Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

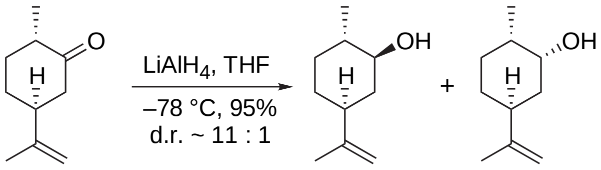
69451 Weinheim, Germany

Total Synthesis of (–)-Colombiasin A and (–)-Elisapterosin B

David C. Harrowven,* David D. Pascoe, Daniela Demurtas, and Heather O. Bourne

Experimental Procedures and Characterisation Data

(1*S*,2*S*,5*S*)-5-Isopropenyl-2-methylcyclohexan-1-ol, 4



3 **4** **4a**

To a stirred suspension of lithium aluminium hydride (2.28 g, 60.0 mmol) in THF (100 mL) at –78 °C was added a solution of (–)-dihydrocarvone (18.1 g, 0.12 mol) in THF (50 mL) over 10 min. After a further 5 min the reaction was quenched with sat. NH$_4$Cl (75 mL) and allowed to warm to RT. The phases were separated and the aqueous phase extracted with ether (3 x 100 mL). The combined organic phases were dried (MgSO$_4$), concentrated *in vacuo* and purified by column chromatography (silica, 10% - 30% ether/petrol) to yield firstly alcohol **4a** (1.3 g, 8.4 mmol, 7%) as a colorless oil, then alcohol **4** as a colorless oil (16.3 g, 105.7 mmol, 88%). Each displayed physical and spectral characteristics consistent with those described in the literature.[1]

Data for **4**:

FT-IR ν_{max} (neat, cm^{-1}) 3345 bw, 2924 m, 2857 w, 1645 w, 1452 m, 1373 w, 1049 m, 887 m.

^{1}H NMR δ_H (300 MHz, CDCl$_3$) 4.70 (2H, s), 3.20 (1H, bt, *J* 9.2 Hz), 2.06-1.94 (2H, m), 1.81-1.65 (2H, m), 1.73 (3H, s), 1.50 (1H, bs), 1.32-1.07 (4H, m), 1.03 (3H, d, *J* 6.3 Hz).

^{13}C NMR δ_C (75 MHz, CDCl$_3$) 149.6 (C), 108.7 (CH$_2$), 76.5 (CH), 44.3 (CH), 40.7 (CH$_2$), 40.2 (CH), 33.4 (CH$_2$), 31.2 (CH$_2$), 21.0 (CH$_3$), 18.5 (CH$_3$).

LRMS $^m/_z$ (EI) 154 (M$^+$, 8%), 136 (100), 121 (98), 107 (100), 93 (95).

Data for **4a**:

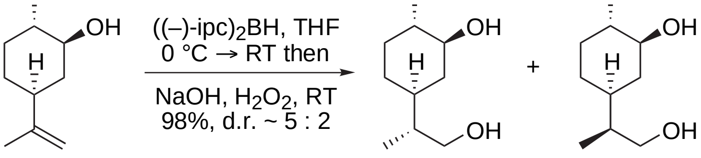
IR ν_{max} (neat, cm^{-1}) 3405 bw, 2923 m, 2871 w, 2855 w, 1643 w, 1451 m, 1374 w, 884 s.

^{1}H NMR (300 MHz) δ_H 4.70 (2H, bs), 3.90 (1H, bs), 2.28 (1H, tt, *J* 12.4, 3.2 Hz), 1.92 (1H, dq, *J* 13.6, 3.4 Hz), 1.81-1.72 (1H, m), 1.73 (3H, s), 1.56-1.37 (5H, m), 1.29-1.13 (1H, m), 0.98 (3H, d, *J* 6.4 Hz).

^{13}C NMR δ_C (75 MHz, CDCl$_3$) 150.3 (C), 108.4 (CH$_2$), 71.0 (CH), 38.7 (CH$_2$), 37.9 (CH), 36.2 (CH), 31.5 (CH$_2$), 28.2 (CH$_2$), 21.0 (CH$_3$), 18.4 (CH$_3$).

LRMS $^m/_z$ (EI) 154 (M$^+$, 4%), 136 (100), 121 (99), 107 (96), 93 (88).

(1*S*,2*S*,2'*R*,5*S*)-5-(1'-Hydroxyprop-2'-yl)-2-methylcyclohexanol 5b and (1*S*,2*S*,2'*S*,5*S*)-5-(1'-hydroxyprop-2'-yl)-2-methylcyclohexanol 5a



4 **5b** **5a**

Using the method of Brown *et al.*[2] – Borane-dimethylsulfide complex (5.4 mL, 57.3 mmol) was added over 5 min to an ice cooled solution of (–)-α-pinene (18.2 mL, 114 mmol) in THF (100 mL). After 1 h alkene **4** (8.84 g, 57.3 mmol) in THF (50 mL) was added *via* syringe over 10 min and the reaction was allowed to warm to RT. After a further 3 h 10% aq. NaOH (22 mL) and 30% aq. H_2O_2 (19 mL) were added sequentially, followed after 16 h by water (50 mL) and chloroform (100 mL). The phases were separated and the aqueous phase extracted with chloroform (2 x 100 mL). The combined organic phases were washed with brine (150 mL), dried ($MgSO_4$), concentrated *in vacuo* and purified by column chromatography (silica, ether) to give a 5 : 2 mixture of diols **5b** and **5a** (9.63 g, 55.9 mmol, 98%) as a colorless oil. Partial separation of the diastereoisomers was achieved by column chromatography on silica using a 3 : 1 : 1 mixture of ether, THF and petrol as the eluting solvent. The enriched samples were then recrystallized from ether/petrol. After a single recrystallization **5b** was attained as a semi-solid contaminated with *ca.* 10% of **5a**, while **5a** was attained as colorless crystals.

Data for **5a** (minor product):

m.p. 83-85 °C (ether/petrol).

FT-IR ν_{max} (neat, cm^{-1}) 3217 bm, 2920 m, 2872 m, 1446 w, 1370 w, 1029 s.

^{1}H NMR δ_H (300 MHz, $CDCl_3$) 3.62 (1H, dd, *J* 10.5, 5.9 Hz), 3.50 (1H, dd, *J* 10.5, 6.4 Hz), 3.15 (1H, td, *J* 10.2, 4.2 Hz), 1.92 (1H, dm, *J* 12.0 Hz), 1.77-1.70 (1H, m), 1.65-1.43 (5H, m), 1.33-1.20 (1H, m), 1.16-0.98 (3H, m), 1.02 (3H, d, *J* 6.3 Hz), 0.91 (3H, d, *J* 6.8 Hz).

^{13}C NMR δ_C (75 MHz, $CDCl_3$) 76.8 (CH), 66.3 (CH_2), 40.43 (CH), 40.40 (CH), 38.3 (CH), 37.8 (CH_2), 33.4 (CH_2), 30.3 (CH_2), 18.5 (CH_3), 13.5 (CH_3).

LRMS $^m/_z$ (EI) 172 (M^+, 3%), 154 (10), 137 (24), 123 (38), 113 (100), 95 (90), 81 (69).

Data for **5b** (major product):

FT-IR ν_{max} (neat, cm^{-1}) 3337 bm, 2920 m, 2872 m, 1453 w, 1373 w, 1041 s.

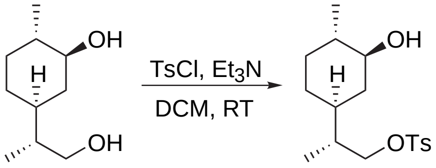
^{1}H NMR δ_H (300 MHz, $CDCl_3$) 3.60 (1H, dd, *J* 10.7, 5.9 Hz), 3.48 (1H, dd, *J* 10.7, 6.4 Hz), 3.15 (1H, dt, *J* 10.2, 4.2 Hz), 1.90 (1H, m), 1.80-1.69 (3H, m), 1.63-1.41 (3H, m), 1.33-0.98 (4H, m), 1.11 (3H, d, *J* 6.4 Hz), 0.89 (3H, d, *J* 7.6 Hz).

^{13}C NMR δ_C (75 MHz, $CDCl_3$) 76.7 (CH), 66.3 (CH_2), 40.5 (CH), 40.3 (CH), 40.0 (CH_2), 38.3 (CH), 33.3 (CH_2), 27.9 (CH_2), 18.5 (CH_3), 13.6 (CH_3).

LRMS $^m/_z$ (EI) 172 (M^+, 2%), 154 (10), 136 (18), 113 (100), 95 (78), 81 (52).

HRMS $^m/_z$ (EI) found: 172.1461, M^+. $C_{10}H_{20}O_2$ requires 172.1463.

(1'*S*,2*R*,3'*S*,4'*S*)-2-(3'-Hydroxy-4'-methylcyclohexyl)propyl *p*-toluenesulfonate, 6



5b **6**

To a stirred solution of diol **5b** (3.01 g, 17.5 mmol) in DCM (125 mL) were added sequentially triethylamine (7.3 mL, 52.5 mmol) and *p*-toluenesulfonyl chloride (10.0 g, 52.5 mmol). After 3 h at RT the solution was concentrated to *ca.* 75 mL and loaded directly onto a chromatography column with silica as the stationary phase. Elution firstly with DCM, then gradient elution with 25% to 75% ether/petrol mixtures, gave tosylate **6** (3.84 g, 11.8 mmol, 67%) as a colorless oil, followed by recovered diol **5b** (902 mg, 5.2 mmol, 30%) as a colorless oil. Data for tosylate **6**:

FT-IR ν_{max} (neat, cm^{-1}) 3402 bw, 2972 w, 2925 m, 2870 w, 1358 s, 1175 s, 1097 m, 962 s, 813 s, 667 s.

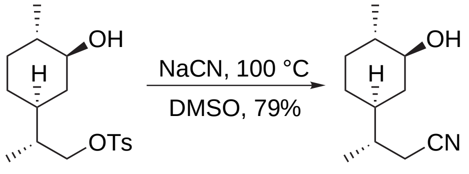
^{1}H NMR δ_H (300 MHz, $CDCl_3$) 7.79 (2H, d, *J* 8.2 Hz), 7.35 (2H, d, *J* 8.2 Hz), 3.95 (1H, dd, *J* 9.5, 6.0 Hz), 3.87 (1H, dd, *J* 9.5, 6.4 Hz), 3.08 (1H, td, *J* 10.2, 4.3 Hz), 2.45 (3H, s), 1.81-1.63 (2H, m), 1.52 (1H, bs), 1.51-1.38 (2H, m), 1.23-1.16 (1H, m), 1.02-0.83 (4H, m), 0.99 (3H, d, *J* 6.4 Hz), 0.87 (3H, d, *J* 7.0 Hz).

^{13}C NMR δ_C (75 MHz, $CDCl_3$) 144.9 (C), 133.3 (C), 130.0 (CH), 128.1 (CH), 76.3 (CH), 73.5 (CH_2), 40.2 (CH), 39.6 (CH_2), 38.0 (CH), 37.5 (CH), 33.0 (CH_2), 27.8 (CH_2), 21.8 (CH_3), 18.4 (CH_3), 13.4 (CH_3).

LRMS $^m/_z$ (ES^+) 675 ($[2M + Na]^+$, 28%), 349 ($[M + Na]^+$, 100).

HRMS $^m/_z$ (ES^+) found: 349.1450, $[M + Na]^+$. $C_{17}H_{26}NaO_4S$ requires 349.1444.

(1'*S*,3*S*,3'*S*,4'*S*)-3-(3'-Hydroxy-4'-methylcyclohexyl)butanenitrile, 7



6 **7**

A solution of tosylate **6** (1.67 g, 5.12 mmol) and sodium cyanide (276 mg, 5.63 mmol) in DMSO (30 mL) was heated to 100 °C for 1 h, then cooled to RT and water (100 mL) added. Following extraction of the aqueous phase with ether (4 x 75 mL), the combined organic phases were washed with water (4 x 100 mL) and brine (2 x 100 mL), dried ($MgSO_4$), and concentrated *in vacuo* to give nitrile **7** as a colorless oil (735 mg, 4.05 mmol, 79%).

FT-IR ν_{max} (neat, cm^{-1}) 3407 bw, 2924 m, 2871 m, 2247 w, 1454 m, 1042 s, 1021 s

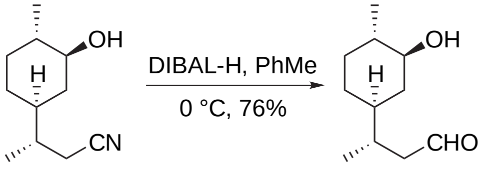
^{1}H NMR δ_H (300 MHz, $CDCl_3$) 3.18 (1H, td, *J* 10.0, 4.2 Hz), 2.38 (1H, dd, *J* 16.8, 5.8 Hz), 2.29 (1H, dd, *J* 16.8, 7.4 Hz),1.99-1.91 (1H, dm, *J* 12.1 Hz), 1.83 (2H, m), 1.69-1.61 (1H, m), 1.60 (1H, bs), 1.53-1.40 (1H, m), 1.33-1.22 (1H, m), 1.11-0.91 (3H, m), 1.08 (3H, d, *J* 7.0 Hz), 1.02 (3H, d, *J* 6.4 Hz).

^{13}C NMR δ_C (75 MHz, $CDCl_3$) 119.2 (C), 76.2 (CH), 40.7 (CH), 40.2 (CH), 39.4 (CH_2), 35.3 (CH), 32.9 (CH_2), 28.2 (CH_2), 22.5 (CH_2), 18.4 (CH_3), 16.8 (CH_3).

LRMS $^m/_z$ (EI) 180 ($[M - H]^+$, 4%), 164 (8), 124 (8), 113 (31), 95 (74), 81 (22), 69 (28), 57 (58).

HRMS $^m/_z$ (EI) found: 181.1465, M^+. $C_{11}H_{19}NO$ requires 181.1467.

(1'*S*,3*S*,3'*S*,4'*S*)-3-(3'-Hydroxy-4'-methylcyclohexyl)butanal, 8



7 **8**

To a solution of nitrile **7** (310 mg, 1.71 mmol) in toluene (20 mL) at 0 °C was added over 5 min DIBAL-H (1 M in hexanes, 5.1 mL, 5.13 mmol). After 1 h chloroform (5 mL) and 2 M HCl (12 mL) were added and the reaction stirred for a further 30 min. Following extraction with chloroform (3 x 30 mL), the combined organic phases were washed with water (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated *in vacuo* to give aldehyde **8** (241 mg, 1.31 mmol, 76%) as a pale yellow oil.

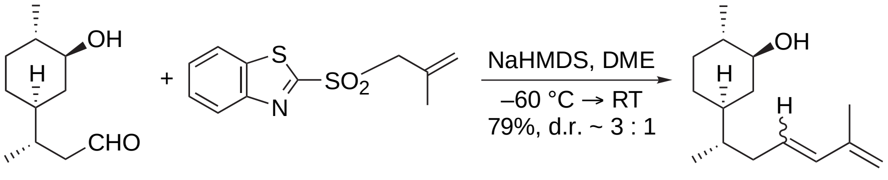
FT-IR ν_{max} (neat, cm^{-1}) 3402 bw, 2923 s, 2857 m, 2721 w, 1721 s, 1453 m, 1376 m, 1043 s, 1019 s.

^{1}H NMR δ_H (300 MHz, $CDCl_3$) 9.76 (1H, dd, *J* 2.7, 1.8 Hz), 3.14 (1H, td, *J* 10.4, 4.0 Hz), 2.47 (1H, ddd, *J* 16.1, 4.8, 1.8 Hz), 2.23 (1H, ddd, *J* 16.1, 8.8, 2.7 Hz), 2.09-1.96 (1H, m), 1.91 (1H, dm, *J* 11.9 Hz), 1.78-1.72 (1H, m), 1.65-1.56 (2H, m), 1.36-1.18 (2H, m), 1.11-0.95 (3H, m), 1.01 (3H, d, *J* 6.4 Hz), 0.93 (3H, d, *J* 7.0 Hz).

^{13}C NMR δ_C (75 MHz, $CDCl_3$) 203.1 (CH), 76.5 (CH), 48.6 (CH_2), 41.7 (CH), 40.4 (CH), 39.3 (CH_2), 33.2 (CH_2), 32.6 (CH), 28.4 (CH_2), 18.4 (CH_3), 17.1 (CH_3).

LRMS $^m/_z$ (CI) 202 ($[M + NH_4]^+$, 100%], 185 (MH^+, 32%), 167 (78), 149 (92), 122 (52), 95 (17).

(1*S*,2*S*,3'*E/Z*,5*S*,6'*S*)-5-(2'-Methylhepa-1',3'-dien-6-yl)-2-methylcyclohexanol, (*Z*)-**10** and (*E*)-**10**



8 **9** (*Z*)-**10** : (*E*)-**10**

Using the method of Kocienski *et al.*[3] – To a mixture of sulfone **9** (667 mg, 2.63 mmol) and aldehyde **8** (485 mg, 2.63 mmol) in DME (30 mL) at –60 °C was added NaHMDS (2 M in THF, 2.6 mL, 5.26 mmol). After 2 h the reaction was allowed to warm to RT over 30 min then stirred at RT for 1 h. The reaction mixture was partitioned between sat. NH_4Cl (10 mL) and ether (30 mL). The aqueous phase was separated and extracted with ether (2 x 30 mL) then the combined organic phases were washed with brine (100 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by column chromatography (silica, 20% ether / petrol) gave a 3 : 1 mixture of dienes (*Z*)-**10** and (*E*)-**10** (464 mg, 2.09 mmol, 79%) as a pale yellow oil. Data was recorded on the mixture.

FT-IR ν_{max} (neat, cm^{-1}) 3360 bw, 2920 s, 2868 m, 1453 m, 1373 m, 1044 s, 1020 m, 966 w, 888 s.

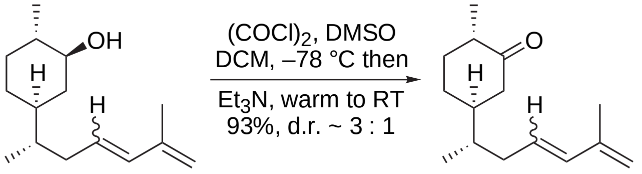
^{1}H NMR δ_H (300 MHz, $CDCl_3$) major isomer (*Z*)-**10** – 5.88 (1H, d, *J* 11.8 Hz), 5.39 (1H, dt, *J* 11.8, 7.4 Hz), 4.95 (1H, s), 4.83 (1H, s), 3.14 (1H, td, *J* 10.4, 4.2 Hz), 2.38-2.27 (1H, m), 2.15 (1H, ddd, *J* 16.1, 8.1, 1.5 Hz), 1.98-1.85 (1H, m), 1.87 (3H, s), 1.75-1.72 (1H, m), 1.58-1.52 (2H, m), 1.46-1.21 (3H, m), 1.31 (1H, bs), 1.14-1.00 (2H, m), 1.01 (3H, d, *J* 6.2 Hz), 0.87 (3H, d, *J* 6.8 Hz). Additional signals attributed to the minor isomer (*E*)-**10** and giving ~ $^1/_3$ the integral of those above – 6.13 (1H, d, *J* 15.7 Hz), 5.62 (1H, dt, *J* 15.7, 7.4 Hz), 4.87 (2H, s), 1.83 (3H, s), 0.85 (3H, d, *J* 6.8 Hz).

^{13}C NMR δ_C (75 MHz, $CDCl_3$) major isomer (*Z*)-**10** – 142.0 (C), 131.7 (CH), 131.0 (CH) 115.2 (CH_2), 76.8 (CH), 41.4 (CH), 40.5 (CH), 39.9 (CH_2), 38.7 (CH), 33.4 (CH_2), 33.2 (CH_2), 28.0 (CH_2), 23.7 (CH_3), 18.5 (CH_3), 16.4 (CH_3). Additional signals attributed to the minor isomer (*E*)-**10** – 142.3 (C), 134.1 (CH), 129.9 (CH), 114.4 (CH_2), 38.2 (CH), 37.7 (CH_2), 18.9 (CH_3).

LRMS $^m/_z$ (EI) 222 (M$^+$, 10%), 189 (6), 161 (4), 122 (5), 109 (100), 93 (12), 82 (18), 67 (32), 55 (19).

HRMS $^m/_z$ (EI) found: 222.1980, M$^+$. $C_{15}H_{26}O$ requires 222.1984.

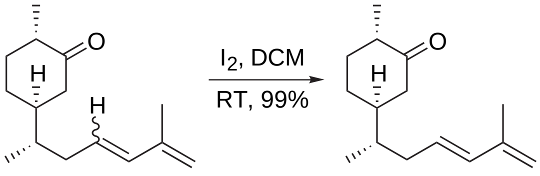
(2*S*,3'*E/Z*,5*S*,6*S*)-5-(2'-Methyl-1',3'-heptadien-6'-yl)-2-methylcyclohexan-1-one, (*Z*)-**11** and (*E*)-**11**



(*Z*)-**10** : (*E*)-**10** (*Z*)-**11** : (*E*)-**11**

To a solution of oxalyl chloride (0.13 mL, 1.44 mmol) in DCM (15 mL) at –78 °C was added dimethyl sulfoxide (0.15 mL, 2.16 mmol). After 15 min a solution of alcohol **6** (160 mg, 0.720 mmol) in DCM (5 mL) was added, followed after 30 min by triethylamine (0.60 mL, 4.32 mmol). After a further 10 min the reaction was warmed to RT, washed with water (10 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by column chromatography (silica, 5% ether / petrol) gave a 3 : 1 mixture of (*Z*)-**11** and (*E*)-**11** as a yellow oil (147 mg, 0.667 mmol, 93%). Data for (*E*)-**11** is given after the following experimental.

(2*S*,3'*E*,5*S*,6*S*)-5-(2'-Methyl-1',3'-heptadien-6'-yl)-2-methylcyclohexan-1-one, (*E*)-**11**



(*Z*)-**11** : (*E*)-**11** (*E*)-**11**

To a solution of dienones (*Z*)-**11** and (*E*)-**11** (d.r. 3 : 1, 383 mg, 1.74 mmol) in DCM (10 mL) was added a solution of iodine (44 mg, 0.1 eq) in DCM (2 mL). After 2 h the reaction mixture was diluted with DCM (30 mL), washed with sat. $Na_2S_2O_3$ (2 x 20 mL) and brine (30 mL), dried ($MgSO_4$), and concentrated *in vacuo* to give dienone (*E*)-**11** (380 mg, 1.72 mmol, 99%) as a pale yellow oil.

FT-IR ν_{max} (neat, cm^{-1}) 2964 m, 2929 m, 2868 m, 1711 vs, 1608 w, 1453 m, 1377 m, 966 m, 822 m.

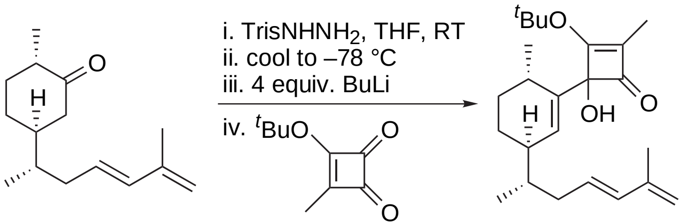
^{1}H NMR δ_H (300 MHz, $CDCl_3$) 6.14 (1H, d, *J* 15.6 Hz), 5.59 (1H, dt, *J* 15.6, 7.2 Hz), 4.88 (2H, s), 2.41-2.27 (2H, m), 2.26-2.05 (3H, m), 1.96 (1H, app. dt, *J* 14.6, 7.2 Hz), 1.87-1.78 (1H, m), 1.83 (3H, s), 1.76-1.67 (1H, ddd, *J* 16.6, 8.1, 3.7 Hz), 1.59-1.38 (2H, m), 1.30 (1H, qd, *J* 12.9, 3.4 Hz), 1.02 (3H, d, *J* 6.6 Hz), 0.90 (3H, d, *J* 7.0 Hz).

^{13}C NMR δ_C (75 MHz, $CDCl_3$) 213.4, (C), 142.2 (C), 134.6 (CH), 129.1 (CH), 114.7 (CH_2), 46.4 (CH_2), 45.2 (CH), 44.7 (CH), 38.2 (CH), 37.5 (CH_2), 35.2 (CH_2), 27.7 (CH_2), 18.9 (CH_3), 16.0 (CH_3), 14.5 (CH_3).

LRMS $^m/_z$ (EI) 220 (M^+, 12%), 205 (3), 109 (100), 69 (42), 55 (50).

HRMS $^m/_z$ (EI) found: 220.1835, M^+. $C_{15}H_{24}O$ requires 220.1827.

(3'*R*,3"*E*,4*RS*,6'*S*,6"*S*)-3-(*tert*-Butoxy)-4-hydroxy-2-methyl-4-(6'-methyl-3'-(2"-methyl-1",3"-heptadien-6-yl)-1-cyclohexenyl)-2-cyclobuten-1-one, 14



(*E*)-**11** **12** **14**

To a solution of $TrisNHNH_2$ (157 mg, 0.526 mmol) in THF (10 mL) under argon was added a solution of dienone (*E*)-**11** (116 mg, 0.526 mmol) in THF (5 mL). After 2 h at RT the temperature was reduced to –78 °C and *t*-BuLi (1.3 M in pentane, 1.7 mL, 2.10 mmol) added. The resulting orange solution was maintained at –78 °C for 2 h then warmed to –20 °C over 20 min. Once N_2 evolution had ceased, the reaction was cooled to –78 °C and a solution of squarate **10** (531 mg, 3.20 mmol) in THF (5 mL) added over 5 min. After a further 20 min water (10 mL) was added and the reaction allowed to warm to RT. Following dilution with ether (20 mL), the aqueous phase was separated and extracted with ether (2 x 20 mL). The combined organic phases were washed with brine (50 mL), dried ($MgSO_4$), concentrated *in vacuo*, and purified by column chromatography (silica, 5% → 50% ether / petrol) to give a ~3 : 2 mixture of cyclobutenones **14** (71 mg, 0.19 mmol, 36%) as a yellow oil. Data was recorded on the mixture.

FT-IR ν_{max} (neat, cm^{-1}) 3383 bw, 2951 m, 2926 m, 2869 w, 1750 m, 1597 vs, 1385 m, 1339 s, 1158 s.

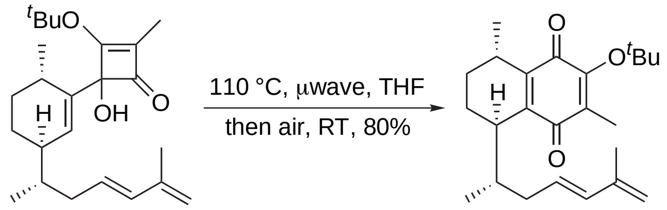
^{1}H NMR δ_H (300 MHz, $CDCl_3$) Integrals for the minor diastereoisomer are italicised and were ~ $^2/_3$ the value of the major diastereoisomer: 6.13 (1H + *1H*, d, *J* 15.5 Hz), 5.95 (*1H*, d, *J* 2.8 Hz), 5.69 (1H, bs), 5.63 (1H + *1H*, dt, *J* 15.5, 7.3 Hz), 4.86 (2H + *2H*, s), 2.17-1.90 (3H + *3H*, m), 1.84 (3H, s), 1.82-1.76 (2H + *2H*, m), 1.80 (*3H*, s), 1.73-1.45 (3H + *3H*, m), 1.57 (9H, s), 1.53 (*9H*, s), 1.44 (3H + *3H*, s), 1.29-1.23 (2H + *2H*, m), 1.17 (3H, d, *J* 7.0 Hz), 1.10 (*3H*, d, *J* 7.0), 0.87 (3H, d, *J* 6.8 Hz), 0.83 (*3H*, d, *J* 6.8 Hz).

^{13}C NMR δ_C (75 MHz, $CDCl_3$) 193.5 (C), 192.4 (C), 180.3 (C), 178.7 (C), 142.3 (2 C), 139.7 (C), 139.2 (C), 134.2 (2 CH), 130.2 (CH), 129.9 (2 CH), 125.7 (CH), 122.4 (C), 121.8 (C), 114.4 (2 CH_2), 94.9 (C), 94.2 (C), 83.7 (C), 83.3 (C), 39.4 (CH), 38.7 (CH), 38.5 (CH), 38.3 (CH), 37.9 (CH_2), 37.8 (CH_2), 31.3 (CH_2), 30.8 (CH_2), 30.5 (CH), 30.0 (CH), 28.9 (C), 28.8 (C), 21.9 (CH_2), 21.0 (CH_2), 20.9 (CH_3), 20.8 (CH_3), 18.9 (2 CH_3), 16.6 (CH_3), 16.5 (CH_3), 9.7 (CH_3), 9.1 (CH_3).

LRMS $^m/_z$ (ES^+) 767 ([2M + Na]$^+$, 8%], 395 ([M + Na]$^+$, 100).

HRMS $^m/_z$ (ES^+) found: 395.2560, [M + Na]$^+$. $C_{24}H_{36}O_3Na$ requires 395.2557.

(3'*E*,6*R*,6'*S*,9*S*)-2-(*tert*-Butoxy)-3,9-dimethyl-6-(2'-methyl-1',3'-heptadien-6'-yl)-6,7,8,9-tetrahydro-1,4-napthalenedione, 18



14 **18**

A solution of cyclobutenone **14** (25 mg, 0.067 mmol) in THF (2 mL) was placed in a sealed tube and heated to 110 °C in a microwave reactor for 30 min. On cooling to RT, the reaction vessel was opened to the atmosphere and stirred in the dark for 24 h. Concentration *in vacuo* and purification by column chromatography (silica, 1% ether / petrol) gave quinone **18** (20 mg, 0.054 mmol, 80%) as a bright yellow oil.

FT-IR ν_{max} (neat, cm^{-1}) 2960 s, 2930 s, 2871 m, 1659 vs, 1646 vs, 1607 s, 1369 s, 1144 vs, 1129 s.

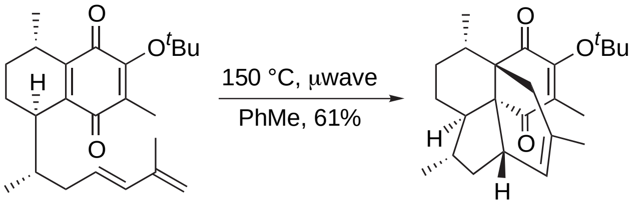
^{1}H NMR δ_H (300 MHz, $CDCl_3$) 6.13 (1H, d, *J* 15.7 Hz), 5.65 (1H, dt, *J* 15.7, 7.0 Hz), 4.86 (2H, bs), 3.02-2.91 (1H, m), 2.87-2.82 (1H, m), 2.18-1.99 (2H, m), 1.97 (3H, s), 1.87-1.80 (1H, obsc. m), 1.84 (3H, s), 1.76-1.72 (1H, m), 1.68-1.59 (1H, m), 1.55-1.43 (1H, m), 1.40 (9H, s), 1.07 (3H, d, *J* 7.0 Hz), 0.92-0.81 (1H, m), 0.82 (3H, d, *J* 6.8 Hz).

^{13}C NMR δ_C (100 MHz, $CDCl_3$) 189.2 (C), 185.2 (C), 154.5 (C), 146.9 (C), 144.8 (C), 142.3 (C), 134.4 (C), 134.3 (CH), 130.1 (CH), 114.6 (CH_2), 84.0 (C), 39.3 (CH_2), 37.1 (CH), 35.3 (CH), 29.7 (CH_3), 26.5 (CH), 26.3 (CH_2), 21.0 (CH_3), 18.9 (CH_3), 18.3 (CH_2), 17.7 (CH_3), 10.9 (CH_3).

LRMS $^m/_z$ (ES^+) 393 ([M + Na]$^+$, 100%).

HRMS $^m/_z$ (ES^+) found: 393.2404, [M + Na]$^+$. $C_{24}H_{34}O_3Na$ requires 393.2400.

(–)-Colombiasin A *tert*-butyl ether, 17



18 **17**

A solution of quinone **18** (13 mg, 35.1 μmol) in toluene (3 mL) was placed in a sealed tube and heated to 150 °C in a microwave reactor for 15 h. After cooling to RT the solvent was removed *in vacuo* and the residue purified by column chromatography (silica, 1% ether / petrol) to give colombiasin A *tert*-butyl ether **17** (7.9 mg, 21.3 μmol, 61%) as a colorless oil, contaminated with *ca.* 10% of an unknown impurity.

FT-IR ν_{max} (neat, cm^{-1}) 2963 m, 2929 s, 1679 s, 1618 w, 1459 w, 1369 m, 1259 w, 1134 m, 1107 m.

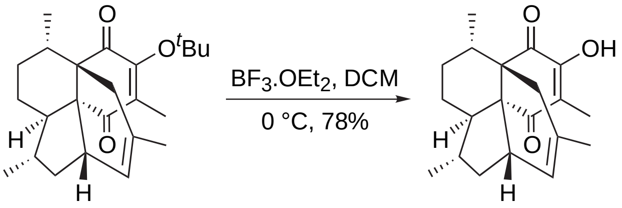
^{1}H NMR δ_H (300 MHz, ($CDCl_3$) 5.64 (1H, bs), 3.10-2.99 (1H, m), 2.39 (1H, bd, *J* 18.9 Hz), 2.14-2.07 (1H, m), 1.93 (3H, s), 1.91-1.74 (6H, obsc. m), 1.56 (3H, bs), 1.40 (9H, s), 1.38-1.28 (3H, m), 1.32 (3H, d, *J* 7.0 Hz), 0.80 (3H, d, *J* 7.0 Hz).

^{13}C NMR δ_C (75 MHz, $CDCl_3$) 203.5 (C), 200.2 (C), 153.4 (C), 137.4 (C), 129.4 (C), 123.3 (CH), 83.3 (C), 63.5 (C), 51.5 (C), 48.3 (CH), 39.6 (CH), 38.9 (CH), 36.4 (CH_2), 33.5 (CH_2), 33.5 (CH), 31.9 (CH_2), 31.3 (CH_2), 29.8 (CH_3), 23.1 (CH_3), 22.5 (CH_3), 18.0 (CH_3), 12.4 (CH_3).

LRMS $^m/_z$ (ES$^+$) 763 ([2M + Na]$^+$, 20%), 425 (25), 393 ([M + Na]$^+$, 100).

HRMS $^m/_z$ (ES$^+$) found: 393.2401, [M + Na]$^+$. $C_{24}H_{34}O_3Na$ requires 393.2400.

(–)-Colombiasin A, 1



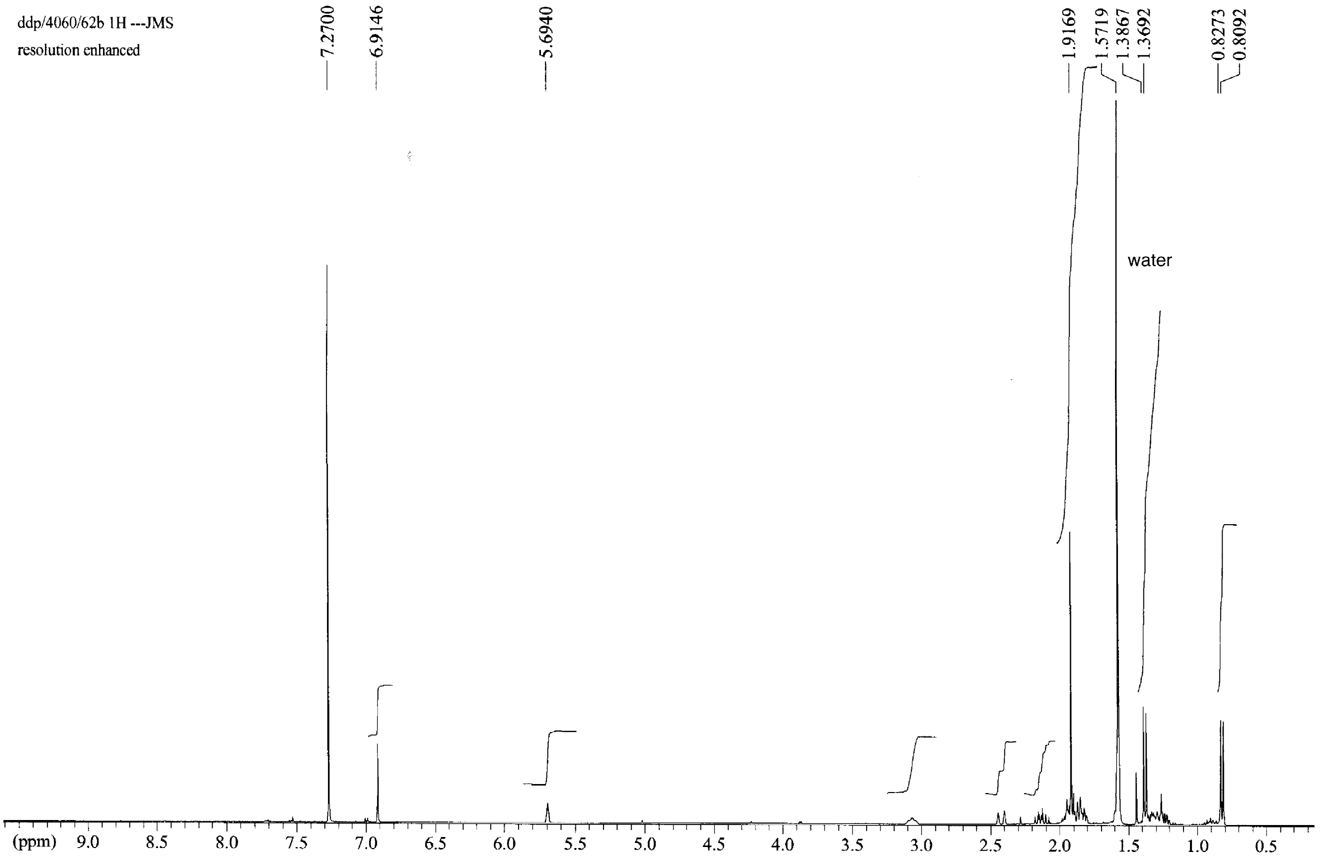
17 **1**

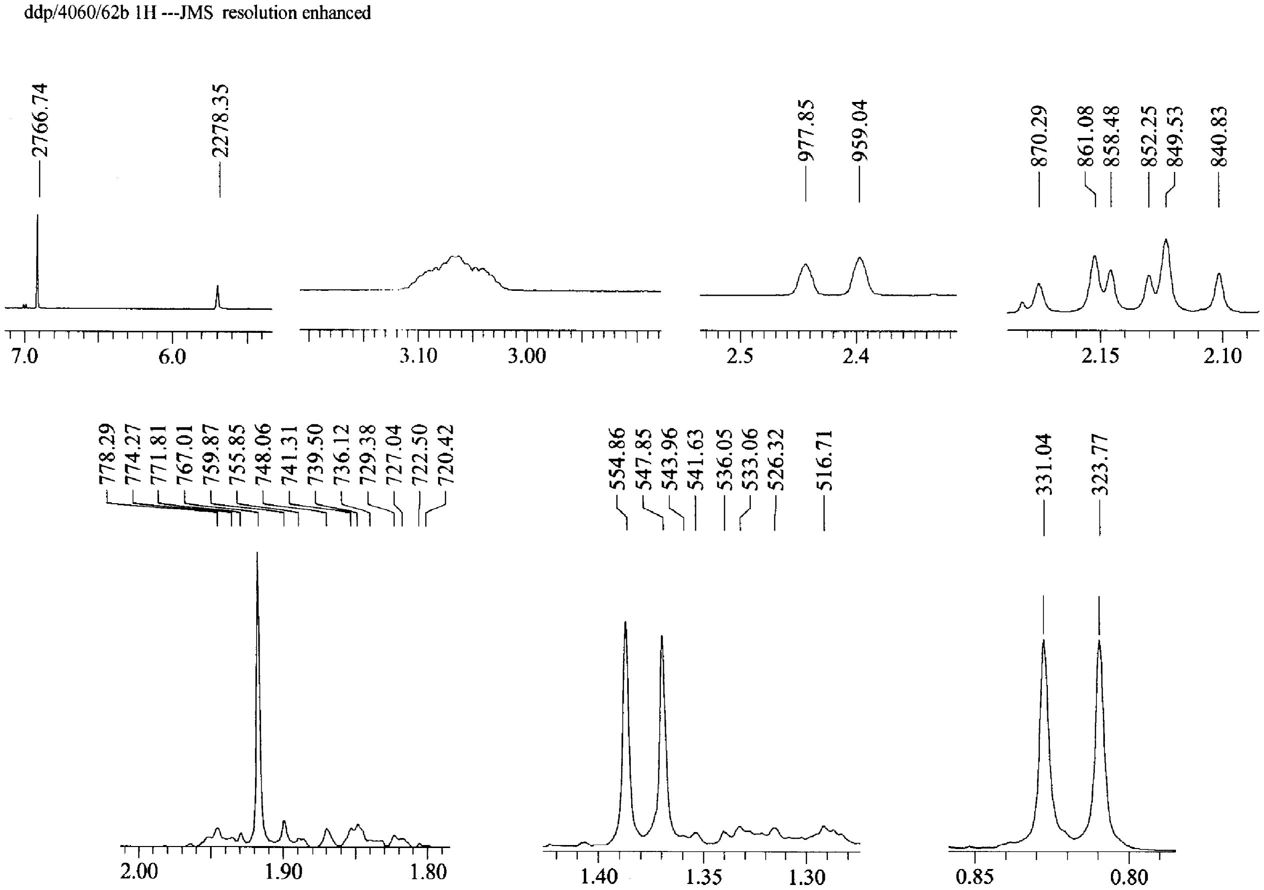
To a solution of (–)-colombiasin A ^{t}butyl ether **17** (3.5 mg, 9.4 μmol) in DCM (1 mL) at 0 °C was added $BF_3.OEt_2$ (1M in DCM, 19 μL, 19 μmol). After 5 min the reaction mixture was loaded directly onto a chromatography column (silica) and eluted with DCM to give colombiasin A **1** (2.3 mg, 7.3 μmol, 78%) as a colorless film. Physical and spectral characteristics were consistent with those described in the literature.[4,5]

$[\alpha]^{25}_D$ –58.7 (c = 0.15, $CHCl_3$). Lit. –55.3 (c = 0.9, $CHCl_3$).[4] Lit. –61.0 (c = 0.1, $CHCl_3$).[5]

FT-IR ν_{max} (neat, cm^{-1}) 3381 bw, 2960 w, 2928 m, 2873 w, 1667 s, 1450 w, 1379 s, 1343 m, 1108 m.

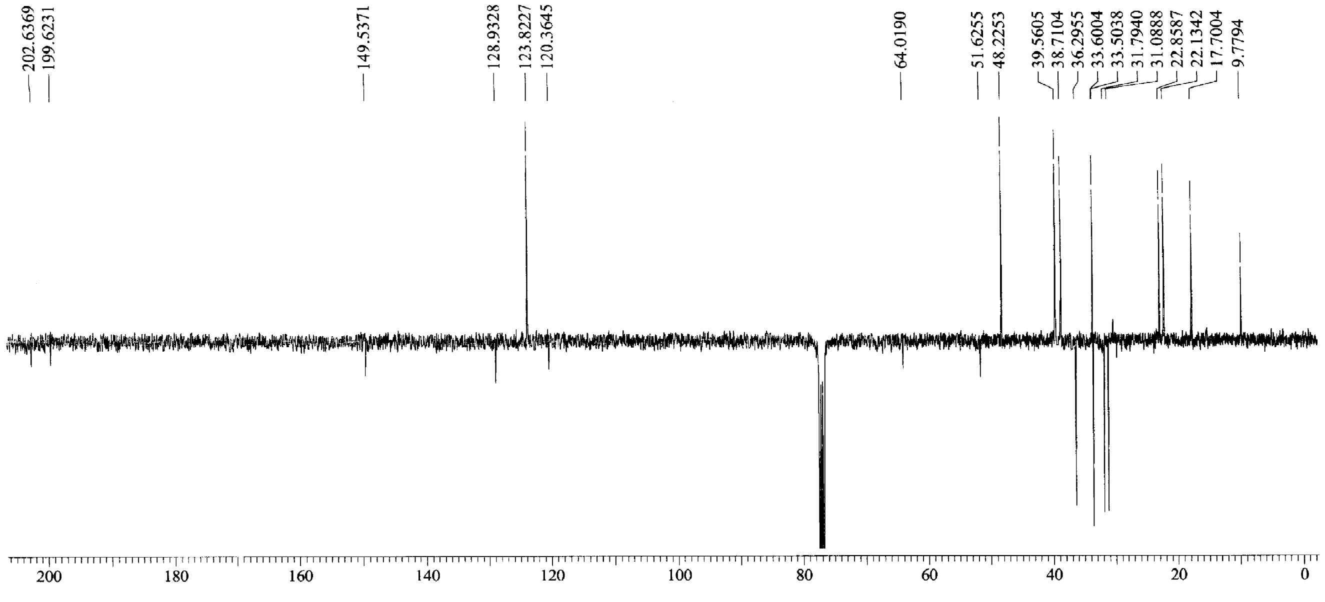
^{1}H NMR δ_H (400 MHz, $CDCl_3$) 6.91 (1H, s), 5.69 (1H, bs), 3.06 (1H, bm), 2.42 (1H, bd, *J* 18.8 Hz), 2.13 (1H, dt, *J* 11.7, 9.0 Hz), 1.98-1.80 (6H, m), 1.92 (3H, s), 1.62-1.55 (1H, m), 1.57 (3H, bs), 1.38 (3H, d, *J* 7.0 Hz), 1.37-1.25 (2H, m), 0.82 (3H, d, *J* 7.3 Hz).





^{13}C NMR δ_C (100 MHz, $CDCl_3$) 202.6 (C), 199.6 (C), 149.5 (C), 128.9 (C), 123.8 (CH), 120.4 (C), 64.0 (C), 51.6 (C), 48.2 (CH), 39.6 (CH), 38.7 (CH), 36.3 (CH_2), 33.6 (CH), 33.5 (CH_2), 31.8 (CH_2), 31.1 (CH_2), 22.9 (CH_3), 22.1 (CH_3), 17.7 (CH_3), 9.8 (CH_3).

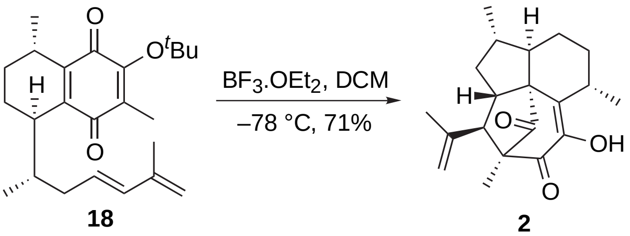
Jmod ^{13}C NMR showing C and CH_2 –ve; CH and CH_3 +ve.



LRMS $^m/_z$ (EI) 314 (M^+, 100%), 299 (28), 286 (33), 271 (19), 243 (18), 206 (27), 201 (24), 145 (26).

HRMS $^m/_z$ (EI) found: 314.1881, M^+. $C_{20}H_{26}O_3$ requires 314.1882.

(–)-Elisapterosin B, 2



18 **2**

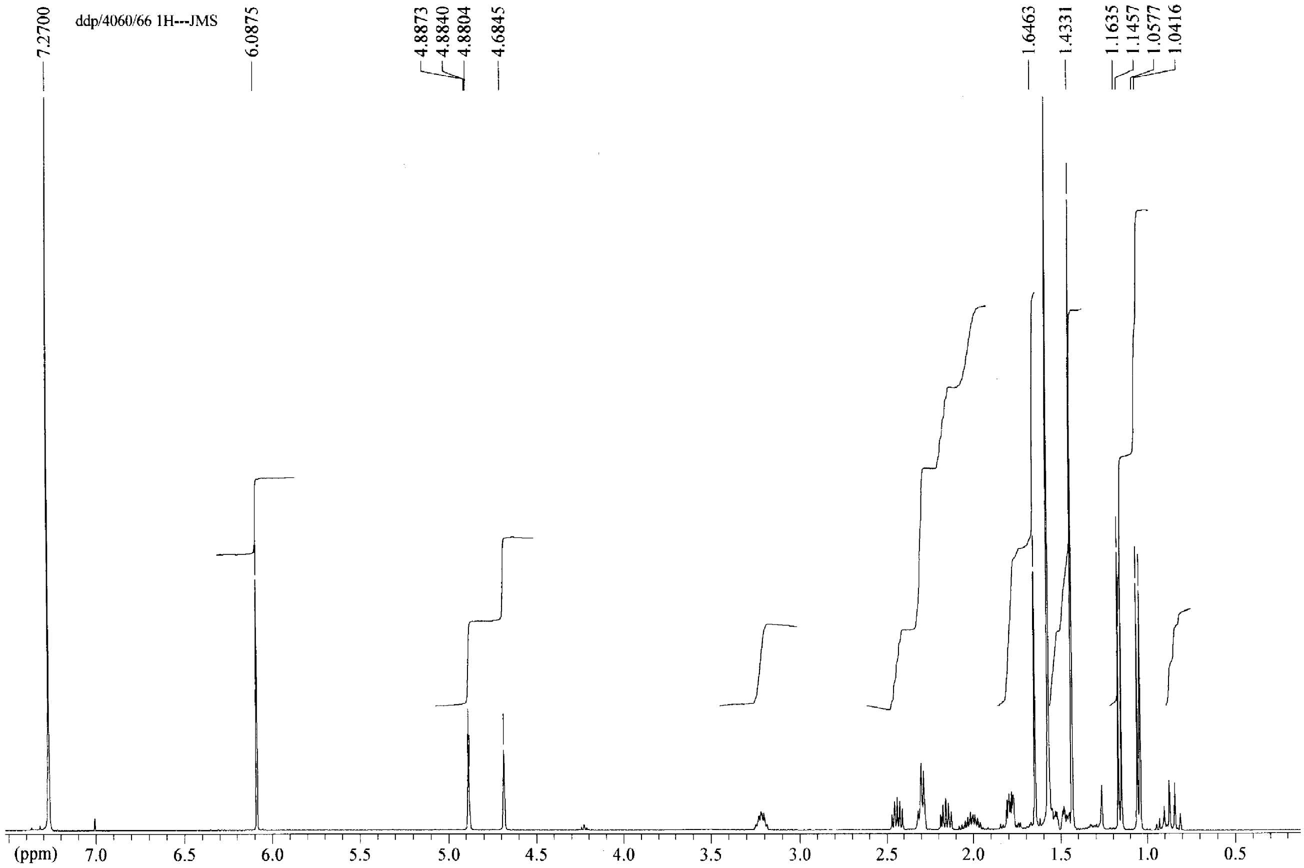
To a solution of quinone **18** (6.5 mg, 17.5 μmol) in DCM (1 mL) at –78 °C and in the dark was added $BF_3.OEt_2$ (1M in DCM, 35 μL, 35.0 μmol). After 1 h sat. $NaHCO_3$ (1 mL) was added. The reaction was warmed to RT and partitioned between ether (5 mL) and brine (3 mL). The organic phase was separated, dried ($MgSO_4$), concentrated *in vacuo*, and purified by column chromatography (silica, 2-5% ether / petrol) to give (–)-elisapterosin B **1** as a white solid (3.9 mg, 18.8 μmol, 71%). Physical and spectral characteristics were consistent with those described in the literature.[6,7]

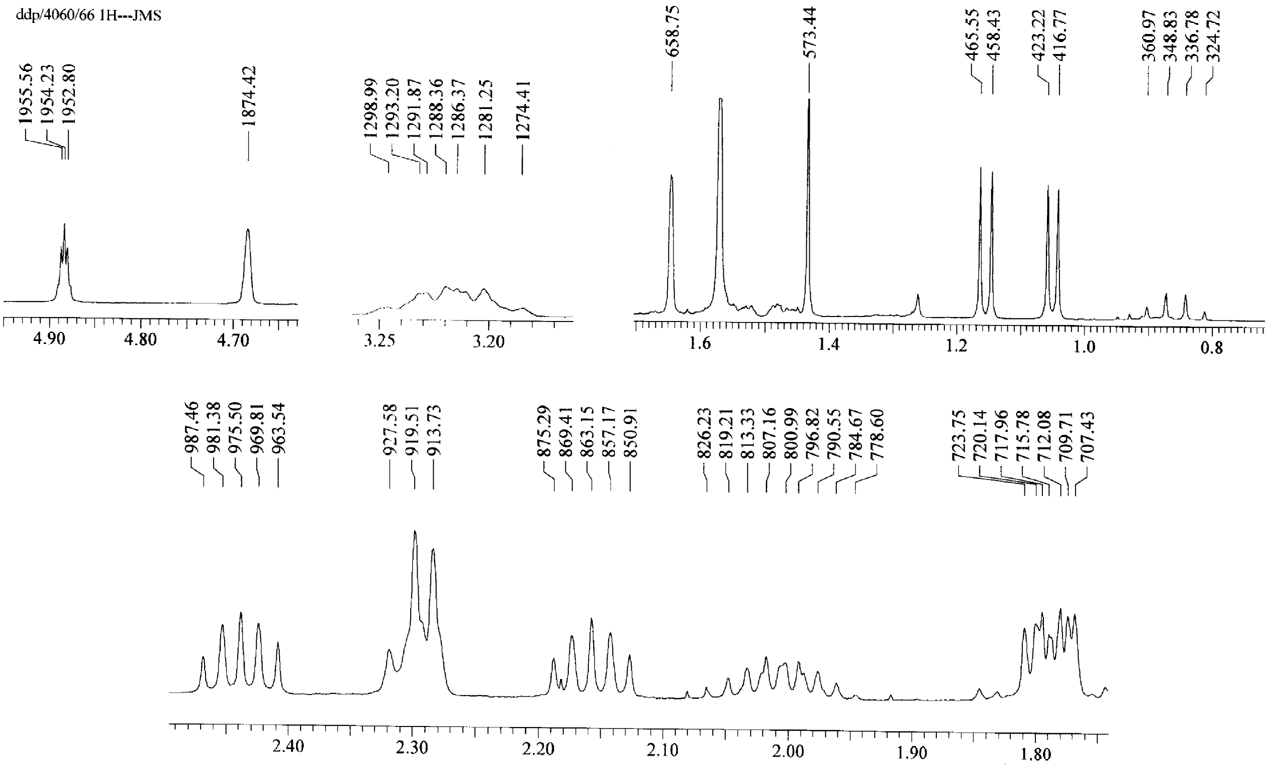
m.p. 48 – 50 °C (ether). Lit.[6,7] not reported.

$[\alpha]^{25}_{D}$ –33.8° (c = 0.10, $CHCl_3$). Lit. –3.0° (c = 4.4, $CHCl_3$).[6] Lit. –31.5° (c = 0.16, $CHCl_3$).[7]

FT-IR ν_{max} (neat, cm^{-1}) 3426 bw, 2931 m, 1757 s, 1660 s, 1618 m, 1386 m, 1365 m, 1043 m, 1032 m.

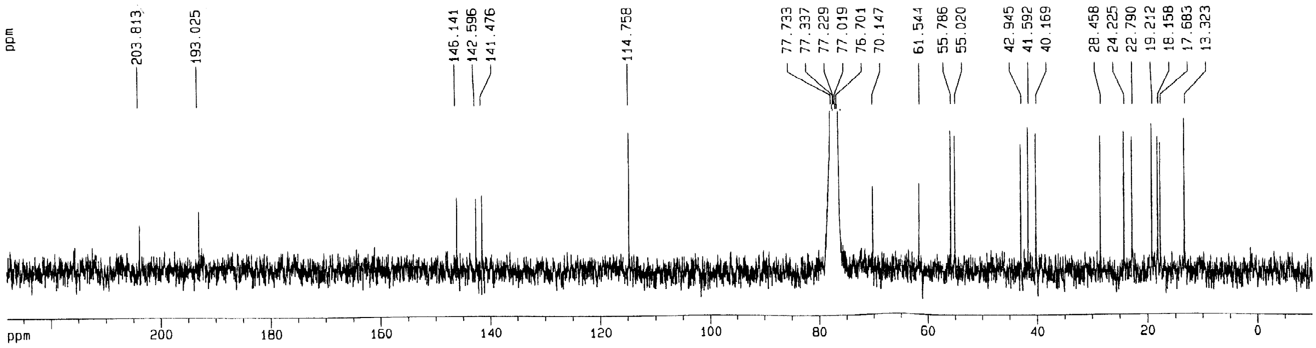
^{1}H NMR δ_H (400 MHz, $CDCl_3$) 6.09 (1H, s), 4.88 (1H, quint, *J* 1.4 Hz), 4.68 (1H, bs), 3.22 (1H, bm), 2.44 (1H, ddd, *J* 11.9, 6.2, 5.6 Hz), 2.33-2.28 (1H, m), 2.29 (1H, d, *J* 5.6 Hz), 2.16 (1H, ddd, *J* 12.2, 6.2, 5.9 Hz), 2.08-1.96 (1H, app ddqd, *J* 12.1, 10.3, 6.4, 5.9 Hz), 1.81-1.76 (2H, m), 1.65 (3H, dd, *J* 1.5, 0.7 Hz), 1.56-1.51 (1H, m), 1.50-1.45 (1H, m), 1.43 (3H, s), 1.15 (3H, d, *J* 7.1 Hz), 1.05 (3H, d, *J* 6.4 Hz), 0.85 (1H, q, *J* 12.1 Hz).





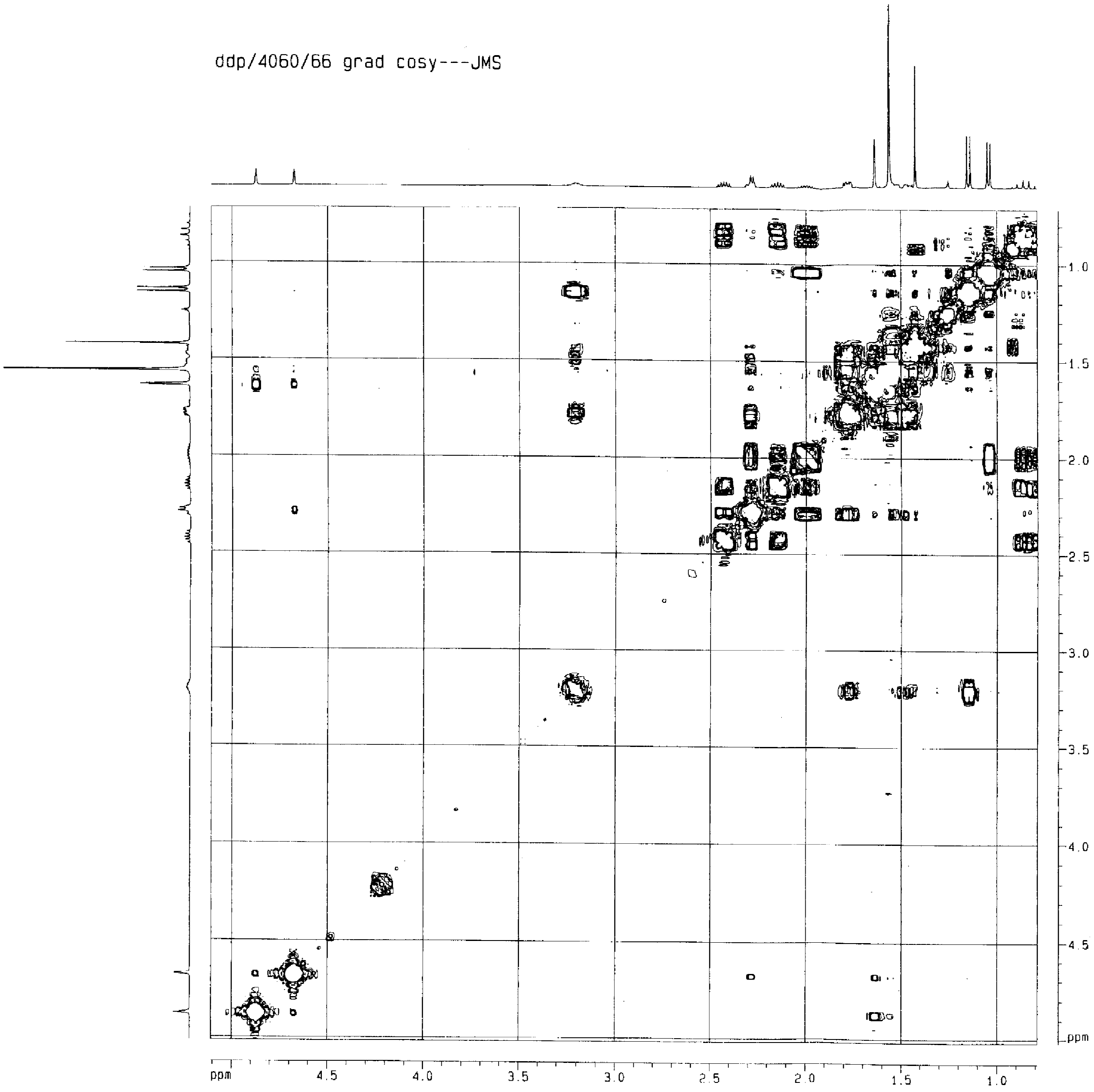
^{1}H-^{1}H COSY reproduced on following page.

^{13}C NMR δ$_C$ (100 MHz, CDCl$_3$) 203.8 (C), 193.0 (C), 146.1 (C), 142.6 (C), 141.5 (C), 114.8 (CH$_2$), 70.1 (C), 61.5 (C), 55.8 (CH), 55.0 (CH), 42.9 (CH$_2$), 41.6 (CH), 40.2 (CH), 28.5 (CH), 24.2 (CH$_2$), 22.8 (CH$_3$), 19.2 (CH$_2$), 18.2 (CH$_3$), 17.7 (CH$_3$), 13.3 (CH$_3$) and reproduced below:



LRMS $^m/_z$ (CI) 315 (MH$^+$, 100%), 287 (12), 271 (8), 243 (6), 206 (50), 109 (34), 93 (18).

HRMS $^m/_z$ (ES$^+$) found: 337.1773, [M + Na]$^+$. C$_{20}$H$_{26}$NaO$_3$ requires 337.1774.



Additional references for the supporting information

[1] T. Hirata, H. Hamada, T. Aoki, T. Suga, *Phytochemistry* **1982**, *21*, 2209-2212.

[2] H. C. Brown, P. V. Ramachandran, *J. Organomet. Chem.* **1995**, *500*, 1-19.

[3] N. D. Smith, P. J. Kocienski, S. D. A. Street, *Synthesis* **1996**, 652-666.

[4] A. D. Rodríguez, C. Ramírez, *Org. Lett.* **2000**, *2*, 507-510.

[5] K. C. Nicolaou, G. Vassilikogiannakis, W. Mägerlein, R. Kranich, *Chem. Eur. J.* **2001**, *7*, 5359-5371.

[6] A. D. Rodríguez, C. Ramírez, I. I. Rodríguez, C. L. Barnes, *J. Org. Chem.* **2000**, *65*, 1390-1398.

[7] A. I. Kim, S. D. Rychnovsky, *Angew. Chem. Int. Ed.* **2003**, *42*, 1267-1270.