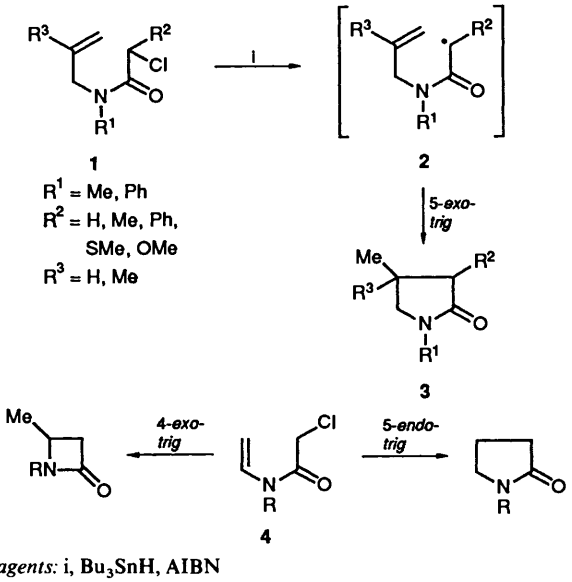
Formation of Five-membered Lactams by 5-*Endo-Trigonal* Radical Cyclisations of 2-Chloro-*N*-(cycloalk-1-enyl)acetamides: New Synthesis of Erythrinane Skeleton

Tatsunori Sato, Nobuyuki Nakamura, Keiko Ikeda, Michiyo Okada, Hiroyuki Ishibashi and Masazumi Ikeda*
Kyoto Pharmaceutical University, Misasagi, Yamashina, Kyoto 607, Japan

Free-radical cyclisations of a range of 2-chloro-*N*-(cycloalk-1-enyl)acetamides have been examined. The enamide **5**, upon treatment with Bu_3SnH in the presence of azoisobutyronitrile, underwent cyclisation *via* the carbamoylmethyl radical **6** in a 'disfavoured' 5-*endo-trig* manner to give octahydro-1-methylindol-2-one **8**. Similarly, the enamides **10** and **11** gave the corresponding octahydroindol-2-ones **12–15**. The *N*-(3,4-dihydro-2-naphthyl) derivative **16**, however, afforded the β-lactam **17** instead of a γ-lactam. The phenyl-substituted congener **24** and the benzocycloheptenyl derivative **29** gave again the five-membered lactams **25** and **30**, respectively. The difference in the mode of cyclisations among substrates **5**, **16**, **24** and **29** has been discussed in terms of the electronic stability and/or the steric congestion of the radical intermediates formed by ring closure of the carbamoylmethyl radical. The carbonyl group incorporated into the five-membered lactams proved to be essential for the 5-*endo-trig* radical cyclisation, by examination of the reactions of the enamides **33** and **38**, in which only the former gave five-membered lactams, *viz.* compounds **34** and **35**. The tandem cyclisation initiated by the carbamoylmethyl radical has also been examined. The method was applied to the synthesis of perhydroerythrinane **58**.

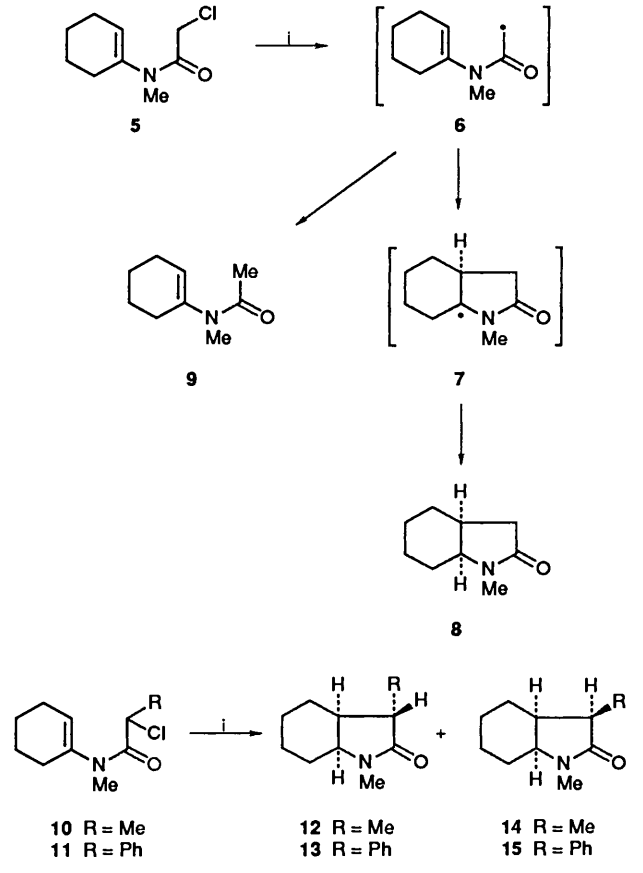
Considerable attention has recently been directed toward the synthesis of nitrogen-containing heterocycles by using free-radical cyclisations.[1] Previously, we reported that the *N*-allylic 2-chloroacetamides **1**, upon treatment with tributyltin hydride in the presence of azoisobutyronitrile (AIBN), underwent 5-*exo-trig* cyclisation *via* the carbamoylmethyl radical **2** to give the five-membered lactams **3**.[2] The high regioselectivity of the reactions and potential utility in natural products field were illustrated by an application to the synthesis of some pyrrolizidine and *Sceletium* alkaloids.[3] As an extension of the carbamoylmethyl radical cyclisations,[4] we have now examined a mode of cyclisations of the *N*-vinylic 2-chloroacetamides **4**. In principle, the ring closure of substrates **4** may occur either in a 4-*exo-trig* manner or in a 5-*endo-trig* manner. We found that the enamides **4** cyclised, in general, in a 'disfavoured' 5-*endo-trig* manner with high degree of efficiency to give five-membered lactams. In this paper, we describe the synthesis of fused five-membered lactams by free-radical cyclisations of various 2-chloro-*N*-(cycloalk-1-enyl)acetamides and also demonstrate the feasibility of the method to the tandem process which provides a new route to the erythrinane skeleton.[5]



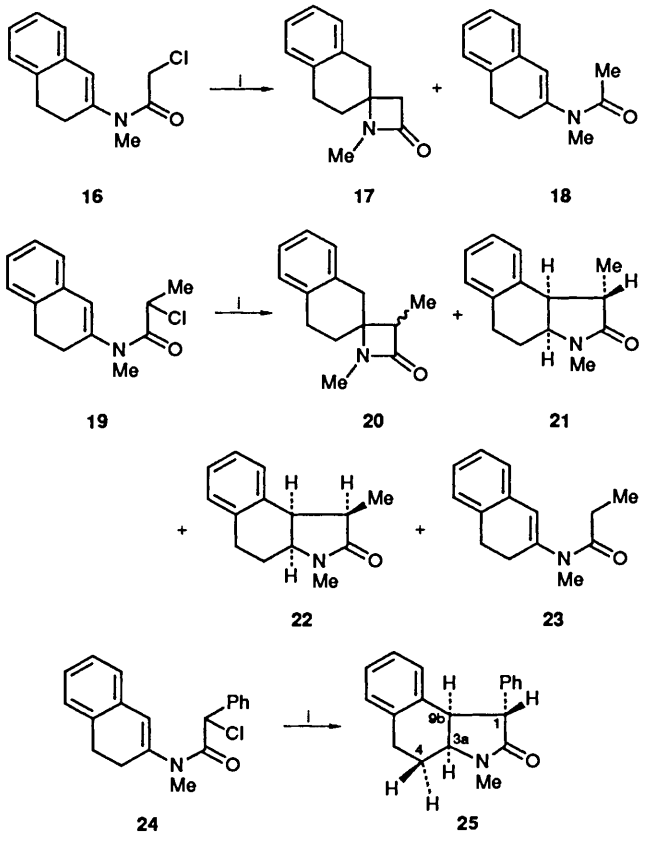
Reagents: i, Bu_3SnH, AIBN

We began our investigation by examining the cyclisation of 2-chloro-*N*-(cyclohex-1-enyl)-*N*-methylacetamide **5**, which was prepared by condensation of cyclohexanone and methylamine followed by *N*-acylation of the resultant imine with chloroacetyl chloride. When a boiling solution of the chloride **5** in toluene was treated with 1.1 mol equiv. of Bu_3SnH in the presence of a catalytic amount of AIBN, the *cis*-octahydroindol-2-one **8** was obtained in 63% yield along with the reduction product **9** (8%) (Scheme 1). The formation of the indolone **8** from **5** may involve the 5-*endo-trig* cyclisation of the carbamoylmethyl radical **6** to give the α-acylamino radical **7**. This step is then followed by an attack of Bu_3SnH from the less hindered site of the radical centre to give the *cis*-fused bicyclic lactam **8**. However, the 5-*endo-trig* cyclisation of radical **6** to give the bicycle **7** has been suggested to be a geometrically disfavoured reaction.[6] Indeed, the inability of pent-4-enyl radical and its related species to undergo 5-*endo-trig* cyclisation is well known.[7] Therefore, the present example is the first success of such 'disfavoured' radical cyclisations.

The 2-chloropropionamide **10** cyclised more cleanly to give, in 73% yield, a mixture of the 3α-Me **12** and the 3β-Me lactams **14** in the ratio 6:1. No reduction product like compound **9** was isolated. Similarly, the 2-chloro-2-phenylacetamide **11** afforded, in 75% yield, a mixture of indolones **13** and **15** in the ratio 2:3. The stereochemistry of the products **12–15** was deduced from the following thermodynamically controlled equilibrium experiments. Thus, when a 6:1 mixture of indolones **12** and **14** was treated with potassium *tert*-butoxide in refluxing *tert*-butyl alcohol for 1 h, a new mixture of **12** and **14** in the ratio 4:1 was obtained. The 3α-Me isomer **12** must be thermodynamically more stable than the 3β-Me isomer **14** for steric reasons, and hence the major product after treatment with



Scheme 1 *Reagents and conditions:* i, Bu_3SnH, AIBN, toluene, reflux



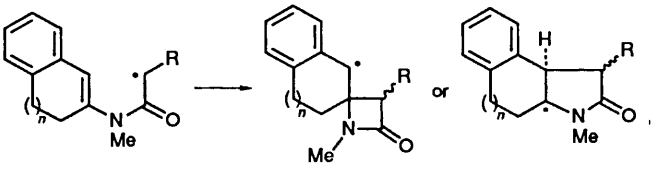
Scheme 2 *Reagents and conditions:* i, Bu_3SnH, AIBN, toluene, reflux

base can be assigned as the 3α-Me isomer **12** that is identical with the major isomer of the cyclisation products. On the other hand, treatment of a 2:3 mixture of indolones **13** and **15** with sodium ethoxide in refluxing ethanol provided only one isomer (**13**) at the complete expense of the other isomer (**15**), indicating that the minor product of the cyclisation products is the relatively stable 3α-Ph isomer **13** and the major one the less stable 3β-Ph isomer **15**. Such predominant formation of the sterically disfavoured products has frequently been observed in radical cyclisations.[1b-d] However, no simple explanation for the present results can be offered at the moment.[8]

In parallel investigations, we also studied the cyclisations of the *N*-(3,4-dihydro-2-naphthyl) derivatives **16**, **19** and **24**, which were prepared from β-tetralone according to the procedure described for the preparation of compound **5**.

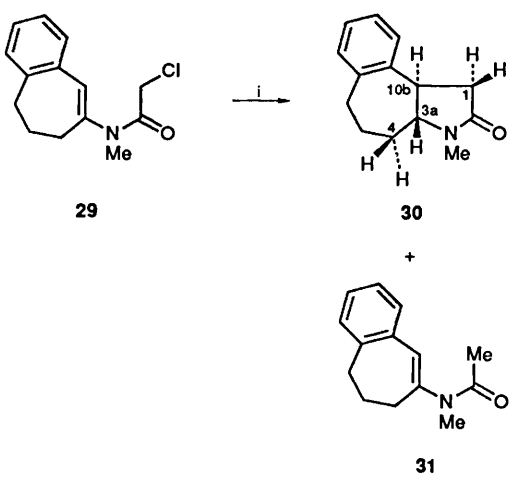
Interestingly, the enamide **16** afforded the β-lactam **17** in 50% yield along with the reduction product **18** (32%) (Scheme 2). No γ-lactam was detected in the reaction mixture. The IR spectrum of β-lactam **17** showed an absorption at 1740 cm^{-1} typical of a β-lactam. The methyl-substituted congener **19**, however, provided both the β-lactam **20** (29%) and the γ-lactams **21** (37%) and **22** (3%) together with the reduction product **23** (12%). The ^1H NMR spectrum of compound **20** showed it to be a mixture of two stereoisomers in the ratio ~1:1. Treatment of compound **22** with potassium *tert*-butoxide in refluxing *tert*-butyl alcohol for 1 h resulted in the formation of a mixture of isomers **21** and **22** having the ratio 91:9 (by GLC), indicating that compound **21** is a thermodynamically more stable 1α-Me isomer and that compound **22** is a less stable 1β-Me isomer. On the other hand, the phenyl-substituted congener **24** gave only the γ-lactam **25**, in 76% yield as a single stereoisomer. The stereochemistry of compound **25** was determined by nuclear Overhauser effect (NOE) difference spectroscopy (see Experimental section).

The difference in the mode of cyclisations among substrates **16**, **19** and **24** may be explained in terms of the electronic stability and/or the steric congestion between the radical intermediates **27** and **28** which are generated by ring closure of the carbamoylmethyl radical **26**. The exclusive formation of the β-lactam **17** from **16** suggests that the benzylic radical **27a**, generated by 4-*exo*-*trig* ring closure*[,9,10] of radical **26a**, might be more stable than the α-acylamino radical **28a**. Inspection of molecular models indicates that the radical intermediate **27a** should be much stabilised due to excellent overlapping of the p-orbital of the radical centre with the neighbouring aromatic π-system.[11] However, if the substituent R(=H) in species **27a** is replaced by a methyl or a phenyl group, a severe steric repulsion between R and the neighbouring geminal substituents becomes evident, and, instead the formation of the α-acylamino radical **28a** predominates to result in an increase in the amount of the γ-lactam products **21**, **22** and **25**.



In sharp contrast to the case of substrate **16**, which gave only the β-lactam **17**, the chloroacetamide **29** provided the γ-lactam

* Formation of β-lactams by 4-*exo*-*trig* radical cyclisation of 2-bromo-*N*-(2,2-diphenylethenyl)acetamides has recently been reported; see ref. 9.



Scheme 3 *Reagents and conditions:* i, Bu_3SnH, AIBN, toluene, reflux

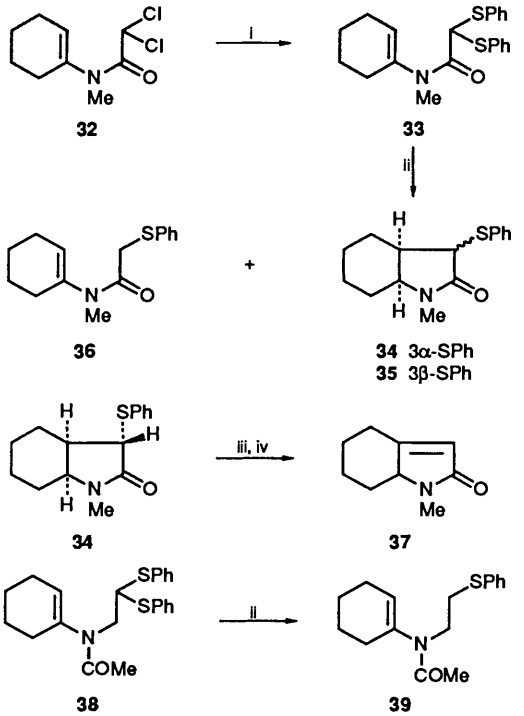
30 in 41% yield along with the reduction product **31** (20%) (Scheme 3). No β-lactam like compound **17** was isolated. NOE difference spectroscopy showed compound **30** to have a *trans* stereochemistry (see Experimental section). Molecular models indicate that the p-orbital of the seven-membered radical intermediate **27b** generated by 4-*exo-trig* cyclisation of species **26b** is almost perpendicular to the neighbouring aromatic π-system in its most conformationally stable form,[11] so that the radical **26b** is expected to cyclise to the relatively stable α-acylamino radical **28b** in preference to the benzylic radical **27b**, leading to the observed γ-lactam **30**.[12] The models also indicate that the *trans* isomer **30** is sterically more favoured compared with the corresponding *cis* isomer, and accordingly the stereochemical outcome of the formation of product **30** may be explained by an attack of Bu_3SnH on a product such as intermediate **28b**, in which the radical centre is tetrahedral.

Next, in order to see whether the carbonyl group in the enamide **5** is essential or not for the success of the 'disfavoured' 5-*endo-trig* cyclisation, we examined the reactions of the enamides **33** and **38**. Treatment of compound **33**, which was prepared from the dichloroacetamide **32** and benzenethiol, with Bu_3SnH in the presence of AIBN gave the 5-*endo-trig* cyclisation products **34** and **35** in 30 and 29% yield, respectively, along with the reduction product **36** (6%) (Scheme 4). Stereochemistry of the phenylthio group in products **34** and **35** was determined as follows. Oxidation of compound **34** with sodium metaperiodate ($NaIO_4$) followed by heating of the resultant sulfoxide in boiling toluene provided the unsaturated lactam **37** in 41% yield as a result of a *syn*-elimination of sulfenic acid. However, the corresponding sulfoxide derived from compound **35** was recovered unchanged.

On the other hand, the enamide **38** gave only the reduction product **39** when treated with Bu_3SnH and AIBN. No 5-*endo-trig* cyclisation product was isolated. Thus, it was shown that the carbonyl group incorporated into the five-membered ring is essential for effecting the 5-*endo-trig* cyclisation, though the exact role of the carbonyl group is obscure at the moment.

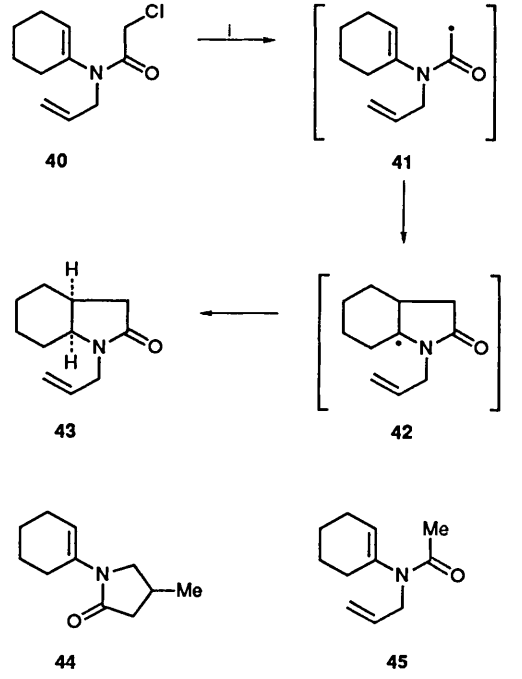
As noted above, the 5-*endo-trig* cyclisation of the carbamoylmethyl radical **6** resulted in the formation of species **7** as a new radical intermediate. Our interest was then turned to the use of the intermediate **7** for the tandem process.

First, we treated the *N*-allylenamide **40** with Bu_3SnH and AIBN: this gave the 5-*endo* cyclisation product **43** as a major product (58% yield) together with a 1:1 mixture of the 5-*exo* cyclisation product **44** and the reduction product **45** (29% total yield). In the light of previous work on the α-acylamino radical cyclisations[1b] and others,[7] the failure of the 5-*endo-trig* cyclisation of the radical intermediate **42** is easily predictable.



Scheme 4 *Reagents and conditions:* i, PhSNa, EtOH, room temperature; ii, Bu_3SnH, AIBN, toluene, reflux; iii, $NaIO_4$, MeOH–acetone, room temperature; iv, $NaHCO_3$, toluene, reflux

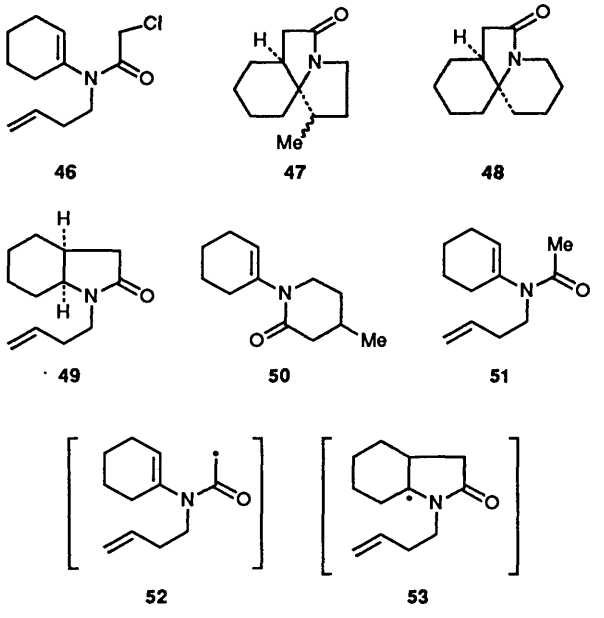
More remarkable is the fact that the carbamoylmethyl radical **41** cyclised predominantly in a 'disfavoured' 5-*endo-trig* manner rather than in a favoured 5-*exo-trig* manner. This preference may be attributable to the high stability of the newly formed α-acylamino radical **42** (Scheme 5).



Scheme 5 *Reagents and conditions:* i, Bu_3SnH, AIBN, toluene, reflux

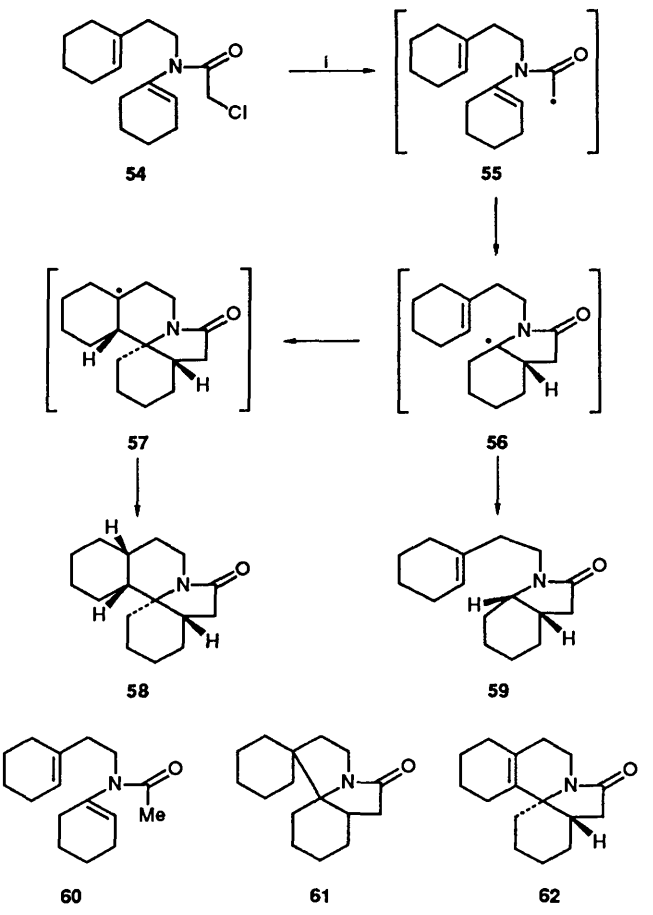
On the other hand, the *N*-(but-3-enyl)enamide **46** gave the expected tandem radical cyclisation products **47** and **48** in 32 and 27% yield, respectively, together with the compounds **49** (7%), **50** (8%) and **51** (6%). The ^1H NMR spectrum of compound **47** showed it to be a mixture of two stereoisomers with respect to the methyl group in a ratio of 3.4:1 (see

Experimental section). Formation of species **47**, **48** and **49** can be explained in terms of the common intermediate **53** generated by 5-*endo-trig* cyclisation of the carbamoylmethyl radical **52**. When the radical **53** cyclised in a 5-*exo-trig* or in a 6-*endo-trig* manner, the products **47** and **48** might result, respectively. The attack of Bu_3SnH on the radical **53** would provide product **49**. On the other hand, the 6-*exo-trig* cyclisation of the carbamoylmethyl radical **52** with an internal but-3-enyl group gives compound **50**.



Having been encouraged by the above experiment, we next examined the cyclisation of the enamide **54** in the hope that the erythrinane skeleton **58** might result.

The compound **54** was easily prepared from commercially available 2-(cyclohex-1-enyl)ethylamine according to the procedure described for the preparation of **5**. Treatment of the enamide **54** with Bu_3SnH and AIBN gave the perhydroerythrinanone **58** in 44% yield along with the compound **59** (9%) and the reduction product **60** (4%) (see Scheme 6). The formation of compound **58** from substrate **54** may involve 5-*endo-trig* cyclisation of the carbamoylmethyl radical **55**, followed by 6-*endo-trig* cyclisation of the resultant α-acylamino radical **56**. No 5-*endo*/5-*exo* cyclisation product **61** was detected from the reaction mixture: this may be due to the severe steric congestion associated with two vicinal quaternary carbon centres in a pyrrolidine ring. Compound **58** was shown to be a single stereoisomer (by ^1H NMR spectroscopy), whose structure was established by direct comparison with an authentic sample prepared by catalytic hydrogenation of 14,15,16,17-tetrahydro-*cis*-erythrinan-8-one **62**[13] over PtO_2 in acetic acid. The stereochemical outcome of the formation of the erythrinane **58** from substrate **54** can be explained by an attack of the alkenic bond on the α-acylamino radical **56** so as to form the *cis*-fused indolizidine ring **57**. This step is then followed by an attack of Bu_3SnH from the less hindered β-face of the radical **57** to lead to compound **58**. This convenient and efficient route to erythrinane skeletons now opens the way to the naturally occurring and biologically important erythroidine-type (non aromatic) *Erythrina* alkaloids.[14]



Scheme 6 *Reagents and conditions:* i, Bu_3SnH, AIBN, toluene, reflux

Experimental

M.p.s were measured on a Yanaco MP-J3 micro melting point apparatus and are uncorrected. IR spectra were recorded on a JASCO-IR-A-100 spectrophotometer. ^1H and ^{13}C NMR spectra were measured on a JEOL JNM-PMX 60 or a Varian XL-300 spectrometer for solutions in $CDCl_3$. δ-Values quoted are relative to tetramethylsilane, and *J*-values are given in Hz. Exact mass (MS) determinations were obtained on a Hitachi M-80 instrument operating at 20 eV. Column chromatography was performed on silica gel 60 PF_{254} for preparative TLC (Nacalai Tesque, Inc.) under pressure. Light petroleum refers to the fraction boiling in the range 80–110 °C.

General Procedure for the Preparation of the Enamides **5**, **10** *and* **11**.—To a solution of *N*-cyclohexylidenemethylamine (1.1 g, 10 mmol) and pyridine (790 mg, 10 mmol) in benzene (10 cm^3) at 0 °C was added a solution of appropriate chloroacetyl chloride (11 mmol) in benzene (2 cm^3) and the mixture was stirred at room temperature for 1 h. Water (10 cm^3) was added and the organic layer was separated. The aqueous layer was further extracted with benzene and the combined organic phases were dried ($MgSO_4$). The solvent was evaporated off and the residue was chromatographed on silica gel [hexane–AcOEt (4:1)] to give the enamide. The following compounds were thus obtained.

2-*Chloro*-N-(*cyclohex*-1-*enyl*)-N-*methylacetamide* **5** (26%), an oil (Found: M^+, 187.0753. $C_9H_{14}ClNO$ requires *M*, 187.0762); $\nu_{max}(CCl_4)/cm^{-1}$ 1655; δ_H(60 MHz) 1.3–2.0 (4 H, m), 2.0–2.4 (4 H, m), 3.0 (3 H, s, NMe), 4.07 (2 H, s, $COCH_2$) and 5.6–5.8 (1 H, m, C=CH).

2-*Chloro*-N-(*cyclohex*-1-*enyl*)-N-*methylpropionamide* **10** (28% , an oil (Found: C, 58.5; H, 8.0; N, 6.7. $C_{10}H_{16}ClNO$ requires C, 58.55; H, 8.0; N, 6.9%); $\nu_{max}(CCl_4)/cm^{-1}$ 1660; δ_H(60 MHz) 1.46–1.96 (4 H, m), 1.59 (3 H, d, *J* 7.0, CMe), 1.96–2.46 (4 H, m), 3.00 (3 H, s, NMe), 4.73 (1 H, q, *J* 7.0, COCH) and 5.6–5.9 (1 H, m, C=CH).

2-*Chloro*-N-(*cyclohex*-1-*enyl*)-N-*methyl*-2-*phenylacetamide* **11** (23%) (Found: C, 68.1; H, 7.0; N, 5.0. $C_{15}H_{18}ClNO$ requires C, 68.3; H, 6.9; N, 5.3%); m.p. 76.5–77.5 °C (from hexane–AcOEt); $\nu_{max}(CCl_4)/cm^{-1}$ 1680; δ_H(60 MHz) 1.33–1.80 (4 H, m), 1.80–2.33 (4 H, m), 2.98 (3 H, s, NMe), 5.37–5.63 (1 H, m, C=CH), 5.73 (1 H, s, COCH) and 7.1–7.7 (5 H, m, ArH).

Radical Cyclisation of Compound **5**: *General Procedure*.—To a boiling solution of the enamide **5** (116 mg, 0.62 mmol) in toluene (20 cm^3) was added a solution of Bu_3SnH (198 mg, 0.68 mmol) and AIBN (10 mg, 0.062 mmol) in toluene (45 cm^3) *via* a syringe during 1 h, and the mixture was heated under reflux for a further hour. After the solvent had been evaporated off, diethyl ether (10 cm^3) and 8% aq. KF (10 cm^3) were added to the residue, and the mixture was stirred vigorously at room temperature for 1 h. The organic layer was separated, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel [hexane–AcOEt (3:1)]. The first fraction gave N-(*cyclohex*-1-*enyl*)-N-*methylacetamide* **9** (8 mg, 8%) as an oil (Found: M^+, 153.1177. $C_9H_{15}NO$ requires *M*, 153.1153); $\nu_{max}(CCl_4)/cm^{-1}$ 1650; δ_H(60 MHz) 1.4–1.9 (4 H, m), 1.9–2.4 (4 H, m), 2.03 (3 H, s, COMe), 2.97 (3 H, s, NMe) and 5.47–5.80 (1 H, m, C=CH). The second fraction gave *cis*-octahydro-1-methylindol-2-one **8** (60 mg, 63%)[15] as an oil, whose spectroscopic data were identical with those of an authentic sample; $\nu_{max}(CCl_4)/cm^{-1}$ 1695; δ_H(60 MHz) 1.1–2.8 (11 H, m), 2.78 (3 H, s, NMe) and 3.47 (1 H, dd, *J* 11 and 6, 7a-H).

Radical Cyclisation of Compound **10**.—Following the general procedure, the enamide **10** (125 mg, 0.62 mmol) was treated with Bu_3SnH (198 mg, 0.68 mmol) and AIBN (10 mg, 0.062 mmol), and the crude material was purified by chromatography on silica gel [hexane–AcOEt (1:1)] to give a mixture of (3S*,3aS*,7aS*)-*octahydro*-1,3-*dimethylindol*-2-*one* **12** and (3R*,3aS*,7aS*)-*octahydro*-1,3-*dimethylindol*-2-*one* **14** (total 75 mg, total 73%) as an oil, whose ratio was estimated to be ~6:1 by ^1H NMR spectroscopy (Found: M^+, 167.1297. $C_{10}H_{17}NO$ requires *M*, 167.1309); $\nu_{max}(CCl_4)/cm^{-1}$ 1690; δ_H for compound **12** (300 MHz) 1.14 (3 H, d, *J* 7.0, 3-Me), 1.17–1.39 (2 H, m), 1.45–1.73 (4 H, m), 1.89–2.05 (3 H, m), 2.25 (1 H, dq, *J* 9.4 and 7.0, 3-H), 2.82 (3 H, d, *J* 0.7, NMe) and 3.35 (1 H, dt, *J* 8.5 and 6.6, 7a-H); δ_C for compound **12** (75 MHz) 13.9, 21.7, 22.2, 25.6, 27.5, 27.7, 39.1, 40.5, 57.4 and 177.2; δ_H for compound **14** (300 MHz) 1.09 (3 H, d, *J* 7.2, 3-Me), 1.17–1.39 (2 H, m), 1.45–1.73 (4 H, m), 1.89–2.05 (3 H, m), 2.45 (1 H, quintet, *J* 7.2, 3-H), 2.77 (3 H, d, *J* 0.7, NMe) and 3.42 (1 H, q, *J* 4.0, 7a-H).

Treatment of a Mixture of Compounds **12** *and* **14** *with Base*.—Potassium *tert*-butoxide (32 mg, 0.28 mmol) was added to a solution of the mixture of compounds **12** and **14** (23 mg, 0.14 mmol), obtained by cyclisation of compound **10**, in *tert*-butyl alcohol (1 cm^3), and the mixture was heated under reflux for 1 h. After the solvent had been evaporated off, water was added to the residue and the whole was extracted with dichloromethane. The extract was dried ($MgSO_4$) and concentrated. The residue was chromatographed on silica gel [hexane–AcOEt (2:1)] to give a mixture of compounds **12** and **14** (20 mg, 87%), whose ratio was estimated to be ~4:1 by 300 MHz ^1H NMR spectroscopy.

Radical Cyclisation of Compound **11**.—Following the general procedure, the enamide **11** (164 mg, 0.62 mmol) was treated with Bu_3SnH (198 mg, 0.68 mmol) and AIBN (10 mg, 0.062 mmol), and the crude material was purified by chromatography on silica gel [hexane–AcOEt (1:1)] to give a mixture of (3R*,3aS*,7aS*)-*octahydro*-1-*methyl*-3-*phenylindol*-2-*one* **13** and (3S*,3aS*,7aS*)-*octahydro*-1-*methyl*-3-*phenylindol*-2-*one* **15** (total 111 mg, total 75%) as an oil, whose ratio was estimated to be ~2:3 by ^1H NMR spectroscopy (Found: C, 78.3; H, 8.5; N, 5.8. $C_{15}H_{19}NO$ requires C, 78.6; H, 8.35; N, 6.1%); $\nu_{max}(CCl_4)/cm^{-1}$ 1695; δ_H for compound **13** (300 MHz) 1.20–2.10 (8 H, m), 2.34–2.44 (1 H, m, 3a-H), 2.91 (3 H, s, NMe), 3.44 (1 H, d, *J* 10.8, 3-H), 3.48 (1 H, dt, *J* 9 and 6.0, 7a-H) and 7.15–7.48 (5 H, m, ArH); δ_H for compound **15** (300 MHz) 1.20–2.10 (8 H, m), 2.45–2.55 (1 H, m, 3a-H), 2.85–3.07 (1 H, m, 3-H), 3.02 (3 H, s, NMe), 3.69 (1 H, q, *J* 6, 7a-H) and 7.15–7.48 (5 H, m, ArH).

Treatment of a Mixture of Compounds **13** *and* **15** *with Base*.—A mixture of compounds **13** and **15** (80 mg, 0.39 mmol) obtained above was dissolved in ethanol (1 cm^3) containing sodium ethoxide (27 mg, 0.39 mmol), and the mixture was heated under reflux for 1 h. After the solvent had been evaporated off, water was added to the residue, the whole was extracted with dichloromethane, and the extract was dried ($MgSO_4$). The solvent was evaporated off and the residue was chromatographed on silica gel [hexane–AcOEt (1:1)] to give the lactam **13** (52 mg, 65%) as the sole product.

General Procedure for the Preparation of 2-*Chloro*-N-(3,4-*dihydro*-2-*naphthyl*)-N-*methylacetamides* **16**, **19** *and* **24**.—β-Tetralone (497 mg, 3.4 mmol) was added to anhydrous methylamine (5 cm^3) at −78 °C, and the mixture was heated at 100 °C in a sealed tube for 1 h. The reaction vessel was cooled to −78 °C, the stopper was removed, and the reaction mixture was allowed to warm to room temperature to remove any excess of methylamine. To the residue cooled to 0 °C were successively added diethyl ether (10 cm^3), triethylamine (412 mg, 4.08 mmol), and a solution of the appropriate chloroacetyl chloride (4.08 mmol) in diethyl ether (5 cm^3). The mixture was stirred at room temperature for 30 min and water (10 cm^3) was added to the reaction mixture. The organic layer was separated, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel [hexane–AcOEt (4:1)] to give an enamide. The following compounds were thus obtained.

2-*Chloro*-N-(3,4-*dihydro*-2-*naphthyl*)-N-*methylacetamide* **16** (23%) (Found: C, 66.3; H, 6.1; N, 6.1. $C_{13}H_{14}ClNO$ requires C, 66.2; H, 6.0; N, 5.9%); m.p. 59–60.5 °C (from hexane–AcOEt); $\nu_{max}(CCl_4)/cm^{-1}$ 1675; δ_H(60 MHz) 2.25–2.7 (2 H, m), 2.8–3.3 (2 H, m), 3.09 (3 H, s, NMe), 4.13 (2 H, s, $COCH_2$), 6.3–6.45 (1 H, m, C=CH) and 6.75–7.35 (4 H, m, ArH).

2-*Chloro*-N-(3,4-*dihydro*-2-*naphthyl*)-N-*methylpropionamide* **19** (91%), an oil (Found: M^+, 249.0937. $C_{14}H_{16}ClNO$ requires *M*, 249.0920); $\nu_{max}(CCl_4)/cm^{-1}$ 1675; δ_H(60 MHz) 1.64 (3 H, d, *J* 7, CMe), 2.3–2.7 (2 H, m), 2.85–3.25 (2 H, m), 3.12 (3 H, s, NMe), 4.85 (1 H, q, *J* 7, COCH), 6.35–6.5 (1 H, m, C=CH) and 6.9–7.35 (4 H, m, ArH).

2-*Chloro*-N-(3,4-*dihydro*-2-*naphthyl*)-N-*methyl*-2-*phenylacetamide* **24** (87%), m.p. 97–98 °C (from hexane–AcOEt) (Found: C, 73.3; H, 5.8; N, 4.45. $C_{19}H_{18}ClNO$ requires C, 73.2; H, 5.8; N, 4.5%); $\nu_{max}(CCl_4)/cm^{-1}$ 1680; δ_H(60 MHz) 2.15–3.2 (4 H, m), 3.12 (3 H, s, NMe), 5.83 (1 H, s, COCH), 6.2–6.35 (1 H, m, C=CH) and 6.75–7.7 (9 H, m, ArH).

Radical Cyclisation of Compound **16**.—Following the general procedure, compound **16** (182 mg, 0.77 mmol) was treated with Bu_3SnH (472 mg, 1.63 mmol) and AIBN (27 mg, 0.16 mmol), and the crude material was purified by chromatography on silica gel [hexane–AcOEt (2:1)]. The first fraction gave N-(3,4-*dihydro*-2-*naphthyl*)-N-*methylacetamide* **18** (49 mg, 32%), an oil (Found: C, 77.4; H, 7.65; N, 6.8. $C_{13}H_{15}NO$ requires C, 77.6; H, 7.5; N, 7.0%); $\nu_{max}(CCl_4)/cm^{-1}$ 1660; δ_H(60 MHz) 2.10 (3 H, s, COMe), 2.2–2.7 (2 H, m), 2.8–3.2 (2 H, m), 3.09 (3 H, s, NMe), 6.25–6.4 (1 H, m, C=CH) and 6.8–7.3 (4 H, m, ArH). The second fraction gave 1-*methylspiro*[*azetidine*-4,2′-1′,2′,3′,4′-*tetrahydronaphthalen*]-4-*one* **17** (77 mg, 50%) (Found: C, 77.45; H, 7.6; N,

6.8. $C_{13}H_{15}NO$ requires C, 77.6; H, 7.5; N, 7.0%); m.p. 93.5–94.5 °C (from hexane); $\nu_{max}(CHCl_3)/cm^{-1}$ 1740; δ_H(60 MHz) 1.45–2.4 (2 H, m), 2.6–3.4 (6 H, m), 2.73 (3 H, s, NMe) and 7.09 (4 H, br s, ArH).

Radical Cyclisation of Compound **19**.—Following the general procedure, compound **19** (1.02 g, 4.08 mmol) was treated with Bu_3SnH (1.90 g, 6.53 mmol) and AIBN (134 mg, 0.82 mmol), and the crude material was purified by chromatography on silica gel [hexane–AcOEt (10:1)]. The first fraction gave N-(3,4-*dihydro*-2-*naphthyl*)-N-*methylpropionamide* **23** (104 mg, 12%), an oil (Found: M^+, 215.1285. $C_{14}H_{17}NO$ requires *M*, 215.1309); $\nu_{max}(CCl_4)/cm^{-1}$ 1665; δ_H(60 MHz) 1.12 (3 H, t, *J* 7, CMe), 2.2–2.7 (2 H, m), 2.39 (2 H, q, *J* 7.4, $COCH_2$), 2.8–3.25 (2 H, m), 3.09 (3 H, s, NMe), 6.25–6.4 (1 H, m, C=CH) and 6.8–7.4 (4 H, m, ArH). The second fraction gave 1,3-*dimethylspiro*-[*azetidine*-4,2′-1′,2′,3′,4′-*tetrahydronaphthalen*]-2-*one* **20** (251 mg, 29%) as an oil, which was shown to be a mixture of two diastereoisomers in a ratio ~1:1 by ^1H NMR spectroscopy (Found: M^+, 215.1308. $C_{14}H_{17}NO$ requires *M*, 215.1309); $\nu_{max}(CCl_4)/cm^{-1}$ 1750; δ_H(60 MHz) 1.02 (3 H × ½, d, *J* 8, CMe of one stereoisomer), 1.20 (3 H × ½, d, *J* 8, CMe of another stereoisomer), 1.55–2.2 (3 H, m), 2.64 (3 H × ½, s, NMe of one stereoisomer), 2.69 (3 H × ½, s, NMe of another stereoisomer), 2.7–3.15 (4 H, m) and 7.02 (4 H, s, ArH). The third fraction gave (1S*,3aS*,9bR*)-1,3,3a,4,5,9b-*hexahydro*-1,3-*dimethylbenz*[e]-*indol*-2-*one* **21** (324 mg, 37%), m.p. 86–87 °C (from light petroleum) (Found: C, 78.0; H, 8.1; N, 6.5. $C_{14}H_{17}NO$ requires C, 78.1; H, 8.0; N, 6.5%); $\nu_{max}(CCl_4)/cm^{-1}$ 1695; δ_H(300 MHz) 1.41 (3 H, d, *J* 7.1, 1-Me), 1.80 (1 H, dtd, *J* 13.0, 7.8 and 5.0, one of 4-H), 1.98 (1 H, ddt, *J* 13.0, 7.2 and 5.0, one of 4-H), 2.35 (1 H, dq, *J* 8.2 and 7.1, 1-H), 2.62–2.81 (2 H, m, 5-H_2), 2.94 (3 H, d, *J* 0.8, NMe), 3.15 (1 H, dd, *J* 8.2 and 7.8, 9b-H), 3.79 (1 H, td, *J* 7.8 and 5.0, 3a-H) and 7.11–7.27 (4 H, m, ArH); δ_C(75 MHz) 16.2, 25.4, 26.7, 28.0, 44.2, 44.4, 57.7, 126.5, 128.59, 128.62, 136.7, 137.3 and 176.1. The fourth fraction gave (1R*,3aS*,-9bR*)-1,3,3a,4,5,9b-*hexahydro*-1,3-*dimethylbenz*[e]*indol*-2-*one* **22** (22 mg, 3%), m.p. 95–96 °C (from light petroleum) (Found: M^+, 215.1301. $C_{14}H_{17}NO$ requires *M*, 215.1309); $\nu_{max}(CCl_4)/cm^{-1}$ 1690; δ_H(300 MHz) 0.90 (3 H, d, *J* 7.7, CMe), 1.67 (1 H, ddt, *J* 17.5, 10.0 and 4.5), 2.14 (1 H, ddt, *J* 13.2, 6.0 and 4.5), 2.16–2.97 (3 H, m), 2.94 (3 H, s, NMe), 3.75–3.87 (2 H, m) and 7.02–7.23 (4 H, m, ArH); δ_C(75 MHz) 15.1, 26.7, 26.8, 27.9, 38.3, 40.7, 59.2, 126.2, 128.5, 130.2, 134.2, 137.5 and 177.2.

Treatment of Compound **22** *with Base*.—A solution of compound **22** (6 mg, 0.028 mmol) and potassium *tert*-butoxide (6.3 mg, 0.056 mmol) in *tert*-butyl alcohol (1 cm^3) was heated under reflux for 1 h. The solvent was evaporated off, dichloromethane (5 cm^3) was added to the residue, and the whole was washed with water. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure to give a mixture of benz[*e*]indolones **21** and **22** (5 mg, 83%), whose ratio was estimated to be 91:9 by GLC analysis.

Radical Cyclisation of Compound **24**.—Following the general procedure, compound **24** (500 mg, 1.6 mmol) was treated with Bu_3SnH (514 mg, 1.76 mmol) and AIBN (26 mg, 0.18 mmol), and the crude material was purified by chromatography on silica gel [hexane–AcOEt (4:1)] to give (1R*,3aS*,9bR*)-1,3,3a,4,5,9b-*hexahydro*-3-*methyl*-1-*phenylbenz*[e]*indol*-2-*one* **25** (336 mg, 76%), m.p. 141–142 °C (from hexane–AcOEt) (Found: C, 82.1; H, 6.9; N, 4.9. $C_{19}H_{19}NO$ requires C, 82.3; H, 6.9; N, 5.05%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1680; δ_H(300 MHz) 1.81 (1 H, dtd, *J* 13.3, 9.5, and 4.7, 4-H$^\beta$), 2.17 (1 H, ddt, *J* 13.3, 6.4 and 4.8, 4-H$^\alpha$), 2.68–2.90 (2 H, m, 5-H_2), 3.03 (3 H, d, *J* 0.6, NMe), 3.56 (1 H, d, *J* 9.5, 1-H), 3.68 (1 H, dd, *J* 9.6 and 7.8, 9b-H), 3.92 (1 H, ddd, *J* 9.0, 7.9 and 4.7, 3a-H), 6.66 (1 H, d, *J* 7.8, ArH) and 6.97–7.43 (8 H, m, ArH); δ_C(75 MHz) 25.2, 26.8, 28.2, 44.8, 56.5, 58.0, 126.3, 126.5, 127.2, 128.5, 128.8, 129.0, 136.1, 136.3, 139.3 and 173.9. NOE difference spectroscopy: when the 3a-H proton was irradiated, the signals for 9b-H and 4-H$^\alpha$ were enhanced (8.3 and 3.3%, respectively): irradiation of the 4-H$^\beta$ proton resulted in a 5.7% enhancement of the signal due to the 1-H proton, while no effect was observed between 1-H and 9b-H.

2-*Chloro*-N-(6,7-*dihydro*-5H-*benzocyclohepten*-8-*yl*)-N-*methylacetamide* **29**.—By use of a procedure similar to that described for the preparation of compound **16**, the imine prepared from 2-benzosuberone (481 mg, 3 mmol) and methylamine (5 cm^3) was *N*-acylated with chloroacetyl chloride (373 mg, 3.3 mmol), and the crude material was purified by chromatography on silica gel [hexane–AcOEt (4:1)] to give the *enamide* **29** (248 mg, 33%), m.p. 64–65 °C (from hexane–AcOEt) (Found: C, 67.5; H, 6.7; N, 5.4. $C_{14}H_{16}ClNO$ requires C, 67.3; H, 6.5; N, 5.6%); $\nu_{max}(CCl_4)/cm^{-1}$ 1665; δ_H(60 MHz) 1.9–2.35 (2 H, m), 2.4–2.75 (2 H, m), 2.75–3.1 (2 H, m), 3.17 (3 H, s, NMe), 4.20 (2 H, s, $COCH_2$), 6.4–6.6 (1 H, m, C=CH) and 6.9–7.45 (4 H, m, ArH).

Radical Cyclisation of Compound **29**.—Following the general procedure, compound **29** (170 mg, 0.68 mmol) was treated with Bu_3SnH (434 mg, 1.5 mmol) and AIBN (22 mg, 0.15 mmol), and the crude material was purified by chromatography on silica gel [hexane–AcOEt (2:1)]. The first fraction gave N-(6,7-*dihydro*-5H-*benzocyclohepten*-8-*yl*)-N-*methylacetamide* **31** (40 mg, 20%) as an oil (Found: M^+, 215.1291. $C_{14}H_{17}NO$ requires *M*, 215.1308); $\nu_{max}(CCl_4)/cm^{-1}$ 1660; δ_H(60 MHz) 1.85–2.35 (2 H, m), 2.16 (3 H, s, COMe), 2.35–2.75 (2 H, m), 2.75–3.15 (2 H, m), 3.16 (3 H, s, NMe), 6.38–6.53 (1 H, m, C=CH) and 7.05–7.40 (4 H, m, ArH). The second fraction gave (3aR*,10bR*)-3,3a,4,5,6,10b-*hexahydrobenzo*[1′,2′:3,4]*cyclohepta*[b]*pyrrol*-2(1H)-*one* **30** (60 mg, 41%) as an oil (Found: M^+, 215.1315. $C_{14}H_{17}NO$ requires *M*, 215.1309); $\nu_{max}(CCl_4)/cm^{-1}$ 1700; δ_H(300 MHz) 1.39–1.53 (1 H, m, 5-H$^\beta$), 1.53–1.67 (1 H, m, 4-H$^\alpha$), 2.08–2.19 (1 H, m, 5-H$^\alpha$), 2.44–2.53 (1 H, m, 4-H$^\beta$), 1.61 (1 H, dd, *J* 16.1 and 8.1, 1-H$^\alpha$), 2.81 (3 H, s, NMe), 2.82–2.96 (2 H, m, 6-H_2), 2.98 (1 H, dd, *J* 16.1 and 12.2, 1-H$^\beta$), 3.06 (1 H, ddd, *J* 11.2, 9.0 and 3.2, 3a-H), 3.47 (1 H, br ddd, *J* 12.1, 9.0 and 8.1, 10b-H) and 7.15–7.29 (4 H, m, ArH); δ_C(75 MHz) 25.3, 26.9, 34.0, 35.8, 35.9, 43.8, 63.8, 124.8, 126.6, 127.1, 129.8, 137.9, 143.1 and 173.9. NOE difference spectroscopy: when the 10b-H proton was irradiated, the signals due to 1-H$^\alpha$ and 4-H$^\alpha$ were enhanced (7 and 5%, respectively), while no effect was observed for 3a-H: irradiation of the 4-H$^\beta$ proton resulted in 2 and 4% enhancement of the signals due to NMe and 3a-H protons, respectively.

2,2-*Dichloro*-N-(*cyclohex*-1-*enyl*)-N-*methylacetamide* **32**.—By use of a procedure similar to that described for the preparation of compound **5**, *N*-cyclohexylidenemethylamine (2 g, 18 mmol) was treated with dichloroacetyl chloride (3.18 g, 21.6 mmol), and the crude material was purified by chromatography on silica gel [hexane–AcOEt (7:1)] to give the *enamide* **32** (874 mg, 22%), m.p. 52–52.5 °C (from hexane–light petroleum) (Found: C, 48.4; H, 5.8; N, 6.3. $C_9H_{13}Cl_2NO$ requires C, 48.7; H, 5.9; N, 6.3%); $\nu_{max}(CCl_4)/cm^{-1}$ 1690; δ_H(60 MHz) 1.35–2.5 (8 H, m), 3.06 (3 H, s, NMe), 5.73–5.96 (1 H, m, C=CH) and 6.37 (1 H, s, $CHCl_2$).

N-(*Cyclohex*-1-*enyl*)-N-*methyl*-2,2-*bis*(*phenylthio*)*acetamide* **33**.—Benzenethiol (436 mg, 3.96 mmol) was added to a solution of sodium ethoxide (269 mg, 3.96 mmol) in ethanol (5 cm^3) at 0 °C, and the mixture was stirred at room temperature for 10

min. To this was added a solution of the enamide **32** (400 mg, 1.8 mmol) in ethanol (1 cm^3) and the mixture was stirred at room temperature overnight. The solvent was removed by evaporation, dichloromethane (10 cm^3) was added to the residue, and the whole was washed with water, then dried ($MgSO_4$). The solvent was evaporated off and the residue was chromatographed on silica gel [hexane–AcOEt (7:1)] to give the *enamide* **33** (338 mg, 51%), m.p. 89–90 °C (from hexane) (Found: C, 68.1; H, 6.2; N, 3.8. $C_{21}H_{23}NOS_2$ requires C, 68.3; H, 6.3; N, 3.8%); $\nu_{max}(CCl_4)/cm^{-1}$ 1655; δ_H(60 MHz) 0.85–2.05 (8 H, m), 2.94 (3 H, s, NMe), 5.05–5.45 (1 H, m, C=CH), 5.17 (1 H, s, SCHS) and 7.05–7.6 (10 H, m, ArH).

Radical Cyclisation of Compound **33**.—Following the general procedure, compound **33** (500 mg, 1.35 mmol) was treated with Bu_3SnH (434 mg, 1.5 mmol) and AIBN (22 mg, 0.15 mmol), and the crude material was purified by chromatography on silica gel [hexane–AcOEt (9:2)]. The first fraction gave N-(*cyclohex*-1-*enyl*)-N-*methyl*-2-(*phenylthio*)*acetamide* **36** (19 mg, 6%) as an oil (Found: C, 69.1; H, 7.4; N, 5.2. $C_{15}H_{19}NOS$ requires C, 68.9; H, 7.3; N, 5.4%); $\nu_{max}(CCl_4)/cm^{-1}$ 1645; δ_H(60 MHz) 1.1–2.3 (8 H, m), 2.99 (3 H, s, NMe), 3.72 (2 H, s, $COCH_2$), 5.5–5.75 (1 H, m, C=CH) and 7.05–7.6 (5 H, m, ArH). The second fraction gave (3R*,3aR*,7aS*)-*octahydro*-1-*methyl*-3-(*phenylthio*)*indol*-2-*one* **35** (101 mg, 29%) as an oil (Found: C, 68.6; H, 7.4; N, 5.5. $C_{15}H_{19}NOS$ requires C, 68.9; H, 7.3; N, 5.4%); $\nu_{max}(CCl_4)/cm^{-1}$ 1690; δ_H(300 MHz) 1.10–1.94 (8 H, m), 2.20 (1 H, quintet, *J* 6.4, 3a-H), 2.81 (3 H, s, NMe), 3.45 (1 H, td, *J* 6.5 and 5.2, 7a-H), 3.51 (1 H, d, *J* 6.8, 3-H), 7.20–7.34 (3 H, m, ArH) and 7.50–7.65 (2 H, m, ArH). The third fraction gave (3S*,3aR*,7aS*)-*octahydro*-1-*methyl*-3-(*phenylthio*)*indol*-2-*one* **34** (105 mg, 30%), m.p. 86–87 °C (from hexane) (Found: C, 68.9; H, 7.45; N, 4.95%); $\nu_{max}(CCl_4)/cm^{-1}$ 1690; δ_H(300 MHz) 1.07–2.12 (8 H, m), 2.48 (1 H, dtd, *J* 11.0, 6.3 and 4.9, 3a-H), 2.83 (3 H, s, NMe), 3.51 (1 H, br dd, *J* 7.9 and 4.0, 7a-H), 4.04 (1 H, d, *J* 6.4, 3-H), 7.17–7.43 (3 H, m, ArH) and 7.48–7.59 (2 H, m, ArH).

1,4,5,6,7,7a-*Hexahydro*-1-*methylindol*-2-*one* **37**.—A solution of sodium metaperiodate (370 mg, 1.73 mmol) in water (5 cm^3) was added dropwise to a solution of compound **34** (225 mg, 0.86 mmol) in acetone (5 cm^3) at 0 °C, and the mixture was stirred at room temperature overnight. The precipitated salts were removed by filtration and the filtrate was concentrated under reduced pressure. Water was added to the residue and the whole was extracted with dichloromethane. The organic phase was dried ($MgSO_4$) and concentrated to give the crude sulfoxide. This sulfoxide was dissolved in toluene (10 cm^3) and the mixture was heated under reflux in the presence of $NaHCO_3$ (78 mg, 0.92 mmol) for 28 h. The insoluble materials were removed by filtration, the filtrate was concentrated under reduced pressure, and the residue was chromatographed on silica gel [hexane–AcOEt (4:1)] to give the *unsaturated lactam* **37** (53 mg, 41%) as an oil (Found: M^+, 151.0972. $C_9H_{13}NO$ requires *M*, 151.0996); $\nu_{max}(CCl_4)/cm^{-1}$ 1690; δ_H(60 MHz) 0.75–3.05 (8 H, m), 2.92 (3 H, s, NMe), 3.63 (1 H, dd, *J* 11.0 and 6.0, 7a-H) and 5.64–5.78 (1 H, m, 3-H).

N-(*Cyclohex*-1-*enyl*)-N-[2,2-*bis*(*phenylthio*)*ethyl*]*acetamide* **38**.—Aluminium chloride (98 mg, 0.74 mmol) was added to a suspension of lithium aluminium hydride (28 mg, 0.74 mmol) in dry diethyl ether (1.5 cm^3) at 0 °C, and the mixture was stirred for 5 min. To this mixture was added a solution of bis(phenylthio)acetonitrile[16] (190 mg, 0.74 mmol) in dry diethyl ether (1 cm^3) at 0 °C, and the mixture was stirred at the same temperature for 1 h. The reaction mixture was made alkaline by addition of 10% aq. NaOH and the whole was extracted with diethyl ether. The extract was dried ($MgSO_4$) and the solvent was evaporated off to give 2,2-bis(phenylthio)ethylamine (140 mg, 74%) as an oil.

This amine was heated with cyclohexanone (54 mg, 0.54 mmol) in refluxing benzene (10 cm^3) with azeotropic removal of water for 1 h. The resultant solution containing *N*-cyclohexylidene-2,2-bis(phenylthio)ethylamine was treated with acetyl chloride (47 mg, 0.6 mmol) in the presence of pyridine (47 mg, 0.6 mmol) at room temperature for 1 h. After usual work-up, the crude material was purified by chromatography on silica gel [hexane–AcOEt (2:1)] to give the *enamide* **38** (80 mg, 37%) as an oil (Found: C, 68.4; H, 6.6; N, 3.7. $C_{22}H_{25}NOS_2$ requires C, 68.9; H, 6.6; N, 3.65%); $\nu_{max}(CCl_4)/cm^{-1}$ 1670; δ_H(60 MHz) 1.4–2.6 (8 H, m), 2.02 (3 H, s, COMe), 3.76 (2 H, d, *J* 7.6, NCH_2), 4.83 (1 H, t, *J* 7.6, SCHS), 5.63–5.92 (1 H, m, C=CH) and 7.1–7.7 (10 H, m, ArH).

Reaction of Compound **38** *with* Bu_3SnH.—Following the general procedure, compound **38** (80 mg, 0.2 mmol) was treated with Bu_3SnH (58.2 mg, 0.22 mmol) and AIBN (5 mg, 0.02 mmol), and the crude material was purified by chromatography on silica gel [hexane–AcOEt (2:1)] to give N-(*cyclohex*-1-*enyl*)-N-[2-(*phenylthio*)*ethyl*]*acetamide* **39** (30 mg, 65%), m.p. 34–35 °C (from hexane–AcOEt) (Found: C, 68.9; H, 7.7; N, 4.6. $C_{16}H_{21}NOS{\cdot}0.25H_2O$ requires C, 68.65; H, 7.7; N, 5.0%); $\nu_{max}(CCl_4)/cm^{-1}$ 1655; δ_H(60 MHz) 1.3–2.4 (8 H, m), 2.00 (3 H, s, COMe), 2.9–3.3 (2 H, m, SCH_2), 3.4–3.8 (2 H, m, NCH_2), 5.5–5.8 (1 H, m, C=CH) and 7.05–7.55 (5 H, m, ArH).

2-*Chloro*-N-(*cyclohex*-1-*enyl*)-N-(*prop*-2-*enyl*)*acetamide* **40**.—A mixture of cyclohexanone (2 g, 20.4 mmol) and prop-2-enylamine (5.8 g, 0.1 mol) in toluene (10 cm^3) was heated in a sealed tube at 100 °C for 2 h. The solvent and excess of prop-2-enylamine were removed by evaporation and the residue was again dissolved in toluene (30 cm^3) containing triethylamine (3 g, 30 mmol) and 4-(dimethylamino)pyridine (248 mg, 2 mmol). To this mixture at 0 °C was added a solution of chloroacetyl chloride (3.4 g, 30 mmol) in toluene (20 cm^3), and the mixture was stirred at the same temperature for 1 h. After saturated aq. $NaHCO_3$ had been added, the organic layer was separated, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel [hexane–AcOEt (20:1)] to give the *enamide* **40** (1.89 g, 44%) as an oil (Found: M^+, 213.0895. $C_{11}H_{16}ClNO$ requires *M*, 213.0918); $\nu_{max}(CCl_4)/cm^{-1}$ 1660; δ_H(60 MHz) 1.4–2.4 (8 H, m), 3.95–4.25 (2 H, m, NCH_2), 4.09 (2 H, s, $COCH_2$), 4.95–5.40 (2 H, m, $CH{=}CH_2$) and 5.45–6.15 (2 H, m, $CH{=}CH_2$ and NC=CH).

Radical Cyclisation of Compound **40**.—Following the general procedure, compound **40** (400 mg, 1.87 mmol) was treated with Bu_3SnH (1.09 g, 3.74 mmol) and AIBN (61 mg, 0.37 mmol), and the crude material was purified by chromatography on silica gel [hexane–AcOEt (10:1)]. The first fraction gave a mixture of 1-(*cyclohex*-1-*enyl*)-4-*methylpyrrolidin*-2-*one* **44** and N-(*cyclohex*-1-*enyl*)-N-(*prop*-2-*enyl*)*acetamide* **45** (total 98 mg, total 29%), whose ratio was estimated to be ~1:1 by ^1H NMR spectroscopy (Found: M^+, 179.1307. $C_{11}H_{17}NO$ requires *M*, 179.1308); $\nu_{max}(CCl_4)/cm^{-1}$ 1700 (for NC=O of **44**) and 1650 (for NC=O of **45**); δ_H for **44** (60 MHz) (diagnostic data only) 1.12 (3 H, d, *J* 6.5, Me), 3.10 (1 H, dd, *J* 9.5 and 6.0, one of NCH_2) and 3.64 (1 H, dd, *J* 9.5 and 7.5, one of NCH_2); δ_H for **45** (60 MHz) (diagnostic data only) 2.04 (3 H, s, COMe) and 3.93–4.16 (2 H, m, NCH_2). The second fraction gave cis-*octahydro*-1-(*prop*-2-*enyl*)*indol*-2-*one* **43** (193 mg, 58%) as an oil (Found: M^+, 179.1310. $C_{11}H_{17}NO$ requires *M*, 179.1308); $\nu_{max}(CCl_4)/cm^{-1}$ 1690; δ_H(60 MHz) 1.2–2.7 (11 H, m), 3.25–3.75 (1 H, m, 7a-H), 3.46 (1 H, dd, *J* 15.5 and 6.5, one of NCH_2), 4.26 (1 H, dd, *J* 15.5 and 5.0, one of NCH_2) and 4.9–6.1 (3 H, m, $CH{=}CH_2$).

N-(*But*-3-*enyl*)-2-*chloro*-N-(*cyclohex*-1-*enyl*)*acetamide* **46**.—Aluminium chloride (6.0 g, 45 mmol) was added to a suspension of lithium aluminium hydride (1.7 g, 45 mmol) in dry diethyl ether (70 cm^3) at 0 °C, and the mixture was stirred at the same temperature for 5 min. To this was added a solution of allyl cyanide(but-3-enonitrile) (3.0 g, 45 mmol) in dry diethyl ether (20 cm^3) and the mixture was stirred at 0 °C for 1 h. The reaction mixture was made alkaline by addition of 10% aq. NaOH and the organic layer was separated. The aqueous layer was further extracted with diethyl ether and the combined organic phases were dried (NaOH pellets). To the organic phase containing but-3-enylamine was added cyclohexanone (4.4 g, 45 mmol), and the whole was heated at 100 °C in a sealed tube for 1 h. The solvent was evaporated off and the residue was distilled *in vacuo* to give *N*-cyclohexylidene-but-3-enylamine (1.3 g, 19%), b.p. 150 °C (bath temperature)/2 mmHg. This imine was used immediately for the next stage.

To a solution of the imine (1.2 g, 8 mmol) in dichloromethane (50 cm^3) at 0 °C was added chloroacetyl chloride (1.0 g, 9 mmol) and the mixture was stirred at the same temperature for 30 min. After saturated aq. $NaHCO_3$ had been added, the organic phase was separated, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel [hexane–AcOEt (5:1)] to give the *enamide* **46** (1.8 g, 40%) as an oil (Found: M^+, 227.1068. $C_{12}H_{18}ClNO$ requires *M*, 227.1075); $\nu_{max}(CCl_4)/cm^{-1}$ 1650; δ_H(60 MHz) 1.4–2.6 (10 H, m), 3.3–3.7 (2 H, m, NCH_2), 4.06 (2 H, s, $COCH_2$), 4.8–5.3 (2 H, m, C=CH_2) and 5.4–6.2 (2 H, m, C*H*=CH_2 and NC=CH).

Radical Cyclisation of Compound **46**.—Following the general procedure, compound **46** (400 mg, 1.8 mmol) was treated with Bu_3SnH (553 mg, 1.9 mmol) and AIBN (29 mg, 0.18 mmol), and the crude material was purified by chromatography on silica gel [hexane–AcOEt (2:1)]. The first fraction gave N-(*but*-3-*enyl*)-N-(*cyclohex*-1-*enyl*)*acetamide* **51** (20 mg, 6%) as an oil (Found: M^+, 193.1438. $C_{12}H_{19}NO$ requires *M*, 193.1465); $\nu_{max}(CCl_4)/cm^{-1}$ 1650; δ_H(60 MHz) 1.4–2.6 (10 H, m), 2.0 (3 H, s, COMe), 3.3–3.7 (2 H, m, NCH_2), 4.8–5.25 (2 H, m, C=CH_2) and 5.4–6.0 (2 H, m, C*H*=CH_2 and NC=CH). The second fraction gave *cis*-1-(but-3-enyl)octahydroindol-2-one **49** as an oil (26 mg, 7%); $\nu_{max}(CCl_4)/cm^{-1}$ 1690; δ_H(60 MHz) 1.1–3.0 (13 H, m), 3.3–3.7 (3 H, m) and 4.7–6.0 (3 H, m). The mass spectrum of this compound showed it to contain a small quantity of unidentified product (*m*/*z* 195): several attempts to obtain an analytically pure sample were unsuccessful. The third fraction gave 1-(*cyclohex*-1-*enyl*)-4-*methylpiperidin*-2-*one* **50** (27 mg, 8%) as an oil (Found: M^+, 193.1454. $C_{12}H_{19}NO$ requires *M*, 193.1465); $\nu_{max}(CCl_4)/cm^{-1}$ 1690 (C=O) and 1650 (C=C); δ_H(60 MHz) 0.8–3.0 (13 H, m), 1.0 (3 H, d, *J* 6, Me), 3.3–3.6 (2 H, m, NCH_2) and 5.4–5.7 (1 H, m, C=CH). The fourth fraction gave *decahydro*-6H-*pyrido*[2,1-i]*indol*-6-*one* **48** (92 mg, 27%) as an oil (Found: M^+, 193.1437. $C_{12}H_{19}NO$ requires *M*, 193.1465); $\nu_{max}(CCl_4)/cm^{-1}$ 1690; δ_H(300 MHz) 1.0–1.45 (5 H, m), 1.45–1.75 (7 H, m), 1.95–2.15 (3 H, m), 2.21 (1 H, dd, *J* 16.3 and 8.1, one of $COCH_2$), 2.36 (1 H, ddd, *J* 16.3, 12.1 and 1.6, one of $COCH_2$), 2.66 (1 H, tdd, *J* 13.2, 3.2 and 1.4, one of NCH_2) and 3.95 (1 H, ddt, *J* 13.2, 4.9 and 1.7, one of NCH_2); δ_C(75 MHz) 19.9, 21.0, 21.5, 24.5, 24.7, 28.7, 33.4, 34.5, 36.7, 41.7, 59.5 and 173.1. The fifth fraction gave *octahydro*-1-*methyl*-1H,5H-*pyrrolo*[2,1-i]*indol*-5-*one* **47** (108 mg, 32%) as an oil (Found: M^+, 193.1477. $C_{12}H_{19}NO$ requires *M*, 193.1465); $\nu_{max}(CCl_4)/cm^{-1}$ 1690; δ_H(300 MHz) 0.95 (3 H, d, *J* 7.3, Me), 1.1–2.0 (9 H, m), 2.10 (1 H, quintet d, *J* 7.3 and 2.7, CHMe), 2.23–2.49 (3 H, m), 2.72–2.85 (1 H, m), 3.09 (1 H, dddd, *J* 11.7, 9.2, 3.8 and 1.3, one of NCH_2) and 3.45 (1 H, dt, *J* 11.7 and 8.1, one of NCH_2) [the spectrum also exhibited a small doublet at δ 1.11 (*J* 6.5), which is assignable as a methyl group of another stereoisomer: the ratio of two stereoisomers was estimated to be ~3.4:1 by the integrated intensities of the peak height of the methyl protons].

2-*Chloro*-N-(*cyclohex*-1-*enyl*)-N-[2-(*cyclohex*-1-*enyl*)*ethyl*]-*acetamide* **54**.—A mixture of 2-(cyclohex-1-enyl)ethylamine (2.5 g, 20 mmol) and cyclohexanone (2.9 g, 30 mmol) in benzene (30 cm^3) was heated under reflux with azeotropic removal of water for 1.5 h. The solvent was evaporated off and the residue was distilled *in vacuo* to give 2-(cyclohex-1-enyl)-*N*-cyclohexylidene ethylamine (2.5 g, 60%), b.p. 180 °C (bath temperature)/2 mmHg. This compound was used immediately for the next stage.

To a solution of the imine (1.0 g, 5 mmol) in dichloromethane (30 cm^3) at 0 °C were added successively triethylamine (0.5 g, 5 mmol) and chloroacetyl chloride (0.6 g, 5 mmol), and the mixture was stirred at the same temperature for 30 min then at room temperature for 1 h. Water (20 cm^3) was added to the reaction mixture and the organic layer was separated. The aqueous layer was further extracted with dichloromethane and the combined organic phases were dried ($MgSO_4$). The solvent was evaporated off and the residue was chromatographed on silica gel [hexane–AcOEt (5:1)] to give the *enamide* **54** (0.5 g, 30%) as an oil (Found: M^+, 281.1542. $C_{16}H_{24}ClNO$ requires *M*, 281.1545); $\nu_{max}(CCl_4)/cm^{-1}$ 1655; δ_H(60 MHz) 1.1–2.6 (18 H, m), 3.3–3.7 (2 H, m, NCH_2), 4.08 (2 H, s, $COCH_2$), 5.43 (1 H, br s, C=CH) and 5.72 (1 H, br s, C=CH).

Radical Cyclisation of Compound **54**.—Following the general procedure, compound **54** (447 mg, 1.6 mmol) was treated with Bu_3SnH (495 mg, 1.7 mmol) and AIBN (26 mg, 0.16 mmol) and the crude material was purified by chromatography on silica gel [hexane–AcOEt (2:1)]. The first fraction gave N-(*cyclohex*-1-*enyl*)-N-[2-(*cyclohex*-1-*enyl*)*ethyl*]*acetamide* **60** (16 mg, 4%) as an oil (Found: M^+, 247.1944. $C_{16}H_{25}NO$ requires *M*, 247.1935); $\nu_{max}(CCl_4)/cm^{-1}$ 1645; δ_H(60 MHz) 1.4–2.4 (18 H, m), 1.98 (3 H, s, COMe), 3.3–4.6 (2 H, m, NCH_2) and 5.3–5.7 (2 H, m, C=CH × 2). The second fraction gave cis-1-[2-(*cyclohex*-1-*enyl*)*ethyl*]*octahydroindol*-2-*one* **59** (36 mg, 9%) as an oil (Found: M^+, 247.1950. $C_{16}H_{25}NO$ requires *M*, 247.1935); $\nu_{max}(CCl_4)/cm^{-1}$ 1690; δ_H(60 MHz) 1.0–3.0 (21 H, m), 3.2–3.7 (3 H, m) and 5.42 (1 H, br s, C=CH). The third fraction gave (5S*,6S*,12R*,13R*)-*perhydroerythrinan*-8-*one* **58** (172 mg, 44%) as an oil (Found: M^+, 247.1942. $C_{16}H_{25}NO$ requires *M*, 247.1935); $\nu_{max}(CCl_4)/cm^{-1}$ 1685; δ_H(300 MHz) 0.8–1.9 (19 H, m), 2.0–2.3 (3 H, m), 2.48 (1 H, dd, *J* 18.8 and 11.0, one of $COCH_2$), 2.68 (1 H, tdd, *J* 13.4, 3.3 and 1.2, one of NCH_2) and 4.01 (1 H, ddd, *J* 13.4, 5.4 and 1.6, one of NCH_2); δ_C(75 MHz) 19.30, 19.34, 24.7, 26.1, 26.8, 27.2, 27.9, 32.6, 34.3, 35.5, 35.6, 36.3, 53.0, 63.1 and 173.2.

Catalytic Hydrogenation of Compound **62**.—Compound **62**[13] (56 mg, 0.2 mmol) was hydrogenated in acetic acid (1 cm^3) over platinum(IV) oxide (32 mg, 0.1 mmol) in a Paar apparatus under 5 kg/cm^2 pressure for 1.5 h. Dichloromethane (10 cm^3) was added to the reaction mixture and the catalyst was filtered off. The filtrate was concentrated and the residue was chromatographed on silica gel [hexane–AcOEt (2:1)]. The first fraction gave unchanged starting material **62** (10 mg, 18%). The second fraction gave compound **58** (22 mg, 39%), whose spectroscopic data were identical with those of the compound obtained above by the cyclisation of compound **54**.

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