Triethylborane-mediated atom-transfer cyclisation of 2-iodo-*N*-(prop-2-enyl)acetamides and related compounds

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The 2-iodo-*N*-(prop-2-enyl)acetamides 1, upon treatment with triethylborane (0.2–0.6 mol equiv.) in boiling benzene, undergo iodine atom-transfer cyclisation to give the 4-(iodomethyl)pyrrolidin-2-ones 2 in high yields. The method has been applied to the synthesis of γ-lactones.

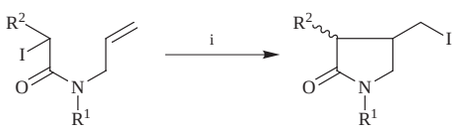
Introduction

In a series of papers,[1] we have demonstrated that the *N*-alkenylcarbamoylmethyl radicals, generated from the corresponding α-halogeno amides, on treatment with tributyltin hydride (TBTH) in the presence of AIBN, undergo cyclisations to give four- to eight-membered lactams. In contrast to the TBTH-mediated radical cyclisation in which the last step is a simple reduction by TBTH, the atom-transfer radical cyclisation can introduce a versatile halogen atom to the cyclised products. Some of these atom-transfer methods of α-halogeno amides include the use of bis(tributyltin) under photochemical conditions,[2] transition metals such as ruthenium(II),[3,4] copper(I),[3b,5] and palladium(0),[6] nickel powder–acetic acid,[7] and electrochemical reactions.[8] Triethylborane in the presence of oxygen has been known to produce ethyl radical which can abstract an iodine atom from iodoalkanes,[9] and this property has been used for the inter- and intra-molecular atom-transfer radical additions of iodoalkanes to alkynes or alkenes.[10] Herein we describe the iodine atom-transfer radical cyclisation of 2-iodo-*N*-(prop-2-enyl)acetamides using triethylborane which provides a new route to 4-(iodomethyl)pyrrolidin-2-ones.[11] Applications of the method to the synthesis of γ-lactones are also presented.

Results and discussion

In a typical experiment, a solution of triethylborane (0.4 mol equiv.) in hexane was added all at once to a solution of 2-iodo-*N*-methyl-*N*-(prop-2-enyl)acetamide **1a** in boiling benzene and the mixture was refluxed for 10 min. After removal of the solvent, the crude material was chromatographed on silica gel to give the 4-(iodomethyl)pyrrolidin-2-one **2a** in 71% yield. When the reaction was carried out at room temperature (rt), the yield of compound **2a** decreased to 32%. Similar treatment of the 2-iodoacetamides **1b**–**e** with triethylborane in benzene either at reflux or at rt gave the corresponding 4-(iodomethyl)pyrrolidin-2-ones **2b**–**e** (Scheme 1), whose yields are given in Table 1. The 2-iodopropanamide **1f** gave product **2f** as a mixture of *cis* and *trans* isomers in the ratio of 1:4.3 (determined by ^{1}H NMR spectroscopy), which were separated by chromatography to give *cis*- and *trans*-**2f**[8b] in 17 and 62% yield, respectively. On the other hand, similar treatment of the bromo congener of iodide **1a** with triethylborane gave no atom-transfer cyclisation product: only the starting material was recovered unchanged.

The known susceptibility of triethylborane to decomposition in the presence of oxygen to form ethyl radical[9] and the observation that compound **1e** was stable in benzene at reflux for 1 h with or without a Lewis acid such as $SnCl_4$ or $BF_3{\cdot}Et_2O$ suggested that the atom-transfer cyclisation of amides **1** was initiated by ethyl radical generated from triethylborane and oxygen to give the carbamoylmethyl radicals **A** (Scheme 2). These radicals then undergo cyclisation to yield new radicals **B**, which may abstract an iodine atom from the starting α-iodo amides **1** to yield the cyclised products **2** and regenerate the radicals **A**.



1a–f **2a–f**

a; R^1 = Me, R^2 = H
b; R^1 = Bn, R^2 = H
c; R^1 = Ph, R^2 = H
d; R^1 = $CH_2CH{=}CH_2$, R^2 = H
e; R^1 = Ts, R^2 = H
f; R^1 = Ts, R^2 = Me

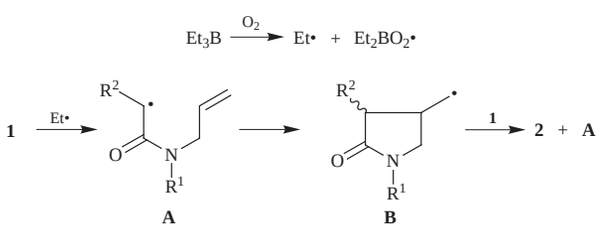
Scheme 1 *Reagents and conditions*: i, Et_3B, benzene, reflux or rt

Table 1 Preparation of the 4-(iodomethyl)pyrrolidin-2-ones **2a**–**f**

Entry	Starting material	Et_3B (mol equiv.)	Temp. (*T*/°C)	Products	Yield (%)
1	**1a**	0.6	80	**2a**	71
2	**1a**	1.2	20	**2a**	32
3	**1b**	0.6	80	**2b**	75
4	**1b**	1.0	20	**2b**	61
5	**1c**	0.4	80	**2c**	77
6	**1c**	1.2	20	**2c**	48
7	**1d**	0.2	80	**2d**	87
8	**1d**	0.2	20	**2d**	81
9	**1e**	0.4	80	**2e**	92
10	**1e**	0.4	20	**2e**	92
11	**1f**	0.6	80	**2f**	17 + 62[a]

[a] Isolated yields of the *cis*- and *trans*-isomer, respectively.

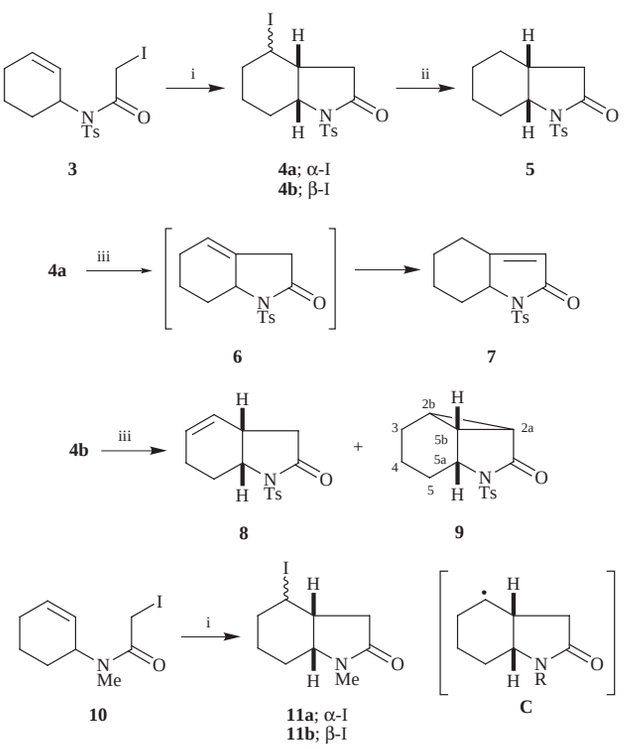
In accord with the previous observation of Curran and Tamine,[2b] cyclisations of the 2-iodoacetamides **1a**–**c** were temperature-dependent. It is believed that high temperature (>80 °C) is required to convert s-*trans* radicals (which cannot cyclise) into s-*cis* radicals such as **A** (which can cyclise) by rotation of the N–CO bond. The exception was the *N*-di(prop-2-enyl) derivative **1d** which efficiently cyclised even at rt. This is because one of the prop-2-enyl groups of substrate **1d** is always



Scheme 2

properly oriented for cyclisation. More interesting is the cyclisation of the *N*-tosyl derivative **1e** which proceeded with high efficiency to give the cyclised product **2e** in high yield regardless of the reaction temperature. This result may be attributed to the lower energy barrier to rotation of the N–CO bond caused by the strong electron-withdrawing effect of the tosyl group. Another interpretation may be derived from consideration of the steric bulkiness of the *N*-tosyl group, which shifts the equilibrium between two rotamers to the easily cyclisable s-*cis* radical.

Since the tosyl derivatives gave good results, we then investigated the cyclisation of *N*-(cyclohex-2-enyl)-2-iodo-*N*-tosylacetamide **3**. Treatment of compound **3** with triethylborane (0.5 molar equiv.) in boiling benzene gave a mixture of two isomeric octahydro-4-iodo-1-tosylindol-2-ones **4a**,**b** in a ratio of ~3:1 and in an almost quantitative yield. The mixture could be separated by careful chromatography on silica gel to give the *endo*-iodide **4a** and *exo*-iodide **4b** in 48 and 24% yield, respectively. The stereochemistry of products **4a** and **4b** was determined by the following chemical evidence. The *cis*-stereochemistry of the ring juncture of products **4a**,**b** was confirmed by reduction of each isomer with TBTH–AIBN to *cis*-octahydro-1-tosylindol-2-one **5** (Scheme 3).[12]

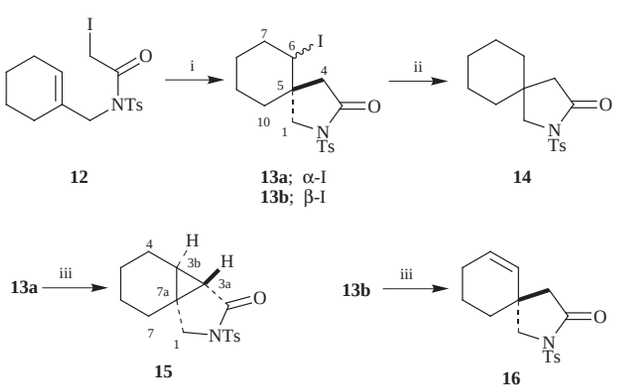


Scheme 3 *Reagents and conditions*: i, Et_3B, benzene, reflux or rt; ii, TBTH, AIBN, benzene, reflux; iii, DBU, benzene, reflux

Treatment of the major isomer **4a** with DBU in benzene gave α,β-unsaturated lactam **7** in 93% yield, while the minor isomer **4b** gave unsaturated latam **8** and tricyclic lactam **9** in 43 and 55% yield, respectively. The formation of product **7** can be rationalised by assuming that the initially formed unsaturated lactam **6** (a Saytzev elimination product) undergoes isomerisation to **7** under the reaction conditions. Taking into account the stereoelectronic effect that exists since the tricyclic compound **9** can be formed when the C-4–I bond and the carbanion formed at the 3-position are antiperiplanar, the C-4–I and C-3a–C-3 bonds in β-iodide **4b** should be *anti*.

Considering the observation of Jolly and Livinghouse[2a] that the *N*-methyl congener **10**, on treatment with bis(tributyltin) under photochemical conditions, gave the *exo*-iodide **11b** as the major product (**11a**:**11b** = 1:5.5) as a result of attack of the iodine atom from the less hindered convex face of the cyclised radical intermediate **C**, it is somewhat surprising that the major product formed from the *N*-tosyl derivative **3** is the *endo*-iodide **4a**, whose iodine atom comes from the more crowded concave face. In order to understand the reasons for this anomalous result, several experiments were carried out. (1) Treatment of compound **10** with triethylborane in boiling benzene also gave the *exo*-iodide **11b** as the major product (**11a**:**11b** = 1:1.4),† which suggested that the nature of the substituent on the nitrogen atom played an important role in deciding the course of the atom-transfer process. (2) A benzene solution of compound **3** was treated with triethylborane at rt to give a 3:1 mixture of compounds **4a** and **4b**, whose ratio was essentially the same as that (3:1) obtained under the refluxing conditions, thereby indicating that any effect of temperature on the ratio of products **4a**,**b** from substrate **3** can be excluded. (3) A similar reaction of substrate **3** using the ditin method afforded approximately equal amounts of products **4a** and **4b**. At the present time, no simple explanation can be offered for the stereochemical outcome observed for the cyclisation of compound **3**.

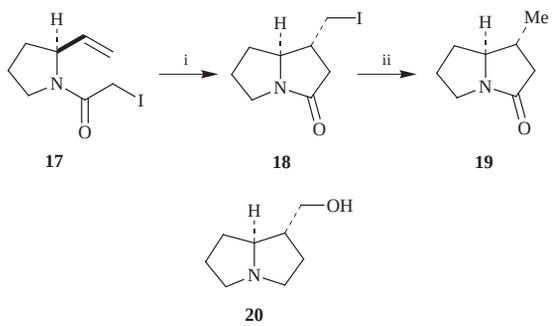
N-[(Cyclohex-1-enyl)methyl]-2-iodo-*N*-tosylacetamide **12**, upon treatment with triethylborane (0.7 mol equiv.), gave isomeric 6-iodo-2-tosyl-2-azaspiro[4.5]decan-3-ones **13a** and **13b** in 40 and 31% yield, respectively (Scheme 4). The stereochemistry of spiro products **13a**,**b** was again confirmed by chemical means. Treatment of each isomer with TBTH–AIBN gave the same spirolactam **14**. Upon treatment with DBU, the major isomer **13a** gave the tricyclic compound **15** in 73% yield, while the minor isomer **13b** gave the unsaturated compound **16** in 85% yield. The structure of tricycle **15** was determined on the basis of its spectroscopic data. The ^{1}H NMR spectrum showed no olefinic proton signal, and the ^{13}C NMR spectrum revealed the presence of one quaternary carbon at δ_C 24.3 and two tertiary carbons at δ_C 25.2 and 31.9. Stereoelectronic considerations indicate that the C-6–I and C-5–C-4 bonds are *anti* for iodide **13a** and *syn* for iodide **13b**, respectively.



Scheme 4 *Reagents and conditions*: i, Et_3B, benzene, reflux; ii, TBTH, AIBN benzene, reflux; iii, DBU, benzene, reflux

† The ^{1}H NMR spectrum of the crude reaction mixture showed it to contain two or three olefinic compounds which might arise by elimination of HI from major products **11a**,**b**. Therefore, the value (1:1.4) of the ratio of products **11a**,**b** is probably not the true one. A similar observation was reported for the ditin method.[2b]

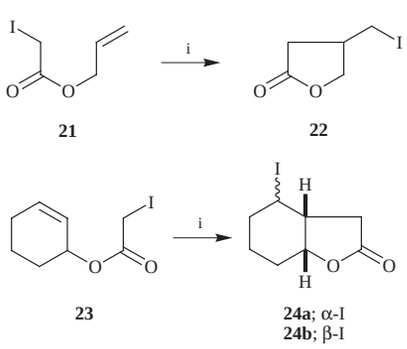
Treatment of *N*-(2-iodoacetyl)-2-vinylpyrrolidine **17**, prepared from (*S*)-prolinol, with triethylborane (0.4 mol equiv.) gave 1-(iodomethyl)pyrrolizidin-3-one **18**[2a,5] in 68% yield as a mixture of the 1-*exo* and 1-*endo* isomers in >95 : <5 (the ratio was determined by the ^{1}H NMR spectrum of the crude product after transformation into 1-methylpyrrolizidin-3-one **19** by sodium borohydride reduction in the presence of a phase-transfer catalyst[13]). Recrystallisation of crude iodide **18** from hexane gave a pure sample of the *exo*-isomer of compound **18**. Compound **18** has already been transformed into (−)-trachelanthamidine **20** (see Scheme 5).[2a,5]



17 **18** **19** **20**

Scheme 5 *Reagents and conditions*: i, Et_3B, benzene, reflux; ii, $NaBH_4$, $CH_3[CH_2]_{15}P^+Bu_3\ Br^-$, toluene, 80 °C

The present method was also effective for formation of the lactone from the corresponding iodoacetates. Thus, the allyl ester **21**, upon treatment with triethylborane in boiling benzene, provided the expected lactone **22** in 46% yield (Scheme 6).



21 **22** **23**

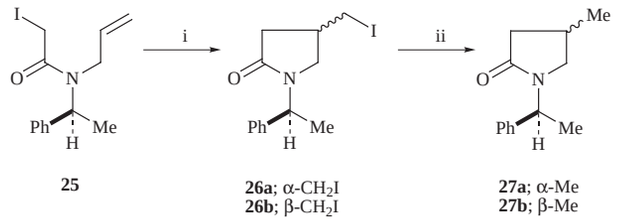
24a; α-I
24b; β-I

Scheme 6 *Reagents and conditions*: i, Et_3B, benzene, reflux

Treatment of homologous ester **23** with triethylborane in boiling benzene gave a mixture of the *endo*-iodide **24a** and *exo*-iodide **24b** in 65% combined yield. The ^{1}H NMR spectrum of the mixture showed the ratio of **24a**,**b** to be ~1 : 5, which closely resembled that (1 : 6) reported with the ditin method.[2b]

Finally, we examined the diastereoselectivity in atom-transfer cyclisation of *N*-allylic iodoacetamides possessing a chiral group on the nitrogen atom. Cardillo *et al.*[14] reported that no diastereoselectivity was observed in the TBTH-mediated radical cyclisation of 2-iodo-*N*-[(*S*)-1-phenylethyl]-*N*-(prop-2-enyl)acetamide **25** to form 4-methylpyrrolidin-2-ones **27a**,**b** in boiling benzene. We treated chiral substrate **25** with triethylborane in benzene at rt or at 0 °C in the hope that some degree of diastereoselectivity might result at lower temperatures, but, unfortunately, in both cases a ~1 : 1 mixture of two diastereoisomers **26a** and **26b** was obtained (the ratio was determined by ^{1}H NMR spectroscopy) (Scheme 7). The stereochemistry of products **26a** and **26b** was determined by their chromatographic separation and transformation into reduced products **27a** and **27b**,[14] respectively.

In summary, this study revealed that triethylborane can be used for the iodine atom-transfer radical cyclisation of α-iodo amides. Advantages of this reagent are that it is cheap, much



25 **26a**; α-CH_2I **26b**; β-CH_2I **27a**; α-Me **27b**; β-Me

Scheme 7 *Reagents and conditions*: i, Et_3B, benzene, rt; ii, $NaBH_4$, $CH_3[CH_2]_{15}P^+Bu_3\ Br^-$, toluene, 80 °C

less toxic than the tin reagents, and easy to handle. In addition, this radical cyclisation is very rapid that does not require a high-dilution method.

Experimental

Mps 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. ^{1}H NMR (60 and 300 MHz) and ^{13}C NMR (75.4 MHz) 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. Optical rotations were measured with a JASCO DIP-360 polarimeter. $[\alpha]_D$-Values are given in 10^{-1} deg cm^2 g^{-1}. Exact mass determinations [electron-impact (EI) and fast-atom bombardment (FAB) mass spectra] were obtained on a JEOL-SX 102A instrument. Column chromatography was performed on silica gel 60 PF_{254} (Nacalai Tesque) under pressure.

Materials

The following radical precursors were prepared according to the reported procedure. 2-Iodo-*N*-methyl-*N*-(prop-2-enyl)-acetamide **1a**,[2b] *N*-benzyl-2-iodo-*N*-(prop-2-enyl)acetamide **1b**,[6] 2-iodo-*N*,*N*-di(prop-2-enyl)acetamide **1d**,[2b] 2-iodo-*N*-(prop-2-enyl)-*N*-(*p*-tolylsulfonyl)acetamide **1e**,[8b] 2-iodo-*N*-(prop-2-enyl)-*N*-(*p*-tolylsulfonyl)propanamide **1f**,[8b] *N*-(cyclohex-2-enyl)-2-iodo-*N*-methylacetamide **10**,[2b] *N*-(2-iodoacetyl)-2-ethenylpyrrolidine **17**,[2a,6] prop-2-enyl 2-iodoacetate **21**,[2b] cyclohex-2-enyl 2-iodoacetate **23**[2b] and 2-iodo-*N*-[(*S*)-1-phenylethyl]-*N*-(prop-2-enyl)acetamide **25**.[14]

2-Iodo-*N*-phenyl-*N*-(prop-2-enyl)acetamide 1c

A mixture of 2-bromo-*N*-phenyl-*N*-(prop-2-enyl)acetamide (985 mg, 3.88 mmol), prepared by acylation of *N*-(prop-2-enyl)aniline with 2-bromoacetyl bromide, and sodium iodide (2.92 g, 19.4 mmol) in acetonitrile (70 cm^3) was stirred at rt for 8 h and the crude material was chromatographed on silica gel [hexane–AcOEt (7 : 1)] to give *title amide* **1c** (1.04 g, 89%) as an oil (Found: M$^+$, 300.9951. $C_{11}H_{12}INO$ requires *M*, 300.9964); $\nu_{max}(CCl_4)$/cm^{-1} 1655; δ_H(60 MHz) 3.55 (2 H, s, CH_2I), 4.27 (2 H, d, *J* 6, $NCH_2CH{=}CH_2$), 4.8–5.3 (2 H, m, $CH_2CH{=}CH_2$), 5.5–6.3 (1 H, m, $CH_2CH{=}CH_2$) and 6.9–7.6 (5 H, m, ArH).

General procedure for the cyclisation of *N*-substituted 2-iodo-*N*-(prop-2-enyl)acetamides 1a–f

To a boiling solution of an amide **1** (0,.365 mmol) in benzene (15 cm^3) was added a 1.01 mol dm^{-3} solution of triethylborane in hexane (0.14 cm^3, 0.146 mmol) all at once, and the mixture was further heated at reflux for 10 min. The reaction mixture was washed with water, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel [hexane–AcOEt (8 : 1–1 : 1)] to give 4-(iodomethyl)pyrrolidin-2-ones **2**. The following compounds were thus obtained (the yields are given in Table 1).

4-(Iodomethyl)-1-methylpyrrolidin-2-one 2a.[2b] An oil; $\nu_{max}(CCl_4)$/cm^{-1} 1695; δ_H(300 MHz) 2.17 (1 H, dd, *J* 16.5 and 6.4, one of 3-H_2), 2.58 (1 H, dd, *J* 16.5 and 9.1, one of 3-H_2), 2.61–2.76 (1 H, m, 4-H), 2.85 (3 H, s, NCH_3), 3.13 (1 H, dd,

J 10.2 and 6.0, one of CH_2I), 3.20 (1 H, dd, *J* 9.9 and 7.8, one of 5-H_2), 3.29 (1 H, dd, *J* 9.9 and 5.7, one of 5-H_2) and 3.53 (1 H, dd, *J* 10.2 and 7.8, one of CH_2I).

1-Benzyl-4-(iodomethyl)pyrrolidin-2-one 2b.[6] An oil; ν_{max}(CCl_4)/cm^{-1} 1665; δ_H(300 MHz) 2.25 (1 H, dd, *J* 20.3 and 10.5, one of 3-H_2), 2.56–2.72 (2 H, m, one of 3-H_2, 4-H), 2.99 (1 H, dd, *J* 10.1 and 5.9, one of CH_2I), 3.15 (1 H, dd, *J* 9.9 and 7.2, one of 5-H_2), 3.23 (1 H, *J* 10.1 and 5.7, one of CH_2I), 3.40 (1 H, dd, *J* 9.9 and 7.7, one of 5-H_2), 4.41 and 4.49 (1 H each, ABq, *J* 14.7, CH_2Ph) and 7.21–7.38 (5 H, m, ArH).

4-(Iodomethyl)-1-phenylpyrrolidin-2-one 2c. Crystals, mp 54–55.5 °C (from hexane–AcOEt) (Found: C, 43.9; H, 3.9; N, 4.6. $C_{11}H_{12}INO$ requires C, 43.9; H, 4.0; N, 4.65%); ν_{max}(CCl_4)/cm^{-1} 1690; δ_H(300 MHz) 2.41 (1 H, dd, *J* 20.2 and 10.6, one of 3-H_2), 2.69–2.84 (2 H, m, one of 3-H_2, 4-H), 3.27 (1 H, dd, *J* 10.0 and 7.5, one of CH_2I), 3.35 (1 H, dd, *J* 10.0 and 5.5, one of CH_2I), 3.60 (1 H, dd, *J* 9.9 and 6.0, one of 5-H_2), 3.98 (1 H, dd, *J* 9.9 and 7.8, one of 5-H_2), 7.16 (1 H, br t, *J* 7.4, ArH), 7.38 (2 H, br t, *J* 8.0, ArH) and 7.58 (2 H, br d, *J* 8.5, ArH).

4-(Iodomethyl)-1-(prop-2-enyl)pyrrolidin-2-one 2d.[2b] An oil; ν_{max}(CCl_4)/cm^{-1} 1670; δ_H(300 MHz) 2.18–2.29 (1 H, m, 4-H), 2.57–2.75 (2 H, m, 3-H_2), 3.09 (1 H, dd, *J* 10.5 and 6.2, one of CH_2I), 3.21 (1 H, dd, *J* 9.5 and 7.5, one of 5-H_2), 3.29 (1 H, *J* 9.5 and 5.5, one of 5-H_2), 3.50 (1 H, dd, *J* 10.5 and 7.5, one of CH_2I), 3.89–3.96 (2 H, m, CH_2CH=CH_2), 5.17–5.24 (2 H, m, CH_2CH=CH_2) and 5.66–5.80 (1 H, m, CH_2C*H*=CH_2).

4-(Iodomethyl)-1-(*p*-tolylsulfonyl)pyrrolidin-2-one 2e. Crystals, mp 131–132 °C (from hexane–AcOEt) (lit.,[8b] 129.5–130 °C); ν_{max}($CHCl_3$)/cm^{-1} 1730; δ_H(300 MHz) 2.27 (1 H, dd, *J* 20.4 and 10.7, one of 3-H_2), 2.45 (3 H, s, ArCH_3), 2.58–2.71 (2 H, m, one of 3-H_2, 4-H), 3.14 (1 H, dd, *J* 10.2 and 6.9, one of CH_2I), 3.21 (1 H, *J* 10.2 and 6.0, one of CH_2I), 3.58 (1 H, dd, *J* 10.2 and 6.3, one of 5-H_2), 4.08 (1 H, dd, *J* 10.2 and 7.8, one of 5-H_2), 7.35 (2 H, d, *J* 8.1, ArH) and 7.93 (2 H, d, *J* 8.4, ArH).

***trans*-4-(Iodomethyl)-3-methyl-1-(*p*-tolylsulfonyl)pyrrolidin-2-one *trans*-2f.** Crystals, mp 157–158 °C (from hexane–AcOEt) (lit.,[8b] 150–151 °C); ν_{max}($CHCl_3$)/cm^{-1} 1730; δ_H(300 MHz) 1.16 (3 H, d, *J* 6.9, 3-Me), 2.01–2.16 (1 H, m, 4-H), 2.25 (1 H, dq, *J* 10.3 and 6.9, 3-H), 2.44 (3 H, s, ArCH_3), 3.11 (1 H, dd, *J* 10.2 and 8.2, one of 5-H_2), 3.34–3.43 (2 H, m, CH_2I), 4.10 (1 H, dd, *J* 10.2 and 7.6, one of 5-H_2), 7.35 (2 H, d, *J* 8.0, ArH) and 7.93 (2 H, d, *J* 8.4, ArH).

***cis*-4-(Iodomethyl)-3-methyl-1-(*p*-tolylsulfonyl)pyrrolidin-2-one *cis*-2f.** *Crystals*, mp 114–115.5 °C (from hexane–AcOEt) (Found: C, 39.55; H, 4.1; N, 3.5. $C_{13}H_{16}INO_3S$ requires C, 39.7; H, 4.1; N, 3.6%); ν_{max}($CHCl_3$)/cm^{-1} 1725; δ_H(300 MHz) 1.05 (3 H, d, *J* 7.3, 3-Me), 2.44 (3 H, s, ArCH_3), 2.66 (1 H, quint, *J* 7.4, 3-H), 2.71–2.81 (1 H, m, 4-H), 2.85 (1 H, d, *J* 10.2, one of CH_2I), 3.16 (1 H, dd, *J* 10.2 and 4.9, one of CH_2I), 3.74 (1 H, dd, *J* 10.5 and 4.8, one of 5-H_2), 3.99 (1 H, dd, *J* 10.5 and 6.4, one of 5-H_2), 7.34 (2 H, d-like, *J* 8.5, ArH) and 7.93 (2 H, d-like, *J* 8.4, ArH).

N-(Cyclohex-2-enyl)-2-iodo-*N*-(*p*-tolylsulfonyl)acetamide 3

Following the procedure described above for the preparation of compound **1c**, 2-bromo-*N*-(cyclohex-2-enyl)-*N*-(*p*-tolylsulfonyl)acetamide[12] (113 mg, 0.30 mmol) was treated sodium iodide (227 mg, 1.52 mmol) in acetonitrile (7 cm^3) to give *title compound* **3** (96 mg, 75%), mp 89.5–91 °C (from hexane–AcOEt) (Found: C, 43.2; H, 4.4; N, 3.2. $C_{15}H_{18}INO_3S$ requires C, 43.0; H, 4.3; N, 3.3%); ν_{max}(CCl_4)/cm^{-1} 1685, 1350 and 1160; δ_H(60 MHz) 1.5–2.3 (6 H, m), 2.43 (3 H, s, ArCH_3), 4.18 (2 H, s, CH_2I), 4.5–5.15 (1 H, m, NCH), 5.2–6.0 (2 H, m), 7.30 (2 H, *J* 8, ArH) and 7.82 (2 H, *J* 8, ArH).

Cyclisation of compound 3

With triethylborane in boiling benzene. Following the general procedure, compound **3** (181 mg, 0.43 mmol) was treated with a 1.01 mol dm^{-3} hexane solution of triethylborane (0.21 cm^3, 0.22 mmol) in boiling benzene (17 cm^3) for 10 min. The crude material was chromatographed on silica gel [hexane–AcOEt (6:1)]. The first fraction gave (3aR*,4S*,7aR*)-*octahydro*-4-*iodo*-1-(p-*tolylsulfonyl*)*indol*-2-*one* **4a** (86 mg, 48%), mp 174–175.5 °C (from hexane–AcOEt) (Found: C, 43.2; H, 4.25; N, 3.3. $C_{15}H_{18}INO_3S$ requires C, 43.0; H, 4.3; N, 3.3%); ν_{max}($CHCl_3$)/cm^{-1} 1730; δ_H(300 MHz) 1.23–1.40 (2 H, m), 1.59–1.74 (1 H, m), 1.80–1.95 (1 H, m), 2.18–2.29 (1 H, m), 2.44 (3 H, s, ArCH_3), 2.45–2.55 (1 H, m), 2.49 (1 H, dd, *J* 17.0 and 9.4, one of 3-H_2), 2.62 (1 H, dd, *J* 17.0 and 13.4, one of 3-H_2), 2.95 (1 H, dt, *J* 13.1 and 6.4, 3a-H), 4.28 (1 H, dt, *J* 12.9 and 4.7, 7a-H), 4.30–4.38 (1 H, m, 4-H), 7.32 (2 H, d, *J* 8.6, ArH) and 7.92 (2 H, d, *J* 8.4, ArH); δ_C(75.5 MHz) 21.6 (CH_3), 24.5 (CH), 24.7 (CH_2), 28.3 (CH_2), 33.2 (CH_2), 36.4 (CH_2), 41.3 (CH), 58.8 (CH), 128.2, 129.5, 135.8, 145.1 and 170.7 (C=O). The second fraction gave (3aR*,4R*,7aR*)-*octahydro*-4-*iodo*-1-(p-*tolylsulfonyl*)-*indol*-2-*one* **4b** (44 mg, 24%), mp 130–131.5 °C (from hexane–AcOEt) (Found: C, 43.3; H, 4.3; N, 3.3%); ν_{max}($CHCl_3$)/cm^{-1} 1730: δ_H(300 MHz) 1.40–1.69 (3 H, m), 1.77–2.03 (2 H, m), 2.32–2.42 (3 H, m), 2.44 (3 H, s, ArCH_3), 2.89–3.01 (1 H, m, 3a-H), 4.55–4.59 (1 H, m, 4-H), 4.61 (dt, *J* 10.6 and 6.1, 7a-H), 7.33 (2 H, d, *J* 8.1, ArH) and 7.94 (2 H, d, *J* 8.5, ArH); δ_C(75.5 MHz) 20.3 (CH_2), 21.7 (CH_3), 28.9 (CH_2), 29.6 (CH), 30.8 (CH_2), 36.3 (CH_2), 43.6 (CH), 57.8 (CH), 128.3, 129.6, 135.9, 145.1 and 171.2 (C=O).

With triethylborane in benzene at rt. A 1.01 mol dm^{-3} hexane solution of triethylborane (0.1 cm^3, 0.11 mmol) was added to a solution of compound **3** (45 mg, 0.11 mmol) in benzene (4 cm^3) at rt, and the mixture was stirred at the same temperature for 10 min. The crude material was chromatographed on silica gel [hexane–AcOEt (6:1)] to give a mixture of isomers **4a**,**b** (34 mg, 76%). The ^{1}H NMR spectrum of the crude material showed the ratio of compounds **4a**,**b** to be ~3:1.

With bis(tributyltin) in benzene under photochemical conditions. A mixture of compound **3** (44 mg, 0.11 mmol) and bis(tributyltin) (7 mg, 0.01 mmol) in benzene (4 cm^3) in a Pyrex tube was irradiated with a 350 W high-pressure mercury lamp for 10 min at 5 °C. After completion of the reaction, a 1.0 mol dm^{-3} diethyl ether solution of iodine (0.01 cm^3), diethyl ether (1 cm^3) and DBU (8 mg, 0.05 mmol) were successively added to the reaction mixture. The solvent was evaporated off and the residue was chromatographed on silica gel [hexane–AcOEt (6:1)] to give a mixture of compounds **4a**,**b** (35 mg, 80%). The ^{1}H NMR spectrum of the crude material showed the ratio of products **4a**,**b** to be ~1:1.

cis-Octahydro-1-(*p*-tolylsulfonyl)indol-2-one 5

From compound 4a. A solution of TBTH (87 mg, 0.52 mmol) and AIBN (16 mg, 0.048 mmol) in benzene (2 cm^3) was added to a boiling solution of iodo compound **4a** (100 mg, 0.24 mmol) in benzene (2 cm^3) and the mixture was refluxed for 8 h. 8% aq. KF (3 cm^3) was added to the mixture and the whole was stirred vigorously at rt for 30 min. The organic layer was separated, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel [hexane–AcOEt (5:1)] to give title compound **5** (15 mg, 21%), mp 146.5–147 °C (from hexane–AcOEt); ν_{max}($CHCl_3$)/cm^{-1} 1730; δ_H(300 MHz) 1.15–1.38 (3 H, m), 1.51–1.79 (4 H, m), 2.24 (1 H, dd, *J* 15.4 and 6.5), 2.31–2.60 (2 H, m), 2.43 (3 H, s, ArCH_3), 2.49 (1 H, d, *J* 15.4), 4.29 (1 H, dt, *J* 10.2 and 6.0, 7a-H), 7.32 (2 H, d, *J* 8.4, ArH) and 7.94 (2 H, d, *J* 8.4, ArH). Mp of this compound was identical with that (147–147.5 °C) of an authentic sample prepared according to the method reported in the literature,[12] but which was itself not reported therein.

From compound 4b. Similar treatment of stereoisomer **4b** (100 mg, 0.24 mmol) gave title compound **5** (24 mg, 34%).

1,4,5,6,7,7a-Hexahydro-1-(*p*-tolylsulfonyl)indol-2-one 7

To a solution of compound **4a** (51 mg, 0.12 mmol) in benzene (3 cm^3) was added DBU (0.09 cm^3, 0.61 mmol) and the mixture was refluxed for 1 h. The mixture was diluted with water and

extracted with diethyl ether. The extract was dried ($MgSO_4$) and concentrated. The residue was chromatographed on silica gel [hexane–AcOEt (2:1)] to give *title compound* **7** (33 mg, 93%), mp 148–149 °C (from hexane–AcOEt) (Found: C, 61.6; H, 5.9; N, 4.8. $C_{16}H_{17}NO_3S$ requires C, 61.8; H, 5.9; N, 4.8%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1725; δ_H(300 MHz) 1.17–1.39 (2 H, m), 1.51 (1 H, qt, *J* 13.5 and 2.9), 1.83–1.95 (1 H, m), 1.96–2.07 (1 H, m), 2.23 (1 H, tdd, *J* 13.1, 5.8 and 2.5, one of 7-H_2), 2.42 (3 H, s, ArCH_3), 2.76 (1 H, dt, *J* 13.6 and 2.1, one of 4-H_2), 2.91–3.02 (1 H, m), 4.41 (1 H, dd, *J* 11.0 and 5.8, 7a-H), 5.64 (1 H, br s, 3-H), 7.32 (2 H, d, *J* 8.5, ArH) and 7.95 (2 H, d, *J* 8.5, ArH); δ_C(75.5 MHz) 21.7 (CH_3), 23.0 (CH_2), 26.9 (CH_2), 29.2 (CH_2), 35.2 (CH_2), 63.8 (CH), 117.3, 127.9, 129.6, 136.3, 144.7 and 167.0 (C=O).

cis-1,3,3a,6,7,7a-Hexahydro-1-(*p*-tolylsulfonyl)indol-2-one 8 and octahydro-1-(*p*-tolylsulfonyl)cycloprop[*cd*]indol-2-one 9

Following the procedure described above for the preparation of compound **7**, compound **4b** (47 mg, 0.11 mmol) was treated with DBU (0.08 cm^3, 0.56 mmol) and the crude material was chromatographed on silica gel [hexane–AcOEt (3:1)]. The first fraction gave the *ene lactam* **8** (14 mg, 43%), mp 108–109 °C (from hexane–AcOEt) (Found: C, 61.4; H, 5.9; N, 4.7. $C_{16}H_{17}NO_3S$ requires C, 61.8; H, 5.9; N, 4.8%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1720; δ_H(300 MHz) 1.51–1.65 (2 H, m, 7-H_2), 2.10–2.18 (2 H, m, 6-H_2), 2.29 (1 H, dd, *J* 17.1 and 12.0, one of 3-H_2), 2.44 (3 H, s, ArCH_3), 2.56 (1 H, dd, *J* 17.1 and 8.4, one of 3-H_2), 2.81–2.95 (1 H, m, 3a-H), 4.42 (1 H, ddd, *J* 11.8, 7.4 and 3.1, 7a-H), 5.63 (1 H, ddt, *J* 9.9, 3.8 and 2.0, 5-H), 5.80–5.89 (1 H, m, 4-H), 7.33 (2 H, *J* 8.5, ArH) and 7.96 (2 H, d, *J* 8.5, ArH). The second fraction gave *tricycle* **9** (18 mg, 55%), mp 131–132.5 °C (from hexane–AcOEt) (Found: C, 61.85; H, 5.9; N, 4.9%); $\nu_{max}(CCl_4)/cm^{-1}$ 1720; δ_H(300 MHz) 1.03–1.22 (1 H, m), 1.33–1.46 (2 H, m), 1.51–1.65 (1 H, m), 1.79–2.03 (2 H, m), 1.86 (1 H, dd, *J* 9.0 and 6.7, 2a-H), 2.19 (1 H, dq, *J* 14.2 and 4.2), 2.28 (1 H, q, *J* 7.4, 5b-H), 2.43 (3 H, s, ArCH_3), 4.68 (1 H, ddd, *J* 7.6, 3.5 and 2.1, 5a-H), 7.32 (2 H, d, *J* 8.5, ArH) and 7.92 (2 H, d, *J* 8.5, ArH); δ_C(75.5 MHz) 14.4 (CH_2), 18.6 (CH_2), 19.6 (CH), 21.7 (CH_3), 22.1 (CH), 25.6 (CH_2), 26.1 (CH), 54.7 (CH), 128.3, 129.4, 135.6, 144.9 and 172.3 (C=O).

Cyclisation of compound 10

Following the general procedure, compound **10** (323 mg, 1.16 mmol) was treated with a 1.01 mol dm^{-3} hexane solution of triethylborane (1.63 cm^3, 1.65 mmol) in boiling benzene (47 cm^3) for 10 min. The crude material was chromatographed on silica gel (AcOEt) to give a mixture of indolinones **11a**,**b** [2b] (153 mg, 43%) as an oil; $\nu_{max}(CCl_4)/cm^{-1}$ 1695; δ_H for **11a** (300 MHz) 1.09–2.55 (7 H, m), 2.80 (3 H, s, NMe), 2.85–3.0 (1 H, m, 3a-H), 3.44 (1 H, dt, *J* 10.4 and 6.3, 7a-H) and 4.33 (1 H, ddd, *J* 12.9, 5.6 and 4.6, 4-H); δ_H for **11b** (300 MHz) 1.09–2.55 (8 H, m), 2.77 (3 H, s, NMe), 3.55 (1 H, q, *J* 4.6, 7a-H) and 4.06 (1 H, ddd, *J* 10.8, 9.0 and 4.1, 4-H). The ^{1}H NMR spectrum of the crude material showed the ratio of products **11a**,**b** to be ~1:1.4 by the integrated intensity of the signals due to the C-4 protons (δ 4.33 and 4.06, respectively).

N-[(Cyclohex-1-enyl)methyl]-2-iodo-*N*-(*p*-tolylsulfonyl)-acetamide 12

A solution of *N*-[(cyclohex-1-enyl)methyl]toluene-*p*-sulfonamide (838 mg, 3.16 mmol) in dry benzene (8 cm^3) was added slowly to a suspension of sodium hydride (60% dispersion in mineral oil, 379 mg, 9.45 mmol) in dry benzene (2 cm^3) at 0 °C, and the mixture was stirred at the same temperature for 10 min. To this mixture was added a solution of bromoacetyl bromide (1.47 g, 7.26 mmol) in dry benzene (4 cm^3) and the mixture was heated at reflux for 9 h. Water was added to the reaction mixture and the whole was extracted with diethyl ether. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel [hexane–AcOEt (10:1)] to give 2-*bromo*-N-[(*cyclohex*-1-*enyl*)*methyl*]-N-(p-*tolylsulfonyl*)*acetamide* (810 mg, 72%), mp 82–83 °C (from hexane–AcOEt) (Found: C, 49.95; H, 5.3; N, 3.4. $C_{16}H_{20}BrNO_3S$ requires C, 49.75; H, 5.2; N, 3.6%); $\nu_{max}(CCl_4)/cm^{-1}$ 1695; δ_H(60 MHz) 1.4–2.2 (8 H, m), 2.43 (3 H, s), 4.10 (2 H, s), 4.38 (2 H, br s), 5.4–5.7 (1 H, br), 7.27 (2 H, d, *J* 8.5) and 7.78 (2 H, d, *J* 8.5).

The amide (917 mg, 2.37 mmol) thus obtained was treated with sodium iodide (1.94 g, 12.9 mmol) in acetonitrile (50 cm^3) according to the general procedure described above for the preparation of compound **1c**, to give title compound **12** (864 mg, 84%) as a low melting solid [Found: $(M + H)^+$, 434.0298. $C_{16}H_{21}INO_3S$ requires *m*/*z*, 434.0287]; $\nu_{max}(CCl_4)/cm^{-1}$ 1695; δ_H(60 MHz) 1.4–2.2 (8 H, m), 2.42 (3 H, s), 3.93 (2 H, s), 4.37 (2 H, br s), 5.4–5.7 (1 H, br), 7.25 (2 H, d, *J* 8.5) and 7.76 (2 H, d, *J* 8.5).

Cyclisation of compound 12

Following the general procedure, compound **12** (144 mg, 0.33 mmol) was treated with a 1.01 mol dm^{-3} hexane solution of triethylborane (0.24 cm^3, 0.24 mmol) in boiling benzene (15 cm^3) and the crude material was chromatographed on silica gel [hexane–AcOEt (6:1)]. The first fraction gave (5R*,6R*)-6-*iodo*-2-(p-*tolylsulfonyl*)-2-*azaspiro*[4.5]*decan*-3-*one* **13b** (45 mg, 31%), mp 147.5–148.5 °C (from hexane–AcOEt) (Found: C, 44.3; H, 4.6; N, 3.1. $C_{16}H_{20}INO_3S$ requires C, 44.35; H, 4.65; N, 3.2%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1730; δ_H(300 MHz) 1.37–1.70 (5 H, m), 1.86–2.01 (2 H, m), 2.13–2.23 (1 H, m), 2.38 (1 H, d, *J* 17.5, one of 4-H_2), 2.43 (3 H, s, ArCH_3), 2.70 (1 H, d, *J* 17.5, one of 4-H_2), 3.75 and 3.78 (1 H each, ABq, *J* 10.2, 1-H_2), 4.28 (1 H, dd, *J* 10.5 and 3.8, 6-H), 7.34 (2 H, d, *J* 8.5, ArH) and 7.93 (2 H, d, *J* 8.5, ArH). The second fraction gave (5R*,6S*)-6-*iodo*-2-(p-*tolylsulfonyl*)-2-*azaspiro*[4.5]*decan*-3-*one* **13a** (57 mg, 40%), mp 158–159 °C (from hexane–AcOEt) (Found: C, 44.3; H, 4.6; N, 3.1%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1730; δ_H(300 MHz) 1.37–1.71 (5 H, m), 1.89–2.05 (3 H, m), 2.43 (1 H, d, *J* 17.6, one of 4-H_2), 2.44 (3 H, s, ArCH_3), 2.52 (1 H, d, *J* 17.6, one of 4-H_2), 3.76 and 3.80 (1 H, each, ABq, *J* 10.5, 1-H_2), 4.27 (1 H, t, *J* 6.1, 6-H), 7.34 (2 H, d, *J* 8.5, ArH) and 7.94 (2 H, d, *J* 8.5, ArH).

2-(*p*-Tolylsulfonyl)-2-azaspiro[4.5]decan-3-one 14

From *endo*-iodide 13a. Following the procedure described for the preparation of compound **5**, compound **13a** (56 mg, 0.13 mmol) was treated with TBTH (75 mg, 0.26 mmol) and AIBN (5 mg, 0.025 mmol) to give *title compound* **14** (14 mg, 35%), mp 116–116.5 °C (from hexane–AcOEt) (Found: C, 62.5; H, 6.9; N, 4.6. $C_{16}H_{21}NO_3S$ requires C, 62.5; H, 6.9; N, 4.6%); $\nu_{max}(CCl_4)/cm^{-1}$ 1740; δ_H(300 MHz) 1.42 (9 H, br s), 1.58 (1 H, s), 2.27 (2 H, s, 4-H_2), 2.44 (3 H, s, ArCH_3), 3.65 (2 H, s, 1-H_2), 7.34 (2 H, d, *J* 8.1 ArH) and 7.91 (2 H, d, *J* 8.1 ArH); δ_C(75.5 MHz) 21.7 (CH_3), 22.5 (CH_2), 25.4 (CH_2), 35.7 (CH_2), 36.6 (quaternary C), 44.8 (CH_2), 57.7 (CH_2), 128.0, 129.6, 135.2, 145.1 and 172.6 (C=O).

From *exo*-iodide 13b. Similar treatment of compound **13b** (54 mg, 0.13 mmol) gave title compound **14** (37 mg, 95%).

Octahydro-2-(*p*-tolylsulfonyl)benzo[1,3]cyclopropa[1,2-*c*]pyrrol-3-one 15

Following a procedure similar to that described for the preparation of compound **7**, compound **13a** (54 mg, 0.13 mmol) was treated with DBU (0.1 cm^3, 0.64 mmol) and the crude material was chromatographed on silica gel [hexane–AcOEt (3:1)] to give *title spirotricycle* **15** (28 mg, 73%), mp 162.5–163.5 °C (from hexane–AcOEt) (Found: C, 62.65; H, 6.2; N, 4.3. $C_{16}H_{19}NO_3S$ requires C, 62.9; H, 6.3; N, 4.6%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1720; δ_H(300 MHz) 1.10–1.53 (5 H, m), 1.55–1.71 (2 H, m), 1.74–2.01 (3 H, m), 2.44 (3 H, s, ArCH_3), 3.55 (1 H, d, *J* 9.8), 3.93 (1 H, dd, *J* 9.8 and 1.0), 7.33 (2 H, d, *J* 8.0, ArH) and 7.89 (2 H, d, *J* 8.0, ArH); δ_C(75.5 MHz) 20.9 (CH_2), 21.2 (CH_2), 21.7 (CH_3), 22.9 (CH_2), 24.3 (quaternary C), 24.7 (CH_2), 25.2 (CH), 31.9 (CH), 53.7 (CH_2), 128.0, 129.6, 135.2, 144.9 and 173.1 (C=O).

2-(*p*-Tolylsulfonyl)-2-azaspiro[4.5]dec-6-en-3-one 16

Following a procedure similar to that described for the preparation of compound **7**, compound **13b** (45 mg, 0.10 mmol) was treated with DBU (0.16 cm^3, 1.07 mmol) and the crude material was chromatographed on silica gel [hexane–AcOEt (3:1)] to give *title ene lactam* **16** (27 mg, 85%), mp 110.5–111.5 °C (from hexane–AcOEt) (Found: C, 62.7; H, 6.2; N, 4.4%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1730; δ_H(300 MHz) 1.45–1.69 (4 H, m), 1.96–2.05 (2 H, m), 2.27 and 2.41 (1 H each, ABq, *J* 17.1, 4-H_2), 2.45 (3 H, s, ArCH_3), 3.62 and 3.72 (1 H, each, ABq, *J* 10.1, 1-H_2), 5.41 (1 H, dt, *J* 10.0 and 2.2, 6-H), 5.81 (1 H, dt, *J* 9.9 and 3.8, 7-H), 7.34 (2 H, d, *J* 8.4, ArH) and 7.91 (2 H, d, *J* 8.4, ArH); δ_C(75.5 MHz) 19.2 (CH_2), 21.7 (CH_3), 24.7 (CH_2), 33.3 (CH_2), 37.1 (quaternary C), 46.3 (CH_2), 57.7 (CH_2), 128.0, 129.7, 130.0, 130.4, 135.2, 145.1 and 172.3 (C=O).

Cyclisation of compound 17

Following the general procedure, compound **17** (269 mg, 1.02 mmol) was treated with a 1.01 mol dm^{-3} hexane solution of triethylborane (0.40 cm^3, 0.41 mmol) in boiling benzene (40 cm^3) for 10 min. The crude material was chromatographed on silica gel (AcOEt) to give (1*R*,7a*S*)-1-(iodomethyl)pyrrolizidin-3-one **18** (183 mg, 68%) containing a trace amount of its (1*S*,7a*S*) isomer. The mixture was recrystallised from hexane to give pure compound **18**, mp 46 °C (lit.,[2a] 48–49 °C); $[\alpha]_D^{21}$ −22.9 (*c* 2.10, EtOH) {lit.,[2a] $[\alpha]_D^{25}$ −23.9 (*c* 1.13, EtOH)}; $\nu_{max}(CCl_4)/cm^{-1}$ 1680; δ_H(300 MHz) 1.38–1.52 (1 H, m), 1.97–2.21 (2 H, m), 2.23–2.32 (1 H, m), 2.35–2.57 (2 H, m), 2.63 (1 H, dd, *J* 15.8 and 8.5), 3.02–3.13 (1 H, m), 3.23 (1 H, dd, *J* 10.5 and 7.6), 3.32 (1 H, dd, *J* 10.5 and 5.4) and 3.51–3.66 (2 H, m).

(1*R*,7a*S*)-1-Methylpyrrolizidin-3-one 19

Tributyl(hexadecyl)phosphonium bromide (17 mg, 0.032 mmol) and aq. sodium borohydride (61 mg, 1.62 mmol in 0.27 cm^3) were added successively to a solution of iodide **18** containing its trace (1*S*,8*S*) isomer (total both isomers 86 mg, 0.32 mmol) in toluene (0.27 cm^3) and the mixture was heated at 80 °C for 2 h. The reaction mixture was extracted with ethyl acetate and the extract was washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (AcOEt) to give title product **19**[1d] (34 mg, 76%) as an oil. The product ratio of 1-*exo*:1-*endo* isomers was estimated to be >95:<5 by integrated intensity of the peak heights of signals due to the 1-methyl doublets appearing at δ 1.16 and 0.98, respectively.

Cyclisation of compound 21

Following the general procedure, compound **21** (207 mg, 0.92 mmol) was treated with a 1.01 mol dm^{-3} hexane solution of triethylborane (0.9 cm^3, 0.92 mmol) in boiling benzene (35 cm^3) for 10 min. The crude material was chromatographed on silica gel [hexane–AcOEt (3:1)] to give dihydro-4-(iodomethyl)furan-2(3*H*)-one[2b] **22** (95 mg, 46%) as an oil; $\nu_{max}(CCl_4)/cm^{-1}$ 1790; δ_H(300 MHz) 2.36 (1 H, dd, *J* 17.7 and 7.5, one of 3-H_2), 2.71 (1 H, dd, *J* 17.7 and 8.4, one of 3-H_2), 2.89 (1 H, septuplet, *J* ~7, 4-H), 3.23 (1 H, dd, *J* 10.2 and 7.1, one of ICH_2), 3.28 (1 H, dd, *J* 10.2 and 6.5, one of ICH_2), 4.03 (1 H, dd, *J* 9.3 and 6.6, one of 5-H_2) and 4.45 (1 H, dd, *J* 9.4 and 7.3, one of 5-H_2).

Cyclisation of compound 23

Following the general procedure, compound **23** (150 mg, 0.56 mmol) was treated with a 1.01 mol dm^{-3} hexane solution of triethylborane (0.56 cm^3, 0.56 mmol) in boiling benzene (23 cm^3) for 10 min. The crude material was chromatographed on silica gel [hexane–AcOEt (4:1)] to give a mixture of (3a*R**,4*S**,7a*R**)- and (3a*R**,4*R**,7a*R**)-*cis*-hexahydro-4-iodobenzofuran-2(3*H*)-ones **24a**,**b**[2b] (98 mg, 65%); $\nu_{max}(CCl_4)/cm^{-1}$ 1780; δ_H(300 MHz) for the major isomer **24b** 1.50–1.78 (3 H, m), 1.91–2.06 (1 H, m), 2.23–2.44 (2 H, m), 2.55 (1 H, d, *J* 17.2, one of 3-H_2), 2.73 (1 H, dd, *J* 17.2 and 6.7, one of 3-H_2), 2.83–2.92 (1 H, m, 3a-H), 3.86 (1 H, ddd, *J* 12.2, 10.8 and 4.0, 4-H) and 4.47 (1 H, q, *J* 3.6, 7a-H); δ_H(300 MHz) for the minor isomer **24a** (diagnostic data only) 3.12–3.24 (1 H, m, 3a-H) and 4.27 (1 H, dt, *J* 12.7 and 5.1, 4-H). The ^{1}H NMR spectrum of the mixture showed the ratio of products **24a** and **24b** to be ~1:5.1 by the integrated intensity of the peak heights of the signals due to the C-4 protons appearing at δ 4.27 and 3.86, respectively. Recrystallisation of the mixture from hexane–AcOEt gave a pure sample of compound **24b**; mp 105.5–107 °C (lit.,[2b] 97–99 °C).

Cyclisation of compound 25

Compound **25** (115 mg, 0.35 mmol) was treated with a 1.01 mol dm^{-3} hexane solution of triethylborane (0.35 cm^3, 0.35 mmol) in benzene (15 cm^3) at rt for 10 min. The ^{1}H NMR spectrum of the crude material showed it to contain approximately equal amounts of (4S)- and (4R)-4-*iodomethyl*-N-[(S)-1-*phenylethyl*]-*pyrrolidin*-2-*one* **26a** and **26b**, which were separated by chromatography on silica gel [hexane–AcOEt (3:1)]. The first fraction gave *S*-isomer **26a** (50 mg, 43%) as an oil (Found: C, 47.8; H, 5.2; N, 4.0. $C_{13}H_{16}INO_3$ requires C, 47.4; H, 4.9; N, 4.25%); $[\alpha]_D^{26}$ −93.1 (*c* 0.75, $CHCl_3$); $\nu_{max}(CCl_4)/cm^{-1}$ 1670; δ_H(300 MHz) 1.54 (3 H, d, *J* 7.1, CHCH_3), 2.25 (1 H, dd, *J* 16.1 and 6.4, one of 3-H_2), 2.44–2.57 (1 H, m, 4-H), 2.61 (1 H, dd, *J* 16.1 and 8.5, one of 3-H_2), 3.05 (1 H, dd, *J* 10.1 and 7.3), 3.14 (1 H, dd, *J* 10.1 and 7.8), 3.18 (1 H, dd, *J* 10.0 and 7.4), 3.26 (1 H, dd, *J* 10.0 and 5.7), 5.50 (1 H, q, *J* 7.1, C*H*CH_3) and 7.25–7.39 (5 H, m, ArH). The second fraction gave *R*-isomer **26b** (31 mg, 27%) as an oil (Found: C, 47.1; H, 5.0; N, 3.9%); $[\alpha]_D^{26}$ −66.6 (*c* 1.0, $CHCl_3$); $\nu_{max}(CCl_4)/cm^{-1}$ 1670; δ_H(300 MHz) 1.53 (3 H, d, *J* 7.2, CHCH_3), 2.20 (1 H, dd, *J* 19.4 and 9.4, one of 3-H_2), 2.58–2.72 (3 H, m, one of 3-H_2, 4-H, one of 5-H_2), 3.02 (1 H, dd, *J* 10.0 and 7.6, one of ICH_2), 3.13 (1 H, dd, *J* 10.0 and 5.7, one of ICH_2), 3.42–3.51 (1 H, m, one of 5-H_2), 5.50 (1 H q, *J* 7.1, C*H*CH_3) and 7.26–7.40 (5 H, m, ArH).

When the reaction was carried out at 0 °C, essentially the same result as that above was obtained. Thus, compounds **26a** (38 mg, 39%) and **26b** (22 mg, 23%) were obtained from substrate **25** (97 mg, 0.295 mmol).

(4*S*)- and (4*R*)-4-Methyl-*N*-[(*S*)-1-phenylethyl]pyrrolidin-2-one 27a and 27b

Following the procedure described for the preparation of compound **19**, compound **26a** (46 mg, 0.14 mmol) was treated with sodium borohydride (28 mg, 0.74 mmol) in the presence of tributyl(hexadecyl)phosphonium bromide (7 mg, 0.015 mmol), and work-up gave compound **27a**[14] (25 mg, 88%) as an oil; $\nu_{max}(CCl_4)/cm^{-1}$ 1680; δ_H(300 MHz) 1.09 (3 H, d, *J* 6.7, 4-CH_3), 1.51 (3 H, d, *J* 7.1, PhCHCH_3), 2.07 (1 H, dd, *J* 16.5 and 7.2, one of 3-H_2), 2.22–2.39 (1 H, m, 4-H), 2.57 (1 H, dd, *J* 16.5 and 8.4, one of 3-CH_2), 2.87 (1 H, dd, *J* 9.4 and 6.4, one of 5-H_2), 3.09 (1 H, dd, *J* 9.4 and 7.6, one of 5-H_2), 5.49 (1 H q, *J* 7.1, PhC*H*CH_3) and 7.23–7.38 (5 H, m, ArH).

Similar treatment of isomeric iodide **26b** (29 mg, 0.093 mmol) gave compound **27b**[14] (18 mg, 96%) as an oil; $\nu_{max}(CCl_4)/cm^{-1}$ 1680; δ_H(300 MHz) 0.97 (3 H, d, *J* 6.8, 4-CH_3), 1.51 (3 H, d, *J* 7.1, PhCHCH_3), 2.03 (1 H, dd, *J* 16.5 and 6.3, one of 3-H_2), 2.29–2.41 (1 H, m, 4-H), 2.51 (1 H, dd, *J* 9.4 and 6.5, one of 5-H_2), 2.59 (1 H, dd, *J* 16.5 and 8.4, one of 3-H_2), 3.42 (1 H, dd, *J* 9.3 and 7.5, one of 5-H_2), 5.50 (1 H, q, *J* 7.1, PhC*H*CH_3) and 7.24–7.38 (5 H, m, ArH).

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