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Gold-Catalyzed Annulations of 2-Alkynyl Benzaldehydes with Vinyl Ethers: Synthesis of Dihydronaphthalene, Isochromene, and Bicyclo[2.2.2]octane Derivatives

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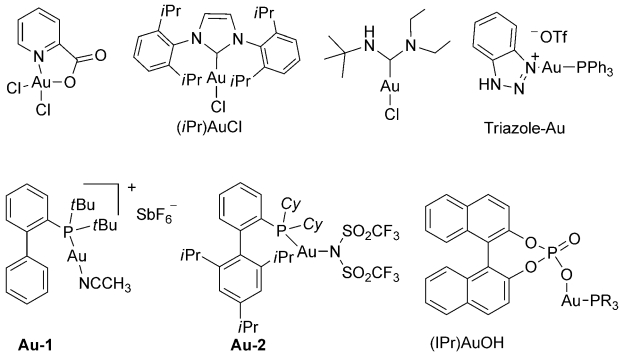
Dedicated to Chancellor Professor Emeritus Chang Ning Wu

Abstract: With the suitable selection of a gold catalyst as well as the appropriate control of the reaction conditions, various new gold-catalyzed cyclizations of 2-alkynyl benzaldehyde with acyclic or cyclic vinyl ethers have been developed. Acetal-tethered dihydronaphthalene and isochromenes were obtained from the reactions of 2-alkynyl benzaldehydes with acyclic vinyl ethers under mild conditions. And, more interestingly, the gold-catalyzed reactions of 2-alkynyl benzaldehyde with a cyclic vinyl ether afforded the bicyclo[2.2.2]octane derivative involving two molecules of cyclic vinyl ethers. These products contain interesting substructures that have been found in many biologically active molecules and natural products. In addition, a gold-catalyzed homo-dimerization of 2-phenylethynyl benzaldehyde **1a** was observed when the reaction was carried out in the absence of vinyl ether, affording a set of separable diastereomeric products. Plausible mechanisms for these transformations are discussed; a gold-containing benzopyrylium was regarded as the crucial intermediate by which a number of these new transformations took place.

Keywords: annulation · cyclization · gold · reaction mechanisms · synthetic methods

Introduction

For more than a decade now, gold-catalyzed transformations have been used extensively in the field of synthetic organic chemistry to rapidly and effectively construct interesting organic frameworks.[1] The development of gold catalysts with improved catalytic activity and stability has also attracted interest.[2] Selected recent notable examples include N,O-chelating gold(III) catalysts,[3] *N*-heterocyclic carbene (NHC) or acyclic carbene gold catalysts,[4] cationic gold acetonitrile complexes[5] containing Buchwald-type phosphine ligands[6] and cationic gold-triazole complexes.[7] On the other hand, counteranions, such as super acid anions including the bis(trifluoromethanesulfonyl)imide (NTf_2),[8] phosphates,[9] and even hydroxide,[10] have been found to play a significant role in the catalytic activities of gold catalysts. (Scheme 1)



Scheme 1. Selected examples of recently developed gold catalysts.

Due to their easy activation by various transition-metal catalysts and Lewis acids, the readily available 2-alkynyl benzaldehyde **1** has served as versatile scaffold in a number of transformations[11] of which gold-catalyzed annulations stand out.[12] Notably, Yamamoto and co-workers reported a gold-catalyzed benzannulation of 2-alkynyl benzaldehyde with an alkyne, furnishing naphthalene derivative **2** in a highly efficient manner.[13] A formal Diels–Alder-type [4+2]-cycloaddition mechanism for this gold-catalyzed annulation was proposed, but a stepwise mechanism via intermediate **B** was also suggested and supported by substituent effects. When copper was used as catalyst decarbonylation occurred to yield **3** as the main product.[14] The group of Yamamoto extended their formal [4+2]-cycloaddition protocol to alkenes, obtaining dihydronaphthalene derivative **4**, but in this case the copper catalyst exhibited better catalytic activity than gold.[15] Carbocation intermediate **B** was called for to account for the observed regio- and stereoselectivities. However, when vinyl ether was employed in the annulation

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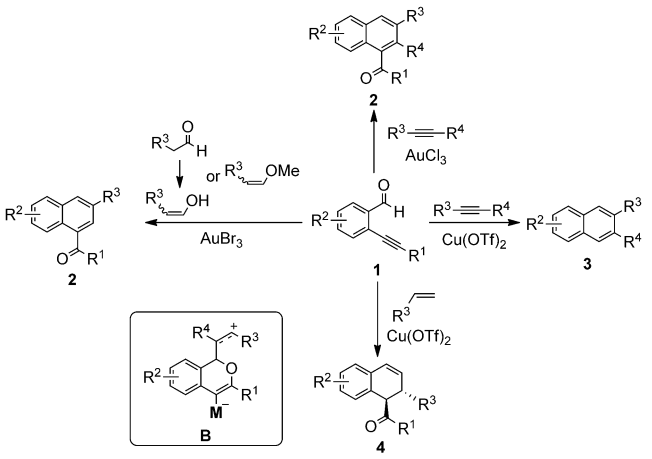
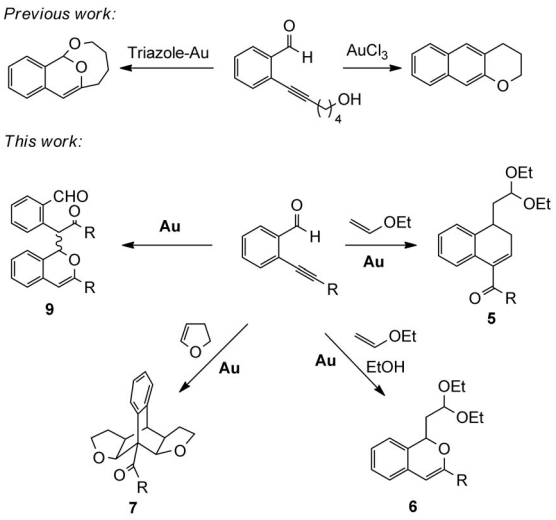
with 2-alkynyl benzaldehyde, the reaction yielded nathphalene **2**, rather than dihydronaphthalene **4**; this result has been ascribed to the elimination of alcohol. This outcome was corroborated by work reported by the Porco group.[16] Aldehydes or acetals having α-protons have been effectively involved in this gold-catalyzed annulation, but these substrates served as an enol source instead of a carbonyl source, affording the naphthalene product **2**, once again, due to the elimination of a water molecule (Scheme 2).[17]

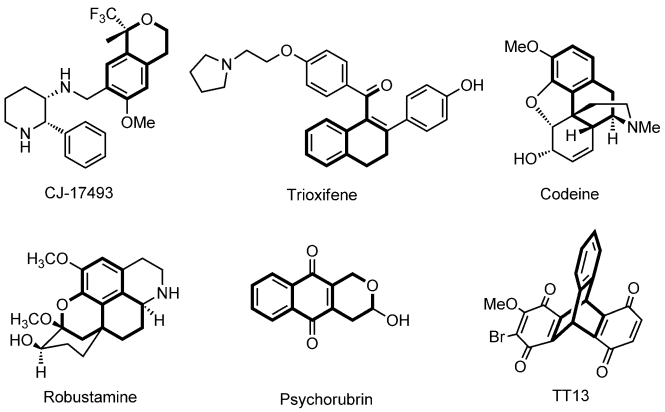


Scheme 2. Yamamoto's group pioneered the gold or copper-catalyzed annulation of 2-alkynyl benzaldehyde with alkyne, alkene, vinyl ether, or aldehyde. R_4 is H or alkyl in **B**.

In line with our continuing interest in gold catalysis and ligand effects,[18] we posited that a gold catalyst containing a suitable ligand may help to stabilize the carbocation intermediate and veer the reaction toward new synthetic paths. Recently, we reported the gold-catalyzed intramolecular annulations of 2-(ynol)aryl aldehydes, in which different gold catalysts furnished benzochromanes or benzobicyclo-[4.3.1]acetals (Scheme 3).[19] Thus, we envisioned that the reaction of 2-alkynyl benzaldehyde with a vinyl ether might yield a synthetically interesting product if a suitable gold catalyst could be found. Herein, we are pleased to report that, by selecting **Au-1** as the catalyst, the reaction of 2-alkynyl benzaldehyde with vinyl ether produced acetal-tethered dihydronaphthalene **5** and isochromene **6**, rather than naphthalene **2**. Furthermore, a symmetrical bicyclo-[2.2.2]octane **7** was produced from the reaction of 2-alkynyl benzaldehyde with a cyclic vinyl ether. By using (*i*Pr)Au as the catalyst, a homo-dimerization of 2-alkynyl benzaldehyde took place, affording a set of separable diastereomers **9** (Scheme 3). These interesting cyclic products are potentially useful synthetic templates of biologically active molecules and natural products such as codeine,[20] CJ-17493,[21] psychorubrin,[22] trioxifene,[23] regalamine, robustamine,[24] and the trypticene analogue TT13[25] (Scheme 4). To the best of our knowledge, the synthesis of similar cyclic compounds are rare, and, normally, harsh reaction conditions are needed.[26]



Scheme 3. New developments on gold-catalyzed annulations of 2-alkynyl benzaldehydes with vinyl ethers.

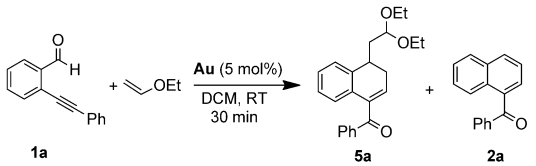


Scheme 4. Selected examples of biologically active compounds containing dihydronaphthalene, isochromene, or bicyclo[2.2.2]octane substructures.

Results and Discussion

Although for the most part the selection of gold catalysts relies on an empirical trial and error approach, some patterns on ligand effect in gold catalysis have emerged recently.[18a–c] For example, the cationic gold complex **Au-1**, developed by Echavarren and co-workers, exhibited excellent stability and catalytic activity in the cycloisomerization of enynes due to its bulky and electron-rich phosphine ligand.[27] Accordingly, we first employed **Au-1** as the catalyst in the reaction of 2-phenylethynyl benzaldehyde with ethyl vinyl ether. To our delight, along with Yamamoto's naphthalene product **2a**, which was obtained in low yield, we isolated the acetal-tethered dihydronaphthalene derivative **5a** as the major product, under mild conditions (Table 1, entry 1). Other traditional gold catalysts were also investigated in this reaction, but only phosphine gold chloride with silver activators showed good catalytic activities (Table 1, entries 2 and 3); other catalysts such as AuCl,

Table 1. Discovery of a new gold-catalyzed annulation of 2-alkynyl benzaldehyde with vinyl ether.[a,c]



Entry	Au cat.	Yield [%][b]
1	**Au-1**	52 (9)
2	$PPh_3AuCl/AgOTf$	50 (20)
3	$PPh_3AuCl/AgNTf_2$	50 (10)
4	AuCl	complex
5	$AuCl_3$	complex
6	triazole Au	complex
7	(*i*Pr)$PPh_3AuCl/AgOTf$	complex
8	AgOTf	complex

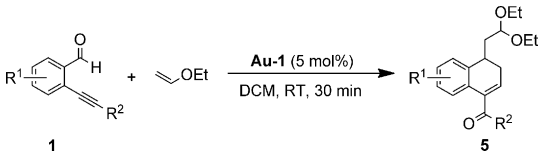
[a] General reaction conditions: 2-(phenylethynyl)benzaldehyde **1a** (0.2 mmol), ethyl vinyl ether (1.0 mmol), Au (5 mol%), CH_2Cl_2 (1.0 mL). [b] Yields of the isolated product; the yields of product **2a** are presented in parentheses. [c] Reaction of **1a** with TfOH (5 mol%) gave a complex reaction mixture along with unreacted **1a**.

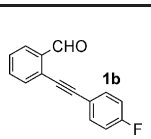
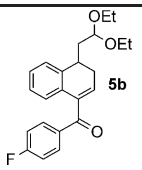
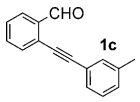
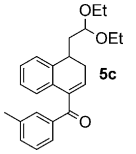
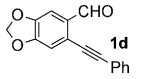
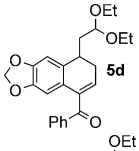
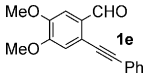
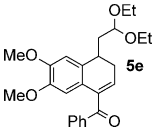
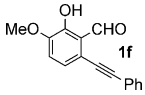
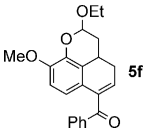
$AuCl_3$, triazole gold, and (*i*Pr)AuCl/AgOTf, as well as AgOTf failed to give any identifiable product (Table 1, entries 4–7). The fragility of this reaction may be due to the instability of ethyl vinyl ether to acidic conditions.[28] Next, various 2-alkynyl benzaldehyde substrates with different substituents on the aromatic ring were prepared for use in this new gold-catalyzed annulation with vinyl ether, and the results are summarized in Table 2. All the reactions gave the desired dihydronaphthalene derivatives in moderate yields at, or below, room temperature. Mechanistically, the tethered acetal might have been generated from an oxonium intermediate reacting with an alkoxide anion.[29]

Thus, we wondered if the oxonium intermediate could be intramolecularly trapped by an adjacent phenolic hydroxyl group or if the desired product would be formed preferably in the presence of additional ethanol. To our satisfaction, when substrate **1f** was employed in this reaction, the reaction intermediate was indeed trapped by the adjacent phenolic hydroxyl group, furnishing the structurally interesting tricyclic compound **5f** as the main product (Table 2, entry 5).[30] However, when two equivalents of ethanol were added to the reaction, a new acetal-tethered isochromene **6a**, rather than the corresponding dihydronaphthalene derivative, was obtained in good yield (Table 3, entry 1).

Since isochromene derivatives are also attractive substrates in organic chemistry, we investigated the gold-catalyzed annulation of 2-alkynyl benzaldehydes with vinyl ether in the presence of alcohol. Our results are outlined in Table 3. All the desired products were obtained in good yields. It should be noted that, for substrate **1f**, the intramolecular trapping was bypassed by an intermolecular quenching with ethanol (Table 3, entry 6), which could be explained by the fact that alkoxide is a stronger nucleophile than phenoxide. Other alcohols such methanol and isopropanol were tested in this reaction, and similar products were obtained in good yields (Table 3, entries 7 and 8).

Table 2. Scope of the gold-catalyzed annulation of 2-alkynyl benzaldehyde with vinyl ether.[a]

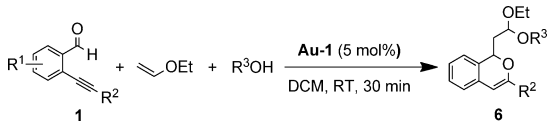


Entry	Substrate	Product	Yield [%][b]
1[c]			67
2			56
3			51[d]
4			53[d]
5			41

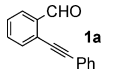
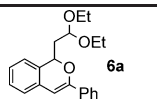
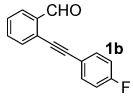
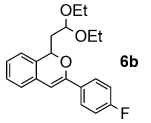
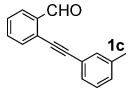
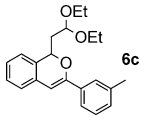
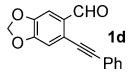
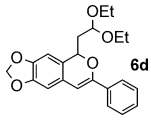
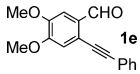
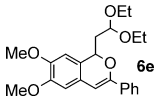
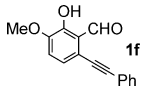
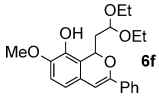
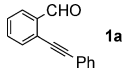
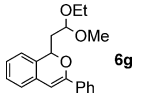
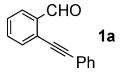
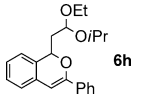
[a] General reaction conditions: 2-alkynyl benzaldehyde **1** (0.145 mmol), ethyl vinyl ether (0.72 mmol), **Au-1** (5 mol%), CH_2Cl_2 (1.0 mL). [b] Yield of the isolated product. [c] Reaction time: 15 min. [d] Ethyl vinyl ether (1.45 mmol) was used and the reaction was carried out at 0°C.

Plausible mechanisms for the formations of these new products have been proposed, as outlined in Scheme 5. The generation of intermediate **A** from a gold catalyst and 2-alkynyl benzaldehyde substrate is well-accepted,[31] whereas the subsequent annulation with vinyl ether to form **C** is not clear. It could be either a concerted step, as in a Diels–Alder-type reaction, or in stepwise fashion, beginning with the formation of **B**. According to previous literature reports, the existence of **B** is supported by substituent effects, regio- and stereoselectivities.[13–17] In our case, the formation of acetal-tethered isochromene **6** in the presence of alcohol also implies the generation of intermediate **B**. However, intermediate **A** was not trapped by alcohol before the formation of **B**, demonstrating the different catalytic activity of the gold catalyst.[32] Once intermediate **C** was formed, it could transform into **D**, which reacted with another molecule of vinyl ether, generating intermediate **E**. Gold and ethoxide elimination and quenching of the oxonium ion with ethoxide took place in **E**, affording **5** as the product and re-generating the gold catalyst.[33,28] A competitive elim-

Table 3. Gold-catalyzed annulation of 2-alkynyl benzaldehyde with vinyl ether in the presence of alcohol.[a]



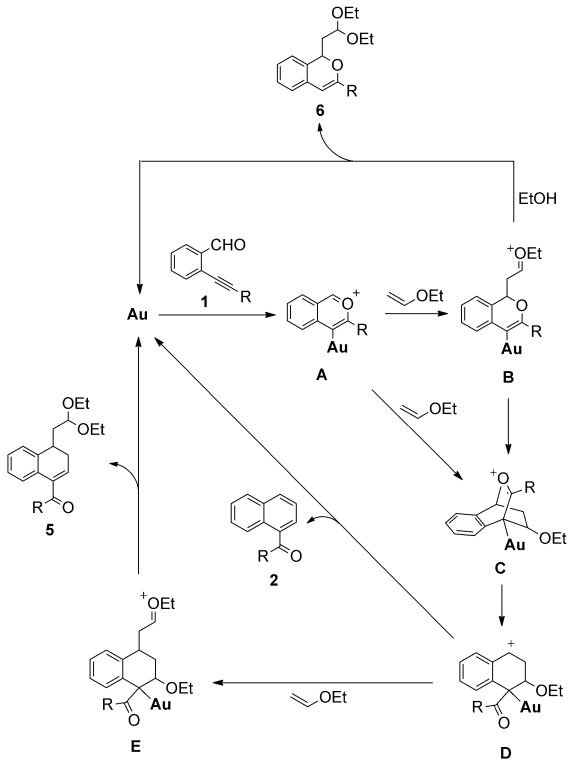
1 6

Entry	Substrate	Product	Yield [%][b]
1			86
2[c]			82
3			71
4			54[d]
5			51[d]
6			56
7			89
8			81

[a] General reaction conditions: 2-alkynyl benzaldehyde **1** (0.145 mmol), ethyl vinyl ether (0.72 mmol), alcohol (0.29 mmol), **Au-1** (5 mol%), CH_2Cl_2 (1.0 mL). [b] Yield of the isolated product. [c] Reaction time: 10 min. [d] The reaction was carried out at 0 °C.

ination in **D** also occurred, furnishing naphthalene **2** as the product. With the selection of an appropriate gold catalyst, the elimination could be controlled.

Because gold alkoxide elimination took place at the stage of intermediate **E**, we envisioned that this elimination might have been prevented if a cyclic vinyl ether was chosen as the annulation partner. Thus, the readily available 2,3-dihydrofuran was employed in the reaction, and as expected, the gold alkoxide elimination was successfully prevented; instead, a new bicyclo[2.2.2]octane derivative **7** was produced, in which two molecules of cyclic vinyl ether were involved. Catalyst **Au-2**[34] showed the best catalytic activity and therefore it was selected for subsequent reactions. Various substrates, having different substituents on the aromatic rings, were employed in this new gold-catalyzed annulation with 2,3-dihydrofuran, and the corresponding products **7a**–**i** were isolated (Table 4). 3,4-Dihydro-2*H*-pyran was also employed



Scheme 5. Proposed mechanisms for the gold-catalyzed annulations of 2-alkynyl benzaldehyde with vinyl ether.

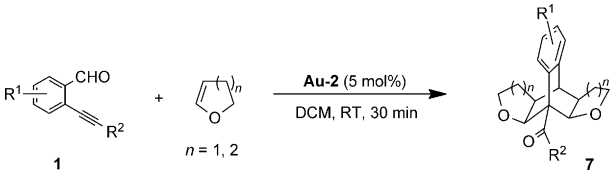
as the cyclic vinyl ether due to its easy availability, and the corresponding product **7j** was obtained in moderate yield.[35]

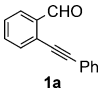
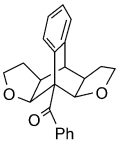
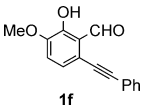
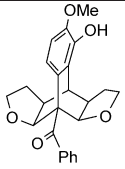
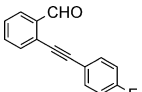
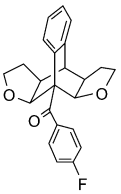
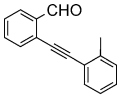
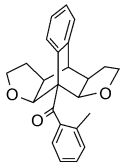
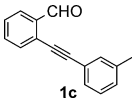
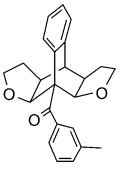
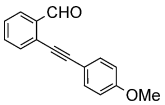
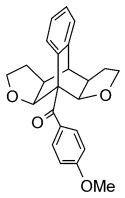
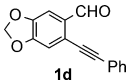
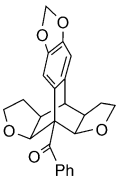
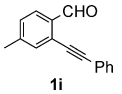
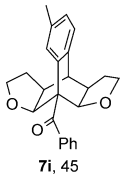
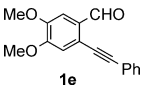
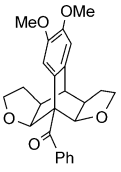
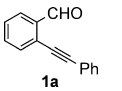
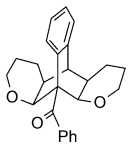
The structure of product **7** was determined by using ^1H, ^{13}C, DEPT, gCOSY, HMQC, and HMBC NMR spectroscopy as well as HRMS, and finally confirmed by using X-ray crystallography (the ORTEP-3 diagram of **7a** is shown in Figure 1).

A plausible mechanism for the formation of the bicyclo-[2.2.2]octane derivative is outlined in Scheme 6. After intermediate **A** is generated, a formal [4+2] cycloaddition to 2,3-dihydrofuran could take place either through a concerted or stepwise fashion to yield intermediate **G**. Intermediate **G** could transform itself into **H**, which then reacts with a second molecule of 2,3-dihydrofuran, generating **I**, before finally furnishing product **7** and regenerating the gold catalyst. However, an alternative possibility should also be taken into account, namely, elimination of gold catalyst from **H** could generate tetrahydronaphthofuran derivative **8**, which would then undergo an inverse-electron-demand Diels–Alder reaction with the second molecule of 2,3-dihydrofuran, furnishing the final product **7**.[36]

During our investigations on these gold-catalyzed annulations, homo-dimerization of 2-alkynyl benzaldehyde was observed when (*i*Pr)AuCl/AgOTf was employed as the catalyst, in the absence of vinyl ether (Scheme 7).[16] A set of separable diastereoisomers **9a** and **9b** was obtained in good yield, in a 3:5 ratio. The formation of this dimer has been ascribed to a gold-catalyzed hydrolysis of the 2-alkynyl benzal-

Table 4. Gold-catalyzed annulation of 2-alkynyl benzaldehyde with cyclic vinyl ether.[a]



Reactant	Product[b]	Reactant	Product[b]
 1a	 7a, 51	 1f	 7f, 27
 1b	 7b, 32	 1g	 7g, 65
 1c	 7c, 52	 1h	 7h, 45
 1d	 7d, 41	 1i	 7i, 45
 1e	 7e, 69	 1a	 7j,[c] 37

[a] General reaction conditions: 2-alkynyl benzaldehyde **1** (0.145 mmol), 2,3-dihydrofuran (0.72 mmol), **Au-2** (5 mol%), and CH_2Cl_2 (1.0 mL). [b] Yield of the isolated product. [c] 3,4-Dihydro-2*H*-pyran was used as cyclic vinyl ether.

dehyde substrate, generating ketone **10**, which then serves as a nucleophile for attacking the electrophilic intermediate **A**. The structure of the dimer was also confirmed by X-ray crystallography. The ORTEP-3 diagram of the anti-isomer **9b** is shown in Figure 2.

Conclusion

We have investigated the gold-catalyzed annulations of 2-alkynyl benzaldehyde with acyclic or cyclic vinyl ethers under very mild conditions, and found a number of synthetically interesting transformations. With the selection of an appropriate gold catalyst, the reactions of various 2-alkynyl benzaldehydes with acyclic vinyl ethers afforded dihydronaphthalene derivatives as the products, whereas acetal-tethered isochromenes were obtained when the reaction was conducted in the presence of alcohol. Interestingly, a new bicyclo[2.2.2]octane derivative was isolated from the reaction of 2-alkynyl benzaldehyde with cyclic vinyl ether. The various mechanisms of formation of these reactions have been discussed. Lastly, it was found that 2-alkynyl benzaldehyde undergoes dimerization under gold catalysis in the absence of vinyl ether.

Experimental Section

General methods: ^{1}H and ^{13}C NMR spectra were recorded at 500 and 126 (or 400 and 101) MHz, respectively, by using $CDCl_3$ as a solvent. The chemical shifts are reported in δ (ppm) values (^{1}H and ^{13}C NMR relative to $CHCl_3$, $\delta=7.26$ ppm for ^{1}H NMR and $\delta=77.0$ ppm for ^{13}C NMR and $CFCl_3$ ($\delta=0$ ppm for ^{19}F NMR), multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and br (broad). Coupling constants, *J*, are reported in Hertz (Hz). Solvents (tetrahydrofuran, ether, dichloromethane and DMF) were dried using a commercial solvent purification system. All other reagents and solvents were employed without further purification. The products were purified using a commercial flash chromatography system or a regular glass column. TLC was developed on silica gel 60 F254 aluminum sheets. Exact molecular weight of new compound was obtained by high-resolution electrospray ionization mass spectrometry (HREIMS).

General procedure for the formation of dihydronaphthalenes (5): Catalyst **Au-1** (5.61 mg, 0.0072 mmol) was added to the solution of 2-phenylethynyl benzaldehyde **1a** (30 mg, 0.145 mmol) and ethyl vinyl ether (70 μL, 0.72 mmol) in CH_2Cl_2 (1.0 mL). The mixture was stirred for 30 min at room temperature; afterwards the reaction mixture was quenched with water and extracted with CH_2Cl_2. The solvent in the organic layer was removed under reduced pressure and the residue was subjected to flash column chromatography (eluent: ethyl acetate/*n*-hexane = 1:10) to give product **5a** (26.5 mg, 52%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=1.13$–1.16 (3H, t, $J=7.2$ Hz), 1.23–1.26 (3H, t, $J=7.2$ Hz), 1.84–1.88 (1H, m), 1.93–2.0 (1H, m), 2.42–2.49 (1H, m), 2.68–2.74 (1H, m), 3.01–3.06 (1H, m), 3.39–3.59 (3H, m), 3.63–3.71 (1H, m), 4.44–4.47 (1H, t, $J=6.4$ Hz), 6.39–6.42 (1H, dd, $J=6.4$, 3.2 Hz), 7.12–7.17 (1H, m), 7.19–7.20 (2H, m), 7.27–7.30 (1H, d, $J=8.0$ Hz), 7.40–7.44 (2H, t, $J=7.8$ Hz), 7.52–7.56 (1H, t, $J=7.4$ Hz), 7.83–7.85 ppm (2H, d, $J=7.2$ Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): $\delta=15.3$, 15.4, 29.0, 33.3, 37.3, 60.8, 61.0, 101.1, 126.3, 126.8, 127.8, 127.9, 128.3, 129.8, 131.1, 132.8, 135.2, 138.0, 138.3, 138.8, 196.7 ppm; HRMS (ESI) calcd for $C_{23}H_{26}NaO_3^+$: 373.1774 [$M+Na^+$]; found: 373.1775.

General procedure for the formation of isochromenes (6): Catalyst **Au-1** (5.61 mg, 0.0072 mmol) was added to the solution of 2-phenylethynyl benzaldehyde **1a** (30 mg, 0.145 mmol, ethyl vinyl ether (70 μL, 0.72 mmol), and ethanol (17 μL, 0.29 mmol) in CH_2Cl_2 (1.0 mL). The mixture was stirred for 30 min at room temperature; afterwards the reaction mixture was quenched with water and extracted with CH_2Cl_2. The solvent in the organic layer was removed under reduced pressure and the

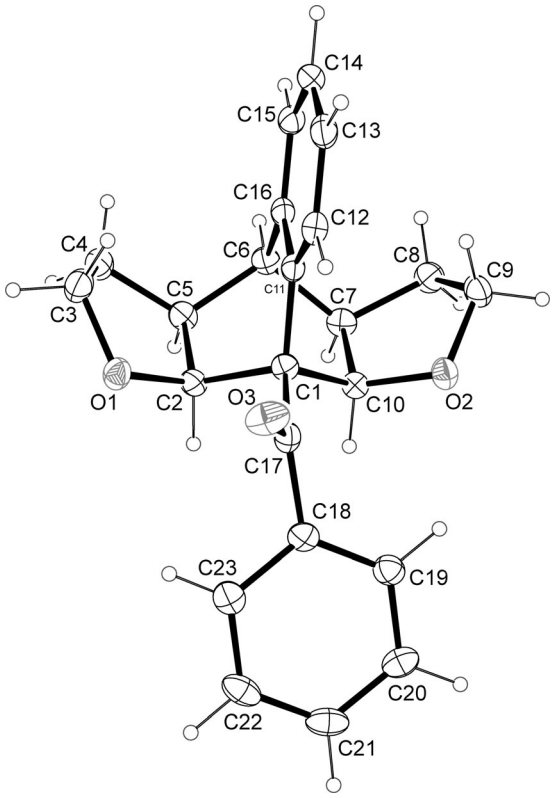
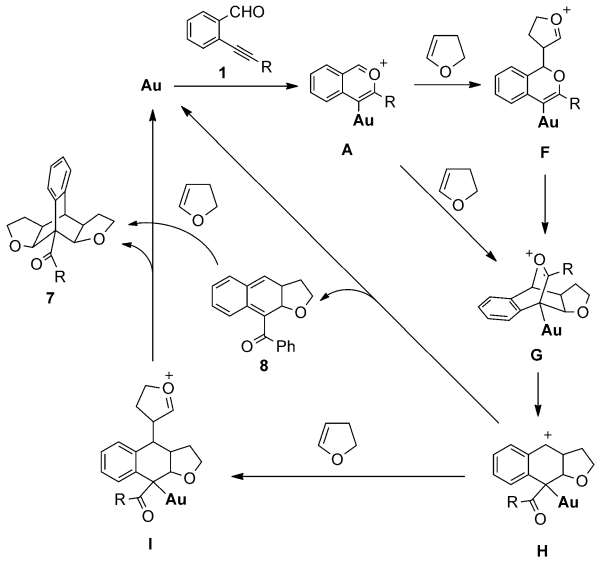
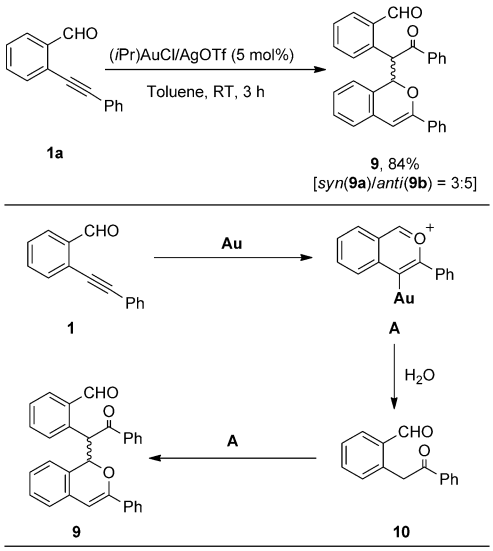


Figure 1. ORTEP-3 diagram of bicyclo[2.2.2]octane derivative **7a**, showing 40% probability ellipsoids. H atoms are shown as small spheres of arbitrary radii. Selected bond lengths [Å] and angles [°]: O1-C2, 1.4285(17); O1-C3, 1.4380(18); O2-C9, 1.4419(18); O2-C10, 1.4338(16); O3-C17, 1.2100(18); O2-C10-C1, 111.15(11); O1-C2-C3, 111.78(11); C2-C1-C10, 104.06(11).



Scheme 6. Proposed mechanism for the gold-catalyzed annulation of 2-alkynyl benzaldehyde with cyclic vinyl ether.

residue was subjected to flash column chromatography (eluent: ethyl acetate/*n*-hexane = 1:10) to give product **6a** (41 mg, 87%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.21–1.24 (3H, t, J = 7.6 Hz), 1.27–1.31 (3H, t, J = 7.2 Hz), 2.09–2.16 (1H, m), 2.42–2.49 (1H, m), 3.51–3.59 (1H, m), 3.61–3.71 (2H, m), 3.76–3.84 (1H, m), 4.90–4.93 (1H, dd, J = 7.6, 3.8 Hz), 5.50–5.53 (1H, dd, J = 9.6, 4.0 Hz), 6.47 (1H, s), 7.09–7.13 (2H, t, J = 8.0 Hz), 7.18–7.27 (2H, m), 7.34–7.43 (3H, m), 7.76–7.78 ppm (2H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 15.39, 15.41, 37.9, 60.9, 62.2, 75.0, 99.9, 100.6, 123.7, 124.0, 124.9, 126.6, 128.0, 128.4, 128.7, 130.9, 131.0, 134.6, 151.3 ppm; HRMS (ESI) calcd for $C_{21}H_{24}NaO_3^+$: 347.1618 [M+ Na^+]; found: 347.1622.



Scheme 7. Gold-catalyzed homo-dimerization of 2-alkynyl benzaldehyde and the proposed mechanism.

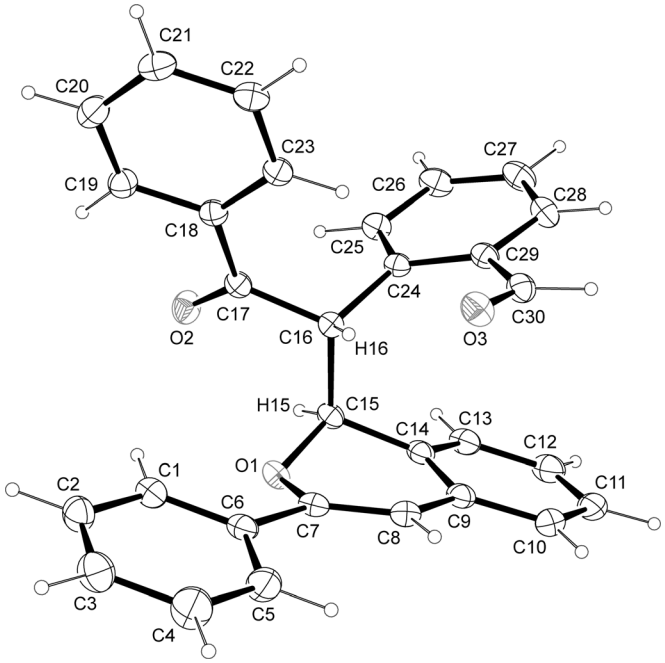


Figure 2. ORTEP-3 diagram of product **9b**, showing one diastereoisomer of the racemic mixture at 40% probability ellipsoids. H atoms are shown as small spheres of arbitrary radii. Selected bond lengths [Å] and angles [°]: O1-C7, 1.3795(15); O1-C15, 1.4447(15); O2-C17, 1.2157(15); O3-C30, 1.2117(16); C15-C16, 1.5531(17); C7-O1-C15, 114.70(9); O1-C7-C8, 121.07(11); O1-C15-C16, 106.72(9).

General procedure for the formation of bicyclo[2.2.2]octanes (7): Catalyst **Au-2** (6.93 mg, 0.0072 mmol) was added to the solution of 2-phenyl-

ethynyl benzaldehyde **1a** (30 mg, 0.145 mmol) and 2,3-dihydrofuran (55 μL, 0.72 mmol) in CH_2Cl_2 (1.0 mL). The mixture was stirred for 30 min at room temperature; afterwards the reaction mixture was quenched with water and extracted with CH_2Cl_2. The solvent in the organic layer was removed under reduced pressure and the residue was subjected to a flash column chromatography (eluent: ethyl acetate/*n*-hexane = 1:10) to give product **7a** (26 mg, 51%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.13–1.21 (2H, m), 1.81–1.89 (2H, m), 2.54–2.61 (2H, m), 2.91–2.97 (3H, m), 3.29–3.35 (2H, q, J = 7.2 Hz), 4.48–4.50 (2H, d, J = 8.4 Hz), 7.05–7.18 (3H, m), 7.30–7.34 (2H, t, J = 7.6 Hz), 7.38–7.41 (1H, t, J = 6.8 Hz), 7.58–7.59 (1H, d, J = 7.2 Hz), 7.83–7.85 ppm (2H, d, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 30.3, 43.8, 44.2, 62.2, 68.5, 81.0, 126.4, 126.8, 127.3, 127.6, 129.0, 129.6, 130.8, 134.9, 137.8, 140.3, 204.0 ppm; HRMS (ESI) calcd for $C_{23}H_{23}O_3^+$: 347.1642 [$M+H^+$]; found: 347.1642.

General procedure for the formation of the dimer 9: (*i*Pr)AuCl (6.9 mg, 0.0072 mmol) and AgOTf (1.86 mg, 0.0072 mmol) were added to the solution of 2-phenylethynyl benzaldehyde **1a** (30 mg, 0.145 mmol) in toluene (1.0 mL). The mixture was stirred for 3 h at room temperature; afterwards, the reaction mixture was quenched with water and extracted with CH_2Cl_2. The solvent in the organic layer was removed under reduced pressure and the residue was subjected to flash column chromatography (eluent: ethyl acetate/*n*-hexane = 1:10) to give the separable diastereoisomers **9a** (*syn*, 10.1 mg, 32%) as yellow liquid and **9b** (anti, 16.3 mg, 52%) as a white solid. For **9a**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 6.28–6.31 (1H, d, J = 9.6 Hz), 6.60 (1H, s), 6.99–7.08 (4H, m), 7.12–7.27 (8H, m), 7.36–7.50 (3H, m), 7.60–7.64 (1H, t, J = 7.4 Hz), 7.85–7.87 (2H, d, J = 8.4 Hz), 7.99–8.01 (1H, d, J = 7.6 Hz), 9.64 ppm (1H, s); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 49.1, 79.8, 101.0, 124.4, 124.5, 126.0, 126.5, 127.6, 127.9, 128.36, 128.4, 128.6, 128.7, 129.6, 129.8, 130.4, 133.2, 133.5, 133.8, 134.7, 135.1, 136.9, 150.7, 192.9, 198.5 ppm; HRMS (ESI) calcd for $C_{30}H_{22}NaO_3^+$: 453.1461 [$M+Na^+$]; found: 453.1465. For **9b**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.92–5.94 (1H, d, J = 7.6 Hz), 6.17–6.20 (1H, d, J = 9.6 Hz), 6.58 (1H, s), 6.65–6.68 (1H, t, J = 7.4 Hz), 7.03–7.11 (3H, m), 7.18–7.19 (3H, m), 7.24–7.28 (2H, t, J = 7.2 Hz), 7.35–7.39 (2H, t, J = 7.6 Hz), 7.46–7.55 (4H, m), 7.77–7.80 (1H, d, J = 8.0 Hz), 7.98–8.00 (2H, d, J = 8.0 Hz), 9.57 ppm (1H, s); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 46.1, 79.9, 100.5, 123.8, 125.1, 125.2, 125.4, 127.0, 128.0, 128.1, 128.2, 128.57, 128.66, 128.68, 129.3, 131.3, 133.2, 133.6, 134.0, 134.5, 135.5, 136.9, 150.7, 191.9, 198.2 ppm; HRMS (ESI) calcd for $C_{30}H_{22}NaO_3^+$: 453.1461 [$M+Na^+$]; found: 453.1464.

Acknowledgements

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[1] a) H.-S. Yeom, J. Koo, H.-S. Park, Y. Wang, Y. Liang, Z.-X. Yu, S. Shin, *J. Am. Chem. Soc.* **2012**, *134*, 208; b) T. J. Brown, D. Weber, M. R. Gagné, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2012**, *134*, 9134; c) C. R. Solorio-Alvarado, A. M. Echavarren, *J. Am. Chem. Soc.* **2010**, *132*, 11881; d) H. Li, R. A. Widenhoefer, *Org. Lett.* **2009**, *11*, 2671; e) G. Zhang, X. Huang, G. Li, L. Zhang, *J. Am. Chem. Soc.* **2008**, *130*, 1814; f) Z. Zhang, C. F. Bender, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2007**, *129*, 14148; g) A. S. K. Hashmi, L. Schwarz, J.-H. Choi, T. M. Frost, *Angew. Chem.* **2000**, *112*, 2382; *Angew. Chem. Int. Ed.* **2000**, *39*, 2285; h) A. S. K. Hashmi, T. M. Frost, J. W. Bats, *J. Am. Chem. Soc.* **2000**, *122*, 11553; i) Y. Ito, M. Sawamura, T. Hayashi, *J. Am. Chem. Soc.* **1986**, *108*, 6405.

[2] a) M. Rudolph, A. S. K. Hashmi, *Chem. Commun.* **2011**, *47*, 6536; b) W. He, C. Li, L. Zhang, *J. Am. Chem. Soc.* **2011**, *133*, 8482; c) C. Winter, N. Krause, *Angew. Chem.* **2009**, *121*, 6457; *Angew. Chem. Int. Ed.* **2009**, *48*, 6339; d) A. Corma, A. Leyva-Pérez, M. Sabater, *Chem. Rev.* **2011**, *111*, 1657; e) A. Saito, T. Konishi, Y. Hanzawa, *Org. Lett.* **2010**, *12*, 372; f) A. S. K. Hashmi, *Pure Appl. Chem.* **2010**, *82*, 657; g) N. T. Patil, Y. Yamamoto, *Chem. Rev.* **2008**, *108*, 3395.

[3] a) S. Wang, L. M. Zhang, *J. Am. Chem. Soc.* **2006**, *128*, 8414; b) S. Wang, L. Zhang, *J. Am. Chem. Soc.* **2006**, *128*, 14274; c) A. S. K. Hashmi, M. Rudolph, J. P. Weyrauch, M. Wölfle, W. Frey, J. W. Bats, *Angew. Chem.* **2005**, *117*, 2858; *Angew. Chem. Int. Ed.* **2005**, *44*, 2798; d) A. S. K. Hashmi, J. P. Weyrauch, M. Rudolph, E. Kurpejović, *Angew. Chem.* **2004**, *116*, 6707; *Angew. Chem. Int. Ed.* **2004**, *43*, 6545; e) A. Dar, K. Moss, S. M. Cottrill, R. V. Parish, C. A. McAuliffe, R. G. Pritchard, B. Beagley, J. Sandbank, *J. Chem. Soc. Dalton Trans.* **1992**, 1907.

[4] a) H. Clavier, S. P. Nolan, *Chem. Commun.* **2010**, *46*, 841; b) A. S. K. Hashmi, C. Lothschütz, C. Böhling, T. Hengst, C. Hubbert, F. Rominger, *Adv. Synth. Catal.* **2010**, *352*, 3001; c) M. Pažický, A. Loos, M. J. Ferreira, D. Serra, N. Vinokurov, F. Rominger, C. Jäkel, A. S. K. Hashmi, M. Limbach, *Organometallics* **2010**, *29*, 4448; d) A. S. K. Hashmi, T. Hengst, C. Lothschütz, F. Rominger, *Adv. Synth. Catal.* **2010**, *352*, 1315; e) C. Bartolomé, Z. Ramiro, D. García-Cuadrado, P. Pérez-Galán, M. Raducan, C. Bour, A. M. Echavarren, P. Espinet, *Organometallics* **2010**, *29*, 951; f) C. Bartolomé, D. García-Cuadrado, Z. Ramiro, P. Espinet, *Organometallics* **2010**, *29*, 3589; M. Alcarazo, T. Stork, A. Anoop, W. Thiel, A. Fürstner, *Angew. Chem.* **2010**, *122*, 2596; *Angew. Chem. Int. Ed.* **2010**, *49*, 2542; h) X. Bantreil, J. Broggi, S. P. Nolan, *Annu. Rep. Prog. Chem. Sect. B: Org. Chem.* **2009**, *105*, 232; i) S. Díez-González, N. Marion, S. P. Nolan, *Chem. Rev.* **2009**, *109*, 3612; j) E. Aldeco-Perez, A. J. Rosenthal, B. Donnadieu, P. Parameswaran, G. Frenking, G. Bertrand, *Science* **2009**, *326*, 556; k) C. Bartolomé, Z. Ramiro, P. Pérez-Galán, C. Bour, M. Raducan, A. M. Echavarren, P. Espinet, *Inorg. Chem.* **2008**, *47*, 11391; l) R. E. Kinder, Z. Zhang, R. A. Widenhoefer, *Org. Lett.* **2008**, *10*, 3157; m) N. Marion, P. Carlqvist, R. Gealageas, P. de Fremont, F. Maseras, S. P. Nolan, *Chem. Eur. J.* **2007**, *13*, 6437; n) N. Marion, S. Diez-González, P. de Frémont, A. R. Noble, S. P. Nolan, *Angew. Chem.* **2006**, *118*, 3729; *Angew. Chem. Int. Ed.* **2006**, *45*, 3647; o) D. Bourissou, O. Guerret, F. P. Gabbaï, G. Bertrand, *Chem. Rev.* **2000**, *100*, 39; p) A.-L. Lee, *Annu. Rep. Prog. Chem.* **2011**, *107*, 369.

[5] a) C. Ferrer, C. H. M. Amijs, A. M. Echavarren, *Chem. Eur. J.* **2007**, *13*, 1358; b) E. Herrero-Gómez, C. Nieto-Oberhuber, S. López, J. Benet-Buchholz, A. M. Echavarren, *Angew. Chem.* **2006**, *118*, 5581; *Angew. Chem. Int. Ed.* **2006**, *45*, 5455; c) C. Ferrer, A. M. Echavarren, *Angew. Chem.* **2006**, *118*, 1123; *Angew. Chem. Int. Ed.* **2006**, *45*, 1105.

[6] a) F. M. Istrate, F. Gagosz, *Org. Lett.* **2007**, *9*, 3181; b) C. Nieto-Oberhuber, M. P. Muñoz, S. López, E. Jiménez-Núñez, C. Nevado, E. Herrero-Gómez, M. Raducan, A. M. Echavarren, *Chem. Eur. J.* **2006**, *12*, 1677; c) C. Nieto-Oberhuber, S. López, A. M. Echavarren, *J. Am. Chem. Soc.* **2005**, *127*, 6178; d) S. D. Walker, T. E. Barder, J. R. Martinelli, S. L. Buchwald, *Angew. Chem.* **2004**, *116*, 1907; *Angew. Chem. Int. Ed.* **2004**, *43*, 1871; e) E. R. Strieter, D. G. Blackmond, S. L. Buchwald, *J. Am. Chem. Soc.* **2003**, *125*, 13978; f) S. Kaye, J. M. Fox, F. A. Hicks, S. L. Buchwald, *Adv. Synth. Catal.* **2001**, *343*, 789.

[7] a) Q. Wang, S. Aparaj, N. G. Akhmedov, J. L. Petersen, X. Shi, *Org. Lett.* **2012**, *14*, 1334; b) D. Wang, L. N. S. Gautam, C. Bollinger, A. Harris, M. Li, X. Shi, *Org. Lett.* **2011**, *13*, 2618; c) D. Wang, Y. Zhang, R. Cai, X. Shi, *Beilstein J. Org. Chem.* **2011**, *7*, 1014; d) D. Wang, Y. Zhang, A. Harris, L. N. S. Gautam, Y. Chen, X. Shi, *Adv. Synth. Catal.* **2011**, *353*, 2584; e) D. Wang, X. Ye, X. Shi, *Org. Lett.* **2010**, *12*, 2088; f) Y. Chen, D. Wang, J. L. Petersen, N. Akhmedov, X. Shi, *Chem. Commun.* **2010**, *46*, 6147; g) W. Yan, Q. Wang, Y. Chen, J. L. Petersen, X. Shi, *Org. Lett.* **2010**, *12*, 3308.

[8] a) L. Ricard, F. Gagosz, *Organometallics* **2007**, *26*, 4704; b) A. K. Buzas, F. M. Istrate, F. Gagosz, *Angew. Chem.* **2007**, *119*, 1159; *Angew. Chem. Int. Ed.* **2007**, *46*, 1141; c) A. Buzas, F. Gagosz, *Org. Lett.* **2006**, *8*, 515; d) A. Buzas, F. Gagosz, *J. Am. Chem. Soc.* **2006**,

128, 12614; e) N. Mézailles, L. Ricard, F. Gagosz, *Org. Lett.* **2005**, *7*, 4133.

[9] a) A. Z. González, D. Benitez, E. Tkatchouk, W. A. Goddard III, F. D. Toste, *J. Am. Chem. Soc.* **2011**, *133*, 5500; b) A. Z. González, F. D. Toste, *Org. Lett.* **2010**, *12*, 200; c) H. Teller, S. Flügge, R. Goddard, A. Fürstner, *Angew. Chem.* **2010**, *122*, 1993; *Angew. Chem. Int. Ed.* **2010**, *49*, 1949; d) I. Alonso, B. Trillo, F. López, S. Montserrat, G. Ujaque, L. Castedo, A. Lledós, J. L. Mascareñas, *J. Am. Chem. Soc.* **2009**, *131*, 13020; e) G. L. Hamilton, E. J. Kang, M. Mba, F. D. Toste, *Science* **2007**, *317*, 496; f) A. D. Melhado, M. Luparia, F. D. Toste, *J. Am. Chem. Soc.* **2007**, *129*, 12638; g) R. L. LaLonde, B. D. Sherry, E. J. Kang, F. D. Toste, *J. Am. Chem. Soc.* **2007**, *129*, 2452.

[10] a) S. Gaillard, C. S. J. Cazin, S. P. Nolan, *Acc. Chem. Res.* **2012**, *45*, 778; b) A. S. K. Hashmi, A. M. Schuster, S. Gaillard, L. Cavallo, A. Poater, S. P. Nolan, *Organometallics* **2011**, *30*, 6328; c) I. I. F. Boogaerts, S. P. Nolan, *J. Am. Chem. Soc.* **2010**, *132*, 8858.

[11] a) K. Gao, J. Wu, *J. Org. Chem.* **2007**, *72*, 8611; b) D. Zheng, S. Li, J. Wu, *Org. Lett.* **2012**, *14*, 2655; c) S. Li, J. Wu, *Org. Lett.* **2011**, *13*, 712; d) N. A. Markina, R. Mancuso, B. Neuenswander, G. H. Lushington, R. C. Larock, *ACS Comb. Sci.* **2011**, *13*, 265; e) Z. Chen, J. Wu, *Org. Lett.* **2010**, *12*, 4856; f) Q. Ding, J. Wu, *Org. Lett.* **2007**, *9*, 4959; g) W. Sun, Q. Ding, X. Sun, R. Fan, J. Wu, *J. Comb. Chem.* **2007**, *9*, 690; h) J. Barluenga, H. Vázquez-Villa, A. Ballesteros, J. M. González, *Org. Lett.* **2003**, *5*, 4121.

[12] a) X. Yao, C.-J. Li, *Org. Lett.* **2006**, *8*, 1953; b) N. Asao, K. Sato, Menggenbateer, Y. Yamamoto, *J. Org. Chem.* **2005**, *70*, 3682; c) N. Asao, T. Nogami, K. Takahashi, Y. Yamamoto, *J. Am. Chem. Soc.* **2002**, *124*, 764; d) N. T. Patil, Y. Yamamoto, *J. Org. Chem.* **2004**, *69*, 5139; e) N. Asao, C. S. Chan, K. Takahashi, Y. Yamamoto, *Tetrahedron* **2005**, *61*, 11322; f) N. T. Patil, N. K. Pahadi, Y. Yamamoto, *J. Org. Chem.* **2005**, *70*, 10096; g) K. Sato, N. Asao, Y. Yamamoto, *J. Org. Chem.* **2005**, *70*, 8977.

[13] N. Asao, K. Takahashi, S. Lee, T. Kasahara, Y. Yamamoto, *J. Am. Chem. Soc.* **2002**, *124*, 12650.

[14] N. Asao, T. Nogami, S. Lee, Y. Yamamoto, *J. Am. Chem. Soc.* **2003**, *125*, 10921.

[15] N. Asao, T. Kasahara, Y. Yamamoto, *Angew. Chem.* **2003**, *115*, 3628; *Angew. Chem. Int. Ed.* **2003**, *42*, 3504.

[16] A. B. Beeler, S. Su, C. A. Singleton, J. A. Porco, Jr., *J. Am. Chem. Soc.* **2007**, *129*, 1413.

[17] N. Asao, H. Aikawa, Y. Yamamoto, *J. Am. Chem. Soc.* **2004**, *126*, 7458.

[18] a) W. Wang, G. B. Hammond, B. Xu, *J. Am. Chem. Soc.* **2012**, *134*, 5697; b) R. Döpp, C. Lothschütz, T. Wurm, M. Pernpointner, S. Keller, F. Rominger, A. S. K. Hashmi, *Organometallics* **2011**, *30*, 5894; c) D. Benitez, N. D. Shapiro, E. Tkatchouk, Y. Wang, W. A. Goddard III, F. D. Toste, *Nat. Chem.* **2009**, *1*, 482; d) L.-P. Liu, D. Malhotra, Z. Jin, R. S. Paton, K. N. Houk, G. B. Hammond, *Chem. Eur. J.* **2011**, *17*, 10690; e) L.-P. Liu, D. Malhotra, R. S. Paton, K. N. Houk, G. B. Hammond, *Angew. Chem.* **2010**, *122*, 9318; *Angew. Chem. Int. Ed.* **2010**, *49*, 9132; f) L.-P. Liu, G. B. Hammond, *Chem. Asian J.* **2009**, *4*, 1230; g) L.-P. Liu, G. B. Hammond, *Org. Lett.* **2009**, *11*, 5090; h) L.-P. Liu, B. Xu, M. S. Mashuta, G. B. Hammond, *J. Am. Chem. Soc.* **2008**, *130*, 17642.

[19] L.-P. Liu, G. B. Hammond, *Org. Lett.* **2010**, *12*, 4640.

[20] P. Magnus, N. Sane, B. P. Fauber, V. Lynch, *J. Am. Chem. Soc.* **2009**, *131*, 16045.

[21] Y. Shishido, H. Wakabayashi, H. Koike, N. Ueno, S. Nukui, T. Yamagishi, Y. Murata, F. Naganeo, M. Mitzutani, K. Shimada, Y. Fujiwara, A. Sakakibara, O. Suga, R. Kusano, S. Ueda, Y. Kanai, M. Tsuchiya, K. Satake, *Bio. Med. Chem.* **2008**, *16*, 7193.

[22] T. Hayashi, F. T. Smith, K.-H. Lee, *J. Med. Chem.* **1987**, *30*, 2005.

[23] M. E. Lieberman, J. Gorski, V. C. Jordan, *J. Biol. Chem.* **1983**, *258*, 4741.

[24] a) M. K. Yusupov, D. A. Abdullaeva, K. A. Aslanov, A. S. Sadykov, *Chem. Nat. Compd.* **1975**, *11*, 395; b) M. K. Yusupov, B. Chommadov, *Chem. Nat. Compd.* **1995**, *31*, 87.

[25] a) E. M. Perchellet, Y. Wang, R. L. Weber, K. Lou, D. H. Hua, J.-P. H. Perchellet, *Anticancer Drugs* **2004**, *15*, 929; b) B. Wang, E. M. Perchellet, Y. Wang, M. Tamura, D. H. Hua, J. P. Perchellet, *Anticancer Drugs* **2003**, *14*, 503.

[26] a) Y. Liu, S. Ma, *Org. Lett.* **2012**, *14*, 720; b) K. Morimoto, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2011**, *76*, 9548; c) D. Lu, Y. Zhou, Y. Li, S. Yan, Y. Gong, *J. Org. Chem.* **2011**, *76*, 8869; d) M.-B. Zhou, W.-T. Wei, Y.-X. Xie, Y. Lei, J.-H. Li, *J. Org. Chem.* **2010**, *75*, 5635; e) R. Mancuso, S. Mehta, B. Gabriele, G. Salerno, W. S. Jenks, R. C. Larock, *J. Org. Chem.* **2010**, *75*, 897; f) S. V. Ley, D. M. Mynett, W.-J. Koot, *Synlett* **1995**, 1017; g) H. Yang, R. G. Carter, *Tetrahedron* **2010**, *66*, 4854; h) F. Foubelo, B. Moreno, M. Yus, *Tetrahedron* **2004**, *60*, 4655; i) K. V. Auwers, K. J. Möller, *J. Prakt. Chem.* **1925**, *109*, 124.

[27] a) V. López-Carrillo, A. M. Echavarren, *J. Am. Chem. Soc.* **2010**, *132*, 9292; b) E. Jiménez-Núñez, C. K. Claverie, C. Bour, D. J. Cárdenas, A. M. Echavarren, *Angew. Chem.* **2008**, *120*, 8010; *Angew. Chem. Int. Ed.* **2008**, *47*, 7892; c) C. Nieto-Oberhuber, P. Pérez. -Galán, E. Herrero. -Gómez, T. Lauterbach, C. Rodríguez, S. López, C. Bour, A. Rosellón, D. J. Cárdenas, A. M. Echavarren, *J. Am. Chem. Soc.* **2008**, *130*, 269; d) M. P. Muñoz, J. Adrio, J. C. Carretero, A. M. Echavarren, *Organometallics* **2005**, *24*, 1293.

[28] a) R. Eliason, M. M. Kreevoy, *J. Phys. Chem.* **1974**, *78*, 2658; b) M. M. Kreevoy, R. Eliason, *J. Phys. Chem.* **1968**, *72*, 1313.

[29] A. S. K. Hashmi, *Angew. Chem.* **2010**, *122*, 5360; *Angew. Chem. Int. Ed.* **2010**, *49*, 5232.

[30] a) F. J. Fañanás, A. Mendoza, T. Arto, B. Temelli, F. Rodríguez, *Angew. Chem.* **2012**, *124*, 5014; *Angew. Chem. Int. Ed.* **2012**, *51*, 4930. This report was published during the course of our investigations; in this report the authors treated akynyl benzaldehyde with an alkynediolto give a spirocycle (i.e., the core structure of Berkelic acid); b) Mechanistically, there is a possibility that phenolic OH can react with the acetal to yield final product **5 f**.

[31] a) Z.-L. Hu, W.-J. Qian, S. Wang, S.-Z. Wang, Z.-J. Yao, *Org. Lett.* **2009**, *11*, 4676; b) Z.-L. Hu, W.-J. Qian, S. Wang, S. Wang, Z.-J. Yao, *J. Org. Chem.* **2009**, *74*, 8787; c) Y.-C. Hsu, C.-M. Ting, R.-S. Liu, *J. Am. Chem. Soc.* **2009**, *131*, 2090; d) C. H. Oh, J. H. Lee, S. J. Lee, J. I. Kim, C. S. Hong, *Angew. Chem.* **2008**, *120*, 7615; *Angew. Chem. Int. Ed.* **2008**, *47*, 7505; e) S. Bhunia, K.-C. Wang, R.-S. Liu, *Angew. Chem.* **2008**, *120*, 5141; *Angew. Chem. Int. Ed.* **2008**, *47*, 5063; f) D. Yue, N. D. Cá, R. C. Larock, *J. Org. Chem.* **2006**, *71*, 3381; g) D. Yue, N. D. Cá, R. C. Larock, *Org. Lett.* **2004**, *6*, 1581; h) J. Barluenga, H. Vázquez-Villa, A. Ballesteros, J. M. González, *J. Am. Chem. Soc.* **2003**, *125*, 9028; i) N. Iwasawa, M. Shido, H. Kusama, *J. Am. Chem. Soc.* **2001**, *123*, 5814.

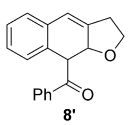
[32] a) N. Asao, Menggenbateer, Y. Seya, Y. Yamamoto, M. Chen, W. Zhang, A. Inoue, *Synlett* **2012**, 66; b) H. Aikawa, S. Tago, K. Umetsu, N. Haginiwa, N. Asao, *Tetrahedron* **2009**, *65*, 1774; c) K. Sato, Menggenbateer, N. Asao, *Tetrahedron* **2008**, *64*, 787; d) N. Asao, H. Aikawa, *J. Org. Chem.* **2006**, *71*, 5249; e) N. Asao, K. Sato, *Org. Lett.* **2006**, *8*, 5361.

[33] Under acidic conditions, ethyl vinyl ether is sensitive and could serve as source of ethanol along with intermediate **E**.

[34] P. Pérez-Galán, N. Delpont, E. Herrero-Gómez, F. Maseras, A. M. Echavarren, *Chem. Eur. J.* **2010**, *16*, 5324.

[35] A. S. K. Hashmi, M. C. Blanco, *Eur. J. Org. Chem.* **2006**, 4340. This report indicates that the twofold addition to alkynes in gold catalysis is often difficult.

[36] Compound **8** is difficult to isolate because of its non-aromatic structure. However, we were able to isolate compound **8′** as minor product, which in theory could have been generated from **8** through aromatization. This result further supports the proposed Diels–Alder mechanism.



8′

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