Photocyclization of Enamides. XXXIII.[1] Total Syntheses of (±)-Agroclavines, (±)-Fumigaclavine B, and (±)-Lysergene[2]

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Total syntheses of several ergoline-type alkaloids, (±)-agroclavine (21), (±)-agroclavine I (24), (±)-fumigaclavine B (28), and (±)-lysergene (33), were accomplished *via* a route involving reductive photocyclization of the enamide 5 followed by oxidative cleavage of the dihydrofuran ring.

Keywords enamide; reductive photocyclization; ergot alkaloid; agroclavine; agroclavine I; fumigaclavine B; lysergene; total syntheses

In Parts XXIV[3] and XXIX,[4] we reported the total syntheses of four ergoline alkaloids having an oxygen function in a substituent at the 8-position *via* a route involving reductive photocyclization of the enamide A as shown in Chart 1. Our synthetic route consisted of oxidative cleavage of a dihydrofuran ring and lithium aluminum hydride reduction of the photocylized lactam B to furnish 9-hydroxy derivatives C as the common key intermediates. However, when a benzoyl group was employed as the protective group for the indolinic nitrogen as reported previously,[3,4] it was necessary to carry out the highly selective reduction of the lactam carbonyl group in the presence of the *N*-benzoyl group or to reintroduce a protective group onto the nitrogen after deprotection caused by the reductive process involved.

In order to avoid the above inconvenience caused by the use of benzoyl as a protective group, we employed the enamide **5** bearing a *p*-methoxyphenylsulfonyl group on nitrogen of the indoline moiety in place of the benzoyl group in A, hoping to develop an improved synthesis of ergoline-type alkaloids, and succeeded in straightforward total syntheses of four ergoline alkaloids including fumigaclavine B and lysergene, which had eluded synthetic attack,[5] according to the route developed for depyrrole analogs[6] and a new procedure for the conversion of indolines to indoles.[4]

Preparation of the Key Intermediates 9, 11, 12, and 14 The tricyclic ketone **4**, which carries a *p*-methoxyphenylsulfonyl group on nitrogen, was prepared as follows in four steps from the known compound **1**[7] in 73% overall yield. Replacement of the *N*-benzoyl group by a *p*-methoxyphenylsulfonyl group was performed by acid hydrolysis of **1** followed by sulfonylation with *p*-methoxyphenylsulfonyl chloride to give **2** in 87% yield. Compound **2** was oxidized with *m*-chloroperbenzoic acid to give the epoxide **3** in 90% yield. Then the conversion of the epoxide **3** to the ketone **4** was investigated in order to avoid a tedious step involving the use of very hygroscopic magnesium dibromide in the conversion employed previously.[7] The conversion was achieved in 93% yield by adding the epoxide **3** dropwise to refluxing toluene in the presence of *p*-toluenesulfonic acid.[8] The ketone **4** showed a strong infrared (IR) absorption at 1712 cm^{-1} (CO). The tricyclic ketone **4** thus obtained was converted to the enamine by treatment with methylamine, and acylation of this enamine with furan-3-carbonyl chloride in the presence of triethylamine afforded the enamide **5** in 90% yield. The enamide **5** showed the proton nuclear magnetic resonance (^{1}H-NMR) signal of an olefinic proton at δ 6.41 as a doublet (J=2 Hz) and a strong IR absorption at 1630 cm^{-1} (NCO). Irradiation of the enamide **5** by the procedure established previously,[3] namely, in the presence of sodium borohydride in benzene and methanol (8 : 1, v/v) at 5 °C by using a high pressure mercury lamp through a Pyrex filter, afforded a complex mixture of products which had lost the *p*-methoxyphenylsulfonyl group. This is in agreement with the known result[9] on the cleavage of the sulfonamide group by irradiation under almost the same conditions. On the other hand, irradiation of the enamide **5** under the same condition described above except for the use of a uranyl glass filter in place of a Pyrex filter gave the desired product in good yield. This photocyclized product was found to be a mixture of three isomeric lactams **6**, **7**, and **8**, which were separated by repeated chromatography on a medium-pressure column in 53%, 21%, and 6% isolated yields, respectively. The structures of **6**—**8** were established to be as expected from their mass spectra (MS), which exhibited a molecular ion peak at m/z 452, two mass units larger than that of the enamide **5**, and from their IR absorptions at 1640—1636 cm^{-1} (NCO). Their stereochemistries were established by comparison of their ^{1}H-NMR spectra with those of the *N*-benzoyl derivatives.[3] That is, the D/E-*cis*-fusion and the *trans* relationship between 11b- and 11c-H for the three lactams **6**—**8**, and the C/D-*trans* structure for **6** and **8** and *cis* structure for **7** were determined. Furthermore, the relative configuration between 5a- and 6a-H was also deduced as being *cis* for **6** and **7** and *trans* for **8**. The ratio of the three stereoisomeric products **6**—**8**

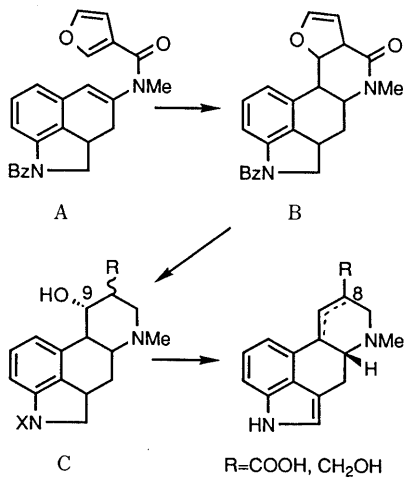

Chart 1

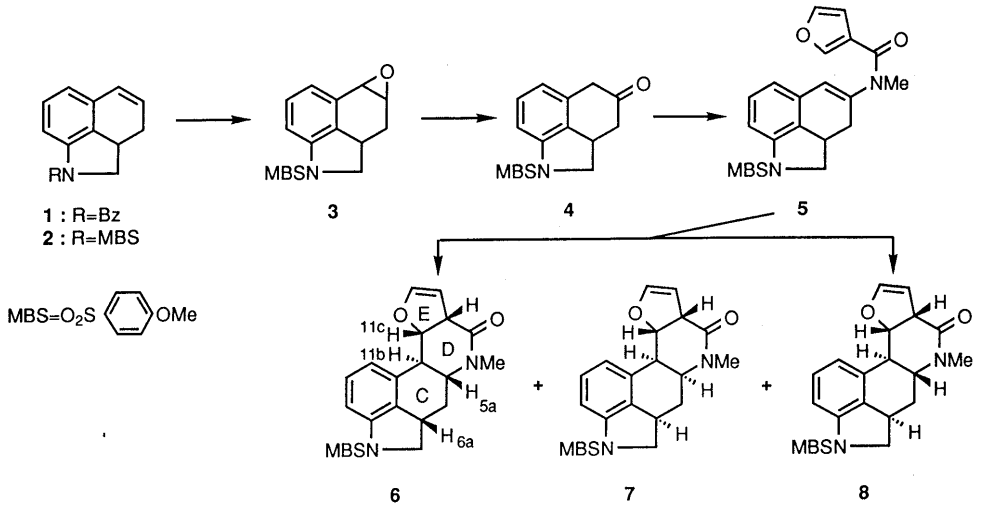

Chart 2

was almost identical with that of the three *N*-benzoyl lactams B which were previously obtained by the reductive photocyclization of the *N*-benzoyl enamide A,[3] and was not influenced by the solvent used.

Of the cyclized lactams **6**—**8**, the 5a,6a-*cis*-lactams **6** and **7** were used for the total syntheses of agroclavines, fumigaclavine B and lysergene. Ring opening of the dihydrofuran ring of the photocyclized lactams **6** and **7** was accomplished according to the procedure described previously.[4] Ozonolysis of the *trans*-lactam **6** in methylene dichloride at −30 °C followed by reduction with lithium aluminum hydride afforded the diol **9** in 45% yield. The diol **9** was treated with mesyl chloride in pyridine at 0 °C to give the monomesylate **10** in 89% yield, and this product was reduced with sodium borohydride in dimethyl sulfoxide (DMSO)[10] at 80 °C to give the 8-methyl-9-ol **11** in 74% yield. By the same procedure, the *cis*-lactam **7** was converted to the diol **12** in 58% yield and then the epimeric 8-methyl-9-ol **14** was obtained from **12** *via* the corresponding mesylate **13** in 46% yield. The stereochemistries of these products **9**, **11**, **12**, and **14** were established from the ^{1}H-NMR spectra, particularly the coupling constants between the two hydrogens at the 9- and 10-positions (8—11 Hz) and between those at 8- and 9-positions (5—6 Hz). The 1,3-diaxial relationship of 3- and 5-H was deduced from the signal pattern of 4-Hax which appears as a quartet (J=11.5—12 Hz) at δ 1.44—1.21. These data were consistent with a stable chair conformation of ring D with the 9-hydroxy group in the equatorial orientation, as shown by the structures D for **9** and **11**, and E for **12** and **14** in Chart 3.

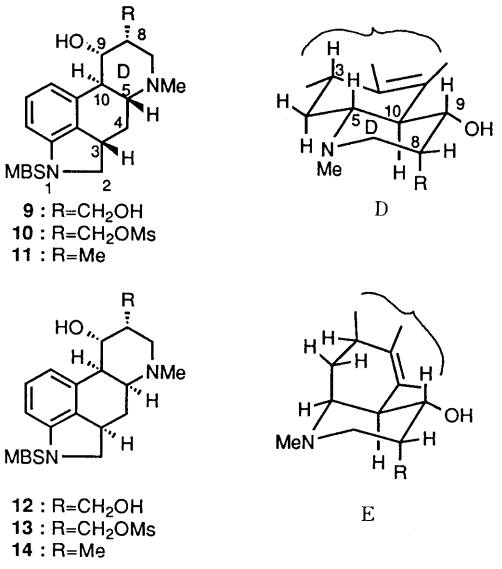

Chart 3

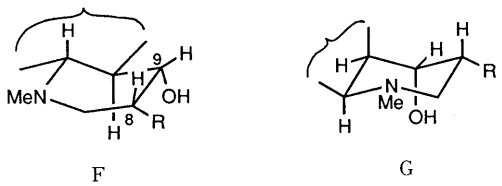

Chart 4

These compounds **9**, **11**, **12** and **14** bear all the necessary functional groups for their conversions to ergot alkaloids having an ergoline skeleton.

Total Synthesis of (±)-Agroclavine (21) and (±)-Agroclavine I (24) Agroclavine (**21**), having a C/D-*trans*-8,9-didehydroergoline structure, occupies an important position in the biosynthetic pathway[5] of ergot alkaloids. Its isomer, agroclavine I (**24**), was isolated from a *Penicillium kapuscinski* strain in 1984 and proposed to have a C/D-*cis*-8,9-didehydroergoline structure.[11] It was later synthesized by two groups.[12,13] For the synthesis of these two alkaloids, the regioselective introduction of a double bond into the 8,9-position from both the C/D-*trans*- **11** and *cis*-alcohols **14** was investigated. In the case of the C/D-*trans*-alcohol, we had previously investigated various methods of the depyrrole analogs.[6] However, the desired product was obtained only as a minor product with thionyl chloride. This result was explained as follows: the reactive intermediate would exist mostly in the stable chair form D (Chart 3) in equilibrium with the less favored boat form F (Chart 4), and the small amount of the latter form F would account for the poor formation of the desired compound having the 8,9-double bond as a result of *trans*-diaxial elimination of the 9-hydroxy group and 8-hydrogen. This suggests that the C/D-*cis*-alcohol **14** may give stereoselec-

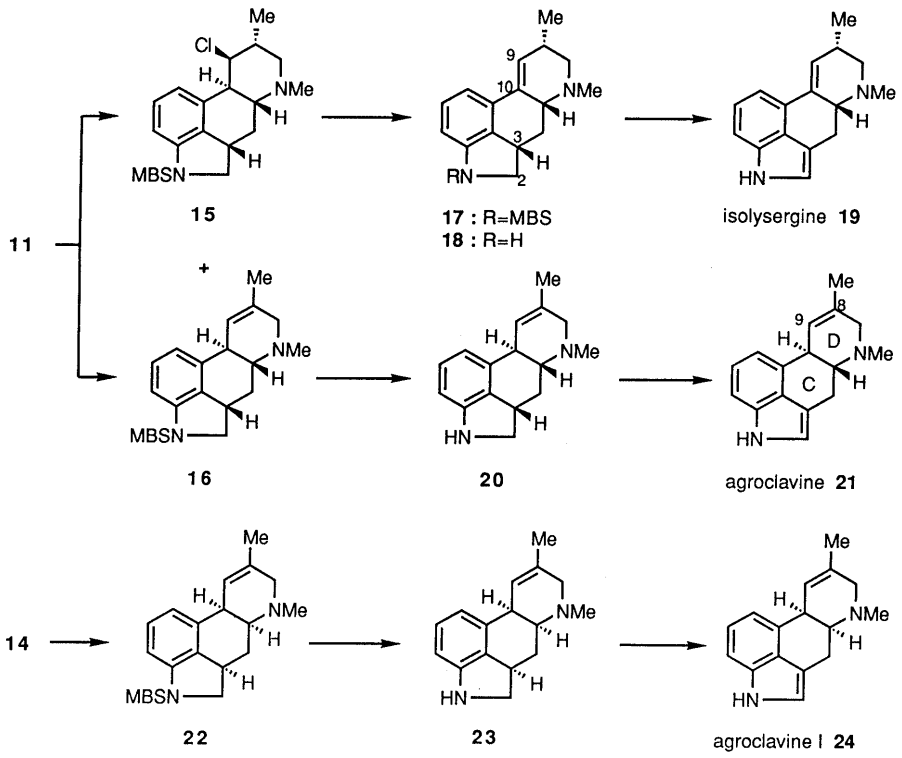

Chart 5

tively the desired compound having the 8,9-double bond since the existence of another conformation G having the 9α-axial hydroxy group and 8β-axial hydrogen in the reactive intermediate would become possible due to the C/D-*cis*-structure in **14**.

Treatment of the C/D-*trans*-9α-alcohol **11** with thionyl chloride in benzene under reflux afforded the inverted 9β-chloride **15** in 64% yield together with the 8,9-dehydrated product **16** in 24% yield, the result being in agreement with the case of the depyrrole analogs.[6] The structures of these products were firmly established from their ^{1}H-NMR signals at δ 4.71 (br s, 9-H) and 1.32 (d, J=8 Hz, 8-Me) for **15** and δ 5.97 (br s, 9-H) and 1.74 (br s, 8-Me) for **16**. On the other hand, under the same conditions, the C/D-*cis*-9α-alcohol **14** was smoothly converted in 64% yield into the dehydrated product **22**, which showed ^{1}H-NMR signals at δ 5.28 (br s, 9-H) and 1.60 (br s, 8-Me). Treatment of the 9β-chloride **15** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in benzene under reflux afforded in 89% yield the unsaturated amine **17**, which was characterized as having a double bond at the 9,10-position by the ^{1}H-NMR signals at δ 6.39 (br dd, J=5, 2 Hz, 9-H) and 1.18 (d, J=7 Hz, 8-Me).

Reductive cleavage of the protecting group of indoline in **17** was achieved by treatment with lithium aluminum hydride in dimethoxyethane (DME) under reflux to give 2,3-dihydroisolysergine (**18**) in 93% yield. Removal of the protecting group of indoline in **16** and **22** was also performed smoothly with sodium in liquid ammonia to afford **20** and **23** in quantitative yields. Finally, the conversion of the indolines **18**, **20**, and **23** into the corresponding indoles was carried out by applying the new procedure reported previously.[4] Treatment of the indolines **18**, **20**, and **23** with 0.5 mol eq of phenylseleninic anhydride in the presence of 3 mol eq of indole at 40 °C in tetrahydrofuran (THF) gave (±)-isolysergine (**19**), (±)-agroclavine (**21**), and (±)-agroclavine I (**24**) in good yields respectively. The product **19** was identical with an authentic sample of unnatural isolysergine, which was prepared by the known procedure[14] from natural lysergene given by Professor Yamatodani, by direct comparison. The product **21** was found to be identical with natural agroclavine by direct comparison and the ^{1}H-NMR of the product **24** was found to be identical with that reported for natural agroclavine I.[11] Thus, we have completed total syntheses of both (±)-agroclavine (**21**) and (±)-agroclavine I (**24**).

Total Synthesis of (±)-Fumigaclavine B (28) Fumigaclavine B (**28**) was isolated in 1961 by Spilsbury and Wilkinson,[15] who proposed the structure having an 8β-methyl configuration on the basis of its conversion into lysergine (9,10-didehydro-6,8β-dimethylergoline) upon soda-lime distillation. In 1974,[16] this proposed structure was revised by Bach *et al.*, based on ^{1}H-NMR analysis, to that having α-axial 8-methyl group and a β-axial 9-hydroxy group with a C/D-*trans* ring juncture. Polonsky *et al.*[17] supported this structure, showing that hydroboration of agroclavine gave fumigaclavine B along with isofumigaclavine B, but the stereochemical structure remained unestablished.

Thus, we planned the synthesis of this compound having the proposed structure by inverting the 9α-hydroxy group in **11**. Inversion of the 9α-hydroxy group to its epimeric β-orientation was performed according to the procedure applied to the depyrrole analog.[6] Treatment of **11** with mesyl chloride in pyridine at room temperature gave the mesylate **25** in quantitative yield. When the mesylate **25**, without purification, was treated with potassium superoxide[18] in DMSO in the presence of 18-crown-6-ether at room temperature, the 9β-hydroxy derivative **26** and dehydro derivative **17** were obtained in 54% and 10% yields, respectively. The minor product **17** was identical with the

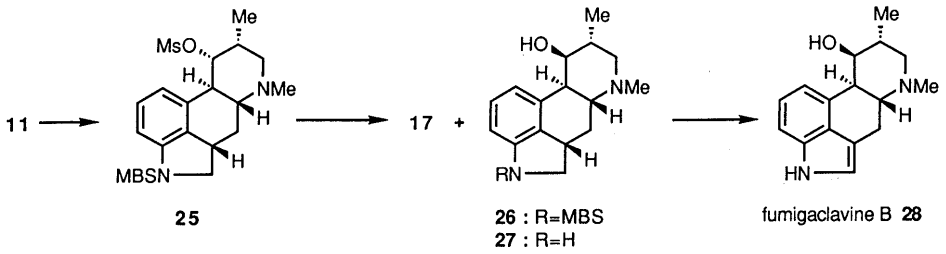

Chart 6

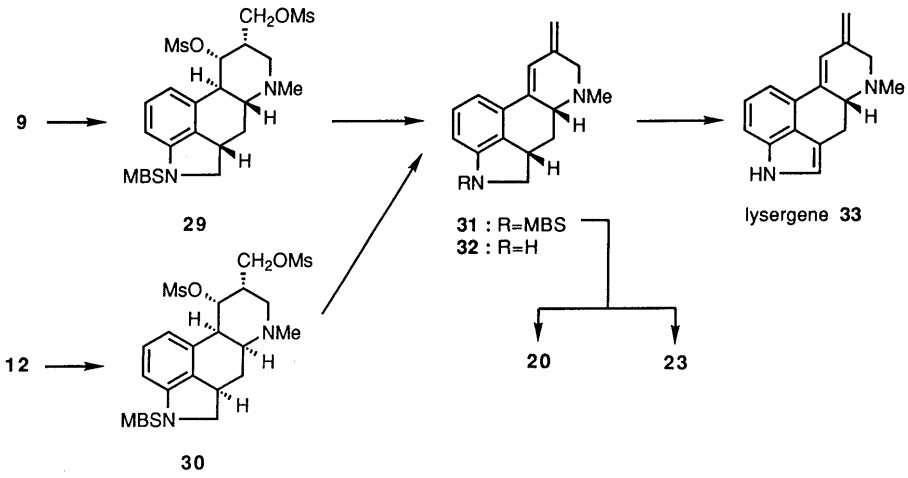

Chart 7

product which had been prepared by dehydrohalogenation of the chloride **15**. The ^{1}H-NMR spectrum of **26** showed signals at δ 4.32 (br s, 9-H), 2.95 (br d, J=10 Hz, 10-H), and 1.20 (d, J=7 Hz, 8-Me), thus confirming its stereochemistry. Treatment of **26** with sodium in liquid ammonia removed the protective group on nitrogen of the indoline moiety to afford 2,3-dihydrofumigaclavine B (**27**) and subsequent treatment with phenylseleninic anhydride in the presence of indole gave (±)-fumigaclavine B (**28**) in 76% yield from **26**. This was found to be identical with natural fumigaclavine B upon comparison of their spectral data, thus firmly establishing the proposed stereostructure of fumigaclavine B (**28**) and completing its first total synthesis.

Having thus synthesized (±)-fumigaclavine B (**28**), we rechecked its ^{1}H-NMR assignment by using the decoupling technique and nuclear Overhauser effect (NOE) measurement, and found that the previous assignment[16] for the hydrogens at the 4-, 5-, 7-, and 10-positions must be revised.

Total Synthesis of (±)-Lysergene (33) Lysergene (**33**) has a diene structure,[19] and total synthesis of this alkaloid was achieved by double elimination of two hydroxy groups in the diols **9** and **12**. The C/D-*trans*-diol **9** and the C/D-*cis*-diol **12** were mesylated with mesyl chloride in pyridine at room temperature to give the dimesylate **29** in 85% yield from **9** and the dimesylate **30** in 81% yield from **12**, respectively. Treatment of the dimesylates **29** and **30** with potassium *tert*-butoxide in DMSO at room temperature brought about smooth double elimination of the two mesyloxy groups to afford the same diene **31** in 52% yield from **29** and 51% yield from **30**, respectively. The ^{1}H-NMR spectrum of **31** showed three broad singlets due to two olefinic protons at δ 6.79, 4.99 and 4.88. Reductive cleavage of the protecting group of **31** was achieved with lithium aluminum hydride in DME under reflux to give 2,3-dihydrolysergene (**32**). Without purification, **32** was then converted into (±)-lysergene (**33**), upon dehydrogenation with phenylseleninic anhydride in the presence of indole, in 58% yield from **31**. The final product **33** was found to be identical with natural lysergene[19] by direct comparison, thus completing its first total synthesis.

Alternatively, treatment of the diene **31** with sodium in liquid ammonia brought about reductive cleavage of the protecting group and concomitant reduction of the diene structure to afford a mixture of the C/D-*trans*- **20** and *cis*-amines **23** in the ratio of 2:1. Dehydrogenation with phenylseleninic anhydride in the presence of indole afforded (±)-agroclavine (**21**) and (±)-agroclavine I (**24**) in 45% and 23% isolated yields from **31**, respectively. These products **21** and **24** were identical with the samples prepared from **16** and **22**.

Experimental

The ^{1}H-NMR spectra were measured with JEOL PMX-60 (60 MHz) and Varian XL-200 (200 MHz) instruments for solutions in deuteriochloroform unless otherwise stated (with tetramethylsilane as an internal reference), and the IR spectra were measured with a Hitachi 215 machine for solutions in chloroform unless otherwise stated. MS were taken with a Hitachi 80 spectrometer. All melting points were determined with a Kofler-type hot-stage apparatus and are uncorrected. Reactions were performed under a nitrogen atmosphere. Extracts from the reaction mixture were washed with water, dried over anhydrous sodium sulfate, and evaporated under reduced pressure. Thin layer chromatography (TLC) was performed on pre-coated Silica gel 60F-254 plates (0.25 mm thick, Merck) and preparative-TLC (p-TLC) on pre-coated Silica gel 60F-254 plates (0.5 mm thick, Merck), and spots were detected by ultraviolet (UV) irradiation of the plate at 254 and 300 nm. Medium-pressure column chromatography was undertaken on a 530-4-10V apparatus (Yamazen) using Lobar grosse B (310-25, Lichroprep Si60,

Merck) column. For flash column chromatography, Merck Kiesel gel 60 (230—400 mesh) was used. Ether refers to diethyl ether.

1-[(4-Methoxyphenyl)sulfonyl]-1,2,2a,3-tetrahydrobenz[*cd*]indole (2) A solution of 1-benzoyl-1,2,2a,3-tetrahydrobenz[*cd*]indole (**1**)[7] (6.54 g) in methanol (275 ml) containing concentrated hydrochloric acid (25 ml) was refluxed for 8 h. The reaction mixture was concentrated to a small volume and then diluted with water, and washed with benzene. The aqueous layer was made alkaline with 10% aqueous sodium carbonate and extracted with benzene. The extract was washed, dried, and evaporated to give a brown oil which was, without further purification, treated in benzene (100 ml) under reflux with 4-(methoxyphenyl)sulfonyl chloride (5.16 g) in the presence of triethylamine (3 g). After 5 h, the reaction mixture was cooled and washed with aqueous sodium bicarbonate and water. The organic layer was dried, and evaporated. The residue was crystallized from ether to give the sulfonamide **2** (7.13 g, 87%), mp 134—138 °C (colorless crystals from ethyl acetate–ether). IR: 1354, 1162 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.91 (2H, br d, J=9 Hz, ArH), 7.43 (1H, d, J=8 Hz, 8-H), 7.18 (1H, t, J=8 Hz, 7-H), 6.96 (2H, br d, J=9 Hz, ArH), 6.76 (1H, d, J=8 Hz, 6-H), 6.49 (1H, dd, J=9, 3 Hz, 5-H), 5.96 (1H, ddd, J=9, 6, 2 Hz, 4-H), 4.38 (1H, m, 2-H), 3.84 (3H, s, OMe), 3.45—3.16 (2H, m, 2- and 2a-H), 2.50 (1H, m, 3-H_{eq}), 1.99 (1H, m, 3-H_{ax}). *Anal.* Calcd for $C_{18}H_{17}NO_3S$: C, 66.03; H, 5.23; N, 4.28. Found: C, 65.91; H, 5.11; N, 4.31.

4,5-Epoxy-1,2,2a,3,4,5-hexahydro-1-[(4-methoxyphenyl)sulfonyl]benz[*cd*]indole (3) *m*-Chloroperbenzoic acid (80%, 3.04 g) was added all at once to a solution of the sulfonamide **2** (4 g) in chloroform (100 ml). The solution was swirled until all the peracid was dissolved and then kept at 5°C for 3 h. The reaction mixture was washed with aquous sodium thiosulfate, 5% aqueous sodium hydroxide, and water. The organic layer was dried and evaporated, and the residue was crystallized from ethyl acetate–hexane to give the epoxide **3** (3.7 g, 90%), mp 165—168 °C (colorless crystals from benzene–hexane). IR: 1356, 1160 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.75 (2H, br d, J=9 Hz, ArH), 7.55 (1H, d, J=8 Hz, 8-H), 7.22 (1H, t, J=8 Hz, 7-H), 7.11 (1H, d, J=8 Hz, 6-H), 6.92 (2H, br d, J=9 Hz, ArH), 4.31 (1H, dd, J=11, 9 Hz, 2-H), 3.81 (3H, s, OMe), 3.79 (1H, d, J=4 Hz, 5-H), 3.65 (1H, dd, J=4, 3 Hz, 4-H), 3.32 (1H, dd, J=11, 10 Hz, 2-H), 3.06 (1H, m, 2a-H), 2.61 (1H, ddd, J=14, 7, 3 Hz, 3-H_{eq}), 1.32 (1H, dd, J=14, 11 Hz, 3-H_{ax}). *Anal.* Calcd for $C_{18}H_{17}NO_4S$: C, 62.96; H, 4.99; N, 4.08. Found: C, 63.20; H, 4.91; N, 4.19.

1-[(4-Methoxyphenyl)sulfonyl]-1,2,2a-3-tetrahydrobenz[*cd*]-indol-4(5*H*)-one (4) A toluene solution (220 ml) of *p*-toluenesulfonic acid (1.23 g) was refluxed for 0.5 h with a Dean-Stark apparatus to remove water, and then a solution of the epoxide **3** (2 g) in toluene (15 ml) was added dropwise to the resulting stirred solution under reflux. After being refluxed for 1 h, the mixture was ice-cooled and washed with aqueous saturated sodium bicarbonate and water. The organic layer was dried and evaporated. The residue was crystallized from benzene to give the ketone **4** (1.86 g, 93%), mp 149—151 °C (colorless needles from benzene–hexane). IR: 1712 (CO), 1358, 1160 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.78 (2H, br d, J=9 Hz, ArH), 7.49 (1H, d, J=8 Hz, 8-H), 7.24 (1H, t, J=8 Hz, 7-H), 6.94 (2H, br d, J=9 Hz, ArH), 6.83 (1H, d, J=8 Hz, 6-H), 4.41 (1H, dd, J=9, 8 Hz, 2-H), 3.83 (3H, s, OMe), 3.50 (1H, m, 2a-H), 3.46 (2H, s, 5-H_2), 3.38 (1H, dd, J=11, 9 Hz, 2-H), 2.96 (1H, dd, J=16, 5 Hz, 3-H_{eq}), 2.13 (1H, dd, J=16, 12 Hz, 3-H_{ax}). *Anal.* Calcd for $C_{18}H_{17}NO_4S \cdot 1/5C_6H_6$: C, 64.23; H, 5.11; N, 3.90. Found: C, 64.30; H, 5.06; N, 3.75.

***N*-[1-[(4-Methoxyphenyl)sulfonyl]-1,2,2a,3-tetrahydrobenz[*cd*]indol-4-yl]-*N*-methyl-3-furancarboxamide (5)** Anhydrous methylamine gas was bubbled into a boiling solution of the ketone **4** (2.1 g) in toluene (300 ml) under a nitrogen stream for 6 h; water was removed as it was formed. The mixture was refluxed further to remove the excess of methylamine by bubbling nitrogen. Triethylamine (1 g) was added to the resulting ice-cooled, stirred solution and then a solution of freshly prepared furan-3-carbonyl chloride (0.8 g) in anhydrous benzene (50 ml) was added dropwise. After being refluxed for 2 h the mixture was cooled, diluted with benzene, and washed. The organic layer was dried and evaporated. Flash chromatography (methylene dichloride) of the residue gave the enamide **5** (2.48 g, 90%) as a pale yellow glass. IR: 1630 (NCO), 1355, 1160 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.82—7.70 (3H, m, 2′-H and ArH), 7.42 (1H, d, J=7 Hz, 8-H), 7.32 (1H, t, J=2 Hz, 5′-H), 7.17 (1H, t, J=7 Hz, 7-H), 6.95 (2H, br d, J=9 Hz, ArH), 6.73 (1H, d, J=7 Hz, 6-H), 6.58 (1H, dd, J=2, 1 Hz, 4′-H), 6.41 (1H, d, J=2 Hz, 5-H), 4.31 (1H, m, 2a-H), 3.84 (3H, s, OMe), 3.30—3.25 (2H, m, 2-H_2), 3.21 (3H, s, NMe), 2.52—2.22 (2H, m, 3-H_2). High-resolution MS *m/z*: Calcd for $C_{24}H_{22}N_2O_5S$ (M^+) 450.1247. Found: 450.1246.

Reductive Photocyclization of the Enamide 5 A solution of a mixture of the enamide **5** (1.3 g) and sodium borohydride (1.3 g) in benzene–methanol (8 : 1, 900 ml) was irradiated with a high-pressure (300 W) mercury lamp through an uranyl glass filter (Eikosha, Osaka, Japan, PIH-300) at 5°C for 2 h. The reaction mixture was washed and the organic layer was dried and evaporated to afford a crystalline residue, which was chromatographed on a medium-pressure column (acetonitrile: methylene dichloride = 1 : 4). (3aβ,5aβ,6aβ,11bα,11cβ)-5,5a,6,6a,7,8,11b,11c-Octahydro-8-[(4-methoxyphenyl)sulfonyl]-5-methylfuro[4,3-*fg*]quinolin-4(3a*H*)-one (**6**) (694 mg, 53%) was obtained from the first fraction. The residue obtained from the second fraction was rechromatographed on a medium-pressure column (benzene : methanol = 98.5 : 1.5) to give (3aβ,5aα,6aα,11bα,11cβ)-5,5a,6,6a,7,8,11b,11c-octahydro-8-[(4-methoxyphenyl)sulfonyl]-5-methylfuro[4,3-*fg*]quinolin-4(3a*H*)-one (**7**) (275 mg, 21%) and (3aβ,5aβ,6aα,11bα,11cβ)-5,5a,6,6a,7,8,11b,11c-octahydro-8-[(4-methoxyphenyl)sulfonyl]-5-methylfuro[4,3-*fg*]quinolin-4(3a*H*)-one (**8**) (79 mg, 6%). The lactam **6**: mp 222—224 °C (colorless crystals from methylene dichloride–ethyl acetate). IR: 1640 (NCO), 1355, 1160 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.80 (2H, br d, J=8 Hz, ArH), 7.45 (1H, d, J=8 Hz, 9-H), 7.39 (1H, d, J=8 Hz, 11-H), 7.22 (1H, t, J=8 Hz, 10-H), 6.96 (2H, br d, J=8 Hz, ArH), 6.44 (1H, t, J=2.5 Hz, 2-H), 5.34 (1H, t, J=2.5 Hz, 3-H), 4.84 (1H, dd, J=12, 10 Hz, 11c-H), 4.31 (1H, m, 7-Hβ), 3.84 (3H, s, OMe), 3.82 (1H, dt, J=12, 2.5 Hz, 3a-H), 3.52 (1H, ddd, J=12, 10, 3 Hz, 5a-H), 3.31—3.10 (2H, m, 6a-H and 7-Hα), 3.02 (3H, s, NMe), 2.91 (1H, t, J=10 Hz, 11b-H), 2.58 (1H, dt, J=12, 4 Hz, 6-H_{eq}), 1.51 (1H, br q, J=12 Hz, 6-H_{ax}). MS *m/z*: 452 (M^+). *Anal.* Calcd for $C_{24}H_{24}N_2O_5S$: C, 63.70; H, 5.35; N, 6.19. Found: C, 63.69; H, 5.10; N, 6.03. The lactam **7**: mp 237—239 °C (dec.) (colorless crystals from methylene dichloride–ethyl acetate). IR: 1638 (NCO), 1358, 1162 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.80 (2H, br d, J=8 Hz, ArH), 7.48 (1H, d, J=8 Hz, 9-H), 7.23 (1H, t, J=8 Hz, 10-H), 7.10 (1H, d, J=8 Hz, 11-H), 6.97 (2H, br d, J=8 Hz, ArH), 6.38 (1H, t, J=2.5 Hz, 2-H), 5.30 (1H, t, J=2.5 Hz, 3-H), 4.46 (1H, dd, J=11, 10 Hz, 11c-H), 4.27 (1H, m, 7-Hβ), 3.86 (3H, s, OMe), 3.78 (1H, dt, J=11, 2.5 Hz, 3a-H), 3.56 (1H, ddd, J=12.5, 5, 3 Hz, 5a-H), 3.34—3.10 (3H, m, 11b-H, 7-Hα, and 6a-H), 3.08 (3H, s, NMe), 2.32 (1H, dt, J=12, 3 Hz, 6-H_{eq}), 1.39 (1H, br q, J=12 Hz, 6-H_{ax}). MS *m/z*: 452 (M^+). *Anal.* Calcd for $C_{24}H_{24}N_2O_5S \cdot 1/10CH_2Cl_2$: C, 62.79; H, 5.29; N, 6.08. Found: C, 62.69; H, 5.37; N, 6.12. The lactam **8**: mp 231—233 °C (colorless crystals from methylene dichloride–ethyl acetate). IR: 1636 (NCO), 1358, 1162 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.80 (2H, br d, J=8 Hz, ArH), 7.51 (1H, d, J=8 Hz, 9-H), 7.38—7.20 (2H, m, 10- and 11-H), 6.96 (2H, br d, J=8 Hz, ArH), 6.38 (1H, t, J=2.5 Hz, 2-H), 5.32 (1H, t, J=2.5 Hz, 3-H), 5.06 (1H, t, J=10 Hz, 11c-H), 4.42 (1H, m, 7-Hβ), 4.04 (1H, td, J=10, 2.5 Hz, 3a-H), 3.85 (3H, s, OMe), 3.40—3.08 (3H, m, 5a-H, 6a-H, and 7-Hα), 2.98 (3H, s, NMe), 2.86 (1H, t, J=10 Hz, 11b-H), 2.14 (1H, m, 6-H_{eq}), 1.98 (1H, m, 6-H_{ax}). MS *m/z*: 452 (M^+). *Anal.* Calcd for $C_{24}H_{24}N_2O_5S \cdot 1/5CH_2Cl_2$: C, 61.91; H, 5.24; N, 5.97. Found: C, 61.94; H, 5.26; N, 6.27.

(3β,8α,9α)-2,3-Dihydro-8-hydroxymethyl-1-[(4-methoxyphenyl)sulfonyl]-6-methylergolin-9-ol (9) Ozone gas was slowly bubbled at −30 °C into a solution of the *trans*-lactam **6** (900 mg) in methylene dichloride (70 ml) in the presence of oil violet until the violet color disappeared (10 min). Removal of the solvent gave the residue, which was dissolved in anhydrous THF (200 ml), and this solution was added dropwise to a solution of lithium aluminum hydride (300 mg) in anhydrous ether (200 ml) under reflux. The mixture was refluxed for an additional 2 h, and treatment in the usual way gave a crystalline residue, which was recrystallized from methanol to give the diol **9** (400 mg, 45%) as colorless needles, mp 200—201.5 °C. IR (Nujol): 3500—3150 (OH), 1355, 1160 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ ($CDCl_3$–CD_3OD): 7.82—7.72 (3H, m, 12-H, and ArH), 7.36 (1H, d, J=8 Hz, 14-H), 7.14 (1H, t, J=8 Hz, 13-H), 6.98 (2H, br d, J=8 Hz, ArH), 4.22 (1H, m, 2-Hβ), 4.15 (1H, dd, J=11, 7 Hz, C$\underline{H}_2$OH), 4.02 (1H, m, 2-Hα), 3.98 (1H, dd, J=11, 5 Hz, 9-H), 3.89 (1H, dd, J=11, 5 Hz, C$\underline{H}_2$OH), 3.86 (3H, s, OMe), 3.14 (1H, m, 3-H), 3.02 (1H, dd, J=12, 3 Hz, 7-H_{eq}), 2.93 (1H, t, J=11 Hz, 10-H), 2.50—2.32 (2H, m, 4-H_{eq} and 7-H_{ax}), 2.31 (3H, s, NMe), 2.19 (1H, m, 8-H), 2.02 (1H, br t, J=11 Hz, 5-H), 1.21 (1H, br q, J=12 Hz, 4-H_{ax}). *Anal.* Calcd for $C_{23}H_{28}N_2O_5S$: C, 62.14; H, 6.35; N, 6.30. Found: C, 62.21; H, 6.39; N, 6.29.

(3β,8α,9α)-2,3-Dihydro-8-methanesulfonyloxymethyl-1-[(4-methoxyphenyl)sulfonyl]-6-methylergolin-9-ol (10) Mesyl chloride (0.1 ml) was added dropwise to a stirred solution of the diol **6** (115 mg) in pyridine (2 ml) under ice-cooling, and the mixture was stirred at 0 °C for an additional 3.5 h. Then 10% aqueous ammonium hydroxide was added to the reaction mixture, which was then extracted with methylene dichloride. The extract was washed, dried, and evaporated to give a crystalline residue which was recrystallized from ether to afford the monomesylate **10** (120 mg, 89%) as colorless crystals, mp 233—235 °C (dec.). IR: 1360, 1160 (NSO_2

and OSO_2) cm^{-1}. ^{1}H-NMR (60 MHz) δ: 4.82—4.56 (2H, m, 8-C$\underline{H}_2$OMs), 4.22 (1H, m, 2-Hβ), 4.06 (1H, m, 9-H), 3.85 (3H, s, OMe), 3.06 (3H, s, OMs), 2.42 (3H, s, NMe). *Anal.* Calcd for $C_{24}H_{30}N_2O_7S_2$: C, 55.15; H, 5.79; N, 5.36. Found: C, 55.13; H, 5.86; N, 5.29.

(3β,8α,9α)-2,3-Dihydro-1-[(4-methoxyphenyl)sulfonyl]-6,8-dimethylergolin-9-ol (11) Sodium borohydride (108 mg) was added to a stirred solution of the monomesylate **10** (140 mg) in DMSO (1 ml) at 10 °C, and the mixture was heated at 80°C for 8 h. Water was added to the cooled reaction mixture and the whole was extracted with ethyl acetate. The extract was washed, dried, and evaporated. The residue was purified by p-TLC (methylene dichloride : methanol = 9 : 1) to afford the alcohol **11** (85 mg, 74%), mp 199—200 °C (colorless needles from chloroform–ether). IR: 3608 (OH), 1354, 1162 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.81 (2H, br d, J = 8 Hz, ArH), 7.67 (1H, d, J = 8 Hz, 12-H), 7.42 (1H, d, J = 8 Hz, 14-H), 7.16 (1H, t, J = 8 Hz, 13-H), 6.95 (2H, br d, J = 8 Hz, ArH), 4.23 (1H, m, 2-Hβ), 3.89 (1H, dd, J = 11, 5 Hz, 9-H), 3.84 (3H, s, OMe), 3.20—2.96 (2H, m, 2-Hα and 3-H), 2.94—2.78 (2H, m, 7-H_{eq} and 10-H), 2.45—2.30 (2H, m, 4-H_{eq} and 7-H_{ax}), 2.32 (3H, s, NMe), 2.14 (1H, m, 8-H), 1.95 (1H, br t, J = 11 Hz, 5-H), 1.22 (1H, br q, J = 12 Hz, 4-H_{ax}), 1.19 (3H, d, J = 7 Hz, 8-Me). *Anal.* Calcd for $C_{23}H_{28}N_2O_4S$: C, 64.46; H, 6.59; N, 6.54. Found: C, 64.55; H, 6.47; N, 6.23.

(3α,8α,9α,10α)-2,3-Dihydro-8-hydroxymethyl-1-[(4-methoxyphenyl)-sulfonyl]-6-methylergolin-9-ol (12) According to the procedure given for the preparation of **9**, ozonolysis of the *cis*-lactam **7** (1.08 g) in methylene dichloride (75 ml) in the presence of oil violet followed by reduction with lithium aluminum hydride (1.5 g) in anhydrous ether–THF (1 : 1, 300 ml) gave a crystalline residue, which was recrystallized from methylene dichloride–ether to afford the diol **12** (620 mg, 58%) as pale yellow crystals, mp 172—174 °C. IR: 3500—3150 (OH), 1355, 1160 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.78 (2H, br d, J = 8 Hz, ArH), 7.40 (1H, d, J = 8 Hz, 14-H), 7.16 (1H, t, J = 8 Hz, 13-H), 7.03 (1H, d, J = 8 Hz, 12-H), 6.93 (2H, br d, J = 8 Hz, ArH), 4.25 (1H, br dd, J = 9, 8 Hz, 2-Hβ), 4.10—3.96 (2H, m, C$\underline{H}_2$OH), 3.84 (3H, s, OMe), 3.71 (1H, dd, J = 9, 5 Hz, 9-H), 3.34 (1H, dd, J = 9, 5 Hz, 10-H), 3.26 (1H, m, 5-H), 3.22 (1H, dd, J = 12, 9 Hz, 2-Hα), 3.01 (1H, m, 3-H), 2.79 (2H, m, 7-H_2), 2.41 (3H, s, NMe), 2.11 (1H, m, 4-H_{eq}), 1.93 (1H, m, 8-H), 1.44 (1H, br q, J = 11.5 Hz, 4-H_{ax}). *Anal.* Calcd for $C_{23}H_{28}N_2O_5S$: C, 62.14; H, 6.35; N, 6.30. Found: C, 62.01; H, 6.29; N, 6.28.

(3α,8α,9α,10α)-2,3-Dihydro-1-[(4-methoxyphenyl)sulfonyl]-6,8-dimethylergolin-9-ol (14) According to the mesylation procedure described for **9**, treatment of the diol **12** (460 mg) in pyridine (2 ml) with mesyl chloride (0.4 ml) followed by flash chromatography (methylene dichloride : methanol = 98 : 2) gave the monomesylate **13** (430 mg, 81%) as a pale yellow glass. IR: 1360, 1160 (NSO_2 and OSO_2) cm^{-1}. ^{1}H-NMR (60 MHz) δ: 3.85 (3H, s, OMe), 3.07 (3H, s, Ms), 2.47 (3H, s, NMe). Sodium borohydride (450 mg) was added to a stirred solution of the above mesylate **13** (300 mg) in DMSO (6 ml) at 10 °C and the mixture was heated at 80 °C for 2 h. The same work-up as described for the preparation of **11** followed by a flash chromatography (methylene dichloride : methanol = 95 : 5) gave the alcohol **14** (139 mg, 57%) as a colorless glass. IR: 3432 (OH), 1356, 1162 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.74 (2H, br d, J = 8 Hz, ArH), 7.35 (1H, d, J = 8 Hz, 14-H), 7.11 (1H, t, J = 8 Hz, 13-H), 6.95—6.84 (3H, m, 12-H and ArH), 4.19 (1H, br dd, J = 9, 8 Hz, 2-Hβ), 3.79 (3H, s, OMe), 3.60 (1H, dd, J = 8, 5 Hz, 9-H), 3.18 (1H, dd, J = 12, 9 Hz, 2-Hα), 3.12 (1H, m, 5-H), 2.98 (1H, br dd, J = 8, 6 Hz, 10-H), 2.92 (1H, m, 3-H), 2.61 (1H, dd, J = 12, 4 Hz, 7-H_{eq}), 2.36 (1H, dd, J = 12, 4 Hz, 7-H_{ax}), 2.33 (3H, s, NMe), 2.08 (1H, m, 4-H_{eq}), 1.98 (1H, m, 8-H), 1.30 (1H, br q, J = 12 Hz, 4-H_{ax}), 1.07 (3H, d, J = 7 Hz, 8-Me). High-resolution MS m/z: Calcd for $C_{23}H_{28}N_2O_4S$ (M^+) 428.1768. Found: 428.1777.

Reaction of the Alcohol 11 with Thionyl Chloride Thionyl chloride (17.2 ml) was added dropwise to a stirred, ice-cooled solution of the alcohol **11** (259 mg) in benzene (80 ml), and the mixture was gently refluxed for 1.5 h. The excess of thionyl chloride and the solvent were removed. Then 10% aqueous sodium carbonate was added to the residue, and the resulting solution was extracted with methylene dichloride. The extract was washed, dried and evaporated. Flash chromatography (methylene dichloride : methanol = 97 : 3) of the residue gave (3β,8α,9β)-9-chloro-2,3-dihydro-1-[(4-methoxyphenyl)sulfonyl]-6,8-dimethylergoline (**15**) (180 mg, 64%) and (3β,8α,9β)-8,9-didehydro-2,3-dihydro-1-[(4-methoxyphenyl)-sulfonyl]-6,8-dimethylergoline (**16**) (60 mg, 24%). The chloride **15**: mp 161.5—164 °C (colorless needles from methanol). IR: 1370, 1180 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.80 (2H, br d, J = 8 Hz, ArH), 7.42 (1H, d, J = 8 Hz, 14-H), 7.23 (1H, t, J = 8 Hz, 13-H), 6.96 (2H, br d, J = 8 Hz, ArH), 6.88 (1H, d, J = 8 Hz, 12-H), 4.71 (1H, br s, 9-H), 4.25 (1H, m, 2-Hβ), 3.84 (3H, s, OMe), 3.32—3.04 (3H, m, 2-Hα, 3-H, and 10-H), 2.89 (1H, dd, J = 12, 4 Hz, 7-H_{ax}), 2.63 (1H, br d, J = 12 Hz, 7-H_{eq}), 2.60—2.25 (3H, m, 4-Heq, 5-H, and 8-H), 2.37 (3H, s, NMe), 1.32 (3H, d, J = 8 Hz, 8-Me), 1.28 (1H, m, 4-H_{ax}). *Anal.* Calcd for $C_{23}H_{27}ClN_2O_3S$: C, 61.80; H, 6.09; N, 6.27. Found: C, 61.53; H, 6.06; N, 6.33. The unsaturated amine **16**: a pale brown glass. IR: 1360, 1170 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.81 (2H, br d, J = 8 Hz, ArH), 7.42 (1H, d, J = 8 Hz, 14-H), 7.22 (1H, t, J = 8 Hz, 13-H), 7.05—6.90 (3H, m, 12-H and ArH), 5.97 (1H, br s, 9-H), 4.25 (1H, m, 2-Hβ), 3.85 (3H, s, OMe), 3.43 (1H, m, 10-H), 3.36—2.96 (4H, m, 2-Hα, 3-H, and 7-H_2), 2.62—2.35 (2H, m, 4-H_{eq} and 5-H), 2.44 (3H, s, NMe), 1.74 (3H, br s, 8-Me), 1.40 (1H, q, J = 11.5 Hz, 4-H_{ax}). High-resolution MS m/z: Calcd for $C_{23}H_{26}N_2O_3S$ (M^+) 410.1663. Found: 410.1682.

(3β,8α)-9,10-Didehydro-2,3-dihydro-1-[(4-methoxyphenyl)sulfonyl]-6,8-dimethylergoline (17) A solution of the chloride **15** (67 mg) and DBU (1.6 ml) in benzene (50 ml) was heated under reflux for 40 h. The reaction mixture was cooled and washed, and the organic layer was dried and evaporated. The residue was purified by p-TLC (methylene dichloride : methanol = 96 : 4) to afford **17** (53 mg, 89%), mp159—160 °C (colorless crystals from methanol). IR: 1356, 1162 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.82 (2H, br d, J = 8 Hz, ArH), 7.43 (1H, dd, J = 8, 1.5 Hz, 14-H), 7.28—7.14 (2H, m, 12- and 13-H), 6.96 (2H, br d, J = 8 Hz, ArH), 6.39 (1H, br dd, J = 5, 2 Hz, 9-H), 4.29 (1H, m, 2-Hβ), 3.86 (3H, s, OMe), 3.32—3.06 (2H, m, 2-Hα and 3-H), 2.90—2.44 (3H, m, 4-H_{eq} and 7-H_2), 2.48 (3H, s, NMe), 2.42—2.31 (2H, m, 5- and 8-H), 1.21 (1H, m, 4-H_{ax}), 1.18 (3H, d, J = 7 Hz, 8-Me). *Anal.* Calcd for $C_{23}H_{26}N_2O_3S$: C, 67.29; H, 6.38; N, 6.82. Found: C, 67.16; H, 6.48; N, 6.71.

(3β)-2,3-Dihydroisolysergine (18) Lithium aluminum hydride (30 mg) was added in small portions to a solution of the unsaturated amine **17** (20 mg) in anhydrous DME (6 ml) at room temperature, and the mixture was refluxed for 5 h. Treatment in the usual way gave a residue, which was purified by p-TLC (chloroform : methanol = 9 : 1) to afford **18** (11 mg, 93%) as a colorless powder. ^{1}H-NMR (200 MHz) δ: 7.10—6.92 (2H, m, 12- and 13-H), 6.53 (1H, dd, J = 7, 1.5 Hz, 14-H), 6.38 (1H, br d, J = 4 Hz, 9-H), 3.73 (1H, m, 2-Hβ), 3.38—3.08 (2H, m, 3-H and 2-Hα), 2.94 (1H, m, 5-H), 2.80—2.30 (4H, m, 4-H_{eq}, 7-H_2, and 8-H), 2.54 (3H, s, NMe), 1.44 (1H, br q, J = 11 Hz, 4-H_{ax}), 1.23 (3H, d, J = 7 Hz, 8-Me). High-resolution MS m/z: Calcd for $C_{16}H_{20}N_2$ (M^+) 240.1625. Found: 240.1626.

(±)-Isolysergine (19) A solution of the amine **18** (9 mg), phenylseleninic anhydride (6.7 mg), and indole (13 mg) in THF (2 ml) was heated at 40°C for 2 h. The solvent was partly evaporated off, and 10% aqueous sodium carbonate 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 purified by p-TLC (chloroform : methanol = 92 : 8) to afford (±)-isolysergine (**19**), mp 112—114 °C (from acetone–hexane). IR: 3500 (NH) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.98 (1H, br s, NH), 7.28—7.14 (3H, m, 12—14-H), 6.94 (1H, br s, 2-H), 6.43 (1H, br dd, J = 5, 2 Hz, 9-H), 3.47 (1H, dd, J = 14, 6 Hz, 4-H_{eq}), 3.30 (1H, m, 5-H), 2.78 (1H, ddd, J = 14, 11, 2 Hz, 4-H_{ax}), 2.83—2.60 (2H, m, 7-H_2), 2.60 (3H, s, NMe), 2.54 (1H, m, 8-H), 1.21 (3H, d, J = 7 Hz, 8-Me). The IR and ^{1}H-NMR spectra and *Rf* value of (±)-(**19**) were found to be identical with those of a sample prepared by the reported procedure[14] from natural lysergene[19] provided by Professor Yamatodani. High-resolution MS m/z: Calcd for $C_{16}H_{18}N_2$ (M^+) 238.1468. Found: 238.1461.

(3β)-2,3-Dihydroagroclavine (20) Sodium (10 mg) was added in small portions over 10 min to liquid ammonia (*ca.* 100 ml), and a solution of the amine **16** (55 mg) in THF (1 ml) was added dropwise to the resulting solution. The mixture was stirred for a further 1 h before excess of ammonium chloride was added to stop the reaction. Ammonia was evaporated off, the residue was treated with water and the mixture was extracted with methylene dichloride. The extract was dried and evaporated to give a crystalline residue, which was recrystallized from ether to give **20** (30 mg, 94%) as colorless crystals, mp 139—141 °C. IR: 3400 (NH) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.09 (1H, t, J = 8 Hz, 13-H), 6.79 (1H, d, J = 8 Hz, 12-H), 6.57 (1H, d, J = 8 Hz, 14-H), 6.02 (1H, br s, 9-H), 3.69 (1H, m, 2-Hβ), 3.60 (1H, m, 2-Hα), 3.50 (1H, m, 10-H), 3.40—3.00 (4H, m, 1-H, 3-H, and 7-H_2), 2.57 (1H, ddd, J = 11, 9.5, 2 Hz, 5-H), 2.49 (1H, m, 4-H_{eq}), 2.45 (3H, s, NMe), 1.74 (3H, br s, 8-Me), 1.54 (1H, q, J = 11 Hz, 4-H_{ax}). High-resolution MS m/z: Calcd for $C_{16}H_{20}N_2$ (M^+) 240.1626. Found: 240.1630.

(±)-Agroclavine (21) A mixture of **20** (15 mg), phenylseleninic anhydride (10.5 mg) and indole (20.6 mg) in THF (4.5 ml) was heated at 40°C for 1.5 h. Following work-up as described for the preparation of **19**, (±)-agroclavine (**21**) (13.2 mg, 89%) was obtained, mp 182—184 °C (dec.)

(from ether) (lit.[20] mp 189—191 °C (dec.)). ^{1}H-NMR (200 MHz) δ: 7.98 (1H, br s, NH), 7.20—7.03 (3H, m, 12—14-H), 6.94 (1H, br s, 2-H), 6.20 (1H, br s, 9-H), 3.76 (1H, br, $W_{1/2}$ = 18 Hz, 10-H), 3.34 (1H, dd, J = 14, 4 Hz, 4-H_{eq}), 3.26 (1H, br d, J = 15 Hz, 7-H_{eq}), 2.96 (1H, br d, J = 15 Hz, 7-H_{ax}), 2.80 (1H, ddd, J = 14, 12, 1.5 Hz, 4-H_{ax}), 2.56 (1H, ddd, J = 12, 9, 4 Hz, 5-H), 2.52 (3H, s, NMe), 1.79 (3H, br s, 8-Me). The IR and ^{1}H-NMR spectra and *Rf* value of (±)-(**21**) were found to be identical with those of natural agroclavine provided by Professor Yamatodani. High-resolution MS *m/z*: Calcd for $C_{16}H_{18}N_2$ (M^+) 238.1468. Found: 238.1476.

(3α,10α)-8,9-Didehydro-2,3-dihydro-1-[(4-methoxyphenyl)sulfonyl]-6,8-dimethylergoline (22) According to the dehydration procedure described for **11**, treatment of **14** (115 mg) and thionyl chloride (5 ml) in benzene (25 ml) followed by purification by p-TLC (methylene dichloride : methanol = 95 : 5) gave **22** (70 mg, 64%) as a colorless glass. IR: 1354, 1160 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.80 (2H, br d, J = 8 Hz, ArH), 7.37 (1H, d, J = 8 Hz, 14-H), 7.20 (1H, t, J = 8 Hz, 13-H), 7.00—6.90 (3H, m, 12-H and ArH), 5.28 (1H, br s, 9-H), 4.25 (1H, dd, J = 10, 8 Hz, 2-Hβ), 3.85 (3H, s, OMe), 3.73 (1H, br, $W_{1/2}$ = 13 Hz, 10-H), 3.25 (1H, dd, J = 12.5, 10 Hz, 2-Hα), 3.19 (1H, m, 5-H), 3.01 (1H, m, 3-H), 2.92 (2H, br s, 7-H_2), 2.56 (3H, s, NMe), 2.07 (1H, m, 4-H_{eq}), 1.60 (3H, br s, 8-Me), 1.20 (1H, q, J = 12 Hz, 4-H_{ax}). High-resolution MS *m/z*: Calcd for $C_{23}H_{26}N_2O_3S$ (M^+) 410.1663. Found: 410.1677.

(±)-Agroclavine I (24) According to the deprotection procedure described for **16**, deprotection of **22** (41 mg) in liquid ammonia (*ca.* 50 ml) with sodium (8 mg) gave (3β)-2,3-dihydroagroclavine I (**23**) as a colorless glass. ^{1}H-NMR (200 MHz) δ: 7.08 (1H, t, J = 8 Hz, 13-H), 6.70 (1H, d, J = 8 Hz, 12-H), 6.52 (1H, d, J = 8 Hz, 14-H), 5.40 (1H, br s, 9-H), 3.76 (1H, br, $W_{1/2}$ = 12 Hz, 10-H), 3.68 (1H, m, 2-Hβ), 3.30 (1H, ddd, J = 12, 5.5, 3 Hz, 5-H), 3.20—3.04 (2H, m, 2-Hα and 3-H), 2.96 (2H, br s, 7-H_2), 2.60 (3H, s, NMe), 2.16 (1H, ddd, J = 12, 4, 3 Hz, 4-H_{eq}), 1.63 (3H, br s, 8-Me), 1.38 (1H, m, 4-H_{ax}). Without purification, a mixture of **23**, phenylseleninic anhydride (17 mg) and indole (33 mg) in THF (6 ml) was heated at 40 °C for 2 h. Following work-up as described for the preparation of **19**, (±)-agroclavine I (**24**) (17 mg, 71% from **22**) was obtained, mp 152—154 °C (from ether) (lit.[13] mp 157—158 °C). ^{1}H-NMR (200 MHz) δ: 7.98 (1H, br s, NH), 7.26—6.98 (3H, m, 12—14-H), 6.90 (1H, br s, 2-H), 5.57 (1H, br s, 9-H), 4.03 (1H, br, 10-H), 3.46 (1H, dt, J = 10, 5 Hz, 5-H), 3.18 (2H, br s, 7-H_2), 3.04 (1H, dd, J = 15, 5 Hz, 4-H_{eq}), 2.87 (1H, br dd, J = 15, 10 Hz, 4-H_{ax}), 2.64 (3H, s, NMe), 1.67 (3H, br s, 8-Me). The ^{1}H-NMR data for (±)-(**24**) were found to be identical with those reported for natural agroclavine I.[11] High-resolution MS *m/z*: Calcd for $C_{16}H_{18}N_2$ (M^+) 238.1468. Found: 238.1451.

(3β,8α,9β)-2,3-Dihydro-1-[(4-methoxyphenyl)sulfonyl]-6,8-dimethylergolin-9-ol (26) According to the mesylation procedure described for **9**, treatment of the alcohol **11** (50 mg) in pyridine (1 ml) with mesyl chloride (0.4 ml) at room temperature for 5 h gave the mesylate **25**. ^{1}H-NMR (60 MHz) δ: 4.70 (1H, dd, J = 11, 5 Hz, 9-H), 3.80 (3H, s, OMe), 2.96 (3H, s, OMs), 2.27 (3H, s, NMe), 1.33 (3H, d, J = 7 Hz, 8-Me). Without purification, the mesylate **25** was dissolved in DMSO (1.85 ml) containing 18-crown-6-ether (150 mg). Potassium superoxide (50 mg) was added to the resulting solution, and the mixture was stirred vigorously at room temperature for 1 h. Then water was added to the reaction mixture, and the whole was extracted repeatedly with ethyl acetate. The combined extracts were washed with brine, dried, and evaporated. The residue was purified by p-TLC (chloroform : methanol = 92 : 8) to afford the alcohol **26** (27 mg, 54%) and the unsaturated amine **17** (5 mg, 10%), which was identical with the sample prepared from **15** upon comparison of their *Rf* values and IR and ^{1}H-NMR spectra. **26**: mp 149—152 °C (colorless crystals from ether–methylene dichloride). IR: 1355, 1160 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.83 (2H, br d, J = 8 Hz, ArH), 7.43 (1H, d, J = 8 Hz, 14-H), 7.24 (1H, t, J = 8 Hz, 13-H), 7.02—6.91 (3H, m, 12-H and ArH), 4.32 (1H, br s, 9-H), 4.25 (1H, m, 2-Hβ), 3.86 (3H, s, OMe), 3.28—3.10 (2H, m, 2-Hα and 3-H), 2.95 (1H, br d, J = 10 Hz, 10-H), 2.73 (1H, br dd, J = 10, 4 Hz, 7-H_{ax}), 2.60 (1H, br d, J = 10 Hz, 7-H_{eq}), 2.50 (1H, br t, J = 10 Hz, 5-H), 2.47 (1H, br d, J = 10 Hz, 4-H_{eq}), 2.36 (3H, s, NMe), 2.06 (1H, m, 8-H), 1.25 (1H, m, 4-H_{ax}), 1.20 (3H, d, J = 7 Hz, 8-Me). High-resolution MS *m/z*: Calcd for $C_{23}H_{28}N_2O_4S$ (M^+) 428.1774. Found; 428.1768.

(±)-Fumigaclavine B (28) According to the deprotection procedure described for **16**, deprotection of **26** (29 mg) in liquid ammonia (*ca.* 50 ml) with sodium (5 mg) gave (3β)-2,3-dihydrofumigaclavine B (**27**) as a colorless powder. ^{1}H-NMR (200 MHz) δ ($CDCl_3$–CD_3OD): 7.06 (1H, t, J = 8 Hz, 13-H), 6.74 (1H, d, J = 8 Hz, 12-H), 6.58 (1H, d, J = 8 Hz, 14-H), 4.36 (1H, br s, 9-H), 3.64 (1H, m, 2-Hβ), 3.22—3.03 (2H, m, 2-Hα and 3-H), 2.96 (1H, br d, J = 10 Hz, 10-H), 2.81 (1H, dd, J = 12, 4 Hz, 7-H_{ax}), 2.74—2.44 (3H, m, 4-H_{eq}, 5-H, and 7-H_{eq}), 2.40 (3H, s, NMe), 2.05 (1H, m, 8-H), 1.34 (1H, m, 4-H_{ax}), 1.23 (3H, d, J = 7 Hz, 8-Me). Without purification, a mixture of **27**, phenylseleninic anhydride (12 mg) and indole (22 mg) in THF (6 ml) was heated at 40 °C for 2 h. Following work-up as described for the preparation of **19**, (±)-fumigaclavine (**28**) (13 mg, 76% from **26**) was obtained, mp 198—200 °C (dec.) (from 95% ethanol). ^{1}H-NMR (200 MHz) δ: 8.02 (1H, br s, NH), 7.18—6.96 (3H, m, 12—14-H), 6.86 (1H, br s, 2-H), 4.50 (1H, br s, 9-H: 10% intensity increase upon irradiation at δ 1.26 and 11% intensity increase upon irradiation at δ 2.12), 3.34 (1H, d, J = 11 Hz, 4-H_{eq}), 3.29 (1H, br d, J = 9 Hz, 10-H: 16% intensity increase upon irradiation at δ 1.26), 2.81 (1H, dd, J = 11, 4 Hz, 7-H_{ax}: 4% intensity increase upon irradiation at δ 2.12), 2.68 (1H, td, J = 11, 1.5 Hz, 4-H_{ax}), 2.58 (1H, dd, J = 11, 2 Hz, 7-H_{eq}: 5% intensity increase upon irradiation at δ 1.26), 2.58 (1H, m, 5-H), 2.41 (3H, s, NMe), 2.12 (1H, m, 8-H: 14% intensity increase upon irradiation at δ 1.26), 1.26 (3H, d, J = 7 Hz, 8-Me). The IR and ^{1}H-NMR spectra of (±)-(**28**) were found to be identical with those of natural fumigaclavine B provided by Dr. Polonsky. High-resolution MS *m/z*: Calcd for $C_{16}H_{20}N_2O$ (M^+) 256.1574. Found: 256.1568.

(3β,8α,9α)-2,3-Dihydro-9-methanesulfonyloxy-8-methanesulfonyloxymethyl-1-[(4-methoxyphenyl)sulfonyl]-6-methylergoline (29) Mesyl chloride (0.2 ml) was added to a solution of the *trans*-diol **8** (120 mg) in pyridine (3 ml) at 0 °C, and the solution was stirred at room temperature for 5 h. The resulting solution was worked up in the same manner as described for the preparation of **10**, and the residue was recrystallized from methylene dichloride–methanol to give the dimesylate **29** (144 mg, 85%) as colorless needles, mp 162—163 °C (dec.). IR: 1360, 1175, 1160 (NSO_2 and OSO_2) cm^{-1}. ^{1}H-NMR (60 MHz) δ: 4.90 (1H, m, 9-H), 4.61 (2H, m, 8-C$\underline{H}_2$OMs), 3.80 (3H, s, OMe), 3.03 and 3.00 (each 3H, s, Ms × 2), 3.26 (3H, s, NMe). *Anal.* Calcd for $C_{25}H_{32}N_2O_9S_3 \cdot 1/5CH_2Cl_2$: C, 49.00; H, 5.29; N, 4.54. Found: C, 49.14; H, 5.27; N, 4.56.

(3α,8α,9α,10α)-2,3-Dihydro-9-methanesulfonyloxy-8-methanesulfonyloxymethyl-1-[(4-methoxyphenyl)sulfonyl]-6-methylerogoline (30) According to the mesylation procedure described above, treatment of the *cis*-diol **12** (120 mg) in pyridine (3 ml) with mesyl chloride (0.2 ml) gave the dimesylate **30** (138 mg, 81%), mp 182—184 °C (dec.) (colorless crystals from methylene dichloride–methanol). IR: 1360, 1180, 1160 (NSO_2 and OSO_2) cm^{-1}. ^{1}H-NMR (60 MHz) δ: 4.82 and 4.59 (each 1H, m, 8-C$\underline{H}_2$OMs), 4.54 (1H, m, 9-H), 4.27 (1H, m, 3-H), 3.85 (3H, s, OMe), 3.09 and 2.60 (each 3H, s, Ms × 2), 2.46 (3H, s, NMe). *Anal.* Calcd for $C_{25}H_{32}N_2O_9S_3$: C, 49.99; H, 5.37; N, 4.66. Found: C, 49.72; H, 5.42; N, 4.67.

(3β)-9,10-Didehydro-2,3-dihydro-1-[(4-methoxyphenyl)sulfonyl]-6-methyl-8-methyleneergoline (31) From the *trans*-dimesylate **29**: Potassium *tert*-butoxide (120 mg) was added to a solution of the dimesylate **29** (144 mg) in DMSO (3 ml) at 10°C, and the resulting solution was stirred at room temperature for 2 h. Water was added to the reaction mixture and the whole was extracted with ethyl acetate. The extract was washed, dried and evaporated. The residue was purified by p-TLC (ethyl acetate) to give the diene **31** (48 mg, 52%), mp 147—149 °C (dec.) (pale yellow needles from ethyl acetate). IR: 1600 (diene), 1360, 1160 (NSO_2) cm^{-1}. ^{1}H-NMR (200 MHz) δ: 7.71 (2H, br d, J = 8 Hz, ArH), 7.35 (1H, d, J = 8 Hz, 14-H), 7.22 (1H, d, J = 8 Hz, 12-H), 7.14 (1H, t, J = 8 Hz, 13-H), 6.86 (2H, br d, J = 8 Hz, ArH), 6.79 (1H, br s, 9-H), 4.99 and 4.88 (each 1H, br s, C=CH_2), 4.22 (1H, br t, J = 7 Hz, 2-Hβ), 3.78 (3H, s, OMe), 3.40 (1H, d, J = 14 Hz, 7-H_{eq}), 3.30—3.04 (4H, m, 2-Hα, 3-H, 5-H, and 7-H_{ax}), 2.38 (1H, dt, J = 12, 4 Hz, 4-H_{eq}), 2.34 (3H, s, NMe), 1.21 (1H, q, J = 12 Hz, 4-H_{ax}). *Anal.* Calcd for $C_{23}H_{24}N_2O_3S \cdot 1/3H_2O$: C, 66.64; H, 6.00; N, 6.75. Found; C, 66.49; H, 5.73; N, 6.60. From the *cis*-dimesylate **30**: According to the procedure described above, treatment of a solution of the *cis*-dimesylate **30** (138 mg) in DMSO (3 ml) with potassium *tert*-butoxide (120 mg) gave the diene **31** (45 mg, 51%), which was identical with the sample prepared from the *trans*-dimesylate **30** upon comparison of their *Rf* values and IR and ^{1}H-NMR spectra.

(±)-Lysergene (33) According to the deprotection procedure described for **17**, deprotection of **31** (24 mg) in DME (5 ml) with lithium aluminum hydride (30 mg) gave (3β)-2,3-dihydrolysergene (**32**) as a yellow powder. IR: 3400 (NH), 1620 (diene) cm^{-1}. ^{1}H-NMR (60 MHz) δ: 6.77 (1H, br s, 9-H), 4.98 and 4.86 (each 1H, br s, C=CH_2), 2.43 (3H, s, NMe). Without purification, a mixture of **32**, phenylseleninic anhydride (6.5 mg) and indole (14.5 mg) in THF (4 ml) was heated at 40 °C for 2 h. Following work-up as described for the preparation of **19**, (±)-lysergene (**33**) (8 mg, 58% from **31**) was obtained, mp 210—212 °C (dec.) (from acetone). ^{1}H-NMR (200 MHz) δ ($CDCl_3$–CD_3OD): 7.34—7.26 (3H, m, 12—14-H), 7.02 and 6.98 (each 1H, br s, 2- and 9-H), 5.12 and 5.01 (each 1H, br s, C=CH_2), 3.60—3.20 (4H, m, 4-H_{eq}, 5-H, and 7-H_2), 2.77 (1H, ddd, J = 14, 11, 2 Hz, 4-H_{ax}), 2.58 (3H, s, NMe). The IR and ^{1}H-NMR spectra and *Rf* value of

(±)-(**33**) were found to be identical with those of natural lysergene.[19] High-resolution MS *m/z*: Calcd for $C_{16}H_{16}N_2$ (M^+) 236.1312. Found: 236.1322.

Reaction of the Diene 31 with Sodium in Liquid Ammonia According to the deprotection procedure given for **16**, treatment of the diene **30** (28 mg) in liquid ammonia (*ca.* 15 ml) with sodium (5 mg) gave a mixture of **20** and **23** in the ratio of 2:1, which was, without purification, dehydrogenated with phenylseleninic anhydride (10 mg) and indole (22 mg) in THF (6 ml) at 40 °C for 2 h. Usual work-up followed by purification by p-TLC (methylene dichloride : methanol = 92 : 8) afforded (±)-agroclavine (**21**) (6.5 mg, 45%) and (±)-agroclavine I (**24**) (3.1 mg, 23%). These products were identical with the sample prepared from **16** and **22** upon comparison of their *Rf* values and IR and ^{1}H-NMR spectra, respectively.

Acknowledgements We thank Professor S. Yamatodani of Kobe Women's University, Japan, for samples of natural agroclavine and lysergene, and Dr. J. Polonsky of I. C. S. N., Gif-sur-Yvette, France, for the specimen of natural fumigaclavine B. We are grateful to Misses H. Kamioka and Y. Shinohara for technical assistance.

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