# Reactions of Organic Anions. LII[1]. Reactions of Organic Thiocyanates with Carbanions in Aqueous Medium

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Organic thiocyanates are used as insecticides, analytical reagents etc., and also as starting materials and intermediates in organic synthesis[2].

We have found that aliphatic and aromatic thiocyanates are effective alkylthiolating or arylthiolating agents for carbanions generated in a two-phase catalytic system.

In organic thiocyanates, a partial positive charge is distributed between the C-atom of the CN group, the S-atom, and the C-α atom. One can therefore expect that nucleophilic agents will attack all of these three positions[3]. In the case of carbanions that are relatively soft bases, the S-atom should be the preferred site of nucleophilic attack. In addition, nucleophilic attack on the S-atom is favoured by the ability of sulfur to stabilize negative charge by filling up unoccupied 3d orbitals. The ununsual affinity of the sulfur atom to nucleophilic attack ("thiophilic attack") has been observed in reactions of cyclic sulfides with butyllithium[4] and has been discussed by Beak and Worley[5] who studied the reaction of thiobenzophenone with organolithium compounds.

Hitherto, only few examples of nucleophilic reactions of carbanions with thiocyanates have been reported. The reaction with lithium acetylenides results in substitution of the CN group to give 1-alkynyl thioethers[6] whereas the reaction with Grignard reagents is more complicated[7]. The low number of examples of such reactions is probably due to the fact that organic thiocyanates are readily converted into disulfides by base[8], i.e. under the conditions used for the generation of carbanions.

$$2\ \text{R—SCN} + 2\ \text{NaOH} \longrightarrow \text{R—S—S—R} + \text{NaCN} + \text{NaOCN}$$

We tried to preclude this undesired side reaction by generating the carbanion in a two-phase catalytic system in which no base is present in the organic phase. These conditions have already been used in other reactions of base/water-sensitive species such as dihalocarbenes[9], α-chloroethers[10], etc.; they are particularly suitable for the generation of trichloromethyl anions[11] and carbanions derived from CH-acidic compounds such as phenylacetonitriles[12]. We investigated the reaction of carbanions generated from chloroform, phenylacetonitrile, and 2-phenylpropanenitrile with alkyl and aryl thiocyanates.

The reaction between ethyl thiocyanate (**1b**) and chloroform in the presence of 50% aqueous sodium hydroxide and catalytic amounts of triethylbenzylaminium chloride (TEBA) is moderately exothermic and gives ethyl trichloromethyl sulfide (**2b**) in high yield.

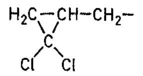
$$2\ \underset{\textbf{1}}{\text{R—S—CN}} + \text{CHCl}_3 \xrightarrow{\text{NaOH/H}_2\text{O/TEBA}} \underset{\textbf{2}}{\text{R—S—CCl}_3} + \text{NaCN}$$

The physical properties of **2b** (b.p., refraction index) were identical with the literature values[13]; compound **2b** was additionally identified by elemental analysis, I.R. spectrum (disappearance of the SCN band at 2200 $\text{cm}^{-1}$, and presence of the C-Cl stretching band at 600–800 $\text{cm}^{-1}$), and $^1$H-N.M.R. spectrum (0.2–0.25 ppm upfield shift of C-α protons).

The reaction of chloroform with other thiocyanates under the same conditions proceeded analogously. The results are summarized in the Table.

Known methods of synthesis of trichloromethyl sulfides are: chlorination of methyl sulfides[14] (limited to dimethyl sulfide and some aryl methyl sulfides), free-radical addition of trichloromethanesulfenyl chloride to alkenes[15], the reaction of trichloromethyl anions with thiosulfonic acid esters[16], and the reaction of dichloromethyl sulfides with phosphorus(V) chloride[13]. Considering the availability of the starting thiocyanates, the simplicity of the procedure and the yields and purity of the trichloromethyl sulfides obtained, the method described here seems to be superior to the known methods. The products are compounds of practical importance[2,17,18].

**Table.** Two-Phase Reaction of Chloroform with Base and Organic Thiocyanates (**1**→**2**).

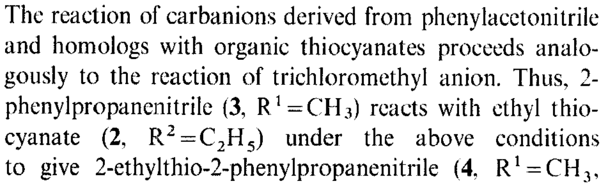
| | R | Yield (%) | Physical Properties of **2** Obtained b.p./torr | $n_D^{23}$ | Lit. values b.p./torr | $n_D^{20}$ | References |
|---|---|---|---|---|---|---|---|
| **a** | $CH_3$ | 61 | 58/35 | 1.5118 | 61/38 | – | 16 |
| **b** | $C_2H_5$ | 64 | 65–67/23 | 1.5122 | 61–62/15 | 1.5094 | 13 |
| **c** | $n$-$C_3H_7$ | 67 | 66–67/10 | 1.5011 | 70–71/12 | 1.5048 | 13 |
| **d** | $C_6H_5$ | 60 | 124–126/16<br>(m.p. 35.5°) | – | 86–87/0.7<br>(m.p. 34–36°) | – | 13 |
| **e** | $C_6H_5$-$CH_2$— | 80 | 128–129/7<br>(m.p. 37–39°) | – | 92–94/0.1<br>(m.p. 37–38°) | 1.5802 | 13 |
| **f** | $n$-$C_5H_{11}$ | 86 | 96–98/11 | 1.4993 | new compounds, satisfactory analyses were obtained | | |
| **g** | Cl—$(CH_2)_3$— | 77 | 128–130/15 | 1.5332 | | | |
| **h** | NC—$(CH_2)_3$— | 70 | 105/0.2 | 1.5263 | | | |
| **i** |  | 76 | 77/0.05 | 1.5453 | | | |

The trichloromethyl anion is known to be a very short-living species and to undergo rapid dissociation to dichlorocarbene and chloride ion[19].

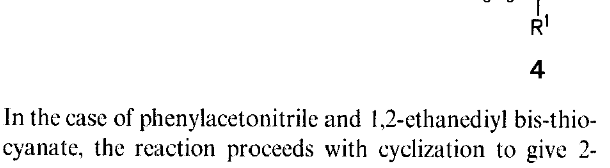
$$CCl_3^{\ominus} \longrightarrow :CCl_2 + Cl^{\ominus}$$

The high yields of trichloromethyl sulfides (**2**) obtained in our reaction can therefore be rationalized in terms of a high reaction rate for the *S*-trichloromethylation of **1**, which exceeds the rate of dichlorocarbene formation.

The reaction of carbanions derived from phenylacetonitrile and homologs with organic thiocyanates proceeds analogously to the reaction of trichloromethyl anion. Thus, 2-phenylpropanenitrile (**3**, $R^1=CH_3$) reacts with ethyl thiocyanate (**2**, $R^2=C_2H_5$) under the above conditions to give 2-ethylthio-2-phenylpropanenitrile (**4**, $R^1=CH_3$, $R^2=C_2H_5$).

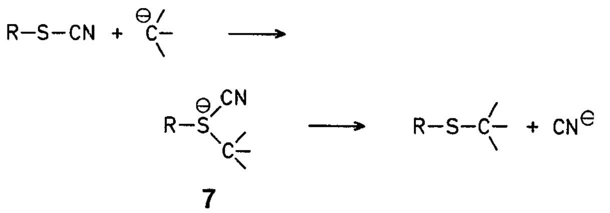


In the case of phenylacetonitrile and 1,2-ethanediyl bis-thiocyanate, the reaction proceeds with cyclization to give 2-cyano-2-phenyl-1,3-dithiolane (**6**).



The structure of the product was established on the basis of the elemental analysis and the ¹H-N.M.R. spectrum.

With the available data it cannot be decided whether substitution of the cyano group in thiocyanates by carbanions proceeds via thiophilic attack and formation of an intermediate anionic adduct or synchronously according to an $S_N2$ type mechanism (via **7** as an intermediate or transition state).



**7**

The alkyl and aryl thiocyanates used as starting materials were prepared by known methods[2]. The ¹H-N.M.R. spectra were recorded on a Jeol JNM-60 H spectrometer in $CCl_4$ using TMS as an internal standard. The I.R. spectra were recorded on a Perkin-Elmer 237-grating spectrometer. All new compounds (marked by an asterisk) gave satisfactory elemental analyses.

**Reaction of Organic Thiocyanates with Chloroform and Base; General Procedure:**

The thiocyanate (0.2 mol), chloroform (76g, 0.6 mol), and TEBA (0.5 g, ~0.002 mol) were vigorously stirred; to this solution, 50% aqueous sodium hydroxide (40 ml) was added portionwise. The reaction was slightly exothermic; the temperature rose to 40° and was then held at 40° for 3–4 h. The mixture was then diluted with water, the organic layer separated, and the aqueous layer extracted with chloroform. The extracts were washed with water, dried, and the solvent evaporated. The residue was distilled in vacuo; in the case of solid products, the distillate was recrystallized.

**Preparation of 2-Alkylthio-2-phenylpropanenitriles; General Procedure:**

A mixture of 2-phenylpropanenitrile (13.1g, 0.1 mol), alkyl thiocyanate (0.2 mol), TEBA (0.2g, 0.001 mol), and 50% aqueous sodium hydroxide (15 ml) was stirred at 50° for 4 h. The products were purified by distillation in vacuo.

*2-Ethylthio-2-phenylpropanenitrile** (**4**, $R^1=CH_3$, $R^2=C_2H_5$); yield: 14.7g (77%); b.p. 88–91°/0.05 torr; $n_D^{23}$: 1.5378.

*2-Pentylthio-2-phenylpropanenitrile** (**4**, $R^1=CH_3$, $R^2=n$-$C_5H_{11}$); yield: 15.8g (68%); b.p. 108–112/0.1 torr; $n_D^{23}$: 1.5332.

**2-Cyano-2-phenyl-1,3-dithiolane* (6):**

The reaction was carried out with phenylacetonitrile (23.4 g, 0.2 mol), 1,2-ethanediyl bis-thiocyanate (28.8g, 0.2 mol), TEBA (0.5g, 0.002 mol), and 50% aqueous sodium hydroxide (40 ml) as described above; yield: 18.7g (45%); b.p. 152–157°/0.3 torr. The product was recrystallized from ethanol; m.p. 72°.

¹H-N.M.R. ($CCl_4$): δ = 3.7 (s, 4H), 7.3–8.2 ppm (m, 5H).

**2,2-Dichlorocyclopropylmethyl Thiocyanate (1i):**

*1-Bromomethyl-2,2-dichlorocyclopropane:* A mixture of allyl bromide (60.5g, 0.5 mol), chloroform (120g, 1 mol), and TEBA (1.5g) was vigorously stirred and to this mixture, 50% aqueous sodium hydroxide (120 ml) was added dropwise. The temperature of the mixture was held at 35–40° for 3 h. The mixture was then diluted with water, extracted with chloroform, the extract dried, the solvent removed, and the residue distilled at reduced pressure; yield: 36.2 g (36%); b.p. 79°/25 torr; $n_D^{20}$: 1.5143 (Ref.[20], b.p. 77°/23 torr; $n_D^{25}$: 1.5150).

*2,2-Dichlorocyclopropylmethyl Thiocyanate**: A mixture of 1-bromomethyl-2,2-dichlorocyclopropane (20.4 g, 0.1 mol), potassium thiocyanate (10.7 g, 0.11 mol), and 90% ethanol (30 ml) was refluxed for 6 h. After the usual work-up, the product was distilled in vacuo; yield: 15.3 g (84%); b.p. 91–92°/0.4 torr; $n_D^{25}$: 1.5268.

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