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[(NHC)Au^{I}]-Catalyzed Formation of Conjugated Enones and Enals: An Experimental and Computational Study

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Abstract: The [(NHC)Au^{I}]-catalyzed (NHC = N-heterocyclic carbene) formation of α,β-unsaturated carbonyl compounds (enones and enals) from propargylic acetates is described. The reactions occur at 60 °C in 8 h in the presence of an equimolar mixture of [(NHC)AuCl] and $AgSbF_6$ and produce conjugated enones and enals in high yields. Optimization studies revealed that the reaction is sensitive to the solvent, the NHC, and, to a lesser extent, to the silver salt employed, leading to the use of [(I*t*Bu)AuCl]/$AgSbF_6$ in THF as an efficient catalytic system. This transformation proved to have a broad scope, enabling the stereoselective formation of (*E*)-enones and -enals with great structural diversity. The effect of substitution at the propargylic and acetylenic positions has been investigated, as well as the effect of aryl substitution on the formation of cinnamyl ketones. The presence or absence of water in the reaction mixture was found to be crucial. From the same phenylpropargyl acetates, anhydrous conditions led to the formation of indene compounds via a tandem [3,3] sigmatropic rearrangement/intramolecular hydroarylation process, whereas simply adding water to the reaction mixture produced enone derivatives cleanly. Several mechanistic hypotheses, including the hydrolysis of an allenol ester intermediate and S_N2' addition of water, were examined to gain an insight into this transformation. Mechanistic investigations and computational studies support [(NHC)AuOH], produced in situ from [(NHC)AuSbF$_6$] and H_2O, instead of cationic [(NHC)AuSbF$_6$] as the catalytically active species. Based on DFT calculations performed at the B3LYP level of theory, a full catalytic cycle featuring an unprecedented transfer of the OH moiety bound to the gold center to the C≡C bond leading to the formation of a gold–allenolate is proposed.

Keywords: carbenes · density functional calculations · enones · gold · potential energy surface

Introduction

Conjugated enones arguably represent one of the most useful building blocks in organic synthesis;[1] two of their main uses are as reactants in 1,4 addition and Diels–Alder reactions.[2,3] α,β-Unsaturated ketones and aldehydes are usually obtained by aldol- or Knoevenagel-type condensation reactions[4] and by the Horner–Wadsworth–Emmons reaction.[5,6] These methods generally require strong basic media and therefore functional group compatibility and selectivity issues can be problematic. Other methods that afford enones include the use of widely available propargylic alcohols.[7] The Meyer–Schuster rearrangement[8] of propargylic alcohols, involving a formal 1,3-shift of the hydroxy moiety, and the Rupe rearrangement,[9] proceeding via a 1,3-enyne, produce isomeric α,β-unsaturated carbonyl compounds (Scheme 1). Despite some reports on the utilization of the Meyer–Schuster reaction under mild conditions,[10,11] these isomerization reactions have not been widely used or

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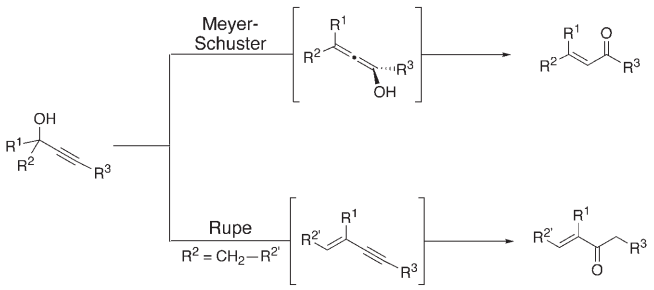


Scheme 1. Meyer–Schuster and Rupe rearrangements of propargylic alcohols.

developed. Several reports on the use of transition metals to activate the C≡C bond for Meyer–Schuster rearrangement have appeared, but their use has had only limited success in terms of scope and reaction conditions.[12]

The activation of C≡C bonds towards cyclization or functionalization with Au^{I} or Au^{III} salts is attracting huge interest.[13] Beyond the widespread interest in the cycloisomerization of polyunsaturated systems,[14] numerous processes have been reported for the mild and efficient formation of C–C, C–N, C–O, and C–S bonds by both inter- and intramolecular reactions. As a testimony to the high potential of this chemistry, and despite being in its infancy, total syntheses of complex natural products featuring gold-catalyzed transformations as the key step have already been reported.[15]

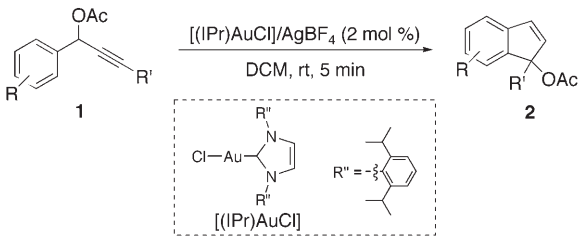
Capitalizing on early work conducted with $PtCl_2$,[16] it has been found that propargylic acetates have played a special role in the field of gold-catalyzed activation of alkynes because of the ability of the ester function to migrate.[17] Thus, upon coordination of the gold center to the alkyne moiety, the acetate undergoes 1,2- or 1,3-migration leading, respectively, to a gold carbene or to an allene poised for subsequent reaction.[18,19] We investigated these two types of activation and took advantage of the 1,2- and 1,3-migration to form [*n*.1.0]bicyclic compounds and indenes, respectively.[20,21] Of note, although additional types of rearrangement of the acetate moiety have been proposed,[22] the propensity of an acetate to behave as a leaving group has never been observed in the context of gold catalysis.

Herein, we report the formation of α,β-unsaturated ketones and aldehydes from propargylic acetates promoted by [(NHC)AuCl] catalysts in conjunction with a silver salt (NHC=N-heterocyclic carbene). The transformation, which can be viewed as a formal S_N2' process, occurs under extremely mild conditions and does not require the addition of base or acid. Furthermore, computational studies were performed in order to gain an insight into the mechanistic aspects of this transformation and led to the proposal of [(NHC)AuOH] as the active species in this catalytic system.

Abstract in Catalan: *Es descriu la reacció de formació de compostos de carbonil α,β-insaturats (enones i enals) a partir d'acetats propargílics catalitzada per [(NHC)Au^{I}] (NHC= carbè N-heterocíclic). Les reaccions tenen lloc a 60°C en 8 h en presència d'una mescla equimolar de [(NHC)AuCl] i $AgSbF_6$ i produeix rendiments alts d'enones i enals conjugats. Estudis d'optimització van mostrar que la reacció era sensible al solvent, el NHC, i, en menor grau, a la natura de la sal de plata emprada; això va portar a escollir [(ItBu)AuCl]/$AgSbF_6$ en THF com a sistema catalític eficient. La transformació va mostrar posseir un ampli espectre, i es va aconseguir la formació estereoselectiva d'(E)-enones i -enals amb gran diversitat estructural. La influència de la substitució en les posicions propargílica i acetilènica va ser investigada, així com la substitució d'aril per donar lloc a la formació de cinamilcetones. La presència o absència d'aigua en el medi de reacció es va mostrar com a crucial. A partir dels mateixos fenilpropargilacetats, condicions anhidres van portar a la formació de compostos indènics mitjançant una reacció tàndem de reorganització sigmatròpica [3,3] i hidroarilació intramolecular, mentre que l'addició d'aigua a la reacció portava de manera neta a derivats del tipus enona. Diverses hipòtesis mecanístiques, entre elles la hidròlisi d'un intermedi del tipus al.lenol ester i l'addició S_N2' d'aigua, han estat examinades per millorar la comprensió del procés. Les dades mecanístiques i els estudis computacionals suggereixen que l'espècie catalítica activa és [(NHC)AuOH], produït in situ a partir de [(NHC)AuSbF$_6$] i H_2O, i no el complex catiònic [(NHC)AuSbF$_6$]. A partir d'estudis DFT realitzats al nivell B3LYP, es proposa un cicle catalític complet, que inclou un nou tipus d'etapa consistent en la transferència d'un grup OH des de l'or cap a l'enllaç C≡C per produir un complex oral.lenolat.*

Results and Discussion

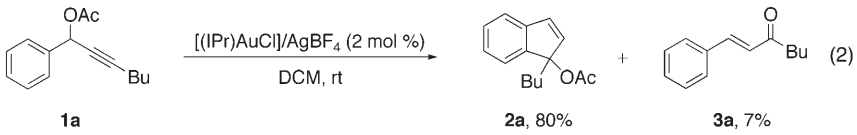
Investigation of by-product formation: In the context of gold-catalyzed alkyne activation, we recently reported an unprecedented type of 1,5-enyne cycloisomerization catalyzed by cationic [(NHC)AuX] complexes (X = BF_4, PF_6, or SbF_6).[20] Further investigation of the activity of NHC-containing gold complexes allowed us to observe the tandem [3,3] rearrangement/intramolecular hydroarylation of phenylpropargyl acetates **1** leading to indenes **2** [Eq. (1)].[21]



(1)

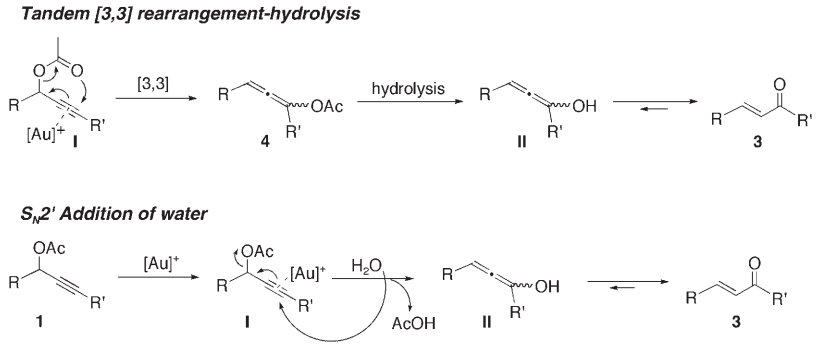
In the course of these studies, we observed, in the ^1H NMR spectrum of the crude product, the formation of a very minor amount (ca. 5%) of an unidentified by-product. More disturbing, these observations were found to be irre-

producible. We then carried out a scale-up experiment (10 mmol) to isolate and fully characterize this by-product. After purification, the ^{1}H NMR spectrum of the by-product exhibited two doublets at $\delta = 7.55$ and 6.75 ppm ($J = 16.2$ Hz), characteristic of two vinylidene protons of a disubstituted olefin placed in an *E* arrangement. In addition, a signal typical of a carbonylic carbon atom ($\delta = 200.9$ ppm) was observed in its ^{13}C NMR spectrum and permitted unequivocal characterization of α,β-unsaturated ketone **3a** [Eq. (2)].



(2)

To rationalize the formation of conjugated enone **3**, we envisaged the two mechanisms depicted in Scheme 2. The first mechanism relies on the gold-catalyzed formation of



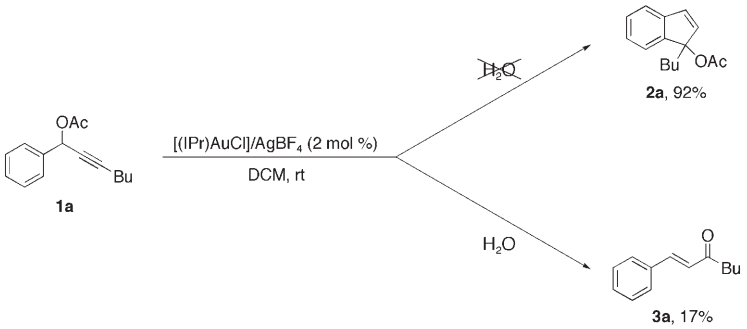
Scheme 2. Mechanisms envisioned for the formation of **3**.

allene **4**, which was shown to be a plausible intermediate en route to indenes **2**,[21] followed by further hydrolysis under the reaction conditions. Alternatively, the C≡C bond could be activated by a cationic gold species allowing nucleophilic attack of water on **I**. Rather than a classical hydration product,[23] the presence of a leaving group at the propargylic position would allow for the formation of allenol **II**, which further tautomerizes to the conjugated enone **3**. At this point in our studies, it was unclear whether the departure of the AcO^- fragment would be assisted by the gold species, nevertheless, the overall process could be considered as an S_N2' reaction. More importantly, regardless of the adopted mechanism, the presence of water appeared mandatory for production of the enone compound. We then thought that anhydrous conditions should inhibit the formation of **3** and yield only indene **2**. Conversely, addition of water should promote the formation of the enone.

To validate our hypothesis, we carried out two experiments under identical conditions, one with anhydrous dichloromethane (DCM) and one with DCM saturated with water, respectively. The presence of water dramatically changed the outcome of the reaction, affording selectively either the indene or the enone (Scheme 3). The use of anhydrous DCM rendered the formation of **2a** almost quantitative and simply adding water to the reaction mixture produced **3a** cleanly as the (*E*)-olefin, albeit in poor yield (the starting propargylic acetate accounting for the remaining mass balance).

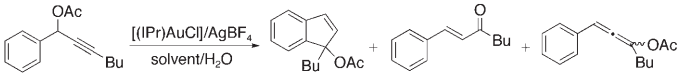
Optimization studies: After control experiments with only [(IPr)AuCl] and with no metal catalyst, which led to the recovery of the starting propargylic acetate **1a**, $AgBF_4$ alone was found, as expected, to produce the [3,3]-rearranged allene **4a**.[21] We then attempted complete conversion of the precursors into enone products. Reaction at room temperature, even with a prolonged reaction time, led to only partial conversion (Table 1, entry 2). On the other hand, increasing the temperature permitted total conversion of **1a**, but yielded allene **4a** as a by-product along with substantial amounts of oligomerized products (Table 1, entry 3).

We then screened a large number of solvents (Table 1, entries 4–12). 1,2-Dichloroethane and 1,4-dioxane proved no better than DCM and were not very selective (Table 1, entries 4 and 12), whereas using acetone resulted in the formation of a complex mixture of products (Table 1, entry 7). THF provided by far the best results, allowing conversion of **1a** into **3a** almost quantitatively (Table 1, entry 8). As water seemed to act as a reagent in this reaction, its concomitant use as solvent was attractive, notably for environmental rea-



Scheme 3. Critical role of water in the reaction of phenylpropargyl acetate **1**.

Table 1. Optimization of solvents in the formation of **3a**.[a]



1a **2a** **3a** **4a**

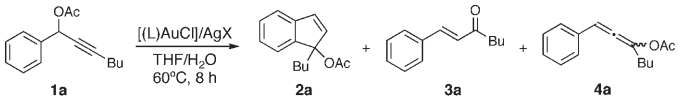
Entry	Solvent	T [°C]	t	Yield [%][b]		
				2a	**3a**	**4a**
1	DCM	25	5 min	–	17	–
2	DCM	25	24 h	–	58	–
3[c]	DCM	45	24 h	–	72	12
4[c]	DCE	80	2 h	8	64	4
5	DMF	90	24 h	–	3	–
6	pentane	40	24 h	no reaction		
7	acetone	50	4 h	unidentified mixture of products		
8	THF	65	4 h	–	90	–
9	toluene	90	24 h	–	–	10
10	H_2O	90	24 h	no reaction		
11	Et_2O	40	24 h	no reaction		
12[c]	1,4-dioxane	90	4 h	–	56	–

[a] Reaction conditions: alkyne **1a** (0.5 mmol), [(IPr)AuCl]/$AgBF_4$ (2 mol%), solvent (5 mL), H_2O (0.5 mL). [b] As determined by ^1H NMR spectroscopy. [c] Substantial amounts of oligomerized by-products were formed.

sons.[24] Unfortunately, as with DMF, pentane, Et_2O, and, to a lesser extent, toluene, precursor **1a** was recovered unreacted after 24 h (Table 1, entries 5, 6, and 9–11) under these conditions. We attribute these last observations to the insolubility of the gold species in these solvents. On the other hand, THF seems to possess the right combination of miscibility with water and solubility of the [(NHC)AuCl] complex to allow for complete conversion.

Next, we optimized the ligand on the gold center (Table 2). Steric hindrance of the ligand appeared to be crucial for the selectivity of the reaction. The more sterically encumbered the ligand, the more selective the formation of α,β-unsaturated ketone **3a** (Table 2, entries 1–4) proved to be. Hence, the extremely bulky I*t*Bu, compared with IPr and IMes,[25] yielded enone **3a** cleanly (Table 2, entry 3),

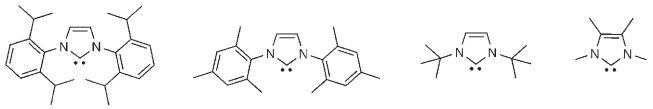
Table 2. Optimization of ligands and silver salts in the formation of **3a**.



1a **2a** **3a** **4a**

Entry	L	AgX	Yield [%][b]		
			2a	**3a**	**4a**
1	IPr	$AgBF_4$	–	90	–
2	IMes	$AgBF_4$	–	87	6
3	I*t*Bu	$AgBF_4$	–	98	–
4[c]	ITM	$AgBF_4$	6	63	4
5	I*t*Bu	$AgPF_6$	–	95	–
6	I*t*Bu	$AgSbF_6$	–	96	–

[a] Reaction conditions: alkyne **1a** (0.5 mmol), [(L)AuCl]/AgX (2 mol%), THF (5 mL), H_2O (0.5 mL). [b] As determined by ^1H NMR spectroscopy. [c] Substantial amounts of oligomerized by-products were formed.

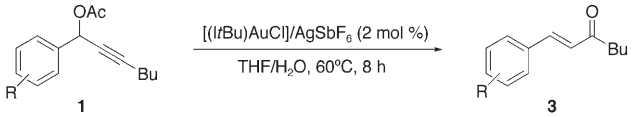


IPr IMes I*t*Bu ITM

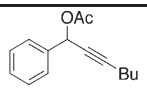
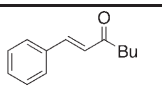
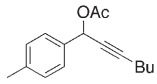
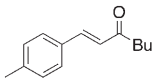
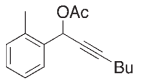
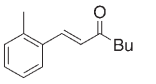
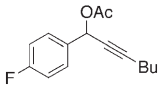
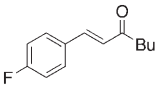
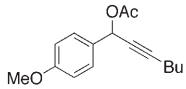
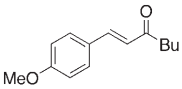
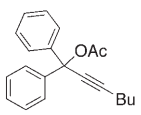
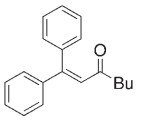
whereas the use of unencumbered ITM resulted in the formation of substantial amounts of oligomerized products (Table 2, entry 4). Finally, silver salts $AgBF_4$, $AgPF_6$, and $AgSbF_6$ were screened and showed similar behavior (Table 2, entries 3, 5, and 6).

Reaction scope: Next, we investigated the scope of this Au^I-catalyzed reaction. We first examined the effect of substitution on the phenyl ring (Table 3). Overall, the reaction was

Table 3. Gold-catalyzed formation of cinnamyl ketones.[a]



1 **3**

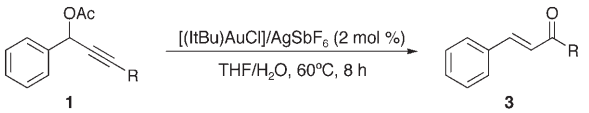
Entry	Propargyl acetate	**1**	Enone	**3**	Yield [%][b]
1		**1a**		**3a**	98
2		**1b**		**3b**	97
3		**1c**		**3c**	98
4		**1d**		**3d**	91
5		**1e**		**3e**	89
6		**1f**		**3f**	88

[a] Reaction conditions: alkyne **1** (1 mmol), [(I*t*Bu)AuCl]/$AgSbF_6$ (2 mol%), THF (10 mL), H_2O (1 mL). [b] Yield of isolated product, average of two runs.

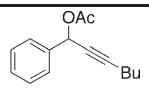
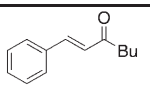
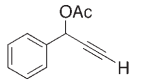
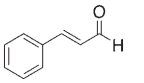
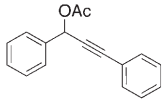
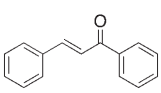
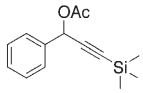
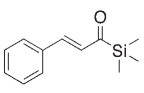
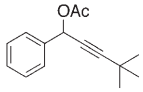
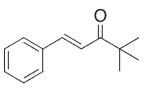
not affected by aromatic substitution and cinnamyl ketones possessing neutral, electron-withdrawing, and electron-donating groups were produced in excellent yields (Table 3, entries 1–5). In the case of electron-rich arenes, the formation of addition products, either on the alkene or the ketone moiety, as described by Hashmi and Dyker and their coworkers, was not observed.[26] This is probably due to the oxidation state of the gold atom (Au^I); since this type of reactivity has only been described with Au^{III} species. In addition, this highlights the chemoselectivity of the present catalytic system and its robustness towards disproportionation under the reaction conditions. Of note, although conjugated enones were produced from **1a** in 4 h, with **1b–e** extended reaction times were required. The tertiary acetate **1f** reacted similarly, yielding trisubstituted olefin **3f** in good yield (Table 3, entry 6). It is noteworthy that the procedure is extremely simple to perform and does not require any precautions as the gold complex is air- and moisture-stable.

Next, we turned our attention to the effect of acetylenic substitution. The results are presented in Table 4. A termi-

Table 4. Effect of acetylenic substitution on the gold-catalyzed reaction.[a]



1 3

Entry	Propargyl acetate	1	Enone/enal	3	Yield [%][b]
1		**1a**		**3a**	98
2		**1g**		**3g**	90
3		**1h**		**3h**	92
4[c]		**1i**		**3i**	nr
5[c]		**1j**		**3j**	nr

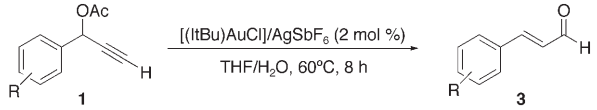
[a] Reaction conditions: alkyne **1** (1 mmol), [(I*t*Bu)AuCl]/$AgSbF_6$ (2 mol %), THF (10 mL), H_2O (1 mL). [b] Yield of isolated product, average of two runs. nr = no reaction [c] [(I*t*Bu)AuCl]/$AgSbF_6$ (10 mol %), 24 h.

nal alkyne was tested as it would afford an α,β-unsaturated aldehyde, which is an extremely valuable building block. Cinnamaldehyde **3g** was produced in excellent yield (Table 4, entry 2). Similarly, *trans*-chalcone **3h** was obtained, showing the compatibility of the reaction with phenylacetylenes (Table 4, entry 3). We examined the possibility of obtaining acylsilanes by subjecting precursor **1i** to gold catalysis. The TMS-containing alkyne did not react even with a high catalyst loading (10 mol %), at an elevated temperature, and/or after a prolonged reaction time (entry 4). The lack of reactivity of silylated alkynes, notably towards cycloisomerization, has already been reported.[27] Interestingly, the presence of a *tert*-butyl group at the acetylenic position resulted in a similar lack of reactivity (Table 4, entry 5). We therefore believe that more than the electronic effect of the TMS group, it is its bulky character that inhibits its reactivity.

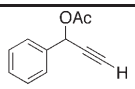
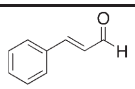
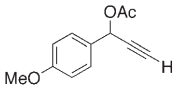
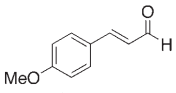
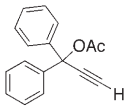
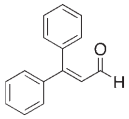
Because of the high potential of enals as electrophiles in organic synthesis, we decided to subject more terminal alkynes to our catalytic system. As shown in Table 5, the reaction is tolerant to aryl substitution (Table 5, entries 1 and 2). Furthermore, a tertiary acetate was converted into a trisubstituted enal (Table 5, entry 3).

All the substrates examined up to this point possessed an aryl moiety at the propargylic position, therefore yielding enones or enals that have a fully conjugated π system from the carbonyl through to the aryl. We envisaged that this full conjugation could be a major driving force for the formation of the enones. To address this possibility and to further expand the scope of the reaction, we tested alkyl and benzyl

Table 5. Gold-catalyzed formation of cinnamaldehydes.[a]



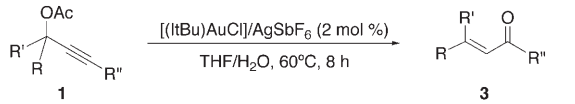
1 3

Entry	Propargyl acetate	1	Enal	3	Yield [%][b]
1		**1g**		**3g**	90
2		**1k**		**3k**	83
3		**1l**		**3l**	96

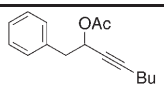
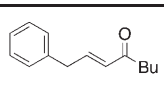
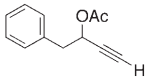
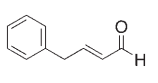
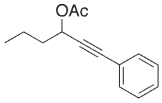
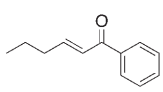
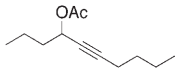
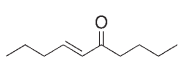
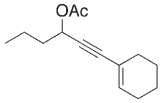
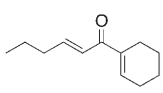
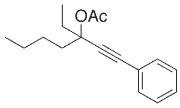
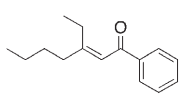
[a] Reaction conditions: alkyne **1** (1 mmol), [(I*t*Bu)AuCl]/$AgSbF_6$ (2 mol %), THF (10 mL), H_2O (1 mL). [b] Yield of isolated product, average of two runs.

acetates (Table 6). When subjected to gold catalysis, benzylpropargyl acetate **1m** afforded butyl ketone **3m** in good yield (Table 6, entry 1), expanding the scope of this enone synthesis to systems that are not fully conjugated. Even without the driving force of full conjugation, the scope of the reaction proved remarkably broad. α,β-Unsaturated aldehydes can be produced (Table 6, entry 2) in excellent yield, as can phenyl (Table 6, entry 3) or divinyl ketones (Table 6, entry 5).

Table 6. Gold-catalyzed formation of unactivated enones.[a]



1 3

Entry	Propargyl acetate	1	Enone/enal	3	Yield [%][b]
1		**1m**		**3m**	87
2		**1n**		**3n**	94
3		**1o**		**3o**	82 (*E*:*Z*, 12:1)
4		**1p**		**3p**	94
5		**1q**		**3q**	89
6		**1r**		**3r**	90 (*E*:*Z*, 1.2:1)

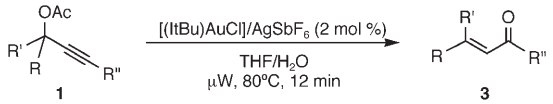
[a] Reaction conditions: alkyne **1** (1 mmol), [(I*t*Bu)AuCl]/$AgSbF_6$ (2 mol %), THF (10 mL), H_2O (1 mL). [b] Yield of isolated product, average of two runs.

Totally unactivated propargyl acetate **1p** afforded dialkyl enone **3p** in excellent yield (Table 6, entry 4), highlighting the efficiency of this synthetic method. In addition, trisubstituted enone **3r** was produced in a good overall yield, but, as expected, with poor *E*:*Z* selectivity as ethyl and butyl groups have only slight structural differences.

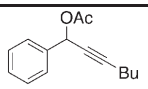
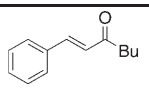
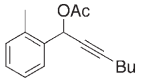
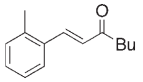
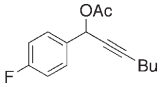
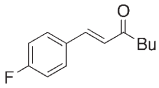
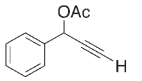
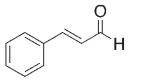
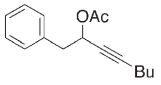
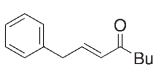
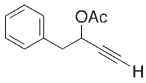
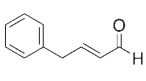
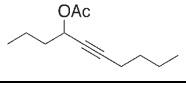
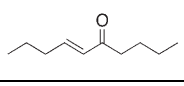
Gold-catalyzed transformations usually have extremely short reaction times (e.g., minute time frame), even those performed at room temperature. A possible drawback of the catalytic system presented herein is the lengthy reaction time (i.e., 8 h) required for the synthesis of enones or enals. As we wished this protocol to be as user friendly as possible to synthetic chemists, we investigated the use of microwave heating to shorten the reaction time.

Microwave-assisted organic and organometallic syntheses have recently witnessed a remarkable explosion in interest, notably because of their ability to shorten reaction times considerably.[28] After tests to optimize reaction conditions,[29] enone **1a** was produced in high yield under microwave heating after only 12 minutes at 80 °C in THF (Table 7, entry 1). We screened more substrates and were able to obtain α,β-unsaturated ketones and aldehydes, even with strongly unactivated dialkyl substrates (entry 7), in excellent yields and in remarkably shortened reaction times (Table 7). Most of the conjugated compounds produced by microwave heating did not require further purification by column chromatography and were found to be >95% pure by ^{1}H NMR spectroscopy. It should be noted that under these conditions, the NHC-containing gold catalytic system proved remarkably robust.[30]

Table 7. Microwave-assisted gold-catalyzed formation of conjugated enones and enals.[a]



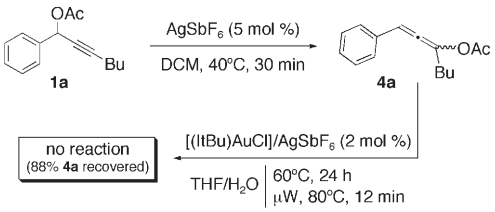
1 3

Entry	Propargyl acetate	1	Enone/enal	3	Yield [%][b]
1[c]		**1a**		**3a**	98
2[c]		**1c**		**3c**	99
3		**1d**		**3d**	90
4[c]		**1g**		**3g**	98
5		**1m**		**3m**	93
6[c]		**1n**		**3n**	93
7[c]		**1p**		**3p**	95

[a] Reaction conditions: alkyne **1** (1 mmol), [(I*t*Bu)AuCl]/$AgSbF_6$ (2 mol%), THF (10 mL), H_2O (1 mL). [b] Yield of isolated product, average of two runs. [c] No purification by silica gel column chromatography was needed.

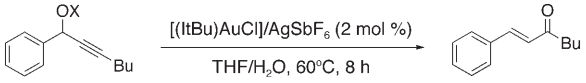
Mechanistic studies

Allenes as intermediates? In view of the striking effect of water on the outcome of the reaction, as depicted in Scheme 3, we investigated the possible mechanisms for this transformation. The first pathway we envisaged involves a [3,3] sigmatropic rearrangement of the propargylic acetate to allene **4** (see Scheme 2) followed by hydrolysis of the ester group to yield allenol **II**, the tautomer of enone **3**.[31] To address this possibility, we synthesized and isolated allene **4a** by silver-catalyzed [3,3] sigmatropic rearrangement of propargylic acetate **1a**[32] and subjected it to the catalytic conditions for enone formation. Strikingly, even after a prolonged reaction time, both under conventional and microwave-assisted heating, the formation of enone **3a** was not observed (Scheme 4), ruling out a possible hydrolysis pathway under these reaction conditions.



Scheme 4. Formation of allene **4a** and its subjection to gold catalysis.

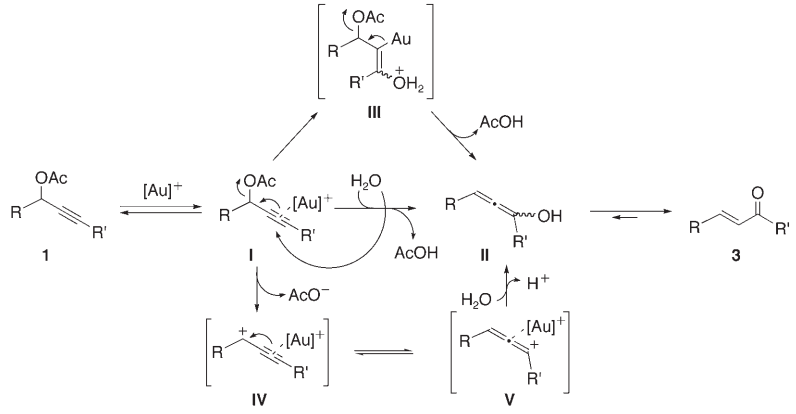
Additional information supporting the non-involvement of allenes as intermediates in the formation of enones was provided by the experiments shown in Scheme 5. In an attempt to evaluate the effect of a hypothetical leaving group at the propargylic position and to gather further information related to the reaction mechanism, we synthesized analogues of acetate **1a** and tested them for the production of enone **3a**. Alcohol **5** did not react under our catalytic conditions and was almost fully recovered (89%). This seems to exclude a Meyer–Schuster-like pathway in which a formal rearrangement of the propargylic alcohol assisted by gold would have been involved.[8] Interestingly, precursor **6**, the methyl ether analogue of **1a**, afforded enone **3a** in moderate yield.[33] We believe that this last result strongly supports the nonparticipation of allene **4a** as a possible intermediate



Scheme 5. Effect of *O*-substitution on the formation of **3a**.

because of the inability of methoxy groups to undergo [3,3] rearrangements.[34]

An S_N2'-like mechanism? An "intuitive" mechanism we could propose for the transformation of propargyl acetate **1** to enone **3** is depicted in Scheme 6.



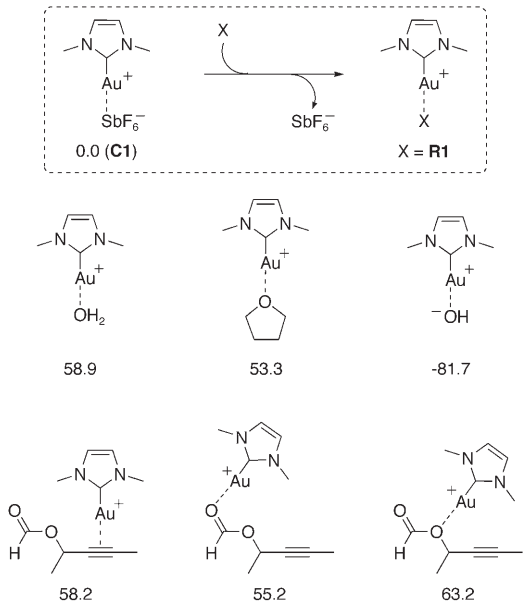
Scheme 6. "Intuitive" mechanism for the formation of **3** from **1**.

Three possible S_N2'-like mechanisms were considered: 1) A concerted mechanism with assistance of cationic gold, in accordance with most proposals on gold homogeneous catalysis, to render the alkyne more prone to nucleophilic attack (middle pathway); 2) a stepwise mechanism involving the addition of water and the formation of a vinylgold species **III** followed by expulsion of acetic acid (top path); 3) another stepwise mechanism proceeding by the release of AcO^- and subsequent addition of water (bottom path). We evaluated the possibility of these S_N2' mechanisms with the help of computational chemistry. DFT calculations at the B3LYP level of theory were carried out on a model system in which the leaving group was formate, the propargylic and alkyne substituents were methyl groups, and the NHC was represented by IDM (*N*,*N*′-dimethylimidazol-2-ylidene). All the energetic data discussed are enthalpies calculated at 298.15 K and 1 atm ($\Delta H_{G,298.15}$).

Unexpectedly, these calculations failed to support the mechanisms proposed in Scheme 6. Following the middle path, the nucleophilic addition of water onto a complex in which the cationic gold species is bound to the alkyne, we were not able to locate a transition state leading to allenol **II**. Our trial optimizations all reverted to the reactants. When optimizing the vinylgold intermediate **III** proposed in the top path, it was found to be unstable, reverting to **I** and water. We consider these results conclusive because neither of the paths relating to species **II** or **III** involves charge separation, which, therefore, makes them very unlikely to be affected by solvation effects. Finally, the lower path, with acetate as the leaving group leading to complete charge separation and intermediate **IV**, is difficult to analyze by gas phase calculations and would require solvation effects to be considered. However, it was found to have an energy 200 kcal mol^{-1} greater than that of **I**. We strongly believe that such a large energy gap prohibits the formation of **IV**, therefore rendering the bottom pathway highly unlikely, even in the condensed phase.

An alternative S_N2' mechanism: The mechanistic proposals in Scheme 6 are based on the assumption that the role of the gold catalyst is to activate the alkyne. This is exemplified by the initial formation of species **I**. The unexpected failure of our calculations to support this mechanism prompted us to examine the possibility that the cationic gold species activates a water molecule or another coordinating species in solution. From an experimental point of view, the former possibility is not infeasible, as the experiments reported above showed that in the absence of water a different chemical transformation takes place (see above).

The energies of the different gold species that may be formed in the reaction mixture from the cationic [(NHC)AuSbF$_6$] complex are reported in Scheme 7. Cationic complexes of the type [(NHC)AuX], where X is a noncoordinating ligand, are known to exist experimentally and have been characterized:[35] the energies are given relative to [(NHC)AuSbF$_6$] (**C1**). Two groups of ligands have been analyzed: neutral (**1**, H_2O, THF) and anionic (SbF_6^-, OH^-).



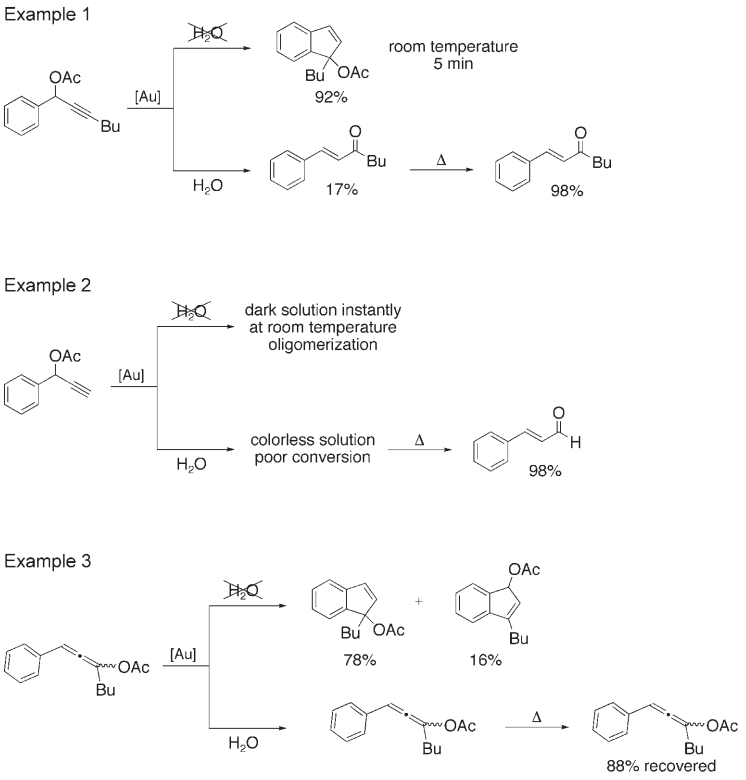
Scheme 7. Relative binding energies of ligands to gold species present in the reaction mixture (energies in kcal mol^{-1}).

Comparison between the different groups is hampered by the lack of solvation effects, but analysis of the trends within each group is informative. Regarding the neutral species, of the three possible complexes that can form between **1** and a cationic NHC–gold species, the most stable one involves the coordination of gold to the carbonyl oxygen atom and not to the triple bond as expected. Moreover, the calculations indicate that the THF–gold complex is more stable than the corresponding complexes with the propargylic formate.

The very stable complex formed by the association of a hydroxide anion and the cationic gold center caught our attention.[36,37] The [(NHC)AuOH] species **C2** could be the active form of the catalyst in solution. We decided to analyze the possible formation of this complex from the initial species **C1**. Direct reaction of **C1** with water can indeed produce **C2**, but the reaction is endothermic by 48.9 kcal mol^{-1} because the other product, $HSbF_6$, is a high-energy compound with strong acidity. In the presence of water, $HSbF_6$ would be strongly solvated. We found in fact that its association with four water molecules leads to a reasonable network of hydrogen bonds, with abstraction of the proton from the antimonate and a species better described as $SbF_6^-\cdots H_7O_3^+$. Formation of [(NHC)AuOH] (**C2**) and $SbF_6^-\cdots H_7O_3^+$ from [(NHC)AuSbF$_6$] and four water molecules is exothermic by 21.1 kcal mol^{-1}, thus favorable. **C2** is therefore likely to be present under the reaction conditions. On the other hand, the protonated water cluster is unlikely to play any role in the subsequent reaction as it is not acidic enough to transfer its proton to the weak basic centers in the reaction medium. In contrast, the hydroxy complex **C2** is a viable catalyst.[38]

In addition, the fact that from the exact same propargylic acetate, two very different compounds are produced in the presence or absence of water can be attributed to two distinct catalytic species. It should also be noted that not only the nature of the products but the reaction conditions are dramatically altered for the transformation to proceed. Thus, extended reaction time and heating are required for the formation of enones, whereas indenes are produced at room temperature in minutes, as shown in Scheme 8. From observations, the presence of water slows down the reaction significantly and leads to a new type of product. This means that water does not only allow the formation of enones, but inhibits the pathway leading to indenes. We therefore believe that these observations, together with the results of our computational studies, strongly support two distinct catalytic species for the formation of indenes and enones, [(NHC)AuX] (X is a non-coordinating ligand) and [(NHC)AuOH], respectively.

Following the general S_N2' scheme presented earlier, but with complex **C2** as the active species, we propose the catalytic cycle presented in Scheme 9. In contrast to our first suggestion, in which the gold center was thought to activate the carbon–carbon triple bond of **1**, the gold instead activates water by forming the hydroxide complex **C2** and releases a solvated cluster of $HSbF_6$. At this point in our study, the possibility of a Brønsted acid catalyzed reaction

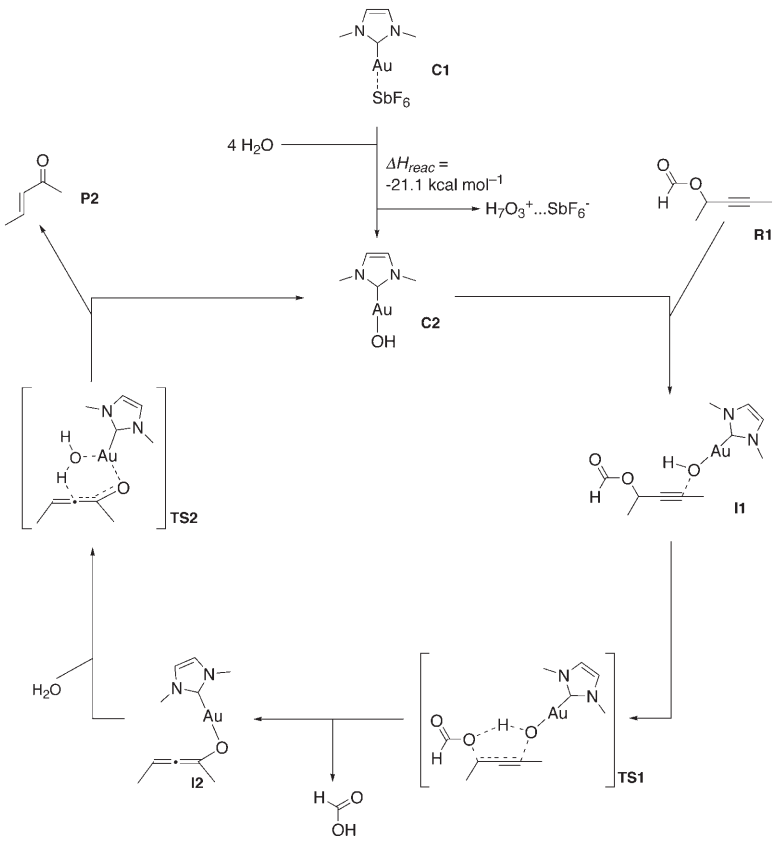


Scheme 8. Influence of water on the reactivity.

could not be overruled and accordingly two control reactions were performed. Alkyne **1a**, when heated at 60 °C for 16 h in THF and water in the presence of up to 20 mol % of HPF_6, was mainly recovered (80 %) along with degradation products (15 %) and traces of **3a** (<5 %). When HBF_4 was employed under the same conditions, only a small amount of degradation (5 %) was observed along with unreacted alkyne **1a**. It seems reasonable then to exclude the possibility of strong Brønsted acids acting as catalysts in this transformation.

To verify the suggested mechanism, all the stationary points in the catalytic cycle were calculated and are presented in the potential energy profile (Figure 1). The optimized geometries of some key structures (**I1**, **TS1**, and **I2**) are shown in Figure 2. Unless stated otherwise, all the energies discussed are given relative to the free reactant **R1** and the gold complex **C2**.

In the first step of the reaction a complex (**I1**) between **C2** and **R1** is formed with an energy of −4.8 kcal mol^{-1}. The complex rearranges to transition state **TS1**, in which the proton of the hydroxy group of **C2** has been transferred to the inner oxygen atom of **R1**. The oxygen atom of **C2** binds in a concerted process to the most electron-deficient carbon atom of the triple bond in **R1**, "delivering" the oxygen atom to the alkyne.[39] Formic acid is formed and acts as a leaving group. A possible alternative transition state involves the transfer of the proton to the carbonyl oxygen atom. However, this TS was found to have a higher energy than **TS1**. The transition state has an energy of 20.6 kcal mol^{-1} and the for-



Scheme 9. Proposed reaction mechanism for the gold-catalyzed production of α,β-unsaturated carbonyl compounds based on calculations.

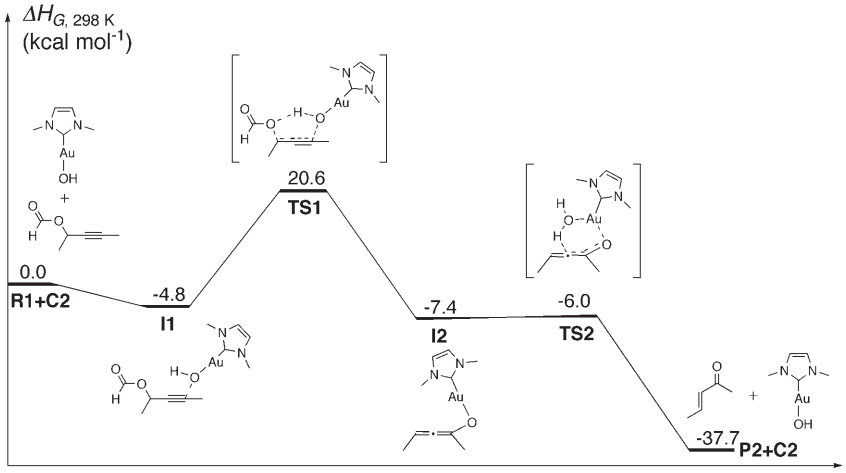


Figure 1. Computed potential energy profile for the gold-catalyzed formation of enones.

mation of gold allenolate **I2** is exothermic by 7.4 kcal mol^{-1}. To complete the catalytic cycle, water adds to **I2**, proceeding through a cyclic six-membered ring TS (**TS2**), to give the enone and regenerating catalyst **C2**. The barrier for this step is only 1.4 kcal mol^{-1} relative to **I2** and the overall process is exothermic by nearly 40 kcal mol^{-1} relative to the free reactants. The energy barrier computed for the rate-determining step of the gold-catalyzed reaction, from **I1** to **TS1**, is 25.4 kcal mol^{-1}.

The uncatalyzed reaction: To compare the energetics and to learn more about the catalytic function of the gold complex, the corresponding uncatalyzed reaction was investigated, that is, the addition of water to **R1**.

The reaction mechanism for the uncatalyzed reaction is presented in Scheme 10 and its energy profile in Figure 3. In the first step a reaction complex is formed with water bound to the reactant, forming complex **I3**, exothermic by 9.6 kcal mol^{-1}. Allenol **P1** is formed via transition state **TS3**, with a proton from H_2O being transferred to the carbonyl oxygen of **R1** to form formic acid which departs concomitantly to the formation of the C–O bond. This is in sharp contrast to the gold-catalyzed reaction in which the proton from **C2** is transferred to the inner oxygen atom of **R1** and not to the carbonyl oxygen. An alternative transition state for the uncatalyzed reaction, corresponding to **TS1**, was optimized, however, this six-membered structure was found to have a higher energy than **TS3** (3.4 kcal mol^{-1} above **TS3**).

TS3 has an energy of 26.6 kcal mol^{-1} relative to **R1**+H_2O. The barrier computed for the rate-limiting step of the uncatalyzed reaction, from **I3** to **TS3**, is 36.2 kcal mol^{-1}. This barrier is 10.8 kcal mol^{-1} higher than that for the gold-catalyzed reaction. The catalytic effect is thus properly reproduced.

Finally, we noticed that in the key rate-determining step of the catalyzed reaction, from **I1** to **TS1**, the sum of Mulliken charges in the [(NHC)Au] fragment changes from +0.432 to +0.542 atomic units, a change of 0.090 atomic units. On the other hand, in the uncatalyzed reaction, the Mulliken charge on the proton occupying the equivalent position changes by only 0.045 atomic units (from +0.470 to +0.515 atomic units) in the equivalent step, that is, going from **I3** to **TS3**.

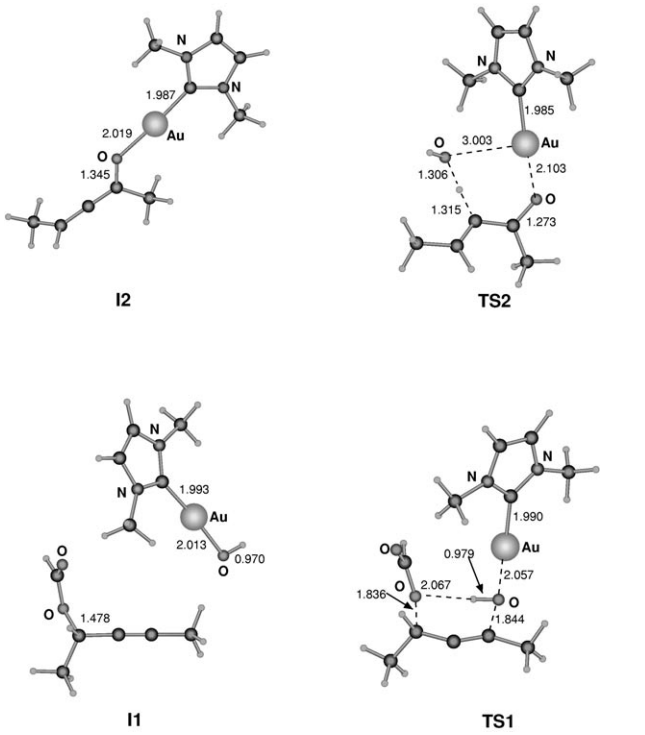
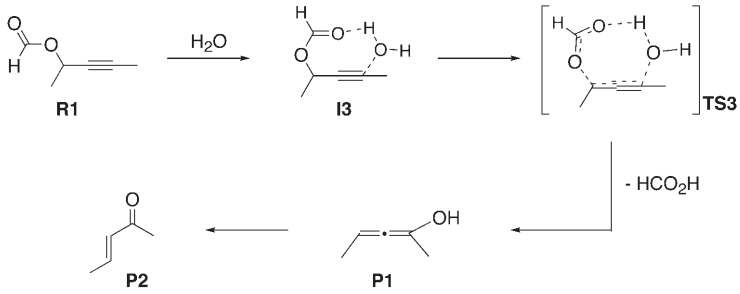


Figure 2. Geometries of stationary points in the gold-catalyzed reaction.



Scheme 10. Plausible mechanism for the uncatalyzed production of α,β-unsaturated carbonyl compounds.

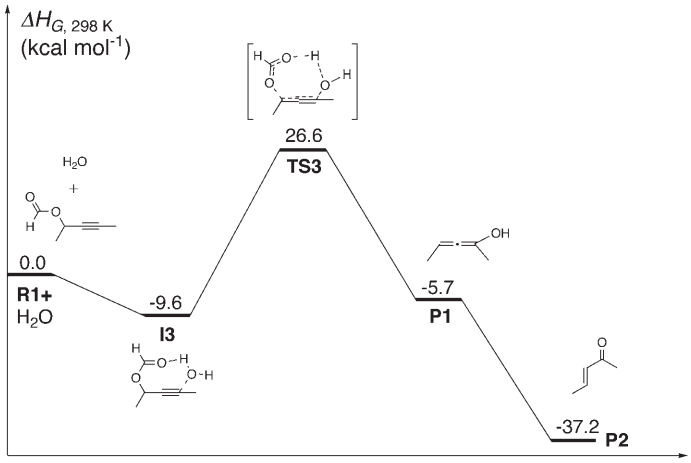


Figure 3. Computed potential energy profile for the uncatalyzed formation of enones.

Therefore, the advantage of replacing a proton by a gold species lies probably in the better ability of the latter to stabilize the positive charge that develops at this position during the reaction cycle.

Conclusion

In summary, we have described a novel type of Au^I-catalyzed transformation that enables the formation of α,β-unsaturated carbonyl compounds from easily accessible propargylic acetates. The use of [(NHC)AuCl] complexes in conjunction with a silver salt has allowed the efficient and stereoselective formation of a wide array of conjugated (*E*)-enones and -enals in high yields. Water has been found to play a crucial role in the outcome of the reaction, which has also been investigated by computational methods. These studies have led to the proposal of an unprecedented type of reactivity in the field of gold catalysis and strongly support [(NHC)AuOH] as the active catalyst. Based on calculations of a full catalytic cycle, this gold species is proposed to deliver its hydroxy moiety to the alkyne to form a gold–allenolate intermediate that is hydrolyzed by water to produce the enone and regenerate [(NHC)AuOH]. Additional research to experimentally verify this unprecedented reactivity of gold(I) complexes is being devised. Further investigations on this novel type of reactivity are ongoing in our laboratories.

Experimental Section

General information: All reagents were used as purchased. Reactions were carried out under anhydrous nitrogen unless otherwise indicated. Dry tetrahydrofuran (THF) and dry dichloromethane (DCM) were purified by passing through a purification column from Innovative Technology Inc. (SPS-400-6). Silver salts were stored in a desiccator wrapped in aluminium foil. [(NHC)AuCl] complexes were synthesized according to literature procedures.[35b] The microwave-assisted reactions were carried out using a Biotage Initiator 2.0. Thin-layer chromatography (TLC) of reaction mixtures was performed on EMD Chemicals silica gel 60 F_{254} plates and visualized using UV light at 254 nm. Flash chromatography was performed on silica gel 60 (230–400 mesh, Silicycle). ^1H and ^{13}C NMR spectra were recorded with a Varian-300, Varian-400, Bruker-300 or Bruker-500 spectrometer at ambient temperature in $CDCl_3$ containing tetramethylsilane. Chemical shifts are given in ppm and are referenced to the peak of tetramethylsilane (0.0 ppm). Some ^1H and ^{13}C NMR signals were assigned by COSY and/or HMBC experiments. Elemental analyses were performed at Robertson Microlit Laboratories, Inc., Madison, NJ (USA).

Synthesis of propargylic acetates 1: Compounds **1a**–**1e**,[21] **1h**,[40] **1i**,[41] and **1p**[42] have already been reported and fully characterized.

General procedures

Alkynylation: In an oven-dried round-bottom flask, the alkyne (13 mmol, 1.3 equiv) and 1.6 M *n*BuLi (12 mmol, 1.2 equiv) were added to THF (20 mL) and stirred for 20 min under nitrogen at −78 °C. The aldehyde or the ketone (10 mmol, 1 equiv) was added and the reaction mixture stirred for 20 min. The mixture was then allowed to warm up to room temperature, quenched with a saturated aqueous NH_4Cl solution, and extracted with diethyl ether. The combined organic layers were washed with brine, dried with magnesium sulfate, filtered, and evaporated to give

the crude propargylic alcohol which was engaged in the next step without further purification.

Acylation: The propargylic alcohol (10 mmol, 1 equiv), 1,2-dichloroethane (DCE) (30 mL), 4-dimethylaminopyridine (DMAP) (0.360 g, 3.0 mmol, 0.3 equiv), Et_3N (5.6 mL, 40 mmol, 4 equiv), and Ac_2O (1.8 mL, 20 mmol, 2 equiv) were added in turn to a round-bottom flask equipped with a condenser. The reaction mixture was heated overnight at 80 °C, quenched with a saturated aqueous NH_4Cl solution, and extracted with diethyl ether. The combined organic layers were washed with brine, dried with magnesium sulfate, filtered, and evaporated to give a crude product that was purified by flash chromatography on silica gel.

Alternatively, the propargylic alcohols could be acylated under microwave-heating conditions as follows. The propargylic alcohol (10 mmol, 1 equiv), DMAP (0.360 g, 3.0 mmol, 0.3 equiv), Et_3N (5.6 mL, 40 mmol, 4 equiv), and Ac_2O (1.8 mL, 20 mmol, 2 equiv) were added in turn to a vial designed for use in a microwave. The reaction mixture was heated under microwave heating at 100 °C for 12 min. The reaction was then quenched with a saturated aqueous NH_4Cl solution and extracted with diethyl ether. The combined organic layers were washed with brine, dried with magnesium sulfate, filtered, and evaporated to give a crude product that was purified by flash chromatography on silica gel when necessary.

Desilylation: Compounds **1g**, **1k**, **1l**, and **1n** were obtained by desilylation of the alkyne. The silylated alkyne (10 mmol, 1 equiv) was diluted with DMSO (17 mL). KF (480 mg, 8.3 mmol, 1.5 equiv) and a few drops of water were added. After 45 min the reaction mixture was quenched with water and extracted with diethyl ether. The combined organic layers were washed with brine, dried with $MgSO_4$, and evaporated to give a crude product purified by flash chromatography on silica gel.

1,1-Diphenylhept-2-ynyl acetate (1f): The above general procedure yielded, after flash chromatography on silica gel (pentane/Et_2O, 98:2), 2.21 g (83 % over two steps) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.37–7.34 (m, 2H; H^{Ar}), 7.23–7.20 (m, 8H; H^{Ar}), 2.16 (dt, J = 6.9, 2.0 Hz, 2H; ≡C-CH_2), 2.03 (s, 3H; OAc), 1.48–1.42 (m, 2H; CH_2), 1.40–1.34 (m, 2H; CH_2), 0.89 ppm (t, J = 7.2 Hz, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 170.1 (C; C=O), 140.2 (C; C^{Ar}), 129.8 (CH; C^{Ar}), 127.9 (CH; C^{Ar}), 127.5 (CH; C^{Ar}), 87.2 (C; *C*≡CH), 82.7 (C; *C*-OAc), 78.2 (CH; C≡*C*H), 31.6 (CH_2), 22.3 (CH_2), 21.0 (CH_3; OAc), 18.7 (CH_2), 13.1 ppm (CH_3); elemental analysis calcd (%) for $C_{21}H_{22}O_2$ (306.40): C 82.32, H 7.24; found: C 82.04, H 7.27.

1-Phenylprop-2-ynyl acetate[43] **(1g)**: The above general procedure yielded, after flash chromatography on silica gel (pentane/Et_2O, 98:2), 1.11 g (64 % over three steps) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.52–7.49 (m, 2H; H^{Ar}), 7.33–7.30 (m, 3H; H^{Ar}), 6.45 (d, J = 2.0 Hz, 1H; C*H*-OAc), 2.66 (d, J = 2.0 Hz, 1H; ≡CH), 1.99 ppm (s, 3H; OAc); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 169.3 (C; C=O), 136.5 (C; C^{Ar}), 128.9 (CH; C^{Ar}), 128.6 (CH; C^{Ar}), 127.6 (CH; C^{Ar}), 80.2 (C; *C*≡CH), 75.5 (CH; C≡*C*H), 65.1 (CH; *C*H-OAc), 20.7 ppm (CH_3; OAc).

4,4-Dimethyl-1-phenylpent-2-ynyl acetate (1j): The above general procedure yielded, after filtration through a plug of Celite, 1.72 g (75 % over two steps) of the title compound. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.53–7.51 (m, 2H; H^{Ar}), 7.39–7.33 (m, 3H; H^{Ar}), 6.49 (s, 1H; C*H*-OAc), 2.08 (s, 3H; OAc), 1.25 ppm (s, 9H; *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 170.1 (C; C=O), 138.1 (C; C^{Ar}), 128.9 (CH; C^{Ar}), 128.7 (CH; C^{Ar}), 128.0 (CH; C^{Ar}), 96.5 (C; C≡*C*-*t*Bu), 75.4 (C; *C*≡C-*t*Bu), 66.1 (CH; *C*H-OAc), 31.0 (CH_3; *t*Bu), 27.7 (C; *t*Bu), 21.5 ppm (CH_3; OAc); HRMS: *m*/*z*: calcd for $C_{21}H_{22}O_2Na$ $[M+Na]^+$: 253.1204; found: 253.1206.

1-(4-Methoxyphenyl)prop-2-ynyl acetate (1k): The above general procedure yielded, after filtration through a plug of silica, 1.59 g (78 % over three steps) of the title compound. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.46 (d, J = 8.7 Hz, 2H; H^{Ar}), 6.90 (d, J = 8.7 Hz, 2H; H^{Ar}), 6.40 (s, 1H; C*H*-OAc), 3.80 (s, 3H; OMe), 2.65 (d, J = 2.3 Hz, 1H; ≡CH), 2.08 ppm (s, 3H; OAc); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 169.9 (C; C=O), 160.4 (C; C^{Ar}-OMe), 129.5 (CH; C^{Ar}), 128.9 (C; C^{Ar}-CH(OAc)), 114.2 (CH; C^{Ar}), 80.7 (C; *C*≡CH), 75.3 (CH; C≡*C*H), 65.2 (CH; *C*H-OAc), 55.5 (CH_3; OMe), 21.2 ppm (CH_3; OAc); HRMS: *m*/*z*: calcd for $C_{12}H_{12}O_3Na$ $[M+Na]^+$: 227.0684; found: 227.0686.

1,1-Diphenylprop-2-ynyl acetate (1l): The corresponding alcohol was purchased and acylated as described above to yield, after flash chromatography on silica gel (pentane/Et_2O, 98:2), 1.80 g (72 %) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.47–7.43 (m, 2H; H^{Ar}), 7.23–7.17 (m, 8H; H^{Ar}), 2.72 (s, 1H; ≡CH), 2.04 ppm (s, 3H; OAc); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 170.1 (C; C=O), 146.4 (C; C^{Ar}), 129.6 (CH; C^{Ar}), 128.4 (CH; C^{Ar}), 126.9 (CH; C^{Ar}), 86.4 (C; *C*≡CH), 84.2 (C; *C*-OAc), 75.2 (CH; C≡*C*H), 21.2 ppm (CH_3; OAc); elemental analysis calcd (%) for $C_{16}H_{20}O_2$ (250.29): C 81.58, H 5.64; found: C 81.36, H 5.77.

1-Phenyloct-3-yn-2-yl acetate (1m): The above general procedure yielded, after flash chromatography on silica gel (pentane/Et_2O, 98:2), 2.12 g (87 % over two steps) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.34–7.22 (m, 5H; H^{Ar}), 5.56 (tt, J = 6.8, 2.0 Hz, 1H; C*H*-OAc), 3.05 (m, 2H; C^{Ar}-CH_2), 2.19 (dt, J = 6.9, 2.0 Hz, 2H; ≡C-CH_2), 2.05 (s, 3H; OAc), 1.51–1.41 (m, 2H; CH_2), 1.40–1.29 (m, 2H; CH_2), 0.90 ppm (t, J = 7.2 Hz, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 170.1 (C; C=O), 136.4 (C; C^{Ar}), 129.9 (CH; C^{Ar}), 128.4 (CH; C^{Ar}), 127.0 (CH; C^{Ar}), 87.4 (C; ≡C), 77.2 (C; ≡C), 65.2 (CH; *C*H-OAc), 41.7 (CH_2; C^{Ar}-CH_2), 30.6 (CH_2; ≡C-CH_2), 22.0 (CH_2), 21.2 (CH_3; OAc), 18.5 (CH_2), 13.8 ppm (CH_3); elemental analysis calcd (%) for $C_{16}H_{20}O_2$ (244.33): C 78.65, H 8.25; found: C 78.86, H 8.07.

1-Phenylbut-3-yn-2-yl acetate (1n): The above general procedure yielded, after flash chromatography on silica gel (pentane/Et_2O, 98:2), 1.51 g (80 % over three steps) of the title compound. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.30–7.23 (m, 5H; H^{Ar}), 5.53 (td, J = 6.8, 2.2 Hz, 1H; C*H*-OAc), 3.07–3.04 (m, 2H; CH_2), 2.44 (d, J = 2.2 Hz, 1H; ≡CH), 2.00 ppm (s, 3H; OAc); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 169.7 (C; C=O), 135.7 (C; C^{Ar}), 129.7 (CH; C^{Ar}), 128.4 (CH; C^{Ar}), 127.1 (CH; C^{Ar}), 80.8 (C; *C*≡CH), 74.5 (CH; C≡*C*H), 64.3 (CH; *C*H-OAc), 41.0 (CH_2), 20.8 ppm (CH_3; OAc); elemental analysis calcd (%) for $C_{12}H_{12}O_2$ (188.22): C 78.01, H 5.87; found: C 77.89, H 5.68.

1-Phenylhex-1-yn-3-yl acetate (1o): The above general procedure yielded, after flash chromatography on silica gel (pentane/Et_2O, 95:5), 1.67 g (77 % over two steps) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.45–7.42 (m, 2H; H^{Ar}), 7.30–7.27 (m, 3H; H^{Ar}), 5.61 (t, J = 6.7 Hz, 1H; C*H*-OAc), 2.09 (s, 3H; OAc), 1.87–1.79 (m, 2H; CH_2-CH(OAc)), 1.59–1.47 (m, 2H; CH_2-CH_3), 0.98 ppm (t, J = 7.4 Hz, 3H; CH_2-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 170.0 (C; C=O), 131.9 (CH; C^{Ar}), 128.6 (CH; C^{Ar}), 128.3 (CH; C^{Ar}), 122.4 (C; C^{Ar}), 86.7 (C; ≡C), 85.2 (C; ≡*C*), 64.4 (CH; *C*H-OAc), 37.0 (CH_2; *C*H_2-CH(OAc)), 21.1 (CH_3; OAc), 18.5 (CH_2; *C*H_2-CH_3), 13.7 ppm (CH_3; CH_2-*C*H_3); elemental analysis calcd (%) for $C_{14}H_{16}O_2$ (216.28): C 77.75, H 7.46; found: C 77.89, H 7.38.

1-Cyclohexenylhex-1-yn-3-yl acetate (1q): The above general procedure yielded, after flash chromatography on silica gel (pentane/Et_2O, 98:2), 1.89 g (86 % over two steps) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 6.13–6.11 (m, 1H; =CH), 5.50 (t, J = 6.6 Hz, 1H; C*H*-OAc), 2.10–2.07 (m, 7H; OAc, =C-CH_2), 1.78–1.70 (m, 2H; CH_2-CH(OAc)), 1.66–1.53 (m, 4H; $CH_2^{cyclohexene}$), 1.50–1.40 (m, 2H; CH_2-CH_3), 0.95 ppm (t, J = 7.4 Hz, 3H; CH_2-*C*H_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 169.6 (C; C=O), 135.9 (CH; =*C*H), 120.0 (C; *C*=CH), 87.1 (C; ≡C), 83.9 (C; ≡*C*), 64.6 (CH; *C*H-OAc), 37.2 (CH_2; *C*H_2-CH(OAc)), 29.1 (CH_2; =C-*C*H_2), 25.7 (CH_2; =CH-*C*H_2), 23.3 ($CH_2^{cyclohexene}$), 21.5 ($CH_2^{cyclohexene}$), 21.2 (CH_3; OAc), 18.5 (CH_2; *C*H_2-CH_3), 13.7 ppm (CH_3; CH_2-*C*H_3); elemental analysis calcd (%) for $C_{14}H_{20}O_2$ (220.31): C 76.33, H 9.15; found: C 76.35, H 9.28.

3-Ethyl-1-phenylhept-1-yn-3-yl acetate (1r): The above general procedure yielded, after flash chromatography on silica gel (pentane/Et_2O, 99:1), 1.73 g (67 % over two steps) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.46–7.41 (m, 2H; H^{Ar}), 7.31–7.26 (m, 3H; H^{Ar}), 2.20–1.90 (m, 7H; OAc + CH_2-CH(OAc)), 1.53–1.30 (m, 4H; CH_2), 1.04 (t, J = 7.4 Hz, 3H; CH_2-*C*H_3), 0.94 ppm (t, J = 7.2 Hz, 3H; CH_2-*C*H_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 169.5 (C; C=O), 132.0 (CH; C^{Ar}), 128.4 (CH; C^{Ar}), 128.3 (CH; C^{Ar}), 123.0 (C; C^{Ar}), 89.0 (C; ≡C), 85.9 (C; ≡*C*), 80.1 (C; *C*-OAc), 37.8 (CH_2), 31.5 (CH_2), 26.5 (CH_2), 22.9 (CH_2), 22.2 (CH_3; OAc), 14.3 (CH_3), 8.7 ppm (CH_3); elemen-

tal analysis calcd (%) for $C_{17}H_{22}O_2$ (258.36): C 79.03, H 8.58; found: C 79.28, H 8.47.

[(NHC)Au^{I}]-catalyzed formation of conjugated enones and enals 3: Compounds **3a**,**b**,[44] **3g**,**h**,[45] **3k**,[45] and **3l**,[46] have already been reported and fully characterized.

General procedures

Conventional heating: $AgSbF_6$ (6.8 mg, 0.02 mmol, 2 mol%) was added o a THF solution (5 mL) of [(I*t*Bu)AuCl] (8.2 mg, 0.02 mmol, 2 mol%) in a screw-cap vial. The solution instantly became cloudy and distilled water (1 mL) was added. The reaction mixture was stirred for 1 min before a THF solution (5 mL) of propargylic acetate **1** (1 mmol, 1 equiv) was added. The vial was then placed in an oil bath at 60 °C and the reaction mixture stirred for 8 h and then allowed to cool to room temperature. The resulting mixture was dissolved in pentane, filtered through Celite, and evaporated. The crude product was purified by flash chromatography on silica gel.

Microwave heating: $AgSbF_6$ (6.8 mg, 0.02 mmol, 2 mol%) was added to a THF solution (5 mL) of [(I*t*Bu)AuCl] (8.2 mg, 0.02 mmol, 2 mol%) in a microwave-designed vial. The solution instantly became cloudy and distilled water (1 mL) was added. The reaction mixture was stirred for 1 min before a THF solution (5 mL) of propargylic acetate **1** (1 mmol, 1 equiv) was added. The vial was then placed in a microwave reactor and heated at 80 °C for 12 min. The resulting mixture was dissolved in pentane, filtered through Celite, and evaporated. The crude product was purified by flash chromatography on silica gel when necessary.

(*E*)-1-(*o*-Tolyl)hept-1-en-3-one (3c): The above general procedure using conventional heating yielded, after flash chromatography on silica gel (pentane/Et_2O, 98:2), 198 mg (98%) of the title compound. The above general procedure using microwave heating yielded, after filtration through a plug of Celite, 200 mg (99%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.86 (d, J = 16.0 Hz, 1H; C^{Ar}-CH=), 7.58 (d, J = 7.0 Hz, 1H; H^{Ar}), 7.29–7.19 (m, 3H; H^{Ar}), 6.67 (d, J = 16.0 Hz, 1H; =CH-C=O), 2.66 (t, J = 7.2 Hz, 2H; CH_2-C=O), 2.45 (s, 3H; C^{Ar}-CH_3), 1.73–1.63 (m, 2H; CH_2CH$_2$CH$_3$), 1.45–1.33 (m, 2H; CH_2CH$_3$), 0.95 ppm (t, J = 7.4 Hz, 3H; CH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 200.9 (C; C=O), 140.0 (C; C^{Ar}-CH=), 138.2 (C; C^{Ar}-CH_3), 133.7 (C; C^{Ar}), 131.0 (CH; C^{Ar}), 130.3 (CH; C^{Ar}), 127.4 (CH; C^{Ar}), 126.6 (CH; C^{Ar}), 126.5 (CH; =CH-C=O), 41.2 (CH_2; CH_2-C=O), 26.7 (CH_2), 22.7 (CH_2), 20.0 (CH_3; C^{Ar}-CH_3), 14.1 ppm (CH_3; CH$_2$CH_3); elemental analysis calcd (%) for $C_{14}H_{18}O$ (202.29): C 83.12, H 8.97; found: C 83.00, H 9.10.

(*E*)-1-(4-Fluorophenyl)hept-1-en-3-one (3d): The above general procedure using conventional heating yielded, after flash chromatography on silica gel (pentane/Et_2O, 95:5), 188 mg (91%) of the title compound. The above general procedure using microwave heating yielded, after flash chromatography on silica gel (pentane/Et_2O, 95:5), 186 mg (90%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.56–7.49 (m, 3H; 2H^{Ar} + C^{Ar}-CH=), 7.11–7.05 (m, 2H; H^{Ar}), 6.68 (d, J = 16.2 Hz, 1H; =CH-C=O), 2.65 (t, J = 7.3 Hz, 2H; CH_2-C=O), 1.71–1.61 (m, 2H; CH_2CH$_2$CH$_3$), 1.44–1.32 (m, 2H; CH_2CH$_3$), 0.94 ppm (t, J = 7.3 Hz, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 200.6 (C; C=O), 164.1 (d, $J_{C\text{-}F}$ = 250 Hz, C; C-F), 141.1 (CH; C^{Ar}-CH=), 131.0 (d, $J_{C\text{-}F}$ = 3.3 Hz, C; C^{Ar}-CH=), 130.3 (d, $J_{C\text{-}F}$ = 8.5 Hz, CH; CH^{Ar}-C^{Ar}-CH=), 126.1 (CH; =CH-C=O), 116.2 (d, $J_{C\text{-}F}$ = 21.8 Hz, CH; CH^{Ar}-CF), 40.9 (CH_2; CH_2-C=O), 26.6 (CH_2), 22.6 (CH_2), 14.1 ppm (CH_3); elemental analysis calcd (%) for $C_{13}H_{15}FO$ (206.26): C 75.70, H 7.33; found: C 75.52, H 7.61.

(*E*)-1-(4-Methoxyphenyl)hept-1-en-3-one (3e): The above general procedure using conventional heating yielded, after flash chromatography on silica gel (pentane/Et_2O, 95:5), 194 mg (89%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.56–7.52 (m, 3H; 2H^{Ar} + C^{Ar}-CH=), 6.95 (d, J = 8.8 Hz, 2H; H^{Ar}), 6.66 (d, J = 16.0 Hz, 1H; =CH-C=O), 3.87 (s, 3H; OMe), 2.66 (t, J = 7.6 Hz, 2H; CH_2-C=O), 1.72–1.65 (m, 2H; CH_2CH$_2$CH$_3$), 1.46–1.36 (m, 2H; CH_2CH$_3$), 0.97 ppm (t, J = 6.8 Hz, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 200.9 (C; C=O), 161.7 (C; C-OMe), 142.3 (CH; C^{Ar}-CH=), 130.1 (CH; C^{Ar}), 127.5 (C; C^{Ar}), 124.4 (CH; =CH-C=O), 114.6 (CH; C^{Ar}), 55.6 (CH_3; OMe), 40.8 (CH_2; CH_2-C=O), 26.9 (CH_2; CH_2CH$_2$CH$_3$), 22.7 (CH_2; CH_2CH$_3$), 14.1 ppm (CH_3; CH_3); elemental analysis calcd (%) for $C_{14}H_{18}O_2$ (218.29): C 77.03, H 8.31; found: C 77.12, H 8.61.

1,1-Diphenylhept-1-en-3-one (3f): The above general procedure using conventional heating yielded, after flash chromatography on silica gel (pentane/Et_2O, 95:5), 233 mg (88%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.41–7.36 (m, 3H; H^{Ar}), 7.35–7.28 (m, 5H; H^{Ar}), 7.22–7.18 (m, 2H; H^{Ar}), 6.58 (s, 1H; =CH), 2.23 (t, J = 7.3 Hz, 2H; CH_2-C=O), 1.52–1.43 (m, 2H; CH_2CH$_2$CH$_3$), 1.24–1.12 (m, 2H; CH_2CH$_3$), 0.80 ppm (t, J = 7.3 Hz, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 202.8 (C; C=O), 153.3 (C; Ph$_2$C=CH), 141.2 (C; C^{Ar}), 139.3 (C; C^{Ar}), 129.7 (CH; C^{Ar}), 129.5 (CH; C^{Ar}), 128.7 (CH; C^{Ar}), 128.6 (CH; C^{Ar}), 128.5 (CH; C^{Ar}), 126.9 (CH; =CH), 43.1 (CH_2; CH_2-C=O), 26.6 (CH_2), 22.5 (CH_2), 14.0 ppm (CH_3); elemental analysis calcd (%) for $C_{19}H_{20}O$ (264.36): C 86.32, H 7.63; found: C 86.15, H 7.51.

(*E*)-1-Phenyloct-2-en-4-one (3m): The above general procedure using conventional heating yielded, after flash chromatography on silica gel (pentane/Et_2O, 98:2), 176 mg (87%) of the title compound. The above general procedure using microwave heating yielded, after flash chromatography on silica gel (pentane/Et_2O, 98:2), 188 mg (93%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.35–7.29 (m, 2H; H^{Ar}), 7.27–7.21 (m, 1H; H^{Ar}), 7.19–7.16 (m, 2H; H^{Ar}), 6.38 (dt, J = 15.8, 6.8 Hz, 1H; CH_2-CH=), 6.09 (dt, J = 15.8, 1.6 Hz, 1H; =CH-C=O), 5.52 (dd, J = 6.8, 1.6 Hz, 2H; CH_2-CH=), 2.53 (t, J = 7.3 Hz, 2H; CH_2-C=O), 1.63–1.53 (m, 2H; CH_2CH$_2$CH$_3$), 1.38–1.26 (m, 2H; CH_2CH$_3$), 0.90 ppm (t, J = 7.3 Hz, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 200.9 (C; C=O), 145.2 (CH; CH_2-CH=), 137.9 (C; C^{Ar}), 131.3 (CH; =CH-C=O), 129.0 (CH; C^{Ar}), 128.9 (CH; C^{Ar}), 126.9 (CH; C^{Ar}), 40.0 (CH_2; CH_2-CH=), 38.9 (CH_2; CH_2-C=O), 26.4 (CH_2), 22.6 (CH_2), 14.1 ppm (CH_3); elemental analysis calcd (%) for $C_{14}H_{18}O$ (202.29): C 83.12, H 8.97; found: C 83.05, H 8.98.

(*E*)-4-Phenylbut-2-enal (3n): The above general procedure using conventional heating yielded, after flash chromatography on silica gel (pentane/Et_2O, 98:2), 137 mg (94%) of the title compound. The above general procedure using microwave heating yielded, after filtration through a plug of Celite, 135 mg (93%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 9.53 (d, J = 7.9 Hz, 1H; CHO), 7.33–7.23 (m, 3H; H^{Ar}), 7.19–7.17 (m, 2H; H^{Ar}), 6.95 (dt, J = 15.5, 6.7 Hz, 1H; CH_2-CH=), 6.09 (ddt, J = 15.5, 7.9, 1.5 Hz, 1H; =CH-C=O), 3.64 ppm (d, J = 6.7 Hz, 2H; CH_2-CH=); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 193.9 (C; C=O), 156.6 (CH; CH_2-CH=), 137.2 (C; C^{Ar}), 133.6 (CH; =CH-C=O), 129.0 (CH; C^{Ar}), 128.9 (CH; C^{Ar}), 127.1 (CH; C^{Ar}), 39.1 ppm (CH_2); elemental analysis calcd (%) for $C_{10}H_{10}O$ (146.19): C 82.16, H 6.89; found: C 82.28, H 7.07.

(*E*)-1-Phenylhex-2-en-1-one (3o): The above general procedure yielded, after flash chromatography on silica gel (pentane/Et_2O, 98:2), 143 mg (82%) of the title compound. The product was collected in two fractions. The first one (110 mg) contained only the *E* olefin, while the second one (33 mg) contained a mixture (*E*:*Z*, 2:1) of the two isomers of the title compound.[47] ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.95–7.91 (m, 2H; H^{Ar}), 7.55 (tt, J = 7.2, 1.4 Hz, 1H; H^{Ar}), 7.49–7.43 (m, 2H; H^{Ar}), 7.07 (dt, J = 15.4, 6.9 Hz, 1H; CH_2-CH=), 6.88 (dt, J = 15.4, 1.3 Hz, 1H; =CH-C=O), 2.34–2.26 (m, 2H; CH_2-CH=), 1.62–1.47 (m, 2H; CH_2CH$_3$), 0.98 ppm (t, J = 7.4 Hz, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 191.1 (C; C=O), 150.1 (CH; CH_2-CH=), 138.2 (C; C^{Ar}), 132.8 (CH; C^{Ar}), 128.70 (CH; C^{Ar}), 128.68 (CH; C^{Ar}), 126.2 (CH; =CH-C=O), 35.0 (CH_2; CH_2-CH=), 21.6 (CH_2; CH_2CH$_3$), 13.9 ppm (CH_3); elemental analysis calcd (%) for $C_{12}H_{14}O$ (174.24): C 82.72, H 8.10; found: C 82.78, H 8.07.

(*E*)-Dec-6-en-5-one[48] **(3p)**: The above general procedure using conventional heating yielded, after flash chromatography on silica gel (pentane/Et_2O, 99:1), 145 mg (94%) of the title compound. The above general procedure using microwave heating yielded, after filtration through a plug of Celite, 147 mg (95%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 6.83 (dt, J = 15.9, 6.9 Hz, 1H; CH_2-CH=), 6.10 (dt, J = 15.9, 1.5 Hz, 1H; =CH-C=O), 2.54 (t, J = 7.3 Hz, 2H; CH_2-C=O), 2.23–2.16 (m, 2H; CH_2-CH=), 1.64–1.44 (m, 4H; CH_2), 1.40–1.28 (m, 2H; CH_2), 0.97–0.89 ppm (m, 6H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 201.2 (C; C=O), 147.3 (CH; CH_2-CH=), 130.7 (CH; =CH-C=

O), 40.0 (CH_2; *C*H_2-C=O), 34.6 (CH_2; *C*H_2-CH=), 26.6 (CH_2), 22.6 (CH_2), 21.6 (CH_2), 14.1 (CH_3), 14.1 ppm (CH_3).

(*E*)-1-Cyclohexenylhex-2-en-1-one (1q): The above general procedure using conventional heating yielded, after flash chromatography on silica gel (pentane/Et_2O, 99:1), 159 mg (89%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 6.87$ (dt, $J = 15.6$, 7.0 Hz, 1H; CH_2-C*H*=CH), 6.64–6.60 (m, 1H; CH_2-C*H*=C), 6.48 (dt, $J = 15.6$, 1.3 Hz, 1H; =CH-C=O), 1.98–1.86 (m, 6H; CH_2-C=), 1.68–1.61 (m, 4H; CH_2), 1.52–1.45 (m, 2H; CH_2), 0.95 ppm (t, $J = 7.4$ Hz, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta = 190.3$ (C; C=O), 155.1 (CH; CH_2-*C*H=CH), 146.2 (CH; CH_2-*C*H=C), 137.8 (C; CH=*C*), 127.7 (CH; =*C*H-C=O), 35.0 (CH_2; *C*H_2-CH=CH), 26.6 (CH_2), 25.8 (CH_2), 24.0 (CH_2), 23.7 (CH_2), 23.2 (CH_2), 13.7 ppm (CH_3); elemental analysis calcd (%) for $C_{12}H_{18}O$ (178.27): C 80.85, H 10.18; found: C 80.69, H 10.26.

3-Ethyl-1-phenylhept-2-en-1-one (3r): The above general procedure yielded, after flash chromatography on silica gel (pentane/Et_2O, 98:2), 195 mg (90%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 7.81$–7.75 (m, 3H; H^{Ar}), 7.48–7.43 (m, 2H; H^{Ar}), 6.70 (br s, 1H; =CH), 2.03–1.92 (m, 4H; C*H*$_2$-CH=), 1.33–1.27 (m, 4H; CH_2), 1.01 (t, $J = 7.3$ Hz, 3H; CH_2-C*H*$_3$), 0.91 ppm (t, $J = 7.4$ Hz, 3H; CH_2-C*H*$_3$). ^{13}C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta = 191.0$ (C; C=O), 163.1 (C; *C*=CH), 139.2 (C; C^{Ar}), 138.7 (C; C^{Ar}), 134.8 (CH; C^{Ar}), 134.7 (CH; C^{Ar}), 129.8 (CH; C^{Ar}), 128.7 (CH; C^{Ar}), 128.6 (CH; C^{Ar}), 118.2 (CH; C=*C*H), 33.0 (CH_2), 32.8 (CH_2), 31.6 (CH_2), 21.9 (CH_2), 21.7 (CH_2), 21.6 (CH_2), 21.2 (CH_2), 13.9 (CH_3), 9.3 (CH_3), 9.1 ppm (CH_3); elemental analysis calcd (%) for $C_{15}H_{20}O$ (216.32): C 83.28, H 9.32; found: C 83.40, H 9.07.

Computational methods: In the computational model, the acetate of reactant **1** was represented by a formate. A methyl group was used as the alkyne substituent. The NHC ligand was represented by IDM (*N*,*N*′-dimethylimidazol-2-ylidene). The stationary points for the uncatalyzed and the gold-catalyzed reactions were fully optimized by DFT at the B3LYP[49,50] level of theory. The gold atom was described by using the LANL2DZ basis set;[51] this basis set includes the Los Alamos effective core potential for the inner electrons and a double-ζ basis set for the outer electrons. To improve the basis set applied to the gold atom, an f polarization shell was added (exponent 1.050).[52] The 6-31+G(d) basis set[53] was used for all remaining atoms. All stationary points were characterized by frequency calculations and transition states were identified by using a single negative eigenvalue in the Hessian matrix. All calculations were performed using the Gaussian03 suite of programs.[54]

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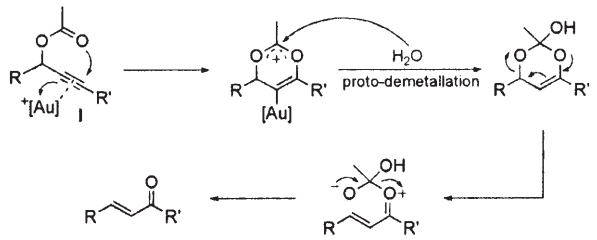

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