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Vinyldiazo Reagents and Metal Catalysts: A Versatile Toolkit for Heterocycle and Carbocycle Construction

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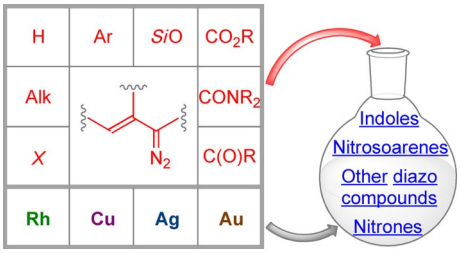
Dedicated to Professor Wenhao Hu on the occasion of his 50th birthday

Over the past decade, vinyldiazo compounds have provided mild, efficient, and highly selective methods for the construction of heterocycles and carbocycles. Dinitrogen extrusion with suitable catalysts provides the carbon framework for [3 + *n*] cycloaddition with a large variety of dipolarophiles. This minireview, covering the latest achievements in the field of metal-catalyzed cyclization reactions with vinyldiazo reagents, focuses on reagent- or catalyst-dependent chemodivergence: different vinyldiazo reagents or metal catalysts direct reactions to different cyclization pathways that give different reaction outcomes. Accordingly, metal-catalyzed cyclization reactions of vinyldiazo compounds with nitrosoarenes, nitrones, indoles, and other diazo compounds are chosen to showcase the controllable versatility of the combination of vinyldiazo reagents and metal catalysts.

1. Introduction

Carbocycle and heterocycle construction is one of the most important topics in organic synthesis.[1] Catalytic intra- and intermolecular transformations of diazo compounds provide mild, efficient, and highly selective methods for the syntheses of cyclic compounds[2] that compliment well-established ring-forming processes (e.g., Diels–Alder cycloaddition, Huisgen cycloaddition, Robinson annulation, and ring-closing metathesis). Recently, efficient and versatile cycloaddition methodologies from combinations of vinyldiazo reagents and metal catalysts have been exhibited in the construction of carbocycles and heterocycles.[3] As depicted in Scheme 1, the common core structure of vinyldiazo reagents is conjugated vinyl and diazo functionalities (C=C–C=N_2), whereas different substituents (e.g., hydro, alkyl, aryl, and silyloxy) and different electron-withdrawing groups (e.g., ester, amide, and ketone) are attached to the vinyl moiety and diazo carbon atom, respectively; rhodium (especially Rh_2L_4) and coinage-metal (including copper, silver, and gold) complexes serve as the catalysts in the ring-forming reactions.

The vinyldiazo compound has a dipolar structure that gives enhanced nucleophilic character to the vinylogous position. However, the extrusion of dinitrogen by a transition-metal compound forms a metallo-vinylcarbene, the dipolar structure of which has enhanced electrophilic character at the vinylogous carbon atom. This umpolung is one of the principal causes for the chemodivergence in catalytic reactions of vinyldiazo compounds.[3]



Scheme 1. Vinyldiazo reagents and metal catalysts employed with selected reactants for heterocycle or carbocycle formation. The toolkit on the left contains the substituted vinyldiazo compound (substituents colored red) and the transition metal of the catalyst used.

This minireview, covering the very latest achievements in the field of metal-catalyzed cyclization reactions with vinyldiazo reagents, focuses on reagent- or catalyst-dependent chemodivergence: 1) different substituents (e.g., hydro vs. silyloxy) or electron-withdrawing groups (e.g., ester vs. amide) installed on vinyldiazo reagents result in divergent cyclization pathways; 2) different metal catalysts (e.g., rhodium vs. copper) lead to distinct cyclization outcomes. Two systematic reviews on metal-catalyzed transformations of vinyldiazo compounds have emphasized methodology development and mechanistic overview.[3] In this review, metal-catalyzed cyclization reactions of vinyldiazo compounds with nitrosoarenes, nitrones, indoles, and other diazo compounds are selected and discussed to showcase the controllable versatility of the combination of vinyldiazo reagents and metal catalysts; we aim to provide an illustrated manual of the cyclization toolkit containing vinyldiazo reagents and metal catalysts, thus promoting its application and expansion by the wider synthetic community.

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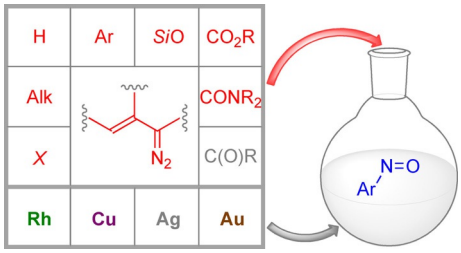
2. Cyclization Reactions of Nitrosoarenes

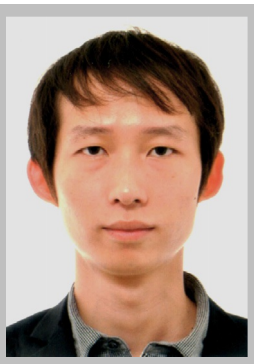
Over the past two decades, nitrosoarenes have been successfully employed in a variety of organocatalyzed and transition-metal-catalyzed ring-forming processes, such as 1,3-dipolar cycloadditions, hetero-Diels–Alder reactions, and annulation reactions involving *ortho*-C(sp^2)–H functionalization.[4] Recently, by treating nitrosoarenes with vinyldiazo reagents in the presence of metal catalysts (Scheme 2), new cyclization methodologies have been developed for the construction of heterocyclic compounds;[5,6] these approaches have proven to be either reagent[5] or catalyst dependent.[6]



Scheme 2. Vinyldiazo reagents and metal catalysts employed in cyclization reactions of nitrosoarenes.

2.1. Cyclization reactions of alkenyldiazoacetates with nitrosoarenes

In 2011, Liu et al.[5] presented gold(I)-catalyzed reactions between alkenyldiazoacetates and nitrosoarenes (Scheme 3). In most cases, gold–alkenylcarbenes, formed by the extrusion of dinitrogen from alkenyldiazoacetates (R^1 = H, Me, Et, Cl, MeO), underwent vinylogous addition with nitrosoarenes **1**; subsequent 6π-electrocyclic ring closure followed by oxidative aromatization produced a series of quinoline *N*-oxides **2** in moderate to good yields (Scheme 3a). Notably, copper(I) and dirhodium(II) catalysts, which were also examined, afforded the same formal [3+3] cycloadducts as those obtained under



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Yang Yu was born in Harbin, China. He received his B.E. degree from East China University of Science and Technology in 2008 and his M.Sc. degree from Shanghai Institute of Organic Chemistry (SIOC) in 2011. He obtained his Ph.D. degree from the University of Hong Kong (HKU) under the supervision of Professor Pauline Chiu in 2015. At HKU, he was engaged in the total synthesis of natural products and rhodium-catalyzed cyclization reactions. Then, he began postdoctoral studies with Professor Michael P. Doyle at the University of Texas at San Antonio in 2016. His current research is focused on the development of novel metal carbene transformations and metal-catalyzed oxidation reactions.

Julietta Yedoyan received her M.Sc. degree in pharmaceutical chemistry from Yerevan State University. After research experience in the groups of Professor Ashot Saghyan (Yerevan State University) and Professor Peter Langer (University of Rostock), she joined the group of Professor Michael P. Doyle at the University of Texas at San Antonio as a research assistant. Her research in the Doyle group focused on highly selective catalytic metal carbene transformations, in particular the cycloaddition reactions of enoldiazo compounds. Currently, she investigates synthetic methods for heterocycle and carbocycle construction as a DAAD Ph.D. scholar under the supervision of Professor Oliver Reiser at the University of Regensburg.

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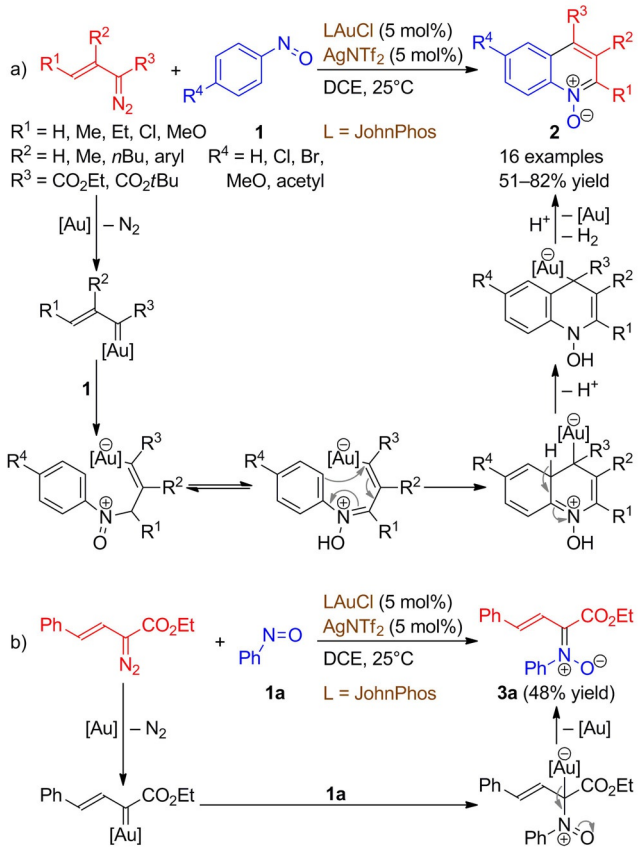
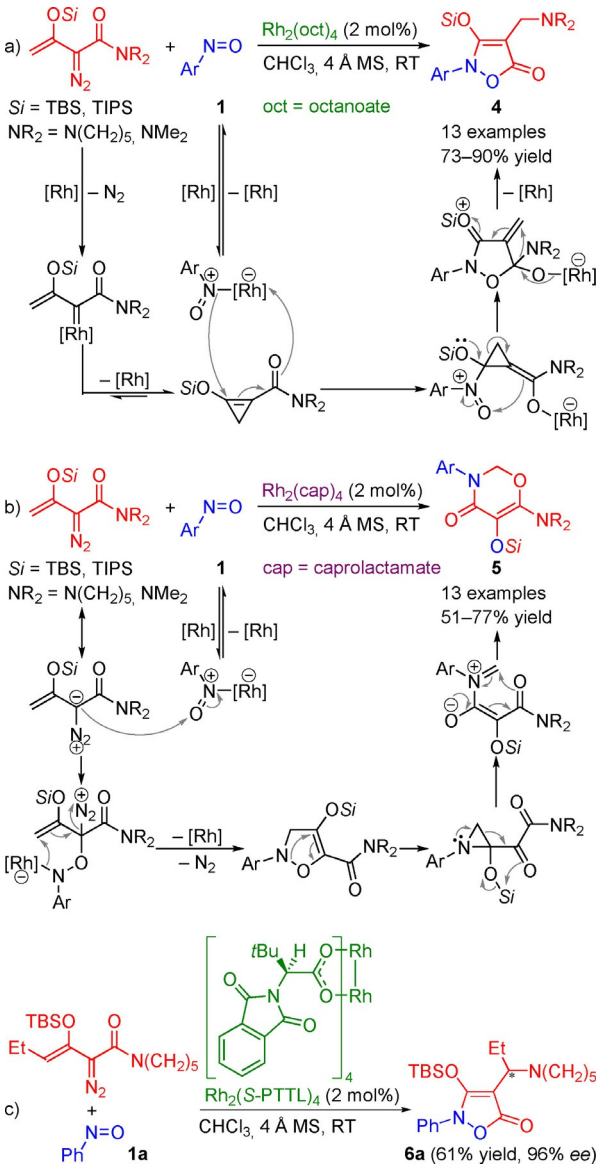


Scheme 3. Gold-catalyzed cyclization reactions of alkenyldiazoacetates with nitrosoarenes. $AgNTf_2$ = silver bis(trifluoromethanesulfonyl)imide; DCE = 1,2-dichloroethane; JohnPhos = (2-biphenylyl)di-*tert*-butylphosphine.



Scheme 4. Rhodium-catalyzed cyclization reactions of enoldiazoacetamides with nitrosoarenes. TBS = *tert*-butyldimethylsilyl; TIPS = triisopropylsilyl.

gold(I) catalysis, albeit in somewhat lower yields.[5] In comparison with the reactions of alkenyldiazoacetates bearing less sterically hindered γ-substituents (Scheme 3a), nucleophilic attack by nitrosobenzene (**1a**) occurred preferentially at the carbene carbon atom over the vinylogous position of the gold–carbene intermediate generated from ethyl (*E*)-styryldiazoacetate (R^1 = Ph), thus furnishing nitrone **3a** in 48% yield (Scheme 3b).

The success of this cyclization reaction (Scheme 3a) was owing to vinylogous addition by the nitrosoarene to form a nitrosonium intermediate that could rapidly tautomerize into its oxime form, thus setting up a sequence of reactions that resulted in the formation of product **2**. Consistent with the electrophilic character of the vinylogous position, chloro and methoxy substituents as R^1 resulted in lower product yields than if R^1 = H or alkyl.[5] Steric influences in this transformation appeared to be significant, and the gold(I) catalyst may have the least steric bias.

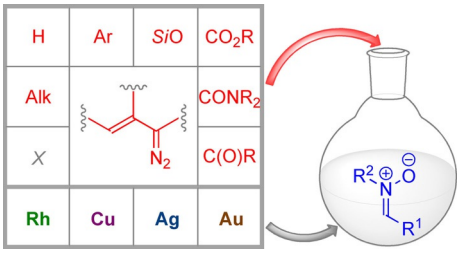
2.2. Cyclization reactions of enoldiazoacetamides with nitrosoarenes

Very recently, Doyle and co-workers[6] reported catalyst-controlled cyclization reactions of enoldiazoacetamides with nitrosoarenes (Scheme 4). Rhodium(II) octanoate [$Rh_2(oct)_4$] and rhodium(II) caprolactamate [$Rh_2(cap)_4$] selectively catalyzed formal [3+2] and [5+1] cyclizations to produce multifunctionalized 5-isoxazolones **4** and 1,3-oxazin-4-ones **5**, respectively. Here, steric effects that would lead to products such as nitrone **3a** from reactions at the metal carbene carbon atom (Scheme 3b) were not evident. Mechanistic studies uncovered distinct catalytic activities and reaction intermediates. $Rh_2(oct)_4$ catalyzed both the generation of donor–acceptor cyclopropenes (by dinitrogen extrusion from enoldiazoacetamides/metallo-enolcarbene formation/intramolecular cyclization) and subsequent aza-Michael addition of nitrosoarenes to the cyclopropenes, and the following five-membered ring closure/cyclopropane opening/dialkylamino migration process delivered the formal [3+2] cycloadducts (Scheme 4a). Rather than directly decomposing enoldiazoacetamides, $Rh_2(cap)_4$ activated nitrosoarenes for electrophilic attack at the diazo carbon atom, and

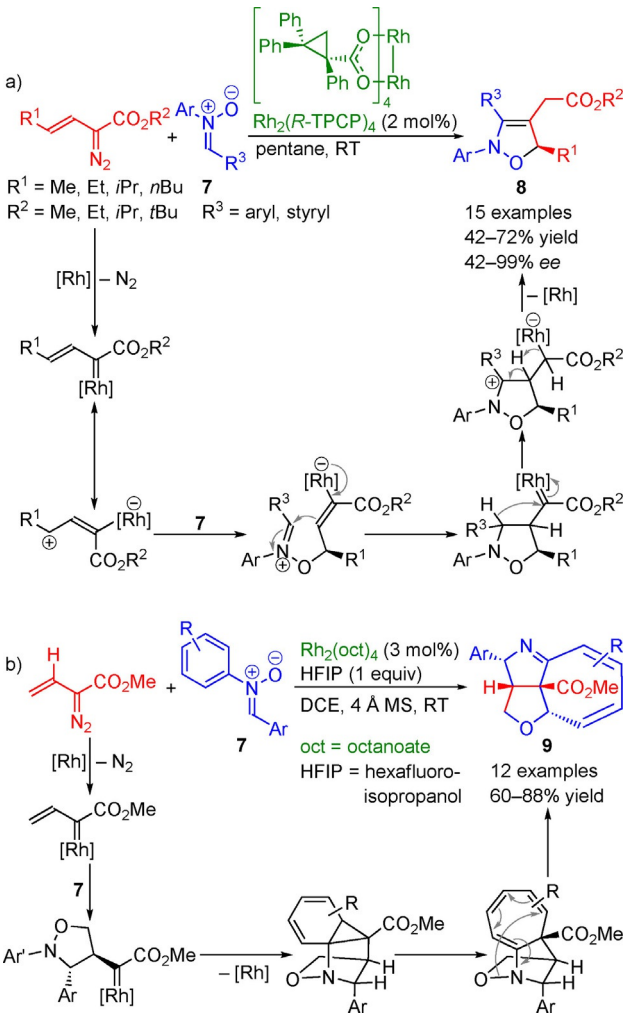
the resulting diazonium intermediates underwent intramolecular nucleophilic addition to the vinylogous position, thus furnishing 4-isoxazolines that rapidly rearranged to 2-acylaziridines; a subsequent aziridine opening/silyl migration/six-membered-ring closure sequence defined the overall [5+1] cyclization (Scheme 4b). Furthermore, a mechanism-inspired enantioselective Rh_2(*S*-PTTL)$_4$-catalyzed reaction between γ-ethyl enoldiazoacetamide and nitrosobenzene produced heterocycle-linked trialkylamine **6a** with 96% *ee* (Scheme 4c).

3. Cyclization Reactions of Nitrones

Nitrones are an important class of dipolar reactants in ring-forming reactions, in which they usually serve as C–N–O-type components for heterocycle construction.[7] As depicted in Scheme 5, various vinyldiazo reagents and metal catalysts have been employed in cyclization reactions of nitrones.[8–13] These highly reagent-[8–11] and catalyst-dependent processes[11–13] provide efficient approaches to distinct heterocyclic compounds. In some cases, the use of an appropriate combination of vinyldiazo reagents and metal catalysts is crucial for achieving compatible reactivity and controllable selectivity.[12,13]



Scheme 5. Vinyldiazo reagents and metal catalysts employed in cyclization reactions of nitrones.

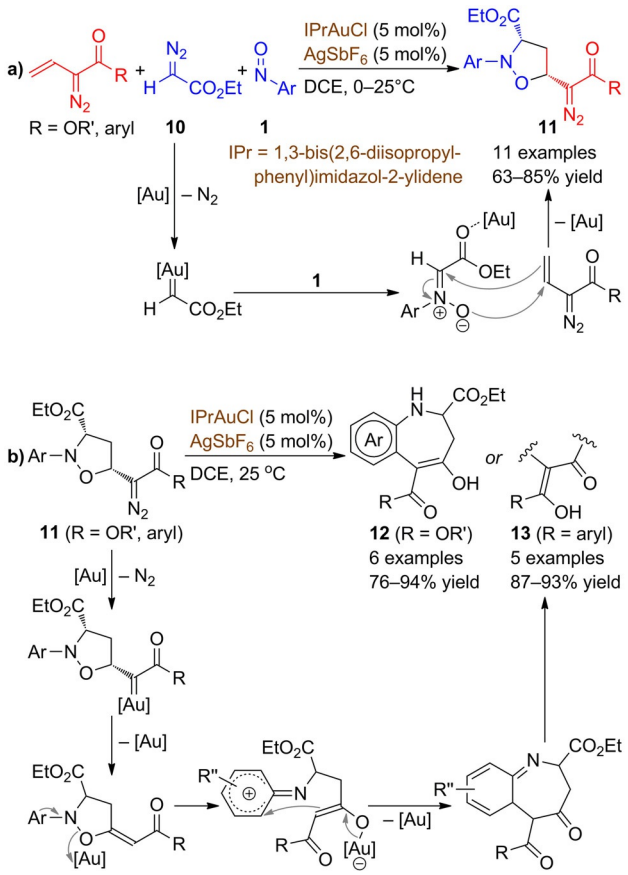


Scheme 6. Rhodium-catalyzed cyclization reactions of alkenyldiazoacetates with nitrones.

3.1. Cyclization reactions of alkenyldiazo compounds with nitrones

Enantioselective dirhodium(II)-catalyzed formal [2+3]-cycloaddition reactions between alkenyldiazoacetates, in which an alkyl group is *trans* at the γ-position, and nitrones were reported by Qin and Davies in 2013.[8] As illustrated in Scheme 6a, Rh_2(*R*-TPCP)$_4$ facilitated dinitrogen extrusion from alkenyldiazoacetates to form rhodium–alkenylcarbenes; nucleophilic attack by nitrones **7** at the vinylogous position of the electrophilic rhodium–alkenylcarbenes followed by five-membered-ring closure produced rhodium–4-isoxazolidinylcarbenes; subsequent [1,3]-hydride abstraction and [1,2]-proton transfer completed this transformation. Interestingly, according to early work from the Doyle group,[9,11] dirhodium(II)-catalyzed cyclization reactions of nitrones with methyl 2-diazo-3-butenoate, which does not bear a substituent at the γ-position (Scheme 6b),[9] and methyl enoldiazoacetate, in which a silyloxy substituent is at the β-position (Scheme 8a, Section 3.2),[11] resulted in distinctly different outcomes. As depicted in Scheme 6b, rhodium–4-isoxazolidinylcarbenes were also generated by rhodium–vinylcarbene formation from methyl 2-diazo-3-butenoate and their formal [2+3] cycloaddition with diarylnitrones.[9] Subsequently, rather than hydride and proton transfer (Scheme 6a),[8] intramolecular aromatic cycloaddition (Buchner ring expansion) occurred; subsequent rearrangement triggered by N–O bond cleavage delivered tricyclic products **9** (Scheme 6b).[9]

As described in Section 2.1 (Scheme 3b)[5] and in other reports,[14] nitrone species can be generated by condensation reactions between nitrosoarenes and diazo compounds. Utilizing this strategy, Pagar and Liu[10] developed a gold(I)-catalyzed three-component reaction of vinyldiazo compounds, ethyl diazoacetate, and nitrosoarenes (Scheme 7). Between these two classes of diazo compounds, the gold(I) complex, generated in situ from IPrAuCl [IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene] and $AgSbF_6$, selectively facilitated dinitrogen extrusion from ethyl diazoacetate (**10**); the resulting gold carbene reacted with nitrosoarenes **1** to form nitrone species that further underwent [3+2] cycloaddition with vinyldiazo compounds to furnish diazo-containing isoxazolidine derivatives **11** (Scheme 7a). The retention of the diazo functionality in products **11** was attributed to catalyst deactivation, as treating

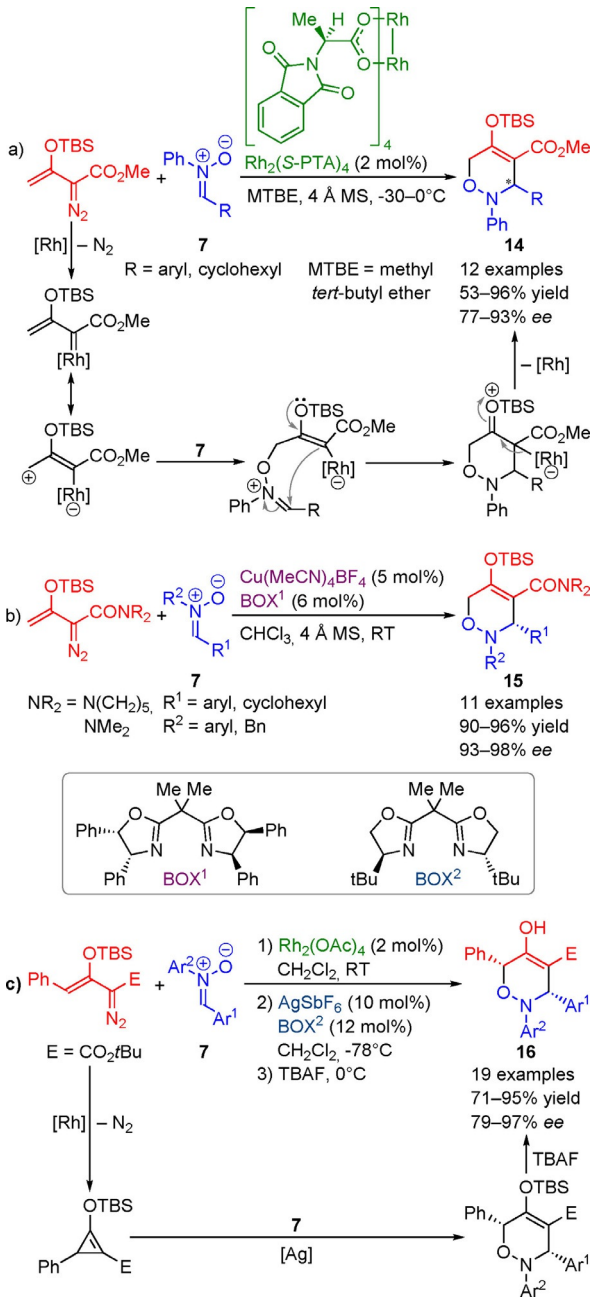


Scheme 7. Gold-catalyzed cyclization reactions of vinyldiazo compounds with in situ generated nitrone species.

compounds **11** with the same gold(I) catalyst led to dinitrogen extrusion to form gold–5-isoxazolidinylcarbenes that further underwent N–O bond cleavage and intramolecular aromatic substitution to afford benzo[*b*]azepine derivatives **12** or **13** (Scheme 7 b).

3.2. Cyclization reactions of enoldiazo compounds with nitrones

In 2011, Doyle and co-workers[11] presented dirhodium(II)-catalyzed formal [3+3]-cycloaddition reactions between methyl enoldiazoacetate and nitrones to produce chiral 3,6-dihydro-1,2-oxazine derivatives **14** in moderate to high yields with good enantioselectivities (Scheme 8 a). In contrast to dirhodium(II)-catalyzed [2+3] cycloadditions of β-unsubstituted alkenyldiazoacetates with nitrones (Scheme 6 a),[8] the enoldiazoacetate furnished [3+3] cycloadducts, in which the silyloxy group enhanced electrophilic ring closure to the metal-bound vinyl carbon atom that was produced following rhodium–enolcarbene formation and vinylogous addition (Scheme 8 a).[11] This efficient synthetic strategy to access enantioenriched six-membered heterocycles in which the enolcarbene serves as the three-carbon component was successfully applied to various 1,3-dipoles and enoldiazo compounds,[15] and the use of an appropriate combination of enoldiazo reagents and metal catalysts was crucial for achieving compatible reactivity and controllable selectivity.[12,13] In contrast to the reactions of enoldiazoacetates, however, the reactions of enoldiazoacetamides with nitrones by using in situ generated chiral bis(oxazoline)-copper(I) complexes exhibited high catalytic activity and exceptional enantiocontrol, whereas with enoldiazoacetamides all of the tested dirhodium(II) catalysts [$Rh_2(OAc)_4$, Rh_2(*S*-PTA)$_4$, Rh_2(*S*-PTTL)$_4$, and Rh_2(*S*-DOSP)$_4$] afforded very low coupling with the nitrone after the enoldiazoacetamide had been fully consumed (Scheme 8 b).[12] Furthermore, with γ-phenyl enoldiazoacetate no [3+3]-cycloaddition product was obtained under the catalysis of $Rh_2(OAc)_4$, but with a chiral silver catalyst high

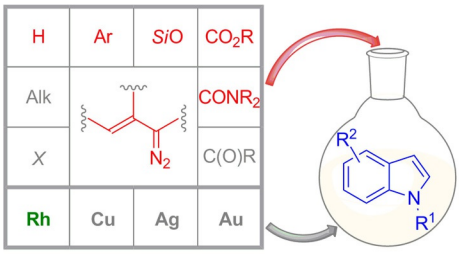


Scheme 8. Metal-catalyzed cyclization reactions of enoldiazo compounds with nitrones. TBAF = tetrabutylammonium fluoride.

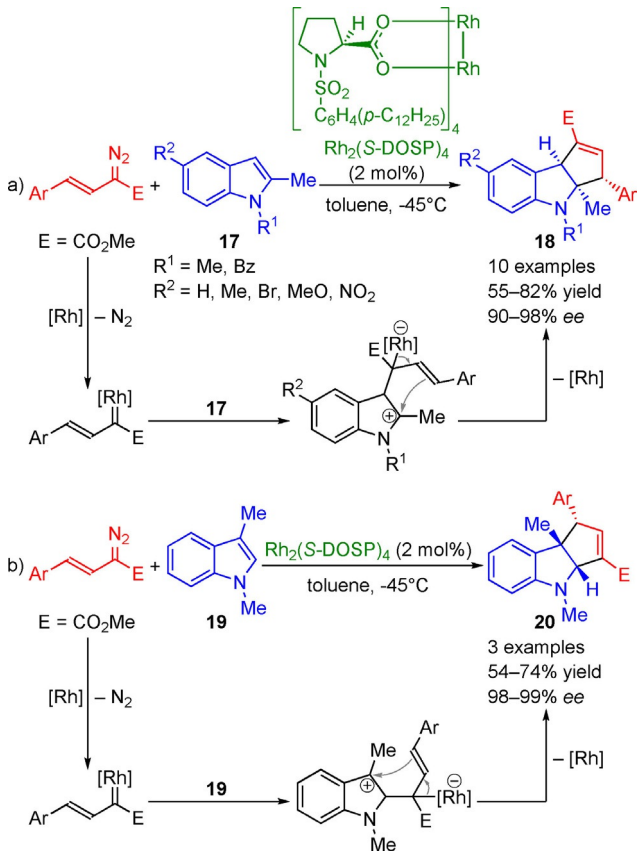
yields and enantioselectivities were achieved by rhodium-catalyzed cyclopropene formation and subsequent silver-catalyzed cycloaddition (Scheme 8c).[13] In this latter case, steric factors appeared to inhibit coupling with the nitrone by using dirhodium(II) catalysts.

4. Cyclization Reactions of Indoles

Catalytic functionalization of indoles has attracted considerable interest over the past few decades. Achieving controllable stereoselectivity is a major focus of research in this area.[16] By using vinyldiazo reagents and rhodium catalysts (Scheme 9), highly regio- and enantioselective dearomatizing annulation reactions of indoles have been developed to produce fused indoline derivatives.[17,18] Reagent- and catalyst-dependent regiocontrol in these transformations is discussed in this section.



Scheme 9. Vinyldiazo reagents and metal catalysts employed in cyclization reactions of indoles.



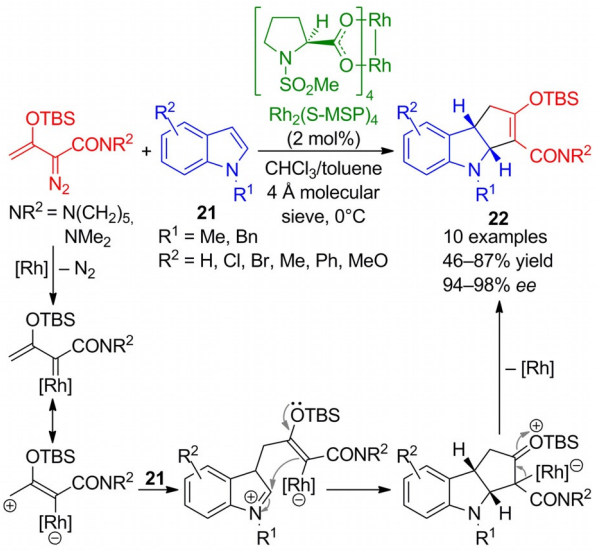
Scheme 10. Rhodium-catalyzed cyclization reactions of arylvinyldiazoacetates with indoles. Bz = benzoyl.

4.1. Cyclization reactions of arylvinyldiazoacetates with indoles

In 2010, Lian and Davies[17] reported Rh_2(*S*-DOSP)$_4$-catalyzed [3+2]-annulation reactions between arylvinyldiazoacetates and indoles (Scheme 10). Electrophilic addition of the carbene carbon atom of rhodium–arylvinylcarbenes generated from arylvinyldiazoacetates occurred at the less sterically hindered C3 position of 2-methylindoles **17**, and subsequent ring closure delivered cyclopentane-fused indolines **18** with excellent enantiocontrol (Scheme 10a). In contrast, electrophilic addition by the carbene carbon atom occurred at the less sterically hindered C2 position of 3-methylindole **19**, thus furnishing the opposite regioisomeric series of fused indolines **20** (Scheme 10b). Notably, the reaction of *N*-methylindole (C2,C3-unsubstituted) with methyl (*E*)-styryldiazoacetate was also examined and only afforded moderate regioselectivity with a 4:1 ratio between **18**- and **19**-type annulation products.[17]

4.2. Cyclization reactions of enoldiazoacetamides with indoles

Recently, highly regio- and enantioselective dearomatizing annulation of C2,C3-unsubstituted indoles was realized by using enoldiazo reagents and chiral dirhodium(II) catalysts.[18] As illustrated in Scheme 11, the sterically compact Rh_2(*S*-MSP)$_4$ catalyst



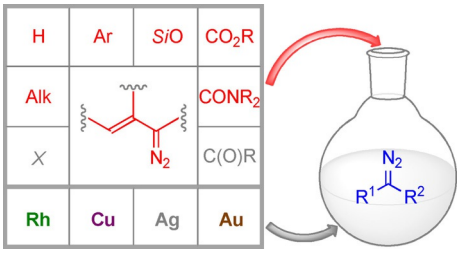
Scheme 11. Rhodium-catalyzed cyclization reactions of enoldiazoacetamides with indoles.

facilitated dinitrogen extrusion from enoldiazoacetamides to form rhodium–enolcarbenes; electrophilic addition by the vinylogous carbon atom of the rhodium–enolcarbenes occurred at the more nucleophilic (electron-rich) C3 position of indoles **21**; subsequent ring closure with elimination of the rhodium

catalyst delivered [3+2]-annulation products **22** with regioisomeric ratios over 20:1. Moreover, catalyst-controlled switchable regioselectivity was achieved in the [3+2] annulation between methyl enoldiazoacetate and *N*-methylindole: sterically bulkier Rh_2(*S*-DOSP)$_4$ and Rh_2(*S*-TFPTTL)$_4$ provided regioisomeric ratios of 5:1 and 1:19, respectively, albeit with significantly diminished enantioselectivities.[18]

5. Cyclization Reactions of Structurally Different Diazo Compounds

The development of selective catalytic cyclization reactions between structurally different diazo compounds is highly intriguing, but several challenges need to be addressed. Can the decomposition of the two diazo compounds be discriminated by the catalyst? Are the intermediates generated from different diazo compounds compatible with each other? Over the past decade, vinyldiazo reagents and metal catalysts have become ideal choices to overcome these challenges (Scheme 12); representative works in the field are included in this section, most of which present reagent- and catalyst-dependent processes.[19–22]

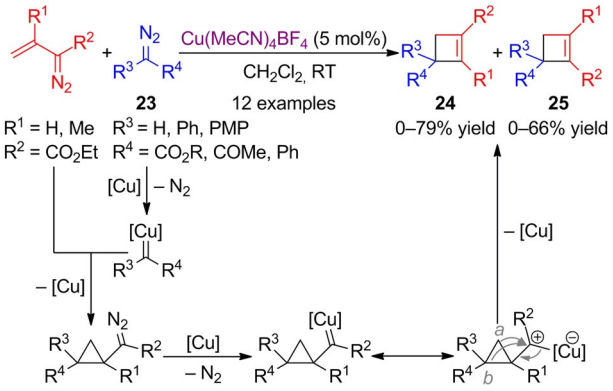


Scheme 12. Vinyldiazo reagents and metal catalysts employed in cyclization reactions of structurally different diazo compounds.

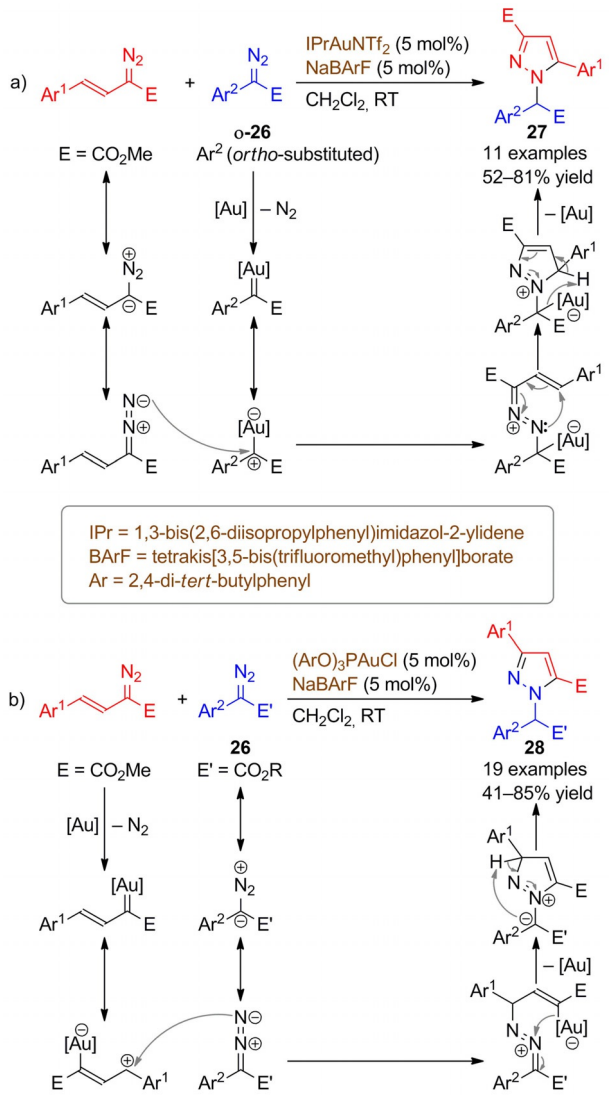
5.1. Cyclization reactions of alkenyl- and arylvinyldiazoacetates with other diazo compounds

In 2009, Barluenga et al.[19] reported the copper(I)-catalyzed formal [3+1] cycloaddition of alkenyldiazoacetates with diazo compounds **23**, including diazoacetates, aryldiazoacetates, phenyldiazomethane, and diphenyldiazomethane (Scheme 13). The copper catalyst [Cu(MeCN)$_4$BF$_4$] decomposed diazo compounds **23** in preference to alkenyldiazoacetates to form copper–carbene intermediates that underwent cyclopropanation with the alkenyldiazoacetates. The resulting cyclopropyldiazoacetates were then decomposed by the copper catalyst to generate copper–cyclopropylcarbenes. Subsequent 1,2-migration of C^a or C^b to the electrophilic carbene carbon atom produced cyclobutenes **24** or **25**, respectively. Notably, enantioselective copper(I)-catalyzed [3+1] cycloaddition of enoldiazoacetates was recently developed by utilizing sulfur ylides as one-carbon-atom synthons, thus furnishing highly enantioenriched cyclobutene derivatives.[23]

In 2015, Sun and co-workers[20] presented catalyst-controlled cyclization reactions between arylvinyldiazoacetates and aryldiazoacetates (Scheme 14). Different gold catalysts selectively



Scheme 13. Copper-catalyzed cyclization reactions of alkenyldiazoacetates with other diazo compounds. PMP = *para*-methoxyphenyl.



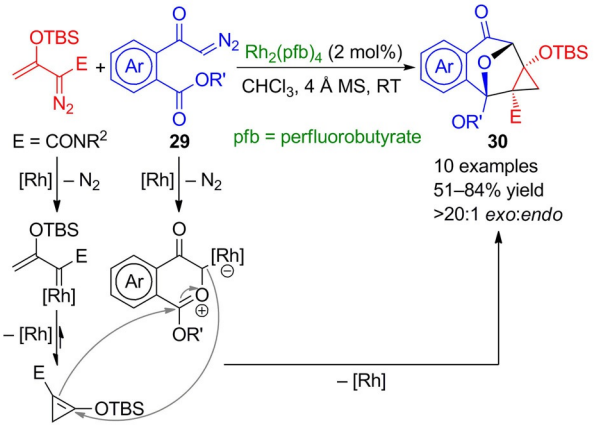
Scheme 14. Gold-catalyzed cyclization reactions of arylvinyldiazoacetates with aryldiazoacetates.

decomposed either arylvinyldiazoacetates or aryldiazoacetates to generate their respective gold–carbene intermediates. With

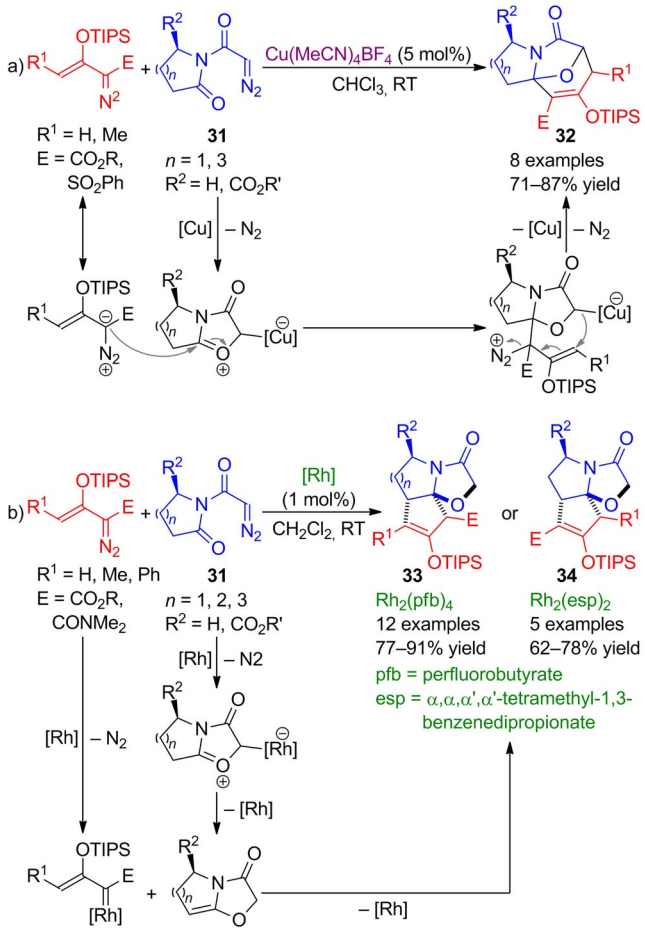
catalysis by an N-heterocyclic carbene gold(I) complex, the preferentially formed gold–arylcarbenes underwent electrophilic addition at the terminal nitrogen atom of the arylvinyldiazoacetates, and subsequent ring closure followed by [1,3]-proton transfer delivered pyrazole derivatives **27** (Scheme 14a).[20] Notbaly, *ortho*-substituents on Ar^2 inhibited C=C bond formation owing to electrophilic attack by the gold–arylcarbenes at the diazo carbon atom of the arylvinyldiazoacetates.[24] Upon changing the catalyst to a triarylphosphite gold(I) complex, gold–arylvinylcarbenes were preferentially formed, and they underwent electrophilic addition from their vinylogous position to the terminal nitrogen atom of aryldiazoacetates **26**; subsequent ring closure followed by [1,4]-proton transfer produced formal [3+2]-cycloadducts **28** (Scheme 14b).[20]

5.2. Cyclization reactions of enoldiazo compounds with other diazo compounds

Recently, highly selective cyclization reactions between enoldiazo compounds and other diazo compounds were developed by the Doyle group (Schemes 15 and 16).[21,22] Under the catalysis of rhodium(II) perfluorobutyrate [Rh_2(pfb)$_4$], donor–acceptor cyclopropenes and carbonyl ylides were generated by carbene formation/intramolecular cyclization from enoldiazoacetamides and α-diazoketones **29**, respectively; subsequent [2+3] cycloaddition produced cyclopropane-fused benzoxa[3.2.1]octane derivatives **30** (Scheme 15).[21] The rapid generation of the relatively stable cyclopropenes to trap the transient carbonyl ylides inhibited other competing reaction pathways (e.g., carbonyl ylide dimerization).[21] In cyclization reactions of enoldiazo compounds with α-diazocarboximides, the copper(I) catalyst [$Cu(MeCN)_4BF_4$] preferentially decomposed α-diazocarboximides **31** to form carbonyl ylides (isomünchnones) that further underwent [3+3] cycloaddition with enoldiazo compounds, thus furnishing epoxypyrrolo[1,2-*a*]azepine derivatives **32** (Scheme 16a).[22] By contrast, dirhodium(II) catalysts facilitated dinitrogen extrusion from both diazo compounds to generate rhodium–enolcarbenes and cyclic ketene–N,O-acetals



Scheme 15. Rhodium-catalyzed cyclization reactions of enoldiazoacetamides with α-diazoketones.



Scheme 16. Metal-catalyzed cyclization reactions of enoldiazo compounds with α-diazocarboximides.

(through [1,4]-proton transfer of isomünchnones), and subsequent [3+2] cycloaddition furnished cyclopenta[2,3]pyrrolo[2,1-*b*]oxazoles **33** or **34** with moderate to high regioselectivities that were tuned by electronic (i.e., in the case of [Rh_2(pfb)$_4$]) and steric (i.e., in the case of [Rh_2(esp)$_2$], esp = α,α,α′,α′-tetramethyl-1,3-benzenedipropionate) influences of the catalyst ligands (Scheme 16b).[22]

6. Conclusions

Vinyldiazo compounds are dipolar reagents that activate the conjugated double bond towards electrophilic addition reactions that are manifested in cycloaddition processes such as that shown in Scheme 7a. However, treatment of vinyldiazo compounds with a variety of transition-metal complexes as catalysts reverses the polarity (umpolung) of the vinyl–carbon unit to activate the conjugated double bond for nucleophilic addition, which is revealed in cycloaddition processes such as those shown in Scheme 6 (cycloaddition to the C=C) and Scheme 8 (cycloaddition to the C=C–carbene). The nature of the cycloaddition process leading to either outcome is dependent on the vinyldiazo substituents, the reacting dipole, and the catalyst, but there is growing evidence that the substitu-

ents of the vinyldiazo compound have a major role in determining the nature of the cycloaddition process. Silyl-protected enoldiazo compounds, in particular, utilize an oxygen lone pair of electrons to facilitate [3+*n*]-cycloaddition reactions. Enoldiazoacetates and -acetamides are a subclass of vinyldiazo compounds that are directly accessed in high yields from diazoacetoacetates and -acetamides by treatment with silyl triflate/triethylamine. These compounds are exceptionally stable at or below room temperature, having no tendency to undergo intramolecular dipolar cycloaddition to form 3*H*-pyrazoles, and they have remarkable versatility in catalytic cyclization reactions. Their intermolecular [3+*n*]-cycloaddition reactions have allowed the facile syntheses of carbocyclic and heterocyclic compounds that occur with high selectivities. Still, all of the factors that govern these processes have not yet been determined, and the full range of substituents on vinyldiazo compounds that are suitable for cycloaddition has not been established.

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Conflict of interest

The authors declare no conflict of interest.

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