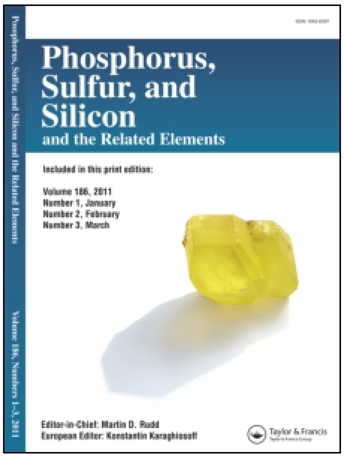

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A New Method for the Synthesis of Isothiocyanates from Dithiocarbamates or Alkyl Amines Using Chlorosilanes as Decomposition Reagents

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A series of isothiocyanates were prepared in good yields by the decomposition of dithiocarbamates using chlorosilanes such as Me_3SiCl, Me_2SiCl_2, $MeSiCl_3$, *and* $SiCl_4$ *as decomposition reagents. Alkyl isothiocyanates were obtained by a facile one-pot method in high yield from alkyl amines using these inexpensive decomposition reagents in the presence of a base.*

Keywords Isothiocyanates; chlorosilanes; decomposition reagents; Me_3SiCl; Me_2SiCl_2; $MeSiCl_3$; $SiCl_4$

INTRODUCTION

Isothiocyanates are one of the most important synthetic intermediates for the preparation of both sulfur-and nitrogen-containing organic compounds, especially for heterocycles such as thiadiazole, triazole, thiouracil, and thiopyrimidine.[1] The isothiocyanate functionality is frequently encountered in natural products, including marine susquiterpenes.[2] The synthesis of isothiocyanates has been extensively studied over past decades because they play an important role as anti proliferatives[3] and enzyme inhibitors for the HIV virus.[4] There have

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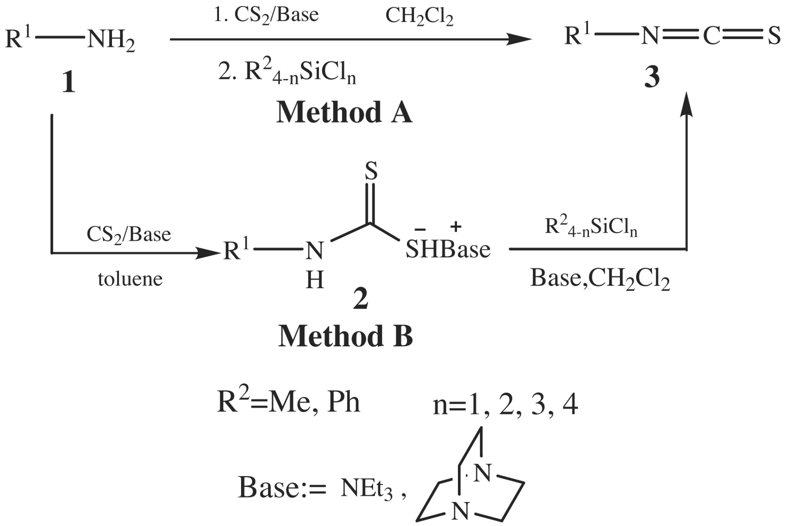
been numerous methods reported for the preparation of isothiocyanates from amine,[5] organic halides,[6] olefins,[7] aldoximes,[8] isocyanides[9] and dithiocarbamates.[10] However, most of them suffer from low yields and the use of environmentally unattractive reagents such as phosgene, thiophosgene, and its derivatives.[5,11]

RESULTS AND DISCUSSION

Among the literature methods, the most widely used procedures for the synthesis of isothiocyanates involve the decomposition of dithiocarbamates using heavy metals,[12] ethyl chlorocarbonates, and clop[13] as reagents. Herein we report for the first time the application of chlorosilanes such as Me_3SiCl, Me_2SiCl_3, $MeSiCl_3$, and $SiCl_4$, as decomposition reagents for the preparation of various isothiocyanates, thus avoiding phosgene and phosgene substitutes (Scheme 1). The experimental results for the synthesis of $PhCH_2NCS$ (**3a**) are listed in Table 1.

Chlorosilanes are not only important intermediates used to manufacture siloxanes and silanes — the building blocks for many silicone products.[14] but they are also versatile synthetic auxiliaries for the synthesis of some important classes of organic compounds.[15] Much of organosilicon chemistry is driven by the formation of strong Si-F, Si-O, and Si-S bonds at the expense of other weaker bonds. The high-bond energy of the Si-O bond makes it thermodynamically very favorable to



SCHEME 1

TABLE I Preparation of $PhCH_2NCS$ (3a) From Dithiocarbamates. Method B[a] Using Chlorosilanes $R^2_{4-n}SiCl_n$ as Decomposition Reagents

n	Chlorosilanes	$R^2_{4-n}SiCl_n$/sub.	Time (h)	Yield (%)[b]
1	Me_3SiCl	2:1	6	45
1	Me_3SiCl	4:1	6	85
1	Me_3SiCl	6:1	4	85
1	$Me_2PhSiCl$	4:1	6	79
2	Me_2SiCl_2	1:1	4	78
2	Me_2SiCl_2	2:1	4	91
2	Me_2SiCl_2	4:1	4	92
2	$MePhSiCl_2$	4:1	10	82
3	$MeSiCl_3$	2:1	4	90
3	$MeSiCl_3$	4:1	4	90
3	$PhSiCl_3$	2:1	5	87
4	$SiCl_4$	2:1	4	91
4	$SiCl_4$	4:1	4	92

[a] The reaction was performed at r.t. in dichloromethane.
[b] Isolated yield based on dithiocarbamate.

enable a reagent with a weak Si-X bond (X = Cl, Br, I) to react with an appropriate oxygen-containing organic molecule to form a silicon-oxygen bonded intermediate, which then can be transformed to another product in a subsequent step.[16]

As show in Table I, benzyl isothiocyanate were obtained in good yields using various chlorosilanes as decomposition reagents. The yield of benzyl isothiocyanate was low when two equivalents of Me_3SiCl were used and high in the case of four equivalents of Me_3SiCl with respect to the dithiocarbamates. However, two equivalents of Me_2SiCl_2, $MeSiCl_3$, and $SiCl_4$ were enough to convert the dithiocarbamates to isothiocyanate. We also found that Me_2SiCl_2, $MeSiCl_3$, and $SiCl_4$ were better decomposition reagents than other chlorosilanes like $Me_2PhSiCl$, $MePhSiCl_2$, and $PhSiCl_3$. A possible mechanism of this reaction is shown in Scheme 2. Byproducts of the reaction are a Bis [silyl] suljane and a polymer with Si-S bonds. The main driving force is the formation of the Si-S bond at the expense of the weaker C-S bond.

Alkyl and aryl isothiocyanates were obtained in high yields using chlorosilanes such as Me_3SiCl, Me_2SiCl_2, $MeSiCl_3$, and $SiCl_4$ as decomposition reagents in the presence of a base within 3–6 h (Method B). We found that alkyl isothiocyanates can also be obtained in good yields by a convenient one-pot method (Method A) directly from alkyl amines using these inexpensive decomposition reagents. However, the

TABLE II Preparation of Isothiocyanates From Amines or Dithiocarbamates Using Chlorosilanes in Dichloromethane[a]

R	Chlorosilane	Chlorosilane/ sub.	M. P. (lit.) (°C)	Method	Time (h)	Yield (%)[d]
$C_6H_5CH_2$	Me_3SiCl	4:1	oil (oil[17])	A	6	90[c](3a)
$C_6H_5CH_2$	Me_2SiCl_2	2:1	oil (oil[17])	B	4	92[b](3a)
$C_6H_5CH(CH_3)$	Me_2SiCl_2	2:1	oil (oil[13])	A	6	90[c](3b)
$C_6H_5CH(CH_3)$	Me_2SiCl_2	2:1	oil (oil[13])	B	4	90[b](3b)
4-$CH_3OC_6H_4CH_2$	$MeSiCl_3$	2:1	oil (oil[18])	A	6	89[c](3c)
$PhCH_2CH(CO_2Et)$	$SiCl_4$	2:1	oil (oil[5])	A	6	86[c](3d)
C_6H_5	Me_3SiCl	4:1	oil (oil[5])	B	4	86[b](3e)
C_6H_5	Me_2SiCl_2	2:1	oil (oil[5])	A	12	31[c](3e)
4-Cl-C_6H_4	Me_2SiCl_2	2:1	42 (42-43[13])	A	4	84[b](3f)
4-Cl-C_6H_4	$SiCl_4$	2:1	42 (42-43[13])	A	20	trace(3f)
2-CH_3-C_6H_4	Me_2SiCl_2	2:1	oil (oil[10])	B	4	85[b](3g)
4-$CH_3OC_6H_4$	$MeSiCl_3$	2:1	oil (oil[19])	B	4	86[b](3h)

[a] The reaction was performed at r.t.

[b] Isolated yield based on dithiocarbamate.

[c] Isolated yield based on amine.

[d] All products were identified by ^1H NMR, ^{13}C NMR, IR, and mass spectrometry.

yields of aryl isothiocyanates by this method were low, owing to their lower basicly. The expermental results are summarized in Table 2.

In conclusion, in this article we report a new method for the synthesis of isothiocyanates from dithiocarbamates using chlorosilanes such as Me_3SiCl, Me_2SiCl_2, $MeSiCl_3$, and $SiCl_4$ as decomposition reagents avoiding phosgene and phosgene substitutes. An efficient one-pot synthetic procedure for the preparation of alkyl isothiocyanates from amines in satisfactory yields using chlorosilanes as decomposition reagents was also developed. Advantages of the new methods are good yields, simplicity, safety, and environmental acceptability.

EXPERIMENTAL SECTION

Melting points were obtained with a capillary melting-point apparatus and are uncorrected. Infrared spectra were recorded on a Thermo Nicolet Avatar 370 spectrophotometer, ^1H NMR spectra ($CDCl_3$) were performed on a Brukes Advance 400 spectrometer using TMS as internal standard. Organic solvents were obtained from commercial sources. Preparative TLC separations were carried out with silica gel GF-245 coated on glass plates.

General Procedure

Method A

To a solution of the amine (1.5 mmol) and 1,4-diazabicyclo[2,2,2] octane (3 mmol) in dry dichloromethane (20 mL), carbon disulfide (2 mmol) was added dropwise over 1 h at 0°C. After the mixture was stirred for 1 h at the same conditions, a solution of the chlorosilane (3 mmol) in dry dichloromethane (20 mL) was added at 0°C. Then the mixture was allowed to warm up to r.t. and stirred for the specified time (monitored by TLC). The mixture was washed with water (20 mL) and saturated aqueous Na_2CO_3 and dried over anhydrous $MgSO_4$. After evaporating the solvent, the crude product was purified by preparative silica gel TLC using cyclohexane, ethyl acetate (10:1) as an eluent.

3a was prepared by Method A ^{1}H NMR ($CDCL_3$) δ 7.20–.35 (5H, m, ArH); 4.59 (2H, s, CH_2); ^{13}C NMR ($CDCL_3$) 134.3, 132, 129.0, 128.6, 126.9, 48; IR $v_{\max}$/cm^{-1}(Nujol): 3063, 2924, 2858, 2088(NCS), 1605, 1531, 1494, 1447, 1199, 698; EI-MS m/z 149 (M^+, 100).

Method B

The chlorosilanes (3 mmol) were added to the respective dithiocarbamate (1.5 mmol) and triethylmaine (1.5 mmol) in dry dichloromethane (20 mL) over 20 min at 0°C. After the mixture was stirred for 1 h at the same condition, it was allowed to warm up to r.t. and was further stirred for 5 h (monitored by TLC). The mixture was washed with water (20 mL) and saturated aqueous Na_2CO_3 and dried over anhydrous $MgSO_4$. After evaporating the solvent, the crude product was purified by preparative silica gel TLC using cyclohexane-ethyl acetate (10:1) as an eluent.

3b was prepared by Method B, oil, ^{1}H NMR ($CDCl_3$) δ: 7.17~7.34 (5H, m, ArH: 4.99 (q, J = 6.8 Hz, 1H, CH); 1.78 (d, J = 4.8 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$) 140.2, 132.4, 128.9, 128.2, 125.5, 57.1, 25°, IR $v_{\max}$/cm^{-1}(Nujol): 3063, 2931, 2087(NCS), 1603, 1493, 1453, 1345, 1021, 699: EI-MS m/z 163 (M^+, 100).

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