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Sequential gold-catalyzed reactions of 1-phenylprop-2-yn-1-ol with 1,3-dicarbonyl compounds

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ABSTRACT

A variety of sequential gold-catalyzed reactions of 1-phenylprop-2-yn-1-ol with 1,3-dicarbonyl compounds are directed towards different outcomes by a suitable choice of the catalytic system, feature of 1,3-dicarbonyl and reaction conditions.

1. Introduction

Gold catalysts are assuming growing popularity in organic synthesis [1]. In contrast to classic Lewis acids, which are known to form strong σ-complexes, the salts of transition metals can operate as bifunctional Lewis acids activating either (or both) carbon–carbon multiple bonds via π-bonding and/or forming σ-complexes by coordinating with heteroatoms [2]. Although gold catalysis has attained a substantial advance in the nucleophilic activations of alkynes and alkenes, only limited examples have focused on the activation of pre-electrophiles [3]. In particular, an effective bidentate chelation of gold catalysts to propargylic alcohols has been reported providing an excellent reactivity for the Meyer–Schuster rearrangement under mild conditions [4]. Moreover, gold catalysts may also act as propargylic alcohol-activating agents in propargylic substitution reactions (Scheme 1) [5].

Recently, efficient methods for the preparation of tetrasubstituted furans through propargylation of 1,3-dicarbonyl compounds-cyclization tandem processes have been developed. It was discovered that $InCl_3$, could catalyze that transformation efficiently while simple iron, copper and silver salts were proven to be ineffective [6]. Moreover, a process, which proceeds in a one-pot manner, involves the initial propargylation of the 1,3-dicarbonyl compound promoted by trifluoroacetic acid, and subsequent cycloisomerization of the resulting γ-ketoalkyne catalyzed by a ruthenium(II) complex [7]. When the ruthenium/TFA catalyzed reaction of secondary propargylic alcohols was carried out with cyclic 1,3-diones the nature of the resulting products was found to be dependent on the ring size of the dicarbonyl compound employed: whereas furan-ring formation has been selectively obtained starting from acyclic 1,3-dicarbonyl compounds and 1,3-cyclohexanediones (Scheme 2a), the use of 1,3-cyclopentanedione leads, instead, to products via a pyran-ring formation (Scheme 2b) [8].

As an extension of our studies of gold catalysis in promoting sequential reaction by accomplishing a dual role catalysis through a twofold coordination of a lone pair of heteroatoms and π-electrons of C–C multiple bonds [9], we decided to investigate the use of gold as an alternative catalyst in the reaction of propargylic alcohols with 1,3-dicarbonyl compounds. The development of novel synthetic routes, allowing the facile assembly of more complex scaffolds from readily available and inexpensive precursors, still remains an important objective for synthetic organic chemists. Hereafter we report the preliminary results of our investigation.

2. Results and discussion

At the outset, we tested Au(III) catalysts in the reaction of 1-phenylprop-2-yn-1-ol **1** with 2,4-pentanedione **2a**. Au(III) catalysts have been reported to give the best results compared to Au(I) catalysts in promoting the selective nucleophilic substitution of propargylic alcohols [5a]. Surprisingly, a mixture of products was isolated in different organic solvents at different temperatures (Scheme 3; Table, entries 1–8). By contrast when the reaction

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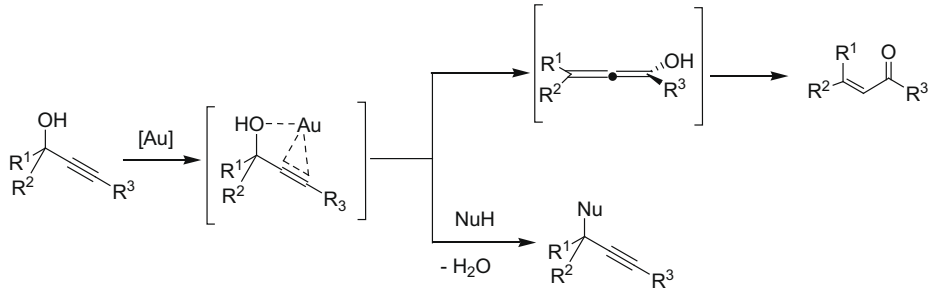
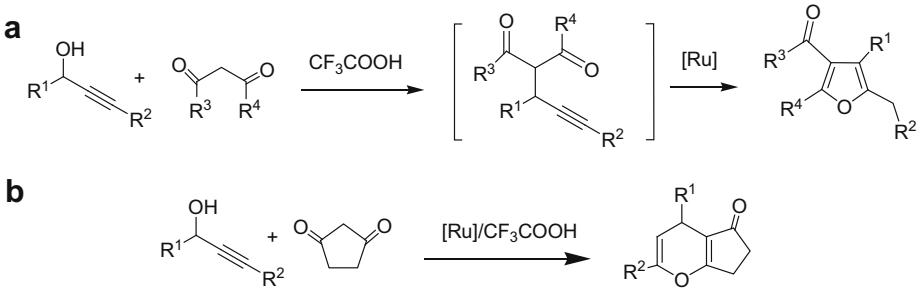
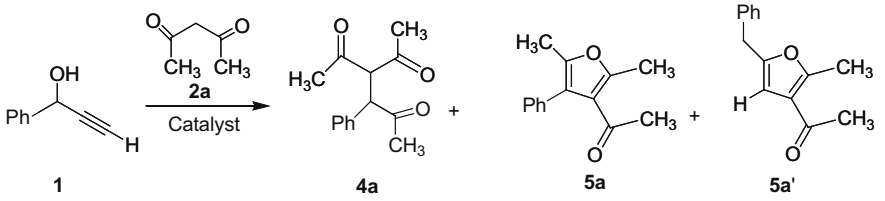


Scheme 1.



Scheme 2.



Scheme 3.

was catalyzed by [AuClPPh$_3$]/AgOTf the furan **5a** was isolated as the only reaction product in 80% yield (Table 1, entry 9). AgOTf should help generate a more electrophilic gold species. AgOTf alone did not efficiently catalyze the reaction under the same conditions (Table 1, entry 10).

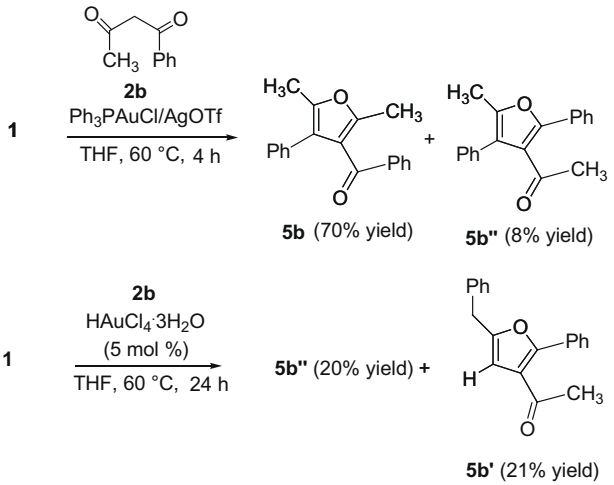
When the reaction was studied by using other 1,3-dicarbonyl compounds, we observed a variety of intriguing results. The reaction of **1** with the 1-phenyl-1,3-butanedione **2b** containing aryl and alkyl ketone fragments gave rise only to the formation of furan derivatives (Scheme 4).

In the presence of Ph$_3$PAuCl (5 mol%)/AgOTf (10 mol%), as catalytic system, the reaction of **1** (2 equiv.) with **2b** (1 equiv.) led, in good yield, the tetrasubstituted furan **5b** derived from the cycliza-

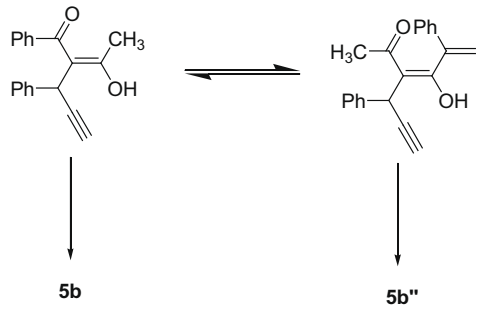
Table 1
Gold-catalyzed reaction of **1** with **2a.**

Entry	**2a**/**1**	Solvent	Catalyst	Temperature (°C)/time (h)	Yield of **4a** (%)[a]	Yield of **5a** (%)[a]	Yield of **5a′** (%)[a]
1	10	Neat	$NaAuCl_4 \cdot 2H_2O$	75/1	–	–	–
2	3	THF	$HAuCl_4 \cdot 3H_2O$	60/0.5	44	–	28
3	3	THF	$HAuCl_4 \cdot 3H_2O$	rt/2.5	14	–	16
4	5	THF	$HAuCl_4 \cdot 3H_2O$	60/5	18		32
5	5	DCE	$HAuCl_4 \cdot 3H_2O$	60/24	–	–	22
6	5	CH_3CN	$HAuCl_4 \cdot 3H_2O$	60/5	45	21	–
7	0.5	THF	$HAuCl_4 \cdot 3H_2O$	60/5.5	–	–	17
8	1.2	Neat	$HAuCl_4 \cdot 3H_2O$	60/24	–	–	–
9	5	THF	PPh_3AuCl/AgOTf	60/4		80	
10	5	THF	AgOTf	60/24		22	

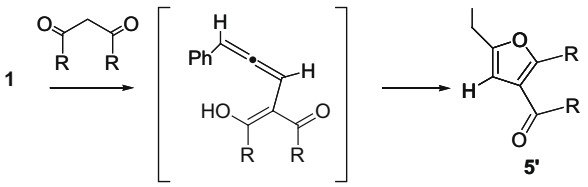
[a]Yields refer to single runs, and are given for pure isolated products.



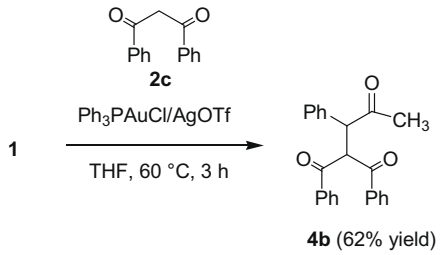
Scheme 4.



Scheme 5.



Scheme 6.



Scheme 7.

tion involving the oxygen of the alkyl ketone fragment. Regioisomeric furan **5b**″ was isolated as minor byproduct. Surprisingly, by using $HAuCl_4 \cdot 3H_2O$ as catalyst we observed a loss of efficiency and different products distribution. The formation of the tetrasubstituted furans **5b** and **5b**″ can be readily explained through the *exo-dig* annulation reaction of the two isomeric enol intermediates arising from the nucleophilic substitution reaction of **1** with **2b** (Scheme 5).

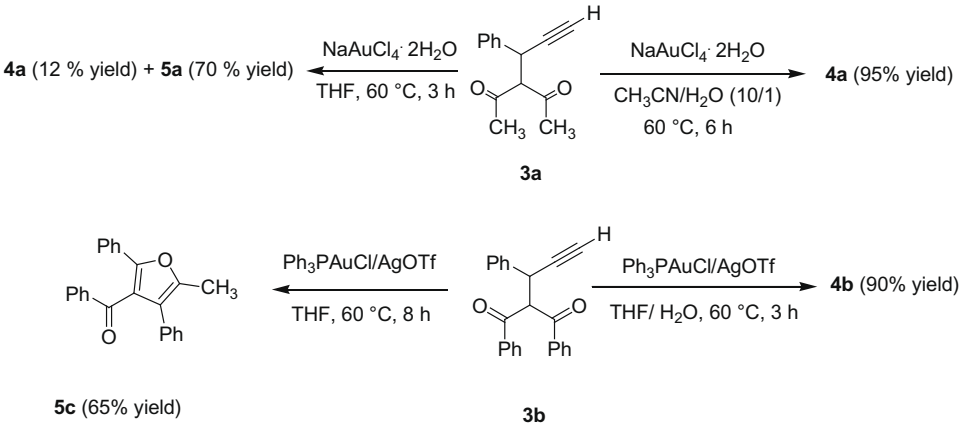
On the other hand, the Au(III)-catalyzed formation of the trisubstituted furan **5b**′ should involve the competitive allenylation (Scheme 6) of the 1,3-dicarbonyl/cyclization reaction with a mechanism that proceeds by an S_N2' pathway [10]. The regioselectivity of the nucleophilic trapping can depend on the competition between an S_N2' or a cationic mechanism. This latter mechanism can be favored by $Au(PPh_3)^+$ [11].

A different sequence of gold-catalyzed reactions was observed when **1** was reacted with the 1,3-diphenylpropanedione **2c** in the presence of Ph_3PauCl (5 mol%)/AgOTf (10 mol%). In this transformation, hydrative alkylation occurs regioselectively leading **4b** in good yield (Scheme 7) [12].

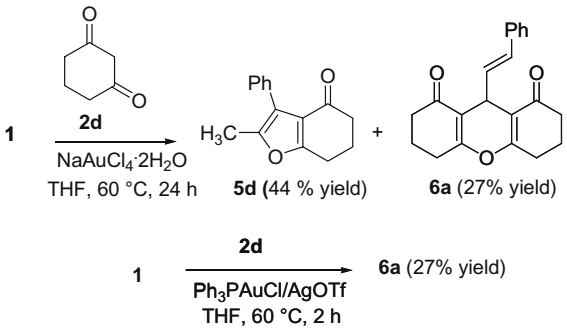
Very likely, the $Au(PPh_3)^+$ coordination with **1** promotes the generation of a carbocation, which is subsequently trapped by the dicarbonyl **2c** to form the substitution product **3b**. Next, regioselective hydration occurs. The competition of the gold-catalyzed hydration of intermediates **3** versus their gold-catalyzed cyclization to furans may depends on a combination of electronic, coordinating, and medium factors. In order to confirm that, we prepared, according to the literature [13], the substitution product **3a–b**, and then treated them with a catalytic amount of gold catalysts (5 mol%) (Scheme 8).

The results observed show that the amount of water, in the reaction medium, plays a pivotal role to direct the reaction towards the hydrative pathway. Indeed **3a** undergoes $NaAuCl_4 \cdot 2H_2O$ catalyzed hydration in high yield in aqueous CH_3CN at 60 °C. By using anhydrous THF instead of aqueous CH_3CN, cyclization of **3a** occurs to give the furan derivative **5a**. The formation of the derivative **4** can be also observed by using the $Ph_3PAuCl/AgOTf$ catalytic system in THF/H_2O with the derivative **3b** which is less prone to undergo the annulation reaction. Indeed, the Au(I)-catalyzed cyclization of **3b** requires long reaction time: after 8 h we isolated **5c** in 65% yield, but the starting **3b** was also recovered in 35% yield. The product **5c** is only accessible by a two step synthesis.

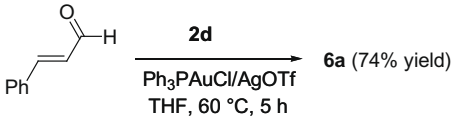
To compare the feature of the catalysis by gold versus the reported ruthenium/TFA-catalyzed coupling of secondary propargylic alcohols with cyclic 1,3-diones [8], we investigated the reaction of **1** with 1,3-cyclohexanediones **2d–e** and 1,3-cyclopentanedione **2f**, respectively. In our cases, the 6,7-dihydro-5H-benzofuran-4-one derivative **5d** has been isolated in moderate yield only in the presence of Au(III) catalysts. Attempts to promote related coupling reaction under Au(I) catalysis resulted in the formation of more complicated reaction mixtures from which the 9-((*E*)-styryl)-3,4,5,6,7,9-hexahydro-2H-xantene-1,8-dione **6a** has been separated by uncharacterized byproducts. The formation of **6a** occurs, also, to some extent under Au(III) catalysis (Scheme 9).



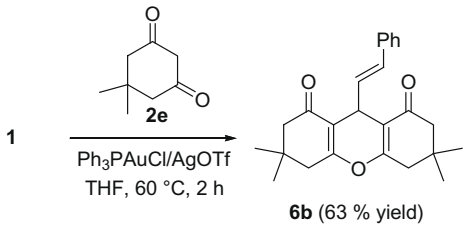
Scheme 8.



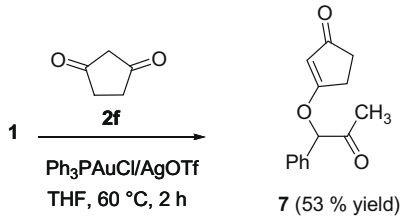
Scheme 9.



Scheme 10.



Scheme 11.



Scheme 12.

Considering that **6a** has been previously prepared by the reaction of cyclohexan-1,3-dione **2d** with cinnamaldehyde, it can be suggested that **1** can also undergo fast gold-catalyzed Meyer-Schuster rearrangement to give the cinnamaldehyde, which subsequently generates **6a** [14]. To shed a light on this aspect, we reacted cynnamaldehyde with **2d** under our reaction conditions and we isolated the derivative **6a** in good yield (Scheme 10).

The formation of 3,4,5,6,7,9-hexahydro-2H-xantene-1,8-dione derivatives in satisfactory synthetic yields through the gold-catalyzed cascade reaction can be accomplished by a suitable choice of the **1**/1,3-cyclohexanedione derivative ratio (i.e. **6b** was isolated in 63% yield by reacting an excess of **1** with **2e** (**1**/**2e** = 2) in anhydrous THF at 60 °C under the presence of Ph_3PauCl (5 mol%)/AgOTf (10 mol%) catalytic system (Scheme 11).

Remarkably, in contrast to the reactions with 1,3-cyclohexanediones, when 1,3-cyclopentanedione is used as a substrate the sequential gold-catalyzed O-propargylation/hydration reaction prevails to give as main reaction product the 3-(2-oxo-1-phenylpropxy)-cyclopent-2-enone **7** (Scheme 12).

In summary, gold-catalyzed sequential C-alkylation/cyclization, C-alkylation/hydration and O-alkylation/hydration reactions of 1-phenyl-prop-2-yn-1-ol with 1,3-dicarbonyl compounds are directed by a suitable choice of the gold catalytic system, substrates and reaction conditions. In the presence of 1,3-cyclohexandione derivatives a cascade gold-catalyzed reaction of 1-phenylprop-2-yn-1-ol can accomplish the formation 3,4,5,6,7,9-hexahydro-2H-xantene-1,8-dione derivatives. Further investigation on the application of the gold-catalyzed reactions of propargylic alcohols with 1,3-dicarbonyls is ongoing and will be reported in due course.

3. Experimental

Temperatures are reported as bath temperature. Solvents used in extraction and purification were distilled prior to use. Compounds were visualized on analytical thin-layer chromatograms (TLC) by UV light (254 nm). The products, after usual work-up, were purified by flash chromatography on silica gel (230–400 mesh) eluting with *n*-hexane/ethyl acetate mixtures. ^1H NMR and ^{13}C NMR spectra were recorded with a Bruker AC 200 E spectrometer or Varian Mercury 300. Mass spectra were recorded with a Varian Saturn 2100 T GC/MS instrument. IR were recorded with a Perkin–Elmer 683 spectrometer. Only the most significant IR absorptions are given. All starting materials, catalysts, and solvents if not otherwise stated, are commercially available and were used as purchased, without further purification. The products **4b** [12b], **5a** [7], **5d** [8], **6a–b** [14] were known and where determined using comparison of their physical and spectral data with those reported in literature.

*3.1. $HAuCl_4 \cdot 3H_2O$ catalyzed reaction of 1-phenylprop-2-yn-1-ol 1 with 2,4-pentanedione (**2a**)*

To a solution of 1-phenylprop-2-yn-1-ol **1** (0.88 mmol, 90 mg) in THF (1 mL) were added the 1,3-dicarbonyl compound **2a** (2.04 mmol, 204 mg) and $HAuCl_4 \cdot 3H_2O$ (0.034 mmol, 13 mg). The mixture was stirred at 60 °C and monitored by TLC or GC–MS. After 0.5 h, the solvent was removed by evaporation. The residue was purified by chromatography on silica gel (230–400 mesh) eluting with *n*-hexane/ethyl acetate mixture 95/5 to afford the pure derivatives **4a** and **5a′**.

*3.2. 3-Acetyl-4-phenyl-hexane-2,5-dione (**4a**)*

69 mg; 44% yield; IR (neat): ν = 1750, 1700, 740, 690 cm^{-1}. ^1H NMR ($CDCl_3$, 300.20 MHz) δ = 1.88 (s, 3H), 2.08 (s, 3H), 2.28 (s, 3H), 4.52 (d, *J* = *11.4* Hz, 1H), 4.64 (d, *J* = *11.4* Hz, 1H), 7.22 (m, 2H), 7.32 (m, 3H). ^{13}C NMR ($CDCl_3$, 75.49 MHz) δ = 28.6, 30.1, 30.7, 58.6, 70.3, 128.2, 128.6, 129.3, 143.2, 201.6, 202.5, 205.9. MS (70 EV, EI, relative intensity): 214 [$(M-H_2O)^+$, 100].

*3.3. 1-(5-Benzyl-2-methyl-furan-3-yl)-ethanone (**5a′**)*

41 mg; 28% yield; IR (neat): ν = 1670, 1550, 670 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz) δ = 2.30 (s, 3H), 2.53 (s, 3H), 3.90 (s, 2H), 6.19 (s, 2H), 7.22–7.36 (m, 5H). ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ = 14.3, 29.0, 34.1, 106.8, 122.0, 126.7, 128.5, 131.6, 137.3, 152.4, 157.3, 194.1. MS (70 EV, EI, relative intensity): 214 [M^+, 100], 199 (73), 171 (30).

*3.4. Ph_3PAuCl/AgOTf catalyzed reaction of 1-phenylprop-2-yn-1-ol 1 with 2,4-pentanedione (**2a**)*

To a solution of 1-phenylprop-2-yn-1-ol **1** (1.52 mmol, 200 mg) in THF (2 mL) were added the 1,3-dicarbonyl compound **2a**

(7.06 mmol, 758 mg), Ph_3PAuCl (0.036 mmol, 37 mg) and AgOTf (0.152 mmol, 40 mg). The mixture was stirred at 60 °C and monitored by TLC or GC–MS. After 4.0 h, the solvent was removed by evaporation. The residue was purified by chromatography on silica gel (230–400 mesh) eluting with *n*-hexane/ethyl acetate mixture 95/5 to afford the pure **5a** (258 mg, 80% yield).

3.5. Ph_3PAuCl/AgOTf catalyzed reaction of 1-phenylprop-2-yn-1-ol 1 with 1-phenyl-1,3-butanedione (**2b**)

To a solution of 1-phenylprop-2-yn-1-ol **1** (2.17 mmol, 293 mg) in THF (2 mL) were added the 1,3-dicarbonyl compound **2b** (1.09 mmol, 180 mg), Ph_3PAuCl (0.055 mmol, 27 mg) and AgOTf (0.11 mmol, 28 mg). The mixture was stirred at 60 °C and monitored by TLC or GC–MS. After 4.0 h, the solvent was removed by evaporation. The residue was purified by chromatography on silica gel (230-400 mesh) eluting with *n*-hexane/ethyl acetate mixture 85/15 to afford the pure derivatives **5b** and **5b″**.

3.6. (2,5-Dimethyl-4-phenyl-furan-3-yl)-phenyl-methanone (**5b**)

210 mg; 70% yield; IR (neat): ν = 1650, 1580, 710, 680 cm^{-1}. ^1H NMR ($CDCl_3$, 300.20 MHz) δ = 2.29 (s, 3H), 2.31 (s, 3H), 7.08–7.65 (m, 10H). ^{13}C NMR ($CDCl_3$, 75.49 MHz) δ = 11.8, 12.4, 34.1, 121.5, 126.2, 127.2, 127.5, 127.7, 128.9, 129.2, 132.1, 132.5, 138.1, 146.6, 154.5, 192.2. MS (70 EV, EI, relative intensity): 276 [M^+, 100], 199 (23), 105 (45).

3.7. 1-(5-Methyl-2,4-diphenyl-furan-3-yl)-ethanone (**5b″**)

22 mg; 8% yield; IR (neat): ν = 1690, 1600, 730, 690 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz) δ = 2.20 (s, 3H), 2.35 (s, 3H), 7.16–7.48 (m, 10H). MS (70 EV, EI, relative intensity): 276 [M^+, 70], 261 (100).

3.8. $HAuCl_4 \cdot 3H_2O$ Catalyzed reaction of 1-phenylprop-2-yn-1-ol 1a with 1-phenyl-1,3-butanedione (**2b**)

To a solution of 1-phenylprop-2-yn-1-ol **1** (1.11 mmol, 147 mg) in THF (1 mL) were added the 1,3-dicarbonyl compound **2a** (0.55 mmol, 90 mg) and $HAuCl_4 \cdot 3H_2O$ (0.028 mmol, 11 mg). The mixture was stirred at 60 °C and monitored by TLC or GC–MS. After 24 h, the solvent was removed by evaporation. The residue was purified by chromatography on silica gel (230-400 mesh) eluting with *n*-hexane/ethyl acetate mixture 85/15 to afford the pure derivatives **5b″** (30 mg; 20% yield) and **5b′**.

3.9. 1-(5-Benzyl-2-phenyl-furan-3-yl)-ethanone (**5b′**)

33 mg; 21% yield; IR (neat): ν = 1670, 1590, 680 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz) δ = 2.35 (s, 3H), 4.01 (s, 2H), 6.18 (s, 1H), 7.25–7.87 (m, 10H). MS (70 EV, EI, relative intensity): 276 [M^+, 100], 261 (90), 233 (16).

3.10. Ph_3PAuCl/AgOTf catalyzed reaction of 1-phenylprop-2-yn-1-ol 1 with 1,3-diphenyl-propane-1,3-dione (**2c**)

To a solution of 1-phenylprop-2-yn-1-ol (**1**) (1.51 mmol, 200 mg) in THF (2 mL) were added the 1,3-dicarbonyl compound **2c** (0.76 mmol, 170 mg), Ph_3PAuCl (0.038 mmol, 19 mg) and AgOTf (0.076 mmol, 20 mg). The mixture was stirred at 60 °C and monitored by TLC or GC–MS. After 3.0 h, the solvent was removed by evaporation. The residue was purified by chromatography on silica gel (230–400 mesh) eluting with *n*-hexane/ethyl acetate mixture 80/20 to afford the pure derivatives **4b** (167 mg, 62% yield).

3.11. Gold(III) catalyzed hydration reaction of 3-(1-phenylprop-2-ynyl)-pentane-2,4-dione (**3a**)

To a solution of 3-(1-phenylprop-2-ynyl)-pentane-2,4-dione (**3a**) (0.41 mmol, 89 mg) in CH_3CN (2 mL) were added water (0.2 mL) and $NaAuCl_4 \cdot 2H_2O$ (0.020 mmol, 8 mg). The mixture was stirred at 60 °C and monitored by TLC or GC–MS. After 6.0 h, the mixture was filtered through a short pad of florisil (EtOAc) and the solvents were evaporated under reduced pressure to give the corresponding derivative **4a** (90 mg, 94% yield).

3.12. Ph_3PAuCl/AgOTf catalyzed hydration reaction of 1,3-diphenyl-2-(1-phenylprop-2-ynyl)-propane-1,3-dione (**3b**)

To a solution of 1,3-diphenyl-2-(1-phenylprop-2-ynyl)-propane-1,3-dione (**3b**) (0.30 mmol, 100 mg) in anhydrous THF (2 mL) were added water (2.95 mmol, 53 mg), Ph_3PAuCl (0.015 mmol, 8 mg) and AgOTf (0.029 mmol, 8 mg). The mixture was stirred at 60 °C and monitored by TLC or GC–MS. After 6.0 h, the mixture was filtered through a short pad of florisil (EtOAc) and the solvents were evaporated under reduced pressure to give the corresponding derivative **4b** (96 mg, 90% yield).

3.13. (Methyl-2,4-diphenyl-furan-3-yl)-phenyl-methanone (**5c**)

65 mg; 65% yield; IR (neat): ν = 1650, 1590, 670 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz) δ = 2.45 (s, 3H), 7.13–7.83 (m, 15H). ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ = 12.3, 121.8, 123.5, 126.2, 126.9, 127.2, 128,1, 128.2, 128.4, 129.2, 129.8, 132.3, 133.1, 137.6, 148.1, 150.8, 193.7 MS (70 EV, EI, relative intensity): 238 [M^+, 100], 261 (22), 105 (32).

3.14. Ph_3PAuCl/AgOTf catalyzed reaction of trans-cynnamaldehyde with cyclohexan-1,3-dione (**2d**)

To a solution of *trans*-cynnamaldehyde (0.78 mmol, 100 mg) in anhydrous THF (2 mL) were added the 1,3-dicarbonyl compound **2d** (2.27 mmol, 255 mg), Ph_3PAuCl (0.04 mmol, 19 mg) and AgOTf (0.08 mmol, 19 mg). The mixture was stirred at 60 °C and monitored by TLC or GC–MS. After 6.0 h, the solvent was removed by evaporation. The residue was purified by chromatography on silica gel (230–400 mesh) eluting with *n*-hexane/ethyl acetate mixture 50/50 to afford the pure derivative **6a** (180 mg, 74% yield).

3.15. Ph_3PAuCl/AgOTf catalyzed reaction of 1-phenylprop-2-yn-1-ol 1 with dimedone (**2e**)

To a solution of 1-phenylprop-2-yn-1-ol **1** (1.51 mmol, 200 mg) in anhydrous THF (2 mL) were added the 1,3-dicarbonyl compound **2e** (0,76 mmol, 106 mg), Ph_3PAuCl (0.038 mmol, 19 mg) and AgOTf (0.076 mmol, 20 mg). The mixture was stirred at 60 °C and monitored by TLC or GC–MS. After 2.0 h, the solvent was removed by evaporation. The residue was purified by chromatography on silica gel (230–400 mesh) eluting with *n*-hexane/ethyl acetate mixture 60/40 to afford the pure derivative **6b** (94 mg, 63% yield).

3.16. Ph_3PAuCl/AgOTf catalyzed reaction of 1-phenylprop-2-yn-1-ol 1 with 1,3-cyclopentanedione (**2f**)

To a solution of 1-phenylprop-2-yn-1-ol **1** (0.76 mmol, 100 mg) in anhydrous THF (2 mL) were added the 1,3-dicarbonyl compound **2f** (2,27 mmol, 223 mg), Ph_3PAuCl (0.038 mmol, 19 mg) and AgOTf (0.076 mmol, 20 mg). The mixture was stirred at 60 °C and monitored by TLC or GC–MS. After 2.0 h, the solvent was removed by evaporation. The residue was purified by chromatography on silica

gel (230–400 mesh) eluting with *n*-hexane/ethyl acetate mixture 90/10 to afford the pure derivative **7**.

3.17. 3-(2-Oxo-1-phenylpropoxy)-cyclopent-2-en-1-one (**7**)

90 mg; 53% yield; IR (neat): ν = 1730, 1700,1590, 670 cm^{-1}. ^1H NMR ($CDCl_3$, 300.20 MHz) δ = 2.18 (s, 3H, CH_3), 2.38–2.54 (m, 2H, CH_2 protons 4a–b), 2.64–2.89 (m, 2H, CH_2 protons 5a–b), 5.20 (s, 1H, C*H* proton 2a), 5.45 (s, 1H, C*H* proton 8a), 7.36–7.49 (m, 5H, C*H* aromatic). ^{13}C NMR ($CDCl_3$, 75.49 MHz) δ = 25.3 (CH_3), 28.4 (CH_2 carbon 5), 34.0 (CH_2 carbon 4), 87.6 (*C*H carbon 8), 106.8 (*C*H carbon 2), 126.8 (*C*H carbons 12 and 16), 129.1 (*C*H carbons 13 and 15), 129.5 (*C*H carbon 14), 132.9 (*C* carbon 11), 187.9 (*C* carbon 3), 201.5 (*C*O carbon 9), 205.3 (*C*O carbon 1). The structure was confirmed by one and two-dimensional NMR experiments. Namely ^1H NMR, ^{13}C NMR, NOE Difference Spectroscopy, DEPT (Distortionless Enhancement by Polarization Transfer), HETCOR 2D (the two-dimensional C,H-Correlation by Polarization Transfer) and HETCORLR 2D (the two-dimensional Long-Range C,H-Correlation by Polarization Transfer). The HETCOR 2D experiment yield cross-signal for all protons and ^{13}C nuclei that are connected by a ^{13}C, ^1H coupling over one bond. Instead HETCORLR 2D experiment yield cross-signal for ^{13}C, ^1H coupled over more than one bond, generally two and three. Therefore the assignment of one member of a spin-coupled pair leads immediately to the assignment of the other. Proton and carbons are numbered as shown in Fig. 1 and the assignment of the peaks in the spectra was done as follow. The peaks position and integral value in the ^1H NMR spectrum showed that, identifying the broad peak centered at 7.42 ppm as the aromatic resonance and imposing to that signal an integral value of five, peak at 2.18 ppm identifies the methyl resonance, peaks at 5.20, 5.45 ppm identify the methine resonances and multiplets in the range 2.38–2.54 and 2.64–2.89 ppm identify the methylene resonances. The peaks position in the ^{13}C NMR spectrum and the DEPT experiment identify that peak at 25.3 ppm is due to a methyl carbon, peaks at 87.6, 106.8, 126.8, 129.1, 129.5 ppm are all due to methine carbons, peaks at 28.4 and 34.0 ppm are due to methylene carbons and peaks at 132.9, 187.9, 201.5 and 205.3 ppm are all due to quaternary carbons. Carbon-13 peaks at 201.5 and 205.3 ppm, for their resonance position can be assigned to carbonyl carbons. The HETCOR 2D experiment shows, beside the obvious correlations of the aromatic moiety, the correlations ^1H–^{13}C between peaks at 2.18 ppm and 25.3 ppm confirming the methyl nature of signals, correlations between peaks at 5.20 ppm and 106.8, and between peaks at 5.45 ppm and 87.6 ppm confirming the methine nature of those signals. While the correlations ^1H–^{13}C between multiplet in the range 2.38–2.54 ppm and peak at 34.0 ppm and between multiplet in the range 2.64–2.89 ppm and peak at 28.4 ppm allow to assign those signals to the methylenes of the five membered ring. The carbons connectivity, in the backbone, as been inferred from HETCORLR experiment. The long range correlation ^1H–^{13}C between peaks at 2.18 ppm and 201.5 ppm allows assigning the latter resonance to carbonyl C-9 and the resonance at 205.3 to carbonyl C-1. The long range correlation ^1H–^{13}C between peaks at 2.18 ppm and 87.6 ppm allows assigning the latter resonance to methine C-8 and the resonance at 106.8 to methine C-2, assignment confirmed by long range correlation ^1H–^{13}C between peaks at 5.20 ppm and 28.4 ppm. The long range correlation ^1H–^{13}C between multiplet in the range 2.38–2.54 and peaks at 205.3 and 187.9 ppm allows assigning the resonance at 187.9 ppm to carbon C-3 and resonance at 34.0 ppm to carbon C-4. The long range correlation ^1H–^{13}C between peak at 5.45 ppm and both peaks at 132.9 and 126.8 ppm allows assigning the former resonance to carbon C-11 and the latter to carbons C-12 and C-16 confirming as well the assignment of resonance at 87.6 ppm to carbon C-8. MS (70 EV, EI, relative intensity): 230 [M+, 100], 187 (23), 105 (23).

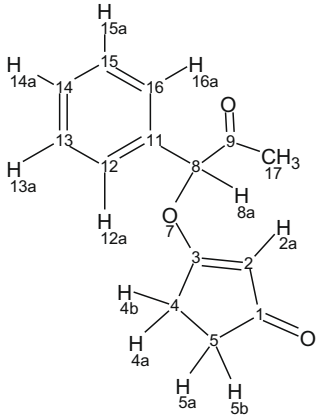


Fig. 1. Proton and carbons numbering for 3-(2-oxo-1-phenylpropoxy)cyclopent-2-en-1-one (**7**).

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