Photocyclisation of Enamides. Part 35.[1,2] New Total Syntheses of the Ergot Alkaloids (±)-Chanoclavine-I and (±)-Isochanoclavine-I using a Fragmentation of 3-Amino Alcohols

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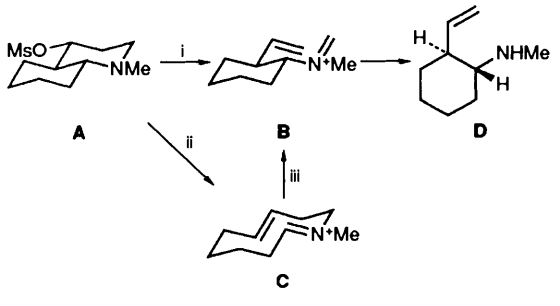
A new synthetic route involving the fragmentation reaction of 3-amino alcohols for the total synthesis of 6,7-secoergoline alkaloids was developed and then successfully applied to the total syntheses of (±)-chanoclavine-I and (±)-isochanoclavine-I.

In continuation of our synthesis of ergot alkaloids[3] which features a strategy of first building up the ergoline skeleton by enamide photocyclisation followed by elaboration of particular structural features, attention has been focussed on the application of a common skeletal compound to the synthesis of other members of this group of alkaloids,[4] namely the ring-opened and modified components, thereby establishing a general synthetic methodology for all members of ergot alkaloids. We picked the fragmentation reaction of the 3-amino alcohols, the structure commonly appearing in the photocyclised products, as the key reaction for the synthesis of ring-opened alkaloids of the chanoclavine type.[4]

Heterolytic fragmentation of 3-amino alcohol derivatives had been developed by Grob,[5] who demonstrated that by base treatment the bicyclic mesate **A** underwent smooth fragmentation *via* either peripheral cleavage or internal cleavage[6] to give the iminium compound **B**, which was then hydrolysed to the cyclohexane derivative **D** (Scheme 1). Previous studies[5] on this reaction have only been carried out on some simple 3-amino alcohol systems, therefore leaving the reaction mechanism to be clarified. We first investigated the fragmentation of model compounds having a 1-hydroxy-2-substituted octahydrobenzo[*f*]quinoline structure and the results were then successfully applied to the total syntheses of (±)-chanoclavine-I and (±)-isochanoclavine-I.



Scheme 1 *Reactions:* i, peripheral cleavage; ii, internal cleavage; iii, aza-Cope rearrangement

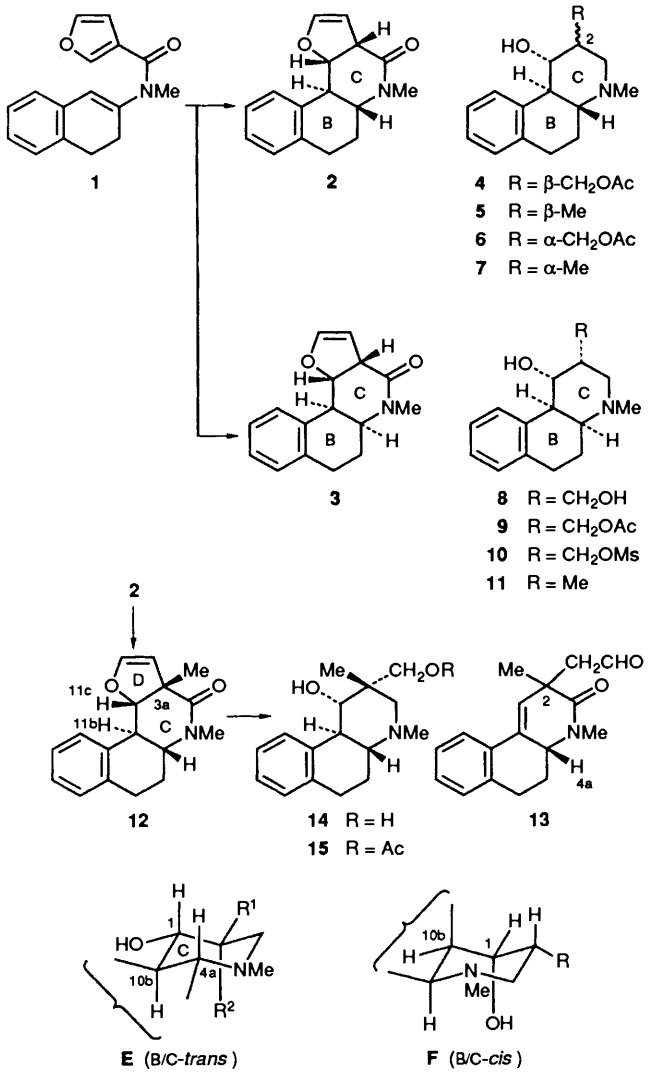
Results and Discussion

Preparation of 1-*Hydroxyoctahydrobenzo*[f]*quinolines.*—1-Hydroxy-1,2,3,4,4a,5,6,10b-octahydrobenzo[*f*]quinolines were considered to be substrates suitable for preliminary investigation of the fragmentation. Seven benzo[*f*]quinolines having two types of substituent (methyl and acetoxymethyl groups) at the 2-position and different ring junctures (B/C) were synthesized. The B/C-*trans*-2-monosubstituted derivatives **4**–**7**, which have one substituent at the 2-position and a B/C-*trans* structure, had already been prepared from the lactam **2** obtained by reductive photocyclisation of the enamide **1**.[7] The B/C-*cis*-2-monosubstituted derivatives **9** and **11** were prepared from the photocyclised B/C-*cis*-lactam **3** according to the reported procedure[7] as follows. Ozonolytic cleavage of the dihydrofuran ring in the *cis*-lactam **3** in methanol, followed by reduction with lithium aluminium hydride, afforded the amino diol **8** in 76% yield. Selective acetylation of the primary hydroxy group in the diol **8** was achieved by treatment with acetic anhydride in methylene dichloride in the presence of 4-(dimethylamino)pyridine (DMAP) at 0 °C to give the monoacetate **9** in 74% yield. When the diol **8** was treated with methanesulphonyl chloride (mesyl chloride) in pyridine at 0 °C, the monomesate **10** was prepared in 80% yield, which was then reduced with sodium borohydride in dimethyl sulfoxide (DMSO),[8] to give the 2-methyl alcohol **11** in 62% yield. The B/C-*trans*-2-disubstituted derivative **14** was prepared *via* a route involving methylation at the 3a-position of the photocyclised lactam **2** as follows. Lithium diisopropylamide (LDA) was added to a solution of the lactam **2** and methyl iodide in tetrahydrofuran (THF) at −40 °C to give the desired 3a-methyl lactam **12** in 87% yield. Inverse addition of methyl iodide to a solution of the lithiated lactam, prepared from compound **2** with LDA, gave the desired lactam **12** in only 54% yield, as well as formation of the ring-opened methylated lactam **13** in 2% yield. The stereochemistry of compound **12** as having a C/D-*cis*-11b,11c-*anti* configuration was deduced from the similarity of its proton nuclear magnetic resonance (^{1}H NMR) spectrum with that of the starting lactam **2** and also by the observation of a nuclear Overhauser effect (NOE) (24%) between the 3a-methyl group and 11c-hydrogen. The by-product **13** was also characterised from its spectral data except on the relative configuration of the 4a-hydrogen and the substituent at the 2-position. Ring opening of the dihydrofuran ring of the methyl lactam **12** by the two-step method involving ozonolysis and lithium aluminium hydride reduction gave the diol **14** in 79% yield. Selective acetylation of the diol **14** was performed by treatment with acetic anhydride in methylene dichloride in the presence of DMAP at 0 °C to afford the monoacetate **15** in 99% yield.

The stereochemistry of the B/C-*trans*-amino alcohols **4**–**7**, and **15** was established from their ^{1}H NMR spectra, particularly the coupling constants (10–11 Hz) between the 1- and 10b-proton and those (10–11 Hz) between the 4a- and 10b-proton. The results were consistent with a stable chair conformation for ring C with the 1-hydroxy group in an equatorial orientation, as shown by the structure **E**. On the other hand, the axial orientation of the 1-hydroxy group in the B/C-*cis*-amino alcohols **9** and **11** was deduced from the coupling constants (3

Table 1 Fragmentation of the 3-amino alcohol derivatives **4**, **5** and **16**–**20**

Substrate	Reaction conditions	Yield (%) of products				
		22 or **23**	**24** or **26**	**25** or **27**	**29**	**30**
4	MsCl in pyridine, 0 °C, 3.5 h	34				
4	MsCl, Et_3N in CH_2Cl_2, 0 °C, 5 h	39				
4	MsCl, Et_3N in toluene, 0 °C, 2.5 h	54				
5	MsCl, Et_3N in toluene, 0 °C, 2 h	44				
16	80% EtOH, 20 °C, 4 days	30	Trace	20		
16	80% EtOH, 50 °C, 6 h	29	9	29		
16	80% EtOH, 70 °C, 6 h	39	Trace	44		
16	Absolute EtOH, 50 °C, 6 h	11	16	44		
16	Neat, 110 °C, 7 h	Trace	24	Trace		
17	80% EtOH, 70 °C, 4 h	27	20	31		
17	Neat, 110 °C, 5 h	Trace	33	Trace		
18	80% EtOH, 70 °C, 29 h	30		27		
18	Neat, 110 °C, 13 h	Trace		11		
19	80% EtOH, 70 °C, 26 h	25		30		
20	80% EtOH, 20 °C, 22 h				32	6
20	80% EtOH, 70 °C, 2 h				50	25
20	Absolute EtOH, 50 °C, 4 h				79	6
20	Absolute EtOH, 70 °C, 4 h				73	11
20	Neat, 110 °C, 3.5 h				39	



Hz) between the 1- and 10b-proton in their ^1H NMR spectra, as shown by the conformation **F**. Thus we have prepared seven benzo[*f*]quinolines, compounds **4**–**7**, **9**, **11** and **15**, and the fragmentation of these compounds was investigated as described below.

Fragmentation Reaction of Benzo[f]*quinolines.*—For facilitating ring opening, five amino alcohols, compounds **6**, **7**, **9**, **11** and **15**, were first treated with mesyl chloride in pyridine or toluene in the presence of triethylamine to give the corresponding mesates **16**–**20** in good yield. Under the same mesylating conditions, the B/C-*trans*-amino alcohols **4** and **5** with a 2-equatorial substituent gave no isolable mesyl derivative, and instead underwent smooth fragmentation as shown in Table 1. The 2-acetoxymethyl-1-ol **4** gave the *E*-amine **22** in 34–54% yield, together with the chloride **21**. The 2-methyl-1-ol **5** gave the *E*-amine **23** in 44% yield under the same mesylating conditions. The structures of these products **22** and **23** were characterised as having an *E*-double bond and a methylamino group in a *trans* configuration on the tetrahydronaphthalene ring from their mass, IR and ^1H NMR spectra, particularly the coupling constants (15 Hz) between two olefinic protons and those (8–9 Hz) between the 1- and 2-proton in their ^1H NMR signals.

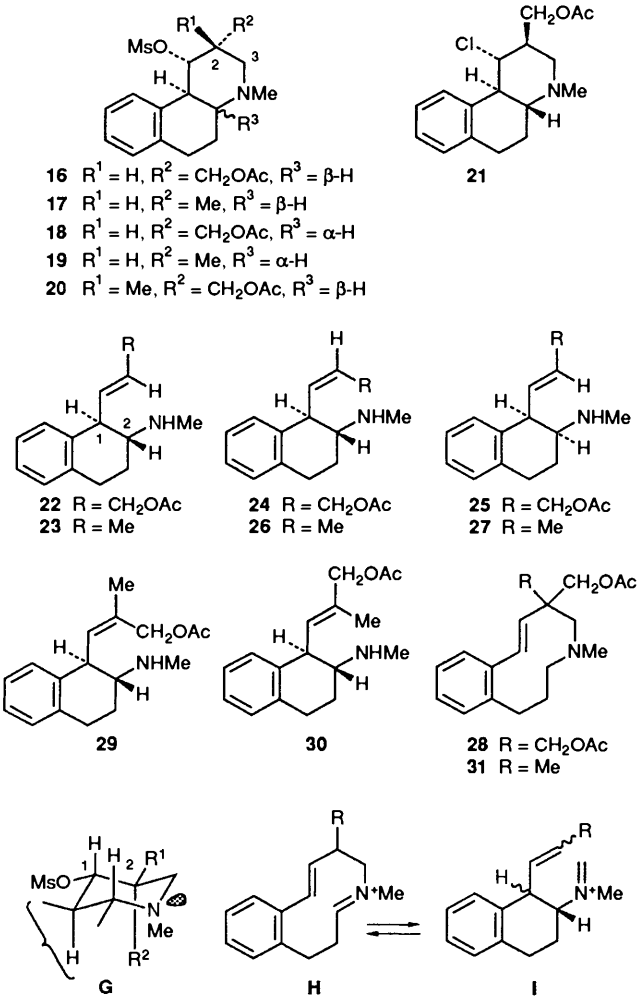
The isolated mesate **16**[7b] was then subjected to fragmentation under various conditions and the results obtained are summarised in Table 1. Stirring of an 80% ethanolic solution of the mesate **16** at 20 °C for 4 days gave a mixture of the *E-trans*- and *E-cis*-amine **22** and **25** in 30 and 20% isolated yield, respectively, together with a trace amount of the *Z-trans*-amine **24**. Heating of the mesate **16** in either 80% ethanol or absolute ethanol at 50–70 °C for 6 h afforded three amines, compounds **22**, **24** and **25**, in 67–83% combined yields as shown in Table 1. Heating of the mesylester **16** without solvent at 110 °C for 7 h gave the *Z*-amine **24** as the major product in 24% yield. The fragmentation of the 2-methyl-B/C-*trans*-mesate **17**[7b] proceeded smoothly to give the amines **23**, **26** and **27** in the yields shown in Table 1. The structures of the *Z-trans*-amines **24** and **26** were established from the coupling constants (10–11 Hz) between the two olefinic protons and those (9–10 Hz) between the 1- and 2-proton in their ^1H NMR spectra. The structure of the *E-cis*-amines **25** and **27** was deduced from the coupling constants (15–16 Hz) between the two olefinic protons and those (5–6 Hz) between the 1- and 2-proton in their ^1H NMR spectra. Similarly, the fragmentation of the B/C-cis-mesates **18** and **19** was carried out in 80% ethanol or without solvent and the stereoisomers **22** and **25** from **18**, and **23** and **27**

from **19**, were obtained in the yields shown in Table 1, though the consumption of the starting compounds **18** and **19** required a longer reaction time as compared with the B/C-*trans*-mesates **16** and **17**. Marked differences between the 2β-substituted amino alcohols **4** and **5** and the 2α-substituted amino alcohols **6**, **7**, **9** and **11** in their mesylation properties and also in the reactivity of the isolated mesylesters **16**–**19** in the fragmentation can be explained as follows. As Grob[5] has suggested that the fragmentation of the 3-amino alcohol derivates requires an extended, *anti*-periplanar relationship between the leaving group, the C–C bond which is undergoing cleavage, and the nitrogen lone pair electrons,[5] the 1,2-*trans*-amino alcohols **4** and **5** can exist preferentially in the conformation **G** with an α-axial *N*-methyl group and β-equatorial lone-pair electrons;[9] therefore the fragmentation of these amino alcohols **4** and **5** would proceed readily, even under the mesylating conditions, *via* the presumably formed mesate *in situ*. On the other hand, there exists considerable steric repulsion between the 2α-axial substituent and the α-axial methyl group on nitrogen in the conformation **G** of the 1,2-*cis*-mesates **16** and **17**. The ^{1}H NMR spectra of the B/C-*cis*-mesylesters **18** and **19** suggest that the mesyloxy group at the 1-position would be in an axial orientation as shown in the conformation **F**, which would be unfavourable to fragmentation, thus retarding the fragmentation of B/C-*cis*-mesates **18** and **19** compared with that of the B/C-*trans*-mesates **16** and **17** which have an equatorial mesyloxy group at the 1-position.

Next, in order to establish the reaction pathway of the fragmentation, we investigated the reaction of compounds **16** and **18** in the presence of sodium borohydride. The mesates **16** and **18** were treated with sodium borohydride in 80% ethanol, and reacetylation of the crude products gave the identical benzazecine **28** in 55–79% yield. The structure of the product **28** was easily established from its spectral data, particularly by the ^{1}H NMR signals of olefinic protons at δ 6.90 (d, *J* 16 Hz, 8-H) and 5.26 (dd, *J* 16, 9 Hz, 7-H). This finding, and the result that a mixture of stereoisomers was obtained by fragmentation of the mesates **16**–**19**, indicated that both the ring-opened iminium **I** (formed *via* peripheral cleavage) and the azecine **H** (formed *via* internal cleavage) would exist in an equilibrium as intermediates in the fragmentation. Since the ten-membered intermediates **H** would possibly exist in various conformations due to flexibility, we assumed that the yields and ratios of products **22**–**27** were greatly influenced by subtle difference in the reaction conditions employed.

When the B/C-*trans*-2-disubstituted mesylester **20** was subjected to the fragmentation as shown in Table 1, the *Z*-amine **29** was obtained as a major product, in addition to the *E*-amine **30** as a minor product. The relative configurations of the two substituents on the tetrahydronaphthalene moiety of both products **29** and **30** were established to be *trans* by the coupling constants (10 Hz) between the 1- and 2-protons of their ^{1}H NMR spectra. The configurations of olefinic double bonds were suggested to be *Z* in compound **29** and *E* in compound **30**, by comparison of the signal pattern due to the allylic methylene protons [δ 4.86 and 4.74 (ABq, *J* 13 Hz), in **29**; δ 4.62 (s) in **30**] in their ^{1}H NMR spectra with that of the natural alkaloids, isochanoclavine-I and chanoclavine-I. Oppolzer[10] and Stauffacher[11] have independently reported that isochanoclavine-I and chanoclavine-I exhibited ^{1}H NMR signals of allylic methylene protons at δ ~4.6 as an AB quartet and δ 4.4 as a singlet, respectively. The major product **29** has the stereochemistry readily suggested from the reaction course on the direct cleavage between the 2- and 3-position in the fragmentation compound of **20**. However, the minor product **30** has the stereochemistry suggested from the reaction course *via* the azecine derivative **H**. Further treatment of the B/C-*trans*-2-disubstituted mesate **20** with sodium borohydride in 80% ethanol, followed by reacetylation, gave the benzazecine **31** in 74% yield. The structure of compound **31** was deduced from its ^{1}H NMR spectrum [δ 6.81 (d, *J* 16.5 Hz, 8-H) and 5.30 (d, *J* 16.5 Hz, 7-H)].

Thus, we have developed a new and simple synthetic method for 6,7-secoergolines using the fragmentation reaction of the 3-amino alcohol derivatives, particularly giving the expected compounds **22**, **23** and **29** as major products from the amino alcohols **4**, **5** and **20** having the 2β-substituent and B/C-*trans*-ring junction, respectively.

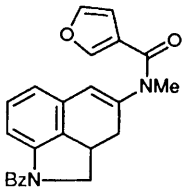


Total Synthesis of (±)-*Chanoclavine-I and* (±)-*Isochanoclavine-I*.—According to the results on the model compounds shown in the previous chapter, the total synthesis of 6,7-secoergolines was carried out by applying fragmentation of the amino alcohols **38** and **40** which are readily available from the known[3a] photocyclised lactams **33** and **34** and are different in respect of their stereochemistry at the C/D ring junction.

Two amino alcohols, compounds **38** and **40**, were synthesized from the known[3a] key intermediates **33** and **34** which had been obtained by reductive photocyclisation of the enamide **32**[3a] and successfully used as the common intermediates in the total synthesis of ergoline-type alkaloids.[3] The C/D-*trans*-lactam **33**[3a] was methylated with methyl iodide and LDA at −40 °C in THF as described above, to give the desired 3a-methyl lactam **35** in 89% yield as the sole product. The stereochemistry of compound **35** as having the D/E-*cis*-11b,11c-*anti* configuration was deduced from the similarity of its ^{1}H NMR spectrum with that of the starting lactam **33** and also by the observation of NOE (25%) between the 3a-methyl group and the 11c-

Table 2 Fragmentation of the mesylesters **42** and **47**

Substrate	Reaction conditions	Yield (%) of products 43	44	45	48	49
42	Neat, 50 °C, 4 h	11	43	5		
42	Et_2NH, 50 °C, 4 h	16		5		
42	Et_2NH, absolute EtOH, 50 °C, 3 h	33		Trace		
42	(i) Et_2NH (−15 °C);					
42	(ii) absolute EtOH, 50 °C, 3 h	56		Trace		
47	Absolute EtOH, 50 °C, 3.5 h				11	22
47	Absolute EtOH, reflux, 3.5 h				11	11
47	DMSO, 120 °C, 3 h				27	11
47	Ethylene glycol, 120 °C, 0.5 h				36	4
47	Ethylene glycol, 50 °C, 3 h				22	38



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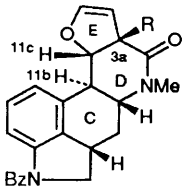

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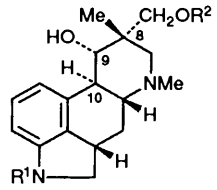
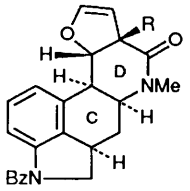
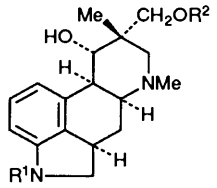
35 R = Me



36 $R^1 = R^2 = H$
37 $R^1 = CH_2Ph$, $R^2 = H$
38 $R^1 = R^2 = Ac$



34 R = H
39 R = Me

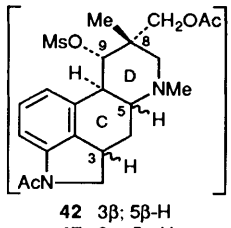


40 $R^1 = R^2 = Ac$
41 $R^1 = CH_2Ph$, $R^2 = Ac$

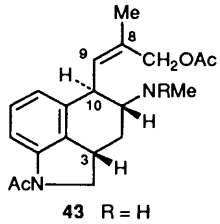
hydrogen. Ring opening of the dihydrofuran ring of the methyl lactam **35** by the two-step method[3b] involving ozonolysis and lithium aluminium hydride reduction gave the debenzoylated amino diol **36** in 53% yield together with the *N*-benzyl derivative **37** in 6% yield. Selective acetylation of the primary hydroxy and secondary amino groups in compound **36** was performed by treatment with acetic anhydride in pyridine at 0 °C to afford the desired amino alcohol **38** in 93% yield. The equatorial orientation of the 9-hydroxy group on the acetate **38** was suggested from the coupling constants (11 Hz) between the 9- and 10-proton in its ^1H NMR spectrum. In a similar manner, the known C/D-*cis*-lactam **34**[3a] was converted into the desired amino alcohol **40** *via* the 3a-methyl lactam **39** in 67% overall yield. The 9-hydroxy group of the acetate **40** was suggested to have an equatorial orientation upon consideration of the coupling constants (11 Hz) between the 9- and 10-proton in its ^1H NMR spectrum. We then thoroughly investigated the fragmentation of these substrates *via* their 9-mesates.

Treatment of the acetate **38** with one mol equiv. amount of mesyl chloride led to only recovery of the starting compound **38**, while similar treatment with an excess of mesyl chloride gave an intractable mixture. We then investigated direct formation of the desired allyl acetate **43** from the acetate **38** by fragmentation *via* the presumed mesate intermediate **42**. The acetate **38** was treated with mesyl chloride (20 mol equiv.) in pyridine at 20 °C for 3 h and the mixture was then warmed at 50 °C for 4 h to give the desired fragmentation products **43**, **44** and **45** in 11, 43 and 5% isolated yield, respectively. Since the major product **44** would be formed by sulphonation of the desired product **43** with the excess of mesyl chloride used, we investigated several reaction conditions where diethylamine was used as a quencher of the unchanged mesyl chloride as shown in Table 2. Best results were obtained when, after addition of diethylamine to a solution of the mesylated reaction mixture at −15 °C, the mixture was diluted with anhydrous ethanol and heated at 50 °C for 3 h. Thereby the desired allyl acetate **43** was isolated in 56% yield. The stereochemistry of the products **43** and its isomer **45** was deduced by comparison of their ^1H NMR spectra with those of natural isochanoclavine-I and chanoclavine-II.[10,11] The structure of the minor product **45** was deduced as the 5,10-*cis*-*E*-allyl acetate judging from the coupling constant (6 Hz) between the 5- and 10-proton and the signal pattern (singlet) of allylic methylene protons. The product **44** was identical with the sample which was prepared by mesylation of the product **43**. Furthermore, treatment of the reaction mixture, which was obtained from the acetate **38**, mesyl chloride, pyridine and diethylamine at 20 °C, with sodium borohydride in anhydrous ethanol followed by reacetylation gave the 10-membered-ring amine **46** in 59% yield.

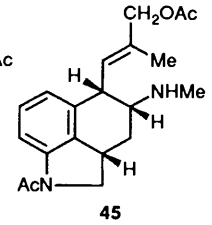
Next we investigated the fragmentation reaction of the C/D-*cis*-acetate **40**. Mesylation of the C/D-*cis*-acetate **40** in pyridine gave the corresponding unstable mesyl derivative **47** which was without purification used in the next fragmentation reaction. According to the procedure exploited for the benzo[*f*]-quinolines, the mesate **47** was treated in absolute ethanol at 50 °C for 3.5 h to give two products, **48** and **49**, in 11 and 22% yield, respectively. Structure of the minor product **48** was deduced to be the 5,10-*trans*-*E*-allyl acetate judging from the signal pattern of 10-H which appeared as a triplet (*J* 10 Hz) and that of the allylic methylene protons which appeared as a



42 3β; 5β-H
47 3α; 5α-H



43 R = H
44 R = Ms



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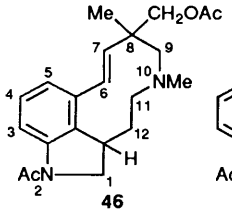

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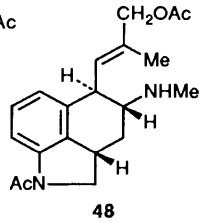

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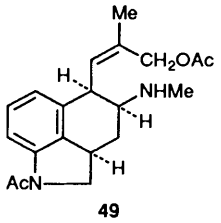

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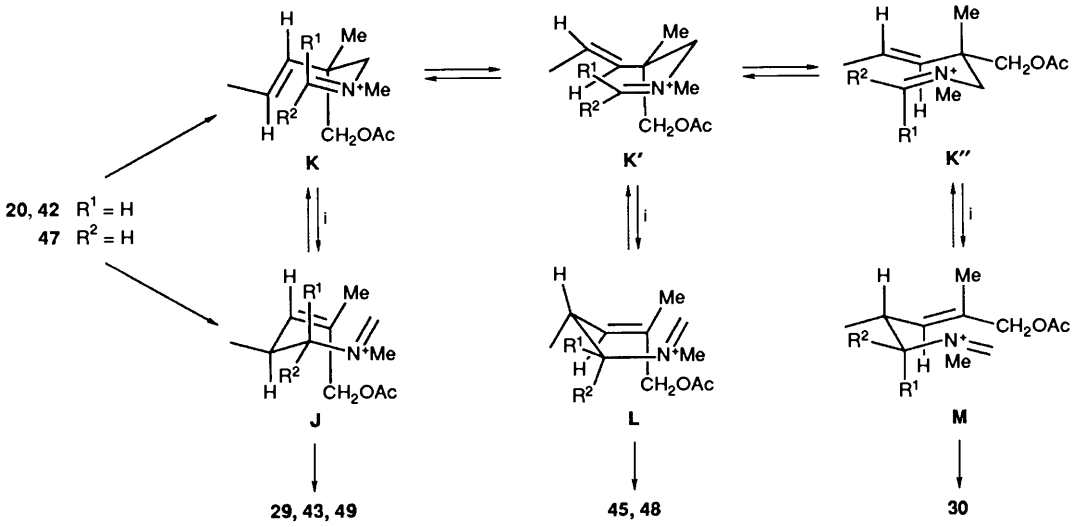
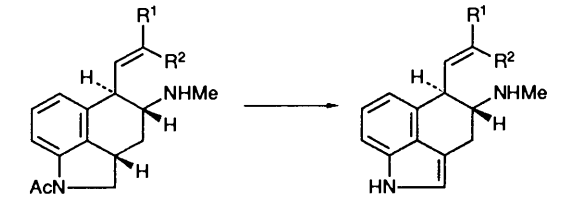


Scheme 2 *Reaction:* i, aza-Cope rearrangement

singlet. Similarly, the structure of the product **49** was deduced to be the 5,10-*cis*-Z-allyl acetate judging from the coupling constant (6 Hz) of the 5- and 10-proton and the signal pattern (AB quartet) of the allylic methylene protons.[12] Interestingly, yields and ratios of the products **48** and **49** were not influenced by the solvent used but by the reaction temperature as shown in Table 2. The desired allyl acetate **48** for the synthesis of chanoclavine-I was obtained in 36% isolated yield by warming a solution of the mesyl compound **47** in ethylene glycol at 120 °C. The relationship between the substrates **38** and **40** and their products (**43** and **45**) and (**48** and **49**) is summarised as follows. C/D-*trans*-Z-Product **43** has the expected structure from the proposed mechanism of the the fragmentation of the starting substrate **38**. Similarly, the allyl acetate **49** is an expected product from compound **47**. On the other hand, the allyl acetates **45** and **48** have the unexpected structures from the starting substrates **38** and **40** following consideration of the stereochemistry of C/D-ring and the relationships between the 9-hydrogen and the 8-methyl group. This result can be explained as follows. The allyl acetates **43** and **49** would be obtained by hydrolysis of the intermediate **J**, while the allyl acetates **45** and **48** would be produced from the intermediate **L** *via* the conformational conversion of **K** to boat-like intermediate **K'**, followed by aza-Cope rearrangement (Scheme 2). The requirement of a higher temperature for the formation of compound **48** can be reasonably explained by the proposed mechanism involving conformational inversion of **K** to **K'**. Results obtained in the previously described fragmentation of the disubstituted benzo[*f*]quinoline **20** can be reasonably explained by conformational exchange of the intermediate **K** to **K''** as follows. The ten-membered-ring intermediate **K**, formed from compound **20**, would be transformed into **K''** *via* **K'** by the rotation of single bonds around C=C and C=N double bonds. Additionally, since 3,5-*syn*-products are known to be more stable in the ergot group of alkaloids,[3a,13] the number of the products formed by the fragmentation of the two substrates **42** and **47** would be limited to two (**43** and **45** from **42**; **48** and **49** from **47**) in each case.

Finally, total synthesis of the natural alkaloids was completed by the conversion of the allyl acetates **43** and **48** into the respective target molecules. Hydrolysis of the acetates **43** and **48** by heating in methanol containing conc. hydrochloric acid at 80 °C followed by dehydrogenation[3b] with benzeneseleninic anhydride in the presence of 3 mol equiv. of indole and 10 mol equiv. of triethylamine in THF afforded the indole derivatives **50** (83% yield from **43**) and **51** (67% yield from **48**). The ^{1}H



NMR and IR spectra of the synthetic compounds **50** and **51** were found to be completely identical with those of authentic samples[14] of (±)-isochanoclavine-I and (±)-chanoclavine-I, respectively, provided by Professor Somei. Thus, we have succeeded in the total synthesis of (±)-isochanoclavine-I and (±)-chanoclavine-I *via* a fragmentation of 3-amino alcohol derivatives.

Experimental

^{1}H NMR spectra were measured with JEOL PMX-60 (60 MHz), Varian XL-200 (200 MHz), and VXR-500 (500 MHz) instruments for solutions in deuteriochloroform unless otherwise stated (tetramethylsilane as internal reference); *J*-values are given in Hz. IR spectra were measured with a Hitachi 215 machine for solutions in chloroform unless otherwise stated. Mass spectra were taken with a Hitachi M-80 spectrometer. M.p.s were determined with a Kofler-type hot-stage apparatus and are uncorrected. Reactions were performed under nitrogen. Extracts from the reaction mixtures were washed with water, dried over anhydrous sodium sulfate, and evaporated under reduced pressure. TLC was performed on precoated silica gel 60F-254 (0.25 mm thick, Merck) and preparative TLC (PLC) on precoated silica gel 60F-254 (0.5 mm thick, Merck), with UV detection at 254 and 300 nm. Medium-pressure column chromatography was undertaken on a 530-4-10V apparatus (Yamazen) with Lobar grosse B (310-25, Lichroprep Si60, Merck) as column absorbent. For flash column chromatography, Merck Kieselgel 60 (230–400 mesh) was used. Ether refers to diethyl ether. Light petroleum refers to the fraction boiling in the range 80–110 °C.

(1α,2α,4aα,10bα)-(±)-1,2,3,4,4a,5,6,10b-*Octahydro*-1-*hydroxy*-4-*methylbenzo*[f]*quinolin*-2-*ylmethanol* **8**.—Ozone gas was slowly bubbled into a solution of the *cis*-lactam **3**[7a] (300 mg) in methanol (20 cm^3) at −30 °C in the presence of Oil Violet[15] (1–2 mg) until the violet colour disappeared (5 min). Removal of the solvent gave a residue, which was dissolved in anhydrous THF (50 cm^3), and this solution was added dropwise to a suspension of lithium aluminium hydride (500 mg) in anhydrous ether (50 cm^3) under reflux. The mixture was refluxed for an additional 2 h, and then treatment in the usual way[9a] gave a crystalline residue, which was recrystallised from methanol to give the *diol* **8** (220 mg, 76%) as crystals, m.p. 189–190 °C; δ_H (200 MHz) 7.33 (1 H, m, 10-H), 7.28–7.12 (3 H, m, 7-, 8- and 9-H), 4.73 (1 H, br t, *J* 4, 1-H), 3.91 (2 H, s, OH × 2), 3.73 (2 H, d, *J* 5, CH_2OH), 3.08 (1 H, br t, *J* 4, 10b-H), 2.96 (1 H, m, 6-H^{eq}), 2.90 (1 H, m, 4a-H), 2.70 (1 H, br ddd, *J* 17, 6 and 3 Hz, 6-H^{ax}), 2.60–2.48 (2 H, m, 3-H_2), 2.34 (3 H, s, NMe), 2.26 (1 H, m, 5-H^{eq}) and 1.90–1.64 (2 H, m, 2-H and 5-H^{ax}) (Found: C, 72.7; H, 8.9; N, 5.5. $C_{15}H_{21}NO_2$ requires C, 72.8; H, 8.6; N, 5.7%).

(1α,2α,4aα,10bα)-(±)-1,2,3,4,4a,5,6,10b-*Octahydro*-1-*hydroxy*-4-*methylbenzo*[f]*quinolin*-2-*ylmethyl Acetate* **9**.—Acetic anhydride (0.03 cm^3) was added dropwise to a stirred solution of the diol **8** (100 mg) and DMAP (52 mg) in ice-cooled methylene dichloride (20 cm^3), and the mixture was stirred at 0 °C for an additional 3.5 h. Then further methylene dichloride was added and the solution was washed successively with 10% aq. sodium carbonate and water. The organic layer was dried and evaporated to give a residue, which was purified by PLC (ethyl acetate) to afford the *acetate* **9** (87 mg, 74%) as an amorphous solid, ν_{max}/cm^{-1} 3512 (OH) and 1730 (OAc); δ_H(200 MHz) 7.32–7.12 (4 H, m, ArH), 4.55 (1 H, br t, *J* 3, 1-H), 4.38 (1 H, dd, *J* 11 and 7, C*H*HOAc), 3.95 (1 H, dd, *J* 11 and 7, CH*H*OAc), 3.08 (1 H, br dd, *J* 4 and 3, 10b-H), 3.00 (1 H, m, 6-H^{eq}), 2.83 (1 H, m, 4a-H), 2.69 (1 H, m, 6-H^{ax}), 2.58 (1 H, dd, *J* 11 and 4, 3-H^{eq}), 2.42 (1 H, t, *J* 11, 3-H^{ax}), 2.36 (3 H, s, NMe), 2.25 (1 H, m, 5-H^{eq}), 2.11 (3 H, s, OAc), 2.04 (1 H, m, 2-H) and 1.71 (1 H, m, 5-H^{ax}) (Found: M^+, 289.167. $C_{17}H_{23}NO_3$ requires M, 289.168).

(1α,2α,4aα,10bα)-(±)-1,2,3,4,4a,5,6,10b-*Octahydro*-1-*hydroxy*-4-*methylbenzo*[f]*quinolin*-2-*ylmethyl Methanesulphonate* **10**.—Mesyl chloride (0.1 cm^3) was added dropwise to a stirred solution of the diol **8** (250 mg) in ice-cooled pyridine (3 cm^3), and the mixture was stirred at 0 °C for an additional 1 h. Then 10% aq. ammonium hydroxide was added, and the mixture was extracted with methylene dichloride. The extract was washed, dried and evaporated. The residue was purified by flash chromatography (methylene dichloride) to give the *monomesyl* derivative **10** (190 mg, 80%) as crystals, m.p. 120–122 °C (from methylene dichloride–ether); ν_{max}/cm^{-1} 3608 (OH); 1360 and 1174 (SO_2); δ_H(60 MHz) 4.50 (1 H, br dd, *J* 4 and 2, 1-H), 2.97 (3 H, s, Ms) and 2.31 (3 H, s, NMe) (Found: C, 58.4; H, 7.0; N, 4.4. $C_{16}H_{23}NO_4S$·$\frac{1}{20}$ CH_2Cl_2 requires C, 58.5; H, 7.1; N, 4.2%).

(1α,2α,4aα,10bα)-(±)-1,2,3,4,4a,5,6,10b-*Octahydro*-2,4-*dimethylbenzo*[f]*quinolin*-1-*ol* **11**.—Sodium borohydride (130 mg) was added to a stirred solution of the monomesyl compound **10** (190 mg) in DMSO (3 cm^3) at 10 °C, and the mixture was heated at 80 °C for 8 h. After being cooled the reaction mixture was treated with water, and this mixture was extracted with ethyl acetate. The extract was washed, dried and evaporated. The residue was purified by PLC (methylene dichloride–methanol, 9:1) to afford the *alcohol* **11** (84 mg, 62%) as crystals, m.p. 100–101 °C (from light petroleum); ν_{max}/cm^{-1} 3616 (OH); δ_H(200 MHz) 7.34–7.10 (4 H, m, ArH), 4.45 (1 H, br d, *J* 3, 1-H), 3.08 (1 H, br s, 10b-H), 3.00 (1 H, m, 6-H^{eq}), 2.75 (1 H, br s, 4a-H), 2.64 (1 H, m, 6-H^{ax}), 2.53 (1 H, dd, *J* 12 and 4, 3-H^{eq}), 2.30 (3 H, s, NMe), 2.26 (1 H, t, *J* 12, 3-H^{ax}), 2.24 (1 H, m, 5-H^{eq}), 1.94–1.60 (2 H, m, 2-H and 5-H^{ax}) and 0.97 (3 H, d, *J* 7, 2-Me) (Found: C, 77.7; H, 9.2; N, 6.0. $C_{15}H_{21}NO$ requires C, 77.9; H, 9.15; N, 6.05%).

Methylation of the Lactam **2**.—(*a*) A solution of LDA, prepared from diisopropylamine (0.28 cm^3) and butyllithium (1.57 mol dm^{-3} solution in hexane) (1.2 cm^3) at −40 °C, was added dropwise to a stirred solution of the lactam **2** (100 mg) and methyl iodide (0.073 ml) in anhydrous THF (10 cm^3) at −40 °C. Addition of LDA was stopped when the red colour of the reaction mixture became permanent. After being stirred at −40 °C for 10 min the mixture was treated with water and was then extracted with methylene dichloride. The extract was washed, dried and evaporated to give a residue, which was chromatographed on a medium-pressure column (ethyl acetate–hexane, 3:2) to afford (3aα,5aα,11bβ,11cα)-(±)-5,5*a*,6,7,11*b*,11*c*-*hexahydro*-3*a*,5-*dimethylbenzo*[f]*furo*[3,2-c]*quinolin*-4(3*a*H)-*one* **12** (90 mg, 87%) as crystals, m.p. 118–120 °C (from ether); ν_{max}/cm^{-1} 1640 (NCO); δ_H(200 MHz) 7.90 (1 H, m, 11-H: 24% intensity increase upon irradiation at δ 1.44), 7.34–7.08 (3 H, m, 8-, 9- and 10-H), 6.40 (1 H, d, *J* 3, 2-H), 5.37 (1 H, d, *J* 3, 3-H), 4.46 (1 H, d, *J* 10, 11c-H), 3.48 (1 H, ddd, *J* 13, 11 and 3, 5a-H), 3.18–2.82 (3 H, m, 7-H_2 and 11b-H), 3.11 (3 H, s, NMe), 2.56 (1 H, m, 6-H^{eq}), 1.86 (1 H, br qd, *J* 12 and 6.5, 6-H^{ax}) and 1.44 (3 H, s, 3a-Me: 2% intensity increase upon irradiation at δ 4.46) (Found: C, 75.7; H, 7.2; N, 5.1. $C_{17}H_{19}NO_2$ requires C, 75.8; H, 7.1; N, 5.2%).

(*b*) A solution of the lactam **2** (550 mg) in anhydrous THF (10 cm^3) was added at −78 °C to a stirred solution of LDA, prepared from diisopropylamine (0.25 cm^3) and butyllithium (1.55% mol dm^{-3} solution in hexane) (1.3 cm^3) at −78 °C, and the mixture was stirred at −78 °C for 10 min, then methyl iodide (1 cm^3) was added. After the mixture had been stirred at −78 °C for 10 min and then at −40 °C for 40 min, water was added and the reaction mixture was extracted with methylene dichloride. The extract was washed, dried and evaporated. The residue was purified as above (*a*) to give the same methyl lactam **12** (314 mg, 54%) and 2,3,4,4*a*,5,6-*hexahydro*-2,4-*dimethyl*-3-*oxobenzo*[f]*quinolin*-2-*ylacetaldehyde* **13** (11 mg, 2%) as a pale yellow oil, ν_{max}/cm^{-1} 1725 (CHO) and 1630 (NCO); δ_H(200 MHz) 9.75 (1 H, dd, *J* 3 and 1, CHO), 7.48 (1 H, m, 10-H), 7.32–7.12 (3 H, m, 7-, 8- and 9-H), 5.86 (1 H, d, *J* 1.5, 1-H), 4.10 (1 H, br ddd, *J* 13, 3 and 1.5, 4a-H), 3.16–3.00 (2 H, m, 6-H_2), 3.12 (3 H, s, NMe), 3.11 (1 H, dd, *J* 16.5 and 1, C*H*HCHO), 2.61 (1 H, dd, *J* 16.5 and 3, CH*H*CHO), 2.60 (1 H, m, 5-H^{eq}), 1.80 (1 H, m, 5-H^{ax}) and 1.45 (3 H, s, 2-Me) (Found: M^+, 269.141. $C_{17}H_{19}NO_2$ requires M, 269.141).

(1α,2α,4aβ,10bα)-(±)-1,2,3,4,4a,5,6,10b-*Octahydro*-1-*hydroxy*-2,4-*dimethylbenzo*[f]*quinolin*-2-*ylmethanol* **14**.—According to the procedure given for the preparation of compound **8**, ozonolysis of the lactam **12** (150 mg) in methanol (10 cm^3) in the presence of Oil Violet (1–2 mg) was followed by reduction with lithium aluminium hydride (350 mg) in anhydrous ether–THF (1:1; 50 cm^3). The crude product was purified by flash chromatography (methylene dichloride–methanol, 9:1) to afford the *diol* **14** (119 mg, 79%) as crystals, m.p. 128–132.5 °C (from ether); δ_H(200 MHz) 7.77 (1 H, m, 10-H), 7.32–7.06 (3 H, m, 7-, 8- and 9-H), 3.96 (1 H, dd, *J* 11 and 2.5, C*H*HOH), 3.81 (1 H, d, *J* 10.5, 1-H), 3.73 (1 H, d, *J* 11, CH*H*OH), 3.11 (1 H, t, *J* 10.5, 10b-H), 2.87–2.66 (2 H, m, 6-H_2), 2.86 (1 H, d, *J* 12, 3-H^{eq}), 2.22 (1 H, dd, *J* 12 and 2.5, 3-H^{ax}), 2.20 (3 H, s, NMe), 2.05 (1 H, m, 5-H^{eq}), 1.85–1.53 (2 H, m, 4a-H and 5-H^{ax}) and 0.92 (3 H, s, 2-Me) (Found: C, 73.5; H, 9.1; N, 5.4. $C_{16}H_{23}NO_2$ requires C, 73.5; H, 8.9; N, 5.4%).

(1α,2α,4aβ,10bα)-(±)-1,2,3,4,4a,5,6,10b-*Octahydro*-1-*hydroxy*-2,4-*dimethylbenzo*[f]*quinolin*-2-*ylmethyl Acetate* **15**.—According to the acetylation procedure described for compound **8**, treatment of the diol **14** (98 mg) in methylene dichloride (17 cm^3) with acetic anhydride (0.04 cm^3) in the presence of DMAP (52.4 mg), followed by recrystallisation of the crude product from ethyl acetate, gave the *acetate* **15** (113 mg, 99%) as crystals, m.p. 148.5–149.5 °C; ν_{max}/cm^{-1} 1735 (OAc); δ_H(200 MHz) 7.64 (1 H, m, 10-H), 7.32–7.10 (3 H, m, 7-, 8- and 9-H), 4.64 and 4.44 (2 H, ABq, *J* 11, CH_2OAc), 3.84 (1 H, br d, *J* 11, 1-H), 2.98–2.68 (2 H, m, 6-H_2), 2.76 (1 H, d, *J* 12, 3-H^{eq}), 2.71 (1 H, t, *J* 11, 10b-H), 2.18 (3 H, s, NMe), 2.10 (3 H, s, OAc), 2.02 (1 H, m, 5-H^{eq}), 1.90 (1 H, d, *J* 12, 3-H^{ax}), 1.90–1.58 (2 H, m, 4a-H and 5-H^{ax}), 1.16 (3 H, s, 2-Me) (Found: C, 71.1; H, 8.45; N, 4.5. $C_{18}H_{25}NO_3$ requires C, 71.25; H, 8.3; N, 4.6%).

(1α,2α,4aα,10bα)-(±)-1,2,3,4,4a,5,6,10b-*Octahydro*-4-*methyl*-1-*methylsulfonyloxybenzo*[f]*quinolin*-2-*ylmethyl Acetate* **18**.—Mesyl chloride (0.2 cm^3) was added dropwise to a stirred, ice-cooled solution of the acetate **9** (40 mg) in pyridine (1 cm^3), and the mixture was then stirred at room temperature for an additional 2 h. Then 10% aq. ammonium hydroxide was added, and the mixture was extracted with methylene dichloride. The extract was washed, dried and evaporated to give a crystalline residue, which was recrystallised from ether to afford the *monomesyl derivative* **18** (40 mg, 79%) as crystals, m.p. 100–101 °C; δ_H(200 MHz) 7.37–7.12 (4 H, m, ArH), 5.61 (1 H, br s, 1-H), 4.19 (1 H, dd, *J* 11 and 8, C*H*HOAc), 4.04 (1 H, dd, *J* 11 and 7, CH*H*OAc), 3.46 (1 H, br s, 10b-H), 3.06 (3 H, s, Ms), 3.02 (1 H, m, 6-H^{eq}), 2.87 (1 H, br s, 4a-H), 2.75–2.58 (2 H, m, 6-H^{ax} and 3-H^{eq}), 2.45–2.16 (3 H, m, 2-H, 3-H^{ax} and 5-H^{eq}), 2.38 (3 H, s, NMe), 2.10 (3 H, s, Ac) and 1.75 (1 H, m, 5-H^{ax}) (Found: C, 59.1; H, 7.0; N, 3.8. $C_{18}H_{25}NO_5S$ requires C, 58.8; H, 6.9; N, 3.8%).

(1α,2α,4aα,10bα)-(±)-1,2,3,4,4a,5,6,10b-*Octahydro*-2,4-*dimethylbenzo*[f]*quinolin*-1-*yl Methanesulfonate* **19**.—According to the mesylation procedure described for compound **9**, treatment of the alcohol **11** (145 mg) in pyridine (3 cm^3) with mesyl chloride (0.1 cm^3), followed by purification by PLC (methylene dichloride–methanol, 98:2), gave the *monomesyl derivative* **19** (150 mg, 78%) as crystals, m.p. 95–97 °C (from ether); ν_{max}/cm^{-1} 1352, 1334 and 1174 (OMs); δ_H(60 MHz) 5.33 (1 H, m, 1-H), 3.40 (1 H, br t, *J* 3, 10b-H), 3.00 (3 H, s, Ms), 2.30 (3 H, s, NMe) and 1.03 (3 H, d, *J* 6, 2-Me) (Found: C, 61.9; H, 7.4; N, 4.3. $C_{16}H_{23}NO_3S$ C, 62.1; H, 7.5; N, 4.5%).

(1α,2α,4aβ,10bα)-(±)-1,2,3,4,4a,5,6,10b-*Octahydro*-2,4-*dimethyl*-1-*methylsulfonyloxybenzo*[f]*quinolin*-2-*ylmethyl Acetate* **20**.—Mesyl chloride (114.6 mg) was added dropwise to a stirred, ice-cooled solution of the acetate **15** (202 mg) in toluene (40 cm^3) in the presence of triethylamine (0.17 ml), and the mixture was then stirred at 0 °C for 1 h. Then 10% aq. ammonium hydroxide was added, and the mixture was extracted with benzene. The extract was washed, dried and evaporated to give a crystalline residue, which was recrystallised from ether–methanol to afford the *mesate* **20** (222 mg, 87%) as crystals, m.p. 189–192 °C; δ_H(200 MHz) 7.48 (1 H, m, 10-H), 7.38–7.15 (3 H, m, 7-, 8- and 9-H), 5.19 (1 H, d, *J* 11, 1-H), 4.56 and 4.41 (2 H, ABq, *J* 11, CH_2OAc), 3.10–2.65 (4 H, m, 3-H^{eq}, 6-H_2 and 10b-H), 2.98 (3 H, s, Ms), 2.17 (3 H, s, NMe), 2.12 (3 H, s, OAc), 2.06–1.56 (4 H, m, 3-H^{ax}, 4a-H and 5-H_2) and 1.32 (3 H, s, 2-Me) (Found: M^+, 381.160. $C_{19}H_{27}NO_5S$ requires M, 381.161).

Fragmentation of the Acetate **4**.—(*a*) Mesyl chloride (0.1 cm^3) was added dropwise to a stirred solution of the acetate **4** (29 mg) in pyridine (1.5 cm^3) at 0 °C, and the mixture was stirred at 0 °C for an additional 3.5 h. Then 10% aq. ammonium hydroxide was added and the mixture was extracted with methylene dichloride. The extract was washed, dried and evaporated to give a residue, which was separated by PLC (methylene dichloride–methanol, 19:1) to afford (1α,2β,4aβ,10bα)-(±)-1-chloro-1,2,3,4,4a,5,6,10b-octahydro-4-methylbenzo[*f*]quinolin-2-ylmethyl acetate **21** (1 mg, 5%) and [1′α(E),2′β]-(±)-3-[1′,2′,3′,4′-*tetrahydro*-2′-(*methylamino*)-1′-*naphthyl*]*prop*-2-*enyl acetate* **22** (9 mg, 34%) as an oil, ν_{max}/cm^{-1} 3320 (NH) and 1732 (OAc); δ_H(200 MHz) 7.25–7.10 (4 H, m, ArH), 5.78 (1 H, dt, *J* 15 and 5.5, 2-H), 5.71 (1 H, dd, *J* 15 and 8, 3-H), 4.67 (2 H, br d, *J* 5, CH_2OAc), 3.50 (1 H, br t, *J* 8, 1′-H), 3.00–2.82 (2 H, m, 4′-H_2), 2.75 (1 H, ddd, *J* 10, 8 and 3, 2′-H), 2.57 (3 H, s, NMe), 2.24 (1 H, m, 3′-H^{eq}), 2.10 (3 H, s, OAc) and 1.72 (1 H, m, 3′-H^{ax}) (Found: M^+, 259.154. $C_{16}H_{21}NO_2$ requires M, 259.157). The chloride **21** was identical with the sample reported before[7b] upon comparison of their R_f-values and IR and ^{1}H NMR spectra.

(*b*) Mesylation of the acetate **4** (29 mg) with mesyl chloride (0.02 cm^3) in the presence of triethylamine (0.05 cm^3) in either methylene dichloride (3 cm^3) or toluene (3 cm^3), and then purification by the same procedure (*a*), gave the same chloride **21** and the same allyl acetate **22**, as shown in Table 1.

Fragmentation of the Amine **5**.—The amine **5** (50 mg) was treated with mesyl chloride (0.05 cm^3) in the presence of triethylamine (0.1 cm^3) in toluene (8 cm^3) as described above. The crude product was purified by PLC (ether–methanol, 1:1) to afford [1α(E),2β]-(±)-1,2,3,4-*tetrahydro*-N-*methyl*-1-(*prop*-1′-*enyl*)*naphthalen*-2-*amine* **23** (19 mg, 44%) as an oil, ν_{max}/cm^{-1} 3316 (NH); δ_H(200 MHz) 7.24–7.04 (4 H, m ArH), 5.70 (1 H, dq, *J* 15 and 6, 2′-H), 5.34 (1 H, ddq, *J* 15, 9 and 2, 1′-H), 3.31 (1 H, br t, *J* 9, 1-H), 2.94–2.72 (2 H, m, 4-H_2), 2.60 (1 H, ddd, *J* 10, 8 and 3, 2-H), 2.52 (3 H, s, NMe), 2.24 (1 H, m, 3-H^{eq}), 1.80 (3 H, dd, *J* 6 and 2, Me) and 1.64 (1 H, m, 3-H^{ax}) (Found: M^+, 201.146. $C_{14}H_{19}N$ requires M, 201.152).

Fragmentation of the Mesyl Derivative **16**.—The mesyl compound **16** (50 mg) was treated in either 80% aq. ethanol (6 cm^3) or absolute ethanol (6 cm^3) or neat at the temperature and for the reaction time described in Table 1. After the reaction mixture had been ice-cooled, 10% aq. ammonium hydroxide was added, and the mixture was extracted with methylene dichloride. The organic layer was washed with water, dried and evaporated to give a residue, which was separated by PLC (ether–methanol, 1:1) to give the allyl acetates **22**, **24** and **25** in the isolated yields shown in Table 1.

[1′α(Z),2′B]-(±)-3-[1′,2′,3′,4′-*Tetrahydro*-2′-(*methylamino*)-1′-*naphthyl*]*prop*-2-*enyl acetate* **24**: an oil, ν_{max}/cm^{-1} 3328 (NH) and 1732 (OAc); δ_H(200 MHz) 7.24–7.06 (4 H, m, ArH), 5.86 (1 H, dt, *J* 11 and 7, 2-H), 5.52 (1 H, br t, *J* 11, 3-H), 4.84 (2 H, dd, *J* 7 and 1, CH_2OAc), 3.65 (1 H, dd, *J* 11 and 9, 1′-H), 3.00–2.83 (2 H, m, 4′-H_2), 2.61 (1 H, ddd, *J* 10, 9 and 3, 2′-H), 2.55 (3 H, s, NMe), 2.30 (1 H, m, 3′-H^{eq}), 2.12 (3 H, s, OAc) and 1.68 (1 H, m, 3′-H^{ax}) (Found: M^+, 259.155. $C_{16}H_{21}NO_2$ requires M, 259.157).

[1′α(E),2′α]-(±)-3-[1′,2′,3′,4′-*Tetrahydro*-2′-(*methylamino*)-1′-*naphthyl*]*prop*-2-*enyl acetate* **25**: an oil, ν_{max}/cm^{-1} 3320 (NH) and 1734 (OAc); δ_H(200 MHz) 7.25–7.08 (4 H, m, ArH), 5.91 (1 H, dd, *J* 16 and 8.5, 3-H), 5.64 (1 H, dt, *J* 16 and 6, 2-H), 4.57 (2 H, dd, *J* 6 and 1, CH_2OAc), 3.74 (1 H, dd, *J* 8.5 and 6, 1′-H), 3.04–2.76 (3 H, m, 2′-H and 4′-H_2), 2.53 (3 H, s, NMe), 2.05 (3 H, s, OAc), 1.98 (1 H, m, 3′-H^{eq}) and 1.78 (1 H, m, 3′-H^{ax}) (Found: M^+, 259.156).

Fragmentation of the Mesyl Derivative **17**.—The mesyl compound **17** (50 mg) was treated in either 80% aq. ethanol (6 cm^3) or absolute ethanol (6 cm^3) or neat at the temperature and for the reaction time described in Table 1. Similar work-up

as above gave the amines **23**, **26** and **27** in the isolated yields shown in Table 1. [1α(Z),2β]-(±)-1,2,3,4-*Tetrahydro*-N-*methyl*-1-(*prop*-1-*enyl*)*naphthalen*-2-*amine* **26**: an oil, ν_{max}/cm^{-1} 3316 (NH); δ_H(200 MHz) 7.20–7.08 (4 H, m, ArH), 5.89 (1 H, dqd, *J* 10, 6.5, and 0.5, 2′-H), 5.34 (1 H, tq, *J* 10 and 2, 1′-H), 3.69 (1 H, br t, *J* 10, 1-H), 2.92–2.73 (2 H, m, 4-H_2), 2.55 (1 H, m, 2-H), 2.50 (3 H, s, NMe), 2.25 (1 H, m, 3-H^{eq}), 1.82 (1 H, dd, *J* 6.5 and 2, Me) and 1.60 (1 H, m, 3-H^{ax}) (Found: M$^+$, 201.148. $C_{14}H_{19}N$ requires M, 201.152).

[1α(E),2α]-(±)-1,2,3,4-*Tetrahydro*-N-*methyl*-1-(*prop*-1′-*enyl*)*naphthalen*-2-*amine* **27**: an oil, ν_{max}/cm^{-1} 3315 (NH); δ_H(500 MHz) 7.22–7.05 (4 H, m, ArH), 5.57 (1 H, dq, *J* 15 and 6, 2′-H), 5.52 (1 H, br dd, *J* 15 and 8, 1′-H), 3.70 (1 H, dd, *J* 8 and 5, 1-H), 3.00–2.80 (3 H, m, 2-H and 4-H_2), 2.54 (3 H, s, NMe), 2.00 (1 H, m, 3-H^{eq}), 1.79 (1 H, m, 3-H^{ax}) and 1.71 (3 H, d, *J* 6, Me) (Found: M$^+$, 201.148).

Fragmentation of the Mesyl Derivatives **18** *and* **19**.—The mesylester **18** (50 mg) or **19** (50 mg) was treated in 80% aq. ethanol (6 cm^3) or neat at the temperature and for the time described in Table 1. Similar work-up as given for the fragmentation of compound **16** gave the amines **22** and **25** from the mesate **18**, and the amines **23** and **27** from the mesate **19**, respectively, in the isolated yields shown in Table 1. These products were identical with the samples prepared above upon comparison of their R_f-values and IR and ^{1}H NMR spectra.

(E)-(±)-1,2,3,4,5,6-*Hexahydro*-4-*methyl*-4-*benzazecin*-6-*ylmethyl Acetate* **28**.—(a) *From compound* **16**. A solution of the mesyl compound **16** (20 mg) in 80% aq. ethanol (3 cm^3) was stirred at room temperature in the presence of sodium borohydride (60 mg) for 2 h. The solvent was removed and water was added to the residue. The mixture was extracted with methylene dichloride. The extract was washed, dried and evaporated to give the hydrolysed amino alcohol, which was dissolved in pyridine (1 cm^3), and acetic anhydride (0.2 cm^3) was added to the resulting ice-cooled solution. The mixture was then stirred at room temperature for 3 h, when 10% aq. sodium carbonate was added and the mixture was extracted with methylene dichloride. The extract was washed, dried and evaporated to give a residue, which was purified by PLC (methylene dichloride–methanol, 19:1) to afford the *benzazecine* **28** (12 mg, 79%) as an oil, ν_{max}/cm^{-1} 1734 (OAc); δ_H(200 MHz) 7.32–7.10 (4 H, m, ArH), 6.90 (1 H, d, *J* 16, 8-H), 5.26 (1 H, dd, *J* 16 and 9, 7-H), 4.16 (2 H, m, CH_2OAc), 3.16–1.38 (9 H, m, 1-, 2-, 3- and 5-H_2, and 6-H), 2.42 (3 H, s, NMe) and 2.09 (3 H, s, OAc) (Found: M$^+$, 273.173. $C_{17}H_{23}NO_2$ requires M, 273.173).

(b) *From compound* **18**. A solution of the acetate **18** (20 mg) in 80% aq. ethanol (3 cm^3) was stirred in the presence of sodium borohydride (60 mg) at room temperature for 8 h. Similar acetylation of the crude product as described above gave the benzazecine **28** (8 mg, 55%), which was identical with the sample prepared before upon comparison of their R_f-values and IR and ^{1}H NMR spectra.

Fragmentation of the Mesyl Derivative **20**.—The amine **20** (50 mg) was treated in either 80% aq. ethanol (6 cm^3) or absolute ethanol (6 cm^3) or neat at the temperature and for the time described in the relevant entry in Table 1. After similar work-up to that given for the fragmentation of compound **16**, the crude product was separated by PLC (ethyl acetate–triethylamine, 92:8) to afford the allyl acetates **29** and **30** in the isolated yields shown in Table 1.

[1′α(Z),2′β]-(±)-2-*Methyl*-3-[1′,2′,3′,4′-*tetrahydro*-2′-(*methylamino*)-1′-*naphthyl*]*prop*-2-*enyl acetate* **29**: pale yellow crystals, m.p. 146–149 °C (from ether); ν_{max}/cm^{-1} 1730 (OAc); δ_H(200 MHz) 7.28–7.00 (4 H, m, ArH), 5.34 (1 H, br d, *J* 10, 3-H), 4.86 and 4.74 (2 H, ABq, *J* 13, CH_2OAc), 3.77 (1 H, br t, *J* 10, 1′-H), 3.00–2.82 (2 H, m, 4′-H_2), 2.63 (1 H, ddd, *J* 10, 9 and 3, 2′-H), 2.56 (3 H, s, NMe), 2.26 (1 H, m, 3′-H^{eq}), 2.11 (3 H, s, OAc), 1.89 (3 H, d, *J* 2, Me) and 1.70 (1 H, m, 3′-H^{ax}) (Found: M$^+$, 273.175. $C_{17}H_{23}NO_2$ requires M, 273.173).

[1′α(E),2′β]-(±)-2-*Methyl*-3-[1′,2′,3′,4′-*tetrahydro*-2′-(*methylamino*)-1′-*naphthyl*]*prop*-2-*enyl acetate* **30**: a pale yellow oil, ν_{max}/cm^{-1} 1730 (OAc); δ_H(200 MHz) 7.24–7.00 (4 H, m, ArH), 5.41 (1 H, br d, *J* 10, 3-H), 4.62 (2 H, s, CH_2OAc), 3.78 (1 H, br t, *J* 9.5, 1′-H), 3.02–2.80 (2 H, m, 4′-H_2), 2.70 (1 H, br ddd, *J* 10, 9 and 3, 2′-H), 2.54 (3 H, s, NMe), 2.28 (1 H, m, 3′-H^{eq}), 2.10 (3 H, s, OAc), 1.90 (3 H, d, *J* 1.5, Me) and 1.75 (1 H, m, 3′-H^{ax}) (Found: M$^+$, 273.175).

(E)-(±)-1,2,3,4,5,6-*Hexahydro*-4,6-*dimethyl*-4-*benzazecin*-6-*ylmethyl Acetate* **31**.—A solution of the mesyl compound **20** (9 mg) in 80% aq. ethanol (1 cm^3) was stirred in the presence of sodium borohydride (20 mg) at room temperature for 1 h. The solvent was removed and water was added to the residue. The mixture was extracted with methylene dichloride. The extract was washed, dried and evaporated to give a residue, which was dissolved in pyridine (0.5 cm^3), and acetic anhydride (0.1 cm^3) was added to the resulting, ice-cooled solution. The mixture was then stirred at room temperature for 3 h. Then 10% aq. sodium carbonate was added and the mixture was extracted with methylene dichloride. The extract was washed, dried and evaporated to give a residue, which was purified by PLC (methylene dichloride–methanol, 98:2) to afford the *benzazecine* **31** (5 mg, 74%) as an oil, ν_{max}/cm^{-1} 1730 (OAc); δ_H(200 MHz) 7.33–7.12 (4 H, m, ArH), 6.81 (1 H, d, *J* 16.5, 8-H), 5.30 (1 H, d, *J* 16.5, 7-H), 4.16 (2 H, br s, CH_2OAc), 2.97–2.68 (2 H, m, 1-H_2), 2.38–2.05 (4 H, m, 3- and 5-H_2), 2.36 (3 H, s, NMe), 2.09 (3 H, s, OAc), 1.78–1.53 (2 H, m, 2-H_2) and 1.15 (3 H, s, 6-Me) (Found: M$^+$, 287.187. $C_{18}H_{25}NO_2$ requires M, 287.188).

(3*a*α,5*a*α,6*a*α,11*b*β,11*c*α)-(±)-8-*Benzoyl*-5,5a,6,6*a*,7,8,11*b*,11*c*-*octahydro*-3*a*,5-*dimethylfuro*[3,2-c]*indolo*[4,3-fg]*quinolin*-4-(3*a*-H)-*one* **35**.—Following the procedure given for compound **12**, alkylation of the lithium enolate of compound **33**[3a] (50 mg), prepared from diisopropylamine (0.092 cm^3) and butyllithium (0.4 cm^3; 1.59 mol dm^{-3} solution in hexane) with methyl iodide (0.024 cm^3), followed by purification of the crude product by a medium-pressure column chromatography (methylene dichloride–methanol, 99:1), afforded the *methyl lactam* **35** (46 mg, 89%) as crystals, m.p. 210–212 °C (from methanol–ether); ν_{max}/cm^{-1} 1638 (NCO); δ_H(200 MHz) 7.70–6.94 (8 H, m, ArH), 6.39 (1 H, d, *J* 2.5, 2-H), 5.37 (1 H, d, *J* 2.5, 3-H), 4.45 (1 H, d, *J* 10.5, 11c-H: 24% intensity increase upon irradiation at δ 1.45), 4.44 (1 H, br, 7-H^β), 3.76 (1 H, t, *J* 11.5, 7-H^α), 3.60 (1 H, ddd, *J* 12.5, 10.5 and 3, 5a-H), 3.40 (1 H, m, 6a-H), 3.08 (3 H, s, NMe), 3.00 (1 H, t, *J* 10.5, 11b-H), 2.70 (1 H, m, 6-H^{eq}), 1.68 (1 H, br q, *J* 12, 6-H^{ax}) and 1.45 (3 H, s, 3a-Me: 2% intensity increase upon irradiation at δ 4.45) (Found: C, 74.8; H, 6.1; N, 7.1. $C_{25}H_{24}N_2O_3$ requires C, 75.0; H, 6.0; N, 7.0%).

Ozonolysis of the Methyl Lactam **35**.—According to the procedure given for the preparation of compound **8**, ozonolysis of the methyl lactam **35** (1 g) in methanol (100 cm^3) in the presence of Oil Violet, followed by reduction with lithium aluminium hydride (1.5 g) in anhydrous ether–THF (1:1; 300 cm^3), gave a crystalline residue, which was recrystallised from methanol to afford (3β,8α,9α)-(±)-2,3-*dihydro*-9-*hydroxy*-6,8-*dimethylergolin*-8-*ylmethanol* **36** (384 mg, 53%) as crystals, m.p. 222–225 °C (decomp.); ν_{max}(Nujol)/cm^{-1} 3276 (NH); δ_H[200 MHz; $(CD_3)_2SO$] 7.39 (1 H, d, *J* 8, 12-H), 6.82 (1 H, t, *J* 8, 13-H), 6.36 (1 H, d, *J* 8, 14-H), 3.72 (2 H, br s, CH_2OH), 3.52–3.28 (2 H, m, 2-H^β and 9-H^{eq}), 3.04–2.84 (2 H, m, 2-H^α and 3-H), 2.84 (1 H, d, *J* 11.5, 7-H^{eq}), 2.80 (1 H, t, *J* 10.5, 10-H), 2.40

(1 H, br d, *J* 11, 4-H^{eq}), 2.23 (3 H, s, NMe), 1.94 (1 H, br t, *J* 10.5, 5-H), 1.80 (1 H, d, *J* 11.5, 7-H^{ax}), 1.20 (1 H, q, *J* 11, 4-H^{ax}), 0.92 (3 H, s, 8-Me) (Found: C, 70.6; H, 8.5; N, 9.5. $C_{17}H_{24}N_2O_2$ requires C, 70.8; H, 8.4; N, 9.7%).

Mother liquor was separated by PLC (methylene dichloride–methanol, 9:1) to give (3β,8α,9α)-(±)-1-*benzyl*-2,3-*dihydro*-9-*hydroxy*-6,8-*dimethylergolin*-8-*ylmethanol* **37** (57 mg, 6%) as crystals, m.p. 196–198 °C (from ethyl acetate); δ_H(200 MHz) 7.54–7.20 (6 H, m, 12-H and ArH), 7.06 (1 H, br t, *J* 8, 13-H), 6.41 (1 H, d, *J* 8, 14-H), 4.46 and 3.91 (2 H, ABq, *J* 14.5, NC*H*$_2$Ph), 3.96 (1 H, br dd, *J* 11 and 2, C*H*HOH), 3.88 (1 H, d, *J* 10, CH*H*OH), 3.66 (1 H, dd, *J* 11 and 8, 9-H), 3.50 (1 H, t, *J* 8, 2-H^{β}), 3.37 (1 H, br t, *J* 11, 10-H), 3.15 (1 H, m, 3-H), 2.93 (1 H, d, *J* 12, 7-H^{eq}), 2.72 (1 H, dd, *J* 12 and 8, 2-H^{α}), 2.58 (1 H, d, *J* 8, 9-OH), 2.40 (1 H, br ddd, *J* 11, 4.5 and 2, 4-H^{eq}), 2.29 (3 H, s, NMe), 2.28 (1 H, dd, *J* 12 and 1.5, 7-H^{ax}), 2.12 (1 H, ddd, *J* 11.5, 10.5 and 2, 5-H), 1.38 (1 H, q, *J* 11.5, 4-H^{ax}) and 0.95 (3 H, s, 8-Me) (Found: M$^+$, 378.231. $C_{24}H_{30}N_2O_2$ requires M, 378.231).

(3β,8α,9α)-(±)-1-*Acetyl*-2,3-*dihydro*-9-*hydroxy*-6,8-*dimethylergolin*-8-*ylmethyl Acetate* **38**.—Acetic anhydride (0.32 cm^3) was added dropwise to a stirred, ice-cooled solution of the diol **36** (93 mg) in pyridine (10 cm^3), and the mixture was stirred at room temperature for an additional 3 h. Then 10% aq. sodium carbonate was added and the mixture was extracted with methylene dichloride. The extract was washed, dried and evaporated to give a crystalline residue, which was recrystallised from ether–methylene dichloride to afford the *acetate* **38** (112 mg, 93%) as pale yellow crystals, m.p. 226–228.5 °C; ν_{max}/cm^{-1} 1732 (OAc) and 1650 (NAc); δ_H(200 MHz) 7.90 (1 H, d, *J* 8, 14-H), 7.77 (1 H, d, *J* 8, 12-H), 7.17 (1 H, t, *J* 8, 13-H), 4.60 and 4.42 (2 H, ABq, *J* 11, C*H*$_2$OAc), 4.20 (1 H, t, *J* 9, 2-H^{β}), 3.61 (1 H, br d, *J* 11, 9-H), 3.60 (1 H, m, 2-H^{α}), 3.39 (1 H, m, 3-H), 2.99 (1 H, br t, *J* 10, 10-H), 2.91 (1 H, d, *J* 12, 7-H^{eq}), 2.47 (1 H, m, 4-H^{eq}), 2.31 (3 H, s, NMe), 2.24 (3 H, s, NAc), 2.11 (3 H, s, OAc), 2.07 (1 H, t, *J* 10, 5-H), 2.00 (1 H, d, *J* 12, 7-H^{ax}), 1.41 (1 H, br q, *J* 12, 4-H^{ax}) and 1.08 (3 H, s, 8-Me) (Found: C, 66.55; H, 7.4; N, 7.5. $C_{21}H_{28}N_2O_4 \cdot \frac{1}{10} CH_2Cl_2$ requires C, 66.5; H, 7.5; N, 7.35%).

(3*a*α,5*a*β,6*a*β,11*b*β,11*c*α)-(±)-8-*Benzoyl*-5,5*a*,6,6*a*,7,8,11*b*,11*c*-*octahydro*-3a,5-*dimethylfuro*[3,2-c]*indolo*[4,3-fg]*quinolin*-4(3a-H)-*one* **39**.—Following the procedure given for compound **12**, alkylation of the lithium enolate of compound **34** (100 mg), prepared from diisopropylamine (0.18 cm^3) and butyllithium (0.8 cm^3; 1.59 mol dm^{-3} solution in hexane), with methyl iodide (0.048 cm^3), followed by purification of the crude product by medium-pressure column chromatography (methylene dichloride–methanol, 99:1), afforded the *methyl lactam* **39** (98 mg, 95%) as pale yellow crystals, m.p. 289–291 °C (decomp.) (from methanol–ether); ν_{max}/cm^{-1} 1632 (NCO); δ_H(200 MHz) 7.64–7.00 (8 H, m, ArH), 6.32 (1 H, d, *J* 2.5, 2-H), 5.33 (1 H, d, *J* 2.5, 3-H), 4.34 (1 H, br, 7-H^{β}), 4.20 (1 H, d, *J* 10.5, 11c-H), 3.74 (1 H, t, *J* 11.5, 7-H^{α}), 3.63 (1 H, br ddd, *J* 12, 6 and 2.5, 5a-H), 3.41 (1 H, m, 6a-H), 3.22 (1 H, dd, *J* 10.5 and 5.5, 11b-H), 3.05 (3 H, s, NMe), 2.38 (1 H, br d, *J* 11, 6-H^{eq}), 1.55 (1 H, q, *J* 12, 6-H^{ax}) and 1.34 (3 H, s, 3a-Me) (Found: C, 74.7; H, 6.05; N, 6.9. $C_{25}H_{24}N_2O_3$ requires C, 75.0; H, 6.0; N, 7.0%).

Ozonolysis of the Methyl Lactam **39** *and Acetylation of the Product*.—According to the procedure given for the preparation of compound **8**, ozonolysis of the methyl lactam **39** (316 mg) in methanol (120 cm^3) in the presence of Oil Violet, followed by reduction with lithium aluminium hydride (450 mg) in anhydrous ether–THF (1:1; 100 cm^3), gave a crystalline residue, which was dissolved in pyridine (9 cm^3). Then acetic anhydride (0.72 cm^3) was added to this solution at 0 °C and the resulting mixture was kept at room temperature for 15 h. After a similar work-up to that described for compound **9**, the residue was purified by medium-pressure column chromatography (methylene dichloride–methanol, 96:4) to give the acetate **40** (207 mg, 70% and the *N*-benzyl derivative **41** (35 mg, 11%).

(3α,5α,8α,9α)-(±)-1-*Acetyl*-2,3-*dihydro*-9-*hydroxy*-6,8-*dimethylergolin*-8-*ylmethyl acetate* **40**: pale yellow crystals, m.p. 220–222 °C (from ethyl acetate); ν_{max}/cm^{-1} 1730 (OAc) and 1650 (NAc); δ_H(200 MHz) 7.90 (1 H, d, *J* 8, 14-H), 7.16 (1 H, t, *J* 8, 13-H), 7.06 (1 H, br d, *J* 8, 12-H), 4.59 and 4.44 (2 H, ABq, *J* 10, C*H*$_2$OAc), 4.20 (1 H, br t, *J* 8.5, 2-H^{β}), 3.61 (1 H, dd, *J* 12 and 9, 2-H^{α}), 3.42–3.20 (3 H, m, 3-, 5-, and 9-H), 3.12 (1 H, dd, *J* 11 and 5, 10-H), 2.58 (1 H, d, *J* 12, 7-H^{eq}), 2.43 (3 H, s, NMe), 2.33 (1 H, d, *J* 12, 7-H^{ax}), 2.25 (3 H, br s, NAc), 2.13 (1 H, m, 4-H^{eq}), 2.10 (3 H, s, OAc), 1.65 (1 H, br q, *J* 11.5, 4-H^{ax}) and 1.00 (3 H, s, 8-Me) (Found: C, 67.8; H, 7.6; N, 7.5. $C_{21}H_{28}N_2O_4$ requires C, 67.7; H, 7.6; N, 7.5%).

(3α,5α,8α,9α)-(±)-1-*Benzyl*-2,3-*dihydro*-9-*hydroxy*-6,8-*dimethylergolin*-8-*ylmethyl acetate* **41**: pale yellow crystals, m.p. 184–186 °C (from ethyl acetate); ν_{max}/cm^{-1} 1730 (OAc); δ_H(200 MHz) 7.46–7.24 (5 H, m, ArH), 7.04 (1 H, t, *J* 8, 13-H), 6.72 (1 H, d, *J* 8, 12-H), 6.40 (1 H, d, *J* 8, 14-H), 4.61 and 4.44 (2 H, ABq, *J* 10, C*H*$_2$OAc), 4.48 and 3.95 (2 H, ABq, *J* 15, NC*H*$_2$Ph), 3.53 (1 H, t, *J* 7.5, 2-H^{β}), 3.35 (1 H, dd, *J* 10.5 and 4, 9-H), 3.31 (1 H, m, 5-H), 3.07 (1 H, dd, *J* 10.5 and 5, 10-H), 3.06 (1 H, m, 3-H), 2.78 (1 H, br dd, *J* 13 and 8, 2-H^{α}), 2.57 (1 H, d, *J* 12, 7-H^{eq}), 2.43 (3 H, s, NMe), 2.31 (1 H, d, *J* 12, 7-H^{ax}), 2.09 (1 H, m, 4-H^{eq}), 2.08 (3 H, s, OAc), 1.60 (1 H, q, *J* 12, 4-H^{ax}) and 1.00 (3 H, s, 8-Me) (Found: C, 74.2; H, 7.7; N, 6.7. $C_{26}H_{32}N_2O_3$ requires C, 74.25; H, 7.7; N, 6.7%).

Fragmentation of the Acetate **38**.—Mesyl chloride (20 mol equiv.) was added by portions to a solution of the acetate **38** in pyridine (0.11 mol dm^{-3}) at 0 °C and the resulting solution was stirred at 20 °C for 3 h. This reaction mixture was used for the next fragmentation reaction.

(*a*) The reaction mixture prepared from the acetate **38** (20 mg) was warmed at 50 °C for 4 h, and then 10% aq. ammonium hydroxide was added and the mixture was extracted with methylene dichloride. The organic layer was washed, dried and evaporated. The residue was purified by PLC (methylene dichloride–methanol, 92:8) to afford the allyl acetates **43** (2 mg, 11%), **44** (8 mg, 43%), and **45** (1 mg, 5%).

[2*a*α,4β,5α(Z)]-(±)-3-{1-*Acetyl*-1,2,2*a*,3,4,5-*hexahydro*-4-(*methylamino*)*benz*[cd]*indol*-5-*yl*}-2-*methylprop*-2-*enyl acetate* **43**: pale yellow crystals, m.p. 117–119.5 °C (from acetone); ν_{max}/cm^{-1} 1724 (OAc) and 1656 (NAc); δ_H*(200 MHz) 7.88 (1 H, d, *J* 8, 14-H), 7.18 (1 H, t, *J* 8, 13-H), 6.70 (1 H, d, *J* 8, 12-H), 5.37 (1 H, br d, *J* 10, 9-H), 4.96 and 4.64 (2 H, ABq, *J* 13, C*H*$_2$OAc), 4.25 (1 H, t, *J* 9, 2-H^{β}), 3.84 (1 H, t, *J* 10, 10-H), 3.67 (1 H, br t, *J* 10, 2-H^{α}), 3.42 (1 H, m, 3-H), 2.89 (1 H, br t, *J* 10, 5-H), 2.62 (3 H, s, NMe), 2.55 (1 H, m, 4-H^{eq}), 2.25 (3 H, s, NAc), 2.11 (3 H, s, OAc), 1.89 (3 H, d, *J* 1, 8-Me) and 1.66 (1 H, br q, *J* 12, 4-H^{ax}) (Found: C, 69.95; H, 7.6; N, 8.0. $C_{20}H_{26}N_2O_3$ requires C, 70.15; H, 7.65; N, 8.2%).

[2*a*α,4β,5α(Z)]-(±)-3-{1-*Acetyl*-1,2,2*a*,3,4,5-*hexahydro*-4-(N-*methyl*-N-*methylsulfonylamino*)*benz*[cd]*indol*-5-*yl*}-2-*methylprop*-2-*enyl acetate* **44**: pale yellow crystals, m.p. 170–171 °C (from ethyl acetate); ν_{max}/cm^{-1} 1732 (OAc) and 1656 (NCO); δ_H*(200 MHz) 7.91 (1 H, d, *J* 8, 14-H), 7.19 (1 H, t, *J* 8, 13-H), 6.74 (1 H, d, *J* 8, 12-H), 5.43 (1 H, br d, *J* 10, 9-H), 4.73 (2 H, br s, C*H*$_2$OAc), 4.30–4.08 (2 H, m, 2-H^{β} and 5-H), 3.86 (1 H, t, *J* 10, 10-H), 3.70–3.36 (2 H, m, 2-H^{α} and 3-H), 2.88 and 2.87 (each 3 H, s, NMe and NMs), 2.25 (1 H, m, 4-H^{eq}), 2.25 (3 H, s, NAc),

* Numbering scheme for compounds **43–45**, **48** and **49–51** follows the ergoline system.

2.13 (3 H, s, OAc), 1.90 (3 H, d, *J* 1, 8-Me) and 1.85 (1 H, m, 4-H^{ax}) (Found: M$^+$, 420.172. $C_{21}H_{28}N_2O_5S$ requires M, 420.172).

[2*a*α,4β,5β(E)]-(±)-3-{1-*Acetyl*-1,2,2*a*,3,4,5-*hexahydro*-4-(*methylamino*)*benz*[cd]*indol*-5-*yl*}-2-*methylprop*-2-*enyl acetate* **45**: a pale yellow oil, ν_{max}/cm^{-1} 1730 (OAc) and 1656 (NAc); δ_H*(200 MHz) 7.87 (1 H, br d, *J* 8, 14-H), 7.16 (1 H, td, *J* 8 and 1, 13-H), 6.76 (1 H, d, *J* 8, 12-H), 5.39 (1 H, dd, *J* 11 and 1.5, 9-H), 4.50 (2 H, s, C*H*$_2$OAc), 4.25 (1 H, t, *J* 8.5, 2-H$^{\beta}$), 4.17 (1 H, br dd, *J* 11 and 6, 10-H), 3.64 (1 H, br dd, *J* 11 and 9, 2-H$^{\alpha}$), 3.41 (1 H, m, 3-H), 3.14 (1 H, ddd, *J* 12, 6 and 3, 5-H), 2.52 (3 H, s, NMe), 2.28 (1 H, m, 4-H^{eq}), 2.25 (3 H, s, NAc), 2.05 (3 H, s, OAc), 1.99 (3 H, d, *J* 1.5, 8-Me) and 1.53 (1 H, q, *J* 12, 4-H^{ax}) (Found: M$^+$, 342.193. $C_{20}H_{26}N_2O_3$ requires M, 342.194).

The sulfonamide **44** was identical with a sample prepared by reaction of the allyl acetate **43** with mesyl chloride in pyridine upon comparison of their R_f-values and IR and ^{1}H NMR spectra.

(*b*) Diethylamine (3 cm^3) was added to the ice-cooled reaction mixture prepared from the acetate **38** (20 mg) and the mixture was warmed at 50 °C for 4 h. Similar work-up as above gave two allyl acetates, **43** (3 mg, 16%) and **45** (1 mg, 5%), both of which were identical with the samples prepared above (*a*) upon comparison of their R_f-values and IR and ^{1}H NMR spectra.

(*c*) Diethyalmine (0.12 cm^3) and ethanol (3 cm^3) were added to the ice-cooled reaction mixture prepared from the acetate **38** (20 mg) and the mixture was warmed at 50 °C for 3 h. Similar work-up as above gave the allyl acetate **43** (6 mg, 33%), which was identical with the sample prepared above (*a*) upon comparison of their R_f-values and IR and ^{1}H NMR spectra.

(*d*) Diethylamine (0.52 cm^3) was added to the reaction mixture prepared from the acetate **38** (78 mg), which was cooled to −15 °C, and ethanol (10 cm^3) was added to the mixture at 20 °C. The resulting mixture was warmed at 50 °C for 3 h. Similar work-up as above gave the allyl acetate **43** (40 mg, 56%), which was identical with the sample prepared above (*a*) upon comparison of their R_f-values and IR and ^{1}H NMR spectra.

(E)-(8α,12*a*β)-(±)-2-*Acetyl*-1,2,8,9,10,11,12,12*a*-*octahydro*-8,10-*dimethylazecino*[4,5-cd]*indol*-8-*ylmethyl Acetate* **46**.—Mesyl chloride (0.16 ml) was added to a stirred solution of the acetate **38** (50 mg) in pyridine (1.5 cm^3) at 0 °C, and the mixture was then stirred at room temperature for 3 h. Diethylamine (0.31 cm^3) was added to this reaction mixture cooled to −15 °C. After 20 min, ethanol (10 cm^3) and sodium borohydride (50 mg) were added to the mixture at 0 °C, and the mixture was then stirred at room temperature for 3 h. Water was added to the reaction mixture and the whole was extracted with methylene dichloride. The extract was washed, dried and evaporated. The residue was purified by PLC (methylene dichloride–methanol, 96:4) to give the *benzazecine* **46** (28 mg, 59%) as pale yellow crystals, m.p. 133.5–135.5 °C (from methanol–ether); ν_{max}/cm^{-1} 1730 (OAc) and 1652 (NAc); δ_H(200 MHz) 8.10 (1 H, d, *J* 8, 5-H), 7.21 (1 H, t, *J* 8, 4-H), 6.95 (1 H, d, *J* 8, 3-H), 6.67 (1 H, d, *J* 17, 6-H), 5.71 (1 H, d, *J* 17, 7-H), 4.19 (1 H, t, *J* 9, 1-H$^{\beta}$), 4.06 and 4.04 (2 H, ABq, *J* 13, C*H*$_2$OAc), 3.80 (1 H, m, 12a-H), 3.65 (1 H, br d, *J* 10, 1-H$^{\alpha}$), 2.52–2.02 (4 H, m, 9- and 11-H^2), 2.44 (3 H, s, NMe), 2.24 (3 H, s, NAc), 2.10 (3 H, s, OAc), 1.92–1.49 (2 H, m, 12-H$_2$) and 1.25 (3 H, s, 8-Me) (Found: M$^+$, 356.208. $C_{21}H_{28}N_2O_3$ requires M, 356.210).

Fragmentation of the Acetate **40**.—Mesyl chloride (0.1 cm^3) was added to a solution of the acetate **40** (20 mg) in pyridine (0.5 cm^3) at 0 °C and the resulting solution was stirred at room temperature for 3 h. Then 10% aq. ammonium hydroxide was added, and the mixture was extracted with methylene dichloride. The extract was washed, dried and evaporated to give a residue, which was, without purification, dissolved in either absolute ethanol (3 cm^3), DMSO (0.5 cm^3) or ethylene glycol (2 cm^3). The mixture was treated at the temperature and for the time described in the relevant entry in Table 2. After similar work-up as given for the fragmentation of compound **16**, the crude product was separated by PLC (methylene dichloride–methanol, 92:8) to afford the allyl acetates **48** and **49** in the isolated yields shown in Table 2.

[2*a*α,4β,5α(E)]-(±)-3-{1-*Acetyl*-1,2,2*a*,3,4,5-*hexahydro*-4-(*methylamino*)*benz*[cd]*indol*-5-*yl*}-2-*methylprop*-2-*enyl acetate* **48**: pale yellow crystals, m.p. 79–82 °C (from acetone); ν_{max}/cm^{-1} 1732 (OAc) and 1652 (NAc); δ_H*(200 MHz) 7.88 (1 H, d, *J* 8, 14-H), 7.18 (1 H, t, *J* 8, 13-H), 6.73 (1 H, d, *J* 8, 12-H), 5.46 (1 H, br d, *J* 10, 9-H), 4.64 (2 H, s, C*H*$_2$OAc), 4.25 (1 H, br t, *J* 10, 2-H$^{\beta}$), 3.66 (1 H, br t, *J* 10.5, 2-H$^{\alpha}$), 3.59 (1 H, br t, *J* 10, 10-H), 3.43 (1 H, m, 3-H), 2.70 (1 H, br ddd, *J* 12, 10 and 3, 5-H), 2.53 (1 H, m, 4-H^{eq}), 2.50 (3 H, s, NMe), 2.26 (3 H, s, NAc), 2.11 (3 H, s, OAc), 1.89 (3 H, d, *J* 1, 8-Me) and 1.39 (1 H, q, *J* 12, 4-H^{ax}) (Found: M$^+$, 342.195. $C_{20}H_{26}N_2O_3$ requires M, 342.194).

[2*a*α,4β,5β(Z)]-(±)-3-{1-*Acetyl*-1,2,2a,3,4,5-*hexahydro*-4-(*methylamino*)*benz*[cd]*indol*-5-*yl*}-2-*methylprop*-2-*enyl acetate* **49**: pale yellow crystals, m.p. 144–146 °C (from ethyl acetate); ν_{max}/cm^{-1} 1730 (OAc) and 1654 (NAc); δ_H*(200 MHz) 7.86 (1 H, d, *J* 8, 14-H), 7.15 (1 H, t, *J* 8, 13-H), 6.71 (1 H, d, *J* 8, 12-H), 5.32 (1 H, br d, *J* 11, 9-H), 4.98 and 4.76 (2 H, ABq, *J* 12, C*H*$_2$OAc), 4.24 (1 H, t, *J* 8.5, 2-H$^{\beta}$), 4.17 (1 H, dd, J 11 and 6, 10-H), 3.64 (1 H, br dd, *J* 11 and 9, 2-H$^{\alpha}$), 3.38 (1 H, m, 3-H), 3.06 (1 H, br ddd, *J* 11.5, 6 and 3, 5-H), 2.53 (3 H, s, NMe), 2.26 (1 H, m, 4-H^{eq}), 2.24 (3 H, s, NAc), 2.12 (3 H, s, OAc), 1.79 (3 H, br s, 8-Me) and 1.53 (1 H, q, *J* 12, 4-H^{ax}) (Found: M$^+$, 342.194).

(±)-*Isochanoclavine-I* **50**.—A solution of compound **43** (26.5 mg) in a mixture of conc. hydrochloric acid (0.38 cm^3) and methanol (5 cm^3) was warmed at 80 °C for 3 h. Removal of the solvent gave a residue, which was dissolved in anhydrous THF (8 cm^3), and triethylamine (0.1 cm^3), indole (27.6 mg), and benzeneseleninic anhydride (21.2 mg) were added in turn to this solution at room temperature. The resulting mixture was warmed at 50 °C for 2 h, the solvent was partly evaporated off, 10% aq. sodium carbonate was added to the residue, and the mixture was extracted with methylene dichloride. The extract was washed, dried and evaporated to give a residue, which was purified by PLC (chloroform–methanol–28% aq. ammonium hydroxide, 9:1:0.02) to afford (±)-isochanoclavine-I **50** (16.4 mg, 83%) as pale brown crystals, m.p. 190–192 °C (decomp.) (from aq. methanol) [lit.,[14] 200–201 °C decomp.)]; δ_H*(200 mHz; [$^2H_5$]pyridine) 11.64 (1 H, br s, 1-H), 7.45 (1 H, d, *J* 7, 12- or 14-H), 7.40–7.20 (2 H, m, 2- and 13-H), 7.09 (1 H, d, *J* 7, 14- or 12-H), 5.53 (1 H, br d, *J* 10, 9-H), 4.74 and 4.60 (2 H, ABq, *J* 12, C*H*$_2$OH), 4.30 (1 H, br dd, *J* 10 and 8, 10-H), 3.44 (1 H, dd, *J* 14 and 3, 4-H^{eq}), 3.00–2.89 (2 H, m, 4-H^{ax} and 5-H) 2.44 (3 H, s, NMe) and 2.19 (3 H, d, *J* 1, 8-Me) (Found: C, 73.5; H, 7.75; N, 10.8. Calc. for $C_{16}H_{20}N_2O$: C, 73.7; H, 7.9; N, 10.7%). IR and ^{1}H NMR spectra and R_f-value of compound (±)-**50** were found to be identical with those of (±)-isochanoclavine-I donated by Professor Somei.

(±)-*Chanoclavine-I* **51**.—According to the procedure given for compound **50**, hydrolysis of compound **48** (30 mg) in methanol (6 cm^3) containing conc. hydrochloric acid (0.5 cm^3) gave a crude product. Without purification, a mixture of the crude product, triethylamine (0.06 cm^3), indole (31 mg), benzene seleninic anhydride (20 mg), and THF (9 cm^3) was

* Numbering scheme for compounds **43–45**, **48** and **49–51** follows the ergoline system.

heated at 40 °C for 3 h. Work-up as given for the preparation of compound **50** gave (±)-chanoclavine-I **51** (15 mg, 67%) as pale yellow crystals, m.p. 192–194 °C (decomp.) (from acetone) [lit.,[14] 194–195 °C (decomp.)]; δ_H*(200 MHz; [$^2H_5$]pyridine) 11.54 (1 H, br s, 1-H), 7.42 (1 H, d, *J* 8, 12- or 14-H), 7.38–7.18 (2 H, m, 2- and 13-H), 7.03 (1 H, d, *J* 8, 14- or 12-H), 5.89 (1 H, br d, *J* 10, 9-H), 4.46 (2 H, s, CH_2OH), 4.21 (1 H, dd, *J* 10 and 8, 10-H), 3.42 (1 H, dd, *J* 14 and 3, 4-H^{eq}), 3.02 (1 H, br td, *J* 9 and 3, 5-H), 2.89 (1 H, dd, *J* 14 and 9, 4-H^{ax}), 2.40 (3 H, s, NMe) and 2.03 (3 H, br s, 8-Me) (Found: M^+, 256.158. Calc. for $C_{16}H_{20}N_2O$: M, 256.158). IR and ^1H NMR spectra and the R_f-value of the product (±)-**51** were found to be identical with those of (±)-chanoclavine-I supplied by Professor Somei.

* Numbering scheme for compounds **43**–**45**, **48** and **49**–**51** follows the ergoline system.

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