Stereoselective Transformation of Ajmaline into Three Minor *Gelsemium* Alkaloids, Koumidine, (19*Z*)-Anhydrovobasinediol [(19*Z*)-Taberpsychine] and *N*-Demethoxyrankinidine and their Absolute Configuration

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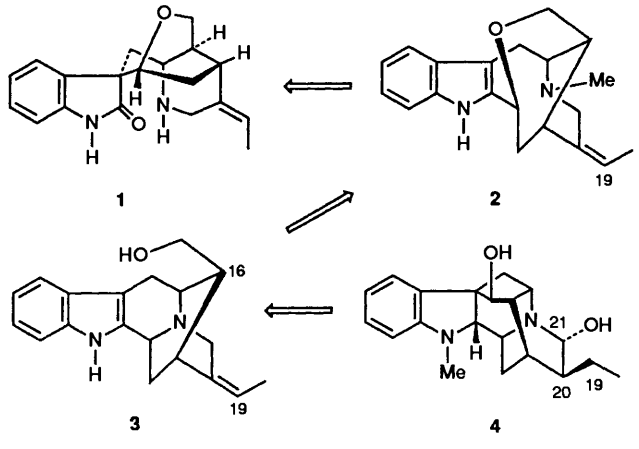
Ajmaline was converted into new *Gelsemium* alkaloids, 19*Z*-anhydrovobasinediol [(19*Z*)-taberpsychine] and *N*-demethoxyrankinidine, *via* koumidine along the biomimetic sequence, and the absolute configuration of these alkaloids was determined by these transformations.

The genus *Gelsemium*, belonging to the family Loganiaceae, comprises three species. Along them, *Gelsemium elegans* Benth., native to South Eastern Asia, has been used in traditional Chinese medicine, as well as a remedy for certain kinds of skin ulcers, and more recently has been used as an analgesic for the palliation of various acute cancer pains.[1] Recent intensive research on the chemical components of these plants resulted in the isolation of many new indole and oxindole alkaloids.[2] The structure of koumidine **3**, one of the minor constituents of *G. elegans*, was first published[3] as having an 19*E* ethylidene side-chain as in the common sarpagine class of indole alkaloids. By careful spectroscopic analysis, the configuration of the side-chain was revised to the 19*Z* form.[2d,4] The structures of new minor alkaloids, (19*Z*)-anhydrovobasinediol [(19*Z*)-taberpsychine] **2**[2d] and *N*-demethoxyrankinidine **1**,[2e] were also elucidated by spectroscopic analysis, but as yet their absolute configuration remains unsettled.[5] Koumidine **3**, 19*Z*-anhydrovobasinediol **2**, and *N*-demethoxyrankinidine **1** may be biogenetically related in that the C/D-ring cleavage of koumidine **3** would generate compound **2** and subsequent oxidative rearrangement to oxindole would serve to generate compound **1**.[2d] We designed the synthesis of these alkaloids from the known compound ajmaline **4**[6] along the above biomimetic sequence (Scheme 1).



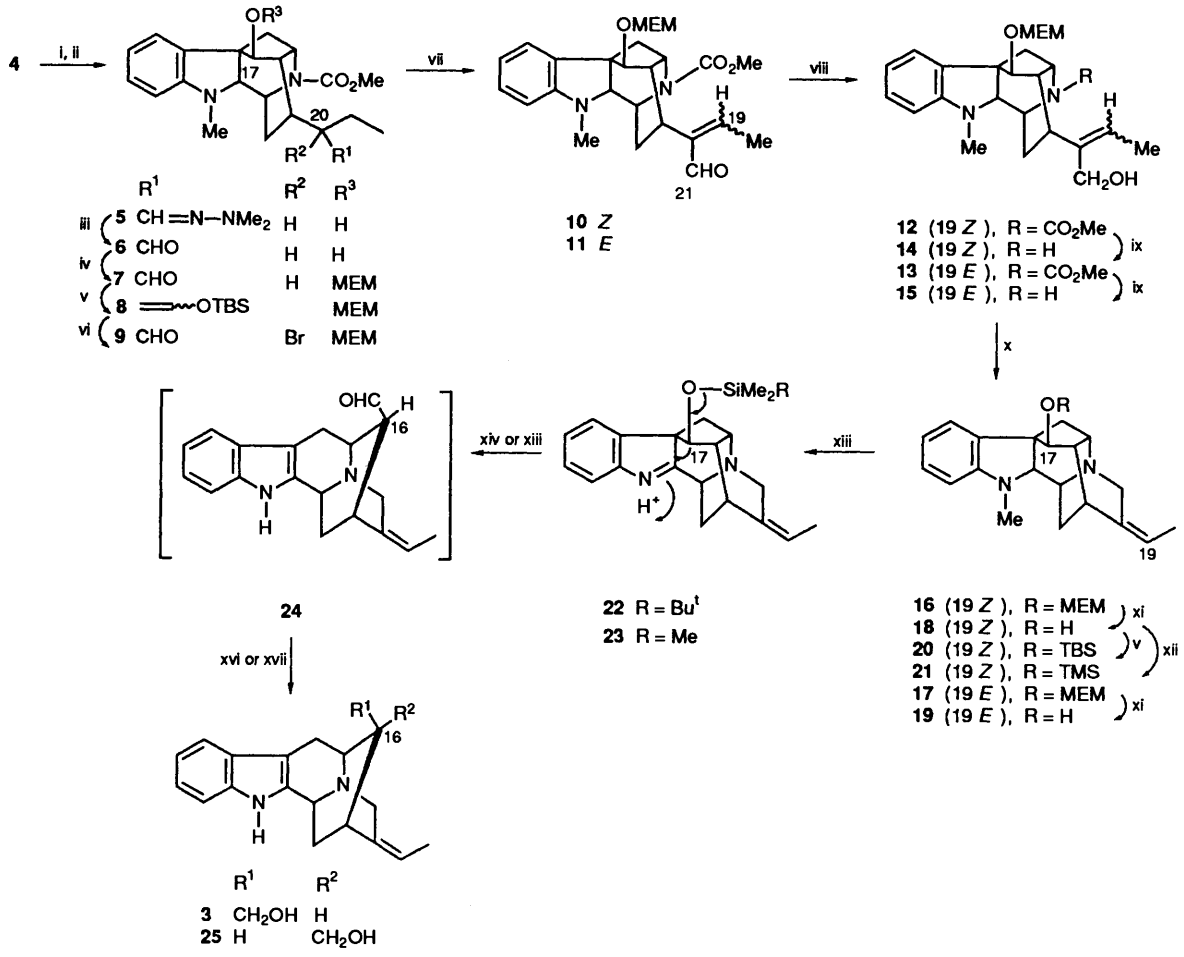
Scheme 1

Initially, koumidine **3** was prepared from ajmaline **4**. Our synthetic pathway contains (i) stereoselective introduction of a *Z*-olefin bond at C^{19}–C^{20} in ajmaline **4** and (ii) indoline-to-indole transformation without epimerization at C^{16}. Ajmaline **4** was converted into the hydrazone derivative **5** in two steps (i, *N*,*N*-dimethylhydrazine and a catalytic amount of H_2SO_4 in EtOH; ii, methyl chloroformate in 1 mol dm^{-3} NaOH–CH_2Cl_2) in 79% overall yield to liberate the masked aldehyde existing as an amino acetal function and to protect the N^b as the methylcarbamate.[7] The hydrazone was hydrolysed with copper(II) chloride in aq. tetrahydrofuran (THF) (pH 7)[8] to afford the aldehyde **6** in 75% yield. In the ^1H NMR spectrum, the signals due to the aldehyde group were observed at δ 9.62 and 9.59.† Attempts at direct conversion of ajmaline **4** into the aldehyde **6** by reaction with chloroformates gave solely the carbonate (21-OCO_2R) derivatives. After the 17-hydroxy group in compound **6** had been protected as the methoxyethoxymethyl (MEM) ether **7** in 81% yield, the aldehyde was converted into the silyl enol ether **8** in 71% yield by treatment with t-butyldimethylsilyl trifluoromethanesulphonate (TBSOTf), and then bromine was selectively introduced into the α-position of the aldehyde in 76% yield by treatment with *N*-bromosuccinimide (NBS) in dry THF at −18 °C. To create the double bond at the C^{19}–C^{20} position, the bromide **9** was treated with 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) in dry dimethylformamide (DMF) to give two α,β-unsaturated aldehydes, the desired 19*Z*-olefin **10** and 19*E*-olefin **11** in 60 and 12% yield, respectively. The geometry of two olefins was confirmed by NOE experiments. Irradiation of the 18-methyl protons (δ 2.15, 2.13) in *Z*-isomer **10** led to enhancement (17%) of the C-21 aldehyde proton (δ 10.20, 10.19), while 25% enhancement was observed between the C-19 olefinic proton (δ 6.56) and C-21 aldehyde proton (δ 9.34, 9.32) in the *E*-isomer **11**. The major α,β-unsaturated aldehyde **10** was reduced with $NaBH_4$ to give the primary alcohol **12** in 88% yield. After deprotection of the N^b-carbamate by alkaline hydrolysis (NaOH in aq. ethylene glycol), the amine **14** was treated with mesyl chloride in dry pyridine to afford the ring-closure product **16** in 62% yield by bond formation between N^b and C-21. By removal of the MEM ether in compound **16**, deoxyajmaline derivative **18** (m.p. 279–281 °C) was obtained in 95% yield.

By the same sequential treatment, the minor, 19*E*-olefin **11** gave the *Rauwolfia* alkaloid tetraphyllicine **19**,[9] m.p. 294–296 °C; $[\alpha]_D^{16}$ +16° (*c* 0.4 in pyridine). Direct comparison of synthetic alkaloid **19** with an authentic sample established their identity in all respects (TLC, mixed m.p., IR, ^1H NMR and mass spectra).

The next requirement of this work was the transformation of the indolenine moiety to an indole ring. If we could prepare the indolenine derivative having a properly protected hydroxy group on C^{17}, we could expect to obtain the indole derivative **24** by the fragmentation as shown in Scheme 2. First we protected the C-17 hydroxy group in compound **18** as the TBS ether **20** and prepared its indolenine derivative **22** by lead tetraacetate oxidation.[10] After removal of the TBS group in compound **22**

† Ajmaline derivatives possessing a carbamate function in the molecule are often shown by their ^1H and ^{13}C NMR spectra to occur as a mixture of rotation isomers.

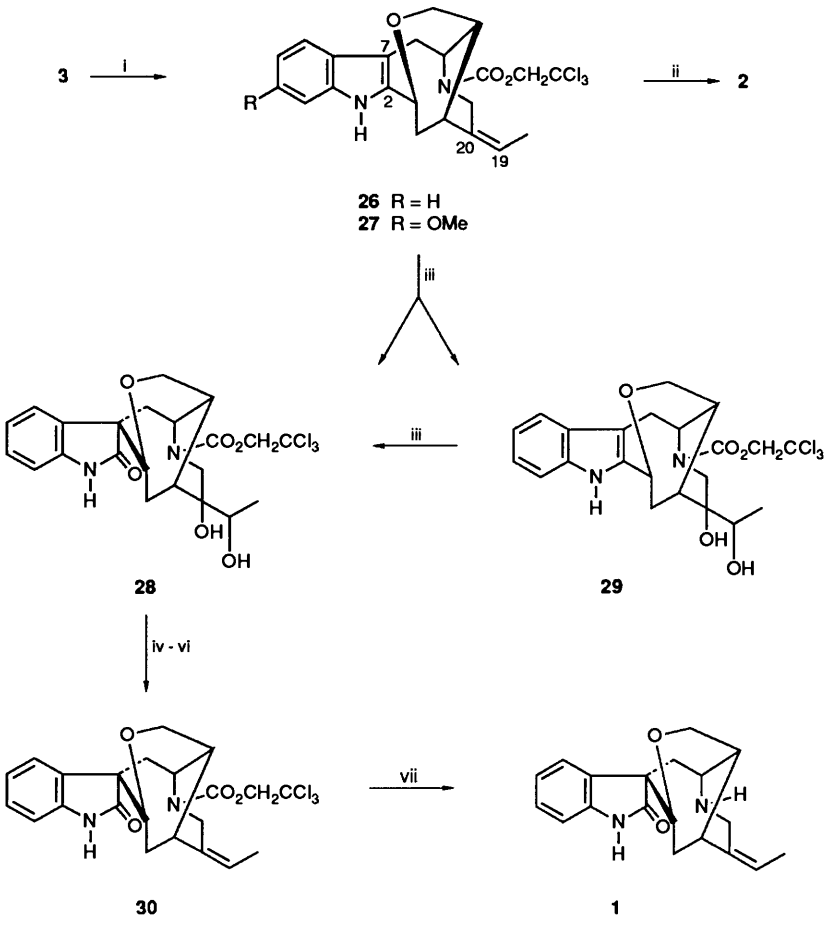


Scheme 2 *Reagents:* i, *N,N*-Dimethylhydrazine, cat. H_2SO_4, 3 Å molecular sieves, dry EtOH; ii, methyl chloroformate, 1 mol dm^{-3} NaOH, CH_2Cl_2; iii, $CuCl_2$, aq. THF, phosphate buffer; iv, MEM chloride, diisopropylethylamine, dry CH_2Cl_2; v, TBSOTf, Et_3N, dry CH_2Cl_2; vi, NBS, dry THF; vii, DBU, dry DMF; viii, $NaBH_4$, MeOH; ix, NaOH, ethylene glycol, water; x, mesyl chloride, Py; xi, conc. HCl, MeOH; xii, TMSOTf, Et_3N, dry CH_2Cl_2; xiii, $Pb(OAc)_4$, dry CH_2Cl_2; xiv, Bu_4NF, THF; xv, AcOH–THF–water (3:1:1); xvi, $NaBH_4$, MeOH; xvii, $NaBH_3CN$

by use of tetrabutylammonium fluoride in THF at room temperature, the resulting aldehyde **24** was immediately reduced with $NaBH_4$ in MeOH to afford, however, 16-*epi*-koumidine **25** [(19*Z*)-normacusine B, m.p. 169–173 °C] as the sole product. Strong nucleophilicity of the fluoride anion presumably led to the epimerization at C^{16} in the aldehyde derivative **24**. To prevent epimerization at C^{16}, the 17-hydroxy group of compound **18** was protected as the trimethylsilyl (TMS) ether, which could be easily removed under mild conditions, and then compound **21** was oxidized with $Pb(OAc)_4$ in dry dichloromethane at −70 °C to −10 °C to give the unstable indolenine **23** in 63% overall yield from the alcohol **18**. The indolenine **23** was successively treated with aq. AcOH–THF at 0 °C and then with sodium cyanoborohydride to afford koumidine **3**, $[\alpha]_D^{23}$ −23.5° (*c* 0.6 in MeOH), in 77% overall yield from substrate **23**. The ^1H NMR, IR, UV, mass spectral and $[\alpha]_D$ data and m.p. were identical with those of natural koumidine.

Koumidine **3** was treated with 2,2,2-trichloroethyl chloroformate in aq. THF in the presence of a large excess of magnesium oxide to give the carbamate **26** in 58% yield. The resulting carbamate **26** was reduced with lithium aluminium hydride to afford the desired (19*Z*)-anhydrovobasinediol **2**, $[\alpha]_D^{23}$ −151° (*c* 0.3 in $CHCl_3$), in 86% yield. The ^1H NMR, IR, UV, mass spectral and $[\alpha]_D$ data were identical with those of natural (19*Z*)-anhydrovobasinediol.

We next turned our attention to the conversion of koumidine **3** into the oxindole alkaloid **1**. We had found an efficient method for the stereoselective oxidation–rearrangement of sarpagine-type indole alkaloids by the use of osmium tetraoxide.[11] In the case of the gardnerine series such as compound **27**, which has a methoxy group at C-6 of the indole ring, the oxidation with OsO_4 proceeded predominantly on the C^2–C^7 bond (indole moiety) rather than on the C^{19}–C^{20} (ethylidene side-chain).[12] However, by the same procedure, the demethoxy indole **26** gave the oxindole diol **28** and the diol **29** in 38 and 37% yield, respectively. Attempts at regioselective oxidation by increasing the reactivity of the indole nuclear using the N^a anion or N^a-trimethylsilyl derivative were ineffective. Furthermore, application of the general procedure, by using t-butyl hypochlorite,[13] to compound **26** gave the undesired oxindole having the opposite configuration at C^7. In turn, the indole **29** was subjected to OsO_4 oxidation to give compound **28**, identical with the oxindole derived directly from compound **26**. The oxindole thus obtained stereoselectively had the natural 7*S* configuration, as confirmed by a comparison of the CD spectrum with that of humanthenine-type alkaloids.[11] The 19*Z* ethylidene double bond was regenerated by a three-step sequence.[14] Thus, diol **28** was treated with trimethyl orthoformate in the presence of pyridium toluene-*p*-sulphonate (PPTS) to give the corresponding 2-methoxy-1,3-dioxolane, which was refluxed in acetic anhydride and then the N^a-acetyl group was removed by alkaline hydrolysis to afford the desired olefinic compound **30** in 74% yield from diol **28**. Finally the protecting group on N^b was removed with Zn in acetic acid to furnish *N*-demethoxyrankinidine **1** {m.p. 268–270 °C (decomp.), $[\alpha]_D^{24}$ −166° (*c* 0.45 in MeOH)} in 78% yield. The synthetic compound **1** had spectral properties (^1H NMR, ^{13}C NMR, IR,



Scheme 3 *Reagents:* i, $ClCO_2CH_2CCl_3$, MgO, aq. THF; ii, $LiAlH_4$, THF; iii, OsO_4, THF–Py; iv, pyridinium toluene-*p*-sulphonate, trimethyl orthoformate, THF; v, Ac_2O; vi, 1 mol dm^{-3} NaOH–MeOH; vii. Zn, AcOH

UV, high-resolution mass, and CD) in accord with those of the natural product.

In conclusion, we have undertaken a biogenetically patterned synthesis of three minor *Gelsemium* alkaloids, koumidine, (19*Z*)-anhydrovobasinediol [(19*Z*)-taberpsychine], and *N*-demethoxyrankinidine, starting from ajmaline, in a stereoselective manner. Since the absolute configuration of ajmaline has already been established, the structure, including the absolute configuration, of the three products was determined.

Experimental

M.p.s were measured on a Yamato MP-21 apparatus and are uncorrected. IR spectra were measured with a Hitachi 260 spectrophotometer, and UV spectra were measured in ethanol with a Hitachi U3400 spectrophotometer. ^1H NMR spectra were recorded on a JEOL JNM FX-270, a JNM GX-270 (270 MHz), or a JEOL GSX500 (500 MHz) spectrometer with tetramethylsilane as internal standard. *J*-Values are given in Hz. ^{13}C NMR spectra were measured with a JEOL GSX400 (100.4 MHz) or a JNM GX-270 (67.8 MHz) spectrometer with tetramethylsilane as internal standard. Mass spectra were taken with a Hitachi RMU-6E or an RMU-7M spectrometer. CD spectra were measured with a JASCO J-500A spectrometer for solutions in MeOH. Optical rotations were measured on a JASCO DIP-140 polarimeter. Elemental analyses were measured with a Perkin-Elmer 240 elemental analyser. TLC was performed on Merk precoated silica gel 60F-254 plates. Column chromatography utilized Merk Silica gel 60 [70–230 and 230–400 mesh (for flash chromatography)], prepacked column [Kusano CPS-HS-221-05 (for medium-pressure column chromatography)], and Merk Al_2O_3 (activity II–III).

Preparation of the Carbamate **5** *from Ajmaline* **4**.—A mixture of compound **4** (5.020 g, 15.3 mmol), *N*,*N*-dimethylhydrazine (4.70 cm^3, 61.9 mmol), a catalytic amount of H_2SO_4, molecular sieves 3 Å, and ethanol (100 cm^3) was heated under reflux for 5 h. The filtrate obtained upon filtration of the molecular sieves was concentrated under reduced pressure and then basified with aq. NH_4OH. The aq. layer was extracted with chloroform and the extract was washed with water, dried ($MgSO_4$) and evaporated. The residue was dissolved in 1 mol dm^{-3} NaOH–CH_2Cl_2 (1:4; 250 cm^3), and methyl chloroformate (1.42 cm^3, 18.4 mmol) was added to the mixture at 0 °C. After 30 min additional methyl chloroformate (0.25 cm^3, 3.2 mmol) was added to the reaction mixture, which was then stirred at 0 °C for 10 min. The organic layer was separated and the aq. layer was extracted with dichloromethane. The combined organic layers were washed with water, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel flash column chromatography with ethyl acetate–hexane (2:1) to give the carbamate **5** (5.166 g, 79%) as an amorphous powder, λ_{max}(EtOH)/nm 290, 245 and 206; ν_{max}($CHCl_3$)/cm^{-1} 3400, 1690 and 1460; δ_H(270 MHz; $CDCl_3$) 6.44 and 6.40* (1 H, each d, *J* 7.3, 21-H), 3.69 (3 H, s, CO_2Me) and 2.75, 2.74 and 2.72 (each 3 H, s, 3 × NMe); *m*/*z* 426 (M^+, 17%), 282 (61), 144 (98) and 113 (100).

Hydrolysis of the Carbamate **5**.—Copper(II) chloride was

* See footnote on p. 1773.

added portionwise to a solution of the hydrazone **5** (6.186 g, 14.5 mmol) in a mixture of THF (218 cm^3), water (29 cm^3) and phosphate buffer (0.07 mol dm^{-3}, pH 7; 87 cm^3) at room temperature in the following manner: 0 min, 3.902 g (29.0 mmol); 18 h, 1.952 g (14.5 mmol); 25 h, 1.013 g (7.5 mmol). After the final additional of $CuCl_2$ the mixture was stirred at room temperature for 17 h. After concentration to remove ethanol the reaction mixture was diluted with ice–water and basified with aq. NH_4OH. The whole mixture was extracted with chloroform and the extract was washed with water, dried ($MgSO_4$) and evaporated. The residue was purified by silica gel flash column chromatography with ethyl acetate–hexane (2:3) to give the *free aldehyde* **6** (4.175 g, 75%) as an amorphous powder (Found: M^+, 384.2050. $C_{22}H_{28}N_2O_4$ requires M, 384.2048); λ_{max}(EtOH)/nm 290, 247 and 206; ν_{max}($CHCl_3$)/cm^{-1} 3450, 1720, 1690 and 1460; δ_H(270 MHz; $CDCl_3$) 9.62 (d, *J* 3.4) and 9.59 (d, *J* 4.3) (together 1 H, 21-H), 3.73 and 3.72 (3 H, each s, CO_2Me), 2.76 and 2.73 (3 H, each s, NMe) and 0.87 (3 H, td, *J* 7.4, 1.3, 18-H_3); *m/z* 384 (M^+, 65%), 240 (32), 198 (28), 173 (80), 168 (30) and 144 (100).

Preparation of the Methoxyethoxymethyl Ether **7**.—Methoxyethoxymethyl chloride (MEMCl) (45 mm^3, 0.394 mmol) was added to a solution of the alcohol **6** (100 mg, 0.260 mmol) and diisopropylethylamine (68 mm^3, 0.390 mmol) in dry dichloromethane (2 cm^3) at 0 °C. The mixture was stirred at room temperature for 1.5 h and was then heated under reflux for 1.5 h. Additional diisopropylethylamine (90 mm^3, 0.517 mmol) and MEMCl (45 mm^3, 0.394 mmol) were added to the reaction mixture at 0 °C and the mixture was heated under reflux for 3 h. Cold 5% aq. sodium carbonate was added to the reaction mixture and the whole was extracted with chloroform. The extract was washed with water, dried ($MgSO_4$), and evaporated. The residue was purified by MPLC with ethyl acetate–hexane (2:5) to afford the MEM ether **7** (100 mg, 81%) as an amorphous powder, λ_{max}(EtOH)/nm 292, 248 and 205; ν_{max}($CHCl_3$)/cm^{-1} 1720, 1690, 1460, 1120 and 1040; δ_H(270 MHz; $CDCl_3$) 9.60 (d, *J* 3.4) and 9.57 (d, *J* 4.6) (together 1 H, 21-H), 3.73 and 3.71 (3 H, each s, CO_2Me), 3.384 and 3.382 (3 H, each s, OMe), 0.863 and 0.855 (3 H, each t, *J* 7.5, 18-H_3); *m/z* 472 (M^+, 75%), 252 (33), 182 (52), 144 (54), 89 (98) and 59 (100).

Preparation of the Silyl Enol Ether **8**.—TBSOTf (73 mm^3, 0.318 mmol) was added to a solution of compound **7** (100 mg, 0.212 mmol) and triethylamine (44 mm^3, 0.316 mmol) in dry dichloromethane (1 cm^3) and the mixture was stirred for 1.5 h. Further triethylamine (73 mm^3, 0.525 mmol) and TBSOTf (73 mm^3, 0.318 mmol) were added to the reaction mixture at 0 °C and the mixture was then stirred at the same temperature for 1 h. Cold 5% aq. sodium carbonate was added to the mixture and the whole was extracted with dichloromethane. The extract was washed with water, dried ($MgSO_4$), and evaporated. The residue was separated by MPLC with 10% ethyl acetate–hexane to give the *silyl ether* **8** (87 mg, 71%) as an amorphous powder (Found: M^+, 586.3419. $C_{32}H_{50}N_2O_6Si$ requires M, 586.3435); λ_{max}(EtOH)/nm 292, 248 and 205; ν_{max}($CHCl_3$)/cm^{-1} 1690, 1460 and 840; δ_H(270 MHz; $CDCl_3$) 6.14 (1 H, br s, 21-H), 1.00 (3 H, t, *J* 7.5, 18-H_3), 0.128, 0.118, 0.111 and 0.107 (6 H, each s, $SiMe_2$) and 0.92 (9 H, s, SiBu^t); *m/z* 586 (M^+, 82%), 336 (97), 241 (33), 182 (67), 144 (61), 89 (100) and 59 (98).

Bromination of the Silyl Enol Ether **8**.—A solution of NBS (27 mg, 0.152 mmol) in dry THF (2 cm^3) was added dropwise to a solution of compound **8** (80 mg, 0.136 mmol) in dry THF (2 cm^3) at −18 °C and the mixture was stirred at the same temperature for 30 min. Saturated aq. ammonium chloride was added and the whole was extracted with chloroform. The extract was washed with water, dried ($MgSO_4$) and evaporated. The residue was purified by MPLC with ethyl acetate–hexane (1:4) to yield compound **9** (57 mg, 76%) as an amorphous powder, λ_{max}(EtOH)/nm 291, 244 and 205; ν_{max}($CHCl_3$)/cm^{-1} 1710, 1690, 1470 and 1110; δ_H(270 MHz; $CDCl_3$) 9.39 and 9.35 (1 H, each s, 21-H), 3.72 and 3.70 (3 H, each s, CO_2Me) and 1.09 (3 H, t, *J* 6.7, 18-H_3); *m/z* 552 (M^+ + 2, 10%), 550 (M^+, 12), 182 (31), 144 (46), 89 (98) and 59 (100).

Preparation of α,β-Unsaturated Aldehydes from Bromide **9**.—DBU (20 mm^3, 0.134 mmol) was added to a solution of the bromide **9** (57 mg, 0.103 mmol) in dry DMF (1 cm^3) and the mixture was stirred at room temperature for 16 h. Saturated aq. ammonium chloride was added and the whole was extracted with chloroform. The extract was washed with water, dried ($MgSO_4$) and evaporated. DMF was removed by Kugelrohr apparatus and the residue was purified by MPLC with ethyl acetate–hexane (2:3) to afford *Z*-olefin **10** (29 mg, 60%) and *E*-olefin **11** (6 mg, 12%). *Compound* **10** was an amorphous powder (Found: M^+, 470.2396. $C_{26}H_{34}N_2O_6$ requires M, 470.2414); λ_{max}(EtOH)/nm 292, 251sh, 230 and 206; ν_{max}($CHCl_3$)/cm^{-1} 1690, 1670, 1460 and 1110; δ_H(500 MHz; $CDCl_3$) 10.20 and 10.19 (1 H, each s, 21-H), 6.67 (1 H, q-like, *J* 7.7, 19-H) and 2.15 and 2.13 (3 H, each d, *J* 7.7, 18-H_3); *m/z* 470 (M^+, 100%), 381 (26), 250 (74), 182 (91), 144 (90), 89 (90) and 59 (73).

Compound **11** was an amorphous powder (Found: M^+, 470.2409); λ_{max}(EtOH)/nm 293, 252, 224 and 207; ν_{max}($CHCl_3$)/cm^{-1} 1690, 1455 and 1110; δ_H(500 MHz; $CDCl_3$) 9.34 and 9.32 (1 H, each s, 21-H), 6.56 (1 H, q-like, *J* 7.4, 19-H) and 2.07 and 2.03 (3 H, each d, *J* 7.4 18-H_3); *m/z* 470 (M^+, 79%), 381 (19), 250 (50), 182 (61), 144 (63), 89 (66) and 59 (100).

$NaBH_4$ *Reduction of Z-Olefin* **10**.—Sodium borohydride (2.1 mg, 0.056 mmol) was added to a solution of enal **10** (25 mg, 0.053 mmol) in methanol (0.5 cm^3) and the mixture was stirred at room temperature for 30 min. Water was added, and the whole was extracted with chloroform. The extract was washed with water, dried ($MgSO_4$) and evaporated. The residue was separated by MPLC with ethyl acetate–hexane (2:1) to afford the *enol* **12** (22 mg, 88%) as an amorphous powder (Found: M^+, 472.2572. $C_{26}H_{36}N_2O_6$ requires M, 472.2573); λ_{max}(EtOH)/nm 291, 248 and 202; ν_{max}($CHCl_3$)/cm^{-1} 3450, 1690, 1455 and 1110; δ_H(270 MHz; $CDCl_3$) 4.23 (2 H, br s, 21-H_2), 5.49 and 5.44 (1 H, q, *J* 7.0, 19-H), 3.70 and 3.64 (3 H, each s, CO_2Me) and 1.70 and 1.69 (3 H, each d, *J* 7.0, 18-H_3); *m/z* 472 (M^+, 68%), 366 (14), 252 (22), 182 (55), 144 (68), 89 (53) and 59 (100).

$NaBH_4$ *Reduction of* E-*Olefin* **11**.—Identical treatment of enal **11** (370 mg, 0.786 mmol) in methanol (7.4 cm^3) with sodium borohydride (30 mg, 0.793 mmol) afforded the *enol* **13** (243 mg, 65%) as an amorphous powder (Found: M^+, 472.2585); λ_{max}(EtOH)/nm 291, 248 and 202; ν_{max}($CHCl_3$)/cm^{-1} 3450, 1690, 1460 and 1120; δ_H(270 MHz; $CDCl_3$) 4.06 (2 H, br s, 21-H_2), 5.60 (1 H, m, 19-H), 3.73 and 3.72 (3 H, each s, CO_2Me) and 1.70 (3 H, d, *J* 6.7, 18-H_3); *m/z* 472 (M^+, 60%), 366 (18), 252 (13), 182 (59), 144 (70), 138 (26), 89 (58) and 59 (100).

Hydrolysis of the Alcohol **12**.—A mixture of the enol carbamate **12** (100 mg, 0.212 mmol), sodium hydroxide (240 mg), ethylene glycol (4 cm^3) and water (0.8 cm^3) was heated under reflux for 6 h. Water was added to the reaction mixture and the whole was extracted with chloroform. The extract was washed with water, dried ($MgSO_4$) and evaporated. The residue was passed through a short column of silica gel to give the free amine **14** (77 mg, 87%) as an amorphous powder, ν_{max}($CHCl_3$)/cm^{-1} 3300, 1480, 1100 and 1040.

Hydrolysis of the Alcohol **13**.—Identical treatment of the enal carbamate **13** (190 mg, 0.402 mmol) with sodium hydroxide (480

mg), ethylene glycol (8 cm^3) and water (1.6 cm^3) (reaction time 1 h) afforded the free amine **15** (141 mg, 85%) as an amorphous powder, $\nu_{max}(CHCl_3)/cm^{-1}$ 3400, 1480, 1090 and 1040.

Preparation of Compound **16**.—Mesyl chloride (0.30 cm^3, 3.876 mmol) was added to a solution of the amine **14** (1556 mg, 3.754 mmol) in dry pyridine (60 cm^3) at 0 °C and the mixture was stirred at room temperature for 30 min. After the addition of ice–water the reaction mixture was basified with aq. NH_4OH. The aq. layer was extracted with chloroform. The extract was washed with water, dried ($MgSO_4$), and evaporated. The residue was separated by silica gel flash column chromatography with 2% methanol–chloroform to afford *compound* **16** (925 mg, 62%) as an amorphous powder (Found: M^+, 396.2399. $C_{24}H_{32}N_2O_3$ requires M, 396.2411); λ_{max}(EtOH)/nm 292, 249 and 205; $\nu_{max}(CHCl_3)/cm^{-1}$ 1100, 1040 and 1020; δ_H(270 MHz; $CDCl_3$) 5.30 (1 H, qt, *J* 6.7 and 2.3, 19-H), 3.6 (1 H, 21-H), 3.29 (1 H, br d, *J* 16.5, 21-H) and 1.56 (3 H, d, *J* 6.7, 18-H_3); *m/z* 396 (M^+, 100%), 307 (33), 291 (35), 183 (37), 144 (24) and 59 (66).

Preparation of **17**.—Identical treatment of a solution of compound **15** (140 mg, 0.338 mmol) in dry pyridine (3 cm^3) with mesyl chloride (29 mm^3, 0.375 mmol) afforded *compound* **17** (98 mg, 73%) as an amorphous powder (Found: M^+, 396.2410); λ_{max}(EtOH)/nm 291, 248 and 205; $\nu_{max}(CHCl_3)/cm^{-1}$ 1110, 1040 and 1020; δ_H(270 MHz; $CDCl_3$) 5.26 (1 H, q-like, *J* 6.7, 19-H), 3.55 (1 H, d, *J* 12.2, 21-H), 3.4 (1 H, 21-H) and 1.65 (3 H, dt, *J* 6.7 and 1.6, 18-H_3); *m/z* 396 (M^+, 100%), 307 (32), 291(31), 183 (36), 144 (20) and 59 (45).

Hydrolysis of Compound **16**.—Conc. HCl (1 drop) was added to a solution of compound **16** (50 mg, 0.126 mmol) in methanol (1 cm^3) at 0 °C and the mixture was refluxed for 5 h. The reaction mixture was diluted with chloroform and then basified with cold 5% aq. sodium carbonate. The whole was extracted with 5% methanol–chloroform. The extract was washed with water, dried ($MgSO_4$) and evaporated. The residue was crystallized from acetone to afford the *alcohol* **18** (37 mg, 95%) as needles, m.p. 279–281 °C (Found: C, 76.9; H, 7.75; N, 8.9. $C_{20}H_{24}N_2O{\cdot}\frac{1}{4}H_2O$ requires C, 76.76; H, 7.89; N, 8.95%); λ_{max}(EtOH)/nm 292, 248 and 205; ν_{max}(KBr)/cm^{-1} 3050, 1605 and 740; δ_H(270 MHz; $CDCl_3$) 5.31 (1 H, qt, *J* 6.7 and 2.2, 19-H), 4.44 (1 H, s, 17-H), 3.62 (1 H, d, *J* 16.8, 21-H), 3.29 (1 H, br d, *J* 16.8, 21-H), 3.46 (1 H, d, *J* 9.8, 3-H), 2.78 (3 H, s, N^aMe), 2.64 (1 H, s, 2-H) and 1.57 (3 H, d, *J* 6.7, 18-H_3); 11% NOE was observed between 15-H, (δ 2.65) and 19-H (δ 5.31); *m/z* 308 (M^+, 100%), 291 (6), 277 (9), 183 (40), 182 (17), 157 (13), 144 (16) and 131 (6).

Preparation of Tetraphyllicine **19**.—Identical treatment of compound **17** (47 mg, 0.119 mmol) in methanol (1.5 cm^3) with catalytic conc. HCl afforded tetraphyllicine **19** (28 mg, 77%) as needles, m.p. 294–296 °C (lit.,[9] 274–275 °C); $[\alpha]_D^{16}$ +16° (*c* 0.4 in pyridine) {natural $[\alpha]_D^{11}$ +19° (in pyridine)} (Found: C, 76.85; H, 7.8; N, 8.95. Calc. for $C_{20}H_{24}N_2O{\cdot}\frac{1}{5}H_2O$: C, 76.98; H, 7.88; N, 8.98%); λ_{max}(EtOH)/nm 291, 249 and 205; ν_{max}(KBr)/cm^{-1} 3050, 1605, 765 and 740; δ_H[270 MHz; $CDCl_3$ + CD_3OD (1:1)] 5.29 (1 H, q-like, *J* 6.7, 19-H), 4.38 (1 H, d, *J* 0.9, 17-H), 3.48 (1 H, d, *J* 9.2, 21-H), 2.76 (3 H, s, N^aMe), 2.64 (1 H, s, 2-H) and 1.68 (3 H, dq, *J* 6.7 and 1.1, 18-H_3); 7% NOE was observed between 18-H_3 (δ 1.68) and 21-H (δ 3.3); *m/z* 308 (M^+, 100%), 291 (5), 277 (8), 183 (45), 182 (22), 168 (12), 157 (16), 144 (25) and 131 (11). It was identical with an authentic sample (TLC, mixed m.p.).

Preparation of the TBS Ether **20**.—TBSOTf (90 mm^3, 0.392 mmol) was added to a stirred mixture of the alcohol **18** (100 mg, 0.324 mmol) and triethylamine (68 mm^3, 0.489 mmol) in dry dichloromethane (10 cm^3) at 0 °C and the mixture was stirred at the same temperature for 1 h. After the addition of further TBSOTf (45 mm^3, 0.196 mmol) at 0 °C the reaction mixture was stirred at 0 °C for 1 h. Cold 5% aq. sodium carbonate was added to the mixture and the whole was extracted with chloroform. The extract was washed with water, dried ($MgSO_4$) and evaporated. The residue was purified by silica gel column chromatography with 2% methanol–chloroform to give compound **20** (110 mg, 80%) as an amorphous powder, λ_{max}(EtOH)/nm 291, 249 and 205; δ_H(270 MHz; $CDCl_3$) 5.32 (1 H, qt, *J* 6.7 and 2.3, 19-H), 4.33 (1 H, s, 17-H), 1.57 (3 H, dd, *J* 6.7 and 0.6 18-H_3), 0.97 (9 H, s, $SiBu^t$) and 0.15 and 0.14 (each 3 H, s, $SiMe_2$); *m/z* 422 (M^+, 100%), 278 (31), 277 (31), 182 (36) and 73 (21).

Preparation of the Indolenine **22** *from the Indoline* **20**.—Lead tetraacetate was added portionwise to a stirred solution of compound **20** (39 mg, 0.092 mmol) in dry dichloromethane (1 cm^3) at −70 °C in the following manner: 0 min, 48 mg (0.097 mmol); 20 min, 48 mg; 40 min, 48 mg; 80 min, 48 mg. The reaction mixture was stirred at −70 °C for 40 min, the temperature was gradually raised to 0 °C during 30 min, and the mixture was stirred at 0 °C for 3 h. Cold aq. 5% sodium carbonate was added to the reaction mixture and the whole was extracted with 5% methanol–chloroform. The organic layer was washed with water, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel flash column chromatography with 2% methanol–chloroform to give compound **22** (22 mg, 59%) was an amorphous powder, λ_{max}(EtOH)/nm 253, 225sh, 221 and 214sh; $\nu_{max}(CHCl_3)/cm^{-1}$ 1590 and 830; δ_H(270 MHz; $CDCl_3$) 5.37 (1 H, qt, *J* 6.7 and 2.2, 19-H), 4.16 (1 H, dd, *J* 7.6 and 2.5, 3-H), 1.60 (3 H, d, *J* 6.7, 18-H_3), 0.94 (9 H, s, $SiBu^t$) and −0.01 and −0.09 (each 3 H, s, $SiMe_2$); *m/z* 406 (M^+, 100%), 349 (22), 248 (39), 247 (34), 181 (21), 168 (39) and 73 (40).

Preparation of 16-epi-*Koumidine* **25**.—A solution of Bu_4NF in THF (148 mm^3, 0.148 mmol) was added to a solution of **25** (30 mg, 0.074 mmol) in THF (0.6 cm^3). The mixture was stirred at 0 °C for 15 min and then at room temperature for 15 min. Water was added to the reaction mixture and the whole was extracted with 5% methanol–chloroform. The extract was washed with water, dried ($MgSO_4$) and evaporated. The resulting aldehyde was subjected to the next reaction without chromatographic purification.

Sodium borohydride (5.6 mg, 0.148 mmol) was added to a solution of aldehyde in methanol (0.5 cm^3) at 0 °C and the reaction mixture was stirred at room temperature for 30 min. Cold 5% aq. sodium carbonate was added to the reaction mixture and the whole was extracted with 5% methanol–chloroform. The extract was washed with water, dried ($MgSO_4$) and evaporated. The residue was purified by silica gel column chromatography with 5–10% methanol–chloroform to give 16-epi-*koumidine* **25** (13 mg, 60%) as needles, m.p. 169–173 °C (Found: C, 76.3; H, 7.6; N, 9.3. $C_{19}H_{22}N_2O{\cdot}\frac{1}{4}H_2O$ requires C, 76.35; H, 7.59; N, 9.37%); λ_{max}(EtOH)/nm 289sh, 279 and 226; ν_{max}(KBr)/cm^{-1} 3230, 1450, 1030 and 740; δ_H(270 MHz; CD_3OD) 5.34 (1 H, qt, *J* 7.0 and 2.4, 19-H), 4.17 (1 H, dd, *J* 10.1 and 2.1, 3-H), 3.46 (2 H, d, *J* 7.3, 17-H_2) and 1.60 (3 H, d, *J* 7.0, 18-H_3); δ_C(67.8 MHz; CD_3OD) 138.2 (s, C-2), 51.6 (d, C-3), 56.8 (d, C-5), 27.9 (t, C-6), 104.0 (s, C-7), 128.8 (s, C-8), 119.9 (d, C-9), 118.6 (d, C-10), 122.1 (d, C-11), 112.0 (d, C-12), 136.3 (s, C-13), 35.9 (t, C-14), 35.7 (d, C-15), 45.3 (d, C-16), 65.3 (t, C-17), 12.6 (q, C-18), 118.7 (d, C-19), 139.0 (s, C-20) and 54.1 (t, C-21); *m/z* 294 (M^+, 100%), 293 (95), 277 (11), 263 (36), 182 (11), 169 (82) and 168 (53).

Preparation of the Indolenine **23** *from the Indoline Alcohol* **18**.—TMSOTf (188 mm^3, 0.973 mmol) was added to a stirred

mixture of compound **18** (200 mg, 0.649 mmol) and triethylamine (0.14 cm^3, 1.006 mmol) in dry dichloromethane (4 cm^3) at 0 °C and the mixture was stirred at room temperature for 30 min. The reaction mixture was diluted with chloroform and the organic layer was washed with water, dried ($MgSO_4$) and evaporated. The resulting trimethylsilyl ether was subjected to the next reaction without chromatographic purification.

To a stirred solution of the trimethylsilyl ether in dry dichloromethane (4 cm^3) was added $Pb(OAc)_4$ in the following manner. Initially, $Pb(OAc)_4$ (320 mg, 0.650 mmol) was added to the mixture at −68 °C and the mixture was stirred at the same temperature for 20 min. After the addition of one more mole equivalent of $Pb(OAc)_4$ at −68 °C, the temperature was gradually raised to −15 °C during 30 min and the mixture was stirred at from −15 °C to −8 °C for 3 h. $Pb(OAc)_4$ (320 mg) was added to the mixture cooled to −68 °C and the temperature was raised to −15 °C during 20 min. After 3 h, further $Pb(OAc)_4$ (160 mg, 0.325 mmol) was added at −68 °C. The temperature was raised to −15 °C during 20 min and the mixture was stirred at from −15 °C to −10 °C for 1 h. Further $Pb(OAc)_4$ (160 mg) was added at −68 °C and the temperature was raised to −15 °C during 15 min. The mixture was stirred at −15 °C for 40 min and then was diluted with chloroform and washed with cold 5% aq. sodium hydrogen carbonate. The aq. layer was extracted with chloroform. The combined organic layers were washed with water, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel flash column chromatography with 3% methanol–chloroform to give compound **23** (149 mg, 63%) as an amorphous powder, λ_{max}(EtOH)/nm 261, 226sh, 221 and 215sh.

Preparation of Koumidine **3** *from the Indolenine* **23**.—To a solution of **23** (202 mg, 0.554 mmol) in THF (1.2 cm^3) at 0 °C were added water (1.2 cm^3) and acetic acid (3.6 cm^3) and the mixture was stirred at the same temperature for 1 h. Sodium cyanoborohydride (105 mg, 1.671 mmol) was added to the reaction mixture still cooled to 0 °C and the mixture was then stirred at room temperature for 50 min. The mixture was diluted with 5% methanol–chloroform and basified with cold aq. NH_4OH. The aq. layer was extracted with 5% methanol–chloroform. The extract was washed with water, dried ($MgSO_4$), and evaporated. The residue was purified by silica gel column chromatography with 1–5% methanol–chloroform to afford koumidine **3** (126 mg, 77%) as needles, m.p. 202–204 °C (natural koumidine has m.p. 200–201 °C; $[\alpha]_D^{23}$ −23.8° (*c* 0.6 in MeOH) {natural $[\alpha]_D^{20}$ −20.8° (*c* 1.8 in MeOH)} (Found: M^+, 294.1733. Calc. for $C_{19}H_{22}N_2O$: M, 294.1731); λ_{max}(EtOH)/nm 289sh, 282 and 227; ν_{max}(KBr)/cm^{-1} 3200, 1450, 1035, 1220 and 740; δ_H(270 MHz; CD_3OD) 5.37 (1 H, qt, *J* 6.7, 2.6, 19-H), 4.12 (1 H, dd, *J* 9.8 and 3.7, 3-H), 3.76 (1 H, br d, *J* 17.1, 21-H), 3.52 (1 H, dd, *J* 10.7 and 6.4, 17-H), 3.15 (1 H, dd, *J* 10.8 and 9.0, 17-H) and 1.61 (3 H, dt, *J* 6.7 and 1.5, 18-H_3); *m/z* 294 (M^+, 100%), 293 (91), 277 (14), 263 (44), 249 (11), 182 (11), 169 (99), 168 (67), 156 (10) and 115 (10). It was identical with an authentic sample on comparison of chromatographic behaviour (TLC), mixed m.p. and ^1H NMR data.

Preparation of the Carbanate **26** *from Koumidine* **3**.—2,2,2-Trichloroethyl chloroformate (0.36 cm^3, 2.615 mmol) was added to a stirred mixture of koumidine **3** (52 mg, 0.177 mmol) and magnesium oxide (145 mg, 3.596 mmol) in THF (4 cm^3)–water (1 cm^3) at 0 °C and the mixture was then stirred at room temperature for 30 min. After the addition of further $ClCO_2CH_2CCl_3$ (0.05 cm^3, 0.363 mmol) to the mixture at 0 °C the reaction mixture was stirred at room temperature for 30 min. Cold water (5 cm^3) was added to the mixture and the whole was extracted with chloroform. The extract was washed with brine, dried ($MgSO_4$) and evaporated. The residue was purified by silica gel flash column chromatography with 30% ethyl acetate–hexane to give compound **26** (48 mg, 58%) as an amorphous powder, λ_{max}(EtOH)/nm 293sh, 284 and 223; δ_H(500 MHz; $CDCl_3$) 7.95 and 7.90 (1 H, each s, N^aH), 5.47 and 5.38 (1 H, q-like, *J* 6.9, 19-H), 5.18 (1 H, d, *J* 9.1, 3-H) and 1.63 and 1.53 (3 H, d, *J* 6.9, 18-H_3); *m/z* 470 (M^+ + 2, 36%), 468 (M^+, 37), 434 (18), 368 (12), 44 (40) and 36 (100).

Preparation of (19Z)-*Anhydrovobasinediol* **2** *from the Carbamate* **26**.—Lithium aluminium hydride (42 mg, 1.105 mmol) was added to a solution of compound **26** (48 mg, 0.102 mmol) in dry THF (2 cm^3) at 0 °C and the mixture was stirred at room temperature for 1.5 h. After decomposition of excess of lithium aluminium hydride with aq. THF, the reaction mixture was filtered. The filtrate was concentrated, and purified by silica gel flash column chromatography with 3% methanol–chloroform to give compound **2** (27 mg, 86%) as an amorphous powder, $[\alpha]_D^{23}$ −151° (*c* 0.3 in $CHCl_3$) {natural (19*Z*)-anhydrovobasinediol has $[\alpha]_D^{23}$ −180° (*c* 0.4 in $CHCl_3$)}; λ_{max}(EtOH)/nm 292, 285, 280sh and 224; ν_{max}($CHCl_3$)/cm^{-1} 3460, 1460, 1340 and 1075; δ_H(500 MHz; $CDCl_3$) 7.92 (1 H, s, N^aH), 5.43 (1 H, q-like, *J* 6.9, 19-H), 5.12 (1 H, d, *J* 9.9, 3-H), 2.60 (3 H, s, N^bMe) and 1.60 (3 H, d, *J* 6.9, 18-H_3); *m/z* 308 (M^+, 100%), 293 (25), 279 (12), 154 (15) and 122 (90). It was identical with an authentic sample on comparison of ^1H NMR and chromatographic behaviour.

Osmylation of the Carbamate **26**. A solution of osmium tetraoxide (51 mg, 0.021 mmol) in dry THF (1 cm^3) was added dropwise to a solution of compound **26** (45 mg, 0.096 mmol) in a mixture of dry THF (1 cm^3) and dry pyridine (1 cm^3) at −20 °C. The mixture was then stirred at the same temperature for 40 min. Aq. sodium hydrogen sulphite [100 mg in water (2 cm^3)] was added and the mixture was stirred at room temperature for 1.5 h. Water was added to the reaction mixture and the whole was extracted with chloroform. The extract was washed with brine, dried ($MgSO_4$) and evaporated. The residue was purified by MPLC with 2% methanol–chloroform to afford the oxindole **28** (19 mg, 38%) and the indole **29** (18 mg, 37%). *Compound* **28**: amorphous powder (Found: M^+, 518.0764. $C_{22}H_{25}Cl_3N_2O_6$ requires M, 518.0775); λ_{max}(EtOH)/nm 279sh, 251 and 208; δ_H(500 MHz; $CDCl_3$) 1.30 and 1.27 (3 H, each d, *J* 6.3, together 18-H_3); *m/z* 520 (M^+ + 2, 12%), 518 (12), 372 (12), 146 (82) and 36 (100); CD $\Delta\varepsilon$/nm (*c* 0.21 mmol dm^{-3}, MeOH; 25 °C) −36.2 (209), +11.3 (227), −6.6 (254) and −1.9 (280). Compound **29**: amorphous powder, λ_{max}(EtOH)/nm 293sh, 284 and 223; δ_H(500 MHz; $CDCl_3$) 8.12 and 8.10 (1 H, each s, N^aH), 5.21 and 5.20 (1 H, each d, *J* 10.2, 3-H) and 1.30 and 1.27 (3 H, each d, *J* 6.3, 18-H_3).

Preparation of the Oxindole **28** *from the Indole* **29**.—A solution of OsO_4 (16.1 mg, 0.063 mmol) in dry THF (0.6 cm^3) was added dropwise to a stirred mixture of the indole **29** (28 mg, 0.056 mmol), dry THF (0.6 cm^3) and dry pyridine (0.6 cm^3) at −28 °C and the mixture was stirred at from −28 °C to −15 °C for 1.5 h. Aq. sodium hydrogen sulphite [60 mg in water (0.6 cm^3)] was added to the mixture at 0 °C and the mixture was then stirred at room temperature for 2 h. Water was added to the reaction mixture and the whole was extracted with chloroform. The extract was washed with brine, dried ($MgSO_4$) and evaporated. The residue was separated by MPLC with 2% methanol–chloroform to give the oxindole **28** (16 mg, 55%) and the starting material **29** (6 mg, 21% recovery).

Preparation of the Olefinic Compound **30** *from the Oxindole* **28**.—Pyridinium toluene-*p*-sulphonate (11 mg, 0.044 mmol) and trimethyl orthoformate (48 mm^3, 0.439 mmol) were added to a solution of compound **28** (45 mg, 0.087 mmol) in dry THF

(1 cm^3). The mixture was stirred at room temperature for 3 h. The solution was passed through a short column of silica gel and was then concentrated. The resulting 1,3-dioxolane was dissolved in acetic anhydride (1 cm^3) and the solution was refluxed for 2 h. The reaction mixture was diluted with ice–water and basified with cold aq. NH_4OH. The whole was extracted with chloroform and the extract was washed with water, dried ($MgSO_4$) and evaporated. The residue was dissolved in 1 mol dm^{-3} NaOH–methanol (1 cm^3) and the mixture was stirred at room temperature for 1 h. Water was added to the reaction mixture and the whole was extracted with chloroform. The extract was washed with brine, dried ($MgSO_4$), and evaporated. The residue was purified by MPLC with ethyl acetate–hexane (1:2) to afford *compound* **30** (31 mg, 74%) as an amorphous powder (Found: M^+, 484.0731. $C_{22}H_{23}Cl_3N_2O_4$ requires **M**, 484.0722); λ_{max}(EtOH)/nm 279, 250 and 206; ν_{max}($CHCl_3$)/cm^{-1} 3440, 1710, 1420 and 1120; δ_H(270 MHz; $CDCl_3$) 8.24 and 8.19 (1 H, each s, N^aH), 5.67 (1 H, m, 19-H) and 1.74 (3 H, d, *J* 5.9, 18-H_3); *m/z* 486 (M^+ + 2, 26%), 484 (M^+, 29), 339 (20), 310 (25), 208 (23), 146 (100) and 133 (24).

Preparation of N-*Demethoxyrankinidine* **1**.—Zinc dust was added to a solution of compound **24** (28 mg, 0.058 mmol) in acetic acid (1 cm^3) at room temperature in the following manner: 0 min, 40 mg (0.612 mmol); 2 h, 15 mg (0.229 mmol); 4 h, 30 mg (0.459 mmol). The mixture was stirred for 2 h and was then filtered, and diluted with ice–water. The mixture was basified with cold aq. NH_4OH and the whole was extracted with 10% methanol–chloroform. The extract was washed with brine, dried ($MgSO_4$), and evaporated. The residue was crystallized from acetone to afford compound **1** (14 mg, 78%) as prism, m.p. 268–270 °C (lit.,[2e] 258–260 °C); $[\alpha]_D^{24}$ −166° (*c* 0.45 in MeOH) {lit.,[2e] $[\alpha]_D^{22}$ −169.2° (*c* 0.052 in MeOH)} (Found: M^+, 310.1671. Calc. for $C_{19}H_{22}N_2O_2$: M, 310.1679); λ_{max}(EtOH)/nm 278sh, 252 and 207; ν_{max}(KBr)/cm^{-1} 3280 and 1700; δ_H(500 MHz; $CDCl_3$) 5.23 (1 H, q-like, *J* 6.6, 19-H), 4.33 (1 H, d, *J* 10.5, 17-H^α), 4.05 (1 H, dd, *J* 10.5 and 4.7, 17-H^β), 3.88 (1 H, d, *J* 16.8, 21-H^β), 3.59 (1 H, d, *J* 8.5, 3-H), 3.32 (1 H, d, *J* 16.8, 21-H^α) and 1.60 (3 H, d, *J* 6.6, 18-H_3); δ_C(100.4 MHz; $CDCl_3$) 181.1 (s, C-2), 73.9 (d, C-3), 54.3 (d, C-5), 33-7 (t, C-6), 58.7 (s, C-7), 135.3 (s, C-8), 125.1 (d, C-9), 122.9 (d, C-10), 128.1 (d, C-11), 109.7 (d, C-12), 139.3 (s, C-13), 29.7 (t, C-14), 33.9 (d, C-15 and -16), 66.9 (t, C-17), 12.7 (q, C-18), 118.8 (d, C-19), 138.7 (s, C-20) and 41.1 (t, C-21); *m/z* 310 (M^+, 96%), 295 (38), 164 (51) and 108 (100); CD $\Delta\varepsilon$/nm (*c* 0.35 mmol dm^{-3}, MeOH; 24 °C) −21.2 (210), +17.4 (229), −7.7 (256) and −2.4 (282). It was identical with an authentic sample on comparison of mixed m.p. and spectroscopic data.

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