METAL-CATALYZED FURAN SYNTHESIS. A REVIEW

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Introduction

Furans are five-membered aromatic heterocycles containing one oxygen atom that are commonly found in many important compounds such as natural products, pharmaceuticals and polymers.[1] Moreover, furans can be utilized as synthetic intermediates to access other useful compounds.[2-6] The synthesis of this fundamental structural building block has received significant attention and a wide variety of approaches are available to the synthetic practitioner.[7-10] This review highlights metal-catalyzed furan syntheses that have been reported over the past decade. It is not intended to be exhaustive but rather all of the fundamentally different approaches are covered.

There are two main strategies to the synthesis of substituted furan rings. The first involves the construction of the ring itself, and the second approach is the functionalization of already prepared furan rings. This review focuses exclusively on the former case and includes a few judiciously chosen experimental procedures.

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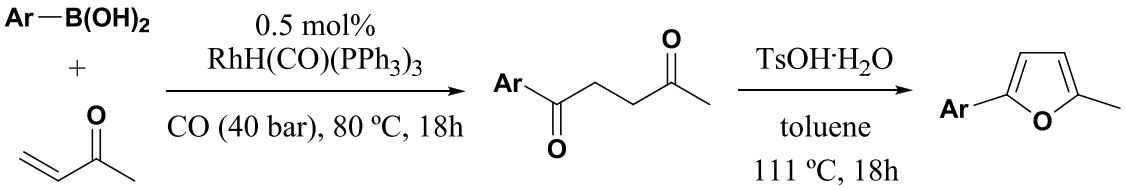
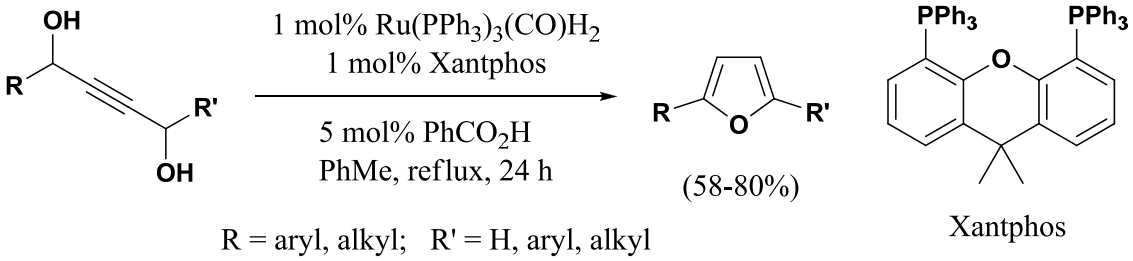
I. Synthesis of Disubstituted Furans

The classical approach to the synthesis of furans is the cyclization of 1,4-diketones mediated by strong mineral acids. This is commonly referred to as the Paal-Knorr reaction.[11,12] The limited availability of different 1,4-diketones and the requirement for a strong acid are both limitations of this procedure. Accordingly, one-pot procedures for the synthesis of furans *via* the metal-catalyzed formation of 1,4-diketone intermediates have been developed. For example, Castanet and co-workers have reported the rhodium-catalyzed carbonylative conjugate addition of arylboronic acids to methyl vinyl ketone to generate 1,4-diketones which are then cyclized to furans on addition of acid (*Scheme 1*).[13]



Scheme 1

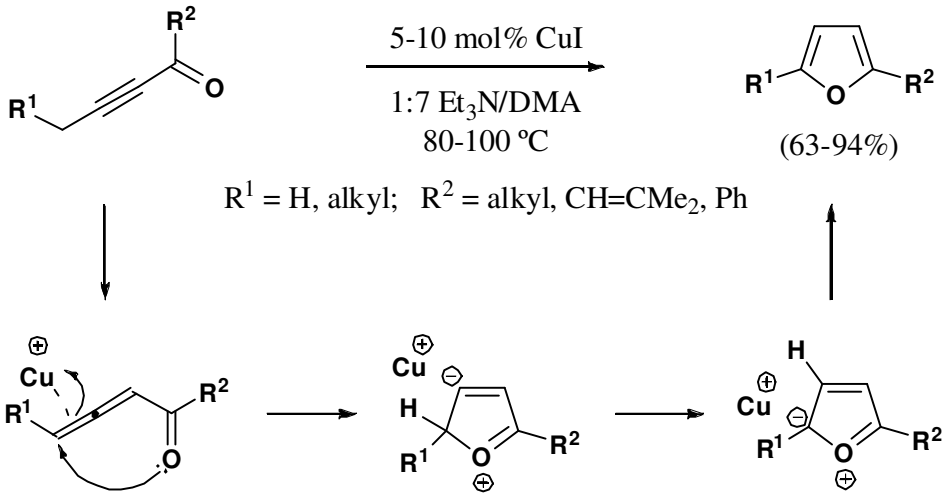
Williams *et al.* demonstrated the ruthenium-catalyzed isomerization of 1,4-alkynediols and their subsequent cyclization into furans (*Scheme 2*).[14] However, the corresponding fully saturated 1,4-diketones were also isolated along with the furans, but in most cases the furan was the major product.



R = aryl, alkyl; R' = H, aryl, alkyl

Scheme 2

A host of other approaches to furan synthesis from alkyne containing substrates have been described in the literature. Gevorgyan has been particularly focused on furan formation and his group has produced a number of different approaches to their preparation (*vide infra*). Starting from alkynyl ketones, they showed that copper(I) iodide efficiently catalyzed the cycloisomerization to furans (*Scheme 3*).[15] A triethylamine-Cu(I)-catalyzed isomerization of the alkynyl ketone to an allenyl ketone occurs followed by cyclization *via* attack of the carbonyl oxygen onto the allene. This intermediate undergoes a deprotonation-protonation isomerization into a more stable isomer which then converts into the furan product. Marshall and co-workers reported the Rh(I)- and Ag(I)-catalyzed cycloisomerization of allenyl aldehydes and ketones.[16,17] Hashmi *et al*. have also described the palladium-catalyzed cycloisomerization of allenyl ketones into 2,4-disubstituted furans and undertaken significant mechanistic studies.[18]



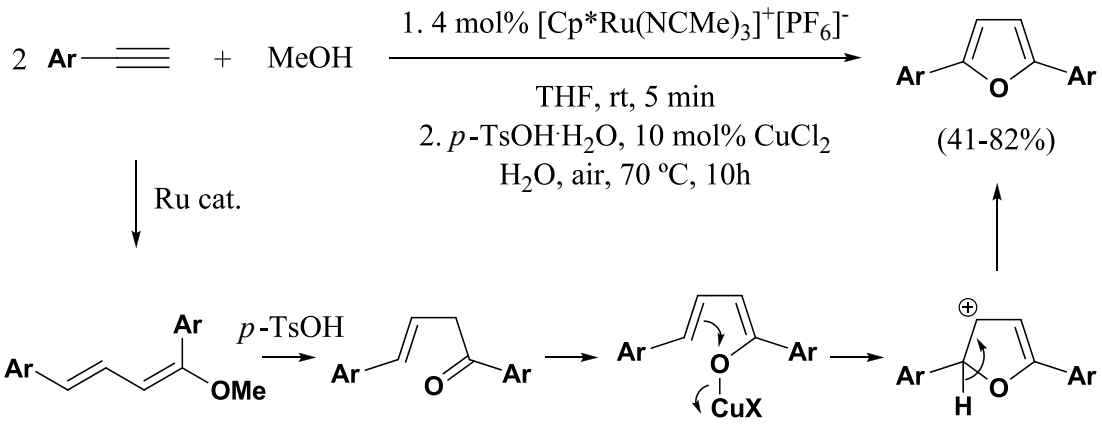
Scheme 3

Representative procedure for the CuI-catalyzed synthesis of 2-hexyl-5-methoxyfuran.[15]

A mixture of 1-methoxydec-2-yn-4-one (182 mg, 1 mmol), CuI (9.6 mg, 0.05 mmol), anhydrous DMA (2.2 mL), and Et_3N (0.3 mL) was stirred in a Wheaton microreactor (3 mL) under argon atmosphere at 80 °C for 3 h. The mixture was cooled, diluted (water, 15 mL), and extracted with hexane. Combined organic extracts were filtered (anhydrous Na_2CO_3), concentrated under

reduced pressure, and chromatographed over a short column (alumina; hexane as eluent) to provide 2-hexyl-5-methoxyfuran (142 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.81 (dd, 1H, J = 2.4, 0.9 Hz), 4.99 (d, 1H, J = 3.0 Hz), 3.80 (s, 3H), 2.49 (t, 2H, J = 7.9 Hz), 1.52-1.65 (m, 2H), 1.24-1.37 (m, 6H), 0.88 (t, 3H, J = 6.9 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 160.7, 146.8, 105.6, 79.6, 58.0, 32.0, 29.2, 28.4 (x2), 23.0, 14.5; MS m/z (relative intensity) 182 (M^+, 10), 111 (100); $C_{11}H_{18}O_2$.

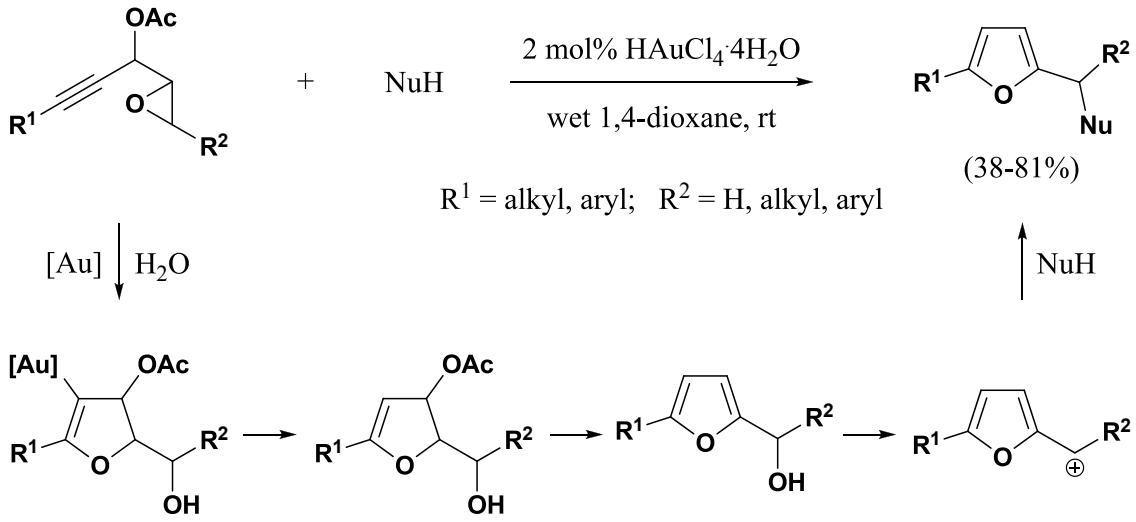
Beller and Dixneuf disclosed a sequential one-pot ruthenium- and copper-catalyzed furan synthesis (*Scheme 4*). In this protocol, two alkyne molecules and an alcohol are combined under ruthenium catalysis to generate a 1,3-dienyl ether, in just five minutes. This is converted into the ketone by the acid and then cyclized to the furan by the copper(II) salt; only symmetrical furans can be prepared by this route.



Scheme 4

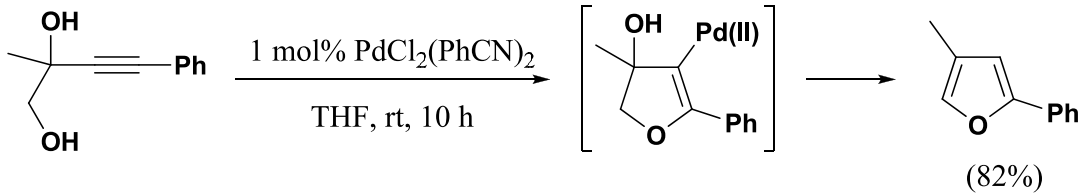
Liang and co-workers reported a gold-catalyzed approach to furans from 1-oxiranyl-2-alkynyl esters and a range of nucleophiles including alcohols, furans and pyrroles (*Scheme 5*).[19,20] The reaction is proposed to proceed through activation of the alkyne by the gold species followed by nucleophilic attack by the epoxide oxygen with either pre- or post-opening of the three-membered ring with water. Protiodeauration and aromatization through loss of acetic acid provides the furan ring which loses water by gold catalysis to generate a carbocationic intermediate which is trapped

by a nucleophile. This reaction was shown to have a reasonably wide substrate scope and it generally works quite well; however, the synthesis of the starting materials is lengthy.



Scheme 5

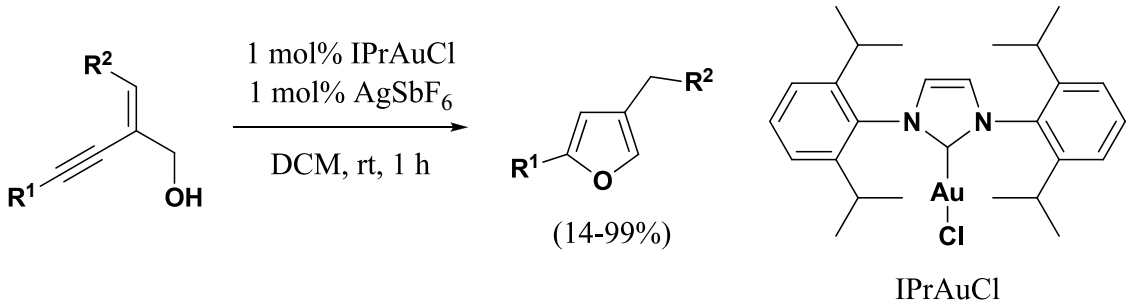
A related reaction was disclosed by Utimoto *et al.* in 1985, whereby furans were formed by a palladium(II)-catalyzed cyclodehydration of 3-alkyn-1,2-diols (*Scheme 6*).[21] The reaction is proposed to proceed by activation of the alkyne by Pd(II), followed by cyclization *via* attack of an hydroxyl group. Protonolysis and dehydration then yield the furan. This reaction can also be effected by various other metal catalysts including Mo,[22,23] Ag,[24] Ru, [25] Au[26,27] and Cu salts.[28]



Scheme 6

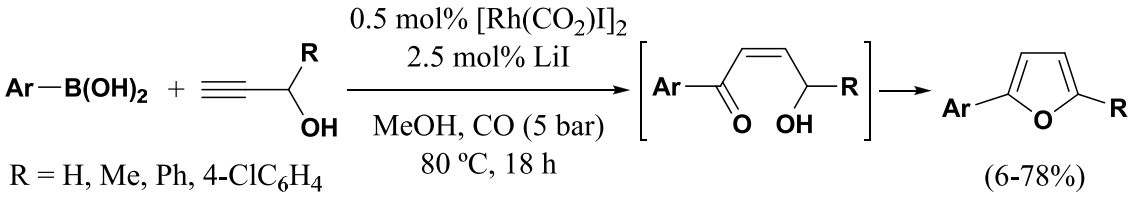
Another popular route for furan synthesis is the cyclization of readily prepared 2-alkynylallyl alcohols. A variety of metals have been utilized as catalysts for this reaction including Mo,[29] Pd,[30]

Ag[31] and Au[32] salts. Notably, Hashmi has developed very mild conditions for this process utilizing a Au(I) catalyst at room temperature (*Scheme 7*).[33] Note that trisubstituted furans can be readily prepared by this method with appropriately substituted substrates.



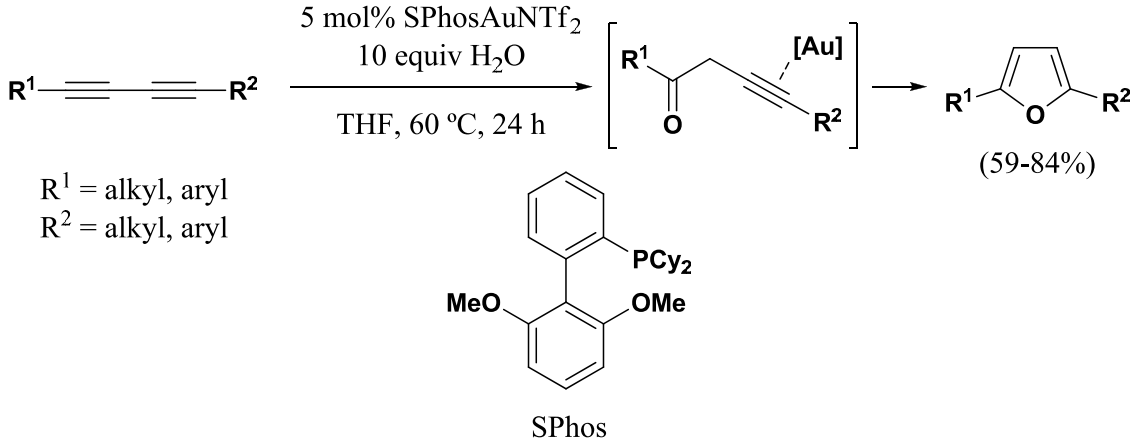
Scheme 7

Sauthier, Castanet and co-workers developed a rhodium-catalyzed carbonylative addition-cyclization approach to furans formed by a dehydrative cyclization of *in-situ* generated hydroxy enones (*Scheme 8*).[34] This reaction was shown to work well apart from with substrates containing aryl groups bearing *ortho* or *meta* substituents; presumably unfavorable steric interactions are to blame here.



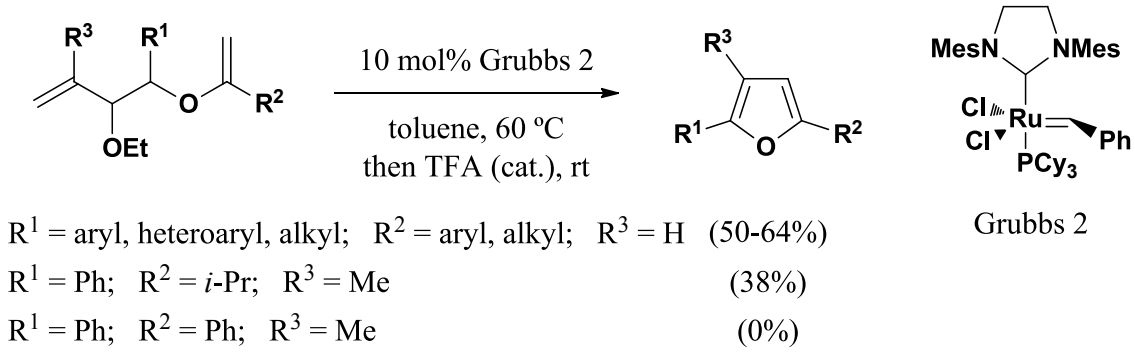
Scheme 8

An interesting study was reported by Skrydstrup and co-workers on the gold(I)-catalyzed synthesis of furans by the hydration of 1,3-diynes and subsequent cyclization (*Scheme 9*).[35] A more recent study into this process has been undertaken by Nolan using his Au(IPr)OH pre-catalyst.[36] Experimentation has shown that only one alkyne is hydrated before cyclization occurs.



Scheme 9

Donohoe and co-workers reported a ring-closing metathesis approach to the construction of furans using Grubbs' second generation catalyst (*Scheme 10*).[37] The cyclization is shown to occur in moderate yields for all of the reported examples, however when $R^2 = CF_3$ no reaction occurs and the preparation of the diene substrates requires three steps. Attempts to obtain trisubstituted furans by this method were less successful with one reaction failing and a second providing only a low yield of product.

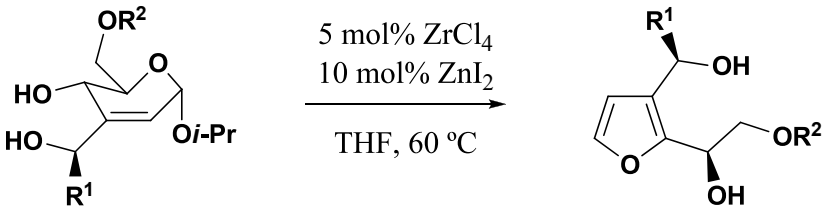


R^1 = aryl, heteroaryl, alkyl; R^2 = aryl, alkyl; R^3 = H (50-64%)
R^1 = Ph; R^2 = *i*-Pr; R^3 = Me (38%)
R^1 = Ph; R^2 = Ph; R^3 = Me (0%)

Scheme 10

An alternative approach to furan synthesis from hex-2-enopyranoside derivatives was disclosed by Shaw and co-workers.[38] Inexpensive D-glucal can be converted in several steps into

substituted hex-2-enopyranosides which can be rearranged to furans upon treatment with catalytic zirconium chloride and zinc iodide (*Scheme 11*). The authors do not propose a mechanism, but a Lewis acid catalyzed ring-opening ring-closing aromatization sequence seems likely. While this appears to be an inexpensive and efficient route to enantiomerically pure furan derivatives, a relatively large number of synthetic steps are required.

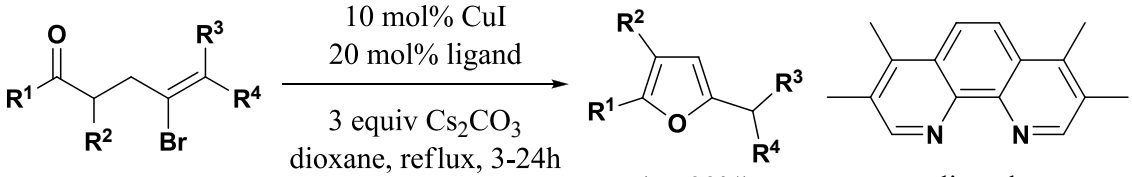


R^1 = alkyl, aryl; R^2 = Piv, Ac (74-86%)

Scheme 11

II. Synthesis of Trisubstituted Furans

Metal-catalyzed coupling reactions have proven to be a popular strategy for furan synthesis. Li and co-workers disclosed a copper-catalyzed intramolecular *O*-vinylation of ketones with vinyl bromides to access furans (*Scheme 12*).[39] This reaction works very well for a range of 2,5-disubstituted and 2,3,5-trisubstituted furans as well as for one example of a tetrasubstituted furan. The authors also demonstrated that an aldehyde (R^1 = R^3 = R^4 = H, R^2 = Ph) takes part in the reaction efficiently to generate a 2,4-disubstituted furan in 97% yield.

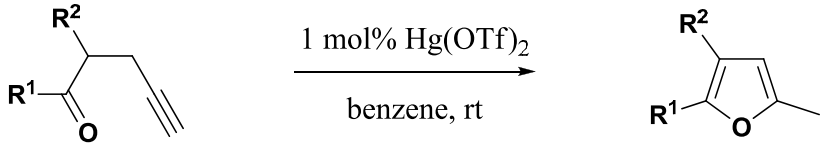


(55-99%) ligand

R^1 = alkyl, aryl; R^2, R^3, R^4 = H, alkyl, aryl

Scheme 12

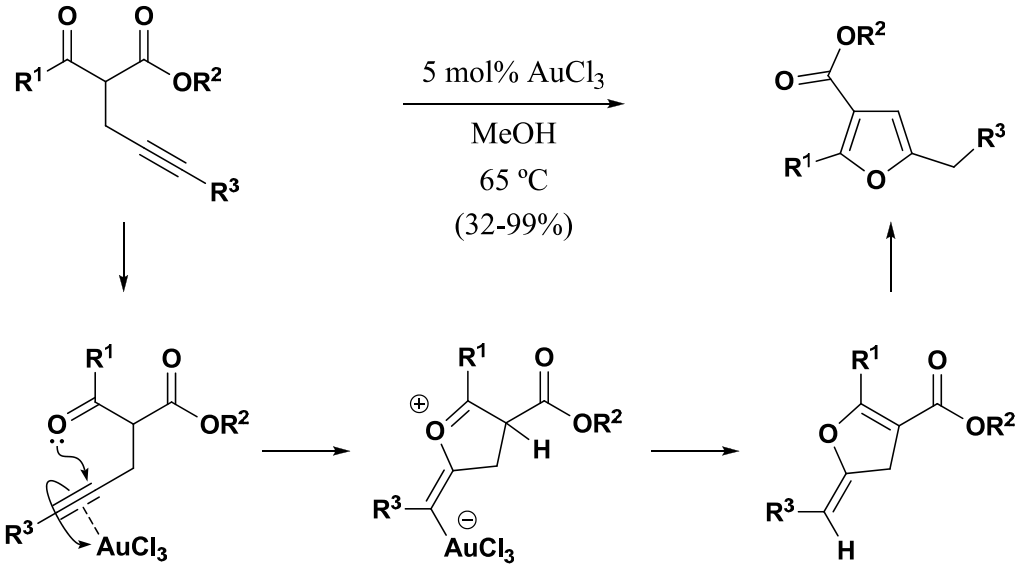
However, the most popular synthetic routes to trisubstituted furans are metal-catalyzed cyclizations and cycloisomerizations. For example, Nishizawa and co-workers reported the mercury triflate catalyzed 5-*exo-dig* cyclization of 1-alkyn-5-ones (*Scheme 13*).[40] This reaction works very well however mercury triflate is very toxic and only substrates bearing terminal alkynes can be used. The presence of internal alkynes leads to mixtures of products being formed. A lone example of such a substrate with an internal alkyne cyclizing to a furan catalyzed by $PdCl_2$ has been reported.[41]



R^1 = alkyl, Ph; R^2 = H, alkyl, ester (70-99%)

Scheme 13

The use of gold-catalysis has been shown to overcome the limitation of the requirement for a terminal alkyne in this process. Krause demonstrated the utility of a gold(I) catalytic system in this regard and prepared a range of di-, tri- and tetrasubstituted furans from internal alkynes.[42] Rodríguez and Moran demonstrated that gold(III) chloride in refluxing methanol is suitable for the cyclization of a range of propargylic substituted β-ketoesters (*Scheme 14*).[43] The mechanism of this cycloisomerization is proposed to proceed through alkyne activation by Au(III) and subsequent 5-*exo-dig* intramolecular attack by the ketone oxygen to form a zwitterionic intermediate. Protodemetalation regenerates the gold catalyst and releases the heterocycle which isomerizes to the furan product. A related indium triflate catalyzed cyclization has also been reported.[44]



R^1 = alkyl, aryl; R^2 = Me, Et; R^3 = H, alkyl, aryl, heteroaryl

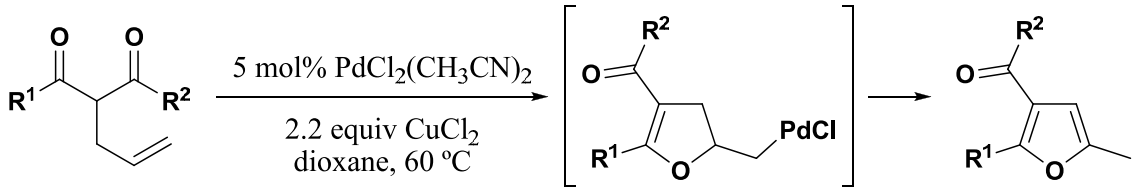
Scheme 14

$AuCl_3$ catalyzed synthesis of methyl 5-benzyl-2-methylfuran-3-carboxylate. Typical procedure.[43]

A flask was charged with methyl 2-acetyl-5-phenylpent-4-ynoate (50 mg, 0.22 mmol), $AuCl_3$ (3.3 mg, 0.011 mmol, 5 mol%) and methanol (1 mL) and heated at reflux for 12 h open to air. The volatiles were removed in vacuo *and the mixture was purified by flash chromatography (5:1 petroleum ether/EtOAc on silica gel) to give methyl 5-benzyl-2-methylfuran-3-carboxylate as a pale yellow oil (36.5 mg,73%). IR (neat): 1080 (s), 1214 (s), 1438 (m), 1581 (m), 1713 (s), 2953 (w) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.53 (3H, s), 3.79 (3H, s), 3.90 (2H, s), 6.23 (1H, s), 7.20-7.28 (3H, m), 7.29-7.35 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 34.6, 51.6, 107.3, 114.1, 127.0, 128.9 (2C), 129.1 (2C), 137.8, 152.9, 158.8, 165.0. MS: m/z (M+23) 253.1. HRMS: m/z calc'd for $C_{14}H_{14}NaO_3$ 253.0835, found 253.0835.*

Han and Widenhoefer disclosed the palladium-catalyzed oxidative cyclization of α-allyl-β-diketones to furans (*Scheme 15*).[45] The mechanism of this process is proposed to proceed through alkene activation by Pd(II) and subsequent intramolecular attack by the ketone oxygen to presumably afford a palladium sigma complex. β-Hydride elimination releases the heterocycle

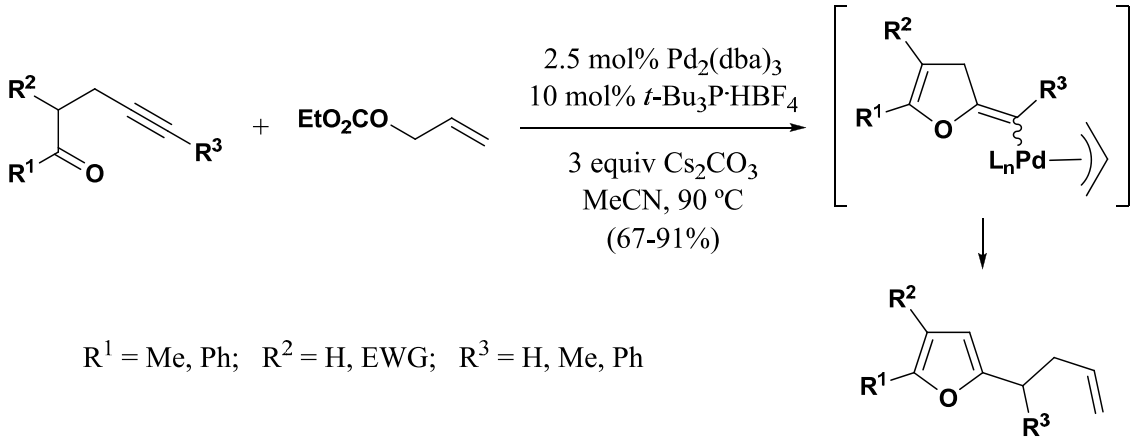
which isomerizes to the furan. The Pd(0) is then re-oxidized to Pd(II) by the $CuCl_2$. There are several interesting features of this process. First, for unsymmetrical diketones complete regioselectivity was observed when R^1 was alkyl and R^2 was aryl. Second, α-homoallyl-β-diketones and α-*bis*-homoallyl-β-diketones also undergo cyclization to furans. The authors propose that palladium-catalyzed olefin isomerization occurs prior to the cyclization event.



R^1, R^2 = alkyl, aryl, heteroaryl (61-72%)

Scheme 15

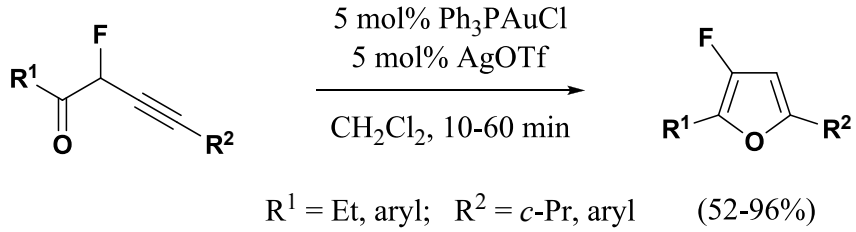
Saito *et al.* developed a similar 5-*exo-dig* cyclization/allylation process catalyzed by palladium but with alkynes instead of alkenes (*Scheme 16*).[46] In this case, β-hydride elimination is not possible and a reductive elimination occurs instead. The substrate scope tested was somewhat limited and substituted allyl carbonates were shown to lead to mixtures of products.



R^1 = Me, Ph; R^2 = H, EWG; R^3 = H, Me, Ph

Scheme 16

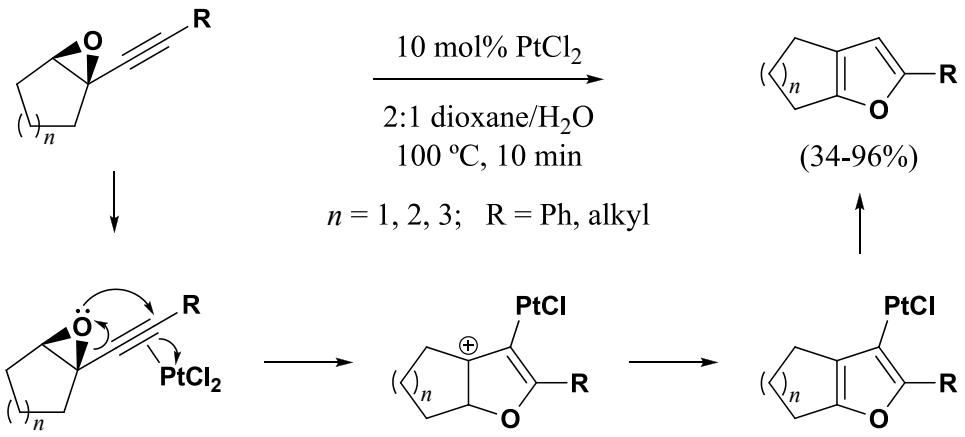
Dembinski *et al.* reported the gold(I)/silver catalyzed synthesis of 3-fluorofurans through a 5-*endo-dig* cyclization (*Scheme 17*).[47] The α-fluoroketone substrates are prepared by fluorination of the *tert*-butylsilyl enol ether of the corresponding aryl(alkyl)-3-yn-1-ones. This procedure compares very favorably to other methods to prepare fluorinated furans as Selectfluor is used as the fluorine source rather than Freon gas (CBr_2F_2).[48]



R^1 = Et, aryl; R^2 = *c*-Pr, aryl (52-96%)

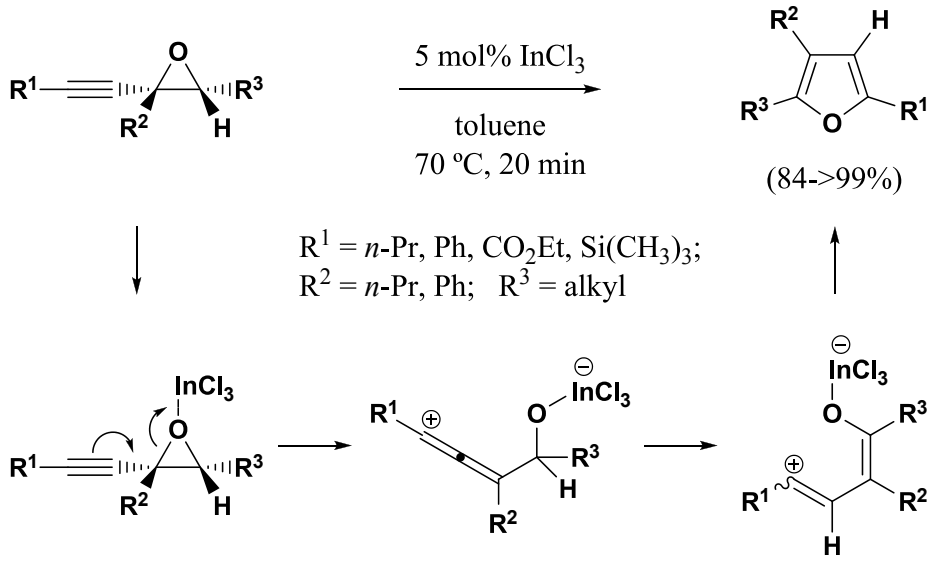
Scheme 17

The cyclization of propargylic oxiranes with $AuCl_3$ in acetonitrile was reported by Hashmi and co-workers in 2004.[49] More recently, Yoshida *et al.* developed superior conditions for this process with $PtCl_2$ in a 2:1 mixture of dioxane and water at 100 °C (*Scheme 18*).[50] A notable feature of this reaction is that it is completed within ten minutes. The reaction mechanism is proposed to involve activation of the alkyne by Pt(II), followed by attack of the epoxide oxygen. Aromatization and protiodemetalation then furnish the furan product.



Scheme 18

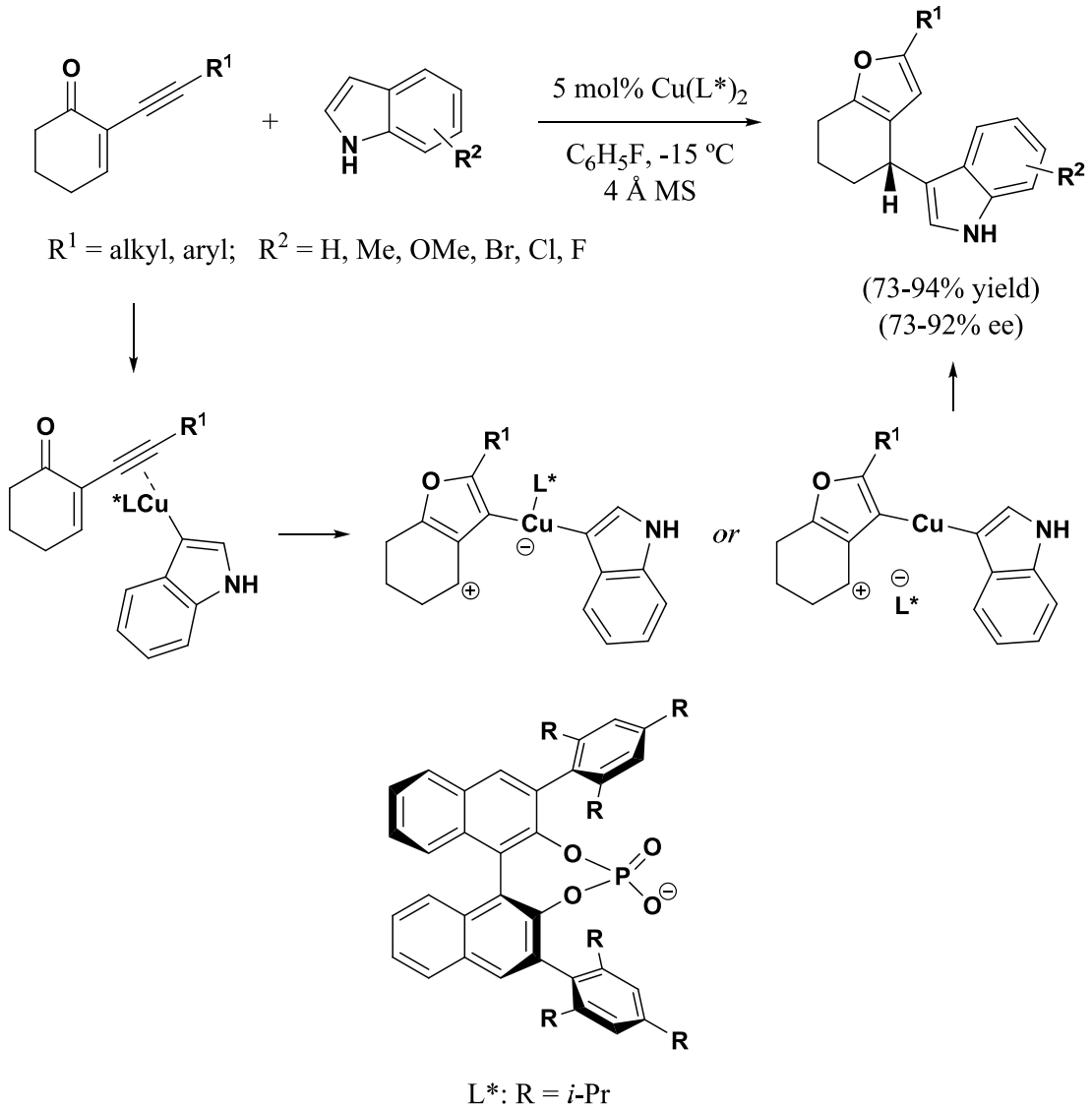
More recently, Kang and Connell reported an indium chloride catalyzed cycloisomerization of propargylic oxiranes (*Scheme 19*).[51] Indium chloride is a Lewis acid and the mechanism of furan formation is quite different from that with $PtCl_2$. The authors propose that the $InCl_3$ activates the epoxide leading to formation of a zwitterionic allene species which undergoes a 1,3-hydride shift followed by cyclization and loss of $InCl_3$. The reaction works very well for all of the substrates tested, however the scope was insufficiently studied.



Scheme 19

The cyclization of 2-(1-alkynyl)-2-alkene-1-ones has attracted considerable attention in the literature with a variety of metal salts being used as catalysts for this process, namely Au,[52,53] Cu,[54] Pd[55] and Pt.[56] Li *et al.* reported a one-pot Pd/Cu-catalyzed Sonogashira coupling/cyclization variation of this process.[57] In addition, Toste and co-workers have developed an enantioselective copper(II)-catalyzed version of this reaction (*Scheme 20*).[58] Mechanistic studies suggested that the active catalyst is a copper-indole complex which activates the alkyne to attack from the carbonyl oxygen. The chiral anionic phosphate ligand, either attached to copper or not, then directs intramolecular addition of an indole group to the carbocation with selectivity for one face. The

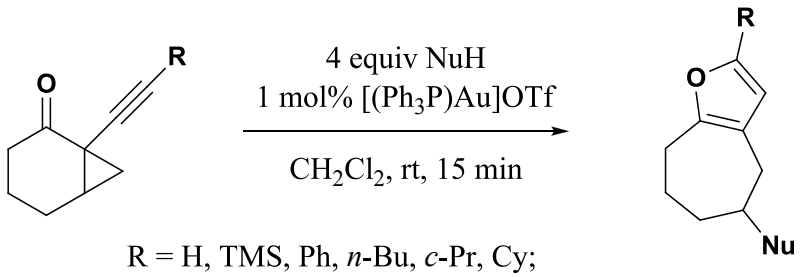
products are generated in very good yields and enantioselectivities, however the reaction is limited to the use of indoles as nucleophiles.



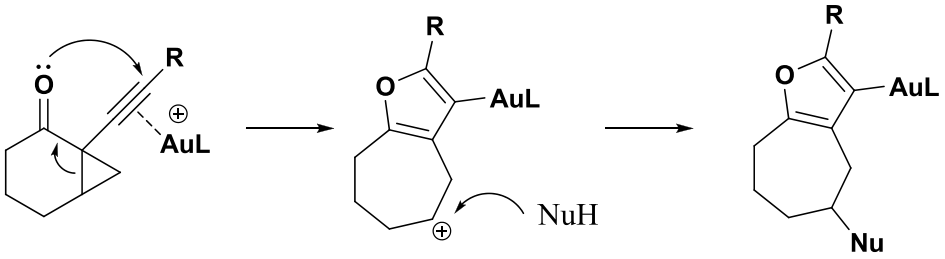
Scheme 20

Zhang and Schmalz developed a Au(I)-catalyzed cyclization/ring-opening process with 1-(1-alkynyl)cyclopropyl ketones to generate furans in very good yields (*Scheme 21*).[59] The authors proposed two possible mechanisms, the first (A) involving initial furan formation with concomitant cyclopropyl ring opening followed by nucleophilic attack on the resulting carbocation, and the second (B) involving nucleophilic cyclopropyl ring opening followed by

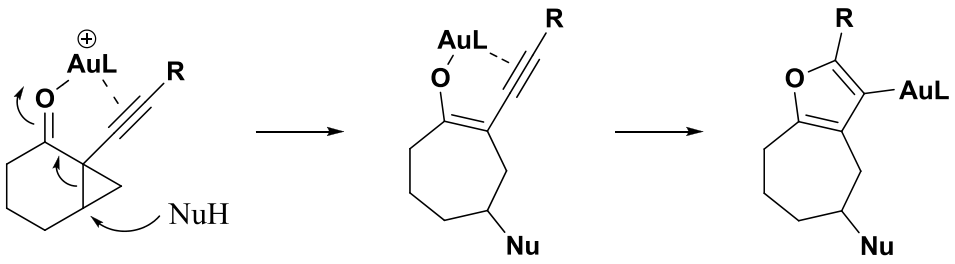
cyclization to the furan; protiodeauration then furnishes the products. The absence of any reaction taking place without a nucleophile present, or with triethylsilane as the nucleophile, led them to postulate that a carbocation intermediate is not formed and that the latter mechanism (B) is more likely.



Possible mechanism A



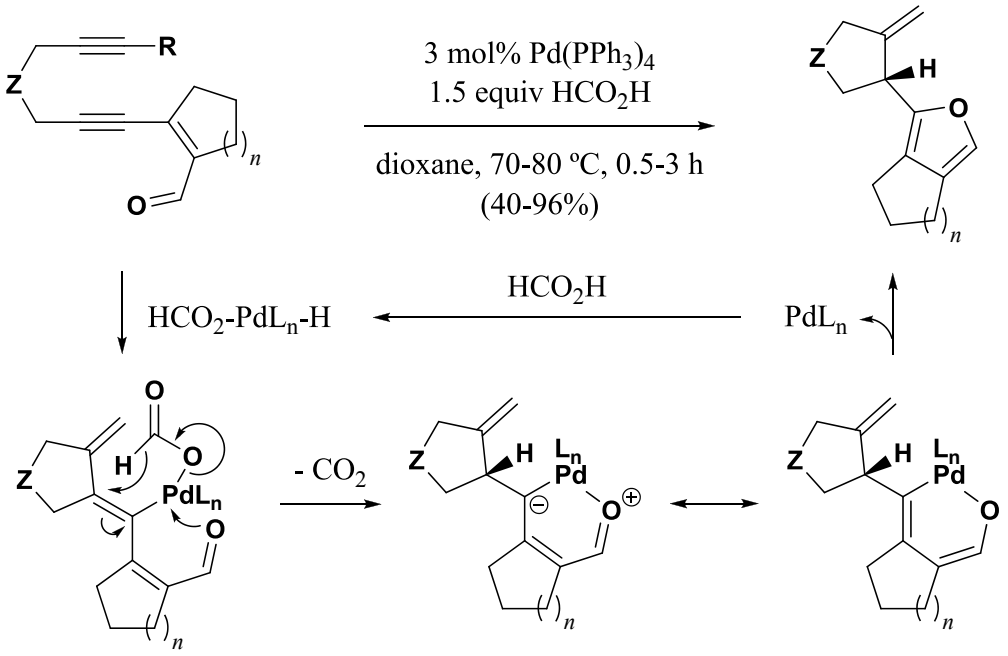
Possible mechanism B



Scheme 21

Tandem cyclizations are notable methods for the construction of polycycles from simple, easily prepared starting materials. Oh and co-workers have been active in this area and have reported the Pd-catalyzed cycloreduction of yne-enynals to complex furan containing molecules (*Scheme 22*).[60] The reaction is proposed to proceed *via* formation of a HPdOCOH species which undergoes consecutive hydropalladation and carbopalladation to generate a vinylpalladium

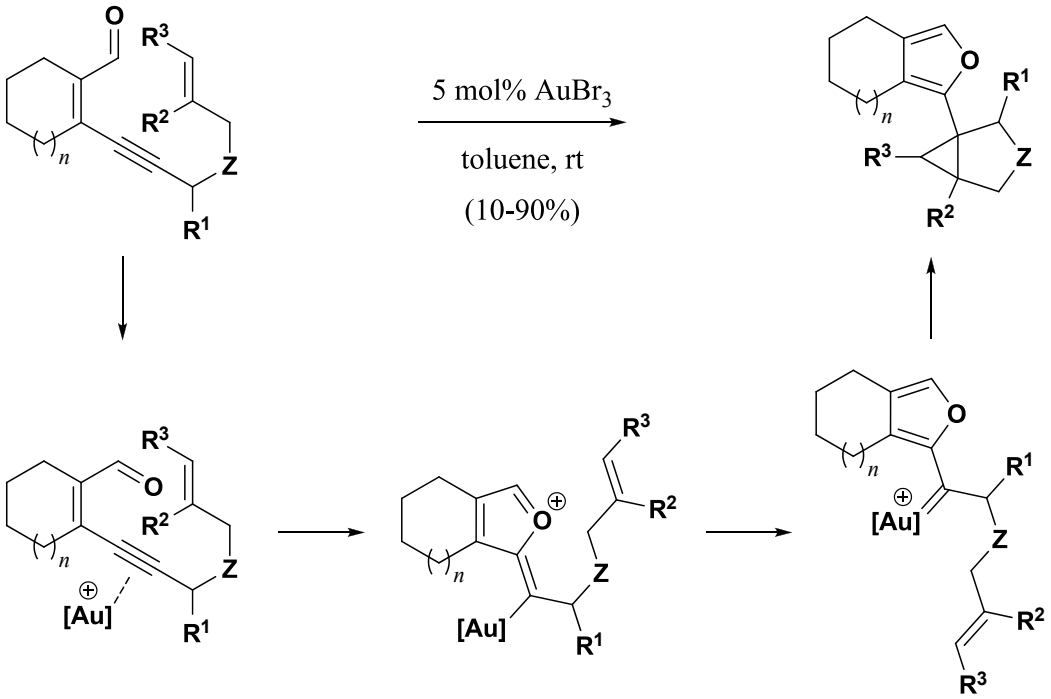
intermediate. The carbonyl oxygen then attacks the Pd center which releases carbon dioxide and induces a hydride transfer. Subsequent reductive elimination generates the furan ring.



n = 1, 2, 3; R = H, CO_2Et; Z = CH_2, $(CH_2)_2$, CHOBn, CHOTBS, $C(CO_2Et)_2$, NTs

Scheme 22

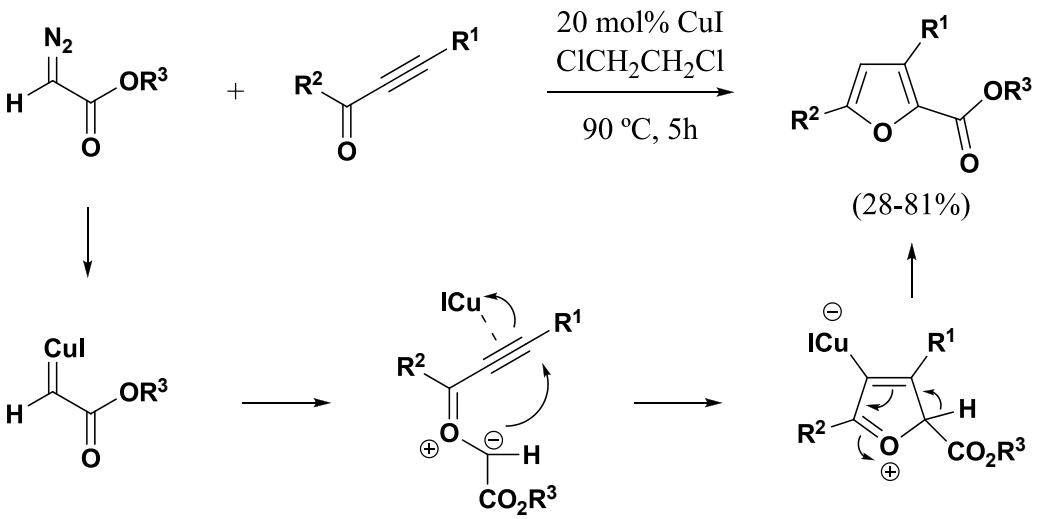
Oh and co-workers have also described a gold-catalyzed polycyclization of enynals to furans (*Scheme 23*).[61] The mechanism of this reaction is believed to involve activation of the alkyne by the gold complex and nucleophilic attack by the carbonyl oxygen. Then, electron redistribution is proposed to generate a Au-carbenoid intermediate which undergoes cyclopropanation with the pendant alkene. Although the reaction is shown to have broad scope, oxygen linkers (*i.e.* Z = O) are incompatible with the reaction. The authors demonstrated that several platinum complexes can also catalyze this reaction.



n =1-3; Z = $C(CO_2Et)_2$, NTs, NPh, $C(CH_3)_2$; R^1 = H, OBn; R^2 = H, Me, Ph; R^3 = H, Ph

Scheme 23

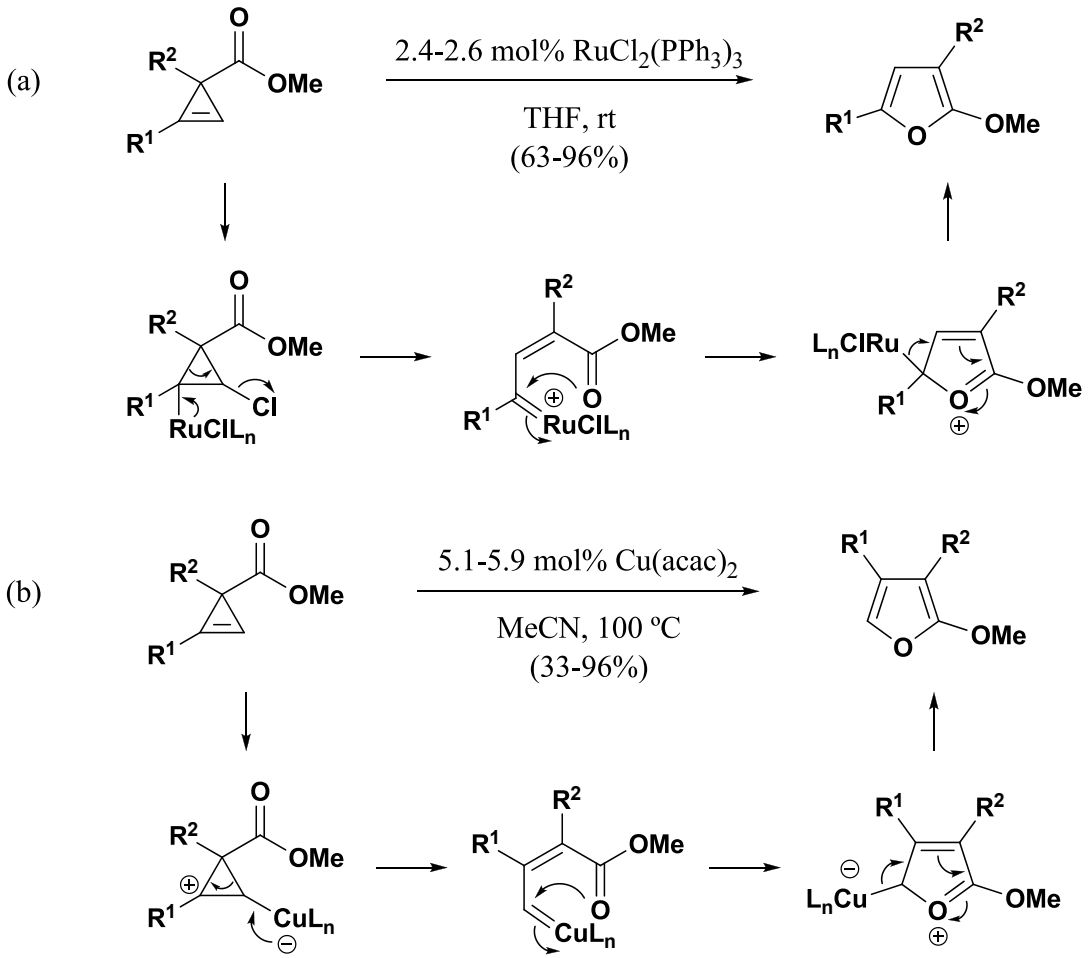
Another synthetic strategy toward ring synthesis is cycloaddition. Liang *et al.* reported a copper(I)-catalyzed [4+1] cycloaddition between diazoacetates and α,β-acetylenic ketones (*Scheme 24*).[62] The authors propose that the reaction proceeds through formation of a copper carbene complex which reacts with the ketone to generate a carbonyl ylid which undergoes cyclization through alkyne activation by the CuI, and subsequent aromatization and protiodecupration to produce the furan. Although this reaction works very well in many cases, the diazoacetate has to be added to the reaction mixture at 90 ^{o}C *via* syringe pump over five hours.



R^1 = Ph, 4-BrC_6H_4, *n*-C_5H_{11}; R^2 = aryl; R^3 = Et, *t*-Bu

Scheme 24

The Ma research group has been interested in the rearrangement of cyclopropenes into furans and has reported the use of Pd, Ru and Cu catalysts toward this end.[63,64] Starting from the same starting materials, Pd and Ru catalysts were shown to lead to the formation of 2,3,5-trisubstituted furans (*Scheme 25a*) whereas Cu catalysis led to the construction of 2,3,4-trisubstituted furans (*Scheme 25b*). The authors rationalized this different reactivity profile by suggesting that chlororuthenation occurs with the chlorine attacking the least substituted carbon of the alkene, whereas in the copper-catalyzed process, cupration occurs with formation of the most stable carbocation. These intermediates then undergo ring-opening followed by ring-closing and loss of the metal to generate the furan products. The substrate scope for each reaction was well studied and the experimental procedures are operationally simple.



Scheme 25

Representative procedure for the Ru-catalyzed protocol.[64]

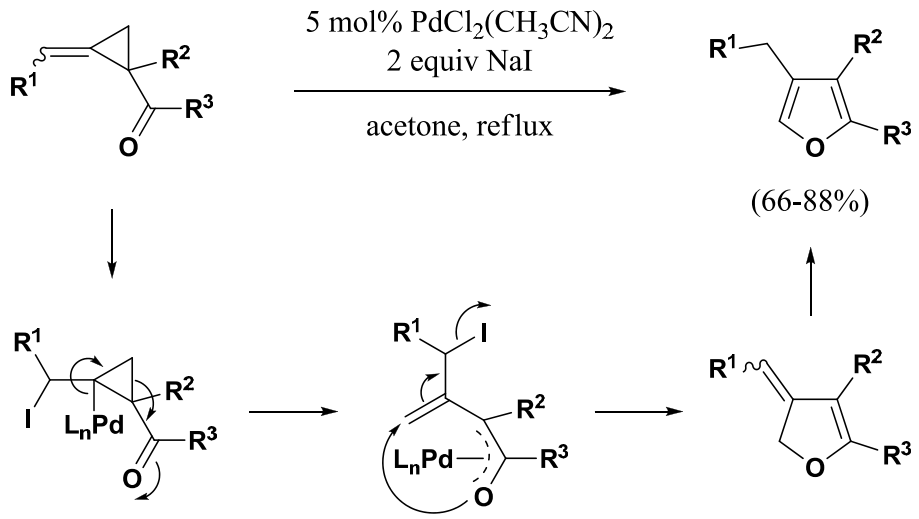
[$RuCl_2(PPh_3)_3$] (5 mg, 5.2x10^{-3} mmol), dimethyl 2-butylcycloprop-2-ene-1,1-dicarboxylate (42 mg, 0.20 mmol), and THF (2 mL) were added sequentially to a Schlenk reaction tube that had been evacuated and backfilled with argon. The resulting mixture was stirred at room temperature. After 11 h, the reaction was complete as monitored by TLC. Evaporation and column chromatography on silica gel (eluent: petroleum ether/ethyl acetate, 5:1) afforded methyl 5-butyl-2-methoxyfuran-3-carboxylate as an oil (40 mg, 95% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.15 (s, 1H), 4.05 (s, 3 H), 3.76 (s, 3H), 2.48 (t, J = 7.4 Hz, 2H), 1.62–1.48 (m, 2H), 1.42–1.26 (m, 2H), 0.90 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 163.6, 160.9, 146.0, 105.8, 91.1, 57.9, 51.0, 29.5, 27.1, 22.0, 13.7; IR (neat): 2955, 2873, 1720, 1607, 1470, 1407, 1279, 1212, 1138,

1089 cm^{-1}; MS (EI): m/z (%): 212 (20.53) [M$^+$], 169 (100) [M$^+$ -C$_3$H$_7$]; HRMS (EI): m/z: calcd for C$_{11}$H$_{16}$O$_4^+$ [M$^+$]: 212.1049; found: 212.1052.

Representative procedure for the Cu-catalyzed protocol. [64]

[Cu(acac)$_2$] (3 mg, 0.011 mmol), dimethyl 2-butylcycloprop-2-ene-1,1-dicarboxylate (41 mg, 0.19 mmol), and CH$_3$CN (2 mL) were added sequentially to a Schlenk reaction tube with a screw cap that had been evacuated and backfilled with argon. The resulting mixture was heated at reflux at 100 ^{o}C. After 48 h the reaction was complete as monitored by TLC. Evaporation and column chromatography on silica gel (eluent: petroleum ether/ethyl acetate, 10:1) afforded methyl 4-butyl-2-methoxyfuran-3-carboxylate as an oil (36 mg, 88% yield). ^{1}H NMR (300 MHz, CDCl$_3$): δ 6.63 (t, J = 1.2 Hz, 1H), 4.05 (s, 3H), 3.78 (s, 3H), 2.54 (td, J = 7.6, 0.8 Hz, 2H), 1.58–1.44 (m, 2 H), 1.43–1.28 (m, 2 H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75.4 MHz, CDCl$_3$): δ 164.1, 162.9, 128.8, 127.3, 90.6, 57.4, 50.9, 31.0, 24.8, 22.4, 13.9; IR (neat): 2954, 1712, 1606, 1583, 1473, 1436, 1412, 1319, 1299, 1214, 1094 cm^{-1}; MS (EI): m/z (%): 212 (14.03) [M$^+$], 170 (100) [M+H$^+$ -C$_3$H$_7$]; HRMS (EI): m/z: calcd for C$_{11}$H$_{16}$O$_4^+$ [M$^+$]: 212.1049; found: 212.1051.

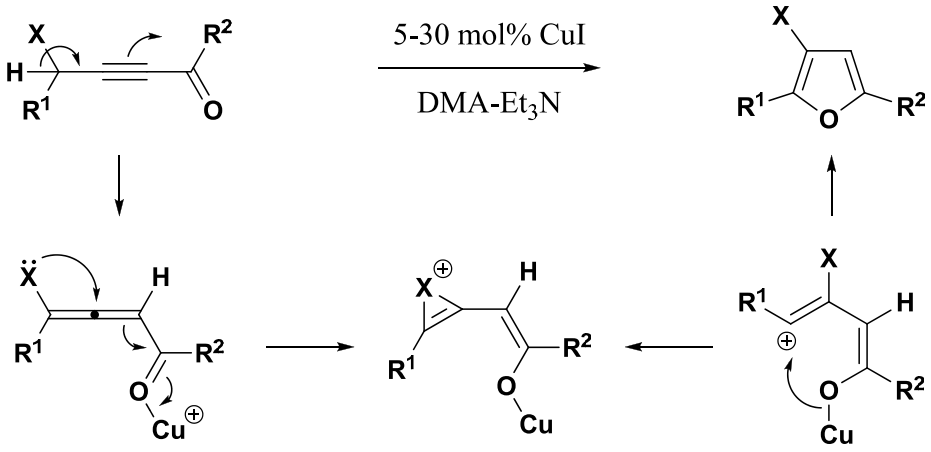
Ma and co-workers have also demonstrated the Pd(II)-catalyzed rearrangement of alkylidenecyclopropyl ketones to furans (*Scheme 26*).[65] The proposed mechanism for this transformation involves iodopalladation of the alkene followed by ring-opening to generate a palladium enolate. This then undergoes an unusual ring closure by nucleophilic addition to the allyl iodide followed by isomerization to the furan. This mechanism is supported by the fact that the reaction proceeds in a similar fashion with just catalytic sodium iodide, *i.e.* with no palladium source; however, the reaction is not as clean in this case.



R^1 = alkyl; R^2 = H, CO_2Et, SO_2Ph; R^3 = alkyl, aryl

Scheme 26

Further research from Gevorgyan has concentrated on the synthesis of furans through allene starting materials or intermediates. Key to this work is the 1,2-migration of a variety of functional groups, namely sulfide,[66] selenide,[67] halide,[68] alkyl and aryl moieties.[69] Despite the apparent similarity of these processes they proceed *via* different mechanisms. The cycloisomerization of the sulfur and selenium substrates was shown to be efficiently catalyzed by CuI; however, the latter (selenium) required reflux temperature whereas the former (sulfur) occurred at room temperature (*Scheme 27*). The postulated mechanism proceeds through a propargyl-allenyl isomerization which then undergoes a thermally-induced and Cu-catalyzed 1,2-migration of the sulfur or selenium group. Finally, ring closure occurs to generate the furan.

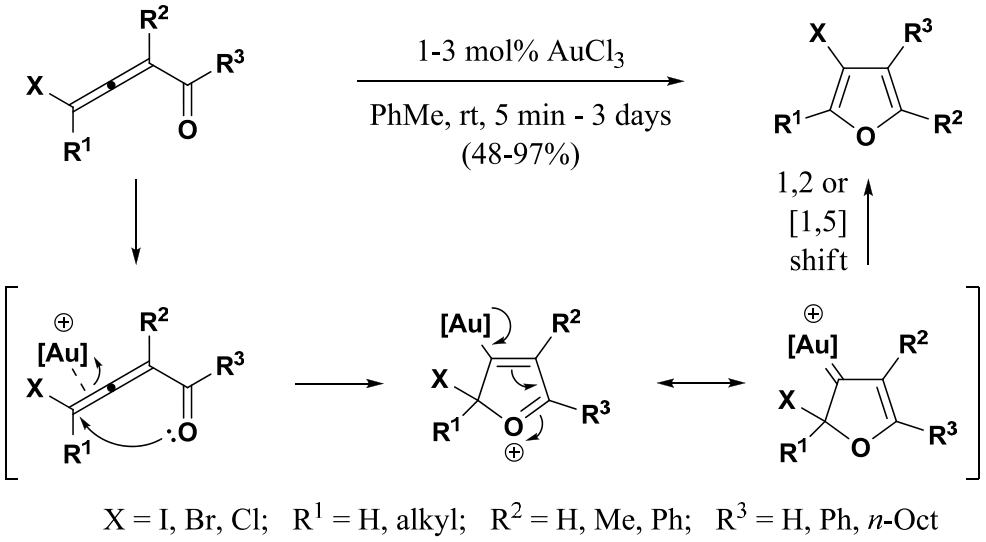


X = SPh, $SC_{12}H_{25}$; R^1 = Me, *n*-Bu, $(CH_2)_3OTHP$;
R^2 = H, Me, *t*-Bu, $(CH_2)_2CO_2Me$, $CHCMe_2$, Ph; (71-95%)

X = SePh; R^1 = *n*-Bu, Bn; R^2 = H, Me, *t*-Bu, Ph; (53-84%)

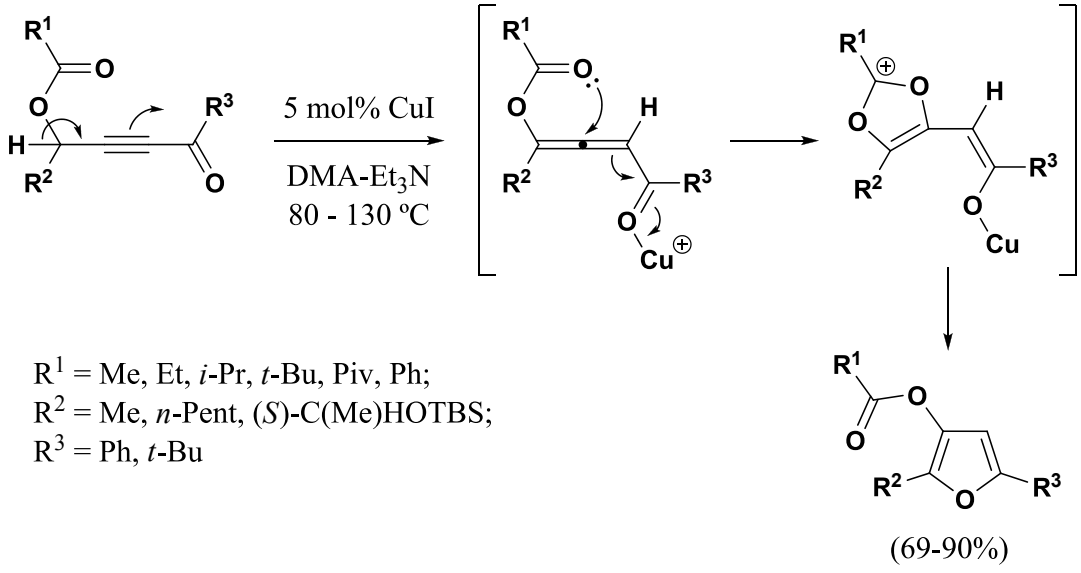
Scheme 27

The Cu-catalyzed cycloisomerization of allenyl ketones bearing substituents other than sulfur and selenium was inefficient. However, it was found that a range of Lewis acids catalyzed the 1,2-shift of alkyl and aryl groups by a similar mechanism.[69] For haloallenyl ketones, $AuCl_3$ was determined to be the catalyst of choice for the transformation, but a different mechanism was delineated (*Scheme 28*).[68] In this case, the distal allene π-bond is activated by the gold complex and the carbonyl oxygen attacks to form an oxonium/carbenoid intermediate which undergoes 1,2- or 1,5-halogen migration and loss of gold to generate the product. The mechanism of this process was investigated by DFT calculations.[70] A variety of di-, tri- and tetrasubstituted furans were prepared by this method in moderate to excellent yields.



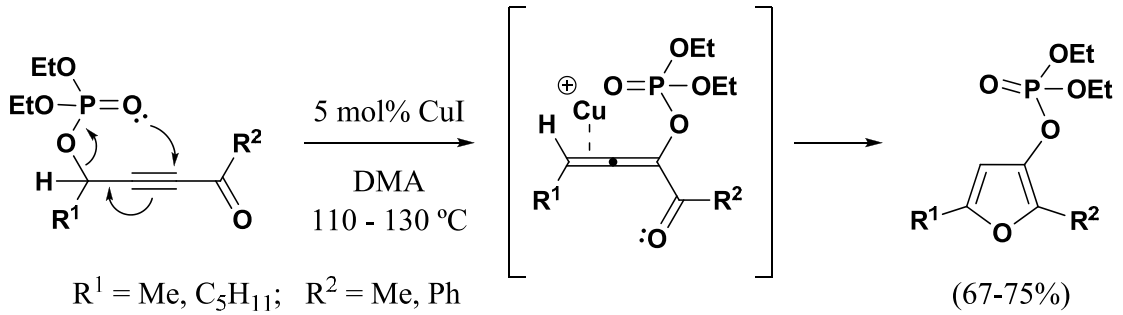
Scheme 28

Gevorgyan has also demonstrated the Cu-catalyzed formation of furans through a formal 1,2-acyloxy group migration in propargyl acetates (*Scheme 29*).[71,72] The mechanism proceeds through a propargyl-allenyl isomerization followed by intramolecular conjugate addition of the acyl group to form a dioxolenylium intermediate. Cyclization to the furan re-generates the copper catalyst.



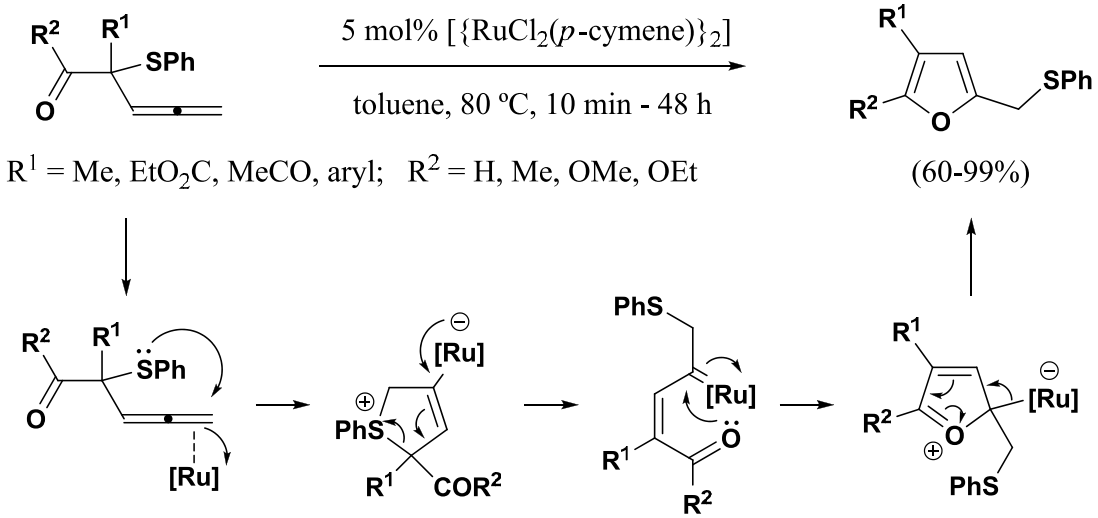
Scheme 29

This reaction has also been shown to be successful for propargyl phosphates; however, the reaction proceeds through a [3,3]-migration/cycloisomerization in this case (*Scheme 30*). This suite of transformations from Gevorgyan's laboratory allows access to a range of furans in generally excellent yields.



Scheme 30

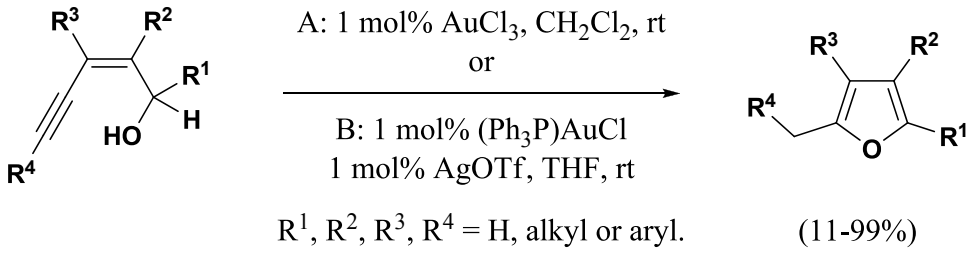
Wang and co-workers have developed a Ru-catalyzed rearrangement of allenyl sulfides to furans (*Scheme 31*).[73] The proposed mechanism involves cyclization of the sulfur onto the allene followed by ring opening to generate a Ru-alkylidene species, which re-cyclizes and then loses the metal to form the furan. The authors went on to show that the synthesis of the allenyl sulfide substrates and the subsequent cycloisomerization can both be catalyzed in a one-pot tandem process.



Scheme 31

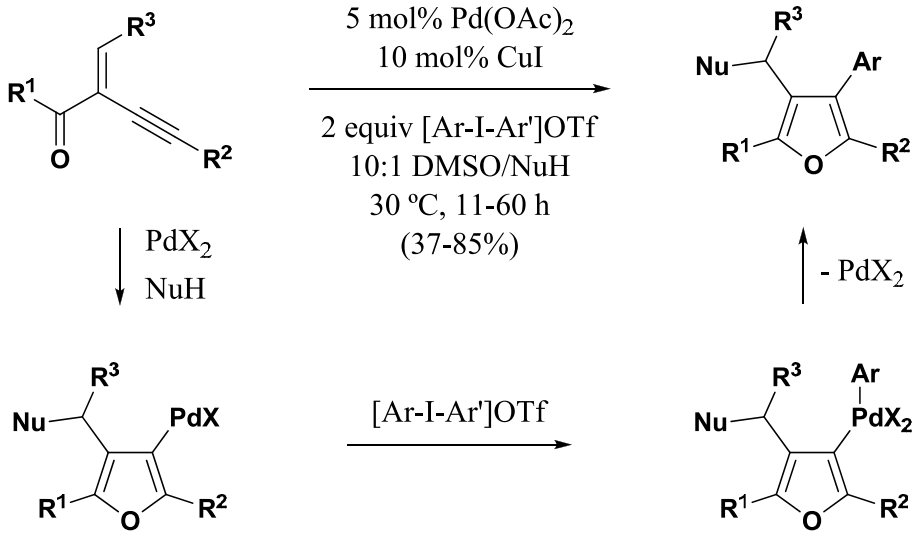
III. Synthesis of Tetrasubstituted Furans

The cycloisomerization of 2-en-4-yn-1-ols has garnered significant attention and a number of catalytic systems have been reported based on Ru,[74,75] Pd[76] and Au.[77] Notably, Liu and co-workers prepared a range of substituted furans including eight tetrasubstituted examples using gold-catalysis (*Scheme 32*).[78] In a similar manner, Ma *et al.* have reported a stepwise Sonogashira coupling and Au(I)-catalyzed, or Pd(II)-catalyzed, cyclization process to access tetrasubstituted furans.[79]



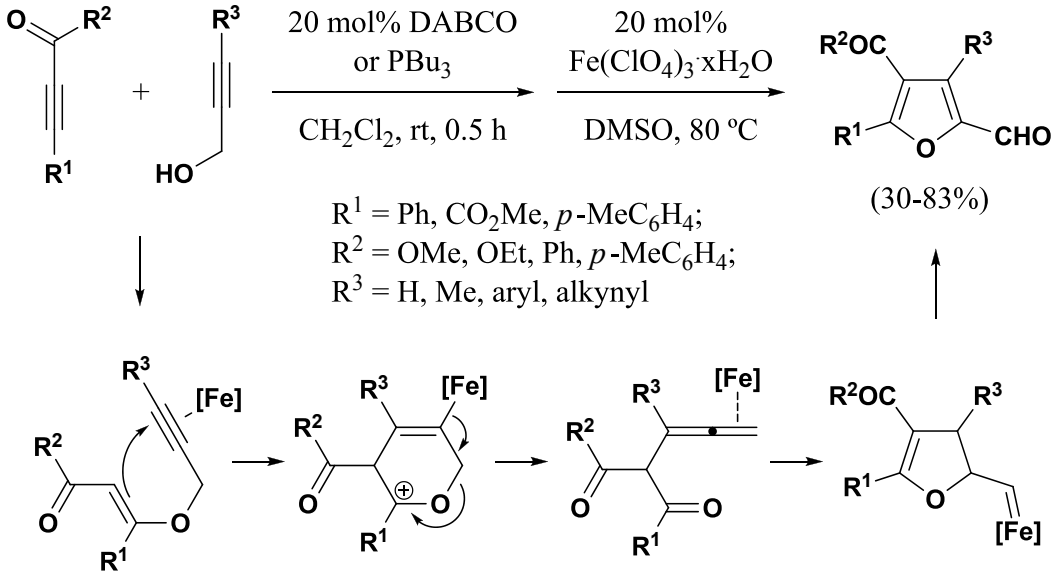
Scheme 32

Zhang and co-workers have reported a number of papers concerned with the utility of 2-(1-alkynyl)-2-alken-1-ones in synthesis, including a three-component furan synthesis by a Pd(II/IV)-catalytic cycle utilizing diaryliodonium salts (*Scheme 33*).[80] The mechanism is postulated to involve nucleophilic attack of the carbonyl oxygen onto the Pd(II)-activated alkyne followed by addition of the alcohol nucleophile. The furanylpalladium(II) intermediate is then envisaged to be oxidized to Pd(IV) by the diaryliodonium salt. Subsequent reductive elimination yields the product and re-generates the Pd(II) catalyst. This reaction allows for the facile access to a range of tetrasubstituted furans in good yields. The role of the CuI is unclear but yields are lower without it. Other results from the Zhang group have demonstrated a related Pd-catalyzed tetrasubstituted furan synthesis from the reaction of 2-(1-alkynyl)-2-alken-1-ones with nucleophiles and allylic chlorides.[81,82]



Scheme 33

The cyclization of propargyl vinyl ethers has also received considerable attention with several different metal catalysts being utilized for the preparation of furans, including Cu[83,84] and Au.[85,86] Jiang has recently published an Fe-catalyzed process which generally gives good yields of furans and requires a relatively inexpensive catalyst (*Scheme 34*).[87] The authors presented a one-pot process whereby DABCO, or tributylphosphine, catalyzed the addition of propargyl alcohols to activated alkynes and the resulting propargyl vinyl ethers were cyclized to the furan by the iron catalyst. The iron species activates the alkyne to nucleophilic attack from the alkene, and the subsequent heterocycle collapses to form an allene intermediate which re-cyclizes to give the furan after loss of the metal and aromatization.



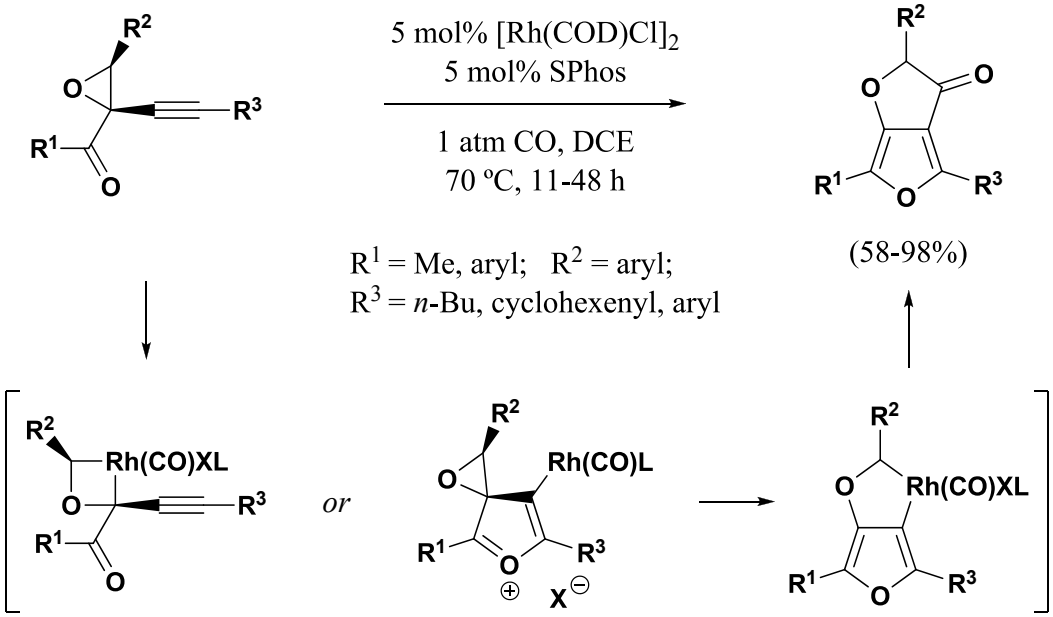
Scheme 34

Representative procedure: synthesis of 4-benzoyl-5-phenylfuran-2-carbaldehyde.[87]

A solution of 1,3-diphenylprop-2-yn-1-one (103 mg, 0.5 mmol), prop-2-yn-1-ol (28 mg, 0.5 mmol), and PBu_3 (0.1mmol) in CH_2Cl_2 was stirred for 30 min at room temperature. The solvent was evaporated under reduced pressure. $Fe(ClO_4)_3$ and DMSO were added at 80 ^oC under atmospheric pressure. After completion of the reaction (monitored by TLC), the solvent was evaporated under reduced pressure. Water was added, and the aqueous solution was extracted with diethyl ether. The combined extracts were dried with anhydrous $MgSO_4$. The solvent was removed, and the crude product was separated by column chromatography to give pure 4-benzoyl-5-phenylfuran-2-carbaldehyde (101 mg, 73%). IR (KBr): 3028, 2834, 1650, 1602, 763 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 9.70 (s, 1H), 7.78-7.83 (m, 4H), 7.53-7.57 (m, 1H), 7.32-7.44 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 190.4, 177.5, 159.8, 150.3, 137.0, 133.6, 130.7, 129.7, 128.7, 128.6, 128.2, 128.1, 123.7, 122.7. HRMS (EI): calcd for $C_{18}H_{12}O_3$ 276.0786, found 276.0780.

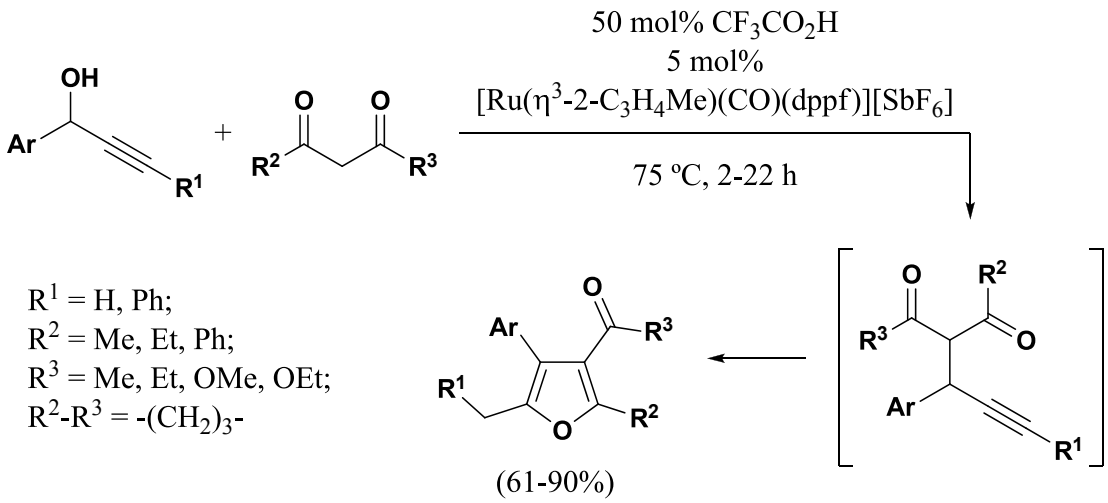
Zhang and co-workers have reported the Rh-catalyzed rearrangement of 1-(1-alkynyl)oxiranyl ketones to furans which proceeds through an unexpected C-C bond cleavage (*Scheme 35*).[88] The authors propose two mechanisms for this process. The first involves oxidative addition to the

epoxide followed by cycloisomerization, carbon monoxide insertion and reductive elimination. The second involves cyclization of the ketone onto the activated alkyne followed by epoxide C-C bond cleavage, carbon monoxide insertion and reductive elimination. Evidence for and against either pathway was not presented; nonetheless, this appears to be a useful process.



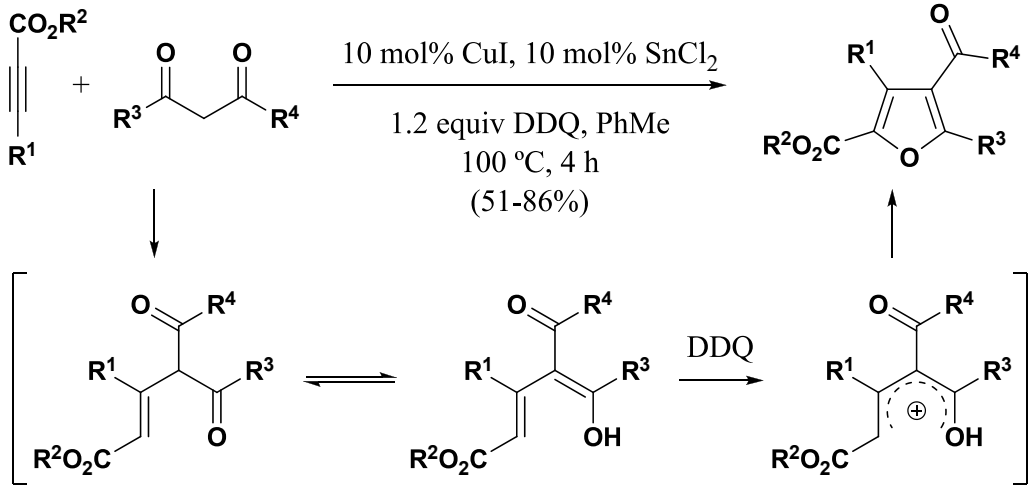
Scheme 35

Cadierno, Gimeno and co-workers have developed a one-pot Ru-catalyzed propargylation-cycloisomerization approach to furan synthesis (*Scheme 36*).[89,90] Half an equivalent of trifluoroacetic acid was required for efficient reaction. This transformation was shown to work well for a range of substrates, but limited to 1-arylpropargyl alcohol derivatives.



Scheme 36

An impressive related strategy was recently reported by Jiang and co-workers whereby alkynoates reacted with 1,3-dicarbonyls to furnish furans (*Scheme 37*).[91] The reaction required catalytic Cu(I) and Sn(II) as well as a stoichiometric amount of an oxidant (DDQ) to proceed. The authors postulated that the Cu(I) activated the 1,3-dicarbonyl while the Sn(II) activated the alkyne leading to conjugate addition. Subsequently, the oxidant (DDQ) is believed to remove a hydride from this intermediate leading to cyclization to the furan.

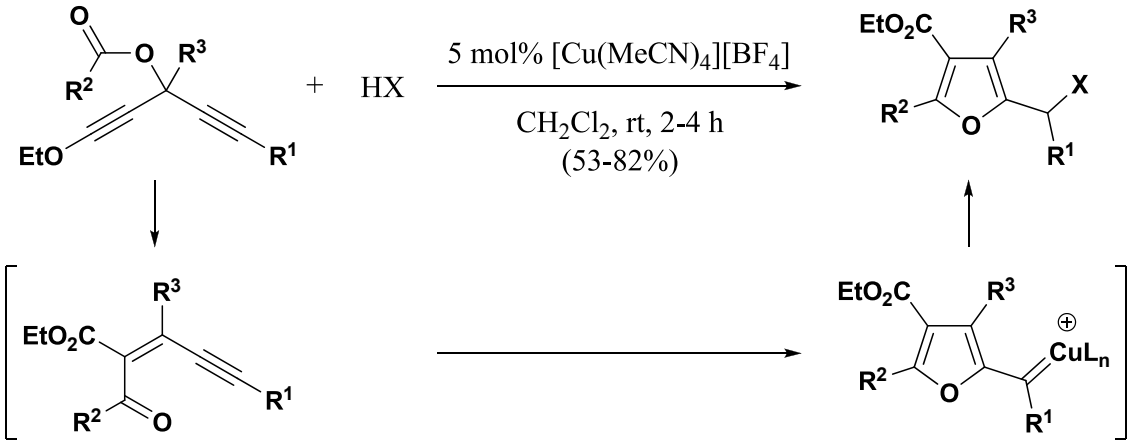


Scheme 37

Representative procedure: synthesis of diethyl 4-Acetyl-5-phenylfuran-2,3-dicarboxylate

To a stirring mixture of diethyl but-2-ynedioate (85 mg, 0.50 mmol) and 1-phenylbutane-1,3-dione (81 mg, 0.5 mmol) were added successively 2 mL of toluene, $SnCl_2$ (9.5 mg, 0.05 mmol), CuI (9.5 mg, 0.05 mmol), and DDQ (135.6 mg, 0.6 mmol). The mixture was stirred at 100 ^oC for 4 h in a round-bottom flask. After cooling, the solvent was diluted with water and extracted with diethyl ether. The ether layer was washed with saturated salt water and dried with anhydrous $MgSO_4$. The resulting mixture was then analyzed by GC and GC-MS. Volatiles were removed under reduced pressure, and the crude product was subjected to isolation by PTLC (GF254) and eluted with a 10:2 petroleum ether-diethyl ether mixture to give 142.3 mg (86%) of diethyl 4-acetyl-5-phenylfuran-2,3-dicarboxylate as a pale yellow viscous oil. IR (KBr): 3065, 2996, 2938, 1724, 1659, 1597, 1410, 1252, 1171, 1060, 942, 910, 864, 772, 697 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.72-7.70 (m, 2H), 7.57-7.53 (m, 1H), 7.45-7.41 (m, 2H), 4.36 (q, 2H, J = 7.2 Hz), 3.94 (q, 2H, J = 7.2 Hz), 2.41 (s, 3H), 1.34 (t, 3H, J = 7.2 Hz), 1.05 (t, 3H, J = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.8, 262.2, 159.3, 157.4, 140.4, 137.8, 133.2, 128.8, 128.5, 125.5, 122.1, 67.8, 61.7, 14.0, 13.9, 13.5. GC-MS m/z (rel intens): 330.07 (M^+, 69.67), 240.92 (100).

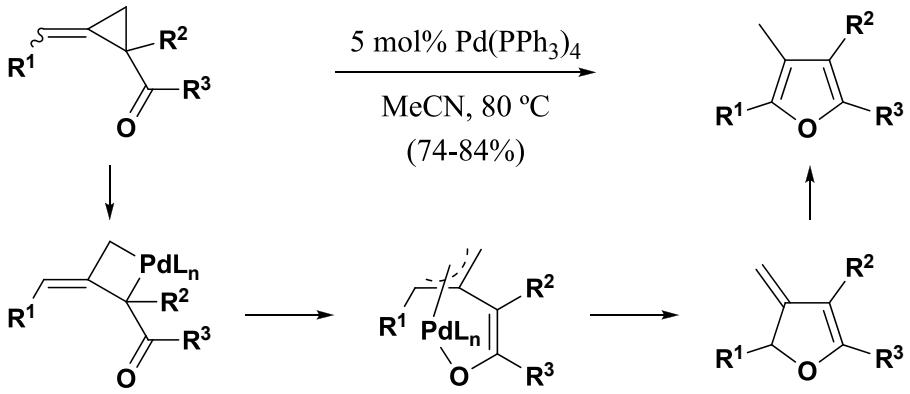
Barluenga and co-workers have shown that *bis*-propargylic esters rearrange to enynones upon addition of Cu(I) catalysts, which subsequently cycloisomerize to copper(I) 2-furylcarbene complexes (*Scheme 38*).[92] These complexes react with silanes and germanes to generate furans in very good yields. The copper carbene intermediates can also be oxidized by air to generate ketones or reacted with ethyl diazoacetate to form alkenes. The substrate scope and functional group tolerance of this reaction was well studied.



R^1 = C_5H_{11}, C(Me)=CH_2, Ph, TMS; R^2 = Me, Et, *t*-Bu, CH=CH_2;
R^3 = H, Me; X = $SiEt_3$, $SiMe_2Et$, $SiMe_2Ph$, $SiHEt_2$, $GeEt_3$

Scheme 38

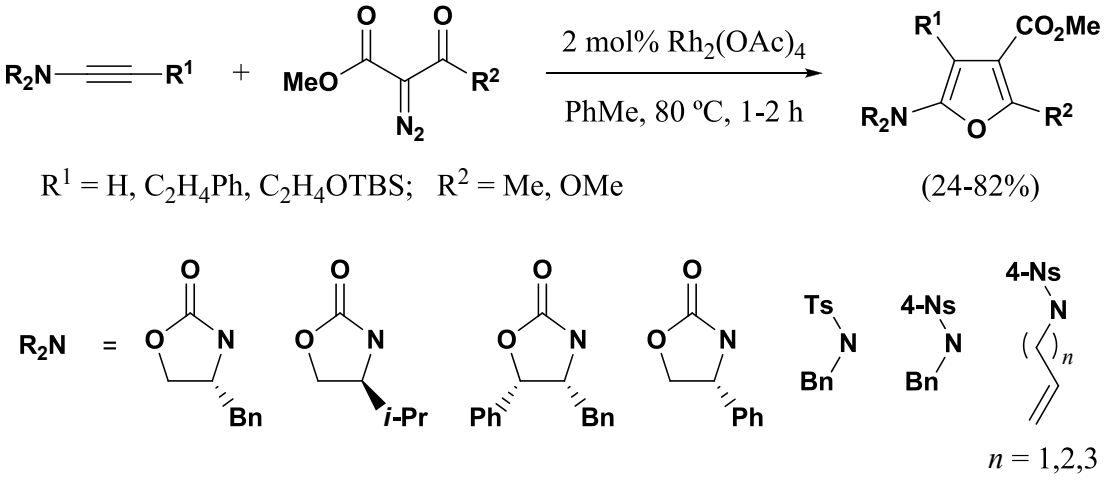
Ma and co-workers disclosed the Pd(0)-catalyzed rearrangement of alkylidenecyclopropyl ketones to furans. This process is quite different to the Pd(II)-catalyzed process discussed earlier as no sodium iodide is required and tetrasubstituted furans are generated from the same starting materials (*Scheme 39*).[65] This transformation is proposed to proceed *via* oxidative addition to the cyclopropane to generate a palladacyclobutane intermediate. Rearrangement leads to an allylic palladium enolate species which undergoes reductive elimination, followed by isomerization, to furnish the furan ring. Unfortunately, the reported substrate scope is somewhat limited.



R^1 = alkyl; R^2 = $COCH_3$, CO_2Et, SO_2Ph; R^3 = Me, Ph

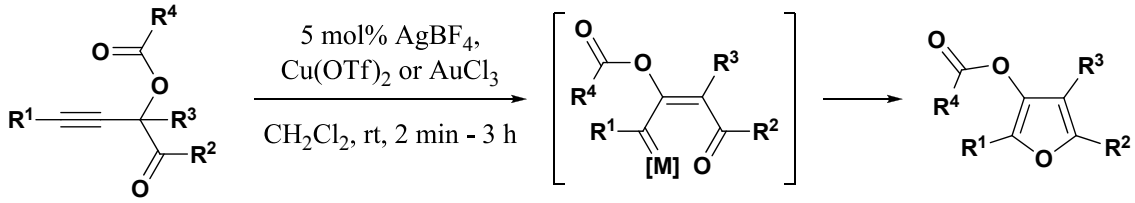
Scheme 39

Li and Hsung developed a Rh-catalyzed synthesis of 2-amidofurans utilizing a cyclopropenation reaction of ynamides (*Scheme 40*).[93] Upon formation of the cyclopropene, a rearrangement occurs to generate the furan. The reaction works well for a range of ynamides and diazo compounds derived from 1,3-dicarbonyl compounds. The reaction was also found to be effective with the corresponding iodonium ylids in place of the diazo compounds. In these cases, the reactions were run at room temperature and in dichloromethane; however, yields were generally lower. Although the authors could not obtain proof for cyclopropene intermediates, the reaction can be considered to be a formal [3+2] cycloaddition.



Scheme 40

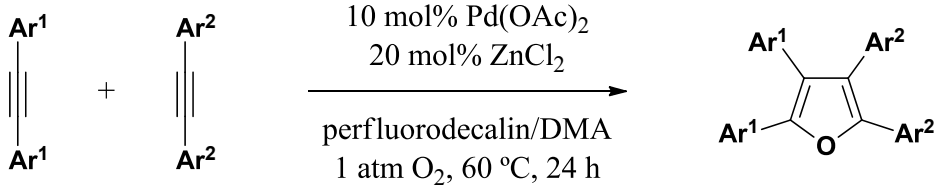
Further work by Gevorgyan and co-workers has demonstrated the rearrangement of alkynyl ketones to provide tetrasubstituted furans in very good yields (*Scheme 41*). The reaction was shown to work with Ag(I), Cu(II) and Au(III) catalysts and the mechanism was determined to be quite complicated, but considerable mechanistic studies were undertaken. Simply viewed, the metal activates the alkyne allowing a [2,3]-rearrangement of the acyl group to generate a metal-alkylidene intermediate which cyclizes to the furan. Substrates with phosphate and tosyl groups in place of acyl were also found to be effective in the reaction.



R^1 = *n*-Bu, *t*-Bu, Ph, TMS; R^2 = Me, Ph; R^3 = Me, Ph; R^4 = Me, *t*-Bu (60-99%)

Scheme 41

A novel Pd-catalyzed oxidation/cyclization of alkynes to generate furans has been reported by Jiang and coworkers (*Scheme 42*).[94,95] The reaction was shown to work well for the preparation of tetra-arylsubstituted furans; however, a statistical mixture of products was formed when two different alkynes were used. The study was also limited to the use of symmetrical alkynes. The authors did not propose a mechanism for this reaction. Overall, this is a nice process but it is severely limited.



(46-95%)

Scheme 42

Conclusion

A variety of different strategies for the preparation of substituted furan rings are available to the synthetic chemist. Over the past decade, the majority of those reported have been based on cycloisomerization and cyclization processes however there are other methods available such as intramolecular couplings and ring closing metathesis. No doubt further and more imaginative approaches to furan synthesis will appear in the literature over the coming decade and beyond.

References

1. X. L. Hou, Z. Yang and H. N. C. Wong, *"Progress in Heterocyclic Chemistry"*, Vol. 15, p. 167, G. W. Gribble and T. L. Gilchrist, ed. Pergamon, Oxford, 2003.
2. R. P. Singh, B. M. Foxman and L. Deng, *J. Am. Chem. Soc*., **132**, 9558 (2010).
3. C. Ouairy, P. Michel, B. Delpech, D. Crich and C. Marazano, *J. Org. Chem*., **75**, 4311 (2010).
4. Y. Guindon, M. Therien, Y. Girard and C. Yoakim, *J. Org. Chem*., **52**, 1680 (1987).
5. B. H. Lisphutz, *Chem. Rev*., **86**, 795 (1986).
6. D. J. Goldsmith, E. Kennedy and R. G. Campbell, *J. Org. Chem*., **40**, 3571 (1975).
7. N. T. Patil and Y. Yamamoto, *ARKIVOC*, 121 (2007).
8. S. F. Kirsch, *Org. Biomol. Chem.*, **4**, 2076 (2006).
9. R. C. D. Brown, *Angew. Chem., Int. Ed.,* **44**, 850 (2005).
10. X. L. Hou, H. Y. Cheung, T. Y. Hon, P. L. Kwan, T. H. Lo, S. Y. Tong and H. N. C. Wong, *Tetrahedron*, **54**, 1955 (1998).
11. L. Knorr, *Ber*., **17**, 2863 (1884).
12. C. Paal, *Ber*., **17**, 2756 (1884).
13. H. Chochois, M. Sauthier, E. Maerten, Y. Castanet and A. Mortreux, *Tetrahedron*, **62**, 11740 (2006).
14. S. J. Pridmore, P. A. Slatford, J. E. Taylor, M. K. Whittlesey and J. M. J. Williams, *Tetrahedron*, **65**, 8981 (2009).
15. A. V. Kel'in and V. Gevorgyan, *J. Org. Chem.*, **67**, 95 (2002).
16. J. A. Marshall and E. D. Robinson, *J. Org. Chem.*, **55**, 3450 (1990).
17. J. A. Marshall and G. S. Bartley, *J. Org. Chem.*, **59**, 7169 (1994).
18. A. S. K. Hashmi, T. L. Ruppert, T. Knöfel and J. W. Bats, *J. Org. Chem.*, **62**, 7295 (1997).
19. X.-Z. Shu, X.-Y. Liu, H.-Q. Xiao, K.-G. Ji, L.-N. Guo, C.-Z. Qi and Y.-M. Liang, *Adv. Synth. Catal.*, **349**, 2493 (2007).
20. K.-G. Ji, X.-Z. Shu, J. Chen, S.-C. Zhao, Z.-J. Zheng, X.-Y. Liu and Y.-M. Liang, *Org. Biomol. Chem.*, **7**, 2501 (2009).
21. Y. Wakabayashi, Y. Fukuda, H. Shiragami, K. Utimoto and H. Nozaki, *Tetrahedron*, **41**, 3655 (1985).
22. F. E. McDonald, C. B. Connolly, M. M. Gleason, T. B. Towne and K. D. Treiber, *J. Org. Chem.*, **58**, 6952 (1993).
23. F. E. McDonald and M. M. Gleason, *J. Am. Chem. Soc*., **118**, 6648 (1996).
24. S. J. Hayes, D. W. Knight, M. D. Menzies, M. O'Halloran and W.-F. Tan, *Tetrahedron Lett.*, **48**, 7709 (2007).

25. Y. Yada, Y. Miyake and Y. Nishibayashi, *Organometallics*, **27**, 3614 (2008).

26. M. Egi, K. Azechi and S. Akai, *Org. Lett.*, **11**, 5002 (2009).

27. A. Aponick, C.-Y. Li, J. Malinge and E. F. Marques, *Org. Lett.*, **11**, 4624 (2009).

28. B. Gabriele, P. Plastina, M. V. Vetere, L. Veltri, R. Mancuso and G. Salerno, *Tetrahedron Lett.*, **51**, 3567 (2010).

29. F. E. McDonald and C. C. Schultz, *J. Am. Chem. Soc.*, **116**, 9363 (1994).

30. F.-L. Qing, W.-Z. Gao and J. Ying, *J. Org. Chem.*, **65**, 2003 (2000).

31. J. A. Marshall and C. A. Sehon, *J. Org. Chem.*, **60**, 5966 (1995).

32. C. Praveen, P. Kiruthiga and P. T. Perumal, *Synlett*, 1990 (**2009**).

33. A. S. K. Hashmi, T. Haffner, M. Rudolph and F. Rominger, *Eur. J. Org. Chem.*, 667 (**2011**).

34. J. Dheur, M. Sauthier, Y. Castanet and A. Mortreux, *Adv. Synth. Catal.*, **352**, 557 (2010).

35. S. Kramer, J. L. H. Madsen, M. Rottländer and T. Skyrdstrup, *Org. Lett.*, **12**, 2758 (2010).

36. P. Nun, S. Dupuy, S. Gaillard, A. Poater, L. Cavallo and S. P. Nolan, *Catal. Sci. Technol.*, **1**, 58 (2011).

37. T. J. Donohoe, L. P. Fishlock, A. R. Lacy and P. A. Procopiou, *Org. Lett.*, **9**, 953 (2007).

38. M. Saquib, I. Husain, B. Kumar and A. K. Shaw, *Chem. Eur. J.*, **15**, 6041 (2009).

39. L. Chen, Y. Fang, Q. Zhao, M. Shi and C. Li, *Tetrahedron Lett.*, **51**, 3678 (2010).

40. H. Imagawa, T. Kurisaki and M. Nishizawa, *Org. Lett.*, **6**, 3679 (2004).

41. M. Picquet, C. Bruneau and P. H. Dixneuf, *Tetrahedron*, **55**, 3937 (1999).

42. V. Belting and N. Krause, *Org. Biomol. Chem.*, **7**, 1221 (2009).

43. A. Rodríguez and W. J. Moran, *Tetrahedron Lett.*, **52**, 2605 (2011).

44. H. Tsuji, K.-I. Yamagata, Y. Ueda and E. Nakamura, *Synlett*, 1015 (**2011**).

45. X. Han and R. A. Widenhoefer, *J. Org. Chem.*, **69**, 1738 (2004).

46. A. Saito, Y. Enomoto, Y. Hanzawa, *Tetrahedron Lett.*, **52**, 4299 (2011).

47. Y. Li, A. Wheeler and R. Dembinski, *Adv. Synth. Catal.*, **352**, 2761 (2010).

48. P. Li, Z. Chai, G. Zhao and S.-Z. Zhu, *Synlett*, 2547 (**2008**).

49. A. S. K. Hashmi and P. Sinha, *Adv. Synth. Catal.*, **346**, 432 (2004).

50. M. Yoshida, M. Al-Amin, K. Matsuda and K. Shishido, *Tetrahedron Lett.*, **49**, 5021 (2008).

51. J. Y. Kang and B. T. Connell, *J. Org. Chem.*, **76**, 2379 (2011).

52 T. Yao, X. Zhang and R. C. Larock, *J. Am. Chem. Soc*., **126**, 11164 (2004).

53. T. Yao, X. Zhang and R. C. Larock, *J. Org. Chem.*, **70**, 7679 (2005).

54. N. T. Patil, H. Wu and Y. Yamamoto, *J. Org. Chem.*, **64**, 7687 (1999).

55. Y. Xiao and J. Zhang, *Chem. Commun.*, 3594 (**2009**).

56. C. H. Oh, V. R. Reddy, A. Kim and C. Y. Rhim, *Tetrahedron Lett.*, **47**, 5307 (2006).

57. J. Yang, C. Wang, X. Xie, H. Li, E. Li and Y. Li, *Org. Biomol. Chem.*, **9**, 1342 (2011).

58. V. Rauniyar, Z. J. Wang, H. E. Burks and F. D. Toste, *J. Am. Chem. Soc*., **133**, XXXXX (2011).

59. J. Zhang and H.-G. Schmalz, *Angew. Chem., Int. Ed.*, **45**, 6704 (2006).

60. C. H. Oh, H. M. Park and D. I. Park, *Org. Lett.*, **9**, 1191 (2007).

61. C. H. Oh, S. J. Lee., J. H. Lee and Y. J. Na, *Chem. Commun.*, 5794 (**2008**).

62. L.-B. Zhao, Z.-H. Guan, Y. Han, Y.-X. Xie, S. He and Y.-M. Liang, *J. Org. Chem.*, **72**, 10276 (2007).

63. S. Ma and J. Zhang, *J. Am. Chem. Soc*., **125**, 12386 (2003).

64. J. Chen and S. Ma, *Chem. Asian. J.*, **5**, 2415 (2010). http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)1861-471X

65. S. Ma, L. Lu and J. Zhang, *J. Am. Chem. Soc*., **126**, 9645 (2004).

66. J. T. Kim, A. V. Kel'in and V. Gevorgyan, *Angew. Chem., Int. Ed.*, **42**, 98 (2003).

67. A. S. Dudnik, A. W. Sromek, M. Rubina, J. T. Kim, A. V. Kel'in and V. Gevorgyan, *J. Am. Chem. Soc*., **130**, 1440 (2008).

68. A. W. Sromek, M. Rubina and V. Gevorgyan, *J. Am. Chem. Soc*., **127**, 10500 (2005).

69. A. S. Dudnik and V. Gevorgyan, *Angew. Chem., Int. Ed.*, **46**, 5195 (2007).

70. Y. Xia, A. S. Dudnik, V. Gevorgyan and Y. Li, *J. Am. Chem. Soc*., **130**, 6940 (2008).

71. A. W. Sromek, A. V. Kel'in and V. Gevorgyan, *Angew. Chem., Int. Ed.*, **43**, 2280 (2004).

72. T. Schwier, A. W. Sromek, D. M. L. Yap, D. Chernyak and V. Gevorgyan, *J. Am. Chem. Soc*., **129**, 9868 (2007).

73. L. Peng, Z. Zhang, M. Ma and J. Wang, *Angew. Chem., Int. Ed.*, **46**, 1905 (2007).

74. B. Seiller, C. Bruneau and P. H. Dixneuf, *J. Chem. Soc., Chem. Commun.*, 493 (**1994**).

75. B. Seiller, C. Bruneau and P. H. Dixneuf, *Tetrahedron*, **51**, 13089 (1995).

76. B. Gabriele, G. Salerno and E. Lauria, *J. Org. Chem.*, **64**, 7687 (1999).

77. Y. Liu, F. Song, Z. Song, M. Liu and B. Yan, *Org. Lett.*, **7**, 5409 (2005).

78. X. Du, F. Song, Y. Lu, H. Chen and Y. Liu, *Tetrahedron*, **65**, 1839 (2009).

79. X. Zhang, Z. Lu, C. Fu and S. Ma, *J. Org. Chem.*, **75**, 2589 (2010).

80. W. Li and J. Zhang, *Chem. Commun.*, **46**, 8839 (2010).

81. Y. Xiao and J. Zhang, *Angew. Chem., Int. Ed.*, **47**, 1903 (2008).

82. Y. Xiao and J. Zhang, *Adv. Synth. Catal.*, **351**, 617 (2009).

83. H. Cao, H. Jiang, W. Yao and X. Liu, *Org. Lett.*, **11**, 1931 (2009).

84. H. Cao, H. Jiang, G. Yuan, Z. Chen, C. Qi and H. Huang, *Chem. Eur. J*., **16**, 10553 (2010).

85. M. H. Suhre, M. Reif and S. F. Kirsch, *Org. Lett.*, **7**, 3925 (2005).

86. A. Gille, J. Rehbein and M. Hiersemann, *Org. Lett.*, **13**, 2122 (2011).

87. H. Jiang, W. Yao, H. Cao, H. Huang and D. Cao, *J. Org. Chem.*, **75**, 5347 (2010).

88. T. Wang, C.-H. Wang and J. Zhang, *Chem. Commun.*, **47**, 5578 (2011).

89. V. Cadierno, J. Gimeno and N. Nebra, *Adv. Synth. Catal.*, **349**, 382 (2007).

90. V. Cadierno, J. Díez, J. Gimeno and N. Nebra, *J. Org. Chem.*, **73**, 5852 (2008).

91. W. Liu, H. Jiang, M. Zhang and C. Qi, *J. Org. Chem.*, **75**, 966 (2010).

92. J. Barluenga, L. Riesgo, R. Vicente, L. A. López and M. Tomás, *J. Am. Chem. Soc*., **130**, 13528 (2008).

93. H. Li and R. P. Hsung, *Org. Lett.*, **11**, 4462 (2009).

94. A. Wang, H. Jiang and Q. Xu, *Synlett*, 929 (**2009**).

95. Y. Wen, S. Zhu, H. Jiang, A. Wang, Z. Chen, *Synlett*, 1023 (**2011**).