Reactions of 1-acylamino-1-(trimethylsiloxy)alkanes: versatile precursors to acylimines

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1-Acylamino-1-(trimethylsiloxy)alkanes react with carbon and heteroatom nucleophiles to give the corresponding 1-substituted-1-acylaminoalkanes. The 1-acylamino-1-(trimethylsiloxy)alkanes can also give rise to enamides, and by this route the mild antibiotic tuberin, and the isomeric (*Z*)-tuberin have been prepared. A further example of their reactions is illustrated with the acid-catalysed intramolecular cyclisation onto a carbon–carbon double bond. These transformations show that 1-acylamino-1-(trimethylsiloxy)alkanes are versatile precursors to synthetically useful acylimines.

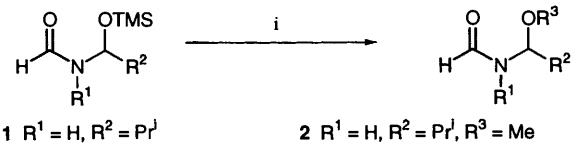
Introduction

N-Acylimines and *N*-acyliminium salts are synthetically useful intermediates that have been utilised in a wide variety of transformations.[1] They are normally generated and used *in situ*; indeed in almost all cases they are too unstable to be stored for any length of time. During the course of our work in the area of natural product syntheses[2,3] we discovered that bis(trimethylsilyl)formamide (BSF) adds to aldehydes to give 1-formamido-1-(trimethylsiloxy)alkanes.[4] Initial results showed that these adducts were not only reasonably stable,† but were also versatile precursors to *N*-acylimines. After a detailed study of the addition of BSF and other silylated amides to aldehydes, ketone and acetals[3] we now report in full the extent of our investigations concerning the reactivity of these adducts, including the preparation of the mild antibiotic tuberin and its isomer (*Z*)-tuberin.

Results and discussion

Substitution reactions

Alcohols. In order to establish the viability of nucleophilic substitution reactions of BSF–aldehyde adducts, the displacement of the trimethylsiloxy group by methanol to give an α-methoxy derivative was investigated. It was anticipated that cleavage of the silicon–oxygen bond, leading to fragmentation to the aldehyde and formamide, might occur in the presence of an alcohol, but this did not prove to be a problem. Addition of two mole equivalents of methanol to the BSF–isobutyraldehyde adduct **1**‡ in CCl_4, in the presence of trimethylsilyl (TMS) triflate, gave the methoxy adduct **2** as an oil (Scheme 1). The use



1 R^1 = H, R^2 = Pr^j — **2** R^1 = H, R^2 = Pr^j, R^3 = Me

4 R^1 = H, R^2 = CH_2Ph — **3** R^1 = H, R^2 = Pr^j, R^3 = Et

6 R^1 = Me, R^2 = Pr^j — **5** R^1 = H, R^2 = CH_2Ph, R^3 = Me

8 R^1 = Ph, R^2 = Pr^j — **7** R^1 = R^3 = Me, R^2 = Pr^j

9 R^1 = Ph, R^2 = Pr^j, R^3 = Me

TMS = $SiMe_3$

Scheme 1 *Reagents and conditions:* i, ROH, TMSOTf (cat.), room temp.

† These adducts may be stored in a freezer at −40 °C, or for up to a week at room temperature without significant decomposition.

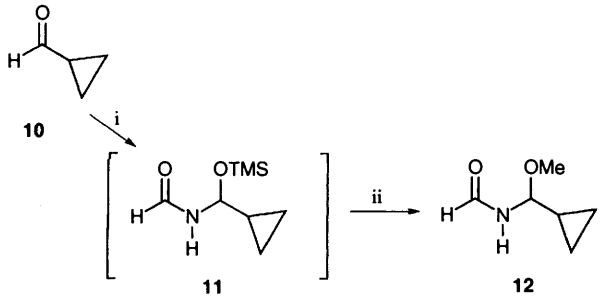
‡ The syntheses of all 1-amido-1-(trimethylsiloxy)alkanes mentioned in this article are detailed in the preceding paper.

of TMS triflate in the presence of an alcohol undoubtedly results in the formation of the corresponding trimethylsilyl ether and trifluoromethanesulfonic acid (triflic acid) which is probably the active catalyst. TMS triflate was preferred to triflic acid for these reactions because the former can be stored for a longer period of time without decomposition and therefore is a more convenient reagent. Using neat methanol as reaction solvent an excellent yield (96%) of the methoxy adduct **2** was obtained. In some early attempts at the preparation of adduct **2** it appeared that the reactions gave a mixture of the methoxy adduct **2** and the unexpected ethoxy adduct **3**. The source of the ethanol was traced to reagent-grade chloroform containing ethanol as stabiliser. The crude reaction product had been transferred to a chromatography column with chloroform, which presumably still contained some catalyst, allowing the conversion of methoxy adduct **2** into the ethoxy adduct **3**. Indeed, dissolution of the methoxy adduct **2** in distilled reagent-grade chloroform with a catalytic quantity of TMS triflate gave a mixture of adducts **2** and **3**. In order to further verify its structure the pure ethoxy adduct **3** (89%) was also prepared by the normal method using ethanol as solvent.

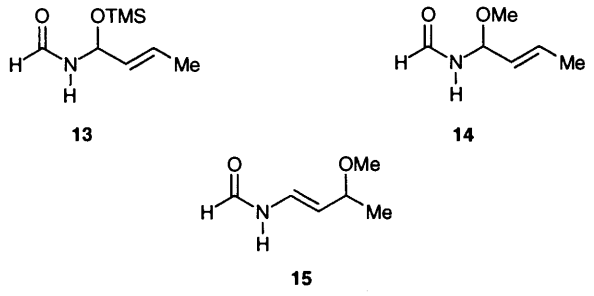
In a similar fashion the methoxy derivative **5** was prepared in 76% yield from the BSF–phenylacetaldehyde adduct **4**, but analogous treatment of *N*-methyl adduct **6** gave only a poor yield (18%) of the corresponding derivative **7**. In this case no other product was isolated, which suggested that a substantial amount of the adduct **6** had decomposed to the corresponding amide and aldehyde. The volatile aldehyde could have been lost, during removal of methanol under reduced pressure, and the amide might have been trapped on the chromatography column. In another experiment the *N*-phenyl methoxy adduct **9** was obtained (61%) from the α-trimethylsiloxy adduct **8**, but this time the fate of the remaining material was accounted for by the isolation of formanilide (37%). Again the aldehyde was presumably lost with removal of the solvent under reduced pressure. Thus it appears that the only significant side-reaction was the decomposition of adduct **8** to give the corresponding amide and aldehyde.

The α-methoxy derivatives could also conveniently be prepared from the aldehydes in a 'one-pot' procedure. For example, addition of cyclopropanecarbaldehyde **10** to a solution of BSF and TMS triflate led to formation of the BSF–cyclopropyl aldehyde adduct **11** *in situ*, was converted into the corresponding methoxy adduct **12** (46%) by addition of excess of methanol (Scheme 2).

With the BSF–crotonaldehyde adduct **13** a nucleophile could in principle add either α- or γ- to the nitrogen. Using the one-pot method, addition of crotonaldehyde to a solution of BSF and a catalytic quantity of TMS triflate, followed by addition of methanol, gave a product whose proton NMR spectrum

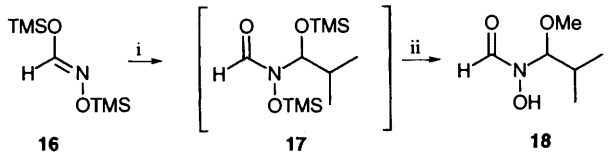


Scheme 2 *Reagents and conditions:* i, CCl_4, BSF, TMSOTf (cat.), room temp.; ii, excess of methanol



indicated to be a mixture of the methoxy adducts **14** and **15** (both of which were unstable).

As noted previously[3] bis(trimethylsilyl)formhydroxamic acid **16** is a particularly reactive bis-silylated derivative, and even at room temperature no catalyst was required for formation of adduct **17** (69%). This adduct was slightly unstable and decomposed on attempted bulb-to-bulb distillation at reduced pressure, but as before the more stable methoxy adduct **18** was simply prepared (46%) by quenching of the reaction with a solution of TMS triflate in methanol. The overall yield of this reaction was also improved to 88% by performing the initial step in the absence of solvent (Scheme 3).

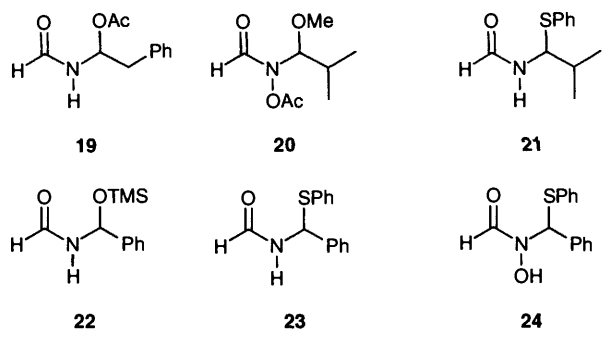


Scheme 3 *Reagents and conditions:* i, Pr^iCHO (neat); ii, TMSOTf (cat.), MeOH

Some of the methoxy derivatives described above were also prepared by heating of the corresponding α-trimethylsiloxy adducts in refluxing methanol. For example, the BSF–cyclopropanecarbaldehyde adduct **11** was converted into the corresponding methoxy adduct **12**, by heating at reflux in methanol for 3 h, but prolonged heating resulted in decomposition to unidentifiable material so the catalysed route was always the preferred method.

Acetic acid. Treatment of the BSF–phenylacetaldehyde adduct **4** with acetic acid at room temperature for 7 days gave the corresponding acetoxy adduct **19** in 79% yield. Evidently, acetic acid is a strong enough acid to catalyse a slow loss of the trimethylsiloxy group from adduct **4**. With methoxy derivative **18** and acetic acid on the other hand the only products obtained were those with ^1H NMR spectra consistent with the *O*-acetyl isobutyraldehyde oxime (30%) and the acetylated methoxy adduct **20** (48%).

Thiophenol. Amides which contain α-sulfur atoms have been used as radical precursors in a variety of synthetically useful cyclisation reactions.[5] We thought such precursors might conveniently be prepared from BSF–aldehyde adducts.



Addition of thiophenol to a solution of the BSF–isobutyraldehyde adduct **1** gave no change until a catalytic amount of TMS triflate was added, whereupon a rapid reaction took place to give the phenylsulfanyl adduct **21** in 68% yield. This adduct was also prepared by the more convenient 'one-pot' method. Addition of isobutyraldehyde to a solution of BSF and a catalytic quantity of TMS triflate formed the BSF–isobutyraldehyde adduct **1** *in situ*, and subsequent addition of thiophenol gave compound **21** (30%). The rather poor yield of the reaction was improved to 68% by passage of the reaction mixture through a pad of flash silica gel prior to the addition of thiophenol. The silica probably brings about N-desilylation and retains the excess of BSF which might otherwise have acted as an acid scavenger and thus interfered with the addition of thiophenol to adduct **1**.

The BSF–benzaldehyde adduct **22** had been found to be rather unstable, but it was predicted that the corresponding phenylsulfanyl derivative **23** ought to be less so. This adduct was prepared in 83% yield directly from benzaldehyde in a similar manner to the preparation of the NH analogue **21**, and was indeed found to be more stable than the trimethylsiloxy derivative **22**. Interestingly the adduct began to precipitate out of the reaction mixture after only 30 s.

It was also found that an α-methoxy group could in the same way be displaced with thiophenol. Thus treatment of the methoxy adduct **18** with a solution of TMS triflate in thiophenol gave the phenylsulfanyl adduct **24** in quantitative yield.

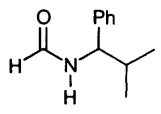
Phenylmagnesium bromide. The addition of oxygen and sulfur nucleophiles to BSF–aldehyde adducts has been used to demonstrate that these adducts may be used as *N*-acylimine precursors. However, for synthetic purposes it is more useful to be able to form carbon–carbon bonds. Addition of two equivalents of phenylmagnesium bromide to the BSF–isobutyraldehyde adduct **1** gave no isolable product. However, it was found that addition of 3.6 mole equivalents of this reagent gave a moderate 40% yield of the addition product **25**. As the Grignard reagent was prepared on a very small scale it may be that the actual quantity of active reagent present was significantly less than calculated.

Attempted addition of phenylmagnesium bromide to the adduct **6** was unsuccessful, the only isolable product being benzhydrol **26**, which could be formed *via* attack of the Grignard reagent at the formyl carbon. It is possible that the corresponding reaction with the BSF–isobutyraldehyde adduct **1** was successful only because the secondary amide would have been protected by deprotonation.

Allyl nucleophiles. The addition of allyltrimethylsilane to the BSF–isobutyraldehyde adduct **1** was attempted, in the presence of TMS triflate, at low temperature. This reaction gave the ether **27** as the product (76%) and only went to completion after warming to room temperature. Storage of the reaction mixture at room temperature for a longer period of time gave the same product. A structurally similar compound has been prepared by the electrochemical oxidation of dimethylformamide.[6] The use

of titanium tetrachloride as catalyst gave no isolable product, but boron trifluoride–diethyl ether gave a poor yield (16%) of the desired allyl-substituted adduct **28**.

It appeared that allyltrimethylsilane was not quite reactive enough to allow satisfactory allylation of the *N*-acyliminium ion generated from adduct **1**. Indeed, it was found that the more reactive reagent allyltributylstannane [7] with boron trifluoride–diethyl etherate gave an excellent yield (93%) of the desired product **28**. A similar reaction of the *N*-methyl adduct **6** with allyltributylstannane was also successful, but gave adduct **29** in only a modest 36% yield.



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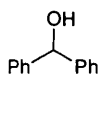

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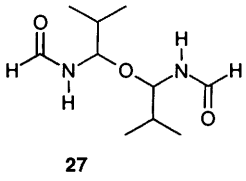

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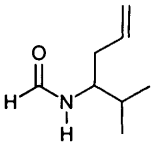

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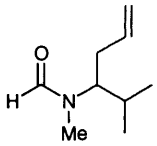

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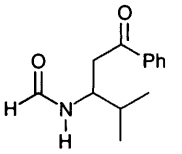

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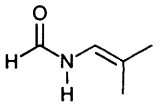

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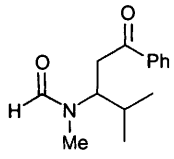

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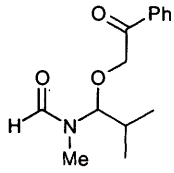

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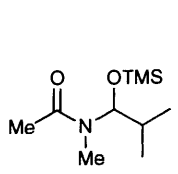
Acetophenone silyl enol ether. It has previously been shown that acylimines react with silyl enol ethers,[8] so a logical extension to this work was to test this type of procedure with our α-(trimethylsiloxy)formamides. It was found that the addition of the silyl enol ether of acetophenone to the BSF–isobutyraldehyde adduct **1**, in the presence of TMS triflate, gave the acetophenone derivative **30**, along with the enamide **31** as significant side-product (60% total; **30**/**31** = 1.2). It was hoped to avoid formation of the enamide **31** by performing the reaction at −78 °C, but this proved to be unsuccessful. However, the use of an excess of silyl enol ether gave better yields of both products (93% total) and an increased preference for the desired acetophenone derivative (**30**/**31** = 2).

Addition of acetophenone silyl enol ether to *N*-formyl-*N*-methyl adduct **6** was unsatisfactory. It gave only a very poor yield of a compound believed (from its ^{1}H NMR spectrum) to be the acetophenone derivative **32**, accompanied by recovered starting material **6** (45%) and also a compound believed (from its ^{1}H NMR spectrum) to be the ether **33**. This ether is most probably derived from an oxidation product of acetophenone silyl enol ether.

In a similar fashion addition of acetophenone silyl enol ether to the *N*-methylacetamido adduct **34** gave the desired product **35** (36%), but this was again accompanied by the related ether **36** (16%), even though the silyl enol ether had been purified prior to use and appeared to be pure by its ^{1}H NMR spectrum.

Reduction. Reduction of *N*-acyliminium ions derived from methanal has been reported as a method for the *N*-methylation of amides, lactams and ureas.[9] As the addition of amides to higher aldehydes does not give stable adducts it is unlikely that this method could be successfully applied to the alkylation of amides. However, the preparation and then reduction of BSF–aldehyde adducts in a similar manner to this would achieve the N-alkylation of formamide. This approach was shown to be



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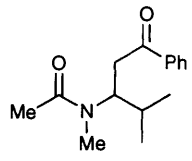

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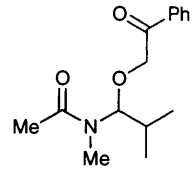

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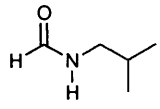

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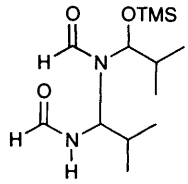

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viable by the reduction of the BSF–isobutyraldehyde adduct **1**. Treatment of this adduct with triethylsilane and trifluoroacetic acid (TFA) in chloroform gave *N*-isobutylformamide **37** in 70% yield.

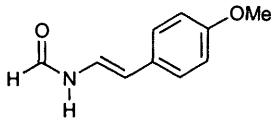
Alkyllithium reagents. Substitution of the trimethylsiloxy group of the BSF–isobutyraldehyde adduct **1**, by an alkyl group was attempted by the use of alkyllithium reagents. Treatment of the adduct with butyl- or methyl-lithium, at −78 °C, somewhat surprisingly, resulted only in clean deprotonation of the secondary amide functionality. It was found that quenching such a reaction with saturated aq. ammonium chloride and subsequent work-up gave an excellent 81% recovery of starting material. This was unexpected as it was thought that the BSF–aldehyde adducts would not survive an aqueous work-up. If, instead of quenching at −78 °C, the reaction mixture was allowed to warm to room temperature and stirred for several hours before quenching, no product could be isolated. However, if the reaction mixture was allowed to warm to room temperature and then immediately quenched, starting material (25%) and the unusual dimer **38** (51%) were obtained. It was somewhat disappointing that no α-alkyl product could be isolated.

Elimination reactions: formation of enamides

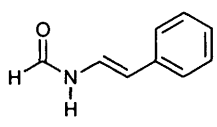
Enamides obtained as by-products of attempted substitution reactions. An enamide was the usual by-product obtained after unsuccessful substitution reactions of β-hydrogen-containing BSF–aldehyde adducts. In some cases this was accompanied by the aldehyde which was presumably formed, along with formamide, by decomposition of the adduct. For example, reaction of the BSF–isobutyraldehyde adduct **1** with anisole, in the presence of either titanium tetrachloride or TMS triflate as catalyst, gave the enamide **31** as the only isolable product (26%) instead of the anticipated arylated product. Heating of a solution of the adduct **1** and cyclopentadiene at reflux in carbon tetrachloride also gave the enamide **31** in better yield (79%), instead of the hoped for Diels–Alder adduct.

The displacement of the trimethylsiloxy group of compound **1** by cyanide was attempted by treatment with a solution of trimethylsilyl cyanide at room temperature, but this also gave the enamide **31**. A similar result was obtained in the presence of a catalytic amount of TMS triflate, but with the use of zinc iodide as a catalyst the major product isolated was the ether **27** (51%), along with enamide **31** (34%).

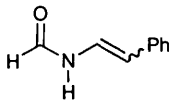
As formation of the enamide **31** appeared to be simple, it was decided to investigate this further. Treatment of the BSF–isobutyraldehyde adduct **1** with TMS triflate gave only a poor yield of the enamide **31**. However, this enamide could conveniently be prepared by heating of the adduct **1** at reflux in acetic acid (81%), or by stirring it in formic acid at room temperature. It was noted though that treatment of the *N*-



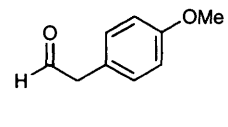
tuberin **39**



demethoxytuberin **40**



40 *E*
41 *Z*



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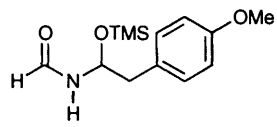

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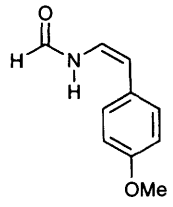
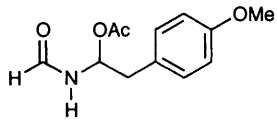


Z-tuberin **44**



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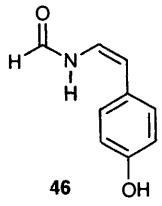

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methyl adduct **6** with formic acid did not give the enamide in this case; only a complex mixture was obtained.

Synthesis of tuberin. The enamide tuberin **39**, which has been isolated from *Streptomyces amakusaensis*, shows weak antibiotic properties towards some mycobacteria.[10,11] It has been previously synthesized[11] *via* a Curtius rearrangement but only in poor yield.

(*a*) *Demethoxytuberin.*—Initially, the synthesis of demethoxytuberin **40** under a variety of conditions was investigated. Heating of the BSF–phenylacetaldehyde adduct **4** in carbon tetrachloride or acetic anhydride gave phenylacetaldehyde and both the *E* and *Z* isomers of the enamide (**40** and **41**). Treatment of compound **4** with TMS triflate (room temperature: $CHCl_3$; 3 h) gave a moderate total yield (41%) of enamides **40** and **41** (~6:1 *E*:*Z*); a similar result was obtained at −78 °C. The use of sodium hydride in a base-mediated elimination gave a similar result, but warming in the presence of triethylamine resulted in the isolation of phenylacetaldehyde only.

In another study the related methoxy compound **5** was heated at reflux in chloroform (48 h). This gave a much cleaner reaction than for the same reaction with the BSF–phenylacetaldehyde adduct **4**, but only a moderate yield (50% total yield; 5.25:1 *E*:*Z*) of product was obtained. Upon treatment with acetic acid containing TMS triflate (5 min), acetate **19** eliminated with much greater selectivity for the *E*-isomer **40**, but again in only a moderate yield (49% total yield; 23.5:1 *E*:*Z*). It was most convenient to form the acetate **19** from adduct **4** *in situ* and then allow it to react further; this gave a 46% yield of the *E*-isomer and 14% of the *Z*. In the presence of acetic anhydride a similar reaction gave approximately the same yield (56% total yield; 1.4:1 *E*:*Z*), but with a greater proportion of the *Z*-isomer. At this point attention was switched to the preparation of tuberin.

(*b*) *Tuberin.*—*p*-Methoxyphenylacetaldehyde **42** was prepared from *p*-methoxybenzaldehyde *via* a Darzens reaction.[12] This aldehyde was then treated with BSF to give an excellent yield of the adduct **43** (88%). Treatment of this adduct **43** with acetic acid, containing a catalytic amount of TMS triflate, for 10 min gave a good overall yield (73%) of the *E* and *Z* enamides [tuberin **39** and (*Z*)-tuberin **44**] in a 1.7:1 ratio.

The adduct **43** could be converted into the corresponding acetate **45** by being stirred in acetic acid for 24 h, but heating of the adduct **43** at reflux in acetic acid for 2 h gave directly a good yield (80%) of tuberin **39** and its *Z*-isomer **44** (4:1), presumably *via* the acetate **45**. Formation of tuberin **39** and its *Z* isomer **44** by warming in acetic acid at temperatures below its boiling point required longer reaction times and gave lower yields. This may be because the enamides take part in other reactions if kept in acetic acid for too long (Table 1). The synthetic tuberin **39** was identical with the natural material§ in all respects, and an intimate mixture of the two had a melting point identical with that of the pure material.

Table 1 Formation of tuberin **39** and *Z*-tuberin **44** by treatment of the BSF–*p*-methoxyphenylacetaldehyde adduct **43** with acetic acid

Temperature (*T*/°C)	Time (*t*/h)	Total yield (%)	*trans*/*cis* Quotient
117–118	2	80	4.0
80–90	4	72	1.8
60–70	42	57	3.1
50–60	48	37	2.7

(c) Attempted preparation of (*Z*)-demethyltuberin. (*Z*)-Demethyltuberin **46** is a naturally occurring potent platelet aggregation inhibitor.[13] It was hoped to prepare this from (*Z*)-tuberin **44** by the use of boron tribromide, following a known procedure used for the conversion of tuberin **39** into demethyltuberin.[10] The ^1H NMR spectrum taken of the reaction mixture indicated that isomerisation of the double bond had taken place as well as demethylation, presumably giving demethyltuberin, but this was not isolated.

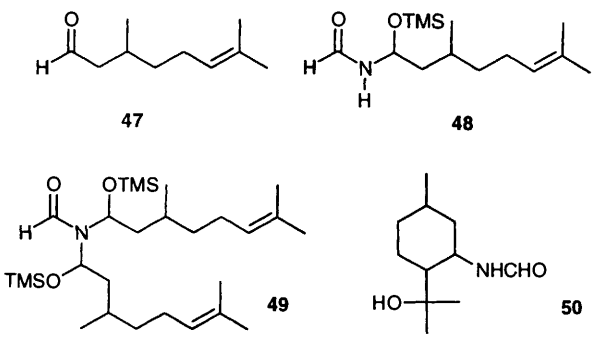
Cyclisation reactions

Cyclisation of the BSF–citronellal adduct in formic acid. Cyclisations involving addition of alkenes (or alkynes) to *N*-acyliminium species have found a great deal of synthetic use;[14] however, owing to the lack of suitable precursors, acyclic species do not appear to have received as much attention as endocyclic acyliminium ions (*e.g.*, those from the reduction of cyclic imides). The BSF–citronellal adduct **48** was chosen as a suitable model compound for cyclisation studies. Citronellal **47** was prepared by the buffered pyridinium chlorochromate (PCC)[15] oxidation of citronellol and converted into the BSF–adduct **48** in 80% yield, along with 16% of the bis-adduct **49**.

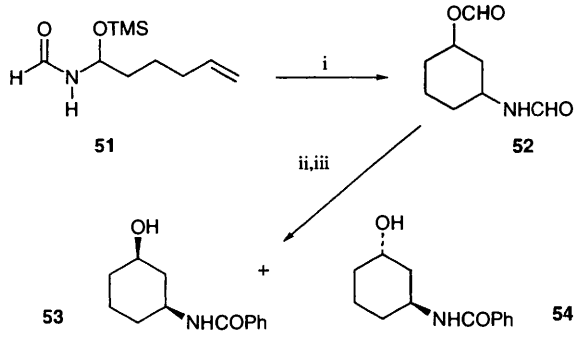
The adduct **48** was treated with formic acid at room temperature for 2 h to give the alcohol **50** in 82% yield. Cleavage of the *O*-formyl moiety presumably occurred on chromatography, and it was not possible to establish whether the compound was stereochemically pure or whether a mixture of stereoisomers was present. In a similar fashion to the intermolecular reactions, the synthesis and subsequent cyclisation of the BSF–citronellal adduct **48** could be carried out in 'one-pot' to give an excellent yield of the alcohol **50** (92% conversion, 86% yield).

Cyclisation of the BSF–hex-5-enal adduct in formic acid. Hex-5-enal was prepared by the buffered PCC oxidation of hex-5-en-

§ We thank Dr R. B. Herbert (University of Leeds) for a sample of authentic tuberin.



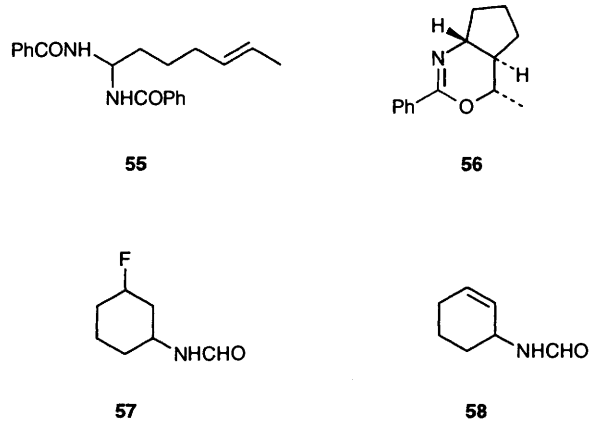
1-ol, and this was converted into the BSF adduct **51** in 80% yield. Treatment of this adduct with formic acid at room temperature for 40 min gave the diformyl derivative **52** (93%). Again it was not possible to establish directly whether compound **52** was a pure stereoisomer or a mixture; however, the corresponding benzamido alcohols **53** and **54** are known[16] and are reported to be separable. The diformyl derivative **52** was hydrolysed in aq. sodium hydroxide and then N-benzoylated with benzoyl chloride (Scheme 4). The benzamides



Scheme 4 *Reagents and conditions:* i, HCO_2H, room temp., 0.6 h (93%); ii, aq. NaOH (3 equiv.), 16 h; iii, NaOH (4 equiv.), PhCOCl (4 equiv.) (64%, two steps)

53 and **54** were obtained as a mixture which appeared to be homogeneous by TLC and was purified by chromatography on flash silica gel. Crystallisation from chloroform gave the *cis*-isomer **53** as crystals. Analysis of the residue by HPLC showed the presence of further compound **53** and another component, which was presumed to be the *trans*-isomer **54**. Some of this was isolated by HPLC and its identity confirmed. The ratio of the *cis* to *trans* isomers was 85:15, which indicates that the cyclisation is quite selective in favour of the *cis*-product. This would be expected if steric interactions were to be avoided in the proposed cyclic transition state (Fig. 1).

Cyclisation of the BSF–hex-5-enal adduct in the presence of boron trifluoride–diethyl ether. It has been reported[17] that the bis-amide **55** readily cyclises at room temperature *via* a Diels–Alder reaction of an intermediate acylimine to give



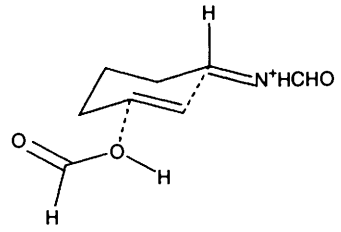


Fig. 1

bicycle **56**. However, treatment of our BSF–hex-5-enal adduct **51** with boron trifluoride–diethyl ether gave no Diels–Alder product, and instead the fluoride **57** (57%) and the cycloalkene **58** (16%) were isolated. Under similar conditions, but with a shorter reaction time, only fluoride **57** was isolated (71%).

Conclusions

1-Acylamino-1-(trimethylsiloxy)alkanes have been shown to be versatile precursors to acylimines by their ready reaction with alcohols, acetic acid, thiophenol, Grignard reagents, allyl nucleophiles and silyl enol ethers to give the corresponding 1-functionalised 1-(acylamino)alkanes. However, the reactions of the related N-substituted compounds were less successful and, in reactions with poorer nucleophiles, ethers (such as **27**, **33** and **36**) are formed. 1-Acylamino-1-(trimethylsiloxy)-alkanes also can give rise to enamides, as illustrated in the preparation of the mild antibiotic tuberin. A further example of the reactions of 1-acylamino-1-trimethylsiloxy)alkanes is illustrated with the acid-catalysed, intramolecular addition of carbon–carbon double bonds to the intermediate acyliminium ion.

Experimental

Experimental protocols such as the drying and purification of reaction solvents, instrumentation and other such details are identical with those described elsewhere.[3] Ether *as solvent* refers to diethyl ether. UV–VIS spectra were recorded on a Pye Unicam PU 8800 spectrophotometer using 1 cm cells.

N-(1-Methoxy-2-methylpropyl)formamide 2: Method A

A solution of TMS triflate (0.03 cm^3 of a 0.52 mol dm^{-3} solution in carbon tetrachloride, 0.016 mmol, 2 mol%) in methanol (0.06 cm^3, 1.5 mmol, 2.0 equiv.) was added to a solution of *N*-[2-methyl-1-(trimethylsiloxy)propyl]formamide **1** (141 mg, 0.743 mmol) at room temperature under nitrogen. After 2 h the solvent was removed under reduced pressure, and purification of the residue by flash column chromatography [silica (12 g); (1:1) light petroleum–ether] gave the *title compound* **2** (45 mg, 46%) as an oil, R_f 0.31 (ether) (Found: C, 54.65; H, 9.85; N, 10.45%; M^+, 131.0946. $C_6H_{13}NO_2$ requires C, 54.9; H, 10.0; N, 10.7%; M, 131.0946); $\nu_{max}(CCl_4)/cm^{-1}$ 3440 (NH), 2970, 1705 (C=O) and 1490; δ_H(90 MHz; CCl_4) 8.4 (0.6 H, s, CHO of major rotamer), 8.2 (0.4 H, d, *J* 11, CHO of minor rotamer), 7.4–6.1 (1 H, br m, NH), 4.95 and 4.1 (1 H, 2 dd, *J* 6 and 10, NHC*H*OMe of major and minor rotamers), 3.4 (3 H, s, OMe), 1.85 (1 H, m, C*H*Me_2) and 1.0 (6 H, d, *J* 7, CHMe_2); *m*/*z* 131 (0.2%, M^+), 116 (2, M − Me), 100 (29, M − OMe), 88 (100, M − Pr^i), 60 (27) and 55 (20).

Method B in neat methanol

(TMS triflate (0.1 cm^3, 0.052 mmol, 4 mol%) was added to a solution of compound **1** (237 mg, 1.25 mmol) in dry methanol (2.5 cm^3) at room temperature under nitrogen. After 10 min the solvent was removed under reduced pressure and purification of the residue by flash column chromatography [silica (20 g); ethyl acetate] gave the *title compound* **2** (158 mg, 96%) as an oil, identical with a fully characterised sample by TLC and ^1H NMR analysis (see above).

N-(1-Ethoxy-2-methylpropyl)formamide 3
TMS triflate (0.01 cm^3 of a 0.52 mol dm^{-3} solution in carbon tetrachloride, 0.005 mmol, 2 mol%) was added to a solution of compound **1** (61 mg, 0.321 mmol) in dry ethanol (2.5 cm^3) at room temperature under nitrogen. Solvent was removed under reduced pressure after 30 min, and purification of the residue by flash column chromatography [silica (1.5 g); (1:1) light petroleum–ether] gave the *title compound* **3** (42 mg, 89%) as an oil, R_f 0.40 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3440 (NH), 1705 (C=O) and 1490; δ_H(90 MHz; CCl_4) 8.3 (0.7 H, s, CHO of major rotamer), 8.1 (0.3 H, d, *J* 12, CHO of minor rotamer), 7.2 and 6.5 (1 H, 2 br m, NH of minor and major rotamers), 4.95 and 4.15 (1 H, 2 dd, *J* 6 and 10, NHC*H*OSiMe_3 of major and minor rotamers), 3.5 (2 H, m, OCH_2Me), 1.8 (1 H, octet, *J* 6, C*H*Me_2), 1.2 and 1.15 (3 H, 2 t, *J* 7, OCH_2*Me* of minor and major rotamers) and 0.95 and 0.90 (6 H, 2 d, *J* 6, CH*Me*$_2$ of major and minor rotamers); *m/z* 102 (100%, $M^+ - Pr^i$), 101 (24, M – NHCHO), 100 (60, M – OEt) and 74 (82, $M - Pr^i - CO$) (Found: M^+, 145.1107. $C_7H_{15}NO_2$ requires M, 145.1103).

N-(1-Methoxy-2-phenylethyl)formamide 5
TMS triflate [0.04 cm^3 of a 0.26 mol dm^{-3} solution in dichloromethane (DCM) 0.01 mmol, 1 mol%] was added to a stirred solution of *N*-[2-phenyl-1-(trimethylsiloxy)ethyl]formamide **4** (219 mg, 0.92 mmol) in dry methanol (4 cm^3) at room temperature under nitrogen. After 20 min the solvent was removed under reduced pressure, and purification of the residue by flash column chromatography [silica (10 g); ether] gave the *title compound* **5** (125 mg, 76%) as needles, mp 120–121 °C (from ether) (Found: C, 67.2; H, 7.4; N, 7.7%; M^+, 179.0942. $C_{10}H_{13}NO_2$ requires C, 67.0; H, 7.3; N, 7.8%; M, 179.0946); R_f 0.24 (ether); ν_{max}(Nujol)/cm^{-1} 3350 (NH), 1690 (C=O) and 1490; δ_H(90 MHz; $CDCl_3$) 8.2 (1 H, s, CHO), 7.3 (5 H, s, ArH), 7.0–6.3 (1 H, br, NH), 5.5 and 4.6 [1 H, 2 m, NHC*H*OMe of major rotamer (68%) and minor rotamer (32%)], 3.35 and 3.30 (3 H, 2 s, OMe of major and minor rotamers) and 2.95 (2 H, m, CH_2Ph); *m/z* 147 (17%, M^+ – HOMe), 134 (6, M – NH_2CHO), 88 (100, M – $PhCH_2$) and 60 (25).

N-(1-Methoxy-2-methyl)propyl-N-methylformamide 7
TMS triflate (0.02 cm^3 of a 0.26 mol dm^{-3} solution in DCM, 0.005 mmol, 1 mol%) was added to a solution of *N*-1-methyl-*N*-[2-methyl-1-(trimethylsiloxy)propyl]formamide **6** (78 mg, 0.388 mmol) in dry methanol (7 cm^3) at room temperature under nitrogen. After 30 min the solvent was removed under reduced pressure, and chromatography on flash silica gel (5 g) with ether as eluent gave the *title compound* **7** (10 mg, 18%), R_f 0.31 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 1690 (C=O) and 1100; $\delta_H(CDCl_3$; 90 MHz) 8.26 and 8.15 [1 H, 2 s, CHO of minor rotamer (14%) and major rotamer (84%)], 5.00 and 3.89 (1 H, 2 d, *J* 9, NC*H*OMe of minor and major rotamers), 3.24 and 3.21 (3 H, 2 s, OMe of minor and major rotamers), 2.78 and 2.74 (3 H, 2 s, NMe of minor and major rotamers), 2.00 (1 H, d heptet, *J* 6.5 and 9, C*H*Me_2) and 1.05 and 0.8 (6 H, 2 d, *J* 6.5, diastereotopic CH*Me*$_2$); *m/z* 145 (0.1%, M^+), 114 (9, M – OMe), 102 (100, $M - Pr^i$), 57 (28) and 42 (55) (Found: M^+, 145.1101. $C_7H_{15}NO_2$ requires M, 145.1103).

N-(1-Methoxy-2-methylpropyl)-N-phenylformamide 9
To a stirred solution of *N*-[2-methyl-1-(trimethylsiloxy)propyl]-*N*-phenylformamide **8** (134 mg, 0.504 mmol) in dry methanol (4 cm^3), under nitrogen at room temperature, was added TMS triflate (0.02 cm^3 of a 0.52 mol dm^{-3} solution in carbon tetrachloride, 0.01 mmol, 2% of adduct). After 4 h the solvent was removed under reduced pressure, and purification of the residue by flash column chromatography [silica (20 g); (2:1) light petroleum–ether] gave the *title compound* **9** (63 mg, 61%) as hexagonal plates, mp 43–46 °C (from light petroleum) (Found: C, 69.75; H, 8.4; N, 6.75%; M^+, 207.1266. $C_{12}H_{17}NO_2$ requires C, 69.54; H, 8.27; N, 6.76%; M, 207.1259); R_f 0.62 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3070, 3040, 1690 (C=O), 1595, 1495 and 1250; $\delta_H(CDCl_3$; 90 MHz) (two rotamers in the ratio 9:1), 8.4 and 8.2 (1 H, 2 s, CHO of major and minor rotamer), 7.25 (5 H, s, ArH), 5.2 and 4.1 (1 H, 2 d, *J* 10, N–CH–O of major and minor rotamers), 3.35 (3 H, s, OMe), 1.65 (1 H, m, C*H*Me_2) and 0.95 and 0.6 (6 H, 2 d, *J* 7, diastereotopic CH*Me*$_2$); *m/z* 207 (2%, M^+), 176 (2, M – OMe), 164 (6, $M - Pr^i$), 136 (2, $M - Pr^i - CO$), 104 (11, $M - Pr^i - CO$ – MeOH), 87 (100, M – PhNCHO) and 77 (14, Ph^+); and formanilide (23 mg, 37%).

N-[Cyclopropyl(methoxy)methyl]formamide 12
A solution of cyclopropanecarbaldehyde **10** (34 mg, 0.488 mmol) in dry carbon tetrachloride (0.8 cm^3) was added to a stirred solution of BSF (0.27 cm^3, 1.26 mmol, 2.6 equiv.) and TMS triflate (0.04 cm^3 of a 0.52 mol dm^{-3} solution in carbon tetrachloride, 0.021 mmol, 4%) in dry carbon tetrachloride (0.2 cm^3), under nitrogen at room temperature. After 1 h dry methanol (5 cm^3) was added and the solution was stirred for 2 h. After 1 h, purification by flash column chromatography [silica (10 g); ether] gave the *title compound* **12** (29 mg, 46%) as an oil, R_f 0.45 (ethyl acetate); $\nu_{max}(CCl_4)/cm^{-1}$ 3430, 3380, 3080, 2750, 1695 (C=O) and 1085; δ_H(90 MHz; CCl_4) 8.25 (0.7 H, s, CHO of major rotamer), 8.10 (0.3 H, d, *J* 11, CHO of minor rotamer), 7.9–6.6 (1 H, br m, NH), 4.85 and 4.2 (1 H, 2 d, *J* 5 and 9, NC*H*OMe of major and minor rotamers), 3.3 (3 H, s, OMe), 1.05 (1 H, m, cyclopropyl methine) and 0.6 and 0.5 (4 H, 2 d, *J* 7, cyclopropyl CH_2 of minor and major rotamers); *m/z* 129 (0.5%, M^+), 128 (7, M – H), 114 (22, M – Me), 98 (100, M – OMe), 88 (77, M – cyclopropyl radical), 70 (58, M – OMe – CO) and 60 (31, M – cyclopropyl radical – CO) [Found: $(M - 1)^+$, 128.0706. $C_6H_{10}NO_2$ requires *m/z*, 128.0711].

N-Hydroxy-N-(1-methoxy-2-methylpropyl)formamide 18.
Method A
A solution of bis(trimethylsilyl)formhydroxamic acid **16** (0.3 cm^3, 256 mg, 1.25 mmol) and isobutyraldehyde (0.1 cm^3, 1.1 mmol) in dry carbon tetrachloride was stirred under nitrogen for 2 days at room temperature. This solution was then poured into a solution of TMS triflate (0.3 cm^3, 0.078 mmol, 6 mol%) in dry methanol (10 cm^3). Solvent was removed under reduced pressure after 20 min and the residue was purified by flash column chromatography [silica (8 g); ether] to give the *title compound* **18** as an oil (75 mg, 46%), R_f 0.27 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3170 (OH), 1675 (C=O) and 1100; $\delta_H(CCl_4$; 90 MHz) (ratio of high to low-field rotamers was 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) and 1.05 and 0.9 (6 H, 2 d, *J* 7, diastereotopic CH*Me*$_2$); *m/z* 147 (0.5%, M^+), 117 (6, M – CH_2O), 104 (2, $M - Pr^i$), 87 (100, M – HCONOH) and 55 (50, M – HCONOH – HOMe) (Found: M^+, 147.0894. Calc. for $C_6H_{13}NO_3$: M, 47.0895).

Method B
Isobutyraldehyde (71 mg, 0.987 mmol) was added to bis(trimethylsilyl)formhydroxamic acid **16** (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 carbon tetrachloride, 0.052 mmol, 5%) was added and after a further 30 min the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (10 g); ether] gave the *title compound* **18** (129 mg, 88%) as an oil. TLC and ^1H NMR data were identical with those of a fully characterised sample (see above).

1-Formamido-2-phenylethyl acetate 19
N-[2-Phenyl-1-(trimethylsiloxy)ethyl]formamide **4** (519 mg,

2.19 mmol) was dissolved in glacial acetic acid (15 cm^3) and the solution was stirred at room temperature for 7 days. Solvent was removed under reduced pressure and purification of the residue by flash column chromatography [silica (30 g); ether] gave the *title compound* **19** (344 mg, 79%) as an oil, R_f 0.26 (ether); ν_{max}(film)/cm^{-1} 3300 (NH), 1740 (MeC=O), 1700 (NHC=O) and 1225; δ_H(90 MHz; $CDCl_3$) 8.3 (0.7 H, d, *J* 11, CHO of major rotamer), 8.15 (0.3 H, s, CHO of minor rotamer), 7.3 (5 H, s, ArH), 7.1–6.1 (1 H, br, NH), 6.6 and 6.15 (1 H, 2 dt, *J* 6 and 10, NHC*H*OAc of minor and major rotamers), 3.15 (2 H, m, CH_2Ph) and 2.05 (3 H, s, OAc); *m/z* 147 (100%, M^+ − AcOH), 118 (56, M − AcOH − CHO), 91 (53, $PhCH_2^+$) and 43 (27) (Found: M^+, 207.0890. $C_{11}H_{13}NO_3$ requires M, 207.0895).

N-[2-Methyl-1-(phenylsulfanyl)propyl]formamide 21

Thiophenol (0.02 cm^3, 0.19 mmol, 1.1 mol equiv.) was added to a solution of compound **1** (33 mg, 0.173 mmol) in dry carbon tetrachloride (1 cm^3). TMS triflate (0.04 cm^3 of a 0.22 mol dm^{-3} solution in carbon tetrachloride, 0.09 mmol, 5 mol%) was added and the mixture was stirred at room temperature, under nitrogen for 10 min. Solvent was removed under reduced pressure, and purification of the residue by flash column chromatography [silica (2 g); (1 : 1) light petroleum–ether] gave the *title compound* **21** (25 mg, 68%) as plates, mp 65–66 °C (from light petroleum); R_f 0.38 (ether) (Found: C, 63.25; H, 7.3; N, 6.5%; M^+, 209.0878. $C_{11}H_{15}NOS$ requires C, 63.1; H, 7.3; N, 6.7%; M, 209.0874); ν_{max}(CCl_4)/cm^{-1} 3440 (NH), 2970, 1700 (C=O) and 1470; δ_H(90 MHz; $CDCl_3$) 8.08 (1 H, s, CHO), 7.53–7.19 (5 H, m, ArH), 5.7 (1 H, m, NH), 5.45 (0.7 H, dd, *J* 5 and 10, SC*H*NH of major rotamer), 4.47 (0.3 H, dd, *J* 5 and 11, SCHNH of minor rotamer), 2.1 (1 H, m, C*H*Me_2) and 1.08 (6 H, d, *J* 7, CH*Me*$_2$); *m/z* 209 (3%, M^+), 166 (1, M − Pr^i), 110 (100, PhSH) and 100 (60, M − PhS).

Compound 21 'one-pot' synthesis from aldehyde

Isobutyraldehyde (0.07 cm^3, 0.77 mmol) was added to a stirred solution of BSF (0.5 cm^3, 2.3 mmol, 3.0 equiv.) and TMS triflate (0.08 cm^3 of a 0.26 mol dm^{-3} solution in carbon tetrachloride, 0.02 mmol, 3%) in dry carbon tetrachloride (3 cm^3), under nitrogen at room temperature. After 2 h the mixture was filtered through flash silica gel (5 g) with ether (30 cm^3) and then the solvent was removed under reduced pressure. To the resulting oil were added dry carbon tetrachloride (5 cm^3) and thiophenol (0.08 cm^3, 0.78 mmol, 1.01 equiv.) under nitrogen at room temperature, followed by TMS triflate (0.08 cm^3 of a 0.26 mol dm^{-3} solution in carbon tetrachloride, 0.02 mmol, 3 mol%). After 16 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* **21** (109 mg, 68%) as plates, mp 65–66 °C; R_f 0.38 (ether), identical with a fully characterised sample (see above).

N-[Phenyl(phenylsulfanyl)methyl]formamide 23

Benzaldehyde (0.078 cm^3, 0.77 mmol) was added dropwise to a solution of BSF (0.5 cm^3, 2.3 mmol, 3 equiv.) and TMS triflate (0.05 cm^3 of a 0.52 mol dm^{-3} solution in carbon tetrachloride, 0.03 mmol, 3 mol%) in dry carbon tetrachloride (3 cm^3) at room temperature under nitrogen. After 8 h the solvent was removed under reduced pressure and the mixture was filtered through flash silica gel (5 g) with ether (50 cm^3). Solvent was removed under reduced pressure, the mixture was dissolved in dry carbon tetrachloride (3 cm^3), and thiophenol (0.1 cm^3, 0.97 mmol, 1.3 equiv.) and then TMS triflate (0.05 cm^3 of a 0.52 mol dm^{-3} solution in carbon tetrachloride, 0.03 mmol, 3 mol%) were added. After 30 s a white precipitate formed and recrystallisation from ether gave the *title compound* **23** (156 mg, 83%) as needles, mp 131–132 °C (Found: C, 69.05; H, 5.4; N, 5.7%; M^+, 243.0722. $C_{14}H_{13}NOS$ requires C, 69.1; H, 5.4; N, 5.75%; M, 243.0718); R_f 0.48 (ether); ν_{max}($CHCl_3$)/cm^{-1} 3430 (NH), 1690 (C=O) and 1485; δ_H(90 MHz; $CDCl_3$) 8.25 (1 H, s, CHO), 7.6 (10 H, m, ArH), 7.3–6.6 (1 H, br, NH) and 6.8 and 6.0 (1 H, 2 d, *J* 10, PhSC*H*NH); *m/z* 133 (47%, M^+ − PhSH), 110 (100, PhSH), 104 (76, $PhCN^+H$), 77 (53, Ph^+) and 51 (42).

N-Hydroxy-N-[phenyl(phenylsulfanyl)methyl]formamide 24

To a stirred solution of compound **18** (49 mg, 0.335 mmol) in thiophenol (1 cm^3) under nitrogen at room temperature was added TMS triflate (0.05 cm^3 of a 0.26 mol dm^{-3} solution in carbon tetrachloride, 0.013 mmol, 4%). After 1 h the solvent was removed under a stream of dry nitrogen to leave the *title compound* **24** (76 mg, 100%) as an oil, R_f (0.24 [(1 : 1) light petroleum–ether]; ν_{max}($CHCl_3$)/cm^{-1} 3150 (OH), 1660 (C=O), 1640, 905 and 860; δ_H($CDCl_3$; 90 MHz) 9.0–7.0 (1 H, br s, OH), 7.6–7.2 (6 H, m, ArH and CHO), 4.35 (1 H, 2 d, *J* 9, NCHS), 2.4 (1 H, d heptet, *J* 7 and 9, C*H*Me_2) and 1.2 and 1.05 (6 H, 2 d, *J* 7, diastereotopic CH*Me*$_2$); *m/z* 225 (1%, M^+), 165 (1, M − HONCHO), 116 (50, M − SPh), 110 (100, HSPh), 88 (11, M − SPh − CO), 77 (20, Ph^+) and (44, M − SPh − CO − H_2O) (Found: M^+, 225.0822. $C_{11}H_{15}NO_2S$ requires M, 225.0823).

N-[2-Methyl-1-phenylpropyl]formamide 25

Bromobenzene (0.22 cm^3, 2.1 mmol, 3.6 equiv.) and magnesium (51 mg, 2.06 mmol, 3.6 equiv.) were dissolved in dry ether (1 cm^3) and kept at room temperature for 30 min, then compound **1** (111 mg, 0.58 mmol) was added in dry ether (3.5 cm^3). After 20 h the solution was poured into dil. hydrochloric acid (0.4 mol dm^{-3}, 10 cm^3), extracted with ether (4 × 10 cm^3), and the extract was washed with brine, dried ($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by flash column chromatography [silica (4 g); ether] gave the *title compound* **25** (40 mg, 40%) as an oil; R_f 0.60 (EtOAc) (Found: C. 74.7; H, 8.6; N, 7.85%; M^+, 177.1152. $C_{11}H_{15}NO$ requires C, 74.55; H, 8.5; N, 7.9%; M, 177.1154); ν_{max}(CCl_4)/cm^{-1} 3440 (NH), 2970, 1700 (C=O) and 1490; δ_H(90 MHz; CCl_4) 8.1 and 8.0 (1 H, 2 s, CHO of minor and major rotamers), 7.9 (1 H, br d, *J* 9, NH), 7.30 and 7.25 (5 H, 2 s, Ph of minor and major rotamer), 4.75 (0.8 H, t, *J* 8.5, NHC*H* of major rotamer), 4.10 (0.2 H, dd, *J* 7 and 9, NHC*H*Ph of minor rotamer), 2.05 (1 H, m, C*H*Me_2) and 0.95 and 0.85 (6 H, 2 d, *J* 7, diastereotopic CH*Me*$_2$); *m/z* 177 (5%, M^+), 134 (100, M − Pr^i), 106 (37, M − Pr^i − CO), 79 (18) and 77 (11, Ph^+).

Bis-(1-formamido-2-methylpropyl) ether 27

Allyltrimethylsilane (0.2 cm^3, 1.26 mmol, 6 equiv.) was added to a stirred solution of compound **1** (49 mg, 0.256 mmol) in dry DCM (2 cm^3) at room temperature under nitrogen. The resulting solution was stirred for 15 min and then TMS triflate (0.02 cm^3 of a 0.26 mol dm^{-3} solution in DCM, 0.0052 mmol, 2.5 mol%) was added. After 8 h the solution was allowed to warm to −40 °C and after a further 48 h it was allowed to warm to room temperature. Solvent was removed under reduced pressure, and purification of the residue by flash column chromatography [silica (5 g); ethyl acetate] gave the *title compound* **27** (21 mg, 76%), R_f (0.26 (EtOAc); ν_{max}($CHCl_3$)/cm^{-1} 3430 (NH), 1690 (C=O) and 1140; δ_H(400 MHz; $CDCl_3$) (spectrum complex due to the presence of two diastereoisomers and rotamers) 8.33–8.09 (2 H, m, NCHO), 6.76–6.67, 6.50–6.19 and 6.07–6.03 (2 H total, 3 m, NH), 5.23–5.10, 4.71–4.65 and 4.47–4.39 (2 H total, 3 m, Me_2CHC*H*O), 1.93–1.77 (2 H, m, Me_2C*H*) and 1.01–0.90 (12 H, m, *Me*$_2$CH); *m/z* 199 (0.3%, M^+ − OH), 173 (2%, M − Pr^i), 100 (100) and 43 (23, Pr^{i+}) [Found: $(M - Pr^i)^+$, 173.0926. $C_7H_{13}N_2O_3$ requires *m/z* 173.0926 Found: (M^+ − OH) 199.1449. $C_{10}H_{19}N_2O_2$ requires *m/z* 199.1446].

N-(1-Isopropylbut-3-enyl)formamide 28, using allyl(trimethyl)-silane

Boron trifluoride–diethyl ether (0.07 cm^3, 0.57 mmol, 1.0 equiv.) was added to a solution of compound **1** (108 mg, 0.570 mmol) and allyl(trimethyl)silane (0.4 cm^3, 2.5 mmol, 4.4 equiv.) in dry DCM (5 cm^3) at −78 °C. The resulting solution was stirred for 4 h and was then allowed to warm to room temperature over a period of 1 h. The solution was poured into aq. sodium hydrogen carbonate (10 cm^3) and was then extracted with ether (3 × 10 cm^3); the organic phase was washed with brine (10 cm^3), dried with magnesium sulfate and evaporated under reduced pressure. Chromatography of the residue on flash silica gel (10 g) gave the *title compound* **28** (13 mg, 16%) as an oil with TLC, IR, and ^1H NMR data identical with those of a fully characterised sample (see below).

N-(1-Isopropylbut-3-enyl)formamide 28, using allyl(tributyl)-stannane

To a stirred solution of compound **1** (186 mg, 0.981 mmol) and allyl(tributyl)stannane (0.61 cm^3, 1.97 mmol, 2.0 equiv.) in dry DCM (5 cm^3), at −78 °C under nitrogen, was added freshly distilled boron trifluoride–diethyl ether (0.13 cm^3, 1.06 mmol, 1.1 mol equiv.). After 10 min at −78 °C the solution was slowly allowed to warm to room temperature (over a period of 7 h); after 1 h at room temperature the mixture was treated with 2 mol dm^{-3} hydrochloric acid (14 cm^3), the solution was extracted with ether (3 × 20 cm^3), and the extracts were dried with magnesium sulfate and then evaporated under reduced pressure. Purification of the residue by flash column chromatography [silica (20 g); (1:1) light petroleum–ether] gave the *title compound* **28** (129 mg, 93%) as an oil, R_f 0.28 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3430 (NH), 3280 (NH), 3080, 2750, 1690 (C=O), 1640, 990 and 910; δ_H(400 MHz; $CDCl_3$) 8.18 (0.7 H, d, *J* 1.5, CHO of major rotamer), 7.95 (0.3 H, d, *J* 11.8, CHO of minor rotamer), 5.72 (1 H, m, C*H*=CH_2), 5.60–5.42 (0.3 H, br m, NH of minor rotamer), 5.42–5.20 (0.7 H, br, NH of major rotamer), 5.07 (2 H, m, CH=CH_2), 3.95 (0.7 H, tdd, *J* 6 and 9 and 10, HCONHC*H* of major rotamer), 3.14 (0.3 H, tdd, *J* 5.5 and 9 and 10, CHONHC*H* of minor rotamer), 2.28 (1 H, m, one of CH_2CH=CH_2), 2.14 (1 H, m, one of CH_2CH=CH_2), 1.76 (0.7 H, octet, *J* 6, C*H*Me_2 of major rotamer), 1.74 (0.3 H, d septet, *J* 7 and 5.5, C*H*Me_2 of minor rotamer), 0.93 and 0.88 (1.8 H, 2 d, *J* 7, diastereotopic CH*Me*$_2$ of minor rotamer), 0.92 and 0.89 (4.2 H, 2 d, *J* 6, diastereotopic CH*Me*$_2$ of major rotamer); δ_C(100 MHz; $CDCl_3$) 164.7 (CHO of minor rotamer), 161.2 (CHO of major rotamer), 134.8 (*C*H=CH_2 of major rotamer), 134.2 (*C*H=CH_2 of minor rotamer), 118.3 (CH=*C*H_2 of minor rotamer), 117.2 (CH=*C*H_2 of major rotamer), 58.3 (*C*HNH-CHO of minor rotamer), 52.8 (*C*HNHCHO of major rotamer), 37.5 (*C*H_2CH=CH_2 of minor rotamer), 36.5 (*C*H_2CH=CH_2 of major rotamer), 32.1 (*C*HMe_2 of minor rotamer), 31.3 (*C*HMe_2 of major rotamer), 19.6 and 17.4 (CH*Me*$_2$, diastereotopic, of minor rotamer) and 19.3 and 17.9 (CH*Me*$_2$, diastereotopic, of major rotamer); *m/z* 142 (1%, $[M + 1]^+$), 141 (0.3, M^+), 100 (100, M − allyl), 98 (27, M − Pr^i), 72 (31, M − allyl − C_2H_4) and 55 (54) (Found: M^+, 141.1147. $C_8H_{15}NO$ requires M, 141.1154).

N-(1-Isopropylbut-3-enyl)-N-methylformamide 29

To a stirred solution of compound **6** (91 mg, 0.449 mmol) and allyl(tributyl)stannane (0.24 cm^3, 0.774 mmol, 1.7 equiv.) in dry DCM (2 cm^3) at −78 °C under nitrogen was added freshly distilled boron trifluoride–diethyl ether (0.056 cm^3, 0.45 mmol, 1.01 equiv.). After 1.5 h at −78 °C the solution was slowly allowed to warm to room temperature, 2 mol dm^{-3} hydrochloric acid (10 cm^3) was added, the solution was extracted with ether (3 × 20 cm^3), the extracts were dried with magnesium sulfate and then the solvent was removed under reduced pressure. Flash column chromatography [silica (20 g); (1:1) light petroleum–ether] of the residue gave the *title compound* **29** (25 mg, 36%) as an oil, R_f 0.38 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3080, 1675 (C=O), 1640 and 1405; $\delta_H(CCl_4$; 90MHz) 8.15 and 8.05 [1 H, 2 s, CHO of minor rotamer (30%) and major rotamer (70%)], 6.15–5.6 (1 H, m, C*H*=CH_2), 5.5–5.1 (2 H, m, CH=CH_2), 4.25 and 3.2 (1 H, 2 dt, *J* 4 and 10, MeNC*H*Pr^i of minor and major rotamers), 2.95 and 2.90 (3 H, 2 s, NMe of minor and major rotamers), 2.8–2.3 (2 H, m, MeNCHCH_2), 1.9 (1 H, m, C*H*Me_2) and 1.3 and 1.1 (6 H, 2 d, *J* 7, diastereotopic CH*Me*$_2$); *m/z* 155 (21%, M^+), 114 (100, M − allyl) and 112 (8, M − Pr^i) (Found: M^+, 155.1312. $C_9H_{17}NO$ requires M, 155.1311).

N-(2-Methyl-1-phenacylpropyl)formamide 30

To a stirred solution of compound **1** (59 mg, 0.310 mmol) and acetophenone silyl enol ether (0.5 cm^3, 2.4 mmol, 7.7 equiv.) in dry carbon tetrachloride (0.5 cm^3) was added TMS triflate (0.07 cm^3 of a 0.26 mol dm^{-3} solution in CCl_4, 0.018 mmol, 6 mol%). The solution was stirred at room temperature under nitrogen for 24 h and then the solvent was removed under reduced pressure. Purification of the residue by flash column chromatography [silica (20 g); ethyl acetate] gave the *title compound* **30** (42 mg, 62%) as needles (Found: C, 70.9; H, 7.65; N, 6.3%; M^+, 219.126 14. $C_{13}H_{17}NO_2$ requires C, 71.2; H, 7.82; N, 6.39%; M, 219.1259); mp 124–125 °C (from ethyl acetate); R_f 0.21 (ether); $\nu_{max}(CHCl_3)/cm^{-1}$ 3420 (NH), 1680 (both C=O), 1600 and 1385; δ_H(400 MHz; $CDCl_3$) (two rotamers in the ratio 5:2) (major rotamer) 8.17 (1 H, d, *J* 1.6, CHO), 7.95–7.45 (5 H, m, ArH), 6.34 (1 H, br d, *J* 9, NH), 4.21 (1 H, dddd, *J* 4.8, 5.5, 8.0 and 9.2, Pr^iCHN), 3.38 (1 H, dd, *J* 5.5 and 17.1, one of diastereotopic PhCOCH_2), 3.14 (1 H, dd, *J* 4.8 and 17.1, one of diastereotopic PhCOCH_2), 2.08 (1 H, d heptet, *J* 8.0 and 6.8, C*H*Me_2) and 0.99 and 0.92 (6 H, 2 d, *J* 6.8, diastereotopic C*Me*$_2$) (and minor rotamer) 8.10 (1 H, d, *J* 11.7, CHO), 7.95–7.45 (5 H, m, ArH), 6.00 (1 H, br t, *J* 11, NH), 3.87 (1 H, dddd, *J* 3.8, 5.8, 8.2 and 10.4, Pr^iCHN), 3.28 (1 H, dd, *J* 8.2 and 17.4, one of diastereotopic PhCOCH_2), 3.05 (1 H, dd, *J* 3.8 and 17.4, one of diastereotopic PhCOCH_2), 2.08 (1 H, d heptet, *J* 5.8 and 6.7, C*H*Me_2) and 0.98 and 0.97 (6 H, 2 d, *J* 6.7, diastereotopic CH*Me*$_2$); *m/z* 219 (2%, M^+), 176 (25, M − Pr^i), 114 (3), 105 (100, $PhCO^+$) and 77 (24, Ph^+); and *N*-2-methylprop-1-enyl)formamide **31** (10 mg, 31%) as an oil, whose ^1H NMR spectrum was identical with that of a fully characterised sample (see below).

N-(2-Methylprop-1-enyl)formamide 31

A stirred solution of compound **1** (124 mg, 0.652 mmol) in dry acetic acid (12 cm^3) was refluxed for 2 h. Solvent was removed under reduced pressure, and purification of the residue by flash column chromatography [silica (4 g); ether] gave the *title compound* **31** (52 mg, 81%) as an oil, R_f 0.28 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3450 (NH), 1690 (C=O) and 1310; $\delta_H(CCl_4$; 90 MHz) 9.3–8.4 (1 H, br, NH), 8.1 (0.3 H, d, *J* 11, CHO of minor rotamer), 7.95 (0.7 H, s, CHO of major rotamer), 6.45 and 6.0 (1 H, 2 d, *J* 10, olefinic H of major and minor rotamers) and 1.7 (6 H, 2 s, CH=C*Me*$_2$); *m/z* 99 (67%, M^+), 84 (20, M − Me), 70 (78, M − CHO), 56 (100) and 43 (56, Pr^{i+}) (Found: M^+, 99.0685. C_5H_9NO requires M, 99.0684).

N-Methyl-N-(2-methyl-1-phenacylpropyl)acetamide 35 and N-methyl-N-(2-methyl-1-phenacyloxypropyl)acetamide 36

To a mixture of *N*-methyl-*N*-[2-methyl-1-(trimethylsiloxy)propyl]acetamide **34** (22 mg, 0.101 mmol) and the silyl enol ether of acetophenone (0.17 cm^3, 0.81 mmol, 7.9 equiv.), at room temperature under nitrogen, was added TMS triflate (0.02 cm^3 of a 0.26 mol dm^{-3} solution in CCl_4, 0.005 mmol, 5%). After 1 h the reaction mixture was concentrated and the residue was purified by flash column chromatography [silica (10 g); ether] to give N-*methyl*-N-[2-*methyl*-1-(*trimethylsiloxy*)*propyl*]*acetamide* **36** (4.5 mg, 16%) as an oil, R_f 0.22 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3070 (ArH), 1705 (PhC=O), 1655 (NC=O) and 1115; $\delta_H(CDCl_3$;

400 MHz) (major rotamer; 60%) 7.95–7.40 (5 H, m, ArH), 5.48 (1 H, d, *J* 9.5, OC*H*NMe), 4.76 (1 H, d, *J* 16.5, one of PhCOCH_2), 4.64 (1 H, d, *J* 16.5, other one of PhCOCH_2), 2.86 (3 H, s, NMe), 2.11 (3 H, s, MeCO), 1.97 (1 H, d heptet, *J* 6.5 and 9.5, C*H*Me$_2$) and 1.13 and 0.80 (6 H, 2 d, *J* 6.5, C*Me*$_2$ diastereotopic) (minor rotamer; 40%) 7.95–7.40 (5 H, m, ArH), 4.75 (1 H, d, *J* 16.5, one of PhCOCH_2), 4.74 (1 H, d, *J* 9.5, OC*H*NMe), 4.53 (1 H, d, *J* 16.5, one of PhCOCH_2), 2.78 (3 H, s, NMe), 2.06 (3 H, s, MeCO), 2.05 (1 H, d heptet, *J* 6.5 and 9.5, C*H*Me$_2$) and 1.16 and 0.83 (6 H, 2 d, *J* 6.5, CH*Me*$_2$ diastereotopic); *m/z* 220 (38%, $M^+ - Pr^i$), 178 (44, $M - Pr^i - O{=}C{=}CH_2$), 128 (71, $M - PhCOCH_2O$), 119 (19, $PhCOCH_2^+$), 105 (100, $PhCO^+$), 86 (81, $M - PhCOCH_2O - O{=}C{=}CH_2$) and 77 (56, Ph^+) [Found: $(M - 43)^+$, 220.0973. $C_{12}H_{14}NO_3$ requires *m/z*, 220.0974] and N-*methyl*-N-(2-*methyl*-1-*phenacylpropyl*)*acetamide* **35** (9 mg, 36%) as an oil, R_f 0.16 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3070, 1685 (PhC=O), 1650 (NC=O) and 1400; $\delta_H(CDCl_3$; 400 MHz) (major rotamer; 60%) 7.95–7.40 (5 H, m, ArH), 4.11 (1 H, ddd, *J* 4.2, 8.6 and 10.0, CH_2CHNMe), 3.29 (1 H, dd, *J* 8.6 and 16.6, one of PhCOCH_2), 3.15 (1 H, dd, *J* 4.2 and 16.6, one of PhCOCH_2), 2.71 (3 H, s, NMe), 1.96 (3 H, s, NAc), 1.89 (1 H, d heptet, *J* 6.5 and 10.0, C*H*Me$_2$) and 1.03 and 0.92 (6 H, 2 d, *J* 6.5, C*Me*$_2$, diastereotopic), (minor rotamer; 40%) 7.95–7.40 (5 H, m, ArH), 4.28 (1 H, dt, *J* 5 and 10, CH_2CHNMe), 3.35 (1 H, dd, *J* 10 and 15.5, one of PhCOCH_2), 3.28 (1 H, dd, *J* 5 and 15.5, one of PhCOCH_2), 2.93 (3 H, s, NMe), 2.16 (3 H, s, NAc), 2.13 (1 H, d heptet, *J* 6.5 and 10, C*H*Me$_2$) and 1.03 and 0.89 (6 H, 2 d, *J* 6.5, CH*Me*$_2$, diastereotopic); *m/z* 247 (3%, M^+), 204 (27, $M - Pr^i$), 162 (28, $M - Pr^i - O{=}C{=}CH_2$), 128 (4, $M - PhCOCH_2$), 105 (100, $PhCO^+$), 86 (8, $M - PhCOCH_2$ – ketene) and 77 (19, Ph^+) (Found: M^+, 247.1577. $C_{15}H_{21}NO_2$ requires M, 247.1572).

N-Isobutylformamide 37

A solution of compound **1** (86 mg, 0.456 mmol) in dry chloroform (2 cm^3) was added dropwise to a solution of triethylsilane (0.11 cm^3, 0.69 mmol, 1.5 equiv.) and TFA (0.35 cm^3, 4.5 mmol, 10 mol equiv.) in dry chloroform (3 cm^3). The solution was stirred at room temperature under nitrogen for 2 h, diluted with ethyl acetate (20 cm^3), washed with saturated aq. sodium hydrogen carbonate (5 cm^3), dried ($MgSO_4$), and evaporated under reduced pressure. Chromatography of the residue on flash silica gel (10 g) gave crude *N*-isobutylformamide, which was further purified by bulb-to-bulb distillation (90–100 °C/20 mmHg) to give the *title compound* **37** (32 mg, 70%) as an oil, R_f 0.55 (ether); $\nu_{max}(CHCl_3)/cm^{-1}$ 1710 (C=O); δ_H(90 MHz; $CDCl_3$) 8.2 (0.75 H, s, CHO of major rotamer), 8.0 (0.25 H, d, *J* 12, CHO of minor rotamer), 6.8–5.9 (1 H, br, NH), 3.15 and 3.05 (2 H, 2 t, *J* 7, NHCH_2 of major and minor rotamers), 1.8 (1 H, m, *J* ~ 7, C*H*Me$_2$) and 0.95 (6 H, d, *J* 7, CH*Me*$_2$); *m/z* 101 (6%, M^+), 86 (3, M – Me), 59 (46), 58 (56, $M - Pr^i$), 46 (51), 41 (30, $CH_2{=}CHCH_2^+$) and 30 (100, $M - Pr^i$ – CO) (Found: M^+, 101.0841. $C_5H_{11}NO$ requires M, 101.0841).

N-(1-Formamido-2-methylpropyl)-*N*-[2-methyl-1-(trimethylsiloxy)propyl]formamide 38

To a solution of compound **1** (56 mg, 0.295 mmol) in dry tetrahydrofuran (THF) (2 cm^3) at −71 °C was added methyllithium (0.40 cm^3 of a 1.5 mol dm^{-3} solution in hexanes, 0.60 mmol, 2.0 equiv.) dropwise. The solution was warmed to room temperature over a period of 4 h and was immediately quenched with saturated aq. ammonium chloride (5 cm^3). Water (5 cm^3) was added, the mixture was extracted with ether (3 × 20 cm^3), and the ether fractions were combined and dried ($MgSO_4$). The solvent was removed under reduced pressure, and purification of the residue flash column chromatography [silica (10 g); (1:1) light petroleum–ether] gave the *title compound* **38** (22 mg, 51%) as an oil, R_f 0.52 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3410 (NH), 3330 br (NH), 1695 (NHC=O), 1675 (NC=O), 1255 and 880; δ_H(90 MHz; CCl_4) 8.2–8.0 (2 H, m, CHO), 7.6 (1 H, br m, NH), 5.0–4.4 (2 H, m, NHC*H*N and NC*H*OSiMe$_3$), 2.7–1.9 (2 H, m, C*H*Me$_2$), 1.0–0.7 (12 H, m, CH*Me*$_2$) and 0.15 (9 H, s, SiMe$_3$); *m/z* 245 (7%, $M^+ - Pr^i$), 172 [56, HCON(SiMe$_3$)=CHPr^i], 146 (71, HCONH=CHOSiMe$_3$), 102 (26, $Me_2Si{=}O^+CH{=}NH$), 100 (30, HCONH=CHPr^i), 75 (48, $Me_2Si{=}O^+H$) and 73 (100, $SiMe_3^+$) (Found: M^+, 288.1866. $C_{13}H_{28}N_2O_3Si$ requires M, 288.1869); and substrate **1** (14 mg, 25% recovery), whose ^{1}H NMR data were identical with those of a fully characterised sample.

Tuberin 39 [(*E*)-*N*-(4-methoxystyryl)formamide] and (*Z*)-tuberin 44 [(*Z*)-*N*-(4-methoxystyryl)formamide]

TMS triflate (0.03 cm^3 of a 0.26 mol dm^{-3} solution in DCM, 0.008 mmol, 1 mol%) was added to a solution of *N*[2-(4-methoxyphenyl)-1-(trimethylsiloxy)ethyl]formamide **43** (see below) (143 mg, 0.536 mmol) in glacial acetic acid (15 cm^3) at room temperature. After 10 min the solvent was removed under reduced pressure, and purification of the residue by flash column chromatography [silica (20 g); ether] gave (*Z*)-tuberin **44** (26 mg, 27%) as needles, mp 74–75 °C (from benzene) (lit.,[13] 72–74 °C) (Found: C, 67.7; H, 6.2; N, 7.75%; M^+, 177.0790. Calc. for $C_{10}H_{11}NO_2$: 67.78; H, 6.26; N, 7.90%; M, 177.0790); R_f 0.33 (ether); λ_{max}(MeOH)/nm 273 and 212 (ε 28 000 and 17 000); ν_{max}(Nujol)/cm^{-1} 3260 (NH), 1650 (C=O), 1605, 1520, 1245 and 740; $\delta_H(CDCl_3$; 90 MHz) 8.50 (0.4 H, d, *J* 11, CHO of minor rotamer), 8.30 (0.6 H, s, CHO of major rotamer), 8.30–7.50 (1 H, br, NH), 7.35 (2 H, d, *J* 9, ArH), 7.1 and 6.55 (1 H, dd, *J* 10 and 11, ArCH=C*H*NH of major and minor rotamers), 7.05 (2 H, d, *J* 9, ArH), 5.90 and 5.80 (1 H, 2 d, *J* 10, ArC*H*=CHNH) and 3.90 (3 H, s, OMe); *m/z* 177 (100%, M^+), 162 (3, M – Me), 148 (10, M – CHO), 134 (53, M – Me – CO), 121 (20, M – CHO – HCN) and 77 (15, Ph^+); and tuberin **39** (43 mg, 46%) as prisms, mp 132–133 °C (lit.,[11] 132–133 °C), mixed mp with natural tuberin§ 132–133 °C) (Found: C, 67.7; H, 6.2; N, 7.9 M^+, 177.0790); R_f 0.24 (EtOAc); λ_{max}(MeOH)/nm 285 and 216 nm (ε 10 000 and 6 900); ν_{max}(Nujol)/cm^{-1} 3220 (NH), 3160 (NH), 1640 (C=O), 1605, 1505, 1250 and 965; $\delta_H(CDCl_3$; 90 MHz) 8.39 (0.3 H, d, *J* 10.9, CHO of minor rotamer), 8.17 (0.7 H, s, CHO of major rotamer), 7.41 (1 H, dd, *J* 10.5 and 14.5, ArCH=C*H*), 7.25 (2 H, d, *J* 9, ArH), 6.83 (2 H, d, *J* 9, ArH), 6.15 and 6.05 (1 H, 2 d, *J* 14.5, ArC*H*=CH of major and minor rotamers), 3.8 (3 H, s, OMe) and 1.60 (1 H, s, NH); *m/z* 177 (100%, M^+), 148 (10, M – CHO), 134 (48, M – COMe) and 121 (16).

Related reactions. (a) TMS triflate (0.03 cm^3 of a 0.26 mol dm^{-3} solution in DCM, 0.008 mmol, 1 mol%), *N*-[2-(4-methoxyphenyl)-1-(trimethylsiloxy)ethyl]formamide **43** (see later) (170 mg, 0.637 mmol) in a mixture of acetic acid (17 cm^3) and acetic anhydride (20 cm^3) (10 min at room temp.) gave (*Z*)-tuberin **44** (15 mg, 13%) and tuberin **39** (37 mg, 33%).

(b) A solution of compound **43** (502 mg, 1.88 mmol) in acetic acid (15 cm^3), heated at reflux for 2 h, gave (*Z*)-tuberin **44** (53 mg, 16%) and tuberin **39** (213 mg, 64%).

Demethoxytuberin 40 and (*Z*)-demethoxytuberin 41 [(*E*)- and (*Z*)-*N*-styrylformamide]

TMS triflate (0.02 cm^3 of a 0.26 mol dm^{-3} solution in DCM, 0.005 mmol, 1 mol%) was added to a solution of compound **4** (82 mg, 0.347 mmol) in acetic acid (9 cm^3) at room temperature. After 30 min 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 (*Z*)-N-*styrylformamide* **41** (8 mg, 14%) as rods, mp 88 °C (from benzene) (Found: C, 73.7; H, 6.1; N, 9.55%; M^+, 147.0685. C_9H_9NO requires C, 73.45; H, 6.16; N, 9.52%; M, 147.0684); R_f 0.48 (ether); λ_{max}(MeOH)/nm 267 and 210 (ε 3700 and 2400); ν_{max}(Nujol)/cm^{-1} 3260 (NH), 1645 (C=O) and 1255; $\delta_H(CDCl_3$; 90 MHz) 8.7–7.3 (1 H, br, NH), 8.4 (0.5 H, d, *J* 11, CHO of one

rotamer), 8.2 (0.5 H, s, CHO of other rotamer), 7.4 (5 H, s, ArH), 7.05 and 6.55 (1 H, 2 dd, *J* 10 and 11, PhCH=C*H* of each rotamer) and 5.90 and 5.80 (1 H, 2 d, *J* 10, PhC*H*=CH of each rotamer); *m/z* 147 (100%, M^+), 118 (62, M − CHO), 91 (75, $PhCH_2^+$) and 65 (17); and (*E*)-N-*styrylformamide* **40** (23 mg, *46%*), *mp* 104–105 °C (from ether) (Found: C, 73.25; H, 6.15; N, 9.3%; M^+, 147.0684); R_f 0.29 (ether); λ_{max}(MeOH)/nm 275 and 218 (ε 1200 and 650); ν_{max}(Nujol)/cm^{-1} 3220 (NH), 1665 (C=O), 1250 and 950; δ_H($CDCl_3$; 90 MHz) 8.75–7.5 (1 H, br m, NH), 8.2 and 8.05 [1 H, 2 s, CHO of minor rotamer (44%) and major rotamer (56%)], 7.6 (1 H, d, *J* 14, PhCH=C*H*), 7.3 (5 H, s, ArH) and 6.25 and 6.15 (1 H, 2 d, *J* 14, PhC*H* of major and minor rotamers); *m/z* 147 (100%, M^+), 118 (52, M − CHO), 91 (42) and 65 (12).

Related reactions. (a) TMS triflate (0.03 cm^3 of a 0.26 mol dm^{-3} solution in DCM, 0.08 mmol) and compound **4** (175 mg, 0.738 mmol) in a mixture of acetic acid (1 cm^3) and acetic anyhdride (10 cm^3) gave a 56% combined yield of isomers **41** and **40** in the ratio 1 : 1.4.

(b) TMS triflate (0.01 cm^3 of a 0.26 mol dm^{-3} solution in DCM, 0.003 mmol, 2 mol%), and compound **19** (35 mg, 0.167 mmol) in acetic acid (5 cm^3) at room temp. for 5 min gave compounds **41** (0.5 mg, 2%) and **40** (11 mg, 47%).

(c) Compound **5** (19 mg, 0.106 mmol) in refluxing chloroform (2 cm^3; 48 h) gave compounds **41** (1.2 mg, 8%) and **40** (6.5 mg, 42%).

N-[2-(4-Methoxyphenyl)-1-(trimethylsiloxy)ethyl]formamide 43

4-Methoxyphenylacetaldehyde[12] **42** (379 mg, 2.52 mmol) as a solution in dry carbon tetrachloride (7 cm^3) was added dropwise to a solution of BSF (1.7 cm^3, 7.94 mmol, 3.2 equiv.) and TMS triflate (0.1 cm^3 of a 0.26 mol dm^{-3} solution in CCl_4, 0.026 mmol, 1 mol%) in dry carbon tetrachloride (8 cm^3) at room temperature under nitrogen. After 30 min the solvent was removed under reduced pressure, and purification of the residue by flash column chromatography [silica (12 g); (1 : 1) light petroleum–ether] gave an oil, which was further purified by bulb-to-bulb distillation (149–155 °C/0.1 mmHg) to give the *title compound* **43** (591 mg, 88%) as an oil (Found: C, 58.55; H, 8.0; N, 5.5%; M^+, 267.1293. $C_{13}H_{21}NO_3Si$ requires C, 58.39; H, 7.92; N, 5.24%; M, 267.1291); R_f 0.41 (ether); ν_{max}(film)/cm^{-1} 3290 (NH), 1685 (C=O), 1515 and 1255; δ_H($CDCl_3$; 90 MHz) 8.25 (0.7 H, s, CHO of major rotamer), 8.2 (0.3 H, d, *J* 12, CHO of minor rotamer), 7.3 (2 H, d, *J* 9, ArH), 6.95 (2 H, d, *J* 9, ArH), 6.5–5.6 (1 H, br m, NH), 5.8 (0.7 H, dt, *J* 5 and 10, NHC*H*OSiMe_3 of major rotamer), 5.2 (0.3 H, dt, *J* 5 and 10, NHC*H*OSiMe_3 of minor rotamer), 3.85 (3 H, s, OMe), 2.9 (2 H, m, ArCH_2) and 0.05 (9 H, s, SiMe_3); *m/z* 252 (3%, M^+ − Me), 222 (7, M − formamide), 177 (29, M − HOTMS), 146 (89, M − $ArCH_2$) and 73 (100, $SiMe_3^+$).

N-[3,7-Dimethyl-1-(trimethylsiloxy)oct-6-enyl]formamide 48

Citronellal **47** (56 mg, 0.364 mmol) was added to a mixture of BSF (0.40 cm^3, 1.87 mmol, 5.1 equiv.) and TMS triflate (0.03 cm^3 of a 0.26 mol dm^{-3} solution in CCl_4, 0.008 mmol, 2%), at room temperature under nitrogen. After 30 min the mixture was purified by flash column chromatography [silica (2.5 g); (2 : 1) light petroleum–ether] to give the *title compound* **48** (79 mg, 80%) as an oil, R_f 0.62 (ether); ν_{max}(CCl_4)/cm^{-1} 3415 (NH), 2750, 1700 (C=O) and 1250; δ_H($CDCl_3$; 90 MHz) 8.2 and 8.1 [1 H, 2 s, CHO of minor rotamer (10%) and major rotamer (90%)], 6.3–5.4 (1 H, br m, NH), 5.7 (1 H, m, NH-C*H*OSiMe_3), 5.1 (1 H, t, *J* 6, olefinic H), 2.0 (2 H, q, *J* 6, allylic CH_2), 1.6 and 1.7 (6 H, 2 s, allylic Me), 1.6–1.1 (5 H, m), 0.9 (3 H, d, *J* 6, C*H*Me) and 0.15 (9 H, s, SiMe_3); *m/z* 256 (0.3%, M^+ − Me), 211 (2, M − Me − H_2NCHO), 181 (10, M − HOSiMe_3), 146 (7, $Me_3SiOCH{=}NH^+CHO$), 136 (36, M − HOSiMe_3 − H_2NCHO), 121 (33) and 75 (100, $H^+O{=}SiMe_2$) (Found: M^+, 271.1975. $C_{14}H_{29}NO_2Si$ requires M, 271.1966).

N-[2-(1-hydroxy-1-methylethyl)-5-methylcyclohexyl]formamide 50

Compound **48** (37 mg, 0.135 mmol) was dissolved in dry formic acid (5 cm^3) at room temperature and the solution was stirred for 2 h. Solvent was removed under reduced pressure and the resulting oil was chromatographed on flash silica gel (2 g), with ethyl acetate as eluent, to give the *title compound* **50** (22 mg, 82%) as an oil, R_f 0.24 (EtOAc); ν_{max}(CCl_4)/cm^{-1} 3560–3120 (NH, OH), 2750, 1685 (C=O), 1500 and 1140; δ_H(CCl_4; 90 MHz) 8.3 and 8.25 (1 H, 2 s, CHO of major and minor rotamers), 7.5 (1 H, br s, OH or NH), 4.5 and 3.8 (1 H, 2 m, C*H*NH of minor and major rotamers) and 2.6–0.8 (18 H, m); *m/z* 181 (48%, $M^+ - H_2O$), 166 (13, M − H_2O − Me), 136 (100, M − H_2O − H_2NCHO), 121 (87, M − H_2O − H_2NCHO − Me) and 59 (14, Me_2CO^+H) (Found: M^+, 199.1571. $C_{11}H_{21}NO_2$ requires M, 199.1572).

'One-pot' preparation of *N*-[2-(1-hydroxy-1-methylethyl)-5-methylcyclohexyl]formamides 50 from aldehyde

Citronellal **47** (41 mg, 0.266 mmol) was added to a mixture of BSF (0.29 cm^3, 1.3 mmol, 5.1 equiv.) and TMS triflate (0.05 cm^3 of a 0.26 mol dm^{-3} solution in CCl_4, 0.01 mmol, 5%), at room temperature under nitrogen. After 50 min, formic acid (5 cm^3) was added and the mixture was stirred at room temperature for 15 min. Purification of the product by flash column chromatography [silica (2.5 g); (2 : 1) light petroleum–ether] gave the *title compound* **50** (45 mg, 86%) as an oil, identical with a fully characterised sample by ^1H NMR spectroscopy and TLC (see above), and citronellal (3 mg, 7% recovery).

N-[1-(Trimethylsiloxy)hex-5-enyl]formamide 51

Hex-5-enal [283 mg of a solution (40%) in ether, 1.2 mmol as a solution in dry carbon tetrachloride (3 cm^3) was added to a stirred solution of BSF (1.0 cm^3, 4.67 mmol, 4 equiv.) and TMS triflate (0.1 cm^3 of a 0.52 mol dm^{-3} solution in carbon tetrachloride, 0.0052 mmol, 4% relative to aldehyde) in dry carbon tetrachloride (2 cm^3), under nitrogen at room temperature. After 18 h 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* **51** (161 mg, 65%) as an oil, R_f 0.24 [(1 : 1) light petroleum–ether]; ν_{max}(film)/cm^{-1} 3280 (NH), 3080, 2750, 167 (C=O), 1250 and 845; δ_H(CCl_4; 90 MHz) 8.2 and 8.1 [1 H, 2 s, CHO of minor rotamer (13%) and major rotamer (87%)], 6.3–5.3 (1 H, br, NH), 6.0–5.4 (2 H, m, O–CH–N and C*H*=CH_2), 5.2–4.8 (2 H, m, CH=CH_2), 2.05 (2 H, q, *J* 7, CH_2CH=CH_2), 1.8–1.2 (4 H, m, C$H_2CH_2CH_2CH{=}CH_2$) and 0.15 (9 H, s, SiMe_3); *m/z* 200 (12%, M^+ − Me), 145 (88, M − $[CH_2]_3CH{=}CH_2$), 102 (100, $Me_2Si{=}O^+CH{=}NH$), 75 (60, $HO^+{=}SiMe_2$) and 73 (74, $SiMe_3^+$) (Found: M^+, 215.1338. $C_{10}H_{21}NO_2Si$ requires M, 215.1342).

Treatment of hex-5-enal with BSF (3 mol equiv.) overnight, under similar conditions, gave an 80% yield of compound **51**.

cis- and *trans*-3-Formamidocyclohexyl formate 52

A solution of compound **51** (84 mg, 0.391 mmol) in dry formic acid (4 cm^3) at room temperature was stirred under nitrogen for 16 h. Solvent was removed under reduced pressure and the resulting oil was chromatographed on flash silica gel (2 g), with ethyl acetate as eluent, to give an inseparable mixture of cis- and trans-3-*formamidocyclohexyl formate* **52** (63 mg, 93%) as an oil; R_f 0.28 (EtOAc); ν_{max}($CHCl_3$)/cm 3430 (NH), 2750, 1720 (OC=O), 1685 (NHC=O), 1500 and 1180; δ_H($CDCl_3$; 90 MHz) 8.05 (1 H, br s, C*H*ONH), 8.0 (1 H, s, CHO–O), 6.55 (1 H, br, NH), 4.9 (1 H, m, C*H*OCHO), 4.0 (1 H, m, C*H*NHCHO) and 2.4–1.0 (8 H, m); *m/z* 171 (2%, M^+), 125 (28, M − HCO_2H),

97 (13, M − HCO_2H − CO), 80 (100, M − HCO_2H − $HCONH_2$), 71 (19, H_2C=CHNHCHO) and 46 (45, HCO_2H) (Found: M^+, 171.0890. $C_8H_{13}NO_3$ requires M, 171.0895).

***cis*- and *trans*-*N*-(3-Hydroxycyclohexyl)benzamide 53 and 54**

Compound **52** (138 mg, 0.805 mmol) was treated with aq. sodium hydroxide (99 mg, 2.48 mmol, 3.1 equiv. in 5 cm^3) for 16 h at room temperature. Further sodium hydroxide (130 mg, 3.25 mmol, 4.0 mol equiv.) was added, followed by benzoyl chloride (0.37 cm^3, 3.2 mmol, 4 equiv.). After 2.5 h the solution was extracted with warm chloroform (6 × 10 cm^3), and the extracts were combined, washed with water (10 cm^3), and evaporated under reduced pressure. Purification of the residue by flash column chromatography [silica (10 g); ethyl acetate] gave a mixture of the *cis* and *trans* benzamides **53** and **54** (114 mg, 64%) as a solid. The solid was dissolved in warm chloroform and the solution was allowed to cool slowly to give *cis*-*N*-(3-hydroxycyclohexyl)benzamide **53** (63 mg) as crystals mp 152–153 °C (from EtOAc) (lit.,[16] 153–154 °C); R_f 0.34 (EtOAc); $\nu_{max}(CHCl_3)/cm^{-1}$ 3500 (OH), 3320 (NH), 1620 (C=O), 1535 and 1015 (Found: C, 71.2; H, 8.0; N, 6.45%; M^+, 219.1255. Calc. for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39%; M, 219.1259); $\delta_H(CDCl_3)$; 400 MHz) 7.79–7.75 (32 H, m, *ortho* ArH), 7.50–7.38 (3 H, m, *meta* and *para* ArH), 6.96 (1 H, br, NH), 4.19 (1 H, tq, *J* 3.5 and 8, C*H*NH), 3.98 (1 H, tt, *J* 3.5 and 8, C*H*OH), 2.11 (1 H, td, *J* 3 and 13, equatorial [NH]CHC*H*HCH[OH] and 1.91–1.38 (8 H, m); *m*/*z* 219 (5%, M^+), 201 (11, M − H_2O), 122 (29, $PhCO_2H$), 105 (100, $PhCO^+$) and 77 (59, Ph^+).

HPLC of the residue showed that it contained further compound **53** (28 mg) and trans-N-(3-*hydroxycyclohexyl)benzamide* **54** (17 mg); preparative HPLC gave a small quantity of pure compound **54** (1.5 mg), R_f 0.34 (EtOAc); $\nu_{max}(CHCl_3)/cm^{-1}$ 3610 (OH), 3440 (NH), 3010 (ArH), 1655 (C=O) and 1515; $\delta_H(CDCl_3)$; 400 MHz 7.76–7.71 (2 H, m, *ortho* ArH), 7.52–7.40 (3 H, m, *meta* and *para* ArH), 5.96 (1 H, br, NH), 4.42 (1 H, tq, *J* 3.5 and 8, C*H*NH), 4.14 (1 H, tt, *J* 2.5 and 5, C*H*OH) and 2.06–1.55 (9 H, m); *m*/*z* 219 (7%, M^+), 201 (3, M − H_2O), 122 (57, $PhCO_2H$), 105 (100, $PhCO^+$) and 77 (59, Ph^+) (Found: M^+, 219.1257)

***N*-(3-Fluorocyclohexyl)formamide 57 and *N*-(cyclohex-2-enyl)-formamide 58**

To a stirred solution of compound **51** (131 mg, 0.607 mmol) in dry DCM (3 cm^3), at room temperature under nitrogen, was added freshly distilled boron trifluoride–diethyl ether (0.15 cm^3, 1.22 mmol, 2.0 equiv.) dropwise. After 50 min, water (5 cm^3) was added and the solution was extracted with DCM (3 × 10 cm^3). The DCM extracts were combined, washed with brine (10 cm^3), dried ($MgSO_4$), and evaporated under reduced pressure. Chromatography of the resulting oil on flash silica gel (10 g) with ether as eluent gave N-(*cyclohex-2-enyl)formamide* **58** (11 mg, 16%) as an oil, R_f 0.34 (ether); $\nu_{max}(CCl_4)/cm^{-1}$ 3440 (NH), 3030, 2740, 1700 (C=O) and 1485; $\delta_H(CDCl_3)$; 90 MHz) 8.15 (0.7 H, s, CHO of major rotamer), 8.15 (0.3 H, d, *J* 11.5, CHO of minor rotamer), 6.0–4.8 (1 H, br, NH), 5.9 (1 H, td, *J* 3 and 9, CH_2CH=CHCHNH), 5.55 (1 H, d, *J* 9, CH_2CH=CH-C*H*NH), 4.6 (0.7 H, m, C*H*NHCHO of major rotamer), 4.0 (0.3 H, m, C*H*NHCHO of minor rotamer) and 2.15–1.4 (6 H, m); *m*/*z* 125 (89%, M^+), 97 (62, M − C_2H_4), 80 (100, M − $HCONH_2$), 69 (66, M − CO − C_2H_4) and 54 (57, H_2C=CH-CH=CH_2) (Found: M^+ 125.0847. $C_7H_{11}NO$ requires M, 125.0841); and N-(3-*fluorocyclohexyl)formamide* **57** (50 mg, 57%) as an oil, R_f 0.31 (EtOAc); $\nu_{max}(CCl_4)/cm^{-1}$ 3440 and 3300 br (NH), 2750, 1695 (C=O), 1495 and 1385; $\delta_H(CCl_4$; 90 MHz) 7.9 (1 H, s, CHO), 7.4 (1 H, br, NH), 4.2–3.5 (2 H, m, CHF and C*H*NHCHO) and 2.5–1.1 (8 H, m); *m*/*z* 145 (11%, M^+), 125 (15, M − HF), 102 (16), 84 (37), 80 (100, M − HF − $HCONH_2$), 71 (34, H_2C=CHNHCHO), 46 (84) and 43 (52, H_2C=$CHNH_2$) (Found: M^+, 145.0897. $C_7H_{12}NOF$ requires M, 145.0903).

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