Intramolecular azomethine ylide cycloaddition reactions to give octahydroindoles

Iain Coldham,*[a] Katherine M. Crapnell,[a] Jonathan D. Moseley[b] and Rémi Rabot[a]

[a] *School of Chemistry, University of Exeter, Stocker Road, Exeter, UK EX4 4QD*
[b] *AstraZeneca Pharmaceuticals, Process R&D Department, Avlon Works, Severn Road, Bristol, UK BS10 7ZE*

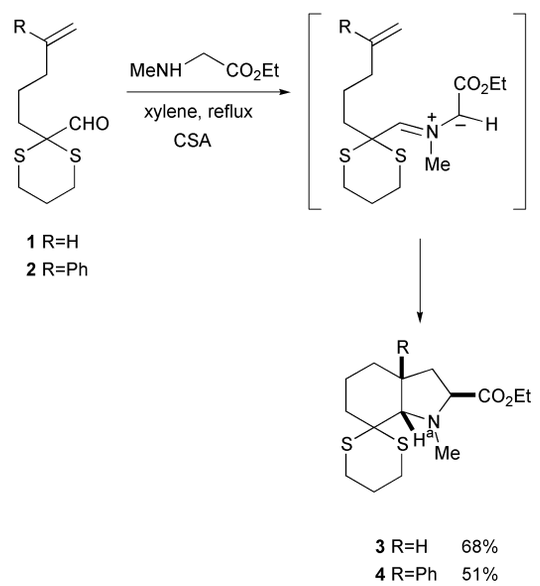
Received (in Cambridge, UK) 18th May 2001, Accepted 21st June 2001
First published as an Advance Article on the web 10th July 2001

The aldehyde 2-formyl-2-(pent-4-enyl)-1,3-dithiane **1**, containing both alkene and aldehyde functional groups, is a good substrate for intramolecular dipolar cycloaddition reactions after condensation with various *N*-alkyl α-amino-esters. This paper reports the optimization, scope and stereoselectivity of this reaction to give octahydroindoles (2-azabicyclo[4.3.0]nonanes).

Introduction

Of the many carbon–carbon bond forming reactions in synthetic organic chemistry, one of the most efficient is an intramolecular cycloaddition reaction. This process commonly sets up two new sigma bonds and two new rings in one step, often with a high degree of stereoselectivity. It is not surprising therefore that intramolecular cycloaddition reactions have been used to access many different bicyclic and polycyclic ring systems.[1] Although less well studied than the Diels–Alder cycloaddition reaction, the dipolar cycloaddition reaction of an azomethine ylide with an alkene or alkyne dipolarophile is an effective method for the formation of ring systems.[2] The intramolecular version of this reaction has been finding increasing use for the synthesis of substituted pyrrolidines, dihydropyrroles and pyrroles.[3]

As part of our efforts towards the synthesis of polycyclic amine natural products such as manzamine A,[4] we have studied the intramolecular azomethine ylide cycloaddition reaction. A convenient and direct approach to the required dipole uses the condensation of an α-amino-ester with an aldehyde. We were therefore interested in cycloaddition reactions using hept-6-enal derivatives, as these give rise, on condensation with a secondary amine, ylide formation and intramolecular cycloaddition, to the desired octahydroindole (2-azabicyclo[4.3.0]nonane) ring system. This ring system was first prepared using an azomethine ylide cycloaddition reaction by Confalone and co-workers (Scheme 1).[5,6] They reported that the cycloadducts **3** and **4** were formed as 'the major product' on refluxing *N*-methylglycine (sarcosine) ethyl ester (10 mmol) and the aldehyde **1** or **2** (5 mmol) in xylene (15 cm^3) with camphorsulfonic acid (CSA) (10 mg) and a Dean–Stark trap for 1–3 days.[5b] The presence of the octahydroindole ring system in many natural products prompted us to reinvestigate this reaction in more detail and to determine its scope and stereoselectivity.



Scheme 1

Results and discussion

In agreement with the report by Confalone and Earl,[5b] heating sarcosine ethyl ester with the parent hept-6-enal failed to give any cycloaddition products. A low yield of the self aldol condensation product of hept-6-enal was the only isolable product from this reaction. It appears, therefore, that it is preferable, although not always a necessity,[6] to have an aldehyde substrate that is blocked towards enolization. We therefore prepared the aldehyde **1**[5b] and studied the condensation and subsequent intramolecular cycloaddition using different secondary amines.

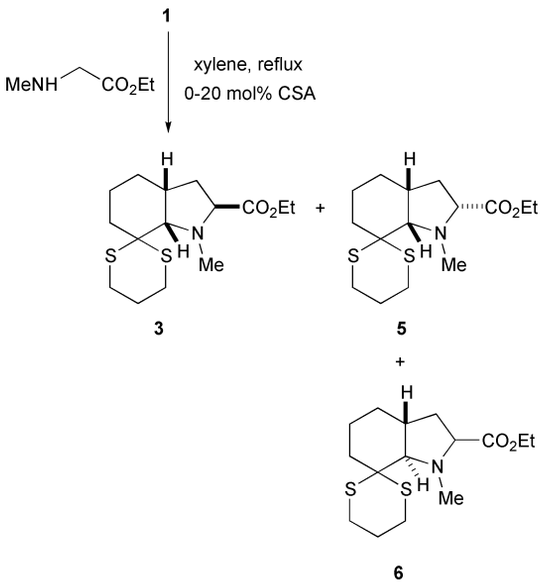
Following the work of Confalone and Earl,[5b] the aldehyde **1** was treated with two equivalents of sarcosine ethyl ester in xylene, with CSA (1 mol%) and heated using a Dean–Stark trap for 16 h. This reaction gave predominantly the desired cycloadduct **3**, together with a small amount of an inseparable mixture of two other cycloaddition products, tentatively assigned as the *endo* product **5** and one diastereomer of the *trans*-ring-fused cycloadduct **6**, together with some recovered aldehyde **1** (Scheme 2). Changing the solvent to the lower-boiling toluene or higher-boiling *o*-dichlorobenzene resulted in lower yields of the cycloaddition products. Switching to more polar solvents (such as propionitrile or *N*-methylpyrrolidinone) resulted in no cycloadduct after heating for several days and only recovered aldehyde **1** was obtained.

The stereochemistry of the major product **3** was assigned by Confalone and Earl on the basis of related compounds and on the chemical shift and coupling constant of the peak corresponding to the ring junction proton H^a in the ^1H NMR spectrum (δ 3.11, d, J 7).[5b] Our spectroscopic data (^1H NMR, $CDCl_3$, δ 3.07, d, J 7.5) agreed with their assignment and were

 DOI: 10.1039/b104390k

Table 1 Cycloaddition of sarcosine ethyl ester and **1** with varying amounts of CSA

Entry	CSA (mol%)	Yield (%)	Ratio **3** : (**5** + **6**)	Recovered **1** (%)
1	0	42	80 : 20	23
2	1	53	80 : 20	12
3	5	68	70 : 30	0
4	10	91	66 : 34	0
5	20	83	78 : 22	0
6	100	0	—	21



Scheme 2

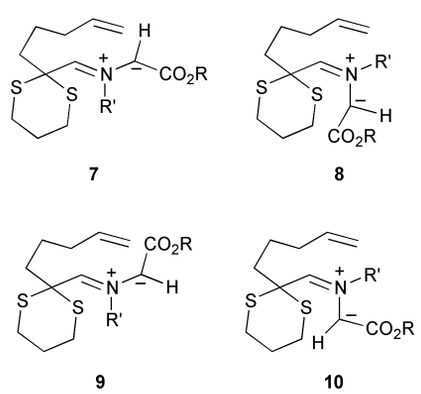


Fig. 1

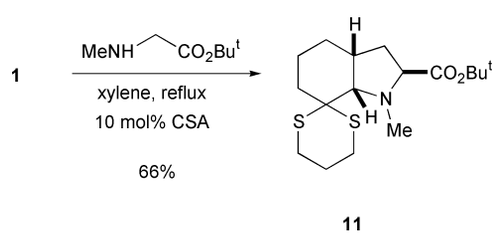
backed up by ^{1}H NMR NOESY experiments, which confirmed that the ring junction stereochemistry is *cis* and that there was no NOE between the proton α to the ester group and the ring junction protons, suggesting, but not proving, the *exo* orientation of the ester group. Of the two minor products, it appeared that the diastereomer **6** with a *trans*-fused ring junction was formed to a greater extent (~3 : 1), since the major set of peaks in the ^{1}H NMR spectrum included the proton (δ 2.82, d, J 12) α to the nitrogen atom at the ring junction with a relatively large coupling constant.

On subjecting the mixture of the two minor diastereomers **5** and **6** to the same reaction conditions, none of the diastereomer **3** was obtained. This suggests that the cycloaddition reaction is irreversible and that the stereochemistry arises from a kinetic rather than a thermodynamic process. There are four possible ylides from which cycloaddition can occur, illustrated in Fig. 1. For the formation of the *cis*-fused bicyclic ring system, the *W*- and *U*-shaped ylides **7** and **8** both give rise to the *endo* cycloadduct **5**, whereas the two *S*-shaped ylides **9** and **10** lead to the *exo* cycloadduct **3**. The preference for the *exo* product **3** can therefore be explained by a preference for one (or both) of the *S*-shaped ylides, with cycloaddition occurring by a concerted suprafacial pathway.

In order to gain a fuller understanding of this reaction prior to its use for the synthesis of other polycyclic amines, we carried out a study to determine the optimum conditions and their influence on the diastereomer ratio of the cycloadducts. Reducing the relative ratio of the secondary amine sarcosine ethyl ester and the aldehyde **1** from 2 : 1 to 1 : 1 gave almost identical results. Altering the amount of CSA present in the reaction did have some influence on the yield and ratio of products, as indicated in Table 1. With no acid catalyst (entry 1), the reaction was slow, although the same diastereomer ratio was observed. Optimum yields were obtained with about 10 mol% of CSA (entry 4), although in these cases a reasonable quantity of the two minor diastereomers **5** and **6** was formed. No cycloadducts were obtained using one equivalent (100 mol%) of CSA.

Changing the acid to pyridinium toluene-*p*-sulfonate had a detrimental effect on the yield of the cycloadducts. Alternative reaction conditions, refluxing one equivalent of sarcosine ethyl ester hydrochloride salt and aldehyde **1** in xylene, with one equivalent of diisopropylethylamine, gave similar results [64% yield, ratio **3** : (**5** + **6**) 78 : 22] to the reaction of the free base of sarcosine ethyl ester.

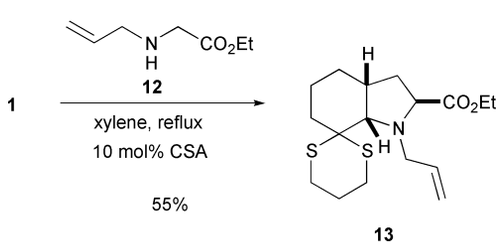
Cycloaddition of the aldehyde **1** with sarcosine *tert*-butyl ester (two equivalents) under the optimized conditions (xylene, 10 mol% CSA, reflux with a Dean–Stark trap for 16 h) gave a reasonable yield (66%) of the diastereomer **11** (Scheme 3). A



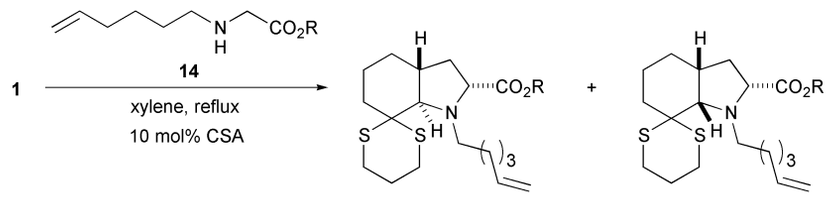
Scheme 3

small amount (15%) of a mixture of two other diastereomers was also formed. This result suggests that the ylide stereochemistry is not influenced significantly by the size of the ester group when using a sarcosine ester as the secondary amine component.

To explore the scope of the cycloaddition reaction further, we investigated the influence of the nitrogen substituent. Using *N*-allylglycine ethyl ester **12**,[7] rather than sarcosine ethyl ester, the desired cycloadduct **13** was obtained (Scheme 4). In addition,



Scheme 4



Scheme 5

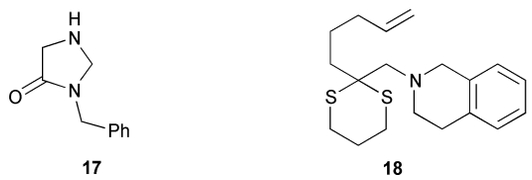


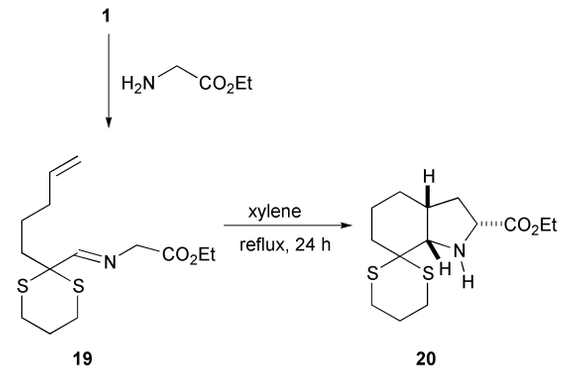
Fig. 2

another product (15%), tentatively assigned as a *trans*-fused diastereomer, was formed (^{1}H NMR, $CDCl_3$, δ 2.88, 1H, d, J 10 for the ring junction proton α to the nitrogen atom). Using a secondary amine with a bulkier *N*-substituent, namely, *N*-hex-5-enyl glycine ethyl ester **14a**, a good yield of two stereoisomeric cycloadducts **15a** and **16a** was obtained (Scheme 5). In this case, the major product was determined (^{1}H NMR NOESY between the two protons in the pyrrolidine ring α to the nitrogen atom) to be the *endo* stereoisomer **16a**. The minor product was the *trans*-fused diastereomer **15a**. Using the bulkier *tert*-butyl ester **14b**, the *endo* stereoisomer **16b** was the only product observed. Therefore, using a large substituent on the nitrogen atom favours the transition state (**7** or **8**) leading to the *endo* cycloadduct.

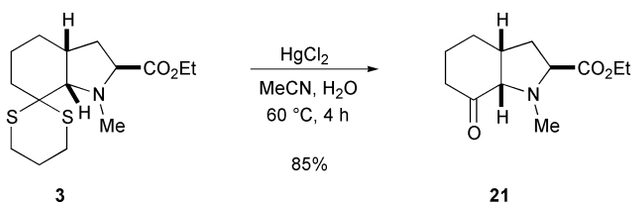
Attempted cycloaddition with methylaminoacetonitrile, L-proline methyl ester or 3-benzylimidazolidin-4-one **17**[8] (Fig. 2) all failed and only a low yield of recovered aldehyde **1** was isolated. Tetrahydroisoquinoline has been reported to allow azomethine ylide formation and cycloaddition;[9] however, using this secondary amine and aldehyde **1** resulted in only the *N*-alkylated product **18** (51%). This product presumably arises by reduction of the intermediate iminium ion, possibly by excess tetrahydroisoquinoline.

Grigg has developed methods for the formation of azomethine ylides from imines using prototropic shift.[10] The required imine **19** was prepared from the aldehyde **1** and glycine ethyl ester [dehydration with $HC(OMe)_3$, 50 °C]. Subsequent treatment with silver acetate and DBU in MeCN at 0 °C, to effect the Lewis acid-promoted prototropic shift and cycloaddition, caused only decomposition. However, thermal conditions from the imine **19**, or preferably directly from the aldehyde **1**, were effective and a good yield (72%) of a mixture of cycloadducts was obtained (Scheme 6). The identity of the major product **20** (~60% of the mixture) with *endo* stereochemistry was established by conversion to the *p*-nitrobenzamide derivative (*p*-nitrobenzoyl chloride, K_2CO_3, CH_2Cl_2, 88%) followed by X-ray crystallographic analysis. Therefore, cycloaddition of the azomethine ylide bearing a hydrogen atom on the nitrogen atom gives rise to predominantly the *endo* cycloadduct, possibly from a preference for the *W*-shaped ylide **7** (R′ = H).

The cycloaddition product **3** was converted to the ketone **21** using mercuric chloride in aqueous MeCN (Scheme 7). This deprotection was best accomplished on warming to 60 °C with 2.2 equivalents of $HgCl_2$. The ketone **21** was found to be unstable to chromatography but could be isolated by simple aqueous extraction.



Scheme 6



Scheme 7

Conclusion

This paper outlines the formation of several bicyclic amines by 1,3-dipolar cycloaddition reactions of azomethine ylides derived from aldehyde **1**. Optimum conditions have been developed for this cycloaddition reaction. The yield of the cycloadduct shows considerable dependence on the conditions of the reaction and on the structure of the secondary amine used to couple with the aldehyde **1**. Successful results were obtained with α-amino-ester derivatives. The diastereoselectivity in the cycloaddition reaction depends on the geometry of the ylide, which is influenced by the steric environment of the substituents. We have therefore determined aspects of the scope and selectivity of the intramolecular azomethine ylide cycloaddition reaction, which provides a convenient approach to functionalised octahydroindoles.

Experimental

General

IR spectra were recorded as liquid films on NaCl plates unless otherwise stated, using a Nicolet FT-IR Magna 550 spectrometer. Elemental analyses were recorded on a Carlo Erba EA1110 elemental analyser. ^{1}H NMR spectra were recorded on a Bruker AC 300 MHz or a Bruker DRX 400 MHz spectrometer using the residual solvent peak as an internal reference. Chemical shifts are given in parts per million. Coupling constants, J, are given in Hz. ^{13}C NMR spectra were recorded on the above spectrometers operating at 75 or 100 MHz respectively and were proton decoupled. Additional analyses by

DEPT, COSY, NOESY or HMQC experiments were performed where necessary. Mass spectra were recorded on a Kratos Profile HV3 spectrometer, a Micromass Quattro II spectrometer or a ThermoQuest AS2000 GCMS machine, using electron impact (EI) or chemical ionisation (CI) techniques, as reported. Accurate mass measurements were performed on the Kratos Profile spectrometer, a Finnigan MAT 900 XLT spectrometer or a Micromass Autospec spectrometer.

Petrol refers to light petroleum (bp 40–60 °C). Flash column chromatography was performed on silica gel 60H (230–400 mesh) (Merck 9385). Thin layer chromatography was performed on Kieselgel $60F_{254}$ 0.25 mm plates, and visualised by UV irradiation at 254 nm or potassium permanganate dip.

2-Formyl-2-(pent-4-enyl)-1,3-dithiane 1 [11]

According to the literature method,[11] alkylation of dithiane with pent-4-enyl bromide, followed by DMF gave, after column chromatography, eluting with petrol–ethyl acetate (EtOAc) (19 : 1), the aldehyde **1** (63%) as an oil, δ_H(300 MHz, $CDCl_3$) 1.53–1.60 (2H, m, CH_2), 1.77–1.83 (3H, m, 3 × CH), 2.02–2.09 (3H, m, CH_2C= and CH), 2.62 (2H, ddd, *J* 14.5, 4.0 and 3.0, 2 × CH), 3.01 (2H, ddd, *J* 14.5, 13.0 and 2.5, 2 × CH), 4.98 (1H, br d, *J* 10.0, CH=), 5.00 (1H, br d, *J* 17.0, CH=), 5.72 (1H, ddt, *J* 17.0, 10.0 and 6.5, CH=) and 9.01 (1H, s, CHO); data in accord with the literature.[11]

Ethyl 1-methyl-7-(propane-1,3-diyldithio)octahydroindole-2-carboxylate 3,[5b] 5, 6

To a solution of the aldehyde **1** (200 mg, 0.93 mmol) in xylene (4 cm^3) were added sarcosine ethyl ester (218 mg, 1.86 mmol) and CSA (22 mg, 0.09 mmol). The mixture was heated under reflux using a Dean–Stark trap containing 4 Å molecular sieves. After 16 h, the solvent was evaporated and the residue was purified by column chromatography, eluting with hexane–EtOAc (95 : 5), to give the (2*RS*,4*SR*,9*RS*)-ester **3** (173 mg, 0.55 mmol, 59%) as needles, R_f 0.19 (petrol–EtOAc, 95 : 5); mp 78–80 °C (Found: C, 56.92; H, 8.19; N, 4.16. $C_{15}H_{25}NO_2S_2$ requires C, 57.11; H, 7.99; N, 4.44%); ν_{max}($CHCl_3$)/cm^{-1} 1720 (C=O); δ_H(400 MHz, $CDCl_3$) 1.23 (3H, t, *J* 7.0, CH_3CH_2), 1.38–1.49 (1H, m, $CH^AH^BCH_2S$), 1.55–1.58 (1H, m, CH^CH^DS), 1.59–1.63 (2H, m, CH_2S), 1.66–1.68 (1H, m, $CH^AH^BCH_2S$), 1.76 (1H, ddd, *J* 12.5, 7.0 and 2.0, CH^EH^FCHN), 1.79–1.87 (1H, m, $CH_2CH^GH^HCH$), 1.97–2.02 (1H, m, $CH_2CH^GH^HCH$), 2.07 (1H, dd, *J* 12.5 and 9.0, CH^EH^FCHN), 2.52–2.54 (1H, m, $CH^IH^JCH_2CS$), 2.55–2.58 (1H, m, CHCHN), 2.60–2.63 (1H, m, CH^KH^LCS), 2.64–2.66 (1H, m, CH^CH^DS), 2.81 (3H, s, CH_3N), 2.88 (1H, ddd, *J* 14.5, 12.0 and 2.5, $CH^IH^JCH_2CS$), 3.07 (1H, d, *J* 7.5, CHCHN), 3.16 (1H, ddd, *J* 15.0, 12.0 and 2.5, CH^KH^LCS), 3.77 (1H, dd, *J* 9.0 and 2.0, $CHCO_2Et$) and 4.10 (2H, q, *J* 7.0, CH_2CH_3); δ_C(100 MHz, $CDCl_3$) 14.3 (CH_3CH_2), 18.4 (CH_2CH_2S), 25.6 (CH_2CH_2CH), 25.7 (CH_2CH_2CS), 26.5 (CH_2S), 27.0 (CH_2CS), 33.9 (CH_2S), 35.2 (CH_2CHN), 37.0 (CHCHN), 38.3 (CH_3N), 57.4 (CS_2), 60.1 (CH_2CH_3), 65.6 ($CHCO_2Et$), 69.9 (CHCHN) and 174.7 (C=O) (Found: M^+, 315.1341. $C_{15}H_{25}NO_2S_2$ requires *M*, 315.1327); *m*/*z* (EI) 315 (M^+, 34%), 242 (M − CO_2Et, 32), 134 (100) and 101 (32); and a mixture of esters **5** and **6** (95 mg, 0.30 mmol, 32%) as an oil, R_f 0.11 (petrol–EtOAc, 95 : 5); ν_{max}($CHCl_3$)/cm^{-1} 1720 (C=O); δ_H(300 MHz, $CDCl_3$) 1.28 (6H, t, *J* 7.0, 2 × CH_3CH_2), 1.31–1.49 (4H, m, 2 × CH_2), 1.58–1.63 (6H, m, 2 × CH_2 and 2 × CH), 1.71–1.96 (6H, m, 2 × CH_2 and 2 × CH), 2.05–2.12 (2H, m, 2 × CH), 2.36–2.42 (2H, m, 2 × CH), 2.58–2.63 (4H, m, 4 × CH), 2.75 (6H, s, 2 × CH_3N), 2.82 (1H, d, *J* 12.0, CHCHN), 2.85–3.04 (3H, m, 3 × CH), 3.10–3.26 (4H, m, 4 × CH), 3.83–3.88 (2H, m, 2 × $CHCO_2Et$) and 4.14 (4H, q, *J* 7.0, 2 × CH_2CH_3); δ_C(100 MHz, $CDCl_3$) 14.1 (CH_3), 14.2 (CH_3), 22.7 (CH_2), 23.1 (CH_2), 24.8 (CH_2), 25.0 (CH_2), 25.8 (CH_2), 25.9 (CH_2), 26.3 (CH_2), 26.6 (CH_2), 27.0 (CH_2), 27.8 (CH_2), 29.8 (CH_2), 30.1 (CH_2), 33.0 (CH_2), 37.1 (CH_3N), 37.2 (CH_3N), 38.9 (CH), 45.1 (CH), 54.1 (C), 59.9 (C), 60.3 (CH_2), 61.6 (CH_2), 64.0 (CH), 65.6 (CH), 72.3 (CH), 79.3 (CH) and 175.1 (C=O) (Found: M^+, 315.1326. $C_{15}H_{25}NO_2S_2$ requires *M*, 315.1327); *m*/*z* (EI) 315 (M^+, 3%), 242 (M − CO_2Et, 3) and 85 (100).

tert-Butyl 1-methyl-7-(propane-1,3-diyldithio)octahydroindole-2-carboxylate 11

In the same way as the amine **3**, the aldehyde **1** (330 mg, 1.5 mmol) in xylene (10 cm^3), sarcosine *tert*-butyl ester (440 mg, 3.0 mmol) and CSA (36 mg, 0.15 mmol) gave, after purification by column chromatography, eluting with hexane–EtOAc (97 : 3) the *amine* **11** (340 mg, 1.0 mmol, 66%) as an oil, R_f 0.15 (hexane–EtOAc, 95 : 5); ν_{max}($CHCl_3$)/cm^{-1} 1710 (C=O); δ_H(400 MHz, $CDCl_3$) 1.44 [9H, s, $(CH_3)_3C$], 1.45–1.52 (1H, m, CH), 1.57–1.70 (4H, m, 4 × CH), 1.70–1.87 (2H, m, CH^AH^BCHN and CH), 1.98–2.06 (2H, m, CH^AH^BCHN and CH), 2.53–2.69 (4H, m, CHCHN and 3 × CH), 2.83 (3H, s, CH_3N), 2.90 (1H, td, *J* 13.5 and 2.0, CH), 3.09 (1H, d, *J* 7.5, CHCHN), 3.18 (1H, td, *J* 13.5 and 2.0, CH) and 3.68 (1H, dd, *J* 8.5 and 1.5, CHCO); δ_C(100 MHz, $CDCl_3$) 18.5 (CH_2), 25.7 (CH_2), 25.8 (CH_2), 26.6 (CH_2), 27.1 (CH_2), 28.2 (CH_3), 33.6 (CH_2), 35.2 (CH_2), 37.0 (CH), 38.4 (CH_3), 57.3 (C), 66.4 (CH), 70.0 (CH), 80.5 (C) and 174.2 (C=O) (Found: MH^+, 344.1723. $C_{17}H_{30}NO_2S_2$ requires *M*, 344.1718); *m*/*z* (CI) 344 (MH^+, 100%) and 242 (M − $CO_2{}^tBu$, 5).

The stereochemistry of the product **11** is assigned on the basis of the NMR similarity to the product **3**. In addition, the coupling constant of *J* 7.5 (δ 3.09) across the ring-fused protons is indicative of a *cis*-fused ring junction and NOE experiments (^{1}H NMR, C_6D_6) gave, on irradiation of the peak corresponding to CHCHN, an enhancement (7.3%) of the peak corresponding to CHCHN, but essentially no enhancement (0.6%) of the peak corresponding to CHCO, suggesting the *exo* diastereomer **11**.

Ethyl 1-allyl-7-(propane-1,3-diyldithio)octahydroindole-2-carboxylate 13

To a solution of the aldehyde **1** (250 mg, 1.16 mmol) in xylene (4 cm^3) were added *N*-allylglycine ethyl ester **12**[7] (330 mg, 2.31 mmol) and CSA (28 mg, 0.12 mmol). The mixture was heated under reflux using a Dean–Stark trap containing 4 Å molecular sieves. After 16 h, the solvent was evaporated and the residue was purified by column chromatography, eluting with petrol–EtOAc (98 : 2) to give the *amine* **13** (220 mg, 0.64 mmol, 55%) as an oil, R_f 0.18 (petrol–EtOAc, 95 : 5); ν_{max}($CHCl_3$)/cm^{-1} 1710 (C=O); δ_H(400 MHz, $CDCl_3$) 1.22 (3H, t, *J* 7.1, CH_3), 1.37–1.45 (1H, m, CH), 1.52–1.72 (5H, m, CH^AH^BCHN and 4 × CH), 1.75–1.89 (1H, m, CH), 1.94–2.05 (1H, m, CH), 2.10–2.20 (1H, m, CH^AH^BCHN), 2.49–2.67 (3H, m, 3 × CH), 2.69–2.75 (1H, m, CH), 2.89 (1H, td, *J* 13.5 and 2.0, CH), 3.13–3.24 (2H, m, 2 × CH), 3.74 (1H, dd, *J* 14.0 and 8.0, CH), 3.80 (1H, d, *J* 8.5, $CHCO_2Et$), 4.02–4.13 (3H, m, CH and CH_2O), 5.01 (1H, d, *J* 10.0, CH=), 5.15 (1H, d, *J* 17.0, CH=) and 5.93–6.05 (1H, m, CH=); δ_C(100 MHz, $CDCl_3$) 14.3 (CH_3), 18.0 (CH_2), 25.8 (2 × CH_2), 26.5 (CH_2), 27.1 (CH_2), 34.6 (CH_2), 35.2 (CH_2), 36.8 (CH), 53.8 (CH_2), 58.4 (C), 60.1 (CH_2), 62.3 (CH), 68.4 (CH), 116.2 (CH_2), 136.9 (CH) and 175.2 (C=O) (Found: MH^+, 342.1560. $C_{17}H_{28}NO_2S_2$ requires *M*, 342.1561); *m*/*z* (CI) 342 (MH^+, 100%) and 236 (11).

The *cis*-fused ring junction in **13** was confirmed by NOE experiments (^{1}H NMR, $C_6D_5CD_3$) in which enhancements (9 and 7.5%) of each ring junction proton were observed on irradiation of the other. No enhancement of the peak corresponding to CHCO was observed.

N-(Hex-5-enyl)glycine ethyl ester 14a

To a solution of glycine ethyl ester (100 mg, 1.0 mmol) in MeCN (2 cm^3) was added $NaHCO_3$ (2.4 g, 29 mmol) and

6-bromohex-1-ene (0.2 cm^3, 1.5 mmol). The mixture was heated under reflux for 1 h, then was cooled to room temperature and water (10 cm^3) was added. The solution was extracted with CH_2Cl_2 (3 × 10 cm^3), and the combined organic layers were washed with water (25 cm^3), dried over $MgSO_4$ and evaporated. Purification by column chromatography, eluting with petrol–EtOAc (1 : 1) gave the *amine* **14a** (65 mg, 0.35 mmol, 36%) as an oil, R_f 0.19 (EtOAc); $\nu_{max}(CHCl_3)/cm^{-1}$ 1730 (C=O) and 1630 (C=C); δ_H(300 MHz, $CDCl_3$) 1.28 (3H, t, *J* 7.0, CH_3), 1.40–1.56 (4H, m, $CH_2CH_2CH_2N$), 1.69 (1H, br s, NH), 2.07 (2H, q, *J* 7.0, CH_2C=C), 2.60 (2H, t, *J* 7.0, CH_2N), 3.39 (2H, s, CH_2CO), 4.17 (2H, q, *J* 7.0, CH_2CH_3), 4.94 (1H, br d, *J* 9.5, CH=), 4.95 (1H, br d, *J* 17.0, CH=) and 5.78 (1H, ddt, *J* 17.0, 9.5 and 7.0, CH=); δ_C(75 MHz, $CDCl_3$) 14.2 (CH_3), 26.4 (CH_2), 29.5 (CH_2), 33.6 (CH_2), 49.4 (CH_2), 51.0 (CH_2), 60.7 (CH_2), 114.5 (CH_2), 138.7 (CH) and 172.6 (C=O) (Found: M^+, 185.1418. $C_{10}H_{19}NO_2$ requires *M*, 185.1416); *m*/*z* (EI) 185 (M^+, 3%), 116 (M − CO_2Et, 26) and 112 ($C_5H_6NO_2$, 100).

N-(Hex-5-enyl)glycine *tert*-butyl ester 14b

In the same way as the ester **14a**, glycine *tert*-butyl ester (780 mg, 6.0 mmol) and 6-bromohex-1-ene (1.0 cm^3, 7.5 mmol) gave the *amine* **14b** (310 mg, 1.4 mmol, 24%) as an oil, R_f 0.27 (EtOAc); $\nu_{max}(CHCl_3)/cm^{-1}$ 1730 (C=O); δ_H(300 MHz, $CDCl_3$) 1.43–1.51 (4H, m, $CH_2CH_2CH_2N$), 1.46 [9H, s, $(CH_3)_3C$], 2.05 (2H, q, *J* 7.0, CH_2C=C), 2.58 (2H, t, *J* 7.0, CH_2CH_2N), 3.28 (2H, s, CH_2CO), 4.95 (1H, br d, *J* 10.0, CH=), 4.96 (1H, br d, *J* 17.0, CH=) and 5.69 (1H, ddt, *J* 17.0, 10.0 and 7.0, CH=); δ_C(75 MHz, $CDCl_3$) 26.5 (CH_2), 28.1 (CH_3), 29.5 (CH_2), 33.6 (CH_2), 49.4 (CH_2), 51.8 (CH_2), 81.2 (C), 114.5 (CH_2), 138.7 (CH) and 171.9 (C=O) (Found: MH^+, 214.1810. $C_{12}H_{24}NO_2$ requires *M*, 214.1807); *m*/*z* (CI) 214 (MH^+, 28%), 200 (14) and 158 (100).

Ethyl 1-(hex-5-enyl)-7-(propane-1,3-diyldithio)octahydroindole-2-carboxylate 15a, 16a

In the same way as the amine **3**, the aldehyde **1** (60 mg, 0.28 mmol) in xylene (1.2 cm^3), *N*-(hex-5-enyl)glycine ethyl ester **14a** (100 mg, 0.56 mmol) and CSA (1 mg, 0.04 mmol), gave, after purification by column chromatography, eluting with hexane–EtOAc (19 : 1), the recovered aldehyde **1** (6 mg, 0.03 mmol, 11%); the (2*SR*,4*SR*,9*RS*)-*ester* **16a** (58 mg, 0.15 mmol, 55%) as an oil, R_f 0.30 (petrol–EtOAc, 9 : 1); $\nu_{max}(CHCl_3)/cm^{-1}$ 1715 (C=O) and 1635 (C=C); δ_H(400 MHz, $CDCl_3$) 1.26 (3H, t, *J* 7.0, CH_3), 1.41–1.49 (3H, m, 3 × CH), 1.56–1.67 (4H, m, 4 × CH), 1.68–1.74 (1H, m, CH^AH^BCHN), 1.78–1.88 (2H, m, CH_2), 2.00–2.11 (2H, m, CH_2), 2.12–2.14 (2H, m, CH_2C=), 2.15–2.21 (1H, m, CH^AH^BCHN), 2.51–2.64 (2H, m, 2 × CH), 2.63–2.68 (1H, m, $CHCHN$), 2.70–2.74 (1H, m, CH), 2.91 (1H, ddd, *J* 15.0, 12.5 and 2.5, CH), 3.10–3.14 (1H, m, CH^CH^DN), 3.17 (1H, d, *J* 7.5, $CHCHN$), 3.21 (1H, ddd, *J* 15.0, 12.5 and 3.0, CH), 3.29–3.36 (1H, m, CH^CH^DN), 3.87 (1H, dd, *J* 8.0 and 1.0, $CHCO_2Et$), 4.09–4.17 (2H, m, OCH_2), 4.94 (1H, ddt, *J* 10.5, 2.5 and 1.5, CH=), 5.03 (1H, br d, *J* 17.0, CH=) and 5.85 (1H, ddt, *J* 17.0, 10.5 and 7.0, CH=); δ_C(100 MHz, $CDCl_3$) 14.3 (CH_3), 18.0 (CH_2), 25.8 (CH_2), 26.6 (CH_2), 26.7 (2 × CH_2), 27.1 (CH_2), 28.1 (CH_2), 33.7 (CH_2), 34.6 (CH_2), 35.2 (CH_2), 36.7 (CH), 50.2 (CH_2), 58.6 (C), 60.1 (CH_2), 62.5 (CH), 68.8 (CH), 114.0 (CH_2), 139.4 (CH) and 175.3 (C=O) (Found: M^+, 383.1951. $C_{20}H_{33}NO_2S_2$ requires *M*, 383.1953); *m*/*z* (EI) 383 (M^+, 40%), 310 (M − CO_2Et, 32), 202 (66) and 187 (100); and the (2*RS*,4*SR*,9*RS*)-*ester* **15a** (18 mg, 0.05 mmol, 17%) as an oil; R_f 0.26 (petrol–EtOAc, 9 : 1); $\nu_{max}(CHCl_3)/cm^{-1}$ 1720 (C=O) and 1630 (C=C); δ_H(400 MHz, $CDCl_3$) 1.27 (3H, t, *J* 7.0, CH_3), 1.32–1.39 (1H, m, CH^AH^BCHN), 1.41–1.60 (7H, m, 7 × CH), 1.70–1.91 (3H, m, 3 × CH), 2.04–2.06 (1H, m, $CHCHN$), 2.07–2.14 (3H, m, CH and CH_2C=), 2.23 (1H, dt, *J* 12.5 and 8.5, CH^AH^BCHN), 2.55–2.65 (3H, m, 3 × CH), 2.86 (1H, d, *J* 10.0, $CHCHN$), 2.88–2.93 (1H, m, CH), 2.98 (1H, ddd, *J* 15.0, 13.0 and 3.0, CH), 3.25 (1H, ddd, *J* 15.0, 13.0 and 3.0, CH), 3.85–3.90 (1H, m, CH), 3.91 (1H, dd, *J* 8.5 and 6.0, $CHCO_2Et$), 4.11–4.20 (2H, m, OCH_2), 4.95 (1H, ddt, *J* 10.5, 2.5 and 1.5, CH=), 4.99 (1H, dq, *J* 17.0 and 2.5, CH=) and 5.85 (1H, ddt, *J* 17.0, 10.5 and 7.0, CH=); δ_C(100 MHz, $CDCl_3$) 14.4 (CH_3), 23.1 (CH_2), 24.8 (CH_2), 26.5 (2 × CH_2), 26.7 (CH_2), 27.7 (CH_2), 29.7 (CH_2), 33.3 (CH_2), 33.8 (CH_2), 37.3 (CH_2), 38.8 (CH), 48.6 (CH_2), 54.6 (C), 59.7 (CH), 60.0 (CH_2), 71.2 (CH), 114.1 (CH_2), 139.3 (CH) and 175.3 (C=O) (Found: M^+, 383.1958. $C_{20}H_{33}NO_2S_2$ requires *M*, 383.1953); *m*/*z* (EI) 383 (M^+, 28%), 310 (M − CO_2Et, 41), 202 (100) and 187 (65).

The results of NOESY experiments (^{1}H NMR, $CDCl_3$) indicated that the major diastereomer was the *endo* product **16a**, since irradiation at δ 3.17 ($CHCHN$) caused an NOE at δ 3.87 ($CHCO_2Et$).

The results of NOESY experiments (^{1}H NMR, $CDCl_3$) indicated that the minor diastereomer was the *trans*-fused product **15a**, since irradiation at δ 2.23 (CH^AH^BCHN) caused an NOE at δ 3.91 ($CHCO_2Et$) and at δ 2.05 ($CHCHN$), and irradiation at δ 1.35 (CH^AH^BCHN) caused an NOE at δ 2.86 ($CHCHN$); the larger coupling constant for the ring junction proton α to the nitrogen atom ($CHCHN$) of **15a** (δ 2.86, d, *J* 10.0) also fits with this assignment.

tert-Butyl 1-(hex-5-enyl)-7-(propane-1,3-diyldithio)octahydroindole-2-carboxylate 16b

In the same way as the amine **3**, the aldehyde **1** (68 mg, 0.31 mmol) in xylene (1.5 cm^3), *N*-(hex-5-enyl)glycine *tert*-butyl ester **14b** (130 mg, 0.62 mmol) and CSA (1 mg, 0.04 mmol), gave, after purification by column chromatography, eluting with hexane–EtOAc, 9 : 1, the *ester* **16b** (74 mg, 0.18 mmol, 58%) as an oil, R_f 0.25 (hexane–EtOAc, 9 : 1); $\nu_{max}(CHCl_3)/cm^{-1}$ 1710 (C=O) and 1630 (C=C); δ_H(300 MHz, $CDCl_3$) 1.42 [9H, s, $(CH_3)_3C$], 1.44–1.83 (10H, m, 4 × CH_2 and 2 × CH), 2.03–2.09 (5H, m, 2 × CH_2 and CH), 2.47–2.75 (4H, m, 4 × CH), 2.81–3.08 (3H, m, 3 × CH), 3.10 (1H, d, *J* 7.5, $CHCHN$), 3.14–3.38 (1H, m, CH), 3.71 (1H, d, *J* 8.0, CHCO), 4.96 (1H, br d, *J* 10.5, CH=), 4.97 (1H, br d, *J* 17.0, CH=) and 5.81 (1H, ddt, *J* 17.0, 10.5 and 7.0, CH=); δ_C(75 MHz, $CDCl_3$) 18.1 (CH_2), 22.9 (CH_2), 24.5 (CH_2), 25.8 (CH_2), 26.6 (CH_2), 26.8 (CH_2), 27.2 (CH_2), 28.1 (CH_3), 33.6 (CH_2), 33.8 (CH_2), 35.2 (CH_2), 36.6 (CH), 50.4 (CH_2), 58.6 (C), 63.2 (CH), 69.0 (CH), 80.5 (C), 114.1 (CH_2), 139.2 (CH) and 189.6 (C=O) (Found: MH^+, 412.2339. $C_{22}H_{38}NO_2S_2$ requires *M*, 412.2344); *m*/*z* (CI) 412 (MH^+, 100%), 330 (27) and 306 (35).

The stereochemistry of the cycloadduct **16b** was assigned tentatively on the basis of the NMR spectroscopic similarity with the *endo* product **16a**; for example, the ring junction proton α to the nitrogen atom is at δ 3.10 for **16b** and at δ 3.17 for **16a**, whereas for the isomer **15a** this proton resonates at δ 2.86; in addition, the proton α to the nitrogen atom at δ 3.10 for **16b** is a doublet, *J* 7.5, indicating a *cis*-fused ring junction.

N-[2-(Propane-1,3-diyldithio)hept-6-enyl]-1,2,3,4-tetrahydroisoquinoline 18

To a solution of the aldehyde **1** (200 mg, 0.93 mmol) in xylene (4 cm^3) were added 1,2,3,4-tetrahydroisoquinoline (0.23 cm^3, 1.86 mmol) and CSA (22 mg, 0.09 mmol). The mixture was heated under reflux using a Dean–Stark trap containing 4 Å molecular sieves. After 16 h, the solvent was evaporated and the residue was purified by column chromatography, eluting with petrol–EtOAc (9 : 1) to give the *amine* **18** (158 mg, 0.48 mmol, 51%) as an oil, R_f 0.29 (petrol–EtOAc, 9 : 1); $\nu_{max}(CHCl_3)/cm^{-1}$ 1640 (C=C); δ_H(400 MHz, $CDCl_3$) 1.59–1.64 (2H, m, CH_2CH_2CS), 1.97–2.01 (4H, m, CH_2CH_2CS and CH_2CH_2S), 2.05–2.09 (2H, m, CH_2C=), 2.74–2.81 (2H, m, 2 × CH^AH^BS), 2.88–3.00 (8H, m, 2 × CH^AH^BS, NCH_2CH_2, NCH_2CS), 3.90 (2H, s, NCH_2Ar), 4.97 (1H, br d, *J* 10.0, CH=), 5.01 (1H, br d, *J* 17.0, CH=), 5.80 (1H, ddt, *J* 17.0, 10.0 and 6.5, CH=) and

6.99–7.13 (4H, m, Ar); δ_C(100 MHz, $CDCl_3$) 23.8 (CH_2), 25.3 (CH_2), 26.2 (2 × CH_2), 28.9 (CH_2), 33.9 (CH_2), 37.0 (CH_2), 52.9 (CH_2), 54.6 (C), 57.7 (CH_2), 63.9 (CH_2), 114.9 (CH_2), 125.5 (CH), 126.0 (CH), 126.5 (CH), 128.7 (CH), 134.5 (C), 135.4 (C) and 138.4 (CH=) (Found: MH^+, 334.2017. $C_{19}H_{28}NS_2$ requires *M*, 334.2019); *m*/*z* (CI) 334 (MH^+, 4%) and 244 (100).

Ethyl 7-(propane-1,3-diyldithio)octahydroindole-2-carboxylate 20

A solution of glycine ethyl ester (240 mg, 2.3 mmol) and the aldehyde **1** (325 mg, 1.5 mmol) in xylene (10 cm^3) was heated under reflux using a Dean–Stark trap. After 48 h, the solvent was evaporated and the residue was purified by column chromatography, eluting with petrol–EtOAc (4 : 1 to 1 : 1) to give a mixture of four cycloaddition products (325 mg, 72%), the major fraction containing the *amine* **20** and another product (85% of the total, 7 : 3 ratio) as an oil; data for partially purified amine **20**: R_f 0.32 (petrol–EtOAc, 1 : 1); ν_{max}($CHCl_3$)/cm^{-1} 1725 (C=O); δ_H(400 MHz, $CDCl_3$) 1.24 (3H, t, *J* 7.0, CH_3), 1.38–1.50 (2H, m, 2 × CH), 1.72–1.78 (2H, m, CH and C*H*^{A}H^{B}CHN), 1.88–2.06 (4H, m, 2 × CH_2), 2.24–2.33 (2H, m, CH^A*H*^{B}CHN and C*H*CHN), 2.60–2.80 (3H, m, 3 × CH), 2.85–2.96 (2H, m, 2 × CH), 3.57 (1H, d, *J* 3.5, CHC*H*N), 3.83 (1H, dt, *J* 10.5 and 4.0, C*H*CO_2Et) and 4.18 (2H, q, *J* 7.0, C*H*$_2$$CH_3$); δ_C(100 MHz, $CDCl_3$) 14.2 (CH_3), 20.8 (CH_2), 25.4 (CH_2), 25.6 (CH_2), 26.3 (CH_2), 27.2 (CH_2), 32.4 (CH_2), 35.3 (CH), 36.5 (CH_2), 51.4 (C), 57.4 (CH), 61.0 (CH_2), 63.6 (CH) and 174.9 (C=O) (Found: M^+, 301.1162. $C_{14}H_{23}NO_2S_2$ requires *M*, 301.1170); *m*/*z* (EI) 301 (M^+, 18%) and 145 ($C_7H_{15}NO_2$, 100).

Ethyl 1-*p*-nitrobenzoyl-7-(propane-1,3-diyldithio)octahydroindole-2-carboxylate

To a solution of the amine **20** (50 mg, 0.17 mmol) in CH_2Cl_2 (3 cm^3) was added K_2CO_3 (59 mg, 0.43 mmol) and *p*-nitrobenzoyl chloride (63 mg, 0.34 mmol) at room temperature. After 2 h, the solvent was evaporated and the residue was purified by column chromatography, eluting with petrol–EtOAc (1 : 1 to 0 : 1) to give the *p-nitrobenzamide* of **20** (67 mg, 0.15 mmol, 88%); recrystallisation from petrol–EtOAc gave needles, R_f 0.40 (petrol–EtOAc, 1 : 1); mp 131–134 °C; ν_{max}($CHCl_3$)/cm^{-1} 1755 (C=O), 1520 (NO_2) and 1340 (NO_2); δ_H(300 MHz, $CDCl_3$) 1.21 (3H, t, *J* 7.0, CH_3), 1.23–1.28 (2H, m, 2 × CH), 1.59–1.77 (5H, m, 5 × CH), 1.87–1.92 (2H, m, 2 × CH), 2.28–2.34 (1H, m, CH), 2.52–2.71 (5H, m, 5 × CH), 2.91–2.99 (2H, m, CHC*H*N and C*H*CO_2Et), 4.10 (2H, q, *J* 7.0, CH_2O), 7.67 (2H, d, *J* 8.5, Ar) and 8.22 (2H, d, *J* 8.5, Ar); δ_C(75 MHz, $CDCl_3$) 14.2 (CH_3), 17.5 (CH_2), 21.1 (CH_2), 24.0 (CH_2), 25.3 (CH_2), 25.8 (CH_2), 26.8 (CH_2), 37.2 (CH), 38.3 (CH_2), 51.3 (C), 55.3 (CH), 60.4 (CH_2), 61.2 (CH), 123.4 (CH), 128.4 (CH), 143.2 (C), 147.8 (C), 170.1 (C=O) and 171.3 (C=O) (Found: MH^+, 451.1366. $C_{21}H_{27}N_2O_5S_2$ requires *M*, 451.1361); *m*/*z* (CI) 451 (MH^+, 100%), 315 (24) and 139 (94).

Ethyl 1-methyl-7-oxooctahydroindole-2-carboxylate 21

To a solution of $HgCl_2$ (510 mg, 1.9 mmol) in 80% aqueous MeCN (14 cm^3) was added a solution of the dithiane **3** (270 mg, 0.9 mmol) in 80% aqueous MeCN (10 cm^3). The mixture was heated at 60 °C for 4.5 h and was then filtered. The mixture was washed with aqueous NH_4OAc (20 cm^3), water (20 cm^3) and brine (20 cm^3), and the organic layer was dried over $MgSO_4$. Evaporation of the solvent gave the *ketone* **21** (160 mg, 0.7 mmol, 85%) as an oil, R_f 0.58 (EtOAc); ν_{max}($CHCl_3$)/cm^{-1} 1725 (C=O) and 1705 (C=O); δ_H(400 MHz, $CDCl_3$) 1.27 (3H, t, *J* 7.0, C*H*$_3$$CH_2$), 1.30–1.39 (1H, m, C*H*^{A}H^{B}CHN), 1.82–1.91 (4H, m, C*H*$_2$C*H*$_2$$CH_2$CO), 2.01–2.05 (1H, m, CH^A*H*^{B}CHN), 2.32–2.37 (2H, m, CH_2CO), 2.52 (3H, s, CH_3N), 2.88–2.93 (1H, m, C*H*CHN), 3.48 (1H, d, *J* 8.5, CHC*H*N), 3.78 (1H, dd, *J* 8.5 and 2.5, C*H*CO_2Et) and 4.14 (2H, q, *J* 7.0, C*H*$_2$O); δ_C(100 MHz, $CDCl_3$) 14.3 (CH_3), 22.9 (CH_2), 28.3 (CH_2), 34.8 (CH_2), 36.6 (CH_3), 38.3 (CH_2), 41.2 (CH), 60.3 (CH_2), 64.7 (CH), 71.3 (CH), 173.7 (C=O) and 219.2 (C=O) (Found: MH^+, 226.1423. $C_{12}H_{20}NO_3$ requires *M*, 226.1418); *m*/*z* (CI) 226 (MH^+, 4%) and 222 ($C_{12}H_{16}NO_3$, 100).

Acknowledgements

We thank the EPSRC and Zeneca Pharmaceuticals (now AstraZeneca) for a CASE Studentship (to K.M.C.). The EPSRC mass spectrometry service at the University of Wales, Swansea and the EPSRC X-ray service at the University of Southampton are thanked.

References

1 (*a*) E. Ciganek, *Org. React.*, 1984, **32**, 1; (*b*) W. Carruthers, *Cycloaddition Reactions in Organic Synthesis*, Pergamon Press, 1990; (*c*) W. R. Roush, *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon Press, 1991, vol. 5, p. 513; (*d*) P. A. Wade, *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon Press, 1991, vol. 4, p. 1111; (*e*) M. Harmata, *Tetrahedron*, 1997, **53**, 6235.

2 A. Padwa, *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon Press, 1991, vol. 4, p. 1069.

3 For some recent examples, see (*a*) L. E. Overman and J. E. Tellew, *J. Org. Chem.*, 1996, **61**, 8338; (*b*) M. Banwell, B. Flynn and D. Hockless, *Chem. Commun.*, 1997, 2259; (*c*) P. Garner, P. B. Cox, J. T. Anderson, J. Protasiewicz and R. Zaniewski, *J. Org. Chem.*, 1997, **62**, 493; (*d*) D. J. Denhart, D. A. Griffith and C. H. Heathcock, *J. Org. Chem.*, 1998, **63**, 9616; (*e*) O. Irie, K. Samizu, J. R. Henry and S. M. Weinreb, *J. Org. Chem.*, 1999, **64**, 587; (*f*) C. J. Lovely and H. Mahmud, *Tetrahedron Lett.*, 1999, **40**, 2079; (*g*) B. B. Snider, Y. Ahn and B. M. Foxman, *Tetrahedron Lett.*, 1999, **40**, 3339; (*h*) E. Vedejs, A. Klapars, B. N. Naidu, D. W. Piotrowski and F. C. Tucci, *J. Am. Chem. Soc.*, 2000, **122**, 5401; (*i*) M. S. Novikov, A. F. Khlebnikov, O. V. Besedina and R. R. Kostikov, *Tetrahedron Lett.*, 2001, **42**, 533.

4 I. Coldham, S. J. Coles, K. M. Crapnell, J.-C. Fernàndez, T. F. N. Haxell, M. B. Hursthouse, J. D. Moseley and A. B. Treacy, *Chem. Commun.*, 1999, 1757.

5 (*a*) P. N. Confalone and E. M. Huie, *J. Am. Chem. Soc.*, 1984, **106**, 7175; (*b*) P. N. Confalone and R. A. Earl, *Tetrahedron Lett.*, 1986, **27**, 2695.

6 For other examples, see (*a*) S. Kanemasa, K. Doi and E. Wada, *Bull. Chem. Soc. Jpn.*, 1990, **63**, 2866; (*b*) L. M. Harwood and I. A. Lilley, *Tetrahedron Lett.*, 1993, **34**, 537; (*c*) M. G. B. Drew, L. M. Harwood, D. W. Price, M.-S. Choi and G. Park, *Tetrahedron Lett.*, 2000, **41**, 5077; (*d*) R. Grigg, V. Savic and M. Thornton-Pett, *Tetrahedron*, 1997, **53**, 10633; (*e*) J. D. Harling and B. S. Orlek, *Tetrahedron*, 1998, **54**, 14905; (*f*) Q. Cheng, W. Zhang, Y. Tagami and T. Oritani, *J. Chem. Soc., Perkin Trans. 1*, 2001, 452.

7 T. L. Gilchrist, R. C. Wasson, F. D. King and G. Wootton, *J. Chem. Soc., Perkin Trans. 1*, 1987, 2517.

8 U. Pfeiffer, M. T. Riccaboni, R. Erba and M. Pinza, *Liebigs Ann. Chem.*, 1988, 993.

9 B. Wang, M. P. Mertes, K. B. Mertes and F. Takusagawa, *Tetrahedron Lett.*, 1990, **31**, 5543.

10 R. Grigg, *Chem. Soc. Rev.*, 1987, **16**, 89.

11 K. F. Burri, R. A. Cardone, W. Y. Chen and P. Rosen, *J. Am. Chem. Soc.*, 1978, **100**, 7069.