz, 1H, overlapped with $CHCl_3$), 7.17-7.12 (m, 1H), 7.05 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.02-6.95 (m, 2H), 6.87 (d, *J* = 7.3 Hz, 1H), 6.33-6.24 (m, 2H); ^{13}C NMR δ 149.4, 141.5, 140.9, 132.4, 132.2, 132.0, 131.7, 130.0, 127.0, 126.9, 126.7, 126.1, 125.6, 125.2, 122.9, 121.9, 121.6, 120.5, 119.0, 115.5; HRMS (DART, positive): m/z calcd. for $C_{20}H_{14}N$ $[M + H]^+$ 268.1122, found 268.1121.

Benzo[6,7]-8-phenylazepino[3,2,1-*jk*]-9*H*-carbazole (3h)

Isolated by PTLC (hexane/DCM = 15/1). The title compound was obtained as a yellow solid, 99%; mp 102 °C; ^{1}H NMR δ 7.98 (d, *J* = 7.6 Hz, 1H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.72 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.47-7.40 (m, 1H), 7.40-7.33 (m, 3H), 7.33-7.26 (m, 4H), 7.18-7.11 (m, 2H), 7.08-7.01 (m, 2H), 6.72 (dd, *J* = 7.6, 0.9 Hz, 1H), 6.61 (s, 1H); ^{13}C NMR δ 151.1, 143.8, 143.4, 142.3, 141.5, 131.9, 131.7, 131.5, 129.5, 129.1, 128.3, 128.0, 127.9, 127.7, 127.3, 126.6, 125.6, 124.9, 122.6, 122.0, 120.8, 120.0, 119.1, 116.2; HRMS (DART, positive): m/z calcd. for $C_{26}H_{18}N$ $[M + H]^+$ 344.1433, found 344.1434.

Benzo[6,7]-8-(3-methylphenyl)azepino[3,2,1-*jk*]-9*H*-carbazole (3i)

Isolated by PTLC (hexane/DCM = 15/1). The title compound was obtained as a yellow solid, 86%; mp 106 °C; ^{1}H NMR δ 7.98 (d, *J* = 7.9 Hz, 1H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.72 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.45-7.40 (m, 1H), 7.31 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.27-7.23 (m, 1H, overlapped with $CHCl_3$),

7.18-7.09 (m, 4H), 7.08-7.01 (m, 3H), 6.73 (dd, *J* = 7.7, 1.0 Hz, 1H), 6.60 (s, 1H), 2.36 (s, 3H); ^{13}C NMR δ 151.2, 140.0, 143.5, 142.4, 141.6, 138.0, 132.0, 131.7, 131.6, 129.9, 129.5, 128.5, 128.3, 128.2, 128.1, 127.5, 126.7, 126.4, 125.7, 125.1, 122.7, 122.2, 120.9, 120.6, 119.1, 116.4, 21.6; HRMS (DART, positive): m/z calcd. for $C_{27}H_{19}N$ $[M + H]^+$ 358.1590, found 358.1590.

Benzo[6,7]-8-(3-methoxylphenyl)azepino[3,2,1-*jk*]-9*H*-carbazole (3j)

Isolated by PTLC (hexane/DCM = 15/1). The title compound was obtained as a yellow solid, 93%; mp 146 °C; ^{1}H NMR δ 7.98 (d, *J* = 7.7 Hz, 1H), 7.80 (d, *J* = 8.5 Hz, 1H), 7.71 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.45-7.40 (m, 1H), 7.33-7.26 (m, 3H), 7.17-7.10 (m, 2H), 7.07-7.01 (m, 2H), 6.88 (dd, *J* = 7.6, 7.6 Hz, 2H), 6.83 (dd, *J* = 2.4, 2.3 Hz, 1H), 6.75 (dd, *J* = 7.4, 0.9 Hz, 1H), 6.62 (s, 1H), 3.79 (s, 3H); ^{13}C NMR δ 159.5, 151.1, 144.9, 143.6, 142.3, 141.5, 131.9, 131.6, 131.4, 129.5, 129.2, 128.0, 127.7, 127.3, 126.6, 125.6, 124.9, 122.6, 122.0, 121.6, 120.8, 120.5, 119.1, 116.2, 114.7, 113.2, 55.3; HRMS (DART, positive): m/z calcd. for $C_{27}H_{20}NO$ $[M + H]^+$ 374.1540, found 374.1539.

Benzo[6,7]-8-(4-biphenyl)azepino[3,2,1-*jk*]-9*H*-carbazole (3k)

Isolated by PTLC (hexane/DCM = 15/1). The title compound was obtained as a yellow solid, 98%; mp 167-168 °C; ^{1}H NMR δ 7.98 (d, *J* = 7.7 Hz, 1H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.73 (d, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.48-7.41 (m, 3H), 7.38-7.28 (m, 5H), 7.17-7.12 (m, 2H), 7.08-7.02 (m, 2H), 6.81 (d, *J* = 7.6 Hz, 1H), 6.68 (s, 1H); ^{13}C NMR δ 151.2, 143.4, 142.4, 142.4, 141.5, 140.7, 140.6, 131.9, 131.7, 131.5, 129.6, 129.5, 128.8, 128.0, 127.8, 127.4, 127.4, 127.1, 127.0, 126.7, 125.7, 125.0, 122.7, 122.1, 120.8, 120.6, 119.1, 116.3; HRMS (DART, positive): m/z calcd. for $C_{32}H_{22}N$ $[M + H]^+$ 420.1746, found 420.1747.

Benzo[6,7]-8-(4-chlorophenyl)azepino[3,2,1-*jk*]-9*H*-carbazole (3l)

Isolated by PTLC (hexane/DCM = 15/1). The title compound was obtained as a yellow solid, 86%; mp 129 °C; ^{1}H NMR δ 7.98 (d, *J* = 7.6 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.72 (d, *J* = 7.3 Hz, 1H), 7.46-7.41 (m, 1H), 7.36-7.29 (m, 4H), 7.23-7.19 (m, 2H), 7.18-7.13 (m, 1H), 7.11 (dd, *J* = 7.7, 1.6 Hz, 1H) 7.07-7.01 (m, 2H), 6.68 (d, *J* = 7.7 Hz, 1H), 6.59 (s, 1H); ^{13}C NMR δ 151.1, 143.8, 143.4, 142.3, 141.5, 131.9, 131.7, 131.5, 129.5, 129.1, 128.3, 128.0, 127.9, 127.7, 127.3, 126.6, 125.6, 124.9, 122.6, 122.0, 120.8, 120.0, 119.1, 116.2; HRMS (DART, positive): m/z calcd. for $C_{26}H_{17}ClN$ $[M + H]^+$ 378.1045, found 378.1044.

Benzo[6,7]-8-(4-trifluoromethylphenyl)azepino[3,2,1-*jk*]-9*H*-carbazole (3m)

Isolated by PTLC (hexane/DCM = 15/1). The title compound was obtained as a yellow solid, 97%; mp 197 °C; ^{1}H NMR δ 7.99 (d, *J* = 7.7 Hz, 1H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.73 (d, *J* = 7.4 Hz, 1H),

7.62 (d, *J* = 8.2 Hz, 2H), 7.44 (ddd, *J* = 7.8, 1.0, 1.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.32 (dd, *J* = 7.3, 7.3 Hz, 2H), 7.20-7.15 (m, 1H), 7.12 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.05 (m, 2H), 6.63 (d, *J* = 7.8 Hz, 1H), 6.01 (s, 1H); ^{13}C NMR δ 151.3, 147.1, 142.5, 142.3, 141.5, 132.6, 132.1, 131.0, 129.9, 129.7, 129.5, 127.7, 127.2, 127.2, 126.9, 125.8, 125.3 (q, $J_{C\text{-}F}$ = 3.6 Hz, 1C), 125.0, 123.1, 122.7, 122.2, 120.9, 120.6, 119.4, 116.2; HRMS (DART, positive): m/z calcd. for $C_{27}H_{17}F_3N$ $[M + H]^+$ 412.1309, found 412.1310.

Benzo[6,7]-8-(4-methylphenyl)azepino-5-methoxy-[3,2,1-*jk*]-9*H*-carbazole (3n)

Isolated by PTLC (hexane/DCM = 15/1). The title compound was obtained as a white solid, 77%; mp 183 °C; ^{1}H NMR δ 8.27 (d, *J* = 7.8 Hz, 1H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.40-7.25 (m, 3H), 7.19-7.14 (m, 4H), 7.13-6.99 (m, 3H), 6.68 (d, *J* = 8.4 Hz, 1H), 6.49 (d, *J* = 8.4 Hz, 1H), 6.46 (s, 1H), 4.00 (s, 3H), 2.38 (s, 3H); ^{13}C NMR δ 155.8, 152.5, 143.8, 141.8, 141.1, 141.0, 137.5, 132.3, 131.7, 129.2, 129.2, 129.2, 129.0, 129.0, 126.7, 125.1, 124.9, 123.5, 122.1, 121.2, 121.0, 116.1, 115.6, 103.4, 55.7, 21.4; HRMS (DART, positive): m/z calcd. for $C_{28}H_{22}NO$ $[M + H]^+$ 388.1694, found 388.1696.

Benzo[*g*] benzo[4,5]-8-(4-methylphenyl)azepino[3, 2, 1-*jk*]-9*H*-carbazole (3o) and Benzo[*c*] benzo[6,7]-8-(4-methylphenyl)azepino[3, 2, 1-*jk*]-9*H*-carbazole (3o')

Isolated by PTLC (hexane/DCM = 15/1). The title compound was obtained as a white solid, 88% (3o/3o' = 3/2); mp 60-61 °C; ^{1}H NMR δ 8.70 (d, *J* = 8.2 Hz, 0.4H), 8.63 (d, *J* = 8.2 Hz, 0.6H), 8.52 (dd, *J* = 6.5, 1.9 Hz, 0.6H), 8.25 (d, *J* = 7.9 Hz, 0.4H), 8.01 (d, *J* = 8.0 Hz, 0.4H), 7.97-7.92 (m, 1H), 7.86 (d, *J* = 8.9 Hz, 0.4H), 7.73-7.68 (m, 0.4H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.62-6.57 (m, 0.6H), 7.53 (dd, *J* = 7.2, 7.2 Hz, 0.4H), 7.48-7.40 (m, 2H), 7.37-7.33 (m, 0.6H), 7.24-7.14 (m, 7.2H), 7.12-7.07 (m, 1H), 6.81 (d, *J* = 7.6 Hz, 0.4H), 6.71 (s, 0.6H), 6.69 (s, 0.4H), 2.41 (s, 1.8H), 2.40 (s, 1.2H); ^{13}C NMR δ 151.1, 148.5, 144.3, 143.7, 141.8, 141.1, 141.1, 140.9, 140.8, 140.0, 137.7, 137.6, 132.0, 132.0, 131.7, 131.6, 131.5, 131.0, 131.0, 130.5, 129.8, 129.5, 129.4, 129.3, 129.2, 129.2, 129.2, 129.1, 128.9, 128.1, 128.0, 127.8, 127.6, 127.4, 127.2, 127.0, 126.8, 125.4, 125.2, 124.4, 124.3, 124.3, 123.4, 123.2, 123.1, 122.6 122.5, 121.9, 121.1, 120.6, 119.4, 116.7, 116.2, 21.4, 21.4 (three pairs of peaks at the aromatic region were overlapped); HRMS (DART, positive): m/z calcd. for $C_{31}H_{22}N$ $[M + H]^+$ 408.1747, found 408.1747.

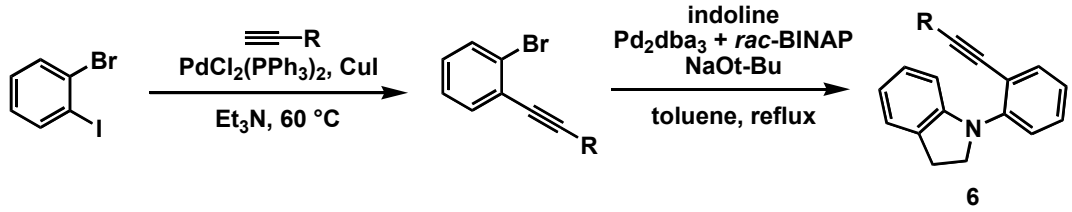
Naphtho[2',3':6,7]-8-(4-methoxyphenyl)azepino-[3,2,1-*jk*]-9*H*-carbazole (3q)

Isolated by PTLC (hexane/DCM = 7/1). The title compound was obtained as a yellow solid, 85%; mp 124-125 °C; ^{1}H NMR δ 8.04 (d, *J* = 7.7 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.72 (s, 1H), 7.68 (d, *J* = 6.9 Hz, 1H), 7.58 (s, 1H), 7.53 (d, *J* = 6.2 Hz, 1H), 7.50-7.46 (m, 1H),

7.38-7.30 (m, 3H), 7.27-7.22 (m, 2H, overlapped with $CHCl_3$), 7.08 (dd, J = 7.6, 7.6 Hz, 1H), 6.92 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 7.6 Hz, 1H), 6.82 (s, 1H), 3.86 (s, 3H); ^{13}C NMR δ 159.4, 149.2, 142.5, 142.0, 140.7, 136.1, 134.4, 131.6, 131.5, 131.1, 131.0, 130.6, 128.5, 127.7, 127.5, 127.5, 127.1, 126.8, 126.7, 125.9, 125.9, 122.6, 122.3, 120.7, 119.2, 118.0, 116.6, 113.8, 55.5; HRMS (DART, positive): m/z calcd. for $C_{31}H_{22}NO$ $[M + H]^+$ 424.1693, found 424.1696.

Synthetic schemes of substrates in 2.1.2.: Compounds **4**[29] and **8m**[30] are known.

Preparation of 1-(2-(2-alkynyl)phenyl)-1*H*-indoline derivatives (6)

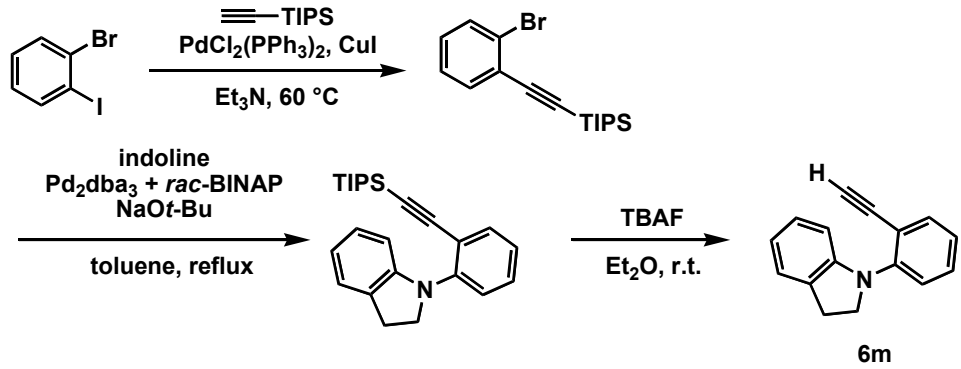


6

Sonogashira coupling was performed under the literature conditions[31]: A dry Schlenk tube was charged with 1-bromo-2-iodobenzene (1.0 eq.), $PdCl_2(PPh_3)_2$ (5 mol%), CuI (5 mol%), alkyne (1.5 eq.) and triethylamine (0.25 M) was added to the reaction vessel. The reaction mixture was then stirred at room temperature for 8 h. The bromides produced in the first step were purified by a short column and subjected to the next Pd-catalyzed amination without isolation.

The Pd-catalyzed amination was performed under the literature conditions[32]: A dry Schlenk tube was charged with crude product (1.0 eq.), Pd_2dba_3 (2 mol%), *rac*-BINAP (4 mol%), NaO*t*-Bu (1.3 eq.) and toluene (0.25 M). The solution was stirred at 125 °C (oil bath temperature) for 24 h. After cooling, it was filtered by silica gel and the solvents were removed. The residue was then purified by flash silica gel column chromatography on silica gel to give desired indoline derivatives **6**.

Preparation of *N*-(2-ethynylphenyl)indoline (6m)

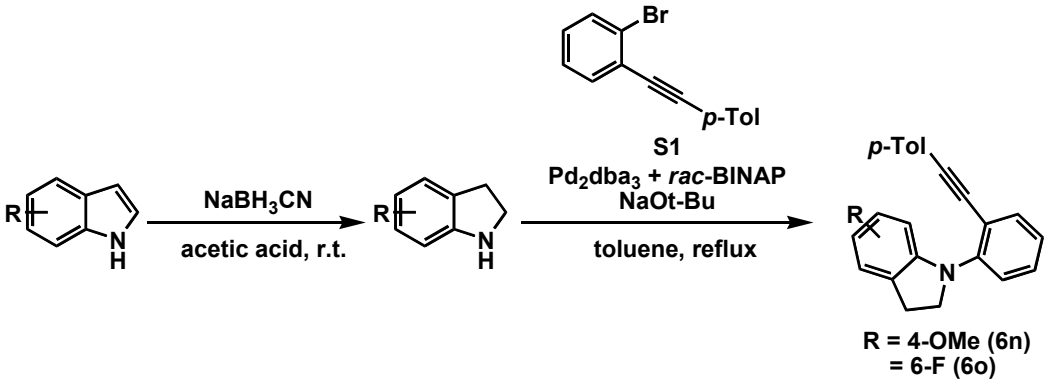


6m

First, Sonogashira coupling of 1-bromo-2-iodobenzene with triisopropylsilylacetylene was conducted under the reported literature.[33] A dry Schlenk tube was charged with 2-bromo-1-iodobenzene (0.5 mmol), $PdCl_2(PPh_3)_2$ (0.01 mmol), CuI (0.02 mmol), triisopropylsilylacetylene (0.75 mmol) and triethylamine (1.0 ml). The solution was stirred at 60 ℃ (oil bath

temperature) for 24 h. After cooling, the obtained bromide was purified by a short column and subjected to the next Pd-catalyzed amination without complete isolation: Pd-catalyzed amination was conducted under the same condition as the latter step in the preparation of **6**, and the crude product was subjected to the desilylation[34]: A dry Schlenk tube was charged with triisopropylsilylalkyne (0.29 mmol), tetrabutylammoniumfluoride (0.34 mmol), and diethyl ether (1.16 ml). The solution was stirred at room temperature for 5 minutes, and filtered by silica gel. The solvents were removed and the residue was purified by PTLC to give **6m** (60.6 mg, 68% in three steps).

Preparation of substituted indoline derivatives (6n, 6o)

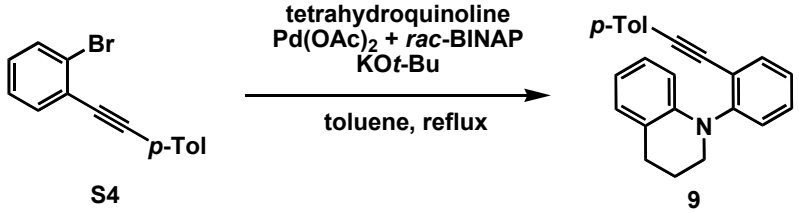


First, 6-fluoroindoline was produced via hydrogenation of the corresponding substituted indoles[35]: A dry Schlenk tube was charged with 6-fluoroindole (0.5 mmol), $NaBH_3CN$ (1.0 mmol) and acetic acid (0.2 ml). The solution was stirred at room temperature for 2 h, then quenched with 5 ml of 2M NaOH, and the organic material was extracted by CH_2Cl_2. The organic layer was washed with brine, and dried over Na_2SO_4. After removal of solvent, the crude products were purified by PTLC (hexane/ethyl acetate = 5/1) to give 6-fluoroindoline (39.5 mg, 57%).

The Pd-catalyzed amination was conducted under the same condition as the latter step in the preparation of **6**, to give **6n** (23.4 mg, 18% in two steps).

4-Methoxyindoline derivative **6o** was synthesized under the same conditions as above to give **3o** (77.1 mg, 62% in two steps)

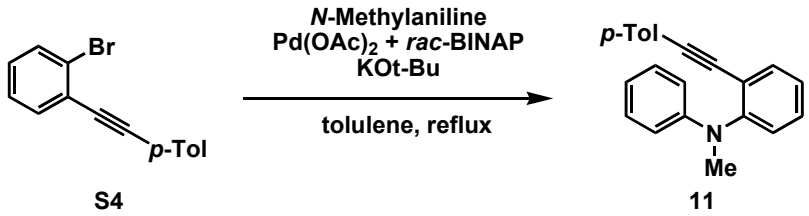
Preparation of 1-(2-(2-(4-methylphenyl)ethynyl)phenyl)-1,2,3,4-tetrahydroquinoline (9)



Pd-Catalyzed amination was conducted[36]: A dry Schlenk tube was charged with **S4** (0.36 mmol),

tetrahydroquinoline (0.43 mmol), $Pd(OAc)_2$ (0.018 mmol), *rac*-BINAP (0.020 mmol), KO*t*-Bu (0.50 mmol) and toluene (0.66 ml). The solution was stirrd at 100 °C for 24 h, and filtered by silica gel, then the solvents were removed. The residue was then purified by flash silica gel column chromatography (hexane/toluene = 5/1) to give desired product **9**.

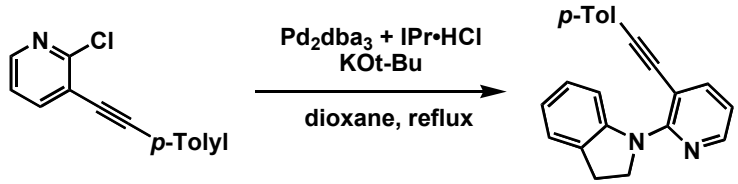
Preparation of *N*-methyl-*N*-phenyl-2-(2-(4-methylphenyl)ethynyl)benzenamine (11)



S4 **11**

The preparation of **11** was the same as the preparation of **9** using *N*-methylaniline instead of tetrahydroquinoline, and desired **11** was produced (99.6 mg, 72%).

Preparation of 1-(3-(2-(4-methylphenyl)ethynyl)pyridin-2-yl)indoline (6p)



S5 **6p**

In this scheme, **S5** was synthesized under the reported conditions[37]. Next, Pd-catalyzed amination was conducted under modified conditions: A dry schlenk tube was charged with **S2** (0.50 mmol), indoline (0.56 mmol), Pd_2dba_3 (0.005 mmol), IPr·HCl (0.02 mmol), KO*t*-Bu (0.75 mmol) and 1.5 ml of dioxane. The solution was stirred at 110 ℃ (oil bath temperature) for 5 h, and then filtered by silica gel. After removal of solvent, desired **6p** was obtained (75.1 mg, 48%).

General procedures for the cycloisomerization in Table 5 and 6

Ph_3PAuCl (0.0050 mmol), AgOTf (0.0050 mmol), and *N*-(2-alkynylphenyl)indoline derivatives **6** (0.050 mmol) were placed in a Schlenk tube under an argon atmosphere in globe box, which was then evacuated and backfilled with argon (×3). To the reaction vessel was added pyridine (0.0050 mmol) and anhydrous DCE (0.50 mL), then the solution was stirred at 40 °C (oil bath temperature). The reaction mixture was cooled to room temperature, and the solution was filtered by silica gel.

The crude product was subjected to the next oxidation reaction without purification under the reported condition. The crude product and DDQ (0.05 mmol) were placed in another Schlenk tube under air, which was then evacuated and backfilled with argon (×3). To the reaction vessel was added benzene (1.0 ml), then the solution was stirred at room temperature. After 1 hour, the solu-

tion was quenched by sat. aqueous $NaHCO_3$, and organic material was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4. After removal of solvent, the crude products were purified by PTLC to give **8**.

Characterization data for new compounds in 2.1.2.

(*Z*)-10-(4-Methylbenzylidene)indolo[1,2-*a*]indole (5)

Isolated by PTLC (hexane/DCM = 10/1). The title compound was obtained as a yellow solid (22.0 mg, 71%). The stereochemistry was determined by the correlation between the vinylic and aromatic protons in the NOESY spectrum; mp 134-135 °C; ^{1}H NMR δ 8.57 (d, *J* = 8.2 Hz, 1H), 8.48 (d, *J* = 8.2 Hz, 1H), 7.80 (d, *J* = 7.4 Hz, 1H), 7.55-7.66 (m, 4H), 7.27-7.43 (m, 5H), 7.07 (s, 1H), 6.85 (s, 1H), 2.44 (s, 3H); ^{13}C NMR δ 138.2, 136.8, 136.2, 136.0, 133.5, 133.1, 130.3, 129.5, 129.0, 128.5, 128.4, 124.8, 123.0, 122.7, 122.0, 122.0, 121.4, 115.4, 114.4, 97.9, 21.5; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{18}N$ ($[M+H]^+$) 308.1434, found 308.1431.

1-(2-(2-(4-Methylphenyl)ethynyl)phenyl)indoline (6a)

Isolated by flash silica gel column chromatography (hexane/ethyl acetate = 10/1). The title compound was obtained as a white solid (305.8 mg, 92%); mp 66-68 °C; ^{1}H NMR δ 7.56 (dd, *J* = 1.7, 7.8 Hz, 1H), 7.40 (dd, *J* = 1.1, 8.0 Hz, 1H), 7.29 (ddd, *J* = 1.7, 7.4, 7.4 Hz, 1H), 7.14-7.20 (m, 3H), 7.06-7.12 (m, 3H), 7.02 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.74 (ddd, *J* = 1.0, 7.3, 7.3 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 4.11 (t, *J* = 8.3 Hz, 2H), 3.16 (t, *J* = 8.3 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR δ 148.6, 146.9, 138.4, 134.0, 131.3, 130.9, 129.2, 126.9, 124.8, 123.9, 122.2, 120.6, 118.9, 118.7, 110.0, 95.6, 87.6, 54.2, 29.1, 21.6 (a pair of peaks at the aromatic region was overlapped); HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{20}N$ ($[M+H]^+$) 310.1590, found 310.1588.

1-(2-(2-(3-Methylphenyl)ethynyl)phenyl)indoline (6b)

Isolated by PTLC (hexane/ethyl acetate = 10/1). The title compound was obtained as brown oil (77.4 mg, 74%); ^{1}H NMR δ 7.56 (dd, *J* = 1.6, 7.8 Hz, 1H), 7.40 (dd, *J* = 1.1, 8.1 Hz, 1H), 7.29 (ddd, *J* = 1.7, 7.4, 7.4 Hz, 1H), 7.18 (dd, *J* = 6.4, 6.4 Hz, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.06-7.12 (m, 3H), 7.00-7.05 (m, 2H), 6.75 (ddd, *J* = 1.1, 7.4, 7.4 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 4.11 (t, *J* = 8.5 Hz, 2H), 3.16 (t, *J* = 8.5 Hz, 2H), 2.28 (s, 3H); ^{13}C NMR δ 148.6, 146.9, 138.1, 134.0, 132.1, 130.9, 129.3, 129.2, 128.5, 128.3, 126.9, 124.8, 123.9, 123.4, 122.2, 118.8, 118.7, 110.0, 95.6, 87.9, 54.2, 29.1, 21.4; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{20}N$ ($[M+H]^+$) 310.1590, found 310.1590.

1-(2-(2-(2-Methylphenyl)ethynyl)phenyl)indoline (6c)

Isolated by PTLC (hexane/ethyl acetate = 10/1). The title compound was obtained as brown oil (78.8 mg, 73%); ^{1}H NMR δ 7.60 (dd, *J* = 1.7, 7.8 Hz, 1H), 7.40 (dd, *J* = 1.1, 8.0 Hz, 1H), 7.29-7.33 (m, 1H), 7.25 (d, *J* = 7.7 Hz, 1H), 7.06-7.20 (m, 5H), 7.01 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.72 (ddd, *J* = 1.0, 7.4, 7.4 Hz, 1H), 6.67 (d, *J* = 7.8 Hz, 1H), 4.09 (t, *J* = 8.4 Hz, 2H), 3.15 (t, *J* = 8.4 Hz, 2H), 2.30 (s, 3H); ^{13}C NMR δ 148.7, 146.5, 140.0, 134.0, 131.8, 130.7, 129.4, 129.2, 128.2, 120.8, 125.5, 124.7, 123.9, 123.3, 122.1, 119.4, 118.6, 109.7, 93.9, 91.7, 54.1, 29.0, 20.4; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{20}N$ ($[M+H]^+$) 310.1590, found 310.1590.

1-(2-(2-(4-Methoxyphenyl)ethynyl)phenyl)indoline (6d)

Isolated by PTLC (hexane/ethyl acetate = 10/1). The title compound was obtained as brown oil (79.9 mg, 56%); ^{1}H NMR δ 7.57 (dd, *J* = 1.6, 7.9 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.30 (ddd, *J* = 1.6, 7.7, 7.7 Hz, 1H), 7.17-7.23 (m, 3H), 7.10 (ddd, *J* = 1.1, 7.4, 7.4 Hz, 1H), 7.00-7.06 (m, 1H), 6.79-6.83 (m, 2H), 6.69-6.77 (m, 2H), 4.12 (t, *J* = 8.5 Hz, 2H), 3.80 (s, 3H), 3.18 (t, *J* = 8.5 Hz, 2H); ^{13}C NMR δ 159.7, 148.6, 146.7, 133.6, 132.9, 130.8, 129.0, 126.9, 124.8, 123.9, 122.3, 119.1, 118.7, 115.8, 114.1, 110.0, 95.4, 86.9, 55.4, 54.2, 29.1; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{20}NO$ ($[M+H]^+$) 326.1539, found 326.1539.

1-(2-(2-(3-Methoxyphenyl)ethynyl)phenyl)indoline (6e)

Isolated by PTLC (hexane/ethyl acetate = 10/1). The title compound was obtained as brown oil (123.4 mg, 71%); ^{1}H NMR δ 7.57 (dd, *J* = 1.5, 7.7 Hz, 1H), 7.38 (d, *J* = 7.9 Hz, 1H), 7.27-7.32 (m, 1H), 7.14-7.18 (m, 2H), 7.09 (ddd, *J* = 1.2, 7.5, 7.5 Hz, 1H), 7.02 (dd, *J* = 7.9, 7.9 Hz, 1H), 6.88 (d, *J* = 7.4 Hz, 1H), 6.80-6.84 (m, 1H), 6.68-6.75 (m, 3H), 4.09 (t, *J* = 8.5 Hz, 2H), 3.73 (s, 3H), 3.15 (t, *J* = 8.5 Hz, 2H); ^{13}C NMR δ 159.5, 148.5, 146.9, 134.1, 130.9, 129.5, 129.5, 126.9, 124.9, 124.7, 124.0, 123.9, 122.2, 118.8, 118.6, 115.9, 115.2, 110.1, 95.5, 88.1, 55.5, 54.2, 29.3; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{19}NNaO$ ($[M+Na]^+$) 348.1359, found 348.1359.

1-(2-(2-(2-Methoxyphenyl)ethynyl)phenyl)indoline (6f)

Isolated by PTLC (hexane/ethyl acetate = 10/1). The title compound was obtained as brown oil (121.3 mg, 80%); ^{1}H NMR δ 7.60 (dd, *J* = 1.5, 7.7 Hz, 1H), 7.43 (dd, *J* = 0.7, 7.9 Hz, 1H), 7.19-7.28 (m, 3H), 7.15 (d, *J* = 7.1 Hz, 1H), 7.06 (ddd, *J* = 0.9, 7.6, 7.6 Hz, 1H), 7.01 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.80-6.87 (m, 2H), 6.69-6.76 (m, 2H), 4.18 (t, *J* = 8.5 Hz, 2H), 3.80 (s, 3H), 3.15 (t, *J* = 8.5 Hz, 2H); ^{13}C NMR δ 159.8, 148.5, 146.8, 134.1, 133.2, 130.8, 129.6, 129.0, 126.7, 124.7, 123.6, 121.7, 120.4, 118.9, 118.5, 112.8, 110.6, 109.8, 92.0, 91.4, 55.7, 53.9, 29.0; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{19}NNaO$ ($[M+Na]^+$) 348.1359, found 348.1359.

1-(2-(2-Phenylethynyl)phenyl)indoline (6g)

Isolated by PTLC (hexane/ethyl acetate = 20/1). The title compound was obtained as brown oil (68.0 mg, 40%); ^{1}H NMR δ 7.57 (dd, *J* = 1.8, 7.7 Hz, 1H), 7.40 (dd, *J* = 1.0, 8.0 Hz, 1H), 7.29 (ddd, *J* = 1.7, 7.3, 7.3 Hz, 1H), 7.26 (m, 5H), 7.18 (d, *J* = 7.2 Hz, 1H), 7.09 (ddd, *J* = 0.9, 7.8, 7.8 Hz, 1H), 7.02 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.74 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 4.10 (t, *J* = 8.3 Hz, 2H), 3.16 (t, *J* = 8.4 Hz, 2H); ^{13}C NMR δ 148.5, 146.9, 134.1, 131.4, 130.9, 129.4, 128.4, 128.2, 126.9, 124.9, 123.9, 123.6, 122.2, 118.8, 118.7, 110.0, 95.4, 88.2, 54.2, 29.1; HRMS (ESI, positive): *m/z* calcd. for $C_{22}H_{18}N$ ($[M+H]^+$) 296.1434, found 296.1430.

1-(2-(2-(4-Chlorophenyl)ethynyl)phenyl)indoline (6h)

Isolated by PTLC (hexane/DCM = 10/1). The title compound was obtained as brown oil (62.8 mg, 63%); ^{1}H NMR δ 7.56 (dd, *J* = 1.6, 7.7 Hz, 1H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.29-7.35 (m, 1H), 7.07-7.16 (m, 3H), 7.17-7.26 (m, 3H), 7.02 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.75 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 4.08 (t, *J* = 8.5 Hz, 2H), 3.16 (t, *J* = 8.5 Hz, 2H); ^{13}C NMR δ 148.3, 146.9, 134.2, 133.9, 132.6, 130.8, 129.6, 128.7, 126.8, 124.8, 123.8, 122.2, 122.0, 118.8, 118.2, 109.9, 94.4, 89.1, 54.2, 29.0 ; HRMS (ESI, positive): *m/z* calcd. for $C_{22}H_{17}{}^{35}ClN$ ($[M+H]^+$) 330.1044, found 330.1044.

1-(2-(2-(3-Chlorophenyl)lethynyl)phenyl)indoline (6i)

Isolated by flash silica gel column chromatography (hexane/ethyl acetate = 40/1). The title compound was obtained as brown oil (108.9 mg, 79%); ^{1}H NMR δ 7.55 (dd, *J* = 1.4, 7.9 Hz, 1H), 7.39 (dd, *J* = 1.0, 8.2 Hz, 1H), 7.31 (ddd, *J* = 1.7, 7.3, 7.3 Hz, 1H), 7.15-7.24 (m, 4H), 7.07-7.12 (m, 2H), 7.02 (dd, *J* = 7.7, 7.7 Hz, 1H), 6.76 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 1H), 4.08 (t, *J* = 8.4 Hz, 2H), 3.16 (t, *J* = 8.4 Hz, 2H); ^{13}C NMR δ 148.3, 147.1, 134.2, 134.1, 131.3, 130.9, 129.8, 129.6, 129.5, 128.5, 126.9, 125.4, 125.0, 123.9, 122.3, 119.0, 118.1, 110.0, 94.2, 89.5, 54.3, 29.2; HRMS (ESI, positive): *m/z* calcd. for $C_{22}H_{17}{}^{35}ClN$ ($[M+H]^+$) 330.1044, found 330.1044.

1-(2-(2-(4-Trifluoromethylphenyl)ethynyl)phenyl)indoline (6j)

Isolated by flash silica gel column chromatography (hexane/ethyl acetate = 10/1). The title compound was obtained as a yellow solid (59.6 mg, 59%); mp 86-87 °C; 7.58 (dd, *J* = 1.5, 7.7 Hz, 1H), 7.51 (d, *J* = 8.3 Hz, 2H), 7.39 (dd, *J* = 1.1, 8.4 Hz, 1H), 7.34 (ddd, *J* = 1.7, 7.4, 7.4 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 6.3 Hz, 1H), 7.08-7.14 (m, 1H), 7.02 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.76 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.69 (d, *J* = 7.9 Hz, 1H), 4.09 (t, *J* = 8.5 Hz, 2H), 3.17 (t, *J* = 8.5 Hz, 2H); ^{13}C NMR δ 148.2, 147.1, 134.1, 131.6, 130.9, 130.0, 129.9, 129.7, 127.4 (q, *J* = 1.68 Hz), 126.8,

125.2 (q, *J* = 3.83 Hz), 124.9, 123.9, 122.2, 119.0, 117.8, 110.0, 94.2, 90.6, 54.3, 29.1; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{17}F_3N$ ($[M+H]^+$) 364.1308, found 364.1305.

1-(2-(2-(1-Naphthyl)ethynyl)phenyl)indoline (6k)

Isolated by flash silica gel column chromatography (hexane/ethyl acetate = 40/1). The title compound was obtained as brown oil (72.4 mg, 33%); ^{1}H NMR δ 8.10 (d, *J* = 7.9 Hz, 1H), 7.16 (dd, *J* = 8.8, 8.8 Hz, 2H), 7.70 (dd, *J* = 1.5, 7.7 Hz, 1H), 7.52 (dd, *J* = 1.0, 7.2 Hz, 1H), 7.30-7.46 (m, 5H), 7.22 (dd, *J* = 1,1.1, 7.5 Hz, 1H), 7.14 (ddd, *J* = 1.3, 7.4, 7.4 Hz, 1H), 7.02 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.71-6.77 (m, 2H), 4.11 (t, *J* = 8.4 Hz, 2H), 3.17 (t, *J* = 8.4 Hz, 2H); ^{13}C NMR δ 149.0, 146.8, 134.1, 133.3, 133.3, 130.8, 130.3, 129.6, 128.7, 128.2, 127.0, 126.8, 126.4, 125.3, 124.9, 124.3, 122.5, 121.3, 119.6, 118.9, 109.7, 93.4, 92.9, 54.3, 29.2 (a pair of peaks at the aromatic region was overlapped); HRMS (ESI, positive): *m/z* calcd. for $C_{26}H_{20}N$ ($[M+H]^+$) 346.1590, found 346.1587.

1-(2-(2-(4-Phenylphenyl)ethynyl)phenyl)indoline (6l)

Isolated by flash silica gel column chromatography (hexane/ethyl acetate = 40/1). The title compound was obtained as a white solid (30.5 mg, 12%); mp 160-161 °C; ^{1}H NMR δ 7.55-7.61 (m, 3H), 7.49-7.53 (m, 2H), 7.40-7.45 (m, 3H), 7.28-7.36 (m, 4H), 7.19 (d, *J* = 7.3 Hz, 1H), 7.11 (ddd, *J* = 1.2, 7.4, 7.4 Hz, 1H), 7.04 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.76 (ddd, *J* = 0.9, 7.4, 7.4 Hz, 1H), 6.72 (d, *J* = 7.9 Hz, 1H), 4.12 (t, *J* = 8.4 Hz, 2H), 3.18 (t, *J* = 8.4 Hz, 2H); ^{13}C NMR δ 148.5, 146.9, 140.9, 140.5, 134.1, 131.8, 130.9, 129.4, 129.0, 127.7, 127.1, 127.1, 126.9, 124.9, 123.9, 122.5, 122.2, 118.8, 118.7, 110.0, 95.4, 89.0, 54.3, 29.1 ; HRMS (ESI, positive): *m/z* calcd. for $C_{28}H_{22}N$ ($[M+H]^+$) 372.1747, found 372,1747.

1-(2-Ethynylphenyl)indoline (6m)

Isolated by flash silica gel column chromatography (hexane/ethyl acetate = 30/1). The title compound was obtained as a brown solid (60.6 mg, 68%); mp 43-44 °C; ^{1}H NMR δ 7.55 (dd, *J* = 1.6, 7.9 Hz, 1H), 7.42 (dd, *J* = 1.0, 8.5 Hz, 1H), 7.28-7.31 (m, 1H), 7.16 (d, *J* = 7.3 Hz, 1H), 7.07 (ddd, *J* = 1.1, 7.4, 7.4 Hz, 1H), 7.02 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.74 (ddd, *J* = 1.0, 7.3, 7.3 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 1H), 4.05 (t, *J* = 8.6 Hz, 2H), 3.27 (s, 1H), 3.15 (t, *J* = 8.6 Hz, 2H); ^{13}C NMR δ 148.7, 148.0, 135.0, 130.9, 129.9, 126.9, 125.0, 124.0, 122.0, 119.0, 118.0, 110.0, 82.6, 82.2, 54.2, 29.1; HRMS (ESI, positive): *m/z* calcd. for $C_{16}H_{14}N$ ($[M+H]^+$) 220.1121, found 220.1119.

6-Fluoro-1-(2-(2-(4-methylphenyl)ethynyl)phenyl)indoline (6n)

Isolated by flash silica gel column chromatography (hexane/ethyl acetate = 5/1). The title compound was obtained as brown oil (23.4 mg, 18%); ^{1}H NMR δ 7.57 (dd, *J* = 1.5, 7.7 Hz, 1H), 7.38

(dd, *J* = 1.0, 8.1 Hz, 1H), 7.32 (ddd, *J* = 1.6, 7.3, 8.1 Hz, 1H), 7.19 (d, *J* = 8.2 Hz, 2H), 7.14 (ddd, *J* = 1.3, 7.6, 7.6 Hz, 1H), 7.09 (d, *J* = 7.9 Hz, 2H), 7.00-7.06 (m, 1H), 6.39 (ddd, *J* = 2.3, 8.0, 9.3 Hz, 1H), 6.34 (dd, *J* = 2.3, 10.5 Hz, 1H), 4.12 (t, *J* = 8.4 Hz, 2H), 3.11 (t, *J* = 8.4, 2H), 2.33 (s, 3H); ^{13}C NMR δ 163.1 (d, *J* = 240.2 Hz), 150.5 (d, *J* = 11.9 Hz), 145.8, 138.6, 134.1, 131.4, 129.3, 129.2, 125.9 (d, *J* = 2.4 Hz), 124.9 (d, *J* = 10.4 Hz), 124.7, 122.9, 120.4, 119.5, 104.4 (d, *J* = 22.7 Hz), 97.7 (d, *J* = 27.7 Hz), 95.8, 87.1, 55.0, 28.3, 21.6; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{19}FN$ ($[M+H]^+$) 328.1496, found 328.1494.

4-Methoxy-1-(2-(2-(4-methylphenyl)ethynyl)phenyl)indoline (6o)

Isolated by flash silica gel column chromatography (hexane). The title compound was obtained as brown oil (77.1 mg, 54%); ^{1}H NMR δ 7.55 (dd, *J* = 1.4, 7.7 Hz, 1H), 7.41 (dd, *J* = 0.4, 8.2 Hz, 1H), 7.26 (ddd, *J* = 1.5, 7.2, 8.0 Hz, 1H), 7.19-7.24 (m, 2H), 7.05-7.10 (m, 3H), 7.00 (dd, *J* = 8.0, 8.0 Hz, 1H), 6.39 (d, *J* = 7.9 Hz, 1H), 6.33 (d, *J* = 8.2 Hz, 1H), 4.13 (t, *J* = 8.6 Hz, 2H), 3.84 (s, 3H), 3.11 (t, *J* = 8.6 Hz, 2H), 2.32 (s, 3H); ^{13}C NMR δ 156.6, 150.4, 147.1, 138.4, 134.0, 131.3, 129.2, 129.1, 128.3, 123.9, 122.6, 120.6, 119.1, 117.3, 103.9, 101.8, 95.3, 87.5, 55.4, 54.6, 26.1, 21.6; HRMS (ESI, positive): *m/z* calcd. for $C_{24}H_{22}NO$ ($[M+H]^+$) 340.1696, found 340.1696.

1-(3-(2-(4-Methylphenyl)ethynyl)pyridin-2-yl)indoline (6p)

Isolated by PTLC (hexane/ethyl acetate = 10/1). The title compound was obtained as a white solid (75.1 mg, 48%); mp 93-94 °C; ^{1}H NMR δ 8.26 (dd, *J* = 1.9, 4.8 Hz, 1H), 7.79 (dd, *J* = 2.0, 7.7 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.15-7.22 (m, 3H), 7.07-7.11 (m, 3H), 6.90 (dd, *J* = 4.8, 7.6 Hz, 1H), 6.85 (ddd, *J* = 0.9, 7.4, 7.4 Hz, 1H), 4.38 (t, *J* = 8.3 Hz, 2H), 3.16 (t, *J* = 8.3 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR δ 156.7, 147.4, 145.5, 142.5, 138.8, 131.8, 131.2, 129.3, 126.5, 124.6, 120.6, 120.2, 116.7, 113.7, 109.3, 97.3, 86.4, 52.8, 29.1, 21.7; HRMS (ESI, positive): *m/z* calcd. for $C_{22}H_{19}N_2$ ($[M+H]^+$) 311.1543, found 311.1543.

6-(4-Methylphenyl)indolo[1,7-*ab*][1]benzazepine (8a)

Isolated by PTLC (hexane/toluene = 10/1). The title compound was obtained as a yellow solid (14.1 mg, 93); mp 108-111 °C; ^{1}H NMR δ 7.39 (d, *J* = 3.7 Hz, 1H), 7.15 (m, 5H), 7.06 (dd, *J* = 7.2 Hz, 1H), 6.86 (m, 3H), 6.70 (dd, *J* = 7.7, 7.7 Hz, 1H), 6.50 (d, *J* = 3.5 Hz, 1H), 6.34 (dd, *J* = 1.1, 7.6 Hz, 1H) 6.02 (s, 1H), 2.37 (s, 3H); ^{13}C NMR δ 143.7, 143.2, 141.6, 140.6, 137.3, 133.6, 131.8, 131.7, 130.2, 129.7, 129.1, 129.0, 127.7, 125.6, 125.1, 124.8, 122.0, 120.9, 120.8, 106.5, 21.4; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{17}N$ ($[M]^+$) 307.1356, found 307.1356.

6-(3-Methylphenyl)indolo[1,7-*ab*][1]benzazepine (8b)

Isolated by PTLC (hexane/ethyl acetate = 10/1). The title compound was obtained as yellow oil (15.8 mg, 98%);^{1}H NMR δ 7.41 (d, *J* = 3.6 Hz, 1H), 7.26 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.12-7.18 (m, 2H), 7.06-7.12 (m, 3H), 6.82-6.92 (m, 3H), 6.72 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.51 (d, *J* = 3.5 Hz, 1H), 6.32 (dd, *J* = 0.9, 7.5 Hz, 1H), 6.02 (s, 1H), 2.37 (s, 3H); ^{13}C NMR δ 143.5, 143.3, 143.2, 141.4, 138.0, 133.5, 131.7, 131.5, 130.2, 129.6, 129.5, 128.2, 128.1, 127.6, 126.0, 125.5, 125.0, 124.7, 121.9, 120.7, 120.7, 106.3, 21.5; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{17}N$ ($[M]^+$) 307.1356, found 307.1356.

6-(2-Methylphenyl)indolo[1,7-*ab*][1]benzazepine (8c)

Isolated by PTLC (hexane/ethyl acetate = 10/1). The title compound was obtained as yellow oil (13.8 mg, 87%);^{1}H NMR δ 7.41 (d, *J* = 3.5 Hz, 1H), 7.23-7.30 (m, 3H), 7.16-7.19 (m, 1H), 7.06-7.13 (m, 2H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.87 (dd, *J* = 1.0, 7.4 Hz, 1H), 6.78 (dd, *J* = 1.4, 7.7 Hz, 1H), 6.63 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.50 (d, *J* = 3.5 Hz, 1H), 6.02 (dd, *J* = 0.7, 7.4 Hz, 1H), 5.89 (s, 1H), 2.30 (s, 3H); ^{13}C NMR δ 142.6, 142.6, 141.4, 136.6, 133.8, 131.7, 131.5, 130.5, 130.2, 129.6, 129.5, 127.6, 127.3, 126.2, 125.2, 125.2, 123.8, 122.2, 120.9, 120.6, 106.3, 19.6 (a pair of peaks at the aromatic reagion was overlapped.); HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{17}N$ ($[M]^+$) 307.1356, found 307.1356.

6-(4-Methoxylphenyl)indolo[1,7-*ab*][1]benzazepine (8d)

Isolated by PTLC (hexane/ethyl acetate = 10/1). The title compound was obtained as yellow oil (13.8 mg, 86%);^{1}H NMR δ 7.41 (d, *J* = 3.6 Hz, 1H), 7.18-7.23 (m, 2H), 7.17 (dd, *J* = 1.0, 8.0 Hz, 1H), 7.08 (ddd, *J* = 1.9, 7.1, 8.1 Hz, 1H), 6.83-6.93 (m, 5H), 6.73 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.52 (d, *J* = 3.6 Hz, 1H), 6.37 (dd, *J* = 0.7, 7.6 Hz, 1H), 6.04 (s, 1H), 3.84 (s, 3H); ^{13}C NMR δ 159.0, 143.6, 142.7, 141.4, 135.7, 133.3 ,131.6, 131.5, 130.1, 130.0, 129.6, 127.7, 125.6, 125.0, 124.7, 121.8, 120.8, 120.7, 113.7, 106.4, 55.3; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{17}NO$ ($[M]^+$) 323.1305, found 323.1305.

6-(3-Methoxylphenyl)indolo[1,7-*ab*][1]benzazepine (8e)

Isolated by PTLC (hexane/toluene = 10/1). The title compound was obtained as yellow oil (15.6 mg, 96%); ^{1}H NMR δ 7.42 (d *J* = 3.4 Hz, 1H), 7.29 (dd, *J* = 8.2, 8.2 Hz, 1H), 7.16 (d, *J* = 7.9 Hz, 1H), 7.08-7.13 (m, 1H), 6.84-6.92 (m, 6H), 6.72 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.52, (d, *J* = 3.6 Hz, 1H), 6.35 (d, *J* = 7.3 Hz, 1H), 6.05 (s, 1H), 3.81 (s, 3H); ^{13}C NMR δ 159.8, 144.9, 143.6, 143.1, 141.6, 133.7, 131.9, 131.7, 130.4, 129.6, 129.5, 127.5, 125.6, 125.1, 124.8, 122.1, 121.5, 120.9, 120.9, 114.6, 113.2, 106.5, 55.4; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{17}NO$ ($[M]^+$) 323.1305, found

323.1306.

6-(2-Methoxylphenyl)indolo[1,7-*ab*][1]benzazepine (8f)

Isolated by PTLC (hexane/toluene = 3/1). The title compound was obtained as a yellow solid (14.3 mg, 88%); mp 127-128 °C; ^{1}H NMR δ 7.39 (d, *J* = 3.6 Hz, 1H), 7.33 (ddd, *J* = 1.8, 7.8, 7.8 Hz, 1H), 7.20 (dd, *J* = 1.8, 7.4 Hz, 1H), 7.04-7.12 (m, 2H), 7.00 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.94 (d, *J* = 8.1 Hz, 1H), 6.89 (d, *J* = 8.1 Hz, 1H), 6.85 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.78 (dd, *J* = 1.6, 7.7 Hz, 1H), 6.64 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.48 (d, *J* = 3.5 Hz, 1H), 6.11 (d, *J* = 7.4 Hz, 1H), 5.94 (s, 1H), 3.73 (s, 3H); ^{13}C NMR δ 157.4, 142.4, 141.5, 140.1, 133.9, 132.3, 132.2, 131.5, 130.9, 130.4, 129.5, 129.0, 127.3, 125.1, 125.0, 123.7, 122.0, 121.0, 120.7, 120.4, 111.3, 106.2, 55.9; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{17}NNaO$ ($[M+Na]^+$) 346.1202, found 346.1203.

6-Phenylindolo[1,7-*ab*][1]benzazepine (8g)

Isolated by PTLC (hexane/DCM = 5/1). The title compound was obtained as a yellow solid (14.6 mg, >99%); mp 136-137 °C; ^{1}H NMR δ 7.42 (d, *J* = 3.5 Hz, 1H), 7.32-7.40 (m, 3H), 7.28-7-31 (m, 2H), 7.17 (dd, *J* = 1.1, 8.0 Hz, 1H), 7.08-7.12 (m, 1H), 6.85-6.93 (m, 3H), 6.72 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.53 (d, *J* = 3.5 Hz, 1H), 6.32 (dd, *J* = 0.9, 7.1 Hz, 1H), 6.04 (s, 1H); ^{13}C HMR δ 143.6, 143.4, 143.2, 141.5, 133.6, 132.0, 131.6, 130.3, 129.6, 129.1, 128.4, 127.6, 127.5, 125.6, 125.1, 124.8, 122.0, 120.8, 106.5 (a pair of peaks at the aromatic region was overlapped); HRMS (ESI, positive): *m/z* calcd. for $C_{22}H_{15}N$ ($[M]^+$) 293.1199, found 293.1198.

6-(4-Chlorophenyl)indolo[1,7-*ab*][1]benzazepine (8h)

Isolated by PTLC (hexane/DCM = 5/1). The title compound was obtained as a yellow solid (14.2 mg, 88%); mp 126-127 °C; ^{1}H NMR δ 7.42 (d, *J* = 3.5 Hz, 1H), 7.33-7.37 (m, 2H), 7.20-7.24 (m, 2H), 7.17 (dd, *J* = 1.0, 8.0 Hz, 1H), 7.11 (ddd, *J* = 1.7, 7.6, 8.1 Hz, 1H), 6.91 (ddd, *J* = 1.0, 7.4, 7.4 Hz, 1H), 6.84-6.89 (m, 2H), 6.72 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.53 (d, *J* = 3.7 Hz, 1H), 6.27 (dd, *J* = 0.6, 7.3 Hz, 1H), 6.01 (s, 1H); ^{13}C NMR δ 143.7, 142.1, 141.9, 141.6, 133.7, 133.4, 132.3, 131.8, 130.6, 130.5, 129.4, 128.7, 127.3, 125.7, 125.2, 124.6, 122.1, 121.1, 121.0, 106.6; HRMS (ESI, positive): *m/z* calcd. for $C_{22}H_{14}{}^{35}ClN$ ($[M]^+$) 327.0809, found 327.0810.

6-(3-Chlorophenyl)indolo[1,7-*ab*][1]benzazepine (8i)

Isolated by PTLC (hexane/DCM = 5/1). The title compound was obtained as yellow oil (16.6 mg, >99%); ^{1}H NMR δ 7.40 (d, *J* = 3.7 Hz, 1H), 7.26-7.34 (m, 3H), 7.13-7.20 (m, 2H), 7.10 (dd, *J* = 1.7, 7.4 Hz, 1H), 6.82-6.92 (m, 3H), 6.73 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.52 (d, *J* = 3.8 Hz, 1H), 6.26 (d, *J* = 7.4 Hz, 1H), 6.01 (s, 1H); ^{13}C NMR δ 145.2, 143.6, 141.9, 141.6, 134.4, 133.8, 132.5, 131.8,

130.7, 129.8, 129.3, 129.2, 127.7, 127.4, 127.2, 125.7, 125.2, 124.6, 122.1, 121.1, 121.0, 106.6; HRMS (ESI, positive): *m/z* calcd. for $C_{22}H_{14}{}^{35}ClN$ ($[M]^+$) 327.0809, found 327.0810.

6-(4-Trifluoromethylphenyl)indolo[1,7-*ab*][1]benzazepine (8j)

Isolated by PTLC (hexane/DCM = 10/1). The title compound was obtained as a yellow solid (9.1 mg, 51%); mp 119-120 °C; ^{1}H NMR δ 7.64 (d, *J* = 8.2 Hz, 2H), 7.38-7.44 (m, 3H), 7.18 (d, *J* = 7.8 Hz, 1H), 7.13 (ddd, *J* = 1.7, 7.7, 7.7 Hz, 1H), 6.84-6.95 (m, 3H), 6.73 (ddd, *J* = 2.0, 7.6, 7.6 Hz, 1H), 6.52-6.55 (m, 1H), 6.22 (d, *J* = 7.4 Hz, 1H), 6.01 (s, 1H); ^{13}C NMR δ 147.1 (q, *J* = 1.44 Hz), 143.7, 142.0, 141.6, 133.8, 132.7, 131.9, 130.8, 129.8, 129.5, 129.2, 127.1, 125.8, 125.7, 125.5 (q, *J* = 3.83 Hz), 125.2, 124.5, 122.1, 121.2, 121.0, 106.6; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{14}F_3N$ ($[M]^+$) 361.1073, found 361.1073.

6-(1-Naphthyl)indolo[1,7-*ab*][1]benzazepine (8k)

Isolated by PTLC (hexane/DCM = 5/1). The title compound was obtained as a yellow solid (17.0 mg, 98%); mp 138-140 °C; ^{1}H NMR δ 8.05 (d, *J* = 8.5 Hz, 1H), 7.86 (dd, *J* = 8.5, 8.5 Hz, 2H), 7.35-7.54 (m, 5H), 7.06-7.15 (m, 2H), 6.96 (d, *J* = 8.2 Hz, 1H), 6.88 (ddd, *J* = 1.9, 7.4, 7.4 Hz, 1H), 6.78 (dd, *J* = 1.5, 7.6 Hz, 1H), 6.49-.6.54 (m, 2H), 6.06 (s, 1H), 5.96 (d, *J* = 7.3, 1H); ^{13}C NMR δ 142.2, 141.4, 141.3, 140.6, 133.8, 133.7, 132.9, 132.1, 131.4, 130.5, 129.3, 128.2, 127.8, 126.5, 126.2, 126.2, 125.9, 125.8, 125.1, 125.1, 124.6, 122.1, 120.8, 120.5, 106.2 (a pair of peaks at the aromatic region was overlapped): *m/z* calcd. for $C_{26}H_{17}N$ ($[M]^+$) 343.1356, found 343.1356.

6-(4-Phenylphenyl)indolo[1,7-*ab*][1]benzazepine (8l)

Isolated by PTLC (hexane/ethyl acetate = 10/1). The title compound was obtained as a yellow solid (14.0 mg, 76%); mp 163-164 °C; ^{1}H NMR δ 7.59-7.67 (m, 4H), 7.42-7.49 (m, 3H), 7.34-7.40 (m, 3H), 7.19 (dd, *J* = 0.9, 7.8 Hz, 1H), 7.12 (ddd, *J* = 2.1, 7.3, 7.9 Hz, 1H), 6.86-6.95 (m, 3H), 6.76 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.54 (d, *J* = 3.4 Hz, 1H), 6.42 (dd, *J* = 0.8, 7.4 Hz, 1H), 6.11 (s, 1H); ^{13}C NMR δ 143.7, 142.9, 142.5, 141.6, 140.9, 140.4, 133.6, 132.0, 132.0, 131.7, 130.4, 129.6, 129.5, 128.9, 127.5, 127.4, 127.2, 125.7, 125.1, 124.8, 122.0, 120.9, 120.9, 106.5; HRMS (ESI, positive): *m/z* calcd. for $C_{28}H_{19}N$ ($[M]^+$) 369.1512, found 369.1514.

5-Fluoro-6-(4-methylphenyl)indolo[1,7-*ab*][1]benzazepine (8n)

Isolated by PTLC (hexane/toluene = 10/1). The title compound was obtained as a yellow solid (12.3 mg, 71%); mp 119-121 °C; ^{1}H NMR δ 7.40 (d, *J* = 3.5 Hz, 1H), 7.20-7.25 (m, 1H), 7.11-7.17 (m, 5H), 7.03 (dd, *J* = 1.9, 7.6 Hz, 1H), 7.00 (dd, *J* = 7.2, 7.2 Hz, 1H), 6.78 (d, *J* = 8.2 Hz, 1H), 6.66 (dd, *J* = 8.4, 11.6 Hz, 1H), 6.56 (d, *J* = 3.5 Hz, 1H), 6.36 (s, 1H), 2.36 (s, 3H); ^{13}C NMR 157.6

(d, *J* = 247.46 Hz), 147.7 (d, *J* = 7.75 Hz), 142.5, 141.4 (d, *J* = 3.28 Hz), 139.9, 137.0, 133,3, 132.6, 130.0, 129.5, 128.9, 127.9, 127.5 (d, *J* = 3.28 Hz), 126.7 (d, *J* = 2.68 Hz), 125.1, 121.9, 121.2 (d, *J* = 11.03 Hz), 124.9 (d, *J* = 13.41 Hz), 112.4 (d, *J* = 25.63 Hz), 107.0, 21.3; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{16}FN$ ($[M]^+$) 325.1261, found 325.1262.

3-Methoxy-6-(4-methylphenyl)indolo[1,7-*ab*][1]benzazepine (8o)

Isolated by PTLC (hexane/toluene = 10/1). The title compound was obtained as yellow oil (8.0 mg, 62%); ^{1}H NMR δ 7.32 (d, *J* = 3.5 Hz, 1H), 7.17-7.19 (m, 4H), 7.05 (dd, *J* = 1.7, 7.5 Hz, 1H), 6.86-6.91 (m, 2H), 6.81 (dd, *J* = 1.6, 7.6 Hz, 1H), 6.61 (d, 3.5 Hz, 1H), 6.27 (d, 8.3 Hz, 1H), 6.12 (d, 8.4 Hz, 1H), 5.86 (s, 1H), 3.85 (s, 3H), 2.38 (s, 3H); ^{13}C NMR δ 153.2, 144.3, 143.1, 140.9, 140.9, 137.2, 133.4, 130.1, 129.7, 129.3, 129.1, 129.0, 125.9, 125.3, 124.3, 122.5, 121.3, 120.7, 103.3, 101.0, 55.4, 21.4; HRMS (ESI, positive): *m/z* calcd. for $C_{24}H_{19}NO$ ($[M]^+$) 337.1461, found 337.1462.

6-(4-Methylphenyl)pyrido[3',2':6,7]azepino[3,2,1-*hi*]indoline (8p)

Isolated by PTLC (hexane/ethyl acetate = 10/1). The title compound was obtained as a yellow solid (30.5 mg, 97%); mp 130 °C (decomp.); ^{1}H NMR δ 7.84 (dd, *J* = 1.7, 4.9 Hz, 1H), 7.13-7.20 (m, 4H), 6.92 (dd, *J* = 1.3, 7.3 Hz, 2H), 6.50-6.60 (m, 2H), 6.36 (d, *J* = 7.8, 1H), 5.94 (s, 1H), 4.19 (dd, *J* = 8.4 Hz, 2H), 2.91 (t, *J* = 8.4 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR δ 160.0, 151.3, 146.7, 143.4, 139.9, 138.9, 137.5, 133.8, 130.2, 129.4, 129.1, 128.8, 127.7, 125.9, 124.3, 122.5, 117.1, 47.3, 27.6, 21.3; HRMS (ESI, positive): *m/z* calcd. for $C_{22}H_{19}N_2$ ($[M+H]^+$) 310.1541, found 310.1543.

1-(2-(2-(4-Methylphenyl)ethynyl)phenyl)-1,2,3,4-tetrahydroquinoline (9)

Isolated by flash silica gel column chromatography (hexane/toluene = 5/1). The title compound was obtained as a white solid (66.6 mg, 57%); mp 81-83 °C; ^{1}H NMR δ 7.58 (dd, *J* = 1.6, 7.8 Hz, 1H), 7.27-7.35 (m, 2H), 7.18 (ddd, *J* = 1.7, 7.7, 7.7 Hz, 1H), 7.12-7.15 (m, 2H), 7.07 (d, *J* = 7.9 Hz, 2H), 7.03 (dd, *J* = 1.2, 7.5 Hz, 1H), 6.89 (ddd, *J* = 1.6, 7.0, 7.0 Hz, 1H), 6.65 (ddd, *J* = 1.1, 7.3, 7.3 Hz, 1H), 6.40 (dd, 0.9, 8.0 Hz, 1H) 3.69 (m, 2H), 2.88 (t, *J* = 6.4 Hz, 2H), 2.32 (s, 3H), 2.04-2.11 (m, 2H); ^{13}C NMR δ 149.8, 145.0, 138.4, 133.9, 131.3, 123.0, 129.4, 129.1, 128.4, 126.9, 125.4, 123.0, 122.4, 120.5, 117.9, 115.1, 94.7, 85.9, 51.2, 28.1, 22.6, 21.8; HRMS (ESI, positive): *m/z* calcd. for $C_{24}H_{22}N$ ($[M+H]^+$) 324.1747, found 324.1745.

7-(4-Methylphenyl)-2,3-dihydrobenzo[6,7]azepino[3,2,1-*ij*]quinoline (10)

Isolated by PTLC (hexane/ethyl acetate = 10/1). The title compound was obtained as a yellow solid (15.3 mg, 94%); mp 68-70 °C; ^{1}H NMR δ 7.28 (d, *J* = 8.0 Hz, 2H), 7.12-7.22 (m, 4H), 7.09 (d, *J* =

7.6 Hz, 1H), 6.92-7.02 (m, 2H), 6.84 (s, 1H), 6.79 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.64 (d, *J* = 7.6 Hz, 1H), 4.00-4.08 (m, 1H), 3.53-3.63 (m, 1H), 2.90-3.00 (m, 2H), 2.39-2.50 (m, 1H), 2.37 (s, 3H), 1.96-2.05 (m, 1H); ^{13}C NMR δ 153.5, 150.7, 144.8, 141.4, 137.1, 134.6, 133.1, 131.0, 130.1, 130.1, 129.0, 129.0, 128.9, 128.9, 128.4, 122.8, 122.6, 117.7, 48.8, 27.1, 21.2, 20.6; HRMS (ESI, positive): *m/z* calcd. for $C_{24}H_{22}N$ ([M+H]$^+$) 324.1747, found 324.1742.

_N_-Methyl-_N_-phenyl-2-(2-(4-methylphenyl)ethynyl)benzenamine (11)

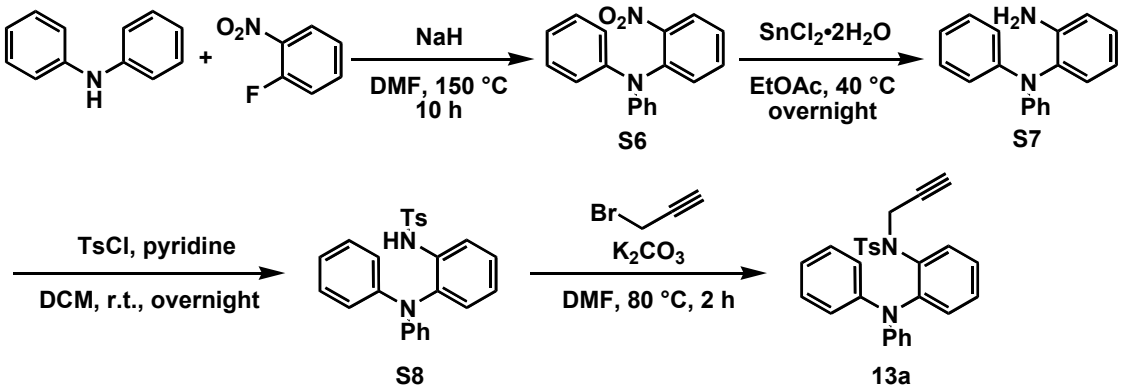
Isolated by flash silica gel column chromatography (hexane/toluene = 3/1). The title compound was obtained as brown oil (99.6 mg, 72%); ^{1}H NMR δ 7.56 (dd, *J* = 1.4, 7.7 Hz, 1H), 7.31 (ddd, *J* = 1.6, 7.5, 8.1 Hz, 1H), 7.13-7.26 (m, 4H), 7.10 (d, *J* = 8.1 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.72-6.80 (m, 3H), 3.36 (s, 3H), 2.30 (s, 3H); ^{13}C NMR δ 150.2, 149.2, 138.4, 133.9, 131.5, 129.5, 129.0, 128.9, 127.7, 125.2, 122.0, 120.3, 118.1, 114.9, 95.0, 86.7, 39.9, 21.6; HRMS (ESI, positive): *m/z* calcd. for $C_{22}H_{20}N$ ([M+H]$^+$) 298.1590, found 298.1588.

5-Methyl-10-(4-methylphenyl)dibenzo[*b,f*]azepine (12)

Isolated by PTLC (hexane/toluene = 3/1). The title compound was obtained as a yellow solid (12.2 mg, 82%); mp 128-129 °C; ^{1}H NMR δ 7.33 (d, *J* = 8.1 Hz, 2H), 7.21-7.30 (m, 2H), 7.18 (dd, *J* = 0.5, 8.4 Hz, 2H), 7.15 (dd, *J* = 8.1, 8.1 Hz, 2H), 7.05 (d, *J* = 8.1 Hz, 1H), 7.00 (ddd, *J* = 1.1, 7.4, 7.4 Hz, 1H), 6.97 (s, 1H), 6.90 (ddd, *J* = 1.1, 7.9, 7.9 Hz, 1H), 6.87 (dd, *J* = 2.1, 7.7 Hz, 1H), 3.39 (s, 3H), 2.39 (s, 3H); ^{13}C NMR δ 153.9, 153.0, 144.3, 140.9, 137.3, 134.7, 132.9, 130.7, 130.3, 129.6, 129.2, 129.1, 129.0, 128.5, 123.2, 118.8, 117.9, 38.8, 21.3 (a pair of peaks at the aromatic region was overlapped); HRMS (ESI, positive): *m/z* calcd. for $C_{22}H_{20}N$ ([M+H]$^+$) 298.1590, found 298.1590.

Synthetic schemes of substrates in 2.2.

Preparation of 13a



Diphenylamine (3.0 mmol, 1.0 eq.) and 2-fluoronitrobenzene (3.3 mmol, 1.1 eq.) were placed in a

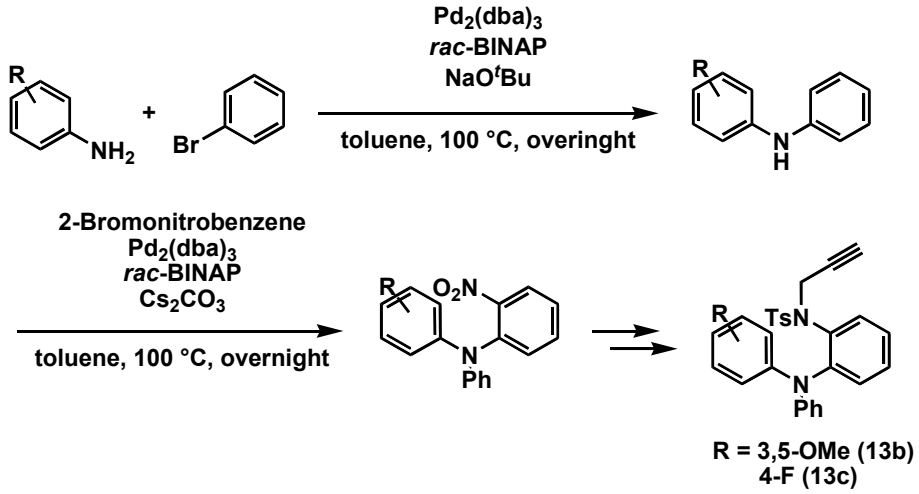
round-bottom flask, which was then evacuated and backfilled with argon (×3). Anhydrous DMF (10.5 ml) was added to the reaction vessel, then the solution was stirred at room temperature. NaH (4.5 mmol, 1.5 eq.) was added and the reaction solution was stirred at 150 °C for 10 h. After cooling, the solution was quenched with 1N HCl, and extracted by ethyl acetate. The organic layer was dried over Na_2SO_4 and filtrated. After removal of solvent from the filtrate, the obtained **S6** was subjected to the next reduction reaction without isolation.

S6 (2.1 mmol, 1.0 eq.), and $SnCl_2 \cdot 2H_2O$ (7.875 mmol, 3.75 eq.) were placed in a round-bottom flask, which was then evacuated and backfilled with argon (×3). Ethyl acetate (10.5 ml) was added to the reaction vessel and the resulting solution was stirred at 40 °C overnight. After cooling, 1N NaOH (10.5 ml) was added and stirred at room temperature for 10 min. The reaction mixture was filtered by celite to remove precipitate. The organic material was extracted by ethyl acetate, and the organic layer was dried over Na_2SO_4 and filtrated. After removal of solvent from the filtrate, the obtained **S7** was subjected to the next sulfonylation reaction of amino group without further purification.

S7 (0.84 mmol, 1.0 eq.) was placed in a Schlenk tube and then evacuated and backfilled with argon (×3). Pyridine (1.68 mmol, 2.0 eq.) was added to the reaction vessel, and *p*-toluenesulfonyl chloride (1.01 mmol, 1.2 eq.) in 1.0 ml of dichloromethane was added dropwise. The reaction mixture was stirred at room temperature overnight, and then quenched with 1N HCl. The organic material was extracted by ethyl acetate, and the organic layer dried over Na_2SO_4, then filtrated. After removal of solvent from the filtrate, the obtained **S3** was subjected to the next propargylation of amino group without isolation.

S8 (0.5 mmol, 1.0 eq.), and K_2CO_3 (1.0 mmol, 2.0 eq.) were placed in a Schlenk tube and then evacuated and backfilled with argon (×3). To the reaction vessel was added propargyl bromide (0.6 mmol, 1.2 eq.) and anhydrous DMF (4.0 ml), then the solution was heated at 80 °C for 2 h. After cooling, the solution was quenched using sat. NH_4Cl. The organic material was extracted by ethyl acetate. After washing by H_2O, the organic layer was dried over Na_2SO_4, and then the solvent was removed. The crude products were purified by flash silica gel column chromatography (hexane/ethyl acetate = 3:1) to give desired **13a** (16% in total yield of four steps).

Preparation of 13b and 13c



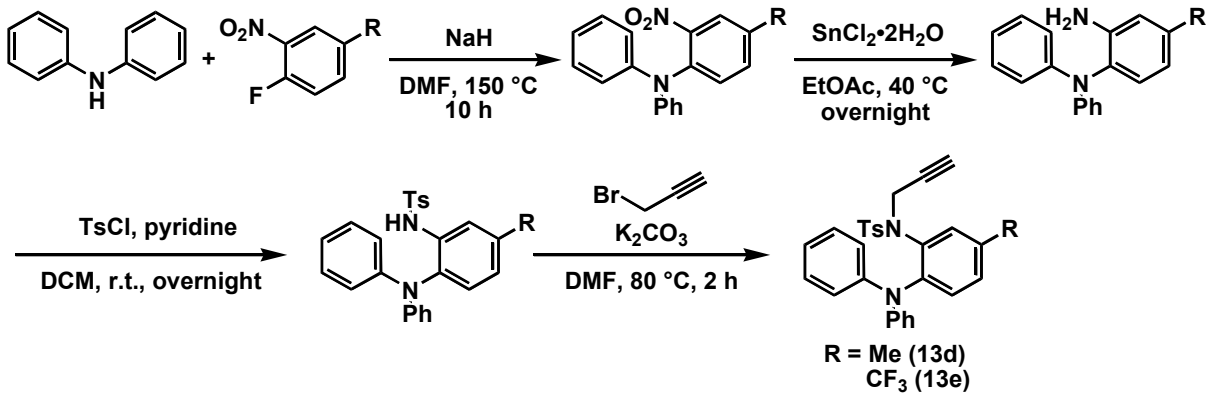
$Pd_2(dba)_3$ (0.003 mmol, 0.3 mol%), *rac*-BINAP (0.008 mmol, 0.8 mol%) and NaO^tBu (1.4 mmol, 1.4 eq.) were added in a round-bottom flask, and then evacuated and backfilled with argon (×3). To the reaction vessel was added bromobenzene (1.0 mmol, 1.0 eq.), 4-fluoroaniline (1.2 mmol, 1.2 eq.), and toluene (1.57 ml, 0.63 M). The reaction mixture was stirred at 100 °C overnight. After cooling, the solution was filtered by short column, then purified by flash silica gel column chromatography (hexane/ethyl acetate = 4:1) to give desired 4-fluoro-*N*-phenylaniline.

Subsequent Buchwald-Hartwig cross coupling was conducted under the reported conditions[38]: $Pd_2(dba)_3$ (0.03 mmol), *rac*-BINAP (0.1 mmol), Cs_2CO_3 (0.6 mmol) were added in a round bottom flask, then evacuated and backfilled with argon (×3). To the reaction vessel was added 4-fluoro-*N*-phenylaniline (0.5 mmol, 1.0 eq.), 2-bromonitrobenzene (0.6 mmol, 1.2 eq.) and toluene (0.9 ml, 0.6 M). The reaction mixture was stirred at 100 °C overnight. After cooling, the solution was filtered by short column. The solvent was removed, and the crude product was subjected to the next reaction without further purification.

Following reactions were the same conditions as synthesis of **13** to give **13c** (126.1 mg, 27% in total yield of five steps).

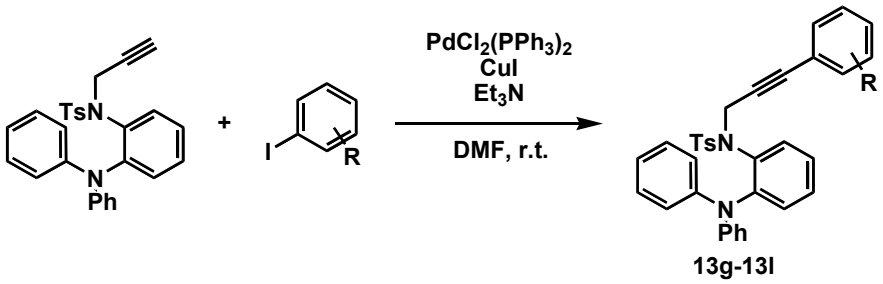
3,5-Methoxydiphenylamine derivative **13b** was synthesized under the same conditions as above (89.1 mg, 17% in total yield of five steps).

Preparation of 13d and 13e



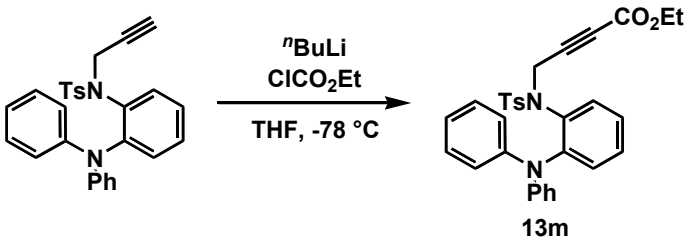
The preparation of **13d** and **13e** was the same as the preparation of **13a** using 4-fluoro-3-nitrotoluene and 2-fluoro-5-trifluoronitrobenzene, respectively, in place of 2-fluoronitrobenzene, and desired **13d** (105.3 mg, 8% in total yield) and **13e** (141.6 mg, 9% in total yield) was obtained.

Preparation of 13g-13l



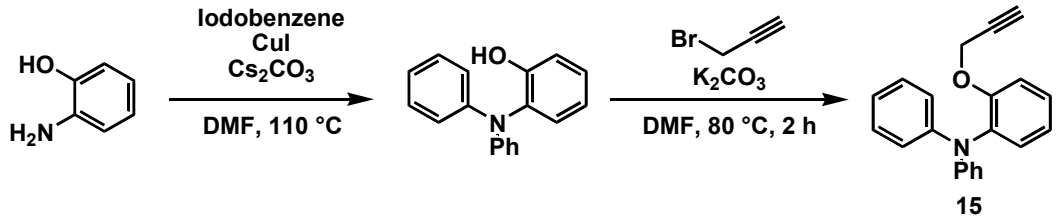
Sonogashira coupling was conducted under the literature conditions.[39] A dry Schlenk tube was charged with **13a** (1.0 eq.), $PdCl_2(PPh_3)_2$ (3 mol%), CuI (3 mol%), iodobenzene derivatives (1.2 eq.), triethylamine (1.2 ml) and DMF (5.0 ml). Reaction mixture was then stirred at room temperature overnight. The reaction mixture was poured into water, and extracted with dichloromethane. The organic layer was successively washed with water, dried over anhydrous Na_2SO_4 and then filtered. The solvent from the filtrate was removed under reduced pressure to give a crude product, which was purified by PTLC to give pure compounds **13g-13l**.

Preparation of 13m



Synthesis of **13m** was conducted under the literature conditions[40]: To a solution of **13a** (0.30 mmol) in THF (0.9 ml) at -78 °C under argon, *n*-BuLi (2.0 mmol) was added dropwise. After stirring for 5 min, ethyl chloroformate (0.36 mmol) was added slowly to the above solution. After stirring at -78 °C for 2 h, the reaction was gradually warmed to room temperature. The mixture was washed with sat. NH_4Cl solution. The aqueous phase was extracted with ethyl acetate (10 ml × 3). The combined organic phase was dried over anhydrous Na_2SO_4 and then filtered. The solvent from the filtrate was removed under reduced pressure to give crude products, which were purified by PTLC (dichloromethane only) to give pure compound **13m**.

Preparation of 15

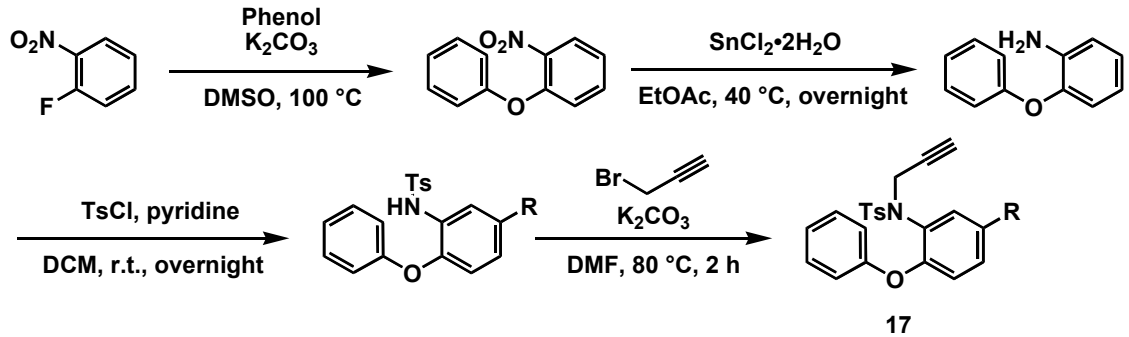


15

Synthesis of 2-diphenylaminophenol was conducted under the reported conditions[41]: 2-aminophenol (1.0 mmol), CuI (20 mol%) and Cs_2CO_3 (3.0 eq.) were added in a Schlenk tube, then evacuated and backfilled with argon (×3). To the solution iodobenzene (3.0 eq.) and DMF (2 ml) were added and stirred overnight at 110 °C. The solution was quenched with 1N HCl, and extracted by ethyl acetate, then the organic layer was dried over Na_2SO_4. After Na_2SO_4 was filtrated, the solvent was removed from the filtrate and the crude product was purified by flash silica gel column chromatography (hexane/ethyl acetate = 9/1) to give 2-diphenylaminophenol (66%).

Subsequent propargylation was conducted under the same conditions as the synthesis of **1** to give **15** (160.4 mg, 81%).

Preparation of 17



17

Synthesis of 1-nitro-2-phenoxybenzene was conducted under the reported conditions[42]: Phenol (2.0 mmol) and K_2CO_3 (2.0 eq.) were added to a Schlenk tube, then evacuated and backfilled with

argon (×3). To the solution 2-fluoronitrobenzene (1.0 eq.) and DMSO (3 ml) were added and stirred overnight at 100 °C. The reaction mixture was quenched with H_2O, then extracted by ethyl acetate. The combined organic layer was dried over Na_2SO_4 and then filtered. The solvent from the filtrate was removed under reduced pressure to give a nitro compound, which was subjected to the next step without isolation.

Subsequent reduction of nitro group, tosylation and propargylation was done under same conditions as synthesis of **1** to give **17** (22% in total yield of four steps).

Characterization data for new compounds in 2.2.

***N*-(2-(Diphenylamino)phenyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (13a)**

Isolated by silica gel column chromatography (hexane/ethyl acetate = 3/1). The title compound was obtained as a brown solid, 16% in total yield; mp 193-195 °C; ^{1}H NMR δ 7.62 (d, *J* = 8.4 Hz, 2H), 7.35-7.27 (m, 2H), 7.25-7.18 (m, 7H), 7.08-7.02 (m, 5H), 6.99 (dd, *J* = 7.4, 7.4 Hz, 2H), 3.98 (brs, 1H), 3.03 (brs, 1H), 2.40 (s, 3H), 1.99 (dd, *J* = 2.3, 2.5 Hz, 1H); ^{13}C NMR δ 148.0, 147.8, 143.6, 137.0, 135.4, 131.7, 129.9, 129.6, 129.2, 129.2, 128.6, 124.9, 123.7, 122.7, 78.5, 73.8, 38.3, 21.7; HRMS (ESI, positive): *m/z* calcd. For $C_{28}H_{24}N_2NaO_2S$ ($[M+Na]^+$) 475.1451, found 475.1451.

***N*-(2-((3,5-Dimethoxyphenyl)(phenyl)amino)phenyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (13b)**

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as red oil, 27% in total yield; ^{1}H NMR δ 7.66-7.61 (m, 2H), 7.35-7.28 (m, 2H), 7.25-7.19 (m, 5H), 7.10-7.04 (m, 3H), 7.02-6.96 (m, 1H), 6.23 (d, *J* = 2.1 Hz, 2H), 6.15 (t, *J* = 2.2 Hz, 1H), 4.01 (brs, 1H), 3.69 (s, 6H), 3.14 (brs, 1H), 2.41 (s, 3H), 1.99 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR δ 161.3, 149.9, 147.7, 147.5, 143.6, 137.0, 135.6, 131.6, 129.9, 129.8, 129.2, 129.1, 128.7, 125.2, 124.0, 122.9, 102.3, 95.2, 78.6, 73.8, 55.5, 38.4, 21.7; HRMS (ESI, positive): *m/z* calcd for $C_{30}H_{28}N_2NaO_4S$($[M+Na]^+$)535.1661, found 535.1662.

***N*-(2-((4-Fluorophenyl)(phenyl)amino)phenyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (13c)**

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as a light yellow solid, 17% in total yield; mp 180 °C; ^{1}H NMR δ 7.63 (d, *J* = 8.4 Hz, 2H), 7.36-7.14 (m, 7H), 7.10-6.86 (m, 8H), 4.01 (brs, 1H), 3.01 (brs, 1H), 2.42 (s, 3H), 1.99 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR δ 158.9 (d, *J* = 241.8 Hz), 148.3, 147.9, 144.2 (d, *J* = 2.6 Hz), 143.7, 136.9, 135.2, 131.6, 130.0, 129.3, 129.2, 128.6, 125.7 (d, *J* = 8.2 Hz), 124.9, 123.3, 122.7, 115.9 (d, *J* = 22.5 Hz), 78.4, 73.9, 53.6, 38.4, 21.7; HRMS (ESI, positive): *m/z* calcd for $C_{28}H_{23}FN_2NaO_2S$ ($[M+Na]^+$) 493.1357,

found 493.1356.

_N_-(2-(Diphenylamino)-5-methylphenyl)-4-methyl-_N_-(prop-2-yn-1-yl)benzenesulfonamide (13d)

Isolated by recrystallization (hexane/dichloromethane). The title compound was obtained as a white solid, 8% in total yield; mp 150-152 °C; ^{1}H NMR δ 7.62 (d, *J* = 8.2 Hz, 2H), 7.24-7.17 (m, 7H), 7.12 (dd, *J* = 1.6, 8.2 Hz, 1H), 7.06-7.00 (m, 5H), 6.96 (dd, *J* = 7.4, 7.4 Hz, 2H), 3.91 (brs, 1H), 3.08 (brs, 1H), 2.40 (s, 3H), 2.25 (s, 3H), 2.01 (dd, *J* = 2.4, 2.4 Hz, 1H); ^{13}C NMR δ 148.0, 144.7, 143.6, 137.0, 135.3, 135.2, 132.2, 130.7, 129.6, 129.1, 129.1, 128.6, 123.3, 122.4, 78.5, 73.7, 38.3, 21.7, 20.9; HRMS (ESI, positive): *m/z* calcd. For $C_{29}H_{26}N_2NaO_2S$ ($[M+Na]^+$) 489.1607, found 489.1608

_N_-(2-(Diphenylamino)-5-(trifluoromethyl)phenyl)-4-methyl-_N_-(prop-2-yn-1-yl)benzenesulfonamide (13e)

Isolated by silica gel column chromatography (hexane/ethyl acetate = 10/1). The title compound was obtained as a white solid, 9% in total yield; mp 121-122 °C; ^{1}H NMR δ 7.59 (d, *J* = 8.3 Hz, 2H), 7.50 (dd, *J* = 2.1, 8.5 Hz, 1H), 7.38 (d, *J* = 8.5 Hz, 1H), 7.35-7.22 (m, 7H), 7.14-7.04 (m, 6H), 3.97 (brs, 1H), 2.92 (brs, 1H), 2.42 (s, 3H), 2.01 (dd, *J* = 2.4, 2.4 Hz, 1H); ^{13}C NMR δ 151.7, 147.7, 144.2, 136.2, 134.4, 129.5, 129.4 (q, *J* = 3.9 Hz), 129.3, 128.6, 128.6, 126.6 (q, *J* = 3.3 Hz,), 125.6 (q, *J* = 33.4 Hz), 124.6, 123.9, 123.7 (q, *J* = 272.4 Hz), 77.9, 74.5, 38.0, 21.7; HRMS (ESI, positive): *m/z* calcd. For $C_{29}H_{23}F_3N_2NaO_2S$ ($[M+Na]^+$) 543.1325, found 543.1326

_N_-(2-(Diphenylamino)phenyl)-4-methyl-_N_-(3-phenylprop-2-yn-1-yl)benzenesulfonamide (13f)

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as a white solid, 58%; mp 159 °C; ^{1}H NMR δ 7.68 (d, *J* = 7.1 Hz, 2H), 7.39-7.29 (m, 2H), 7.29-7.20 (m, 8H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 4H), 7.08-7.03 (m, 3H), 7.01 (dd, *J* = 6.9, 6.9 Hz, 2H), 4.18 (brs, 1H), 3.15 (brs, 1H), 2.34 (s, 3H); ^{13}C NMR δ 148.2 148.2, 143.4, 137.4, 135.8, 131.5, 131.4, 129.9, 129.5, 129.3, 129.2, 128.7, 128.4, 128.3, 124.9, 123.9, 122.7, 122.6, 85.4, 84.1, 39.3, 21.6; HRMS (ESI, positive): *m/z* calcd for $C_{34}H_{28}N_2NaO_2S$ ($[M+Na]^+$) 551.1765, found 551.1764.

_N_-(2-(Diphenylamino)phenyl)-_N_-(3-(4-methoxyphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (13g)

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as a light yellow solid, 56%; mp 114 °C; ^{1}H NMR δ 7.68 (d, *J* = 8.2 Hz, 2H), 7.39-7.27 (m, 2H), 7.27-7.21

(m, 5H), 7.20-7.14 (m, 2H), 7.11 (dd, *J* = 0.7, 7.7 Hz, 3H), 7.07-6.96 (m, 6H), 6.76 (d, *J* = 8.4 Hz, 2H), 4.16 (brs, 1H), 3.79 (s, 3H), 3.13 (br, 1H), 2.35 (s, 3H); ^{13}C NMR δ 159.7, 148.2, 148.2, 143.3, 137.4, 135.8, 132.9, 131.5, 129.9, 129.5, 129.3, 129.2, 128.7, 124.9, 123.9, 122.7, 114.7, 113.9, 85.3, 82.6, 55.4, 39.4, 21.6; HRMS (ESI, positive): *m/z* calcd for $C_{35}H_{30}N_2NaO_3S$ ([M+Na]$^+$) 581.1869, found 581.1869.

_N_-(2-(Diphenylamino)phenyl)-_N_-(3-(3-methoxyphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (13h)

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as a yellow solid, 50%; mp 114 °C; ^{1}H NMR δ 7.68 (d, *J* = 8.2 Hz, 2H), 7.38-7.34 (m, 1H), 7.33-7.28 (m, 1H), 7.28-7.17 (m, 7H), 7.16-7.08 (m, 5H), 7.07-6.98 (m, 3H), 6.83 (dd, *J* = 2.4, 8.3 Hz, 1H), 6.65 (d, *J* = 7.6 Hz, 1H), 6.59 (s, 1H), 4.17 (brs, 1H), 3.77 (s, 3H), 3.13 (brs, 1H), 2.35 (s, 3H); ^{13}C NMR δ 159.3, 148.2, 148.2, 143.5, 137.3, 135.8, 131.4, 129.9, 129.5, 129.3, 129.3, 129.2, 128.7, 124.9, 124.0, 123.9, 123.6, 122.7, 117.0, 114.4, 85.3, 84.0, 55.4, 39.2, 21.6; HRMS (ESI, positive): *m/z* calcd for $C_{35}H_{30}N_2NaO_3S$ ([M+Na]$^+$) 581.1869, found 581.1869.

_N_-(2-(Diphenylamino)phenyl)-_N_-(3-(2-methoxyphenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (13i)

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as a light red solid, 51%; mp 189 °C; ^{1}H NMR δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.40-7.33 (m, 2H), 7.32-7.27 (m, 1H), 7.27-7.21 (m, 5H), 7.15-7.07 (m, 6H), 7.06-6.97 (m, 3H), 6.95 (dd, *J* = 1.8, 7.7 Hz, 1H), 6.86-6.77 (m, 2H), 4.23 (brs, 1H), 3.77 (s, 3H), 3.14 (brs, 1H), 2.27 (s, 3H); ^{13}C NMR δ 160.1, 148.3, 148.2, 143.2, 137.2, 135.8, 133.3, 131.8, 129.8, 129.8, 129.3, 129.2, 129.1, 128.8, 124.7, 123.9, 122.7, 120.3, 111.9, 110.5, 88.1, 82.1, 55.6, 39.6, 21.6; HRMS (ESI, positive): *m/z* calcd for $C_{35}H_{30}N_2NaO_3S$ ([M+Na]$^+$) 581.1868, found 581.1869.

_N_-(2-(Diphenylamino)phenyl)-4-methyl-_N_-(3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-yl)benzenesulfonamide (13j)

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as a white solid, 62%; mp 154 °C; ^{1}H NMR δ 7.67 (d, *J* = 6.7 Hz, 2H), 7.50 (d, *J* = 7.8 Hz, 2H), 7.39-7.30 (m, 2H), 7.22-7.29 (m, 5H), 7.17 (dd, *J* = 7.4, 7.7 Hz, 4H), 7.13-7.04 (m, 5H), 7.01 (t, *J* = 7.4 Hz, 2H), 4.18 (brs, 1H), 3.19 (brs, 1H), 2.35 (s, 3H); ^{13}C NMR δ 148.2, 148.1, 143.5, 137.3, 135.7, 131.7, 131.3, 130.2 (q, *J* = 33.1 Hz), 130.1, 129.7, 129.3, 129.2, 128.7, 126.4 (q, *J* = 1.5 Hz), 125.2 (q, *J* = 3.9 Hz), 124.9, 123.9, 123.9 (q, *J* = 271.8 Hz), 122.8, 86.8, 84.1, 39.1, 21.6 HRMS (ESI, positive): *m/z* calcd for $C_{35}H_{27}F_3N_2NaO_2S$ ([M+Na]$^+$) 619.1634, found 619.1638.

_N_-(2-(Diphenylamino)phenyl)-_N_-(3-(4-fluorophenyl)prop-2-yn-1-yl)-4-methylbenzenesulfonamide (13k)

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as a white solid, 28%; mp 147 °C; ^{1}H NMR δ 7.67 (d, *J* = 8.2 Hz, 2H), 7.38-7.29 (m, 2H), 7.28-7.20 (m, 5H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 4H), 7.07-6.98 (m, 5H), 6.93 (dd, *J* = 8.7, 8.7 Hz, 2H), 4.13 (brs, 1H), 3.14(brs, 1H), 2.34 (s, 3H); ^{13}C NMR δ 162.6 (d, *J* = 250.0 Hz), 148.2, 148.2, 143.4, 137.4, 135.8, 133.4 (d, *J* = 8.3 Hz), 131.4, 129.9, 129.6, 129.3, 129.2, 128.7, 124.9, 123.9, 122.8, 118.7 (d, *J* = 3.6 Hz), 115.6 (d, *J* = 22.1 Hz), 84.4, 83.8 (d, *J* = 1.5 Hz), 39.2, 21.6; HRMS (ESI, positive): *m/z* calcd for $C_{34}H_{27}FN_2NaO_2S$ ([M+Na]$^{+}$) 569.1669, found 569.1669.

_N_-(3-(4-Chlorophenyl)prop-2-yn-1-yl)-_N_-(2-(diphenylamino)phenyl)-4-methylbenzenesulfonamide (13l)

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as a light yellow solid, 79%; mp 165 °C; ^{1}H NMR δ 7.70-7.62 (m, 2H), 7.39-7.29 (m, 2H), 7.27-7.14 (m, 9H), 7.13-7.08 (m, 4H), 7.07-7.03 (m, 1H), 7.03-6.93 (m, 4H), 4.13 (brs, 1H), 3.14 (brs, 1H), 2.35 (s, 3H); ^{13}C NMR δ 148.2, 148.2, 143.5, 137.3, 135.7, 134.5, 132.7, 131.3, 130.0, 129.6, 129.3, 129.2, 128.7, 128.6, 124.9, 123.9, 122.8, 121.1, 85.2, 84.3, 39.2, 21.6; HRMS (ESI, positive): *m/z* calcd for $C_{34}H_{27}ClN_2NaO_2S$ ([M+Na]$^{+}$) 585.1374, found 585.1374.

Ethyl 4-((_N_-(2-(diphenylamino)phenyl)-4-methylphenyl)sulfonamido)but-2-ynoate (13m)

Isolated by PTLC (dichloromethane). The title compound was obtained as a white solid, 34%; mp 128 °C; ^{1}H NMR δ 7.63 (d, *J* = 8.2 Hz, 2H), 7.36-7.29 (m, 2H), 7.27-7.20 (m, 7H), 7.10-7.02 (m, 6H), 7.00 (dd, *J* = 7.4, 7.4 Hz, 2H), 4.15 (q, *J* = 7.2 Hz, 2H), 4.07 (brs, 1H), 3.03 (brs, 1H), 2.41 (s, 3H), 1.27(t, *J* = 7.2 Hz, 3H); ^{13}C NMR δ 152.9, 148.2, 148.1, 143.9, 136.4, 135.0, 131.5, 130.3, 129.6, 129.5, 129.3, 128.6, 125.2, 123.8, 122.9, 82.2, 77.3, 62.1, 38.3, 21.7, 14.1, ; HRMS (ESI, positive): *m/z* calcd for $C_{31}H_{28}N_2NaO_4S$ ([M+Na]$^{+}$)547.1663, found 547.1662.

_N_-(2-(Diphenylamino)phenyl)-4-methyl-_N_-(3-(_p_-tolyl)prop-2-yn-1-yl)benzenesulfonamide (13o)

Isolated by PTLC (hexane/dichloromethane = 1/2) The title compound was obtained as a white solid, 53%; mp 159 °C; ^{1}H NMR δ 7.68 (d, *J* = 8.1 Hz, 2H), 7.37-7.33 (m, 1H), 7.33-7.28 (ddd, *J* = 1.6, 7.3, 7.3 Hz, 1H), 7.28-7.21 (m, 5H), 7.18 (d, *J* = 8.1 Hz, 2H), 7.11 (dd, *J* = 0.7, 8.1 Hz, 4H), 7.03-6.97 (m, 5H), 6.95 (d, *J* = 7.9 Hz, 2H), 4.18 (brs, 1H), 3.12 (brs, 1H), 2.35 (s, 3H), 2.32 (s, 3H); ^{13}C NMR δ 148.2, 148.2, 143.4, 138.6, 137.4, 135.8, 131.5, 131.4, 129.9, 129.5, 129.3, 129.2,

129.0, 128.7, 124.9, 123.9, 122.7, 119.5, 85.5, 83.4, 39.3, 21.6, 21.6; HRMS (ESI, positive):*m/z* calcd for $C_{35}H_{30}N_2NaO_2S$ ($[M+Na]^+$) 565.1924, found 565.1920.

General procedure for the cycloisomerization in Table 7, and 8

2-Propargyltosylaminodiphenylaniline derivative **13** (0.050 mmol) was placed in a Schlenk tube in air. This reaction vessel was evacuated and backfilled with argon (×3), then gold(I) complex (10 mol%) and silver salt (10 mol%) were placed to the reaction vessel in globe box. After solvent (0.5 ml) was added, the solution was stirred at room temperature for 1 h. The solution was filtered by silica gel. After removal of solvent, the crude products were filtered by short column, and purified by PTLC to give desired cyclized product **14**.

7-Methylene-12-phenyl-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b,e*][1,4]diazocine (14a)

Isolated by PTLC (dichloromethane). The title compound was obtained as a brown solid 99%; mp 146-148 °C; ^{1}H NMR δ 7.80-7.74 (m, 1H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.34 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.28-7.22 (m, 3H), 7.20-7.16 (m, 2H), 7.12 (d, *J* = 8.2 Hz, 2H), 7.04 (dd, *J* = 8.1, 8.1 Hz, 2H), 6.90 (d, *J* = 8.1 Hz, 2H), 6.78 (dd, *J* = 7.2, 7.2 Hz, 1H) 6.42 (d, *J* = 8.6 Hz, 2H), 5.38 (s, 1H), 5.20 (s, 1H), 4.54 (s, 2H), 2.29 (s, 3H); ^{13}C NMR δ 147.8, 143.6, 143.3, 131.8, 139.7, 139.6, 137.0, 136.0, 131.2, 130.4, 129.5, 129.4, 129.0, 128.5, 127.7, 127.4, 126.8, 126.7, 126.6, 119.2, 117.8, 115.4, 54.7, 21.6; HRMS (ESI, positive): *m/z* calcd. For $C_{28}H_{24}N_2NaO_2S$ ($[M+Na]^+$) 475.1451, found 475.1452.

8,10-Dimethoxy-7-methylene-12-phenyl-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b,e*][1,4]diazocine (14b)

Isolated by PTLC (hexane/ethyl acetate = 5/1). The title compound was obtained as a light yellow solid, >99%; mp 146 °C; ^{1}H NMR δ 7.71 (d, *J* = 7.6 Hz, 1H), 7.28-7.22 (m, 2H), 7.20-7.12 (m, 3H), 7.04 (dd, *J* = 8.0, 8.0 Hz, 2H), 6.94 (d, *J* = 7.9 Hz, 2H), 6.79 (dd, *J* = 6.9 Hz, 1H), 6.48 (d, *J* = 8.2 Hz, 2H), 6.37 (d, *J* = 2.3 Hz, 1H), 6.33 (d, *J* = 2.3 Hz, 1H), 5.40 (s, 1H), 5.34 (s, 1H), 4.36 (s, 2H), 3.78 (s, 3H), 3.70 (s, 3H), 2.30 (s, 3H); ^{13}C NMR δ 160.4, 159.2, 147.6, 144.4, 143.0, 139.9, 137.3, 136.8, 135.5, 130.7, 129.4, 129.0, 127.7, 127.4, 126.8, 126.7, 121.4, 120.4, 119.5, 116.2, 104.0, 97.1, 56.3, 55.9, 55.5, 21.6; HRMS (ESI, positive):*m/z* calcd for $C_{30}H_{28}N_2NaO_4S$ ($[M+Na]^+$) 535.1662, found 535.1662.

12-(4-Fluorophenyl)-7-methylene-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b,e*][1,4]diazocine (14c)

Isolated by PTLC (hexane/ethyl acetate = 5/1). The title compound was obtained as yellow oil, 99%; ^{1}H NMR δ 7.79-7.74 (m, 1H), 7.41 (dd, *J* = 1.4, 7.6 Hz, 1H), 7.30-7.26 (m, 1H), 7.23-7.11

(m, 7H), 6.90 (d, *J* = 8.1 Hz, 2H), 6.72-6.64 (m, 2H), 6.39-6.28 (m, 2H), 5.37 (s, 1H), 5.21 (s, 1H), 4.55 (s, 2H), 2.29 (s, 3H); ^{13}C NMR δ 156.9 (d, *J* = 237.9 Hz), 144.2 (d, *J* = 1.9 Hz), 143.5, 142.9, 142.6, 139.7, 139.0, 137.5, 136.0, 131.4, 130.3, 129.5, 129.4, 128.5, 127.5, 127.0 (d, *J* = 5.0 Hz), 126.2, 118.9, 116.9, 116.9, 115.6, 115.4, 54.5, 21.5; HRMS (ESI, positive):*m/z* calcd for $C_{28}H_{23}FN_2NaO_2S$ ($[M+Na]^+$) 493.1357, found 493.1356.

3-Methyl-7-methylene-12-phenyl-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b,e*][1,4]diazocine (14d)

Isolated by PTLC (hexane/diethyl ether = 1/1). The title compound was obtained as brown oil, 82%; ^{1}H NMR δ 8.00 (d, *J* = 1.8 Hz, 1H), 7.55 (dd, *J* = 1.6, 7.3 Hz, 1H), 7.42-7.33 (m, 4H), 7.18 (dd, *J* = 1.4, 7.7 Hz, 1H), 7.10-7.02 (m, 4H), 6.92 (d, *J* = 8.0 Hz, 2H), 6.81 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.40 (d, *J* = 7.9 Hz, 2H), 5.37 (s, 1H), 5.19 (s, 1H), 4.56 (s, 2H), 2.28 (s, 3H), 1.55 (s, 3H); ^{13}C NMR δ 147.9, 143.3, 143.3, 142.3, 139.2, 139.2, 136.9, 135.9, 134.4, 131.0, 130.3, 129.4, 129.4, 129.0, 128.2, 128.1, 127.7, 126.2, 119.0, 118.3, 115.5, 54.5, 21.6, 21.4 (a pair of aromatic peaks was overlapped) ; HRMS (ESI, positive): *m/z* calcd. For $C_{29}H_{26}N_2NaO_2S$ ($[M+Na]^+$) 489.1607, found 489.1606.

7-Methylene-12-phenyl-5-tosyl-3-trifluoromethyl-5,6,7,12-tetrahydrodibenzo[*b,e*][1,4] diazocine (14e)

Isolated by PTLC (hexane/diethyl ether = 1/1). The title compound was obtained as a brown solid, 95%; mp 149-151 °C; ^{1}H NMR δ 8.00 (d, *J* = 1.8 Hz, 1H), 7.55 (dd, *J* = 1.7, 7.4 Hz, 1H), 7.42-7.33 (m, 4H), 7.81 (dd, *J* = 1.4, 7.7 Hz, 1H), 7.09-7.02 (m, 4H), 6.91 (d, *J* = 8.2 Hz, 2H), 6.80 (dd, *J* = 7.4 Hz, 1H), 6.39 (d, *J* = 7.8 Hz, 2H), 5.36 (s, 1H), 5.19 (s, 1H), 4.56 (s, 2H), 2.28 (s, 3H); ^{13}C NMR δ 147.3, 144.1, 144.0, 140.3, 140.2, 140.0, 139.2, 135.3, 130.9, 130.8, 129.8, 129.7, 129.5, 129.2, 128.0, 127.7, 124.7 (q, *J* = 21.5 Hz), 123.7 (q, *J* = 272.7 Hz), 123.5 (q, *J* = 4.5 Hz), 123.0 (q, *J* = 3.9 Hz), 119.9, 116.5, 115.4, 54.7, 21.6; HRMS (ESI, positive): *m/z* calcd. For $C_{29}H_{23}F_3N_2NaO_2S$ ($[M+Na]^+$) 543.1325, found 543.1326.

(*E*)-7-Benzylidene-12-phenyl-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b*,*e*][1,4]diazocine (14f)

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as a yellow solid, 94%. The stereochemistry was determined by the correlation between the vinylic and methylene protons in the NOESY spectrum; mp 196 °C; ^{1}H NMR δ 7,71-7.62 (m, 1H), 7.32-7.24 (m, 2H), 7.23-7.13 (m, 4H), 7.13-7.03 (m, 7H), 6.97-6.86 (m, 3H), 6.85-6.74 (m, 3H), 6.60 (d, *J* = 8.6 Hz, 2H), 6.53 (s, 1H), 4.54 (brs, 1H), 4.43 (brs, 1H), 2.28 (s, 3H); ^{13}C NMR 147.8, 143.5, 143.3, 139.7, 137.7, 136.7, 136.1, 135.1, 135.1, 133.0, 132.3, 130.8, 129.5, 129.2, 129.0, 128.9, 128.0, 128.0, 127.7, 127.6, 127.2, 126.9, 126.8, 124.9, 119.9, 116.8, 57.0, 21.6; HRMS (ESI, positive):*m/z*

calcd for $C_{34}H_{28}N_2NaO_2S$ ($[M+Na]^+$) 551.1764, found 551.1764.

(*E*)-7-(4-Methoxybenzylidene)-12-phenyl-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b*,*e*][1,4] diazocine (14g)

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as colorless oil, 41%; ^{1}H NMR δ 8.24 (s, 1H), 7.78 (dd, *J* = 1.4, 7.9 Hz, 1H), 7.65 (dd, *J* = 1.5, 8.2 Hz, 1H), 7.40 (dd, *J* = 1.5, 7.9 Hz, 1H), 7.36 (d, *J* = 8.6 Hz, 2H), 7.22-7.18 (m, 2H), 7.18-7.12 (m, 4H), 7.12-7.00 (m, 5H), 6.91-6.88 (m, 2H), 6.82 (s, 1H), 6.79 (d, *J* = 8.2 Hz, 2H), 4.08 (s, 2H), 3.81 (s, 3H), 2.20 (s, 3H); ^{13}C NMR δ 158.3, 148.7, 148.1, 143.2, 142.8, 136.6, 136.0, 135.8, 134.6, 132.6, 132.2, 130.5, 129.9, 129.3, 129.2, 128.6, 128.0, 127.4, 126.9, 125.3, 125.0, 124.8, 123.6, 123.4, 120.1, 114.2, 55.4, 42.8, 21.5; HRMS (ESI, positive): *m/z* calcd for $C_{35}H_{30}N_2NaO_3S$ ($[M+Na]^+$) 581.1870, found 581.1869.

(*E*)-7-(3-Methoxybenzylidene)-12-phenyl-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b*,*e*][1,4] diazocine (14h)

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as a yellow solid, 53%; mp 91 °C; ^{1}H NMR δ 7.66 (dd, *J* = 1.6, 8.8 Hz, 1H), 7.30-7.26 (m, 1H), 7.25-7.04 (m, 9H), 7.00 (dd, *J* = 7.9, 7.9 Hz, 1H), 6.96-6.89 (m, 3H), 6.82 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.63 (dd, *J* = 2.4, 8.4 Hz, 1H), 6.59 (d, *J* = 4.0 Hz, 2H), 6.51 (s, 1H), 6.43 (d, *J* = 4.0 Hz, 1H), 6.27 (s, 1H), 4.54 (brs, 1H), 4.42 (brs, 1H), 3.54 (s, 3H), 2.29 (s, 3H); ^{13}C NMR δ 159.2, 147.9, 143.5, 143.3, 139.8, 138.1, 137.8, 136.7, 136.2, 135.4, 133.1, 132.4, 130.8, 129.5, 129.2, 129.1, 129.0, 128.1, 127.8, 127.6, 126.9, 126.9, 124.9, 121.7, 120.0, 116.9, 113.8, 113.6, 57.0, 55.1, 21.6; HRMS (ESI, positive): *m/z* calcd for $C_{35}H_{30}N_2NaO_3S$ ($[M+Na]^+$) 581.1869, found 581.1869.

(*E*)-7-(2-Methoxybenzylidene)-12-phenyl-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b*,*e*][1,4] diazocine (14i)

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as brown oil, 50%; ^{1}H NMR δ 7.70 (d, *J* = 8.2 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.25-7.11 (m, 6H), 7.06 (dd, *J* = 8.0, 8.0 Hz, 3H), 7.00 (d, *J* = 7.8 Hz, 1H), 6.91 (d, *J* = 8.1 Hz, 2H), 6.81 (q, *J* = 8.2 Hz, 2H), 6.77 (d, *J* = 4.3 Hz, 1H), 6.68 (s, 1H), 6.58 (d, *J* = 8.1 Hz, 2H), 6.45 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.04 (d, *J* = 7.7 Hz, 1H), 4.69 (brs, 1H), 4.26 (brs, 1H), 3.81 (s, 3H), 2.29 (s, 3H); ^{13}C NMR δ 157.6, 147.8, 144.0, 143.1, 140.2, 137.8, 136.6, 136.2, 133.9, 132.7, 131.6, 130.2, 129.8, 129.5, 129.2, 128.8, 128.5, 127.7, 127.4, 127.1, 126.6, 125.9, 124.4, 120.0, 119.8, 116.9, 110.4, 56.8, 55.5, 21.6 (a pair of peaks at the aromatic region was overlapped); HRMS (ESI, positive): *m/z* calcd for $C_{35}H_{30}N_2NaO_3S$ ($[M+Na]^+$) 581.1868, found 581.1869.

(*E*)-12-Phenyl-5-tosyl-7-(4-(trifluoromethyl)benzylidene)-5,6,7,12-tetrahydrodibenzo[*b*,*e*][1,4] diazocine (14j)

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as a white solid, 85%; mp 172 °C; ^{1}H NMR δ 7.64 (dd, *J* = 1.5, 8.2 Hz, 1H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.31-7.23 (m, 4H), 7.20-7.01 (m, 6H), 6.86-6.98 (m, 5H), 6.83 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.58 (d, *J* = 8.1 Hz, 2H), 6.52 (s, 1H), 4.54 (brs, 1H), 4.51 (brs, 1H), 2.30 (s, 3H); ^{13}C NMR δ 147.8, 143.7, 143.5, 140.4, 139.7, 138.2, 137.7, 136.2, 136.1, 133.0, 130.7, 130.1, 129.5, 129.5, 129.2, 129.2, 129.0 (q, *J* = 32.2 Hz), 128.1, 127.8, 127.7, 127.0, 126.9, 125.3, 125.1 (q, *J* = 3.9 Hz), 124.6 (q, *J* = 237.5 Hz), 120.2, 116.9, 56.9, 21.6 HRMS (ESI, positive): *m/z* calcd for $C_{35}H_{27}F_3N_2NaO_2S$ ($[M+Na]^+$) 619.1635, found 619.1638.

(*E*)-7-(4-Fluorobenzylidene)-12-phenyl-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b*,*e*][1,4]diazocine (14k)

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as a yellow solid, 87%; mp 193 °C; ^{1}H NMR δ 7.65 (dd, *J* = 1.4, 8.0 H, 1H), 7.30-7.20 (m, 4H), 7.20-7.11 (m, 3H), 7.08 (dd, *J* = 7.7, 7.7 Hz, 3H), 6.97-6.88 (m, 3H), 6.82 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.76 (d, *J* = 7.2 Hz, 4H), 6.58 (d, *J* = 8.0 Hz, 2H), 6.47 (s, 1H), 4.52 (brs, 1H), 4.42 (brs, 1H), 2.29 (s, 3H); ^{13}C NMR δ 162.0 (d, *J* = 217.8 Hz), 147.8, 143.7, 143.4, 139.8, 137.7, 136.1, 136.5, 135.3 (d, *J* = 1.2 Hz), 132.9, 132.8, 132.8, 131.0, 130.8, 130.6 (d, *J* = 8.1 Hz), 129.5, 129.2, 129.1, 128.0, 127.8, 126.9 (d, *J* = 4.2 Hz), 125.0, 120.0, 116.9, 115.1 (d, *J* = 21.5 Hz), 57.0, 21.6 (a pair of peaks at the aromatic region was overlapped.); HRMS (ESI, positive): *m/z* calcd for $C_{34}H_{27}FN_2NaO_2S$ ($[M+Na]^+$) 569.1669, found 569.1669.

(*E*)-7-(4-Chlorobenzylidene)-12-phenyl-5-tosyl-5,6,7,12-tetrahydrodibenzo[*b*,*e*][1,4]diazocine (14l)

Isolated by PTLC (hexane/dichloromethane = 1/2). The title compound was obtained as a yellow solid, 89%; mp 210 °C; ^{1}H NMR δ 7.64 (d, *J* = 8.0 Hz, 1H), 7.32-7.21 (m, 4H), 7.20-7.10 (m, 3H), 7.08 (t, *J* = 7.3 Hz, 3H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.96-6.89 (m, 3H), 6.82 (dd, *J* = 7.2, 7.2 Hz, 1H), 6.72 (d, *J* = 8.3 Hz, 2H), 6.57 (d, *J* = 8.2 Hz, 2H), 6.45 (s, 1H), 4.52 (brs, 1H), .4.44 (brs, 1H), 2.29 (s, 3H); ^{13}C NMR δ 147.8, 143.6, 143.4, 139.7, 137.7, 136.4, 136.2, 136.1, 135.2, 133.0, 132.9, 130.8, 130.7, 130.3, 129.5, 129.5, 129.2, 128.3, 127.9, 127.9, 127.7, 126.9, 126.9, 125.1, 120.1, 116.9, 57.0, 21.6; HRMS (ESI, positive): *m/z* calcd for $C_{34}H_{27}O_2ClNaO_2S$ ($[M+Na]^+$) 585.1373, found 585.1374.

Ethyl (*E*)-2-(12-phenyl-5-tosyl-5,12-dihydrodibenzo[*b,e*][1,4]diazocin-7(6H)-ylidene)acetate (14m)

Isolated by PTLC (dichloromethane). The title compound was obtained as yellow oil, 98%; ^{1}H NMR δ 7.62 (dd, *J* = 1.5, 7.7 Hz, 1H),7.31-7.51 (m, 4H), 7.17 (dd, *J* = 1.1, 8.0 Hz, 1H), 6.99-7.14 (m, 8H), 6.76 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.51 (d, *J* = 7.8 Hz, 2H), 5.73 (s, 1H), 4.88 (brs, 1H), 4.20 (brs, 1H), 4.02 (q, *J* = 7.1 Hz, 2H), 2.31 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR δ 165.1, 154.6, 147.4, 143.9, 140.8, 139.2, 137.4, 137.1, 136.3, 134.0, 130.8, 129.6, 129.6, 129.6, 128.9, 127.9, 126.5, 126.4, 125.9, 125.1, 119.6, 116.9, 115.1, 60.1, 56.4, 21.6, 14.2; HRMS (ESI, positive): *m/z* calcd for $C_{31}H_{28}N_2NaO_4S$ ([M+Na]$^+$) 547.1661, found 547.1662.

4-(4-methoxyphenyl)-*N*,*N*-diphenyl-1-tosyl-1,2-dihydroquinolin-8-amine (14g')

Isolated by PTLC (hexane/dichloromethane = 1/2) The title compound was obtained as a white solid, 70%; mp 237 °C; ^{1}H NMR δ 7.42 (d, *J* = 8.2 Hz, 2H), 7.30-7.14 (m, 9H), 7.09-6.99 (m, 5H), 6.79-6.73 (m, 2H), 6.70-6.60 (m, 3H), 5.36 (dd, *J* = 2.6, 6.0 Hz, 1H), 4.26 (dd, *J* = 6.0, 18.2 Hz, 1H), 3.80 (s, 3H), 3.26 (dd, *J* = 2.6, 18.6 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR δ 159.2, 146.5, 143.2, 138.5, 137.3, 134.9, 130.5, 129.9, 129.2, 129.2, 129.1, 128.9, 128.6, 128.2, 127.7, 127.5, 122.7, 121.5, 113.3, 55.4, 53.6, 44.1, 21.5; HRMS (ESI, positive): *m/z* calcd for $C_{35}H_{30}N_2NaO_3S$ ([M+Na]$^+$) 581.1870, found 581.1869.

***N*,*N*-diphenyl-4-(*p*-tolyl)-1-tosyl-1,2-dihydroquinolin-8-amine (14o')**

Isolated by PTLC (hexane/dichloromethane = 1/2) The title compound was obtained as light yellow oil, 43%; ^{1}H NMR δ 7.44-7.40 (m, 2H), 7.30-7.15 (m, 9H), 7.08-6.99 (m, 7H), 6.66-6.59 (m, 3H), 5.39 (dd, *J* = 2.5, 6.0 Hz, 1H), 4.27 (dd, *J* = 6.0, 18.3 Hz, 1H), 3.27 (dd, *J* = 2.3, 18.4 Hz, 1H), 2.33 (s, 3H), 2.27 (s, 3H); ^{13}C NMR δ146.5, 143.2, 138.9, 137.4, 137.2, 135.2, 134.8, 129.7, 129.5, 129.3, 129.0, 128.9, 128.7, 128.6, 128.5, 128.1, 127.6, 127.5, 123.0, 121.6, 44.1, 21.5, 21.3; HRMS (ESI, positive): *m/z* calcd for $C_{35}H_{30}N_2NaO_2S$ ([M+Na]$^+$) 565.1920, found 565.1920.

***N*,*N*-Diphenyl-2-(prop-2-yn-1-yloxy)aniline (15)**

Isolated by flash silica gel column chromatography (hexane/ethyl acetate = 9/1). The title compound was obtained as brown oil, 81%; ^{1}H NMR δ 7.24-7.16 (m, 6H), 7.12 (dd, *J* = 0.9, 7.9 Hz, 1H), 7.05-6.97 (m, 5H), 6.93 (dd, *J* = 7.3, 7.3 Hz, 2H), 4.48 (d, *J* = 2.4 Hz, 2H), 2.40 (dd, *J* = 2.4 Hz, 1H); ^{13}C NMR δ 154.0, 147.7, 136.8, 130.2, 129.0, 126.5, 123.2, 122.0, 121.8, 116.6, 78.8, 75.4, 56.8; HRMS (ESI, positive): m/z calcd. For $C_{21}H_{17}NNaO$ ([M+Na]$^+$) 322.1202, found 322.1202.

_N_,_N_-Diphenyl-2H-chromen-8-amine (16')

Isolated by PTLC (hexane/ethyl acetate = 15/1). The title compound was obtained as orange oil, 59%; ^{1}H NMR δ 7.23-7.15 (m, 4H), 7.07-7.00 (m, 4H),7.00-6.98 (m, 3H), 6.83 (d, J = 4.9 Hz, 2H), 6.41 (dt, J_t = 1.8 Hz, J_d = 9.9 Hz, 1H), 5.72 (dt, J_t = 3.5, J_d = 9.9 Hz, 1H), 4.52 (dd, J = 1.8, 3.5 Hz, 2H); ^{13}C NMR 150.0, 147.7, 134.3, 129.7, 129.0, 124.7, 124.5, 124.0, 122.8, 121.9, 121.8, 121.7, 65.2; HRMS (ESI, positive): *m/z* calcd. For $C_{21}H_{18}NO$ ($[M+H]^+$) 300.1383, found 300.1383.

4-Methyl-_N_-(2-oxopropyl)-_N_-(2-phenoxyphenyl)benzenesulfonamide (17)

Isolated by PTLC (hexane/ethyl acetate = 4/1). The title compound was obtained as a white solid, 22% in total yield; mp 100-102 °C; ^{1}H NMR δ 7.63 (d, J = 8.3 Hz, 2H), 7.45 (dd, J = 1.7, 7.9 Hz, 1H), 7.29-7.16 (m, 5H), 7.12-7.07 (m, 1H), 7.05 (ddd, J = 1.4, 7.7, 7.7 Hz, 1H), 6.77-6.71 (m, 3H), 4.51 (d, J = 1.8 Hz, 2H), 2.38 (s, 3H), 2.18 (t, J = 2.5 Hz, 1H); ^{13}C NMR δ 155.7, 155.1, 143.5, 137.1, 133.5, 130.0, 129.8, 129.5, 128.2, 127.9, 124.1, 123.0, 119.6, 118.1, 78.5, 73.5, 40.2, 21.6; HRMS (ESI, positive): *m/z* calcd. For $C_{22}H_{19}NNaO_3S$ ($[M+Na]^+$) 400.0978, found 400.0979.

4-Methyl-_N_-(2-oxopropyl)-_N_-(2-phenoxyphenyl)benzenesulfonamide (18')

Isolated by PTLC (hexane/ethyl acetate = 3/1). The title compound was obtained as a brown solid, 72%; mp 88-89 °C; ^{1}H NMR δ 7.62 (d, J = 8.0 Hz, 1H), 7.56 (d, 8.1 Hz, 2H), 7.25 (dd, J = 7.7, 7.7 Hz, 2H), 7.22-7.15 (m, 3H), 7.12-7.03 (m, 2H), 6.66 (d, J = 8.3 Hz, 1H), 6.61 (d, J = 8.6 Hz, 2H), 4.41 (s, 2H), 2.37 (s, 3H), 2.30 (s, 3H); ^{13}C NMR δ 204.9, 155.1, 154.3, 143.7, 136.5, 133.5, 129.9, 129.5, 128.8, 127.9, 124.3, 123.1, 119.5, 117.6, 60.3, 27.3, 21.7 (a pair of aromatic region was overlapped); HRMS (ESI, positive): m/z calcd. For $C_{22}H_{21}NNaO_4S$ ($[M+Na]^+$) 418.1084, found 418.1080.

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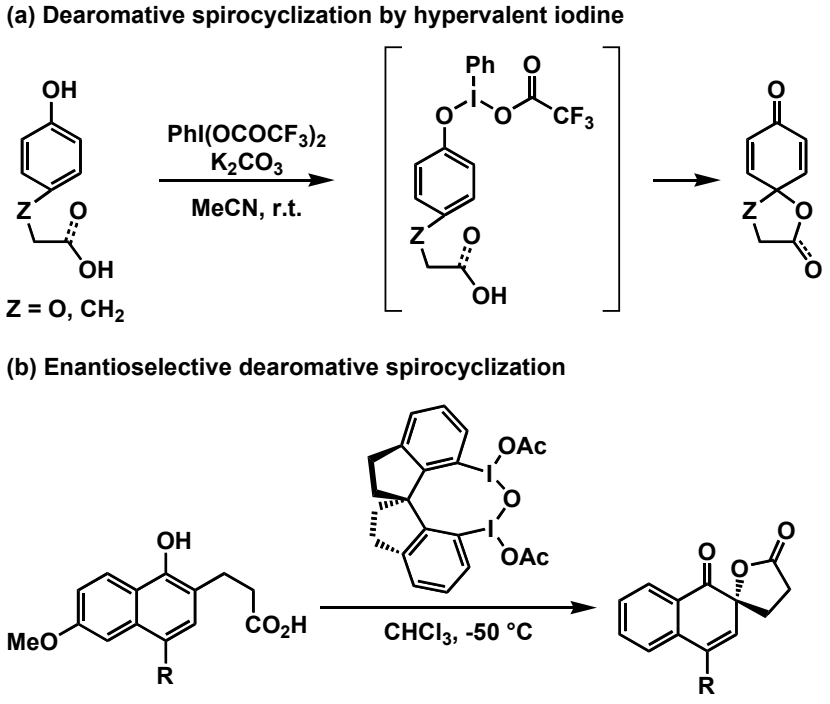
Chapter 3

Catalytic Dearomative Spirocyclization of Phenols via Gold Carbenoid Species Derived from Ynamides

Backgrounds

The spirocyclic skeleton is a unique structure found in various natural products and biologically active compounds.[1] Azaspirocyclic skeleton is also important, because it is a substructure of biologically active gabapentin lactam and a key synthetic intermediate of a natural product, crinine.[2,3] Therefore, many synthetic chemists developed the synthetic strategies for spirocyclic skeletons. One of the most common strategies is the dearomative spirocyclization of phenols to give spirocyclohexadienones, and there are mainly three strategies.[4] The first one is oxidative spirocyclization of phenols. In 1987, Kita and co-workers reported the first example of dearomative spirocyclization of phenols by using hypervalent iodine, where phenols act as an electrophile (Scheme 1a).[5a] The reaction is considered to proceed via phenoxy-λ^3-iodane species, which was intramolecularly attacked by nucleophiles. After their intensive works, they developed an enantioselective spirocyclization of phenols using chiral hypervalent iodine in 2008 (Scheme 1b).[5b] This reaction was the first example of highly enantioselective reaction mediated by chiral hypervalent iodine. The rigid structure of 1,1'-spirobiindane skeleton of chiral hypervalent iodine was the key to high enantioselectivity, and the use of *m*CPBA as a co-oxidant could lower the loading of hypervalent iodine to a catalytic amount.

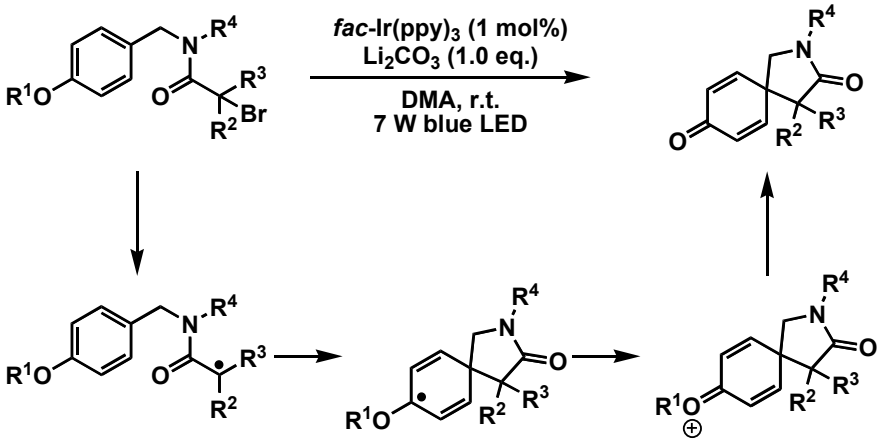
Scheme 1. Oxidative spirocyclization of phenols by hypervalent iodine



The second one is radical spirocyclization. In 2016, Zhang and co-workers reported the radical spirocyclization of phenols under mild conditions using photocatalyst (*fac*-Ir(ppy)$_3$) and blue LED

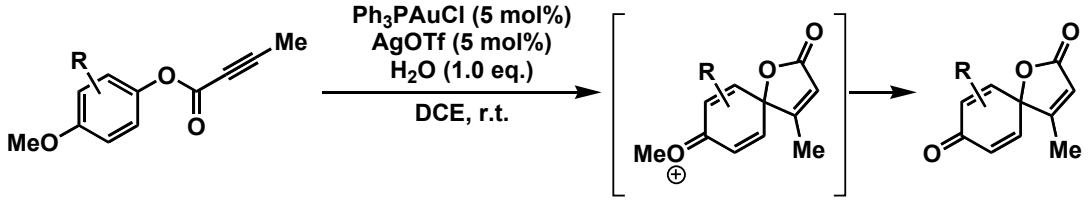
(Scheme 2).[6] The visible light excited the Ir(III) catalyst to generate Ir(III)* species. Ir(III)* species gave a single electron to bromo compound along with the homolytic cleavage of C-Br bond to provide a radical intermediate and Ir(IV) complex. The resulting radical intermediate underwent C-C bond formation at the *ipso*-position and a single electron transferred to Ir(IV) complex to complete the catalytic cycle along with the formation of an oxonium intermediate. It was converted to the product by aid of base.

Scheme 2. Radical spirocyclization of phenols



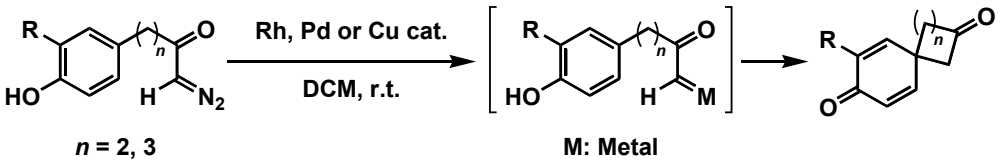
The third one is *ipso*-Friedel-Crafts-type spirocyclization. In 2014, Aparece and Vadola developed gold(I)-catalyzed 5-*endo-dig* spirocyclization of alkyne-containing phenol derivatives, where anisyl moiety acts as a nucleophile to alkyne (Scheme 3).[7] They found that the use of H_2O as an additive promoted the dearomative spirocyclization and the anhydrous condition induced 6-*endo-dig* hydroarylation to give coumarin selectively. The presence of water was considered important for the demethylation from an oxonium intermediate.

Scheme 3. *ipso*-Friedel-Crafts type spirocyclization of phenol derivatives



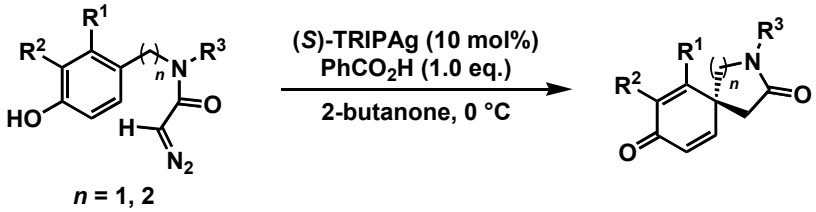
Metal carbenoid species were used for the *ipso*-Fridel-Crafts-type spirocyclization.[8,9] For a pioneering work, Iwata and co-workers reported transition metal-catalyzed dearomative spirocyclization of phenols using metal carbenoid species prepared from diazoketones in 1985 (Scheme 4).[8b,8c] They used rhodium, palladium, and copper catalysts for the generation of metal carbenoid species. However, the scope of substrates was limited.

Scheme 4. Dearomative spirocyclization via metal carbenoid species



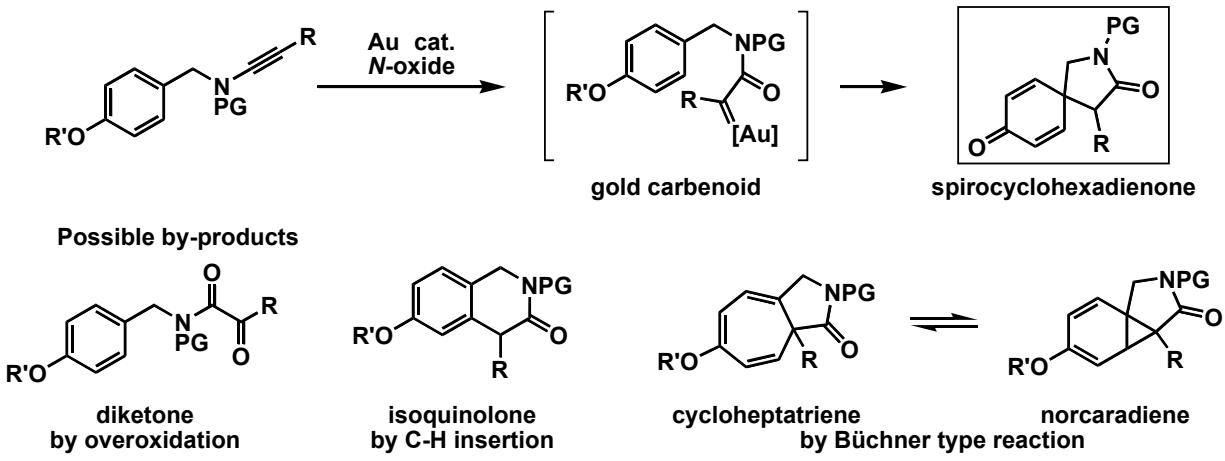
Recently, Nemoto and co-workers developed an enantioselective dearomative spirocyclization of phenols using a chiral silver catalyst and diazoketones (Scheme 5).[9] The high enantioselectivity was achieved by a chiral counteranion and the addition of benzoic acid. Compared to rhodium carbenoid, which promoted Büchner type reaction and C-H insertion, the lower bond order of silver carbenoid resulted in a more carbocationic character, which facilitates spirocyclization. However, these reactions used poisonous diazo compounds for the generation of metal carbenoid species.

Scheme 5. Enantioselective dearomative spirocyclization via Ag-carbenoid species



Against this background, the author envisioned gold(I)-catalyzed dearomative spirocyclization of phenol derivatives via gold carbenoid species derived from ynamide (Scheme 6). This strategy did not use hazardous diazo compounds to generate metal carbenoid species and could introduce substituents (R) easily. To achieve the transformation, suppression of possible side reactions, such as overoxidation, C-H insertion, and Büchner type reaction, was a difficult problem to be solved.

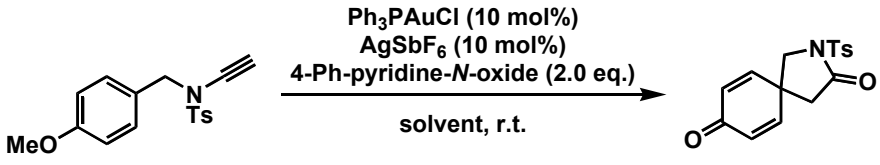
Scheme 6. Concept of this work



Results and Discussion

First, the author conducted screening of solvents by using terminal ynamide **1a** (Table 1). When the reaction was examined by using DCE as a sole solvent, the desired spirocyclic compound **2a** was obtained in low yield (Entry 1). According to previous work,[7] the author considered that the addition of water would be effective for this reaction (see, Scheme 3). Various ratio of mixed solvent of DCE and water were examined (Entries 2-4). As a result, the addition of water improved the yield and the 1/4 mixed solvent of DCE and water gave the highest yield of **2a** (Entry 4). In contrast, the reaction using water as a sole solvent gave only trace amount of **2a** without the consumption of **1a**.

Table 1. Screening of solvent



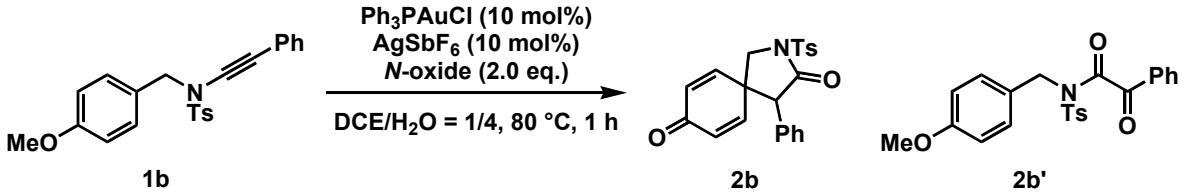
1a **2a**

Entry	Solvent	Time /h	Yield /%[a]
1	DCE	1	ca. 27
2	DCE/H_2O = 4/1	5	55
3	DCE/H_2O = 1/1	5	54
4	DCE/H_2O = 1/4	5	60
5	H_2O	5	trace

[a] NMR yields was measured using 1,1,2,2-tetrachloroethane as an internal standard.

Next, the author subjected internal ynamide **1b** to gold(I)-catalyzed spirocyclization. Preliminary experiments showed the 1/4 mixed solvent of DCE and water was suitable for spirocyclization. The author then started the screening of *N*-oxides oxidants (Table 2). The use of pyridine *N*-oxide gave the desired spirocyclic compound **2b** in moderate yield along with the complete consumption of **1b** (Entry 1). The major by-product was an overoxidized product, diketone **2b'**. The reaction of 4-phenylpyridine *N*-oxide was complete within 30 min, but the yield was not improved (Entry 2). To inhibit the generation of diketone, sterically hindered pyridine *N*-oxides were used (Entries 3-5). However, the yield was not improved. Next, quinoline *N*-oxides were examined (Entries 6 and 7). The use of quinoline *N*-oxide improved the yield slightly (Entry 6). The use of sterically more hindered quinoline *N*-oxide was not effective (Entry 7). The author determined quinoline *N*-oxide as the best oxidant, but the formation of diketone by-product could not be fully prevented.

Table 2. Screening of oxidants

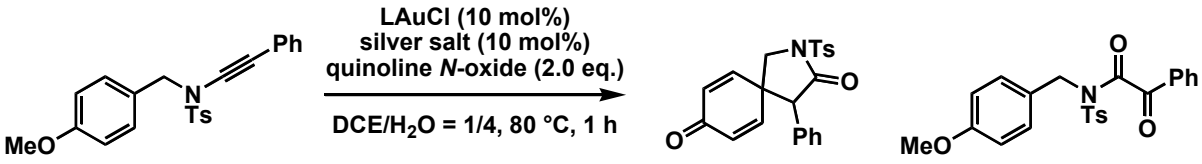


Entry	*N*-oxide	Yield of **2b** /%[a]	Yield of **2b'** /%[a]
1	Pyridine	51	19
2[b]	4-Ph-pyridine	(46)	-
3[c]	2,6-Br_2-pyridine	18	Trace
4	2,6-Me_2-pyridine	40	24
5	2-Me-pyridine	51	48
6	quinoline	54	46
7	8-Me-quinoline	26	31

[a] NMR yields was measured using 1,1,2,2-tetrachloroethane as an internal standard. When the total yield of **2b** and **2b'** exceeded 100%, the yields were calculated by the ratio of **2b** and **2b'**, determined by ^{1}H-NMR. Isolated yield was shown in parentheses. [b] The reaction was conducted for 30 min. [c] The reaction was conducted at room temperature.

To accelerate the *ipso*-Friedel-Crafts reaction and inhibit the over-oxidation, phosphine ligands and silver salts were examined (Table 3). Electron-deficient ligands were ineffective: the yield of **2b** was lower and the yield of the diketone increased (Entries 2 and 3). Almost no effect was observed by silver salts (Entries 1, 4 and 5). While the reaction did not proceed in the absence of gold catalysts, only a slight loss of yield was observed in the absence of silver salts (Entries 6 and 7). The author considered that silver salts are not significant for this transformation and further screened the ligands under silver salt-free conditions.

Table 3. Screening of phosphine ligands and silver salts



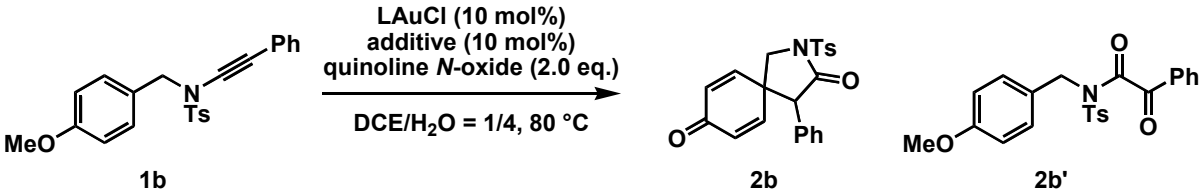
1b **2b** **2b'**

Entry	L	Silver salt	Yield of **2b** /%[a]	Yield of **2b'** /%[a]
1	PPh_3	$AgSbF_6$	54	46
2	$P(C_6F_5)_3$	$AgSbF_6$	17	83
3	$P(4\text{-}CF_3C_6H_4)_3$	$AgSbF_6$	33	67
4	PPh_3	AgOTf	53	47
5	PPh_3	$AgBF_4$	51	49
6[b]	None	$AgSbF_6$	Trace	Trace
7	PPh_3	None	48	52

[a] NMR yields was measured by using 1,1,2,2-tetrachloroethane as an internal standard. When the total yield of **2b** and **2b'** exceeded 100%, the yields were calculated by the ratio of **2b** and **2b'**, determined by ^{1}H-NMR. [b] The reaction was conducted without gold complexes.

Next, NHC ligands and additives were examined (Table 4). When the reaction was conducted for 3 h using the IPr ligand, the yield was low due to the low conversion along with formation of the diketone as a by-product (Entry 1). When the reaction time was prolonged to 24 h, the yield was improved. More important still, the amount of diketone did not increase (Entry 2). The catalytic activity was drastically decreased in DCE as a single solvent and the yield of **2b** was low because of low conversion (Entry 3). Other NHC ligands were examined and IPr gave the best results (Entries 2, 4-7). These results indicated that the bulkiness around the gold catalyst inhibited the generation of diketone, and high yield of spirocyclic product **2b** was achieved.[10] Judging from entries 1 and 2, the author speculated that quinoline generated from quinoline *N*-oxide suppressed the formation of diketone and added quinolone as an additive (Entry 8). Gratifyingly, the isolated yield was improved to 85%. The reaction could also be conducted by the larger reaction scale (Entry 9). It is noteworthy that the present reaction smoothly proceeded under air and the comparable yield was achieved (Entry 10).

Table 4. Screening of NHC ligand and additive



1b **2b** **2b'**

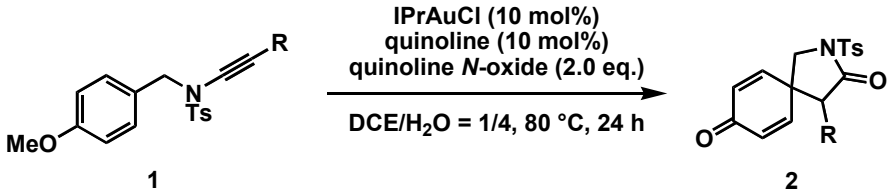
Entry	L	Additive	Time /h	Yield of **2b** /%[a]	Yield of **2b'** /%[a]
1	IPr	None	3	35	20
2	IPr	None	24	78 (75)	22
3[b]	IPr	None	24	14	-
4	SIPr	None	24	(72)	-
5	ICy	None	24	29	71
6	IMes	None	24	59 (57)	41
7	SIMes	None	24	(63)	-
8	IPr	Quinoline	24	(85)	-
9[c]	IPr	Quinoline	24	(79)	-
10[d]	IPr	Quinoline	24	77	23

[a] NMR yields were measured using 1,1,2,2-tetrachloroethane as an internal standard. When the total yield of **2b** and **2b'** exceeded 100%, the yields were calculated by the ratio of **2b** and **2b'**, determined by ^{1}H-NMR. Isolated yields were shown in parentheses. [b] DCE (0.5 mL) was used as a sole solvent. [c] The reaction was conducted four times as much scale as other entries: **1b** (0.20 mmol), Au cat. (10 mol%), quinoline (10 mol%), quinoline *N*-oxide (0.2 mmol), DCE (0.4 mL), H_2O (7.6 mL), 80 °C, 24 h. [d] The reaction was conducted under air.

Under the optimized conditions (Entry 8 in Table 4), various ynamides were examined for the spirocyclization (Table 4). The reactions of haloaryl-substituted ynamides **1c**-**1g** gave the desired compounds **2c**-**2g** in good to excellent yields (Entries 1-5). In the reactions of **1d**, **1g** and *p*-methoxycarbonyl-substituted ynamide **1h**, DCE content in the mixed solvent was increased because of low solubility of the ynamides (Entries 2, 5 and 6). The best substrate for this transformation was *p*-trifluoromethylphenyl-substituted ynamide **1i** that gave spirocyclic product **2i** in 98% (Entry 7). Sterically hindered substrate **1j** showed low reactivity (Entry 8). Electron-donating group substituted-ynamides **1k**-**1n** were not suitable for this reaction and the yield was low to moderate because of the formation of a significant amount of diketones (Entries 9-12). Heteroaryl-substituted ynamide **1o** could also be used for this reaction and pyridyl-substituted product **2o** was obtained in moderate yield (Entry 13). When terminal alkyne **1a** was subjected to the reaction under the opti-

mized conditions, **2a** was obtained in low yield (Entry 14). After screening of conditions, the reaction of terminal alkyne **1a** proceeded in the presence of chloro(triphenylphosphine)gold(I) and 4-phenylpyridine *N*-oxide at room temperature to give **2a** in moderate yield.

Table 4. Scope of alkyne terminus



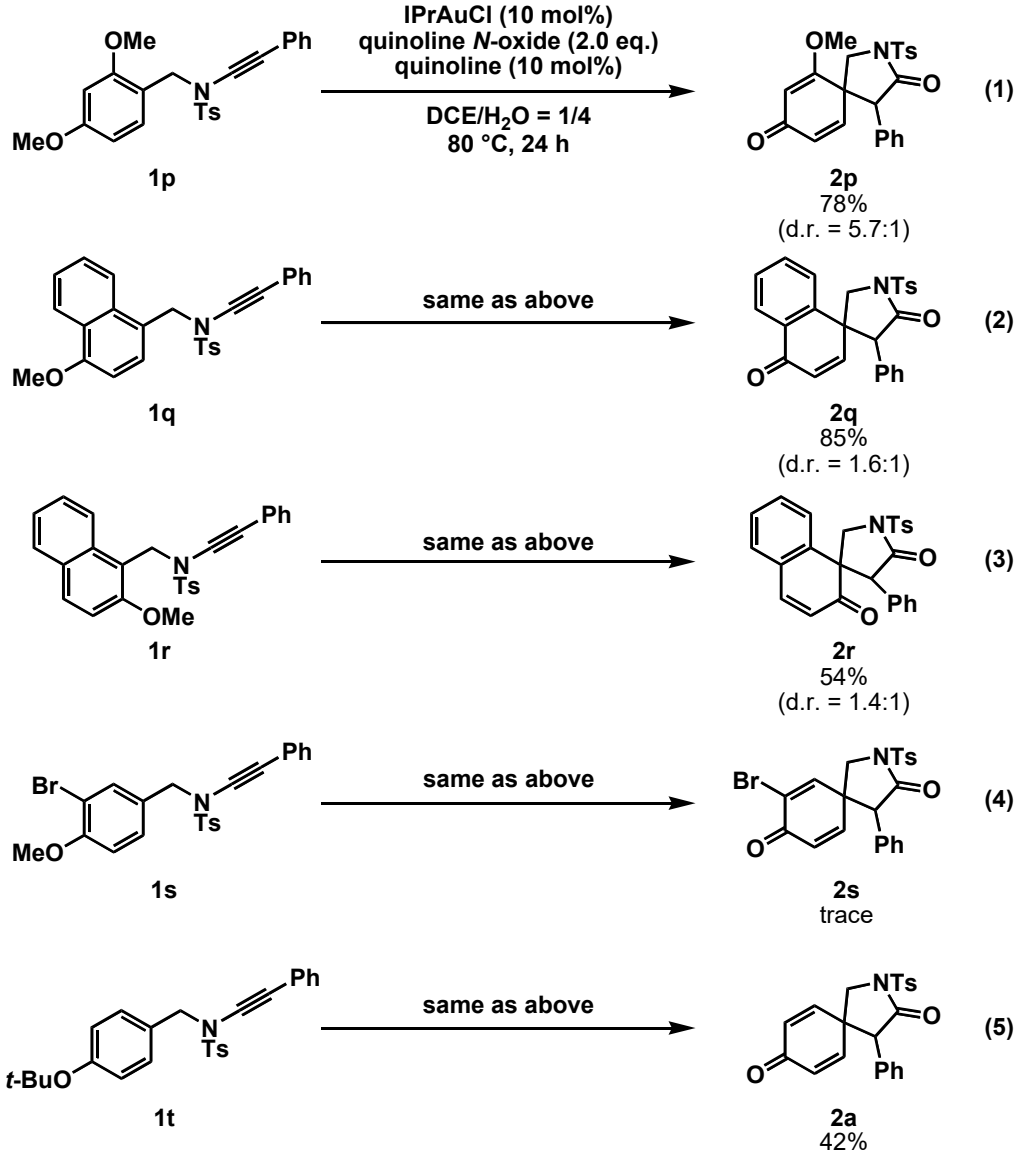
1 2

Entry	R	Yield /%[a]	Entry	R	Yield /%[a]
1	4-FC_6H_4 (**1c**)	68 (**2c**)	8	2-$CF_3C_6H_4$ (**1j**)	27, 35[b] (**2j**)
2	4-ClC_6H_4 (**1d**)	30, 79[b] (**2d**)	9	4-MeC_6H_4 (**1k**)	37, 51[c] (**2k**)
3	4-BrC_6H_4 (**1e**)	85 (**2e**)	10	3-MeC_6H_4 (**1l**)	52 (**2l**)
4	3-ClC_6H_4 (**1f**)	82 (**2f**)	11	2-MeC_6H_4 (**1m**)	49 (**2m**)
5	4-Br-2-FC_6H_3 (**1g**)	31, 69[b] (**2g**)	12	4-$MeOC_6H_4$ (**1n**)	trace, 14[c] (**2n**)
6	4-(CO_2Me)C_6H_4 (**1h**)	55, 86[b] (**2h**)	13	3-Pyridyl (**1o**)	67 (**2o**)
7	4-$CF_3C_6H_4$ (**1i**)	98 (**2i**)	14	H (**1a**)	22, 53[d] (**2a**)

[a] Isolated yield. [b] Quinoline (20 mol%), DCE (0.2 mL) and H_2O (0.4 mL) were used. [c] Ph_3PAuCl (10 mol%), quinoline (20 mol%) and quinoline *N*-oxide (0.1 mmol) were used in a mixed solvent of PhCl (0.2 mL) and H_2O (0.8 mL) at 100 °C for 24 h. [d] **1o** (0.05 mmol), Ph_3PAuCl (10 mol%), 4-phenylpyridine *N*-oxide (0.1 mmol) were used in a mixed solvent of DCE (0.1 mL) and H_2O (0.4 mL) at r.t. for 5 h.

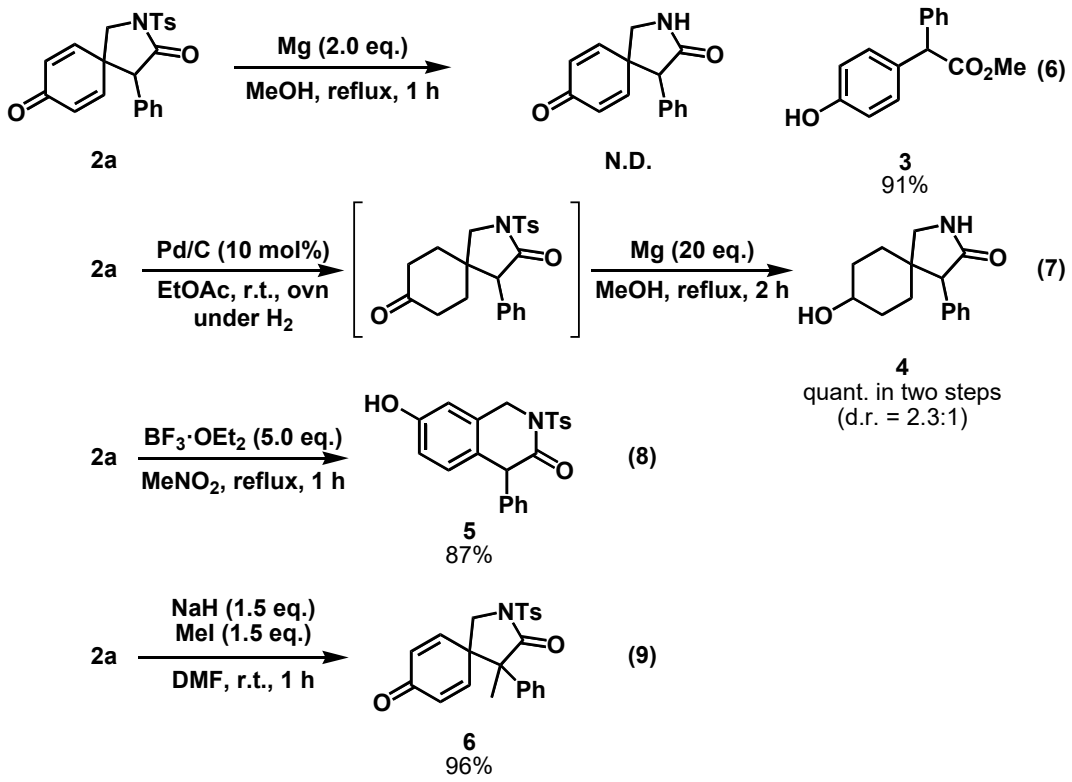
Next, the author examined the reaction of substrates possessing other alkoxy-substituted aryl groups (Scheme 7). The reaction of 2,4-dimethoxybenzylamine derived substrate **1p** gave spirocyclic product **2p** in good yield with moderate diastereoselectivity [Equation (1)]. The author subjected naphthol derivatives **1q** and **1r** in the present spirocyclization [Equation (2) and (3)]. 1-Naphthol derivative **1q** was a good substrate and tricyclic compound **2q** was obtained in high yield. When 2-naphthol derivative **1r** was subjected to the reaction, the desired product **2r** was obtained in moderate yield. This reaction required an electron-donating group on the arene moiety. Actually, 3-bromo-4-methoxybenzylamine derivative **1s** gave only a trace amount of spirocyclic compound **2s** [Equation (4)]. This result indicated that the nucleophilicity of *ipso* position was important. The reaction of *tert*-butoxy-substituted substrate **1t** also gave spirocyclic product **2a** in moderate yield [Equation (5)].

Scheme 7. Scope of substrates possessing other alkoxy-substituted aryl groups



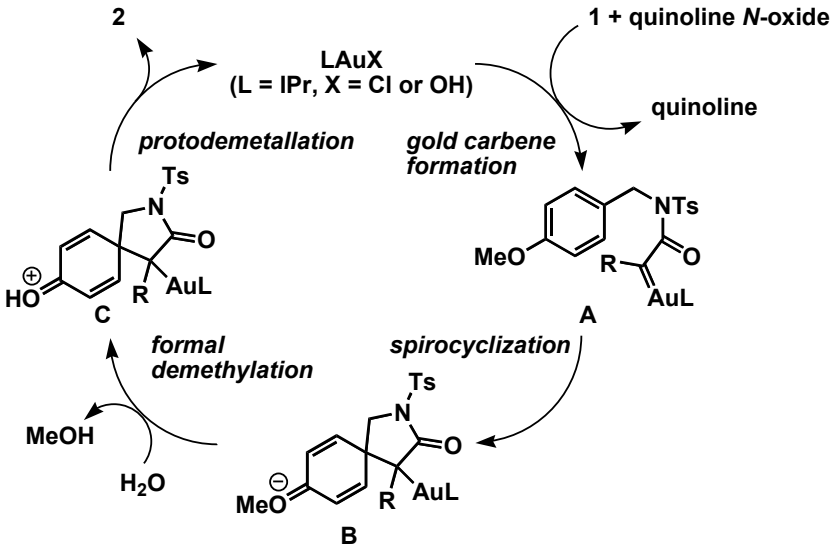
Some synthetic transformations of **2b** were demonstrated (Scheme 8). The deprotection of the tosyl group was conducted using magnesium in methanol, but diarylacetate **3** was obtained by re-aromatization of the cyclohexadienone moiety along with C-C bond cleavage [Equation (6)].[11] To prevent the rearomatization, Pd-catalyzed hydrogenation of the cyclohexadienone moiety was carried out prior to deprotection of the tosyl group [Equation (7)]. The reaction proceeded smoothly to give gabapentin lactam derivative **4** quantitatively in two steps.[3] Lewis acid-mediated rearrangement of **2b** gave dihydroisoquinolone derivative **5** in high yield [Equation (8)].[12] Methylation adjacent to carbonyl group proceeded under basic conditions to provide **6** in high yield [Equation (9)].

Scheme 8. Synthetic applications of **2b**



The possible reaction mechanism was depicted in Scheme 9. The initial step is the formation of gold carbenoid species **A** from ynamide and *N*-oxide. The carbenoid species react at a highly nucleophilic *ipso* position to provide spirocycle **B**. The spirocycle **B** react to give **C** by aid of water.[7] In this transformation, the water acts as a reactant to promote the formal demethylation step where nucleophilic addition of water along with elimination of methanol, and quinoline may also promote this step by increasing the basicity.[13] Finally, protodemetallation of **C** yields spirocyclic product **2** and the gold catalyst is regenerated.

Scheme 9. Plausible reaction mechanism



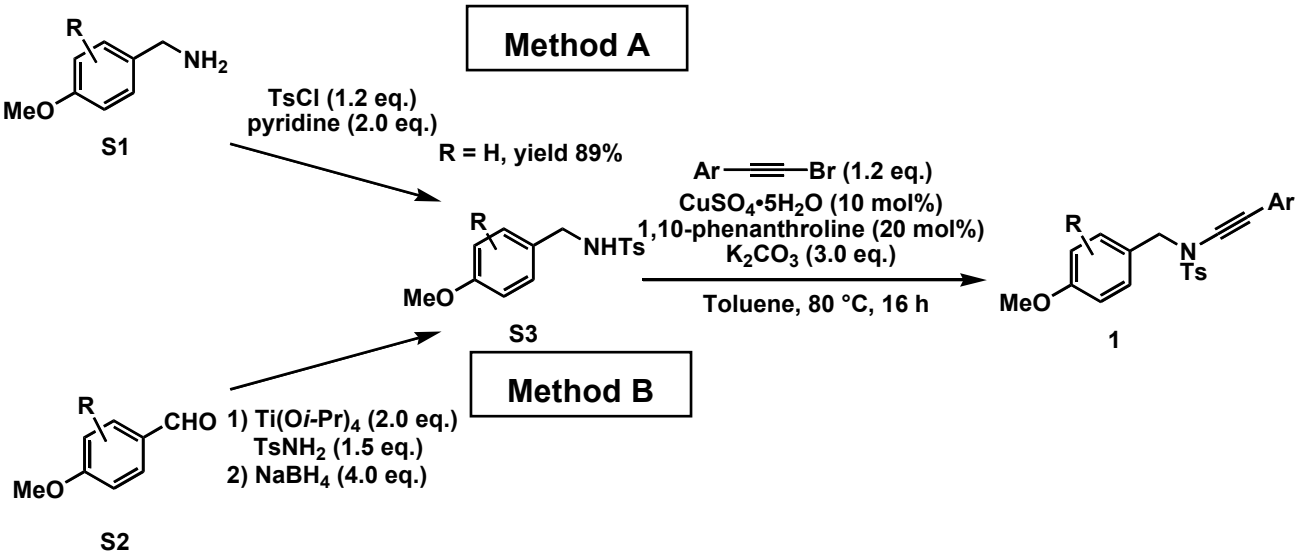
Conclusion

The author developed catalytic dearomative spirocyclization of phenol derivatives via gold carbenoid species derived from ynamides. This reaction demonstrated new reactivity of gold carbenoid species. The use of IPr as a relatively bulky NHC ligand was important to suppress the generation of diketone by-product. The author speculated that the bulkiness shielded the gold carbenoid species from the second attack of *N*-oxide, which is derived into the formation of diketone as a major by-product. In addition, the strong electron-donating ability of NHC ligand would improve the reactivity toward spirocyclization. The presence of water as a co-solvent was crucial for the high reactivity. In the plausible reaction mechanism, water acted as a nucleophile in formal demethylation step to convert intermediate **B** to **C**. The reactivity drastically decreased by using DCE as a sole solvent (Table 4, Entry 3). From these results, the author speculated that the counter anion of gold catalyst, chloride, exchanged to hydroxide in the presence of excess water and the gold-hydroxide complexes were the active species. The obtained spirocyclohexadienones were readily transformed into various compounds.

Experimental Section

General information: ^{1}H NMR spectra were recorded on JEOL ECX-500 (500 MHz) spectrometers. The chemical shifts were reported in parts per million (δ) relative to internal standard TMS (0 ppm) for $CDCl_3$. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; dd, doublet of doublets; dt, triplet of doublet; m, multiplet; q, quartet. The coupling constants, *J*, are reported in Hertz (Hz). ^{13}C NMR spectra were obtained by JEOL ECX-500 (125 MHz) spectrometers and referenced to the internal solvent signals (central peak is 77.16 ppm in $CDCl_3$). $CDCl_3$ was used as a NMR solvent. High-resolution mass spectra (HRMS) were measured on a JMS-T100CS with ESI (Electro Spray Ionization) method. Preparative thin-layer chromatography (PTLC) was performed with silica gel-precoated glass plates (Wakogel B-5F) prepared in our laboratory, Flash column chromatography was performed over silica gel 200-300. All reagents were weighed and handled in air and backfilled under argon at room temperature. Unless otherwise noted, all reactions were performed under an argon atmosphere. All reagents were purchased from Wako, Kanto, Aldrich, TCI and Strem and used without further purification.

Preparation of *N*-(4-methoxybenzyl)-4-methyl-*N*-(arylethynyl)benzenesulfonamide (1):



Method A:

Preparation of Ts-protected *p*-methoxybenzylamine derivatives: A dry Schlenk tube equipped with a rubber septum was charged with **S1** (1.0 mmol). Pyridine (2.0 mmol) and DCM (2.0 mL) were added to the reaction vessel under argon atmosphere. TsCl (1.2 mmol) was added slowly. The

reaction mixture was stirred overnight at room temperature and quenched with 1N HCl solution. The solution was extracted with EtOAc, the organic extract was dried over Na_2SO_4. The dry organic extract was filtered, and evaporated under reduced pressure. The crude products were semi-purified by crystallization from hexane and DCM to give **S3**.[14] *N*-(4-methoxybenzyl)-4-methylbenzenesulfonamide was obtained in 89%. Other **S3** products were used for the next reaction without further purification.

Preparation of bromo-alkyne: To a solution of the terminal alkyne (1 equiv) in anhydrous acetone (conc = 0.30 M) were added *N*-bromosuccinimide (1.2 equiv) and $AgNO_3$ (10 mol %). After 3 h at room temperature, the resulting mixture was then filtrated and the filtrate was extracted with hexane (3 × 30 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under vacuum (25°C, 200 mbar) to afford the title compounds.[15a]

Preparation of ynamide: To a dry flask were added Ts-protected *p*-methoxybenzylamine derivatives (0.5 mmol), $CuSO_4$•$5H_2O$ (10 mol%), 1,10-phenanthroline (20 mmol) and K_2CO_3 (1.0 mmol). Then toluene (2.0 mL) and bromoalkyne (1.2 mmol) were added, and the resulting mixture was stirred at 80 °C for 12 h under an atmosphere of argon. When the reaction was complete, the crude mixture was cooled down to room temperature, filtered through celite and washed with ethyl acetate. After solvent evaporation, the residue was purified by flash column chromatography on silica gel (eluent: hexane: ethyl acetate = 5:1) to afford compound **1**.[15b]

Method B:

Preparation of Ts-protected *p*-methoxybenzylamine derivatives: A 30 mL dry two-necked pear-shaped flask equipped with a glass stopper and argon balloon was charged with **S2** (1.0 mmol), $TsNH_2$ (1.5 mmol), Ti(O*i*-Pr)$_4$ (2.0 mmol), and toluene (4.2 mL). The solution was refluxed for 3 h. After removal of the solvent under reduced pressure, MeOH (4.2 mL) and THF (4.2 mL) were added, and the reaction vessel equipped with argon balloon was cooled to 0 °C. To the cooled solution, $NaBH_4$ (4.0 mmol) was slowly added. The reaction mixture was warmed to room temperature and stirred for 1 h. The solution was poured into ice cold water and extracted with EtOAc (×3). The organic extracts were combined, washed with brine, and dried over Na_2SO_4. The dry organic extract was filtered, and evaporated under reduced pressure. The crude products were semi-purified by crystallization from hexane and DCM to give **S3**. **S3** were used for the next reaction without further purification.[16]

Next steps are the same as Method A.

Preparation *N*-(4-methoxybenzyl)-*N*-ethynyl-*p*-toluenesulfonamide (1a):

To a stirred solution of *N*-(4-methoxybenzyl)-4-methylbenzenesulfonamide (1 mmol) in dry DMF (20 mL) was added Cs_2CO_3 (1.3 eq.) at room temperature. After 30 min, a solution of (trimethylsilyl)ethynyl iodonium trifluoromethanesulfonate salt (1.3 mmol) in dry CH_2Cl_2 (8 mL) was added dropwise. Stirring was continued until starting materials disappeared (TLC monitoring, typically 5 h). Then, ether was added (10 mL) and the combined organic layers were extracted with water and brine, dried over anhydrous Na_2SO_4 and concentrated to dryness. Purification of the residue by flash chromatography on silica gel using a gradient mixture of EtOAc/hexanes as eluent afforded ynamides **1a** in good yields.[17]

Preparation of [(NHC)AuCl]:

The protocol is the complete same as the reference.[18] ICyAuCl was synthesized in the same way as IPrAuCl, and its ^{1}H-NMR matched the data of the reference.[19]

General procedure for reaction in Table 4:

Condition A: IPrAuCl (3.1 mg, 0.0050 mmol), quinoline *N*-oxide·nH_2O (18.1 mg, 0.10 mmol; calculated as n = 2), and *N*-(4-methoxybenzyl)-4-methyl-*N*-(phenylethynyl)benzenesulfonamide **1** (0.050 mmol), were placed in a Schlenk tube, which was then evacuated and backfilled with argon (×3). To the reaction vessel, H_2O (0.40 mL) and a solution of 50 mM quinoline in DCE (0.10 mL) were added. The solution was then stirred at 80 °C (oil bath temperature). The reaction mixture was cooled to room temperature and the solvent was evaporated. The obtained crude product was purified by PTLC to give products **2**.

Condition B: Ph_3PAuCl (2.4 mg, 0.0050 mmol), quinoline *N*-oxide·nH_2O (18.1 mg, 0.010 mmol; calculated as n = 2), and *N*-(4-methoxybenzyl)-4-methyl-*N*-(phenylethynyl)benzenesulfonamide **1** (0.050 mmol), were placed in a Schlenk tube, which was then evacuated and backfilled with argon (×3). To the reaction vessel, H_2O (0.80 mL) and a solution of 50 mM quinoline in PhCl (0.20 mL) were added. The solution was then stirred at room temperature. After removal of solvent, the crude product was purified by PTLC to give products **2**.

1-(4-Hydroxyphenyl)-1-methoxycarbonyl-1-phenylmethane (**3**)

A dry Schlenk tube equipped with a rubber septum was charged with **2b** (19.7 mg, 0.05 mmol), and activated Mg (2.5 mg, 0.1 mmol). MeOH (0.50 mL) was added to the reaction vessel, and it was capped with a glass stopper under argon atmosphere. The resulting solution was refluxed for 1 h,

then filtered through a short pad of celite. The filtrate was evaporated under reduced pressure. The crude products were purified by preparative TLC (elution: hexane/EtOAc = 1/1) to give the title compound **3** (11.1 mg, 91%) as a colorless oil.

8-Hydroxy-4-phenyl-2-azaspiro[4.5]decan-3-one (**4**)

A dry Schlenk tube equipped with a rubber septum was charged with **2b** (23.0 mg, 0.058 mmol), dry 10% Pd/C (5.0 mg, 0.005 mmol), and EtOAc (1.0 mL). The reaction vessel was evacuated and backfilled with argon (×3), then backfilled with H_2 (×3). The reaction mixture was stirred at room temperature overnight. After the consumption of starting material, the reaction vessel was evacuated and backfilled with argon (×3). The resulting solution was filtered through a short pad of celite and washed with EtOAc. The filtrate was evaporated under reduced pressure. The crude product was used directly in the next step. A dry Schlenk tube equipped with a rubber septum was charged with crude product, activated Mg (25.0 mg, 1.0 mmol). MeOH (0.50 mL) was added to the reaction vessel, and it was capped with a glass stopper under argon atmosphere. The resulting solution was refluxed for 2 h. The resulting solution was filtered through a short pad of celite. The filtrate was evaporated under reduced pressure to give pure **4** quantitatively without further purification.

2-Tosyl-6-hydroxy-4-phenyl-1,2-dihydroisoquinolin-3(4*H*)-one (**5**)

A dry Schlenk tube equipped with a rubber septum was charged with **2b** (19.5 mg, 0.05 mmol), and $BF_3 \cdot Et_2O$ (31 μL, 0.25 mmol). $MeNO_2$ (1.5 mL) was added to the reaction vessel, and it was capped with a glass stopper under argon atmosphere. The resulting solution was refluxed for 1 h and quenched with sat. $NaHCO_3$ solution. The solution was extracted with EtOAc, the organic extract was dried over Na_2SO_4. The dry organic extract was filtered, and evaporated under reduced pressure. The crude products were purified by preparative TLC (elution: hexane/EtOAc = 3/2) to give **5** (17.0 mg, 87%) as an off-white solid.

2-Tosyl-4-methyl-4-phenyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (**6**)

A dry Schlenk tube equipped with a rubber septum was charged with **2b** (18.9 mg, 0.048 mmol), ca. 50% NaH in oil (4.0 mg, ca. 0.087 mmol), and DMF (0.5 mL). The solution was stirred for 30 min at room temperature. MeI (4.7 μL, 0.075 mmol) in DMF (0.5 mL) was added to the solution and the reaction mixture was stirred for 1 h. After consumption of starting material, water was added and the solution was extracted with EtOAc (×3). The combined organic layer was dried over Na_2SO_4. The dry organic extract was filtered and evaporated under reduced pressure. The crude products were purified by preparative TLC (elution: hexane/EtOAc = 1/1) to give **6** (18.9 mg, 96%) as a white solid.

2) Characterization data for new compounds

***N*-(4-Methoxybenzyl)-*N*-ethynyl-*p*-toluenesulfonamide (1a)**

Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as an off-white solid, 70%; mp 121 °C; ^{1}H NMR δ 7.75 (d, *J* = 8.5 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 4.43 (s, 2H), 3.79 (s, 3H), 2.67 (s, 1H), 2.44 (s, 3H); ^{13}C NMR δ 159.8, 144.8, 134.9, 130.4, 129.9, 127.8, 126.4, 114.0, 76.4, 59.9, 55.4, 54.9, 21.8; HRMS (ESI, positive): m/z calcd. for $C_{17}H_{17}NNaO_3S$ $[M + Na]^+$ 338.0821, found 338.0821.

***N*-(4-Methoxybenzyl)-4-methyl-*N*-(phenylethynyl)benzenesulfonamide (1b)**

Synthesized by Method A. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as a white solid, 89%; mp 81 °C; ^{1}H NMR δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.27-7.22 (m, 7H, overlapped with $CHCl_3$), 6.83 (d, *J* = 8.4 Hz, 2H), 4.51 (s, 2H), 3.79 (s, 3H), 2.44 (s, 3H); ^{13}C NMR δ 159.9, 144.7, 134.9, 131.3, 130.6, 129.8, 128.3, 127.9, 127.8, 126.6, 123.0, 114.0, 82.9, 71.6, 55.4, 55.4, 21.8; HRMS (ESI, positive): m/z calcd. for $C_{23}H_{21}NNaO_3S$ $[M + Na]^+$ 414.1133, found 414.1134.

***N*-((4-Fluorophenyl)ethynyl)-*N*-(4-methoxybenzyl)-4-methylbenzenesulfonamide (1c)**

Synthesized by Method A. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as a white solid, 90%; mp 59-60 °C; ^{1}H NMR δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.25-7.19 (m, 4H), 6.94 (dd, *J* = 8.6, 8.6 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 4.50 (s, 2H), 3.79 (s, 3H), 2.44 (s, 3H); ^{13}C NMR δ 162.3 (d, $J_{C\text{-}F}$ = 249.4 Hz, 1C), 159.9, 144.7, 134.9, 133.3 (d, $J_{C\text{-}F}$ = 8.4 Hz, 1C), 130.5, 129.9, 127.9, 126.6, 119.0 (d, $J_{C\text{-}F}$ = 3.6 Hz, 1C), 115.6 (d, $J_{C\text{-}F}$ = 22.1 Hz, 1C), 114.0, 82.4, 70.5, 55.4, 55.4, 21.8; HRMS (ESI, positive): m/z calcd. for $C_{23}H_{20}FNNaO_3S$ $[M + Na]^+$ 432.1040, found 432.1040.

***N*-((4-Chlorophenyl)ethynyl)-*N*-(4-methoxybenzyl)-4-methylbenzenesulfonamide (1d)**

Synthesized by Method A. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as a white solid, 61%; mp 87-89 °C; ^{1}H NMR δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.28-7.19 (m, 4H), 7.15 (d, *J* = 8.3 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 4.51 (s, 2H), 3.79 (s, 3H), 2.45 (s, 3H); ^{13}C NMR δ 159.8, 144.8, 134.8, 133.6, 132.4, 130.5, 129.8, 128.6, 127.8, 126.4, 121.5, 114.0, 83.6, 70.7, 55.4, 55.3, 21.7; HRMS (ESI, positive): m/z calcd. for $C_{23}H_{20}{}^{35}ClNNaO_3S$ $[M + Na]^+$ 448.0745, found 448.0745.

_N_-((4-Bromophenyl)ethynyl)-_N_-(4-methoxybenzyl)-4-methylbenzenesulfonamide (1e)

Synthesized by Method A. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as a white solid, 74%; mp 75 °C; ^{1}H NMR δ 7.78 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 8.8 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.6 Hz, 2H), 7.08 (d, J = 8.6 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 4.50 (s, 2H), 3.79 (s, 3H), 2.45 (s, 3H); ^{13}C NMR δ 159.9, 144.8, 134.9, 132.6, 131.6, 130.6, 129.9, 127.9, 126.5, 122.0, 121.8, 114.0, 82.4, 70.8, 55.4, 55.3, 21.8; HRMS (ESI, positive): m/z calcd. for $C_{23}H_{20}{}^{79}BrNNaO_3S$ $[M + Na]^+$ 492.0241, found 492.0239

_N_-((3-Chlorophenyl)ethynyl)-_N_-(4-methoxybenzyl)-4-methylbenzenesulfonamide (1f)

Synthesized by Method A. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as a white solid, 84%; mp 113 °C; ^{1}H NMR δ 7.78 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 7.9 Hz, 2H), 7.25-7.14 (m, 5H), 7.10 (dt, J = 7.4, 1.5 Hz, 1H), 6.84 (d, J = 8.8 Hz, 2H), 4.51 (s, 2H), 3.80 (s, 3H), 2.45 (s, 3H); ^{13}C NMR δ 159.9, 144.8, 134.8, 134.1, 130.8, 130.5, 129.9, 129.5, 129.1, 127.8, 127.8, 126.3, 124.8, 114.0, 84.0, 70.6, 55.4, 55.3, 21.7; HRMS (ESI, positive): m/z calcd. for $C_{23}H_{20}{}^{35}ClNNaO_3S$ $[M + Na]^+$ 448.0747, found 448.0745.

_N_-((4-Bromo-2-fluorophenyl)ethynyl)-_N_-(4-methoxybenzyl)-4-methylbenzenesulfonamide (1g)

Synthesized by Method A. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as a white solid, 87%; mp 73-74 °C; ^{1}H NMR δ 7.79 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.6 Hz, 2H, overlapped with $CDCl_3$), 7.20 (dd, J = 8.7, 1.8 Hz, 1H), 7.17 (dd, J = 8.3, 2.0 Hz, 1H), 7.09 (t, J = 7.9 Hz, 1H), 6.82 (d, J = 8.7 Hz, 2H), 4.52 (s, 2H), 3.79 (s, 3H), 2.44 (s, 3H); ^{13}C NMR δ 162.0 (d, $J_{C\text{-}F}$ = 255.1 Hz, 1C), 159.9, 144.8, 134.8, 133.6 (d, $J_{C\text{-}F}$ = 1.8 Hz, 1C), 130.6, 129.8, 127.8, 127.4 (d, $J_{C\text{-}F}$ = 3.6 Hz, 1C), 126.2, 121.6 (d, $J_{C\text{-}F}$ = 8.9 Hz, 1C), 119.2 (d, $J_{C\text{-}F}$ = 24.1 Hz, 1C), 114.0, 111.0 (d, $J_{C\text{-}F}$ = 15.8 Hz, 1C), 88.7 (d, $J_{C\text{-}F}$ = 3.0 Hz, 1C), 64.7, 55.4, 55.3, 21.7; HRMS (ESI, positive): m/z calcd. for $C_{23}H_{19}{}^{79}BrFNNaO_3S$ $[M + Na]^+$ 510.0148, found 510.0145.

Methyl 4-(((_N_-(4-methoxybenzyl)-4-methylphenyl)sulfonamido)ethynyl)benzoate (1h)

Synthesized by Method A. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as a white solid, 91%; mp 80 °C; ^{1}H NMR δ 7.91 (d, J = 8.5 Hz, 2H), 7.79 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.28-7.22 (m, 4H), 6.84 (d, J = 8.6 Hz, 2H), 4.53 (s, 2H), 3.90 (s, 3H), 3.80 (s, 3H), 2.45 (s, 3H); ^{13}C NMR δ 166.7, 159.9, 144.9, 134.8, 130.5, 130.4, 129.9, 129.5, 128.7, 128.0, 127.8, 126.3, 114.0, 86.1, 71.8, 55.4, 55.3, 52.2, 21.7; HRMS (ESI, positive): m/z calcd. for $C_{25}H_{23}NNaO_5S$ $[M + Na]^+$ 472.1191, found 472.1189.

_N_-(4-Methoxybenzyl)-4-methyl-_N_-((4-(trifluoromethyl)phenyl)ethynyl)benzenesulfonamide (1i)

Synthesized by Method A. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as pale yellow oil, 84%; ^{1}H NMR δ 7.79 (d, J = 8.3 Hz, 2H), 7.49 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 8.2 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 7.24 (d, J = 8.8 Hz, 2H, overlapped with $CHCl_3$), 6.84 (d, J = 8.8 Hz, 2H), 4.53 (s, 2H), 3.80 (s, 3H), 2.45 (s, 3H); ^{13}C NMR δ 159.9, 144.9, 134.8, 130.8, 130.5, 129.9, 129.2 (q, J_{C-F} = 32.5 Hz, 1C), 127.8, 127.0 (q, J_{C-F} = 1.5 Hz, 1C), 126.2, 125.2 (q, J_{C-F} = 3.9 Hz, 1C), 124.0 (q, J_{C-F} = 272.4 Hz, 1C), 114.0, 85.4, 71.1, 55.4, 55.2, 21.7; HRMS (ESI, positive): m/z calcd. for $C_{24}H_{20}F_3NNaO_3S$ $[M + Na]^+$ 482.1008, found 482.1009.

_N_-(4-Methoxybenzyl)-4-methyl-_N_-((2-(trifluoromethyl)phenyl)ethynyl)benzenesulfonamide (1j)

Synthesized by Method A. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as a white solid, 83%; mp 76-78 °C; ^{1}H NMR δ 7.78 (d, J = 8.3 Hz, 2H), 7.57 (d, J = 7.8 Hz, 1H), 7.40 (t, J = 7.2 Hz, 1H), 7.35-7.24 (m, 6H, overlapped with $CHCl_3$), 6.83 (d, J = 8.6 Hz, 2H), 4.54 (s, 2H), 3.78 (s, 3H), 2.43 (s, 3H); ^{13}C NMR δ 159.8, 144.8, 135.0, 133.2, 131.4, 130.5, 130.1 (q, J_{C-F} = 30.4 Hz, 1C), 129.8, 127.8, 127.0, 126.4, 125.8 (q, J_{C-F} = 5.1 Hz, 1C), 123.6 (d, J_{C-F} = 272.1 Hz, 1C), 121.5 (d, J_{C-F} = 2.1 Hz, 1C), 114.0, 88.5, 68.3, 55.5, 55.4, 21.7; HRMS (ESI, positive): m/z calcd. for $C_{24}H_{20}F_3NNaO_3S$ $[M + Na]^+$ 482.1008, found 482.1008.

_N_-(4-Methoxybenzyl)-4-methyl-_N_-(_p_-tolylethynyl)benzenesulfonamide (1k)

Synthesized by Method A. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as pale yellow oil, 93%; ^{1}H NMR δ 7.88 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 7.26-7.23 (m, 2H, overlapped with $CHCl_3$), 7.14 (d, J = 8.2 Hz, 2H), 7.05 (d, J = 7.7 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 4.50 (s, 2H), 3.78 (s, 3H), 2.43 (s, 3H), 2.31 (s, 3H); ^{13}C NMR δ 159.8, 144.6, 138.0, 135.0, 131.4, 130.6, 129.8, 129.1, 127.9, 126.7, 119.9, 114.0, 82.1, 71.5, 55.4, 55.4, 21.8, 21.5; HRMS (ESI, positive): m/z calcd. for $C_{24}H_{23}NNaO_3S$ $[M + Na]^+$ 428.1291, found 428.1291.

_N_-(4-Methoxybenzyl)-4-methyl-_N_-(_m_-tolylethynyl)benzenesulfonamide (1l)

Synthesized by Method A. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as pale yellow oil, 93%; ^{1}H NMR δ 7.78 (d, J = 8.4 Hz, 2H),

7.31 (d, *J* = 8.1 Hz, 2H), 7.27-7.23 (m, 2H, overlapped with $CHCl_3$), 7.13 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.05 (dd, *J* = 7.5, 5.8 Hz, 3H), 6.83 (d, *J* = 8.6 Hz, 2H), 4.50 (s, 2H), 3.79 (s, 3H), 2.43 (s, 3H), 2.28 (s, 3H); ^{13}C NMR δ 159.8, 144.6, 138.0, 135.0, 131.9, 130.6, 129.8, 128.7, 128.3, 128.2, 127.9, 126.7, 122.8, 114.0, 82.5, 71.7, 55.4, 21.8, 21.3; HRMS (ESI, positive): m/z calcd. for $C_{24}H_{23}NNaO_3S$ $[M + Na]^+$ 428.1290, found 428.1291.

_N_-(4-Methoxybenzyl)-4-methyl-_N_-(_o_-tolylethynyl)benzenesulfonamide (1m)

Synthesized by Method A. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as pale yellow oil, 95%; ^{1}H NMR δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 7.31-7.27 (m, 2H, overlapped with $CHCl_3$), 7.22 (d, *J* = 7.5 Hz, 1H), 7.18-7.13 (m, 2H), 7.11-7.07 (m, 1H), 6.86 (d, *J* = 8.4 Hz, 2H), 4.56 (s, 2H), 3.82 (s, 3H), 2.47 (s, 3H), 2.22 (s, 3H); ^{13}C NMR δ 159.9, 144.7, 139.6, 135.0, 131.3, 130.6, 129.9, 129.4, 127.9, 127.7, 126.7, 125.5, 122.8, 114.1, 86.5, 70.7, 55.4, 55.4, 21.8, 20.7; HRMS (ESI, positive): m/z calcd. for $C_{24}H_{23}NNaO_3S$ $[M + Na]^+$ 428.1291, found 428.1291.

_N_-(4-Methoxybenzyl)-_N_-((4-methoxyphenyl)ethynyl)-4-methylbenzenesulfonamide (1n)

Synthesized by Method A. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as a white solid, 92%; mp 73-74 °C; ^{1}H NMR δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H, overlapped with $CHCl_3$), 7.20 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 4.50 (s, 2H), 3.78 (s, 3H), 3.78 (s, 3H), 2.44 (s, 3H); ^{13}C NMR δ 159.8, 159.5, 144.6, 135.0, 133.3, 130.5, 129.8, 127.9, 126.8, 115.0, 114.0, 114.0, 81.4, 71.2, 55.5, 55.4, 21.8; HRMS (ESI, positive): m/z calcd. for $C_{24}H_{23}NNaO_4S$ $[M + Na]^+$ 444.1239, found 444.1240.

_N_-(4-Methoxybenzyl)-4-methyl-_N_-(pyridin-3-ylethynyl)benzenesulfonamide (1o)

Synthesized by Method A. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as brown oil, 70%; ^{1}H NMR δ 8.46-8.42 (m, 2H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.54-7.50 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.8 Hz, 2H), 7.20-7.15 (m, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 4.53 (s, 2H), 3.80 (s, 3H), 2.45 (s, 3H); ^{13}C NMR δ 160.0, 151.9, 148.1, 145.0, 138.0, 134.8, 130.6, 130.0, 127.9, 126.3, 123.0, 120.3, 114.1, 85.9, 68.8, 55.4, 55.3, 21.8; HRMS (ESI, positive): m/z calcd. for $C_{22}H_{20}N_2NaO_3S$ $[M + Na]^+$ 415.1085, found 415.1087.

_N_-(2,4-Dimethoxybenzyl)-_N_-(phenylethynyl)-_p_-toluenesulfonamide (1p)

Synthesized by Method B. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as a off-white solid, 32% (2 steps); mp 81 °C; ^{1}H NMR δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.22-7.17 (m, 6H), 6.42 (dd, *J* = 8.2, 2.4 Hz, 1H), 6.37 (d, *J* = 2.4 Hz, 1H), 4.58 (s, 2H), 3.76 (s, 3H), 3.65 (s, 3H), 2.41 (s, 3H); ^{13}C NMR δ 161.4, 159.0, 144.4, 135.2, 131.9, 131.0, 129.7, 128.3, 127.9, 127.4, 123.4, 115.1, 104.1, 98.5, 83.3, 71.0, 55.5, 55.4, 50.5, 21.8 (a pair of peaks on the aromatic region is overlapped); HRMS (ESI, positive): m/z calcd. for $C_{24}H_{23}NNaO_4S$ $[M + Na]^+$ 444.1240, found 444.1241..

_N_-(4-Methoxynaphthylmethyl)-_N_-(phenylethynyl)-_p_-toluenesulfonamide (1q)

Synthesized by Method B. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as a white solid, 45% (2 steps); mp 141 °C; ^{1}H NMR δ 8.29 (d, *J* = 8.3 Hz, 1H), 8.15 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 2H), 7.60-7.46 (m, 2H), 7.38-7.31 (m, 3H), 7.22-7.16 (m, 3H), 7.12-7.06 (m, 2H), 6.72 (d, *J* = 8.0 Hz, 1H), 4.89 (s, 2H), 3.99 (s, 3H), 2.45 (s, 3H); ^{13}C NMR δ 156.6, 144.8, 134.3, 132.9, 131.1, 129.9, 129.7, 128.2, 128.0, 127.6, 127.4, 126.0, 125.5, 123.6, 123.0, 122.7, 121.5, 102.9, 82.8, 71.9, 55.7, 53.7, 21.8; HRMS (ESI, positive): m/z calcd. for $C_{27}H_{23}NNaO_3S$ $[M+Na^+]$ 464.1291, found 464.1293.

_N_-(2-Methoxynaphthylmethyl)-_N_-(phenylethynyl)-_p_-toluenesulfonamide (1r)

Synthesized by Method B. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as a pale yellow solid, 54% (2 steps); mp 130 °C; ^{1}H NMR δ 8.07 (d, *J* = 8.6 Hz, 1H), 7.91 (d, *J* = 8.3 Hz, 2H), 7.82 (d, *J* = 8.9 Hz, 1H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.51-7.43 (m, 1H), 7.37-7.30 (m, 3H), 7.19 (d, *J* = 8.9 Hz, 1H), 7.12-7.06 (m, 3H), 6.89-6.82 (m, 2H), 5.08 (s, 2H), 3.76 (s, 3H), 2.42 (s, 3H); ^{13}C NMR δ 156.8, 144.6, 134.5, 133.7, 131.4, 130.6, 129.9, 129.1, 128.5, 128.1, 128.1, 127.5, 127.1, 123.8, 123.3, 123.2, 114.1, 113.0, 82.8, 71.0, 56.6, 45.2, 21.8; HRMS(ESI, positive): m/z calcd. for $C_{27}H_{23}NNaO_3S$ $[M+Na^+]$ 464.1291, found 464.1292.

_N_-(3-Bromo-4-methoxybenzyl)-_N_-(phenylethynyl)-_p_-toluenesulfonamide (1s)

Synthesized by Method B. Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as a pale yellow solid, 68% (2 steps); mp 108 °C; ^{1}H NMR δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.42 (s, 1H), 7.34-7.20 (m, 7H), 6.80 (d, *J* = 8.5 Hz, 2H), 4.47 (s, 2H), 3.84 (s, 3H), 2.42 (s, 3H); ^{13}C NMR δ 156.0, 144.9, 134.7, 134.0, 131.3, 129.9, 129.5, 128.4, 128.0, 127.9, 127.8, 122.8, 111.8, 111.6, 82.5, 71.8, 56.4, 54.7, 21.8; HRMS(ESI, positive): m/z calcd. for

$C_{23}H_{20}{}^{79}BrNNaO_3S$ [M+Na^+] 492.0239, found 492.0241.

***N*-(4-*tert*-Butoxybenzyl)-*N*-(phenylethynyl)-*p*-toluenesulfonamide (1t)**

Synthesized by Method B from *p-tert*-butoxybenzaldehyde.[20] Isolated by flash silica gel column chromatography (hexane/EtOAc = 7/3). The title compound was obtained as pale-yellow oil, 74%; ^{1}H NMR δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 2H), 7.26-7.20 (m, 7H), 6.92 (d, 8.4 Hz, 2H), 4.54 (s, 2H), 2.44 (s, 3H), 1.33 (s, 9H); ^{13}C NMR δ 155.7, 144.7, 134.9, 131.2, 129.9, 129.8, 129.3, 128.3, 127.9, 127.8, 124.1, 122.9, 82.8, 78.8, 71.5, 55.4, 28.9, 21.8; HRMS(ESI, positive): m/z calcd. for $C_{26}H_{27}NNaO_3S$ [M+Na^+] 456.1604, found 456.1603.

2-Tosyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2a)

Isolated by PTLC (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as a white solid, 53%; mp 165 °C; ^{1}H NMR δ 7.95 (d, *J* = 8.3 Hz, 2H), 7.40 (d, *J* = 8.3 Hz, 2H), 6.80 (d, *J* = 10.1 Hz, 2H), 6.35 (d, *J* = 10.1 Hz, 2H), 3.92 (s, 2H), 2.62 (s, 2H), 2.48 (s, 3H); ^{13}C NMR δ 184.4, 169.7, 147.6, 146.1, 134.6, 130.4, 130.1, 128.3, 53.8, 42.1, 40.9, 21.9; HRMS (ESI, positive): m/z calcd. for $C_{16}H_{15}NNaO_4S$ [M + $Na]^+$ 340.0614, found 340.0614.

4-Phenyl-2-tosyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2b)

Isolated by flash silica gel column chromatography (hexane/DCM/EtOAc = 4/5/1). The title compound was obtained as a pale pink solid, 85%; mp 188 °C; ^{1}H NMR δ 8.01 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.2 Hz, 2H), 7.25-7.18 (m, 3H), 6.91-6.85 (m, 3H), 6.63 (dd, *J* = 10.2, 3.1 Hz, 1H), 6.36 (dd, *J* = 10.1, 1.8 Hz, 1H), 6.09 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.01 (d, *J* = 10.4 Hz, 1H), 3.94 (d, *J* = 10.4 Hz, 1H), 3.91 (s, 1H), 2.49 (s, 3H); ^{13}C NMR δ 184.6, 170.4, 147.2, 146.2, 145.5, 134.7, 132.0, 131.0, 131.0, 130.2, 129.2, 128.8, 128.7, 128.4, 58.6, 52.1, 47.1, 21.9; HRMS (ESI, positive): m/z calcd. for $C_{22}H_{19}NNaO_4S$ [M + $Na]^+$ 416.0925, found 416.0927.

***N*-(4-Methoxybenzyl)-*N*-tosyl-2-oxo-2-phenylacetamide (2b')**[21]

The NMR data of the title compound were accorded with those in the literature.

4-(4-Fluorophenyl)-2-tosyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2c)

Isolated by flash silica gel column chromatography (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as a pale pink solid, 68%; mp >198 °C decomp.; ^{1}H NMR δ 8.00 (d, *J* = 8.2 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 6.95-6.88 (m, 4H), 6.86 (dd, *J* = 9.9, 3.0 Hz, 1H), 6.65 (dd, *J* = 10.1, 3.0 Hz, 1H), 6.37 (dd, *J* = 10.1, 1.8 Hz, 1H), 6.12 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.01 (d, *J* = 10.4 Hz, 1H), 3.96-3.90 (m, 2H), 2.49 (s, 3H); ^{13}C NMR δ 184.4, 170.1, 146.9, 146.3, 145.1, 134.6, 132.4,

131.2, 131.0, 131.0, 130.2, 128.4, 126.6 (d, $J_{C\text{-}F}$ = 3.6 Hz, 1C), 115.8 (d, $J_{C\text{-}F}$ = 21.8 Hz, 1C), 57.8, 52.0, 47.3, 21.9; HRMS (ESI, positive): m/z calcd. for $C_{22}H_{18}FNNaO_4S$ $[M + Na]^+$ 434.0833, found 434.0833.

4-(4-Chlorophenyl)-2-tosyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2d)

Isolated by PTLC (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as a pale yellow solid, 79%; mp 154-155 °C; ^{1}H NMR δ 8.00 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 6.87-6.83 (m, 3H), 6.64 (dd, *J* = 10.0, 3.0 Hz, 1H), 6.40-6.36 (m, 1H), 6.14-6.10 (m, 1H), 4.01 (d, *J* = 10.4 Hz, 1H), 3.93 (d, *J* = 10.4 Hz, 1H), 3.91 (s, 1H), 2.49 (s, 3H); ^{13}C NMR δ 184.2, 169.7, 146.6, 146.2, 144.8, 134.7, 134.4, 132.4, 131.1, 130.4, 130.1, 129.2, 128.9, 128.3, 57.8, 51.9, 47.1, 21.8; HRMS (ESI, positive): m/z calcd. for $C_{22}H_{18}ClNNaO_4S$ $[M + Na]^+$ 450.0539, found 450.0537.

4-(4-Bromophenyl)-2-tosyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2e)

Isolated by PTLC (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained pale yellow solid, 85%; mp 133 °C; ^{1}H NMR δ 8.00 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 7.9 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 1H), 6.85 (dd, *J* = 10.0, 3.1 Hz, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 6.63 (dd, *J* = 10.3, 3.1 Hz, 1H), 6.38 (dd, *J* = 10.0, 1.8 Hz, 1H), 6.12 (dd, *J* = 10.3, 1.8 Hz, 1H), 4.00 (d, *J* = 10.6 Hz, 1H), 3.93 (d, *J* = 10.6 Hz, 1H), 3.89 (s, 3H), 2.49 (s, 3H); ^{13}C NMR δ 184.3, 169.8, 146.7, 146.3, 144.9, 134.5, 132.5, 132.0, 131.3, 130.8, 130.2, 129.8, 128.4, 123.0, 58.0, 52.0, 47.2, 21.9; HRMS (ESI, positive): m/z calcd. for $C_{22}H_{18}{}^{79}BrNNaO_4S$ $[M + Na]^+$ 494.0034, found 494.0032.

4-(3-Chlorophenyl)-2-tosyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2f)

Isolated by PTLC (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as a pale yellow solid, 82%; mp 156-157 °C; ^{1}H NMR δ 8.01 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.24-7.21 (m, 1H), 7.16 (t, *J* = 7.8 Hz, 1H), 6.90-6.85 (m, 2H), 6.82-6.78 (m, 1H), 6.63 (dd, *J* = 10.2, 3.1 Hz, 1H), 6.39 (dd, *J* = 10.1, 1.8 Hz, 1H), 6.14 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.00 (d, *J* = 10.5 Hz, 1H), 3.94 (d, *J* = 10.5 Hz, 1H), 3.90 (s, 1H), 2.49 (s, 3H); ^{13}C NMR δ 184.3, 169.6, 146.6, 146.2, 144.8, 134.5, 134.4, 132.7, 132.3, 131.1, 130.1, 129.9, 129.0, 128.9, 128.3, 127.4, 57.9, 52.0, 47.0, 21.8; HRMS (ESI, positive): m/z calcd. for $C_{22}H_{18}{}^{35}ClNNaO_4S$ $[M + Na]^+$ 450.0538, found 450.0537.

4-(4-Bromo-2-fluorophenyl)-2-tosyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2g)

Isolated by PTLC (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as a pale yellow solid, 69%; mp 182-183 °C; ^{1}H NMR δ 7.99 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 7.9 Hz, 2H), 7.19 (dd,

J = 8.3, 1.8 Hz, 1H), 7.15 (dd, *J* = 9.6, 1.8 Hz, 1H), 6.90-6.82 (m, 2H), 6.76-6.72 (m, 1H), 6.34 (dd, *J* = 10.1, 1.8 Hz, 1H), 6.17 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.20 (s, 1H), 4.03 (d, *J* = 10.5 Hz, 1H), 3.96 (d, *J* = 10.5 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR δ 184.2, 168.9, 160.5 (d, $J_{C\text{-}F}$ = 252.4 Hz, 1C), 146.7, 146.2, 144.3 (d, $J_{C\text{-}F}$ = 1.5 Hz, 1C), 134.3, 132.3 (d, $J_{C\text{-}F}$ = 4.8 Hz, 1C), 132.0, 131.3, 130.1, 128.3, 127.7 (d, $J_{C\text{-}F}$ = 3.3 Hz, 1C), 123.3 (d, $J_{C\text{-}F}$ = 9.2 Hz, 1C), 119.5 (d, $J_{C\text{-}F}$ = 25.6 Hz, 1C), 117.5 (d, $J_{C\text{-}F}$ = 15.2 Hz, 1C), 52.2, 52.1, 47.1, 21.8; HRMS (ESI, positive): m/z calcd. for $C_{22}H_{17}{}^{79}BrFNNaO_4S$ $[M + Na]^+$ 511.9940, found 511.9938.

Methyl 4-(3,8-dioxo-2-tosyl-2-azaspiro[4.5]deca-6,9-dien-4-yl)benzoate (2h)

Isolated by PTLC (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as a brown solid, 86%; mp >100 °C decomp.; ^{1}H NMR δ 8.01 (d, *J* = 8.4 Hz, 2H), 7.89 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 8.2 Hz, 2H), 6.88 (dd, *J* = 10.0, 3.0 Hz, 1H), 6.64 (dd, *J* = 10.1, 3.0 Hz, 1H), 6.37 (dd, *J* = 10.0, 2.1 Hz, 1H), 6.08 (dd, *J* = 10.1, 2.1 Hz, 1H), 4.04-3.94 (m, 3H), 3.88 (s, 3H), 2.00 (s, 3H); ^{13}C NMR δ 184.2, 169.6, 166.4, 146.6, 146.3, 144.8, 135.7, 134.4, 132.4, 131.1, 130.4, 130.2, 129.8, 129.2, 128.4, 58.2, 52.3, 52.1, 47.1, 21.9; HRMS (ESI, positive): m/z calcd. for $C_{24}H_{21}NNaO_6S$ $[M + Na]^+$ 474.0983, found 474.0982.

2-Tosyl-4-(4-(trifluoromethyl)phenyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2i)

Isolated by PTLC (/DCM/EtOAc = 4/1). The title compound was obtained as a white solid, 98%; mp 93-94 °C; ^{1}H NMR δ 8.01 (d, *J* = 8.2 Hz, 2H), 7.49 (d, *J* = 8.2 Hz, 2H), 7.43 (d, *J* = 8.2 Hz, 2H), 7.06 (d, *J* = 8.2 Hz, 2H), 6.90 (dd, *J* = 10.1, 3.0 Hz, 1H), 6.64 (dd, *J* = 10.2, 3.0 Hz, 1H), 6.40 (dd, *J* = 10.1, 1.8 Hz, 1H), 6.12 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.05-3.95 (m, 3H), 2.50 (s, 3H); ^{13}C NMR δ 184.1, 169.5, 146.5, 146.3, 144.5, 134.8, 134.7 (q, $J_{C\text{-}F}$ = 1.2 Hz, 1C), 132.6, 131.3, 130.8 (q, $J_{C\text{-}F}$ = 32.8 Hz, 1C), 130.2, 129.7, 128.4, 125.6 (q, $J_{C\text{-}F}$ = 3.6 Hz, 1C), 123.7 (q, $J_{C\text{-}F}$ = 272.4 Hz, 1C), 58.0, 52.1, 47.2, 21.9; HRMS (ESI, positive): m/z calcd. for $C_{23}H_{18}F_3NNaO_4S$ $[M + Na]^+$ 484.0801, found 484.0802.

2-Tosyl-4-(2-(trifluoromethyl)phenyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2j)

Isolated by PTLC (hexane/toluene/DCM/EtOAc = 3/2/4/1). The title compound was obtained as a pale yellow solid, 35%; mp 72 °C; ^{1}H NMR δ 8.01 (d, *J* = 8.4 Hz, 2H), 7.63 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.46-7.38 (m, 3H), 6.95 (d, *J* = 7.6 Hz, 2H), 6.87-6.82 (m, 1H), 6.60 (dd, *J* = 10.3, 3.2 Hz, 1H), 6.30 (dd, *J* = 10.1, 1.8 Hz, 1H), 6.20 (dd, *J* = 10.3, 1.8 Hz, 1H), 4.32 (s, 1H), 4.06 (d, *J* = 10.6 Hz, 1H), 3.97 (d, *J* = 10.6 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR δ 184.3, 170.3, 147.1, 146.3, 144.7, 134.4, 132.0, 131.5, 131.2, 130.7, 130.3 (q, $J_{C\text{-}F}$ = 1.5 Hz, 1C), 130.2, 129.0, 128.5, 127.0 (q, $J_{C\text{-}F}$ = 5.4 Hz, 1C), 124.8, 122.6, 54.8, 52.5, 46.6, 21.9; HRMS (ESI, positive): m/z calcd. for $C_{23}H_{18}F_3NNaO_4S$

$[M + Na]^+$ 484.0801, found 484.0801.

4-(*p*-Tolyl)-2-tosyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2k)

Isolated by flash silica gel column chromatography (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as a pale yellow solid, 51%; mp 86-87 °C; ^{1}H NMR δ 8.01 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.01 (d, *J* = 7.9 Hz, 2H), 6.85 (dd, *J* = 10.1, 3.1 Hz, 1H), 6.77 (d, *J* = 7.9 Hz, 2H), 6.63 (dd, *J* = 10.1, 3.1 Hz, 1H), 6.35 (dd, *J* = 10.1, 1.8 Hz, 1H), 6.10 (dd, *J* = 10.3, 1.8 Hz, 1H), 3.99 (d, *J* = 10.4 Hz, 1H), 3.90 (d, *J* = 10.4 Hz, 1H), 3.86 (s, 1H), 2.49 (s, 3H), 2.26 (s, 3H); ^{13}C NMR δ 184.7, 170.5, 147.3, 146.1, 145.7, 138.5, 134.7, 132.0, 131.0, 130.1, 129.5, 129.0, 128.4, 127.9, 58.4, 52.0, 47.2, 21.9, 21.2; HRMS (ESI, positive): m/z calcd. for $C_{23}H_{21}NNaO_4S$ $[M + Na]^+$ 430.1085, found 430.1084.

4-(*m*-Tolyl)-2-tosyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2l)

Isolated by flash silica gel column chromatography (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as a pale yellow solid, 52%; mp 143-144 °C; ^{1}H NMR δ 8.02 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 8.1 Hz, 2H), 7.12-7.06 (m, 1H), 7.04 (d, *J* = 7.5 Hz, 1H), 6.88 (dd, *J* = 10.1, 3.1 Hz, 1H), 6.66 (d, *J* = 8.1 Hz, 2H), 6.61 (dd, *J* = 10.2, 3.1 Hz, 1H), 6.36 (dd, *J* = 10.0, 1.8 Hz, 1H), 6.12 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.00 (d, *J* = 10.4 Hz, 1H), 3.91 (d, *J* = 10.4 Hz, 1H), 3.84 (s, 1H), 2.49 (s, 3H), 2.22 (s, 3H); ^{13}C NMR δ 184.7, 170.6, 147.4, 146.1, 145.7, 138.5, 134.7, 131.7, 131.0, 131.0, 130.2, 129.6, 129.5, 128.7, 128.5, 126.2, 58.6, 52.1, 46.9, 21.9, 21.4; HRMS (ESI, positive): m/z calcd. for $C_{23}H_{21}NNaO_4S$ $[M + Na]^+$ 430.1083, found 430.1084.

4-(*o*-Tolyl)-2-tosyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2m)

Isolated by flash silica gel column chromatography (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as a pale yellow solid, 49%; mp 87-88 °C; ^{1}H NMR δ 8.03 (d, *J* = 8.2 Hz, 2H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.17-7.08 (m, 2H), 7.03-6.98 (m, 1H), 6.95 (dd, *J* = 10.1, 3.1 Hz, 1H), 6.60-6.57 (m, 1H), 6.46 (dd, *J* = 10.3, 3.2 Hz, 1H), 6.33 (dd, *J* = 10.1, 1.8 Hz, 1H), 6.17 (dd, *J* = 10.3, 1.8 Hz, 1H), 4.09 (s, 1H), 4.01 (d, *J* = 10.6 Hz, 1H), 3.92 (d, *J* = 10.6 Hz, 1H), 2.51 (s, 3H), 2.09 (s, 3H); ^{13}C NMR δ 184.5, 171.7, 163.8, 147.9, 146.2, 145.8, 137.2, 134.7, 131.4, 131.3, 130.8, 130.4, 130.2, 128.7, 128.5, 126.6, 55.0, 52.3, 46.0, 21.9, 20.2; HRMS (ESI, positive): m/z calcd. for $C_{23}H_{21}NNaO_4S$ $[M + Na]^+$ 430.1083, found 430.1084.

4-(4-Methoxyphenyl)-2-tosyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2n)

Isolated by flash silica gel column chromatography (hexane/DCM/EtOAc = 5/4/1). The title com-

pound was obtained as a vermilion solid, 14%; mp 70 °C; ^{1}H NMR δ 8.01 (d, *J* = 8.2 Hz, 2H), 7.41 (d, *J* = 8.1 Hz, 2H), 6.85 (dd, *J* = 9.9, 2.8 Hz, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.73 (d, *J* = 8.7 Hz, 2H), 6.64 (dd, *J* = 10.2, 2.8 Hz, 1H), 6.36 (dd, *J* = 9.9, 1.7 Hz, 1H), 6.11 (dd, *J* = 10.2, 1.7 Hz, 1H), 4.00 (d, *J* = 10.6 Hz, 1H), 3.90 (d, *J* = 10.6 Hz, 1H), 3.87 (s, 1H), 3.74 (s, 3H), 2.49 (s, 3H); ^{13}C NMR δ 184.5, 170.5, 159.5, 147.2, 146.0, 145.6, 134.6, 132.0, 130.9, 130.2, 130.0, 128.3, 122.7, 114.0, 57.9, 55.2, 51.8, 47.3, 21.8; HRMS (ESI, positive): m/z calcd. for $C_{23}H_{21}NNaO_5S$ $[M + Na]^+$ 446.1033, found 446.1033.

4-(Pyridin-3-yl)-2-tosyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2o)

Isolated by PTLC (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as a brown solid, 67%; mp 75-76 °C; ^{1}H NMR δ 8.49 (dd, *J* = 4.8 1.6 Hz, 1H), 8.19 (d, *J* = 2.2 Hz, 1H), 8.00 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.34-7.30 (m, 1H), 7.21-7.17 (m, 1H), 6.89 (dd, *J* = 9.9, 3.1 Hz, 1H), 6.67 (dd, *J* = 10.2, 3.1 Hz, 1H), 6.40 (dd, *J* = 9.9, 1.7 Hz, 1H), 6.13 (dd, *J* = 10.2, 1.7 Hz, 1H), 4.04 (d, *J* = 10.4 Hz, 1H), 4.01-3.97 (m, 2H), 2.50 (s, 3H); ^{13}C NMR δ 184.1, 169.3, 150.3, 150.0, 146.4, 146.2, 144.3, 136.8, 134.5, 133.0, 131.6, 130.3, 128.4, 126.8, 123.4, 56.2, 52.2, 47.5, 21.9; HRMS (ESI, positive): m/z calcd. for $C_{21}H_{18}N_2NaO_4S$ $[M + Na]^+$ 417.0879, found 417.0879.

6-Methoxy-4-phenyl-2-tosyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2p)

Isolated by PTLC (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as a pale-brown solid, 78%; diastereomeric mixture; ^{1}H NMR δ 8.08-7.98 (m, 2H), 7.46-7.36 (m, 2H), 7.24-7.12 (m, 3H), 6.96-6.86 (m, 2H), 6.69 (d, *J* = 9.9 Hz, 0.85H), 6.41 (d, *J* = 10.2 Hz, 0.15H), 6.28 (dd, *J* = 9.9, 1.5 Hz, 0.85H), 5.99 (dd, *J* = 10.1, 1.5 Hz, 0.15H), 5.66 (d, *J* = 1.5 Hz, 0.15H), 5.10 (d, *J* = 1.3 Hz, 0.85H), 4.32-3.88 (m, 3H), 3.79 (s, 0.45H), 3.14 (s, 2.55H), 2.49 (s, 3H); ^{13}C NMR δ 186.5, 186.2, 173.0, 171.1, 170.3, 170.0, 146.0, 145.5, 143.7, 142.2, 135.4, 134.8, 131.3, 131.1, 130.2, 130.1, 129.8, 129.6, 129.1, 129.0, 128.8, 128.6, 128.5, 128.5, 128.5, 128.4, 105.2, 103.3, 56.9, 56.7, 56.3, 55.1, 51.7, 51.4, 49.2, 48.5, 21.9, 21.9; HRMS (ESI, positive): m/z calcd. for $C_{23}H_{21}NNaO_5S$ $[M + Na]^+$ 446.1033, found 446.1036.

2'-Phenyl-1'-tosyl-4*H*-spiro[naphthalene-1,3'-pyrrolidine]-4,5'-dione (2q)

Isolated by PTLC (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as yellow oil, 85%; diastereomeric mixture; ^{1}H NMR δ 8.13 (d, *J* = 7.4 Hz, 0.61H), 8.11-8.03 (m, 2H), 7.86-7.80 (m, 0.39H), 7.74-7.41(m, 4H), 7.29-7.27 (m, 0.39H), 7.24-7.11 (m, 1H), 7.11-6.98 (m, 2H), 6.97-6.90 (m, 0.78H), 6.77-6.60 (m, 2H), 6.59-6.50 (m, 1.22H), 6.24 (d, *J* = 10.4 Hz, 0.61H), 4.50 (d, *J* = 10.8 Hz, 0.39H), 4.39 (s, 0.61H), 4.35 (d, *J* = 10.8 Hz, 0.61H), 4.28 (d, *J* = 10.8 Hz, 0.39H), 4.18-4.09 (m, 1H), 2.55-2.49 (m, 3H); ^{13}C NMR δ 183.4, 183.3, 170.5, 170.3, 149.0, 146.2, 146.1,

146.0, 141.7, 141.7, 134.8, 134.7, 133.5, 132.9, 132.6, 131.5, 131.3, 131.0, 130.2, 130.1, 130.0, 129.9, 129.5, 128.8, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.1, 128.0, 127.6, 127.3, 125.8, 124.7, 61.4, 59.9, 55.3, 55.1, 47.3, 46.9, 21.9 (a pair of peaks on alkyl region is overlapped); HRMS (ESI, positive): m/z calcd. for $C_{26}H_{21}NNaO_4S$ $[M + Na]^+$ 466.1084, found 466.1086.

2'-Phenyl-1'-tosyl-2*H*-spiro[naphthalene-1,3'-pyrrolidine]-2,5'-dione (2r)

Isolated by PTLC (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as a brown solid, 54%; diastereomeric mixture (d.r. = 1.4:1); mp >200 °C decomp; ^{1}H NMR δ 8.15-8.03 (m, 2H), 7.76-7.69 (d, J = 7.9 Hz, 0.58H), 6.64-7.54 (m, 0.58H), 7.47-7.39 (m, 3H), 7.33-7.27 (m, 1H), 7.25-7.01 (m, 4H), 6.99-6.89 (m, 0.84H), 6.63-6.53 (m, 2H), 6.18 (d, *J* = 9.9 Hz, 0.42H), 5.66-5.58 (d, *J* = 9.9 Hz, 0.58H), 4.71 (d, *J* = 10.3 Hz, 0.42H), 4.39 (d, *J* = 10.8 Hz, 0.58H), 4.36-4.30 (m, 1H), 4.30-4.23 (m, 1H), 2.54-2.48 (m, 3H); ^{13}C NMR δ 199.9, 199.3, 170.3, 169.8, 147.0, 145.9, 145.5, 145.3, 140.6, 140.2, 135.2, 134.7, 131.5, 131.2, 130.9, 130.8, 130.7, 130.3, 130.2, 130.0, 129.9, 129.9, 129.8, 129.3, 128.7, 128.7, 128.6, 128.5, 128.3, 128.1, 127.9, 127.6, 126.8, 126.3, 124.8, 124.7, 63.2, 62.7, 56.4, 55.6, 54.1, 53.4, 22.0, 21.9 (two pairs of peaks on the aromatic region are overlapped); HRMS (ESI, positive): m/z calcd. for $C_{26}H_{21}NNaO_4S$ $[M + Na]^+$ 466.1084, found 466.1085.

1-(4-Hydroxyphenyl)-1-methoxycarbonyl-1-phenylmethane (3)[22]

Isolated by PTLC (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as colorless oil, 91%; ^{1}H NMR δ 7.40-7.21 (m, 5H, overlapped with $CHCl_3$), 7.16 (d, *J* = 8.7 Hz, 2H), 6.76 (d, *J* = 8.7 Hz, 2H), 5.10 (s, 1H), 4.97 (s, 1H), 3.74 (s, 3H); ^{13}C NMR δ 173.6, 155.0, 139.0, 130.9, 130.0, 128.8, 128.6, 127.4, 115.6, 56.3, 52.5; HRMS (ESI, positive): m/z calcd. for $C_{15}H_{14}NaO_3$ $[M + Na]^+$ 265.0835, found 265.0834.

8-Hydroxy-4-phenyl-2-azaspiro[4.5]decan-3-one (4)

The title compound was obtained as a white solid, quant.; diastereomeric mixture; mp 95 °C; ^{1}H NMR (CD_3OD) δ 7.37-7.23 (m, 3H), 7.22-7.18 (m, 0.6H), 7.17-7.10 (m, 1.4H), 3.41-3.26 (m, 4H), 1.94-1.17 (m, 7H), 1.14-1.05 (m, 0.3H), 0.89-0.77 (m, 0.7H); ^{13}C NMR δ 181.1, 180.6, 137.3, 136.7, 130.9, 130.7, 129.5, 129.4, 128.3, 128.3, 70.2, 60.9, 50.8, 44.3, 44.1, 35.7, 32.5, 32.0, 31.2, 31.2, 31.2, 31.1, 30.6, 30.5 (two pairs of peaks on the alkyl region are overlapped); HRMS (ESI, positive): m/z calcd. for $C_{15}H_{19}NNaO_2$ $[M + Na]^+$ 268.1308, found 268.1309.

7-Hydroxy-4-phenyl-2-tosyl-1,2-dihydroisoquinolin-3(4*H*)-one (**5**)

Isolated by flash silica gel column chromatography (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as a white solid, 87%; mp 182 °C; ^{1}H NMR δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.28-7.14 (m, 6H,), 6.88 (d, *J* = 6.6 Hz, 2H), 6.81 (dd, *J* = 8.2, 2.4 Hz, 1H), 6.56 (d, *J* = 2.4 Hz, 1H), 5.79 (brs, 1H), 5.09 (d, *J* = 15.2, 1H), 4.69 (s, 1H), 4.55 (d, *J* = 15.2 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR δ 170.0, 156.5, 145.1, 136.0, 135.5, 134.2, 129.5, 129.0, 128.6, 127.9, 127.7, 127.7, 124.0, 115.4, 115.1, 55.6, 48.0, 21.8; HRMS (ESI, positive): m/z calcd. for $C_{22}H_{19}NNaO_4S$ $[M + Na]^+$ 416.0927, found 416.0925.

4-Methyl-4-phenyl-2-tosyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (**6**)

Isolated by flash silica gel column chromatography (hexane/DCM/EtOAc = 5/4/1). The title compound was obtained as a white solid, 96%; mp 135 °C; ^{1}H NMR δ 8.05 (d, *J* = 8.3 Hz, 2H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.26-7.17 (m, 3H), 6.87 (d, *J* = 7.3 Hz, 2H), 6.80 (dd, *J* = 10.3, 3.0 Hz, 1H), 6.41 (dd, J = 10.3, 1.7 Hz, 1H), 6.23 (dd, *J* = 10.3, 1.7 Hz, 1H), 6.17 (dd, *J* = 10.3, 3.0 Hz, 1H), 3.84 (d, *J* = 10.5Hz, 1H), 3.80 (d, *J* = 10.5 Hz, 1H), 2.53 (s, 3H), 1.34 (s, 3H); ^{13}C NMR δ 184.6, 174.4, 146.7, 146.5, 146.2, 137.2, 134.6, 131.5, 131.1, 130.2, 129.0, 128.5, 128.4, 126.6, 58.5, 50.9, 48.6, 22.0, 20.0; HRMS (ESI, positive): m/z calcd. for $C_{23}H_{21}NNaO_4S$ $[M + Na]^+$ 430.1084, found 430.1084.

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Chapter 4

Concluding Remarks

In this thesis, the author explained the gold(I)-catalyzed construction of nitrogen-containing medium-sized rings and azaspirocyclic compounds.

In Chapter 2, the author disclosed 7-*endo*-*dig*-selective cycloisomerization of 2-alkynydiphenylamines and 8-*exo*-*dig*-selective cycloisomerization of 2-propargylaminotriphenylamines, which gave dibenzazepines and dibenzodiazocines, respectively. The reaction of carbazole-containing 2-alkynyldiphenylamine derivatives gave π-conjugated multicyclic compounds. The consecutive cycloisomerization and oxidation of indoline-containing 2-alkynyldiphenylamine derivatives provided tetracyclic indole-containing compounds under mild conditions. This strategy was applied for the reaction of 2-alkynyl-*N*-methyldiphenylamine to give *N*-methyldibenzazepine. On the other hand, the reaction of 2-propargylaminotriphenylamines possessing a terminal alkyne moiety proceeded via 8-*exo*-*dig* cyclization under mild conditions using Ph_3PAuCl. In contrast, the use of IPrAuCl was important for the reaction of internal alkynes.

In Chapter 3, the author disclosed dearomative spirocyclization of phenol derivatives using gold carbenoid species derived from ynamides and *N*-oxide, which provided azaspirocyclohexadienones. The reaction proceeded even under air without the use of hazardous diazo compounds. The use of IPr as the ligand and water as the co-solvent surppressed the formation of diketone by-products. Some of the obtained products were transformed into synthetically important compounds.

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早稲田大学　博士（理学）　学位申請　研究業績書

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講演	“Gold(I)-Catalyzed 8-*exo-dig* Selective Cycloisomerization for the Synthesis of Dibenzodiazocine Derivatives” XXVIII International Conference on Organometallic Chemistry, Florence (Italy), July 2018, P246. Asahi Takaki, Daisuke Inoue, Mamoru Ito, Kyalo Stephen Kanyiva, Takanori Shibata 「カチオン性金触媒による環化異性化反応を用いた含窒素中員環合成」 第 113 回有機合成シンポジウム, 名古屋大学（愛知）, 2018 年 6 月, A-16. 伊藤守, 川崎涼介, 井上大輔, 高木朝日, Kyalo Stephen Kanyiva, 柴田高範 「金(Ⅰ)触媒を用いた 8-*exo-dig* 選択的環化異性化によるジベンゾジアゾシン誘導体の合成」 日本化学会第 98 春季年会, 日本大学（千葉）, 2018 年 3 月, 2H2-16. 高木朝日, 井上大輔, 伊藤　守, カニヴァ　ステイヴィン　キャロ, 柴田高範 「イナミドから調製される α-オキソ金カルベノイド種を用いたフェノール類の脱芳香化を伴う触媒的スピロ環化反応」 日本化学会第 98 春季年会, 日本大学（千葉）, 2018 年 3 月, 2H2-15. 伊藤　守, 川崎涼介, カニヴァ　ステイヴィン　キャロ, 柴田高範 “Construction of Dibenzazepine Skeleton via Au(I)-Catalyzed Cycloisomerization on 7-Position of Indoline” 26th ISHC Congress, Regensburg (Germany), September 2017, TUE-P56 Daisuke Inoue, Mamoru Ito, Ryosuke Kawasaki, Kyalo Stephen Kanyiva, Takanori Shibata 「カチオン性金触媒による環化異性化反応を用いたジベンゾアゼピン誘導体の合成」 第 73 回有機合成化学協会関東支部シンポジウム, 学習院大学（東京）, 2017 年 5 月, A04. 伊藤守, 川崎涼介, Kyalo Stephen Kanyiva, 柴田高範 「金(I)触媒を用いた環化異性化によるインドリン骨格を有するジベンゾアゼピン誘導体の合成」 日本化学会第 97 春季年会, 慶應義塾大学（神奈川）, 2017 年 3 月, 1E2-09. 井上大輔, 伊藤　守, カニヴァ　ステイヴィン　キャロ, 柴田高範 “Efficient Synthesis of Dibenzazepine Derivatives by Cationic Au(I)-Catalyzed Cycloisomerization” Catalysis and Fine Chemicals, Taipei (Taiwan), November 2016, YO-04. Mamoru Ito, Ryosuke Kawasaki, Kyalo Stephen Kanyiva, Takanori Shibata 「金触媒による環化異性化反応をジベンゾアゼピン誘導体の合成」 第 63 回有機金属化学討論会, 早稲田大学,（東京）, 2016 年 9 月, O2-16. 伊藤　守, 川崎　涼介, カニヴァ　ステイヴィン　キャロ, 柴田　高範

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講演	“Efficient synthesis of 4-substituted tryptophan derivatives via Ir-catalyzed C-H bond activation: Total synthesis of cis-clavicipitic acid” Pacifichem, Honolulu, December 2015, Organic 2546. Mamoru Ito, Yuki Tahara, Takanori Shibata “Enantioselective synthesis of γ-amino acids via sp^3 C-H Bond activation using by Ir(I)-catalyst” Pacifichem, Honolulu, December 2015, Organic 1355. Masamichi Michino, Mamoru Ito, Yuki Tahara, Takanori Shibata 「Ir 触媒による sp^3 C-H 結合活性化を用いたγ-ラクタムとγ-アミノ酸の不斉合成」 第 45 回 複素環化学討論会, 早稲田大学（東京）, 2015 年 11 月, 1P-22. 道野 仁理, 伊藤 守, 田原 優樹, Kyalo Stephen Kanyiva, 柴田 高範 「イリジウム触媒による炭素－水素結合活性化を鍵反応とした cis-クラビシピチン酸の全合成」 第 45 回 複素環化学討論会, 早稲田大学（東京）, 2015 年 11 月, 2P-12. 伊藤 守, 田原 優樹, カニヴァ キャロ ステイヴィン, 柴田 高範 「遷移金属触媒を用いるC-H結合活性化反応および[2+2+2]付加環化反応を利用した新規アミノ酸誘導体の合成」 第 108 回 有機合成シンポジウム, 早稲田大学（東京）, 2015 年 11 月, O-01. 田原　優樹, 伊藤　守, 大日方 秀平, 道野　仁理, Kyalo Stephen Kanyiva, 柴田　高範 “Enantioselective Synthesis of γ-Amino Acid Derivatives via Iridium Catalyzed Activation of sp^3 C-H Bond” 250th American Chemical Society National Meeting & Exposition, Boston, MA, August 2015, ORGN112. Yuki Tahara, Masamichi Michino, Mamoru Ito, Takanori Shibata 「イリジウム触媒を用いる炭素－水素結合活性化を起点としたクラビシピチン酸の全合成」 日本化学会第 95 春季年会, 日本大学（千葉）, 2015 年 3 月, 2G3-11. 伊藤　守, 田原優樹, 柴田高範 「イリジウム触媒を用いるエナンチオ選択的C-H結合活性化を利用したγ-アミノ酸類の不斉合成」 日本化学会第 95 春季年会, 日本大学（千葉）, 2015 年 3 月, 2E5-12. 道野仁理, 伊藤　守, 田原優樹, 柴田高範 “Enantioselective Synthesis of γ-Amino Acid Derivatives via Ir(I)-Catalyzed sp^3 C-H Bond Activation” XXVI International Conference on Organometallic Chemistry, Sapporo (Japan), July 2014, 3P105. Mamoru Ito, Shun Yuzawa, Yu-ki Tahara, Takanori Shibata