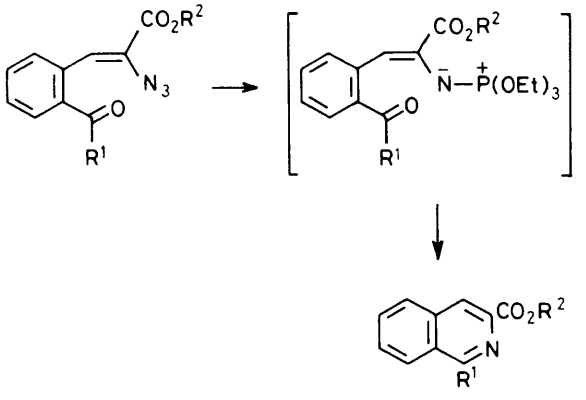
Vinyl Azides in Heterocyclic Synthesis. Part 9.[1] Synthesis of the Isoquinolone Alkaloid Siamine by Intramolecular Aza-Wittig Reaction

Michael Kennedy, Christopher J. Moody, Charles W. Rees, and Juan J. Vaquero
Department of Chemistry, Imperial College of Science and Technology, London SW7 2AY

The isoquinolone alkaloid siamine (**1**) has been synthesised from 3,5-dibenzyloxybenzoic acid (**2**) by a route which incorporates an intramolecular aza-Wittig reaction as the key step. The benzaldehyde (**5**), prepared from the benzoic acid (**2**) by the dihydro-oxazole method, is converted into the vinyl azides (**6**) and (**7**), which on treatment with triethyl phosphite give the isoquinolone (**8**) and the 1-ethoxyisoquinoline (**9**) respectively. The synthesis is completed by transformation of the isoquinoline 3-ester (**9**) into the corresponding 3-methylisoquinoline (**12**), complete dealkylation of which with boron tribromide gives siamine (**1**).

In one of the earlier parts of this series,[2] we described a new route to isoquinolines based on the intramolecular aza-Wittig reaction. Isoquinolines are formed under mild neutral conditions by spontaneous cyclisation of iminophosphoranes derived from azidocinnamates containing *ortho*-carbonyl substituents by treatment with triethyl phosphite (TEP) (Scheme 1). Particularly interesting was the fact that even less reactive ester (R^1 = OEt) and carboxylic acid (R^1 = OH) carbonyl groups readily participated in the intramolecular aza-Wittig reaction to give 1-ethoxyisoquinolines or isoquinolones respectively.

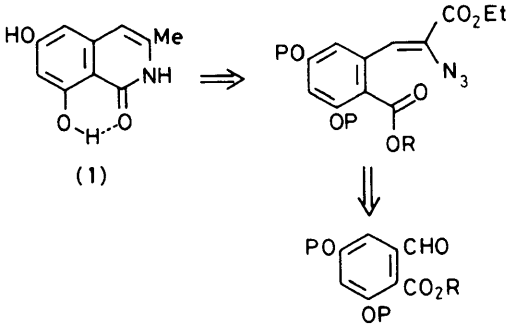


Scheme 1.

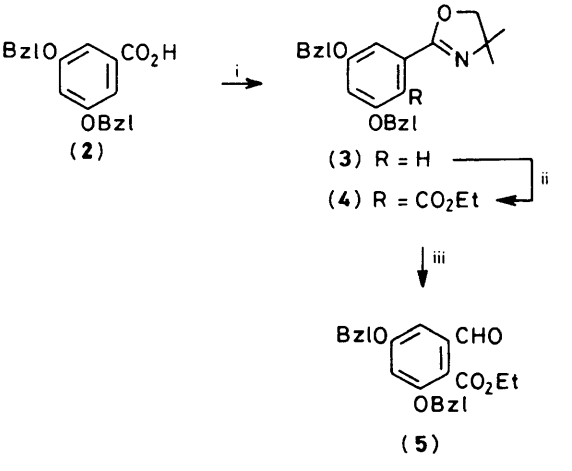
We now report an application of the intramolecular aza-Wittig reaction to the synthesis of siamine (**1**), one of the simpler isoquinoline alkaloids,[3] isolated from the seeds and leaves of *Cassia siamea*,[4,5,6] and previously prepared by a classical route.[4,5]

Results and Discussion

From the outset it was recognised that siamine (**1**) could result from an intramolecular aza-Wittig reaction of an appropriately substituted azidocinnamate with the ethyl ester substituent serving as a potential methyl group (Scheme 2). It was also decided to investigate both the preparation of the desired isoquinolone and the corresponding 1-ethoxyisoquinoline in the expectation that the latter derivative might be easier to handle in the subsequent transformations. As usual, the required azidocinnamates would be prepared from the corresponding benzaldehyde. Benzyl ethers were chosen as protecting groups for the phenolic hydroxy groups, and therefore the benzaldehyde (**5**) became the initial target. This was prepared from known[7] 3,5-dibenzyloxybenzoic acid (**2**) using the standard oxazoline chemistry developed by Meyers and co-workers.[8a] Thus the benzoic acid (**2**) was converted into the dihydro-oxazole (**3**) (93%), which was lithiated using butyl-lithium in 1,2-dimethoxyethane (DME), and the resulting aryl-lithium species quenched with ethyl chloroformate to give the ester (**4**) (77%). The dihydro-oxazole group was transformed into an aldehyde in the usual way[8b] by reaction with neat iodomethane and reduction of the resulting *N*-methyloxazolinium salt with sodium borohydride to give the required benzaldehyde (**5**) (51%) (Scheme 3).



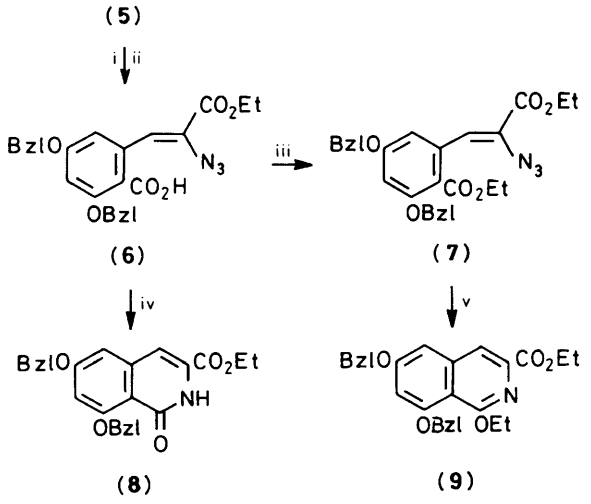
Scheme 2. P = protecting group; R = H or Et



Scheme 3. [Bzl = $PhCH_2$] *Reagents:* i, $SOCl_2$; $HOCH_2CMe_2NH_2$; $SOCl_2$; ii, BuLi, DME, −78 °C; EtO_2CCl; iii, MeI, reflux; $NaBH_4$, MeOH, H_3O^+

Condensation of the aldehyde (**5**) with ethyl azidoacetate in ethanolic sodium ethoxide under the standard conditions[9] resulted in cleavage of the ester group and gave the *ortho*-carboxy azidocinnamate (**6**), although in modest yield (37%). The facile cleavage of the ester is probably due to participation by the negatively charged oxygen atom in the tetrahedral intermediate formed by attack of ethyl azidoacetate on the aldehyde. A better yield (58%) of the *ortho*-carboxy azidocinnamate (**6**) could be obtained by prior hydrolysis of the ester (**5**) to the corresponding *ortho*-carboxy benzaldehyde, which exists as 5,7-dibenzyloxy-3-hydroxyphthalide, followed by condensation with ethyl azidoacetate (Scheme 4). Esterification of the acid (**6**) using iodoethane and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in acetonitrile[10] then gave the azidocinnamate (**7**) (75%).

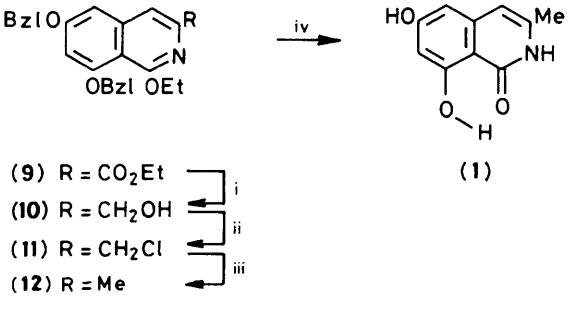
The azidocinnamates (**6**) and (**7**) were the desired intermediates for the key intramolecular aza-Wittig reactions. Treatment of the azide (**6**) with TEP in tetrahydrofuran (THF)



Scheme 4. [Bzl = $PhCH_2$] *Reagents:* i, KOH, dioxane, water; ii, $EtO_2CCH_2N_3$, NaOEt, EtOH, −15 °C; iii, EtI, DBU, MeCN; iv, TEP, THF; v, TEP, C_6H_6

at room temperature gave the isoquinolone (**8**) in 65% yield. The cyclisation proceeded in higher yield with the ester (**7**) which gave the 1-ethoxyisoquinoline (**9**) in 94% yield on reaction with TEP in benzene (Scheme 4).

As expected, the very polar isoquinolone (**8**) proved difficult to handle and gave poor results on attempted reduction of the ester group, and therefore the synthesis was completed from the 1-ethoxyisoquinoline (**9**). The ester substituent of compound (**9**) was reduced in a high yielding indirect sequence. Thus reduction of the ester (**9**) with sodium bis(2-methoxyethoxy)-



Scheme 5. [Bzl = $PhCH_2$] *Reagents:* i $NaAlH_2(OCH_2CH_2OMe)_2$, THF; ii, $SOCl_2$, C_6H_6, then $NaHCO_3$; iii, $LiAlH_4$, THF; iv, BBr_3, CH_2Cl_2

aluminium hydride[11] gave the alcohol (**10**), which was converted into the required 3-methylisoquinoline (**12**) [70% from (**9**)] *via* the chloride (**11**) (Scheme 5). Finally, treatment of the 6,8-dibenzyloxy-1-ethoxyisoquinoline (**12**) with boron tribromide in dichloromethane[12] resulted in simultaneous cleavage of the ethyl and benzyl ethers to give siamine (**1**) in 71% yield.

The spectra (i.r., u.v., ^{1}H n.m.r., m.s.) of synthetic siamine were identical with those described for the natural product.[4,6]

Experimental

For general points see ref. 9.

2-(3,5-*Dibenzyloxyphenyl*)-4,5-*dihydro*-4,4-*dimethyloxazole* (**3**).—Thionyl chloride (4.4 ml, 60 mmol) was added to a stirred suspension of 3,5-dibenzyloxybenzoic acid (**2**) (6.68 g, 20 mmol) in benzene (15 ml). The mixture was refluxed for 1 h, and then evaporated to leave an oily residue which crystallised under vacuum. The crude product was dissolved in dichloromethane (10 ml), and added dropwise to a stirred solution of 2-amino-2-methylpropan-1-ol (3.6 g, 0.04 mol) in dichloromethane (10 ml) at 0 °C. The mixture was stirred at room temperature for 6 h, filtered, and the filtrate was washed with water, dried ($MgSO_4$) and evaporated to give 3,5-dibenzyloxy-*N*-(2-hydroxy-1,1-dimethylethyl)benzamide (7.90 g, 98%) as a clear oil which crystallised on standing. Thionyl chloride (1.55 g) was added dropwise to the above amide (1.72 g). When the addition was complete, the solution was poured into dry ether (15 ml), and, after swirling, the ether was decanted off. The remaining oil was dissolved in ethanol (15 ml) and poured into cold aqueous sodium hydroxide (20%; 40 ml). The resulting precipitate was filtered off, washed with water, and dried to give the *title compound* (**3**) (1.56 g, 95%) (93% overall), m.p. 85—87 °C (Found: C, 77.2; H, 6.6; N, 3.6. $C_{25}H_{25}NO_3$ requires C, 77.5; H, 6.5; N, 3.6%); $\nu_{max.}$($CHCl_3$) 1 640 and 1 590 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.36 (6 H, s), 4.07 (2 H, s), 5.02 (4 H, s), 6.71 (1 H, m), and 7.18—7.50 (12 H, m); *m/z* 387 (M^+, 11%), 296 (6), and 91 (100).

Ethyl 2,4-*Dibenzyloxy*-6-(4,5-*dihydro*-4,4-*dimethyloxazol*-2-*yl*)*benzoate* (**4**).—A solution of butyl-lithium in hexane (1.6M; 1.77 ml, 2.83 mmol) was added dropwise to a stirred solution of the dihydro-oxazole (**3**) (1.00 g, 2.58 mmol) in DME (10 ml) at −78 °C under nitrogen. The resulting green solution was stirred at −78 °C for 1.5 h, treated with ethyl chloroformate (freshly distilled from $CaCO_3$) (1 ml, 10 mmol), and stirred for a further 1 h at −78 °C. The cooling bath was removed, and the mixture was stirred for 2 h at room temperature. Water (5 ml) was added cautiously followed by ether (20 ml) and more water (20 ml). The ether layer was separated, and the aqueous layer was extracted with ether (2 × 20 ml). The combined ether extracts were washed with saturated aqueous sodium hydrogen carbonate, dried ($MgSO_4$), evaporated, and the residue chromatographed to give the *title compound* (**4**) (0.91 g, 77%) as a colourless oil (Found: C, 73.25; H, 6.4; N, 3.4. $C_{28}H_{29}NO_5$ requires C, 73.2; H, 6.3; N, 3.05%); $\nu_{max.}$($CHCl_3$) 1 725, 1 650, and 1 605 cm^{-1}; δ (250 MHz; $CDCl_3$) 1.26—1.41 (9 H, m), 4.04 (2 H, s), 4.31 (2 H, q, *J* 7.5 Hz), 5.04 (2 H, s), 5.07 (2 H, s), 6.64 (1 H, d, *J* 2.25 Hz), 7.10 (1 H, d, *J* 2.25 Hz), and 7.20—7.42 (10 H, m); *m/z* 459 (M^+, 0.4%), 369 (2), 117 (100), and 91 (23).

Ethyl 2,4-*Dibenzyloxy*-6-*formylbenzoate* (**5**).—A mixture of the dihydro-oxazole (**4**) (1.02 g, 2.2 mmol) and iodomethane (3 ml) were heated at reflux under nitrogen for 4 days. The iodomethane was evaporated to give a yellow foam (1.23 g) which consisted mainly of the *N*-methyloxazolinium salt (80% by ^{1}H n.m.r.). The above salt (1.13 g) was dissolved in dry methanol (20 ml) and the stirred solution was cooled to 0 °C.

Sodium borohydride (0.11 g, 2.88 mol) was added in 4 portions over 2 h, and the resulting mixture was stirred for a further 2 h at room temperature. Hydrochloric acid (2M; 10 ml) was added, stirring was continued overnight, and the mixture was extracted with ether–ethyl acetate (1:1; 3 × 20 ml). The organic extracts were combined, washed with aqueous sodium thiosulphate (10%), saturated brine, dried ($MgSO_4$), and evaporated, and the residue chromatographed to give the *title compound* (**5**) [0.40 g, 51% from (**4**)], m.p. 85—86 °C (Found: C, 73.8; H, 5.6. $C_{24}H_{22}O_5$ requires C, 73.85; H, 5.6%); $\nu_{max.}$($CHCl_3$) 1 725, 1 705, and 1 600 cm^{-1}; δ (250 MHz; $CDCl_3$) 1.33 (3 H, t, *J* 7.7 Hz), 4.42 (2 H, q, *J* 7.7 Hz) 5.100 (2 H, s), 5.107 (2 H, s), 6.81 (1 H, d, *J* 2.25 Hz), 7.08 (1 H, d, *J* 2.25 Hz), 7.28—7.46 (10 H, m), and 9.99 (1 H, s); *m/z* 390 (M^+, 2%), 345 (2), 316 (1), 299 (15), 271 (3), 227 (3), 181 (2), 135 (2), and 91 (100).

Ethyl 2-*Azido*-3-(2-*carboxy*-3,5-*dibenzyloxyphenyl*)-*propenoate* (**6**).—A mixture of the ester (**5**) (500 mg, 1.28 mmol) in dioxane (30 ml) and potassium hydroxide (154 mg) in water (10 ml) was stirred at room temperature for 14 h. The mixture was acidified to pH 3, and extracted with dichloromethane (3 × 20 ml). The organic extracts were combined, washed with saturated brine, dried ($MgSO_4$), and evaporated to give 5,7-*dibenzyloxy*-3-*hydroxyphthalide* (430 mg, 93%), m.p. 130—132 °C (Found: C, 73.0; H, 5.0. $C_{22}H_{18}O_5$ requires C, 72.9; H, 5.0%); $\nu_{max.}$($CHCl_3$) 3 260 br, 1 765, 1 620, and 1 610 cm^{-1}; δ (250 MHz; $CDCl_3$) 5.04 (2 H, s), 5.21 (2 H, s), 6.43 (1 H, br s), 6.54 (1 H, s), 6.70 (1 H, s), and 7.27—7.48 (10 H, m); *m/z* 362 (M^+, 2%), 318 (3), 271 (2), 256 (5), and 91 (100).

A solution of the above hydroxyphthalide (1.00 g, 2.76 mmol) and ethyl azidoacetate (1.51 g, 11.71 mmol) in ethanol (8 ml) was added dropwise to a stirred solution of sodium ethoxide [from sodium (0.35 g, 15.22 mmol)] in ethanol (8 ml) at −20 °C. The mixture was stirred at −20 °C for 1 h, at −15 °C for 2 h, and then allowed to reach room temperature. The reaction mixture was poured into ice-cold hydrochloric acid (1M; 50 ml) and extracted with dichloromethane (3 × 50 ml). The organic extracts were combined, washed with saturated brine, dried ($MgSO_4$), and evaporated, and the residue was chromatographed to give the *title compound* (**6**) (0.75 g, 58%) as pale yellow crystals, m.p. 119.5—121 °C (Found: 65.7; H, 4.8; N, 8.6. $C_{26}H_{23}N_3O_6$ requires C, 66.0; H, 4.9; N, 8.9%); $\nu_{max.}$($CHCl_3$) 2 140, 1 720, and 1 597 cm^{-1}; δ (250 MHz; $CDCl_3$) 1.38 (3 H, t, *J* 7.6 Hz), 4.35 (2 H, q, *J* 7.6 Hz), 5.14 (2 H, s), 5.20 (2 H, s), 6.69 (1 H, d, *J* 2.25 Hz), 7.06 (1 H, d, *J* 2.25 Hz), 7.30—7.47 (10 H, br s), and 7.90 (1 H, s); *m/z* 473 (M^+, 0.2%), 445 (1), 354 (2), 345 (1), 254 (1), and 91 (41).

Ethyl 2-*Azido*-3-(3,5-*dibenzyloxy*-2-*ethoxycarbonylphenyl*)-*propenoate* (**7**).—DBU (254 mg, 1.67 mmol) was added dropwise to a stirred suspension of the acid (**6**) (780 mg, 1.65 mmol) in dry acetonitrile at 0 °C under nitrogen. The cooling bath was removed, iodoethane (390 mg, 2.5 mmol) was added dropwise, and the mixture was stirred at room temperature for 4 h with exclusion of light. The mixture was diluted with dichloromethane (60 ml), and then washed with water (2 × 40 ml). The organic layer was dried ($MgSO_4$), evaporated, and the residue chromatographed to give the *title compound* (**7**) (620 mg, 75%) as a clear oil which crystallised on standing, m.p. 103—105 °C (Found: C, 67.1; H, 5.3; N, 8.3. $C_{28}N_{27}N_3O_6$ requires C, 67.1; H, 5.4; N, 8.4%); $\nu_{max.}$($CHCl_3$) 2 020, 1 715, 1 623, 1 600, and 1 575 cm^{-1}; δ (250 MHz; $CDCl_3$) 1.26—1.43 (6 H, 2 × t), 4.27—4.43 (4 H, m), 5.07 (2 H, s), 5.10 (2 H, s), 6.58 (2 H, d), 6.93 (1 H, s), and 7.29—7.48 (10 H, m); *m/z* 473 (M^+ − 28, 5%), 457 (1), 428 (2), 382 (3), 374 (10) 181 (4), and 91 (100).

Ethyl 6,8-*Dibenzyloxy*-1-*oxoisoquinoline*-3-*carboxylate* (**8**).—A solution of the azide (**6**) (513 mg, 1.1 mmol) and triethyl phosphite (200 mg, 1.2 mmol) in dry THF (14 ml) was stirred at room temperature for 18 h. The solvent was evaporated and the residue was dried at 70 °C and 0.1 mmHg for 3 h to give a yellow solid which was purified by chromatography to give the *title compound* (**8**) (302 mg, 65%) as crystals, m.p. 163—164 °C (Found: C, 72.4; H, 5.0; N, 3.3. $C_{26}H_{23}NO_5$ requires C, 72.7; H, 5.4; N, 3.3%); $\nu_{max.}$($CHCl_3$) 3 370, 1 715, 1 657, and 1 600 cm^{-1}; δ (250 MHz; $CDCl_3$) 1.42 (3 H, t, *J* 7.7 Hz), 4.43 (2 H, q, *J* 7.7 Hz), 5.12 (2 H, s), 5.28 (2 H, s), 6.70 (2 H, s), 7.15 (1 H, s), 7.22—7.67 (10 H, m), and 8.75 (1 H, br s); *m/z* 429 (M^+, 16%), 352 (2), 339 (5), 323 (2), 312 (3), 265 (2), 179 (2), and 91 (100).

Ethyl 6,8-*Dibenzyloxy*-1-*ethoxyisoquinoline*-3-*carboxylate* (**9**).—A solution of the azide (**7**) (752 mg, 1.5 mmol) and triethyl phosphite (497 mg, 3 mmol) in dry benzene (50 ml) was heated under reflux for 12 h. The solvent was evaporated, and the triethyl phosphate by-product was distilled off at 75 °C and 0.2 mmHg to give the *title compound* (**9**) (647 mg, 94%) as a solid, m.p. 128.5—130 °C (Found: C, 73.7; H, 6.1; N, 3.1. $C_{28}H_{27}NO_5$ requires C, 73.5; H, 5.9; N, 3.1%); $\nu_{max.}$($CHCl_3$) 1 720, 1 615, and 1 573 cm^{-1}; δ (250 MHz; $CDCl_3$) 1.35—1.50 (6 H, 2 × t), 4.43 (2 H, q, *J* 6.6 Hz), 4.62 (2 H, q, *J* 6.6 Hz), 5.17 (4 H, s), 6.80 (1 H, d, *J* 1.75 Hz), 6.85 (1 H, d, *J* 1.75 Hz), 7.30—7.65 (10 H, m), and 7.93 (1 H, s); *m/z* 457 (M^+, 9%), 442 (3), 324 (3), 181 (3), 149 (3), and 91 (100).

6,8-*Dibenzyloxy*-1-*ethoxyisoquinolin*-3-*ylmethanol* (**10**).—A solution of sodium bis(2-methoxyethoxy)aluminium hydride (3.4M; 0.15 ml, 0.5 mmol) was added to a stirred solution of the ester (**9**) (230 mg, 0.5 mmol) in dry THF (6 ml). The mixture was stirred at room temperature for 1 h, a further portion of reducing agent (0.15 ml, 0.5 mmol) was added, and stirring was continued for 1 h. Aqueous work-up and ether extraction gave an off-white solid which was purified by chromatography to give the *title compound* (**10**) (175 mg, 84%), m.p. 127—129 °C (Found: C, 75.15; H, 6.2; N, 3.4. $C_{26}H_{25}NO_4$ requires C, 75.2; H, 6.0; N, 3.4%); $\nu_{max.}$($CHCl_3$) 3 400, 1 623, 1 605, and 1 575 cm^{-1}; δ (250 MHz; $CDCl_3$) 1.39 (3 H, t, *J* 6.6 Hz), 3.36 (1 H, br s), 4.50 (2 H, q, *J* 6.6 Hz), 4.66 (2 H, br s), 5.13 (4 H, s), 6.64 (1 H, d, *J* 2 Hz), 6.67 (1 H, d, *J* 2 Hz), 6.93 (1 H, s), and 7.20—7.64 (10 H, m); *m/z* 415 (M^+, 8%), 320 (3), 181 (5), 149 (5), 108 (7), and 91 (100).

6,8-*Dibenzyloxy*-3-*chloromethyl*-1-*ethoxyisoquinoline* (**11**).—Thionyl chloride (0.75 ml, 8.7 mmol) was added to a stirred solution of the alcohol (**10**) (240 mg, 0.58 mmol) in dry benzene (20 ml) at room temperature. The mixture was stirred for 1.5 h, and then evaporated to dryness. The residual solid was dissolved in dichloromethane (60 ml), the solution was washed with saturated aqueous sodium hydrogen carbonate (2 × 20 ml), dried ($MgSO_4$), and evaporated to give the *title compound* (**11**) (248 mg, 99%), m.p. 135—137 °C (Found: C, 71.8; H, 5.6; N, 3.2. $C_{26}H_{24}ClNO_3$ requires C, 72.0; H, 5.5; N, 3.2%); $\nu_{max.}$($CHCl_3$) 1 618 and 1 572 cm^{-1}; δ (250 MHz; $CDCl_3$) 1.38 (3 H, t, *J* 6.6 Hz), 4.51 (2 H, q, *J* 6.6 Hz), 4.58 (2 H, s), 5.13 (4 H, s), 6.67 (1 H, d, *J* 2 Hz), 6.71 (1 H, d, *J* 2 Hz), 7.13 (1 H, s), and 7.28—7.64 (10 H, m); *m/z* 433 (M^+, 3%) 399 (1), 338 (4), 279 (3), 181 (7), 149 (14), and 91 (100).

6,8-*Dibenzyloxy*-1-*ethoxy*-3-*methylisoquinoline* (**12**).—Lithium aluminium hydride (13 mg, 0.34 mmol) was added to a stirred solution of the chloride (**11**) (160 mg, 0.37 mmol) in dry THF (4 ml), and the mixture was heated under reflux for 1 h. More lithium aluminium hydride (50 mg, 1.31 mmol) was added, and the mixture refluxed for a further 1 h. Water (4 ml) was added cautiously, and the mixture was stirred at room temperature for 1 h. The liquid was decanted from the aluminium salts, and then extracted with ether (3 × 15 ml). The ether extracts were combined, washed with saturated brine

(2 × 15 ml), dried ($MgSO_4$), evaporated, and the residue purified by chromatography to give the *title compound* (**12**) (123 mg, 84%), m.p. 117 °C (Found: C, 78.3; H, 6.4; N, 3.5. $C_{26}H_{25}NO_3$ requires C, 78.2; H, 6.3; N, 3.5%); $\nu_{max.}$($CHCl_3$), 1 622 and 1 572 cm^{-1}; δ (250 MHz; $CDCl_3$) 1.37 (3 H, t, *J* 6.6 Hz), 2.43 (3 H, s), 4.48 (2 H, q, *J* 6.6 Hz), 5.12 (2 H, s), 5.14 (2 H, s), 6.59 (1 H, d, *J* 2 Hz), 6.61 (1 H, d, *J* 2 Hz), 6.84 (1 H, s), and 7.26—7.63 (10 H, m); *m/z* 399 (M^+, 16%), 384 (4), 370 (2), 181 (5), 149 (1), and 91 (100).

6,8-*Dihydroxy*-3-*methylisoquinolone* (*Siamine*) (**1**).—A solution of boron tribromide in dichloromethane (1M; 0.3 ml, 0.3 mmol) was addded to a solution of the isoquinoline (**12**) (20.3 mg, 0.05 mmol) in dichloromethane (1.5 ml). The mixture was stirred at room temperature under nitrogen for 20 h, and diluted with dichloromethane (1 ml) and water (2 ml). After 1 h, the mixture was extracted with ethyl acetate (3 × 15 ml), and the organic extracts were combined, washed with saturated brine, dried ($MgSO_4$), and evaporated. The residual solid was purified by chromatography to give the *title compound* (**1**) (7.0 mg, 71%), m.p. 260—264 °C (lit.,[5] 268, 264—267, 267—268 °C) (Found: C, 62.95; H, 4.7; N, 7.2. Calc. for $C_{10}H_9NO_3$ C, 62.8; H, 4.7; N, 7.3%); δ [250 MHz; $(CD_3)_2CO$] 2.26 (3 H, s), 6.20 (1 H, s), 6.22 (1 H, d, *J* 2.2 Hz), 6.33 (1 H, d, *J* 2.2 Hz), 9.20 (1 H, br), 10.24 (1 H, br s, NH), and 12.97 (1 H, s, C-8 OH); *m/z* 191 (M^+, 100%).

Acknowledgements

We gratefully acknowledge a N.A.T.O. Science Foundation Programme award (J. J. V.), a Pfizer Postgraduate Scholarship (M. K.), and financial support from Glaxo Group Research (Greenford).

References

1 Part 8, R. E. Bolton, C. J. Moody, C. W. Rees, and G. Tojo, *J. Chem. Soc., Perkin Trans. 1*, 1987, 931.
2 D. M. B. Hickey, A. R. Mackenzie, C. J. Moody, and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1987, 921.
3 B. D. Krane and M. Shamma, *J. Nat. Prod.*, 1982, **45**, 377.
4 B. Z. Ahn and F. Zymalkowski, *Tetrahedron Lett.*, 1976, 821.
5 B. Z. Ahn, U. Degen, C. Lienjayetz, P. Pachaly, and F. Zymalkowski, *Arch. Pharm.* (*Weinheim Ger.*), 1978, **311**, 569.
6 S. M. El-Sayyad, S. A. Ross, and H. M. Sayed, *J. Nat. Prod.*, 1984, **47**, 708.
7 N. Katagiri, J. Nakano, and T. Kato, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2710.
8 (a) A. I. Meyers, D. L. Temple, D. Haidukewych, and E. D. Mihelich, *J. Org. Chem.*, 1974, **39**, 2787; (b) A. R. Leed, S. D. Boettger, and B. Ganem, *ibid.*, 1980, **45**, 1098.
9 L. Henn, D. M. B. Hickey, C. J. Moody, and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1984, 2189.
10 N. Ono, T. Yamada, T. Saito, K. Tanaka, and A. Kaji, *Bull. Chem. Soc. Jpn.*, 1978, **51**, 2401.
11 N. Cohen, R. J. Lopresti, and G. Saucy, *J. Am. Chem. Soc.*, 1979, **101**, 6710.
12 J. B. Press, *Synth. Commun.*, 1979, **9**, 407.

Received 7th August 1986; *Paper* 6/1610