ACS Catalysis

Review

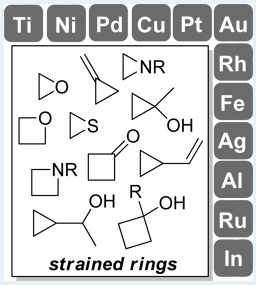
pubs.acs.org/acscatalysis

Recent Advances in the Metal-Catalyzed Ring Expansions of Three- and Four-Membered Rings

Daniel J. Mack[§] and Jon T. Njardarson*[,‡]

[‡]Department of Chemistry and Biochemistry, University of Arizona, 1306 E. University Blvd., Tucson, Arizona 85721, United States
[§]Department of Chemistry and Chemical Biology, Baker Laboratory, Cornell University, Ithaca, New York 14853, United States

ABSTRACT: New catalytic ring-expansion reactions of strained ring (hetero- and carbocyclic) substrates reported in the last six years (2006−2012) are presented. As evident from the diversity of new approaches, this is a vibrant area of research. Metals ranging from magnesium to gold have been used as catalysts. Some of these reactions allow access to enantioenriched products by employing catalysts decorated with chiral organic motifs (primarily C-2 symmetric).



KEYWORDS: *ring expansion, catalysis, strained rings, heterocycles, cyclopropane, cyclobutane*

Ring expansions of strained rings have attracted the interest of organic chemists for decades. Of these, the classic ring expansion of vinyl cyclopropanes to cyclopentene products is best known and studied.[1] This Review covers the literature from 2006 to the present with the aim of summarizing new contributions to the ring expansion of three- and four-membered rings using metal catalysis. To keep the coverage reasonable in scope, we have chosen to focus the review, with few exceptions, only on ring expansions wherein no external atoms have been added to the product during the catalytic ring-expansion process. To best calibrate and educate the reader about new advancements being made in this exciting field, we have separated the topics on the basis of ring size and whether the ring-expansion substrates are hetero- or carbocyclic. With the majority of new contributions in the last six years being focused on cyclopropane and cyclobutane substrates, we have further divided those contributions into smaller segments arranged according to unique substitution patterns critical to the ring expansions being presented:

Three-membered rings

(1) heterocyclic
  (a) oxiranes
  (b) thiiranes
  (c) aziridines
  (d) other
(2) cyclopropanes
  (a) methylenecyclopropanes
  (b) vinyl- and alkynyl-substituted cyclopropanes
  (c) cyclopropanes containing endo- and exocyclic alcohols

Four-membered rings

(1) heterocyclic
  (a) oxetanes
  (b) thietanes
  (c) azetidines
  (d) other
(2) cyclobutanes
  (a) cyclobutanones
  (b) cyclobutanols

THREE-MEMBERED RINGS

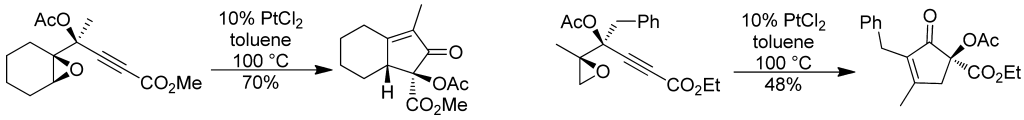
New heterocyclic contributions have been focused primarily on ring-expanding oxirane and aziridine substrates. With cyclopropanes being the most studied substrate class covered in this review, we have divided our coverage of their ring expansions into three sections on the basis of the position and nature of key substituents (olefins, alkynes, and alcohols).

Heterocyclic Three-Membered Rings. *Oxiranes.* In the last six years, several new metal-catalyzed oxirane ring expansions have been reported. A diversity of metals, ranging from early to late transition metals such as iron to late ones such as gold, have been used. These new contributions are detailed in the following Schemes.

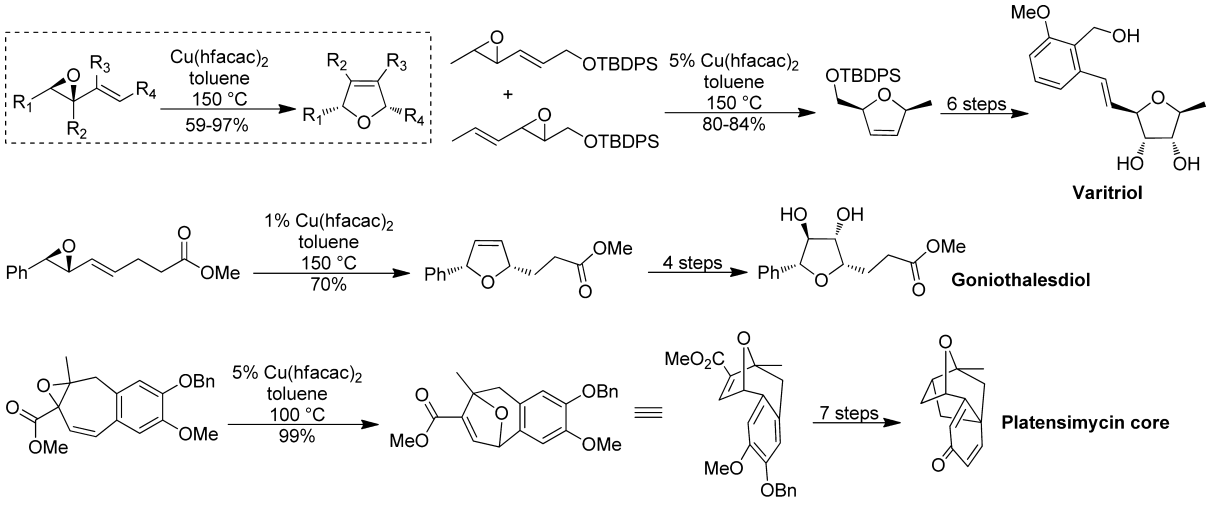
In 2006, Professor Sarpong reported the platinum(II)-catalyzed ring expansion of oxiranes substituted with propargylic ester groups to cyclopentenone products (Scheme 1).[2] Yields for this new reaction range from 48% to 75%. Trisubstituted oxiranes embedded within a ring were primarily used for these studies. The authors postulate that an interplay between a platinum-complexed alkyne and the adjacent acetate results in the formation of a platinum carbene intermediate that reacts with the oxirane to form a pyran. This pyran product then proceeds to open and follow a platinum-enabled Nazarov-type cyclization pathway to form the cyclopentenone product. This is a nice

Received: November 28, 2012
Revised: January 8, 2013
Published: January 14, 2013

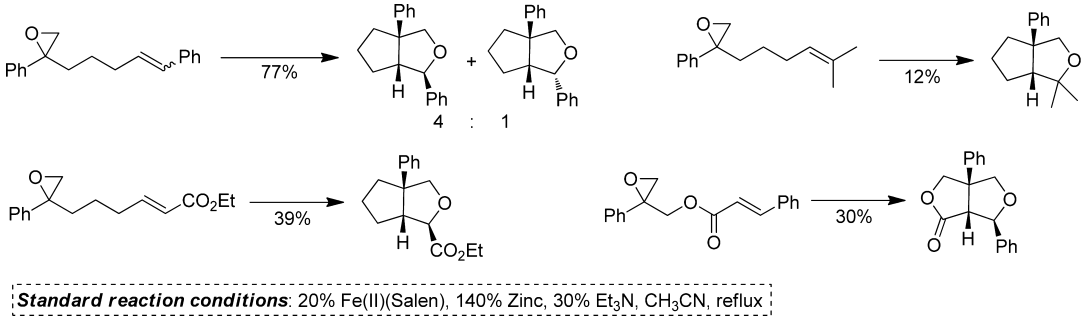
Scheme 1. Platinum-Catalyzed Ring Expansion of Propargylic Oxiranes



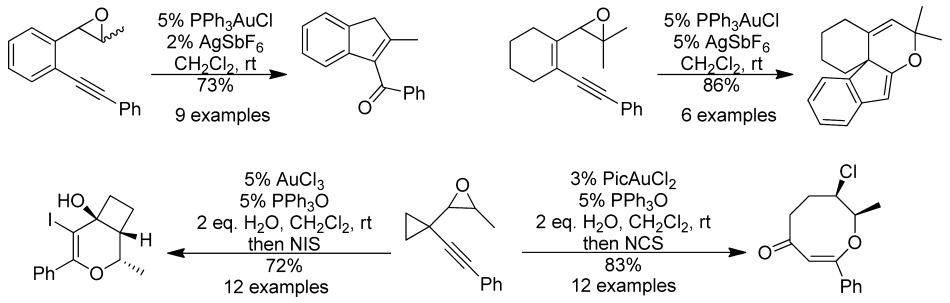
Scheme 2. Copper-Catalyzed Ring Expansion of Vinyl Oxiranes



Scheme 3. Iron-Catalyzed Ring Expansion of Aryl-Substituted Oxiranes



Scheme 4. Gold-Catalyzed Ring Expansion of Alkyne-Tethered Oxiranes



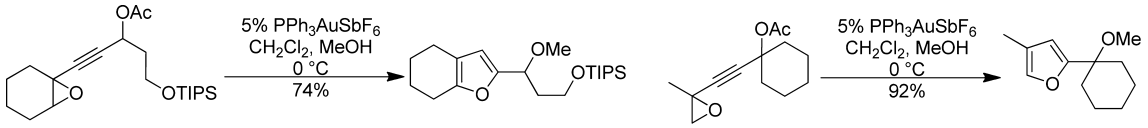
new entry to access densely substituted cyclopentenone products from an easily assembled propargylic precursor.

In the past few years, our group has developed and studied the copper-catalyzed ring expansion of vinyl oxiranes (Scheme 2).[3] We demonstrated that $Cu(hfacac)_2$, a stable and inexpensive catalyst, was uniquely suited for this catalytic challenge. Using toluene as solvent, vinyl oxirane substrates ring-expand stereoselectively[4] in uniformly high yields (59−97%). Ring expansions can even be performed without solvent, which is a testament to the robustness of this reaction. We have showcased the strength and versatility of this new catalytic reaction by employing it in concise total syntheses of the natural products varitriol,[5] goniothalesdiol and platensimycin. Recently, we have shown that the mechanism of this unique ring expansion proceeds through an in situ reduction pathway to form a Cu(I)(hfacac) catalyst, which then proceeds to insert into the C−O oxirane bond, rearrange to form a six-membered metallocycle, and reductively eliminate to form the 2,5-dihydrofuran product.[6]

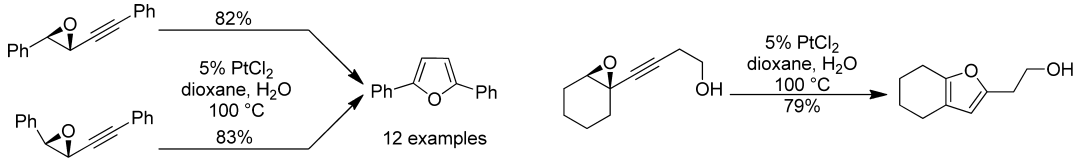
Professor Hilt has extended and greatly improved his intriguing iron-catalyzed stilbene oxide olefin addition approach[7] to

dx.doi.org/10.1021/cs300771d | ACS Catal. 2013, 3, 272−286

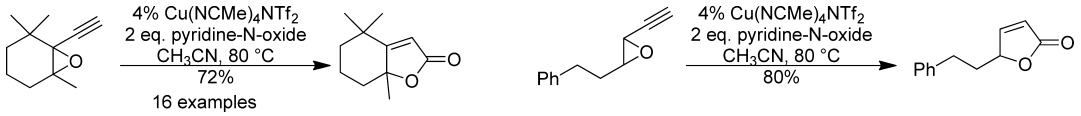
Scheme 5. Gold-Catalyzed Oxidative Ring Expansion of Alkynyl Oxiranes



Scheme 6. Platinum-Catalyzed Ring Expansion of Alkynyl Oxiranes



Scheme 7. Copper-Catalyzed Ring Expansion of Alkynyl Oxiranes



form substituted tetrahydrofurans to also include intramolecular variants (Scheme 3).[8] Fifteen examples of 1,1-disubstituted oxiranes containing an aryl group and a linear fragment containing olefins substituted in a variety of ways are reported. Yields of the cycloadducts range from 0 to 88%, with styrenyl or ene-yne groups separated by three atoms from the oxirane being the optimal substrate class (57−88%). Yields drop significantly when electron-deficient olefins are used as acceptors (29−39%); 1,2-epoxides perform poorly and separating the olefin acceptor from the oxirane by one additional atom results in no product being formed. Hilt proposes that zinc reduces iron(II) in situ to an iron(I) catalyst, which then opens the oxirane bond by delivering an electron, forming an iron(II)alkoxide complex containing a benzylic radical. Following a 5-exo radical cyclization, a back electron transfer generates a carbocation, which is then immediately trapped by the iron-complexed alkoxide.

Professor Liu has studied and reported on the gold-catalyzed ring expansions of oxirane substrates tethered to an alkyne separated by an aryl,[9] alkenyl, or cyclopropyl[10] group (Scheme 4). In his earlier report, he demonstrated that a gold(I) catalyst in the presence of a silver additive in methylene chloride at room temperature could convert *ortho*-alkynyl styrene oxide substrates to substituted indenes. Aryl substitution of the terminal alkyne was essential for this reaction to proceed. Interestingly, this ring expansion could be expanded to include trisubstituted oxiranes simply by omitting the gold catalyst and employing only $AgSbF_6$ as catalyst. When a cyclohexene was used instead of an aryl group to separate the oxirane from the alkyne, the ring expansion followed a different pathway, forming tetracyclic pyran products. Cyclohexenes were the only olefins evaluated, and again, the reaction was limited to aryl-substituted alkynes. In both cases, the authors propose that a gold-activated alkyne is attacked by the oxirane (7-endo for the aryl scenario and 6-exo for the alkene case) to form gold carbene intermediates, which then proceed to form the products. The cyclopropane-tethered substrates react to form a cyclobutyl allyl gold cation intermediate, which is then trapped with water to form the cyclobutane products shown, or alternatively, the cyclobutanol is ring-opened in situ and trapped with a halide to form the eight-membered heterocycle. Both of these two ring expansions failed when alkyl-substituted alkynes were used.

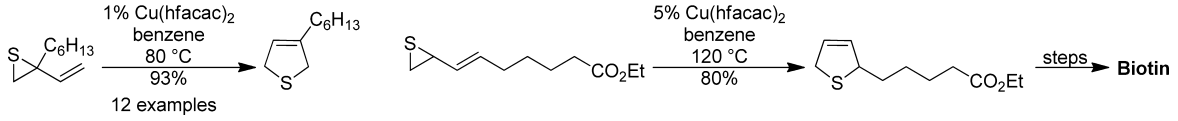
Ring expansions of alkynyl oxiranes to furans have been known for some time now and can be catalyzed by a variety of different metals and acids. Professor Pale and his group have recently reported new mechanistic insights for this ring expansion that demonstrate that alcohols such as methanol promote the reaction.[11] In 2010, his group demonstrated that propargyl acetate-substituted oxiranes (Scheme 5) could be ring-expanded mildly in high yields using a gold catalyst in a methylene chloride−methanol solvent mixture.[12] In this new ring expansion, the desired furan is formed, and the acetate is replaced with the solvent (methanol). As little as 2 equiv of methanol is enough to form the products, and methanol can be replaced with a range of other, more functionally desirable, alcohols. Pale invokes the intermediacy of an activated oxygenated allene, formed via an intramolecular attack of the acetate group onto the gold-activated alkyne, which then cyclizes to form the furan product. The nucleophile is incorporated by attack onto the activated allylic acetate thus generated. In a separate report, Professor Pale has shown that alkynyl oxiranes can also be ring-expanded using a silver catalyst (AgOTf) with the help of a Bronsted acid (*p*-TsOH).[13]

Yoshida has demonstrated that platinum can be added to the list of metals capable of ring-expanding alkynyl oxiranes to furan products (Scheme 6).[14] Yields for this catalytic procedure range from 34% to 92%. Of particular note is the tolerance of free hydroxyl groups. The mechanism involves activation of the alkyne by the platinum catalyst, followed by oxirane attack, rearomatization, and eventual protonation by water of the 3-furanyl platinum intermediate to regenerate the catalyst.

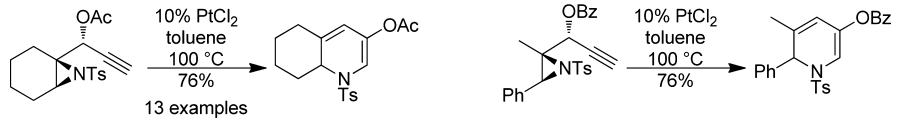
Recently, Professor Gagosz published a copper-catalyzed procedure for converting alkynyl oxirane substrates to butenolides (Scheme 7).[15] The second oxygen atom is incorporated from pyridine-*N*-oxide, which the authors postulated attacks the copper(I)-activated alkyne in a S_N2' fashion to form an alkoxy-activated allene and a copper alkoxide, which then undergoes a cyclization, followed by elimination of pyridine and protonation of a vinyl copper intermediate. This new catalytic ring-expansion reaction, which is run in refluxing acetonitrile, is generally high-yielding and tolerant of a variety of functional groups.

dx.doi.org/10.1021/cs300771d | *ACS Catal.* 2013, 3, 272−286

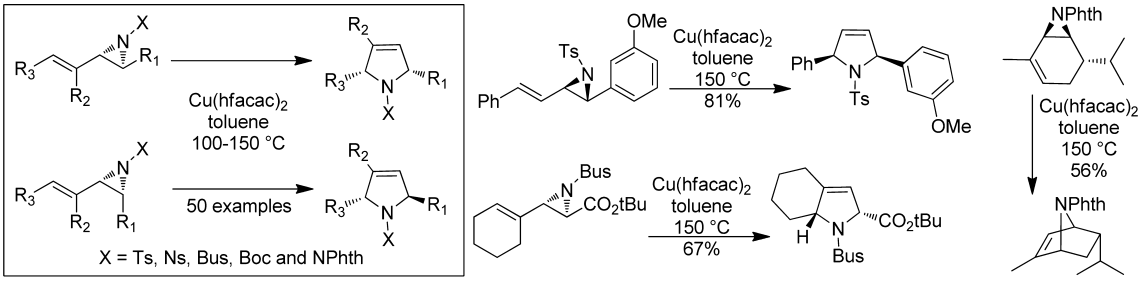
Scheme 8. Copper-Catalyzed Ring Expansion of Vinyl Thiiranes



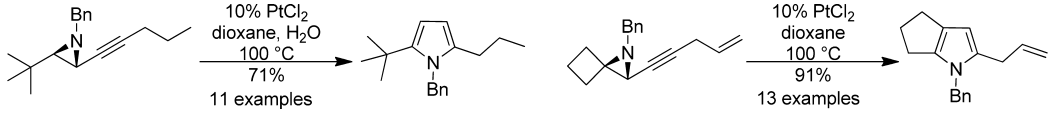
Scheme 9. Platinum-Catalyzed Ring Expansion of Propargylic Aziridines



Scheme 10. Copper-Catalyzed Ring Expansion of Vinyl Aziridines



Scheme 11. Platinum-Catalyzed Ring Expansion of Alkynyl Aziridines



Thiiranes. Ring expansions of thiiranes are few and far between. The only reported ring expansion of a thiirane in the last 10 years or so is from our laboratory (Scheme 8).[16] We demonstrated that vinyl thiiranes could be catalytically ring-expanded in high to excellent yields using $Cu(hfacac)_2$, the same catalyst that worked so well for ring-expanding vinyl oxiranes. The main competing pathways the catalyst needed to avoid were desulfurization and nucleophilic ring opening to form dihydrothiines. All other catalysts we evaluated succumbed to these highly competitive pathways. This new catalytic ring-expansion reaction is reasonably broad in scope. It was used to achieve concise formal total syntheses of biotin and Plavix.

Aziridines. Several new catalytic aziridine ring-expansion reactions have been published in the past few years. These reactions primarily employ late transition metals and sulfonylated aziridine substrates connected to either an adjacent olefin or alkyne.

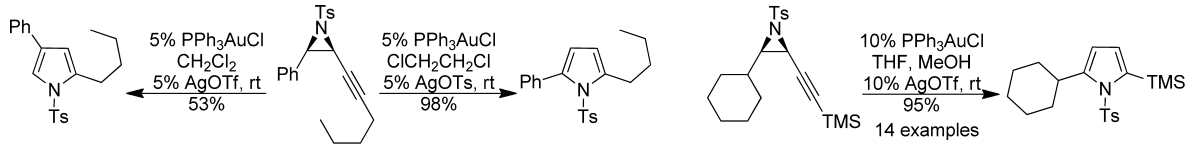
Sarpong has extended his platinum-catalyzed ring-expansion studies (Scheme 1) also to include aziridines (Scheme 9).[17] Interestingly, instead of cyclopentenone products, 1,2-dihydropyridines are formed exclusively when propargylic aziridines are subjected to the same platinum-catalyzed conditions. Yields are uniformly high and substituents of variable size are tolerated on the aziridine and the alkyne. This method is not limited to propargylic acetates or nitrogen sulfonamide groups. Ring expansion of a chiral aziridine substrate revealed that chirality of the starting substrate was retained in the product. The authors propose that the reaction proceeds via a carboxylate-assisted formation of a platinum carbene, which is then captured by the nitrogen aziridine atom and the resulting fused bicyclic aziridinium ion fragments to form the 1,2-dihydropyridine product.

In 2008, we published our first report wherein we demonstrated that vinyl aziridine substrates could be ring-expanded with $Cu(hfacac)_2$ (Scheme 10).[18] Reactions were generally high-yielding, and the 24 substrates initially disclosed demonstrated that functional group tolerance was great and that hindered, bicyclic, electron-poor and electron-rich vinyl aziridines could be ring-expanded using these reaction conditions. In advancing this method to access chiral 3-pyrroline products, we learned that the ring expansion is stereoselective, which means that a chiral 2,5-substituted 3-pyrroline of any configuration can be accessed by synthesizing the appropriately configured vinyl aziridine.[19] The requisite chiral aziridines are readily accessed by adding bifunctional nucleophiles, such as α-bromo esters or sulfur ylides, to an imine. This reaction accommodates several nitrogen atom substituents. Of these, the nosyl (Ns) group is optimal. Using this protecting group, the product is produced using shorter reaction times and lower temperatures, and easier deprotection conditions are needed to remove the nosyl group. Recent mechanistic investigations[5] have revealed that the ring expansion proceeds via an in situ reduction to form a copper(I) complex, which then undergoes a C−N insertion followed by allylic transposition and reductive elimination to form the 3-pyrroline product.

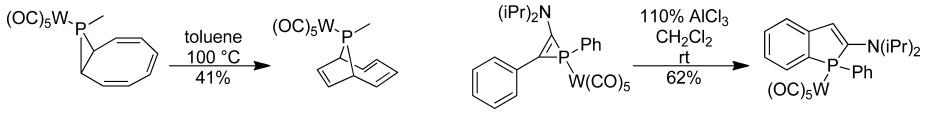
Yoshida has reported that his conditions for ring-expanding alkynyl oxiranes can be successfully expanded to benzyl-protected alkynyl aziridines (Scheme 11). In a separate report, he has shown that sulfonamide-protected *cis*-alkynyl aziridines can be converted to 3-iodo-substituted pyrroles by using platinum(II) chloride in combination with iodine.[20] He has since used mechanistic insights to take the platinum-catalyzed ring expansion a step further by investigating spirocyclobutane-substituted alkynyl

dx.doi.org/10.1021/cs300771d | ACS Catal. 2013, 3, 272−286

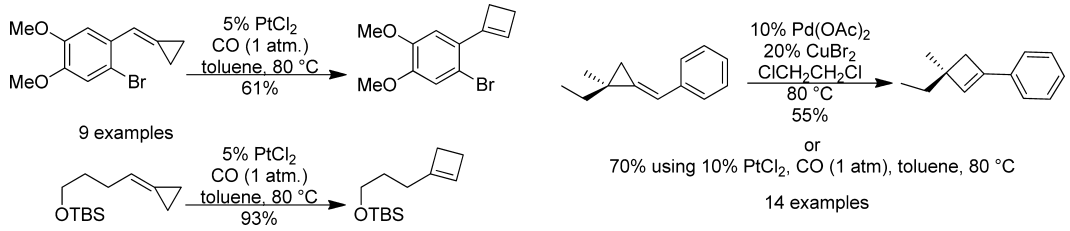
Scheme 12. Gold-Catalyzed Ring Expansion of Alkynyl Aziridines



Scheme 13. Ring Expansion of Vinyl- and Aryl-Substituted Phosphiranes



Scheme 14. Platinum- and Palladium-Catalyzed Ring Openings of Methylene Cyclopropanes



aziridine substrates.[21] This special class of substrates undergoes the same platinum-catalyzed ring expansion, except the intermediate cation presumably generated initiates a cyclobutane ring expansion before rearomatization. The aziridine precursors needed for this study are easily assembled from a cyclobutanone electrophile and a chloride-substituted zinc allene nucleophile. Yields for this intriguing double ring-expansion reaction are 50−90%.

About the same time in 2009, Professors Davies[22] and Hou[23] reported gold-catalyzed ring expansions of alkynyl aziridines (Scheme 12). Both used tosyl-protected cis-substituted aziridines as substrates and PPh_3AuCl as their gold source for their studies. Professor Davies noted significant counterion and solvent effects on the reaction. For example, silver(I) tosylate in dichloroethane produced the 2,5-substituted pyrrole product, but silver(I) triflate in methylene chloride afforded primarily the 2,4-substituted pyrrole. By switching the solvent to toluene while still using silver(I) triflate, the reaction again favored the 2,5-pyrrole product. The authors propose that the intermediate 2-pyrroline cation undergoes a 1,2-alkyl shift prior to aromatization and that this shift is sensitive to counterion and solvent effects. Professor Hou proposes a similar mechanism for his gold-catalyzed ring expansion, which differs primarily in the use of solvents. Yields for the 14 examples reported in his study are uniformly high.

Other. Little attention has been paid to the ring expansion of three-membered rings whose backbone contains atoms other than some combination of C, H, O, or N. Interestingly, in the past few years, two research groups have reported on the ring expansion of phosphiranes. In the first report,[24] by Professor Lammertsma and co-workers, they demonstrated that a monophosphorinated cyclooctatetraene substrate could be ring-expanded thermally in modest yields to the corresponding [4.2.1]-phosphabicyclic product (Scheme 13). The phosphirane isomer containing the tungsten substituent anti to the carbocycle ring-expands to form a single product, whereas the syn isomer ring-expands less efficiently and affords both isomers of the [4.2.1]-phosphabicyclic product. In the second report, Professor Mathey presents the serendipitous discovery of an aryl phosphirane ring expansion promoted by aluminum trichloride.[25] Three examples are reported in this study. In addition to the one shown, the ring expansion also proceeds when the phenyl phosphorus substituent is replaced with either a methoxy- or a 2-chloroethyl group.

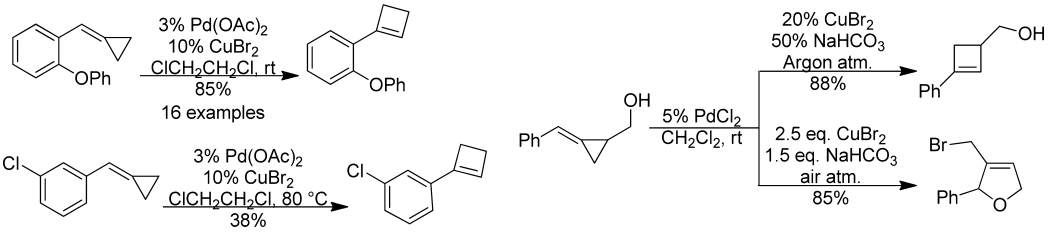
Cyclopropanes. *Methylene Cyclopropanes.* Important new contributions have been made to the catalytic ring-expansion literature for methylene cyclopropanes[26] in the past few years. Metals ranging from magnesium to gold have been employed to facilitate these new ring-expansion reactions.

Professor Fürstner has made several noteworthy contributions to this class of reactions. In 2006, he demonstrated that platinum(II) dichloride and an atmosphere of carbon monoxide were well suited to ring-expand methylene cyclopropane substrates to cyclobutenes (Scheme 14).[27] Yields were shown to be modest to excellent, aryl- and alkyl-substituted substrates ring-expanded, and functional groups such as aryl bromides and silyl ethers were tolerated. The authors propose that coordination of platinum to the olefin moiety results in the formation of a carbocation, which then undergoes a facile ring expansion to form a cyclobutane-substituted platinum carbene en route to the cyclobutene product. In a follow up study,[28] wherein his team focused on accessing enantiomerically pure cyclobutenes containing quaternary carbon centers, Professor Fürstner reports that this same ring expansion can also be accomplished using a palladium catalyst along with a copper additive. Both contributions are valuable because these cyclobutene products are hard to access using other methodologies.

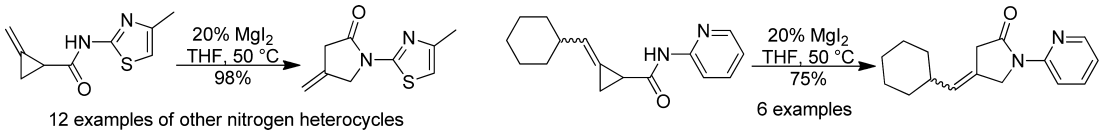
In a photo finish, following the publication of Fürstner's platinum-catalyzed ring-expansion reaction, Professor Shi and his team reported the same reaction using a palladium(II)-catalyzed approach (Scheme 15).[29] Only aryl-substituted substrates were shown to work in this study, and electron-rich substrates ring expanded faster, at lower temperatures, and in higher yields than electron-poor aromatic ones did. The authors propose an initial bromo palladation of the double bond, followed by formation of an exocyclic palladium carbene, ring expansion, and elimination. Unlike Fürstner's mechanism,

dx.doi.org/10.1021/cs300771d | ACS Catal. 2013, 3, 272−286

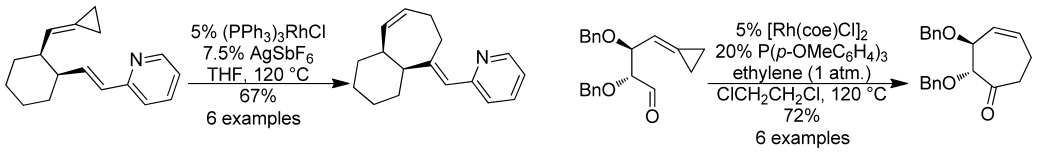
Scheme 15. Palladium-Catalyzed Ring Opening of Methylene Cyclopropanes



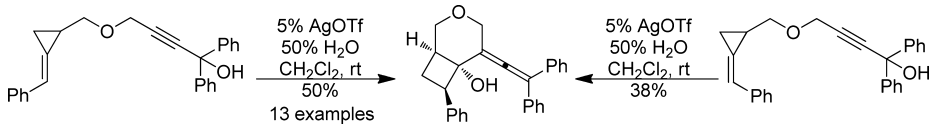
Scheme 16. Magnesium-Catalyzed Ring Opening of Methylene Cyclopropanes



Scheme 17. Rhodium-Catalyzed Ring Openings of Methylene Cyclopropanes



Scheme 18. Silver-Catalyzed Ring Opening of Methylene Cyclopropanes



no carbocation intermediates are proposed. Shi and his team have since expanded the scope of this new ring expansion to substrates with a methylene alcohol group attached to the cyclopropane.[30] By increasing the amount of copper(II) bromide and performing the reaction in the presence of air, they are able to divert the reaction pathway to favor the formation of brominated 2,5-dihydrofuran products. In both cases, only aryl-substituted olefins were explored. The authors propose that the heterocyclic product is formed by initial attack of bromide to either of the cyclopropane tetrahedral carbons, thus generating an allyl palladium species that goes on to form the product.

Professor Lautens has designed a ring expansion that employs an activated methylene cyclopropane substrate (amide attached to the cyclopropane) linked to a heteroaryl amide capable of additional activation through in situ chelation to a magnesium ion (Scheme 16).[31] Upon chelation, the magnesium releases an iodide atom, which attacks the cyclopropane to form an allyl iodide, and a magnesium enolate fragments; the two then combine to form the lactam product. Twelve different nitrogen amide heterocycles are shown to be competent. Further substrate scope studies are presented with pyridine as the heterocyclic chelation partner. For these substrates, yields range from 39% to 82%, and reaction times, from 12 to 49 h.

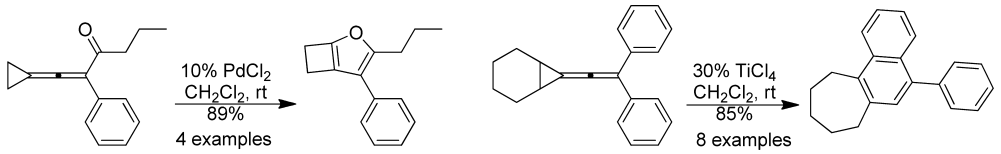
Following his initial success with ring-opening methylene cyclopropanes, Professor Fürstner turned his attention to evaluating intramolecular ring-expansion variants (Scheme 17).[32] He has shown that by using a directing group (pyridine), he can strategically guide how the metal adds to the methylene cyclopropane. This strategy is showcased for 1,5-dienes substituted with a pyridine group at one end and a cyclopropane at the other. Using this substrate class, he is able to guide the Wilkinsons catalyst with the aid of a silver(I) additive to ring-expand substrates to cycloheptene products. In the second scenario, he takes cues from the hydroacylation literature and now uses an aldehyde as a metal-directing group. This strategy takes advantage of an initial aldehyde C(=O)−H insertion step, which places the rhodium in close proximity to the methylene cyclopropane ready to add and ring-expand to a cycloheptenone product. For this approach, a different rhodium catalyst ([Rh(coe)Cl)]2, coe = cyclooctene) is used along with an electron-rich triaryl phosphine additive.

Professor Shi has also expanded his methylene cyclopropane ring-expansion program to include intramolecular variants (Scheme 18).[33] He has designed a clever silver-catalyzed cationic cyclization cascade that converts an alkynol tether methylene cyclopropane starting material to a tetrasubstituted pyran product decorated with a cyclobutane and an allene. Yields for the reaction range from modest to good. Apart from a single substrate, all reported examples employ only aryl substitutents. The diaryl alkynol group serves as the site of initiation. The resulting allene cation is captured by the olefin of the methylene cyclopropane to form an excocyclic cyclopropyl cation, which then proceeds to ring-expand to a cyclobutane before being quenched with water.

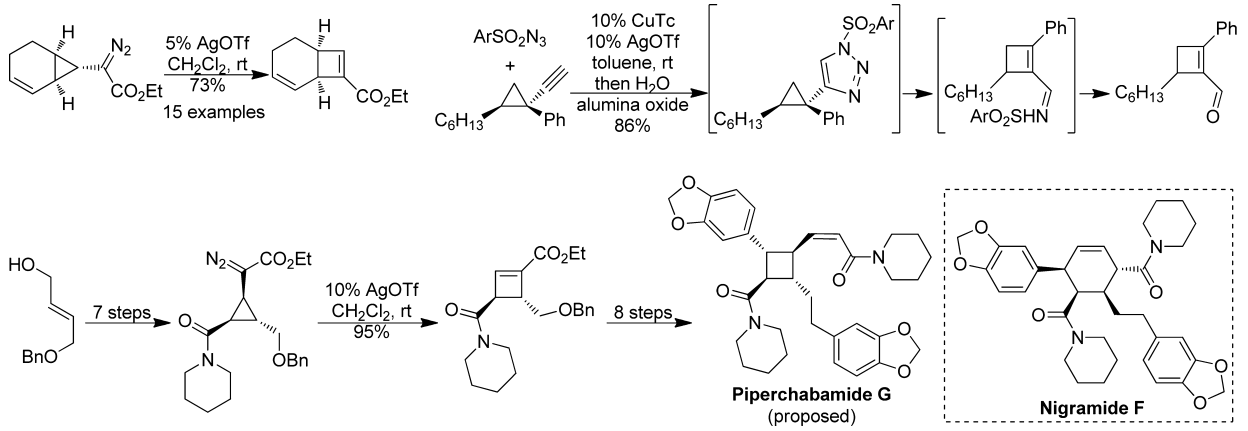
Vinylidine cyclopropanes have also been explored as catalytic ring-expansion substrates. In one recent report (Scheme 19),[34] a palladium-catalyzed ring-expansion reaction to form cyclobutane-fused furan substrates is described, whereas in another,[35] a new titanium-catalyzed approach to form highly substituted napthalenes is presented.

dx.doi.org/10.1021/cs300771d | ACS Catal. 2013, 3, 272−286

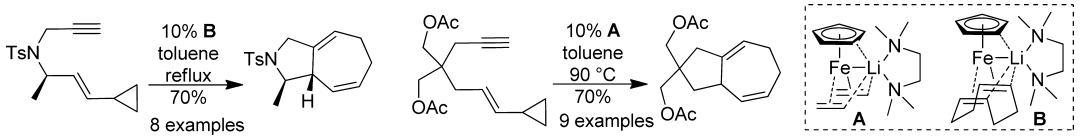
Scheme 19. Titanium- and Palladium-Catalyzed Ring Opening of Vinylidene Cyclopropanes



Scheme 20. Silver-Catalyzed Ring Opening of α-Diazo and α-1,2,3-Triazole Cyclopropanes



Scheme 21. Iron-Catalyzed Ring Opening of Vinyl Cyclopropanes



Vinyl- and Alkynyl Substituted Cyclopropanes. Many creative new contributions have been made for this particular ring-expansion class in the past few years. Approaches to small rings, such as cyclobutanes to complex fused-ring systems containing seven-membered rings, have been disclosed.

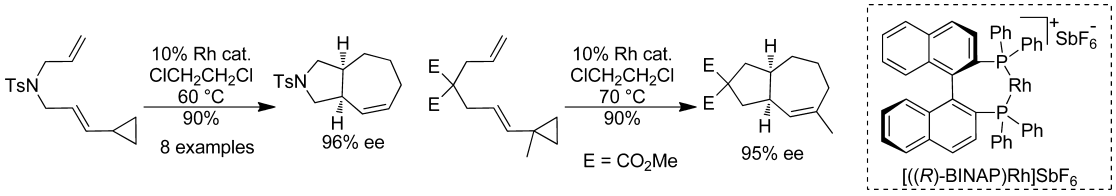
Professor Tang has made several contributions to this class of ring expansions. His first disclosure described the silver-catalyzed ring expansion of stabilized α-diazo cyclopropyl substrates to cyclobutene products (Scheme 20).[36] Using silver(I) triflate as catalyst, a variety of different compounds can be ring-expanded at room temperature. The main drawback of this strategy is the need to form and to work with unstable diazo substrates. In his follow-up studies, he tackled this challenge head-on and reported a new silver-catalyzed ring-expansion procedure that avoids the preparation of any diazo compounds. It has been previously shown that sulfonylated 1,2,3-triazoles, products of the copper-catalyzed click reaction, can serve as diazo compound equivalents. Professor Tang has since developed a one-pot procedure for this task, starting from alkynyl cyclopropanes.[37] This procedure relies on an initial cycloaddition (click reaction, Ar = 3,5-*bis*-CF_3−C_6H_3) to form a 1,2,3-triazole adduct, which fragments to form a silver carbene intermediate stabilized by an α-imino group that then undergoes the same ring-expansion chemistry as his diazo substrates did. His cyclobutene imino product can be either hydrolyzed to aldehydes or reduced to sulfonyl-protected primary amines. Professor Tang has elegantly applied his new catalytic ring-expansion method to the total synthesis of members of an intriguing family of cyclobutane natural products (Scheme 20), wherein piperchabamide G and pipercyclobutanimde A served as his primary synthetic targets.[38] Using his method, he was able to synthesize both reported structures and convincingly demonstrate that both natural products had been missassigned and where, in fact, chabamide and nigramide F, respectively. Recently, a gold-catalyzed approach to similar cyclobutene products has been reported.[39] An alkyne and an external oxygen atom source (diphenyl sulfoxide) serve as the key ingredients needed to form a stabilized gold carbene adjacent to a cyclopropyl group.

Fürstner has published a new iron-catalyzed ring-expansion ([5 + 2] cycloaddition) reaction, which relies on the use of low-valent iron complexes (**A** and **B**, Scheme 21) as catalysts.[40] These complexes are easily accessed from ferrocene by the addition of lithium metal in the presence of an olefin (ethylene in the case of **A** and cyclooctadiene in the case of **B**) and tetramethylethylene-diamine (TMEDA). Both catalysts produce the fused bicyclic products in good to excellent yields. Catalyst **B** was shown to perform better for substrates with more substituents.

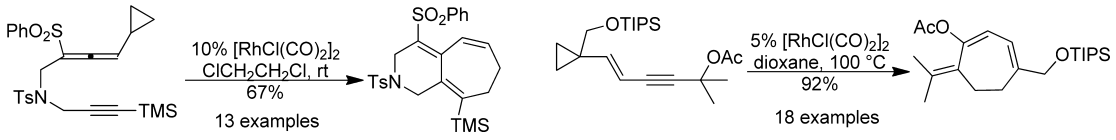
With his seminal rhodium-catalyzed vinyl cyclopropane [5 + 2] report in 1995,[41] Professor Wender opened up an exciting area of research that continues to inspire new ring-expansion development and entice researchers to use other metal catalysts as testing grounds. In 2006, he reported the first catalytic asymmetric variant for cyclizing olefin-tethered vinyl cyclopropane substrates (Scheme 22).[42] By using a cationic rhodium(I) BINAP catalyst with an SbF_6 counterion, he was able to demonstrate that chiral fused bicyclic substrates could be accessed in high yields and with modest to excellent enantioselectivity. The main drawbacks of this new asymmetric ring-expansion reaction are high catalyst loadings and long reaction times (1.5−8 days).

dx.doi.org/10.1021/cs300771d | *ACS Catal.* 2013, 3, 272−286

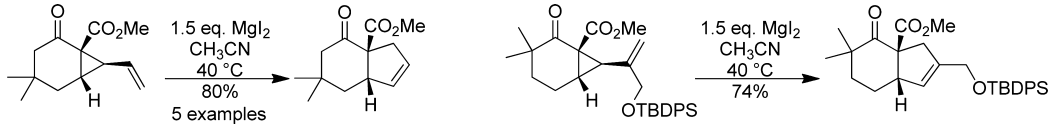
Scheme 22. Asymmetric Rhodium-Catalyzed Ring Opening of Vinyl Cyclopropanes



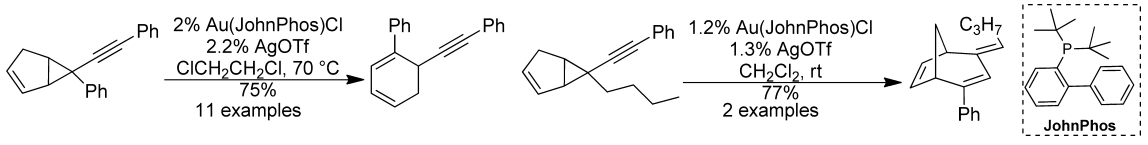
Scheme 23. Rhodium-Catalyzed Ring Openings of Vinyl and Allenyl Cyclopropanes



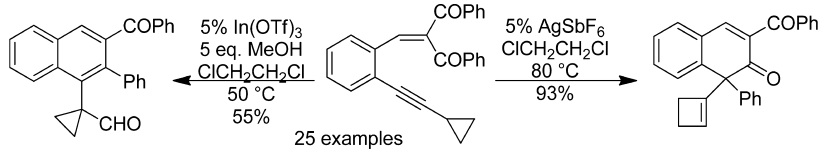
Scheme 24. Magnesium-Catalyzed Ring Opening of Vinyl Cyclopropanes



Scheme 25. Gold-Catalyzed Ring Opening of Alkynyl Cyclopropanes



Scheme 26. Silver- and Indium-Catalyzed Ring Openings of Alkynyl Cyclopropanes



Interesting new variations on the rhodium-catalyzed ring expansion introduced by Wender continue to appear in the literature. Mukai[43] has reported one involving an allene and alkyne, and Tang[44] has disclosed an intriguing eneyne-substituted case (Scheme 23). The same rhodium catalyst is used in both cases. Results for a good number of substrates are reported, for which yields generally range from modest to excellent. All examples in Mukai's study employ a sulfonylated allene, whereas most of the substrates in Tang's study contain either a tertiary or phenyl-substituted secondary propargylic alcohol ester. It is important to note that the mechanism by which Tang's rhodium-catalyzed ring expansion is proposed to proceed is distinctly different from that of Wender and Mukai.

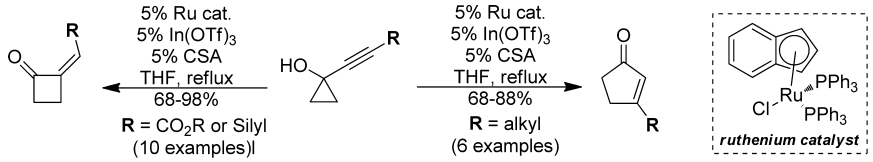
Professor Lambert has shown for a handful of doubly activated vinyl cyclopropane substrates that magnesium(II) iodide is well suited to facilitate a ring expansion to cyclopentene products (Scheme 24).[45] The mechanism is proposed to involve magnesium bis-coordination to the β-ketoester group, followed by reversible attack of an iodide atom onto the olefin terminus and a displacement of the alkyl iodide by the β-ketoester enolate.

In 2011, Professor Barluenga and co-workers reported gold-catalyzed ring expansion of cyclopropanes decorated with both a vinyl and alkynyl group (Scheme 25).[46] Using a gold(I) catalyst substituted with a large phosphine ligand (JohnPhos) in the presence of silver(I) triflate, he was able to ring-expand vinylcyclopropane substrates to 1,3-hexadiene products. Interestingly, when the phenyl quaternary substituent was replaced with an alkyl group, the mechanistic path diverged to form a [3.2.1] bicyclic product. Diversity of substrates studied was not broad, as exemplified by only aryl-substituted alkynes being used and no additional substituents on the cyclopentene cyclopropane fragment being evaluated. After initial coordination of the gold catalyst to the alkyne, the cyclohexene product is formed, followed by a 3-exo cyclopropyl C−C bond alkyne cyclization while the bicyclic product follows an initial 6-endo attack by the alkene π-bond.

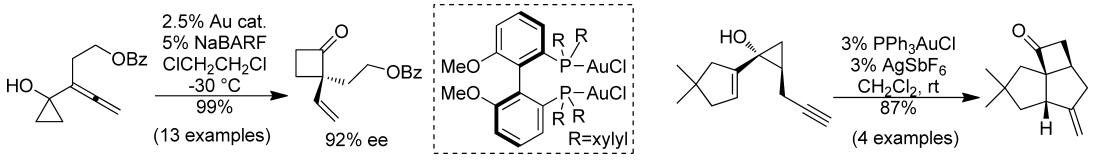
Zhang has reported on the catalyst-dependent behavior of a very specific class of molecules: namely, aryl substrates containing an alkynyl cyclopropane in an ortho relationship to a doubly activated enone (Scheme 26).[47] Upon treatment of these substrates with a silver(I) catalyst, a ring expansion to form a naphthalen-2(1*H*)-one core decorated with a cyclobutene-containing quaternary center resulted, but subjecting these same substrates to indium(III) triflate afforded a naphthalene substituted with a formylcyclopropyl group. The authors propose that following initial cyclization to form the fused ring system, a common methylene cyclopropyl cation intermediate serves as the point of divergence where in one

dx.doi.org/10.1021/cs300771d | ACS Catal. 2013, 3, 272−286

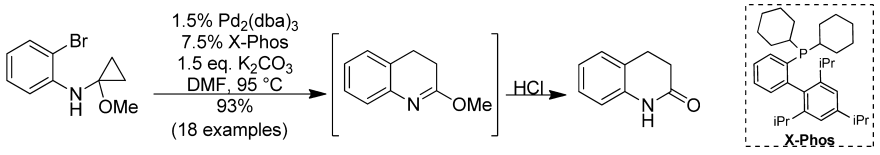
Scheme 27. Ruthenium-Catalyzed Ring Opening of Alkynyl Cyclopropanols



Scheme 28. Gold-Catalyzed Ring Openings of Cyclopropanols



Scheme 29. Palladium-Catalyzed Ring Opening of Cyclopropane Aminals



case an aryl shift occurs while for the other pathway, the cation is trapped with methanol.

Cyclopropanes Containing endo- and exo-Cyclic Alcohols. Cyclopropanol architectures have and continue to serve as attractive ring-expansion motifs. In the past few years, several new catalytic contributions have been made that use these reactive motifs.

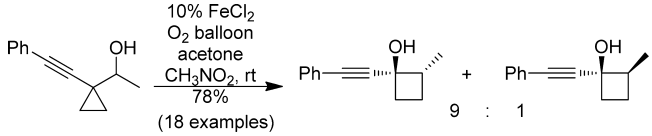
Professor Trost has shown that an indene-derived ruthenium complex (Scheme 27) can be employed effectively with the aid of indium(III) triflate and a Bronsted acid (CSA) to ring-expand alkyne-substituted cyclopropanol substrates.[48] Ring expansion is strongly dependent on the nature of the alkyne substituent. Cyclobutanone products are formed when the alkyne is substituted with silyl or carboxylate groups, whereas cyclopentenone is preferred for alkyl groups. The authors propose, for the alkyl-substituted alkynes, an insertion mechanism involving a ruthenium metallocycle intermediate that following a reductive elimination step forms the cyclopentenone products. The cyclobutanone products are believed to originate from a pathway involving an initial alkyne coordination, followed by alcohol-driven ring expansion aided by either the ability of silicon to stabilize β-cation charge or the Michael acceptor capabilities of the carboxylate group.

Professor Toste is a prolific and important contributor to the field of metal-catalyzed ring-expansion reactions. He has recently reported the first enantioselective gold-catalyzed 1,2-alkyl migration reaction (Scheme 28).[49] Allene-substituted cyclopropanols served as the substrates for his study. Axially chiral cold catalyst in the presence of a large noncoordinating boron counterion (BARF) was used to form chiral cyclobutanone products in excellent yields and ee's. Aryl and alkyl allene substituents decorated with a variety of different functional groups were tolerated. Catalyst loadings as low as 0.5 mol % could be employed for this reaction. In a separate ring-expansion report on gold catalysis,[50] Professor Toste and his team showcased that cyclopropanols substituted with vinyl and propargylic groups in a cis relationship could be ring-expanded to cyclobutanone products fused to a five-membered ring containing an exo-cyclic olefin. The authors propose an initial alkyne coordination of the gold catalyst, followed by a 6-exo-dig cyclization and a semipinacol rearrangement. Only of handful of substrates were studied. The product shown was advanced in six additional steps to the natural product ventricos-7(13)-ene.

Professor Tsuritani and colleagues have shown that cyclopropane aminal substrates containing an aniline fragment with an ortho-bromo, -iodo, or -chloro group can be ring-expanded with palladium to quinolone products (Scheme 29).[51] The catalyst, temperature, base, and phosphine additive are all critical to the success of this reaction. For example, slightly lower temperatures or alternative bases lead to drastic reduction in yields. The authors propose that following an initial aryl halide insertion of the palladium catalyst, an aniline-assisted cyclopropane insertion results in a seven-membered palladacycle that then undergoes a reductive elimination to form the 2-alkoxy iminoquinoline shown. This product can be treated with aqueous hydrochloric acid to form a lactam.

Professor Jiao has shown that simple iron(II) chloride in the presence of oxygen and an appropriate solvent mixture (acetone/nitromethane) can be used as a catalyst to ring-expand alkynylcyclopropyl alkanol substrates to cyclobutanol products (Scheme 30).[52] The authors postulate that this mild,

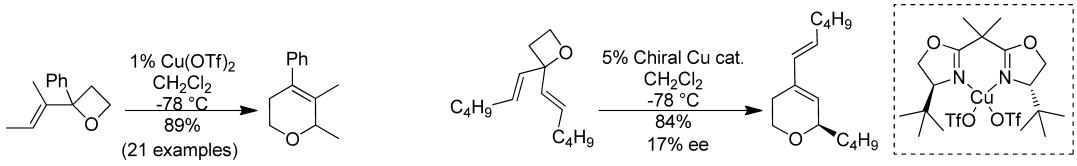
Scheme 30. Iron-Catalyzed Ring Opening of Alkylnylcyclopropyl Alkanols



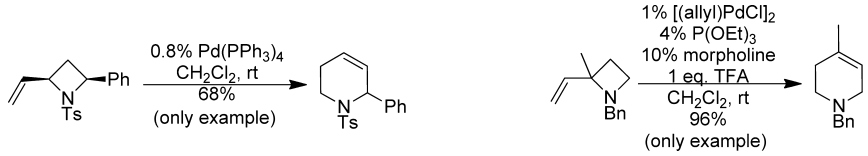
intriguing ring-expansion reaction proceeds through an initial oxidation of the catalyst to iron(III), followed by coordination to the alkyne and cyclopropyl cation formation. After 1,2-alkyl shift, the resulting alkyne-stabilized cyclobutyl cation is trapped with a hydroxyl group bound to the alkyne-complexed iron. All but one example employ aryl alkynes. Yields are reduced significantly when large alkyl (*t*-butyl and *i*-propyl) groups are

dx.doi.org/10.1021/cs300771d | ACS Catal. 2013, 3, 272−286

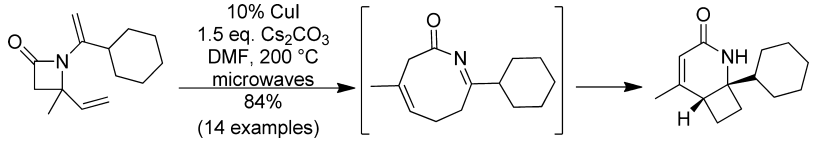
Scheme 31. Copper-Catalyzed Ring Opening of Vinyl Oxetanes



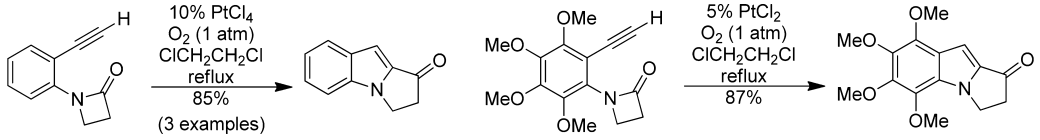
Scheme 32. Palladium-Catalyzed Ring Openings of Vinyl Azetidines



Scheme 33. Copper-Catalyzed Ring Opening of N-Vinyl Lactams



Scheme 34. Platinum-Catalyzed Ring Opening of *N*-Aryl Lactams



used and, as expected, based on the proposed mechanism, primary alcohol substrates are incompetent.

FOUR-MEMBERED RINGS

Examples of catalytic ring expansions of four-membered rings are far fewer than those for three-membered rings. The primary reason for this difference is simply that there are not many reliable methods to synthesize four-membered rings, but there are numerous to access three-membered rings. The exciting new ring-expansion results presented in the following sections suggest that more attention should be paid to develop a useful route to make the precursors used for these studies. The majority of new four-membered ring catalytic ring-expansion contributions have employed cyclobutane[53] derivatives.

Heterocyclic Four-Membered Rings. *Oxetanes.* In 2012, our group reported the first catalytic vinyl oxetane ring-expansion reaction (Scheme 31).[54] Copper(II) triflate was shown to be the best catalyst for the task. Yields ranged from very good to excellent for the substrates studied. Our mechanistic investigations revealed that select Bronsted acids could also facilitate this reaction, although in most cases at a much slower rate and with less efficiency. These insights confirmed that the reaction proceeded through an allylic cation, which then underwent a 6-endo cyclization to form the product. These mechanistic insights provided us with an opportunity to explore chiral counterion catalysis opportunities. In a proof of principle experiment, we have demonstrated that chiral bisoxazoline catalysts can be used to form chiral products from achiral vinyl oxetane precursors. By using Bronsted acids instead of copper catalysts, we have been able to access products using this strategy in enantiomeric ratios as high as 95:5.

Thietanes. Thietanes continue to be a neglected heterocyclic motif when it comes to catalytic ring expansions. Since 2006, only one ring-expansion study has been reported.[55] This reaction, which goes beyond the defined scope of this Review, involves a copper-catalyzed insertion of a nitrene into aryl thietane substrates.

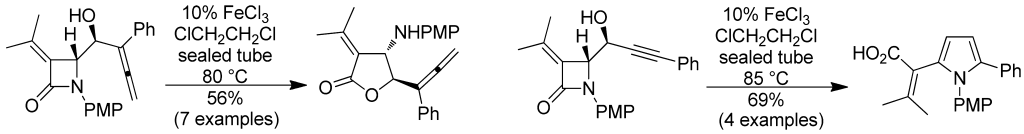
Azetidines. Catalytic conversions of vinyl azetidines to tetrahydropyridine products have not been systematically investigated in the past. Two different research groups have recently reported similar advances toward this goal (Scheme 32). Professor Tunge has shown that a sulfonyl-protected vinyl azetidine can be ring-expanded in the presence of a palladium(0) catalyst.[56] A few years later, Professor Yudin similarly demonstrated that a benzyl-protected vinyl azetidine could be ring-expanded using a palladium catalyst aided by several additives (triethyl phosphite, morpholine, and trifluoroacetic acid).[57] These results match results of an earlier report by Professors Hiemstra and Rutjes.[58] The mechanism is believed to proceed through a palladium allyl intermediate, which is then attacked in a 6-endo fashion by the nitrogen atom.

Professor Yudin has reported that copper catalysts can aid the aza-Claisen rearrangements of N-vinyl-substituted β-lactam substrates (Scheme 33).[59] The reaction does proceed without a catalyst, but yields were uniformly higher when a copper catalyst was employed. The scope of this reaction is quite broad, as exemplified by the diverse range of substrates that were shown that could be successfully ring-expanded in this study.

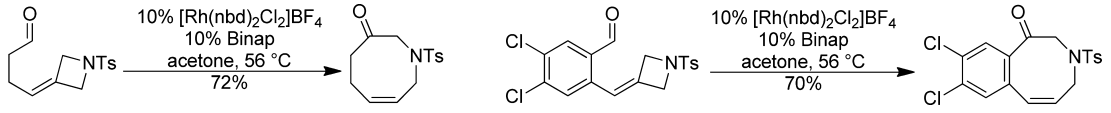
Using Aryl lactams substituted with *ortho*-alkynyl groups, Professor Zhang has shown that platinum(II) and platinum(IV) chlorides can be used to ring-expand and form useful indole products (Scheme 34).[60] Only a handful of substrates where studied. When the alkyne terminus is substituted with an alkyl

dx.doi.org/10.1021/cs300771d | ACS Catal. 2013, 3, 272−286

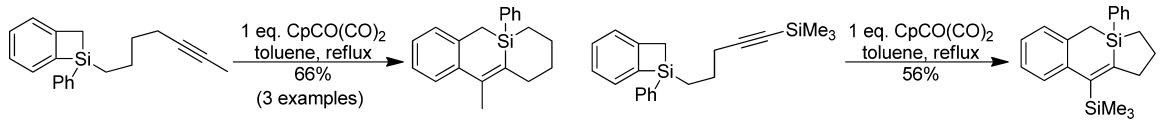
Scheme 35. Iron-Catalyzed Ring Openings of Alkylhydroxy Lactams



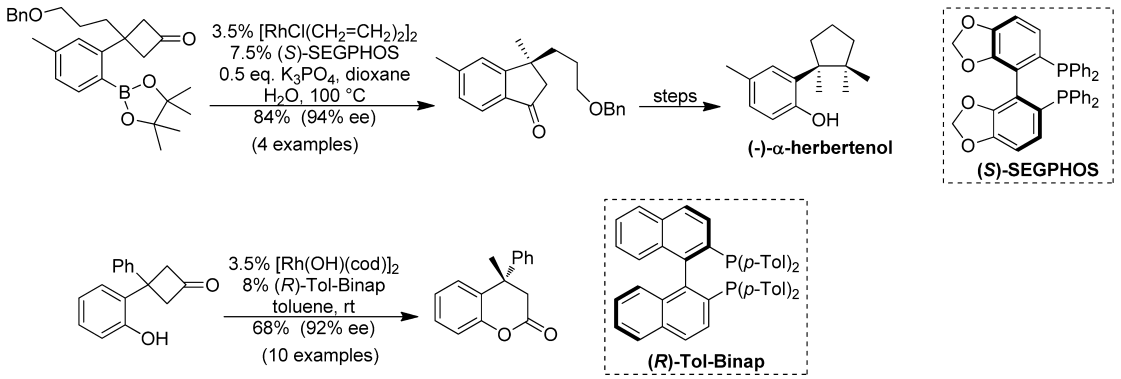
Scheme 36. Rhodium-Catalyzed Ring Opening of Azetidines



Scheme 37. Rhodium-Catalyzed Ring Opening of Azetidines



Scheme 38. Rhodium-Catalyzed Ring Openings of Aryl Cyclobutanones



or aryl group, the yields for the products shown drop because one-third of the starting material leads to an alternate fused indole product. The authors propose a 5-endo-dig cyclization of the lactam nitrogen onto a platinum-activated alkyne complex. The resulting spiro intermediate then rearranges to the fused architecture containing a platinum carbene, which then leads to the product. The authors have employed this new catalytic ring-expansion reaction toward a formal synthesis of 7-methoxymitosene (example on the right in Scheme 34).[61]

Professor Alcaide has shown that PMP-protected (PMP = 4-methoxyphenyl) lactams substituted with alkynols or allenols at the carbon bearing the nitrogen atom produce drastically different products when treated with iron(III) chloride as catalyst (Scheme 35).[62] Allenol-substituted precursors form γ-lactones, whereas alkynol-substituted ones form pyrrole-substituted acrylic acid products. The more intriguing pyrrole-forming mechanism is believed to involve an initial Meyer−Schuster rearrangement step, which is then followed by lactam opening by the resulting allenol, aminocyclization, and dehydration. The structural variety of the substrates studied was quite narrow.

As part of a larger rhodium-catalyzed study evaluating the capacity of rhodium acyl intermediates to insert into strain rings, Professor Aissa has demonstrated that azetidines tethered to an aldehyde through an *exo*-olefin tether can be ring-expanded to eight-membered rings (Scheme 36).[63] Only two azetidine examples (both shown) were reported. Sulfonamide group protection was shown to be essential as amide and carbamate-protected azetidines failed. A fairly high mole percent of both the rhodium catalyst and the binap additive was needed. Although yields were good for both examples reported, reaction times were long (44 h). Rhodium hydroacylations are well documented reactions that have been studied extensively. These particular substrates were designed so that the initial rhodium acyl species could first add across the olefin before fragmenting and cyclizing to form a nine-membered metallocycle that finally undergoes a reductive elimination to form the product.

Other. A new cobalt-mediated silacyclobutane ring expansion has recently been reported (Scheme 37).[64] Although still not catalytic, it is an interesting route to access fused tricyclic silicon-containing frameworks. The highest yielding substrates of the four covered in this study are shown below. The authors propose a mechanism involving an initial insertion of cobalt complex into the silicon aryl bond, followed by dissociation of a CO ligand and coordination to the tethered alkyne group.

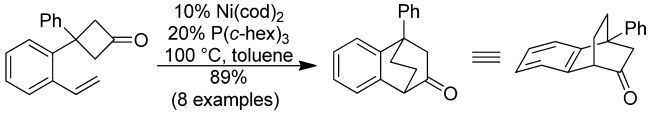
Cyclobutanes. *Cyclobutanones.* Professor Murakami has shown that 3-aryl-substituted cyclobutanone substrates containing a reactive functional group (phenol[65] or a boronic ester[66]) can be ring-opened asymmetrically using chiral rhodium catalysts (Scheme 38). Using (*S*)-SEGPHOS as a chiral phosphine additive, he was able to convert achiral cyclobutanone substrates substituted with a boronic ester into 2,3-dihydro indenone products bearing a chiral quaternary center. One of the products (shown) from this study was used to synthesize the natural product herbertenol. In a separate study, a phenol group was

dx.doi.org/10.1021/cs300771d | *ACS Catal.* 2013, 3, 272−286

used to trap the intermediate generated from ring-opening the cyclobutanone fragment. Althought SEGPHOS was also shown to be well suited for this reaction, (*R*)-Tol-Binap proved to be more successful in affording products containing chiral quaternary centers with high enantioselectivity. It is worth noting that this strategy can also be extended to benzylic alcohols and benzylic cyclobutanone substrates without much loss in yield but a dramatic drop in enantioselectivity. For both reactions, the authors propose an initial addition step of an *ortho*-rhodium species (aryl or arylalkoxy) onto the cyclobutanone carbonyl group. This addition step is followed by a fragmentation of the rhodium cyclobutanol and protonolysis of the terminal rhodium alkyl species.

Professor Murakami has expanded his ring-expansion studies of 3-aryl-substituted cyclobutanones to also include styrenyl substrates (Scheme 39).[67] This new reaction offers an alternative route to aryl fused bicyclo[2.2.2]octane architectures. The proposed mechanistic pathway is initiated by an oxidative nickel-mediated cyclization between the olefin and carbonyl groups. The resulting metallocycle then undergoes a fragmentation (*β*-carbon elimination), followed by a reductive elimination of a seven-membered metallocycle.

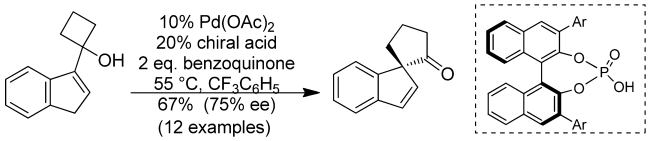
Scheme 39. Nickel-Catalyzed Ring Opening of Styrenyl Cyclobutanones



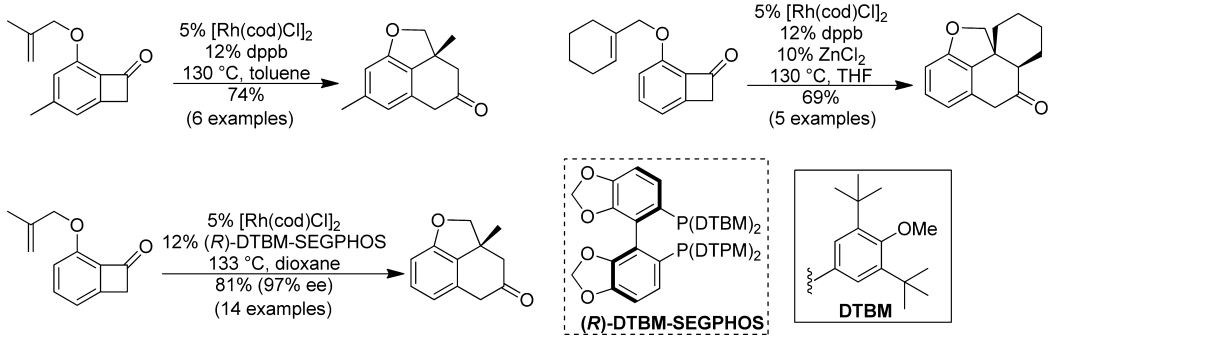
Professor Dong has recently reported on the catalytic ring expansion of aryl fused cyclobutanone substrates decorated with an allylated ortho phenol (Scheme 40).[68] Complex *β*-tetralone products can be accessed using this new rhodium-catalyzed approach. For certain classes of substrates, additional help from a Lewis acid ($ZnCl_2$) and a different solvent (THF instead of toluene) is needed to make the ring expansion succeed. The authors propose that the rhodium catalyst starts by inserting into the aryl−acyl bond, and the resulting rhodacycle then adds across the adjacent olefin to form a seven-membered rhodacycle that finally undergoes a reductive elimination to afford the product. Professor Dong and his team have since demonstrated that this excellent new transformation can also be done asymmetrically.[69] Excellent levels of enantioselectivity can be achieved by replacing the dppb ligand with an axially chiral ligand ((*R*)-DTBM-SEGPHHOS) and using dioxane instead of toluene as solvent. All of the examples in this study, except one, employ 1,1-disubstituted allyl tethers.

Cyclobutanols. Professor Cramer has made important contributions toward enantioselective ring expansions of cyclobutanol substrates (Scheme 41). He has separately studied allenic-[70] and 3-aryl[71]-substituted substrates using in situ-formed chiral rhodium catalysts (DTBM = 3,5-di-*tert*-butyl-4-methoxyphenyl). Using these two new reactions, complex cyclohexenone and indane substrates bearing chiral quaternary centers can be accessed. Although reaction conditions are quite

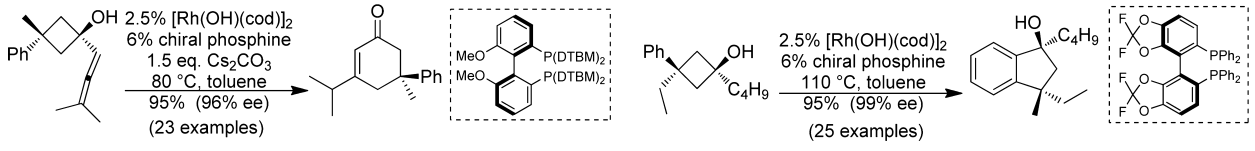
Scheme 43. Palladium-Catalyzed Ring Opening of Indenyl Cyclobutanols



Scheme 40. Rhodium-Catalyzed Ring Opening of Aryl Fused Cyclobutanones



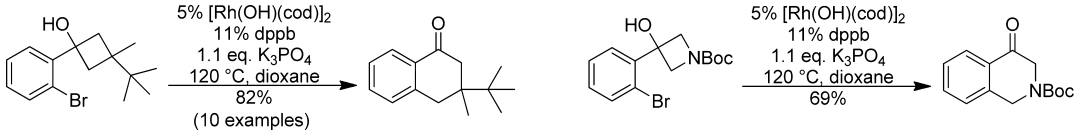
Scheme 41. Rhodium-Catalyzed Ring Openings of 3-Aryl and Allenyl Cyclobutanols



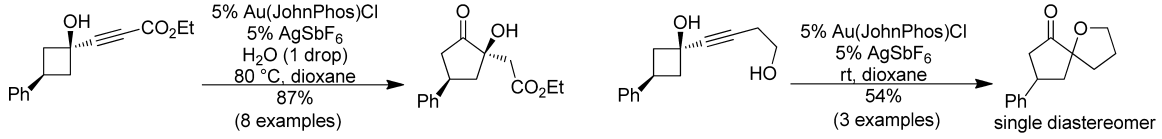
Scheme 42. Palladium-Catalyzed Ring Opening of Allenyl Cyclobutanols

dx.doi.org/10.1021/cs300771d | ACS Catal. 2013, 3, 272−286

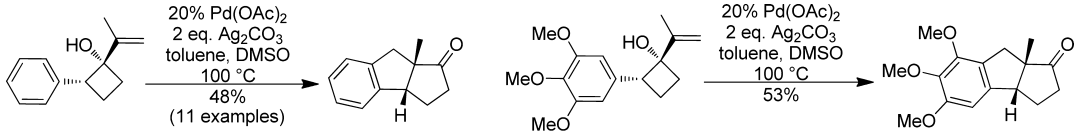
Scheme 44. Rhodium-Catalyzed Ring Opening of Haloaryl Cyclobutanols



Scheme 45. Gold-Catalyzed Ring Opening of Alkynyl Cyclobutanols



Scheme 46. Palladium-Catalyzed Ring Opening of Allylic 2-Aryl Cyclobutanols



similar for both reactions, the indane-forming reaction is quite sensitive to the structure of the chiral additive used (chiral ferrocenyl phosphine ligands are optimal for many of the substrates, for example). Yields and enantioselectivities for the substrates reported are uniformly high. The common proposed initial mechanistic step for both reactions involves fragmentation of the cyclobutanol group to form a γ-rhodium ketone intermediate, which cyclizes to form a seven-membered rhodacycle in the case of the allene, whereas the rhodium group migrates to an aryl group and then attacks the carbonyl group in the other scenario. It is important to note that simultaneously, Professor Murakami developed an identical rhodium-catalyzed asymmetric ring-expansion protocol for 3-aryl-substituted substrates to form chiral indane products.[72] He also identified difluorophos (shown) as the optimal chiral phosphine for this reaction.

Professor Trost has shown the achiral cyclobutanols substituted with an alkoxy allene group can be catalytically ring-expanded to form chiral cyclopentanone products (Scheme 42).[73] Using his established chiral bis-phosphine ligand framework in combination with a palladium catalyst and two additives (benzoic acid and triethylamine), highly enantioenriched products are afforded in excellent yields. Assignment of the absolute configuration was made by converting the substrate shown to a known *trans*-diol.[74] Hydropalladation of the alkoxyallene fragment generates an allyl-palladium intermediate, which then undergoes an asymmetric Wagner−Meerwein shift to form the product.

Professor Rainey has recently disclosed a new palladium-catalyzed enantioselective ring expansion of indene-substituted cyclobutanol substrates (Scheme 43).[75] The reaction design involves activation of the indene moiety to form a cationic *p*-allyl complex, which is then followed by a semipinacol rearrangement of the cyclobutanol. By using a chiral Bronsted acid, a counterion pairing is achieved with the palladium intermediate that results in spirocyclic products being formed with modest to excellent selectivity (48−96% ee). This mode of activation and use of chiral counterion catalysis is an exciting direction in the field of catalytic ring expansions.

Professor Murakami has developed a new catalytic ring-expansion approach that converts benzylic cyclobutanol substrates substituted with an *ortho*-bromide to α-tetralone products (Scheme 44).[76] Yields range from modest to high for the substrates studied. Murakami also demonstrated that by replacing dppb (1,4-bis(diphenylphosphino)butane) with a chiral phosphine ((*R*)-tol-BINAP), he is able to asymmetrically ring-expand to form chiral tetralone products. The authors propose a mechanism in which a rhodium alkoxide reacts with the aryl bromide to form a spirocyclic rhodacycle, which then fragments to a seven-membered one before undergoing a reductive elimination step to form the product. Although this approach will likely never serve as the chosen route to such products, it is mechanistically interesting.

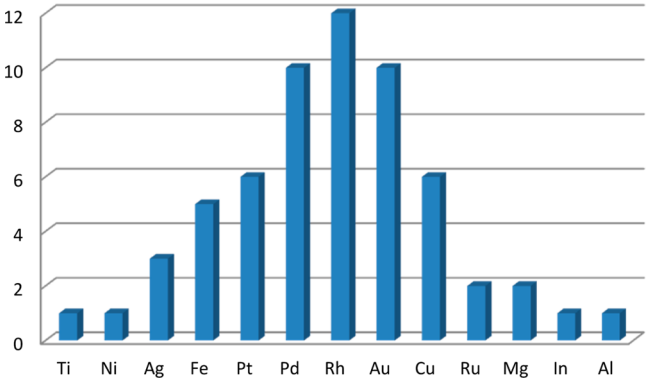
Professor Shin has reported a new twist in the catalytic ring expansions of alkynyl cyclobutanol substrates (Scheme 45).[77] When this gold-catalyzed reaction is run in the presence of water or if homo-propargylic substrates are used, a ring expansion to form cyclopentanone products with an α-oxy quaternary center are afforded. Silver(I) hexafluoroantimonate(V) is also critical for success. Heating is required for generating α-hydroxy ketone products. This new reaction relies on initial inter- or intramolecular alkyne hydration prior to a gold-catalyzed α-ketol ring-expansion step.

Professor Orellana has designed a palladium-catalyzed ring-expansion protocol that converted allylic cyclobutanols bearing a 2-aryl group to benzodiquinane products (Scheme 46).[78] Silver(II) carbonate is an essential base for this transformation, which is also aided by heat and the appropriate solvent mixture (toluene and DMSO). The only structural variation in the substrates reported is the aryl group, with both electron-rich and -poor aryl groups being accommodated. Yields range from poor to good. The authors propose that palladium activation of the olefin promotes a 1,2-alkyl shift to form a cyclopentanone containing an α-quaternary center bearing a β-alkyl palladium intermediate, which then inserts into an aryl C−H to form the product.

It should be clear from this summary that the study of metal-catalyzed ring expansions of strained rings is alive and well, with many new and creative contributions being made in the past few years. The diversity of approaches being pursued is inspiring. One measure of this diversity (Scheme 47) is the range of different metals being used for catalysis. Expensive metals, such

dx.doi.org/10.1021/cs300771d | *ACS Catal.* 2013, 3, 272−286

Scheme 47. Frequency of Metals Used for New Catalytic Ring Expansion Reactions



as rhodium, gold, platinum, and palladium are used in more than 60% of the new reactions presented in our coverage. We hope that future contributions involve more use of widely available, stable, and less expensive metal catalysts. Ring expansion reactions employing chiral catalysts are one of the most exciting scientific fronts presented in this review. We look forward to watching and learning about new advances (Schemes 22, 28, 31, 38, and 41–43). All of the chiral motifs used for these new asymmetric ring-expansion reactions are C2-symmetric, and all but two use axial chirality (BINAP type architecture) to induce asymmetry. Clearly, there is much room for development and applications of other, hopefully inexpensive and readily available, chiral motifs for catalytic ring-expansion purposes. We look forward to new contributions to emerge in the coming years.

AUTHOR INFORMATION

Corresponding Author

*E-mail: njardars@email.arizona.edu.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We thank the NSF (CHE-0848324) and the University of Arizona for financial support.

ABBREVIATIONS

Ac = acetate
BARF = tetrakis(pentafluorophenyl)borate
Binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl
Bn = benzyl
c-hex = cyclohexyl
cod = cyclooctadiene
Cp = cyclopentadiene
CSA = camphorsulfonic acid
dba = *trans*-dibenzylideneacetone
DMF = *N*,*N*-dimethylformamide
dppb = 1,4-bis(diphenylphosphino)butane
DMSO = dimethylsulfoxide
DTBM = 3,5-di-*tert*-butyl-4-methoxyphenyl
Hfacac = hexafluoroacetylacetone
JohnPhos = (2-biphenyl)di-*tert*-butylphosphine
nbd = norbornadiene
NCS = *N*-chlorosuccinimide
NIS = *N*-iodosuccinimide
Ph = phenyl
pic = picolate
PMP = 4-methoxyphenyl
Salen = *N*,*N*′-bis(salicylidene)ethylenediamine
SEGPHOS = 5,5′-bis(diphenylphosphino)-4,4′-bi-1,3-benzodioxole
Tc = thiophene-2-carboxylate
Tf = trifluoromethanesulfonate
TFA = trifluoroacetic acid
TMS = trimethylsilyl
Ts = *p*-toluenesulfonate
XPhos = 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl

REFERENCES

(1) Hudlicky, T.; Reed, J. W. *Angew. Chem., Int. Ed.* **2010**, *49*, 4864–4876.
(2) Pujanauski, B. G.; Prasad, B. A. B.; Sarpong, R. *J. Am. Chem. Soc.* **2006**, *128*, 6786–6787. Similar products can be accessed by treatment of alkyne-substituted allylic acetates with a palladium catalyst: Rautenstrauch, V. *J. Org. Chem.* **1984**, *49*, 950–952.
(3) Batory, L. A.; McInnis, C. E.; Njardarson, J. T. *J. Am. Chem. Soc.* **2006**, *128*, 16054–16055.
(4) Brichacek, M.; Batory, L. A.; Njardarson, J. T. *Angew. Chem., Int. Ed.* **2010**, *49*, 1648–1651.
(5) Brichacek, M.; Batory, L. A.; McGrath, N. A.; Njardarson, J. T. *Tetrahedron* **2010**, *66*, 4832–4840.
(6) (a) Mack, D. J.; Njardarson, J. T. *Chem. Sci.* **2012**, *3*, 3321–3325. (b) Mustard, T. J. L.; Mack, D. J.; Njardarson, J. T.; Cheong, P. H.-Y. *J. Am. Chem. Soc.* **2013**, ASAP; DOI: 10.1021/ja310065z.
(7) (a) Hilt, G.; Bolze, P.; Kieltsch, I. *Chem. Commun.* **2005**, 1996–1998. (b) Hilt, G.; Walter, C.; Bolze, P. *Adv. Synth. Catal.* **2006**, *348*, 1241–1247.
(8) Hilt, G.; Bolze, P.; Heitbaum, M.; Hasse, K.; Harms, K.; Massa, W. *Adv. Synth. Catal.* **2007**, *349*, 2018–2026.
(9) Lin, G.-Y.; Li, C.-W.; Hung, S.-H.; Liu, R.-S. *Org. Lett.* **2008**, *10*, 5059–5062.
(10) (a) Yang, C.-Y.; Lin, M.-S.; Liao, H.-H.; Liu, R.-S. *Chem.—Eur. J.* **2010**, *16*, 2696–2699. (b) Liao, H.-H.; Liu, R.-S. *Chem. Commun.* **2011**, *47*, 1339–1341.
(11) Blanc, A.; Tenbrink, K.; Weibel, J.-M.; Pale, P. *J. Org. Chem.* **2009**, *74*, 5342–5348.
(12) Blanc, A.; Alix, A.; Weibel, J.-M.; Pale, P. *Eur. J. Org. Chem.* **2010**, 1644–1647.
(13) Blanc, A.; Tenbrink, K.; Weibel, J.-M.; Pale, P. *J. Org. Chem.* **2009**, *74*, 4360–4363.
(14) Yoshida, M.; Al-Amin, M.; Shishido, K. *Synthesis* **2009**, 2454–2466.
(15) Gronnier, C.; Kramer, S.; Odabachian, Y.; Gagosz, F. *J. Am. Chem. Soc.* **2012**, *134*, 828–831.
(16) Rogers, E.; Araki, H.; Batory, L. A.; McInnis, C. E.; Njardarson, J. T. *J. Am. Chem. Soc.* **2007**, *129*, 2768–2769.
(17) Motamed, M.; Bunnelle, E. M.; Singaram, S. W.; Sarpong, R. *Org. Lett.* **2007**, *9*, 2167–2170.
(18) Brichacek, M.; Lee, D.; Njardarson, J. T. *Org. Lett.* **2008**, *10*, 5023–5026.
(19) Brichacek, M.; Villalobos, M. N.; Plichta, A.; Njardarson, J. T. *Org. Lett.* **2011**, *13*, 1110–1113.
(20) Yoshida, M.; Easmin, S.; Al-Amin, M.; Hirai, Y.; Shishido, K. *Tetrahedron* **2011**, *67*, 3194–3200.
(21) Yoshida, M.; Maeyama, Y.; Al-Amin, M.; Shishido, K. *J. Org. Chem.* **2011**, *76*, 5813–5820.
(22) (a) Davies, P. W.; Martin, N. *Org. Lett.* **2009**, *11*, 2293–2296. (b) Davies, P. W.; Martin, N. *J. Organomet. Chem.* **2011**, *696*, 159–164.
(23) Chen, D.-D.; Hou, X.-L.; Dai, L.-X. *Tetrahedron. Lett.* **2009**, *50*, 6944–6964.

(24) Bulo, R. E.; Allaart, F.; Ehlers, A. W.; de Kander, F. J. J.; Schakel, M.; Lutz, M.; Spek, A. L.; Lammertsma, K. *J. Am. Chem. Soc.* **2006**, *128*, 12169−12173.
(25) Panichakul, D.; Mathey, F. *Organometallics* **2011**, *30*, 348−351.
(26) Shi, M.; Lu, J.-M.; Wei, Y.; Shao, L.-X. *Acc. Chem. Res.* **2012**, *45*, 641−652.
(27) Furstner, A.; Aissa, C. *J. Am. Chem. Soc.* **2006**, *128*, 6306−6307.
(28) Masarwa, A.; Furstner, A.; Marek, I. *Chem. Commun.* **2009**, 5760−5762.
(29) Shi, M.; Liu, L.-P.; Tang, J. *J. Am. Chem. Soc.* **2006**, *128*, 7430−7431.
(30) Tian, G.-Q.; Yuan, Z.-L.; Zhu, Z.-B.; Shi, M. *Chem. Commun.* **2008**, 2668−2670.
(31) Scott, M. E.; Schwarz, C. A.; Lautens, M. *Org. Lett.* **2006**, *8*, 5521−5524.
(32) Aissa, C.; Furstner, A. *J. Am. Chem. Soc.* **2007**, *129*, 14836−14837.
(33) Yao, L.-F.; Wei, Y.; Shi, M. *J. Org. Chem.* **2009**, *74*, 9466−9469.
(34) Miao, M.; Cao, J.; Zhang, J.; Huang, X.; Wu, L. *Org. Lett.* **2012**, *14*, 2718−2721.
(35) Huang, X.; Su, C.; Liu, Q.; Song, Y. *Synlett.* **2008**, 229−232.
(36) Xu, H.; Zhang, W.; Shu, D.; Werness, J. B.; Tang, W. *Angew. Chem., Int. Ed.* **2008**, *47*, 8933−8936.
(37) Liu, R.; Zhang, M.; Winston-McPherson, G.; Tang, W. *Chem. Commun.* **2013**, DOI; 10.1039/c2cc34609e.
(38) Liu, R.; Zhang, M.; Wyche, T. P.; Winston-McPherson, G.; Bugni, T. S.; Tang, W. *Angew. Chem., Int. Ed.* **2012**, *51*, 7503−7506.
(39) Li, C.-W.; Pati, K.; Lin, G.-Y.; Sohel, S. M. A.; Hung, H.-H.; Liu, R.-S. *Angew. Chem., Int. Ed.* **2010**, *49*, 9891−9894.
(40) Furstner, A.; Majima, K.; Martin, R.; Krause, H.; Kattnig, E.; Goddard, R.; Lehmann, C. W. *J. Am. Chem. Soc.* **2008**, *130*, 1992−2004.
(41) Wender, P. A.; Takahashi, H.; Witulski, B. *J. Am. Chem. Soc.* **1995**, *117*, 4720−4721.
(42) Wender, P. A.; Haustedt, L. O.; Lim, J.; Love, J. A.; Williams, T. J.; Yoon, J.-Y. *J. Am. Chem. Soc.* **2006**, *128*, 6302−6303.
(43) Inagaki, F.; Sugikubo, K.; Miyashita, Y.; Mukai, C. *Angew. Chem., Int. Ed.* **2010**, *49*, 2206−2210.
(44) Li, X.; Zhang, M.; Shu, D.; Robichaux, P. J.; Huang, S.; Tang, W. *Angew. Chem., Int. Ed.* **2011**, *50*, 10421−10424.
(45) Coscia, R. W.; Lambert, T. H. *J. Am. Chem. Soc.* **2009**, *131*, 2496−2498.
(46) Barluenga, J.; Tudela, E.; Vicente, R.; Ballesteros, A.; Tomas, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 2107−2110.
(47) Liu, L.; Zhang, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 6093−6096.
(48) Trost, B. M.; Xie, J.; Maulide, N. *J. Am. Chem. Soc.* **2008**, *130*, 17258−17259.
(49) Kleinbeck, F.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 9178−9179.
(50) Sethofer, S. G.; Staben, S. T.; Hung, O. Y.; Toste, F. D. *Org. Lett.* **2008**, *10*, 4315−4318.
(51) Tsuritani, T.; Yamamoto, Y.; Kawasaki, M.; Mase, T. *Org. Lett.* **2009**, *11*, 1043−1045.
(52) Chen, A.; Lin, R.; Liu, Q.; Jiao, N. *Chem. Commun.* **2009**, 6842−6844.
(53) Seiser, T.; Saget, T.; Tran, D. N.; Cramer, N. *Angew. Chem., Int. Ed.* **2011**, *50*, 7740−7752.
(54) Guo, B.; Schwarzwalder, G.; Njardarson, J. T. *Angew. Chem., Int. Ed.* **2012**, *51*, 5675−5678.
(55) Nair, V.; Nair, S. M.; Devipriya, S.; Sethumadhavan, D. *Tetrahedron Lett.* **2006**, *47*, 1043−1111.
(56) Wang, C.; Tunge, J. A. *Org. Lett.* **2006**, *8*, 3211−3214.
(57) Dubovyk, I.; Pichugin, D.; Yudin, A. K. *Angew. Chem., Int. Ed.* **2011**, *50*, 5924−5926.
(58) Rutjes, F. P. J. T.; Tjen, K. C. M.; Wolf, L. B.; Karstens, W. F. J.; Schoemaker, H. E.; Hiemstra, H. *Org. Lett.* **1999**, *1*, 717−720.
(59) Cheung, L. L. W.; Yudin, A. K. *Org. Lett.* **2009**, *11*, 1281−1284.
(60) Li, G.; Huang, X.; Zhang, L. *Angew. Chem., Int. Ed.* **2008**, *47*, 346−349.
(61) Li, L.; Wang, Y.; Zhang, L. *Org. Lett.* **2012**, *14*, 3736−3739.
(62) Alcaide, B.; Almendros, P.; Quiros, M. T. *Adv. Synth. Catal.* **2011**, *353*, 585−594.
(63) Crepin, D.; Dawick, J.; Aissa, C. *Angew. Chem., Int. Ed.* **2010**, *49*, 620−623.
(64) Agenet, N.; Mirebeau, J.-H.; Petit, M.; Thoubenot, R.; Gandon, V.; Malacria, M.; Aubert, C. *Organometallics* **2007**, *26*, 819−830.
(65) Matsuda, T.; Shigeno, M.; Murakami, M. *J. Am. Chem. Soc.* **2007**, *129*, 12086−12087.
(66) Matsuda, T.; Shigeno, M.; Makino, M.; Murakami, M. *Org. Lett.* **2006**, *8*, 379−3381.
(67) Murakami, M.; Ashida, S. *Chem. Commun.* **2006**, 4599−4601.
(68) Xu, T.; Dong, G. *Angew. Chem., Int. Ed.* **2012**, *51*, 7567−7571.
(69) Xu, T.; Ko, H. M.; Savage, N. A.; Dong, G. *J. Am. Chem. Soc.* **2012**, *134*, 20005−20008.
(70) (a) Seiser, T.; Cramer, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 9294−9297. (b) Seiser, T.; Cramer, N. *Chem.—Eur. J.* **2010**, *16*, 3383−3391.
(71) Seiser, T.; Roth, O. A.; Cramer, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 6320−6323.
(72) Shigeno, M.; Yamamoto, T.; Murakami, M. *Chem.—Eur. J.* **2009**, *15*, 12929−12931.
(73) (a) Trost, B. M.; Xie, J. *J. Am. Chem. Soc.* **2006**, *128*, 6044−6045. (b) Trost, B. M.; Xie, J. *J. Am. Chem. Soc.* **2008**, *130*, 6231−6242.
(74) Brown, M. J.; Harrison, T.; Overman, L. E. *J. Am. Chem. Soc.* **1991**, *113*, 5378−5384.
(75) Chai, Z.; Rainey, T. J. *J. Am. Chem. Soc.* **2012**, *134*, 3615−3618.
(76) Ishida, N.; Sawano, S.; Murakami, M. *Chem. Commun.* **2012**, 1973−1975.
(77) Kim, K.-D.; Yeom, H.-S.; Shin, S.; Shin, S. *Tetrahedron* **2012**, *68*, 5241−5247.
(78) Schweinitz, A.; Chtchemelinine, A.; Orellana, A. *Org. Lett.* **2011**, *13*, 232−235.