Abstract

Title of Document:	DIVERSITY IN CATALYTIC REACTIONS OF PROPARGYLIC DIAZOESTERS
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Propargylic aryldiazoesters, which possess multiple reactive functional groups in a single molecule, were expected to undergo divergent reaction pathways as a function of catalysts. A variety of transition metal complexes including rhodium(II), palladium(II), silver(I), mercury(II), copper(I and II), and cationic gold (I) complexes have been examined to be effective in the catalytic domino reactions of propargylic aryldiazoesters. An unexpected Lewis acid catalyzed pathway was also discovered by using $FeCl_3$ as the catalyst.

Under the catalysis of selected gold catalysts, propargylic aryldiazoesters exist in equilibrium with 1-aryl-1,2-dien-1-yl diazoacetate allenes that are rapidly formed at room temperature through 1,3-acyloxy migration. The newly formed allenes further undergo a metal-free

rearrangement in which the terminal nitrogen of the diazo functional group adds to the central carbon of the allene initiating a sequence of bond forming reactions resulting in the production of 1,5-dihydro-4*H*-pyrazol-4-ones in good yields. These 1,5-dihydro-4*H*-pyrazol-4-ones undergo intramolecular 1,3-acyl migration to form an equilibrium mixture or quantitatively transfer the acyl group to an external nucleophile with formation of 4-hydroxypyrazoles.

In the presence of a pyridine-*N*-oxide, both *E*- and *Z*-1,3-dienyl aryldiazoacetates are formed in high combined yields by Au(I)-catalyzed rearrangement of propargyl arylyldiazoacetates at short reaction times. Under thermal reactions the *E*-isomers form the products from intramolecular [4+2]-cycloaddition with $\Delta H^{\ddagger}_{298} = 15.6$ kcal/mol and $\Delta S^{\ddagger}_{298} = -27.3$ cal/ (mol•degree). The *Z*-isomer is inert to [4+2]-cycloaddition under these conditions. The Hammett relationships from aryl-substituted diazo esters ($\rho = +0.89$) and aryl-substituted dienes ($\rho = -1.65$) are consistent with the dipolar nature of this transformation.

An unexpected reaction for the synthesis of seven-membered conjugated 1,4-diketones from propargylic diazoesters with unsaturated imines was disclosed. To undergo this process vinyl gold carbene

intermediates generated by 1,2-acyloxy migration of propargylic aryldiazoesters undergo a formal [4+3]-cycloaddition, and the resulting aryldiazoesters tethered dihydroazepines undergo an intricate metal-free process to form observed seven-membered conjugated 1,4-diketones with moderate to high yields.

Diversity in Catalytic Reaction of Propargylic Diazoesters

By

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Dissertation submitted to the Faculty of the Graduate School of the
University of Maryland, College Park, in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
2016

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Dedication

To my wife, Lulu Ma for her tireless support throughout this entire process, to my granduncle Changji Qiu and my parents Baifa Qiu and Sumei Sheng.

Acknowledgement

I would like to express deepest gratitude to my advisor, Dr. Michael Doyle, for his support, patience, encouragement, and guidance throughout my entire graduate research program in the United States. His great passion on science has always motivated me, and his thoughtful criticisms have inspired me a lot. Without his great guidance and constant feedback this PhD dissertation would not have been achievable. To me, Dr. Michael Doyle is not only a great mentor in science but also an outstanding mentor in life. Also, I would like to extend my gratitude to Janice Doyle for her help to me and my family in United States.

I would like to thank my advisor Professor Wenhao Hu at East China Normal University in China. He is a person who showed the beauty of organic chemistry to me and fostered my great interests in scientific research. I truly benefit from his insights on science as well as his advice both on my career development and my life.

I would like to thank Professor Anderi Vedernikov, Professor Daniel Falvey, and Professor Lyle Isaacs for serving on Ph.D dissertation committee, and Professor Yanjin Zhang for serving as the Dean's representative. I am really appreciated for their valuable time and advices.

granduncle, my parents, mother-in-law, father-in-law, brother, sister, and my wife for their support and love over the years.

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p-ABSA	4-Acetamidobenzenesulfonyl azide
Ar	aromatic
Bn	benzyl
t-Bu	*tert*-butyl
DCM	dichloromethane
DCE	1,2-dichloroethane
dr	diastereomeric ratio
ee	enantiomeric excess
Et	ethyl
Et_3N	triethylamine
EtOAc	ethyl acetate
equiv	equivalent
h	hour

MLn   transition metal with ligands

Me   methyl

NMR   nuclear magnetic resonance

OAc   acetate

i-Pr   *iso*-propyl

RT   room temperature

SEM   scanning electron microscope

THF   tetrahydrofuran

TMS   trimethylsilyl

Chapter 1: Catalyst Classification in Catalytic Reaction of Propargylic Diazoesters

I. Introduction

1.1 General Information for Diazo Compounds

Diazo compounds are high energy organic compounds bearing a C=N=N functional group. Their general formula can be described as $R_1R_2C=N_2$. Two resonance contributing structures describe the general electronic characteristics of diazo compounds (**Figure 1.1**). These electronic structures describe an electropositive center on the central nitrogen and nucleophilic centers at the terminal nitrogen and the carbon.
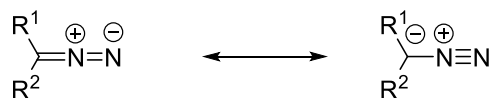
Figure 1.1 Resonance Structures of Diazo Compounds.

Diazo compounds are capable of undergoing a variety of transformations, and numerous reactions involving diazo compounds have been studied over the past hundred years. In general, four types of reactions have been recognized and described in the literature (**Scheme 1.1**): (a) 1,3-dipolar cycloaddition reactions with alkenes or alkynes;[1] (b)

a surprising electrophilic addition to nucleophiles from the terminal

nitrogen position;[2] (c) nucleophilic addition reactions with electrophiles

that occur at the nucleophilic carbon position,[3] and (d) reactions

involving (metal) carbene intermediates.[4]
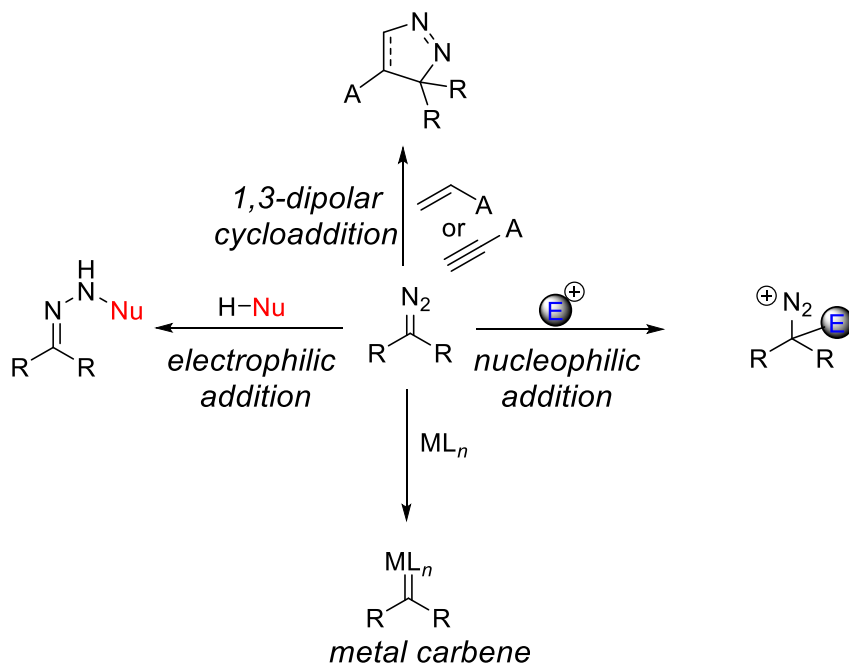
Scheme 1.1 General Reactions of Diazo Compounds.

1.2 Transition Metal-Catalyzed reactions of Diazo Compounds

Catalytic decomposition of diazo compounds occurs by the

extrusion of dinitrogen to produce a variety of reaction products

dependent on the catalyst that is employed.[5] Because of back-bonding

from electrophilic transition metals, their complexes produce

electrophilic metal-stabilized carbenes.[6] The proposed process involves the use of a transition metal complex as a Lewis acid by coordination to the negatively-polarized carbon of the diazo compound to produce an organometallic diazonium ion followed by loss of dinitrogen to furnish the metal-stabilized carbene.[6b,7] The metal-stabilized carbene may be depicted by two resonance contributing structures: one that describes a metal-carbon double bond, not unlike that used to depict stable Fischer carbene,[6-7] and another having a charge separated structure that places a formal positive charge on carbon and a formal negative charge on the metal (**Scheme 1.2**).[8] The depiction of the carbene as a charge-separated species (metal-stabilized carbocation), while deemphasizing back bonding from metal into the carbene, provides focus on their electrophilic reactivity.
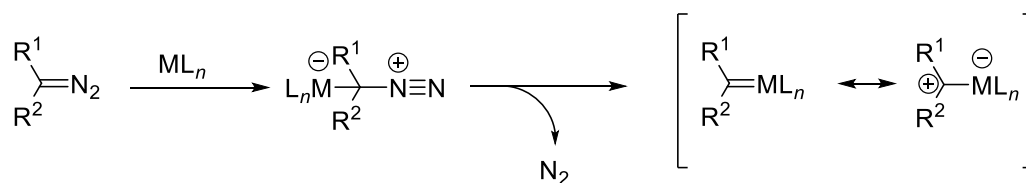
Scheme 1.2 Transition Metal-Catalyzed Decomposition of the Diazo Compounds.

Due to their high electrophilic reactivity, metal-stabilized carbenes have been reported to undergo a wide array of transformations including

cyclopropanation, cyclopropenation, C-H insertion and ylide formation (**Scheme 1.3**).[5a,9] For these processes a simplified catalytic cycle is described in **Scheme 1.4**, and in some cases catalyst loading is under 0.1 mol %.[10] Addition to the carbon-carbon double bond to form cyclopropanes is perhaps the most studied transformation, but C-H insertion and ylide-derived transformations have emerged during the past two decades as viable and synthetically useful transformations.[5b,10-11]

A = CR$_3$, NR$_2$, OR...
Y = CR$_2$
cycloaddition

R^1 = H, alkyl, aryl
Z = COOR, H, CONR$_2$

metal carbene

X = CR$_3$, SiR$_3$, BR$_2$...

insertion

B = NR$_2$, OR, SR...
ylide formation
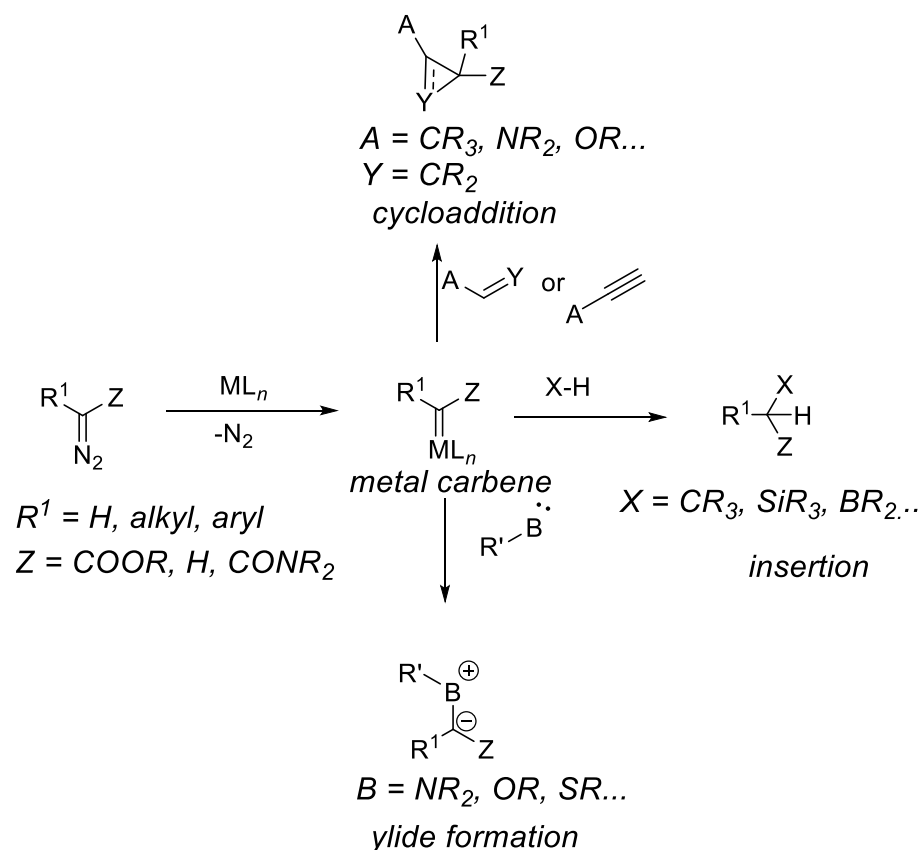
Scheme 1.3 Transition Metal-Catalyzed Reactions of Metal Carbenes Formed from Diazo Compounds.

$R^1R^2C=N_2$

$[L_nM \ominus R^1 \oplus N \equiv N \ R^2]$

$[ML_n]$

N_2

$[R^1R^2C=ML_n]$

SCR^1R^2

S:
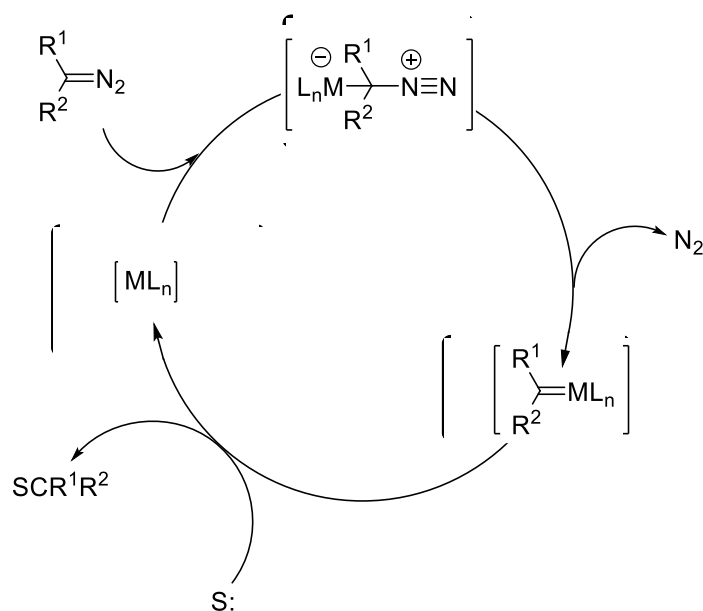
Scheme 1.4 Generally Accepted Mechanism for Metal Catalyzed Decomposition of Diazo Compounds.

1.2.1 Classification of Metal Carbenes

The reactivity profile of metal carbenes is greatly influenced by the electronic nature of the substituents that adorn the carbene center.[12] Because of their relative stabilities and general ease of formation and handling, diazocarbonyl compounds are the most commonly used metal carbene precursors.[13] Three types of metal carbenes have been classified and described by Davies and coworkers: acceptor, acceptor/acceptor, and donor/acceptor metal carbenes (**Scheme 1.5**);[5d,11b,11c] the term "acceptor" refers to an electron-withdrawing group (keto, cyano, nitro, phosphonyl and sulfonyl) bonded to the carbene center, whereas "donor" refers to an electron-donating group (vinyl, aryl and heteroaryl) bonded to the

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carbene center; both terms are relative to hydrogen in their electronic

effects.

Acceptor/acceptor metal carbene   Acceptor metal carbene   Donor/acceptor metal carbene
EWG = electron-withdrawing group (CO_2R, COR, CN, $CONR_2$, $PO(OR)_2$, SO_2R, NO_2, CF_3)
EDG = electron-donating group (aryl, vinyl, heteroaryl)
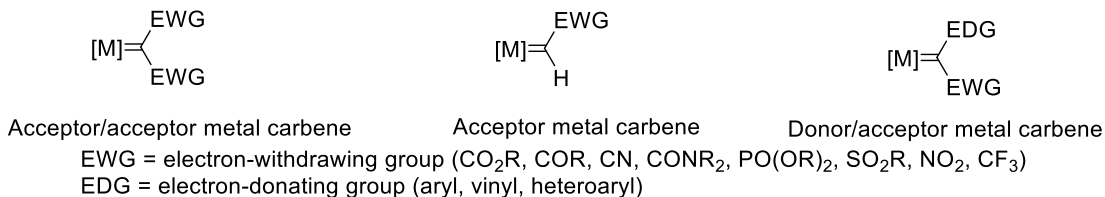
Scheme 1.5 Classification of Substituted Metal Carbene Intermediates.

Due to the electrophilic character of metal carbenes, the electron-

donating group bonded to the carbene center will stabilize metal carbenes,

which results in their increased selectivity compared to the acceptor and

acceptor/acceptor metal carbenes (**Scheme 1.6**).[5b]

Increasing stability and selectivity

Increasing reactivity
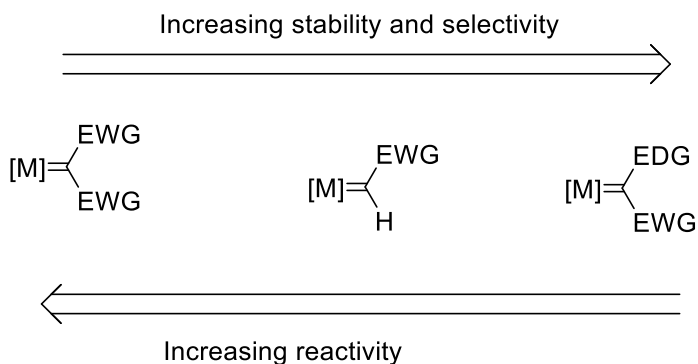
Scheme 1.6 General Reactivity Profiles of Metal Carbenes.

For the past two decades, numerous efforts have been devoted to

the study of catalytically selective reactions of donor/acceptor metal

carbenes, especially aryldiazoacetates.[5c] These donor/acceptor diazo

compounds are easily prepared from corresponding arylacetate esters via a diazo transfer reaction, usually with 4-acetamidobenzenesulfonyl azide (*p*-ABSA).[14] They are stable and storable at room temperature for extended periods of time; and they are capable of undergoing a variety of transformations ranging from cyclopropanation, cyclopropenation, C-H insertion, aromatic substitution, and ylide formation (**Scheme 1.7**).[15]
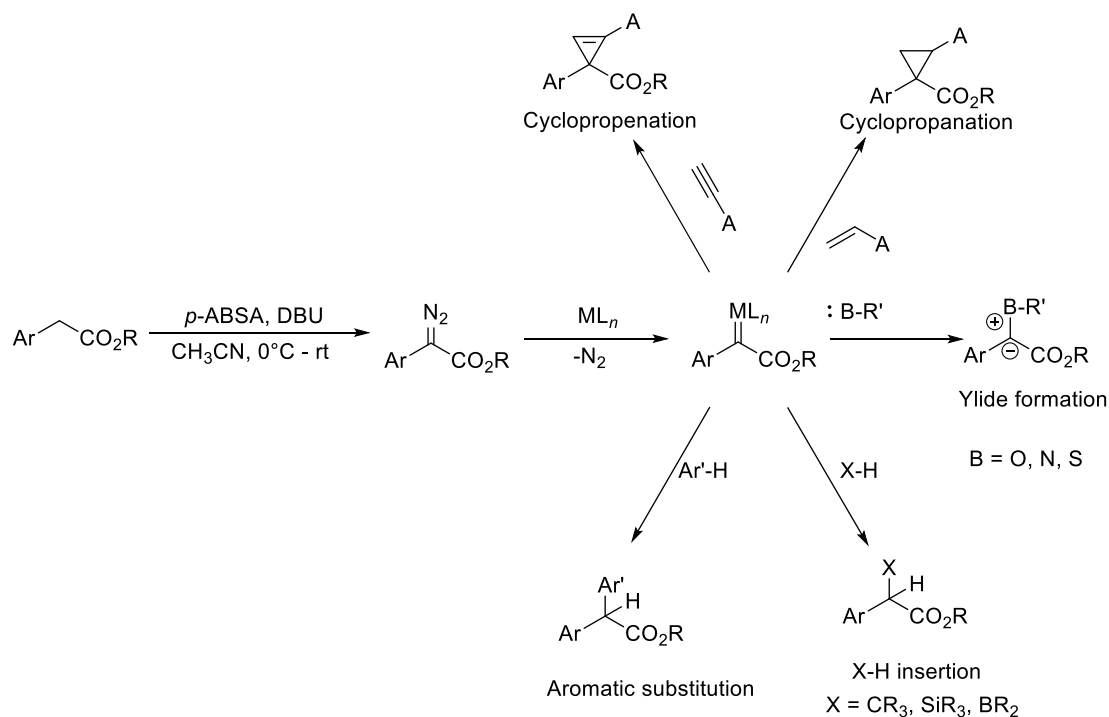
Scheme 1.7 Synthesis of Donor/Acceptor Diazo Compounds and Transformations involving Donor/Acceptor Metal Carbenes.

1.2.2 Transition Metal Complexes for Metal Carbene Transformations

Transition metal complexes have played an important role in the development of synthetic methodology;[4b,16] and their applications to the decomposition of diazo compounds, as well as their subsequent transformations involving metal carbenes, are particular attractive. Transition metal complexes, including those of copper, rhodium, cobalt, iron, palladium, ruthenium, silver, iridium,[17] and gold have been reported to mediate these transformations effectively; [13b] and recent results have shown that the ligands for these transition metals have great influence on the reactivity and selectivity.[18] Copper and rhodium complexes are well-established systems, and their activities and selectivities have been summarized in several excellent reviews.[6a,6b,9,11d]

1.2.2.1 Copper Catalysts in the Decomposition of Diazo Compounds

Since the first discovery of copper-catalyzed decomposition of diazo compounds over a century ago,[19] a variety of copper salts and complexes have been widely used in the catalytic reactions of diazo compounds. These copper salts include copper(I) halides,[20] copper(I) triflate,[21] copper(II) triflate,[22] copper(II) sulfate.[23] The commercial available and conveniently handled tetrakis(acetonitrile)copper(I) hexafluorophosphate $[CuPF_6(MeCN)_4]$[24] and

tetrakis(acetonitrile)copper(I) tetrafluoroborate $[CuBF_4(MeCN)_4]$[25] have shown advantages over other copper salts in several transformations.

Copper(I) is understood to be the catalytically active oxidation state in copper catalyzed reactions of diazo compounds.[21] With four coordination sites copper(I) can be linked to ligands that influence its reactivity and selectivity in reactions with diazo compounds. The first effective chiral ligands used to control enantioselectivity were introduced on copper,[26a] and the most effective of these ligands were multidentate.[5b, 26b] Copper complexes formed from chiral ligands have been widely used in the asymmetric transformations including cyclopropanation,[27] C-H insertion,[28] and [3+3]-cycloaddition of diazo compounds,[29] and the major ligands used for copper(I) complexes are described in **Figure 1.2**. [30]

R = Ph, ^{t}Bu, ^{i}Pr, Bn
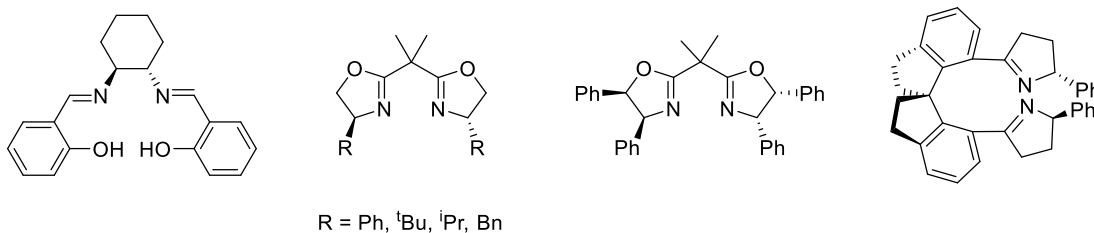
Figure 1.2 Selected Chiral Ligands for Copper Catalysts.

1.2.2.2 Rhodium Complexes in Dinitrogen Extrusion from Diazo Compounds

Dirhodium(II) complexes have emerged as the dominant catalysts for reactions with diazo compounds.[5b,5d,10,15a,31] They possess a paddlewheel structure containing two rhodium atoms that are connected by a rhodium-rhodium single bond and four bidentate ligands that bridge two rhodium atoms in 16-electron rhodium complexes (**Figure 1.3**). The bridging ligands are most commonly carboxylates or carboxamidates, though catalysts based on phosphonate[32] and arylphosphine[33] ligands have also been reported. Dependent on the bridging ligands, they may have water solubility; but most uses have occurred in solvents of moderate polarity such as dichloromethane. Two open coordination sites exist at the axial positions of these paddlewheel complexes, and the axial coordination site is the electrophilic center at which reaction with diazo compounds occurs.
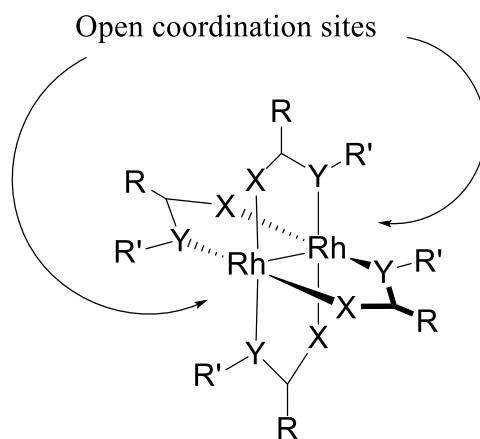
Figure 1.3 General Structural Formula for Homoleptic Dirhodium(II) Carboxylates (X = Y = O) and Carboxamidates (X = O; Y = N).

Chiral dirhodium(II) carboxylates or carboxamidates can be easily prepared from rhodium acetate and corresponding enantiomerically pure amino-protected amino acids or enantiomerically pure amino acid-derived lactams.[8,34] Several excellent reviews describe their catalytic advantages.[5a,5b,5d,10] Recently, these chiral dirhodium(II) complexes have been broadly classified and well summarized according to generality and selectivity in the transformations of rhodium carbenes by a compressive review by Doyle and coworkers (**Figure 1.4**).[35]

Davies's catalysts   Hashimoto's catalysts

$Ar = p\text{-}(^nC_{12}H_{25})C_6H_4$

Rh$_2$(*R*-DOSP)$_4$ Rh$_2$(*R*-PTTL)$_4$ Rh$_2$(*R*-NTTL)$_4$

Doyle's catalysts

Rh$_2$(5R-MEPY)$_4$ Rh$_2$(4R-MEOX)$_4$ Rh$_2$(4S-MPPIM)$_4$ Rh$_2$(4S-MEAZ)$_4$
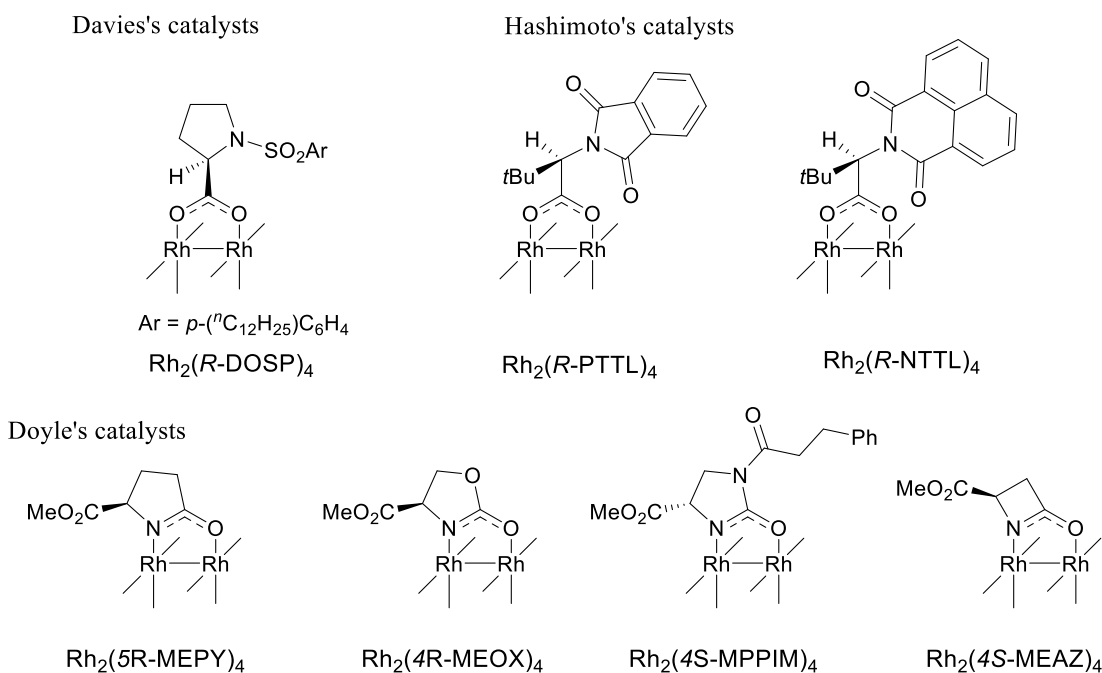
Figure 1.4 Representative Examples of Chiral Dirhodium(II) Carboxylates and Carboxamidates.

1.2.2.3 Gold Complexes in Reactions with Diazo Compounds

Gold complexes have emerged in recent years as powerful catalysts for the construction of C–C, C–N, and C–O bonds in organic synthesis.[36] During the past decade, the chemical community has witnessed a rapidly increasing interest in the gold-catalyzed transformations of diazo compounds, especially α-diazocarbonyl compounds.[37]

Gold(I) complexes, simply described as [LAuY], are two-coordinate, linear species; they are air- and moisture-stable. When Y is a coordinating anion (halides, carboxylates, sulfonates, and triflimide), they are neutral gold(I) complexes. Cationic gold(I) complexes with weakly coordinating anions (BF_4^-, PF_6^-, SbF_6^-, OTf^-, NTf_2^- $BAr^F_4{}^-$), which can be generated in situ via ionization of neutral gold(I) complexes (LAuCl) with soluble silver or sodium salts ($AgSbF_6$, $AgBF_4$, $NaBAr^F_4$), are the most commonly used gold complexes for reactions with α-diazocarbonyl compounds; and the reactivity profiles of formed gold carbene complexes is greatly dependent on the nature of the ligand that is bound to gold. Phosphines, phosphites, and *N*-heterocyclic carbenes are the most commonly used ligands. The most commonly used ligands are listed in **Figure 1.5**.[38]
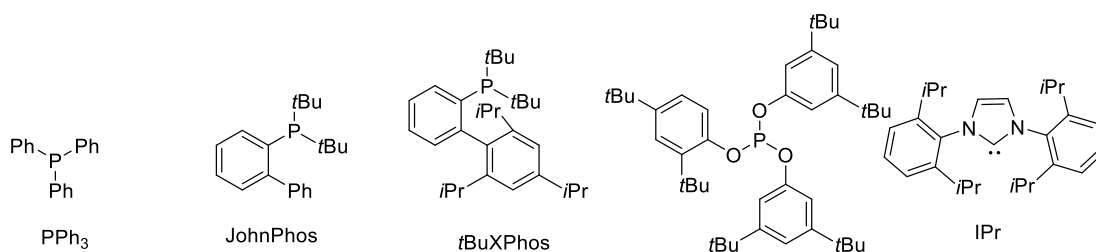
Figure 1.5 Selected Chiral Ligands for Gold(I) Catalysts.

Beside the cationic gold(I) complexes, some simple gold(III) salts such as AuCl₃ and AuCl₃(pyridine), also have been reported as catalysts in decomposition of diazo compounds (**Figure 1.6**). These complexes are subject to disproportionation at higher temperatures, generally observed through the formation of metallic gold.
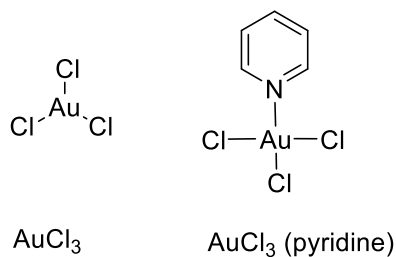
Figure 1.6 Structures for AuCl₃ and AuCl₃(Pyridine).

1.2.2.4 Other Transition Metal Complexes in Reactions with Diazo Compounds

For the past several decades, several other transition metals including cobalt, iron, palladium, ruthenium, silver, iridium also have been investigated, and important progress has been achieved. [6a, 6c, 11a, 17] It

is worthy noted that the ligands for these transition metal complexes always play an important role on the selectivity and reactivity in the transformations of diazo compounds.[18a,34e,39]

1.3 General Information for Alkynes

Alkynes are organic compounds containing a carbon-carbon triple bond. The simplest alkyne is acetylene with the formula C_2H_2, whose four atoms are linear; there are two π-bonds and one σ-bond between two carbon atoms; the hybridization on each carbon atom is sp. Based on the substituents of each acetylenic carbon, alkynes can be simply categorized as terminal and internal alkynes; both of them share the similar linear structure with acetylene (**Figure 1.7**).

$$R\!\!-\!\!\!\equiv\!\!\!-\!\!H \qquad\qquad R\!\!-\!\!\!\equiv\!\!\!-\!\!R$$

terminal alkynes   internal alkynes

Figure 1.7 Two Classes of Alkynes.

Alkynes have played an extremely important role in the history of organic chemistry.[40] Several traditional transformations including hydrogenation, additions of electrophilic reagents, 1,3-dipolar cycloaddition reactions, hydroboration and oxidations have been reported in the last century; these transformations have been commonly used

methods for constructing C-C, C-O, C-B, C-X (X = Cl, Br) bonds (**Scheme 1.8**).[40a, 40c, 40d] Also, their applications in the total synthesis of natural products have been demonstrated by numerous examples.[41]
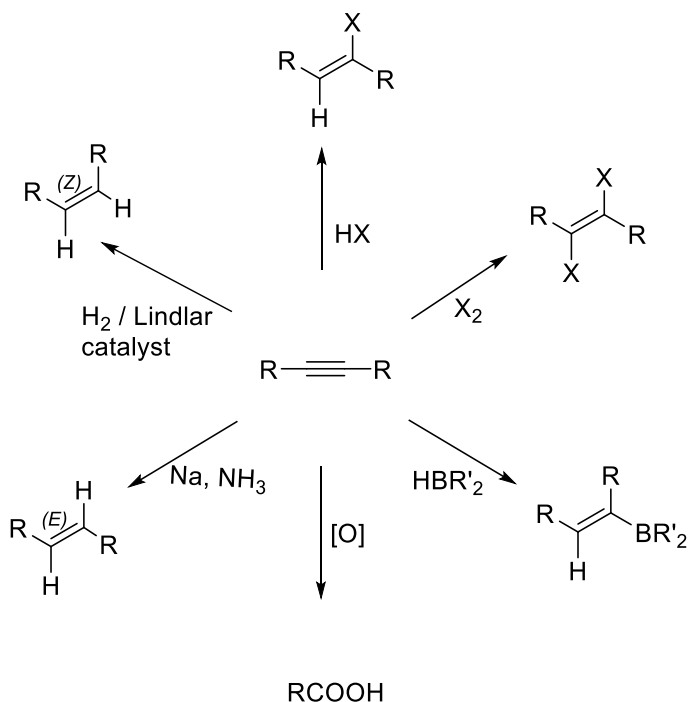
Scheme 1.8 Traditional Transformations of Alkynes.

The transition metal complexes catalyzed transformations of alkynes are particularly attractive because they provide a wide range of synthetically meaningful transformations with high efficiency under mild reaction conditions.[42] Transition metal alkyne complexes, which are formed through π-coordination of an alkyne ligand (or two and more alkyne ligands) to a transition metal center, are proposed as key intermediates in many catalytic transformations.[41b,43] It should be noted

that the alkynes that coordinate to transition metal complexes are usually non-linear; the transition metal alkyne complexes can undergo a variety of transformations ranging from nucleophilic addition reactions,[44] electrophilic addition reactions,[45] and cycloaddition reactions (**Scheme 1.9**).[46] A wide range of transition metal complexes containing cobalt,[47] titanium,[48] zirconium,[49] iron,[50] molybdenum,[51] tungsten,[52] nickel,[53] rhodium,[54] ruthenium,[55] iridium,[56] palladium,[57] mercury,[58] platinum,[59] silver,[60] and gold[55a,59b] have been reported.
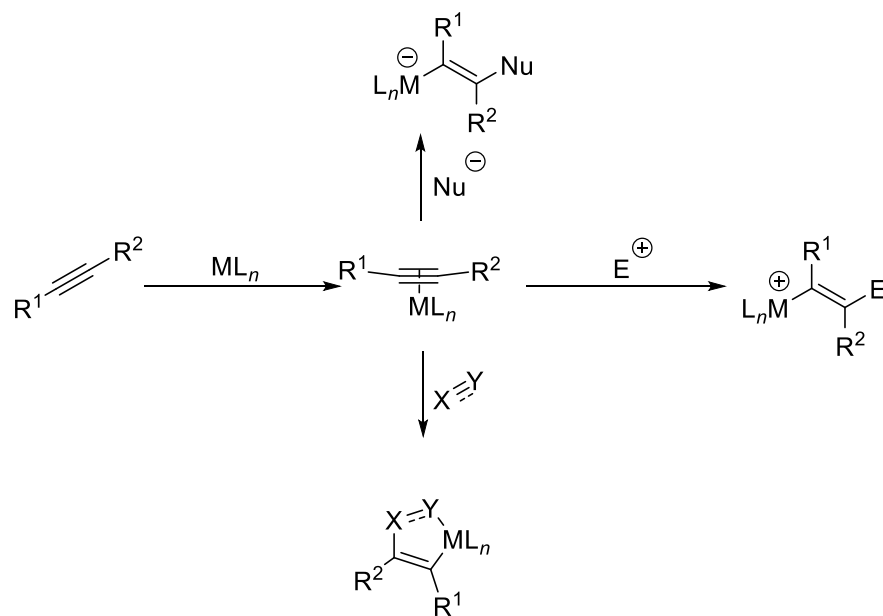
Scheme 1.9 Transition Metal Complexes Catalyzed Reactions of Alkynes.

1.4 My Research Goal

Since both diazo compounds and alkynes can react with a wide array of transition metal complexes to form reactive transition metal complexes which are capable of undergoing further transformations, we asked the question "Is there diversity in product formation if both acetylenic and diazo functionalities are present in the same molecule?" To answer this question, easily accessible propargylic phenyldiazoacetates that combines diazo functionality and a propargylic ester were synthesized for this evaluation.
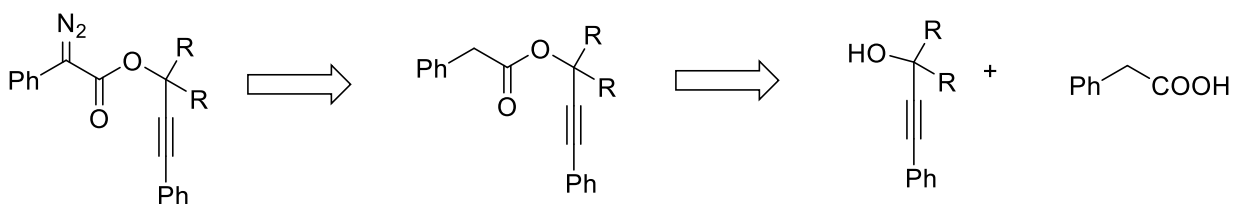
Scheme 1.10 Synthesis of Propargylic Phenyldiazoacetates.

1.4.1 Transition Metal Catalyzed-Domino Reactions involving Diazo Decomposition and Carbene/Alkyne Cascade.

Domino reactions, which are also known as cascade reactions or tandem reactions, are defined as a consecutive series of transformations occurring in one step via highly reactive intermediates.[61] Transition metal complexes catalyzed domino reactions of diazo compounds with tethered

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alkynes have been investigated over the past three decades; [4a] the mechanism for these domino processes always involves dinitrogen extrusion and a subsequent carbene/alkyne cascade to produce a new cyclic metal carbene species, sometimes involving formation of a highly strained cyclopropene that can react with transition metal complex to produce the same cyclic metal carbene species.[64] The newly formed cyclic metal carbene species has been reported to undergo a variety of transformations that include cyclopropanation, C-H insertion,[62], aromatic substitution[63] and 1,3-dipolar cycloaddition.[64] Transition metal complexes including $Rh_2(OAc)_4$, $Pd(OAc)_2$, $Ni(COD)_2$, $Cu(hfacac)_2$, and other dirhodium(II) carboxylates have been reported as the catalysts for selected domino processes.

cyclopropanation;
C-H insertion;
aromatic substitution;
1,3-dipolar cycloaddition
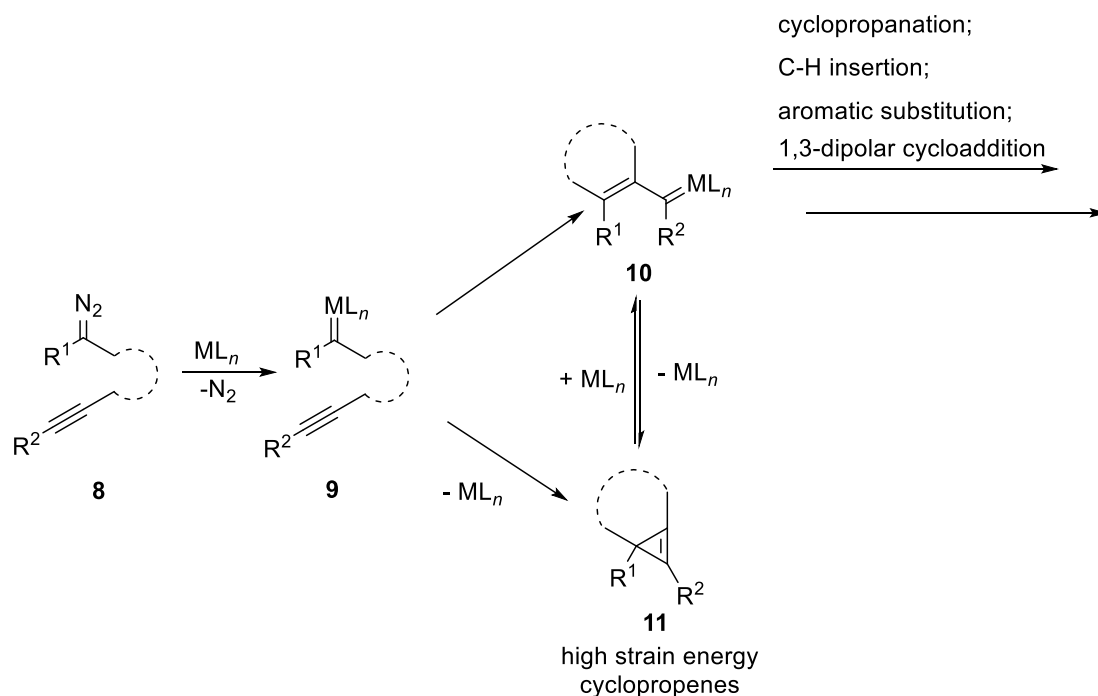
Scheme 1.11 Transition Metal Complexes-Catalyzed Domino Reactions of Diazo Compounds with Tethered Alkynes.

Padwa and coworkers have reported that propargylic phenyldiazoesters can undergo intramolecular domino reactions to produce indene-fused lactone upon treatment with catalytic amount $Rh_2(OAc)_4$; the authors propose that the domino reaction proceeds through rhodium-catalyzed diazo decomposition, carbene/alkyne metathesis and subsequent aromatic substitution.[65] However, the substrate scope of this domino reaction was not fully investigated; other transition metal complexes that can catalyze decomposition of diazo compounds have not been examined in this domino reaction.
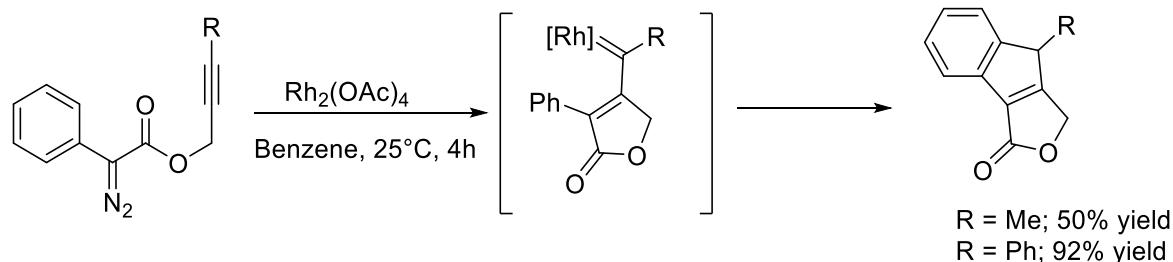
Scheme 1.12 Rh$_2$(OAc)$_4$-Catalyzed Domino Reactions of Propargylic Phenyldiazoesters.

1.4.2 Transition Metal Complexes-Catalyzed Reactions of Propargylic Esters

Propargylic esters are one of the most easily accessible substrates for reactions with transition metals that are initiated at the carbon-carbon triple bond. Numerous examples have been reported;[66] and all involve rearrangement of the ester as the initial step. Two rearrangement pathways are common (**Scheme 1.13**). In one the transition metal complex coordinates with the triple bond to form alkyne complexes **I**, and then the carbonyl oxygen undergoes a 5-exo-dig cyclization to form intermediate **II**, which with back-bonding from gold and successive ring opening finally forms the vinyl transition metal-stabilized carbene intermediates **III**. An alternative pathway is also possible. Instead of 5-exo-dig cyclization, intermediate **I** undergoes a 6-endo-dig cyclization to generate a six-membered-ring intermediates **IV**, which forms allenylic

ester intermediate **V** via a similar back-bonding and ring opening process. In most cases outcomes of the transition metal complexes-catalyzed regioselectivity of propargylic esters can be predicted: if the R^3 unit is a hydrogen atom (terminal alkynes) or an electron-withdrawing group that includes ester, the formation of the metal vinylcarbene complexes though 5-exo-dig cyclization is preferred; alternatively, while when R^3 is an aryl group or alkyl group, allenyl esters, which are generated by 6-endo-dig cyclization, will be the corresponding reaction intermediates. However, a few cases that are not consistent with this simple rule have also been reported.[67] These results indicate that the outcome of regioselectivity can be also influenced by other factors ranging from the structure of transition metal complexes, the substitution pattern at the propargylic moiety, and reaction conditions.
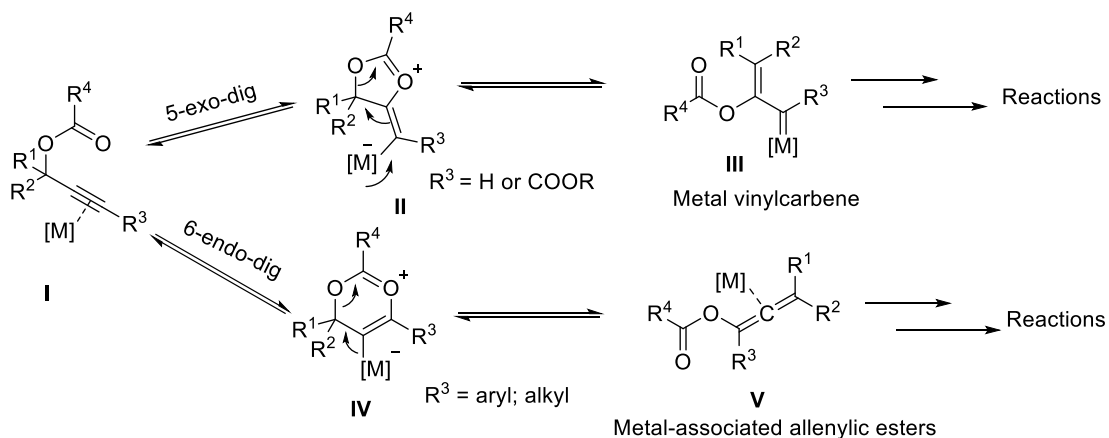
Scheme 1.13 Competitive 1,2- and 1,3-Acyl Migration of Transition Metal Complexes Catalyzed Rearrangement of Propargylic Esters.

Different transition metals including copper,[68] zinc,[69] silver,[68] palladium,[70] ruthenium,[71] rhodium,[66a] platinum,[70,72] and gold[36b,66d,73] have been unveiled to be effective for those reactions of propargylic esters. However, propargylic esters bearing a diazo group have not yet been examined with these transition metal complexes.

1.4.3 Reactivity of Propargylic Phenyldiazoacetates

Two divergent reaction pathways are possible for reactions of propargyl diazoacetates: (a) the diazo functionality reacts with the σ-bond acceptor to displace dinitrogen through back-donation and formation of a metal carbene, followed by addition to the carbon-carbon triple bond to form a derivative metal carbene that completes the domino transformation by electrophilic substitution into the aromatic ring of the original aryldiazoacetates; (b) π-bond-forming reactions that occur initially at the carbon-carbon triple bond followed by nucleophilic addition at a carbonyl oxygen and 1,3-acyloxy migration to produce allene intermediates,[68,74] and then to undetermined product(s) based on subsequent reactions that, although diverse examples are known, the

possible outcome with propargylic diazoacetates is unknown. (**Scheme 1.14**)
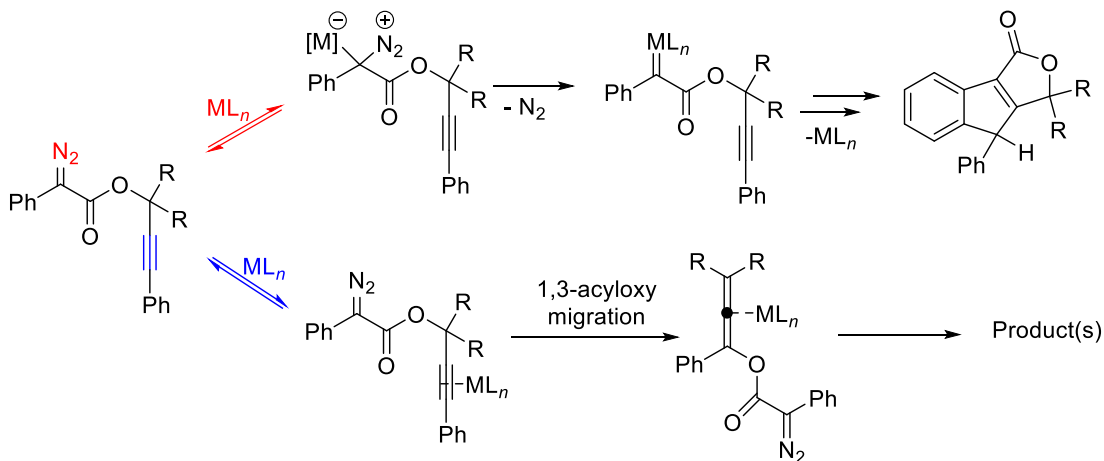
Scheme 1.14 Catalyst-Dependent Divergence of Reaction Pathway Based on σ-Bond Association with a Diazo Functional Group versus π-Bond Association with an Alkyne.

II. Results and Discussion

2.1 Initial Assessments of Transition Metal Complexes

Assessments of transition metal complexes catalysis with phenylpropargyl phenyldiazoacetate **1a** were performed at 20 ℃ in CH_2Cl_2 using 1-5 mol % of catalyst. With 1 mol% $Rh_2(OAc)_4$ the product (**2**) from the cascade transformation of an intermediate metal carbene was formed in 76% isolated yield (**Table 1.1**, entry 1). The more Lewis acidic catalyst $Rh_2(TFA)_4$ was also tested and gave improved yield (83% yield) indicating that dirhodium catalysts prefer the domino process (**Table 1.1**,

entry 2). Three commonly used palladium catalysts Pd(OAc)$_2$, PdCl$_2$(PhCN)$_2$, and [Pd(η_3-C$_3$H$_5$)Cl]$_2$,were further examined. Although all of them produced the cascade product **2a** as the dominated product, their catalytic activities are much lower compared to Rh$_2$(OAc)$_4$. These reactions were monitored every 12 h by TLC (Thin Layer Chromatography), and the starting material **1a** was completely consumed after 48 h. The cascade product was obtained in moderate yields (**Table 1.1**, entries 3-5), but an unexpected elimination product **3a** was observed during the process. AgSbF$_6$, which is widely used in decomposition of diazo compounds, also worked well in the domino cascade reaction. With 5 mol % AgSbF$_6$, the cascade cascade product **2a** was obtained in reasonable yield, and the elimination product **3a** was isolated as another product (**Table 1.1**, entry 6). Au(JohnPhos)SbF$_6$ and IPrAuBF$_4$, recently were reported as effective catalysts in decomposition donor/acceptor diazoacetates,[75] were also surveyed. Au(JohnPhos)SbF$_6$ gave the cascade product in 86% yield, whereas the cascade product **1a** was obtained in 50% yield with IPrAuBF$_4$ (**Table 1.1**, entries 7 and 8). When more Lewis acidic catalysts such as Hg(OTf)$_2$ were employed, the competing product **3a** was obtained as the dominant product, and only 10% of the domino product **2a** was observed. With the Cu(OTf)$_2$ catalysis, the cascade

product **2a** and elimination product **3a** almost were formed in similar yield (**Table 1.1**, entry 11). We found that $CuBF_4(MeCN)_4$ and $CuPF_6(MeCN)_4$ were very effective for this domino reaction (**Table 1.1**, entries 12-13); with 5 mol% $CuPF_6(MeCN)_4$ **2a** was obtained in 90% isolated yield (94% ^{1}H NMR yield) in DCM for 1 h at room temperature, and no other discernable product was observed. Under the catalysis of $FeCl_3$, the elimination product **3a** was isolated as the dominant product in 70% yield (**Table 1.1**, entry 14). Surprisingly, no cascade product **2a** was observed but instead unexpected product **4a** was obtained in 20% yield, which can be easily separated from **2a** by normal phase column chromatography (this part will be discussed later). Moreover, reaction with tetrahydrothiophene gold(I) chloride, $AuCl(C_4H_8S)$, was more complex, forming none of **2a** but produced two isomeric 1*H*-pyrazolines as the dominant products (discussed in the chapter 2). We also performed several reactions of **1a** under the catalysis of chiral catalysts including chiral dirhodium carboxylates such as $Rh_2(S\text{-PTTL})_4$ and $CuPF_6(CH_3CN)_4$ with chiral BOX ligands (*i*-Pr, *t*-Bu, Bn and etc.). Although **2a** is formed in reasonable yield, the analyses from chiral HPLC have shown that the only racemic product **2a** was observed.

Table 1.1 Catalysts Screening of the Reaction with Phenylpropargyl Phenyldiazoacetate **1a**.
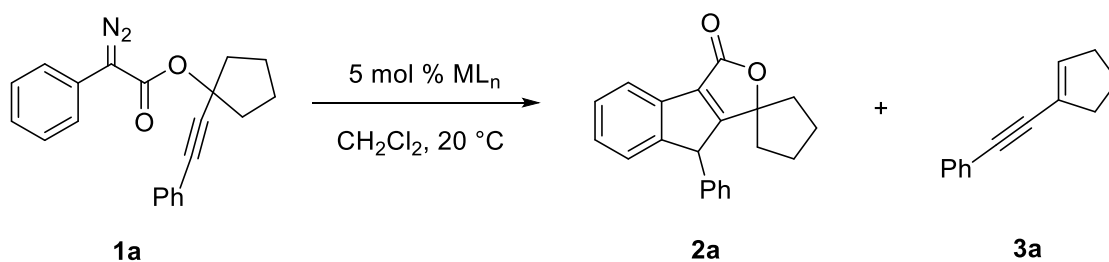
Entry[a]	Catalyst	reaction time	Conversion of **1a**[b], %	Yield of **2a** %	Yield of **3a**, %
1	Rh$_2$(OAc)$_4$[c]	6 h	>95	76	<5
2	Rh$_2$(TFA)$_4$[c]	3 h	>95	83	<5
3	Pd(OAc)$_2$	48h	>95	71	10
4	PdCl$_2$(PhCN)$_2$	48 h	>95	76	11
5	[Pd(η^3-C$_3$H$_5$)Cl]$_2$	48 h	>95	65	15
6	AgSbF$_6$	1 h	>95	65	30
7	Au(JohnPhos)SbF$_6$	10 h	>95	86	4
8	IPrAuBF$_4$	10 h	>95	50	16
9	Hg(OTf)$_2$	48 h	>95	10	80

10	HgCl$_2$	24 h	50	15	76
11	Cu(OTf)$_2$	6 h	>95	40	50
12	CuBF$_4$(MeCN)$_4$	1 h	>95	92	<5
13	CuPF$_6$(MeCN)$_4$	1 h	>95	94 (90)[d]	<5
14	FeCl$_3$[e]	12 h	>95	<5	70
15	AuCl(C$_4$H$_8$S)	72h	>95	<5	<5

[a] Reactions were carried out at 20 ℃ on a 0.20 mmol scale: a solution of **1a** in 2.0 mL CH$_2$Cl$_2$ was added dropwise to a 5 mol % solution of -catalyst in 2.0 mL CH$_2$Cl$_2$ under a nitrogen atmosphere within 10 min, and the resulting reaction mixture was stirred for the stated reaction time. [b] The percent conversion of **1a**, the yield of **2a** and yield of **3a** (in parenthesis) were determined by ^{1}H NMR spectroscopy using 2,4,6-trimethoxy-benzaldehyde as an internal standard. [c] Catalyst loading is 1 mol %. [d] Isolated yield. [e] Temperature was 60°C and DCE was solvent.

2.2 Substrate Scope with CuPF$_6$(MeCN)$_4$

Since CuPF$_6$(MeCN)$_4$ has exhibited very high efficiency and excellent selectivity in formation of domino cascade reaction product during the catalyst screening of **1a**, we became interested in the generality of CuPF$_6$(MeCN)$_4$ to the domino process The propargyl aryldiazoacetates **1b-1j** with different substituents were prepared in the following investigation. First, the influence of substituents on the phenyl group at the *para* position was examined to further understand the formation of the cascade products. Substituents **1b-c** with electron

donating groups (EDG) such as methoxy group and methyl group gave higher yields compared with **1a** (**Table 1.2**, entries 1 and 2); bromo- and chloro-substituted propargylic aryldiazoacetates **1d-e** resulted in corresponding products with slightly decreased yields because elimination product **3a** was formed as a by-product (**Table 1.2**, entries 3 and 4); however, **1f** with a nitro group, which is a strong electron-withdrawing group (EWG), only produced a trace of product (15% yield) under same reaction conditions (elimination product **3a** was obtained in 65% yield separately; **Table 1.2**, entry 5) . Then, substrates with dimethyl as well as other carbocycles that include cyclohexyl and cyclobutyl **1g-i** were found to be compatible in this domino cascade process and furnished the products **2g-i** in good yields (**Table 1.2**, entries 6-8). The substituents on alkyne were also investigated: substrate **1j**, which is derived from cyclopropylacetylene, produces corresponding cascade product **2j** in 85% yield under the same reaction conditions (**Table 1.2**, entry 9).

Table 1.2 Substrates Scope for $CuPF_6(MeCN)_4$ Reaction with Propargyl Diazoacetates
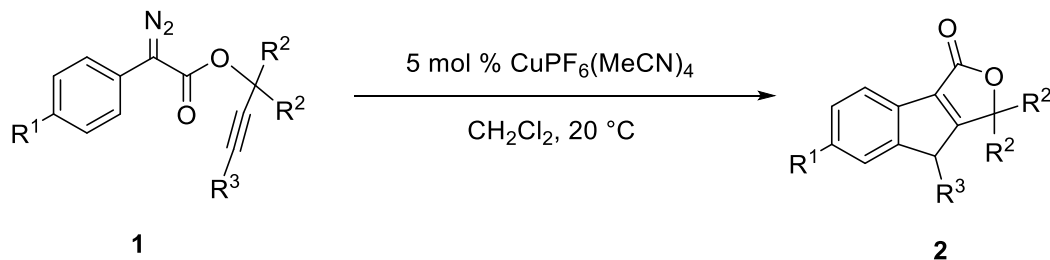
Entry[a]	1 and 2	R^1	R^2	R^3	yield of 2(%)[b]
1	b	OMe	$-(CH_2)_4-$	Ph	98
2	c	Me	$-(CH_2)_4-$	Ph	95
3	d	Br	$-(CH_2)_4-$	Ph	86 (6)[c]
4	e	Cl	$-(CH_2)_4-$	Ph	78 (12)[c]
5	f	NO_2	$-(CH_2)_4-$	Ph	15 (65)[c]
6	g	H	Me	Ph	90
7	h	H	$-(CH_2)_3-$	Ph	90
8	i	H	$-(CH_2)_5-$	Ph	80
9	j	H	$-(CH_2)_4-$	cyclopropyl	85

[a] Reactions were performed at 20 ℃ on a 0.20 mmol scale: a solution of 1 in 2.0 mL CH_2Cl_2 was added dropwise to a 5 mol % solution of $CuPF_6(MeCN)_4$ in 2.0 mL solvent under a nitrogen atmosphere within 10 min, and the resulting reaction mixture was stirred for 1 h. [b] Isolated yield. [c] Isolated yield of elimination product 3a.

2.3 Proposed Mechanism for Copper-Catalyzed Carbene Domino Cascade Process

As shown in **Scheme 1.15**, a plausible mechanism is proposed based on previous reports by Padwa and coworkers.[64,76] The Cu(I) complex reacts with phenyldiazoacetate **A** to produce metal carbene intermediate **B,** which readily undergoes a carbene/alkyne metathesis or cyclopropenation/spontaneous ring opening process to form the cyclic

vinyl carbene intermediate **C**,[77] followed by an intramolecular electrophilic aromatic substitution to furnish indene product **E**.
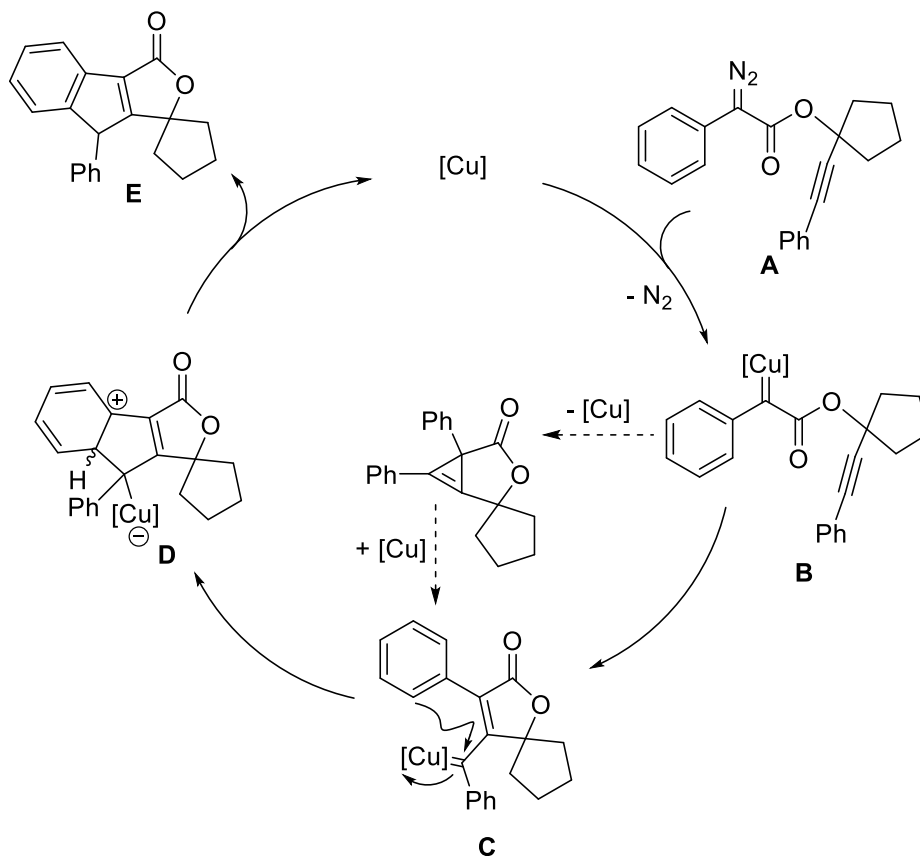
Scheme 1.15 Postulated Copper-Catalyzed Reaction Pathway.

2.4 The Lewis Acid Catalyzed Reactions of Propargyl Phenyldiazoesters

As mentioned before, under the catalysis of FeCl$_3$ an unexpected reaction of **1a** occurred with formation of unexpected lactone **4a** albeit with relatively lower yield. However, the elimination product **3a** was obtained as the dominant product under selected reaction conditions

(**Table 1.3**, entry 1). Other Lewis acids also were examined for this process. $Sc(OTf)_3$, $In(OTf)_3$, and $Zn(OTf)_2$ failed to give the lactone **4a** (**Table 1.3**, entries 2-4). With 10 mol% $ZnBr_2$, lactone **4a** was obtained in 4% yield (**Table 1.3**, entry 5); increasing the catalyst loading of $ZnBr_2$ to 100 mol% resulted in higher yield (**Table 1.3**, entry 6). $BF_3 \cdot Et_2O$ was also tested, and lactone **4a** could be obtained in 20% yield at either $60^\circ C$ or $20^\circ C$ upon the consumption of starting material (**Table 1.3**, entries 7 and 8). However, the formation of elimination product **3a** was always the dominant process with these Lewis acids.

Table 1.3 Lewis Acid Catalyzed Reactions of Propargyl Phenyldiazoesters
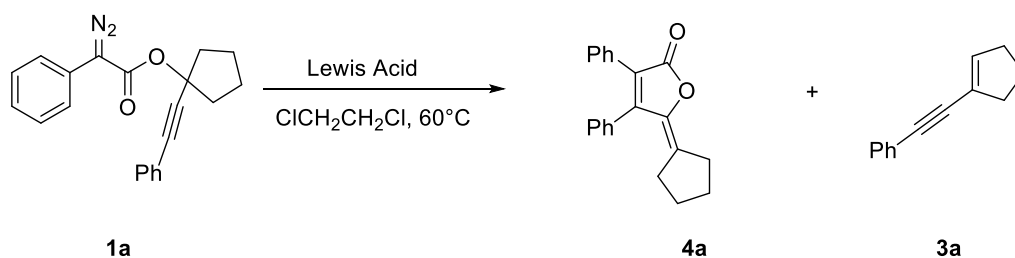
Entry[a]	Lewis acid	reaction time	Conversion of 1a[b]	Yield of 4a[c]	Yield of 3a[c]
1	$FeCl_3$	12 h	>95%	21%	75%
2	$Sc(OTf)_3$	10 h	>95%	<1%	80%
3	$In(OTf)_3$	10 h	>95%	<1%	95%
4	$Zn(OTf)_2$	24 h	>95%	<1%	80%
5	$ZnBr_2$	24 h	>95%	4%	90%
6	$ZnBr_2{}^d$	12 h	>95%	17%	75%

7	BF$_3$•Et$_2$O	1 h	>95%	20%	80%
8[e]	BF$_3$•Et$_2$O	12 h	>95%	20%	65%
9[e]	FeCl$_3$	24 h	50%	3%	45%
10[f]	FeCl$_3$	6 h	>95%	15%	75%

[a]Reactions were performed at 60℃ on a 0.20 mmol scale: a solution of **1a** in 2.0 mL ClCH$_2$CH$_2$Cl was added to a solution of 10 mol% of catalyst in 2.0 mL ClCH$_2$CH$_2$Cl under a nitrogen atmosphere, and the resulting reaction mixture was stirred for stated reaction time. [b]The percent conversion of **1a** was determined ^{1}H NMR spectroscopy using 2,4,6-trimethoxy-benzaldehyde as an internal standard. [c]Isolated yield. [d]1.0 eq. of ZnBr$_2$ was used. [e]Reaction temperature was 20 ℃. [f]Reaction temperature was 80 ℃.

Major efforts were devoted to understanding the mechanism for this unique process. A control experiment was conducted by using propargyl acetate with *tert*-butyl diazoacetate under catalysis of FeCl$_3$; the rearrangement product analog **4g** was obtained in 17% isolated yield together with the major elimination product **3g** (**Scheme 1.16**).
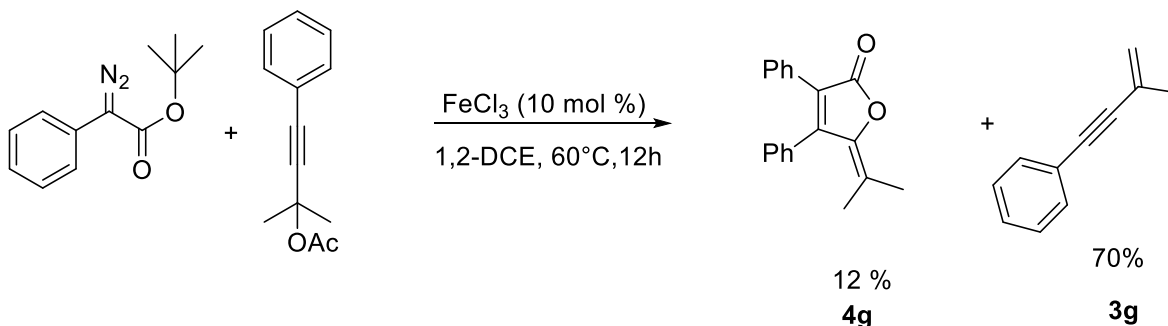
Scheme 1.16 FeCl$_3$-Catalyzed Reaction of Propargyl Acetate with tert-Butyl Diazo Acetate.

Based on this experiment and previous reports,[78] we propose a plausible mechanism for the above rearrangement reaction as shown in

Scheme 1.17. Under the catalysis of FeCl$_3$, ester C-O bond cleavage of **A** occurs, which forms cationic species **G** and anionic species **F**. The conversion of cationic species **G** to the allene carbocation **H** via Meyer−Schuster rearrangement has been documented [79]. The allene carbocation **H** was proposed to be trapped by nucleophilic attack of **F** to produce a key intermediate aryl allene derived compound **I**, and finally cyclization of **I** furnishes product **J**. Also, the formed cationic species **G** is not stable; deprotonation of **G** occurs readily, which forms enyne **L** as another competing product.[80]
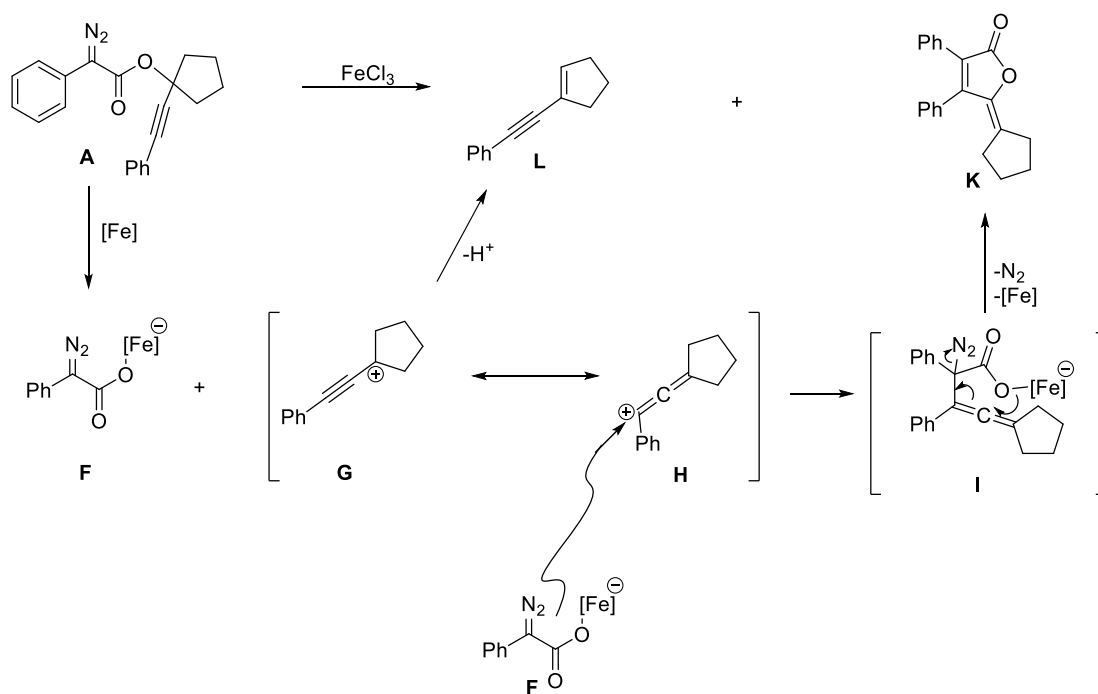
Scheme 1.17 Proposed Mechanism for FeCl$_3$-Catalyzed Reaction of **1a**.

III. Conclusion

In summary, we have disclosed that propargylic phenyldiazoesters were converted into three structurally different products as a function of catalysts. A variety of transition metal complexes that include rhodium(II), palladium(II), silver(I), mercury(II), copper(I and II), and cationic gold (I) complexes have been examined to be effective in the catalytic domino reactions of propargylic aryldiazoesters. $CuPF_6(MeCN)_4$ has been demonstrated as a superior catalyst in the domino cascade reaction for formation of indene derivatives. A Lewis acid catalyzed pathway was also discovered: $FeCl_3$ works as a Lewis acid and selectively gives furanone **4** as a reaction product. Selected gold catalysts exhibit a unique catalytic reactivity, which not only selectively activates the alkyne group but also retains the dinitrogen in the final product, which has been thoroughly investigated and will be reported in the next three chapters.

IV. Experimental Section

4.1 General Information

Unless noted all reactions were carried out under inert atmosphere of dinitrogen in oven-dried glassware with magnetic stirring using freshly distilled solvents. All solvents were purified and dried using standard

methods. Analytical thin layer chromatography (TLC) plates were purchased from EM Science (silica gel 60 F_{254} plates). High-resolution mass spectra (HRMS) were performed on a microTOF-ESI mass spectrometer using CsI as the standard. Accurate masses are reported for the molecular ion $[M+Cs]^+$, $[M+Na]^+$, or $[M+H]^+$. Melting points were determined on an Electrothermo Mel-Temp DLX 104 device and were uncorrected. Column chromatography was performed on CombiFlash® Rf 200 purification system using normal phase disposable columns. IR spectra were recorded using Bruker Vectcr 22 spectrometer. All NMR spectra were recorded on a Bruker spectrometer at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR) or an Agilent spectrometer at 500 MHz (^{1}H NMR) and 125 MHz (^{13}C NMR). Chemical shifts are reported in ppm with the solvent signals as reference (in $CDCl_3$ as solvent), and coupling constants (*J*) are given in Hertz (Hz). The peak information is described as: br = broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = composite of magnetically non-equivalent protons.

4.2 Materials

$Rh_2(OAc)_4$ was purchased from Pressure Chemical Co. and $Rh_2(TFA)_4$, $Pd(OAc)_2$, $PdCl_2(PhCN)_2$, $[Pd(\eta3\text{-}C_3H_5)Cl]_2$, $AgSbF_6$, $Au(JohnPhos)SbF_6$, $IPrAuBF_4$, $Hg(OTf)_2$, $Cu(OTf)_2$, $CuBF4(MeCN)$,

CuPF$_6$(MeCN)$_4$, and FeCl$_3$ were purchased from Sigma-Aldrich. AuCl(C$_4$H$_8$S) was purchased from Strem Chemicals. Other chemicals were obtained from commercial sources and used without further purification.

4.3 Experimental Procedures

1a
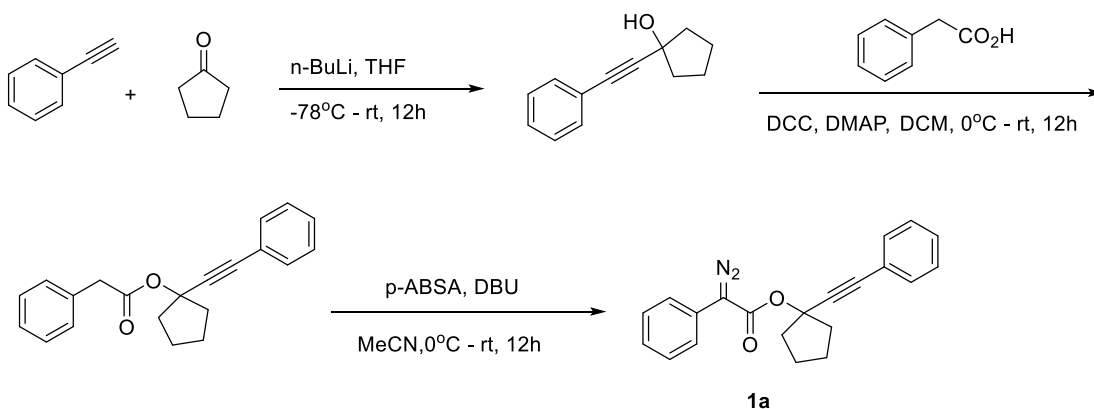
General Procedures for Preparation of 1-(Phenylethynyl)cyclopentyl α-Diazo-α-phenylacetate 1a: To a solution of phenylacetylene (1.02 g, 10.0 mmol) in dry THF (50 mL) was added *n*-BuLi (4.4 mL, 11.0 mmol) dropwise under nitrogen atmosphere at -78°C. After stirring at -78°C for 1 h, cyclopentanone (924 mg, 11 mmol) was added, and the reaction mixture was allowed to warm to room temperature over 1 h. After stirring for another 10 h, the reaction mixture was quenched with aqueous NH$_4$Cl solution (50 mL), and then extracted with diethyl ether (50 mL×2) and dried over anhydrous MgSO$_4$. After evaporating the solvent, the crude product was purified by column

chromatography (hexane/ethyl acetate = 10/1) to give 1-(phenylethynyl)cyclopentan-1-ol as a white solid (1.76 g, 95% yield)

To a solution of 1-(phenylethynyl)cyclopentan-1-ol (930 mg, 5 mmol), phenylacetic acid (816 mg, 6mmol) and DMAP (122 mg, 1 mmol) in dry DCM (30 mL) was added to a solution of DCC (1.24g, 6 mmol) in dry DCM (20 mL) via addition funnel over 20 min at 0°C. The resulting mixture was allowed to warm to room temperature over 1 h, and stirred for another 10 h, and a white solid was formed in the process. The reaction solution was added to 30 mL of hexanes and filtered by Büchner funnel. After evaporating the solvent under reduced pressure, the resulting reaction mixture was purified by column chromatography (hexane/ethyl acetate = 25/1) to give 1-(phenylethynyl)cyclopentyl 2-phenylacetate as a colorless oil (1.29 g, 85% yield).

To a solution of 1-(phenylethynyl)cyclopentyl 2-phenylacetate (1.29 g, 4.2 mmol) and 4-acetamidobenzenesulfonyl azide (*p*-ABSA) (1.20 g, 5 mmol) in dry CH_3CN (30 mL) was added 1,8-diazabicycloundec-7-ene (DBU) (0.76g, 5mmol) dropwise at 0°C. The resulting mixture was allowed to warm to room temperature over 30 min and stirred for another 10 h. The reaction was quenched with aqueous NH_4Cl solution (60 mL) and then extracted with diethyl ether (50 mL×2)

and dried over anhydrous MgSO$_4$. After evaporating the solvent, the resulting mixture was purified by column chromatography (hexane/ethyl acetate = 30/1) to give 1-(phenylethynyl)cyclopentyl α-diazo-α-phenylacetate **1a** as a yellow solid (1.13 g, 82% yield).

Compounds **1b** − **1j** were prepared from the corresponding arylacetic acids, ketones, or alkynes using the same synthetic procedure as **1a**.
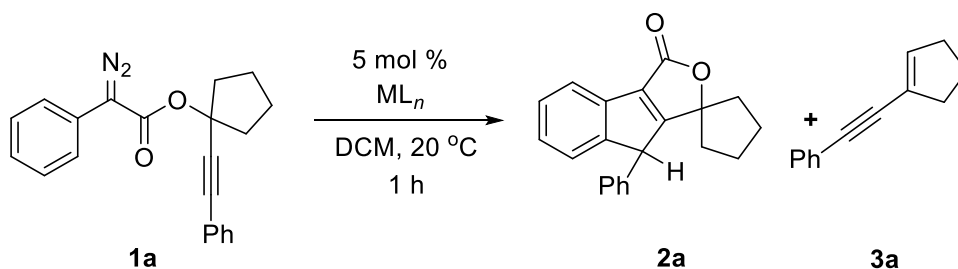
General Procedure for Catalyst Screening: To a flame-dried 10 mL Schlenk flask charged with a magnetic stirring bar, transition metal catalyst (0.010 mmol) and 2.0 mL DCM were added under nitrogen atmosphere [for Rh$_2$(OAc)$_4$ and Rh$_2$(TFA)$_4$, only 1 mol% catalyst was used]. . 1-(Phenylethynyl)cyclopentyl 2-diazo-2-phenylacetate **1a** (0.20 mmol) dissolved in 2.0 mL of DCM was added in one portion into the solution under a flow of nitrogen. The resulting mixture was stirred at room temperature and monitored periodically by TLC. Upon consumption of the 2-diazo-2-phenylacetate **1a** (1 − 48 h), the reaction

mixture was purified by column chromatography (100:1 to 10:1 gradient of hexanes: ethyl acetate as eluents) to afford pure 8'-phenylspiro[cyclopentane-1,1'-indeno[1,2-c]furan]-3'(8'H)-one **2a** and
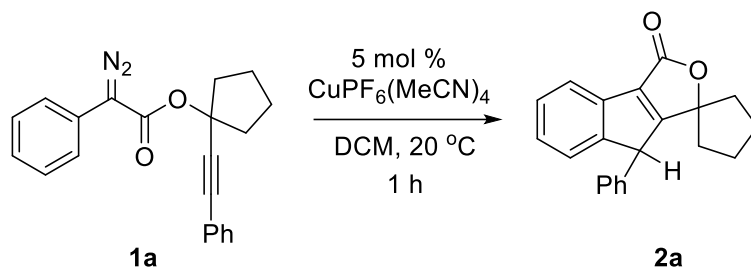
General Procedure for Copper-Catalyzed Domino Cascade Reaction of 1-(Phenylethynyl)cyclopentyl α-Diazo-α-phenylacetate 1a:
To a flame-dried 10 mL Schlenk flask charged with a magnetic stirring bar, $CuPF_6(MeCN)_4$ (0.010 mmol) and 2.0 mL DCM were added under nitrogen atmosphere. 1-(Phenylethynyl)cyclopentyl 2-diazo-2-phenylacetate **1a** (0.20 mmol) dissolved in 2.0 mL of DCM was added in one portion into the solution under a flow of nitrogen. The resulting mixture was stirred for 1 h at room temperature (20 °C). The reaction mixture was purified by column chromatography (100:1 to 10:1 gradient of hexanes: ethyl acetate as eluents) to afford pure 8'-phenylspiro[cyclopentane-1,1'-indeno[1,2-c]furan]-3'[8'H]-one **2a** as a white solid (90% yield)

The same procedure was used with other transition metal complexes.
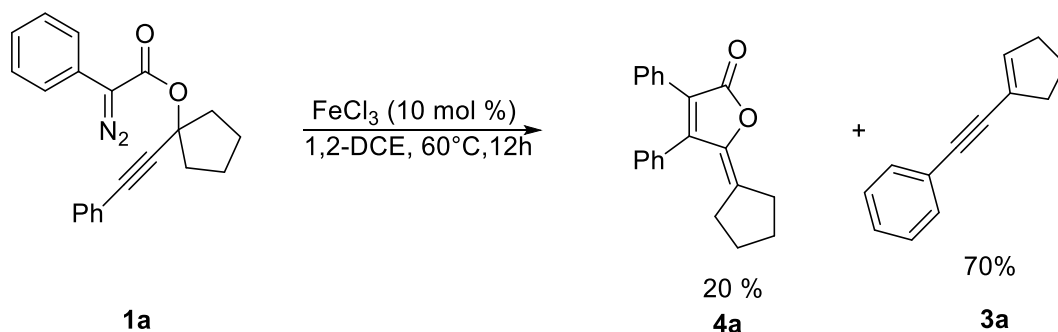
General Procedure for FeCl₃-Catalyzed Reaction of 1-(Phenylethynyl)cyclopentyl α-Diazo-α-phenylacetate 1a: To a flame-dried 10 mL Schlenk flask charged with a magnetic stirbar. FeCl₃ (0.020 mmol) and 2.0 mL DCE were added under nitrogen atmosphere. 1-(Phenylethynyl)cyclopentyl 2-diazo-2-phenylacetate **1a** (0.20 mmol) dissolved in 2.0 mL of DCE was added in one portion into the solution under the flow of nitrogen. The resulting mixture was stirred for 12 h at 60 °C; crude product was purified by column chromatography (100:1 to 10:1 gradient of hexanes: ethyl acetate as eluents) to afford pure **3a** (70%) yield as colorless oil and **4a** (20 % yield) as a white solid.

40
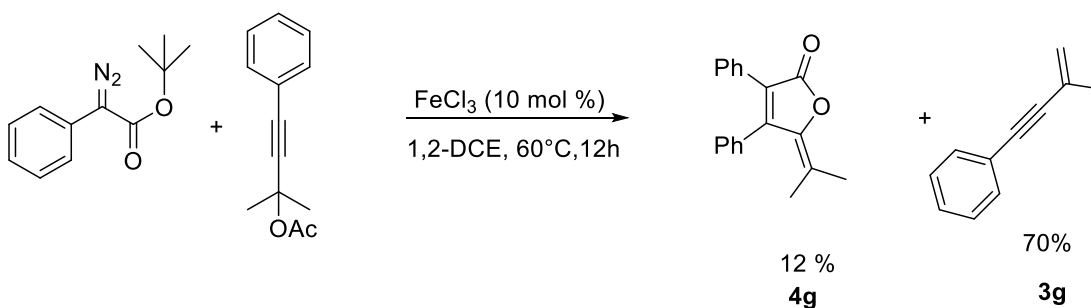
General Procedure for FeCl₃-Catalyzed Reaction of *tert*-Butyl 2-Diazo-2-phenylacetate and 2-Methyl-4-phenylbut-3-yn-2-yl acetate:
To a flame-dried 10 mL Schlenk flask charged with a magnetic stirring bar. FeCl₃ (0.020 mmol) and 2.0 mL DCE were added under a nitrogen atmosphere. *tert*-Butyl 2-diazo-2-phenylacetate (0.20 mmol) and 2-methyl-4-phenylbut-3-yn-2-yl acetate (0.20 mmol) dissolved in 2.0 mL of DCE were added in one portion into the solution under the flow of nitrogen. The resulting mixture was stirred for 12 h at 60 °C; the reaction mixture was purified by column chromatography (100:1 to 10:1 gradient of hexanes: ethyl acetate as eluents) to afford pure **3g** (70% yield) as colorless oil and **4g** (12 % yield) as a white solid.

4.4 Characterization Data

1a
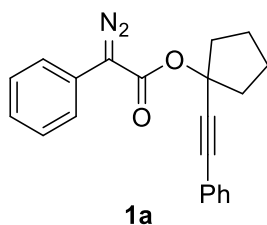
1-(Phenylethynyl)cyclopentyl α-Diazo-α-phenylacetate 1a: 66% yield. Yellow solid, m.p. 52.7 – 54.1°C. ^{1}H NMR (500 MHz, CDCl₃) δ 7.51 (d, J = 7.9 Hz, 2H), 7.47 – 7.43 (comp, 2H), 7.38 (t, J = 7.9 Hz, 2H), 7.31 – 7.27 (comp, 3H), 7.18 (t, J = 7.4 Hz, 1H), 2.46 – 3.39 (comp, 2H),

2.35 – 2.27 (comp, 2H), 1.89 – 1.80 (comp, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.50, 131.82, 128.85, 128.28, 128.11, 125.69, 125.63, 123.95, 122.66, 89.34, 85.08, 82.16, 40.77, 23.44. IR (neat) 2089, 1704, 1353, 1250, 1151, 905 cm^{-1}. HRMS (ESI) m/z calculated for C$_{21}$H$_{18}$N$_2$O$_2$Cs$^+$ [M+Cs]$^+$ 463.0417, found: 463.0419.

1b
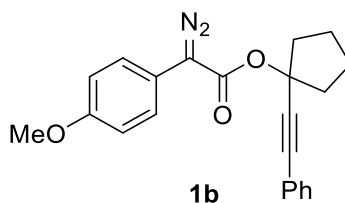
1-(Phenylethynyl)cyclopentyl 2-Diazo-2-(4-methoxyphenyl)acetate 1b: 69% yield. Orange oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.49 – 7.44 (comp, 2H), 7.44 – 7.39 (comp, 2H), 7.33 – 7.28 (comp, 3H), 6.97 – 6.92 (comp, 2H), 3.82 (s, 3H), 2.42 (ddd, J = 12.3, 7.8, 3.7 Hz, 2H), 2.35 – 2.26 (comp, 2H), 1.90 – 1.78 (comp, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 164.06, 157.97, 131.84, 128.27, 128.11, 125.87, 122.72, 117.07, 114.56, 89.46, 85.01, 82.04, 55.35, 40.79, 23.46. IR (neat) 2954, 2075, 1702, 1512, 1255, 1145, 997 cm^{-1}; HRMS (ESI) m/z calculated for C$_{22}$H$_{20}$N$_2$O$_3$Na [M+Na]$^+$ 383.1366, found: 383.1361.

1c
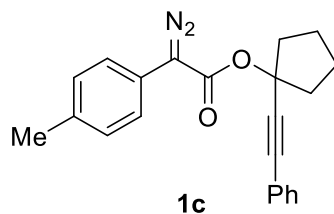
1-(Phenylethynyl)cyclopentyl α-Diazo-α-(p-tolyl)acetate 1c:

64%. Yellow solid, m.p. 60.2 – 61.5°C. ^{1}H NMR (500 MHz, CDCl$_3$) δ

7.49 – 7.44 (comp, 2H), 7.41 (d, J = 8.1 Hz, 2H), 7.32 – 7.27 (comp, 3H),

7.21 (d, J = 8.1 Hz, 2H), 2.46 – 2.40 (comp, 2H), 2.35 (s, 3H), 2.34 –

2.26 (comp, 2H), 1.89 – 1.82 (comp, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ

163.69, 135.50, 131.77, 129.55, 128.22, 128.06, 124.03, 122.66, 122.22,

89.39, 84.99, 82.01, 40.73, 23.41, 20.93. IR (neat) 2087, 1703, 1250,

1150, 906 cm^{-1}. HRMS (ESI) m/z calculated for C$_{22}$H$_{20}$N$_2$O$_2$Na$^+$ [M+Na]$^+$

367.1417, found: 367.1431.
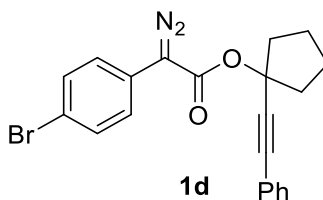
1-(Phenylethynyl)cyclopentyl 2-(4-Bromophenyl)-2-

diazoacetate 1d: 68% yield. Yellow solid, m.p. 80.5 – 82°C. ^{1}H NMR

(500 MHz, CDCl$_3$) δ 7.49 (d, J = 8.8 Hz, 2H), 7.46 – 7.42 (comp, 2H),

7.38 (d, J = 8.8 Hz, 2H), 7.31 – 7.26 (comp, 3H), 2.45 – 2.36 (comp, 2H),

2.34 – 2.26 (comp, 2H), 1.86 – 1.78 (comp, 4H). ^{13}C NMR (125 MHz,

CDCl$_3$) δ 163.12, 131.92, 131.81, 128.36, 128.14, 125.34, 124.87, 122.57,

119.20, 89.14, 85.24, 82.43, 40.77, 23.44. IR (neat) 2088, 1702, 1491,

1245, 1150, 903 cm^{-1}. HRMS (ESI) *m/z* calculated for C$_{21}$H$_{17}$N$_2$O$_2$BrNa$^+$ [M+Na]$^+$ 431.0366, found: 431.0381.

1e
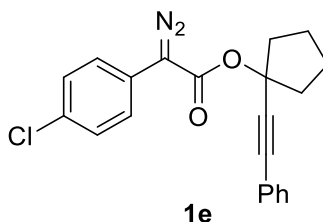
1-(Phenylethynyl)cyclopentyl 2-(4-Chlorophenyl)-2-diazoacetate 1e: 65% yield. Yellow solid, m.p. 56.5 – 58.1℃. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.47 – 7.40 (comp, 4H), 7.34 (d, *J* = 7.1 Hz, 2H), 7.30 – 7.26 (comp, 3H), 2.44 – 2.38 (comp, 2H), 2.34 – 2.27 (comp, 2H), 1.87 – 1.79 (comp, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.18, 131.81, 131.33, 128.99, 128.34, 128.13, 125.06, 124.29, 122.57, 89.15, 85.21, 82.40, 40.76, 23.43. IR (neat) 2088, 1702, 1250, 1150, 745 cm^{-1}. HRMS (ESI) *m/z* calculated for C$_{21}$H$_{17}$N$_2$O$_2$ClCs$^+$ [M+Cs]$^+$ 497.0028, found: 497.0036.

1f
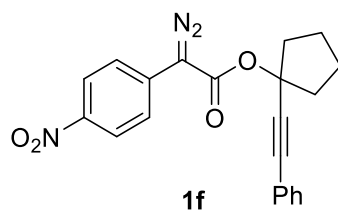
1-(Phenylethynyl)cyclopentyl 2-Diazo-2-(4-nitrophenyl)acetate 1f: 54% yield. Yellow solid, m.p. 113.4 – 114.5℃. ^{1}H NMR (500 MHz,

CDCl3) δ 8.22 (d, J = 9.0 Hz, 2H), 7.68 (d, J = 9.0 Hz, 2H), 7.47 – 7.42 (comp, 2H), 7.32 – 7.27 (comp, 3H), 2.46 – 2.38 (comp, 2H), 2.35 – 2.28 (comp, 2H), 1.92 – 1.78 (comp, 4H). ^{13}C NMR (125 MHz, CDCl3) δ 162.03, 144.95, 134.04, 131.80, 128.49, 128.18, 124.20, 123.18, 122.38, 88.72, 85.57, 83.07, 40.75, 23.42. IR (neat) 2095, 1708, 1594, 1335, 1245, 1152, 903 cm^{-1}. HRMS (ESI) m/z calculated for $C_{21}H_{17}N_3O_4Na^+$ [M+Na]$^+$ 398.1111, found: 398.1135.

1g
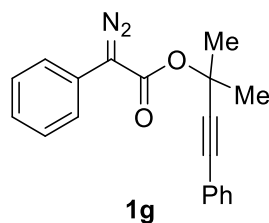
2-Methyl-4-phenylbut-3-yn-2-yl 2-Diazo-2-phenylacetate 1g: 63% yield. Orange oil. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.53 – 7.43 (comp, 4H), 7.41 – 7.35 (comp, 2H), 7.32 – 7.27 (comp, 3H), 7.21 – 7.14 (m, 1H), 1.85 (s, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.35, 131.85, 128.86, 128.39, 128.15, 125.73, 125.70, 124.03, 122.52, 89.95, 84.47, 73.81, 29.44. IR (neat) 2936, 2079, 1705, 1498, 1349, 1247, 1120, 754, 691 cm^{-1}; HRMS (ESI) m/z calculated for $C_{19}H_{16}N_2O_2Na$ [M+Na]$^+$ 327.1104, found: 327.1102.

1h
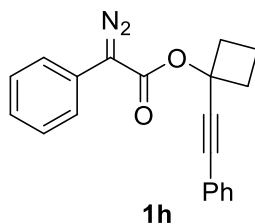
1-(Phenylethynyl)cyclobutyl 2-Diazo-2-phenylacetate 1h: 52% yield. Yellow solid, m.p. 76 – 77 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.52 (dd, J = 8.5, 1.1 Hz, 2H), 7.50 – 7.45 (comp, 2H), 7.42 – 7.36 (comp, 2H), 7.34 – 7.29 (comp, 3H), 7.23 – 7.16 (m, 1H), 2.81 – 2.71 (comp, 2H), 2.62 (ddd, J = 12.7, 9.7, 2.6 Hz, 2H), 2.15 – 2.05 (m, 1H), 2.00 (qdd, J = 9.9, 8.6, 4.9 Hz, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.24, 131.94, 128.90, 128.43, 128.16, 125.80, 125.45, 123.98, 122.54, 89.16, 84.79, 73.26, 37.18, 14.65. IR (neat) 2952, 2081, 1704, 1497, 1351, 1242, 1144, 1088, 754, 691 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{20}$H$_{16}$N$_2$O$_2$Na [M+Na]$^+$ 339.1104, found: 339.1107.

1i
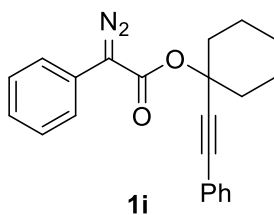
1-(Phenylethynyl)cyclohexyl 2-Diazo-2-phenylacetate 1i: 66% yield. Yellow solid, m.p. 50 – 51 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.53 (dd, J = 8.5, 1.1 Hz, 2H), 7.50 – 7.45 (comp, 2H), 7.42 – 7.36 (comp, 2H),

7.34 − 7.28 (comp, 3H), 7.21 − 7.16 (m, 1H), 2.36 − 2.21 (comp, 2H), 2.09 (comp, 2H), 1.81 − 1.65 (comp, 4H), 1.62 − 1.53 (m, 1H), 1.45 (ddd, J = 13.1, 8.5, 4.8 Hz, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.07, 131.87, 128.85, 128.32, 128.14, 125.79, 125.66, 124.02, 122.70, 89.06, 86.54, 77.10, 37.48, 25.17, 22.72. IR (neat) 2936, 2083, 1707, 1241, 754, 691 cm^{-1}; HRMS (ESI) m/z calculated for C$_{22}$H$_{20}$N$_2$O$_2$Na [M+Na]$^+$ 367.1417, found: 367.1410.

2a
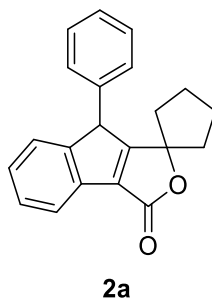
1-(phenylethynyl)cyclopentyl 2-Diazo-2-phenylacetate 2a: 94% yield. White solid, m.p. 128 − 129 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.74 (d, J = 8.0 Hz, 1H), 7.40 - 7.36 (m, 1H), 7.33 - 7.30 (comp., 3H), 7.27 - 7.24 (comp., 2H), 7.08 - 7.06 (comp., 2H), 4.80 (s, 1H), 2.11 - 2.08 (comp., 2H), 2.07 -2.02, (m, 1H), 2.01 - 1.98 (m, 1H), 1.98 − 1.82 m, 1H), 1.81 − 1.69 (m, 1H), 1.67 − 1.55 (m, 1H), 1.33-1.25 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 179.0, 166.4, 152.0, 136.1, 135.9, 134.3, 129.1, 128.1, 127.9, 127.7, 125.0,120.9, 95.5, 52.4, 38.5, 36.7, 24.4. HRMS

(ESI) *m/z* calculated for $C_{21}H_{18}O_2Na$ [M+Na]$^+$ 325.1199, found: 325.1200.

2b
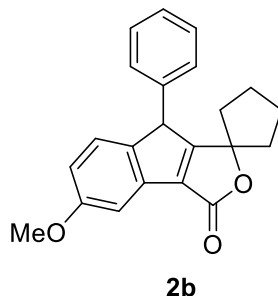
5'-Methoxy-8'-phenylspiro(cyclopentane-1,1'-indeno[1,2-c]furan)-3'(8'H)-one 2b: 98% yield. White solid, m.p. 152 – 153 °C.^{1}H NMR (400 MHz, CDCl$_3$) δ 7.51 (d, J= 8.3 Hz, 1H), 7.22 - 7.20 (comp., 3H), 6.98 - 6.96 (comp., 2H), 6.81 - 6.78 (m, 1H), 6.70 - 6.69 (m, 1H), 4.65 (s, 1H), 3.66 (s, 3H), 1.98 - 1.94 (comp., 2H), 1.88 – 1.86 (m, 1H), 1.78 – 1.74 (m, 1H), 1.71 – 1.66 (m, 1H),1.59 – 1.54 (m, 1H), 1.47 – 1.40 (m, 1H), 1.20-1.12 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) 176.9, 166.5, 159.2, 153.9, 136.1, 135.6, 129.0, 128.1, 127.8, 127.0, 121.3, 112.6, 111.8, 95.4, 55.4, 52.4, 38.3, 36.7, 24.3. HRMS (ESI) *m/z* calculated for $C_{22}H_{21}O_3Na$ [M+Na]$^+$ 355.1305, found: 355.1309.

2c
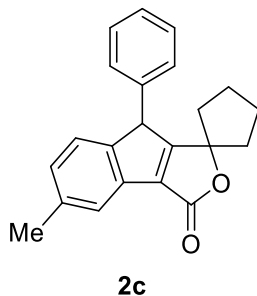
5'-Methyl-8'-phenylspiro[cyclopentane-1,1'-indeno[1,2-c]furan]-3'[8'H]-one 2c: 98% yield. White solid, m.p. 98 – 99 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.51 (d, *J* = 8.4 Hz, 1H), 7.24 - 7.18 (comp., 3H), 7.09 (d, *J* = 8.4 Hz, 1H), 6.98-6.95 (comp., 3H), 4.66 (s, 1H), 2.24 (s, 3H), 1.99 - 1.96 (comp., 2H), 1.93 – 1.86 (m, 1H), 1.82 – 1.75 (m, 1H), 1.73 – 1.64 (m, 1H), 1.63 - 1.56 (m, 4H),1.50-1.41 (m,1H),1.21-1.14 (m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 178.1, 166.6, 152.3, 136.9, 136.2, 136.0, 131.5, 129.1, 128.4, 128.1, 127.8, 125.8, 120.5, 95.4, 52.3, 38.4, 36.7, 24.3, 21.5. HRMS (ESI) *m/z* calculated for C$_{22}$H$_{20}$O$_2$Na [M+Na]$^+$ 339.1361, found: 339.1371.

2d
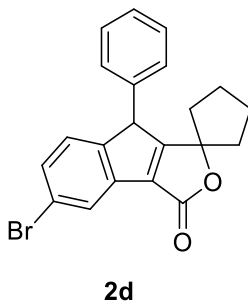
5'-Bromo-8'-phenylspiro(cyclopentane-1,1'-indeno[1,2-c]furan)-3'[8'H}-one 2d: 86% yield. White solid, m.p. 143 – 144 °C. [1]H

NMR (500 MHz, CDCl$_3$) δ 7.57 (d, J = 8.1 Hz, 1H), 7.49 (d, J = 8.1 Hz, 1H), 7.34 – 7.32 (m, 1H), 7.33 – 7.29 (comp., 3H), 7.08 – 6.99 (comp., 2H), 4.77 (s, 1H), 2.10 – 2.04 (comp., 2H), 2.01 – 1.93 (m, 1H), 1.90 – 1.83 (m, 1H), 1.79 – 1.73 (m, 1H), 1.70 – 1.65 (m, 1H), 1.55 – 1.51, (m, 1H), 1.29 – 1.22 (m, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 179.09, 165.92, 153.83, 135.45, 134.89, 133.20, 130.91, 129.27, 128.40, 128.19, 128.05, 122.04, 120.96, 95.44, 52.42, 38.41, 36.72, 24.42, 24.33. C$_{21}$H$_{17}$O$_2$BrNa [M+Na]$^+$ 403.0310, found: 403.0306.

2e
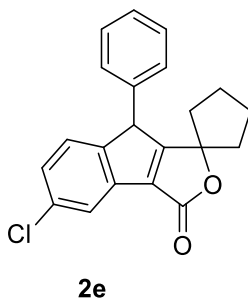
5'-Chloro-8'-phenylspiro[cyclopentane-1,1'-indeno[1,2-c]furan]-3'(8'H)-one 2e: 78% yield. White solid, m.p. 101 – 102 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.56 (d, J = 8.2 Hz, 1H), 7.29-7.24 (comp., 4H), 7.19-7.12 (m, 1H), 6.98-6.96 (comp., 2H), 4.70 (s, 1H), 2.02 – 1.97 (comp., 2H), 1.93 – 1.87 (m, 1H), 1.83 – 1.77 (m , 1H), 1.72 – 1.67 (m, 1H), 1.64 – 1.57 (m, 1H), 1.51 - 1.45 (m, 1H), 1.23-1.15 (m, 1H); ^{13}C NMR (100 MHz, CDCl3) δ 179.1, 166.0, 153.6, 135.5, 135.0, 133.0,

132.8, 129.3, 128.2, 128.1, 125.6, 121.7, 95.5, 52.5, 38.5, 36.8, 24.5, 24.4.

$C_{21}H_{17}O_2ClNa$ [M+Na]$^+$ 359.0815, found: 359.0821.

2f
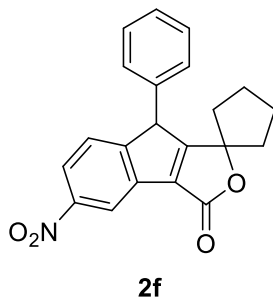
5'-Nitro-8'-phenylspiro[cyclopentane-1,1'-indeno[1,2-c]furan]-3'(8'H)-one 2f: 15% yield. White solid, m.p. 162 – 163 °C.^{1}H NMR (500 MHz, CDCl$_3$) δ 8.34 – 8.30 (m, 1H), 8.09 – 8.06 (m, 1H), 7.87 – 7.82 (m, 1H), 7.36 – 7.32 (m, 3H), 7.05 (s, 2H), 4.90 (s, 1H), 2.15 – 2.07 (m, 2H), 2.03 – 1.98 (m, 1H), 1.92 – 1.87 (m, 1H), 1.84 – 1.78 (m, 1H), 1.75 – 1.71 (m, 1H), 1.59 – 1.56 (m, 1H), 1.33 – 1.29 (m, 1H).^{13}C NMR (125 MHz, CDCl$_3$) δ 183.53, 165.26, 153.04, 146.99, 140.43, 135.21, 133.69, 129.60, 128.72, 128.05, 124.30, 121.13, 120.42, 95.84, 52.92, 38.64, 36.88, 24.54, 24.46. $C_{21}H_{17}NO_4Na$ [M+Na]$^+$ 370.1055, found: 370.1047.

2g
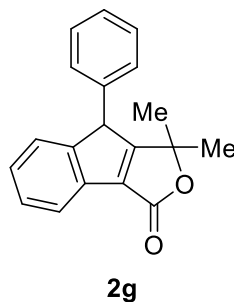
2-Methyl-4-phenylbut-3-yn-2-yl 2-diazo-2-phenylacetate 2g: 90% yield; white solid, m.p. 88 – 89 °C.^{1}H NMR (400 MHz, CDCl$_3$) δ 7.66 (d, *J* = 8.0 Hz, 1H), 7.32-7.28 (m, 1H), 7.24-7.14 (comp., 5H), 6.98-6.96 (comp., 2H), 4.70 (s, 1H), 1.54 (s, 3H), 1.03 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 181.9, 166.2, 151.6, 135.6, 135.1, 134.3, 129.1, 128.2, 127.9, 127.8, 127.0, 121.1, 85.4, 52.5, 26.4, 25.7. C$_{19}$H$_{16}$O$_2$Na [M+Na]$^+$ 299.1043, found: 299.1050.

2h
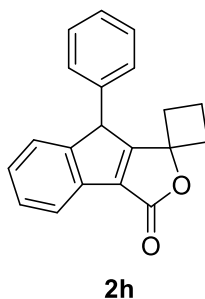
8'-Phenylspiro[cyclobutane-1,1'-indeno[1,2-c]furan]-3'(8'H)-one 2h: 90% yield; white solid, m.p. 150 – 151 °C.^{1}H NMR (400 MHz, CDCl$_3$) δ 7.72 (d, J= 8.2 Hz, 1H), 7.38-7.32 (comp., 4H), 7.27-7.21 (comp., 2H), 7.15-7.13 (comp., 2H), 4.89 (s, 1H), 2.82-2.74 (m, 1H), 2.51-2.47 (comp., 2H), 1.84-1.73 (comp., 2H), 1.60-1.50(m, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 178.2, 166.2, 152.2, 135.8, 135.5, 133.8, 129.0, 128.1, 127.9, 127.0, 125.0, 120.9, 85.9, 52.4, 33.3, 31.7, 12.2. C$_{20}$H$_{16}$O$_2$Na [M+Na]$^+$ 311.1048, found: 311.1062.
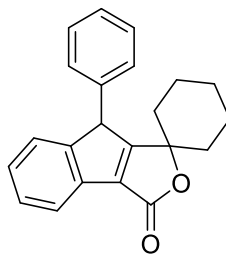
2i

8'-Phenylspiro[cyclohexane-1,1'-indeno[1,2-c]furan]-3'(8'H)-

one 2i: 80% yield; white solid, m.p. 175 – 176 °C. ^{1}H NMR (500 MHz,

CDCl$_3$) δ 7.75 (d, J = 7.4 Hz, 1H), 7.39 – 7.35 (m, 1H), 7.33 – 7.29 (m,

3H), 7.24 (d, J = 7.4 Hz, 1H), 7.21 (d, J = 7.4 Hz, 1H), 7.07 – 7.03

(comp., 2H), 4.76 (s, 1H), 1.85 – 1.77 (comp., 3H), 1.75 – 1.46 (comp.,

3H), 1.43 – 1.39 (comp., 2H), 1.19 – 1.08 (m, 1H), 1.06 – 0.97 (m, 1H).

^{13}C NMR (125 MHz, CDCl$_3$) δ 182.00, 166.60, 151.83, 135.67, 135.23,

134.24, 129.05, 128.25, 127.85, 127.69, 126.94, 125.01, 121.01, 87.36,

52.66, 35.68, 34.67, 24.30, 22.09, 21.70. C$_{22}$H$_{20}$O$_2$Na [M+Na]$^+$339.1361,

found: 339.1364.
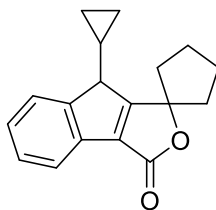
2j

8'-Cyclopropylspiro[cyclopentane-1,1'-indeno[1,2-c]furan]-

3'[8'H]-one 2j: 80% yield; White solid, m.p. 135 – 136 °C. ^{1}H NMR

(500 MHz, CDCl$_3$) δ 7.68 (d, J = 7.4 Hz, 1H), 7.63 (d, J = 7.5 Hz, 1H), 7.37 (t, J = 7.4 Hz, 1H), 7.30 (t, J = 7.5 Hz, 1H), 2.89 (d, J = 9.6 Hz, 1H), 2.57 − 2.47 (m, 1H), 2.17 − 1.89 (m, 7H), 0.93 − 0.83 (m, 1H), 0.81 − 0.69 (m, 3H), 0.46 (td, J = 9.6, 5.0 Hz, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 179.22, 150.67, 135.79, 134.10, 127.70, 126.46, 124.41, 120.80, 95.64, 51.79, 38.78, 36.84, 25.07, 24.92, 11.84, 4.82, 4.33. C$_{18}$H$_{18}$O$_2$Na [M+Na]$^+$ 289.1024, found: 289.1026.

4a
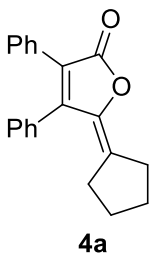
5-Cyclopentylidene-3,4-diphenylfuran-2[5H]-one 4a: 20% yield; White solid, m.p. 93 − 94 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.47 − 7.42 (comp., 3H), 7.41 − 7.37 (comp., 2H), 7.29 − 7.25 (comp., 2H), 7.25 − 7.19 (comp., 3H), 2.77 (t, J = 6.9 Hz, 2H), 1.87 (t, J = 7.2 Hz, 2H), 1.71 − 1.63 (comp., 2H), 1.62 − 1.56 (comp., 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 168.88, 148.98, 141.50, 136.31, 132.76, 129.82, 128.96, 128.95, 128.39, 128.21, 128.08, 125.69, 32.54, 30.49, 27.32, 25.31. HRMS (ESI) *m/z* calculated for C$_{21}$H$_{18}$O$_2$Na [M+Na]$^+$ 325.1199, found: 325.1191.

4g
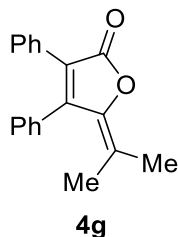
3,4-Diphenyl-5-(propan-2-ylidene)furan-2[5H]-one 4g: 17 %
yield; White solid, m.p. 87 – 88 °C.^{1}H NMR (500 MHz, CDCl$_3$) δ 7.45 –
7.40 (m, 3H), 7.35 – 7.31 (m, 2H), 7.29 – 7.26 (m, 2H), 7.23 – 7.18 (m,
3H), 2.10 (s, 3H), 1.47 (s, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 168.40,
148.80, 144.04, 133.33, 129.71, 129.03, 129.00, 128.90, 128.48, 128.24,
128.04, 127.18, 125.64, 21.19, 19.17. C$_{19}$H$_{16}$O$_2$Na [M+Na]$^+$ 299.1043,
found: 299.1040.

**NMR graphs will be obtained from the supporting information of the
upcoming published paper.**

V. References:

(1) Regitz, M.; Maas, G. In *Diazo Compounds*; Academic Press:
1986, 199.

(2) (a) Li, W.; Liu, X.; Hao, X.; Hu, X.; Chu, Y.; Cao, W.; Qin, S.;
Hu, C.; Lin, L.; Feng, X. *J. Am. Chem. Soc.* **2011**, *133*, 15268-15271; (b)
Liu, Y.; Bakshi, K.; Zavalij, P.; Doyle, M. P. *Org. Lett.* **2010**, *12*, 4304-
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Chapter 2: Unprecedented Rearrangement of Propargyl Aryldiazoacetates. Gold Catalysis Forms Allenes Whose Intramolecular Reaction with the Terminal Diazo Nitrogen Yields 1,5-Dihydro-4H-pyrazol-4-ones

I Introduction

1.1 Discovery of the Rearrangement Process

Because of the positioning of their two reaction centers (diazo and alkyne), we have been intrigued with the reactions of propargyl diazoacetates since both reaction centers are known to initiate reaction processes that are characteristic of their requisite functional groups. In **Chapter 1**, we disclosed that a variety of transition metal complexes that include $Rh_2(OAc)_4$, $Rh_2(tfa)_4$, $Pd(OAc)_2$, $PdCl_2(PhCN)_2$, $[Pd(\eta^3-C_3H_5)Cl]_2$, $AgSbF_6$, $Au(JohnPhos)SbF_6$, $IPrAuBF_4$, $Cu(OTf)_2$, $CuBF_4(MeCN)_4$, and $CuPF_6(MeCN)_4$ undergo carbene/alkyne domino cascade reactions. During the screening of the transition metal complexes with propargyl phenyldiazoacetate, we found that the carbene/alkyne

domino cascade product was not observed under catalysis by AuCl(C$_4$H$_8$S); but, instead, two isomeric 1*H*-pyrazolines that retain dinitrogen were obtained (**Scheme 2.1**).
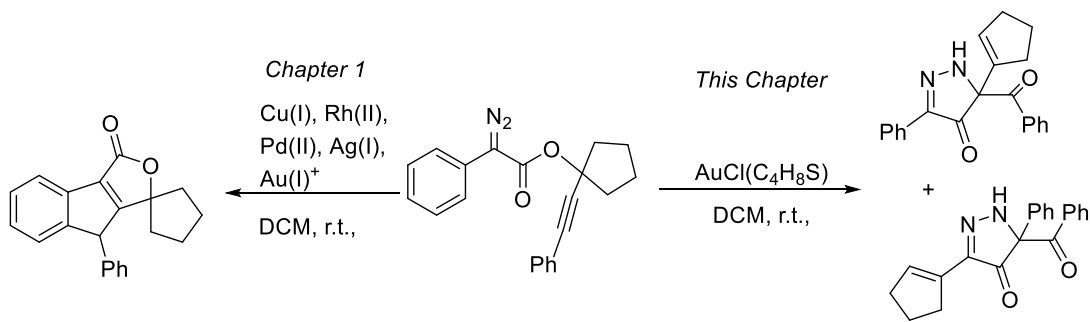
Scheme 2.1 Catalysts Screening Leads to Discovery of the Rearrangement Process.

1.2 General Information for Gold Catalysis

Gold catalysis provides powerful methodologies for unique metallo-organic transformations.[1] Activation of organic functional groups by gold(I) and gold(III) complexes initiates diverse pathways for often unique reactions.[2] Many of the transformations developed with gold complexes involve activating carbon-carbon unsaturated bonds as electrophiles.[3] Alkynes have been recognized as the most successful substrates in gold catalyzed reactions.[4] The most common reaction pattern involves the coordination of gold complexes with internal alkynes that lead to a loss of π-electron density, which allows nucleophilic attack

on the activated alkynes to produce *trans*-alkenyl gold complexes (**Scheme 2.2**).
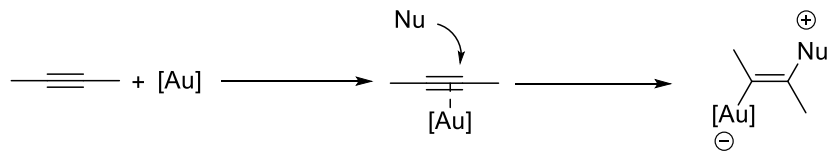
Scheme 2.2 Equation for Gold-Catalyzed Activation of Alkynes toward a variety of Nucleophiles.

1.3 Gold-Catalyzed 1,3-Acyloxy Migration of Propargyl Esters and Subsequent Transformations

One of the most useful of these transformations has been that of propargyl esters, which form allenes by 1,3-acyloxy migration, then undergo varied catalytic reactions.[5] A wide array of subsequent transformations that involve this highly valuable intermediate have been widely used in constructing mono-, bicycles, and other important compounds over the past decade (**Scheme 2.3**).[6]
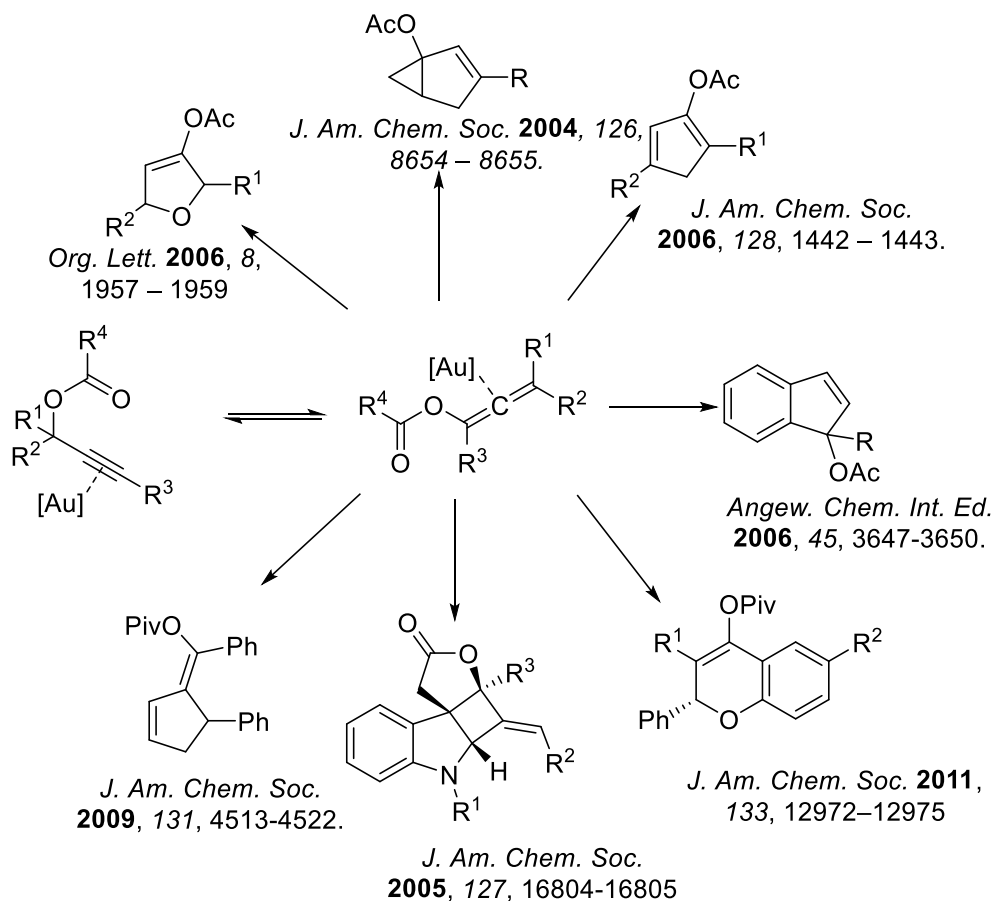
Scheme 2.3 Formation of Allenes and Subsequent Transformations to Form Diverse Carbocycles and Heterocycles.

II. Results and Discussion

2.1 Initial Assessment of Gold Catalysts and Attempts to Determine the Structure of Rearrangement Products

Initial assessment of gold catalysis was evaluated with propargyl aryldiazoacetates using cationic gold(I) catalysts, including those formed from ligated gold(I) chloride and silver salts. Cationic gold catalysts are well-established σ-bond acceptors with aryldiazoacetates,[7] and they have

been widely used for dinitrogen extrusion reactions of diazo compounds that are reported to produce the corresponding gold carbenes.[8] Catalytic reactions of phenylpropargyl phenyldiazoacetate **1** with representative Au(I)$^+$ catalysts formed the product from the carbene-initiated domino transformation **2** in good yield (**Scheme 2.4**). Complete conversion of the reactant was observed at room temperature, and no other discernable product was identified. Each of the gold catalysts was soluble in the reaction solution.

[Au(JohnPhos)(MeCN)]SbF$_6$	86%
AuCl(PPh$_3$)/AgSbF$_6$	83%
(IPr)AuCl/AgSbF$_6$	67%
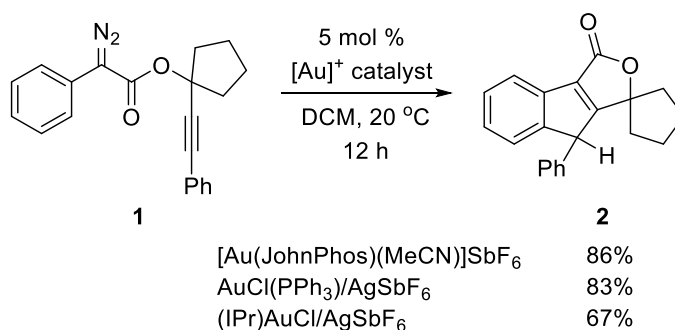
Scheme 2.4 Domino Reaction of Propargyl Phenyldiazoacetate **1** Catalyzed by Cationic Gold(I).

Neutral gold(I) and gold(III) compounds are reported to have varying influences on reactions with diazo and alkyne functional groups.[9] A survey of representative compounds for reactions with **1** at 20 °C revealed that 5 mol % of chloro(tetrahydrothiophene)gold(I) [AuCl(C$_4$H$_8$S)] catalyzed its complete conversion to three discernable products in the highest yield (**Scheme 2.5**). The surprising conversion of

1 to **3** and **4** retained all of the atoms of the reactant but gave extensive rearrangement, including the conversion of the reactant ester to product 1,5-dihydro-4*H*-pyrazol-4-ones.
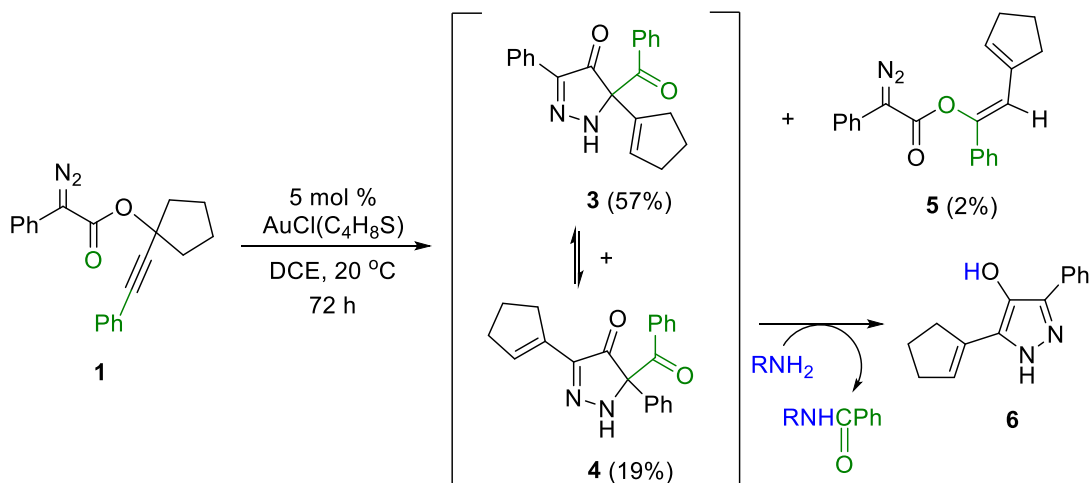
Scheme 2.5 Products from Gold(I)-Catalyzed Rearrangement of Phenylpropargyl Phenyldiazoacetate **1**.

Compounds **3** and **4** were observed spectroscopically to be related as structural isomers, and the crystal structure of **4** was obtained (**Figure 2.1a**) after its isolation from the reaction mixture. Recognition of **3** and **4** as potential benzoyl transfer agents prompted us to convert **3** and **4**, individually and as a mixture, quantitatively to the same 4-hydroxypyrazole **6** by treatment with nucleophilic bases that included hydrazines and amines (X-Ray structure of analog **6′**, **Figure 2.1b**). Compound **5**, although present in very low yield, was confirmed by

spectral and chromatographic comparison with the characterized compound (discussed in the next chapter).[10]

Figure 2.1 X-Ray Structures of 1,5-Dihydro-4*H*-Pyrazol-4-One **4** and Deacylation Product **6´**.

2.2 Optimization of Reaction Conditions and Monitoring the Reaction Process

Under the catalysis of 5 mol% AuCl(C$_4$H$_8$S), different solvents were examined in attempts to increase the yield of 1,5-dihydro-4*H*-pyrazol-4-ones as well as improve the ratios of **3**:**4** at room temperature. Use of chloroform and dichloromethane failed to increase product yields and resulted in the decreased **3**:**4** product ratios (**Table 2.1**, entries 2 and 3). Toluene gave the improved **3**:**4** product ratios compared to 1,2-dichloroethane, but the yield of 1,5-dihydro-4*H*-pyrazol-4-ones was only 29% (**Table 2.1**, entry 4). Polar solvents that include tetrahydrofuran and acetonitrile showed lower yield of product, but had a great influence on the **3**:**4** product ratios (**Table 2.1**, entries 5 and 6). Overall, examination of this reaction as a function of solvent did not provide any improvement in the product yield, but did show significant variation in the **3**:**4** product ratios.

Table 2.1 Solvent Screening for the Reaction of **1** with AuCl(C$_4$H$_8$S)
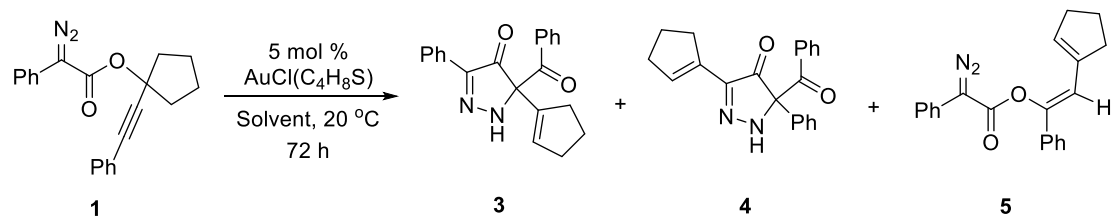
Entry[a]	Solvent[b]	Conversion (%) **1**[c]	Yield (%) **3+4**[c]	Ratio **3:4**[c]	Yield (%) **5**[c]
1	1,2-Dichloroethane	>95	76	72:25	2
2	Chloroform	>95	57	65:35	3
3	Dichloromethane	>95	43	40:60	5
4	Toluene	>95	29	80:20	10
5	Tetrahydrofuran	>95	40	65:35	3
6	Acetonitrile	>95	30	37:63	1

[a]Reactions were carried out on 0.20 mmol scale: a solution of **1** (0.20 mmol) in 2.0 mL of solvent was added to a solution of 5 mol % AuCl(C$_4$H$_8$S) in 2.0 mL of solvent under a nitrogen atmosphere at 20 °C, and the resulting reaction mixture was stirred for 72 h. [b]No reaction occurred for reactions performed in hexane or nitromethane. [c]Conversion of **1**, yields of (**3+4**), **5**. Ratios **3:4** were determined by ^{1}H NMR analysis of characteristic peaks using 2,4,6-trimethoxybenzene as the internal standard.

To determine if this product variation could be due to an equilibrium between **3** and **4** under the reaction conditions, the formation of **3** and **4** in DCE was followed as a function of time over ten days at room temperature with high product accountability, and the results from this investigation (**Figure 2.2**) clearly show an equilibrium between **3** and

4. Slow deacylation resulting in **6** complicates the overall picture, but conclusions can be drawn that compound **3** is the product of kinetic control at room temperature, and **4** is the product of thermodynamic control.
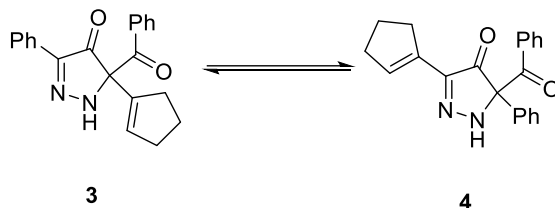
Figure 2.2 Time Course for the Formation of **3**, **4**, and **6** in DCE at 20 ^{0}C. (Yields were determined by ^{1}H NMR and HPLC analyses of the reaction mixture after selected periods of time using 1,3,5-trimethoxybenzene as the internal standard; reported yields are the averages of two runs; reactions and analyses performed by Kostiantyn Marichev.)

Experiments performed at higher temperatures (50 and 84 °C) are consistent with this interpretation (**Table 2.2**). Compound **4** is the major isomer even at lower conversions of diazo compound **1**. At 50 °C the maximum total yield of **3**+**4** is 81% at a 12 h reaction time, and the ratio **3**:**4** is 2:3; whereas at 84 °C the reaction is complete (total yield of **3**+**4** is 80%) after 6 h, and **3**:**4** is 1:1. Continuing the reaction further at these higher temperatures leads to lower product yield as the result of deacylation from which 4-hydroxypyrazole **6** is formed.

Table 2.2 Temperature Screening for the Reaction of **1** with AuCl(C$_4$H$_8$S).
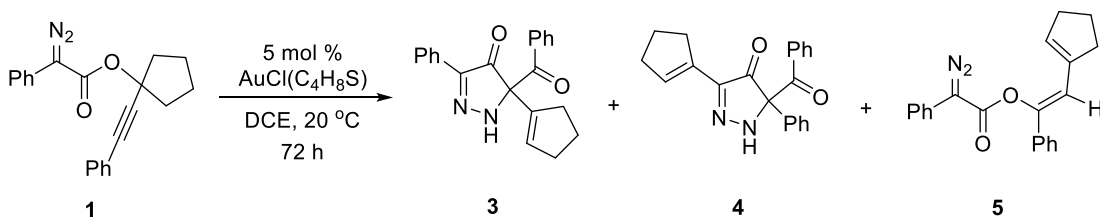
Entry[a]	Temp (°C)	Time (h)	Yield (%) (**3+4**)[b]	Ratio **3:4**[b]
1	50	3	35	45:55
2	50	6	56	42:58
3	50	12	81	40:60
4	50	24	64	37:63
5	84	3	53	48:52
6	84	6	80	45:55
7	84	12	79	43:57
8	84	24	48	45:55
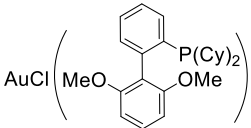
[a]Reactions were carried out on 0.20 mmol scale: a solution of **1** (0.20 mmol) in 2.0 mL of solvent was added to a solution of 5 mol % AuCl(C$_4$H$_8$S) in 2.0 mL of solvent under a nitrogen atmosphere at 20 °C, and the resulting reaction mixture was heated for defined periods of time. [b]Yields and ratios were determined by ^{1}H NMR analyses of the reaction mixture using 1,3,5-trimethoxybenzene as the internal standard.

Cationic gold(I) and the neutral chloro(tetrahydrothiophene)gold(I) catalysts are mutually exclusive for product formation from reactions with **1**. Both catalysts are active at room temperature, and their application provides products from reactions at the diazo functional group [**2** from cationic gold(I)] and the alkyne functional group [**3**, **4**, and **5** from AuCl(C$_4$H$_8$S)] in good yields. Neutral gold(I) chloride complexes having strongly coordinating ligands (**Table 2.3**) show very low or negligible conversion of phenylpropargyl phenyldiazoacetate **1** under the same conditions, even to reaction times of three days. However, heating these complexes to the temperature of refluxing 1,2-dichloroethane for up to 48 h gives the domino reaction product **2** exclusively or as the major product (**Table 2.3**, entries 1-6), albeit usually with low product yield and, generally, low % conversion. The dimethylsulfide coordinated AuCl (**Table 2.3**, entries 9-10) is not as effective a catalyst as its tetrahydrothiophene analog (**Table 2.3**, entries 7-8) with product yields only about half those found with AuCl(C$_4$H$_8$S). Gold(III) catalysts (**Table 2.3**, entries 11-14) are also less efficient than the AuCl(R$_2$S) catalysts in the formation of compounds **3** and **4**, but they afford diene **5** in yields up to 39% and give no evidence for the formation of **2**.

Table 2.3 Screening of Gold(I) and Gold(III) Catalysts in Reactions with Phenylpropargyl Phenyldiazoacetate **1**.
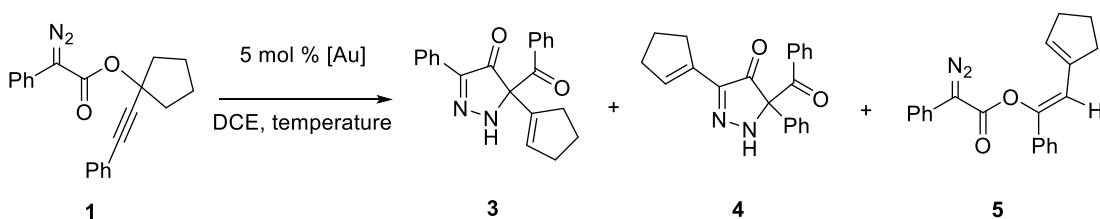
Entry[a]	Gold Catalyst	Temp (°C)	Conversion (%) 1	Yield (%) 2[b]	Yield (%) 3+4[b]	Ratio 3:4[b]	Yield (%) 5[b]
1	AuCl(IPr)	84[d] (20)	68 (<5)	46	–	–	–
2	AuCl(CO)	84 (20)	>95 (14)	16 (9)	14	47:53	9
3	AuCl[P(OMe)$_3$]	84[c] (20)	40 (<5)	25	–	–	3
4	AuCl(PPh$_3$)	84[c] (20)	35 (<5)	23	–	–	–
5	AuCl(PMe$_3$)	84[c] (20)	45 (<5)	20	8	40:60	6
6	AuCl(MeO—P(Cy)$_2$—OMe)	84[c] (20)	70 (<5)	57	–	–	–
7	AuCl(C$_4$H$_8$S)[i]	20	>95	–	76	75:25	2
8	AuCl(C$_4$H$_8$S)	84	>95	–	80	45:55	4
9	AuCl(Me$_2$S)	20	>95	–	42	62:38	3
10	AuCl(Me$_2$S)	84	>95	–	46	45:55	5

73

11[e]	AuPicCl$_2$[j]	20	>95	–	21	50:50	14
12[f]	AuPicCl$_2$[j]	84	>95	–	14	40:60	18
13[g]	AuCl$_3$(Pyridine)[j]	20	>95	–	25	60:40	35
14[h]	AuCl$_3$(Pyridine)[j]	84	>95	–	18	45:55	39

[a]Reactions were performed on 0.10 mmol scale: a solution of **1** (0.10 mmol) in DCE (1.0 mL) was added to a solution of Au-catalyst (5 mol %) in DCE (1.0 mL) under a nitrogen atmosphere at 20 °C (% conversion in parenthesis for entries 1-6) or in refluxing DCE, and the resulting reaction mixture was stirred for defined periods of time. [b]Conversion of **1**, yields of **2**, (**3**+**4**), **5**, and ratios **3**:**4** were determined by ^{1}H NMR analysis of characteristic peaks using 2,4,6-trimethoxybenzene as the internal standard. Reaction times were 72 h for the reactions carried out at 20 °C, and 6 h at 84 °C. Reaction times: [c]12 h; [d]48 h. Yield of product **6**: [e]24%; [f]27%; [g]32%; [h]38%. [i]At 50 °C after 12 h: 81% yield of **3**+**4** with **3**:**4** = 40:60. [j]Reduction of the catalyst to elemental gold is significant.

2.3 Reaction Mechanism

A stepwise mechanism for the neutral gold(I)-catalyzed rearrangement of arylpropargyl aryldiazoacetate **9** is given in **Scheme 2.6**. The AuCl(R$_2$S) catalyzed 1,3-acyloxy rearrangement of **9** produces carboxyallene **C** that undergoes a unique rearrangement between allene **C** and the diazo functional group to form the observed **3** directly in a concerted fashion or stepwise through intermediate **D**. Diene **12** is formed from gold-activated carboxyallene **A,** presumably through gold-coordinated acylium ion intermediate **B**. Compound **10** is formed initially from **A** and undergoes acyl migration to reach equilibrium with **11**. This mechanism explains the formation of **10** from carboxyallene **C**, the

equilibrium that exists between **10** and **11,** and the formation of (*Z*)-diene **12**.
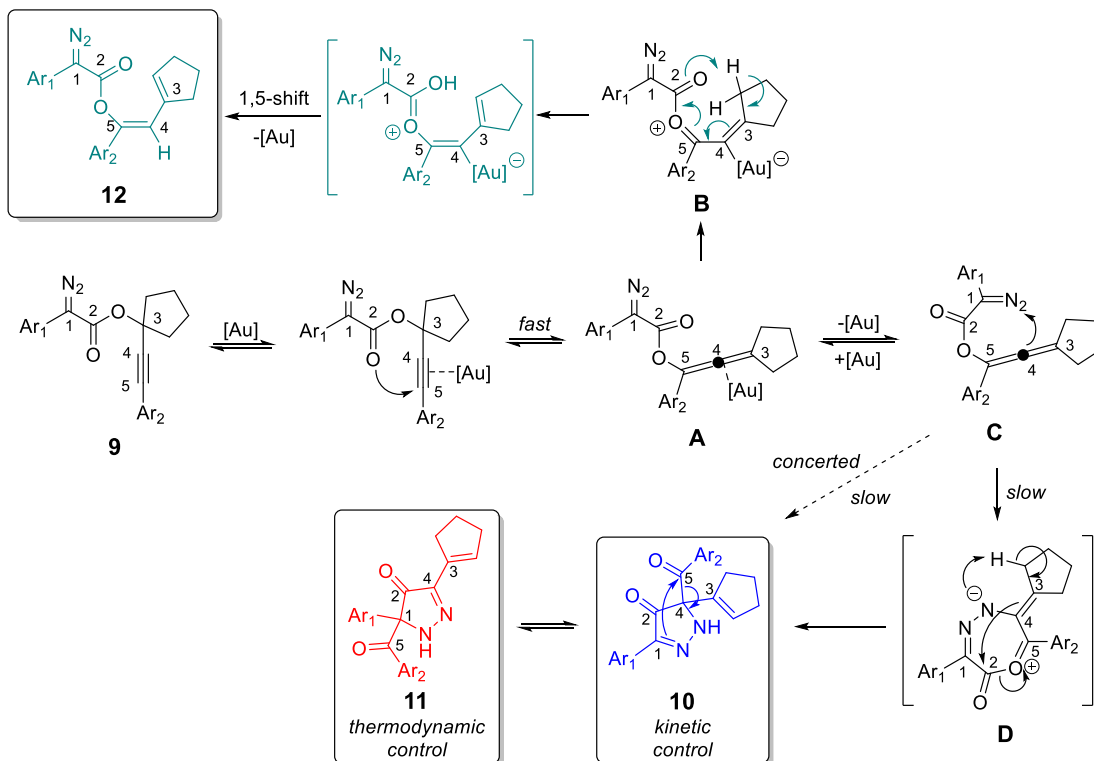
Scheme 2.6 Proposed Mechanism for the Formation of **10**, **11**, and **12** from **9**.

2.3a Formation of Allene

Close examination of the reaction process by NMR spectroscopy revealed that the key transformation in the formation of **3** and **4** was the generation of allene (**Scheme 2.6**), which occurred within 5 min at 20 °C. For these investigations the dimethyl analog (**7**) of cyclopentylpropargyl phenyldiazoacetate **1** was used (Eq 1) to assess the course of the reaction. Allene **8** formation,[6b] which occurs by 1,3-acyloxy transfer, begins to

take place immediately upon addition of the catalyst [5 mol %
AuCl(Me₂S) or AuCl(C₄H₈S)] as the only reaction product, and reaches
an apparent equilibrium (**7:8** = 45:55 with either catalyst).
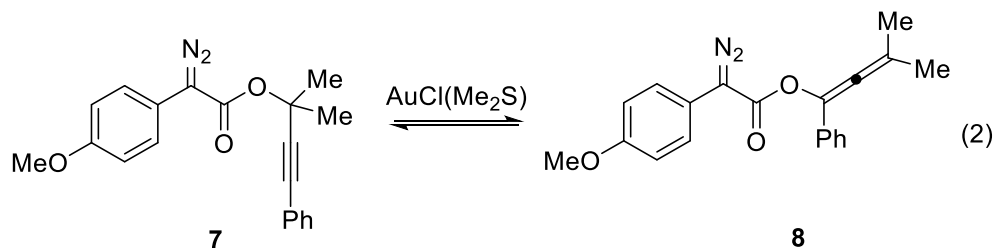
With added gold catalyst up to 2 equiv. based on **7** no further
change in the **7:8** ratio occurred. Confirmation of this process was made
with phenyldimethylpropargyl benzoate under the same conditions
(allene:alkyne = 3:2) and with **1** (allene:alkyne = 1:2).

The validity of the reversibility of Au(I)-catalyzed [3,3]-
rearrangements of propargylic esters has been reported by Toste and
coworkers.[6h] By introducing a stereochemically defined cyclopropane
probe, the authors have disclosed both isomerization of the cyclopropyl
moiety and propargyl moiety which indicates the reversibility of the
gold(I)-catalyzed rearrangement propargylic esters. DFT studies on the
reversibility of propargylic esters supported the experimental evidence.

	trans:cis		dr	
t = 2 min	40:60	59%	1:1	41%
t = 10 min	75:25	33%	1:1	54%
t = 1 h	>97:3	12%	1:1	61%
t = 8 h	--	0%	--	75%
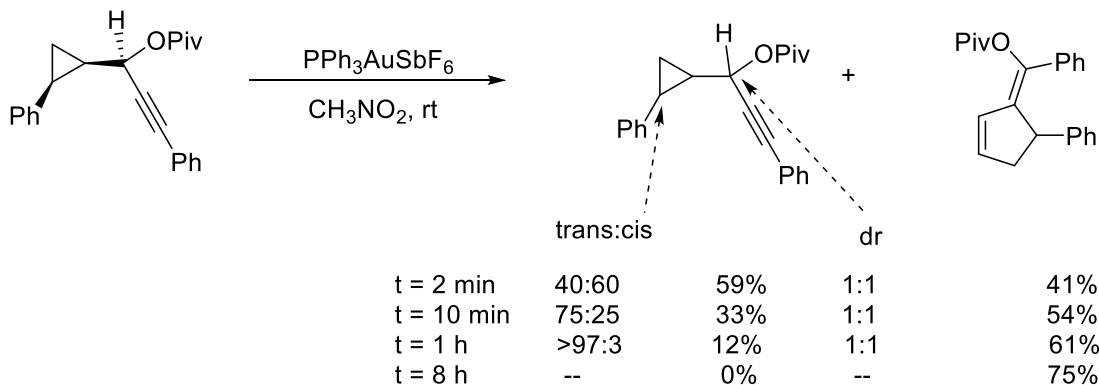
Scheme 2.7 Further Insight into the Mechanism of Au(I)-Catalyzed [3,3]-Rearrangements of Propargylic Esters

With propargyl diazoacetates additional stabilization by the diazo group of the cyclic carbocation intermediate on the pathway to allene formation could be expected. Furthermore, when the allene was isolated from the reaction mixture free of gold catalyst, the allene was observed to undergo slow conversion to the rearranged products corresponding to **3** and **4**, but without any obvious formation of **5**. This conversion was first order in **7** with a rate constant of 1.05×10^{-5} sec^{-1} at 20 °C, and addition of AuCl(Me$_2$S) did not influence the reaction rate. The activation energy measured over 20−60 °C was 18.8 kcal/mol ($R^2 = 0.999$) with $\Delta H^{\ddagger} = 18.2$ kcal/mol and $\Delta S^{\ddagger} = -19.4$ cal/deg-mol at 298 K (reaction and analysis performed by Kostiantyn Marichev).

2.3b Diazo Compounds as Electrophiles in Organic Transformations

Although diazo compounds are normally regarded as nucleophiles, with both the diazo carbon and the terminal nitrogen as nucleophilic centers,[11] there are examples in which the terminal nitrogen atom of diazo compounds exhibits electrophilic reactivity.[12] The formation of **10** can be considered to be initiated by intramolecular electrophilic addition of the *N*-terminus of the aryldiazoacetates onto the central carbon of the allene that is continued with hydrogen.
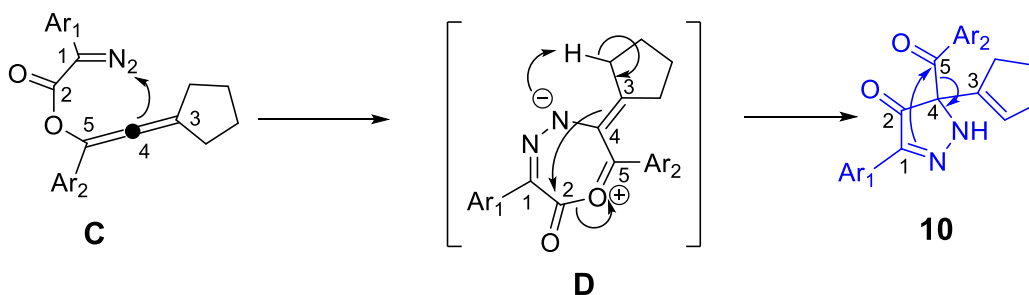
Feng and coworkers discovered a scandium-catalyzed nucleophilic addition to α-diazoesters, in which ketones were the nucleophiles.[13] With chiral *N,N'*-dioxide as the ligands for Sc(OTf)$_3$, the reaction produces the addition products in excellent yields and enantioselectivities. To better understand this unusual process, the authors performed theoretical calculations, which showed that the positive charge on the terminal nitrogen atom greatly increases when the carbonyl oxygen of α-diazoesters coordinates with Sc(OTf)$_3$ These reactions are intermolecular and involve obvious nucleophilic attack on the terminal nitrogen of

diazocarbonyl compounds and result in the formation of hydrazone derivatives (**Scheme 2.8**).

Feng's work

R = Aryl or Alkyl

up to 98% yield
up to 99% ee

L: Ar=2,6-i-Pr$_2$C$_6$H$_3$
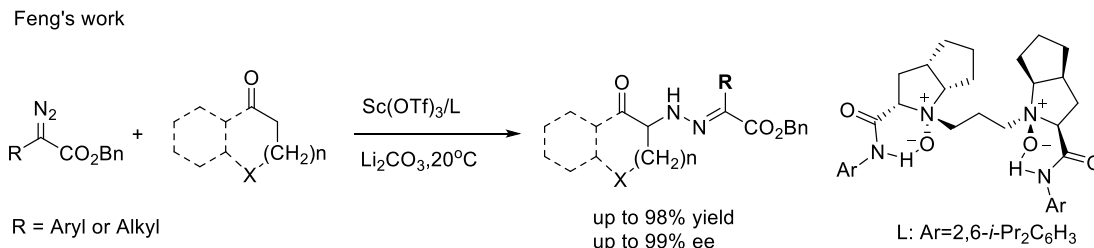
Scheme 2.8 Intermolecular Electrophilic Addition of α-Diazoesters with Ketones.

The intramolecular transformations that involve the electrophilic capability of diazo compounds are also documented in several other reports,[14] which are also referred to as electrocyclization of the diazo group.[15] For instance, in the process of investigating synthetic applications of benzocyclobutenes, Nemoto and coworkers have developed a one-pot reaction for synthesis of 2,3-benzodiazepines. In this reaction, the electrophilic capability of diazo compounds plays an important role in the formation of the cyclic product, which was obviously formed by intramolecular nucleophilic addition to the terminal nitrogen of the diazo group (**Scheme 2.9**).[15b] Enolates were also reported as efficient nucleophiles in the reactions with diazo compounds by Doyle and coworkers, who have discovered that the enedione-diazoester undergoes intramolecular cycloaddition reaction to produce 1,2-diazepine

under basic conditions. The authors proposed a mechanism by which a similar intramolecular nucleophilic attack occurs on the terminal nitrogen process (**Scheme 2.10**).[15a]

Nemoto's work
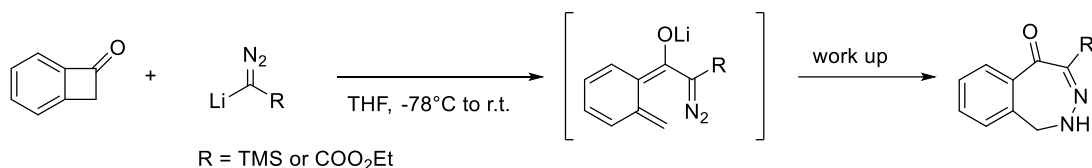
Scheme 2.9 Synthesis of 2,3-Benzodiazepines from Benzocyclobutenes

Doyle's work
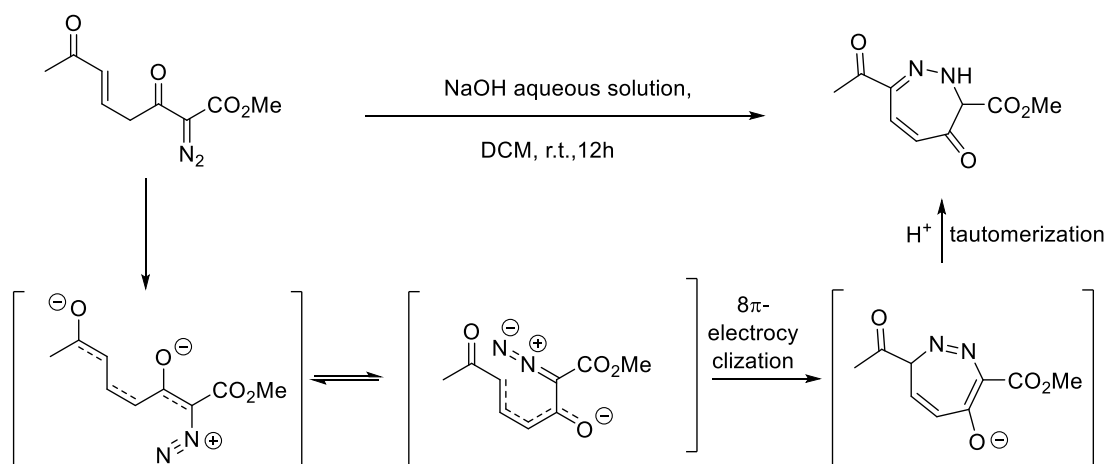
Scheme 2.10 Synthesis of 1,2-Diazepine from Enedione-Diazoester.

2.3c Formation of 1,3-Diene
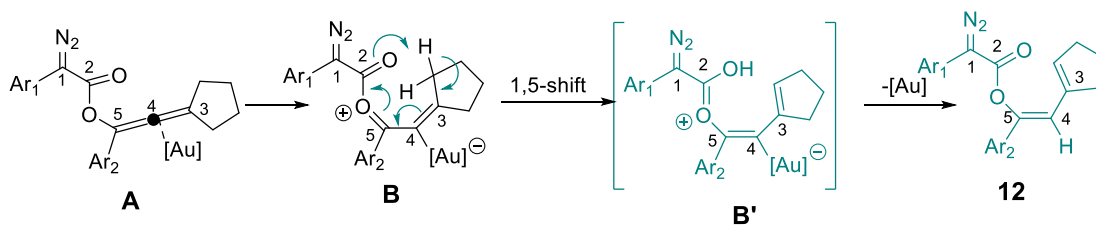
Isomerization of allenes into 1,3-dienes under the catalysis of gold complexes has been reported previously.[16] Gold-allene complexes are considered to be the initial intermediates in these transformations. Based on those reports,[17] we propose a plausible mechanism for formation of 1,3-diene **12**. The (*Z*)-diene **12** was considered to be generated from gold-allene complexes **A**, presumably through gold-coordinated acylium ion intermediate **B**. Acylium ion intermediate **B** underwent intermolecular 1,5-hydrogen shift, which produced the (*Z*)-diene-gold complex **B′**, followed by a proton transfer process of the newly formed (*Z*)-diene-gold complex **B′**, to furnish (*Z*)-diene **12**. It should be noted that when the same reaction was performed in the presence of 4-chloropyridine-*N*-oxide, the isomeric (*E*)-diene could be observed (discussed in next chapter).

Rearrangement of propargyl esters into 1,3-dienes in presence of gold catalysts has also been documented,[18] and this rearrangement has been considered to occur though allene intermediates. Gevorgyan and coworkers developed a cascade process of double 1,3-acyloxy group migration/1,2-migration of hydrogen to produce (*E*)-1,3-dienes from alkynes via a gold-catalyzed cycloisomerization of propargylic esters. The authors proposed a pathway in which a gold-catalyzed 1,3-acyloxy

migration occurs via cyclic intermediates into allenes, followed by hydrogen migration to produce the (*Z*)-1,3-dienes (**Scheme 2.11**).

Scheme 2.11 Formation of 1,3-diene from Gold-Catalyzed Propargyl Esters.

2.4 Substrate Scope

The substrate scope of phenylpropargyl aryldiazoacetates **9a–k** (**Table 2.4**) demonstrates that the AuCl(C$_4$H$_8$S)-catalyzed reaction is broadly appropriate for the synthesis of the 1,5-dihydro-4*H*-pyrazol-4-ones **10** and **11**, and these reactions are tolerant of both electron-donating and electron-withdrawing substituents in the aryl group of the aryldiazoacetate. High total yields of the **10**+**11** composites are observed, and their **10**:**11** ratio is near 3:1 (**Table 2.4**). Substrate **9j** with a 12-membered ring gives a high yield of the **10j**+**11j** composite, but its **10**:**11** ratio is 3:2. Tetrahydropyranyl derivatives **10k**+**11k** are obtained in only 46% yield and a 78:22 **10**:**11** ratio.

Table 2.4 Substrate Scope of Gold(I)-Catalyzed Reaction of Phenylpropargyl Aryldiazoacetates **9**[a]
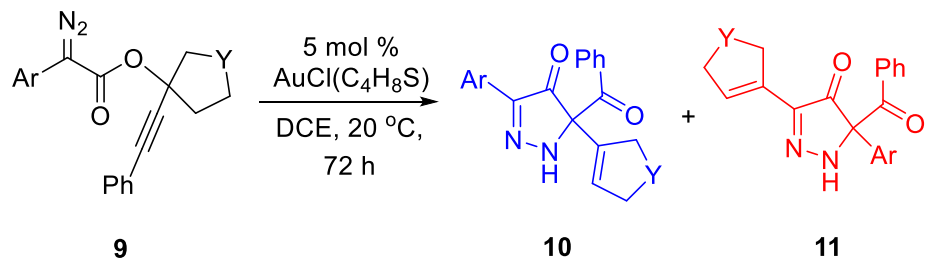
9−11	Ar (Y = CH$_2$)	Yield (%)$^{b, c}$	Ratio 10:11^b
a	C$_6$H$_5$	76	75:25
b	p-MeO-C$_6$H$_4$	75	72:28
c	p-Me-C$_6$H$_4$	85	72:28
d	p-Ph-C$_6$H$_4$	78	88:12
e	p-Br-C$_6$H$_4$	87	85:15
f	p-Cl-C$_6$H$_4$	83	83:17
g	p-CF$_3$-C$_6$H$_4$	73	70:30
h	2-C$_4$H$_3$S^d	67	88:12

9−11	Y (Ar = C$_6$H$_5$)	Yield (%)$^{b, c}$	Ratio 10:11^b
i	(CH$_2$)$_2$	73	78:22
j	(CH$_2$)$_8$	86	59:41

k	CH_2O	46	78:22

With substrates having electron-withdrawing or electron-donating groups (EWG or EDG) in both arene rings, the product outcome is quite similar (**Scheme 2.12**) to those presented in **Table 2.4**. However, having an EWG as Z and an EDG as X (compound **9o**) results in a lower yield of **10o+11o** (47%) but a higher **10**:**11** ratio of 89:11. High yield (79%) and almost exclusive formation of compound **10q** (**10**:**11** = 91:9) are observed from the dimethyl analog **9q**, whereas the unsubstituted aryl analog **9p** results in lower yield of **10p+11p** (68%) with a 88:12 **10**:**11** ratio.

10,11	X	Y	Z	Yield (%)	10:11
l	Cl	CH_2	H	80	77:23
m	OMe	CH_2	H	77	62:38
n	OMe	CH_2	OMe	79	70:30
o	OMe	CH_2	CF_3	47	89:11
p	H	H	H	68	88:12
q	H	H	OMe	79	91:9
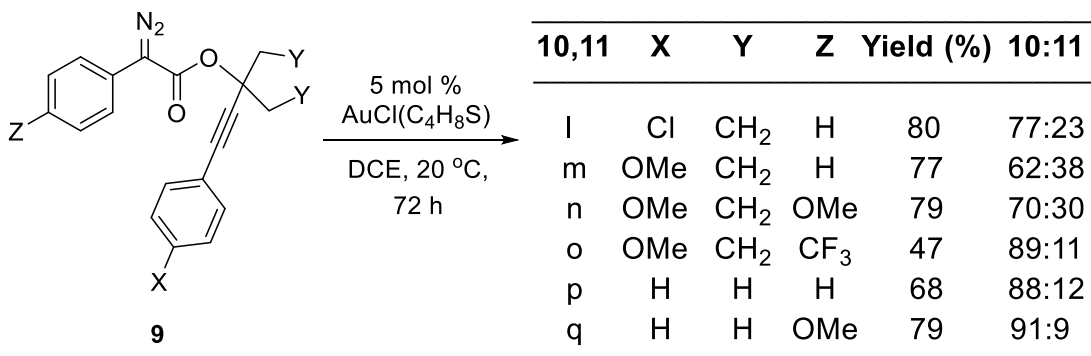
Scheme 2.12 Substrate Scope of Gold(I)-Catalyzed Reaction of Arylpropargyl Aryldiazoacetates **9**.

The cyclobutyl analog **9r** forms neither **10** nor **11**. Instead, treatment of **9r** with 5 mol % AuCl(C$_4$H$_8$S) affords **13** in good yield (70%), but only at 80 °C over 12 h. This product is consistent with initial formation of a gold-carbene intermediate through the diazo functional group. The alternate pathway through a strained allene intermediate is apparently too restrictive and, although the initial step in the 1,3-acyl rearrangement that produces the stabilized intermediate **E** is favorable, release of the C-O bond to form the allene does not occur (**Scheme 2.13**).
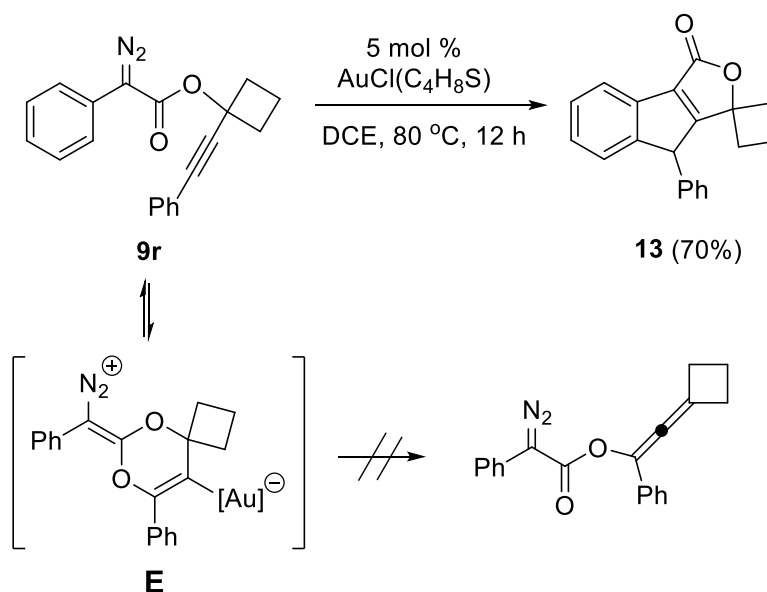
Scheme 2.13 Outcome of Gold(I)-Catalyzed Reaction of Cyclobutyl Propargyl Reactant **9r**.

III. Conclusion

We have discovered a unique gold(I)-catalyzed rearrangement of propargyl aryldiazoacetates and a platform on which catalytic activity of

gold complexes can be assessed. Phenylpropargyl phenyldiazoacetates have two reactive sites for reactions with gold complexes. If initial interaction occurs at the diazo carbon, a gold carbene is the outcome, and a subsequent cascade process results in the formation of a product that is uniquely characteristic of this pathway. If gold coordination occurs with the carbon-carbon triple bond, 1,3-acyloxy migration of the propargylic ester promoted by the diazoester takes place. The corresponding allene formed rapidly is a stable intermediate, and it determines the course of subsequent processes, one of which is to undergo gold-catalyzed formation of a gold-acylacylium ion intermediate to form stable products by cleavage or intramolecular hydrogen migration. Alternatively, the allene intermediate undergoes a complex transformation, not catalyzed by gold, in which the terminal nitrogen of the diazo functional group adds at the central carbon of the allene to initiate a sequence of bond forming reactions resulting in the production of 1,5-dihydro-4*H*-pyrazol-4-ones in good yields. As acyl transfer agents these unique products undergo intramolecular 1,3-acyl migration to form an equilibrium mixture of two isomeric 1,5-dihydro-4*H*-pyrazol-4-ones under the reaction conditions or quantitatively transfer the acyl group to an external nucleophile with formation of 4-hydroxypyrazoles. Cationic gold(I) complexes initiate

their reactions at room temperature exclusively with the diazo functional group of propargyl phenyldiazoacetates, whereas both $AuCl(R_2S)$ and gold(III) catalysts undergo initial reaction exclusively at the carbon-carbon triple bond. Neutral gold(I) chloride complexes having strongly coordinating ligands show very low or negligible conversion of propargyl phenyldiazoacetates at room temperature, but they undergo slow reaction at higher temperatures to give mainly the product from reaction at the diazo functional group, which may have occurred after chloride dissociation,[19] sometimes in competition with products from reaction at the carbon-carbon triple bond.

IV. Experimental Section

4.1 General Information

Unless noted all reactions were carried out under inert atmosphere of dinitrogen in oven-dried glassware with magnetic stirring using freshly distilled solvents. All solvents were purified and dried using standard methods. Analytical thin layer chromatography (TLC) plates were purchased from EM Science (silica gel 60 F_{254} plates). High-resolution mass spectra (HRMS) were performed on a microTOF-ESI mass spectrometer using CsI as the standard. Accurate masses are reported for the molecular ion $[M+Cs]^+$, $[M+Na]^+$, or $[M+H]^+$. Melting points were

determined on an Electrothermo Mel-Temp DLX 104 device and were uncorrected. Column chromatography was performed on CombiFlash®️ Rf 200 purification system using normal phase disposable columns. IR spectra were recorded using Bruker Vector 22 spectrometer. All NMR spectra were recorded on a Bruker spectrometer at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR) or an Agilent spectrometer at 500 MHz (^{1}H NMR) and 125 MHz (^{13}C NMR). Chemical shifts are reported in ppm with the solvent signals as reference (in $CDCl_3$ as solvent), and coupling constants (J) are given in Hertz (Hz). The peak information is described as: br = broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = composite of magnetically non-equivalent protons.

4.2 Materials

AuCl(PPh$_3$), AuCl(PMe$_3$), AuCl[P(OMe)$_3$], Chloro[2-dicyclohexyl(2′,6′-dimethoxybiphenyl)phosphine] gold(I), and AuPicCl$_2$ were purchased from Sigma-Aldrich; AuCl(C$_4$H$_8$S), AuCl(Me$_2$S), AuCl(CO), (IPr)AuCl, and AuCl$_3$(Py) were purchased from Strem Chemicals. All other chemicals were obtained from commercial sources and used as received without further purification.

4.3 Experimental Procedures.
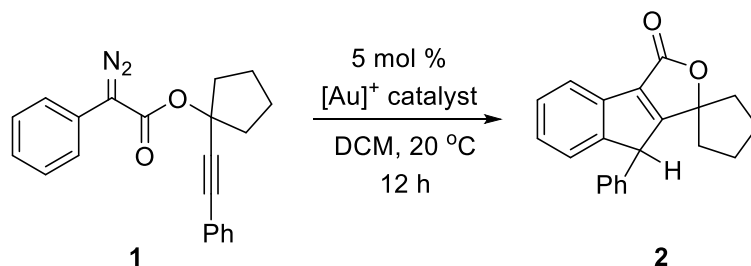
General Procedure for Gold(I)-Catalyzed Domino Cascade Transformation of Phenylpropargyl Phenyldiazoacetates 1: To a flame-dried 10 mL Schlenk flask charged with a magnetic stirring bar cationic gold(I) catalyst (0.010 mmol) and 2.0 mL DCM were added under nitrogen atmosphere. 1-(Phenylethynyl)cyclopentyl 2-diazo-2-phenylacetate **1** (0.20 mmol) dissolved in 2.0 mL of DCM was added in one portion into the solution under the flow of nitrogen. The resulting mixture was stirred for 12 h at room temperature (20 °C); the reaction mixture was purified by column chromatography (100:1 to 10:1 gradient of hexanes:ethyl acetate as eluents) to afford pure 8'-phenylspiro[cyclopentane-1,1'-indeno[1,2-*c*]furan]-3'[8'*H*]-one (**2**) as a white solid.
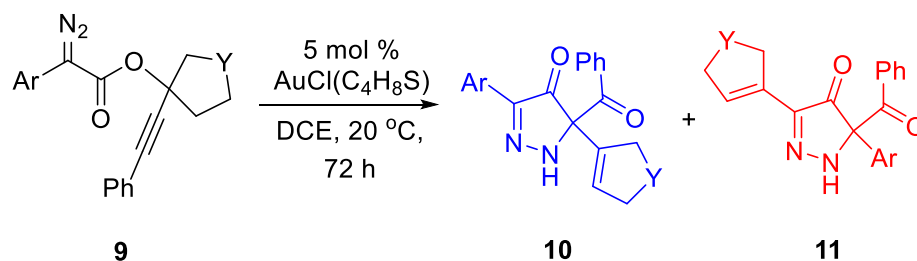
General Procedure for the Synthesis of 1,5-Dihydro-4*H*-pyrazol-4-ones 10 and 11: To a flame-dried 10 mL Schlenk flask charged with a magnetic stirring bar, AuCl(C$_4$H$_8$S) catalyst (0.010 mmol) and 2.0 mL DCE were added under nitrogen atmosphere. Propargyl aryldiazoacetate **1** or **9** (0.20 mmol) dissolved in 2.0 mL of DCE was added in one portion into the solution under the flow of nitrogen. The resulting mixture was stirred for 72 h at room temperature (20 °C). Solvent was evaporated, and products were purified by column chromatography (100:1 to 10:1 gradient of hexanes: ethyl acetate as eluents) to afford pure compounds **10** and **11**.
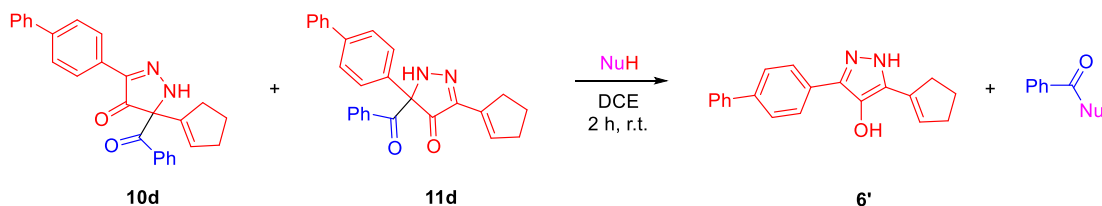
Procedure for the Synthesis of 6d from a Reaction Mixture Containing 10d and 11d: To the reaction mixture after the gold(I)-catalyzed reaction of **9d** that contained 1,5-dihydro-4*H*-pyrazol-4-ones **10d** and **11d** (156 mg, 0.384 mmol) of in DCE (8.0 mL) benzylamine (49.4 mg, 0.461 mmol) dissolved in DCE (0.5 mL) was added in one portion under a nitrogen atmosphere. The resulting mixture was stirred at 20 °C for 2 h, and the white precipitate of **6′** was formed. The precipitate

of **6′** was dissolved by adding methanol (5.0 mL); the solution was filtered through Celite to remove gold particles. Solvents were evaporated, and the obtained mixture of products **6′** and *N*-benzylbenzamide was separated by column chromatography using hexanes/ethyl acetate (v/v 2:1) as the eluent to afford 3-([1,1'-biphenyl]-4-yl)-5-(cyclopent-1-en-1-yl)-1*H*-pyrazol-4-ol **6′.**

Procedure for the Synthesis of 6′ from Pure 10d: To a solution of **10d** (81.0 mg, 0.200 mmol) in DCE (4.0 mL) benzylamine (25.7 mg, 0.240 mmol) dissolved in DCE (0.3 mL) was added in one portion under a nitrogen atmosphere. The resulting mixture was stirred at 20 °C for 2 h. Afterward, DCE was evaporated, and the obtained mixture of products **6′** and *N*-benzylbenzamide was separated by column chromatography using hexanes/ethyl acetate (v/v 2:1) as the eluent to afford compound **6′** (54.0 mg, 89% yield).

Table 2.5 Deacylation of **10d** and **11d** by Nucleophiles

Entry	Substrate	Nucleophile	Isolated yield (%) **6′**
1[a]	**10d**+**11d**	PhNHNH$_2$	80
2[a]	**10d**+**11d**	BnNH$_2$	87

3[a,b]	**10d**+**11d**	MeOH	63
4	**10d**	BnNH$_2$	89
5	**11d**	BnNH$_2$	88
6	**10d**	CyNH$_2$	90
7	**11d**	CyNH$_2$	86

[a]Isolated yields are given only for the deacylation reaction. [b]The reaction was carried out at 65 °C for 12h.

4.4 Kinetic Experiments

Rate constants for the conversion of **8** to **10q** were determined by ^{1}H NMR spectroscopy. The equilibrium mixture **7**+**8** was formed by treatment of **7** (0.1 mmol) with 5 mol % AuCl(Me$_2$S) in DCM. After 5 min the mixture **7**+**8** was separated from gold via silica gel column chromatography (with 19:1 to 9:1 gradient of hexanes:ethyl acetate as eluents). Solvents were evaporated under vacuum at room temperature to afford pure mixture **7**+**8** (See ^{1}H NMR and ^{13}C NMR spectra confirming the formation of allene **8** below; reactions and analyses performed by Kostiantyn Marichev.)
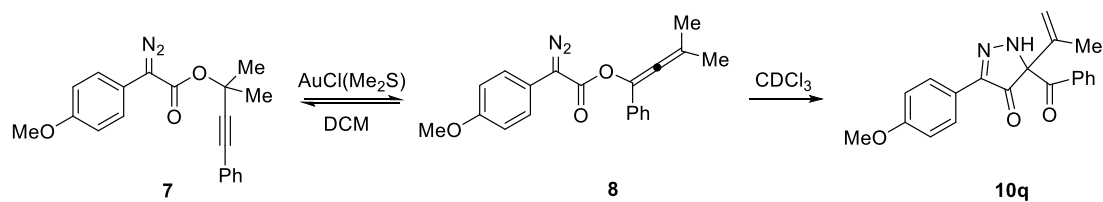
Data collection for the intramolecular conversion of **8** to **10p** was performed at at 20 °C: since **7** is stable in CDCl$_3$ in the absence of catalyst and not self-reactive, we decided to use the mixture **7**+**8** for data collection with **7** as the internal standard. The obtained mixture of **7**+**8** was dissolved in 0.35 mL CDCl$_3$ and placed in an NMR tube. The ratio of **7** [following peak at δ 1.86 (s, 6H, CH$_3$) ppm] to **8** [following peak at δ 1.98 (s, 6H, CH$_3$) ppm] and % conversion of **8** to **10p** (**Figure 2.3**) were determined by ^{1}H NMR analysis (Agilent spectrometer at 500 MHz, ^{1}H NMR).

The first-order rate constant $k = 1.05 \times 10^{-5}\ s^{-1}$ at 20 °C was calculated from the plot of ln[**8**]/[**8**$_{t=0}$] *vs.* time (**Figure 2.4**).

Other first-order rate constants at different temperatures [40 °C (**Figure 2.5**), 45 °C (**Figure 2.6**), 60 °C (**Figure 2.7**)] were determined in the same way: an NMR tube with CDCl$_3$ solution of **7**+**8** was placed into an oil bath with a temperature stability of ±1 °C. Temperature control at

60 ºC was provided by the Agilent 500 MHz spectrometer with a temperature stability of ±0.1 ºC.

An Arrhenius plot (**Table 2.6**, **Figure 2.8**) was obtained from the first-order rate constants determined at the corresponding temperatures. The activation energy E_{act} = 18.8 kcal/mol (R^2 = 0.999) was calculated from the slope of Arrhenius plot (E_{act} = −slope × R). $\Delta H^{\ddagger}$ = 18.2 kcal/mol and $\Delta S^{\ddagger}$ = −19.4 cal/deg-mol were determined from Eyring equation.[20]

Figure 2.3 Stacked ^{1}H NMR Spectra: Determination of Rate Constant for the Conversion of **8** to **10q** at 20 ^{0}C; Reaction and Analysis Performed by Kostiantyn Marichev.

Figure 2.4 First-order Rate Constant at 20 ºC. *(k = 1.05 × 10^{-5} s^{-1})*

Figure 2.5 First-order Rate Constant at 40 ºC. *(k = 7.67 × 10^{-5} s^{-1})*

Figure 2.6 First-order Rate Constant at 45 ^{0}C. *(k = 1.19 × 10^{-4} s^{-1})*

Figure 2.7 First-order Rate Constant at 60 ^{0}C. *(k = 5.17 × 10^{-4} s^{-1})*

Table 2.6 Data for Arrhenius Plot Measured within 20−60 ^{0}C

ln$k$	−11.46	−9.48	−9.04	−7.57
1/T, K^{-1}	0.003413	0.003195	0.003145	0.003003
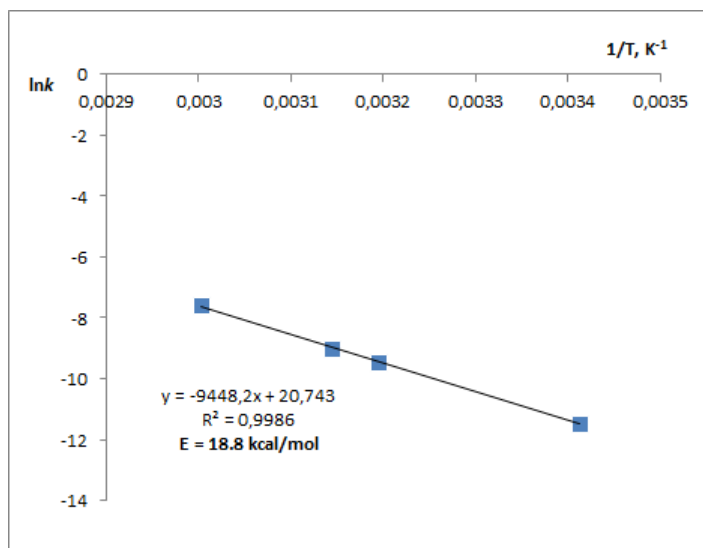
Figure 2.8 Arrhenius Plot: Compound **8** Activation Energy.

Table 2.7 Time Course for the Gold(I)-Catalyzed Reaction of **1**[a]
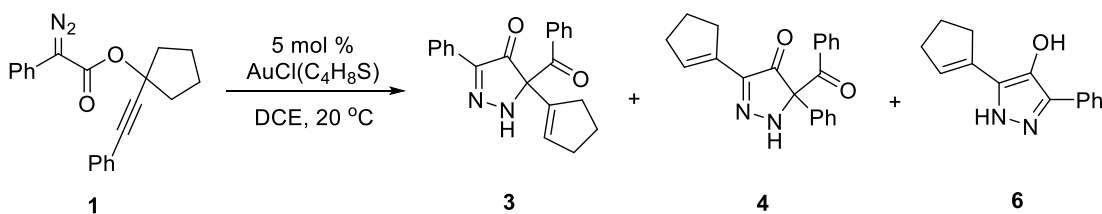
Time (h)	Yield (%) **3**	Yield (%) **4**	Yield (%) **6**	Total yield (%)[a] **3+4+6**
0	0	0	0	0
3	13	2	1	16
6	19	5	2.5	26.5

12	26.5	7	3	36.5
24	39.5	9.5	4	53
36	47	12.5	4	63.5
48	51	15.5	4	70.5
60	54	17.5	4	75.5
72	56	20	5	81
84	55	22.5	5	82.5
96	50.5	25.5	7	83
108	45	29.5	8	82.5
120	40.5	32	10	82.5
132	37	33	11	81
144	35	34	11	80
156	33	34	12	79
168	31.5	35.5	12	79
180	30	36.5	12.5	79

192	29	38	12.5	79.5
204	28	39	13	80
216	28	40	12.5	80.5
228	28	40	12.5	80.5
240	28	40	12.5	80.5

[a]Records the formation of **3**, **4**, and **6** in DCE at 20 ºC in reactions of **1** with 5 mol % AuCl(C$_4$H$_8$S). Yields were determined by ^{1}H NMR analyses of the reaction mixture at the recorded times in the presence of 1,3,5-trimethoxybenzene as the internal standard. Reported yields are the averages of two runs. [a]Yield of **5** was about 2−3% and remained constant within 10 days.

4.5 Characterization Data for New Compounds

9h
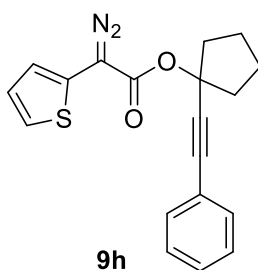
1-(Phenylethynyl)cyclopentyl   2-Diazo-2-(thiophen-2-yl)acetate

9h: 52% yield. Dark-red oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.46 (dd, J = 6.4, 2.9 Hz, 2H), 7.34 – 7.28 (m, 4H), 7.07 – 7.03 (m, 1H), 6.84 (d, J = 3.6 Hz, 1H), 2.49 – 2.41 (m, 2H), 2.31 (dt, J = 15.3, 7.7 Hz, 2H), 1.87 – 1.81 (m, 4H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 163.38, 131.85, 128.34, 128.12, 126.90, 125.92, 125.44, 122.61, 120.88, 89.03, 85.33, 82.90,

40.76, 23.43. IR (neat) 2928, 2076, 1701, 1443, 1285, 1231, 1127, 974, 691 cm^{-1}; HRMS (ESI) m/z calculated for $C_{19}H_{16}N_2O_2SNa$ [M+Na]$^+$ 359.0825, found: 359.0822.

9j
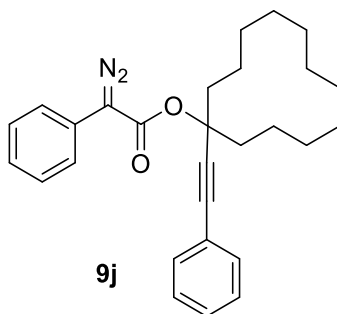
1-(Phenylethynyl)cyclododecyl 2-Diazo-2-phenylacetate 9j: 62% yield. Yellow solid, m.p. 92.5 – 93.5 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.53 (dd, J = 7.6, 0.9 Hz, 2H), 7.50 – 7.44 (comp, 2H), 7.42 – 7.35 (comp, 2H), 7.34 – 7.27 (comp, 3H), 7.19 (ddd, J = 8.6, 2.2, 1.1 Hz, 1H), 2.37 – 2.23 (comp, 2H), 2.12 – 1.98 (comp, 2H), 1.68 (d, J = 8.8 Hz, 2H), 1.43 (comp, 16H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 163.08, 131.87, 128.85, 128.31, 128.14, 125.79, 125.66, 124.01, 122.71, 89.38, 86.21, 79.61, 33.36, 26.08, 25.86, 22.29, 22.07, 19.44. IR (neat) 2928, 2079, 1705, 1470, 1241, 1146, 1006, 754 cm^{-1}; HRMS (ESI) m/z calculated for $C_{28}H_{32}N_2O_2Na$ [M+Na]$^+$ 451.2356, found: 451.2343.

9k
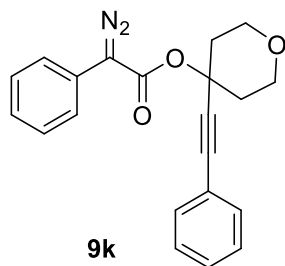
4-(Phenylethynyl)tetrahydro-2*H*-pyran-4-yl   2-Diazo-2-phenylacetate 9k: 65% yield. Yellow solid, m.p. 85 – 86 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.57 – 7.45 (comp, 4H), 7.44 – 7.36 (comp, 2H), 7.36 – 7.28 (comp, 3H), 7.23 – 7.17 (m, 1H), 3.93 (dt, *J* = 9.2, 4.4 Hz, 2H), 3.85 (ddd, *J* = 11.9, 9.0, 2.9 Hz, 2H), 2.45 – 2.38 (comp, 2H), 2.23 (ddd, *J* = 13.1, 9.0, 4.0 Hz, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 163.00, 131.92, 128.92, 128.70, 128.24, 125.89, 125.43, 124.07, 122.15, 87.48, 87.46, 74.12, 64.51, 37.96. IR (neat) 2960, 2086, 1707, 1498, 1241, 1140, 755 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{21}$H$_{18}$N$_2$O$_3$Na [M+Na]$^{+}$ 369.1214, found: 369.1210.

9n
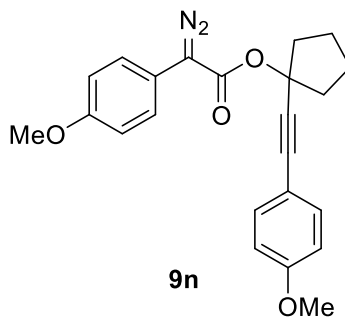
1-((4-Methoxyphenyl)ethynyl)cyclopentyl 2-Diazo-2-(4-methoxyphenyl)acetate 9n: 58% yield. Orange oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.41 (dd, J = 10.1, 9.0 Hz, 4H), 6.94 (d, J = 9.0 Hz, 2H), 6.82 (d, J = 8.9 Hz, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 2.46 – 2.37 (m, 2H), 2.34 – 2.24 (m, 2H), 1.87 – 1.78 (m, 4H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.08, 159.61, 157.94, 133.33, 125.86, 117.13, 114.84, 114.54, 113.75, 88.06, 84.91, 82.25, 55.34, 55.25, 40.83, 23.45. IR (neat) 2956, 2080, 1703, 1511, 1248, 1147, 830, 734 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{23}$H$_{22}$N$_2$O$_4$Na [M+Na]$^+$ 413.1472, found: 413.1483.

9o
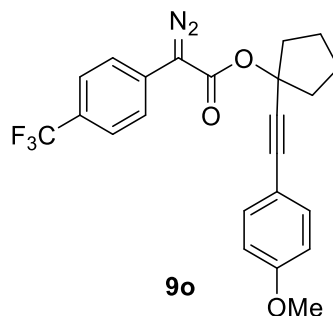
1-((4-Methoxyphenyl)ethynyl)cyclopentyl 2-Diazo-2-(4-(trifluoromethyl)phenyl)acetate 9o: 55% yield. Orange oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.72 – 7.52 (comp, 4H), 7.40 (d, J = 8.6 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 3.81 (s, 3H), 2.50 – 2.37 (comp, 2H), 2.37 – 2.22 (comp, 2H), 1.85 (comp, 4H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 162.76, 159.72, 133.34, 130.32, 127.47 (q, J = 32.5 Hz), 125.73 (q, J = 3.8 Hz),

123.45, 114.62, 113.79, 87.63, 85.31, 82.90, 77.26, 77.00, 76.75, 55.25, 40.82, 23.44. IR (neat) 2957, 2087, 1706, 1509, 1323, 1244, 1070, 832 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{23}H_{19}F_3N_2O_2Na$ [M+Na]$^+$ 451.1240, found: 451.1225.

9q
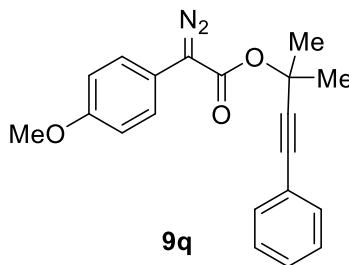
2-Methyl-4-phenylbut-3-yn-2-yl **2-Diazo-2-(4-methoxyphenyl)acetate 9q:** 68% yield. Orange oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.49 − 7.44 (comp, 2H), 7.42 (d, *J* = 9.0 Hz, 2H), 7.34 − 7.28 (comp, 3H), 6.95 (d, *J* = 9.0 Hz, 2H), 3.82 (s, 3H), 1.85 (s, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 163.90, 157.97, 131.85, 128.36, 128.14, 125.94, 122.56, 117.15, 114.55, 90.05, 84.39, 73.66, 55.35, 29.45. IR (neat) 2988, 2079, 1705, 1514, 1258, 1122, 998, 827 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{20}H_{18}N_2O_3Na$ [M+Na]$^+$ 357.1210, found: 357.1209.

3
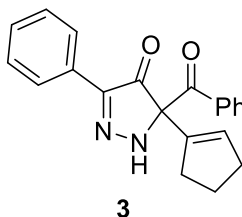
5-Benzoyl-5-(cyclopent-1-en-1-yl)-3-phenyl-1,5-dihydro-4*H*-pyrazol-4-one 3: 57% yield. Yellow solid, m.p. 115–116 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.18 (dd, *J* = 7.9, 1.2 Hz, 2H), 8.08 (dd, *J* = 7.9, 1.2 Hz, 2H), 7.90 (br, 1H), 7.62 – 7.57 (m, 1H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.42 – 7.36 (comp, 3H), 5.88 – 5.84 (m, 1H), 2.50 – 2.41 (comp, 3H), 2.35 – 2.29 (m, 1H), 1.98 – 1.89 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.05, 189.74, 143.83, 138.50, 133.97, 133.43, 131.63, 130.71, 129.19, 129.09, 128.49, 128.35, 125.98, 81.54, 32.43, 32.42, 22.96. IR (neat) 3358, 1721, 1674, 1246, 903 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{21}$H$_{18}$N$_2$O$_2$Na [M+Na]$^+$ 353.1260, found: 353.1247.
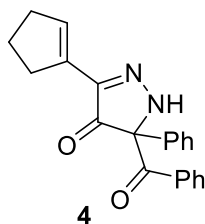
5-Benzoyl-3-(cyclopent-1-en-1-yl)-5-phenyl-1,5-dihydro-4*H*-pyrazol-4-one 4: 19% yield. Yellow solid, m.p. 130–131 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.84 (d, *J* = 7.5 Hz, 2H), 7.66 (br, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.42 – 7.33 (comp, 7H), 6.84 – 6.80 (m, 1H), 2.75 – 2.70 (comp, 2H), 2.56 – 2.49 (comp, 2H), 1.96 – 1.89 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.74, 189.45, 143.16, 135.74, 134.05, 133.70, 133.07, 131.98, 130.94, 129.49, 128.79, 128.46, 126.49, 81.80, 34.07,

32.68, 22.20. IR (neat) 3343, 1732, 1675, 1447, 1231, 738 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{21}$H$_{18}$N$_2$O$_2$Na [M+Na]$^+$ 353.1260, found: 353.1249.

10b
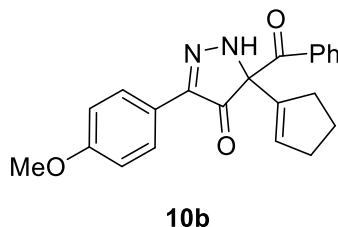
5-Benzoyl-5-(cyclopent-1-en-1-yl)-3-(4-methoxyphenyl)-1,5-dihydro-4*H*-pyrazol-4-one 10b: 54% yield. Yellow solid, m.p. 44–46 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.18 (d, *J* = 7.3 Hz, 2H), 8.03 (d, *J* = 9.0 Hz, 2H), 7.73 (s, 1H), 7.62 – 7.56 (m, 1H), 7.50 – 7.44 (comp, 2H), 6.92 (d, *J* = 9.0 Hz, 2H), 5.87 – 5.82 (m, 1H), 3.84 (s, 3H), 2.52 – 2.39 (comp, 3H), 2.31 (dddd, *J* = 17.5, 9.3, 5.8, 2.1 Hz, 1H), 2.02 – 1.84 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.53, 189.89, 160.49, 144.20, 138.71, 133.93, 133.48, 131.43, 130.72, 128.34, 127.58, 121.69, 113.96, 81.31, 55.30, 32.46, 32.43, 22.96. IR (neat) 3338, 2931, 1712, 1674, 1608, 1510, 1251, 1176, 835 cm^{-1}; HRMS (EI) *m/z* calculated for C$_{22}$H$_{19}$N$_2$O$_3$ [M−H]$^-$ 359.1401, found: 359.1396.

11b
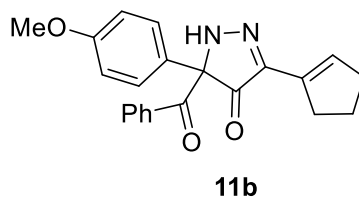
5-Benzoyl-3-(cyclopent-1-en-1-yl)-5-(4-methoxyphenyl)-1,5-dihydro-4*H*-pyrazol-4-one 11b: 21% yield. Yellow solid, m.p. 60.5–61.5 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.86 (d, *J* = 8.5 Hz, 2H), 7.73 (s, 1H), 7.53 – 7.47 (m, 1H), 7.36 (dd, *J* = 11.7, 4.0 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 2H), 6.92 (d, *J* = 7.8 Hz, 2H), 6.82-6.81 (m, 1H), 3.80 (s, 3H), 2.76 – 2.68 (m, 2H), 2.52 (d, *J* = 5.6 Hz, 2H), 1.96 – 1.88 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 193.12, 189.71, 159.84, 143.16, 133.85, 133.64, 133.12, 132.07, 131.02, 128.42, 127.87, 127.78, 114.89, 81.58, 55.31, 34.07, 32.69, 22.21. IR (neat) 3344, 2954, 1736, 1673, 1608, 1510, 1252, 692 cm^{-1}; HRMS (EI) *m/z* calculated for C$_{22}$H$_{19}$N$_2$O$_3$ [M−H]$^-$ 359.1401, found: 359.1406.

10c
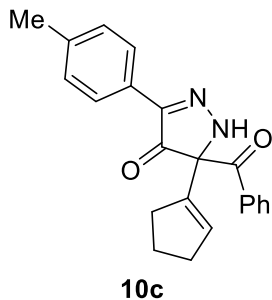
5-Benzoyl-5-(cyclopent-1-en-1-yl)-3-(*p*-tolyl)-1,5-dihydro-4*H*-

pyrazol-4-one 10c: 61% yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$)

δ 8.19 – 8.14 (comp, 2H), 7.97 – 7.92 (comp, 2H), 7.78 (s, 1H), 7.60 –

7.56 (m, 1H), 7.47 – 7.43 (comp, 2H), 7.21 – 7.18 (comp, 2H), 5.85 –

5.82 (m, 1H), 2.46 – 2.38 (comp, 3H), 2.36 (s, 3H), 2.31 – 2.26 (m, 1H),

1.96 – 1.88 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.31, 189.84,

144.23, 139.34, 138.63, 133.95, 133.46, 131.52, 130.73, 129.21, 128.42,

128.34, 125.96, 81.40, 32.45, 32.42, 22.96, 21.42. IR (neat) 3344, 1722,

1676, 1231, 951 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{22}$H$_{20}$N$_2$O$_2$Na

[M+Na]$^+$ 367.1417, found: 367.1404.

11c
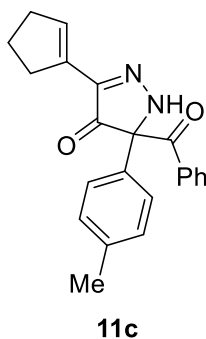
5-Benzoyl-3-(cyclopent-1-en-1-yl)-5-(*p*-tolyl)-1,5-dihydro-4*H*-

pyrazol-4-one 11c: 24% yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$)

δ 7.88 – 7.80 (comp, 2H), 7.67 (s, 1H), 7.51 – 7.47 (m, 1H), 7.37 – 7.32

(comp, 2H), 7.24 – 7.16 (comp, 4H), 6.83 – 6.78 (m, 1H), 2.74 – 2.68

(comp, 2H), 2.55 – 2.48 (comp, 2H), 2.34 (s, 3H), 1.96 – 1.88 (comp,

2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.94, 189.61, 143.22, 138.79, 133.91, 133.65, 133.11, 132.85, 132.04, 131.03, 130.19, 128.42, 126.40, 81.81, 34.07, 32.68, 22.21, 21.14. IR (neat) 3348, 1737, 1675, 1230, 809 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{22}$H$_{20}$N$_2$O$_2$Na [M+Na]$^+$ 367.1417, found: 367.1407.

10d
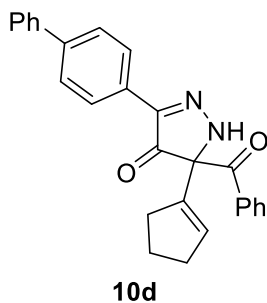
3-([1,1'-Biphenyl]-4-yl)-5-benzoyl-5-(cyclopent-1-en-1-yl)-1,5-dihydro-4*H***-pyrazol-4-one 10d:** 69% yield. Yellow solid, m.p. 49–51 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.23 – 8.15 (comp, 2H), 7.98 (s, 1H), 7.68 – 7.58 (comp, 6H), 7.47 (dt, *J* = 12.5, 7.9 Hz, 5H), 7.37 (t, *J* = 7.4 Hz, 1H), 5.89 (m, 1H), 2.59 – 2.40 (comp, 3H), 2.35 (ddd, *J* = 15.2, 11.0, 4.0 Hz, 1H), 2.04 – 1.86 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.14, 189.76, 143.50, 141.83, 140.49, 138.50, 134.02, 133.48, 131.68, 130.73, 128.82, 128.39, 128.08, 127.58, 127.18, 127.03, 126.38, 81.61, 32.46, 23.00. IR (neat) 3346, 2957, 1725, 1674, 1233, 907, 733 cm^{-1}; HRMS (EI) *m/z* calculated for C$_{27}$H$_{21}$N$_2$O$_2$ [M−H]$^−$ 405.1609, found: 405.1610.

11d
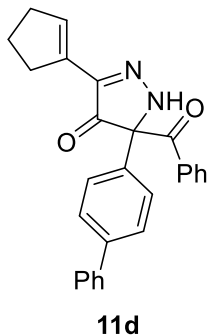
5-([1,1'-Biphenyl]-4-yl)-5-benzoyl-3-(cyclopent-1-en-1-yl)-1,5-dihydro-4*H*-pyrazol-4-one 11d: 9% yield. Yellow solid, m.p. 80–81 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.92 – 7.88 (comp, 2H), 7.78 (s, 1H), 7.67 – 7.61 (comp, 3H), 7.60 – 7.55 (comp, 2H), 7.52 (dd, *J* = 11.1, 3.7 Hz, 1H), 7.48 – 7.42 (comp, 3H), 7.38 (dd, *J* = 15.9, 7.7 Hz, 3H), 6.88 – 6.83 (m, 1H), 2.79 – 2.72 (comp, 2H), 2.58 – 2.51 (comp, 2H), 1.98 – 1.90 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.83, 189.49, 143.22, 141.67, 140.00, 134.63, 134.15, 133.79, 133.14, 132.02, 130.95, 128.86, 128.55, 128.15, 127.73, 127.08, 126.93, 81.60, 34.11, 32.72, 22.24. IR (neat) 3342, 2953, 1728, 1674, 1487, 1229, 1008, 735, 696 cm^{-1}; HRMS (EI) *m/z* calculated for C$_{27}$H$_{21}$N$_2$O$_2$ [M−H]$^{-}$ 405.1609, found: 405.1604.

10e
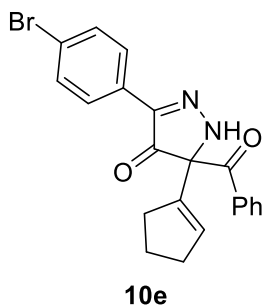
5-Benzoyl-3-(4-bromophenyl)-5-(cyclopent-1-en-1-yl)-1,5-dihydro-4*H*-pyrazol-4-one 10e: 74% yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.19 – 8.14 (comp, 2H), 7.97 – 7.92 (comp, 3H), 7.61 – 7.57 (m, 1H), 7.52 – 7.49 (comp, 2H), 7.47 – 7.43 (comp, 2H), 5.86 – 5.83 (m, 1H), 2.47 – 2.39 (comp, 3H), 2.32 – 2.26 (m, 1H), 1.96 – 1.89 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 191.68, 189.49, 142.70, 138.29, 134.09, 133.31, 131.82, 131.68, 130.75, 128.39, 128.07, 127.39, 123.36, 81.67, 32.45, 32.43, 22.94. IR (neat) 3336, 1724, 1673, 1231, 1009 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{21}$H$_{17}$N$_2$O$_2$NaBr [M+Na]$^+$ 431.0366, found: 431.0350.

11e
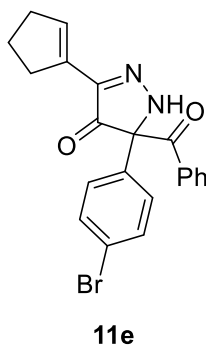
5-Benzoyl-5-(4-bromophenyl)-3-(cyclopent-1-en-1-yl)-1,5-dihydro-4*H*-pyrazol-4-one 11e: 13% yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.83 – 7.79 (comp, 2H), 7.62 (s, 1H), 7.54 – 7.50 (comp, 3H), 7.39 – 7.35 (comp, 2H), 7.26 – 7.23 (comp, 2H), 6.83 – 6.80 (m, 1H), 2.74 – 2.68 (comp, 2H), 2.54 – 2.50 (comp, 2H), 1.95 – 1.89 (comp,

2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.40, 189.05, 143.33, 134.67, 134.55, 133.94, 132.88, 132.62, 131.85, 130.77, 128.66, 128.17, 123.20, 80.98, 77.25, 77.00, 76.75, 34.10, 32.66, 22.19. IR (neat) 3338, 1719, 1674, 1230, 908 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{21}$H$_{17}$N$_2$O$_2$NaBr [M+Na]$^+$ 431.0366, found: 431.0345.
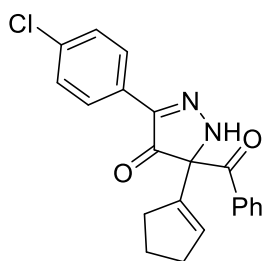
10f

5-Benzoyl-3-(4-chlorophenyl)-5-(cyclopent-1-en-1-yl)-1,5-dihydro-4*H*-pyrazol-4-one 10f: 69% yield. Yellow solid, m.p. 77.5–78.5 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.17 (d, *J* = 8.5 Hz, 2H), 8.02 (d, *J* = 8.5 Hz, 2H), 7.91 (s, 1H), 7.62 – 7.57 (m, 1H), 7.49 – 7.45 (comp, 2H), 7.38 – 7.34 (comp, 2H), 5.87 – 5.83 (m, 1H), 2.49 – 2.39 (comp, 3H), 2.33 – 2.26 (m, 1H), 1.97 – 1.88 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 191.75, 189.51, 142.73, 138.33, 135.04, 134.09, 133.32, 131.79, 130.73, 128.73, 128.39, 127.62, 127.17, 81.66, 32.45, 32.43, 22.94. IR (neat) 3345, 1716, 1673, 1231, 1116 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{21}$H$_{17}$N$_2$O$_2$NaCl [M+Na]$^+$ 387.0871, found: 387.0857.
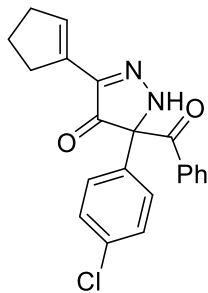
11f

5-Benzoyl-5-(4-chlorophenyl)-3-(cyclopent-1-en-1-yl)-1,5-dihydro-4*H*-pyrazol-4-one 11f: 14% yield. Yellow solid, m.p. 94–95 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.84 – 7.80 (comp, 2H), 7.67 (s, 1H), 7.55 – 7.51 (m, 1H), 7.40 – 7.36 (comp, 4H), 7.34 – 7.30 (comp, 2H), 6.85 – 6.81 (m, 1H), 2.75 – 2.69 (comp, 2H), 2.56 – 2.51 (copm, 2H), 1.96 – 1.90 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.48, 189.12, 143.30, 134.99, 134.50, 134.13, 133.92, 132.89, 131.86, 130.77, 129.67, 128.63, 127.89, 80.94, 34.09, 32.66, 22.19. IR (neat) 3344, 1717, 1671, 1228, 933 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{21}$H$_{17}$N$_2$O$_2$NaCl [M+Na]$^+$ 387.0871, found: 387.0858.
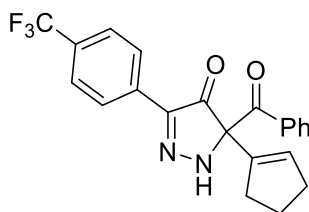
10g

5-Benzoyl-5-(cyclopent-1-en-1-yl)-3-[4-

(trifluoromethyl)phenyl]-1,5-dihydro-4*H*-pyrazol-4-one   10g: 51%

yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.22 – 8.16 (comp, 4H),

8.07 (br, 1H), 7.63 (d, *J* = 8.5 Hz, 2H), 7.60 – 7.56 (m, 1H), 7.50 – 7.47

(comp, 2H), 5.88 – 5.86 (m, 1H), 2.47 – 2.40 (comp, 3H), 2.33 – 2.27 (m,

1H), 1.98 – 1.89 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 191.37,

189.33, 141.91, 138.11, 134.17, 133.55, 133.27, 132.76, 132.61, 131.92

(q, *J* = 30.0 Hz), 129.30, 128.42, 127.85, 125.40 (q, *J* = 3.8 Hz) 124.51 (q,

J = 278.8 Hz), 81.91, 32.44, 32.39, 22.95. IR (neat) 3334, 1709, 1673,

1321, 1120 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{22}$H$_{17}$N$_2$O$_2$F$_3$Na

[M+Na]$^+$ 421.1134, found: 421.1116.

11g
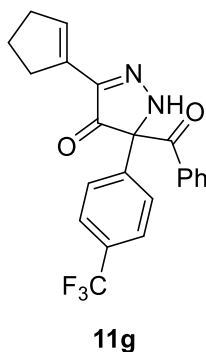
5-Benzoyl-3-(cyclopent-1-en-1-yl)-5-[4-

(trifluoromethyl)phenyl]-1,5-dihydro-4*H*-pyrazol-4-one   11g: 22%

yield. Yellow solid, m.p. 45.5–46.5 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ

7.82 – 7.76 (comp, 2H), 7.68 – 7.63 (comp, 3H), 7.55 – 7.50 (comp, 3H),

7.38 (t, J = 7.8 Hz, 2H), 6.85 – 6.83 (m, 1H), 2.75 – 2.69 (comp, 2H), 2.56 – 2.51 (comp, 2H), 1.97 – 1.89 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.14, 188.85, 143.30, 139.33, 134.84, 134.07, 132.86, 131.76, 130.99 (q, J = 32.5 Hz) 130.59, 128.78, 126.90, 126.37 (q, J = 3.8 Hz), 121.54 (q, J = 270 Hz) 80.84, 34.11, 32.67, 22.18. IR (neat) 3335, 1729, 1675, 1119, 907 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{22}$H$_{17}$N$_2$O$_2$F$_3$Na [M+Na]$^+$ 421.1134, found: 421.1119.

10h
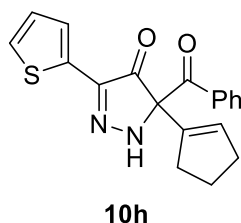
5-Benzoyl-5-(cyclopent-1-en-1-yl)-3-(thiophen-2-yl)-1,5-dihydro-4*H*-pyrazol-4-one 10h: 59% yield.[6] Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.18 (d, J = 7.3 Hz, 2H), 7.82 (s, 1H), 7.80 (dd, J = 3.7, 0.8 Hz, 1H), 7.60 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.8 Hz, 2H), 7.35 (d, J = 5.1 Hz, 1H), 7.08 (dd, J = 4.9, 3.8 Hz, 1H), 5.88 – 5.84 (m, 1H), 2.48 – 2.37 (comp, 3H), 2.37 – 2.26 (m, 1H), 1.91 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 190.69, 189.48, 141.61, 138.34, 134.05, 130.72, 128.39, 127.65, 126.69, 81.21, 32.44, 22.96. IR (neat) 3337, 2926, 1722, 1674,

1228, 731, 692 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{19}$H$_{16}$N$_2$O$_2$SNa [M+Na]$^+$ 359.0825, found: 359.0823.
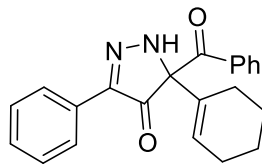
10i

5-Benzoyl-5-(cyclohex-1-en-1-yl)-3-phenyl-1,5-dihydro-4*H*-pyrazol-4-one 10i: 57% yield. Yellow oil. ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.18 (dd, *J* = 5.3, 3.3 Hz, 2H), 8.13 − 7.95 (m, 2H), 7.84 (s, 1H), 7.59 (ddd, *J* = 6.7, 4.0, 1.3 Hz, 1H), 7.52 − 7.43 (comp, 2H), 7.42 − 7.32 (comp, 3H), 5.84 (t, *J* = 2.7 Hz, 1H), 2.11 (comp, 2H), 1.63 (comp, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.26, 190.41, 143.73, 134.13, 133.91, 133.45, 130.83, 129.18, 129.10, 128.54, 128.46, 128.33, 128.24, 127.72, 125.95, 84.94, 25.90, 25.48, 22.57, 21.58. IR (neat) 3343, 2927, 1729, 1674, 1447, 1231, 695 cm^{-1}; HRMS (EI) *m/z* calculated for C$_{22}$H$_{19}$N$_2$O$_2$ [M−H]$^−$ 343.1452, found: 343.1449.
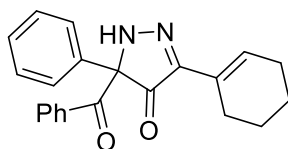

11i

5-Benzoyl-3-(cyclohex-1-en-1-yl)-5-phenyl-1,5-dihydro-4*H*-

pyrazol-4-one 11i: 16% yield. Yellow solid, m.p. 63–64 °C. ^{1}H NMR

(300 MHz, CDCl$_3$) δ 7.83 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.56 (br, 1H), 7.49

(dd, *J* = 10.5, 4.4 Hz, 1H), 7.41 – 7.31 (comp, 7H), 7.02 (m, 1H), 2.40

(comp, 2H), 2.18 (comp, 2H), 1.76 – 1.55 (comp, 4H). ^{13}C NMR (126

MHz, CDCl$_3$) δ 193.10, 189.61, 145.03, 135.93, 133.67, 133.12, 131.49,

130.95, 129.45, 128.74, 128.46, 127.74, 126.52, 82.13, 25.72, 25.17,

22.25, 21.92. IR (neat) 3339, 2927, 1732, 1675, 1447, 1231, 698 cm^{-1};

HRMS (EI) *m/z* calculated for C$_{22}$H$_{19}$N$_2$O$_2$ [M−H]$^-$ 343.1452, found:

343.1448.
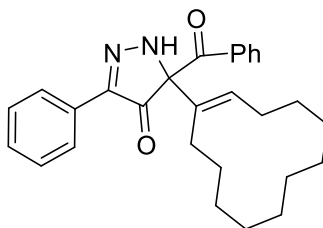
10j

5-Benzoyl-5-(cyclododec-1-en-1-yl)-3-phenyl-1,5-dihydro-4*H*-

pyrazol-4-one 10j: 51% yield. Yellow solid, m.p. 69–70 °C. ^{1}H NMR

(500 MHz, CDCl$_3$) δ 8.15 – 8.05 (comp, 2H), 7.89 (s, 1H), 7.64 – 7.31

(comp, 8H), 5.48 – 5.42 (m, 1H), 2.69 – 2.44 (comp, 2H), 2.32 – 2.18 (m,

1H), 2.09 – 1.96 (m, 1H), 1.55 – 1.19 (comp, 16H). ^{13}C NMR (126 MHz,

CDCl$_3$) δ 192.16, 190.33, 143.53, 143.47, 135.73, 135.03, 133.72, 131.61,

131.36, 129.03, 128.45, 128.23, 127.84, 127.05, 125.94, 85.65, 26.43, 25.53, 25.48, 25.09, 25.05, 24.74, 24.72, 24.10, 22.64, 22.37. IR (neat) 3351, 2928, 1699, 1677, 1448, 1344, 693 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{28}H_{32}N_2O_2Na$ [M+Na]$^+$ 451.2356, found: 451.2347.

11j
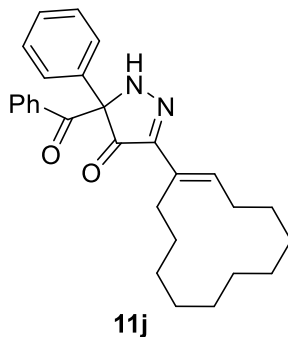
5-Benzoyl-3-(cyclododec-1-en-1-yl)-5-phenyl-1,5-dihydro-4*H*-pyrazol-4-one 11j: 35% yield. Yellow solid, m.p. 71–72 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.85 (dt, *J* = 8.5, 1.5 Hz, 2H), 7.66 (s, 1H), 7.52 – 7.47 (m, 1H), 7.44 – 7.31 (comp, 7H), 6.79 (t, *J* = 8.1 Hz, 1H), 2.57 (t, *J* = 6.8 Hz, 2H), 2.30 – 2.17 (comp, 2H), 1.67 – 1.59 (comp, 2H), 1.54 (dt, *J* = 9.6, 7.2 Hz, 2H), 1.49 – 1.41 (comp, 4H), 1.40 – 1.31 (comp, 6H), 1.30 – 1.23 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 193.42, 189.63, 144.99, 135.98, 135.37, 133.64, 133.23, 130.88, 129.94, 129.45, 128.72, 128.48, 126.47, 81.94, 26.57, 26.11, 25.60, 25.19, 25.14, 24.89, 24.62, 23.69, 22.93, 22.24. IR (neat) 3347, 2924, 2850, 1729, 1672, 1447, 1229,

737, 696 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{28}$H$_{32}$N$_2$O$_2$Na [M+Na]$^+$ 451.2356, found: 451.2349.
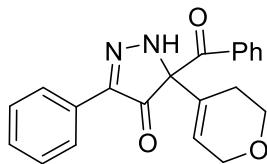
10k

5-Benzoyl-5-(3,6-dihydro-2*H*-pyran-4-yl)-3-phenyl-1,5-dihydro-4*H*-pyrazol-4-one 10k: 36% yield. Yellow solid, m.p. 67–68 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.23 – 8.12 (comp, 2H), 8.10 – 8.03 (m, 1H), 7.84 (dd, *J* = 6.3, 3.1 Hz, 1H), 7.56 – 7.30 (comp, 5H), 7.27 (comp, 2H), 5.91 – 5.88 (m, 1H), 4.22 (dd, *J* = 5.3, 2.6 Hz, 2H), 3.89 (ddt, *J* = 16.8, 11.9, 6.2 Hz, 1H), 3.78 – 3.64 (m, 1H), 2.70 – 2.41 (m, 1H), 2.37 – 2.05 (m, 1H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 191.76, 189.62, 144.05, 134.20, 131.68, 131.58, 130.95, 130.67, 129.36, 128.57, 128.53, 126.70, 126.03, 83.53, 65.33, 64.00, 25.78. IR (neat) 3332, 2925, 2085, 1710, 1677, 1447, 1232, 700 cm^{-1}; HRMS (EI) *m/z* calculated for C$_{21}$H$_{17}$N$_2$O$_3$ [M−H]$^−$ 345.1245, found: 345.1243.
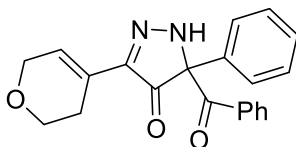
11k

5-Benzoyl-3-(3,6-dihydro-2*H*-pyran-4-yl)-5-phenyl-1,5-dihydro-4*H*-pyrazol-4-one 11k: 10% yield. Yellow solid, m.p. 70–71 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.84 (d, *J* = 8.3 Hz, 2H), 7.73 (s, 1H), 7.52 (td, *J* = 7.6, 1.0 Hz, 1H), 7.44 – 7.33 (comp, 7H), 6.99 (m, 1H), 4.29 (comp, 2H), 3.89 (dd, *J* = 10.5, 5.2 Hz, 2H), 2.54 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.57, 189.28, 143.24, 135.56, 133.80, 133.03, 130.94, 129.56, 128.91, 128.52, 128.51, 126.43, 125.14, 82.38, 65.39, 64.08, 25.06. IR (neat) 3322, 2923, 2085, 1708, 1675, 1447, 1232, 1131, 694 cm^{-1}; HRMS (EI) *m/z* calculated for C$_{21}$H$_{17}$N$_2$O$_3$ [M−H]$^-$ 345.1245, found: 345.1239.

10l
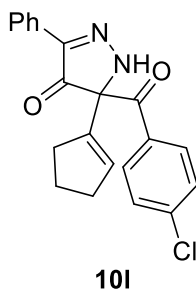
5-(4-Chlorobenzoyl)-5-(cyclopent-1-en-1-yl)-3-phenyl-1,5-dihydro-4*H*-pyrazol-4-one 10l: 62% yield. Yellow solid, m.p. 85–86 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.21 – 8.15 (comp, 2H), 8.08 – 8.03 (comp, 2H), 7.92 (s, 1H), 7.46 – 7.43 (comp, 2H), 7.41 – 7.37 (comp, 3H), 5.85 – 5.82 (m, 1H), 2.47 – 2.40 (comp, 3H), 2.29 – 2.24 (m, 1H), 1.97 – 1.88 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.00, 188.67,

143.90, 140.74, 138.43, 132.36, 132.06, 131.50, 129.28, 128.97, 128.70, 128.53, 125.98, 81.58, 77.26, 77.01, 76.75, 32.50, 32.44, 22.92. IR (neat) 3347, 1724, 1674, 1114, 1010 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{21}$H$_{17}$N$_2$O$_2$NaCl [M+Na]$^+$ 387.0871, found: 387.0855.

11l
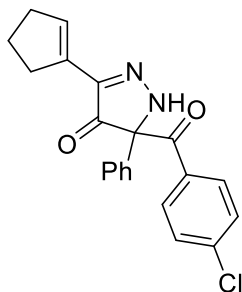
5-(4-Chlorobenzoyl)-3-(cyclopent-1-en-1-yl)-5-phenyl-1,5-dihydro-4*H*-pyrazol-4-one 11l: 18% yield. Yellow solid, m.p. 92–93 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.84 – 7.80 (comp, 2H), 7.77 (s, 1H), 7.40 – 7.36 (comp, 3H), 7.33 – 7.30 (comp, 2H), 7.28 – 7.26 (comp, 2H), 6.82 – 6.79 (m, 1H), 2.75 – 2.71 (comp, 2H), 2.55 – 2.51 (comp, 2H), 1.95 – 1.89 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.74, 188.42, 143.28, 140.46, 135.69, 134.13, 132.65, 131.96, 131.03, 129.62, 128.97, 128.75, 126.69, 82.19, 77.25, 77.00, 76.75, 34.09, 32.69, 22.20. IR (neat) 3342, 1741, 1676, 1091, 907 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{21}$H$_{17}$N$_2$O$_2$NaCl [M+Na]$^+$ 387.0871, found: 387.0856.

10m
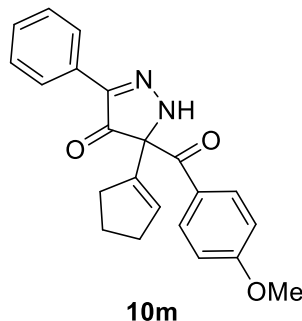
5-(Cyclopent-1-en-1-yl)-5-(4-methoxybenzoyl)-3-phenyl-1,5-dihydro-4_H_-pyrazol-4-one 10m: 48% yield. Yellow solid, m.p. 53–54 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.29 – 8.18 (comp, 2H), 8.11 – 8.02 (comp, 2H), 7.98 (s, 1H), 7.43 – 7.33 (comp, 3H), 6.98 – 6.90 (comp, 2H), 5.88 – 5.79 (m, 1H), 3.89 (s, 3H), 2.52 – 2.37 (comp, 3H), 2.32 – 2.24 (m, 1H), 2.00 – 1.84 (comp, 2H). ^{13}C NMR (126 MHz, cdcl$_3$) δ 192.59, 187.77, 164.22, 144.01, 138.98, 133.58, 131.38, 129.19, 129.12, 128.47, 126.06, 125.99, 113.58, 81.57, 55.53, 32.55, 32.44, 22.96. IR (neat) 3336, 2932, 2842, 1714, 1663, 1596, 1244, 1171, 1028, 842, 732 cm^{-1}; HRMS (EI) *m/z* calculated for C$_{22}$H$_{19}$N$_2$O$_3$ [M−H]$^-$ 359.1401, found: 359.1397.

11m
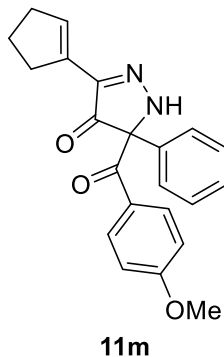
3-(Cyclopent-1-en-1-yl)-5-(4-methoxybenzoyl)-5-phenyl-1,5-dihydro-4_H_-pyrazol-4-one 11m: 29% yield. Yellow solid, m.p. 72–73 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.94 – 7.84 (comp, 2H), 7.78 (s, 1H), 7.50 – 7.42 (m, 1H), 7.41 – 7.34 (comp, 2H), 7.33 – 7.29 (comp, 2H), 6.86 – 6.77 (comp, 3H), 3.81 (s, 3H), 2.77 – 2.69 (comp, 2H), 2.53 (ddd, _J_ = 9.6, 4.8, 2.2 Hz, 2H), 1.93 (dt, _J_ = 15.0, 7.4 Hz, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 193.38, 187.75, 163.91, 143.41, 136.43, 133.87, 133.84, 132.10, 129.43, 128.87, 128.66, 126.73, 125.50, 113.68, 82.22, 55.47, 34.07, 32.70, 22.22. IR (neat) 3310, 2933, 2841, 1736, 1667, 1599, 1510, 1247, 1172, 733 cm^{-1}; HRMS (EI) _m/z_ calculated for C$_{22}$H$_{19}$N$_2$O$_3$ [M−H]$^-$ 359.1401, found: 359.1394.

10n
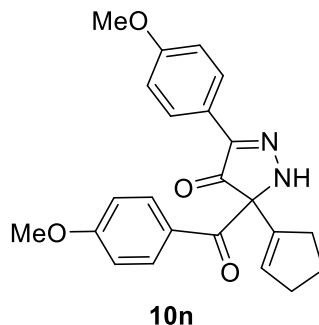
5-(Cyclopent-1-en-1-yl)-5-(4-methoxybenzoyl)-3-(4-methoxyphenyl)-1,5-dihydro-4*H*-pyrazol-4-one 10n: 55% yield. Yellow solid, m.p. 52–53 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.29 – 8.17 (comp, 2H), 8.07 – 7.98 (comp, 2H), 7.90 (s, 1H), 6.97 – 6.87 (comp, 4H), 5.86 – 5.78 (m, 1H), 3.87 (s, 3H), 3.82 (s, 3H), 2.51 – 2.36 (comp, 3H), 2.28 (dddd, *J* = 15.3, 9.3, 5.8, 2.1 Hz, 1H), 1.99 – 1.84 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 193.04, 187.90, 164.17, 160.41, 144.19, 139.17, 133.52, 131.11, 127.55, 126.15, 121.83, 113.93, 113.56, 81.34, 55.51, 55.28, 32.54, 32.43, 22.97. IR (neat) 3340, 2956, 2840, 1717, 1665, 1598, 1508, 1248, 1172, 1029, 837 cm^{-1}; HRMS (EI) *m/z* calculated for C$_{23}$H$_{21}$N$_2$O$_4$ [M−H]$^-$ 389.1507, found: 389.1501.

11n
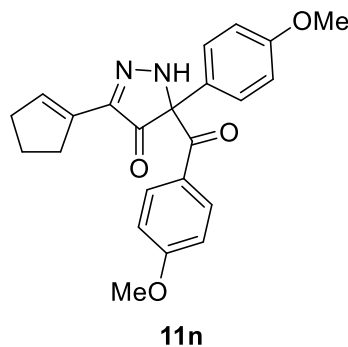
3-(Cyclopent-1-en-1-yl)-5-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-1,5-dihydro-4*H*-pyrazol-4-one **11n:** 24% yield. Yellow solid, m.p. 67–68 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.94 – 7.86 (comp, 2H), 7.83 (s, 1H), 7.24 – 7.17 (comp, 2H), 6.92 – 6.85 (comp, 2H), 6.86 – 6.77 (comp, 3H), 3.81 (s, 3H), 3.80 – 3.77 (s, 3H), 2.77 – 2.67 (comp, 2H), 2.56 – 2.46 (comp, 2H), 1.96 – 1.87 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 193.71, 187.98, 163.84, 159.70, 143.27, 133.91, 133.57, 132.17, 128.46, 128.06, 125.55, 114.81, 113.62, 81.97, 55.46, 55.29, 34.05, 32.70, 22.22. IR (neat) 3337, 2933, 2839, 1721, 1663, 1596, 1508, 1241, 1169, 1027, 839, 734 cm^{-1}; HRMS (EI) *m/z* calculated for C$_{23}$H$_{21}$N$_2$O$_4$ [M−H]$^-$ 389.1507, found: 389.1497.

10o
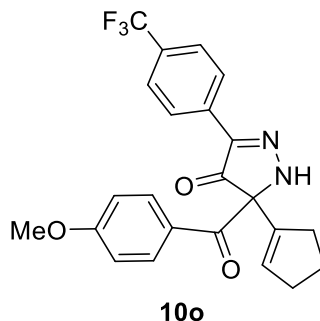
5-(Cyclopent-1-en-1-yl)-5-(4-methoxybenzoyl)-3-[4-(trifluoromethyl)phenyl]-1,5-dihydro-4*H*-pyrazol-4-one 10o: 42% yield. Yellow solid, m.p. 35–36 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.23 (comp, 5H), 7.63 (d, *J* = 8.3 Hz, 2H), 6.99 – 6.91 (comp, 2H), 5.89 – 5.83 (m, 1H), 3.89 (s, 3H), 2.51 – 2.39 (comp, 3H), 2.33 – 2.24 (m, 1H), 2.00 – 1.87 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 191.90, 187.39, 164.36, 141.88, 138.55, 133.60, 131.74, 130.47 (q, *J* = 32.8 Hz), 125.91, 125.36 (q, *J* = 3.8 Hz), 113.64, 81.95, 55.54, 32.52, 32.43, 22.95. IR (neat) 3326, 2930, 2845, 1663, 1596, 1321, 1243, 1164, 1065, 842 cm^{-1}; HRMS (EI) *m/z* calculated for C$_{23}$H$_{18}$F$_3$N$_2$O$_3$ [M−H]$^-$ 427.1275, found: 427.1274.

11o
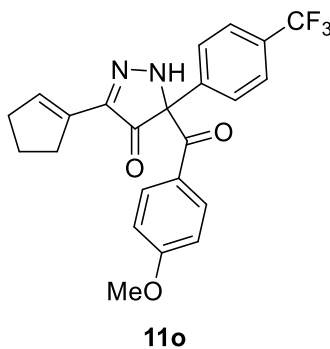
3-(Cyclopent-1-en-1-yl)-5-(4-methoxybenzoyl)-5-[4-(trifluoromethyl)phenyl]-1,5-dihydro-4*H*-pyrazol-4-one 11o: 5% yield. Yellow solid, m.p. 67 – 68 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.85 (dd, *J* = 9.3, 2.6 Hz, 2H), 7.71 (s, 1H), 7.66 (dd, *J* = 8.5, 2.5 Hz, 2H), 7.48 (dd, *J* = 8.5, 2.5 Hz, 2H), 6.92 – 6.76 (comp, 3H), 3.84 (s, 3H), 2.82 – 2.67 (comp, 2H), 2.61 – 2.42 (comp, 2H), 2.00 – 1.84 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.82, 187.09, 164.19, 143.61, 140.05, 134.63, 133.59, 131.88, 130.83 (q, *J* = 34.0 Hz), 127.65, 127.13, 126.34 (q, *J* = 3.8 Hz), 125.21, 125.13, 113.99, 81.24, 55.55, 34.11, 32.68, 22.20. IR (neat) 3337, 2930, 1725, 1667, 1598, 1323, 1243, 1170, 1120, 1070, 841 cm^{-1}; HRMS (EI) *m/z* calculated for C$_{23}$H$_{18}$F$_3$N$_2$O$_3$ [M−H]$^-$ 427.1275, found: 427.1277.
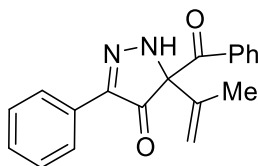
10p

5-Benzoyl-3-phenyl-5-(prop-1-en-2-yl)-1,5-dihydro-4*H*-pyrazol-4-one 10p: 60% yield.[6] Yellow solid, m.p. 39 – 40 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.19 (d, *J* = 7.4 Hz, 2H), 8.08 (d, *J* = 6.7 Hz, 2H), 7.93 (s, 1H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.43 – 7.35 (comp, 3H), 5.27 (s, 1H), 5.20 (s, 1H), 1.91 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 191.96, 189.85, 143.73, 140.34, 134.10, 133.37, 130.72, 129.26, 129.01, 128.51, 128.45, 126.03, 116.67, 84.14, 20.00. IR (neat) 3339, 1727, 1671, 1447, 1229, 692 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{19}$H$_{16}$N$_2$O$_2$Na [M+Na]$^+$ 327.1104, found: 327.1098.
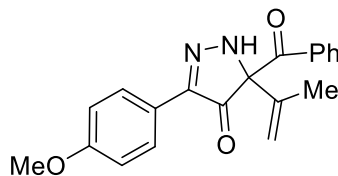
10q

5-Benzoyl-3-(4-methoxyphenyl)-5-(prop-1-en-2-yl)-1,5-dihydro-4*H*-pyrazol-4-one 10q: 72% yield.[6] Yellow solid, m.p. 44–45 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.18 (d, *J* = 7.4 Hz, 2H), 8.03 (d, *J* = 9.0 Hz, 2H), 7.74 (s, 1H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 6.92 (d, *J* = 9.0 Hz, 2H), 5.25 (s, 1H), 5.18 (s, 1H), 3.83 (s, 3H), 1.90 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 192.41, 189.98, 160.52, 144.08, 140.53, 134.05, 133.39, 130.72, 128.43, 127.61, 121.59, 116.51,

113.97, 83.89, 55.30, 20.02. IR (neat) 3342, 2934, 1730, 1674, 1251, 1231, 1173, 835, 690 cm^{-1}; HRMS (EI) *m/z* calculated for $C_{20}H_{17}N_2O_3$ [M−H]$^-$ 333.1245, found: 333.1251.

6
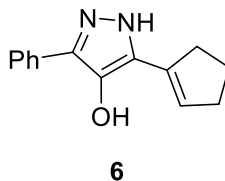
5-(Cyclopent-1-en-1-yl)-3-phenyl-1*H*-pyrazol-4-ol 6: 90% yield. White solid, m. p. 198 – 200 °C (decomp.). ^{1}H NMR (500 MHz, CD$_3$OD) δ 7.85 (dd, *J* = 8.1, 0.9 Hz, 2H), 7.43 (dd, *J* = 10.6, 4.8 Hz, 2H), 7.34 (ddd, *J* = 6.8, 2.4, 1.2 Hz, 1H), 6.48 (dt, *J* = 4.2, 2.1 Hz, 1H), 2.78 (ddd, *J* = 9.8, 4.4, 2.1 Hz, 2H), 2.57 (tdd, *J* = 7.5, 4.8, 2.4 Hz, 2H), 2.07 – 1.93 (comp, 2H). ^{13}C NMR (126 MHz, CD$_3$OD) δ 136.70, 135.08, 134.32, 131.59, 130.43, 128.71, 128.19, 127.49, 126.13, 32.87, 32.62, 22.39. IR (neat) 3249 (br), 1635, 1482, 1274, 1026, 845 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{14}H_{15}N_2O$ [M+H]$^+$ 227.1179, found: 227.1181.

6'
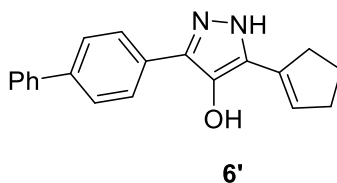
3-([1,1'-biphenyl]-4-yl)-5-(cyclopent-1-en-1-yl)-1H-pyrazol-4-ol

6': 87% yield. White solid, m. p. > 300 °C (decomp.). ^{1}H NMR (300 MHz, DMSO-d6) δ 12.54 (br, 1H), 8.04 – 8.01 (comp, 3H), 7.69 (d, J = 7.3 Hz, 4H), 7.45 (t, J = 7.5 Hz, 2H), 7.34 (t, J = 7.2 Hz, 1H), 6.29 (s, 1H), 2.70 – 2.68 (comp, 2H), 2.49 – 2.47 (comp, 2H), 1.99 – 1.78 (comp, 2H). ^{13}C NMR (126 MHz, DMSO-d6) δ 140.27, 138.71, 135.96, 129.39, 127.79, 127.05, 126.88, 126.30, 126.00, 33.41, 33.31, 22.76. IR (neat) 3246 (br), 1634, 1487, 1269, 1016, 844, 767 cm^{-1}; HRMS (ESI) m/z calculated for $C_{20}H_{19}N_2O$ [M+H]$^+$ 303.1492, found: 303.1496.

NMR graphs will be obtained from the supporting information of the upcoming published paper.

4.6 X-ray Crystal Structure Information for 4 and 6'

```
Bond precision:    C-C = 0.0053 A          Wavelength=0.71073

Cell:              a=17.920(7)      b=6.022(2)           c=15.745(6)
                   alpha=90         beta=99.297(6)       gamma=90
Temperature:       98 K

                   Calculated                 Reported
Volume             1676.8(11)                 1676.8(11)
Space group        P 21/c                     P 1 21/c 1
Hall group         -P 2ybc                    -P 2ybc
Moiety formula     C21 H18 N2 O2              C21 H18 N2 O2
Sum formula        C21 H18 N2 O2              C21 H18 N2 O2
Mr                 330.37                     330.37
Dx,g cm-3          1.309                      1.309
Z                  4                          4
Mu (mm-1)          0.085                      0.085
F000               696.0                      696.0
F000'              696.29
h,k,lmax           21,7,18                    21,7,18
Nref               2970                       2953
Tmin,Tmax          0.994,0.999                0.407,1.000
Tmin'              0.965

Correction method= # Reported T Limits: Tmin=0.407 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.994          Theta(max)= 25.047

R(reflections)= 0.0785( 1994)     wR2(reflections)= 0.1761( 2953)

S = 1.015                    Npar= 226
```

```
Bond precision:    C-C = 0.0131 A           Wavelength=0.71075

Cell:               a=6.727(9)       b=23.55(3)       c=9.860(13)
                    alpha=90         beta=90          gamma=90
Temperature:        98 K

                    Calculated                 Reported
Volume              1562(4)                    1562(4)
Space group         P n a 21                   P n a 21
Hall group          P 2c -2n                   P 2c -2n
Moiety formula      C20 H18 N2 O               C20 H18 N2 O
Sum formula         C20 H18 N2 O               C20 H18 N2 O
Mr                  302.36                     302.36
Dx,g cm-3           1.286                      1.286
Z                   4                          4
Mu (mm-1)           0.080                      0.080
F000                640.0                      640.0
F000'               640.24
h,k,lmax            8,28,11                    8,28,11
Nref                2757[ 1466]                2538
Tmin,Tmax           0.978,0.994                0.474,1.000
Tmin'               0.971

Correction method= # Reported T Limits: Tmin=0.474 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.73/0.92       Theta(max)= 25.043

R(reflections)= 0.0900( 1788)      wR2(reflections)= 0.1984( 2538)

S = 1.039                  Npar= 209
```

Single crystals of $C_{21}H_{18}N_2O_2$ (**4**) and $C_{20}H_{18}N_2O$ (**6′**) were prepared by slow evaporation of **4** solution in hexane/dichloromethane (4:1) and **6′** solution in methanol respectively. A suitable green needle-like crystal (for $C_{21}H_{18}N_2O_2$), with dimensions of 0.42 mm × 0.06 mm × 0.01 mm, and a suitable colorless prism-like crystal (for $C_{20}H_{18}N_2O$),

with dimensions of 0.37 mm $\times$ 0.27 mm $\times$ 0.07 were mounted, using Paratone oil, onto a glass fiber. The data were collected at 98(2) K using a Rigaku AFC12 / Saturn 724 CCD fitted with MoKα radiation (λ = 0.71075 Å). Data collection and unit cell refinement were performed using *CrystalClear* software.[9] The total number of data were measured in the range 5.2° < 2θ < 50.1° and 4.5° < 2θ < 50.1° using ω scans, respectively. Data processing and absorption correction, giving minimum and maximum transmission factors of 0.407 and 1.000 for $C_{21}H_{18}N_2O_2$ and 0.474 and 1.00 for $C_{20}H_{18}N_2O$, were accomplished with *CrystalClear*[10] and *ABSCOR*[10] respectively. The structure, using Olex2,[11] was solved with the ShelXT[12] structure solution program using direct methods and refined (on F^2) with the ShelXL[13] refinement package using full-matrix, least-squares techniques. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atom positions were determined by geometry and refined by a riding model.

Table 2.8 Crystallographic data and structure refinement for cd1309 (**4**) and cd1383 (**6′**)

Identification code	**cd1309**	**cd1383**
Empirical formula	$C_{21}H_{18}N_2O_2$	$C_{20}H_{18}N_2O$
Formula weight	330.37	302.36
Crystal system	Monoclinic	Orthorhombic
Space group	$P\,1\,2_1/c\,1$	$P\,n\,a\,2_1$
a (Å)	17.920(7)	6.727(9)
b (Å)	6.022(2)	23.55(3)
c (Å)	15.745(6)	9.860(13)
α (°)	90	90
β (°)	99.297(6)	90
γ (°)	90	90
Volume (Å^3)	1676.8(11)	1562(4)
Z	4	4
ρ (calc.)	1.309	1.286
λ	0.71075	0.71075
Temp. (K)	98(2)	98(2)

F(000)	696	640
μ (mm^{-1})	0.085	0.080
T$_{min}$, T$_{max}$	0.407, 1.000	0.474, 1.000
2θ$_{range}$ (°)	5.2 to 50.1	4.5 to 50.1
Reflections collected	8256	6848
Independent reflections	2953 [R(int) = 0.094]	2538 [R(int) = 0.067]
Completeness	99.4%	97.6%
Data / restraints / parameters	2953 / 0 / 226	2538 / 1 / 209
Observed data [I > 2σ(I)]	1994	1788
$wR(F^2$ all data)	0.1761	0.1984
$R(F$ obsd data)	0.0785	0.0900
Goodness-of-fit on F^2	1.015	1.04
Largest diff. peak and	0.48/−0.48	0.37 / −0.37

hole (e Å^{-3})		

$$wR_2 = \{ \Sigma [w(F_O{}^2 - F_C{}^2)^2] / \Sigma [w(F_O{}^2)^2] \}^{1/2}$$

$$R_1 = \Sigma ||F_O| - |F_C|| / \Sigma |F_O|$$

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Chapter 3: Unprecedented Intramolecular [4+2]-Cycloaddition Between a 1,3-Diene and a Diazo Ester

I. Introduction

1.1 Isoelectronic Principle and Isoelectronic Systems: Diazo Compounds, Ketenes and Allenes

The term, isoelectronic, is used to describe chemical entities (atoms, molecules, or ions) that have the same number of electrons and the same number of heavy-atoms.[1] The "isoelectronic principle" states that when two or more molecular entities are isoelectronic, they tend to have similar physical and chemical properties.[2] For instance, carbon dioxide and nitrous oxide are isoelectronic with each other; and their physical properties including critical pressure, critical temperature, density of liquid, and dielectric constant of liquid are found to be remarkably similar.[3] More importantly, the isoelectronic principle provides an opportunity for chemists to predict some possible properties and reactions of compounds as being isoelectronic with some already known ones.

Diazo compounds, ketenes and allenes are isoelectronic and share similar electronic structures of cumulated double-bond systems (**Figure 3.1**).[4] Based on the isoelectronic principle, the rich chemistry of allenes and ketenes might provide some clues for us to discover possible properties and reactions of diazo compounds that have not been explored.

$$R^1 \atop R^2 {>}{=}X{=}Y \qquad R^1 \atop R^2 {>}{=}C{=}{<} R^3 \atop R^4 \qquad R^1 \atop R^2 {>}{=}C{=}O \qquad R^1 \atop R^2 {>}{=}\overset{\oplus}{N}{=}\overset{\ominus}{N}$$

Allenes-Ketenes-diazo compounds series   Allenes   Ketenes   Diazo compounds
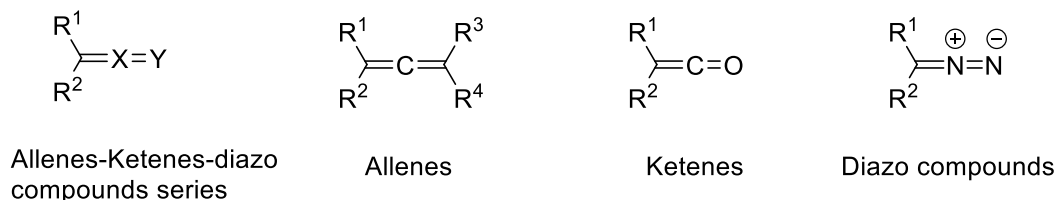
Figure 3.1 Isoelectronic Systems: Allenes-Ketenes-Diazo Compounds

1.2 [4+2]-Cycloaddition of Dienes with Allenes or Ketenes

The Diels-Alder reaction is noted for its ability to construct unsaturated six-membered rings and has been extensively used in synthesis of drugs, natural products, and compounds with biological activity.[5] Allene and ketene have been reported to undergo these reactions and have received considerable attention.[6] However, in the long history of Diels-Alder reactions there has not been a reported example of [4+2]-cycloaddition between a diene and a diazo compound.[7]

1.2.1 4+2]-Cycloaddition of Diene with Allene

Concerted thermal [4+2]-cycloaddition reactions of dienes with highly polarized allenes were extensively investigated in the last century, but favorable competing stepwise [2+2]-cycloaddition reactions diminished their importance.[8] For instance, Houk and coworkers have investigated the cycloaddition reaction of 1,1-difluoroallene and 1,3-butadiene. Although the total yield of [4+2]-adduct and [2+2]-adduct is high, the selectivity in product formation is only moderate (**Scheme 3.1**).[9]

$$
\begin{array}{ccc}
& \text{CF}_2 & \\
& \| & \xrightarrow[\text{90\% yield}]{110°\text{C, 7 h}} \\
& \text{C} & \\
& \| & \\
& \text{CH}_2 &
\end{array}
$$

63%   37%
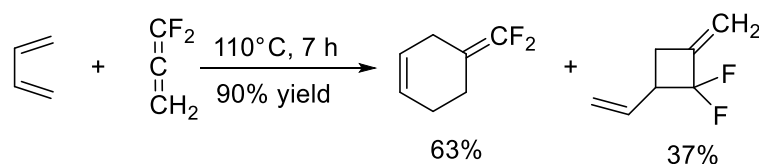
Scheme 3.1 [4+2]- versus [2+2]-Cycloaddition of 1,1-Difluoroallene and 1,3-Butadiene.

Transition metal complex catalyzed allene-diene cycloaddition reactions, although recent in their discovery, have circumvented this competition and become a mainstay of new process developments.[10] Under catalysis of transition metal complexes these [4+2]-cycloaddition reactions were proposed to proceed through a multistep mechanism that always involved organometallic complexes as reaction intermediates; the nature of these transition metal complexes has a great influence on the selectivity of [4+2]-cycloaddition reactions of allenes which have two reactive carbon-carbon double bonds.[11] For instance, Wender and

coworkers reported a transition metal-catalyzed intramolecular [4+2]-cycloaddition of diene-allene.[12] They found, interestingly, that treatment of the diene-allene with Ni(COD)$_2$/P(O-*o*-BiPh)$_3$ gave products with 6,6-fused rings, while when [RhCl(COD)]$_2$/P(O-*o*-BiPh)$_3$ was used as the catalyst, products with 6,5-fused rings were obtained in good yields (**Scheme 3.2**).[12]
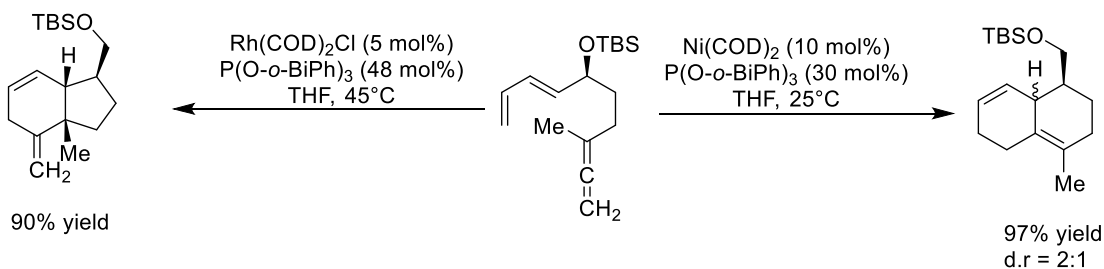
Scheme 3.2 Divergent Outcomes of Transition Metal-Catalyzed [4+2]-Cycloaddition Reactions of Allenes with Dienes.

1.2.2 [4+2]-Cycloaddition of Dienes with Ketenes

The development of [4+2]-cycloaddition reactions of ketenes has been a challenge for a long period of time.[13] One major problem is that ketenes readily undergo [2+2]-cycloaddition reactions with one double bond of dienes.[14] However, diene equivalents that include α,β-unsaturated ketones bearing a strong electron-donating group (EWG) at the α position react with ketenes to produce [4+2]-cycloaddition products under thermal reaction conditions (**Scheme 3.3**).[15]
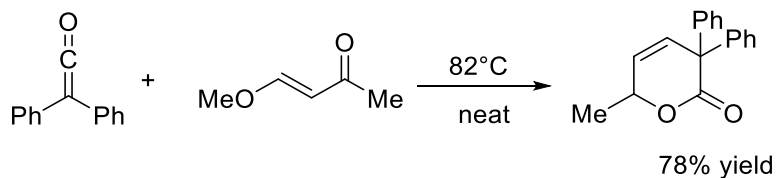
Scheme 3.3 [4+2]-Cycloaddition Reaction of Diphenylketene and (*E*)-4-Methoxybut-3-en-2-one.

Recently, organocatalysis has emerged as a powerful method in organic synthesis.[16] Organocatalyzed [4+2]-cycloaddition reactions of ketenes have also been explored.[17] These transformations involve zwitterionic "ketene" enolates that are generated in situ from the reactions of cinchona alkaloids or *N*-heterocyclic carbenes with ketenes.[17f] These organocatalysts have not only expanded upon the substrate scope of dienes, but have also permitted access to the asymmetric version of these [4+2]-cycloaddition reactions. Cinchona alkaloid-based catalysts were first applied in the [4+2]-cycloaddition reaction of *o*-quinones with ketene enolates, which are derived in situ from readily available acid chlorides.[17b] To inhibit the [2+2]-cycloaddition products, *o*-quinones were used as the dienes so that restoration of aromaticity occurs by [4+2]-cycloaddition (**Scheme 3.4**). Ye and coworkers have developed a chiral *N*-heterocyclic carbene-catalyzed formal [4+2]-cycloaddition of disubstituted ketenes with enones to produce δ-lactones with a quaternary-β-tertiary stereocenter in

good yields with high diastereo- and enantioselectivities.[17f] The authors proposed that the [4+2]-cycloaddition reaction initiated by the nucleophilic addition of *N*-heterocyclic carbene (NHC) to ketenes produce ketene enolates, which could undergo an inverse electron demand Diels–Alder reaction to afford triazolium zwitterionic intermediates, followed by elimination of the NHC to furnish the corresponding δ–lactones (**Scheme 3.5**).

Lectka's work
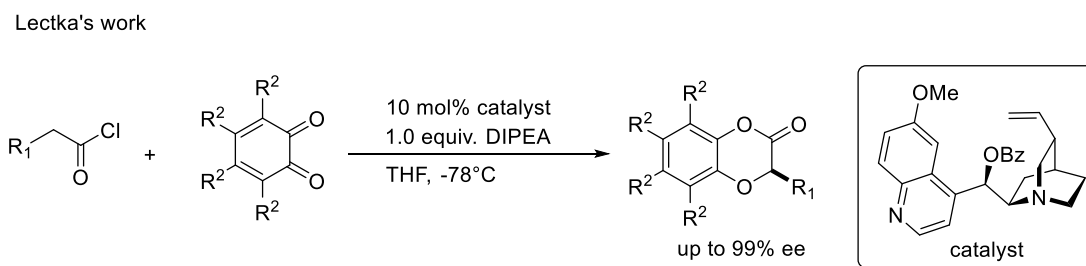
Scheme 3.4 Cinchona Alkaloid-Based Catalyst-Catalyzed [4+2]-Cycloaddition of *o*-Quinones with Ketene Enolates
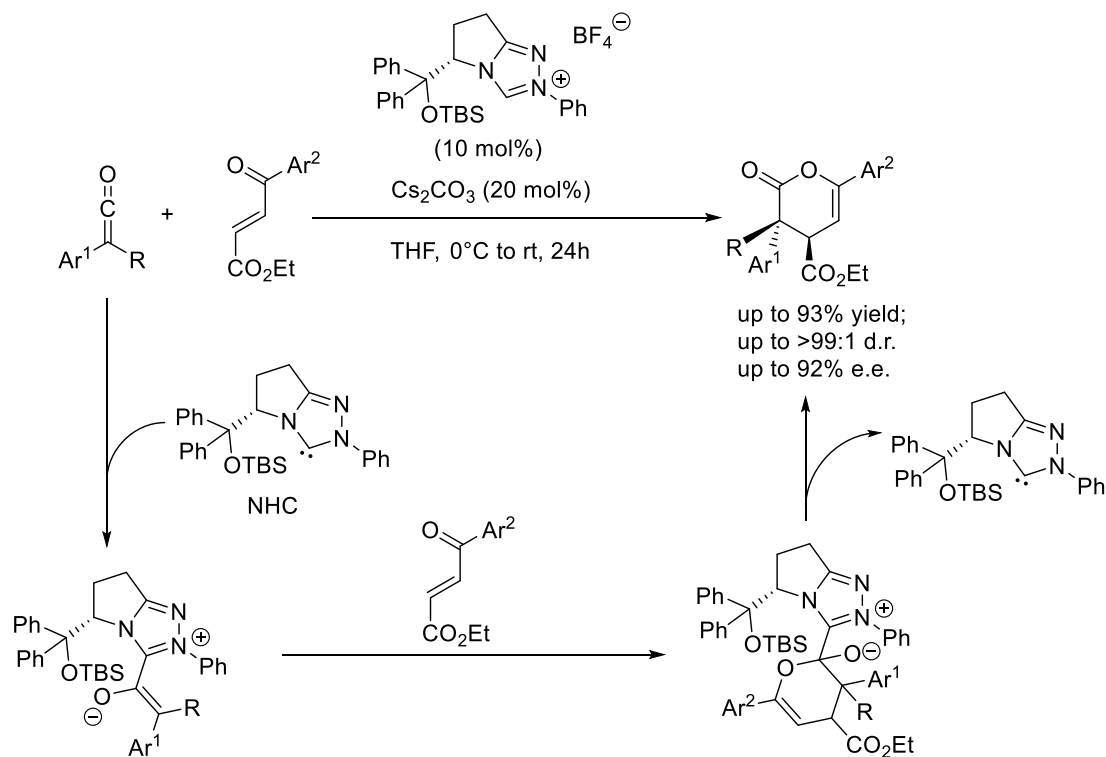
Scheme 3.5 *N*-Heterocyclic Carbene-Catalyzed [4+2]-Cycloaddition Reaction of Ketenes with Enones.

1.3 Original Considerations of [4+2]-Cycloaddition of Diene with Diazo Compounds

Compared with allenes or ketenes, diazo compounds commonly react with one double bond of dienes by dipolar cycloaddition or, following dinitrogen extrusion, by cyclopropanation, but not by [4+2]-cycloaddition (**Scheme 3.6**).[7]
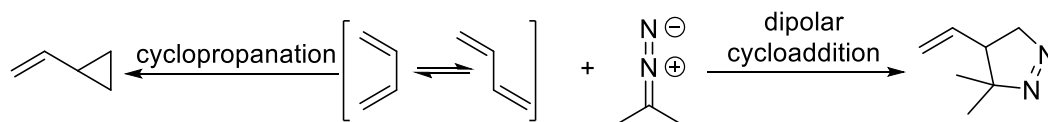
Scheme 3.6 Dipolar Cycloaddition and Cyclopropanation of 1,3-Dienes with Diazo Compounds.

That [4+2]-cycloaddition reactions occur with allenes and ketenes, but not with diazo compounds suggested to us that the facility with which diazo compounds undergo dipolar cycloaddition prevent [4+2]-cycloaddition and that, if dipolar cycloaddition could be electronically and/or sterically inhibited, perhaps [4+2]-cycloaddition should be observed. Inhibition of dipolar cycloaddition with deactivation of the carbon-carbon double bond towards dipolar cycloaddition would require constraints in the alignment of the diazo functional group with either one of the double bonds of the diene. To design such a system we were encouraged by a recent report by M. Brewer and coworkers of a polar intramolecular $[4^{\oplus}+2]$-cycloaddition of aryl-1-aza-2-azoniaallene salts that produced protonated azomethine imines.[18] When they used heteroallenes as starting materials, $[3^{\oplus}+2]$-cycloaddition products, 5,5-bridged bicyclic diazenium salts,[19] were not observed, but instead, $[4^{\oplus}+2]$-cycloaddition products, tricyclic azomethine imine salts containing a 1,2,3,4-tetrahydrocinnoline scaffold, were obtained in good yields. To further understand this transformation, Brewer and Houk have employed computational studies indicating that the formation of a four-membered

ring transition state prevents the formation of the [3⊕+2]-cycloaddition product and favors the [4⊕+2]-cycloaddition (**Scheme 3.7**).[20]
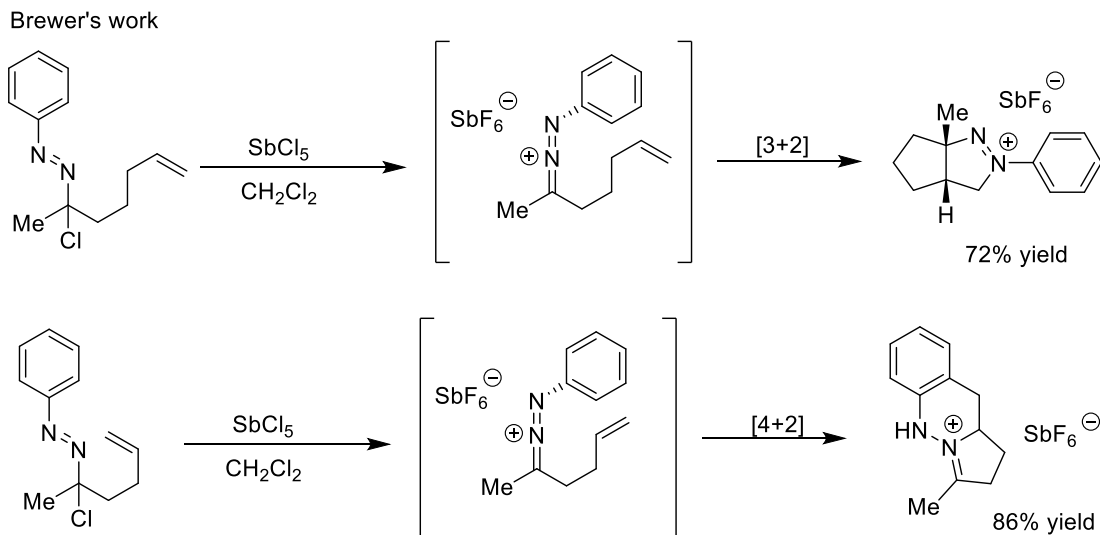
Scheme 3.7 Intramolecular Cycloaddition of 1-Aza-2-Azoniaallene Salts.

One such structural design appropriate for intramolecular [4+2]-cycloaddition between a diene and a diazocarbonyl compound (**Scheme 3.8**) would produce a dipolar azomethine species (**2**) that could serve as a suitable stabilized product. Add to this design activation of the diene with electron-donating substituents, as well as further stabilization of the dipolar azomethine product; and this cycloaddition reaction appears feasible. However, additional constraints that include the linkage between the diene and the diazo units, as well as the geometry of attachment to the diene, remain unresolved.

1   **2**
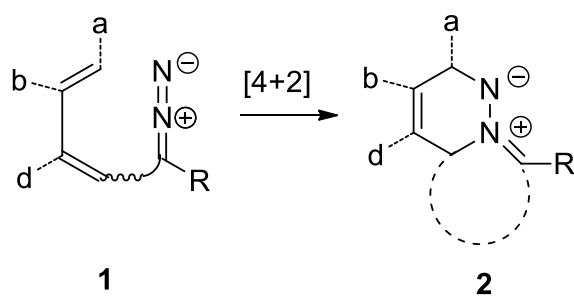
Scheme 3.8 Proposed Intramolecular [4+2]-Cycloaddition of Dienes with Diazo Compounds.

For this investigation we chose to synthesize diene-linked aryldiazoacetates **1** (**Scheme 3.9**). This structure contains the elements of activation and stabilization that we believe to be requirements for diene-diazo [4+2]-cyclization. Gold-catalyzed 1,3-acyloxy migration of propargylic carboxylates is known to form allene intermediates (**3**) suitable for diene formation, and the generation of dienes from propargylic esters through a gold(I)-catalyzed 1,3-migratory cascade involving allene intermediates has been established.[21]
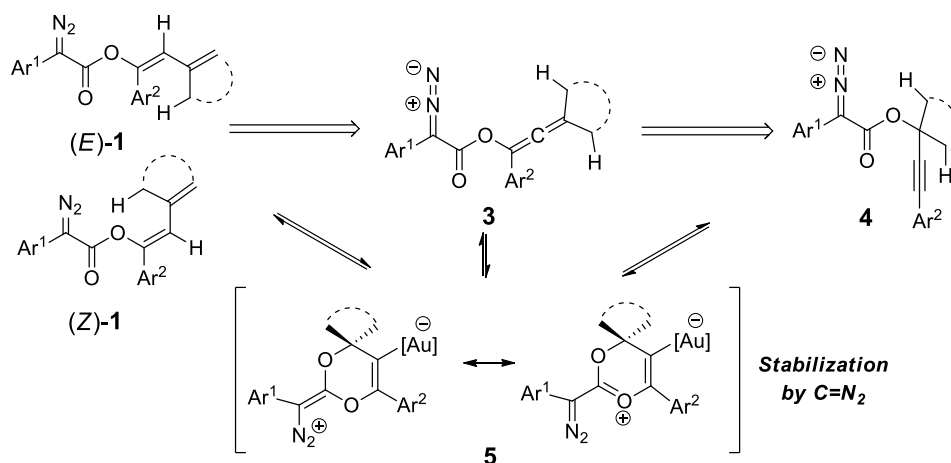
Scheme 3.9 Synthesis of Diene-linked Aryldiazoacetates.

II. Results and Discussion

2.1 Initial Screening of Additives and Reaction Conditions

Treatment of propargyl phenyldiazoacetate **4a** with a broad selection of neutral gold catalysts under various conditions of temperatures and solvents gave either no reaction or 1,5-dihydro-4*H*-pyrazol-4-ones as dominant products (discussed in **Chapter 2**) and minor amounts of diene (*Z*)-**1a**, although not in high yield. Sensing that proton transfer might be limiting this process, a variety of inorganic bases, organic bases, and organic acids were used as additives. Results are shown in **Table 3.1**. Organic bases that include triethylamine (NEt$_3$), pyridine, and 1,8-diazabicycloundec-7-ene (DBU) were found to poison the gold catalyst (**Table 3.1**, entries 1-3). With sodium hydroxide as the base, the starting material **4a** was also recovered in over 95% after 4 days under the same reaction conditions (**Table 3.1**, entry 4). Sodium acetate and sodium bicarbonate changed the yields of (*Z*)-**1a** slightly with over 95% conversion of **4a** (**Table 3.1**, entries 5 and 6). Another mild Lewis base, nitrosobenzene (PhNO), was also tested and was found to slightly deactivate the gold catalyst (**Table 3.1**, entry 7). Interestingly, when 1.0 equivalent of dimethyl sulfoxide (DMSO) was added, the reaction

resulted in the formation of (Z)-**1a** and a product anticipated from a diene-diazo [4+2]-cycloaddition (**2a**) in a combined yield of 30% (**Table 3.1**, entry 8). Further investigations of other organic-oxide-containing bases including triphenylphosphine oxide and pyridine-*N*-oxide have shown that pyridine-*N*-oxide gave improved results (**Table 3.1**, entry 9 and 10). The use of benzoic acid did not yield the [4+2]-cycloaddition product **2a** (**Table 3.1**, entry 11).

Table 3.1 Sreening the Additives for Gold-Catalyzed Reactions of Propargyl Phenyldiazoacetate **4a**.
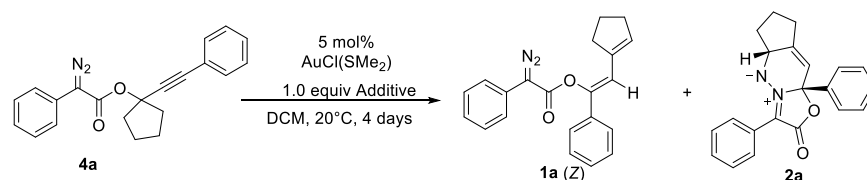
Entry[a]	Additive	Conversion[b]	Yield[c]	(Z)-**1a**:**2a**[c]
1	NEt₃	<10	<10	-[d]
2	Pyridine	<10	<5	-[d]
3	DBU	<10	<10	-[d]
4	NaOH	<10	<10	-[d]
5	NaOAc	>95	15	>20:1

6	NaHCO$_3$	>95	18	>20:1
7	PhNO	80	23	>20:1
8	DMSO	>95	30	60:40
9	Ph$_3$PO	>95	10	>20:1
10	Pyridine-*N*-oxide	>95	74	65:35
11	Benzoic acid	90%	9	>20:1

[a]To a flame-dried 10 mL Schlenk flask charged with a magnetic stirring bar, AuCl(SMe$_2$) (2.90 mg, 0.010 mmol), an additive (0.20 mmol) and 2.0 mL of toluene were added sequentially under nitrogen atmosphere. Then **4a** (0.20 mmol) dissolved in 3.0 mL of toluene was added sequentially into the solution under the flow of nitrogen. The resulting mixture was allowed to stir for 48 h at room temperature. [b]The percent conversion of **4a** was determined ^{1}H NMR spectroscopy using 2,4,6-trimethoxybenzaldehyde as an internal standard. [c]The total yields of [(*Z*)-**1a**+**2a**] and the ratios were determined by the ^{1}H NMR analyses of characteristic absorptions. [d]Not determined.

Pyridine-*N*-oxides with different substituent groups including nitro, methoxy, and chloro at the *para*-position were also tested (**Table 3.2**, entries 1-4). 4-Chloropyridine-*N*-oxide was optimal. 4-Nitropyridine-*N*-oxide **6c** did not give the product from [4+2]-cycloaddition, which might be because of its decreased basicity; however, 4-methoxypyridine-*N*-oxide, which is a stronger base compared to pyridine-*N*-oxide, was found to deactivate the gold catalyst and resulted in a lower yield of products. With 4-chloropyridine-*N*-oxide, gold catalysts that include AuCl, AuCl$_3$, IPrAuCl, PPh$_3$AuCl were examined, but did not give improved results

(**Table 3.2**, entries 5-8). A variety of solvents that include hexanes, tetrahydrofuran (THF), acetonitrile (CH₃CN), and toluene were examined subsequently (**Table 3.2**, entries 9-12): all of the solvents were tolerated, but their use did give significant variation in the (*Z*)-**1a**:**2a** product ratios. Finally, AuCl(Me₂S) and 4-chloropyridine-*N*-oxide were optimal for the reaction performed in toluene at 20℃.

Table 3.2 Optimization of Catalyst and Reaction Condition for Gold-Catalyzed Reactions of Propargyl Phenyldiazoacetate **4a**.
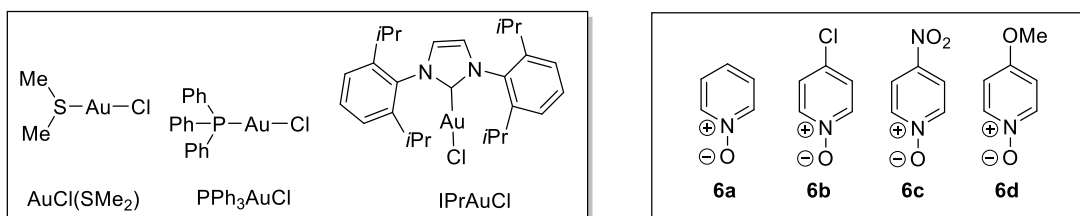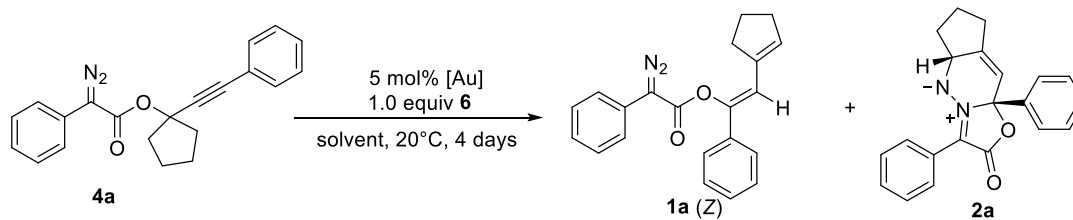
Entry[a]	[Au]	solvent	6	conversion (%)[b]	yield (%)[c]	(*Z*)-1a:2a[d]
1	AuCl(SMe₂)	CH₂Cl₂	**6a**	>95	74	65:35
2	AuCl(SMe₂)	CH₂Cl₂	**6b**	>95	80	62:38
3	AuCl(SMe₂)	CH₂Cl₂	**6c**	>95	<10	-[d]

4	AuCl(SMe₂)	CH₂Cl₂	**6d**	50	31	65:35
5	AuCl	CH₂Cl₂	**6b**	>95	76	65:35
6	AuCl₃	CH₂Cl₂	**6b**	>95	52	67:33
7	IPrAuCl	CH₂Cl₂	**6b**	<5	trace	-[d]
8	PPh₃AuCl	CH₂Cl₂	**6b**	<5	trace	-[d]
9	AuCl(SMe₂)	hexane	**6b**	>95	42	52:48
10	AuCl(SMe₂)	THF	**6b**	>95	81	62:38
11	AuCl(SMe₂)	CH₃CN	**6b**	>95	55	65:35
12	AuCl(SMe₂)	toluene	**6b**	>95	85 (80)[e]	43:57 (40:60)[f]

[a]Reactions were performed at 20℃ on a 0.20 mmol scale: a solution of **4a** in 2.0 mL solvent was added to the solution of **6** (1.0 equiv) and 5 mol% of catalyst 3.0 mL of solvent under a nitrogen atmosphere, and the resulting reaction mixture was stirred for 4 days. [b]The percent conversion of **4a** was determined ^{1}H NMR spectroscopy using 2,4,6-trimethoxybenz-aldehyde as an internal standard. [c]The total yields of [(*Z*)-**1a** + **2a**] and the ratios were determined by the ^{1}H NMR analyses of characteristic absorptions. [d]Not determined. [e]The combined isolated yield of (*Z*)-**1a** and **2a**. [f]The ratio (*Z*)-**1a**:**2a** of the isolated product.

Structures for both the diene (*Z*)-**1e** and cycloaddition product **2f** were confirmed by X-ray diffraction (**Figure 3.2**). Neither the cascade reaction anticipated from initial dinitrogen extrusion by the catalyst at the diazo carbon nor the product(s) from dipolar cycloaddition between the diazo compound and diene were observed, and the absence of the cascade

reaction product indicated a high preference of the gold catalyst for reaction at the carbon-carbon triple bond rather than with the phenyldiazoacetate.
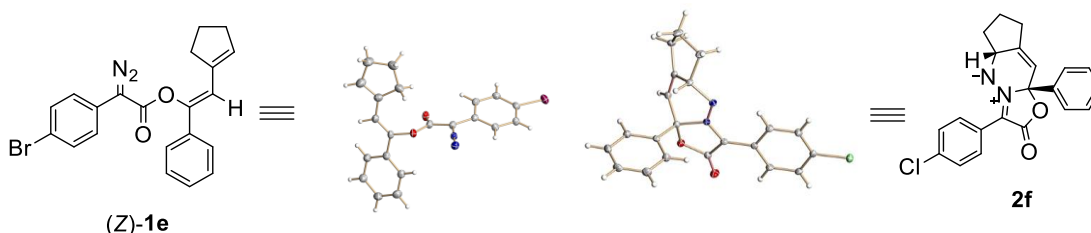
Figure 3.2 X-ray Structures of Diene (*Z*)-**1e** and Cycloaddition Product **2f**.

2.2 Substrate Scope
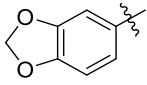
Using optimum reaction conditions (**Table 3.2**, entry 12) the influence of substituents on the arylpropargyl aryldiazoacetate was examined to further understand the formation of diene-linked aryldiazoacetates and the diene-diazo [4+2]-cycloaddition process. As shown in **Table 3.3**, arylacetic acid-derived substituents – including ethers, halides, nitro, trifluoromethyl, alkyl, aryl – underwent the rearrangement reaction smoothly within 4 days at 20°C, affording the diene and cycloaddition products in good to excellent combined yields (**Table 3.3**, entries 1-8). *o*-Bromophenylacetic acid-derived compound **4j** (**Table 3.3**, entry 9) underwent reaction much slower than the *p*-bromophenylacetic acid-derived substitutent **4e**, suggesting a possible

steric influence. We also examined arylacetylene-derived substituents. Generally, those with electron-donating substituents in the *para*-position (**Table 3.3**, entries 10 and 11) underwent rearrangement reaction faster than **4a**. However, those with electron-withdrawing substituents were potential challenges because of the reduced nucleophilicity of *(E)*-**1** dienes that are suggested to be the precursors to cycloaddition products **2**. The success of the *p*-fluorophenylacetylene-substituted **4n** encouraged us to examine more electron-deficient substituents (**4o** and **4p**). The dienes and cycloaddition products from these reactants were successfully obtained in reasonable yields after 20 days at room temperature (**Table 3.3**, entries 14 and 15). However, the *p*-nitrophenylacetylene-substituted **4q** failed to deliver the corresponding diene and cycloaddition product (**Table 3.3**, entry 16) even after 20 days.

Table 3.3 Substrate Scope for Rearrangement Reaction.

Entry[a]	4	Ar[1]	Ar[2]	reaction time (day)[b]	conversion (%)[c]	yield of (Z)-**1** and **2** (%)[d]	(Z)-**1**:**2**[e]

1	**4b**		Ph	4	>95	92	41:59
2	**4c**	4-MeC$_6$H$_4$	Ph	4	>95	94	42:58
3	**4d**	4-PhC$_6$H$_4$	Ph	4	>95	91	42:58
4	**4e**	4-BrC$_6$H$_4$	Ph	4	>95	89	44:56
5	**4f**	4-ClC$_6$H$_4$	Ph	4	>95	88	41:59
6	**4g**	4-FC$_6$H$_4$	Ph	4	>95	84	40:60
7	**4h**	4-CF$_3$C$_6$H$_4$	Ph	4	90	77	42:58
8	**4i**	4-NO$_2$C$_6$H$_4$	Ph	4	85	70	26:74
9	**4j**	2-BrC$_6$H$_4$	Ph	20	>95	75	27:73
10	**4k**	Ph	4-OMeC$_6$H$_4$	2.5	>95	82	50:50
11	**4l**	Ph	4-MeC$_6$H$_4$	3	>95	86	48:52
12	**4m**	Ph	4-ClC$_6$H$_4$	7	>95	85	47:53
13	**4n**	Ph	4-FC$_6$H$_4$	9	>95	81	45:55
14	**4o**	Ph	4-MeO$_2$CC$_6$H$_4$	20	>95	81	45:55
15	**4p**	Ph	4-(OHC)C$_6$H$_4$	20	>95	77	47:53

16	**4q**	Ph	4-NO$_2$C$_6$H$_4$	20	45%	<10%	-[f]

[a]Reactions were performed at 20℃ on 0.20 mmol scale: the solution of **4** in 2.0 mL toluene was added to the solution of **6b** and 5 mol % of AuCl(SMe$_2$) in 3.0 mL of toluene under a nitrogen atmosphere, and the resulting reaction mixture was stirred for the stated reaction time. [b]The reaction time was determined from the disappearance of **4** by thin-layer chromatography or no improved conversion with longer times. [c]The % conversion of **4** was determined by ^{1}H NMR analysis using 2,4,6-trimethoxybenzaldehyde as the internal standard. [d]Isolated combined yields. [e]Isolated ratios. [f]Not determined.

2.3 Kinetic Studies

To determine if both (E)-**1** and (Z)-**1** were formed initially after which (E)-**1** underwent cycloaddition to **2** we examined the gold catalyzed reaction at shorter reaction times. If (E)-**1** was the precursor to **2**, this diene should be observed as an initially formed product. Fortunately, during 6-12 h reaction time at room temperature with relatively low conversion of **4**, both (E)-**1** and (Z)-**1** were obtained at apparent equivalent rates. Isolation of (E)-**1a** by column chromatography at room temperature provided sufficient material to examine if this diene could undergo uncatalyzed formation of **2a** or if cycloaddition required the intervention of a catalyst. In the absence of catalyst, isolated (E)-**1a** underwent quantitative conversion to cycloaddition product **2a** in toluene at room temperature for 4 days. Furthermore, compound (E)-**1a** was dissolved in CDCl$_3$ and the progress of the reaction was monitored by ^{1}H NMR spectroscopy. Reaction was first order in (E)-**1a** with k$_{obs}$ = 9.6×10^{-5} s^{-1} at 41℃ in CDCl$_3$ (**Figure 3.3**); and the addition of the gold catalyst

in amounts similar to those used for reactions with propargyl aryldiazoacetates **4** did not influence the rate of conversion of (*E*)-**1a** to **2a**, confirming that the cycloaddition reaction was uncatalyzed. The variation of the rate constant over temperatures ranging from 20°C to 49°C provided E_{act} = 16.2 kcal/mol, $\Delta H^{\ddagger}_{298}$ = 15.6 kcal/mol and $\Delta S^{\ddagger}_{298}$ = -27.3 cal/(mol•degree).[22] Multiple determinations of reaction rates after separations of (*E*)-**1a** from different reaction mixtures were made to ensure that there was consistency in results. Cycloaddition occurred with rate constants that were independent of the batch source of (*E*)-**1a**.
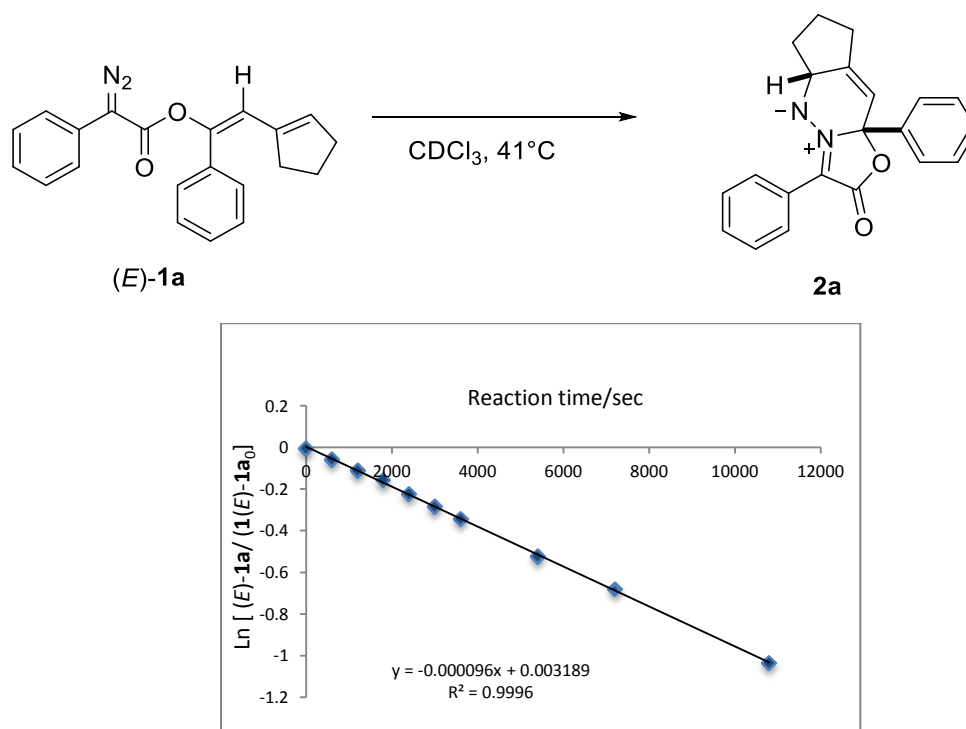
Figure 3.3 Linear Relationship Between Reaction Time and Ln [(*E*)-**1a**/(*E*)-**1a**$_0$]. Reaction Performed in CDCl$_3$ at 41°C.

Surprisingly, the geometrical isomer of (*Z*)-**1a** did not undergo [4+2]-cycloaddition. Stable at room temperature in the absence of catalyst for more than 7 days in toluene, (*Z*)-**1a** underwent complete decomposition resulting in complex mixtures at 60°C in CDCl$_3$ for 24 h that did not include evidence for **2a** or similar cycloaddition products. In contrast, (*E*)-**1a** underwent what is a facile [4+2]-cycloaddition reaction that occurred without evidence for formation of a dipolar cycloaddition product.

The design of (*E*)-**1** with its strategically placed phenyl groups allows the examination of the influence substituents on the rates for cycloaddition for both the dienophile and the diene in the same compound. To perform these determinations we isolated (*E*)-**1** from a representative series of gold-catalyzed reactions of **4**, determined the yields for their conversion to [4+2]-cycloaddition product, and measured the rates for their conversion to **2** at constant temperature. As shown in **Table 3.4**, the intramolecular [4+2]-cycloaddition reaction of (*E*)-**1** gave **2** in high yields with complete diastereocontrol. Reaction rates were dependent on compounds (*E*)-**1** with arylacetic acid-derived substituents Ar^1 and with arylacetylene-derived aryl substituents Ar^2. The *p*-methylsubstituent slightly decreased the reaction rate (**Table 3,4**, entry

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2); other substituents, such as *p*-Ph, *p*-Br, *p*-Cl, and *p*-F, increased the reaction rate (**Table 3,4**, entries 3-6); moreover, the aryldiazoacetate with the strongly electron-withdrawing *p*-NO$_2$ group gave the highest reaction rate (**Table 3.4**, entry 7). In contrast, electron-withdrawing groups on the benzene ring of the phenylacetylene-derived substituents decreased the reaction rate (**Table 3.4**, entries 11-14), whereas electron-donating groups increased the reaction rate (**Table 3.4**, entries 9 and 10). Hammett plots of the intermolecular [4+2]-cycloaddition reaction of (*E*)-**1** showed good correlations between σ values and log (k$_X$/k$_H$) with ρ-values of +0.89 (R^2 = 0.96) for the para-substituted aryldiazo esters and -1.65 (R^2 = 0.95) for the para-substituted aryldienes (Figures **3.4** and **3.5**).[23] The diazo functional group exhibits electrophilic character in these reactions (discussed in **Chapter 2**) while the diene is its nucleophilic partner. In addition, the *o*-bromo substituent underwent a much slower reaction than did the *p*-bromo-derived compound, suggesting a possible steric inhibition (**Table 3.4**, entry 8).

Table 3.4 Product and Kinetic Studies of Intramolecular [4+2]-Cycloaddition.

(E)-1 → 2
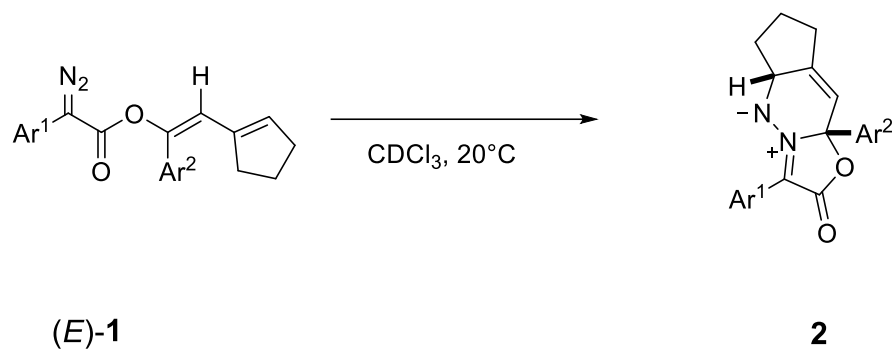
Entry[a]	(E)-1 and 2	Ar[1]	Ar[2]	time[b] (days)	yield of 2 from (E)-1[c]	rate constant[d] (s[-1])
1	a	Ph	Ph	4	90[e]	1.50×10^{-5}
2	c	4-MeC$_6$H$_4$	Ph	4	92[e]	1.47×10^{-5}
3	d	4-PhC$_6$H$_4$	Ph	4	93[e]	2.57×10^{-5}
4	e	4-BrC$_6$H$_4$	Ph	4	90[e]	3.41×10^{-5}
5	f	4-ClC$_6$H$_4$	Ph	4	88[e]	3.04×10^{-5}
6	g	4-FC$_6$H$_4$	Ph	4	91[e]	2.38×10^{-5}
7	i	4-NO$_2$C$_6$H$_4$	Ph	2	85[e]	9.82×10^{-5}
8	j	2-BrC$_6$H$_4$	Ph	21	87	0.33×10^{-5}
9	k	Ph	4-OMeC$_6$H$_4$	4	92[e]	3.71×10^{-5}
10	l	Ph	4-MeC$_6$H$_4$	4	90[e]	3.04×10^{-5}

11	**m**	Ph	4-ClC$_6$H$_4$	7	88[e]	0.72×10^{-5}
12	**n**	Ph	4-FC$_6$H$_4$	7	88[e]	0.86×10^{-5}
13	**o**	Ph	4-MeO$_2$CC$_6$H$_4$	15	89	0.45×10^{-5}
14	**p**	Ph	4-(OHC)C$_6$H$_4$	21	87	0.30×10^{-5}

[a]Reactions were performed at 20 ± 0.5°C on a 0.05 mmol scale: under a nitrogen atmosphere. The solution of (*E*)-**1** in 0.5 mL CDCl$_3$ was monitored by ^{1}H NMR spectroscopy every a period of time until over 80% of (*E*)-**1** was converted into the cycloaddition product **2**. [b]The reaction time was determined from the disappearance of (*E*)-**1** by ^{1}H NMR spectroscopy. [c]Isolated yields from the conversions of (*E*)-**1** to **2**. [d]Determined by ^{1}H NMR. [e]The solution of (*E*)-**1** and (*Z*)-**1** in 0.5 mL CDCl$_3$ was monitored by ^{1}H NMR spectroscopy.
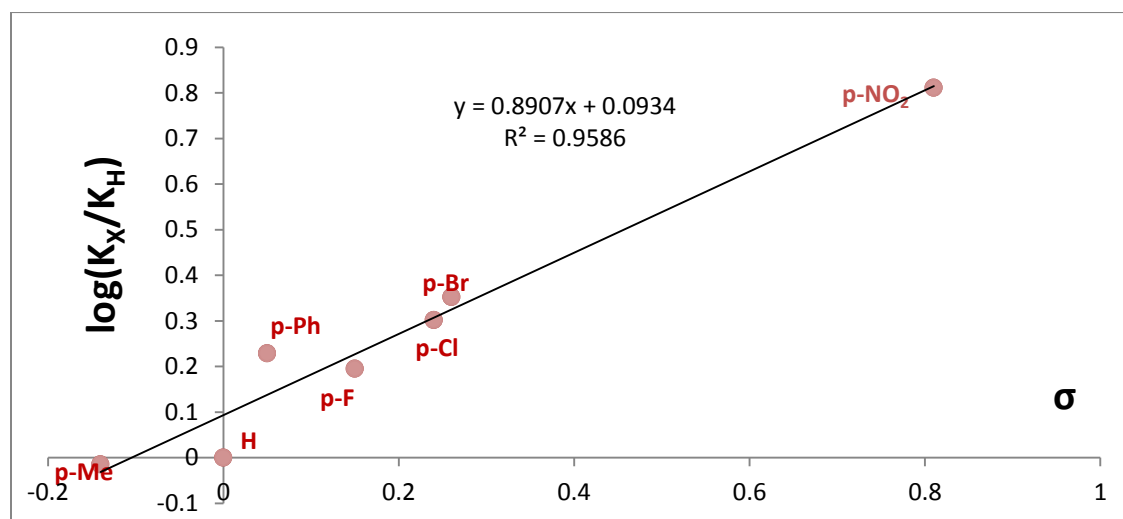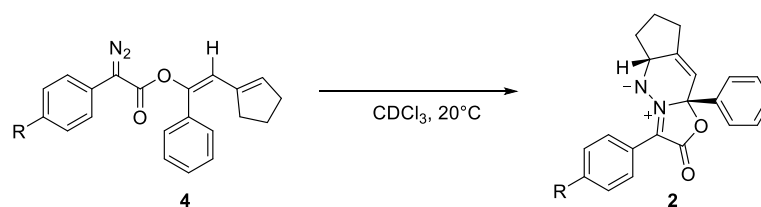
Figure 3.4 Hammett Plot for the *para*-Substituted Aryldiazoesters.
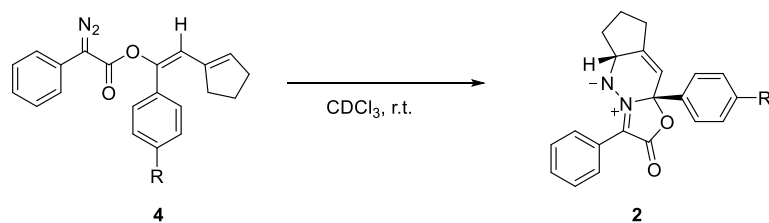
Figure 3.5 Hammett Plot for the *para*-Substituted Aryldienes.

2.4 Reaction Mechanism

A plausible mechanism for the neutral gold(I)-catalyzed formation of diene-diazo and cycloaddition product is outlined in **Scheme 3.10**. Gold-catalyzed 1,3-acyloxy rearrangement of **4a** produces gold-coordinated carboxyallene **A** (discussed in **Chapter 2**). In the presence of 4-chloropyridine *N*-oxide, subsequent protonation of gold-coordinated carboxyallene **A** produces (*E*)- and (*Z*)-gold-coordinated diene-diazo intermediates **B** and **C**, which are protodeaurated by protonated 4-chloropyridine *N*-oxide (Pry-OH $^\oplus$) to produce (*E*)- and (*Z*)-**1a** and regenerate gold catalyst and 4-chloropyridine *N*-oxide. The (*E*)-**1a** further undergoes an intramolecular [4+2]-cycloaddition to furnish the dipolar azomethine species **2a**.
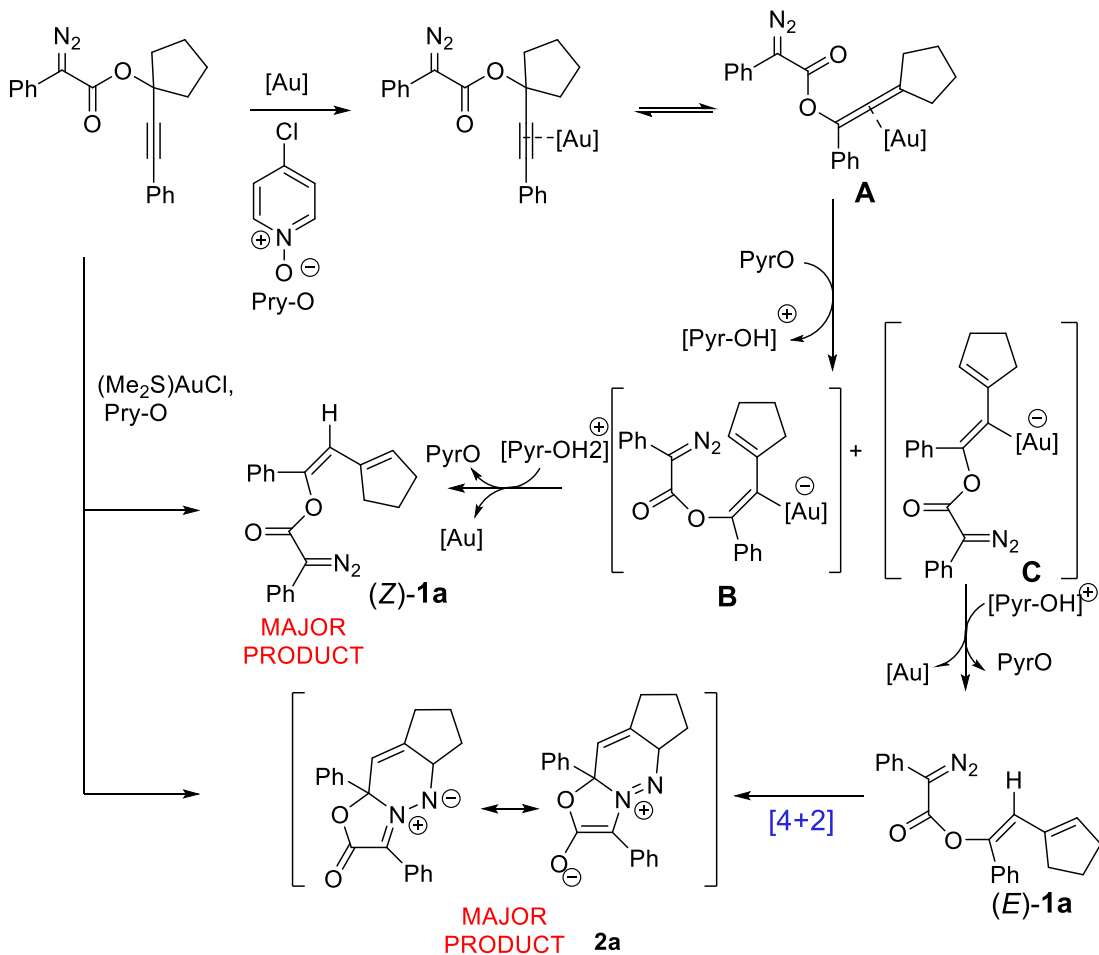
Scheme 3.10 Proposed Mechanism for Gold(I)-Catalyzed Rearrangements in Presence of 4-Chloropyridine *N*-Oxide.

2.4a Gold-Catalyzed Isomerization of Allenes into 1,3-Dienes with an Additive
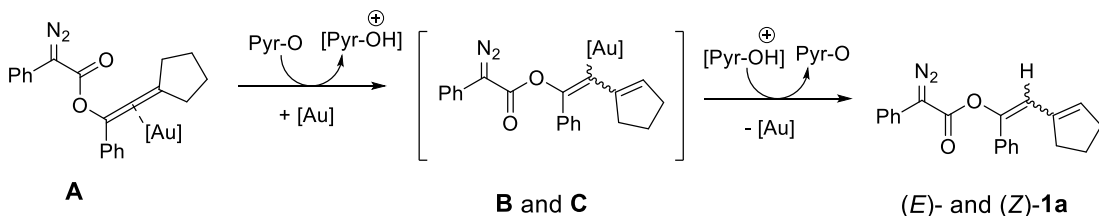
As discussed in **Chapter 2**, gold-coordinated carboxyallene **A**, which is initially formed by gold-catalyzed 1,3-acyloxy rearrangement of

4a, is the key intermediate for further transformation. Gold-catalyzed synthesis of 1,3-dienes via allene intermediates has been reported previously (also discussed in **Chapter 2**). In some cases, additives play an important role in these transformations. For instance, Liu and coworkers found that in presence of AuCl$_3$ and nitrosobenzene, the (3-methylbuta-1,2-dien-1-yl)benzene undergoes isomerization and furnishes (*E*)-(3-methylbuta-1,3-dien-1-yl)benzene in good yield. Nitrosobenzene is found to be essential to this transformation; no 1,3-diene is formed in absence of nitrosobenzene. In the paper, the authors suggested that the role of nitrosobenzene is as a mild base accelerating proton transfer for this isomerization (**Scheme 3.11**).[24]
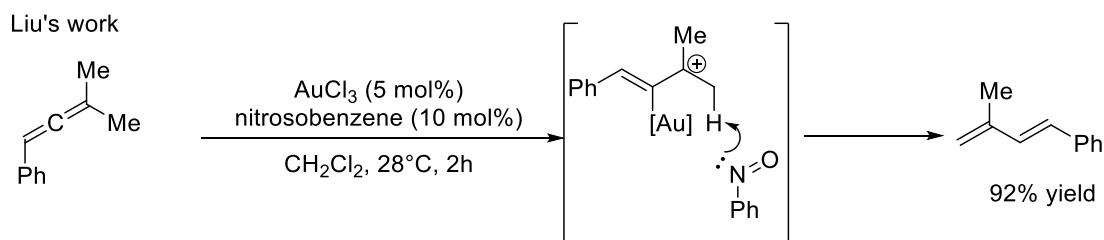
Scheme 3.11 Gold-Catalyzed Isomerization of Unreactive Allenes into 1,3-Dienes.

2.4b Pyridine *N*-Oxides as Mild Bases in Gold Catalysis

Although pyridine-*N*-oxides are noted for their role in oxygen transfer that provides access to α-oxo gold carbenes,[25] uses of pyridine-*N*-oxides as mild bases rather than as oxygen transfer agents have also

been reported.[26] For instance, studies of reactions using diynes as substrates with pyridine-*N*-oxides in presence of BrettPhosAuNTf afforded tricyclicindenes instead of oxidation products. Zhang and coworkers proposed a mechanism which describes the *N*-oxide as a mild base to facilitate the deprotonation of the terminal alkyne to form alkynylgold **E** with subsequent coordination with another BrettPhosAu cation to produce **F**, which further undergoes complex transformations to form intermediate **G**, which react with protonated pyridine *N*-oxide (Pry-OH[⊕]) to produce the tricyclicindenes, and regenerate the gold catalysts and pyridine *N*-oxides (**Scheme 3.12**).[27]
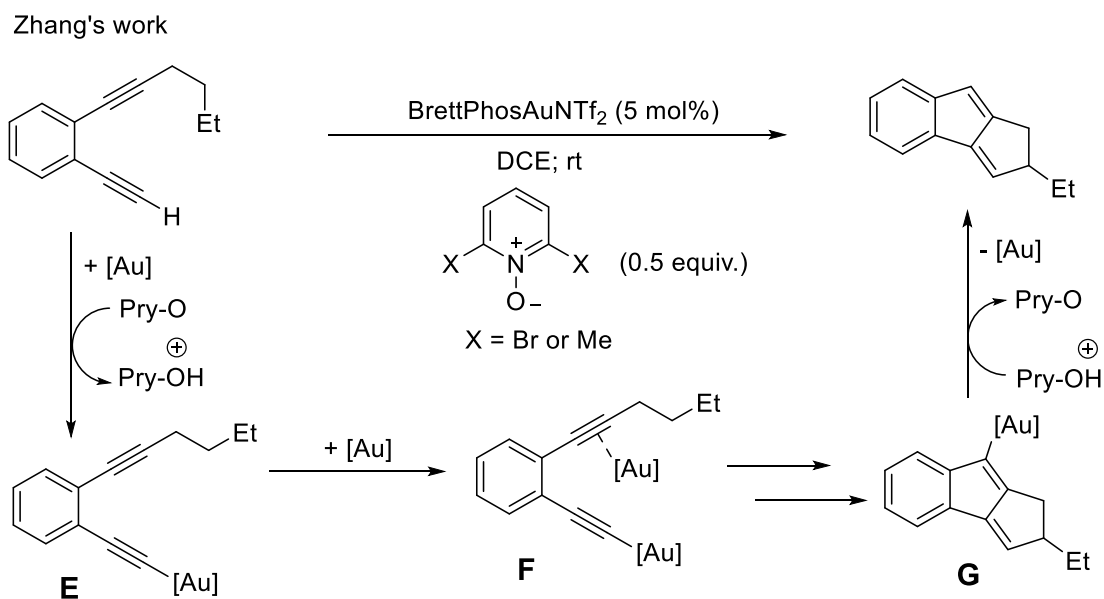
Scheme 3.12 Gold-Catalyzed Rearrangement of Diynes: Pyridine-*N*-Oxides as Mild Bases.

In another example, Zhang and co-workers reported a novel strategy for in situ generation of furan-based ortho-quinodimethanes from 2-(1-alkynyl)-2-alken-1-ones with catalytic amount of pyridine *N*-oxides and Ph$_3$PAuCl. They demonstrated that pyridine-*N*-oxide plays a key role in this transformation and serves as the mild base. Interestingly, replacement of pyridine-*N*-oxide with a series of inorganic and organic bases including K$_2$CO$_3$, 1,4-diazabicyclo[2,2,2]octane (DABCO), Et$_3$N, and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) failed to produce the any desired products (**Scheme 3.13**).[28]
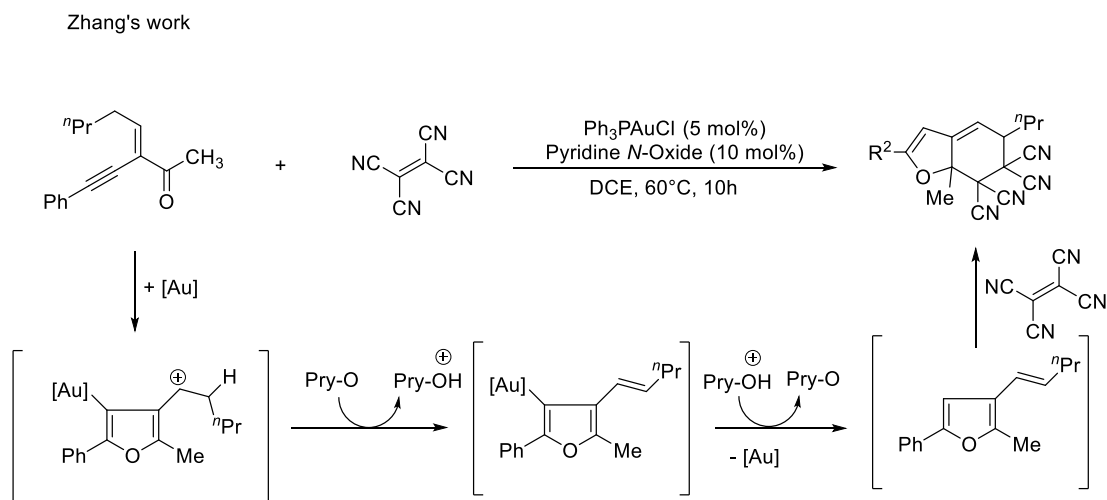
Scheme 3.13 Gold-catalyzed Rearrangement of 2-(1-Alkynyl)-2-Alken-1-Ones: Pyridine-*N*-Oxides as Mild Bases.

2.4c Deuterium Labeling Experiments

Based on the proposed mechanism, we hypothesized that protonated 4-chloropyridine *N*-oxide (Pry-OH$^\oplus$) may undergo deuterium-

hydrogen exchange with external deuterium source such as deuterium oxide (D_2O) to form deuterated 4-chloropyridine *N*-oxide (Pry-OD⊕); if this proposed process occurs, the deuterated dienes should be observed.
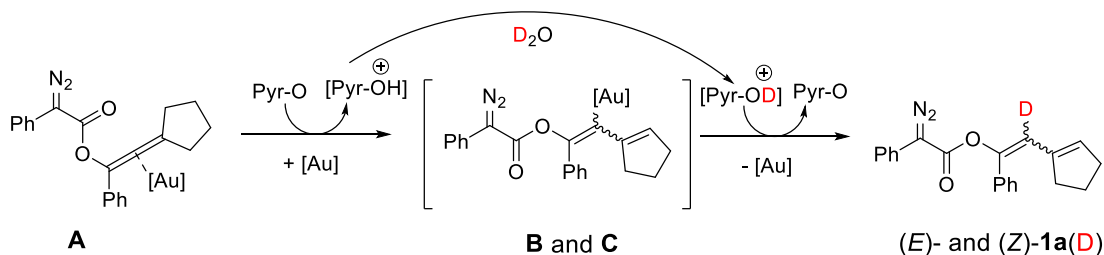
Scheme 3.14 Proposed Deuterium-Hydrogen Exchange Process.

To test our hypothesis, deuterium oxide (D_2O) was added to the reaction mixtures under optimized reaction conditions. And the results were reported in **Scheme 3.15**. Both deuterated diene-diazo and [4+2]-cycloaddition products were obtained; and the percentage of two deuterated products was almost the same even with changing the amount of deuterium oxide (D_2O).

X	$D_{diene}\%^{a}$	$D_{zwitterionic}\%^{b}$
1	43%	45%
2	51%	53%
5	64%	66%
10	79%	81%

[a]$D_{diene}\%$ is the percentage of deuterated diene
[b]$D_{zwitterionic}\%$ is the percentage of deuterated [4+2]-cycloaddition
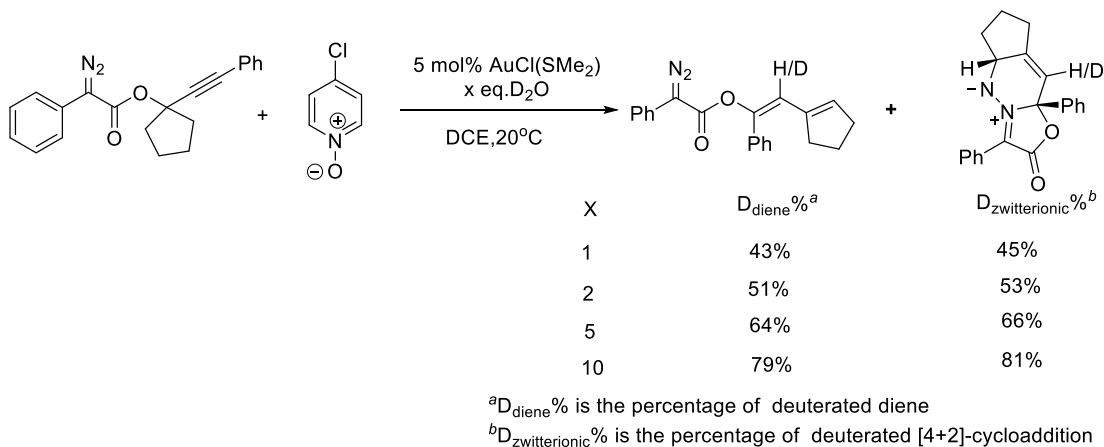
Scheme 3.15 Deuterium Labeling Experiments.

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2.4d Theoretical Study

To further understand this unique intramolecular [4+2]-cycloaddition reaction, we are collaborating with Professor Kenneth Houk's group at UCLA, whose calculated results fit our observations very well. Although there is an intrinsic preference for diazoketones and dienes to give the 1,3-dipolar cycloaddition [3+2]-cycloaddition products, our reaction strongly favors the intramolecular [4+2] across the diazo N=N bond because the tether distortion is much less than that of the 1,3-dipolar cycloaddition (this work will published) .

Figure 3.6 shows the energetics and transition states of intramolecular [4+2] cycloaddition across the N=N double bond of diazo ester for (*E*)- and (*Z*)-alkenes. The (*E*)-alkene is 2.5 kcal/mol stable than the (*Z*)-alkene. The observed product from (*E*)-alkene is formed with a barrier of only 26.9 kcal/mol. The reaction of the (*Z*)-alkene has a much high barrier (39.2 kcal/mol), and the product is slightly unstable compared to the reactant.

Figure 3.6 Energetics and Transition States of Intramolecular [4+2]-Cycloaddition (*E* vs *Z*)

Figure 3.7 shows the two possible competing [4+2] and [3+2] cycloadditions. The observed [4+2] cycloaddition has a lower barrier (by 4 kcal/mol) compared to the (3+2) cycloaddition. Therefore, only the [4+2] product was observed experimentally, although the (3+2) product is more stable.

Figure 3.7 Energetics and Transition States of [4+2]- and [3+2]-Cycloadditions

2.5 Further Applications of [4+2]-Cycloaddition Products

The [4+2]-cycloaddition products formed from (*E*)-**1** are stable dipolar species, and their suitability for dipolar cycloaddition with reactive alkenes and alkynes was examined.[29] Treatment of **2e** with *N*-phenylmaleimide at room temperature for 6 h gave the nitrogen-fused pentacyclic compound **5e** in 85% yield with complete diastereocontrol (eq 2). The structure of **5e** was confirmed by X-ray diffraction (**Figure 3.8**).
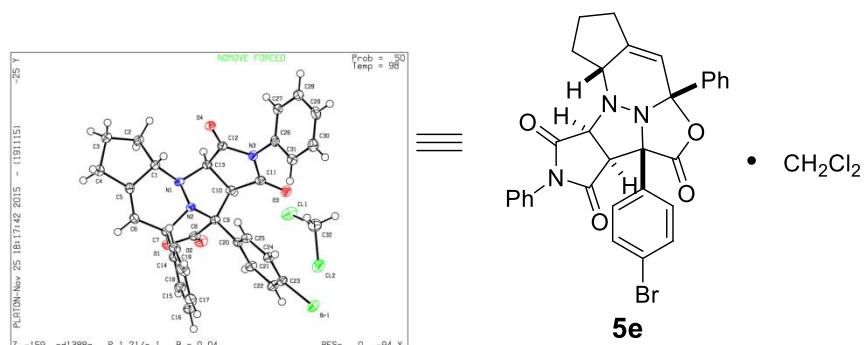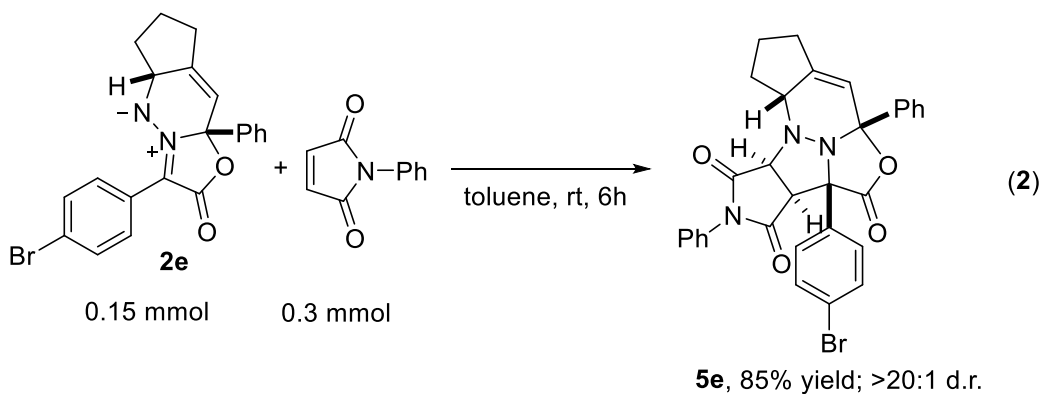
Figure 3.8 X-Ray Structure of **5e**.

III. Conclusion

In summary, aryl-substituted 1-(1,3-dienyl) aryldiazoacetates were formed selectively and in moderate to high yields by Au(I)-catalyzed rearrangement of propargyl phenyldiazoacetates performed in the presence of a pyridine-*N*-oxide. Complete selectivity for Au(I) activation of the alkyne rather than metallocarbene formation from the diazoacetate occurred, and both aryl-substituted 1-(1,3-dienyl) aryldiazoacetates and the products from intramolecular [4+2]-cycloaddition of the diazo N=N bond to the diene were formed. Aryl-substituted (*E*)-1-(1,3-dienyl)

aryldiazoacetates underwent intramolecular [4+2]-diene-diazo cycloaddition under mild conditions without catalysis by the Au(I) reagent used in its formation and without evidence of a competing dipolar cycloaddition.[30] Cycloaddition was first order in the substrate, and both the activation parameters and the Hammett relationships for the conversion of (*E*)-**1** to **2** are consistent with those for other intramolecular Diels-Alder reactions.[31]

IV. Experimental Section

4.1 General Information

Unless noted all reactions were carried out under inert atmosphere of dinitrogen in oven-dried glassware with magnetic stirring using freshly distilled solvents. All solvents were purified and dried using standard methods. Analytical thin layer chromatography (TLC) plates were purchased from EM Science (silica gel 60 F_{254} plates). High-resolution mass spectra (HRMS) were performed on a microTOF-ESI mass spectrometer using CsI as the standard. Accurate masses are reported for the molecular ion $[M+Cs]^+$, $[M+Na]^+$, or $[M+H]^+$. Melting points were determined on an Electrothermo Mel-Temp DLX 104 device and were uncorrected. Column chromatography was performed on CombiFlash® Rf 200 purification system using normal phase disposable columns. IR

spectra were recorded using Bruker Vectcr 22 spectrometer. All NMR spectra were recorded on a Bruker spectrometer at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR) or an Agilent spectrometer at 500 MHz (^{1}H NMR) and 125 MHz (^{13}C NMR). Chemical shifts are reported in ppm with the solvent signals as reference (in CDCl$_3$ as solvent), and coupling constants (J) are given in Hertz (Hz). The peak information is described as: br = broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = composite of magnetically non-equivalent protons.

4.2 Materials

AuCl, AuCl$_3$, (PPh$_3$)AuCl, (IPr)AuCl were purchased from Sigma-Aldrich. AuCl(C$_4$H$_8$S) and AuCl$_3$(C$_5$H$_6$N) were purchased from Strem Chemicals. Pyridine *N*-oxides were purchased from Sigma-Aldrich or prepared according to the literature procedures.[32] Other chemicals were obtained from commercial sources and used without further purification.

4.3 Experimental Procedures

Synthesis of 1-[(4-chlorophenyl)ethynyl]cyclopentyl α-diazo-α-phenylacetate (4m).
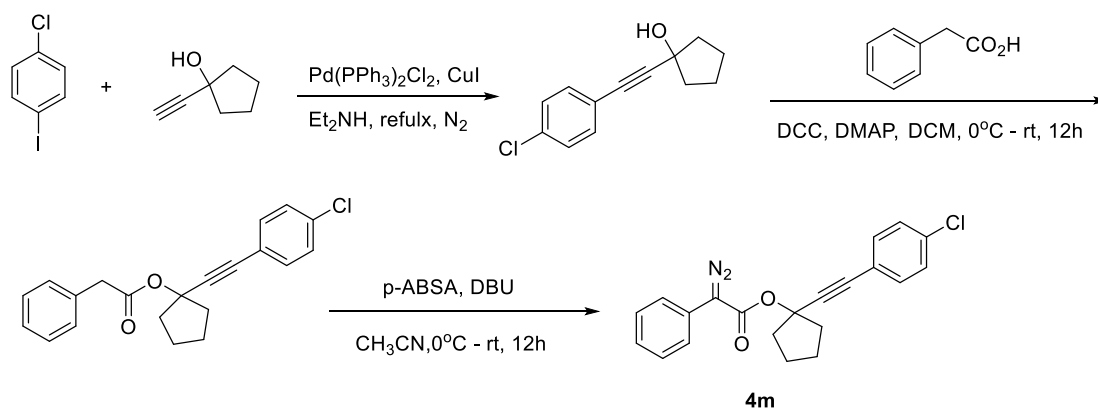
To a solution of Et$_2$NH (20 mL) in an oven-dried flask equipped with a magnetic stirring bar was added 1-ethynylcyclopentan-1-ol (1.10 g, 10.0 mmol), 1-chloro-4-iodobenzene (2.62 g, 11.0 mol), Pd(PPh$_3$)$_2$Cl$_2$ (700 mg, 1.0 mmol), CuI (38 mg, 2.0 mmol), and the reaction mixture was degassed with nitrogen. After stirring under refluxing conditions for 24 h, the solvent of the reaction mixture was removed with the use of a vacuum pump. The residue was purified by column chromatography (hexane/ethyl acetate = 10/1) to give 1-((4-chlorophenyl)ethynyl)cyclopentan-1-ol as a colorless oil (1.98 g, 90% yield).

To a solution of 1-[(4-chlorophenyl)ethynyl]cyclopentan-1-ol (1.10 mg, 5 mmol), phenylacetic acid (816 mg, 6 mmol) and DMAP (122 mg, 1 mmol) in dry DCM (30 mL) was added to a solution of DCC (1.24 g, 6 mmol) in dry DCM (20 mL) via addition funnel over 20 min at 0°C. The

resulting mixture was allowed to warm to room temperature, and stirred for another 10 h, and a white solid was formed in the process. The reaction solution was added to 30 mL of hexanes and then filtered through a Büchner funnel. After evaporating the solvent, the resulting reaction mixture was purified by column chromatography (hexane/ethyl acetate = 25/1) to give the 1-[(4-chlorophenyl)ethynyl]cyclopentyl 2-phenylacetate as a colorless oil (1.39 g, 82% yield).

To a solution of 1-[(4-chlorophenyl)ethynyl]cyclopentyl 2-phenylacetate (1.29 g, 4.1 mmol) and *p*-ABSA (1.20 g, 5 mmol) in dry CH_3CN (30 mL) was added DBU (0.76g, 5mmol) dropwise at $0^{\circ}C$. The resulting mixture was allowed to warm to room temperature, and stirred for another 10 h. The reaction was quenched with aqueous NH_4Cl solution (60 mL), and then extracted with diethyl ether (50 mL×2) and dried over anhydrous $MgSO_4$. After evaporating the solvent, the reaction mixture was purified by column chromatography (hexane/ethyl acetate = 30/1) to give the 1-[(4-chlorophenyl)ethynyl]cyclopentyl α-diazo-α-phenylacetate **4m** as a yellow oil (1.30 g, 85% yield).

Compounds **4n** – **4q** were prepared from corresponding iodo(bromo)-arenes using the same synthetic procedure with **4m**.

General Procedure for Gold Catalyzed Rearrangement of Propargyl Aryldiazoacetates in the Presence of 4-Chloropyridine *N*-Oxide:

To a flame-dried 10 mL Schlenk flask charged with a magnetic stirring bar, AuCl(SMe$_2$) (2.90 mg, 0.010 mmol), 4-chloropyridine *N*-oxide **6b** (25.9 mg, 0.20 mmol) and 2.0 mL toluene were added sequentially under nitrogen atmosphere. Then **4** (0.20 mmol) dissolved in 3.0 mL of toluene was added at once into the solution under the flow of nitrogen. The resulting mixture was allowed to stir for the stated time at room temperature, then purified by column chromatography (with 100:1 to 10:1 gradient of hexanes: ethyl acetate as eluents) to give isolated (*Z*)-**1** and **2**.

General Procedure for Deuterium Labeling Experiments

To a flame-dried 10 mL Schlenk flask charged with a magnetic stirring bar, AuCl(SMe$_2$) (2.90 mg, 0.010 mmol), 4-chloropyridine *N*-oxide **6b** (25.9 mg, 0.20 mmol), x (x = 1.0, 2.0, 5.0, 10.0) equiv. of deuterium oxide (D$_2$O) and 2.0 mL toluene were added sequentially under nitrogen atmosphere. Then **4a** (0.20 mmol) dissolved in 3.0 mL of toluene was added at once into the solution under the flow of nitrogen. The resulting mixture was allowed to stir for the 4 days at room temperature, then purified by column chromatography (with 100:1 to

10:1 gradient of hexanes: ethyl acetate as eluents) to give isolated (*Z*)-**1a** and **2a**. The percentage of deuterated products was determined by ^{1}H NMR analysis.

Kinetic Measurements:

Isolation of (*E*)-**1a:** To a flame-dried 10 mL Schlenk flask charged with a magnetic stirring bar, AuCl(SMe$_2$) (2.90 mg, 0.010 mmol), 4-chloropyridine-*N*-oxide (25.9 mg, 0.20 mmol) and 2.0 mL toluene were added sequentially under nitrogen atmosphere. Then **4** (0.20 mmol) dissolved in 3.0 mL of toluene was added at once into the solution under the flow of nitrogen. The resulting mixture was allowed to stir for 6 - 12 h at room temperature. The mixture of diene (*E*)-**1a** with (*Z*)-**1a** was isolated following the separation on the silica gel column chromatography (with 100:1 to 30:1 gradient of hexanes:ethyl acetate as eluents) and removal solvents in a water bath at 5 - 10$^\mathrm{o}$C under vacuum. The mixture of diene (*E*)-**1a** with (*Z*)-**1a** was obtained as light yellow oil and kept under nitrogen atmosphere at -78$^\mathrm{o}$C. Pure diene (*E*)-**1a** could be isolated by preparative TLC plates.

Data collection for the intermolecular cycloaddition reaction: Because (*E*)-**1a** is inert to [4+2]-cycloaddition and stable in CDCl$_3$ at room temperature, we decided to use the mixture of diene (*E*)-**1a** with

(*Z*)-**1a** for data collection. The mixture of diene (*E*)-**1a** with (*Z*)-**1a** (0.1 M for combined concentration) was diluted in $CDCl_3$ and placed in an NMR tube. The ratio of diene (*E*)-**1a** [δ 6.39 (s, 1H), 5.84 (t, *J* = 2.2 Hz, 1H) with (*Z*)-**1a** (1:1) [δ 6.55 (s, 1H), 5.90 (t, *J* = 2.4 Hz, 1H) was determined by ^{1}H NMR analysis (Agilent spectrometer at 500 MHz for ^{1}H NMR). The NMR tube was placed in an oil bath at 41°C with temperature stability of ±0.5^{o}C for 10.0 min and quenched by dry ice-acetone bath. The ^{1}H NMR spectra were recorded after the heating of each 10.0 (or 30.0) min. A control experiment was carried out which proved that the presence of (*Z*)-**1a** had no effect on the rate of intramolecular [4+2]-reaction or on the yield of products.

Computational methods for determining the progress of the intramolecular cycloaddition reaction: The amount of (*E*)-**1a** was determined by the integration of (*E*)-**1a** olefinic protons at δ = 6.39 (s, 1H, normalized as "1.00"), 5.84 (t, *J* = 2.2 Hz, 1H), and the difference was less than 5%. The amount of (*E*)-**1a**$_0$ was calculated by combined integration of (*E*)-**1a** with **2a** [δ 8.69 (d, *J* = 8.5, 2H), 6. 57 − 6.54 (m, 1H)] or the integration of (*Z*)-**1a** [δ 6.63 (s, 1H), 5.98 (t, *J* = 2.4 Hz, 1H), and the difference of two methods was less than 5%.

For other substituted derivatives: The mixture of diene (*E*)-**1** with (*Z*)-**1** was isolated following the same procedure as **1a** and was used directly for data collection of the intermolecular cycloaddition reaction. The amount of (*E*)-**1** was determined by the integration of (*E*)-**1** olefinic protons $\delta = 6.45 - 6.35$ (s, 1H, normalize as "1.00"), $5.85 - 5.75$, (t, 1H) and the difference was less than 5%. The amount of (*E*)-**1**$_0$ was calculated by combined integration of (*E*)-**1** with **2** [δ 8.80 − 8.60 (d, 2H), 6. 60 − 6.50 (m, 1H)] or the integration of (*Z*)-**1a** [δ 6.70 − 6.50 (s, 1H), 5.95 − 5.87 (t, 1H), and the difference of two methods was less than 5%.

First-order rate constants at different temperatures (20°C, 41°C, 49°C) were obtained by the same procedure: the time in oil bath ranged from every 5 min (49°C) to 1 h (20°C) with a temperature stability of $\pm 0.5^{\circ}$C (**Figure 3.9** to **Figure 3.12**). This intramolecular process was recorded at least 8 times. An Arrhenius plot was obtained from the kinetic rate constants that were obtained and their corresponding temperature (**Table 3.5** and **Figure 3.13**). The activation energy E_{act} was calculated from the slope of Arrhenius plot (E_{act} = -slope $\times$ R). $\Delta H^{\ddagger}_{298}$ and $\Delta S^{\ddagger}_{298}$ were calculated by the Eyring equation.
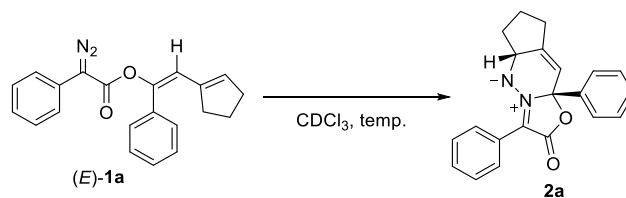
Table 3.5 Data for Arrhenius plot

lnk	-11.09	-10.12	-9.25	-8.52
1/T	0.003411	0.003299	0.003183	0.003104

Figure 3.9 First-order Rate Constant at 49 °C.

Figure 3.10 First-order Rate Constant at 41 °C.

Figure 3.11 First-order Rate Constant at 30 °C.

Figure 3.12 First-order Rate Constant at 20 °C.

Figure 3.13 Arrhenius plot: (*E*)-**1a** Activation Energy.

4.4 Characterization Data for New Compounds

(The characterization data for **4a, 4a-g** has been reported on Chapter 1 and 2.)

4b
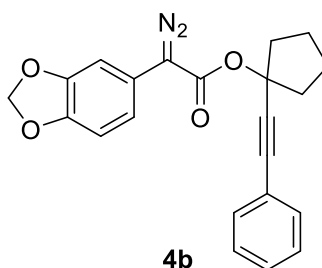
1-(Phenylethynyl)cyclopentyl 2-(benzo[d][1,3]dioxol-5-yl)-2-diazoacetate 4b: 63% yield. Red solid, m.p. 69.1 – 71.0°C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.47 – 7.39 (comp, 2H), 7.31 – 7.24 (comp, 3H), 7.10 (s, 1H), 6.88 (d, J = 8.2 Hz, 1H), 6.82 (d, J = 8.2 Hz, 1H), 5.96 (s, 2H), 2.44 – 2.35 (comp, 2H), 2.33 – 2.25 (comp, 2H), 1.86 – 1.75 (comp, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.79, 148.31, 145.92, 131.81, 128.27, 128.10, 122.64, 118.71, 117.71, 108.73, 105.68, 101.19, 89.33, 85.05, 82.13, 40.75, 23.42. IR (neat) 2085, 1700, 1492, 1235, 903 cm^{-1}. HRMS (ESI) m/z calculated for C$_{22}$H$_{18}$N$_2$O$_4$Na$^+$ [M+Na]$^+$ 397.1159, found: 397.1174.

4h
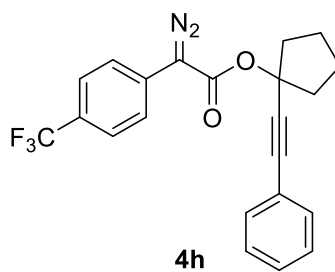
1-(Phenylethynyl)cyclopentyl 2-Diazo-2-[4-(trifluoromethyl)-phenyl]acetate 4h: 58% yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.68 – 7.57 (comp, 4H), 7.47 – 7.43 (comp, 2H), 7.33 – 7.25 (comp, 3H), 2.48 – 2.38 (comp, 2H), 2.37 – 2.26 (comp, 2H), 1.90 – 1.79 (comp, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 162.73, 131.82, 130.27, 128.42, 128.17, 127.47 (q, J = 32.5 Hz), 125.73 (q, J = 3.8 Hz), 124.09 (q, J =

270.2 Hz), 123.45, 122.53, 89.02, 85.39, 82.68, 40.78, 23.45. IR (neat)

2092, 1704, 1325, 1125, 1070, 903 cm^{-1}. HRMS (ESI) *m/z* calculated for

$C_{22}H_{17}N_2O_2F_3Na^+$ [M+Na]$^+$ 421.1134, found: 421.1131.

4i
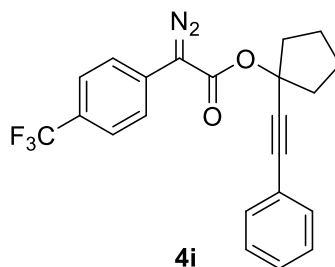
1-(Phenylethynyl)cyclopentyl 2-Diazo-2-(4-nitrophenyl)acetate

4i: 54% yield. Yellow solid, m.p. 113.4 – 114.5℃. ^{1}H NMR (500 MHz,

CDCl$_3$) δ 8.22 (d, *J* = 9.0 Hz, 2H), 7.68 (d, *J* = 9.0 Hz, 2H), 7.47 – 7.42

(comp, 2H), 7.32 – 7.27 (comp, 3H), 2.46 – 2.38 (comp, 2H), 2.35 – 2.28

(comp, 2H), 1.92 – 1.78 (comp, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ

162.03, 144.95, 134.04, 131.80, 128.49, 128.18, 124.20, 123.18, 122.38,

88.72, 85.57, 83.07, 40.75, 23.42. IR (neat) 2095, 1708, 1594, 1335,

1245, 1152, 903 cm^{-1}. HRMS (ESI) *m/z* calculated for $C_{21}H_{17}N_3O_4Na^+$

[M+Na]$^+$ 398.1111, found: 398.1135.

4j
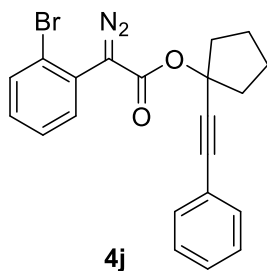
1-(Phenylethynyl)cyclopentyl   2-(2-Bromophenyl)-2-diazoacetate 4j: 60% yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.62 (d, *J* = 8.1 Hz, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.47 – 7.43 (comp, 2H), 7.36 (t, *J* = 7.7 Hz, 1H), 7.31 – 7.27 (comp, 3H), 7.19 (t, *J* = 7.7 Hz, 1H), 2.43 – 2.37 (comp, 2H), 2.33 – 2.25 (comp, 2H), 1.86 – 1.78 (comp, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.77, 133.28, 132.80, 131.80, 129.86, 128.24, 128.08, 127.55, 125.86, 122.69, 89.39, 85.01, 82.29, 40.72, 23.40. IR (neat) 2098, 1700, 1153, 902 cm^{-1}. HRMS (ESI) *m/z* calculated for C$_{21}$H$_{17}$N$_2$O$_2$BrNa$^+$ [M+Na]$^+$ 431.0366, found: 431.0386.

4k
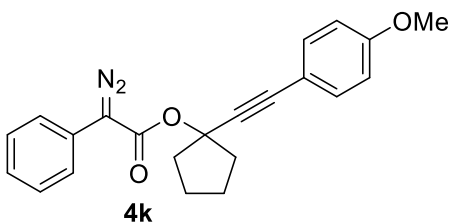
1-[(4-Methoxyphenyl)ethynyl]cyclopentyl   α-Diazo-α-phenyl-acetate 4k: 52% yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.52 (d, *J* = 7.7 Hz, 2H), 7.43 – 7.36 (comp, 4H), 7.18 (t, *J* = 8.5 Hz, 1H), 6.84 – 6.80 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 2.47 – 2.40 (comp, 2H), 2.35 – 2.27 (comp, 2H), 1.88 – 1.80 (comp, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.43, 159.56, 133.24, 128.77, 125.59, 123.86, 114.70, 113.68, 87.89, 84.95, 82.31, 55.15, 40.75, 23.37. IR (neat) 2087, 1702, 1510, 1247,

1149, 903 cm^{-1}. HRMS (ESI) *m/z* calculated for C$_{22}$H$_{20}$N$_2$O$_3$Na$^+$ [M+Na]$^+$

383.1366, found: 383.1364.

4l
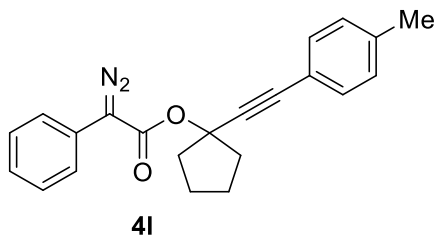
1-(p-Tolylethynyl)cyclopentyl α-Diazo-α-phenylacetate 4l: 60%

yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) 7.51 (d, *J* = 8.1 Hz, 2H),

7.40 – 7.32 (comp, 4H), 7.19 – 7.15 (m, 1H), 7.09 (d, *J* = 8.1 Hz, 2H),

2.46 – 2.38 (comp, 2H), 2.35 – 2.26 (comp, 5H), 1.88 – 1.79 (comp, 4H).

^{13}C NMR (125 MHz, CDCl$_3$) δ 163.49, 138.35, 131.71, 128.86, 128.83,

125.66, 123.95, 119.58, 88.61, 85.21, 82.29, 40.78, 23.43, 21.43. IR (neat)

2079, 1703, 1598, 1498, 1244, 1142, 1003 cm^{-1}. HRMS (ESI) *m/z*

calculated for C$_{22}$H$_{20}$N$_2$O$_2$Na$^+$ [M+Na]$^+$ 367.1417, found: 367.1426.

4m
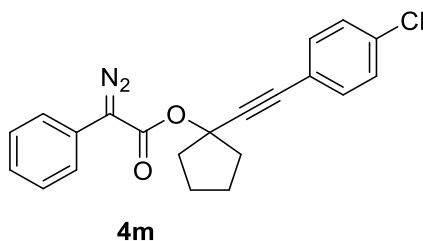
1-[(4-Chlorophenyl)ethynyl]cyclopentyl **α-Diazo-α-**

phenylacetate 4m: 62% yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$)

δ 7.51 (d, *J* = 7.7 Hz, 2H), 7.41 – 7.36 (comp, 4H), 7.27 (d, *J* = 7.7 Hz,

2H), 7.19 (t, J = 9.6 Hz, 1H), 2.47 – 2.38 (comp, 2H), 2.36 – 2.28 (comp,

2H), 1.89 – 1.80 (comp, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.48,

134.30, 133.03, 128.86, 128.44, 125.74, 125.52, 123.93, 121.16, 90.33,

83.96, 81.97, 40.71, 23.44. IR (neat) 2087, 1701, 1149, 903 cm^{-1}. HRMS

(ESI) m/z calculated for C$_{21}$H$_{17}$N$_2$O$_2$ClNa$^+$ [M+Na]$^+$ 387.0871, found:

387.0883.

4n
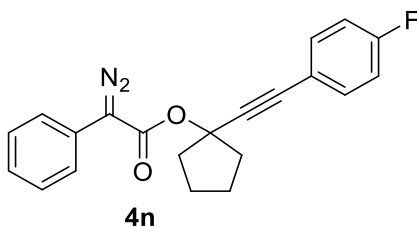
1-[(4-Fluorophenyl)ethynyl]cyclopentyl α-Diazo-α-phenyl-

acetate 4n: 61% yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.50

(d, J = 8.4 Hz, 2H), 7.45 – 7.40 (comp, 2H), 7.40 – 7.35 (comp, 2H), 7.18

(t, J = 7.5, 1H), 7.98 (t, J = 7.5, 1H), 2.45 – 2.38 (comp, 2H), 2.33 – 2.25

(comp, 2H), 1.87 – 1.79 (comp, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ

163.51, 162.52 (d, J = 249.9 Hz), 133.74 (d, J = 8.3 Hz), 128.87, 125.73,

125.58, 123.95, 118.74(d, J = 3.5 Hz), 115.39 (d, J = 22.4 Hz), 89.05,

84.03, 82.07, 40.74, 23.44. IR (neat) 2085, 1702, 1505, 1246, 1147, 905

cm^{-1}. HRMS (ESI) m/z calculated for C$_{21}$H$_{17}$N$_2$O$_2$FNa$^+$ [M+Na]$^+$

371.1166, found: 371.1179.

4o
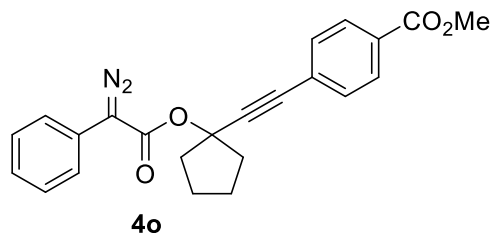
Methyl 4-[(1-(2-Diazo-2-phenylacetoxy)cyclopentyl]ethynyl benzoate 4o: 57% yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.96 (d, J = 8.2 Hz, 2H), 7.52 – 7.48 (comp, 4H), 7.38 (t, J = 7.9 Hz, 2H), 7.18 (t, J = 10.6, 1H), 3.90 (s, 3H), 2.45 – 2.37 (comp, 2H), 2.35 – 2.25 (comp, 2H), 1.88 – 1.79 (comp, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 166.50, 163.49, 131.69, 129.54, 129.28, 128.88, 127.39, 125.77, 125.48, 123.94, 92.38, 84.35, 81.86, 52.16, 40.71, 23.46. IR (neat) 2081, 1703, 1605, 1273, 1145, 1004 cm^{-1}. HRMS (ESI) *m/z* calculated for C$_{23}$H$_{20}$N$_2$O$_4$Na$^+$ [M+Na]$^+$ 411.1315, found: 411.1314.

4p
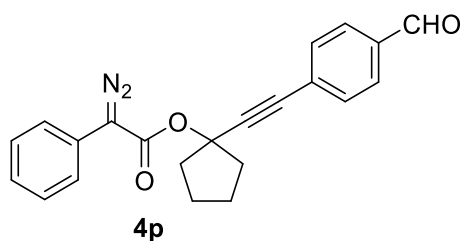
1-[(4-Formylphenyl)ethynyl]cyclopentyl α-Diazo-α-phenyl-acetate 4p: 53% yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.99 (s, 1H), 7.81 (d, J = 8.1 Hz, 2H), 7.60 (d, J = 8.1 Hz, 2H), 7.51 (d, J = 7.7 Hz, 2H), 7.40 (t, J = 7.7 Hz, 2H), 7.19 (t, J = 7.7 Hz, 1H), 2.46 – 2.40

(comp, 2H), 2.36 – 2.29 (comp, 2H), 1.89 – 1.83 (comp, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 191.41, 163.48, 135.47, 132.28, 129.34, 128.97, 128.89, 125.80, 125.42, 123.93, 93.49, 84.23, 81.75, 40.69, 23.47. IR (neat) 2087, 1709, 1497 cm^{-1}. HRMS (ESI) *m/z* calculated for C$_{22}$H$_{18}$N$_2$O$_3$Na$^+$ [M+Na]$^+$ 381.1210, found: 381.1219.

4q
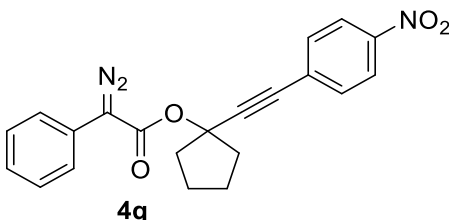
1-[(4-Nitrophenyl)ethynyl]cyclopentyl α-Diazo-α-phenylacetate

4q: 47% yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.14 (d, *J* = 9.0 Hz, 2H), 7.58 (d, *J* = 9.0 Hz, 2H), 7.48 (d, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.19 (t, *J* = 7.5 Hz, 1H), 2.47 – 2.39 (comp, 2H), 2.35 – 2.28 (comp, 2H), 1.88 – 1.82 (comp, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.49, 147.07, 132.48, 129.60, 128.91, 125.86, 125.33, 123.92, 123.37, 94.81, 83.30, 81.56, 40.65, 23.48. IR (neat) 2090, 1703, 1521, 1346, 1150, 906 cm^{-1}. HRMS (ESI) *m/z* calculated for C$_{21}$H$_{17}$N$_3$O$_4$Na$^+$ [M+Na]$^+$ 398.1111, found: 398.1124.

(*Z*)-**1a**
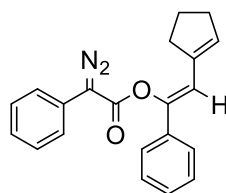
(Z)-2-(Cyclopent-1-en-1-yl)-1-phenylvinyl α-Diazo-α-phenyl-acetate 1a: 32% yield. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.47 (d, J = 7.6 Hz, 2H), 7.40 (d, J = 7.5 Hz, 2H), 7.32 (t, J = 7.6 Hz, 2H), 7.26 (t, J = 7.5 Hz, 2H), 7.20 − 7.18 (m, 1H), 7.15 − 7.12 (m, 1H), 6.55 (s, 1H), 5.90 (t, J = 2.4 Hz, 1H), 2.60 (t, J = 6.4 Hz, 2H), 2.32 (dt, J = 7.6, 2.4 Hz, 2H), 1.90 − 1.80 (comp, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.24, 143.72, 138.56, 135.57, 135.44, 129.03, 128.62, 128.23, 126.09, 124.79, 124.47, 123.83, 115.08, 33.06, 32.19, 23.82. HRMS (ESI) *m/z* calculated for C$_{21}$H$_{18}$N$_2$O$_2$Cs$^+$ [M+Cs]$^+$ 463.0417, found: 463.0437.
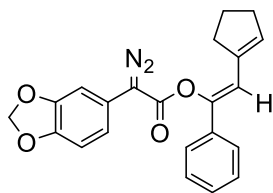
(*Z*)-**1b**

(Z)-2-(Cyclopent-1-en-1-yl)-1-phenylvinyl 2-(Benzo[d][1,3]-dioxol-5-yl)-2-diazoacetate 1b: 38% yield. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.46 (d, J = 7.0 Hz, 2H), 7.34 (t, J = 7.0 Hz, 2H), 7.29 − 7.27 (m, 1H), 7.14 − 7.09 (m, 1H), 6.92 (d, J = 8.2 Hz, 1H), 6.85 (d, J = 8.2 Hz, 1H), 6.61 (s, 1H), 5.97 (t, J = 2.0 Hz, 1H), 5.96 (s, 2H), 2.67 (t, J = 6.3 Hz, 2H), 2.40 (dt J = 7.3, 2.0 Hz, 2H), 1.97 − 1.90 (comp, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 163.61, 148.50, 146.27, 143.75, 138.55, 135.58, 135.42, 128.62, 128.23, 124.47, 124.38, 117.82, 115.06, 108.87, 105.63,

101.33, 33.06, 32.20, 23.83. HRMS (ESI) *m/z* calculated for C22H18N2O4Cs+ [M+Cs]+ 507.0316, found: 507.0319.
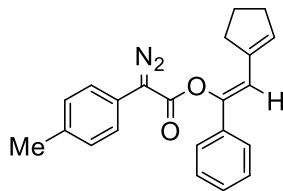
(*Z*)-**1c**

(Z)-2-(Cyclopent-1-en-1-yl)-1-phenylvinyl α-Diazo-α-(*p*-tolyl)-acetate 1c: 40% yield. ^{1}H NMR (500 MHz, CDCl3) δ 7.49 (d, *J* = 7.3 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.34 (t, *J* = 7.3 Hz, 2H), 7.31 -7.28 (m, 1H), 7.22 (d, *J* = 8.5 Hz, 2H), 6.63 (s, 1H), 5.98 (t, *J* = 2.3 Hz, 1H), 2.68 (t, *J* = 6.5 Hz, 2H), 2.40 (dt, *J* = 7.5, 2.3 Hz, 2H), 2.35 (s, 3H), 1.92 − 1.83 (comp, 2H). ^{13}C NMR (125 MHz, CDCl3) δ 163.48, 143.76, 138.60, 136.03, 135.61, 135.38, 129.75, 128.60, 128.20, 124.47, 123.94, 121.40, 115.05, 33.05, 32.19, 23.82, 20.99. HRMS (ESI) *m/z* calculated for C22H20N2O2Cs+ [M+Cs]+ 477.0574, found: 477.0592.
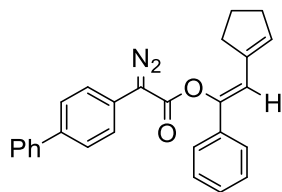
(*Z*)-**1d**

(Z)-2-(Cyclopent-1-en-1-yl)-1-phenylvinyl 2-([1,1'-Biphenyl]-4-yl)-2-diazoacetate 1d: 38% yield. ^{1}H NMR (500 MHz, CDCl3) δ 7.66 − 7.62 (comp, 3H), 7.61 − 7.57 (comp, 3H), 7.51 − 7.47 (comp, 2H), 7.43 −

7.46 (comp, 2H), 7.37 − 7.33 (comp, 3H), 7.30 − 7.28 (m, 1H), 6.64 (s,

1H), 5.99 (t, J = 2.4 Hz, 1H), 2.69 (t, J = 6.5 Hz, 2H), 2.41 (dt, J = 7.5,

2.4 Hz, 2H), 1.88 (tt, J = 7.5, 6.5 Hz, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ

163.27, 143.73, 140.21, 138.93, 138.55, 135.56, 135.52, 128.84, 128.65,

128.26, 127.68, 127.43, 126.87, 124.48, 124.15, 123.64, 115.12, 33.08,

32.20, 23.84. HRMS (ESI) m/z calculated for C$_{27}$H$_{22}$N$_2$O$_2$Cs$^+$ [M+Cs]$^+$

539.0730, found: 539.0757.
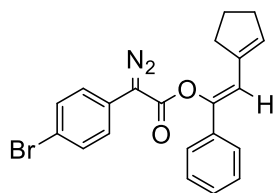
(*Z*)-**1e**

(Z)-2-(Cyclopent-1-en-1-yl)-1-phenylvinyl 2-(4-Bromophenyl)-

2-diazoacetate 1e: 39% yield. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.51 (d, J

= 8.8 Hz, 2H), 7.46 (d, J = 7.5 Hz, 2H), 7.42 (d, J = 8.8 Hz, 2H), 7.36 −

7.32 (comp, 2H), 7.29 (t, J = 7.5 Hz, 1H), 6.62 (s, 1H), 5.98 (t, J = 2.2 Hz,

1H), 2.65 (t, J = 6.3 Hz, 2H), 2.40 (dt J = 8.2, 2.2 Hz, 2H), 1.96 − 1.91

(comp, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 162.97, 143.61, 138.40,

135.65, 135.44, 132.10, 128.65, 128.30, 125.23, 124.43, 123.98, 119.67,

115.15, 33.05, 32.18, 23.80. HRMS (ESI) m/z calculated for

C$_{21}$H$_{17}$N$_2$O$_2$BrCs$^+$ [M+Cs]$^+$ 540.9522, found:540.9539.
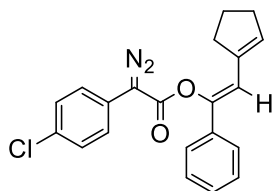
(Z)-1f

(Z)-2-(Cyclopent-1-en-1-yl)-1-phenylvinyl 2-(4-Chlorophenyl)-2-diazo-acetate 1f: 36% yield. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.48 (comp, 4H), 7.38 − 7.33 (comp, 4H), 7.29 (t, J = 7.3 Hz, 1H), 6.62 (s, 1H), 5.99 (t, J = 2.5 Hz ,1H), 2.66 (t, J = 6.6 Hz, 2H), 2.40 (dt, J = 7.6, 2.5 Hz, 2H), 1.97 − 1.90 (comp, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.00, 143.64, 138.42, 135.64, 135.47, 131.83, 129.19, 128.66, 128.31, 124.99, 124.45, 123.41, 115.16, 33.06, 32.19, 23.81. HRMS (ESI) m/z calculated for C$_{21}$H$_{17}$N$_2$O$_2$ClCs^{+} [M+Cs]$^{+}$ 497.0028, found:497.0047.
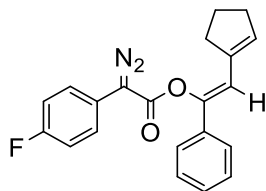
(Z)-1g

(Z)-2-(Cyclopent-1-en-1-yl)-1-phenylvinyl 2-Diazo-2-(4-fluoro-phenyl)-acetate 1g: 34% yield. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.53 − 7.44 (comp, 4H), 7.34 (t, J = 7.5 Hz, 1H), 7.30 − 7.26 (comp, 1H), 7.10 (d, J = 7.5 Hz, 2H), 6.62 (s, 1H), 6.97 (t, J = 2.5 Hz ,1H), 2.66 (t, J = 6.5 Hz ,2H), 2.40 (dt, J = 7.6, 2.5 Hz, 2H), 1.98 − 1.89 (comp, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.33, 161.20 (d, J = 247.9 Hz), 143.70, 138.48,

135.56, 135.53, 128.65, 128.29, 125.81(d, J = 7.8 Hz), 124.46, 120.52 (d, J = 1.9 Hz), 116.15 (d, J = 21.9 Hz), 115.13, 33.07, 32.20, 23.83. HRMS (ESI) m/z calculated for $C_{21}H_{17}N_2O_2FCs^+$ [M+Cs]$^+$ 481.0323, found:481.0338.
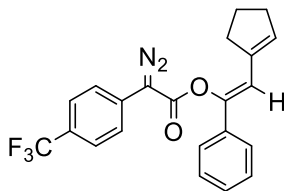
(*Z*)-**1h**

(Z)-2-(Cyclopent-1-en-1-yl)-1-phenylvinyl   2-Diazo-2-[4-(trifluoromethyl)phenyl]acetate 1h: 32% yield. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.69 – 7.64 (comp, 4H), 7.48 (d, J = 8.3 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.32 – 7.28 (m, 1H), 6.65 (s, 1H), 6.01 (t, , J = 2.6 Hz, 1H), 2.67 (t, J = 6.7 Hz, 2H), 2.42(dt, J = 7.8 Hz, 2.6 Hz, 2H), 1.98 – 1.92 (m, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 162.57, 143.55, 138.33, 135.83, 135.37, 129.36, 128.69, 128.41, 127.91 (q, J = 32.4 Hz), 125.93 (q, J = 3.8 Hz), 124.44, 123.96 (q, J = 270.2 Hz), 123.42, 115.24, 33.06, 32.19, 23.81. HRMS (ESI) m/z calculated for $C_{22}H_{17}N_2O_2F_3Cs^+$ [M+Cs]$^+$ 531.0291, found: 531.0317.
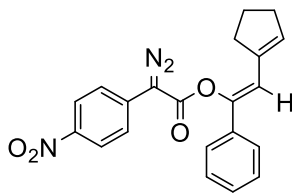
(*Z*)-**1i**

(Z)-2-(Cyclopent-1-en-1-yl)-1-phenylvinyl 2-Diazo-2-(4-nitro-phenyl)-acetate 1i: 18% yield. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.24 (d, J = 9.0 Hz, 2H), 7.70 (d, J = 9.0 Hz, 2H), 7.46 (d, J = 7.4 Hz, 2H), 7.36 (t, J = 7.4 Hz, 2H), 7.32 - 7.28 (m, 1H), 6.64 (s, 1H), 6.01 (t, J = 2.4 Hz, 1H), 2.65 (t, J = 6.4 Hz, 2H), 2.41 (dt, J = 7.5, 2.4 Hz, 2H), 1.97 − 1.91 (comp, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 162.00, 145.34, 143.46, 138.17, 136.11, 135.22, 133.05, 128.75, 128.48, 124.43, 124.37, 123.30, 115.36, 33.09, 32.20, 23.81. HRMS (ESI) m/z calculated for C$_{21}$H$_{17}$N$_3$O$_4$Cs$^+$ [M+Cs]$^+$ 508.0268, found: 508.0286.
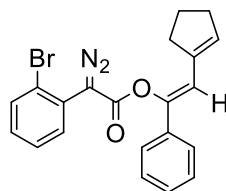
(*Z*)-**1j**

(Z)-2-(Cyclopent-1-en-1-yl)-1-phenylvinyl 2-(2-Bromophenyl)-2-diazo-acetate 1j: 20% yield. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.66 (d, J = 8.0 Hz, 1H), 7.59 (d, J = 7.2 Hz, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.41 − 7.33 (comp, 3H), 7.31 − 7.27 (m, 1H), 7.26 − 7.23 (m, 1H), 6.59 (s, 1H), 5.97 (t, J = 2.2 Hz, 1H), 2.75 − 2.65 (comp, 2H), 2.40 (dt, J = 7.0, 2.2 Hz, 2H), 2.00 − 1.92 (comp, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.78, 144.00, 138.59, 135.56, 135.27, 135.23, 133.34, 130.52 130.51, 128.58,

128.19, 127.83, 124.52, 114.95, 114.91, 33.21, 32.24, 23.80. HRMS (ESI)

m/z calculated for $C_{21}H_{17}N_2O_2BrCs^+$ [M+Cs]$^+$ 540.9522, found: 540.9552.

(Z)-**1k**   OMe
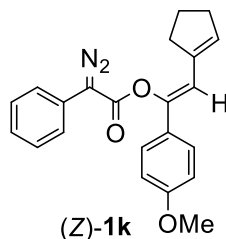
(Z)-2-(Cyclopent-1-en-1-yl)-1-(4-methoxyphenyl)vinyl α-Diazo-α-phenylacetate 1k: 42% yield. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.55 (d, *J* = 8.9 Hz, 2H), 7.42– 7.38 (comp, 4H), 7.21 (t, *J* = 7.4 Hz, 1H), 6.87 (d, *J* = 8.9 Hz, 2H), 6.51 (s, 1H), 5.93 (t, *J* = 2.4 Hz, 1H), 3.80 (s, 3H), 2.66 (t, *J* = 6.8 Hz, 2H), 2.39 (dt, *J* = 7.8, 2.4 Hz, 2H), 1.95 – 1.89 (comp, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 159.69, 143.65, 138.59, 134.37, 129.02, 128.24, 126.06, 125.90, 124.84, 123.82, 114.09, 113.90, 113.42, 55.30, 33.10, 32.15, 23.83. HRMS (ESI) *m/z* calculated for $C_{22}H_{20}N_2O_3Cs^+$ [M+Cs]$^+$ 493.0523, found: 493.0539.

(Z)-**1l**   OMe
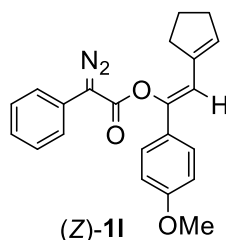
(Z)-2-(Cyclopent-1-en-1-yl)-1-(*p*-tolyl)vinyl α-Diazo-α-phenyl-acetate 1l: 41% yield. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.55(d, *J* = 8.0 Hz, 2H), 7.42 – 7.36 (comp, 4H), 7.21 (t, *J* = 7.57, 1H), 7.15 (d, *J* = 7.7 Hz,

191

2H), 6.58 (s, 1H), 5.95 (t, J = 2.0 Hz, 1H), 2.67 (t, J = 6.6 Hz, 2H), 2.39

(dt, J = 7.6, 2.0 Hz, 2H), 2.34 (s, 3H), 1.97 – 1.89 (comp, 2H). ^{13}C NMR

(125 MHz, CDCl$_3$) δ 163.25, 143.90, 138.61, 138.23, 134.88, 132.79,

129.36, 129.02, 126.05, 124.85, 124.41, 123.82, 114.20, 33.10, 32.17,

23.84, 21.20. HRMS (ESI) m/z calculated for $C_{22}H_{20}N_2O_2Cs^+$ [M+Cs]$^+$

477.0574, found: 477.0587.

(Z)-**1m** Cl
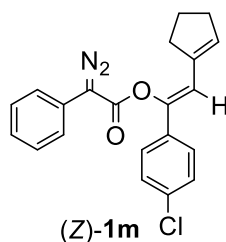
(Z)-1-(4-Chlorophenyl)-2-(cyclopent-1-en-1-yl)vinyl α-Diazo-α-

phenyl-acetate 1m: 40% yield. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.54 (d, J

= 8.5 Hz, 2H), 7.44 – 7.38 (comp, 4H), 7.34 – 7.29 (d, J = 7.4 Hz, 2H),

7.23 (t, J = 7.4 Hz, 1H), 6.61 (s, 1H), 6.00 (t, J = 2.4 Hz, 1H), 2.67 (t, J =

6.3 Hz, 2H), 2.41 (dt, J = 7.7, 2.4 Hz, 2H), 1.98 – 1.91 (comp, 2H). ^{13}C

NMR (125 MHz, CDCl$_3$) δ 163.17, 142.69, 138.40, 136.12, 134.22,

134.02, 129.08, 128.84, 126.21, 125.75, 124.60, 123.84, 115.58, 32.99,

32.22, 23.81. HRMS (ESI) m/z calculated for $C_{21}H_{17}N_2O_2ClCs^+$ [M+Cs]$^+$

497.0028, found: 497.0048.

(Z)-1n
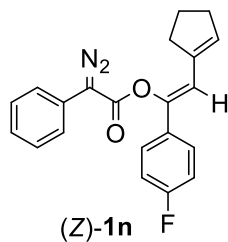
(Z)-2-(Cyclopent-1-en-1-yl)-1-(4-fluorophenyl)vinyl α-Diazo-α-phenylacetate 1n: 36% yield. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.55 (d, J = 8.1 Hz, 2H), 7.46 (d, J = 8.1 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 7.23 (t, J = 8.0 Hz, 1H), 7.04 (t, J = 8.0 Hz, 2H), 6.56 (s, 1H), 5.97 (t, J = 2.5 Hz, 1H), 2.67 (t, J = 6.5 Hz, 2H), 2.40 (dt, J = 7.9, 2.5 Hz, 2H), 1.98 − 1.90 (comp, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.20, 162.65 (d, J = 247.1 Hz), 142.86, 138.40, 135.73 (d, J = 3.3 Hz), 131.90, 129.07, 126.35(d, J = 8.1 Hz), 126.19, 124.64, 123.84, 115.65 (d, J = 21.8 Hz), 115.02, 33.02, 32.19, 23.81. HRMS (ESI) m/z calculated for C$_{21}$H$_{17}$N$_2$O$_2$FCs$^+$ [M+Cs]$^+$ 481.0323, found: 481.0332.

(Z)-1o   CO$_2$Me
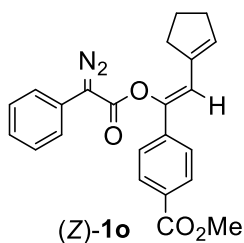
Methyl (Z)-4-(2-(Cyclopent-1-en-1-yl)-1-[(2-diazo-2-phenyl-acetoxy)vinyl]benzoate 1o: 36% yield. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.01(d, J = 8.6 Hz, 2H), 7.56 − 7.52 (comp, 4H), 7.44 − 7.38 (comp, 2H), 7.21 (t, J = 7.4 Hz, 1H), 6.58 (s, 1H), 6.08 − 6.05 (m, 1H), 3.91 (s, 3H),

2.71 – 2.65 (comp, 2H), 2.45 – 2.39 (comp, 2H), 1.99 – 1.91 (comp, 2H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 166.59, 163.15, 142.69, 139.92, 138.48, 137.27, 129.97, 129.09, 126.24, 124.56, 124.23, 123.87, 117.18, 52.12, 32.95, 32.30, 23.82. HRMS (ESI) *m/z* calculated for C$_{23}$H$_{20}$N$_2$O$_4$Cs$^+$ [M+Cs]$^+$ 521.0472, found: 521.0494.

(*Z*)-**1p**   CHO
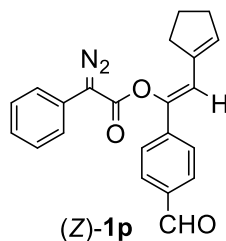
(*Z*)-2-(Cyclopent-1-en-1-yl)-1-(4-formylphenyl)vinyl α-Diazo-α-phenylacetate 1p: 36% yield. ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.98 (s, 1H), 7.86 (d, *J* = 8.6 Hz, 2H), 7.63 (d, *J* = 8.6 Hz, 2H), 7.54 (d, *J* = 7.7 Hz, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.23 (t, *J* = 7.7 Hz, 1H), 6.79 (s, 1H), 6.10 (t, *J* = 2.5 Hz, 1H), 2.69 (t, *J* = 7.3 Hz, 2H), 2.43 (dt, *J* = 7.5, 2.5 Hz, 2H), 1.95 (dd, *J* = 15.0, 7.4 Hz, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 191.41, 163.05, 142.42, 141.42, 138.49, 138.02, 135.66, 130.11, 129.12, 126.31, 124.79, 124.46, 123.87, 118.02, 32.91, 32.35, 23.82. HRMS (ESI) *m/z* calculated for C$_{22}$H$_{18}$N$_2$O$_3$Cs$^+$ [M+Cs]$^+$ 491.0366, found: 491.0393.

2a
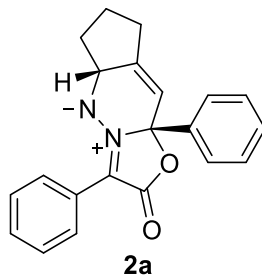
2-Oxo-3,9a-diphenyl-2,5a,6,7,8,9a-hexahydrocyclopenta[e]-oxazolo[3,2-b]pyridazin-4-ium-5-ide 2a: 48% yield. Light yellow solid, 100 °C(dec.); ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.69 d, J = 8.5, 2H), 7.69 – 7.42 (comp, 2H), 7.41 – 7.10 (comp, 6H), 6. 57 – 6.54 (m, 1H), 3.82 (t, J = 8.2 Hz, 1H), 2.66 – 2.36 (comp, 3H), 2.16 – 1.85 (comp, 2H), 1.83 – 1.61 (m, 1H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 163.94, 148.42, 135.16, 130.09, 128.89, 128.10, 127.70, 127.61, 126.01, 125.43, 115.87, 104.8, 96.70, 68.15, 32.15, 29.41, 24.42. HRMS (ESI) m/z calculated for C$_{21}$H$_{19}$N$_2$O$_2{}^+$ [M+H]$^+$ 331.1441, found: 331.1461.

2b
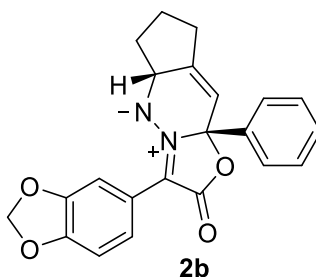
3-(Benzo[d][1,3]dioxol-5-yl)-2-oxo-9a-phenyl-2,5a,6,7,8,9a-hexahydro-cyclopenta[e]oxazolo[3,2-b]pyridazin-4-ium-5-ide 2b: 54% yield. Yellow solid, 100 °C(dec.); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.32 (d,

J = 8.8 Hz, 2H), 7.42 – 7.32 (comp, 3H), 7.28 (d, J = 7.3 Hz, 2H), 6.96 –

6.92 (m, 1H), 6.56 – 6.52 (m, 1H), 6.01 (s, 2H), 3.78 (t, J = 8.6 Hz, 1H),

2.59 – 2.44 (comp., 3H), 2.05 - 1.90 (comp, 2H), 1.80 – 1.74 (m, 1H).[13]C

NMR (125 MHz, CDCl$_3$) δ 163.93, 148.52, 147.28, 146.79, 135.30,

130.04, 128.87, 125.96, 121.87, 120.26, 115.83, 108.13, 105.56, 101.05,

101.01, 96.45, 67.96, 32.23, 29.42, 24.41. HRMS (ESI) *m/z* calculated

for C$_{22}$H$_{19}$N$_2$O$_4$[+] [M+H][+] 375.1339, found: 375.1358.

2c

2-Oxo-9a-phenyl-3-(*p*-tolyl)-2,5a,6,7,8,9a-hexahydrocyclo-

penta[e]-oxazolo[3,2-b]pyridazin-4-ium-5-ide 2c: 54% yield. Light

yellow solid, 100 ℃ (dec.); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.58 (d, J =

8.2 Hz, 2H), 7.39 – 7.36 (m, 1H), 7.36 – 7.27 (comp, 6H), 6.56 – 6.53 (m,

1H), 3.78 (t, J = 8.7 Hz, 1H), 2.58 – 2.44 (comp, 3H), 2.40 (s, 3H), 2.04 –

1.98 (comp, 1H), 1.97 – 1.90 (m, 1H), 1.80 – 1.74 (m, 1H). ^{13}C NMR

(125 MHz, CDCl$_3$) δ 163.99, 148.46, 137.67, 135.32, 130.03, 128.86,

128.80, 126.02, 125.44, 124.90, 115.86, 105.61, 96.56, 68.03, 32.21,

29.43, 24.42, 21.49. HRMS (ESI) *m/z* calculated for C$_{22}$H$_{21}$N$_2$O$_2$[+]

[M+H][+] 345.1598, found: 345.1616.

2d

3-([1,1'-Biphenyl]-4-yl)-2-oxo-9a-phenyl-2,5a,6,7,8,9a-hexahydro-cyclopenta[e]oxazolo[3,2-b]pyridazin-4-ium-5-ide 2d: 53% yield. Light yellow solid, 100 ℃ (dec.); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.80 (d, *J* = 8.7 Hz, 2H), 7.74 (d, *J* = 8.7 Hz, 2H), 7.69 − 7.66 (comp, 2H), 7.49 − 7.45 (comp, 2H), 7.41 − 7.36 (comp, 3H), 7.36 − 7.33 (comp, 3H), 6.60 − 6.57 (m, 1H), 3.84 (t, *J* = 8.7 Hz, 1H), 2.63 − 2.44 (comp, 3H), 2.10 − 2.01 (m, 1H), 2.00 − 1.91 (m, 1H), 1.85 − 1.74 (m, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.95, 148.45, 140.65, 140.00, 135.16, 130.12, 128.91, 128.80, 127.38, 126.97, 126.73, 126.69, 126.01, 125.76, 115.88, 105.38, 96.75, 68.22, 32.18, 29.42, 24.43. HRMS (ESI) *m/z* calculated for C$_{27}$H$_{23}$N$_2$O$_2^+$ [M+H]$^+$ 407.1754, found: 407.1765.

2e
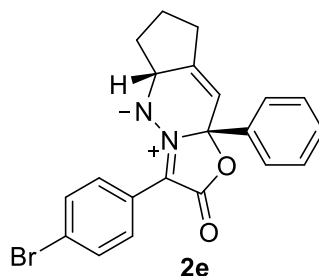
3-(4-Bromophenyl)-2-oxo-9a-phenyl-2,5a,6,7,8,9a-hexahydro-cyclopenta[e]-oxazolo[3,2-b]pyridazin-4-ium-5-ide 2e: 50% yield. Light yellow solid, 100 ℃ (dec.); ^{1}H NMR (500 MHz, CDCl3) δ 8.58 (d, J = 8.8 Hz,, 2H), 7.56 (d, J = 8.8 Hz, 2H), 7.40 – 7.30 (comp, 3H), 7.28– 7.24 (comp, 2H), 6.54 – 5.51 (m, 1H), 3.76 (t, J = 8.7 Hz, 1H), 2.60 – 2.42 (comp, 3H), 2.03 – 1.89 (comp, 2H), 1.80 – 1.72 (m, 1H). ^{13}C NMR (125 MHz, CDCl3) δ 163.71, 148.46, 134.99, 131.24, 130.21, 128.97, 126.89, 126.67, 125.97, 121.20, 115.83, 104.87, 96.98, 68.32, 32.15, 29.42, 24.42. HRMS (ESI) m/z calculated for $C_{21}H_{18}N_2O_2Br^+$ $[M+H]^+$ 409.0546, found: 409.0565.

2f

3-(4-Chlorophenyl)-2-oxo-9a-phenyl-2,5a,6,7,8,9a-hexahydro-cyclopenta[e]oxazolo[3,2-b]pyridazin-4-ium-5-ide 2f: 52% yield. Light yellow solid, 100 ℃ (dec.); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.66 (d, J = 8.6 Hz, 2H), 7.42 (d, J = 8.6 Hz, 2H), 7.38 (t, J = 7.6 Hz, 1H), 7.34 (t, J = 7.6 Hz, 2H), 7.29 (d, J = 7.6 Hz, 2H), 6.55 – 6.52 (m, 1H), 3.79 (t, J = 8.6 Hz, 1H), 2.60 – 2.44 (comp, 3H), 2.04 – 1.92 (comp, 2H), 1.78 (m, 1H).

^{13}C NMR (125 MHz, CDCl$_3$) δ 163.78, 148.45, 134.95, 132.90, 130.20, 128.95, 128.27, 126.64, 126.21, 125.95, 115.79, 104.79, 96.93, 68.26, 32.13, 29.39, 24.41. HRMS (ESI) *m/z* calculated for C$_{21}$H$_{18}$N$_2$O$_2$Cl$^+$ [M+H]$^+$ 365.1051, found: 365.1071.

2g
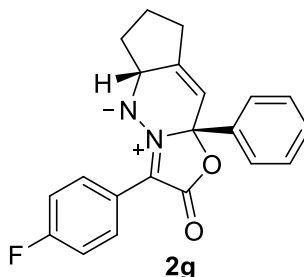
3-(4-Fluorophenyl)-2-oxo-9a-phenyl-2,5a,6,7,8,9a-hexahydro-cyclopenta[e]oxazolo[3,2-b]pyridazin-4-ium-5-ide 2g: 50% yield. Light yellow solid, 100 ℃ (dec.); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.70 (d, *J* = 8.7 Hz, 2H),, 7.41 − 7.32 (comp, 3H), 7.29 (t, *J* = 7.4 Hz, 2H), 7.15 (d, *J* = 7.4 Hz, 2H), 6.57− 6.53 (m, 1H), 3.79 (t, *J* = 8.2 Hz, 1H), 2.62 − 2.40 (comp, 3H), 2.05 − 1.90 (comp, 2H), 1.82 − 1.73 (m, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.93, 161.60 (d, *J*=248.2 Hz), 148.51, 135.07, 130.15, 128.92, 127.54 (d, *J*=7.5 Hz), 125.96, 123.98, 115.5 (d, *J*=21.3 Hz), 114.99, 104.90, 96.82, 68.07, 32.16, 29.40, 24.40. HRMS (ESI) *m/z* calculated for C$_{21}$H$_{18}$N$_2$O$_2$F$^+$ [M+H]$^+$ 349.1347, found: 349.1365.

2h
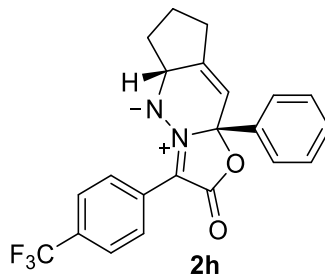
2-Oxo-9a-phenyl-3-(4-(trifluoromethyl)phenyl)-2,5a,6,7,8,9a-hexahydrocyclopenta[e]oxazolo [3,2-b]pyridazin-4-ium-5-ide 2h: 52% yield. Light yellow solid, 100 ℃ (dec.); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.82 (d, J = 8.4 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.40 (t, J = 7.5 Hz, 1H), 7.36 (t, J = 7.5 Hz, 2H), 7.30 (d, J = 7.5 Hz, 2H), 6.57 − 6.54 (m, 1H), 3.83 (t, J = 8.8 Hz, 1H), 2.60 − 2.47 (comp, 3H), 2.06 − 2.01 (m, 1H), 1.98 − 1.93 (m, 1H), 1.82 − 1.77 (m, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.72, 148.39, 134.70, 131.00, 130.33, 129.03, 128.67 (q, J = 32.2 Hz), 128.47 (q, J = 276.4 Hz), 125.89, 125.17, 124.97 (q, J = 3.4 Hz), 115.76, 104.53, 97.19, 68.54, 32.05, 29.38, 24.41. HRMS (ESI) m/z calculated for C$_{22}$H$_{17}$N$_2$O$_2$F$_3$$^+$ [M+H]$^+$ 399.1315, found: 399.1326.

2i

3-(4-Nitrophenyl)-2-oxo-9a-phenyl-2,5a,6,7,8,9a-hexahydro-cyclopenta[e]oxazolo[3,2-b]pyridazin-4-ium-5-ide 2i: 42% yield. Light yellow solid, 100 ℃ (dec.); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.90 (d, J = 9.0 Hz, 2H), 8.30 (d, J = 9.0 Hz, 2H), 7.42 (t, J = 7.3 Hz, 1H), 7.37 (t, J = 7.3 Hz, 2H), 7.28 (d, J = 7.3 Hz, 2H), 6.59 – 6.55 (m, 1H), 3.86 (t, J = 9.0 Hz, 1H), 2.62 – 2.55 (comp, 2H), 2.54 – 2.46 (m, 1H), 2.10– 2.05 (m, 1H), 2.02– 1.95 (m, 1H), 1.86 – 1.79 (m, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.48, 148.35, 145.62, 142.78, 134.34, 133.83, 130.53, 129.14, 125.93, 125.25, 123.52, 115.73, 97.57, 68.95, 31.99, 29.36, 24.43. HRMS (ESI) m/z calculated for C$_{21}$H$_{17}$N$_3$O$_4$Cs$^+$ [M+Cs]$^+$ 508.0268, found: 508.0280.

2j

3-(2-Bromophenyl)-2-oxo-9a-phenyl-2,5a,6,7,8,9a-hexahydro-cyclopenta[e]oxazolo[3,2-b]pyridazin-4-ium-5-ide 2j: 55% yield. Light yellow solid, 100 ℃ (dec.); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.69 – 7.65 (m, 1H), 7.63 – 7.53 (comp, 3H), 7.44 – 7.36 (comp, 4H), 7.29 – 2.25 (m, 1H), 6.54 – 6.51 (m, 1H), 3.81 – 3.76 (m, 1H), 2.62 – 2.55 (m, 1H), 2.53

– 2.45 (m, 1H), 2.44 – 2.38 (m, 1H), 1.96 – 1.86 (comp, 2H), 1.71 –
1.78 (m, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.80, 148.53, 133.35,
132.58, 130.45, 130.22, 128.83, 128.75, 128.04, 127.38, 126.39, 125.01,
115.63, 105.83, 97.98, 68.01, 32.00, 29.32, 24.31. HRMS (ESI) *m/z*
calculated for C$_{21}$H$_{18}$N$_2$O$_2$Br$^+$ [M+H]$^+$ 409.0546, found: 409.0557.

2k

9a-(4-Methoxyphenyl)-2-oxo-3-phenyl-2,5a,6,7,8,9a-

hexahydro-cyclopenta[e]oxazolo[3,2-b]pyridazin-4-ium-5-ide 2k: 42%

yield. Light yellow solid, 100 ℃ (dec.); ^{1}H NMR (500 MHz, CDCl$_3$) δ

8.67 (d, *J* = 8.1 Hz, 2H), 7.47 (t, *J* = 8.1 Hz, 2H), 7.31 (t, *J* = 8.1 Hz, 1H),

7.24(d, *J* = 8.9 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 2H), 6.52 – 6.50 (m, 1H),

3.81 (t, *J* = 8.6 Hz, 1H), 3.78 (s, 3H), 2.59 – 2.44 (m, 3H), 2.04 – 1.99

(m, 1H), 1.96 – 1.90 (m, 1H), 1.79 – 1.76 (m, 1H). ^{13}C NMR (125 MHz,

CDCl$_3$) δ 164.10, 160.84, 148.33, 128.10, 127.79, 127.70, 127.54, 127.01,

125.43, 116.00, 114.16, 105.25, 96.77, 68.13, 55.38, 32.14, 29.41, 24.49.

HRMS (ESI) *m/z* calculated for C$_{22}$H$_{21}$N$_2$O$_3$$^+$ [M+H]$^+$ 361.1547, found:
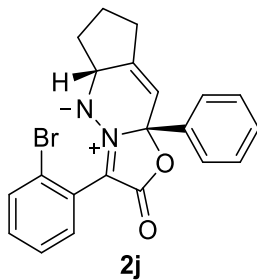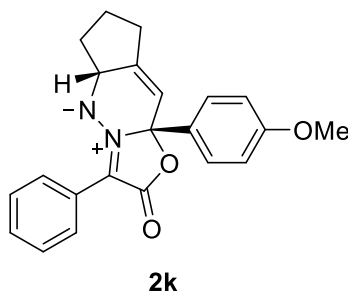
361.1557.

2l
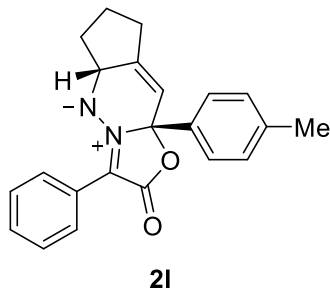
2-Oxo-3-phenyl-9a-(p-tolyl)-2,5a,6,7,8,9a-hexahydrocyclo-penta[e]-oxazolo[3,2-b]pyridazin-4-ium-5-ide 2l: 45% yield. Light yellow solid, 100 ℃ (dec.); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.67 (d, *J* = 8.3 Hz, 2H), 7.47 (t, *J* = 8.3 Hz, 2H), 7.32 (t, *J* = 8.3 Hz, 1H), 7.21(d, *J* = 7.8 Hz, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 6.54 – 6.51 (m, 1H), 3.81 (t, *J* = 8.2 Hz, 1H), 2.60 – 2.41 (comp, 3H), 2.33 (s, 3H), 2.04 – 1.98 (m, 1H), 1.96 – 1.90 (m, 1H), 1.80 – 1.74 (m, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 164.05, 148.26, 140.32, 132.20, 129.53, 128.09, 127.79, 127.55, 126.02, 125.44, 115.99, 105.36, 96.81, 68.13, 32.14, 29.40, 24.46, 21.17. HRMS (ESI) *m/z* calculated for C$_{22}$H$_{21}$N$_2$O$_2$$^+$ [M+H]$^+$ 345.1598, found: 345.1606.

2m

9a-(4-Chlorophenyl)-2-oxo-3-phenyl-2,5a,6,7,8,9a-hexahydro-cyclopenta[e]oxazolo[3,2-b]pyridazin-4-ium-5-ide 2m: 45% yield.

Light yellow solid, 100 ℃(dec.); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.67 (d, J

= 8.4 Hz, 2H), 7.48 (t, J = 7.8 Hz, 2H), 7.35 – 7.29 (comp, 3H), 7.25 (t, J

= 7.8 Hz, 2H), 6.55 - 6.52 (m, 1H), 3.78 (t, J = 8.6 Hz, 1H), 2.60 – 2.42

(comp, 3H), 2.05 – 1.91 (comp, 2H), 1.82 – 1.75 (m, 1H). ^{13}C NMR (125

MHz, CDCl$_3$) δ 163.68, 148.95, 136.31, 133.76, 129.16, 128.15, 127.80,

127.51, 125.46, 115.55, 105.40, 95.95, 68.23, 32.17, 29.44, 24.39.

HRMS (ESI) m/z calculated for C$_{21}$H$_{18}$N$_2$O$_2$Cl$^+$ [M+H]$^+$365.1051, found:
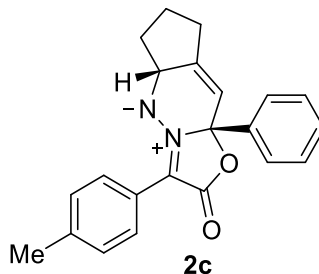
365.1063.

2n

(5aR,9aR)-9a-(4-fluorophenyl)-2-oxo-3-phenyl-2,5a,6,7,8,9a-

hexahydro-cyclopenta[e]oxazolo[3,2-b]pyridazin-4-ium-5-ide 2n: 45%

yield. Light yellow solid, 100 ℃ (dec.); ^{1}H NMR (500 MHz, CDCl$_3$) δ

8.68 (d, J = 8.1 Hz, 2H), 7.48 (t, J = 8.1 Hz, 2H), 7.36 – 7.30 (comp, 3H),

7.04 (t, J = 8.5 Hz, 2H), 6.54 – 6.51 (m, 1H), 3.79 (t, J = 8.6 Hz, 1H),

2.59 – 2.45 (comp, 3H), 2.05 – 2.00 (m, 1H), 1.98 – 1.93 (m, 1H), 1.81 –

1.76 (m, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.76, 163.50 (d, J =

249.6 Hz), 148.83, 131.17 (d, J = 3.3 Hz), 128.25, 128.14, 127.76,

127.56, 125.45, 115.98 (d, J = 21.9 Hz), 115.73, 105.37, 96.05, 68.20, 32.16, 29.43, 24.41. HRMS (ESI) m/z calculated for $C_{21}H_{18}N_2O_2F^+$ [M+H]$^+$349.1347, found: 349.1359.
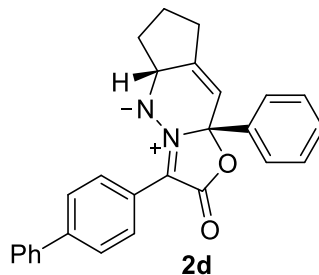

2o

9a-(4-(Methoxycarbonyl)phenyl)-2-oxo-3-phenyl-2,5a,6,7,8,9a-hexahydrocyclopenta[e]oxazolo[3,2-b]pyridazin-4-ium-5-ide 2o: 45% yield. Light yellow solid, 100 ℃ (dec.); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.67 (d, J = 7.5 Hz, 2H), 8.01 (d, J = 8.6 Hz, 2H), 7.48 (t, J = 7.5 Hz, 2H), 7.38 (d, J = 8.6 Hz, 2H), 7.34 (t, J = 7.5 Hz, 1H), 6.56 − 6.53 (m, 1H), 3.91 (s, 3H), 3.76 (t, J = 8.6 Hz, 1H), 2.58 − 2.45 (comp, 3H), 2.06 − 2.00 (m, 1H), 1.97 − 1.92 (m, 1H), 1.81 − 1.74 (m, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 165.98, 163.62, 149.00, 139.65, 131.75, 130.15, 128.17, 127.87, 127.49, 126.10, 125.51, 115.56, 105.52, 95.94, 68.26, 52.39, 32.21, 29.45, 24.36. HRMS (ESI) m/z calculated for $C_{23}H_{21}N_2O_4^+$ [M+H]$^+$389.1496, found: 389.1504.
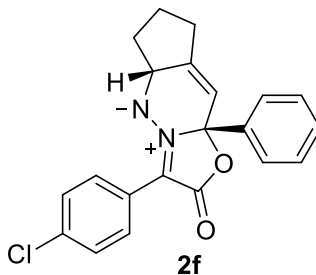
2p

9a-(4-Formylphenyl)-2-oxo-3-phenyl-2,5a,6,7,8,9a-hexahydro-cyclopenta[e]oxazolo[3,2-b]pyridazin-4-ium-5-ide 2p: 41% yield. Light yellow solid, 100 °C (dec.); ^{1}H NMR (500 MHz, CDCl$_3$) δ 10.02 (s, 1H), 8.69 (d, J = 7.7 Hz, 2H), 7.88 (d, J = 8.5 Hz, 2H), 7.52 – 7.47 (comp, 4H), 7.36 (t, J = 7.7 Hz, 1H), 6.58 – 6.55 (m, 1H), 3.78 (t, J = 8.7 Hz, 1H), 2.62 – 2.46 (comp, 3H), 2.08 – 2.02 (m, 1H), 2.00 – 1.94 (m, 1H), 1.83 – 1.74 (m, 1H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 191.41, 163.05, 142.42, 141.42, 138.49, 138.02, 135.66, 130.11, 129.12, 126.31, 124.79, 124.46, 123.87, 118.02, 105.60, 32.91, 32.35, 23.82. HRMS (ESI) m/z calculated for C$_{22}$H$_{19}$N$_2$O$_3$$^+$ [M+H]$^+$359.1390, found: 359.1410.
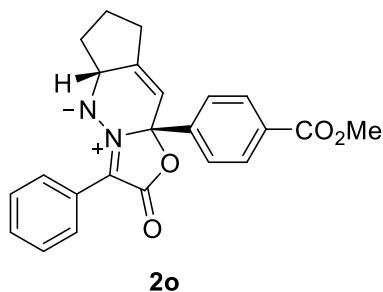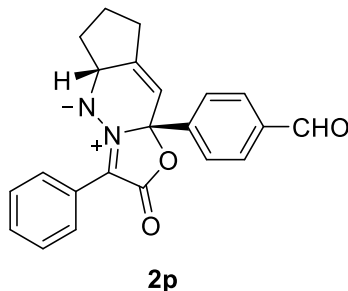
(E)-1a
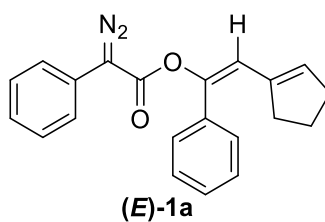
(*E*)-2-(Cyclopent-1-en-1-yl)-1-phenylvinyl α-Diazo-α-phenyl-acetate 1a: ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.49 – 7.44 (comp, 4H), 7.39 – 7.34 (comp, 5H), 7.18 (t, J = 7.4 Hz, 1H), 6.39 (s, 1H), 5.84 (t, J = 2.2 Hz,

1H) 2.34 – 2.30 (comp, 2H), 2.02 - 1.91 (comp, 2H), 1.79 – 1.74 (comp, 2H).:^{13}C NMR (125 MHz, CDCl$_3$) δ 163.83, 146.02, 137.87, 135.16, 134.87, 129.80, 128.92, 128.82, 127.71, 125.94, 125.12, 123.93, 118.69, 33.58, 32.30, 24.11. (The ^{13}C NMR for **1a** contains around 10% of cycloaddition product **2a** because (*E*)-**1a** was converted to **2a** in process of acquiring data.) HRMS (ESI) *m/z* calculated for C$_{21}$H$_{18}$N$_2$O$_2$Cs$^+$ [M+Cs]$^+$ 463.0417, found: 463.0428.

5e
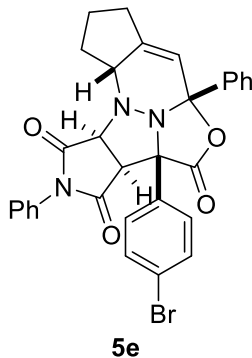
(±)-(3aS,3bR,5aR,9aR,9cS)-3b-(4-bromophenyl)-2,5a-diphenyl-3a,5a,8,9,9a,9c-hexahydro-1H,7H-5-oxa-2,3b1,9b-triazapentaleno-[1,2,3-cd]-s-indacene-1,3,4(2H,3bH)-trione 5e: 85% yield. White solid, 80 ℃ (dec.), .); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.41 –7.37 (comp, 3H), 7.35 –7.25 (comp, 4H), 7.09 –7.01 (comp, 5H), 6.80 – 6.76 (m, 1H), 6.68 – 6.64 (m, 1H), 5.57 – 5.55 (m, 1H), 4.55 –4.50 (comp, 2H), 4.10 (d, *J* = 7.5 Hz, 1H), 2.65–2.50 (comp, 3H), 2.04 – 1.97 (m, 1H), 1.93 – 1.87 (m, 1H), 1.70 – 1.61 (m, 1H). ^{13}C NMR (126 MHz, cdcl$_3$) δ 166.59, 166.17,

163.54, 142.16, 131.11, 124.27, 123.83, 123.77, 122.92, 122.07, 121.68, 121.12, 120.75, 120.66, 118.57, 115.73, 110.53, 93.01, 70.76, 54.53, 54.31, 44.47, 22.95, 21.53, 14.79. HRMS (ESI) *m/z* calculated for $C_{31}H_{25}BrN_3O_4^+$ [M+H]$^+$582.1028, found: 582.1035.

NMR spectra can be obtained from the supporting information of: H. Qiu, H. D. Srinivas, P.Y. Zavalij, M. P. Doyle. *J. Am. Chem. Soc.* **2016**, *138*, 1808–1811.

4.5 X-ray Crystal Structure Information for 2f, (*Z*)-1e, and 5e

Details X-ray analysis of compounds **2f**, (*Z*)-**1e**, and **5e** can be found in supporting information file of our pulished data.[30]

2f

(*Z*)-**1e**
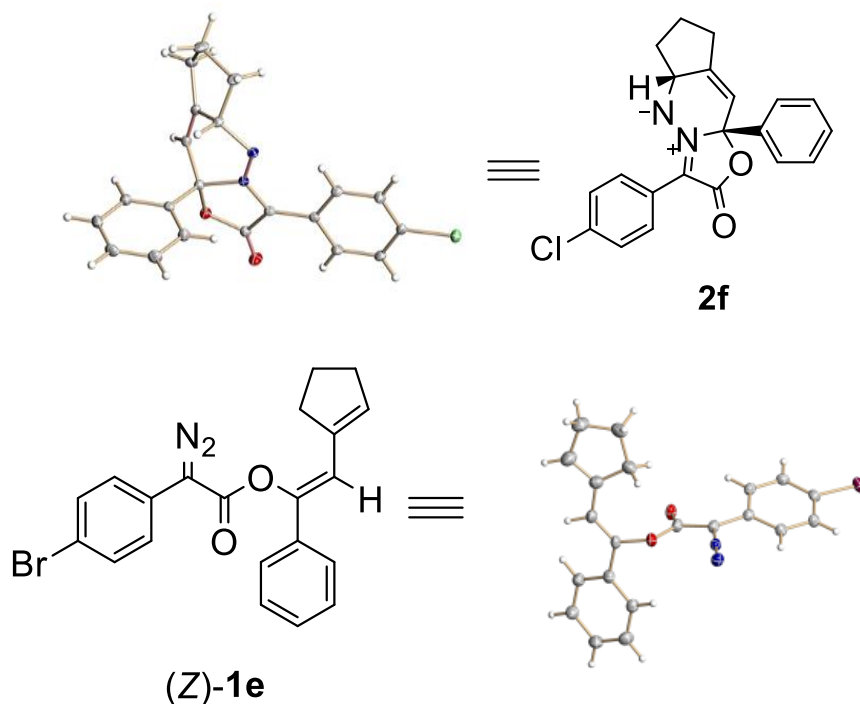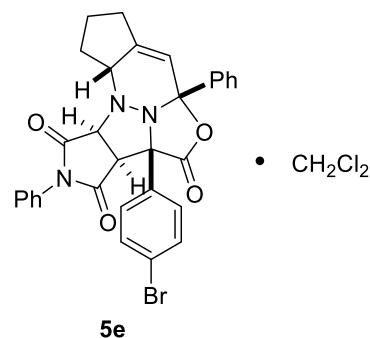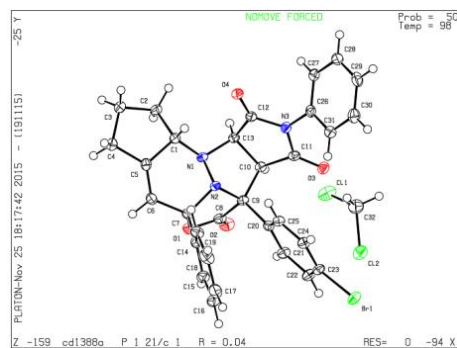
V. References:

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Chapter 4: Unexpected [4+3]-Cycloaddition/Extrusion of Dinitrogen and Rearrangement in Gold-Catalyzed Reactions of Propargylic Diazoesters with Unsaturated Imines

I. Introduction

1.1 Discovery of the Unexpected Cascade Process

With access to metal carbenes from both diazo and acetylenic precursors we considered whether we could selectively form one of two metal carbene intermediates and, in doing so, either retain the unreacted functional group or expect a synergy between the two groups that, like the cascade reactions developed from previously reported reactions of diazo compounds with both functional groups, provides unique access to complex chemical structures (see examples in **Chapter 2** and **Chapter 3**). Using the gold-catalyzed reaction process for [4+3]-cycloaddition established by Toste and coworkers,[1] we have employed the slightly modified propargyl system in which benzoate is replaced by phenyldiazoacetate (**2a**) that was expected to produce dihydroazepines (**3**)

which retained the phenyldiazoacetate functionality. Instead, an unexpected cascade [4+3]-cycloaddition/extrusion of dinitrogen and rearrangement occurred that reorganized the reactant atoms, including conversion of the reactant ester to a diketone.
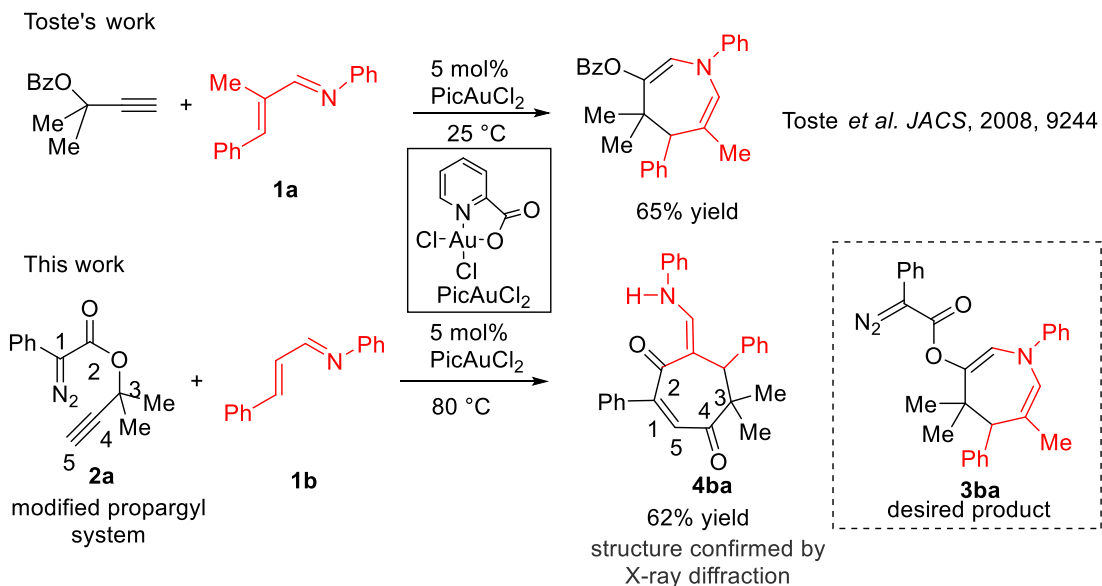
Scheme 4.1 Discovery of the Unexpected Cascade Process.

1.2 Gold Catalyzed 1,2-Acyloxy Migration of Propargyl Esters and Subsequent Reactions

For the past several decades, alkynes have been reported to effectively serve as precursors to metal carbenes via direct reactions with transition metal complexes.[2] Gold catalyzed 1,2-acyloxy migration of propargyl esters is a highly versatile route to access gold vinylcarbene intermediates and has received considerable attention from several

research groups.[3] Similar to other transition metal complex-catalyzed rearrangements of propargyl esters, which have been described in **Chapter 1**, the outcomes of the regioselectivity in the gold catalyzed of propargylic esters are mainly dependent on the R^3 group: if R^3 is a hydrogen atom, the formation of the gold vinylcarbene complexes is preferred.[4] These gold vinylcarbene intermediates are capable of undergoing a variety of intermolecular transformations including cycloaddition, insertion and ylide formation.[4-5]

J. Am. Chem. Soc.,
2008, *130*, 9244–9245

J. Am. Chem. Soc., **2009**,
131, 11654–11655.

J. Am. Chem. Soc.,
2006, *128*, 14480-14481

Chem. Commun.,
2008, 238-240

J. Am. Chem. Soc.,
2007, *129*, 5838-5839

gold vinylcarbene

J. Am. Chem. Soc.,
2009, *131*, 2056-2057

J. Am. Chem. Soc.,
2005, *127*, 18002-18003
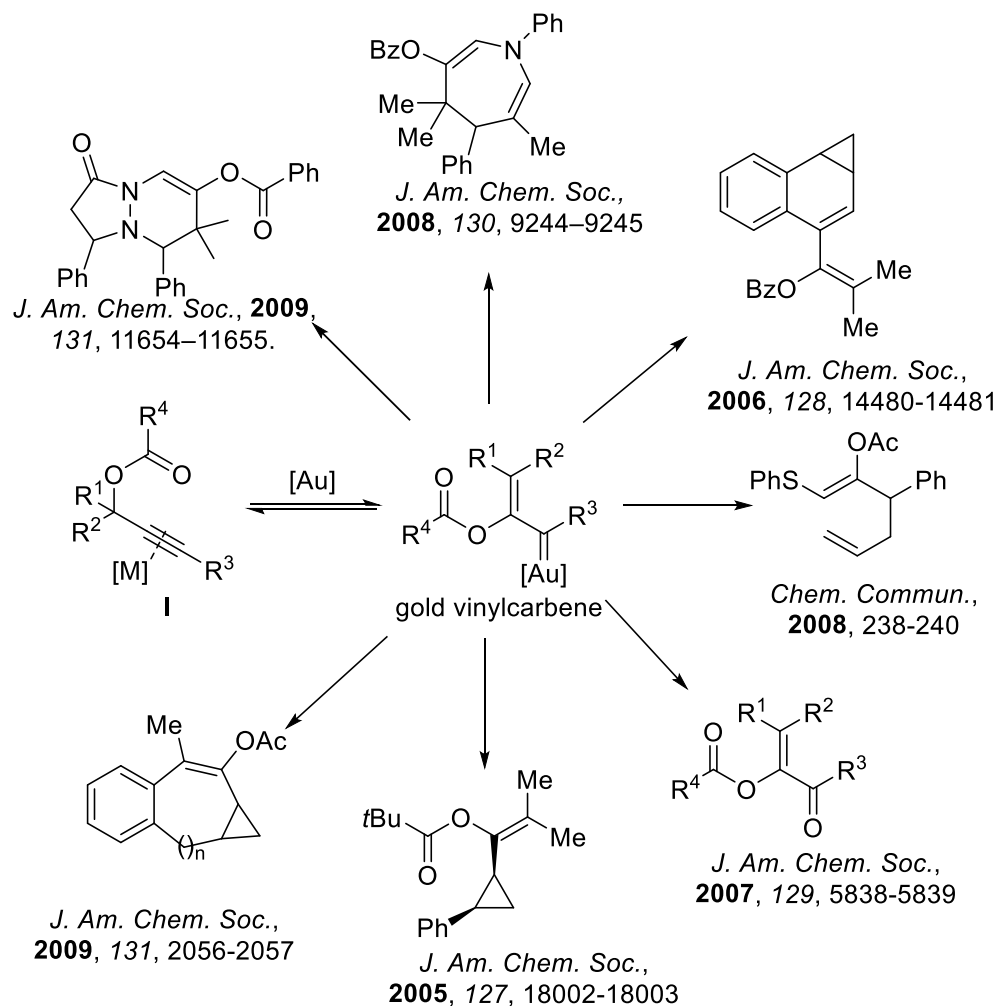
Scheme 4.2 Formation of Gold Vinylcarbenes and Subsequent Transformations.

1.3 [4+3]-Cycloaddition Reactions of Metal Vinylcarbenes with Unsaturated Imines

Cycloaddition reactions of imines with metal carbene species provide access to a wide range of nitrogen-containing heterocyclic compounds with remarkable selectivities and high yields under mild reaction conditions.[6] These reactions typically involve reactive azomethine ylide intermediates.[7] In the process of investigating rhodium-catalyzed azomethine ylide-derived reactions of vinyldiazo compounds with imines, Doyle and coworkers have discovered the first example of a [4+3]-cycloaddition reaction of styryldiazoacetates with α,β-unsaturated imines. This reaction provides rapid entry into substituted dihydroazepine derivatives from easily obtained starting materials. A stepwise mechanism involving addition of α,β-unsaturated imines to a rhodium vinylcarbene intermediate has been proposed.[8]
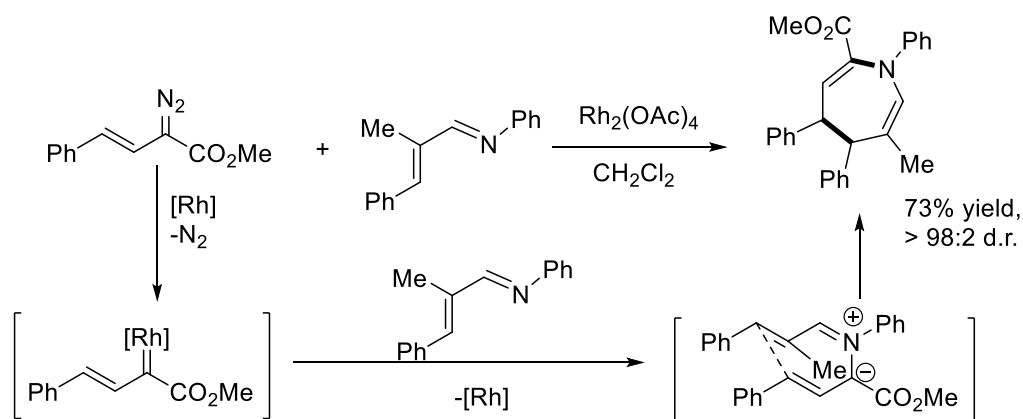
Scheme 4.3 Rhodium-Catalyzed [4+3]-Cycloaddition Reaction of Styryldiazoacetates with α,β-Unsaturated Imines.

By analogy with to the [4+3]-cycloaddition reaction of rhodium vinylcarbenes with α,β-unsaturated imines, Toste and coworkers have demonstrated that propargyl esters can serve as gold vinylcarbene precursors, which undergo similar [4+3]-cycloaddition reactions with α,β-unsaturated imines. Similar to the mechanism proposed by Doyle and coworkers, this formal [4+3]-cycloaddition reaction proceeds via a stepwise process involving addition of the α,β-unsaturated imines to a gold vinylcarbene intermediate to form an allyl−gold intermediate, which undergoes intramolecular cyclization to produce the [4+3]-adduct and regenerates the gold catalyst.[1]

Toste's work
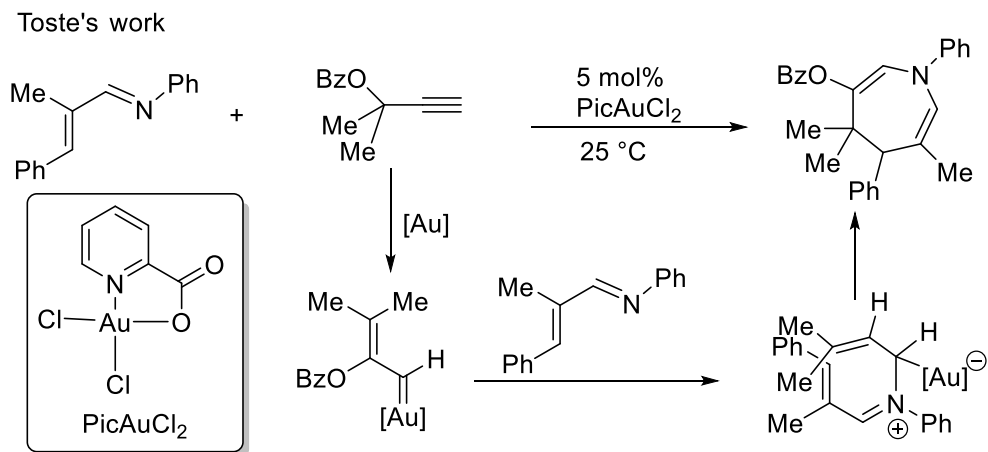
Scheme 4.4 Gold-Catalyzed [4+3]-Cycloaddition Reaction of Propargyl Esters with α,β-Unsaturated Imines.

1.4 Seven-Membered Carbocycles and Previous Synthesis

Seven-membered carbocycles exist in many natural products, and some of them are potential therapeutic compounds, such as ingenol, cortistatin guanacastepene family tropolonoids.[9] However, constructing seven-membered carbocycles is considered to be generally more challenging in comparison to five- and six-membered carbocycles.[10] Although several synthetic approaches that lead to seven-membered carbocycles have been developed over the past decades, discovering novel synthetic methods to highly functionalized seven-membered carbocycles is still in high demand.[11]
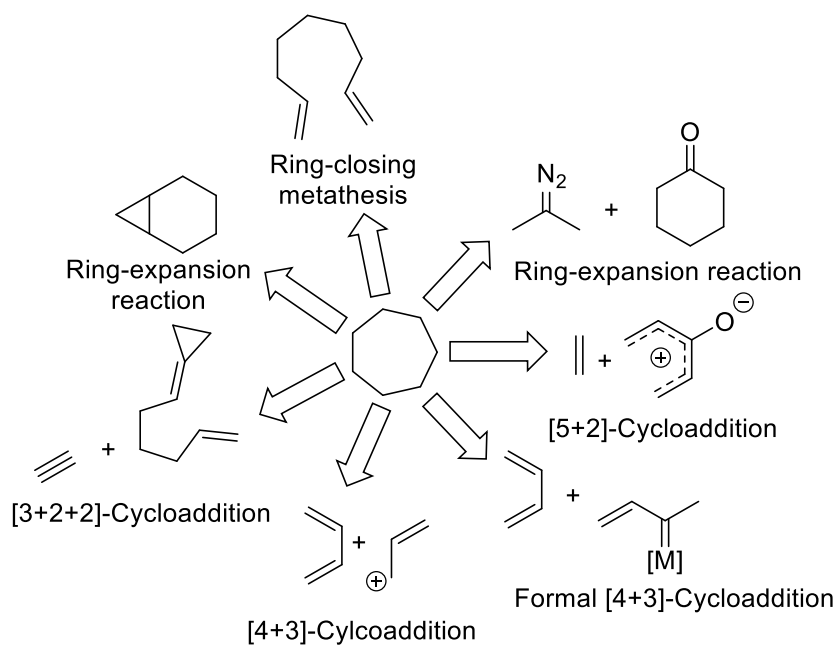
Scheme 4.5 Various Routes to Seven-Membered Carbocycles.

II. Results and Discussion

2.1 Discovery of the Unexpected Cascade Process and Optimization of Reaction Conditions

With 5 mol% AuPicCl$_2$ as the catalyst, treatment of propargyl phenyldiazoacetate **2a** with α-methyl-*trans*-cinnamyl phenylimine **1a**, which was the optimum cinnamylimine previously used in reactions with α,α-dimethylpropargyl benzoate (**Scheme 4.4**), resulted in a complex product mixture that occurred with complete reaction of propargyl phenyldiazoacetate **2a** within 30 minutes at room temperature but with <10% production of the anticipated [4+3]-cycloaddition product **3aa** (**Table 4.1**, entry 1). The use of alternative Au(I) catalysts, including

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AuCl, Au(JohnPhos)SbF$_6$, and IPrAuBF$_4$ that are commonly used in the transformations of propargyl esters, also failed to give the desired [4+3]-cycloaddition product **3aa**. Replacing α-methyl-*trans*-cinnamyl *N*-phenylimine **1a** with *trans*-cinnamyl *N*-phenylimine **1b**, which was disfavored in reactions with α,α-dimethylpropargyl benzoate, under the same reaction conditions for 72 h resulted in a 40% conversion of propargyl phenyldiazoacetate **2a**, but gave as the predominant product **4ba** in 10% isolated yield a compound that did not have the diazo functional group or the anticipated ester functionality and was highly colored (**Table 4.1**, entry 2). Cationic gold catalysts that include (ArO)$_3$PAuSbF$_6$, Au(IPr)SbF$_6$ and Au(JohnPhos)SbF$_6$ failed to give **4ba** at room temperature in dichloromethane (DCM) with low conversion of **1a** (**Table 4.1**, entries 3-5). The use of neutral AuCl produced this unexpected product but in low yield (**Table 4.1**, entry 6), However, increasing the reaction temperature dramatically increased percent conversion and the yield of this product, as well as reducing the reaction time (**Table 4.1**, entries 7-9). At 80°C in 1,2-dichloroethane (DCE) for 6 h in the presence of 5 mol% PicAuCl$_2$ this highly colored product was obtained in 62% isolated yield. A further increase in temperature slightly decreased the yield of this product (**Table 4.1**, entry 10). Changing the

solvent to toluene, acetonitrile, or *N*,*N*-dimethylformamide did not provide improvement (**Table 4.1**, entries 11-13).

Table 4.1 Optimization of gold-catalyzed reaction of propargyl phenyldiazoacetate **2a** with *trans*-cinnamyl phenylimine **1b**

1a, R = Me
1b, R = H

2a

4aa, R = Me
4ba, R = H

3aa, R = Me;
3ba, R = H
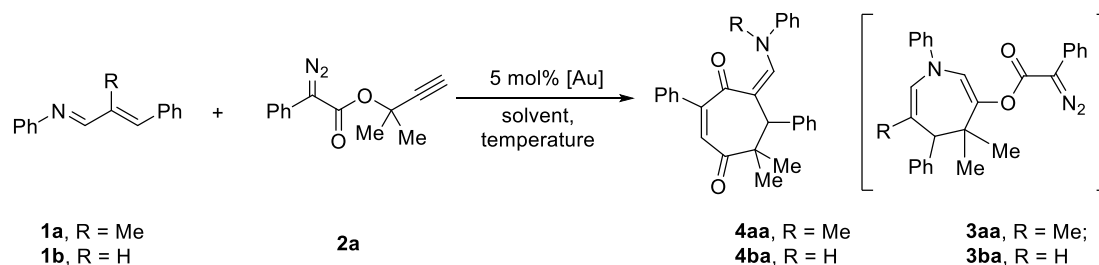
Entry[a]	imines	[Au]	Temperature (^{o}C) /time (h)	solvent	Conversion of **2a**[b] (%)	yield of **4ba**[c] (%)
1[e]	**1a**	PicAuCl$_2$	20/0.5	DCM	>95	--[d]
2	**1a**	Ph$_3$PAuSbF$_6$	20/72	DCM	<10	<5
3	**1a**	IPrAuSbF$_6$	20/24	DCM	<10	<5
4	**1a**	(ArO)PAuSbF$_6$	20/24	DCM	<10	<5
5	**1a**	AuCl	20/24	DCM	25	8
6	**1a**	PicAuCl$_2$	20/72	DCM	40	10
7	**1b**	PicAuCl$_2$	40/48	DCE	60	31

8	**1b**	PicAuCl$_2$	60/12	DCE	85	47
9	**1b**	**PicAuCl$_2$**	**80/6**	**DCE**	**>95**	**65 (62)[e]**
10	**1b**	PicAuCl$_2$	100/2	DCE	>95	57
11	**1b**	PicAuCl$_2$	80/6	toluene	>95	25
12	**1b**	PicAuCl$_2$	80/6	CH$_3$CN	80	38
13	**1b**	PicAuCl$_2$	80/6	DMF	<20	<5

[a]Reactions were performed on 0.20 mmol scale: a solution of **2a** (0.24 mmol) in 2.0 mL solvent was added to a solution of **1b** (or **1a**) (0.20 mmol) and 5 mol% of selected catalyst in 2.0 mL of solvent under a nitrogen atmosphere at stated temperature, and the resulting reaction mixture was stirred for the stated time. [b]The percent conversion of **2a** was determined by ^{1}H NMR spectroscopy using 2,4,6-trimethoxybenzaldehyde as the internal standard. [c]The yield of **4ba** was determined by ^{1}H NMR analyses of characteristic absorptions. [d] Neither **3aa** nor **4aa** was observed. [e] The isolated yield of **4ba**. Ar = 2,4-di-*tert*-butylphenyl.

Attempts to determine the structure of **4** spectroscopically gave partial connectivities, demonstrated the loss of dinitrogen, and pointed to the conversion of the ester to ketones, but its final confirmation awaited X-ray determination. Various derivatives were prepared, but only with **4ha** from the reaction between propargyl phenyldiazoacetate **2a**, and cinnamyl 1-naphthylimine **1h** was a compound suitable for single crystal analysis obtained. X-ray diffraction revealed a structure in which the carbon atoms of the original propargyl phenyldiazoacetate were rearranged, that the ester was converted to a diketone, and depicted the presence of an intramolecular hydrogen bond between nitrogen and a

carbonyl group (**Figure 4.1**). Extrusion of dinitrogen from propargyl phenyldiazoacetate **2a** and the fact that the carbon atoms of seven-membered ring came from three parts of the starting materials demonstrated extensive structural rearrangement.
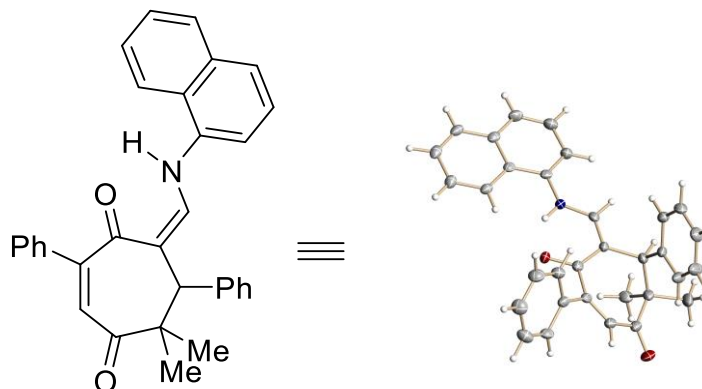
Figure 4.1 X-ray Structure of **4ha**.

2.2 Substrate Scope

In efforts to determine the scope of the gold-catalyzed reaction, structural modifications on both the propargyl aryldiazoacetates and the cinnamyl arylimines were investigated under the optimized reaction conditions (**Table 4.1**, entry 9). Propargylic aryldiazoacetates **2** with electron-donating groups and electron-withdrawing groups at the *para* position underwent the gold-catalyzed transformation smoothly in 6 h with moderate to high yields (**Table 4.2**, entries 1-4). *Ortho* substituted propargylic aryldiazoacetates (**2f** and **2g)** gave reasonable yields of **4bf** and **4bg** (**Table 4.2**, entries 5 and 6). Unsaturated imines **1c-1g** with

arylimine-derived para substituents Ar^1 – including ethers, phenols, and halides –underwent this cycloaddition favorably under the stated reaction conditions (**Table 4.2**, entries 7-11). Sterically hindered 1-naphthylamine-derived **1h** also underwent this transformation smoothly and gave the product **4ha** in 68% yield (**Table 4.2**, entry 12). Imine **1i** with a bulky *N*-mesityl group gave the highest yield in all cases (**Table 4.2**, entry 13). That *p*-nitrocinnamylaldehyde-derived and *p*-methoxycinnamylaldehyde-derived unsaturated imines **1j** and **1k** gave the corresponding products **4ja** and **4ka** in comparable yields shows electronic tolerance in the reactant *trans*-cinnamyl phenylimines (**Table 4.2**, entries 14 and 15). Using cyclopentylpropargyl phenyldiazoacetate, which was easily obtained from 1-ethynylcyclopentanol**,** the rearranged product **4bg** was formed in basically the same yield as its dimethyl analog **4ba** (**Table 4.2**, entry 16).

Table 4.2 Substrate Scope of Gold-Catalyzed Reactions of Propargylic Diazoesters with Unsaturated Imines
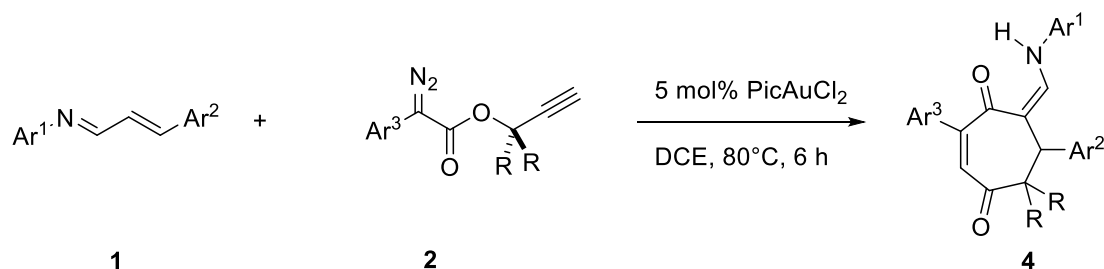
entry	1	Ar^2/Ar^3	2	Ar^1/R	4	yield of 4 (%)
1	1c	4-HOC$_6$H$_4$/Ph	2b	4-MeOC$_6$H$_4$/Me	4cb	68
2	1b	Ph/Ph	2c	4-MeC$_6$H$_4$/Me	4bc	65
3	1b	Ph/Ph	2d	4-BrC$_6$H$_4$/Me	4bd	55
4	1b	Ph/Ph	2e	4-NO$_2$C$_6$H$_4$/Me	4be	43
5	1b	Ph/Ph	2f	2-BrC$_6$H$_4$/Me	4bf	52
6	1b	Ph/Ph	2g	2-NO$_2$C$_6$H$_4$/Me	4bg	55
7	1c	4-HOC$_6$H$_4$/Ph	2a	Ph/Me	4ca	64
8	1d	4-MeOeC$_6$H$_4$/Ph	2a	Ph/Me	4da	65
9	1e	4-BrC$_6$H$_4$/Ph	2a	Ph/Me	4ea	61
10	1f	4-ClC$_6$H$_4$/Ph	2a	Ph/Me	4fa	60
11	1g	4-FC$_6$H$_4$/Ph	2a	Ph/Me	4ga	56
12	1h	2-Naphthyl/Ph	2a	Ph/Me	4ha	68
13	1i	2,4,6-Me$_3$C$_6$H$_2$/Ph	2a	Ph/Me	4ia	70
14	1j	Ph/4-MeOC$_6$H$_4$	2a	Ph/Me	4ja	67

| 15 | **1k** | Ph/4-NO$_2$C$_6$H$_4$ | **2a** | Ph/Me | **4ka** | 59 |
| 16 | **1b** | Ph/ Ph | **2g** | Ph/-(CH$_2$)$_4$- | **4bg** | 65 |

[a]Reactions was performed on a 0.20 mmol scale: a solution of **2** (0.24 mmol) in 2.0 mL solvent was added to a solution of **1** (0.20 mmol) and 5 mol% of PicAuCl$_2$ in 2.0 mL of DCE under a nitrogen atmosphere at 20°C, and the resulting reaction mixture was stirred at 80 ºC for 6 h. Yields are isolated yields after chromatography.

2.3 Isolation of [4+3]-Cycloaddition Products and Kinetic Studies

The extraordinary structural rearrangement that was uncovered in this investigation obviously occurred after the combination of the imine reactant with an intermediate formed by a gold catalyzed reaction with the propargyl phenyldiazoacetate.[1] We understood that gold catalysis occurred with the acetylenic functional group rather than with the diazo group, but was this rearrangement the result of a transformation from the gold-catalyzed [4+3]-cycloaddition product? To address this question propargyl phenyldiazoacetate **2a** was reacted with *N*-phenyl cinnamylimine **1b** at the lower reaction temperature of refluxing CDCl$_3$ in presence of 5 mol% AuPicCl$_2$. An intermediate **3ba** was observed within 5 min that was completely converted to **4ba** after 12 h (**Figure 4.2**). To obtain the separable and relatively stable [4+3]-adducts for further investigation of this cascade process, a variety of reactions with

different starting materials as well as reaction conditions was performed. Fortunately, [4+3]-cycloaddition product **3cb** was isolated by silica-based columns in 36% yield from **1c** and **2b** by quenching the reaction after 5 min at 80ºC in DCE. To determine if intermediate **3** was converted to diketone **4** by a metal-free process or required a catalyst, **3cb** was allowed to react in the absence and presence of 5 mol% AuPicCl$_2$. The stable product **4cb** was obtained in 90% isolated yield from the solution of **3cb** in DCE at 80 °C for 6 h in the absence of any catalysts. However, when the [4+3]-cycloaddition **3cb** was treated with 5 mol% PicAuCl$_2$ in DCE at 80ºC, decomposition occurred within 1 h and resulted in a complex product mixture in which only a trace (less than 10%) of **4cb** was observed (**Scheme 4.6**).
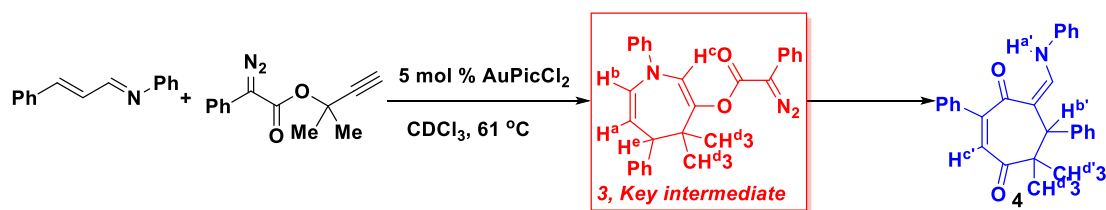
Figure 4.2 ^{1}H NMR Progress of the Gold-Catalyzed Reaction.
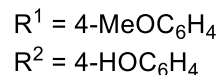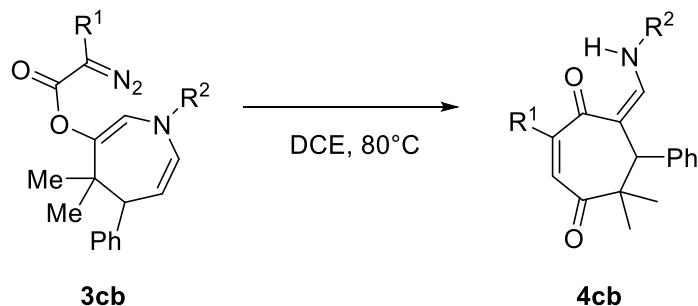
R^1 = 4-MeOC$_6$H$_4$ without 5 mol% PicAuCl$_2$, 90% isolated yield
R^2 = 4-HOC$_6$H$_4$ with 5 mol% PicAuCl$_2$, < 10% yield

Scheme 4.6 Control Experiments for the formation of **4bd** from **3bd**.

Furthermore, we carried out a series of kinetic studies with the isolated [4+3]-cycloaddition product **3cb** for the subsequent transformation. The transformation was first order in **3cb** with a rate constant k$_{obs}$ = 3.6×10^{-4} sec^{-1} at 61 °C in DCE. The variation of the rate constant over temperatures ranging from 61℃ to 75℃ provided E$_{act}$ = 22.6 kcal/mol, $\Delta H^\ddagger_{298}$ = 22.0 kcal/mol and $\Delta S^\ddagger_{298}$ = -9.21 cal/(mol•℃) (**Figure 4.3-4.7**).[12]

R^1 = 4-MeOC$_6$H$_4$
R^2 = 4-HOC$_6$H$_4$

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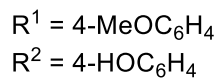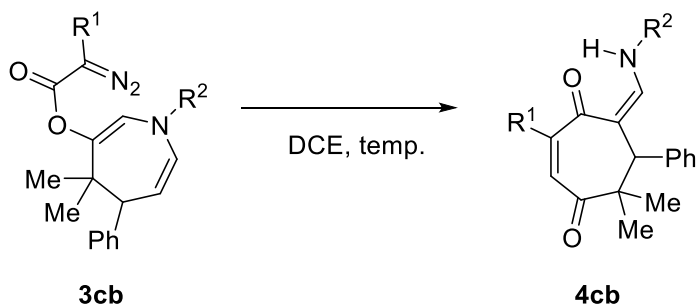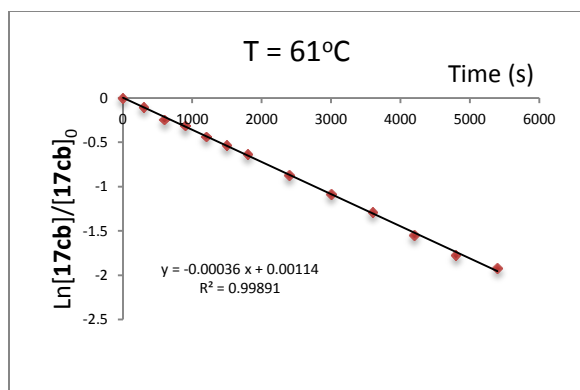
Figure 4.3 First-order Rate Constant at 61 ^{o}C.
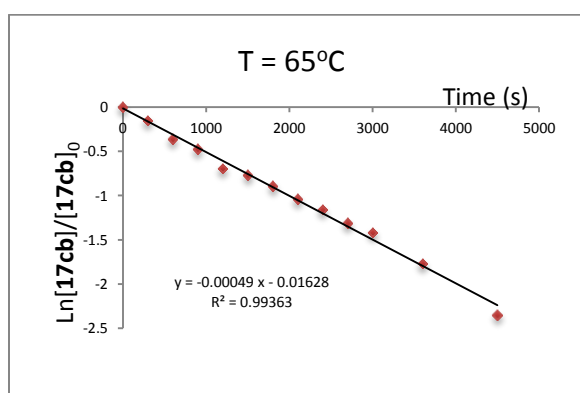
Figure 4.4 First-order Rate Constant at 65°C.

Figure 4.5 First-order Rate Constant at 71 ^{o}C.

Figure 4.6 First-order Rate Constant at 75°C.

Figure 4.7 Arrhenius Plot: **16cb** Activation Energy.

2.4 The Role of the Unsaturated Imines in Diketones Formation

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As shown in precious section, the [4+3]-cycloaddition product **3cb** undergoes a metal free process to form the rearranged products. However, the AuPicCl$_2$, which is capable of destroying the [4+3]-cycloaddition product **3cb**, exists in the reaction mixture. We speculated that there is a base (it might be the unsaturated imine), which prevented the gold species from decomposing the [4+3]-cycloaddition product **3cb** in the reaction mixture. Thus, we carried out several control experiments, and four types of bases were tested in the presence of 5 mol% AuPicCl$_2$. From the **Table 4.3**, we can easily find that: a) adding base increased the yields of diketone **4cb**; and b) decreasing the amount of base resulted in a decreasing the yield of diketone **4cb**. These results supported that the imines also served as a base, which assists in the formation of **4cb** in presence of 5 mol% AuPicCl$_2$. We also found the formation of metallic gold in the presence of imines (**A$_2$** to **A$_4$**), which was confirmed by a SEM (Scanning Electron Microscope) examination.

Figure 4.8 Representative SEM of Metallic Gold.

Table 4.3 Control Experiments

3cb

R^1 = 4-MeOC$_6$H$_4$
R^2 = 4-HOC$_6$H$_4$

4cb
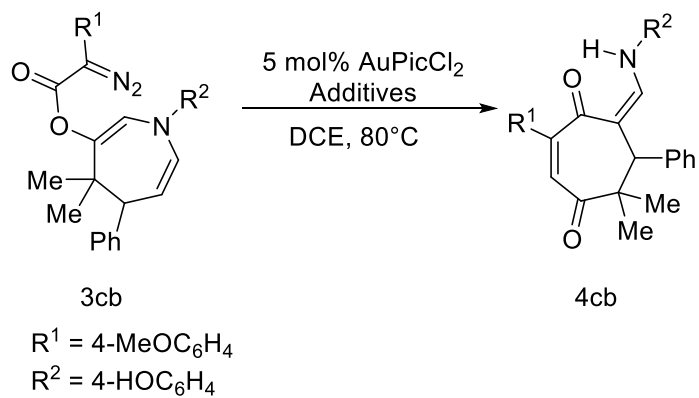
A1
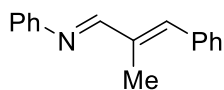
A2
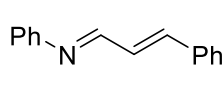
A3
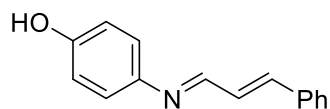
A4

Entry[a]	additive	equiv of additive (mol%)	^{1}HNMR yield (%)
1	A1	50	56
2	A2	50	40
3	A3	50	72

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4	A4	50	73
5	A4	40	69
6	A4	30	63
7	A4	20	55
8	A4	10	45

[a]Reactions was performed on a 0.05 mmol scale: a solution of **3cb** (0.05 mmol) in 0.5mL DCE was added to a solution of stated amount of additive and 5 mol% of PicAuCl$_2$ in 0.5 mL of DCE under a nitrogen atmosphere at 20°C, and the resulting reaction mixture was stirred at 80 °C for 6 h. Yield is determined by ^{1}H NMR analyses of characteristic absorptions.

2.5 Reaction Mechanism

Based on these observations and previous reports,[1] a plausible mechanism for the formation of seven-membered conjugated 1,4-diketones **4** is shown in **Scheme 4.7**. The vinyl gold carbene intermediates generated by 1,2-acyloxy migration of propargylic aryldiazoesters undergo formal [4+3]-cycloaddition with unsaturated imines **2** to afford phenyldiazoacetate-tethered dihydroazepines **3**. We propose that **3** can undergo an intramolecular [3+2]-cycloaddition to form pyrazolines.[13] (The formal [3+2]-cycloaddition might be stepwise, which involves diazo group as an electrophile that has been discussed in Chapter 2, and followed by subsequent ring-closing to produce the [3+2]-adducts.) The resulting pyrazolines undergo nitrogen extrusion,[14] acyloxy

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migration followed by a nucleophilic attack at carbonyl carbon, retro-Michael addition[15] and tautomerization,[16] as shown in **Scheme 4.7**, and finally afford **4** under thermal conditions.
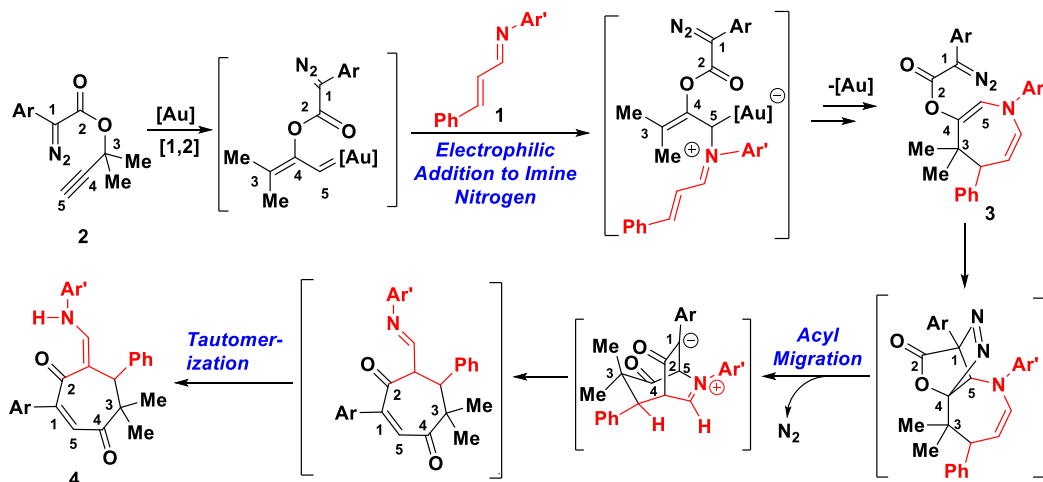
Scheme 4.7 Proposed Mechanism for the Gold-Catalyzed Reaction of Propargyl Arylyldiazoacetates **1** with Unsaturated Imines **2**.

III. Conclusion

In conclusion, we have developed a general and efficient method for the synthesis of seven-membered conjugated 1,4-diketones **4** from easily synthesized materials. To undergo this process vinyl gold carbene intermediates generated by 1,2-acyloxy migration of propargylic aryldiazoesters undergo a formal [4+3]-cycloaddition, and the resulting aryldiazoesters tethered dihydroazepines **3** undergo an intricate metal-free process to form observed **4** with moderate to high yields. Current

efforts aimed at understanding the metal-free process in detail and utilizing propargylic aryldiazoesters as switchable carbene precursors in other transformations are ongoing in our lab.

IV. Experimental Section

4.1 General Information

Unless noted all reactions were carried out under inert atmosphere of dinitrogen in oven-dried glassware with magnetic stirring using freshly distilled solvents. All solvents were purified and dried using standard methods. Analytical thin layer chromatography (TLC) plates were purchased from EM Science (silica gel 60 F_{254} plates). High-resolution mass spectra (HRMS) were performed on a microTOF-ESI mass spectrometer using CsI as the standard. Accurate masses are reported for the molecular ion $[M+Cs]^+$, $[M+Na]^+$, or $[M+H]^+$. Melting points were determined on an Electrothermo Mel-Temp DLX 104 device and were uncorrected. Column chromatography was performed on CombiFlash® Rf 200 purification system using normal phase disposable columns. IR spectra were recorded using Bruker Vector 22 spectrometer. All NMR spectra were recorded on a Bruker spectrometer at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR) or an Agilent spectrometer at 500 MHz ([1]H

NMR) and 125 MHz (^{13}C NMR). Chemical shifts are reported in ppm with the solvent signals as reference (in CDCl$_3$ as solvent), and coupling constants (J) are given in Hertz (Hz). The peak information is described as: br = broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = composite of magnetically non-equivalent protons. The wavelength of maximum absorbance and molar extinction coefficients measurements were performed on a Carey 50 Bio UV-vis spectrometer (200-800 nm) in DCM at room temperature.

4.2 Materials

AuCl(PPh$_3$), AuCl[P(OMe)$_3$], Chloro[2-dicyclohexyl(2′,6′-dimethoxybiphenyl)phosphine] gold(I), and AuPicCl$_2$ were purchased from Sigma-Aldrich; AuCl was purchased from Strem Chemicals. Unsaturated imines[17] and propargylic diazoesters[18] were prepared according to the literature procedures. All other chemicals were obtained from commercial sources and used as received without further purification.

4.3 Experimental Procedures.
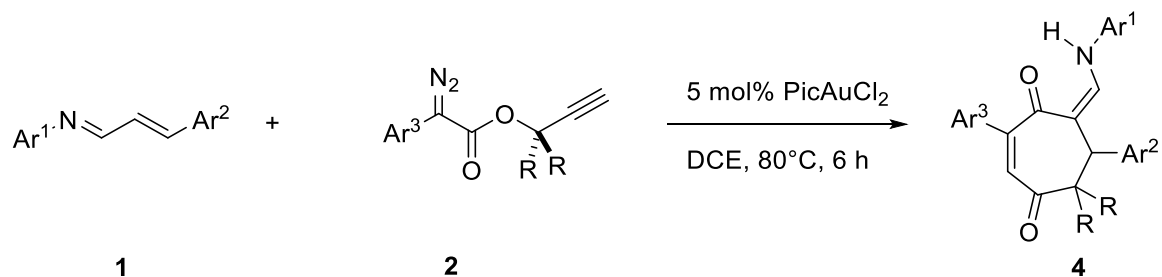
General Procedure for Gold Catalyzed Reaction of Propargylic Diazoesters with Unsaturated Imines: To a flame-dried 10 mL Schlenk flask charged with a magnetic stirring bar, *N*-aryl imine **2** (0.20 mmol), 1,2-dichloroethane (DCE) (2.0 mL) and AuPicCl$_2$ (3.9 mg, 0.01 mmol) were sequentially added under a nitrogen atmosphere. Propargyl diazoester **1** (0.24 mmol) dissolved in 2.0 mL of DCE was added in one portion into the solution under the flow of nitrogen. The mixture was stirred for 6h at 80°C. Solvent was evaporated, and products were purified by column chromatography (100:1 to 10:1 gradient of hexanes: ethyl acetate as eluents) to afford pure compounds **4** as red solids or liquids.

$R^1 = 4\text{-MeOC}_6\text{H}_4$
$R^2 = 4\text{-HOC}_6\text{H}_4$
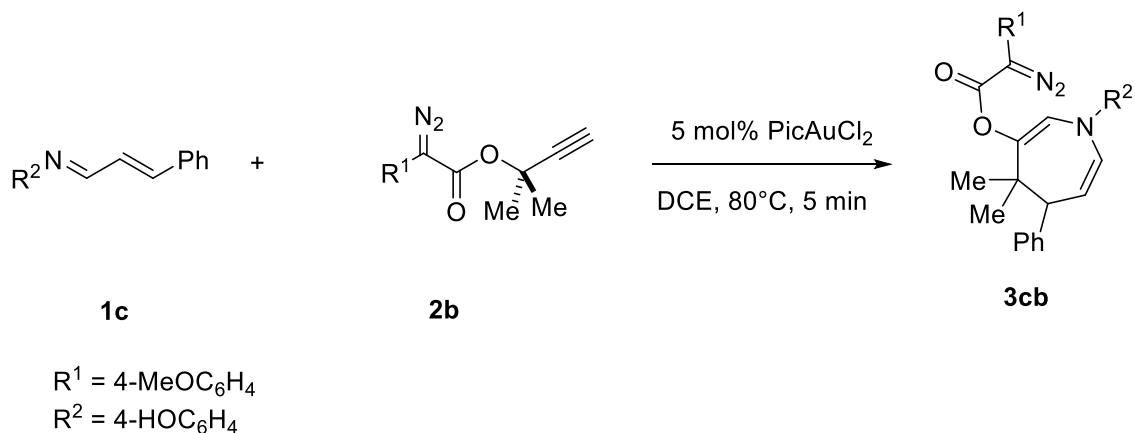
General Procedure for Synthesis of 3cb: To a flame-dried 10 mL Schlenk flask charged with a magnetic stir bar, *N*-aryl imine **1c** (0.20 mmol), 1,2-dichloroethane (DCE) (2.0 mL) and AuPicCl₂ (3.9 mg, 0.01 mmol) were sequentially added under nitrogen atmosphere. Propargyl diazoester **2b** (0.24 mmol) dissolved in 2.0 mL of DCE was added in one portion into the solution under the flow of nitrogen. The mixture was stirred for 5 min at 80°C. The reaction mixture was directly purified by column chromatography (100:1 to 10:1 gradient of hexanes: ethyl acetate as eluents) to afford pure compound **3cb** in 36% isolated yield as a light yellow oil.
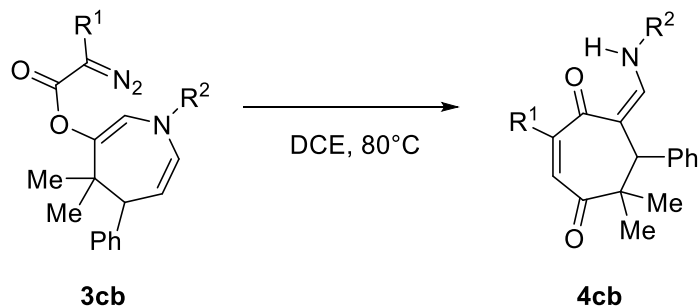
R^1 = 4-MeOC$_6$H$_4$
R^2 = 4-HOC$_6$H$_4$

General Procedure for Synthesis of 4cb from 3cb without Gold Catalyst: To a flame-dried 10 mL Schlenk flask charged with a magnetic stir bar, **3cb** (0.1 mmol) dissolved in 2.0 mL of DCE was added under nitrogen atmosphere, The reaction mixture was stirred for 6h at 80°C. Solvent was evaporated, and products were purified by column chromatography (100:1 to 10:1 gradient of hexanes: ethyl acetate as eluents) to afford pure compound **4cb** in 90% isolated yield.
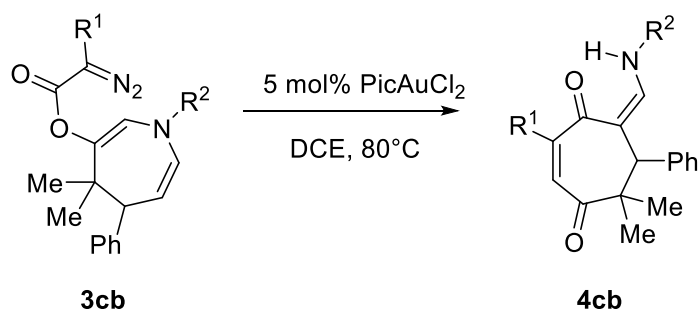
R^1 = 4-MeOC$_6$H$_4$
R^2 = 4-HOC$_6$H$_4$

General Procedure for Synthesis of 4cb from 3cb with Gold Catalyst: To a flame-dried 10 mL Schlenk flask charged with a magnetic stir bar, **3cb** (0.1 mmol) dissolved in 2.0 mL of DCE and AuPicCl$_2$ (2.0 mg, 0.005 mmol) were added under nitrogen atmosphere. The reaction mixture was stirred for 5 min at 80°C. The color of reaction mixture turned dark black. Checking the reaction mixture shows that the starting material was consumed completely, and the yield of **4cb** was less than 10%.

3cb

5 mol% AuPicCl$_2$
50 mol% **1c**

DCE, 80°C

4cb

R^1 = 4-MeOC$_6$H$_4$
R^2 = 4-HOC$_6$H$_4$
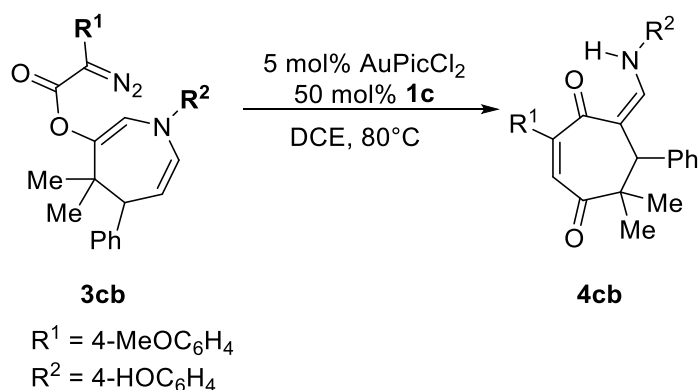
General Procedure for Control Experiment: To a flame-dried 10 mL Schlenk flask charged with a magnetic stir bar, a solution of **3cb** (0.05 mmol) in 0.05 mL of DCE was added to a solution of **1c** (**A4**) and 5 mol% of PicAuCl$_2$ in 0.5 mL of DCE under a nitrogen atmosphere at 20°C. The reaction mixture was stirred for 6 h at 80°C. The solvent was

evaporated; the yield of **4cb** was determined by ^{1}H NMR analysis using 2,4,6-trimethoxybenzaldehyde as an internal standard.

Other stated additives were also tested using the same procedure.

4.4 Characterization Data for New Compounds

2a
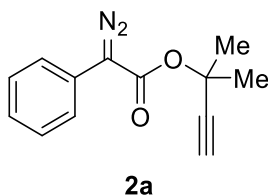
2-Methylbut-3-yn-2-yl 2-Diazo-2-phenylacetate 2a: 80% yield. Yellow solid, m.p. 70.2 – 71.4℃. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.50 (d, J = 8.5 Hz, 2H), 7.38 (t, J = 8.5 Hz, 2H), 7.19 (t, J = 8.5 Hz, 1H), 2.62 (s, 1H), 1.78 (s, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.45, 128.84, 125.75, 125.44, 123.96, 84.51, 72.84, 72.77, 29.21. IR (neat) 2082, 1701, 1286, 1145 cm^{-1}; HRMS (ESI) m/z calculated for C$_{13}$H$_{12}$N$_2$O$_2$Na$^+$ [M+Na]+ 251.0791, found: 251.0796.

2b
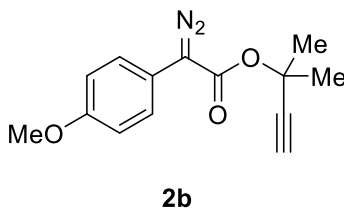
2-Methylbut-3-yn-2-yl 2-Diazo-2-(4-methoxyphenyl)acetate 2b:

75% yield. Red solid, 67.0 – 68.5℃. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.39

(d, J = 9.1 Hz, 2H), 6.93 (d, J = 9.1 Hz, 2H), 3.80 (s, 3H), 2.59 (s, 1H),

1.76 (s, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 164.03, 158.00, 125.89,

116.87, 114.54, 84.62, 72.71, 72.68, 55.34, 29.24. IR (neat) 2084, 1702,

1127, 903 cm-1; HRMS (ESI) m/z calculated for C$_{14}$H$_{14}$N$_2$O$_3$Na

[M+Na]$^+$ 281.0897, found: 281.0900.
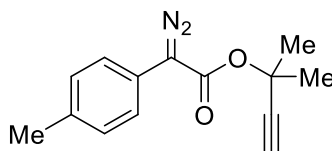
2c

2-Methylbut-3-yn-2-yl 2-Diazo-2-(p-tolyl)-acetate 2c: 78%

yield. Yellow solid, 58.0 – 59.2℃. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.38 (d,

J = 8.4 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 2.61 (s, 1H), 2.35 (s, 3H), 1.78

(s, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.70, 135.60, 129.57, 124.08,

122.07, 84.58, 72.70, 29.22, 20.95. IR (neat) 2083, 1702, 1124, 906 cm-1;

HRMS (ESI) m/z calculated for C$_{14}$H$_{14}$N$_2$O$_2$Na$^+$ [M+Na]$^+$ 265.0947,

found 265.0953.
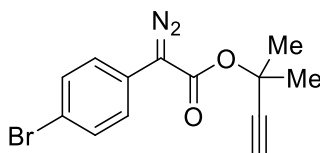
2d

2-Methylbut-3-yn-2-yl 2-(4-Bromophenyl)-2-Diazoacetate 2d:

82% yield. Yellow solid, 90.1 – 91.5℃. ^{1}H NMR (500 MHz, CDCl$_3$) δ

7.49 (d, J = 8.6 Hz, 2H), 7.38 (d, J = 8.6 Hz, 2H), 2.62 (s, 1H), 1.77 (s,

6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.08, 131.93, 125.33, 124.69,

119.28, 84.35, 73.12, 72.93, 29.20. IR (neat) 2087, 1703, 1126, 907 cm^{-1};

HRMS (ESI) m/z calculated for C$_{13}$H$_{12}$N$_2$O$_2$BrNa$^+$ [M+Na]$^+$ 328.9896,

found 328.9891.
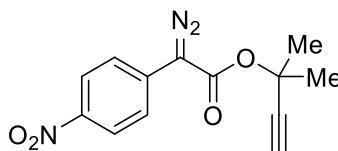
2e

2-Methylbut-3-yn-2-yl 2-Diazo-2-(4-nitrophenyl)acetate 2e: 65%

yield. Yellow solid, 107.2 – 108.5℃. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.22

(d, J = 7.1 Hz, 2H), 7.68 (d, J = 7.1 Hz, 2H), 2.64 (s, 1H), 1.80 (s, 6H).

^{13}C NMR (125 MHz, CDCl$_3$) δ 161.98, 145.00, 133.85, 124.19, 123.18,

84.00, 73.78, 73.28, 29.14. IR (neat) 2095, 1710, 1334, 904 cm-1; HRMS

(ESI) m/z calculated for C$_{13}$H$_{11}$N$_3$O$_4$Na$^+$ [M+Na]$^+$ 296.0642, found

296.0634.
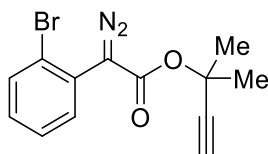
2f

2-Methylbut-3-yn-2-yl 2-(2-Bromophenyl)-2-Diazoacetate 2f:

65% yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.60 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.35 (dd, J = 8.0, 7.7 Hz, 1H), 7.18 (dd, J = 7.8, 7.7 Hz, 1H), 2.60 (s, 1H), 1.74 (s, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.58, 133.16, 132.73, 129.81, 127.44, 125.55, 124.13, 84.39, 72.88, 72.68, 29.05. IR (neat) 2091, 1699, 1117, 754 cm-1; HRMS (ESI) m/z calculated for C$_{13}$H$_{12}$N$_2$O$_2$BrNa$^+$ [M+Na]$^+$ 328.9896, found 328.9893.

2g
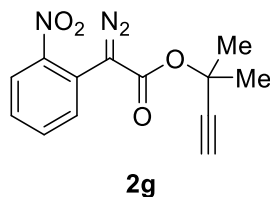
2-Methylbut-3-yn-2-yl 2-Diazo-2-(2-nitrophenyl)acetate 2g: 52% yield. Yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.04 (d, J = 8.2 Hz, 1H), 7.63 (dd, J = 7.9, 2.3 Hz, 1H), 7.55 (d, J = 7.9 Hz, 1H), 7.46 (dd, J = 8.2, 2.3 Hz, 1H), 2.58 (s, 1H), 1.70 (s, 7H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 162.94, 147.17, 133.12, 130.96, 128.74, 125.60, 121.01, 84.18, 73.74, 72.94, 28.97. IR (neat) 2085, 1702, 1513, 1259, 903 cm-1; HRMS (ESI) m/z calculated for C$_{13}$H$_{11}$N$_3$O$_4$Na$^+$ [M+Na]$^+$ 296.0642, found 296.0637.

2h
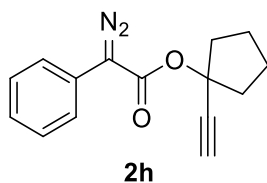
Ethynylcyclopentyl 2-Diazo-2-phenylacetate 2h: 81% yield. Yellow solid, m.p. 31.8 – 33.0℃. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.52 – 7.47 (m, 2H), 7.39 – 7.35 (m, 2H), 7.20 – 7.15 (m, 1H), 2.64 (s, 1H), 2.37 – 2.30 (m, 2H), 2.27 – 2.20 (m, 2H), 1.82 – 1.76 (m, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.64, 128.84, 125.75, 125.37, 123.91, 83.97, 81.27, 73.36, 40.59, 23.32. IR (neat) 2081, 1701, 1598, 1286, 907 cm-1; HRMS (ESI) m/z calculated for C$_{15}$H$_{14}$N$_2$O$_2$Na$^+$ [M+Na]$^+$ 277.0947, found 277.0946.

4ba
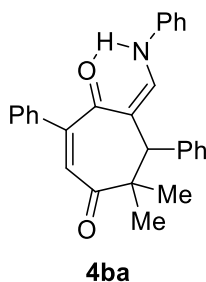
(Z)-5,5-Dimethyl-2,6-diphenyl-7-[(phenylamino)methylene]cyclohept-2-ene-1,4-dione 4ba: 63% yield. Red viscous oil. TLC R$_f$ =0.3 (10:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl$_3$) δ 12.60 (d, J = 12.3 Hz, 1H), 7.58 (d, J = 12.3 Hz, 1H), 7.41 – 7.34 (comp, 5H), 7.34 – 7.27 (comp, 6H), 7.26 – 7.21 (m, 1H), 7.08 (t, J = 7.4 Hz, 1H), 7.00 (d, J = 7.5 Hz, 2H), 6.55 (s, 1H), 4.10 (s, 1H), 1.50 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 206.6, 189.7, 149.2, 147.1, 140.0, 139.8, 138.9, 131.1, 129.8, 129.8, 128.7, 128.4, 128.3,

126.8, 124.2, 116.7, 111.4, 54.5, 52.5, 27.9, 23.2; IR (neat) 2977, 2248, 1625, 1596 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{28}H_{26}NO_2^+$ [M+H]$^+$ 408.1958, found: 408.1944; UV/vis absorption spectra of **4ba** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 308 nm, 411 nm, and corresponding molar extinction coefficients are ε_{308} = 10362 M^{-1} cm^{-1}, ε_{411} = 9534 M^{-1} cm^{-1}.

4cb
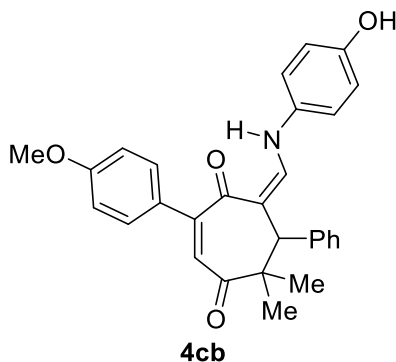
(Z)-7-[(4-hydroxyphenyl)amino]methylene-2-(4-methoxyphenyl)-5,5-dimethyl-6-phenylcyclohept-2-ene-1,4-dione 4cb: 68% yield. Red viscous oil. TLC R$_f$ = 0.15 (5:1 hexanes/EtOAc). ^{1}H NMR (500 MHz, CDCl$_3$) δ 12.72 (d, *J* = 12.3 Hz, 1H), 7.47 (d, *J* = 12.3 Hz, 1H), 7.36 – 7.28 (m, 4H), 7.28 – 7.23 (m, 4H), 6.91 – 6.83 (m, 4H), 6.78 – 6.73 (m, 2H), 6.53 (d, *J* = 1.1 Hz, 1H), 5.86 (s, 1H), 4.10 (s, 1H), 3.81 (s, 3H), 1.48 (s, 3H), 1.21 (s, 3H).^{13}C NMR (125 MHz, CDCl3) δ 207.32, 189.05, 160.19, 153.08, 149.13, 148.13, 140.06, 133.10, 131.12, 129.89, 129.88, 129.47, 128.35, 126.72, 118.49, 116.55, 113.82, 110.71,

55.34, 54.35, 52.77, 27.87, 23.06. HRMS (ESI) *m/z* calculated for $C_{29}H_{28}NO_4^+$ [M+H]$^+$ 454.2018, found: 454.2014; UV/vis absorption spectra of **4cb** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 303 nm, 419 nm, and corresponding molar extinction coefficients are ε_{303} = 9762 M^{-1} cm^{-1}, ε_{419} = 8121 M^{-1} cm^{-1}.

4bc

(Z)-5,5-Dimethyl-6-phenyl-7-[(phenylamino)methylene]-2-(*p*-tolyl)cyclohept-2-ene-1,4-dione 4bc: 65% yield. Red viscous oil. TLC R$_f$ = 0.25 (10:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl3) δ 12.61 (d, *J* = 12.2 Hz, 1H), 7.56 (d, *J* = 12.2 Hz, 1H), 7.37 − 7.28 (comp, 6H), 7.25 − 7.22 (m, 1H), 7.19 − 7.15 (comp, 4H), 7.08 (t, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 7.5 Hz, 2H), 6.54 (s, 1H), 4.09 (s, 1H), 2.36 (s, 3H), 1.49 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 206.8, 189.9, 149.3, 147.0, 140.0, 139.9, 138.9, 136.0, 130.5, 129.8, 129.8, 129.0, 128.4, 128.3, 126.7, 124.2, 116.7, 111.5, 54.5, 52.5, 27.9, 23.2, 21.3; IR (neat) 2973, 1628, 1598 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{29}H_{28}NO_2^+$ [M+H]$^+$

422.2115, found: 422.2118; UV/vis absorption spectra of **4bc** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 311 nm, 405 nm, and corresponding molar extinction coefficients are ε_{311} = 9517 M^{-1} cm^{-1}, ε_{405} = 8119 M^{-1} cm^{-1}.
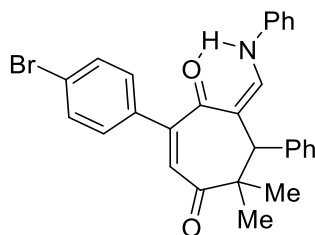
4bd

(Z)-2-(4-Bromophenyl)-5,5-dimethyl-6-phenyl-7-[(phenylamino)-methylene]cyclohept-2-ene-1,4-dione 4bd: 55% yield. Red viscous oil. TLC R_f =0.3 (10:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl3) δ 12.60 (d, *J* = 12.3 Hz, 1H), 7.59 (d, *J* = 12.3 Hz, 1H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.35 – 7.28 (comp, 6H), 7.25 – 7.21 (m, 1H), 7.14 (d, *J* = 8.5 Hz, 2H), 7.10 (t, *J* = 7.4 Hz, 1H), 7.01 (d, *J* = 7.5 Hz, 2H), 6.50 (s, 1H), 4.04 (s, 1H), 1.50 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 206.2, 188.9, 148.2, 147.4, 139.9, 139.6, 137.8, 131.4, 131.3, 130.0, 129.8, 129.7, 128.4, 126.8, 124.4, 123.1, 116.8, 111.4, 54.6, 52.3, 27.9, 23.5; IR (neat) 2975, 1625, 1597 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{28}H_{25}BrNO_2^+$ [M+H]$^+$ 486.1063, found: 486.1052; UV/vis absorption spectra of **4bd** recorded at 20°C in dichloromethane (DCM): UV (λ max)

= 311 nm, 411 nm, and corresponding molar extinction coefficients are $\varepsilon_{311} = 14924$ M^{-1} cm^{-1}, $\varepsilon_{411} = 11984$ M^{-1} cm^{-1}.

4be
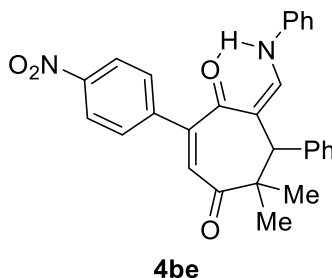
(Z)-5,5-Dimethyl-2-(4-nitrophenyl)-6-phenyl-7-[(phenylamino)-methylene]cyclohept-2-ene-1,4-dione 4be: 43% yield. Red viscous solid. TLC R$_f$ =0.4 (5:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl3) δ 12.61 (d, *J* = 12.4 Hz, 1H), 8.21 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 12.4 Hz, 1H), 7.40 (d, *J* = 8.8 Hz, 2H), 7.38 − 7.30 (comp, 6H), 7.29 − 7.22 (m, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 7.5 Hz, 2H), 6.53 (s, 1H), 4.00 (s, 1H), 1.53 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 205.6, 187.9, 148.0, 147.7, 147.3, 145.7, 139.8, 139.4, 132.8, 129.9, 129.6, 129.5, 128.5, 126.9, 124.7, 123.4, 117.0, 111.5, 54.7, 52.2, 27.9, 23.8; IR (neat) 2926, 1626, 1596 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{28}$H$_{25}$N$_2$O$_4$$^+$ [M+H]$^+$ 453.1809, found: 408.1813; UV/vis absorption spectra of **4be** recorded at 20°C in dichloromethane (DCM): UV (λ max)

= 288 nm, 420 nm, and corresponding molar extinction coefficients are $\varepsilon_{288} = 14841$ M^{-1} cm^{-1}, $\varepsilon_{420} = 6549$ M^{-1} cm^{-1}.

4bf

(Z)-2-(2-Bromophenyl)-5,5-dimethyl-6-phenyl-7-[(phenyl-amino)-methylene]cyclohept-2-ene-1,4-dione 4bf: 52% yield. Red viscous solid. TLC R$_f$ =0.2 (10:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl3) δ 12.44 (d, *J* = 12.3 Hz, 1H), 7.59 (s, 2H), 7.43 − 7.37 (comp, 3H), 7.37 − 7.34 (comp, 2H), 7.34 − 7.27 (comp, 4H), 7.25 − 7.21 (m, 1H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.95 (d, *J* = 7.5 Hz, 2H), 6.46 (s, 1H), 4.37 (s, 1H), 1.49 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 206.6, 188.2, 149.5, 147.4, 140.7, 139.9, 139.8, 132.9, 132.5, 131.1, 130.0, 129.9, 129.7, 128.5, 127.5, 126.9, 124.1, 122.0, 116.6, 110.4, 54.3, 52.6, 27.5, 22.2; IR (neat) 2975, 1759, 1624, 1597 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{28}$H$_{25}$BrNO$_2{}^+$ [M+H]$^+$ 486.1063, found: 486.1020; UV/vis absorption spectra of **4bf** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 311 nm, 410 nm, and corresponding molar extinction coefficients are $\varepsilon_{311} = 8329$ M^{-1} cm^{-1}, $\varepsilon_{410} = 8494$ M^{-1} cm^{-1}.

4bg

(*Z*)-5,5-Dimethyl-2-(2-nitrophenyl)-6-phenyl-7-[(phenylamino)-methylene]cyclohept-2-ene-1,4-dione 4bg: 55% yield. Red viscous solid. TLC R_f =0.3 (5:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl3) δ 12.30 (d, *J* = 12.4 Hz, 1H), 8.19 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.72 (td, *J* = 7.5, 1.3 Hz, 1H), 7.62 − 7.55 (m, 1H), 7.52 − 7.44 (comp, 4H), 7.40 − 7.34 (comp, 2H), 7.31 − 7.26 (comp, 2H), 7.26 − 7.23 (m, 1H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.88 (d, *J* = 7.5 Hz, 2H), 6.58 (s, 1H), 1.49 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 206.5, 187.0, 148.4, 147.7, 147.5, 140.2, 139.6, 135.0, 134.0, 132.2, 131.5, 129.8, 129.7, 129.6, 128.6, 127.0, 124.6, 124.3, 116.8, 110.2, 27.2; IR (neat) 2976, 1623, 1597 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{28}$H$_{25}$N$_2$O$_4^+$ [M+H]$^+$ 453.1809, found: 453.1802; UV/vis absorption spectra of **4bg** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 292 nm, 413 nm, and corresponding molar extinction coefficients are ε_{292} = 9321 M^{-1} cm^{-1}, ε_{413} = 7601 M^{-1} cm^{-1}.

4ca

(Z)-7-[(4-Hydroxyphenyl)amino]methylene-5,5-dimethyl-2,6-diphenylcyclohept-2-ene-1,4-dione 4ca: 64% yield. Red viscous solid. TLC R_f =0.2 (5:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl3) δ 12.71 (d, J = 12.3 Hz, 1H), 7.47 (d, J = 12.3 Hz, 1H), 7.39 – 7.32 (comp, 6H), 7.31 – 7.27 (comp, 3H), 7.26 – 7.21 (m, 1H), 6.88 (d, J = 8.9 Hz, 2H), 6.77 (d, J = 8.9 Hz, 2H), 6.53 (s, 1H), 5.23 (br, 1H), 4.06 (s, 1H), 1.49 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 206.9, 188.8, 152.8, 149.5, 148.2, 140.1, 139.1, 133.3, 130.9, 129.8, 128.7, 128.4, 128.4, 128.3, 126.7, 118.5, 116.5, 110.8, 54.6, 52.6, 27.8, 23.2; IR (neat) 3321, 2975, 1733, 1620 cm^{-1}; HRMS (ESI) m/z calculated for C$_{28}$H$_{26}$NO$_3^+$ [M+H]$^+$ 424.1907, found: 424.1889; UV/vis absorption spectra of **4ca** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 305 nm, 418 nm, and corresponding molar extinction coefficients are ε_{305} = 9592 M^{-1} cm^{-1}, ε_{418} = 8307 M^{-1} cm^{-1}.

4da

(*Z*)-7-[(4-Methoxyphenyl)amino]methylene-5,5-dimethyl-2,6-diphenylcyclohept-2-ene-1,4-dione 4da: 65% yield. Red viscous solid. TLC R_f =0.5 (5:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl3) δ 12.71 (d, *J* = 12.3 Hz, 1H), 7.47 (d, *J* = 12.3 Hz, 1H), 7.39 – 7.32 (comp, 6H), 7.31 – 7.27 (comp, 3H), 7.26 – 7.21 (m, 1H), 6.88 (d, *J* = 8.9 Hz, 2H), 6.77 (d, *J* = 8.9 Hz, 2H), 6.53 (s, 1H), 5.23 (br, 1H), 4.06 (s, 1H), 1.49 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 206.9, 188.8, 152.8, 149.5, 148.2, 140.1, 139.1, 133.3, 130.9, 129.8, 128.7, 128.4, 128.4, 128.3, 126.7, 118.5, 116.5, 110.8, 54.6, 52.6, 27.8, 23.2; IR (neat) 2919, 2850, 1622 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{29}H_{28}NO_3^+$ [M+H]$^+$ 438.2064, found: 438.2057; UV/vis absorption spectra of **4da** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 305 nm, 420 nm, and corresponding molar extinction coefficients are ε_{305} = 10691 M^{-1} cm^{-1}, ε_{420} = 9478 M^{-1} cm^{-1}.

4ea

(Z)-7-[(4-Bromophenyl)amino]methylene-5,5-dimethyl-2,6-diphenylcyclohept-2-ene-1,4-dione 4ea: 61% yield. Red viscous solid,; TLC R_f = (10:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl3) δ 12.55 (d, J = 12.2 Hz, 1H), 7.49 (d, J = 12.2 Hz, 1H), 7.41 (d, J = 8.8 Hz, 2H), 7.39 − 7.31 (comp, 7H), 7.31 − 7.27 (comp, 2H), 7.26 − 7.22 (m, 1H), 6.86 (d, J = 8.8 Hz, 2H), 6.56 (s, 1H), 4.09 (s, 1H), 1.50 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 206.4, 190.2, 149.0, 146.4, 139.8, 139.0, 138.8, 132.7, 131.3, 129.8, 128.8, 128.4, 128.4, 128.3, 126.9, 118.2, 116.7, 111.9, 54.5, 52.4, 27.9, 23.2; IR (neat) 2976, 1623, 1590 cm^{-1}; HRMS (ESI) m/z calculated for $C_{28}H_{25}BrNO_2^+$ [M+H]$^+$ 486.1063, found: 486.1035; UV/vis absorption spectra of **4ea** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 301 nm, 413 nm, and corresponding molar extinction coefficients are ε_{301} = 12017 M^{-1} cm^{-1}, ε_{413} = 11837 M^{-1} cm^{-1}.

4fa

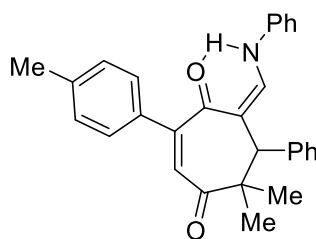**(Z)-7-[(4-Chlorophenyl)amino]methylene-5,5-dimethyl-2,6-diphenylcyclohept-2-ene-1,4-dione 4fa:** 60% yield. Red viscous solid. TLC R$_f$ =0.2 (10:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl3) δ 12.57 (d, J = 12.1 Hz, 1H), 7.49 (d, J = 12.1 Hz, 1H), 7.39 – 7.36 (comp, 3H), 7.35 – 7.31 (comp, 4H), 7.31 – 7.27 (comp, 3H), 7.26 – 7.23 (comp, 2H), 6.92 (d, J = 8.9 Hz, 2H), 6.56 (s, 1H), 4.10 (s, 1H), 1.50 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 206.5, 190.1, 149.0, 146.6, 139.8, 138.8, 138.5, 131.3, 129.8, 129.8, 129.3, 128.8, 128.4, 128.4, 128.3, 126.9, 117.8, 111.8, 54.5, 52.4, 27.9, 23.2; IR (neat) 2976, 1623, 1595 cm^{-1}; HRMS (ESI) m/z calculated for C$_{28}$H$_{25}$ClNO$_2$$^+$ [M+H]$^+$ 442.1568, found: 442.1573; UV/vis absorption spectra of **4fa** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 300 nm, 410 nm, and corresponding molar extinction coefficients are ε$_{300}$ = 6217 M^{-1} cm^{-1}, ε$_{410}$ = 5461 M^{-1} cm^{-1}.
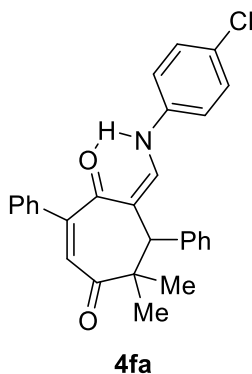
4ga
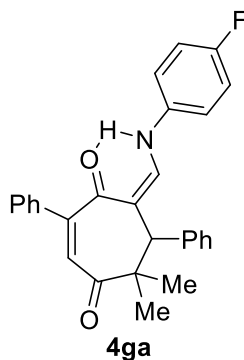
(Z)-7-[(4-Fluorophenyl)amino]methylene-5,5-dimethyl-2,6-diphenylcyclohept-2-ene-1,4-dione 4ga: 56% yield. Red viscous solid. TLC R_f =0.2 (10:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl3) δ 12.64 (d, J = 12.2 Hz, 1H), 7.47 (d, J = 12.2 Hz, 1H), 7.39 − 7.36 (comp, 3H), 7.35 − 7.33 (comp, 2H), 7.32 − 7.31 (m, 1H), 7.31 − 7.26 (comp, 3H), 7.25 − 7.22 (m, 1H), 7.06 − 6.98 (comp, 2H), 6.98 − 6.92 (comp, 2H), 6.55 (s, 1H), 4.09 (s, 1H), 1.50 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 206.5, 189.7, 159.55 (d, J = 244.2 Hz), 149.1, 147.5, 139.9, 138.9, 136.2 (d, J = 2.8 Hz), 131.2, 129.8, 128.8, 128.4, 128.4, 128.3, 126.8, 118.25 (d, J = 8.0 Hz), 116.59 (d, J = 23.1 Hz), 111.4, 54.5, 52.5, 27.9, 23.2; IR (neat) 2975, 1735, 1624, 1600 cm^{-1}; HRMS (ESI) m/z calculated for $C_{28}H_{25}FNO_2^+$ [M+H]$^+$ 426.1864, found: 426.1867; UV/vis absorption spectra of **4ga** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 299 nm, 408 nm, and corresponding molar extinction coefficients are ε_{299} = 8565 M^{-1} cm^{-1}, ε_{408} = 7098 M^{-1} cm^{-1}.
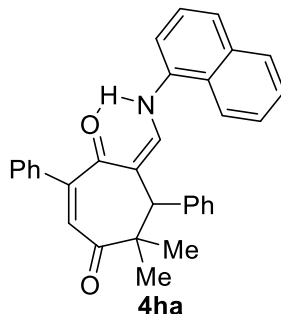
(*Z*)-5,5-Dimethyl-7-(naphthalen-1-ylamino)methylene-2,6-diphenylcyclohept-2-ene-1,4-dione 4ha: 68% yield. Red viscous solid TLC R_f =0.3 (10:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl3) δ 13.43 (d, *J* = 11.8 Hz, 1H), 8.16 − 8.08 (m, 1H), 7.89 − 7.81 (m, 1H), 7.77 (d, *J* = 11.8 Hz, 1H), 7.63 (d, *J* = 8.3 Hz, 1H), 7.55 − 7.50 (comp, 2H), 7.44 (d, *J* = 7.8 Hz, 1H), 7.42 − 7.31 (comp, 9H), 7.29 − 7.23 (m, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 6.61 (s, 1H), 4.22 (s, 1H), 1.54 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 206.9, 190.2, 149.2, 148.3, 139.9, 138.8, 136.2, 134.2, 131.0, 129.9, 128.9, 128.5, 128.5, 128.4, 128.4, 126.8, 126.8, 126.8, 125.7, 124.9, 124.8, 121.1, 112.3, 111.7, 54.4, 52.8, 27.9, 23.0; IR (neat) 2975, 2268, 1616 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{32}H_{28}NO_2^+$ [M+H]$^+$ 458.2115, found: 458.2088; UV/vis absorption spectra of **4ha** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 325 nm, 424 nm, and corresponding molar extinction coefficients are ε_{325} = 3967 M^{-1} cm^{-1}, ε_{424} = 4629 M^{-1} cm^{-1}.

4ia
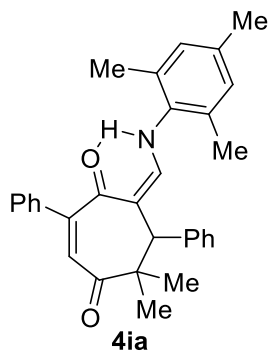
(*Z*)-7-(Mesitylamino)methylene-5,5-dimethyl-2,6-diphenyl-cyclohept-2-ene-1,4-dione 4ia: 70% yield. Red viscous solid. TLC R_f =0.3 (10:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl3) δ 12.13 (d, *J* = 12.5 Hz, 1H), 7.41 – 7.34 (comp, 5H), 7.34 – 7.26 (comp, 4H), 7.24 – 7.18 (m, 1H), 7.06 (d, *J* = 12.5 Hz, 1H), 6.87 (s, 2H), 6.57 (s, 1H), 4.19 (s, 1H), 2.26 (s, 3H), 2.16 (s, 6H), 1.49 (s, 3H), 1.19 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 207.8, 189.1, 155.2, 149.0, 140.3, 138.8, 135.9, 135.9, 131.7, 130.3, 129.9, 129.5, 128.7, 128.4, 128.4, 128.3, 126.6, 109.3, 53.8, 53.2, 27.7, 22.3, 20.8, 18.5; IR (neat) 2974, 1622, 1602 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{31}H_{32}NO_2^+$ [M+H]$^+$ 450.2428, found: 450.2401; UV/vis absorption spectra of **4ia** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 300 nm, 393 nm, and corresponding molar extinction coefficients are ε_{300} = 12797 M^{-1} cm^{-1}, ε_{393} = 7917 M^{-1} cm^{-1}.
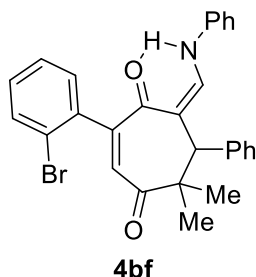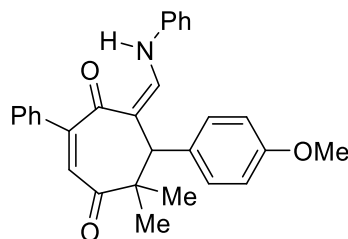
4ja

(Z)-6-(4-methoxyphenyl)-5,5-dimethyl-2-phenyl-7-[(phenyl-amino)methylene]cyclohept-2-ene-1,4-dione 4ja: 67% yield. Red viscous solid. TLC R_f =0.30 (10:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, CDCl$_3$) δ 12.60 (d, J = 12.1 Hz, 1H), 7.57 (d, J = 12.1 Hz, 1H), 7.41 – 7.36 (comp., 3H), 7.35 – 7.30 (comp., 4H), 7.30 – 7.25 (comp., 4H), 7.10 – 7.07 (m, 1H), 7.01 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 6.56 (s, 1H), 4.10 (s, 1H), 3.81 (s, 3H), 1.48 (s, 3H), 1.21 (s, 3H).; ^{13}C NMR (125 MHz, CDCl$_3$) δ 206.90, 189.82, 158.22, 149.17, 147.05, 139.87, 138.91, 131.88, 130.96, 130.85, 129.79, 128.76, 128.44, 128.33, 124.21, 116.76, 113.76, 111.56, 55.25, 53.71, 52.79, 27.83, 22.85.; IR (neat) 2927, 1621, 1427 cm^{-1}; HRMS (ESI) m/z calculated for C$_{29}$H$_{28}$NO$_3{}^+$ [M+H]$^+$ 438.2064, found: 438.2061; UV/vis absorption spectra of **4ja** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 301 nm, 391 nm, and corresponding molar extinction coefficients are ε_{296} = 17213 M^{-1} cm^{-1}, ε_{413} = 16721 M^{-1} cm^{-1}.
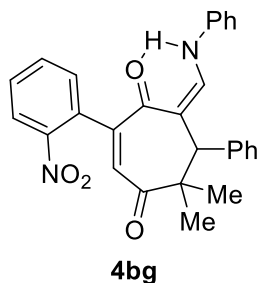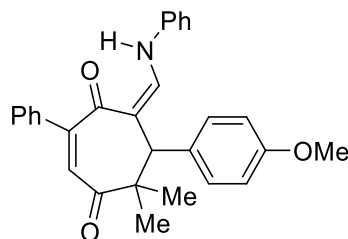
4ja

(Z)-5,5-Dimethyl-6-(4-nitrophenyl)-2-phenyl-7-[(phenyl-amino)methylene]cyclohept-2-ene-1,4-dione 4ka: 59% yield. Red viscous solid. TLC R$_f$ =0.15 (10:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl3) δ 12.66 (d, J = 12.3 Hz, 1H), 8.15 (d, J = 8.8 Hz, 2H), 7.57 (d, J = 12.3 Hz, 1H), 7.52 (d, J = 8.8 Hz, 2H), 7.40 – 7.32 (comp, 5H), 7.25 – 7.20 (comp, 2H), 7.13 (t, J = 7.4 Hz, 1H), 7.06 (d, J = 7.9 Hz, 2H), 6.53 (s, 1H), 4.01 (s, 1H), 1.52 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 204.8, 188.9, 149.9, 148.1, 147.5, 146.4, 139.4, 138.8, 131.4, 130.3, 129.9, 129.0, 128.4, 128.3, 124.8, 123.4, 117.0, 110.6, 55.1, 51.6, 28.0, 24.4; IR (neat) 2925, 1625, 1595 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{28}$H$_{25}$N$_2$O$_4$$^+$ [M+H]$^+$ 453.1809, found: 453.1810; UV/vis absorption spectra of **4ka** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 296 nm, 413 nm, and corresponding molar extinction coefficients are ε$_{296}$ = 36223 M^{-1} cm^{-1}, ε$_{413}$ = 23233 M^{-1} cm^{-1}.

4bh

(Z)-8,11-Diphenyl-10-[(phenylamino)methylene]spiro[4.6]-undec-7-ene-6,9-dione 4bh: 65% yield. Red viscous solid. TLC R_f =0.2 (10:0 hexanes/EtOAc); ^{1}H NMR (400 MHz, CDCl3) δ 12.53 (d, *J* = 12.3 Hz, 1H), 7.61 (d, *J* = 12.3 Hz, 1H), 7.40 – 7.33 (comp, 2H), 7.31 – 7.28 (m, 1H), 7.27 – 7.21 (comp, 6H), 7.17 – 7.11 (comp, 4H), 7.06 – 7.01 (comp, 2H), 6.21 (s, 1H), 3.72 (s, 1H), 2.89 – 2.79 (m, 1H), 2.08 – 1.96 (m, 1H), 1.93 – 1.83 (comp, 3H), 1.78 – 1.67 (comp, 2H), 1.66 – 1.55 (m, 1H); ^{13}C NMR (100 MHz, CDCl3) δ 205.0, 189.2, 149.8, 147.1, 141.5, 139.8, 139.7, 132.2, 129.8, 128.3, 128.3, 128.3, 128.1, 128.0, 126.2, 124.2, 116.7, 112.5, 62.2, 54.9, 40.0, 38.2, 26.3, 24.8; IR (neat) 2949, 1625, 1595 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{30}H_{28}NO_2^+$ [M+H]$^+$ 434.2115, found: 434.2134; UV/vis absorption spectra of **4bh** recorded at 20°C in dichloromethane (DCM): UV (λ max) = 298 nm, 419 nm, and corresponding molar extinction coefficients are ε_{298}= 8390 M^{-1} cm^{-1}, ε_{419} = 5328 M^{-1} cm^{-1}.

3cb

1-(4-hydroxyphenyl)-4,4-dimethyl-5-phenyl-4,5-dihydro-1*H*-azepin-3-yl 2-diazo-2-(4-methoxyphenyl)acetate 3cb: 36% yield. Yellow oil.^{1}H NMR (500 MHz, cdcl$_3$) δ 7.30 (dd, *J* = 16.4, 8.3 Hz, 5H), 7.24 (d, *J* = 6.6 Hz, 2H), 7.09 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 8.9 Hz, 2H), 6.82 − 6.77 (m, 2H), 6.39 (d, *J* = 9.9 Hz, 1H), 6.37 (s, 1H), 5.33 (s, 1H), 4.92 (dd, *J* = 9.8, 6.6 Hz, 1H), 3.80 (s, 3H), 3.57 (d, *J* = 6.4 Hz, 1H), 1.19 (s, 3H), 1.04 (s, 3H). ^{13}C NMR (126 MHz, cdcl$_3$) δ 165.96, 158.08, 152.62, 144.09, 140.75, 138.84, 129.65, 129.17, 127.69, 126.27, 125.86, 124.75, 122.96, 116.62, 115.85, 114.63, 107.79, 55.35, 54.90, 43.75, 28.36, 25.01. IR (neat) 3406, 2086, 1671, 1152, 1253 cm^{-1}; HRMS (ESI) *m/z* calculated for C$_{29}$H$_{28}$N$_3$O$_4^+$ [M+H]$^+$ 482.2080, found: 482.2086.

NMR spectra will be obtained from the Supporting Information of the published paper.

4.5 X-ray Crystal Structure Information for 4ha

Crystal Structure Report for 4ha

A specimen of $C_{32}H_{27}NO_2$, approximate dimensions 0.07 mm × 0.08 mm × 0.47 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker APEX-II CCD system equipped with a graphite monochromator and a MoKα sealed tube (λ = 0.71073 Å). Data collection temperature was 150 K.

The total exposure time was 17.78 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinicunit cell yielded a total of 15657 reflections to a maximum θ angle of 24.99° (0.84 Å resolution), of which 4299 were independent (average redundancy 3.642, completeness = 100.0%, R_{int} =7.86%) and 2251 (52.36%) were greater than 2σ(F^2). The final cell constants of a = 18.041(4) Å, b = 12.292(3) Å, c = 11.066(2) Å, β = 94.663(3)°, V = 2445.9(9) Å^3, are based upon the refinement of the XYZ-centroids of 1326 reflections above 20 σ(I) with 5.328° < 2θ < 41.67°. Data were corrected for absorption effects using the multi-scan method (SADABS). The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.8840 and 0.9940.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P2$_1$/c, with Z = 4 for the formula unit, $C_{32}H_{27}NO_2$. The final anisotropic full-matrix least-squares refinement on F^2 with 404 variables converged at R$_1$ = 5.44%, for the observed data and wR$_2$ = 9.80% for all data. The goodness-of-fit was 1.069. The largest peak in the final difference electron density synthesis was 0.199 e$^-$/Å^3 and the largest hole was -0.182 e$^-$/Å^3 with an RMS deviation of 0.043 e$^-$/Å^3. On the basis of the final model, the calculated density was1.243 g/cm^3 and F(000), 968 e$^-$.

APEX2 Version 2010.11-3 (Bruker AXS Inc.)
SAINT Version 7.68A (Bruker AXS Inc., 2009)
SADABS Version 2008/1 (G. M. Sheldrick, Bruker AXS Inc.)
XPREP Version 2008/2 (G. M. Sheldrick, Bruker AXS Inc.)
XS Version 2008/1 (G. M. Sheldrick, *Acta Cryst.* (2008). A**64**, 112-122)
XL Version 2012/4 (G. M. Sheldrick, (2012) University of Gottingen, Germany)
Platon (A. L. Spek, *Acta Cryst.* (1990). A**46**, C-34).

Table 1. Sample and crystal data for 4ha.

Identification code	2608
Chemical formula	$C_{32}H_{27}NO_2$
Formula weight	457.54
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal size	$0.07 \times 0.08 \times 0.47$ mm
Crystal system	monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 18.041(4) Å $\alpha = 90°$
	b = 12.292(3) Å $\beta = 94.663(3)°$
	c = 11.066(2) Å $\gamma = 90°$
Volume	2445.9(9) Å^3
Z	4
Density (calculated)	1.243 Mg/cm^3
Absorption coefficient	0.077 mm^{-1}
F(000)	968

Table 2. Data collection and structure refinement for 4ha.

Diffractometer	Bruker APEX-II CCD
Radiation source	sealed tube, MoKα
Theta range for	2.01 to 24.99°

data collection	
Index ranges	$-20 \leq h \leq 21$, $-14 \leq k \leq 14$, $-13 \leq l \leq 13$
Reflections collected	15657
Independent reflections	4299 [R(int) = 0.0786]
Coverage of independent reflections	100.0%
Absorption correction	multi-scan
Max. and min. transmission	0.9940 and 0.8840
Structure solution technique	direct methods
Structure solution program	ShelXS-97 (Sheldrick, 2008)
Refinement method	Full-matrix least-squares on F^2
Refinement program	ShelXL-2014 (Sheldrick, 2014)
Function minimized	$\Sigma \, w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	4299 / 0 / 404
Goodness-of-fit on F^2	1.069
Final R indices	2251 data; I>2σ(I) $R_1 = 0.0544$, $wR_2 = 0.0797$
	all data $R_1 = 0.1294$, $wR_2 = 0.0980$
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0150P)^2 + 0.7500P]$, $P = (F_o^2 + 2F_c^2)/3$

Largest diff. peak and hole 0.199 and -0.182 eÅ^{-3}

R.M.S. deviation from mean 0.043 eÅ^{-3}

$$R_{int} = \Sigma |F_o^2 - F_o^2(mean)| / \Sigma [F_o^2]$$

$$R_1 = \Sigma ||F_o| - |F_c|| / \Sigma |F_o|$$

$$GOOF = S = \{\Sigma [w(F_o^2 - F_c^2)^2] / (n - p)\}^{1/2}$$

$$wR_2 = \{\Sigma [w(F_o^2 - F_c^2)^2] / \Sigma [w(F_o^2)^2]\}^{1/2}$$

Table 3. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2) for 4ha.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
C1	0.27599(16)	0.2147(2)	0.2860(3)	0.0371(8)
C2	0.22310(14)	0.2913(2)	0.2500(2)	0.0353(7)
C3	0.15699(15)	0.3060(3)	0.3262(3)	0.0405(8)
C4	0.08121(15)	0.2776(3)	0.2558(3)	0.0437(8)
C5	0.05480(17)	0.3616(3)	0.1603(3)	0.0450(8)
O5	0.98856(11)	0.36475(18)	0.12510(18)	0.0610(7)
C6	0.10421(17)	0.4408(3)	0.1064(3)	0.0414(8)
C7	0.17840(15)	0.4432(2)	0.1021(2)	0.0371(7)
C8	0.23122(15)	0.3540(2)	0.1442(2)	0.0367(7)
O8	0.28433(10)	0.34054(14)	0.07800(16)	0.0399(5)
N1	0.33667(12)	0.19550(19)	0.2260(2)	0.0347(6)
C10	0.39469(15)	0.1210(2)	0.2515(2)	0.0339(7)
C11	0.39531(17)	0.0481(2)	0.3448(3)	0.0420(8)
C12	0.45455(18)	0.9744(3)	0.3645(3)	0.0497(9)
C13	0.51227(19)	0.9752(3)	0.2931(3)	0.0481(9)
C14	0.51321(15)	0.0486(2)	0.1947(3)	0.0377(7)

	x/a	y/b	z/c	U(eq)
C15	0.57043(16)	0.0470(3)	0.1146(3)	0.0414(8)
C16	0.56868(17)	0.1134(3)	0.0167(3)	0.0428(8)
C17	0.50969(16)	0.1871(3)	0.9935(3)	0.0414(8)
C18	0.45387(16)	0.1925(2)	0.0701(3)	0.0355(7)
C19	0.45329(14)	0.1229(2)	0.1721(2)	0.0322(7)
C31	0.16207(16)	0.4125(3)	0.3967(2)	0.0431(8)
C32	0.22399(17)	0.4283(3)	0.4791(3)	0.0418(8)
C33	0.23266(19)	0.5202(3)	0.5496(3)	0.0479(9)
C34	0.1796(2)	0.6015(3)	0.5389(3)	0.0581(10)
C35	0.1182(2)	0.5894(3)	0.4567(3)	0.0667(11)
C36	0.10933(19)	0.4956(3)	0.3885(3)	0.0604(11)
C41	0.08874(15)	0.1693(2)	0.1860(3)	0.0525(9)
C42	0.02121(16)	0.2602(3)	0.3450(3)	0.0674(11)
C71	0.21405(16)	0.5340(2)	0.0407(3)	0.0384(7)
C72	0.18490(18)	0.5762(3)	0.9299(3)	0.0436(8)
C73	0.2208(2)	0.6586(3)	0.8740(3)	0.0565(10)
C74	0.2857(2)	0.7021(3)	0.9282(3)	0.0616(10)
C75	0.3140(2)	0.6625(3)	0.0386(3)	0.0562(10)
C76	0.27907(17)	0.5803(3)	0.0947(3)	0.0459(8)

Table 4. Bond lengths (Å) for 4ha.

C1-N1	1.347(3)	C1-C2	1.376(4)
C1-H1	0.98(2)	C2-C8	1.419(3)
C2-C3	1.526(3)	C3-C31	1.524(4)
C3-C4	1.557(4)	C3-H3	1.00(2)
C4-C5	1.525(4)	C4-C42	1.539(4)
C4-C41	1.550(4)	C5-O5	1.227(3)
C5-C6	1.479(4)	C6-C7	1.344(4)
C6-H6	0.98(2)	C7-C71	1.481(4)
C7-C8	1.502(4)	C8-O8	1.264(3)
N1-C10	1.402(3)	N1-H1A	0.91(3)
C10-C11	1.367(4)	C10-C19	1.428(3)

C11-C12	1.405(4)	C11-H11	0.97(2)
C12-C13	1.357(4)	C12-H12	0.98(3)
C13-C14	1.414(4)	C13-H13	0.95(3)
C14-C15	1.415(4)	C14-C19	1.422(3)
C15-C16	1.355(4)	C15-H15	0.98(2)
C16-C17	1.405(4)	C16-H16	1.00(2)
C17-C18	1.370(4)	C17-H17	0.97(2)
C18-C19	1.416(4)	C18-H18	0.94(2)
C31-C36	1.394(4)	C31-C32	1.397(4)
C32-C33	1.375(4)	C32-H32	0.98(2)
C33-C34	1.383(4)	C33-H33	0.98(3)
C34-C35	1.382(4)	C34-H34	0.99(2)
C35-C36	1.380(4)	C35-H35	1.01(3)
C36-H36	0.99(3)	C41-H41A	0.98
C41-H41B	0.98	C41-H41C	0.98
C42-H42A	0.98	C42-H42B	0.98
C42-H42C	0.98	C71-C76	1.394(4)
C71-C72	1.394(4)	C72-C73	1.376(4)
C72-H72	0.94(3)	C73-C74	1.379(4)
C73-H73	0.99(3)	C74-C75	1.375(4)
C74-H74	0.96(3)	C75-C76	1.367(4)
C75-H75	0.95(3)	C76-H76	0.98(2)

Table 5. Bond angles (°) for 4ha.

N1-C1-C2	123.4(3)	N1-C1-H1	114.2(13)
C2-C1-H1	122.3(13)	C1-C2-C8	119.7(2)
C1-C2-C3	118.4(3)	C8-C2-C3	121.9(3)
C31-C3-C2	111.6(2)	C31-C3-C4	117.6(2)
C2-C3-C4	113.0(2)	C31-C3-H3	106.9(13)
C2-C3-H3	104.7(13)	C4-C3-H3	101.5(13)
C5-C4-C42	110.0(2)	C5-C4-C41	105.7(2)
C42-C4-C41	107.2(3)	C5-C4-C3	114.0(3)
C42-C4-C3	110.2(2)	C41-C4-C3	109.4(2)

O5-C5-C6	117.0(3)	O5-C5-C4	118.9(3)
C6-C5-C4	124.1(3)	C7-C6-C5	131.6(3)
C7-C6-H6	117.1(14)	C5-C6-H6	111.3(14)
C6-C7-C71	120.3(3)	C6-C7-C8	125.6(3)
C71-C7-C8	113.9(2)	O8-C8-C2	122.8(3)
O8-C8-C7	114.0(2)	C2-C8-C7	123.2(2)
C1-N1-C10	129.7(3)	C1-N1-H1A	111.5(18)
C10-N1-H1A	118.7(18)	C11-C10-N1	122.7(3)
C11-C10-C19	121.0(3)	N1-C10-C19	116.3(2)
C10-C11-C12	120.0(3)	C10-C11-H11	120.4(15)
C12-C11-H11	119.7(15)	C13-C12-C11	121.0(3)
C13-C12-H12	121.7(17)	C11-C12-H12	117.3(17)
C12-C13-C14	120.7(3)	C12-C13-H13	122.6(17)
C14-C13-H13	116.7(16)	C13-C14-C15	121.9(3)
C13-C14-C19	119.3(3)	C15-C14-C19	118.8(3)
C16-C15-C14	121.5(3)	C16-C15-H15	119.2(15)
C14-C15-H15	119.3(15)	C15-C16-C17	120.2(3)
C15-C16-H16	122.6(15)	C17-C16-H16	117.2(15)
C18-C17-C16	120.1(3)	C18-C17-H17	120.2(16)
C16-C17-H17	119.7(16)	C17-C18-C19	121.2(3)
C17-C18-H18	117.7(14)	C19-C18-H18	121.0(14)
C18-C19-C14	118.2(3)	C18-C19-C10	123.6(3)
C14-C19-C10	118.1(3)	C36-C31-C32	116.5(3)
C36-C31-C3	125.8(3)	C32-C31-C3	117.7(3)
C33-C32-C31	122.2(3)	C33-C32-H32	120.1(14)
C31-C32-H32	117.7(14)	C32-C33-C34	119.9(3)
C32-C33-H33	119.2(16)	C34-C33-H33	120.8(16)
C35-C34-C33	119.4(3)	C35-C34-H34	117.1(15)
C33-C34-H34	123.3(16)	C36-C35-C34	120.1(4)
C36-C35-H35	118.5(17)	C34-C35-H35	121.4(17)
C35-C36-C31	121.9(3)	C35-C36-H36	118.0(17)
C31-C36-H36	120.1(17)	C4-C41-H41A	109.5
C4-C41-H41B	109.5	H41A-C41-H41B	109.5

C4-C41-H41C	109.5	H41A-C41-H41C	109.5
H41B-C41-H41C	109.5	C4-C42-H42A	109.5
C4-C42-H42B	109.5	H42A-C42-H42B	109.5
C4-C42-H42C	109.5	H42A-C42-H42C	109.5
H42B-C42-H42C	109.5	C76-C71-C72	118.0(3)
C76-C71-C7	119.5(3)	C72-C71-C7	122.5(3)
C73-C72-C71	120.8(3)	C73-C72-H72	120.4(16)
C71-C72-H72	118.8(16)	C72-C73-C74	120.3(3)
C72-C73-H73	121.0(17)	C74-C73-H73	118.7(17)
C75-C74-C73	119.3(4)	C75-C74-H74	122.2(18)
C73-C74-H74	118.5(18)	C76-C75-C74	120.9(4)
C76-C75-H75	118.1(17)	C74-C75-H75	120.8(17)
C75-C76-C71	120.7(3)	C75-C76-H76	122.4(15)
C71-C76-H76	116.9(15)		

Table 6. Torsion angles (°) for 4ha.

N1-C1-C2-C8	0.3(4)	N1-C1-C2-C3	-179.6(3)
C1-C2-C3-C31	108.0(3)	C8-C2-C3-C31	-71.9(3)
C1-C2-C3-C4	-116.9(3)	C8-C2-C3-C4	63.2(4)
C31-C3-C4-C5	59.3(3)	C2-C3-C4-C5	-72.9(3)
C31-C3-C4-C42	-64.9(3)	C2-C3-C4-C42	162.9(3)
C31-C3-C4-C41	177.5(2)	C2-C3-C4-C41	45.3(3)
C42-C4-C5-O5	-34.9(4)	C41-C4-C5-O5	80.5(3)
C3-C4-C5-O5	-159.3(3)	C42-C4-C5-C6	145.0(3)
C41-C4-C5-C6	-99.6(3)	C3-C4-C5-C6	20.7(4)
O5-C5-C6-C7	-162.0(3)	C4-C5-C6-C7	18.1(5)

C5-C6-C7-C71	179.8(3)	C5-C6-C7-C8	6.4(5)
C1-C2-C8-O8	2.4(4)	C3-C2-C8-O8	-177.7(3)
C1-C2-C8-C7	-176.7(3)	C3-C2-C8-C7	3.3(4)
C6-C7-C8-O8	142.0(3)	C71-C7-C8-O8	-31.8(3)
C6-C7-C8-C2	-38.9(4)	C71-C7-C8-C2	147.4(3)
C2-C1-N1-C10	-180.0(3)	C1-N1-C10-C11	3.8(4)
C1-N1-C10-C19	-177.7(3)	N1-C10-C11-C12	179.0(3)
C19-C10-C11-C12	0.6(4)	C10-C11-C12-C13	1.1(5)
C11-C12-C13-C14	-1.8(5)	C12-C13-C14-C15	-176.2(3)
C12-C13-C14-C19	0.8(4)	C13-C14-C15-C16	176.2(3)
C19-C14-C15-C16	-0.9(4)	C14-C15-C16-C17	0.8(4)
C15-C16-C17-C18	0.3(4)	C16-C17-C18-C19	-1.4(4)
C17-C18-C19-C14	1.3(4)	C17-C18-C19-C10	-176.7(3)
C13-C14-C19-C18	-177.4(3)	C15-C14-C19-C18	-0.2(4)
C13-C14-C19-C10	0.8(4)	C15-C14-C19-C10	177.9(2)
C11-C10-C19-C18	176.5(3)	N1-C10-C19-C18	-2.0(4)
C11-C10-C19-C14	-1.5(4)	N1-C10-C19-C14	-180.0(2)
C2-C3-C31-C36	121.6(3)	C4-C3-C31-C36	-11.2(4)
C2-C3-C31-C32	-59.9(3)	C4-C3-C31-C32	167.2(2)
C36-C31-C32-C33	0.5(4)	C3-C31-C32-C33	-178.1(3)
C31-C32-C33-	-0.9(5)	C32-C33-C34-	-0.2(5)

C34		C35	
C33-C34-C35-C36	1.7(6)	C34-C35-C36-C31	-2.1(6)
C32-C31-C36-C35	1.0(5)	C3-C31-C36-C35	179.5(3)
C6-C7-C71-C76	137.2(3)	C8-C7-C71-C76	-48.7(4)
C6-C7-C71-C72	-42.5(4)	C8-C7-C71-C72	131.6(3)
C76-C71-C72-C73	2.2(4)	C7-C71-C72-C73	-178.1(3)
C71-C72-C73-C74	-1.3(5)	C72-C73-C74-C75	-0.1(5)
C73-C74-C75-C76	0.5(5)	C74-C75-C76-C71	0.4(5)
C72-C71-C76-C75	-1.8(4)	C7-C71-C76-C75	178.5(3)

Table 7. Anisotropic atomic displacement parameters (Å^2) for 4ha.

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[\,h^2\,a^{*2}\,U_{11} + ... + 2\,h\,k\,a^*\,b^*\,U_{12}\,]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.0311(18)	0.056(2)	0.0235(17)	0.0004(15)	-0.0017(14)	-0.0018(16)
C2	0.0251(16)	0.056(2)	0.0253(16)	0.0015(14)	0.0034(13)	0.0041(15)
C3	0.0301(18)	0.065(2)	0.0264(17)	0.0026(16)	0.0037(14)	0.0051(16)
C4	0.0273(18)	0.073(2)	0.0311(17)	-0.0013(16)	0.0022(14)	-0.0047(16)
C5	0.0284(19)	0.071(2)	0.0351(18)	-0.0074(16)	0.0010(15)	0.0042(17)
O5	0.0268(13)	0.0972(18)	0.0579(15)	0.0080(12)	-0.0029(11)	0.0034(12)
C6	0.0326(19)	0.057(2)	0.0340(18)	-0.0007(16)	-0.0014(15)	0.0059(17)
C7	0.0319(18)	0.053(2)	0.0260(16)	-0.0072(14)	-0.0029(14)	0.0069(16)

	U$_{11}$	U$_{22}$	U$_{33}$	U$_{23}$	U$_{13}$	U$_{12}$
C8	0.0317(17)	0.047(2)	0.0311(17)	-0.0018(14)	0.0008(14)	0.0022(15)
O8	0.0303(12)	0.0548(13)	0.0357(12)	0.0046(10)	0.0093(10)	0.0075(10)
N1	0.0271(14)	0.0497(17)	0.0275(15)	0.0035(12)	0.0029(12)	0.0057(12)
C10	0.0274(17)	0.0410(18)	0.0320(17)	-0.0017(14)	-0.0063(13)	0.0013(14)
C11	0.037(2)	0.054(2)	0.0349(19)	0.0070(16)	0.0022(16)	0.0061(17)
C12	0.049(2)	0.058(2)	0.041(2)	0.0092(17)	-0.0049(17)	0.0065(18)
C13	0.042(2)	0.050(2)	0.050(2)	0.0017(17)	-0.0051(18)	0.0140(18)
C14	0.0295(17)	0.0411(19)	0.0417(19)	-0.0090(15)	-0.0027(14)	0.0027(14)
C15	0.0269(18)	0.047(2)	0.049(2)	-0.0123(17)	-0.0028(16)	0.0058(16)
C16	0.032(2)	0.048(2)	0.048(2)	-0.0134(17)	0.0072(16)	-0.0048(16)
C17	0.036(2)	0.045(2)	0.044(2)	-0.0047(16)	0.0076(16)	-0.0029(16)
C18	0.0281(18)	0.0364(19)	0.0413(19)	-0.0050(14)	-0.0014(15)	0.0026(15)
C19	0.0258(17)	0.0387(18)	0.0311(17)	-0.0062(13)	-0.0044(13)	-0.0021(14)
C31	0.0265(17)	0.075(2)	0.0285(17)	-0.0004(16)	0.0047(14)	0.0063(17)
C32	0.0303(19)	0.058(2)	0.0373(19)	0.0060(17)	0.0021(15)	0.0046(18)
C33	0.035(2)	0.071(3)	0.037(2)	0.0018(18)	-0.0048(16)	-0.0036(19)
C34	0.062(3)	0.070(3)	0.042(2)	-0.0152(19)	0.0037(19)	0.010(2)
C35	0.056(3)	0.096(3)	0.047(2)	-0.022(2)	-0.0058(19)	0.033(2)
C36	0.041(2)	0.097(3)	0.041(2)	-0.022(2)	-0.0065(17)	0.025(2)
C41	0.038(2)	0.072(2)	0.046(2)	0.0050(18)	-	-

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
					0.0045(16)	0.0088(17)
C42	0.036(2)	0.127(3)	0.040(2)	0.006(2)	0.0097(17)	-0.005(2)
C71	0.0296(18)	0.046(2)	0.0393(18)	-0.0024(15)	0.0009(15)	0.0072(15)
C72	0.038(2)	0.054(2)	0.037(2)	-0.0063(17)	-0.0090(16)	0.0040(18)
C73	0.071(3)	0.052(2)	0.044(2)	0.0075(18)	-0.007(2)	0.001(2)
C74	0.067(3)	0.053(3)	0.065(3)	0.010(2)	0.004(2)	-0.006(2)
C75	0.045(2)	0.061(2)	0.061(3)	0.000(2)	-0.008(2)	-0.008(2)
C76	0.041(2)	0.054(2)	0.041(2)	0.0041(17)	-0.0036(17)	0.0041(17)

Table 8. Hydrogen atomic coordinates and isotropic atomic displacement parameters (Å^2) for 4ha.

	x/a	y/b	z/c	U(eq)
H1	0.2742(12)	0.1728(18)	0.361(2)	0.033(7)
H3	0.1620(12)	0.2461(17)	0.387(2)	0.023(7)
H6	0.0758(13)	0.5023(19)	0.069(2)	0.037(8)
H1A	0.3371(15)	0.238(2)	0.158(2)	0.053(10)
H11	0.3548(14)	0.0468(19)	0.398(2)	0.047(8)
H12	0.4526(16)	-0.077(2)	0.432(3)	0.067(10)
H13	0.5541(15)	-0.072(2)	0.307(2)	0.058(10)
H15	0.6123(14)	-0.003(2)	0.130(2)	0.043(8)
H16	0.6072(14)	0.1108(19)	-0.043(2)	0.047(8)
H17	0.5090(14)	0.235(2)	-0.077(2)	0.051(9)
H18	0.4145(13)	0.2415(18)	0.050(2)	0.031(8)
H32	0.2611(13)	0.3695(19)	0.488(2)	0.034(8)
H33	0.2754(15)	0.525(2)	0.610(2)	0.052(9)
H34	0.1845(14)	0.671(2)	0.584(2)	0.048(9)
H35	0.0798(17)	0.649(2)	0.443(3)	0.076(11)

	x/a	y/b	z/c	U(eq)
H36	0.0647(16)	0.489(2)	0.331(3)	0.070(10)
H41A	0.0398	0.1470	0.1494	0.079(6)
H41B	0.1085	0.1129	0.2422	0.079(6)
H41C	0.1227	0.1797	0.1221	0.079(6)
H42A	-0.0267	0.2457	0.2997	0.083(6)
H42B	0.0172	0.3257	0.3946	0.083(6)
H42C	0.0349	0.1981	0.3977	0.083(6)
H72	0.1413(15)	0.545(2)	-0.108(2)	0.050(9)
H73	0.2004(16)	0.689(2)	-0.205(3)	0.074(11)
H74	0.3099(16)	0.759(2)	-0.113(3)	0.067(10)
H75	0.3560(15)	0.696(2)	0.082(2)	0.057(10)
H76	0.2979(14)	0.5512(19)	0.173(2)	0.042(8)

Table 9. Hydrogen bond distances (Å) and angles (°) for 4ha.

	Donor-H	Acceptor-H	Donor-Acceptor	Angle
N1-H1A···O8	0.91(3)	1.78(3)	2.550(3)	141.0

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Chapter 5: Conclusions

I. Diversity as a Function of Catalyst

Divergent-oriented synthesis (DOS) is a strategy that emphasizes efficiency of chemical library synthesis of small molecules with complexity as well as skeletal diversity. Since both diazo compounds and alkynes can react with a wide array of transition metal complexes to form reactive transition metal complexes that are capable of undergoing further transformations, we asked the question "Is there diversity in product formation if both acetylenic and diazo functionalities are present in the same molecule?" To answer the question, we synthesized propargyl phenyldiazoacetates, which have a possibility to react with either functional group to form reactive transition metal complexes. Catalyst surveys under a variety of reaction conditions led to the discovery of the catalyst-directed divergent outcomes of propargylic diazoeacetates were discussed in Chapter 1.

II. Intramolecular Electrophilic Addition Reaction of Diazo Ester with an Allene

Under catalysis by neutral gold complexes, phenylpropargyl diazoacetates exist in equilibrium with 1-phenyl-1,2-dien-1-yl

diazoacetate allenes that are rapidly formed at room temperature through gold-catalyzed 1,3-acyloxy migration. Interestingly, these gold catalysts react solely with the π-donor rather than with the diazo group. The newly formed allene-aryldiazoacetates subsequently undergo a slow rearrangement that is not catalyzed by gold in which the terminal nitrogen of the diazo functional group adds to the central carbon of the allene initiating a sequence of bond forming reactions resulting in the production of 1,5-dihydro-4H-pyrazol-4-ones in good yields. These 1,5-dihydro-4H-pyrazol-4-ones were found to undergo an intramolecular 1,3-acyl migration to form an equilibrium mixture or quantitatively transfer the acyl group to an external nucleophile with formation of 4-hydroxypyrazoles (Chapter 2).

III. The Fisrt Discovery of Intramolecular [4+2]-Cycloaddition Between a 1,3-Diene and a Diazo Ester

In the process of studying propargyl phenyldiazoacetate with a broad selection of gold catalysts under various conditions of temperature, solvents and additives, we found reactions using a 4-chloropyridine-*N*-oxide in stoichiometric amounts resulted in the formation of (*Z*)-diene and a product anticipated from diene-diazo [4+2]-cycloaddition. This led to the discovery of the first intramolecular. [4+2]-cycloaddition between

a 1,3-diene and a diazo ester. We successfully isolated the (*E*)-diene that was the presumed precursor to the cycloaddition product and studied the kinetic version of this reaction. Thermal reactions with the *E*-isomer form the product from [4+2]-cycloaddition with E_{act} = 16.2 kcal/mol, $\Delta H^{\ddagger}_{298}$ = 15.6 kcal/mol and $\Delta S^{\ddagger}_{298}$ = -27.3 cal/ (mol•deg). The *Z*-isomer is inert to [4+2]-cycloaddition under these conditions; Hammett plots of this unique reaction were also created. In addition, to better understand this intramolecular [4+2]-cycloaddition reaction, we are collaborating with Professor Kenneth Houk's group at UCLA from the viewpoint of computational chemistry, and the calculated results fit our observations very well (Chapter 3).

IV. Intramolecular [3+2]-Cycloaddition with a Diazo with an Alkene and Subsequent Transformation

Cascade reaction, a consecutive series of transformations occurred in one step, is noted for efficient construction of molecular complex, high atom economy and economies of time, labor, and resource management. Due to these benefits, discovery of novel cascade reactions has been in high demand as well as a challenging task of modern organic synthesis. Substrates with multiple functional groups are considered crucial and

fundamental to discovering cascade reactions. Inspired by gold-catalyzed [4+3]-cycloaddition of propargyl esters and unsaturated imines, we decided to use a modified propargyl system in which benzoate is replaced by phenyldiazoacetate that was expected to produce the azepine product that retained the phenyldiazoacetate functionality. Instead, a new and unexpected transformation occurred that reorganized the reactant atoms from the reactant ester to a diketone and rearranged the reactant atoms. To further understand this extensive process, we used the NMR spectroscopy to monitor the process. An intermediate, observed within 5 min that rapidly rearranged to diketone, was isolated by quenching the reaction after 5 min. Purified by silica gel chromatography, the isolated product was converted to the previously observed diketone at 80ºC in 90% yield without added catalyst. Furthermore, we carried out a series of kinetic studies with the isolated [4+3]-cycloaddition product for the subsequent transformation. The transformation was first order in with a rate constant $k_{obs} = 3.6 \times 10^{-4}$ sec^{-1} at 61 °C in DCE. The variation of the rate constant over temperatures ranging from 61℃ to 75℃ provided E_{act} = 22.6 kcal/mol, $\Delta H^{\ddagger}_{298}$ = 22.0 kcal/mol and $\Delta S^{\ddagger}_{298}$ = -9.21 cal/(mol•℃). This work was discussed in Chapter 4.

V. Future Work

This work has demonstrated convincingly that the concept of "diversity as a function of catalyst" can be used in the discovery of novel transformations. The product diversity in a catalytic reaction and divergent reaction pathways could be achieved by the choice of catalysts. Our research with propargylic diazoesters have lead us to discover three new catalyst-free transformations of diazo compounds. The electrophilic capability of diazo compounds plays an important role in those intramolecular transformations. However, intermolecular versions of α-diazoesters with alkenes, allenes, and dienes have not yet been explored. Since the chemical properties of diazo compounds are heavily influenced by their structures as well as the choice of catalysts, I believe that these intermolecular reactions, such as the [4+2]-cycloaddition reaction, will be achieved in the future, although a combination of hard work, reasonable design, and a bit of luck are necessary.

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