MINI-REVIEW ARTICLE

CURRENT
MICROWAVE CHEMISTRY

Microwave-Assisted Homogeneous Gold Catalyzed Organic Transformations

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Abstract: Microwave chemistry is an emerging area of science mainly focusing on various applications of microwave energy into chemical processes. Microwave irradiation has enormous potential to provide controlled energy directly to the molecules of interest. On the other hand, homogeneous gold catalysis has emerged in the last two decades or so as one of the most promising fields in organic and organometallic chemistry. Its efficacy has been established many times for the construction of new C – X (X = O, N, S, *etc.*) and C – C bonds under mild reaction conditions. Although a significant number of reports have appeared in the literature regarding the homogeneous gold-catalyzed organic transformations under microwave conditions, this is the first review article which is going to appear in the literature. This mini-review is designed to give an interesting insight into various homogeneous gold-catalyzed organic reactions under microwave irradiation for the synthesis of a library of electronically and structurally diverse and biologically important organic molecules.

1. INTRODUCTION

Microwave chemistry is a promising area of science of applying microwave energy to various chemical reactions. Current research publications have reported that under certain conditions, microwave energy can significantly increase the rate of product formation of a chemical reaction [1]. The enhanced heating rate under microwave-assisted reaction conditions leads to improved product yield, higher catalyst turnover, milder reaction conditions, and shorter reaction times. [2-3]. The reactivity of chemical compounds under microwave conditions cannot be explained exclusively by the rapid heating of the system, the "microwave effect" is assumed to be a synergistic effect of both thermal and non-thermal effects [4]. Since the efficiency of microwave energy to trigger rapid heating depends on the properties of different compounds, thus reactions can be made selectively and conducted under high pressure without harming the microwave-transparent reaction vessel. As mentioned earlier, since microwave heating is highly polarity-dependent, organic reactions can also be regulated by carefully choosing dielectric properties of solvents and other reaction contents [5]. Besides, the capability of microwaves to enhance the solubility of organic reactants to aqueous media has created an incentive for chemists to develop new methodologies based on water as a solvent. Water itself is an ideal and green solvent for organic transformations, as it is cheap and easily removable from the organic reaction mixture [6, 7].

On the other hand, homogeneous catalysis relates to catalytic reactions where the catalyst is in the same phase as the reactants and it is most important in organic synthesis. This set of reactions, involving several diverse carbon-carbon and carbon-heteroatom bond-forming reactions and asymmetric transformations, is highly demanding synthetic tool for the organic chemists today. Nevertheless, in high-throughput synthesis, the long reaction times that are often needed for complete conversions have restricted the utilization of homogeneous catalysis. Therefore, efficient and practical microwave applications are needed not only for the rapid production of new chemical compounds but in general to boost-up the efficiency of homogeneous catalysis. By the mid-1980s the implementation of microwaves technology was well accepted as an effective heating source for organic reactions [8]. Afterward, several reactions have been reported where significantly higher reaction rates were observed in combinatorial chemistry [9-10]. The use of microwave technology is not only limited as a fast heating technique, but it also has wide applications in biocatalysis [11, 12], biotechnology [13-15], medicinal chemistry [16, 17], analytical chemistry [18-21], and polymer and material science [22-24]. It is also useful for remote sensing and environmental chemistry [25-29]. Generally, very good yields and clean reactions were obtained using only small quantities of energy. A further advantage of using this heating technology is the opportunity to employ milder and less toxic reagents and solvents. The non-inert-atmospheric conditions and easy experimental method of many microwave-assisted reactions provide additional utility in chemical synthesis. Many organic reactions are typically conducted over a few hours using a homogeneous/heterogeneous catalyst. One of the most prac-

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tical reasons in an organic reaction using microwave irradiation is to greatly speed up the process from hours to minutes. This advantage of microwave-assisted processes has provided greater efficiency to chemists in studying less kinetically favored reactions.

While gold has the shortest history in catalysis, ignited by the discovery of its catalytic activity, it has enjoyed the sharpest burst of interest witnessed in the last few decades. This was associated with the revealing of an array of new reactivities, and thus with the progress of a plethora of new transformations. Nowadays, homogeneous gold catalysis is already widely used for cross-coupling [30-35], C–H functionalization [36-38], benzannulation [39-42], oxidation [43], hydrogenation [44], and several other transformations, beginning with addition, cycloaddition, and cycloisomerization [45] reactions involving alkynes and alkenes. Considerable progress has also been achieved in the development of highly stereoselective gold-catalyzed reactions for organic transformations [46-53] as well as in total synthesis [54-58]. This review article is mainly focused to explore the benefits and challenges of the area of microwave-assisted homogeneous gold catalysis after a brief discussion on microwaves-assisted reactions and homogeneous gold catalysis.

2. MICROWAVE-ASSISTED REACTIONS: GENERAL APPROACH

Microwave heating is dependent on the capacity of a given substance to absorb microwave energy and convert that electromagnetic energy into heat [59]. Molecules with a dipole moment make an effort to align them with the oscillating electric field of microwave irradiation, which leads to the rotation [60]. One molecule which is rotationally excited by incident irradiation will strike the second one, transforming rotational energy into translational energy. Thus, a large number of molecules are rotationally excited under microwave irradiation, and when they hit other molecules, rotational energy is converted into translational energy (*i.e,.* kinetic energy), and as a result, heating is detected [61] (Fig. **1**).
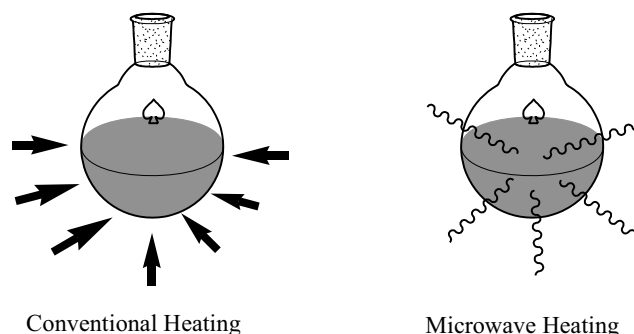
Fig. (1). Comparison of microwave heating versus conventional heating.

There are some differences between conventional heating and microwave-assisted heating. These are: firstly, the heating or thermal reaction initiates from the surface of material only, whereas the microwave-assisted heating or thermal reaction starts consistently and concurrently from the surface to the bulk of the material. Secondly, under conventional heating conditions, the heat transfer needs physical contact between the surface of the materials and the vessel but physical contact between the surface of the materials and the vessel is not necessary under microwave irradiative heating conditions. Thirdly, electric or thermal sources are used for conventional heating while microwave-assisted heating takes place by microwave irradiations. Fourthly, heating of materials occurs through a thermal conduction mechanism under conventional heating conditions as opposed to microwave-assisted heating, where heating of material involves dielectric polarization of materials. Fifthly, the low heating rate was observed employing conventional heating methods in contrast to the higher rate of heating under microwave heating conditions.

Since microwave heating relies on a molecule's dipole moment, polar solvents like dimethylsulfoxide, dimethylformamide, ethanol, and water better transform microwave irradiation into heat relative to non-polar solvents like toluene or hexane. Besides, many other factors are also contributing to the rapid heating of a substance upon microwave irradiation. Factors such as specific heat capacity and the heat of vaporization, as well as the depth to which microwave irradiation will reach the sample, may often have a greater effect on the heating rate than their corresponding dielectric losses. Therefore, all of these variables change as a function of temperature, and the heat of vaporization varies as a function of pressure.

Thus, microwaves can accelerate the rate of reaction, provide improved yields and greater purity, uniform and selective heating with energy-saving, attain higher reproducibility of reactions and help in developing convenient and cleaner green [62, 63] synthetic processes. The main benefits of microwave-assisted organic synthesis are:-

(a) Faster reaction: Based on experimental results it was noticed that the rates of a microwave-assisted chemical reaction can be as much as 1000-fold faster than conventional heating methods. The microwave can use higher temperatures compared to conventional heating systems, and thus the reactions are finished in a few minutes rather than hours.

(b) Improved yield and higher purity: Generally products were obtained in higher yield using microwave irradiation and less formation of side products was observed. As a result, the purification step was found to be quicker and easier.

(c) Low processing costs: Conventional methods of organic synthesis generally require longer heating time, tedious apparatus setup, and excessive use of solvents/reagents resulting in higher processing costs. Microwave synthesis is believed to be an important approach in the direction of green chemistry since this technique is more eco-friendly. Because of its ability to couple directly with the reaction molecules and by passing thermal conductivity leading to a rapid rise in the temperature, microwave-assisted synthesis generally has low processing costs.

(d) Uniform and selective heating: Under the conventional heating condition, the oil bath walls are heated first and the solvent afterward. Despite this dispersed heating in an oil bath, the difference in temperature between both the walls and the solvent is always apparent. Only the solvent and the solute particles are excited under microwave heating which leads to uniform heating of solution. Selective heating is focused on the concept that different materials respond to microwave irradiation differently. Some substances are transparent while others are microwave absorbents.

(e) Greater reproducibility: Due to uniform heating and enhanced control of process parameters, reactions performed under microwave-assisted heating protocol are more reproducible compared to conventional heating. It is also easy to monitor the temperature of the chemical reactions with microwave heating.

(f) Energy-saving process: Microwave-assisted heating is a highly efficient process and helps in significant energy saving. This is mainly because microwaves only heat the sample and not the apparatus, and so the energy consumption is less.

(g) Green synthesis: The microwave-assisted reactions are cleaner and more environmentally friendly than conventional heating methods. Microwaves directly heat the molecules; hence the use of solvents in the chemical reaction may be minimized or excluded. Organic synthesis in the absence of solvent, where reagents are absorbed on mineral support, has a large prospective since it offers an eco-friendly green protocol in synthesis. The use of microwaves has also decreased the number of purification steps needed for chemical reactions involving toxic-reagents to obtain desired products.

(h) Small particle size and narrow distribution: Compared to conventional methods, microwave-assisted synthesis yields smaller particle sizes and narrow particle size distribution. It provides particles with the usual particle size of 12 nm. Nanostructures with smaller sizes, narrower size distributions, and a higher degree of crystallization are obtained under microwave heating in contrast to conventional oil-bath heating.

Although microwave-assisted organic transformations have lots of advantages still it is not free from some demerits [64]. One of the drawbacks of microwave scale-up technology is the insufficient microwave irradiation penetration range into the absorbing materials. This means that solvents or reagents are heated by convection in the center of the large reaction vessel and not by dielectric heating directly in the microwave-assisted heating. The higher temperatures/superheating of the solvent in sealed vessels may facilitate the decomposition of the desired products or may lead to the formation of a thermodynamically stable product preferably to the kinetically favored product. The use of microwaves as a heating source has limited applicability for materials that absorb it. Microwaves cannot heat materials that are transparent to their radiation, such as sulfur. Improper utilization of microwave heating to increase the rate of chemical reactions involving radioisotopes can lead to unregulated radioactive decay. Some issues were also found during the conduct of polar acid-based reactions, with hazardous results, which can harm the polymer vessel used for heating. Microwave reactions may also result in uncontrolled reactions and cause explosions at high-pressure conditions.

Though microwave chemistry is presently being used in both academic and industrial applications, the effect on the pharmaceutical industry [65-67] in particular has contributed to the advancement of microwave-assisted organic synthesis (MAOS) from a laboratory interest in the 1980s and 1990s to a technology now fully adopted. The field has evolved to such an extent that almost every pharmaceutical company and many academic laboratories are now actively using this technology for their research work.

3. HOMOGENEOUS GOLD CATALYSIS: GENERAL APPROACH

Gold-catalyzed reactions have exhibited several unique features. Specifically, with an electron configuration of $[Xe]4f^{14}5d^{10}6s^1$ for the gold atom, gold catalysts mainly exist in +1 and +3 oxidation states. The high oxidation potential of Au(I) to Au(III) permits most Au(I)-catalyzed reactions to perform without much precautions to exclude air. The reluctance to switch between oxidation states ensures the progress of novel modes of catalytic cycles contrary to the classical oxidative addition/reductive elimination pathways common in late transition metal catalysis. Moreover, gold catalysts are remarkably alkynophilic, but not as oxophilic as most Lewis acids. Thus, tolerance towards air and moisture and the nontoxicity make these catalysts greatly user friendly and a premier choice for green chemistry. Also, convenient procedures and without the worry of air and moisture, gold-catalyzed reactions often provide competent access to structures of huge diversity and or complexity from much simpler starting materials. Furthermore, carbon-gold bonds are labile toward protodeauration, but not susceptible to β-hydride elimination, which often occurs in other transition metal-catalyzed reactions, thereby increasing the product selectivity. Gold has only one isotope and therefore lacks a characteristic isotope pattern in mass spectrometry. The nuclear spin of gold is 3/2, but due to very low sensitivity and a quadrupole moment, only a few [79]Au spectra in a highly symmetric environment have been reported. The diamagnetic character of both gold(I) and gold(III) conveniently allows the monitoring of catalytic reactions by NMR. Mössbauer spectroscopy can convey information about the oxidation state.

Over the past two decades, homogeneous gold catalysis has gained increasing attention, allowing for the substitution of unified organic reactions with simpler, selective, and chemically feasible alternatives. The fine-tunability of both the electronic and steric properties of gold catalysts significantly contributed to the development of the research field, with widespread uses in total synthesis and asymmetric catalysis. The key benefit of homogeneous catalysis of gold was that the precise change of the catalyst structure will impact the mechanism of the reaction in a controlled and predictable way. Homogeneous gold catalysis has attracted substantial attention in recent years, and several powerful new
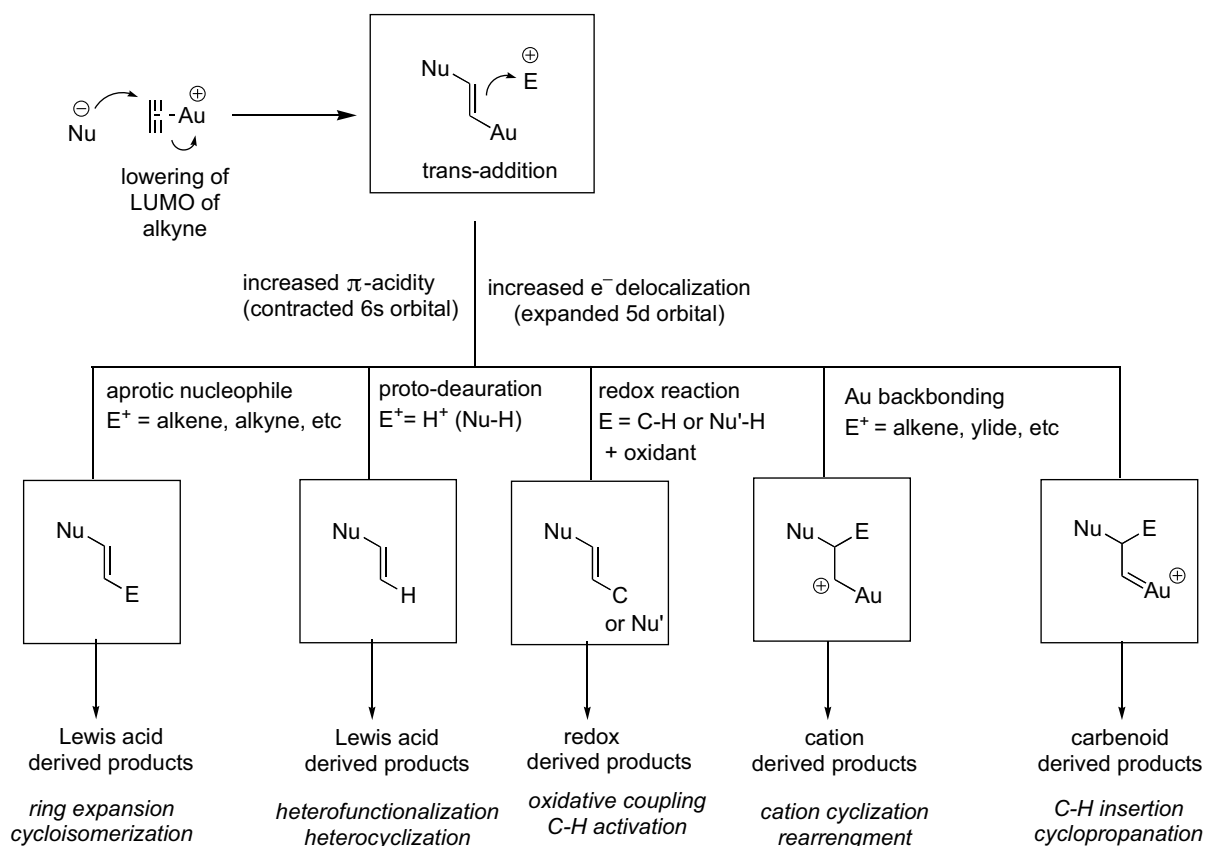
Scheme 1. Mode of reactivity in homogeneous gold catalysis.

reaction cascades have been discovered for the rapid construction of molecular architectures, starting from simple key precursors.

Although there are various types of organic reactions catalyzed by homogeneous gold catalysts, a mainstream of them proceed through some very alike mechanistic steps and involve the activation of a π-system of an alkyne or an allene, or sometimes even an alkene moiety, thereby rendering it susceptible to nucleophilic attack. One of the great advantages of using gold catalysis is a kinetically labile carbon–gold bond that can be readily cleaved under the reaction conditions, thus confirming efficient turnover. As a result, these reactions provide an atom-economical entry into functionalized cyclic and acyclic scaffolds useful for the synthesis of natural and non-natural products under mild conditions with excellent chemoselectivity and high synthetic efficiency. The metal-π-complex may evolve through the usual carbenoid species or also via back-donation down through a 1,2-shift (hydride, halide, *etc.*) that leads to the formation of a metal–vinylidene complex. A general pathway for these transformations is given in Scheme 1 [68].

## 4. MICROWAVE-ASSISTED HOMOGENEOUS GOLD CATALYSIS

The combination of homogeneous catalysis and microwave heating is not only a hot topic but also a research domain expected to influence many modern fields of chemistry. Transition metal-catalyzed reactions that usually took hours or days to complete with regular, thermal heating can now be carried to full conversion in just seconds or minutes with good reproducibility, requiring just a fraction of the energy normally required for a regular, oil-bath-heated reaction. Additionally, the use of microwave heating is often correlated with the benefits of using conventional heating which is not easily achieved. Indeed, under the action of microwaves, transition metal-catalyzed chemistry has been proven much more effective than with normal heating in many cases.

In 2007, Che *et al.* described an elegant method for the preparation of substituted 1,2- dihydro quinolines and quinolines efficiently using Au(I) catalyzed tandem hydroamination- hydroarylation strategy under microwave conditions [69]. In this protocol primary anilines react with two equivalents of aliphatic or aryl alkynes in the presence of 5 mol% N- heterocyclic carbene gold(I) catalyst, Au(IPr)Cl to produce 1,2-dihydro quinolines in excellent yields (Scheme **2**). It has been found that compared to traditional thermal heating conditions, microwave irradiation shortens the reaction time from 12-24h to less than 70 minutes thus proving the efficiency and utility of the use of microwave conditions. The toleration of various functional groups and broad substrate scopes makes this method elegant. On the other hand, the reaction of 2-aminophenone with one equivalent alkyne provides 2,4-disubstituted quinolines under similar experimental conditions (Scheme **3**).
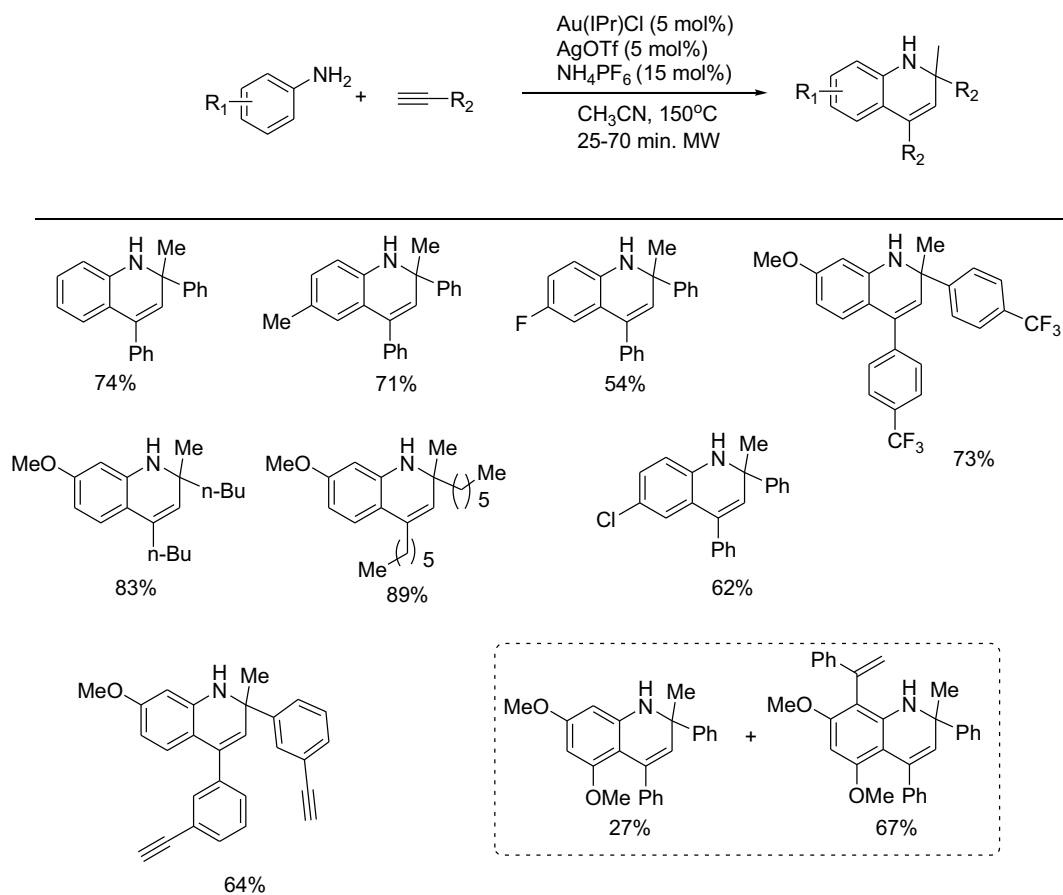
Scheme 2. Gold(I)-catalyzed reactions between primary arylamines and alkynes under microwave conditions.
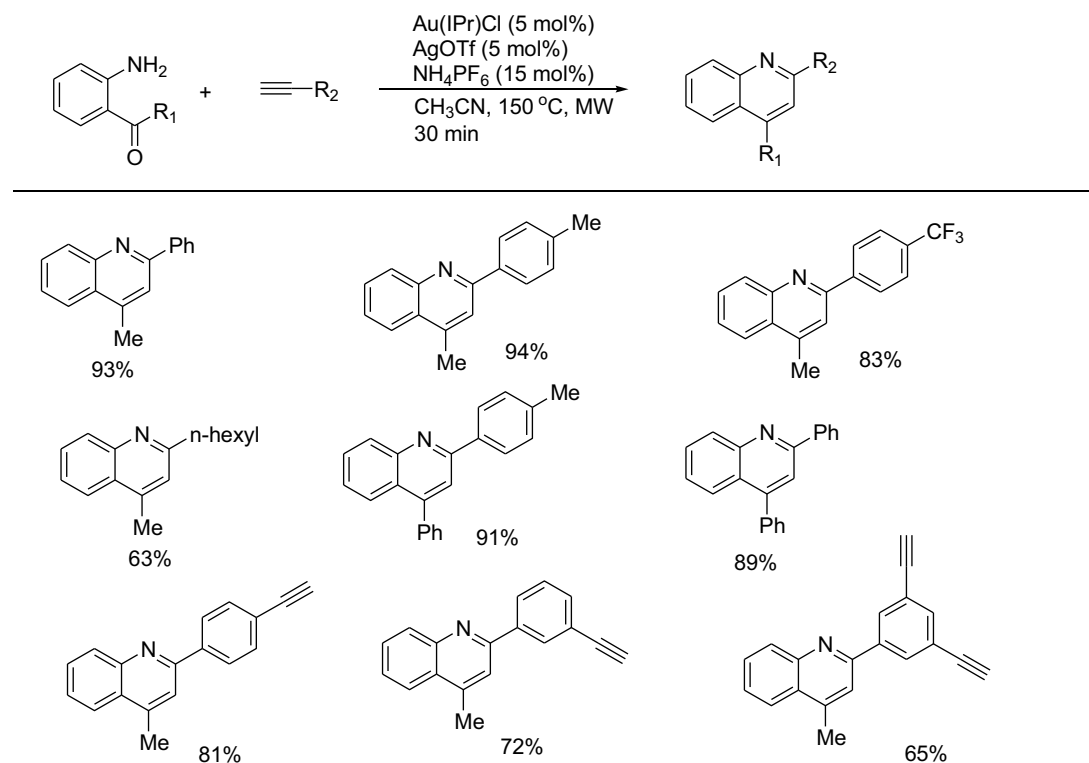
**Scheme 3.** Gold(I)-catalyzed two-component synthesis of quinolines under microwave irradiation.
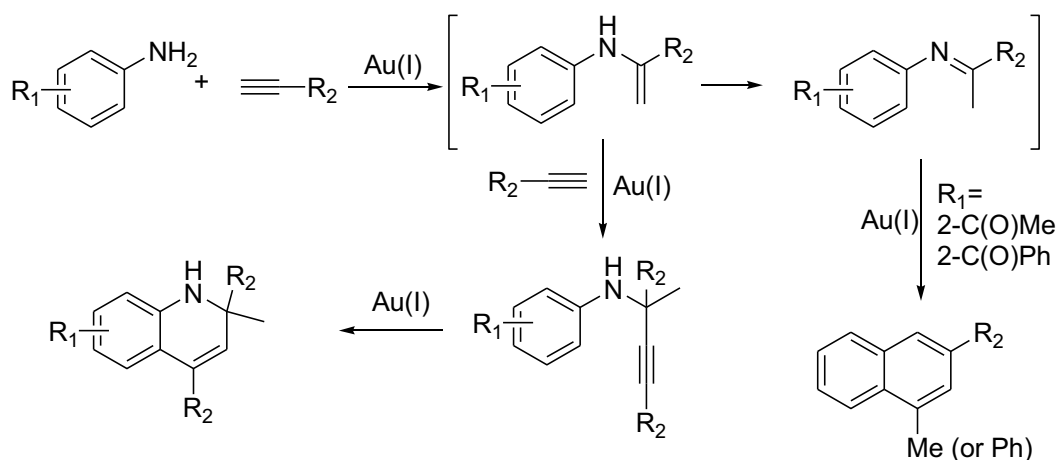
Scheme 4. A plausible mechanism of microwave-assisted gold(I)-catalyzed tandem hydroamination−hydroarylation.

Based on preliminary mechanistic investigations and analyzing previous works on hydroamination reactions, a plausible mechanism was proposed for the synthesis of 1,2-dihydro quinolines and 2,4-disubstituted quinolines through the gold-catalyzed reaction of anilines and alkynes (Scheme **4**). The process involves Au(I) catalyzed activation of alkynes followed by hydroamination of alkynes to generate an enamine intermediate which forms ketimine through tautomerization. Then, the reaction of enamine or ketimine immediately reacts with alkynes to form a propargyl amine intermediate. The intramolecular hydroarylation of the aforementioned intermediate produces 1,2-dihydroquinolines. On the other hand, when ketimine undergoes a condensation/ annulation reaction it produces 2,4-disubstituted quinoline derivatives.

Since the π*-orbital of alkenes are higher in energy level compared to alkynes, the energy gap between the π*-orbital of alkene and HOMO of upcoming nucleophiles is larger compared to the energy gap between π*-orbital of alkyne and the HOMO of upcoming nucleophiles [70]. For this reason, the addition of nucleophiles to an alkene is more difficult compared to alkynes. Thus, the lowering of alkene π*-orbital is necessary to facilitate the nucleophilic addition reaction. For this purpose, a robust and highly carbophilic Lewis acid is required. Like hydroamination of alkynes, the gold catalyst has proved its efficiency for the hydroamination alkenes which has been well documented in several reports [71, 72]. A pleasant report from Che and co-workers described that in presence of a gold catalyst(Au(PR$_3$)Cl) (R= Phenyl or Cyclohexyl) in a combination of AgOTf, alkenes can react through intramolecular tandem isomerization- hydroamination by sulfonamides, aniline derivatives and benzamides under microwave irradiation (Schemes **5** and **6**) [73]. It has been found that tosylamide or O-substituted benzenesulfonamides were transformed to cyclic sulfonamides in excellent yields (95-99%) in the presence of 5 mol% Au(PPh$_3$)Cl/AgOTf catalyst in toluene solvent at 100°C during 12-24h reaction time. Notably, longer reaction time (72h) was required for the intramolecular hydroamination of aliphatic alkenes with sulfonamides, but the dramatic acceleration of reaction was observed under microwave irradiation where 10-40 mins were required for completion of reactions. Also, gold-catalyzed intramolecular hydroamination of benzamides produced the corresponding cyclic products in moderate to good yields(50-90%) during the 13h reaction time at 100°C. Here also, shortening of reaction time from 30h to 30 minutes was observed upon the treatment of the reaction mixture under microwave irradiation affording cyclic products in 57- 60% isolated yields. Similarly, gold-catalyzed intramolecular hydroamination of alkenes with sulfonyl amides provides the products in good yields under microwave irradiation for 40 minutes.

After the success of the aforementioned intramolecular hydroamination of alkenes, Che *et al.* broadened the reaction scope of this type of Lewis acid-catalyzed nucleophilic addition to alkenes from hetero-atom nucleophiles to carbon nucleophiles. Using Au(PPh$_3$)Cl/AgOTf catalytic system, the addition of indoles towards alkenes in intramolecular fashion was developed (Scheme **7**) [74]. The intermolecular hydroarylation of aryl alkenes or conjugated dienes with indoles was achieved in excellent yields through the reaction at the C-3 position of indoles in the presence of 2-5 mol% Au(PPh$_3$)Cl/AgOTf under microwave irradiation in 1,2-dichloroethane affording the desired product in moderate to excellent yields (42-90%) compared to low yield and necessity of longer reaction time under conventional heating. In the case of substrate allylbenzenes, gold-catalyzed migration of the C=C bond takes place and as a result, trans-β-methyl styrenes were formed in situ under the experimental conditions which further react with indole derivatives to furnish the hydroarylation products. The preliminary mechanistic investigation including deuterium labeling experiments recommends a three steps mechanism that is, firstly π-bond of alkene moiety was co-ordinated by the cationic [Au(PPh$_3$)]$^+$ species thus electrophilicity of the alkene was increased by lowering the energy of π*-orbital of alkenes. Secondly, the nucleophilic addition of indoles to gold activated alkene generates organogold(I) intermediate. Now lastly, the proto-deauration of the formed organogold(I) intermediates provides the desired product and releasing the actual catalyst,
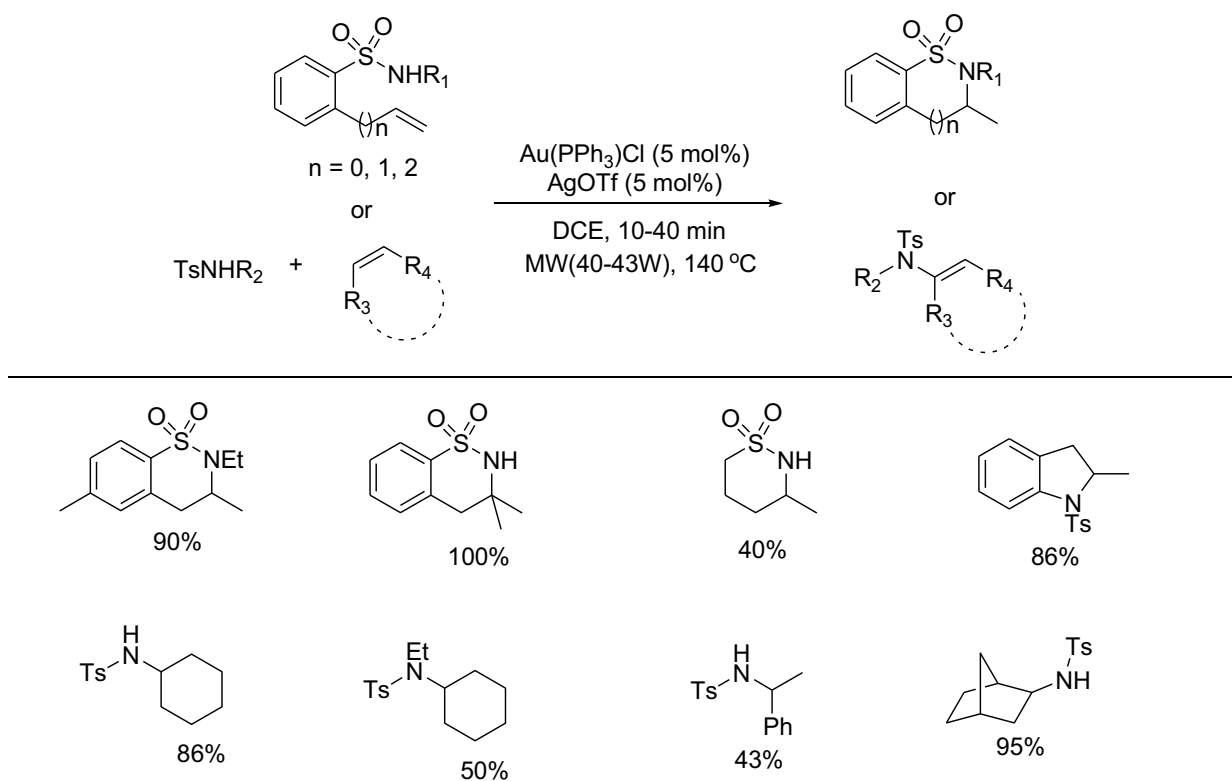
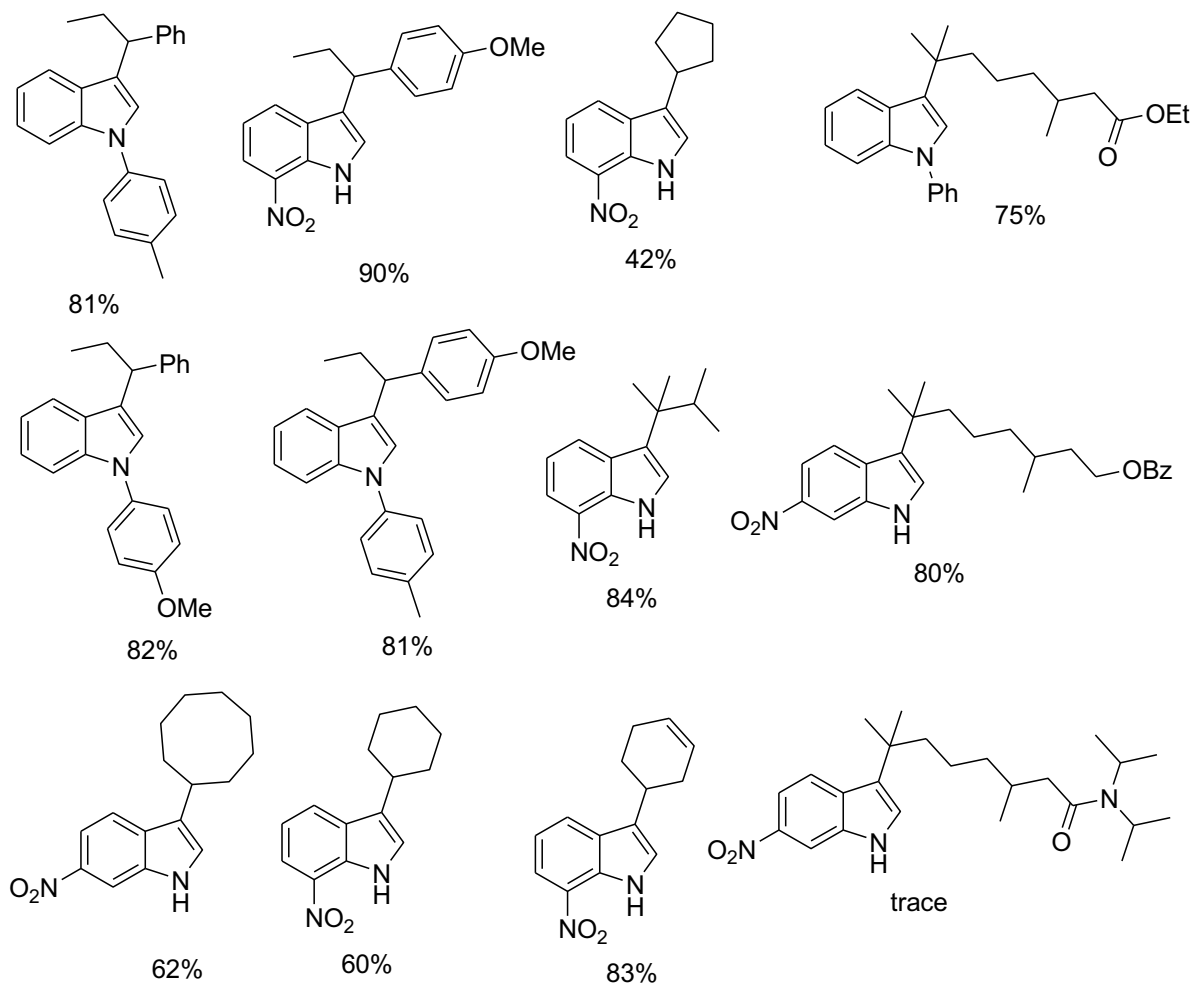**Scheme 5.** Gold catalyzed hydroamination of alkenes under microwave conditions.
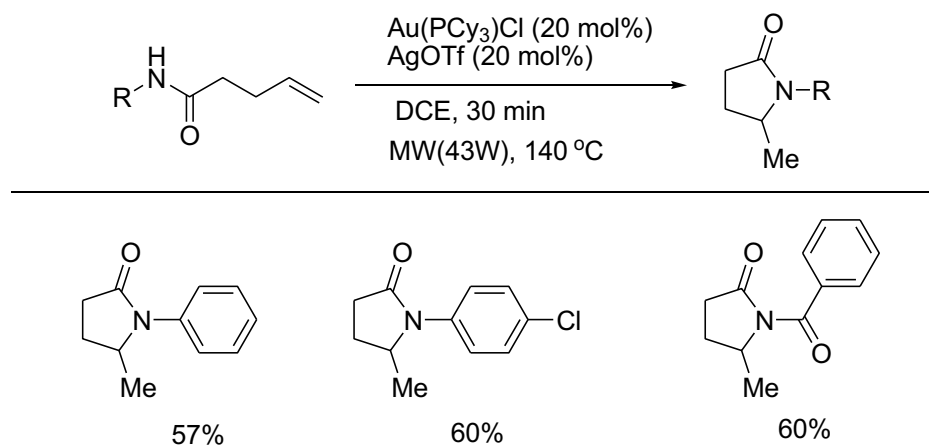

Scheme 6. Intramolecular hydroamination of amides under microwave conditions.

i.e. cationic $[Au(PPh_3)]^+$ species for the next catalytic cycle (Scheme **8**).

Echavarren *et al.* reported a significant article about cationic gold(I) catalyzed intramolecular [4 + 2] cycloaddition of both alkenyl and aryl-substituted enynes to produce the bicyclic and tricyclic compounds, respectively (Scheme **9**) [75]. Compared to conventional heating, the employment of microwave irradiation leads to shortening of the reaction times, and provides greater yields and high regioselectivity. Intramolecular cycloaddition of 1,8-diene-3-yne derivatives through the 5-exo-dig pathway produces hydrindanes. On the

other hand, under this protocol, 1,6-enynes containing an aryl ring provides 2,3,9,9a- tetrahydro-1H- cyclopenta[b] naphthalenes through a 5-exo-dig cyclization followed by a Friedel-Craft-type ring expansion. Interestingly, in some cases, a 6-endo-dig cyclization was observed as a less favorable process mostly, whereas this pathway was found to be major in a few cases.

In 2011, Najera *et al.* reported a comparative study between gold (I) and silver catalyzed hydroamination of inactivated alkenes and dienes using NH-nucleophiles like sulfonamides, anilines, and carbamates under microwave condition
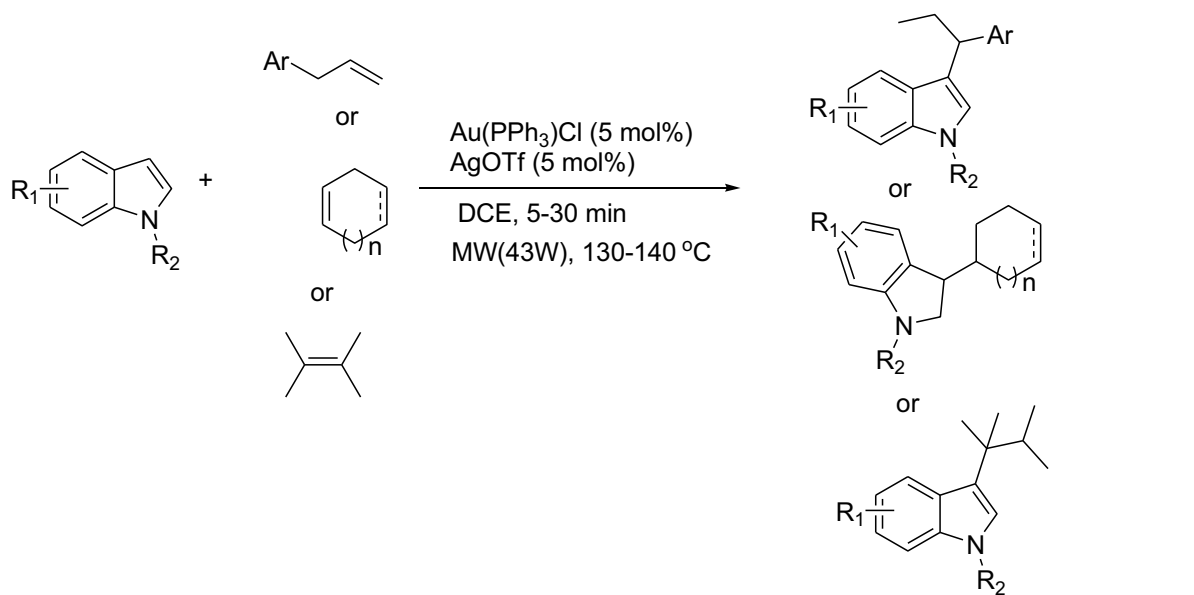
Scheme 7. Gold-catalyzed hydroarylation of indoles with alkenes under microwave conditions.
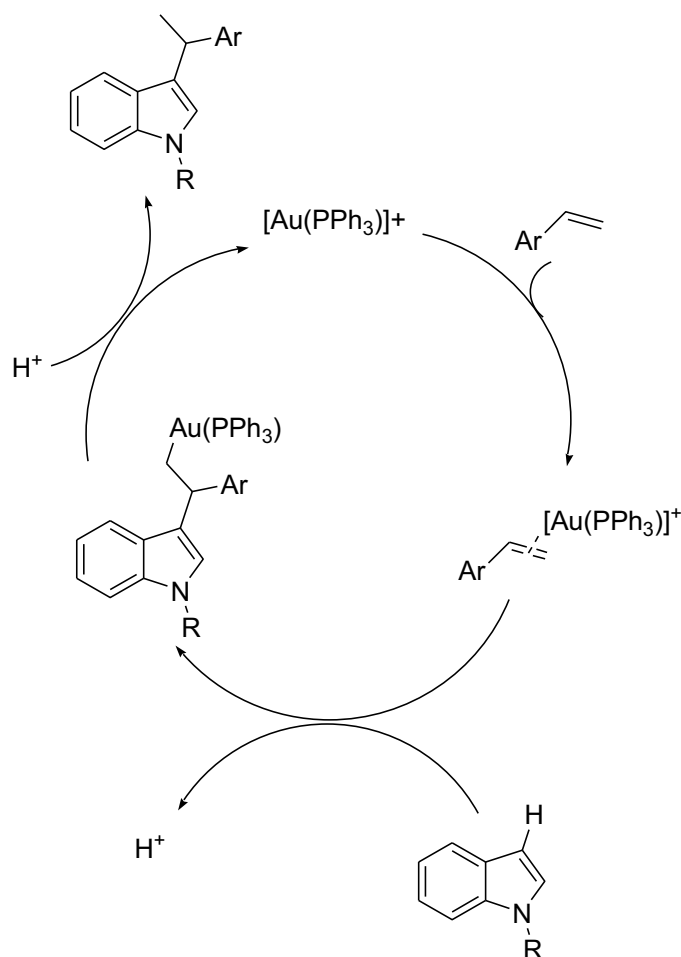
**Scheme 8.** Proposed mechanism of gold(I)-catalysed hydroarylation of styrene derivatives with indoles.

(Scheme **10**) [76]. This study revealed that gold-catalyzed reactions show high turnover compared to silver salts, as higher catalyst loading was required to carry out the reaction. Terminal alkenes, except styrenes, were found to be unsuitable substrates for the silver catalyzed hydroamination reaction contrary to the gold-catalyzed reaction where the aforementioned substrates would easily provide the desired products in good to excellent yields.

In 2013, Stockland *et al.* synthesized various aryl gold compounds under microwave conditions and utilized them to investigate single-component catalysis for hydrophenoxylation of a variety of inactivated internal alkynes (Scheme **11**) [77]. Sterically and electronically diverse phenolic compounds were efficiently added to alkynes in the presence of a gold catalyst containing Johnphos or IPr/SIPr ligands under either microwave or conventional heating and afforded moderate to excellent yields of the vinyl ethers. Lack of necessity of silver salts, acids, or solvent makes this protocol highly appreciable to the chemical community.

Wenzel *et al.*, in 2015, reported a gold-catalyzed, SN¹-type reaction of alcohol to directly afford unsymmetrical ethers (Scheme **12**) and Cbz-protected amines (Scheme **13**) under microwave conditions [78]. The high reproducibility,

toleration of moisture, and moderate to excellent product yields (53–99%) under mild reaction conditions make it more attractive for the synthetic community. Interestingly, it was observed that no symmetric ether was formed under this protocol. Toleration of electronically and structurally diverse wide range of alcohols for the etherification reaction shows the large scope of this method. Notably, gold-catalyzed intermolecular direct amination of alcohols for the synthesis of carbamate-protected amines was unprecedented before this report.

Praveen and co-workers have reported practical and highly efficient double condensation reactions between isatin and 4-hydroxycoumarin in the presence of a gold catalyst under microwave irradiation to obtain spirooxyindoles (Scheme **14**) [79]. Improvement of the product yield from 10% to 79% as well as shortening of the reaction time from 1-2h to 15 minutes was observed moving from conventional heating to utilization of microwave condition in ethanol solvent. High yields, clean reaction, short reaction time, and easy separation of product from the reaction mixture by simple filtration without the necessity of tedious column chromatography make this protocol very much attractive. Investigation of bioactivity of the prepared spirooxindoles [pyrano- bis-2H-1- benzopyrans] revealed that some of the compounds
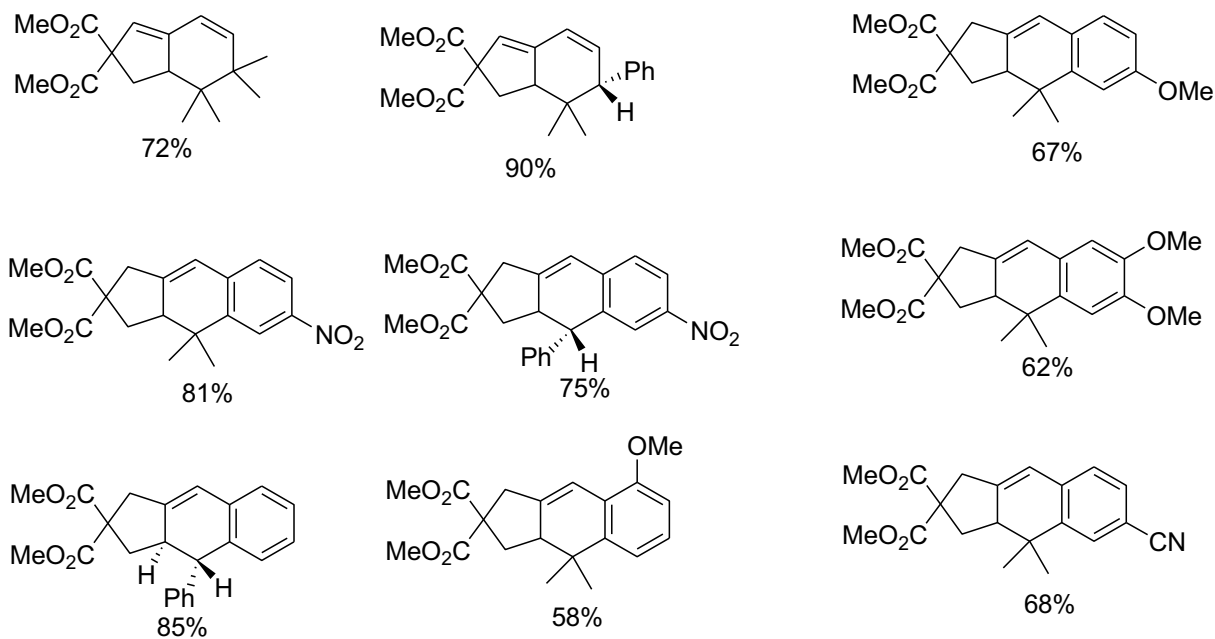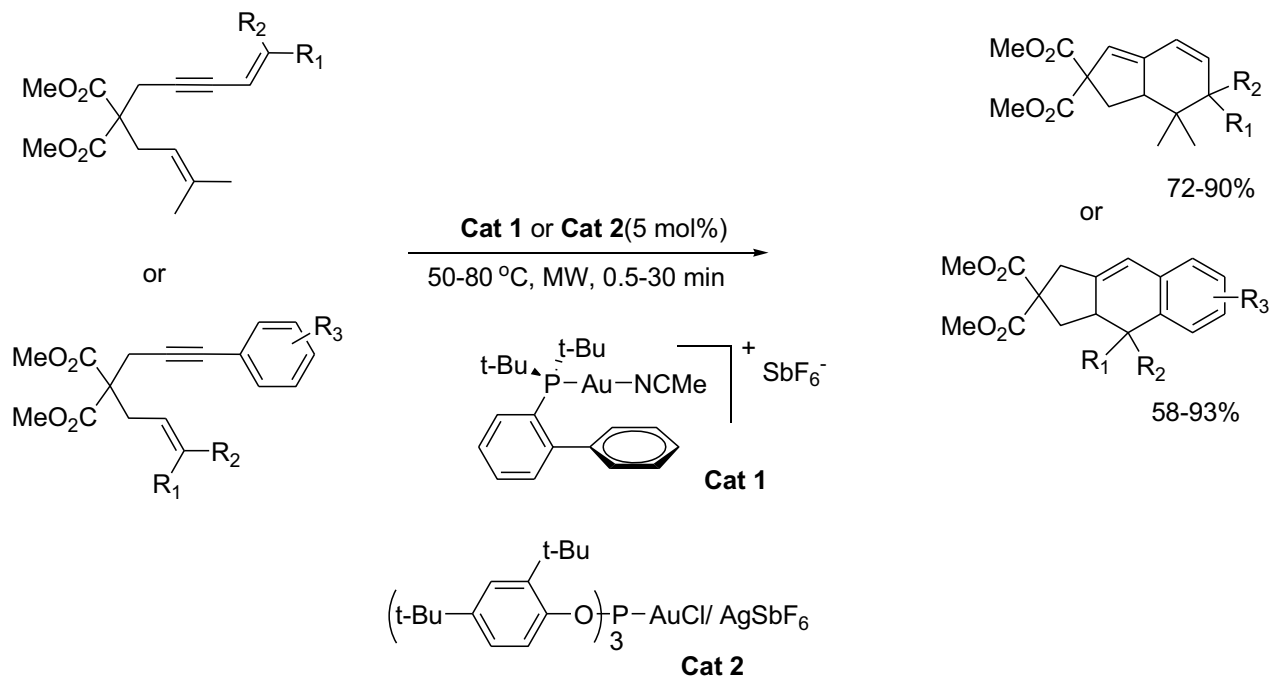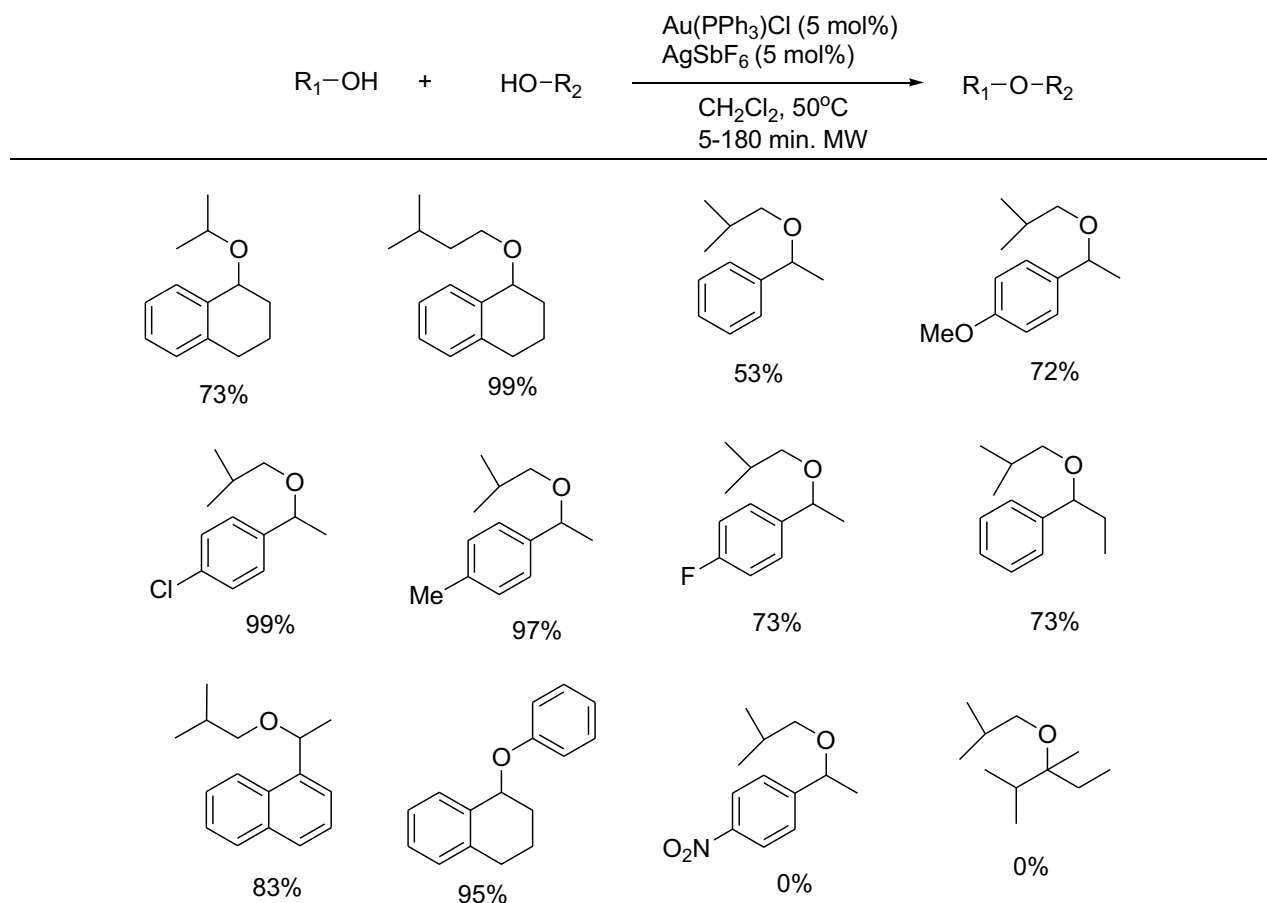
Scheme 9. Microwave-assisted gold-catalyzed intramolecular [4 + 2] cycloaddition of alkenyl- and aryl-substituted enynes.
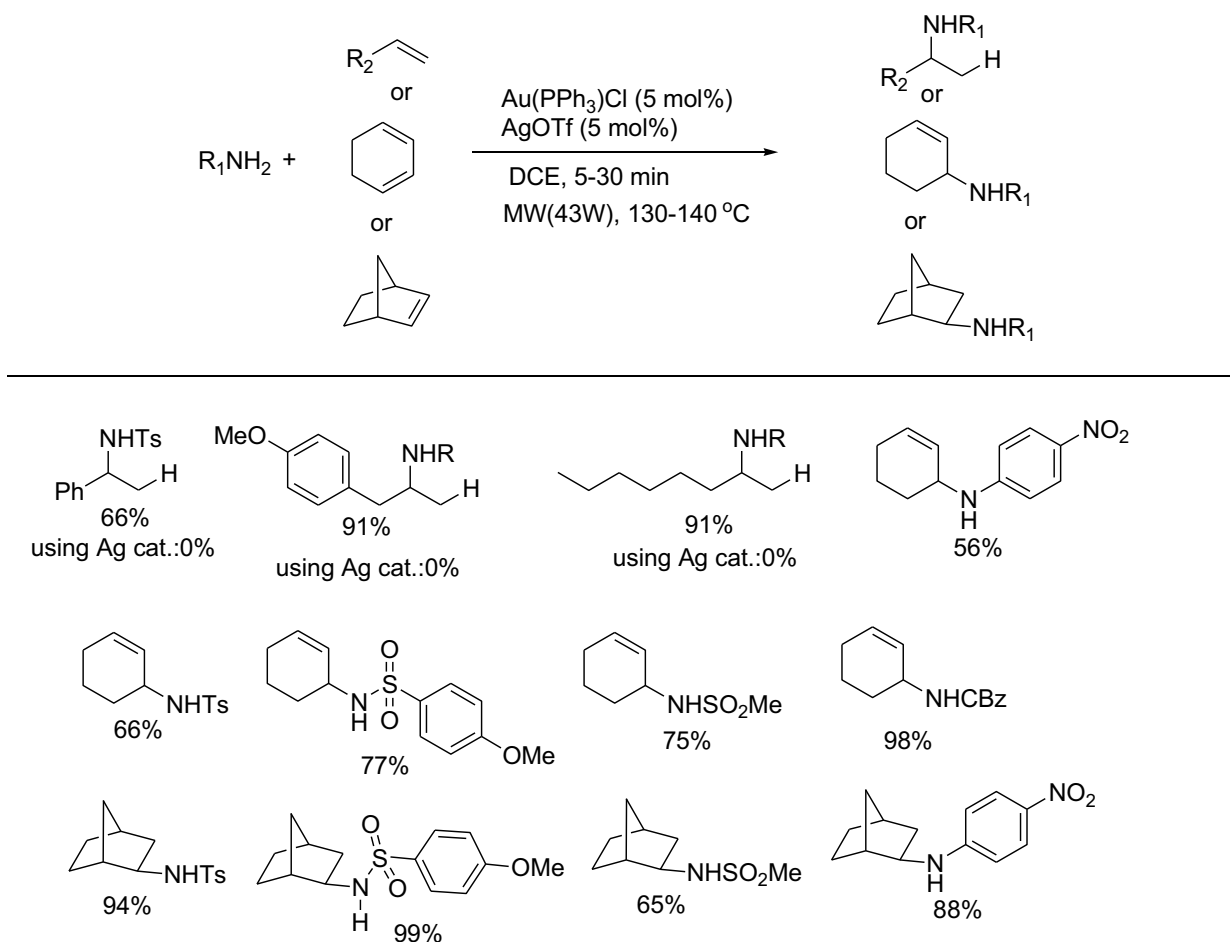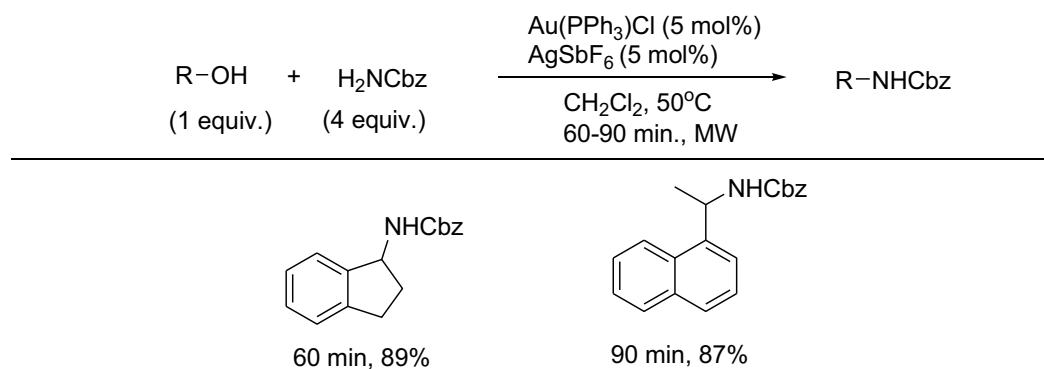
Scheme 10. Hydroamination of alkene, norbornene, and 1,3-cyclohexadiene with different nucleophiles.
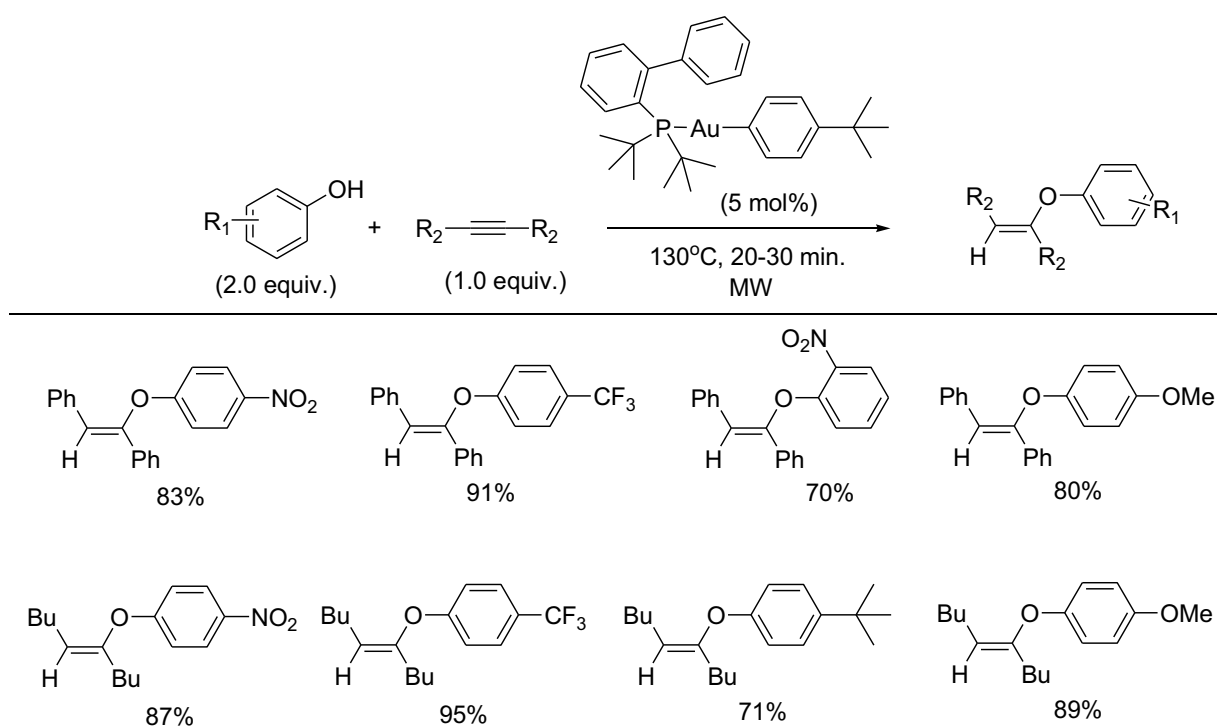
Scheme 11. Gold catalyzed hydrophenoxylation of alkynes under microwave conditions.

$$R_1\text{—OH} \quad + \quad HO\text{—}R_2 \xrightarrow[\substack{CH_2Cl_2,\ 50^oC \\ 5\text{-}180\ \text{min. MW}}]{\substack{Au(PPh_3)Cl\ (5\ mol\%) \\ AgSbF_6\ (5\ mol\%)}} R_1\text{—O—}R_2$$

73% 99% 53% 72%

99% 97% 73% 73%

83% 95% 0% 0%

Scheme 12. Gold-catalyzed SN^1-type reaction of alcohols under microwave conditions.

$$R\text{—OH} \quad + \quad H_2NCbz \xrightarrow[\substack{CH_2Cl_2,\ 50^oC \\ 60\text{-}90\ \text{min., MW}}]{\substack{Au(PPh_3)Cl\ (5\ mol\%) \\ AgSbF_6\ (5\ mol\%)}} R\text{—NHCbz}$$

(1 equiv.)   (4 equiv.)

60 min, 89%   90 min, 87%

Scheme 13. Gold-catalyzed amination of alcohols under microwave conditions.

show strong anti-microbial activity against a wide panel of microbial strain. All the product molecules were examined for their cytotoxic potency against COLO320 cancer cells and found that nitro-compound (shown in dashed box) exhibited significant inhibitory activity with an IC$_{50}$ value of 50.0μM.

Sutherland and Lee *et al.* reported the ipso-iododeboronation reactions with N-iodosuccinimide(NIS) in the presence and absence of gold catalyst and green solvent, dimethyl carbonate under microwave conditions (Scheme 15) [80]. The gold-catalyzed reaction was highly favored for aryl boronic acid substrates which were electron-deficient and sterically hindered. On the other hand, the uncatalyzed reaction resulting in very poor yields proved the significance of the use of a gold catalyst. The gold-catalyzed reaction also produced considerably higher yields for iododeboronation of electron-rich boronic acid substrates than the uncatalyzed procedure. Although, heterocyclic and N-containing aryl boronic acids reacted more effectively under uncatalyzed reaction conditions for these transformations.
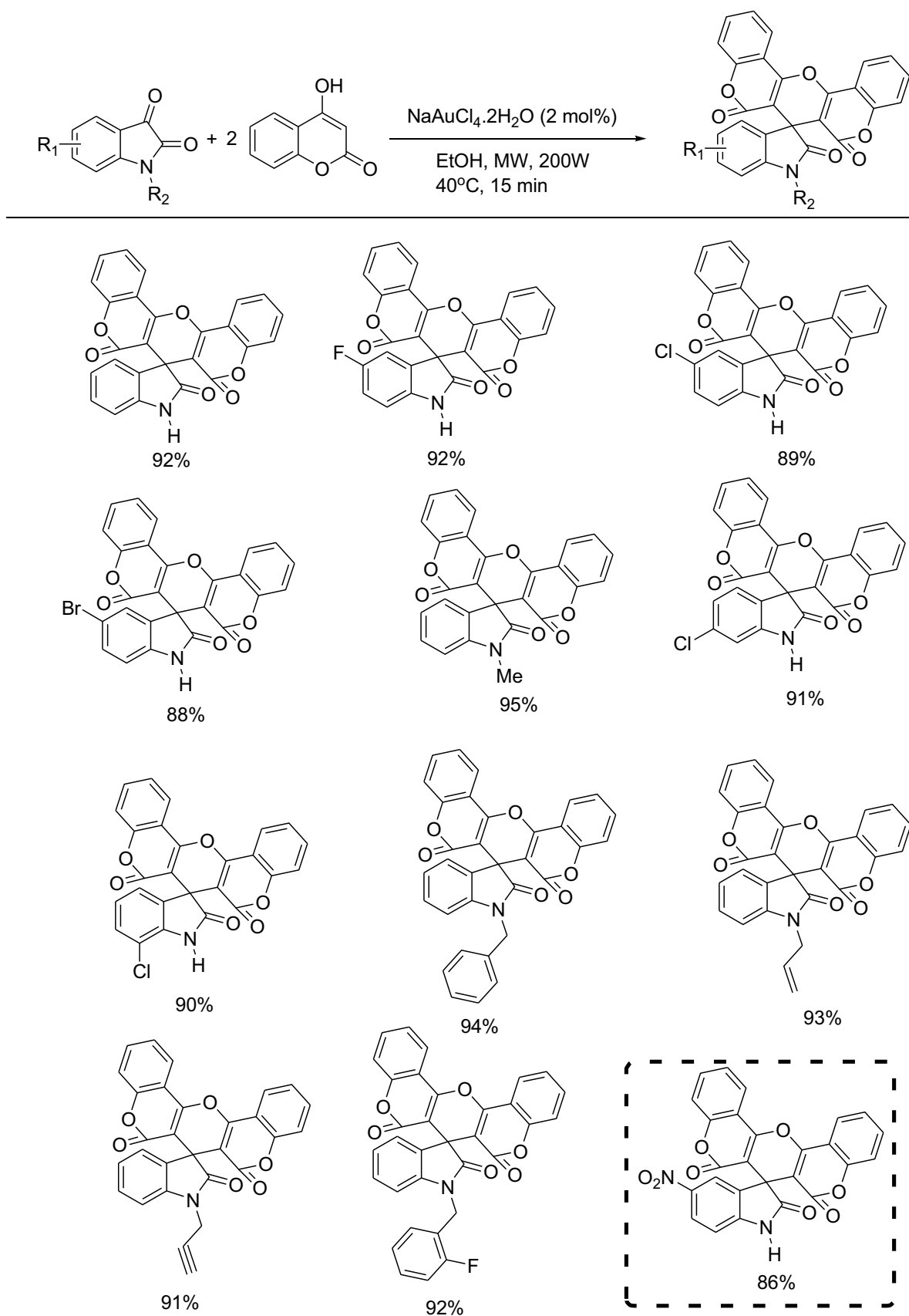
Scheme 14. Gold-catalyzed synthesis of spirooxindoles under microwave conditions.
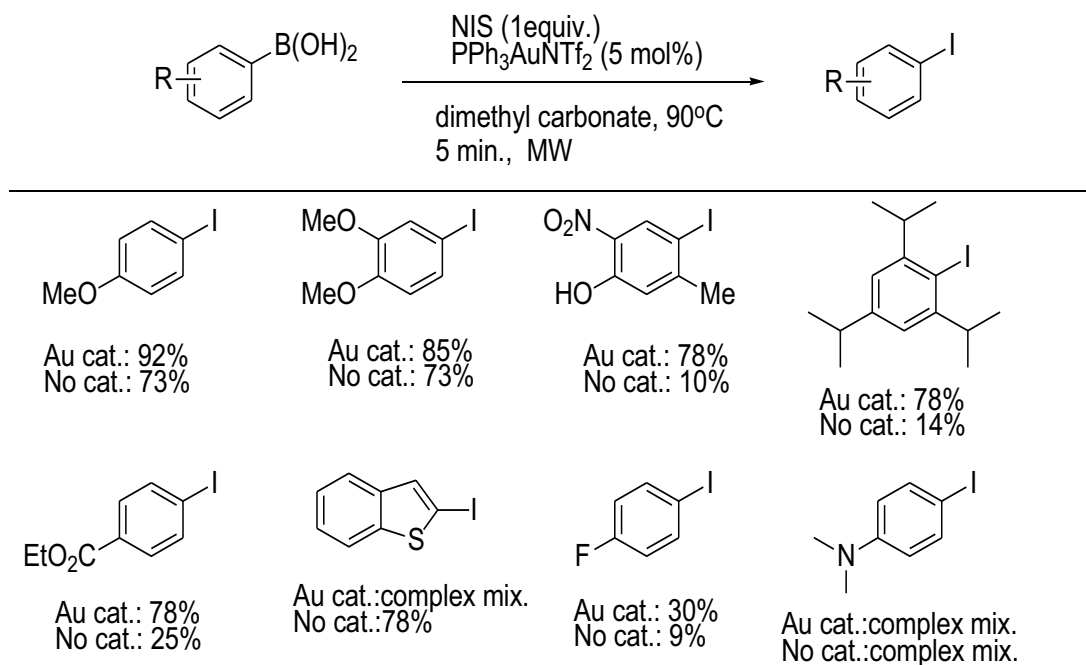
Scheme 15. Iododeboronation with and without a gold catalyst.
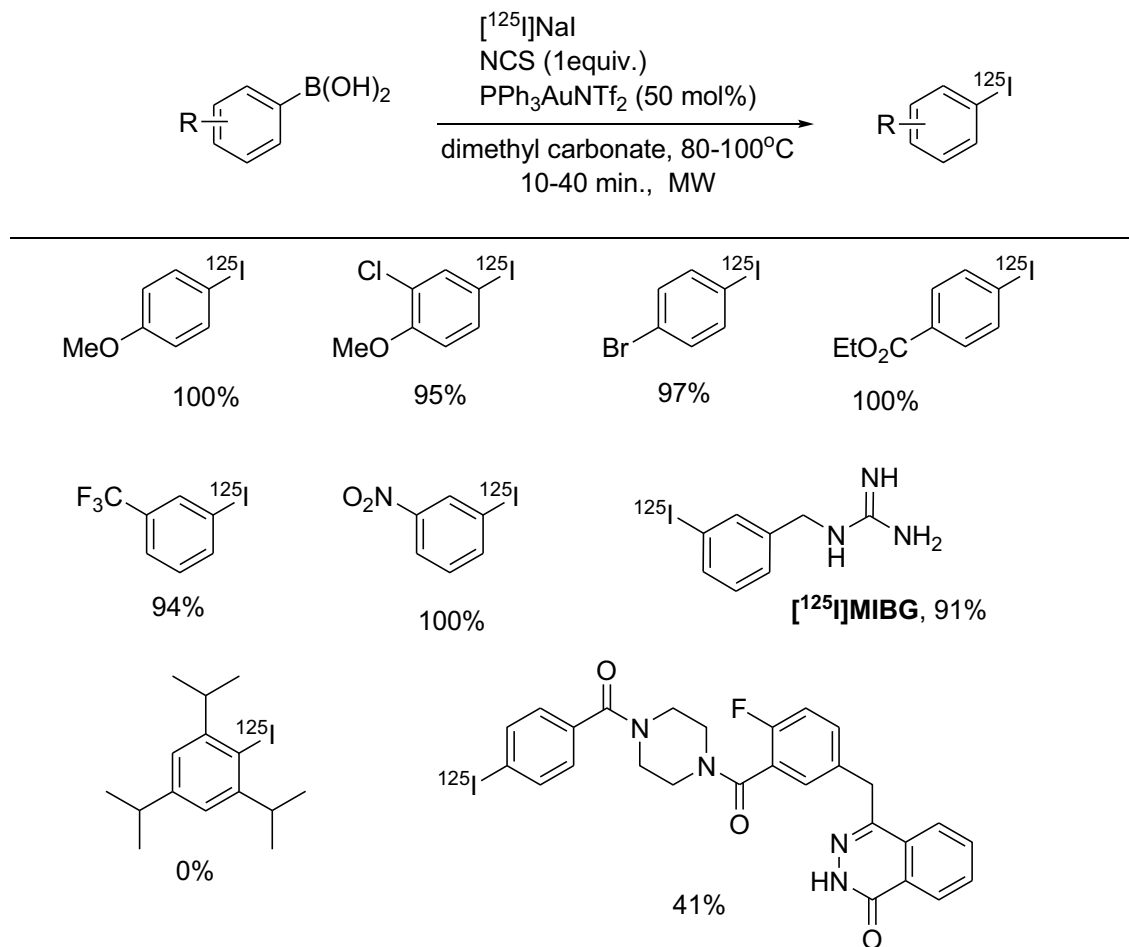
Scheme 16: Microwave-assisted gold-mediated radioiodododeboronation.

Additionally, halogen moieties (Br and Cl) are well tolerated under these reaction conditions, which is useful for further derivatization. The fast reaction and mild experimental conditions of the gold-catalyzed iododeboronation reaction were found to be comfortable for the I-labeling method for arenas and authors have claimed that this is the earliest application to selective radiosynthesis catalyzed by the homogeneous gold catalyst. In this protocol, both electron-rich and electron-poor aryl boronic acids were efficiently converted to the radioiodinated products with excellent radiochemical yields (Scheme **16**). It is well known that, in nuclear medicine, for drug development and disease diagnosis, radiopharmaceuticals containing radioactive iodine in association with single-photon emission computed tomography imaging perform a vital role. An important radiopharmaceutical, namely meta-[^{125}I]iodobenzylguanidine ([^{125}**I**]**MIBG**) used for the imaging and therapy of human norepinephrine transporter-expressing tumors [81-83], was prepared in this microwave-assisted gold-catalyzed iododeboronation reaction conditions.

CONCLUSION AND PERSPECTIVE

Microwave chemistry is an emerging area of science, mainly focusing on the various applications of microwave energy to chemical processes. Microwave irradiation has enormous potential to provide controlled energy directly to the molecules of interest. Over the last few years, the advancement of microwave chemistry has been witnessed in the literature. In near future, it is possible to develop robust microwave-assisted methods for almost every reaction which needs an external heat source and this article represents that the gold-catalyzed reactions can be conducted very efficiently and successfully under microwave conditions. The single-mode microwave irradiation heating allows for easily adjustable and regulated bulk heating that can be done safely and with very low energy consumption. The synthetic chemist can enjoy the benefits of the unique reactions of carbon-carbon bond formation offered by organometallic chemistry that enables the reaction to occur in seconds or minutes, which is a significant achievement since other transition-metal-catalyzed reactions are time-consuming.

Gold complexes have proved to be more effective than other transition metals in various transformations, leading to improved yields and selectivities. They have also shown some very particular properties, making possible new mechanistic pathways and exhibiting sometimes a distinct reactivity. The examples described suggest that the combined perspective of microwave heating and homogeneous gold catalysis can be an almost synergistic approach, in the sense that the combination as such has more potential than its two separate sections alone. However, there are also many other catalytic reactions with significant potential for microwaves heating. For example, it could be anticipated that growing numbers of gold-catalyzed reactions could well respond to microwave heating. In the high-speed generation of combinatorial libraries, it is already clear that modern automated microwave synthesizers have a lot to offer. New research on this subject will possibly include an in-depth analysis of the interaction of microwaves with materials of various chemical natures (solvents, analytics, and structural features of microwave systems) and work on the effects of microwave's physical properties (frequency and intensity) on chemical transformations both in homogeneous and heterogeneous systems [84-86].

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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