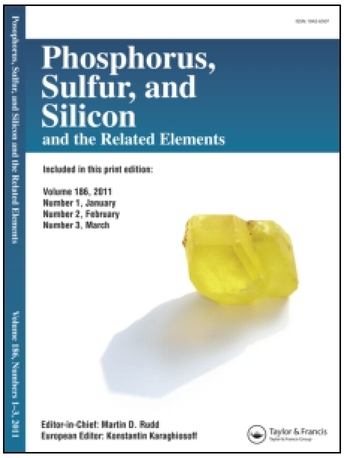

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SYNTHESIS OF ARYL THIOCYANATES FROM ARYL ALKYL SULPHIDES. CONVERSION OF UNACTIVATED ARYL HALIDES INTO ARYL THIOCYANATES

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Aryl alkyl sulphides, easily obtained from aryl halides, can be selectively dealkylated in HMPA by treatment with sodium, sodium methanethiolate or sodium methoxide. The resulting solutions, containing the sodium arenethiolates, when treated with BrCN or ICN, afford the corresponding aryl thiocyanates in moderate to good yields. A by-product is obtained in several cases to whom the structure of $ArSP(O)(NMe_2)_2$ has been attributed.

INTRODUCTION

The synthesis of aryl thiocyanates still represents a problem of considerable interest[1] since a good synthetic method is not yet available. Among the few reported procedures[2,3] the reaction of arenethiolates with cyanogen halides[2] seems to be the easiest way to obtain aryl thiocyanates. This method obviously requires the starting arenethiols to be easily available. We have recently developed a series of procedures to synthesize mono- and poly(mercapto)arenes by dealkylation of the corresponding aryl alkyl sulphides and we report in this paper the extension of these reactions to effect a useful synthesis of aryl thiocyanates.

In previous works we have described the synthesis of mono- and poly(alkylthio)benzenes from the corresponding aryl halides,[4] of bis(alkylthio)benzenes containing two different alkyl groups,[5] and of alkoxy alkylthiobenzenes[6] from dichlorobenzenes. All these reactions can be easily effected with sodium alkanethiolates, using HMPA as solvent. In the same solvent these compounds can be dealkylated in several ways. By treatment with sodium, poly(alkylthio)benzenes are completely dealkylated to the sodium salts of the poly(mercapto)benzenes[7] (Eq. 1), whereas the alkoxy thioalkoxybenzenes give selectively the alkoxy mercaptobenzenes[8] (Eq. 2). By reaction with MeSNa, an S_N2 process occurs[9] and the dealkylation of bis(alkylthio)benzenes selectively takes place at the less sterically hindered alkylthio function[5,9] (Eq. 3). On the contrary, with MeONa the dealkylation process is the result of an E_2 reaction which occurs at the more branched alkyl group[5] (Eq. 4).

$$C_6H_4(SR)_2 \xrightarrow{Na} C_6H_4(SNa)_2 \tag{1}$$

$$C_6H_4(OR)SR \xrightarrow{Na} C_6H_4(OR)SNa \tag{2}$$

$$C_6H_4(SMe)SCHMe_2 \xrightarrow{MeSNa} C_6H_4(SCHMe_2)SNa \qquad (3)$$

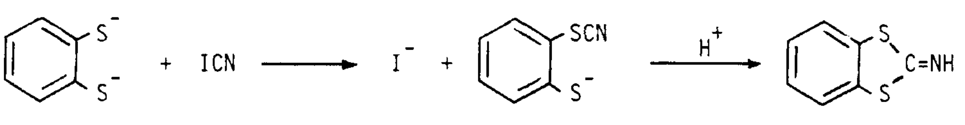
$$C_6H_4(SMe)SCHMe_2 \xrightarrow{MeONa} C_6H_4(SMe)SNa \qquad (4)$$

We have now applied all these methods to the synthesis of aryl thiocyanates which can be effected by simply adding BrCN or ICN to the solution of the thiolates in HMPA. Since the thiolates, produced as reported in Eqs. 1–4, are obtained from the aromatic halides, the present procedure allows the transformation of an unactivated aromatic halide into the corresponding aryl thiocyanate, according to the reaction sequence reported in Eq. 5. In some cases the series of reactions can even be effected in one-pot.

$$ArX \xrightarrow{RSNa} ArSR \xrightarrow[\text{or MeONa}]{\text{Na or MeSNa}} ArSNa \xrightarrow{XCN} ArSCN \qquad (5)$$

RESULTS AND DISCUSSION

Preliminary experiments showed that the best results are obtained when the sodium arenethiolates in HMPA are allowed to react, at room temperature, with the cyanogen halides dissolved in benzene. The experimental conditions employed, the reaction products obtained and the reaction yields are summarized in the table. It can be observed that the present method can be applied both to the aromatic and the heteroaromatic series. Aryl thiocyanates are obtained in moderate to good yields. In general cyanogen iodide gives better results than cyanogen bromide. The *m*- and *p*-bis(mercapto)benzene give the bis substituted compounds *m*- and *p*-$C_6H_4(SCN)_2$. On the contrary, the *ortho* isomer gives rise to the cyclization product **1**, as a result of an intramolecular addition of the arenethiolate to the carbon atom of the SCN function (see scheme). In several cases a by-product was obtained. On the basis of elemental analyses, ^{1}H-nmr and infrared spectra, the structure **2** was assigned to these compounds (see scheme). Thus these products derive from the reaction of arenethiolates with HMPA and formally result from a nucleophilic substitution at



1

$$ArS^- + (NMe_2)_3PO \longrightarrow NMe_2^- + ArSP(O)(NMe_2)_2$$

2

SCHEME

the phosphorus as depicted in the scheme. The mechanism of this reaction is not clear. It can be said, however, that compounds **2** form from ArSNa and HMPA under the catalytic influence of the cyanogen halides or of some other species derived from them, since in the absence of ICN or BrCN the formation of **2** was not observed. In all the previous examples in which arenethiolates were produced in HMPA[4-9] compounds of type **2** were never detected. With ICN the yields of compounds **2** are generally lower than with BrCN and in some cases these by-products are not obtained at all.

In the cases of the quinoline and thiophen derivatives, the reactions were effected starting from the 2- and 4-chloroquinoline and the 2-bromothiophene. The resulting methylthio derivatives, obtained by reaction with MeSNa, were not isolated but directly dealkylated with sodium or with excess MeSNa (see table). These three cases therefore represent examples of the one-pot synthesis of aryl thiocyanates starting from aryl halides. This procedure can in principle be applied to most of the other examples collected in the table and has in fact been tested in the case of the *p*-dichlorobenzene.

In conclusion, although reaction yields are not excellent in most cases, the easiness with which these reactions are carried out and the easy availability of the halogeno derivatives employed as starting materials, make the present procedure a useful synthetic method for the preparation of aryl thiocyanates with several advantages over the other existing methods.

EXPERIMENTAL

Reaction products were identified by comparison of their physical and spectral properties with those reported in the literature and by proton nmr and infrared spectra. C, H, N, and S elemental analyses were carried out on a C. Erba Elemental Analyzer Mod. 1106. Nmr spectra were recorded, in $CDCl_3$ solution, on a 90 MHz Varian EM 390 instrument; infrared spectra were recorded, in CH_2Cl_2 or CS_2 solutions on a Perkin-Elmer 1320 instrument. Commercial HMPA, ICN and BrCN were used without further purification. All the starting aryl alkyl sulphides were prepared from the aromatic halides by reaction with Me_2CHSNa or MeSNa in HMPA as described in previous works.[4-6]

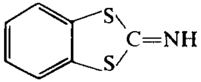
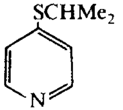
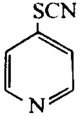
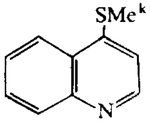
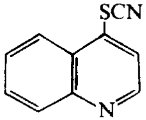
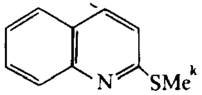
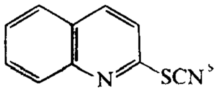
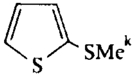
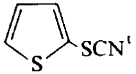
Synthesis of the Aryl Thiocyanates. To a stirred solution of the aryl alkyl sulphide (0.01 mols) in HMPA (20 ml), kept under nitrogen at 90°, small pieces of sodium (Method A[7,8]) or MeSNa (Method B[5,9]) or MeONa (Method C[5]) were added. The detailed procedures for the dealkylations of the sulphides can be found in the cited previous works. The progress of the reaction was monitored by tlc. When the starting sulphides were completely transformed in the corresponding aromatic thiols, the reaction mixtures were cooled to room temperature. A benzene solution of BrCN or ICN (0.05 mols) was added and the mixture was stirred at the room temperature for the time indicated in the table. The mixture was poured on water and extracted with ether. The organic layer was washed with water, dried and the solvent was evaporated. The residue was chromatographed through a silica gel column. Elution with light petroleum/ethyl ether (from 95 : 5 to 50 : 50 depending on the products) afforded the ArSCN; to obtain the $ArSP(O)(NMe_2)_2$ the column was then eluted with chloroform/methanol (98 : 2). Also reported in the table are the results obtained from the *p*-bis(*i*-propylthio)benzene, the 2- and 4-methylthioquinoline and the 2-methylthiothiophene which were prepared from the reaction of the *p*-dichlorobenzene (0.01 mols) with Me_2CHSNa (0.03 mols) and of the 2- and 4-chloroquinoline (0.01 mols) and the 2-bromothiophene (0.01 mols) with MeSNa (0.03 mols) in HMPA at 90°C. The solutions of these aryl alkyl sulphides were directly treated with sodium or with excess MeSNa (see table) and then with the solution of the cyanogen halide according to the procedure described above.

The products obtained and the reaction yields are collected in the table. Physical and spectral data for the reaction products are reported in the footnotes of the same table.

The structure of the $ArSP(O)(NMe_2)_2$ derivatives is strongly supported by the presence of the two singlets at 2.75 and 2.6 δ in the nmr spectra and of two strong absorptions at about 1295 and 1220 cm^{-1} in the infrared spectra. These spectral features are similar to those presented by HMPA (2.75 and 2.6 δ; 1295s and 1215s cm^{-1}).

TABLE I

Syntheses of aryl thiocyanates from the dealkylation of aryl alkyl sulphides and reaction with cyanogen halides in HMPA at 25°C.

Run	Sulphide	Dealkylation Method[a]	Cyanongen Halide	Reaction Time (hr)	Reaction Products[b] ArSCN	% Yield[c]	ArSP(O)(NMe$_2$)$_2$	% Yield[c]
1	$C_6H_5SCHMe_2$	A	BrCN	15	C_6H_5SCN[d]	67.5	$C_6H_5SP(O)(NMe_2)_2$[e]	17.5
2	$C_6H_5SCHMe_2$	A	ICN	15	C_6H_5SCN	63	$C_6H_5SP(O)(NMe_2)_2$	12.5
3	o-$C_6H_4(SCHMe_2)_2$	A	BrCN	6		49		
4	m-$C_6H_4(SCHMe_2)_2$	A	BrCN	1	m-$C_6H_4(SCN)_2$[g]	80	m-$C_6H_4(SCN)SP(O)(NMe_2)_2$[h]	10
5	p-$C_6H_4(SCHMe_2)_2$	A	BrCN	1.5	p-$C_6H_4(SCN)_2$[i]	47	p-$C_6H_4(SCN)SP(O)(NMe_2)_2$[j]	34
6	p-$C_6H_4(SCHMe_2)_2$	A	ICN	3	p-$C_6H_4(SCN)_2$	76.5	p-$C_6H_4(SCN)SP(O)(NMe_2)_2$	19
7	p-$C_6H_4(SCHMe_2)_2$[k]	A	ICN	3	p-$C_6H_4(SCN)_2$	56.5	p-$C_6H_4(SCN)SP(O)(NMe_2)_2$	20
8	m-$C_6H_4(Ph)SCHMe_2$	A	BrCN	3	m-$C_6H_4(Ph)SCN$[l]	34.5	m-$C_6H_4(Ph)SP(O)(NMe_2)_2$[m]	55
9	2-$C_{10}H_7SCHMe_2$	A	BrCN	3	2-$C_{10}H_7SCN$[n]	29	2-$C_{10}H_7SP(O)(NMe_2)_2$[o]	34
10	2-$C_{10}H_7SCHMe_2$	A	ICN	15	2-$C_{10}H_7SCN$	57	2-$C_{10}H_7SP(O)(NMe_2)_2$	22
11		A	ICN	3.5		55.5		
12	p-$C_6H_4(OMe)SMe$	A	ICN	16	p-$C_6H_4(OMe)SCN$[q]	40		
13		A	ICN	8		44		
14		B	ICN	12		33		
15		B	ICN	4.5		35		
16	p-$C_6H_4(SCHMe_2)SMe$	B	ICN	16	p-$C_6H_4(SCHMe_2)SCN$[u]	48		
17	p-$C_6H_4(SCHMe_2)SMe$	C	ICN	18	p-$C_6H_4(SMe)SCN$[v]	58.5		

[a] A: Sodium; B: MeSNa; C: MeONa.

[b] Chemical shifts are in δ and coupling constants in Hz. Infrared absorptions are in cm^{-1}; the values in parentheses refer to spectra recorded in CS_2 solution.

[c] Based on isolated products after column chromatography.

[d] Oil (Lit.[10] b.p. 232°); 7.35 (m); 2160s.

[e] Oil; 7.55 (m, 2 H), 7.25 (m, 3 H), 2.75 (s, 6 H), 2.6 (s, 6 H); (1290s, 1220s). (Found: C, 49.10; H, 6.93; N, 11.50; S, 13.27. $C_{10}H_{17}N_2OPS$ requires: C, 49.15; H, 7.03; N, 11.47; S, 13.12%).

[f] M.p. 128–129°; 8.75 (broad s, 1 H), 7.15 (AA'BB', 4 H); 3300s, 1575s, 1550s. (Found: C, 50.22; H, 2.96; N, 8.29; S, 38.50. $C_7H_5NS_2$ requires: C, 50.27; H, 3.02; N, 8.38; S, 38.33%).

[g] M.p. 52–54° (Lit.[11] m.p. 54°); 7.6 (m, 1 H), 7.5 (m, 3 H); 2165s.

[h] Oil; 7.7–7.2 (m, 4 H), 2.75 (s, 6 H), 2.6 (s, 6 H); 2160s, (1295s, 1225s). (Found: C, 43.34; H, 5.35; N, 13.66; S, 21.43. $C_{11}H_{16}ON_3S_2P$ requires: C, 43.83; H, 5.36; N, 13.94; S, 21.27%).

[i] M.p. 107–109° (Lit.[12] m.p. 106°); 7.5 (s); 2160s.

[j] Oil; 7.65, 7.4 (AA'BB', 4 H), 2.75 (s, 6 H), 2.6 (s, 6 H); 2170s, (1295s, 1225s). (Found: C, 44.00; H, 5.12; N, 13.71; S, 21.28. $C_{11}H_{16}ON_3S_2P$ requires: C, 43.83; H, 5.36; N, 13.94; S, 21.27%).

[k] Obtained *in situ* from the reactions of the *p*-dichlorobenzene with Me_2CHSNa, and of the 2- and 4-chloroquinoline and 2-bromothiophene with MeSNa in HMPA. The sulphides were not isolated but directly dealkylated with Na or MeSNa as indicated in the table.

[l] Oil; 7.6 (m, 1 H), 7.55–7.2 (m, 9 H); 2160s. (Found: C, 73.63; H, 4.54; N, 6.71; S, 15.24. $C_{13}H_9NS$ requires: C, 73.90; H, 4.30; N, 6.63; S, 15.17%).

[m] Oil; 7.75 (m, 1 H), 7.55–7.10 (m, 9 H), 2.75 (s, 6 H), 2.6 (s, 6 H); (1295s, 1225s). (Found: C, 60.04; H, 6.59; N, 8.50; S, 10.21. $C_{16}H_{21}N_2OPS$ requires: C, 59.97; H, 6.62; N, 8.74; S, 10.00%).

[n] M.p. 28–30° (Lit.[13] m.p. 32–33°); 7.9–7.3 (m); 2160s.

[o] Oil; 8.05 (m, 1 H), 7.8–7.2 (m, 6 H), 2.75 (s, 6 H), 2.6 (s, 6 H); (1290s, 1220s). (Found: C, 56.98; H, 6.68; N, 9.31; S, 11.05. $C_{14}H_{19}N_2OPS$ requires: C, 57.11; H, 6.52; N, 9.52; S, 10.89%).

[p] M.p. 51–53° (Lit.[13] m.p. 54–56°); 8.5, 7.3 (AA'BB'); 2170s.

[q] M.p. 34–36° (Lit.[14] m.p. 35°); 7.35, 6.8 (AA'BB', 4 H), 3.75 (s, 3 H); 2180s.

[r] M.p. 101–102° (Lit.[15] b.p. 103/7 mm); 8.75 (d, J = 4.5, 1 H), 8.0 (m, 1 H), 7.65 (d, J = 4.5, 1 H), 7.8–7.4 (m, 3 H); 2180s.

[s] M.p. 72–74° (Lit.[13] m.p. 74–75°); 8.0 (d, J = 8.5, 1 H), 7.9–7.3 (m, 5 H); 2170s.

[t] Oil (Lit.[16] b.p. 108–110°/12 mm); 7.4 (dd, J = 5.2, 1.2, 1 H), 7.25 (dd, J = 3.6, 1.2, 1 H), 6.95 (dd, J = 5.2, 3.6 1 H); 2170s.

[u] Oil; 7.3 (s, 4 H), 3.4 (spt, J = 7.5, 1 H), 1.3 (d, J = 7.5, 6 H); 2140s. (Found: C, 57.25; H, 5.50; N, 6.47; S, 30.81. $C_{10}H_{11}NS_2$ requires: C, 57.37; H, 5.31; N, 6.69; S, 30.63%).

[v] Oil (Lit.[17] b.p. 94°/0.14 mm); 7.3, 7.1 (AA'BB', 4 H), 2.45 (s, 3 H); 2160s.

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