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# Cyanuric chloride/dimethylformamide promoted one-pot conversion of primary alcohols into alkyl thiocyanates

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# Cyanuric chloride/dimethylformamide promoted one-pot conversion of primary alcohols into alkyl thiocyanates

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A convenient and efficient procedure for one-pot conversion of alcohols into corresponding alkyl thiocyanates in the presence of cyanuric chloride/dimethylformamide mixed reagent is described. This approach is efficient and selective for primary alcohols especially substituted benzyl alcohols. This method can be easily applied for the facile conversion of primary alcohols into corresponding thiocyanates, but sterically hindered alcohols produced corresponding thiocyanates in very low yields.

**Keywords:** alcohol; thiocyanation; alkyl thiocyanate; one-pot; cyanuric chloride



## 1. Introduction

Organic thiocyanates have been used extensively in synthetic organic chemistry (*1*), with a wide range of applications particularly in biological and heterocyclic chemistry (*2*). For example, properties such as antiasthmatic (*3*), insecticide (*4*), and biocides (*5*) have been reported for organic thiocyanates. These organo-sulfur compounds are industrially important and have been used as vulcanization accelerators (*6*). Moreover, some organic thiocyanates such as allylic thiocyanates may be isomerized into isothiocyanates on warming (*7*). The latter compounds are also very important in organic synthesis (*8*).

Thiocyanate groups are usually introduced into aliphatic compounds by nucleophilic substitution. The most reliable procedures involve heating the appropriate alkyl halides or tosylates with thiocyanate ion in polar aprotic solvents. The various sources of thiocyanate and isothiocyanates ion such as NaSCN (*9*), potassium thiocyanate (KSCN) (*9*), ammonium thiocyanate ($NH_4SCN$) (*10*), $Zn(SCN)_2$ (*9*), $Me_3SiNCS$ (*11*), $Me_3SiNCS/Bu_4NF$ (*12*), $Me_3SiNCS/TiCl_4$ (*13*), and 1-butyl-3-methylimidazolium thiocyanate ([bmim]SCN) (*14*) were used for thiocyanation reaction.

Another general and more important route for the preparation of alkyl thiocyanates is direct thiocyanation of alcohols. In direct thiocyanation methods, phosphine-based reagents have been used for activation of the hydroxyl group of alcohols. These reagents include $Ph_3P(SCN)_2$ (*15*),

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$Ph_3P(Br)_2/NH_4SCN$ (*16*), $Ph_3P$/Diethylazodicarboxylate/$NH_4SCN$ (*17*), and $Ph_3P$/Dichlorodicyanoquinone/$Bu_4NSCN$ (*18*). Recently, a new ionic liquids-based phosphine has also been reported for the direct conversion of alcohols into alkyl thiocyanates (*19*). In addition, thiols (*20*), silyl ethers (*21*), amines (*22*), and THP-ethers (*23*) can be directly converted into corresponding thiocyanates using phosphine-based reagents.

In the last decade, cyanuric chloride (CC) or 2,4,6–trichloro –1,3,5– triazine (*24*) and its derivatives (*25*) have been utilized in various organic functional group transformations. A literature survey indicates that CC was not used for the conversion of alcohols into alkyl thiocyanates.

## 2. Results and discussion

In continuation of our studies on organo-sulfur chemistry (*26*), we report here the successful use of CC/dimethylformamide (DMF) mixed reagent for one-pot conversion of alcohols into corresponding alkyl thiocyanates, under relatively mild conditions (Scheme 1).

In order to achieve optimal conditions, the reaction of benzyl alcohol with potassium thiocyanate (KSCN) in the presence of CC/DMF was selected as a model reaction, and the effects of the various reaction parameters such as amount, counter ion of the nucleophile, temperature, and base were studied in detail.

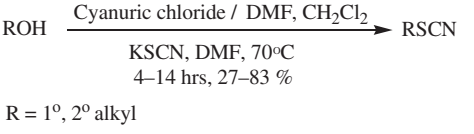


In the first step, the effect of the nucleophile amount was studied. For this purpose, the model reaction was conducted with different amounts of KSCN from 1 to 5 equivalents. The best results were obtained when the reaction was carried out in the presence of 5 equivalents excess of the nucleophile with respect to benzyl alcohol. In addition, the effect of supposedly more soluble thiocyanate salts such as $NH_4SCN$ and tetrabutylammonium thiocyanate was also investigated. Reaction of $NH_4SCN$ has no considerable difference with KSCN but *n*-$Bu_4NSCN$ proved less successful than KSCN.

In the next step, the effect of the base was studied. For this purpose, three organic bases such as triethylamine, 1,8-diazabicyclo[2,2,2]octane, and 1,5-diazabicyclo[5,4,0]-undec-7-ene were used. The results showed no significant difference between reaction in the presence or absence of the base, and hence the subsequent reactions were performed in the absence of the base.

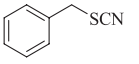
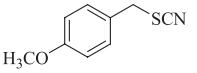
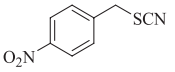
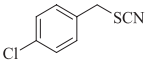
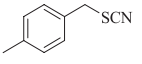
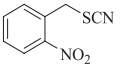
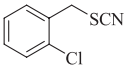
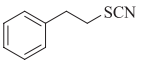
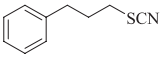
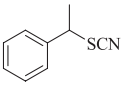
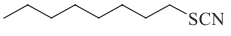
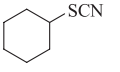
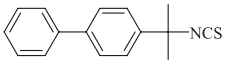
In addition, the effect of the temperature was also investigated. The results revealed that the conversion of benzyl alcohol into benzyl thiocyanate was easily performed at 70 °C, and this temperature was applied for subsequent reactions.

Under optimal conditions, several structurally diverse alcohols were examined for the thiocyanation reaction. Representative results are summarized in Table 1. As is clear from Table 1, primary benzylic alcohols (Entries 1–7) were easily converted into corresponding thiocyanates in good to excellent yields, but secondary (Entries 10 and 12) and tertiary alcohols (Entry 13) produced desired products in very low and negligible yields, respectively, even at higher temperature. In these cases (Entries 10–13), alkyl chlorides produced a major product. In addition, under optimal conditions, non-benzylic primary alcohols (Entries 8, 9, 11) produced corresponding thiocyanates in low yields.




Scheme 1. Conversion of alcohols into alkyl thiocyanates with CC/DMF mixed reagent.

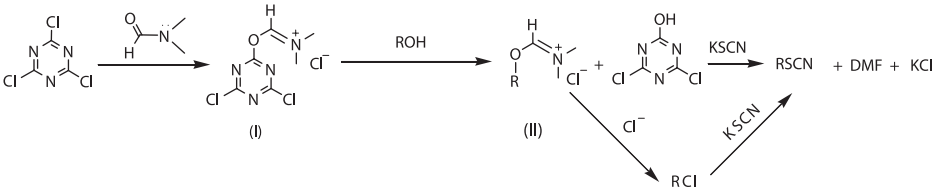
Table 1. Conversion of alcohols into alkyl thiocyanates using CC/DMF and KSCN.

| Entry | Alcohol | Product | Time (h) | Yields (%)[a] | IR(SCN) $cm^{-1}$ | Ref. |
|---|---|---|---|---|---|---|
| 1 | Benzyl alcohol |  | 6 | 76 | 2155 | (*16*) |
| 2 | 4-Methoxy benzyl alcohol |  | 8 | 83 | 2155 | (*21*) |
| 3 | 4-Nitro benzyl alcohol |  | 4 | 72 | 2155 | (*23*) |
| 4 | 4-Chloro benzyl alcohol |  | 5 | 78 | 2155 | (*21*) |
| 5 | 4-Methyl benzyl alcohol |  | 6 | 79 | 2154 | (*27*) |
| 6 | 2-Nitro benzyl alcohol |  | 6 | 81 | 2156 | –[c] |
| 7 | 2-Chloro benzyl alcohol |  | 6 | 79 | 2154 | –[d] |
| 8 | 2-Phenyl ethanol |  | 14 | 65 | 2155 | (*16*) |
| 9 | 3-Phenyl propanol |  | 14 | 70 | 2154 | (*18*) |
| 10 | 1-Phenyl ethanol |  | 14 | 35[b] | 2153 | (*17*) |
| 11 | 1-Octanol |  | 14 | 48[b] | 2155 | (*17*) |
| 12 | Cyclohexanol |  | 14 | 27[b] | 2155 | (*20*) |
| 13 | 2-(4-Biphenyl)-2-propanol |  | 14 | 0[b] | – | – |

Notes: [a]Isolated pure product. [b]GC analysis showed 45, 60, 40 and 0% yield for corresponding alkyl thiocyanates and 55, 40, 60 and 100% for alkyl chlorides for Entries 10–13, respectively. [c]IR (-SCN) in $CCl_4$ 2156 $cm^{-1}$; $^1$H-NMR (250 MHz, $CDCl_3$) $\delta$ 4.47 (2H, s), 7.55–7.77 (1H, d), 7.60–7.65 (1H, t), 7.72–7.76 (1H, t), 8.25–8.27 (1H, d) ppm; $^{13}$C-NMR (60 MHz, $CDCl_3$) $\delta$ 134.62, 132.53, 131.16, 130.38, 129.52, 126.29, 112.13, 36.70 ppm. [d]IR (-SCN) in $CCl_4$ 2154 $cm^{-1}$; $^1$H-NMR (250 MHz, $CDCl_3$) $\delta$ 4.27 (2H, s), 7.28–7.38 (2H, m), 7.42–7.48 (2H, m) ppm; $^{13}$C-NMR (60 MHz, $CDCl_3$) $\delta$ 134.19, 132.33, 131.16, 130.52, 130.16, 127.49, 111.82, 36.25 ppm.

In another attempt, we examined this method for the large-scale preparation of alkyl thiocyanates. The results for preparation of benzyl thiocyanate from benzyl alcohol (20 mmol) as a model compound showed that this method can be easily applied for the large-scale synthesis of this compound.

On the basis of the previous report (*24b*) and our observation, the following mechanism is suggested for this conversion (Scheme 2). At first, positively charged adduct (**I**) is formed from the




Scheme 2. The suggested mechanism for the conversion of alcohols into alkyl thiocyanates with CC/DMF.

reaction of CC with DMF. This positively charged adduct **(I)** interacts with alcohol and produces **(II)**. Nucleophile attack of thiocyanate ion on intermediate **(II)** produces the corresponding alkyl thiocyanate, DMF, and KCl. Also, the chloride ion could be attacked on the intermediate **(II)** to produce alkyl chloride. Under reaction conditions, the chloride leaving groups can be substituted by a thiocyanate ion. In the cases of secondary and tertiary alcohols, alkyl chlorides were formed in the reaction mixture as a major product that cannot be easily converted into alkyl thiocyanates under this reaction condition.

In summary, the present methodology can be applied as an alternative to the all of the phosphine-based reactions for the preparation of primary alkyl thiocyanates. In addition, the reactants (CC and KSCN) are more inexpensive than Mitsunobu and other phosphine-based reagents, and also the side products are innocuous (DMF and potassium chloride).



## 3. Experimental

### 3.1. *General*

Products were characterized by comparison of their spectroscopic data ($^1$H and $^{13}$C NMR, IR) with those reported in the literature. All yields refer to isolated products. The FT-IR spectra of neat samples between NaCl disks were obtained on a BOMEM 450 instrument. The high-field NMR spectra were obtained on a Brucker AC 250 instrument.$^1$H and $^{13}$C chemical shifts are quoted relative to solvent resonance(s) as internal standard.

### 3.2. *General procedure for the conversion of benzyl alcohol into benzyl thiocyanate*

CC (0.183 g, 1.0 mmol) was added to DMF (0.5 ml), maintained at 25 °C. After the formation of a white solid, the reaction was monitored by thin layer chromatography (TLC) until complete disappearance of CC, and $CH_2Cl_2$ (5 ml) was added, followed by the benzyl alcohol (0.09 ml, 0.95 mmol), KSCN (0.491 g, 5 mmol), and DMF (10 ml). Then, the mixture was stirred at 70 °C and monitored (TLC) until completion (6 h). The organic layer was washed with water (3 × 15 ml), and dried over anhydrous $Na_2SO_4$. Evaporation of the solvent and chromatography on a short silica gel column using $n-$hexane/ethyl acetate (9/1) as eluent gave benzyl thiocyanate in 76% yield. IR (-SCN) in $CCl_4$ 2155 cm$^{-1}$; $^1$H-NMR (250 MHz, $CDCl_3$) $\delta$ 4.12 (2H, s), 7.32–7.45 (5H, m) ppm; $^{13}$C-NMR (60 MHz, $CDCl_3$) $\delta$ 134.85, 132.64, 129.68, 129.49, 110.64, 38.76 ppm.

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