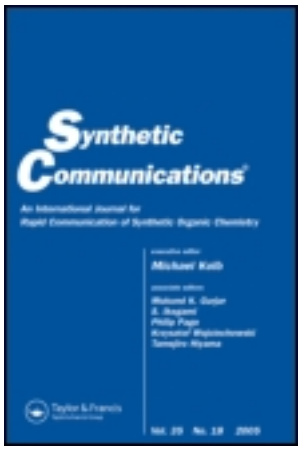

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A Novel Uncatalyzed Insertion Reaction of In Situ Formed Trichlorosilyl Cyanide with Imines: A Facile Silicon Mediated Synthesis of α-Aminonitriles

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A Novel Uncatalyzed Insertion Reaction of In Situ Formed Trichlorosilyl Cyanide with Imines: A Facile Silicon Mediated Synthesis of α-Aminonitriles

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ABSTRACT

The tetrachlorosilane-potassium cyanide reagent combination, (trichloro-silyl cyanide-in situ) is a new, safe and versatile hydrogen cyanide substitute. The reaction of this reagent with saturated aldimines **1a–j** and benzophenone oxime **3,** in absences of any catalyst, affords the corresponding α-aminonitriles **2a–j** and **4**, respectively, in excellent yield. Under the same condition the *bis*-imine **5** yields the imidazo[1,2-a]quinoxaline derivative **6**. Moreover, trichlorosilyl cyanide-in situ undergoes regiospecific addition onto α, β-unsaturated aldimines **7a–e** to give the corresponding

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1,2-addition products **8a–e**, in high yield, under exceedingly mild conditions.

Key Words: Tetrachlorosilane; Aldimines; Trichlorosilylcyanide; Aminonitriles; Synthesis.

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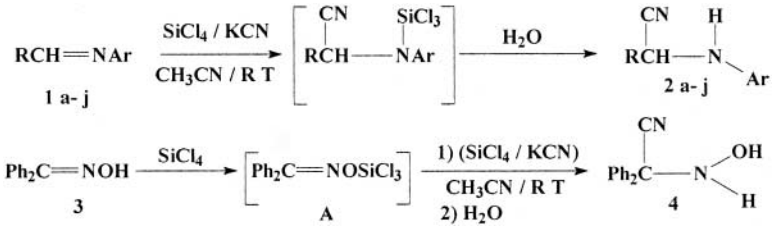
The synthetic exploitation of silicon reagents derived from tetrachlorosilane is considered to be an important undeveloped field in view of the great variety of potential silicon reagents. The in situ generation of safe and easily accessible silicon reagents, derived from tetrachlorosilane and different soft nucleophiles, attracted our attention in the last few years. Recently, we reported the in situ generation of triazidochlorosilane from the reaction of tetrachlorosilane with sodium azide in dry acetonitrile. Triazidochlorosilane showed an enhanced reactivity in comparison with other silyl azides.[1–4] This persuaded us to investigate in situ generation of other silicon reagents *via* interaction of tetrachlorosilane with different stoichiometeric amounts of various nucleophiles. Silyl cyanides are good reagents for introducing cyano-functionality, protecting and activating carbonyl compounds in organic synthesis.[5–8] The reaction of various silyl cyanides with different functional groups required the presence of either Lewis acids,[9–12] Lewis bases[13] or anionic catalysts.[14–15] Besides, the preparation of various silyl cyanides takes place under severe conditions; for example, dicyano-dimethylsilane was prepared by reaction of dichlorodimethylsilane with silver cyanide at 120–140°C for 5–7 days.[16] Due to their hydrolytic susceptibility, sensitivity to air and decomposition on prolonged storage, most silicon reagents should be freshly distilled or freshly prepared. Therefore, the in situ preparation and evaluation of the synthetic potentialities of simple, cheap and new silicon reagents is of great value. Thus, we introduce here the trichlorosilyl cyanide (TCSC in situ) as a stoichiometric reagent combination, prepared in situ from equimolar amounts of tetrachlorosilane and potassium cyanide in dry acetonitrile, and its reaction with different aldimines.

In order to explore the synthetic potentiality of TCSC in situ we decided to examine the cyanosilylation of imines as preliminary study, since the products are important intermediates for synthesis of α-amio acids. Although, it was reported that the in situ formed trimethylsilyl cyanide failed to react with imines,[17] TCSC in situ reacts with *N*-phenyl-*N*-(phenylmethylidene)amine **1a** to give 2-anilino-2-phenylacetonitrile **2a**, in absence of any catalyst under exceedingly mild conditions, in excellent yield (Sch. 1). To demonstrate functional group compatibility



Scheme 1.

for this process and to define the scope of the method, the reaction of several functionalized aldimines has been investigated. In most cases α-aminonitriles **2a–j** (Table 1) are isolated in pure form after aqueous work up. Also, in the number of systems studied the addition process has been devoid of side reactions such as imine cleavage (Sch. 4). In addition, by this method Lewis acids, Lewis bases and various anionic catalysts, which could have a deleterious effect on several functional groups, may be avoided.

The structures of α-aminonitriles were based on spectral and elemental analyses. The IR spectrum of **2a** showed a characteristic weak absorption band at 2235 cm^{-1} for cyano-group and a strong band at 3337 cm^{-1} for NH group. The ^1H NMR of **2a** showed two doublets, one proton each at δ 4.1 and δ 5.42 for the NH (D_2O exchangeable) and CH–protons respectively. The other α-aminonitriles have spectral data compatible with their structures (Table 2). The cyanosilylation of the sterically hinderded bezophenone oxime **3** was, also, investigated. The reaction afforded the corresponding α-aminonitrile **4,** in high yield, in the presence of one mole excess of tetrachlorosilane. Therefore, it seems that the reaction proceeds *via* the *O*-silylated intermediate A, followed by addition of trichlorosilyl cyanide to the carbon-nitrogen double bond (Sch. 1). Compound **4** does not exhibit a nitrile absorption in the IR. However, this is expected, since nitriles that have an electron-withdrawing group α to the nitrile group often have very weak or undetectable absorption in the 2000–2400 cm^{-1} region.[18]

The reaction of the *bis*-imine **5** with two equivalents of TCSC produced the imidazo[1,2-a]quinoxaline **6** in good yield. The structure of **6** was based on analytical and spectral data. The IR spectrum of **6** lacks any absorption bands for carbonitrile groups, instead it showed two absorption bands due to symmetric and asymmetric stretching frequencies of primary amine at 3368 and 3290 cm^{-1}. The ^1H NMR spectrum of **6** displayed a broad, two-proton singlet (D_2O exchangeable) at δ 5.5,

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Table 1. Characterization and IR (cm^{-1}) data of compounds **2a–j**, **4**, **6**, **8a–e** and **10a,b**.

Compd. no.	R	Ar	M.p. °C [lit. M.p.]	Yield (%)	IR cm^{-1}
2a	Ph	Ph	85–87 [85–86][24]	87	2235, 3337
2b	4-BrC_6H_4	Ph	99–100[a]	92	2225, 3348
2c	4-ClC_6H_4	Ph	116 [112–13][24]	89	2246, 3301
2d	4-BrC_6H_4	4-BrC_6H_4	130[b]	89	2241, 3359
2e	4-$MeOC_6H_4$	Ph	108[c]	96	2225, 3329
2f	4-MeC_6H_4	Ph	94–95[d]	84	2240, 3308
2g	Ph	4-ClC_6H_4	123–25 [121–22][25]	87	2243, 3320
2h	Ph	4-$MeOC_6H_4$	73–75 [74–76][24]	85	2233, 3337
2i	4-ClC_6H_4	4-MeC_6H_4	84–85 [81–82][25]	89	2245, 3348
2j	2-HOC_6H_4	Ph	124–26[e]	76	2240, 3312, 3364
4			162–64[f]	93	3343, 3280, 3050
6			155–56[g]	72	3368, 3290, 3191
8a	H		128–29[h]	94	2255, 3345
8b	Cl		137–38[i]	96	2230, 3350
8c	Br		142–44[j]	93	2250, 3375
8d	Me		108–10[k]	92	2228, 3360
8e	MeO		116–17[l]	94	2232, 3346
10a		4-BrC_6H_4	54–56 [55–58][26]	95	
10b		4-ClC_6H_4	45–46 [47–50][26]	92	

[a]Anal. calcd. for $C_{14}H_{11}BrN_2$: C, 58.56; H, 3.86. Found: C, 58.92; H, 3.47.
[b]Anal. calcd. for $C_{14}H_{10}Br_2N_2$: C, 45.94; H, 2.75. Found: C, 45.56; H, 3.01.
[c]Anal. calcd. for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92. Found: C, 75.14; H, 6.39.
[d]Anal. calcd. for $C_{15}H_{14}N_2$: C, 81.05; H, 6.35. Found: C, 80.79; H, 6.83.
[e]Anal. calcd. for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39. Found: C, 75.32; H, 5.68.
[f]Anal. calcd. for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39. Found: C, 74.45; H, 5.53.
[g]Anal. calcd. for $C_{22}H_{16}Cl_2N_4$: C, 64.88; H, 3.96. Found: C, 65.28; H, 4.25.
[h]Anal. calcd. for $C_{16}H_{14}N_2$: C, 82.02; H, 6.02. Found: C, 81.59; H, 6.43.
[i]Anal. calcd. for $C_{16}H_{13}ClN_2$: C, 71.51; H, 4.88. Found: C, 71.27; H, 5.25.
[j]Anal. calcd. for $C_{16}H_{13}BrN_2$: C, 61.36; H, 4.18. Found: C, 61.69; H, 3.93.
[k]Anal. calcd. for $C_{17}H_{16}N_2$: C, 82.23; H, 6.49. Found: C, 82.68; H, 6.05.
[l]Anal. calcd. for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10. Found: C, 76.87; H, 6.52.

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Table 2. ^{1}H NMR and ^{13}C NMR data of compounds of compounds **2a–e**, **6** and **8b,c**.

Compd no.	^{1}H NMR, δ	^{13}C NMR, δ
2a	4.1 (d, 1H, $J=7$ Hz), 5.42 (d, 1H, $J=7$ Hz), 6.8 (d, 2H, $J=8$ Hz), 6.94 (t, 1H), 7.32 (t, 2H), 7.5 (m, 3H), 7.64 (d, 2H, $J=8$ Hz)	51, 115, 118, 122, 127.5, 130, 131, 131.5, 135, 146.
2b	4.1 (d, 1H, NH, $J=7$ Hz), 5.41 (d, 1H, $J=7$ Hz), 6.71 (d, 2H, $J=8$ Hz), 6.92 (t, 1H), 7.23 (m, 2H), 7.5 (d, 2H, $J=8$ Hz), 7.6 (d, 2H, $J=8$ Hz)	
2c	4.1 (d, 1H, NH, $J=7$ Hz), 5.4 (d, 1H, $J=7$ Hz), 6.55 (d, 2H, $J=8$ Hz), 6.95 (t, 1H), 7.25 (t, 2H), 7.4 (d, 2H, $J=8$ Hz), 7.51 (d, 2H, $J=8$ Hz)	50, 115.1, 118.2, 122.2, 128, 131.3, 131.5, 133, 137, 145.
2d	4.18 (d, 1H, $J=7$ Hz), 5.4 (d, 1H, $J=7$ Hz), 6.75 (d, 2H, $J=8$ Hz), 7.4 (d, 2H, $J=8$ Hz), 7.55 (d, 2H, $J=8$ Hz), 7.7 (d, 2H, $J=8$Hz)	49.9, 112, 115, 116, 118, 123, 129, 132, 132.5, 143.
2e	3.84 (s, 3H, CH_3O), 4.06 (d, 1H, $J=7$ Hz), 5.38 (d, 1H, $J=7$ Hz), 6.79 (d, 2H, $J=7$ Hz), 6.95 ((m, 3H), 7.24 (t, 2H), 7.52 (d, 2H, $J=7$ Hz)	49.1, 55.1, 113, 114, 117, 120, 126.6, 127.5, 129.5, 145, 161.
6	5.5 (br. s, 2H, NH_2), 6.98 (d, 2H, $J=7$ Hz), 7.4 (m, 5H), 7.48(d, 2H, $J=7$ Hz), 7.55 (br.s, 1H, NH), 7.96 (d, 2H, $J=7$ Hz), 7.91 (d, 1H, $J=7$ H), 8.57 (br.s, 1H, NH).	112, 118.8, 125, 125.6, 125.8, 128, 130.2, 130.4, 130.6, 131.5, 133.9, 134.9, 135.2, 138, 138.9, 151.9.
8b	4.01 (d, 1H, NH, $J=8$ Hz), 4.99 (dd, 1H, $J=6,8$), 6.28 (dd, 1H, $J=6,16$), 6.63 (d, 2H, $J=8$ Hz), 7.0 (d, 1H, $J=16$ Hz), 7.42 (m, 7H)	
8c	4.06 (d, 1H, NH, $J=8$ Hz), 5.01 (dd, 1H, $J=6,8$ Hz), 6.25 (dd, 1H, $J=6$, 16 Hz), 6.65 (d, 2H, $J=8$ Hz), 7.04 (d, 1H, $J=16$ Hz), 7.38 (m, 7H).	48, 112.5, 116.5, 117.8, 122, 126.5, 128, 129, 133, 136, 136.5, 144

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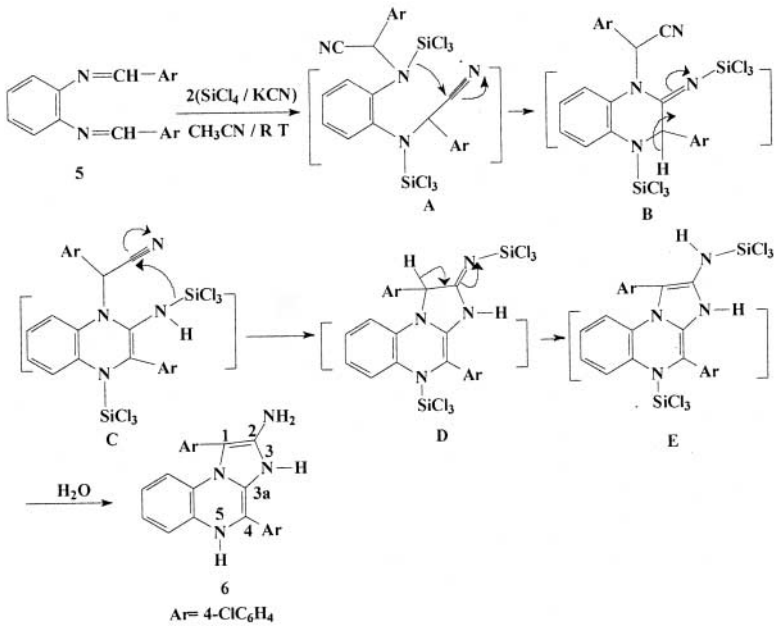
attributable to primary amino-group. The ^{13}C NMR spectrum of **6** showed two characteristic peaks at δ 138.9 and 151.9 assignable for C-3a and C-2 respectively.[19] The plausible mechanism for formation of **6** is shown in (Sch. 2). It seems that the reaction proceeds *via* the formation of the double addition intermediate A, followed by cyclization and tautomerisation to give intermediate C. Further cyclization of C affords intermediate D, which on tautomerisation and hydrolysis yields compound **6** (Sch. 2).

The regioselectivity of the addition of TCSC in situ onto α, β-unsaturated imines was also investigated. When (*E*)-*N*-phenyl-*N*-(3-phenyl-2-propenylidene)amine **7a** reacts with TCSC in situ, (*E*)-1-anilino-3-phenyl-2-propenyl cyanide **8a** was obtained as a sole product in nearly quantitative yield (Sch. 3). Similarly, the reaction of different substituted α, β-unsaturated imines **7b–e** with TCSC afforded exclusively the 1,2-addition products **8b–e**. The structures of compounds **8a–e** were based on spectral and analytical data. The ^{1}H NMR of **8c** displayed a one proton doublet at δ 4.06(exchangeable with D_2O) attributable to NH group; one proton doublet of doublet at δ 5.01 assignable to H_c;



Scheme 2.

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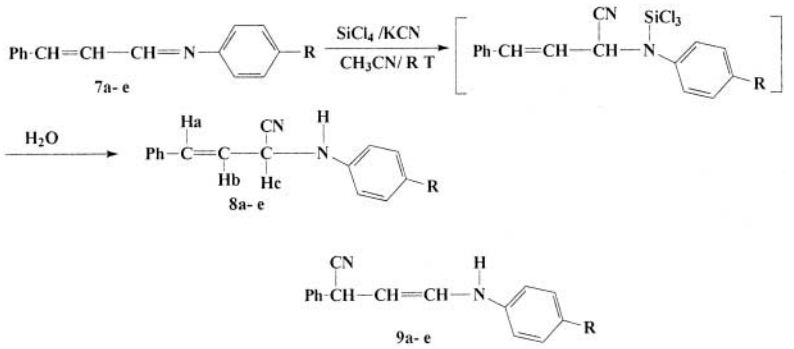
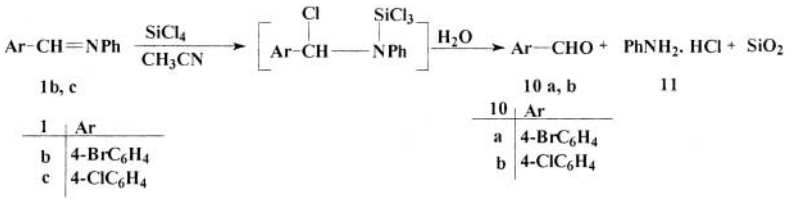


Scheme 3.



Scheme 4.

a doublet of doublet at δ 6.25 assignable to H_b and a doublet integrated for one proton at δ 7.04 attributed to H_a.

The conjugate addition products **9a–e** were not detected in the reaction mixture either by TLC or by ^{1}H NMR analyses of the crude products. The regiospecifity of this reaction is of great value for preparation of β, γ-unsaturated-α-aminonitriles, which are important intermediates for synthesis of β, γ-unsaturated-α-amino acids and amino alcohols. The ^{1}H NMR of **8b,c** showed that the formed β, γ-unsaturated-α-aminonitriles are completely in the E-form and this demonstrates that there is no E-Z-isomerization under the reaction condition.

It is noteworthy that the treatment of different Schiff bases with tetrachlorosilane in acetonitrile at room temperature afforded the corresponding aldehyde and the amine hydrochloride after aqueous work up (Sch. 4).

However, the free aldehydes or its cyanohydrin were not detected in the worked up reaction mixture of different aldimines with TCSC in situ. It is postulated that the activation energy of the addition of TCSC

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in situ onto imines is lower than that of addition of tetrachlorosilane due to the fact is that the silicon–carbon bond is much more weaker than the silicon–chlorine one.[20] Therefore the imine cleavage was not observed under the reaction condition.

In conclusion, the value of this work is not only for introducing a simple cheap method for preparation of α-aminonitriles, but for introducing the reagent combination: tetrachlorosilane–potassium cyanide as a simple, cheap and safe reagent easily obtainable from commercially available materials.

EXPERIMENTAL

Melting points (°C) (uncorrected) were determined using Griffin melting point apparatus. IR spectra were recorded on MATTSON 5000 FTIR Spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a GE Omega GN-300 instrument at 300 and 75 MHz, respectively, using $CDCl_3$ as solvent. Chemical shifts are expressed in δ relative to TMS as an internal standard. Elemental analyses were carried out at the microanalytical unit, Faculty of Science, Mansoura University.

General Procedure for the Reaction of Imines 1a–i and 7a–e with the Reagent Combination of Tetrachlorosilane and Potassium Cyanide: Synthesis of 2-Arylamino-2-Arylacetonitrile 2a–i and (E)-1-Arylamino-3-Aryl-2-Propenyl Cyanide 8a–e

A mixture of tetrachlorosilane (5 mmol, 0.6 mL) and potassium cyanide (5 mmol, 0.325 g) in 20 mL acetonitrile was stirred at room temperature for one half hour with exclusion of moisture. Then, a (5 mmol) solution of each of the imines **1a–i**[21] and **7a–e**[22] in 15–25 mL of dry acetonitrile was added over a period of 15 min. The reaction mixture was stirred at room temperature for 1–3 h, then poured onto crushed-ice (40 g), extracted with chloroform, dried over sodium sulfate and distilled off to give the α-aminonitriles **2a–i** and **8a–e,** which were recrystallized from aqueous-ethanol (Table 1). The benzophenone oxime **3** and *N*-phenyl-*N*-(4-hydroxy-phenylmethylidene)amine **1j** were reacted in the same manner except that 5 mmoles more of tetrachlorosilane were added for protection of the hydroxyl group.

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Reaction of Tetrachlorosilane–Potassium Cyanide Reagent Combination With the *Bis*-Imine 5: Synthesis of 1,4-Di(4-Chlorophenyl)-3,5-Dihydroimidazo [1,2-a]Quinoxalin-2-yl Amine 6

A mixture of tetrachlorosilane (10 mmol, 1.2 mL) and potassium cyanide (10 mmol, 0.65 g) in 35 mL acetonitrile was stirred at room temperature for one half hour, with exclusion of moisture. Then, a solution of N^1, N^2-di-[1-(4-chlorophenyl)methylidene]-1,2-benzenediamine **5**[23] (5 mmol, 1.77 g) in 20 mL acetonitrile was added over a period of 15 min. The reaction mixture was stirred for 4 h and processed in the same manner to give the imidazo[1,2-a]quinoxaline **6** which was recrystallized from ethanol (Table 1).

Reaction of Imines 1b,c with Tetrachlorosilane

A mixture of tetrachlorosilane (5 mmol, 0.6 mL) and/or imine **1b,c** (5 mmol) in 20 mL dry acetonitrile was stirred at room temperature for 6 h, then poured onto crushed-ice (20 g), extracted with chloroform (25 mL). The chloroform extract was washed with water, dried over sodium sulfate and distilled off to give pure 4-chloro- and 4-bromobenzaldehydes **10a,b** respectively. The aqueous layer was basified with sodium hydroxide and extracted with ether. The ether extract was dried and distilled off. The oily residue was identified as aniline (TLC and it gave the usual reactions of aniline).

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