

Palladium-catalyzed arylation of styrene and acrylic acid in water

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Received 27 May 1994

Abstract

Palladium-catalyzed arylations of styrene and acrylic acid are shown to occur in the presence of base (Na_2CO_3 or K_2CO_3) in pure water using simple palladium compounds as catalyst precursors.

Keywords: Palladium; Catalysis; Water; Solvent; Aryl

1. Introduction

The use of water as a reaction medium for transition metal catalyzed reactions is very attractive for organic synthesis [1–9], for both economic and safety reasons. Recently we investigated the carbonylation of aryl iodides [10] and the coupling reactions of aryl halides with boronic acids [11] in neat water in the presence of palladium salts PdX_2 without phosphine ligands. The reactions proceeded, under very mild conditions, with high rates and good yields. In this paper we report the first palladium-catalyzed arylation of water insoluble olefins in neat water without organic co-solvents.

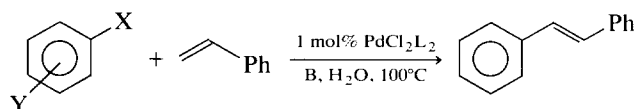
Palladium-catalyzed reaction of olefins with organic halides (Heck reaction) is an important method for carbon–carbon bond formation. These reactions are usually carried out in anhydrous organic solvents [12]. The arylation of olefins has been shown earlier to proceed very smoothly in aqueous-organic media in the presence of $\text{Pd}(\text{OAc})_2$ [15–17], $\text{Pd}(\text{OAc})_2(o\text{-Tol}_3\text{P})_2$ [16,17], or $\text{Pd}(\text{OAc})_2[(m\text{-SO}_3\text{C}_6\text{H}_4)_3\text{P}]_2$ [18]. Water soluble olefins can react with soluble aryl iodides in pure water in the presence of simple palladium salts [16,19]. If both organic reagents are soluble in water, the efficiency of the catalytic system is extremely high (200 000 cycles per palladium atom) in water in the presence of K_2CO_3 [16].

2. Results and discussion

We have studied the possibility of using water as a medium for palladium-catalyzed reactions when both olefin and aryl halide are insoluble in water.

The reaction of styrene with aryl halides catalyzed by 1 mol% $\text{PdCl}_2(o\text{-Tol}_3\text{P})_2$ in an aqueous solution of K_2CO_3 without organic co-solvent has been proved to give poor yields of stilbenes (Table 1, entry 1) owing to low solubility of the base in the organic phase (styrene and aryl iodide). The reaction proceeds smoothly to give stilbene with good yield (Table 1, entry 2) in the presence of Bu_3N as a base instead of K_2CO_3 . The arylation of styrene proceeds in water (Table 1) in the presence of palladium catalyst, K_2CO_3 as a base and the small amount of Bu_3N (10 mol %), method I or Bu_4NBr (5 mol %), method II. The palladium salt $\text{Pd}(\text{OAc})_2$ can be used as a catalyst precursor only for aryl iodides with electron-withdrawing substituents (Table 1, entries 3–5). For less reactive aryl iodides and aryl bromides it is necessary to use the palladium complex with phosphine ligands. We have found that PPh_3 is the efficient ligand in the reaction with bromonitrobenzenes and 5-bromo-2-picoline (Table 1, entries 6, 7, 12), $\text{P}(o\text{-Tol})_3$ for the other arylbromides. It is interesting that the reaction is retarded by addition of organic solvent. For example, the reaction of bromobenzene and styrene occurs in the presence of K_2CO_3 and 5 mol % Bu_4NBr in water:xylene (1:1.26 by volume) to give after 2 h only 6% stilbene (see also Ref. [14]).

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X = Br, I; Y = NH₂, OH, OMe, H, Cl, Br, MeCO,

CHO, NO₂; B = K₂CO₃ + 5 mol % Bu₄NBr

or K₂CO₃ + 10 mol % Bu₃N.

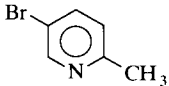
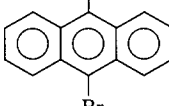
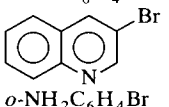
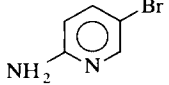
The arylation of acrylic acid proceeds in water without addition of Bu₃N or Bu₄NBr. Both water-soluble and insoluble aryl halides having either electron-withdrawing or electron-donating groups enter the reaction to give substituted cinnamic acids with high yields without any by-product formation (Table 2). It is important that simple palladium salts PdCl₂ and Pd(OAc)₂ can be used as catalyst precursors, and Na₂CO₃ as a base. Even in the case of aryl bromides with electron-donating groups the reaction proceeds in the pres-

ence of catalyst without phosphine ligands. There is no noticeable difference in reactivity between aryl iodides and bromides. We have also shown that even palladium black can be used as a catalyst (Table 1, entry 7). In water the reactivity of Pd-black in the oxidative addition to ArX is increased because the ligand environment of palladium appears to consist of such ligands as OH⁻, HCO₃⁻, CO₃²⁻, X⁻. It is probably the hydrophilicity of these ligands that enables insoluble substrates to react with water-soluble olefins, since the intermediate ArPdXL_n might act as a phase-transfer agent. However, such a catalytic system appears to be completely inactive when applied to water-insoluble styrene (Table 1, entry 1).

3. Experimental section

The palladium complexes Pd(OAc)₂, PdCl₂(PPh₃)₂, PdCl₂[P(*o*-Tol)₃]₂ and aryl halides were prepared by

Table 1
Reaction of ArX with Styrene (1.5 equiv), Catalyst (1 mol%), H₂O, 100°C, Argon

Entry	ArX	Catalyst ^a	Base ^b	t, h	Yield of (E)-ArCH=CHC ₆ H ₅ % ^c
1 ^d	PhBr	A	–	2	6
2 ^e	PhBr	A	–	2.5	85
3	<i>p</i> -O ₂ NC ₆ H ₄ I	B	I	7	(81)
4	<i>p</i> -ClC ₆ H ₄ I	B	I	10	75
5	<i>p</i> -MeOC ₆ H ₄ I	B	I	14	84
6	<i>o</i> -O ₂ NC ₆ H ₄ Br	C	I	3	93 (80)
7	<i>p</i> -O ₂ NC ₆ H ₄ Br	C	I	3	88 (80)
8	<i>p</i> -AcC ₆ H ₄ Br	A	I	2	(90)
9	<i>p</i> -ClC ₆ H ₄ Br	A	I	5	(90)
10 ^f	<i>p</i> -BrC ₆ H ₄ Br	A	I	6	(85)
11	<i>p</i> -MeOC ₆ H ₄ Br	A	I	6	86
12	Br-  -CH ₃	C	I	7	(75)
13 ^f	Br-  -Br	A	I	3	(97)
14	PhBr	A	II	2	86
15	<i>p</i> -MeC ₆ H ₄ Br	A	II	4	86 (71)
16	<i>m</i> -HOC ₆ H ₄ Br	A	II	5	74 (60)
17	Br-  -Br	A	II	2	87 (69)
18 ^g	<i>o</i> -NH ₂ C ₆ H ₄ Br	A	–	4	75 (64)
19 ^g	NH ₂ -  -Br	A	–	5	(70)

^a A = PdCl₂ + 4P(*o*-Tol)₃ or PdCl₂[P(*o*-Tol)₃]₂ + 2P(*o*-Tol)₃; B = Pd(OAc)₂; C = PdCl₂(PPh₃)₂.

^b I. 10 mol % Bu₃N, 1.5 equiv K₂CO₃ or Na₂CO₃; II. 5 mol % Bu₄NBr, 1 equiv K₂CO₃.

^c Yield determined by GLC or TLC and UV-spectroscopy, isolated yields are given in parentheses. Minor amounts of (Z)-ArCH=CHC₆H₅ were observed (5–10%). Products were characterized by UV, ¹H, ¹³C NMR spectroscopy and elemental analysis.

^d K₂CO₃, H₂O;

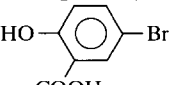
^e 1.5 equiv Bu₃N, H₂O;

^f both bromine atoms were displaced;

^g DMF:H₂O = 1:2.5 (by volume), 1 equiv K₂CO₃.

Table 2

Reaction of ArX with $\text{CH}_2=\text{CHCOOH}$ (1.5 equiv), Na_2CO_3 (3 equiv), 1 mol% PdCl_2 , H_2O , 100°C , Argon

Entry	ArX	<i>t</i> , h	Isolated yield of (E)-ArCH=CHCOOH, %
1	<i>p</i> -AcC ₆ H ₄ I	1	88
2	<i>p</i> -ClC ₆ H ₄ I	6	74
3	<i>p</i> -MeOC ₆ H ₄ I	3	66
4	<i>p</i> -MeC ₆ H ₄ I	5	54
5 ^a	<i>p</i> -O ₂ NC ₆ H ₄ I	3	93
6 ^c	PhI	3	88
7 ^b	PhI	3	89
8	<i>p</i> -O ₂ NC ₆ H ₄ Br	3	94
9	<i>p</i> -OHCC ₆ H ₄ Br	3	92
10 ^c	<i>p</i> -AcC ₆ H ₄ Br	5	93
11 ^c	<i>p</i> -MeOC ₆ H ₄ Br	10	91
12 ^c	<i>m</i> -HO ₂ CC ₆ H ₄ Br	2	86
13		5	70
14	<i>p</i> -HOCC ₆ H ₄ Br	2	65

^a 1 mol% $\text{Pd}(\text{OAc})_2$; ^b 1 mol% Pd-black; ^c reaction carried out without argon.

standard procedures. Analytical grade Na_2CO_3 and K_2CO_3 were used. Acrylic acid, styrene, DMF and water were distilled before use. The yields of the products were determined by TLC on Silufol-254 and UV-spectroscopy (Hitachi-124 spectrophotometer). The isolated products were characterized by UV, ^1H , ^{13}C NMR spectroscopy and elemental analysis.

3.1. Synthesis of substituted stilbenes

3.1.1. 2-Styryl-5-methylpyridine

1 mmol (0.172 g) 2-bromo-5-methylpyridine, 1.5 mmol (0.156 g) styrene, 10 mol % Bu_3N (0.024 ml) and 0.01 mmol (0.007 g) $\text{PdCl}_2(\text{PPh}_3)_2$ were placed in 25 ml round bottom flask 1.5 mmol K_2CO_3 and 1.5 ml H_2O was added to the slurry. The mixture was stirred vigorously at 100°C under argon. The reaction mixture was tested by TLC to check for the completion of the reaction. After 7 h the mixture was treated with dilute HCl and extracted with 3×5 ml of ether. The ether layer was dried over MgSO_4 and then evaporated and recrystallized to give 0.145 g (75% yield) of 2-styryl-5-methylpyridine, mp. 70°C . Anal. Calc. for $\text{C}_{14}\text{H}_{13}\text{N}$: C 86.15, H 6.67, N 7.18. Found: C 86.33, H 6.82, N 7.16%. ^1H -NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$, δ , ppm): 7.20–7.40 (m, 6H, 5H Ph, H Ph–CH=CH–), 7.60 (m, 2H, 3,4H pyridine), 7.91 (d, H, 8 Hz, Ph–CH=CH–), 8.62 (s, H, 1H pyridine).

9,10-Distyrylanthracene was prepared by the method described above and was recrystallized from *o*-xylene to give 97% yield, m.p. $275\text{--}276^\circ\text{C}$. Anal. calc. for

$\text{C}_{30}\text{H}_{22}$: C 94.24, H 5.76. Found: C 93.96, H 5.93%. ^1H -NMR (400 MHz, CDCl_3 , δ): 6.92–6.99 (d, 2H, 16 Hz, Ph–CH=CH–), 7.38 (t, 2H, 4,4'-2H, Ph), 7.48 (m, 8H, 2,3,5,6,2',3',5',6'-8H, Ph), 7.68–7.74 (d, 4H, 2,3,6,7H anthracene), 7.92–7.98 (d, 2H, 16 Hz, Ph–CH=CH–), 8.41 (m, 4H, 1,4,5,8H anthracene).

3.1.2. 3-Styrylphenol

$\text{PdCl}_2[\text{P}(o\text{-Tol})_3]_2$ 0.01 mmol (0.0079 g), $\text{P}(o\text{-Tol})_3$ 0.02 mmol (0.0061 g), styrene 2 mmol (0.208 g), 1.26 ml 1.6 M K_2CO_3 solution in H_2O and Bu_4NBr 0.05 mmol (0.0161 g) were added to 1 mmol (0.416 g) 3-bromophenol. The reaction mixture was stirred vigorously at room temperature (15 min) and then at 100°C under argon. After 5 h it was treated with water and extracted with ether. The yield of (E)-3-styrylphenol (74%) was determined by TLC and UV-spectroscopy. The solvent was removed and the residue was dissolved in dilute solution of NaOH. The solution was filtered and was treated with dilute HCl until it was acidic to litmus. The precipitate was filtered and recrystallized (aqueous EtOH) to give 0.117 g (60% yield) of (E)-3-styrylphenol, m.p. $121\text{--}122^\circ\text{C}$ [20]. ^1H -NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$, δ , ppm): 6.77 (d, 1H, 6 H Ar), 7.08 (m, 2H, 2,4 H Ar), 7.17 (m, 3H, –CH=CH–, 5 H Ar), 7.25 (t, 1H, 4 H Ph), 7.35 (t, 2H, 3,5, H Ph), 7.57 (d, 2,6 H Ph), 8.39 (s, 1H, OH). ^{13}C -NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$, δ , ppm): 113.89, 115.61, 118.89, 127.28, 128.33, 129.25, 129.45, 130.46, 138.26, 139.71, 158.54.

The properties of the stilbenes (Table 1) are consistent with published data for *p*-nitrostilbene [21], *o*-nitrostilbene [22], *p*-chlorostilbene [23], *p*-acetylstilbene [24], *p*-methylstilbene [25], *o*-aminostilbene [21], *p*-distyrylbenzene [26], 3-styrylquinoline [27].

3.1.3. 2-Amino-5-styrylpyridine

2 mmol (0.346 g) 2-amino-5-bromopyridine, 3 mmol (0.313 g) styrene, 1.26 ml 1.6 M K_2CO_3 solution in H_2O , 0.5 ml DMF, 0.02 mmol (0.0157 g) $\text{PdCl}_2[\text{P}(o\text{-Tol})_3]_2$, 0.04 mmol (0.0122 g) $\text{P}(o\text{-Tol})_3$ were placed in a 25 ml round bottom flask. The reaction mixture was stirred vigorously at room temperature (15 min) and then at 100°C under argon. After 5 h it was treated with water and extracted with benzene. The benzene solution was treated with pentane. The precipitate was filtered, recrystallized (acetone : H_2O = 3 : 2) and dried under vacuum to give 0.27 g (70% yield) of (E)-2-amino-5-styrylpyridine (yellow crystals), m.p. $199\text{--}200^\circ\text{C}$. Anal. Calculated for $\text{C}_{13}\text{H}_{12}\text{N}_2$: C 79.59, H 6.12, N 14.29. Found: C 79.72, H 6.10, N 13.98%. ^1H -NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$, δ , ppm): 5.56 (s, 2H, NH_2), 6.57 (d, 1H, 3 H pyridine), 7.00 (d, 1H, Ph–CH=CH–, J = 16.6), 7.11 (d, 1H, Ph–CH=CH–, J = 16.5), 7.20–7.52 (m, 5H, 5 H Ph), 7.73 dd, 1H, 4 H pyridine, J = 8.8, J = 2.4), 8.12 (d, 1H, 6 H pyridine, J = 2.4). ^{13}C -NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$, δ , ppm):

107.06, 121.43, 123.62, 124.74, 124.86, 125.73, 127.45, 132.73, 136.91, 146.88, 158.24.

3.2. Synthesis of substituted cinnamic acids

3.2.1. 3-Carboxy-4-hydroxycinnamic acid

1 mmol (0.217 g) 5-brom-2-hydroxybenzoic acid, 3.9 ml H₂O, 1.9 ml 1.6 M Na₂CO₃ solution in H₂O, 1.5 mmol (0.108 g) acrylic acid and 0.1 ml 0.1 M solution PdCl₂ (0.0018 g, 0.01 mmol) in H₂O were placed in a 25 ml round bottom flask. The reaction mixture was stirred vigorously at room temperature (15 min) and then at 100°C under argon. After 7 h it was cooled, filtered and the filtrate was treated with dilute HCl until it was acidic to litmus. The precipitate was filtered and dissolved in DMSO. The solution was filtered through a bed of silica gel and treated with H₂O. The precipitate was filtered, washed in 3 × 5 ml of water and dried under vacuum to give 0.145 g (70% yield) of 3-carboxy-4-hydroxycinnamic acid, m.p. 240°C (dec.). Anal. calc. for C₁₀H₈O₅: C 57.69, H 3.85. Found: C 57.93, H 3.93%. ¹H-NMR (400 MHz, DMSO-*d*₆, δ, ppm): 6.35 (d, 1H, HO₂C–CH=CH–, *J* = 16.0), 6.94 (d, 1H, 5 H Ar, *J* = 8.6), 7.52 (d, 1H, HO₂C–CH=CH–, *J* = 16.0), 7.82 (d, 1H, 6 H Ar, *J* = 8.7), 7.97 (s, 1H, 2 H Ar). ¹³C-NMR (400 MHz, DMSO-*d*₆, δ, ppm): 114.13, 118.13, 118.69, 126.38, 131.74, 135.20, 143.69, 163.31, 168.43, 172.27.

The properties of the cinnamic acids (Table 2) are consistent with published data for cinnamic acid [28], *p*-acetylcinnamic acid [29], *p*-chlorocinnamic acid [30], *p*-methoxycinnamic acid [29], *p*-methylcinnamic acid [29], *p*-formylcinnamic acid [31], *p*-nitrocinnamic acid [29], *m*-carboxycinnamic acid [29].

Acknowledgements

The research described in this publication was made possible in part by grant NM44000 from the International Science Foundation and by a grant from the Russian Fundamental Research Foundation.

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