Synthesis of Pyrrolidinones *via* Free-radical Cyclisations: Potential Application to the Kainoids

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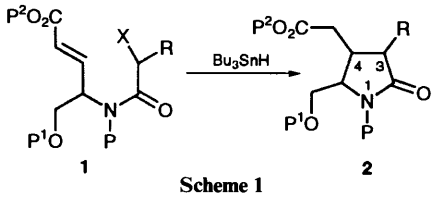
The tin hydride-mediated cyclisation of a range of DL-serine-derived α-chloro amides **1** to form pyrrolidinones has been examined. The yield and stereoselectivity of the cyclisation process was found to be markedly affected by the nature of the substituent at the site of radical generation. Thus, radicals substituted at the α-position by methyl, phenyl, dichloro and sulfanylphenyl substituents underwent smooth cyclisation to give excellent yields (58–95%) of a mixture of diastereoisomeric pyrrolidinones while the hydrogen-substituted congener cyclised in only 31–38% yield. This procedure has potential application to pyrrolidinone/pyrrolidine natural product synthesis and, in particular, to the kainoid amino acids.

There have been numerous studies directed towards the development of new syntheses of the pyrrolidine ring which is present in a wide variety of natural products. For example, the free-radical cyclisations of β-amino radicals have been extensively investigated and applied to the synthesis of a number of biologically important compounds including cyclic amino acids.[1] In comparison, the synthesis of pyrrolidinones using, for example, radical cyclisations has received little attention.[2] Recently, however, the cyclisation of *N*-allylic-α-halogeno amides using tin hydride (or halogen atom-transfer[3]) to form pyrrolidinones has been examined and the success of the cyclisation has been shown to be influenced by reaction temperature and nitrogen substituents. These change either the conformer population or the barrier to rotation around the amide bond.[4] In this paper[5] we report the cyclisation of a range of α-chloro amides **1** (with varying R substituents) to form substituted pyrrolidinones of type **2** (Scheme 1). The effect of

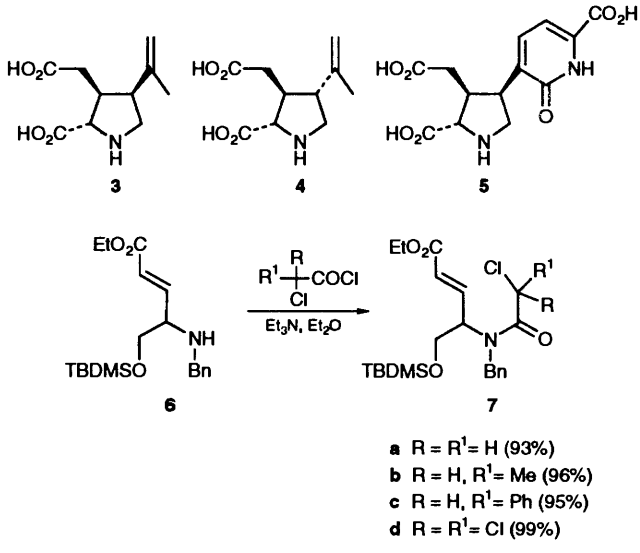


Scheme 1

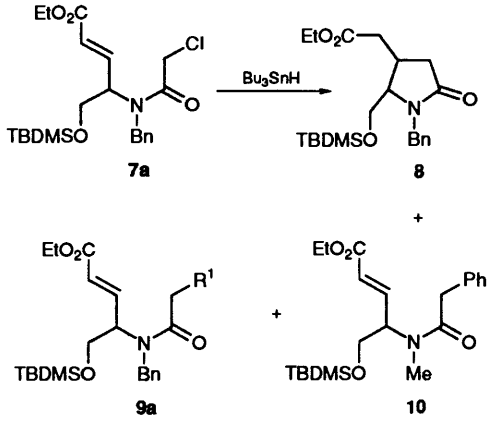
temperature, substituents (at the site of radical generation) and protecting groups (*e.g.* alcohol and ester) on the yield and diastereoselectivity of the cyclisation has been investigated. This approach has potential application to the preparation of a number of pyrrolidinone/pyrrolidine natural products. This includes the synthesis of kainic acid **3**, allokainic acid **4** and acromelic acid A **5** which are members of a group of biologically important amino acids known as the kainoids.[6]

The precursor α-chloro amides **7a–d** were prepared from reaction of the known secondary amine **6**, prepared from DL-serine,[7] with the appropriate acid chloride (Scheme 2). The α-chloro amides **7a–d** were isolated in excellent yield (93–99%) as colourless oils after column chromatography.

We began our investigation by examining the cyclisation of the α-chloro amide **7a**, which on treatment with Bu_3SnH and AIBN (catalytic) in boiling benzene yielded a number of products after chromatography (Scheme 3, Table 1, entry 1). The desired disubstituted pyrrolidinone **8** was isolated in only 31% yield (as predominantly the 4,5-*trans*-isomer) while the ethanamide **9a**, resulting from simple chloro amide **7a** reduction, was formed in 35% yield. In addition, the 1,4-aryl migration product **10** was formed in 13% yield. This presumably results from an intramolecular *ipso*-attack[8] as shown in Scheme 4. When the reaction was carried out at higher temperature, using boiling toluene (Table 1, entry 2) the yield of pyrrolidinone **8** was improved to 38% but its formation was found to be less diastereoselective (*i.e. trans*-/*cis*- ratio 4.2:1). In addition, the by-products **9a** and **10** were still formed in significant yields (15 and 18%, respectively). The ^1H NMR spectrum of **7a** in $CDCl_3$ at room temperature indicated the



Scheme 2 (Bn = benzyl)

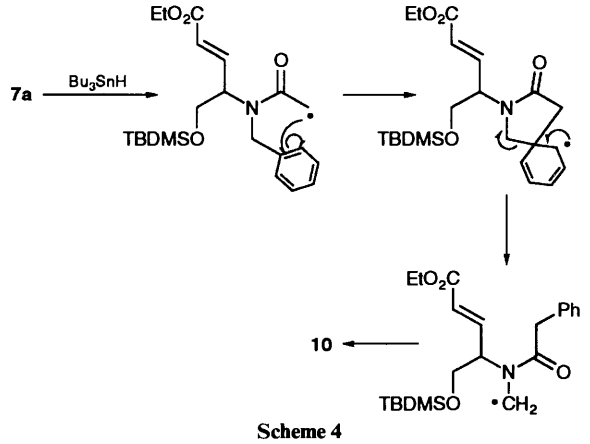


Scheme 3

Table 1 Tin-mediated radical cyclisations of the chloro amides **7**

Entry	Chloride **7**	Reaction temp. (°C)	Products (yield %)	C-4:C-5 *trans*/*cis* ratio
1	**a**	80	**8**(31) + **9a**(35) + **10**(13)	15:1
2	**a**	110	**8**(38) + **9a**(15) + **10**(18)	4.2:1
3	**b**	80	**9b**(4) + **11b**(25) + **12b**(28) + **13b**(28)	2.2:1
4	**c**	80	**11c**(31) + **12c**(31) + **13c**(31)	2:1
5	**c**	110	**11c**(32) + **12c**(32) + **13c**(32)	2:1
6	**d**	80	**15**(77)	5:2
7	**d**	110[a]	**8**(82)	2.7:1

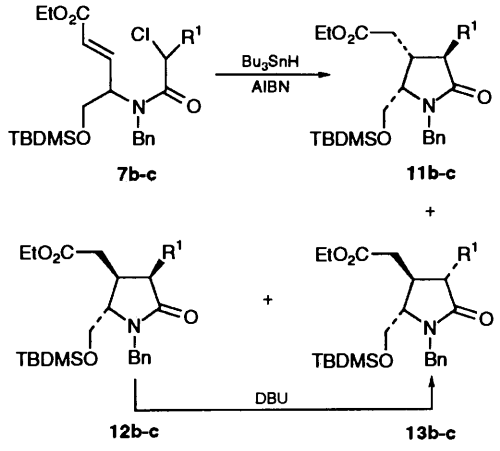
[a] Reaction performed using 3.3 equiv. of Bu_3SnH.



Scheme 4

presence of two amide conformers. However, when the ^1H NMR spectrum of **7a** was recorded at 80 °C ([$^2H_8$]toluene) there was free rotation about the amide bond.[4] It, therefore, seems likely that the formation of **10** occurs because of the high reactivity of the radical derived from **7a** [compared to those generated from substituted analogues **7b,c** (see later)] rather than any conformational effect.

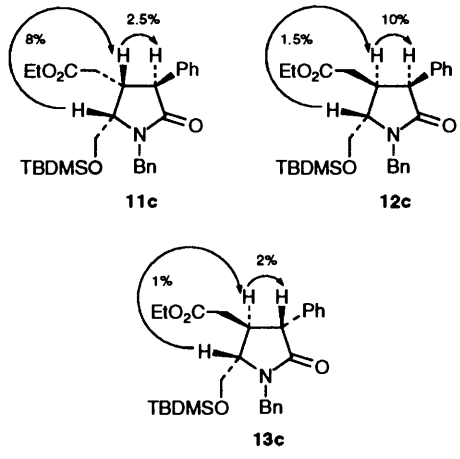
Cyclisations of the substituted chloro amides **7b,c** were found to be much more efficient (Scheme 5). Thus, on reaction of



Scheme 5

chloropropionamide **7b** with Bu_3SnH in boiling benzene, the separable pyrrolidinones **11b–13b** were isolated in a combined yield of 81%, while the non-cyclised by-product **9b** was formed in only 4% yield (Table 1, entry 3). The methyl substituent at the site of radical generation obviously had a dramatic influence on the efficiency of the cyclisation.

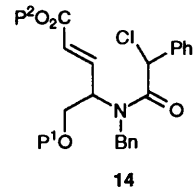
Interestingly, the cyclisation of the chloro-2-phenylacetamide **7c** in refluxing benzene or toluene afforded an almost quantitative combined yield of the separable pyrrolidinones **11c–13c** (Table 1, entries 4 and 5). None of the reduced compound **9c** was apparently formed. Cyclisation using either benzene or toluene as the solvent gave rise to a mixture of pyrrolidinone diastereoisomers **11c–13c** in the ratio 1:1:1. Attempted cyclisation of **7c** in benzene at lower temperature (40 °C) yielded only starting material on TLC analysis and pyrrolidinone **11c–13c** formation was only observed when the reaction temperature was raised to 80 °C. The pyrrolidinones **11c–13c** were again isolated as a 1:1:1 mixture in a combined yield of 73% (determined from the ^1H NMR spectrum). The stereochemistry of the pyrrolidinone diastereoisomers was deduced from NOE experiments (some of which are shown in Scheme 6) and confirmed by base-induced epimerisation experiments using



Scheme 6

DBU. Thus, when treated with DBU in boiling benzene the pyrrolidinone **12c** was cleanly converted into the all-*trans*-pyrrolidinone **13c** by epimerisation at the C-3 position. The epimerisation of pyrrolidinones of type **12** to **13** could be employed in allokainoid amino acid synthesis.

The related α-chloro amides **14e** and **14f*** cyclised in similar yield and diastereoselectivity to **7c**. Thus, cyclisation of **14e** or



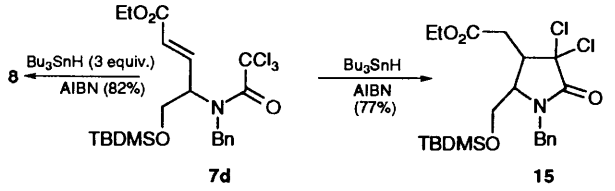
14e P^1 = TBDPS, P^2 = Et
f P^1 = TBDMS, P^2 = Bu^t

14f using Bu_3SnH (1.1 equiv.) in refluxing benzene both

* Chloroamides **14e** and **14f** were prepared in a similar manner (from DL-serine) to **7c**.

produced three pyrrolidinones (in the ratio 1.2:1:1.25 and 1.25:1:1.2, respectively) in 83% yield. The cyclisation of **14e** in toluene also gave similar results. From this it is clear that the alcohol and ester protecting groups exert little influence over the cyclisation.

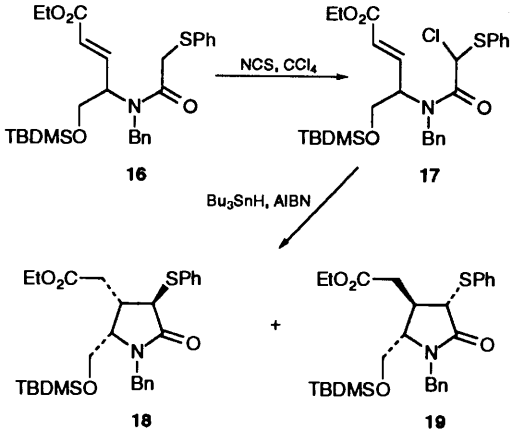
The cyclisation of the trichloroacetamide **7d** was also investigated (Scheme 7). On reaction of **7d** with 1.1 equiv. of



Scheme 7

Bu_3SnH in refluxing benzene the desired dichloro-substituted lactam **15** was isolated in 77% yield after column chromatography (Table 1, entry 6). This is surprising considering the electrophilic nature of the radical derived from **7d**, which was expected[9] to cyclise in low yield onto the electron-poor double bond. Treatment of trichloroacetamide **7d** with 3.3 equiv. of Bu_3SnH in refluxing toluene afforded the disubstituted pyrrolidinone **8** in 82% yield (Table 1, entry 7). This contrasts with the earlier cyclisation of the monochloroacetamide **7a** which yielded predominantly uncyclised by-products (the pyrrolidinone **8** being formed in only 31–38% yield). It is noted that both cyclisation of **7a** and **7d** in toluene afforded the pyrrolidinone **8** in a similar diastereoisomer ratio (*i.e.* 4.2:1 and 2.7:1).

We next investigated the cyclisation of the *S*-phenyl derivative **17** prepared on chlorination of **16*** using *N*-chlorosuccinimide in carbon tetrachloride (Scheme 8).[10] On treatment



Scheme 8

with Bu_3SnH (1.1 equiv.) the separable pyrrolidinones **18** and **19** were isolated in unoptimised yields of 33 and 25%, respectively. The stereochemistry of these isomers was deduced by treatment with DBU (which yielded no C-3 epimerisation) and reduction using Raney nickel[10] in boiling ethanol to give the previously prepared pyrrolidinone **8**.

This work has demonstrated the importance of the substituents at the site of radical generation and temperature on the efficiency of cyclisation of α-chloro amides. Thus, extremely efficient ring formation can be achieved with methyl, phenyl, dichloro and phenylsulfanyl substituents in boiling benzene or toluene. It is also clear that the stereoselectivity observed in the cyclisation of the α-carbamyl radicals differs from that expected for simple 1-substituted hex-5-enyl radicals.[11] The preferential *cis*-product formation found for the cyclisation of β-amino radicals contrasts with the predominant *trans*-(C-3:C-4) product observed here.

Future work will look at the effect of the nitrogen protecting group on the radical cyclisation and the application of this chemistry to natural product synthesis using enantiomerically pure serine.

* Compound **16** was prepared by reaction of the amine **6** with (phenylsulfanyl)acetyl chloride in diethyl ether.

Experimental

IR spectra (ν_{max}) were recorded on a Perkin-Elmer FT IR 1720X spectrophotometer as neat films or emulsions in Nujol; only selected resonances are reported as strong (s), medium (m) or weak (w). ^1H NMR spectra (δ_H) were recorded using JEOL FX 270 and 400 spectrometers. Chemical shifts are quoted on the scale using residual solvent or using tetramethylsilane as an internal standard. *J* Values are given in Hz. ^{13}C NMR spectra (δ_C) were recorded at 67.5 MHz on a FX 270 spectrometer. Mass spectra were recorded on a Kratos MS 25 (low resolution) or a Kratos VG ZAB-1F (high resolution) instrument. Tributyltin hydride (Bu_3SnH) was purchased from Lancaster Chemical Company and distilled before use. TLC was performed on aluminium plates coated with Merck silica gel $60F_{254}$. Compounds were visualised with iodine or a solution of alkaline potassium permanganate. Column chromatography was carried out on silica gel 60 (Merck 7734). M.p.s were recorded on a Kofler hot-stage melting point apparatus and are uncorrected.

General Procedure for the Preparation of the Chloro Amides **7a–d**.—To a solution of the amine **6** (0.21–0.96 mmol, 1 equiv.) in diethyl ether (*ca.* 20 cm^3 $mmol^{-1}$ of amine) at 0 °C was added triethylamine (1.2 equiv.) followed by a solution of the acid chloride (1.2 equiv.) in diethyl ether (*ca.* 5 cm^3 $mmol^{-1}$ of amine). The resultant mixture was then allowed to warm to room temperature after which it was stirred for a further 0.5 h. After dilution of the mixture with water and further diethyl ether, the organic layer was separated, washed with brine, dried ($MgSO_4$) and evaporated under reduced pressure to afford crude product.

Ethyl 4-(2-*chloro*-N-*benzylacetamido*)-5-(tert-*butyldimethylsiloxy*)*pent*-2-*enoate* **7a**. This compound was prepared from the amine **6** (0.35 g, 0.96 mmol) and chloroacetyl chloride (0.09 cm^3, 1.16 mmol) using the general procedure. Purification using column chromatography (silica; ethyl acetate–dichloromethane, 1:32) afforded the *title compound* **7a** (0.39 g, 93%) as a colourless viscous oil; R_F 0.30 (ethyl acetate–dichloromethane, 1:32); ν_{max}(thin film)/cm^{-1} 2929m, 2857m, 1721s, 1662s, 1471m, 1415m, 1368m, 1259m, 1185m, 1107m, 1039w and 838s; δ_H(270 MHz; $CDCl_3$) (mixture of conformers) 7.39–7.23 (5 H, m, aromatics), 7.00 and 6.83 (1 H, 2 × dd, *J* 6 and 16 Hz, CH=C*H*CO_2), 6.09–5.88 (1 H, m, C*H*=$CHCO_2$), 4.97–4.35 (3 H, m, NC*H* and NCH_2Ph), 4.18 (2 H, q, *J* 7, CO_2CH_2), 4.04–3.65 (4 H, m, $NCOCH_2Cl$ and CH_2OSi), 1.28 (3 H, t, *J* 7.3 Hz, $CO_2CH_2CH_3$), 0.87 [9 H, s, $SiC(CH_3)_3$] and 0.04 and 0.02 (6 H, 2 × s, 2 × $SiCH_3$); δ_C(67.5 Hz; $CDCl_3$) 168.1, 167.5, 165.7, 165.2 (CO_2 and NCO), 142.7, 141.8 (*C*H=C), 137.7, 136.7 (C–*C*=C), 129.0, 128.4, 127.8, 127.2, 126.1, 124.4, 123.8 (*C*H=C), 62.9, 62.4, 60.7, 60.5, 59.1, 50.7, 41.8, 41.5 ($NCOCH_2$, CO_2-CH_2, CH_2OSi, NCH and NCH_2Ph), 25.7 [$SiC(CH_3)_3$], 18.1 [$SiC(CH_3)_3$], 14.1 ($CO_2CH_2CH_3$) and −5.7 (2 × $SiCH_3$); *m/z* (CI, NH_3) 440 (M^{35} + H^+, 50%), 406 (100), 308 (40), 257 (35), 201 (50), 184 (55), 148 (30) and 106 (45) (Found: M^{35} + H^+, 440.2024. $C_{22}H_{34}ClNO_4Si$ requires *M* + H^+, 440.2024).

Ethyl 4-(2-*chloro*-N-*benzylpropionamido*)-5-(tert-*butyldimethylsiloxy*)*pent*-2-*enoate* **7b**. This was prepared from amine **6** (0.25 g, 0.69 mmol) and 2-chloropropionyl chloride (0.08 ml,

0.83 mmol) using the general procedure. Purification using column chromatography (silica; ethyl acetate–dichloromethane, 1:32) afforded the *title compound* **7b** (0.3 g, 96%) as a diastereoisomeric mixture; R_F 0.50 and 0.46 (ethyl acetate–dichloromethane, 1:32) (Found: C, 60.8; H, 8.0; N, 3.2. $C_{23}H_{36}ClNO_4Si$ requires C, 60.84; H, 7.99; N, 3.08%); ν_{max}(thin film)/cm^{-1} 2955m, 2857m, 1721s, 1665s, 1464m, 1451m, 1419m, 1368m, 1310m, 1259m, 1184m, 1106m and 839m; δ_H(270 MHz; $CDCl_3$) (mixture of diastereoisomers and conformers) 7.48–7.28 (5 H, m, aromatics), 7.14–6.80 (1 H, m, CH=C*H*CO$_2$), 6.10–5.96 (1 H, m, C*H*=CHCO$_2$), 5.20–3.70 (8 H, m, NC*H*, NCOC*H*Cl, C*H*$_2$OSi, CO$_2$C*H*$_2$ and NC*H*$_2$Ph), 1.82–1.68 (3 H, m, CHClC*H*$_3$), 1.40–1.25 (3 H, m, CO$_2$CH$_2$C*H*$_3$), 0.97–0.91 [9 H, m, SiC(C*H*$_3$)$_3$] and 0.13–0.00 (6 H, m, 2 × SiC*H*$_3$); δ_C(67.5 MHz; $CDCl_3$) 170.4, 165.9 (*C*O$_2$ and N*C*O), 143.6 (*C*H=C), 137.5 (*C*=C), 128.9, 128.4, 127.6, 127.0, 126.8, 126.0, 125.7, 123.2 (*C*H=C), 62.8, 60.7, 60.5, 60.4, 58.7, 50.0, 49.9 (NCO*C*H), CO$_2$*C*H$_2$, *C*H$_2$OSi, N*C*H and N*C*H$_2$Ph), 25.8 [SiC(*C*H$_3$)$_3$], 20.7 (CH*C*H$_3$), 18.1 [Si*C*(CH$_3$)$_3$], 14.2 (CO$_2$CH$_2$*C*H$_3$) and −5.7 (2 × Si*C*H$_3$); *m*/*z* (CI, NH_3) 454 (M^{35} + H^+, 20%), 420 (100), 330 (20), 257 (20), 198 (50), 164 (20) and 106 (25) (Found: M^{35} + H^+, 454.2180. $C_{23}H_{36}ClNO_4Si$ requires for M^{35} + H^+, 454.2180).

Ethyl 4-(2-*chloro*-N-*benzyl*-2-*phenylacetamido*)-5-(tert-*butyldimethylsiloxy*)*pent*-2-*enoate* **7c**. This compound was prepared from amine **6** (0.23 g, 0.63 mmol) and 2-chloro-2-phenylacetyl chloride (0.12 cm^3, 0.75 mmol) using the general procedure. Purification using column chromatography (silica; ethyl acetate–dichloromethane, 1:32) afforded *chloro amide* **7c** (0.31 g, 95%) as a colourless viscous oil; R_F 0.47 (ethyl acetate–dichloromethane, 1:32); ν_{max}(thin film)/cm^{-1} 2920s, 2857m, 1725s, 1670s, 1455m, 1420m, 1370m, 1310m, 1260m, 1180m, 1110m, 1050w and 850m; δ_H(270 MHz; $CDCl_3$) (mixture of diastereoisomers and conformers) 7.42–7.21 (10 H, m, aromatics), 7.01–6.91, 6.87–6.78 and 6.62–6.50 (1 H, m, C*H*=CHCO$_2$), 6.05–5.74 (1 H, m, CH=C*H*CO$_2$), 5.47 and 5.45 (1 H, 2 × s, NCOC*H*Ph), 5.08–3.54 (7 H, m, NC*H*$_2$Ph, CO$_2$C*H*$_2$, C*H*$_2$OSi and NC*H*), 1.30–1.24 (3 H, m, CO$_2$CH$_2$C*H*$_3$), 0.91–0.81 [9 H, m, SiC(C*H*$_3$)$_3$] and 0.00 to −0.08 (6 H, m, 2 × SiCH$_3$); δ_C(67.5 Hz; $CDCl_3$) 168.6, 168.5, 165.8 and 165.7 (*C*O$_2$ and N*C*O), 142.9 and 142.8 (*C*H=CHCO$_2$), 137.1 and 136.9 (*C*=C), 129.2, 129.1, 129.0, 128.9, 128.7, 128.4, 128.3, 128.1, 127.8, 127.4, 126.0, 125.9 and 123.8 (*C*H=C), 63.1, 63.0, 60.4, 59.1, 58.9, 57.9 and 57.2, (NCO*C*H, CO$_2$*C*H$_2$, *C*H$_2$OSi and N*C*H), 50.3 and 50.2 (N*C*H$_2$Ph), 25.7 [SiC(*C*H$_3$)$_3$], 18.0 [Si*C*(CH$_3$)$_3$], 14.1 (CO$_2$CH$_2$*C*H$_3$) and −5.7 and −5.8 (2 × SiCH$_3$); *m*/*z* (CI, NH_3); 518 (M^{37} + H^+, 15%), 516 (M^{35} + H^+, 25), 482 (100), 480 (95) and 91 (30) (Found: M^{35} + H^+, 516.2340. $C_{28}H_{38}ClNO_4Si$ requires for M^{35} + H^+, 516.2337).

Ethyl 4-(2,2,2-*trichloro*-N-*benzylacetamide*)-5-(tert-*butyldimethylsiloxy*)*pent*-2-*enoate* **7d**. This compound was prepared from the amine **6** (0.27 g, 0.74 mmol) and trichloroacetyl chloride (0.1 cm^3, 0.89 mmol) following the general procedure. Purification using column chromatography (dichloromethane) yielded the *title compound* **7d** (0.38 g, 99%) as a colourless oil; R_F 0.59 (dichloromethane); ν_{max}(thin film)/cm^{-1} 2929m, 2857m, 1723s, 1684s, 1471m, 1367m, 1260m, 1184m, 1107m, 1039w, 982vw and 840vs; δ_H(270 MHz; $CDCl_3$) 7.40–7.10 (5 H, m, aromatics), 6.98 (1 H, dd, *J* 16 and 6, C*H*=CHCO$_2$), 6.04–4.77 and 4.42–3.70 (8 H, m, CH=C*H*CO$_2$, CO$_2$C*H*$_2$CH$_3$, C*H*$_2$OSi, NC*H* and NC*H*$_2$Ph), 1.24 (3 H, t, *J* 9.9, CO$_2$CH$_2$C*H*$_3$), 0.85–0.79 [9 H, m, SiC(C*H*$_3$)$_3$] and 0.00 to −0.2 (6 H, m, 2 × SiCH$_3$); δ_C(67.5 Hz; $CDCl_3$) 165.6, 160.2 (*C*O$_2$ and N*C*O), 142.0 (*C*H=CHCO$_2$), 135.0 (*C*=C), 128.7, 128.2, 127.8, 127.2, 126.5, 124.3 and 123.3 (*C*H=C), 63.8, 63.2, 62.1, 61.3, 60.5, 55.9 and 49.8 (N*C*H$_2$Ph, NCO*C*Cl$_3$, N*C*H, CO$_2$*C*H$_2$ and *C*H$_2$OSi), 25.8 [SiC(*C*H$_3$)$_3$], 18.1 [Si*C*(CH$_3$)$_3$], 14.1 (CO$_2$CH$_2$*C*H$_3$) and −5.5 and −5.7 (2 × SiCH$_3$); *m*/*z* (CI, NH_3) 527 (M + NH_4^+, 25%), 525 (M + NH_4^+, 24), 510 (M + NH_4^+, 40), 508 (M + H^+, 38), 438 (60), 378 (98), 376 (100), 342 (30) and 108 (30) (Found: M + H^+, 508.1244. $C_{22}H_{32}Cl_3NO_4Si$ requires for *M* + H^+, 508.1245).

General Procedure for Radical Cyclisation.—A 0.02 mol dm^{-3} solution containing Bu_3SnH (1.1 equiv.) and AIBN (azoisobutyronitrile) (0.1 equiv.) in benzene or toluene (8–20 cm^3) was added dropwise over 1 h to a 0.03 mol dm^{-3} solution of the chloride **7a–c** (0.14–0.35 mmol, 1 equiv.) in boiling benzene or toluene (5-12 cm^3) whilst the latter was stirred under nitrogen. The solution was then refluxed for a further 2 h after which it was evaporated under reduced pressure. Diethyl ether (10–15 cm^3) and aqueous KF (8%; 10–15 cm^3) was added to the residue and the mixture stirred for 2 h. The organic layer was separated, washed with water and brine, dried ($MgSO_4$) and evaporated under reduced pressure to afford crude product which was purified by column chromatography (silica).

Cyclisation of ethyl 4-(2-*chloro*-N-*benzylacetamido*)-5-(tert-*butyldimethylsiloxy*)*pent*-2-*enoate* **7a**. The chloride **7a** (150 mg, 0.34 mmol) was treated with Bu_3SnH (117 mg, 0.40 mmol) and AIBN (6 mg, 0.04 mmol) in boiling benzene (32 cm^3) following the general procedure. After work-up, chromatography of the residue on silica (dichloromethane–ethyl acetate, 5.7:1) afforded the pyrrolidinone **8** (43 mg, 31%) as a mixture of *trans*:*cis* isomers in the ratio 15:1, acetamide **9a** (48 mg, 35%) and the *N*-methyl amide **10** (18 mg, 13%) as colourless oils. Reaction of the chloride **7a** (154 mg, 0.35 mmol) with Bu_3SnH (120 mg, 0.41 mmol) and AIBN (6 mg, 0.04 mmol) in boiling toluene (33 cm^3) yielded the pyrrolidinone **8** (54 mg, 38%) (as a mixture of *trans*:*cis* isomers in the ratio 4.2:1), the acetamide **9a** (21 mg, 15%) and the *N*-methyl amide **10** (26 mg, 18%).

trans-*Pyrrolidinone* **8**. R_F 0.27 (dichloromethane–ethyl acetate, 5.7:1) (Found: C, 65.1; H, 8.8; N, 3.7. $C_{22}H_{35}NO_4Si$ requires C, 65.15; H, 8.70; N, 3.45%); ν_{max}(thin film)/cm^{-1} 2929m, 2857m, 1734s, 1695s, 1419m, 1253m, 1187m, 1115m, 1029w, 990vw and 838m; δ_H(270 MHz; $CDCl_3$) 7.32–7.19 (5 H, m, aromatics), 4.98 (1 H, d, *J* 14.8, NC*H*Ph), 4.02 (2 H, q, *J* 7.3, CO$_2$C*H*$_2$CH$_3$), 3.97 (1 H, d, *J* 14.9, NC*H*Ph), 3.68 (1 H, dd, *J* 3.6 and 10.7, NCHC*H*OSi), 3.57 (1 H, dd, *J* 3.3 and 10.8, CHOSi), 3.10 (1 H, q, *J* 2.6, NCH), 2.79 (1 H, dd, *J* 17.0 and 9.0, NCOCH), 2.62–2.52 (1 H, m, C*H*CH$_2$CO$_2$), 2.32 (1 H, d, *J* 2.0, CHCO$_2$), 2.29 (1 H, d, *J* 2.6, CHCO$_2$), 2.07 (1 H, dd, *J* 16.8 and 3.3, NCOCH), 1.18 (3 H, t, *J* 7.3, CO$_2$CH$_2$C*H*$_3$), 0.85 [9 H, s, SiC(CH$_3$)$_3$] and 0.01 and 0.00 (6 H, 2 × s, 2 × SiCH$_3$); δ_C(67.5 MHz; $CDCl_3$) 174.2 and 171.7 (*C*O$_2$CH$_2$ and N*C*O), 136.6, 128.6, 128.0 and 127.5 (aromatic *C*H=C), 63.7, 62.6 and 60.5 (CO$_2$*C*H$_2$, *C*H$_2$OSi and N*C*H), 44.5 (N*C*H$_2$Ph), 39.3, 36.9, 31.0 (NCO*C*H$_2$, *C*HCH$_2$CO$_2$ and *C*H$_2$CO$_2$), 25.8 [SiC(*C*H$_3$)$_3$], 18.1 [Si*C*(CH$_3$)$_3$], 14.1 (CO$_2$CH$_2$*C*H$_3$) and −5.6 (2 × Si*C*H$_3$); *m*/*z* (CI, NH_3) 406 (M + H^+, 100%) (Found: M + H^+, 406.2414. $C_{22}H_{35}NO_4Si$ requires for *M* + H^+, 406.2414).

cis-*Pyrrolidinone* **8**. The presence of this compound was indicated by the ^{1}H NMR spectrum [δ 5.05 and 3.85 (2 × d, *J* 15.1, NCH$_2$Ph)].

Acetamide **9a**. R_F 0.47 (dichloromethane–ethyl acetate, 5.7:1); ν_{max}(thin film)/cm^{-1} 2929m, 2857m, 1723s, 1652s, 1413m, 1367m, 1258m, 1185m, 1108m, 1031w and 838m; δ_H(270 MHz; $CDCl_3$) 7.40–7.20 (5 H, m, aromatics), 7.04–6.83 (1 H, m, C*H*=CHCO$_2$), 5.97–5.86 (1 H, m, CH=C*H*CO$_2$), 5.01 (1 H, m, NCH), 4.82–3.71 (6 H, m, C*H*$_2$OSi, NC*H*$_2$Ph and CO$_2$C*H*$_2$CH$_3$), 2.29 and 2.13 (3 H, 2 × s, COCH$_3$), 1.30 (3 H, m, CO$_2$CH$_2$C*H*$_3$), 0.90 and 0.89 [9 H, 2 × s, SiC(CH$_3$)$_3$] and 0.04 and 0.00 (6 H, 2 × s, 2 × SiCH$_3$); δ_C(67.5 MHz; $CDCl_3$) 171.6, 165.8 (*C*O$_2$CH$_2$ and N*C*O), 143.9 (*C*H=CHCO$_2$), 137.4 (aromatic CH=*C*), 128.7, 128.6, 128.3, 127.9, 127.3 and 126.1

(aromatic *C*H=C), 123.2 (CH=*C*HCO$_2$), 63.1, 60.3, 58.2 and 51.2 (CO$_2$*C*H$_2$, *C*H$_2$OSi, N*C*H and N*C*H$_2$Ph), 25.7 [SiC(*C*H$_3$)$_3$], 22.2 (NCO*C*H$_3$), 18.0 [Si*C*(CH$_3$)$_3$], 14.1 (CO$_2$CH$_2$*C*H$_3$) and −5.7 (2 × SiCH$_3$); *m/z* (CI, NH$_3$) 406 (M + H$^+$, 100%), 274 (30), 257 (35) and 150 (65) (Found: M + H$^+$, 406.2414. $C_{22}H_{35}NO_4Si$ requires for *M* + H$^+$, 406.2414).

N-*Methylamide* **10**. R_F 0.52 (dichloromethane–ethyl acetate, 5.7:1); ν_{max}(thin film)/cm^{-1} 2955s, 2929s, 2856m, 1722s, 1652s, 1471m, 1399m, 1259m, 1179m, 1113m, 1032w and 838m; δ_H(270 MHz; CDCl$_3$) 7.37–7.19 (5 H, m, aromatics), 6.83 and 6.65 (1 H, 2 × dd, *J* 4.6 and 16, C*H*=CHCO$_2$), 5.83 and 5.62 (1 H, 2 × d, *J* 16, CH=C*H*CO$_2$), 5.35 and 4.58 (1 H, 2 × m, NC*H*), 4.20–4.10 (2 H, m, CO$_2$C*H*$_2$CH$_3$), 3.80–3.63 (4 H, m, C*H*$_2$OSi and NCOC*H*$_2$), 2.90 and 2.80 (2 H, 2 × s, NC*H*$_3$), 1.29–1.23 (3 H, m, CO$_2$CH$_2$C*H*$_3$), 0.85 and 0.83 [9 H, 2 × s, SiC(CH$_3$)$_3$], 0.01 and 0.00 (6 H, 2 × s, 2 × SiCH$_3$); δ_C(67.5 MHz; CDCl$_3$) 171.5, 166.0 (*C*O$_2$CH$_2$ and N*C*O), 143.3 (*C*H=CHCO$_2$), 141.9 (aromatic *C*=CH), 134.6, 128.7 and 126.8 (aromatic *C*H=C), 123.2 (CH=*C*HCO$_2$), 62.5, 60.5 and 55.8 (CO$_2$*C*H$_2$, *C*H$_2$OSi and N*C*H), 41.3 (NCO*C*H$_2$Ph), 32.1 (NCH$_3$), 25.7 [SiC(*C*H$_3$)$_3$], 17.5 [Si*C*(CH$_3$)$_3$], 13.6 (CO$_2$CH$_2$*C*H$_3$) and −5.6 (2 × Si*C*H$_3$); *m/z* (CI, NH$_3$) 406 (M + H$^+$, 50%), 274 (20), 257 (60), 167 (25) and 150 (100) (Found: M + H$^+$, 406.2414. $C_{22}H_{35}NO_4Si$ requires for *M* + H$^+$, 406.2414).

Cyclisation of ethyl 4-(2-*chloro*-N-*benzylpropionamido*)-5-(tert-*butyldimethylsiloxy*)*pent*-2-*enoate* **7b**. The chloride **7b** (150 mg, 0.33 mmol) was treated with Bu$_3$SnH (106 mg, 0.36 mmol) and AIBN (6 mg, 0.04 mmol) in boiling benzene (25 cm^3) following the general procedure. After work-up, chromatography of the residue on silica (dichloromethane–ethyl acetate, 9:1) afforded the pyrrolidinone **11b** (36 mg, 26%), the pyrrolidinone **12b** (39 mg, 28%), the pyrrolidinone **13b** (39 mg, 28%) and the propionamide **9b** (6 mg, 4%).

Pyrrolidinone **11b**. R_F 0.37 (dichloromethane–ethyl acetate, 9:1); ν_{max}(thin film)/cm^{-1} 2929m, 1733s, 1694s, 1427m, 1323w, 1254m, 1173m, 1095m, 1045m and 838m; δ_H(270 MHz; CDCl$_3$) 7.38–7.20 (5 H, m, aromatics), 5.04 (1 H, d, *J* 15.1, NC*H*Ph), 4.11 (2 H, q, *J* 7.3, CO$_2$C*H*$_2$CH$_3$), 3.93 (1 H, d, *J* 15.1, NC*H*Ph), 3.74 (1 H, dd, *J* 11.5 and 2.3, C*H*OSi), 3.56–3.45 (2 H, m, CHOSi and NCH), 2.71–2.54 and 2.49–2.28 (4 H, m, C*H*$_2$CO$_2$, C*H*CH$_2$CO$_2$ and COC*H*CH$_3$), 1.30–1.18 (6 H, m, CO$_2$CH$_2$-C*H*$_3$ and COCHC*H*$_3$), 0.87 [9 H, s, SiC(CH$_3$)$_3$] and 0.04 and 0.00 (6 H, 2 × s, 2 × SiCH$_3$); δ_C(67.5 MHz; CDCl$_3$) 176.8, 172.6 (CO$_2$ and NCO), 136.8 (aromatic *C*=CH), 128.7, 127.9, 127.4 (aromatic C=*C*H), 60.5, 59.1, 58.4 (CO$_2$*C*H$_2$CH$_3$, *C*H$_2$OSi and N*C*H), 44.3 (N*C*H$_2$Ph), 41.3, 40.9 (*C*HCH$_2$CO$_2$ and CH$_3$*C*HCO), 33.6 (*C*H$_2$CO$_2$), 25.8 [SiC(*C*H$_3$)$_3$], 17.9 [Si*C*(CH$_3$)$_3$], 15.1 and 14.1 (CO$_2$CH$_2$*C*H$_3$ and NCOCH*C*H$_3$) and −5.7 and −5.8 (2 × Si*C*H$_3$); *m/z* (CI, NH$_3$) 420 (M + H$^+$, 100%) (Found: M + H$^+$, 420.2570. $C_{23}H_{37}NO_4Si$ requires for *M* + H$^+$, 420.2570).

Pyrrolidinone **12b**. R_F 0.27 (dichloromethane–ethyl acetate, 9:1); ν_{max}(thin film)/cm^{-1} 2929m, 2857m, 1733s, 1695vs, 1429m, 1254m, 1176m, 1114m, 1031w and 838m; δ_H(270 MHz; CDCl$_3$) 7.35–7.18 (5 H, m, aromatics), 4.98 (1 H, d, *J* 15.2, NC*H*Ph), 4.07–3.97 (3 H, m, CO$_2$C*H*$_2$CH$_3$ and NC*H*Ph), 3.69 (1 H, dd, *J* 3.3 and 10.7, C*H*OSi), 3.59 (1 H, dd, *J* 3.6 and 10.7, C*H*OSi), 3.02 (1 H, q, *J* 3.3, NC*H*CH$_2$), 2.87 (1 H, p, *J* 7.6, NCOC*H*CH$_3$), 2.73–2.57 (1 H, m, C*H*CH$_2$CO$_2$), 2.36 (1 H, dd, *J* 16.2 and 6.3, CHCO$_2$), 2.08 (1 H, dd, *J* 16.1 and 9.6, CHCO$_2$), 1.20–1.05 (6 H, m, CO$_2$CH$_2$C*H*$_3$ and COCHC*H*$_3$), 0.85 [9 H, s, SiC(CH$_3$)$_3$], 0.01 and 0.00 (6 H, 2 × s, 2 × SiCH$_3$); δ_C(67.5 MHz; CDCl$_3$) 176.8 and 172.3 (CO$_2$ and NCO), 136.8 (aromatic *C*=CH), 128.7, 128.6, 128.0, 127.9 and 127.4 (aromatic C=*C*H), 62.7, 62.2 and 60.5 (CO$_2$*C*H$_2$, *C*H$_2$OSi and N*C*HCH$_2$), 44.7 (N*C*H$_2$Ph), 38.4, 35.5 and 34.1 (*C*HCH$_2$CO$_2$, CH$_3$*C*HCO and *C*H$_2$CO$_2$), 25.7 [SiC(*C*H$_3$)$_3$], 18.2 [Si*C*(CH$_3$)$_3$], 14.1 and 11.1 (CO$_2$-CH$_2$*C*H$_3$ and NCOCH*C*H$_3$) and −5.6 (2 × Si*C*H$_3$); *m/z* (CI, NH$_3$) 420 (M + H$^+$, 100%) and 330 (20) (Found: M + H$^+$, 420.2570. $C_{23}H_{37}NO_4Si$ requires for *M* + H$^+$, 420.2570).

Pyrrolidinone **13b**. R_F 0.22 (dichloromethane–ethyl acetate, 9:1); ν_{max}(thin film)/cm^{-1} 2929m, 2857m, 1734s, 1700vs, 1456m, 1436m, 1253m, 1180m, 1114m, 1029w and 837m; δ_H(270 MHz; CDCl$_3$) 7.30–7.16 (5 H, m, aromatics), 5.03 (1 H, d, *J* 15.2, NC*H*Ph), 4.06 (2 H, q, *J* 7.3, CO$_2$C*H*$_2$CH$_3$), 3.95 (1 H, d, *J* 15.2, NC*H*Ph), 3.68 (1 H, dd, *J* 3.6 and 10.9, C*H*OSi), 3.55 (1 H, dd, *J* 3.4 and 11.0, C*H*OSi), 3.15–3.08 (1 H, m, NC*H*CH$_2$), 2.41–2.15 (4 H, m, C*H*$_2$CO$_2$, C*H*CH$_2$CO$_2$ and NCOC*H*CH$_3$), 1.26–1.08 (6 H, m, CO$_2$CH$_2$C*H*$_3$ and NCOCHC*H*$_3$), 0.84 [9 H, s, SiC(CH$_3$)$_3$] 0.00 and −0.01 (6 H, 2 × s, 2 × SiCH$_3$); δ_C(67.5 MHz; CDCl$_3$) 176.7, 171.6 (N*C*O and *C*O$_2$), 136.6 (aromatic *C*=CH), 128.6, 128.0, 127.8, 127.3 (aromatic C=*C*H), 62.1, 61.9, 60.6 (CO$_2$*C*H$_2$, *C*H$_2$OSi and N*C*HCH$_2$), 44.4 (N*C*H$_2$Ph), 42.4, 38.4 and 38.3 (*C*HCH$_2$CO$_2$, CH$_3$*C*HCO and *C*H$_2$CO$_2$), 25.8 [SiC(*C*H$_3$)$_3$], 18.2 [Si*C*(CH$_3$)$_3$], 16.4 and 14.1 (CO$_2$CH$_2$*C*H$_3$ and NCOCH*C*H$_3$) and −5.6 (2 × Si*C*H$_3$); *m/z* (CI, NH$_3$) 420 (M + H$^+$, 100%), 330 (45) and 274 (25) (Found: M + H$^+$, 420.2570. $C_{23}H_{37}NO_4Si$ requires for *M* + H$^+$, 420.2570).

Propionamide **9b**. R_F 0.45 (dichloromethane–ethyl acetate, 9:1); ν_{max}(thin film)/cm^{-1} 2929m, 2856m, 1723s, 1652s, 1463m, 1367w, 1259m, 1174m, 1106m, 1038w and 838m; δ_H(270 MHz; CDCl$_3$) 7.40–7.23 (5 H, m, aromatics), 7.03 (1 H, dd, *J* 6 and 16, C*H*=CHCO$_2$), 5.87 (1 H, d, *J* 16, CH=C*H*CO$_2$), 4.99 (1 H, q, *J* 6, NC*H*CH$_2$), 4.72–4.56 (2 H, m, NC*H*$_2$Ph), 4.20 (2 H, q, *J* 7.3, CO$_2$C*H*$_2$CH$_3$), 4.01–3.82 (2 H, m, CH$_2$OSi), 2.35 (2 H, q, *J* 7.2, NCOC*H*$_2$CH$_3$), 1.30–1.10 (6 H, m, 2 × CH$_2$C*H*$_3$), 0.89 [9 H, s, SiC(CH$_3$)$_3$], 0.04 and 0.00 (6 H, 2 × s, 2 × SiCH$_3$); *m/z* (CI, NH$_3$) 420 (M + H$^+$, 100%), 362 (20), 288 (90), 257 (55) and 164 (100) (Found: M + H$^+$, 420.2570. $C_{23}H_{37}NO_4Si$ requires for *M* + H$^+$, 420.2570).

Cyclisation of ethyl 4-(2-*chloro*-N-*benzyl*-2-*phenylaceta-mido*)-5-(tert-*butyldimethylsiloxy*)*pent*-2-*enoate* **7c**. The chloride **7c** (138 mg, 0.27 mmol) was treated with Bu$_3$SnH (86 mg, 0.30 mmol) and AIBN (5 mg, 0.03 mmol) in boiling benzene (30 cm^3) following the general procedure. After work-up, chromatography of the residue on silica (dichloromethane–ethyl acetate, 9:1) afforded the pyrrolidinone **11c** (40 mg, 31%), the pyrrolidinone **12c** (40 mg, 31%) and the pyrrolidinone **13c** (40 mg, 31%). Reaction of the chloride **7c** (150 mg, 0.29 mmol) with Bu$_3$SnH (93 mg, 0.33 mmol) and AIBN (5 mg, 0.03 mmol) in boiling toluene (30 cm^3) yielded the pyrrolidinone **11c** (45 mg, 32%), the pyrrolidinone **12c** (45 mg, 32%) and the pyrrolidinone **13c** (45 mg, 32%).

Pyrrolidinone **11c**. R_F 0.63 (dichloromethane–ethyl acetate, 9:1); m.p. 93–95 °C (Found: C, 70.00; H, 8.25; N, 2.88. $C_{28}H_{39}NO_4Si$ requires C, 69.82; H, 8.16; N, 2.91%); ν_{max}(Nujol)/cm^{-1} 2928m, 2857m, 1733s, 1694s, 1423m, 1253m, 1208m, 1155m, 1096m and 884m; δ_H(400 MHz; C_6D_6) 7.33–7.28 and 7.22–7.09 (10 H, m, aromatics), 5.12 (1 H, d, *J* 15.1, NC*H*Ph), 4.08 (1 H, d, *J* 15.1, NC*H*Ph), 3.85–3.72 (4 H, m, CO$_2$C*H*$_2$CH$_3$, NCOC*H* and NC*H*CH$_2$), 3.60 (1 H, dd, *J* 11.6 and 2.6, C*H*OSi), 3.52 (1 H, dd, *J* 11.6 and 1.7, C*H*OSi), 3.08–2.99 (1 H, m, C*H*CH$_2$CO$_2$), 2.73 (1 H, dd, *J* 16.8 and 10.8, CHCO$_2$), 2.54 (1 H, dd, *J* 16.8 and 4.6, CHCO$_2$), 0.97 [9 H, s, SiC(CH$_3$)$_3$], 0.85 (3 H, t, *J* 7.1, CO$_2$CH$_2$C*H*$_3$) and 0.01 and −0.01 (6 H, 2 × s, 2 × SiCH$_3$); δ_C(67.5 MHz; CDCl$_3$) 174.6 and 172.2 (*C*O$_2$CH$_2$ and N*C*O), 138.4 and 136.7 (aromatic *C*=CH), 128.9, 128.8, 128.7, 128.0, 127.6 and 127.2 (aromatic *C*H=C), 60.5 and 59.1 (CO$_2$*C*H$_2$ and *C*H$_2$OSi), 58.2 and 53.9 (N*C*HCH$_2$ and NCO*C*HPh), 44.7 (N*C*H$_2$Ph), 42.2 (*C*HCHPh), 33.1 (*C*H$_2$CO$_2$), 25.8 [SiC(*C*H$_3$)$_3$], 17.9 [Si*C*(CH$_3$)$_3$], 14.0 (CO$_2$CH$_2$*C*H$_3$) and −5.7 and −5.8 (2 × Si*C*H$_3$); *m/z* (CI, NH$_3$) 482 (M + H$^+$, 100%) (Found: M + H$^+$, 482.2727. $C_{28}H_{39}NO_4Si$ requires for *M* + H$^+$, 482.2727).

Pyrrolidinone **12c**. R_F 0.44 (dichloromethane–ethyl acetate, 9:1); ν_{max}(thin film)/cm^{-1} 2929m, 2857m, 1733s, 1693s, 1426m,

1254m, 1115m and 839m; δ_H(400 MHz; $CDCl_3$) 7.37–7.17 and 7.09–7.07 (10 H, m, aromatics), 5.17 (1 H, d, *J* 14.9, NC*H*Ph), 4.23 (1 H, d, *J* 9.1, NCOC*H*), 4.03 (1 H, d, *J* 14.8, NC*H*Ph), 3.94–3.86 (2 H, m, CO_2CH_2), 3.84 (1 H, dd, *J* 10.9 and 3.0, CHOSi), 3.71 (1 H, dd, *J* 10.9 and 3.3, CHOSi), 3.16 (1 H, q, *J* 3.2, C*H*CH_2OSi), 2.99–2.97 (1 H, m, C*H*CH_2CO_2), 2.00 (1 H, dd, *J* 16.7 and 9.3, CHC*H*CO_2), 1.81 (1 H, dd, *J* 16.8 and 6.3, CHC*H*CO_2), 1.08 (3 H, t, *J* 7.1, $CO_2CH_2CH_3$), 0.91 [9 H, s, $SiC(CH_3)_3$] and 0.08 and 0.07 (6 H, 2 × s, 2 × $SiCH_3$); δ_C(67.5 MHz; $CDCl_3$) 174.4 and 172.0 (CO_2 and NCO), 136.7, 135.8 (aromatic *C*=CH), 129.7, 128.7, 128.5, 128.2, 127.6 and 127.1 (aromatic *C*H=C), 62.6 and 62.2 (CO_2CH_2 and CH_2OSi), 60.3 and 50.9 (NCHCH_2 and NCOCHPh), 44.7 (NCH_2Ph), 36.7, 35.2 (CHCHPh and CH_2CO_2), 25.8 [$SiC(CH_3)_3$], 18.2 [$SiC(CH_3)_3$], 14.0 ($CO_2CH_2CH_3$) and −5.5 and −5.6 (2 × $SiCH_3$); *m*/*z* (CI, NH_3) 482 (M + H^+, 100%) (Found: M + H^+, 482.2727. $C_{28}H_{39}NO_4Si$ requires for *M* + H^+, 482.2727).

Pyrrolidinone **13c**. R_F 0.30 (dichloromethane–ethyl acetate, 9:1); ν_{max}(thin film)/cm^{-1} 2929m, 2857m, 1734s, 1692s, 1497m, 1255m, 1176w, 1127w, 1096w and 838m; δ_H(400 MHz; $CDCl_3$) 7.36–7.24 (10 H, m, aromatics), 5.18 (1 H, d, *J* 15.0, NC*H*Ph), 4.07 (1 H, d, *J* 15.0, NC*H*Ph), 3.95–3.84 (2 H, m, $CO_2CH_2CH_3$), 3.79 (1 H, dd, *J* 11.1 and 3.5, CHOSi), 3.62 (1 H, dd, *J* 11.1 and 3.1, CHOSi), 3.53 (1 H, d, *J* 9.0, NCOCH), 3.32–3.29 (1 H, m, NC*H*CH_2OSi), 2.77–2.70 (1 H, m, C*H*CH_2CO_2), 2.47 (1 H, d, *J* 2, $CHCO_2$), 2.45 (1 H, d, *J* 2.2, C*H*CO_2), 1.07 (3 H, t, *J* 7.1, $CO_2CH_2CH_3$), 0.89 [9 H, s, $SiC(CH_3)_3$] and 0.05 and 0.03 (6 H, 2 × s, 2 × $SiCH_3$); δ_C(67.5 MHz; $CDCl_3$) 174.3 and 171.2 (CO_2CH_2 and NCO), 139.1 and 136.5 (aromatic *C*=CH), 129.8, 128.7, 128.6, 128.4, 128.1, 128.0, 127.5 and 127.1 (aromatic C=CH), 61.4, 61.1, 60.5 and 54.0 (CH_2OSi, CO_2CH_2, NCHCH_2 and NCOCHPh), 44.7 (NCH_2Ph), 39.9 and 37.1 (CHCHPh and CH_2CO_2), 25.8 [$SiC(CH_3)_3$], 18.3 [$SiC(CH_3)_3$], 13.9 ($CO_2CH_2CH_3$) and −5.6 (2 × $SiCH_3$); *m*/*z* (CI, NH_3) 482 (M + H^+, 100%) (Found: M + H^+, 482.2727. $C_{28}H_{39}NO_4Si$ requires for *M* + H^+, 482.2727).

Cyclisation of ethyl 4-(N-*benzyl*-2,2,2-*trichloroacetamido*)-5-(tert-*butyldimethylsiloxy*)*pent*-2-*enoate* **7d**. The trichloride **7d** (150 mg, 0.29 mmol) was treated with Bu_3SnH (93 mg, 0.33 mmol) and AIBN (5 mg, 0.03 mmol) in boiling benzene (30 cm^3) following the general procedure. After work-up, chromatography on silica (dichloromethane) afforded the pyrrolidinone **15** (107 mg, 77%) as a mixture of C-4:C-5 *trans*/*cis* isomers in the ratio 5:2; R_F 0.14 (dichloromethane); ν_{max}(thin film)/cm^{-1} 2929m, 2856m, 1733vs, 1471w, 1423m, 1256m, 1180m, 1101m, 1029w, 968vw and 838m; δ_H(270 MHz; $CDCl_3$) (trans-*isomer*) 7.30–7.11 (5 H, m, aromatics), 5.17 (1 H, d, *J* 15.1, NC*H*Ph), 4.09 (2 H, q, *J* 7.2, CO_2CH_2), 3.91 (1 H, d, *J* 15.1, NC*H*Ph), 3.74 (1 H, dd, *J* 12 and 3.0, CHOSi), 3.50 (1 H, dd, *J* 11.9 and 2.3, CHOSi), 3.30–3.20 (1 H, m, NCH), 3.10 (1 H, dt, *J* 7.9 and 2.6, $CHCCl_2$), 2.90–2.80 (1 H, m, $CHCO_2$), 2.44 (1 H, dd, *J* 16 and 6.6, $CHCO_2$), 1.19 (3 H, t, *J* 7.2, $CO_2CH_2CH_3$), 0.82 [9 H, s, $SiC(CH_3)_3$] 0.01 and 0.00 (6 H, 2 × s, 2 × $SiCH_3$); δ_C(67.5 MHz; $CDCl_3$) 170.6, 170.4, 166.9 and 166.5 (CO_2 and NCO), 135.3, 135.0, 128.8, 128.0, 127.9 and 127.6 (aromatic *C*=CH and C=*C*H), 85.6 and 84.5 (NCO*C*Cl_2), 61.1, 60.5, 60.1, 58.3 and 58.2 (CH_2OSi, CH_2CO_2 and NCH), 48.5 and 46.9 (CHCCl$_2$), 46.7 and 44.6 (NCH_2Ph), 32.8 and 30.5 (CH_2CO_2), 25.7 [$SiC(CH_3)_3$], 18.2 and 18.1 [$SiC(CH_3)_3$], 14.0 and 13.5 ($CO_2CH_2CH_3$) and −5.7 (2 × $SiCH_3$); *m*/*z* (CI, NH_3) 476 (M + H^+, 70%), 474 (M + H^+, 100), 442 (40), 440 (80), 406 (20), 352 (20) and 108 (20) (Found: M + H^+, 474.1634. $C_{22}H_{33}Cl_2NO_4Si$ requires for *M* + H^+, 474.1634).

cis-*Pyrrolidinone* **15**. The presence of the *cis*-isomer was indicated by the ^1H NMR spectrum [δ 4.93 (d, *J* 15.0, NC*H*Ph), 4.26 (d, *J* 14.8, NC*H*Ph) and 3.30–3.20 (m, C*H*CCl_2)].

Preparation of 1-*Benzyl*-4-(*ethoxycarbonylmethyl*)-5-[(tert-*butyldimethylsiloxy*)*methyl*]*pyrrolidin*-2-*one* **8** *by Cyclisation of Ethyl* 4-(2,2,2-*trichloro*-N-*benzylacetamido*)-5-(tert-*butyldimethylsilyloxy*)*pent*-2-*enoate* **7d** *using* 3 *Equiv. of* Bu_3SnH.—A 0.02 mol dm^{-3} solution of Bu_3SnH (100 mg, 0.35 mmol) in toluene (20 cm^3) containing AIBN (5 mg, 0.03 mmol) was slowly added *via* a syringe pump (1 h) to a boiling 0.03 mol dm^{-3} solution of the chloride **7d** (160 mg, 0.31 mmol) in toluene (11 cm^3) whilst the latter was stirred under nitrogen. The solution was then heated at reflux for 1 h after which a mixture of Bu_3SnH (200 mg, 0.69 mmol) and AIBN (10 mg, 0.06 mmol) in toluene (5 cm^3) was added to it in one portion. This mixture was then heated at reflux for a further 3 h, after which the usual work-up afforded crude product. Column chromatography on silica (dichloromethane–ethyl acetate, 5.7:1) afforded the pyrrolidinone **8** (105 mg, 82%) as a mxiture of *trans*/*cis* isomers in the ratio 2.7:1.

Preparation and Cyclisation of Ethyl 4-(2-*Chloro*-2-*phenylsulfanyl*-N-*benzylacetamido*)-5-(tert-*butyldimethylsiloxy*)*pent*-2-*enoate* **17**.—*N*-Chlorosuccinimide (27 mg, 0.2 mmol) was added portionwise to a solution of the sulfide **16** (85 mg, 0.17 mmol) in carbon tetrachloride (3 cm^3) at 0 °C and the mixture was then stirred at room temperature for 4.5 h. After this the precipitated succinimide was filtered off and the filtrate concentrated under reduced pressure to yield crude product **17**. This was dissolved in toluene (6 cm^3) and the solution was heated at reflux. A 0.015 mol dm^{-3} solution of Bu_3SnH (53 mg, 0.18 mmol) in toluene (12 cm^3) containing AIBN (3 mg) was slowly added *via* a syringe pump (0.5 h) to the reaction mixture which was then heated for a further 4 h. The reaction mixture was then evaporated under reduced pressure and worked up to afford crude product. Purification of this by column chromatography (silica; dichloromethane–ethyl acetate, 32:1) afforded the pyrrolidinone **18** (28 mg, 33%) and pyrrolidinone **19** (21 mg, 25%) as colourless oils.

Pyrrolidinone **18**. R_F 0.42 (dichloromethane–ethyl acetate, 32:1); ν_{max}(thin film)/cm^{-1} 2926s, 1734s, 1700s, 1440m, 1254m, 1191w, 1152w, 1097m and 838s; δ_H(270 MHz; $CDCl_3$) 7.61–7.57, 7.38–7.20 and 6.98–6.94 (10 H, m, aromatics), 5.08 (1 H, d, *J* 15.1, NC*H*Ph), 4.09 (2 H, q, *J* 7.2, $CO_2CH_2CH_3$), 3.77 (1 H, d, *J* 15.0, NC*H*Ph), 3.70–3.35 (4 H, m, CH_2OSi, NC*H* and COC*H*SPh), 2.93 (1 H, d, *J* 12, $CHCO_2$), 2.70–2.50 (2 H, m, C*H*CO_2 and C*H*CH_2CO_2), 1.30 (3 H, t, *J* 7, $CO_2CH_2CH_3$), 0.84 [9 H, s, $SiC(CH_3)_3$] and 0.02 and 0.00 (6 H, 2 × s, 2 × $SiCH_3$); δ_C(67.5 MHz; $CDCl_3$) 172.3 and 171.8 (CO_2 and NCO), 135.9, 134.4, 132.1, 128.9, 128.6, 128.1, 127.7 and 127.5 (aromatic *C*=CH), 60.7, 58.9, 58.0 and 54.2 (CHSPh, NCH, CH_2OSi and CO_2CH_2), 44.5 (NCH_2Ph), 38.0 (CHCHSPh), 33.0 (CH_2CO_2), 25.8 [$SiC(CH_3)_3$], 17.9 [$SiC(CH_3)_3$], 13.6 ($CO_2CH_2CH_3$) and −5.7 and −5.8 (6 H, 2 × s, 2 × $SiCH_3$); *m*/*z* (CI, NH_3) 514 (M + H^+, 100%) and 406 (30) (Found: M + H^+, 514.2450. $C_{28}H_{39}NO_4SSi$ requires for *M* + H^+, 514.2447).

Pyrrolidinone **19**. R_F 0.18 (dichloromethane–ethyl acetate, 32:1); ν_{max}(thin film)/cm^{-1} 2919s, 2852s, 1733s, 1693s, 1441m, 1255m, 1157w, 1098m and 838m; δ_H(270 MHz; $CDCl_3$) 7.66–7.62 and 7.33–7.20 (10 H, m, aromatics), 4.97 (1 H, d, *J* 15.1, NCH), 4.16 (1 H, d, *J* 15.1, NC*H*), 4.07 (2 H, q, *J* 7.3, $CO_2CH_2CH_3$), 3.69 (1 H, d, *J* 6.6, C*H*SPh), 3.57–3.45 (2 H, m, CH_2OSi), 3.25 (1 H, q, *J* 5, NCH), 2.52–2.42 (3 H, m, C*H*CH_2CO_2 and CH_2CO_2), 1.32 (3 H, t, *J* 7.1, $CO_2CH_2CH_3$), 0.87 [9 H, s, $SiC(CH_3)_3$] and 0.01 and 0.00 (6 H, 2 × s, 2 × $SiCH_3$); δ_C(67.5 MHz; $CDCl_3$) 172.1 and 171.1 (CO_2 and NCO), 136.4, 133.4, 129.0, 128.7, 128.6, 128.0 and 127.5 (aromatic C=CH), 63.2, 61.6, 60.7 and 52.8 (CHSPh, NCH, CH_2OSi and CO_2CH_2), 45.4 (NCH_2Ph), 38.0 and 36.9 (CHCHSPh and CH_2CO_2), 25.8 [$SiC(CH_3)_3$], 17.5 [SiC-

$(CH_3)_3$], 13.6 ($CO_2CH_2CH_3$) and −5.6 (2 × $SiCH_3$); *m/z* (CI, NH_3) 514 ($M + H^+$, 100%) and 406 (40) (Found: $M + H^+$, 514.2450. $C_{28}H_{39}NO_4SSi$ requires for $M + H^+$, 514.2447).

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