Gold(I)-Catalyzed Synthesis of Dihydrobenzofurans from Aryl Allyl Ethers

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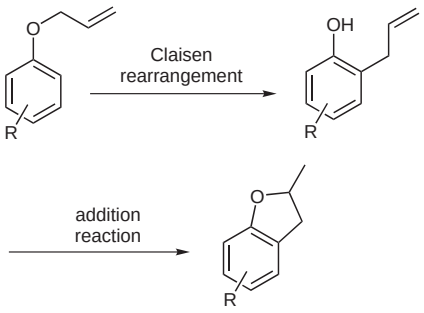
Abstract: Formation of dihydrobenzofurans from aryl allyl ethers was catalyzed by in situ generated PPh_3AuOTf. This reaction appears to proceed by a Claisen rearrangement, followed by addition of the resulting phenol to the allyl group.

Key words: homogeneous catalysis, gold, cyclization, alkenes, Claisen rearrangement

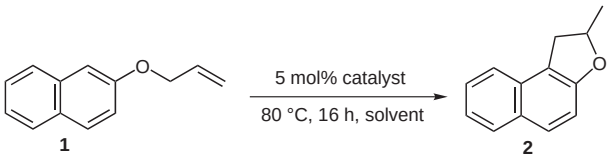
The Claisen rearrangement represents one of the oldest and most effective carbon–carbon bond formation methods.[2] Though traditionally this reaction is conducted thermally at high temperatures, a large number of catalytic systems have been developed for both the aryl and aliphatic variants of the reaction.[2,3] In addition to carbon–carbon bond formation, the product of the aryl Claisen rearrangement is well suited to undergo ring closure via an intramolecular addition reaction to give a dihydrobenzofuran (Scheme 1). As part of our continued interest in cationic gold species as effective Lewis acid catalysts, we sought to catalyze the synthesis of dihydrobenzofurans from allyl aryl ethers in a one-pot process.[4] We describe here our success in mediating this tandem process utilizing PPh_3AuOTf, generated in situ, and report our studies on the mechanism of this reaction.



Scheme 1

Our initial survey of reaction conditions focused upon $AuCl_3$/AgOTf as the catalyst, a system we have successfully applied in the past.[5] Indeed, $AuCl_3$/3AgOTf (5 mol% based on gold) was capable of catalyzing the transformation of compound **1** to **2** at 80 °C in a number of solvents (Table 1). While the reaction proceeded at as low as room temperature, the reaction was too sluggish to be of practical use, thus requiring higher temperatures (80 °C) for completion. Unfortunately, good yields were only obtained with the use of carbon tetrachloride as solvent (Table 1). Based on our recent success in employing PPh_3AuOTf to activate olefins for addition of weak nucleophiles,[6] we tested the catalyst in this system as well. PPh_3AuOTf proved to be the ideal catalyst for conducting this reaction, which when employed in toluene (Table 1) gave an excellent yield of **2**. We found that silver(I) triflate alone as well as triflic acid were capable of catalyzing the same reaction, but at significantly lower yields. Without the phosphine ligand, gold(I) chloride with silver(I) triflate was still able to catalyze the reaction, but with a far lower efficiency.

Table 1 Survey of Catalysts



Catalyst	Solvent	Yield (%)[a]
$AuCl_3$/3AgOTf	Benzene	69
$AuCl_3$/3AgOTf	Toluene	(45)
$AuCl_3$/3AgOTf	CCl_4	(73)
PPh_3AuCl/AgOTf	Toluene	>95 (82)
AuCl/AgOTf	Toluene	65
AgOTf	Toluene	57
HOTf	Toluene	66 (53)

[a] Yield based on ^1H NMR, using an internal standard. Yields in parentheses represent isolated yields.

Having identified our best catalyst system, we applied these conditions to a number of aryl allyl ethers in order to investigate the scope of the reaction (Table 2). For less activated systems than compound **1**, it was found that slightly longer reaction times were required to afford complete conversion. The presence of electron-donating groups on the aromatic ring proved to increase the reaction yield. Furthermore, the best yields were achieved with donating groups *para* to the allyl group, though *meta* electron-donating groups could also be beneficial to the reaction. In addition, the reaction was also tolerant of

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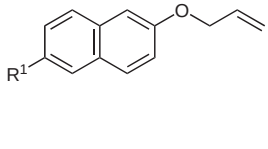
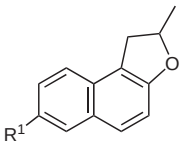
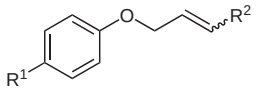
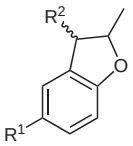
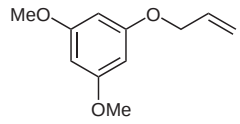
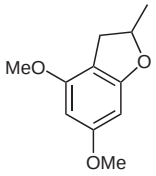
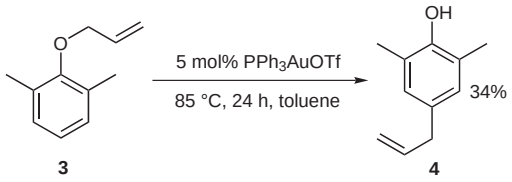
Table 2 Synthesis of Dihydrobenzofurans[a]

Entry	Substrate	Product	Yield (%)[b]
			
1	R^1 = H		82
2	R^1 = Br		81
			
3	R^1 = H, R^2 = H		60[c]
4	R^1 = OMe, R^2 = H		69
5	R^1 = *t*-Bu, R^2 = H		68
6	R^1 = OMe, R^2 = Me		62
7			55

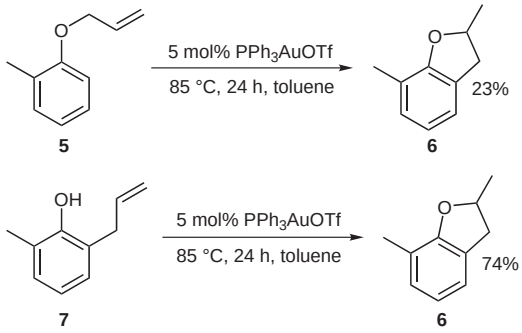
[a] All reactions were run in toluene at 85 °C catalyzed by 5 mol% $PPh_3AuCl/AgOTf$.
[b] All yields are isolated, unless specified otherwise.
[c] Yield based on ^1H NMR using an internal standard.

electron-withdrawing groups on the naphthyl ring as seen in entry 2, Table 2.

We next explored the mechanism of this transformation. As part of demonstrating that the first step of the reaction proceeded through a Claisen rearrangement, we synthesized the 2,6-substituted aryl allyl ether **3**. This compound was subjected to our standard reaction conditions to afford **4** in a 34% yield, in addition to recovery of most of the remaining starting material (Scheme 2). Unable to undergo a tandem rearrangement and cyclization due to the presence of two *ortho* substituents, this substrate instead underwent a [3,3] rearrangement to afford compound **4**, indicating that cationic gold(I) is capable of mediating the rearrangement. We next conducted the reactions shown in Scheme 3 in order to confirm the mechanism shown in Scheme 1 for the one-pot reaction. Compound **5** underwent the tandem reaction to give **6** in a low yield (24%) at 85 °C after 24 hours. If the reaction was run for 12 hours, an intermediate **7** could be isolated and confirmed by NMR. Compound **7** can subsequently be converted to **6** with the same catalyst at much higher efficiency in comparison to the reaction starting from **5**. These results support the proposed two-step mechanism we proposed.

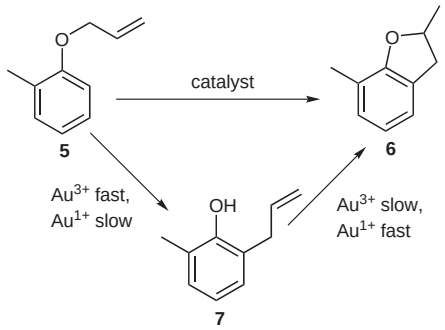


Scheme 2



Scheme 3

Finally, we attempted to compare the rates of the two steps in the tandem reaction process (Scheme 4). Complete conversion of compound **7** to product **6** was found to occur after 10 hours, while the reaction of substrate **5** to compound **6** proceeded to only about 50% conversion after even 24 hours, signifying that the Claisen rearrangement is the slow step in the process. Interestingly, gold(III) was able to catalyze the Claisen rearrangement of compound **1** at 0 °C, without undergoing the second addition step to yield **2**. Gold(I), at such a low temperature, could not mediate the rearrangement step, indicating the difference between the two oxidation states of gold. This difference may be attributed to the increased oxophilicity of gold(III) as compared to gold(I).[7] Presumably, gold(III) binds to the phenol oxygen to speed up the rearrangement step. This observation appears to be general for the reactions we tested.



Scheme 4

In conclusion, we have described a one-pot synthesis of dihydrobenzofurans from aryl allyl ethers by using a gold(I) catalyst, further demonstrating the utility of gold as an effective Lewis acid catalyst.[8,9] We have probed the mechanism of this reaction and revealed that the reaction proceeds by a Claisen rearrangement followed by an intramolecular addition of the resulting phenol to the allyl group.

Representative Procedure for Synthesis of Aryl Allyl Ethers

2-Naphthol (1.44 g, 10 mmol) and allylbromide (1.33 g, 11 mmol) were mixed in 50 mL of acetone and refluxed for 3 h in the presence of K_2CO_3 (5.53 g, 40 mmol). The reaction mixture was filtered and the solvent removed under vacuum. The crude product was purified by using flash column chromatography with 10:1 hexanes–Et_2O as eluent. This yielded 1.74 g (95% yield) of pure 2-(allyloxy)naphthalene (**1**) as a yellow oil.

Representative Procedure for Synthesis of Dihydrobenzofurans

2-(Allyloxy)naphthalene (263 mg, 1 mmol), chlorotriphenylphosphinegold(I) (24.7 mg, 0.05 mmol) and silver(I) triflate (12.8 mg, 0.05 mmol) were mixed in 3 mL of dry toluene in a sealed reaction tube and wrapped with aluminum foil. The mixture was then heated at 85 °C with stirring for 24 h. After removal of the solvent the crude product was purified by using flash column chromatography with 20:1 hexanes–Et_2O as eluent. This yielded 215 mg (82% yield) of pure 1,2-dihydro-2-methylnaphtho[2,1-*b*]furan (**2**) as a yellow oil.

Spectral Data for Selected Compounds

7-Bromo-1,2-dihydro-2-methylnaphtho[2,1-*b*]furan (Table 2, Entry 2)

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.53 (d, 3 H, *J* = 6.3 Hz, CH_3), 3.01 (dd, 1 H, *J* = 7.46, 7.75 Hz, CH_2), 3.53 (dd, 1 H, *J* = 9.24, 5.94 Hz, CH_2), 5.11 (m, 1 H, CH), 7.07 (d, 1 H, *J* = 8.76, ArH), 7.37 (d, 1 H, *J* = 8.76, ArH), 7.47 (dd, 1 H, *J* = 1.96, 6.82 Hz, ArH), 7.52 (d, 1 H, *J* = 8.71 Hz, ArH), 7.90 (d, 1 H, *J* = 1.91 Hz, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.2, 35.9, 80.5, 113.3, 116.2, 118.8, 124.5, 128.2, 129.5, 129.9, 130.3, 130.7, 157.4. HRMS: *m/z* calcd for $C_{13}H_{11}OBr$: 261.9993; found: 261.9988.

5-*tert*-Butyl-2,3-dihydro-2-methylbenzofuran (Table 2, Entry 5)

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.29 (s, 10 H, *t*-Bu), 1.46 (d, 3 H, *J* = 6.31 Hz, CH_3), 2.80 (dd, 1 H, *J* = 7.87, 7.42 Hz, CH_2), 3.29 (dd, 1 H, *J* = 8.74, 6.55 Hz, CH_2), 4.90 (m, 1 H, CH), 6.67 (d, 1 H, *J* = 8.36 Hz, ArH), 7.12 (d, 1 H, *J* = 8.41 Hz, ArH), 7.26 (s, 1 H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.2, 31.9, 34.4, 37.5, 79.8, 108.6, 122.1, 124.80, 126.8, 143.3, 157.4. HRMS: *m/z* calcd for $C_{13}H_{18}O$: 190.1358; found: 190.1379.

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References and Notes

(1) Present address: College of Chemistry, Peking University, Beijing 100871, P. R. of China.
(2) For a recent review: Castro, A. M. M. *Chem. Rev*. **2004**, *104*, 2939.
(3) Hiersemann, M.; Abraham, L. *Eur. J. Org. Chem.* **2002**, 1461.
(4) (a) Kim, K. M.; Kim, H. R.; Ryu, E. K. *Heterocycles* **1993**, *36*, 497. (b) Grant, V. H.; Liu, B. *Tetrahedron Lett.* **2005**, *46*, 1237. (c) Zulfiqar, F.; Kitazume, T. *Green Chem.* **2000**, *2*, 296. (d) Bernard, A. M.; Cocco, M. T.; Onnis, V.; Piras, P. P. *Synthesis* **1997**, 41.
(5) (a) Shi, Z.; He, C. *J. Am. Chem. Soc*. **2004**, *126*, 5964. (b) Shi, Z.; He, C. *J. Org. Chem.* **2004**, *69*, 3669. (c) Shi, Z.; He, C. *J. Am. Chem. Soc.* **2004**, *126*, 13596.
(6) Yang, C.-G.; He, C. *J. Am. Chem. Soc.* **2005**, *127*, 6966.
(7) Sromek, A. K.; Rubina, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2005**, *127*, 10500.
(8) Recent reviews: (a) Hashmi, A. S. K. *Angew. Chem. Int. Ed.* **2005**, *44*, 6990. (b) Hoffmann-Röder, A.; Krause, N. *Org. Biomol. Chem.* **2005**, *3*, 387. (c) Arcadi, A.; Di Giuseppe, S. *Curr. Org. Chem.* **2004**, *8*, 795. (d) De Vos, D. E.; Sels, B. F. *Angew. Chem. Int. Ed.* **2005**, *44*, 30.
(9) Selected recent examples: (a) Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 15978. (b) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 6962. (c) Yao, Y.; Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 11164. (d) Nieto-Oberhuber, C.; Paz Muñoz, M.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 2402. (e) Mamane, V.; Gress, T.; Krause, H.; Fürstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654.