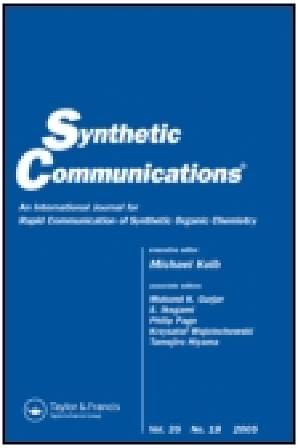

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Copper(I)-Mediated Novel Thiocyanation of Nonactivated Aryl Iodides

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COPPER(I)-MEDIATED NOVEL THIOCYANATION OF NONACTIVATED ARYL IODIDES

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ABSTRACT: Various aryl thiocyanates **2** were easily prepared in acceptable yields by heating aryl iodides **1** with cuprate complex $K[Cu(SCN)_2]$ in *N,N*-dimethylformamide (DMF).

Aryl thiocyanates are versatile starting material for a variety of sulfur-containing compounds,[1] especially heterocycles.[2] Their known preparation methods include electrophilic thiocyanation of activated arenes by thiocyanogen,[3,4] thiocyanogen halide[4,5] or *N*-thiocyanatosuccinimide[6]; treatment of aryldiazonium,[7] *N*-arylpyridinium[8] or activated aryl halides[9] with metal thiocyanate; cyanation of organosulfur compounds;[10-17] and organometallic approaches based on arylthallium[18] and arylzinc[19] compounds. The major drawbacks involved therein are toxic nature or high cost of reagent, low regio- or chemo-selectivity, poor

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accessibility to starting material, formation of side product (especially, isothiocyanate), and unsatisfactory yield.

Unlike alkyl halides, aryl halides are generally too inactive toward thiocyanate anion to afford aryl thiocyanates. Early workers made some attempt to use copper salts for overcoming this difficulty.[20] In most cases, however, the major product was not the expected aryl thiocyanates but their descendants. To our knowledge, the work by Clark and coworkers was the only successful case,[21] where charcoal-supported CuSCN was found to be effective for the thiocyanation of nonactivated haloarenes. However, it is not free from some drawbacks such as the use of large excess of reagent and tedious effort necessary for preparing the supported copper salt. In this paper, we wish to report that the thiocyanation of nonactivated iodoarenes can be effected with ease using a cuprate complex $K[Cu(SCN)_2]$ as the thiocyanating agent in a dipolar aprotic solvent.

In contrast to early report that the reaction between aryl halides and metal thiocyanates in pyridine or aqueous alcohol led to arenethiol and/or disulfide,[20] we found that thiocyanatodurene **2a** could be obtained by the heterogeneous interaction between iododurene **1a** and CuSCN in hot DMF. However, the yield of **2a** was low because of the concurrent formation of considerable amounts of nitrile **3a** and disulfide **4a**. In order to enhance the solubility and improve nucleophilicity of CuSCN, one equiv of KSCN was added to the reaction system to generate the cuprate complex $K[Cu(SCN)_2]$. By this modification, the formation of nitrile **3a** was considerably depressed and the yield of **2a** rose up to 57%. Under these conditions, the thiocyanation proceeded in homogeneous phase. The results are summarized in Table 1. Presence of functionality such as acetamide and phenylthio groups did not affect the yields so much, and the formation of isothiocyanate could not be observed with all substrates examined.

$$\underset{\mathbf{1}}{\mathrm{ArI}} + \mathrm{K[Cu(SCN)_2]} \xrightarrow[\Delta]{\mathrm{DMF}} \underset{\mathbf{2}}{\mathrm{ArSCN}} + (\,\underset{\mathbf{3}}{\mathrm{ArCN}} + \underset{\mathbf{4}}{\mathrm{ArSSAr}}\,)$$

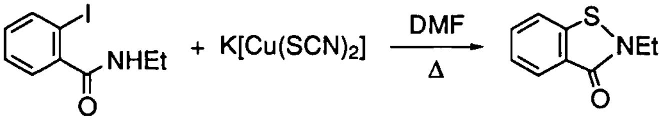
Table 1. Thiocyanation of Substituted Iodoarenes 1[a]

Iodoarene 1			Thiocyanate 2		
	ArI	Conv./%	ArSCN	Yield/%	IR ν_{max}/cm^{-1}
1a	2,3,5,6-Me_4C_6HI	100	2a	57	2150
1b	4-MeC_6H_4I	100	2b[15a]	52	2155
1c	4-$MeOC_6H_4I$	53	2c[15a]	34	2155
1d	4-ClC_6H_4I	68	2d[15a]	43	2160
1e	4-$MeCONHC_6H_4I$	44	2e[15a]	33	2155
1f	2-$MeCONHC_6H_4I$	100	2f	40	2230
1g	4-(PhS)C_6H_4I	94	2g	39	2155

[a] Reaction conditions: Iodoarene 1 2 mmol, CuSCN 2 mmol, KSCN 2 mmol, DMF 5 mL; 140 °C, 12 h under Ar.

The effect of CuSCN/KSCN ratio was also investigated; addition of an equimolar amount of KSCN improved the yield of **2a** considerably, but further addition affected only slightly and a large excess of KSCN was found to work adversely, lowering the yield (Table 2). Among various dipolar aprotic solvents examined, DMF was the solvent of choice. Attempted reaction in HMPA resulted in the formation to **3a** and **4a**. Compared with KSCN, other thiocyanates such as NaSCN, $Ba(SCN)_2{\bullet}2H_2O$ and NH_4SCN gave no better results.

As an extension, we have also applied this procedure to the synthesis of a heterocycle. When *N*-ethyl-2-iodobenzamide was reacted with $K[Cu(SCN)_2]$ in hot DMF, 2-ethyl-1,2-benzisothiazol-3(2*H*)-one **5** was obtained in 52% isolated yield.



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Since nonactivated iodoarenes are readily obtained by the direct iodination of corresponding arenes with iodine-periodic acid,[22] the present new procedure should provide a convenient access to a variety of aryl thiocyanates.

Table 2. Effect of Molar CuSCN/KSCN Ratio on Yield of 2a [a]

CuSCN/equiv	KSCN/equiv	Yield of 2a/%
1	0	33
2	0	30
1	1	57
1	2	61
1	3	49

[a] Reaction conditions: Iododurene **1a** 2 mmol, DMF 5 mL; 140 °C, 12 h under Ar.

Experimental Section

General. Copper(I) thiocyanate and potassium thiocyanate were used after drying *in vacuo* for 6 h. All solvents were used after distillation. All reagents were of commercial quality and purchased from Wako Pure Chemical Industries, Ltd. and Nacalai Tesque, Inc. ^{1}H-NMR spectra were recorded in $CDCl_3$ on a 200-MHz NMR spectrometer. Mass spectra (EI) were determined at 70 eV. Elemental analyses were carried out at Microanalytical Laboratory, Institute for Chemical Research, Kyoto University.

2,3,5,6-Tetramethylphenyl Thiocyanate (2a). The Typical Procedure for Thiocyanation. Under an argon atmosphere, a mixture of iododurene **1a** (0.52 g, 2.0 mmol), CuSCN (0.24 g, 2.0 mmol), KSCN (0.19 g, 2.0 mmol) and DMF (5 mL) was heated with stirring in an oil bath and maintained at 140 °C for 12 h. The reaction mixture gradually turned brown. After cooling, the mixture was diluted with benzene (10 mL) and water (10 mL), and then filtered through a Celite bed. Aqueous phase was extracted with benzene (10 mL x 2) and the combined organic phase was washed with water, dried over Na_2SO_4, and concentrated. The resulting orange-colored oil was chromatographed on silica gel (hexane as eluent) to afford thiocyanate **2a** (57%). Further purification was made by recrystallization from hexane/dichloromethane. Colorless solid, mp 48-49 °C; ^{1}H NMR ($CDCl_3$) δ 2.27 (s, 6 H), 2.52 (s, 6 H), 7.08 (s, 1 H); IR (KBr) 2150, 1465 cm^{-1}; MS (EI) *m/z* 191 (100, M+), 176 (43), 164 (71), 149 (49). Anal. Calcd for $C_{11}H_{13}NS$: C, 69.1; H, 6.9; N, 7.3. Found: C, 69.3; H, 6.9; N, 7.3.

2-Acetylaminophenyl Thiocyanate (2f): Colorless solid, mp 175-177 °C; ^1H NMR ($CDCl_3$) δ 2.30 (s, 3 H), 7.3-7.5 (m, 2 H), 7.7-7.9 (m, 2 H), 10.7 (br s, 1 H); IR (KBr) 3535, 2230, 1550 cm^{-1}; MS (EI) *m/z* 192 (21, M+), 150 (100), 123 (18). Anal. Calcd for $C_9H_8N_2OS$: C, 56.2; H, 4.2; N, 14.6. Found: C, 56.1; H, 4.1; N, 14.6.

4-(Phenylthio)phenyl Thiocyanate (2g): Colorless oil; ^1H NMR ($CDCl_3$) δ 7.2-7.5 (m, 9 H); IR (NaCl) 2155, 1475 cm^{-1}; MS (EI) *m/z* 243 (100, M+), 184 (46), 109 (34). Anal. Calcd for $C_{13}H_9NS_2$: C, 64.2; H, 3.7; N, 5.8. Found: C, 64.3; H, 3.7; N, 5.5.

2-Ethyl-1,2-benzisothiazol-3(2*H*)-one (5). A mixture of *N*-ethyl-2-iodobenzamide (0.55 g, 2.0 mmol), CuSCN (0.24 g, 2.0 mmol), KSCN (0.19 g, 2.0 mmol) and DMF (5 mL) was heated with stirring at 140 °C for 12 h under argon. After usual work up, 2-ethyl-1,2-benzisothiazol-3(2*H*)-one (5)[23] was obtained as a pale yellow oil; ^1H NMR ($CDCl_3$) δ 1.38 (t, $J = 7.2$, 3 H), 3.96 (q, $J = 7.2$, 2 H), 7.3-7.7 (m, 3 H), 8.0-8.1 (m, 1 H); IR (neat) 1650 cm^{-1}.

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