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Cyanation of Iodobenzene Catalyzed by $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$

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The catalytic ability of $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ in a nucleophilic displacement of iodobenzene with cyanide anion was examined. In the presence of 0.5 mol% of the Pd complex and dppf as ligand in NMP, the reaction reached completion at 60°C in 4h to afford benzonitrile in an excellent yield.

KEY WORDS: Aryl Cyanation/ $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$

INTRODUCTION

The inertness of halogens bound to an sp^2 carbon atom prevents a nucleophilic displacement of non-activated aryl halides through the conventional procedures. In certain cases, however, such difficulty is overcome by using a transition-metal complex as exemplified by a pronounced catalysis of nickel or palladium in the reaction between aryl halides and organometallics, amines, thiols and so on.¹⁾ Concerning the reaction of the substrates with cyanide anion, the present author had shown the effectiveness of palladium catalyst: in the presence of a catalytic amount of palladium(II) salt, non-activated aryl halides underwent the nucleophilic displacement with potassium cyanide to afford corresponding aryl cyanides in good yields under mild conditions.²⁾ Detailed investigations revealed that the palladium(II) salt was initially reduced to a metallic palladium, which played the role of an active catalyst. Another important observation was the inhibitory effect of cyanide anion itself on the catalytic reaction: the reaction proceeded most well in hexamethylphosphoric triamide (HMPA) where potassium cyanide was least dissolved. Subsequently, tetrakis(triphenylphosphine)palladium(0) ($\text{Pd}(\text{PPh}_3)_4$) had been shown to be effective for the cyanation, too.³⁾ But the air-sensitive complex was not so reactive and reported catalyst systems were rather complicated: $\text{Pd}(\text{PPh}_3)_4$ -crown ether, -alumina, or -reducing potential.

In the present investigation, we examined the ability of another zero-valent palladium, $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (tris(dibenzylideneacetone)(chloroform)-di-palladium(0)).⁴⁾ The effects on the reaction process of solvent and the addition of various ligand were examined intending to find convenient and effective catalytic systems for the aryl cyanation.

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RESULTS AND DISCUSSION

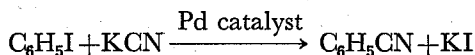
Effect of Solvent. The reaction of iodobenzene with potassium cyanide was examined in the presence of 0.5 mol% of Pd₂(dba)₃·CHCl₃ in various common solvent at 60°C.⁵⁾ As shown in Table 1, in 1-methyl-2-pyrrolidinone (NMP) or tetrahydrofuran (THF) the cyanation

Table 1. Pd (O)-catalyzed Cyanation of Iodobenzene.^{a)}

Run	Solvent	Ligand	Conversion/%	Yield/% ^{b)} C ₆ H ₅ CN
1	AN	—	<1	<1
2	DMF	—	<1	<1
3	THF	—	9	8
4	NMP	—	46	40
5	NMP	PPh ₃	<1	<1
6	NMP	PBu ₃	<1	<1
7	NMP	dppp	6	5
8	NMP	P(<i>o</i> -Tol) ₃	84	79
9	NMP	dppf	100	97

a) In the presence of 1 mmol of iodobenzene, 2 mmol of potassium cyanide, 0.005 mmol of Pd₂(dba)₃·CHCl₃, and 0.02 or 0.04 mmol of ligand (when used) in 0.5 cm³ of the solvent at 60°C for 5h (Runs 1-8) or 4h (Run 9) under nitrogen.

b) Yields were determined by GLC using an internal standard.



took place. Although the catalytic reaction stopped before it reached completion, benzonitrile was obtained selectively in either solvent (87 or 89% after 40 or 8 turnover). On the other hand, the catalytic reaction did not occur in *N,N*-dimethylformamide (DMF) or acetonitrile (AN). Apparently this remarkable effect of solvents could not be attributable to the simple medium effect (e.g., dielectric constant: AN=37.5, DMF=36.71, NMP=32.0, THF=7.58).⁶⁾

Effect of Ligand. The reaction of iodobenzene with potassium cyanide was examined in the presence of 0.5 mol% of Pd₂(dba)₃·CHCl₃ and 4 mol% of phosphorus or 2 mol% of diphosphorus ligand in NMP at 60°C. As shown in Table 1, such ligand as triphenylphosphine (PPh₃), tributylphosphine (PBu₃), or 1,3-bis(diphenylphosphino)propane (dppp) did not improve the reactivity. Whereas the addition of tri(*o*-tolyl)phosphine (P(*o*-Tol)₃) or 1,1'-bis(diphenylphosphino)ferrocene (dppf) gave a favorable catalyst system. Although a clear account of these effects can not be offered at the present stage, the nature of species (including solvent molecules and phosphorus ligands) ligated to palladium(0) did alter its reactivity remarkably.

In conclusion, a new and efficient reaction system, Pd₂(dba)₃·CHCl₃+dppf catalyst in NMP, was developed for aryl cyanation, which might provide a convenient and practical synthetic procedure of aryl cyanides starting from iodoarenes.

EXPERIMENTAL

Materials. $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ was utilized as obtained from Kanto Chemical Co. Potassium cyanide was recrystallized from water. All the solvents were distilled under nitrogen and stored over Molecular Sieve. The other materials were commercial products and used without further purification.

General Procedure. All the reactions were performed in a test tube equipped with a magnetic stirring bar under nitrogen. A mixture composed of potassium cyanide, iodobenzene, $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$, phosphorus ligand (when used), and solvent was degassed by evacuation and flushed with nitrogen. The mixture was then heated at 60°C for 4–5 h with stirring and shaking with aq. NaCl-ether. The organic layer was subjected to GLC analysis.

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