Temperature-Controlled Selectivity toward [1,3]- or [3,3]-Sigmatropic Rearrangement: Regioselective Synthesis of Substituted 3,4-Dihydrocoumarins

Yunkui Liu,* Jianqiang Qian, Shaojie Lou, Zhenyuan Xu*

State Key Laboratory Breeding Base of Green Chemistry-Synthesis Technology, Zhejiang University of Technology, Hangzhou 310014, P. R. of China
E-mail: ykuiliu@zjut.edu; E-mail: greensyn@zjut.edu.cn

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Abstract: Either [1,3]- or [3,3]-sigmatropic rearrangements were selectively accessed by controlling the reaction temperature in the gold(III)-catalyzed tandem rearrangement/cyclization of (*E*)-2-(aryloxymethyl)alk-2-enoates to afford diversely substituted 3,4-dihydrocoumarin derivatives in moderate to good yields and in excellent regioselectivity.

Key words: [1,3]-sigmatropic rearrangement, [3,3]-sigmatropic rearrangement, gold catalyst, tandem reaction, 3,4-dihydrocoumarin

After being neglected in catalysis field for a long time, gold catalysis has become a hot topic in chemistry over the past few years as witnessed by a focus of attention on gold-catalyzed organic transformations recently.[1] Among various gold-catalyzed reactions, those involving sigmatropic skeletal rearrangements have received much attention and served as powerful and highly selective tools to generate molecular diversity and structural complexity.[2–5] The Claisen rearrangement[6] is a 97-year-old reaction, yet it still plays a very important role in modern organic synthesis.[7] Normally, the reaction proceeds via a [3,3]-sigmatropic rearrangement process to afford products with high chemo-, regio- and stereoselectivity. In some cases, however, the reaction may be concomitant with other patterns of rearrangement deviating from the normal [3,3]-sigmatropic rearrangement (e.g. [1,3]-, [2,3]-, [3,5]-rearrangements), often leading to reduced selectivities.[8] On the other hand, we believe that such rearrangements should also be useful tools for organic synthesis provided that selectivity could be well controlled by proper optimization of catalysts, solvents and temperatures. Unfortunately, so far, such efforts have been still limited.[9] As part of our ongoing interest in the application of Baylis–Hillman adducts[10,11] in organic synthesis and gold-catalyzed skeletal rearrangements,[11e] we herein report the first example of gold(III)-catalyzed regiospecific [1,3]-sigmatropic rearrangement[9a–9e] of aryl allyl ethers **1**[12,3j] derived from Baylis–Hillman adducts (Tables 1 and 2). Furthermore, our studies disclose that [1,3]- or [3,3]-sigmatropic rearrangement of **1** could be selectively accessed by controlling the reaction temperature, leading to regioselective synthesis of 3,4-dihydrocoumarin (3,4-DHC) derivatives with diverse substituted patterns in moderate to good yields via a tandem rearrangement/cyclization strategy.

Initially, we selected (*E*)-methyl 3-(4-chlorophenyl)-2-(2-naphthyloxymethyl)-2-enoate (**1a**) as a model substrate for the tandem rearrangement/cyclization reaction and expected the formation of **3a** (Scheme 1, Table 1). The reaction indeed proceeded when **1a** was treated with Ph_3PAuCl–AgOTf (3 mol% based on **1a**) in DCE at 80 °C for eight hours. However, 3-arylidene-3,4-DHC **2a**, apparently generated via a [1,3]-sigmatropic rearrangement/cyclization process (see intermediate **A**), was unexpectedly isolated as the sole product in 16% yield (entry 1). The yield of **2a** was increased to 87% in the presence of AuCl–AgOTf at the same temperature for five hours (entry 2). The best result (up to 96% yield of **2a**) was obtained when a combination of $AuCl_3$ and AgOTf was used in DCE or DCB (1,2-dichlorobenzene) at 80 °C for four hours (entry 3). Interestingly, when the same reaction was conducted at 120 °C for two hours, 4-aryl-3-methylene-3,4-DHC **3a**, arising from normal Claisen rearrangement/cyclization process (see intermediate **B**),[3j] was exclusively obtained in 93% yield (entry 3). It was found that solvent had fundamental influence on the activity and the selectivity of the catalytic system (entry 3). DCE and DCB were equally suitable solvent for the tandem reaction, but DCB was preferred to be used at 120 °C because its higher boiling point allowed the operation to be more easily handled. Shifting solvent to toluene, MeCN, THF or 1,4-dioxane led to a decrease in the yield of products and/or the regioselectivity of the reaction. The reaction could hardly take place without a catalyst (entry 16), or in the presence of AuCl, Ph_3PAuCl, $AuCl_3$ or AgOTf alone at both 80 °C and 120 °C (entries 4–7), indicating that cationic gold(III) or gold(I) species were essential for the reaction due to their more electrophilic properties.[13,14] Catalyst screening experiments revealed that the tandem rearrangement/cyclization of **1a** in the presence of other conventional Lewis and Brønsted acids as catalyst was less effective (entries 8–15).

With optimized reaction conditions in hand, a study of the scope of this temperature-controlled regioselective transformation of **1** into 3,4-DHCs with diverse substituted patterns (**2** vs. **3**) was then undertaken (Scheme 2, Table 2).[15,16] Under conditions A (3 mol% $AuCl_3$ plus 9 mol% AgOTf, DCE, 80 °C), a variety of **1** could be

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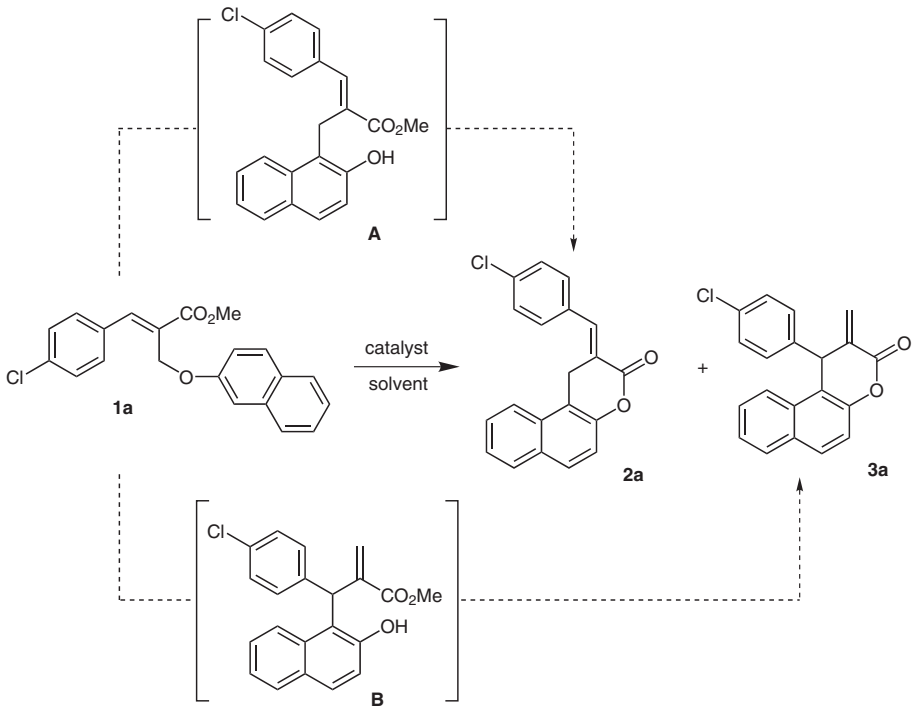
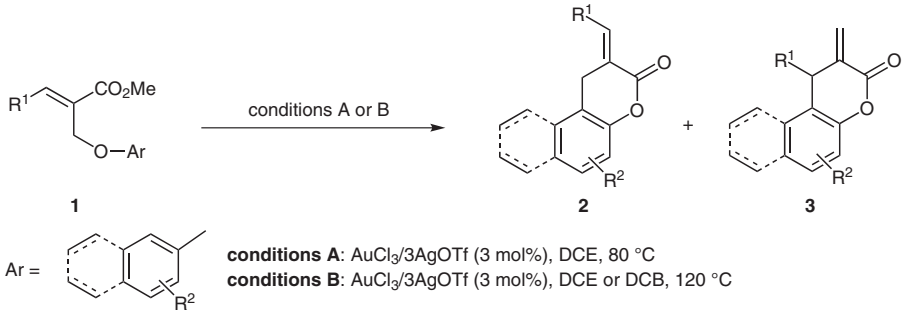
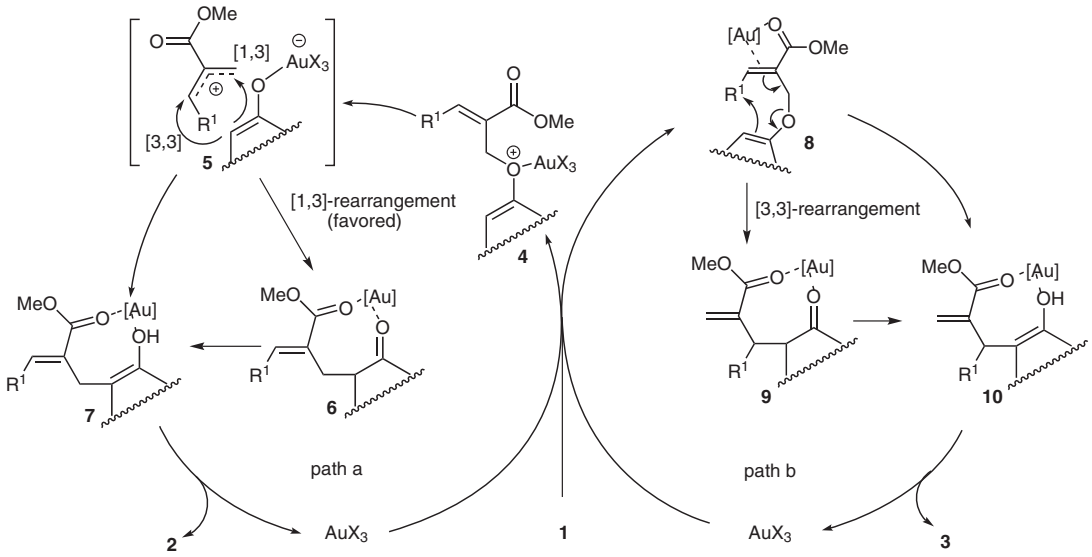


Scheme 1



Scheme 2



Scheme 3 Possible mechanism for the selective formation of **2** or **3**

regiospecifically converted into **2** in moderate to good yields (65–96%, entries 1–12). When R^1 was a phenyl ring substituted with electron-withdrawing groups, the reaction produced **2** in slightly higher yield than those substituted with electron-donating groups (entries 1 and 2 vs. 12; entries 6–9 vs. 4 and 5). As for the substituent Ar, substrates containing electron-rich aryl groups (entries 1–9, 11 and 12) usually afforded the corresponding products in better yields than those possessing electron-deficient aryl rings (entry 10). Under conditions B (3 mol% $AuCl_3$ plus 9 mol% AgOTf, DCE or DCB, 120 °C), allyl ethers **1** derived from 2-naphthol could be regiospecifically transformed into the corresponding products **3** in good yields (entries 1, 2 and 13–15) while those derived from phenol or 4-methylphenol were converted into **3** as major product together with a small amount of **2** (entries 3 and 4).

On the basis of previous reports,[4a,8b] a proposed mechanism to rationalize the regioselectivity in the gold(III)-catalyzed tandem reactions of **1** is depicted in Scheme 3. Under conditions A, the ether oxygen atom of **1** was coordinated to the cationic gold(III) center, resulting in cleavage of the ether bond to generate an ion pair intermediate **5** between the gold(III) phenolate and the corresponding allylic cation. The ease of attack of the α-carbon of the gold(III) phenolate onto the less substituted carbon of the allylic cation led to selective [1,3]-sigmatropic rearrangement (see intermediate **5**), thus **2** could be eventually formed via cyclization of intermediate **7** (Path a). The ion pair mechanism was proven by allylic cation trapping experiment, in which a Friedel–Crafts allylation product **12** was also detected besides the desired **2a** when **1a** and *p*-xylene (**11**) were subjected to reaction under conditions A (Scheme 4).

Table 1 Optimization of Reaction Conditions for the Selective Access to 3,4-DHC Derivatives **2a** and **3a**[a]

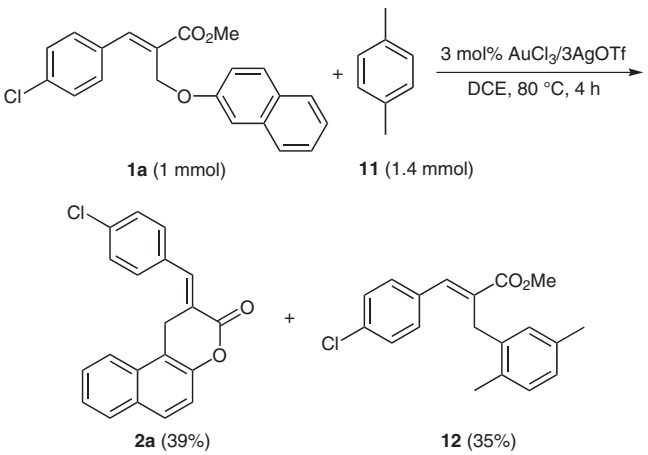
Entry	Catalyst (0.03 mmol)	Solvent	Time (h) at T_1	Time (h) at T_2	Yield (%)[b] T_1 **2a**	Yield (%)[b] T_2 **3a** (**2a**)
1	Ph_3PAuCl–AgOTf	DCE	8.0	3.5	16	79
2	AuCl–AgOTf	DCE	5.0	3.5	87	86 (3)
3	**$AuCl_3$–3AgOTf**	**DCE**	**4.0**	**2.0**	**96**	**93**
		DCB[c]	**4.0**	**2.0**	**96**	**93**
		toluene	4.0	2.5	68	63 (10)
		MeCN	4.5	2.0	72	62 (25)
		THF	6.0	2.5	30	89 (<1)
		dioxane	6.0	3.0	53	65 (20)
4	AuCl	DCE	10.0	3.5	0	3
5	$AuCl_3$	DCE	10.0	3.5	0	7
6	Ph_3PAuCl	DCE	10.0	3.5	0	0
7	AgOTf[d]	DCE	10.0	3.5	0	0
8	$FeCl_3$[e]	DCE	10.0	3.5	15	0 (35)
9	$AlCl_3$[e]	DCE	10.0	3.5	0	0
10	$ZnCl_2$[e]	DCE	10.0	3.5	0	7 (15)
11	$BiCl_3$[e]	DCE	10.0	3.5	5	11 (18)
12	$SnCl_4$[e]	DCE	10.0	3.5	0	29 (35)
13	$Cu(OTf)_2$[e]	DCE	10.0	3.5	0	10 (54)
14	HCl[e,f]	DCE	10.0	3.5	0	4 (32)
15	HOTf[e]	DCE	10.0	3.5	0	27 (28)
16	none	DCE	10.0	3.5	0[g]	0[g]

[a] The reaction was carried out at temperature T_1 (80 °C) or T_2 (120 °C) using **1a** (1.0 mmol), catalyst (3 mol% unless otherwise stated) in solvent (3 mL) under N_2 atmosphere.
[b] Isolated yield.
[c] DCB = 1,2-dichlorobenzene.
[d] The amount of catalyst was 0.09 mmol.
[e] The amount of catalyst was 0.3 mmol.
[f] Aqueous HCl (37%wt) was used.
[g] Compound **1a** was recovered quantitatively.

Table 2 Tandem Rearrangement/Cyclization Reactions of (*E*)-2-(Aryloxymethyl)alk-2-enoates **1** Catalyzed by Gold(III)

Entry	R^1, Ar (**1**)	Time (h)	Conditions	Yield (%)[a] of **2** or **3**
1	4-ClC_6H_4, 2-naphthyl (**1a**)	3.5 2.0	A B (DCE)	96 (only **2a**) 93 (only **3a**)
2	4-BrC_6H_4, 2-naphthyl (**1b**)	3.5 2.0	A B (DCE)	94 (only **2b**) 95 (only **3b**)
3	Ph, Ph (**1c**)	4.0 3.0	A B (DCB)	81 (only **2c**) 59/29 (**3c/2c**)[b]
4	Ph, 4-MeC_6H_4 (**1d**)	3.5 2.5	A B (DCB)	72 (only **2d**) 69/19 (**3d/2d**)[b]
5	3,4-$OCH_2OC_6H_3$, Ph (**1e**)	4.0	A	83 (only **2e**)
6	4-ClC_6H_4, Ph (**1f**)	4.0	A	93 (only **2f**)
7	2-BrC_6H_4, Ph (**1g**)	5.0	A	87 (only **2g**)
8	4-BrC_6H_4, Ph (**1h**)	4.0	A	89 (only **2h**)
9	2,4-$Cl_2C_6H_3$, Ph (**1i**)	4.0	A	91 (only **2i**)
10	Ph, 4-ClC_6H_4 (**1j**)	4.5	A	65 (only **2j**)
11	Ph, 4-MeC_6H_4 (**1k**)	4.0	A	87 (only **2k**)
12	4-$MeOC_6H_4$, 2-naphthyl (**1l**)	4.0	A	90 (only **2l**)
13	Ph, 2-naphthyl (**1m**)	2.0	B (DCE)	86 (only **3m**)
14	4-MeC_6H_4, 2-naphthyl (**1n**)	2.0	B (DCB)	90 (only **3n**)
15	4-$CF_3C_6H_4$, 2-naphthyl (**1o**)	2.5	B (DCB)	89 (only **3o**)

[a] Isolated yield based on **1**.
[b] The individual isomers were separated by column chromatography.



Scheme 4 Trapping of allylic cation

On the other hand, under conditions B, a thermally concerted [3,3]-sigmatropic rearrangement may be predominant, thus **3** could be selectively formed via cyclization of intermediate **10** (Path b). In the process, gold(III) might play a key role in helping to trigger the [3,3]-sigmatropic rearrangement via activation of the R^1-substituted carbon through coordination to the internal C=C bond and/or the carbonyl oxygen atom in **1** (see intermediate **8**).

The 3,4-dihydrocoumarin framework occurs frequently in natural compounds and shows important pharmacological activities.[17] Besides, DHCs serve as important flavor and fragrance compounds in both food and cosmetics.[18] Several methods[19] have been reported for the preparation of functionalized DHCs, the main drawback of some of these methods can be attributed to using harsh reaction conditions, multistep procedures, not easy availability of substrates, poor selectivities or low yields. The present method has characteristic features of high efficiency to tunably produce diversely substituted patterns of 3,4-DHCs with excellent regioselectivities, high yields and easy availability of the starting materials.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

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References and Notes

(1) (a) Hashmi, A. S. K.; Hutching, G. J. *Angew. Chem. Int. Ed.* **2006**, *45*, 7896. (b) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180. (c) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Commun.* **2007**, 333. (d) Li, Z.; Brouwer, C.; He, C. *Chem. Rev.* **2008**, *108*, 3239. (e) Arcadi, A. *Chem. Rev.* **2008**, *108*, 3266. (f) Hashmi, A. S. K.; Rodolph, M. *Chem. Soc. Rev.* **2008**, *37*, 1766. (g) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (h) Skouta, R.; Li, C.-J. *Tetrahedron* **2008**, *64*, 4917. (i) Muzart, J. *Tetrahedron* **2008**, *64*, 5815.

(2) For two reviews on gold-catalyzed [3,3]- and [2,3]-sigmatropic rearrangements of propargylic esters, see: (a) Marion, N.; Nolan, S. P. *Angew. Chem. Int. Ed.* **2007**, *46*, 2750. (b) Marco-Contelles, J.; Soriano, E. *Chem. Eur. J.* **2007**, *13*, 1350.

(3) For selected examples related to [3,3]-sigmatropic rearrangement catalyzed by gold, see: (a) Peng, Y.; Cui, L.; Zhang, G.; Zhang, L. *J. Am. Chem. Soc.* **2009**, *131*, 5062. (b) Bae, H. J.; Baskar, B.; An, S. E.; Cheong, J. Y.; Thangadurai, D. T.; Hwang, I.-C.; Rhee, Y. H. *Angew. Chem. Int. Ed.* **2008**, *47*, 2263. (c) Yu, M.; Zhang, G.; Zhang, L. *Org. Lett.* **2007**, *9*, 2147. (d) Buzas, A. K.; Istrate, F. M.; Gagosz, F. *Org. Lett.* **2007**, *9*, 985. (e) Marion, N.; Gealageas, R.; Nolan, S. P. *Org. Lett.* **2007**, *9*, 2653. (f) Luo, T.; Schreiber, S. L. *Angew. Chem. Int. Ed.* **2007**, *46*, 8250. (g) Wang, S.; Zhang, L. *J. Am. Chem. Soc.* **2006**, *128*, 8414. (h) Zhang, L.; Wang, S. *J. Am. Chem. Soc.* **2006**, *128*, 1442. (i) Wang, S.; Zhang, L. *J. Am. Chem. Soc.* **2006**, *128*, 14274. (j) Reich, N. W.; Yang, C.-G.; Shi, Z.; He, C. *Synlett*

2006, 1278. (k) Zhao, J.; Hughes, C. O.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 7436. (l) Marion, N.; Díez-González, S.; de Frémont, P.; Noble, A. R.; Nolan, S. P. *Angew. Chem. Int. Ed.* **2006**, *45*, 3647. (m) Suhre, M. H.; Reif, M.; Kirsch, S. F. *Org. Lett.* **2005**, *7*, 3925.

(4) For selected examples of [2,3]-sigmatropic rearrangement catalyzed by gold, see: (a) Uemura, M.; Watson, I. D. G.; Katsukawa, M.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 3464. (b) Súarez-Pantiga, S.; Rubio, E.; Alvarez-Rúa, C.; González, J. M. *Org. Lett.* **2009**, *11*, 13. (c) Li, G.; Zhang, G.; Zhang, L. *J. Am. Chem. Soc.* **2008**, *130*, 3740. (d) Pérez, A. G.; López, C. S.; Marco-Contelles, J.; Faza, O. N.; Soriano, E.; de Lera, A. R. *J. Org. Chem.* **2009**, *74*, 2982. (e) Moreau, X.; Goddard, J.-P.; Bernard, M.; Lemière, G.; López-Romero, J. M.; Mainetti, E.; Marion, N.; Mouriès, V.; Thorimbert, S.; Fensterbank, L.; Malacria, M. *Adv. Synth. Catal.* **2008**, *350*, 43. (f) Davies, P. W.; Albrecht, S. J.-C. *Chem. Commun.* **2008**, 238. (g) Gorin, D. J.; Watson, I. D. G.; Toste, F. D. *J. Am. Chem. Soc.* **2008**, *130*, 3736. (h) Shapiro, N. D.; Toste, F. D. *J. Am. Chem. Soc.* **2008**, *130*, 9244. (i) Witham, C. A.; Mauleón, P.; Shapiro, N. D.; Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 5838. (j) Amijs, C. H. M.; López-Carillo, V.; Echavarren, A. M. *Org. Lett.* **2007**, *9*, 4021.

(5) For examples of [1,2]-sigmatropic rearrangement catalyzed by gold, see: (a) Peng, L.; Zhang, X.; Zhang, S.; Wang, J. *J. Org. Chem.* **2007**, *72*, 1192. (b) Sanz, R.; Miguel, D.; Rodríguez, F. *Angew. Chem. Int. Ed.* **2008**, *47*, 7354. (c) Mamane, V.; Hannen, P.; Fürstner, A. *Chem. Eur. J.* **2004**, *10*, 4556.

(6) Claisen, L. *Ber. Dtsch. Chem. Ges.* **1912**, *45*, 3157.

(7) (a) Rhoads, S. J.; Raulins, N. R. *Organic Reactions*, Vol. 22; Wiley: New York, **1974**, 1. (b) Wipf, P. In *Comprehensive Organic Synthesis*, Vol. 5; Trost, B. M.; Fleming, I.; Paquette, L. A., Eds.; Pergamon Press: Oxford, **1991**, 827–873. (c) Luts, R. P. *Chem. Rev.* **1984**, *84*, 205. (d) Ziegler, F. E. *Chem. Rev.* **1988**, *88*, 1423. (e) Castro, A. M. M. *Chem. Rev.* **2004**, *104*, 2939. (f) Ito, H.; Taguchi, T. *Chem. Soc. Rev.* **1999**, *28*, 43. (g) Hiersemann, M.; Abraham, L. *Eur. J. Org. Chem.* **2002**, 1461. (h) Nubbemeyer, U. *Synthesis* **2003**, 961.

(8) (a) Wipf, P.; Rodríguez, S. *Adv. Synth. Catal.* **2002**, *344*, 434. (b) Hiersemann, M.; Abraham, L. *Org. Lett.* **2001**, *3*, 49. (c) Saito, S.; Shimada, K.; Yamamoto, H. *Synlett* **1996**, 720. (d) Nonoshita, K.; Banno, H.; Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1990**, *112*, 316. (e) Schmid, K.; Schmid, H. *Helv. Chim. Acta* **1953**, *36*, 687. (f) Fahrni, P.; Schmid, H. *Helv. Chim. Acta* **1959**, *42*, 1102. (g) Mooney, B. A.; Prager, R. H.; Ward, A. D. *Aust. J. Chem.* **1980**, *33*, 2717.

(9) (a) Grieco, P. A.; Clark, J. D.; Jagoe, C. T. *J. Am. Chem. Soc.* **1991**, *113*, 5488. (b) Grieco, P. A.; Collins, J. L.; Henry, K. J. Jr. *Tetrahedron Lett.* **1992**, *33*, 4735. (c) Palani, N.; Balasubramanian, K. K. *Tetrahedron Lett.* **1993**, *34*, 5001. (d) Palani, N.; Balasubramanian, K. K. *Tetrahedron Lett.* **1995**, *36*, 9527. (e) Nakamura, S.; Ishihara, K.; Yamamoto, H. *J. Am. Chem. Soc.* **2000**, *122*, 8131. (f) Schobert, R.; Siegfried, S.; Gordon, G.; Mulholland, D.; Nieuwenhuyzen, M. *Tetrahedron Lett.* **2001**, *42*, 4561.

(10) (a) Basavaiah, D.; Rao, P. D.; Hyma, R. S. *Tetrahedron* **1996**, *52*, 8001. (b) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811.

(11) (a) Liu, Y.; Li, J.; Zheng, H.; Xu, D.; Xu, Z.; Zhang, Y. *Synlett* **2005**, 2999. (b) Liu, Y.; Xu, X.; Zheng, H.; Xu, D.; Xu, Z.; Zhang, Y. *Synlett* **2006**, 571. (c) Liu, Y. K.; Zheng, H.; Xu, D.; Xu, Z.; Zhang, Y. *Synlett* **2006**, 2492. (d) Liu, Y.; Xu, D.; Xu, Z.; Zhang, Y. *Synlett* **2007**, 1671. (e) Liu, Y.; Mao, D.; Qian, J.; Lou, S.; Xu, Z.; Zhang, Y. *Synthesis* **2009**, 1170.

(12) Basavaiah, D.; Bakthadoss, M.; Pandiaraju, S. *Chem. Commun.* **1998**, 1639.

(13) For an excellent review on ligand effects in homogeneous gold catalysis, see: Grorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351.

(14) For silver salt additives in gold catalysis, see, for example: (a) Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 2402. (b) Watanabe, T.; Oishi, S.; Fujii, N.; Ohno, H. *Org. Lett.* **2007**, *9*, 4821. (c) Lemière, G. G.; Gandon, V.; Agenet, N.; Goddard, J.-P.; de Kozak, A.; Aubert, C.; Fensterbank, L.; Malacria, M. *Angew. Chem. Int. Ed.* **2006**, *45*, 7596. (d) Shi, Z.; He, C. *J. Am. Chem. Soc.* **2004**, *126*, 5964.

(15) **Typical Experimental Procedure for the Synthesis of 2 under Condition A**: $AuCl_3$ (9.1 mg, 0.03 mmol), AgOTf (23.1 mg, 0.09 mmol), and DCE (2 mL) were added to a 10-mL flask. The mixture was stirred at r.t. for 5 min before a DCE solution of **1a** (0.35 g, 1.0 mmol diluted in 1 mL of solvent) was added. Then the reaction mixture was stirred at 80 °C for 4 h. Upon completion of the reaction, the resulting mixture was diluted with CH_2Cl_2 (10 mL) and filtered through Celite. After evaporation of the solvent under vacuum, the residue was purified by column chromatography on silica gel (200–300 mesh) using cyclohexane–EtOAc (12:1) as eluent to give pure **2a**.
Typical Experimental Procedure for the Synthesis of 3 under Condition B: $AuCl_3$ (9.1 mg, 0.03 mmol), AgOTf (23.1 mg, 0.09 mmol), and DCE or DCB (2 mL) were added to a 10-mL sealed vessel. The mixture was stirred at r.t. for 5 min before a DCE or DCB solution of **1a** (0.35 g, 1.0 mmol diluted in 1 mL of solvent) was added. Then the reaction mixture was stirred at 120 °C for 2 h. Upon completion of the reaction, the resulting mixture was diluted with CH_2Cl_2 (10 mL) and filtered through Celite. After evaporation of the solvent under vacuum, the residue was purified by column chromatography on silica gel (200–300 mesh) using cyclohexane–EtOAc (12:1) as eluent to give pure **3a**.

(16) **Representative Data for Compound 2 and 3**:
Compound **2b**: white solid; R_f 0.46 (cyclohexane–EtOAc, 12:1); mp 198.3–201.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.32 (d, 2 H, *J* = 2.5 Hz, CH_2), 7.25 (d, 1 H, *J* = 8.5 Hz, ArH), 7.43–7.85 (m, 9 H, ArH), 8.03 (t, 1 H, *J* = 2.5 Hz, ArCH=). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.12, 112.14, 117.50, 122.28, 122.91, 124.27, 125.25, 127.33, 128.87, 129.25, 130.76, 130.91, 131.74, 132.17, 133.55, 142.13, 147.77, 163.60. IR (KBr): 1711 (C=O), 1630 (C=C) cm^{-1}. GC–MS: *m*/*z* = 364 [M$^+$], 366 [M$^+$ + 2]. HRMS (EI): *m*/*z* calcd for $C_{20}H_{13}O_2Br$: 364.0099; found: 364.0113.
Compound **3c**: white solid; R_f 0.56 (cyclohexane–EtOAc, 12:1); mp 114.5–114.6 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, Me), 4.90 (s, 1 H), 5.72 (s, 1 H), 6.44 (s, 1 H), 6.89–7.33 (m, 8 H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.80, 48.26, 117.04, 124.28, 127.52, 127.76, 128.96, 129.08, 129.26, 129.43, 134.53, 136.88, 140.77, 148.59, 163.26. IR (KBr): 1746 (C=O), 1627 (C=C) cm^{-1}. GC–MS: *m*/*z* = 250 [M$^+$]. HRMS (EI): *m*/*z* calcd for $C_{17}H_{14}O_2$: 250.0994; found: 250.1001.

(17) (a) Donnelly, D. M. X.; Boland, G. M. *Nat. Prod. Rep.* **1995**, *12*, 321. (b) Donnelly, D. M. X.; Boland, G. M. *The Flavonoids: Advances in Research since 1986*; Harborne, J. B., Ed.; Chapman and Hall: London, **1993**, Chap. 6. (c) Posakony, J.; Hirao, M.; Steven, S.; Simon, J. A.; Bedalov, A. *J. Med. Chem.* **2004**, *47*, 2635.

(18) (a) Zeitler, K.; Rose, C. A. *J. Org. Chem.* **2009**, *74*, 1759. (b) Häser, K.; Wenk, H. H.; Schwab, W. *J. Agric. Food Chem.* **2006**, *54*, 6236.

(19) (a) Foucaud, A.; Brine, N. *Synth. Commun.* **1994**, *24*, 2851. (b) Krawczyk, H.; Albrecht, L.; Wojciechowski, J.; Wolf, W. M. *Tetrahedron* **2007**, *63*, 12583. (c) Vida, J. A.; Gut, M. *J. Org. Chem.* **1968**, *33*, 1202. (d) Pickett, J. E.; van Dort, P. C. *Tetrahedron Lett.* **1992**, *33*, 1161. (e) Murakami, M.; Tsuruta, T.; Ito, Y. *Angew. Chem. Int. Ed.* **2000**, *39*, 2484. (f) Henry, C. E.; Kwon, O. *Org. Lett.* **2007**, *9*, 3069. (g) Zhang, Z.; Ma, Y.; Zhao, Y. *Synlett* **2008**, 1091.