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The Cyanation of Aromatic Halides Catalyzed by Nickel(0) Complexes Generated In Situ. I. General Scope and Limitations

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The cyanation of chlorobenzene catalyzed by $Ni(PPh_3)_n$, which was generated in situ from $NiBr_2(PPh_3)_2$–Zn–PPh_3(Ni : Zn : P=1 : 3 : 2 molar ratio), was at first examined with various MCN (M=K, Na)-solvent systems by three procedures in order to clarify the conditions under which the reaction occurs. The effects of the systems and the procedures on the reaction were remarkable. It was observed that the cyanide ion has an inhibitory action on both the reduction of Ni(II) and the oxidative addition of the halide to Ni(0). However, when such MCN-dipolar aprotic solvent systems as KCN–HMPA, KCN or NaCN–MeCN, which give low cyanide concentrations, were used, the reaction readily took place at 50—60 °C without reducing Ni(II) prior to the addition of MCN and adding MCN slowly. Various Y-substituted chlorobenzenes, except for those with Y=*o*-Cl, *o*-CN, and *m*-NO_2, were cyanated to give the corresponding nitriles in fair to good yields. $NiBr_2$–PPh_3 can be used in place of $NiBr_2(PPh_3)_2$ if MCN is added after reduction. In addition, less reactive halides, such as *o*-dichlorobenzene and *o*-chlorobenzonitrile, were fairly smoothly cyanated by the use of $NiBr_2$–1,1′-bis(diphenylphosphino)-ferrocene.

It was first reported by the present authors[1)] and by Cassar[2)] that non-activated aryl halides can react with the cyanide ion under moderate conditions in the presence of Pd and Ni catalysts to afford the corresponding nitriles. Pd(II) salts,[3,4)] $Pd(PPh_3)_4$,[5)] $Ni(PPh_3)_3$ (isolated or generated in situ from $NiCl_2(PPh_3)_2$–Mn·Fe alloy–PPh_3),[6,7)] and $NiClAr(PPh_3)_2$[6)] are known to be homogeneous transition metal catalysts for the cyanation. Recently, $K_3[Co(CN)_4]$, which is formed in situ from $CoCl_2$–KCN–KOH(aq)–H_2 has also been found to be effective.[8)]

Previously, the present authors pointed out that the Pd(II)-catalyzed cyanation proceeds smoothly when KCN–HMPA is used as the MCN(M=K, Na)-solvent system, but fails to proceed in the NaCN–HMPA system, in which cyanide is more soluble.[3)] This suggests that the cyanide ion itself has also an inhibitory action on the catalytic reaction. Hence, the selection of MCN-solvent systems is important for keeping the catalyst active. In the case of the nickel catalysts, however, little has been reported about the utility of dipolar aprotic solvents and the selection of MCN-solvent systems. Cassar et al. mainly used the NaCN–EtOH[2,6)] and MCN–benzene–crown ether systems.[7)] Concerning the use of dipolar aprotic solvents, it has been reported by them that, in DMF, the Ni(0)-catalyzed cyanation occurs only if NaCN is added slowly.[6)]

In this paper, we investigate, under various conditions, the cyanation of aromatic halides catalyzed by Ni(0) phosphine complexes, which were generated in situ from the $NiBr_2(PPh_3)_2$–Zn–PPh_3 and $NiBr_2$–Zn–phosphorus ligand, and define the scope and limitations of the reaction more clearly.

Experimental

Materials. All the solvents were purified by the ordinary methods. The KCN (Merck), NaCN, zinc powder, triphenylphosphine, anhydrous $NiBr_2$ (Nakarai), 1,2-bis(diphenylphosphino)ethane, and 1,1′-bis(diphenylphosphino)ferrocene(Strem) were commercially available. All the aromatic halides were commercially available and were used without further purification. The tri-*o*-tolylphosphine,[9)] dibromobis(triphenylphosphine)nickel,[10)] and dicyanobis(triphenylphosphine)nickel[11)] were prepared according to the literature methods.

Procedures. Four procedures were examined and compared. A typical example of each is described below.

Procedure A: A 30-ml flask was charged with $NiBr_2(PPh_3)_2$ (740 mg, 1.0 mmol), Zn powder (200 mg, 3.0 mmol), PPh_3 (520 mg, 2.0 mmol), and KCN (2.15 g, 33 mmol). This mixture was degassed by evacuation and flushed with nitrogen, and a solution of chlorobenzene (3.38 g, 30 mmol) and naphthalene (about 0.2 g, internal standard) in HMPA (8 ml) was added by the use of a syringe. The mixture was then heated at 60 °C for 6 h with vigorous stirring and, after cooling, shaken with aq NaCl–CH_2Cl_2. The organic layer was subjected to GC analysis.

Procedure B: The catalyst components, $NiBr_2(PPh_3)_2$, Zn, and PPh_3 (1 : 3 : 2 molar ratio), were placed in a flask whose side arm was connected, by means of a ground-glass joint, to a KCN container. After replcing the air with nitrogen, HMPA was added by the use of a syringe. The mixture was heated at 60 °C for 30 min with stirring, and then chlorobenzene was added. After continued heating for 30 min, KCN was added from the KCN container, and the reaction mixture was further heated at 60 °C for 6 h.

Procedure C: This procedure was the same as Procedure B except that the order of the addition of chlorobenzene and KCN was reversed.

Procedure D: Anhydrous $NiBr_2$, Zn powder, and phosphorus ligand (1 : 3 : 4 molar ratio; 1 : 3 : 2 for the bidentate ligand) were placed in a flask fitted with a KCN container. After replacing the air with nitrogen, HMPA was added by the use of a syringe. The mixture was heated at 60 °C for 1 h with stirring, and then KCN was added from the KCN container, followed by the addition of chlorobenzene without delay. The reaction mixture was subsequently further heated at 60 °C for 6 h.

Analysis. The gas-chromatographic analyses were made by the use of a Shimadzu-GC-7A apparatus with He carrier gas, using a 3-m PEG-20M column for the analysis of the *p*-bromo-*N*,*N*-dimethylaniline, *m*-chlorofluorobenzene, methyl *p*-chlorobenzoate, *p*-chloroacetophenone, and 3-bromopyridine and a 3-m EGS column for the analysis of the other halides. The products were identified by comparison with authentic samples, and the yields were determined by using internal standards.

Preparation of Nitriles. Three isolated examples will be described here for illustration.

Benzonitrile: Chlorobenzene (3.38 g, 30 mmol) was cyanated by Procedure A described above. The resulting mixture was poured into water (20 ml), which was then extracted twice with ether (20 ml). The combined extracts were washed with water (10 ml), dried (Na_2SO_4), and concentrated. The residue was distilled to give 2.39 g (77%) of benzonitrile: bp 81—83 °C (20 mmHg (1 mmHg=133.322 Pa)); n_D^{20} 1.5279.

Methyl *p*-Cyanobenzoate: A mixture of methyl *p*-chlorobenzoate (5.12 g, 30 mmol), KCN (2.15 g, 33 mmol), $NiBr_2(PPh_3)_2$ (740 mg, 1.0 mmol), Zn powder (200 mg, 3.0 mmol), PPh_3 (520 mg, 2.0 mmol), and acetonitrile (12 ml) was kept at 50 °C for 6 h while being stirred under nitrogen (Procedure A). The resulting mixture was chromatographed on a silica-gel column, using hexane-ethyl acetate (29/1) as the eluent, to give 3.87 g (80%) of methyl *p*-cyanobenzoate: mp 66—67 °C; ^{1}H NMR ($CDCl_3$) δ=4.0 (3H, s), 7.7 (2H, d, *J*=8.8 Hz), and 8.1 (2H, d, *J*=8.8 Hz).

***p*-Acetylbenzonitrile:** *p*-Chloroacetophenone (4.64 g, 30 mmol) was cyanated in the same manner as methyl *p*-chlorobenzoate. The resulting mixture was chromatographed on a silica-gel column, using hexane-ethyl acetate (9/1) as the eluent, to give 3.58 g (82%) of *p*-acetylbenzonitrile: mp 57—58 °C; ^{1}H NMR ($CDCl_3$) δ=2.6 (3H, s), 7.7 (2H, d, *J*=8.7 Hz), and 8.1 (2H, d, *J*=8.7 Hz).

Solubilities of KCN and NaCN. Saturated solutions were generated by stirring the respective solvents (30 ml) with a large excess of cyanide at 60±1 °C under a nitrogen atmosphere. One-milliliter aliquots were withdrawn at intervals for analysis until it was evident that equilibrium had been attained. Samples were diluted to 100 ml with 0.1 mol l^{-1} NaOH and analyzed for the cyanide ion using a cyanide ion electrode-F-7 pH meter (Horiba).

Results and Discussion

In the Ni(0)-catalyzed cyanation of aromatic halides, the use of $Ni(PPh_3)_3$ generated in situ as a catalyst is convenient and practical because $Ni(PPh_3)_n$(n=3 or 4) and $NiXAr(PPh_3)_2$ are troublesome to prepare and handle. Thus, as the first attempt, the cyanation of bromobenzene with KCN-DMF as the MCN-solvent system was examined according to Procedure A, using four kinds of metals (powder) as reducing agents of Ni(II) (Table 1). The cyanation proceeded catalytically together with the coupling reaction. It is noteworthy that the catalytic cyanation occurred by only heating the reaction mixture, without reducing Ni(II) previously and adding KCN slowly. When NaCN-DMF was used instead of KCN-DMF, however, the reaction did not occur. Of the four metals, Zn was found to be most favorable. In what follows, $NiBr_2(PPh_3)_2$-Zn-PPh_3 (Ni : Zn : P=1 : 3 : 2 molar ratio) and $NiBr_2$-Zn-phosphorus ligand (Ni : Zn : P=1 : 3 : 4; 1 : 3 : 2 for bidentate ligand) will be used as the catalyst systems to generate Ni(0) phosphine complexes in situ.

Table 1. Catalytic Activity of $NiBr_2(PPh_3)_2$-Metal-PPh_3 for the Cyanation of Bromobenzene with KCN[a)]

Metal(powder)	Conversion	Selectivity/%[b)]	
	%	PhCN	Ph-Ph
Zn	100	68	28
Zn	100[c)]	55	40
Mn	91	55	28
Mn-Fe(77-23)[d)]	63	61	23
Mg[e)]	70	77	14

a) Carried out according to Procedure A as described in Experimental Section. $NiBr_2(PPh_3)_2$, 1 mmol (Ni : Metal : P=1 : 3 : 2 molar ratio); PhBr, 10 mmol; KCN, 11 mmol; DMF, 10 ml; temp, 60 °C; time, 4 h. b) Yield based on the halide consumed. c) Chlorobenzene was used as halide. d) Calculated for Mn on the basis of the ratio. e) The reproducibility of the reaction was poor.

$$\mathrm{ArX} + \mathrm{MCN} \xrightarrow[\text{or } \mathrm{NiBr_2\text{-}Zn\text{-}P}\text{ ligand}]{\mathrm{NiBr_2(PPh_3)_2\text{-}Zn\text{-}PPh_3}} \mathrm{ArCN} + \mathrm{MX}$$

M : K,Na

Comparison of MCN-Solvent Systems and Reaction Procedures. The cyanation of chlorobenzene catalyzed by $Ni(PPh_3)_3$, which was generated in situ from $NiBr_2(PPh_3)_2$-Zn-PPh_3, was examined with various MCN(M=K, Na)-solvent systems by means of three procedures: A(catalyst-reactant mixing without pretreatment), B(catalyst reduction-halide addition-cyanide addition), and C(catalyst reduction-cyanide addition-halide addition) (see Experimental section for further details). The results are shown, together with the solubilities of MCN, in Table 2. The effect of MCN-solvent systems is remarkable and appears to be closely related to the solubilities of MCN.

With Procedure A, which is the most convenient of the three procedures, the cyanation proceeded smoothly by the use of certain MCN-dipolar aprotic solvent systems with lower cyanide solubilities than about 15 mmol l^{-1}. Of the systems tested, the KCN-HMPA and KCN-MeCN systems gave especially good results: benzonitrile was obtained in high selectivities (92—95%) at high conversions (99%), together with biphenyl in very low selectivities (2—6%). The KCN-TMU and NaCN-MeCN systems also gave good results. With the KCN-DMF and KCN-THF systems, biphenyl was produced in somewhat high selectivities compared with the above four systems. On the other hand, the KCN-EtOH system (solubility, 51.8 mmol l^{-1}) was not especially useful, though it caused the cyanation to

Table 2. Cyanation of Chlorobenzene with Various MCN-Solvent Systems by Three Procedures

KCN system		Procedure[a]	Conversion/%	Selectivity/%	
Solvent	Solubility[b]/mmol l^{-1}			PhCN	Ph-Ph
Acetone[c]	0.5	A	58	82	10
HMPA	1.5	A	99	95	2
		B	100	88	4
		C	85	88	8
MeCN	1.9	A	99	92	6
		B	21	57	35
		C	74	87	8
TMU[d]	2.1	A	95	91	9
THF	2.4	A	88	86	12
Sulfolane	8.1	A	54	59	28
DMAC[e]	10.8	A	58	91	9
DMF	15.0	A	83	80	19
		B	67	83	20
		C	94	88	13
EtOH	51.8	A	49	47	8
		B	59	63	4
		C	0		
DMSO	131	A	3	—	—
Diglyme	—	A	18	59	26
Monoglyme	—	A	42	73	24
Benzene	—	A	13	7	86

NaCN system		Procedure[a]	Conversion/%	Selectivity/%	
Solvent	Solubility[b]/mmol l^{-1}			PhCN	Ph-Ph
Acetone[c]	0.9	A	76	89	6
MeCN	4.4	A	84	97	2
		B	20	55	37
		C	93	97	3
THF	10.4	A	65	92	8
TMU[d]	10.8	A	78	84	14
Sulfolane	15.0	A	62	65	23
DMAC[e]	123	A	0		
DMF	127	A	0		
		B	89	86	14
		C	0		
EtOH	227	A	0		
		B	33	93	1
HMPA	461	A	0		
		B	95	88	2
		C	0		

a) $NiBr_2(PPh_3)_2$, 1 mmol(Ni : Zn : P=1 : 3 : 2); KCN, 33 mmol; PhCl, 30 mmol; solvent, 8 ml. Procedure A: Ni-Zn-P+KCN+solvent+PhCl, 60 °C-6 h. Procedure B: Ni-Zn-P+solvent, 60 °C-0.5 h, +PhCl, 60 °C-0.5 h, +MCN, 60 °C-6 h. Procedure C: Ni-Zn-P+solvent, 60 °C-0.5 h, +MCN, 60 °C-0.5 h, +PhCl, 60 °C-6 h (see Experimental section). b) Values at 60 °C except for acetone (50 °C). c) Reaction temp, 50 °C. d) *N,N,N′,N′*-Tetramethylurea. e) *N,N*-Dimethylacetamide.

proceed, in contrast with the NaCN-EtOH system (solubility, 227 mmol l^{-1}).

With Procedure B, the catalytic cyanation proceeded even when the NaCN-EtOH (solubility, 227 mmol l^{-1}) and NaCN-HMPA (solubility, 461 mmol l^{-1}) systems were used, giving high cyanide concentrations. The KCN-HMPA and NaCN-HMPA systems gave particularly good results (95—100% conversions, 88% selectivity), near to those obtained using the KCN-HMPA and KCN-MeCN systems by Procedure A. However, the MeCN solvent gave less favorable results than did HMPA: in both KCN-MeCN and NaCN-MeCN systems, the reaction stopped at a conversion of about 20%, and the formation of biphenyl, accompanied by the oxidation of Ni(0) to Ni(II), was remarkable (35—37% selectivities). With the MCN-EtOH systems, the reproducibility of the results was fairly poor, especially with the NaCN-EtOH system, and good results were not obtained.[12)]

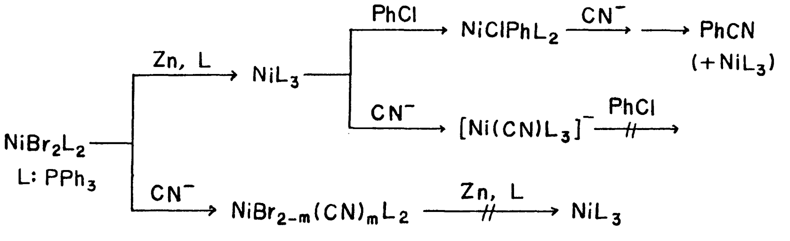
With Procedure C, it was found that the inhibitory effect of the cyanide ion was remarkable and that the cyanation was accomplished by the use of MCN-dipolar aprotic solvent systems with cyanide solubilities lower than about 15 mmol l^{-1}. With the MCN-MeCN systems, Procedure C gave better results than did Procedure B. In the NaCN-DMF system (solubility, 127 mmol l^{-1}), the cyanation was also attempted by adding chlorobenzene 5 min after the addition of NaCN, but the reaction was not initiated, such as when it was added 30 min later. This suggests that the cyanide ion coordinates to $Ni(PPh_3)_3$ rapidly under the conditions used (vide infra).

Distinct differences in the occurrence and progress of the cyanation between these three procedures, A—C, were thus observed. Here, the inhibition by the cyanide ion for the catalytic cyanation will be discussed mainly. With Procedure A, the reduction of $NiBr_2(PPh_3)_2$ by Zn powder appears to compete with the replacement of its bromine atom by a cyano group (Scheme 1). With good systems such as KCN-HMPA and KCN-MeCN, the solution turned reddish from green at an initial stage of the reaction to reveal the formation of $Ni(PPh_3)_3$ by reduction, while with poor systems, such as KCN-DMSO and NaCN-DMF, the solution turned pale yellow, suggesting that no reducible cyanonickel(II) complexes, $NiBr_{2-m}(CN)_m(PPh_3)_2$, were formed. In fact, the cyanation did not occur when $Ni(CN)_2(PPh_3)_2$(yellow) was used instead of $NiBr_2(PPh_3)_2$ in Procedure A. It was observed, however, that the dicyanonickel(II) complex served as a cyanation reagent instead of MCN in the Ni(0)-catalyzed cyanation.[13] Accordingly, even if $NiBr_{2-m}(CN)_m(PPh_3)_2$ is formed in part, it is advantageously converted into reducible $NiBr_{2-m}Cl_m(PPh_3)_2$ when the cyanation of chlorobenzene proceeds.

The results obtained by Procedure C, in which MCN is introduced prior to chlorobenzene, suggest that the cyanide ion also inhibits the oxidative addition of chlorobenzene to $Ni(PPh_3)_3$. Probably, a cyanide ion would coordinate to $Ni(PPh_3)_3$ to form $[Ni(CN)(PPh_3)_3]^-$,[14] for which it is difficult to undergo the oxidative addition of chlorobenzene. Therefore, the systems with low solubilities of MCN may be required also for the cyanation by Procedure C. On the other hand, Procedure B, in which chlorobenzene is introduced prior to MCN, made the cyanation possible even in the systems with relatively high solubilities of MCN, in contrast to Procedure C. This implies that the cyanation is smoothly initiated by a rapid reaction of CN^- with $NiClPh(PPh_3)_2$, which is formed prior to the addition of MCN, and that the concentration of the cyanide ion stays low, thus suppressing the formation of inactive $[Ni(CN)(PPh_3)_3]^-$ as a catalyst and permitting the catalytic cycle.

Biphenyl, the main by-product, is formed by the Ni(0)-catalyzed coupling of aryl halides: $2PhCl + Ni(0) \rightarrow Ph\text{-}Ph + NiCl_2$.[15] This reaction lowers the catalyst turnover of the cyanation because the Ni(0) is oxidized to ineffective Ni(II). This was remarkable in Procedure B in the MeCN solvent (vide supra).

Effect of Temperature and Time. The cyanation of PhCl by KCN was made by means of Procedure A at



Scheme 1.

Table 3. Effects of Temperature and Time[a)]

Solvent	Temp	Time	Conversion	Selectivity/%		PhCN
	°C	h	%	PhCN	Ph-Ph	Ph-Ph
HMPA	40	6	56	80	19	4.2
	60	1	16	85	11	7.7
	60	3	70	93	3	31
	60	6	99	95	2	48
	70	6	100	87	12	7.3
	80	6	35	53	46	1.2
MeCN	40	6	81	97	1	97
	60	6	99	92	6	15
	70	6	26	56	31	1.8
	80	6	18	52	46	1.1
DMF	40	6	2	70	—	—
	60	6	83	80	19	4.2
	80	6	51	66	34	1.9

a) Made by Procedure A. $NiBr_2(PPh_3)_2$, 1 mmol (Ni : Zn : P=1 : 3 : 2); PhCl, 30 mmol; KCN, 33 mmol; solvent, 8 ml.

Table 4. Cyanation of Various Aromatic Halides[a)]

Y-C_6H_4X(mmol)		Solvent (ml)	Temp	Time	Conversion	Selectivity	
Y	X		°C	h	%	%	
H	Cl (100)	HMPA (20)	60	16	67	99	
H	Cl (100)	CH_3CN (20)	50	16	76	95	
H	Br (100)	HMPA (20)	60	16	100	94	
p-NMe_2	Br (30)	HMPA (12)	60	16	89	54	
p-OMe	Cl (30)	HMPA (8)	60	6	98	94	
m-OMe	Cl (30)	HMPA (8)	60	6	100	97	
o-OMe	Cl (30)	HMPA (12)	60	16	98	98	
m-Me	Cl (30)	HMPA (8)	60	6	100	95	
o-Me	Cl (30)	HMPA (12)	60	6	69	97	
o-Me	Cl (30)	HMPA (12)	60	16	91	95	
m-F	Cl (30)	HMPA (8)	60	6	100	99[d)]	
o-Cl	Cl (30)[b)]	HMPA (12)	60	16	11	Mono 28	Di 67
p-CO_2Me	Cl (30)	CH_3CN (12)	50	6	99	97	
m-CF_3	Cl (30)	HMPA (8)	60	6	98	27	
m-CF_3	Cl (30)	CH_3CN (12)	50	6	64	72	
p-CF_3	Cl (30)	HMPA (8)	60	6	99	82	
p-COMe	Cl (30)	CH_3CN (12)	50	6	96	96	
m-CN	Cl (30)	CH_3CN (8)	50	6	76	91	
m-CN	Cl (30)	HMPA (8)	60	6	27	11	
p-CN	Cl (30)	CH_3CN (12)	50	6	96	99	
o-CN	Cl (30)	CH_3CN (12)	60	16	20	70	
o-CN	Cl (30)	HMPA (12)	60	16	29	71	
m-NO_2	Cl (30)	HMPA (12)	60	6	≈0		
3-Br-Py[c)]	(30)	HMPA (8)	60	8	19	12	
3-Br-Py[c)]	(30)	CH_3CN (8)	60	8	77	74	

a) Made by Procedure A. $NiBr_2(PPh_3)_2$, 1 mmol (Ni : Zn : P=1 : 3 : 2); KCN/halide=1.1 molar ratio. b) KCN/*o*-$C_6H_4Cl_2$=2.2 molar ratio. c) 3-Br-Py=3-bromopyridine. d) For *m*-fluorobenzonitrile.

Table 5. Cyanation of Aromatic Halides with the $NiBr_2$-Zn-Phosphorus Ligand Catalyst

Y-C_6H_4Cl(mmol)		$NiBr_2$	L[a)]	HMPA	Procedure[b)]	Time	Conversion	Selectivity	
Y		mmol		ml		h	%	%	
H	(30)	1	PPh_3	8	A	6	59	84	
H	(30)	1	PPh_3	12	D	6	95	94	
H	(15)	0.5	DPPF	6	D	6	47	72	
o-Cl	(15)	0.5	PPh_3	6	D	24	10	Mono 39	Di 51
o-Cl	(15)	0.5	DPPF	6	D	6	33	31	37
						24	68	9	75
o-CN	(15)	0.5	DPPF	6	D	24	94	87	

a) Phosphorus ligand, DPPF=1,1′-bis(diphenylphosphino)ferrocene. b) $NiBr_2$: Zn : L=1 : 3 : 4 molar ratio for PPh_3 and 1 : 3 : 2 for DPPF; KCN/halide=1.1 molar ratio for monohalide and 2.2 for dihalide. Procedure D: Ni-Zn-L+HMPA, 60 °C-1 h, +KCN+halide, 60 °C-6 or 24 h (see Experimental section).

temperatures ranging from 40 to 80 °C in three solvents: HMPA, MeCN, and DMF. The results are shown in Table 3. In all cases, the best results were obtained at about 60 °C. It is noteworthy that the reaction always proceeded fairly smoothly, even at the low temperature of 40 °C (conversion: 81% at 6 h), in MeCN. Generally, at 80 °C the coupling reaction became much more rapid, thus deactivating the catalyst. In the case, for example, of HMPA at 80 °C, the reaction stopped at the low conversion of 35%; the solution turned from reddish brown to black (colloidal nickel), thus revealing the decomposition of the catalyst. Furthermore, the selectivity of biphenyl varied also with the reaction time(conversion), as exemplified by the results obtained with HMPA. The PhCN/Ph-Ph ratio increased with the increase in the conversion, ranging from 7.7 at 16% conversion to 48 at 99% conversion. This suggests that most of the biphenyl is fomed at an initial stage of the reaction.

Cyanation of Various Aromatic Halides. The cyanation of various aromatic halides was examined with the KCN-HMPA and KCN-MeCN systems by means of Procedure A, which is the most convenient of the three (Table 4). At first, the cyanation of chlorobenzene and bromobenzene was attempted at a high halide/Ni ratio of 100 (KCN/Ni=110) in 20 ml of HMPA and MeCN. With the above two systems, good results were obtained even at such a high ratio, whereas with the KCN-DMF system, with a higher cyanide solubility, the cyanation was not initiated under similar conditions. Furthermore, with 20 ml of DMF, the halides were not cyanated even at a halide/Ni ratio of 30 (KCN/Ni=33), which is allowable with 8 ml of DMF.

All the Y-substituted chlorobenzenes were reactive for cyanation except those with Y=*o*-Cl, *o*-CN, and *m*-NO_2; they all gave fair to good yields, regardless of the Hammett σ values for the Y-substituents. In general, *o*-Y-substituted chlorobenzenes, especially those with Y=Cl and CN, were less reactive. However, *o*-chloroanisole and *o*-chlorotoluene were cyanated almost completely during a long reaction time. With *m*-chlorobenzylidyne trifluoride, the MeCN solvent gave a much higher selectivity than that obtained in HMPA. The former solvent was also a better one for *m*- and *p*-chlorobenzonitrile. *m*-Chlorofluorobenzene gave only *m*-fluorobenzonitrile selectively. Further, *p*-bromo-*N,N*-dimethylaniline and 3-bromopyridine also reacted to give fair yields of the nitriles.

Cyanation of Aromatic Halides with $NiBr_2$-Zn-Phosphorus Ligand Catalyst. The use of $NiBr_2$-PPh_3 in place of $NiBr_2(PPh_3)_2$, if it were allowable, would provide a more convenient procedure because it would then be unnecessary to prepare the nickel complex prior to the catalytic cyanation. Therefore, first the cyanation of chlorobenzene was attempted using $NiBr_2$-PPh_3 in place of $NiBr_2(PPh_3)_2$ in Procedure A (Table 5). As a result, the conversion was low (59%) compared with that with $NiBr_2(PPh_3)_2$. The good result of a 94% selectivity at a 95% conversion was, however, obtained by adopting Procedure D, in which a mixture of $NiBr_2$, Zn, and PPh_3 in HMPA was heated at 60 °C for 1 h prior to the addition of KCN and chlorobenzene.

Next, combinations of $NiBr_2$ and three phosphorus ligands (tri-*o*-tolylphosphine, 1,2-bis(diphenylphos phino)ethane, and 1,1′-bis(diphenylphosphino)ferrocene(DPPF)) were used for the cyanation of chlorobenzene and much less reactive halides, such as *o*-dichlorobenzene and *o*-chlorobenzonitrile. The former two ligands were ineffective for the cyanation of chlorobenzene. DPPF was effective, but not so good as PPh_3 (47% conversion, 72% selectivity). DPPF was, however, found to be a good ligand for *o*-dichlorobenzene and *o*-chlorobenzonitrile; the former halide gave *o*-chlorobenzonitrile and phthalonitrile in a total yield of 57% (68% conversion, 84% total selectivity), in contrast to a yield of 9% with PPh_3, while the latter halide gave phthalonitrile in the good yield of 82%. On the other hand, tri-*o*-tolylphosphine and 1,2-bis(diphenylphosphino)ethane were also ineffective for the cyanation of *o*-dichlorobenzene and *o*-chlorobenzonitrile.

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12) Cassar et al. have obtained good results by the use of the NaCN-EtOH system in the in-situ generated $Ni(PPh_3)_3$-catalyzed cyanation of aromatic halides (Ref. 6). However, the results we obtained following their procedure exactly were not so good as those reported by them and moreover, were poorly reproducible.

13) The reaction of PhCl (4.8 mmol) with $Ni(CN)_2(PPh_3)_2$ (2.4 mmol) for 6 h at 60 °C in HMPA (8 ml) in the presence of a nickel catalyst ($NiBr_2(PPh_3)_2$, 1 mmol; Ni : Zn : P=1 : 3 : 2) gave benzonitrile in a 78% yield.

14) The equilibrium between $Ni(PPh_3)_4$ and $Ni(PPh_3)_3$ in toluene is found to lie well to the latter side at room temperature (R. Mynott, A. Mollbach, and G. Wilke, *J. Organomet. Chem.*, **199**, 107 (1980)). Cyanonickel(0)-complex ions $[Ni(CN)_n(PPh_3)_{4-n}]^{n-}$ (n=1—4) are not obtained by the action of CN^- on $Ni(PPh_3)_4$, while it is known that $K_4[Ni(CN)_4]$ undergoes a complete triphenylphosphine displacement of cyanide to give $Ni(PPh_3)_4$ without any intermediate substitution products (H. Behrens and A. Müller, *Z. Anorg. Allg. Chem.*, **341**, 124 (1965); R. del Rosario and L. S. Stuhl, *J. Am. Chem. Soc.*, **106**, 1160 (1984)). Cassar et al. have, however, reported that the IR bands assigned to coordinate cyanide are observed when NaCN is added to a *N,N*-dimethylformamide solution of $Ni(PPh_3)_3$ (Ref. 6). Recently, it has been reported that a related nickel complex anion $[Ni(CN)(P(OMe)_3)_3]^-$ is formed by the reaction of $(K\cdot 18\text{-crown-}6)_2[Ni(CN)_2\{\eta^2\text{-}PhC{\equiv}CPh\}]$ with $P(OMe)_3$ (R. del Rosario and L. S. Stuhl, *Organometallics*, **5**, 1260 (1986)).

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