Synthetic Approaches to the Alkaloids of the Ancistrocladaceae. Part 3.[1] The Total Synthesis of (−)-Ancistrocladinine: Control of the Diastereoisomer Excess in the Synthesis of Axially Chiral Biaryls[2]

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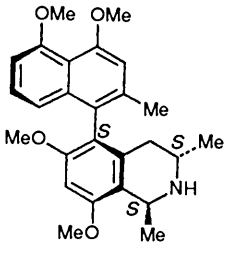
The total synthesis of the naphthylisoquinoline alkaloid (−)-ancistrocladinine [(−)-(*S*,3*S*)-6-hydroxy-5-(4,5-dimethoxy-2-methyl-1-naphthyl)-8-methoxy-3,4-dihydro-1,3-dimethylisoquinoline] is described. The key step was the construction of the disymmetric biaryl linkage by a coupling between the Grignard reagent derived from 2-(3-benzyloxy-2-bromo-5-methoxyphenyl)-1,3-dioxane and (+)-(4*S*,5*S*)-4-methoxymethyl-5-phenyl-2-(1,4,5-trimethoxy-2-naphthyl)-4,5-dihydroxazole. The reactions between the last-mentioned compound and a variety of 2,6-disubstituted phenyl Grignard reagents have been investigated and an attempt has been made to delineate the factors which control the diastereoisomeric excess.

We have utilized the reaction of an aryl Grignard reagent with a chiral oxazoline to generate chiral aryl naphthalenes in the total synthesis of the *Ancistrocladus* alkaloids such as *O*-methylancistrocladine **1**.[1] The versatility of this methodology is now demonstrated by the first total synthesis of the phenolic 3,4-dihydroisoquinoline alkaloid (−)-ancistrocladinine **2**, a minor constituent of *Ancistrocladus heyneanus* Wall.[3]



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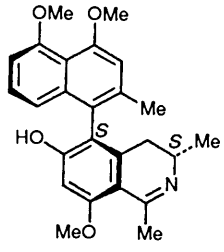

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A methodology for the synthesis of the naphthyl-isoquinoline alkaloids developed by German workers[4] relies on the construction of the biaryl linkage by an intramolecular radical coupling reaction. However, some of the naphthyl-isoquinoline alkaloids are 1,2- or 3,4-dihydroisoquinolines and the above methodology has limitations since the oxidation of tetrahydroisoquinoline alkaloids to the dihydroisoquinolines has proved troublesome.[5]

By use of a chiral oxazoline in the biaryl synthesis previously described,[1] we have secured a significant diastereoisomeric excess of one atropisomer. The required bromo compound **7** was synthesized from the known aldehyde **5**[6] in a sequence outlined in Scheme 1. The acetate **3**[7] was allowed to react with *N*-bromosuccinimide (NBS) in boiling carbon tetrachloride containing a trace of benzoyl peroxide to provide the tribromide **4**. Hydrolysis of this compound gave the hydroxy aldehyde **5** which on benzylation provided the aldehyde **6**. Acetalization then gave the bromo compound **7**.

When the Grignard reagent generated from the bromo compound **7** was allowed to react with the chiral oxazoline **8**[1] a readily separable mixture of the biaryls **9** (49%) and **11** (15%) was obtained as well as the demethylated oxazoline **13**[1] (22%) (Scheme 2). The tentative assignment of the absolute configurations of the diastereoisomers **9** and **11** was based on the comparison between the chemical shifts of the 3′- and 5-protons in their ^{1}H NMR spectra with those of the methyl analogues **10** and **12**,[1] the absolute configuration of which had already been determined.

Quaternization of the oxazoline **9** followed by hydrolysis with potassium hydroxide in aqueous dimethyl sulphoxide and subsequent methylation gave the ester **14** (Scheme 2). Reduction with lithium aluminium hydride then gave the alcohol **15** which was mesylated, reduced and hydrolysed to give the aldehyde **16**. Henry reaction of this compound with nitroethane then yielded the nitrostyrene **17**.

Reduction of the nitrostyrene **17** with lithium aluminium hydride followed by chromatographic resolution[1,8] of the diastereoisomeric mixture of amines gave the butanamides **18** and **19**, the configurations of which were assigned by use of Helmchen's analysis.[9] Acidic hydrolysis of the hydroxy amide **19** followed by acetylation gave the amide **20** which on catalytic hydrogenolysis gave the phenol **21**.

Attempted Bischler–Napieralski ring closure of the phenolic amide **21** did not give the desired product but rather an intractable gum. However, acetylation of the free phenol and ring closure of the resultant acetate **22** with phosphorus oxychloride smoothly gave the dihydroisoquinoline **26**. Base hydrolysis then provided (−)-ancistrocladinine **2** which was further characterized as the diacetate **28**, the physical properties of which were in accordance with those recorded in the literature.[3] In the ^{1}H NMR spectrum of the diacetate **28** the vinylic protons resonate as singlets at δ 5.33 and 6.20. Since naturally occurring (−)-ancistrocladinine **2** has been converted into (−)-ancistrocladine this synthesis also constitutes a formal total synthesis of this alkaloid.[10]

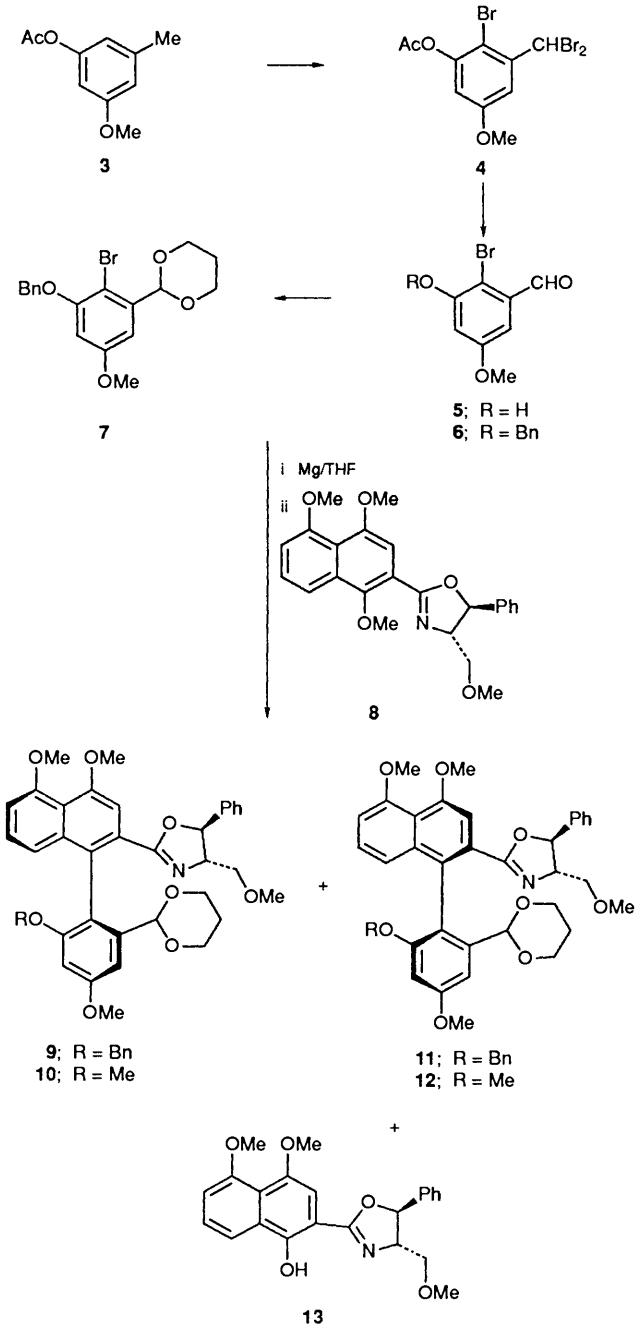
Hydrolysis and acetylation of the butanamide **18** gave the amide **23** which was deprotected to give the phenol **24**. Acetylation of this phenol followed by ring closure and hydrolysis provided 3-*epi*-ancistrocladinine **27** which was also characterized as the derived diacetate **29**.

The factors that govern the diastereoisomeric ratios of the products of the reaction of an aryl Grignard reagent with a chiral oxazoline are poorly understood.[11] This fact prompted an investigation into the reactions of the chiral oxazoline **8** with a variety of related 2,6-disubstituted phenyl Grignard reagents. The acetals **30** and **31** were synthesized from 2-bromo-3,5-dimethoxybenzaldehyde[12] and ethylene glycol or 2,2-dimethylpropane-1,3-diol[13] respectively. The acetal **32** was prepared in a similar fashion from the aldehyde **6** and 2,2-dimethylpropane-1,3-diol.

A solution of each bromide **30**, **31** and **32** in tetrahydrofuran (THF) was converted into its Grignard reagent (2 mol equiv.)

Table 1 Reaction of the oxazoline **8** with Grignard reagents

Products	Yield (%)	Yield (%) of **13**	Ratio	D.e. (%)	Reaction time (h)
33:**34**	77	20	42:58	16	4
10:**12**	65	15	69:31	38	5
35:**36**	72	19	70:30	40	6
9:**11**	64	22	77:23	54	20
37:**38**	69	28	88:12	76	20



Scheme 1

and these were added separately to a solution of the oxazoline **8** in THF and then heated under reflux until all the oxazoline had been consumed. The products **33**/**34**, **35**/**36** and **37**/**38** were completely separated by flash chromatography and the yields obtained are quoted in Table 1. The demethylated oxazoline **13** was also isolated from all the reactions performed and the atropisomers that were eluted first were shown to have the *R* configuration about the biaryl linkage.

The absolute configurations of the biaryl compounds **9**, **10**, **11** and **12** have been confirmed by their conversion into naphthyl-isoquinoline alkaloids of known configuration.[1] The biaryls **34** and **37** were each separately converted into the aldehydes **41**[1] and **16** (Schemes 3 and 4), the absolute configurations of which are known.

Quaternization of the oxazoline **34** followed by base hydrolysis and methylation gave the ester **39**. Reduction of this compound provided the alcohol **40** which was mesylated, reduced and hydrolysed to give the aldehyde **41**. In a similar manner the oxazoline **37** was converted into the aldehyde **16**, *via* the ester **42** and the alcohol **43**. The differences in the chemical shifts of the 3′- and 5-protons in the ^{1}H NMR spectra of the compounds belonging to each atropisomeric series appear to be consistent throughout each series (Table 2). These differences were used to assign the absolute configurations of the biaryls **35** and **36**.

The coupling of a Grignard reagent with an aryloxazoline is thought to involve the addition of the Grignard reagent to the oxazoline to produce a magnesium chelated intermediate followed by the elimination of magnesium and its appropriate gegenions yielding the biaryl.[14] Thus, the coupling of the Grignard reagent derived from the bromo compound **30** with the oxazoline **8** could produce the intermediate **44**. Since there is probably some freedom of rotation about the new bond then its rotamer in which the methoxy group and the dioxolanyl residue have exchanged places is also possible. After elimination the first intermediate would yield the 1′-(*S*) atropisomer and the second the 1′-(*R*) atropisomer. It is seen from Table 1 that the predominant product in this case is the 1′-(*S*) atropisomer but the excess is not great. Presumably the steric effect of the two substituents is little different but the dioxolanyl substitutent possesses two oxygen atoms capable of chelation to the magnesium.

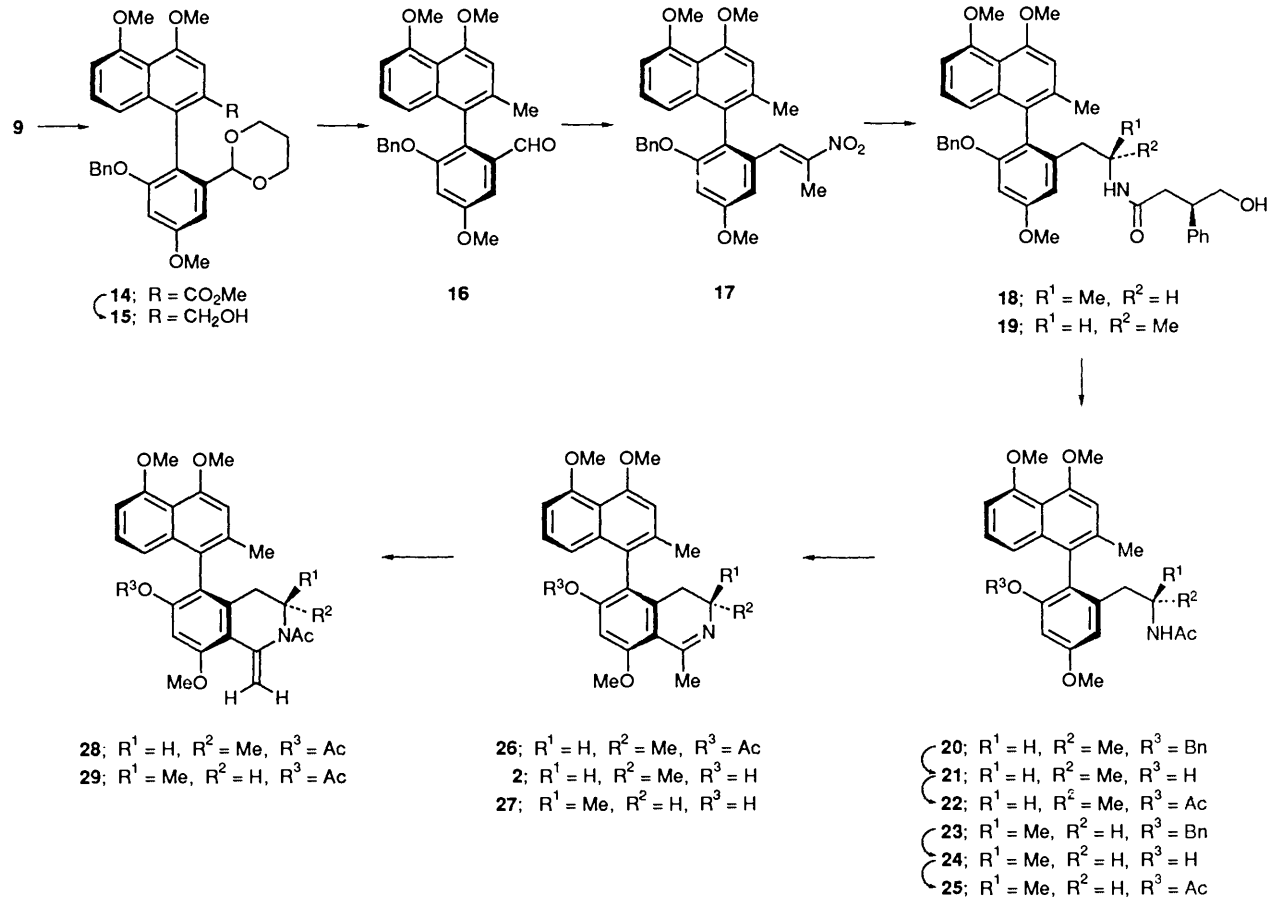
For all of the six-membered acetals it is the 1′-(*R*) atropisomer which predominates and the diastereoisomeric excesses are higher for the dimethyldioxanes than for the unsubstituted dioxanes reflecting their greater bulk. It was also observed that the reactions involving the Grignard reagents with benzyloxy substituents were slower (20 h) than those involving methoxy substituents (4–6 h). Reaction rate, controlled by the bulk of the 2- and 6-substituents therefore appears to influence the diastereoisomeric excess. Warshawsky and Meyers have recently announced similar results.[15]

Experimental

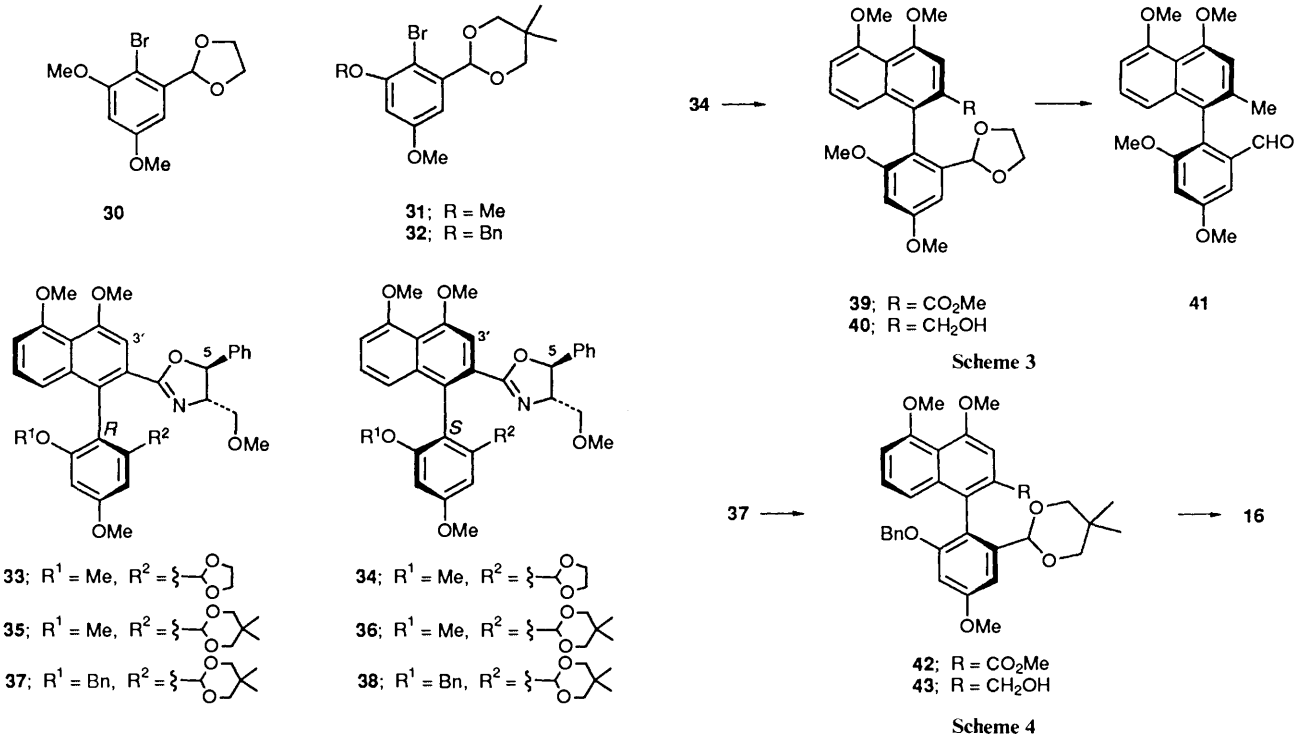
General directions have been given in Parts 1 and 2.[1] *J* Values are given in Hz and $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}.

3-Methoxy-5-methylphenyl Acetate **3**.—This was prepared (93%) by Chattaway's method[16] from 3-methoxy-5-methylphenol,[17] as an oil, b.p. 115 °C at 4 mmHg (lit.,[7] 138–140 °C at 11 mmHg).

2-Bromo-3-dibromomethyl-5-methoxyphenyl Acetate **4**.—A



Scheme 2



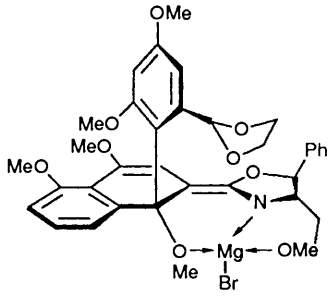
Scheme 3

Scheme 4

solution of the foregoing acetate (27.2 g, 0.15 mol) in carbon tetrachloride (600 cm^3) was heated under reflux with *N*-bromosuccinimide (NBS) (80.8 g, 0.46 mol) and benzoyl peroxide (780 mg) for 72 h. At intervals of 24 and 48 h fresh additions (3.0 g, 0.02 mol) of NBS were made; the course of the reaction can conveniently be followed by ^1H NMR spectroscopy. The cooled suspension was then filtered and the filter cake was washed with a little carbon tetrachloride. The filtrate was washed with water and removal of the solvent left the crude product (63.0 g, 100%) which was used in the next step. In another experiment, a sample crystallized from hexane

Table 2 ^{1}H NMR chemical shifts for biaryls

Compd.	δ 5-H	δ 3′-H	Compd.	δ 5-H	δ 3′-H
33	5.13	7.50	**34**	5.22	7.35
10	5.05	7.52	**12**	5.17	7.35
35	5.06	7.49	**36**	5.16	7.36
9	5.05	7.52	**11**	5.16	7.38
37	5.05	7.49	**38**	5.16	7.40



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as needles of the *tribromide* **4**, m.p. 96–97.5 °C (Found: C, 28.65; H, 2.0; Br, 57.5. $C_{10}H_9Br_3O_3$ requires C, 28.8; H, 2.2; Br, 57.5%); δ_H(80 MHz) 2.36 (3 H, s, MeCO), 3.86 (3 H, s, OMe), 6.69 and 7.48 (2 H, AB, *J* 2.9, ArH) and 7.05 (1 H, s, CH).

2-Bromo-3-hydroxy-5-methoxybenzaldehyde **5**.—The crude bromide **4** (63.0 g, 0.15 mol) was dissolved by warming in ethanol (300 cm^3) and ammonium formate (25.2 g, 0.37 mol) was added. The suspension was heated to boiling and water (100 cm^3) and ethanol (80 cm^3) were added and the whole was stirred and heated under reflux for 24 h. Concentrated hydrochloric acid (8.0 cm^3) was added and the bulk of the ethanol was removed by evaporation under reduced pressure. Water was next added and the crude product (34.9 g, 100%) was separated by filtration and used in the next step. In another experiment, a sample was purified by radical chromatography with 15% ethyl acetate–hexane as eluent and then crystallized from ethyl acetate–hexane whereupon the aldehyde **5** formed yellow laths, m.p. 164–164.5 °C (lit.,[6] 161–162 °C) (Found: C, 41.6; H, 2.9; Br, 34.7%; M$^+$, 232/230. Calc. for $C_8H_7BrO_3$: C, 41.6; H, 3.05; Br, 34.6%; *M*, 232/230); δ_H[80 MHz, $(CD_3)_2CO$] 3.84 (3 H, s, OMe), 6.89 and 6.96 (2 H, AB, *J* 3.0, ArH) and 10.33 (1 H, s, CHO).

3-Benzyloxy-2-bromo-5-methoxybenzaldehyde **6**.—A solution of the crude phenol **5** (34.9 g, 0.15 mol) and benzyl bromide (28.4 g, 0.17 mol) in *N*,*N*-dimethylformamide (DMF) (450 cm^3) was stirred with anhydrous potassium carbonate (22.8 g, 0.18 mol) for 22 h. Work-up gave a crude product which was filtered through a short column of alumina with 5% ethyl acetate–hexane as eluent. The *aldehyde* **6** (31.8 g, 66%) crystallized from hexane as plates, m.p. 93–94 °C (Found: C, 54.4; H, 3.8; Br, 24.95%; M$^+$, 322/320. $C_{15}H_{13}BrO_3$ requires C, 56.1; H, 4.1; Br, 24.9%; *M*, 322/320); δ_H(80 MHz) 3.82 (3 H, s, OMe), 5.16 (2 H, s, CH_2), 6.76 and 7.06 (2 H, AB, *J* 2.8, ArH), 7.32–7.51 (5 H, m, Ph) and 10.42 (1 H, s, CHO).

2-(3-Benzyloxy-2-bromo-5-methoxyphenyl)-1,3-dioxane **7**.—A solution of the aldehyde **6** (12.2 g, 38.0 mmol), propane-1,3-diol (3.48 g, 45.8 mmol) and toluene-*p*-sulphonic acid (200 mg) in benzene (250 cm^3) was heated under reflux in a Dean–Stark apparatus for 16 h. The cooled solution was diluted with ethyl acetate and washed successively with water, sodium hydrogen carbonate and with saturated brine. The *dioxane* **7** (14.4 g, 99%) crystallized from hexane as needles, m.p. 80–81 °C (Found: C, 57.35; H, 5.1; Br, 21.3. $C_{18}H_{19}BrO_4$ requires C, 57.0; H, 5.05; Br, 21.05%); δ_H(80 MHz) 1.31–1.55 (1 H, m, methylene CH), 2.01–2.40 (1 H, m, methylene CH), 3.79 (3 H, s, OMe), 3.84–4.46 (4 H, m, 2 × OCH_2), 5.10 (2 H, s, CH_2Ar), 5.82 (1 H, s, dioxane 2-H), 6.52 and 6.90 (2 H, AB, *J* 2.8, ArH) and 7.28–7.52 (5 H, m, Ph); *m/z* 299 (1%, M$^+$ − Br) and 91 (100).

(+)-(R,4S,5S)-**9** *and* (+)-(S,4S,5S)-*4,5-Dihydro-2-{1-[6-benzyloxy-2-(1,3-dioxan-2-yl)-4-methoxyphenyl]-4,5-dimethoxy-2-naphthyl}-4-methoxymethyl-5-phenyloxazole* **11**.—A solution of the Grignard reagent [from the bromo compound **7** (2.87 g, 7.6 mmol) and magnesium (184 mg)] in anhydrous THF (45 cm^3) was added to a stirred solution of the oxazoline **8** (1.50 g, 3.7 mmol) in THF (30 cm^3) under an atmosphere of argon. The solution was heated under reflux for 20 h, cooled and next poured into saturated aqueous ammonium chloride. Extraction with ethyl acetate gave the crude product which was purified by flash chromatography with 80% ethyl acetate–hexane as eluent. The first band that was eluted, after treatment with acid and further chromatography, yielded the oxazoline **13** (220 mg, 22%). This was followed by the major diastereoisomeric *biaryl* **9** (1.23 g, 49%) which precipitated from isopropyl ether as an amorphous solid; R_F 0.53 (EtOAc); $[\alpha]_D^{20}$ +92.6 (*c* 2.42, THF) (Found: C, 73.05; H, 6.35; N, 1.25. $C_{41}H_{41}NO_8$ requires C, 72.85; H, 6.1; N, 2.05%); δ_H(300 MHz) 1.16 (1 H, br d, *J* 13.5, methylene CH), 1.98–2.11 and 3.26–3.35 (each 1 H, m, methylene CH), 3.37 (3 H, s, OMe), 3.40 (1 H, dd, *J* 9.4, 7.7, CH_AOMe), 3.46–3.55 (1 H, m, methylene CH), 3.66 (1 H, dd, *J* 9.4, 5.2, CH_BOMe), 3.84–3.89 (1 H, m, methylene CH), 3.86, 4.00 and 4.11 (each 3 H, s, OMe), 4.00–4.08 (1 H, m, methylene CH), 4.14 (1 H, ddd, *J* 7.7, 7.1, 5.2, oxazole 4-H), 4.82 (1 H, s, dioxane 2-H), 4.83 (2 H, AB, *J* 13.0, CH_2Ph), 5.05 (1 H, d, *J* 7.7, oxazole 5-H), 6.44 (1 H, d, *J* 2.3, ArH), 6.88 (1 H, dd, $J_{6',7'}$ 7.9, $J_{6',8'}$ 1.6, 6′-H), 6.93 (1 H, d, *J* 2.3, ArH), 7.00–7.20 (11 H, m, ArH), 7.25 (1 H, dd, $J_{7',8'}$ 8.4, $J_{7',6'}$ 7.9, 7′-H) and 7.52 (1 H, s, 3′-H); δ_C 25.48 (CH_2), 55.28, 56.37, 56.51 and 59.01 (each OMe), 67.05 and 69.76 (each CH_2), 73.67 (CH), 74.87 (CH_2), 84.12, 99.89, 100.90, 101.18, 106.03 and 107.60 (each CH), 116.47 (ArC), 120.49 (ArCH), 120.83 (ArC), 125.14 and 125.97 (each ArCH), 126.54 (ArC), 126.59, 126.94, 127.43, 127.00 and 128.23 (each ArCH), 137.15, 137.26, 138.85 and 140.87 (each ArC), 156.25, 156.80, 157.49 and 160.19 (each ArCO) and 165.97 (C=N); λ_{max}/nm 245, 314 and 347 (ε 36 900, 8400 and 4700 respectively); *m/z* 588 (11%), 105 (19), 91 (100) and 87 (92). Further elution supplied the minor diastereoisomeric *biaryl* **11** (370 mg, 15%) which crystallized from ethyl acetate–hexane as prisms, m.p. 175–176 °C; R_F 0.45 (EtOAc); $[\alpha]_D^{20}$ +115.4 (*c* 2.37, THF) (Found: C, 72.8; H, 6.3; N, 1.95. $C_{41}H_{41}NO_8$ requires C, 72.85; H, 6.1; N, 2.05%); δ_H(300 MHz) 1.14 (1 H, br d, *J* 13.2, methylene CH), 1.96–2.09, 3.23–3.32 and 3.48–3.57 (each 1 H, m, methylene CH), 3.37 (3 H, s, OMe), 3.49 (1 H, dd, *J* 9.8, 6.7, CH_AOMe), 3.62 (1 H, dd, *J* 9.8, 5.0, CH_BOMe), 3.80–3.84 (1 H, m, methylene CH), 3.84, 4.02 and 4.10 (each 3 H, s, OMe), 3.99–4.09 (1 H, m, methylene CH), 4.10 (1 H, ddd, *J* 8.2, 6.7, 5.0, oxazole 4-H), 4.86 (3 H, s, dioxane 2-H and CH_2Ph), 5.16 (1 H, d, *J* 8.2, oxazole 5-H), 6.43 (1 H, d, *J* 2.4, ArH), 6.88 (1 H, dd, $J_{6',7'}$ 7.6, $J_{6',8'}$ 1.0, 6′-H), 6.96 (1 H, d, *J* 2.4, ArH), 6.93–7.27 (11 H, m, ArH) and 7.38 (1 H, s, 3′-H); δ_C 25.44 (CH_2), 55.24, 56.31, 56.45 and 59.07 (each OMe), 66.66, 67.03 and 70.02 (each CH_2), 74.19 (CH), 74.47 (CH_2), 84.40, 99.77, 101.15, 101.74, 105.99 and 107.39 (each CH), 118.25 (ArC), 120.47, 125.71, 126.25, 126.57 and 126.94 (each ArCH), 127.13 (ArC), 127.41, 127.86 and 128.06 (each ArCH), 137.05, 137.14, 139.07 and 140.30 (each ArC), 156.26, 156.76, 157.69 and 160.19 (each ArCO) and 165.76 (C=N); λ_{max}/nm 242, 312 and 345 (ε 33 100, 7500 and 4300 respectively); *m/z* 588 (5%), 105 (20), 91 (100) and 87 (94).

(−)-(R)-2-[*3-Benzyloxy-2-(2-hydroxymethyl-4,5-dimethoxy-1-naphthyl)-5-methoxyphenyl*]-1,3-*dioxane* **15**.—A solution of

the oxazoline **9** (1.12 g, 1.6 mmol) and iodomethane (1 cm^3) in anhydrous nitromethane (20 cm^3) was stirred and heated at 60 °C for 22 h. The solvents were removed under reduced pressure and the residue was stirred and heated with potassium hydroxide (1.0 g) in dimethyl sulphoxide–water (10:1, 25 cm^3) at 100 °C (bath) under an argon atmosphere for 24 h. Work-up gave the crude acid (730 mg, 83%) which was stirred in DMF (15 cm^3) with dry potassium carbonate (330 mg) and iodomethane (340 mg) for 2 h at room temperature. Work-up provided the ester **14** (640 mg, 71%). A solution of the above crude ester in anhydrous THF (20 cm^3) was added dropwise to a stirred suspension of lithium aluminium hydride (72 mg) in anhydrous THF (5 cm^3). The mixture was stirred at room temperature for 30 min and then cooled to 0 °C. Saturated aqueous sodium sulphate was added until coagulation occurred and the precipitated salts were filtered off and washed with ethyl acetate. The crude product was purified by radial chromatography with 30% ethyl acetate–hexane as eluent to give the *alcohol* **15** (500 mg, 82%) which precipitated from isopropyl ether as an amorphous solid, R_F 0.14 (40% ethyl acetate–hexane); $[\alpha]_D^{17}$ −55.6 (*c* 0.94, THF) (Found: C, 71.8; H, 6.25. $C_{31}H_{32}O_7$ requires C, 72.1; H, 6.25%); δ_H(300 MHz), 1.19 (1 H, br d, *J* 13.4, methylene CH), 2.01–2.14 (1 H, m, methylene CH), 3.17 (1 H, dd, *J* 8.6, 4.5, D_2O exchangeable CH_2OH), 3.29–3.38 and 3.40–3.49 (each 1 H, m, methylene CH), 3.89, 4.02 and 4.08 (each 3 H, s, OMe), 3.91–3.96 (1 H, m, methylene CH), 4.27 (1 H, dd, *J* 11.8, 8.6, CH_AOH), 4.33 (1 H, dd, *J* 11.8, 4.5, CH_BOH), 4.75 (1 H, s, dioxane 2-H), 4.90 (2 H, AB, *J* 12.7, CH_2Ph), 6.62 (1 H, d, $J_{6,4}$ 2.4, 6-H), 6.85–6.93 (4 H, m, ArH), 7.01 (1 H, d, $J_{4,6}$ 2.4, 4-H), 7.07 (1 H, s, 3′-H), 7.13–7.16 (3 H, m, ArH) and 7.23 (1 H, dd, $J_{7,8}$ 8.8, $J_{7,6}$ 8.4, 7′-H).

(+)-(S)-3-*Benzyloxy*-2-(4,5-*dimethoxy*-2-*methyl*-2-*naphthyl*)-5-*methoxybenzaldehyde* **16**.—(*a*) A solution of methanesulphonyl chloride (91 mg, 0.79 mmol) in dry dichloromethane (2.8 cm^3) was added dropwise to a stirred solution of the alcohol **15** (370 mg, 0.72 mmol) and triethylamine (0.1 cm^3) in dry dichloromethane (5 cm^3) at 0 °C. The solution was stirred at 0 °C for 30 min and work-up gave the crude mesylate (418 mg, 98%) which was dissolved in anhydrous THF (5 cm^3) and added to a stirred suspension of lithium aluminium hydride (100 mg) in anhydrous THF (2 cm^3) at room temperature. The mixture was heated under reflux for 2 h and cooled. An excess of 10% hydrochloric acid was added and the solution was stirred at room temperature for 5 h. Most of the solvent was removed under reduced pressure and the residue was extracted with ethyl acetate. The crude product was subjected to radial chromatography with 20% ethyl acetate–hexane as eluent to give the *aldehyde* **16** (257 mg, 81%) as a light yellow foam; R_F 0.55 (20% ethyl acetate–hexane); $[\alpha]_D^{20}$ +23.2 (*c* 2.57, $CHCl_3$) (Found: C, 76.15; H, 6.1. $C_{28}H_{26}O_5$ requires C, 76.0; H, 5.9%); δ_H(300 MHz) 2.13 (3 H, s, Me), 3.90, 4.00 and 4.03 (each 3 H, s, OMe), 4.96 (2 H, AB, *J* 14.0, CH_2Ph), 6.79–6.82 (3 H, m, ArH), 6.86 (1 H, d, $J_{4,6}$ 2.4, 6-H), 6.93–6.96 (2 H, m, ArH), 7.16–7.24 (5 H, m, ArH) and 9.34 (1 H, s, CHO); *m/z* 442 (34%, M^+), 336 (56), 305 (16), 293 (13) and 91 (100).

(*b*) The alcohol **43** (see below) (307 mg, 0.56 mmol) was mesylated, reduced and hydrolysed in a similar manner as to that described above to give the aldehyde **16** as a light yellow foam (184 mg, 74%); $[\alpha]_D^{18}$ +21.4 (*c* 1.38, $CHCl_3$).

(E)-(−)-(S)-1-[3-*Benzyloxy*-2-(4,5-*dimethoxy*-2-*methyl*-1-*naphthyl*)-5-*methoxyphenyl*]-2-*nitropropane* **17**.—The aldehyde **16** (257 mg, 0.58 mmol), nitroethane (3.0 cm^3), ammonium acetate (50 mg) and acetic acid (0.5 cm^3) were heated at 80 °C (bath) for 2.5 h. The cooled solution was poured into saturated aqueous sodium hydrogen carbonate and the crude product was isolated by extraction with ethyl acetate and purified by radial chromatography with 20% ethyl acetate–hexane as eluent. The *nitrostyrene* **17** (270 mg, 93%) was obtained as a gum; R_F 0.52 (30% ethyl acetate–hexane); $[\alpha]_D^{20}$ −112.0 (*c* 2.46, THF); (Found: C, 72.1; H, 5.85; N, 2.65. $C_{30}H_{29}NO_6$ requires C, 72.15; H, 5.85; N, 2.8%); δ_H(300 MHz) 2.07 (3 H, s, Me), 2.34 (3 H, d, *J* 1.0, CH=C*Me*), 3.86, 3.99 and 4.01 (each 3 H, s, OMe), 4.94 (2 H, AB, *J* 13.6, CH_2Ph), 6.57 and 6.68 (2 H, AB, $J_{4,6}$ 2.3, 4- and 6-H), 6.77–6.80 (3 H, m, ArH), 6.92–6.95 (2 H, m, ArH), 7.21–7.16 (4 H, m, ArH) and 7.37 (1 H, br s, $W_{\frac{1}{2}}$ 3.0, C*H*=CMe); *m/z* 499 (12%, M^+), 393 (20), 347 (30), 316 (40) and 91 (100).

(−)-(S,1R,3S)-**18** *and* (−)-(S,1S,3S)-N-{2-[3-*Benzyloxy*-2-(4,5-*dimethoxy*-2-*methyl*-1-*naphthyl*)-5-*methoxyphenyl*]-1-*methylethyl*}-4-*hydroxy*-3-*phenylbutanamide* **19**.—A solution of the nitrostyrene **17** (406 mg, 0.81 mmol) in anhydrous THF (15 cm^3) was added to a stirred solution of lithium aluminium hydride (100 mg) in THF (5 cm^3) under argon and the mixture was stirred and heated under reflux for 2 h. The mixture was cooled to 0 °C and aqueous sodium hydroxide (30%) was added until coagulation occurred. The precipitated salts were filtered off and washed with hot ethyl acetate. A solution of the crude amines so obtained, 2-hydroxypyridine (158 mg, 1.7 mmol) and (+)-(*S*)-4-phenyl-4,5-dihydrofuran-2(3*H*)-one[1] (270 mg, 1.7 mmol) in anhydrous toluene (10 cm^3) was heated under reflux under an argon atmosphere for 24 h. The solution was next diluted with ethyl acetate and washed in turn with dilute hydrochloric acid and water. Radial chromatography of the crude product with 80% ethyl acetate–hexane as eluent gave the (*S,R,S*)-hydroxy amide **18** as a gum (105.3 mg, 20%); R_F 0.56 (EtOAc); $[\alpha]_D^{20}$ −2.8 (*c* 0.93, THF); δ_H(300 MHz) 0.76 (3 H, d, *J* 6.4, CH*Me*), 2.08–2.14 (2 H, m, methylene CH), 2.10 (3 H, s, ArMe), 2.32 (1 H, dd, *J* 14.6, 8.0, methylene CH), 2.44 (1 H, dd, *J* 14.2, 8.0, methylene CH), 3.08 (1 H, m, CHPh), 3.83, 3.97 and 4.03 (each 3 H, s, OMe), 4.05 (1 H, m, C*H*Me), 4.83 (1 H, br d, *J* 8.0, NHCO), 4.90 (2 H, AB, *J* 13.0, CH_2Ph) 6.51 and 6.56 (2 H, AB, *J* 2.3, ArH), 6.73 (1 H, br d, *J* 7.7, ArH), 6.81 (1 H, s, ArH), 6.84–6.90 (3 H, m, ArH), 6.98–7.05 (2 H, m, ArH) and 7.12–7.24 (7 H, m, ArH); further elution gave the (*S,S,S*)-hydroxy amide **19** (109 mg, 21%) as a gum; R_F 0.46 (EtOAc); $[\alpha]_D^{18}$ −6.0 (*c* 0.78, THF); δ_H(300 MHz) 0.80 (3 H, d, *J* 6.6, CH*Me*), 2.06 (3 H, s, ArMe), 2.08 (1 H, dd, *J* 14.2, 8.0, methylene CH), 2.23 (1 H, dd, *J* 14.2, 5.7, methylene CH), 2.36 (1 H, dd, *J* 14.2, 6.6, methylene CH), 2.44 (1 H, dd, *J* 14.5, 8.2, methylene CH), 3.14 (1 H, m, CHPh), 3.70 (2 H, m, CH_2OH), 3.82, 3.98 and 4.00 (each 3 H, s, OMe), 4.08 (1 H, m, C*H*Me), 4.88 (2 H, AB, *J* 13.0, CH_2Ph), 5.03 (1 H, br d, *J* 7.5, NHCO), 6.48 and 6.52 (2 H, AB, *J* 2.3, ArH), 6.77 (1 H, br d, *J* 7.0, ArH), 6.78 (1 H, s, ArH), 6.89–6.90 (3 H, m, ArH) and 7.08–7.27 (9 H, m, ArH).

(−)-(S,1R)-**23** *and* (−)-(S,1S)-*N*-{2-[3-*Benzyloxy*-2-(4,5-*dimethoxy*-2-*methyl*-1-*naphthyl*)-5-*methoxyphenyl*]-1-*methylethyl*}*acetamide* **20**.—A solution of the hydroxy amide **18** (105.3 mg, 0.17 mmol) in dioxane–1 mol dm^{-3} sulphuric acid (1:1; 5 cm^3) was heated at 90 °C (bath) under argon for 7 h. Water was added and the solution was basified with dilute aqueous sodium hydroxide. Extraction with dichloromethane provided the amine which was treated with pyridine (0.5 cm^3) and acetic anhydride (0.5 cm^3) at room temperature for 2 h. Water was added to the mixture and the product was isolated by extraction with ethyl acetate. The organic layer was washed in turn with dilute hydrochloric acid, saturated aqueous sodium hydrogen carbonate and water. Removal of the solvent provided the crude product which was purified by radial chromatography with 80% ethyl acetate–hexane as eluent to give the amide **23** (67 mg, 68%) as a gum; R_F 0.52 (EtOAc); $[\alpha]_D^{20}$ −4.4 (*c* 0.84, THF); δ_H(300 MHz) 0.92 (3 H, d, *J* 6.4, CH*Me*), 1.69 (3 H, s, NAc), 2.12 (3 H, s,

ArMe), 2.20 (1 H, dd, *J* 14.5, 9.5, CH_A), 2.33 (1 H, dd, *J* 14.5, 5.6, CH_B), 3.83, 4.01 and 4.03 (each 3 H, s, OMe), 4.19 (1 H, m, C*H*Me), 4.87 (1 H, br d, *J* 8.0, NHCO), 4.89 (2 H, AB, *J* 14.3, CH_2Ph), 6.50 and 6.60 (2 H, AB, $J_{4,6}$ 2.3, 4- and 6-H), 6.83 (1 H, s, 3′-H), 6.87–6.90 and 7.12–7.16 (each 3 H, m, ArH) and 7.12 (1 H, dd, $J_{7',8'}$ 8.4 $J_{7',6'}$ 7.8, 7′-H); δ_C 20.79, 21.38 and 23.48 (each Me), 39.07 (CH_2), 46.12 (*C*HMe), 55.36, 56.37 and 56.42 (each OMe), 69.87 (*C*H_2Ph), 99.05, 105.13, 105.18 and 108.97 (each ArCH), 116.20 (ArC), 118.34 (ArCH), 121.62 and 125.32 (each ArC), 126.31, 126.50, 127.25 and 128.18 (each ArCH), 136.01, 136.96, 137.26 and 139.93 (each ArC), 156.09, 157.39, 157.50 and 159.98 (each ArCO) and 169.37 (C=O); *m/z* 513 (8%, M^+), 454 (8) and 348 (19). The hydroxy amide **19** (109 mg, 0.17 mmol) was hydrolysed and acetylated in a similar manner to that described above and purification by radial chromatography with 80% ethyl acetate–hexane as eluent gave the amide **20** (62.6 mg, 71%) as a gum; R_F 0.52 (EtOAc); $[\alpha]_D^{20}$ −27.9 (*c* 0.97, THF); δ_H(300 MHz) 0.84 (3 H, d, *J* 6.4, CH*Me*), 1.70 (3 H, s, NAc), 2.10 (3 H, s, ArMe), 2.18 (1 H, dd, *J* 14.2, 7.4, CH_A), 2.46 (1 H, dd, *J* 14.2, 6.9, CH_B), 3.84, 3.99 and 4.02 (each 3 H, s, OMe), 4.14 (1 H, m, C*H*Me), 4.88 (2 H, AB, *J* 14.0, CH_2Ph), 5.06 (1 H, br d, *J* 8.2, NHCO), 6.50 and 6.60 (2 H, AB, $J_{4,6}$ 2.3, 4- and 6-H), 6.79 (1 H, br d, $J_{6',7'}$ 7.8, 6′-H), 6.80 (1 H, s, 3′-H), 6.86–6.90 (2 H, m, ArH), 6.92 (1 H, dd, $J_{8',7'}$ 8.5, $J_{8',6'}$ 0.9, 8′-H), 7.11–7.16 (3 H, m, ArH) and 7.20 (1 H, dd, $J_{7',8'}$ 8.5, $J_{7',6'}$ 7.8, 7′-H); δ_C 20.57, 20.70 and 23.30 (each Me), 39.16 (CH_2), 45.59 (*C*HMe), 55.29, 56.31 and 56.38 (each OMe), 69.62 (*C*H_2Ph), 96.90, 105.24, 105.72 and 108.75 (each ArCH), 116.10 (ArC), 116.91 (ArCH), 121.68 and 125.49 (each ArC), 126.17, 126.25, 127.16 and 128.10 (each ArCH), 135.39, 136.89, 137.21 and 139.74 (each ArC), 156.00, 157.16, 157.39 and 159.78 (each ArCO) and 169.06 (C=O); *m/z* 513 (10%, M^+), 454 (8) and 348 (14).

(−)-(S,1R)-**24** *and* (−)-(S,1S)-N-{2-[3-*Hydroxy*-2-(4,5-*dimethoxy*-2-*methyl*-1-*naphthyl*)-5-*methoxyphenyl*}-1-*methylethyl*]*acetamide* **21**.—A solution of the acetamide **23** (40.9 mg, 79.7 μmol) in ethyl acetate (4 cm^3), containing concentrated hydrochloric acid (1 small drop), was stirred under a hydrogen atmosphere with palladized charcoal (10%, 5 mg) until absorption ceased. The catalyst was filtered off and the filtrate was washed with saturated aqueous sodium hydrogen carbonate and water. Removal of the solvent gave the crude product which was purified by radial chromatography with 80% ethyl acetate–hexane as eluent to afford the *acetamide* **24** (32.7 mg, 97%) as prisms (from ether–hexane), m.p. 105–107 °C; R_F 0.40 (EtOAc); $[\alpha]_D^{20}$ −35.0 (*c* 0.45, THF) (Found: C, 70.65; H, 7.0; N, 3.05. $C_{25}H_{29}NO_5$ requires C, 70.9; H, 6.9; N, 3.3%); δ_H(300 MHz) 0.91 (3 H, d, *J* 6.4, CH*Me*), 1.73 (3 H, s, NAc), 2.17 (3 H, s, ArMe), 2.14 (1 H, dd, *J* 14.6, 9.1, CH_A), 2.28 (1 H, dd, *J* 14.6, 5.7, CH_B), 3.85, 3.99 and 4.03 (each 3 H, s, OMe), 4.11 (1 H, m, C*H*Me), 4.69 (1 H, s, D_2O exchangeable OH), 4.87 (1 H, br d, *J* 7.6, NHCO), 6.53 and 6.58 (2 H, AB, $J_{4,6}$ 2.5, 4- and 6-H), 6.82 (1 H, br d, $J_{6',7'}$ 7.6, 6′-H), 6.84 (1 H, s, 3′-H), 6.91 (1 H, dd, $J_{8',7'}$ 8.5, $J_{8',6'}$ 0.8, 8′-H) and 7.26 (1 H, dd, $J_{7',8'}$ 8.5, $J_{7',6'}$ 7.0, 7′-H); *m/z* 423 (18%, M^+) and 364 (30). Treatment of the amide **20** (48.5 mg, 94.5 μmol) in an analogous way to that described above gave the *acetamide* **21** (39.4 mg, 98%) as granules (from ether–hexane), m.p. 105–108 °C; $[\alpha]_D^{20}$ −52.7 (*c* 0.42, THF) (Found: C, 70.95; H, 7.0; N, 3.1. $C_{25}H_{29}NO_5$ requires C, 70.9; H, 6.9; N, 3.3%); δ_H(300 MHz) 0.85, (3 H, d, *J* 6.6, CH*Me*), 1.73 (3 H, s, NAc), 2.15 (3 H, s, ArMe), 2.10 (1 H, dd, *J* 14.2, 7.7, CH_A), 2.44 (1 H, dd, *J* 14.2, 6.6, CH_B), 3.85, 3.98 and 4.02 (each 3 H, s, OMe), 4.08 (1 H, m, C*H*Me), 4.61 (1 H, s, D_2O exchangeable OH), 4.97 (1 H, br d, *J* 7.6. NHCO), 6.53 and 6.58 (2 H, AB, $J_{4,6}$ 2.4, 4- and 6-H), 6.82 (1 H, br d, $J_{6',7'}$ 7.2, 6′-H), 6.83 (1 H, s, 3′-H), 6.94 (1 H, dd, $J_{8',7'}$ 8.5, $J_{8',6'}$ 0.8, 8′-H) and 7.27 (1 H, dd, $J_{7',8'}$ 8.5, $J_{7',6'}$ 7.2, 7′-H); *m/z* 423 (32%, M^+) and 364 (48).

(−)-(S,3S)-6-*Hydroxy*-5-(4,5-*dimethoxy*-2-*methyl*-1-*naphthyl*)-8-*methoxy*-3,4-*dihydro*-1,3-*dimethylisoquinoline* [(−)-*Ancistrocladinine*] **2**.—The phenol **21** (48.7 mg, 0.11 mmol) was treated with pyridine (0.5 cm^3) and acetic anhydride (0.5 cm^3) at room temperature for 1.5 h. Work-up as described previously gave the acetate **22** which was subjected to radial chromatography with 80% ethyl acetate–hexane as eluent. A solution of this acetate in anhydrous acetonitrile (2 cm^3) was heated under reflux with freshly distilled phosphoryl chloride (40 mm^3) for 45 min. The solvents were removed under reduced pressure and the residue was dissolved in chloroform (10 cm^3) the solution shaken with saturated aqueous sodium hydrogen carbonate (10%; 10 cm^3) and ether (50 cm^3). Removal of the solvent provided *O*-acetylancistrocladinine **26** (43.6 mg, 89%); δ_H (300 MHz) 1.20 (3 H, d, *J* 6.7, CH*Me*), 1.64 (3 H, s, OAc), 1.95 (1 H, dd, *J* 16.2, 12.3, CH_A), 2.07 (3 H, s, ArMe), 2.14 (1 H, dd, *J* 16.2, 4.9, CH_B), 2.60 (1 H, d, *J* 1.5, N=CMe), 3.84 (1 H, m, C*H*Me), 3.94, 3.99 and 4.01 (each 3 H, s, OMe), 6.76–6.82 (4 H, m, ArH) and 7.23 (1 H, dd, $J_{7',8'}$ 8.2, $J_{7',6'}$ 8.0, 7′-H). A solution of the foregoing acetate in methanol (2 cm^3) was treated with 10% aqueous sodium hydroxide (0.2 cm^3) at room temperature under an argon atmosphere and the solution was stirred for 10 min. Most of the methanol was removed under reduced pressure and water was added to the residue; the pH was then adjusted to 7 with dilute hydrochloric acid. Extraction with chloroform provided synthetic *ancistrocladinine* **2** (35.9 mg, 80%) which crystallized from acetone as needles, m.p. 255–258 °C (deceomp) [lit.,[3] 235–238 °C (decomp.)]; R_F 0.24 (10% methanol–$CHCl_3$); $[\alpha]_D^{20}$ −148.9 (*c* 0.48, pyridine) [lit.,[3] $[\alpha]_D^{25}$ −321.8 (*c* 1.06, pyridine)] (Found: M^+, 405.1940. $^{12}C_{25}{}^1H_{27}{}^{14}N^{16}O_4$ requires *M*, 405.1940); δ_H(300 MHz) 0.80 (3 H, d, *J* 6.0, CH*Me*), 1.75 (1 H, dd, *J* 16.1, 11.0, CH_A), 1.93 (1 H, dd, *J* 16.1, 4.8, CH_B), 2.11 (3 H, s, ArMe), 2.18 (3 H, br s, $W_{\frac{1}{2}}$ 2.5, N=CMe), 2.84 (1 H, m, C*H*Me), 3.76, 3.86 and 3.87 (each 3 H, s, OMe), 6.13 (1 H, s, 7-H), 6.70 (1 H, s, 3′-H), 6.70 (1 H, br d, $J_{6',7'}$ 8.0, 6′-H), 6.99 (1 H, br d, $J_{8',7'}$ 8.5, 8′-H) and 7.19 (1 H, dd, $J_{7',8'}$ 8.5, $J_{7',6'}$ 8.0, 7′-H); λ_{max}/nm 231, 306, 320 and 335 nm (ε 38 700, 7500, 7000 and 7470 respectively); *m/z* 405 (100%, M^+), 406 (27), 404 (30), 390 (22) and 202 (33). Acetylation (acetic anhydride–pyridine, room temperature, 2 h) and purification of the crude product by radial chromatography with 80% ethyl acetate–hexane as eluent gave N,O-*diacetoxyancistrocladinine* **28** (60%) which crystallized from ether as prisms, m.p. 198–200 °C (lit.,[3] 204–206 °C); R_F 0.28 (EtOAc); $[\alpha]_D^{20}$ +72.0 (*c* 0.88, $CHCl_3$) [lit.,[3] $[\alpha]_D$ +88.62 ($CHCl_3$)] (Found: M^+, 489.2150. $^{12}C_{29}{}^1H_{31}{}^{14}N^{16}O_6$ requires *M*, 489.2151); δ_H(300 MHz) 1.09 (3 H, d, 6.7, CH*Me*), 1.66 (3 H, s, OAc), 2.06 (1 H, dd, *J* 17.0, 3.8, CH_A), 2.07 (3 H, s, ArMe), 2.23 (3 H, s, NAc), 2.52 (1 H, dd, *J* 17.0, 6.3; CH_B), 3.96, 3.98, 4.01 (each 3 H, s, OMe), 4.66 (1 H, m, C*H*Me), 5.33 (1 H, s, vinyl-H), 6.20 (1 H, s, vinyl-H), 6.73 (1 H, s, 7-H), 6.75 (1 H, s, 3′-H), 6.76 (1 H, dd, $J_{8',7'}$ 8.4, $J_{8',6'}$ 0.9, 8′-H), 6.78 (1 H, br d, $J_{6',7'}$ 7.8, 6′-H) and 7.20 (1 H, dd, $J_{7',8'}$ 8.4, $J_{7',6'}$ 7.8, 7′-H); *m/z* 489 (94%, M^+), 432 (100), 404 (39), 390 (44) and 202 (58).

(−)-(S,3R)-6-*Hydroxy*-5-(4,5-*dimethoxy*-2-*methyl*-1-*naphthyl*-8-*dimethoxy*-3,4-*dihydro*-1,3-*dimethylisoquinoline* **27**.—The acetamide **24** (32.7 mg, 77.3 μmol) was acetylated, ring closed and hydrolysed in a manner similar to that described above to give the *isoquinoline* **27** (40.7 mg, 94%) which crystallized from acetone as prisms, m.p. 191–195 °C; $[\alpha]_D^{18}$ −100.4 (*c* 0.23, pyridine) (Found: M^+, 405.1940. $^{12}C_{25}{}^1H_{27}{}^{14}N^{16}O_4$ requires *M*, 405.1940); δ_H(300 MHz) 0.70 (3 H, d, *J* 6.0, CH*Me*), 1.60 (1 H, dd, *J* 16.6, 9.6, CH_A), 1.93 (1 H, dd, *J* 16.6, 5.4, CH_B), 2.18 (3 H, s, ArMe), 2.26 (3 H, br s, $W_{\frac{1}{2}}$ 2.5, N=CMe), 2.39 (1 H, m, C*H*Me), 3.78, 3.80 and 3.84 (each 3 H, s, OMe), 6.12 (1 H, s, 7-H), 6.61 (1 H, br d, $J_{6',7'}$ 7.8, 6′-H), 6.73 (1 H, s, 3′-H), 6.94 (1 H, br d, $J_{8',7'}$ 8.0, 8′-H) and 7.07 (1 H, dd,

$J_{7',8'}$ 8.0, $J_{7',6'}$ 7.8, 7′-H); λ_{max}/nm 231, 305, 320 and 335 nm (ε 48 900, 10 200, 9600 and 10 100 respectively); *m/z* 405 (100%, M^+), 406 (28), 404 (30), 390 (25) and 202 (58). Acetylation as before (acetic anhydride–pyridine, room temperature, 2 h) and purification of the crude product by radial chromatography with 80% ethyl acetate–hexane as eluent gave the *diacetate* **29** (60%) which crystallized from ether as prisms, m.p. 188–192 °C; $[\alpha]_D^{19}$ −31.7 (*c* 0.16, $CHCl_3$); (Found: M^+, 489.2150. $^{12}C_{29}{}^{1}H_{31}{}^{14}N^{16}O_6$ requires *M*, 489.2151); δ_H(300 MHz) 1.02 (3 H, d, 6.7, CH*Me*), 1.65 (3 H, s, OAc), 1.96 (1 H, dd, *J* 17.0, *J* 3.8, CH_A), 2.07 (3 H, s, ArMe), 2.21 (3 H, s, NAc), 2.58 (1 H, dd, *J* 17.0, *J* 6.6, CH_B), 3.96, 3.98, 4.01 (each 3 H, s, OMe), 4.72 (1 H, m, C*H*Me), 5.32 (1 H, s, vinyl-H), 6.21 (1 H, s, vinyl-H), 6.73 (1 H, s, 7-H), 6.75 (1 H, s, 3′-H), 6.75 (1 H, br d, $J_{8',7'}$ 8.2, 8′-H), 6.78 (1 H, br d, $J_{6',7'}$ 8.0, 6′-H) and 7.20 (1 H, dd, $J_{7',8'}$ 8.2, $J_{7',6'}$ 8.0, 7′-H).

2-(2-*Bromo*-3,5-*dimethoxyphenyl*)-1,3-*dioxolane* **30**.—This compound was prepared from 2-bromo-3,5-dimethoxybenzaldehyde[12] (2.0 g, 8.2 mmol) and ethylene glycol (560 mg, 9.0 mmol). It crystallized from hexane as spars (2.34 g, 99%) of the *dioxolane* **30**, m.p. 84–84.5 °C (Found: C, 46.0; H, 4.6; Br, 27.85%; M^+, 288/290. $C_{11}H_{13}BrO_4$ requires C, 45.7; H, 4.55; Br, 27.65%; *M*, 288/290); δ_H(80 MHz) 3.82 and 3.87 (each 3 H, s, OMe), 4.11 (4 H, d, *J* 2.0, 2 × CH_2), 6.13 (1 H, s, CH) and 6.51 and 6.80 (2 H, AB, *J* 2.8, ArH).

2-(2-*Bromo*-3,5-*dimethoxyphenyl*)-5,5-*dimethyl*-1,3-*dioxane* **31**.—This compound was prepared from 2-bromo-3,5-dimethoxybenzaldehyde[12] (3.5 g, 14.3 mmol) and 2,2-dimethoxypropane-1,3-diol[13] (1.93 g, 18.6 mmol). Crystallization from hexane provided the *dioxane* **31** (4.72 g, 100%) as needles, m.p. 78–79 °C (Found: C, 50.7; H, 5.95; Br, 24.2%; M^+, 332/330. $C_{14}H_{19}BrO_4$ requires C, 50.75; H, 5.8; Br, 24.18%; M, 332/330); δ_H(80 MHz) 0.80 (3 H, s, Me_{ax}), 1.56 (3 H, s, Me_{eq}), 3.73 (4 H, s, 2 × CH_2), 3.83 and 3.85 (each 3 H, s, OMe), 5.71 (1 H, s, CH) and 6.49 and 6.93 (2 H, AB, *J* 2.8, ArH).

2-(3-*Benzyloxy*-2-*bromo*-5-*methoxyphenyl*)-5,5-*dimethyl*-1,3-*dioxane* **32**.—This compound was prepared from the aldehyde **6** (3.5 g, 10.9 mmol) and 2.2-dimethoxypropane-1,3-diol (1.47 g, 14.2 mmol). It crystallized from hexane as needles (4.4 g, 99%) of the *dioxane* **32**, m.p. 91–92 °C (Found: C, 59.4; H, 5.95; Br, 19.4%; M^+. 408/406. $C_{20}H_{23}BrO_4$ requires C, 59.0; H, 5.7; Br, 19.6%; *M*, 408/406); δ_H(80 MHz) 0.80 (3 H, s, Me_{ax}), 1.31 (3 H, s, Me_{eq}), 3.73 (4 H, s, 2 × CH_2), 3.79 (3 H, s, OMe), 5.11 (2 H, s, CH_2Ph), 5.73 (1 H, s, CH), 6.52 and 6.94 (2 H, AB, *J* 2.8, ArH) and 7.31–7.48 (5 H, m, Ph).

(+)-(R,4S,5S)-**33** *and* (+)-(S,4S,5S)-4,5-*Dihydro*-2-{1[2-(1,3-*dioxolan*-2-*yl*)-4,6-*dimethoxyphenyl*]-4,5-*dimethoxy*-2-*naphthyl*}-4-*methoxymethyl*-5-*phenyloxazole* **34**.—A solution of the Grignard reagent [from magnesium (100 mg) and the bromo compound **30** (1.16 g, 3.6 mmol)] in THF (10 cm^3) was added *via* a cannula to a solution of the oxazoline **8** (800 mg, 2.0 mmol) in THF (10 cm^3) under argon and the solution was heated under reflux for 6 h. Work-up as previously described gave the crude product which was purified by flash chromatography with 60% ethyl acetate–hexane as eluent. The first band that was eluted yielded, after acid treatment and further chromatography, the oxazoline **13** (154 mg, 20%). This was followed by the minor diastereoisomeric *biaryl* **33** (377 mg, 32%) which crystallized from ethyl acetate–hexane as plates, m.p. 144–145 °C; R_F 0.32 (70% ethyl acetate–hexane); $[\alpha]_D^{19}$ +134.3 (*c* 0.73, THF); (Found: C, 69.75; H, 6.2; N, 2.15. $C_{34}H_{35}NO_8$ requires C, 69.75; H, 6.0; N, 2.4%); δ_H(300 MHz) 3.39, 3.51, 3.87, 3.98 and 4.07 (each 3 H, s. OMe), 3.43 (1 H, dd, *J* 9.5, 7.8, CH_AOMe), 3.61–3.76 (2 H. m. CH_2), 3.69 (1 H, dd, *J* 9.5, 5.0, CH_BOMe), 3.89–3.96 (2 H, m, CH_2), 4.18 (1 H, ddd, *J* 7.8, 7.0, 5.0, oxazole 4-H), 5.13 (1 H, d, *J* 7.0, oxazole 5-H), 5.15 (1 H, s, dioxolane 2-H), 6.47 and 6.80 (each 1 H, d, *J* 2.3, ArH), 6.90 (1 H, br d, $J_{6',7'}$ 7.3, 6′-H), 6.98 (1 H, dd, $J_{8',7'}$ 8.5, $J_{8',6'}$ 0.8, 8′-H), 7.09–7.12 (2 H, m, ArH), 7.23–7.29 (4 H, m, ArH) and 7.50 (1 H, s, 3′-H); δ_C 55.34, 55.78, 56.41, 56.65 and 59.15 (each OMe), 64.99 and 65.13 (each CH_2), 73.63 (CH), 74.93 (CH_2), 84.16, 99.50, 101.31, 101.41, 106.22 and 107.82 (each CH), 118.66 (ArC), 120.20 (ArCH), 121.58 (ArC), 125.23 (ArCH), 126.52 and 126.69 (each ArC), 126.77, 127.52 and 128.31 (each ArCH), 137.24, 138.09 and 140.94 (each ArC), 156.41, 157.08, 158.72 and 160.29 (each ArCO) and 165.73 (C=N); λ_{max}/nm 246, 304, 311 and 346 (ε 41 000, 10 600, 10 200 and 5700 respectively); *m/z* 585 (1%, M^+), 513 (30) and 512 (100). Further elution supplied the major diastereoisomeric *biaryl* **34** (514 mg, 44%) which crystallized from ethyl acetate–hexane as needles, m.p. 175–176 °C; R_F 0.22 (70% ethyl acetate–hexane); $[\alpha]_D^{20}$ +125.6 (*c* 1.0, THF) (Found: C, 69.75; H, 5.95; N, 2.3. $C_{34}H_{35}NO_8$ requires C, 69.75; H, 6.0; N, 2.4%); δ_H(300 MHz) 3.39, 3.54, 3.86. 3.97 and 4.07 (each 3 H, s, OMe), 3.49 (1 H, dd, *J* 9.8, 7.0, CH_AOMe), 3.56–3.71 (2 H, m, CH_2), 3.65 (1 H, dd, *J* 9.8, 4.6, CH_BOMe), 3.81–3.94 (2 H, m, CH_2), 4.15 (1 H, ddd, *J* 7.9, 7.0, 4.6, oxazole 4-H), 5.16 (1 H, s, dioxolane 2-H), 5.22 (1 H. d, *J* 7.9, oxazole 5-H), 6.46 and 6.83 (each 1 H, d, *J* 2.4, ArH). 6.89 (1 H, br d, $J_{6',7'}$ 7.8, 6′-H), 6.95–6.99 (3 H, m, ArH), 7.20–7.29 (4 H, m, ArH) and 7.35 (1 H, s, 3′-H); δ_C 55.32, 56.09, 56.43, 56.57 and 59.22 (each OMe), 64.98 and 65.19 (each CH_2), 74.17 (CH), 74.69 (CH_2), 84.48, 99.71, 101.33, 101.60, 106.30 and 107.56 (each CH), 118.46 (ArC), 120.04 (ArCH), 121.23 (ArC), 125.71 (ArCH), 126.31 (ArC), 126.79 (ArCH), 127.20 (ArC), 127.51 and 128.19 (each ArCH), 137.11, 138.29 and 140.55 (each ArC), 156.47, 157.04, 159.12 and 160.40 (each ArCO) and 165.69 (C=N); λ_{max}/nm 240, 307 and 340 (ε 41 200, 10 400, 10 200 and 5700 respectively); *m/z* 585 (1%, M^+), 513 (51) and 512 (100).

(+)-(R,4S,5S)-**35** *and* (+)-(S,4S,5S)-4,5-*Dihydro*-2-{1-[4,6-*dimethoxy*-2-(5,5-*dimethyl*-1,3-*dioxan*-2-*yl*)*phenyl*]-4,5-*dimethoxy*-2-*naphthyl*}-4-*methoxymethyl*-5-*phenyloxazole* **36**.—A solution of the Grignard reagent [from magnesium (78 mg) and the bromo compound **31** (1.06 g, 3.6 mmol)] in THF (10 cm^3) was added *via* a cannula to a solution of the oxazoline **8** (660 mg, 1.6 mmol) in THF (10 cm^3) under argon and the solution was heated under reflux for 16 h. Work-up as previously described gave the crude product which was purified by flash chromatography with 50% ethyl acetate–hexane as eluent. The first band that was eluted yielded the oxazoline **13** (120 mg, 21%). This was followed by the major diastereoisomeric *biaryl* **35** (513 mg, 50%) which crystallized from ethyl acetate–hexane as plates, m.p. 136–137 °C; R_F 0.46 (60% ethyl acetate–hexane); $[\alpha]_D^{17}$ +146.8 (*c* 2.02, THF) (Found: C, 70.6; H. 6.3; N, 2.0. $C_{37}H_{41}NO_8$ requires C, 70.8; H, 6.6; N, 2.2%); δ_H(300 MHz) 0.55 (3 H, s, Me_{ax}), 1.22 (3 H, s, Me_{eq}), 2.93 and 3.16 (each 1 H, d, $J_{ax,eq}$ 11.1, dioxane 4- and 6-H_{ax}), 3.36 and 3.50 (each 1 H, dd, $^2J_{eq,ex}$ 11.1, $^4J_{eq,eq}$ 2.6, dioxane 4- and 6-H_{eq}), 3.39 (1 H, dd, *J* 9.4, 8.0, CH_AOMe), 3.65 (1 H, dd, *J* 9.4, 5.1, CH_BOMe), 3.38, 3.52, 3.89, 3.99 and 4.09 (each 3 H, s, OMe), 4.16 (1 H, ddd, *J* 8.0, 7.0, 5.1, oxazole 4-H), 4.62 (1 H, s, dioxane 2-H), 5.06 (1 H, d, *J* 7.0, oxazole 5-H), 6.46 (1 H, d, *J* 2.3, ArH), 6.89 (1 H, br d, $J_{6',7'}$ 7.8, 6′-H), 6.95 (1 H, d, *J* 2.3, ArH), 6.98 (1 H, dd, $J_{8',7'}$ 8.5, $J_{8',6'}$ 0.9, 8′-H), 7.12–7.15 (2 H, m, ArH), 7.21–7.30 (4 H, m, ArH) and 7.49 (1 H, s, 3′-H); δ_C 21.61 and 23.31 (each Me), 30.00 (dioxane C-5), 55.34, 55.76, 56.37, 56.57 and 59.10 (each OMe), 73.61 (CH), 74.92 and 77.41 (each CH_2), 84.09, 99.19, 100.00, 100.94, 106.03 and 107.66 (each CH), 118.50 (ArC), 120.44 (ArCH), 120.48 (ArC), 125.20 (ArCH), 126.57 (ArC), 126.67 (ArCH), 126.87 (ArC), 127.52 and 128.32 (each ArCH), 137.12, 138.68 and 140.96 (each ArC), 156.33, 156.69, 158.67 and 160.43 (each

ArCO) and 165.67 (C=N); *m/z* 627 (2%, M^+), 513 (35), 512 (100), 351 (18) and 350 (21); further elution supplied the minor diastereoisomeric *biaryl* **36** (220 mg, 22%) as a gum; R_F 0.29 (60% ethyl acetate–hexane); $[\alpha]_D^{20}$ +108.4 (*c* 0.60, THF) (Found: C, 70.5; H, 6.25; N, 1.9. $C_{37}H_{41}NO_8$ requires C, 70.8; H, 6.6; N, 2.2%); δ_H(300 MHz) 0.53 (3 H, s, Me_{ax}), 1.19 (3 H, s, Me_{eq}), 2.96 and 3.16 (each 1 H, d, $J_{ax,eq}$ 11.0, dioxane 4- and 6-H_{ax}), 3.37 and 3.46 (each 1 H, dd, $^2J_{eq,ax}$ 11.1, $^4J_{eq,eq}$ 2.6, dioxane 4- and 6-H_{eq}), 3.49 (1 H, dd, *J* 9.8, 6.6, CH_AOMe), 3.61 (1 H, dd, *J* 9.8, 4.9, CH_BOMe), 3.38, 3.53, 3.87, 3.99 and 4.08 (each 3 H, s, OMe), 4.09 (1 H, ddd, *J* 8.1, 6.6, 4.9, oxazole 4-H), 4.64 (1 H, s, dioxane 2-H), 5.16 (1 H, d, *J* 8.1, oxazole 5-H), 6.43 (1 H, d, *J* 2.4, ArH), 6.89 (1 H, br d, $J_{6',7'}$ 7.4, 6′-H), 6.90–7.02 (4 H, m, ArH), 7.20–7.23 (4 H, m, ArH) and 7.36 (1 H, s, 3′-H); δ_C 21.50 and 23.16 (each Me), 29.91 (dioxane C-5), 55.26, 56.03, 56.33, 56.46 and 59.13 (each OMe), 74.23 (CH), 74.55, 77.08 and 77.34 (each CH_2), 84.54, 99.42, 99.67, 101.38, 106.09 and 107.39 (each CH), 118.29 and 120.15 (each ArC), 120.23, 125.14 and 125.85 (each ArCH), 126.37 (ArC), 126.62 (ArCH), 127.30 (ArC), 127.44 and 128.07 (each ArCH), 136.95, 138.80 and 140.43 (each ArC), 156.32, 156.62, 158.83 and 160.46 (each ArCO) and 165.84 (C=N); *m/z* 627 (4%, M^+), 513 (36), 512 (100), 351 (38) and 350 (45).

(+)-(R,4S,5S)-**37** *and* (+)-(S,4S,5S)-4,5-*Dihydro*-2-{1-[6-*benzyloxy*-4-*methoxy*-2-(5,5-*dimethyl*-1,3-*dioxan*-2-*yl*)*phenyl*]-4,5-*dimethoxy*-2-*naphthyl*}-4-*methoxymethyl*-5-*phenyloxazole* **38**.—A solution of the Grignard reagent [from magnesium (87 mg) and the bromo-compound **32** (1.46 g, 3.6 mmol)] in THF (10 cm^3) was added *via* a cannula to a solution of the oxazoline **8** (730 mg, 1.8 mmol) in THF (15 cm^3) under argon and the solution was heated under reflux for 20 h. Work-up as previously described gave the crude product which was purified by flash chromatography with 50% ethyl acetate–hexane as eluent. The first band that was eluted yielded the oxazoline **13** (200 mg, 28%). This was followed by the major diastereoisomeric *biaryl* **37** (777 mg, 61%) which precipitated from isopropyl ether as an amorphous solid; R_F 0.55 (50% ethyl acetate–hexane); $[\alpha]_D^{20}$ +89.0 (*c* 0.92, THF) (Found: C, 73.35; H, 6.4; N, 1.75. $C_{43}H_{45}NO_8$ requires C, 73.4; H, 6.45; N, 2.0%); δ_H(300 MHz) 0.56 (3 H, s, Me_{ax}), 1.21 (3 H, s, Me_{eq}), 2.96 and 3.20 (each 1 H, d, $J_{ax,eq}$ 11.1, dioxane 4- and 6-H_{ax}), 3.36 and 3.52 (each 1 H, dd, $^2J_{eq,ax}$ 11.1, $^4J_{eq,eq}$ 2.6, dioxane 4- and 6-H_{eq}), 3.36 (1 H, dd, *J* 9.4, 7.7, CH_AOMe), 3.65 (1 H, dd, *J* 9.4, 5.2, CH_BOMe), 3.37, 3.85, 4.01 and 4.11 (each 3 H, s, OMe), 4.14 (1 H, ddd, *J* 7.7, 7.0, 5.2, oxazole 4-H), 4.72 (1 H, s, dioxane 2-H), 4.84 (2 H, AB, *J* 13.0, CH_2Ph), 5.05 (1 H, d, *J* 7.0, oxazole 5-H), 6.45 (1 H, d, *J* 2.3, ArH), 6.88–6.93 (3 H, m, ArH), 6.96 (1 H, d, *J* 2.3, ArH), 7.00–7.20 (9 H, m, ArH), 7.25 (1 H, dd, *J* 8.3, *J* 7.9, 7′-H) and 7.49 (1 H, s, 3′-H); δ_C 21.58 and 23.26 (each Me), 29.99 (dioxane C-5), 55.29, 56.38, 56.54 and 59.05 (each OMe), 69.84 (CH_2), 73.71 (CH), 74.86, 77.36 and 77.41 (each CH_2), 84.16, 99.96, 100.62, 101.54, 106.01 and 107.62 (each CH), 118.47 (ArC), 120.61 (ArCH), 120.90 (ArC), 125.18, 126.03 and 126.62 (each ArCH), 126.94 (ArC), 126.98, 126.94, 127.47, 128.03 and 128.28 (each ArCH), 137.17, 137.29, 138.81 and 140.89 (each ArC), 156.31, 156.62, 157.54 and 160.25 (each ArCO) and 166.02 (C=N); *m/z* 703 (1%, M^+), 588 (22), 115 (41) and 91 (100); further elution supplied the minor diastereoisomeric *biaryl* **38** (97 mg, 8%) which crystallized from ethyl acetate–hexane as prisms, m.p. 205–206 °C; R_F 0.43 (50% ethyl acetate–hexane); $[\alpha]_D^{20}$ +115.1 (*c* 1.24, THF) (Found: C, 73.15; H, 6.65; N, 1.8. $C_{43}H_{45}NO_8$ requires C, 73.4; H, 6.45; N, 2.0%); δ_H(300 MHz) 0.54 (3 H, s, Me_{ax}), 1.20 (3 H, s, Me_{eq}), 2.99 and 3.19 (each 1 H, d, $J_{ax,eq}$ 11.1, dioxane 4- and 6-H_{ax}), 3.38 and 3.48 (each 1 H, dd, $^2J_{eq,ax}$ 11.1, $^4J_{eq,eq}$ 2.6, dioxane 4- and 6-H_{eq}), 3.50 (1 H, dd, *J* 9.8, 6.8, CH_AOMe), 3.61 (1 H, dd, *J* 9.8, 4.9, CH_BOMe), 3.36, 3.81, 4.00 and 4.10 (each 3 H, s, OMe), 4.09 (1 H, ddd, *J* 8.3, 6.8, 4.9, oxazole 4-H), 4.73 (1 H, s, dioxane 2-H), 4.86 (2 H, s, CH_2Ph), 5.16 (1 H, d, *J* 8.3, oxazole 5-H), 6.42 (1 H, d, *J* 2.3, ArH), 6.88–6.91 (3 H, m, ArH), 7.00–7.09 (7 H, m, ArH), 7.19–7.25 (4 H, m, ArH) and 7.40 (1 H, s, 3′-H); δ_C 21.48 and 23.13 (each Me), 29.91 (dioxane C-5), 55.22, 56.30, 56.45 and 59.10 (each OMe), 70.04 (CH_2), 74.21 (CH), 74.47, 77.06 and 77.33 (each CH_2), 84.49, 99.66, 101.04, 101.89, 106.03 and 107.39 (each CH), 118.24 (ArC), 120.45 (ArCH), 120.65 (ArC), 125.67 and 126.29 (each ArCH), 126.43 (ArC), 126.61 and 126.98 (ArCH), 127.28 (ArC), 127.42, 127.92 and 128.03 (each ArCH), 136.99, 137.17, 138.85 and 140.32 (each ArC), 156.26, 156.60, 157.69 and 160.26 (each ArCO) and 165.64 (C=N); λ_{max}/nm 242 and 309 (ε 35 000 and 8500); *m/z* 703 (1%, M^+), 588 (15), 115 (32) and 91 (100).

(+)-(S)-*Methyl* 1-[2-(1,3-*Dioxolan*-2-*yl*)-4,6-*dimethoxyphenyl*]-4,5-*dimethoxynaphthalene*-2-*carboxylate* **39**.—The oxazoline **34** (316 mg, 0.54 mmol) was quaternized, hydrolysed and methylated in an analogous way to that described for the synthesis of compound **14**. The *ester* **39** (549 mg, 82%) crystallized from ethyl acetate–hexane as prisms, m.p. 173–174 °C; $[\alpha]_D^{16}$ +2.3 (*c* 3.09, THF) (Found: C, 65.8; H, 6.0%; M^+, 454. $C_{25}H_{26}O_8$ requires C, 66.0; H, 5.75%; M, 454); δ_H(300 MHz) 3.59, 3.62, 3.91, 3.94 and 4.05 (each 3 H, s, OMe), 3.62–3.84 (4 H, m, 2 × CH_2), 5.08 (1 H, s, dioxolane 2-H), 6.60 and 6.84 (2 H, AB, *J* 2.4, ArH), 6.88–7.29 (3 H, m, ArH) and 7.39 (1 H, s, 3-H).

(+)-(S)-2-[2-(2-*Hydroxymethyl*-4,5-*dimethoxy*-1-*naphthyl*)-3,5-*dimethoxyphenyl*]-1,3-*dioxolane* **40**.—The foregoing ester (211 mg, 0.46 mg) was reduced with lithium aluminium hydride in a manner similar to that described above to give the *alcohol* **40** (195 mg, 100%) as prisms (from ethyl acetate–hexane), m.p. 219–200 °C; $[\alpha]_D^{18}$ +106.0 (*c* 0.98, $CHCl_3$) (Found: C, 67.3; H, 6.5%; M^+, 426. $C_{24}H_{26}O_7$ requires C, 67.6; H, 6.15%; M, 426); δ_H(300 MHz) 3.59, 3.93, 3.97 and 4.04 (each 3 H, s, OMe), 3.66–3.86 (4 H, m, 2 × CH_2), 5.06 (1 H, s, dioxolane 2-H), 6.62 (1 H, d, *J* 2.4, ArH) and 6.78–7.32 (5 H, m, ArH).

(−)-(R)-2-(4,5-*Dimethoxy*-2-*methyl*-1-*naphthyl*)-3,5-*dimethoxybenzaldehyde* **41**.—Mesylation, reduction and acid hydrolysis of the alcohol **40** (195 mg, 0.46 mmol) gave the aldehyde **41** (150 mg, 97%), m.p. 153–155 °C (lit.,[1] m.p. 155–157) (from dichloromethane–hexane); $[\alpha]_D^{19}$ −7.2 (*c* 5.70, THF), identical with an authentic sample.[1]

(−)-(R)-2-[3-*Benzyloxy*-2-(2-*hydroxymethyl*-4,5-*dimethoxy*-1-*naphthyl*)-5-*methoxyphenyl*]-5,5-*dimethyl*-1,3-*dioxane* **43**.—The oxazoline **37** (872 mg, 1.2 mmol) was quaternized, hydrolysed and methylated in an analogous way to that described for the synthesis of compound **14**. Purification of the crude product by flash chromatography gave the *ester* **42** (549 mg, 82%) as a gum; $[\alpha]_D^{16}$ +22.8 (*c* 1.6, THF) (Found: C, 71.05; H, 6.45. $C_{34}H_{36}O_8$ requires C, 71.3; H, 6.35%); δ_H(300 MHz) 0.56 (3 H, s, Me_{ax}), 1.20 (3 H, s, Me_{eq}), 3.02 and 3.08 (each 1 H, d, $J_{ax.eq}$ 11.0, H_{ax}), 3.44 and 3.48 (each 1 H, dd, $J_{ax,eq}$ 11.0, $J_{eq.eq}$ 2.7, H_{eq}), 3.58, 3.89, 4.02 and 4.09 (each 3 H, s, OMe), 4.57 (1 H, s, dioxane H), 4.92 (2 H, AB, *J* 14.0, CH_2Ph), 6.58 (1 H, d, $J_{3,5}$ 2.4, 3-H), 6.87–6.90 (2 H, m, ArH), 6.94 (1 H, dd, $J_{6',7'}$ 7.0, $J_{6',8'}$ 0.9, 6′-H), 6.98 (1 H, d, $J_{5,3}$ 2.4, 5-H), 7.10–7.13 (3 H, m, ArH), 7.07 (1 H, dd, $J_{8',7'}$ 8.5, $J_{8',6'}$ 0.9, 8′-H), 7.25 (1 H, dd, $J_{7',8'}$ 8.5, $J_{7',6'}$ 7.0, 7′-H) and 7.38 (1 H, s, 3′-H). Reduction of the foregoing ester as described above gave the *alcohol* **43** (97%) as an amorphous solid; $[\alpha]_D^{16}$ −47.4 (*c* 1.02, THF) (Found: C, 72.85; H, 6.7. $C_{33}H_{36}O_7$ requires C, 72.75; H, 6.65%); δ_H(300 MHz) 0.57 (3 H, s, Me_{ax}), 1.20 (3 H, s, Me_{eq}), 3.03 and 3.11 (each 1 H, d, $J_{ax,eq}$ 11.1, H_{ax}), 3.13 (1 H, dd, *J* 8.3, 4.8, CH_2OH), 3.46 and 3.54 (each 1 H, dd, $J_{ax.eq}$ 11.1, $J_{eq.eq}$ 2.6, H_{eq}), 3.89, 4.02 and 4.09

(each 3 H, s, OMe), 4.30 (2 H, ddd, J 11.7, 8.3, 4.8, CH_2OH), 4.63 (1 H, s, dioxane 2-H), 4.91 (2 H, AB, J 12.6, CH_2Ph), 6.62 (1 H, d, J 2.4, ArH), 6.85–6.93 (4 H, m, ArH), 7.04 (1 H, d, J 2.4, ArH), 7.13–7.17 (3 H, m, ArH), 7.23 (1 H, dd, $J_{7',8'} = J_{7',6'}$ 7.0, 7′-H) and 7.06 (1 H, s, 3′-H); m/z 544 (35%, M^+), 422 (21), 337 (22), 321 (22) and 91 (100).

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