Regioselective total synthesis of edulane and its angular analogue

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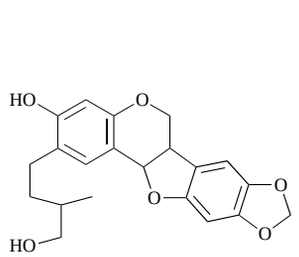
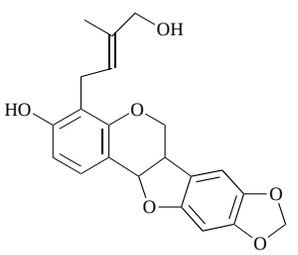
1 PERKIN

Herein we describe a 10-step total synthesis of edulane 3 and its angular analogue 18 from phloroglucinol. The key step involves $ZnCl_2$-catalysed condensation of the appropriately substituted 2*H*-chromenes 8, 9 and 10 with the 2-alkoxy-1,4-benzoquinones 11 and 12, respectively.

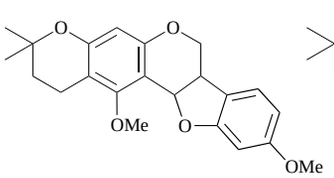
A large number of naturally occurring isoflavonoid phytoalexins possessing a furan ring system are biologically active,[1] *e.g.* carbenegrin A-I **1** and carbenegrin A-II **2** isolated from the



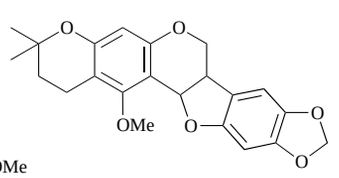
1 Carbenegrin A-I



2 Carbenegrin A-II



3 Edulane



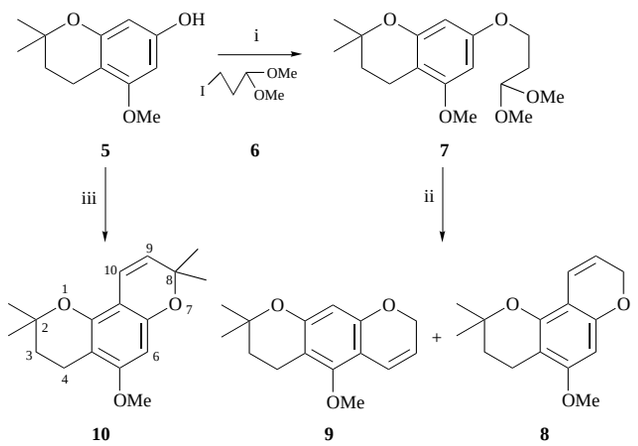
4 Neorautanin

roots of the plant 'carbeeca de negra', have been shown to have potent anti snake venom activity.[2] Because of the significant biological activity associated with the pterocarpans, considerable efforts have recently been directed towards the total synthesis of such naturally occurring compounds.[3,4] Thus, a one-step, Ti^{IV}-catalysed synthesis of substituted pterocarpans has been developed by Engler *et al.* through the reaction of 2-alkoxy-1,4-benzoquinones with appropriately substituted 2*H*-chromenes.[3b,c,5] We have also reported an essentially quantitative method for the synthesis of this class of compounds using $ZnCl_2$ as catalyst.[6]

In continuation of our work on the regioselective[6,7] and enantioselective[8] synthesis of substituted pterocarpans, we have attempted a total synthesis of edulane **3**, a pterocarpan isolated from the root bark of the *Neorautania edulis* by Brink *et al.*,[9] and its angular analogue **18**. Herein we describe this 10-step synthesis from phloroglucinol.

Results and discussion

7-Hydroxy-5-methoxychroman **5** was prepared from phloroglucinol in a 5-step synthesis.[10] 3-Iodopropanal dimethyl acetal **6**[11] on reaction with chroman **5** in K_2CO_3–acetone under reflux gave the acetal **7** (74%; Scheme 1), acid-catalysed cyclisation[4] of which in dry dioxane gave the chromenes **8** and **9** (64%; 1:2 ratio). It was found that an increase in either the reaction time or the temperature led to complete decomposition of the product. Signals at δ 6.70 (1 H, d, *J* 9.81 Hz) and 5.5 (1 H, td, *J* 3.84 and 9.8 Hz) in the ^{1}H NMR spectrum confirmed the identity of

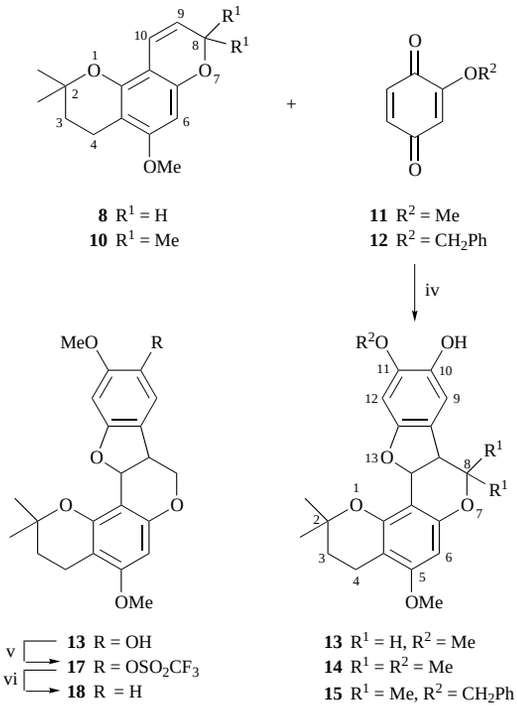


5 **6** **7** **10** **9** **8**

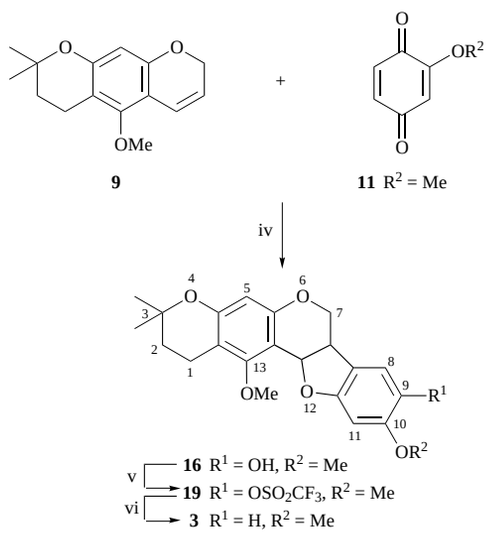
Scheme 1 *Reagents and conditions*: i, K_2CO_3, acetone, reflux, 12 h; ii, dry dioxane, *p*-TsOH, 68 °C, 2 h; iii, pyridine, 3-methylbut-2-enal, 140 °C, 48 h

the chromenes **8** and **9**. In order to ascertain the linear and angular fusion of the chromenes formed, NOE studies on **8** and **9** were carried out. Irradiation of the methoxy proton signal of chromene **8** at δ 3.76 led to an enhancement of the single aromatic proton singlet at δ 5.97. This indicated that the two aromatic carbons, *i.e.* the one bearing the methoxy and the other unsubstituted, are adjacent. This is possible only in the angular chromene **8**. Likewise, irradiation of the methoxy signal of chromene **9** at δ 3.74 gave enhancement of the olefinic proton at δ 6.61 indicating it to be the linear compound. Base-catalysed thermal cyclisation[12] of 7-hydroxy-5-methoxychroman **5** with 3-methylbut-2-enal in pyridine gave the chromene **10** (68%), which was confirmed by the appearance of two one-proton doublets with *J* 9.7 Hz at δ 5.37 and 6.59 for 9- and 10-H, respectively. An irradiation study of this chromene clearly confirmed it to be the angular compound.

The 2*H*-chromenes **8**, **9** and **10** were subjected to $ZnCl_2$-catalysed condensation with 2-alkoxy-1,4-benzoquinones **11** and **12** to afford the corresponding pterocarpans **13, 14, 15** and **16** in good yields (Schemes 2 and 3). The appearance of an OH absorption (*ca.* 3550 cm^{-1}) in the IR spectra and a signal at δ_H *ca.* 5.5 (1 H, d, *J* 6.5 Hz) in each case confirmed the formation of pterocarpans. The pterocarpans **13** and **16** were conveniently converted into their corresponding trifluoromethanesulfonates (triflates) **17** and **19** by treatment with trifluoromethanesulfonic anhydride in the presence of pyridine at −78 °C in 77 and 88% yields respectively.[3b] The disappearance of the OH absorption in the IR spectrum and the 1 H singlet at δ 5.21 (5.29 in the case of **19**) confirmed the formation of triflates. The triflates **19** and **17** when heated with a mixture of palladium(II) acetate, 1,1′-bis(diphenylphosphino)ferrocene, triethylamine and formic acid gave edulane **3** (84%) and its analogue **18** (78%) (Schemes 2 and 3).[3b] The formation of edulane **3** and its analogue **18** was confirmed by the appearance of signals at δ 6.48 and 7.12 (both



Scheme 2 *Reagents and conditions*: iv, $ZnCl_2$ (1.5 equiv.), CH_2Cl_2, room temp; v, $(CF_3SO_2)_2O$, pyridine, −78 °C, 4 h; vi, $Pd(OAc)_2$, 1,1′-bis(DPP)ferrocene, Et_3N, HCO_2H, 75 °C, 1 h



Scheme 3 *Reagents and conditions*: iv, $ZnCl_2$ (1.5 equiv.), CH_2Cl_2, room temp; v, $(CF_3SO_2)_2O$, pyridine, −78 °C, 4 h; vi, $Pd(OAc)_2$, 1,1′-bis(DPP)ferrocene, Et_3N, HCO_2H, 75 °C, 1 h

1 H, d) and δ 6.43 (1 H, dd) in their ^{1}H NMR spectra. This was further confirmed by mass spectral evidence.

Experimental

Diphenyl diselenide, trifluoromethanesulfonic anhydride, palladium(II) acetate and 1,1′-bis(diphenylphosphino)ferrocene [bis(DPP)ferrocene] were purchased from the Aldrich Chemical Co. 2-Methoxy-1,4-benzoquinones was prepared from vanillin using aqueous H_2O_2.[13] Melting points are uncorrected. TLC analyses were carried out on glass plates coated with TLC grade silica gel. Silica gel (100–200 mesh) were used for column chromatography. Laboratory solvents were purified and predried before use according to standard procedures. Light petroleum (LP; bp 60–80 °C) was used for column chromatography. IR spectra were recorded on a Perkin-Elmer 688 spectrometer. NMR spectra were recorded either on Bruker AM 500, Varian VXR 300S or Bruker-200 instruments using $CDCl_3$ as the solvent containing $SiMe_4$ as an internal standard with chemical shifts (δ) expressed as ppm downfield with respect to $SiMe_4$. *J* Values are given in Hz. Elemental analyses were performed on a CEST 1106 elemental analyser. Mass spectra were recorded on a Hewlett Packard MS Engine 5989-A mass spectrometer.

7-(3′,3′-Dimethoxypropoxy)-2,2-dimethyl-3,4-dihydro-5-methoxybenzo[1,2-*b*]pyran 7

A mixture of K_2CO_3 (200 mg, 1.45 mmol) and 7-hydroxy-5-methoxy-2,2-dimethylchroman **5** (300 g, 1.4 mmol) in dry acetone (25 ml) was stirred for 10 min at 5–10 °C. 3-Iodopropanal dimethyl acetal **6** (0.45 ml, 2.0 mmol) in dry acetone (10 ml) was then gradually added to the mixture after which it was refluxed overnight. The mixture was evaporated under reduced pressure and extracted with dichloromethane (4 × 50 ml) and the combined extracts were washed with water and brine, dried (Na_2SO_4) and evaporated under reduced pressure. The product was chromatographed over silica gel and eluted with LP–ethyl acetate (98:2) to give the title compound **7** as a light yellow oil (320 mg, 74%); ν_{max}/cm^{-1} 2947, 1624, 1591, 1499, 1453, 1393, 1123 and 814; δ_H(300 MHz, $CDCl_3$) 1.30 [6 H, s, 2,2-$(CH_3)_2$], 1.74 (2 H, t, *J* 6.77, 3-H), 2.05 (2 H, q, *J* 6.04, 12.26, 2′-H), 2.55 (2 H, t, *J* 6.77, 4-H), 3.35 (6 H, s, 3′-OCH_3), 3.78 (3 H, s, 5-OCH_3), 3.97 (2 H, t, *J* 6.28, 1′-H), 4.61 (1 H, t, *J* 5.86, 3′-H), 6.0 (1 H, d, *J* 2.4, Ar-H) and 6.03 (1 H, d, *J* 2.4, Ar-H); *m/z* 310 (M^+, 71%), 295 (100), 247 (29), 239 (71), 153 (47) and 75 (59).

3,4-Dihydro-2,2-dimethyl-5-methoxy-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*′]dipyran 8 and 6,7-dihydro-8,8-dimethyl-5-methoxy-2*H*,8*H*-benzo[1,2-*b*:5,4-*b*′]dipyran 9

To a solution of toluene-*p*-sulfonic acid (catalytic amount) in dry dioxane (25 ml) was added the alkylated chroman **7** (1 g, 3.2 mmol) in dry dioxane (15 ml). The mixture was heated at 68 °C under a N_2 atmosphere for 2 h and then allowed to cool to room temperature. After 15 mins, it was diluted with water (25 ml) and extracted with dichloromethane. The extract was washed with water and brine, dried (Na_2SO_4) and concentrated. The resultant oil was subjected to silica gel column chromatography and eluted with LP–ethyl acetate (99:1 and 98:2) to afford the chromenes **8** and **9** as colourless oils. Chromene **8** (170 mg, 21.5%); ν_{max}/cm^{-1} 3019, 1979, 2940, 1621, 1453, 1216, 1117, 1025 and 755; δ_H(300 MHz, $CDCl_3$) 1.31 [6 H, s, 2,2-$(CH_3)_2$], 1.74 (2 H, t, *J* 6.95, 3 H), 2.54 (2 H, t, *J* 6.96, 4-H), 3.76 (3 H, s, OCH_3), 4.69 (2 H, q, *J* 1.65, 8-H), 5.55 (1 H, td, *J* 3.84, 9.8, 9-H), 5.97 (1 H, s, 6-H) and 6.70 (1 H, d, *J* 9.81, 10-H); δ_C(125 MHz, $CDCl_3$) 16.93, 26.93, 32.46, 55.62, 65.51, 74.5, 91.03, 102.85, 105.30, 116.15, 120.2, 150.38, 154.0 and 158.2; *m/z* 246 (M^+, 99%), 191 (80) and 161 (100). The chromene **9** (330 mg, 42%); ν_{max}/cm^{-1} 3026, 2979, 2940, 1617, 1479, 1216, 1143 and 762; δ_H(300 MHz, $CDCl_3$) 1.31 [6 H, s, 8,8-$(CH_3)_2$], 1.75 (2 H, t, *J* 6.77, 7-H), 2.65 (2 H, t, *J* 6.77, 6-H), 3.74 (3 H, s, OCH_3), 4.69 (2 H, q, *J* 1.83, 2-H), 5.64 (1 H, td, *J* 9.88, 3.84, 3-H), 6.10 (1 H, s, 10-H) and 6.61 (1 H, d, *J* 9.88, 4-H); δ_C(125 MHz, $CDCl_3$) 17.08, 26.95, 32.61, 61.53, 65.38, 74.64, 100.8, 107.7, 108.8, 118.4, 119.9, 154.2, 154.69 and 155.43; *m/z* 246 (M^+, 86%), 191 (69) and 83 (100).

3,4-Dihydro-2,2,8,8-tetramethyl-5-methoxy-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*′]dipyran 10

3-Methylbut-2-enal (0.87 ml, 9.0 mmol) was added to a mixture of 7-hydroxy-5-methoxychroman **5** (1.8 g, 9.0 mmol) and dry pyridine (2.9 ml, 36 mmol) at 140 °C (oil-bath temp.). After the mixture had been heated under reflux for 12 h it was treated with 3-methylbut-2-enal (0.87 ml, 9.0 mmol) and refluxing continued for 36 h. The mixture was then evaporated to dryness under reduced pressure to remove the pyridine, after which it was diluted with water (20 ml) and extracted with ethyl acetate. The extract was washed with water and brine, dried (Na_2SO_4) and evaporated to afford an oily residue. This was subjected to

column chromatography and eluted with LP–ethyl acetate (98:2) to give the chromene **10** as a colourless oil (1.67 g, 68%); ν_{max}/cm^{-1} 3024, 2974, 2935, 1622, 1587, 1479, 1221 and 1149; δ_H(300 MHz, $CDCl_3$) 1.30 [6 H, s, 2,2-$(CH_3)_2$], 1.40 [6 H, s, 8,8-$(CH_3)_2$], 1.73 (2 H, t, *J* 6.8, 3-H), 2.54 (2 H, t, *J* 6.77, 4-H), 3.76 (3 H, s, OCH_3), 5.37 (1 H, d, *J* 9.7, 9-H), 5.97 (1 H, s, 6-H) and 6.59 (1 H, d, *J* 9.7, 10-H); δ_C(50 MHz, $CDCl_3$) 16.75, 26.73, 27.78, 32.34, 55.35, 74.23, 75.87, 91.36, 102.05, 103.71, 117.17, 125.17, 150.11, 152.44 and 158.04; *m/z* 274 (M^+, 56%), 259 (100), 203 (85) and 181 (49).

Synthesis of the pterocarpans 13, 14, 15 and 16: General procedure

To a well stirred solution of the 2-alkoxy-1,4-benzoquinone (**11** or **12**) (1 mol equiv.) in dichloromethane, $ZnCl_2$ (1.5 mol equiv.) was added, followed by a solution of the 2*H*-chromene (**8, 9** or **10**) (1 mol equiv.) in dichloromethane at room temperature under nitrogen atmosphere. After completion of the reaction (monitored by TLC), the mixture was diluted with water to quench the reaction and then extracted with dichloromethane. The extract was washed with water and brine, dried (Na_2SO_4) and concentrated *in vacuo*. The products were chromatographed over silica gel using LP–ethyl acetate (92:8) as eluent to afford the title compounds.

3,4,8a,13a-Tetrahydro-10-hydroxy-5,11-dimethoxy-2,2-dimethyl-2*H*,8*H*-benzofuro[2′,3′:4,5]pyrano[2,3-*h*][1]benzopyran 13

The 2*H*-chromene **8** (200 mg, 0.81 mmol), 2-methoxy-1,4-benzoquinone **11** (110 mg, 0.81 mmol) and $ZnCl_2$ (160 mg, 1.21 mmol) gave compound **13** as a colourless solid (190 mg, 62%); mp 85–88 °C; ν_{max}/cm^{-1} 3552, 3026, 1620, 1492, 1453, 1216 and 1130; δ_H(300 MHz, $CDCl_3$) 1.28 (3 H, s, CH_3), 1.45 (3 H, s, CH_3), 1.78 (2 H, m, 3-H), 2.58 (2 H, m, 4-H), 3.33 (1 H, m, 8a-H), 3.61 (1 H, t, *J* 11, 8ax-H), 3.78 (3 H, s, OCH_3), 3.84 (3 H, s, OCH_3), 4.17 (1 H, q, *J* 4.9, 10.9, 8eq-H), 5.21 (1 H, s, OH), 5.56 (1 H, d, *J* 6.4, 13a-H), 6.02 (1 H, s, 6-H), 6.51 (1 H, s, 12-H) and 6.82 (1 H, s, 9-H); *m/z* 384 (M^+, 100%), 328 (61) and 165 (15) (Found: C, 68.77; H, 6.28. $C_{22}H_{24}O_6$ requires C, 68.74; H, 6.29%).

3,4,8a,13a-Tetrahydro-10-hydroxy-5,11-dimethoxy-2,2,8,8-tetramethyl-2*H*,8*H*-benzofuro[2′,3′:4,5]pyrano[2,3-*h*][1]benzopyran 14

The 2*H*-chromene **10** (160 mg, 0.58 mmol), 2-methoxy-1,4-benzoquinone **11** (80 mg, 0.58 mmol) and $ZnCl_2$ (120 mg, 0.87 mmol) gave compound **14** as a colourless solid (130 mg, 55%), mp 94–96 °C; δ_H(300 MHz, $CDCl_3$) 0.94 (3 H, s, CH_3), 1.23 (3 H, s, CH_3), 1.48 [6 H, s, 2-$(CH_3)_2$], 1.83 (2 H, m, 3-H), 2.58 (2 H, m, 4-H), 3.12 (1 H, d, *J* 6.95, 8a-H), 3.78 (3 H, s, OCH_3), 3.86 (3 H, s, OCH_3), 5.25 (1 H, s, OH), 5.48 (1 H, d, *J* 6.95, 13a-H), 6.02 (1 H, s, 6-H), 6.51 (1 H, s, 12-H) and 6.86 (1 H, s, 9-H); δ_C(75 MHz, $CDCl_3$) 16.82, 19.87, 25.0, 27.54, 28.42, 32.07, 48.73, 55.37, 56.13, 74.64, 76.28, 76.45, 91.40, 94.71, 100.98, 102.53, 110.89, 119.28, 139.31, 146.74, 153.0, 154.25, 154.41 and 159.03; *m/z* 412 (M^+, 91.2%), 397 (100), 341 (83.3) and 178 (29.4) (Found: C, 69.93; H, 6.89. $C_{24}H_{28}O_6$ requires C, 69.87; H, 6.85%).

3,4,8a,13a-Tetrahydro-10-hydroxy-5-methoxy-11-benzyloxy-2,2,8,8-tetramethyl-2*H*,8*H*-benzofuro[2′,3′:4,5]pyrano[2,3-*h*]-[1]benzopyran 15

The 2*H*-chromene **10** (180 mg, 0.65 mmol), 2-benzyloxy-1,4-benzoquinone **12** (140 mg, 0.65 mmol) and $ZnCl_2$ (130 mg, 0.97 mmol) gave compound **15** as a colourless solid (190 mg, 61%), mp 96–98 °C; ν_{max}/cm^{-1} 3539, 3427, 3019, 1617, 1596, 1492, 1341, 1216 and 762; δ_H(500 MHz, $CDCl_3$) 0.95 (3 H, s, CH_3), 1.24 (3 H, s, CH_3), 1.48 (3 H, s, CH_3), 1.50 (3 H, s, CH_3), 1.84 (2 H, m, 3-H), 2.60 (2 H, m, 4-H), 3.13 (1 H, d, *J* 7.0, 8a-H), 3.79 (3 H, s, OCH_3), 5.07 (2 H, s, OCH_2), 5.33 (1 H, s, OH), 5.49 (1 H, d, *J* 7.0, 13a-H), 6.03 (1 H, s, 6-H), 6.61 (1 H, s, 12-H), 6.89 (1 H, s, 9-H) and 7.38 (5 H, m, ArH); δ_C(75 MHz, $CDCl_3$) 16.81, 19.86, 24.92, 27.51, 28.45, 32.05, 48.70, 55.34, 71.34, 74.64, 76.21, 76.43, 91.39, 96.07, 100.92, 102.52, 111.07, 119.87, 127.89, 128.39, 128.70, 136.27, 139.57, 145.85, 153.02, 154.14, 154.39 and 159.01; *m/z* 488 (M^+, 53%), 473 (47), 397 (100) and 341 (78.4) (Found: C, 73.71; H, 6.59. $C_{30}H_{32}O_6$ requires C, 73.75; H, 6.60%).

1,2,7a,12a-Tetrahydro-10,13-dimethoxy-9-hydroxy-3,3-dimethyl-3*H*,7*H*-benzofuro[2′,3′:4,5]pyrano[3,2-*g*][1]-benzopyran 16

The 2*H*-chromene **9** (120 mg, 0.49 mmol), 2-methoxy-1,4-benzoquinone **11** (67 mg, 0.49 mmol) and $ZnCl_2$ (99 mg, 0.74 mmol) gave compound **16** as a colourless solid (131 mg, 71%), mp 165–168 °C; ν_{max}/cm^{-1} 3552, 3019, 2927, 2854, 1624, 1587, 1492, 1216, 1143 and 762; δ_H(300 MHz, $CDCl_3$) 1.32 (3 H, s, CH_3), 1.34 (3 H, s, CH_3), 1.77 (2 H, t, *J* 6.6, 2-H), 2.75 (2 H, dt, *J* 2.4, 6.6, 1-H), 3.37 (1 H, m, 7a-H), 3.60 (1 H, t, *J* 11, 7ax-H), 3.84 (3 H, s, OCH_3), 3.95 (3 H, s, OCH_3), 4.16 (1 H, dd, *J* 4.95, 10.95, 7eq-H), 5.29 (1 H, s, OH), 5.60 (1 H, d, *J* 6.6, 12a-H), 6.22 (1 H, s, 5-H), 6.50 (1 H, s, 11-H) and 6.83 (1 H, s, 8-H); δ_C(75 MHz, $CDCl_3$) 17.17, 26.57, 27.06, 32.39, 39.89, 56.21, 61.52, 66.30, 74.57, 75.42, 94.94, 100.97, 106.28, 108.62, 110.32, 118.13, 139.73, 146.84, 153.11, 155.23, 156.33 and 159.27; *m/z* 384 (M^+, 15%), 179 (15), 149 (34), 97 (44) and 57 (100) (Found: C, 68.74; H, 6.26. $C_{22}H_{24}O_6$ requires C, 68.74; H, 6.29%).

3,4,8a,13a-Tetrahydro-5,11-dimethoxy-2,2-dimethyl-2*H*,8*H*-benzofuro[2′,3′:4,5]pyrano[2,3-*h*][1]benzopyran-10-yl trifluoromethanesulfonate 17

To a solution of the pterocarpan **13** (70 mg, 0.182 mmol) in dichloromethane (10 ml) was added pyridine (0.061 ml, 0.75 mmol) at −78 °C, followed after 1 h, by trifluoromethanesulfonic anhydride (0.061 ml, 0.364 mmol). The mixture was stirred at −78 °C for 4 h, after which it was warmed to room temperature and poured into water (25 ml). The aqueous layer was separated and extracted with dichloromethane (3 × 25 ml) and the combined extracts were washed with water and brine, dried (Na_2SO_4) and concentrated under reduced pressure to give a colourless solid. This was chromatographed over silica gel with LP–ethyl acetate (95:5) as eluent to give compound **17** as a colourless solid (72 mg, 77%), mp 125–127 °C; ν_{max}/cm^{-1} 3029, 2979, 2400, 1617, 1492, 1420, 1222 and 762; δ_H(300 MHz, $CDCl_3$) 1.44 [6 H, s, 2,2-$(CH_3)_2$], 1.81 (2 H, m, 3-H), 2.60 (2 H, m, 4-H), 3.41 (1 H, m, 8a-H), 3.65 (1 H, t, *J* 10.9, 8ax-H), 3.78 (3 H, s, OCH_3), 3.85 (3 H, s, OCH_3), 4.17 (1 H, dd, *J* 4.9, 10.9, 8eq-H), 5.69 (1 H, d, *J* 6.6, 13a-H), 6.03 (1 H, s, 6-H), 6.58 (1 H, s, 12-H) and 7.08 (1 H, s, 9-H); δ_C(125 MHz, $CDCl_3$) 16.93, 26.02, 27.85, 32.27, 39.34, 55.65, 56.56, 66.27, 75.06, 76.84, 91.07, 96.52, 100.85, 103.4, 118.37, 118.97, 132.39, 152.65, 154.7, 155.56, 159.42 and 160.56; *m/z* 516 (M^+, 64%), 383 (97) and 327 (100) (Found: C, 53.53; H, 4.47; S, 6.21. $C_{23}H_{23}SO_8F_3$ requires C, 53.49; H, 4.49; S, 6.24%).

1,2,7a,12a-Tetrahydro-10,13-dimethoxy-3,3-dimethyl-3*H*,7*H*-benzofuro[2′,3′:4,5]pyrano[3,2-*g*][1]benzopyran-9-yl trifluoromethanesulfonate 19

In a manner similar to that described for the preparation of the triflate **17**, the pterocarpan **16** (60 mg, 0.156 mmol) was converted into **19** with pyridine (0.052 ml, 0.64 mmol) and trifluoromethanesulfonic anhydride (0.052 ml, 0.31 mmol). Silica gel column chromatography of the crude product with 5% ethyl acetate–LP as eluent, afforded the title compound as a colourless solid (70.8 mg, 88%), mp 176–179 °C; ν_{max}/cm^{-1} 3019, 2979, 2400, 1624, 1584, 1499, 1420, 1222, 1143 and 755; δ_H(300 MHz, $CDCl_3$) 1.33 (3 H, s, CH_3), 1.35 (3 H, s, CH_3), 1.78 (2 H, t, *J* 6.77, 2-H), 2.75 (2 H, dt, *J* 2.2, 6.77, 1-H), 3.47 (1 H, m, 7a-H), 3.64 (1 H, t, *J* 10.6, 7ax-H), 3.86 (3 H, s, OCH_3), 3.95 (3 H, s, OCH_3), 4.16 (1 H, dd, *J* 4.9, 10.9, 7eq-H), 5.74 (1 H, d, *J* 6.7,

12a-H), 6.22 (1 H, s, 5-H), 6.58 (1 H, s, 11-H) and 7.09 (1 H, s, 8-H); δ_C(75 MHz, $CDCl_3$) 17.2, 26.58, 27.11, 32.34, 39.43, 56.42, 61.57, 65.99, 74.75, 76.85, 96.22, 101.12, 105.48, 108.91, 118.38, 118.67, 132.44, 152.59, 155.24, 156.72, 159.29 and 160.07; *m/z* 516 (M^+, 34%), 383 (100), 368 (19), 313 (12) and 83 (53) (Found: C, 53.50; H, 4.49, S, 6.20. $C_{23}H_{23}SO_8F_3$ requires C, 53.49; H, 4.49; S, 6.21%).

3,4,8a,13a-Tetrahydro-5,11-dimethoxy-2,2-dimethyl-2*H*,8*H*-benzofuro[2′,3′:4,5]pyrano[2,3-*h*][1]benzopyran 18

The triflate **17** (60 mg, 0.11 mmol) was dissolved in *N*,*N*-dimethylformamide (3 ml) under an argon atmosphere at room temperature. Palladium(II) acetate (15.9 mg, 0.070 mmol), 1,1′-bis(diphenylphosphino)ferrocene (31 mg, 0.056 mmol), triethylamine (0.334 ml, 2.4 mmol) and aqueous formic acid (0.15 ml, 3.8 mmol) was added at 75 °C to the reaction mixture which was then stirred for 1 h. After completion of the reaction (monitored by TLC), the mixture was cooled to room temperature, diluted with water (10 ml) and extracted with dichloromethane (2 × 25 ml). The combined extracts were washed with water and brine, dried (Na_2SO_4) and concentrated *in vacuo*. Column chromatography of the residue over silica gel using LP–ethyl acetate (97:3) afforded compound **18** (32 mg, 78%), mp 151–152 °C; ν_{max}/cm^{-1} 3019, 2979, 1617, 1597, 1505, 1466, 1446, 1216, 1117 and 760; δ_H(300 MHz, $CDCl_3$) 1.23 (3 H, s, CH_3), 1.46 (3 H, s, CH_3), 1.83 (2 H, m, 3-H), 2.59 (2 H, m, 4-H), 3.35 (1 H, m, 8a-H), 3.52 (1 H, t, *J* 10.9, 8ax-H), 3.77 (3 H, s, OCH_3), 3.78 (3 H, s, OCH_3), 4.17 (1 H, q, *J* 5.2, 11.1, 8eq-H), 5.61 (1 H, d, *J* 6.8, 13a-H), 6.03 (1 H, s, 6-H), 6.43 (1 H, dd, *J* 2.8, 8.14, 10-H), 6.48 (1 H, d, *J* 2.3, 12-H) and 7.12 (1 H, d, *J* 8.0, 9-H); δ_C(125 MHz, $CDCl_3$) 16.96, 25.94, 27.96, 32.29, 39.15, 55.61, 55.69, 66.67, 74.93, 75.98, 91.0, 97.28, 101.5, 103.19, 106.2, 119.65, 124.65, 154.8, 155.54, 159.18, 161.23 and 161.47; *m/z* 368 (M^+, 100%), 312 (71), 221 (31) and 165 (32) (Found: C, 71.72; H, 6.56. $C_{22}H_{24}O_5$ requires C, 71.72; H, 6.57%).

1,2,7a,12a-Tetrahydro-10,13-dimethoxy-3,3-dimethyl-3*H*,7*H*-benzofuro[2′,3′:4,5]pyrano[3,2-*g*][1]benzopyran 3

In a manner similar to that for the preparation of compound **18**, the triflate **19** (40 mg, 0.077 mmol) was converted into edulane **3** by heating a mixture of triflate **19** with palladium(II) acetate (10.6 mg, 0.050 mmol), 1,1′-bis(diphenylphosphino)-ferrocene (21 mg, 0.037 mmol), triethylamine (0.223 ml, 1.60 mmol) and formic acid (0.1 ml, 2.53 mmol) to 75 °C for 2 h. Column chromatography of the resulting solid over silica gel with LP–ethyl acetate (97:3) as eluent afforded the title compound **3** (23.7 mg, 84% yield); mp 177–178 °C; ν_{max}/cm^{-1} 3019, 2979, 2400, 1624, 1584, 1499, 1479, 1347, 1216, 1143 and 767; δ_H(300 MHz, $CDCl_3$) 1.32 (3 H, s, CH_3), 1.34 (3 H, s, CH_3), 1.77 (2 H, t, *J* 6.5, 2-H), 2.76 (2 H, t, *J* 6.5, 1-H), 3.40 (1 H, m, 7a-H), 3.60 (1 H, t, *J* 10.98, 7ax-H), 3.77 (3 H, s, OCH_3), 3.96 (3 H, s, OCH_3), 4.16 (1 H, m, 7eq-H), 5.66 (1 H, d, *J* 6.6, 12a-H), 6.22 (1 H, s, 5-H), 6.42 (1 H, d, *J* 2.2, 11-H), 6.46 (1 H, dd, *J* 6.52, 2.2, 9-H) and 7.13 (1 H, d, *J* 8, 8-H); δ_C(75 MHz, $CDCl_3$) 17.2, 26.54, 27.17, 32.41, 39.19, 55.56, 61.6, 66.38, 74.63, 75.97, 97.05, 100.98, 106.22, 108.70, 119.37, 124.66, 155.26, 156.42, 159.34, 160.99 and 161.12; *m/z* 368 (M^+, 3%), 86 (90), 83 (100) and 47 (51) (Found: C, 71.69; H, 6.59. $C_{22}H_{24}O_5$ requires C, 71.72; H, 6.57%).

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