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Gold(III)-Catalyzed Tandem Reaction of *O*-Arylhydroxylamines with 1,3-Dicarbonyl Compounds: Highly Selective Synthesis of 3-Carbonylated Benzofuran Derivatives

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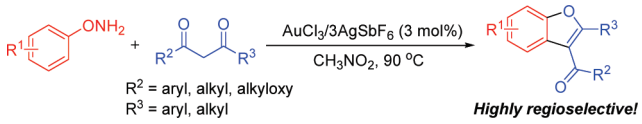
Received July 10, 2010



A highly regioselective protocol for the synthesis of 3-carbonylated benzofuran derivatives has been developed involving the gold(III)-catalyzed tandem condensation/rearrangement/cyclization reaction of *O*-arylhydroxylamines with 1,3-dicarbonyl compounds.

3-Carbonylated benzofuran (3-CBF) derivatives represent an important class of members in the benzofuran[1] family exhibiting unique biological and pharmacological activities.[2] To date, many approaches have been explored for the construction of benzofuran scaffold with different functional patterns,[3−5] among which, however, those related to the synthesis of 3-CBFs have a lack of development. Representative methods include Pd-catalyzed cascade carbonylative annulation of *o*-hydroxyarylacetylenes in the presence of CO gas,[4a−c] tandem Michael addition/cyclization of quinones with 1,3-dicarbonyl compounds or *β*-(dimethylamino)vinyl ketones,[4d−f] CuI-catalyzed coupling of 1-bromo-2-iodobenzenes and *β*-keto esters,[4g] and BBr_3-mediated domino ring cleavage/deprotection/annulation reaction of 2-alkylidenetetrahydrofurans.[4h] Unfortunately, most of these procedures suffer from one or more limitations such as the requirement of highly toxic CO gas, multistep processes, high catalyst loading, and/or not easy availability of starting materials. Recently, oxidative annulation protocol has been developed as an alternative to 3-CBFs with high efficiency, as exemplified in the $FeCl_3$-mediated ring closure of α-arylketones[4i] and the Fe(III)-catalyzed tandem oxidative coupling/cyclization reaction of phenols with *β*-keto esters.[4j] However, harsh reaction conditions and using external oxidants represent the main drawbacks. Li[4k] and co-workers have

(1) (a) Hou, X.-L.; Yang, Z.; Wong, H. N. C. Furans and Benzofurans. In *Progress in Heterocyclic Chemistry*; Gribble, G. W., Gilchrist, T. L., Eds; Pergamon: Oxford, England, 2002; Vol. 14, pp139−179. (b) Donnelly, D. M. X.; Meegnan, M. J. In *Furans and Their Benzo Derivatives: (iii) Synthesis and Application In Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: NewYork, 1984; Vol. 4, p 657. (c) *The Chemistry of Heterocyclic Compounds: Benzofurans*; Weissberger, A., Taylor, E. C., Eds.; John Wiley and Sons: New York, 1974; Vol. 29, p 1. (d) Cagniant, P.; Cagniant, D. Recent Advances in the Chemistry of Benzo[*b*]furan and Its Derivatives. Part I: Occurrence and Synthesis. In *Advances in Heterocyclic Chemistry*; Katritzky, A. R., Boulton, A. J., Eds.; Academic Press: New York, 1975; Vol. 18, pp 337−482.

(2) (a) Pôças, E. S. C.; Lopes, D. V. S.; da Silva, A. J. M.; Pimenta, P. H. C.; Leitão, F. B.; Netto, C. D.; Buarque, C. D.; Brito, F. V.; Costa, P. R. R.; Noël, F. *Bioorg. Med. Chem.* **2006**, *14*, 7962. (b) Baxendale, I. R.; Griffiths-Jones, C. M.; Ley, S. V.; Tranmer, G. K. *Synlett* **2006**, 427. (c) Kálai, T.; Várbiró, G.; Bognár, Z.; Pálfi, A.; Hantó, K.; Bognár, B.; Ösz, E.; Sümegi, B.; Hideg, K. *Bioorg. Med. Chem.* **2005**, *13*, 2629. (d) Hong, Y.; Kania, R. S. U.S. Patent 5137395, 2005. (e) Carlsson, B.; Singh, B. N.; Temciuc, M.; Nilsson, S.; Li, Y.-L.; Mellin, C.; Malm, J. *J. Med. Chem.* **2002**, *45*, 623. (f) Romines, W. H.; Kania, R. S.; Lou, J.; Collins, M. R.; Cripps, S. J.; He, M.; Zhou, R.; Palmer, C. L.; Deal, J. G. WO2003106462, 2003. (g) Pieters, L.; Van Dyck, S.; Gao, M.; Bai, R.; Hamel, E.; Vlietinck, A.; Lemière, G. *J. Med. Chem.* **1999**, *42*, 5475. (h) Singh, S. N.; Fletcher, R. D.; Fisher, S. G.; Singh, B. N.; Lewis, H. D.; Deedwania, P. C.; Massie, B. M.; Colling, C.; Layyeri, D. *N. Eng. J. Med.* **1995**, *333*, 77. (i) Boyle, E. A.; Mangan, F. R.; Markwell, R. E.; Smith, S. A.; Thomson, M. J.; Ward, R. W.; Wyman, P. A. *J. Med. Chem.* **1986**, *29*, 894.

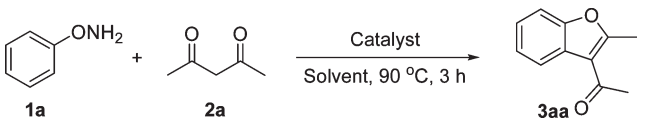
(3) For recent reviews on the synthesis of benzofurans, see: (a) Patil, N. T.; Yamamoto, Y. *Chem. Rev.* **2008**, *108*, 3395. (b) Zeni, G.; Larock, R. C. *Chem. Rev.* **2006**, *106*, 4644. (c) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873. (d) Ziegert, R. E.; Torang, J.; Knepper, K.; Brase, S. *J. Comb. Chem.* **2005**, *7*, 147. (e) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079. (f) Horton, D. A.; Bourne, G. T.; Smythe, M. L. *Chem. Rev.* **2003**, *103*, 893. (g) Metwally, M. A.; Abdel-Wahab, B. F.; El-Hiti, G. A. *Curr. Org. Chem.* **2010**, *14*, 48.

(4) For recent examples on the synthesis of 3-carbonylated benzofurans, see: (a) Liao, Y.; Smith, J.; Fathi, R.; Yang, Z. *Org. Lett.* **2005**, *7*, 2707. (b) Liao, Y.; Reitman, M.; Zhang, Y.; Fathi, R.; Yang, Z. *Org. Lett.* **2002**, *4*, 2607. (c) Nan, Y.; Miao, H.; Yang, Z. *Org. Lett.* **2000**, *2*, 297. (d) Mothe, S. R.; Susanti, D.; Chan, P. W. H. *Tetrahedron Lett.* **2010**, *51*, 2136. (e) Fakhari, A. R.; Nematollahi, D.; Shamsipur, M.; Makarem, S.; Davarani, S. S. H.; Alizadeh, A.; Khavasi, D. R. *Tetrahedron* **2007**, *63*, 3894. (f) Cheng, X.-M.; Liu, X.-W. *J. Comb. Chem.* **2007**, *9*, 906. (g) Lu, B.; Wang, B.; Zhang, Y.; Ma, D. *J. Org. Chem.* **2007**, *72*, 5337. (h) Bellur, E.; Langer, P. *J. Org. Chem.* **2005**, *70*, 7686. (i) Liang, Z.; Hou, W.; Du, Y.; Zhang, Y.; Pan, Y.; Mao, D.; Zhao, K. *Org. Lett.* **2009**, *11*, 4978. (j) Guo, X.; Yu, R.; Li, H.; Li, Z. *J. Am. Chem. Soc.* **2009**, *131*, 17387. (k) Huang, X.-C.; Liu, Y.-L.; Liang, Y.; Pi, S.-F.; Wang, F.; Li, J.-H. *Org. Lett.* **2008**, *10*, 1525. (l) Dudley, M. E.; Morshed, M. M.; Hossain, M. M. *Synthesis* **2006**, 1711.

(5) For recent examples on the synthesis of benzofuran derivatives other than 3-carbonylated benzofurans, see: (a) Mehta, S.; Larock, R. C. *J. Org. Chem.* **2010**, *75*, 1652. (b) Hu, J.; Wu, L.-Y.; Wang, X.-C.; Hu, Y.-Y.; Niu, Y.-N.; Liu, X.-Y.; Yang, S.; Liang, Y.-M. *Adv. Synth. Catal.* **2010**, *352*, 351. (c) Jaseer, E. A.; Prasad, D. J. C.; Sekar, G. *Tetrahedron* **2010**, *66*, 2077. (d) Geary, L. M.; Hultin, P. G. *Org. Lett.* **2009**, *11*, 5478. (e) Tsuchikama, K.; Hashimoto, Y.-K.; Endo, K.; Shibata, T. *Adv. Synth. Catal.* **2009**, *351*, 2850. (f) Menon, R. S.; Findlay, A. D.; Bissember, A. C.; Banwell, M. G. *J. Org. Chem.* **2009**, *74*, 8901. (g) Du, H.-A.; Zhang, X.-G.; Tang, R.-Y.; Li, J.-H. *J. Org. Chem.* **2009**, *74*, 7844. (h) Contiero, F.; Jones, K. M.; Matts, E. A.; Porzello, A.; Tomkinson, N. C. O. *Synlett* **2009**, 3003. (i) Bi, H.-P.; Guo, L.-N.; Gou, F.-R.; Duan, X.-H.; Liu, X.-Y.; Liang, Y.-M. *J. Org. Chem.* **2008**, *73*, 4713. (j) Takeda, N.; Miyata, O.; Naito, T. *Eur. J. Org. Chem.* **2007**, 1491. (k) Luca, L. D.; Giacomelli, G.; Nieddu, G. *J. Org. Chem.* **2007**, *72*, 3955. (l) Gabriele, B.; Mancuso, R.; Salerno, G.; Costa, M. *J. Org. Chem.* **2007**, *72*, 9278. (m) Nagamochi, M.; Fang, Y.-Q.; Lautens, M. *Org. Lett.* **2007**, *9*, 2955. (n) Oppenheimer, J.; Johnson, W. L.; Tracey, M. R.; Hsung, R. P.; Yao, P.-Y.; Liu, R.; Zhao, K. *Org. Lett.* **2007**, *9*, 2361. (o) Nakamura, I.; Mizushima, Y.; Yamagishi, U.; Yamamoto, Y. *Tetrahedron* **2007**, *63*, 8670. (p) Kumar, M. P.; Liu, R.-S. *J. Org. Chem.* **2006**, *71*, 4951. (q) Carril, M.; SanMartin, R.; Tellitu, I.; Domínguez, E. *Org. Lett.* **2006**, *8*, 1467. (r) Nakamura, I.; Mizushima, Y.; Yamamoto, Y. *J. Am. Chem. Soc.* **2005**, *127*, 15022. (s) Fürstner, A.; Davies, P. W. *J. Am. Chem. Soc.* **2005**, *127*, 15024. (t) Yue, D.; Yao, T.; Larock, R. C. *J. Org. Chem.* **2005**, *70*, 10292. (u) Green, M. P.; Pichlmair, S.; Marques, M. M. B.; Martin, H, J.; Diwald, O.; Berger, T.; Mulzer, J. *Org. Lett.* **2004**, *6*, 3131. (v) Miyata, O.; Takeda, N.; Naito, T. *Org. Lett.* **2004**, *6*, 1761. (w) Maimone, T. J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 9990.

Published on Web 08/13/2010 DOI: 10.1021/jo101357d

TABLE 1. Optimization of Reaction Conditions[a]



1a 2a 3aa

entry	catalyst (0.03 mmol)	solvent	yield (%)
1	$AuCl_3$/3AgOTf	DCE[b]	46
		dioxane	58
		THF[c]	45
		toluene	22
		CH_3CN[c]	5
		CH_3NO_2	78
2	$AuCl_3$/3$AgNTf_2$	CH_3NO_2	79
3	$AuCl_3$/3$AgSbF_6$	CH_3NO_2	82
4	$AuCl_3$/$AgSbF_6$	CH_3NO_2	73
5	$AuCl_3$/3$AgBF_4$	CH_3NO_2	67
6	$AuCl_3$	CH_3NO_2	10
7	AuCl/AgOTf	CH_3NO_2	51
8	AuCl/$AgSbF_6$	CH_3NO_2	40
9	PPh_3AuCl/AgOTf	CH_3NO_2	31
10	PPh_3AuNTf_2	CH_3NO_2	46
11	$AgSbF_6$[d]	CH_3NO_2	0
12	$AlCl_3$[e]	CH_3NO_2	41
13	$ZnCl_2$[e]	CH_3NO_2	25
14	$FeCl_3$[e]	CH_3NO_2	36
15	$Cu(OTf)_2$[e]	CH_3NO_2	7
16	HCl[e,f]	CH_3NO_2	0
17	HOTf[e]	CH_3NO_2	< 3
18	$MeSO_3H$[e]	CH_3NO_2	0
19	none	CH_3NO_2	0

[a]Carried out on 1 mmol of **1a** and 1.2 mmol of **2a** in the presence of catalyst in solvent (3 mL) at 90 °C for 3 h. [b]DCE = 1,2-dichloroethane. [c]The reaction temperature at reflux. [d]The amount of catalyst is 0.09 mmol. [e]The amount of catalyst is 0.3 mmol. [f]Aqueous HCl (37 wt %) was used.

developed a mild and general route for the synthesis of 3-CBFs involving cycloaddition of arynes with iodonium ylides. Despite significant advance, a stoichiometric amount of iodobenzene byproduct is generated in the method. Owing to their importance in medicinal chemistry, it is still highly desirable to develop general and efficient new approaches to 3-CBFs.

On the other hand, the study of recently popularized gold[6]-catalyzed tandem reactions[7] has resulted in significant achievements in the construction of various heterocycles.[3a,8] In this regard, we once reported an efficient and highly selective approach to 4*H*-chromene derivatives via gold(III)-catalyzed condensation/annulation tandem reaction of ketones with phenols,[8h] and a temperature-controlled highly regioselective synthesis of 3,4-dihydrocoumarin derivatives via gold(III)-catalyzed tandem rearrangement/cyclization of (*E*)-2-(aryloxymethyl)alk-2-enoates.[8i] Recently, Tomkinson[5h] and Naito[5v] have developed efficient methods for the synthesis of benzofurans involving methanesulfonic acid (2 equiv) or trifluoroacetyl triflate (5 equiv)-triggered [3,3]-sigmatropic rearrangement of oxime ethers generated from the condensation of *O*-arylhydroxylamines with monoketones. In light of their reports, we envisioned that 3-CBFs might be accessed when 1,3-dicarbonyl compounds were used as substrates. Herein, we present a gold(III)-catalyzed (only with 3 mol %) highly selective protocol for the synthesis of 3-CBFs via one-pot tandem reaction of *O*-arylhydroxylamines with 1,3-dicarbonyl compounds.

Initially, the model reaction between *O*-phenylhydroxylamine **1a** and acetylacetone **2a** was investigated under a broad range of reaction conditions (Table 1; Table 1S in the SI). When **1a** was subjected to react with **2a** in the presence of $AuCl_3$/3AgOTf (3 mol % based on **1a**) in DCE at 90 °C for 3 h, the target product **3aa** was isolated in 46% yield (entry 1). The $AuCl_3$/3AgOTf catalytic system showed the best performance in nitromethane among several solvents examined, affording **3aa** in 78% yield (entry 1). It was found that silver salts had profound effects on the tandem reaction.[9] While employment of $AgBF_4$, AgCN, $AgNO_2$, or AgF in combination with $AuCl_3$ showed a modest catalytic activity for the reaction (Table 1S, SI), a combination of $AgNTf_2$ with $AuCl_3$ displayed almost equal effectiveness as $AuCl_3$/3AgOTf (entry 2 vs 1), and a $AuCl_3$/3$AgSbF_6$ combined system was identified to be the best choice for the reaction (entry 3). A combined system of $AuCl_3$ and $AgSbF_6$ with a molar ratio of 1:1 was less effective than the $AuCl_3$/3$AgSbF_6$ system (entry 4). Cationic Au(I) catalysts were not suitable for the reaction (entries 7−10). The reaction could hardly take place without a catalyst (entry 19), or in the presence of $AuCl_3$ or $AgSbF_6$ alone (entries 6, 11). Using a range of other conventional Lewis or Brønsted acids as catalyst resulted in far less effectiveness even at a catalyst loading of 30 mol % (entries 12−18), indicating that cationic gold(III) species were indispensable in reaching high reactivity for the tandem reaction.

Subsequently, the scope of 1,3-dicarbonyl compounds was investigated under the optimized reaction conditions by fixing *O*-phenylhydroxylamine **1a** as a model substrate (Table 2). Both acyclic (entries 1, 2, and 5−10) and cyclic 1,3-diketones (entries 3, 4) are suitable substrates for the reaction, generally furnishing desired products in good to excellent yields (81−93%, entries 1−10 except 2). For unsymmetrical aryl alkyl 1,3-diketones, the present reaction

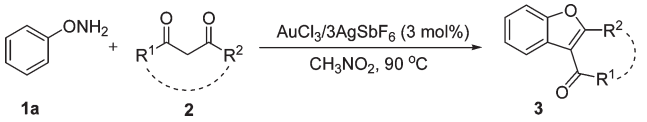
(6) For reviews on gold catalysts, see: (a) Hashmi, A. S. K.; Rodolph, M. *Chem. Soc. Rev.* **2008**, *37*, 1766. (b) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (c) Marion, N.; Nolan, S. P. *Chem. Soc. Rev.* **2008**, *37*, 1776. (d) Li, Z.; Brouwer, C.; He, C. *Chem. Rev.* **2008**, *108*, 3239. (e) Arcadi, A. *Chem. Rev.* **2008**, *108*, 3266. (f) Skouta, R.; Li, C.-J. *Tetrahedron* **2008**, *64*, 4917. (g) Muzart, J. *Tetrahedron* **2008**, *64*, 5815. (h) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180. (i) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Commun.* **2007**, 333. (j) Hashmi, A. S. K.; Hutching, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896.

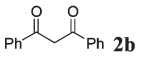
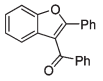
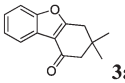
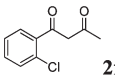
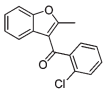
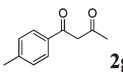
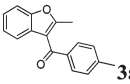
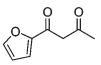
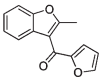
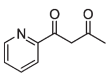
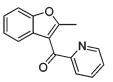
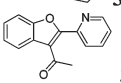
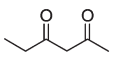
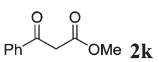
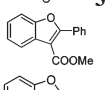
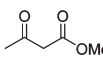
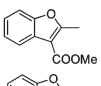
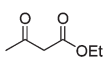
(7) For reviews on tandem reactions, see: (a) Enders, D.; Grondal, C.; Hüttl, M. R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 1570. (b) Tietze, L. F.; Bell, H. P.; Brasche, G., Eds. *Domino Reactions in Organic Synthesis*; Wiley-VCH: Weinheim, Germany, 2006. (c) Nicolaou, K. C.; Montagnon, T.; Snyder, S. A. *Chem. Commun.* **2003**, 551. (d) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115.

(8) For recent examples on the synthesis of heterocylces via gold-catalyzed tandem reactions, see: (a) Ye, L.; Cui, L.; Zhang, G.; Zhang, L. *J. Am. Chem. Soc.* **2010**, *132*, 3258. (b) Zhang, Q.; Cheng, M.; Hu, X.; Li, B.-G.; Ji, J.-X. *J. Am. Chem. Soc.* **2010**, *132*, 7256. (c) Kothandaraman, P.; Rao, W.; Foo, S. J.; Chan, P. W. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 4619. (d) Nakamura, I.; Okamoto, M.; Terada, M. *Org. Lett.* **2010**, *12*, 2453. (e) Ueda, M.; Sato, A.; Ikeda, Y.; Miyoshi, T.; Naito, T.; Miyata, O. *Org. Lett.* **2010**, *12*, 2594. (f) Liu, Y.; Xu, W.; Wang, X. *Org. Lett.* **2010**, *12*, 1448. (g) Zhou, Y.; Zhai, Y.; Ji, X.; Liu, G.; Feng, E.; Ye, D.; Zhao, L.; Jiang, H.; Liu, H. *Adv. Synth. Catal.* **2010**, *352*, 373. (h) Liu, Y.; Qian, J.; Lou, S.; Zhu, J.; Xu, Z. *J. Org. Chem.* **2010**, *75*, 1309. (i) Liu, Y.; Qian, J.; Lou, S.; Xu, Z. *Synlett* **2009**, 2971. (j) Shi, Y.; Roth, K. E.; Ramgren, S. D.; Blum, S. A. *J. Am. Chem. Soc.* **2009**, *131*, 18022. (k) Aponick, A.; Li, C.-Y.; Palmes, J. A. *Org. Lett.* **2009**, *11*, 121. (l) Luo, T.; Schreiber, S. L. *J. Am. Chem. Soc.* **2009**, *131*, 5667. (m) Uemura, M.; Watson, I. D. G.; Katsukawa, M.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 3464.

(9) For an excellent review on ligand effects in homogeneous gold catalysis, see: (a) Grorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351. For silver salt additives in gold catalysis, see for examples: (b) 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. (c) Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2402. (d) Shi, Z.; He, C. *J. Am. Chem. Soc.* **2004**, *126*, 5964.

TABLE 2. Au(III)-Catalyzed Tandem Reaction of *O*-Phenylhydroxylamine 1a with Different 1,3-Dicarbonyl Compounds 2[a]

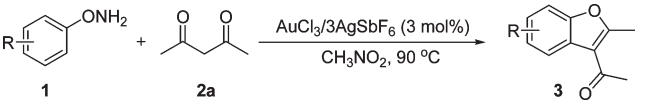


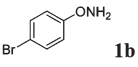
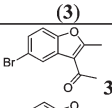
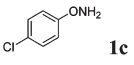
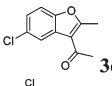
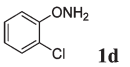
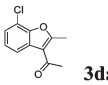
entry	substrate (2)	time (h)	product (3)	yield (%)
1	 **2a**	3	 **3aa**	82
2	 **2b**	10	 **3ab**	56[b]
3	 **2c**	6	 **3ac**	89
4	 **2d**	8	 **3ad**	83
5	 **2e**	3	 **3ae**	92
6	 **2f**	3	 **3af**	90
7	 **2g**	3	 **3ag**	93
8	 **2h**	3	 **3ah**	87
9	 **2i**	3	 **3ai**  **3'ai**	86 (93:7)[c]
10	 **2j**	4	 **3aj**  **3'aj**	45 36
11	 **2k**	8	 **3ak**	45[d]
12	 **2l**	8	 **3al**	54[d]
13	 **2m**	8	 **3am**	56[d]
14	 **7**	10	 **8**	0[e] (0[e,f])
15	 **9**	10	 **10**	0[e] (0[e,f])

[a]Reaction conditions: **1a** (1 mmol), **2** (1.2 mmol), $AuCl_3/3AgSbF_6$ (0.03 mmol), CH_3NO_2 (3 mL), 90 °C. [b]The reaction temperature at 100 °C. [c]The ratio of **3ai** to **3′ai**; determined on the basis of ^1H NMR analysis. [d]Phenol was detected as minor product. [e]Phenol was detected as major product. [f]Preparative *O*-phenyloxime ether was directly used as substrate.

exhibited excellent regioselectivity for the formation of 2-alkyl-3-aroyl-substituted benzofuran isomer predominantly

TABLE 3. Au(III)-Catalyzed Tandem Reaction of Acetylactone 2a with Different *O*-Arylhydroxylamines 1[a]



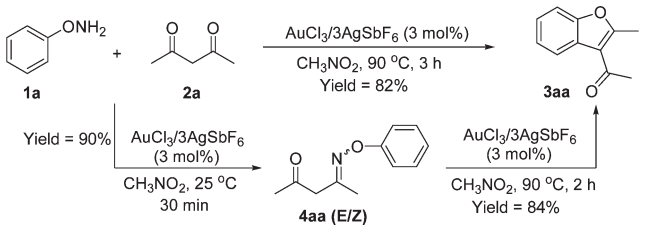
entry	Substrate (1)	time (h)	product (3)	yield (%)
1	 **1b**	4	 **3ba**	83
2	 **1c**	3	 **3ca**	86
3	 **1d**	3	 **3da**	81
4	**1e**	5	**3ea**	64[b]
5	**1f**	3	**3fa**	89
6	**1g**	3	**3ga**	86
7	**1h**	4	**3ha**	62
8	**1i**	4	**3ia**	42
9	**1j**	3	**3ja**	49
10	**1k**	4	R^4 = Me, R^5 = H **3ka**; R^4 = H, R^5 = Me **3'ka**	45 (92:8)[c]

[a]Reaction conditions: **1** (1 mmol), **2a** (1.2 mmol), $AuCl_3/3AgSbF_6$ (0.03 mmol), CH_3NO_2 (3 mL), 90 °C. [b]The reaction temperature at 100 °C. [c]The ratio of **3ka** to **3′ka**; determined on the basis of ^1H NMR analysis.

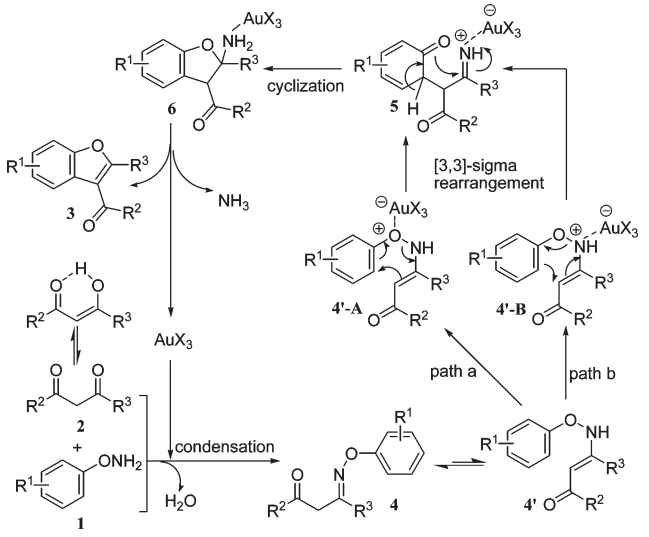
(100% for **3ae**−**h**, entries 5−8; 93% for **3ai**, entry 9). When unsymmetrical dialkyl 1,3-diketone **2j** was subjected to react with **1a**, two regioisomeric products **3aj** and **3′aj** in a ratio of 55:45 were isolated in a total yield of 81% (entry 10). The reactions of β-keto esters with **1a** resulted in regiospecific formation of 3-alkoxycarbonyl-substituted benzofurans in modest yields (45−56%, entries 11−13). In these cases, a small amount of phenol was detected as the minor product. Monoketones as well as their preparative *O*-phenyloxime ethers were also examined for the reaction (entries 14 and 15). Unfortunately, none of the desired product was obtained while phenol was always detected as the major product, suggesting the decomposition of reaction intermediates.

Next, the substitution variation of *O*-arylhydroxylamines **1** was investigated (Table 3). Both para- and ortho-substituted *O*-arylhydroxylamines **1** were able to react with **2a** affording target products in moderate to good yields (entries 1−3 and 5−9). Meta-substituted **1** gave predominantly one isomer within which the carbon at the less sterically hindered

SCHEME 1



SCHEME 2. Proposed Mechanism



position was incorporated into the benzofuran scaffold (>99% for **3ea**, entry 4; 92% for **3ka**, entry 10). Generally, electron-deficient *O*-arylhydroxylamines **1** reacted with **2a** more smoothly than those substituted with electron-donating groups and afforded higher yields of desired products (entries 1−7 vs entries 8−10). A range of functional groups including halo (F, Cl, and Br), methyl, trifluoromethyl, and ester groups were well tolerated under the reaction conditions.

Finally, preliminary mechanistic experiments revealed that the condensation intermediate, i.e. β-phenoxyimino ketone **4aa**, was able to be isolated in 90% yield upon treatment of **1a** and **2a** in nitromethane at 25 °C for 30 min in the presence of 3 mol % of $AuCl_3/3AgSbF_6$. Subsequent employment of **4aa** under the standard reaction conditions for 2 h also afforded the desired product **3aa** in 84% yield (Scheme 1). On the basis of these facts, a proposed mechanism regarding the gold(III)-catalyzed tandem reaction of **1** with **2** is depicted in Scheme 2. First, gold(III)-catalyzed condensation of **1** and **2** formed intermediate **4**,[10] which might be isomerized into **4′** under the reaction conditions.[10a,11] Either the oxygen atom (path a) or the nitrogen atom (path b) in the arylhydroxylamine moiety would coordinate to the cationic Au(III) center and then trigger the [3,3]-σ rearrangement of **4′**.[5h,v,8i] Since electron-deficient *O*-arylhydroxyamines **1** showed better reactivity than their electron-rich counterparts, **4′** undergoing [3,3]-σ rearrangement via path a is more likely to give **5**. Intramolecular annulation of **5** followed by elimination of one molecule of NH_3 from **6** eventually furnished **3**.

In summary, we have developed a unique gold(III)-catalyzed tandem reaction of *O*-arylhydroxyamines with 1,3-dicarbonyl compounds, which furnished a variety of 3-carbonylated benzofuran derivatives with excellent regioselectivity.

Experimental Section

$AuCl_3$ (9.1 mg, 0.03 mmol), $AgSbF_6$ (30.8 mg, 0.09 mmol), and CH_3NO_2 (2 mL) were added to a 10-mL flask in a glovebox. The mixture was stirred at rt for 5 min before a CH_3NO_2 solution (1 mL) of **1a** (1.0 mmol, 0.11 g) and **2a** (1.2 mmol, 0.12 g) was added. Then the reaction mixture was stirred at 90 °C. Upon completion, 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) with petroleum ether−EtOAc (6:1) as eluent to give pure **3aa** (143 mg, 82%). Yellow oil; R_f 0.35 (cyclohexane−EtOAc, 6:1); IR (neat, cm^{-1}) ν 1661; ^1H NMR ($CDCl_3$/TMS, 500 MHz) δ 7.95−7.93 (m, 1H), 7.46−7.44 (m, 1H), 7.33−7.28 (m, 2H), 2.78 (s, 3H), 2.64 (s, 3H); ^{13}C NMR ($CDCl_3$/TMS, 125 MHz) δ 194.3, 162.8, 153.6, 126.1, 124.4, 124.0, 121.4, 117.6, 111.0, 31.2, 15.4; MS (EI, 70 eV) *m*/*z* (%) 174 (40) [M^+], 159 (100). For more details, see the Supporting Information.

Acknowledgment. Financial support from the Natural Science Foundation of Zhejiang Province (No. Y407168), the Foundation of Education of Zhejiang Province (No. Z200803599), and the Opening Foundation of Zhejiang Provincial Top Key Discipline is gratefully acknowledged.

Supporting Information Available: Experimental procedures and characterization data of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

(10) (a) Abbiati, G.; Arcadi, A.; Bianchi, G.; Di Goiseppe, S.; Marinelli, F.; Rossi, E. *J. Org. Chem.* **2003**, *68*, 6959. (b) Arcadi, A.; Bianchi, G.; Di Giuseppe, A.; Marinelli, F. *Green Chem.* **2003**, *5*, 64.

(11) Liu, X.-Y.; Ding, P.; Huang, J.-S.; Che, C.-M. *Org. Lett.* **2007**, *9*, 2645.