Synthesis of 1-acylamino-1-(trimethylsiloxy)alkanes by trimethylsilyl trifluoromethanesulfonate-catalysed addition of bis(trimethylsilyl)amides to aldehydes

A. Peter Johnson,* Richard W. A. Luke, Robert W. Steele and Andrew N. Boa

School of Chemistry, University of Leeds, Leeds LS2 9JT, UK

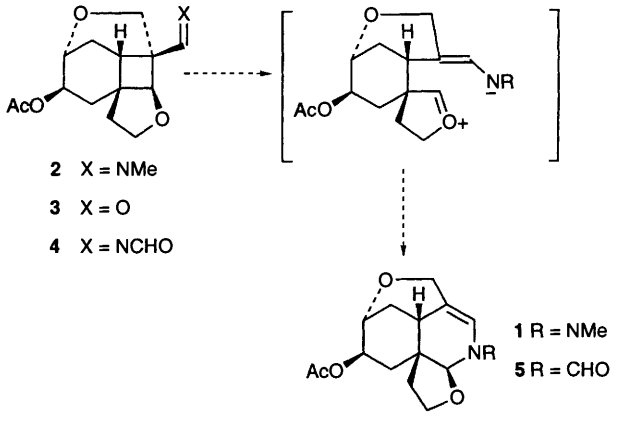
Bis(trimethylsilyl)formamide reacts with aldehydes in refluxing chloroform, or at room temperature with catalysis by trimethylsilyl trifluoromethanesulfonate, to give 1-acylamino-1-(trimethylsiloxy)alkanes; similar results are obtained with other bis(trimethylsilyl)amides, but surprisingly not with bis(trimethylsilyl)acetamide, and addition of bis(trimethylsilyl)formamide to ketones and acetals can also be accomplished using TMS triflate as catalyst.

Introduction

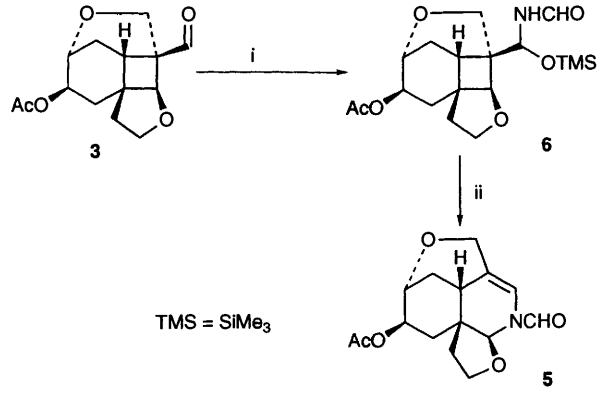
As part [1] of our studies directed towards the total synthesis [2] of the indole alkaloid gelsemine we wished to prepare the enamine **1** by rearrangement of the imine **2** under acidic conditions. The imine **2** was made from the corresponding aldehyde **3** by addition of *N*,*N*-bis(trimethylsilyl)methylamine, as this methodology has several advantages over other ways of preparing imines.[3-6] Unfortunately, treatment of the imine **2** with acid failed to effect rearrangement and it was reasoned that this might be due to insufficient electron-withdrawing character of the imine carbon–nitrogen double bond. On the other hand, in view of the greater electron-withdrawing character of *N*-acylimines over imines, it was expected that a species such as **4** might successfully rearrange. *N*-Acylimines and iminium salts have been shown to be versatile synthetic intermediates which undergo reactions with nucleophiles,[7] dienes [8] and dienophiles.[9] Until now *N*-acylimine precursors were most commonly prepared from α-alkoxy-*N*-acylamines (generated by electrochemical oxidation of an amide in the presence of an alcohol [10]) or α-hydroxy-*N*-acylamines. The latter species have been generated from reduction of cyclic imides [11] or by acid-catalysed addition of a primary amide to a particularly reactive aldehyde [7a] (*e.g.* formaldehyde or ethyl glyoxylate). These procedures are not generally applicable to the synthesis of acyclic *N*-acylimine precursors as the adducts show a marked tendency to revert back to the amide and aldehyde (or ketone).[12] Thus there appeared to be a need for reliable methods of preparing acyclic *N*-acylimines.

Although there was no precedent for the addition of silylated amides to aldehydes, the reaction of bis(trimethylsilyl)formamide (BSF) **7** with aldehyde **3** was attempted. Treatment of aldehyde **3** with six equivalents of BSF in refluxing chloroform gave the adduct **6** in good yield. In contrast to the reaction forming the *N*-methylimine, elimination of the trimethylsiloxy group did not occur under the reaction conditions. This may be accounted for by the fact that the nitrogen lone pair is partially delocalised into the carbonyl group. Treatment of the adduct **6** with triflic acid at room temperature in dichloromethane gave the desired enamide **5**, presumably by the mechanism shown in Scheme 1. See also Scheme 2.

The novel reaction of BSF **7** with an aldehyde, and the use of the resulting adduct as an *N*-acylimine precursor, promised significant synthetic potential,[13,14] particularly as there are very few methods available for the preparation of *N*-acylimine precursors from simple aldehydes and amides. A thorough investigation of the limitations of this new reaction and the synthetic potential of the resulting α-trimethylsiloxy amides was therefore undertaken.[13]



Scheme 1



Scheme 2 *Reagents and conditions:* i, BSF **7** (6 equiv.), $CHCl_3$, reflux, 96 h; ii, TfOH, room temp., 24 h

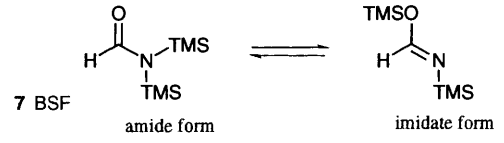
In general, it is possible to prepare silylated amides by the reaction of the corresponding primary or secondary amide with trimethylsilyl chloride (TMSCl) and triethylamine. In the work described here, BSF **7** was prepared by the method of Bredereck and co-workers.[15] BSF has been shown to act as a silylating agent [15,16] (*e.g.*, 1,3-dicarbonyl compounds are converted into the corresponding silyl enol ethers [15]), and will undergo electrophilic attack at the carbonyl carbon [15] (*e.g.*, with malononitrile). In the context of this work it is also important to note that it has been observed to act as an N-nucleophile,[15,16] in one case by addition to an *N*-acylimine intermediate.[17]

Table 1 Formation of BSF–aldehyde adducts under thermal conditions[a]

Adduct	Aldehyde	BSF (mol equiv.)	Time (t/h)[b]	Yield (%)
8	Bu^{t}CHO	1.7	96	6
9	Pr^{i}CHO	1.4	17	48
10	PrCHO	1.2	144	78
	PhCHO			0
	$PhCH_2CHO$			0[c]
	(*E*)-CH_3CH=CHCHO			0

[a] In refluxing $CHCl_3$ or CCl_4. [b] Time for completion of reaction as indicated by TLC. [c] Silyl enol ether isolated.

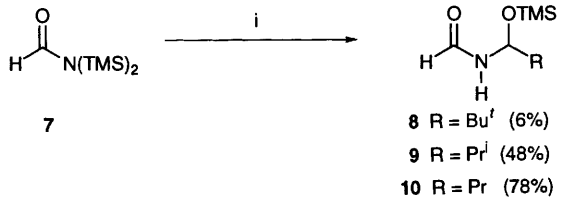
In principle, silylated amides can have two different structures: the amide or the imidate. There was originally some debate[15–19] about which form was adopted by BSF, so Yoder *et al.*[19] examined the IR spectra of [^{14}N]- and [^{15}N]-BSF. Both of these showed a very intense peak at 1659 cm^{-1} and as the frequency observed is apparently independent of the mass of the nitrogen atom it could not correspond to a C=N vibration and had to be due to C=O. Thus BSF exists in the amide form, but interestingly, bis(trimethylsilyl)acetamide (BSA) is believed to exist in the imidate form, as the IR spectrum of [^{14}N]-BSA has a peak at 1698 cm^{-1} which shifts to 1675 cm^{-1} in the ^{15}N derivative.



Results and discussion

Thermal reactions of BSF with aldehydes

A series of simple saturated aldehydes was used to establish the generality of the reaction of BSF with aldehydes. As the first example, pivalaldehyde was heated at reflux in chloroform with a slight excess of BSF for four days. After purification the BSF adduct **8** was obtained, though in poor yield. Under similar conditions BSF and isobutyraldehyde gave a better yield of the adduct **9**, and with butyraldehyde the adduct **10** was obtained in a respectable yield of 78% (Scheme 3, Table 1). ^{1}H NMR



Scheme 3 *Reagents and conditions:* i, $CHCl_3$, reflux, 17–144 h

analysis indicated that the initial product of the reaction was an N-silylated adduct, which was protodesilylated by chromatography on flash silica gel. The three adducts **8–10** may conveniently be stored in a freezer at −40 °C, or at room temperature for up to a week without decomposition.

The attempted addition of BSF to benzaldehyde or crotonaldehyde, using conditions similar to those described above, was unsuccessful. In neither case was it possible to isolate a stable product. When phenylacetaldehyde was heated with BSF, at reflux in chloroform, ^{1}H NMR spectroscopy indicated formation of the corresponding silyl enol ether[20] **11** (as a mixture of *E* and *Z* isomers). Somewhat surprisingly, it was possible to purify this silyl enol ether by flash chromatography. As BSF has been reported to convert 1,3-dicarbonyl compounds into their silyl enol ethers,[15] it is reasonable that phenylacetaldehyde should undergo similar reaction, even when this is not the case for simple saturated aldehydes, since its enol should be more stable due to conjugation of the double bond with the aromatic ring. In view of this result it seemed likely that the addition of BSF to other readily enolisable aldehydes could be problematic under these conditions.

Reactions of BSF with aldehydes in the presence of a catalyst

The reactions of BSF with aldehydes under thermal conditions were not uniformly successful and, even when successful, required long reaction times. It was therefore desirable to find a catalyst which would allow the reaction to proceed rapidly, at room temperature and with a wider range of aldehydes. As nucleophilic addition to a carbonyl compound is involved, we thought the use of a Lewis acid as catalyst ought to be effective. Titanium tetrachloride was the first potential candidate tested, but its use gave complex mixtures and it was not possible to isolate any identifiable material from these reactions. Presumably this Lewis acid catalyses further reactions/decomposition of the product.

Trimethylsilyl trifluoromethanesulfonate (TMS triflate) has been used as a catalyst for many reactions, including the addition of 2-(trimethylsiloxy)pyridine to butyraldehyde dimethyl acetal[21] which is in some ways similar to the addition of BSF to aldehydes. Although BSF is believed to exist in the amide form,[19] it is possible that a small amount of the imidate is in equilibrium with it and that this is the reactive form. In this case TMS triflate could catalyse equilibration between the two forms and thus increase the rate of reaction.

The addition of BSF **7** to butyraldehyde in the presence of TMS triflate was therefore attempted. TLC indicated rapid formation of the BSF–butyraldehyde adduct **10**, accompanied by a substantial amount of an unknown compound, which was subsequently identified as an equimolar mixture of the two diastereoisomers of the BSF–bisbutyraldehyde adduct **12**. In a similar fashion BSF **7** and benzaldehyde gave the corresponding bis-adduct **13** and a small amount of the mono-adduct **14**. The bis-adduct is probably formed by reaction of the appropriate N-silylated mono-adduct with a further molecule of aldehyde, but nevertheless this result was encouraging in the light of the failure of the thermal reaction between benzaldehyde and BSF.

Although the bis-adducts are useful compounds in their own right, it would be desirable to avoid their formation. The course of the reaction was not significantly different at low temperature (−50 °C), but it was found that the use of excess of BSF **7** at room temperature gave a much more favourable ratio of mono- to bis-adducts. Thus, using five equivalents of BSF **7** the BSF–benzaldehyde adduct **14** was obtained in 93% yield. Preparation of the BSF–phenylacetaldehyde adduct **15** by this method was equally impressive. Under thermal conditions, BSF **7** had converted phenylacetaldehyde into the corresponding silyl enol ether **11**, but in the presence of TMS triflate an excellent yield of the crystalline adduct **15** was obtained. Further examples of the preparation of adducts by reaction of BSF **7** with aldehydes, in the presence of a catalytic quantity of TMS triflate, are given in Table 2.

The conditions described above allow a variety of BSF–mono-aldehyde adducts to be prepared in good yield. Increasing the excess of BSF **7** improved the yield of the BSF–

Table 2 Preparation of BSF–aldehyde mono-adducts catalysed by TMS triflate

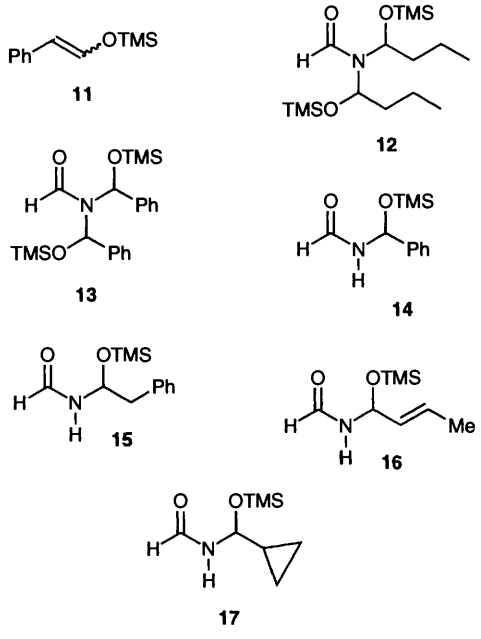
Adduct	Aldehyde	BSF/(mol equiv.)	Time (t/h)[a]	Yield (%)	Mp or bp (mmHg)/°C
8	Pivalaldehyde	1.6	20	85	55–57
9	Isobutyraldehyde	1.5	1	59	73–80 (0.3)
9	Isobutyraldehyde	2.5	3	80	
9	Isobutyraldehyde	3.4	2.5	93	
10	Butyraldehyde	5.0	1	63	98–100 (0.3)
14	Benzaldehyde	5.4	8	93	*b*
15	Phenylacetaldehyde	1.6	24	35	82–83
15	Phenylacetaldehyde	2.3	72	97	
16	Crotonaldehyde	3.9	21	40	*b*
17	Cyclopropanecarbaldehyde	3.0	0.2	31	*b*

[a] Time for completion of reaction as indicated by TLC. [b] Adducts were unstable and decomposed upon attempted distillation under reduced pressure.

Table 3 Addition of BSF to ketones catalysed by TMS triflate

Adduct	Ketone	BSF (mol equiv.)	Time (t/h)	Yield (%)
18	Acetone	2.9	168	38[a]
19	Cyclopentanone	3.5	120	13[a]
20	Methyl pyruvate	3.5	24	83[b]

[a] Product decomposed upon attempted distillation. [b] Mp 91–92 °C.



isobutyraldehyde adduct **9** until an excellent yield was obtained with 3.4 equivalents. Although it has not been examined in detail, it appears that the extent of the excess of BSF **7** required to give good yields varies from one aldehyde to another. Of particular note is the relatively small excess required to give an excellent yield of the BSF–pivalaldehyde adduct **8**. This may be because, in this case, formation of the bis-adduct is disfavoured for steric reasons.

Reactions of BSF with ketones

The analogous, TMS triflate-catalysed reaction between BSF **7** and ketones (in place of aldehydes) was found in general to be less successful (Table 3). Acetone and cyclopentanone gave poor yields of the corresponding mono-adducts **18** and **19** respectively and required long reaction times. At elevated temperatures the rate of the reaction was increased significantly, but unfortunately much lower yields were obtained. Methyl pyruvate, a particularly reactive ketone, gave the corresponding mono-adduct **20** in 85% yield, but the rate of reaction in this case was still slower than that observed for aldehydes.

Addition of BSF to an acetal

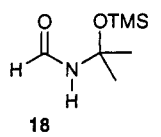
The addition of BSF **7** to an acetal in a similar manner to that described should give an adduct with an O-alkyl group. However, it was not possible to achieve this in the presence of TMS triflate, and the use of titanium tetrachloride was equally unsuccessful. This result is surprising in view of the fact that silyl enol ethers have been found to react with acetals but *not* with the parent aldehydes or ketones.[22] Noyori and co-workers[23] used TMS triflate for the addition of silyl enol ethers to acetals, and they found that the addition of a hindered base, such as dicyclohexylmethylamine, was necessary if an acetal derived from formaldehyde was used. We found that the presence of a small amount of diisopropylethylamine allowed the addition of BSF to propionaldehyde diethyl acetal, in the presence of TMS triflate, to give both the adduct **21** (21%) and bis-adduct **22** (37%). The role of the base in this and Noyori's example is unclear.

Other silylated amides

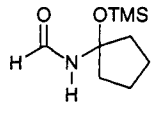
As the addition of BSF to aldehydes gave excellent yields of the corresponding adducts, a variety of other silylated amides were prepared so that their reactions with aldehydes could be investigated in order to establish whether this chemistry is applicable to silylated amides in general.

The addition of bis(trimethylsilyl)acetamide[19] (BSA, **23**) to isobutyraldehyde was attempted under both thermal conditions and in the presence of TMS triflate, but in neither case was it possible to isolate a product. This result was somewhat surprising given the ready addition of BSF **7** to aldehydes. The most obvious difference in nature between the two silylated amides is that BSA **23** exists in the imidate form whereas BSF **7** has the amide form.[19] A particularly attractive mechanism for the addition of the imidate form of BSF **7** to aldehydes involves a cyclic transition state. If the transition state is a pseudo-chair, as shown in Scheme 4, then the formyl hydrogen of BSF **7** would occupy a pseudo-axial position (assuming that imidate BSF was *E*). A similar transition state involving BSA **23** would be less favourable due to steric interactions as the methyl group of the acetamide would occupy this pseudo-axial position. This argument of course would only be valid if the reaction proceeds under kinetic control.

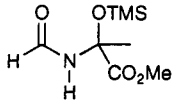
Trifluorobis(trimethylsilyl)acetamide **24** was prepared according to a known procedure,[24] and is believed to exist as a mixture of the amide and imidate forms. Attempted addition of compound **24** to isobutyraldehyde, in the presence of TMS



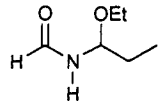
18



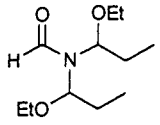
19



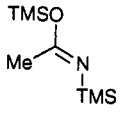
20



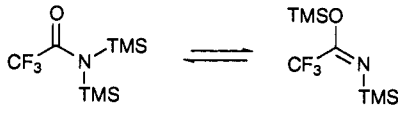
21



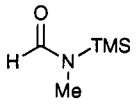
22



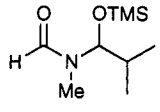
23



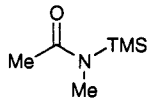
24



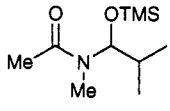
25



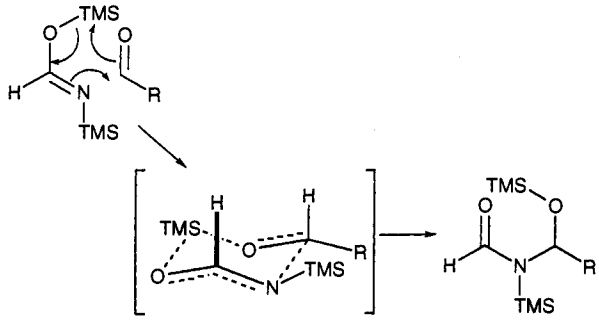
26



27



28

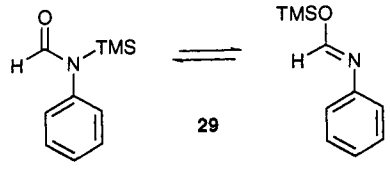


Scheme 4

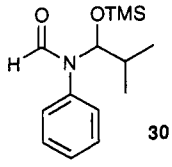
triflate, was unsuccessful. The lack of reactivity might be explained by the steric interactions postulated as one possible explanation for the failure of BSA to react, or more likely by the reduced nucleophilicity of the amide nitrogen due to the extra electron-withdrawing effect of the trifluoroacetyl group.

N-Methyl-*N*-(trimethylsilyl)formamide **25**, is reported to exist in the amide form and can be prepared in the normal manner.[25] Addition of isobutyraldehyde to a solution of compound **25** and a catalytic amount of TMS triflate gave the adduct **26** in 96% yield. The properties of the adduct **26** were similar to those of the corresponding BSF–isobutyraldehyde adduct **9**. The rates of addition of these two silylated amides, to isobutyraldehyde, appeared to be similar and a competition experiment was carried out in order to determine the relative rates more precisely. This result suggests that, under these conditions, *N*-methyl-*N*-(trimethylsilyl)formamide **25** is approximately 3.5 times as reactive towards isobutyraldehyde as is BSF **7**. This result helps to explain the formation of bis-adducts as the major product when approximately equimolar quantities of BSF **7** and aldehydes were mixed in the presence of TMS triflate, since the initially formed N-silylated mono-adduct should be more reactive towards the remaining aldehyde than is BSF.

N-Methyl-*N*-(trimethylsilyl)acetamide **27** was prepared in the usual manner, and is believed to exist in the amide form.[25] Addition of this silylated amide **27** to isobutyraldehyde, in the presence of TMS triflate, gave the adduct **28** (48%). This was surprising since BSA **23** did not react.



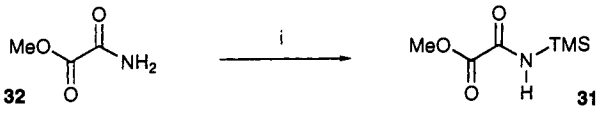
29



30

N-(Trimethylsilyl)formanilide **29**, which is believed to exist as a mixture of the amide and the imidate forms, was prepared in the usual manner.[26] Addition of this silylated amide to isobutyraldehyde, in the presence of TMS triflate, gave an excellent yield of the adduct **30** (99%).

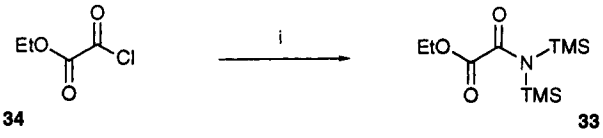
Ethyl *N*,*N*-bis(trimethylsilyl)oxamate **33** does not appear to have been synthesized previously. Treatment of methyl oxamate **32** with two equivalents of TMSCl and triethylamine in refluxing benzene gave only the mono-*N*-trimethylsilyl oxamate **31** (Scheme 5). Conversion of compound **31** into methyl



32 31

Scheme 5 *Reagents and conditions:* i, TMSCl (2 equiv.) Et_3N, PhH, reflux

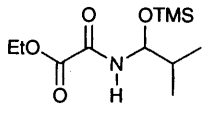
N,*N*-bis(trimethylsilyl)oxamate by deprotonation with sodium hydride or potassium hydride and quenching with TMSCl was unsuccessful. However, an alternative approach, which involved addition of sodium hexamethyldisilylamide to ethyl oxalyl chloride **34**, was successful (Scheme 6). Addition of



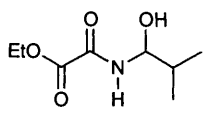
34 33

Scheme 6 *Reagents and conditions:* i, $NaN(TMS)_2$, PhH, 4 °C

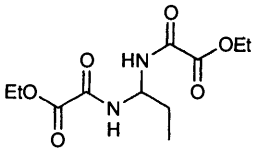
isobutyraldehyde to a solution of the oxamate **33** and a catalytic quantity of TMS triflate gave the silyloxy-adduct **35** (23%), recovered oxamate, and the hydroxy adduct **36** (11%). Presumably this latter adduct resulted from hydrolysis of compound **35** on work-up, and it is unusual for an adduct such as **36** to be stable. When the reaction time was reduced a slightly better yield (24%) of the silyloxy-adduct **35** was obtained. The silylated oxamate **33** could also be added to



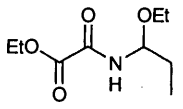
35



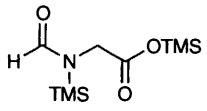
36



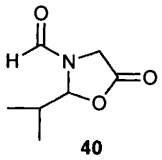
37



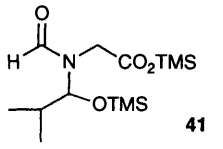
38



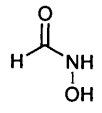
39



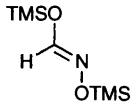
40



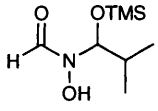
41



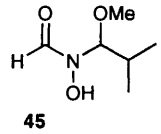
42



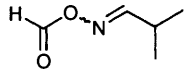
43



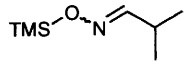
44



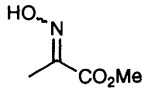
45



46



47



48

propionaldehyde diethyl acetal to give a mixture of the bis-adduct **37** (69%) and mono-adduct **38** (10%).

Silylation of *N*-formylglycine proceeded smoothly to give an excellent yield of *N*-formyl-*N*,*O*-bis(trimethylsilyl)glycine **39**. It was envisaged that addition of compound **39** to isobutyraldehyde would give directly the oxazolidinone **40**. Addition of isobutyraldehyde to a solution of compound **39** and a catalytic quantity of TMS triflate gave a product which appeared to be the adduct **41**, by IR and ^{1}H NMR spectroscopy, and which was obtained in a crude state by bulb-to-bulb distillation from the reaction mixture. A complex mixture resulted when cyclisation of compound **41** was attempted in acetic anhydride. However, when, instead of attempting to isolate compound **41**, we treated the reaction mixture with formic acid, then the desired oxazolidinone **40** was obtained (58%). It was possible that this oxazolidinone **40** might be available *via* direct reaction of *N*-formylglycine with isobutyraldehyde; however, when this reaction was attempted under acidic conditions a complex mixture was produced.

Next formhydroxamic acid **42** was prepared from hydroxylamine hydrochloride and ethyl formate[27] and silylation of acid **42** under the usual conditions gave bis(trimethylsilyl)formhydroxamic acid **43**. A series of bis(trimethylsilyl)hydroxamic acids had been found to exist in the imidate form[28] and as the IR spectrum of compound **43** contains characteristic absorptions in common with these compounds it is possible that it also exists in the imidate form. Since formhydroxamic acid **42** decomposes above its melting point (81–82 °C) some decomposition might be expected in refluxing benzene. This point was borne out by the excellent yield of compound **43** obtained with a short reaction time (93%; reflux, 0.25 h) *vs.* the relatively poor yield obtained over a longer period (35%; reflux, 1 h). Bis(trimethylsilyl)formhydroxamic acid **43** was a particularly reactive silylated amide, and even at room temperature no catalyst was required for formation of the isobutyraldehyde adduct **44** (69%). The adduct **44** was slightly unstable and decomposed on attempted bulb-to-bulb distillation at reduced pressure, but the more stable methoxy-adduct **45** was prepared (46%) by quenching the reaction with a solution of TMS triflate in methanol.† We also found that the yield of this reaction could be improved to 88% by performing the initial step in the absence of solvent. When the preparation of the trimethylsilyloxy-adduct **44** was attempted in the presence of catalytic TMS triflate the only isolable products were formyl oxime **46** and *O*-trimethylsilyl isobutyraldehyde oxime **47** in low yields.

Finally, addition of bis(trimethylsilyl)formhydroxamic acid **43** to methyl pyruvate, followed by a methanolic solution of TMS triflate was attempted, but this only gave the oxime **48** in a meagre 18% yield.

Spectral properties of the BSF–bisbutyraldehyde adduct 12 as representative of this class of compounds

The ^{1}H NMR spectrum of compound **12** is complicated by the presence of two diastereoisomers and hindered rotation about the C–N bond of the amide. The latter effect results in one side-chain being shielded and one being deshielded at any point in time (on the NMR time-scale). Thus the formyl proton of each diastereoisomer resonates at its own unique frequency and two signals are observed. All other types of protons in the compound can give rise to up to four signals; similar protons in different diastereoisomers can have distinct chemical shifts and within each diastereoisomer the two side-chains are distinguishable. The ^{13}C NMR spectrum is also complicated by the presence of diastereoisomers and rotamers. As in the ^{1}H NMR spectrum, two signals are observed for the formyl carbon (one due to each diastereoisomer) and all other types of carbon can give rise to up to four signals.[29]

Spectral properties of the BSF–monophenylacetaldehyde adduct 15 as representative of this class of compounds

Two rotamers are present due to restricted rotation about the C–N bond of the formamide. Each rotamer has its own ^{1}H NMR spectrum and so the spectrum observed is a combination of these. Peaks due to each rotamer can be distinguished as the C*H*O-N*H* coupling in the s-*trans*-rotamer is much larger than in the s-*cis*-rotamer.[30] In this case the rotamers are present in the ratio 3:1, the major component being the s-*cis*-rotamer. This ratio corresponds to a free-energy difference of 0.65 kcal per mole‡ between the two isomers.[31] The spectrum of each rotamer is presented separately below in the Experimental section. For a given rotamer, each proton of the methylene group has a different chemical shift as they are adjacent to an asymmetric carbon and are thus diastereotopic. Separate peaks for each rotamer are also observed in the ^{13}C NMR spectrum.

Conclusions

There does not appear to be any clear-cut explanation for the reactivity of some silylated amides towards aldehydes and

† See following paper for a more detailed study of the reactions of *N*-(α-trimethylsiloxy)amides.

‡ 1 cal = 4.184 J.

the absence of such reactivity in others. BSA **23** and trifluorobis(trimethylsilyl)acetamide **24** failed to react, but *N*-methyl-*N*-(trimethylsilyl)formamide **25**, *N*-phenyl-*N*(trimethylsilyl)formamide **29** and *N*-methyl-*N*-(trimethylsilyl)acetamide **27** reacted cleanly. Bis(trimethylsilyl)-formhydroxamic acid **43** was particularly reactive, which may be attributable to the α effect,[32] and did not require the use of a catalyst in its reactions with aldehydes. Addition of silylated amides to ketones is also possible, but good yields are only achieved with reactive compounds such as methyl pyruvate. BSF **7** also adds to propionaldehyde diethyl acetal, but only in poor yield.

Experimental

Mp were measured on a Reichert hot stage and are uncorrected. Elemental analyses were performed by the staff of the Micro-Analytical Unit of the School of Chemistry of the University of Leeds. IR spectra were recorded on a Perkin-Elmer 1420 Ratio Recording IR spectrometer, using polystyrene (ν_{max} 1601 cm^{-1}) as standard. NMR spectra were recorded on either a Perkin-Elmer R32 (^1H at 90 MHz), a JEOL FX 90Q (^1H at 90 MHz and ^{13}C at 22.5 MHz) or a Bruker AM400 spectrometer (^1H at 400 MHz and ^{13}C at 100 MHz). Resonances are reported in parts per million downfield from tetramethylsilane (internal standard), and *J*-values are given in Hz. Low-resolution mass spectra (electron impact) were recorded on a Kratos MS25 mass spectrometer, and high-resolution measurements determined on a Kratos MS9/50 mass spectrometer. TLC was carried out using Camlab pre-coated TLC plates (Sil G-25 UV_{254}) and the products visualised either under UV light at 254 nm, by exposure to iodine vapour, or by dipping in a solution of cerium(IV) ammonium sulfate in sulfuric acid (10 g in 300 cm^3 of 3 mol dm^{-3} H_2SO_4) and warming. Column chromatography was carried out on Camlab flash silica gel (230–400 mesh). Diethyl ether (referred to as ether) and benzene were distilled from sodium wire, and chloroform, dichloromethane (DCM), and tetrachloromethane were distilled from phosphorus pentaoxide. Triethylamine was distilled from calcium hydride, and formic acid from boric anhydride. All purified solvents were stored over 4 Å molecular sieves (except for triethylamine and formic acid). Light petroleum refers to the fractions boiling at 30–40 °C and was distilled prior to use, as was ethyl acetate. Ether for chromatography was used as purchased.

Bis(trimethylsilyl)formamide 7[15]

To a stirred solution of formamide (8 cm^3, 0.20 mol) and triethylamine (62 cm^3, 0.44 mol, 2.2 equiv.) in dry benzene (80 cm^3), at room temperature under nitrogen, was added TMSCl (51 cm^3, 0.40 mol, 2.2 equiv.) over a period of 1.5 h. The solution was heated at reflux for 1 h and then was allowed to cool to room temperature. Triethylamine hydrochloride was removed by filtration under nitrogen and was washed with dry benzene (3 × 20 cm^3). The organic solutions were combined and the solvent was removed under reduced pressure (oil pump). The resulting oil was distilled (81–82 °C/20 mmHg) through a short Vigreux column to give the *title compound* **7** (28.24 g, 75%) as an oil, $\nu_{max}(CCl_4)/cm^{-1}$ 1660 (C=O), 1410 and 1385; δ_H(90 MHz; $CDCl_3$) 8.50 (1 H, s, CHO) and 0.28 (18 H, s, $SiMe_3$).

***N*-[2,2-Dimethyl-1-(trimethylsiloxy)propyl]formamide 8**

To a solution of pivalaldehyde (0.35 cm^3, 3.2 mmol) in dry chloroform (10 cm^3) was added BSF **7** (1.2 cm^3, 5.6 mmol, 1.7 equiv.). The solution was heated at reflux under nitrogen for 4 days after which the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (30 g); (1:1) light petroleum–ether] gave the *title compound* **8** (40 mg, 6%) as crystals, mp 55–57 °C (Found: C, 53.4; H, 10.4; N, 6.85%; M^+, 203.1348. $C_9H_{21}NO_2Si$ requires C, 53.15; H, 10.4; N, 6.9%; M, 203.1341); R_f 0.78 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3440 (N–H), 2760, 1690 (C=O) and 1500; δ_H(90 MHz; CCl_4) (where separate peaks are seen for each rotamer the ratio of the low field to the high field peak is 2:1) 8.05 and 7.90 (1 H, 2 s, CHO of major and minor rotamers), 6.35–6.0 (1 H, br, NH), 5.15 and 4.4 (1 H, 2 d, *J* 10, N–CHO of major and minor rotamers), 0.85 (9 H, s, CMe_3) and 0.1 (9 H, s, $SiMe_3$); *m/z* 203 (M^+, 0.4%), 188 (12, M − Me), 146 (100, M − CMe_3), 102 (71, NH=CHO^+=$SiMe_2$) and 73 (73, $SiMe_3^+$).

***N*-[2-methyl-1-(trimethylsiloxy)propyl]formamide 9**

To a solution of isobutyraldehyde (0.3 cm^3, 3.3 mmol) in dry chloroform (6 cm^3) was added BSF **7** (1.0 cm^3, 4.7 mmol, 1.4 equiv.). The solution was heated at reflux for 17 h, under a silica gel guard tube to exclude moisture, after which the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (15 g); (3:1) light petroleum–ether] gave an oil, which was further purified by bulb-to-bulb distillation (73–80 °C/0.3 mmHg) to give the *title compound* **9** (301 mg, 48%) as an oil (Found: C, 50.6; H, 9.95; N, 7.3%; M^+, 189.1187. $C_8H_{19}NO_2Si$ requires C, 50.75; H, 10.1; N, 7.4%; M, 189.1185); R_f 0.55 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3440 (NH), 1710 (C=O) and 1490; δ_H(90 MHz; CCl_4) (two rotamers present in ratio 4:1) 8.1 (0.8 H, s, major rotamer of CHO), 8.1 (0.2 H, d, *J* 11, minor rotamer of CHO), 7.35 and 6.60 (1 H, 2 br m, NH, of major and minor rotamers), 5.25 and 4.6 (1 H, 2 d, *J* 7 and 10 N–CH–O of minor and major rotamers), 1.75 (1 H, octet, *J* 7, C*H*Me_2), 0.95 (6 H, d, *J* 7, CH*Me*$_2$) and 0.15 (9 H, s, $SiMe_3$); *m/z* 174 (M^+ − Me, 11%), 146 (67, M − $CHMe_2$), 102 (96, NH=CHO^+=$SiMe_2$), 75 (99, HO^+=$SiMe_2$) and 73 (100, $SiMe_3^+$).

***N*-[1-(Trimethylsiloxy)butyl]formamide 10**

To a solution of butyraldehyde (0.35 cm^3, 4.0 mmol) in dry chloroform (10 cm^3) was added BSF **7** (0.95 g, 5.02 mmol, 1.2 equiv.). The solution was heated at reflux, under a silica gel guard tube to exclude moisture, for 6 days, after which the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (30 g); (1:1) light petroleum–ether] gave an oil, which was further purified by bulb-to-bulb distillation (98–100 °C/0.3 mmHg) to give the *title compound* **10** (676 mg, 78%) as an oil (Found: C, 50.9; H, 10.3; N, 7.65%; M^+, 189.1184); R_f 0.58 (ether); $\nu_{max}(CHCl_3)/cm^{-1}$ 3430 (NH), 1690 (C=O) and 1500; δ_H(90 MHz; CCl_4) (two rotamers present in ratio 3:1) 8.05 and 7.95 (1 H, 2 s, CHO of major and minor rotamers), 6.65–6.35 (1 H, br, NH), 5.45 and 4.85 (1 H, 2 m, N–CH–O of major and minor rotamers), 1.8–1.15 (4 H, m, CH_2CH_2), 0.95 (3 H, t, *J* 6, CH_2CH_2*Me*) and 0.15 (9 H, s, $SiMe_3$); *m/z* 189 (M^+, 0.6%), 174 (11, M − Me), 146 (53, M − $CH_2CH_2CH_3$), 102 (86, NH=CHO^+=$SiMe_2$) and 75 (100, HO^+=$SiMe_2$).

***N*,*N*-Bis-[1-(trimethylsiloxy)butyl]formamide 12**

To a solution of butyraldehyde (0.35 cm^3, 4.0 mmol) in dry chloroform (6 cm^3) was added BSF **7** (1.1 cm^3, 5.1 mmol, 1.3 equiv.) and TMS triflate (0.38 cm^3 of a 0.52 mol dm^{-3} solution in tetrachloromethane, 0.2 mmol, 5 mol% with respect to the aldehyde). The solution was stirred at room temperature with a silica gel guard tube to exclude moisture for 5 h, after which the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (15 g); (2:1) light petroleum–ether] gave an equimolar mixture of the two diastereoisomers of the *title compound* **12** (221 mg, 34%) as an oil (Found: C, 54.05; H, 10.55; N, 4.2%; M^+, 333.2144. $C_{15}H_{35}NO_3Si_2$ requires C, 54.0; H, 10.6; N, 4.25%; M, 333.2155); R_f 0.72 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 2960, 1680 (C=O) and 1255; δ_H(400 MHz; $CDCl_3$) 8.45 and 8.40 (1 H, 2 s, CHO of each diastereoisomer), 5.85 (1 H, 2 t, *J* 6.0, N–CH–O deshielded by carbonyl, separate peaks for each diastereoisomer), 5.00 (1 H, t, *J* 6.0, N–CH–O shielded by

carbonyl), 1.9–1.1 (8 H, m, CH_2CH_2), 0.95 (6 H, t, *J* 7, CH_2CH_2Me) and 0.142, 0.138, 0.138 and 0.118 (18 H, 4 s, $SiMe_3$); δ_C(22.5 MHz; $CDCl_3$) 162.0, 161.3 (CHO, of each diastereoisomer), 79.2, 77.8, 75.0, 74.9 (N–CH–O of the two side-chains, in each diastereoisomer), 41.7, 41.5, 38.6 and 38.1 ($CHCH_2CH_2Me$ of the two side-chains, in each diastereoisomer), 18.4, 18.3 and 18.2 ($CHCH_2CH_2Me$ of the two side-chains, in each diastereoisomer), 13.3 (CH_2CH_2Me) and 0.1, −0.1, −0.2 and −0.4 ($SiMe_3$ of the two side-chains, in each diastereoisomer); *m/z* 290 (1%, M − CH_2CH_2Me), 218 (32, M − CH_2CH_2Me − $HCOCH_2CH_2Me$), 145 (61, $MeCH_2CH_2CH{=}O^+SiMe_3$) and 73 (100, TMS^+).

N,N-Bis[phenyl(trimethylsiloxy)methyl]formamide 13 and N-[phenyl(trimethylsiloxy)methyl]formamide 14

Benzaldehyde (0.3 cm^3, 2.9 mmol) was added dropwise to a solution of BSF **7** (0.75 cm^3, 3.5 mmol, 1.2 equiv.) and TMS triflate (0.06 cm^3 of a 0.52 mol dm^{-3} solution in tetrachloromethane, 0.03 mmol, 1 mol% of aldehyde) in dry chloroform (6 cm^3). The solution was stirred at room temperature with a silica gel guard tube to exclude moisture for 24 h, after which the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (40 g); (3:1) light petroleum–ether] gave an oil, which was further purified by bulb-to-bulb distillation (130–138 °C/0.2 mmHg) to give an equimolar mixture of the two diastereoisomers of N,N-*bis[phenyl(trimethylsiloxy)methyl]formamide* **13** (384 mg, 65%) as an oil (Found: C, 63.05; H, 7.95; N, 3.45%; M^+, 401.1827. $C_{21}H_{31}NO_3Si_2$ requires C, 62.8; H, 7.8; M, 3.5%; M, 401.1842); R_f 0.59 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 2960 and 1680 (C=O); δ_H(90 MHz; CCl_4) 8.5 and 8.3 (1 H, s, CHO of each diastereoisomer), 7.6–7.0 (10 H, m, ArH), 6.75 (1 H, m, N–CH–O deshielded by formyl), 5.3 (1 H, m, N–CH–O shielded by formyl) and 0.2, 0.1, 0.05 and −0.35 (18 H, 4 s, $SiMe_3$ shielded and deshielded by formyl and of each diastereoisomer); *m/z* 295 (4%, M − PhCHO), 222 (25), 179 (100, $PhCH{=}O^+SiMe_3$) and 73 (5, $SiMe_3^+$) and N-[*phenyl(trimethylsiloxy)methyl]formamide* **14** (147 mg, 22%) as an oil; ^1H NMR spectrum identical with that of a more fully characterised sample (see below).

N-[Phenyl(trimethylsiloxy)methyl]formamide 14

A solution of benzaldehyde (92 mg, 0.86 mmol) in dry tetrachloromethane (7 cm^3) was added dropwise to a solution of BSF **7** (1 cm^3, 4.7 mmol, 5.4 equiv.) and TMS triflate (0.05 cm^3 of a 0.52 mol dm^{-3} solution in CCl_4, 0.026 mmol, 3 mol%) in dry tetrachloromethane (5 cm^3). After stirring of the mixture at room temperature under nitrogen for 8 h the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (8 g); (1:1) light petroleum–ether] gave the *title compound* **14** (179 mg, 93%) as an oil, R_f 0.55 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3420 (NH), 1700 (C=O), 1485 and 1255; δ_H(90 MHz; CCl_4) 8.1 and 7.95 [1 H, 2 s, CHO of minor rotamer (20%) and major rotamer (80%)], 7.6–6.6 (1 H, br, NH), 7.3 (5 H, s, ArH), 6.45 and 5.85 (1 H, 2 d, *J* 9, $NHCHOSiMe_3$ of major and minor rotamers) and 0.15 and 0.05 (9 H, s, $SiMe_3$ of major and minor rotamers). No further data could be obtained as the compound decomposed on attempted vacuum distillation.

N-[2-Phenyl-1-(trimethylsiloxy)ethyl]formamide 15

Phenylacetaldehyde (0.3 cm^3, 2.6 mmol) was added dropwise to a solution of BSF **7** (1.3 cm^3, 6.1 mmol, 2.3 equiv.) and TMS triflate (0.2 cm^3 of a 0.26 mol dm^{-3} solution in tetrachloromethane 0.05 mmol, 2 mol% of aldehyde) in dry CCl_4 (7 cm^3). The solution was stirred at room temperature with a silica gel guard tube to exclude moisture for 72 h, after which the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (30 g); (1:1) light petroleum–ether] gave an oil, which was further purified by bulb-to-bulb distillation (80–84 °C/0.3 mmHg) to give the *title compound* **15** (600 mg, 97%) as crystals, mp 82–83 °C (Found: C, 60.8; H, 8.15; N, 5.85%; M^+, 237.1184. $C_{12}H_{19}NO_2Si$ requires C, 60.7; H, 8.1; N, 5.9%; M, 237.1185); R_f 0.62 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3440 (NH), 2960, 1705 (C=O) and 1490; δ_H(400 MHz; $CDCl_3$) 8.02 (0.25 H, d, *J* 10.0, CHO of minor rotamer), 8.01 (0.75 H, s, CHO of major rotamer), 7.23 (5 H, m, ArH), 6.93 (0.25 H, t, *J* 10.0, NH of minor rotamer), 6.71 (0.75 H, d, *J* 9.0, NH of major rotamer), 5.72 (0.75 H, ddd, *J* 4.6, 6.9 and 9.0, N–CH–O of major rotamer), 5.06 (0.25 H, dt, *J* 5.9 and 10.0, N–CH–O of minor rotamer), 2.94 (0.25 H, dd, *J* 6.0 and 13.0, CH*H*Ph of minor rotamer), 2.93 (0.25 H, dd, *J* 10.0 and 13.0, CH*H*Ph of minor rotamer), 2.90 (0.75 H, dd, *J* 4.6 and 13.4, C*H*HPh of major rotamer), 2.83 (0.75 H, dd, *J* 6.9 and 13.4, CH*H*Ph of major rotamer) and 0.001 and 0.000 (9 H, 2 s, $SiMe_3$ of minor and major rotamers); δ_C(22.5 MHz; $CDCl_3$) 163.5 and 160.0 (minor and major rotamers of CHO), 136.2 and 135.7 (quaternary aromatic C in major and minor rotamers), 129.8, 128.3 and 128.1 [*ortho* and *meta* aromatic C of the rotamers; 129.8 has a high-field shoulder on it (presumably its minor rotamer), 128.3 is smaller than the other two (presumably it is the minor rotamer of 128.1)], 126.8 and 126.5 (*para* aromatic C of minor and major rotamers), 78.9 and 73.1 ($NHCHOSiMe_3$ of minor and major rotamers), 44.9 and 43.9 (CH_2Ph of minor and major rotamers) and −0.1 and −0.4 ($SiMe_3$ of minor and major rotamers); *m/z* 222 (4%, M − Me), 146 (100, M − $PhCH_2$), 102 (51, $NH{=}CHO^+{=}SiMe_2$), 75 (55, $HO^+{=}SiMe_2$) and 73 (85, $SiMe_3^+$).

(Under similar conditions, treatment of phenylacetaldehyde with 1.6 mol equiv. of BSF **7** for 1 day gave compound **15** in 35% yield.)

N-[2,2-Dimethyl-1-(trimethylsiloxy)propyl]formamide 8

Pivalaldehyde (0.35 cm^3, 3.2 mmol) was added dropwise to a solution of BSF **7** (1.1 cm^3, 5.1 mmol, 1.6 equiv.) and TMS triflate (0.1 cm^3 of a 0.52 mol dm^{-3} solution in tetrachloromethane, 2 mol%) in dry chloroform (6 cm^3). The solution was stirred at room temperature, using a silica gel guard tube to exclude moisture, for 20 h, after which the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (20 g); (1:1) light petroleum–ether] gave the *title compound* **8** (554 mg, 85%) as crystals, identical with a fully characterised sample by ^1H NMR spectroscopy and TLC (see above).

N-[2-Methyl-1-(trimethylsiloxy)propyl]formamide 9

Isobutyraldehyde (0.40 cm^3, 4.1 mmol) was added dropwise to a solution of BSF **7** (3.0 cm^3, 14.0 mmol, 3.4 equiv.) and TMS triflate (0.15 cm^3 of a 0.52 mol dm^{-3} solution in tetrachloromethane, 0.078 mmol, 2 mol%) in dry tetrachloromethane (16 cm^3). The solution was stirred at room temperature under nitrogen for 2.5 h, after which the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (20 g); (1:1) light petroleum–ether] gave the *title compound* **9** (720 mg, 93%) as an oil, identical with a fully characterised sample by ^1H NMR spectroscopy and TLC. (Under similar conditions, treatment of isobutyraldehyde with 2.5 mol equiv. of BSF for 3 h gave compound **9** in 80% yield, whereas treatment with 1.5 mol equiv. of BSF for 1 h gave compound **9** in 59% yield.)

N-[1-(Trimethylsiloxy)butyl]formamide 10

Butyraldehyde (0.09 cm^3, 1.0 mmol) was added dropwise to a solution of BSF **7** (1.1 cm^3, 5.1 mmol, 5.0 equiv.) and TMS triflate (0.7 cm^3 of a 0.26 mol dm^{-3} solution in tetrachloromethane, 0.18 mmol, 18 mol%) in dry chloroform (5 cm^3). The solution was stirred at room temperature under nitrogen for 1 h, after which the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (40 g); (2:1) light petroleum–ether] gave the *title*

compound **10** (118 mg, 63%) as an oil, identical with a fully characterised sample by ^{1}H NMR spectroscopy and TLC.

N-[1-(Trimethylsiloxy)but-2-enyl]formamide 16

Crotonaldehyde (0.05 cm^3, 0.6 mmol) was added dropwise to a solution of BSF **7** (0.5 cm^3, 2.34 mmol, 3.9 equiv.) and TMS triflate (0.03 cm^3 of a 0.26 mol dm^{-3} solution in DCM, 0.008 mmol, 1 mol%) in dry tetrachloromethane (5 cm^3) under nitrogen at room temperature. After 1 h thiophenol (0.07 cm^3, 0.68 mmol, 1.1 mol equiv.) was added and after a further 21 h the solvent was removed under a stream of nitrogen. Purification of the residue by flash column chromatography [silica (20 g); (1:1) light petroleum–ether] gave the *title compound* **16** (42 mg, 40%) as an oil, R_f 0.52 (ether); ν_{max}(film)/cm^{-1} 3290 (NH), 2960, 1680 (C=O), 1520 and 1250; δ_H(400 MHz; $CDCl_3$) [major rotamer (55%)] 8.12 (1 H, dd, *J* 0.9 and 1.4, CHO), 6.11 (1 H, br d, *J* 9.0, NH), 5.94 (1 H, qdddd, *J* 1.1, 0.9, 1.3, 5.0 and 9.2, NHC*H*OSiMe$_3$), 5.81 (1 H, dqd, *J* 1.2, 6.6 and 15.2, CH=C*H*Me), 5.45 (1 H, qdd, *J* 1.6, 5.0 and 15.2, C*H*=CHMe), 1.70 (3 H, ddd, *J* 1.1, 1.6 and 6.6, CH=CH*Me*) and 0.16 (9 H, s, SiMe$_3$); [minor rotamer (45%)] 8.18 (1 H, d, *J* 11.8, CHO), 6.21 (1 H, br dd, *J* 9.0 and 12.0, NH), 5.86 (1 H, dqd, *J* 1.3, 6.6 and 15.4, CH=C*H*Me), 5.53 (1 H, qdd, *J* 1.6, 5.0 and 15.4, C*H*=CHMe), 5.36 (1 H, qddd, *J* 1.1, 1.3, 5.0 and 9.2, NHC*H*OSiMe$_3$), 1.70 (3 H, ddd, *J* 1.1, 1.6 and 6.6, CH=CH*Me*) and 0.15 (9 H, s, SiMe$_3$); *m/z* 187 (2%, M$^+$), 172 (3, M − Me), 147 (4), 102 (25) and 75 (100) (Found: M$^+$, 187.1028. $C_8H_{17}NO_2Si$ requires M, 187.1029).

N-[1-Cyclopropyl-1-(trimethylsiloxy)methyl]formamide 17

To a stirred solution of BSF **7** (1.0 cm^3, 4.67 mmol, 3.0 equiv.) and TMS triflate (0.1 cm^3 of a 0.52 mol dm^{-3} solution in tetrachloromethane, 0.0052 mmol, 3% relative to aldehyde) in dry tetrachloromethane (1 cm^3) under nitrogen at room temperature was added cyclopropanecarbaldehyde (111 mg, 1.58 mmol). After 10 min the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (30 g); (1:1) light petroleum–ether] gave the *title compound* **17** (92 mg, 31%) as an oil, R_f 0.41 (ether); ν_{max}(CCl_4)/cm^{-1} 3430 (NH), 3090, 3010, 2750, 1700 (C=O), 1250 and 890; δ_H (90 MHz; CCl_4) 8.25 and 8.10 [1 H, 2 s, CHO of minor rotamer (25%) and major rotamer (75%)], 7.9–7.0 (1 H, br m, NH), 5.3 and 4.80 (1 H, 2 dd, *J* 6 and 9, NHC*H*OSiMe$_3$ of major and minor rotamers), 1.10 (1 H, m, C*H*Me$_2$), 0.40 (4 H, m, cyclopropyl CH_2) and 0.15 (9 H, s, SiMe$_3$); *m/z* 187 (2%, M$^+$), 172 (8, M − Me), 146 (23, M − cyclopropyl radical), 118 (5, M − cyclopropyl radical − CO), 102 (100, Me$_2$Si=O$^+$CH=NH), 75 (75, Me$_2$Si=O$^+$H) and 73 (79, SiMe$_3^+$ (Found: M$^+$, 187.1036. $C_8H_{17}NO_2Si$ requires M, 187.1029).

N-[1-Methyl-1-(trimethylsiloxy)ethyl]formamide 18

Acetone (0.058 cm^3, 0.79 mmol) was added dropwise to a stirred solution of BSF **7** (0.5 cm^3, 2.3 mmol, 2.9 equiv.) and TMS triflate (0.1 cm^3 of a 0.26 mol dm^{-3} solution in tetrachloromethane, 0.026 mmol, 3 mol% of ketone) in dry tetrachloromethane (3 cm^3) at room temperature under nitrogen. After 7 days the solvent was removed under reduced pressure and purification of the residue by flash column chromatography [silica (20 g); (1:1) light petroleum–ether] gave the *title compound* **18** (52 mg, 38%) as an oil, R_f 0.38 (ether); ν_{max}(CCl_4)/cm^{-1} 3220 (NH), 1700 (C=O) and 1255; δ_H(90 MHz; CCl_4) 9.0–7.9 (1 H, br m, NH), 8.45 (1 H, d, *J* 12, CHO), 1.6 (6 H, s, Me) and 0.2 (9 H, s, SiMe$_3$); no further data could be obtained due to decomposition of this compound.

N-[1-(Trimethylsiloxy)cyclopentyl]formamide 19

Cyclopentanone (0.06 cm^3, 0.68 mmol) was added dropwise to a stirred solution of BSF **7** (0.5 cm^3, 2.34 mmol, 3.5 equiv.) and TMS triflate (0.1 cm^3 of a 0.26 mol dm^{-3} solution in DCM, 0.026 mmol, 4 mol%) in dry terachloromethane (5 cm^3) at room temperature under nitrogen. After 5 days the solvent was removed under reduced pressure and purification of the residue by flash column chromatography [silica (10 g); (2:1) light petroleum–ether] gave the *title compound* **19** (18 mg, 13%) as an oil, R_f 0.48 (ether); ν_{max}($CHCl_3$)/cm^{-1} 3400 (NH), 1690 (C=O), and 1250; δ_H(90 MHz; $CDCl_3$) 8.6 (1 H, d, *J* 11, CHO), 7.9–7.2 (1 H, br m, NH), 2.3–1.5 (8 H, m, [CH_2]$_4$) and 0.15 (9 H, s, SiMe$_3$); *m/z* 201 (31%, M$^+$), 186 (15, M − Me), 172 (38), 118 (100), 102 (68, Me$_2$Si=O$^+$CH=NH) and 75 (75, Me$_2$Si=O$^+$H) (Found: M$^+$, 201.1185. $C_9H_{19}NO_2Si$ requires M, 201.1185).

Methyl 2-formamido-2-(trimethylsiloxy)propanoate 20

Methyl pyruvate (0.06 cm^3, 0.66 mmol) was added dropwise to a stirred solution of BSF **7** (0.5 cm^3, 2.34 mmol, 3.5 equiv.) and TMS triflate (0.06 cm^3 of a 0.52 mol dm^{-3} solution in tetrachloromethane, 0.031 cm^3, 5 mol%) in dry tetrachloromethane (5 cm^3) at room temperature under nitrogen. After 21 h the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (20 g); ether] gave the *title compound* **20** (122 mg, 83%) as needles, mp 91–92 °C (from EtOAc) (Found: C, 43.9; H, 7.9; N, 6.5%; M$^+$, 219.0928. $C_8H_{17}NO_4Si$ requires C, 43.8; H, 7.8; N, 6.4%; M, 219.0927); R_f 0.62 (ether); ν_{max}($CHCl_3$)/cm^{-1} 3400 (NH), 1750 (MeOC=O), 1695 (NHC=O) and 1285; δ_H(90 MHz; $CDCl_3$) 9.3 (0.5 H, d, *J* 13, CHO of one rotamer), 8.9 (0.5 H, s, CHO of other rotamer), 8.1–7.2 (1 H, br m, NH), 4.2 (3 H, s, OMe), 2.05 and 1.95 (together 3 H, each s, CMe of each rotamer) and 0.25 (9 H, s, SiMe$_3$); *m/z* 204 (4%, M$^+$ − Me), 160 (28, M − CO_2Me), 118 (65) and 102 (100, Me$_2$Si=O$^+$CH=NH).

N-(1-Ethoxypropyl)formamide 21 and N,N-bis-(1-ethoxypropyl)formamide 22

Propionaldehyde diethyl acetal (0.1 cm^3, 0.62 mmol) was added to a solution of BSF **7** (0.5 cm^3, 2.34 mmol, 3.8 equiv.), Hünig's base (*N*-ethyldiisopropylamine) (0.02 cm^3, 0.06 mmol, 10 mol%) and TMS triflate (0.1 cm^3 of a 0.26 mol dm^{-3} solution in DCM, 0.026 mmol, 4 mol%) in dry DCM (6 cm^3) under nitrogen at room temperature. After 24 h the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (10 g); (1:1) light petroleum–ether] gave N,N-*bis*(1-*ethoxypropyl*)*formamide* **22** (25 mg, 37%) as an oil, R_f 0.62 (ether); ν_{max}(CCl_4)/cm^{-1} 2980, 1680 (C=O) and 1240; δ_H(90 MHz; CCl_4) 8.55 and 8.50 (1 H, 2 s, CHO of each diastereoisomer), 5.50 and 5.40 (1 H, 2 dd, *J* 3 and 5, NC*H*OEt deshielded by formyl; one dd for each diastereoisomer), 4.50 and 4.40 (1 H, 2 dd, *J* 3 and 5, NC*H*OEt shielded by formyl; one dd for each diastereoisomer), 3.6 (4 H, m, OCH_2), 1.75 (4 H, m, $CHCH_2CH_3$), 1.25 (6 H, t, *J* 7, OCH_2CH_3) and 1.05 (6 H, t, *J* 7, $CHCH_2CH_3$); *m/z* 188 (8%, M$^+$ − Et) 171 (2, M − HOEt), 130 (5), 102 (13), 87 (100) and 59 (63) (Found: M$^+$, 217.1677. $C_{11}H_{23}NO_3$ requires M, 217.1678).

Also isolated was N-(1-*ethoxypropyl*)*formamide* **21** (17 mg, 21%) as an oil, R_f 0.26 (ether); ν_{max}(CCl_4)/cm^{-1} 3415 (NH), 2980, 1705 (C=O) and 1490; δ_H(90 MHz; CCl_4) 8.25 (0.6 H, s, CHO of major rotamer), 8.15 (0.4 H, d, *J* 12, CHO of minor rotamer), 7.5–6.5 (1 H, br m, NH), 5.15 and 4.40 (1 H, 2 dt, *J* 6 and 10, NHC*H*OEt of major and minor rotamers), 3.5 (2 H, m, OCH_2), 1.6 (2 H, m, $CHCH_2Me$), 1.15 and 1.10 (3 H, 2 t, *J* 7, OCH_2CH_3 of minor and major rotamers) and 0.9 (3 H, t, *J* 7, $CHCH_2CH_3$); *m/z* 130 (1%, M$^+$ − H), 102 (90, M − Et), 86 (100, M − OEt), 74 (77) and 56 (86) [Found: (M − 1)$^+$, 130.0868. $C_6H_{12}NO_2$ requires *m/z*, 130.0868].

N-Methyl-N-[2-methyl-1-(trimethylsiloxy)propyl]formamide 26

Isobutyraldehyde (0.08 cm^3, 0.88 mmol) was added dropwise to a stirred solution of *N*-methyl-*N*-(trimethylsilyl)formamide[25]

25 (0.45 g, 4.0 equiv.) and TMS triflate (0.04 cm^3 of a 0.26 mol dm^{-3} solution in DCM, 0.01 mmol, 1 mol%) in dry tetrachloromethane (5 cm^3) under nitrogen at room temperature. After 2 h the solvent was removed under reduced pressure, and purification of the residue by flash column chromatography [silica (15 g); (1:1) light petroleum–ether] gave the *title compound* **26** (171 mg, 96%) as an oil (Found: C, 52.85; H, 10.35; N, 6.8%; M^+, 203.1341. $C_9H_{21}NO_2Si$ requires C, 53.15; H, 10.4; N, 6.9% M, 203.1342); R_f 0.72 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 1685 (C=O), 1255 and 1095; δ_H(90 MHz; CCl_4) 8.05 and 8.0 [1 H, 2 s, CHO of major rotamer (67%) and minor rotamer (33%)], 5.3 and 4.4 (1 H, 2 d, *J* 9, NC*H*OSiMe$_3$ of minor and major rotamers), 2.8 and 2.7 (3 H, 2 s, NMe of minor and major rotamers), 1.9 (1 H, septet, *J* 7, C*H*Me$_2$), 1.0 and 0.8 (6 H, 2 d, *J* 7, diastereotopic CH*Me*$_2$) and 0.1 (9 H, s, SiMe$_3$); *m/z* 203 (M^+, 0.2%), 188 (2, M − Me), 160 (100, M − Pr^i), 116 (38), 73 (83, TMS^+).

Competition reaction between BSF 7 and *N*-methyl-*N*-(trimethylsilyl)formamide 25 with isobutyraldehyde

Isobutyraldehyde (0.30 cm^3, 3.3 mmol, 7 mol% of silylated amides) was added to a mixture of BSF **7** (4.629 g, 0.0244 mol), *N*-methyl-*N*-(trimethylsilyl)formamide[25] **25** (3.181 g, 0.0243 mmol) and TMS triflate (0.10 cm^3, 0.52 mmol, 16 mol% of aldehyde) at room temperature under nitrogen. After 37 min the solvent was removed under reduced pressure and purification of the residue by flash column chromatography [silica (300 g); (1:1) light petroleum–ether] gave N-*methyl*-N-[2-*methyl*-1-(*trimethylsiloxy*)*propyl*]*formamide* **26** (459 mg, 68%), identical (^{1}H NMR) with a fully characterised sample, and N-[2-*methyl*-(*trimethylsiloxy*)*propyl*]*formamide* **9** (121 mg, 19%), identical (^{1}H NMR) with a fully characterised sample.

***N*-Methyl-*N*-[2-methyl-1-(trimethylsiloxy)propyl]acetamide 28**

Isobutyraldehyde (0.10 cm^3, 1.1 mmol) was added dropwise to a solution of *N*-methyl-*N*-(trimethylsilyl) acetamide[25] **27** (693 mg, 4.77 mmol, 4.3 equiv.) and TMS triflate (0.05 cm^3 of a 0.26 mol dm^{-3} solution in tetrachloromethane, 0.013 mmol, 1 mol%) in dry tetrachloromethane (8 cm^3) under nitrogen at room temperature. After 1 h the solvent was removed under reduced pressure, and purification of the residue by flash column chromatography [silica (30 g); (1:1) light petroleum–ether] gave the *title compound* **28** (114 mg, 48%) as an oil, R_f 0.55 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 1660 (C=O), 1250 and 1070; δ_H(90 MHz; CCl_4) 5.70 and 4.90 [1 H, 2 d, *J* 8, NC*H*OSiMe$_3$ of major rotamer (81%) and minor rotamer (19%)], 2.9 and 2.8 (3 H, 2 s, NMe of major and minor rotamers), 2.1 and 2.05 (3 H, 2 s, Ac of major and minor rotamers), 1.85 (1 H, m, C*H*Me$_2$), 1.1 and 0.85 (6 H, 2 d, *J* 8, diastereotopic CH*Me*$_2$) and 0.2 and 0.15 (9 H, 2 s, SiMe$_3$ of minor and major rotamers); *m/z* 217 (0.3%, M^+), 202 (2, M − Me), 174 (98, M − Pr^i), 132 (100, M − Pr^i − CH_2CO), 73 (94, $SiMe_3^+$) and 43 (73, $MeCO^+$) (Found: M^+, 217.1678. $C_{10}H_{23}NO_2Si$ requires M, 217.1683).

***N*-[2-Methyl-1-(trimethylsiloxy)propyl]-*N*-phenylformamide 30**

To a stirred solution of *N*-(trimethylsilyl)formanilide[26] **29** (210 mg, 10.9 mmol, 4.8 equiv.) and TMS triflate (0.1 cm^3 of a 0.52 mol dm^{-3} solution in tetrachloromethane, 0.052 mmol, 2% of aldehyde) under nitrogen at room temperature was added isobutyraldehyde (164 mg, 2.27 mmol) dropwise. After 1 h the solvent was removed under reduced pressure, and purification of the residue by flash column chromatography [silica (80 g); (1:1) light petroleum–ether] gave the *title compound* **30** (601 mg, 99%) as an oil, which was further purified by bulb-to-bulb distillation (115–120 °C/0.2 mmHg) (Found: C, 63.45; H, 8.8; N, 5.5%; M^+, 265.1491. $C_{14}H_{23}NO_2Si$ requires C, 63.35; H, 8.7; N, 5.3%; M, 265.1498); R_f 0.67 (ether); ν_{max}(film)/cm^{-1} 3060, 1685 (C=O), 1595, 1495, 1250 and 1075; δ_H(90 MHz; $CDCl_3$) 8.31 and 8.23 (1 H, 2 s, CHO of minor and major rotamers), 7.26 (5 H, s, ArH), 5.57 (0.85 H, d, *J* 9.6, N–CH–O of major rotamer), 4.61 (0.15 H, d, *J* 8.6, N–CH–O of minor rotamer), 1.6 (1 H, m, C*H*Me$_2$), 0.83 and 0.64 (6 H, 2 d, *J* 6.5, diastereotopic CH*Me*$_2$) and 0.11 and 0.10 (9 H, 2 s, SiMe$_3$ of minor and major rotamers); δ_C(22.5 MHz; $CDCl_3$) 163.1 and 162.5 (CHO of major and minor rotamers), 138.6, 129.0, 127.1 and 126.5 (Ar of major rotamer), 137, 128, 127 and 126 (Ar of minor rotamer), 90.3 and 81.7 (N–CH–O of minor and major rotamers), 32 and 31.4 (*C*HMe$_2$ of minor and major rotamers), 19.1 and 17.4 (diastereotopic CH*Me*$_2$ of major rotamer), 18.7 and 18.2 (diastereotopic CH*Me*$_2$ of minor rotamer) and 0.02 and −0.14 (SiMe$_3$ of minor and major rotamers); *m/z* 265 (1%, M^+), 250 (2, M − Me), 222 (11, M − Pr^i), 193 (46, M − $HCOPr^i$), 178 (31, M − $HCOPr^i$ − Me), 145 (56, M − CHONPh), 104 (26, Ph^+NCH) and 73 (100, $SiMe_3^+$).

Ethyl *N*,*N*-bis(trimethylsilyl)oxamate 33

Sodium (2.67 g, 0.116 mol) was slowly added to a solution of iron(III) nitrate nonahydrate (0.05 g, 0.124 mmol, 0.1 mol%) in liquid ammonia (100 cm^3). The resulting dark red–brown solution was stirred for 1 h, then dry benzene was added (100 cm^3) and the ammonia was allowed to evaporate off overnight. Hexamethyldisilazane (25 cm^3, 0.118 mol, 1.02 equiv.) was slowly added to the solution, which was then heated at reflux for 5 h (after which the evolution of ammonia gas had ceased). The solution was cooled in an ice-bath and ethyl oxalyl chloride **34** (9 cm^3, 0.081 mol, 0.7 equiv.) was added dropwise (over a period of 2 h) so that the temperature of the solution was maintained at less than 5 °C; the resulting solution was stirred at room temperature overnight. The solution was filtered under nitrogen, the flask was rinsed with dry benzene (2 × 20 cm^3), and solvent was removed under reduced pressure. The resulting pale yellow solution was purified by bulb-to-bulb distillation (100–110 °C/6 mmHg) to give the *title compound* **33** (6.26 g, 30%) as an oil, $\nu_{max}(CCl_4)/cm^{-1}$ 2980, 1745 (OC=O), 1700 (NC=O), 1245, 1100 and 900; δ_H(90 MHz; $CDCl_3$) 4.15 (2 H, q, *J* 7, C*H*$_2$Me), 1.3 (3 H, t, *J* 7, CH$_2$*Me*), 0.2 and 0.05 (18 H, 2, 2 × SiMe$_3$). Satisfactory mass spectra and microanalyses could not be obtained due to the ease of hydrolysis of this compound.

Ethyl *N*-[2-methyl-1-(trimethylsiloxy)propyl]oxamate 35

A solution of isobutyraldehyde (157 mg, 2.18 mmol) in dry tetrachloromethane (2 cm^3) was added dropwise to a solution of ethyl *N*,*N*-bis(trimethylsilyl)oxamate **33** (1.08 g, 4.14 mmol, 1.9 equiv.) and TMS triflate (0.1 cm^3 of a 0.52 mol dm^{-3} solution in CCl_4, 0.052 mmol, 2%) in dry tetrachloromethane (2 cm^3). The solution was stirred at room temperature, under nitrogen, for 17 h and then the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (30 g); (4:1) light petroleum–ether] gave the *title compound* **35** (135 mg, 24%) as an oil, R_f 0.69 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3400 (NH), 1760 (EtOC=O), 1700 (NHC=O) and 1275; δ_H(90 MHz; CCl_4) 7.2 (1 H, br d, *J* 10, NH), 5.2 (1 H, dd, *J* 6 and 10, NHC*H*OSiMe$_3$), 4.35 (2 H, q, *J* 7, OC*H*$_2$Me), 1.8 (1 H, m, C*H*Me$_2$), 1.5 (3 H, t, *J* 7, OCH$_2$*Me*), 1.0 (6 H, d, *J* 7, CH*Me*$_2$) and 0.2 (9 H, s, SiMe$_3$); δ_C(22.5 MHz; $CDCl_3$) 160.6 (NHC=O), 155.6 (OC=O), 78.8 (NHCHO), 63.1 (O*C*H$_2$Me), 34.7 (Me$_2$*C*H), 17.0 (OCH$_2$*Me*), 13.9 (*Me*$_2$CH) and −0.2 (SiMe$_3$); *m/z* 246 (4%, M^+ − Me), 218 (29, M − Pr^i), 190 (12, M − Pr^i − CO), 174 (25, M − Pr^i − CO_2), 162 (4, M − Pr^i − C_2H_4 − CO), 146 (32, M − Pr^i − C_2H_4 − CO_2), 75 (41, $Me_2Si{=}O^+H$), 73 (100, $SiMe_3^+$) (Found: M^+, 261.1395. $C_{11}H_{23}NO_4Si$ requires M, 261.1396).

Ethyl *N*-[2-methyl-1-(trimethylsiloxy)propyl]oxamate 35 and ethyl *N*-(1-hydroxy-2-methylpropyl)oxamate 36

A solution of isobutyraldehyde (77 mg, 1.07 mmol) in dry CCl_4 (3 cm^3) was slowly added to a solution of ethyl *N*,*N*-bis(trimethylsilyl)oxamate **33** (0.932 g, 3.57 mmol, 3.3 equiv.) and TMS triflate (0.1 cm^3 of a 0.52 mol dm^{-3} solution in

CCl_4, 0.052 mmol, 1%) in dry CCl_4 (1 cm^3). The solution was stirred at room temperature under nitrogen for 5 days and then the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (20 g); (1:1) light petroleum–ether] gave ethyl N-[2-*methyl*-1-(*trimethylsiloxy*)*propyl*]*oxamate* **35** (64 mg, 23%) as an oil, ^1H NMR data identical with those of a fully characterised sample, and *ethyl* N-(1-*hydroxy*-2-*methylpropyl*)*oxamate* **36** (23 mg, 11%) as a solid, R_f 0.43 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3320 (OH and NH), 1700 (C=O) and 1280; δ_H(90 MHz; CCl_4) 7.6 (1 H, d, *J* 9, NH), 5.2 (1 H, dd, *J* 7 and 9, OCHN), 4.9–4.6 (1 H, s, OH), 4.4 (2H, q, *J* 7, CH_2Me), 2.0 (1 H, octet, *J* 7, C*H*Me_2), 1.55 (3 H, t, *J* 7, CH_2*Me*) and 1.15 and 1.10 (6 H, 2 d, *J* 7, diastereotopic CH*Me*$_2$); *m/z* 172 (0.8%, $M^+ - OH$), 171 (0.5, $M - H_2O$), 146 (15, $M - Pr^i$), 118 (26, $M - Pr^i - C_2H_4$), 90 (29, $M - Pr^i - C_2H_4 - CO$), 73 (48, $Me_2CHCH{=}O+H$) (Found: M^+, 189.0991. $C_8H_{15}NO_4$ requires M, 189.1001) (Found: $[M - 1]^+$, 188.0916. $C_8H_{14}NO_4$ requires *m/z*, 188.0923).

Diethyl *N,N'*-propane-1,1-diyldioxamate 37 and ethyl *N*-(1-ethoxypropyl)oxamate 38

To a stirred solution of propionaldehyde diethyl acetal (442 mg, 3.34 mmol) and ethyl *N,N*-bis(trimethylsilyl)oxamate **33** (963 mg, 3.69 mmol, 1.1 equiv.) in dry tetrachloromethane (3 cm^3), at room temperature under nitrogen, was added TMS triflate (0.06 cm^3, 0.31 mmol, 9%). The solution was stirred for 20 min and then a further portion of TMS triflate (0.1 cm^3, 0.52 mmol, 15%) was added. After 1 h the solvent was removed under reduced pressure, and the resulting oil was purified by flash column chromatography [silica (70 g); (2:1) light petroleum–ether] to give *ethyl* N-(1-*ethoxypropyl*)*oxamate* **38** (66 mg, 10%) as an oil, R_f 0.59 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3400 (NH), 1730 (OC=O), 1710 (NHC=O) and 1510; δ_H(90 MHz; CCl_4) 7.5–7.0 (1 H, m, NH), 5.05 (1 H, dt, *J* 10 and 6, NHC*H*OEt), 4.3 (2 H, q, *J* 7, CO_2CH_2Me), 3.55 (2 H, m, CHOCH_2Me), 1.9–1.6 (2 H, m, CHCH_2Me), 1.45 (3 H, t *J* 7, CO_2CH_2*Me*), 1.2 (3 H, t, *J* 7, CHOCH_2*Me*) and 1.0 (3 H, t, *J* 7, CHCH_2*Me*); *m/z* 203 (0.4%, M^+), 174 (41, M – Et), 158 (37, M – OEt), 130 (21, M – Et – CO_2), 118 (24), 87 (100, $Et^+O{=}CHEt$), 59 (80, $H^+O{=}CHEt$) (Found: M^+, 203.1158. $C_9H_{17}NO_4$ requires M, 203.1157).

Also obtained was *diethyl* N,N'-*propane*-1,1-*diyldioxamate* **37** (345 mg, 69%) as an oil, R_f 0.62 (EtOAc); $\nu_{max}/(CHCl_3)/cm^{-1}$ 3400 (NH), 1760 (EtOC=O), 1715 (NHC=O) and 1510; δ_H(90 MHz; $CDCl_3$) 8.25 (2 H, br d, *J* 8, NH), 5.5 (1 H, m, NHC*H*NH), 4.4 (4 H, 2 q, *J* 7, OCH_2Me), 1.85 (2 H, m, MeCH_2CH), 1.45 (6 H, 2 t, OCH_2*Me*), 1.1 (3 H, m, *Me*CH_2CH); *m/z* 245 (21%, $M^+ - Et$), 174 (7, $M - CO_2 - CO - C_2H_4$), 158 (50, M – NHCOCO_2Et), 58 (29, $H_2N^+{=}CHEt$), 44 (75, MeCHO) and 29 (100, CHO^+) (Found: M^+, 274.1155. $C_{11}H_{18}N_2O_6$ requires M, 274.1165).

[*N*-Formyl-*N*-(trimethylsilyl)glycinate 39

To a stirred suspension of *N*-formylglycine (4.194 g, 0.041 mol) and triethylamine (15.1 cm^3, 0.11 mol, 2.7 equiv.) in dry benzene (80 cm^3) under nitrogen at room temperature was added trimethylsilyl chloride (12.8 cm^3, 0.10 mol, 2.4 equiv.) dropwise. The solution was heated at reflux for 3 h, then was cooled, and filtered under nitrogen. The solvent was removed under reduced pressure to give an orange-yellow oil, which was distilled (102–103 °C/0.4 mmHg) to give the *title compound* **39** (8.22 g, 82%) as an oil, $\nu_{max}(CCl_4)/cm^{-1}$ 1730 (OC=O), 1670 (NC=O) 1250 and 1090; δ_H(90 MHz; CCl_4) 8.55 and 8.40 [1 H, 2 s, CHO of major rotamer (60%) and minor rotamer (34%)], 4.00 (2 H, s, CH_2), 0.50 and 0.45 (18 H, 2 s, $SiMe_3$). Satisfactory mass spectra and microanalyses could not be obtained due to the ease of hydrolysis of this compound.

Trimethylsilyl *N*-formyl-*N*-[2-methyl-1-(trimethylsiloxy)-propyl]glycinate 41

To a mixture of isobutyraldehyde (0.050 cm^3, 0.55 mmol) and trimethylsilyl *N*-formyl-*N*-(trimethylsilyl)glycinate **39** (196 mg, 0.793 mmol, 1.4 equiv.) at room temperature was added TMS triflate (0.1 cm^3 of a 0.26 mol dm^{-3} solution in CCl_4, 0.026 mmol, 5 mol%). After 50 min the mixture was distilled bulb-to-bulb (77–87 °C/0.05 mmHg) to give the *title compound* **41** as an oil, ν_{max}(film)/cm^{-1} 1735 (OC=O), 1675 (NC=O), 1255 and 1210; δ_H(90 MHz; CCl_4) 8.25 (1 H, s, CHO), 5.6 (0.2 H, d, *J* 9, NC*H*O-$SiMe_3$ of minor rotamer), 4.7 (0.8 H, d, *J* 9, NC*H*O$SiMe_3$ of major rotamer), 4.1 (2 H, s, N$CH_2CO_2SiMe_3$), 1.95 (1 H, m, C*H*Me_2), 1.05 (6 H, d, *J* 7, CH*Me*$_2$), 0.4 (18 H, s, $SiMe_3$).

2-Isopropyl-5-oxooxazolidine-3-carbaldehyde 40

To a stirred solution of trimethylsilyl *N*-formyl-*N*-(trimethylsilyl)glycine **39** (609 mg, 2.46 mmol) and isobutyraldehyde (0.25 cm^3, 2.8 mmol, 1.1 equiv.), under nitrogen was added TMS triflate (0.1 cm^3 of a 0.26 mol dm^{-3} solution in CCl_4, 0.026 mmol, 1 mol%). After 40 min at room temperature the mixture was treated with formic acid (20 cm^3) added rapidly in one portion and after a further 10 min the formic acid was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (40 g); ether] gave the *title compound* **40** (223 mg, 58%) as an oil, R_f 0.19 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 1810 (OC=O), 1690 (NC=O) and 1160; δ_H(90 MHz; CCl_4) (a 1:1 mixture of the two rotamers) 8.25 and 8.20 (1 H, 2 s, CHO of each rotamer), 5.8 and 5.6 (1 H, 2 d, *J* 5, OC*H*NCHO of each rotamer), 4.35 (0.5 H, d, *J* 17, NC*H*HCO of one rotamer), 4.35 (0.5 H, d, *J* 18, NC*H*HCO of other rotamer), 4.0 (0.5 H, d, *J* 17, NCH*H*CO of one rotamer), 3.75 (0.5 H, d, *J* 18, NCH*H*CO of other rotamer), 2.2 (1 H, m, C*H*Me_2) and 1.1 (6 H, d, *J* 7, CH*Me*$_2$); *m/z* 157 (5%, M^+), 114 (100, $M - Pr^i$), 86 (94, $M - Pr^i - CO$), 58 (89, $M - Pr^i - CO - CO$) and 43 (23, Pr^{i+}) (Found: M^+, 157.0736. $C_7H_{11}NO_3$ requires M, 157.0739). Also isolated was *N*-formylglycine (49 mg, 19%).

Trimethylsilyl *O*-(trimethylsilyl)formhydroxamate 43

To a suspension of formhydroxamic acid [27] **42** (8.1 g, 0.133 mol) in dry benzene (100 cm^3) containing triethylamine (37.5 cm^3, 0.269 mmol, 2.02 equiv.) was added trimethylsilyl chloride (34 cm^3, 0.268 mmol, 2.02 equiv.) dropwise under nitrogen during 1.5 h. The solution was heated at reflux for 0.25 h and was then allowed to cool. The triethylamine hydrochloride precipitate was removed by filtration under nitrogen and rinsed with dry benzene (80 cm^3). The solvent was removed under reduced pressure and the product was distilled (70–71 °C/23 mmHg) to give the *title compound* **43** (25.32 g, 93%) as an oil, $\nu_{max}(CCl_4)/cm^{-1}$ 1630 and 1250; δ_H(90 MHz; CCl_4) 7.75 and 6.5 (1 H, 2 s, CHO) and 0.2, 0.15, 0.1 and 0.05 (18 H, 4 s, $SiMe_3$). Satisfactory mass spectra and microanalyses could not be obtained due to the ease of hydrolysis of this compound. (Under similar conditions addition of trimethylsilyl chloride over a period of 2 h and heating at reflux for 1 h gave compound **43** in 35% yield.)

***N*-[2-Methyl-1-(trimethylsiloxy)propyl]formhydroxamic acid 44**

Isobutyraldehyde (0.08 cm^3, 0.88 mmol) was added to a solution of trimethylsilyl *O*-(trimethylsilyl)formhydroxamate **43** (0.387 g, 1.88 mmol, 2.1 equiv.) in dry tetrachloromethane (2 cm^3), at room temperature under nitrogen. After 5 h the solvent was removed under reduced pressure and the resulting mixture of oil and solid was washed with dry tetrachloromethane. The tetrachloromethane solution was evaporated under reduced pressure to give the *title compound* **44** as an oil (125 mg, 69%), R_f 0.60 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3500–2700 (OH), 1680 (C=O) and 1255; δ_H(90 MHz; CCl_4) 9.4–7.5 (1 H, br s, OH), 8.15 and 8.05 [1 H, 2 s, CHO of minor rotamer (20%) and major rotamer (80%)], 5.2 and 4.6 (1 H, 2 d, *J* 8, N–CH–O of minor and major rotamers), 2.2 (1 H, m, C*H*Me_2), 1.0 and 0.9 (6 H, 2 d, *J* 7, diastereotopic CH*Me*$_2$) and 0.15 (9 H, s, $SiMe_3$); *m/z*

205 (M^+, 2%), 190 (4, M − Me), 162 (4, M − Pr^i), 145 (82, M − HCONOH) and 73 (100, $SiMe_3^+$). Attempted distillation of this product resulted in decomposition.

***N*-(1-Methoxy-2-methylpropyl)formhydroxamic acid 45**

Isobutyraldehyde (71 mg, 0.99 mmol) was added to (trimethylsilyl *O*-trimethylsilylformhydroxamate **43** (295 mg, 1.09 mmol, 1.1 equiv.) at room temperature under nitrogen. After 4 days a solution of dry methanol (10 cm^3) containing TMS triflate (0.2 cm^3 of a 0.26 mol dm^{-3} solution in tetrachloromethane 0.052 mmol, 5%) was added and after a further 30 min solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (10 g); ether] gave the *title compound* **45** (129 mg, 88%) as an oil, R_f 0.27 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3170 (OH), 1675 (C=O) and 1100; δ_H(90 MHz; CCl_4) (ratio of high- to low-field rotamers is 3:1) 9.6–8.3 (1 H, br s, OH), 8.5 and 8.0 (1 H, 2 s, CHO of each rotamer), 4.8 and 4.05 (1 H, 2 d, *J* 7, C*H*OMe of each rotamer), 3.3 (3 H, s, OMe), 2.3 (1 H, octet, *J* 7, C*H*Me_2), 1.05 and 0.9 (6H, 2 d, *J* 7, diastereotopic CH*Me*$_2$); *m*/*z* 147 (M^+, 0.5%), 117 (6, M − CH_2O), 104 (2, M − Pr^i), 87 (100, M − HCONOH) and 55 (50, M − HCONOH − HOMe) (Found: M^+, 147.0894. $C_6H_{13}NO_3$ requires M, 147.0895).

Acknowledgements

We would like to thank the SERC for financial support of this work.

References

1 A. P. Johnson and R. W. Steele, unpublished results.
2 Z. Sheikh, R. Steel, A. S. Tasker and A. P. Johnson, *J. Chem. Soc., Chem. Commun.*, 1994, 763; J. K. Dutton, R. W. Steel, A. S. Tasker, V. Popsavin and A. P. Johnson, *J. Chem. Soc., Chem. Commun.*, 1994, 765.
3 T. Morimoto and M. Sekiya, *Chem. Lett.*, 1985, 1371.
4 N. Duffaut and J.-P. Dupin, *Bull. Soc. Chim. Fr.*, 1966, 3205.
5 E. Oliveros-Desherces, M. Riviere, J. Parello and A. Lattes, *Synthesis*, 1974, 812.
6 C. Krüger, E. G. Rochow and U. Wannagat, *Chem. Ber.*, 1963, **96**, 2132.
7 (*a*) H. E. Zaugg, *Synthesis*, 1984, 181; (*b*) H. Hiemstra, H. P. Fortgens, S. Stegenge and W. N. Speckamp, *Tetrahedron Lett.*, 1985, **26**, 3151; H. Hiemstra, H. P. Fortgens and W. N. Speckamp, *Tetrahedron Lett.*, 1985, **26**, 3155; G. A. Kraus and K. N. Neuenschwander, *J. Chem. Soc., Chem. Commun.*, 1982, 134; P. N. W. van der Vliet, J. A. M. Hamersma and W. N. Speckamp, *Tetrahedron*, 1985, **41**, 2007; J. A. M. Hamersma, P. M. M. Nossin and W. N. Speckamp, *Tetrahedron*, 1985, **41**, 1999; R. M. Williams, R. W. Armstrong, L. K. Maruyama, J.-S. Dung and O. P. Anderson, *J. Am. Chem. Soc.*, 1985, **107**, 3246.
8 S. M. Weinreb and J. I. Levin, *Heterocycles*, 1979, **12**, 949; S. M. Weinreb and R. R. Staib, *Tetrahedron*, 1982, **38**, 3087.
9 R. R. Schmidt, *Synthesis*, 1972, 333.
10 K. Nyberg, *Acta Chem. Scand., Ser. B*, 1974, **28**, 825; S. D. Ross, M. Finkelstein and R. C. Petersen, *J. Am. Chem. Soc.*, 1966, **88**, 4657; *J. Org. Chem.*, 1966, **31**, 128; K. Nyberg and R. Servin, *Acta Chem. Scand., Ser. B*, 1976, **30**, 640; T. Shono, *Tetrahedron*, 1984, **40**, 811.
11 J. C. Hubert, W. Steege, W. N. Speckamp and H. O. Huisman, *Synth. Commun.*, 1971, **1**, 103; A. R. C. Oostveen, J. J. J. de Boer and W. N. Speckamp, *Heterocycles*, 1977, **7**, 171.
12 W. N. Speckamp and H. Hiemstra, *Tetrahedron*, 1985, **41**, 4367. For stable adducts see: A. Einhorn and T. Mauermayer, *Liebigs Ann. Chem.*, 1905, **343**, 282; G. Gormley, Jr., Y. Y. Chan and J. Fried, *J. Org. Chem.*, 1980, **45**, 1447.
13 A. P. Johnson, R. W. A. Luke and R. W. Steele, *J. Chem. Soc., Chem. Commun.*, 1986, 1658.
14 E. C. Roos, M. C. Lopez, M. A. Brook, H. Hiemstra, W. N. Speckamp, B. Kaptein, J. Kamphuis and H. E. Schoemaker, *J. Org. Chem.*, 1993, **58**, 3259; E. C. Roos, H. Hiemstra, W. N. Speckamp, B. Kaptein, J. Kamphuis and H. E. Schoemaker, *Recl. Trav. Chim. Pays-Bas*, 1992, **111**, 360; *Synlett*, 1992, 451.
15 W. Kantlehner, W. Kugel and H. Bredereck, *Chem. Ber.*, 1972, **105**, 2264.
16 W. Kantlehner, P. Fischer, W. Kugel, E. Möhring and H. Bredereck, *Liebigs. Ann. Chem.*, 1978, 512.
17 P. H. Milner, A. W. Guest, F. P. Harrington, R. J. Ponsford, T. C. Smale and A. W. Stachulski, *J. Chem. Soc., Chem. Commun.*, 1984, 1335.
18 G. Schirawski and U. Wannagat, *Monatsh. Chem.*, 1969, **100**, 1901.
19 C. H. Yoder, W. C. Copenhafer and B. DuBeshter, *J. Am. Chem. Soc.*, 1974, **96**, 4283.
20 D. Ladjama and J. J. Riehl, *Synthesis*, 1979, 504.
21 R. Noyori, S. Murata and M. Suzuki, *Tetrahedron*, 1981, **37**, 3899.
22 S. Murata, M. Suzuki and R. Noyori, *J. Am. Chem. Soc.*, 1980, **102**, 3248.
23 S. Murata, M. Suzuki and R. Noyori, *Tetrahedron Lett.*, 1980, **21**, 2527.
24 D. Stalling, C. W. Gehrke and R. W. Zumwalt, *Biochem. Biophys. Res. Commun.*, 1968, **31**, 616.
25 A. Komoriya and C. H. Yoder, *J. Am. Chem. Soc.*, 1972, **94**, 5285.
26 C. H. Yoder and A. D. Belber, *J. Organomet. Chem.*, 1976, **114**, 251.
27 K. Achiwa and M. Sekiya, *Chem. Lett.*, 1981, 1213.
28 J. Rigaudy, E. Lytwyn, P. Wallach and N. K. Cuong, *Tetrahedron Lett.*, 1980, **21**, 3367.
29 G. C. Levy, R. L. Lichter and G. L. Nelson, *Carbon-13 Nuclear Magnetic Resonance Spectroscopy*, Wiley, New York, 2nd edn., 1980.
30 M. T. Rogers and L. A. LaPlanche, *J. Phys. Chem.*, 1965, **69**, 3648.
31 E. L. Eliel, in *Stereochemistry of Carbon Compounds*, McGraw-Hill, New York, 1962, p. 207.
32 J. O. Edwards and R. G. Pearson, *J. Am. Chem. Soc.*, 1962, **84**, 16; J. L. Kice and E. Legan, *J. Am. Chem. Soc.*, 1973, **95**, 3912.

Paper 5/06196B
Received 19*th September* 1995
Accepted 16*th November* 1995