Nitrile-Group Transfer from Solvents to Aryl Halides. Novel Carbon−Carbon Bond Formation and Cleavage Mediated by Palladium and Zinc Species

Feng-Hong Luo, Chi-I Chu, and Chien-Hong Cheng*

Department of Chemistry, National Tsing Hua University, Hsinchu, Taiwan 300, Republic of China

Received September 26, 1997

The palladium phosphine complexes $Pd(PPh_3)_2Cl_2/PPh_3$, $Pd(PBu_3)_2Cl_2$, and $Pd(dppp)_2Cl_2$ (dppp = 1,2-bis(diphenylphosphino)propane) in the presence of zinc metal powder catalyze nitrile-group transfer from organic nitriles RCN (R = Me, Et, *n*-Pr, Bn, Ph) to bromoarenes to give the corresponding ArCN compounds. Only ortho-disubstituted bromoarenes (1-bromo-2-methylnaphthalene (**1**), 2-bromo-*m*-xylene, 2-bromomesitylene (**3**), 1-bromo-2-methoxynaphthalene, and 9-bromoanthracene) afforded good yields of the cyanation products. Analysis of the reaction mixture of **3** with benzyl cyanide using $Pd(PBu_3)_2Cl_2$ as the catalyst showed the presence of dibenzyl ketone and a cyclic product, 2,4,6-tribenzyl-5-phenylpyrimidine, in addition to 2,4,6-trimethylbenzonitrile. To understand the mechanistic features of these catalytic reactions, a number of experiments were performed and the results are summarized as follows: (i) the palladium intermediate $Pd(PPh_3)_2$(2-Me-Np)Br (**6**; 2-Me-Np = 2-methylnaphthyl), which can be prepared separately from the oxidative addition of **1** to $Pd(PPh_3)_4$, was detected from ^{1}H NMR spectra in the catalytic cyanation of **1** in acetonitrile; (ii) heating **6** in acetonitrile in the presence of Zn powder or $ZnBr_2$ at 160 °C afforded 1-cyano-2-methylnaphthalene (**2**) in 76 and 45% yields, respectively; (iii) heating **6** in acetonitrile alone gave no cyanation product but the imine product CH_3(2-Me-Np)C=NH (**7**) in 35% yield; (iv) treatment of **7** by $ZnBr_2$ at 160 °C afforded **2** in 44% yield. On the basis of these results, a mechanism involving the cooperation of two metals, palladium and zinc, with the former responsible for C−C bond formation and the latter for C−C bond cleavage, is proposed to account for the observed catalytic reactions.

Introduction

While great advances in metal-mediated C−C bond formation have occurred in recent years, the reverse C−C bond cleavage is much less developed.[1] Because of their weak coordinating ability, small polarity, and strong bond energy, C−C bonds are notably unreactive toward metal complexes.[1] In most cases, the C−C bond cleavage promoted by metal complexes relied on the use of strained cyclic compounds.[2,3] Successful examples of the activation of unstrained C−C bonds are limited to substrates containing directing groups for precoordination to the metals.[3−7] The development of new methods for selective cleavage of C−C bonds is a great challenge to organometallic chemists. We report here an unprecedented activation of C−C bonds mediated by metal complexes of the nickel family and zinc that act cooperatively, leading to cleavage of a C−C bond of the nitrile solvents and the transfer of the nitrile-group to aryl halides (eq 1).

$$\mathrm{ArX} \xrightarrow{\mathrm{RCN}} \mathrm{ArCN} \qquad (1)$$

Results and Discussion

Nitrile Group Transfer. Heating 1-bromo-2-methylnaphthalene (**1**) in acetonitrile in the presence of $PdCl_2(PPh_3)_2$, PPh_3, and zinc powder at 160 °C led to transfer of a nitrile group from acetonitrile to **1** and the isolation of 1-cyano-2-methylnaphthalene (**2**) in good yield. A minor product, 2-methylnaphthalene, from hydrogenolysis of **1** was also isolated. Under similar reaction conditions, cyanation of the ortho-disubstituted bromoarenes 2-bromo-*m*-xylene, 2-bromomesitylene (**3**),

(1) Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals*; Wiley: New York, 1994; p 329.

(2) Selected references: (a) Perthuisot, C.; Jones, W. D. *J. Am. Chem. Soc.* **1994**, *116*, 3647. (b) Periana, R. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 7346. (c) Schwarz, H.; Schröder, D.; Schalley, C. A. *J. Am. Chem. Soc.* **1994**, *116*, 11089. (d) Green, M. L. H.; Baretta, A.; Chong, K. S.; Cloke, F. G. N.; Feigenbaum, A. *J. Chem. Soc., Dalton. Trans.* **1983**, 861. (e) Green, M. L. H.; Baretta, A.; Cloke, F. G. N.; Feigenbaum, A.; Prout, K.; Gourdon, A. *J. Chem. Soc., Chem. Commun.* **1981**, 156. (f) Eilbracht, P.; Dahler, P. *J. Organomet. Chem.* **1977**, *127*, C48. (g) Elibracht, P. *Chem. Ber.* **1976**, *109*, 3136.

(3) Bishop, K. C. *Chem. Rev.* **1976**, *76*, 461 and references therein.

(4) (a) Gozin, M.; Weisman, A.; Ben-David, Y.; Milstein, D. *Nature* **1993**, *364*, 699. (b) Chiang, H.-J.; Liu, C.-S. *J. Organomet. Chem.* **1993**, *458*, 167. (c) Muetterties, E. L.; Jesson, J. P.; Parshall, G. W.; Kane, A. R.; Gerlach, D. H. *J. Am. Chem. Soc.* **1971**, *93*, 3543. (d) Schwarz, H.; Zummack, W.; Eller, K. *J. Am. Chem. Soc.* **1990**, *112*, 621. (e) Spencer, J. L.; Nicholls, J. C. *Organometallics* **1994**, *13*, 1781.

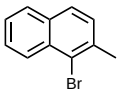
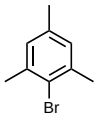
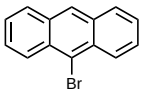
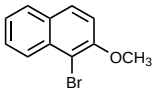
(5) Suggs, J. W.; Jun, C.-H. *J. Am. Chem. Soc.* **1986**, *108*, 4679 and references therein.

(6) (a) Crabtree, R. H.; Dion, R. P. *J. Chem. Soc., Chem. Commun.* **1984**, 1260. (b) Crabtree, R. H.; Dion, R. P.; Gibboni, D. J.; McGrath, D. V.; Holt, E. M. *J. Am. Chem. Soc.* **1986**, *108*, 7222.

(7) (a) Bricout, H.; Carpentier, J.-F.; Mortreux, A. *Tetrahedron Lett.* **1997**, *38*, 1053. (b) Bianchini, C.; Casares, J. A.; Peruzzini, M.; Romerosa, A.; Zanobini, F. *J. Am. Chem. Soc.* **1996**, *118*, 4585.

S0276-7333(97)00842-X CCC: $15.00
Publication on Web 02/13/1998

Table 1. Results of Cyanation of Aryl Halides Catalyzed by Metal Complexes of the Nickel Family[a]

				product yield/%[b,c]	
entry no.	RX	solvent	catalyst	RCN	RH
1		CH_3CN	$Pd(PPh_3)_2Cl_2$/8 PPh_3	76(69)	20(18)
2		CH_3CN	$Pd(P(Bu_3)_2Cl_2$[d]	81	17
3		CH_3CN	$Pd(dppe)Cl_2$[d]	47	23
4		CH_3CN	$Pd(dppm)Cl_2$[d]	6	23
5		CH_3CN	$Pd(dppp)Cl_2$[d]	90	8
6		CH_3CN	$Pd(P(o\text{-tol})_3)_2Cl_2$/8 $P(o\text{-tol})_3$[d]	20	11
7		CH_3CN	$Ni(PPh_3)_2Cl_2$/5 PPh_3	23	29
8		CH_3CN	$Pd(PPh_3)_2Cl_2$/8 PPh_3	94(76)	5(3)
9		CH_3CN	$Pd(PBu_3)_2Cl_2$	100	0
10		CH_3CH_2CN	$Pd(PBu_3)_2Cl_2$	61	0
11		$CH_3(CH_2)_2CN$	$Pd(PBu_3)_2Cl_2$	50	1
12		$PhCH_2CN$	$Pd(PBu_3)_2Cl_2$	97	0
13		CH_3CN	$Pt(PPh_3)_2Cl_2$/8 PPh_3	39	9
14		CH_3CN	$Pd(PPh_3)_2Cl_2$/8 PPh_3	77(60)	7
15		CH_3CN	$Pd(PBu_3)_2Cl_2$	80	0
16		CH_3CN	$Ni(PPh_3)_2Cl_2$/40 PPh_3	42	10
17		CH_3CN	$Ni(PPh_3)_2Cl_2$/40 PPh_3	78	7
18		CH_3CN	$Pd(PBu_3)_2Cl_2$	(70)	(18)
19		CH_3CN	$Ni(PPh_3)_2Cl_2$/20 PPh_3	0	62
20		CH_3CN	$Pd(PPh_3)_2Cl_2$/8 PPh_3	30(28)	22(20)
21		CH_3CN	$Pd(PBu_3)_2Cl_2$	32	10

[a] Reaction conditions for palladium-catalyzed reactions: aryl halide, 5.0 mmol; palladium complex, 0.50 mmol; Zn, 20 mmol; phosphine, variable; RCN, 30 mL; 24 h; 160 °C. Reaction conditions for nickel-catalyzed reactions: aryl halide, 2.0 mmol; $Ni(PPh_3)_2Cl_2$, 0.20 mmol; Zn, 8 mmol; PPh_3, variable; CH_3CN, 10 mL; 24 h; 90 °C. Reaction conditions for platinum-catalyzed reactions: aryl halide, 4.0 mmol; $Pt(PPh_3)_2Cl_2$, 0.40 mmol; Zn, 16 mmol; PPh_3, 3.2 mmol; CH_3CN, 24 mL; 24 h; 210 °C. See Experimental Section for detailed reaction conditions. [b] Yields determined by ^1H NMR using $HCON(Et)_2$ as an internal standard. [c] Yields in parentheses are isolated yields. [d] Bu = *n*-butyl, dppp = 1,2-bis(diphenylphosphino)propane, dppm = bis(diphenylphosphino)methane, dppe = 1,2-bis(diphenylphosphino)ethane, $P(o\text{-tol})_3$ = tri-*o*-tolylphosphine.

1-bromo-2-methoxynaphthalene, and 9-bromoanthracene also occurs in acetonitrile to afford the corresponding aromatic nitriles[8] in fair to excellent yields (Table 1). For bromoarenes (ArBr) with one or no substituent at the ortho position, only a trace of the corresponding nitriles was produced. The main products were the phosphonium salt ($PPh_3Ar^+X^-$) and the hydrogenolysis compounds (ArH).

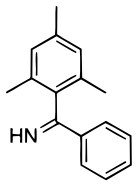
The yield of cyanation depends greatly on the amount of PPh_3 used in the reaction solution. By using the reaction of **1** in acetonitrile in the presence of $PdCl_2(PPh_3)_2$, PPh_3, and zinc powder at 160 °C as the example, the yield of **2** increases as the PPh_3 to palladium ratio grows from 0 to 4. Beyond this value, saturation occurs and the yield remains constant within experimental error. At a low PPh_3 to palladium ratio, rapid decomposition of the palladium complex was observed, leading to low conversion of **1**. The reaction of **1** in acetonitrile to give compound **2** consumes a stoichiometric amount of zinc metal. The best yields of **2** were obtained when 2−4 equiv of zinc metal powder relative to compound **1** was employed.

In addition to the $Pd(PPh_3)_2Cl_2/PPh_3$ system, several other palladium systems also show catalytic activity for the cyanation of **1** in acetonitrile. As shown in Table 1, the activities of $Pd(PBu_3)_2Cl_2$ and $Pd(dppp)Cl_2$ are comparable or superior to that of the $PdCl_2(PPh_3)_2/PPh_3$ system. On the other hand, $Pd(dppe)Cl_2$ and $Pd(dppm)Cl_2$ are much less active. It is noteworthy that the other members of the nickel family also reveal catalytic activity for the cyanation of **1**, although the reaction temperature differs drastically. Some of the results of

(8) These products were characterized by ^1H and ^{13}C NMR, IR, and microanalysis.

cyanation of haloarenes catalyzed by nickel and platinum systems are listed in Table 1. As revealed in entries 16, 17, and 19, the cyanation takes place at 90 °C for $Ni(PPh_3)_2Cl_2/PPh_3$ but at 210 °C for $Pt(PPh_3)_2Cl_2$. In general, nickel and platinum complexes show less selectivity for the cyanation of haloarenes compared to palladium complexes. An exception is the cyanation of *o*-chlorotoluene by $Ni(PPh_3)_2Cl_2$ in the presence of 40 equiv of PPh_3, giving the corresponding cyanation product in 78% yield. Both palladium and platinum complexes do not exhibit significant activity toward chloroarenes. Excess PPh_3 was required for the cyanation of haloarenes catalyzed by $Ni(PPh_3)_2Cl_2$ to prevent the nickel complex from decomposition to the inactive metal.

Other organic nitriles also readily undergo transfer of the nitrile group to aryl halides in the presence of a palladium complex and zinc metal. For example, **3** was converted in propionitrile, *n*-butyronitrile, and benzyl cyanide at 160 °C in the presence of $Pd(PBu_3)_2Cl_2$ and Zn to 2,4,6-trimethylbenzonitrile in 61, 50, and 97% yields (entries 10−12), respectively. According to these data, acetonitrile and benzyl cyanide appear to be the best solvents for the transfer of a nitrile group to aryl halide. It is interesting to note that nitrile-group transfer to **3** took place even in benzonitrile, affording 2,4,6-trimethylbenzonitrile, albeit in low yield (15%). The main product isolated is the imine **4** in 55% yield.[9]



4

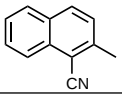
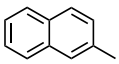
While there is no doubt that, in the present cyanation reaction, the nitrile group in the solvent RCN is transferred to aryl halide to give the product, it is not yet clear where the R group of the solvent goes. To unravel this obscurity, the mixture from the reaction of benzyl cyanide with **3** (entry 12 of Table 1) was analyzed. In addition to the cyanation product 2,4,6-trimethylbenzonitrile, dibenzyl ketone and cyclic product **5** in 39 and 30% yields, respectively, were isolated from the reaction mixture (eq 2). It is conceivable that the observed dibenzyl ketone results from nucleophilic addition of a benzyl group, generated from the cleavage of benzyl cyanide during cyanation, to a benzyl cyanide followed by hydrolysis. On the other hand, product **5** is likely from the addition of a benzyl group to three other benzyl cyanide units followed by cyclization and deamination (vide infra). Nucleophilic addition of Grignard reagents to nitriles is known to give products similar to **5**.[10,11]

(9) Spectral data for **4** are as follows. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.09 (s, 6 H), 2.33 (s, 3 H), 6.91 (s, 2 H), 7.38 (dd, J = 8.0 Hz, J = 7.2 Hz, 2 H), 7.46 (t, J = 8.0 Hz, 1 H), 7.72 (d, J = 7.2 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.5 (q), 21.0 (q), 127.6 (d), 128.3 (d), 128.5 (d), 128.5 (s), 130.9 (d), 134.2 (s), 137.6 (s), 137.7 (s), 178.6 (s). IR (neat): 3238, 3232, 2927, 2858, 1606, 1572, 1448 cm^{-1}. HRMS: calcd for $C_{16}H_{16}N$ 222.1282, found 222.1283.

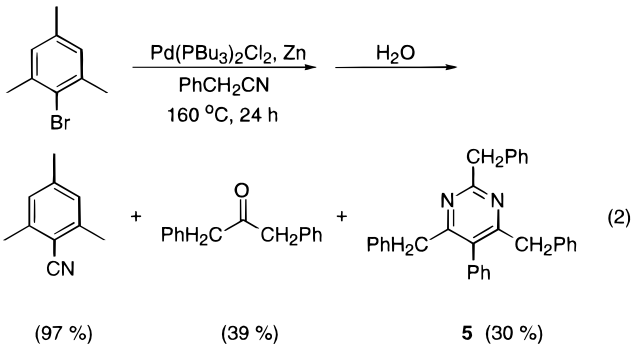
(10) Rabesiaka, P. J. *Bull. Soc. Chim. Fr.* **1970**, 1440.

(11) Wakefield, B. J. *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: New York, 1982; Vol. 7, p 18.

Table 2. Results of the Reaction of 6 with Acetonitrile[a,b]

		yield/%	
entry no.	reagent (amt/mmol)		
1[c]			
2	Zn (0.5)	19	2
3	Zn (2.0)	76	trace
4	$ZnBr_2$ (2.2)	45	
5	ZnI_2 (2.3)	36	
6	$ZnCl_2$ (2.0)	11	
7	$ZnBr_2$ (2.2), PPh_3 (4.0)	36	
8	$ZnBr_2$ (2.2), Zn (2.0), PPh_3 (4.0)	67	trace
9[d]	Zn (2.0), PPh_3 (4.0)		trace
10[d]	PPh_3 (4.0)		trace
11	$AlCl_3$ (2.0)		100

[a] Reaction conditions: **6**, 0.5 mmol; CH_3CN, 30 mL; temperature, 160 °C; reaction time, 24 h. [b] Product yields were determined from ^{1}H NMR spectra using DMF as the internal standard. [c] Methyl-(2-methyl-1-naphthyl)ketimine (**7**) was observed in 35% yield. [d] Most of the starting compound **6** remained unreacted.

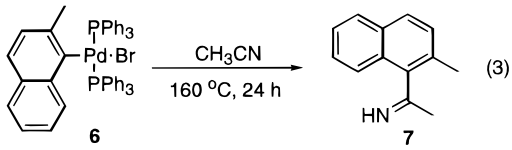


(2)

Mechanistic Studies. During the cyanation of **1** in acetonitrile in the presence of $PdCl_2(PPh_3)_2$, PPh_3, and zinc powder, the palladium intermediate **6** was observed by ^{1}H NMR spectroscopy.[12] This intermediate shows characteristic signals for the 2-methylnaphthyl group at δ 2.24 (s) (methyl protons) and δ 6.24 (d), 6.84 (d), 6.92 (dd), and 6.97 (dd) (aromatic protons) in the ^{1}H NMR spectrum.[13] Interestingly, **6** can be prepared in good yield from oxidative addition of **1** to $Pd(PPh_3)_4$ (see Experimental Section) and is thermally very stable. The structure of **6** consisting of two PPh_3 groups, a 2-methylnaphthyl group, and a bromide as the ligands was determined on the basis of the analytical data and the spectral data obtained. It is noteworthy that **6** acts as an effective catalyst for the cyanation of **1** in the presence of PPh_3, $ZnBr_2$, and zinc powder in acetonitrile to give **2** in 77% yield and 2-methylnaphthalene in 21% yield. To understand how **6** reacts with organic nitrile to yield **2**, a series of control reactions were carried out and the results are shown in Table 2. Heating **6** alone in acetonitrile at 160 °C did not produce the desired product **2** but the imine **7** in 35% yield (entry 1).[13]

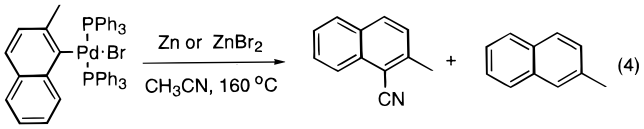
(12) The catalytic reaction (see Experimental Section) was allowed to proceed for ca. 4 h and was then cooled to room temperature. The solvent was removed in vacuo, and some of the residue was dissolved in chloroform-*d* for the ^{1}H NMR measurement.

(13) The other NMR signals of the naphthyl protons are likely buried in the region for the coordinated PPh_3.

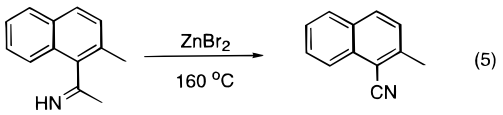


(3)

Clearly, **7** results from the insertion of acetonitrile into the palladium−carbon bond in **6** followed by protonation. To yield the cyanation product **2** from **6**, either zinc metal or zinc halide is required. Thus, treatment of **6** in acetonitrile at 160 °C in the presence of 4 equiv of Zn metal or 4.4 equiv of $ZnBr_2$ afforded 76 and 45% of **2**, respectively (entries 3 and 4) (eq 4). In the presence



(4)

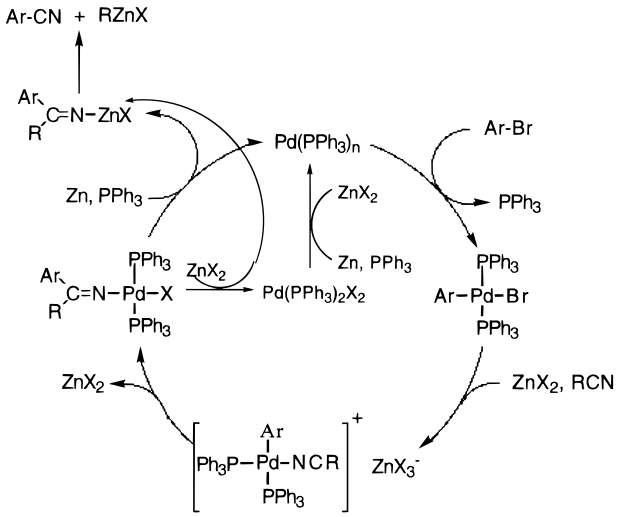


(5)

of excess PPh_3, the requirement of reaction conditions for obtaining **2** is different. Heating **6**, Zn, and excess PPh_3 in acetonitrile did not give **2**. However, replacement of Zn by $ZnBr_2$ in the above solution or addition of $ZnBr_2$ to the above solution, followed by heating, led to the formation of **2** in 36 and 67% yields, respectively (entries 7 and 8). It should be noted that, in the real catalytic cyanation, excess phosphine, zinc halide, and zinc metal are present in solution. Consequently, the reaction conditions of entry 8 are close to the real catalytic conditions. While heating **6** did not give **2** but **7**, the latter was converted to **2** in 44% yield on treating with $ZnBr_2$ at 160 °C for 12 h (eq 5).

The observations of intermediate **6** and its reaction with acetonitrile to yield **7** suggest that the catalysis involves oxidative addition and insertion of RCN into the Ar−Pd bond to give the palladoimine $Pd(PPh_3)_2$-(N=CR(Ar))X, and subsequently protonation of the palladoimine to afford the imine compound **7**. Further transformation of the latter in the presence of $ZnBr_2$ to the cyanation product indicates that $ZnBr_2$ instead of the palladium complex is responsible for the C−R bond cleavage to give the cyanation product. A possible intermediate from the reaction of imine **7** and $ZnBr_2$ is Zn(N=CR(Ar))X, which undergoes β-elimination to give ArCN and RZnX. The enhancement of Zn metal in the transformation of complex **6** to the cyanation product **2** (entries 3 and 8) suggests a facile reaction of **6** with RCN and Zn to yield Zn(N=CR(Ar))X. Alternatively, Zn-(N=CR(Ar))X may be produced from complex **6**, RCN, and ZnX_2. The formation of RZnX is supported by the observation of dibenzyl ketone and products **4** and **5** during catalytic cyanation. These products may be viewed as resulting from further reaction of RZnX with the nitrile solvent used. Insertion of a nitrile group into RZnX to give an imine and then the corresponding ketone is known.[14] The observation that the transformation from complex **6** to **2** is inhibited by excess PPh_3 but is enhanced by the presence of $ZnBr_2$ may be rationalized by the necessity of a coordination site for the

Scheme 1



nitrile solvent. In the presence of excess PPh_3, the chance for the dissociation of a phosphine ligand in **6** is small and thus no coordination site is available for nitrile solvent. However, the presence of $ZnBr_2$, which is known to be a Lewis acid, facilitates the removal of the halide ligand from **6** and creates a vacant coordinating site for a solvent molecule. On the basis of the foregoing mechanistic studies, it is clear that the success of the present catalytic cyanation requires the cooperation of two metals, palladium and zinc, with the former responsible for C−C bond formation and the latter for the bond cleavage. Scheme 1 outlines a possible mechanism for the cyanation reaction based on this cooperation, while Scheme 2 summarizes the proposed pathways for the formation of dibenzyl ketone and product **5**.

Several methods are known in the literature for the preparation of aryl nitriles.[15] Similar to the nitrile-transfer catalysis, one of these methods, the substitution reaction of aryl halides with a metal cyanide catalyzed by a nickel[16] or palladium complex,[17] involves oxidative addition of an aryl halide to a Ni(0) or Pd(0) species as a key step in the reaction. Nucleophilic additions of zinc−,[14] lithium−,[18] magnesium−[19] or aluminum−carbon[20] bonds to a nitrile group to afford an imine and

(14) (a) Kishi, Y.; Hannick, S. M. *J. Org. Chem.* **1983**, *48*, 3883. (b) Jolly, P. W. *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: New York, 1982; Vol. 6, p 84. (c) Bellassoued, M.; Gaudemar, M. *J. Organomet. Chem.* **1974**, *81*, 139.

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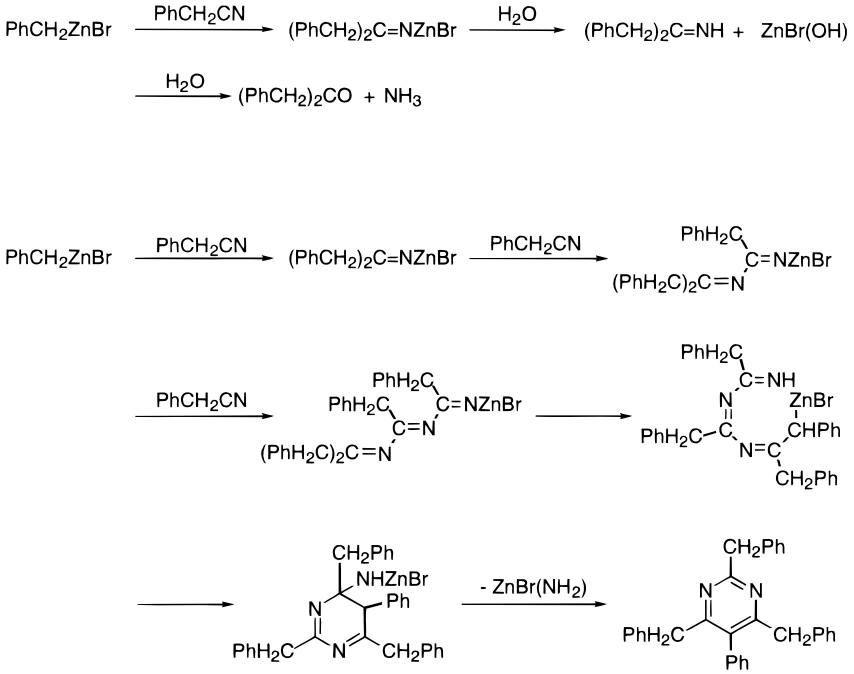
Scheme 2



the corresponding ketone after hydrolysis were reported previously, but no example of such an insertion with a palladium complex is known. Carbon−carbon cleavage in the imine **7** by zinc(II) is a key step for success of the catalytic cyanation. This chemistry is completely unknown in the literature. Investigations in this area may lead to development of new methods of C−C bond activation and may find useful application in organic synthesis.

Experimental Section

All reactions were performed under dry nitrogen, and all solvents were dried by standard methods. ^{1}H and ^{13}C NMR experiments were performed on a Varian Unity 400 spectrometer, while ^{31}P NMR experiments were recorded on a Bruker AM-400 spectrometer using 85% H_3PO_4 as an external standard. GC/MS analyses were performed on a Varian Model 3400 gas chromatograph connected to a Finnigan Mat Magnum mass detector. Infrared spectra were obtained on a Bomem MB-100 spectrophotometer, while mass spectra were recorded on a JEOL JMS-D100 system. Melting points measurements were carried on a Mel-Temp apparatus and are uncorrected. Microanalytical data were obtained on a Heraeus CHN-O-RAPID instrument.

Tri-*n*-butylphosphine (Merck), bis(diphenylphosphino)-methane, 1,2-bis(diphenylphosphino)ethane, 1,2-bis(diphenylphosphino)propane, tri-*o*-tolylphosphine, and tri-*p*-tolylphosphine (Strem), palladium dichloride (Balance Precious Metal), and 1-bromo-2,6-dimethylbenzene, 1-bromo-2-methylnaphthalene, 1-bromo-2-naphthol, 2-bromo-1,3,5-trimethylbenzene, 1-bromo-2,6-dichlorobenzene, 2-chloro-1,2,3-trimethylbenzene, *o*-chlorotoluene, 9-bromoanthracene (TCI), triphenylphosphine, and 1-bromo-2,6-dimethoxybenzene (Aldrich) were used as purchased. $Pd(PBu_3)_2Cl_2$, $Pd(PPh_3)_2Cl_2$, $Pd[P(o\text{-tolyl})_3]_2Cl_2$, $Pd[P(p\text{-tolyl})_3]_2Cl_2$, $Pd(dppe)Cl_2$, $Pd(dppm)Cl_2$, and $Pd(dppp)Cl_2$,[21] $Pd(PPh_3)_4$,[22] and $Pt(PPh_3)_2Cl_2$[23] were prepared according to reported methods.

$Pd(PPh_3)_2Cl_2$-Catalyzed Cyanation of 1-Bromo-2-methylnaphthalene. In a 300 mL autoclave equipped with a mechanical stirrer were added $Pd(PPh_3)_2Cl_2$ (0.350 g, 0.500 mmol), PPh_3 (1.05 g, 4.0 mmol), zinc powder (1.30 g, 20.0 mmol), 1-bromo-2-methylnaphthalene (1.10 g, 5.00 mmol), and acetonitrile (30 mL). The system was evacuated, flushed with nitrogen gas three times, and then heated with stirring at 160 °C for 24 h. The mixture on cooling to ambient temperature was filtered through Celite to remove solid material. Concentration followed by separation on a silica gel column using a mixture of dichloromethane and hexanes as eluent afforded 1-cyano-2-methylnaphthalene (**2**; 0.576 g, 3.45 mmol) in 69% yield. Spectral data for **2** are as follows. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.71 (s. 3 H), 7.33 (d, J = 8.5 Hz, 1 H), 7.51 (dd, J = 8.1 Hz, J = 7.2 Hz, 1 H), 7.62 (dd, J = 8.3 Hz, J = 7.2 Hz, 1 H), 7.82 (d, J = 8.1 Hz, 1 H), 7.90 (d, J = 8.5 Hz, 1 H), 8.15 (d, J = 8.3 Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.0 (q), 108.9 (s), 116.8 (s), 124.5 (d), 126.3 (d), 127.3 (d), 128.1 (d), 128.2 (d), 130.9 (s), 132.3 (d), 132.4 (s), 142.6 (s). IR (KBr): 2214 (ν_{CN}) cm^{-1}. HRMS: calcd for $C_{12}H_9N$ 167.0734, found 167.0742. Anal. Calcd for $C_{12}H_9N$: N, 8.38; C, 86.23; H, 5.39. Found: N, 8.31; C, 86.20; H, 5.50. Mp: 85−87 °C.

Similar reaction conditions were employed for the cyanation of ortho-disubstituted bromoarenes such as 2-bromo-*m*-xylene, 2-bromomesitylene, 1-bromo-2-methoxynaphthalene, and 9-bromoanthracene. The yields of the cyanation products are presented in Table 1, while important spectral data are shown below.

2,4,6-Trimethylbenzonitrile. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 3 H), 2.48 (s, 6 H), 6.93 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.5 (q), 21.5 (q), 110.3 (s), 117.5 (s), 128.1 (d), 141.9 (s), 142.7 (s). IR (KBr): ν_{max} 2211, 1601, 1458, 1376, 1305, 1254, 1041, 900, 862, 725, 690, 503, 481, 435 cm^{-1}. MS (EI): *m/z* (relative intensity) 130 (88), 131 (9), 144 (17), 145 (M^+, 100), 146 (16). HRMS: calcd for $C_{10}H_{11}N$ 145.0891, found 145.0905. Anal. Calcd for $C_{10}H_{11}N$: N, 9.66, C, 82.76; H, 7.58. Found: N, 9.62; C, 82.83; H, 7.58. Mp: 48−50 °C.

2,6-Dimethylbenzonitrile. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.51 (s, 6 H), 7.11 (d, J = 7.2 Hz, 2 H), 7.34 (t, J = 7.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.5 (q), 113.1 (s), 117.0 (s), 127.1 (d), 131.9 (d), 141.9 (s). IR (KBr): ν_{max} 2213, 1959, 1888, 1819, 1691, 1592, 1470, 1383, 1300, 1261, 1200, 1172, 1088, 1038, 982, 783, 727, 598, 569, 407 cm^{-1}. MS (EI): *m/z*

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(relative intensity) 166 (73), 117 (7), 130 (40), 131 (M^+, 100), 132 (16). HRMS: calcd for C_9H_9N 131.0734, found 131.0744. Anal. Calcd for C_9H_9N: N, 10.69; C, 82.44; H, 6.67. Found: N, 10.65; C, 82.29; H, 6.92. Mp: 89−90 °C.

2-Methoxy-1-naphthonitrile. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.07 (s, 3 H), 7.27 (d, J = 8.8 Hz, 1 H), 7.45 (dd, J = 8.0 Hz, J = 7.6 Hz, 1 H), 7.63 (dd, J = 8.8 Hz, J = 7.6 Hz, 1 H), 7.83 (d, J = 8.0 Hz, 1 H), 8.03 (d, J = 8.8 Hz, 1 H), 8.09 (d, J = 8.8 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.6 (q), 95.0 (s), 112.0 (d), 115.7 (s), 124.0 (d), 125.0 (d), 128.0 (s), 128.4 (d), 129.2 (d), 133.6 (s), 135.0 (d), 161.6 (s). IR (KBr): ν_{max} 2215, 1624, 1586, 1508, 1468, 1434, 1340, 1283, 1257, 1181, 1148, 1081, 1042, 1020, 908, 811, 774, 745, 600, 449 cm^{-1}. MS (EI): *m*/*z* (relative intensity) 140 (100), 141 (26), 183 (M^+, 74), 184 (11). HRMS: calcd for $C_{12}H_9ON$ 183.0684, found 183.0680. Anal. Calcd for $C_{12}H_9ON$: N, 7.65; C, 78.69; H, 4.92. Found: N, 7.57; C, 78.44; H, 4.97. Mp: 95−96 °C.

$Pd(PBu_3)_2Cl_2$-Catalyzed Cyanation of 2-Bromo-1,3,5-trimethylbenzene in Benzyl Cyanide. In a 100 mL round-bottom side-arm flask were added $Pd(PBu_3)_2Cl_2$ (0.116 g, 0.200 mmol), zinc powder (0.520 g, 8.0 mmol), 2-bromo-1,3,5-trimethylbenzene (0.398 g, 2.00 mmol), and benzyl cyanide (5.0 mL). The system was evacuated, flushed with nitrogen gas three times, and then heated with stirring to 160 °C for 24 h. The mixture on cooling to ambient temperature was filtered through Celite to remove solid material. Concentration, followed by separation on a silica gel column using a mixture of dichloromethane and hexanes (1/1 v/v) as eluent afforded 2,4,6-trimethylbenzonitrile (0.287 g, 1.94 mmol) in 97% yield, dibenzyl ketone (0.163 g, 0.78 mmol) in 39% yield, and 2,4,6-tribenzyl-5-phenylpyrimidine (**5**; 0.255 g, 0.60 mmol) in 30% yield. Important spectral data for 2,4,6-trimethylbenzonitrile are shown above, while those for dibenzyl ketone and **5** are shown below.

Dibenzyl Ketone. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.73 (s, 4 H), 7.16 (d, J = 7.6 Hz, 4 H), 7.28 (t, J = 7.2 Hz, 2 H), 7.33 (dd, J = 7.6 Hz, J = 7.2 Hz, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 49.1 (t), 127.0 (d), 128.7 (d), 129.5 (d), 134.0 (s), 205.6 (s). IR (KBr): ν_{max} 3030, 1716, 1602, 1496, 1453, 1411, 1328, 1056, 753, 731, 699, 531, 478 cm^{-1}. MS (EI): *m*/*z* (relative intensity) 118 (100), 92 (29), 210 (M^+, 65), 211 (12). HRMS: calcd for $C_{15}H_{14}O$ 210.1045, found 210.1052.

2,4,6-Tribenzyl-5-phenylpyrimidine (5). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 4 H), 4.32 (s, 2 H), 6.87 (m, 6 H), 7.12 (m, 6 H), 7.33 (m, 6 H), 7.44 (d, J = 8.0 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 41.5 (t), 45.6 (t), 126.2 (d), 126.3 (d), 128.0 (d), 128.1 (d), 128.3 (d), 128.4 (d), 129.0 (d), 129.4 (d), 129.8 (d), 131.1 (s), 135.5 (s), 138.0 (s), 138.6 (s), 166.8 (s), 167.6 (s). IR (KBr): ν_{max} 3060, 3029, 2924, 2852, 1602, 1551, 1536, 1494, 1454, 1404, 1074, 1030, 762, 723, 699 cm^{-1}. MS (EI): *m*/*z* (relative intensity) 91 (20), 425 (100), 426 (M^+, 67), 427 (18). HRMS: calcd for $C_{31}H_{26}N_2$ 426.2096, found 426.2076.

Similar reaction conditions using $Pd(PBu_3)_2Cl_2$ as the catalyst were employed for the cyanation of 2-bromo-*m*-xylene, 2-bromomesitylene, 1-bromo-2-methoxynaphthalene, and 9-bromoanthracene. The yields of the cyanation products are presented in Table 1.

Synthesis of Bromo(2-methyl-1-naphthyl)bis(triphenylphosphine)palladium(II) (6). In a 250 mL side-arm flask containing $Pd(PPh_3)_4$ (11.54 g, 10.0 mmol) under an atmosphere of nitrogen were added 1-bromo-2-methylnaphthalene (3.32 g, 15.0 mmol) and toluene (100 mL). The system was purged by nitrogen gas three times and was then heated to 100 °C with stirring for 24 h. On cooling to room temperature, the solution was evacuated to remove the solvent. The residue was redissolved in dichloromethane and was filtered through Celite. Addition of ether to the filtrate led to precipitation of the desired white product in 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.24 (s, 3 H), 6.24 (d, J = 8.0 Hz, 1 H), 6.84 (d, J = 8.0 Hz, 1 H), 6.92 (dd, J = 8.1 Hz, J = 7.6 Hz, 1 H), 6.97 (dd, J = 8.2 Hz, J = 7.6 Hz, 1 H), 7.13 (dd, J = 7.0 Hz, J = 7.0 Hz, 12 H), 7.21 (d, J = 8.2 Hz, 1 H), 7.24 (t, J = 7.0 Hz, 6 H), 7.42 (dd, J_{HP} = 14.8 Hz, J = 7.0 Hz, 12 H), 8.54 (d, J = 8.1 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.3 (q), 123.3 (d), 123.4 (d), 123.5 (d), 127.1 (d), 127.5 (dt, J_{CP} = 4.8 Hz), 128.1 (d), 129.7 (d), 130.8 (d), 131.3 (t, J_{CP} = 23.9 Hz), 132.5 (s), 134.5 (dt, J_{CP} = 6.2 Hz), 136.8 (t, J_{CP} = 4.5 Hz), 138.4 (t, J_{CP} = 3.4 Hz), 159.5 (s). Anal. Calcd for $C_{47}H_{39}P_2PdBr$: C, 66.25; H, 4.61. Found: C, 66.25; H, 4.65. Mp: 230 °C dec.

Formation of Methyl(2-methyl-1-naphthyl)ketimine (7) from Bromo(2-methyl-1-naphthyl)bis(triphenylphosphine)palladium(II). In a 300-mL autoclave containing bromo(2-methyl-1-naphthyl)bis(triphenylphosphine)palladium(II) (0.425 g, 0.500 mmol) under an atmosphere of nitrogen was added acetonitrile (30 mL) via a syringe. The system was evacuated, flushed with nitrogen gas three times, and then heated with stirring at 160 °C for 24 h. The mixture on cooling to ambient temperature was filtered through Celite to remove the solid material. Concentration, followed by separation on a silica gel column using a mixture of dichloromethane and hexanes as eluent, afforded an oily product (0.032 g, 0.175 mmol) in 35% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.42 (s, 3 H), 2.45 (s, 3 H). 5.6 (b, 1 H), 7.31 (d, J = 8.8 Hz, 1 H), 7.46 (m, 2 H), 7.68 (d, J = 8.0 Hz, 1 H), 7.73 (d, J = 7.2 Hz, 1 H), 7.82 (d, J = 7.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4 (q), 28.1 (q), 124.3 (d), 125.3 (d), 126.6 (d), 127.9 (d), 128.1 (d), 128.5 (d), 129.2 (s), 129.7 (s), 131.8 (s), 138.8 (s), 181.1 (s). IR (KBr): ν_{max} 3241, 3191, 3040, 2914, 2850, 1634, 1508, 1427, 1324, 1266, 1180, 1098, 930, 868, 813, 784, 744, 518, 440 cm^{-1}. MS (EI): *m*/*z* (relative intensity) 115 (78), 139 (46), 140 (19), 141 (32), 168 (80), 181 (100), 183 (M^+, 55), 184 (10). HRMS: calcd for $C_{13}H_{13}N$ 183.1048, found 183.1031.

$Ni(PPh_3)_2Cl_2$-Catalyzed Cyanation of 1-Bromo-2-methylnaphthalene. To a 50-mL side-arm flask containing $Ni(PPh_3)_2Cl_2$ (0.130 g, 0.200 mmol), zinc powder (0.520 g, 8.00 mmol), 1-bromo-2-methylnaphthalene (0.440 g, 2.00 mmol), and triphenylphosphine (0.262 g, 1.0 mmol) under 1 atm of nitrogen was added acetonitrile (10 mL). The system was then stirred at 90 °C for 24 h. After filtration through Celite to remove the solid material, the solution was concentrated and then separated on a silica gel column using a mixture of dichloromethane and hexanes as eluent to afford 1-cyano-2-methylnaphthalene (0.077 g, 0.46 mmol) in 23% yield.

The cyanation of *o*-chlorotoluene was carried out under similar reaction conditions to give *o*-tolunitrile in 78% yield.

Acknowledgment. We thank the National Science Council of the Republic of China (Grant No. NSC 83-0208-M-007-095) for support of this research.

OM970842F