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Journal of Molecular Catalysis A: Chemical 143 (1999) 203–210

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

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Palladium-catalyzed cross-carbonylation of phenolic compounds with aldehydes to give benzofuran-2(3*H*)-one derivatives

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Received 15 May 1998; accepted 21 August 1998

Abstract

Palladium-catalyzed cross-carbonylation of naphthols and phenols having appropriate substituents with aldehydes in the presence of CF_3COOH as a cocatalyst gives the corresponding benzofuran-2(3*H*)-one derivatives. Under similar conditions, cyclocarbonylation reaction of 2-hydroxybenzyl alcohols also takes place effectively.

Keywords: Carbonylation; Phenol; Aldehyde; Benzofuranone; Palladium

1. Introduction

Since various compounds containing benzofuranone and isobenzofuranone nuclei are known to show interesting biological activities [1,2], the synthesis of these units has currently attracted considerable attention. As generally recognized, transition metal-catalyzed carbonylation is one of the most useful strategies for the synthesis of five-membered lactones [3–7]. Indeed, various methods to construct them have recently been developed [8–17]; they usually involve intramolecular carbonylative cyclization of haloalcohols or unsaturated alcohols. Meanwhile, in the context of our study of palladium-catalyzed reactions using phenolic substrates [18–23], we observed that the carbonylation of allyl alcohols with phenols as nucleophiles could take place under relatively mild conditions in the presence of a palladium catalyst; the use of acetic acid as a cocatalyst was essential for the reaction to proceed smoothly [22]. As depicted in Eq. (1), it has also been found that using a similar catalyst system of $Pd(PPh_3)_4$–CF_3COOH, treatment of 1- or 2-naphthols with aldehydes under carbon monoxide effectively affords naphthofuran-2(3*H*)-one analogues [24]. Furthermore, in the further investigation into this unique three-component tandem reaction with respect to the scope and limitation, certain phenols have also appeared to be able to undergo the reaction to produce the corresponding

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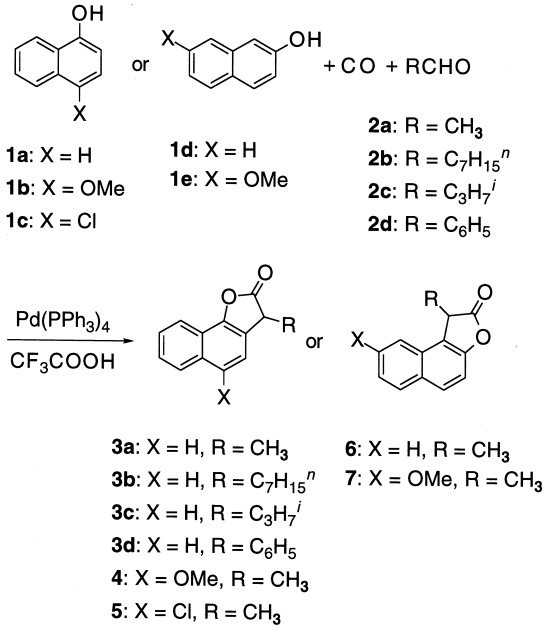
1381-1169/99/$ - see front matter
PII: S1381-1169(98)00388-4

benzofuranones. Details of these studies on the synthesis of furanones are described herein.



(1)

2. Experimental

2.1. Analyses and materials

^{1}H NMR spectra were recorded at 400 or 600 MHz for $CDCl_3$ solutions. MS data were obtained by EI. GLC analysis was carried out using a silicone OV-17 column (i.d. 2.6 mm × 1.5 m) or with a CBP-1 capillary column (i.d. 0.5 mm × 25 m).

The complex $Pd(PPh_3)_4$ [25] and alcohol **12b** [26] were prepared by the methods reported previously. Other starting materials were commercially available.

2.2. General procedure for the cross-carbonylation reaction of naphthols or phenols with aldehydes

A mixture of a naphthol or a phenol (2 mmol), an aldehyde (2–10 mmol), a palladium catalyst (0.05–0.1 mmol), a carboxylic acid (0.02–0.1 mmol), and C_6H_6 (5 ml) was placed in a 50 ml stainless steel autoclave. Then, carbon monoxide (3–10 atm at room temperature) was charged and the mixture was magnetically stirred at 80–160°C for 5–18 h. After cooling, the reaction mixture was poured into water, extracted with ether, and dried over sodium sulfate. Product was isolated by column chromatography on silica gel using hexane–methylene chloride or hexane–ethyl acetate as eluent.

2.3. Reaction of 1-naphthol with aldehydes under oxidative conditions

Cs_2CO_3 was placed in a 100-ml two-necked flask (652 mg, 2 mmol), which was then dried at 150°C in vacuo for 2 h. Then, $Pd(OAc)_2$ (11 mg, 0.05 mmol), PPh_3 (26 mg, 0.1 mmol), 1-naphthol (144 mg, 1 mmol), an aldehyde (1 mmol), bromobenzene (314 mg, 2 mmol), and DMF (5 ml) were added, and the resulting mixture was stirred under N_2 at 120°C for 27–30 h. After cooling, the reaction mixture was extracted with diethyl ether and dried over sodium sulfate. Product was isolated by column chromatography on silica gel using hexane–ethyl acetate as eluent.

2.4. Products

3-Methylnaphtho[1,2-*b*]furan-2(3*H*)-one (**3a**): mp 80–81°C; ^{1}H NMR δ 1.66 (d, 3H, $J = 7.8$ Hz), 3.93 (q, 1H, $J = 7.8$ Hz), 7.37 (d, 1H, $J = 8.3$ Hz), 7.51–7.59 (m, 2H), 7.67 (d, 1H, $J = 8.3$ Hz), 7.88 (dd, 1H, $J = 1.5$, 7.3 Hz), 8.04 (dd, 1H, $J = 1.0$, 8.3 Hz); IR (KBr) 1792 cm^{-1}; MS m/z 198 (M^+). Anal. Calcd. for $C_{13}H_{10}O_2$: C, 78.77; H, 5.09. Found: C, 78.66; H, 5.09.

3-Heptylnaphtho[1,2-*b*]furan-2(3*H*)-one (**3b**): mp 59–60°C; ^{1}H NMR δ 0.85 (t, 3H, $J = 6.8$ Hz), 1.23–1.45 (m, 10H), 2.04–2.09 (m, 2H),3.90 (t, 1H, $J = 6.1$ Hz), 7.36 (d, 1H,

$J = 8.3$ Hz), 7.49–7.57 (m, 2H), 7.65 (d, 1H, $J = 8.3$ Hz), 7.87 (d, 1H, $J = 7.3$ Hz), 8.02 (d, 1H, $J = 8.3$ Hz); MS m/z 282 (M^+). Anal. Calcd. for $C_{19}H_{22}O_2$: C, 80.81; H, 7.85. Found: C, 80.97; H, 7.91.

3-Isopropylnaphtho[1,2-*b*]furan-2(3*H*)-one (**3c**): mp 60–61°C; ^{1}H NMR δ 1.03 (d, 3H, $J = 6.8$ Hz), 1.13 (d, 3H, $J = 6.8$ Hz), 2.54–2.59 (m, 1H), 3.84 (d, 1H, $J = 3.9$ Hz), 7.40 (d, 1H, $J = 8.3$ Hz), 7.51–7.59 (m, 2H), 7.66 (d, 1H, $J = 8.3$ Hz), 7.88 (d, 1H, $J = 8.8$ Hz), 8.04 (d, 1H, $J = 8.3$ Hz); IR (KBr) 1794 cm^{-1}; MS m/z 226 (M^+). Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.58; H, 6.30.

3-Phenylnaphtho[1,2-*b*]furan-2(3*H*)-one (**3d**): mp 129–130°C; ^{1}H NMR δ 5.07 (s, 1H), 7.24–7.39 (m, 6H), 7.54–7.62 (m, 2H), 7.68 (d, 1H, $J = 8.3$ Hz), 7.90 (d, 1H, $J = 7.8$ Hz), 8.09 (d, 1H, $J = 8.3$ Hz); MS m/z 260 (M^+). Anal. Calcd. for $C_{18}H_{12}O_2$: C, 83.06; H, 4.65. Found: C, 83.34; H, 4.61.

5-Methoxy-3-methylnaphtho[1,2-*b*]furan-2(3*H*)-one (**4**): mp 86–87°C; ^{1}H NMR δ 1.65 (d, 3H, $J = 7.3$ Hz), 3.90 (q, 1H, $J = 7.8$ Hz), 4.01 (s, 3H), 6.69 (s, 1H), 7.53 (ddd, 1H, $J = 1.5$, 7.3, 8.8 Hz), 7.59 (ddd, 1H, $J = 1.0$, 6.9, 7.9 Hz), 7.97 (d, 1H, $J = 8.3$ Hz), 8.27 (d, 1H, $J = 8.3$ Hz); IR (KBr) 1794 cm^{-1}; HRMS m/z (M^+) Calcd for $C_{14}H_{12}O_3$: 228.0787. Found: 228.0789. Anal. Calcd. for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.30; H, 5.57.

5-Chloro-3-methylnaphtho[1,2-*b*]furan-2(3*H*)-one (**5**): mp 106.5–107.5°C; ^{1}H NMR δ 1.64 (d, 3H, $J = 7.8$ Hz), 3.92 (q, 1H, $J = 7.8$ Hz), 7.47 (s, 1H), 7.61–7.67 (m, 2H), 8.02–8.07 (m, 1H), 8.25–8.30 (m, 1H); IR (KBr) 1794 cm^{-1}; MS m/z 232, 234 (M^+). Anal. Calcd. for $C_{13}H_9O_2Cl$: C, 67.11; H, 3.90; Cl, 15.24. Found: C, 66.99; H, 4.00; Cl, 15.16.

3-Methylnaphtho[2,1-*b*]furan-2(3*H*)-one (**6**): mp 126–127°C; ^{1}H NMR δ 1.79 (d, 3H, $J = 7.8$ Hz), 4.11 (q, 1H, $J = 7.8$ Hz), 7.36 (d, 1H, $J = 8.8$ Hz), 7.45 (ddd, 1H, $J = 1.0$, 6.8, 8.3 Hz), 7.57 (ddd, 1H, $J = 1.5$, 6.8, 8.3 Hz), 7.77 (d, 1H, $J = 8.3$ Hz), 7.84 (d, 1H, $J = 9.3$ Hz), 7.90 (d, 1H, $J = 8.3$ Hz); IR (KBr) 1794 cm^{-1}; MS m/z 198 (M^+). Anal. Calcd. for $C_{13}H_{10}O_2$: C, 78.77; H, 5.09. Found: C, 78.45; H, 5.14.

5-Methoxy-3-methylnaphtho[2,1-*b*]furan-2(3*H*)-one (**7**): mp 116°C; ^{1}H NMR δ 1.78 (d, 3H, $J = 7.3$ Hz), 3.95 (s, 3H), 4.06 (q, 1H, $J = 7.8$ Hz), 6.99 (d, 1H, $J = 2.5$ Hz), 7.11 (dd, 1H, $J = 2.4$, 8.8 Hz), 7.20 (d, 1H, $J = 8.3$ Hz), 7.75 (d, 1H, $J = 8.8$ Hz), 7.78 (d, 1H, $J = 9.3$ Hz); IR (KBr) 1802 cm^{-1}; MS m/z 228 (M^+). Anal. Calcd. for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.52; H, 5.39.

3-Methyl-5,6-methylenedioxybenzo[*b*]furan-2(3*H*)-one (**9a**): mp 185.5–186°C; ^{1}H NMR δ 1.52 (d, 3H $J = 7.3$ Hz), 3.65 (q, 1H, $J = 7.3$ Hz), 5.96 (s, 2H), 6.67 (s, 1H), 6.71 (s, 1H); IR (KBr) 1809 cm^{-1}; HRMS m/z (M^+) Calcd for $C_{10}H_8O_4$: 192.0423. Found: 192.0416. Anal. Calcd. for $C_{10}H_8O_4$: C, 62.50; H, 4.20. Found: C, 62.44; H, 4.12.

4,5,6-Trimethoxy-3-methylbenzo[*b*]furan-2(3*H*)-one (**9b**): oil.; ^{1}H NMR δ 1.58 (d, 3H, $J = 7.8$ Hz), 3.76 (q, 1H, $J = 7.8$ Hz), 3.82 (s, 3H), 3.86 (s, 3H), 3.97 (s, 3H), 6.49 (s, 1H); ^{13}C NMR δ 15.69, 15.73, 38.03, 56.41, 60.73, 61.18, 91.59, 112.00, 138.25, 149.37, 150.17, 154.51, 178.32; HRMS m/z (M^+) Calcd. for $C_{12}H_{14}O_5$: 238.0841. Found: 238.0836.

4,6-Dimethoxy-3-methylbenzo[*b*]furan-2(3*H*)-one (**9c**): mp 73.5–74.5°C; ^{1}H NMR δ 1.55 (d, 3H, $J = 7.3$ Hz), 3.71 (q, 1H, $J = 7.3$ Hz), 3.81 (s, 3H), 3.82 (s, 3H), 6.23 (s, 1H), 6.32 (s, 1H); ^{13}C NMR δ 15.19, 37.38, 55.47, 55.74, 89.30, 94.26, 107.77, 154.76, 156.71, 161.52, 178.65; HRMS m/z (M^+) Calcd. for $C_{11}H_{12}O_4$: 208.0736. Found: 208.0743.

6-Methoxy-3,4-dimethylbenzo[*b*]furan-2(3*H*)-one (**9d**): mp 61.5–62°C; ^{1}H NMR δ 1.57 (d, 3H, $J = 7.3$ Hz), 2.30 (s, 3H), 3.66 (q, 1H, $J = 7.3$ Hz), 3.79 (s, 3H), 6.48 (s, 1H), 6.53 (s, 1H); ^{13}C NMR $\delta = 15.83$, 18.55, 37.87, 55.56, 94.95, 111.10, 118.90, 135.58, 154.28, 160.13, 178.56; HRMS m/z (M^+) Calcd. for $C_{11}H_{12}O_3$: 192.0786. Found: 192.0786.

4-Methoxy-3,6-dimethylbenzo[*b*]furan-2(3*H*)-one (**10**): oil.; ^{1}H NMR δ 1.55 (d, 3H, $J = 7.8$ Hz), 2.37 (s, 3H), 3.70–3.75 (m, 1H),

3.84 (s, 3H), 6.47 (s, 1H), 6.57 (s, 1H); HRMS m/z (M^+) Calcd. for $C_{11}H_{12}O_3$: 192.0786. Found: 192.0785.

(1-Hydroxy-2-naphthyl)(3-pyridyl)methanone (**11b**): mp 91–92°C; ^{1}H NMR δ 7.26 (d, 1H, $J = 8.8$ Hz), 7.47–7.51 (m, 2H), 7.58 (ddd, 1H, $J = 1.5$, 6.8, 8.3 Hz), 7.68 (ddd, 1H, $J = 1.0$, 6.8, 8.3 Hz), 7.79 (d, 1H, $J = 8.3$ Hz), 8.05 (dt, 1H, $J = 7.8$, 2.0 Hz), 8.54 (d, 1H, $J = 8.3$ Hz), 8.84 (d, 1H, $J = 3.4$ Hz), 8.97 (s, 1H), 13.8 (s, 1H); MS m/z 249 (M^+). Anal. Calcd for $C_{16}H_{11}NO_2$: C, 77.10; H, 4.45; N, 5.62. Found: C, 77.08; H, 4.73; N, 5.51.

Compounds **11a** [27], **13a** [28], and **13b** [29] are known and were compared with those authentic specimens.

3. Results and discussion

3.1. Reaction of naphthols

The reaction of 1-naphthol **1a** (2 mmol) with acetaldehyde **2a** (6 mmol) in the presence of $Pd(PPh_3)_4$ (0.05 mmol) in C_6H_6 under CO (5 atm) at 120°C for 18 h gave 3-methylnaphtho[1,2-*b*]furan-2(3*H*)-one **3a** in a yield of 32% (Entry 1 in Table 1). When CF_3COOH (0.05 mmol) was added to the reaction, the yield of **3a** remarkably increased up to 97% (Entry 2). $PdCl_2/PPh_3$ could also be used in place of $Pd(PPh_3)_4$ (Entry 3). Relatively weaker acids, CH_3COOH and C_6H_5COOH showed essentially no effect on the reaction, and a stronger one, TsOH was less effective than CF_3COOH (Entries 4–6). While an increase in the CO pressure to 10 atm showed no significant influence on the reaction, a decrease to 3 atm somewhat reduced the yield of **3a** (Entries 7 and 8). The reaction temperature also affected the product yield (Entries 2 and 9–11); a maximum yield of **3a** was obtained at 120°C. Furanone **3a** was almost quantitatively produced, when the amount of **2a** was increased to 10 mmol (Entry 12).

Table 1
Reaction of 1-naphthol **1a** with acetaldehyde **2a**[a]

Entry	Acid	Temperature (°C)	CO pressure (atm)	Yield of **3a** (%)[b]
1	-	120	5	32
2	CF_3COOH	120	5	97
3[c]	CF_3COOH	120	5	84
4	CH_3COOH	120	5	28
5	C_6H_5COOH	120	5	26
6	TsOH	120	5	54
7	CF_3COOH	120	3	81
8	CF_3COOH	120	10	96
9	CF_3COOH	80	5	67
10	CF_3COOH	100	5	93
11	CF_3COOH	140	5	82
12[d]	CF_3COOH	120	5	~100

[a]Unless otherwise noted, the reaction was carried out under the following 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) for 18 h.
[b]Determined by GLC analysis based on amount of **1a** used.
[c]$PdCl_2$ (0.05 mmol) and PPh_3 (0.2 mmol) was used in place of $Pd(PPh_3)_4$.
[d]**2a** (10 mmol).

Table 2
Reaction of naphthols with aldehyde[a]

Entry	**1**	**2**	Product (%)[b]
1[c]	**1a**	**2b**	**3b** (94)
2[d]	**1a**	**2c**	**3c** (79)
3[e]	**1a**	**2d**	**3d** (54)
4[e,f]	**1a**	**2d**	**3d** (63)
5	**1b**	**2a**	**4** (86)
6	**1c**	**2a**	**5** (37)
7	**1d**	**2a**	**6** (78)
8	**1e**	**2a**	**7** (88)

[a]Unless otherwise noted, the reaction was carried out under the following 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]Determined by GLC analysis based on amount of **1** used.
[c]**2b** (3 mmol), $Pd(PPh_3)_4$ (0.1 mmol) and CF_3COOH (0.1 mmol) at 125°C.
[d]**2c** (5 mmol), $Pd(PPh_3)_4$ (0.1 mmol) and CF_3COOH (0.1 mmol) at 125°C.
[e]**2d** (2 mmol).
[f]$Pd(OAc)_2$ (0.1 mmol) and PPh_3 (0.4 mmol) was used in place of $Pd(PPh_3)_4$.

Table 2 summarizes the results for the reactions of **1a** with aldehydes **2b–d** (1–2.5 equiv.) and of naphthols **1b–e** 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. When aliphatic or aromatic aldehydes **2b–d** were used in place of **2a**, the corresponding 3-alkyl- and 3-arylnaphthofuran-2(3*H*)-ones **3b–d** were produced in fair to good yields, as was **3a**. In the reaction with **2d**, the use of $Pd(OAc)_2/PPh_3$ gave a somewhat better result than that of $Pd(PPh_3)_4$ (Entry 4 versus 3). The reactions of **1b–e** with **2a** also gave furanones **4–7**. Note that naphtho[2,1-*b*]furan-2(3*H*)-ones **6** and **7** were exclusively formed in the reaction using 2-naphthols **1d** and **1e** as substrates, no [2,3-*b*] isomers being detected.

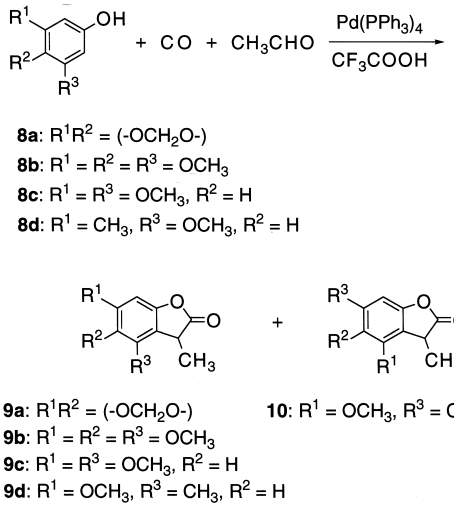
3.2. Reaction of phenols

When 3,4-methylenedioxyphenol **8a** (2 mmol) was treated with **2a** (10 mmol) in the presence of $Pd(PPh_3)_4$ (0.1 mmol) and CF_3COOH (0.1 mmol) in C_6H_6 (5 ml) under CO (5 atm) at 120°C for 18 h, 3-methyl-5,6-methylenedioxybenzo[*b*]furan-2(3*H*)-one **9a** was exclusively produced in a yield of 43% (Eq. (2) and Entry 1 in Table 3). Formation of 3-methyl-4,5-methylenedioxy isomer was not observed, which may be due to steric reasons. In this case, CF_3COOH was also found to be the most effective among the acids examined (Entries 1–4). A decrease in the amount of CF_3COOH to 0.05 mmol slightly enhanced the yield of **9a**, while it was reduced by a further decrease to 0.02 mmol (Entries 5 and 6). When the reaction was carried out at 140°C, both the reaction rate and product yield were considerably enhanced (54% within 5 h; Entry 7). At 160°C, while the reaction was also completed within 5 h, the product was obtained in a lower yield (Entry 8). As for the reaction of **1a** with **2a**, a maximum yield of **9a** was obtained under 5 atm of CO (Entry 1 versus 9 and 10). In contrast to the reaction of **8**, treatment of phenol itself or 4-methoxyphenol with **2a** or **2b** gave no expected coupling product [24]. Consequently, we examined the reaction using phenols bearing two or more electron-donating substituents to obtain other benzofuranone derivatives. As expected, the corresponding furanones **9b** and **9c** were produced from **8b** and **8c**, respectively (Entries 11 and 12). The reaction of **8d** gave a mixture of furanones **9d** and **10** (Entry 13).

Table 3
Reaction of phenols with acetaldehyde **2a**[a]

Entry	**8**	Acid (mmol)	Temperature (°C)	CO pressure (atm)	Product (%)[b]
1	**8a**	CF_3COOH (0.1)	120	5	**9a** (43)
2	**8a**	CCl_3COOH (0.1)	120	5	**9a** (35)
3	**8a**	HCOOH (0.1)	120	5	**9a** (11)
4	**8a**	TsOH (0.1)	120	5	**9a** (35)
5	**8a**	CF_3COOH (0.05)	120	5	**9a** (47)
6	**8a**	CF_3COOH (0.02)	120	5	**9a** (43)
7[c]	**8a**	CF_3COOH (0.05)	140	5	**9a** (54)
8[c]	**8a**	CF_3COOH (0.05)	160	5	**9a** (30)
9	**8a**	CF_3COOH (0.05)	140	10	**9a** (49)
10	**8a**	CF_3COOH (0.05)	140	3	**9a** (30)
11	**8b**	CF_3COOH (0.05)	140	5	**9b** (50)
12	**8c**	CF_3COOH (0.1)	120	5	**9c** (39)
13	**8d**	CF_3COOH (0.05)	140	5	**9d** (39), **10** (15)

[a]Unless otherwise noted, the reaction was carried out under the following conditions: **8** (2 mmol), **2a** (10 mmol), and $Pd(PPh_3)_4$ (0.1 mmol) in C_6H_6 (5 ml) for 18 h.
[b]Determined by GLC analysis based on **8** used.
[c]For 5 h.

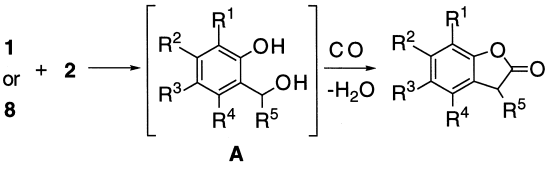


(2)

3.3. Reaction scheme

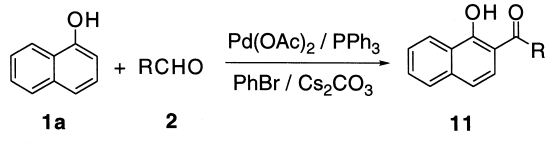
The first step of the three-component reaction may involve nucleophilic addition of naphthol **1** or phenol **8** to aldehyde **2**, which may be promoted by CF_3COOH, to give dihydroxy intermediate **A** (Scheme 1); this may be followed by carbonylation under the influence of palladium species. Such a reaction of phenolic compounds with aldehydes is known to be catalyzed by acidic species including carboxylic acids [30,31].

As a control experiment, a mixture of **1a** (2 mmol) and **2b** (3 mmol) was heated at 120°C under N_2 for 24 h in the absence of the catalyst, formation of an adduct of **1a** to **2b** (ca. 30%) being detected by GC-MS. However, its attempted isolation by column chromatography on silica gel failed; dihydroxy compounds such as **A** are known to be acid-sensitive [31]. Thus, in situ oxidation of an adduct **A** was examined by using bromobenzene as an oxidant [32]. When



Scheme 1.

1a (1 mmol) was treated with **2d** (1 mmol) in the presence of bromobenzene (2 mmol), Cs_2CO_3 (2 mmol), $Pd(OAc)_2$ (0.05 mmol), and PPh_3 (0.1 mmol) in DMF under N_2 at 120°C for 30 h, an adduct of **1a** to **2d**, 2-benzoyl-1-naphthol **11a** was obtained in 63% yield, as expected (Eq. (3)). This may not only support the above mechanism in respect to formation of adduct **A** during the treatment of **1** with **2**, but also suggest that this reaction itself may be applicable to acylation of naphthols. The reaction using 3-pyridinecarboxaldehyde **2e** in place of **2d** also afforded the corresponding ketone **11b** in 54% yield.



	Yield (%)
11a: R = C_6H_5	63
11b: R = 3-pyridyl	54

(3)

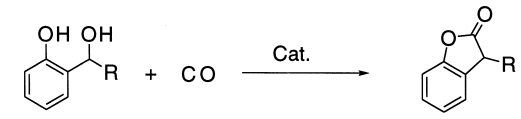
The electron-donating substituents on the phenolic substrates seem to enhance their nucleophilicity to promote the first step [33]. While without such substituents the adduct formation appears to be difficult to occur, naphthols may readily undergo the reaction with aldehydes, since the loss of resonance energy during the reaction course may be less significant than that in the case using phenols. It was confirmed that

Table 4
Carbonylation of 2-hydroxybenzyl alcohols[a]

Entry	12	Catalyst	Product (%)[b]
1	**12a**	$Pd(PPh_3)_4$	**13a** (32)
2	**12a**	$Pd(OAc)_2 + 4PPh_3$	**13a** (25)
3	**12a**	$Pd(PPh_3)_4 + CH_3COOH$	**13a** (40)
4	**12a**	$Pd(PPh_3)_4 + C_6H_5COOH$	**13a** (59)
5	**12a**	$Pd(PPh_3)_4 + CF_3COOH$	**13a** (17)
6	**12b**	$Pd(OAc)_2 + 4PPh_3$	**13b** (90)
7	**12b**	$Pd(OAc)_2 + 4PPh_3 + CF_3COOH$	**13b** (~ 100)

[a] Reaction conditions: **12** (2 mmol), and Pd-catalyst (0.1 mmol) in C_6H_6 (5 ml) under CO (5 atm) at 125°C for 20 h.
[b] Determined by GLC analysis based on **12** used.

simple benzofuranones **13a**,**b**, bearing no electron-donating substituent on the aromatic moiety, could be obtained, when 2-hydroxybenzyl alcohols **12a**,**b** were treated under similar conditions (Eq. (4) and Table 4). In these reactions, addition of appropriate acids also increased the furanone yield. Formation of **13** may suggest that the second step in Scheme 1 does not require electron donating substituents to proceed smoothly.



12a: R = H
12b: R = C_6H_5

13a: R = H
13b: R = C_6H_5

(4)

In contrast to these 2-hydroxybenzyl alcohols **12**, treatment of benzyl alcohol itself in the presence of phenol under carbon monoxide gave no carbonylation products, being recovered both the substrates. As this example, carbonylation of benzyl alcohols using transition metal complexes is generally recognized to be very difficult under halogen free conditions [3–6], though they may be carbonylated in the presence of hydrogen halides such as HCl [34] and HI [35]. Thus, it may be considered that in the present cross-carbonylation of **1** or **8** with **2** and the carbonylation of **12** which proceed under relatively mild conditions, the phenolic hydroxyl group in intermediate **A** or **12** may play an important role to smoothly form the corresponding key benzylpalladium intermediate. While the mode of this transformation is not yet definitive, it is conceivable that the functional group accelerates the formation of the benzylic cation which reacts with Pd(0) species generated in the medium to give the key intermediate. The phenolic function 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, since 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, which has been confirmed by ^1H NMR [36].

References

[1] R. Anacardio, A. Arcadi, G. D'Anniballe, F. Marinelli, Synthesis (1995) 831 and references therein.
[2] P.V. Ramachandran, G.-M. Chen, H.C. Brown, Tetrahedron Lett. 37 (1996) 2205, and references therein.
[3] H. Bahrmann, B. Cornils, C.D. Frohning, A. Mullen, in: J. Falbe (Ed.), New Syntheses with Carbon Monoxide, Springer, New York, 1980.
[4] G. Wilkinson, F.G.A. Stone, E.W. Abel (Eds.), Comprehensive Organometallic Chemistry, Vol. 8, Pergamon, Oxford, 1982.
[5] H.M. Colquhoun, J. Holton, D.J. Thompson, M.V. Twigg, New Pathways for Organic Synthesis, Plenum, New York, 1984.
[6] H.M. Coloquhoun, D.J. Thompson, M.V. Twigg, Carbonylation, Plenum, New York, 1991.
[7] M. Beller, B. Cornils, C.D. Frohnong, C.W. Kohlpaintner, J. Mol. Catal. A: Chemical 104 (1995) 17.
[8] B.E. Ali, K. Okuro, G. Vasapollo, H. Alper, J. Am. Chem. Soc. 118 (1996) 4264.
[9] P. Kalck, R. Naigre, S. Sirol, FR2.721.926 (1996), Chem. Abstr., 124: 317531f.
[10] B. Gabriele, G. Salerno, F. De Pascali, M. Costa, G.P. Chiusoli, J. Chem. Soc., Perkin Trans. 1 (1997) 147.
[11] N.M. Kablaoui, F.A. Hicks, S.L. Buchwald, J. Am. Chem. Soc. 119 (1997) 4424.
[12] W.-J. Xiao, H. Alper, J. Org. Chem. 62 (1997) 3422.
[13] T. Sugioka, E. Yoneda, K. Onitsuka, S.-W. Zhang, S. Takahashi, Tetrahedron Lett. 38 (1997) 4989.
[14] D.Y. Lee, C.S. Cho, L.H. Jiang, X. Wu, S.C. Shim, D.H. Oh, Synth. Commun. 27 (1997) 3449.
[15] M. Brunner, H. Alper, J. Org. Chem. 62 (1997) 7565.
[16] A. Ogawa, H. Kuniyasu, N. Sonoda, T. Hirao, J. Org. Chem. 62 (1997) 8361.
[17] E.-I. Negishi, H. Makabe, I. Shimoyama, G. Wu, Y. Zhang, Tetrahedron 54 (1998) 1095.
[18] K. Itoh, M. Miura, M. Nomura, Tetrahedron Lett. (1992) 5369.
[19] T. Satoh, K. Kokubo, M. Miura, M. Nomura, Organometallics 13 (1994) 4431.
[20] T. Satoh, M. Ikeda, M. Miura, M. Nomura, J. Mol. Catal. A: Chemical 111 (1996) 25.
[21] T. Satoh, T. Itaya, M. Miura, M. Nomura, Chem. Lett. (1996) 823.
[22] T. Satoh, M. Ikeda, Y. Kushino, M. Miura, M. Nomura, J. Org. Chem. 62 (1997) 2662.
[23] M. Miura, T. Tsuda, T. Satoh, M. Nomura, Chem. Lett. (1997) 1103.

[24] T. Satoh, T. Tsuda, Y. Kushino, M. Miura, M. Nomura, J. Org. Chem. 61 (1996) 6476, A preliminary communication of this work.
[25] R.F. Heck, Palladium Reagents in Organic Syntheses, Academic Press, New York, 1985.
[26] J.J. Talley, I.A. Evans, J. Org. Chem. 49 (1984) 5267.
[27] O. Piccolo, L. Filippini, L. Tinucci, E. Valoti, A. Citterio, Tetrahedron 42 (1986) 885.
[28] M. Watanabe, M. Date, K. Kawanishi, T. Hori, S. Furukawa, Chem. Pharm. Bull. 39 (1991) 41.
[29] A. Bistrzycki, J. Flatau, Ber 28 (1895) 989.
[30] J.C. Martini, N.W. Franke, G.M. Singerman, J. Org. Chem. 35 (1970) 2904.
[31] W. Nagata, K. Okada, T. Aoki, Synthesis (1979) 365.
[32] Y. Tamaru, Y. Yamada, K. Inoue, Y. Yamamoto, Z. Yoshida, J. Org. Chem. 48 (1983) 1286.
[33] B.M. Trost, F.D. Toste, J. Am. Chem. Soc. 118 (1996) 6305.
[34] G. Cavinato, L. Toniolo, J. Mol. Catal. 78 (1993) 9.
[35] Y.-S. Lin, A. Yamamoto, Bull. Chem. Soc. Jpn. 71 (1998) 723.
[36] Y. Kushino, K. Itoh, M. Miura, Nomura, J. Mol. Catal. 89 (1994) 151.