Palladium-Catalyzed Coupling Reaction of Aromatic Compounds

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The oxidative coupling reaction of aromatic compounds proceeds catalytically with palladium salt under oxygen pressure. Yields and isomer distributions are attributed to the reaction variables such as temperature, additives, and the nature of the substituent on a benzene ring. Naphthalene was converted mainly into 1-substituted products and *o*-xylene into 4-substituted products. The coupling of diphenyl ether afforded diphenylene oxide with coupling dimers. An intramolecular two stage dehydrogenation process is proposed.

Palladium compounds have recently attracted much attention from the viewpoint of synthetic organic chemistry and theoretical interest.[1] Van Helden and Verberg[2] reported on the oxidative coupling of benzene derivatives by palladium chloride and sodium acetate in acetic acid solution. Subsequent studies by Davidson and Triggs[3] showed no precipitation of metallic palladium under oxygen pressure. No coupling proceed catalytically since excess acetic acid existed in the reaction system. We have reported[4] on the palladium-catalyzed coupling reaction of styrene with benzene under oxygen pressure in the absence of acetic acid. This paper gives a detailed description of the palladium-catalyzed coupling of aromatic compounds.[5]

Results

Coupling of Alkylbenzenes. Coupling of toluene gave six isomers, 2,2'-, 2,3'-, 2,4'-, 3,3'-, 3,4'-, and 4,4'-dimethylbiphenyls. Yields and isomer distributions of bitolyls at several temperatures are given in Table 1. *Meta*-substituted bitolyls were major products and the yield of *ortho*-substituted bitolyls increased with increasing temperature. However, the system of palladium chloride and sodium acetate[6] accelerated the formation of *ortho*-substituted bitolyls with decreasing temperature. The difference may be due to the reaction process. The former is a catalytic reaction whereas the latter is stoichiometric, precipitating palladium black during the course of reaction. Methyl group shows a high degree of steric effect on the coupling. Namely, yields of biaryls at 150 °C were 7500, 5700, 4100, 400, and zero percent from toluene, *o*-xylene, *m*-xylene, *p*-xylene, and mesitylene as starting material, respectively. The coupling product of *o*-xylene consisted of 1% of 2,3,2',3'-, 24% of 2,3,3',4'-, and 75% of 3,4,3',4'-tetramethylbiphenyls, whereas that of naphthalene contained 43% of 1,1'-, 50% of 1,2'-, and 7% of 2,2'-binaphthyls. The former is contributed by steric requirement and the latter by electronic factor.

Table 1. Yield and isomer distribution of dimethylbiphenyl[a]

Reation		Compositions (%)						
Temp. °C	Press. kg/cm²	2,2'	2,3'	2,4'	3,3'	3,4'	4,4'	yield[c] (%)
120	50	2	12	8	31	36	11	1840
150	50	2	13	10	28	35	12	5140
180	50	2	19	13	24	30	12	2270
120	13	2	17	13	28	31	9	480
150[b]	50	2	12	8	32	34	12	7500

a) Carried out with $Pd(OAc)_2$ (0.5 mmol) and toluene (50 ml).
b) Acetylacetone (0.5 mmol) was added.
c) Based on $Pd(OAc)_2$ used.

Table 2. Effect of palladium compounds on coupling of toluene[a]

Pd compound	Bitolyl yield %[b]
$Pd(OAc)_2$	5140
$Pd(OAc)_2$ + acetylacetone	7400
$Pd(acac)_2$	5400
$Pd(OAc)_2(PPh_3)_2$	1700
$Pd(PPh_3)_4$	310
$PdCl_2$ + KOAc (1 : 5)	200

a) Carried out with Pd compound (0.5 mmole), toluene (50 ml).
b) Based on Pd compound used.

Table 3. Effect of β-diketone on coupling of dimethyl phthalate[a]

β-Diketone	Biaryl yield %[b]
Acetylacetone	5200
Benzoylacetone	3600
Trifluoroacetylacetone	3070
Ethyl acetoacetate	3000
——	2130
Acetoacetanilide	1570
Salicylaldehyde	500

a) Carried out with $Pd(OAc)_2$ (1 mmol), β-diketone (1 mmol), dimethyl phthalate (100 ml) and O_2-N_2 (1 : 1) (50 kg/cm²) at 150°C for 6 hr.
b) Based on $Pd(OAc)_2$ used.

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Effect of Palladium Compounds. Various palladium compounds can be used as catalyst (Table 2). Palladium acetylacetonate as well as palladium acetate are effective catalysts. Tetrakis(triphenylphosphine)palladium shows lower activity, precipitating palladium metal during the course of reaction.

Effect of Additives. Addition of an equimolar amount of acetylacetone to palladium acetate increased the yield of the coupling products (Tables 1 and 2). The influence of several β-diketones on the yield of bitolyl is shown in Table 3. Acetylacetone highly activated palladium acetate for the coupling.

Effect of Reaction Variables. Increase in oxygen pressures increases the yields of coupling products but not pressure above 25 kg/cm^2. Under 50 kg/cm^2 of the mixture of nitrogen and oxygen (1 : 1), use of less than 10 mmol/l of palladium acetate is recommended since the overall yield of biaryls does not increase in the presence of excess palladium acetate. Addition of solvent to this system remarkably decreased the yield of coupling products. However, mesitylene or butyl acetate can be applied in as little an amount as possible for the coupling of high melting compounds such as anthracene, phenanthrene, and acenaphthene.

Coupling of Diphenyl Ether. Diphenyl ether was considerably converted into diphenylene oxide, an intramolecular coupling product, with dimerized products. However, the reaction of diphenylmethane involved a small amount of fluorene, an intramolecular coupling product, with dibenzylbiphenyl, benzophenone, and fluorenone. The coupling of anisole gave dimethoxybiphenyl containing only 2% of *ortho*-disubstituted isomer (Table 4).

TABLE 4. COUPLING OF DIPHENYL ETHER AND THE RELATED DERIVATIVES[a]

Aromatic compound	Products	Yield %[b]
Diphenyl ether	Diphenylene oxide	3080
	Dimers of diphenyl ether	4610
Diphenylmethane	Fluorene	340
	Dimers of diphenylmethane	5010
	Benzophenone	4120
	Fluorenone	230
Anisole[c]	Dimethoxybiphenyl[d]	740

a) Carried out with $Pd(OAc)_2$ (0.15 mmol), acetylacetone (0.15 mmol), aromatic compound (15 ml).
b) Based on $Pd(OAc)_2$ used.
c) Reaction temperature, 120°C.
d) The compositions are 2,2'- 2%, 2,3'- 10%, 2,4'- 21%, 3,3'- 17%, 3,4'- 29%, 4,4'- 21%.

Discussion

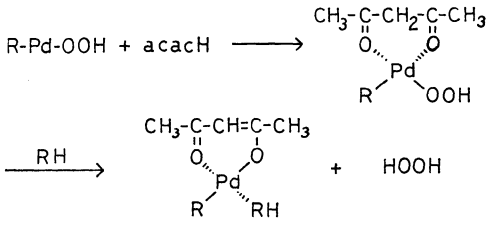
Davidson and Triggs[3] proposed an intermolecular coupling process of σ-phenylpalladium(II) complex on the basis of isolation of palladium(I) complex and measurement of kinetic isotope effect. Unger and Fouty[6] suggested the intramolecular reaction through a diarylpalladium(II) complex for explaining the isomer distribution of bitolyls.

Under oxygen pressure in the absence of acetic acid the coupling reaction is catalytic and thus the yield of biaryl was greatly enhanced. In this system, palladium remaining in the solution can be reoxidized to its active oxidation state by the action of molecular oxygen.

Oxygen adduct complex $Pd(PPh_3)_2O_2$[7,8] takes part in the oxidation of the coordinating triphenylphosphine to triphenylphosphine oxide. Stern[9] explained the mechanism by assuming that the oxygen adduct palladium(0) complex serves to abstract hydrogen from aromatic nucleus and concurrently changes to a σ-arylpalladium(II) complex. By applying this mechanism, the overall process for the palladium-catalyzed coupling can be represented as follows.

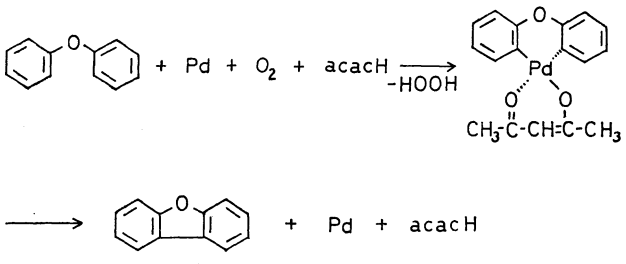
$$PdX_2 + 2RH \longrightarrow R\text{-}Pd\text{-}R + 2HX$$
$$R\text{-}Pd\text{-}R \longrightarrow R\text{-}R + Pd$$
$$Pd + O_2 + RH \longrightarrow R\text{-}Pd\text{-}OOH$$
$$R\text{-}Pd\text{-}OOH + acacH \longrightarrow R\text{-}Pd\text{-}acac + HOOH$$
$$R\text{-}Pd\text{-}acac + RH \longrightarrow R\text{-}Pd\text{-}R + acacH$$

where RH denotes an aromatic compound, and acacH acetylacetone. The key step of the mechanism is a reoxidation of palladium(0) with molecular oxygen. The effect of addition of acetylacetone to this system may be explained by assuming the formation of a stable *cis*-diaryl palladium complex which is active on subsequent coupling in analogy with *cis*-hydroxo-olefin complex[1b] known in the Wacker process.



The two stage coupling mechanism was proposed based on the primary isotope effects[10] in the competitive coupling between benzene and benzene-d_6 and also the characteristic isomer distributions of biaryls.

Isomer distribution of the coupling products changes remarkably with the substituent. The coupling of *o*-xylene is attributed to steric effect of methyl group while naphthalene is influenced by polar effect. The



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reaction of diphenyl ether affords an intramolecular ring closure which is facilitated *via* a stable transition state of a six π electron system, whereas the reaction of diphenylmethane does not favor a ring formation.

The possibility exists that biphenyl formation may involve homolytic substitution of phenyl radical.[11] However, it is well-known that a radical can not exist in the presence of oxygen. The presence of excess 2,6-di-*tert*-butyl-*p*-cresol does not influence the coupling at all. Thus the reaction mechanism involving free radicals is unlikely.

In contrast to the Wacker process and acetoxylation of olefins, the palladium-catalyzed oxidative coupling is markedly inhibited in the presence of mineral acid, polar solvent, sodium acetate, lithium chloride, and some metal ions. The coupling process favors the simple system consisting of palladium acetate and aromatic compounds under oxygen pressure. For prevention of explosion, oxygen should be diluted with an inert gas.

Experimental

Palladium acetate,[12] palladium acetylacetonate[13] and tetrakis(triphenylphosphine)palladium[8] were prepared according to literatures. Palladium chloride (Nippon Engelhald Co.) and a gaseous mixture of oxygen and nitrogen (1 : 1) (Nippon Sanso Co.) were used. Benzene, toluene, and *o*-xylene were distilled before use. Other chemicals were reagent grade and were used without further purification.

Bis(triphenylphosphine)palladium Acetate. To a stirred solution of palladium acetate (0.224 g) in ether (25 ml) was added a solution of triphenylphosphine (0.786 g) in ether (25 ml). After stirring at room temperature for 1 hr, yellow precipitates formed were collected, washed with ether and dried, mp 118—120 °C. Found: C, 64.77; H, 4.99%. Calcd for $C_{40}H_{36}O_4P_2Pd$: C, 64.14; H, 4.84%.

General Procedure. In a glass vessel (250 ml) were placed palladium acetate, acetylacetone, aromatic compound and some additives when necessary. The glass vessel was inserted into a stainless steel autoclave (300 ml) and subjected to a pressure of 50 kg/cm^2 with a gaseous mixture of oxygen and nitrogen (1 : 1) at room temperature. The autoclave was heated at 150 °C for 4 hr with shaking 35 times per minute. After cooling, the filtrate was analyzed with a Shimadzu GC 4APT gas chromatograph on silicone SE 30 (20% on Diasolid, 1 m long) and Apiezon L (5% on Diasolid, 2 m long) columns using helium as a carrier gas. Products were identified with authentic samples by glc and also by comparison of their melting points (if isolated), IR and mass spectra.[14]

Coupling Reaction of Diphenyl Ether. The reaction was carried out in an autoclave (100 ml). The resulting products were analyzed by glc (SE 30 column). Stilbene was used as an internal standard for diphenylene oxide, and pyrene was used for the coupling dimers. The fraction boiling at 200—240 °C/1 mmHg was collected from the reaction mixture. The mass spectrum shows the molecular ion at *m/e* 338 which is consistent with the dimer of diphenyl ether.

Coupling of Naphthalene. A mixture of naphthalene (50 g), palladium acetate (0.112 g), and acetylacetone (0.050 g) was shaken at 150 °C for 4 hr. The resulting solution was analyzed by glc (SE 30 column) at 240 °C. Triphenylethylene was used as an internal standard. Binaphthyl was obtained in 4500% yield based on palladium acetate used. The composition was shown to be 43% of 1,1′-, 50% of 1,2′-, and 7% of 2,2′-binaphthyls. After removal of naphthalene by distillation, the residue was chromatographed over alumina using benzene as a solvent. Evaporation of benzene gave 6.9 g of crude binaphthyls which was extracted with hot methanol (110 ml) to afford 1,1′-binaphthyl (1.4 g) having mp 157—158 °C. After recrystallization from ethanol, mass spectroscopy showed the molecular ion 254 identical with 1,1′-binaphthyl. The residue was again treated with a mixture of benzene (25 ml) and ethanol (75 ml). The undissolved material (0.3 g) was collected by filtration. Recrystallization from benzene gave 2,2′-binaphthyl mp 182—183 °C. Mass spectroscopy showed the molecular ion to be identical with 2,2′-binaphthyl. 1,2′-Binaphthyl was identified by comparison of glc retention time with that of an authentic specimen prepared from 2-tetralone and 1-bromonaphthalene according to the modified procedure by M. Orchin[15] for the synthesis of 2-ethylbiphenyl.

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