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ACYL THIOCYANATES—III

THE SYNTHESIS OF STABLE AROYL THIOCYANATES

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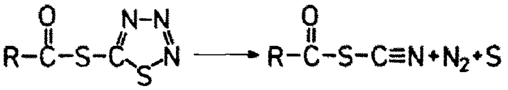
Abstract—Two methods are devised for the synthesis of aroyl thiocyanates. One method is based on the thermal breakdown of 5-aroylthio-1,2,3,4-thiatriazoles to aroyl thiocyanates, nitrogen and sulfur. The other method is based on the reaction between thioacid salts and cyanogen halides. The latter synthesis also gives rise to diacyldisulfides. A hypothesis for the disulfide formation is advanced. These investigations have revealed that 2,4,6-tribromobenzoyl- and 2,4,6-triiodobenzoyl thiocyanate are stable compounds which can be kept at room temperature for prolonged periods without decomposition, while 2,6-dimethyl-4-nitrobenzoyl and 3,4,5-trimethoxybenzoyl thiocyanate are of intermediate stability. The former thiocyanates are the first examples of stable acyl thiocyanates.

Recently one of us reported evidence for the existence of acyl and aroyl thiocyanates.[1-3] Due to a pronounced tendency to isomerize to the isomeric isothiocyanates no acyl or aroyl thiocyanate were isolated in the pure state. The aim of this paper is to describe the synthesis of some selected aroyl thiocyanates. Apparently aroyl thiocyanates may isomerize either by unimolecular or by bimolecular mechanisms depending on the substitution of the ring.[2] In order to obtain stable compounds it therefore seems necessary to choose substrates which exhibit low S_N1 reactivity as well as low S_N2 reactivity. These requirements are met in the 2,4,6-tribromobenzoyl, 2,4,6-triiodobenzoyl and 2,6-dimethyl-4-nitrobenzoyl systems.[4]

Mainly two synthetic pathways have been exploited in the present work, these will be dealt with separately.

Acyl thiocyanates from 5-acylthio-1,2,3,4-thiatriazoles. Elimination of nitrogen and sulfur from the 5-substituted 1,2,3,4-thiatriazole nucleus to produce cyano derivatives appears to be a general reaction. In the case of 5-acylthio-1,2,3,4-thiatriazoles (**1**) the cyano derivative formed is an acyl thiocyanate.



1 **2**

a: R = 2,4,6-tribromophenyl
b: R = 2,4,6-triiodophenyl
c: R = 2,6-dimethyl-4-nitrophenyl
d: R = 3,4,5-trimethoxyphenyl

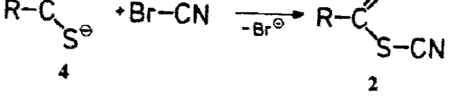
The thiatriazoles **1a–1d** were prepared from the corresponding acid chloride and sodium 1,2,3,4-thiatriazole-5-thiolate.[2] Although 2,4,6-tribromobenzoyl chloride (**3a**), and 2,4,6-triiodobenzoyl chloride (**3b**) are believed to be very unreactive[†] (e.g. **3a** on reflux in 8% KOHaq hydroxide for 30 min is only hydrolysed to an extent of 28%)[4] no difficulty was encountered in the preparation of **1a** and **b**.

The decomposition of the thiatriazoles could conveniently be followed by IR spectroscopy, since the –S–C≡N stretching vibration of the thiocyanate develops as a sharp band at 2165 cm^{-1}.

The thermal stability of **1a**, **1b**, **1c** and **1d** far exceeds that of normal 5-aroylthio-1,2,3,4-thiatriazoles as exemplified by the observation, that a sample of **1a** kept at 75° contained considerable amounts of thiatriazole even after 2·5 hr. On melting or during refluxing in benzene solution the extrusion of nitrogen and sulfur takes place. The acyl thiocyanates formed are in the case of **1b**, **1c** and **1d** unstable in boiling benzene, it is therefore necessary to maintain the thermolyses time at a minimum.

Usually acyl isothiocyanates are found to be present in the thermolyses mixture in varying amounts depending on the time and whether or not a solvent is used. The isothiocyanates are much more reactive towards nucleophilic reagents than are the thiocyanates. The former could therefore be removed from the mixture by dissolving in chloroform containing 1% of ethanol, in which the N-aroyl-O-ethylthiocarbamates formed are only slightly soluble. The removal of elemental sulfur from the products proved a severe problem, which was only solved by repeated recrystallization, resulting in loss of acyl thiocyanate.

Monothiobenzoates and cyanogen halides. In order to avoid the elevated temperature necessary to induce decomposition of the thiatriazole nucleus another synthetic pathway for the acyl thiocyanates was explored. The reaction between the salts of monothiobenzoic acids and cyanogen halides proceeds with a velocity acceptable for synthetic purposes at about −5 to −15°.



4 **2**

a: R = 2,4,6-tribromophenyl
b: R = 2,4,6-triiodophenyl

The monothiobenzoic acids were synthesized using conventional methods.[5] The reaction of cyanogen bromide with **4a** and **b** at −15° in ether or pentane produced the acyl thiocyanates **2a** and **2b** in fair yield (73 and 80%, respectively). The products are stable under these experimental conditions and since they are also

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[†] See, however, Ref. 8 for an investigation of the hydrolyses of these acid chlorides.

stable towards cyanogen bromide an excess of this reagent may be used. The only side product found in these reactions was diacyl disulfide† meaning that the combined yields of thiocyanate and disulfide were always quantitative. In no case was any isothiocyanate detected. Similar results were found using cyanogen chloride, resulting in 5–20% higher yields.

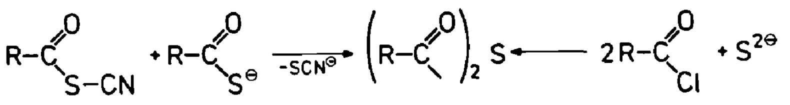
Under similar experimental conditions the reaction of the benzoyl thiolate with cyanogen bromide gave a high yield of dibenzoyl disulfide. However, absorptions at 2160 and 1980 cm^{-1} indicated that minor amounts of benzoyl thiocyanate and benzoyl isothiocyanate were formed. On attempted purification the 2160 cm^{-1} absorption disappeared while the 1980 cm^{-1} reached a maximum.

The authentic isothiocyanates were prepared according to Takamizawa *et al.*[6]

In one case, namely the reaction between 2,4,6-triiodobenzoyl chloride **3b** and KSCN, the mixture was found to contain apart from 2,4,6-triiodobenzoyl isothiocyanate, a minor amount of the corresponding thiocyanate **2b** (9% pure material).

The IR spectra of the isothiocyanates showed strong -N=C=S absorptions at 1950–1990 cm^{-1} and C=N absorptions in the 1690–1710 cm^{-1} region.

Further investigations are needed to clarify the mechanism of the disulfide formation. However, the possibility that the disulfides are products from the reaction of acyl thiocyanates with thioacid salts is ruled out by the observation that acyl thiocyanates react with thioacid salts to give a quantitative yield of diacyl sulfide. The diacylsulfides were identified by comparison with a sample synthesized from acid chloride and sulfide ion.[7]

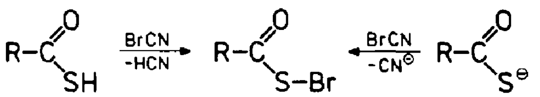


When free thioacid reacted with cyanogen bromide a quantitative yield of diacyl disulfide was formed. This finding is in contrast to the expected ease of oxidation of thioacid salts *versus* free thioacid. Cyclic voltammetry confirmed that the thioacid salts are far more easily oxidized than the free thioacids. The following peak potentials were found from the voltammograms:‡

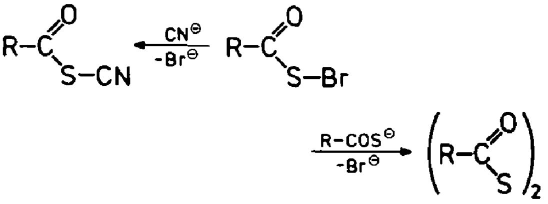
Monothioacid	E_p (V)	Potassium salt E_p (V)
Benzoic	1·35	0·42
2,4,6-Triiodibenzoic	1·23	0·47
2,4,6-Tribromobenzoic	1·28	0·61
3,4,5-Trimethoxybenzoic	1·37	0·63

We thus infer that the oxidation mechanism cannot be a simple electron transfer reaction between thioacid and cyanogen bromide.

It seems most likely that the primary product formed in the reaction of the free thioacid as well as in the reaction of thioacid salts with cyanogen bromide is the acyl sulfenic acid bromide. This is supported by the belief that cyanogen bromide is polarized with bromine as the positive end of the dipole.[9]



The sulfenic acid bromide so formed may then react with cyanide ion to form acyl thiocyanate or with thioacid salt to form diacyl disulfide.



EXPERIMENTAL

Experimental details are as those given in Ref. 2. NMR spectra were obtained using a Varian A-60 A instrument (60 Mc/s and with TMS as internal standard).

5-Aroylthio-1,2,3,4-thiatriazoles. These thiatriazoles were obtained from the corresponding acid chloride and sodium 1,2,3,4-thiatriazole-5-thiolate as described in Ref. 2. The yields obtained were: **1a** 97%; **1b** 96%; **1c** 100%; and **1d** 90%. (Found for **1c**: C, 40·60; H, 2·76; N, 18·84; S, 21·53. Calc. for $C_{10}H_8N_4O_3S_2$: C, 40·55; H, 2·72; N, 18·92; S, 21·60%). Recrystallization of thiatriazoles **1a**, **1b** and **1d** resulted in loss of material, the thiatriazoles were therefore used without purification.)

Mono thiobenzoic acids. The acids were prepared according to Ref. 7. Only dry dioxan was used as solvent for the acid chlorides. The potassium salts were recrystallized from acetonitrile.

Potassium mono thiobenzoate, m.p. >260° (dec). (Found: C, 47·31; H, 2·93; S, 17·99. Calc. for C_7H_5OSK: C, 47·74; H, 2·86; S, 18·20%).

Potassium 2,4,6-*tribromomonothiobenzoate*, m.p. >260° (dec). (Found: C, 20·34; H, 0·82; S, 7·86. Calc. for $C_7H_2Br_3OSK$: C, 20·34; H, 0·97; S, 7·73%).

Potassium 2,4,6-*triiodomonothiobenzoate*, m.p. >260° (dec). (Found: C, 17·13; H, 0·66; S, 6·78. Calc. for C_7H_2IOSK: C, 17·41; H, 0·42; S, 6·64%).

Decomposition of 5-aroylthio-1,2,3,4-*triatriazoles.* A 10% soln of the thiatriazole in benzene was refluxed for 20–50 min. Petrol ether was added and after cooling the ppt was filtered off. The filtrate was evaporated and the crude product was recrystallized from cyclohexane giving the pure thiocyanate.

2,4,6-*Tribromobenzoylthiocyanate* (**2a**). Reaction time 35 min, yield 97%, m.p. 106–7°. The IR spectrum shows absorptions for (SCN) at 2165 cm^{-1} and for (C=O) at 1765, 1730 cm^{-1}. (Found: C, 24·28; H, 0·58; N, 3·50; S, 8·40; Br, 59·85. Calc. for $C_8H_2Br_3NOS$: C, 24·18; H, 0·50; N, 3·53; S, 8·06; Br, 59·70%).

2,4,6-*Triiodobenzoyl thiocyanate* (**2b**). Reaction time 50 min, yield 91%, m.p. 143·5–144·5°. The IR spectrum shows absorptions for (SCN) at 2160 cm^{-1} and for (C=O) at 1760 cm^{-1}. (Found: C, 17·70; H, 0·40; N, 2·51; S, 6·04; Br, 70·40. Calc. for $C_8H_2I_3NOS$: C, 17·76; H, 0·37; N, 2·59; S, 5·93; I, 70·39%).

2,4-*Dimethyl-4-nitrobenzoyl thiocyanate* (**2c**). Reaction time

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†The diacyl disulfides were identified by comparison with samples prepared by oxidation of the monothioacid salts with iodine using a method described in *Org. Synth. Coll.* **III**, 116 (1965).

‡The potentials were measured using an Ag/AgCl electrode as reference electrode. The values are corrected to the calomel reference by addition of −0·22 V. The potassium salt of 2,4,6-tribromobenzoic acid gave rise to a corrected peak potential of 1·66 V.

20 min, yield 83%, m.p. 131–132°. The IR spectrum shows absorptions for (SCN) at 2170 cm^{-1} and (C=O) at 1755 cm^{-1}.

3,4,5-*Trimethoxybenzoyl thiocyanate* (**2d**). Reaction time 25 min, yield 65%, m.p. 105–6°. IR: (SCN) 2165 cm^{-1} (C=O) 1725 cm^{-1}. (Found: C, 52·45; H, 4·39; N, 5·30. Calc. for $C_{11}H_{11}NSO_4$: C, 52·17; H, 4·38; N, 5·53%). In another experiment the decomposition of **2d** was carried out in boiling chloroform (containing 1% of EtOH), which after the reaction was completed, was evaporated. When crystallized several times from ether the ethylthiocarbamate was found as a minor product (yield approx. 2%), m.p. 131·5–132°. The IR and NMR spectrum is identical with the authentic one.

N-3,4,5-*Trimethoxybenzoyl*-O-*ethyl thiocarbamate.* 3,4,5-Trimethoxybenzoyl isothiocyanate (300 mg) was dissolved in chloroform containing 10% EtOH. After 2 hr the solvent was evaporated and the product recrystallized from 40% EtOH giving the pure compound, m.p. 131·5–132°. (Found: C, 52·16; H, 5·77; N, 4·59; S, 10·83. Calc. for $C_{13}H_{17}O_3N$: C, 52·17; H, 5·73; N, 4·68; S, 10·68%). The NMR spectrum shows signals at $\delta = 1{\cdot}47$ (tri), $\delta = 3{\cdot}87$ (si), $\delta = 4{\cdot}63$ (qu) and $\delta = 6{\cdot}99$ ppm (si).

Mono thiobenzoates and cyanogen halides. To a stirred suspension 10 mmol powdered potassium thiobenzoate in 250 ml dry ether were added dropwise a solution of 15 mmol cyanogen halide (cyanogen-bromide or -chloride) in 100 ml ether. The temp. was constantly held at −12 to −15° by means of a ice/MeOH bath. After additional 2 hr the mixture was filtered the remaining inorganic solid washed with ether on the filter and the combined aliquots evaporated. After recrystallization from cyclohexane the pure benzoyl thiocyanate was isolated.

Cyanogen halide	Yield of $C_6H_2Br_3COSCN$	Yield of $C_6H_2I_3COSCN$	Yield of C_6H_5COSCN
CN—Br	51%	73%	~0
CN—Cl	80%	85%	~0

The insoluble remanens contains disulfide. Recrystallization from ether gave the pure product.

Di(2,4,6-*tribromobenzoyl*)*disulfide*, m.p. 163–163·5°. (Found: C, 22·66; H, 0·56; S, 8·77; Br, 63·76. Calc. for $C_{14}H_4O_2S_2Br_6$: C, 22·64; H, 0·54; S, 8·62; Br, 63·88%).

Di(2,4,6-*triiodobenzoyl-disulfide*, m.p. 225–226°. (Found: C, 16·40; H, 0·46; S, 6·14; I, 74·00. Calc. for $C_{14}H_4O_2S_2I_6$: C, 16·33; H, 0·38; S, 6·22; I, 73·96%).

Dibenzoyl disulfide, m.p. 136–136·5°. (Found: C, 61·35; H, 3·75; S, 23·19. Calc. for $C_{14}H_{10}O_2S_2$: C, 61·31; H, 3·65; S, 23·36%).

Mono thioacids and cyanogen bromide. General procedure: the mono thioacid (0·5 mmol) was dissolved in dry ether (6 ml). To this soln was added dropwise a soln of BrCN (0·7 mmol) in dry ether (10 ml). The mixture was kept at 0°. After 2 hr the solvent was evaporated giving an almost analytical pure product. Recrystallization from ether gave the pure product.

Potassium mono thio-2,4,6-*tribromobenzoate and* 2,4,6-*tribromobenzoyl thiocyanate.* The thiocyanate (330 mg) was dissolved in dioxan (20 ml). To this soln was added dropwise a soln of the monothiobenzoate (200 mg) in dioxan (5 ml). After 8 hr at room temp. the mixture was filtered. The ppt was identified as KSCN by means of IR. After evaporation the crude product was recrystallized from dry ether to give the pure di(2,4,6-tribromobenzoyl)-sulfide, m.p. 158–158·5°. (Found: C, 23·58; H, 0·60; S, 4·42. Calc. for $C_{14}H_4O_2SBr_6$: C, 23·50; H, 0·56; S, 4·47%). The authentic di(2,4,6-tribromobenzoyl)sulfide was prepared according to Ref. 7.

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