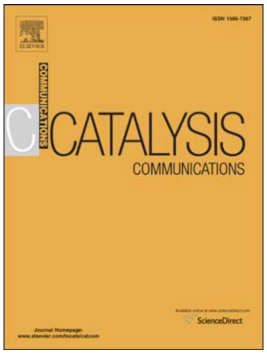

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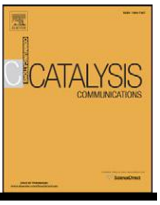

Catalytic hydration of alkynes to ketones by a salen-gold(III) complex

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ABSTRACT

A general atom-economical approach for the synthesis of ketones is demonstrated through hydration of a wide range of alkynes catalyzed by a salen-gold(III) complex in the presence of trifluoroacetic acid as the cocatalyst. Various terminal and internal alkynes were suitable substrates for the catalytic system.

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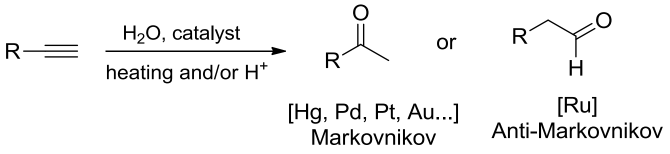
1. Introduction

The hydration of alkynes is a reaction of prime interest for the formation of carbonyl derivatives considering the wide availability of alkynyl substrates and the fundamental importance of carbonyl compounds in organic synthesis [1-3]. Meanwhile, the reaction proceeded by the addition of water to the metal–alkyne complex with 100% atom economy is environmentally friendly and consistent with the sustainable chemistry [4-6].

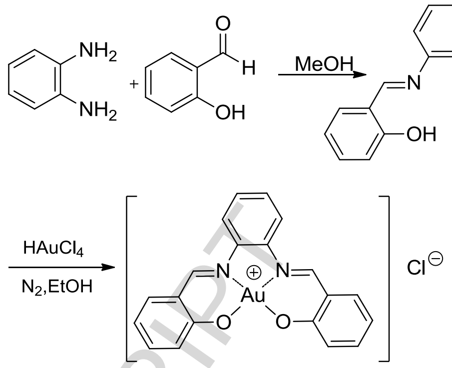
In the 19th century, the hydration of alkynes to ketones was first accomplished through the mediation of Hg compounds as the catalysts in acidic media [7]. In order to replace the highly toxic mercury salts, other less harmful transition-metal-complex catalysts including Rh[8], Pd[9], Ru[10], Cu[11], Pt[12], Co[13] and Au[14-16] have also been applied in the transformation. All metals lead to ketones following the Markovnikov rule except Ru (Scheme 1).



Scheme 1 Catalytic hydration of alkynes

In the last two decades, the use of gold complexes as the catalysts for organic reactions has increased substantially due to their excellent catalytic activities in both heterogeneous and homogeneous systems [17, 18]. In homogeneous gold catalysis, two oxidation states of Au are used as pre-catalysts, Au(I) and Au(III)[19]. Au(I) is isoelectronic to Hg(II) with lower toxic and has the similar “alkynephilicity” to the latter[20]. Thus Au(I) coordinated with the phosphines [21, 22] and nitrogen heterocyclic carbene ligands [23, 24] has been widely applied in the hydration of alkynes. For instance, Teles and Tanaka first reported the $[AuMe(PPh_3)]$ as the catalyst for the hydration of alkynes to ketones in acidic media [14, 21]. Recently, several water-soluble Au(I) *N*-heterocyclic carbene complexes were synthesized and also employed in the hydration of alkynes by Silbestri [24]. However, only a limited number of examples of well defined organogold(III) complexes acting as the catalysts for the hydration of alkynes were reported[25,26]. Au(III) can easily disproportionate to Au(I) and Au(0) and therefore a four-dentate chelate ligand is helpful to stabilize the Au(III) center and show a square planar environment, and this type of Au(III) complex makes a stable catalyst.[25, 27-29]

Meanwhile, salen-type Schiff bases, which can be prepared by condensation of aldehydes and amines [30], are able to stabilize various metals in different oxidation states with four coordinating sites and control the performance of metals in a large variety of useful catalytic transformations [31]. Thus, the coordination of Au(III) and salen ligand is eye-catching especially for their more accessible synthesis conditions and the great importance for catalysis, such as the cross-coupling reaction[32, 33], Mannich reaction[28] and domino reaction[34]. In 2008, Iglesias reported the hydroamination reaction of alkyne with amine catalyzed by the salen-Au(III) under acidic condition[35]. However, there was no report about the nucleophilic addition of water to alkynes catalyzed by salen-Au(III). Herein, we report the easily available salen–Au(III) complex (salen=*N,N'*-bis(salicylidene)*o*-phenylenediamine) (Scheme 2) as catalyst to promote the hydration of alkynes in the presence of the CF_3COOH as cocatalyst.



Scheme 2 synthesis of the salen-Au(III) complex

2. Experimental

2.1. *General*

All reagents were purchased from commercial sources and used without treatment. The products were purified by column chromatography over silica gel. ^1H NMR spectra were recorded on a Bruker AMX500 (500 MHz) spectrometer and tetramethylsilane (TMS) was used as a reference. Elemental analysis was performed on a Vario EL III recorder. IR spectroscopy was recorded on a Nicolet IS-10 spectrometer. Most products were known compounds and were identified by comparison of their physical and spectra data with those of authentic samples.

2.2. *Catalyst preparation*

2.2.1. *Preparation of salenH$_2$*

o-Phenylenediamine (108 mg, 1 mmol) in 5 mL MeOH was added to a stirred mixture of salicylaldehyde (244 mg, 2 mmol) in 10 mL MeOH. The resulting orange mixture was stirred overnight at room temperature. The solid product was collected by filtration, washed with cool alcohol and dried in vacuo (256 mg, yield: 81%).

2.2.2. *Preparation of salen-Au(III) complex*

The homogeneous salen-Au(III) complex was obtained as follows. An ethanolic solution of $HAuCl_4 \cdot 3H_2O$ (1 mmol/15 mL) was added to a solution of the ligand (316 mg, 1 mmol) in EtOH (15 mL) at room temperature under inert atmosphere. The resulting mixture was stirred under reflux for 4 h, then cooled to room temperature and concentrated under vacuum. The residue was washed several times with diethyl ether, filtered and dried to afford the respective complex in good yield (493mg, yield: 88%). IR: ν (cm^{-1}) = 1615, 1555.

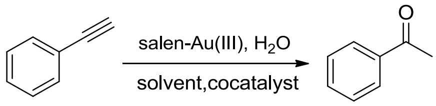
2.3. *Typical Procedure for the hydration of alkynes*

Alkyne (0.5 mmol), catalyst (2.0 mol %), H_2O (4.0 equiv, 0.04 mL) and CF_3COOH (2.0 mol %) were dissolved in MeOH (0.4 mL) and the homogeneous solution was stirred in a sealed tube at 80°C for 5 h. After the completion of the reaction, the mixture was cooled to room temperature, and then CH_2Cl_2 (10 mL) and H_2O (10 mL) were added to it. The organic layer were separated and washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified over silica gel by column chromatography (25 % EtOAc in hexane).

3. Results and Discussion

The salen-Au(III) complex was synthesized according to the reaction sequence shown in Scheme 2 and applied as the catalyst for the hydration of phenylacetylene. The reaction conditions were optimized and the results were summarized in Table 1. Poor yields of the corresponding products were observed when salen-Au(III) or CF_3COOH was only used (Table 1, entries 1 and 2). Various cocatalysts were examined (table 1, entries 3-8) and the best yield was obtained in the presence of 2 mol % of CF_3COOH as the cocatalyst. Then, several solvents were screened for the hydration and quantitively yield was achieved when methanol was used as the solvent in a 10:1 volume ratio with water (Table 1, entries 9-12). Trials in pure water proved unsuccessful. Meanwhile, $HAuCl_4$ was employed directly as the catalyst under the optimized conditions but exhibited less catalytic activity than the salen-Au(III) complex (Table 1, entry 13), indicating that the efficiency of the catalyst was enhanced by the addition of the salen ligand.

Table 1. Optimization of the reaction conditions[a]

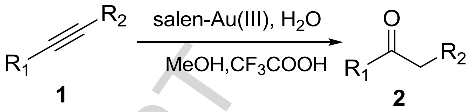


entry	solvent	solvent/H_2O(V/V)	cocatalyst	yield [b] /%
1	MeOH	1/1	--	trace
2[c]	MeOH	1/1	CF_3COOH	trace
3	MeOH	1/1	CF_3COOH	78
4	MeOH	1/1	CH_3COOH	43
5	MeOH	1/1	H_2SO_4	71
6	MeOH	1/1	NH_4PF_6	34
7	MeOH	1/1	$AgPF_6$	39
8	MeOH	1/1	AgOTf	31
9	MeOH	10/1	CF_3COOH	93
10	MeCN	10/1	CF_3COOH	75
11	1,4-dioxane	10/1	CF_3COOH	68
12	H_2O	/	CF_3COOH	trace
13 [d]	MeOH	10/1	CF_3COOH	77

[a] reaction conditions: phenylacetylene (0.5 mmol), catalyst (2.0 mol %), H_2O (4.0 equiv, 0.04 mL), cocatalyst (2.0 mol %) and solvent were stirred in a sealed tube at 80°C for 5 h.
[b] Isolated yield.
[c] no salen-Au(III) was used.
[d] $HAuCl_4$ was used as the catalyst.

Furthermore, the substrate scope for the hydration of alkynes was explored under the optimized conditions. The reactivity of several terminal alkynes was investigated firstly. The influence of the electronic effects of the substituent on the phenyl ring was tested in the reaction, and both electron-withdrawing and electron-donating groups were well tolerated, affording the desired products with satisfactory yields (Table 2, entries 2-10). To our surprise, the phenylacetylene derivatives bearing the amino group exhibited weak reactivity and only moderate yields were obtained. A substituent on the *o*-position resulted in lower yield because of steric hindrance effects (Table 2, entries 2 vs 13). Heterocyclic terminal alkynes, including 2-ethynylthiophene, 2-ethynylpyridine both reacted efficiently to give products in 91 and 92 % yields, respectively (Table 2, entries 15 and 16). Aliphatic terminal alkynes, 1-dodecyne, also effectively participated in the hydration reaction affording the product in 96 % yield (Table 2, entry 17). This protocol was then applicable to the internal alkynes. Because of steric hindrance effects, the alkyne possessing aryl/aryl substituents was more reluctant participant than the terminal counterparts toward hydration[14] and resulted only 34% yield (Table 2, entry 18). On the other hand, the 5-decyne with smaller steric hindrance effects was found suitable substrates in the present catalytic system (Table 2, entry 19).

Table 2. Scope of substrates[a]



entry	R_1	R_2	Product	yield [b] /%
1	Ph	H	2a	93
2	4-MeC_6H_4	H	2b	93
3	4-$MeOC_6H_4$	H	2c	94
4	4-*n*-$C_3H_7C_6H_4$	H	2d	91
5	4-*n*-$C_4H_9C_6H_4$	H	2e	95
6	4-*n*-$C_5H_{11}C_6H_4$	H	2f	92
7	4-FC_6H_4	H	2g	87
8	4-ClC_6H_4	H	2h	91
9	4-BrC_6H_4	H	2i	90
10	4-$NO_2C_6H_4$	H	2j	92
11	4-$NH_2C_6H_4$	H	2k	78
12	3-$NH_2C_6H_4$	H	2l	68
13	3-MeC_6H_4	H	2m	89
14	2-MeC_6H_4	H	2n	90
15	2-Thienyl	H	2o	91
16	2-Pyridyl	H	2p	92
17	*n*-$C_{10}H_{21}$	H	2q	96
18	Ph	Ph	2r	34
19	*n*-C_5H_{11}	*n*-C_5H_{11}	2s	94

[a] reaction conditions: alkyne (0.5 mmol), catalyst (2.0 mol %), H_2O (4.0 equiv, 0.04 mL), CF_3COOH (2.0 mol %) in 0.4 mL MeOH were stirred in a sealed tube at 80°C for 5 h.
[b] Isolate yield.

4. Conclusions

In summary, a salen-Au(III) complex was synthesized and then applied as the catalyst in a general atom-economical approach for the synthesis of ketones through hydration of alkynes. CF_3COOH proved to be the most efficient cocatalyst for this reaction. Various terminal and internal alkynes were investigated and excellent yields (up to 96%) were achieved in most cases.

5. Supplementary Material

Supplementary data associated with this article can be found, in the online version.

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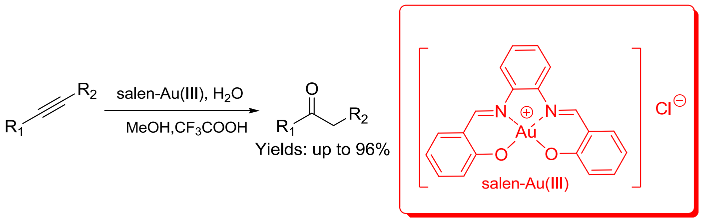

Graphical abstract

Highlights:

- A salen-Au(III) complex has been synthesized by a facile route.
- The salen-Au(III) exhibited excellent catalytic ability in the hydration of alkynes.
- Both terminal and internal alkynes were suitable substrates for the catalytic system.
- Excellent yields (up to 96%) were achieved in most cases.