

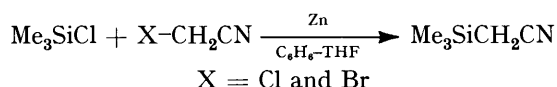
## A Simple Preparation of Trimethylsilylacetonitrile and a Novel Ring-opening of Epoxides with Trimethylsilylacetonitrile Anion

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Trimethylsilylacetonitrile (TMSAN) is prepared from halogenoacetonitrile and chlorotrimethylsilane using zinc as a halogen acceptor. TMSAN anion reacts with carbonyl compounds and epoxides to give  $\alpha\beta$ -unsaturated nitriles (1) and  $\gamma$ -trimethylsilyloxynitriles (4) and (6), respectively. The formation of the latter compounds is explained by the intermediacy of (3) which is generated by 1,4-migration of the trimethylsilyl group. Nitriles (4) and (6) are readily transformed to  $\gamma$ -lactone derivatives (5) and (7) with hydrochloric acid in aqueous methanol.

TRIMETHYLSILYLACETONITRILE (TMSAN) has broad synthetic applicability as a  $C_1$  or  $C_2$  synthon because it possesses two reaction sites. The trimethylsilylmethyl group is reactive towards proton-specific bases and the cyano group reacts with nucleophiles or acids. The presence of the trimethylsilyl group facilitates generation of the anion and results in extraordinary reactivity, because of the remarkable affinity of organosilyl groups for oxygen, which is well known for intramolecular migration<sup>1-4</sup> and intermolecular oxygen abstraction reactions.<sup>5-9</sup> Nevertheless the reported preparations of TMSAN use intractable materials<sup>10,11</sup> which do not allow large scale reactions. We report herein an improved preparation of TMSAN, and the reaction of TMSAN anion with epoxides to give consecutive ring-opened products (6) involving intramolecular migration of a trimethylsilyl group. Transformations of (4) and (6) to  $\gamma$ -lactone derivatives are also described.

Prolonged reflux of a mixture of chlorotrimethylsilane, halogenoacetonitrile  $XCH_2CN$  ( $X = Cl$  and  $Br$ ), and 2–3 mol. equiv. of granular zinc in benzene–tetrahydrofuran (1 : 1) gave TMSAN in 61% ( $X = Cl$ ) and 81% ( $X = Br$ ) yield as the result of dehalogenative coupling. When magnesium ribbon was used instead of granular zinc, separation of TMSAN was difficult and the yield was low. Although quenching of acetonitrile

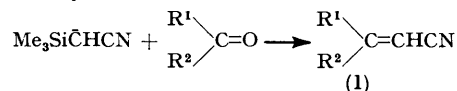


anion with chlorotrimethylsilane is the most straightforward route to TMSAN, the product is invariably contaminated with significant amounts of tris(trimethylsilyl)ketenimine which cannot be separated by distillation.<sup>12-14</sup> Previous syntheses used cyanogen<sup>10</sup> or sodium cyanide<sup>11</sup> and the relatively expensive chloromethyltrimethylsilane. Therefore our dehalogenative coupling method is more effective for selective preparation of TMSAN.

TMSAN anion was generated by the action of 1 mol. equiv. of *n*-butyl-lithium or lithium di-isopropylamide (LDA) in ether at  $-78^\circ C$ . Quenching these solutions with water regenerated TMSAN.

Carbonyl compounds were first used to check the character and reactivity of TMSAN anion. Olefin formation from an  $\alpha$ -silyl carbanion and carbonyl compounds is a well known reaction.<sup>5,6,15</sup> In this case the reaction proceeded smoothly to give  $\alpha\beta$ -unsaturated

nitriles (1).<sup>16</sup> Benzaldehyde, cinnamaldehyde, and cyclohexanone reacted with 1 mol. equiv. of TMSAN anion to give cinnamonitrile,<sup>17</sup> 5-phenylpenta-2,4-dienitrile,<sup>18</sup> and cyclohexylideneacetonitrile<sup>19</sup> in 77, 95, and 73% yield, respectively.



- a;  $R^1 = Ph$ ,  $R^2 = H$   
 b;  $R^1 = PhCH=CH$ ,  $R^2 = H$   
 c;  $R^1R^2 = [CH_2]_6$

The products were identified by comparison of spectral data with literature values. The results show that TMSAN anion can be used in place of cyanomethylenetriphenylphosphorane<sup>20,21</sup> or diethyl cyanomethylphosphonate,<sup>22-24</sup> with high reactivity and greater ease of handling.

Two possible products were expected for ring-opening of epoxides by TMSAN anion. The first is an  $\alpha$ -trimethylsilyl- $\gamma$ -hydroxynitrile, which could be transformed into an  $\alpha$ -methylene- $\gamma$ -lactone by a Peterson-type reaction and hydrolysis. The second is a cyclopropane derivative formed by spontaneous elimination of lithium trimethylsiloxy from the intermediate (2) as in Peterson-type reactions. However, unexpected results were obtained.

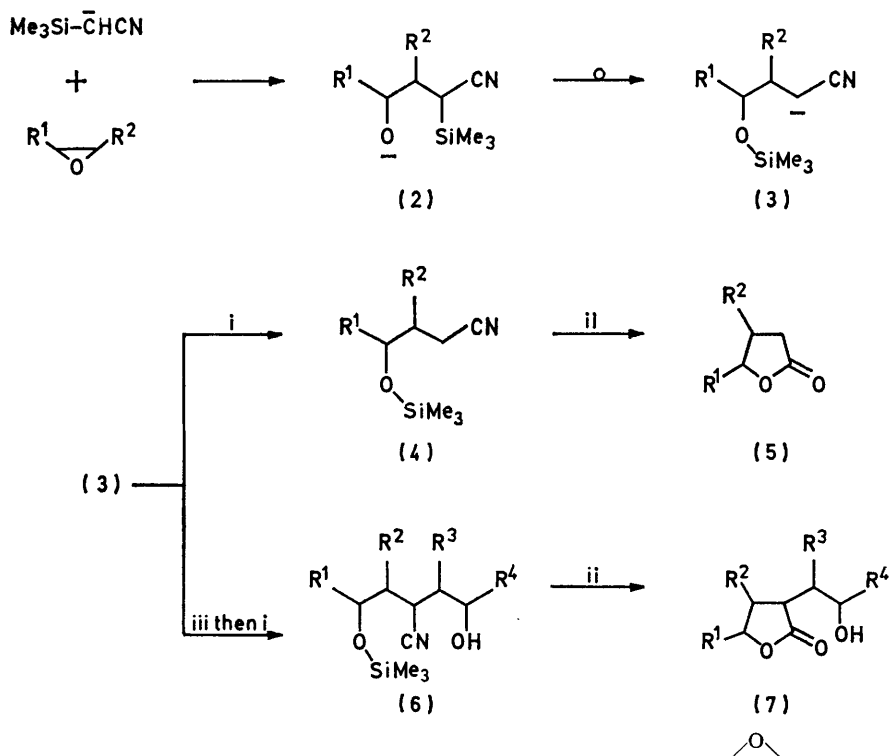
The reaction of TMSAN anion with 1 mol. equiv. of propylene oxide in dimethoxyethane between  $-30$  and  $-20^\circ C$  for 6 h gave unexpectedly 4-trimethylsilyloxyvaleronitrile (4a) in 94% yield after quenching with water. The structure was determined by analysis, and from the n.m.r. spectrum. The absence of a  $\nu(OH)$  band in the i.r. spectrum also supported the trimethylsilyl ether structure. These data were consistent with those found for an authentic sample, obtained by the normal fission of propylene oxide with acetonitrile anion<sup>25</sup> and quenching with chlorotrimethylsilane. The rate of the ring-opening reaction was not accelerated either by the addition of a catalytic amount of copper(I) iodide, or by the use of lithium bis(trimethylsilylcyanomethyl)copper(I).<sup>26</sup>

But-1-ene oxide gave exclusively 4-trimethylsilyloxyhexanenitrile (4b) (84%) under the same conditions. However, at higher temperatures ( $-20$  to  $20^\circ C$ ), a mixture of (4) and (6) was obtained in both cases, and could be separated by silica gel chromatography. Compounds (4c and d) were obtained as minor products from similar reactions of styrene oxide and cyclohexene oxide, respectively, even using a 1 : 1 mole ratio of reactants.

$\gamma$ -Trimethylsilyloxynitriles (6) were obtained selectively in good yields, by reaction of TMSAN anion with 2 mol. equiv. of the epoxides at room temperature. Formally, the nitriles (6) consist of two molecules of epoxide and a molecule of TMSAN. Their identities were confirmed by elemental analyses and n.m.r. spectra. A typical example is (6a), which shows unequivocally separated signals for the trimethylsilyl group at  $\delta$  0.12 (minor) and 0.15 (major). The splitting of the trimethylsilyl group results from discrimination among isomers caused by the presence of two asymmetric alkoxy carbon atoms. This supposition is based on the observation that the phenomenon was detected in the case of the 2,6-bis-

been reported,<sup>26-30</sup> the double anion behaviour of TMSAN anion is at present unique.

$\gamma$ -Trimethylsilyloxynitriles (4) and (6) are precursors of  $\gamma$ -lactone derivatives because a cyano group may be easily converted into carbonyl. In fact, an analogous transformation has been reported for  $\gamma$ -hydroxynitriles.<sup>27,30,31</sup> Acidic conditions were selected for the simultaneous desilylation and hydrolysis of the cyano group in nitriles (4) and (6) to give  $\gamma$ -lactones. *ca.* 2M-HCl in aqueous methanol was chosen as a standard reagent for lactonization based on the results in Table 2. The results are summarized in Table 1. The identities of the  $\gamma$ -lactones were confirmed by the presence of



SCHEME Reagents: i,  $\text{H}_2\text{O}$ ; ii, 2M-HCl-aqueous MeOH; iii,  $\text{R}^3\text{CH}-\text{CHR}^4$

(trimethylsilyloxy)nitrile (6a') and not in the case of the nitrile formed from isobutene oxide, where exchange between a trimethylsilyl group and a hydroxy proton is precluded. Moreover, the apparent non-equivalence within the *gem*-dimethyl group in (6a) reflects the magnetic anisotropy induced by the cyano group.

The results strongly indicate the intermediacy of the carbanion (3) which is generated by 1,4-migration of a trimethylsilyl group from the carbon atom to the oxyanion of (2). The carbanion (3) is then converted into (4) by protonation or into (6) by subsequent ring-opening of the epoxide. The isolation of (6e and f) which were obtained by the consecutive interaction of different types of epoxides, supports the stepwise process *via* intermediate (3) as shown in the Scheme. This stepwise behaviour of TMSAN anion should have wide synthetic applicability as a double anion equivalent. Although an intramolecular epoxynitrile cyclization has

$\nu_{\text{C}=\text{O}}$  around  $1780\text{ cm}^{-1}$  and by comparison with authentic samples.<sup>32,33</sup>

The direction of ring-opening of epoxides with TMSAN anion is more selective than that with diethylmalonate anion. For example, the former reagent selectively cleaves styrene oxide, while the latter is nonselective, in spite of a contrary statement in the literature.<sup>34</sup> Therefore,  $\gamma$ -lactone formation *via*  $\gamma$ -trimethylsilyloxynitriles is more effective than the diethylmalonate method.

#### EXPERIMENTAL

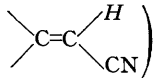
I.r. spectra were recorded with JASCO IR-403G and IR-S instruments. A JEOL C-60HL instrument was used to record  $^1\text{H}$  n.m.r. spectra, using tetramethylsilane as internal standard.  $\gamma$ -Caprolactone<sup>32</sup> and *trans*-2-hydroxycyclohexylacetic acid lactone<sup>33</sup> were prepared according to the literature.

*Preparation of Trimethylsilylacetonitrile.*—To a suspension

of chlorotrimethylsilane (36 g, 0.33 mol) and two equivalents of activated granular zinc (38 g, 0.58 mol) in benzene-THF (1:1; 400 ml) was added a solution of bromoacetonitrile (34.8 g, 0.29 mol) in benzene (20 ml) with gentle heating. The mixture was then refluxed for 16 h and poured into buffer solution (AcONa-AcOH) (300 ml). The organic layer was separated and the water layer extracted with benzene (4 × 200 ml). The combined extracts were washed with buffer solution (300 ml) several times and dried (CaCl<sub>2</sub>). After removal of the solvent the residue was distilled under reduced pressure giving pure product (29.6 g, 81%), b.p. 65–70 °C at 20 mmHg (Found: C, 52.9; H, 10.1; N, 12.35. C<sub>5</sub>H<sub>11</sub>NSi requires C, 53.05; H, 9.8; N, 12.35%; ν<sub>max</sub> (CCl<sub>4</sub>) 2 215 cm<sup>-1</sup> (C≡N); δ(CCl<sub>4</sub>) 0.23 (9 H, s, H<sub>3</sub>CSi) and 1.53 (2 H, s, CH<sub>2</sub>CN).

A similar procedure using chloroacetonitrile (36 h reflux) also gave TMSAN (61%).

**Reaction of TMSAN Anion with Benzaldehyde.**—To a solution of LDA formed from di-isopropylamine (0.516 g, 5.10 mmol) and n-butyl-lithium (4.6 ml, 1.1M) in THF (15 ml) was added a solution of TMSAN (0.567 g, 5.00 mmol) in THF (5 ml) at -78 °C. The mixture was stirred for 40 min at this temperature. A solution of benzaldehyde (0.529 g, 4.99 mmol) in THF (5 ml) was added to the

5.41 (1H, d, *J* 13.2 Hz, ) and 6.7–7.6 (8 H, m, Ph and olefinic protons).

**Reaction of TMSAN Anion with Cyclohexanone.**—To a TMSAN anion solution, formed from TMSAN (0.569 g, 5.02 mmol) and an equivalent amount of LDA, was added cyclohexanone (0.498 g, 5.07 mmol) at -78 °C. The mixture was treated as described above to give compound (1c) (0.442 g, 73%); ν<sub>max</sub> (CCl<sub>4</sub>) 2 230 (C≡N) and 1 633 cm<sup>-1</sup> (C=C); δ(CCl<sub>4</sub>) 1.67br (6 H, cyclohexyl), 2.2–2.5 (4 H, m, cyclohexyl), and 5.03br (1 H, s, olefin).

**Reaction of TMSAN Anion with Epoxides.**—(a) **Propylene oxide.** To a solution of LDA formed from di-isopropylamine (1.265 g, 12.5 mmol) and n-butyl-lithium (8.9 ml, 1.4M) in DME (20 ml) was added a solution of TMSAN (1.360 g, 12.0 mmol) in DME (5 ml) at -78 °C. The mixture was stirred for 40 min at this temperature. A solution of propylene oxide (0.604 g, 10.4 mmol) in DME (3 ml) was added dropwise at -78 °C and the temperature of the mixture was raised gradually to -30 °C. After stirring for an additional 6 h between -30 and -20 °C, saturated aqueous NH<sub>4</sub>Cl (20 ml) was added and the organic layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5 × 25 ml). The combined

TABLE I

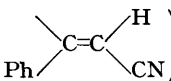
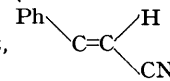
Isolated yields of products

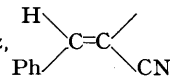
	R <sup>1</sup>	R <sup>2</sup>	Yield (%)		R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	Yield (%)	
			(4)	(5)					(6)	(7)
a	Me	H	94	72	Me	H	H	Me	80	52
b	Et	H	84	51	Et	H	H	Et	61	71
c	Ph	H	42 <sup>a</sup>	72	Ph	H	H	Ph	42	51
d	[CH <sub>2</sub> ] <sub>4</sub>		25 <sup>a</sup>	28	[CH <sub>2</sub> ] <sub>4</sub>			[CH <sub>2</sub> ] <sub>4</sub>	51	63
e					Me	H	H	Et	73 <sup>b</sup>	
f					Me	H		[CH <sub>2</sub> ] <sub>4</sub>	60 <sup>b</sup>	

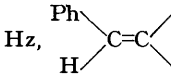
<sup>a</sup> Yield from separation of a mixture of (4) and (6). <sup>b</sup> Isolated as bis(trimethylsiloxy)derivatives.

TMSAN anion solution at -78 °C and the mixture was stirred for 1 h at -78 °C and 4 h at room temperature. It was quenched with aqueous NH<sub>4</sub>Cl and the organic layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (6 × 20 ml). The combined extracts were washed with saturated brine and dried (MgSO<sub>4</sub>). After removal of the solvent the residue was purified by column chromatography giving 1:1 *Z*- and *E*-cinnamonitrile (1a) (0.499 g, 77%); ν<sub>max</sub> (CCl<sub>4</sub>) 2 235

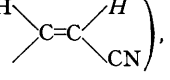
(C≡N) and 1 620 cm<sup>-1</sup> (C=C), δ(CCl<sub>4</sub>) 5.42 (1 H, d, *J* 12 Hz,

, 5.86 (1 H, d, *J* 16.5 Hz, ,

7.10 (1 H, d, *J* 12 Hz, , 7.37 (1 H, d, *J* 16.5

Hz, , and 7.4–7.9 (5 H, m, Ph).

**Reaction of TMSAN Anion with Cinnamaldehyde.**—To a TMSAN anion solution, formed from TMSAN (0.564 g, 4.98 mmol) and an equivalent amount of LDA, was added cinnamaldehyde (0.663 g, 5.02 mmol) at -78 °C. The mixture was treated as for the reaction with benzaldehyde, to give compound (1b) (0.782 g, 95%); ν<sub>max</sub> (CCl<sub>4</sub>) 2 232

cm<sup>-1</sup> (C≡N); δ(CCl<sub>4</sub>) 5.20 (1 H, d, *J* 7.5 Hz, ,

extracts were washed with saturated brine twice and dried (MgSO<sub>4</sub>). The residue, after removal of solvent under reduced pressure, was purified by silica gel column chromatography eluting with benzene to give 4-trimethylsiloxyvaleronitrile (4a) (1.68 g, 94%), b.p. 65–70 °C at 3 mmHg (Found: C, 56.3; H, 9.85; N, 8.3. C<sub>8</sub>H<sub>17</sub>NOSi requires C, 56.1; H, 10.0; N, 8.2%); ν<sub>max</sub> (CCl<sub>4</sub>) 2 265 cm<sup>-1</sup> (C≡N); δ(CCl<sub>4</sub>) 0.13 (9 H, s, H<sub>3</sub>CSi), 1.17 (3 H, d, *J* 6.0 Hz, H<sub>3</sub>CCHO), 1.67 (2 H, q, *J* 5.8 Hz, CH<sub>2</sub>CH<sub>2</sub>CN), 2.07 (2 H, t, *J* 6.1 Hz, CH<sub>2</sub>CN), and 3.94 (1 H, *J* 5.6 Hz, sextet CHOSi).

(b) **But-1-ene oxide.** To a TMSAN anion solution (8.05 mmol) in DME (12 ml) was added a solution of but-1-ene oxide (0.559 g, 7.75 mmol) in DME (3 ml) and the mixture was treated as described for the reaction with propylene oxide, giving 4-trimethylsiloxyacetonitrile (4b) (1.207 g, 84%), b.p. 67 °C at 3 mmHg (Found: C, 58.6; H, 10.5; N, 7.6. C<sub>9</sub>H<sub>19</sub>NOSi requires C, 58.3; H, 10.35; N, 7.55%); ν<sub>max</sub> (CCl<sub>4</sub>) 2 270 cm<sup>-1</sup> (C≡N); δ(CCl<sub>4</sub>) 0.12 (9 H, s, H<sub>3</sub>CSi), 0.86 (3 H, t, *J* 6.0 Hz, H<sub>3</sub>CCH<sub>2</sub>), 1.38 (2 H, q, *J* 6.0 Hz, H<sub>3</sub>CCH<sub>2</sub>), 1.63 (2 H, q, *J* 6.3 Hz, CH<sub>2</sub>CH<sub>2</sub>CN), 2.26 (2 H, t, *J* 6.5 Hz, CH<sub>2</sub>CN), and 3.59 (1 H, quintet, *J* 6.0 Hz, CHOSi).

(c) **Styrene oxide.** To a TMSAN anion solution (8.04 mmol) in DME (25 ml) was added a solution of styrene oxide (0.967 g, 8.04 mmol) in DME (5 ml) and the mixture was treated as described above. Purification by chromatography gave 4-phenyl-4-trimethylsiloxybutyronitrile (4c) (0.783 g, 42%) [and compound (6c) (0.478 g, 34%) as side product], b.p. 85 °C at 0.7 mmHg (Found: C, 66.85; H,

7.95; N, 5.85.  $C_{13}H_{19}NOSi$  requires C, 66.9; H, 8.2; N, 6.0%;  $\nu_{\max}$  ( $CCl_4$ ) 2 234  $cm^{-1}$  ( $C\equiv N$ );  $\delta(CCl_4)$  0.03 (9 H, s,  $H_3CSi$ ), 1.2—2.8 (4 H, m,  $2 \times CH_2$ ), 4.65 (1 H, t,  $J$  6.0 Hz,  $CHOSi$ ), and 7.10 (5 H, s, Ph).

(d) *Cyclohexene oxide*. To a TMSAN anion solution (10.1 mmol) in DME (20 ml) was added a solution of cyclohexene oxide (1.07 g, 10.9 mmol) in DME (4 ml) at  $-78^\circ C$  and the mixture was stirred for 13 h at room temperature. Work-up as described above afforded (2-trimethylsilyloxy-cyclohexyl)acetonitrile (4d) (0.539 g, 25%) [and (6d) (0.786 g, 51%)], b.p.  $100^\circ C$  at 0.5 mmHg (Found: C, 62.55; H, 10.25; N, 6.7.  $C_{11}H_{21}NOSi$  requires C, 62.5; H, 10.0; N, 6.65%;  $\nu_{\max}$  ( $CCl_4$ ) 2 250  $cm^{-1}$  ( $C\equiv N$ );  $\delta(CCl_4)$  0.13 (9 H, s,  $H_3CSi$ ), 1.0—2.0 (10 H, m, cyclohexyl), 2.36 (2 H, d,  $J$  4.5 Hz,  $CH_2CN$ ), and 3.3br (1 H,  $CHOSi$ ).

*Reaction of TMSAN Anion with Two Equivalents of Epoxide*.—(a) *Propylene oxide*. To a TMSAN anion solution (7.01 mmol) in THF (18 ml) was added a solution of propylene oxide (0.849 g, 14.6 mmol) in THF (5 ml) at  $-78^\circ C$ . The mixture was warmed to room temperature gradually and stirred for 14 h. Saturated aqueous  $NH_4Cl$  solution (15 ml) was added to the mixture and the organic layer was extracted with  $CH_2Cl_2$  ( $5 \times 20$  ml). The combined extracts were washed twice with saturated brine and dried ( $MgSO_4$ ). The residue, after removal of the solvent under reduced pressure, was purified by silica gel column chromatography eluting with  $CHCl_3$  to give 4-cyano-2-hydroxy-6-trimethylsilyloxyheptane (6a) (1.188 g, 80%), b.p.  $109$ — $111^\circ C$  at 0.5 mmHg (Found: C, 57.4; H, 10.0; N, 6.3.  $C_{11}H_{23}NO_2Si$  requires C, 57.6; H, 10.1; N, 6.1%;  $\nu_{\max}$  ( $CCl_4$ ) 3 630 (OH) and 2 250  $cm^{-1}$  ( $C\equiv N$ );  $\delta(CCl_4)$  0.12 and 0.15 (9 H, each s,  $H_3CSi$ ), 1.03 (3 H, d,  $J$  6.3 Hz,  $H_3CCHO$ ), 1.05 (3 H, d,  $J$  6.5 Hz,  $H_3CCHO$ ), 1.4—2.0 (4 H, m,  $2 \times CH_2$ ), 2.70 (1 H, quintet,  $J$  6.6 Hz,  $CHCN$ ), 2.8br (1 H, OH), and 3.9br (2 H,  $2 \times CH_2CHO$ ).

When the reaction mixture was quenched with an excess of  $Me_3SiCl$ , 4-cyano-2,6-bis(trimethylsilyloxy)heptane (6a') (76%) was obtained by distillation of the residue after removal of the solvent, b.p.  $90$ — $100^\circ C$  at 2 mmHg (Found: C, 55.65; H, 10.45; N, 4.65.  $C_{14}H_{31}NO_2Si_2$  requires C, 55.75; H, 10.35; N, 4.65%;  $\nu_{\max}$  ( $CCl_4$ ) 2 260  $cm^{-1}$  ( $C\equiv N$ );  $\delta(CCl_4)$  0.12 and 0.14 (18 H each s,  $H_3CSi$ ), 1.17 (6 H, d,  $J$  6.8 Hz,  $2 \times H_3CCHO$ ), 1.2—1.8 (4 H, m,  $2 \times CH_2$ ), 2.72 (1 H, quintet,  $J$  7.4 Hz,  $CHCN$ ), and 3.94 (2 H, quintet,  $J$  6.3 Hz,  $2 \times CHOSi$ ).

(b) *But-1-ene oxide*. To a solution of TMSAN anion (9.96 mmol) in THF (18 ml) was added a solution of but-1-ene oxide (1.458 g, 2.02 mmol) in THF (4 ml) at  $-78^\circ C$ . The mixture was treated similarly to (a) above. After removal of the solvent, the residue was distilled giving 5-cyano-3-hydroxy-7-trimethylsilyloxy-nonane (6b), (1.565 g, 61%) b.p.  $125^\circ C$  at 1.5 mmHg (Found: C, 60.65; H, 10.85; N, 5.5.  $C_{13}H_{27}NO_2Si$  requires C, 60.65; H, 10.55; N, 5.45%;  $\nu_{\max}$  ( $CCl_4$ ) 3 650 (OH) and 2 270  $cm^{-1}$  ( $C\equiv N$ );  $\delta(CCl_4)$  0.15 (9 H, s,  $H_3CSi$ ), 0.92 (3 H, t,  $J$  6.8 Hz,  $H_3CCH_2$ ), 1.3—1.8 (8 H, m,  $4 \times CH_2$ ), 2.3br (1 H, OH), 2.9br (1 H,  $CHCN$ ), and 3.7br (2 H, CHO).

(c) *Styrene oxide*. To a solution of TMSAN anion (10.0 mmol) in THF (20 ml) was added a solution of styrene oxide (2.399 g, 20.0 mmol) in THF (4 ml) at  $-78^\circ C$ . The mixture was treated similarly to (a) above. After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography eluting with  $CHCl_3$  to give 3-cyano-1-hydroxy-1,5-diphenyl-5-trimethylsilyloxy-pentane (6c) (1.489 g, 42%) (Found: C, 71.6; H,

7.9; N, 4.0.  $C_{21}H_{27}NO_2Si$  requires C, 71.35; H, 7.7; N, 3.95%;  $\nu_{\max}$  ( $CCl_4$ ) 3 640 (OH) and 2 265  $cm^{-1}$  ( $C\equiv N$ );  $\delta(CCl_4)$   $-0.05$ ,  $0.03$ , and  $0.05$  (9 H, each s,  $H_3CSi$ ), 1.5—2.1 (4 H, m,  $2 \times CH_2$ ), 2.75br (1 H, s, OH), 3.8br (1 H,  $CHCN$ ), 4.7br (2 H,  $2 \times CHO$ ), and 7.3 (10 H, m,  $2 \times Ph$ ).

(d) *Cyclohexene oxide*. To a solution of TMSAN anion (8.04 mmol) in THF (15 ml) was added a solution of cyclohexene oxide (1.603 g, 16.33 mmol) in THF (4 ml) at  $-78^\circ C$ . After similar treatment of the mixture to (a) above, the residue was purified by silica gel column chromatography, eluting with  $CHCl_3$  to give (2-hydroxycyclohexyl)-(2-trimethylsilyloxy-cyclohexyl)acetonitrile (6d) (1.271 g, 51%) (Found: C, 65.9; H, 10.1; N, 4.55.  $C_{17}H_{31}NO_2Si$  requires C, 66.0; H, 10.15; N, 4.55%;  $\nu_{\max}$  ( $CCl_4$ ) 3 630 (OH) and 2 245  $cm^{-1}$  ( $C\equiv N$ );  $\delta(CCl_4)$  0.14 and 0.16 (9 H, each s,  $H_3CSi$ ), 0.9—2.1 (20 H, m,  $2 \times$  cyclohexyl), 2.38 (1 H, d,  $J$  3.9 Hz, OH), 3.26 (1 H, t,  $J$  5.6 Hz,  $CHCN$ ), and 3.2—3.7br (2 H,  $2 \times CHO$ ).

(e) *Isobutene oxide*. To a solution of TMSAN anion (8.04 mmol) in THF (15 ml) was added a solution of isobutene oxide (1.169 g, 16.2 mmol) in THF (5 ml) at  $-78^\circ C$ . Similarly, the residue was purified by silica gel column chromatography, eluting with  $CHCl_3$  to give 4-cyano-2-hydroxy-2,6-dimethyl-6-trimethylsilyloxyheptane (1.547 g, 75%), b.p.  $112$ — $116^\circ C$  at 0.6 mmHg (Found: C, 60.45; H, 10.75; N, 5.4.  $C_{13}H_{27}NO_2Si$  requires C, 60.65; H, 10.55; N, 5.45%;  $\nu_{\max}$  ( $CCl_4$ ) 3 640 (OH) and 2 270  $cm^{-1}$  ( $C\equiv N$ );  $\delta(CCl_4)$  0.13 (9 H, s,  $H_3CSi$ ), 1.24 (3 H, s,  $H_3CC$ ), 1.29 (6 H, s,  $H_3CC$ ), 1.35 (3 H, s,  $H_3CC$ ), 1.6—2.0 (4 H, m,  $2 \times CH_2$ ), 2.36 (1 H, s, OH), and 2.8br (1 H,  $CHCN$ ).

*Stepwise Addition of Different Epoxides to TMSAN Anion*.—(a) 4-Cyano-2,6-bis(trimethylsilyloxy)octane (6e). To a solution of TMSAN anion (8.1 mmol) in dimethoxyethane (DME) (25 ml), propylene oxide (0.468 g, 8.05 mmol) in DME (5 ml) and but-1-ene oxide (0.585 g, 8.05 mmol) in DME (5 ml) were added at interval of 3 h between  $-30$  and  $-20^\circ C$ . After stirring for 12 h at room temperature, the mixture was quenched with an excess of  $Me_3SiCl$  (1.5 ml, 12 mmol) at room temperature. The solvent was removed under reduced pressure, and the residue was dissolved in ether (50 ml), filtering from  $LiCl$ . The crude product, after removal of the solvent, was distilled giving product (6e) (1.84 g, 73%), b.p.  $100$ — $110^\circ C$  at 0.3 mmHg (Found: C, 56.85; H, 10.4; N, 4.5.  $C_{15}H_{33}NO_2Si_2$  requires C, 57.1; H, 10.55; N, 4.45%;  $\nu_{\max}$  ( $CCl_4$ ) 2 265  $cm^{-1}$  ( $C\equiv N$ );  $\delta(CCl_4)$  0.12 (9 H, s,  $H_3CSi$ ), 0.15 (9 H, s,  $H_3CSi$ ), 0.90 (3 H, t,  $J$  6.8 Hz,  $H_3CCH_2$ ), 1.17 (3 H, d,  $J$  6.3 Hz,  $H_3CCHO$ ), 1.4—1.8 (6 H, m,  $3 \times CH_2$ ), 2.74 (1 H, quintet,  $J$  6.9 Hz,  $CHCN$ ), and 4.0 (2 H, m,  $2 \times CHOSi$ ).

(b) 2-(trans-2-Trimethylsilyloxy-cyclohexyl)-4-trimethylsilyloxyvaleronitrile (6f). To a solution of TMSAN anion (7.99 mmol) in DME (25 ml), propylene oxide (0.466 g, 8.02 mmol) in DME (5 ml) and cyclohexene oxide (0.791 g, 8.06 mmol) in DME (5 ml) were added at intervals of 3 h between  $-30$  and  $-20^\circ C$ . After stirring for 12 h at room temperature, the mixture was quenched with  $Me_3SiCl$  (1.5 ml, 12 mmol) at room temperature. The solvent was removed under reduced pressure, and the residue dissolved in ether (50 ml), filtering from  $LiCl$ . The crude product, after removal of the solvent, was purified by silica gel column chromatography giving product (6f) (1.644 g, 60%), b.p.  $118$ — $120^\circ C$  at 0.3 mmHg (Found: C, 59.6; H, 10.3; N, 4.35.  $C_{17}H_{35}NO_2Si_2$  requires C, 59.7; H, 10.35; N, 4.1%;  $\nu_{\max}$  ( $CCl_4$ ) 2 255  $cm^{-1}$  ( $C\equiv N$ );  $\delta(CCl_4)$  0.14 (18 H, s,  $H_3CSi$ ), 1.18 (3 H, d,  $J$  6.3 Hz,  $H_3CCHO$ ), 2.1—1.0 (11 H,

m), 3.5—2.5 (2 H, m, CHOSi and CHCN), and 3.9 (1 H, m, CHOSi).

**Lactonization of  $\gamma$ -Trimethylsiloxy nitriles.**—(a)  $\gamma$ -Valerolactone (5a). To a solution of 4-trimethylsiloxyvaleronitrile (4a) (1.357 g, 7.91 mol) in methanol (20 ml) was added concentrated HCl (2 ml) and the mixture was refluxed for 7 h. After removal of methanol under reduced pressure the residue was dissolved in water (10 ml) and hydrolysed with an excess of NaHCO<sub>3</sub> for 1 h. The mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (4 × 30 ml). The combined extracts were washed twice with water and dried (MgSO<sub>4</sub>). After removal of the solvent, purification of the residue by chromatography gave  $\gamma$ -valerolactone (0.571 g, 72%).

Yields of  $\gamma$ -valerolactone from (4a) under other acidic conditions are summarized in Table 2.

TABLE 2  
Yields of  $\gamma$ -valerolactone

Reagent	Solvent	Conditions T/°C (t/h)	Yield (%)
2M-HCl	MeOH	60 (7)	72
dry HCl	Et <sub>2</sub> O	40 (1)	52
BF <sub>3</sub> ·2MeOH	MeOH	70 (5)	40
TiCl <sub>4</sub>	CH <sub>2</sub> Cl <sub>2</sub>	40 (1)	15
4M-HCl	Dioxan	90 (4)	63
<i>p</i> -MeC <sub>6</sub> H <sub>4</sub> SO <sub>3</sub> H	EtOH	80 (2)	20

(b)  $\gamma$ -Caprolactone (5b). Analogous treatment of (4b) (0.936 g, 5.05 mmol) in methanol (20 ml) gave (5b) (0.291 g, 51%),  $\nu_{\max}$  (CCl<sub>4</sub>) 1 783 cm<sup>-1</sup> (C=O);  $\delta$ (CCl<sub>4</sub>) 1.00 (3 H, t, *J* 6.5 Hz, H<sub>3</sub>CCH<sub>2</sub>), 1.4—2.5 (6 H, m, 3 × CH<sub>2</sub>), and 4.33 (1 H, quintet, *J* 6.3 Hz, CHO).

(c) 4-Phenyl- $\gamma$ -butyrolactone (5c). Analogous treatment of (4c) (0.535 g, 2.29 mmol) in MeOH (18 ml) gave (5c) (0.268 g, 72%) [and methyl 4-methoxy-4-phenylbutyrate (10.077 g, 16%) as a side product] (Found: C, 74.2; H, 6.15. C<sub>10</sub>H<sub>10</sub>O<sub>2</sub> requires C, 74.05; H, 6.2%);  $\nu_{\max}$  (CCl<sub>4</sub>) 1 785 cm<sup>-1</sup> (C=O);  $\delta$ (CCl<sub>4</sub>) 1.9—2.6 (4 H, m, 2 × CH<sub>2</sub>), 5.41 (1 H, m, PhCHO), and 7.25 (5 H, s, Ph).

(d) *trans*-2-Hydroxycyclohexylacetic acid lactone (5d). Analogous treatment of (4d) (0.487 g, 2.30 mmol) in MeOH (7 ml) gave 2-methoxycarbonylcyclohexanol which was converted into (5d) (0.090 g, 28%) by refluxing a benzene solution (10 ml) with toluene-*p*-sulphonic acid (0.050 g)  $\nu_{\max}$  (CCl<sub>4</sub>) 1 783 cm<sup>-1</sup> (C=O);  $\delta$ (CCl<sub>4</sub>) 1.2—2.5 (11 H, m) and 3.69br (1 H, CHO).

(e) 2-(2-Hydroxypropyl)- $\gamma$ -valerolactone (7a). Analogous treatment of (6a') (1.042 g, 3.46 mmol) in MeOH (18 ml) gave pure oily lactone (7a) (0.282 g, 52%) (Found: C, 60.65; H, 9.1. C<sub>9</sub>H<sub>14</sub>O<sub>3</sub> requires C, 60.75; H, 8.9%);  $\nu_{\max}$  (CCl<sub>4</sub>) 3 500 (OH) and 1 774 cm<sup>-1</sup> (C=O);  $\delta$ (CDCl<sub>3</sub>) 1.23 (3 H, d, *J* 6.5 and 0.9 Hz, H<sub>3</sub>CCHO), 1.39 (3 H, dd, *J* 6.8 and 2.6, H<sub>3</sub>CCHO), 1.5—3.7 (5 H, m, OH and 2 × CH<sub>2</sub>), 3.9br (1 H, CHC=O), and 4.75 (2 H, m, 2 × CHO).

(f) 2-(2-Hydroxybutyl)- $\gamma$ -caprolactone. Analogous treatment of (6b) (1.129 g, 4.38 mmol) in MeOH (10 ml) gave pure oily lactone (7b) (0.538 g, 71%) (Found: C, 64.3; H, 10.0. C<sub>10</sub>H<sub>18</sub>O<sub>3</sub> requires C, 64.5; H, 9.75%);  $\nu_{\max}$  (CCl<sub>4</sub>) 3 500 (OH) and 1 774 cm<sup>-1</sup> (C=O);  $\delta$ (CCl<sub>4</sub>) 0.95 (3 H, t, *J* 7.1 Hz, H<sub>3</sub>CCH<sub>2</sub>), 1.01 (3 H, t, *J* 7.1 Hz, H<sub>3</sub>CCH<sub>2</sub>), 1.2—2.9 (8 H, m, 4 × CH<sub>2</sub>), 3.25br (1 H, OH), 3.5br (1 H, CHC=O), 4.29 (1 H, quintet, *J* 6.2 Hz, CHO), and 4.37 (1 H, quintet, *J* 6.2 Hz, CHO).

(g) 2-(2-Hydroxy-2-phenylethyl)-4-phenyl- $\gamma$ -butyrolactone (7c). Analogous treatment of (6c) (0.413 g, 1.17 mmol) in MeOH (15 ml) and H<sub>2</sub>O (10 ml) gave pure oily lactone

(7c) (0.144 g, 51%) (Found: C, 76.7; H, 6.65. C<sub>18</sub>H<sub>18</sub>O<sub>3</sub> requires C, 76.55; H, 6.45%);  $\nu_{\max}$  (CCl<sub>4</sub>) 3 630 (OH) and 1 774 cm<sup>-1</sup> (C=O);  $\delta$ (CCl<sub>4</sub>) 1.2—2.8 (5 H, m, 2 × CH<sub>2</sub> and CH), 3.6br (1 H, OH), 4.8 (1 H, m, PhCHO), 5.34 (1 H, t, *J* 6.3 Hz, PhCHO), and 7.2 (10 H, m, 2 × Ph).

(h) *trans*-2-Hydroxy-1-(2-hydroxycyclohexyl)cyclohexylacetic acid lactone (7d). Analogous treatment of (6d) (0.771 g, 2.49 mmol) in MeOH (10 ml) gave pure oily lactone (7d) (0.365 g, 62%) (Found: C, 70.25; H, 9.55. C<sub>14</sub>H<sub>22</sub>O<sub>3</sub> requires C, 70.55; H, 9.3%);  $\nu_{\max}$  (CCl<sub>4</sub>) 3 600 (OH) and 1 778 cm<sup>-1</sup> (C=O),  $\delta$ (CCl<sub>4</sub>) 1.0—2.1 (18 H, ring protons), 2.40 (1 H, t, *J* 11.6 Hz, CHC=O), 2.73br (1 H, s, OH), and 3.6br (2 H, 2 × CH-O).

[7/1627 Received, 12th September, 1977]

#### REFERENCES

- I. Matsuda, K. Itoh, and Y. Ishii, *J. Chem. Soc. (C)*, 1969, 701.
- I. Matsuda, K. Itoh, and Y. Ishii, *J. Organometallic Chem.*, 1969, **19**, 339.
- I. Matsuda, K. Itoh, and Y. Ishii, *J. Chem. Soc. (C)*, 1971, 1850.
- A. G. Brook, *Accounts Chem. Res.*, 1974, **7**, 77.
- D. J. Peterson, *J. Org. Chem.*, 1968, **33**, 780.
- K. Shimoji, H. Taguchi, K. Oshima, H. Yamamoto, and H. Nozaki, *J. Amer. Chem. Soc.*, 1974, **96**, 1620; *Bull. Chem. Soc. Japan*, 1974, **47**, 2529.
- K. Naumann G. Zon, and K. Mislow, *J. Amer. Chem. Soc.*, 1969, **91**, 7012.
- L. Horner and W. D. Balzer, *Tetrahedron Letters*, 1965, 1157.
- H. Suzuki, M. Ohashi, K. Itoh, I. Matsuda, and Y. Ishii, *Bull. Chem. Soc. Japan*, 1975, **48**, 1922.
- M. Prober, *J. Amer. Chem. Soc.*, 1955, **77**, 3224.
- K. Shiina and M. Kumada, *Memorials Faculty Eng. Osaka City Univ.*, 1962, **3**, 195 (*Chem. Abs.*, 1963, **58**, 3455f).
- G. A. Cornowicz and R. West, *J. Amer. Chem. Soc.*, 1971, **93**, 1714.
- J. Llonch and E. Frainnet, *Compt. rend.*, 1973, **276C**, 1803.
- D. S. Watt, *Synth. Comm.*, 1974, **4**, 127.
- T. H. Chan and E. Chang, *J. Org. Chem.*, 1974, **39**, 3264.
- I. Ojima, M. Kumagai, and Y. Nagai, *Tetrahedron Letters*, 1974, 4005.
- C. J. Pouchert, 'The Aldrich Library of IR Spectra,' 2nd edn., p. 979F; C. J. Pouchert and J. R. Campbell, 'The Aldrich Library of NMR Spectra,' vol. 7, p. 121A.
- T. J. van Bergen and R. M. Kellogg, *J. Org. Chem.*, 1971, **36**, 1705.
- G. Descotes and P. Laconche, *Bull. Soc. chim. France*, 1968, 2149.
- G. P. Schiemenz and H. Engelhard, *Chem. Ber.*, 1961, **94**, 578.
- S. Trippett and D. M. Walker, *J. Chem. Soc.*, 1961, 1266.
- W. S. Wadsworth, jun., and W. D. Emmons, *J. Amer. Chem. Soc.*, 1961, **83**, 1733.
- B. Deshamps, G. Lefebvre, and J. Seyden-Penne, *Tetrahedron*, 1973, **29**, 2437.
- A. Loupy, K. Sogadji, and J. Seyden-Penne, *Synthesis*, 1977, 126.
- K. Enoki, T. Yao, T. Kaku, K. Ishii, and K. Sasai, *J.P. 74/14,424* (*Chem. Abs.*, 1974, **81**, 3392n).
- C. R. Johnson, R. W. Herr, and D. M. Wieland, *J. Org. Chem.*, 1973, **38**, 4263.
- G. Stork, L. D. Cama, and D. R. Coulson, *J. Amer. Chem. Soc.*, 1974, **96**, 5268.
- G. Stork and J. F. Cohen, *J. Amer. Chem. Soc.*, 1974, **96**, 5270.
- J. Y. Lallemand and M. Onanga, *Tetrahedron Letters*, 1975, 585.
- R. Achini and W. Oppolzer, *Tetrahedron Letters*, 1975, 369.
- N. R. Easton, J. H. Gardner, and J. R. Stevens, *J. Amer. Chem. Soc.*, 1947, **69**, 2941.
- S. E. Boxer and R. P. Linstead, *J. Chem. Soc.*, 1931, 74; 1932, 115.
- M. S. Newman and C. A. V. Werf, *J. Amer. Chem. Soc.*, 1945, **67**, 233.
- R. R. Russell and C. A. V. Werf, *J. Amer. Chem. Soc.*, 1947, **69**, 11.