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Au^{I}-Catalyzed Tandem [3,3] Rearrangement–Intramolecular Hydroarylation: Mild and Efficient Formation of Substituted Indenes[**]

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Recent reports have highlighted the use of gold(I) and gold(III) complexes as efficient homogeneous catalysts in several organic transformations.[1] Notably, gold catalysts, in both oxidation states, enable the cycloisomerization of enynes.[2] Based on these earlier studies, we reasoned that the electron-rich phenyl ring could replace an alkene moiety and lead to

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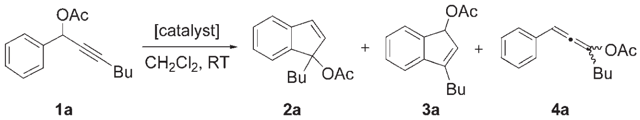
valuable cyclized products. Surprisingly, the only related examples of intramolecular hydroarylation employ a heteroatom-containing tether to provide indoles, benzofurans, or coumarins.[3] Carbocycles, especially indenes, are compounds of great interest as synthetic targets and building blocks for pharmaceutical[4] and materials chemistry.[5] As the inter- or intramolecular formation of indenes usually requires high temperature and/or a prolonged reaction time,[6] a mild and efficient assembly protocol would be highly desirable.

Keeping in mind that propargylic acetates, in the presence of cationic gold complexes, undergo 1,2-migration of the acetate group and subsequent formation of carbenoid species,[7] we first examined the reactivity of **1a** with an equimolar amount of [(IPr)AuCl] (IPr = *N*,*N*′-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) and AgBF$_4$. After five minutes at room temperature, the reaction with **1a** cleanly yielded indene **2a** (Table 1, entry 1). Interestingly, although the formation of indenes from aryl propargyl acetates such as **1a** has two precedents in the literature, both leading to products of type **5**,[8] the structure of **2a** is unexpected (see Scheme 3). Reaction of **1a** with AgBF$_4$ (Table 1, entry 3) resulted in the formation of allene **4a**, which showed only minor decomposition and no formation of cyclized product upon prolonged stirring.[9] [(IPr)AuCl] alone was found to be inactive toward alkyne **1a** (Table 1, entry 2).

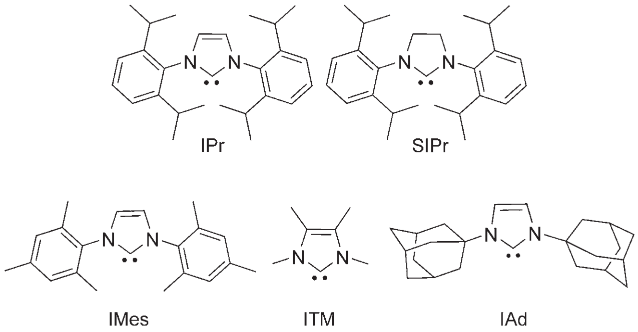
Table 1: Catalyst optimization.[a]



Entry	Catalyst (2 mol%)	*t*	**2a** [%][b]	**3a** [%][b]	**4a** [%][b]
1	[(IPr)AuCl]/AgBF$_4$	5 min	92	–	–
2	[(IPr)AuCl]	overnight	no reaction		
3	AgBF$_4$	30 min	–	–	87
4	[(IPr)AuCl]/AgPF$_6$	5 min	90	–	–
5	[(IPr)AuCl]/AgSbF$_6$	5 min	73	–	–
6	[(SIPr)AuCl]/AgBF$_4$	5 min	88	5	–
7	[(IMes)AuCl]/AgBF$_4$	5 min	76	3	–
8	[(ITM)AuCl]/AgBF$_4$	5 min	54	23	11
9	[(IAd)AuCl]/AgBF$_4$	15 min	89	–	–
10	[(PPh$_3$)AuCl]/AgBF$_4$	5 min	51	32	8
11	AuCl	30 min	unidentified mixture		
12	AuCl/AgBF$_4$	5 min	unidentified mixture		
13	PtCl$_2$	overnight	–	–	53

[a] Reaction conditions: alkyne **1a** (0.5 mmol), catalyst (2 mol%), CH$_2$Cl$_2$ (20 mL). [b] NMR spectroscopic yields with respect to 1,2-dichloroethane.

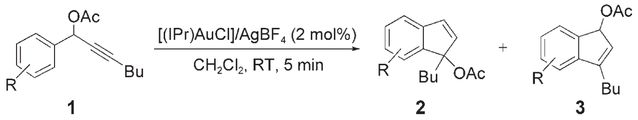
To gauge the influence of the ligand in this transformation, we carried out reactions with various [(NHC)AuCl] complexes[10] (NHC = N-heterocyclic carbene, Scheme 1) and silver tetrafluoroborate. Sterically demanding NHCs led to sluggish reactions (Table 1, entry 9) while less encumbered NHCs,[11] as well as PPh$_3$, led to poor selectivity (Table 1, entries 8 and 10).[12] Further optimization revealed that tetrafluoroborate or hexafluorophosphate were both suitable counterions (Table 1, entries 1 and 4), whereas hexafluoroantimonate produced a significant amount of oligomerization (Table 1, entry 5). It is noteworthy that AuCl alone or in conjunction with AgBF$_4$ did not lead to **2a** (Table 1, entries 11 and 12). Furthermore, PtCl$_2$, which has been reported recently to catalyze a closely related reaction,[8b] did not lead to **2a** under our conditions (Table 1, entry 13).

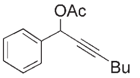
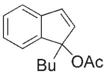
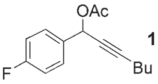
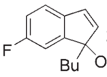
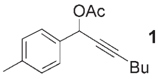
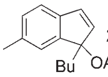
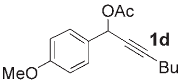
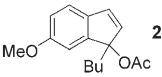
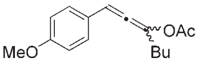
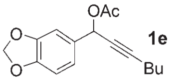
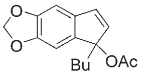
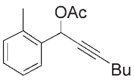
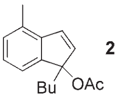
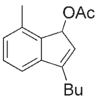
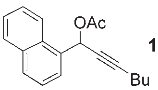
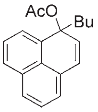
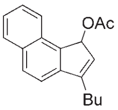
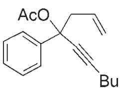
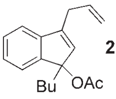
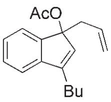


Scheme 1. Structures of NHC ligands.

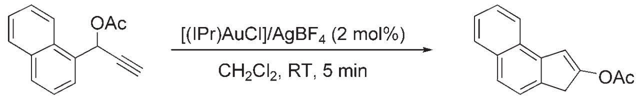
The scope of the reaction was investigated with a variety of reactants **1**, and the results are presented in Table 2. The formation of indenes **2** was found to be compatible with electron-poor or electron-rich arenes **1b–d**. Benzodioxole **1e** reacted regioselectively to give **2e** in excellent yield. *Ortho*-substituted arenes **1f** and **1g** gave **2f** and **2g**′ and led to the formation of indenes of type **3** as minor products. Interest-

Table 2: Gold(I)-catalyzed formation of indenes from propargylic acetates.



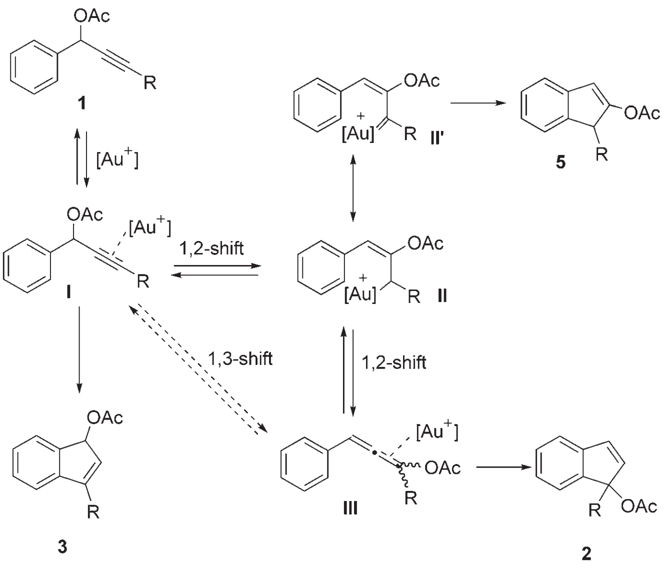
1		Major product	Minor product
	**1a**	 **2a** (92%)	
	**1b**	 **2b** (81%)	
	**1c**	 **2c** (78%)	
	**1d**	 **2d** (63%)	 **4d** (13%)
	**1e**	 **2e** (90%)	
	**1f**	 **2f** (88%)	 **3f** (9%)
	**1g**	 **2g′** (78%)	 **3g** (11%)
	**1h**	 **2h** (67%)	 **3h** (18%)

ingly, the naphthalene **1g** produced the phenalene **2g**′ regioselectively.[13] To further explore the generality of this transformation, we carried out the reaction using **1h**, which cleanly produced indenes **2h** and **3h**.[14] Strikingly, no trace of bicyclo[3.1.0] compounds was observed,[2a,h] thus highlighting the chemoselectivity of the reaction. Furthermore, the latter reaction shows that tertiary acetates are also suitable substrates in this transformation. Finally, varying the substituent at the acetylenic position with a phenyl group in place of the butyl group resulted in oligomerization of the starting material. On the other hand, with a proton at the acetylenic position, the formation of **5i** was observed, resulting primarily from a 1,2-migration of the propargylic acetate group in **1i** (Scheme 2). In this latter case, the reactivity of the aryl propargyl acetate is similar to that observed in transformations reported by the research groups of Uemura and Sarpong with ruthenium and platinum catalysts, respectively.[8] Therefore, it appears that the behavior of the $[(\mathrm{IPr})\mathrm{Au}]^+$ catalyst and, subsequently, the outcome of the reaction are highly dependent on the substitution pattern at the acetylenic position. The apparent 1,3-migration of the acetate moiety in products of type **2** and the observation of allene **4d** led us to propose the mechanism depicted in Scheme 3. π Complexation of the in situ generated cationic gold complex to the C≡C bond and subsequent direct nucleophilic attack by the electron-rich phenyl ring would lead to products of type **3**.[15,16] On the other hand, electrophilic activation of the alkyne could trigger two successive 1,2-migrations (or a single 1,3-migration) of the acetate group[17] to produce allene **III**, which would be further activated by the $[\mathrm{Au}^+]$ fragment for hydroarylation,[18,19] thus leading to products of type **2**.[20] To gain insight into the mechanism, we synthesized allenes **4a**,**c**,**d** by treating **1a**,**c**,**d** with $AgSbF_6$ and subjected the allenes to cyclization conditions. We observed the formation of the corresponding indenes **2a**,**c**,**d** after 15 minutes (Table 3).



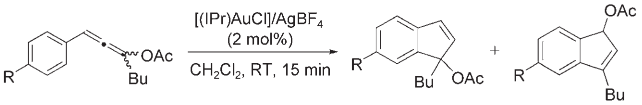
1i **5i** (77% yield)

Scheme 2. An example of gold(I)-catalyzed formation of an indene from a terminal alkyne.

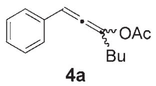
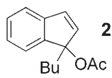
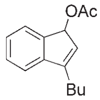
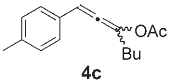
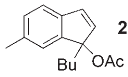
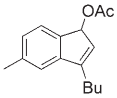
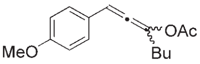
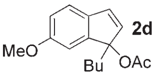
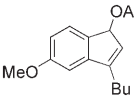


Scheme 3. Proposed mechanism.

Table 3: Gold(I)-catalyzed formation of indenes from aryl allenes.



4 **2** **3**

4	2	3
 **4a**	 **2a** (78%)	 **3a** (16%)
 **4c**	 **2c** (65%)	 **3c** (24%)
 **4d**	 **2d** (62%)	 **3d** (14%)

Unexpectedly, the reaction times were slightly longer than with the propargylic acetates. This could be a consequence of a higher "alkynophilicity" than "allenophilicity" of the $[(\mathrm{IPr})\mathrm{Au}]^+$ fragment, a difference which is not observed starting from **1** as a result of the mandatory proximity of the gold center to the newly formed allene moiety.[21] Finally, the minor formation of **3a**,**c**,**d**, products of the direct hydroarylation of the alkyne, emphasizes the reversibility of the gold(I)-catalyzed [3,3] rearrangement and the advantage of using alkynes in this reaction for a higher selectivity.

In summary, we have described a novel type of metal-mediated formation of indenes from aryl propargyl acetates. This chemoselective transformation proceeds under extremely mild reaction conditions. Studies aimed at exploring mechanistic aspects of this transformation and developing further uses of [(IPr)AuCl][22] are ongoing.

Experimental Section

General Procedure: $AgBF_4$ (2 mg, 0.02 mmol) was added in the absence of light to a solution of [(IPr)AuCl] (12.4 mg, 0.02 mmol) in anhydrous CH_2Cl_2 (35 mL) in a round-bottom flask equipped with a septum. The solution instantly became cloudy. A solution of propargylic acetate **1** (1 mmol) in anhydrous CH_2Cl_2 (5 mL) was then injected through the septum. When TLC analysis showed total consumption of the starting material, the solvent was removed under vacuum. The resulting mixture was dissolved in pentane, filtered through celite, and evaporated. The crude oil was purified by flash chromatography on silica gel.

2a: The above general procedure employing **1a** (230 mg) yielded **2a** after flash chromatography on silica gel (pentane/methyl *tert*-butyl ether, 95:5). Yield: 212 mg, 92 %; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 7.35 (d, $J = 7.2$ Hz, 1H, ArH), 7.24–7.14 (m, 2H, ArH), 7.21–7.18 (m, 1H, ArH), 6.70 (d, $J = 5.7$ Hz, 1H, $C_{Ar}CH{=}CH$), 6.56 (d, $J = 5.7$ Hz, 1H, $C_{Ar}CH{=}CH$), 2.22 (dt, $J = 12.6$, 4.5 Hz, 1H, CCH_2CH_2), 1.99 (s, 3 H, OAc), 1.93 (dt, $J = 12.6$, 4.5 Hz, 1 H, CCH_2CH_2), 1.32–1.19 (m, 4 H, $CH_2CH_2CH_3$), 0.83 ppm (t, $J = 7.5$ Hz, 3 H, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.0$ (C=O), 145.8 (C_{Ar}), 142.4 (C_{Ar}), 137.9 ($C_{Ar}H$), 132.4 ($C_{Ar}CH{=}CH$), 128.7 ($C_{Ar}H$), 126.2 ($C_{Ar}CH{=}CH$), 122.2 ($C_{Ar}H$), 121.7 ($C_{Ar}H$), 91.0 (COAc), 35.7 (CCH_2CH_2), 26.4 ($CH_2CH_2CH_3$), 23.1 (CH_2CH_3), 21.9 (CH_3, OAc), 14.0 ppm (CH_2CH_3). Elemental analysis (%) calcd for $C_{15}H_{18}O_2$ (M_r 230.30): C 78.23, H 7.88; found: C 78.15, H 7.94.

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Keywords: alkynes · allenes · gold · hydroarylation · indenes

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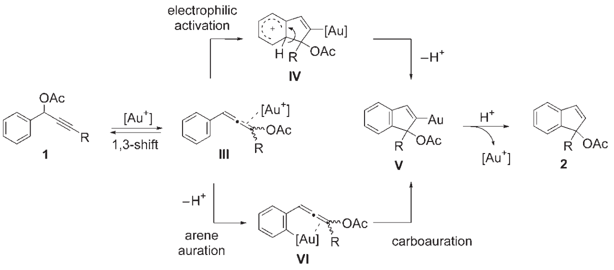
[20] Cyclization occuring through C–H activation and arene auration cannot at this time be ruled out (see scheme below); for examples of arene gold(III) complexes involved in catalytic transformations, see: Z. Shi, C. He, *J. Am. Chem. Soc.* **2004**, *126*, 13596–13597.



[21] An alternate explanation would imply that the reaction might not go through a discrete allene intermediate; hence, a concerted mechanism would be worth consideration.

[22] For an example of diazoacetate transfer catalyzed by [(IPr)AuCl], see: M. R. Fructos, T. R. Belderrain, P. de Frémont, N. M. Scott, S. P. Nolan, M. M. Díaz-Requejo, P. J. Pérez, *Angew. Chem.* **2005**, *117*, 5418–5422; *Angew. Chem. Int. Ed.* **2005**, *44*, 5284–5288.