Synthetic Approaches to the Naphthyl-isoquinoline Alkaloids. Part 1. Dehydroancistrocladisine[1]

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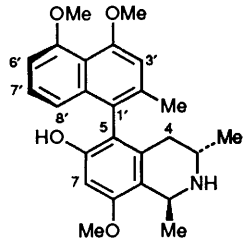
A synthesis of (±)-7-(4,5-dimethoxy-2-methyl-1-naphthyl)-6,8-dimethoxy-1,3-dimethylisoquinoline (dehydroancistrocladisine) **19**, the racemic form of a degradation product of the unusual naphthyl-isoquinoline alkaloid ancistrocladisine **3**, is recorded. The key step relied on oxazoline chemistry for the construction of the biaryl linkage.

The naphthyl-isoquinoline alkaloids are found only in tropical lianas of the plant families Ancistrocladaceae and Dioncophyllaceae. The family Ancistrocladaceae contains one genus, *Ancistrocladus*, which contains about 20 species that are distributed in the Indian archipelago, tropical Asia, and tropical West Africa.[2] Most of the structural studies, carried out by Govindachari and his co-workers,[3] have been confined to the *Ancistrocladus* alkaloids, but two members of the Dioncophyllaceae have been investigated.[4]

The naphthyl-isoquinoline alkaloids can be divided into three groups depending on the position of the linkage between the two ring systems. The largest group is the 5-1′ linked alkaloids exemplified by (−)-ancistrocladine **1** from *A. heyneanus*,[5-7] *A.*



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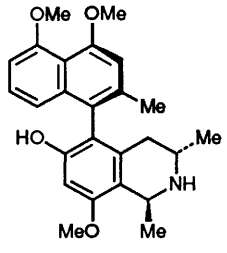

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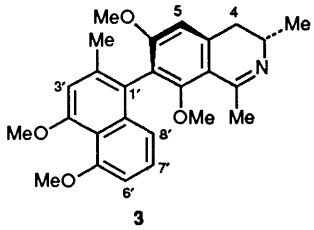

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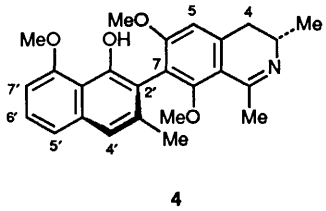

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hamatus,[8,9] *A. tectorius*,[10,11] and *A. congolensis*,[12] and its atropisomer (+)-hamatine **2** from *A. hamatus*[8] and *A. tectorius*.[11] The 7-1′ and the 7-2′ linked alkaloids are represented by (−)-ancistrocladisine **3** from *A. heyneanus*[13,14] and (−)-ancistrocladidine **4** also from *A. heyneanus*.[14,15] These alkaloids are structurally unusual isoquinoline alkaloids on account of the methyl group at the 3-position and oxygenation at the 6- and 8-positions of the isoquinoline ring which points to a polyketide origin.[4,5] Another remarkable structural feature of these alkaloids is that they exist as thermally stable atropisomers because of the restricted rotation about the naphthyl-isoquinoline linkage. We were therefore attracted to the problem of the total synthesis of these alkaloids, a challenge that has also been taken up by Bringmann and his co-workers.[16]

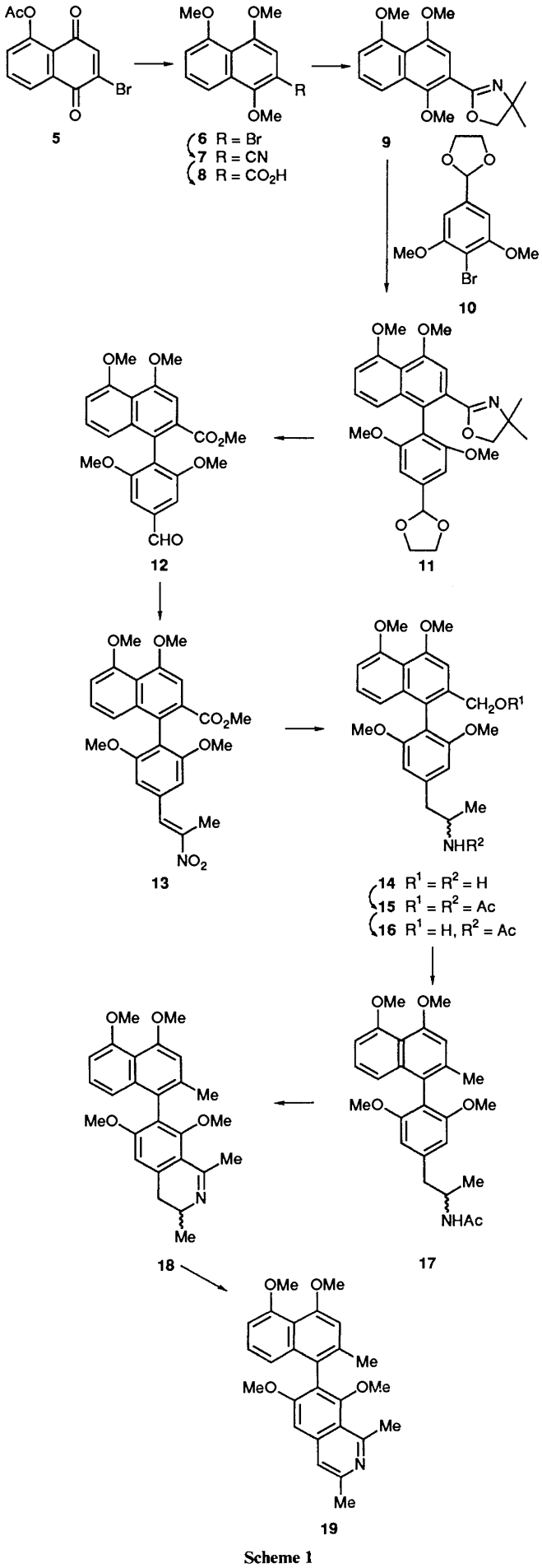
Our synthetic plan was to construct the biaryl linkage of these alkaloids by using the biaryl synthesis of Meyers in which the *o*-methoxy group in an *o*-(methoxyaryl)oxazoline is displaced by an aryl Grignard reagent.[17] By using a chiral oxazoline this method offers the opportunity to construct atropisomeric biaryls in which one diastereoisomer is in excess.[18] Before embarking on such an asymmetric synthesis we deemed it sagacious to first test this methodology by the synthesis of a racemic compound. For this purpose we chose dehydroancistrocladisine **19** (see Scheme 1) a product obtained in optically active form by Govindachari and his co-workers by dehydrogenation of (−)-ancistrocladisine **3**.[13]

The oxazoline **9** required for the biaryl synthesis was available in a few steps from the known bromo-juglone **5**.[19] This compound was first converted, by an adaptation of the method of Jung and Hagenah,[19] into the bromonaphthalene **6** which was then allowed to react with copper(I) cyanide which provided the nitrile **7**. Hydrolysis of this nitrile provided the acid **8** which was converted into the oxazoline **9** by the usual method.[17] The bromo compound **10** was readily available by ketalization of the known aldehyde,[20] and the derived Grignard reagent was caused to react with the oxazoline **9**.

The resultant biaryl **11** was converted by deprotection and methylation into the intermediate **12** and this under the conditions of the Henry reaction yielded the nitrostyrene **13**. Reduction of this compound with lithium aluminium hydride yielded the racemic amphetamine **14** which on acetylation provided the *N*,*O*-diacetyl compound **15**. *O*-Deacetylation of the diacetate **15** was achieved with sodium methoxide in methanol and the resultant alcohol **16** was deoxygenated by the method of Morita *et al.*[21] This reaction afforded the *N*-acetylamphetamine **17** which on Bischler–Napieralski cyclization supplied ancistrocladisine **18** as an inseparable mixture of diastereoisomers. This mixture of diastereoisomers was then dehydrogenated with Raney nickel in boiling naphthalene and this reaction yielded racemic dehydroancistrocladisine **19** which had properties in close agreement with those recorded in the literature.[13]

Experimental

M.p.s were determined with a Kofler hot-stage apparatus. All organic extracts were washed with saturated brine, and were then dried with anhydrous sodium sulphate prior to evaporation under diminished pressure. Radial chromatography was carried out on a Harrison Research Chromatotron with plates coated with Merck Kieselgel 60 PF_{254}. NMR spectra were recorded for solutions in deuteriochloroform at 80 MHz with a Bruker WP-80 instrument or at 300 MHz with a Bruker AM-300 instrument.



Scheme 1

J Values are given in Hz. Electronic spectra were recorded with a Hewlett-Packard 8450A spectrophotometer. Mass spectra were determined at 35 eV using a Hewlett-Packard 5986 instrument.

2-Bromo-1,4,5-trimethoxynaphthalene **6**.—A solution of 1,5-diacetoxynaphthalene[22] (12 g, 49.2 mmol) in warm acetic acid (500 ml) was added dropwise to a solution of *N*-bromosuccinimide (35.6 g) in acetic acid (500 ml) and water (1000 ml) at 55–60 °C over 10 min. This solution was stirred for a further 45 min and then diluted with water (1000 ml). The mixture was cooled in an ice-bath and the quinone was collected by filtration, dissolved in ether–dichloromethane (5:1; 300 ml), and the solution shaken with sodium dithionite (25 g) in water (250 ml) for 10 min, and finally shaken with water (2 × 150 ml). The organic layer was next stirred vigorously with dimethyl sulphate (23 ml) and tetrabutylammonium bromide (2 g) in water (250 ml) under argon at 0 °C and sodium hydroxide (16 g) in water (250 ml) was added dropwise over 0.5 h. The dark red mixture was stirred for 15 h at room temperature and the organic layer was separated, washed with concentrated ammonia solution, and dried. Removal of the solvent and filtration of the crude product through a short column of alumina with hexane as eluent gave the naphthalene **6** (10.7 g, 73%) which formed prisms (from hexane), m.p. 115–116 °C (lit.,[19] 115–117 °C).

1,4,5-Trimethoxynaphthalene-2-carbonitrile **7**.—A mixture of copper(I) cyanide (4.6 g, 51.3 mmol) and the bromonaphthalene **6** (5.97 g, 20.1 mmol) in dry *N,N*-dimethylformamide (DMF) (100 ml) was heated under reflux under nitrogen for 16 h. The dark solution was cooled, poured into 1,2-diaminoethane (10 ml) in water (100 ml) and extracted with ethyl acetate. Removal of the solvent gave the *nitrile* **7** (4.17 g, 88%) which crystallized from hexane as needles, m.p. 125.5–126 °C (Found: C, 68.9; H, 5.6; N, 5.7%; M^+, 243. $C_{14}H_{13}NO_3$ requires C, 69.1; H, 5.4; N, 5.75%; M, 243); δ_H(80 MHz) 3.95, 3.98 and 4.15 (each 3 H, s, OMe), 6.95 (1 H, s, 3-H), 7.04 (1 H, dd, $J_{6,7}$ 7.7, $J_{6,8}$ 1.1, 6-H), 7.52 (1 H, dd, $J_{7,8}$ 8.4, $J_{6,7}$ 7.7, 7-H) and 7.82 (1 H, dd, $J_{7,8}$ 8.4, $J_{6,8}$ 1.1, 8-H).

1,4,5-Trimethoxynaphthalene-2-carboxylic Acid **8**.—A solution of the nitrile **7** (3.9 g, 16.0 mmol) and potassium hydroxide (8 g) in methanol (75 ml) and water (20 ml) was heated under reflux for 72 h. Most of the methanol was removed by distillation and the residue was diluted with water and washed with ether. Acidification of the aqueous layer and the usual work-up gave the *acid* **8** (3.5 g, 84%) which crystallized from ether–hexane as pale yellow needles, m.p. 124–125 °C (Found: C, 64.55; H, 5.8%; M^+, 262. $C_{14}H_{14}O_5$ requires C, 64.1; H, 5.4%; M, 262). Methylation of the acid (DMF, potassium carbonate, methyl iodide) gave the *methyl ester* (100%) which crystallized from hexane as needles, m.p. 71–71.5 °C (Found: C, 65.2; H, 5.9%; M^+, 276. $C_{15}H_{16}O_5$ requires C, 65.2; H, 5.85%; M, 276); δ_H(80 MHz) 3.97 and 3.98 (each 6 H, s, OMe), 7.18 (1 H, s, 3-H), 6.98 (1 H, dd, $J_{6,7}$ 7.0, $J_{6,8}$ 1.0, 6-H), 7.47 (1 H, dd, $J_{7,8}$ 8.5, $J_{7,6}$ 7.0, 7-H) and 7.86 (1 H, dd, $J_{8,7}$ 8.5, $J_{8,6}$, 1.0, 8-H).

4,5-Dihydro-4,4-dimethyl-2-(1,4,5-trimethoxy-2-naphthyl)-oxazole **9**.—Oxalyl chloride (0.63 ml, 7.4 mmol) was added to a solution of the acid **8** (970 mg, 3.7 mmol) in dry dichloromethane (25 ml) under argon at room temperature. The deep red solution was stirred for 2.5 h and the excess of oxalyl chloride was removed under reduced pressure. A solution of the crude acid chloride in dry dichloromethane (10 ml) was added dropwise to a solution of 2-amino-2-methylpropan-1-ol (691 mg, 7.8 mmol) in dry dichloromethane (10 ml) at 5 °C. The solution was then stirred at room temperature for 2 h, filtered and the orange filtrate was treated with thionyl chloride (0.6 ml) at 0 °C. After 1.5 h at room temperature the solution was cooled

to 0 °C and diluted cautiously with water (40 ml). The organic layer was extracted with dilute hydrochloric acid and the aqueous layers were combined and washed with dichloromethane. Basification with dilute aqueous sodium hydroxide and isolation of the product by extraction with ether provided the *oxazoline* **9** (986 mg, 85%) as needles (from dichloromethane–hexane), m.p. 101–102 °C (Found: C, 68.7; H, 7.05; N, 4.2%; M^+, 315. $C_{18}H_{21}NO_4$ requires C, 68.55; H, 6.7; N, 4.45%; M, 315); δ_H(80 MHz) 1.44 (6 H, s, 2 × Me), 3.91, 3.97 and 3.99 (each 3 H, s, OMe), 4.17 (2 H, s, CH_2), 6.94 (1 H, dd, $J_{6,7}$ 7.5, $J_{6,8}$ 1.0, 6-H), 7.17 (1 H, s, 3-H), 7.45 (1 H, dd, $J_{7,8}$ 8.5, $J_{7,6}$ 7.5, 7-H) and 7.84 (1 H, dd, $J_{8,7}$ 8.5, $J_{8,6}$ 1.0, 8-H).

2-(4-*Bromo*-3,5-*dimethoxyphenyl*)-1,3-*dioxolane* **10**.—A solution of 4-bromo-3,5-dimethoxybenzaldehyde[20] (7.1 g, 29.0 mmol), ethylene glycol (2.2 g, 35.6 mmol), and toluene-*p*-sulphonic acid (100 mg) in benzene (200 ml) was heated under reflux in a Dean–Stark apparatus for 20 h. The solution was cooled, washed with saturated aqueous sodium hydrogen carbonate, and with water. Removal of the solvent and crystallization of the residue from hexane afforded the *acetal* **10** (8.2 g, 98%) as prisms, m.p. 45–47 °C (Found: C, 45.45; H, 4.35; Br, 27.7%; 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) 3.92 (6 H, s, 2 × OMe), 4.06 (4 H, m, CH_2), 5.79 (1 H, s, 2-H) and 6.72 (2 H, s, ArH).

2-{1-[4-(1,3-*Dioxolan*-2-*yl*)-2,6-*dimethoxyphenyl*]-4,5-*dimethoxy*-2-*naphthyl*}-4,4-*dimethyl*-4,5-*dihydrooxazole* **11**.—The Grignard reagent [from the bromo compound **10** (4.45 g, 15.4 mmol) and magnesium turnings (380 mg) in dry tetrahydrofuran (THF) (25 ml)] was added *via* a cannula to a solution of the oxazoline **9** (1.61 g, 5.1 mmol) in dry THF (25 ml) and the solution was stirred at room temperature for 16 h and then heated under reflux for 2 h. The cooled solution was diluted with ethyl acetate, poured into saturated aqueous ammonium chloride and the separated organic layer was washed with water. Removal of the solvent and radial chromatography of the residue with 50–80% ethyl acetate–hexane as eluent afforded the *oxazoline* **11** (2.04 g, 81%) which crystallized from ethyl acetate–hexane as prismatic needles, m.p. 160–161 °C (Found: C, 68.35; H, 6.5; N, 2.9%; M^+, 493. $C_{28}H_{31}NO_7$ requires C, 68.15; H, 6.35; N, 2.85%; M, 493); δ_H(300 MHz) 1.21 (6 H, s, 2 × Me), 3.64 (6 H, s, 2 × OMe), 3.70 (2 H, s, CH_2), 3.97 and 4.05 (each 3 H, s, OMe), 4.08–4.24 (2 H, m, CH_2O_2), 5.87, (1 H, s, CHO_2), 6.77 (2 H, s, 3′- and 5′-H), 6.88 (1 H, dd, $J_{6,7}$ 7.5, $J_{6,8}$ 1, 6-H), 7.07 (1 H, dd, $J_{8,7}$ 8.5, $J_{8,6}$ 1.0, 8-H), 7.22 (1 H, dd, $J_{7,8}$ 8.5, $J_{7,6}$ 7.5, 7-H) and 7.27 (1 H, s, 3-H); λ_{max}(MeOH)/nm 206, 236, 308 and 336 (ε 50 500, 40 400, 9300 and 5000).

Methyl 1-(4-*Formyl*-2,6-*dimethoxyphenyl*)-4,5-*dimethoxynaphthalene*-2-*carboxylate* **12**.—A solution of the oxazoline **11** (437 mg, 0.9 mmol) in dry nitromethane (5 ml) was heated at 60 °C with methyl iodide (1 ml) for 24 h. The solvents were removed under reduced pressure and the salt and sodium hydroxide (350 mg) were dissolved in THF–methanol (5:1; 25 ml) and water (5 ml) and the solution was heated under reflux for 35 h. The cooled solution was acidified to pH 4 with concentrated hydrochloric acid and next stirred for 15 min at room temperature. Work-up provided the crude acid (390 mg, 100%) which was dissolved in anhydrous DMF (15 ml) and stirred with anhydrous potassium carbonate (250 mg) and methyl iodide (0.3 ml) at room temperature for 16 h. The mixture was poured into saturated brine and extraction with dichloromethane provided the *ester* **12** (334 mg, 90%) which crystallized from dichloromethane–hexane as plates, m.p. 248–249 °C (Found: C, 67.15; H, 5.35%; M^+, 410. $C_{23}H_{22}O_7$ requires C, 67.3; H, 5.4%; M, 410); δ_H(80 MHz) 3.66, 3.98 and 4.06 (each 3 H, s, OMe), 3.69 (6 H, s, 2 × OMe), 6.87–7.18 (3 H, m, 6-, 7- and 8-H), 7.22 (2 H, s, 3′- and 5′-H), 7.44 (1 H, s, 3-H) and 10.04 (1 H, s, CHO).

Methyl 1-[2,6-*Dimethoxy*-4-(E)-2-*nitropropenyl*)*phenyl*]-4,5-*dimethoxynaphthalene*-2-*carboxylate* **13**.—A mixture of the aldehyde **12** (710 mg, 1.7 mmol), freshly distilled nitroethane (7 ml) and ammonium acetate (240 mg) was heated at 80 °C (bath) for 1 h. Acetic acid (2.5 ml) was then added and the yellow solution was heated under reflux for 1.5 h. The cooled mixture was poured into saturated aqueous sodium hydrogen carbonate and extracted with ethyl acetate and the extract was worked up to provide the crude product. This was subjected to radial chromatography with 30% ethyl acetate–hexane as eluent. The *nitrostyrene* **13** (649 mg, 80%) formed yellow prisms (from dichloromethane–hexane), m.p. 199–200 °C (Found: C, 64.45; H, 5.55; N, 3.1%; M^+, 467. $C_{25}H_{25}NO_8$ requires C, 64.25; H, 5.4; N, 3.0%; M, 467); δ_H(300 MHz) 2.59 (3 H, d, *J* 1.0, Me), 3.64 (6 H, s, 2 × OMe), 3.69, 3.99 and 4.07 (each 3 H, s, OMe), 6.76 (2 H, s, 3′- and 5′-H), 6.94 (1 H, dd, $J_{6,7}$ 7.8, $J_{6,8}$ 0.9, 6-H), 7.03 (1 H, dd, $J_{8,7}$ 8.5, $J_{8,6}$ 0.9, 8-H), 7.29 (1 H, dd, $J_{7,8}$ 8.5, $J_{7,6}$ 7.8, 7-H), 7.43 (1 H, s, 3-H) and 8.18 (1 H, br s, $W_{\frac{1}{2}}$ 3.5 Hz, vinyl H); λ_{max}/nm 210, 244 and 345 (ε 57 200, 48 000 and 19 900 respectively).

1-[4-(2-*Aminopropyl*)-2,6-*dimethoxyphenyl*]-4,5-*dimethoxy*-2-*naphthylmethanol* **14**.—A solution of the nitrostyrene **13** (200 mg, 0.43 mmol) in anhydrous THF (6 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (60 mg) in anhydrous THF (10 ml) under gentle reflux under argon. The mixture was heated under reflux for 2.5 h and then cooled to 0 °C. Aqueous sodium hydroxide (30%) was added until coagulation occurred and the suspension was filtered through Celite and the solids were extracted further with boiling ether. Removal of the solvent gave the *amine* **14** which crystallized from dichloromethane–hexane as prisms (145 mg, 82%), m.p. 104–106 °C (Found: C, 67.35; H, 7.5; N, 3.05%; M^+, 411. $C_{24}H_{29}NO_5 \cdot H_2O$ requires C, 67.1; H, 7.25; N,3.25%; M, 411); δ_H(300 MHz) 1.23 (3 H, d, *J* 6.3, CH*Me*), 2.62 (1 H, dd, *J* 13.2, *J* 8.5, CH_A), 2.83 (1 H, dd, *J* 13.2, *J* 5.1, CH_B), 3.32 (1 H, m, C*H*Me), 3.62 (6 H, s, 2 × OMe), 3.97 and 4.04 (each 3 H, s, OMe), 4.40 (2 H, s, CH_2OH), 6.56 (2 H, s, 3′- and 5′H), 6.84 (1 H, br d, $J_{6,7}$ 7.7, 6-H), 6.88 (1 H, dd, $J_{8,7}$ 8.5, $J_{8,6}$ 0.9, 8-H), 7.07 (1 H, s, 3-H) and 7.21 (1 H, dd, $J_{7,8}$ 8.5, $J_{7,6}$ 7.7, 7-H).

N-{2-[2-(*Hydroxymethyl*-4,5-*dimethoxy*-1-*naphthyl*)-3,5-*dimethoxyphenyl*]-1-*methylethyl*}acetamide **16**.—The amino alcohol **14** (190 mg, 0.46 mmol) was stirred with pyridine (1.5 ml) and acetic anhydride (0.12 ml) at 35–40 °C for 2.5 h. Warm water was added to the solution and the crude product was isolated by extraction with dichloromethane. The *diacetate* **15** (210 mg, 92%) crystallized as prisms (from ethyl acetate), m.p. 178–179.5 °C (Found: C, 67.7; H, 6.9; N, 2.65%; M^+, 495. $C_{28}H_{33}NO_7$ requires C, 67.85; H, 6.7; N, 2.85%; M, 495); δ_H(80 MHz) 1.22 (3 H, d, *J* 6.5, CH*Me*), 2.00 and 2.01 (each 3 H, s, Ac), 2.80–2.92 (2 H, m, CH_2CH), 3.61 (6 H, s, OMe), 3.96 and 4.02 (each 3 H, s, OMe), 4.38 (1 H, m, C*H*Me), 4.92 (2 H, s, CH_2O), 6.50 (2 H, s, ArH), 6.79–7.27 (3 H, m, ArH) and 6.99 (1 H, s, ArH). The diacetate **15** (200 mg, 0.4 mmol) was stirred with methanolic sodium methoxide [from sodium (40 mg) and methanol (20 ml)] at room temperature for 1.5 h when the compound had dissolved. The solution was poured into hydrochloric acid (10%) and the crude product was isolated by extraction with ethyl acetate and crystallized from dichloromethane–hexane to afford the *alcohol* **16** (148 mg, 81%) as prisms, m.p. 161–162 °C (Found: C, 66.5; H, 7.05; N, 2.7%; M^+, 453. $C_{26}H_{31}NO_6 \cdot H_2O$ requires C, 66.2; H, 7.05; N, 2.95%; M, 453); δ_H(300 MHz) 1.22 (3 H, d, *J* 6.7, CHMe), 2.00 (3 H, s, NAc), 2.31 (1 H, t, *J* 5.6, D_2O exchangeable OH), 2.74 (1 H, dd, *J* 13.4, 7.8,

CH_A), 2.99 (1 H, dd, J 13.4, 5.8, CH_B), 3.61 (6 H, s, 2 × OMe), 3.97 and 4.04 (each 3 H, s, OMe), 4.37 (1 H, m, C*H*Me), 4.39 (2 H, d, J 5.6, CH_2OH), 5.44 (1 H, br d, J 8.4, NH) 6.55 (2 H, s, 2- and 6-H), 6.84 (1 H, br d, $J_{6',7'}$ 7.8, 6'-H) 6.87 (1 H, dd, $J_{8',7'}$ 8.5, $J_{8',6'}$ 1, 8'-H), 7.07 (1 H, s, 3'-H) and 7.21 (1 H, dd, $J_{7',8'}$ 8.5, $J_{7',6'}$ 7.8, 7'-H).

N-{2-[4-(4,5-*Dimethoxy*-2-*methyl*-1-*naphthyl*)-3,5-*dimethoxyphenyl*]-1-*methylethyl*}acetamide **17**.—A solution of chlorotrimethylsilane (61 mg, 0.56 mmol) in anhydrous acetonitrile (2.6 ml) was added dropwise to a stirred mixture of the alcohol **16** (100 mg, 0.22 mmol) and anhydrous sodium iodide (86 mg, 0.54 mmol) in anhydrous acetonitrile (3 ml) at 35–40 °C (bath). After 1 h, acetic acid (0.4 ml) and zinc dust (100 mg) were added and the colourless mixture was stirred at 80 °C for 4.5 h. Work-up gave the *acetamide* **17** (94 mg, 97%) which crystallized from dichloromethane–hexane as prisms, m.p. 174–175.5 °C (Found: C, 70.25; H, 7.45; N, 3.0%; M^+, 437. $C_{26}H_{31}NO_5$ requires C, 69.95; H, 7.2; N, 3.15%; M, 437); δ_H(300 MHz) 1.22 (3 H, d, J 6.6, CH*Me*), 1.99 (3 H, s, NAc), 2.12 (3 H, s, ArMe), 2.75 (1 H, dd, J 13.0, 8.0, CH_A), 2.97 (1 H, dd, J 13.0, 6.0, CH_B), 4.37 (1 H, apparent quintet, (C*H*Me), 5.40 (1 H, br d, J 8.0, N*H*Ac), 6.52 (2 H, s, 2- and 6-H), 6.76 (1 H, br d, $J_{6',7'}$ 7.8, 6'-H), 6.82 (1 H, s, 3'-H), 6.87 (1 H, br d, $J_{8',7'}$ 8.2, 8'-H) and 7.17 (1 H, dd, $J_{7',8'}$ 8.2, $J_{7',6'}$ 7.8, 7'-H); λ_{max}(EtOH)/nm (207, 230, 305, 320 and 335 (ε32 700. 33 300, 6000, 4800 and 3900).

(±)-7-(4,5-*Dimethoxy*-2-*methyl*-1-*naphthyl*)-6,8-*dimethoxy*-1,3-*dimethylisoquinoline* (*Dehydroancistrocladisine*) **19**.—A solution of the acetamide **17** (200 mg, 0.46 mmol) and phosphoryl chloride (0.2 ml) in acetonitrile (10 ml) was heated under reflux for 30 min. The solvents were removed under reduced pressure and the residue in chloroform (10 ml) was shaken with 10% aqueous sodium hydroxide and ether. Removal of the solvent gave the crude product **18** (189 mg) which, dissolved in the minimum amount of dichloromethane and added to a mixture of naphthalene (2 g) and dry W2 Raney nickel (*ca.* 1 g), was stirred and heated under a stream of argon, to remove the dichloromethane. Next it was heated under reflux under argon for 3 h. The cooled residue was dissolved in ethyl acetate and the solution filtered through Celite; the naphthalene was then removed by steam distillation. Extraction of the pot residue with ethyl acetate and radial chromatography of the crude product with 50% ethyl acetate–hexane as eluent afforded racemic *dehydroancistrocladisine* **19** (45 mg, 24%) which crystallized from ether as prisms, m.p. 207–208 °C (lit.,[13] 210–211 °C) (Found: C, 74.9; H, 6.8; N, 3.3. $C_{28}H_{33}NO_7$ requires C, 74.8; H, 6.5; 3.35%); δ_H(300 MHz) 2.20 (3 H, s, 2'-Me), 2.64 (3 H, s, 3-Me), 3.03 and 3.20 (each 3 H, s, 1-Me and 8-OMe), 3.75, 3.99 and 4.04 (each 3 H, s, OMe), 6.79 (1 H, br d, $J_{7',8'}$ 8.0, 8'-H), 6.85, 6.91 and 7.29 (each 1 H, s, 4-, 5- and 3'-H), 6.92 (1 H, dd, $J_{6',7'}$ 7.5, $J_{6',8'}$ 1, 6'-H) and 7.20 (1 H, dd, $J_{7',8'}$ 8.0, $J_{7',6'}$ 7.5, 7'-H); λ_{max}(MeOH)/nm 236, 307, 319 and 334 (ε 92 900, 16 800, 14 600 and 10 100); *m/z* 417 (100%, M^+), 418 (24) and 387 (20).

References

1 Preliminary communication: M. A. Rizzacasa and M. V. Sargent, *J. Chem. Soc., Chem. Commun.*, 1989, 301.
2 J. D. Hooker, *The Flora of British India*, Reeve and Co., Ashford, 1875, vol. 1, p. 299.
3 T. R. Govindachari and P. C. Parthasarathy, *Heterocycles*, 1977, **7**, 661.
4 G. Bringmann in *The Alkaloids*, ed. A. Brossi, Academic Press, New York, 1986, vol. 29, p. 141.
5 T. R. Govindachari and P. C. Parthasarathy, *Indian J. Chem.*, 1970, **8**, 567; *Tetrahedron*, 1971, **27** 1013.
6 T. R. Govindachari, P. C. Parthasarathy and H. K. Desai, *Indian J. Chem.*, 1971, **9**, 931.
7 T. R. Govindachari, K. Nagarajan, P. C. Parthasarathy, T. G. Rajagopalan, H. K. Desai, G. Kartha, S. L. Chen and K. Nakanishi, *J. Chem. Soc., Perkin Trans. 1*, 1974, 1413.
8 T. R. Govindachari, P. C. Parthasarathy, T. G. Rajagopalan, H. K. Desai, K. S. Ramachandran and E. Lee, *Indian J. Chem.*, 1975, **13**, 641.
9 H. K. Desai, D. H. Gawad, T. R. Govindachari, B. S. Joshi, P. C. Parthasarathy, K. S. Ramachandran, K. R. Ravindranath, A. R. Sidhaye and N. Viswanathan, *Indian J. Chem., Sect. B*, 1976, **14**, 473.
10 J. P. Foucher, J. L. Pousset, A. Cavé and R. R. Paris, *Plantes Méd. Phytothér.*, 1975, **9**, 26.
11 Z. X. Chen, B. D. Wang, K. W. Quin, B. E. Zhang, Q. L. Su and Q. C. Lin, *Yaoxue Xuebao*, 1981, **16**, 519.
12 J. P. Foucher, J. L. Pousset, A. Cavé, A. Bouquet and R. Paris, *Plantes Méd. Phytothér.*, 1975, **9**, 87.
13 T. R. Govindachari, P. C. Parthasarathy and H. K. Desai, *Indian J. Chem.*, 1972, **10**, 1117.
14 T. R. Govindachari, P. C. Parthasarathy, T. G. Rajagopalan, H. K. Desai, K. S. Ramachandran and E. Lee, *J. Chem. Soc., Perkin Trans. 1*, 1975, 2134.
15 T. R. Govindachari, P. C. Parthasarathy and H. K. Desai, *Indian J. Chem.*, 1973, **11**, 1190.
16 G. Bringmann and H. Reuscher, *Tetrahedron Lett.*, 1989, 5249 and earlier papers.
17 A. I. Meyers, R. Gabel and E. D. Mihelich, *J. Org. Chem.*, 1978, **43**, 1372.
18 A. I. Meyers, J. R. Flisak and R. A. Aitken, *J. Am. Chem. Soc.*, 1987, **109**, 5446.
19 M. E. Jung and J. A. Hagenah, *J. Org. Chem.*, 1987, **52**, 1889.
20 I. Kompis and A. Wick, *Helv. Chim. Acta*, 1977, **60**, 3025.
21 T. Morita, Y. Okamoto and H. Sakurai, *Synthesis*, 1981, 32.
22 A. Leman, *Ann. Chim. (Paris)*, 1935, **9**, 357.

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