# Organic & Biomolecular Chemistry

**PAPER**

# Kinetics and mechanism of the racemic addition of trimethylsilyl cyanide to aldehydes catalysed by Lewis bases†

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The mechanism by which four Lewis bases, triethylamine, tetrabutylammonium thiocyanate, tetrabutylammonium azide and tetrabutylammonium cyanide, catalyse the addition of trimethylsilyl cyanide to aldehydes is studied by a combination of kinetic and spectroscopic methods. The reactions can exhibit first or second order kinetics corresponding to three different reaction mechanisms. Spectroscopic evidence for the formation of hypervalent silicon species is obtained for reaction between all of the tetrabutylammonium salts and trimethylsilyl cyanide. The reactions are accelerated by the presence of water in the reaction mixture, an effect which is due to a change in the reaction mechanism from Lewis to Brønsted base catalysis. Tetrabutylammonium thiocyanate is shown to be an excellent catalyst for the synthesis of cyanohydrin trimethylsilyl ethers on a preparative scale.

## Introduction

Cyanohydrin synthesis achieved by the base-catalysed addition of cyanide to aldehydes was one of the first reactions to be mechanistically studied[1] and remains one of the fundamental carbon–carbon bond forming reactions used in organic synthesis.[2] However, whilst cyanide salts are still used in cyanohydrin synthesis,[3] other cyanide sources are now often used to avoid potential side reactions,[4] render cyanohydrin synthesis irreversible and directly produce protected cyanohydrins suitable for further manipulation. Examples of these cyanide sources include trimethylsilyl cyanide,[5–12] ethyl cyanoformate,[12,13] diethyl cyanophosphonates[12,14,15] and acyl cyanides.[12,16] Another advantage of these cyanide sources is that, when used with a suitable chiral catalyst, they permit the asymmetric synthesis of cyanohydrin derivatives.[17] We have developed metal (salen) complexes as highly effective catalysts for asymmetric cyanohydrin synthesis[18] and have also studied the mechanism of asymmetric cyanohydrin synthesis using trimethylsilyl cyanide as the cyanide source.[19,20] During this work, we became aware that surprisingly little work had been done on the kinetics and mechanism of racemic cyanohydrin synthesis using cyanide sources other than alkali metal cyanides. Thus, Umani-Ronchi and co-workers had studied the indium tribromide catalysed

reactions between ketones and trimethylsilyl cyanide,[6] and Denmark and Chung had studied the use of various amines and phosphines as Lewis base catalysts for the reaction between aldehydes and trimethylsilyl cyanide.[7] Therefore, we undertook a project to investigate the mechanism of cyanohydrin trimethylsilyl ether formation using trimethylsilyl cyanide as the cyanide source and dichloromethane as solvent (Scheme 1), in order to allow comparison of the results with our previous work on the kinetics of asymmetric cyanohydrin synthesis.[19,20]
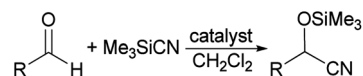
The addition of trimethylsilyl cyanide to aldehydes is known to be catalysed by both Lewis acids[5,6] and Lewis bases.[7–12] However, preliminary attempts to study the kinetics of cyanohydrin trimethylsilyl ether formation catalysed by a range of Lewis acids (titanium isopropoxide, aluminium triflate, zinc iodide) were unsuccessful as in all cases catalyst decomposition occurred during the reaction. In contrast, Lewis bases were found to be kinetically well-behaved catalysts and in this manuscript we present the results obtained using four Lewis bases in dichloromethane solution and discuss how the differing kinetic data obtained correspond to three different mechanisms for cyanohydrin trimethylsilyl ether formation.
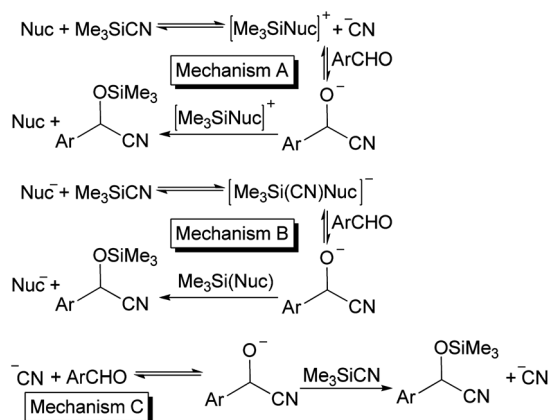
## Results and discussion

Four Lewis base catalysts were selected for this study. Triethylamine **1** has been shown to be an effective catalyst for the

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†Electronic supplementary information (ESI) available: Kinetic data for reactions catalysed by Lewis bases **1–4**, ^{1}H NMR spectra of cyanohydrin trimethylsilyl ethers and NMR spectra showing the formation of hypervalent silicon species. See DOI: 10.1039/c2ob25188d



**Scheme 1** Synthesis of cyanohydrin trimethylsilyl ethers.

**Scheme 2** Possible mechanisms for the addition of trimethylsilyl cyanide to aldehydes.



**Fig. 1** Plot of [catalyst] against $k_{obs}$ for each of catalysts **1–4**. $k_{obs}$ is the average of two experiments carried out at the same catalyst concentration. Solid line and filled diamonds = **1** ($m = 3$, $n = 4$) ($y = 0.7194x - 0.0937$; $R^2 = 0.993$); short dashed line and empty squares = **2** ($m = n = 4$) ($y = 0.6659x - 0.1304$; $R^2 = 0.9995$); dotted line and filled triangles = **3** ($m = 4$, $n = 2$) ($y = 1.9527x + 0.1756$; $R^2 = 0.994$); long dashed line and empty circles = **4** ($m = 5$, $n = 3$) ($y = 0.4411x + 0.0109$; $R^2 = 0.989$).

addition of many cyanide sources including trimethylsilyl cyanide to aldehydes[12] and the kinetics of the addition of trimethylsilyl cyanide to aldehydes catalysed by triethylamine have previously been reported.[7] The relatively large size of triethylamine suggested that the reaction mechanism was most likely to be that shown in Scheme 2A. Tetrabutylammonium thiocyanate **2** and tetrabutylammonium azide **3** were selected as both these anions are known to catalyse the addition of trimethylsilyl cyanide to aldehydes[10] and isothiocyanate was found to be the most effective of a series of ligands (X) in VO(salen)X-catalysed asymmetric cyanohydrin synthesis.[20] The small, linear nature of thiocyanate and azide would facilitate the formation of hypervalent silicon intermediates,[21] so that the reaction mechanism could be that shown in Scheme 2A or B.‡ Finally, tetrabutylammonium cyanide **4** was selected as an organic solvent soluble source of cyanide, since it[9] and other species which contain cyanide anions[10,15] are also known to catalyse the addition of trimethylsilyl cyanide and other cyanide reagents to aldehydes. Mechanistically, the cyanide anions could form a hypervalent silicon complex (Scheme 2B) as previously proposed[9,22] or could directly add to the aldehyde (Scheme 2C). It was anticipated that a thorough analysis of the reaction kinetics of the addition of trimethylsilyl cyanide to a range of aromatic aldehydes catalysed by each of these four catalysts would allow the reaction mechanisms to be determined.

Initial kinetic studies using catalysts **1–4** were carried out at 0 °C in dichloromethane using benzaldehyde as substrate with initial concentrations of benzaldehyde and trimethylsilyl cyanide of 0.53 M and 0.56 M respectively. The catalyst concentration (0.01 M for triethylamine, $9.4 \times 10^{-3}$ M for tetrabutylammonium thiocyanate and $2.3 \times 10^{-3}$ M for both tetrabutylammonium azide and tetrabutylammonium cyanide) was adjusted so as to give a convenient reaction rate to allow the reactions to be monitored by UV analysis of samples withdrawn at regular

intervals. All of the reactions carried out under these conditions were kinetically well behaved and could be followed to >90% conversion.

Differences between catalysts **1–4** were immediately apparent from this study. Thus, whilst reactions catalysed by **1** and **4** were found to follow first order kinetics, reactions catalysed by tetrabutylammonium salts **2** and **3** were found to follow second order kinetics.† Reactions were then carried out at various initial concentrations of benzaldehyde and trimethylsilyl cyanide to determine the order with respect to each reactant.† These experiments showed that reactions catalysed by triethylamine **1** or tetrabutylammonium cyanide **4** gave reactions which were first order in benzaldehyde concentration, but zero order in trimethylsilyl cyanide concentration. Reactions catalysed by tetrabutylammonium salts **2** and **3** were found to be first order in both benzaldehyde and trimethylsilyl cyanide concentration.

To complete the determination of the rate equations, reactions were carried out at different catalyst concentrations to allow the order with respect to catalyst **1–4** to be determined.†

Fig. 1 shows that in each case the reactions were first order in catalyst concentration. As a result, the rate equations for reactions catalysed by complexes **1–4** were found to be:

- Rate = 0.072(±0.017)[**1**][PhCHO]
- Rate = 0.67(±0.01)[**2**][Me₃SiCN][PhCHO]
- Rate = 195(±4)[**3**][Me₃SiCN][PhCHO]
- Rate = 441(±11)[**4**][PhCHO]

The rate equation for cyanohydrin trimethylsilyl ether synthesis catalysed by triethylamine **1** is identical to that previously determined by Denmark and Chung under slightly different conditions.[7] It is consistent with the mechanism shown in Scheme 2A provided that the second step of the mechanism is rate determining and that the first step is irreversible or has an equilibrium which favours formation of free cyanide.[7] Similarly, the rate equation for reactions catalysed by tetrabutylammonium cyanide **4** is consistent with the mechanism shown in Scheme 2C, again provided that the first step is rate determining. In this case, the first step of Scheme 2A would be a degenerate process and it therefore becomes equivalent to Scheme 2C, so

‡ It is also possible that azide and thiocyanate will undergo addition to the aldehyde under the reaction conditions. This has been shown to occur for azide addition,[32] however, under our reaction conditions we were unable to detect any such species by mass spectrometry, NMR spectroscopy or UV spectroscopy. Thus, whilst we cannot fully discount this possibility we have no evidence to support it.
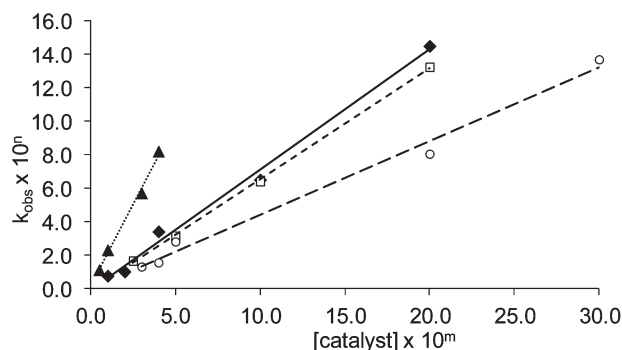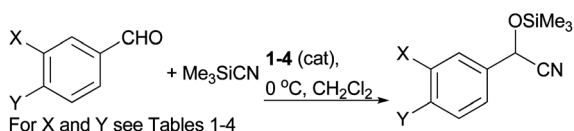
**Scheme 3** Synthesis of cyanohydrin trimethylsilyl ethers from substituted benzaldehydes.

**Table 1** Rate data for the addition of trimethylsilyl cyanide to substituted benzaldehydes catalysed by triethylamine **1**[a]

| Aldehyde | $\sigma$ | $k$ (s$^{-1}$)[b] |
| --- | --- | --- |
| 3-ClC$_6$H$_4$CHO | 0.37 | 0.00139 ± 0.00008 |
| 3-FC$_6$H$_4$CHO | 0.34 | 0.00122 ± 0.00008 |
| 4-ClC$_6$H$_4$CHO | 0.23 | 0.00072 ± 0.00004 |
| 4-FC$_6$H$_4$CHO | 0.06 | 0.00098 ± 0.00008 |
| PhCHO | 0 | 0.00065 ± 0.00007 |
| 4-MeSC$_6$H$_4$CHO | 0 | 0.00078 ± 0.00008 |
| 3-MeC$_6$H$_4$CHO | −0.06 | 0.00056 ± 0.00007 |
| 4-MeC$_6$H$_4$CHO | −0.14 | 0.00092 ± 0.00007 |
| 3,4-Me$_2$C$_6$H$_3$CHO | −0.24 | 0.00042 ± 0.00001 |
| 4-MeOC$_6$H$_4$CHO | −0.27 | 0.00055 ± 0.00005 |

[a] All reactions carried out at 0 °C with [aldehyde]$_0$ = 0.49 M, [Me$_3$SiCN]$_0$ = 0.56 M and [**1**] = 0.001 M. [b] Average of two experiments.

that the two mechanisms have identical kinetic features. The rate equations for catalysts **2** and **3** could however be interpreted as being consistent with the mechanism shown in Scheme 2A or B, provided that the first step of the mechanism is not rate limiting. However, as azide and thiocyanate are both small linear species, the large difference in rate constant (almost a factor of 300) between reactions catalysed by **2** and **3**, is suggestive of either a change in mechanism between the two catalysts, or both reactions proceeding by the mechanism shown in Scheme 2B. In the mechanism shown in Scheme 2B, the anion is coordinated to the hypervalent silicon during the cyanide transfer step and so can influence the rate of this step both sterically and electronically. In contrast, in the mechanism shown in Scheme 2A, the anion is dissociated from the tetravalent silicon and so would be expected to have only a small influence on the rate of cyanide transfer.

To investigate the extent of charge transfer to the aldehyde in the rate determining step of the mechanism, a Hammett analysis of the reaction using various *meta*- and/or *para*-substituted benzaldehydes was undertaken with each of catalysts **1–4** (Scheme 3). Each of these kinetic experiments was carried out in duplicate† and Tables 1–4 detail the resulting rate data. In all cases, each of the substituted benzaldehydes was found to give a good fit to the same reaction order determined for reactions using benzaldehyde. The average of the two rate constants ($k_{avg}$) was used to construct the Hammett plot. In the case of reactions catalysed by triethylamine **1**, no correlation between the substituent constants and the rate of reaction was observed,† but for catalysts **2–4** there was a clear correlation as shown in Fig. 2.

All of the data given in Tables 1–4 was obtained by manual sampling of reactions carried out at 0 °C. However, reactions catalysed by tetrabutylammonium thiocyanate **2** and involving the less electron-rich aromatic aldehydes were also fast enough to be monitored *in situ* in a stopped-flow kinetics system.† These

**Table 2** Rate data for the addition of trimethylsilyl cyanide to substituted benzaldehydes catalysed by tetrabutylammonium thiocyanate **2**[a]

| Aldehyde | $\sigma$ | $k$ (M$^{-1}$ s$^{-1}$)[b] |
| --- | --- | --- |
| 3,5-F$_2$C$_6$H$_3$CHO | 0.68 | 0.28 ± 0.04 |
| 4-F$_3$CC$_6$H$_4$CHO | 0.53 | 0.097 ± 0.007 |
| 3-ClC$_6$H$_4$CHO | 0.37 | 0.035 ± 0.002 |
| 3-FC$_6$H$_4$CHO | 0.34 | 0.00299 ± 0.00006 |
| 4-ClC$_6$H$_4$CHO | 0.23 | 0.0083 ± 0.0002 |
| 4-FC$_6$H$_4$CHO | 0.06 | 0.00052 ± 0.00005 |
| PhCHO | 0 | 0.00064 ± 0.00002 |
| 4-MeSC$_6$H$_4$CHO | 0 | 0.00077 ± 0.00001 |
| 3-MeC$_6$H$_4$CHO | −0.06 | 0.00034 ± 0.00001 |
| 4-MeC$_6$H$_4$CHO | −0.14 | 0.00066 ± 0.00002 |
| 3,4-Me$_2$C$_6$H$_3$CHO | −0.24 | 0.00010 ± 0.00001 |
| 4-MeOC$_6$H$_4$CHO | −0.27 | 0.00014 ± 0.00001 |

[a] All reactions carried out at 0 °C with [aldehyde]$_0$ = 0.49 M, [Me$_3$SiCN]$_0$ = 0.56 M and [**2**] = 9.4 × 10$^{-3}$ M. [b] Average of two experiments.

**Table 3** Rate data for the addition of trimethylsilyl cyanide to substituted benzaldehydes catalysed by tetrabutylammonium azide **3**[a]

| Aldehyde | $\sigma$ | $k$ (M$^{-1}$ s$^{-1}$)[b] |
| --- | --- | --- |
| 4-ClC$_6$H$_4$CHO | 0.23 | 0.204 ± 0.007 |
| 4-FC$_6$H$_4$CHO | 0.06 | 0.058 ± 0.008 |
| PhCHO | 0 | 0.057 ± 0.001 |
| 4-MeSC$_6$H$_4$CHO | 0 | 0.070 ± 0.008 |
| 3-MeC$_6$H$_4$CHO | −0.06 | 0.029 ± 0.002 |
| 4-MeC$_6$H$_4$CHO | −0.14 | 0.030 ± 0.008 |
| 3,4-Me$_2$C$_6$H$_3$CHO | −0.24 | 0.0051 ± 0.0004 |
| 4-MeOC$_6$H$_4$CHO | −0.27 | 0.0088 ± 0.0001 |

[a] All reactions carried out at 0 °C with [aldehyde]$_0$ = 0.49 M, [Me$_3$SiCN]$_0$ = 0.56 M and [**3**] = 2.3 × 10$^{-3}$ M. [b] Average of two experiments.

**Table 4** Rate data for the addition of trimethylsilyl cyanide to substituted benzaldehydes catalysed by tetrabutylammonium cyanide **4**[a]

| Aldehyde | $\sigma$ | $k$ (s$^{-1}$)[b] |
| --- | --- | --- |
| 3-ClC$_6$H$_4$CHO | 0.37 | 0.0323 ± 0.0007 |
| 3-FC$_6$H$_4$CHO | 0.34 | 0.0113 ± 0.0005 |
| 4-ClC$_6$H$_4$CHO | 0.23 | 0.0093 ± 0.0006 |
| 4-FC$_6$H$_4$CHO | 0.06 | 0.0018 ± 0.0001 |
| PhCHO | 0 | 0.00132 ± 0.00009 |
| 4-MeSC$_6$H$_4$CHO | 0 | 0.00097 ± 0.00005 |
| 3-MeC$_6$H$_4$CHO | −0.06 | 0.00040 ± 0.00002 |
| 4-MeC$_6$H$_4$CHO | −0.14 | 0.00033 ± 0.00001 |
| 3,4-Me$_2$C$_6$H$_3$CHO | −0.24 | 0.00024 ± 0.00001 |
| 4-MeOC$_6$H$_4$CHO | −0.27 | 0.00013 ± 0.00001 |

[a] All reactions carried out at 0 °C with [aldehyde]$_0$ = 0.49 M, [Me$_3$SiCN]$_0$ = 0.56 M and [**4**] = 2.3 × 10$^{-4}$ M. [b] Average of two experiments.

reactions were carried out at 17 °C and also gave a Hammett plot with a large positive slope (2.7), thus providing further evidence of the robustness of the kinetic data used to construct the Hammett plots.

It is apparent from Fig. 2 that reactions catalysed by catalysts **2–4** all have large positive reaction constants (+3.0 to +3.6)
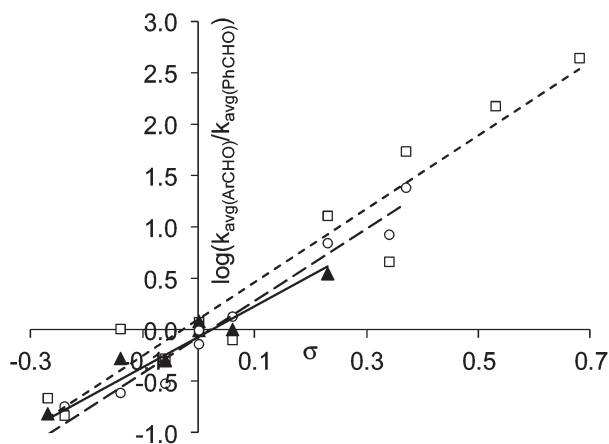
**Fig. 2** Hammett plots for reactions catalysed by catalysts **2–4**. Short dashed line and empty squares = **2** ($y = 3.58x + 0.1$; $R^2 = 0.93$). Solid line and filled triangles = **3** ($y = 2.98x - 0.07$; $R^2 = 0.91$). Long dashed line and empty circles = **4** ($y = 3.50x - 0.07$; $R^2 = 0.97$).
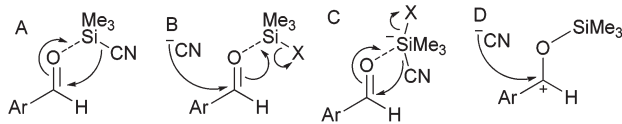


**Fig. 3** Possible modes of Lewis acid activation of aldehydes by tetra- or pentavalent silicon species.

which implies that there is a significant movement of negative charge towards the benzylic carbon atom of the aldehyde in the rate-determining transition state. This is consistent with nucleophilic addition of cyanide to the carbonyl being the rate-determining step for reactions catalysed by catalysts **2–4**. Tetra- or pentavalent silicon species are known to possess Lewis acidity[23] and hence could activate the aldehyde as illustrated in Fig. 3. However, this would result in a decrease in electron density at the benzylic carbon atom of the coordinated aldehyde and hence would be expected to decrease the magnitude of the reaction constant. The large magnitude of the observed reaction constants for reactions catalysed by tetrabutylammonium salts **2–4** suggests that any such activation of the aldehyde by silicon-based Lewis acids is of at most minor importance and the reactions are dominated by Lewis base activation of the trimethylsilyl cyanide. In contrast, the absence of a Hammett correlation for reactions catalysed by triethylamine, even though the aldehyde is involved in the rate-determining step of the mechanism, could be explained by the initial coordination of the aldehyde to the trimethylsilyl cyanide, which would withdraw electron density from the benzylic carbon atom and offset the subsequent increase in electron density at this carbon atom during the nucleophilic addition of cyanide (*cf*. Fig. 3D).

To allow the activation parameters ($\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$ and $\Delta G^{\ddagger}$) for reactions catalysed by **1–4** to be determined and compared, a variable-temperature kinetics study was carried out using each of the catalysts with benzaldehyde as substrate.† The resulting Eyring plot is shown in Fig. 4 and the derived activation parameters are given in Table 5.

It is apparent from the $\Delta H^{\ddagger}$ data in Table 5 that triethylamine **1** differs from the three tetrabutylammonium-based catalysts **2–4**
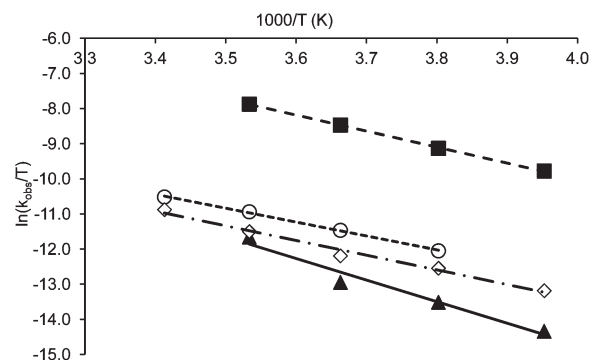


**Fig. 4** Eyring plots for reactions catalysed by **1–4**. Solid line and filled triangles = **1** ($y = -6.13x + 9.80$; $R^2 = 0.96$). Short dashed line and empty circles = **2** ($y = -3.96x + 3.02$; $R^2 = 1.00$). Long dashed line and filled squares = **3** ($y = -4.56x + 8.22$; $R^2 = 1.00$). Long and short dashed line and empty diamonds = **4** ($y = -4.18x + 3.29$; $R^2 = 0.99$).

**Table 5** Activation parameters for reactions catalysed by catalysts **2–4**

| Catalyst | $\Delta H^{\ddagger a}$ (kJ mol$^{-1}$) | $\Delta S^{\ddagger a}$ (J mol$^{-1}$ K$^{-1}$) | $\Delta G^{\ddagger a,b}$ (kJ mol$^{-1}$) |
|---|---|---|---|
| 1 | 53.2 ± 5.0 | −68 ± 18 | 71.8 ± 9.9 |
| 2 | 33.0 ± 6.8 | −128 ± 24 | 68.0 ± 13.3 |
| 3 | 38.1 ± 5.3 | −78 ± 20 | 59.4 ± 10.8 |
| 4 | 35.9 ± 2.5 | −96 ± 9 | 62.1 ± 5.0 |
| 1 + H$_2$O | 15.2 ± 3.6 | −202 ± 13 | 70.4 ± 7.1 |

$^a$ For details of the error analysis see the ESI.† $^b$ At 0 °C.

in having a significantly larger enthalpy of activation. This is consistent with the other kinetic data and in particular with reactions catalysed by triethylamine following the reaction shown in Scheme 2A requiring the complete cleavage of the Si–CN bond, prior to nucleophilic addition of cyanide to the carbonyl; whilst reactions catalysed by tetrabutylammonium salts **2–4** follow the mechanisms shown in Scheme 2B/C in which this bond has to be (at most) partially broken prior to the cyanohydrin-forming transition state.

The $\Delta S^{\ddagger}$ data has to be interpreted with care as it is well known that the extrapolation of the data shown in Fig. 4 to 1000/$T = 0$, necessary to obtain the entropies of activation, results in relatively large errors being associated with the calculated entropies.[24] Nevertheless, it is notable that the reaction catalysed by triethylamine has the least negative entropy of activation and this is significantly less negative than the entropy of activation for the reaction catalysed by tetrabutylammonium thiocyanate **2**. This is consistent with the triethylamine and tetrabutylammonium thiocyanate catalysed reactions occurring by the mechanisms shown in Scheme 2A and B respectively, as the latter, involving a hypervalent silicon species, will have a much more ordered transition state. The less negative entropy of activation observed for reactions catalysed by tetrabutylammonium azide **3** compared to tetrabutylammonium thiocyanate **2** may be related to the symmetrical nature of the azide group, which makes its coordination to silicon through either terminal nitrogen degenerate and hence results in an increase in the disorder of the transition state relative to that for tetrabutylammonium thiocyanate **2**. The entropy of activation for the reaction catalysed by

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**Table 6**  NMR data for hypervalent silicon cyanide complexes

| Entry | Compound | $\delta_H$ | $\delta_C$ |
|---|---|---|---|
| 1 | Me$_3$SiCN[a] | +0.31 | −1.88 |
| 2 | Me$_3$SiNCS[a] | +0.08 | +2.15 |
| 3 | Me$_3$SiN$_3$[a] | +0.28 | −0.93 |
| 4 | (Me$_3$Si)$_2$O[a] | +0.07 | +2.07 |
| 5 | PNP$^+$ [Me$_3$SiCl(NC)]$^-$ [a,b] | −0.02 | +1.89 |
| 6 | Li$^+$ [Me$_3$SiCl(NC)]$^-$ [c] | | +1.93 |
| 7 | Li$^+$ [Me$_3$Si(NC)$_2$]$^-$ [c] | | +1.91 |
| 8 | Me$_3$SiCN + Et$_3$N[a] | +0.31 | −1.88 |
| 9 | Me$_3$SiCN + Bu$_4$NSCN[a,d] | −0.01 | +1.80 |
| 10 | Me$_3$SiCN + Bu$_4$NN$_3$[a,d] | +0.01 | +1.64 |
| 11 | Me$_3$SiCN + Bu$_4$NCN[a,d] | +0.04 | +1.79 |

[a] In CDCl$_3$. [b] PNP = bis(triphenylphosphoranylidene)ammonium. Data taken from ref. 25b. [c] In thf-d$_8$. Data taken from ref. 25a. [d] Signals due to Me$_3$SiCN were also present.

tetrabutylammonium cyanide **4** is less negative than that for the tetrabutylammonium thiocyanate catalysed reaction and is consistent with the mechanism shown in Scheme 2C.

The $\Delta G^{\ddagger}$ data also has quite large errors associated with it. However, the Gibbs free energies of activation for reactions catalysed by **1** and **2** appear to be similar and higher than those of reactions catalysed by **3** and **4** which are also similar. This is consistent with the rate constants determined for reactions catalysed by **1–4**, as those for reactions catalysed by **1** and **2** were around three orders of magnitude lower than those for reactions catalysed by tetrabutylammonium salts **3** and **4**.

To investigate the formation of hypervalent silicon complexes from trimethylsilyl cyanide and Lewis bases **1–4**, NMR studies were carried out. $^1$H and $^{13}$C NMR data of hypervalent silicon species obtained by treatment of trimethylsilyl cyanide with chloride or cyanide have been reported in the literature and formed the basis of our study.[25] Table 6 presents the literature data for relevant four- and five-coordinate silicon species and the data we have observed when equimolar amounts of trimethylsilyl cyanide and Lewis bases **1–4** were mixed in CDCl$_3$. Entries 1–4 give the NMR data of tetravalent silicon species that could be formed *in situ* from mixtures of trimethylsilyl cyanide and Lewis bases **2–4** and entries 5–7 give the literature data reported for hypervalent silicon complexes derived from trimethylsilyl cyanide. When the NMR spectrum of a 1 : 1 mixture of trimethylsilyl cyanide and triethylamine was recorded (entry 8), no change in the spectrum relative to that of trimethylsilyl cyanide was observed and in particular, there was no evidence for the formation of hypervalent silicon species.

In contrast, the $^1$H and $^{13}$C NMR spectra of 1 : 1 mixtures of trimethylsilyl cyanide and Lewis bases **2–4** (entries 9–11) showed clear evidence of hypervalent silicon species being formed *in situ*. The $^1$H NMR spectra all showed a new peak at −0.01 to +0.04 ppm consistent with the literature data of −0.02 ppm for a closely related hypervalent silicon species (Table 6, entries 5 and 9–11) and the $^{13}$C NMR spectra showed a new signal at +1.64 to +1.80 ppm consistent with the literature data of +1.89 to +1.93 ppm for related hypervalent silicon species (Table 6, entries 5–7 and 9–11). Integration of the trimethylsilyl signals for trimethylsilyl cyanide and the hypervalent silicon species in the $^1$H NMR spectra of the mixtures indicated

that 10–14% of the trimethylsilyl cyanide had been converted into a hypervalent silicon species. However, trimethylsilyl cyanation reactions involving Lewis bases **2–4** are carried out at a trimethylsilyl cyanide to Lewis base ratio of between 60 and 2400 : 1. Therefore, even if all of the Lewis base forms a hypervalent silicon species, then for virtually all of the reaction there will be far more trimethylsilyl cyanide than hypervalent species present. Thus, if the hypervalent silicon species is to be the catalytically active form of trimethylsilyl cyanide for cyanohydrin synthesis, then it will have to have a rate constant 2–3 orders of magnitude greater than that of trimethylsilyl cyanide to compensate for its lower concentration.

The combination of the kinetic and spectroscopic data indicate that triethylamine does not form a hypervalent silicon species with trimethylsilyl cyanide and that it therefore catalyses the formation of cyanohydrin trimethylsilyl ethers through the mechanism shown in Scheme 2A with the nucleophilic addition of cyanide to the carbonyl being rate determining. This does require that during the reaction, [Me$_3$SiNEt$_3$]$^+$ CN$^-$ should accumulate and this species was not detected by $^1$H or $^{13}$C NMR spectroscopy of an equimolar amount of trimethylsilyl cyanide and triethylamine. However, the kinetics experiments were carried out using just 2 mol% of triethylamine, so a 50-fold excess of trimethylsilyl cyanide is present which will shift the first equilibrium in Scheme 2A in favour of formation of [Me$_3$SiNEt$_3$]$^+$ CN$^-$.

In contrast, tetrabutylammonium salts **2–4** do form hypervalent silicon species with trimethylsilyl cyanide and in the case of catalysts **2** and **3** these are the most reactive cyanide-containing species present in solution, so cyanohydrin trimethylsilyl ether synthesis follows the mechanism shown in Scheme 2B. For reactions catalysed by tetrabutylammonium cyanide **4**, although a hypervalent silicon species is formed *in situ*, cyanide ions are also present and the kinetics suggest that these rather than the hypervalent silicon species attack the carbonyl compound, thus giving the mechanism shown in Scheme 2C with the first step rate determining.

During the course of this work, it became apparent that reactions catalysed by **1–4** were sensitive to the presence of water. This was particularly notable for the hygroscopic tetrabutylammonium salts **3** and **4**. The reactions were greatly accelerated by the presence of water and the rate equation also changed. Fig. 5 shows the progress of the addition of trimethylsilyl cyanide to 3,4-dimethylbenzaldehyde catalysed by tetrabutylammonium azide **3**. In this case, the reaction in the presence of water is an order of magnitude faster than that under anhydrous condition, reaching 86% conversion after 124 rather than 1813 seconds. The presence of water was also found to change the rate equation from second order to first order.†

The effect of water on reactions catalysed by triethylamine and tetrabutylammonium thiocyanate was studied quantitatively. Fig. 6 shows the effect of adding 2 or 10 mol% of water (relative to benzaldehyde) to reactions catalysed by triethylamine. The significant rate enhancement due to the water is again apparent in Fig. 6. In this case, the reactions followed first order overall kinetics under both anhydrous and hydrated reaction conditions and were first order in benzaldehyde concentration and zero order in trimethylsilyl cyanide concentration. Reactions carried out at various concentrations of triethylamine showed that in the
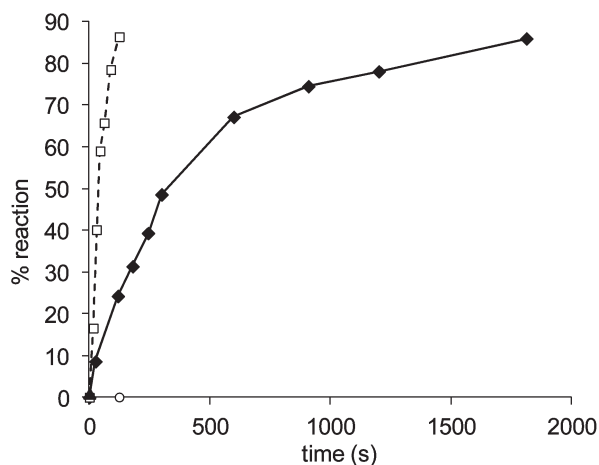
**Fig. 5** Comparison of the rate of reaction between 3,4-dimethylbenzaldehyde and $Me_3SiCN$ under anhydrous reaction conditions (filled diamonds and solid line) and in the presence of water (empty squares and broken line).
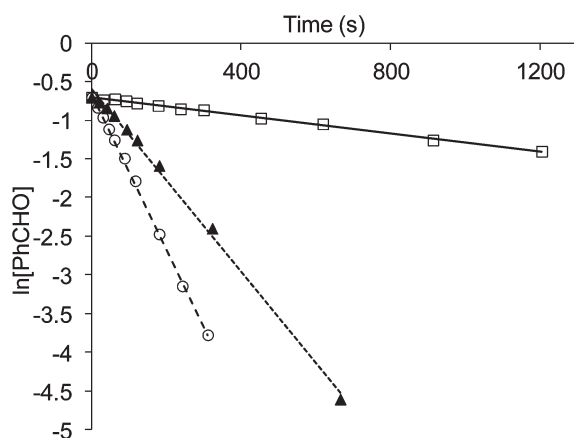


**Fig. 6** First order kinetics plots for the reaction between benzaldehyde and $Me_3SiCN$ catalysed by triethylamine **1** under anhydrous reaction conditions (empty squares and solid line). ($y = -0.0006x - 0.7041$; $R^2 = 0.997$); in the presence of 2 mol% water (filled triangles and short dashed line) ($y = -0.0059x - 0.5916$; $R^2 = 0.997$); and in the presence of 10 mol% water (empty circles and long dashed line) ($y = -0.01x - 0.65$; $R^2 = 0.999$).

presence of water, the reactions still exhibited first order kinetics with respect to triethylamine concentration.†

A Hammett analysis was also carried out using wet triethylamine as catalyst and, as for the analysis carried out using anhydrous triethylamine as catalyst, no correlation between the substituent constant and relative rate of reaction was apparent.† Finally, a variable temperature kinetics study was carried out using wet triethylamine as catalyst.† The results of this study are included in Table 5 and it is apparent that the activation parameters in the presence of water are very different to those of triethylamine (or catalysts **2–4**) under anhydrous conditions. In particular, the enthalpy of activation is much lower and there is a much more negative entropy of activation in the presence of water.

The addition of trimethylsilyl cyanide to benzaldehyde catalysed by 1 mol% of tetrabutylammonium thiocyanate **2** was also
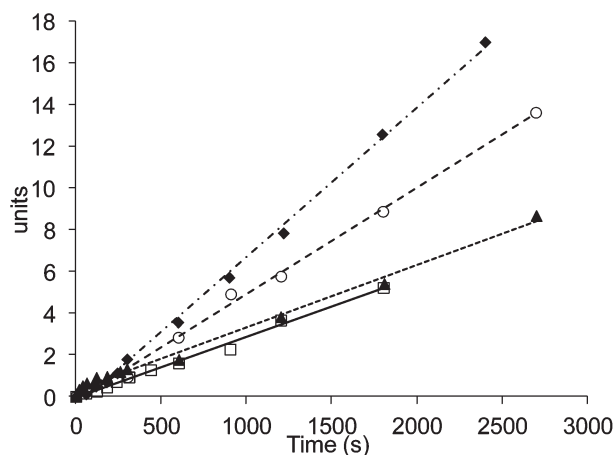


**Fig. 7** Second order kinetics plots for the reaction between benzaldehyde and $Me_3SiCN$ catalysed by tetrabutylammonium thiocyanate **2** under anhydrous reaction conditions (empty squares and solid line) ($y = 0.0029x - 0.0504$; $R^2 = 0.994$); in the presence of 1 mol% water (filled triangles and short dashed line) ($y = 0.003x + 0.3075$; $R^2 = 0.993$); in the presence of 5 mol% water (empty circles and long dashed line) ($y = 0.0051x - 0.2043$; $R^2 = 0.997$); and in the presence of 10 mol% water (filled diamonds and long and short dashed line) ($y = 0.0072x - 0.4646$; $R^2 = 0.998$). The units for the vertical scale are: $\ln[(B_0A_t)/(B_tA_0)]/(A_0 - B_0)$ where: $A = [PhCHO]$, $B = [Me_3SiCN]$ and the subscripts 0 and $t$ refer to initial concentrations and concentrations at time $t$, respectively, and the concentration of benzaldehyde was monitored during the reactions.

accelerated in the presence of water. In this case, the reactions followed second order kinetics under both anhydrous conditions and in the presence of 1–10 mol% of water (relative to benzaldehyde). As shown in Fig. 7, the rate enhancement due to water was much more modest in this case and the time required for the reaction to reach 70% conversion decreased by just a factor of two from 1200 seconds under anhydrous conditions to 600 seconds in the presence of 10 mol% water.

Water and other protic additives are known to react rapidly with trimethylsilyl cyanide to form hydrogen cyanide,[26] which can be the cyanide source in asymmetric cyanohydrin synthesis.[27] In the presence of a Brønsted base ($X^-$ or $Et_3N$), hydrogen cyanide will add to aldehydes to form a cyanohydrin which can then be silylated by trimethylsilyl cyanide reforming cyanide. This alternative reaction pathway appears to account for the kinetic behaviour observed for triethylamine catalysed reactions in the presence of water. In particular, if the reaction between trimethylsilyl cyanide and water is fast, then the reaction would be expected to show first order kinetics in benzaldehyde and triethylamine concentrations and to be independent of the trimethylsilyl cyanide concentration. The activation parameters will be totally different to those observed under anhydrous conditions as they correspond to the transition state for a different reaction. Thus, in the presence of water, the reaction mechanism reverts to that established by Lapworth over a century ago.[1] Reactions catalysed by tetrabutylammonium thiocyanate **2** show a much lower rate acceleration in the presence of water than those catalysed by compounds **1**, **3** or **4**. This is consistent with the $pK_a$ values for the conjugate acids of the bases since, in water, thiocyanic acid (HSCN) has a much lower $pK_a$

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**Table 7** Comparison of Lewis acids for the addition of $Me_3SiCN$ to benzaldehyde[a]

| Catalyst | Conversion[b] (%) |
|---|---|
| $AlCl_3$ | 73 |
| $Al(OTf)_3$ | 98 |
| $FeCl_3$ | 88 |
| $Ti(O^iPr)_4$ | 20 |
| $ZnBr_2$ | 28 |
| $ZnI_2$ | 83 |

[a] Reactions carried out at room temperature in $CH_2Cl_2$ for one hour, using 10 mol% of catalyst and 1.2 equivalents of $Me_3SiCN$. [b] Determined by ^{1}H NMR spectroscopy.

$(-1.1)$[28] than those of hydrazoic acid (HN$_3$, p$K_a$ 4.7),[29] hydrogen cyanide (HCN, p$K_a$ 9.0)[30] or triethylammonium (Et$_3$NH$^+$, p$K_a$ 10.8).[31] Thus, thiocyanate is the weakest Brønsted base amongst the catalysts studied and hence would be expected to be the least effective catalyst for the addition of hydrogen cyanide to aldehydes.

Previous work has shown that triethylamine, tetrabutylammonium azide and tetrabutylammonium cyanide are all effective catalysts for the preparation of cyanohydrins.[10,12] However, the preparative utility of tetrabutylammonium thiocyanate **2** had not previously been investigated. Therefore, since the mechanistic studies had shown tetrabutylammonium thiocyanate to be such an effective catalyst and one which was much less affected by moisture present in the reaction mixture than the other tetrabutylammonium salts, a preparative study of the utility of catalyst **2** was undertaken. To allow the catalytic efficiency of tetrabutylammonium thiocyanate to be compared with other catalysts, the effectiveness of six Lewis acids as catalysts for the addition of trimethylsilyl cyanide to benzaldehyde was investigated. Table 7 compares the results obtained using 10 mol% of each catalyst for one hour at room temperature and clearly shows that aluminium triflate is the most effective of these Lewis acidic catalysts.

Therefore, aluminium triflate and tetrabutylammonium thiocyanate were both used as catalysts for the addition of trimethylsilyl cyanide to a range of aromatic and aliphatic aldehydes. For this study the catalyst loading was reduced to 5 mol% and the reaction time extended to two hours, giving the results shown in Table 8. In every case, tetrabutylammonium thiocyanate was found to be a more effective catalyst than aluminium triflate and for the more electron-deficient aldehydes, total conversion was obtained in the tetrabutylammonium thiocyanate catalysed reactions under these conditions. This provided a very convenient and high yielding synthesis of pure cyanohydrin trimethylsilyl ethers.

## Conclusions

Lewis bases **1–4** catalyse the addition of trimethylsilyl cyanide to aldehydes by three distinct mechanisms. The formation of hypervalent silicon species could be detected for the reaction between trimethylsilyl cyanide and tetrabutylammonium salts **2–4**, but not triethylamine **1**. Thus triethylamine appears to react with trimethylsilyl cyanide to generate cyanide anions which then add to the aldehyde. In contrast, for tetrabutylammonium

**Table 8** Comparison of $Al(OTf)_3$ and $Bu_4NNCS$ as catalysts for the addition of $Me_3SiCN$ to aldehydes[a]

| | Conversion[b] (%) | |
|---|---|---|
| Aldehyde | $Al(OTf)_3$ | $Bu_4NNCS$ |
| PhCHO | 81 | 94 |
| $3,5-F_2C_6H_3CHO$ | 93 | 100 |
| $3,4-Cl_2C_6H_3CHO$ | 96 | 100 |
| $4-F_3CC_6H_4CHO$ | 77 | 100 |
| $3-ClC_6H_4CHO$ | 84 | 100 |
| $3-FC_6H_4CHO$ | 62 | 100 |
| $4-ClC_6H_4CHO$ | 64 | 100 |
| $4-BrC_6H_4CHO$ | 63 | 100 |
| $4-FC_6H_4CHO$ | 68 | 91 |
| $4-MeSC_6H_4CHO$ | 72 | 88 |
| $3-MeC_6H_4CHO$ | 58 | 80 |
| $4-MeC_6H_4CHO$ | 55 | 87 |
| $3,4-Me_2C_6H_3CHO$ | 50 | 76 |
| $4-MeOC_6H_4CHO$ | 41 | 66 |
| $4-^tBuOC_6H_4CHO$ | — | 72 |

[a] Reactions carried out at room temperature in $CH_2Cl_2$ for two hours, using 5 mol% of catalyst and 1.2 equivalents of $Me_3SiCN$. [b] Determined by ^{1}H NMR spectroscopy.

salts **2** and **3** it is the hypervalent silicon complex which reacts with the aldehyde. Tetrabutylammonium cyanide **4** can directly provide cyanide anions to add to the aldehyde.

Reactions involving catalysts **1–4** are accelerated by the presence of water and this appears to be due to a change in mechanism from Lewis base-catalysed trimethylsilyl cyanide addition to Brønsted base-catalysed hydrogen cyanide addition. Tetrabutylammonium thiocyanate was shown to be a particularly effective catalyst for the synthesis of cyanohydrin trimethylsilyl ethers from a range of aldehydes.

## Experimental

Aldehyde concentrations were calculated by measuring UV absorbance maxima at the appropriate wavelength using a Biochrom Libra S12 UV-visible spectrophotometer. Stopped flow experiments were carried out using an Applied Photophysics SX stopped flow spectrometer used in absorbance mode with the monochromator set at the appropriate wavelength for the aldehyde being used. NMR spectra were recorded on a Bruker Avance 300 spectrometer operating at 300 MHz for ^{1}H and 75 MHz for [13]C. Infrared spectra were recorded using a Varian 800 FT-IR Scimitar series spectrometer fitted with an ATR attachment. Positive ion electrospray mass-spectra were recorded on a Waters LCT Premier LCMS spectrometer.

### General procedure for kinetic experiments with manual sampling

A solution of the appropriate catalyst in $CH_2Cl_2$ was added to a 5 mL round bottomed flask fitted with a Suba Seal stopper. $CH_2Cl_2$ was added to dilute the solution to the desired volume. An aliquot (0.5 μL) was taken *via* a microsyringe and diluted into $CH_2Cl_2$ (3 mL); this sample provided the reference for UV measurements. Aldehyde (0.94 mmol) was then added and

another aliquot (0.5 μL) taken to calculate the concentration at time = 0. Me$_3$SiCN (0.14 mL, 1.03 mmol) was added and simultaneously a timer was started. Samples (0.5 μL) were taken and diluted into CH$_2$Cl$_2$ (3 mL) at appropriate intervals and the UV absorbance measured to determine the concentration of the remaining aldehyde. The amount of CH$_2$Cl$_2$ used to dissolve the catalyst in a particular reaction was varied to ensure that the total initial reaction volume (CH$_2$Cl$_2$ + aldehyde + Me$_3$SiCN) was kept constant at 2.0 mL.

### General procedure for stopped-flow kinetic experiments

Solutions of aldehyde (1.96 mol L$^{-1}$) and Me$_3$SiCN (1.12 mol L$^{-1}$) in CH$_2$Cl$_2$ were prepared. The aldehyde solution was combined with an equal volume of CH$_2$Cl$_2$ solution containing Bu$_4$NNCS (4 mmol L$^{-1}$). The combined aldehyde and catalyst solution was placed into one of the syringes on the stopped flow unit and the Me$_3$SiCN solution placed into the other. On mixing the reagents, data was collected automatically over a time period of between 10 seconds and 60 minutes depending on the aldehyde.

### General procedure for Bu$_4$NNCS-catalysed cyanohydrin trimethylsilyl ether synthesis

An aldehyde (1.0 mmol) was added to a solution of Bu$_4$NNCS (15 mg, 0.05 mmol) in dry CH$_2$Cl$_2$ (1.75 mL). To this solution, Me$_3$SiCN (119 mg, 1.2 mmol) was added and the reaction was stirred for 2 hours at room temperature. The solution was then passed through a short silica plug, eluting with CH$_2$Cl$_2$ and the solvent was evaporated *in vacuo*. All the cyanohydrin trimethylsilyl ethers had spectroscopic data identical to those reported previously.[19e]

**2-Trimethylsilyloxy-phenylacetonitrile.**[19e] IR: 3092, 2972, 2243, 1592 cm$^{-1}$; ^{1}H NMR (300 MHz, CDCl$_3$): δ 0.24 (s, 9H, Si(CH$_3$)$_3$), 5.50 (s, 1H, CHO), 7.3–7.5 (m, 5H, ArH); ^{13}C NMR (75 MHz, CDCl$_3$): δ −0.3 (Si(CH$_3$)$_3$), 63.6 (CHO), 119.2 (CN), 126.3 (CHAr), 128.9 (CHAr), 129.3 (CHAr), 136.2 (CAr); MS (ESI, pos.) *m/z* 206 (MH$^+$).

**2-Trimethylsilyloxy-(3,5-difluorophenyl)acetonitrile.**[19e] IR: 3096, 2962, 2903, 2243, 1626, 1602 cm$^{-1}$; ^{1}H NMR (300 MHz, CDCl$_3$): δ 0.27 (s, 9H, Si(CH$_3$)$_3$), 5.50 (s, 1H, CHO), 6.84 (tt, 1H, $^3J_{(H,F)}$ = 8.8 Hz, $^4J_{(H,H)}$ = 2.4 Hz, CHAr), 6.9–7.1 (2H, m, CHAr); ^{13}C NMR (75 MHz, CDCl$_3$): δ −0.4 (Si(CH$_3$)$_3$), 62.4 (CHO), 104.8 (t, $^2J_{(C,F)}$ = 25.1 Hz, CHAr), 109.3 (d, $^2J_{(C,F)}$ = 26.9 Hz, CHAr), 118.2 (CN), 140.0 (t, $^3J_{(C,F)}$ = 9.1 Hz, CAr), 163.2 (dd, $^1J_{(CF)}$ = 249.4 Hz, $^3J_{(C,F)}$ = 12.4 Hz, CAr); MS (ESI, pos.) *m/z* 259 (M + H$_2$O)$^+$.

**2-Trimethylsilyloxy-(3,4-dichlorophenyl)acetonitrile.**[19e] IR: 3094, 3025, 2961, 2901, 2242, 1595, 1568 cm$^{-1}$; ^{1}H NMR (300 MHz, CDCl$_3$): δ 0.26 (s, 9H, Si(CH$_3$)$_3$), 5.44 (s, 1H, CHO), 7.31 (dd, 1H, $^3J_{(H,H)}$ = 8.4 Hz, $^4J_{(H,H)}$ = 2.0 Hz, CHAr), 7.50 (d, 1H, $^3J_{(H,H)}$ = 8.4 Hz, CHAr), 7.57 ppm (d, 1H, $^4J_{(H,H)}$ = 2.0 Hz, CHAr); ^{13}C NMR (75 MHz, CDCl$_3$): δ −0.3 (Si(CH$_3$)$_3$), 62.4 (CHO), 118.4 (CN), 125.4 (CHAr), 128.3 (CHAr), 131.0

(CHAr), 133.3 (CAr), 133.7 (CAr), 136.3 (CAr); MS (ESI, pos.) *m/z* 296 (M + Na$^+$).

**2-Trimethylsilyloxy-(4-trifluoromethylphenyl)acetonitrile.**[19e] IR: 2981, 2350, 1584, 1515 cm$^{-1}$; ^{1}H NMR (300 MHz, CDCl$_3$): δ 0.27 (s, 9H, Si(CH$_3$)$_3$), 5.55 (s, 1H, CHO), 7.61 (d, 2H, $^3J_{(H,H)}$ = 8.1 Hz, CHAr), 7.70 (d, 2H, $^3J_{(H,H)}$ = 8.1 Hz, CHAr); ^{13}C NMR (75 MHz, CDCl$_3$): δ −0.3 (Si(CH$_3$)$_3$), 63.0 (CHO), 118.5 (CN), 122.4 (CHAr), 126.0 (q, $^2J_{(C,F)}$ = 4 Hz, ArC), 126.6 (CHAr), 131.55 (q, $^1J_{(C,F)}$ = 33 Hz, CF$_3$), 140.0 (ArC); MS (ESI, pos.) *m/z* 296 (M + Na$^+$).

**2-Trimethylsilyloxy-(3-chlorophenyl)acetonitrile.**[19e] IR: 2971, 2884, 2355, 1636, 1596 cm$^{-1}$; ^{1}H NMR (300 MHz, CDCl$_3$): δ 0.26 (s, 9H, Si(CH$_3$)$_3$), 5.44 (s, 1H, CHO), 7.3–7.4 (m, 2H, CHAr), 7.4–7.5 (m, 2H, CHAr); ^{13}C NMR (75 MHz, CDCl$_3$): δ −0.3 (Si(CH$_3$)$_3$), 62.9 (CHO), 118.6 (CN), 124.3 (CHAr), 126.4 (CHAr), 129.5 (CHAr), 130.2 (CHAr), 134.9 (CAr), 138.1 (CAr); MS (ESI, pos.) *m/z* 280 (M + Na$^+$ + H$_2$O), 240 (MH$^+$).

**2-Trimethylsilyloxy-(3-fluorophenyl)acetonitrile.**[19e] IR: 3078, 2976, 2360, 1592 cm$^{-1}$; ^{1}H NMR (300 MHz, CDCl$_3$): δ 0.25 (s, 9H, Si(CH$_3$)$_3$), 5.49 (s, 1H, CHO), 7.0–7.1 (m, 1H, CHAr), 7.1–7.2 (m, 1H, CHAr), 7.2–7.3 (m, 1H, CHAr), 7.3–7.4 (m, 1H, CHAr); ^{13}C NMR (75 MHz, CDCl$_3$): δ −0.3 (Si(CH$_3$)$_3$), 62.9 (CHO), 113.5 (d, $^2J_{(C,F)}$ = 23 Hz), 116.4 (d, $^2J_{(C,F)}$ = 21 Hz), 118.8 (CN), 121.9 (d, $^4J_{(C,F)}$ = 3 Hz, CHAr), 130.7 (d, $^3J_{(C,F)}$ = 8 Hz, CHAr), 138.7 (d, $^3J_{(C,F)}$ = 7 Hz, CAr) 163.0 (d, $^1J_{(C,F)}$ = 246 Hz, CF); MS (ESI, pos.) *m/z* 224 (MH$^+$).

**2-Trimethylsilyloxy-(4-chlorophenyl)acetonitrile.**[19e] IR: 2971, 2352, 1595 cm$^{-1}$; ^{1}H NMR (300 MHz, CDCl$_3$): δ 0.24 (s, 9H, Si(CH$_3$)$_3$), 5.46 (s, 1H, CHO), 7.3–7.5 (m, 4H, CHAr); ^{13}C NMR (75 MHz, CDCl$_3$): δ −0.2 (Si(CH$_3$)$_3$), 63.0 (CHO), 118.8 (CN), 127.7 (CHAr), 129.2 (CHAr), 134.8 (CAr), 135.3 (CAr); MS (ESI, pos.) *m/z* 280 (M + Na$^+$ + H$_2$O).

**2-Trimethylsilyloxy-(4-bromophenyl)acetonitrile.**[19e] IR: 2970, 2230, 1590 cm$^{-1}$; ^{1}H NMR (300 MHz, CDCl$_3$): δ 0.24 (s, 9H, Si(CH$_3$)$_3$), 5.45 (s, 1H, CHO), 7.35 (d, 2H, $^3J_{(H,H)}$ = 8.3 Hz), 7.55 (d, 2H, $^3J_{(H,H)}$ = 8.3 Hz); ^{13}C NMR (75 MHz, CDCl$_3$): δ −0.3 (Si(CH$_3$)$_3$), 63.0 (CHO), 118.7 (CN), 123.5 (CHAr), 127.9 (CHAr), 132.1 (CAr), 135.3 (CAr); MS (ESI, pos.) *m/z* 324 and 326 (M + Na$^+$ + H$_2$O), 284 and 286 (MH$^+$).

**2-Trimethylsilyloxy-(4-fluorophenyl)acetonitrile.**[19e] IR: 2972, 2330, 1596, 1507 cm$^{-1}$; ^{1}H NMR (300 MHz, CDCl$_3$): δ 0.24 (s, 9H, Si(CH$_3$)$_3$), 5.47 (s, 1H, CHO), 7.09 (t, 2H, $^3J_{(H,H)}$ = $^3J_{(H,F)}$ = 6.3 Hz), 7.42 (dd, 2H, $^3J_{(H,H)}$ = 6.3 Hz, $^4J_{(H,F)}$ = 3.9 Hz); ^{13}C NMR (75 MHz, CDCl$_3$): δ −0.3 (Si(CH$_3$)$_3$), 63.0 (CHO), 116.1 (d, $^2J_{(C,F)}$ = 22 Hz, CHAr), 119.1 (CN), 128.4 (d, $^3J_{(C,F)}$ = 9 Hz, CHAr), 132.3 (d, $^4J_{(C,F)}$ = 3 Hz, CAr), 163.2 (d, $^1J_{(C,F)}$ = 247 Hz, CF); MS (ESI, pos.) *m/z* 224 (MH$^+$).

**2-Trimethylsilyloxy-(4-thiomethylphenyl)acetonitrile.**[19e] IR: 2970, 2920, 2834, 2240, 1590, 1560 cm$^{-1}$; ^{1}H NMR (300 MHz, CDCl$_3$): δ 0.23 (s, 9H, Si(CH$_3$)$_3$), 2.50 (s, 3H, SCH$_3$), 5.45 (1H, s, CHO), 7.27 (d, 2H, $^3J_{(H,H)}$ = 7.6 Hz, CHAr), 7.38 (d, 2H, $^3J_{(H,H)}$ = 7.7 Hz, CHAr); ^{13}C NMR (75 MHz, CDCl$_3$): δ −0.3 (Si(CH$_3$)$_3$), 15.4 (SCH$_3$), 63.3 (CHO), 119.1 (CN), 126.5 (CHAr), 126.8 (CHAr), 127.1 (CAr), 139.4 (CAr); MS (ESI, pos.) *m/z* 292 (M + Na$^+$ + H$_2$O), 252 (MH$^+$).

**2-Trimethylsilyloxy-(3-methylphenyl)acetonitrile.**[19e] IR: 3052, 2971, 2882, 2358, 1606 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 0.23 (s, 9H, Si(CH$_3$)$_3$), 2.39 (s, 3H, ArCH$_3$), 5.45 (1H, s, CHO), 7.1–7.2 (m, 1H, CHAr), 7.2–7.3 (m, 3H, CHAr); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ −0.3 (Si(CH$_3$)$_3$), 21.4 (ArCH$_3$), 63.7 (CHO), 119.3 (CN), 123.5 (CHAr), 127.0 (CHAr), 129.9 (CHAr), 130.1 (CHAr), 136.1 (CAr), 138.8 (CAr); MS (ESI, pos.) $m/z$ 260 (M + Na$^+$ + H$_2$O).

**2-Trimethylsilyloxy-(4-methylphenyl)acetonitrile.**[19e] IR: 3020, 2968, 2820, 2352, 1604 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 0.22 (s, 9H, Si(CH$_3$)$_3$), 2.37 (s, 3H, ArCH$_3$), 5.45 (1H, s, CHO), 7.22 (d, 2H, $^3J_{(H,H)}$ = 7.9 Hz), 7.35 (d, 2H, $^3J_{(H,H)}$ = 7.9 Hz); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ −0.2 (Si(CH$_3$)$_3$), 21.2 (ArCH$_3$), 63.6 (CHO), 119.3 (CN), 126.4 (CHAr), 129.6 (CHAr), 133.4 (CAr), 139.4 (CAr); MS (ESI, pos.) $m/z$ 260 (M + Na$^+$ + H$_2$O).

**2-Trimethylsilyloxy-(3,4-dimethylphenyl)acetonitrile.**[19e] IR: 3017, 2960, 2924, 2239 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 0.21 (s, 9H, Si(CH$_3$)$_3$), 2.26 (s, 3H, ArCH$_3$), 2.28 (s, 3H, ArCH$_3$), 5.41 (1H, s, CHO), 7.1–7.3 (m, 3H, CHAr); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ −0.2 (Si(CH$_3$)$_3$), 19.6 (ArCH$_3$), 19.8 (ArCH$_3$), 63.6 (CHO), 119.4 (CN), 123.9 (CHAr), 127.6 (CHAr), 130.1 (CHAr), 133.7 (CAr), 137.4 (CAr), 138.0 (CAr); MS 274 (M + Na$^+$ + H$_2$O).

**2-Trimethylsilyloxy-(4-methoxyphenyl)acetonitrile.**[19e] IR: 3002, 2960, 2840, 2742, 2270, 1596, 1577 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 0.21 (s, 9H, Si(CH$_3$)$_3$), 3.83 (s, 3H, OCH$_3$), 5.44 (1H, s, CHO), 6.93 (d, 2H, $^3J_{(H,H)}$ = 8.5 Hz), 7.39 (d, 2H, $^3J_{(H,H)}$ = 8.5 Hz); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ −0.2 (Si(CH$_3$)$_3$), 55.3 (OCH$_3$), 63.3 (CHO), 114.3 (CAr), 119.3 (CN), 127.9 (CHAr), 128.5 (CHAr), 160.3 (CAr); MS (ESI, pos.) $m/z$ 236 (MH$^+$).

**2-Trimethylsilyloxy-(4-*tert*-butoxyphenyl)acetonitrile.**[19e] IR: 3063, 3036, 2978, 2904, 2240, 1608, 1508 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 0.22 (s, 9H, Si(CH$_3$)$_3$), 1.36 (s, 9H, OC(CH$_3$)$_3$), 5.46 (1H, s, CHO), 7.02 (d, 2H, $^3J_{(H,H)}$ = 8.4 Hz, CHAr), 7.36 (d, 2H, $^3J_{(H,H)}$ = 8.4 Hz, CHAr); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ −0.2 (Si(CH$_3$)$_3$), 28.8 (C(CH$_3$)$_3$), 63.4 (CHO), 79.0 (OCMe$_3$), 119.3 (CN), 124.2 (CAr), 127.2 (CHAr), 130.9 (CHAr), 156.4 (CAr); MS (ESI, pos.) $m/z$ 278 (M + H).

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