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Synthetic Studies on Lythraceae Alkaloids *via* [3+2]Cycloaddition. II.[1) Total Synthesis of (±)-Decaline and (±)-Vertaline[2,3)

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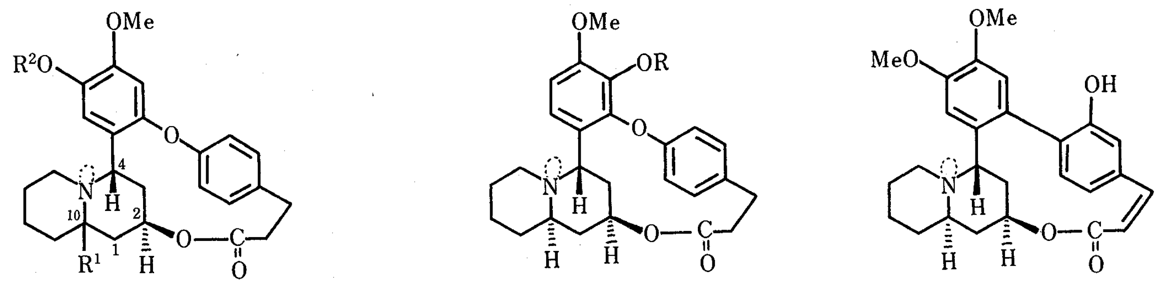
An efficient total synthesis of (±)-decaline and (±)-vertaline, lactonic biphenyl ether Lythraceae alkaloids, was achieved. The [3+2]cycloaddition of the nitrone (**24**) with the olefin (**10**), prepared *via* the Ullmann reaction catalyzed by a phase-transfer reagent, produced the adduct (**11**) which, upon treatment with methanesulfonyl chloride followed by reductive cleavage of the N–O bond, gave the isomeric quinolizidinols (**13** and **14**) in a one-pot operation. Through the use of inter- and intramolecular Mitsunobu reaction as an inversion procedure at C-2, **13** was converted into (±)-decaline (**1**). On the other hand, the *cis*-quinolizidinol (**14**) was transformed in two steps to (±)-vertaline (**2**).

Keywords——[3+2]cycloaddition; (±)-decaline; (±)-vertaline; Lythraceae alkaloid; Ullmann reaction; phase-transfer cayalyst

In 1962, during the course of isolation and structural studies[4) of the alkaloids from *Decodon verticillatus*, Ferris isolated seven alkaloids, two of which were decaline and vertaline. An X-ray study[5) of vertaline hydrobromide established the structure and absolute stereochemistry of vertaline to be as shown in **2**. On the basis of spectroscopic and chemical criteria Ferris[6) showed that decaline (**1**) had the same structure as vertaline with the exception of opposite configuration at C-10. Concerning the relative stereochemistry at C-2 and 4 in both alkaloids, the lactone group and biphenyl ether are linked to the quinolizidine ring in axial and equatorial orientations respectively. Besides these two, four other similar Lythraceae alkaloids[7) (**3**—**6**) with the structural features of fourteen-membered lactonic biphenyl ethers have been isolated so far. The isolation of these alkaloids has been of considerable interest to synthetic chemists[8) because of their unique structural features and the antiinflamatory activity[9) of a related alkaloid, cryogenine (**7**).



1 $R^1=\beta$-H, $R^2=Me$ **3** $R^1=\beta$-H, $R^2=H$
2 $R^1=\alpha$-H, $R^2=Me$ **4** $R^1=\alpha$-H, $R^2=H$

5 R=H
6 R=Me

7

Fig. 1

In the previous papers,[1,10] one of the authors (KS) presented a general synthetic procedure for constructing 2,4-disubstituted *trans*- and *cis*-quinolizidines *via* an intermolecular [3+2]cycloaddition of a cyclic nitrone with a monosubstituted olefin, and synthesized several Lythraceae alkaloids efficiently. In connection with our interest both in the synthesis of Lythraceae alkaloids and in an extension of the applicability of this methodology, we chose these two lactonic biphenyl ether alkaloids, decaline (**1**) and vertaline (**2**), as targets for total synthesis. In 1983, we briefly reported[2] a total synthesis of these molecules, and we describe here the experimental details of our synthetic studies.

From a retrosynthetic perspective, we envisaged that decaline and vertaline might be prepared from the isoxazolidine (**11**) by our strategy[10] described previously. Compound **11** in turn might be constructed by a regio- and stereoselective [3+2]cycloaddition of the cyclic nitrone **24** with the olefin **10** which should be available by Ullmann reaction[11] of the bromide (**9**) with the phenol (**22**).

The Ullmann reaction of the bromide (**9**), derived from 6-bromoveratraldehyde (**8**) with allylmagnesium bromide, with methyl 3-(4-hydroxyphenyl)propionate[12] (**22**) in pyridine in the presence of copper (II) oxide and potassium carbonate at 120—150 °C for 3.5 h gave the expected biphenyl ether (**10**) in 35% yield along with a fair amount (59% recovery) of the debrominated alcohol (**23**).

To improve the yield of **10**, we investigated the Ullmann reaction in the presence of various phase-transfer catalysts. To our knowledge, the use of a phase-transfer catalyst in the Ullmann reaction has not yet been reported in the literature. Firstly, 18-crown-6 (entry 4 in Table I) was used as a catalyst in the coupling reaction of **9** with **22**. As we had expected, the yield of the biphenyl ether (**10**) was raised to 51% and that of the undesired debrominated product (**23**) was suppressed to 34%. A series of phase-transfer catalysts was examined (Table I).

It was found that the presence of a catalyst not only raised the yield of **10** but also considerably suppressed debromination of the starting bromide (**9**). However, no improvement appeared in the reaction time. Comparing the crown ether type catalyst with the quaternary ammonium salt type, the latter may be preferable because of the lower yield of **23**. The best choice seems to be tetrabutylammonium hydrogen sulfate.

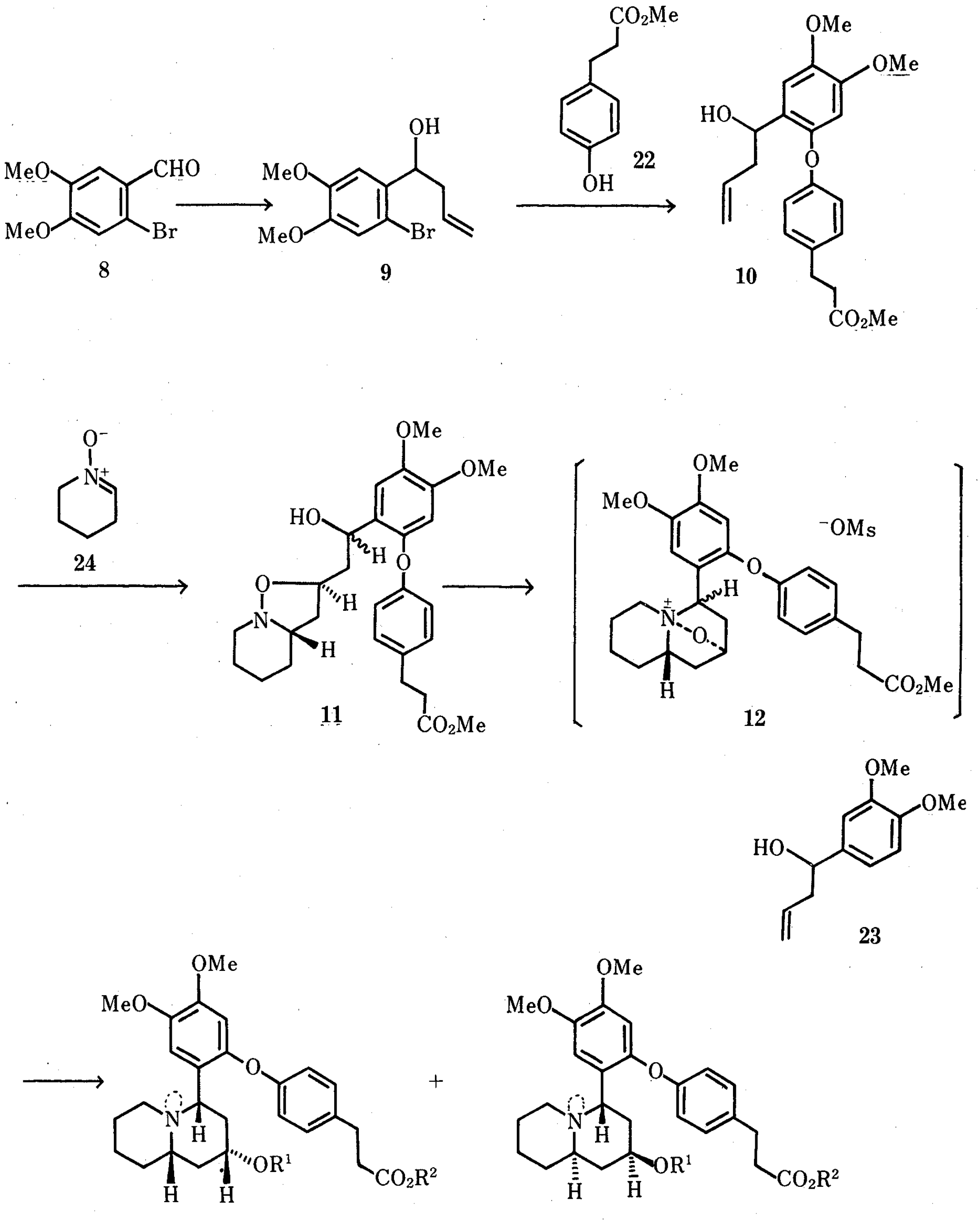
Having the desired homoallylic alcohol (**10**) in hand, we proceeded to examine the [3+2]cycloaddition reaction. On heating of **10** with 3,4,5,6-tetrahydropyridine 1-oxide (**24**)[13] in toluene under reflux, the adduct (**11**) was obtained in 99% yield as two inseparable diastereoisomers. The molecular ion peak appeared at *m/z* 485 in the mass spectrum (MS), and the relative stereochemistry shown in **11** at the future C-2 and C-10 of the quinolizidine nucleus, as well as the regiochemistry of the cycloaddition, were determined from the eventual

TABLE I. Reaction Conditions and Yields in the Ullmann Reaction of **9** with **22**

Entry	Additive	Reaction time (h)	Yield (%) of **10**	Yield (%) of **23**
1	None	3.5	35	59
2	Dibenzo-18-crown-6	4	44	31
3	Dicyclohexyl-18-crown-6	5	50	31
4	18-crown-6	5	51	34
5	$Bu_4\overset{+}{N}\overset{-}{Br}$	5	52	21
6	$Bu_4\overset{+}{N}\overset{-}{I}$	4	50	22
7	$Bu_4\overset{+}{N}\overset{-}{HSO_4}$	3.5	48	15

conversion of **11** to the natural substances.

Subsequent reaction of **11** with methanesulfonyl chloride in CH_2Cl_2 in the presence of triethylamine followed by treatment with zinc-aqueous acetic acid in a one-pot operation afforded the desired quinolizidinols **13** and **14** *via* the presumed intermediate (**12**) in 43.9 and 50.7% yields, respectively. The quinolizidine ring of the alcohol (**13**) was considered to be trans-fused on the basis of the Bohlmann bands in the infrared (IR) spectrum. The axial orientation of C-2H could be deduced from the nuclear magnetic resonance (NMR) absorption of the corresponding acetate (**15**), derived from **13** by a standard procedure, at δ 4.61 with a half-height width of 24 Hz. On the other hand, the alcohol **14** showed a mass spectrum similar to that of **13** and the absence of Bohlmann bands suggested it to be the *cis*-



13 : $R^1=H$, $R^2=Me$
15 : $R^1=Ac$, $R^2=Me$
17 : $R^1=R^2=H$

14 : $R^1=H$, $R^2=Me$
16 : $R^1=Ac$, $R^2=Me$
18 : $R^1=R^2=H$

Chart 1

isomer. The indicated structure of **14** was confirmed by a transformation to the acetate (**16**), whose NMR (100 MHz) spectrum was identical with that of the an authentic sample.[14)]

Thus, the stage was set for completion of a total synthesis of decaline and vertaline. The conversion of the hydroxy acid (**18**), prepared by basic hydrolysis of **16**, to (±)-vertaline (**2**) was accomplished by two macrolide-forming reactions. The first one is the Mukaiyama–Corey[8f,15)] procedure (method A). Treatment of **18** with 2,2′-dipyridyl disulfide in the presence of triphenylphosphine followed by refluxing in xylene at high dilution gave (±)-vertaline, mp 225.5 °C (lit.[8d)] 224—225 °C), in 58.9% yield. The chromatographic properties and the spectral data (IR, NMR, MS) of synthetic vertaline were identical with those of an authentic sample. The second approach that we examined is the methodology recently developed by Masamune[16)] (method B). Thus, **17** was treated with triethylamine and diphenyl phosphochloridate followed by refluxing in benzene in the presence of 4-(dimethylamino)pyridine at high dilution to afford (±)-**2** in 54.1% yield.

To complete a total synthesis of decaline from **13**, it is necessary to lactonize the molecule with an S_N2 inversion at the hydroxybearing carbon (C-2) in the quinolizidine ring. Various attempts at constructing a fourteen-membered lactone ring with the inversion in the hydroxy acid (**17**), *e.g.* intramolecular Mitsunobu reaction,[17)] the Kellog procedure,[18)] *etc.*, did not produce (±)-decaline, even in small quantities as checked by thin-layer chromatography (TLC) analysis. The lactonization was finally achieved by the use of the *N,N*-dimethylformamide (DMF)–dineopentyl acetal method.[19)] Treatment of **17** with DMF–dineopentyl acetal in refluxing toluene at high dilution afforded two products. The major product (28.4% yield) was identified as **26**, whose IR spectrum showed formate and amide carbonyl absorptions at 1720 and 1630 cm^{-1}, respectively; axial orientation of C–2H was indicated by the NMR absorption at δ 4.84 (a multiplet with half-height width 24 Hz). The formation of **26** might be explainable in terms of an intervention of the four-membered intermediate **25**, as shown in Chart 2.

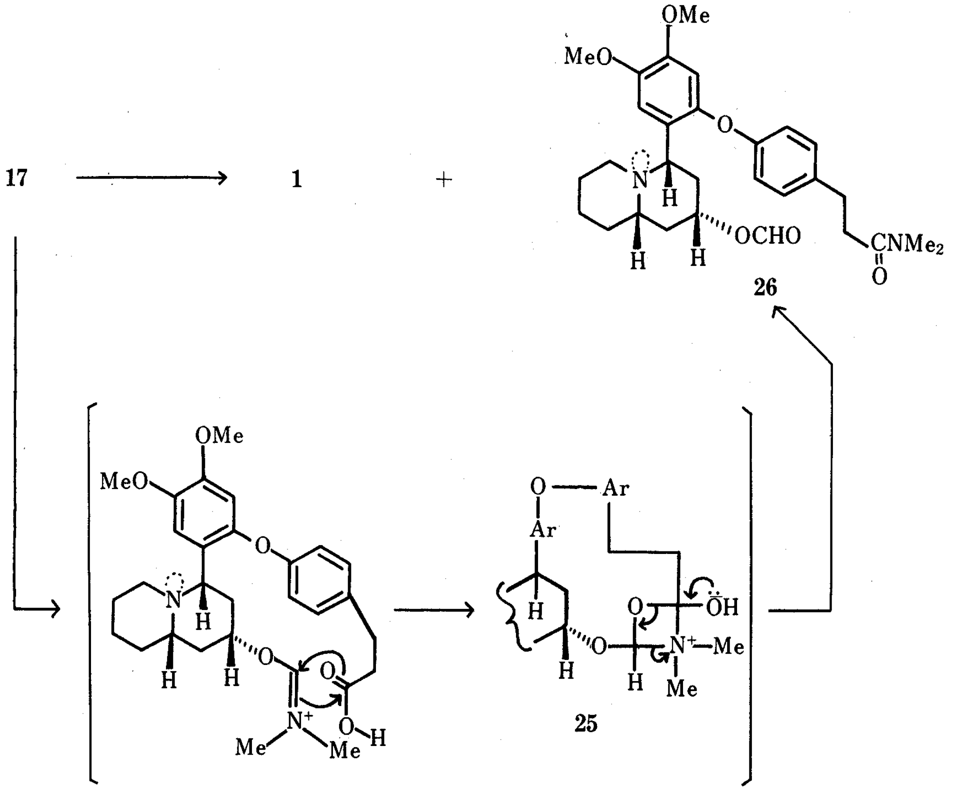
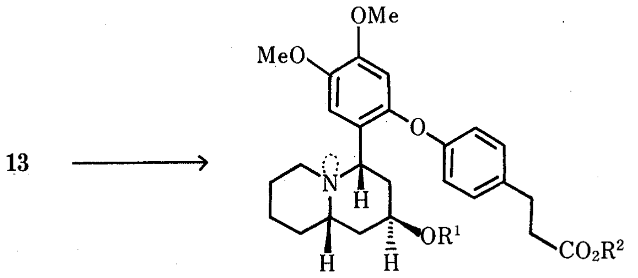


Chart 2

As the minor product, (±)-decaline (**1**), mp 197—197.5 °C (lit.[8a)] 196—197 °C), was obtained in 9.7% yield. Identity of the synthetic material with an authentic sample was established by comparisons of TLC behavior, and IR, NMR, and mass spectra. To improve the yield of the final step, the intermolecular S_N2 inversion of the configuration at C-2 was attempted by various procedures. Mesylation of the hydroxy ester (**13**) followed by treatment with cesium propionate[20)] furnished the inverted propionate (**19**) in 41.5% yield. The inversion at C-2 is supported by the observation that the equatorial proton at C-2 appeared at δ 4.92 as a multiplet with a half-height width of 8 Hz.

The inversion at C-2 was accomplished more effectively by employing the intermolecular Mitsunobu reaction.[17)] Treatment of **13** with diethyl azodicarboxylate and triphenylphosphine in the presence of benzoic acid afforded the benzoate (**21**) in 77.2% yield. The configuration at C-2 in **21** was also confirmed by the NMR absorption at δ 5.15 (a multiplet with a half-height width of 8 Hz), which indicated the axial orientation. Finally, **21** was converted to (±)-decaline (**1**) by successive hydrolysis and lactonization under the same conditions (method A and B) as described for vertaline in 57.4 and 44.7% yields, respectively.



19 : R^1=COEt, R^2=Me
20 : R^1=R^2=H
21 : R^1=COPh, R^2=Me

Chart 3

An efficient total synthesis of decaline and vertaline was thus achieved in 9.8 and 11.2% overall yields from 6-bromoveratraldehyde, respectively, and we were thus able to extend the applicability of our methodology for the total synthesis of the quinolizidine alkaloids. Furthermore, during the course of the synthetic study, it was found that the use of a phase-transfer catalyst in the Ullmann reaction of an aryl bromide with a phenol derivative not only enhanced the yield of the biphenyl ether but also suppressed the formation of the undesired debrominated product.

Experimental

Melting points were determined on a Yanagimoto MP-S2 apparatus and are uncorrected. IR spectra were obtained on a Hitachi 125 grating spectrometer and NMR spectra on a JEOL PMX-60 or JEOL PS-100 spectrometer with tetramethylsilane as an internal standard. When peak multiplicities are reported, the following abbreviations are used: s, singlet; d, doublet; t, triplet; m, multiplet; br, broadened. Ordinary mass spectra were measured with a Hitachi M-52G instrument, while high-resolution mass spectroscopy was performed on a JEOL TMS-01SG-2 spectrometer. Unless otherwise specified, all reactions were carried out under an atmosphere of dry argon or nitrogen and extracts were dried over anhydrous Na_2SO_4. Column chromatography was carried out with silica gel (Wako gel C-200) and alumina (ICN grade III).

4-Bromo-5-(1-hydroxybut-3-en-1-yl)veratrole (9)——A solution of allyl bromide (0.21 ml) and 6-bromoveratraldehyde (0.5 g) in dry tetrahydrofuran (THF) (5 ml) was added dropwise to a stirred mixture of Mg (74 mg) in dry THF (1 ml) at room temperature (RT). The whole was stirred for 4 h, then sat. NH_4Cl solution was added and the mixture was extracted with benzene. The extract was washed with brine, then dried, and the solvent was evaporated off to give the residue, which was chromatographed on silica gel with AcOEt–hexane (1 : 2, v/v) as an eluent to afford **9**

(0.51 g, 87.7%) as a colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1}: 3570 (OH), 1635 (C=C). NMR (CCl_4) δ: 3.72 (6H, s, -OMe × 2), 4.70—6.16 (4H, m, olefinic H and Ar-$\underset{|}{\text{C}}$(OH)$\underline{\text{H}}$), 6.79, 6.91 (1H each, s, Ar-H). MS *m*/*z*: 288 and 286 (M^+). High-resolution MS (*m*/*z*): Calcd for $C_{12}H_{15}BrO_3$: 288.0186 and 286.0203. Found: 288.0202 and 186.0173.

General Procedure for the Ullmann Reaction of 9 with 22——A mixture of the bromide (**9**) (1 mmol), methyl 3-(4-hydroxyphenyl)propionate[12] (2 mmol), and K_2CO_3 (5.8 mmol) in dry pyridine (1.5 ml) was heated with (or without) a phase-transfer catalyst (*ca.* 0.1 mmol) in the presence of CuO (5 mmol) at 120—150 °C for 3.5—5 h, then cooled. H_2O and $CHCl_3$ (5 ml each) were added to the reaction mixture, which was filtered with the aid of celite. The filtrate was successively washed with 10% HCl (3—4 times), H_2O, sat. $NaHCO_3$ solution (2—3 times), and H_2O, then dried. Removal of the solvent gave a residue, which was chromatographed on silica gel with AcOEt–hexane (1 : 4, v/v) as an eluent to afford the debrominated alcohol (**23**) as colorless needles, mp 76.9—77.0 °C, after recrystallization from benzene–hexane. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1}: 3600 (OH), 1642 (C=C). NMR ($CDCl_3$) δ: 2.15 (1H, br s, -O$\underline{\text{H}}$, D_2O disappeared), 2.40 (2H, t, J=6 Hz, -C$\underline{\text{H}}_2$—⟍), 3.77 (6H, s, -OMe × 2), 4.52 (1H, t, J=6 Hz, Ar-$\underset{|}{\text{C}}$(OH)$\underline{\text{H}}$), 4.83—6.00 (3H, m, olefinic H), 6.67—6.87 (3H, m, Ar-H). MS *m*/*z*: 208 (M^+). High-resolution MS (*m*/*z*): Calcd for $C_{12}H_{16}O_3$: 208.1097. Found: 208.1076. From the later fraction eluted with the same solvent, the biphenyl ether (**10**) was obtained as a pale yellow oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1}: 3575 (OH), 1720 ($-\underset{\overset{\|}{\text{O}}}{\text{C}}-\text{O}-$), 1630 (C=C). NMR ($CDCl_3$) δ: 2.15—3.15 (7H, m), 3.55, 3.61, 3.73 (3H each, s, -OMe × 3), 4.65—6.05 (4H, m), 6.33 (1H, s, Ar-H), 6.72 (2H, d, J=9 Hz, Ar-H), 6.98 (1H, s, Ar-H), 7.02 (2H, d, J=9 Hz, Ar-H). MS *m*/*z*: 386 (M^+). High-resolution MS (*m*/*z*): Calcd for $C_{22}H_{26}O_6$: 386.1729. Found: 386.1734. The phase-transfer catalyst, the reaction time, and the yields of both **23** and **10** are indicated in Table I.

The Isoxazolidine (11)——A mixture of 1-hydroxypiperidine (90 mg) and HgO (yellow) (381 mg) in dry CH_2Cl_2 (7 ml) was stirred at −13—−5 °C for 1 h. After filtration, dry toluene (3.3 ml) was added to the filtrate and the CH_2Cl_2 was evaporated off. Then a solution of **10** (170 mg) in toluene (5 ml) was added to the resulting toluene solution of the nitrone (**24**) and the mixture was refluxed for 1.5 h. The organic layer was washed with brine, dried and evaporated to leave the residue, which was chromatographed on silica gel with $CHCl_3$ as an eluent to afford **11** (211 mg, 99%) as a colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1}: 3500 (OH), 1730 ($-\underset{\overset{\|}{\text{O}}}{\text{C}}-\text{O}-$). NMR ($CDCl_3$) δ: 3.54, 3.62, 3.74 (3H each, s, -OMe × 3), 4.84 (1H, m, Ar$\underset{|}{\text{C}}$(OH)$\underline{\text{H}}$), 6.23 (1H, s, Ar-H), 6.62 (2H, d, J=9 Hz, Ar-H), 6.92 (2H, d, J=9 Hz, Ar-H), 6.94 (1H, s, Ar-H). MS *m*/*z*: 485 (M^+). High-resolution MS (*m*/*z*): Calcd for $C_{27}H_{35}NO_7$: 485.2411. Found: 485.2409.

The *trans*-Quinolizidinol (13) and the *cis*-Quinolizidinol (14)——Triethylamine (4.5 ml) was added dropwise to a stirred solution of **11** (1.8 g) and methanesulfonyl chloride (1.53 ml) in dry CH_2Cl_2 (30 ml) at 0 °C. The resulting mixture was stirred at 0 °C for 1.2 h. After evaporation of the solvent and the excess reagents, the residue was taken up with 50% aqueous AcOH (36 ml) and the solution was treated with Zn dust (6.6 g) at room temperature for 2.5 h. The mixture was filtered with the aid of celite and the filtrate was concentrated to leave a residue, which was chromatographed on silica gel with $CHCl_3$–MeOH (97 : 3, v/v) as an eluent to afford **13** (0.76 g, 43.9%) as a colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1}: 3600 (OH), 2795, 2750 (Bohlmann bands), 1738 ($-\underset{\overset{\|}{\text{O}}}{\text{C}}-\text{O}-$). NMR ($CDCl_3$) δ: 3.67, 3.76, 3.91 (3H each, s, -OMe × 3), 6.45 (1H, s, Ar-H), 6.67 (2H, d, J=8 Hz, Ar-H), 7.12 (2H, d, J=8 Hz, Ar-H), 7.13 (1H, s, Ar-H). MS *m*/*z*: 469 (M^+). High-resolution MS (*m*/*z*): Calcd for $C_{27}H_{35}NO_6$: 469.2463. Found: 469.2421. From the next fraction, eluted with $CHCl_3$–MeOH (95 : 5, v/v), **14** (0.88 g, 50.7%) was obtained as a colorless oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1}: 3600 (OH), 1737 ($-\underset{\overset{\|}{\text{O}}}{\text{C}}-\text{O}-$). NMR ($CDCl_3$) δ: 3.66, 3.77, 3.90 (3H each, s, -OMe × 3), 4.65 (1H, m, C-2H), 6.57 (1H, s, Ar-H), 6.81 (2H, d, J=8 Hz, Ar-H), 7.08 (1H, s, Ar-H), 7.16 (2H, d, J=8 Hz, Ar-H). MS *m*/*z*: 469 (M^+). High-resolution MS (*m*/*z*): Calcd for $C_{27}H_{35}NO_6$: 469.2463. Found: 469.2461.

Acetylation of 13——A solution of **13** (40 mg) in acetic anhydride (0.5 ml) and pyridine (0.5 ml) was stirred at room temperature for 15 h. After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel with $CHCl_3$ as an eluent to afford **15** (43 mg, 98.9%) as a pale brown oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1}: 2800, 2755 (Bohlmann bands), 1740 ($-\text{O}-\underset{\overset{\|}{\text{O}}}{\text{C}}-$). NMR (100 MHz, $CDCl_3$) δ: 1.90 (3H, s, $-\text{O}-\underset{\overset{\|}{\text{O}}}{\text{C}}-\text{CH}_3$), 3.34 (1H, dd, J=12 and 3 Hz, C-4H), 3.57, 3.64, 3.80 (3H each, s, -OMe × 3), 4.61 (1H, m, $W_{1/2}$=24 Hz, C-2H), 6.32 (1H, s, Ar-H), 6.64 (2H, d, J=9 Hz, Ar-H), 6.98 (1H, s, Ar-H), 7.00 (2H, d, J=9 Hz, Ar-H). MS *m*/*z*: 511 (M^+). High-resolution MS (*m*/*z*): Calcd for $C_{29}H_{37}NO_7$: 511.2570. Found: 511.2581.

Acetylation of 14——A solution of **14** (0.75 g) in acetic anhydride (5 ml) and pyridine (5 ml) was stirred at room temperture for 4 h. After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel with $CHCl_3$–MeOH (98 : 2, v/v) as an eluent to afford the actate (**16**)[8e] (0.68 g, 83.2%) as a pale brown oil. IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1}: 1730 ($-\underset{\overset{\|}{\text{O}}}{\text{C}}-$). NMR (100 MHz, $CDCl_3$) δ: 3.65, 3.76, 3.90 (3H each, s, -OMe × 3), 4.54 (1H, t, J=6 Hz, C-4H), 5.10 (1H, m, $W_{1/2}$=13 Hz, C-2H), 6.48 (1H, s, Ar-H), 6.72 (2H, d, J=8 Hz, Ar-H), 7.02 (1H, s, Ar-H), 7.07 (2H, d, J=8 Hz, Ar-H). MS *m*/*z*: 511 (M^+).

(±)-Vertaline (2)——(Method A) A solution of **16** (120 mg) and LiOH (60 mg) in aqueous MeOH (H_2O 2 ml, MeOH 6 ml) was stirred at room temperature for 2 h. After removal of MeOH, the residual liquid was adjusted to pH 6 with 10% HCl by using bromothymol blue as an indicator. The mixture was then extracted with CH_2Cl_2 and the extract was dried. Removal of the solvent gave the crude hydroxy acid (**18**) as a pale green foam, which was taken up with CH_2Cl_2 (2.1 ml). The resulting solution was treated with 2,2′-dipyridyl disulfide (78 mg) and triphenylphosphine (92 mg) at room temperature for 1 h. After evaporation of the solvent, the residue was refluxed in xylene (447 ml) for 20 h and the solvent was removed *in vacuo*. The residue was chromatographed on alumina with Et_2O–hexane (2 : 3, v/v) as an eluent to afford (±)-vertaline (**2**) (57 mg, 58.9%) as colorless prisms, mp 225.5 °C (lit.[8d] 224—225 °C), after recrystallization from MeOH. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1719 (–$\underset{\overset{\|}{\mathrm{O}}}{\mathrm{C}}$–O–). NMR (100 MHz, $CDCl_3$) δ: 3.40 (1H, dd, $J=12$ and 4 Hz, C-4H), 3.84, 3.89 (3H each, s, –OMe × 2), 4.86 (1H, m, $W_{1/2}=9$ Hz, C-2H), 6.48 (1H, dd, $J=9$ and 2 Hz, Ar-H), 6.74, 6.83 (1H each, s, Ar-H), 6.92 (1H, dd, $J=9$ and 2 Hz, Ar-H), 7.23 (2H, br s, Ar-H). MS m/z: 437 (M^+, 100%). High-resolution MS (m/z): Calcd for $C_{26}H_{31}NO_5$: 437.2200. Found: 437.2197. (Method B) The *cis*-acetate (**16**) (150 mg) was hydrolyzed to **17** as mentioned in method A. Then the crude hydroxy acid (**18**) was treated with triethylamine (0.041 ml) followed by diphenyl phosphochloridate (0.063 ml) at 0 °C. The mixture was stirred for 0.5 h, then filtered. The filtrate, after dilution with benzene (100 ml), was maintained at 5 °C and this cold solution was added over a period of 8 h to a stirred, warm (80 °C) solution of 4-(dimethylamino)pyridine (109 mg) in benzene (180 ml). After the addition had been completed, the resulting solution was kept at reflux for 14 h, then the solvent was removed to give a residue, which was chromatographed on silica gel with $CHCl_3$–MeOH (95 : 5, v/v) as an eluent to afford (±)-**2** (69.3 mg, 54.1%).

(±)-Decaline (1) (DMF Dineopentylacetal Method)——The hydroxy acid (**17**) was prepared from the corresponding hydroxy ester (**13**) (58 mg) by the procedure described above. A solution of the crude **17** in toluene (2 ml) and a solution of DMF dineopentylacetal (0.05 ml) in toluene (2 ml) were added dropwise at the same time to refluxing toluene (3 ml) over a period of 12 h. The resulting mixture was heated at 130 °C for 12 h and the solvent was then evaporated off to leave a residue, which was chromatographed on silica gel with $CHCl_3$ as an eluent to afford the amide formate (**26**) (17 mg, 28.4%) as a pale yellow oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 2800, 2760 (Bohlmann bands), 1720 (–O–$\underset{\overset{\|}{\mathrm{O}}}{\mathrm{C}}$–H), 1630 ($Me_2N$–$\underset{\overset{\|}{\mathrm{O}}}{\mathrm{C}}$–). NMR (100 MHz, $CDCl_3$) δ: 2.95 (6H, s, –NMe_2), 3.44 (1H, dd, $J=12$ and 3 Hz, C-4H), 3.75, 3.91 (3H each, s, –OMe × 2), 4.84 (1H, m, $W_{1/2}=24$ Hz, C-2H), 6.44 (1H, s, Ar-H), 6.76 (2H, d, $J=9$ Hz, Ar-H), 7.08 (1H, s, Ar-H), 7.12 (2H, d, $J=9$ Hz, Ar-H), 7.96 (1H, s, –O–$\underset{\overset{\|}{\mathrm{O}}}{\mathrm{C}}$–H). MS m/z: 510 (M^+). High-resolution MS (m/z): Calcd for $C_{29}H_{38}N_2O_6$: 510.2728. Found: 510.2692. From the next fraction, eluted with the same solvent, (±)-decaline (**1**) (5 mg, 9.7%) was obtained as colorless prisms, mp 197—197.5 °C (lit.[8a] 196—197 °C), after recrystallization from MeOH. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 2790, 2750 (Bohlmann bands), 1728 (–O–$\underset{\overset{\|}{\mathrm{O}}}{\mathrm{C}}$–). NMR (100 MHz, $CDCl_3$) δ: 2.80 (1H, dd, $J=12$ and 3 Hz, C-4H), 3.78, 3.80 (3H each, s, –OMe × 2), 4.79 (1H, m, $W_{1/2}=8$ Hz, C-2H), 6.34 (1H, dd, $J=9$ and 2.5 Hz, Ar-H), 6.63 (1H, s, Ar-H), 6.79 (1H, dd, $J=9$ and 2.5 Hz, Ar-H), 6.80 (1H, s, Ar-H), 7.08 (2H, m, Ar-H). MS m/z: 437 (M^+, 100%). High-resolution MS (m/z): Calcd for $C_{26}H_{31}NO_5$: 437.2202. Found: 437.2239.

The Propionate (19)——Methanesulfonyl chloride (0.03 ml) was added dropwise to a stirred solution of **13** (68 mg) in CH_2Cl_2 (5 ml) in the presence of triethylamine (0.2 ml) at 0 °C and the mixture was stirred at the same temperature for 1 h. After removal of the solvent and the excess reagents, the residue was extracted with CH_2Cl_2 and the extracts was washed with H_2O, dried and evaporated. The resulting crude mesylate was taken up with DMF (1 ml) and the solution was treated with cesium propionate (36 mg) at 90 °C for 42 h. Evaporation of the solvent gave a residue, which was chromatographed on silica gel with $CHCl_3$ as an eluent to afford **19** (27 mg, 41.5%) as a colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 2800, 2780 (Bohlmann bands), 1732 (–O–$\underset{\overset{\|}{\mathrm{O}}}{\mathrm{C}}$–). NMR (100 MHz, $CDCl_3$) δ: 1.92 (3H, t, $J=8$ Hz, –$\underset{\overset{\|}{\mathrm{O}}}{\mathrm{C}}$–$CH_2$–$C\underline{H}_3$), 2.00 (2H, q, $J=8$ Hz, –$\underset{\overset{\|}{\mathrm{O}}}{\mathrm{C}}$–$C\underline{H}_2$–$CH_3$), 3.58, 3.68, 3.84 (3H each, s, –OMe × 3), 4.92 (1H, m, $W_{1/2}=8$ Hz, C-2H), 6.38 (1H, s, Ar-H), 6.62 (2H, d, $J=8$ Hz, Ar-H), 7.00 (2H, d, $J=8$ Hz, Ar-H), 7.04 (1H, s, Ar-H). MS m/z: 525 (M^+). High-resolution MS (m/z): Calcd for $C_{30}H_{39}NO_7$: 525.2725. Found: 525.2703.

The Benzoate (21)——A solution of diethyl azodicarboxylate (0.14 ml) in dry THF (0.5 ml) was added dropwise to a stirred solution of **13** (190 mg) and triphenylphosphine (168 mg) in dry THF (3 ml) in the presence of benzoic acid (78 mg) over a period of 15 min at room temperature. The mixture was stirred at the same temperature for 3.5 h and the solvent was evaporated off to give a residue, which was chromatographed on silica gel with $CHCl_3$ as an eluent to afford **21** (179 mg, 77.2%) as a colorless oil. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 2800, 2775 (Bohlmann bands), 1725 (–O–$\underset{\overset{\|}{\mathrm{O}}}{\mathrm{C}}$–). NMR (100 MHz, $CDCl_3$) δ: 3.56, 3.71, 3.85 (3H each, s, –OMe × 3), 5.15 (1H, m, $W_{1/2}=8$ Hz, C-2H), 6.43 (1H, s, Ar-H), 6.54 (2H, d, $J=8$ Hz, Ar-H), 6.84 (2H, d, $J=8$ Hz, Ar-H), 7.04 (1H, s, Ar-H), 7.38 (4H, m, Ar-H), 7.78 (2H, dd, $J=8$ and 2 Hz, Ar-H). MS m/z: 573 (M^+). High-resolution MS (m/z): Calcd for $C_{34}H_{39}NO_7$: 573.2726. Found: 573.2729.

(±)-Decaline (1) from 21——(Method A) The benzoate (**21**) (160 mg) was hydrolyzed to the corresponding hydroxy acid (**20**) by the same procedure as described for **2** (method A). The crude **20** was taken up with CH_2Cl_2 (2 ml) and the solution was treated with 2,2′-dipyridyl disulfide (90 mg) and triphenylphosphine (106 mg) at room temperature for 1 h. Evaporation of the solvent gave a residue, which was refluxed in xylene (400 ml) for 18 h, then the solvent was removed to leave an oil. The crude material was chromatographed on silica gel with $CHCl_3$ as an eluent to afford (±)-**1** (70 mg, 57.4%), which was identical with an authentic sample. (Method B) The crude hydroxy acid (**20**), prepared from **21** (100 mg), was treated with triethylamine (0.024 ml) followed by diphenyl phosphochloridate (0.037 ml) at 0 °C and the mixture was stirred for 0.5 h, then filtered. The filtrate, after dilution with benzene (70 ml), was maintained at 5 °C and this cold solution was added over a period of 8 h to a stirred, warm (80 °C) solution of 4-(dimethylamino)pyridine (65 mg) in benzene (105 ml). After the addition had been completed, the resulting solution was kept at reflux for 13 h and the solvent was removed to leave a residue, which was chromatographed on silica gel with $CHCl_3$ as an eluent to afford (±)-**1** (34 mg, 44.7%).

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