ORGANIC
LETTERS

2004
Vol. 6, No. 14
2437−2439

Palladium(II)-Catalyzed Sequential Hydroxylation–Carboxylation of Biphenyl Using Formic Acid as a Carbonyl Source

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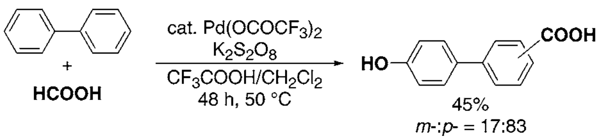
Received May 7, 2004

ABSTRACT



A simultaneous hydroxylation–carboxylation of biphenyl occurred to give 4′-hydroxy-4-biphenylcarboxylic acid, which has wide potential application as a polyester monomer.

The cleavage and functionalization of an unreactive C−H bond by the aid of transition metal catalysts is one of the hottest topics in organic and organometallic chemistry.[1,2] Since their first report in 1967,[3] Fujiwara and co-workers developed the electrophilic subsitution of an aromatic hydrogen atom by palladium(II) under acidic conditions.[1] The resulting organopalladium species, an aryl−Pd σ-complex, reacts with alkenes,[4] carbon monoxide,[5] carbon dioxide,[6] and oxygen, providing a variety of substituted arenes.[7] Here we report our unexpected finding of a simultaneous hydroxylation−carboxylation of biphenyl to provide 4′-hydroxy-4-biphenylcarboxylic acid, which has wide potential application as a polyester monomer. Efficient carboxylation of other aromatic compounds is also presented. The use of formic acid is the key for the present carboxylation reactions.[8,9]

When biphenyl (**1**) was treated with formic acid and $K_2S_2O_8$ in a mixture of trifluoroacetic acid and dichloromethane[10] at 50 °C, using $Pd(OCOCF_3)_2$ as a catalyst,

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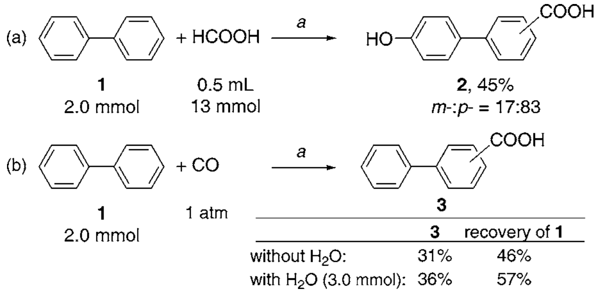
10.1021/ol049166l CCC: $27.50

Scheme 1. Hydroxylation−Carboxylation of Biphenyl (**1**)



	3	recovery of **1**
without H_2O:	31%	46%
with H_2O (3.0 mmol):	36%	57%

[a] $Pd(OCOCF_3)_2$ (20 mol), $K_2S_2O_8$ (6 mmol), CF_3COOH (2 mL), CH_2Cl_2 (1 mL), 48 h, 50 °C, and then treatment with H_2O

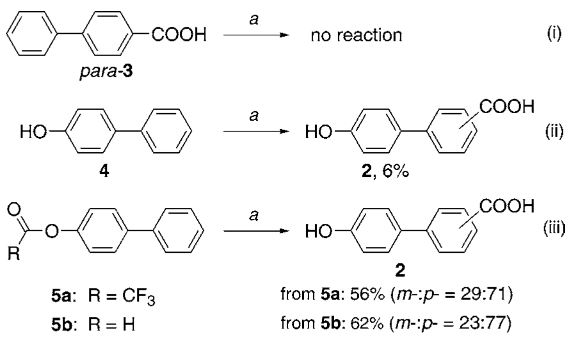
hydroxy-biphenylcarboxylic acid **2** was obtained in 45% (Scheme 1a).[11] This is the first example in which the two reactions, hydroxylation[7] and carboxylation,[5] proceeded simultaneously on one molecule with such high chemoselectivity. The reaction of benzene at 50 °C also gave 4-hydroxybenzoic acid (4% yield), but benzoic acid was the major product (58%). At 40 °C, 4-hydroxybenzoic acid, 2-hydroxybenzoic acid, and benzoic acid were formed in 2, 8, and 17% yields, respectively. From naphthalene, a mixture of 1-hydroxy-5-naphthoic acid (6% yield) and 1-hydroxy-4-naphthoic acid (6% yield) was obtained.

Although decomposition of formic acid into CO and H_2O may be anticipated, the reaction was confirmed to be unique for formic acid on the basis of the following control experiments. Biphenylcarboxylic acid **3**[12] was the major product when **1** was treated with CO (1 atm) instead of formic acid under otherwise the same reaction conditions; no trace of **2** was detected either in the absence or in the presence of water (Scheme 1b).

The reaction temperature was essential for the chemoselectivity. When the reaction of **1** with formic acid was carried out at 40 °C, 4-hydroxybiphenyl (**4**) was the major product (30% yield) and **3** was obtained in 7%. At 80 °C,[13] on the other hand, the simple carboxylation product **3** was obtained in 40% yield. No trace of **2** was found in either case. It is likely that the electrophilic substitution of an aromatic C−H bond by Pd(II) initiates both the hydroxylation and the carboxylation reactions.[1] The temperature dependency of the reaction may be explained as follows: at 40 °C, the aryl−Pd σ-complex intermediate preferentially underwent the oxidation to **4**, and at 80 °C, the aryl−Pd predominantly gave biphenylcarboxylic acid **3**.

The reaction process of the hydroxylation−carboxylation was disclosed by subjecting several possible intermediates to the reaction conditions. The results are summarized in reactions i−iii in Scheme 2. (i) No reaction proceeded with 4-biphenylcarboxylic acid (*para*-**3**). (ii) The carboxylation took place for 4-hydroxybiphenyl (**4**) to give the hydroxycarboxylic acid **2**, but the yield was low (6%). Byproducts due to the oxidative dimerization of **4** lowered the yield of **2**. (iii) 4-Biphenyl esters of trifluoroacetic acid (**5a**) and formic acid (**5b**) provided **2** after aqueous workup in 56 and 62% yields, respectively. These yields are much higher than that from **4** or from **1**. Thus, observations i−iii strongly suggest that, at 50 °C, biphenyl (**1**) was first oxidized to give a protected hydroxybiphenyl either **5a** or **5b**,[14] followed by subsequent carboxylation. The final product **2** was obtained after aqueous workup.

Scheme 2. Control Experiments Using Possible Intermediates **3**−**5**



[a] Substrate **3**, **4**, **5a**, or **5b** (2 mmol), HCOOH (0.5 mL, 13 mmol), $Pd(OCOCF_3)_2$ (20 mol), $K_2S_2O_8$ (6 mmol), CF_3COOH (2 mL), CH_2Cl_2 (1 mL), 48 h, 50 °C, and then treatment with H_2O.

The existence of a trace amount of water, which may possibly be included in or be generated from formic acid, played an essential role for the hydroxylation−carboxylation reaction.[15] Trifluoroacetic anhydride is known to react with water immediately to form trifluoroacetic acid. Thus, when **1** was treated in the presence of 0.25 mL of trifluoroacetic anhydride under otherwise the same reaction conditions as in Scheme 1a, **2** was not given at all but the simple carboxylation product **3** was obtained in 46% yield.

The system is effective not only for the sequential hydroxylation−carboxylation of biphenyl but also for the simple carbonylation of aromatic C−H bonds. The results are summarized in Table 1. Carbonylation of benzene (**6a**) with formic acid was performed in trifluoroacetic acid. Benzoic acid (**7a**) was obtained with a catalyst turnover number (TON) of 106 at 80 °C for 70 h (Table 1, entry 1). The TON is higher than the reported values for the conventional Fujiwara carbonylation with CO.[5c,d] The higher reactivity with ortho−para orientation was observed for electron-rich arenes. This substituent-effect agrees with the electrophilic nature of the reaction.[5] Thus, from toluene (**6b**), regioisomers of toluic acid were obtained in an ortho:meta:para ratio of 25:10:65 (entry 2). The orientation was sensitive to steric factors; cumene (**6c**) and *tert*-butylbenzene (**6d**) afforded the corresponding carboxylic acids with meta−para orientation (entries 3, 4). It is noteworthy that the highest

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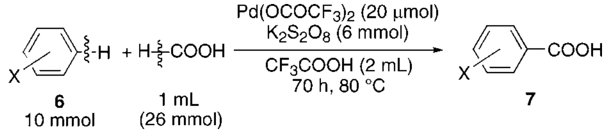
(10) Existence of the cosolvent dichloromethane was essential for obtaining **2**. In the absence of dichloromethane, **1** did dissolve and no reaction took place.

(11) Byproducts were mostly of higher molecular weights, possibly isomers of functionalized biphenyl dimers, as was suggested by size exclusion chromatography.

(12) A mixture of meta and para isomers was obtained. The ortho carbonylated product was obtained not as 2-biphenylcarboxylic acid but as a mixture of benzo[*c*]chromen-6-one and 9-fluorenone. See Supporting Information for details.

(13) 1,2-Dichloroethane was used as a cosolvent instead of dichloromethane.

Table 1. Palladium-Catalyzed Carboxylation of Benzene and Its Derivatives Using Formic Acid as a Carbonyl Source[a]



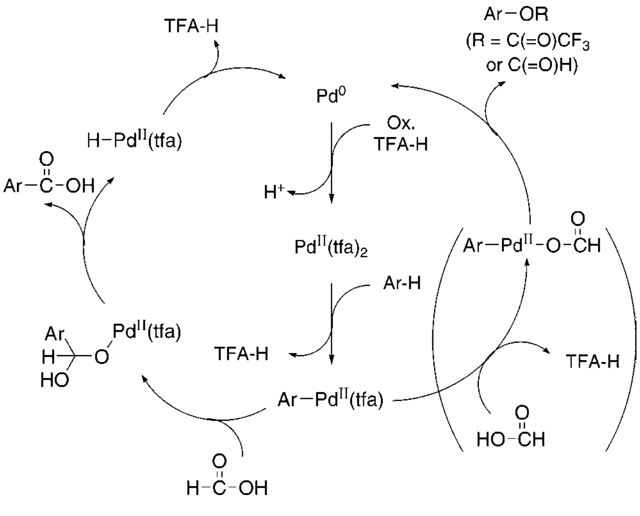
entry	**6** (X)	TON	o:m:p
1	**6a** (H)	106[b]	
2	**6b** (Me)	99[c]	25:10:65
3	**6c** (*iso*-Pr)	30[d]	13:20:67
4	**6d** (*tert*-Bu)	106	0:33:67
5	**6e** (OAc)	130[e]	42:0:58
6	**6f** (I)	36	20:20:60
7	**6g** (Cl)	6	48:20:32
8	**1** (Ph)[f]	120[g]	8[h]:18:74

[a] A mixture of arenes (10 mmol) and formic acid (1 mL, 26 mmol) in trifluoroacetic acid (2 mL) was heated at 80 °C for 70 h in the presence of $Pd(OCOCF_3)_2$ (20 µmol) and $K_2S_2O_8$ (6 mmol). [b] Dimerization product (biphenyl) was not detected. [c] Regioisomers of dimethylbiphenyls were obtained as byproducts with a TON of 22. [d] Complex mixture was produced as byproducts resulting from radical oxidation of **6c**. [e] Products were obtained as hydroxybenzoic acid after aqueous workup. [f] Product was **2**. [g] 4-Hydroxybiphenyl was obtained as a byproduct with a TON of 5. [h] Ortho-carbonylated product was obtained not as 2-biphenylcarboxylic acid but as a mixture of benzo[*c*]chromen-6-one and 9-fluorenone in a ratio of 65:35.

TON (130) was achieved with phenyl acetate (**6e**), which afforded a mixture of *ortho*- and *para*-hydroxybenzoic acid after aqueous workup (entry 5). Aryl halides gave carboxylated products, leaving the halogen−carbon bond untouched (entries 6, 7). Phenol and anisol gave complex mixtures as products, while electron-deficient arenes such as α,α,α-trifluorotoluene and acetophenone were inert under the reaction conditions.

Although the mechanism of neither the hydroxylation nor the carboxylation is clear at this moment, possible reaction pathways are drawn in Scheme 3. Under the reaction conditions, an electrophilic substitution of Pd(II) on an arene is known to give the arylpalladium complex, Ar−Pd(tfa).[1] Reductive elimination of Ar−OR (R = $CF_3C(=O)$ or $HC(=O)$) may proceed from either Ar−Pd(tfa) or Ar−Pd−OCOH[16] (the right half of Scheme 3). Reductive elimination through Pd(IV) species was also proposed.[14b] As an alternative route to $ArOCOCF_3$, metal-catalyzed trifluoroacetoxylation by peracid may be suggested.[17] For the carboxylation, the common intermediate Ar−Pd(tfa) may possibly add to a carbonyl group of formic acid in a nucleophilic manner.[18] The subsequent β-hydride elimination would give the carboxylation product (the left half of Scheme 3). Although the oxidative addition of a formyl C−H to a low-valent metal has been reported,[19] it is less probable to proceed under the current reaction conditions where the electron-deficient Pd(II) predominates. Another possible pathway for the carboxylation is the decomposition of formic acid into CO and H_2O. In fact, the carbonylation of Ar−Pd(tfa) by CO is well-known.[5] However, the decomposition of formic acid was not detected in TFA at 50 °C for 80 h, at least in the absence of palladium. Thus, even if the decomposition of formic acid is the key step for the carbonylation, the decomposition should take place on the Pd metal, and probably, the CO thus produced would directly undergo the carbonylation without being released from the metal center.

Scheme 3. Possible Reaction Pathways for the Hydroxylation−Carboxylation of Biphenyl



In conclusion, we found that the sequential hydroxylation−carboxylation of biphenyl (**1**) provides hydroxybiphenylcarboxylic acid (**2**). The para-substituted isomer, 4′-hydroxy-4-biphenylcarboxylic acid, is an attractive monomer for polyaromatic esters, widely used as engineering plastic with extremely high thermal stability. This new route may be more advantageous than conventional processes, which employ multiple-step methods involving production of hydroxybiphenyl **4**, protection of its hydroxyl group, and then carboxylation of the protected **4**.[20]

Supporting Information Available: Experimental procedure for the hydroxy-carboxylation of **1** and **6a**, the carboxylation of **1** and **6a−g**, control experiments, and characterization of all the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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