Enantioselective Synthesis of (+)-Indolizidine, (+)-Laburnine and (+)-Elaeokanines A and C using the Diels–Alder Reaction of α-(2-*exo*-Hydroxy-10-bornylsulfinyl)maleimide

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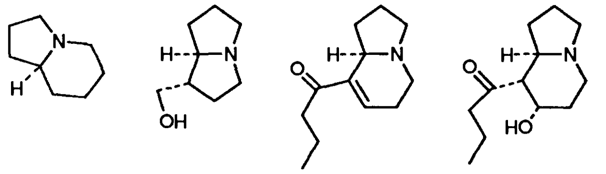
The Diels–Alder adduct **5** derived from the *N*-butynylmaleimide **6** and cyclopentadiene has been transformed into the tetracyclic lactams **12** and **19** *via* a common precursor **9**. The lactams **12** and **19** have been converted into (+)-indolizidine **1** and (+)-laburnine **2**, respectively, *via* retro-Diels–Alder reaction. Similar methodology has been successfully applied to the synthesis of (+)-elaeokanine A **3** and (+)-elaeokanine C **4**.

In the preceding paper,[1] we described a convenient route to chirally functionalised pyrrolines. The route involves (i) an asymmetric Diels–Alder reaction using a chiral sulfinylmaleimide, (ii) diastereoselective reduction, (iii) stereoselective *N*-acyliminium addition and (iv) retro-Diels–Alder reaction. The reaction sequence would provide a useful, enantioselective route to functionalised pyrrolizidines and indolizidines. We now report the utilisation of this sequence in the synthesis of bicyclic alkaloids **1**–**4**.[2]



1 **2** **3** **4**

Results and Discussion

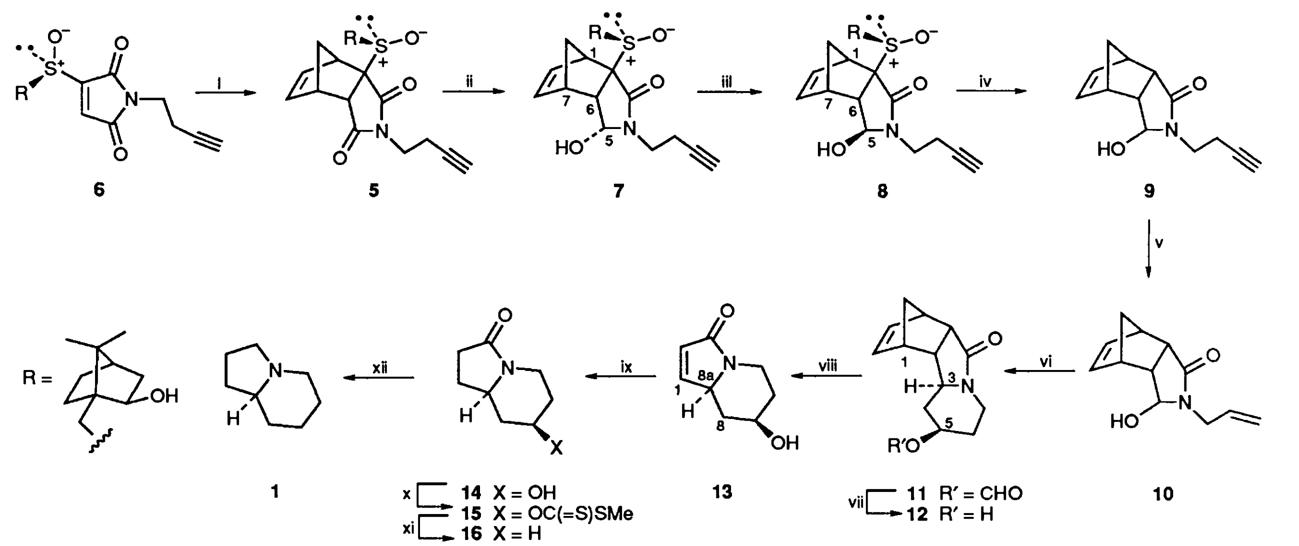
Synthesis of (+)-Indolizidine and (+)-Laburnine.—Indolizidine **1**, although not naturally occurring, has been considered as a typical synthetic target molecule[3] because of the widespread occurrence of indolizidine alkaloids in Nature.[4] On the other hand, one of the pyrrolizidine alkaloids, 1-(hydroxymethyl)pyrrolizidine **2**, has been isolated, and named trachelanthamidine[5] and laburnine[6] for the (−)- and (+)-enantiomer, respectively. Along with a number of racemic syntheses[7] of compound **2**, some enantioselective syntheses of (−)-**2**[8] and (+)-**2**[8a,9] have been reported.

The synthesis of (+)-indolizidine **1** is depicted in Scheme 1 and commences with a Diels–Alder adduct **5**,[1] which is easily available from the *N*-(3-butynyl)maleimide **6** and cyclopentadiene. The adduct **5** was transformed into the hydroxy lactam **7** by sodium borohydride reduction according to the procedure described previously.[10] The regiochemistry of the hydroxy group in compound **7** could be confirmed by coupling (*J* 4.2 Hz) of 5-H with 6-H in the ^{1}H NMR spectrum. The stereochemistry of the hydroxy group in compound **7** is of little importance since the stereocentre is subsequently obliterated, and is assigned as depicted in Scheme 1. Strong support for the assignment was provided by epimerisation of compound **7** into compound **8**: treatment of compound **7** with sodium ethoxide in ethanol at room temperature for 5 h afforded epimer **8** in quantitative yield. Comparison of two molecular models for epimers **7** and **8** suggests that the dihedral angle between 5-H and 6-H in compound **8** is nearly 90°. It seemed obviously that the lack of coupling (*J* 0 Hz) between the 5-H and 6-H protons in the ^{1}H NMR spectrum of epimer **8** shows a *trans* relationship between the two hydrogens.

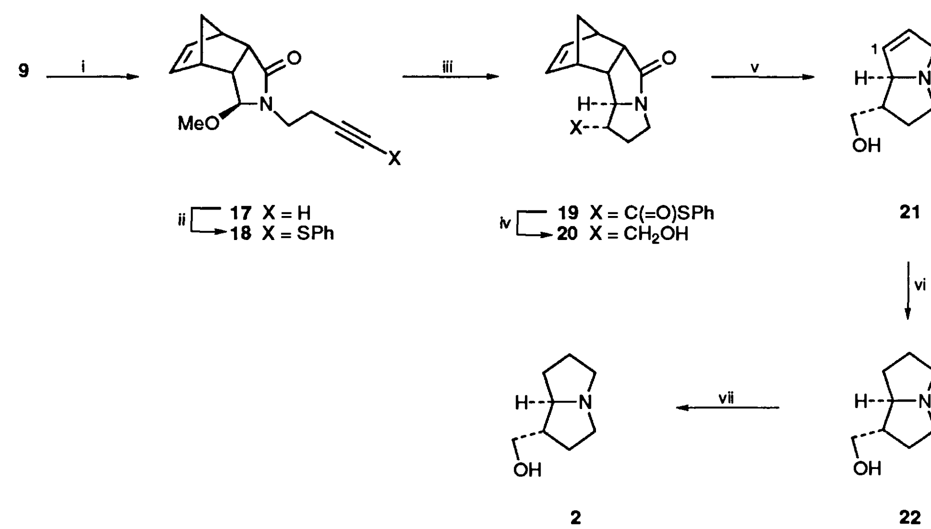
Desulfinylation of compound **8** with samarium(II) diiodide in the presence of hexamethylphosphoric triamide (HMPA) afforded the hydroxy lactam **9** in 88% yield. Partial hydrogenation of alkyne **9** over Pd–$BaSO_4$ afforded the but-3-enyl lactam **10** in 99% yield. Exposure of ene-ol **10** to formic acid at room temperature for 12 h furnished the formyl ester **11** in 92% yield. The transformation of the alcohol **10** into ester **11** had been accomplished by Speckamp and co-workers[11] in a racemic series and the spectroscopic data of our compounds **10** and **11** were in good agreement with those reported. Hydrolysis of formate **11** produced the alcohol **12**, which upon flash vacuum pyrolysis (FVP) (450 °C; 0.5 Pa) afforded the bicyclic alcohol **13** as a crystalline material in 83% yield. The minor product (< 5% yield) was assumed to be the C(8a)-epimer of **13** arising from thermal isomerisation[12] during FVP, but was not fully characterised. Careful hydrogenation of the unsaturated lactam **13** over platinum on alumina in methanol gave the saturated lactam **14**, in 99% yield. It was observed that, in hydrogenation using other catalysts (*e.g.* PtO_2 or Pd–C), a by-product, the C(8a)-epimer of **13**, was invariably formed also. Attempts to transform the alcohol **14** into indolizidine **1** by tosylation followed by reduction with lithium aluminium hydride were unsuccessful. Removal of the hydroxy group in compound **14** was therefore accomplished by the formation of the xanthate **15** (80% yield), and subsequent reduction of compound **15** with tributyltin hydride[13] and 2,2′-azoisobutyronitrile (AIBN) in benzene (reflux, 10 h, 76% yield). The spectroscopic data of the lactam **16** obtained were in good agreement with those of the racemate prepared previously.[14] Finally, reduction of lactam **16** with lithium aluminium hydride afforded indolizidine **1** {$[\alpha]_D^{24}$ +9.0 (*c* 0.74, EtOH);† lit.,[3d] $[\alpha]_D^{23}$ +9.3 ± 0.6 (*c* 1.77, EtOH)}.

On the other hand the hydroxy lactam **9** was treated with pyridinium toluene-*p*-sulfonate (PPTS)[15] in methanol to give the methoxy lactam **17** in 90% yield (Scheme 2). Treatment of methoxy lactam **17** with diphenyl disulfide and lithium hexamethyldisilazide (LiHMDS) afforded the phenylthio lactam **18** in 96% yield. Exposure of sulfide **18** to formic acid at room temperature for 12 h gave the tetracyclic lactam **19** in 80% yield. A similar *N*-acylimino cyclisation has been developed, albeit in a monocyclic system.[16] For the monocyclic system, *N*-acylimino addition resulted in the formation

† Units for $[\alpha]_D$ are 10^{-1} deg cm^2 g^{-1}.

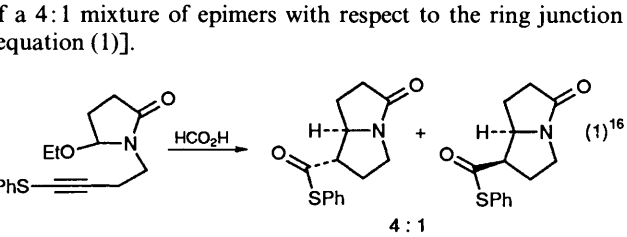


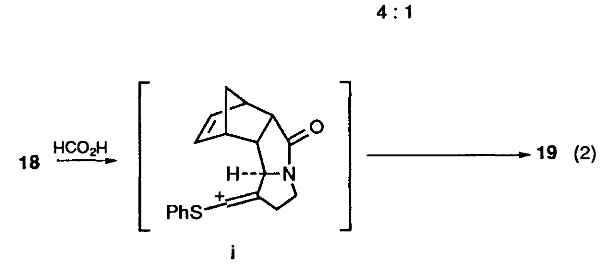
Scheme 1 *Reagents and conditions:* i, ref. 1; ii, $NaBH_4$, EtOH–H^+; iii, EtONa, EtOH; iv, SmI_2, Bu^{t}OH, HMPA, THF; v, H_2, 5% Pd–$BaSO_4$, pyridine (cat.), MeOH; vi, HCO_2H; vii, KOH, aq. EtOH; viii, FVP (450 °C; 0.5 Pa); ix, H_2, 5% Pt on alumina, MeOH; x, NaH, imidazole (cat.), CS_2; then MeI; xi, Bu_3SnH, AIBN (cat.), PhH; xii, $LiAlH_4$, Et_2O



Scheme 2 *Reagents and conditions:* i, PPTS, MeOH; ii, lithium hexamethyldisilazide; then $(PhS)_2$; iii, HCO_2H; iv, $NaBH_4$, MeOH; v, FVP (500 °C; 1.3×10^{-3} Pa); vi, H_2, PtO_2,EtOH; vii, $LiAlH_4$, THF

of a 4:1 mixture of epimers with respect to the ring junction [equation (1)].

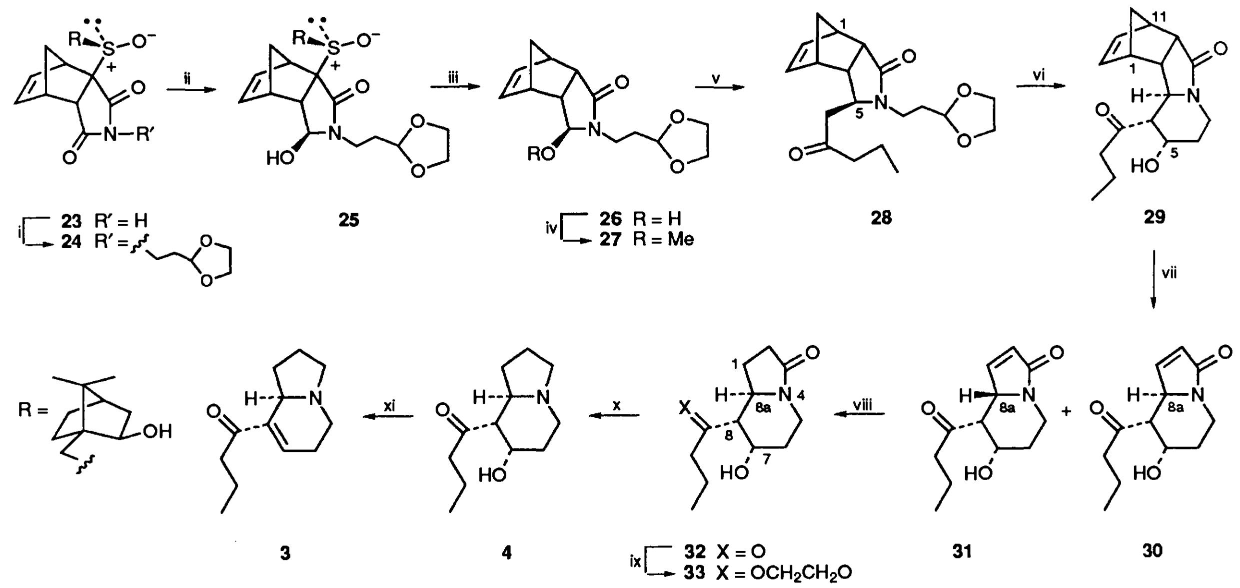




With the lactam **18** fused with a bicyclo[2.2.1]heptene system, the cyclisation proceeded with high diastereoselectivity, *via* the vinyl cation (**i**) [16] being captured by formic acid from the sterically less hindered convex face [equation (2)]. Reduction of the thioester **19** with sodium borohydride afforded the alcohol **20** in 97% yield. FVP (500 °C; 1.3×10^{-3} Pa) of tetracycle **20** produced the α,β-unsaturated lactam **21** in 86% yield. No other by-product such as lactam **22** was detected in the crude product. Catalytic hydrogenation of unsaturated lactam **21** over platinum oxide followed by reduction of the resulting saturated lactam **22** with lithium aluminium hydride furnished (+)-laburnine **2** {$[\alpha]_D^{25}$ +11.1 (*c* 1.1, EtOH); lit.,[6] $[\alpha]_D$ +15.4 (*c* 1.44, EtOH); lit.,[8a] $[\alpha]_D^{22}$ +14.6 (*c* 3.25, EtOH); lit.,[9] $[\alpha]_D^{20}$ +13.63 (*c* 1.22, EtOH)}, whose ^1H NMR and ^{13}C NMR spectra were in good agreement with those of its enantiomer (−)-**2** reported previously.[8c]

Synthesis of (+)-Elaeokanine A and (+)-Elaeokanine C.—(+)-Elaeokanine A **3** and (−)-elaeokanine C(−)-**4**, the *Elaeocarpus* family of the indolizidine alkaloids, have been isolated and their structures have been determined.[17] Although a number of syntheses of elaeokanines **3** and **4** have been achieved in racemic form,[18] only a few enantioselective syntheses[17b,19] of compounds **3** and **4** have been reported to date.

Having achieved the synthesis of bicyclic alkaloids **1** and **2** *via* intramolecular *N*-acylimino addition, we extended the method-



Scheme 3 *Reagents and conditions:* i, NaH, dimethylformamide, 2-(2-bromoethyl)-1,3-dioxolane; ii, $NaBH_4$, EtOH; iii, SmI_2, Bu^{t}OH, HMPA, THF; iv, PPTS, MeOH; v, BF_3·ET_2O, 2-(trimethylsiloxy)-pent-1-ene, CH_2Cl_2; vi, conc. HCl; vii, FVP (425 °C; 0.5 Pa); viii separation; H_2, 5% Pt on alumina, Bu^{t}OH; ix, PPTS, ethylene glycol, $(EtO)_3CH$, 4 Å molecular sieves; x, $LiAlH_4$, THF; then 10% H_2SO_4; xi, aq. NaOH, EtOH

ology to an intermolecular *N*-acylimino addition, which would enable us to attempt synthesis of the other bicyclic alkaloids previously mentioned. The sequence would allow the enantioselective synthesis of elaeokanine A and elaeokanine C (Scheme 3). The starting material **23** is easily available by asymmetric Diels–Alder reaction, as was described in the preceding paper.[1] Treatment of compound **23** with 2-(2-bromoethyl)-1,3-dioxolane and sodium hydride gave the acetal **24** in 93% yield. Regioselective reduction of one of the imidocarbonyls in compound **24** with sodium borohydride (to give lactam **25**) followed by desulfinylation with samarium(II) diiodide afforded the hydroxy lactam **26** in 64% yield. Under the $NaBH_4$ reduction conditions followed by 'basic work-up',[1] the thermodynamically more stable γ-hydroxy lactam **25** was produced exclusively. Treatment of the alcohol **26** with PPTS in methanol gave the methoxy lactam **27**, which was subjected to an *N*-acylimino addition with 2-(trimethylsiloxy)pent-1-ene.[20] The choice of Lewis acid was crucial,[21] and the use of $TiCl_4$ or $SnCl_4$ as a Lewis acid for the addition was inefficient, resulting in cleavage of the dioxolane ring and/or decomposition of starting material. After several attempts, the reaction of the lactam **27** with the silyl enol ether in the presence of BF_3·Et_2O complex was found to give the required acetal **28** in 91% yield, as a single product. Although the spectroscopic data of compound **28** were of no help in the assignment of the stereochemistry of the newly created C(5) position, the relative stereochemistry could be tentatively assigned as depicted in Scheme 3, and was subsequently confirmed by the ultimate success of the synthesis of the target molecules **3** and **4**. Acid-catalysed aldol cyclisation of compound **28** produced the keto alcohol **29** in 79% yield. FVP (435 °C; 0.5 Pa) of compound **29** proceeded smoothly to give the pyrrolidines **30** and **31** in the ratio 3:1, in quantitative yield. The major product **30** was isolated in 52% yield by crystallisation from the crude product. The minor product was assumed to be epimer **31** which would arise from isomerisation during the heating, and was inseparable from its epimer **30** on chromatography. Hydrogenation of compound **30** over 5% Pt on alumina produced the saturated lactam **32** in quantitative yield. Other catalysts such as platinum oxide for the hydrogenation resulted in the formation of a ~1:1 mixture of C(8a) epimers. After the carbonyl group in keto lactam **32** had been protected as the ethylene ketal, the resulting ketal **33** was treated with lithium aluminium hydride followed by acid to give (+)-elaeokanine C **4** {$[\alpha]_D^{26}$ +36.9 (*c* 0.58, $CHCl_3$); lit.,[19b] $[\alpha]_D^{23}$ +47 (*c* 0.4, $CHCl_3$)}. The enantiomeric excess of compound **4** was estimated as >93%, judging from ^{19}F NMR analysis of the Mosher's amide derivative.[22] Treatment of compound **4** with sodium hydroxide (10% aq. NaOH in ethanol; reflux; 1 h) furnished (+)-elaeokanine A **3** {$[\alpha]_D^{26}$ +63.0 (*c* 0.93, $CHCl_3$); lit.,[19a] $[\alpha]_D^{22}$ +49 (*c* 0.5, $CHCl_3$); lit.,[19b] $[\alpha]_D^{23}$ +47 (*c* 0.31, $CHCl_3$)} in 66% yield.

In conclusion, we have shown that the use of a bicyclo[2.2.1]heptene moiety as a control element provides a highly diastereoselective *N*-acylimino addition, and generates pyrrolidine derivatives through retro-Diels–Alder reaction. The methodology has been applied to the enantioselective synthesis of some alkaloids.

Experimental

General.—The general experimental conditions were as in the preceding paper.[1] ^{19}F NMR spectra were measured in $CDCl_3$ with $CFCl_3$ as internal standard and were taken with a JEOL GX-270 (254 MHz) spectrometer.

(1R,2R,5R,6S,7S)-(+)-4-(*But-3″-ynyl*)-5-*hydroxy*-2-({(1′S,2′R,4′R,R$_S$)-2′-*hydroxy*-7′,7′-*dimethylbicyclo*[2′.2′.1′]-*heptan*-1′-*yl*}*methylsulfinyl*)-4-*azatricyclo*[5.2.1.0^{2,6}]*dec*-8-*en*-3-*one* **7**.—To a solution of compound **5**[1] (9.70 g, 23 mmol) in dry methanol (300 cm^3) at 0 °C was added sodium borohydride (5.40 g, 0.12 mmol) in one portion. To the mixture were added 2–3 drops of ethanolic hydrochloric acid [prepared from 3 drops of conc. hydrochloric acid and ethanol (5 cm^3)] at regular intervals (~15 min). After 3 h, the excess of sodium borohydride was decomposed by careful addition of cold water (100 cm^3) and the aqueous phase was neutralised by addition of dil. hydrochloric acid using a pH test paper. Most of the methanol was evaporated off and the aqueous phase was extracted with dichloromethane (100 cm^3 × 5). The combined extracts were washed with saturated brine (100 cm^3), dried, and concentrated. The residual solid was recrystallised from aq. methanol to give *compound* **7** (7.56 g, 78%) as needles, m.p. 205–206 °C (Found: C, 66.0; H, 7.5; N, 3.2. $C_{23}H_{31}NO_4S$ requires C, 66.16; H, 7.48; N, 3.36%); $[\alpha]_D^{26}$ +51.8 [*c* 1.0, tetrahydrofuran (THF)]; ν_{max}(KBr)/cm^{-1} 3380, 3310, 2940, 1650, 1460, 1350 and 1030; δ_H 0.90 (3 H, s, Me), 1.34 (3 H, s, Me), 1.06–2.06 (7 H, m, bornyl H), 1.50 (1 H, d, *J* 8.5, 10-H^a), 2.21 (1 H, d, *J* 8.5, 10-H^b), 2.50–2.80 (2 H, m, 2″-H_2), 2.74 (1 H, t, *J* 2.7, 4″-H), 3.27 (1 H, br s, 1- or 7-H), 3.51 (1 H, dd, *J* 7.6 and 4.2, 6-H), 3.58 (1 H, br t, *J* 6.8, NC*H*H), 3.69 (1 H, d, *J* 13, SC*H*H), 3.70 (1 H, d, *J* 6.8, NCH*H*), 3.76 (1 H, d, *J* 13, SCH*H*), 3.89 (1 H, br s, 7- or 1-H), 4.30 (1 H, ddd, *J* 4.0, 3.5 and 3.2, 2′-H), 4.83 (1 H, br d, *J* 3.2, OH), 5.81 (1 H, dd, *J* 7.6 and 5.4, 5-H), 6.25 (1 H, dd, *J* 5.5 and 3.2, CH=), 6.73 (1 H, dd, *J* 5.5 and 2.8, CH=) and 8.55 (1 H, d, *J* 5.4, OH); *m/z* 418 (M^+ + 1), 400, 334, 316, 265 and 199.

The C-5 Epimer **8**.—To a solution of sodium ethoxide in ethanol [prepared from sodium (50 mg) and absolute ethanol (20 cm^3)] was added compound **7** (50 mg, 0.12 mmol), and the mixture was stirred at room temperature for 5 h. The mixture was then quenched with cold water (5 cm^3) and the solvent was evaporated off. The aqueous phase was extracted with dichloromethane (5 cm^3 × 5). The combined extracts were washed with saturated brine (10 cm^3), dried and concentrated. The residue was purified by chromatography on silica with hexane–ethyl acetate (1:1) to give compound **8** (50 mg, 100%) as an oil, δ_H 0.87 (3 H, s, Me), 1.12 (3 H, s, Me), 1.61–1.98 (9 H, m, bornyl H and 10-H_2), 2.04 (1 H, t, *J* 2.7, 4″-H), 2.77 (1 H, d, *J* 4.2, 6-H), 2.41 (2 H, dt, *J* 6.6 and 2.7, 2″-H_2), 2.99 (1 H, d, *J* 13, C*H*HS), 3.24 (1 H, d, *J* 13, CH*H*S), 3.30 (1 H, br s, 7-H), 3.39 (1 H, dt, *J* 13 and 6.6, 1″-H^a), 3.45 (1 H, dt, *J* 13 and 6.6, 1″-H^b), 3.56 (1 H, br s, 1-H), 3.75 (1 H, d, *J* 3.2, OH), 3.88 (1 H, d, *J* 8.3, 5-H), 4.02 (1 H, ddd, *J* 7.6, 3.7 and 3.2, 2′-H), 4.82 (1 H, d, *J* 8.3, OH), 6.26 (1 H, dd, *J* 5.5 and 2.9, CH=) and 6.33 (1 H, dd, *J* 5.5 and 2.9, CH=). The 5-H proton in compound **8** appears at δ 3.88, coupled (*J* 8.3 Hz) with the hydroxy proton in the ^{1}H NMR spectrum, whereas no coupling with the 6-H proton was observed.

(1R,2S,5R/S,6R,7S)-(+)-4-(*But-3′-ynyl*)-5-*hydroxy*-4-*azatricyclo*[5.2.1.0^{2,6}]*dec*-8-*en*-3-*ones* **9**.—To a degassed solution of compound **7** (900 mg, 2.15 mmol), *tert*-butyl alcohol (2 cm^3, 21.5 mmol) and HMPA (3.9 cm^3, 21.5 mmol) in dry THF (50 cm^3) was added SmI_2 (108 cm^3, 10.8 mmol; 0.1 mol dm^{-3} in THF) *via* cannula under a stream of argon. After being stirred at room temperature for 15 min, the intense purple suspension was quenched with cold, 1 mol dm^{-3} hydrochloric acid (30 cm^3). The mixture was then diluted with diethyl ether (30 cm^3) and the organic layer was separated. The aqueous layer was extracted with diethyl ether (20 cm^3 × 3). The combined extracts were washed successively with 2% aq. sodium thiosulfate (15 cm^3) and saturated brine (15 cm^3), dried, and concentrated. The residue was purified by column chromatography on silica with hexane–ethyl acetate (1:2→1:4) to give *compound* **9**:

(a) (5R)-*Epimer* (335 mg, 72%): plates, m.p. 157–158 °C (from hexane–ethyl acetate) (Found: C, 71.7; H, 6.8; N, 6.2. $C_{13}H_{15}NO_2$ requires C, 71.86; H, 6.96; N, 6.45%); $[\alpha]_D^{25}$ +148.8 (*c* 2.06, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3290, 3060, 2990, 1650, 1460, 1360 and 1110; δ_H 1.42 (1 H, d, *J* 8.4, 10-H^a), 1.59 (1 H, dt, *J* 8.4 and 1.7, 10-H^b), 2.00 (1 H, t, *J* 2.7, 4′-H), 2.43 (2 H, dt, *J* 6.8 and 2.7, 2′-H_2), 3.06 (1 H, m, 6-H), 3.11 (1 H, m, 1- or 7-H), 3.11 (1 H, d, *J* 9.0, OH), 3.14 (1 H, dd, *J* 8.8 and 4.4, 2-H), 3.27 (1 H, m, 7- or 1-H), 3.35 (2 H, t, *J* 6.8, 1′-H_2), 5.28 (1 H, dd, *J* 9.0 and 7.0, 5-H), 6.12 (1 H, dd, *J* 5.6 and 3.0, CH=) and 6.25 (1 H, dd, *J* 5.6 and 2.7, CH=); *m/z* 217 (M^+), 199, 171, 160, 112 and 66.

(b) (5S)-*Epimer* (75 mg, 16%): needles, m.p. 143–144 °C (from hexane–ethyl acetate) (Found: C, 71.9; H, 6.9; N, 6.4%); $[\alpha]_D^{24}$ +68.8 (*c* 1.09, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3300, 3070, 2960, 1660, 1470, 1320, 1250 and 1060; δ_H 1.39 (1 H, d, *J* 8.5, 10-H^a), 1.59 (1 H, dt, *J* 8.5 and 1.7, 10-H^b), 2.01 (1 H, t, *J* 2.7, 4′-H), 2.36 (2 H, dt, *J* 6.0 and 2.7, 2′-H_2), 2.66 (1 H, m, 6-H), 3.15–3.27 (4 H, m, 1-, 2- and 7-H and OH), 3.28 (1 H, dt, *J* 14 and 6.6, NC*H*H), 3.45 (1 H, dt, *J* 14 and 6.6, NCH*H*), 4.70 (1 H, d, *J* 7.6, 5-H) and 6.10 (2 H, br s, CH=); *m/z* 217 (M^+), 200, 178, 151, 112 and 66.

(1R,2S,5R/S,6R,7S)-(+)-4-(*Buten*-3-*yl*)-5-*hydroxy*-4-*azatricyclo*[5.2.1.0^{2,6}]*dec*-8-*en*-3-*one* **10**.—A suspension of alkyne **9** (1.7 g, 7.8 mmol) and 5% Pd on $BaSO_4$ (400 mg) and dry pyridine (0.5 cm^3) in dry methanol (15 cm^3) was hydrogenated at 1 atm for 15 h. The mixture was filtered and the filter was washed with methanol (10 cm^3). The combined filtrate and washings were concentrated. The residue was purified by column chromatography on silica with hexane–ethyl acetate (1:4) to give compound **10**[11] (1.7 g, 99%) as a 7:3 epimeric mixture, m.p. 134–135 °C (from hexane–ethyl acetate); $[\alpha]_D^{25}$ +91.3 (*c* 1.1, $CHCl_3$). The spectroscopic data were in good agreement with those of the racemate (lit.,[11] m.p. 110–112 °C).

(1S,2R,3S,5R,10S,11R)-(+)-9-*Oxo*-8-*azatetracyclo*-[9.2.1.0^{2,10}.0^{3,8}]*tetradec*-12-*en*-5-*yl Formate* **11**.—Compound **10** (88 mg, 0.4 mmol) was dissolved in 90% formic acid (1 cm^3) and the mixture was stirred at room temperature for 12 h. After being diluted with cold water (10 cm^3), the aqueous phase was extracted with dichloromethane (5 cm^3 × 5). The combined extracts were washed successively with 5% aq. sodium hydrogen carbonate (20 cm^3) and saturated brine (20 cm^3), dried, and concentrated. The residue was purified by column chromatography on silica with hexane–ethyl acetate (1:4) to give compound **11** (91 mg, 92%) as prisms, m.p. 132–133 °C (from hexane–ethyl acetate); $[\alpha]_D^{25}$ +80.9 (*c* 1.03, $CHCl_3$). The spectroscopic data were in good agreement with those of the racemate (lit.,[11] m.p. 145–148 °C).

(1S,2R,3S,5R,10S,11R)-(+)-5-*Hydroxy*-8-*azatetracyclo*-[9.2.1.0^{2,10}.0^{3,8}]*tetradec*-12-*en*-9-*one* **12**.—A solution of formate **11** (55 mg, 0.22 mmol) in ethanol (5 cm^3) was treated with 2 mol dm^{-3} KOH (5 drops). After being stirred at room temperature for 2 h, the mixture was evaporated and 1 mol dm^{-3} hydrochloric acid (5 cm^3) was added. The aqueous phase was extracted with dichloromethane (5 cm^3 × 5) and the extracts were washed with brine (10 cm^3), dried, and concentrated. The residue was purified by column chromatography on silica with chloroform–methanol (20:1) to give *compound* **12** (49 mg, 95%) as prisms, m.p. 134–135 °C (from hexane–ethyl acetate) (Found: C, 71.1; H, 7.9; N, 6.5. $C_{13}H_{17}NO_2$ requires C, 71.20; H, 7.82; N, 6.39%); $[\alpha]_D^{24}$ +72.3 (*c* 1.3, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3320, 3060, 2990, 1650, 1460, 1270 and 1070; δ_H 1.31–1.34 (2 H, m), 1.38 (1 H, d, *J* 8.5, 14-H^a), 1.59 (1 H, d, *J* 8.5, 14-H^b), 1.83 (1 H, br s, OH), 190 (1 H, br d, *J* 12), 2.16 (1 H, br d, *J* 12), 2.45–2.48 (1 H, m, 2-H), 2.50 (1 H, dt, *J* 13 and 3.4, 7α-H), 2.86 (1 H, br d, *J* 12, 3-H), 3.08 (1 H, br s, 1- or 11-H), 3.12 (1 H, m, 10-H), 3.25 (1 H, br s, 11- or 1-H), 3.71 (1 H, m, 5-H), 4.07 (1 H, ddd, *J* 13, 3.4 and 1, 7β-H), 6.10 (1 H, dd, *J* 5.6 and 2.9, CH=) and 6.21 (1 H, dd, *J* 5.6 and 2.9, CH=); *m/z* 219 (M^+), 202 and 153.

(7R,8aS)-(+)-6,7,8,8a-*Tetrahydro*-7-*hydroxyindolizin*-3(5H)-*one* **13**.—Compound **12** (490 mg, 2.24 mmol) was subjected to FVP (sublimation temp. 200 °C, quartz tube: length 48 cm, diameter 16 mm; oven temp. 450 °C; 0.5 Pa; 4 h) to give *compound* **13** (285 mg, 83%) as needles, m.p. 94–95 °C (from pentane–ethyl acetate) (Found: C, 62.8; H, 7.0; N, 9.0. $C_8H_{11}NO_2$ requires C, 62.72; H, 7.24; N, 9.14%); $[\alpha]_D^{25}$ +90.2 (*c* 1.0, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3220, 2930, 1690, 1460 and 1070; δ_H 1.02 (1 H, dt, *J* 12 and 11, 8β-H), 1.32 (1 H, dq, *J* 13 and 5.4, 6β-H), 1.72 (1 H, br s, OH), 2.01 (1 H, br d, *J* 13, 6α-H), 2.34 (1 H, ddt, *J* 12, 2 and 2, 8α-H), 2.90 (1 H, dt, *J* 13 and 3.5, 5α-H), 3.9–4.0 (2 H, m, *CH*OH and 8a-H), 4.31 (1 H, ddd, *J* 13, 5.4 and 1.5, 5β-H), 6.15 (1 H, dd, *J* 5.9 and 1.5, 2-H) and 7.03 (1 H, dd, *J* 5.9 and 1.5, 1-H); *m/z* 153 (M^+), 135, 109 and 96.

The minor product (< 5% yield) could not be isolated in pure form, but the structure was assumed to be that of the C(8a) epimer of compound **13** by the ^1H NMR spectrum of the crude pyrolysate. Selected ^1H NMR spectral data of the epimer: δ_H 3.29 (1 H, dt, *J* 12.9 and 3.7, 5α-H), 4.16 (1 H, dd, *J* 13.4 and 5.9, 5β-H), 6.17 (1 H, dd, *J* 6.0 and 1.6, 2-H) and 7.07 (1 H, dd, *J* 6.0 and 1.3, 1-H).

(7R,8aR)-(+)-7-*Hydroxyindolizidin*-3-*one* **14**.—A mixture of unsaturated lactam **13** (270 mg, 1.76 mmol) and 5% Pt on alumina (40 mg) in dry methanol (10 cm^3) was hydrogenated at 1 atm for 4 h. The mixture was filtered through a short pad of Celite, and the solid filter was washed with methanol (10 cm^3). The combined filtrate and washings were concentrated. The residue was purified by column chromatography on silica with chloroform–methanol (10 : 1) to give *compound* **14** (270 mg, 99%) as prisms, m.p. 104–106 °C (from hexane–ethyl acetate) (Found: C, 61.9; H, 8.55; N, 9.1. $C_8H_{13}NO_2$ requires C, 61.91; H, 8.44; N, 9.03%); $[\alpha]_D^{24}$ +49.0 (*c* 3.0, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3250, 2940, 1660, 1470 and 1080; δ_H 1.18 (1 H, q, *J* 12, 8β-H), 1.35 (1 H, m, 6β-H), 1.62–1.70 (1 H, m, 1α-H), 1.98 (1 H, br d, *J* 13, 1β-H), 2.14–2.29 (2 H, m, 6α- and 8α-H), 2.39 (2 H, dd, *J* 8 and 7, 2-H_2), 2.67 (1 H, dt, *J* 13 and 3, 5α-H), 3.50–3.55 (1 H, m, 8a-H), 3.64 (1 H, br d, *J* 4, OH), 3.77 (1 H, m, 7-H) and 4.12 (1 H, ddd, *J* 14, 5 and 2, 5β-H); *m/z* 155 (M^+), 137, 127, 110 and 83.

(+)-S-*Methyl* O-(7R,8aR)-3-*Oxoindolizidin*-7-*yl Dithiocarbonate* **15**.—To a suspension of sodium hydride (60% dispersion; 80 mg, 2 mmol) in dry THF (10 cm^3) was added a solution of the alcohol **14** (200 mg, 1.3 mmol) in dry THF (2 cm^3) followed by imidazole (5 mg). The mixture was heated at reflux for 1 h, and carbon disulfide (0.78 cm^3, 13 mmol) was added. After the mixture had been stirred at that temperature for 0.5 h, iodomethane (0.81 cm^3, 13 mmol) was added. The mixture was then stirred at that temperature for 10 min, cooled to 0 °C, and partitioned between water (10 cm^3) and dichloromethane (30 cm^3). The aqueous phase was extracted with dichloromethane (5 cm^3 × 3). The combined organic phases were washed with saturated brine (20 cm^3), dried, and concentrated. The residue was purified by column chromatography on silica with ethyl acetate to give *compound* **15** (254 mg, 80%) as pale yellow prisms, m.p. 84–85 °C (from hexane–ethyl acetate) (Found: C, 48.8; H, 6.3; N, 6.0. $C_{10}H_{15}NO_2S_2$ requires C, 48.97; H, 6.17; N, 5.71%); $[\alpha]_D^{25}$ +67.7 (*c* 1.1, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 2960, 1680, 1420, 1210 and 1050; δ_H 1.41 (1 H, q, *J* 11, 8β-H), 1.56–1.69 (2 H, m, 1- and 6-H), 2.19–2.33 (2 H, m, 1- and 8α-H), 2.39–2.46 (3 H, m, 2-H_2 and 6-H), 2.56 (3 H, s, SMe), 2.77 (1 H, dt, *J* 13 and 3, 5α-H), 3.62 (1 H, ddt, *J* 11, 7 and 4, 8a-H), 4.24 (1 H, ddd, *J* 14, 5 and 2, 5β-H) and 5.67 (1 H, tt, *J* 11 and 4, 7α-H); *m/z* 246 (M^+ + 1), 198, 148 and 110.

(8aS)-(+)-*Indolizidin*-3-*one* **16**.—A mixture of xanthate **15** (40 mg, 0.16 mmol), tributyltin hydride (0.065 cm^3, 0.24 mmol) and a catalytic amount of AIBN in dry benzene (1 cm^3) was heated at reflux in a sealed tube for 10 h. After being cooled, the mixture was charged directly to a silica column, and elution with ethyl acetate gave compound **16** (17 mg, 76%) as an oil, b.p. 80–85 °C/1.5 mmHg; $[\alpha]_D^{24}$ +31.1 (*c* 2.0, $CHCl_3$). The spectroscopic data were in good agreement with those of the racemate.[14]

(8aS)-(+)-*Indolizidine* **1**.-To a solution of lactam **16** (60 mg, 0.43 mmol) in dry diethyl ether (10 cm^3) was added lithium aluminium hydride (32 mg, 0.86 mmol) and the mixture was heated at reflux for 1 h. After being cooled to 0 °C, the mixture was quenched by sequential addition of water (0.04 cm^3), 15% aq. sodium hydroxide (0.04 cm^3), and water (0.04 cm^3). The mixture was dried by addition of anhydrous magnesium sulfate, filtered, and concentrated under atmospheric pressure to give indolizidine **1** (40 mg, 74%) as an oil, b.p. 75–80 °C/25 mmHg (Kugelrohr); $[\alpha]_D^{24}$ +9.0 (*c* 0.74, EtOH) {lit.,[3d] $[\alpha]_D^{23}$ +9.3 ± 0.6 (*c* 1.77, EtOH) for 100% e.e.}.

(1R,2S,5S,6R,7S)-(+)-4-(*But*-3′-*ynyl*)-5-*methoxy*-4-*azatricyclo*[5.2.1.0^2,6^]*dec*-8-*en*-3-*one* **17**.—A solution of the alcohol **9** (330 mg, 1.52 mmol) in dry methanol (10 cm^3) was treated with PPTS (380 mg, 1.52 mmol) at room temperature for 15 h. After removal of the solvent, the residue was purified by column chromatography on silica with hexane–ethyl acetate (2:1) to give *compound* **17** (315 mg, 90%). Recrystallisation from hexane gave prisms, m.p. 46–48 °C (Found: C, 72.7; H, 7.4; N, 5.9. $C_{14}H_{17}NO_2$ requires C, 72.70; H, 7.41; N, 6.06%); $[\alpha]_D^{25}$ +69.2 (*c* 1.06, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3310, 2980, 1680, 1450, 1380, 1250, 1070 and 990; δ_H 1.42 (1 H, d, *J* 8.6, 10-H^a), 1.60 (1 H, dt, *J* 8.6 and 1.5, 10-H^b), 1.98 (1 H, t, *J* 2.6, 4′-H), 2.33 (2 H, dt, *J* 7.0 and 2.6, 2′-H_2), 2.66 (1 H, ddd, *J* 8.5, 4.1 and 1.0, 6-H), 3.06–3.17 (3 H, m, 1′-H^a, 2-H and 1- or 7-H), 3.25 (3 H, s, OMe), 3.27 (1 H, br s, 7- or 1-H), 3.52 (1 H, ddd, *J* 14, 7 and 7, 1′-H^b), 4.52 (1 H, s, 5-H) and 6.12 (2 H, br t, *J* 2, CH=); *m/z* 231 (M^+), 216, 200, 165, 126 and 66.

(1R,2S,5S,6R,7S)-(+)-5-*Methoxy*-4-[4′-(*phenylthio*)*but*-3′-*ynyl*]-4-*azatricyclo*[5.2.1.0^2,6^]*dec*-8-*en*-3-*one* **18**.—To a solution of hexamethyldisilane (0.43 cm^3, 2.05 mmol) in dry THF (10 cm^3) at −70 °C was added dropwise butyllithium (1.23 cm^3, 2.04 mmol; 1.66 mol dm^{-3} in hexane). After the mixture had been stirred for an additional 0.5 h at that temperature, a solution of compound **17** (190 mg, 0.82 mmol) in dry THF (10 cm^3) was added dropwise and the mixture was stirred for 15 min. To the mixture was added a solution of diphenyl disulfide (536 mg, 2.46 mmol) in dry THF (5 cm^3). The reaction mixture was allowed to warm to room temperature over a period of 1 h and quenched with saturated aq. ammonium chloride (15 cm^3) followed by diethyl ether (15 cm^3). The organic layer was separated and the aqueous layer was extracted with diethyl ether (10 cm^3 × 3). The combined organic phases were washed with saturated brine (20 cm^3), dried, and concentrated. The residue was purified by flash chromatography on silica with hexane–ethyl acetate (1:1) to give *compound* **18** (266 mg, 96%) as an oil (Found: C, 70.6; H, 6.3; N, 4.1. $C_{20}H_{21}NO_2S$ requires C, 70.78; H, 6.24; N, 4.13%); $[\alpha]_D^{25}$ +19.2 (*c* 0.83, $CHCl_3$); ν_{max}(neat) 2970, 1690, 1440, 1340 and 1080; δ_H 1.40 (1 H, d, *J* 8.3, 10-H^a), 1.58 (1 H, d, *J* 8.3, 10-H^b), 2.61 (2 H, dt, *J* 6.6 and 2.2, 2′-H_2), 2.66 (1 H, dd, *J* 8.5 and 4.0, 2-H), 3.08 (1 H, br s, 1- or 7-H), 3.11–3.20 (2 H, m, 6-H and 1′-H^a), 3.23 (3 H, s, OMe), 3.28 (1 H, br s, 7- or 1-H), 3.60 (1 H, dt *J* 13 and 6.6, 1′-H^b), 4.49 (1 H, s, 5-H), 6.10 (2 H, m, CH=) and 7.18–7.42 (5 H, m, ArH); *m/z* 339 (M^+), 308, 273, 230 and 160.

S-*Phenyl*(1S,2R,3R,4S,9S,10R)-(+)-8-*Oxo*-7-*azatetracyclo*[8.2.1.0^2,9^.0^3,7^]*tridec*-11-*ene*-4-*carbothioate* **19**.—Compound **18** (700 mg, 2.06 mmol) was treated with 90% formic acid (4 cm^3) at room temperature for 15 h. After being diluted with water (20 cm^3), the aqueous phase was extracted with dichloromethane (20 cm^3). The combined organic phases washed with saturated aq. sodium hydrogen carbonate (20 cm^3) and the aqueous phase was back-extracted with dichloromethane (5 cm^3 × 3). The combined organic phases were washed with saturated brine (20 cm^3), dried, and concentrated. The residue was purified by flash chromatography on silica with hexane–ethyl acetate (1:2) to give *compound* **19** (535 mg, 80%) as an oil (Found: M^+, 325.1155. $C_{19}H_{19}NO_2S$ requires M, 325.1135); $[\alpha]_D^{24}$ +129.3 (*c* 1.25, $CHCl_3$); ν_{max}(neat)/cm^{-1} 2970, 1690, 1680, 1440, 1340, 1280 and 1020; δ_H 1.42 (1 H, d, *J* 8.5, 13-H^a), 1.64 (1 H, dt, *J* 8.5 and 1.8, 13-H^b), 2.15–2.42 (2 H, m, 5-H_2), 2.79 (1 H, dt, *J* 11 and 10, 4-H), 2.94 (1 H, ddd, *J* 9.0, 4.2 and 2.4, 2-H), 3.08 (1 H, ddd, *J* 12, 10 and 3.7, 6β-H), 3.15 (1 H, br s, 1- or 10-H), 3.20 (1 H, dd, *J* 9.0 and 4.5, 9-H), 3.28 (1 H, br s, 10- or 1-H), 3.30 (1 H, dd, *J* 9.8 and 2.4, 3-H), 3.67 (1 H, dt, *J* 12 and 8.3, 6α-H), 6.23 (2 H, br t, *J* 1.7, CH=) and 7.45 (5 H, br s, ArH); *m/z* 325 (M^+), 297, 259, 216, 188, 150 and 122.

(1S,2R,3R,4S,9S,10R)-(+)-4-*Hydroxymethyl-7-azatetracyclo*[8.2.1.0^{2,9}.0^{3,7}]*tridec-11-en-8-one* **20**.—To a solution of compound **19** (500 mg, 1.54 mmol) in methanol (10 cm^3) at 0 °C was added sodium borohydride (116 mg, 3.1 mmol) in one portion. The mixture was stirred at that temperature for 0.5 h and quenched with cold, 3% hydrochloric acid (20 cm^3). After removal of the solvent, the aqueous layer was extracted with dichloromethane (15 cm^3 × 3). The combined extracts were washed with saturated brine (20 cm^3), dried, and concentrated. The residue was purified by flash chromatography on silica with ethyl acetate and then with chloroform–methanol (10:1) to give *compound* **20** (326 mg, 97%) as an oil (Found: M^+, 219.1258. $C_{13}H_{17}NO_2$ requires M, 219.1258); $[\alpha]_D^{24}$ +47.3 (*c* 2.25, $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 3390, 3000, 1660, 1430, 1250, 1210 and 1090; δ_H 1.38 (1 H, d, *J* 8.3, 13-H^a), 1.61 (1 H, br d, *J* 8.3, 13-H^b), 1.55–1.70 (1 H, m, 5α-H), 1.75–1.90 (1 H, m, 4-H), 2.05–2.16 (1 H, m, 5β-H), 2.85–3.05 (4 H, m, 2-, 3-, 6β-H and OH), 3.12 (1 H, br, 1- or 10-H), 3.15 (1 H, dd, *J* 9.3 and 4.6, 9-H), 3.23 (1 H, br, 10- or 1-H), 3.54 (1H, dt *J* 11 and 8, 6α-H), 3.64 (1 H, dd, *J* 11 and 6.8, C*H*HOH), 3.78 (1 H, dd, *J* 11 and 5, CH*H*OH) and 6.25 (2 H, br s, CH=); *m/z* 219 (M^+), 202, 165, 154, 136, 122 and 66.

(7S,7aR)-(+)-5,6,7,7a-*Tetrahydro-7-(hydroxymethyl)pyrrolizin-3-one* **21**.—In a manner similar to compound **13**, FVP (oven temp. 500 °C at 1.3 × 10^{-3} Pa, sublimation temp. 165 °C) of compound **20** (55 mg, 0.25 mmol) afforded *compound* **21** (33 mg, 86%) after chromatography on silica with chloroform–methanol (10:1), as prisms, m.p. 62–64 °C (from diethyl ether) (Found: C, 62.6; H, 7.15; N, 9.2. $C_8H_{11}NO_2$ requires C, 62.72; H, 7.24; N, 9.14%); $[\alpha]_D^{26}$ +38.6 (*c* 0.9, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3400, 2900, 1670, 1570, 1390, 1250, 1030 and 810; δ_H 1.79 (1 H, m, 7-H), 2.07 (1 H, ddt, *J* 13, 11 and 9.3, 6α-H), 2.17 (1 H, br s, OH), 2.36 (1 H, dddd, *J* 13, 8.3, 7.2 and 2.2, 6β-H), 3.35 (1 H, ddd, *J* 11, 9.3 and 2.2, 5α-H), 3.54 (1 H, ddd, *J* 11, 9.3 and 8.3, 5β-H), 3.69 (1 H, br t, *J* 11, C*H*HOH), 3.90 (1 H, br dd, *J* 11 and 4.3, CH*H*OH), 4.14 (1 H, d, *J* 9.8, 7a-H), 6.27 (1 H, dd, *J* 5.7 and 1.6, 1-H) and 7.31 (1 H, dd, *J* 5.7 and 1.8, 2-H); *m/z* 153 (M^+), 134, 106, 95 and 67.

(7S,7aR)-(+)-7-(*Hydroxymethyl)pyrrolizidin-3-one* **22**.—A mixture of compound **21** (44 mg, 0.28 mmol) and PtO_2 (6.5 mg) in dry ethanol (10 cm^3) was hydrogenated at room temperature under atmospheric pressure for 4 h. The mixture was filtered through a short pad of Celite. The solid filter was washed with chloroform (5 cm^3 × 2), and the combined filtrate and washings were concentrated. The residue was purified by chromatography on silica with chloroform–methanol (10:1) to give *compound* **22** (43 mg, 99%) as an oil, b.p. 175–180 °C/1 mmHg (Kugelrohr) (Found: M^+, 155.0954. $C_8H_{13}NO_2$ requires M, 155.0946); $[\alpha]_D^{25}$ +17.0 (*c* 1.95, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3570, 2890, 1650, 1460, 1420 and 1050; δ_H 1.85–2.0 (3 H, m), 2.1–2.5 (3 H, m), 2.65–2.8 (1 H, m), 2.8 (1 H, br, OH), 3.1–3.2 (1 H, m) and 3.5–3.8 (4 H, m); *m/z* 155 (M^+), 138, 114, 97, 84 and 69.

(+)-*Laburnine* **2**.—To a solution of compound **22** (30 mg, 0.19 mmol) in THF (5 cm^3) was added lithium aluminium hydride (15 mg, 0.39 mmol) and the mixture was heated at reflux for 4 h. After being cooled to 0 °C, the mixture was quenched by sequential addition of water (0.02 cm^3), 15% aq. sodium hydroxide (0.02 cm^3), and water (0.02 cm^3). The mixture was dried by addition of anhydrous magnesium sulfate (~200 mg), filtered and concentrated. The residue was purified by flash chromatography on silica with chloroform–methanol–triethylamine (5:4:1) to give (+)-laburnine **2** (16 mg, 60%) as an oil, b.p. 80–85 °C/0.5 mmHg (Kugelrohr); $[\alpha]_D^{25}$ +11.1 (*c* 1.1, EtOH) {lit.,[6] $[\alpha]_D$ +15.4 (*c* 1.44, EtOH); lit.,[8a] $[\alpha]_D^{22}$ +14.6 (*c* 3.25, EtOH); lit.,[9] $[\alpha]_D^{20}$ +13.63 (*c* 1.22, EtOH)}, whose ^{1}H NMR and ^{13}C NMR spectra were in good agreement with those of its enantiomer (−)-**2** reported by Ishibashi *et al.*[8c]

(1R,4S)-(+)-N-[2″-(1,3-*Dioxolan-2-yl)ethyl*]-2-exo-({(1′S,2′R,4′R,R$_S$)-2′-*hydroxy-7′,7′-dimethylbicyclo*[2.2.1]*heptan-1′-yl*}*methylsulfinyl)bicyclo*[2.2.1]*hept-5-ene-2*-endo,3-endo-*dicarboximide* **24**.—To a suspension of sodium hydride (60% dispersion; 890 mg, 22.3 mmol, washed with dry diethyl ether three times) in dry *N,N*-dimethylformamide (30 cm^3) at 0 °C was added compound **23**[1] (4.04 g, 11.1 mmol) in one portion. After being stirred at that temperature for 0.5 h, the mixture was allowed to warm gradually to room temperature over a period of 0.5 h. 2-(2-Bromoethyl)-1,3-dioxolane (1.96 cm^3, 16.7 mmol) was added *via* syringe. After being stirred for 12 h, the mixture was cooled to 0 °C and was quenched with cold water (10 cm^3). The mixture was partitioned between chloroform (50 cm^3) and saturated brine (20 cm^3) and the organic layer was separated. The aqueous layer was extracted with chloroform (15 cm^3 × 3) and the combined organic phases were dried and concentrated. The residue was purified by flash chromatography on silica with hexane–ethyl acetate (2:1) to give *compound* **24** (4.77 g, 93%) as needles, m.p. 69–71 °C (from hexane–diethyl ether–ethanol) (Found: C, 61.8; H, 7.6; N, 3.2. $C_{24}H_{33}NO_6S$ requires C, 62.19; H, 7.18; N, 3.02%); $[\alpha]_D^{24}$ +7.1 (*c* 1.08, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3450, 2960, 1700, 1180 and 1030; δ_H 0.90 (3 H, s, Me), 1.15 (4 H, s + m, Me and 10-H^a), 1.45–1.89 (9 H, m, bornyl H and 2″-H_2), 2.29 (1 H, d, *J* 9, 10-H^b), 3.09 (1 H, d, *J* 13, SC*H*H), 3.46 (1 H, d, *J* 13, SCH*H*), 3.48 (2 H, s, 3- and 1- or 7-H), 3.53 (2 H, t, *J* 7, NCH_2), 3.63 (1 H, br d, *J* 3, OH), 3.79–3.9 (4 H, m, OCH_2CH_2O), 3.95 (1 H, br s, 7- or 1-H), 4.02 (1 H, m, 2′-H), 4.85 (1 H, t, *J* 4, C*H*OCH_2), 6.27 (1 H, dd, *J* 5 and 3, CH=) and 6.34 (1 H, d, *J* 5, CH=); *m/z* 464 (M^+ + 1), 463 (M^+), 446, 312, 311 and 109.

(1R,2R,5S,6S,7S)-(+)-4-[2-(1,3-*Dioxolan-2-yl)ethyl*]-5-*hydroxy*-2-({(1′S,2′R,4′R,R$_S$)-2′-*hydroxy-7′,7′-dimethylbicyclo*[2′.2′.1′]*heptan-1′-yl*}*methylsulfinyl*)-4-*azatricyclo*[5.2.1.0^{2,6}]-*dec-8-en-3-one* **25**.—A mixture of compound **24** (1.65 g, 3.56 mmol) and sodium borohydride (540 mg, 14.3 mmol) in ethanol (20 cm^3) was heated at reflux for 3 h. After being cooled to 0 °C, the mixture was quenched with cold water (10 cm^3) and most of the ethanol was evaporated off. The aqueous phase was partitioned between chloroform (30 cm^3) and saturated brine (30 cm^3) and the organic layer was separated. The aqueous phase was extracted with chloroform (10 cm^3 × 5) and the combined organic phases were dried and concentrated. The residue was purified by chromatography on silica with ethyl acetate to give *compound* **25** (1.18 g, 71%) as prisms, m.p. 167–168 °C (from pentane–ethyl acetate) (Found: C, 61.6; H, 7.2; N, 3.0. $C_{24}H_{35}NO_6S$ requires C, 61.92; H, 7.58; N, 3.01%); $[\alpha]_D^{24}$ +48.5 (*c* 1.13, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3437, 2953, 2879, 1667, 1455, 1142, 1078 and 1034; δ_H 0.86 (3 H, s, Me), 1.12 (4 H, br s, Me and bornyl H), 1.4–2.11 (11 H, m, bornyl H, OH, NCH_2CH_2 and $10\text{-}H_2$), 2.75 (1 H, d, *J* 3.9, 6-H), 3.10 (1 H, d, *J* 13, C*H*HSO), 3.26 (1 H, d, *J* 13, CH*H*SO), 3.27 (1 H, br s, 7-H), 3.25–3.5 (2 H, m, NCH_2), 3.60 (1 H, br s, 1-H), 3.8–4.1 (5 H, m, OCH_2CH_2O and 2'-H), 4.20 (1 H, br, OH), 4.62 (1 H, br, 5-H), 4.88 (1 H, t, *J* 4.4, C*H*OCH_2) and 6.25 (2 H, s, CH=); *m/z* 466 (M^+ + 1), 465 (M^+), 448, 295 and 247.

(+)-(1R,2S,5S,6R,7S)-4-[2'-(1,3-*Dioxolan*-2-*yl*)*ethyl*]-5-*hydroxy*-4-*azatricyclo*[5.2.1.$0^{2,6}$]*dec*-8-*en*-3-*one* **26**.—To a degassed solution of compound **25** (740 mg, 1.6 mmol), *tert*-butyl alcohol (1.5 cm^3, 16 mmol) and HMPA (2.9 cm^3, 16 mmol) in THF (30 cm^3) was added SmI_2 (64 cm^3, 6.4 mmol; 0.1 mol dm^{-3} in THF) *via* cannula under a stream of argon. After being stirred for an additional 15 min, the intense purple-coloured suspension was quenched with water (20 cm^3). After removal of the solvent, the mixture was partitioned between chloroform (50 cm^3) and saturated aq. ammonium chloride (20 cm^3). The mixture was stirred vigorously for 10 min and acidified by careful addition of 3% hydrochloric acid until a pH test paper indicated pH 3–4. The organic layer was separated and the aqueous phase was extracted with chloroform (20 cm^3 × 5). The combined organic phases were washed with saturated brine (50 cm^3), dried and concentrated. The residue was passed through a short pad of silica with ethyl acetate–methanol (100:1) to remove most of the HMPA. The eluent was concentrated and the residue was purified by flash chromatography on silica with ethyl acetate–methanol (100:1) to give *compound* **26** (390 mg, 92%) as needles, m.p. 116–118 °C (from hexane–ethyl acetate) (Found: C, 63.2; H, 7.4; N, 5.4. $C_{14}H_{19}NO_4$ requires C, 63.38; H, 7.22; N, 5.28%); $[\alpha]_D^{25}$ +84.6 (*c* 2.0, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3199, 2988, 1637, 1350 and 1116; δ_H 1.39 (1 H, d, *J* 8.4, 10-H^a), 1.57 (1 H, d, *J* 8.4, 10-H^b), 1.75–2.0 (2 H, m, 2'-H_2), 2.66 (1 H, dd, *J* 8 and 4, 6-H), 3.1–3.45 (5 H, m, 1-, 2- and 7-H and 1'-H_2), 3.8–4.1 (4 H, m, OCH_2CH_2O), 4.17 (1 H, d, *J* 7, OH), 4.54 (1 H, d, *J* 7, 5-H), 4.87 (1 H, t, *J* 4.6, OCHO), 6.03 (1 H, dd, *J* 5.4 and 2.4, CH=) and 6.09 (1 H, dd, *J* 5.4 and 3, CH=); *m/z* 265 (M^+), 247, 199, 183 and 161.

(1R,2S,5S,6R,7S)-(+)-4-[2'-(1,3-*Dioxolan*-2-*yl*)*ethyl*]-5-*methoxy*-4-*azatricyclo*[5.2.1.$0^{2,6}$]*dec*-8-*en*-3-*one* **27**.—To a solution of compound **26** (130 mg, 0.49 mmol) in dry methanol (5 cm^3) was added PPTS (62 mg, 0.25 mmol) and the mixture was stirred for 12 h. The solvent was evaporated off and the residue was purified by flash chromatography on silica with hexane–ethyl acetate (1:4) to give *compound* **27** (134 mg, 98%) as an oil (Found: M^+, 279.1474. $C_{15}H_{21}NO_4$ requires M, 279.1469); $[\alpha]_D^{26}$ +85.9 (*c* 3.0, $CHCl_3$); ν_{max}(neat)/cm^{-1} 3061, 2974, 2883, 1682, 1455 and 1079; δ_H 1.41 (1 H, d, *J* 8.4, 10-H^a), 1.59 (1 H, d, *J* 8.4, 10-H^b), 1.65–1.95 (2 H, m, 2'-H_2), 2.66 (1 H, dd, *J* 8.3 and 3.9, 6-H), 2.9–3.55 (5 H, m, 1-, 2- and 7-H and 1'-H_2), 3.23 (3 H, s, OMe), 3.8–4.0 (4 H, m, OCH_2CH_2O), 4.36 (1 H, s, 5-H), 4.85 (1 H, t, *J* 4.8, OCHO), 6.05 (1 H, dd, *J* 5 and 2.7, CH=) and 6.11 (1 H, dd, *J* 5 and 2.7, CH=); *m/z* 279 (M^+), 213, 170, 119 and 99.

(1R,2S,5S,6R,7S)-(+)-4-[2'-(1,3-*Dioxolan*-2-*yl*)*ethyl*]-5-(2''-*oxopentyl*)-4-*azatricyclo*[5.2.1.$0^{2,6}$]*dec*-8-*en*-3-*one* **28**.—To a solution of compound **27** (255 mg, 0.91 mmol) in dry dichloromethane (15 cm^3) at 0 °C was added boron trifluoride-diethyl ether complex (0.17 cm^3, 1.82 mmol) *via* syringe. After being stirred for 10 min, the mixture was treated with a solution of 2-(trimethylsiloxy)pent-1-ene[20] (0.39 cm^3, 3.64 mmol) in dry dichloromethane (10 cm^3). The mixture was allowed to warm to room temperature and was stirred for an additional 2 h. The mixture was then quenched with cold, saturated brine (25 cm^3) and the organic phase was separated. The aqueous phase was extracted with dichloromethane (10 cm^3 × 3), and the combined organic phases were dried and concentrated. The residue was purified by flash chromatography on silica with hexane–ethyl acetate (1:4) to give *compound* **28** (276 mg, 91%) as an oil (Found: M^+, 333.1957. $C_{19}H_{27}NO_4$ requires M, 333.1940); $[\alpha]_D^{25}$ +86.9 (*c* 2, $CHCl_3$); ν_{max}(neat)/cm^{-1} 2962, 2875, 1710, 1673 and 1132; δ_H 0.94 (3 H, t, *J* 7.3, Me), 1.30 (1 H, d, *J* 8.6, 10-H^a), 1.53 (1 H, d, *J* 8.6, 10-H^b), 1.63 (2 H, sep, *J* 7.3, 4''-H_2), 1.7–1.85 (2 H, m, 2'-H_2), 2.31 (1 H, ddd, *J* 9, 3.2 and 3.2, 6-H), 2.42 (2 H, br t, *J* 7.3, 3''-H_2), 2.48 (1 H, dd, *J* 17.5 and 9.6, 1''-H^a), 2.73 (1 H, dt, *J* 14.7 and 6.8, NC*H*H), 2.82 (1 H, dd, *J* 17.5 and 3.5, 1''-H^b), 3.05 (1 H, dd, *J* 9 and 4.5, 2-H), 3.20 (1 H, br s, 7-H), 3.25 (1 H, br s, 1-H), 3.44 (1 H, ddd, *J* 9.6, 3.5 and 3.2, 5-H), 3.65 (1 H, dt, *J* 14.7 and 7, NCH*H*), 3.8–4.0 (4 H, m, OCH_2CH_2O), 4.83 (1 H, t, *J* 4.6, OCHO) and 6.15 (2 H, br s, CH=); *m/z* 333 (M^+), 290, 267, 262, 248 and 196.

(1S,2R,3R,4R,5S,10S,11R)-(+)-4-*Butyryl*-5-*hydroxy*-8-*azatetracyclo*[9.2.1.$0^{2,10}$.$0^{3,8}$]*tetradec*-12-*en*-9-*one* **29**.—Compound **28** (543 mg, 1.63 mmol) was dissolved in conc. hydrochloric acid (2 cm^3) and the mixture was stirred at room temperature for 3 h. After the mixture had been partitioned between chloroform (10 cm^3) and water (5 cm^3), cold, saturated aq. sodium hydrogen carbonate (10 cm^3) was added. The organic layer was separated and the aqueous layer was extracted with chloroform (5 cm^3 × 3). The combined organic phases were washed with saturated brine (10 cm^3), dried, and concentrated. The residue was purified by flash chromatography on silica with chloroform–methanol (50:1) to give *compound* **29** (370 mg, 79%) as prisms, m.p. 140–142 °C (from hexane–ethyl acetate) (Found: C, 70.7; H, 8.0; N, 4.8. $C_{17}H_{23}NO_3$ requires C, 70.56; H, 8.01; N, 4.84%); $[\alpha]_D^{26}$ +103.7 (*c* 3.0, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3280, 3058, 2962, 2876, 1702, 1646 and 1465; δ_H 0.96 (3 H, t, *J* 7.4, Me), 1.33 (1 H, d, *J* 8.3, 14-H^a), 1.57 (1 H, d, *J* 8.3, 14-H^b), 1.67 (2 H, sextet, *J* 7.3, 3'-H_2), 1.75–1.9 (2 H, m, 6-H_2), 2.28 (1 H, ddd, *J* 9.3, 3.7 and 2.8, 2-H), 2.48 (1 H, dt, *J* 12.5 and 7.3, 2'-H^a), 2.49 (1 H, d, *J* 11, 4-H), 2.63 (1 H, dt, *J* 12.5 and 7.3, 2'-H^b), 2.66 (1 H, br s, OH), 2.91 (1 H, dt, *J* 13.2 and 3.4, 7-H_{ax}), 3.02 (1 H, dd, *J* 9.3 and 4.5, 10-H), 3.14 (1 H, br s, 1- or 11-H), 3.22 (1 H, br s, 11- or 1-H), 3.48 (1 H, dd, *J* 11 and 2.8, 3-H), 3.85 (1 H, dd, *J* 13.2 and 4.4, 7-H_{eq}), 4.41 (1 H, br s, 5-H) and 6.20 (2 H, br s, CH=); *m/z* 289 (M^+), 223, 153, 152 and 135.

(7S,8R,8aR)-(+)-8-*Butyryl*-6,7,8,8a-*tetrahydro*-7-*hydroxy*-*indolizin*-3(5H)-*one* **30**.—As described earlier, compound **29** (150 mg, 0.52 mmol) was subjected to FVP (oven temp. 425 °C at 0.5 Pa, sublimation temp. 200 °C; 4 h) to afford a mixture of epimers **30** and **31** (115 mg, 99%) in the ratio 3:1. The *major product* **30** (60 mg, 52%) was separated from the minor product **31** by recrystallisation from diethyl ether–ethyl acetate, as needles, m.p. 182–184 °C (Found: C, 64.5; H, 7.7; N, 6.2. $C_{12}H_{17}NO_3$ requires C, 64.55; H, 7.68; N, 6.27%); $[\alpha]_D^{26}$ +150.9 (*c* 1.0, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3219, 2962, 2933, 2875, 2726, 1703 and 1651; δ_H 0.92 (3 H, t, *J* 7.3, Me), 1.52–1.70 (3 H, m, 3'-H_2 and 6-H_{ax}), 1.97 (1 H, br d, *J* 14, 6-H_{eq}), 2.26 (1 H, dd, *J* 11 and 1.7, 8-H), 2.48 (1 H, dt, *J* 17 and 7.3, 2'-H^a), 2.62 (1 H, dt, *J* 17 and 7.3, 2'-H^b), 2.86 (1 H, br s, OH), 3.26 (1 H, dt, *J* 13 and 3.4, 5-H_{ax}), 4.15 (1 H, dd, *J* 13 and 5.6, 5-H_{eq}), 4.55 (1 H, br s, 7-H), 4.57 (1 H, br d, *J* 11, 8a-H), 6.19 (1 H, dd, *J* 5 and 1, 2-H) and 7.09 (1 H, d, *J* 5, 1-H); *m/z* 223 (M^+), 153, 136, 135, 134 and 71.

The minor product could not be isolated in pure form; however, the ^1H NMR spectrum of the crude reaction mixture suggested the structure **31**. Selected ^1H NMR data of compound **31**: δ_H 2.94 (1 H, dt, *J* 13 and 3.5, 5-H_{ax}), 4.28 (1 H, dd, J 13 and 5.5, 5-H_{eq}), 6.19 (1 H, m, overlapping with the 2-H of compound **30**) and 6.87 (1 H, dd, J 5.9 and 1.0, 1-H).

(7S,8R,8aR)-(+)-8-*Butyryl*-7-*hydroxyindolizidin*-3-*one* **32**.—A mixture of compound **30** (120 mg, 0.54 mmol) and 5% Pt on alumina (360 mg) in *tert*-butyl alcohol (10 cm^3) was hydrogenated at room temperature at 1 atm for 6h. The mixture was filtered and the solid filter was washed with chloroform (20 cm^3). The combined filtrate and washings were concentrated and the residue was purified by flash chromatography on silica with chloroform–methanol (50:1) to give *compound* **32** (121 mg, 100%) as needles, m.p. 172–174 °C (from hexane–diethyl ether–ethanol) (Found: C, 63.7; H, 8.55; N, 6.2. $C_{12}H_{19}NO_3$ requires C, 63.98; H, 8.50; N, 6.22%); $[\alpha]_D^{26}$ +113.4 (c 1.0, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3246, 2964, 2930, 2874, 1702, 1652 and 1472; δ_H 0.94 (3 H, t, J 7.3, Me), 1.5–1.8 (2 H, m), 1.64 (2 H, sep, J 7.3, 3'-H_2), 1.92 (1 H, br d, J 14, 6-H_{eq}), 2.25–2.40 (3 H, m), 2.47 (1 H, d, J 11, 8-H), 2.47 (1 H, dt, J 17 and 7, 2'-H^a), 2.61 (1 H, dt, J 17 and 7, 2'-H^b), 2.87 (1 H, br s, OH), 3.08 (1 H, dt, J 13 and 3, 5-H_{ax}), 3.96 (1 H, ddd, J 13, 5.5 and 1.2, 5-H_{eq}), 4.04 (1 H, dt, J 11 and 7, 8a-H) and 4.38 (1 H, br s, 7-H); m/z 225 (M^+), 182, 181, 139, 138 and 136.

Hydrogenation using other catalysts (*e.g.*, platinum oxide, methanol, room temp., 1 atm, 3 h) resulted in an inseparable 1.4:1 mixture of compound **32** and its C(8a) epimer; selected ^{1}H NMR data: δ_H 3.62 (1 H, dt, J 10.3 and 7.1, 5-H_{ax}) and 4.16 (1 H, ddd, J 13.6, 5.1 and 1.6, 8a-H).

(7S,8R,8aR)-(+)-7-*Hydroxy*-8-(2-*propyl*-1,3-*dioxolan*-2-*yl*)-*indolizin*-3-*one* **33**.—A mixture of keto lactam **32** (70 mg, 0.31 mmol), triethyl orthoformate (4 cm^3), ethylene glycol (3 cm^3), a pinch of toluene-*p*-sulfonic acid monohydrate and 4 Å molecular sieves (powder, 10 mg) was heated at 130 °C for 10 h. After being cooled, the mixture was filtered and the solid filter was washed with chloroform (20 cm^3). The combined filtrate and washings were washed with saturated aq. sodium hydrogen carbonate (10 cm^3). The aqueous layer was back-extracted with chloroform (5 cm^3 × 3). The combined organic phases were washed with saturated brine (15 cm^3), dried, and concentrated. The residue was purified by flash chromatography on silica with chloroform–methanol (70:1) to give *compound* **33** (76 mg, 91%) as prisms, m.p. 167–169 °C (from hexane–ethyl acetate) (Found: C, 62.2; H, 8.6; N, 5.05. $C_{14}H_{23}NO_4$ requires C, 62.43; H, 8.61; N, 5.20%); $[\alpha]_D^{26}$ +63.2 (c 1.0, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3308, 2959, 2931, 2899, 2872 and 1660; δ_H 0.93 (3 H, t, J 7, Me), 1.2–2.1 (8 H, m), 2.2–2.4 (3 H, m), 3.07 (1 H, dt, J 13, 3, 5-H_{ax}), 3.57 (1 H, br d, J 1.2, OH), 3.7–4.2 (6 H, m) and 4.27 (1 H, br s, C*H*OH); m/z 269 (M^+), 236, 136, 126, 116, 115 and 71.

(+)-*Elaeokanine C* **4**.—A mixture of compound **33** (50 mg, 0.17 mmol) and lithium aluminium hydride (14 mg, 0.37 mmol) in dry THF (10 cm^3) was heated at reflux for 2 h. The mixture was quenched with cold water (1 cm^3) and partitioned between chloroform (10 cm^3) and 10% aq. sodium hydroxide (10 cm^3). The organic layer was separated and the aqueous layer was extracted with dichloromethane (5 cm^3 × 3). The combined organic phases were dried and concentrated.

The crude product (48 mg) was treated with 10% sulfuric acid (3 cm^3) at room temperature for 2 h. After being diluted with 10% aq. sodium hydroxide (5 cm^3), the aqueous phase was extracted with dichloromethane (10 cm^3 × 5). The combined extracts were dried and concentrated. The residue was purified by flash chromatography on silica with ethyl acetate–triethylamine (19:1) to give compound **4** (30 mg, 76%) as an oil; $[\alpha]_D^{26}$ +36.9 (c 0.58, $CHCl_3$) {lit.,[19b] $[\alpha]_D^{23}$ +47 (c 0.4, $CHCl_3$)}. ^{1}H NMR and IR spectra were in good agreement with those of an authentic sample.[20]

The enantiomeric excess of our synthetic product **4** was estimated as >93% as judged by the Mosher's amide derivative of compound **4**. To a solution of compound **4** (5 mg, 0.02 mmol) in dichloromethane (3 cm^3) containing pyridine (1 drop) were added (+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid chloride (MTPACl) (10 mg) and 4-(dimethylamino)pyridine (10 mg). After being stirred at room temperature overnight, the mixture was evaporated. The residue was purified by flash chromatography on silica with chloroform–methanol (120:1) to give the MTPA amide (8 mg, 79%). On the other hand, racemate (±)-**4** was prepared from racemate (±)-**26** starting with the Diels–Alder reaction from cyclopentadiene and maleimide followed by a Mitsunobu coupling of the adduct with 2-(2-bromoethyl)-1,3-dioxolane.

The Mosher's amide of racemate (±)-**4** resolved to a pair of singlets which gave signals at δ_F −71.75 and −71.80 (trichlorofluoromethane as internal standard) in the ^{19}F NMR spectrum, whereas the Mosher's amide of synthetic compound (+)-**4** resonated at δ_F −71.80. In the ^{1}H NMR spectrum of the Mosher's amide of (±)-**4**, the methyl signals in the butanone side-chain resonated at δ 0.868 and 0.885 each as a triplet, while the methyl signal in (+)-**4** was at δ 0.868.

(+)-*Elaeokanine A* **3**.—By the literature method,[14] compound **4** (30 mg, 0.14 mmol) was transformed into elaeokanine A **3** (18 mg, 66%). The spectroscopic data of our product **3** were in good agreement with those[20] reported previously; $[\alpha]_D^{26}$ +63.0 (c 0.93, $CHCl_3$) {lit.,[19a] $[\alpha]_D^{22}$ +49 (c 0.5, $CHCl_3$); lit.,[19b] $[\alpha]_D^{23}$ +47 (c 0.31, $CHCl_3$)}.

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