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Preparation of *t*-Butyl Sulfides by a Novel Ligand-Transfer Reaction of Aryl Thiocyanates.

F. Dean Toste and Ian W. J. Still*

J. Tuzo Wilson Research Laboratories, Erindale College, University of Toronto in Mississauga, Mississauga, Ontario, Canada L5L 1C6.

Abstract: Aryl *t*-butyl sulfides are prepared in good to excellent yields by the reaction of aryl thiocyanates with $(t\text{-Bu})_2Cu(CN)Li_2$.

The thiocyanate functionality has long been recognized as possessing two possible sites for attack by nucleophiles, at sulfur and at carbon. An early report suggested that the reaction with carbon nucleophiles proceeded mainly by attack at the (harder) carbon electrophilic site, especially with relatively bulky Grignard reagents.[1,2] Softer nucleophiles in contrast, such as phosphines[3a] and phosphites,[3b] appear to react mainly at the sulfur electrophilic site. We have recently described an efficient and regioselective electrophilic preparation of aryl thiocyanates[4] and we became interested in trying to modify the reactivity of carbon nucleophiles towards the thiocyanate functionality, in order to prepare aryl *t*-butyl sulfides. The preparation of *t*-butyl sulfides is most often achieved by the reaction of the corresponding thiol with isobutylene in the presence of acid.[5,6] *t*-Butyl is a versatile and easily removable protecting group for thiols[5] but, in addition the *t*-butyl sulfide moiety in aryl *t*-butyl sulfides[7a] (and *t*-butylsulfonyl in the analogous sulfones[7b]) has found extensive use as an *ortho*-directing group for the lithiation of substituted arenes. Julia and coworkers[6] have also reported replacement of the *t*-butylsulfonyl functionality by organometallic reagents in a nickel-catalyzed process.

Based on a report that Ni(II) and Cu(II) salts catalyze nucleophilic attack on aryl selenocyanates *at selenium*[8] we have investigated the possibility that Ni(II) salts might change the normal reactivity pattern of aryl thiocyanates towards organometallics. Examination of the reaction of N,N-dimethyl-4-thiocyanatoaniline **1c** with several organometallic reagents (*t*-BuM: M = MgBr, ZnCl, MnCl), showed only minor changes in the S:C attack ratio in the presence of Ni(II) catalysts (see Table 1). However, when the corresponding reaction was carried out with $t\text{-Bu}_2Cu(CN)Li_2$[9] in THF at -78°C, the aryl *t*-butyl sulfide was obtained as the only observable product. In effect, the *t*-butyl ligand of the copper complex is exchanged for a cyanide ligand.[10]

Table 1. Product ratios for the reaction of N,N-dimethyl-4-thiocyanatoaniline **1c** with various organometallic reagents at -78 °C in THF.

t-BuM	Catalyst	Ratio		
		ArS^{t}Bu	:	ArSH^a
t-BuMgBr	none	1		99
t-BuMgBr	$(PPh_3)_2NiCl_2$	1		5
t-BuMgBr	$Ni(acac)_2$	1		3
t-BuZnCl	none	--		--
t-BuZnCl	$(PPh_3)_2NiCl_2$	1		8
t-BuMnCl	none	--		--
t-$Bu_2Cu(CN)Li_2$	none	99		1

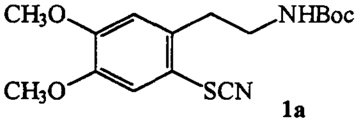
[a] Presumably as a result of attack of *t*-BuM at the cyanide carbon atom.

Table 2. Yields of aryl *t*-butyl sulfides from the reaction of various aryl thiocyanates with *t*-$Bu_2Cu(CN)Li_2$ in THF at -78 °C.

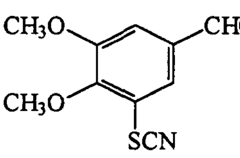
Entry	ArSCN^a	Isolated Yield of ArSBu (%)
1	**1a**	67
2	**1b**	65
3	**1c**	99
4	**1d**^{b}	73
5	**1e**^{b}	78
6	**1f**	38

[a] Reaction with 3,5-dinitrophenyl thiocyanate was unsuccessful.

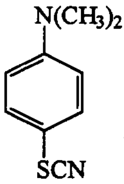
[b] These compounds were prepared from the readily available thiols by the procedure of Harpp et al.[11]



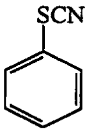
1a



1b



1c



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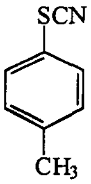
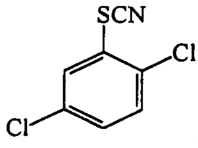


1e



1f

We have been able to extend this reaction to the preparation of several aryl *t*-butyl sulfides from the corresponding aryl thiocyanates **1a-f** (Table 2). The effectiveness of the ligand transfer reaction appears to be somewhat diminished only by the presence of electron-withdrawing substituents (entry 6). Several reactive functional groups are tolerated, although nitro groups are reduced under the reaction conditions.

Table 3. Effect of varying the cuprate ligand on the product ratio for the reaction of higher order cuprates with **1c** at -78°C in THF.

RM	Ratio		
	ArSR	:	ArSH
MeMgBr	3		2
$Me_2Cu(CN)Li_2$	3		1
s-$Bu_2Cu(CN)Li_2$	1		20
t-$Bu_2Cu(CN)Li_2$	99		1

Evidence for the type of mechanism involved is seen in Table 3. Very little success was achieved with the higher-order *s*-butyl or methyl cuprate reagents, or with the simple Grignard reagent, MeMgBr. These results suggest that, in the case where a stable (*t*-butyl) radical may be formed, a radical mechanism may be favoured, while in those cases where the radical is relatively unstable (methyl, *s*-butyl) a polar mechanism operates. In the former circumstance it seems likely that a single electron transfer (SET) process, mediated by copper, may be followed.[12]

General Procedure: To a tan slurry of *t*-$Bu_2Cu(CN)Li_2$[13] (2.0 equiv.) in dry THF, at -78°C under argon, was slowly added the aryl thiocyanate (1.0 equiv.). The reaction mixture was stirred for 4h at -78°C, then allowed to slowly warm to room temperature.[14] To the reaction mixture was then added a solution of satd. ammonium chloride, and the biphasic solution was allowed to stir, open to the atmosphere, until the aqueous layer became distinctly blue in colour (at least 2 h). The organic layer was separated, washed with satd. NaCl, dried (Na_2SO_4) and concentrated to afford the crude product. Flash chromatography afforded the products (Table 2), the purity of which was verified by ^1H-NMR, ^{13}C-NMR and TLC.

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References and Notes

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9. We have also investigated the reaction of aryl thiocyanates with lower order, Gilman-type cuprates (e.g., t-Bu_2CuLi) prepared from CuI or $CuBr.SMe_2$. Although product ratios were similar, we prefer to use the higher order cuprate shown, as it provides better yields due to greater ease of work-up.
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