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DEOXYGENATION OF ISOCYANATES TO ISONITRILES

A MECHANISTIC STUDY BY NUCLEAR MAGNETIC RESONANCE

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Abstract—Carbon-13 NMR has been used to show that the deoxygenation of isocyanates to isonitriles with t-butyldiphenylsilyl lithium proceeds via the intermediates (**7** and **8**). The silyl carboxamide (**1**) can be isolated but is thermally unstable rearranging to a mixture of silyl formamides (**2**). The spectroscopic properties of the silyl carboxamide (**1**) were found to be substantially different from those previously claimed for such compounds.

We have previously described how the conversion of an isocyanate to an isonitrile can be accomplished using t-butyldiphenylsilyl lithium[1] (Scheme 1). This reaction bears a formal resemblance to the Peterson type deoxygenation of epoxides to olefins,[2] which proceeds *via* an intermediate β-hydroxy silane anion. The stereochemical outcome of the Peterson reaction indicates that expulsion of siloxide from this intermediate occurs in a synchronous process through a 4-membered cyclic transition state[3] (Scheme 2). We wished to investigate whether the isocyanate deoxygenation involved an analogous 3-membered transition state or whether other processes intervened.

^{13}C NMR at low temperature proved to be an effective method for investigating the deoxygenation process. In order to minimise the complexity of the low field region of the carbon spectra, we chose to use an alkyl isocyanate as substrate, cyclohexyl isocyanate being the most suitable as it was the highest yielding of the alkyl isocyanates previously investigated.[1]

RESULTS

Initially we obtained spectra of species likely to be present in the reaction mixture, under the same conditions as the reaction required, i.e. in solution in tetrahydrofuran (THF). The chemical shift of the quaternary carbon α to silicon in the silyl species proved very sensitive to the environment of the silicon; shifts for these carbons along with those of the isocyanate and isonitrile carbons of the substrate and product are recorded in Table 1.

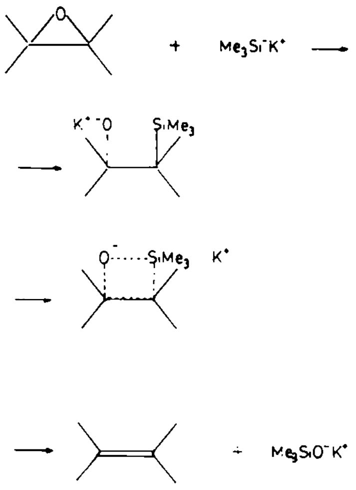
The reaction was observed by mixing pre-cooled (−80°) solutions of the silyl anion and the isocyanate in THF in an NMR tube and then rapidly introducing the tube into the spectrometer probe at −60°. At the concentrations used carbon spectra with adequate signal to noise could be obtained in about 5 min (corresponding to the accumulation of about 400 transients). In this way the progress of the reaction through a range of times and temperatures could be monitored. Figure 1 shows a sequence of spectra obtained during a single run of this type; only the low-field region of each spectrum is presented.

If the reaction mixture is maintained at −50° for slightly more than 1 hr, the resonance due to t-butyldiphenylsilyl lithium (δ 157.5) disappears completely, being replaced by a resonance at δ 181.1 (B in Fig. 1), without concomitant formation of detectable amounts of lithium t-butyldiphenylsiloxide or cyclohexyl isonitrile.

$$\mathrm{R{-}N{=}C{=}O} \quad + \quad \mathrm{Ph_2{}^tBuSi^-Li^+}$$

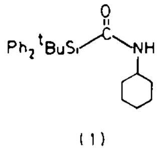
$$\longrightarrow \quad \mathrm{R{-}N{=}C} \quad + \quad \mathrm{Ph_2{}^tBuSiO^-Li^+}$$

Scheme 1.



Scheme 2.

The reaction was quenched with one equivalent of water at this stage, and simple work-up to remove salts then allowed the isolation of an adduct (**1**) of the silyl anion and the isocyanate as a colourless oil.



(1)

Compound **1** had a molecular weight of 365. Its ^{13}C NMR spectrum showed sets of resonances characteristic of both the t-butyldiphenylsilyl and mono-substituted cyclohexyl groups, and in addition a signal at δ 182.6 which was a singlet in the off-resonance decoupled spectrum. The ^{1}H NMR spectrum confirmed the presence of the t-butyldiphenylsilyl and cyclohexyl groups, and also showed a broad doublet at δ 5.7 and a multiplet at δ 4.1.

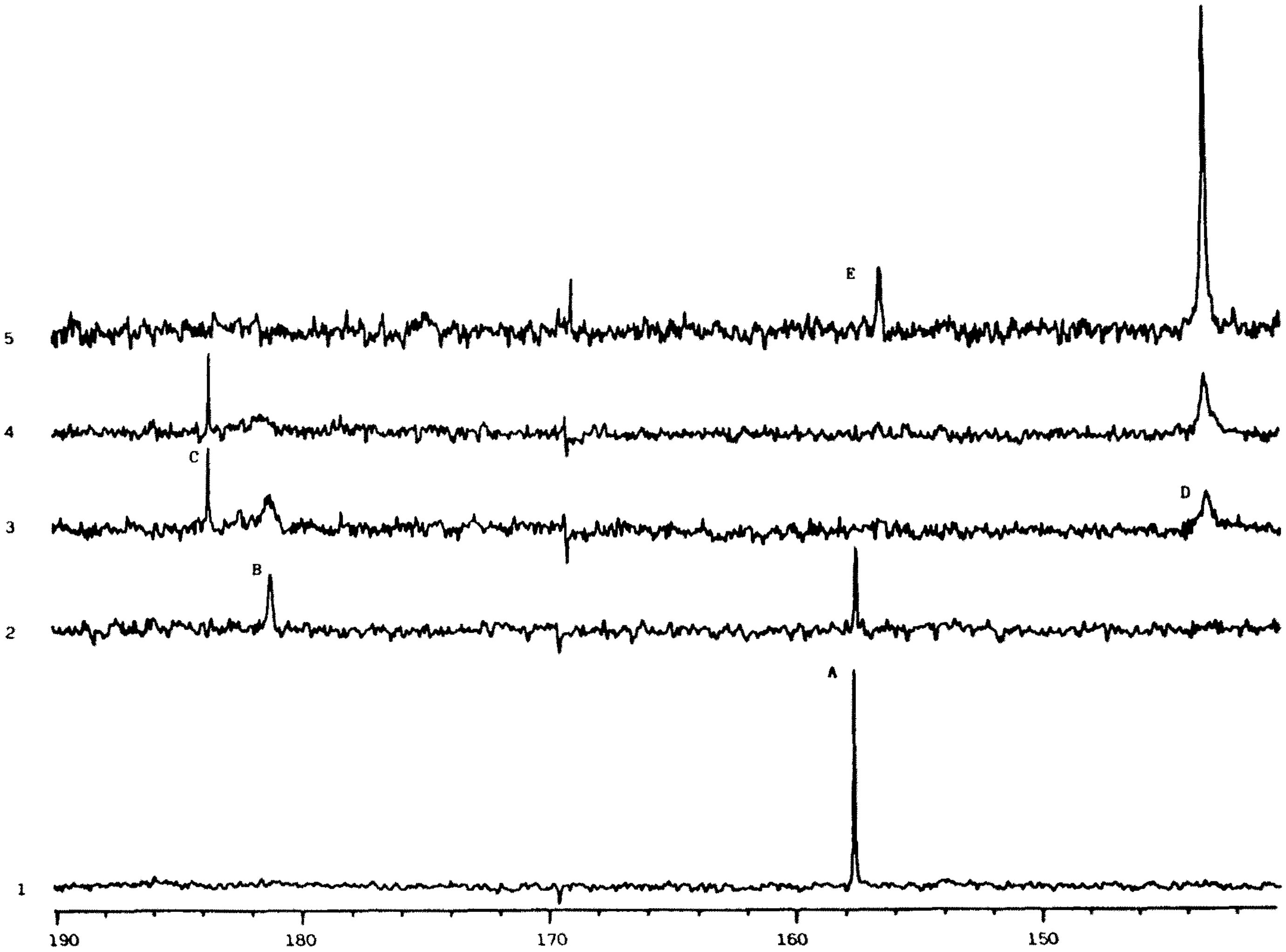


Fig. 1. Partial ^{13}C NMR spectra of the progress of the deoxygenation of cyclohexyl isocyanate by t-butyldiphenylsilyl lithium in THF. (1) – 50°C, immediately after mixing, A: Ph$_2{}^t$BuSi Li$^+$; (2) – 50°C, 1 hr, B: first intermediate; (3) – 10°C, 1.5 hr, C: second intermediate, D: Ph$_2{}^t$BuSiO$^-$Li$^+$; (4) – 10°C, 2.5 hr; (5) room temperature, E: cyclohexyl isonitrile. The peak at about δ 169.5 which shows temperature dependent phase changes is a quad image of the intense THF resonance at δ 67.7.

Table 1. Characteristic ^{13}C and ^{29}Si chemical shifts[a]

Compound	$\delta^{13}C$	$\delta^{29}Si^{e}$
$Ph_2{}^tBuSiCl$	133.1^b	13.1
$Ph_2{}^tBuSiOH$	137.5^b	-9.2
$Ph_2{}^tBuSiO^-Li^+$	143.5^b	-21.9
$Ph_2{}^tBuSi^-Li^+$	157.5^b	+6.6
Cyclohexyl Isocyanate	123.8^c	
Cyclohexyl Isonitrile	157.3^d	

a) In solution in THF

b) Shift of the quaternary aromatic carbon

c) Shift of the isocyanate carbon

d) Shift of the isonitrile carbon

e) Relative to TMS = 0·0

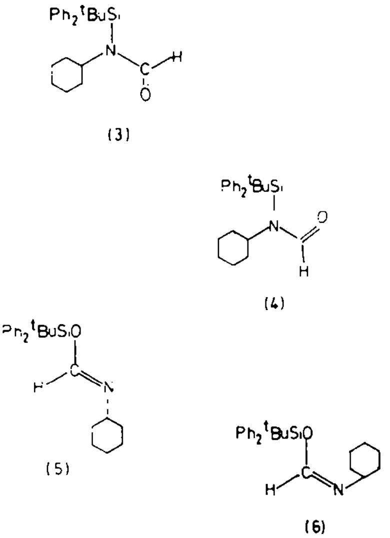
Irradiation of the δ 5.7 signal caused that at δ 4.1 to collapse to a triplet of triplets, the first-order pattern expected for the methine of a mono-substituted cyclohexane. Only a single resonance appeared in the ^{29}Si NMR spectrum, at δ-17.5 IR absorptions at 3420 and 1595 cm^{-1} indicated the likely presence of an N–H bond and some form of carbonyl. These data are consistent with adduct **1** being N-cyclohexyl-t-butyldiphenylsilylcarboxamide. The CO absorption at 1595 cm^{-1}, however, is substantially different from that quoted for the CO of the only secondary silyl carboxamide previously reported in the lit.[4] and we will return to this point shortly. Compound **1** is the protonated form of the expected product of nucleophilic attack by the silyl anion on the isocyanate from which direct expulsion of siloxide should be observed if the analogy with the Peterson synthesis holds.

If rather than quenching the reaction at −50°, when this first intermediate is present, it is instead warmed to about −10° and monitored further, immediate formation of the final products is not observed. Instead a new resonance appears at δ 183.9, and it is only after this has been present for some time that formation of the siloxide and isonitrile products can be detected. This resonance, presumably due to a second intermediate (C in Fig. 1), reaches its maximum intensity while the first intermediate is still present in solution, and when some formation of siloxide has already occurred. Quenching the reaction with water at this stage therefore yields a mixture of carboxamide (**1**), cyclohexyl isonitrile, t-butyldiphenylsilanol and a new substance (**2**).

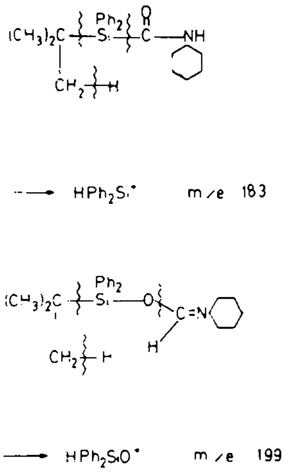
The ^{13}C NMR spectrum of this mixture revealed two new low-field resonances at δ 150.5 and δ 143.9 which were doublets in the off-resonance decoupled spectrum. In the IR spectrum the 1595 cm^{-1} absorption due to carboxamide (**1**) was still present, together with a new band at 1660 cm^{-1}. Substance **2** was very involatile and sensitive to hydrolysis, properties which precluded its isolation from the mixture for characterisation. However, we observed that carboxamide (**1**) is unstable at room temperature—on standing over several hours features characteristic of the new substance (**2**) appear in the spectra of **1**. Complete conversion of **1** to **2** could be brought about by refluxing for 30 min in THF. In this protonated form no further reaction of **2** is observed, allowing therefore the preparation of a sample for characterisation.

The molecular weight of **2** was also 365. In its ^{13}C spectrum there appeared, in addition to the signals at δ 150.5 and δ 143.9, a double set of signals characteristic of the t-butyldiphenylsilyl and cyclohexyl groups. Likewise, the proton spectrum showed signals characteristic of these groups, as for **1**. However, in the case of **2** there were two cyclohexyl methine resonances, at δ 2.9 (major) and δ 3.9 (minor), the former being a triplet of triplets. A doublet at δ 6.9 proved to be coupled to both the δ 3.9 proton signal ($J \sim 1.0$ Hz) and to the carbon resonating at δ 143.9 (demonstrated by selective proton-carbon decoupling). There was no immediately evident signal of this type associated with the δ 2.9 methine; however an NOE difference experiment from this methine enhanced a singlet at δ 7.7 (previously obscured by the complex aromatic signals) by 12.6%. Proton irradiation at δ 7.7 collapsed the δ 150.5 carbon doublet, completing the association of this set of signals. The silicon-29 spectrum of **2** showed two signals, at δ-1.6 and δ-2.7; the IR spectrum showed a strong band at 1660 cm^{-1}.

These observations indicated that substance **2** was a mixture of two compounds, most likely two out of the four possible N or O-silylated formamides (**3**–**6**). This idea was confirmed by treating N-cyclohexyl formamide sequentially with n-butyl lithium and t-butyldiphenylsilylchloride, which yielded a substance having spectroscopic properties identical to those of **2**. It was not possible to unambiguously determine the sites of silylation from the spectroscopic data; however the mass-spectral fragmentations indicated probable O-silylation. Thus carboxamide **1** has the base peak in its mass spectrum at 183, corresponding to the diphenyl silyl cation, while that for **2** appears at 199 corresponding to the diphenyl siloxide cation. Interestingly the thermal rearrangement of **1** to **2** can be observed in the spectrometer, the 183 peak gradually falling in intensity over a period of a few minutes to be replaced by that at 199 (Scheme 3).



Mixture (2).



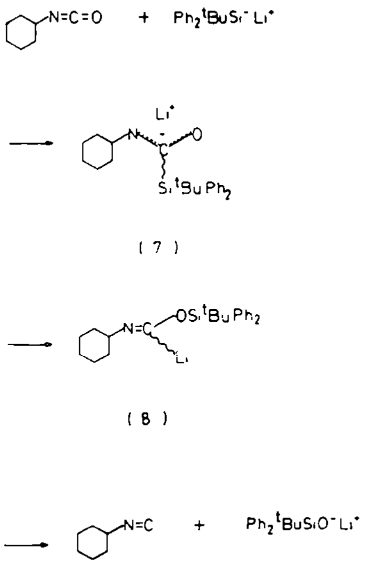
Scheme 3.

DISCUSSION

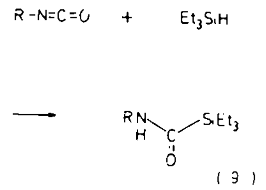
Given the structures for the protonated intermediates (**1** and **2**), a reasonable mechanism for the deoxygenation process is that depicted in Scheme 4 involving initial attack by the silyl anion on the isocyanate followed by silicon migration from C to O revealing a carbanion which subsequently fragments to isonitrile plus siloxide. This is supported by the observation that the mixture **2** prepared by silylation of N-cyclohexyl formamide can itself be converted to cyclohexyl isonitrile by treatment with a further equivalent of n-butyl lithium. The deoxygenation therefore involves a novel type of C to O silicon rearrangement and differs in this respect from the Peterson reaction.

There remains the question of the frequency of the CO absorption in the IR spectrum of **1**. In the only previous report claiming the preparation of secondary silyl carboxamides, Ojima and Inaba describe their formation by heating together triethyl silane and an alkyl isocyanate in the presence of palladium chloride at 80°[4] (Scheme 5). The compounds were characterized on the basis of proton NMR and an IR spectrum showing an N-H absorption together with a band at $1650\,\text{cm}^{-1}$. In view of both the observed thermal instability of **1** and the well documented tendency for silicon substitution of carbonyl compounds to reduce the IR CO absorption frequency by about $50\,\text{cm}^{-1}$ relative to the analogous alkyl derivatives,[6] we felt it was unlikely that the products of these reactions were in fact silyl carboxamides. In addition, compound **10** (Scheme 6) of unambiguous structure,[5] has a reported CO stretching frequency of $1560\,\text{cm}^{-1}$, confirming that the expected frequency shift is observed in silyl amides.

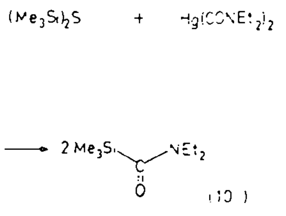
We therefore repeated the silane/isocyanate addition reaction. Careful recording of the IR spectrum either of the crude reaction mixture or of the product isolated by distillation, in solution in anhydrous carbon tetrachloride, revealed the band at $1650\,\text{cm}^{-1}$, but there was no evidence of an absorption at $3250\,\text{cm}^{-1}$ as previously claimed. Brief exposure of this reaction to the air did however lead to a mixture showing absorptions at 3440 and $3680\,\text{cm}^{-1}$. The proton spectrum in dry carbon tetrachloride corresponded to that claimed previously,



Scheme 4.



Scheme 5.



Scheme 6.

the cyclohexyl methine appearing as a clean triplet of triplets. However the carbon spectrum revealed that the low field signal which was expected to be the silyl carboxamide CO, if the original structure claimed for this compound was correct, was in fact a doublet in the off-resonance decoupled spectrum indicating the presence of a formyl component. There can therefore be no doubt that the product of this hydrosilylation reaction has been incorrectly formulated.[8] The true structure is almost certainly one of the four possible triethylsilyl formamides, the presently available evidence being insufficient to determine this unambiguously.

CONCLUSIONS

Our observations by ^{13}C NMR of the deoxygenation have led to the identification of two intermediates on the pathway between silyl anion plus isocyanate to siloxide plus isonitrile, allowing us to propose a mechanism for the reaction. In order to confirm that the physical data for carboxamide (**1**) were fully consistent with its structure we have been required to demonstrate that a previous literature report regarding secondary silyl carboxamides was incorrect. Compound **1** therefore represents the first example of this class of substance.

EXPERIMENTAL

Proton NMR spectra were recorded at 300 MHz unless otherwise stated. Silicon NMR spectra were recorded at a frequency of 59.64 MHz. Carbon-13 spectra were recorded on a Bruker WH 300 spectrometer at a frequency of 75.47 MHz in a 10-mm broadband probe. The $\pi/2$ pulse length was 28 μsec. Accumulations were in 16 K data, a spectral width of 18,500 Hz being digitised with a pulse repetition time of 1.2 sec for 10–12 μsec pulses. Broadband proton decoupling was applied throughout the acquisition and relaxation delay periods; for off-resonance decoupled spectra the irradiation frequency was offset 3000 Hz downfield from ^{1}H δ 5.0. Exponential multiplication with a line broadening of 1–2 Hz preceded Fourier transformation. The 8 K real points after transformation gave a digital resolution of 2.2 Hz/point. For variable temp experiments the cooling was produced by direct evaporation of liquid N_2 into the probe.

IR spectra were recorded as soln spectra on a Perkin–Elmer 681 spectrometer and Mass Spectra on a VG micromass ZAB 1F spectrometer.

THF was distilled from Na/benzophenone, and cyclohexyl isocyanate was distilled for calcium hydride. All apparatus was pre-dried at 100° overnight.

Preparation of t-butyldiphenylsilyl lithium.[7] To excess finely divided Li was added dropwise a soln of t-butyldiphenylsilylchloride (5 ml; 19.2 mmol) in THF (20 ml). The mixture was stirred at room temp. for 6 hr to give a green/black soln of the silyl anion (0.77 M). The precipitated LiCl was allowed to settle and the supernatant removed by syringe when required.

Typical procedure for NMR observations. A soln of t-butyldiphenylsilyl lithium (0.77 M; 2 ml; 1.54 mmol) in THF was introduced by syringe into a 10 mm o.d. NMR tube (pre-dried, sealed with a septum and purged with N_2). After addition of d^6-benzene (200 μL) and tetramethylsilane (50 μL) and cooling in a MeOH/dry ice bath, a pre-cooled soln of cyclohexyl isocyanate (0.2 ml; 1.54 mmol) in THF (1 ml) was added and the solns mixed by shaking on a whirlimixer. The tube was then introduced rapidly into the probe of the spectrometer which had been pre-cooled to − 60°.

Preparation of N-cyclohexyl t-butyldiphenylsilyl carboxamide (**1**). A soln of t-butyldiphenylsilyl lithium and cyclohexyl isocyanate in THF, prepared as described above, was warmed to − 50° and held for approx. 1 hr until ^{13}C NMR indicated consumption of the silyl anion. The tube was rapidly removed from the spectrometer, returned to the cooling bath and quenched with water (28 μL; 1.54 mmol). After warming to room temp., the soln was taken up in hexane, filtered through celite and evaporated under reduced pressure to yield a viscous oil (**1**).[10] IR(CHCl$_3$): 3420, 3010, 2940, 1595, 1490 cm^{-1}; ^{1}H NMR(CDCl$_3$) δ 7.7 (m; 4H; Ar) 7.4 (m; 6H; Ar), 5.7 (bd; 1H; N$\underline{H}$), 4.1 (m; 1H; C$\underline{H}$N), 1.9–1.10 (m; 10H; C$\underline{H}_2$'s), 1.2 (s; 9H; 3 × Me), ^{13}C NMR(CDCl$_3$) δ 182.6 (s; $\underline{C}$=0), 131.7 (s; Ar), 136.0, 129.8, 127.9 (d; Ar), 46.1 (d; $\underline{C}$HN), 32.8, 25.3, 24.4 (t; $\underline{C}H_2$'s), 27.4 (q; 3 × CH$_3$), 18.1 (s; Me$_3\underline{C}$Si), ^{29}Si NMR (CDCl$_3$) δ-17.5. MS *m/e* (relative intensity) 365 (1), 308 (10), 199 (22), 183 (100), 105 (15), High Resolution MS: Expected: 365.2175; Found: 365.2177.

Thermal rearrangement of **1**. A soln of the silyl carboxamide (**1**) in THF was refluxed for 30 min and the solvent removed under reduced pressure to give a quantitative yield of a viscous liquid. IR (CHCl$_3$): 2940, 1660, 1430 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.7 (s), 6.9 (d) (1H; OC$\underline{H}$=N), 7.2–7.8 (m; 10H; Ar), 3.9, 2.9 (tt) (1H; ($\underline{C}H_2)_2$C$\underline{H}$N), 1.0–2.0 (m; 10H; C$\underline{H}_2$'s), 1.2, 1.15 (s; 9H; 3 × CH$_3$), ^{13}C NMR (CDCl$_3$) δ 150.5, 143.9 (d; N=C$\underline{H}$O), 135.5, 135.2, 130.4, 130.0, 128.7, 128.1 (d; Ar), 132.4, 131.8 (s; Ar), 60.9, 53.8 (d; $\underline{C}$HN), 35.0, 33.8 (t; $\underline{C}H_2$'s), 26.6, 26.4, 25.9, 25.5, 25.0, 24.7 (region too crowded to assign off-resonance spectrum CH$_2$'s and CH$_3$'s) 19.2, 19.1 (s; 2 × Me$_3\underline{C}$Si), ^{29}Si NMR (CDCl$_3$) -1.6, -2.7, MS *m/e* (relative intensity): 365 (0.5), 308 (80), 199 (100), High Resolution MS: Expected 365.2175; Found: 365.2177.

Preparation of N-*cyclohexcyl*, N-*t-butyldiphenylsilyl formamide* (**2**). To a soln of N-cyclohexyl formamide (1 g; 7.87 mmol) in THF (20 ml) was added at − 60° a soln of n-BuLi (1.6 M; 5.4 ml; 8.66 mmol) in hexane. The white suspension was stirred at room temp. for 10 min and quenched with t-butyldiphenylsilyl chloride (2.17 ml; 7.87 mmol) to give a clear yellow soln. After stirring for 2 hr, the solvent was removed under reduced pressure and the residue distilled to give a clear viscous liquid (2.8 g; 97%) b.p. 200° at 0.15 mmHg.

Spectroscopic data identical to the product from thermal rearrangement of **1**.

Reaction of triethylsilane and cyclohexyl isocyanate. A mixture of triethylsilane (1.59 ml; 10 mmol), cyclohexyl isocyanate (1.25 ml; 10 mmol) and palladium chloride (25 mg) was heated at 90° for 12 hr. The mixture was distilled to give a clear liquid (0.7 g; 30%; increasing the reaction time to 20 hr increased the yield to 75%) b.p. 78–84°/0.2 mmHg (lit: 72°/0.2 mmHg).[4] IR (CCl$_4$): 2930, 1650, 1230 cm^{-1}, ^{1}H NMR (CCl$_4$) δ 7.45 (1H; s), 3.0 (br; 1H), 1.2–1.8 (m; 10H; CH$_2$'s), 0.95 (t; 3H; C$\underline{H}_3$CH$_2$Si), 0.75 (t; 2H; C$\underline{H}_2$Si), ^{13}C NMR (d^6-Benzene) δ 151.8 (d; H$\underline{C}$O, 61.2 (d; CH$_2\underline{C}$HCH$_2$).

Reaction of n-butyl lithium with N-*cyclohexyl*, N-*t-butyldiphenylsilyl formamide.* To a soln of N-cyclohexylformamide (1.44 g; 11.3 mmol) in dry THF (20 ml) was added at − 60° a soln of n-BuLi in hexane (1.6 M; 7.8 ml; 12.4 mmol). The white suspension was stirred at room temp for 10 min and quenched with t-butyldiphenylsilyl chloride (2.95 ml; 11.3 mmol) to give a clear yellow soln. The mixture was stirred for 30 min, cooled to − 20° and a soln of n-BuLi in hexane (1.6 M; 7.8 ml; 12.4 mmol) added over 10 min. The mixture was stirred for 15 min and the solvent removed under reduced pressure. Subsequent fractional distillation of the residue gave a clear liquid (295 mg; 25%). Spectroscopy showed this to be identical to a previously prepared sample of cyclohexyl isonitrile. IR (CHCl$_3$): 2140 cm^{-1}, ^{1}H NMR (CDCl$_3$; 60 MHz), δ 3.75 (br; 1H), 1.4–1.9 (br; 10 H).

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[8] During the preparation of this manuscript a report appeared in the literature[9] describing how the structure assigned by Ojima and Inaba for the adduct of triethylsilane/butyl isocyanate was incorrect. The authors claim that the compound is the O-silyl formimidate and not the C-silyl amide.

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[10] A repeat of this reaction under laboratory conditions gave a yield of 96%.