Stereocontrolled Assembly of Tetrasubstituted Tetrahydrofurans: A Concise Synthesis of Virgatusin

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Supporting information and spectra

General methods for tetrahydrofuran synthesis: (4*S*, 2'*R*, 3'*S*, 4'*S*, 5'*S*)-4-benzyl-3-(2',5'-diphenethyl-4'-vinyltetrahydrofuran-3'-carbonyl)-oxazolidin-2-one 11a

Method 1 - Mediated by boron trifluoride etherate (Table 1, entry 1)

Boron trifluoride etherate (1.90 ml, 14.1 mmol) and hydrocinnamaldehyde (1.85 ml, 14.0 mmol) were sequentially added to a solution of **9** (3.15 g, 7.01 mmol) in dry dichloromethane (150 ml) at -78°C . The reaction mixture was stirred for 2 hours at -78°C and for $13\frac{1}{2}$ hours at room temperature. The reaction mixture was quenched with brine (100 ml) and then extracted with ethyl acetate (3×50 ml). The combined organic extracts were washed with water (50 ml), then dried (MgSO_4), filtered and evaporated under reduced pressure to give the crude product which was purified by flash chromatography eluting with 20:80 diethyl ether-petrol, to give **11a** (3.26 g, 91 %) as a pale yellow oil, R_F 0.41 (30% ethyl acetate in hexane); $[\alpha]_{\text{D}}^{18} +33$ (c 3.4, CHCl_3); $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3082 s, 3062 s, 2927 s, 2861 w, 1736 s, 1693 s, 1639 m, 1603 s, 1584 w, 1495 s, 1454 s, 1385 s, 1347 s, 918 s, 748 s, and 699 s; δ_{H} (500 MHz, CDCl_3) 7.25-7.07 (15 H, m), 5.80 (1 H, dt, J 16.5, 10.5), 5.033 (1 H, d, J 10.5), 5.028 (1 H, d, J 16.5), 4.55 (1 H, m), 4.24 (1 H, t, J 7.5), 4.14 (1 H, td, J 7.5, 5.0), 4.07-4.02 (3 H, m), 3.14 (1 H, dd, J 13.5, 3.0), 3.09 (1 H, dt, J 10.5, 7.5), 2.81-2.73 (2 H, m), 2.63-2.56 (3 H, m), 1.97-1.83 (2 H, m), 1.77 (1 H, m) and 1.66 (1 H, m,); δ_{C} (75 MHz, CDCl_3) 174.1, 153.8, 142.5, 142.2, 136.2, 135.5, 129.9, 129.4, 129.0, 128.9, 128.8, 127.9, 127.8, 126.3, 126.28, 117.9, 82.2, 81.3, 66.2, 55.9, 55.0, 53.0, 38.4, 37.5, 34.4, 33.0 and 32.9; m/z (ES+) 532 (73%, $[\text{M}+\text{Na}]^+$), 527 (58, $[\text{M}+\text{NH}_4]^+$), 510 (100, $[\text{M}+\text{H}]^+$), 376 (91) and 309 (33); HRMS (ES+) found $[\text{M}+\text{Na}]^+$ 532.2441, $\text{C}_{33}\text{H}_{35}\text{NO}_4\text{Na}$ requires 532.2464. Anal. Calcd for $\text{C}_{33}\text{H}_{35}\text{NO}_4$: C, 77.8; H, 6.9; N, 2.8. Found: C, 77.5; H, 7.1; N, 2.7.

Method 2 - Mediated by trimethylsilyl triflate (Table 2, entry 1)

Trimethylsilyl trifluoromethanesulfonate (5 μ l, 0.03 mmol, 20 mol%) was added to a solution of (4*S*, 6'*S*, 7'*R*)-4-benzyl-3-(2',2'-dimethyl-7'-phenethyl-2',3',6',7'-tetrahydro-[1',2']oxasilepine-6'-carbonyl)oxazolidin-2-one **9** (0.062 g, 0.14 mmol) and hydrocinnamaldehyde (18 μ l, 0.14 mmol) in dry dichloromethane (4 ml) at -78°C . The reaction mixture was stirred for 14 $\frac{1}{4}$ hours at -78°C . The reaction mixture was quenched with brine (10 ml) and then extracted with ethyl acetate (3 $\times$ 10 ml). The combined organic extracts were washed with water (10 ml), then dried (MgSO_4), filtered and evaporated under reduced pressure to give the crude product which was purified by flash column chromatography eluting with gradient elution: 20:80 to 35:75 diethyl ether-petrol to give **11a** (0.060 g, 86%) as a pale yellow oil whose data agreed with that reported above.

(4*S*, 2'*R*, 3'*S*, 4'*S*, 5'*R*)-4-benzyl-3-(5'-benzyloxymethyl-2'-phenethyl-4'-vinyltetrahydrofuran-3'-carbonyl)-oxazolidin-2-one **12a**

Method 1 (Table 1, entry 2)

Carried out according to the general method using boron trifluoride etherate (9 μ l, 0.07 mmol), benzyloxyacetaldehyde (0.0065 g, 0.043 mmol), **9** (0.015 g, 0.033 mmol) in dry dichloromethane (1.5 ml) at -78°C . The reaction mixture was stirred for 2 $\frac{1}{2}$ hours at -78°C and for 16 $\frac{1}{4}$ hours at room temperature. After work up the crude product was purified by flash chromatography eluting 30:70 diethyl ether-petrol, to give **12a** (0.011 g, 65%) as a pale yellow oil viscous oil, R_F 0.29 (50% diethyl ether in petrol); $[\alpha]_D^{18} +33$ (c 0.45, CH_2Cl_2); $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3028 m, 2925 m, 2862 m, 1782 s, 1721 m, 1692 s, 1639 w, 1603 w, 1496 m, 1454 m, 1385 s, 1351 s, 1290 m, 1270 m, 1210 s, 1104 s, 1053 m,

911 s, 733 s, and 700 s; δ_{H} (500 MHz, CDCl_3); 7.32-7.07 (15 H, m), 5.84 (1 H, dt, J 17.5, 10.0), 5.06 (1 H, d, J 17.0), 5.02 (1 H, d, J 10.0), 4.57 (1 H, m), 4.53-4.48 (2 H, m), 4.36 (1 H, t, J 8.0), 4.27 (1 H, dt, J 9.0, 4.5), 4.21 (1 H, td, J 8.0, 4.5), 4.09-4.03 (2 H, m), 3.47 (1 H, d, J 7.0), 3.46 (1 H, d, J 7.0), 3.23 (1 H, m), 3.17 (1 H, dd, J 13.0, 3.0), 2.76 (1 H, m), 2.60 (1 H, dd, J 13.0, 10.0), 2.56 (1 H, m) and 1.99-1.82 (2 H, m); δ_{C} (75 MHz, CDCl_3) 173.8, 153.8, 142.2, 138.6, 135.52, 135.47, 129.8, 129.4, 128.9, 128.8, 128.7, 128.1, 127.9, 127.8, 126.2, 118.4, 82.9, 80.9, 73.8 C, 71.0 C, 66.2, 55.9, 54.4, 52.6, 38.4, 36.8, and 33.0; m/z (ES+) 548 (58%, $[\text{M}+\text{Na}]^+$), 544 (32, $[\text{M}+\text{NH}_4]^+$), 527 (41, $[\text{M}+\text{H}]^+$), 526 (100, $[\text{M}+\text{H}]^+$), 508 (33, $[\text{M}-\text{OH}]^+$), 466 (52), 349 (88, $[\text{M}-\text{PhCH}_2\text{CHCH}_2\text{CO}_2\text{N}]^+$), 332 (56) and 302 (33); HRMS (ES+) found $[\text{M}+\text{H}]^+$ 526.2609, $\text{C}_{33}\text{H}_{36}\text{NO}_4$ requires 526.2593.

Method 2 (Table 2, entry 2)

Carried out on according to the general method using TMSOTf (50 μl , 0.28 mmol, 5 mol%), **9** (2.65 g, 5.89 mmol) and benzyloxyacetaldehyde (0.889 g, 5.92 mmol) in dry dichloromethane (80 ml) at -78°C . The reaction mixture was stirred for $2\frac{3}{4}$ hours at -78°C . A further aliquot of TMSOTf (150 μl , 0.827 mmol, 14 mol%) was added to the reaction mixture which was stirred for a further $2\frac{1}{4}$ hours at -78°C . Further TMSOTf (200 μl , 1.10 mmol, 19 mol%) was added to the reaction mixture which was stirred for a further 4 hours at -78°C and for a further $8\frac{1}{4}$ hours at room temperature. Work-up and purification by flash column chromatography eluting with 30:70 diethyl ether-petrol gave **12a** (2.35 g, 76%) as a pale yellow viscous oil whose data agreed with that reported above.

(4*S*, 2'*R*, 3'*S*, 4'*S*, 5'*R*) and (4*S*, 2'*R*, 3'*S*, 4'*S*, 5'*S*)-4-benzyl-3-(2'-phenethyl-5'-phenyl-4'-vinyltetra-hydrofuran-3'-carbonyl)-oxazolidin-2-one **13a** and **13b**

Method 1 (Table 1, entry 3)

Carried out according to the general method using boron trifluoride etherate (0.360 ml, 2.67 mmol), benzaldehyde (0.270 ml, 2.66 mmol) and **9** (0.034 g, 0.076 mmol) in dry dichloromethane (1 ml) at -78°C . The reaction mixture was stirred for $4\frac{1}{2}$ hours at -78°C and at room temperature for $22\frac{1}{2}$ hours. Work-up and flash chromatography eluting with 15:85 ethyl acetate-petrol gave **13a** and **13b** (0.024 g, 65% as a 93:7 mixture of diastereoisomers), as a pale yellow viscous oil, R_F 0.07 (10% ethyl acetate in hexane); $[\alpha]_D^{21} +45$ (c 0.65, CH_2Cl_2); $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3063 m, 3028 m, 2923 m, 1779 s, 1694 s, 1640 w, 1603 w, 1495 s, 1454 s, 1385 s, 1351 s, 1209 s, 1106 s and 700 s; δ_{H} (500 MHz, CDCl_3 , signals for **13a**) 7.29-7.09 (15 H, m), 5.23 (1 H, d, J 8.0), 5.21 (1 H, dt, J 17.0, 10.0), 4.90 (1 H, dd, J 17.0, 1.5), 4.79 (1 H, dd, J 10.0, 1.5), 4.60 (1 H, m), 4.40 (1 H, t, J 8.0), 4.29 (1 H, td, J 8.0, 4.5), 4.08 (1 H, t, J 9.0), 4.04 (1 H, dd, J 9.0, 3.0), 3.44 (1 H, m), 3.18 (1 H, dd, J 13.5, 3.5), 2.87 (1H, ddd, J 14.0, 10.5, 4.5), 2.67 (1 H, ddd, J 14.0, 10.5, 6.5), 2.59 (1 H, dd, J 13.5, 9.5), 2.11 (1 H, m), 1.99 (1 H, m); signals for **13b** visible at 5.84 (1 H, dt, J 17.0, 10.0), 5.01 (1 H, d, J 10.0) and 2.54 (1 H, dd, J 13.5, 9.5); δ_{C} (75 MHz, CDCl_3); 173.2, 153.0, 141.7, 139.2, 136.1, 135.0, 129.4, 129.0, 128.5, 128.4, 128.1, 127.8, 127.4, 126.8, 125.9, 117.0, 83.3, 82.2, 65.8, 56.2, 55.8, 52.2, 38.0, 36.2 and 32.5; m/z (ES+) 504 (100%, $[\text{M}+\text{Na}]^+$); HRMS (ES+) found $[\text{M}+\text{Na}]^+$ 504.2136, $\text{C}_{31}\text{H}_{31}\text{NO}_4\text{Na}$ requires 504.2151.

Method 1 - extended reaction time (Table 1, entry 4)

Carried out according to the general method using boron trifluoride etherate (0.360 ml, 2.67 mmol), benzaldehyde (0.270 ml, 2.66 mmol) and **9** (1.20 g, 2.67 mmol) in dry dichloromethane (60 ml) at $-78\text{ }^{\circ}\text{C}$. The reaction mixture was stirred for $27\frac{1}{4}$ hours at $-78\text{ }^{\circ}\text{C}$ and at room temperature for $90\frac{1}{4}$ hours. The reaction mixture was quenched with brine (30 ml) and then extracted with ethyl acetate ($3 \times 30\text{ ml}$). The combined organic extracts were washed with water (30 ml), dried (MgSO_4), filtered and evaporated under reduced pressure to give the crude product which was purified by flash chromatography eluting with 15:85 ethyl acetate-petrol, to give **13a**, **13b** and an unidentified diastereoisomer **13c** (1.00 g, 78% as an 80:12:8 mixture of diastereoisomers) as a pale yellow viscous oil, R_F 0.10 (10% ethyl acetate in hexane); $[\alpha]_D^{21} +41$ (c 6.2, CH_2Cl_2); signals for **13c** visible at δ_H (500 MHz, CDCl_3) 5.72 (1 H, dt, J 17.0, 10.0), 5.03 (1 H, d, J 10.0), 3.33 (1 H, dd, J 13.5, 3.5) and 2.40 (1 H, dd, J 13.5, 11.0), whose other data agree with that reported above.

Method 1 - reaction at reflux (Table 1, entry 5)

Carried out according to the general method using boron trifluoride etherate (5 μl , 0.04 mmol), benzaldehyde (4 μl , 0.04 mmol) and **9** (0.017 g, 0.038 mmol) in dry dichloromethane (2 ml) at room temperature. The reaction mixture was stirred for $1\frac{1}{2}$ hours at room temperature and then refluxed for $165\frac{1}{4}$ hours. Work-up and flash chromatography eluting with 15:85 ethyl acetate-petrol, gave **13a**, **13b** and **13c** (0.010 g, 74% as a 73:15:12 mixture of diastereoisomers), as a pale yellow viscous oil, R_F 0.15 (30% diethyl ether in petrol); $[\alpha]_D^{21} +43$ (c 0.15, CH_2Cl_2), whose other data agree with that reported above.

Method 2 (Table 2, entry 3)

Carried out according to the general method using trimethylsilyl trifluoromethanesulfonate (5 μl , 0.03 mmol, 8 mol%), **9** (0.15 g, 0.34 mmol) and benzaldehyde (35 μl , 0.34 mmol) in dry dichloromethane (8.0 ml) at $-78\text{ }^{\circ}\text{C}$. The reaction mixture was stirred for $5\frac{1}{2}$ hours at $-78\text{ }^{\circ}\text{C}$. Work-up and flash column chromatography

eluting with 20:80 diethyl ether-petrol gave **13a** (0.13 g, 81%) as a pale yellow viscous oil; $[\alpha]_D^{19} +23$ (c 0.22, CH_2Cl_2), whose other data agreed with that reported above.

(4*S*, 2'*R*, 3'*S*, 4'*S*, 5'*R*) and (4*S*, 2'*R*, 3'*S*, 4'*S*, 5'*S*)-3-(5'-benzo-[1,3]-dioxol-5-yl-2'-phenethyl-4'-vinyltetrahydrofuran-3'-carbonyl)-4-benzyloxazolidin-2-one 14a and 14b

Method 1 (Table 1, entry 6)

Carried out according to the general method using boron trifluoride etherate (31 μl , 0.23 mmol), piperonal (0.035 g, 0.23 mmol), **9** (0.10 g, 0.23 mmol) in dry dichloromethane (7 ml) at -78°C . The reaction mixture was stirred for 3 hours at -78°C and for 124 $\frac{1}{4}$ hours at room temperature. Work-up and flash chromatography eluting with gradient elution: 20:80 to 50:50 ethyl acetate-petrol gave **14a** and **14b** (0.051 g, 37% by ^1H nmr, as a 9:91 diastereomeric mixture) and an unidentified product, as a pale yellow oil, R_F 0.41 (30% ethyl acetate in hexane); $[\alpha]_D^{19} +73$ (c 2.2, CH_2Cl_2); $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3027 w, 2925 m, 1779 s, 1694 s, 1642 w, 1603 w, 1490 s, 1444 s, 1385 s, 1250 s, 1039 s and 700 s; δ_{H} (500 MHz, CDCl_3 , signals for **14a**); 7.35-7.16 (10 H, m), 6.98-6.76 (3 H, m), 5.95 (2 H, s), 5.87 (1 H, dt, J 17.0, 9.5), 5.08 (1 H, d, J 10.0), 4.98 (1 H, d, J 17.0), 4.75 (1 H, d, J 9.5), 4.69-4.55 (2 H, m), 4.62 (1 H, t, J 9.0), 4.09-4.17 (2 H, m), 3.23 (1 H, dd, J 13.5, 3.5), 3.17 (1 H, q, J 9.5), 2.87 (1 H, m), 2.69 (1 H, m), 2.61 (1 H, dd, J 13.5, 9.5), 2.05 (1 H, m), 1.96 (1 H, m); signals for **14b** visible at 5.33 (1 H, dt, J 17.0, 10.0), 5.22 (1 H, d, J 8.0), 4.90 (1 H, d, J 10.0) and 4.44 (1 H, t, J 8.5); (75 MHz, CDCl_3) 173.0, 153.4, 148.0, 147.7, 135.5, 135.3, 134.7, 129.8, 129.4, 128.9, 128.8, 128.6, 127.8, 126.3, 120.5, 119.0, 108.4, 107.2, 101.4, 85.6, 82.7, 66.3, 61.1, 56.0, 54.0, 38.5, 37.3, and 32.3; m/z (ES+) 602 (56), 404 (36, $[\text{M}-\text{C}_6\text{H}_3\text{CH}_2(\text{O})_2]^+$), 391 (100), 159 (51), 114 (39) and 101 (61).

Method 2 (Table 2, entry 4)

Carried out according to the general method using trimethylsilyl trifluoromethanesulfonate (5 μ l, 0.03 mmol, 15 mol%), **9** (0.080 g, 0.18 mmol) and piperonal (0.027 g, 0.18 mmol) in dry dichloromethane (5 ml) at -78°C . The reaction mixture was stirred for $14\frac{1}{4}$ hours at -78°C . Further trimethylsilyl trifluoromethanesulfonate (5 μ l, 27.6 μ mol, 15 mol%) was added to the reaction mixture. The reaction mixture was stirred for $7\frac{3}{4}$ hours at -78°C . Work-up and flash column chromatography eluting with gradient elution: 20:80 to 50:50 diethyl ether-petrol, gave **14a** (0.068 g, 72%) as colourless viscous oil, R_F 0.30 (50% diethyl ether in petrol); $[\alpha]_D^{20} +16$ (c 0.15, CH_2Cl_2); $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3071 w, 2919 m, 1779 s, 1691 s, 1637 w, 1603 w, 1503 m, 1490 s, 1444 s, 1385 s, 1239 s, 1038 s and 700 s; δ_H (500 MHz, CDCl_3); 7.25-7.09 (10 H, m), 6.73 (1 H, s), 6.70 (1 H, d, J 7.5), 6.67 (1 H, d, J 7.5), 5.87 (2 H, s), 5.26 (1 H, m), 5.14 (1 H, d, J 8.0), 4.91 (1 H, d, J 16.5), 4.82 (1 H, d, J 10.0), 4.59 (1 H, m), 4.37 (1 H, t, J 8.5), 4.25 (1 H, m), 4.09-4.03 (2 H, m), 3.38 (1 H, q, J 8.5), 3.17 (1 H, dd, J 13.5, 3.5), 2.86 (1 H, ddd, 14.5, 9.5, 5.0), 2.65 (1 H, m), 2.58 (1 H, dd, J 13.5, 10.0), 2.08 (1 H, m) and 1.96 (1 H, m); δ_C (75 MHz, CDCl_3) 173.6, 153.4, 148.0, 147.2, 142.1, 136.6, 135.5, 133.7, 129.8, 129.4, 128.9, 128.8, 127.9, 126.3, 120.5, 117.4, 108.4, 107.8, 101.4, 83.6, 82.5, 66.3, 56.7, 55.4, 52.5, 38.4, 36.6 and 33.0; m/z (ES+) 548 (60%, $[\text{M}+\text{Na}]^+$), 508 (35, $[\text{M}-\text{OH}]^+$), 405 (32, $[\text{M}-\text{C}_6\text{H}_3\text{CH}_2\text{O}_2]^+$), 404 (100, $[\text{M}-\text{C}_6\text{H}_3\text{CH}_2\text{O}_2]^+$), 376 (43) and 331 (84); HRMS (ES+) found $[\text{M}+\text{Na}]^+$ 548.2067, $\text{C}_{32}\text{H}_{31}\text{NO}_6\text{Na}$ requires 548.2049.

(4*S*, 2'*R*, 3'*S*, 4'*S*, 5'*S*) and (4*S*, 2'*R*, 3'*S*, 4'*S*, 5'*R*)-4-benzyl-3-(2'-phenethyl-5'-styryl-4'-vinyltetrahydrofuran-3'-carbonyl)-oxazolidin-2-one 15a and 15b

Method 1 (Table 1, entry 7)

Carried out according to the general method using boron trifluoride etherate (17 μ l, 0.13 mmol), *trans*-cinnamaldehyde (16 μ l, 0.13 mmol) and **9** (0.056 g, 0.13 mmol) in dry dichloromethane (3.5 ml) at -78°C . The reaction mixture was stirred for 1 hour at -78°C and for 187 $\frac{1}{2}$ hours at room temperature. Work-up and flash chromatography eluting with gradient elution: 15:85 to 30:70 diethyl ether-petrol, gave **15a**, **15b** and an unidentified diastereoisomer **15c** (0.025 g, 39% as an 11:78:11 mixture of diastereoisomers), as a pale yellow oil, R_F 0.16 (30% diethyl ether in petrol); $[\alpha]_D^{24} +71$ (c 1.7, CH_2Cl_2); $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3027 m, 2924 m, 1779 s, 1693 s, 1641 w, 1495 m, 1454 m, 1386 s, 1350 m, 1209 m, 1107 m, 749 m and 699 s; δ_{H} (500 MHz, CDCl_3 , signals for **15b**) 7.34-7.08 (15 H, m), 6.54 (1 H, d, J 16.0), 6.17 (1 H, dd, J 16.0, 7.5), 5.79 (1 H, dt, J 17.0, 10.0), 5.07 (1 H, d, J 17.0), 5.06 (1 H, d, J 10.0), 4.60 (1 H, m), 4.50 (1 H dd, J 10.0, 8.5), 4.41-4.36 (2 H, m), 4.10-4.03 (2 H, m), 3.18 (1 H, dd, J 13.5, 3.5), 3.06 (1 H, q, J 10.0), 2.79 (1 H, m), 2.59 (1 H, m), 2.57 (1 H, dd, 13.5, 9.5), 1.95 (1 H, m) and 1.86 (1 H, m); signals for **15a** visible at 6.56 (1 H, d, J 16.0), 6.12 (1 H, dd, J 16.0, 7.5), 4.74 (1 H, t, J 7.5); signals for **15c** visible at 5.65 (1 H, dt, J 17.0, 10.0), 4.26 (1 H, m), 3.40 (1 H, m), 3.31 (1 H, dd, J 13.0, 3.0), 2.86 (1 H, m), 2.65 (1 H, m) and 2.40 (1 H, dd, J 13.0, 10.5); δ_{C} (75 MHz, CDCl_3) 173.0, 153.5, 142.1, 136.9, 135.5, 135.3, 132.9, 129.8, 129.4, 128.94, 128.88, 128.80, 128.2, 128.1, 127.9, 127.1, 126.3, 119.0, 84.9, 82.7, 66.3, 59.0, 56.0, 53.7, 38.5, 37.2 and 32.7; m/z (ES^+) 508 (55%, $[\text{M}+\text{H}]^+$), 405 (32), 404 (100) and 374 (44); HRMS (ES^+) found $[\text{M}+\text{Na}]^+$ 508.2508, $\text{C}_{33}\text{H}_{33}\text{NO}_4$ requires 508.2488.

Method 2 (Table 2, entry 5)

Carried out according to the general method using trimethylsilyl trifluoromethanesulfonate (5 μ l, 0.03 mmol, 6 mol%), **9** (0.20 g, 0.45 mmol) and *trans*-cinnamaldehyde (65 μ l, 0.52 mmol) in dry dichloromethane (7 ml) at -78°C . The reaction mixture was stirred for 6 hours at -78°C . Work-up and flash column chromatography eluting with gradient elution: 20:80 to 50:50 diethyl ether-petrol, gave (4*S*, 2'*R*, 3'*S*, 4'*S*, 5'*S*)-4-benzyl-3-(2'-phenethyl-5'-styryl-4'-vinyltetrahydrofuran-3'-carbonyl)-oxazolidin-2-one **15a** and **15b** (0.22 g, 95% as a 97:3 mixture of diastereoisomers), as a pale yellow viscous oil, R_F 0.38 (50% diethyl ether in petrol);

$[\alpha]_D^{18} +16$ (*c* 0.55, CH₂Cl₂); $\nu_{\max}/\text{cm}^{-1}$ (neat) 3061 s, 3027 s, 2924 s, 2858 s, 1779 s, 1693 s, 1641 w, 1495 m, 1454 m, 1385 s, 1347 m, 1209 m, 1107 m, 749 m and 699 s δ_{H} (500 MHz, CDCl₃, signals for **15a**) 7.34-7.08 (15 H, m), 6.56 (1 H, d, *J* 16.0), 6.12 (1 H, dd, *J* 16.0, 7.5), 5.78 (1 H, dt, *J* 17.0, 10.0), 5.07-5.02 (2 H, m), 4.74 (1 H, t *J* 7.5), 4.59 (1 H, m), 4.36 (1 H, t, *J* 8.0), 4.25 (1 H, dt, *J* 8.0, 4.5), 4.10-4.04 (2 H, m), 3.31 (1 H, m), 3.18 (1 H, dd, *J* 13.5, 3.0), 2.82 (1 H, m), 2.62 (1 H, m), 2.60 (1 H, dd, 13.5, 10.0), 2.01 (1 H, m) and 1.91 (1 H, m); signals for **15b** visible at 6.17 (1 H, dd, *J* 16.0, 7.5), 4.49 (1 H, m) and 3.06 (1 H, q, *J* 10.0); δ_{C} (75 MHz, CDCl₃) 173.6, 153.4, 142.1, 137.0, 135.9, 135.5, 132.9, 129.9, 129.4, 129.0, 128.88, 128.81, 128.2, 127.9, 127.6, 127.1, 126.3, 118.1, 83.0, 82.7, 66.3, 56.2, 55.9, 52.7, 38.4, 37.2 and 32.9; *m/z* (ES⁺) 522 (60%), 508 (37), 507 (35, [M+H]⁺), 506 (100), 404 (78), 392 (31) and 374 (33); HRMS (ES⁺) found [M+Na]⁺ 530.2294, C₃₃H₃₃NO₄Na requires 530.2307.

(4*S*, 2'*S*, 3'*S*, 4'*S*, 5'*S*)-4-benzyl-3-[2'-(3,4-dimethoxyphenyl)-5'-phenethyl-4'-vinyltetrahydrofuran-3'-carbonyl]-oxazolidin-2-one 16a

Method 2 (Table 2, entry 6)

Carried out according to the general method using trimethylsilyl trifluoromethanesulfonate (5.5 μl , 30 μmol , 10 mol%), **10** (0.146 g, 0.303 mmol) and 3-phenylpropionaldehyde (40 μl , 0.30 mmol) in dry dichloromethane (7.0 ml) at -78°C . The reaction mixture was stirred for 5³/₄ hours at -78°C . Work-up and high performance liquid chromatography eluting with gradient elution: 35:65 to 95:5 acetonitrile-water, gave **16a** (0.068 g, 41%) as a pale yellow oil; R_{F} 0.38 (50% ethyl acetate in hexane); $[\alpha]_D^{18} +74$ (*c* 0.40, CH₂Cl₂); $\nu_{\max}/\text{cm}^{-1}$ (neat) 3027 w, 2935 m, 2862 w, 1781 s, 1692 s, 1639 w, 1602 w, 1517 s, 1162 m, 1108 m, 1050 m, 1028 s, 911 s, 732 s, 701 s and 647 m;

δ_{H} (500 MHz, CDCl_3) 7.32-7.18 (10 H, m), 6.97 (1 H, s), 6.94 (1 H, d, J 8.0), 6.82 (1 H, d, J 8.0), 5.97 (1 H, dt, J 17.5, 10.0), 5.18 (1 H, d, J 17.5), 5.16 (1 H, d, J 10.0), 5.14 (1 H, d, J 9.0), 4.68 (1 H t, J 9.0), 4.59 (1 H, m), 4.30 (1 H, m), 4.05 (1 H, dd, J 9.0, 2.5), 3.99 (1 H, t, J 9.0) 3.88 (3 H, s), 3.85 (3 H, s), 3.39 (1 H, q, J 9.0), 3.24 (1 H, dd, J 13.5, 3.5), 2.91 (1 H, ddd, J 15.5, 10.5, 5.0), 2.69 (1 H, m), 2.64 (1 H, dd, J 13.5, 10.0), 1.99 (1 H, m) and 1.85 (1 H, m); δ_{C} (75 MHz, CDCl_3) 173.2, 153.1, 149.4, 142.4, 135.5, 132.1, 129.8, 129.4, 128.9, 128.8, 127.8, 126.3, 119.7, 118.4, 111.4, 110.2, 84.5, 81.2, 66.2, 56.3, 56.0, 55.3, 54.5, 38.4, 34.9 and 32.9 (29 signals expected, 27 signals visible); m/z (ES+) 564 (52%, $[\text{M}+\text{Na}]^+$), 542 (30, $[\text{M}+\text{H}]^+$), 524 (72, $[\text{M}-\text{OH}]^+$), 404 (73, $[\text{M}-\text{C}_6\text{H}_3(\text{OCH}_3)_2]^+$), 366 (54, $[\text{M}-\text{PhCH}_2\text{CHCH}_2\text{CO}_2\text{N}]^+$), 365 (100, $[\text{M}-\text{PhCH}_2\text{CHCH}_2\text{CO}_2\text{N}]^+$) and 347 (37); HRMS (ES+) found $[\text{M}+\text{H}]^+$ 542.2545, $\text{C}_{33}\text{H}_{36}\text{NO}_6$ requires 542.2543.

(4*S*, 2'*S*, 3'*S*, 4'*S*, 5'*R*)-4-benzyl-3-[2'-(3,4-dimethoxyphenyl)-5-phenyl-4'-vinyltetrahydrofuran-3'-carbonyl]-oxazolidin-2-one 17a

Method 2 (Table 2, entry 7)

Carried out according to the general method using trimethylsilyl trifluoromethanesulfonate (5 μl , 0.03 mmol, 10 mol%), **10** (0.136 g, 0.283 mmol) and benzaldehyde (29 μl , 0.29 mmol) in dry dichloromethane (6.5 ml) at -78°C . The reaction mixture was stirred for $5\frac{3}{4}$ hours at -78°C . Work-up and high performance liquid chromatography eluting with gradient elution: 20:80 to 95:5 acetonitrile-water, gave **17a** (0.049 g, 34%) as a pale yellow oil, R_{F} 0.29 (50% EtOAc in petrol); $[\alpha]_{\text{D}}^{24}$ (+80 c 2.4, CH_2Cl_2); $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3063 w, 3029 w, 2960 w, 2934 w, 1779 s, 1690 s, 1639 w, 1594 w, 1518 s, 1454 m, 1386 s, 1264 s, 1027 s and 700 m; δ_{H} (500 MHz, CDCl_3) 7.36-7.18 (10 H, m), 7.11 (1 H, d, J 1.5), 7.07 (1 H, dd, J 8.0, 1.5), 6.86 (1 H, d, J 8.0), 5.42 (1

H, d, *J* 9.5), 5.34 (1 H, dt, *J* 17.0, 9.5), 5.29 (1 H, d, *J* 9.5), 5.05 (1 H, d, *J* 17.0), 4.91 (1 H, d, *J* 9.5) 4.90 (1 H, t, *J* 9.5), 4.62 (1 H, m), 4.05 (1 H, dd, *J* 9.0, 2.5), 4.00 (1 H, m) 3.91 (3 H, s), 3.87 (3 H, s), 3.70 (1 H q, *J* 9.5), 3.25 (1 H, dd, *J* 13.5, 3.0) and 2.63 (1 H, dd, *J* 13.5, 10.0); δ_C (75 MHz, CDCl₃) 173.0, 153.1, 149.6, 149.5, 139.6, 135.5, 131.1, 129.8, 129.4, 128.6, 128.0, 127.8, 127.5, 119.8, 117.7, 111.5, 110.6, 84.6, 83.6, 66.1, 57.0, 56.3, 56.0, 53.6 and 38.5 (27 signals expected, 25 signals visible); *m/z* (ES⁺) 514 (17%, [M+H]⁺), 497 (34, [M–OH]⁺), 496 (85, [M–OH]⁺), 376 (50, [M–C₆H₄(OCH₃)₂]⁺), 358 (51), 348 (64), 337 (100, [M–PhCH₂CH(CH₂)CO₂N]⁺) and 319 (76); HRMS (ES⁺) found [M+H]⁺ 514.2220, C₃₁H₃₂NO₆ requires 514.2230.

Preparation of (4*S* 2'*S*, 3'*S*, 4'*S*, 5'*R*) and (4*S* 2'*S*, 3'*S*, 4'*S*, 5'*S*)-3-[5'-benzo[1,3]dioxol-5-yl-2'-(3',4'-dimethoxyphenyl)-4'-vinyltetrahydrofuran-3'-carbonyl]-4-benzylloxazolidin-2-one **18a and **18b****

Method 2 (Table 2, entry 8)

Carried out according to the general method using trimethylsilyl trifluoromethanesulfonate (6 μ l, 0.03 mmol, 10 mol%), **10** (0.15 g, 0.32 mmol) and piperonal (0.049 g, 0.33 mmol) in dry dichloromethane (7.5 ml) at -78°C . The reaction mixture was stirred for 6³/₄ hours at -78°C . Work-up and high performance flash chromatography eluting with gradient elution: 20:80 to 95:5 acetonitrile-water, gave **18a** and **18b** (0.11 g, 63% as a 91:9 mixture of diastereoisomers), as a pale yellow viscous liquid, R_F 0.30 (50% diethyl ether in petrol); $[\alpha]_D^{25} +52$ (*c* 1.3, CH₂Cl₂); $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 2994 w, 2956 m, 2922 s, 2851 m, 1778 s, 1691 s, 1640 w, 1607 w, 1517 s, 1504 s, 1490 s, 1462 m, 1445 s, 1386 s, 1350 m, 1261 s, 1239 s, 1103 m, 1035 s, 930 m and 701 s; δ_H (500 MHz, CDCl₃, signals for **18a**); 7.33–6.78 (11 H, m), 5.97 (2 H, s), 5.40 (1 H, dt, *J*

17.0, 9.5), 5.33 (1 H, d, J 9.5), 5.24 (1 H, d, J 9.5), 5.06 (1 H, d, J 17.0), 4.94 (1 H, d, J 9.5), 4.87 (1 H, t, J 9.5), 4.61 (1 H, m), 4.06 (1 H, dd, J 9.0, 2.5), 3.99 (1 H, t, J 9.0), 3.91 (3 H, s), 3.88 (3 H, s), 3.64 (1 H, q, J 9.5), 3.26 (1 H, dd, J 13.5, 10.0), 2.63 (1 H, dd, J 13.5, 9.5); signals for **18b** visible at 5.98 (2 H, s), 5.83 (1 H, ddd, J 17.0, 10.0, 8.0), 5.13 (1 H, d, J 10.0), 4.73 (1 H, t, J 9.0) and 3.06 (1 H, dd, J 13.5, 3.0); δ_c (75 MHz, $CDCl_3$) 172.9, 153.1, 149.6, 149.5, 148.0, 136.3, 135.5, 133.7, 131.0, 129.8, 129.4, 129.4, 129.3, 127.8, 120.8, 119.9, 117.7, 111.5, 110.5, 108.4, 101.4, 84.5, 83.5, 77.6, 66.2, 57.1, 56.3, 53.5, 38.5 (30 signals expected, 29 signals seen); signals for **18b** visible at 135.7, 121.1, 120.2, 118.9, 110.9, 110.7, 107.6, 85.6, 81.6, 66.4 and 54.1; m/z (ES⁺) 541 (45%, $[M-OH]^+$), 540 (100, $[M-OH]^+$), 418 (55), 402 (30), 392 (58) and 363 (90); HRMS (ES⁺) found $[M+Na]^+$ 580.1971, $C_{32}H_{31}NONa$ requires 580.1947.

(4*S*, 2'*S*, 3'*R*, 4'*R*, 5'*R*)-[5'-benzo[1,3]dioxol-5-yl-2'-(3',4'-dimethoxyphenyl)-4'-hydroxymethyltetrahydrofuran-3'-yl]-methanol **19**

Water (0.22 ml), 4-methylmorpholine *N*-oxide (0.039 g, 0.33 mmol) and potassium osmate dihydrate (3 mg, 0.009 mmol, 5 mol%) were sequentially added to a solution of **18** (0.108 g, 194 μ mol, 91:9 diastereomeric mixture) in dry THF (2.2 ml). The reaction mixture was stirred for 40 hours at room temperature. Water (5 ml) was added to the reaction mixture which was then extracted with dichloromethane (5×10 ml). The combined organic extracts were dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the crude diol. The crude diol was dissolved in methanol (2 ml) followed by addition of a solution sodium metaperiodate (0.051 g, 0.024 mmol) in methanol-water (3.2:1, 3.8 ml). The reaction mixture was stirred for 3 $\frac{1}{2}$ hours at room temperature. The reaction mixture was filtered and the residue washed with dichloromethane. Water (5 ml) was added to the organic filtrate and the aqueous layer was extracted with

dichloromethane (4×20 ml). The combined organic extracts were dried (MgSO_4), filtered and evaporated under reduced pressure to give the crude aldehyde. The crude aldehyde was dissolved in THF (1.5 ml) followed by the addition of a solution of sodium borohydride (0.045 g, 0.98 mmol) in water (0.8 ml). The reaction mixture was stirred for $14\frac{3}{4}$ hours at room temperature. The reaction mixture was quenched with aqueous 1 M hydrochloric acid solution (0.4 ml) then extracted with dichloromethane (3×20 ml). The combined organic extracts were dried (MgSO_4), filtered and evaporated under reduced pressure to give the crude product which was purified by flash chromatography gradient elution: 40:60-70:30 ethyl acetate-petrol, to give **19** (0.036 g, 48% as a 74:26 mixture of diastereoisomers), as a pale yellow oil, R_F 0.21 (ethyl acetate); $[\alpha]_D^{24} +14$ (c 0.55, CH_2Cl_2); $\nu_{\text{max}}/\text{cm}^{-1}$ (neat) 3368 br, 2956 s, 2924 s, 2851 w, 1608 m, 1593 m, 1516 s, 1503 s, 1489 s, 1462 s, 1444 s, 1260 s, 1029 s, 932 w, and 809 m; δ_H (300 MHz, CDCl_3); 7.03-6.77 (6 H, m), 5.97 (2 H, s), 5.12 (1 H, d, J 8.5), 4.50 (1 H, d, J 9.5), 3.92 (3 H, s), 3.90 (3 H, s), 3.78 (1 H, dd, J 10.5, 3.5), 3.63 (1 H, t, J 10.5), 3.38 (1 H, dd, J 10.5, 4.5), 3.18 (1 H, t, J 10.5), 2.60 (1 H, m), 2.27 (1 H, m); signals for minor diastereoisomer visible at 5.98 (2 H, s), 5.13 (1 H, d, J 8.5), 3.88 (3 H, s) and 3.14 (1 H, t, J 10.0); δ_C (75 MHz, CDCl_3) 148.1, 148.0, 146.7, 146.1, 131.8, 131.4, 118.8, 118.1, 110.1, 108.9, 107.1, 106.0, 100.1, 81.6, 80.2, 62.8, 62.1, 54.9, 54.2, 49.9 (21 signals expected, 20 signals seen); signals for minor diastereoisomer visible at 148.0, 147.5, 119.4, 117.6, 109.9, 108.6, 107.2, 103.6, 62.0, 54.1 and 49.7; m/z (ES+) 411 (13%, $[\text{M}+\text{Na}]^+$), 353 (100) and 335 (52); HRMS (ES+) found $[\text{M}+\text{Na}]^+$ 411.1428, $\text{C}_{21}\text{H}_{24}\text{O}_7\text{Na}$ requires 411.1420.

(+)-Virgatusin 1

A solution of **19** (17 mg, 0.044 mmol, 74:26 diastereomeric mixture) in dry THF (1.5 ml) was added to a mixture of sodium hydride (5.4 mg, 60% dispersion in mineral oil, 0.14 mmol) in dry THF (0.10 ml). The reaction mixture was stirred for 1¹/₂ at room temperature. Methyl iodide (8.5 μ l, 0.14 mmol) was added to the reaction mixture and the reaction mixture was stirred at room temperature for 20¹/₂ hours. The reaction mixture was diluted with diethyl ether, dried (MgSO₄), filtered and evaporated under reduced pressure to give the crude product which was purified by flash chromatography eluting with 60:40 ethyl acetate-petrol, to give **1** (9 mg, 50 %) as a 74:26 mixture of diastereoisomers, as a pale yellow oil whose data agreed with that reported in the literature¹ for the enantiomeric compound. R_F 0.57 (ethyl acetate); $[\alpha]_D^{22} +16$ (c 0.40, CH₂Cl₂) (lit.⁷⁸ $[\alpha]_D^{25} -12.7$ (c 0.5, CH₂Cl₂); ν_{max}/cm^{-1} (neat) 3434 w, 2929 s, 1727 s, 1607 m, 1516 m, 1491 m, 1445 m, 1382 w, 1269 s, 1234 s, 1193 w, 1124 m, 1073 w 1037 m, 937 w, 809 w and 741 w; δ_H (300 MHz, CDCl₃) 6.93-6.77 (6 H, m), 5.96 (2 H, s), 5.08 (1 H, d, J 7.5), 4.73 (1 H, d, J 8.0), 3.93 (3 H, s), 3.90 (3 H, s), 3.53 (2 H, m), 3.36 (3 H, s), 3.09 (3 H, s), 3.08 (1 H, m), 2.96 (1 H, m), 2.61 (1 H, m), 2.33 (1 H, m); signals for minor diastereoisomer visible at 5.97 (2 H, s), 5.10 (1 H, m), 4.71 (1 H, d, J 7.5) and 3.08 (3 H, s); δ_C (75 MHz, CDCl₃) 148.9, 148.5, 147.4, 146.6, 134.1, 132.8, 119.6, 118.8, 110.9, 109.6, 107.9, 107.1, 101.0, 82.6, 81.5, 73.1, 73.0, 59.1, 58.7, 55.92, 55.85, 50.9, 46.6; signals for minor diastereoisomer visible at 118.5, 110.7, 110.9, 108.1 and 51.1; m/z (ES⁺) 439 (47%, [M+Na]⁺), 413 (48), 367 (85) and 335 (100); HRMS (ES⁺) found [M+Na]⁺ 439.1724, C₂₃H₂₈O₇Na requires 439.1733.

¹ Huang, Y.-L.; Chen, C.-C.; Hsu, F.-L.; Chen, C.-F. *J. Nat. Prod.* **1996**, *59*, 520.

NMR SPECTRA

Siloxane 9

Siloxane 9

Siloxane 10

Siloxane 10

Compound 11a (Table 1, Entry 1; Table 2, Entry 2)

Compound 11a (Table 1, Entry 1; Table 2, Entry 2)

Compound 12a (Table 1, Entry 2; Table 2, Entry 2)

Compound 12a (Table 1, Entry 2; Table 2, Entry 2)

Compounds 13a/13b (93:7, Table 1, Entry 3)

Compounds 13a/13b (93:7, Table 1, Entry 3)

Compounds 13a/13b + 13c (unknown stereochemistry) (80:12:8, Table 1, Entry 4)

Compounds 14a/14b (9:91, Table 1, Entry 6)

Compounds 14a/14b (9:91, Table 1, Entry 6)

Compound 14a (Table 2, Entry 4)

Compound 14a (Table 2, Entry 4)

Compounds 15a/15b + 15c (unknown stereochemistry) (11:78:11, Table 1, Entry 7)

Compounds 15a/15b (97:3, Table 2, Entry 5)

Compounds 15a/15b (97:3, Table 2, Entry 5)

Compound 16 a (Table 2, Entry 6)

Compound 16 a (Table 2, Entry 6)

Compound 17a (Table 2, Entry 7)

Compound 17a (Table 2, Entry 7)

Compounds 18a/18b (91:9, Table 2, Entry 8)

Compounds 18a/18b (91:9, Table 2, Entry 8)

Compound 19

Compound 19

Compound 1 (virgatusin)

Compound 1 (virgatusin)