Nucleophilic Displacement Catalyzed by Transition Metal. III.[1] Kinetic Investigation of the Cyanation of Iodobenzene Catalyzed by Palladium(II)

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The nucleophilic displacement of iodobenzene with potassium cyanide was carried out in HMPA in the presence of palladium(II) acetate. The reaction obeys the following kinetics;

$$d[C_6H_5CN]/dt = k[Pd(OAc)_2]_0(M_{KCN})^{2/3}$$

A reaction scheme composed of two cycles has been proposed: in one cycle Pd^0 activates iodobenzene and in the other cycle Pd^{2+} assists the dissolution of potassium cyanide.

In a previous paper,[2] we reported that the nucleophilic displacement of non-activated aryl halides by cyanide anions takes place in the presence of palladium-

$$ArX + KCN \xrightarrow{Pd(II)} ArCN + KX$$

(II) salts. The scope of the reaction revealed that the palladium(II) salt is initially reduced to a lower-valent species, which plays the role of an active catalyst, and that the cyanide ligand retards the reduction. It is particularly interesting to note that a cyanide anion in the solution is a retarder of the reaction. In order to obtain an insight into the mechanism of the reaction, we studied the reaction from the kinetic viewpoint. The results and the most plausible scheme for the reaction will be presented in this paper.

Results and Discussion

The reaction of iodobenzene with potassium cyanide

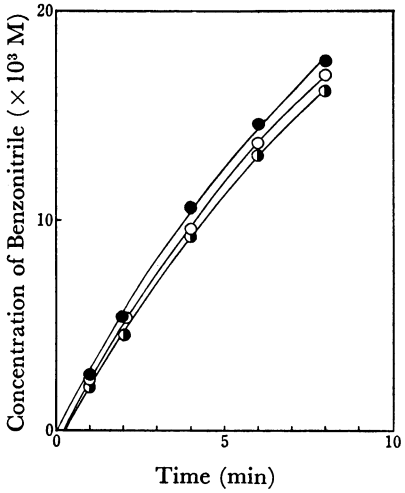

Fig. 1. Effect of concentration of iodobenzene.
KCN 1.03 mmol, $Pd(OAc)_2$ 1.03×10^{-3} M, HMPA 7.7 ml, 102±1 °C, under N_2 C_6H_5I ● 7.07×10^{-2} M ○ 4.36×10^{-2} M ◑ 2.36×10^{-2} M.

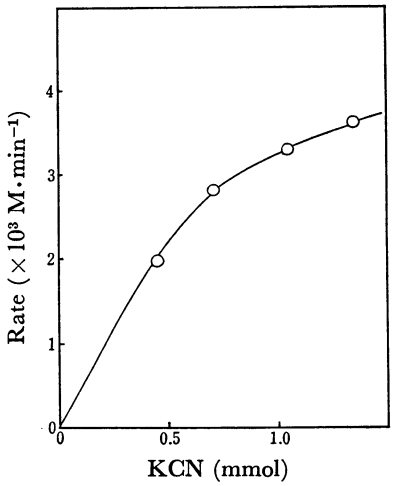

Fig. 2. Effect of amount of potassium cyanide on reaction rate.
$Pd(OAc)_2$ 1.74×10^{-3} M, C_6H_5I 4.36×10^{-2} M, HMPA 7.7 ml, 102±1 °C, under N_2.

was carried out in hexamethylphosphoric triamide (HMPA) at 102 °C using palladium(II) acetate as a catalyst. Benzonitrile was obtained in a quantitative yield, and by-products such as biphenyl were not detected on GLC. Since the reaction system is heterogeneous and there remains an undetermined variable (*vide infra*), we resigned to calculate numerical values for the rate constants.

Effect of Concentrations of Reactants. As is shown in Fig. 1, the initial rate for the appearance of benzonitrile was independent of the initial concentration of iodobenzene, which ranged from 2.36×10^{-2} M to 7.07×10^{-2} M. On the other hand, the rate increased non-linearly with the amount (weight) of potassium cyanide, as illustrated in Fig. 2. The analysis of the order with the method of integration[3] revealed that the kinetics obeys a two-thirds-order (r=0.992) for the amount of potassium cyanide. A linear relationship directed at the origin was observed between the rate and the concentration of palladium(II) acetate, provided that the concentration was greater than 1.04×10^{-3} M (Fig. 3).

Thus, Eq. 1 shows the rate expression determined experimentally, where $[Pd(OAc)_2]_0$ stands for the initial concentration of palladium(II) acetate and M_{KCN}

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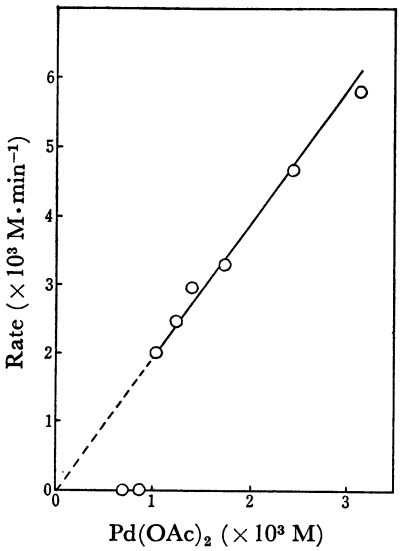


Fig. 3. Effect of concentration of palladium(II) acetate on reaction rate.
KCN 1.01 mmol, C_6H_5I 4.36×10^{-2} M, HMPA 7.7 ml, 102±1 °C, under N_2.

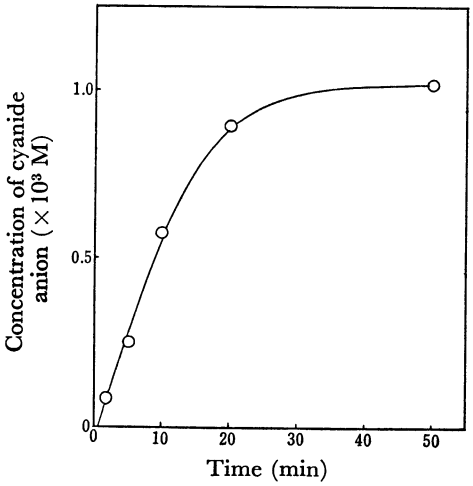


Fig. 4. Dissolution of potassium cyanide in HMPA. (Plot of concentration of cyanide anion *vs.* time)
KCN 2.02 mmol, HMPA 15.4 ml, 102±1 °C, under N_2.

means the amount of potassium cyanide in the reaction mixture.

$$d[C_6H_5CN]/dt = k[Pd(OAc)_2]_0(M_{KCN})^{2/3}$$
$$[Pd(OAc)_2]_0 \geq 1.04 \times 10^{-3}M$$

Rate of Dissolution of Potassium Cyanide into HMPA. Concentrations of potassium cyanide in HMPA at 102 °C were measured at appropriate time intervals after mixing both materials; the result is shown in Fig. 4. It is noteworthy that the concentration-time profile has an asymptote of about 1×10^{-3} M, which is almost identical to the minimum concentration of palladium(II) acetate necessary for the catalytic reaction. This observation seems to reveal that the cyanide anion in the solution[4] is trapped rapidly by a palladium(II) acetate at the very initial stage of the reaction to form the cyanide salt, which is inactive for initiation of the reaction.

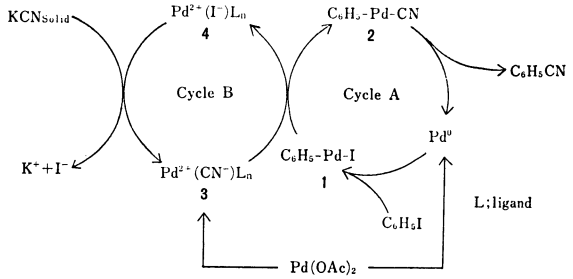
$$Pd(OAc)_2 + CN^- \xrightarrow[fast]{} Pd^{2+}(CN^-)L_n \not\rightarrow Pd^0$$
$$\downarrow \qquad \uparrow$$
$$Pd^0 \qquad KCN_{solid}$$

L; ligand (OAc^-, solvent, *etc.*)

The fact that potassium tetracyanopalladate(II) or palladium(II) cyanide is an inactive catalyst under the present conditions[2,5] supports this idea. Thus, in order to have a catalytic reaction, the initial concentration of palladium(II) acetate must exceed that of potassium cyanide in the solution.

The initial rate of dissolution of potassium cyanide into HMPA can be calculated to be 6×10^{-5} M·min^{-1}, which is far smaller (1/30—1/100) than the rates of the appearance of benzonitrile (2×10^{-3}—6×10^{-3} M·min^{-1}, *cf.* Figs. 1—3). This result suggests that the cyanide anions which contribute to the reaction comes directly from the potassium cyanide in the solid state, if not all.

Reaction Scheme. The results and discussion presented above leads to the following scheme as the most plausible mechanism for the reaction:



The low-valent palladium species (Pd^0) which comes from palladium(II) acetate[6] reacts with iodobenzene to give an oxidative-addition adduct (**1**). A methathesis of **1** with the cyanopalladium complex (**3**) produces the phenylcyanopalladium(II) complex (**2**), which subsequently yields benzonitrile and regenerates Pd^0 to ensure the catalytic cycle A. This is the well-known sequence of oxidative addition, methathesis, and reductive elimination in transition metal catalysis.[7] Supporting evidence for this is presented by the reaction of arylmercury(II) compound with potassium cyanide in the presence of palladium(II) chloride.

$$p\text{-}CH_3\text{-}C_6H_4\text{-}HgCl + KCN + PdCl_2 \longrightarrow$$
$$p\text{-}CH_3\text{-}C_6H_4\text{-}CN\ (+\ KCl + HgCl_2 + Pd)$$

In this case *p*-methylbenzonitrile was obtained quantitatively based on palladium(II) chloride.[8]

The cycle B represents a cyanide-carrier. Palladium(II) species draws the cyanide anion away from solid potassium cyanide and transfers it to **1** in methathesis.

The fact that the overall reaction rate is independent of the concentration of iodobenzene implies that the rate-determining step is the process for the abstraction of cyanide anions from the solid surface by palladium(II) species. Under such a circumstance the reaction rate is proportional to the stoichiometric concentration of

palladium(II) acetate and to the surface area of potassium cyanide in solid state, that is, the two-thirds-order of the amount of potassium cyanide; thus the experimentally derived Eq. 1 is consistent with the reaction scheme.

It should be noted that, in constructing the reaction scheme, we have assumed that almost all the palladium species in the reaction mixture is used as a cyanide-carrier (cycle B) and that the steady-state concentration of palladium species in cycle A is quite low.

That a cyano-complex such as **3** can provide the cyanide anions to form another complex, **2**, has been confirmed with a control experiment: when palladium(II) acetate ($[Pd(OAc)_2]/[KCN]=1/4$) was added into a homogeneous solution of iodobenzene and potassium cyanide in HMPA containing a small amount of water and the solution was heated at 102 °C for 30 min, no reaction took place. However, when additional palladium(II) acetate (half the amount to the initial palladium(II) acetate) was added to this reaction solution and the solution was kept at 102 °C for 30 min, benzonitrile was obtained in a 86% yield (based on potassium cyanide used). Since all palladium(II) cations initially added were consumed to form tetracyanopalladate(II) anions, there remained no species to yield Pd^0, whereas Pd^0 could be produced from the second portion of palladium(II) acetate because there remained scarcely any cyanide anions in the solution.

The existence of an appreciable amount of an iodo-complex, **4**, in the reacting solution can be shown from the absorption spectra. A pale-yellow reaction solution turns to reddish brown during the reaction, then comes back to pale-yellow at the end of the reaction. The reddish brown solution exhibits absorption similar to that of palladium(II) iodide solution at 500 nm or higher wavelengths, as is illustrated in Fig. 5.[9]

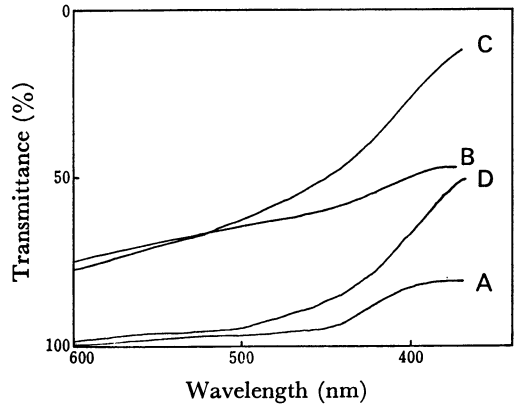


Fig. 5. Electronic spectra.
(A) $Pd(OAc)_2$, (B) PdI_2, (C) Reaction solution-in progress, (D) Reaction solution-terminate.
The concentrations of palladium(II) salts and other reaction conditions (C,D) are identical with those of Fig. 2.

Experimental

Materials. Palladium(II) acetate was prepared according to the literature.[10] HMPA and iodobenzene were commercial reagents and were dried over Molecular Sieves-(3A). Potassium cyanide was recrystallized from water and was ground by the use of a mortar.

Procedure. All reactions were performed in a 30-ml flask equipped with a magnetic stirrer and a three-way trap under a nitrogen stream. A mixture composed of potassium cyanide, iodobenzene, naphthalene (internal standard), and HMPA was stirred for 30 min at 102±1 °C. Then, a HMPA solution of palladium(II) acetate was added at once to start the reaction. Each aliquot (0.4 ml) taken out at appropriate time intervals was quenched with 5 ml of 12.5% aqueous sodium chloride, and the organic materials were extracted with 3 ml of ether. The ether layer was washed with 5 ml of 12.5% aqueous sodium chloride, dried over sodium sulfate, and subjected to the analysis on GLC (Hitachi Perkin-Elmer F6D, 35% silicon DC 200 on celite 545, 2 m, 140 °C, 0.8 kg·cm^{-2} of N_2).

The standard reaction mixture was composed of 1.01 mmol of potassium cyanide, 0.34 mmol of iodobenzene, 0.011 mmol of palladium(II) acetate, and 7.7 ml of HMPA. The concentration of each reagent was changed as indicated in Figs. 1—3.

The reaction rates were computed based on the amount of benzonitrile yielded at 2 min after the initiation.

Reaction of Arylmercury(II) Compound with Potassium Cyanide in the Presence of Palladium(II) Chloride. Into a solution of 65.8 mg (0.2 mmol) of *p*-chloromercuritoluene and 13.0 mg (0.2 mmol) of potassium cyanide in DMF (2.5 ml) was added 2.5 ml of 0.02 M solution of palladium(II) chloride in DMF. The mixture was kept at 50 °C for 1 h. The analysis by GLC revealed 5.8 mg (0.05 mmol) of *p*-methylbenzonitrile (a 99% yield based on $PdCl_2$) and a small amount of *p,p'*-bitolyl.

Solubility of Potassium Cyanide. To 2.02 mmol of potassium cyanide kept at 102 °C under nitrogen was added 15.4 ml of HMPA preheated to 102 °C; the concentrations of cyanide anions in the stirred mixture were measured at appropriate time intervals by the aid of a cyanide-ion electrode (Toa Electronic Ltd., CN-125).

Absorption Spectra. The spectra were recorded on a Hitachi Spectrophotometer 124. The reaction mixture was diluted with HMPA by a factor of 3 when it was submitted to the spectroscopy.

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References

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2) K. Takagi, T. Okamoto, Y. Sakakibara, A. Ohno, S. Oka, and N. Hayama, *Bull. Chem. Soc. Jpn.*, **48**, 3298 (1975); K. Takagi, T. Okamoto, Y. Sakakibara, and S. Oka, *Chem. Lett.*, **1973**, 471.

3) K. J. Laidler, "Chemical Kinetics," 2nd ed., McGraw-Hill, New York (1965), p. 5.

4) The mixture composed of potassium cyanide, iodobenzene, and HMPA was stirred for 30 min at 102 °C (see Experimental). Thus, the palladium(II) acetate was added to the mixture containing about 1×10^{-3} M of cyanide anions.

5) P. M. Maitlis, "Organic Chemistry of Palladium," Vol. 1, Academic Press, New York (1971), p. 32.

6) In a previous paper,[2] the reduced palladium species (Pd^0) was supposed to be the active catalyst for this palladium-

(II)-catalyzed cyanation from the following observations:

(1) The catalytic activity was greatly enhanced by the addition of a reductant such as potassium hydroxide or potassium carbonate.

(2) The cyanide ($Pd(CN)_2$ or $K_2Pd(CN)_4$), which is reduced with difficulty, was a less effective catalyst than the other palladium(II) salts examined.

(3) Palladium(II) acetate was spontaneously reduced to palladium metal on standing in HMPA under nitrogen.

7) L. Cassar, S. Ferra, and M. Foa, "Homogeneous Catalysis-II," Advances in Chemistry Series No. 132, American Chemical Society, Washington (1974), p. 252; D. G. Morrell and J. K. Kochi, *J. Am. Chem. Soc.*, **97**, 7262 (1975) and references cited therein.

8) An early report concerning a similar reaction described only unsatisfactory results (<20% yield); P. M. Henry, *J. Org. Chem.*, **36**, 1886 (1971).

9) Normally, organopalladium complexes (containing iodide ligand) are white; J. K. Klabunde and J. Y. E. Low, *J. Am. Chem. Soc.*, **96**, 7674 (1974).

10) T. A. Stephenson, S. M. Morehouse, A. R. Powell, J. P. Heffer, and G. Wilkinson, *J. Chem. Soc., A*, **1965**, 3632.