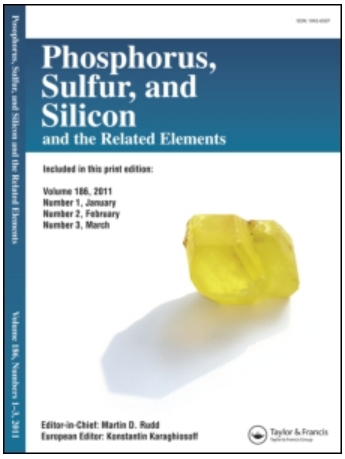

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THE REACTION OF O-SILYLATED α-KETOLS WITH TRIMETHYLSILYL CYANIDE

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The reactions of a series of O-silylated α-ketols with trimethylsilyl cyanide have been investigated. Formation of the expected 0-trimethylsilyl cyanohydrins as major products has been shown to be accompanied by the hitherto unsuspected formation of a disiloxane by a proposed intramolecular S_N2 displacement mechanism. The latter reaction is, surprisingly, independent of the substitution pattern in the silylated ketol. Formation of the side-product, however, increases in all cases with increasing dilution. The α,β-epoxynitrile **9**, a second side-product expected, along with the observed disiloxane, by our proposed mechanism was synthesized by an unambiguous route. A control experiment showed the epoxynitrile to be completely destroyed under the usual conditions of reaction with trimethylsilyl cyanide. ^{13}C NMR data have been obtained for most of the compounds in this study.

Key words: trimethylsilyl cyanide; α-ketols (O-silylated); α,β-epoxynitrile; disiloxane.

INTRODUCTION

The reaction of simple aldehydes and ketones with HCN to produce cyanohydrins has been known for many years and was one of the earliest reactions to be studied from the mechanistic standpoint.[2] In recent years, it has often been found to be more convenient to use trimethylsilyl cyanide instead of HCN.[3] We have used the latter reaction successfully[4] for the synthesis of **1a**, an intermediate in the synthesis of the tetronic acid derivatives **2**, employing the general procedure described by Evans and Truesdale.[5] Interest in the synthetic utility of trimethylsilyl cyanide[6] and of O-silyl cyanohydrins[7,8] has recently been intense.

We recently attempted to extend our earlier work[4] to the preparation of **1b**, which we hope to be able to convert eventually to thiotetromycin **3**, an interesting thiolactone antibiotic first reported by Omura *et al.*[9] To our surprise, while we obtained the expected **1b** (from **4b**) in 88% yield, a second product shown to be present on careful TLC analysis was subsequently isolated by flash chromatography. This finding has prompted us to undertake the structural elucidation of the second product as well as a systematic examination of trimethylsilyl cyanide addition to the series of O-silylated α-ketols **4a-c**, the results of which we now report.

RESULTS AND DISCUSSION

The ketones **4a** and **4b** required for this study were made by O-silylation of the readily available α-ketols by the procedure previously described,[4] in yields of 93% and 92%, respectively. Compound **4c** is new and was made by selective and essentially quantitative O-silylation of 3,3-dimethyl-1,2-butanediol to give **5**, followed

by oxidation with Jones' reagent, in an overall yield of 44%. The relatively modest yield in the oxidation step may be attributed to steric hindrance by the *t*-butyl group. A fourth compound, **6**, was prepared as a reference system, in 90% yield, by standard treatment of 1-butanol with *t*-butyldiphenylsilyl chloride. The spectral characteristics of compounds **4a–c**, **5**, and **6** (IR, ^1H and ^{13}C NMR) are listed in Table I, along with the data for the corresponding O-trimethylsilyl cyanohydrins **1a–c**.

When the crude product from the reaction of **4b** with trimethylsilyl cyanide was subjected to careful flash chromatography a minor product (6%) was also isolated. By a combination of IR, ^1H and ^{13}C NMR, and mass spectral analyses, we have

TABLE I

Spectral characteristics for **1a–c**, **4a–c**, **5** and **6**

Compound	IR(cm^{-1})[a]	^1H-NMR(δ)[b]	^{13}C-NMR(δ)[c,d]
4a	1743, 1722, 1117, 822	7.69(m, 4H), 7.45(m, 6H), 4.15(s, 2H), 2.18(s, 3H), 1.13(s,9H)	208.5(*CO*), 69.9(*CH*$_2$), 26.6(*CH*$_3$)
4b	1743, 1729, 1117, 815	7.57(m, 4H), 7.29(m, 6H), 4.14(s, 2H) 2.52(q, J = 7.5 Hz, 2H), 1.07(s, 9H), 1.01(t, J = 7.5 Hz, 3H)	211.2(*CO*), 69.6(*CH*$_2$), 31.9(*CH*$_2$), 7.2(*CH*$_3$)
4c	(CCl_4)1736, 1560, 1117	7.58(m, 4H), 7.28(m, 6H),4.35(s, 2H), 1.07(s, 9H), 0.97(s, 9H)	211.9(*CO*), 65.5(*CH*$_2$), 42.4(*C*(CH$_3$)$_3$), 26.2(C(*CH*$_3$)$_3$)
1a	1265, 1117, 850	7.63(m, 4H), 7.35(m, 6H), 3.60(two d, J = 10.5 Hz, 2H), 1.62(s, 3H), 1.12(s, 9H), 0.23(s, 9H)	121.3(*CN*), 70.5(*C*–CN), 70.3(*CH*$_2$), 25.9(*CH*$_3$), 1.2(Si(*CH*$_3$)$_3$)[e]
1b	1265, 1117, 850	7.77(m, 4H), 7.33(m, 6H), 3.68(two d, J = 10.5 Hz, 2H), 1.83(m, 2H), 1.09(s, 9H), 1.03(t, J = 7.5 Hz, 3H), 0.17(s, 9H)	120.6(*CN*), 74.3(*C*–CN), 68.2(*CH*$_2$O), 31.4(*CH*$_2$), 7.9(*CH*$_3$), 1.2(Si(*CH*$_3$)$_3$)[e]
1c	1258, 1117, 843	7.73(m, 4H), 7.43(m, 6H), 3.72(two d, J = 10.5 Hz, 2H), 1.15(s, 9H), 1.08(s, 9H), 0.19(s, 9H)	119.8(*CN*), 80.1(*C*–CN), 66.7 (*CH*$_2$), 38.7(*C*(CH$_3$)$_3$), 25.3((C(*CH*$_3$)$_3$), 1.2((Si(*CH*$_3$)$_3$)[e]
5	3578, 1110, 1068, 829	7.70(m, 4H), 7.42(m, 6H), 3.90–3.23(m, 3H), 2.79(s, 1H, exch. D_2O), 1.11(s, 9H), 0.88(s, 9H)	135.6(*C-2'*, *6'*), 133.2(*C-1'*), 129.8(*C-4'*), 127.8(*C-3'*, *5'*), 78.8(*CH*(OH)), 64.7(*CH*$_2$), 33.2,25.9(C–*C*(*CH*$_3$)$_3$), 26.9, 19.2(Si(*C*(*CH*$_3$)$_3$)
6	1110, 822	7.70(m, 4H), 7.38(m, 6H), 3.70(t, J = 6.5 Hz, 2H), 1.83–0.63(m, 7H), 1.11(s, 9H)	135.6(*C-2'*, *6'*), 134.3(*C-1'*), 129.5(*C-4'*), 127.6(*C-3'*, *5'*), 63.8(*C-1*), 34.9(*C-2*), 27.0,19.3(Si-*C*(*CH*$_3$)$_3$), 19.1(*C-3*), 14.0(*C-4*)

[a] Spectra recorded as liquid films (neat) unless otherwise indicated.

[b] At 60 MHz, in $CDCl_3$ solution.

[c] At 400 MHz, in $CDCl_3$ solution.

[d] For clarity, the signals due to the silyl *t*-butyl and phenyl substituents in **4a–c** and **1a–c** are omitted. They were essentially constant (±0.1 ppm), as follows: δ 135.5(*C*—2',6'), 132.6(*C*—*1'*), 130.0(*C*—*4'*), 127.8(*C*—*3'*,*5'*), 26.7(C(*CH*$_3$)$_3$), 19.2(*C*(CH$_3$)$_3$).

[e] For compounds **1a–c**, chirally induced chemical shift differences could readily be detected for the C—1' (~0.3 ppm), C—2',6' (~0.1 ppm) and even, in the case of **1b**, for the C—4' carbons ($\delta\Delta$ = 0.027 ppm), separated by *seven* bonds from the chiral centre. Ingold and coworkers[10] have recently reported similar chemical shift differences for α-tocopherol and related compounds at aromatic carbons up to five bonds from the nearest chiral centre and have examined these effects and their variation with bond separation in great detail.

shown that this compound is 1-*t*-butyl-1,1-diphenyl-3,3,3-trimethyldisiloxane, **7**. A plausible mechanism for its formation is shown in Scheme 1 (Path b) and involves the intramolecular S_N2 displacement of *t*-butyldiphenylsilanolate ion in the intermediate **8**, followed by silylation of the silanolate ion with excess trimethylsilyl cyanide to produce **7**, in competition with trapping of **8** by trimethylsilyl cyanide to give **1b**, the major product (Path a).[11]

While such S_N2 displacements of silanolate leaving groups are not common, it is well known that intramolecular S_N2 reactions leading to 3-membered rings are kinetically favorable, while the loss of the considerable steric bulk in the particular silanolate leaving group used in this instance may also be a factor. Displacement of silanolates from acyloxysilanes, by nucleophilic attack at C=O, has been found

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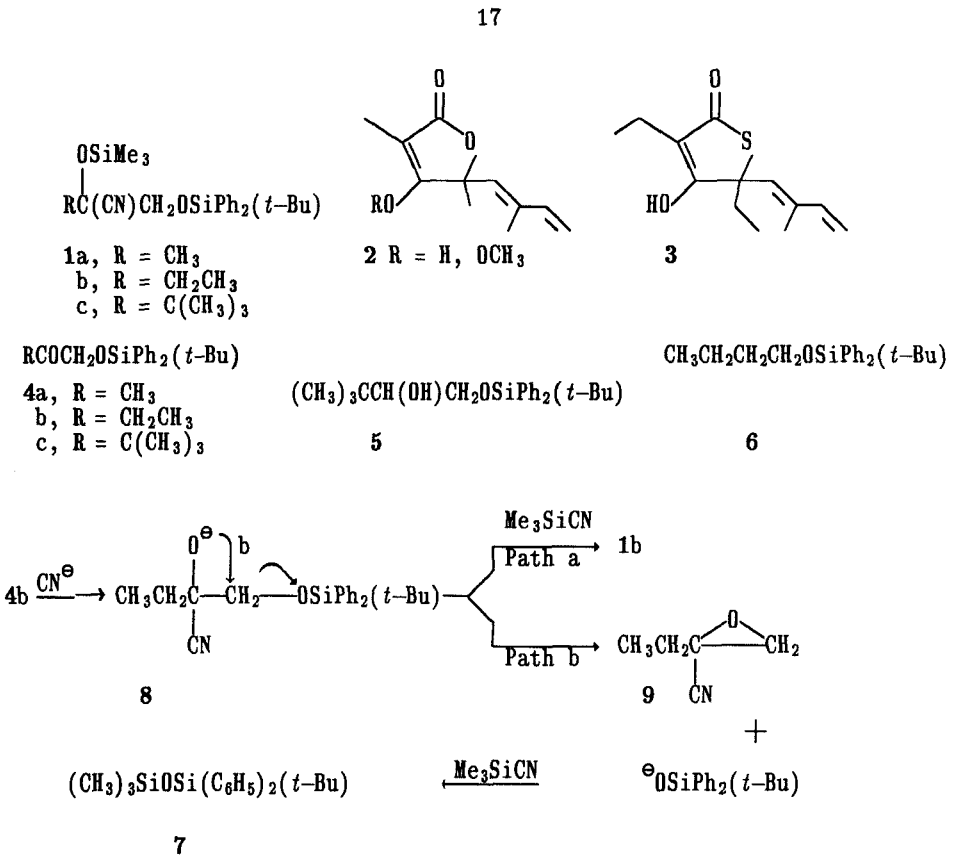
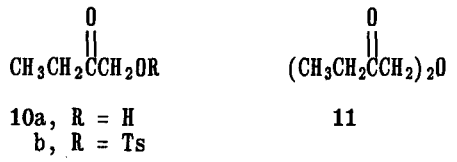


Scheme 1. Proposed Mechanism for the Formation of the Disiloxane **7**.



by Hudrlik and Feasley[12] to compete with nucleophilic attack at silicon under certain conditions, with increasing bulk of the silicon substituents favouring the former process. Displacements of silanolate assisted by prior protonation or silylation of the oxygen atom are also known,[13] although we do not think prior silylation to produce an oxonium ion is likely in our system, for steric reasons. We have ruled out direct *intermolecular* displacement of the silanolate leaving group by S_N2 attack of cyanide ion at C—1 in **4b**, for two reasons. Firstly, none of the (stable) 3-oxopentanenitrile expected from this reaction could be detected. Secondly, prolonged treatment of the model compound **6** with trimethylsilyl cyanide under our standard reaction conditions (see Experimental) led only to the quantitative recovery of starting material.

We next sought evidence that this unusual side-reaction was a general one by studying the analogous reactions of **4a** and **4c** with trimethylsilyl cyanide at a standard (ketone) concentration of 6 M. We hoped by this means to discover whether any pronounced substituent effect in the ketone could be observed. The product mixtures were analyzed by HPLC and, surprisingly, the results showed no significant effect of increasing substitution in the starting ketone—the relative yields of **1a–c** (in relation to **7**) being 91–92% in all cases, although the net conversion of **4c** to products was only 78%. In a series of experiments in which we varied the concentration of the reactant, using hexane as solvent, we can see from Table II that decreasing the concentration of the reactants has a dramatic effect in increasing the relative amount of **7** produced, to as much as 30% at a concentration of 1 M. We feel that this result lends strong support to our proposed mechanism for the formation of **7**, since decreasing concentration should disfavour Path a (bimolecular reaction) in Scheme 1 while leaving Path b unaffected.

The reactions of epoxides in general with trimethylsilyl cyanide have been studied extensively by Olah *et al.*[14] α,β-Epoxynitriles do not appear to have been widely investigated but, interestingly, epoxy isonitriles have been found in a series of fungal metabolites possessing potent antimicrobial activity.[15] We thought it would therefore be of interest to synthesize the epoxynitrile **9** by an unambiguous route in order to examine its reactivity towards trimethylsilyl cyanide under the conditions used to react our series of silylated α-ketols.

We were able to synthesize the epoxynitrile **9**, starting from 1-hydroxy-2-buta-

TABLE II

Variation in Relative Yield of **7** with Concentration of Ketone (**4b**)

Concentration of ketone **4b** (mol, in hexane)	Overall yield (%)	Relative yield[a] of **1b** (%)	Relative yield[a] of **7** (%)
Neat (no solvent)	85.0	94.3	5.7
6.0	96.0	91.1	8.9
1.0	93.2	69.6	30.4

[a] As estimated by HPLC analysis (see Experimental).

none **10a** (also used in the preparation of **4b**). Conversion of this α-ketol into its O-toluenesulfonyl derivative **10b** initially proved to be difficult but was finally achieved in approximately 90% crude yield, using triethylamine at 0°C as catalyst.[16] The crude product was shown by ^{1}H NMR to be a mixture of **10b** with the symmetrical ether **11**, in a ratio of 82:18, but was used in the next step without further purification, as it was felt that **11** was unlikely to interfere. The impure **10b** was subjected to reaction with potassium cyanide in the presence of 18-crown-6 at 0–3°C, to afford the known 2,3-epoxy-2-ethylpropanenitrile (**9**) in 27% overall yield. The mechanism of this transformation appears to parallel that of Path b in Scheme 1. The structure of the epoxynitrile was confirmed by IR, ^{1}H and ^{13}C NMR, and mass spectral analysis.

The results from our study of the reactions of the O-silylated ketols **4a–c** with trimethylsilyl cyanide show that side-products should be expected from such reactions, except at very high concentrations of reactants or, preferably, in the complete absence of solvent. The O-tosylation problems encountered in the formation of **10b** from 1-hydroxy-2-butanone serve to reinforce our finding that even apparently straightforward reactions of α-ketols and their O-silylated derivatives must be interpreted with great care.

EXPERIMENTAL

FT-IR spectra were recorded on a Nicolet 5DX instrument and the ^{1}H NMR spectra were obtained at 60 MHz (Varian T-60). ^{13}C NMR spectra and 400 MHz ^{1}H NMR spectra were obtained using a Varian XL-400 spectrometer. Mass spectra were recorded under electron impact conditions on a VG11-250S instrument operating at 70 eV, unless stated otherwise. Flash chromatography was carried out on silica gel supplied by E. Merck (Darmstadt), with 230–400 mesh size. TLC (analytical and preparative) was carried out on silica gel supplied by E. Merck (Darmstadt). The purity of titled compounds was shown to be ≥98% by ^{1}H NMR and TLC analyses. HPLC analyses of product mixtures were performed on a Varian Vista 6500 instrument with polychrome diode detector, using a Waters μPorasil^R (3.9 mm × 30.0 cm) column, with a flow-rate of 1 mL/min (hexane:ethyl acetate = 9:1). Semi-preparative scale purifications were conducted on a Dupont Zorbax Sil^R (9.4 mm × 25.0 cm) column, flow-rate = 3 mL/min, using the same solvent system. Elemental analysis was performed by the Scandinavian Microanalytical Laboratory, Box 25, DK-2730, Herlev, Denmark. Melting points and boiling points are uncorrected.

Anhydrous reactions were performed in oven-dried glassware (140°C, 6 h), which was then cooled under nitrogen. All syringes were oven-dried and cooled in a desiccator before use. Dichloromethane was distilled from phosphorus pentoxide and stored over 4-Å molecular sieves. Benzene, toluene, diethyl ether, and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl before use. Hexane, triethylamine and pyridine were stirred over calcium hydride (72 h) and distilled, followed by storage over 3-Å molecular sieves. Methanol was distilled from magnesium and acetone was purified by stirring with $KMnO_4$, followed by distillation.

1-(t-Butyldiphenylsilyloxy)-2-propanone (**4a**). This compound was prepared from acetol in 93% yield, as described previously,[4] and purified by distillation to a pale yellow liquid, bp 144–153°C (0.9 mm). (A colourless product could be obtained by flash chromatography, using hexane:ethyl acetate = 30:1 to 10:1 as eluant but the distilled liquid was >98% pure.)

Spectral data, see Table I; MS: *m/z* (%) 256(11), 255(51), 241(14), 228(19), 227(100), 200(16), 199(86), 183(6), 181(14), 177(31), 117(5), 105(6), 78(5), 77(12); HRMS calcd. for $C_{15}H_{15}O_2Si$(M—C_4H_9) 255.0841, found 255.0808.

1-(t-Butyldiphenylsilyloxy)-2-butanone (**4b**). This compound was prepared in a yield of 92%, by the O-silylation procedure used for **4a**, as a colourless liquid, bp 152–156°C (0.8 mm). Spectral data, see Table I; MS: *m/z* (%) 270(19), 269(78), 255(15), 227(12), 200(23), 199(100), 191(42), 183(12), 181(17), 139(15), 135(12), 105(15), 78(10), 77(21); HRMS calcd. for $C_{16}H_{17}O_2Si$(M—C_4H_9) 269.0998, found 269.1025.

1-(t-Butyldiphenylsilyloxy)-3,3-dimethyl-2-butanone (**4c**). 3,3-Dimethyl-1,2-butanediol was selectively O-silylated by treatment with *t*-butyldiphenylsilyl chloride under the conditions used to prepare **4a, b** above, in almost quantitative yield. IR and NMR data (see Table I) indicated that compound **5** was at least 95% pure and it was thus used for the next step without further purification; MS: *m/z* (%) 299(3), 229(27), 200(20), 199(100), 184(8), 183(41), 135(11), 105(13), 77(7). To a solution of **5** (10.7 g, 0.03 mol) in acetone (25 mL) was added dropwise with stirring a solution of chromic acid (prepared from sodium dichromate (4.0 g) and sulfuric acid (3 mL) and diluting to 20 mL with water). When the reaction mixture remained orange it was diluted with water (200 mL) and extracted with diethyl ether (3 × 120 mL). Washing the combined ether layers (satd. $NaHCO_3$ aq., NaCl aq.) and drying ($MgSO_4$) gave crude **4c** on evaporation. The partly crystalline product afforded white plates on dissolving in 95% ethyl alcohol at 25°C and cooling to −20°C, mp 76.5–77.5°C (44%, based on 3,3-dimethyl-1,2-butanediol). Spectral data, see Table I; MS: *m/z* (%) 299(7), 298(26), 297(100), 267(7), 240(13), 239(58), 211(7), 199(16), 189(7), 183(20), 181(14), 163(15), 135(13), 105(9), 77(5). Anal. calcd. for $C_{22}H_{30}O_2Si$: C, 74.57; H, 8.47. Found: C, 74.38; H, 8.56.

1-(t-Butyldiphenylsilyloxy)butane (**6**). This compound was also prepared by the general silylation procedure above, from 1-butanol, as a colourless liquid (90%), bp 135–139°C (0.5 mm). Spectral data, see Table I; MS: *m/z* (%) 257(6), 256(27), 255(100), 200(10), 199(59), 184(11), 183(55), 123(18), 105(7), 77(5); HRMS calcd. for $C_{16}H_{19}OSi(M—C_4H_9)$ 255.1205, found 255.1154.

Preparation of O-Trimethylsilyl Cyanohydrins (**1a–c**) *Representative Synthetic Procedure* (**1b**): Trimethylsilyl cyanide (0.42 mL, 3.0 mmol) was added to a mixture of **4b** (0.98 g, 3.0 mmol) and freshly prepared potassium cyanide/18-crown-6 catalyst[5] (0.05 g), in dry hexane (3 mL) at 0°C. After addition, the reaction mixture was stirred for 48 h at 25°C, under nitrogen. Hexane (20 mL) was added and the solution filtered through Celite. The filtrate was washed with water (3 × 20 mL), brine (20 mL) and dried ($MgSO_4$). Evaporation afforded crude **1b**, which could be purified by HPLC or flash chromatography, eluting with hexane:ethyl acetate = 30:1, to afford pure **1b** as a colourless liquid (88%), bp 185°C (0.7 mm).[17] (For a discussion of the isolation and identification of the side product **7**, see below.)

Spectral data, see Table I; MS; *m/z* (%) 368(11), 271(100), 269(53), 199(13), 197(15), 193(30), 191(32), 145(17), 135(33), 105(8), 77(2); HRMS calcd. for $C_{20}H_{26}NO_2Si_2(M—C_4H_9)$ 368.1502, found 368.1482.

Also prepared by the above procedure were **1a**, bp 190°C (0.8 mm)[17] (69%) and **1c**, bp 180°C (0.7 mm)[17] (74%), the spectral data for which also appear in Table I. MS (**1a**): *m/z* (%) 354(15), 327(6), 271(100), 255(51), 199(6), 197(10), 193(17), 177(28), 135(17), 105(6); HRMS calcd. for $C_{19}H_{24}NO_2Si_2(M—C_4H_9)$ 354.1346, found 354.1347. MS (**1c**): *m/z* (%) 423(6), 396(54), 366(15), 313(43), 297(100), 271(77), 262(33), 239(59), 199(29), 197(35), 193(23), 135(49), 105(10), 91(17), 77(6); HRMS calcd. for $C_{22}H_{30}NO_2Si_2(M—C_4H_9)$ 396.1815, found 396.1820.

1-t-Butyl-1,1-diphenyl-3,3,3-trimethyldisiloxane (**7**). This compound was separated from **1a**, **1b**, or **1c** prepared as above and was isolated by careful flash chromatography (hexane:ethyl acetate = 30:1) or, more conveniently, by preparative HPLC, using hexane:ethyl acetate = 9:1. Compound **7** was a colourless oil, bp 309°C[17]; IR (liquid film): *ν* 1595, 1265, 1117, 1082, 840 cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 7.63 (m, 4H), 7.36 (m, 6H), 1.02 (s, 9H), 0.13 (s, 9H); ^{13}C NMR ($CDCl_3$): *δ* 136.1 (*C—1'*), 135.0 (*C—2',6'*), 129.3 (*C—4'*), 127.5 (*C—3',5'*), 26.8 ($C(CH_3)_3$), 19.2 ($C(CH_3)_3$), 2.2 ($Si(CH_3)_3$); MS: *m/z* (%) 313(2), 273(10), 272(27), 271(100), 255(7), 197(6), 195(7), 193(37), 183(19), 135(8), 105(7); HRMS calcd. for $C_{18}H_{25}OSi_2$ (M—CH_3) 313.1444, found 313.1423.

2,3-Epoxy-2-ethylpropanenitrile (**9**). 1-Hydroxy-2-butanone **10a** (2.65 g, 0.03 mol) was added to a solution of p-toluenesulfonyl chloride (6.9 g, 0.036 mol) and triethylamine (5.1 mL, 0.036 mol) in dichloromethane (15 mL) at 0°C during 1.5 h, with stirring. After stirring a further 6 h at 0°C and standing overnight at 0°C, the reaction mixture was poured into ice-water (75 mL) and extracted (CH_2Cl_2, 3 × 70 mL). The combined extracts were washed (satd. NH_4Cl 150 mL, brine 150 mL), dried ($MgSO_4$), and evaporated to give the crude 1-tosyloxy-2-butanone (**10b**) as an oil (6.44 g, 90%). IR (liquid film): *ν* 1743, 1729, 1602, 1370, 1180, 1019, 970, 822 cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 7.75 and 7.32 (dd, *J* = 8.0 Hz, 4H aromatic), 4.55 (s, 2H, CH_2O), 2.52 (q, *J* = 7.0 Hz, 2H, CH_2), 2.48 (s, 3H, $ArCH_3$), 1.05 (t, *J* = 7.0 Hz, 3H, CH_3). (The presence, and the amount, of the symmetrical ether **11** as contaminant can easily be determined from the ^1H NMR signal at *δ* ($CDCl_3$) 4.07 (s, 4H, CH_2). Compound **11** also showed similar signals to **10b** in the ^1H NMR at *δ* ($CDCl_3$) 2.65 (q, *J* = 7.0 Hz, 4H, CH_2) and 1.13 (t, *J* = 7.0 Hz, 6H, CH_3); ^{13}C NMR ($CDCl_3$): *δ* 203.3 (C=O), 47.9 (CH_2O), 33.0 (CH_2CO), 7.6 (CH_3); IR (liquid film): *ν* 1743, 1722, 1413, 1110 cm^{-1}.)

To a solution of the crude tosylate **10b** (6.44 g, 0.027 mol) in dichloromethane (15 mL) at 0°C was added potassium cyanide (1.7 g, 0.027 mol) and 18-crown-6 (0.1 g). After stirring 48 h at 0–3°C,

dichloromethane (50 mL) was added and the solution washed (water 2 × 50 mL, brine 50 mL) and dried ($MgSO_4$). Evaporation and distillation gave the product **9** as a colourless liquid, bp 28–30°C (1.2 mm), literature[18] bp 152° (0.7 g, 27%, based upon **10a**). IR (liquid film): ν 2249, 1469, 1054, 913 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.13 (d, J = 5.15 Hz, 1H) and 2.81 (d, J = 5.13 Hz, 1H, CH_2O), 1.85–1.69 (12-line m, 2H, CH_2), 1.08 (br t, J = 7.47 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 117.9 (*CN*), 51.8 (*C—3*), 49.1 (*C—2*), 26.9 (CH_2), 8.6 (CH_3); GC—MS (only one major component over range 50–200°C): *m/z* (%) 96(9), 82(60), 68(17), 67(27), 66(48), 64(15), 58(8), 57(100), 54(14), 52(58); HRMS calcd. for C_4H_4NO (M—CH_3) 82.0293, found 82.0308.

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