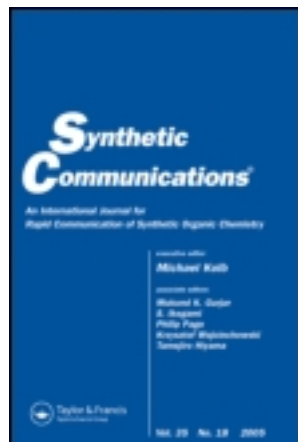


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Efficient and Novel Method for Thiocyanation of Aromatic Compounds Using Trichloroisocyanuric Acid/Ammonium Thiocyanate/Wet SiO₂

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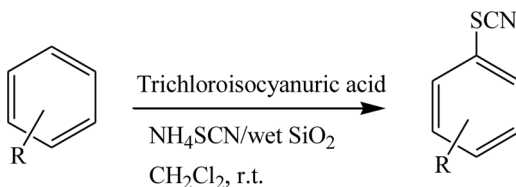
EFFICIENT AND NOVEL METHOD FOR THIOCYANATION OF AROMATIC COMPOUNDS USING TRICHLOROISOCYANURIC ACID/AMMONIUM THIOCYANATE/WET SiO₂

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GRAPHICAL ABSTRACT



Abstract An efficient and novel method for thiocyanation of aromatic and heteroaromatic compounds using trichloroisocyanuric acid/ammonium thiocyanate/wet SiO₂ is described.

Keywords Aromatic; thiocyanation; trichloroisocyanuric acid; wet SiO₂

INTRODUCTION

Aromatic and heteroaromatic thiocyanato compounds are useful intermediates in the synthesis of sulfur-containing heterocycles such as 2-aminobenzothiazoles, 1,3-thiazine derivatives, and 2-iminobenzoxathioles.^[1] Furthermore, aryl thiocyanates can be easily transformed into various sulfur-containing functional groups^[2] such as thiophenols, thiocarbamates, and dithiourethanes. They are particularly useful for producing drugs and pharmaceuticals.^[3] Several methods have been developed for the thiocyanation of arenes by using various reagents under certain conditions including arylthallium bistrifluoroacetates/potassium thiocyanate,^[4a] antimony(V) chloride/lead(II) thiocyanate,^[4b] phenyl iodine(III) bis(trifluoroacetate)/trimethylsilyl isothiocyanate (TMSNCS),^[4c] and *N*-bromosulfonamides/potassium

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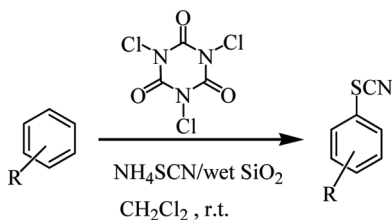
thiocyanate (KSCN).^[4d] Other reagents have been applied to the thiocyanation of indoles and aromatic amines such as bromine/potassium thiocyanate,^[2b] ceric ammonium nitrate (CAN)/ammonium thiocyanate,^[5a] iodine/ammonium thiocyanate,^[5b] ferric chloride/ammonium thiocyanate,^[5c] and oxone/ammonium thiocyanate.^[5d] Very recently, 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ)/NH₄SCN,^[6a] BrMe₂SBr/NH₄SCN,^[6b] HIO₃/NH₄SCN,^[6c] I₂O₅/NH₄SCN,^[6d] and *p*-toluene sulfonic acid/NH₄SCN^[6e] have been reported for thiocyanation of aromatic and heteroaromatic compounds. However, some of these methods suffer from some drawbacks such as the requirement for strong oxidizing reagents, toxicity of the reagents,^[4b] and poor yields for some compounds.^[5d] In the case of molecular bromine, which is hazardous and difficult to handle, reactions need to be performed at -70 °C to -60 °C. Hence, a new method for the thiocyanation of aromatic and heteroaromatic compounds could be valuable.

Any simplification in handling procedures would be highly convenient in terms of risk reduction, economic advantage, and environment protection.^[7] On the other hand, there is intense current research and general interest in heterogeneous systems because of the perceived opportunities such systems present for basic research and because of the unquestioned importance they have in industry and development technologies.^[8] The use of trichloroisocyanuric acid, which is used primarily as a disinfectant, has found wide applications in organic chemistry.^[9,10] In recent years, Zolfigol and coworkers reported the mononitration and dinitration of phenols by using trichloroisocyanuric acid/NaNO₂/wet SiO₂.^[11] Also, we used this reagent for the iodination of aromatic compounds in conjunction with I₂ and wet SiO₂ in CH₂Cl₂.^[12] Herein, in a continuation of our study, we report a novel and efficient approach for the thiocyanation of aromatic and heteroaromatic compounds using trichloroisocyanuric acid/NH₄SCN/wet SiO₂.

RESULTS AND DISCUSSION

To begin our study, effects of various reaction parameters on the thiocyanation of aromatic ring were examined. The reaction was carried out with different molar ratios of aromatic compound/trichloroisocyanuric acid/ammonium thiocyanate, and we found that 1:1:1 is the most suitable ratio. In the solvent study, we found that CH₂Cl₂ was the best solvent in this method. Different aromatic compounds were also subjected to thiocyanation in the presence of trichloroisocyanuric acid, ammonium thiocyanate, and wet SiO₂ (50% w/w) in dichloromethane (DCM) at room temperature (Scheme 1).

Under the optimized conditions, a wide range of substrates including benzene, toluene, xylenes, anisols, anilines, acetanilide, *p*-chloroacetanilide, and naphthalene were investigated, as shown in Table 1. Anilines and the other substituted aromatic compounds were thiocyanated under these conditions, giving selectively *para*-thiocyanated products (Table 1, entries 2, 6, 9, 12, 13, and 15). Also, when the reaction was performed on anilines and aromatic compounds without *para*-substituent, thiocyanation occurred at the *para* position (Table 1, entries 3, 5, 7, 8, 10, and 11). Heteroaromatic compounds such as thiophene and pyrrole were also easily transformed into the monothiocyanated products in 2 min (Table 1, entries 17 and 18).



Scheme 1. Thiocyanation of aromatic compounds by trichloroisocyanuric acid and ammonium thiocyanate/wet SiO₂.

As expected, all the substrates underwent thiocyanation reaction and afforded the corresponding products in excellent yields. Anilines, thiophene, and pyrrole were converted to the corresponding thiocyanated product in a very short time. Trichloroisocyanuric acid as a commercially available reagent (slightly soluble in CH₂Cl₂) has been used for the in situ generation of HOCl in the presence of wet SiO₂.^[13] We think that the presence of wet SiO₂ acts as a heterogeneous effective surface area for in situ generation of the HOCl and then the SCN⁺ ion is generated by oxidation of the SCN⁻.

Trichloroisocyanuric acid was converted to cyanuric acid during the reaction as a highly polar compound that is completely insoluble in CH₂Cl₂ and was adsorbed by silica gel, efficiently making the workup easy. However, the corresponding products were obtained by simple filtration and subsequent evaporation of the solvent.

To conclude, we have developed a novel method for aromatic and heteroaromatic thiocyanation using a combination of trichloroisocyanuric acid/NH₄SCN/wet SiO₂. The method is mild and gives mono- and regioselective thiocyanato products in good to excellent yields within short reaction time. Moreover, cheapness and availability of the reagents and easy workup of the reaction make this method attractive for organic chemists.

EXPERIMENTAL




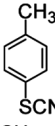
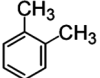
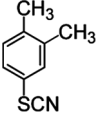
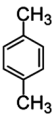
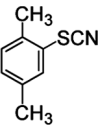
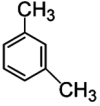
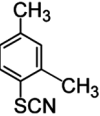

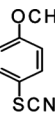
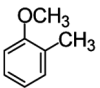
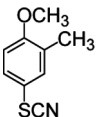
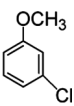
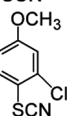

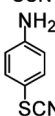
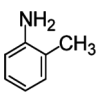
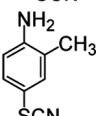
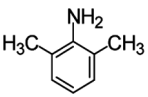
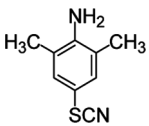
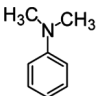
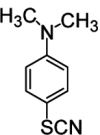
The products were purified by column chromatography. Fourier transform (FT)–infrared (IR) spectra were recorded on a Perkin-Elmer RXI spectrometer. NMR spectra were recorded on a Bruker Avance DPX 250-MHz instrument. All products were identified by comparison with authentic samples.

Aromatic compound (1 mmol) was added to a mixture of trichloroisocyanuric acid (0.196 g, 1 mmol), ammonium thiocyanate (0.076 g, 1 mmol), and wet SiO₂ (50% w/w, 1 g) while stirring in CH₂Cl₂. The progress of the reaction was monitored by thin-layer chromatography (TLC). After completion of the reaction, the mixture was filtered. The filtrate was dried over anhydrous MgSO₄ and then applied on a silica-gel column (using n-hexane as eluent) to afford corresponding thiocyanato product.

1-Methoxy-4-thiocyanatobenzene (Entry 6)

Solid mp 32–33 °C (lit.^[14] 33–34 °C). IR (KBr): 3050, 2910, 2160 (SCN), 1620 cm⁻¹. ¹H NMR (CDCl₃), δ = 3.83 (s, 3H), 6.85(d, 2H), 7.48 (d, 2H).

Table 1. Thiocyanation of various aromatic and heteroaromatic compounds using trichloroisocyanuric acid/ammonium thiocyanate/wet SiO₂ in CH₂Cl₂ at room temperature

Entry	Substrate	Product ^a	Reaction time (min)	Isolated yield (%)
1			60	94
2			50	92
3			47	97
4			58	96
5			45	93
6			17	93
7			17	93
8			20	95
9			2	98
10			2	95
11			3	96
12			3	98

(Continued)

Table 1. Continued

Entry	Substrate	Product ^a	Reaction time (min)	Isolated yield (%)
13			2	95
14			60	96
15			15	98
16			57	97
17			2	93
18			2	97

^aThe products were identified by comparison of their physical constants and IR and NMR spectra with those of authentic samples.

1-Methoxy-2-methyl-4-thiocyanatobenzene (Entry 7)

Oil (lit.^[4c] oil). IR (KBr): 2988, 2150 (SCN), 1596, 1479, 1260, 880 cm^{-1} . ¹H NMR (CDCl_3): $\delta = 2.50$ (s, 3 H), 3.89 (s, 3 H), 6.81–7.2 (m, 3 H).

4-Thiocyanatobenzamine (Entry 9)

Mp 50–51 °C (lit.^[5d] mp 51–52 °C). IR (KBr): 3403, 3350, 2137 (SCN), 1627, 1591, 1432, 818 cm^{-1} .

2-Methyl-4-thiocyanatobenzamide (Entry 10)

Solid; mp 70–71 °C (lit.^[15] 70–71 °C). ¹H NMR (CDCl_3): $\delta = 2.44$ (s, 3 H), 3.75 (br s, 2 H), 6.43–6.62 (m, 2 H), 7.18–7.52 (m, 1 H). IR (KBr): 3354, 3243, 2145 (SCN), 1628, 1592, 1492, 1298, 821 cm^{-1} .

2,6-Dimethyl-4-thiocyanatobenzamide (Entry 11)

Solid; mp 85–87 °C (lit.^[16] 87–88 °C). IR (KBr): 2928, 2147 (SCN), 1615, 1592, 1460, 1288 cm^{-1} .

N,N-Dimethyl-4-thiocyanatobenzenamine (Entry 12)

Solid; mp 72–74 °C (lit.^[5d] 73–74 °C). IR (KBr): 2922, 2137 (SCN), 1586, 1503, 1362, 1077, 802 cm⁻¹.

N-Methyl-4-thiocyanatobenzenamine (Entry 13)

Liquid. IR (film): m3385 (NH), 2908, 2142 (SCN), 1596, 1508, 1305, 1181, 814 (N–H), 745 (C–S) cm⁻¹. ¹H NMR (CDCl₃): δ 2.84 (s, 3H, CH₃), 4.12 (br., 1H, NH), 6.58 (d, 2H, *J* = 8.67 Hz, 2-, 6- H), 7.38 (d, 2H, *J* = 8.64 Hz, 3-, 5-H).

2-Thiocyanatothiophene (Entry 17)

Oil (lit.^[17] oil). IR (neat): 3012, 2158 (SCN), 1412, 1215, 850, 728 cm⁻¹. ¹H NMR (CDCl₃): δ = 7.50–8.12 (m, 3 H).

2-Thiocyanato-1*H*-pyrrole (Entry 18)

Oil (lit.^[5d] oil). IR (neat): 3340, 2952, 2159 (SCN), 1530, 1422, 1029, 737 cm⁻¹. ¹H NMR (CDCl₃): δ = 6.26 (m, 1 H), 6.61 (m, 1 H), 6.95 (m, 1 H), 8.83 (br., 1 H).

ACKNOWLEDGMENT

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