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PALLADIUM(II) CATALYZED SYNTHESIS OF ARYL CYANIDES FROM ARYL HALIDES

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In the presence of Pd(II) salts, substitution reaction of aryl halides with potassium cyanide occurs readily which affords a simple and beneficial method for aryl cyanide synthesis.

The conversion of aryl halides into the corresponding cyanides has been usually effected by Rosenmund-von Braun reaction,$^{1)}$ which is characterized by the use of a stoichiometric amount of cuprous cyanide as a source of cyanide group. Recently palladium(II) catalyzed aromatic nuclear oxidation such as acetoxylation$^{2)}$ and nitration$^{3)}$ has been reported, but little attentions have been paid on the catalytic displacement of halogen atoms in non-activated aromatic halides by the nucleophiles. We wish to report the synthesis of aryl cyanides by the substitution reaction of aryl halides with cyanide ion in the presence of a catalytic amount of palladium(II) salts.

$$\mathrm{ArX} \quad + \quad \mathrm{KCN} \quad \xrightarrow[\mathrm{DMF}]{\mathrm{Pd(II)}} \quad \mathrm{ArCN} \quad + \quad \mathrm{KX} \qquad (\mathrm{X} = \mathrm{I\ or\ Br})$$

Aryl halides react easily with potassium cyanide in dimethylformamide to give aryl cyanides in high yields. As an example, a mixture of 2.34 g (10 mmol) of *p*-iodoanisole, 1.04 g (16 mmol) of KCN, and 7.9 mg (0.05 mmol) of palladium cyanide in 5ml of dimethylformamide was refluxed overnight with stirrrng under nitrogen. No metallic palladium precipitated after the reaction. The reaction mixture was then shaken with ether-water. The ether extract was evaporated to yield 1.00 g (75.2%) of *p*-methoxybenzonitrile. The product was analytically pure without further purification. Other results are listed in Table 1.

Table 1. Catalytic Cyanation of Aryl Halide

Aryl Halide	Catalyst	Temp. (°C)	Time (hr)	Conversion[c)] (%)	Selectivity of Aryl Cyanide[c)] (%)
Iodobenzene	$Pd(CN)_2$	140	2.0	100	84
Iodobenzene[a)]	$Pd(OAc)_2$	140	3.0	100	72
Iodobenzene	$Pd(OAc)_2$	140	2.0	100	72
Bromobenzene	$Pd(CN)_2$[b)]	150	12.0	72	84
Bromobenzene	$Pd(CN)_2$	153	11.5	91	80
1-Bromonaphthalene	$Pd(CN)_2$	140	2.0	64	95

Aryl halide: 2 mmol, Catalyst: 0.04 mmol, KCN: 4 mmol, DMF: 2 ml.

a) Iodobenzene: 4 mmol, KCN: 6 mmol. b) 0.08 mmol. c) Values on glc analysis.

No reaction took place when palladium(II) catalyst was absent. In the presence of the catalyst, the reaction proceeded smoothly in contrast with the similar reaction of aryl halides with cuprous salts,[4)] which cannot be catalytic since alkali-metal salts depress the reaction.[5)] Additives such as phosphine or phosphite depressed the reaction completely even in twice mole to palladium and the exclusion of air and moisture in the reaction system was necessary to obtain the reproducible results. No by-products such as biphenyls were detected on glc analysis.

The following features of this reaction are believed to be of practical value in preparative work: (i) The selectivity of nitriles is high. (ii) The reaction rate is sufficiently fast even below the refluxing temperature of the solvent (DMF).[6)] (iii) The isolation of the products from the reaction mixture is easily effected by the ether-extraction without the troublesome treatment which is necessary to decompose the complex in Rosenmund-von Braun reaction.

To examine the scope and limitation of the catalytic reaction, competitive reactions were carried out. The results are listed in Table 2. The ease of displacement of halogen atoms from the aromatic nucleus is in the order of $I > Br > Cl$.

Table 2. Competitive Cyanation of Substituted Aryl Halides

Aryl Halides (1 mmol / 1 mmol)	Conversion (mmol)
Iodobenzene/*p*-Iodotoluene	0.25 / 0.18
p-Iodotoluene/*p*-Iodoanisole	0.09 / 0.07
m-Iodotoluene/*p*-Iodoanisole	0.16 / 0.13
o-Iodotoluene/*p*-Iodoanisole	0.14 / 0.13
p-Chloroiodobenzene/*p*-Iodotoluene	0.34*/ 0.11

Reaction temp.: 140°C, Reaction time: 1 hr, $Pd(CN)_2$: 0.04 mmol, KCN: 4 mmol, DMF: 2 ml. The selectivities of aryl cyanides in all reactions were sufficiently high (>93%). **p*-Chlorobenzonitrile.

Chlorobenzene failed to react under our reaction conditions. Although the effect of the substituents is relatively small compared with the S_N reaction of activated aryl halides,7) a distinct tendency of substituent effect was observed in Table 2. An electron-attracting substituent accelerated the reaction and electron-releasing substituents retarded.

At the present stage only a speculative view can be advanced concerning the mechanism of the reaction. The above observations are not accommodated to the nucleophilic substitution of aromatic halides activated, for example, by the π-coordination of palladium(II) to the aromatic ring. In view of the small *ortho*-effect compared with that of the palladium-catalyzed aromatic substitution of olefins,8) a phenylpalladium intermediate is also less plausible. The four center process which was assumed in the exchange reaction of aryl halides with cuprous salts9) seems more likely. Indeed both reactions show similar features except for the inhibition by air and the reaction being catalytic for the reaction of palladium.

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References and Notes

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5) Catalytic replacement of aryl halides with alkali-metal halides was also achieved by the catalysis of nickel-phosphine complexes (to be published).

6) For comparison, Friedman *et al.*10) obtained 1-cyanonaphthalene in 94% yield in the reaction of 1-bromonaphthalene (1.00 mol) with CuCN (1.15 mol) in DMF under reflux (153°C) for 4 hrs.

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