Gold-catalyzed C–O bond forming reactions for the synthesis of six-membered O-heterocycles

Navjeet Kaur¹ · Pranshu Bhardwaj¹ · Meenu Devi¹ · Yamini Verma¹ · Pooja Grewal¹

© Springer Nature Switzerland AG 2019

Abstract

The heterocycles are present in the drugs and pesticides in a major proportion and development of new strategies for the synthesis of these compounds is attractive topic for the synthetic and medicinal chemists. Synthesis of heterocycles is one of the important areas in synthetic organic chemistry. The present manuscript reported the synthesis of six-membered heterocycles with oxygen heteroatom using gold catalysts. This review covered interesting discoveries in the past few years.

Keywords Gold · Catalysis · Heterocycles · Oxygen

1 Introduction

Heterocycles are the most explored compounds as they are present in biologically active natural products, key intermediates and pharmaceutically important molecules including anti-bacterial, anti-inflammatory, anti-viral, antioxidant and anti-tumoral agents [1–38]. These heterocycles are widespread in materials, corrosion inhibitors, agrochemicals, herbicides, and among others. They act as key components in organic synthesis, constitute a significant proportion of drug molecules and have industrial applications such as cosmetics reprography, plastics, and information storage [39–76].

A wide range of reactions, including annulation, cyclization and cascade reactions, are reported for the synthesis of heterocycles. The metal and non-metal catalyzed synthesis of heterocycles is one of the straightforward method and many starting materials were easily converted into cyclic compounds [77–86]. Catalytic protocol is employed for the synthesis of heterocycles, carbocycles and complex natural products. These catalytic systems make the synthetic strategies simpler and easier retrosynthetic processes. Due to the importance of these heterocycles and catalytic systems, the present documentation is highly

attractive and useful for the synthetic chemists. Overall, these findings will be a useful tool for the design and synthesis of heterocycles with medicinally active key intermediate in large quantity and with facial manner [87–90].

The present review article concentrated on the synthesis of several six-membered oxygen containing heterocyclic compounds using gold catalysts.

1.1 Gold-catalyzed synthesis of six-membered heterocycles with oxygen heteroatom

1.1.1 Synthesis of six-membered one oxygen containing heterocycles

Sherry et al. [91] used a tandem Claisen rearrangement/heterocyclization for the synthesis of dihydropyrans (Scheme 1). The aldehyde was formed when propargyl vinyl ether was subjected to $[(PPh_3PAu)_3O]BF_4$. The dihydropyran was obtained when formed aldehyde was treated under same catalyst, but in wet dioxane. The dihydropyran was formed in 86% yield when this two step reaction was combined into a single step using wet dioxane [92].

✉ Navjeet Kaur, nvjithaans@gmail.com | ¹Department of Chemistry, Banasthali Vidyapith, Banasthali, Rajasthan 304022, India.

Scheme 1

Scheme 2

Scheme 3

When reactions were stopped at partial conversion authors isolated a small amount of ketone. Ketone underwent cyclization under reaction condition (Scheme 2) [93].

He and co-workers [94] produced simple olefins from intermolecular addition of both carboxylic acids and phenols at 85 °C in the presence of $Ph_3PAuOTf$. Mixed products were obtained when some terminal olefins migrated to an internal position, but further migration does not occur. However, allylic benzenes not migrated to more stable styrenes and different functional groups were tolerated (Scheme 3).

Forsyth and co-workers [95] performed Au-catalyzed nucleophilic bis-spiroketalization for the synthesis of the rings of azaspiracid which possessed a trioxadispiroketal core structure (Scheme 4).

Marine toxins family has azaspiracid which causes diverse chronic effects on pancreas, liver, and thymus and human poisoning [96, 97]. Its complete structure has been fully established [98], and many methods have been reported for its synthesis [99, 100]. Kazama and co-workers [101] synthesized azaspiracid fragment. Authors concentrated on the synthesis of rings in one step spiroketalization with Au catalyst. Coupling of subunits (formed from simple precursors) afforded alkynediol-based system (Scheme 5).

Initially, ketone was synthesized through Markovnikov alkyne hydration with Au, followed by the formation of enone by β -elimination of methoxy group. The desired product was obtained by Au-mediated intramolecular

Scheme 4

Scheme 5

conjugate addition of the nucleophilic hydroxyl group (Scheme 6) [102].

The dihydropyrans were formed upon cycloisomerization of hydroxyallenes (Scheme 7) [103]. Both Au(I) and Au(III) pre-catalysts were found to be competent and provided dihydropyrans (the 6-endo-cyclization product) with ~60% yield. No trace of 5-exo-isomer was observed. Interestingly, the presence of Ag salts and the solvent hardly

affected the yield which led to cationic Au species. With cationic Au catalysts the reaction time decreased considerably in non-coordinating solvents. The tetrahydropyridine was formed in good yield when the process was extended to aminoallene.

Heterocyclic ketones were formed when homopropargylic ethers with pendent nucleophiles were reacted in aqueous solvent with gold catalysts [104, 105]. The

Scheme 6

Scheme 7

Scheme 8

reactions are tolerant of functionality and ambient atmosphere, efficient, and operationally simple. The product thermodynamics predicted the diastereoselectivity. Water-saturated dichloromethane was utilized as a solvent to ensure the smooth alkyne hydration. The simpler Au species were able to effect the elementary steps in this sequence in the presence of sodium tetrachloroaurate(III) catalyst. The reactions occurred reproducibly and smoothly at 35 °C. Although for many reactions sodium tetrachloroaurate(III) was found to be a suitable catalyst, the preferable catalyst for slower reactions was produced from Ph_3PAuCl /silver hexafluoroantimonate(V) system. More electrophilic catalyst was generated when silver(I) served to abstract the chloride from Ph_3PAuCl (Scheme 8). Ketone was obtained by Au mediated hydration of the alkyne. Enone was formed upon methanol elimination. The cyclized product was obtained when enone underwent metal-mediated conjugate addition.

A racemic mixture of pyran was obtained (determined by a GC experiment with a chiral stationary phase) when substrate underwent cyclization with Au catalyst under standard atmospheric condition. The tetrahydropyran was produced when homopropargylic ether was reacted in the presence of silver hexafluoroantimonate(V) (5 mol %) and chloro(triphenylphosphine)gold(I) (5 mol%) under standard atmospheric conditions in unpurified dichloromethane (Scheme 9). A mixture of diastereomers was obtained as a single diastereomer in 60% yield upon similar treatment of ether [106–110].

Du and co-workers [111] developed a highly efficient cyclization of (Z)-enynols in the presence of gold catalyst under mild reaction conditions (Scheme 10) [112–114].

The coinage metals are utilized for the construction of bioactive target molecules via functionalized allenes. These bioactive molecules include the fragrance compound linalool oxide, the alkaloids isochrysotricine and

Scheme 9

Scheme 10

Scheme 11

isocyclocapitelline, as well as bejarol, boivinianin B, and varitriol [115–119]. During the total synthesis of natural sesquiterpenoid (*R,R,R*)-bejarol and its (*3R,5S,9R*)-isomer, the propargyl acetate underwent $\text{SN}2'$ -substitution with methylmagnesium cuprate to afford the desired allene as a mixture of diastereomers with regard to the allenic chirality axis (Scheme 11). Dihydropyran was obtained by Au-catalyzed cycloisomerization upon deprotection of the silyl ether. The formed dihydropyran was transformed readily into the target molecule.

The cycloisomerization of 2-alkynyl-1,5-diol was performed with AuCl to afford dioxabicyclo[4.2.1] ketal and its further transformation product tetrahydropyran [120]. The intermediates were produced when Au catalyst activated one of the oxygen atoms. The formed intermediates were rearranged to oxonium intermediates (Scheme 12).

Excellent yields of olefin-possessing spiroketals (and enantiomer) were obtained when monopropargylic triols underwent Au(I)-catalyzed intramolecular cyclization under mild conditions [121] (Scheme 13). A variety of

Scheme 12

Scheme 13

Scheme 14

different substituted triols was synthesized which cyclized to afford substituted 5- and 6-membered ring spiroketals. Similarly, Zhang et al. [122] reported Au-catalyzed double intramolecular hydroalkoxylation for the preparation of bisbenz-annelated spiroketal core of natural bioactive rubromycins.

The alk-4-yn-1-ones underwent Au-catalyzed cyclization to afford different oxygen heterocyclic compounds depending on the reaction solvent and the substitution pattern in the substrate. Thus, substituted furans were formed by a 5-exodig cycloisomerization of alkynones with one substituent at C-3, whilst 4*H*-pyrans were obtained by 6-endo-dig cyclization of substrates containing two substituents at C-3 (Scheme 14) [123].

Various substituted nitrogen- or oxygen possessing heterocycles were formed by homogeneous carboamination,

carboalkoxylation and carbolactonization of terminal alkenes via oxidative Au catalysis. Deuterium-labeling studies established the indispensable role of gold(I)/gold(III) catalysis and the nature of the alkene functionalization (Scheme 15) [124].

A strong decrease in catalyst loading was observed with improved selectivity and stability of Au catalysts in additives and/or THF solvent. Interestingly, the synthesis of 5,6-dihydro-2*H*-pyrans from β -hydroxyallenes by *endo*-cycloisomerization is also strongly affected by additives and solvent. The β -hydroxyallenes were less reactive as compared to α -hydroxyallenes. The best results were reported with cationic Au catalyst $\text{Ph}_3\text{PAuBF}_4$ (produced in situ from silver tetrafluoroborate and Ph_3PAuCl) or AuCl (Scheme 16). Interestingly, Ag salts alone not promoted the reaction. The reaction was completed at room

Scheme 15

Scheme 16

Scheme 17

temperature within 1 h in toluene or CH_2Cl_2 , whereas slower but more selective reaction occurred with additives or THF solvent. The epimerization of aryl-substituted β -hydroxyallenes during cyclization was prevented upon addition of pyridine [125, 126].

Many five- and six-membered heterocyclic compounds were synthesized with Au catalyst by *endo*-cycloisomerization of allenes containing nucleophilic substituents at α - or β -position. Main characteristics of these transformations are the chirality transfer from the allenic axis of chirality to the new stereogenic center in the cyclization product and the high reactivity of allene in the presence of Lewis-acidic, carbophilic Au(I) or Au(III) catalysts. Recent contributions included the applications in the total synthesis of natural products such as the β -carboline alkaloids (–)-isochrysotricine and (–)-isocyclocapitelline and the optimization of chirality transfer employing σ -donor ligands to Au. Authors started developing new synthetic methods using allenes under homogeneous Au catalysis for stereoselective synthesis of functionalized allenes [126–130]. This strategy concentrated on *endo*-cycloisomerizations of chiral allenes possessing a nucleophilic substituent in the homoallylic (β) or allylic (α) position. On the other hand,

other researchers studied Au-catalyzed intermolecular additions to allenes [131, 132] or *exo*-selective cyclizations [133–137], (Scheme 17). This reaction occurred with perfect atom economy [138, 139].

1.1.2 Synthesis of six-membered one oxygen containing polyheterocycles

Yang and He [106] reported alkylation of arenes with epoxides in the presence of Au catalyst. The *endo* addition product 3-chromanols formed exclusively in good yield when (phenoxymethyl)oxiranes were treated with gold(III) chloride/silver trifluoromethanesulfonate (2.5% based on Au) in dichloroethane (Scheme 18) [140].

Planar chiral isochromene-chromium complexes were afforded with high enantioselectivity by Au(I) -catalyzed asymmetric cyclization of 1,3-dihydroxymethyl-2-alkynylbenzene chromium complexes [141]. The combination of Ag salts and Au pre-catalysts largely influenced the enantioselectivities of the cyclized isochromene-chromium complexes. Regardless of the nature of the Au pre-catalyst, the use of silver hexafluoroantimonate(V) resulted in excellent enantioselectivities (Scheme 19).

Scheme 18

Scheme 19

Scheme 20

Ketals are crucial targets and key structures in organic synthesis [142–144]. Bicyclic, fused, and spiroketals are present in natural compounds. Various biomedically important non-natural and natural systems possess spiroketals [145–148]. Most common method for the synthesis of spiroketals is the cyclocondensation of ketone diols among other developed methods [149, 150] (Scheme 20). One-pot cycloisomerization on alkynediols with Au catalyst built complex ketal systems and offered many advantages. For example, cycloisomerization of alkynediols in the presence of gold catalyst are more

atom economical, exothermic, and more compatible than ketones under different reaction conditions. This protocol was applied for the construction of many natural compounds [151–154]. Bisbenzannelated spiroketal core of rubromycins was synthesized by Li and co-workers [122]. These natural compounds exhibit various pharmacological properties, like inhibition of the reverse transcriptase of HIV I, inhibition of DNA polymerase, or inhibition of DNA helicase [155–158]. The basic structure motif share natural isolated compounds such as purpurumycin, γ -rubromycin, or heliquinomycin. Moderate yields of spiroketals were

Scheme 21

Scheme 22

Scheme 23

obtained by Au-catalyzed cycloisomerization of alkynediols along with benzofuran in notable amounts [159].

Dai and Shi [160] reported that α -epoxyketones underwent intramolecular cycloisomerisation with their tethered alkynes in the presence of Au(I) catalyst to synthesize six-membered heterocycles. The epoxyketones were isomerized into 1,3-diketones which underwent a subsequent intramolecular addition of a carbon or an oxygen nucleophile to the alkynes with Au(I) catalyst (Scheme 21).

He and co-workers [161] described that epoxides underwent an intra- and intermolecular hydroarylation with gold(III) chloride/silver trifluoromethanesulfonate. The intramolecular reaction was found to be stereospecific. The addition occurred only at the less hindered terminal carbon with an intermolecular reaction of 1,3,5-trimethoxybenzene with propylene oxide. In contrast to this, well-known Friedel–Crafts reaction with Lewis acid/

Bronsted acid catalyst formed carbon–carbon bonds at the more substituted carbon. The reaction occurred through an SN^2 mechanism with an aryl-Au(III) species (Scheme 22).

The 2-(1-alkynyl)aryldimines and several nucleophiles underwent a tandem nucleophilic addition and cyclization with carbophilic Lewis acids, like nickel chloride, $\text{In}(\text{OTf})_3$, and $\text{AuCl}(\text{PPh}_3)/\text{AgNTf}_2$, to deliver 1,3-disubstituted-1,2-dihydroisoquinolines. Gold(I) catalysts needed appropriate proton sources, among these catalysts, by which a number of substrates and nucleophiles can be used for this tandem reaction (Scheme 23) [162].

The benzopyrans possessing quaternary stereocenters were formed in excellent enantioselectivity when propargyl esters underwent carboalkoxylation with 3,5-(*t*-Bu)₂-4-MeO-MeOBIPHEP-Au complex (Scheme 24) [163]. The amount of catalyst was decreased without significant loss of yield or enantioselectivity.

Scheme 24

Scheme 25

Scheme 26

The product as well as unexpected dimer were obtained from substrates bearing additional nucleophilic groups such as amide or ester moieties with both the Au(I) and Au(III) catalysts through the formation of eight new bonds (Scheme 25) [164].

Wang et al. [165] in 2011 used propargylic pivalates for the enantioselective construction of chromenyl derivatives with Au catalyst. The metal activated axially chiral allene was produced from an initial 1,3-pivaloxy migration, formed chiral allene was converted into achiral carbocation with Au catalyst. The achiral carbocation, contain a chiral ligand at the Au functionality, is stabilized by the

oxygen atom of the migrated group. Therefore, the enantioenriched oxonium compound was formed by dynamic kinetic asymmetric 6-endo-trig cyclization. The C3-substituted chromenyl pivalate was obtained upon carbodemetalation of the vinyl Au moiety present in oxonium compound via 1,3-alkyl migration. Interestingly, the vinyl pivalate moiety of chromenyl pivalate was transformed into ketone in the presence of lithium aluminium hydride, then the ketone afforded enantioenriched chromanones (Scheme 26) [166].

Uemura et al. [167] reported that propargyl pivalates underwent Au-catalyzed enantioselective

Scheme 27

Scheme 28

cascade 1,2-O-Piv-1,4-allyl migration for the synthesis of benzopyran (Scheme 27). An efficient and highly enantioselective (R)-MeO-DTBM-BIPHEP-(AuCl)₂-silver hexafluoroantimonate(V) catalyzed transformation occurred with propargyl pivalates containing various groups at the propargylic, the aromatic ring, and the allylic positions, system. Mechanism has proposed that the Au-promoted 1,2-pivaloxy migration of substrate bearing a terminal alkyne moiety synthesized carbene. The oxonium intermediate was prepared when carbene underwent a nucleophilic attack of ether oxygen atom at the electrophilic center [166].

Simple *ortho*-alkynylbenzaldehydes underwent base-promoted domino nucleophilic addition/annulation in the presence of alcohols (Scheme 28). They focused on to rationalize the relationship between the nature of the substitution on the cyclisation mode and the alkynyl terminus and the selective preparation of the isobenzofuran framework [168, 169].

The fused heterobicyclic alkenes were synthesized [170]. The oxabicycloalkene was formed as a single diastereomer in 90% yield when alcohol was treated with gold(III) chloride (5 mol%). The tandem cyclization reactions were stereospecific and consistent with earlier observations of stereospecific cyclopropanations (Scheme 29) [171].

Hashmi and co-workers [172] in their intramolecular hydroalkoxylation of alkynes studied that dimerization products were synthesized through benzylic carbon–hydrogen activation pathway with Au catalyst. Isotope labeling studies have suggested that ketone oxygen comes from the alcohol which supported the benzylic carbon–hydrogen and ketone oxidation mechanism (Scheme 30). Carbon–hydrogen activation occurred at benzylic position in the presence of Au catalyst at room temperature in a neutral solvent. The Au-catalyzed transformation of substrates takes place to afford isochromene derivatives via 6-endo-dig cyclization [164].

Watanabe et al. [173] synthesized benzofurans by intramolecular addition of simple arenes to tethered allenes with Au(I) catalyst. To produce 6-membered rings preferentially presence of electron-donating substitutions on the arene was needed (Scheme 31).

1.1.3 Synthesis of six-membered one oxygen containing heterocycles fused with aromatics

With electron rich arenes reaction occurred at 50 °C. Longer reaction times and higher temperatures were needed for less-electron-rich substrates. The halide substituents were tolerated in this reaction for further functionalization of the ring. The high diastereoselectivity was

Scheme 29

Scheme 30

Scheme 31

observed in reaction which resulted in exclusive formation of trans products. X-ray analysis confirmed the inversion of configuration of carbon atom linked to aryl ring. Easy control of stereochemistry of starting epoxide offered a good route to synthesize 3-chromanols stereospecifically (Scheme 32) [164].

In Au-catalyzed enantioselective addition BIPHEP is used as a chiral atropisomeric biaryl diphosphine ligand. Although the Au-catalyzed reactions are well investigated, because of intrinsic inertness of carbon=carbon (with respect to alkynes and allenes) participating in nucleophilic addition reactions assisted by π -electrophilic

activation, the use of non-activated olefinic carbon-carbon double bonds is still largely unexplored [174]. The desired arylated products were synthesized with enantiomeric excess of 98% when enynes were treated with 3,5-(*t*-Bu)₂-4-MeO-MeOBIPHEP(AuCl)₂ and silver trifluoromethanesulfonate at room temperature in diethylether for 15–20 h. The same protocol was also used in asymmetric synthesis of bicyclo[4.1.0]heptene derivatives by gold(I)-catalyzed cycloisomerization of 1,6-enynes [175] (Scheme 33).

Nonaromatic epoxides were obtained by Au-catalyzed epoxyalkyne cycloisomerisation which afforded

Scheme 32

Scheme 33

Scheme 34

heterocycle. An attack of epoxide at the activated alkyne via 6-*exo-dig* furnished key intermediate whose structure is shown by its Au-carbenoid resonance form which provided heterocycle by a Nazarov-type cyclisation Scheme 34 [176].

Sethofer et al. [177] reported a highly enantioselective polyene cyclization where transition metal-assisted alkyne

activation acted as cyclization initiating event. The enyne reacted with silver hexafluoroantimonate(V) and monocationic Au(I) complexes in the presence of sterically encumbered phosphines. The fused bicyclic compounds were formed in the presence of 3,5- $(t\text{-Bu})_2$ -4-MeO-MeOBIPHEP with good enantiomeric excess values (Scheme 35, 36).

Scheme 35

Scheme 36

Naturally occurring brazilane and synthetic analogues were synthesized by this short and efficient strategy. The complex molecular frameworks were produced

stereoselectively from *cis*-2,4-dien-1-als and allylsilanes by catalytic [4 + 3] annulation. Addition product was obtained (Scheme 37, 38, 39) upon nucleophilic attack of

Scheme 37

Scheme 38

an allylsilane derivative onto allyl cation species. The addition product afforded a new allyl cation by an ionisation/

nucleophilic attack. Allyl cation underwent carbocyclisation to provide annulated product [176, 178].

Scheme 39

Scheme 40

Scheme 41

Liu and co-workers [179] developed an intramolecular cycloaddition of diynes with tethered arenes in the presence of Au catalyst. Deuterium-labeling studies have shown that the vinylgold(I) was formed in the first step of reaction i.e. intramolecular arylation of one alkyne. The target product was produced from vinylgold(I) by either a Nazarov cyclization or 5-*exo-dig* addition (Scheme 40).

1.1.4 Synthesis of six-membered one oxygen containing heterocycles fused with other heterocycles

In some cases electron-rich arenes served as good nucleophiles [180, 181]. An alkynyl ether functionality initiated a furan-yne cyclization with Au complex [Mes₃PAu]NTf₂ to afford a tetracyclic system rather than a phenol (Scheme 41) [182, 183].

Scheme 42

Scheme 43

Scheme 44

Liu and co-workers [184] reported that 2-(ynol)aryl aldehydes underwent Au-catalyzed annulations for the construction of benzobicycloacetals and benzochromanes. With gold(III) chloride catalyst benzochromanes were synthesized, whereas with the use of triazole-Au catalyst benzobicyclo[5.3.1]acetals were obtained. The cyclization of benzaldimine-chromium complexes and *o*-alkynyl benzaldehyde with Au(I) catalyst and alcohol nucleophiles provided 1-anti-functionalized heterocycle chromium complexes stereoselectively (Scheme 42, 43, 44) [185]. A single planar chiral chromium complex was employed in this strategy for the preparation of enantiomerically pure *cis*- and *trans*-1,3-dimethylisochromans [183].

Alkynols underwent heterocyclization reactions in the presence of Au catalyst to afford fused bicyclic systems.

Good yield of desired cycloetherification/hydroxylation product was reported when 2-azetidinone-tethered bis-homopropargylic alcohol was treated with gold(III) chloride. A (methoxymethyl)oxy moiety in place of free hydroxyl group underwent Au-catalyzed reaction to provide cyclization product smoothly albeit in lower yield. The protective group at the hydroxy moiety not influenced the regioselectivity (5-exo cyclization). The oxycyclization/hydroxylation adduct with concomitant methoxymethyl ether cleavage was synthesized by Au-catalyzed oxycyclizations of trishomopropargylic alcohol. On the other hand, the reactivity was affected substantially when a phenyl substituent was present at the terminal alkyne carbon, as shown by the fact that a complex mixture of products was obtained from phenyl alkynol (Scheme 45) [186–188].

Scheme 45

Scheme 46

Scheme 47

Gagne and co-workers [189] reported the synthesis of polyether skeletons from epoxyallenes by Au(I)-catalyzed cascade nucleophilic cyclisation in CH₂Cl₂ at room temperature. A variety of functional groups such as esters, sulfones, sulfonamides, and ethers were tolerated under catalytic conditions. Bicyclic medium-ring ethers are present in many polyether natural products. These fused bicyclic medium-ring ethers were synthesized under Au catalysis (Scheme 46) [176, 190].

1.1.5 Synthesis of six-membered two oxygen containing heterocycles

Good yields of α -pyrones were obtained in sequential alkyne activation of propiolic acids and terminal alkynes with Au(I) catalyst. Different substituents bearing α -pyrones were produced from reactions involving propiolic acids (Scheme 47) [191].

A straightforward preparation of substituted α -pyrones was performed in good yields upon rearrangement of β -alkynylpropiolactones with Au(I) catalyst (Scheme 48) [192].

Scheme 48

Scheme 49

Scheme 50

An enyne allene was prepared when substrates underwent Au-catalyzed [3,3]-sigmatropic rearrangement. The activation of alkyne functionality in enyne allene induced a 6-endo-dig cyclization to afford oxocarbenium intermediate. In one route elimination provided a vinyl pyrone (Scheme 49). A number of nucleophiles also trapped oxocarbenium intermediate. Using different reaction conditions and nucleophiles the attack of electrophilic intermediate oxocarbenium at three distinct sites was controlled [164].

Piera et al. [193] reported an efficient pathway for the generation of unsaturated δ -lactones in which there was Au-catalyzed intramolecular nucleophilic attack of a carboxy ester on an allene (Scheme 50).

The carbon–fluorine bonds were formed by fluorination of a C–M bond (an alternative method) in addition to fluorometallation of unsaturated carbon–carbon bonds. This intramolecular reaction is a good strategy to prepare fluorinated heterocyclic compounds. The transition metal-catalyzed fluorination of multi carbon–carbon

Scheme 51

Scheme 52

bond reactions is less investigated due to the scarcity of protocols for the fluorination of C–M bonds. So far, only three metals, palladium, gold, and silver were employed in these reactions. Schuler et al. [194] in 2008 developed an alkoxyfluorination of alkynes in the presence of Au catalyst which involved a sequential alkoxyauration reaction and oxidative fluorination of the vinyl-gold bond with Select-Fluor as the fluorine source. However, alkoxyhydrogenation product was formed in significant amounts due to the protonolysis of vinyl-gold bond. For this transformation the presence of difluorine substitution at the α -position of carbonyl group was needed. Without difluorine substitution only hydroalkoxylation occurred. The β -hydroxy- α,α -difluoroynones underwent Au-catalyzed intramolecular 6-endo-dig cyclization under mild conditions (Scheme 51).

These results have showed that Au catalysis was compatible with electrophilic fluorinating reagents [195].

Schreiber and co-workers [196, 197] reacted diynes and electron-rich arenes for the preparation of pyrones in the presence of Au(I) catalyst. The rearrangement of alkyne into an allene was the first step supported by racemization of enantio-enriched substrates (Scheme 52, 53). Traditional preparations of pyrones involved the lactonization of ketoesters [198, 199]. Alternatives which have attracted the attention are transition-metal catalyzed cycloaddition [200] and annulation reactions [201], but most of them have limitations including the need for harsh reaction conditions or the poor regioselectivity. Different complex pyrones were obtained from readily available propargyl propiolate by Au-catalyzed cascade process [164].

Scheme 53

Scheme 54

Genet and Michelet [202] reported very good to excellent yields of addition of carboxylic acids to alkynes, despite their lower nucleophilicity. Five- or six-membered lactones were produced based on the electronic nature of the alkynyl substituent (Scheme 54).

Toste and co-workers [203] synthesized carbonylic products when sulfoxides acted as an oxygen donor to Au(I)-carbenoids. Good yields of enamine were obtained also from sulfines by this transformation. A similar intramolecular redox system was used by Li and Zhang [204]. They utilized propargyl alcohols in place of simple alkynes which were oxidized and rearranged into diketones (Scheme 55).

Carbonyl compounds were prepared upon addition of water to alkynes. Synthesis of carbonyl compounds by hydration of alkynes without energy-intensive redox chemistry is an atom-economical method. In 1881 Kucherov reported that hydration of alkynes occurred with Hg(II) salts under mild conditions and this reaction has

many applications in synthesis. The Kucherov reaction was unsuitable for sustainable organic synthesis due to toxicity of mercury and problems of their disposal and handling. Alternative alkyne hydration catalysts were developed in order to replace the Hg(II) by more-active and less-toxic metal catalysts. In 1976 Au catalyst (HAuCl_4) was used for catalytic hydration of alkynes [205]. Later on a new protocol was examined for the hydration of alkyne under neutral conditions with sodium tetrachloroaurate catalyst. Excellent yields of hydration of internal and terminal alkynes were reported [206–208]. The phenylacetylene and hept-1-yne were hydrated under acidic or neutral conditions with a number of Au(III) organometallic compounds, possessing Au–Mes or Au– C_6F_5 2,4,6-trimethylphenyl units, and chloro ligands [209]. Mononuclear complexes containing electronegative ligands like $\text{PR}_4[\text{Au}(\text{Ar})\text{Cl}_3]$ or $\text{NBu}_4[\text{Au}(\text{C}_6\text{F}_5)_2\text{Cl}_2]$ afforded the best results and have same activity as that of sodium tetrachloroaurate(III). In acidic media higher turnover numbers were obtained. Schulz

Scheme 55

Scheme 56

and Teles [210], Teles et al. [211] performed hydration of propargyl alcohol in the presence of gold(I)-acid catalytic system. Moreover, Au(I)-acid catalyzed addition of alcohols to alkynes occurred. The catalysts were produced from (a) [AuCl(PPh₃)] and AgY (Y) nonnucleophilic counterion), from (b) [AuX(PPh₃)](X Cl, MeSO₃, CF₃CO₂, NO₃) and boron trifluoride, or from (c) [AuMe(PPh₃)] by protonolysis of the Au–C bond in the presence of strong acid which afforded a non-nucleophilic counterion (HBF₄, sulfuric acid, MeSO₃H). Reactions occurred under mild conditions (20–50 °C). The formed enol ethers were trapped as ketals or hydrolyzed to carbonyl compounds (Scheme 56) [164].

1.1.6 Synthesis of six-membered two oxygen containing polyheterocycles

Although propargyl amines were produced from Au–acetylide species, no report is there on Au-catalyzed synthesis of propargyl alcohol. The catalytic cycle was arrested as Au was oxophilic and binded the propargyl alcohol irreversibly. Li and co-workers [212] synthesized 1-alkynyl-1*H*-isochromenes when propargyl alcohol–Au complex underwent an intramolecular nucleophilic addition by tethering an alkynyl group to the ortho position of an aryl aldehyde. This reaction not takes place successfully with simple aryl aldehydes. The neighboring alkynyl group acted as chelating ligand and the intermediate proposed in this reaction was similar to that reported by Yamamoto

and Asao [213] earlier. The reaction synthesized isoflavanones through a completely different pathway if salicylaldehyde was utilized [214]. Au(I) activated the carbonyl proton, which was subsequently added to alkyne. Azaflavanones were formed in lower yields from *o*-tosylaminobenzaldehyde and only aromatic alkynes acted in this reaction [215] (Scheme 57, 58). Li and Yao [216] reacted terminal alkynes and *o*-alkynyl benzaldehydes in catalytic amounts of a phosphine Au(I) complex and a tertiary base in a mixture of toluene and water to afford remarkable results. Moderate to high yields of 1-alkynyl-1*H*-isochromenes were obtained [164, 217].

Harkat et al. [218] utilized unactivated ω -acetylenic acids for the synthesis of different ring-sized lactones. The nucleophilicity of carboxylic group was boosted employing potassium carbonate in catalytic amounts to synthesize carboxylate anion. The limitations and regioselectivity of the reaction were investigated by gold(I) chloride catalyzed cycloisomerization of δ - and γ -acetylenic acids [219]. Both endo- and exo- derivatives were obtained by intramolecular cyclization of δ - and γ -acetylenic acids. Uchiyama and co-workers [220] described that γ -acetylenic acids underwent a regiocontrolled intramolecular 6-endo-dig cyclization with acid catalyst. In contrast to this, in Au-catalyzed cycloisomerization reaction the exo-dig cyclization predominated to provide lactones as a single stereoisomer in major amounts (Scheme 59, 60) [164].

Scheme 57

Scheme 58

Scheme 59

Scheme 60

The dienes served as good participants in Diels–Alder reaction (Scheme 61). The desired 1,3-dienes were synthesized when propargylic pivalates underwent double migratory reaction under reaction conditions. The

1,3-dienes by intra- and intermolecular Diels–Alder reactions afforded good yields of cycloadducts with good selectivity [166, 221].

Scheme 61

Scheme 62

Skouta and Li [222, 223] generated isoflavanone-type compounds by annulation of salicylaldehyde with arylalkyne. The mechanism has proposed that an oxidative addition occurred around the Au center to produce an acyl Au(III) hydride intermediate which underwent an alkyne insertion and reductive elimination to afford enone. Then, the enone ultimately afforded compound via an intramolecular Michael-type reaction (Scheme 62). This annulation reaction was extended with alkynes and 2-tosylaminobenzaldehydes for the construction of azaisoflavanones. The desired product was not obtained from 2-aminobenzaldehyde. The reaction was improved possibly with tosylamine greatly due to increased acidity of the hydrogen on nitrogen [176].

The natural heterocyclic compounds chromones exhibit various biological activities. The oxacyclic systems were prepared by several methods such as iodocyclizations

[224], metal-catalyzed cycloadditions [225], or O-arylation processes [226]. The chromones were produced from alkynol framework by Au catalyzed cycloisomerization [227]. Highly functionalized frameworks were obtained upon further migration of group R1. The isomerization reaction competed with the desired gold assisted cycloisomerization therefore only moderate yields were observed (Scheme 63), in [159].

The isocoumarins were formed exclusively upon cyclization of γ -acetylenic esters with gold(III) chloride (Scheme 64) [164].

He [228] and Reetz [229] developed hydroarylation of electron deficient alkynes and normal alkynes with Au(III) catalyst, respectively. In the former case, coumarin derivatives were obtained when reaction was extended to an intramolecular fashion. Strong Bronsted acids do not catalyze the hydroarylation of electron-deficient alkynes. An

Scheme 63

Scheme 64

Scheme 65

attractive route for the formation of new carbon–carbon bond is intra and intermolecular hydroarylation of alkynes [230–232]. Although other metal catalysts like platinum, palladium, scandium and zirconium salts are also active in the hydroarylation of alkynes, best or comparable results were reported with Au but with a lower catalyst loading. Shi and He's [233] isotope labeling and spectroscopic experiments have indicated that in hydroarylation reaction an arenegold intermediate was involved. Kharasch and Isbell [234] in 1931 synthesized arylgold(III) complexes in the presence of anhydrous Au(III) chloride in neat toluene, benzene, or other aromatic compounds at room temperature [235–238]. This auration reaction occurred by base promoted transmetalation of aryl boronic acid or in an electrophilic manner [239, 240]. Authors reported that electron-deficient alkynes underwent both intra- and

intermolecular hydroarylation. The intermolecular reactions proceeded smoothly without solvent at rt in small amounts of gold(III) chloride and silver trifluoromethanesulfonate, whereas synthesis of coumarins by intramolecular version required the higher catalyst loading and higher temperature (Scheme 65) [164, 216].

1.1.7 Synthesis of six-membered two oxygen containing heterocycles fused with aromatics

The reaction of diazo ketones with alkynes and rhodium catalyst formed alkenyl rhodium carbenoids. The reactivity of alkenyl rhodium carbenoids has been the subject of considerable investigation [241–246]. Vinylogous acceptor-substituted carbenoids [247, 248] were generated by ring opening of cyclopropenyl ketones. An intramolecular

Scheme 66

Scheme 67

trapping occurred with an alkene of vinylogous acceptor-substituted carbenoids [249–261]. The cycloisomerization of appropriately substituted cyclopropene-ones occurred with transition metal catalyst through intramolecular cyclopropanation of olefin and its synthetic potential remained unexplored. The 3-allyl-1,2-diphenylcyclopropene was rearranged into substituted bicyclo-[3.1.0]hex-2-ene with Ag catalyst and it constituted one of the first examples of such a process [252]. The 3-aza- or 3-oxabicyclo[4.1.0]heptanes I were synthesized in excellent diastereoselectivities and high yields by Au-catalyzed cycloisomerization of cyclopropene-ones [253–261]. The [4.1.0] bicycloheptan-2-ones were formed from isopropylidene group by ozonolysis [262], this method was comparable to copper-catalyzed intramolecular cyclopropanation of

dialko alkenyl ketones, [263, 264] in terms of diastereoselectivity and efficiency (Scheme 66).

1.1.8 Synthesis of six-membered two oxygen containing heterocycles fused with other heterocycles

The allene (45%) was formed together with bridged dihydropyran in trace amounts from 2'-hydroxyflavone ether with an internal nucleophile and PtCl_2 (Scheme 67). Bridged dihydropyran originated from intramolecular trapping of the oxonium ion by the adjacent 2'-hydroxy group. The bridged dihydropyran product was formed upon replacing PtCl_2 to $\text{NaAuCl}_4 \cdot \text{H}_2\text{O}$ and PtCl_4 . The bridged dihydropyran was obtained in 44% yield upon addition of 1,1,1,2,2,2-hexafluoroisopropanol as a proton source

Scheme 68

Scheme 69

which promoted the protodemetalation over metal dissociation [265].

1.1.9 Synthesis of six-membered oxygen and nitrogen containing heterocycles

The alkynyl- β -lactams by direct bisheterocyclization afforded optically pure tricyclic bridged acetals containing a 2-azetidinone nucleus with regiocontrolled Au/Bronsted acid co-catalyst [266, 267]. The desired ketal was produced when terminal alkyne was treated with gold(III) chloride/*p*-toluenesulfonic acid catalytic system. A polar ketone was formed in appreciable amounts from hydration of alkyne. Better activity was displayed by [AuClPPh₃]/silver trifluoromethanesulfonate/*p*-toluenesulfonic acid system. In contrast, the reaction of terminal alkynyl dioxolane with precious metal/acid co-catalyst furnished 6,8-dioxabicyclo[3.2.1]octane derivative as sole products (Scheme 68) by initial attack of the oxygen atom on the external alkyne carbon through an exclusive 7-*endo*/5-*exo* bis-oxycyclization. Competition between the 7-*endo* and 6-*exo* oxycyclizations favored the former, despite that this was more demanding energetically [268].

Furan analogues were generated by an intramolecular addition of -OH group to a C-C triple bond. The cyclization of monoallylic diols with Au(I) catalyst is an efficient protocol for the synthesis of tetrahydropyran analogs (Scheme 69) [183, 269, 270].

A reaction was reported with internal alkynes. The six-membered 1,3-oxazine heterocyclic compounds were produced by a preferable 6-*endo-dig* cyclization. Good yields of vinylgold species were obtained by deprotonation of intermediate with base and *N*-heterocyclic carbene ligand (Scheme 70). The reactions were unsuccessful with phosphane ligand [271, 272]. These intermediates acted as catalysts also in the presence of acid [273].

Bioactive fused heterocycles were synthesized in this protocol. The pyrido/pyrrolo[2,1-*b*]benzo[*d*] [1, 3] oxazin-1-ones [274] (Scheme 71), pyrido/pyrrolo[2,1-*a*] [1, 3] benzoxazinones [275] (Scheme 72), and benzo[*e*]indolo[1,2-*a*]pyrrolo[2,1-*c*] [1, 4] diazepine-3,9-diones (Scheme 73) were generated efficiently by cycloisomerization in the presence of [Au{P(*t*-Bu)₂(*o*-biphenyl)}{CH₃CN}]SbF₆ catalyst. An intramolecular cycloaddition occurred with enol lactone intermediate [276]. The desired products were produced from intermediate by subsequent intermolecular hydroamination and cyclization. The tricyclic lactam was synthesized efficiently in a straightforward one-pot pathway in which various carbon-carbon and carbon-nitrogen bonds were formed from simple starting substrates [183, 277].

Mixtures of 3,6-dihydro-1,2-oxazines and 4,5-dihydroisoxazoles were obtained from allenic hydroxylamine ethers having exchanged positions of the hetero atoms. The cationic Au(I) complexes Ph₃PAuBF₄ shifted the regioselectivity in favor of isoxazoles (Scheme 74) [278, 279].

Scheme 70

Scheme 71

Scheme 72

In contrast to this, the *N*-Boc-protected hydroxylamine ethers were treated with $\text{Au}(\text{I})$ chloride to afford oxazines via a 6-*endo*-cyclization. This process was versatile because same-hydroxyallenes underwent Mitsunobu reaction to synthesize allenic hydroxylamine ethers precursors for the

preparation of heterocyclic compounds stereoselectively [280, 281].

Shin and co-workers [282] reported that in intramolecular hydroamination of alkynes and imine derivatives the homopropargylic trichloroacetimidates rapidly underwent

Scheme 73

Scheme 74

Scheme 75

6-*exo-trig* cyclizations under mild conditions (0 °C) in the presence of $\text{Ph}_3\text{PAuBF}_4$. They successfully employed

both internal and terminal alkynes, and *anti*-addition product was formed exclusively in all cases (Scheme 75).

Scheme 76

Scheme 77

Trichloroacetimidates were obtained from homopropargyl and propargyl alcohols which underwent intramolecular hydroamination of trichloroacetimidates with Au(I) catalyst [283]. Several trichloroacetimidates underwent an efficient hydroamination under mild condition in the presence of cationic gold(I) complex (2–5 mol%). An orthogonality of the Au-catalyzed protocol has been reported with stoichiometric electrophile (Scheme 75) [164, 216].

Dixon and co-workers [284] reacted alkynoic acids with primary amines by Au(I)-catalyzed cascade. Good yields of multi-ring heterocyclic compounds were afforded. The alkynoic acids provided enol lactone intermediates, which produced *N*-acyl iminium intermediates subsequently upon reacting with primary amines. The multi-ring heterocyclic compounds were formed when tethered electron rich heterocyclic products attacked the iminium. Suitable candidates for additions were internal and terminal alkynes. Control experiments employing a HOTf and/or phosphorine base (BEMP) have confirmed that a Lewis acid assisted Bronsted acid is the active catalyst for the final two steps in the sequence (Scheme 76) [216].

Kimber [285] synthesized α -vinyl-substituted tetrahydro isoquinolines by intramolecular hydroarylation of allenamides in the presence of gold(I) catalyst (Scheme 77). The hydroarylation was impeded when R=Boc due to its steric hindrance [286].

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

- Balaban AT, Oniciu DC, Katritzky AR (2004) Aromaticity as a cornerstone in heterocyclic chemistry. *Chem Rev* 104:2777–2812
- Martins MAP, Cunico W, Pereira CMP, Flores AFC, Bonacorso HG, Zanatta N (2004) 4-Alkoxy-1, 1, 1-trichloro-3-alken-2-ones: preparation and applications in heterocyclic synthesis. *Curr Org Synth* 1:391–403
- Majumdar P, Pati A, Patra M, Behera RK, Behera AK (2014) Acid hydrazides, potent reagents for synthesis of oxygen-, nitrogen-, and/or sulfur-containing heterocyclic rings. *Chem Rev* 114:2942–2977
- Xiong Y, Schaus SE, Porco JA (2013) Metal-catalyzed cascade rearrangements of 3-alkynyl flavone ethers. *Org Lett* 15:1962–1965
- Kaur N (2015) Palladium-catalyzed approach to the synthesis of 5-heterocycles. *Catal Rev* 57:478–564
- Kaur N, Verma Y, Grewal P, Bhardwaj P, Devi M (2019) Application of titanium catalysts for the syntheses of heterocycles. *Synth Commun* 49:1847–1894
- Kaur N (2019) Ionic liquid: an efficient and recyclable medium for the synthesis of fused six-membered oxygen heterocycles. *Synth Commun* 49:1679–1707
- Kaur N (2019) Multiple nitrogen-containing heterocycles: metal and non-metal assisted synthesis. *Synth Commun* 49:1633–1658
- Kaur N, Grewal P, Bhardwaj P, Devi M, Verma Y (2019) Nickel-catalyzed synthesis of five-membered heterocycles. *Synth Commun* 49:1543–1577

10. Kaur N (2019) Gold and silver assisted synthesis of five-membered oxygen and nitrogen containing heterocycles. *Synth Commun* 49:1459–1485
11. Kaur N (2018) Synthesis of six- and seven-membered and larger heterocycles using Au and Ag catalysts. *Inorg Nano Metal Chem* 48:541–568
12. Domling A (2006) Recent developments in isocyanide based multi-component reactions in applied chemistry. *Chem Rev* 106:17–89
13. Kaur N (2019) Applications of palladium dibenzylideneacetone as catalyst in the synthesis of five-membered *N*-heterocycles. *Synth Commun* 49:1205–1230
14. Kaur N (2019) Copper catalyzed synthesis of seven and higher-membered heterocycles. *Synth Commun* 49:879–916
15. Kaur N (2019) Ionic liquid assisted synthesis of *S*-heterocycles. *Phosphorus Sulfur Silicon Relat Elem* 194:165–185
16. Kaur N (2019) Nickel catalysis: six membered heterocycle syntheses. *Synth Commun* 49:1103–1133
17. Kaur N (2019) Seven-membered *N*-heterocycles: metal and non-metal assisted synthesis. *Synth Commun* 49:987–1030
18. Kaur N, Bhardwaj P, Devi M, Verma Y, Grewal P (2019) Synthesis of five-membered *O*, *N*-heterocycles using metal and non-metal. *Synth Commun* 49:1345–1384
19. Kaur N (2019) Synthetic routes to seven and higher membered *S*-heterocycles by use of metal and nonmetal catalyzed reactions. *Phosphorus Sulfur Silicon Relat Elem* 194:186–209
20. Kaur N (2019) Synthesis of six-membered *N*-heterocycles using ruthenium catalysts. *Catal Lett* 14:1513–1539
21. Kaur N (2015) Benign approaches for the microwave-assisted synthesis of five-membered 1,2-*N,N*-heterocycles. *J Heterocycl Chem* 52:953–973
22. Kaur N (2017) Methods for metal and non-metal catalyzed synthesis of six-membered oxygen containing poly-heterocycles. *Curr Org Synth* 14:531–556
23. Kaur N (2017) Photochemical reactions: synthesis of six-membered *N*-heterocycles. *Curr Org Synth* 14:972–998
24. Kaur N (2017) Ionic liquids: promising but challenging solvents for the synthesis of *N*-heterocycles. *Mini Rev Org Chem* 14:3–23
25. Kaur N (2016) Metal catalysts for the formation of six-membered *N*-polyheterocycles. *Synth React Inorg Met Org Nano Met Chem* 46:983–1020
26. Kaur N (2017) Applications of gold catalysts for the synthesis of five-membered *O*-heterocycles. *Inorg Nano Met Chem* 47:163–187
27. Orru RVA, de Greef M (2003) Recent advances in solution-phase multi-component methodology for the synthesis of heterocyclic compounds. *Synthesis* 10:1471–1499
28. Reddy CR, Ranjan R, Kumaraswamy P, Motati DR, Grée R (2014) 1-Aryl propargylic alcohols as handy synthons for the construction of heterocycles and carbocycles. *Curr Org Chem* 18:2603–2645
29. Kaur N (2014) Palladium-catalyzed approach to the synthesis of five-membered *O*-heterocycles. *Inorg Chem Commun* 49:86–119
30. Kaur N, Kishore D (2014) Nitrogen-containing six-membered heterocycles: solid-phase synthesis. *Synth Commun* 44:1173–1211
31. Kaur N, Kishore D (2014) Solid-phase synthetic approach toward the synthesis of oxygen containing heterocycles. *Synth Commun* 44:1019–1042
32. Kaur N (2014) Microwave-assisted synthesis of five membered *O*-heterocycles. *Synth Commun* 44:3483–3508
33. Kaur N (2014) Microwave-assisted synthesis of five membered *O,N*-heterocycles. *Synth Commun* 44:3509–3537
34. Kaur N (2014) Microwave-assisted synthesis of five membered *O,N,N*-heterocycles. *Synth Commun* 44:3229–3247
35. Kaur N (2018) Synthesis of six and seven-membered heterocycles under ultrasound irradiation. *Synth Commun* 48:1235–1258
36. Kaur N (2018) Photochemical reactions as key steps in five-membered *N*-heterocycles synthesis. *Synth Commun* 48:1259–1284
37. Kaur N (2018) Solid-phase synthesis of sulfur containing heterocycles. *J Sulfur Chem* 39:544–577
38. Uredi D, Motati DR, Watkins EB (2018) A unified strategy for the synthesis of β -carbolines, γ -carbolines, and other fused. Azaheteroaromatics under mild, metal-free conditions. *Org Lett* 20:6336–6339
39. Kaur N (2015) Metal catalysts: applications in higher membered *N*-heterocycles synthesis. *J Iran Chem Soc* 12:9–45
40. Kaur N (2015) Insight into microwave-assisted synthesis of benzo derivatives of five membered *N,N*-heterocycles. *Synth Commun* 45:1269–1300
41. Kaur N (2015) Synthesis of fused five-membered *N,N*-heterocycles using microwave irradiation. *Synth Commun* 45:1379–1410
42. Kaur N (2014) Microwave-assisted synthesis of seven membered *S*-heterocycles. *Synth Commun* 44:3201–3228
43. Kaur N (2015) Six membered *N*-heterocycles: microwave-assisted synthesis. *Synth Commun* 45:1–34
44. Kaur N (2015) Polycyclic six membered *N*-heterocycles: microwave-assisted synthesis. *Synth Commun* 45:35–69
45. Kaur N (2018) Copper catalysts in the synthesis of five-membered *N*-polyheterocycles. *Curr Org Synth* 15:940–971
46. Kaur N (2018) Recent developments in the synthesis of nitrogen containing five-membered polyheterocycles using rhodium catalysts. *Synth Commun* 48:2457–2474
47. Kaur N (2015) Microwave-assisted synthesis: fused five membered *N*-heterocycles. *Synth Commun* 45:789–823
48. Kaur N (2015) Six membered heterocycles with three and four *N*-heteroatoms: microwave-assisted synthesis. *Synth Commun* 45:151–172
49. Kaur N (2015) Application of microwave-assisted synthesis in the synthesis of fused six-membered heterocycles with *N*-heteroatom. *Synth Commun* 45:173–201
50. Kaur N (2015) Microwave-assisted synthesis of fused polycyclic six membered *N*-heterocycles. *Synth Commun* 45:273–299
51. Kaur N (2015) Review of microwave-assisted synthesis of benzo fused six-membered *N,N*-heterocycles. *Synth Commun* 45:300–330
52. Kaur N, Kishore D (2014) Synthetic strategies applicable in the synthesis of privileged scaffold: 1,4-benzodiazepine. *Synth Commun* 44:1375–1413
53. Kaur N (2015) Environmentally benign synthesis of five membered 1,3-*N,N*-heterocycles by microwave irradiation. *Synth Commun* 45:909–943
54. Kaur N (2015) Advances in microwave-assisted synthesis for five membered *N*-heterocycles synthesis. *Synth Commun* 45:432–457
55. Kaur N (2014) Microwave-assisted synthesis of five membered *S*-heterocycles. *J Iran Chem Soc* 11:523–564
56. Kaur N (2015) Review on the synthesis of six membered *N,N*-heterocycles by microwave irradiation. *Synth Commun* 45:1145–1182
57. Kaur N (2015) Greener and expeditious synthesis of fused six-membered *N,N*-heterocycles using microwave irradiation. *Synth Commun* 45:1493–1519
58. Kaur N (2015) Applications of microwaves in the synthesis of polycyclic six membered *N,N*-heterocycles. *Synth Commun* 45:1599–1631

59. Kaur N (2015) Synthesis of five-membered *N,N,N*- and *N,N,N,N*-heterocyclic compounds: applications of microwaves. *Synth Commun* 45:1711–1742
60. Kaur N (2018) Ruthenium catalysis in six-membered *O*-heterocycles synthesis. *Synth Commun* 48:1551–1587
61. Kaur N (2018) Green synthesis of three to five-membered *O*-heterocycles using ionic liquids. *Synth Commun* 48:1588–1613
62. Kaur N (2018) Ultrasound-assisted green synthesis of five-membered *O*- and *S*-heterocycles. *Synth Commun* 48:1715–1738
63. Kaur N (2018) Photochemical mediated reactions in five-membered *O*-heterocycles synthesis. *Synth Commun* 48:2119–2149
64. Kaur N (2018) Mercury-catalyzed synthesis of heterocycles. *Synth Commun* 48:2715–2749
65. Kaur N (2018) Photochemical irradiation: seven and higher membered *O*-heterocycles. *Synth Commun* 48:2935–2964
66. Kaur N (2018) Synthesis of seven and higher membered nitrogen containing heterocycles using photochemical irradiation. *Synth Commun* 48:2815–2849
67. Kaur N (2018) Ruthenium catalyzed synthesis of five-membered *O*-heterocycles. *Inorg Chem Commun* 99:82–107
68. Patil NT, Yamamoto Y (2008) Coinage metal-assisted synthesis of heterocycles. *Chem Rev* 108:3395–3442
69. Kaur N (2015) Role of microwaves in the synthesis of fused five membered heterocycles with three *N*-heteroatoms. *Synth Commun* 45:403–431
70. Kaur N (2015) Recent impact of microwave-assisted synthesis on benzo derivatives of five membered *N*-heterocycles. *Synth Commun* 45:539–568
71. Kaur N, Kishore D (2014) Microwave-assisted synthesis of seven and higher membered *N*-heterocycles. *Synth Commun* 44:2577–2614
72. Kaur N, Kishore D (2014) Microwave-assisted synthesis of six-membered *S*-heterocycles. *Synth Commun* 44:2615–2644
73. Kaur N, Kishore D (2014) Microwave-assisted synthesis of seven and higher membered *O*-heterocycles. *Synth Commun* 44:2739–2755
74. Kaur N (2019) Palladium acetate and phosphine assisted synthesis of five-membered *N*-heterocycles. *Synth Commun* 49:483–514
75. Kaur N (2019) Application of silver-promoted reactions in the synthesis of five-membered *O*-heterocycles. *Synth Commun* 49:743–789
76. Kaur N (2019) Synthesis of seven and higher-membered heterocycles using ruthenium catalysts. *Synth Commun* 49:617–661
77. Alberico D, Scott ME, Lautens M (2007) Aryl bond formation by transition-metal-catalyzed direct arylation. *Chem Rev* 107:174–238
78. Kaur N (2017) Gold catalysts in the synthesis of five-membered *N*-heterocycles. *Curr Organocatal* 4:122–154
79. Dick AR, Sanford MS (2006) Transition metal catalyzed oxidative functionalization of carbon-hydrogen bonds. *Tetrahedron* 62:2439–2463
80. Kaur N (2015) Palladium catalysts: synthesis of five-membered *N*-heterocycles fused with other heterocycles. *Catal Rev* 57:1–78
81. Kaur N, Kishore D (2014) Microwave-assisted synthesis of six membered *O,O*-heterocycles. *Synth Commun* 44:3082–3111
82. Kaur N, Kishore D (2014) Microwave-assisted synthesis of six membered *O*-heterocycles. *Synth Commun* 44:3047–3081
83. Kaur N, Tyagi R, Kishore D (2014) Expedient protocols for the installation of 1,5-benzazepine based privileged templates on 2-position of α , β -enone incorporated derivatives of the 1,4-benzodiazepine nucleus linked through a phenoxy spacer. *J Heterocycl Chem* 51:E340–E343
84. Kaur N, Kishore D (2014) Synthesis of 2-(oxadiazolo, pyrimido, imidazolo, and benzimidazolo) substituted analogues of 1,4-benzodiazepin-5-carboxamides linked through a phenoxy bridge. *J Chem Sci* 126:1861–1867
85. Kaur N, Kishore D (2014) Synthesis of oxadiazolo, pyrimido, imidazolo and benzimidazolo containing derivatives of 1,4-benzodiazepin-5-(4'-methylpiperazinyl)-carboxamide through phenylamino spacer. *Synth Commun* 44:2789–2796
86. Kaur N, Kishore D (2013) Application of chalcones in heterocycles synthesis: synthesis of 2-(isoxazolo, pyrazolo and pyrimido) substituted analogues of 1,4-benzodiazepin-5-carboxamides linked through an oxyphenyl bridge. *J Chem Sci* 125:555–560
87. Zeni G, Larock RC (2006) Synthesis of heterocycles via palladium-catalyzed oxidative addition. *Chem Rev* 106:4644–4680
88. Jimenez-Gonzalez L, Garcia-Munoz S, Alvarez-Corral M, Munoz-Dorado M, Rodriguez-Garcia I (2006) Silver-catalyzed asymmetric synthesis of 2,3-dihydrobenzofurans: a new chiral synthesis of pterocarpans. *Chem Eur J* 12:8762–8779
89. Kaur N, Bhardwaj P, Devi M, Verma Y, Grewal P (2019) Photochemical reactions in five and six-membered polyheterocycles synthesis. *Synth Commun* 49:2281–2318
90. Li Z, He C (2006) Recent advances in silver-catalyzed nitrene, carbene, and silylene-transfer reactions. *Eur J Org Chem* 2006:4313–4322
91. Sherry BD, Maus L, Laforteza BN, Toste FD (2006) Gold(I)-catalyzed synthesis of dihydropyrans. *J Am Chem Soc* 128:8132–8133
92. Ney J, Wolfe JP (2005) Selective synthesis of 5- or 6-aryl octahydrocyclopenta[b]pyrroles from a common precursor through control of competing pathways in a Pd-catalyzed reaction. *J Am Chem Soc* 127:8644–8651
93. Li Z, Zhang J, Brouwer C, Yang C-G, Reich NW, He C (2006) Brønsted acid catalyzed addition of phenols, carboxylic acids, and tosylamides to simple olefins. *Org Lett* 8:4175–4178
94. Mori M, Sakakibara N, Kinoshita A (1998) Remarkable effect of ethylene gas in the intramolecular enyne metathesis of terminal alkynes. *J Org Chem* 63:6082–6083
95. Li Y, Zhou F, Forsyth CJ (2007) Gold(I)-catalyzed bis-spiroketalization: synthesis of the trioxadispiroketal-containing A–D rings of azaspiracid. *Angew Chem Int Ed* 46:279–282
96. McMahon I, Silke J (1996) Winter toxicity of unknown aetiology in mussels. *Harmful Algae News* 14:2
97. Ito E, Satake M, Ofuji N, Kurita N, McMahon T, James K, Yasumoto T (2000) Multiple organ damage caused by a new toxin azaspiracid, isolated from mussels produced in Ireland. *Toxicon* 38:917–930
98. Satake M, Ofuji K, Naoki H, James KJ, Furey A, McMahon T, Silke J, Yasumoto T (1998) Azaspiracid, a new marine toxin having unique spiro ring assemblies, isolated from Irish mussels, *Mytilus edulis*. *J Am Chem Soc* 120:9967–9968
99. Nicolau KC, Kotifs TV, Vyskocil S, Petrovic G, Ling T, Yamamda YMA, Tang W, Frederick MO (2004) Structural revision and total synthesis of azaspiracid-1, part 2: definition of the ABCD domain and total synthesis. *Angew Chem Int Ed* 43:4318–4324
100. Inoki S, Mukaiyama TA (1990) Convenient method for the stereoselective preparation of trans-(2-hydroxymethyl)tetrahydrofurans by the oxidative cyclization of 5-hydroxy-1-alkenes with molecular oxygen catalyzed by cobalt(II) complex. *Chem Lett* 1:67–70
101. Inoue Y, Itoh Y, Kazama H (1980) Reaction of dialkyl-substituted alkynes with carbon dioxide catalyzed by nickel(0) complexes. Incorporation of carbon dioxide in alkyne dimers and novel cyclotrimerization of the alkynes. *Bull Chem Soc Jpn* 53:3329–3333
102. Gaunt MJ, Spencer JB (2001) Derailing the Wacker oxidation: development of a palladium-catalyzed amidation reaction. *Org Lett* 3:25–28

103. Gockel B, Krause N (2006) Golden times for allenes: gold-catalyzed cycloisomerization of β -hydroxyallenes to dihydropyrans. *Org Lett* 8:4485–4488
104. Jung HH, Floreancig PE (2006) Gold-catalyzed heterocycle synthesis using homopropargylic ethers as latent electrophiles. *Org Lett* 8:1949–1951
105. Jung HH, Floreancig PE (2007) Gold-catalyzed synthesis of oxygen- and nitrogen-containing heterocycles from alkynyl ethers: application to the total synthesis of andrachcinidine. *J Org Chem* 72:7359–7366
106. Yang C-G, He C (2005) Gold(I)-catalyzed intermolecular addition of phenols and carboxylic acids to olefins. *J Am Chem Soc* 127:6966–6967
107. Hegedus LS, Allen GF, Bozell JJ, Waterman EL (1978) Palladium-assisted intramolecular amination of olefins. Synthesis of nitrogen heterocycles. *J Am Chem Soc* 100:5800–5807
108. Pugin B, Venanti LM (1981) Palladium-promoted cyclization reactions of aminoalkenes. *J Organomet Chem* 214:125–133
109. Hegedus LS, McKearin J (1982) Palladium-catalyzed cyclization of omega-olefinic tosamides. Synthesis of nonaromatic nitrogen heterocycles. *J Am Chem Soc* 104:2444–2451
110. Pugin B, Venanti LM (1983) Palladium-catalyzed oxidation of amino alkenes to cyclic imines or enamines and amino ketones. *J Am Chem Soc* 105:6877–6881
111. Du XW, Song FJ, Lu YH, Chen HY, Liu YH (2009) A general and efficient synthesis of substituted furans and dihydrofurans via gold-catalyzed cyclization of (Z)-2-en-4-yn-1-ols. *Tetrahedron* 65:1839–1845
112. Tsuda T, Morikawa S, Hasegawa N, Saegusa T (1990) Nickel(0)-catalyzed cycloaddition of silyl diynes with carbon dioxide to silyl bicyclic alpha-pyrone. *J Org Chem* 55:2978–2981
113. Louie J, Gibby JE, Farnworth MV, Tekavec TN (2002) Efficient nickel catalyzed [2 + 2 + 2] cycloaddition of CO₂ and diynes. *J Am Chem Soc* 124:15188–15189
114. Van Orden LJ, Patterson BD, Rychnovsky SD (2007) Total synthesis of leucascandrolide A: a new application of the Mukaiyama Aldol–Prins reaction. *J Org Chem* 72:5784–5793
115. Volz F, Krause N (2007) Golden opportunities in natural product synthesis: first total synthesis of (–)-isocyclocapitelline and (–)-isochrysotricine by gold-catalyzed allene cycloisomerization. *Org Biomol Chem* 5:1519–1521
116. Volz F, Wadman SH, Hoffmann-Roder A, Krause N (2009) Gold catalysis in stereoselective natural product synthesis: (+)-lin-alool oxide, (–)-isocyclocapitelline, and (–)-isochrysotricine. *Tetrahedron* 65:1902–1910
117. Miura T, Shimada M, De Mendoza P, Deutsch C, Krause N, Murakami M (2009) Stereoselective synthesis of *syn*-configured α -allenols by rhodium-catalyzed reaction of alkynyl oxiranes with arylboronic acids. *J Org Chem* 74:6050–6054
118. Sawama Y, Sawama Y, Krause N (2008) First total synthesis of (R,R,R)- and (3R,5S,9R)-bejarol by gold-catalyzed allene cycloisomerization and determination of absolute configuration of the natural product. *Org Biomol Chem* 6:3573–3579
119. Steinborn D, Gerisch M, Heinemann FW, Scholz J, Schenzel KZ (1995) Structure and constitution of dichloro(tetraalkyl cyclobutadiene)platinum(II) complexes. *Allg Anorg Chem* 621:1421–1425
120. Diver ST, Giessert AJ (2004) Enyne metathesis (enyne bond reorganization). *Chem Rev* 104:1317–1382
121. Aponick A, Li C-Y, Palmes JA (2009) Au-catalyzed cyclization of monopropargylic triols: an expedient synthesis of monounsaturated spiroketals. *Org Lett* 11:121–124
122. Zhang Y, Xue JJ, Xin ZJ, Xie ZX, Li Y (2008) Gold-catalyzed double intramolecular alkyne hydroalkoxylation: synthesis of the bisbenzannulated spiroketal core of rubromycins. *Synlett* 6:0940–0944
123. Belting V, Krause N (2009) Gold-catalyzed cycloisomerization of alk-4-yn-1-ones. *Org Biomol Chem* 7:1221–1225
124. Zhang G, Cui L, Wang Y, Zhang L (2010) Homogeneous gold-catalyzed oxidative carboheterofunctionalization of alkenes. *J Am Chem Soc* 132:1474–1475
125. Deutsch C, Gockel B, Hoffmann-Roder A, Krause N (2007) Golden opportunities in stereoselective catalysis: optimization of chirality transfer and catalyst efficiency in the gold-catalyzed cycloisomerization of α -hydroxyallenes to 2,5-dihydrofurans. *Synlett* 11:1790–1794
126. Krause N, Belting V, Deutsch C, Erdsack J, Fan H-T, Gockel B, Hoffmann-Roder A, Morita N, Volz F (2008) Golden opportunities in catalysis. *Pure Appl Chem* 80:1063–1069
127. Zimmer R, Dinesh CU, Nandan E, Khan FA (2000) Palladium-catalyzed reactions of allenes. *Chem Rev* 100:3067–3126
128. Marshall JA (2000) Synthesis and reactions of allylic, allenic, vinylic, and arylmetal reagents from halides and esters via transient organopalladium intermediates. *Chem Rev* 100:3163–3186
129. Krause N, Hoffmann-Roder A (2004) Synthesis of allenes with organometallic reagents. *Tetrahedron* 60:11671–11694
130. Ma S (2005) Some typical advances in the synthetic applications of allenes. *Chem Rev* 105:2829–2872
131. Nishina N, Yamamoto Y (2006) Gold catalyzed intermolecular hydroamination of allenes with arylamines and resulting high chirality transfer. *Angew Chem* 118:3392–3395
132. Nishina N, Yamamoto Y (2006) Gold catalyzed intermolecular hydroamination of allenes with arylamines and resulting high chirality transfer. *Angew Chem Int Ed* 45:3314–3317
133. Patil NT, Lutete LM, Nishina N, Yamamoto Y (2006) Gold-catalyzed intramolecular hydroamination of allenes: a case of chirality transfer. *Tetrahedron Lett* 47:4749–4751
134. Zhang Z, Liu C, Kinder RE, Han X, Qian H, Widenhoefer RA (2006) Highly active Au(I) catalyst for the intramolecular *exo*-hydrofunctionalization of allenes with carbon, nitrogen, and oxygen nucleophiles. *J Am Chem Soc* 128:9066–9073
135. Zhang Z, Widenhoefer RA (2007) Gold(I) catalyzed intramolecular enantioselective hydroalkoxylation of allenes. *Angew Chem* 119:287–289
136. Zhang Z, Widenhoefer RA (2007) Gold(I)-catalyzed intramolecular enantioselective hydroalkoxylation of allenes. *Angew Chem Int Ed* 46:283–285
137. LaLonde RL, Sherry BD, Kang EJ, Toste FD (2007) Gold(I) catalyzed enantioselective intramolecular hydroamination of allenes. *J Am Chem Soc* 129:2452–2453
138. Trost BM (1995) Atomökonomische synthesen—eine herausforderung in der organischen chemie: die homogenkatalyse als wegweisende methode. *Angew Chem* 107:285–307
139. Trost BM (1995) Atom economy: a challenge for organic synthesis—homogeneous catalysis leads the way. *Angew Chem Int Ed* 34:259–281
140. Seiche W, Schuschkowski A, Breit B (2005) Bidentate ligands by self-assembly through hydrogen bonding: a general room temperature/ambient pressure regioselective hydroformylation of terminal alkenes. *Adv Synth Catal* 347:1488–1494
141. Murai M, Uenishi J, Uemura M (2010) Gold(I)-catalyzed asymmetric synthesis of planar chiral arene chromium complexes. *Org Lett* 12:4788–4791
142. Ballini R, Petrini M (2008) Nitroalkanes as key building blocks for the synthesis of heterocyclic derivatives. *ARKIVOC* 9:195–223
143. Lopez-Herrera FJ, Sarabia-Garcia F (1997) Condensation of *D*-mannosaldehyde derivatives with ethyl diazoacetate. An easy and stereoselective chain elongation methodology for carbohydrates: application to new syntheses for KDO and 2-deoxy- β -KDO. *Tetrahedron* 53:3325–3346

144. Weibel J-M, Blanc A, Pale P (2008) Ag-mediated reactions: coupling and heterocyclization reactions. *Chem Rev* 108:3149–3173
145. Perron F, Albizzati KF (1989) Chemistry of spiroketals. *Chem Rev* 89:1617–1661
146. Aho JE, Pihko PM, Rissa TK (2005) Nanometric spiroketals in natural products: structures, sources, and synthetic strategies. *Chem Rev* 105:4406–4440
147. Rama Raju B, Saikia AK (2008) Asymmetric synthesis of naturally occurring spiroketals. *Molecules* 13:1942–2038
148. Blunt JW, Copp BR, Hu WP, Munro MHG, Northcote PT, Prinsep MR (2009) Marine natural products. *Nat Prod Rep* 26:170–244
149. Brimble MA, Bryant CJ (2006) Synthesis of the spiroketal-containing anti-helicobacter pylori agents. *Chem Commun* 43:4506–4508
150. Izquierdo-Cubero I, Plaza Lopez-Espinosa MT, Kari N (1994) Synthesis of optically active chalcogran from L-sorbose. *Carbohydr Res* 261:231–242
151. Antoniotti S, Genin E, Michelet V, Genet J-P (2005) Highly efficient access to strained bicyclic ketals via gold-catalyzed cycloisomerization of bis-homopropargylic diols. *J Am Chem Soc* 127:9976–9977
152. Liu L-P, Hammond GB (2009) Highly efficient and tunable synthesis of dioxabicyclo[4.2.1] ketals and tetrahydropyrans via gold-catalyzed cycloisomerization of 2-alkynyl-1,5-diols. *Org Lett* 11:5090–5092
153. Liu B, De Brabander JK (2006) Metal-catalyzed regioselective oxy-functionalization of internal alkynes: an entry into ketones, acetals, and spiroketals. *Org Lett* 8:4907–4910
154. Hashmi ASK, Buhrlé M, Wolfe M, Rudolph M, Wietek M, Rominger F, Frey W (2010) Gold catalysis: tandem reactions of diyne-diols and external nucleophiles as an easy access to tricyclic cage-like structures. *Chem Eur J* 16:9846–9854
155. Brockmann H, Lenk W, Schwantje G, Zeek A (1966) Robromycins. *Tetrahedron Lett* 7:3525–3530
156. Goldman ME, Salituro GS, Bowen JA, Williamson JM, Zink L, Scleif WA, Emini EA (1990) Inhibition of human immunodeficiency virus-1 reverse transcriptase activity by robromycins: competitive interaction at the template primer site. *Mol Pharmacol* 38:20–28
157. Trani A, Dallanoce C, Pranzoni G, Ripamonti F, Goldstein BP, Cibiatti R (1997) Semisynthetic derivatives of purpurumycin as potential topical agents for vaginal infections. *J Med Chem* 40:967–971
158. Chino M, Nishikawa K, Umekia M, Hayashi C, Yamazaki T, Tsuchida T, Sawa T, Hamada M, Takeuchi T (1996) Heliquinomycin, a new inhibitor of DNA helicase, produced by streptomyces sp. MJ929-SF2. Taxonomy, production, isolation, physicochemical properties and biological activities. *J Antibiot* 49:752–757
159. Alcaide B, Almendros P, Alonso JM (2011) Gold-catalyzed cyclizations of alkynol-based compounds: synthesis of natural products and derivatives. *Molecules* 16:7815–7843
160. Dai L-Z, Shi M (2009) Gold(I) catalysis: selective synthesis of six- or seven-membered heterocycles from epoxy alkynes. *Eur J Org Chem* 19:3129–3133
161. Rhee JU, Krische MJ (2005) Alkynes as synthetic equivalents to stabilized Wittig reagents: intra- and intermolecular carbonyl olefinations catalyzed by Ag(I), BF₃, and HBF₄. *Org Lett* 7:2493–2495
162. Obika S, Kono H, Yasui Y, Yanada R, Takemoto Y (2007) Concise synthesis of 1,2-dihydroisoquinolines and 1H-isochromenes by carbophilic Lewis acid-catalyzed tandem nucleophilic addition and cyclization of 2-(1-alkynyl)arylaldimines and 2-(1-alkynyl) arylaldehydes. *J Org Chem* 72:4462–4468
163. Kleinbeck F, Toste FD (2009) Gold(I)-catalyzed enantioselective ring expansion of allenylcyclopropanols. *J Am Chem Soc* 131:9178–9179
164. Arcadi A (2008) Alternative synthetic methods through new developments in catalysis by gold. *Chem Rev* 108:3266–3325
165. Wang Y, Kuzniewski CN, Rauniyar V, Hoong C, Toste FD (2011) Chiral (acyclic diaminocarbene)gold(I)-catalyzed dynamic kinetic asymmetric transformation of propargyl esters. *J Am Chem Soc* 133:12972–12975
166. Shiroodi RK, Gevorgyan V (2013) Metal-catalyzed double migratory cascade reactions of propargylic esters and phosphates. *Chem Soc Rev* 42:4991–5001
167. Uemura M, Watson IDG, Katsukawa M, Toste FD (2009) Gold(I)-catalyzed enantioselective synthesis of benzopyrans via rearrangement of allylic oxonium intermediates. *J Am Chem Soc* 131:3464–3465
168. Arcadi A, Abbiati G, Rossi E (2011) Tandem imination/annulation of γ - and δ -ketoalkynes in the presence of ammonia/amines. *J Organomet Chem* 696:87–98
169. Dell'Acqua M, Facoetti D, Abbiati G, Rossi E (2010) Selective base-promoted synthesis of dihydroisobenzofurans by domino addition/annulation reactions of *ortho*-alkynylbenzaldehydes. *Synthesis* 41:2367–2378
170. Zhang L, Kozmin SA (2005) Gold-catalyzed assembly of heterobicyclic systems. *J Am Chem Soc* 127:6962–6963
171. Zhang L, Sun J, Kozmin SA (2006) Gold and platinum catalysis of enyne cycloisomerization. *Adv Synth Catal* 348:2271–2296
172. Hashmi ASK, Schafer S, Wolfe M, Diez Gil C, Fischer P, Laguna A, Blanco MC, Gimeno MC (2007) Gold-catalyzed benzylic C–H activation at room temperature. *Angew Chem Int Ed* 46:6184–6187
173. Watanabe T, Oishi S, Fujii N, Ohno H (2007) Gold-catalyzed hydroarylation of allenes: a highly regioselective carbon–carbon bond formation producing six-membered rings. *Org Lett* 9:4821–4824
174. Bandini M, Gualandi A, Monari M, Romaniello A, Savoia D, Tragni M (2011) Allylic alcohols: valuable synthetic equivalents of non-activated alkenes in gold-catalyzed enantioselective alkylation of indoles. *J Organomet Chem* 696:338–347
175. Chao CM, Beltrami D, Toullec PY, Michelet V (2009) Asymmetric Au(I)-catalyzed synthesis of bicyclo[4.1.0]heptene derivatives via a cycloisomerization process of 1,6-enynes. *Chem Commun* 45:6988–6990
176. Das A, Sohle SMA, Liu R-S (2010) Carbo- and heterocyclization of oxygen- and nitrogen-containing electrophiles by platinum, gold, silver and copper species. *Org Biomol Chem* 8:960–979
177. Sethofer SG, Mayer T, Toste FD (2010) Gold(I)-catalyzed enantioselective polycyclization reactions. *J Am Chem Soc* 132:8276–8277
178. Lin C-C, Teng T-M, Tsai C-C, Liao H-Y, Liu R-S (2008) Gold-catalyzed deoxygenative nazarov cyclization of 2,4-dien-1-als for stereoselective synthesis of highly substituted cyclopentenones. *J Am Chem Soc* 130:16417–16423
179. Lian J-J, Chen P-C, Lin Y-P, Ting H-C, Liu R-S (2006) Gold catalyzed intramolecular [3 + 2]-cycloaddition of arenyne-yne functionalities. *J Am Chem Soc* 128:11372–11373
180. Gronnier C, Odabachian Y, Gagosz F (2011) Gold(I)-catalyzed formation of dihydroquinolines and indoles from *N*-aminophenyl propargyl malonates. *Chem Commun* 47:218–220
181. Park C, Lee PH (2008) Indium-mediated regio- and chemoselective synthesis of α -hydroxyalkyl allenic esters and gold-catalyzed cyclizations to ethyl 2-naphthoate derivatives. *Org Lett* 10:3359–3362
182. Hashmi ASK, Rudolph M, Huck J, Frey W, Bats JW, Hamzic M (2009) Gold catalysis: switching the pathway of the furan-yne cyclization. *Angew Chem Int Ed* 48:5848–5852

183. Huang H, Zhou Y, Liu H (2011) Recent advances in the gold-catalyzed additions to C–C multiple bonds. *Beilstein J Org Chem* 7:897–936
184. Liu LP, Hammond GB (2010) Gold-catalyzed cascade annulations of 2-(ynol)aryl aldehydes: facile synthesis of benzochromanes and benzobicyclo[*n*.3.1]acetals. *Org Lett* 12:4640–4643
185. Kotera A, Uenishi J, Uemura M (2010) Gold-catalyzed stereoselective reaction of tricarbonylchromium complexes of *ortho*-alkynyl benzaldehydes and benzaldimines with nucleophiles. *J Organomet Chem* 695:2180–2190
186. Cefalo DR, Kiely AF, Wuchrer M, Jamieson JY, Schrock RR, Hoveyda AH (2001) Enantioselective synthesis of unsaturated cyclic tertiary ethers by Mo catalyzed olefin metathesis. *J Am Chem Soc* 123:3139–3140
187. Chilot JJ, Doutheau A, Gore J (1982) Heterocyclisation de diols $\beta\gamma'$ -alleniques. *Tetrahedron Lett* 23:4693–4696
188. Ting PC, Bartlett PA (1984) Stereocontrolled synthesis of *trans*-2,5-disubstituted tetrahydrofurans. *J Am Chem Soc* 106:2668–2671
189. Tarselli MA, Zuccarello JL, Lee SJ, Gagne MR (2009) Gold(I)-catalyzed cascade cyclization of allenyl epoxides. *Org Lett* 11:3490–3492
190. Yang CG, Reich NW, Shi Z, He C (2005) Intramolecular additions of alcohols and carboxylic acids to inert olefins catalyzed by silver(I) triflate. *Org Lett* 7:4553–4556
191. Luo T, Dai M, Zheng S-L, Schreiber SL (2011) Syntheses of α -pyrones using gold-catalyzed coupling reactions. *Org Lett* 13:2834–2836
192. Dombay T, Blanc A, Weibel J-M, Pale P (2010) Gold(I)-catalyzed cycloisomerization of β -alkynylpropiolactones to substituted α -pyrones. *Org Lett* 12:5362–5365
193. Piera J, Krumlinde P, Strubing D, Backvall J-H (2007) Gold-catalyzed cyclization of allene-substituted malonate esters: synthesis of β , γ -unsaturated δ -lactones. *Org Lett* 9:2235–2237
194. Schuler M, Silva F, Bobbio C, Tessier A, Gouverneur V (2008) Gold(I)-catalyzed alkoxyhalogenation of β -hydroxy- α , α -difluoropyrones. *Angew Chem Int Ed* 47:7927–7930
195. Liu G (2012) Transition metal-catalyzed fluorination of multi carbon-carbon bonds: new strategies for fluorinated heterocycles. *Org Biomol Chem* 10:6243–6248
196. Burke MD, Schreiber SL (2004) A planning strategy for diversity-oriented synthesis. *Angew Chem Int Ed* 43:46–58
197. Luo T, Schreiber SL (2007) Complex α -pyrones synthesized by a gold-catalyzed coupling reaction. *Angew Chem Int Ed* 46:8250–8253
198. Ma S, Yu S, Yin S (2003) Studies on K_2CO_3 -catalyzed 1,4-addition of 1,2-allenic ketones with diethyl malonate: controlled selective synthesis of β , γ -unsaturated enones and α -pyrones. *J Org Chem* 68:8996–9002
199. Hachiya I, Shibuya H, Shimizu M (2003) Novel 2-pyrone synthesis via the nucleophilic addition of active methine compounds to 2-alkynone. *Tetrahedron Lett* 44:2061–2063
200. Fukuyama T, Higashibeppu Y, Yamaura R, Ryu I (2007) Ru-catalyzed intermolecular [3 + 2 + 1] cycloaddition of α , β -unsaturated ketones with silylacetylenes and carbon monoxide leading to α -pyrones. *Org Lett* 9:587–589
201. Kishimoto Y, Mitani I (2005) Solvent-free synthesis of 2-pyrones from alkynes and carbon dioxide catalyzed by Ni(1,5-cyclooctadiene)2/trialkylphosphine catalysts. *Synlett* 14:2141–2146
202. Genin E, Toullec PY, Antonietti S, Brancour C, Genet J-P, Michelet V (2006) Room temperature Au(I)-catalyzed exo-selective cycloisomerization of acetylenic acids: an entry to functionalized γ -lactones. *J Am Chem Soc* 128:3112–3113
203. Shapiro ND, Toste FD (2007) Rearrangement of alkynyl sulfoxides catalyzed by gold(I) complexes. *J Am Chem Soc* 129:4160–4161
204. Li G, Zhang L (2007) Gold-catalyzed intramolecular redox reaction of sulfinyl alkynes: efficient generation of α -oxo gold carbenoids and application in insertion into R–CO bonds. *Angew Chem Int Ed* 46:5156–5159
205. Norman ROC, Parr WJE, Thomas CB (1976) The reactions of alkynes, cyclopropanes, and benzene derivatives with gold(III). *J Chem Soc Perkin Trans 1* 18:1983–1987
206. Fukuda Y (1991) Utimoto, K Efficient transformation of methyl propargyl ethers into α , β -unsaturated ketones. *Bull Chem Soc Jpn* 64:2013–2015
207. Fukuda Y, Utimoto K (1991) Effective transformation of unactivated alkynes into ketones or acetals with a gold(III) catalyst. *J Org Chem* 56:3729–3731
208. Imai K, Imai K, Utimoto K (1987) Regioselective hydration of alkynones by palladium catalysis. *Tetrahedron Lett* 28:3127–3130
209. Casado R, Contel M, Laguna M, Romero P, Sans S (2003) Organometallic gold(III) compounds as catalysts for the addition of water and methanol to terminal alkynes. *J Am Chem Soc* 125:11925–11935
210. Schulz M, Teles JH (2000) U.S. Patent 6,037,482 for BASF, 14 March 2000
211. Teles JH, Brode S, Chabanas M (1998) Cationic gold(I) complexes: highly efficient catalysts for the addition of alcohols to alkynes. *Angew Chem Int Ed* 37:1415–1418
212. Yao X-Q, Li C-J (2006) Water-triggered and gold(I)-catalyzed cascade addition/cyclization of terminal alkynes with *ortho*-alkynylaryl aldehyde. *Org Lett* 8:1953–1955
213. Asao N (2006) Gold- and copper-catalyzed [4 + 2] benzannulations between enynal or enynone units and 2π -systems. *Synlett* 11:1645–1656
214. Bartlett PA, Chapuis C (1986) Synthesis of polyether-type tetrahydrofurans via hydroperoxide cyclization. *J Org Chem* 51:2799–2806
215. Nakata T, Schmid G, Vranesic B, Okigawa M, Smith-Palmer T, Kishi Y (1978) A total synthesis of lasalocid A. *J Am Chem Soc* 100:2933–2935
216. Li Z, Brouwer C, He C (2008) Gold catalyzed organic transformations. *Chem Rev* 108:3239–3265
217. Zeni G, Larock RC (2004) Synthesis of heterocycles via palladium π -olefin and π -alkyne chemistry. *Chem Rev* 104:2285–2310
218. Harkat H, Weibel J-M, Pale P (2006) A mild access to γ - or δ -alkylidene lactones through gold catalysis. *Tetrahedron Lett* 47:6273–6276
219. Marchal E, Uriac P, Legouin B, Toupet L, van de Weghe P (2007) Cycloisomerization of γ - and δ -acetylenic acids catalyzed by gold(I) chloride. *Tetrahedron* 63:9979–9990
220. Uchiyama M, Ozawa H, Takuma K, Matsumoto Y, Yonehara M, Hiroya K, Sakamoto T (2006) Regiocontrolled intramolecular cyclizations of carboxylic acids to carbon-carbon triple bonds promoted by acid or base catalyst. *Org Lett* 8:5517–5520
221. Li G, Zhang G, Zhang L (2008) Au-catalyzed synthesis of (1Z,3E)-2-pivaloxy-1,3-dienes from propargylic pivalates. *J Am Chem Soc* 130:3740–3741
222. Skouta R, Li C-J (2007) Gold(I)-catalyzed annulation of salicylaldehydes and aryl acetylenes as an expedient route to isoflavonones. *Angew Chem Int Ed* 46:1117–1119
223. Skouta R, Li C-J (2007) Au(I)-catalyzed annulation of 2-tosylaminobenzaldehyde and alkynes. *Synlett* 11:1759–1762
224. Raffa G, Belot S, Balme G, Monteiro N (2011) Iodocyclization versus diiodination in the reaction of 3-alkynyl-4-methoxycoumarins with iodine: synthesis of 3-iodofuro[2,3-*b*]chromones. *Org Biomol Chem* 9:1474–1478
225. Wang L, Peng S, Wang J (2011) Palladium-catalyzed cascade reactions of coumarins with alkynes: synthesis of highly

- substituted cyclopentadiene fused chromones. *Chem Commun* 47:5422–5424
226. Zhao J, Zhao Y, Fu H (2011) Transition-metal-free intramolecular Ullmann-type *O*-arylation: synthesis of chromone derivatives. *Angew Chem Int Ed* 50:3769–3773
227. Renault J, Qian Z, Uriac P, Goualt N (2011) Electrophilic carbon transfer in gold catalysis: synthesis of substituted chromones. *Tetrahedron Lett* 52:2476–2479
228. Shi Z, He C (2004) Efficient functionalization of aromatic C–H bonds catalyzed by gold(III) under mild and solvent-free conditions. *J Org Chem* 69:3669–3671
229. Reetz MT, Sommer K (2003) Gold-catalyzed hydroarylation of alkynes. *Eur J Org Chem* 18:3485–3496
230. Nevado C, Echavarren AM (2005) Transition metal-catalyzed hydroarylation of alkynes. *Synthesis* 2:167–182
231. Nevado C, Echavarren AM (2005) Intramolecular hydroarylation of alkynes catalyzed by platinum or gold: mechanism and *endo* selectivity. *Chem Eur J* 11:3155–3164
232. Soriano E, Marco-Contelles J (2006) Mechanisms of the transition metal-mediated hydroarylation of alkynes and allenes. *Organometallics* 25:4542–4553
233. Shi Z, He C (2004) An Au-catalyzed cyclialkylation of electron-rich arenes with epoxides to prepare 3-chromanols. *J Am Chem Soc* 126:5964–5965
234. Kharasch MS, Isbell HS (1931) The chemistry of organic gold compounds. III. Direct introduction of gold into the aromatic nucleus (preliminary communication). *J Am Chem Soc* 53:3053–3059
235. Porter KA, Schier A, Schmidbaur H (2003) Auration of thiophene and furan: structures of the 2-mono- and 2,2-diaurated products. *Organometallics* 22:4922–4927
236. Fuchita Y, Utsunomiya Y, Yasutake M (2001) Synthesis and reactivity of arylgold(III) complexes from aromatic hydrocarbons via C–H bond activation. *J Chem Soc Dalton Trans* 16:2330–2334
237. de Graaf PWJ, Boersma J, van der Kerk GJM (1976) Preparation and properties of arylgold compounds. Scope and limitations of the auration reaction. *J Organomet Chem* 105:399–406
238. Liddle KS, Parkin C (1972) Synthesis and properties of monoarylgold(III) complexes. *J Chem Soc Chem Commun* 1:26a–26a
239. Partyka DV, Esswein AJ, Zeller M, Hunter AD, Gray TG (2007) Gold(I) pyrenyls: excited-state consequences of carbon–gold bond formation. *Organometallics* 26:3279–3282
240. Partyka DV, Zeller M, Hunter AD, Gray TG (2006) Relativistic functional groups: aryl carbon–gold bond formation by selective transmetalation of boronic acids. *Angew Chem Int Ed* 45:8188–8191
241. Padwa A, Krumpke KE, Zhi L (1989) Cycloalkenone formation by the intramolecular addition of α -diazo ketone to an acetylenic pi-bond. *Tetrahedron Lett* 30:2633–2636
242. Padwa A, Chiacchio U, Garreau Y, Kassir JM, Krumpke KE, Schoffstall AM (1990) Generation of vinylcarbenes by the intramolecular addition of alpha-diazo ketones to acetylenes. *J Org Chem* 55:414–416
243. Padwa A, Krumpke KE, Garreau Y, Chiacchio U (1991) Rhodium(II)-catalyzed cyclization reactions of alkynyl-substituted alpha-diazo ketones. *J Org Chem* 56:2523–2530
244. Padwa A, Krumpke KE (1992) Application of intramolecular carbenoid reactions in organic synthesis. *Tetrahedron* 48:5385–5453
245. Padwa A, Krumpke KE, Kassir JM (1992) Rhodium carbenoid mediated cyclizations of *o*-alkynyl-substituted alpha-diazoacetophenones. *J Org Chem* 57:4940–4948
246. Padwa A, Austin DJ, Gareau Y, Kassir JM, Xu SL (1993) Rearrangement of alkynyl and vinyl carbenoids via the rhodium (II)-catalyzed cyclization reaction of alpha-diazo ketones. *J Am Chem Soc* 115:2637–2647
247. Davies HML, Denton JR (2009) Application of donor/acceptor-carbenoids to the synthesis of natural products. *Chem Soc Rev* 38:3061–3071
248. Bonge HT, Hanse T (2010) Insights on Rh(II) carbenoid reactivity. *Tetrahedron Lett* 51:5378–5381
249. Hoyer TR, Dinsmore CJ, Johnson DS, Korkowski PF (1990) Alkyne insertion reactions of metal-carbenes derived from enynyl-alpha-diazo ketones [R'CN₂COCR₂CH₂CC(CH₂)_{n-2}CH:CH₂]. *J Org Chem* 55:4518–4520
250. Hoyer TR, Dinsmore CJ (1991) Rhodium (II) acetate catalyzed alkyne insertion reactions of alpha-diazo ketones: mechanistic inferences. *J Am Chem Soc* 113:4343–4345
251. Harvey DF, Sigano DM (1996) Carbene-alkyne-alkene cyclization reactions. *Chem Rev* 96:271–288
252. Padwa A, Blacklock TJ, Loza R (1982) Mechanistic aspects of the silver (I)-promoted rearrangement of cyclopropene derivatives. *J Org Chem* 47:3712–3721
253. Zhu Z-B, Shi M (2008) Gold(I)-catalyzed cycloisomerization of arylvinylcyclopropenes: an efficient synthetic protocol for the construction of indene skeletons. *Chem Eur J* 14:10219–10222
254. Bauer JT, Hadfield MS, Lee A-L (2008) Gold catalysed reactions with cyclopropenes. *Chem Commun* 47:6405–6407
255. Benitez D, Shapiro ND, Tkatchouk E, Wang Y, Goddard WA, Toste FD (2009) A bonding model for gold(I) carbene complexes. *Nat Chem* 1:482–486
256. Li C, Zeng Y, Wang J (2009) Au-catalyzed isomerization of cyclopropenes: a novel approach to indene derivatives. *Tetrahedron Lett* 50:2956–2959
257. Zhou Y, Trewyn BG, Angelici RJ, Woo LK (2009) Catalytic reactions of carbene precursors on bulk gold metal. *J Am Chem Soc* 131:11734–11743
258. Li C, Zeng Y, Zhang H, Feng J, Zhang Y, Wang J (2010) Gold(I)-catalyzed cycloisomerization of enynes containing cyclopropenes. *Angew Chem* 122:6557–6561 (*Angew Chem Int Ed* 49: 6413–6417)
259. Seraya E, Slack E, Ariafard A, Yates BF, Hyland CJT (2010) Experimental and theoretical investigation into the gold-catalyzed reactivity of cyclopropenylmethyl acetates. *Org Lett* 12:4768–4771
260. Hadfield MS, Bauer JT, Glen PE, Lee A-L (2010) Gold(I)-catalysed alcohol additions to cyclopropenes. *Org Biomol Chem* 8:4090–4095
261. Hadfield MS, Lee A-L (2011) Gold(I)-catalysed synthesis of conjugated trienes. *Chem Commun* 47:1333–1335
262. Miede F, Meyer C, Cossy J (2010) Synthesis of 3-oxa- and 3-azabicyclo[4.1.0]heptanes by gold-catalyzed cycloisomerization of cyclopropenes. *Org Lett* 12:4144–4147
263. Hon Y-S, Chang R-C (1991) The studies of carbenoid reactions of α -O-allyl- or α -N-allyl- α' -diazo propanone derivatives catalyzed by various metal ions. *Heterocycles* 32:1089–1099
264. Miede F, Meyer C, Cossy J (2011) Rhodium-catalyzed cycloisomerization involving cyclopropenes: efficient stereoselective synthesis of medium-sized heterocyclic scaffolds. *Angew Chem* 123:6054–6059
265. Majumdar KC, De RN, Khan AT, Chattopadhyay SK, Dey K, Patra A (1988) Studies of [3,3]sigmatropic rearrangements: rearrangement of 3-(4-*p*-tolylxybut-2-ynyl)oxy[1]benzopyran-2-one. *J Chem Soc Chem Commun* 12:777–779
266. Alcaide B, Almendros P, Carrascosa R, Torres MR (2010) Gold/acid-Co-catalyzed regiodivergent preparation of bridged ketals via direct bis-oxycyclization of alkynic acetonides. *Adv Synth Catal* 352:1277–1283
267. Alcaide B, Almendros P, Carrascosa R (2011) Straightforward synthesis of bridged azaoxa skeletons: gold-catalyzed

- aminoketalization of Garner's aldehyde derived alkynes. *Chem Eur J* 17:4968–4971
268. Alcaide B, Almendros P (2011) Gold-catalyzed heterocyclizations in alkynyl- and allenyl- β -lactams. *Beilstein J Org Chem* 7:622–630
269. Aponick A, Biannic B (2008) Gold-catalyzed dehydrative cyclization of allylic diols. *Synthesis* 20:3356–3359
270. Bandini M, Monari M, Romaniello A, Tragni M (2010) Gold catalyzed direct activation of allylic alcohols in the stereoselective synthesis of functionalized 2-vinyl-morpholines. *Chem Eur J* 16:14272–14277
271. Hashmi ASK, Schuster A, Rominger F (2009) Gold katalyse: isolierung von vinylgold komplexen ausgehend von alkinen. *Angew Chem* 121:8396–8398
272. Hashmi ASK, Schuster A, Rominger F (2009) Gold catalysis: isolation of vinylgold complexes derived from alkynes. *Angew Chem Int Ed* 48:8247–8249
273. Stephen A, Hashmi K (2010) Gold-catalyzed synthesis of *N,O*-heterocycles. *Pure Appl Chem* 82:657–668
274. Zhou Y, Zhai Y, Ji X, Liu G, Feng E, Ye D, Zhao L, Jiang H, Liu H (2010) Gold(I) catalyzed one-pot tandem coupling/cyclization: an efficient synthesis of pyrrolo-/pyrido[2,1-*b*]benzo[*d*][1,3]oxazin-1-ones. *Adv Synth Catal* 352:373–378
275. Feng E, Zhou Y, Zhang D, Zhang L, Sun H, Jiang H, Liu H (2010) Gold(I)-catalyzed tandem transformation: a simple approach for the synthesis of pyrrolo/pyrido[2,1-*a*][1,3]benzoxazinones and pyrrolo/pyrido[2,1-*a*]quinazolinones. *J Org Chem* 75:3274–3282
276. Patil NT, Mutyala AK, Lakshmi PGV, Gajula B, Sridhar B, Potireddygar GR, Rao TP (2010) Au(I)-catalyzed cascade reaction involving formal double hydroamination of alkynes bearing tethered carboxylic groups: an easy access to fused dihydrobenzimidazoles and tetrahydroquinazolines. *J Org Chem* 75:5963–5975
277. Zhou Y, Feng E, Liu G, Ye D, Li J, Jiang H, Liu H (2009) Gold-catalyzed one-pot cascade construction of highly functionalized pyrrolo[1,2-*a*]quinolin-1(2*H*)-ones. *J Org Chem* 74:7344–7348
278. Winter C, Krause N (2009) Structural diversity through gold catalysis: stereoselective synthesis of *N*-hydroxypyrrolines, dihydroisoxazoles, and dihydro-1,2-oxazines. *Angew Chem* 121:6457–6460
279. Winter C, Krause N (2009) Structural diversity through gold catalysis: stereoselective synthesis of *N*-hydroxypyrrolines, dihydroisoxazoles, and dihydro-1,2-oxazines. *Angew Chem Int Ed* 48:6339–6342
280. Krause N, Aksin-Artok O, Breker V, Deutsch C, Gockel B, Poonoth M, Sawama Y, Sawama Y, Sun T, Winter C (2010) Combined coinage metal catalysis for the synthesis of bioactive molecules. *Pure Appl Chem* 82:1529–1536
281. Krause N, Aksin-Artok O, Asikainen M, Breker V, Deutsch C, Erdsack J, Fan H-T, Gockel B, Minkler S, Poonoth M, Sawama Y, Sawama Y, Sun T, Volz F, Winter C (2012) Combined coinage metal catalysis for the synthesis of bioactive molecules. *J Organometal Chem* 704:1–8
282. Kang J-E, Kim H-B, Lee J-W, Shin S (2006) Gold(I) catalyzed intramolecular hydroamination of alkyne with trichloroacetimides. *Org Lett* 8:3537–3540
283. Lloyd-Jones GC, Margue RG, Vries JG (2005) Rate enhancement by ethylene in the Ru-catalyzed ring-closing metathesis of enynes: evidence for an “ene-then-yne” pathway that diverts through a second catalytic cycle. *Angew Chem Int Ed* 44:7442–7447
284. Yang T, Campbell L, Dixon DJ (2007) A Au(I)-catalyzed *N*-acyl iminium ion cyclization cascade. *J Am Chem Soc* 129:12070–12071
285. Singh S, Elsegood MRJ, Kimber MC (2012) An Au(I) catalyzed allenamide cyclization giving access to an α -vinyl-substituted tetrahydroisoquinoline building block. *Synlett* 23:565–568
286. Lu T, Lu Z, Ma Z-X, Zhang Y, Hsung RP (2013) Allenamides: a powerful and versatile building block in organic synthesis. *Chem Rev* 113:4862–4904

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.