Communications

Synthesis of Naphthofuran-2(3*H*)-one Derivatives by Palladium-Catalyzed Three-Component Coupling Using Naphthols, Aldehydes, and Carbon Monoxide

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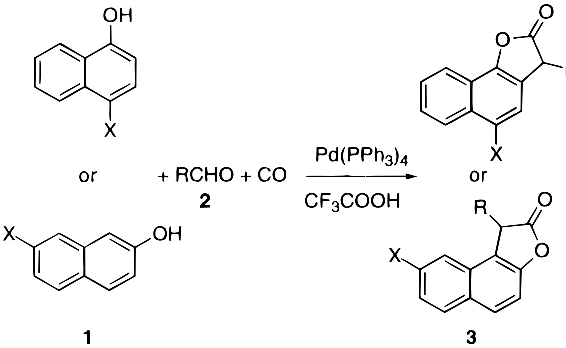
Received June 10, 1996

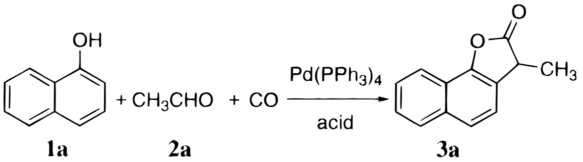
Benzofuranone and isobenzofuranone nuclei are found in various naturally occurring compounds, and a number of their natural and synthetic derivatives are known to exhibit interesting biological properties.[1] Thus, new, effective synthetic routes to them are of considerable interest. Meanwhile, transition metal-catalyzed carbonylation may be one of the most useful strategies for the synthesis of lactones, and indeed, various methods to construct them, including benzofuranones, have been developed;[2] they usually involve intramolecular carbonylative cyclization of halo alcohols or unsaturated alcohols. In the context of our study of synthesis of heterocyclic compounds by means of homogeneous catalysis,[3] we have found that naphthofuran-2(3*H*)-one analogues can be efficiently produced by three-component tandem reaction using 1- or 2-naphthols, aldehydes, and carbon monoxide in the presence of a palladium catalyst (eq 1).



(1)

When a mixture of 1-naphthol (**1a**) (2 mmol) and acetaldehyde (**2a**) (6 mmol) was heated in the presence of $Pd(PPh_3)_4$ (0.05 mmol) in C_6H_6 (5 mL) under CO (5 atm) at 120 °C for 18 h, 3-methylnaphtho[1,2-*b*]furan-2(3*H*)-one (**3a**) was produced in a yield of 32% (entry 1 in Table 1). Addition of CF_3COOH (0.05 mmol) as cocatalyst was found to remarkably enhance the yield of **3a** (97%) (entry 2). Other acids such as CH_3COOH, C_6H_5COOH, and TsOH, however, were not as effective as CF_3COOH (entries 3−5). Furanone **3a** was almost quantitatively produced, when the amount of **2a** was increased to 10 mmol in the presence of CF_3COOH (entry 6).

Table 1. Reaction of 1-Naphthol (1a) with Acetaldehyde (2a) under Carbon Monoxide[a]



entry	acid	yield of **3a** (%)[b]	entry	acid	yield of **3a** (%)[b]
1	none	32	4	C_6H_5COOH	26
2	CF_3COOH	97	5	TsOH	54
3	CH_3COOH	28	6[c]	CF_3COOH	~100

[a] Reaction conditions: **1a** (2 mmol), **2a** (6 mmol), $Pd(PPh_3)_4$ (0.05 mmol), and acid (0.05 mmol) in C_6H_6 (5 mL) under CO (5 atm) at 120 °C for 18 h. [b] Determined by GLC analysis. [c] **2a** (10 mmol) was used.

Table 2 summarizes the results for the reactions of **1a** with aldehydes **2b**−**d** (1−2.5 equiv) and of **1b**−**d** with **2a** (5 equiv) using $Pd(PPh_3)_4$ or a combination of $Pd(OAc)_2$ and PPh_3 in the presence of CF_3COOH. It can be seen that 3-alkyl- and 3-arylnaphthofuran-2(3*H*)-ones **3b**−**g** could be produced in fair to good yields.[4] Note that naphtho[2,1-*b*]furan-2(3*H*)-ones **3f** and **3g** were exclusively formed in the reaction using 2-naphthols **1c** and **1d** as substrates, no [2,3-*b*] isomers being detected. In contrast to the high reactivity of naphthols, treatment of phenol or 4-methoxyphenol with **2a** or **2b** gave no expected coupling product.

The present three-component reaction may involve the initial nucleophilic addition of naphthol **1** to aldehyde **2**, which may be promoted by CF_3COOH, to give dihydroxy intermediate **I**,[5,6] followed by carbonylation under the influence of palladium species used, as depicted in Scheme 1 with **1a** as the representative. The inertness of phenols for this reaction seems to be attributable to the difficulty of the corresponding first step, i.e., nucleophilic addition of phenols to **2** under the conditions employed. Actually, it was confirmed that benzofuranones **5a** and **5b** could be obtained, when 2-hydroxybenzyl alcohols **4a** and **4b** were treated under similar reaction conditions (eq 2). In these reactions, addition of appropriate acids also increased the lactone yield. On the other hand, treatment of 1-(2-naphthyl)ethanol (**6**)

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[1] (a) Anacardio, R.; Arcadi, A.; D'Anniballe, G.; Marinelli, F. *Synthesis* **1995**, 831 and references therein. (b) Ramachandran, P. V.; Chen, G.-M.; Brown, H. C. *Tetrahedron Lett.* **1996**, *37*, 2205 and references therein.

[2] (a) Bahrmann, H.; Cornils, B.; Frohning, C. D.; Mullen, A. *New Syntheses with Carbon Monoxide*; Falbe, J., Ed.; Springer-Verlag: New York, 1980. (b) *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 8. (c) Colquhoun, H. M.; Holton, J.; Thompson, D. J.; Twigg, M. V. *New Pathways for Organic Synthesis*; Plenum: New York, 1984. (d) Coloquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation*; Plenum: New York, 1991.

[3] (a) Okuro, K.; Furuune, M.; Miura, M.; Nomura, M. *J. Org. Chem.* **1993**, *58*, 7606. (b) Miura, M.; Enna, M.; Okuro, K.; Nomura, M. *J. Org. Chem.* **1995**, *60*, 4999. (c) Satoh, T.; Itaya, T.; Okuro, K.; Miura, M.; Nomura, M. *J. Org. Chem.* **1995**, *60*, 7267.

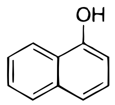
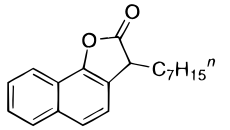
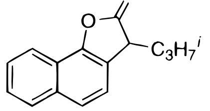
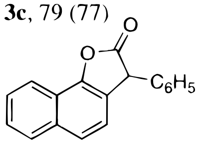
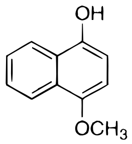
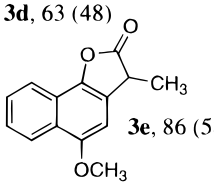
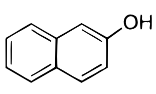
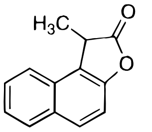
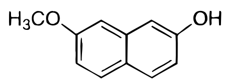
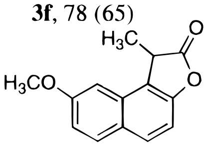
[4] In the reaction with **2b**, a small amount of aldol type dimerization product (<10%) of the aldehyde was detected by GC-MS, suggesting that the side reaction is not significant.

[5] Such a reaction of phenolic compounds with aldehydes is well-known to be catalyzed by acidic species including carboxylic acids, e.g.: (a) Martini, J. C.; Franke, N. W.; Singerman, G. M. *J. Org. Chem.* **1970**, *35*, 2904. (b) Nagata, W.; Okada, K.; Aoki, T. *Synthesis* **1979**, 365.

[6] It has been confirmed by ^1H NMR that a part of $Pd(PPh_3)_4$ is transformed into hydridopalladium species in the presence of an equimolar amount of CF_3COOH in benzene-d_6 at room temperature: Kushino, Y.; Itoh, K.; Miura, M.; Nomura, M. *J. Mol. Catal.* **1994**, *89*, 151. Thus, Pd(II) species such as $(PPh_3)_2Pd(H)(O_2CCF_3)$ could also catalyze the initial reaction.

S0022-3263(96)01087-0 CCC: $12.00

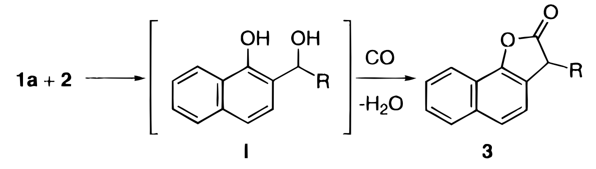
Table 2. Reaction of Naphthols 1a–d with Aldehydes 2a–d under Carbon Monoxide[a]

1	2	product,[b] % yield[c]
 **1a**	$C_7H_{15}{}^nCHO$[d] **2b**	 **3b**, 94 (81)
1a	$C_3H_7{}^iCHO$[e] **2c**	 **3c**, 79 (77)
1a	C_6H_5CHO[f] **2d**	 **3d**, 63 (48)
 **1b**	**2a**	 **3e**, 86 (58)
 **1c**	**2a**	 **3f**, 78 (65)
 **1d**	**2a**	 **3g**, 88 (76)

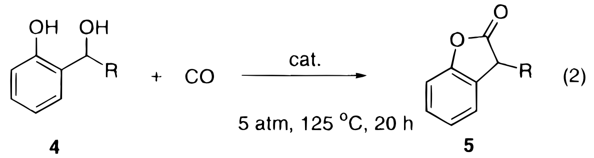
[a] Reaction conditions: **1** (2 mmol), **2** (10 mmol), $Pd(PPh_3)_4$ (0.05 mmol), and CF_3COOH (0.05 mmol) in C_6H_6 (5 mL) under CO (5 atm) at 120 °C for 18 h. [b] All new compounds were characterized by ^1H NMR, IR, and MS data and elemental analyses. [c] GLC yield based on amount of **1** used. Value in parentheses indicates yield after purification. [d] Reaction was carried out using **2b** (3 mmol), $Pd(PPh_3)_4$ (0.1 mmol), and CF_3COOH (0.1 mmol) at 125 °C. [e] Reaction was carried out using **2c** (5 mmol), $Pd(PPh_3)_4$ (0.1 mmol), and CF_3COOH (0.1 mmol) at 125 °C. [f] Reaction was carried out using **2d** (2 mmol) in the presence of $Pd(OAc)_2$ (0.1 mmol) and PPh_3 (0.4 mmol), in place of $Pd(PPh_3)_4$.

in the presence of phenol under carbon monoxide gave no carbonylation products, with only a trace amount of ether **7** being detected.[7] In this example, carbonylation of benzylic alcohols using transition metal complexes is generally recognized to be very difficult, compared with that of the corresponding halides.[2] Thus, it may be considered that, in the present cross-carbonylation of **1** with **2** and the carbonylation of **4** which proceed under relatively mild conditions, the phenolic hydroxyl group in **I** or **4** may play an important role to smoothly form the corresponding key benzylpalladium intermediate.[8]

Scheme 1

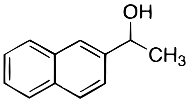


I **3**



4 **5**

	cat.	% yield
4a: R=H	$Pd(PPh_3)_4$	32
	$Pd(PPh_3)_4 + C_6H_5COOH$	59
4b: R=C_6H_5	$Pd(OAc)_2 + 4PPh_3$	90
	$Pd(OAc)_2 + 4PPh_3 + CF_3COOH$	~100



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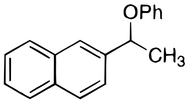

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Acknowledgment. This work was partly supported by a Grant-in-aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, Japan.

Supporting Information Available: Experimental procedure and spectral and analytical data for the new compounds **3a–g** (2 pages).

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(7) In contrast to alcohol **6**, its carboxylate derivatives and α-arylethyl bromides have been reported to be capable of being carbonylated in the presence of palladium catalysts: (a) Baird, J. M.; Kern, J. R.; Lee, G. R.; Morgans, D. J.; Sparacino, M. L. *J. Org. Chem.* **1991**, *56*, 1928. (b) Arzoumanian, H.; Buono, G.; Choukrad, M.; Petrignani, J.-F. *Organometallics* **1988**, *7*, 59.

(8) While the mode of the transformation from **I** or **4** to the corresponding organopalladium species is not definitive at the present stage, it may be reasonable to consider that the functional group accelerates the formation of the benzylic cation which reacts with Pd(0) species to give the key palladium intermediate. The OH group may also act as a ligand to stabilize the intermediate. On the other hand, the possibility that hydridopalladium species formed from Pd(0) species and CF_3COOH also participates in the reaction cannot be excluded.[6]