A Specific and Efficient Synthesis of (±)-Dihydrocorynantheol

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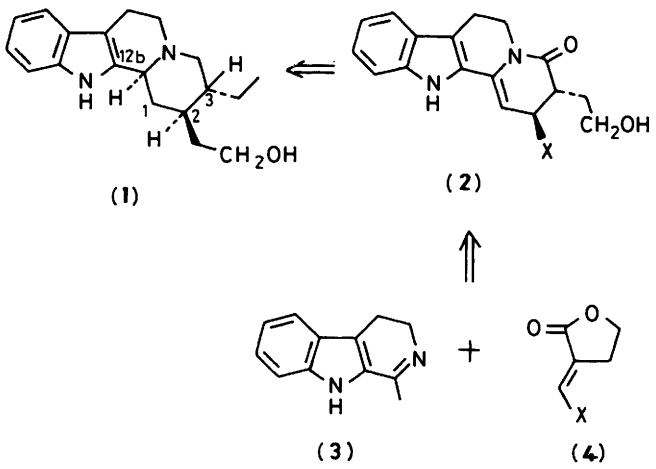
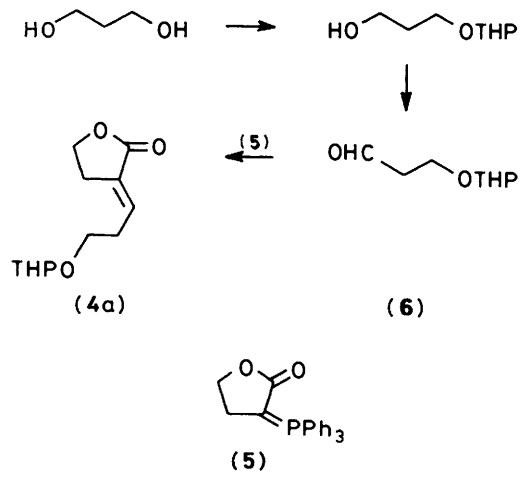
A specific and efficient synthesis of (±)-dihydrocorynantheol (**1**) is reported. Starting with the easily accessible imine (**3**), ring D was built *via* stereoselective reaction with the lactone (**4a**), thus providing the complete carbon skeleton of (**1**); subsequent elaboration gave the desired alkaloid (**1**).

In our previous paper[1] we discussed a basic strategy for the construction of ring D of indoloquinolizidine alkaloids culminating in the synthesis of (±)-deplancheine. We now report the application of this method to a convenient and efficient, stereoselective synthesis of (±)-dihydrocorynantheol (**1**)†[,2–5] as a further example of its usefulness in the preparation of Corynanthé-type alkaloids. The strategy chosen for this total synthesis evolved from the retrosynthetic reasoning outlined in Scheme 1. The first phase of this approach involved the elaboration of the enamide (**2a**), embodying the entire carbon skeleton of (**1**), from the imine (**3**)[6] and the (*E*)-lactone (**4a**). This was to be prepared in a totally stereoselective manner by the reaction of dihydro-3-(triphenylphosphoranylidene)furan-2(3*H*)-one (**5**)[7] with the protected aldehyde (**6**), readily available from propane-1,3-diol (Scheme 2). Addition of (**3**) to (**4a**) by reaction at 80 °C for 30 h in dimethylformamide, by alkylation–cyclisation in a two-reaction one-pot sequence, gave with a high degree of steoselectivity a 19:1 diastereoisomeric mixture (71% yield) from which the major isomer (**2a**) was successfully isolated by standard silica gel chromatography. The predominant diastereoisomer may be presumed to have the 'correct' stereochemistry at C-2 and C-3 (*i.e.*, 2*S**,3*R**) as suggested by Zimmerman's theoretical considerations[8] on the stereochemical outcome of the ketonisation of enolates in Michael addition. As documented in our previous study,[9] this proposal was confirmed by analogy with closely related enamides (**2b**) and (**2c**), prepared by alkylation of (**3**) with the appropriate 3-alkylidenefuran-2(3*H*)-ones (**4b**) and (**4c**), respectively. In particular, we examined the ^{1}H n.m.r. spectra of (**2b**) in which the 2-H proton appears at δ 2.15 as a doublet of triplets with coupling constants of 6.2 and 2.5 Hz. This suggests that ring D adopts a half-chair conformation in which 2-H lies in the plane of π-enamide system and the C-3 substituent is axially disposed owing to steric strain with both the C-2 residue and the carbonyl group in the alternative conformation. To complete the stereoselective elaboration of ring D in the target molecule, it is necessary to reduce the double bond in the enamide moiety from the face opposite to the C-2 alkyl appendage. Kametani and co-workers[4] accomplished this task, albeit in low yields or without appreciable stereoselectivity, by catalytic hydrogenation in the presence of PtO_2 or Pd–C, respectively. In our hands, total stereoselectivity was attained in the formation of the 'desired' stereoisomer (**7**) (78% yield) by chemoselective reduction of the carbonyl group [lithium aluminium hydride in refluxing tetrahydrofuran (THF)] and, without isolation, by addition of an equimolar amount of sodium borohydride to the intermediate iminium derivative (**11**). The remarkable stereoselectivity in the latter reduction may presumably be ascribed to the following steric as well as electronic effects. The underside



THP = tetrahydro-2*H*-pyran-2-yl
a; X = CH_2CH_2OTHP
b; X = Pr^i
c; X = Et

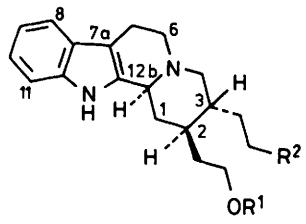
Scheme 1.



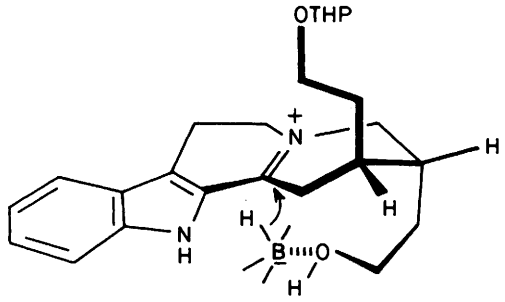
Scheme 2.

approach of the hydride ion towards the imino π-bond of (**11**) is preferred in view of the steric hindrance of the bulky C-2 residue. Moreover, hydride delivery to the C-12b position by the alkanol side chain at C-3 is considered to be of importance. The final stage of the synthesis, mainly the removal of the undesired hydroxy group, was achieved *via* the reduction of the selenide (**8**), readily available from (**7**) by the *o*-nitroselenophenyl cyanate–tributylphosphine method.[10] Deprotection of the

† This compound occurs in laevorotatory form in the bark of *Aspidosperma marcgravium* Woodson (S. Gilbert, L. D. Antonaccio, and C. Djerassi, *J. Org. Chem.*, 1962, **27**, 4702).



(7) R^1 = THP, R^2 = OH
(8) R^1 = THP, R^2 = *o*-$O_2NC_6H_4Se$-
(9) R^1 = H, R^2 = *o*-$O_2NC_6H_4Se$-
(10) R^1 = H, R^2 = *o*-$H_2NC_6H_4Se$-



(11)

hydroxy group located on the C-2 appendage *via* acid hydrolysis (pyridinium toluene-*p*-sulphonate, ethanol) gave the corresponding alcohol (**9**) which, without purification, was treated with triphenylstannane[11] in refluxing toluene to afford the target molecule (**1**) in 55% yield [starting from (**7**)]. A similar result was obtained by treatment of (**9**) with W-2 Raney nickel in ethanol at room temperature in comparable yield. To our surprise, an attempt to carry out such a reaction using tri-n-butylstannane–azoisobutyronitrile under typical conditions was thwarted, the aminoselenide (**10**) being the only isolable product.

The racemic dihydrocorynantheol so obtained was identical (mass spectra and t.l.c.) with a sample kindly supplied by Professor Takano, Tohoku University, Aobayama, and the structure was further corroborated by ^{13}C n.m.r. analysis.

Experimental

I.r. spectra were recorded on a Perkin-Elmer 681 spectrometer in chloroform solutions, u.v. spectra on a Perkin-Elmer model 554 in ethanol. ^1H N.m.r. spectra were recorded on Varian EM-360 A (60 MHz), Bruker WP-80 (80 MHz), and Varian XL-200 (200 MHz) spectrometers with deuteriochloroform as solvent, unless otherwise stated, and tetramethylsilane as internal standard. ^{13}C N.m.r. spectra were taken on a Varian XL-100 spectrometer at 25.2 MHz, using tetramethylsilane as internal reference. Mass spectra (electron impact) were determined using Varian 112 (model 212 for high-resolution spectra) and CH-7 spectrometers. Gas chromatography was carried out using columns packed with 30% silicone gum rubber SE-30 on Chromosorb P. H.p.l.c. was performed on a Perkin-Elmer system (2/2 dual pump module, LC-85 spectrophotometric u.v. detector) and a Lichrosorb RP-8 (10 mμ, Merck) column with acetonitrile–methanol as the mobile phase. T.l.c. was performed on 0.25 mm thick layers of silica gel GF_{254} (Merck) on glass plates. Compounds were detected on developed chromatograms by fluorescence quenching (λ 254 or 365 nm) or visualised with cerium(IV) ammonium sulphate (CAS, 1% in 85% phosphoric acid); R_F and colour (CAS spray on t.l.c.) of products are given. Flash chromatography (f.c.) was carried out as described by Still *et al.*[12] and performed with silica gel S (Merck) 230—400 mesh. All solvents were purified by standard procedures before use.

Synthesis of (E)-*Dihydro*-3-[3-(*tetrahydro*-2H-*pyran*-2-*yl*)-*oxypropylidene*]*furan*-2(3H)-*one* (**4a**).—To a stirred solution of propane-1,3-diol (5 g, 66 mmol) in dry dichloromethane (200 ml), pyridinium toluene-*p*-sulphonate (1.6 g, 6.6 mmol) and dihydropyran (6 ml, 66 mmol) were added at room temperature. After 4 h the solution was washed with brine, dried, and evaporated to dryness. The residual oil was purified by f.c. with ethyl acetate–hexane (7:3) as eluant yielding pure 3-[(tetrahydro-2*H*-pyran-2-yl)oxy]propan-1-ol (7.6 g, 72%), b.p. 59—60 °C at 0.1 mmHg; δ_H 1.30—2.10 (8 H, m), 3.30—4.25 (6 H, m, CH_2O), and 4.62 (1 H, m, OCHO).

A solution of the preceding protected alcohol (4.8 g, 30 mmol) in dichloromethane (200 ml) was added to a slurry of sodium acetate (6.74 g, 69 mmol) and pyridinium chlorochromate (10.34 g, 48 mmol) in the same solvent (50 ml) dropwise during 10 min. The mixture was stirred at room temperature for 24 h when diethyl ether (300 ml) was added to precipitate the chromium salts. The dark brown solution was then filtered through Florisil, dried, and concentrated to afford a clear oil (4.3 g). F.c. with ethyl acetate–hexane (7:3) as eluant furnished pure 3-[(tetrahydro-2*H*-pyran-2-yl)oxy]propanal (**6**) (2.98 g, 63%), b.p. 60—62 °C at 0.5 mmHg; $\nu_{max.}$ 2 940 and 1 720 cm^{-1}; $\delta_H(CCl_4)$ 2.60 (2 H, dt, *J* 5.2 and 1.0 Hz, CH_2CHO), 4.55 (1 H, m, OCHO), and 9.84 (1 H, t, *J* 1.0 Hz, *CHO*); *m/z* 158 (M^+, 3%), 157 (13), 101 (21), and 85 (100).

The preceding compound (**6**) (1.4 g, 8.8 mmol) was dissolved in dry benzene (50 ml). Recrystallised dihydro-3-(triphenylphosphoranylidene)furan-2(3*H*)-one (**5**)[7] (3.05 g, 8.8 mmol) was added under nitrogen and the progress of the reaction monitored by t.l.c. After 4 h at reflux, the solution was cooled, washed with brine, dried, and evaporated to give a colourless viscous oil (1.9 g). F.c. with diethyl ether–dichloromethane (9:1) as eluant yielded compound (**4a**) (1.3 g, 66%) as a thick oil, 95% pure by g.l.c.; $\nu_{max.}$ 1 750 and 1 680 cm^{-1}; δ_H 2.94 (2 H, m, CH_2CH_2OCO), 3.30—4.10 (4 H, m, 2 × OCH_2), 4.42 (2 H, t, *J* 8 Hz, CH_2OCO), 4.60 (1 H, m, OCHO), and 6.83 (1 H, tt, *J* 7.5 and 2.5 Hz, HC=); *m/z* 227 (M^+ + 1, 9%), 196 (10), 171 (14), 142 (33), and 125 (100).

(E)-*Dihydro*-3-*isobutylidenefuran*-2(3H)-*one* (**4b**).—Compound (**4b**) was prepared by the method described for (**4a**) by the reaction of the ylide (**5**) and 2-methylpropanal on a 5 mmol scale, and was obtained in 90% yield, as a colourless oil, >95% pure by g.l.c.; $\nu_{max.}$ 1 745 and 1 675 cm^{-1}; δ_H (60 MHz) 1.16 (6 H, d, *J* 7 Hz, Me_2C), 2.46 (1 H, m, Me_2CH), 2.93 (2 H, dt, *J* 7 and 2.5 Hz, CH_2CH_2OCO), 4.45 (2 H, t, *J* 7 Hz, CH_2OCO), and 6.65 (1 H, dt, *J* 7.5 and 2.5 Hz, HC=).

(E)-*Dihydro*-3-*propylidenefuran*-2(3H)-*one* (**4c**).—Compound (**4c**) was prepared by the method described for (**4a**) by the reaction of (**5**) and propanal, and was obtained in 84% yield as a colourless oil, 95% pure by g.l.c.; $\nu_{max.}$ 1 760 and 1 665 cm^{-1}; δ_H (60 MHz) 1.12 (3 H, t, *J* 7 Hz, CH_3CH_2), 2.21 (2 H, quint., *J* 7 Hz, CH_3CH_2), 2.83 (2 H, br, t, *J* 7 Hz, OCH_2CH_2), 4.40 (2 H, t, *J* 7 Hz, OCH_2), and 6.75 (1 H, tt, *J* 7.5 and 2.5 Hz, HC=).

(2S*,3R*)-2,6,7,12-*Tetrahydro*-3-(2-*hydroxyethyl*)-2-[2-(*tetrahydro*-2H-*pyran*-2-*yloxyethyl*]*indolo*[2,3-a]*quinolizin*-4(3H)-*one* (**2a**).—To a solution of 4,9-dihydro-1-methyl-3*H*-pyrido[3,4-*b*]indole (**3**)[6] (0.92 g, 5 mmol) in dry *N*,*N*-dimethylformamide (10 ml) the lactone (**4a**) (1.24 g, 5.5 mmol) was added and the solution was heated to 80 °C under nitrogen

for 30 h. The solution was cooled, solvent removed under reduced pressure, and the dark residue purified by f.c. with ethyl acetate as eluant to afford the *tetracyclic ketone* (**2a**) (1.37 g, 67%) R_F 0.37 (ethyl acetate–propan-2-ol–ammonia, 48:2:1) (orange-yellow spot) as a colourless foam which did not crystallise, >95% pure by h.p.l.c. (Found: C, 70.05; H, 7.4; N, 6.8. $C_{24}H_{30}N_2O_4$ requires C, 70.2; H, 7.4; N, 6.8%); $\nu_{max.}$ 3 460, 1 665, and 1 645 cm^{-1}; $\lambda_{max.}$ (log ε) 231 (4.46), 309 (4.28), and 321 nm (4.30); δ_H 2.65 (1 H, br, dt, *J* 7 and 2.5 Hz, 3-H), 3.00 (2 H, m, 7-H), 4.55 (1 H, m, OCHO), 4.68 (1 H, dt, *J* 12 and 6 Hz, 6β-H), 5.50 (1 H, d, *J* 6.1 Hz, 1-H), and 8.12 (1 H, br, s, NH); *m/z* 410 (M^+, 43%), 366 (15), 365 (39), 325 ($M^+ - C_5H_9O$, 100), 281 (95), 237 (64), 235 (34), 184 (22), and 144 (16). A less polar compound (82 mg, 4%) with R_F 0.42 (ethyl acetate–propan-2-ol–ammonia, 48:2:1, orange spot), thought to be a diastereoisomer of compound (**2a**) was isolated in an impure state; $\lambda_{max.}$ 230, 310, and 320 nm; *m/z* 410 (M^+, 56%) and 325 ($M^+ - C_5H_9O$, 100).

(2R*,3R*)-2,6,7,12-*Tetrahydro*-3-(2-*hydroxyethyl*)-2-*isopropylindolo*[2,3-a]*quinolizin*-4(3H)-*one* (**2b**).—By the procedure described for the preparation of (**2a**), the *isopropyl derivative* (**2b**) was obtained in 56% yield by the reaction of the unsaturated lactone (**4b**) with the imine (**3**), as a colourless glass which did not crystallise, R_F 0.22 (ethyl acetate–chloroform, 7:3) (orange spot), >95% pure by h.p.l.c. (Found: C, 74.3; H, 7.5; N, 8.7. $C_{20}H_{24}N_2O_2$ requires C, 74.05; H, 7.5; N, 8.6%); $\nu_{max.}$ 3 460, 1 665, and 1 640 cm^{-1}; $\lambda_{max.}$ (log ε) 231 (4.48), 312 (4.30), and 320 nm (4.29); δ_H (200 MHz) 0.95 (3 H, d, *J* 6.7 Hz, diastereotopic Me), 1.00 (3 H, d, *J* 6.7 Hz, diastereotopic Me), 1.6—1.9 (3 H, m, CH_2CH_2OH and Me_2CH), 2.15 (1 H, dt, *J* 6.2 and 2.5 Hz, 2-H), 2.78 (1 H, m, 3-H), 2.94 (2 H, m, 7-H), 3.38 (1 H, ddd, $J_{6\alpha,6\beta}$ 13.2 Hz, $J_{6\alpha,7\alpha}$ 5.8 Hz, $J_{6\alpha,7\beta}$ 9.1 Hz, 6α-H), 3.72 (2 H, t, *J* 5.8 Hz, CH_2OH), 4.78 (1 H, dt, $J_{6\alpha,6\beta}$ 13.2 Hz, $J_{6\beta,7\alpha} \approx J_{6\beta,7\beta}$ = 3.7 Hz, 6β-H), 5.43 (1 H, d, *J* 6.2 Hz, 1-H), and 8.30 (1 H, s, NH); *m/z* 324 (M^+, 17%), 282 (17), 281 (80), 260 (20), 259 (100), 237 (13), 235 (15), and 199 (17).

(2S*,3R*)-2-*Ethyl*-2,6,7,12-*tetrahydro*-3-(2-*hydroxyethyl*)-*indolo*[2,3-a]*quinolizin*-4(3H)-*one* (**2c**).—By the procedure described for the preparation of (**2a**), the *enamide* (**2c**) was obtained in 65% yield by the reaction of the lactone (**4c**) with (**3**) as a colourless glass, R_F 0.24 (ethyl acetate–chloroform, 7:3; orange-yellow spot), >95% pure by h.p.l.c. (Found: C, 73.7; H, 7.1; N, 8.9. $C_{19}H_{22}N_2O_2$ requires C, 73.5; H, 7.1; N, 9.0%); $\nu_{max.}$ 3 455, 1 665, and 1 645 cm^{-1}; $\lambda_{max.}$ (log ε) 227 (4.50), 308 (4.30), and 319 nm (4.27); δ_H (200 MHz) 0.94 (3 H, t, *J* 7.0 Hz, $MeCH_2$), 1.48 (2 H, dq, $J_1 = J_2$ = 7.0 Hz, CH_2Me), 1.81 (2 H, m, CH_2CH_2OH), 2.20 (1 H, m, 2-H), 2.67 (1 H, m, 3-H), 2.86 (2 H, m, 7-H), 3.54 (1 H, ddd, $J_{6\alpha,6\beta}$ 13.0, $J_{6\alpha,7\alpha}$ 6.0, $J_{6\alpha,7\beta}$ 9.0 Hz, 6α-H), 3.74 (2 H, t, *J* 6.0 Hz, CH_2OH), 4.60 (1 H, dt, $J_{6\alpha,6\beta}$ 13.0, $J_{6\beta,7\beta} \approx J_{6\beta,7\beta}$ = 5.0, 6β-H), 5.54 (1 H, d, *J* 6.0 Hz, 1-H), 7.30 (1 H, br, d, *J* 8.3 Hz, 8-H), 7.48 (1 H, br, d, *J* 8.1 Hz, 11-H), and 8.84 (1 H, s, NH); δ_C 11.7 (C-13), 20.6 (C-7), 27.4 (C-14), 33.7 (C-16), 37.8 (C-2), 39.5 (C-6), 44.0 (C-3), 60.4 (C-15), 102.8 (C-1), 110.8 (C-7a), 111.0 (C-11), 118.5 (C-8), 119.3 (C-10), 122.8 (C-9), 126.3 (C-12b), 128.0 (C-9a), 129.1 (C-12a), 137.4 (C-11a), and 172.2 p.p.m. (C=O); *m/z* 310 (M^+, 24%), 281 (37), 263 (100), 237 (61), 168 (28), 183 (37), 167 (24), and 144 (48).

Reduction of (**2a**) *to* (2R*,3R*,12bS*)-1,2,3,4,6,7,12,12b-*Octahydro*-3-(2-*hydroxyethyl*)-2-[2-(*tetrahydro*-2H-*pyran*-2-*yloxy*)*ethyl*]*indolo*[2,3-a]*quinolizine* (**7**).—To a slurry of lithium aluminium hydride (74 mg, 2.0 mmol) in dry tetrahydrofuran (50 ml) cooled in an ice–salt bath was added a solution of (**2a**) (820 mg, 2.0 mmol) in the same solvent (100 ml). The cold bath was removed, the mixture refluxed under nitrogen, and the progress of the reaction followed by t.l.c. analysis. After 3 h, the mixture was allowed to cool to ambient temperature and sodium borohydride (39 mg, 1.0 mmol) in propan-2-ol (2 ml) was added, whereupon the colour of the suspension turned from green to pale yellow. After 1 h the reaction was cooled to 0 °C and decomposed by addition of water (2 ml), 15% aqueous sodium hydroxide (2 ml), and finally water (10 ml). The aluminates were filtered off and washed with chloroform. The combined organic layers were dried and evaporated to leave a yellowish oil (0.73 g). F.c. with ethyl acetate–diethylamine (19:1) as eluant yielded the tetracycle (**7**) (621 mg, 78%); R_F 0.28 (ethyl acetate–propan-2-ol–ammonia, 48:2:1, pale green spot), as a pale yellow gum. Trituration with diethyl ether gave (**7**) as an off-white powder of indefinite m.p.; >95% pure in h.p.l.c.; $\nu_{max.}$ 3 470 cm^{-1}; $\lambda_{max.}$ (log ε) 228 (4.58), 281 (3.88), and 290 nm (sh) (3.78); δ_H 4.58 (1 H, br, t, *J* 7 Hz, OCHO) and 7.78 (1 H, s, NH); δ_C 21.7 (C-7), 25.4 (3-CH_2), 30.8 (2-CH_2), 34.1 (C-1), 37.8* (C-2), 38.0* (C-3), 53.1 (C-6), 59.8 (C-4), 60.3 (CH_2OH), 61.2 (C-12b), 65.2 (CH_2OCO), 99.2 (OCO), 107.2 (C-7a), 110.8 (C-11), 117.7 (C-8), 118.8 (C-9), 120.7 (C-10), 127.2 (C-7b), 135.2 (C-12a), and 136.2 p.p.m. (C-11a) (Found: M^+, *m/z* 398.256 82. $C_{24}H_{34}N_2O_3$ requires *M*, 398.256 75).

(2R*,3R*,12bS*)-1,2,3,4,6,7,12,12b-*Octahydro*-3-[2-(2-*nitrophenylseleno*)*ethyl*]-2-[2-(*tetrahydro*-2H-*pyran*-2-*yloxy*)*ethyl*]-*indolo*[2,3-a]*quinolizine* (**8**).—Tri-n-butylphosphine (241 mg, 1.19 mmol) was injected dropwise during 5 min into a magnetically stirred solution of (**7**) (398 mg, 1.0 mmol) and 2-nitrophenylselenocyanate (270 mg, 1.19 mmol) in dry tetrahydrofuran (5 ml) under nitrogen. After 12 h at room temperature, a substantial amount of (**7**) remained (t.l.c.). More 2-nitrophenylselenocyanate (113.5 mg, 0.5 mmol) and tri-n-butylphosphine (101 mg, 0.5 mmol) were added and, after a further 3 h at ambient temperature, the solvent was removed *in vacuo*. F.c. of the yellow residue (1.2 g) with ethyl acetate–chloroform (1:1) as eluant yielded the yellow *protected selenide* (**8**) (477 mg, 82%); R_F 0.65 (ethyl acetate–propan-2-ol–ammonia, 48:2:1; green spot) (Found: C, 62.1; H, 6.4; N, 7.2. $C_{30}H_{37}N_3O_4Se$ requires C, 61.8; H, 6.4; N, 7.2%); $\nu_{max.}$ 3 470, 2 870, 2 805, and 2 750 cm^{-1}; δ_H 4.57 (1 H, m, OCHO), 7.88 (1 H, s, NH), and 8.31 (1 H, dd, *J* 8 and 1.5 Hz, *o*-nitro proton); *m/z* 582 (M^+, 3%), 397 (12), 344 (11), 342 (10), 278 (100), 201 (22), 199 (26), 184 (15), and 170 (28).

Reduction of the Selenide (**8**) *to* (2R*,3R*,12bS*)-3-*Ethyl*-1,2,3,4,6,7,12,12b-*octahydro*-2-(2-*hydroxyethyl*)*indolo*[2,3-a]-*quinolizine*, (±)-*Dihydrocorynantheol* (**1**).—Compound (**8**) (400 mg, 0.68 mmol) and pyridinium toluene-*p*-sulphonate (16 mg) were dissolved in absolute ethanol (20 ml) and the mixture was stirred at 50 °C for 3 h. The solution was diluted with ethyl acetate (80 ml), washed with water, and dried to give the almost pure deprotected selenide (**9**) (333 mg, 98.5%) with R_F 0.38 (ethyl acetate–propan-2-ol–ammonia, 48:2:1) as a green spot.

(a) The deprotected selenide (**9**) (200 mg, 0.4 mmol) was heated in toluene (5 ml) in preheated oil-bath (120—125 °C) and triphenylstannane (704 mg, 2.0 mmol) was added during 10 min. The resulting solution was warmed at reflux for 5 h, and then cooled to room temperature. The mixture was evaporated to dryness and the recovered pale yellow oil was separated by p.l.c. [chloroform–methanol (9:1) as developer] to yield pure (±)-dihydrocorynantheol (**1**) (81 mg, 68%) as a crystalline solid; R_F 0.26 (chloroform–methanol, 9:1; green spot). Recrystallisation from chloroform gave colourless prisms, m.p. 179—180 °C (lit.,[3] 178—180.5 °C) (Found: C, 76.8; H, 9.4; N, 9.4. Calc. for $C_{19}H_{26}N_2O$: C, 76.5; H, 8.8; N, 9.4%); $\nu_{max.}$ 3 470, 2 800, and 2 760 cm^{-1}; $\lambda_{max.}$ (log ε) 277 (4.55), 281 (3.85), and 292 nm (sh) (3.81); δ_C 11.2 (CH_3), 22.3† (C-7), 22.4† (CH_2CH_3), 35.7† (C-

† Values may be interchanged.

$2CH_2$), 36.6† (C-1), 38.1 (C-2), 48.8 (C-3), 54.3 (C-6), 60.3 (C-4), 61.3 (C-12b), 61.6 (COH), 107.6 (C-7a), 111.8 (C-11), 118.4 (C-8), 119.6 (C-10), 121.8 (C-7b), 135.5 (C-12a), and 136.4 p.p.m. (C-11a); *m/z* 298 (M^+, 76%), 297 (100), 253 (11), 225 (19), 184 (10), 170 (26), 169 (23), and 156 (16).

(*b*) A solution of (**9**) (100 mg, 0.2 mmol) in ethanol (2 ml) was added to a slurry of W-2 Raney nickel (0.5 g, wet weight in ethanol), and the mixture was shaken at room temperature until the yellow colour disappeared (5 min) and then filtered through a plug of Celite. The collected Raney nickel was washed immediately with ethanol (10 ml). The combined filtrate and ethanol washes were evaporated to give a dark syrup which was chromatographed with chloroform–methanol (9:1) to yield dihydrocorynantheol (**1**) (39 mg, 65%), m.p. 177—179 °C (chloroform) identical with the sample just described.

Reduction of (**8**) *with Tri-n-butylstannane–Azoisobutyronitrile* (AIBN).—To a solution of (**9**) (200 mg, 0.4 mmol) in dry toluene (5 ml) warmed under nitrogen at 125 °C was added dropwise during 5 min a solution of tri-n-butylstannane (465 mg, 1.6 mmol) and AIBN (5 mg) in toluene (2 ml). The resulting solution was warmed at reflux for 3 h, and then cooled to ambient temperature and concentrated *in vacuo*. The residual yellow oil (0.71 g) was chromatographed with chloroform–methanol (19:1) as eluant to leave the amino derivative (**10**) as a pale yellow powder (133 mg, 71%), R_F 0.50 (chloroform–methanol, 17:3; green spot); $\nu_{max.}$ 3 470, 3 360, 2 805, 2 765, and 1 605 cm^{-1}; $\lambda_{max.}$ 226, 284, and 291 nm; δ_H 3.62 (2 H, br s, NH_2), 6.65 (1 H, br, t, *J* 7.5 Hz, 4′-H), 6.70 (1 H, br d, *J* 7.5 Hz, 6′-H), and 8.48 (1 H, br s, NH); δ_C 21.6 (C-7), 24.6 (3-CH_2), 29.7† (2-CH_2), 31.7† (CH_2Se), 35.2 (C-1), 36.9 (C-3), 40.7 (C-2), 53.0 (C-6), 59.7 (C-12b), 59.9† (C-4), 60.3 † (CH_2OH), 107.7 (C-7a), 111.0 (C-11), 113.9 (C-2′), 114.7 (C-6′), 118.0 † (C-8), 118.7 † (C-4′), 119.7 (C-10), 121.2 (C-9), 127.3 (C-7b), 130.0 (C-5′), 134.7 (C-12a), 136.2 † (C-11a), 137.6† (C-3′), and 148.4 p.p.m. (C-1′) (Found: M^+, *m/z* 467.163 80. $C_{25}H_{31}N_3O^{78}Se$ requires *M*, 467.163 89).

† Values may be interchanged.

References

1 L. Calabi, B. Danieli, G. Lesma, and G. Palmisano, *Tetrahedron Lett.*, 1982, 2139.
2 C. Vamvacas, W. v. Philipsborn, E. Schlitter, H. Schmid, and P. Karrer, *Helv. Chim. Acta*, 1957, **40**, 1793.
3 F. E. Zielger and J. G. Sweeny, *Tetrahedron Lett.*, 1969, 1097.
4 T. Kametani, N. Kanaya, H. Hino, S.-P. Huang, and M. Ihara, *Heterocycles*, 1980, **14**, 1771.
5 S. Takano, K. Shibuya, M. Takahashi, S. Hatakeyama, and K. Ogasawara, *Heterocycles*, 1981, **16**, 1125.
6 R. H. F. Manske, W. H. Perkins, and R. Robinson, *J. Chem. Soc.*, 1927, 11.
7 S. Fliszàr, R. F. Hudson, and G. Salvadori, *Helv. Chim. Acta*, 1963, **46**, 1580.
8 H. E. Zimmerman and W. H. Chiang, *J. Am. Chem. Soc.*, 1959, **81**, 3634.
9 B. Danieli, G. Lesma, G. Palmisano, and S. Tollari, *Synthesis*, in the press.
10 P. A. Grieco, S. Gilman, and M. Nishizawa, *J. Org. Chem.*, 1976, **41**, 1485.
11 D. L. J. Clive, G. Chittattu, and C. K. Wong, *J. Chem. Soc., Chem. Commun.*, 1978, 41.
12 W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.

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