Asymmetric formal total synthesis of (−)-swainsonine†

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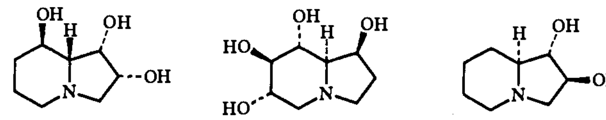
A new concise noncarbohydrate-based enantioselective approach to (−)-swainsonine **1** is described, utilizing the kinetic resolution of α-furfuryl amide **4** and the Sharpless AD reaction of **9a** as key steps. Kinetic resolution of α-furfuryl amide **4** using the modified Sharpless asymmetric epoxidation reagent with D-(−)-DIPT as the chiral ligand, gave the chiral building block the dihydropyridone **5**. Reduction of the α,β-unsaturated ketone **6a** with sodium boranuide gave the 3β-OH product **7**. Dihydroxylation of **9a**, with Sharpless AD reagent using DHQ-CLB as the chiral ligand, provided the 1,2-glycols **10a** and **10b** in ratio of 10:1. Detosylation of the triol **11** afforded the amino alcohol, which underwent intramolecular cyclization by treatment with CCl_4–PPh_3–Et_3N giving (−)-8-benzyloxy-swainsonine **12**. Compound **12** was converted into the acetonide **13**, which underwent subsequent formal deprotections to afford (−)-swainsonine **1**.

Polyhydroxylated indolizidine alkaloids, typified by swainsonine **1**,[1] castanospermine **2**,[2] lentiginosine **3**[3] and their derivatives are of considerable importance due to their potent activities as inhibitors of glycosidase and glycoprotein processing (Fig. 1).[4] These compounds have also exhibited interesting anticancer, antiviral, antiretroviral and immunoregulatory activity.[5] Consequently, much attention has been devoted to the synthesis of (−)-swainsonine **1**, a naturally occurring trihydroxyindolizidine first isolated from the fungus *Rhizoctonia leguminicola*[6] and later found in the plants *Swainsona canescens*[1b] and *Astraagalus lentiginosus*[1c] and also in the fungus *Metarhizium anisopliae*.[5c,6–18] Whilst most of the previous methodologies utilized carbohydrates as starting material,[6–13] others used *R*-glutamic acid,[14] D-tartaric acid,[15] D-malic acid[16] and D-isoascorbic acid[17] as the chiral precursors. However, to the best of our knowledge, only one approach to the target compound **1** has been reported,[18] starting from a racemic allylic alcohol derivative instead of the above mentioned chiral pool.

Notwithstanding this plethora of methods, interest in the synthesis of swainsonine **1** and its analogues remains undiminished. Development of general methods which could have flexibility for the construction of these compounds and analogues continues to be important to probe structure–activity relationships. We have previously developed an efficient method for the kinetic resolution of α-furfuryl amide by using the modified Sharpless asymmetric epoxidation reagent[19] (Scheme 1). This reaction afforded two versatile chiral building blocks, both of them are very suitable to be used for elaboration of the skeleton of many types of alkaloids.[20]

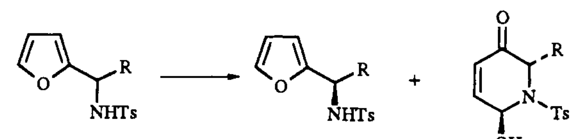
As part of a program designed to develop a new general strategy for the enantioselective synthesis of biologically active alkaloids and explore the use of the reaction in alkaloid synthesis, we undertook a synthesis of (−)-swainsonine **1**, utilizing the α-furfuryl amide **4** as starting material.

Our synthetic strategy is illustrated in Scheme 2 in which an optically active dihydropyridone **5**, as key intermediate, was prepared from α-furfuryl amide **4** by the earlier mentioned kinetic resolution. Stereoselective reduction of **6a** followed by benzylation gave the 3β-benzyloxy product **8**. The Sharpless



1 **2** **3**

Fig. 1



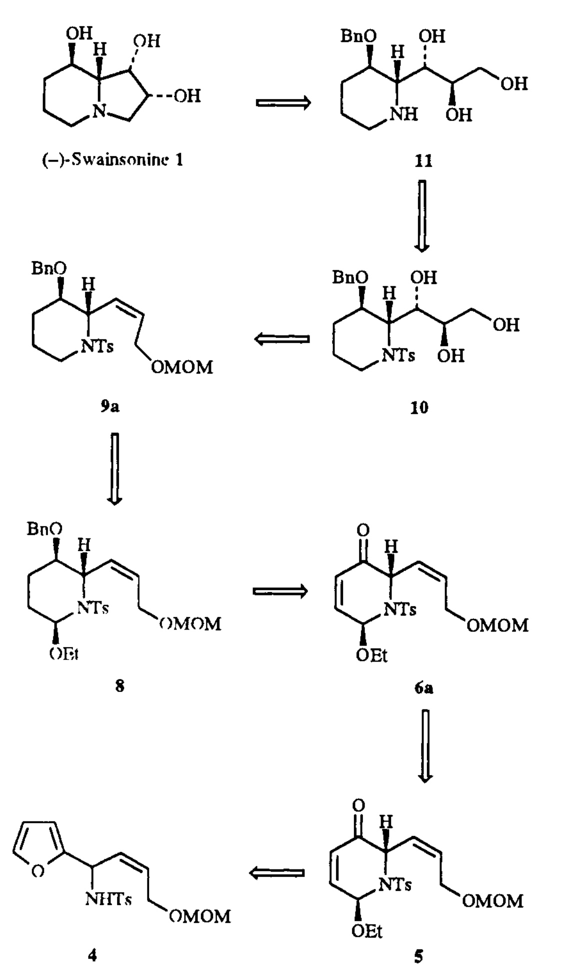
4 ***(R)*-4** **(2*S*, 6*S*)-5**

Scheme 1

asymmetric dihydroxylation (AD) of **9a** yielded the 1,2-glycol **10**. An intramolecular cyclization of the detosylated compound **11** would lead to (−)-swainsonine **1**.

The synthesis of (−)-swainsonine **1** is illustrated in Scheme 3. Kinetic resolution of the α-furfuryl amide **4** by the reported procedure[19] using D-(−)-DIPT as chiral ligand yielded (*R*)-**4** (46%) and the (2*S*,6*S*)-dihydropyridinone **5** (42%). The stereochemistry of **5** was assigned by a 2D-NOESY spectrum, in which no NOE correlation was found between 2-H and 6-H (Fig. 2). Preliminary attempts to reach **9** in two steps by directly exposing **5** to a solution of sodium boranuide in formic acid[21] followed by benzylation of the resulting alcohol was unsuccessful, the reduction of **5** giving a complex mixture. Therefore, we circumvented this problem by first treatment of **5** with triethyl orthoformate in anhydrous Et_2O in the presence of a catalytic amount of $BF_3{\cdot}Et_2O$[22] to give a separable mixture of **6a** (92%) and the deprotected product **6b** (5%). Next, reduction of **6a** with sodium boranuide in methanol at −40 to −30 °C[23] afforded solely the alcohol **7** (88%), with the desired sense of stereochemistry as shown in **7**. In the 2D-NOESY spectrum of **7**, no NOE between 2-H and 3-H was found; the value of $J_{2,3}$ 11.5 Hz also indicates the *trans*-configuration of the protons at position 2 and 3 (Fig. 3). Subsequent benzylation of the alcohol **7**[24] followed by reduction with a solution of sodium boranuide in formic acid at −5 to 0 °C[21] furnished a separable mixture of **9a** (80%) and the MOM deprotected product **9b** (10%).

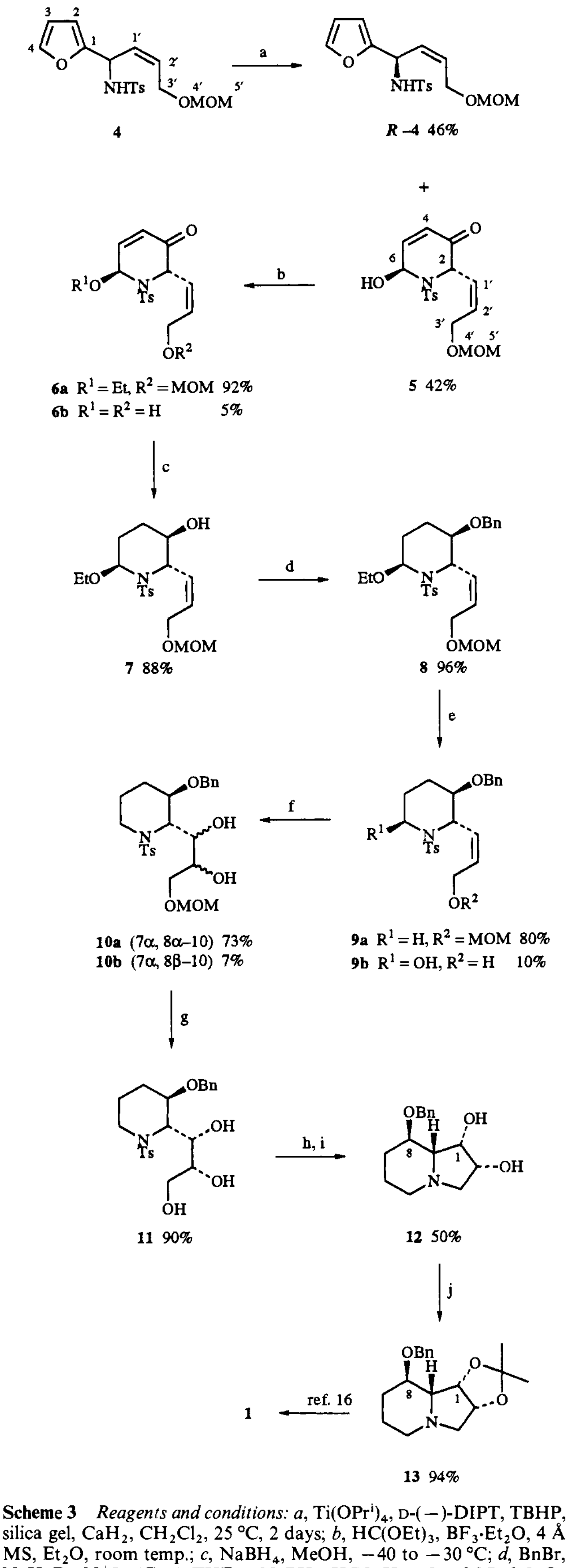
† Preliminary communication, W. S. Zhou, W. G. Xie, Z. H. Lu and X. F. Pan, *Tetrahedron Lett.*, 1995, **36**, 1291.
D-(−)-DIPT = D-(−)-Diisopropyl tartrate.
DHQ-CLB = Dihydroquinine-4-chlorobenzoate.



Scheme 2

Having the pivotal intermediate **9a** in hand, we next tried to convert **9a** into the desired diol **10a**. Thus, the Sharpless asymmetric dihydroxylation reagent (DHQ-CLB as chiral ligand) was tried out on **9**;[25] no reaction, however, occurred. Fortunately, we eventually found that the reaction when performed in an ultrasonic cleaner, proceeded smoothly to form a separable mixture of the desired diol **10a** and its epimer **10b** in a ratio of 10:1, respectively, in 80% combined yield. The stereochemical assignments for these products were based on the Sharpless empirical rule, the major isomer **10a** being judged to have the desired 7*S*,8*R* configuration. Further confirmation of this assignment was provided by transformation of **10a** to a known compound, *vide infra*. In contrast, the use of DHQD-CLB as chiral ligand resulted in the reverse and somewhat lower diastereoselectivity (**10a**:**10b** 1:4). The inherent diastereoselectivity of the olefin **9a** without chiral ligand was 2.5:1 in favour of **10a** as observed from dihydroxylation with OsO_4–NMO.

Removal of the MOM group in **10a** by treatment with *p*-TsOH[26] gave the triol **11** (90%). Deprotection of **11** by treatment with sodium naphthalide[27] and then, without purification, direct treatment of the so-formed crude product with PPh_3, CCl_4 and Et_3N in DMF[28] gave intramolecular cyclization to afford 8-benzyloxy-swainsonine **12** in 50% overall yield from **11**. Attempts to obtain swainsonine **1** by debenzylation of **11** were unsuccessful, mainly because of problems of isolation. To complete the formal synthesis of the target molecule, the diol **12** was converted into the known acetonide **13**[29] (90%) by treatment with dimethoxypropane in the presence of a catalytic amount of *p*-TsOH {$[\alpha]_D^{20}$ −64.2 (*c* 0.5, $CHCl_3$), lit.,[16] $[\alpha]_D^{26}$ −58.9 (*c* 0.27, $CHCl_3$)}; this



Scheme 3 *Reagents and conditions: a*, $Ti(OPr^i)_4$, D-(−)-DIPT, TBHP, silica gel, CaH_2, CH_2Cl_2, 25 °C, 2 days; *b*, $HC(OEt)_3$, BF_3·Et_2O, 4 Å MS, Et_2O, room temp.; *c*, $NaBH_4$, MeOH, −40 to −30 °C; *d*, BnBr, NaH, $Bu_4N^+I^-$ (Cat.), THF; *e*, $NaBH_4$, HCO_2H, −5 to 0 °C; *f*, OsO_4 (Cat.), NMO, DHQ-CLB, trace $MeSO_2NH_2$, acetone-H_2O, ultrasonication; *g*, *p*-TsOH, Bu^tOH, reflux; *h*, Na/naphthalene, DME, −60 °C; *i*, Ph_3P, CCl_4, Et_3N, DMF; *j*, $MeC(OMe)_2Me$, *p*-TsOH, CH_2Cl_2

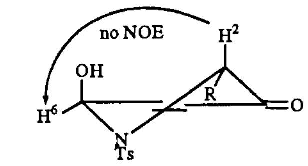


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Fig. 2

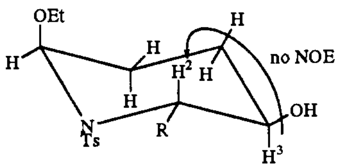

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Fig. 3

compound would then deliver **1** by sequential hydrogenolysis using Pd–C in ethanol and acidic hydrolysis, according to the results of Kibayashi.[16]

In conclusion, we have developed an efficient procedure for preparing the polyhydroxylated indolizidine alkaloid, swainsonine, by employing the kinetic resolution of α-furfuryl amide **4** and Sharpless asymmetric dihydroxylation in an overall yield of 19% from **5** to **13** in eight steps. The synthesis of the other structure-related polyhydroxylated indolizidine alkaloid, castanospermine **2** is currently under investigation.

Experimental

All solvents were distilled prior to use. THF and DME were dried over sodium–benzophenone and freshly distilled before use. Melting points were determined with a Buchi 535 melting point apparatus and are uncorrected. Optical rotations, $[\alpha]_D$, were measured on a digital polarimeter in a 1 dm cell and are recorded in units of 10^{-1} deg cm^2 g^{-1}. IR spectra were recorded on a FTIR instrument. ^{1}H and ^{13}C NMR spectra were determined on a Bruker-AMX-400 spectrometer. Chemical shifts were reported in ppm relative to internal TMS, unless otherwise indicated. Mass spectra were measured on ZAB-HS MS spectrometer. Titanium(IV) isopropyl tartrate (DIPT) was purified by reduced pressure distillation and stored under inert atmosphere. *tert*-Butyl hydroperoxide (TBHP) was obtained from Merk-Schuchardt Co. and was purified before use according to a standard procedure.[30] Calcium hydride was obtained from Fluka Co. The starting racemic α-furfuryl amide **4**, could be readily prepared from the reaction of *N*-furfuryltoluene-*p*-sulfonylimine[31] with 3-methoxymethoxy prop-2-ynyllithium at −70 °C followed by catalytic hydrogenation with P-2Ni.[32] Reaction of *N*-furfuryltoluene-*p*-sulfonylimine with 3-methoxymethoxy prop-2-ynyllithium at −70 °C in freshly distilled THF gave crystalline *N*-[1-(2-furyl)-4-methoxymethoxybut-2-ynyl]toluene-*p*-sulfonamide (80%), selective catalytic hydrogenation of which on P-2Ni in ethanol gave mainly the *cis*-olefin product **4** (95%), which was identified by the value (*J* 7.4 Hz) between the two protons on the side-chain double bond.

N-[1-(1-Furyl)-4-methoxymethoxybut-2-ynyl]toluene-*p*-sulfonamide

To a solution of N-furfuryltoluene-*p*-sulfonylimine (20 g, 80 mmol) in freshly distilled THF (100 cm^3) was slowly added 3-methoxymethoxyprop-2-ynyllithium (1.1 mol dm^{-3}; 80 cm^3) at −70 °C. The reaction mixture was stirred at the same temperature for 1 h, after which it was treated with saturated aq. NH_4Cl (20 cm^3). The resulting mixture was filtered through a pad of silica gel and the filtrate was concentrated to give an oil. This was purified by flash column chromatography on silica gel to afford the crystalline title compound **14** (23 g, 80%), mp 96.0–97.5 °C; ν_{max}(film)/cm^{-1} 3150, 2923, 1606 and 1470; δ_H($CDCl_3$) 7.72, 7.25 (each d, each 2 H, *J* 10.2, aryl), 6.27 (d, 1 H, *J* 3.2, 4-H), 6.22 (t, 1 H, *J* 3.0, 7.4, 3-H), 5.58 (d, 1 H, *J* 14.8, C*H*NHTs), 5.38 (d, 1 H, *J* 2.0, 2-H), 4.52 (d, 2 H, *J* 3.3, OCH_2O), 3.99 (d, 2 H, *J* 1.6, C*H*$_2$OMOM), 3.29 (s, 3 H, OCH_3) and 2.39 (s, 3 H, $PhCH_3$); *m/z* (FABMS) 348 (M^+ − 1) and 332 (M^+ + 1 − H_2O) (Found: C, 58.3; H, 5.3; N, 4.5. Calc. for $C_{17}H_{19}NO_5S$: C, 58.48; H, 5.48; N, 4.58%).

N-[1-(2-Furyl)-4-methoxymethoxybut-2-enyl]toluene-*p*-sulfonamide 4

To a hydrogen-saturated solution of $Ni(OAc)_2$·$4H_2O$ (800 mg, 4.5 mmol) in dry ethanol (20 cm^3) was added dropwise a solution of $NaBH_4$ in ethanol (10 cm^3; containing 120 mg, 3.4 mmol of $NaBH_4$); Et_3N (0.5 cm^3) was then injected into the mixture until no more hydrogen was evolved. A solution of the amide **14** (12.0 g, 5.7 mmol) in ethanol (50 cm^3) was then added to the mixture after which it was stirred for 1 h. When the catalytic hydrogenation was complete (TLC), the resulting mixture was filtered through a pad of silica gel, evaporated and the residue extracted with ethyl acetate. The extract was dried (Na_2SO_4) and worked up and the product purified by flash column chromatography on silica gel to yield (±)-**4** (11.5 g, 95%), mp 80.0–82.0 °C; ν_{max}(film)/cm^{-1} 3262, 2940, 1598, 1440 and 1158; δ_H($CDCl_3$) 7.69, 7.24 (each d, each 2 H, *J* 8.3, aryl), 6.18 (d, 1 H, *J* 3.2, 4-H), 6.06 (d, 1 H, *J* 9.2, C*H*NHTs), 5.64 (m, 2 H, 1′-, 2′-H), 5.31 (t, 1 H, *J* 7.5, 6.4, 3-H), 5.20 (d, 1 H, *J* 7.3, 2-H), 4.56 (d, 2 H, *J* 1.4, OCH_2O), 4.07 (d, 2 H, *J* 2.0, 3′-H), 3.33 (s, 3 H, OCH_3) and 2.39 (s, 3 H, $PhCH_3$); *m/z* (FABMS) 350 (M^+ − 1), 332 (M^+ + 1 − H_2O) and 290 (100) (Found: C, 58.1; H, 6.11; N, 4.44. Calc. for $C_{17}H_{21}NO_5S$: C, 58.14; H, 6.03; N, 4.56%).

Compound (*R*)-4 and (2*S*,6*S*)-6-hydroxy-2-(3-methoxymethoxyprop-1-enyl)-1,2,3,6-tetrahydropyridin-3-one 5

To a solution of $Ti(OiPr)_4$ (1 equiv.) in CH_2Cl_2 was added D-(−)-DIPT (1 equiv.), CaH_2 (1% equiv.) and silica gel (1% equiv.) under N_2 at −10 to 0 °C. After the mixture had been stirred for 10 min, the (±)-amide **4** (2.0 g, 5.7 mmol) in CH_2Cl_2 (5 cm^3) was added to it and stirring was continued for a further 10 min; anhydrous TBHP (2.8 equiv., 8.5 mol dm^{-3}) was then injected into the mixture. After the reaction mixture had been stirred for 3 days at room temperature, 10% aqueous tartaric acid (18 cm^3) was added to it at −20 °C. Vigorous stirring of the mixture was continued at room temperature for 2 h until the aqueous layer became clear. The mixture was then filtered through a pad of Celite and the filtrate concentrated under reduced pressure to give a syrup. This was dissolved in ether (100 cm^3) and treated with $FeSO_4$ (4 equiv.) in water (20 cm^3) for 1 h at 0 °C with vigorous stirring. The organic layer was separated, washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure to give an oil, which was purified by flash column chromatography on silica gel to afford (*R*)-**4** (0.92 g, 46%), mp 78.5–80.0 °C, $[\alpha]_D^{20}$ +7.2 (*c* 1.0, MeOH); other spectrum data were almost identical with those of (±)-**4**. The oxidation product **5** (0.88 g, 42%) had $[\alpha]_D^{20}$ −9.0 (*c* 1.0, MeOH); ν_{max}(film)/cm^{-1} 3310, 2934, 1693, 1342, 1161 and 1044; δ_H($CDCl_3$) 7.71–7.28 (each d, *J* = *J*′ 7.0, each 2 H, aryl), 6.91 (dd, *J* 4.5, 5.8, 1 H, 5-H), 6.02 (m, 2 H, 1′-, 2′-H), 5.82 (d, *J* 9.0, 1 H, 4-H), 5.72 (d, *J* 4.6, 1 H, 6-H), 5.16 (d, *J* 8.5, 1 H, 2-H), 4.69 (d, *J* 2.4, 2 H, OCH_2O), 4.44 (dd, *J* 6.3, 7.5, 1 H, 3′-H), 4.23 (m, 1 H, 3′-H), 3.42 (s, 1 H, OCH_3) and 2.40 (s, 3 H, $PhCH_3$); *m/z* (FABMS) 368 (M^+ + 1) and 350 (M^+ + 1 − H_2O) (Found: C, 55.3; H, 5.9; N, 4.0. Calc. for $C_{17}H_{21}NO_6S$: C, 55.57; H, 5.76; N, 3.81%).

(2*S*,6*S*)-6-Ethoxy-2-[(*Z*)-3′-methoxymethoxyprop-1′-enyl]-1-tosyl-1,2,3,6-tetrahydropyridin-3-one 6a and (2*S*,6*S*)-6-hydroxy-2-[(*Z*)-3′-hydroxyprop-1-enyl]-1-tosyl-1,2,3,6-tetrahydropyridin-3-one 6b

To a stirred solution of compound **5** (1.0 g, 2.7 mmol) in anhydrous ether under nitrogen, dried 4 Å molecular sieves and $(EtO)_3CH$ (1 cm^3) were added. With continued stirring under N_2, catalytic $BF_3{\cdot}Et_2O$ (0.1 cm^3) was then injected into the mixture. After the mixture had been stirred overnight at room temperature, water (5 cm^3) was added to it and the organic layer was separated; the aqueous phase was then extracted with ethyl acetate. The combined organic phase and extract were washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated. Purification of the residue by column chromatography on silica gel gave **6a** as a yellow oil (1.0 g, 92%); $[\alpha]_D^{20}$ −20.3 (*c* 1.0, MeOH); ν_{max}(film)/cm^{-1} 3033, 2932, 1349, 1165 and 1047; $\delta_H(CDCl_3)$ 7.66 (d, *J* 8.3, 2 H, aryl), 7.26 (d, *J* 6.8, 2 H, aryl), 6.82 (dd, *J* 9.5, 5.7, 1 H, 5-H), 5.87 (d, *J* 9.5, 1 H, 4-H), 5.80 (m, 2 H, 1′-, 2′-H), 5.68 (d, *J* 6.7, 1 H, 6-H), 5.13 (d, *J* 7.7, 1 H, 2-H), 4.70 (d, *J* 1.0, 2 H, OCH_2O), 4.41 (dd, *J* 5.7, 8.3, 1 H, 3′-H), 4.26 (dd, *J* 10.2, 5.2, 1 H, 3′-H), 3.98, 3.70 (each m, each 1 H, OCH_2CH_3), 3.43 (s, 3 H), 2.40 (s, 3 H) and 1.25 (t, *J* 7.0, 6.9, 3 H, OCH_2CH_3); $\delta_C(CDCl_3)$ 14.75, 21.40, 55.21, 58.88, 62.84, 78.93, 64.20, 95.68, 126.72, 126.89 (2 C), 126.98, 129.82 (2 C), 131.87, 142.71, 136.18, 144.03 and 191.79; *m/z* (FABMS) 394 (M^+ − 1) and 378 (M^+ − OH) (Found: C, 57.95; H, 6.45; N, 3.8. Calc. for $C_{19}H_{25}NO_6S$: C, 57.70; H, 6.37; N, 3.54%).

The second fraction eluted afforded **6b** (55 mg, 5%), $[\alpha]_D^{20}$ −15.2 (*c*, 1.0, MeOH); ν_{max}(film)/cm^{-1} 3056, 2953, 1700, 1343, 1160 and 1092; $\delta_H(CDCl_3)$ 7.80 (d, *J* 8.3, 2 H, aryl), 7.31 (d, *J* 8.0, 2 H, aryl), 7.04 (dd, *J* 5.38, 4.91, 1 H, 5-H), 6.36 (d, *J* 5.39, 1 H, 4-H), 6.22 (d, *J* 4.88, 1 H, 6-H), 5.57, 5.51 (each m, each 1 H, 1′-, 2′-H), 5.09 (d, *J* 5.92, 1 H, 2-H), 4.33 (d, *J* 12.0, 1 H, 3′-H), 4.22 (dd, *J* 6.0, 12.0, 1 H, 3′-H) and 2.45 (s, 3 H, $PhCH_3$); $\delta_C(CDCl_3)$ 21.43, 61.35, 64.86, 77.44, 126.87, 128.07 (2 C), 129.33 (2 C), 131.79, 132.85, 142.27, 136.50, 143.84 and 188.22; *m/z* (FABMS) 324 (M^+ + 1), 306 (M^+ + 1 − H_2O) and 288 (M^+ + 1 − 2 H_2O) (Found: C, 55.45; H, 5.1; N, 4.7. Calc. for $C_{15}H_{17}NO_5S$: C, 55.71; H, 5.30; N, 4.33%).

(2*S*,3*R*,6*S*)-6-Ethoxy-2-[(*Z*)-3′-methoxymethoxyprop-1′-enyl]-1-tosylpiperidin-3-ol 7

To a cold (−50 to −30 °C) stirred solution of compound **6a** (1.0 g, 2.5 mmol) in MeOH (10 cm^3) was added sodium boranuide (1.5 g, 40 mmol) portionwise. The reaction mixture was stirred at −40 °C for 2 h after which it was diluted with water (5 cm^3) and evaporated under reduced pressure to remove the methanol. The residue was diluted with ethyl acetate (50 cm^3) and neutralized with 5% aqueous HCl. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (2 × 15 cm^3). The combined organic layer and extracts were washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel to give **7** (890 mg, 88%), as a colourless oil, $[\alpha]_D^{20}$ −57.1 (*c* 1.5, MeOH); ν_{max}(film)/cm^{-1} 3029, 2990, 2863, 1500, 1344, 1168 and 960; $\delta_H(CDCl_3)$ 7.60 (d, *J* 8.1, 2 H, aryl), 7.31 (d, *J* 8.1, 2 H, aryl), 6.05 (t, *J* 10.6, 4.9, 1 H, 1′-H), 5.81 (m, 1 H, 2′-H), 4.86 (dd, *J* 4.7, 4.4, 1 H, 2-H), 4.62 (d, *J* 2.0, 2 H, OCH_2O), 4.45 (d, *J* 12, 2, 1 H, 6-H), 4.37 (m, 2 H), 3.62 (m, 1 H, 3-H), 3.39 (s, 3 H, OCH_3), 3.15 (m, 1 H), 2.37 (s, 3 H, $PHCH_3$), 2.35 (d, *J* 3.6, 1 H), 1.92 (m, 1 H), 1.61 (m, 1 H), 1.30 (m, 1 H) and 1.13 (t, 3 H); *m/z* (FABMS) 400 (M^+ + 1), 382 (M^+ + 1 − H_2O) and 354 (100) (Found: C, 56.7; H, 7.1; N, 3.77. Calc. for $C_{19}H_{29}NO_6S$: C, 57.12; H, 7.32; N, 3.51%).

(2*S*,3*R*,6*S*)-3-Benzyloxy-6-ethoxy-2-[(*Z*)-3′-methoxymethoxyprop-1′-enyl]piperidine 8

To a stirred solution of compound **7** (800 mg, 2.0 mmol) in anhydrous THF (20 cm^3) under N_2 were added NaH (53 mg, 1.1 equiv.) in anhydrous THF (5 cm^3) and catalytic Bu_4NI (5 mg) in anhydrous THF (2 cm^3). The mixture was stirred for 20 min after which BnBr (0.3 cm^3, 1.1 equiv.) was injected into it. The mixture was stirred for 1 h after which it was poured into ice-cold water, and extracted with ethyl acetate (3 × 30 cm^3). The combined extracts were washed with brine, dried ($MgSO_4$) and evaporated and the residue was purified by chromatography on silica gel to provide **8** (940 mg, 96%); $[\alpha]_D^{20}$ −53.8 (*c* 1.0, MeOH); ν_{max}(film)/cm^{-1} 3031, 2946, 2881, 1495, 1343, 1164, 1101, 1047 and 668; $\delta_H(CDCl_3)$ 7.58 (d, *J* 8.18, 2 H, aryl), 7.33–7.11 (m, 7 H, aryl), 6.04 (t, *J* 10.6, 11.0, 1 H, 1′-H), 5.83 (m, 1 H, 2′-H), 4.88 (dd, *J* 5.7, 6.0, 1 H, 2-H), 4.71 (s, 2 H, OCH_2O), 4.44 (d, *J* 3.8, 1 H, 6-H), 4.37 (m, 4 H), 3.63 (m, 1 H, 3-H), 3.40 (s, 3 H, OCH_3), 3.02 (m, 1 H), 2.37 (s, 3 H, $PHCH_3$), 2.34 (d, *J* 3.6, 1 H), 1.94 (m, 2 H), 1.59 (m, 1 H), 1.29 (m, 1 H) and 1.14 (t, 3 H, OCH_2CH_3); *m/z* (FABMS) 490 (M^+ + 1) and 334 (100) (Found: C, 63.9; H, 7.1; N, 3.1. Calc. for $C_{26}H_{35}NO_6S$: C, 63.78; H, 7.21; N, 2.86%).

(2*S*,3*R*)-3-Benzyloxy-2-[(*Z*)-3′-methoxymethoxyprop-1′-enyl]-1-tosylpiperidine 9a and (2*S*,3*R*,6*S*)-3-benzyloxy-2-[(*Z*)-3′-hydroxyprop-1′-enyl]-1-tosylpiperidin-6-ol 9b

To a stirred cold (−50 °C) mixture of compound **8** (700 mg, 1.4 mmol) and formic acid was added portionwise sodium boranuide (160 mg, 4.3 mmol), and the resulting mixture was stirred at −50 °C for 0.5 h. Formic acid was removed under reduced pressure from the mixture which was then diluted with water and extracted with ethyl acetate (3 × 20 cm^3). The combined extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$) and evaporated and the residue was purified on silica gel to give **9a** as an oil (510 mg, 80%). The second fraction afforded **9b** (55 mg, 10%). Compound **9a**: $[\alpha]_D^{20}$ −60.1 (*c* 1.0, MeOH); ν_{max}(film)/cm^{-1} 3030, 2942, 2874, 1339 and 1152; $\delta_H[(CD_3)_2CO]$ 7.68 (d, *J* 10.3, 2 H, aryl), 7.31 (m, 7 H, aryl), 5.63 (m, 2 H, 1′-, 2′-H), 5.07 (m, 1 H, 2-H), 4.62 (s, 2 H, CH_2OPh), 4.57 (m, 2 H, OCH_2O), 4.30 (dd, *J* 5.2, 7.1, 1 H, 3′-H), 4.19 (m, 1 H, 3′-H), 3.64 (m, 1 H, 3-H), 3.48 (m, 1 H, 6-H), 3.33 (s, 3 H, OCH_3), 2.90 (m, 1 H, 6-H), 2.40 (s, 3 H, $PhCH_3$), 1.85 (m, 1 H), 1.53 (m, 1 H) and 1.44 (m, 2 H); $\delta_C[(CD_3)_2CO]$ 144.32, 143.53, 139.74, 133.14 (2 C), 130.51, 130.31 (2 C), 129.04, 128.36, 128.30, 128.20 (2 C), 123.54, 96.61, 76.52, 70.76, 64.42, 55.23, 53.17, 41.13, 25.99, 24.51 and 21.34; *m/z* (FABMS) 446 (M + 1) (Found: C, 64.4; H, 6.7; N, 3.45. Calc. for $C_{24}H_{31}NO_5S$: C, 64.69; H, 7.01; N, 3.14%).

Compound **9b**: $[\alpha]_D^{20}$ −56.4 (1.0, MeOH); ν_{max}(film)/cm^{-1} 3029, 2928, 1346, 1162 and 1089; $\delta_H[(CD_3)_2CO]$ 7.16 (d, *J* 8.2, 2 H, aryl), 7.32 (m, 7 H, aryl), 5.95 (m, 1 H, 1′-H), 5.67 (m, 1 H, 2′-H), 5.52 (br, 1 H, 2-H), 4.96 (br, 1 H, 6-H), 4.56 (d, *J* 2.81, 2 H, CH_2OPh), 4.33 (m, 1 H, 3-H), 3.94 (dd, *J* 6.7, 8.6, 1 H, 3′-H), 3.21 (m, 1 H, 3′-H), 2.43 (s, 3 H, $PhCH_3$), 1.79 (m, 2 H), 1.64 (m, 1 H) and 1.28 (m, 1 H); $\delta_C[(CD_3)_2CO]$ 144.40, 144.30, 139.41; 132.64 (2 C), 130.73 (2 C), 129.14, 128.80 (2 C), 128.44, 128.36, 127.34 (2 C), 81.27, 76.16, 70.82, 61.08, 57.77, 30.46, 21.51 and 21.40; *m/z* (FABMS) 418 (M^+ + 1), 400 (M^+ + 1 − H_2O) and 382 (M^+ + 1 − 2 H_2O) (Found: C, 63.8; H, 6.6; N, 3.35. Calc. for $C_{22}H_{27}NO_5S$: C, 63.29; H, 6.52; N, 3.35%).

(2*R*,3*R*,7*S*,8*R*)-3-Benzyloxy-2-(1′,2′-dihydroxy-3′-methoxymethoxypropyl)-1-tosylpiperidine 10a and (2*R*,3*R*,7*R*,8*S*)-3-benzyloxy-2-(1′,2′-dihydroxy-3′-methoxymethoxypropyl)-1-tosylpiperidine 10b

Method A. To a stirred solution of compound **9a** (400 mg, 0.9 mmol) in acetone (9 cm^3) were added DHQ-CLB (5 mg) a catalytic amount of $MeSO_2NH_2$ and OsO_4 (2 mg cm^{-3} in toluene; 1 cm^3). After the mixture had been stirred at room temperature for 0.5 h it was treated dropwise with *N*-methylmorpholine *N*-oxide (NMO) (490 mg, 3.6 mmol) in water (3 cm^3) and placed in an ultrasonic cleaner for 4 h. After this, $NaHSO_3$ (190 mg, 2 equiv.) was added to the mixture and stirring was continued at room temperature for a further 1 h. The mixture was then concentrated and extracted with ethyl acetate–butanol (2:1). The combined extracts were washed with 1% aqueous HCl and brine, dried (Na_2SO_4) and evaporated under reduced pressure. Purification of the residue by chromatography on silica gel provided a 10:1 mixture of the diol **10a** (310 mg, 73%) and **10b** (30 mg, 7%). In a manner similar to that described above, reactions with either DHQD-CLB as the chiral ligand or without any ligand yielded **10a** and **10b** in a ratio of 1:4 and 2.5:1 respectively. Compound **10a** formed colourless crystals, mp 140–142 °C; $[\alpha]_D^{20}$ −70.5 (*c* 1.0, MeOH); ν_{max}(film)/cm^{-1} 3352, 3245, 2924, 1324 and 1152; δ_H($CDCl_3$) 7.58 (d, *J* 8.1, 2 H, aryl), 7.35 (m, 5 H, aryl), 7.16 (d, *J* 8.1, 2 H, aryl), 4.69 (s, 2 H, OCH_2Ph), 4.51 (d, *J* 2.1, 2 H, OCH_2O), 4.28 (m, 2 H, 3′-H), 4.02, 3.78 (each 1 H for OH), 3.92 (m, 2 H, 1′-, 2′-H), 3.85 (m, 1 H, 3-H), 3.59 (m, 1 H, 2-H), 3.39 (s, 3 H, OCH_3), 3.08 (m, 2 H, 6-H), 2.39 (s, 3 H, $PhCH_3$), 2.04 (m, 1 H), 1.69 (m, 1 H), 1.51 (d, *J* 12.2, 1 H) and 1.06 (m, 1 H); δ_C($CDCl_3$) 143.37, 143.30, 139.8, 129.86 (2 C), 128.46 (2 C), 127.80, 127.50 (2 C), 126.65 (2 C), 97.01, 73.41 (2 C), 70.58, 70.47, 68.54, 55.61, 53.80, 43.29, 26.01, 22.85 and 21.49; *m/z* (FABMS) 480 (M + 1) and 344 (100) (Found: C, 60.3; H, 7.2; N, 2.9. Calc. for $C_{24}H_{33}NO_7S$: C, 60.1; H, 6.9; N, 2.92%).

Compound **10b**, $[\alpha]_D^{20}$ −33.8 (*c* 0.5, MeOH); δ_H($CDCl_3$) 7.64 (d, *J* 8.28, 2 H, aryl), 7.28 (m, 7 H, aryl), 4.69 (d, *J* 1.0, 2 H, OCH_2Ph), 4.54 (d, *J* 2.0, 2 H, OCH_2O), 4.30 (m, 2 H, 3′-H), 3.99, 3.91 (2 H for OH), 3.96 (m, 2 H, 1′-, 2′-H), 3.74 (m, 1 H, 3-H), 3.45 (m, 1 H, 2-H), 3.41 (s, 3 H, $PhCH_3$), 3.08 (m, 2 H, 6-H), 2.40 (s, 3 H, OCH_3), 1.82 (m, 2 H), 1.57 (m, 1 H) and 1.25 (m, 1 H); *m/z* (FABMS) 480 (M^+ + 1) and 344 (100) (Found: C, 60.2; H, 7.0; N, 2.8. Calc. for $C_{24}H_{33}NO_7S$: C, 60.11; H, 6.94; N, 2.92%).

Method B. To a stirred solution of compound **9a** (20 mg, 0.045 mmol) in acetone (3 cm^3), were added DHQD-CLB (1 mg), a catalytic amount of $MeSO_2NH_2$ and OsO_4 (2 mg cm^{-3} in toluene; 0.2 cm^3). After being stirred at room temperature for 0.5 h the mixture was treated dropwise with aqueous *N*-methylmorpholine *N*-oxide (NMO) (24 mg, 0.1 mmol) in water (1 cm^3) and placed in an ultrasonic cleaner for 4 h. After this, $NaHSO_3$ (9 mg, 2 equiv.) was added to the mixture and stirring was continued at room temperature for a further 1 h. The mixture was then concentrated and extracted with ethyl acetate–butanol (2:1). The combined extracts were washed with 1% aqueous HCl and brine, dried (Na_2SO_4), and evaporated under reduced pressure and the residue purified by chromatography on silica gel to provide a 1:4 mixture of the diol **10a** (3.0 mg, 14%) and **10b** (13.0 mg, 58%). Compound **10a** formed colourless crystals, mp 139–142 °C, $[\alpha]_D^{20}$ −67.3 (*c* 0.3, MeOH); **10b**, $[\alpha]_D^{20}$ −35.0 (*c* 1.3, CH_3OH).

Method C. To a stirred solution of compound **9a** (20 mg, 0.045 mmol) in acetone (3 cm^3), was added a catalytic amount of $MeSO_2NH_2$ and OsO_4 (2 mg cm^{-3} in toluene; 0.2 cm^3). After being stirred at room temperature for 0.5 h, aqueous *N*-methylmorpholine *N*-oxide (NMO) (24 mg, 0.1 mmol) in water (1 cm^3) was added dropwise to the reaction mixture which was then placed in an ultrasonic cleaner for 4 h. After this $NaHSO_3$ (9 mg, 2 equiv.) was added to the mixture and stirring was continued at room temperature for a further 1 h. The mixture was concentrated and extracted with ethyl acetate–butanol (2:1) and the combined extracts were washed with 1% aqueous HCl and brine, dried (Na_2SO_4), and evaporated under reduced pressure. Purification of the residue by chromatography on silica gel provided a 2.5:1 mixture of the diol **10a** (13.0 mg, 58%) and **10b** (5.0 mg, 23%). Compound **10a** formed colourless crystals, mp 142–143 °C; $[\alpha]_D^{20}$ −69.4 (*c* 1.3, MeOH); **10b**, $[\alpha]_D^{20}$ −36.2 (*c* 0.5, MeOH).

(2*R*,3*R*,7*S*,8*R*)-3-Benzyloxy-1-tosyl-2-(1′,2′,3′,-trihydroxypropyl)piperidine 11

To a solution of compound **10a** (80 mg, 0.15 mmol) in Bu^tOH, was added catalytic *p*-TsOH. After the mixture had been stirred under reflux for 2 h it was concentrated by removal of the Bu^tOH under reduced pressure and extracted with BuOH–ethyl acetate (1:1). The combined extracts were washed with aqueous saturated $NaHCO_3$ and brine, dried (Na_2SO_4), and evaporated. Purification of the residue by flash column chromatography on silica gel gave **11** (65 mg, 90%), $[\alpha]_D^{20}$ −79.8 (*c* 0.5, MeOH); δ_H($CDCl_3$) 7.58 (d, *J* 8.3, 2 H, aryl), 7.20 (m, 7 H, aryl), 4.68 (dd, *J* 7.0, 1.0, 1 H, 3-H), 4.50 (s, 2 H, OCH_2Ph), 4.38 (dd, *J* 10.2, 3.7, 2 H, 3′-H), 3.69 (m, 1 H, 2-H), 3.44 (m, 2 H, 1′-, 2′-H), 2.53 (m, 1 H), 2.38 (s, 3 H, $PhCH_3$), 2.30 (m, 1 H), 1.80 (m, 1 H), 1.62 (m, 1 H) and 1.26 (m, 2 H); *m/z* (FABMS) 436 (M + 1) (Found: C, 60.4; H, 6.9; N, 3.5. Calc. for $C_{22}H_{29}NO_6S$: C, 60.67; H, 6.71; N, 3.22%).

(1*S*,2*R*,8*R*,8a*R*)-8-Benzyloxyindolizidine-1,2-diol 12

To a cold (−75 °C) solution of Na naphthalide in DME under N_2, was added **11** (20 mg, 0.05 mmol) in DME (2 cm^3). The mixture was stirred at −75 °C for 1 h and then diluted with water and stirred for a further 30 min. After this, it was extracted with ethyl acetate–BuOH (1:1) and the extract washed with brine, dried and concentrated. Chromatography of the residue on silica gel with light petroleum as eluent gave naphthalene after which BuOH as eluent gave the crude product. Without further purification, the crude product was dissolved in DMF (5 cm^3) and PPh_3 (2 equiv.), CCl_4 and Et_3N were added to the solution. After being stirred at room temperature overnight, the brown reaction mixture was diluted with MeOH (2 cm^3), evaporated under reduced pressure and extracted with ethyl acetate–BuOH (1:1). The extracts were washed with brine, dried (Na_2SO_4) and evaporated. Purification of the residue by chromatography on silica gel afforded the title compound **12** (6 mg, 50%); $[\alpha]_D^{20}$ −79.4 (*c* 1.0, in methanol); δ_H(CD_3OD) 7.35–7.28 (m, 5 H, aryl), 4.69 (s, 2 H, CH_2OPh), 4.32 (m, 1 H, 1-H), 4.29 (m, 1 H, 2-H), 4.04 (m, 1 H, 8-H), 3.94 (m, 1 H, 8a-H), 3.85 (m, 1 H, 3-H), 3.81 (m, 1 H, 3-H), 3.59 (m, 1 H, 5-H), 3.08 (m, 1 H, 5-H), 2.05 (m, 1 H), 1.69 (m, 1 H) and 1.51, 1.05 (each m, each 1 H); *m/z* (FABMS) 264 (M^+ + 1) and 91 (100) (Found: C, 68.0; H, 8.4; N, 5.1. Calc. for $C_{15}H_{21}NO_3$: C, 68.40; H, 8.04; N, 5.34%).

(1*S*,2*R*,8*R*,8a*R*)-8-Benzyloxy-1,2-isopropylidenedioxyindolizidine 13

To a solution of compound **12** (10 mg, 0.04 mmol) in CH_2Cl_2 were added a catalytic quantity of *p*-TsOH and 2,2-dimethoxypropane (0.1 cm^3), and the mixture was stirred for 6 h. After this it was diluted with saturated aqueous $NaHCO_3$ (2 cm^3), and extracted with $CHCl_3$. The combined extracts were washed with brine, dried (Na_2SO_4), concentrated and chromatographed on silica gel to give **13** (11 mg, 94%), $[\alpha]_D^{20}$ − 64.2 (*c* 0.5, $CHCl_3$) {lit.,[16] $[\alpha]_D^{26}$ −58.9 (*c* 0.27, $CHCl_3$)}; δ_H($CDCl_3$) 7.37–7.21 (m, 5 H, aryl), 4.68 (dd, *J* 6.4, 6.3, 1 H, 1-H), 4.61 (s, 2 H, OCH_2Ph), 4.39 (m, 1 H, 2-H), 3.51 (m, 1 H, 8-H), 3.12 (m, 1 H, 8a-H), 2.44 (dd, *J* 3.2, 7.2, 1 H, 3-H), 2.32 (t, *J* 8.3, 10.3, 1 H, 3-H), 2.08 (d br, 1 H, 5-H), 1.94 (m, 1 H, 5-H), 1.68 (m, 2 H, 6-H), 1.53 (s, 4 H, CH_3 and 7-H), 1.35 (s, 3 H, CH_3) and 1.25 (m, 1 H, 7-H); *m/z* (FABMS) 304 (M^+ + 1) and 214 (100) (Found: C, 70.9; H, 8.5; N, 4.8. $C_{18}H_{25}NO_3$: C, 71.26; H, 8.31; N, 4.62%).

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References

1 (*a*) F. P. Guengerich, S. J. Dimari and H. P. Broquist, *J. Am. Chem. Soc.*, 1973, **95**, 2055; (*b*) S. M. Colegate, P. R. Dorling and C. R. Huxtable, *Aust. J. Chem.*, 1979, **32**, 2257; (*c*) R. J. Molyneux and L. F. James, *Science*, 1982, **216**, 190; (*d*) D. Davis, P. Schwaru, T. Hernandez, M. Mitchell, B. Warnock and A. D. Elbein, *Plant. Physiol.*, 1984, **76**, 972; (*e*) N. Yasuda, H. Tsutsumi and T. Takaya, *Chem. Lett.*, 1984, 1201.

2 (*a*) L. D. Hohenschutz, E. A. Bell, P. J. Jewess, D. P. Leworthy, R. J. Pryce, E. Arnold and J. Clardy, *Phytochemistry*, 1981, **20**, 811; (*b*) R. J. Nash, L. E. Fellows, J. V. Dring, C. H. Striton, D. Carter, M. P. Hegarty and E. A. Bell, *Phytochemistry*, 1988, **27**, 1403.

3 (*a*) I. Pastuszak, R. J. Molyneux, L. F. James and A. D. Elbein, *Biochemistry*, 1990, **29**, 1886; (*b*) R. J. Molyneux, *J. Nat. Prod.*, 1990, **53**, 609; (*c*) H. Yoda, H. Kitayama, T. Katagiri and K. Takabe, *Tetrahedron: Asymmetry*, 1993, 4, 1455.

4 For recent reviews, see (*a*) A. D. Elbein and R. J. Molyneux, *Alkaloids: Chemical and Biological Perspectives*, S. W. Pelletier, ed., Wiley, New York, 1987, vol. 5, ch. 1, pp. 1–54; (*b*) A. D. Elbein, *Crit. Rev. Biochem.*, 1984, **16**, 21; (*c*) C. L. Fellows, *Chem. Br.*, 1987, **23**, 842; (*d*) P. Vogel, *Studies in Natural Products Chemistry*, Atta-ur-Rahman, ed., Elsevier, Amsterdam, 1993, vol. 12, p. 275.

5 (*a*) M. J. Humphries, K. Matsumoto, S. L. White and K. Olden, *Cancer Res.*, 1986, **46**, 5215; (*b*) M. J. Humphries, K. Olden, *Pharmacol. and Ther.*, 1989, **44**, 85; (*c*) T. Kino, N. Inamura, K. Nakahara, S. Kiyoto, T. Goto, H. Terano, M. Kohsaka, H. Aoki and H. Imanaka, *J. Antibiot.*, 1985, **38**, 936; (*d*) J. W. Dennis, *Cancer Res.*, 1986, **46**, 5131.

6 (*a*) F. P. Cuengerich, S. J. DiMari and H. P. Broquist, *J. Am. Chem. Soc.*, 1973, **95**, 2055; (*b*) M. J. Schneider, F. S. Ungemach, H. P. Broquist, T. M. Harris, *Tetrahedron*, 1983, **39**, 29.

7 (*a*) M. H. Ali, L. Hough and A. C. Richardson, *J. Chem. Soc., Chem. Commun.*, 1984, 447; (*b*) M. H. Ali, L. Hough and A. C. Richardson, *Carbohydr. Res.*, 1985, **136**, 225.

8 T. Suami, K. I. Tadano and Y. Limura, *Chem. Lett.*, 1984, 513.

9 (*a*) G. W. J. Fleet, M. J. Gough and P. W. Smith, *Tetrahedron Lett.*, 1984, **25**, 1853; (*b*) B. P. Bashyal, G. W. J. Fleet, M. J. Gough and P. W. Smith, *Tetrahedron*, 1987, **43**, 3083.

10 H. Steoi, H. Takeno and M. Hashimoto, *J. Org. Chem.*, 1985, **50**, 3948.

11 R. B. Bennett III, J. R. Choi, W. Montgomery and J. K. Cha, *J. Am. Chem. Soc.*, 1989, **111**, 2580.

12 W. H. Pearson and K. C. Lin, *Tetrahedron Lett.*, 1990, **31**, 7571.

13 S. A. Miller and A. R. Chamberlin, *J. Am. Chem. Soc.*, 1990, **112**, 8100.

14 (*a*) N. Ikota and A. Hanaki, *Chem. Pharm. Bull.*, 1987, **35**, 2140; (*b*) N. Ikata, A. Hanaki, *Chem. Pharm. Bull.*, 1990, **38**, 2712.

15 J. M. Dener, D. J. Hart and S. Ramesh, *J. Org. Chem.*, 1988, **53**, 6022.

16 M. Naruse, S. Aoyagi and C. Kibayashi, *J. Org. Chem.*, 1994, **59**, 1358.

17 M. P. Heitz and L. E. Overman, *J. Org. Chem.*, 1989, **54**, 2591.

18 C. E. Adams, F. J. Walker and K. B. Sharpless, *J. Org. Chem.*, 1985, **50**, 420.

19 (*a*) W. S. Zhou, Z. H. Lu and Z. M. Wang, *Tetrahedron Lett.*, 1991, **32**, 1467; (*b*) W. S. Zhou, Z. H. Lu and Z. M. Wang, *Tetrahedron*, 1993, **49**, 2641.

20 (*a*) Z. H. Lu and W. S. Zhou, *J. Chem. Soc., Perkin Trans. 1*, 1993, 593; (*b*) Z. H. Lu and W. S. Zhou, *Tetrahedron*, 1993, **49**, 4659.

21 Y. Shishido and C. Kibayashi, *J. Org. Chem.*, 1992, **57**, 2876.

22 J. E. McMurry, V. Farina, W. J. Scott, A. H. Davidson, D. R. Summers and A. Shenvi, *J. Org. Chem.*, 1984, **49**, 3803.

23 J. H. Schauble, G. J. Walter and J. G. Morin, *J. Org. Chem.*, 1974, **39**, 755.

24 S. Czernechi, C. Georgoulis and C. Provelenghiou, *Tetrahedron Lett.*, 1976, 3535.

25 (*a*) L. Wang and K. B. Sharpless, *J. Am. Chem. Soc.*, 1992, **114**, 7568; (*b*) E. N. Jecobsen, I. Marco, W. S. Mungal, G. Schroder and K. B. Sharpless, *J. Am. Chem. Soc.*, 1988, **110**, 1968; (*c*) V. S. Martin, S. S. Woodard, T. Katastuki, Y. Yamada, M. Ikeda and K. B. Sharpless, *J. Am. Chem. Soc.*, 1981, **103**, 6237.

26 H. Monti, G. Leandri, M. Klos-Ringnet and C. Corriol, *Synth. Commun.*, 1983, **13**, 1021.

27 S. Ji, L. B. Gortler, A. Waring, A. Battisti, S. Bank and W. D. Closson, *J. Am. Chem. Soc.*, 1967, **89**, 5311.

28 G. Rassu, G. Casiraghi, L. Pinna, P. Spanu and F. Ulgheri, *Tetrahedron*, 1993, **49**, 6627.

29 M. E. Evans, F. W. Parrish and L. Long, *J. Carbohydr. Res.*, 1967, **3**, 453.

30 T. Shono, Y. Matsumura, K. Tsubata and K. Uchida, *J. Org. Chem.*, 1986, **51**, 2590.

31 R. Albercht, G. Kresez and B. Makar, *Chem. Ber.*, 1964, **97**, 483.

32 S. C. Jain, W. L. Roelofs and J. Meinwald, *J. Org. Chem.*, 1983, **48**, 2274.

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