Mendeleev Commun., 2006, **16(5)**, 250–251

Catalytic thiocyanation of aryldiazonium salts in the presence of copper salts

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DOI: 10.1070/MC2006v016n05ABEH002403

Aryldiazonium fluoroborates readily react with potassium thiocyanate in the presence of the Cu^I/Cu^{II}/Phen catalytic system to give arylthiocyanates in high yields.

Arylthiocyanates are of interest as compounds with high biological activity[1] and convenient sources of ArS^-.[2] Methods for synthesising these compounds involve the cyanation of sulfinates and Bunte salts[3] or rhodanation of activated arenes with alkaline-metal rhodanides in the presence of an oxidant.[4] Yet another approach involves iodine replacement in aryl iodides on treatment with copper(I) rhodanide.[5] Furthermore, a synthesis of arylthiocyanates based on the reaction of arylsulfenyl halides with potassium cyanide was also reported.[6] However, unlike in nitrile synthesis, Sandmeyer-type reactions are uncommon in syntheses of these compounds. There have been only a few examples of studies that deal with reactions of aryldiazonium salts with alkaline-metal thiocyanates on treatment with stoichiometric amounts of Fe^{III} salts,[7(*a*)] copper powder[7(*b*)] or copper(II) acetate.[7(*c*)]

In continuation of our studies on catalytic cyanation[8] and halogenation[8(*b*)] of aryldiazonium salts, we developed a method for synthesising arylthiocyanates based on the reaction of aryldiazonium salts with potassium thiocyanate involving cocatalysis by Cu^I and Cu^{II} salts.

We used the thiocyanation of 4-fluorophenyldiazonium fluoroborate **1a** with potassium thiocyanate as the model reaction for catalyst screening. The fluorine label allowed us to monitor the progress of the reaction and the composition of the products by means of ^{19}F NMR spectroscopy.

Since the oxidation potential of SCN^- is close to that of I^-, it could be expected that this reaction would occur without a catalyst. In fact, the formation of 4-fluorophenyl thiocyanate **2a** is observed under these conditions, but its yield is extremely low, whereas fluorobenzene **3** is the major reaction product identified (Table 1, entry 1). Addition of 10 mol% copper(I) salts and 1,10-phenanthroline increases the yield of **2a** significantly (Table 1, entry 2). On the other hand, the use of Cu^{II} tetrafluoroborate (20%) proved to be inefficient under these conditions as the yield of aryl rhodanide was as low as 27% (Table 1, entry 3). As before,[8] the two-component Cu^I/Cu^{II} catalyst was the optimum variant (Table 1, entry 4); the yield of ArSCN could be increased by performing the reaction at a lower temperature (Table 1, entry 5).

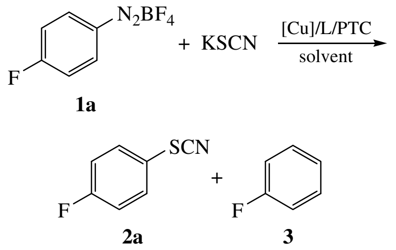
Table 1 Conditions and catalyst systems (solvent, MeCN).[a]

Entry	Cu^I (mol%)	Cu^{II} (mol%)	L	PTC	*T*/°C	Yield[b] (%) 2a	Yield[b] (%) 3
1	0	0	—	Dibenzo-18-crown-6	20	10	36
2	10	0	phen	Dibenzo-18-crown-6	20	53	40
3	0	20	phen	Dibenzo-18-crown-6	20	27	45
4	10	10	phen	Dibenzo-18-crown-6	20	77	19
5	10	10	phen	Dibenzo-18-crown-6	0	84	8
6	10	10	phen	TEBACl	0	82	9
7	10	10	phen	—	0	83	12
8	10	10	bpy	Dibenzo-18-crown-6	20	76	14
9[c]	10	10	phen	—	20	76	17

[a] 10% PTC, $(MeCN)_4CuBF_4$, $Cu(BF_4)_2$ and ligand were added to a suspension of KSCN (2 mmol) in 1 ml of the solvent. A solution of compound **1a** in 2 ml of the solvent was then added over a period of several minutes to the resulting mixture. [b] According to ^{19}F NMR data. [c] Cu^I and Cu^{II} rhodanides were synthesised separately just before the reaction from the appropriate copper borofluorides and potassium rhodanide.

The nature of the phase-transfer catalyst does not affect the aryl thiocyanate yield. What is more, the solubility of potassium thiocyanate is sufficient for performing the reaction without a phase-transfer catalyst (Table 1, entries 5–7). The replacement of phenanthroline with α,α′-bipyridyl decreases the yield of **2a** insignificantly (Table 1, entries 7, 8). Analogous results were previously observed in similar reactions with potassium cyanide[8] and bromide.[8(*b*)]

As we showed previously in a similar reaction with potassium bromide,[8(*b*)] the yield of the product strongly depended on the nature of the anion in the catalyst. Maximum product yields were achieved with copper bromides, whereas the use of copper fluoroborates decreased the yields despite their higher solubility. Copper bromides can be either used as ready salts or generated separately from suitable copper salts just before the reaction. Since the use of the respective copper salts is difficult in the case of thiocyanates, we prepared them *in situ* from $(MeCN)_4CuBF_4$ and $Cu(BF_4)_2$ by reactions with KSCN and then used them as catalysts in the reaction. However, we observed that in the case of rhodanation, the nature of the anion in the catalyst did not affect the yield and ratio of the reaction products (Table 1, entry 9).



Scheme 1

Under the optimum conditions found, we synthesised a series of aryl thiocyanates containing electron-donating substituents **2a**–**d** and electron-withdrawing substituents **2e**–**i**. In a typical procedure, a solution of an aryldiazonium salt in acetonitrile is added at 0–5 °C to KSCN (6 mmol), $(MeCN)_4CuBF_4$ (0.3 mmol), $Cu(BF_4)_2$ (0.3 mmol), 1,10-phenanthroline (0.3 mmol) in acetonitrile.[†] Note that the effect of the substituent is much stronger

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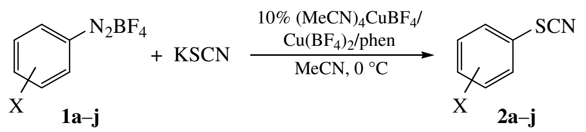
[†] The ^1H and ^{13}C NMR spectra for the aryl thiocyanates synthesised match those reported in the literature. Aryldiazonium fluoroborates were synthesised by diazotization of appropriate amines with sodium nitrite in a 15% HBF_4 solution at 0–5 °C.

General procedure. A solution of $(MeCN)_4CuBF_4$ (0.3 mmol) and $Cu(BF_4)_2$ (0.3 mmol) in acetonitrile (1 ml) and then 1,10-phenanthroline (0.3 mmol) were added in a two-necked flask under argon to a suspension of KSCN (6 mmol) in acetonitrile (3 ml). After stirring for 10 min, the reaction mixture was cooled with an ice bath, and a solution of a diazonium salt (3 mmol) in acetonitrile (3–10 ml) was added with vigorous stirring in such a way that the temperature did not exceed 0–5 °C. After gas evolution had ceased, cooling was removed; the reaction mixture was allowed to heat to room temperature and poured into diethyl ether (50 ml). The precipitate was filtered off and washed two times with diethyl ether. The combined organic fractions were concentrated *in vacuo*. Column chromatography (SiO_2, hexane–EtOAc, 95:5 or 90:10 for **2h** and **2i**) gave a pure aryl thiocyanate, either as a yellow oil or as yellow (**2h**) or orange (**2i**) crystals.

in this case than for the bromide ion[8(b)] and is similar to that observed in the reaction with cyanide.[8(a)] In fact, the yield is as small as 65% for 4-methoxyphenyldiazonium fluoroborate **1d** compared to 84% for phenyldiazonium fluoroborate **1b** (Table 2, entries 1, 4). On the other hand, the yield is 91% for 4-nitro-substituted substrate **1i** (Table 2, entry 9). Steric requirements affect the product yield very strongly. Indeed, the presence of just one *ortho*-methyl group decreases the yield to 46% (Table 2, entry 10).



Scheme 2

Table 2 Synthesis of ArSCN.

Entry	X	ArSCN	Isolated yield (%)
1	4-F	**2a**[9]	82
2	H	**2b**[10]	84
3	4-Me	**2c**[9,10]	78
4	4-MeO	**2d**[9]	65
5	4-Cl	**2e**[7(b)]	86
6	3-Cl	**2f**[10]	82
7	3,5-Cl_2	**2g**[11]	89
8	4-Ac	**2h**[12]	88
9	4-NO_2	**2i**[12]	91
10	2-Me	**2j**[7(b)]	46

In conclusion, note that we were the first to develop a catalytic method for the thiocyanation of aryldiazonium salts with potassium thiocyanate in the presence of the Cu^I/Cu^{II}/phen catalytic system to give aryl thiocyanates in high yields.

This study was supported by the Russian Foundation for Basic Research (grant no. 05-03-32941).

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Received: 4th July 2006; Com. 06/2748