LETTERS

Catalytic Cyanation of Aryl Halides with NaCN in the Presence of Crowned Phosphine Complexes of Palladium under Solid-liquid Two-phase Conditions

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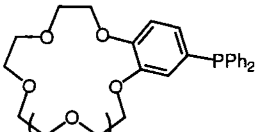
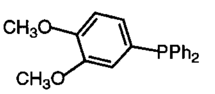
Abstract: The cyanation of aryl halides with powdered NaCN in dioxane is efficiently catalyzed by crowned phosphine complexes of palladium to give aryl cyanides in good yields. Owing to the proximity effect of the crowned complexes, the catalytic efficiency is superior to those of mixed systems of unmodified phosphine complexes of palladium with the corresponding crown ethers.

The cyanation of aromatic halides with inexpensive alkali metal cyanides is an important synthetic tool, which is achieved by the use of Ni or Pd phosphine complexes under very mild conditions.[1] However, alkali metal cyanides are insoluble in common organic solvents, whereas in such solvents in which the cyanide salts are too soluble, an excess of cyanide anion deactivates these catalysts.[2] In order to keep the concentration of cyanide anion moderate, the good combination of solvent and cyanide salt,[2c,3] and the use of phase transfer catalysts[2a,4] or Al_2O_3[5] have been investigated. However, these cyanations require strict reaction conditions. Recently, it has been reported that phosphine complexes modified with crown ethers efficiently react with slightly soluble alkali metal salts.[6-8] Therefore we studied the catalytic cyanation with sodium cyanide using the crowned phosphine complexes of palladium.

The cyanation of phenyl bromide with powdered NaCN in dioxane successfully proceeded in the presence of $PdCl_2$-$\{PPh_2(bc\text{-}5)\}_2$ or $PdCl_2\{PPh_2(bc\text{-}6)\}_2$ (PPh_2(bc-5)=17-diphenylphosphino-2,5,8,11,14-pentaoxa-bicyclo-[13.4.0]-nonadeca-15,17,19-triene, PPh_2(bc-6)=20-diphenylphosphino-2,5,8,11,14,17-hexaoxa-bicyclo-[16.4.0]-docosa-18,20,22-triene) to give benzonitrile in a considerable turnover number (see Table 1).[9] These catalysts were unfortunately inactive for the cyanation using an aqueous solution of NaCN in toluene at 100°C.



n= 0, PPh_2(bc-5)
1, PPh_2(bc-6)



PPh_2(dmp)

The turnover number of the solid-liquid cyanation was improved by the addition of small amounts of Zn powder and free PPh_2(bc-5). The Zn powder is likely to reduce $PdCl_2\{PPh_2(bc\text{-}5)\}_2$ to the catalytically active species as reported before.[2c] In fact, $PhPdBr\{PPh_2(bc\text{-}5)\}_2$ was active without Zn powder (see Table 2).[10] The addition of the phosphine mostly contributes to stabilization of the catalytically active species as described below.

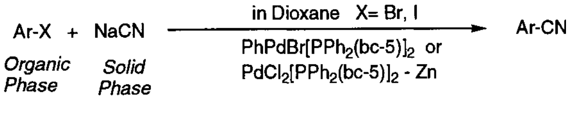


Table 1. Catalytic cyanation of PhBr with powdered NaCN in dioxane in the presence of $PdCl_2L_2$[a]

$PdCl_2L_2$ /L=	Additives	Turnover Number (PhCN/Pd)[b]
PPh_2(bc-5)	Zn	264
PPh_2(bc-5)[c]	Zn	113
PPh_2(bc-5)		215
PPh_2(bc-5)[d]		191
PPh_2(bc-6)	Zn	258
PPh_3	Benzo-15-crown-5[e], Zn	170
PPh_3	Zn	30

[a] A suspension of PhBr (25 mmol), powdered NaCN (75 mmol), Zn powder (2 mmol), $PdCl_2L_2$ (0.05 mmol) and L (0.1 mmol) in dioxane (10 ml) was vigorously stirred under reflux for 20 h. [b] The turnover number was determined by GLC using naphthalene as an internal standard. [c] Toluene (10 ml) was used instead of dioxane. [d] In the absence of free PPh_2(bc-5). [e] Benzo-15-crown-5 (0.2 mmol) was added

Table 2. Catalytic cyanation of aryl halides with powdered NaCN in dioxane in the presence of *trans*-$PhPdBrL_2$[a]

Aryl Halide	Catalyst	Yield/%[a)]
C_6H_5Br	$PhPdBr\{PPh_2(bc\text{-}5)\}_2$	85
	$PhPdBr\{PPh_2(bc\text{-}5)\}_2$[b]	89
	$PhPdBr\{PPh_2(dmp)\}_2$[c]	71
	$PhPdBr\{PPh_2(dmp)\}_2$	21
p-$CH_3C_6H_4Br$	$PhPdBr\{PPh_2(bc\text{-}5)\}_2$	92 (77)[d]
p-ClC_6H_4Br[e]	$PhPdBr\{PPh_2(bc\text{-}5)\}_2$	93 (81)[d]
p-$CH_3OC_6H_4Br$	$PhPdBr\{PPh_2(bc\text{-}5)\}_2$	86
C_6H_5I	$PhPdBr\{PPh_2(bc\text{-}5)\}_2$	91
m-ClC_6H_4I[f]	$PhPdBr\{PPh_2(bc\text{-}5)\}_2$	87

[a] A suspension of aryl halide (7.5 mmol), powdered NaCN (22.5 mmol), *trans*-$PhPdBrL_2$ (0.025 mmol) and L (0.05 mmol) in dioxane (5 ml) was vigorously stirred under reflux for 20 h. [a] GLC yield. [b] Zn (0.1 mg atom) was added. [c] Benzo-15-crown-5 (0.1 mmol) was added. [d] Isolated yield. [e] *p*-ClC_6H_4CN. [f] *m*-ClC_6H_4CN

The addition of benzo-15-crown-5 was effective in increasing the catalytic activity of $PdCl_2(PPh_3)_2$. Though a large amount of the benzocrown was used, the activity of the mixed system was still inferior to that of $PdCl_2\{PPh_2(bc\text{-}5)\}_2$. The crowned phosphine and PPh_2(dmp) (PPh_2(dmp)=1,2-dimethoxy-4-diphenylphosphino-benzene) are almost equivalent in both electronic and steric effects. However, the catalytic activity of $PhPdBr\{PPh_2(dmp)\}_2$ was very poor as compared with that of $PhPdBr\{PPh_2(bc\text{-}5)\}_2$. The addition of benzo-15-crown-5 also enhanced the catalytic activity of $PhPdBr\{PPh_2(dmp)\}_2$, but the yield was still below the level of $PhPdBr\{PPh_2(bc\text{-}5)\}_2$. The crowned phosphine itself is known to be upon the same extractability level with benzo-15-crown-5.[6b] Therefore, the high reactivity of the crowned complexes is likely attributed to a proximity effect as in enzyme chemistry. That is to say, the intramolecular substitution of the palladium complex with the cyanide anion extracted with the side crown arm is much faster than the corresponding intermolecular reaction in the mixed catalyst system. Analogous proximity effects are observed in other reactions of crowned phosphine complexes.[6a,7,11]

The biphasic cyanation of iodides as well as aryl bromides was also achieved. As aryl chlorides were inert under these conditions, bromo or iodo chlorobenzenes gave the corresponding chlorobenzonitriles in good yields. These biphasic reactions have the advantage in that the product and the cyanide salt are easily separated from the reaction mixture.

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References and Notes

(1) G. P. Ellis and T. M. Romney-Alexander, *Chem Rev.*, **1987**, *87*, 779; V. V. Grushin and H. Alper, *Chem Rev.*, **1994**, *94*, 1047.

(2) (a) L. Cassar, *Ann. N. Y. Acad. Sci.*, **1980**, *333*, 208; (b) P. J. Peerce-Landers and R. J. Jasinski, *J. Electrochem. Soc.*, **1983**, *130*, 1862; (c) Y. Sakakibara, F. Okuda, A. Shimobayashi, K. Kirino, M. Sakai, N. Uchino, and K. Takagi, *Bull. Chem. Soc. Jpn.*, **1988**, *61*, 1985.

(3) K. Takagi, K. Sasaki, and Y. Sakakibara, *Bull. Chem. Soc. Jpn.*, **1991**, *64*, 1118; Y. Sakakibara, Y. Ido, K. Sasaki, M. Sakai, and N. Uchino, *Bull. Chem. Soc. Jpn.*, **1993**, *66*, 2776.

(4) H. Prochazka and M. Siroky, *Coll. Czech. Chem. Commun.*, **1983**, *48*, 1765; N. Sato and M. Suzuki, *J. Heterocycl. Chem.*, **1987**, *24*, 1371; E. Piers and F. F. Fleming, *Can. J. Chem.*, **1993**, *71*, 1867.

(5) J. R. Dalton and S. L. Regen, *J. Org. Chem.*, **1979**, *44*, 4443.

(6) (a) T. Okano, M. Iwahara, T. Suzuki, H. Konishi, and J. Kiji, *Chem. Lett.*, **1986**, 1467; (b) T. Okano, M. Iwahara, H. Konishi, and J. Kiji, *J. Organomet. Chem.*, **1988**, *346*, 267.

(7) M. Sawamura, H. Nagata, H. Sakamoto, and S. Ito, *J. Am. Chem. Soc.*, **1992**, *114*, 2586 .

(8) G. M. Gary, *Comments Inorg. Chem.*, **1995**, *17*, 94.

(9) These dichloro compounds were prepared by the previously reported procedure.[6]

(10) This phenyl compound was prepared as follows. To a mixture of $PdCl_2$ (0.05 g) and PPh_2(bc-5) (0.51 g) in DMSO (4 ml) at 130°C, $NH_2NH_2 \cdot H_2O$ (0.07 ml) was added. After addition of benzene (30 ml), the solution was washed with water (10 ml) several times. After concentration and dryness, the residue was treated with PhBr (0.3 ml) in benzene (4 ml) under reflux for 20 h to give *trans*-PhPdBr$\{PPh_2(\text{bc-5})\}_2$ as orange crystals (0.21 g, 64 %, mp. 97-100 °C). ^{1}H-NMR(270 MHz, $CDCl_3$, δ) : 3.7-4.2 (32H, m), 6.23 (2H, dd, J=7.3 and 7.8Hz), 6.35 (1H, t, J= 7.3Hz), 6.62 (2H, d, J=7.8Hz), 6.78 (2H, d, J=8.4Hz), 7.0 (2H, m), 7.1-7.7 (22H, m). ^{13}C-NMR(67.8 MHz, $CDCl_3$, δ) : 68.7, 69.0, 69.4, 69.5, 70.5, 70.6, 71.2, 71.3, 113.0, 121.8, 122.5, 125.3, 127.7, 127.8, 128.6, 129.5, 132.3, 134.3, 136.3, 148.4, 150. 8, 156.3. ^{31}P-NMR(109.3 MHz, $CDCl_3$, δ) : 22.7.

(11) E. M. Hyde, B. L. Show, and I. Shepherd, *J. Chem. Soc., Dalton Trans.*, **1978**, 1686.