10.1071/CH14030_AC

Australian Journal of Chemistry 2014, 67(8 & 9), 1189-1194

Development of the Claisen Rearrangement / Organocatalytic Diels-Alder Approach to the Eunicellins

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Supplementary Information

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General Experimental Techniques

^{1}H nuclear magnetic resonance spectra were recorded for deuterochloroform, deuterobenzene or deuteromethanol solutions on Varian Inova 400 (400 MHz) and Varian Inova 500 (500 MHz) instruments. Chemical shifts are given in parts per million (ppm) quoted relative to tetramethylsilane (δ = 0 ppm) and referenced to residual solvent as internal standard. When quoting multiplicity, the following abbreviations are used; s - singlet, br s – broad singlet, d – doublet, t – triplet, q – quartet, sept – septet, m- multiplet. Coupling constants (*J*) are given in Hertz (Hz), to the nearest 0.5 Hz.

Proton decoupled ^{13}C nuclear magnetic resonance spectra were recorded on Varian Inova 400 (100 MHz) and Varian Inova 500 (125 MHz) instruments in the solvent indicated. Chemical shifts are given in parts per million (ppm) quoted relative to tetramethylsilane (δ = 0 ppm) and referenced to residual solvent as internal standard.

Two dimentional NMR spectra were recorded on a Varian Inova 500 (500 MHz) instrument fitted with gradient coils. Gradient COSY experiments were typically aquired with 256 slices in F_1 and 2048 slices in F_2. NOE difference experiments were aquired with a mixing time of 500 msec.

Optical rotations were measured on a Jasco DIP-1000 digital polarimeter in a cell length of 1 dm. Specific rotations are given as $[\alpha]_D^T$ with implied units of °dm^{2}g^{-1}. Temperature (T) is given in °C and concentration (c) is expressed as g / 100 mL.

Infrared spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrometer in the region of 4000-650 cm^{-1}. Samples were analysed as thin films from chloroform, or from the solvent indicated.

Mass spectra were recorded at Bio21 (The University of Melbourne), CSIRO (Clayton), or the EPSRC Mass Spectrometry Service Center (University of Swansea). Electrospray ionisation (ESI) low- and high-resolution spectra were recorded at Bio21 using a hybrid linear ion trap and Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer (Finnigan LTQ-FT). High-resolution electron impact (EI) spectra were recorded at CSIRO on a ThermoQuest MAT95XL instrument. High-resolution chemical ionisation (CI) spectra were recorded at the

EPSRC Mass Spectrometry Service Center on a Finnigan MAT 95XP double focusing mass spectrometer.

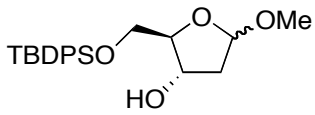
Elemental analysis was performed at CMAS (Chemical and MicroAnalytical Services) Belmont, Australia.

Melting points were determined on an Electrothermal Engineering IA9100 or Büchi 510 melting point apparatus and are uncorrected.

Analytical thin layer chromatography was carried out on glass backed, pre-coated 0.25 mm Merck 60 F_{254} silica plates. Spots were visualised by UV absorbance, or by staining with 20% w/w phosphomolybdic acid in ethanol. Flash chromatography was carried out on Merck Kieselgel 60 (230-400 mesh) silica, or where indicated, Brockman grade I neutral alumina (150 mesh, Aldrich) under a pressure of nitrogen.

Anhydrous THF, diethyl ether, and dichloromethane were dried by passage through a packed column of neutral alumina under a nitrogen atmosphere, and toluene was passed through a further column containing R3-11 copper based catalyst (BASF Australia).[1] All other solvents were purified according to standard procedures. All non-aqueous reactions were carried out under an atmosphere of nitrogen (or argon where indicated) in a dual manifold using Schlenk techniques in anhydrous solvents. Petroleum spirit refers to the fraction boiling between 40-60 °C. Ether refers to diethyl ether.

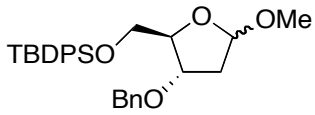
(2R,3R,5S)- and (2R,3S,5S)-3-Benzyloxy-2-(tert-butyldiphenylsilanyloxymethyl)-5-hydroxy-2,3,4,5-tetrahydrofuran (S1)[2]



To a stirred solution of 2-deoxy-*D*-ribose (1.84 g, 13.7 mmol) in methanol (60 mL) was added HCl (4.5 mL, 1.0 M solution in Et_2O, 4.5 mmol). The resulting solution was stirred for 1 h, before pyridine (9 mL) was added, and the solvents were removed *in vacuo*. Pyridine (9 mL) was again added, removed *in vacuo*, and the residue dried under high vacuum for 1 h. Pyridine (15 mL) and TBDPSCl (3.56 mL, 13.7 mmol) were added to the crude material, and the reaction was stirred for 20 h at room temperature. The solvent was removed *in vacuo*, and the reaction was quenched by the addition of water (30 mL). EtOAc (30 mL) was added and the layers were separated. The aqueous phase was extracted with EtOAc (2 × 30 mL), and the combined organic portions were washed with a saturated aqueous solution of copper sulfate (2 × 60 mL), and then dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue was purified by column chromatography, (1:1 EtOAc/petrol) to yield the epimeric products as a clear colourless oil (3.48 g, 66%)

R_f 0.18 and 0.27 (Et_2O:hexane, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67-7.71 (m, 8H, Ar), 7.39-7.47 (m, 12H, Ar), 5.13 (d, *J* = 4.5 Hz, 1H, OC*H*OMe), 5.08 (dd, *J* = 5.5, 2 Hz, 1H, OC*H*OMe), 4.53 (m, 1H), 4.31 (dd, *J* = 10.5, 6 Hz, 1H), 4.19 (m, 1H), 3.96 (m, 1H), 3.84 (dd, *J* = 10.5, 5 Hz, 1H), 3.76 (dd, *J* = 11, 3.5 Hz, 1H), 3.63 (dd, *J* = 10, 7.5 Hz, 1H), 3.61 (m, 1H), 3.40 (s, 3H, OCH_3), 3.29 (s, 3H, OCH_3), 2.86 (d, *J* = 10.5 Hz, 1H), 2.20 (m, 2H), 2.05 (m, 1H), 2.02 (m, 1H), 1.92 (d, *J* = 4 Hz, 1H), 1.09 (s, 18H, 2 × SiC(CH_3)$_3$). These data agree with those previously reported.[2]

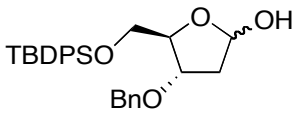
(2R,3R,5S)- and (2R,3S,5S)-3-Benzyloxy-2-(tert-butyldiphenylsilanyloxymethyl)-5-hydroxy-2,3,4,5-tetrahydrofuran (S2)[2]



To a solution of the methyl acetals **S1** (900 mg, 2.33 mmol.) in THF (20 mL) at 0 °C was added NaH (140 mg, 60 % dispersion in mineral oil, 3.5 mmol.). The suspension was stirred at room temperature for 2 h, and benzyl bromide (0.47 mL, 3.95 mmol) was added. The mixture was stirred at room temperature for a further 18 h, and quenched by addition of water (20 mL). The aqueous phase was extracted with ether (3 × 20 mL), and the combined organic portions were dried ($MgSO_4$) and solvent was removed *in vacuo*. Purification by column chromatography (ether :hexane, 1:1) furnished the benzyl ethers (1.05 g, 94%) as a colourless oil.

R_f 0.65 and 0.70 (hexane:ether, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 7.62-7.79 (m, 4H), 7.24-7.48 (m, 11H), 5.09-5.11 (m, 1H), 4.48-4.58 (m, 2H), 4.20-4.26 (m, 1H), 4.09-4.12 (m, 1H), 3.65-3.71 (m, 2H), 3.42 (s, 3H), 3.41 (s, 3H), 2.16-2.24 (m, 1H), 2.08 (d, J = 14 Hz, 1H), 1.08 (s, 9H), 1.05 (s, 9H). These data agree with those previously reported.[2]

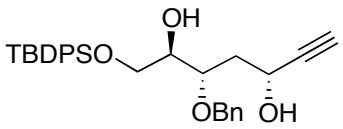
(2*R*,3*R*,5*S*)- and (2*R*,3*S*,5*S*)-3-Benzyloxy-2-(*tert*-butyldiphenylsilanyloxymethyl)-5-hydroxy-2,3,4,5-tetrahydrofuran (S3)[2]



The methyl acetals **S2** (680 mg, 0.14 mmol) were dissolved in AcOH, acetone and water (8:1:1, 50 mL) and the solution was heated to 65 °C in an open flask for 3 h. Et_2O (50 mL) was added and the organic phase washed with saturated aqueous $NaHCO_3$ solution (5 × 30 mL), until evolution of gas ceased. The solvent was removed *in vacuo* to yield the hemiacetals (645 mg, 98%) as a yellow oil. No further purification was required.

R_f 0.20 (hexane:Et_2O, 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.45 (m, 11H, Ar), 6.63-6.69 (m, 4H, Ar), 6.29 (m, 1H), 5.32-5.47 (dd, J = 11, 4.5 Hz, 1H), 4.52-4.64 (m, 1H), 4.45-4.47 (m, 1H), 4.43 (m, 2H), 4.30 (m, 1H), 4.18-4.23 (m, 1H) 3.75-3.78 (m, 1H), 3.47-3.65 (m, 2H), 3.25 (m, 1H), 2.18-2.24 (m, 2H), 2.08-2.15 (m, 2H), 1.07 (s, 9H, $SiC(CH_3)_3$), 1.05 (s, 9H, $SiC(CH_3)_3$). These data agree with those previously reported.[2]

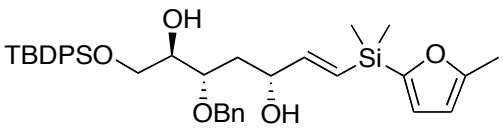
(2*R*,3*R*,5*S*)-3-Benzyloxy-1-(*tert*-butyldiphenylsilanyloxymethyl)-hept-6-yne-2,5-diol (17) [2]



To a stirred solution of the lactols **S3** (1.74 g, 3.76 mmol) in THF (20 mL) at 0 °C was added ethynylmagnesium bromide (18.8 mL, 0.5 M solution in THF, 9.4 mmol) and the solution was stirred for a further 2 h at 0 °C. The reaction was warmed to room temperature and a saturated aqueous solution of NH_4Cl (10 mL) was added and the layers were separated. The aqueous phase was extracted with Et_2O (2 × 20 mL) and the combined organic portions were washed with brine (20 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to yield the crude product as a 3:1 mixture of isomers (determined by proton NMR spectroscopy). The mixture was purified by column chromatography (1:2 EtOAc/petrol) to yield a single diastereoisomer as a crystalline solid. The product was recrystallised (Et_2O/petrol) to give colourless needles (1.30 g, 71%).

R_f 0.30 (Et_2O:hexane 1:2); m.p. 80-82 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64-7.66 (m, 4H, Ar), 7.36-7.46 (m, 5H, Ar), 7.25-7.32 (m, 4H, Ar), 7.19-7.21 (m, 2H, Ar), 4.63 (ddd, *J* = 7.5, 5.5, 2 Hz, 1H, C*H*OH), 4.51 (q, *J* = 11.5 Hz, 1H, CH_2OPh), 3.87-3.75 (m, 4H), 3.32 (br s, 1H, O*H*), 2.78 (br s, 1H, O*H*), 2.47 (d, *J* = 2 Hz, 1H, C≡C*H*), 2.17-2.10 (m, 1H, C*H*H), 2.01 (dt, J = 14.5, 5 Hz, 1H, C*H*H), 1.08 (s, 9H, SiC(CH_3)$_3$). These data agree with those previously reported.[2]

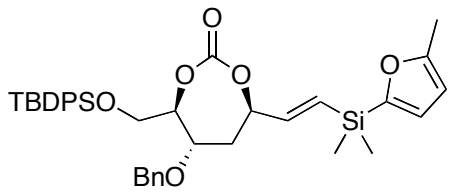
(2*R*,3*S*,5*R*,E)-3-(Benzyloxy)-1-(tert-butyldiphenylsilyloxy)-7-(dimethyl(5-methylfuran-2-yl)silyl)hept-6-ene-2,5-diol (19)



To a stirred solution of the alkyne **17** (414 mg, 0.85 mmol) and *dimethyl(5-methylfuran-2-yl)silane* (238 mg, 1.7 mmol) in THF (40 mL) was added the catalyst $Pt(DVDS)_2$ (85 μL, 0.1 M solution, 8.5 μmmol). The mixture was stirred at room temperature for 20 min, water (20 mL) was added, and the aqueous phase was extracted with Et_2O (3 × 20 mL). The organic extracts were dried (Mg_2SO_4) and the solvent was removed *in vacuo*. The residue purified by column chromatography, (1:2 Et_2O/petrol) to yield the vinyl silane **19** (425 mg, 80 %) as a pale yellow oil.

R_f 0.43 (2:1 Et_2O/hexane); $[\alpha]_D^{22}$ -10.1 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.64-7.69 (m, 4H, Ar), 7.43-7.67 (m, 5H, Ar), 7.31-7.27 (m, 4H, Ar), 7.21-7.23 (m, 2H, Ar), 6.52 (d, *J*= 3 Hz, 1H, furan C*H*), 6.11 (dd, *J* = 18.5, 5 Hz, 1H, C*H*=CH), 5.97-5.93 (m, 2H), 4.53 (AB q, J = 11.5 Hz, 1H, OCH_2Ph), 4.34 (dd, *J* = 10.5, 5 Hz, 1H, C*H*OH), 3.89 (dd, *J* = 10.5, 5.5 Hz, 1H, CH_2OH), 3.78-3.73 (m, 3H), 3.21 (br s, 1H, O*H*), 2.72 (br s, 1H,O*H*), 2.30 (s, 3H, furan CH_3), 1.80-1.77 (m, 2H), 1.07 (s, 9H, SiC(CH_3)$_3$), 0.31 (s, 6H, Si(CH_3)$_2$); ^{13}C NMR (125 MHz $CDCl_3$) 156.7, 150.0, 137.7, 135.5, 133.0, 132.9, 128.9, 128.8, 128.4, 128.0, 127.82, 127.79, 125.7, 121.7, 105.7, 78.2, 72.9, 72.0, 71.9, 64.5, 36.7, 26.9, 19.3, 13.7, -2.88, -2.92; IR(film) 3394 br, 2955, 2858, 1590, 1427, 1249, 1111, 1017, 922, 844, 821, 784, 734, 699 cm^{-1}; MS (ESI$^-$) *m/z* (rel intensity) 727 [100, (M-H)$^-$]; HRMS (ESI$^-$) 627.2967 (627.2962 calcd for $C_{37}H_{47}O_5Si_2$, [M-H]$^-$).

(4R,5S,7R)-5-(Benzyloxy)-4-((tert-butyldiphenylsilyloxy)methyl)-7-((E)-2-(dimethyl(5-methylfuran-2-yl)silyl)vinyl)-1,3-dioxepan-2-one (22)

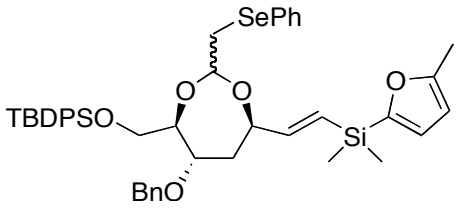


To a solution of the diol **19** (30 mg, 0.048 mmol) in CH_2Cl_2 (2 mL) was added pyridine (25 μL, 0.31 mmol), triethylamine (43 μL, 0.31 mmol) and powdered 4 Å molecular sieves (one spatula tip). The mixture was cooled to -78 °C and triphosgene (25 mg, 0.083 mmol) was added. The mixture was stirred at -78 °C for 1 h, and quenched by addition of saturated aqueous $NaHCO_3$ solution (5 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 5 mL),

the organic extracts were dried (Mg_2SO_4) and the solvent was removed *in vacuo*. The residue purified by column chromatography, eluted in 10:80:2 Et_2O/petrol/NEt_3, to yield the carbonate **22** (25 mg, 80%) as a colourless oil.

R_f 0.40 (1:4 EtOAc/hexane); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.35-7.31 (m, 4H, Ar), 7.52-7.35 (m, 5H, Ar), 7.32-7.27 (m, 4H, Ar), 7.24-7.22 (m, 2H, Ar), 6.55 (d, *J* = 3 Hz, 1H, furan C*H*), 6.09-6.07 (m, 2H), 5.97 (m, 1H, furan C*H*), 5.12 (ddd, *J* = 11, 3.5, 1.5 Hz, 1H, OC*H*CH=CH), 4.55 (d, *J* = 11.5, 1H, OCH_2Ph), 4.45, (d, *J* = 11.5, 1H, OCH_2Ph), 4.41-4.38 (dt, *J* = 8, 5 Hz, 1H, OC*H*), 4.00-3.97 (dt, *J* = 6.5, 3.5 Hz, 1H, OC*H*), 3.90-3.89 (m, 3H), 2.34 (s, 3H, furan CH_3), 2.16-2.12 (m, 1H, CH_2), 2.05 (ddd, *J* = 14.5, 11, 3.5 Hz, 1H, CH_H), 1.05 (s, 9H, SiC(CH_3)$_3$), 0.33 (s, 6H, Si(CH_3)$_2$); ^{13}C NMR (125 MHz $CDCl_3$) 157.0, 155.6, 151.7, 144.2, 137.3, 135.6, 135.5, 132.8, 132.6, 129.8, 129.7, 129.3, 128.5, 128.0, 127.8, 127.78, 127.74, 127.73, 127.65, 122.0, 105.8, 80.6, 78.2, 71.9, 71.5, 62.3, 46.2, 34.2, 26.7, 19.2, 13.7, 11.5, -3.1, -3.2; IR(film) 2931, 1750, 1428, 1364, 1250, 1204, 1112, 908, 732, 701 cm^{-1}; MS (ESI$^+$) *m/z* (rel intensity) 1331 [60], 677 [100, (M + Na)$^+$); HRMS (ESI$^+$) 677.2725 (677.2725 calcd for $C_{38}H_{46}O_6Si_2Na$, [M + Na]$^+$)

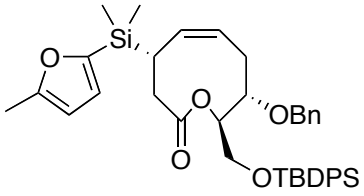
(((2S,4R,5S,7R)- and (((2R,4R,5S,7R)-5-(Benzyloxy)-7-((E)-2-(dimethyl(5-methylfuran-2-yl)silyl)vinyl)-2-(phenylselanylmethyl)-1,3-dioxepan-4-yl)methoxy)(tert-butyl)diphenylsilane (21)



A solution of the diol **19** (1.57 g, 2.50 mmol), phenylselenoaldehyde diethyl acetal (822 mg, 3.01 mmol) and PPTS (31 mg, 0.12 mmol) in toluene (120 mL) was heated to reflux under Dean-Stark conditions for 1 h. Water (50 mL) was added and the aqueous phase was extracted with Et_2O (3 × 50 mL). The organic extracts were dried (Mg_2SO_4), the solvent was removed *in vacuo* and the resulting product was purified by column chromatography (1:10 EtOAc/petrol) to yield the title compounds **22** (1.80 g, 89 %) as a pale yellow oil.

R_f 0.36 (1:4 EtOAc/hexane); MS (ESI^+) *m/z* (rel intensity) 833 [20, $(M + Na)^+$], 683 [100]; HRMS (ESI^+) 833.2566 (833.2573 calcd for $C_{45}H_{54}O_5SeSiNa$, $[M + Na]^+$)

(4S,8S,9R,Z)-8-(Benzyloxy)-9-((tert-butyldiphenylsilyloxy)methyl)-4-(dimethyl(5-methylfuran-2-yl)silyl)-3,4,8,9-tetrahydrooxonin-2(7H)-one (24)



Method 1

To a stirred solution of the carbonate **22** (45 mg, 0.070 mmol) in toluene (5 mL) in the absence of light, was added Petasis reagent (0.33 mL, 0.33 M solution in toluene, 0.11 mmol). The solution was heated to reflux for 20 h, allowed to cool to room temperature and filtered through a plug of silica. The solvent was removed *in vacuo* and the residue was purified by column chromatography (1:20 Et_2O/petrol) to yield the lactone **24** (33 mg, 73 %) as a yellow oil.

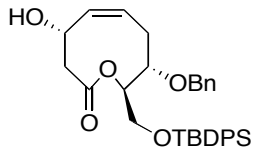
Method 2

The selenoacetals **21** (1.80 g, 2.22 mmol) were dissolved in CH_2Cl_2 (40 mL) and MeOH (200 mL), and water (30 mL) were added until the material began to precipitate. To this cloudy mixture was added $NaHCO_3$ (205 mg, 2.44 mmol) and $NaIO_4$ (1.42 g, 6.66 mmol) to form a cream/white suspension. After 3 h, the reaction was quenched by the addition of water (200 mL). The organic phase was isolated and the aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic portions were dried ($MgSO_4$) and the solvent removed *in vacuo* to yield what was presumed to be the selenoxides.

To a stirred solution of the selenoxides in toluene (200 mL) was added DBU (1.01 g, 6.66 mmol), and the reaction was heated to reflux under Dean-Stark conditions for 19 h. After being allowed to cool to room temperature, the solvent was removed *in vacuo* and the material was purified by flash chromatography (1:20 Et_2O/petrol) to yield the lactone **24** (1.06 g, 74%) as a pale yellow oil.

R_f 0.58 (1:4 EtOAc/hexane); $[\alpha]_D^{22}$ 26.4 (*c* 0.78, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.69-7.66 (m, 4H, Ar), 7.42-7.33 (m, 6H, Ar), 7.26-7.21 (m, 5H, Ar), 6.56 (d, *J* = 2.5 Hz, 1H, furan C*H*), 5.97 (d, *J* = 2.5 Hz, 1H, furan, C*H*), 5.70 (td *J* = 11, 5 Hz, 1H, CH=C*H*), 5.43 (t, *J* = 11 Hz, 1H, CH=C*H*), 4.58-4.65 (m, 2H), 4.40 (d, *J* = 12 Hz, 1H, OC*H*HPh), 4.13 (ddd, *J* = 10, 6, 3 Hz, 1H, C*H*OBn) 3.83-3.85 (m, 2H, CH_2OSi), 2.70 (ddd, *J* = 14.5, 12, 3 Hz, 1H, C*H*H), 2.66 (td, J = 12.5, 6.5 Hz, 1H, C*H*Si), 2.55 (dd, J = 14, 6 Hz, 1H, C*H*H), 2.34 (s, 3H, furan CH_3), 2.28-2.35 (m, 1H, C*H*H), 2.19 (dd, *J* = 14, 12.5 Hz, 1H, C*H*H), 1.03 (s, 9H, SiC(CH_3)$_3$), 0.25 (s, 6H, Si(CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 157.1, 155.0, 138.2, 135.6, 135.5, 133.49, 133.43, 130.6, 129.6, 128.3, 127.57, 122.4, 105.8, 78.4, 71.2, 64.1, 35.1, 26.89, 26.82, 23.4, 19.3, 13.7, -4.7, -5.3; IR (film) 2930, 2858, 1738, 1428, 1365, 1217, 1112, 909, 772, 733, 701 cm^{-1}; MS (ESI$^+$) *m/z* (rel intensity) 1328 [60, $(2M+Na)^+$], 675 [100, $(M + Na)^+$]; HRMS (ESI$^+$) 675.2932 (675.2932 calcd for $C_{39}H_{48}O_5Si_2Na$, $[M + Na]^+$)

(4S,8S,9R,Z)-8-(Benzyloxy)-9-((tert-butyldiphenylsilyloxy)methyl)-4-hydroxy-3,4,8,9-tetrahydrooxonin-2(7H)-one (24a)

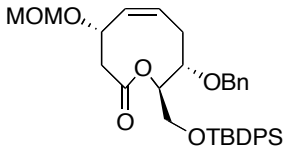


A solution of the lactone **24** (7.0 g, 10.7 mmol) and rose bengal (210 mg, 0.21 mmol) in CH_2Cl_2 (350 mL) under an atmosphere of oxygen at -78 °C was irradiated with a white halogen lamp for 8 h. The reaction was quenched by addition of water and allowed to warm to room temperature. The mixture was diluted with CH_2Cl_2 (400 mL) and the organic phase washed with saturated aqueous $NaHCO_3$ (3 × 400 mL), dried (Mg_2SO_4) and the solvent was removed *in vacuo.* The resulting residue was dissolved in DMF (350 mL), and was treated with $NaHCO_3$ (2.1 mg, 25.2 mmol) KF (1.47 mg, 25.2 mmol) and 30 % aqueous H_2O_2 (59.7 mL, 50 mmol). The resulting solution was stirred at room temperature for 18 h, and the solvent was removed under high vacuum. Water (500 mL) and EtOAc (500 mL) were added, and the aqueous phase was extracted with EtOAc (3 × 300 mL). The combined organic extracts were dried (Mg_2SO_4), the solvent removed *in vacuo* and the residue was purified by

column chromatography, (1:5 EtOAc/petrol) to yield the alcohol **24a** (4.62 g, 81%) as a colourless oil.

R_f 0.32 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$ 26.5 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.59-7.63 (m, 4H, Ar), 7.25-7.43 (m, 11H, Ar), 5.68 (td, *J* = 11, 6.5 Hz, 1H, C*H*=CH), 5.57 (dd, *J* = 11, 8.5 Hz, 1H, C*H*=CH), 5.00-5.06 (m, 1H, C*H*OH), 4.69 (dt, *J* = 7, 3.5 Hz, 1H, OC*H*), 4.60 (d, *J* = 12 Hz, 1H, OC*H*HPh), 4.41 (d, *J* = 12 Hz, 1H, OC*H*HPh), 4.07-4.10 (m, 1H, C*H*OBn), 3.81 (d, *J* = 4 Hz, 2H, CH_2OSi), 2.98 (dd, *J* = 13.5, 7 Hz, 1H, C*H*HC=O), 2.45-2.54 (m, 2H), 2.32 (dd, *J* = 13.5, 10 Hz, 1H, C*H*HC=O) 1.04 (s, 9H, Si(CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 138.0, 135.6, 135.5, 134.0, 133.4, 133.3, 129.72, 129.69, 128.4, 127.7, 127.6, 127.5, 127.3, 77.1, 71.3, 65.3, 64.0, 42.0, 28.7, 26.8, 19.3; IR(film) 3429, 2956, 1744, 1427, 1268, 1235, 1112, 1054, 738, 699 cm^{-1}; MS (ESI$^+$) *m/z* (rel intensity) 553 [100, (M+Na)$^+$]; HRMS (ESI$^+$) 553.2381 (553.2381 calcd for $C_{32}H_{38}O_5SiNa$, [M + Na]$^+$)

(4S,8S,9R,Z)-8-(Benzyloxy)-9-((tert-butyldiphenylsilyloxy)methyl)-4-(methoxymethoxy)-3,4,8,9-tetrahydrooxonin-2(7H)-one (27)

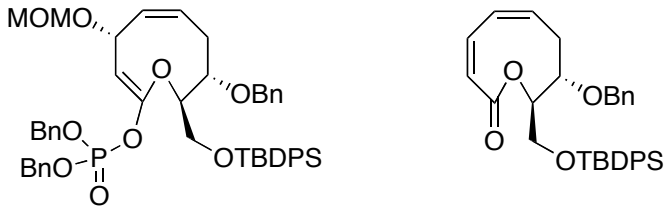


To a stirred solution of the above alcohol (1.80 g, 3.4 mmol) in $CH_2(OMe)_2$ (50 mL) was added P_2O_5 (1.70 g, 12 mmol). The mixture was stirred at room temperature for 2 h and the solvent was decanted off from the solids. The solids were washed with CH_2Cl_2 (50 mL) and the combined organic extracts were washed with saturated aqueous $NaHCO_3$ solution (50 mL). The organic phase was dried (Mg_2SO_4) and the solvent was removed *in vacuo*. The resulting residue was purified by column chromatography, (1:10 EtOAc/petrol) to yield the methoxymethyl ether **27** (1.70 g, 85%) as a colourless oil.

R_f 0.49 (1:4 EtOAc/hexane); $[\alpha]_D^{22}$ 3.0 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.60-7.64 (m, 4H, Ar), 7.23-7.42 (m, 11H, Ar), 5.76 (tdd, *J* = 11, 6, 1 Hz, 1H, C*H*=CH), 5.51 (dd, J = 11, 9 Hz, 1H, C*H*=CH), 4.91 (dd, J = 16, 9 Hz, 1H, C*H*OCH_2OCH_3), 4.69 (d, *J* = 7 Hz, 1H, OC*H*HOCH_3) 4.66-4.68 (m, 1H), 4.57-4.59 (m, 2H), 4.41 (d, *J* = 12 Hz, 1H, OC*H*HPh), 4.06-

4.09 (m, 1H), 3.80-3.81 (m, 2H, CH_2OSi), 3.38 (s, 3H, CH_2OCH_3), 2.96 (dd, *J* = 13.5, 7 Hz, 1H, C*H*HC=O), 2.43-2.55 (m, 2H), 2.35 (dd, *J* = 13.5, 10 Hz, 1H, C*H*HC=O), 1.04 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 138.1, 135.7, 135.6, 133.4, 133.3, 129.7, 128.7, 127.7, 127.6, 127.5, 94.6, 77.1, 69.0, 64.0, 55.5, 40.2, 28.6, 19.3; IR(film) 2931, 2858, 1748, 1428, 1275, 1226, 1104, 1068, 1035, 740, 700 cm^{-1}; MS (ESI$^+$) *m/z* (rel intensity) 627 [15], 597 [100, (M+Na)$^+$]; HRMS (ESI$^+$) 597.2644 (597.2643 calcd for $C_{34}H_{42}O_6SiNa$, [M + Na]$^+$)

(2E,4R,5Z,8S,9R)-8-(Benzyloxy)-9-((tert-butyldiphenylsilyloxy)methyl)-4-(methoxymethoxy)-4,7,8,9-tetrahydrooxonin-2-yl diphenyl phosphate (28) and (3Z,5Z,8S,9R)-8-(Benzyloxy)-9-((tert-butyldiphenylsilyloxy)methyl)-8,9-dihydrooxonin-2(7H)-one (28a)



To a solution of the lactone **27** (213 mg, 0.36 mmol), HMPA (170 μL, 1.0 mmol) and diphenylphosphoryl chloride (206 μL, 1.0 mmol) in THF (10 m) at -78 °C was added lithium hexamethyldisilazane (540 μL, 1.0 M solution in THF, 0.54 mmol) dropwise. After being stirred at -78 °C for 20 min, the reaction was quenched by addition of saturated aqueous NH_4Cl solution (10 mL). The aqueous phase was extracted with Et_2O (3 × 15 mL) and the combined organic extracts were dried (Mg_2SO_4). The solvent was removed *in vacuo* and the resulting product was purified by column chromatography (20:80:1 Et_2O/hexane/NEt_3) to yield the enol phosphate **28** (191 mg, 72 %) as a colourless oil and the diene **28a** (9 mg, 5 %) as a colourless oil.

Data for the enol phosphate **28**

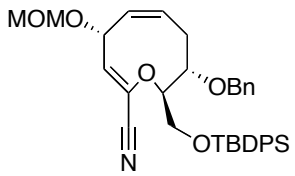
R_f 0.51 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$ 21.0 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.63-7.71 (m, 4H), 7.05-7.41 (m, 21H), 5.80 (dd, *J* = 10.9, 8.4 Hz, 1H), 5.65 (m, 1H), 5.55-5.50

(m, 1H), 5.26 (dd, *J* = 5.2, 2.0 Hz, 1H), 4.62-4.68 (m, 2H), 4.47 (td, *J* = 9.5, 3 Hz, 1H), 4.45 (d, *J* = 11.2 Hz, 1H), 4.00 (dd, *J* = 11.6, 1.6 Hz, 1H), 3.88 (dd, *J* = 11.6, 1.7 Hz, 1H), 3.80 (dt, *J* = 9.4, 1.6, 1.56 Hz, 1H), 3.38 (s, 3H), 3.04 (ddd, *J* = 14.2, 11.7, 2.8 Hz, 1H), 2.60 (q, *J* = 7.2 Hz, 1H), 2.53 (ddd, *J* = 14.2, 5.3, 3.2 Hz, 1H), 1.06 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 129.6, 129.55, 128.1, 128.0, 127.9, 127.8, 127.7, 127.3, 127.1, 125.3, 125.2, 125.1, 125.07, 124.9, 120.2, 120.15, 120.1, 120.0, 199.9, 101.7, 94.0, 85.3, 78.0, 71.5, 67.5, 54.9, 26.7; IR(film) 2927, 1741, 1591, 1489, 1191, 1025, 955, 744 cm^{-1}; MS (ESI$^+$) *m/z* (rel intensity) 1634 [15, $(2M+Na)^+$], 829 [100, $(M+Na)^+$]; HRMS (ESI$^+$) 829.2929 (829.2932 calcd for $C_{46}H_{51}O_9PSiNa$, $[M + Na]^+$)

Data for the diene **28a**

R_f 0.53 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$186.6 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.61-7.67 (m, 4H, Ar), 7.22-7.41 (m, 21H, Ar), 6.36 (dd, *J* = 12.5, 6 Hz, 1H, C*H*=CHC=O), 5.94 (d, *J* = 12 Hz, 1H, CH=C*H*C=O), 5.86 (ddd, *J* = 12, 6, 0.5 Hz, 1H, C*H*=CH), 5.65-5.76 (m, 1H), 5.08 (ddd, *J* = 7.5, 4.5, 3 Hz, 1H, OC*H*), 4.59 (d, *J* = 11.5 Hz, 1H, C*H*HOPh), 4.37 (d, *J* = 11.5 Hz, 1H, C*H*HOPh), 3.81-3.87 (m, 3H), 3.70-3.79 (m, 1H), 2.40-2.43 (m, 3H), 1.02 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.0, 137.8, 137.6, 135.6, 134.8, 133.9, 133.2, 129.6, 128.4, 127.72, 127.68, 127.63, 127.60, 127.56, 124.6, 122.2, 71.5, 71.2, 63.7, 63.7, 32.9, 26.8, 19.3; IR(film) 2930, 2857, 1716, 1427, 1268, 1198, 1111, 740, 700 cm^{-1}; MS (ESI$^+$) *m/z* (rel intensity) 535 [35, $(M+Na)^+$], 530 [100, $(M+NH_4)^+$], 436 [50].

(2Z,4*R*,5Z,8*S*,9*R*)-8-(Benzyloxy)-9-((tert-butyldiphenylsilyloxy)methyl)-4-(methoxymethoxy)-4,7,8,9-tetrahydrooxonine-2-carbonitrile (29)

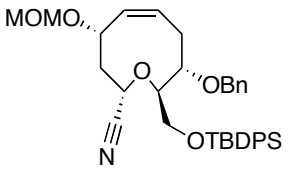


A solution of the enol phosphate **28** (111 mg, 0.14 mmol) Pd_2dba_2 (135 mg, 0.015 mmol), dppf (33 mg, 0.060 mmol) copper cyanide (18 mg, 0.21 mmol) and TMEDA (39 μL, 0.06 mmol) in 1,4-dioxane (12 mL) was heated to reflux for 20 h. The mixture was cooled, filtered through a plug of celite and the solvent was removed *in vacuo*. The resulting residue was

purified by column chromatography (1:5 EtOAc/petrol) to yield the nitrile **29** (57 mg, 72%) as a pale yellow oil.

R_f 0.57 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$ 101.7 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.62-7.77 (m, 6H, Ar), 7.09-7.42 (m, 9H, Ar), 6.15 (d, *J* = 5 Hz, 1H, C*H*=CCN), 5.76 (ddd, *J* = 11.5, 9.5, 5.5 Hz, 1H, C*H*=CH), 5.69-5.60 (m, 2H), 4.59-4.69 (m, 3H), 4.40-4.46 (m, 2H), 4.29 (dd, *J* = 12, 1.5 Hz, 1H, CH*H*OSi), 3.94 (dd, *J* = 12, 1.5 Hz, 1H, CH*H*OSi), 3.59 (dt, *J* = 3, 1.5 Hz, 1H, C*H*O), 3.39 (s, 3H, OCH_3), 2.90-3.01 (m, 1H, C*H*H), 2.54 (ddd, *J* = 14, 5.5, 3 Hz, 1H, C*H*H), 1.11 (s, 9H, SiC(CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.9, 143.3, 137.9, 135.7, 135.6, 134.8, 133.3, 132.7, 132.0, 130.4, 129.73, 129.65, 128.9, 128.5, 128.4, 128.3, 127.9, 127.73, 127.69, 127.5, 125.4, 115.3, 94.3, 85.3, 78.0, 72.1, 68.5, 61.4, 55.6, 27.8, 26.9, 19.3.; IR(film) 2930, 1622, 1428, 1337, 1158, 1104, 1037, 118, 740, 700 cm^{-1}; MS (ESI$^+$) *m/z* (rel intensity) 829 [30], 606 [100, (M+Na)$^+$]; HRMS (ESI$^+$) 606.2646 (606.2644 calcd for $C_{35}H_{41}O_5NSiNa$, [M + Na]$^+$)

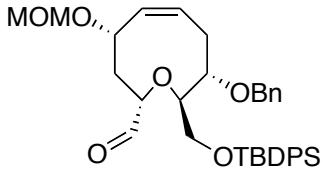
(2S,4S,8S,9R,Z)-8-(Benzyloxy)-9-((tert-butyldiphenylsilyloxy)methyl)-4-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonine-2-carbonitrile (30)



To a solution of the unsaturated nitrile **29** (141 mg, 0.24 mmol) in MeOH (15 mL) was added magnesium turnings (116 mg, 4.8 mmol) and iodine (3 mg, 0.01 mmol). After several minutes, evolution of gas was observed, and the mixture was stirred at room temperature for 3 h, after which time a white precipitate had formed. To this mixture was added 1 M HCl solution until the solids dissolved (pH ~ 7) and the solution was extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried (Mg_2SO_4), and the solvent was removed *in vacuo*. The resulting product was purified by column chromatography (1:4 Et_2O/petrol) to yield the title compound **30** (119 mg, 81%) as a colourless oil.

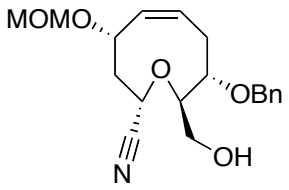
R_f 0.50 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$ -15.5 (*c* 1.46, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.66-7.71 (m, 4H, Ar), 7.18-7.43 (m, 11H, Ar), 5.78 (td, *J* = 11, 6 Hz, 1H, C*H*=CH), 5.69 (dd, *J* = 11, 8.5 Hz, 1H, C*H*=CH), 4.84 (dd, *J* = 7.5, 6 Hz, 1H, C*H*OCH_2OCH_3), 4.62-4.70 (m, 3H), 4.54 (d, *J* = 7 Hz, 1H, OC*H*H), 4.40 (d, *J* = 11.5 Hz, 1H, OC*H*H), 4.13 (dd, *J* = 11.5, 1.5 Hz, 1H, CH*H*OSi), 3.91 (dt, *J* = 9, 3 Hz, 1H, C*H*OBn), 3.82 (dd, *J* = 11.5, 4 Hz, 1H, C*H*O), 3.76 (ddd, *J* = 9, 4, 2 Hz, 1H, CH*H*OSi), 3.37 (s, 3H, OCH_3), 2.56 (ddd, *J* = 14, 11, 3 Hz, 1H, C*H*H), 2.44 (ddd, *J* = 14, 5.5, 3.5 Hz, 1H, C*H*H), 2.36 (ddd, *J* = 15, 6, 4 Hz, 1H, C*H*H), 2.28 (m, 1H, C*H*H), 1.09 (s, 9H, $SiC(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 135.8, 135.6, 133.9, 133.5, 129.7, 129.6, 128.38, 128.35, 127.74, 127.67, 127.64, 127.61, 127.36, 118.1, 94.3, 77.5, 75.4, 71.7, 68.6, 64.9, 62.9, 55.5, 38.9, 27.1, 26.9, 19.3; IR(film) 2931, 2857, 1472, 1454, 1428, 1152, 1089, 1068, 1027, 978, 911, 823, 781, 735, 699 cm^{-1}; MS (ESI^+) *m/z* (rel intensity) 608 [100, $(M+Na)^+$]; HRMS (ESI^+) 608.2802 (608.2803 calcd for $C_{35}H_{43}O_5NSiNa$, $[M + Na]^+$)

Attempted synthesis of (2S,4S,8S,9R,Z)-8-(Benzyloxy)-9-((tert-butyldiphenylsilyloxy)methyl)-4-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonine-2-carbaldehyde (31)



To a stirred solution of the nitrile **29** (18 mg, 0.03 mmol) in CH_2Cl_2 (3 mL) at -78 °C was added DIBAL-H (30 μL, 1.0 M solution in CH_2Cl_2, 0.03 mmol) dropwise. After stirring at -78 °C for 2 h, EtOAc (0.1 mL) was added, and the mixture stirred at -78 °C for 15 min before being allowed to warm to room temperature. CH_2Cl_2 (5 mL) and saturated aqueous sodium potassium tartrate (5 mL) were added, and the organic phase was washed with water (5 mL), brine (5 mL) and dried (Mg_2SO_4). The solvent was removed *in vacuo,* and analysis of the crude product by ^{1}H NMR spectroscopy showed that the starting material was recovered.

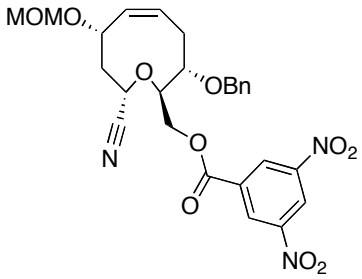
(2S,4S,8S,9R,Z)-8-(Benzyloxy)-9-(hydroxymethyl)-4-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonine-2-carbonitrile (30a)



To a solution of the silyl ether **30** (300 mg, 0.51 mmol) in THF (30 mL) was added a solution of TBAF (1.0 mL of a 1.0 solution in THF, 1.0 mmol). The solution was stirred at room temperature for 1 h, and water (50 mL) and Et_2O (50 mL) were added. The aqueous phase was extracted with Et_2O (3 × 50 mL) and the combined organic extracts were dried (Mg_2SO_4). The solvent removed *in vacuo,* and the resulting residue was purified by column chromatography (1:2 Et_2O/petrol) to yield the alcohol **30a** (170 mg, 95%) as a colourless oil.

R_f 0.15 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$ 38.7 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.26-7.37 (m, 5H, Ar), 5.58-5.7 (m, 2H, C*H*=C*H*), 4.85 (ddd, *J* = 11, 5, 1 Hz, 1H, C*H*OCH_2OCH_3), 4.69 (d, *J* = 11.5 Hz, 1H, OC*H*H), 4.65 (dd, *J* = 7, 2 Hz, 1H, OC*H*H), 4.54 (dd, *J* = 7, 2 Hz, 1H, OC*H*H), 4.53-4.55 (m, 1H), 4.51 (d, *J* = 11.5 Hz, 1H, OC*H*H), 4.13 (dd, *J* = 12.5, 3 Hz, 1H), 3.81-3.86 (m, 1H), 3.67 (m, 1H), 3.36 (d, *J* = 2 Hz, 3H, OCH_3), 2.42-2.52 (m, 3H), 2.54 (ddt, *J* = 15, 5.5, 2 Hz, 1H, C*H*H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.8, 134.7, 128.5, 128.0, 127.9, 125.9, 118.3, 94.4, 75.1, 74.6, 71.8, 68.6, 64.1, 60.6, 55.6, 39.0, 26.5; IR(film) 3474, 2934, 1453, 1211, 1151, 1112, 1073, 1028, 742, 698 cm^{-1}; MS (ESI^+) *m/z* (rel intensity) 371 [100], 370 [80, $(M+Na)^+$]; HRMS (ESI^+) 370.1626 (390.1625 calcd for $C_{19}H_{25}O_5NSiNa$, [M + $Na]^+$)

((2R,3S,7S,9S,Z)-3-(Benzyloxy)-9-cyano-7-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonin-2-yl)methyl 3,5-dinitrobenzoate (30b)



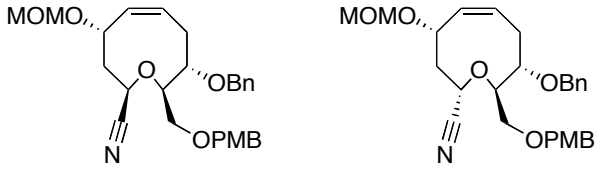
To a solution of the alcohol **30a** (9 mg, 0.026 mmol) in CH_2Cl_2 (1 mL) was added pyridine (5 μL, 0.06 mmol), DMAP (1 mg, 0.009 mmol), and 3,5-dinitrobenzoyl chloride (8 mg, 0.035 mmol). The resulting mixture was stirred at room temperature for 1 h and loaded directly onto a silica gel column. The product was eluted in 1:2 Et_2O/petrol to yield the title compound **30b** (12 mg, 77 %) as a colourless crystalline solid. The product was recrystallised (isopropanol) to give colourless plates.

R_f 0.35 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$ 52.5 (*c* 1.0, $CHCl_3$); m.p. 109-110 °C; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 9.19-9.21 (m, 1H, Ar), 9.01 (dd, *J* = 2, 1 Hz, 2H, Ar), 7.27-7.31 (m, 2H, Ar), 7.20-7.23 (m, 2H, Ar), 7.09-7.12 (m, 1H, Ar), 5.71-5.80 (m, 2H, C*H*=C*H*), 4.99 (dd, *J* = 12, 2 Hz, 1H, OC*H*), 4.89 (dd, *J* = 10, 5.5 Hz, 1H, OC*H*CN), 4.73 (d, *J* = 11.5 Hz, 1H, OC*H*H), 4.67 (dd, *J* = 7, 1 Hz, 1H), 4.54-4.61 (m, 3H), 4.44 (d, *J* = 11.5 Hz, 1H, OC*H*H), 3.98 (dt, *J* = 9.5, 2.5 Hz, 1H, OC*H*), 3.77 (dt, *J* = 9.5, 2.5 Hz, 1H, OC*H*), 3.37 (s, 3H, OCH_3), 2.46-2.59 (m, 3H), 2.34 (ddd, *J* = 15, 5.5, 1.5 Hz, 1H, C*H*H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.1, 148.5, 137.2, 135.0, 133.5, 129.5, 129.4, 128.5, 128.4, 128.1, 127.9, 125.6, 122.3, 117.9, 94.3, 72.2, 74.1, 72.9, 71.0, 68.3, 64.4, 55.5, 38.8, 26.0; IR(film) 2926, 1733, 1543, 1343, 1276, 1166, 1152, 1109, 1068, 1026, 918, 750, 719, 699 cm^{-1}; MS (CI, NH_3) *m/z* (rel intensity) 573 [5], 559 [100, $(M+NH_4)^+$]; HRMS (CI, NH_3) 559.2027 (559.2035 calcd for $C_{26}H_{31}O_{10}N_4$, [M + NH_4]$^+$)

Space group P2(1)2(1)1(1), Unit Cell Dimensions *a* = 7.2957(3) Å, *b* = 13.6588(4) Å, *c* = 25.9129(9) Å, α = 90°, β = 90°, γ = 90°, 2582.23(16) Å^3, Z = 4, D = 1.393 Mg/m3, F(000) = 1366, Mol. Formula $C_{26}H_{27}O_{10}N_3$, Mw = 541.5067.

The X-ray data have been deposited with the Cambridge Crystallographic Data Cantre and assigned the deposit code CCDC 974195.

(2R,4S,8S,9R,Z)-8-(Benzyloxy)-9-((4-methoxybenzyloxy)methyl)-4-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonine-2-carbonitrile (32) and (2S,4S,8S,9R,Z)-8-(Benzyloxy)-9-((4-methoxybenzyloxy)methyl)-4-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonine-2-carbonitrile (32a)



To a solution of the alcohol **30a** (100 mg, 0.29 mmol) and *para*-methoxybenzyl chloride (110 μL, 0.6 mmol) in THF (18 mL) was added NaH (18.5 mg, 60% dispersion in mineral oil, 0.30 mmol). The resulting mixture was stirred at room temperature for 8 h, and tetrabutylammonium iodide (55 mg, 0.15 mmol) was added. The mixture was stirred at room temperature for 18 h, and the reaction was quenched by addition of saturated aqueous NH_4Cl solution (20 mL). The aqueous phase was extracted with Et_2O (3 × 20 mL) and the combined organic extracts were dried (Mg_2SO_4). The solvent was removed *in vacuo* and the resulting product was purified by column chromatography (1:5 EtOAc/petrol) to yield the *syn* product (94 mg, 70%) and the *anti* product (9 mg, 7%) as colourless oils.

Data for the *syn* product **32**

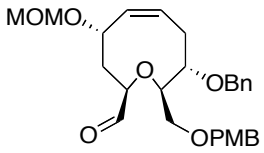
R_f 0.49 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$108.1 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.21-7.34 (m, 6H, Ar), 6.86-6.90 (m, 3H, Ar), 5.86 (td, *J* = 11.5, 5.5 Hz, 1H, C*H*=CH), 5.49 (dd, *J* = 10.5, 9.5 Hz, 1H, C*H*=CH), 4.81 (td, *J* = 9.5, 7 Hz, 1H, C*H*OCH_2OCH_3), 4.65 (d, *J* = 6.5 Hz, 1H, OC*H*H), 4.57 (d, *J* = 11.5 Hz, 1H, OC*H*H), 4.52 (d, *J* = 6.5 Hz, 1H, OC*H*H), 4.49 (d, *J* = 2.5 Hz, 2H), 4.32 (d, *J* = 11.5 Hz, 1H, OC*H*H), 4.20 (dd, *J* = 12, 5 Hz, 1H, OC*H*CN), 3.82 (s, 2H), 3.79 (s, 3H, ArOCH_3), 3.75 (dt, *J* = 7.5, 3.5 Hz, 1H, C*H*OBn), 3.65 (dd, *J* = 10.5, 3 Hz, 1H, C*H*HOPMB), 3.45 (dd, *J* = 10.5, 5.5 Hz, 1H, C*H*HOPMB), 3.45 (m, 4H), 2.60-2.53 (m, 2H), 2.43-2.48 (m, 1H, C*H*H), 1.93 (ddd, *J* = 13.5, 10, 5 Hz, 1H, C*H*H); ^{13}C NMR (125 MHz, $CDCl_3$) 159.2, 137.8, 133.1, 141.4, 130.0, 129.8, 129.6, 128.6, 128.4, 127.8, 127.7, 119.0, 114.0, 113.8, 94.3, 85.5, 77.5, 73.0, 71.7, 69.7, 69.5, 68.3, 65.0, 55.4, 55.3, 55.2, 37.9, 27.8; IR(film) 2930, 1512, 1246, 1089, 1028, 817, 698 cm^{-1}; MS (ESI^+) *m/z* (rel

intensity) 490 [100, $(M+Na)^+$]; HRMS (ESI^+) 490.2200 (490.2200 calcd for $C_{27}H_{33}O_6NNa$, $[M + Na]^+$)

Data for the *anti* product **32a**

R_f 0.48 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$ 30.7 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.21-7.34 (m, 6H, Ar), 6.84-6.92 (m, 3H, Ar), 5.65-5.74 (m, 2H, C*H*=C*H*), 4.89 (dd, *J* = 10, 5.5 Hz, 1H, OC*H*CN), 4.57-4.65 (m, 4H), 4.41 (d, *J* = 11.5 Hz, 1H, OC*H*H), 4.36 (d, *J* = 11 Hz, 1H, OC*H*H), 3.97 (dd, *J* = 11, 2 Hz, 1H, C*H*HOPMB), 3.88 (dt, *J* = 9.5, 3, Hz, 1H, C*H*OBn), 3.78 (s, 3H, ArOCH_3), 3.74 (dt, *J* = 9.5, 2.5 Hz, 1H, OC*H*), 3.67 (dd, *J* = 11, 3 Hz, 1H, C*H*HOPMB), 3.35 (s, 3H, CH_2OCH_3), 2.53 (ddd, *J* = 13.5, 10, 2.5 Hz, 1H, C*H*H), 2.37-2.43 (m, 2H), 2.29 (ddd, *J* = 15, 5.5, 2.5 Hz, 1H, C*H*H); ^{13}C NMR (125 MHz, $CDCl_3$) 159.2, 138.0, 134.2, 130.2, 129.5, 128.6, 128.4, 127.7, 126.6, 118.4, 113.8, 94.3, 75.0, 74.9, 73.1, 71.8, 68.6, 67.4, 64.3, 55.5, 55.2, 38.8, 26.9; IR(film) 2934, 1612, 1513, 1454, 1247, 1091, 1032 cm^{-1}; MS (ESI^+) *m/z* (rel intensity) 490 [100, $(M+Na)^+$]; HRMS (ESI^+) 490.2199 (490.2200 calcd for $C_{27}H_{33}O_6NNa$, $[M + Na]^+$)

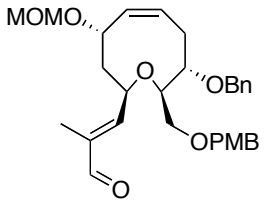
(2S,4S,8S,9R,Z)-8-(Benzyloxy)-9-((4-methoxybenzyloxy)methyl)-4-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonine-2-carbaldehyde (32b)



To a solution of the nitrile **32** (65 mg, 0.14 mmol) in CH_2Cl_2 (10 mL) at -78 °C was added DIBAL-H (150 μL, 1.0 M solution in CH_2Cl_2, 0.15 mmol) dropwise. After stirring at -78 °C for 2 h, EtOAc (0.1 mL) was added, and the mixture stirred at -78 °C for 15 min before being allowed to warm to room temperature. CH_2Cl_2 (20 mL) and saturated aqueous sodium potassium tartrate (20 mL) were added, and the organic phase was washed with water (20 mL), brine (20 mL) and dried (Mg_2SO_4). The solvent was removed *in vacuo* and the resulting product was purified by column chromatography (1:5 EtOAc/petrol) to yield the aldehyde **32b** (59 mg, 90%) as a colourless oil.

R_f 0.20 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$ 73.4 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 9.69 (d, *J* = 1.5 Hz, 1H, C*H*=O), 7.29-7.34 (m, 3H, Ar), 7.18-7.24 (m, 4H, Ar), 6.84-6.87 (m, 2H, Ar), 5.84 (tdd, *J* = 12, 5.5, 1.5 Hz, 1H, C*H*=CH), 5.56 (t, *J* = 9.5 Hz, 1H, C*H*=CH), 4.80 (td, *J* = 10, 7 Hz, 1H, C*H*OCH_2OCH_3), 4.65 (d, *J* = 6.5 Hz, 1H, OC*H*H), 4.62 (d, *J* = 11.5 Hz, 1H, OC*H*H), 4.52 (d, *J* = 6.5 Hz, 1H, OC*H*H), 4.37-4.42 (m, 2H), 4.33 (d, *J* = 11.5 Hz, 1H, OC*H*H), 3.77-3.81 (m, 1H, OC*H*CH=O), 3.79 (s, 3H, OCH_3), 3.63 (dt, *J* = 9, 3 Hz, 1H, C*H*OBn), 3.58 (dd, *J* = 10, 2 Hz, 1H, C*H*HOPMB), 3.43 (dd, *J* = 10, 7 Hz, 1H, C*H*HOPMB), 3.33 (s, 3H, OCH_3), 3.30 (ddd, *J* = 9.5, 7.5, 2.5 Hz, 1H, OC*H*), 2.67 (ddd, *J* = 14.5, 12, 3.5 Hz, 1H, C*H*H), 2.43 (ddd, *J* = 14, 5, 2.5 Hz, 1H, C*H*H), 2.16 (ddd, *J* = 13.5, 12, 6.5 Hz, 1H, C*H*H), 1.86 (ddd, *J* = 13.5, 10, 5.5 Hz, 1H, C*H*H); ^{13}C NMR (125 MHz, $CDCl_3$) 203.6, 159.3, 137.9, 132.5, 129.6, 128.6, 128.4, 127.79, 127.77, 113.8, 94.3, 86.6, 84.8, 77.9, 72.9, 71.5, 71.4, 68.8, 55.3, 55.2, 34.4, 27.8; IR(film) 2917, 1730, 1513, 1247, 1089, 1032, 916 cm^{-1}; MS (ESI^+) *m/z* (rel intensity) 493 [100, $(M+Na)^+$]; HRMS (ESI^+) 493.2196 (493.2197 calcd for $C_{27}H_{34}O_7Na$, $[M + Na]^+$)

(*E*)-3-((2*R*,4*S*,8*S*,9*R*,*Z*)-8-(Benzyloxy)-9-((4-methoxybenzyloxy)methyl)-4-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonin-2-yl)-2-methylacrylaldehyde (33)

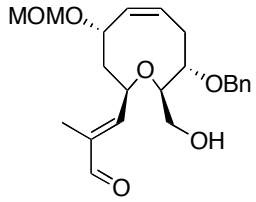


A solution of the aldehyde **32b** (75 mg, 0.16 mmol) and 2-(triphenylphosphoranylidene) propionaldehyde (95 mg, 0.30 mmol) in toluene (10 mL) was heated to reflux for 8 h. The reaction mixture was loaded directly onto a silica gel column and eluted in 1:4 EtOAc, to yield the α,β-unsaturated aldehyde **33** (57 mg, 70%) as a colourless oil.

R_f 0.28 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$ 28.0 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 9.21 (s, 1H, C*H*=O), 7.13-7.30 (m, 7H, Ar), 6.79-6.83 (m, 2H, Ar), 6.38 (d, *J* = 7.5 Hz, 1H, C*H*=C(CH_3)(CHO), 5.85 (td, *J* = 11.5, 5.5 Hz, 1H, C*H*=CH), 5.55 (t, *J* = 9.5 Hz, 1H, C*H*=CH), 4.88 (td, *J* = 9.5, 6.5 Hz, 1H, C*H*OCH_2OCH_3), 4.64 (d, *J* = 6.5 Hz, 1H, OC*H*H),

4.57 (d, *J* = 11.5 Hz, 1H, OC*H*H), 4.50 (d, *J* = 6.5 Hz, 1H, OC*H*H), 4.31-4.37 (m, 3H), 4.28 (d, *J* = 11.5 Hz, 1H, OC*H*H), 3.75 (s, 3H, OCH_3), 3.74-3.79 (m, 1H, C*H*OBn), 3.36 (d, *J* = 3.5 Hz, 2H, CH_2OPMB), 3.30 (s, 3H, OCH_3), 3.21 (dt, *J* = 8.5, 3.5 Hz, 1H, OC*H*), 2.66 (ddd, *J* = 14, 11.5, 3.5 Hz, 1H, C*H*H), 2.41 (dt, *J* = 14, 4.5 Hz, 1H, C*H*H), 2.10 (ddd, *J* = 13.5, 11.5, 6.5 Hz, 1H, C*H*H), 1.63-1.68 (m, 1H, C*H*H), 1.61 (s, 3H, CH=C(CH_3)(CHO)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.8, 159.3, 159.2, 138.1, 137.2, 132.6, 129.5, 128.8, 128.3, 127.8, 127.7, 113.7, 94.3, 83.5, 78.6, 78.0, 72.8, 71.6, 69.8, 69.2, 55.3, 55.2, 38.0, 27.8, 9.4; IR(film) 2921, 1689, 1513, 1248, 1066, 1036, 772 cm^{-1}; MS (ESI$^+$) *m/z* (rel intensity) 551 [20], 533 [100, (M+Na)$^+$], 493 [30], 457 [25]; HRMS (ESI$^+$) 533.2510 (533.2510 calcd for $C_{30}H_{38}O_7Na$, (M+Na)$^+$)

(E)-3-((2R,4S,8S,9R,Z)-8-(Benzyloxy)-9-(hydroxymethyl)-4-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonin-2-yl)-2-methylacrylaldehyde (33a)

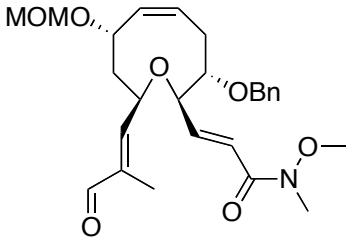


To a stirred solution of the PMB ether **33** (45 mg, 0.088 mmol) in CH_2Cl_2 (10 mL) was added pH 7 buffer (1 mL, 0.05 M NaH_2PO_4, 0.29 M NaOH in H_2O) and DDQ (40 mg g, 0.18 mmol). The resulting mixture was stirred at room temperature for 1 h, and quenched by addition of saturated aqueous $NaHCO_3$ solution (10 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL) and the combined organic extracts were dried (Mg_2SO_4). The solvent was removed *in vacuo* and the crude material was purified by flash chromatography (1:2 EtOAc/Petrol) to yield the alcohol **33a** (28 mg, 80%) as a colourless oil.

R_f 0.22 (1:1 EtOAc/hexane); $[\alpha]_D^{22}$ 33.7 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 9.42 (s, 1H, C*H*=O), 7.28-7.36 (m, 5H, Ar), 6.42 (dq, *J* = 8, 1.5 Hz, 1H, C*H*=C(CH_3)(CHO)), 5.89 (tdd, *J* = 11.5, 5.5, 1 Hz, 1H, CH=C*H*), 5.60 (dd, *J* = 11, 9 Hz, 1H, C*H*=CH), 4.91 (td, *J* = 9.5 7 Hz, 1H, C*H*CH_2OCH_3), 4.66-4.70 (m, 2H), 4.55 (d, *J* = 6.5 Hz, 1H, OC*H*H), 4.44-4.48 (m,

2H), 3.80 (dt, *J* = 7.5, 3.5 Hz, 1H, C*H*OBn), 3.56 (dd, *J* = 4, 2 Hz, 2H, CH_2OH), 3.36 (s, 3H, OCH_3), 3.26 (dt, *J* = 7.5, 6.5 Hz, 1H, OC*H*) 2.65 (ddd, *J* = 14.5, 12, 3 Hz, 1H, C*H*H), 2.49 (dt, *J* = 14, 5 Hz, 1H, C*H*H), 2.15 (ddd, *J* = 13.5, 11, 6 Hz, 1H, C*H*H), 1.72 (d, *J* = 1.5 Hz, 3H, CH=C(CH_3)(CHO)), 1.66-1.71 (m, 1H, C*H*H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.6, 152.7, 138.4, 137.9, 132.7, 128.6, 128.5, 127.9, 127.8, 94.4, 84.0, 78.0, 77.8, 71.6, 69.3, 63.0, 55.4, 38.1, 27.6, 9.5; IR(film) 3485, 2924, 1688, 1098, 1067, 1031, 699 cm^{-1}; MS (ESI$^+$) *m/z* (rel intensity) 413 [100, (M+Na)$^+$], 86 [20]; HRMS (ESI$^+$) 413.1934 (413.1935 calcd for $C_{22}H_{30}O_6Na$, (M+Na)$^+$)

(*E*)-3-((2*R*,3*S*,7*S*,9*R*,*Z*)-3-(Benzyloxy)-7-(methoxymethoxy)-9-((*E*)-2-methyl-3-oxoprop-1-enyl)-2,3,4,7,8,9-hexahydrooxonin-2-yl)-N-methoxy-N-methylacrylamide (35)

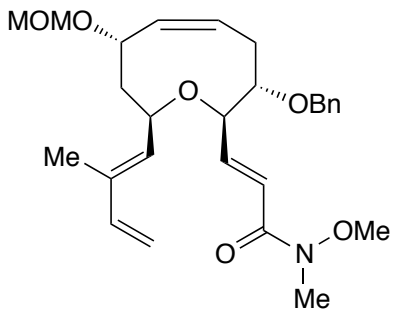


To a solution of the alcohol **33a** (28 mg, 0.072 mmol) in CH_2Cl_2 (2 mL) at 0 °C was added triethylamine (50 μL, 0.36 mmol) and the mixture stirred for 10 min. To this was added a solution of SO_3.pyridine (29 mg, 0.18 mmol) in DMSO (0.5 mL) dropwise. The resulting mixture was stirred at 0 °C for 3 h, until oxidation was deemed complete by TLC analysis. *N*-Methoxy-*N*-methyl-2-(triphenylphosphoranylidene) acetamide **34** (36 mg, 0.10 mmol) was added and the mixture stirred at room temperature for 16 h. The reaction mixture was loaded directly onto a silica gel column, eluted in 1:1 Et_2O/hexane, to yield the amide **35** (19 mg, 55 %) as a colourless oil.

R_f 0.22 (1:1 EtOAc/hexane); $[\alpha]_D^{22}$ 17.2 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 9.38 (s, 1H, C*H*=O), 7.27-7.34 (m, 5H, Ar), 6.97 (dd, *J* = 15.5, 5.5 Hz, 1H, C*H*=CHCON), 6.56 (d, *J* = 15.5 Hz, 1H, CH=C*H*CON), 6.43 (dq, *J* = 8, 1 Hz, 1H, C*H*=C(CH$_3$)(CHO)), 5.89 (td, *J* = 11.5, 5.5 Hz, 1H, C*H*=CH), 5.63 (dd, *J* = 11, 9 Hz, 1H, C*H*=CH), 4.91 (td, *J* = 9.5, 6.5 Hz, 1H, C*H*OCH$_2$OCH$_3$), 4.68 (d, *J* = 6.5 Hz, 1H, OC*H*H), 4.62 (d, *J* = 11.5 Hz, 1H, OC*H*H),

4.54 (d, *J* = 6.5 Hz, 1H, OC*H*H), 4.44 (d, *J* = 11.5 Hz, 1H, OC*H*H), 4.39-4.42 (m, 1H), 3.81 (ddd, *J* = 8, 5.5, 1.5 Hz, 1H, OC*H*), 3.6-3.63 (m, 1H), 3.59 (s, 3H, CH_3), 3.35 (s, 3H, CH_3), 3.22 (s, 3H, CH_3), 2.73 (ddd, *J* = 14, 11.5, 3 Hz, 1H, C*H*H), 2.45 (ddd, *J* = 14, 5, 3.5 Hz, 1H, C*H*H), 2.15 (ddd, *J* = 14, 10.4, 6 Hz, 1H, C*H*H), 1.74-1.79 (m, 1H), 1.68 (d, *J* = 1 Hz, 3H, CH=C(CH_3)(CHO)); ^{13}C NMR (125 MHz, $CDCl_3$) 194.6, 152.4, 145.3, 138.1, 137.8, 133.3, 128.4, 128.1, 127.78, 127.76, 119.1, 94.4, 82.9, 81.6, 77.8, 72.1, 69.1, 61.7, 55.4, 38.2, 29.7, 28.0, 9.5; IR(film) 2925, 1689, 1666, 1636, 1381, 1096, 1029, 746, 699 cm^{-1}; MS (ESI$^+$) *m/z* (rel intensity) 496 [100, (M+Na)$^+$], 474 [100, (M+H)$^+$]; HRMS (ESI$^+$) 496.2304 (496.2306 calcd for $C_{26}H_{35}NO_7Na$, (M+Na)$^+$).

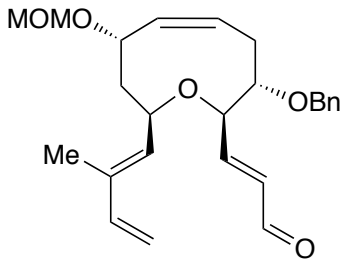
(E)-3-((2R,3S,7S,9R,Z)-3-(Benzyloxy)-7-(methoxymethoxy)-9-((E)-2-methylbuta-1,3-dienyl)-2,3,4,7,8,9-hexahydrooxonin-2-yl)-N-methoxy-N-methylacrylamide (35a)



To a solution of methyltriphenylphosphonium bromide (90 mg, 0.25 mmol, pre-dried at 100°C under high vac. for 2 h) in THF (5 mL) at 0 °C was a solution of KO^{t}Bu (250 μL, 1.0 M in THF, 0.25 mmol) dropwise. The resulting solution was stirred at 0 °C for 0.5 h. To a solution of the α,β-unsaturated aldehyde **35** (19 mg, 0.04 mmol) in THF (2 mL) was added the phosphorous ylide solution (1 mL, 0.05 mmol) dropwise by cannula. The mixture was stirred at 0 °C for 2 h, the reaction was quenched by addition of water (5 mL). The aqueous phase was extracted with Et_2O (3 × 10 mL) and the combined organic extracts were dried (Mg_2SO_4). The solvent was removed *in vacuo* and the resulting product was purified by column chromatography (1:2 EtOAc/petrol) to yield the title compound **35a** (15 mg, 80%) as a colourless oil.

R_f 0.43 (1:1 EtOAc/hexane); $[\alpha]_D^{22}$ 5.5 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.27-7.35 (m, 5H, Ar), 7.03 (dd, *J* = 15.5, 4.5 Hz, 1H, C*H*=CHCON), 6.59 (d, *J* = 15.5 Hz, 1H, CH=C*H*CON), 6.28 (ddd, *J* = 17.5, 10.5 0.5 Hz, 1H, C*H*=CH_2), 5.86 (tdd, *J* = 11, 5.5, 1 Hz, 1H, C*H*=CH), 5.62 (dd, *J* = 11, 9 Hz, 1H, C*H*=CH), 5.52 (d, *J* = 9 Hz, 1H, C*H*=C(CH_3)(CHO)), 5.14 (d, *J* = 17.5 Hz, 1H, CH=CHH_{trans}), 5.00 (d, *J* = 10.5 Hz, 1H, CH=CHH_{cis}), 4.89 (td, *J* = 9, 6 Hz, 1H, C*H*OCH_2OCH_3), 4.68 (d, *J* = 6.5 Hz, 1H, OC*H*H), 4.61 (d, *J* = 11.5 Hz, 1H, OC*H*H), 4.54 (d, *J* = 6.5 Hz, 1H, OC*H*H), 4.45 (d, *J* = 11.5 Hz, 1H, OC*H*H), 4.28 (ddd, *J* = 10, 9, 5 Hz, 1H, OC*H*), 3.83 (ddd, *J* = 8.5, 4.5, 1.5 Hz, 1H, OC*H*), 3.62 (s, 3H, CH_3), 3.58 (dt, *J* = 8.5, 3 Hz, 1H, C*H*OBn), 3.36 (s, 3H, CH_3), 3.32 (s, 3H, CH_3), 2.73 (ddd, *J* = 14, 11.5, 3 Hz, 1H, C*H*H), 2.42 (ddd, *J* = 14, 5, 4 Hz, 1H, C*H*H), 2.10 (ddd, *J* = 14, 10, 5.5 Hz, 1H, C*H*H), 1.73 (ddd, *J* = 14, 9.5, 5 Hz, 1H, C*H*H), 1.68 (d, *J* = 1 Hz, 1H, CH=C(CH_3)(CHO)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.2, 140.8, 137.9, 134.5, 133.7, 132.9, 128.4, 127.8, 127.7, 127.5, 118.4, 113.1, 94.3, 82.1, 82.0, 78.0, 72.1, 69.3, 61.7, 55.3, 39.6, 29.7, 28.0, 12.1; IR(film) 2924, 1665, 1636, 1455, 1380, 1152, 1097, 1032, 914, 747, 699 cm^{-1}; MS (ESI^+) *m/z* (rel intensity) 494 [100, $(M+Na)^+$]; HRMS (ESI^+) 494.2511 (494.2513 calcd for $C_{27}H_{37}O_6NNa$, $(M+Na)^+$).

(E*)-3-((2*R*,3*S*,7*S*,9*R*,Z*)-3-(Benzyloxy)-7-(methoxymethoxy)-9-((E*)-2-methylbuta-1,3-dienyl)-2,3,4,7,8,9-hexahydrooxonin-2-yl)acrylaldehyde (36)

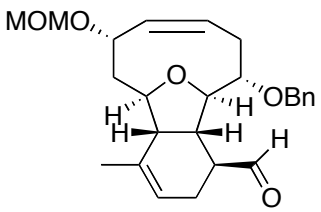


To a solution of the above amide **35a** (24 mg, 0.051 mmol) in Et_2O (1 mL) at -78 °C was added DIBAL-H solution (40 μL of a 1.5 M solution in toluene, 0.60 mmol) and the solution stirred at -78 °C for 1 h. EtOAc (0.1 mL) was added, and the mixture stirred at -78 °C for 15 min. before being allowed to warm to room temperature. Et_2O (2 mL) and saturated aqueous sodium potassium tartrate (2 mL) were added, and the aqueous phase extracted with Et_2O (3 × 5 mL). The combined organic portions were washed with water (10 mL), brine (10 mL)

and dried (Mg_2SO_4), and the solvent was removed *in vacuo* to yield the crude aldehyde. The product was purified by column chromatography (1:2 EtOAc/petrol) to yield the title compound **36** (19 mg, 90%) as a colourless oil.

R_f 0.65 (1:1 EtOAc/hexane); $[\alpha]_D^{22}$ 15.0 (*c* 1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 9.41 (d, *J* = 8 Hz, 1H, CH=O), 7.28-7.36 (m 5H, Ar), 6.74 (dd, *J* = 15.5, 4.5 Hz, 1H, C*H*=CHCHO), 6.29 (ddd, *J* = 17.5, 10.5, 0.5 Hz, 1H, CH=CH_2), 6.24 (ddd, *J* = 15.5, 8, 1.5 Hz, 1H, CH=C*H*CHO), 5.86 (ddt, *J* = 11.5, 5.5, 1 Hz, 1H, C*H*=CH), 5.65 (dd, *J* = 11, 9 Hz, 1H, C*H*=CH), 5.47 (dq, *J* = 9, 1.5 Hz, 1H, C*H*=C(CH_3)), 5.14 (d, *J* = 17.5 Hz, 1H, CH=CHH_{trans}), 5.03 (d, *J* = 10.5 Hz, 1H, CH=CHH_{cis}), 4.86 (td, *J* = 9, 6 Hz, 1H, C*H*OCH_2OCH_3), 4.66-4.69 (m, 2H), 4.54 (d, *J* = 6.5 Hz, 1H, OC*H*H), 4.40 (d, *J* = 11.5 Hz, 1H, OC*H*H), 4.25 (ddd, *J* = 10, 9, 5 Hz, 1H, OC*H*), 3.85 (ddd, *J* = 8.5, 4.5, 1.5 Hz, 1H, OC*H*), 3.58 (dt, *J* = 8.5, 3Hz, 1H, C*H*OBn), 3.56 (s, 3H, OCH_3), 2.74 (ddd, *J* = 14.5, 12, 3.5 Hz, 1H, C*H*H), 2.46 (ddd, *J* = 14, 5.5, 3.5 Hz, 1H, C*H*H), 2.11 (ddd, *J* = 14, 10, 6 Hz, 1H, C*H*H), 1.73 (ddd, *J* = 14, 9.5, 4.5Hz, 1H, C*H*H), 1.66 (d, *J* = 1.5 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.4, 156.8, 140.5, 137.6, 134.9, 134.1, 132.1, 131.5, 128.5, 128.0, 127.2, 113.5, 94.3, 81.6, 81.3, 78.5, 71.8, 69.2, 55.3, 39.5, 27.9, 12.2; IR(film) 2927, 1691, 1151, 1101, 1032, 913, 699 cm^{-1}; MS (ESI^+) *m/z* (rel intensity) 435 [100, $(M+Na)^+$]; HRMS (ESI^+) 435.2143 (435.2142 calcd for $C_{25}H_{32}O_5Na$, $(M+Na)^+$).

(*1*S,*2*R,*3*S,*5*Z,*7*S,*9*R,*10*R,*11*Z,*14*S)-*3-(Benzyloxy)-7-(methoxymethoxy)-14-formyl-cladiella-5(6),11(12)-diene (37)

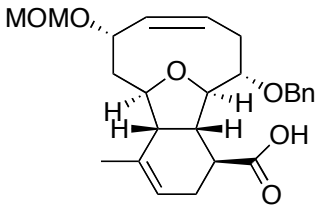


To a stirred solution of the tetraene **36** (81 mg, 0.20 mmol) in MeCN/H_2O (19:1, 2 mL) was added (5*S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one **14** (20 mg, 0.08 mmol). The mixture was stirred at room temperature for 4 days and the solvent removed *in vacuo*. The residue was

purified by column chromatography (1:4 EtOAc/petrol) to yield the title compound **37** (68 mg, 84%) as a colourless oil.

R_f 0.34 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$ 2.9 (*c* 0.8, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 9.67 (d, *J* = 0.5 Hz, 1H, H13), 7.26-7.39 (m, 5H, Ar), 5.80-5.86 (m, 1H, H5), 5.50-5.54 (m, 2H, H6, H12), 4.82-4.86 (m, 1H, H7), 4.76 (d, *J* = 7 Hz, 1H, OC*H*H), 4.59-4.64 (m, 2H), 4.54 (d, *J* = 7 Hz, 1H, OC*H*H), 4.22 (dd, *J* = 4.5, 1.5 Hz, 1H, H2), 4.20 (ddd, *J* = 7.5, 4.5, 1.5 Hz, 1H, H9), 3.51 (dt, *J* = 6, 1.5 Hz, 1H, H3), 3.39 (s, 3H, OCH_3), 2.90 (t, *J* = 8 Hz, 1H, H10), 2.52 (td, *J* = 8.5, 4.5 Hz, 1H, H1), 2.44-2.49 (m, 3H, H4 and H14), 2.32-2.37 (m, 1H, H13), 2.28 (ddd, *J* = 14.5, 11.5, 4.5 Hz, 1H, H8), 2.05-2.11 (m, 1H, H13), 1.84 (dt, *J* = 14.5, 1.5 Hz, 1H, H8), 1.73 (d, *J* = 1.5 Hz, 3H, H17); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.2 (C18), 138.5 (CH), 134.5 (CH), 134.2 (CH), 128.3 (CH), 127.7 (CH), 127.5 (C5), 127.2 (CH), 119.9 (CH), 93.4 (CH_2), 86.7 (C2), 83.2 (C9), 76.9 (C3), 70.8 (CH_2), 68.1 (C7), 55.2 (CH_2), 47.9 (C14), 44.3 (C10), 40.6 (C1), 37.5 (C8), 27.4 (C4), 23.4 (C3), 22.8 (C17); IR(film) 2922, 1721, 1452, 1149, 1098, 1040, 919, 731, 698 cm^{-1}; MS (ESI$^+$) *m/z* (rel intensity) 435 [100, $(M+Na)^+$], 430 [25, $(M+NH_4)^+$], 351 [30]; HRMS (ESI$^+$) 435.2142 (435.2142 calcd for $C_{25}H_{32}O_5Na$, $(M+Na)^+$)

(*1*S,*2*R,*3*S,*5*Z,*7*S,*9*R,*10*R,*11*Z,*14*S)-*3-(Benzyloxy)-7-(methoxymethoxy)-cladiella-5(6),11(12)-dienyl-14-methanoic acid (37a)*

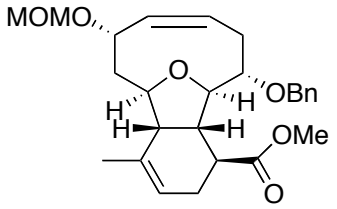


To a solution of the aldehyde **37** (11 mg, 0.027 mmol) in acetone (1 mL) and water (0.4 mL) at 0 °C was added 2-methyl-2-butene (0.4 mL), NaH_2PO_3 (35 mg, 0.26 mmol) and $NaClO_2$ (7 mg, 0.076 mmol). The mixture was stirred at 0 °C for 1 h and water (5 mL) and EtOAc (5 mL) were added. The aqueous phase extracted with EtOAc (2 × 5 mL) and the combined organic portions were dried (Mg_2SO_4). The solvent removed *in vacuo* and the product was

purified by column chromatography (EtOAc) to yield the title compound **37a** as a colourless solid (11.5 mg, quantitative). The product was recrystallised (Et_2O/hexane) to give colourless needles.

R_f 0.08 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$ 37.5 (*c* 1.0, $CHCl_3$); m.p. 152-153 °C; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.24-7.35 (m, 5H, Ar), 5.83 (td, *J* = 11, 6 Hz, 1H), 5.51-5.55 (m, 2H), 4.88-4.92 (m, 1H), 4.78 (d, *J* = 7 Hz, 1H), 4.58 (d, *J* = 6 Hz, 1H), 4.55 (d, *J* = 7 Hz, 1H), 4.54-4.56 (m, 1H), 4.23-4.23 (m, 1H), 4.21 (ddd, *J* = 9.5, 4, 2 Hz, 1H), 3.53 (d, *J* = 7 Hz, 1H), 3.38 (s, 3H), 3.00 (t, *J* = 9 Hz, 1H), 2.57 (td, *J* = 11, 5 Hz, 1H), 2.35-2.47 (m, 4H), 2.29 (ddd, *J* = 14.5, 11.5, 4 Hz, 1H), 2.17 (dddd, *J* = 17.5, 10.5, 4.5, 2 Hz, 1H), 1.91 (dt, *J* = 14, 1.5 Hz, 1H), 1.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.0, 138.5, 134.2, 132.4, 128.2, 127.6, 127.5, 127.3, 121.0, 93.4, 87.5, 83.3, 77.7, 70.7, 68.2, 55.2, 43.8, 42.9, 41.8, 36.6, 28.1, 27.8, 22.8; IR(film) 2932, 1727, 1704, 1440, 1150, 1097, 1084, 1039, 1027, 753, 701 cm^{-1}; MS (ESI^+) *m/z* (rel intensity) 451 [100, $(M+Na)^+$], 367 [35]; HRMS (ESI^+) 451.2091 (451.2091 calcd for $C_{25}H_{32}O_6Na$, $(M+Na)^+$)

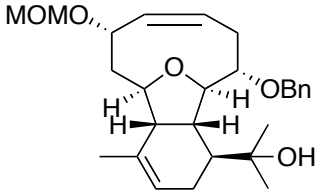
(*1*S,*2*R,*3*S,*5*Z,*7*S,*9*R,*10*R,*11*Z,*14*S)-*3-(Benzyloxy)-7-(methoxymethoxy)-14-methoxyformyl-cladiella-5(6),11(12)-diene (38)



To a solution of the carboxylic acid **37a** (11.5 mg, 0.027 mmol) in toluene (0.4 mL) and MeOH (0.1 mL) was added trimethylsilyl diazomethane (20 μL, 2.0 M solution in Et_2O, 0.04 mmol). After 15 min the solvent was removed *in vacuo*. The residue was purified by column chromatography (1:4 EtOAc/petrol) to yield the title compound **38** (10 mg, 90%) as a colourless oil.

R_f 0.47 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$ 54.0 (*c* 0.2, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.27-7.37 (m, 5H, Ar), 5.82 (tdd, *J* = 11, 6, 1 Hz, 1H, H5), 5.50-5.54 (m, 2H, H6 and H12), 4.88-4.92 (m, 1H, H7), 4.77 (d, *J* = 7 Hz, 1H), 4.58 (s, 2H), 4.54 (d, *J* = 7 Hz, 1H), 4.19 (ddd, *J* = 9.5, 4, 2 Hz, 1H, H9), 4.14 (dd, *J* = 2, 1.5 Hz, 1H, H2), 3.65 (s, 3H, OCH_3), 3.50 (d, *J* = 7 Hz, 1H, H3), 3.38 (s, 3H, OCH_3), 2.99 (t, *J* = 9 Hz, 1H, H10), 2.52 (td, *J* = 11, 5 Hz, 1H), 2.43-2.49 (m, 1H), 2.34-2.41 (m, 2H), 2.24-2.32 (m, 2H), 2.11 (dddd, *J* = 17, 11, 5, 2.5 Hz, 1H), 1.89 (dt, *J* = 14.5, 2 Hz, 1H), 1.75 (d, *J* = 1.5 Hz, 1H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5, 138.6, 134.2, 132.6, 128.2, 127.6, 127.4, 127.3, 121.2, 93.5, 87.6, 83.3, 77.9, 70.6, 68.2, 55.2, 51.8, 43.7, 43.3, 42.2, 36.6, 27.94, 27.91 22.9; IR(film) 2926, 1731, 1439, 1165, 1150, 1098, 1039, 916, 701 cm^{-1}; MS (ESI^+) *m/z* (rel intensity) 465 [100, $(M+Na)^+$], 460 [20, $(M+NH_4)^+$], 381 [20]; HRMS (ESI^+) 465.2247 (465.2247 calcd for $C_{26}H_{34}O_6Na$, $(M+Na)^+$)

(*1*S,*2*R,*3*S,*5Z*,*7*S,*9*R,*10*R,*11Z*,*14*S)-*3-(Benzyloxy)-7-(methoxymethoxy)-18-hydroxy -cladiella-5(6),11(12)-diene (39)

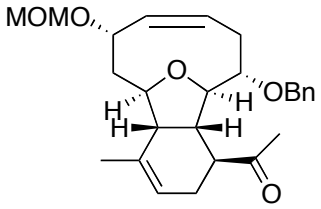


To a solution of the ester **38** (6 mg, 0.014 mmol) in Et_2O (1 mL) at -78 °C was added methyl lithium (28 μL, 1.6 M solution in Et_2O, 0.045 mmol). The resulting solution was stirred at -78 °C for 30 min and quenched by addition of saturated aqueous NH_4Cl solution (2 mL). The aqueous phase extracted with EtOAc (3 × 5 mL) and the combined organic portions were dried (Mg_2SO_4). The solvent was removed *in vacuo* and the product was purified by column chromatography (1:2 EtOAc/petrol) to yield the title compound **39** (4 mg, 64%) as a colourless, amorphous solid.

R_f 0.12 (1:2 EtOAc/hexane); $[\alpha]_D^{22}$ 9.6 (*c* 0.27, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.26-7.40 (m, 5H), 5.84 (dddd, *J* = 10.75, 9.72, 6.66, 0.76 Hz, 1H), 5.50 (dd, *J* = 11.42, 8.75 Hz, 1H), 5.45-5.47 (m, 1H), 4.74 (d, *J* = 6.61 Hz, 1H), 4.72-4.73 (m, 1H), 4.69 (d, *J* = 12.38 Hz,

1H), 4.61 (d, *J* = 12.30 Hz, 1H), 4.53 (d, *J* = 6.59 Hz, 1H), 4.34 (dd, *J* = 8.04, 1.86 Hz, 1H), 4.22 (t, *J* = 4.24, 4.24 Hz, 1H),3.38-3.39 (m, 1H), 3.38 (s, 3H), 2.63-2.7 (m, 3H), 2.44 (dt, *J* = 14.5, 6.5 Hz, 1H), 2.28 (ddd, *J* = 13.94, 11.23, 5.25 Hz, 1H), 2.10-2.14 (m, 2H), 1.72 (dt, *J* = 13.89, 1.17, 1.17 Hz, 1H), 1.68 (s, 3H), 1.36 (dt, *J* = 6.50, 3.23, 3.23 Hz, 1H), 1.20 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 135.1, 134.2, 128.3, 127.8, 127.5, 127.2, 120.6, 93.2, 86.6, 82.5, 76.0, 73.4, 70.9, 68.2, 55.2, 47.0, 43.3, 40.7, 39.3, 29.2, 27.8, 26.1, 22.4, 22.2; ; IR(film) 3451, 2929, 1452, 1376, 1149, 1094, 1040, 918, 734, 700 cm^{-1}; MS (ESI^+) *m/z* (rel intensity) 465 [100, $(M+Na)^+$], 460 [20, $(M+NH_4)^+$], 381 [15]; HRMS (ESI^+) 465.2612 (465.2612 calcd for $C_{27}H_{38}O_5Na$, $(M+Na)^+$)

(*1*S,*2*R,*3*S,*5*Z,*7*S,*9*R,*10*R,*11*Z,*14*S)-*3-(Benzyloxy)-7-(methoxymethoxy) -cladiella-5(6),11(12)-dienyl-18-one (41)

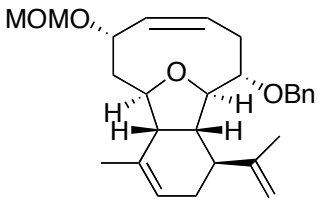


To a stirred solution of the aldehyde **37** (55 mg, 0.13 mmol) in Et_2O (15 mL) at -78 °C was added methyl lithium solution (125 μL, 1.6 M solution in Et_2O, 0.2 mmol). After stirring at -78 °C for 20 min, the reaction was quenched by addition of saturated aqueous NH_4Cl solution (10 mL). The aqueous phase extracted with EtOAc (3 × 10 mL) and the combined organic portions were dried (Mg_2SO_4) and reduced *in vacuo*. The resulting residue was redissolved in CH_2Cl_2 (10 mL) and celite (100 mg) was added, followed by pyridinium chlorochromate (43 mg, 0.2 mmol). The deep red solution was stirred at room temperature for 1 h, and filtered through a plug of silica, eluted with CH_2Cl_2 (50 mL). The solvent was removed *in vacuo* and the product was purified by column chromatography (1:1 Et_2O/petrol) to yield the ketone **41** (50 mg, 88 %) as a colourless oil.

R_f 0.23 (1:2 EtOAc/hexane); $[\alpha]_D^{21}$ 24.6 (*c* 0.27, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.25-7.39 (m, 5H, Ar), 5.82 (tdd, *J* = 11, 6, 1 Hz, 1H, H5), 5.50-5.54 (m, 2H, H6, H12), 4.89-4.93 (m, 1H, H7), 4.77 (d, *J* = 6.5 Hz, 1H), 4.58 (d, *J* = 3.5 Hz, 2H), 4.55 (d, *J* = 6.5 Hz, 1H), 4.19

(ddd, J = 9.5, 4, 2 Hz, 1H, H9), 4.00 (dd, J = 2.5, 1.5 Hz, 1H, H2), 3.59 (d, J = 7 Hz, 1H), 3.38 (s, 3H, -OCH_3), 2.99 (app t, J = 9 Hz, 1H, H10), 2.66 (td, J = 11, 5 Hz, 1H), 2.40-2.47 (m, 2H), 2.32-2.38 (m, 2H), 2.27 (ddd, J = 14.5, 11.5, 4 Hz, 1H), 2.18 (s, 3H, $COCH_3$), 1.90 (dt, J = 14.5, 2 Hz, 1H), 1.76 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.6, 138.6, 134.1, 132.8, 128.2, 128.1, 127.7, 127.4, 120.8, 93.4, 88.1, 83.4, 78.0, 68.1, 55.1, 49.5, 47.9, 43.7, 42.2, 36.6, 29.2, 28.1, 27.6, 22.8; IR(film) 2915, 1706, 1452, 1363, 1149, 1100, 1086, 1040, 735, 700 cm^{-1}; MS (ESI$^+$) *m/z* (rel intensity) 449 [100, $(M+Na)^+$], 444 [30], 365 [20]; HRMS (ESI$^+$) 449.22985 (449.22985 calcd for $C_{26}H_{34}O_5Na$, $(M+Na)^+$).

(*1*S,*2*R,*3*S,*5*Z,*7*S,*9*R,*10*R,*11*Z,*14*S)-*3-(Benzyloxy)-7-(methoxymethoxy) -cladiella-5(6),11(12),14(15)-triene (42)



To a solution of the ketone **41** (100 mg, 0.23 mmol) and DMAP (28 mg, 0.23 mmol) in THF (10 mL) at -40 °C was added a solution of bis(cyclopentadienyl)-chloro(dimethylaluminum)-methylenetitanium (0.6 mL of a 0.5 M solution in toluene, 0.3 mmol) dropwise. The mixture was stirred at -40 °C for 30 min. and allowed to warm to room temperature over 1 h. The solution was recooled to -10 °C and quenched carefully by addition of saturated aqueous NaOH solution until evolution of gas ceased. Et_2O (20mL) was added, and the solution was filtered through a plug a celite. The solvent was removed *in vacuo* and the resulting product was purified by column chromatography, (1:4 Et_2O/petrol) to yield the triene **42** (73 mg, 75 %) as a yellow crystalline solid. A sample of the product was recrystallised (4:1 MeOH/water) to give fine, colourless needles.

R_f 0.44 (1:2 EtOAc/hexane); m.p. 84-85.5 °C; $[\alpha]_D^{19}$ -3.0 (*c* 0.5, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.26-7.35 (m, 5H, Ar), 5.81 (dddd, J = 11, 10, 6, 1 Hz, 1H, H5), 5.48-5.53 (m, 2H, H6 and H12), 4.89-4.92 (m, 1H, H7), 4.83-4.84 (m, 1H, H15), 4.77 (d, J = 7 Hz, 1H), 4.60 (s, 2H), 4.55 (d, J = 7 Hz, 1H), 4.25 (t, J = 2.0 Hz, 1H, H2), 4.21 (ddd, J = 10, 4, 2 Hz, 1H), 3.38

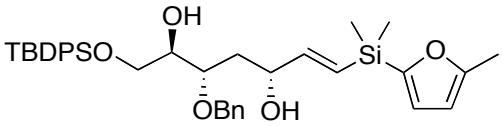
(s, 3H), 3.32 (dt, *J* = 7, 1.5 Hz, 1H), 2.94 (t, *J* = 9 Hz, 1H), 2.33-2.45 (m, 2H), 2.27 (ddd, *J* = 14.5, 11.5, 4.5 Hz, 1H), 2.17 (td, *J* = 11.5, 4.5 Hz, 1H), 2.05-2.12 (m, 1H), 1.90 (dt, *J* = 14.5, 2 Hz, 1H), 1.74 (s, 3H), 1.58 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.1, 138.5, 134.0, 131.4, 128.2, 127.6, 127.4, 127.3, 123.0, 115.9, 112.8, 93.4, 85.6, 83.0, 77.9, 70.3, 68.4, 55.1, 44.2, 44.1, 43.8, 36.5, 30.5, 28.8, 23.0, 19.4; IR(film) 2924, 2854, 1454, 1150, 1099, 1040, 918, 734, 699 cm^{-1}; MS (ESI^+) *m/z* (rel intensity) 449 [30], 447, [75 $(M+Na)^+$], 433 [100], 363 [20], 349 [25]; HRMS (ESI^+) 447.25062 (447.25058 calcd for $C_{27}H_{36}O_4Na$, $(M+Na)^+$)

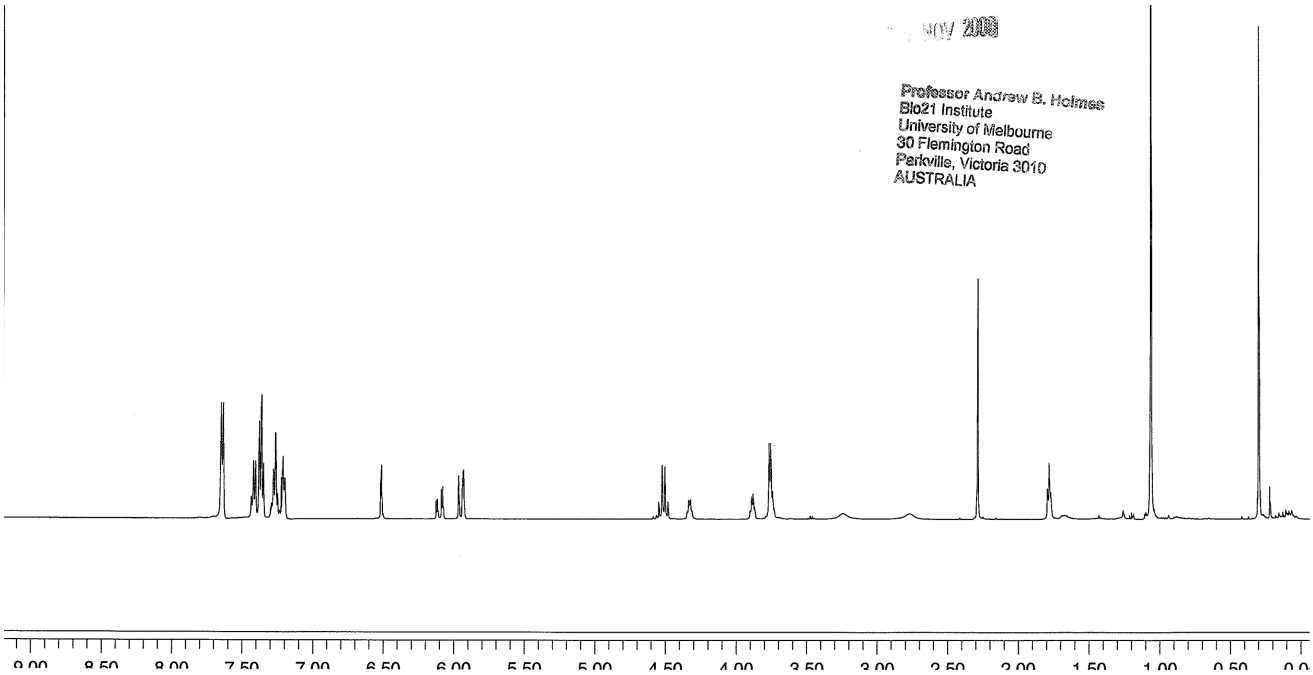
Space group P2(1)2(1)2(1), Unit Cell Dimensions *a* = 5.2539(3) Å, *b* = 17.363(2) Å, *c* = 25.103(3) Å, α = 90°, β = 90°, γ = 90°, V = 2290.0(4) $Å^3$, Z = 4, D = 1.231 Mg/m3, F(000) = 920, Mol. formula = $C_{27}H_{36}O_4$, Mw = 424.5723.

The X-ray data have been deposited with the Cambridge Crystallographic Data Cantre and assigned the deposit code CCDC 974196.

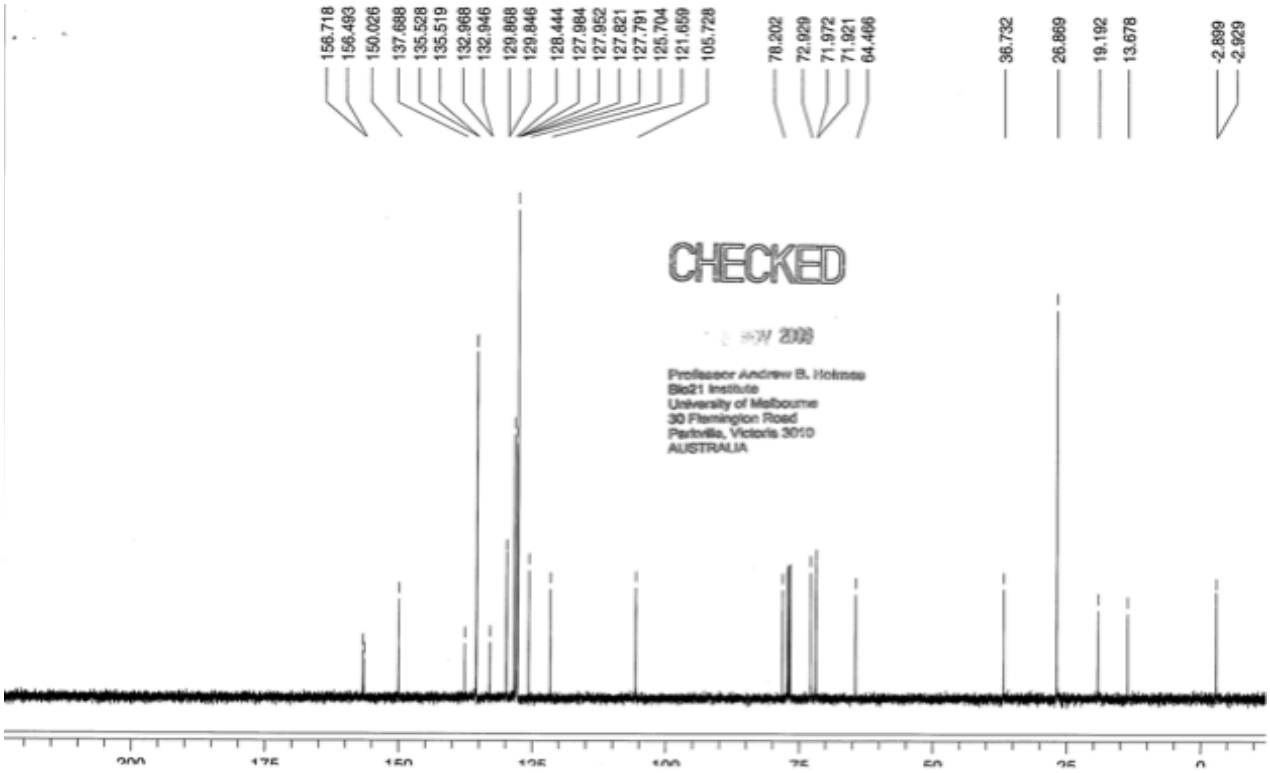
(2R,3S,5R,E)-3-(Benzyloxy)-1-(tert-butyldiphenylsilyloxy)-7-(dimethyl(5-methylfuran-2-yl)silyl)hept-6-ene-2,5-diol (19)

^{1}H NMR (500 MHz, $CDCl_3$)

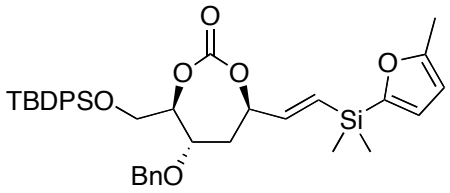




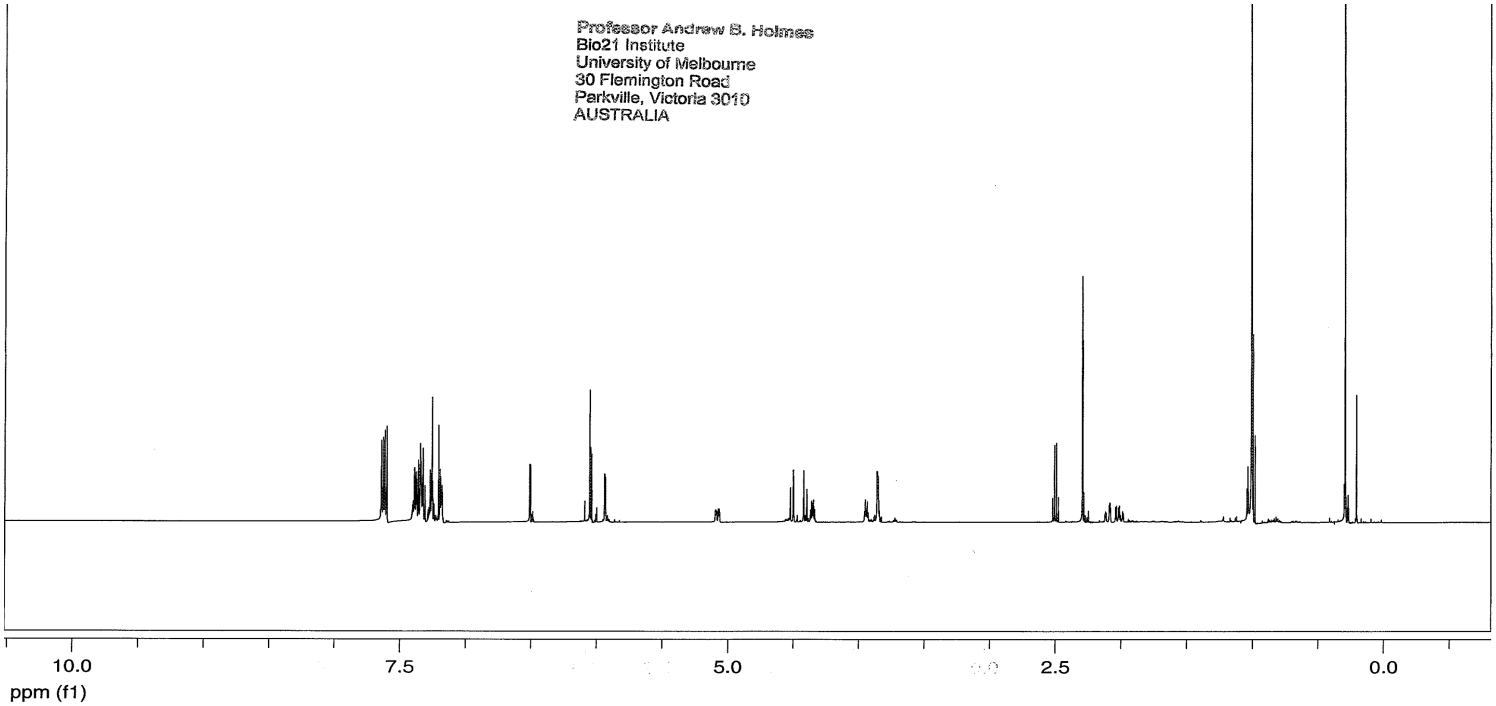
^{13}C NMR (125 MHz, $CDCl_3$)



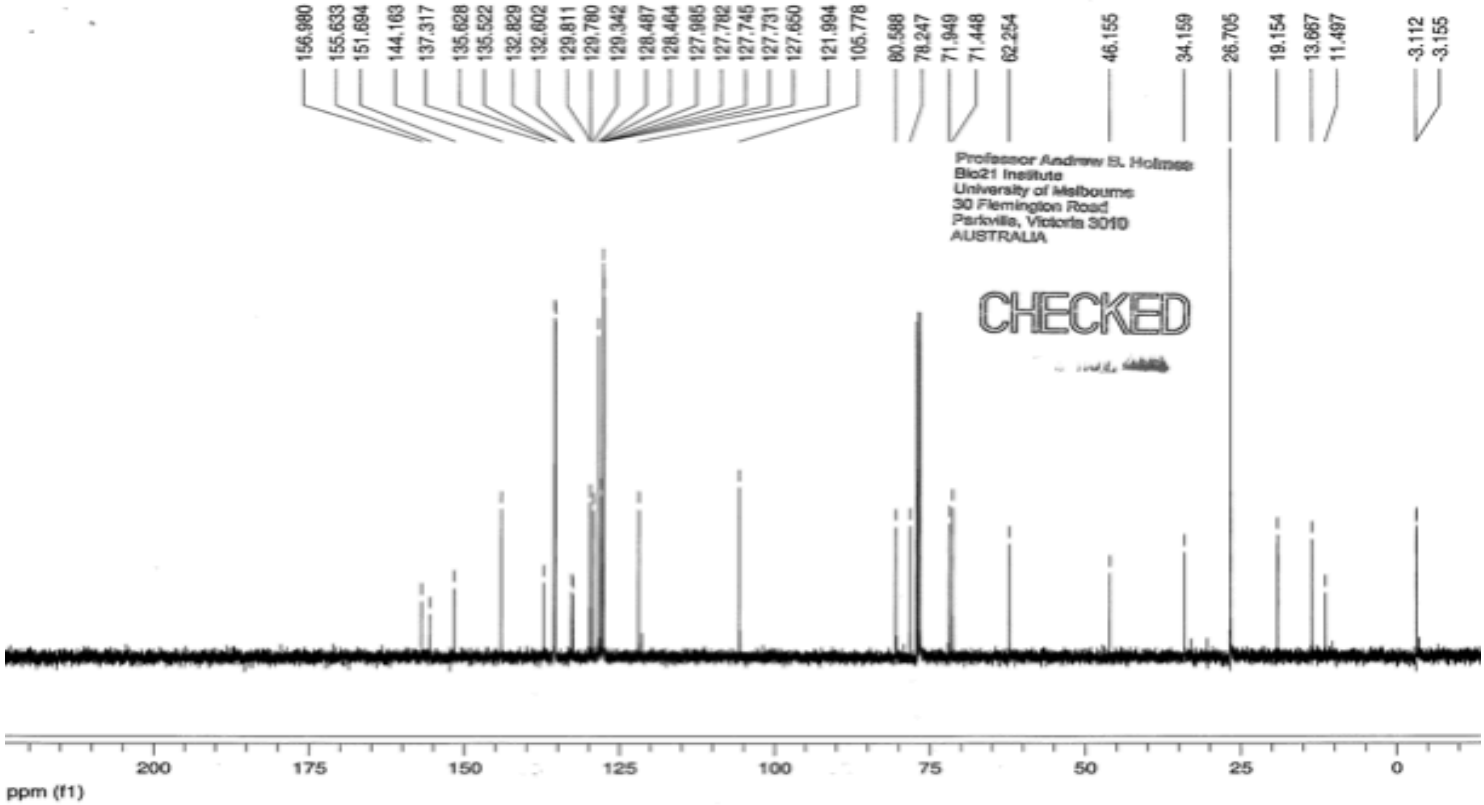
(4R,5S,7R)-5-(Benzyloxy)-4-((tert-butyldiphenylsilyloxy)methyl)-7-((E)-2-(dimethyl(5-methylfuran-2-yl)silyl)vinyl)-1,3-dioxepan-2-one (22)



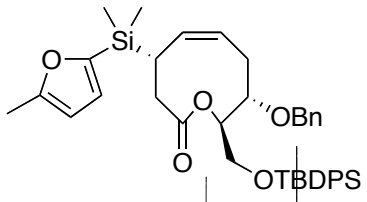
^{1}H NMR (500 MHz, $CDCl_3$)



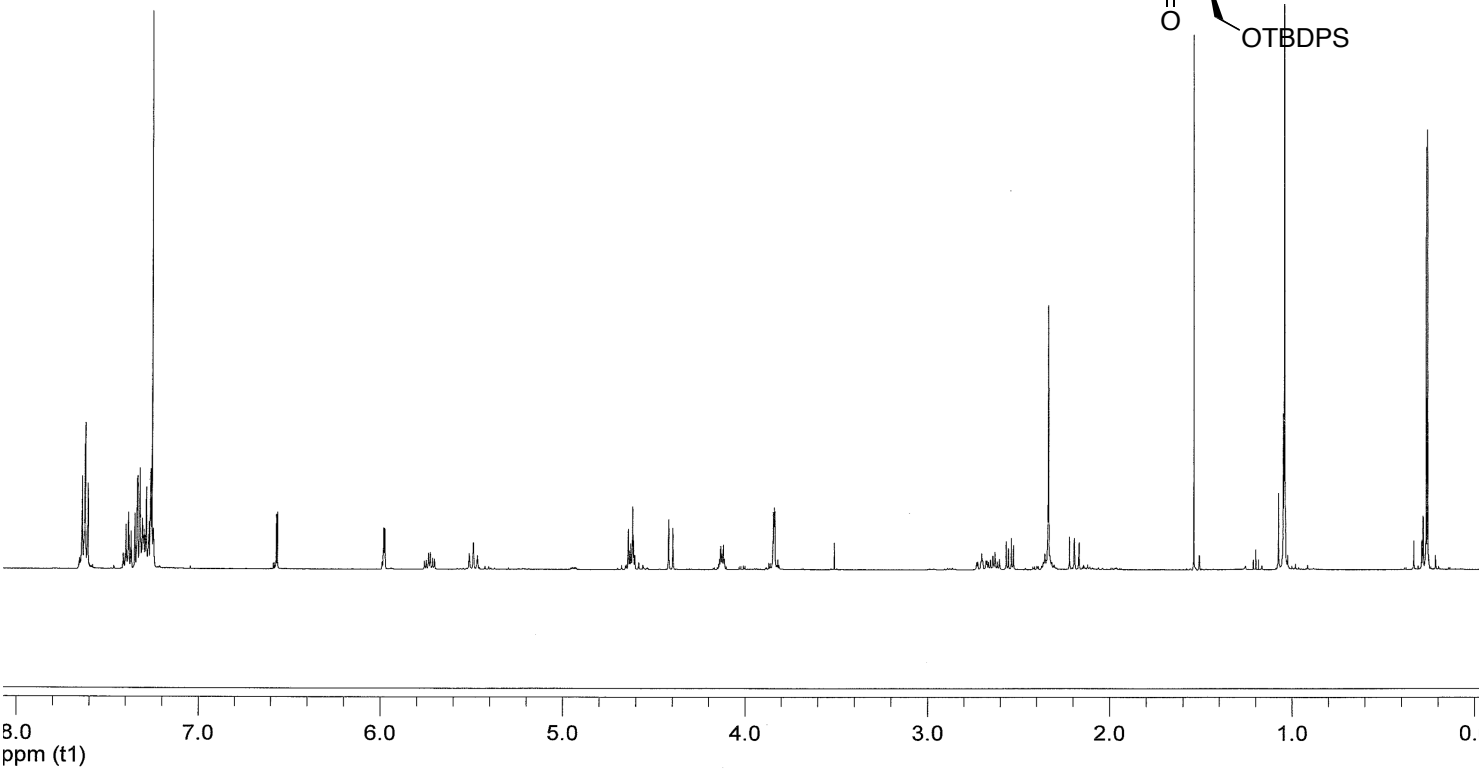
^{13}C NMR (125 MHz, $CDCl_3$)



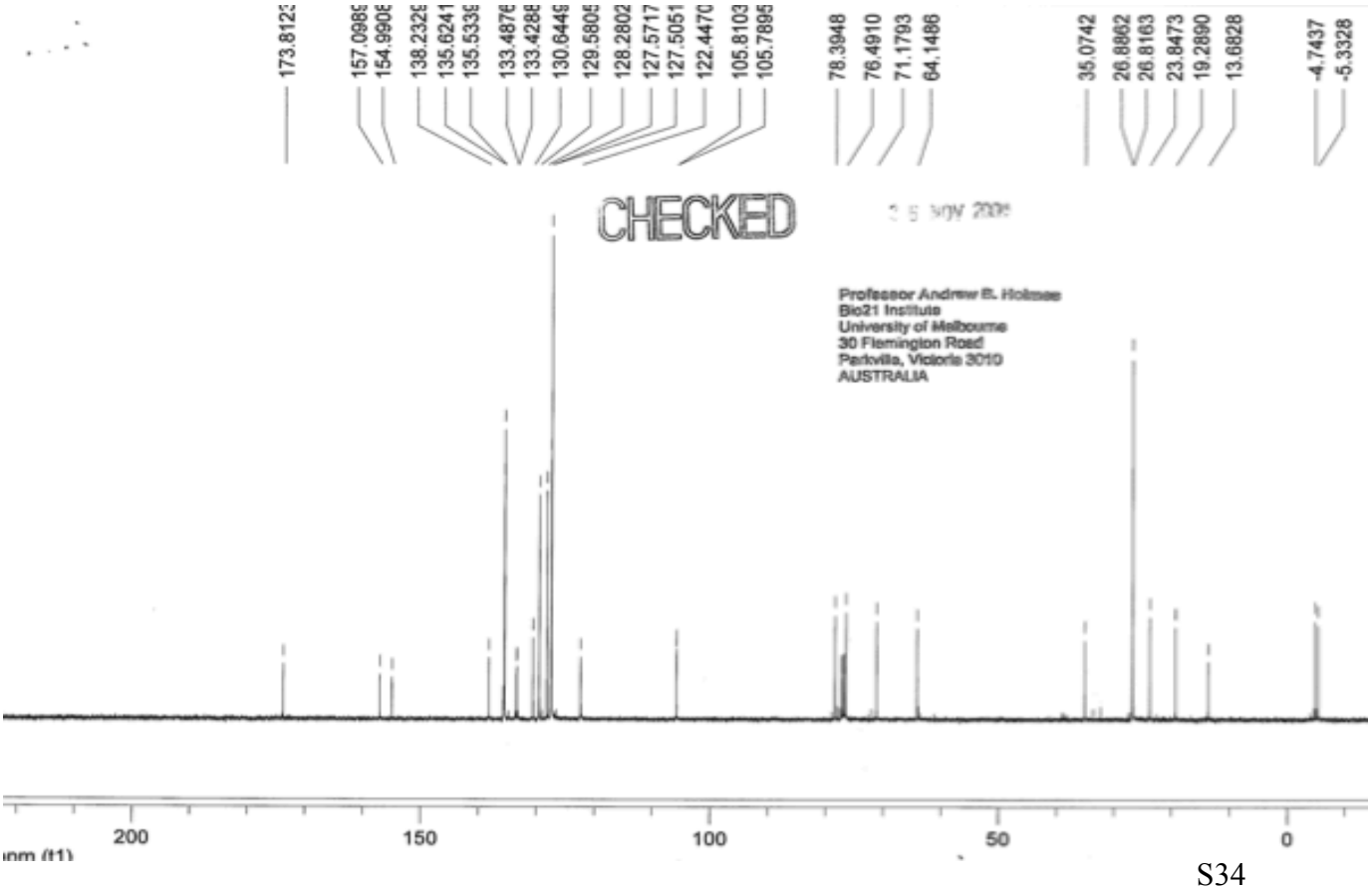
(4S,8S,9R,Z)-8-(Benzyloxy)-9-((tert-butyldiphenylsilyloxy)methyl)-4-(dimethyl(5-methylfuran-2-yl)silyl)-3,4,8,9-tetrahydrooxonin-2(7H)-one (24)

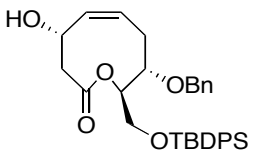


^{1}H NMR (500 MHz, $CDCl_3$)



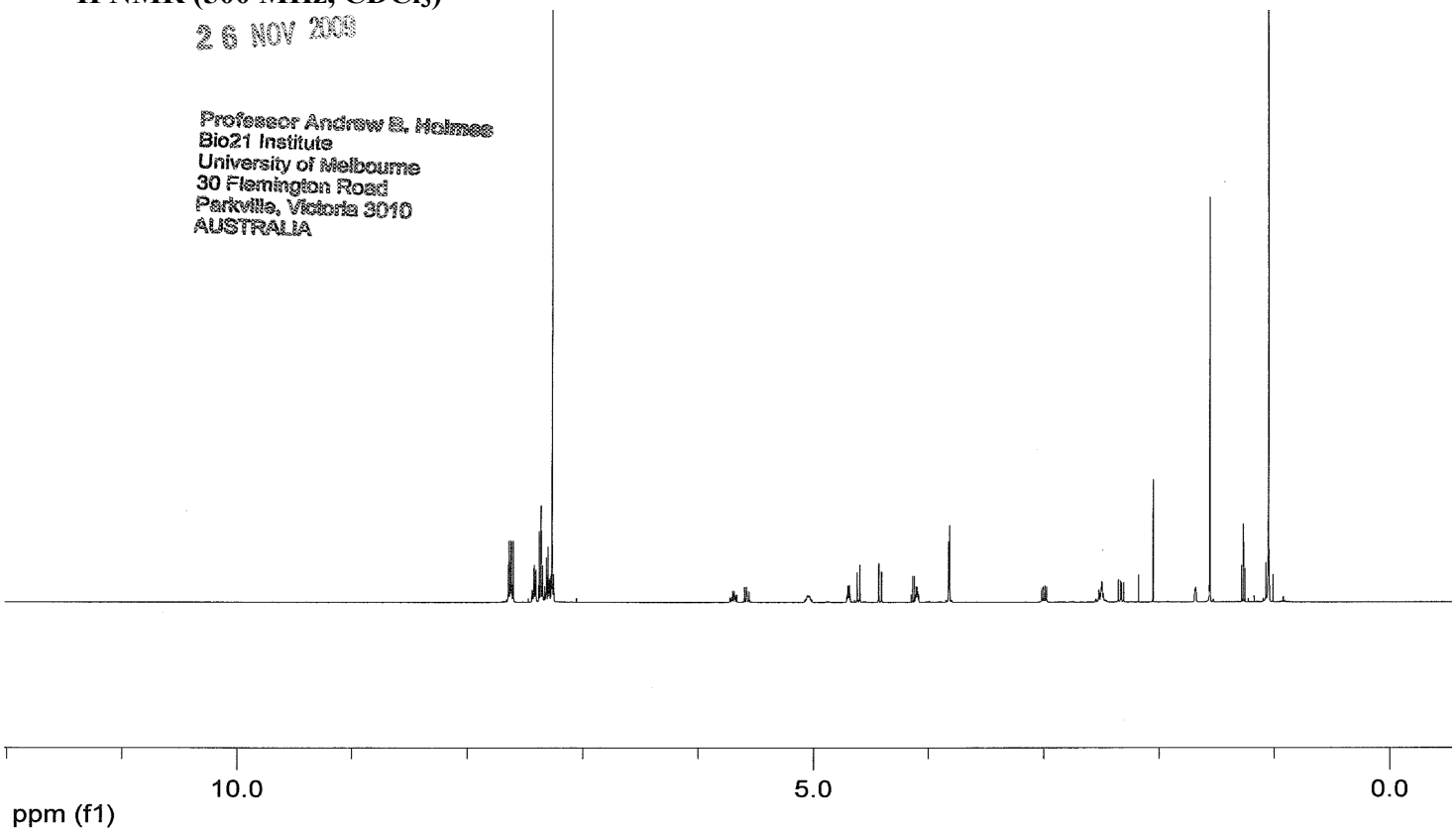
^{13}C NMR (125 MHz, $CDCl_3$)



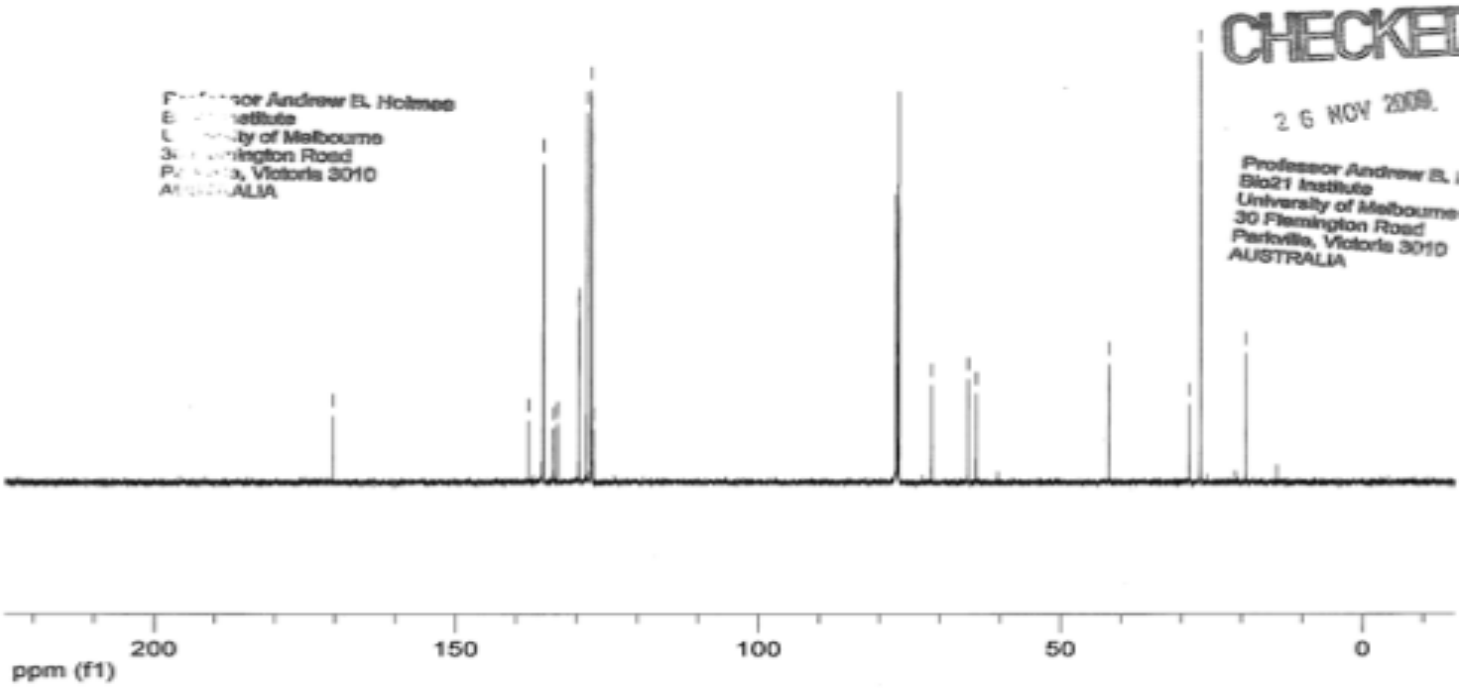


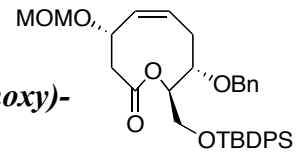
(4S,8S,9R,Z)-8-(Benzyloxy)-9-((tert-butyldiphenylsilyloxy)methyl)-4-hydroxy-3,4,8,9-tetrahydrooxonin-2(7H)-one (24a)

^{1}H NMR (500 MHz, $CDCl_3$)



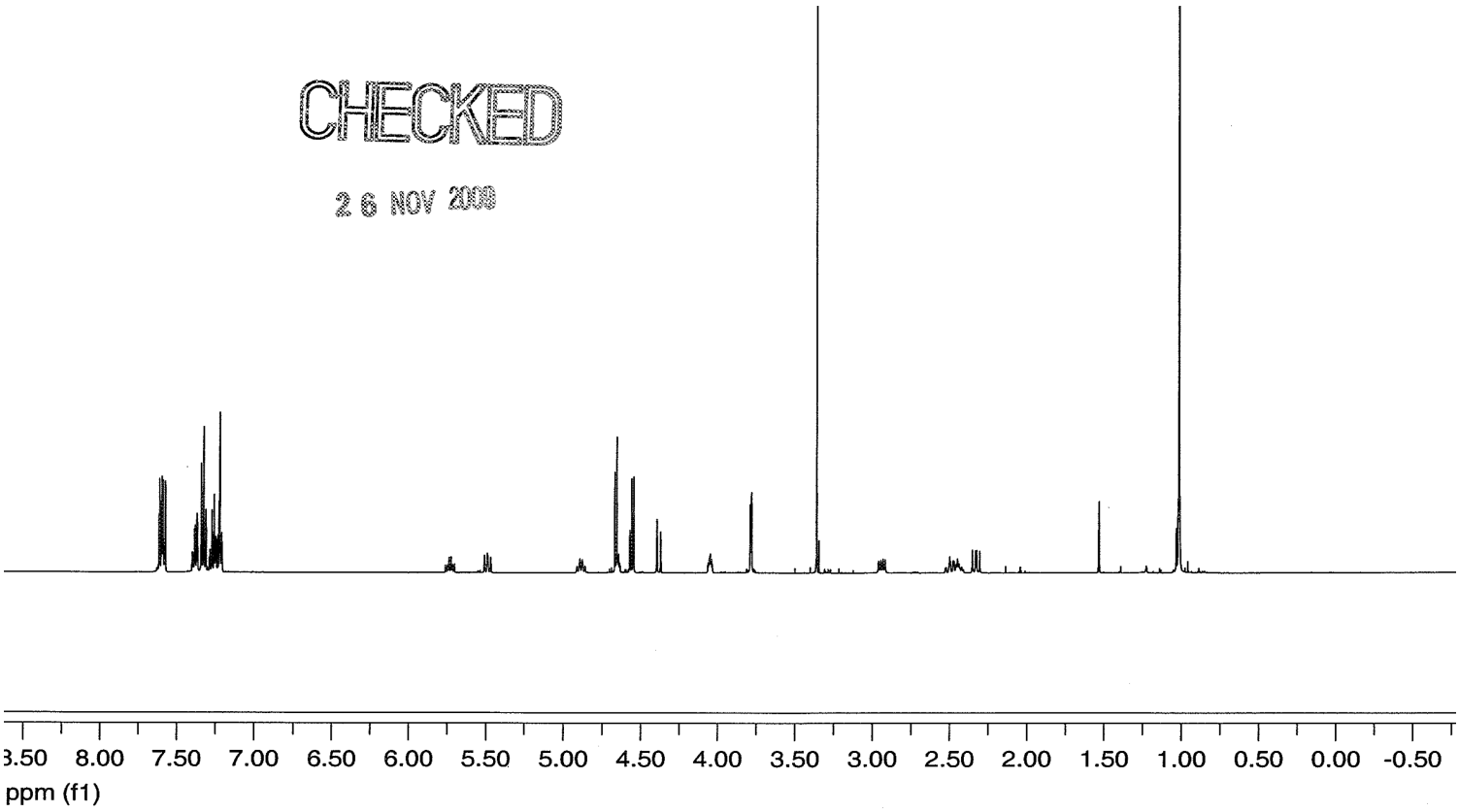
^{13}C NMR (125 MHz, $CDCl_3$)



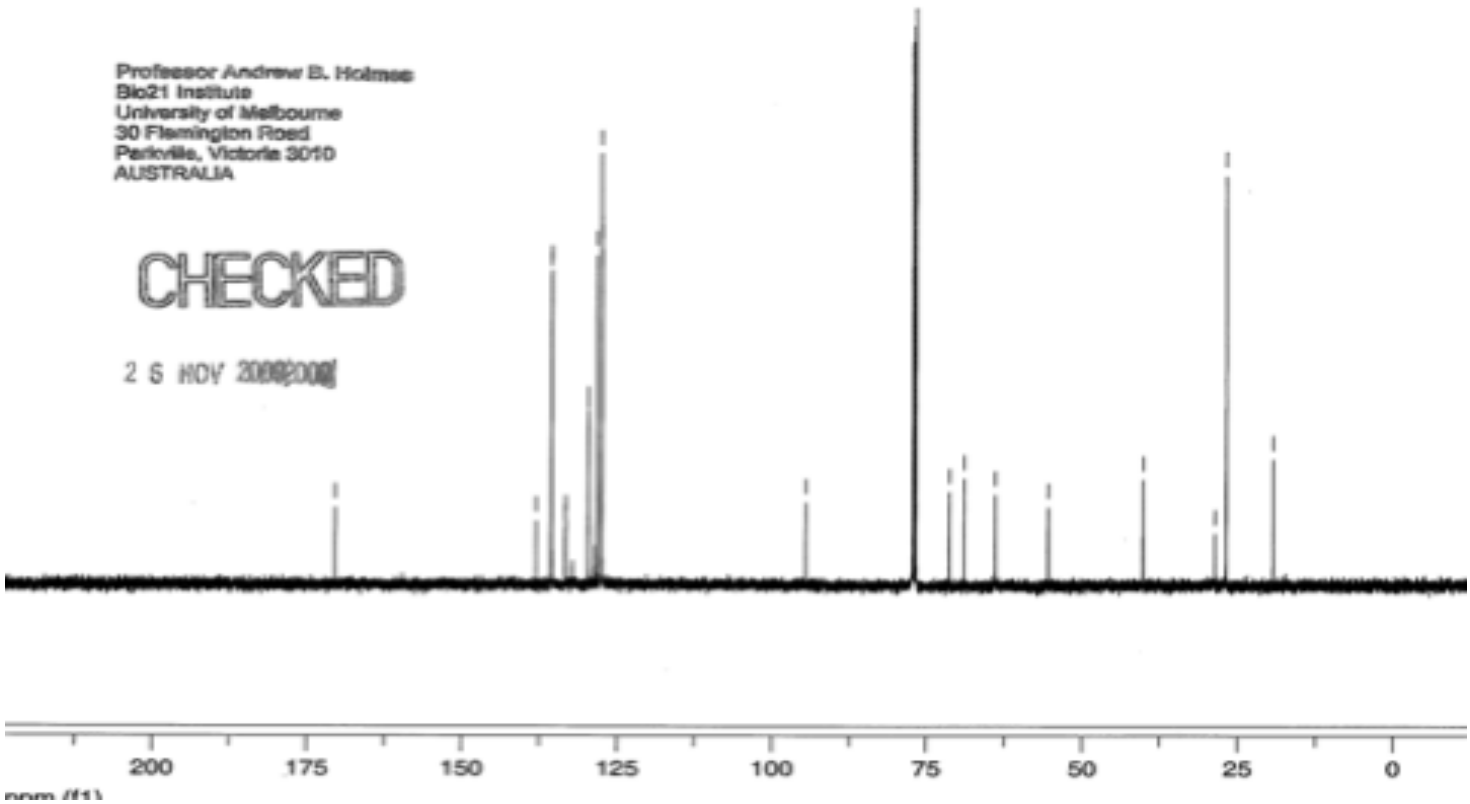


(4S,8S,9R,Z)-8-(Benzyloxy)-9-((tert-butyldiphenylsilyloxy)methyl)-4-(methoxymethoxy)-3,4,8,9-tetrahydrooxonin-2(7H)-one (27)

^{1}H NMR (500 MHz, $CDCl_3$)

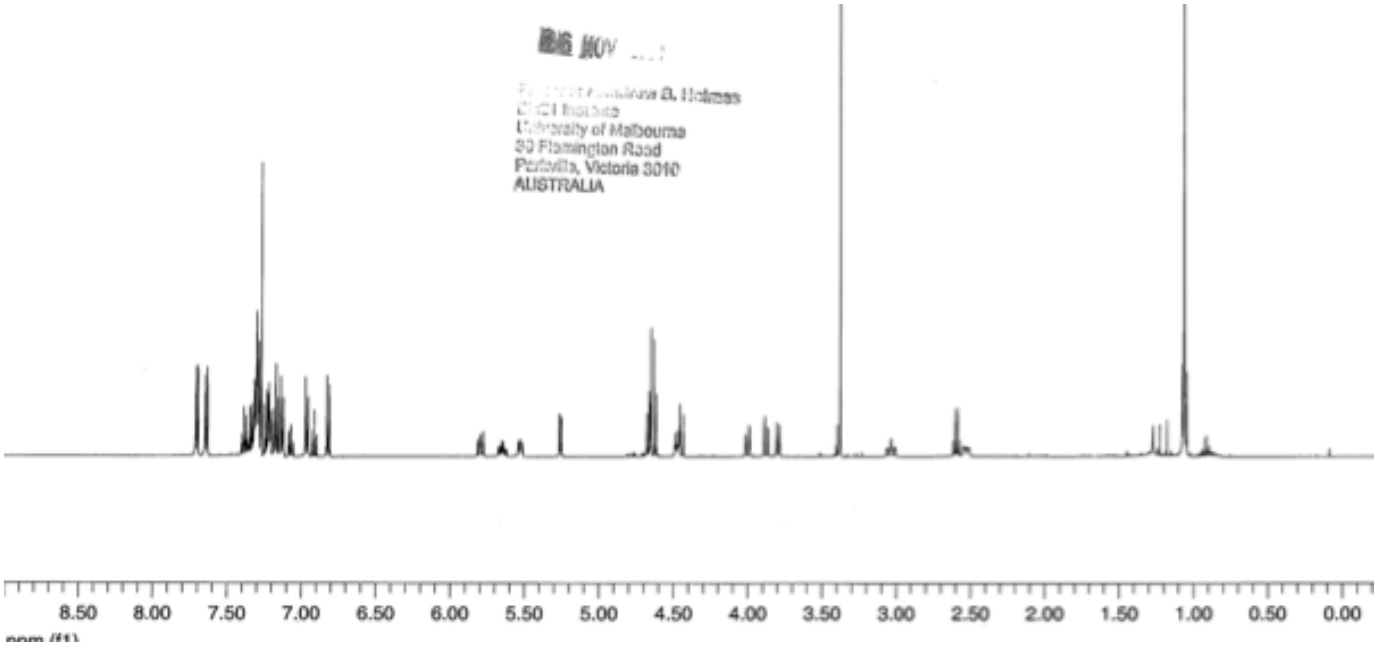


^{13}C NMR (125 MHz, $CDCl_3$)

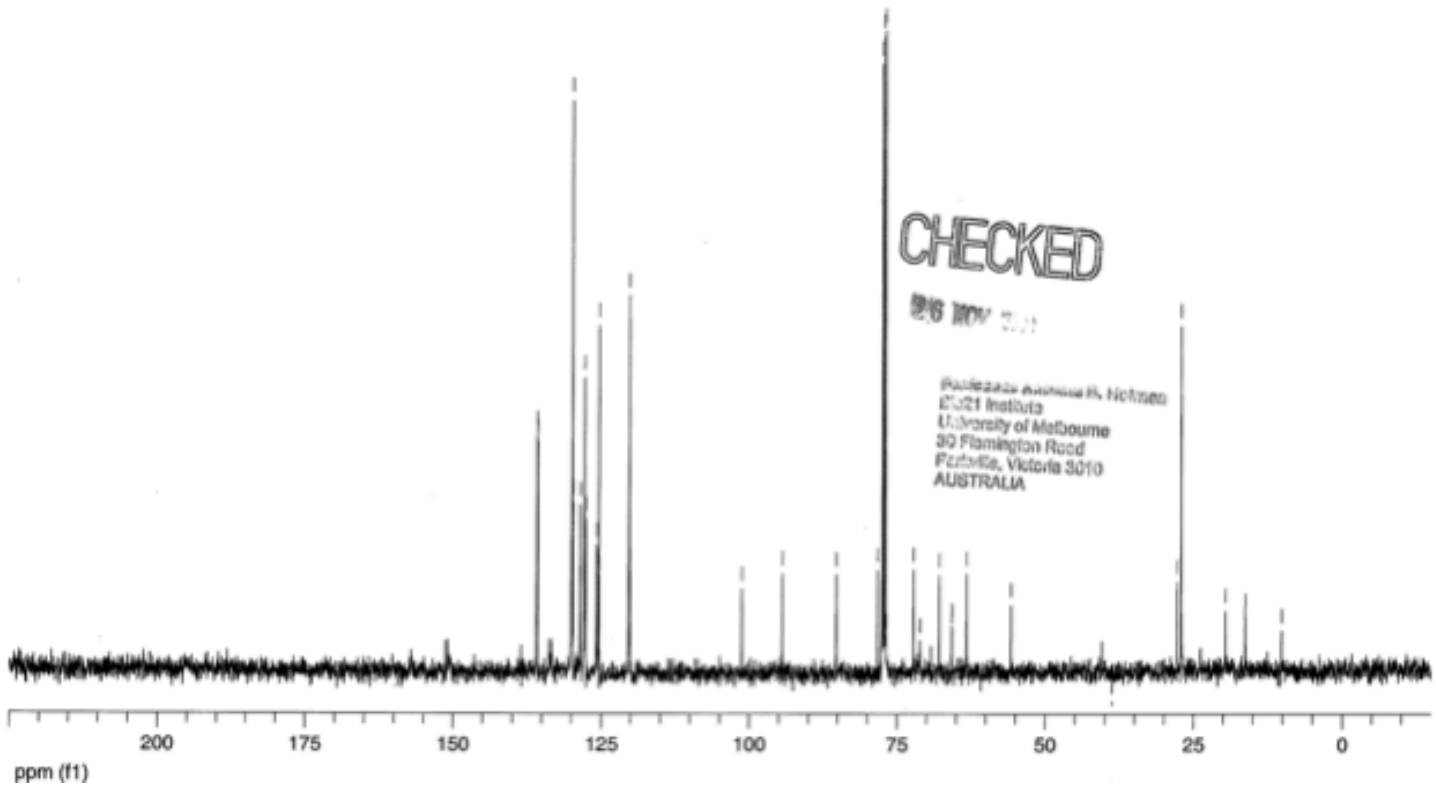


(2E,4R,5Z,8S,9R)-8-(Benzyloxy)-9-((tert-butyldiphenylsilyloxy)methyl)-4-(methoxymethoxy)-4,7,8,9-tetrahydrooxonin-2-yl diphenyl phosphate (28)

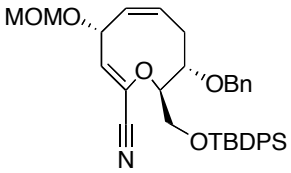
^{1}H NMR (500 MHz, $CDCl_3$)



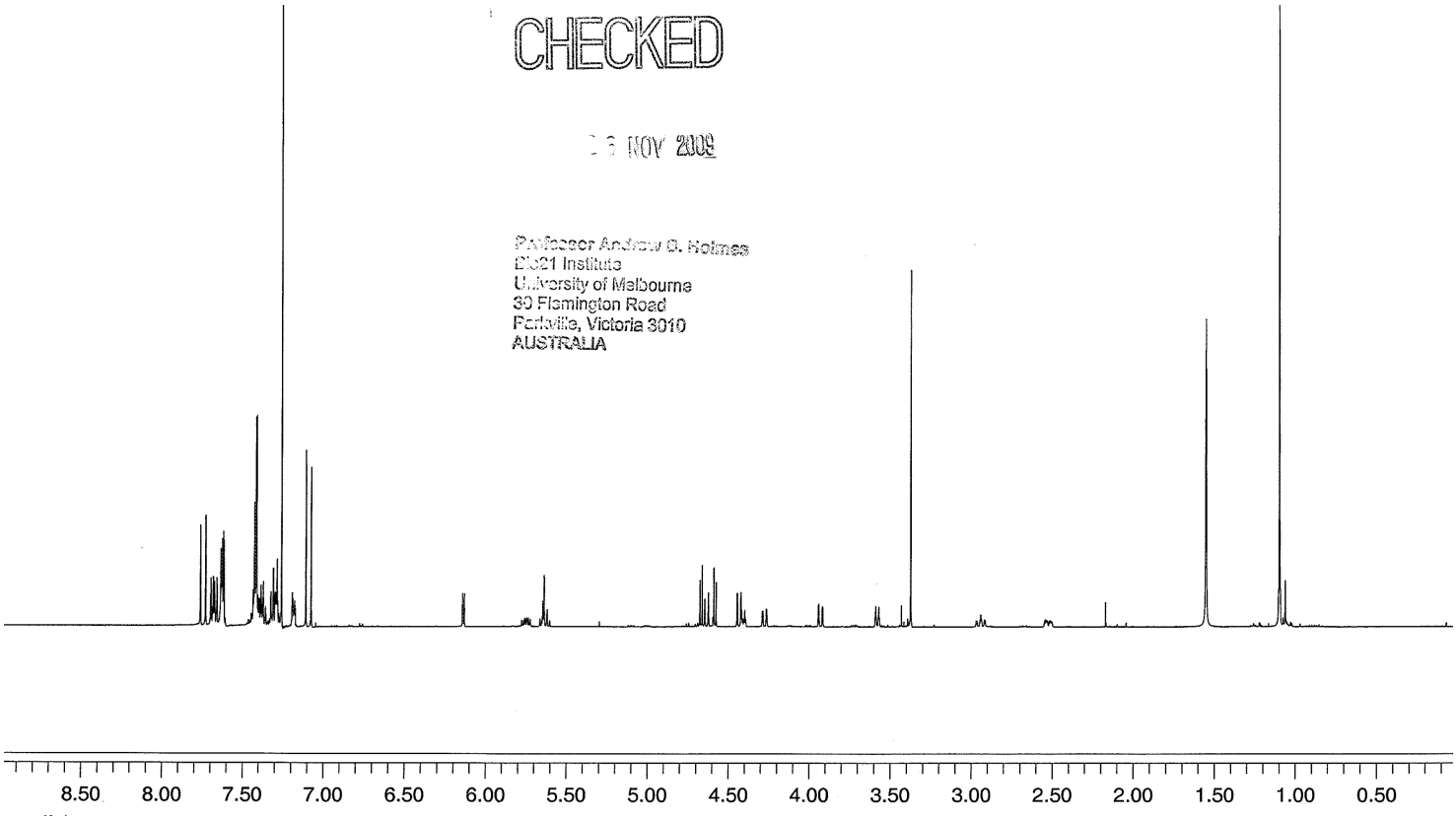
^{13}C NMR (125 MHz, $CDCl_3$)



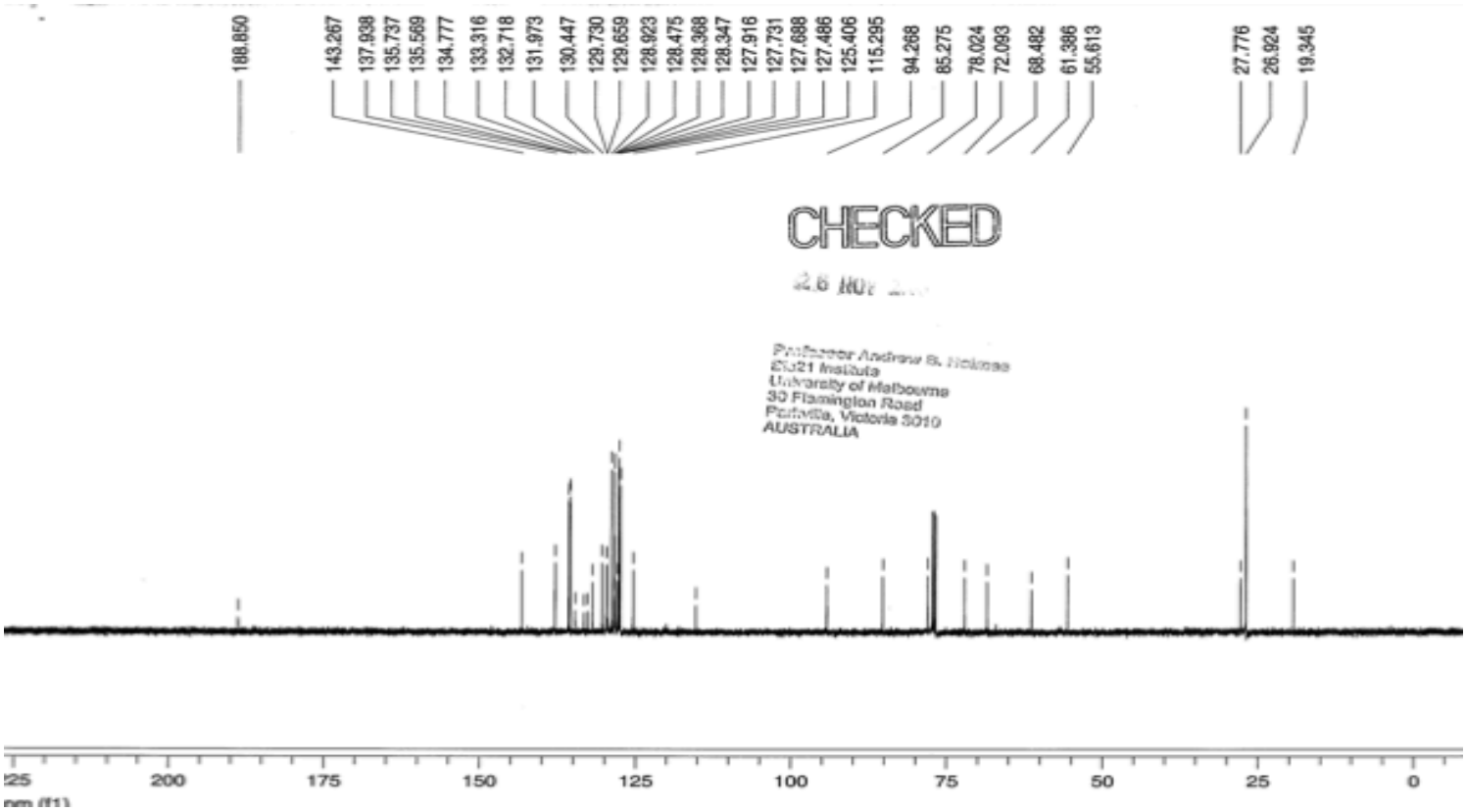
(2Z,4R,5Z,8S,9R)-8-(Benzyloxy)-9-((tert-butyldiphenylsilyloxy)methyl)-4-(methoxymethoxy)-4,7,8,9-tetrahydrooxonine-2-carbonitrile (29)

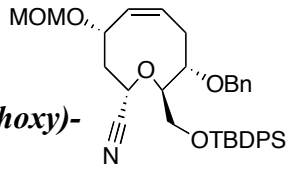


^{1}H NMR (500 MHz, $CDCl_3$)



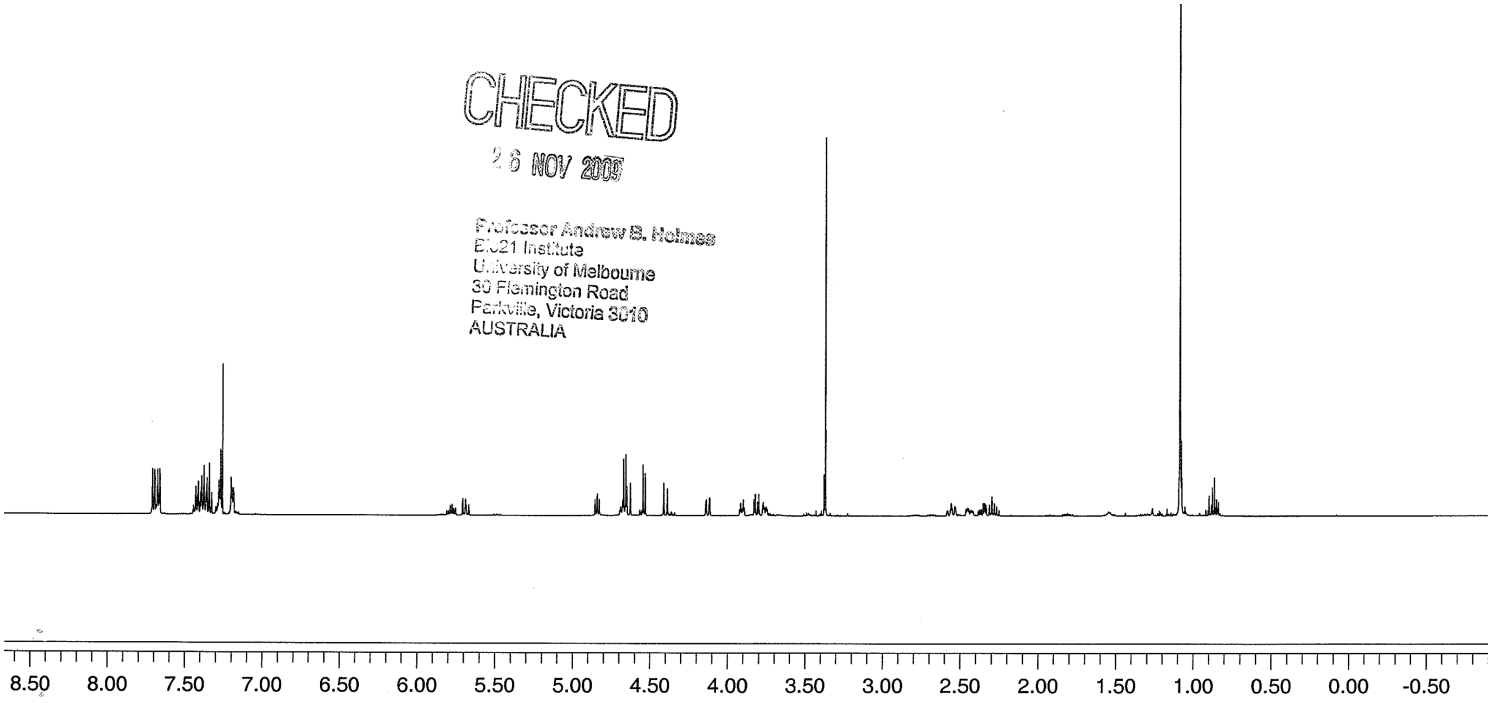
^{13}C NMR (125 MHz, $CDCl_3$)



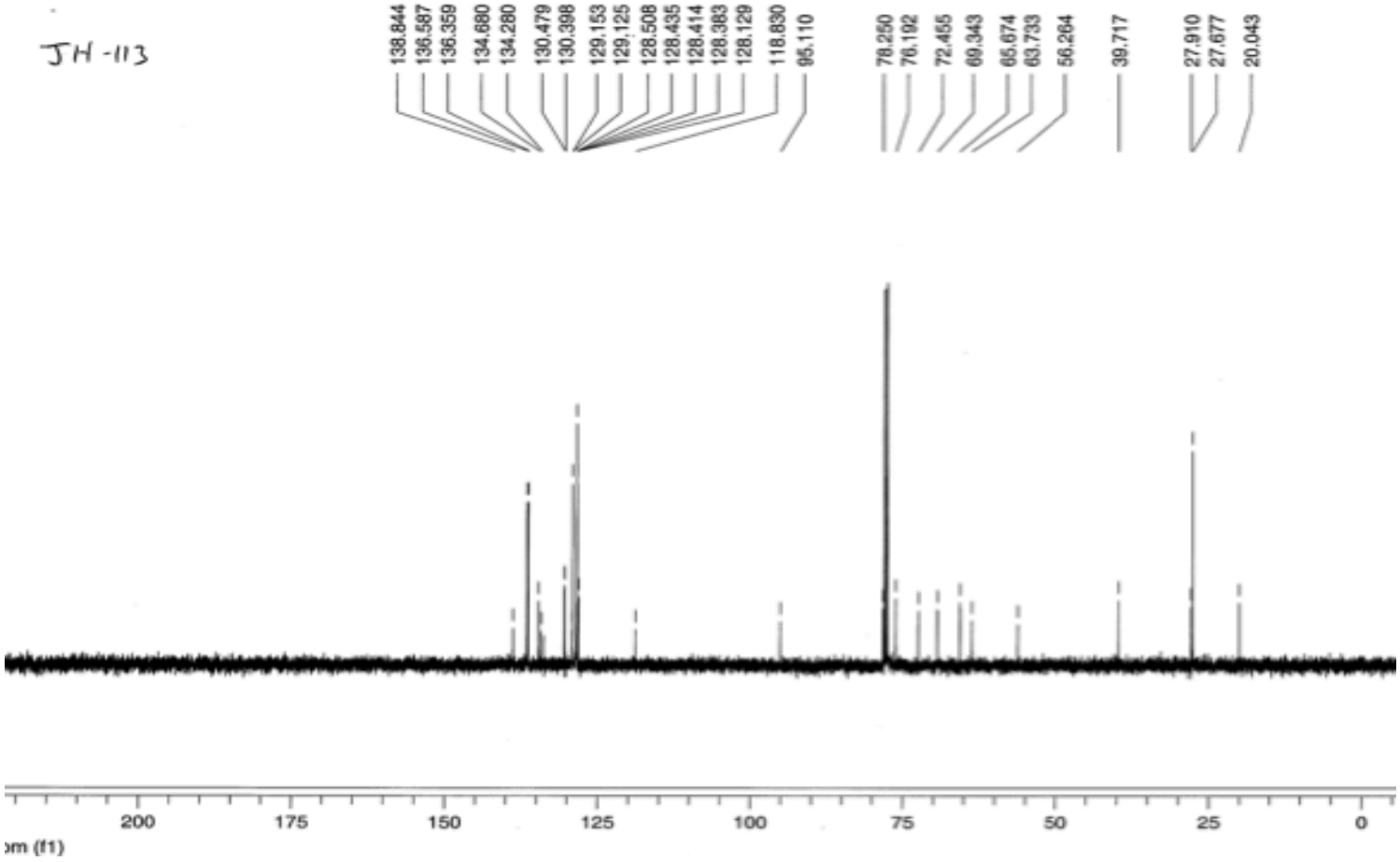


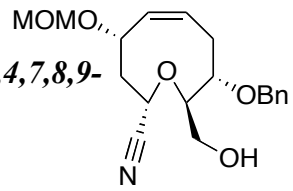
(2S,4S,8S,9R,Z)-8-(Benzyloxy)-9-((tert-butyldiphenylsilyloxy)methyl)-4-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonine-2-carbonitrile (30)

^{1}H NMR (500 MHz, $CDCl_3$)



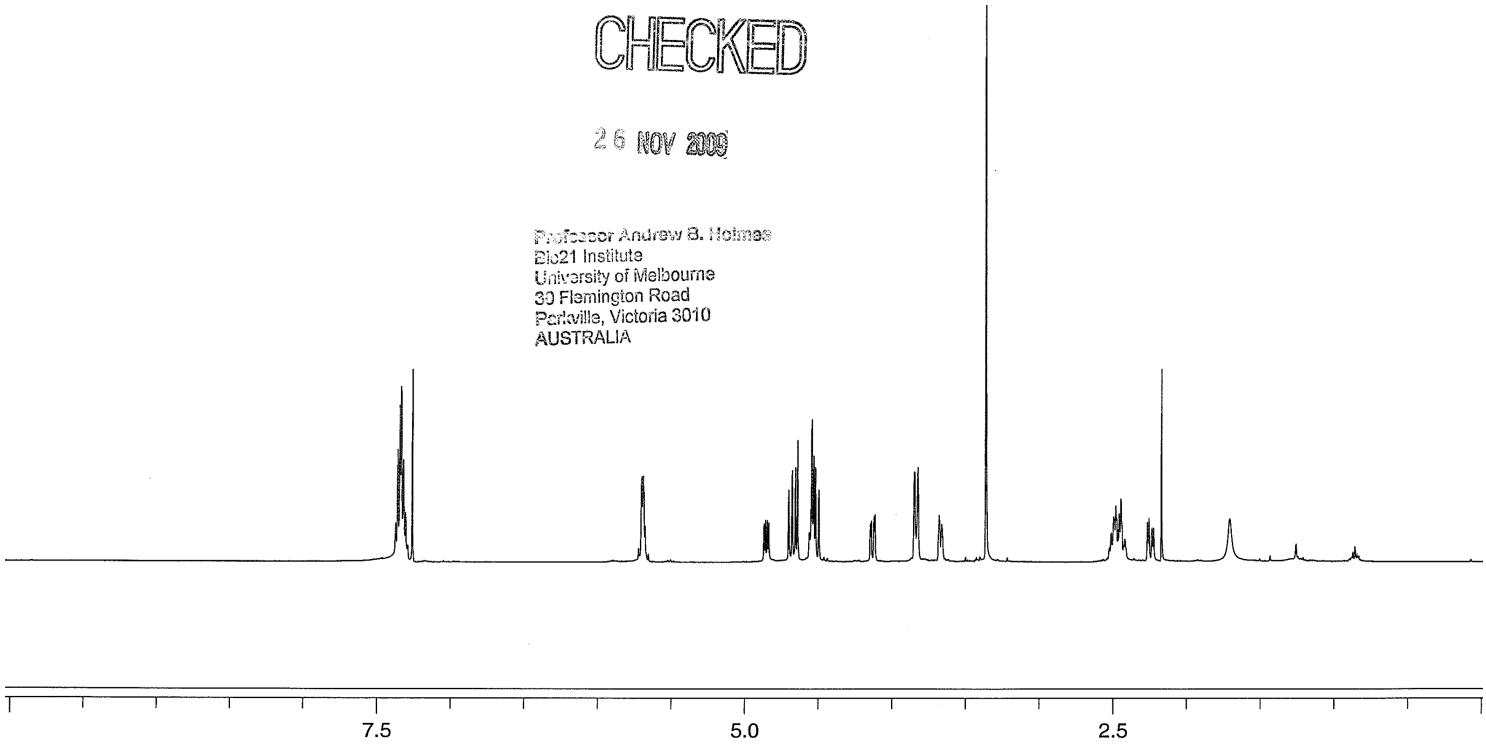
^{13}C NMR (125 MHz, $CDCl_3$)



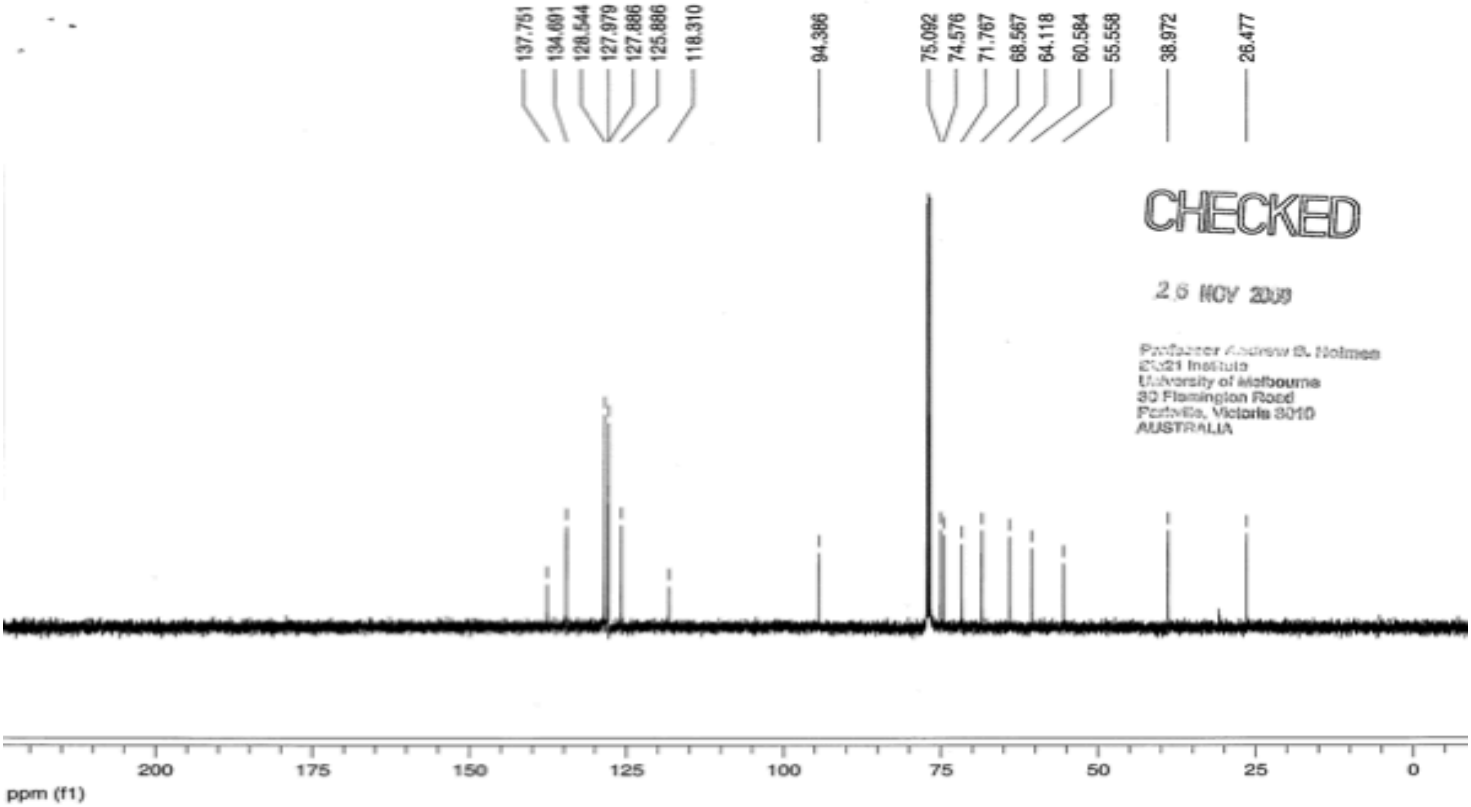


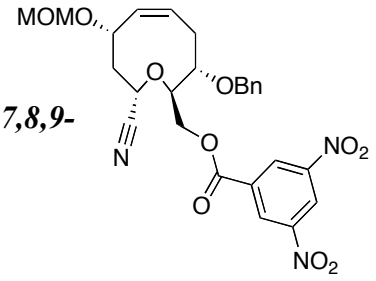
(2S,4S,8S,9R,Z)-8-(Benzyloxy)-9-(hydroxymethyl)-4-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonine-2-carbonitrile (30a)

^{1}H NMR (500 MHz, $CDCl_3$)



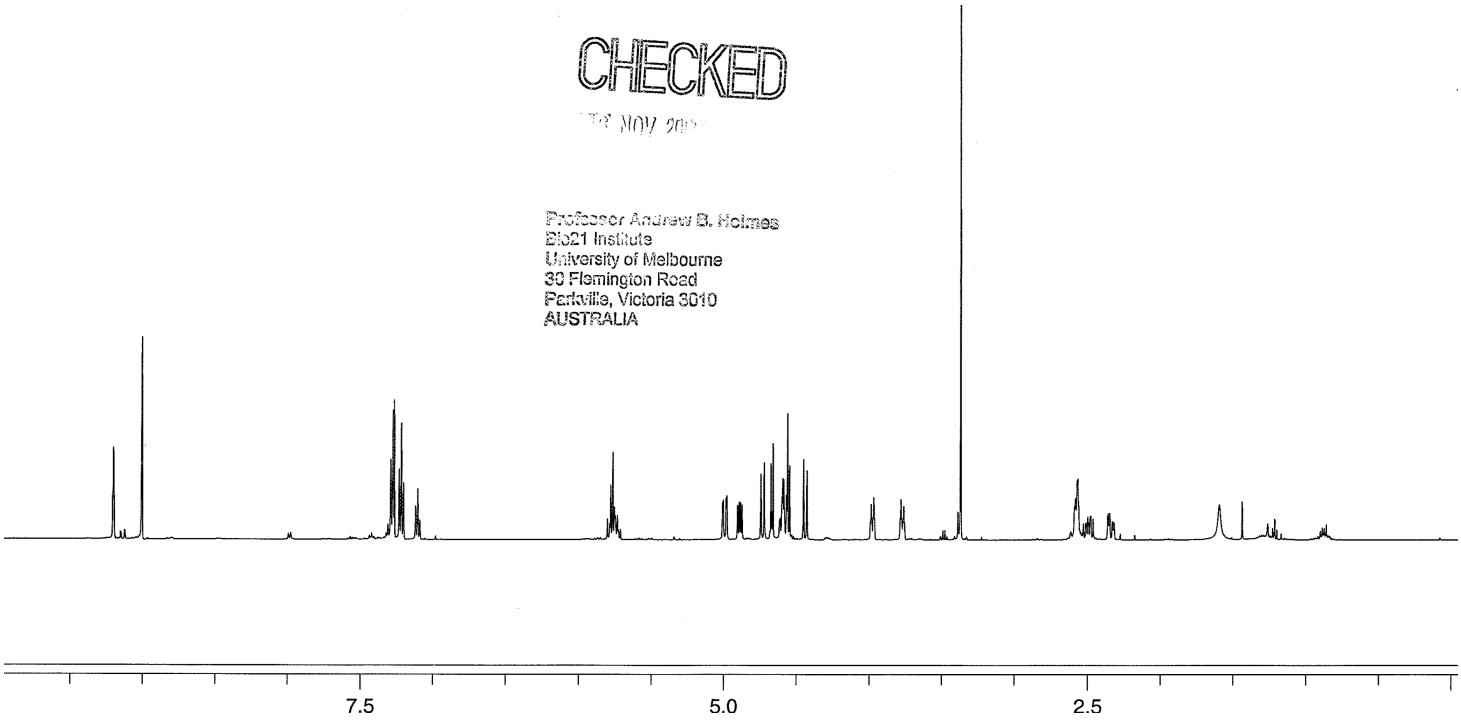
^{13}C NMR (125 MHz, $CDCl_3$)



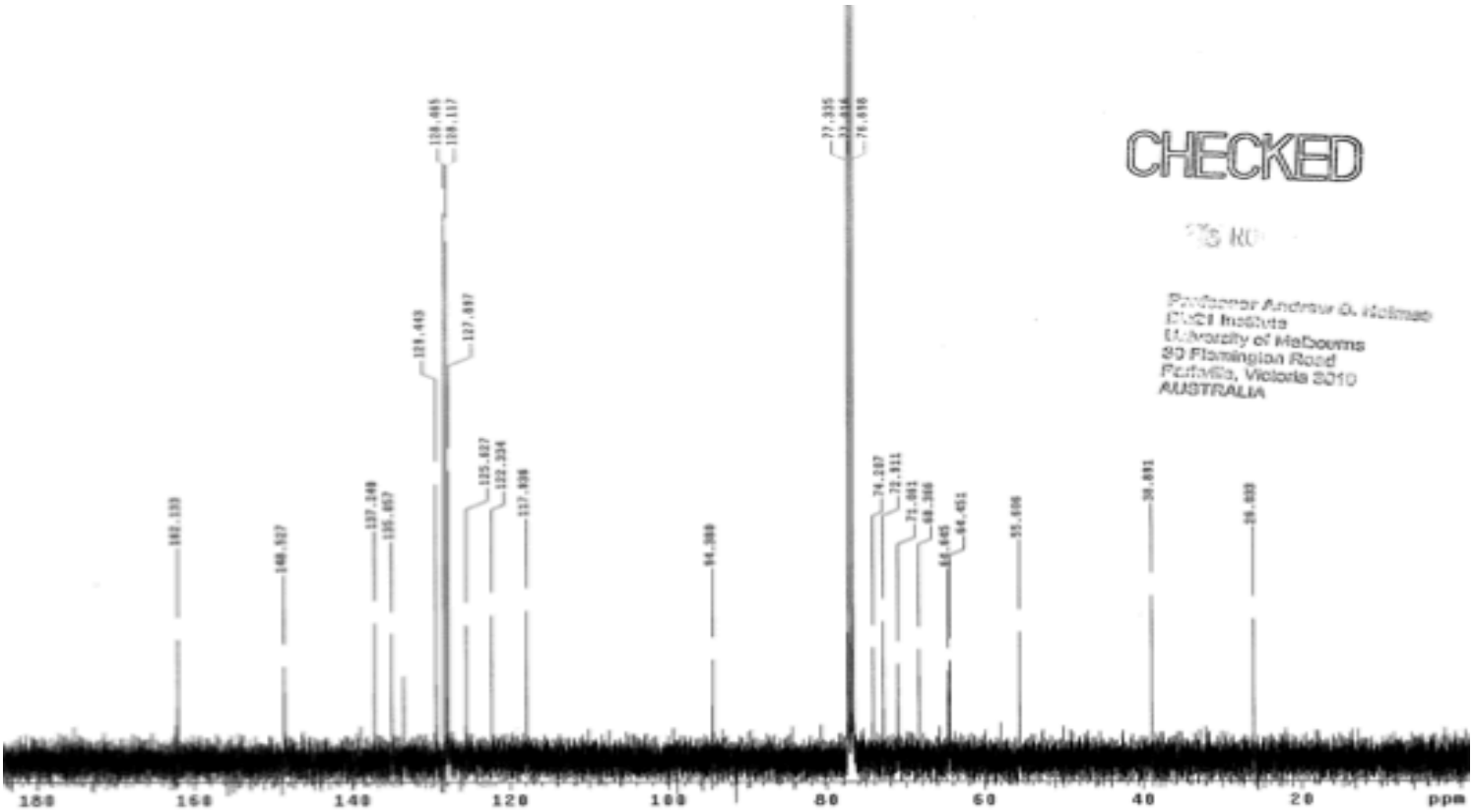


((2R,3S,7S,9S,Z)-3-(Benzyloxy)-9-cyano-7-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonin-2-yl)methyl 3,5-dinitrobenzoate (30b)

^{1}H NMR (500 MHz, $CDCl_3$)

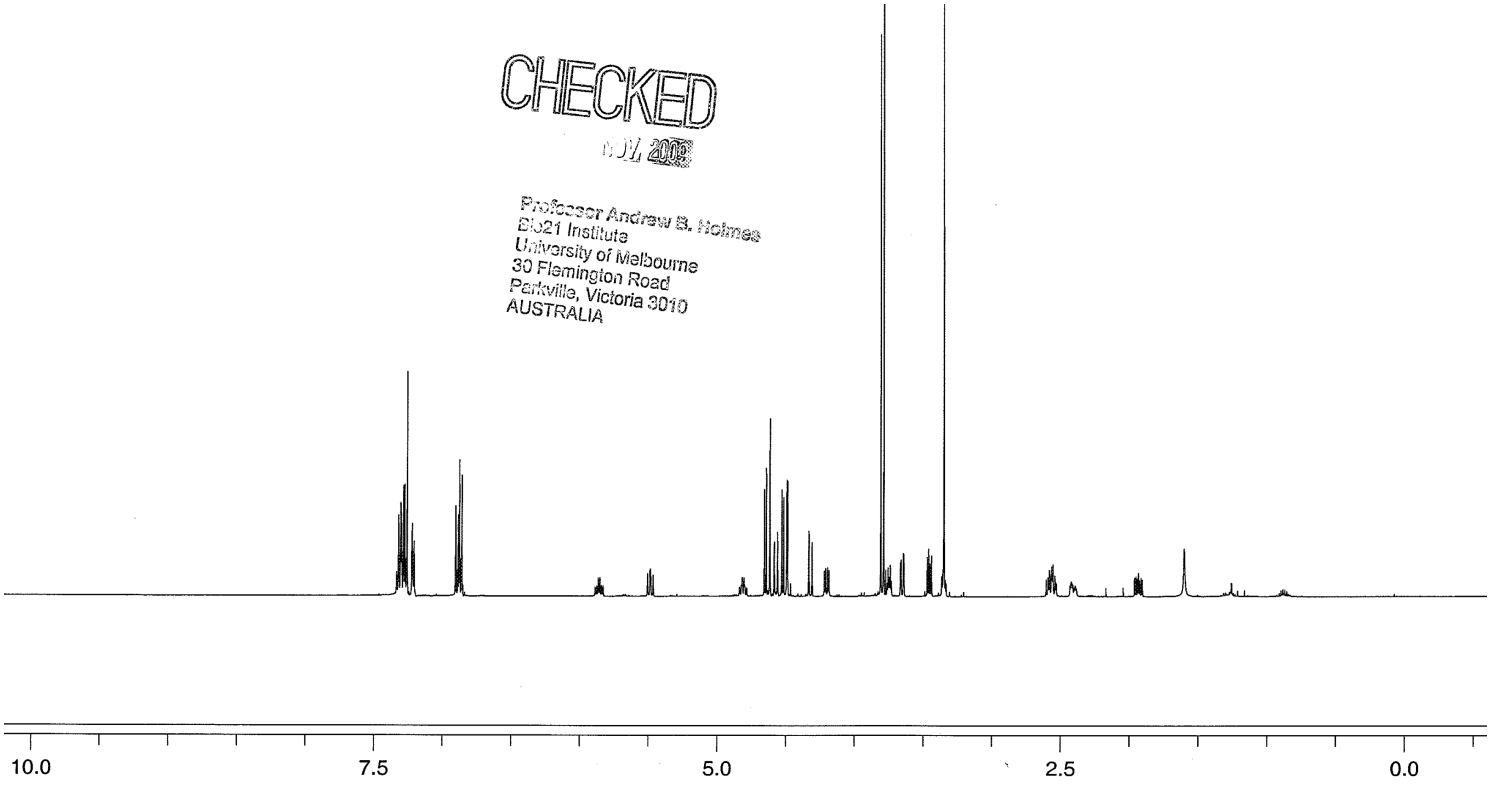


^{13}C NMR (125 MHz, $CDCl_3$)

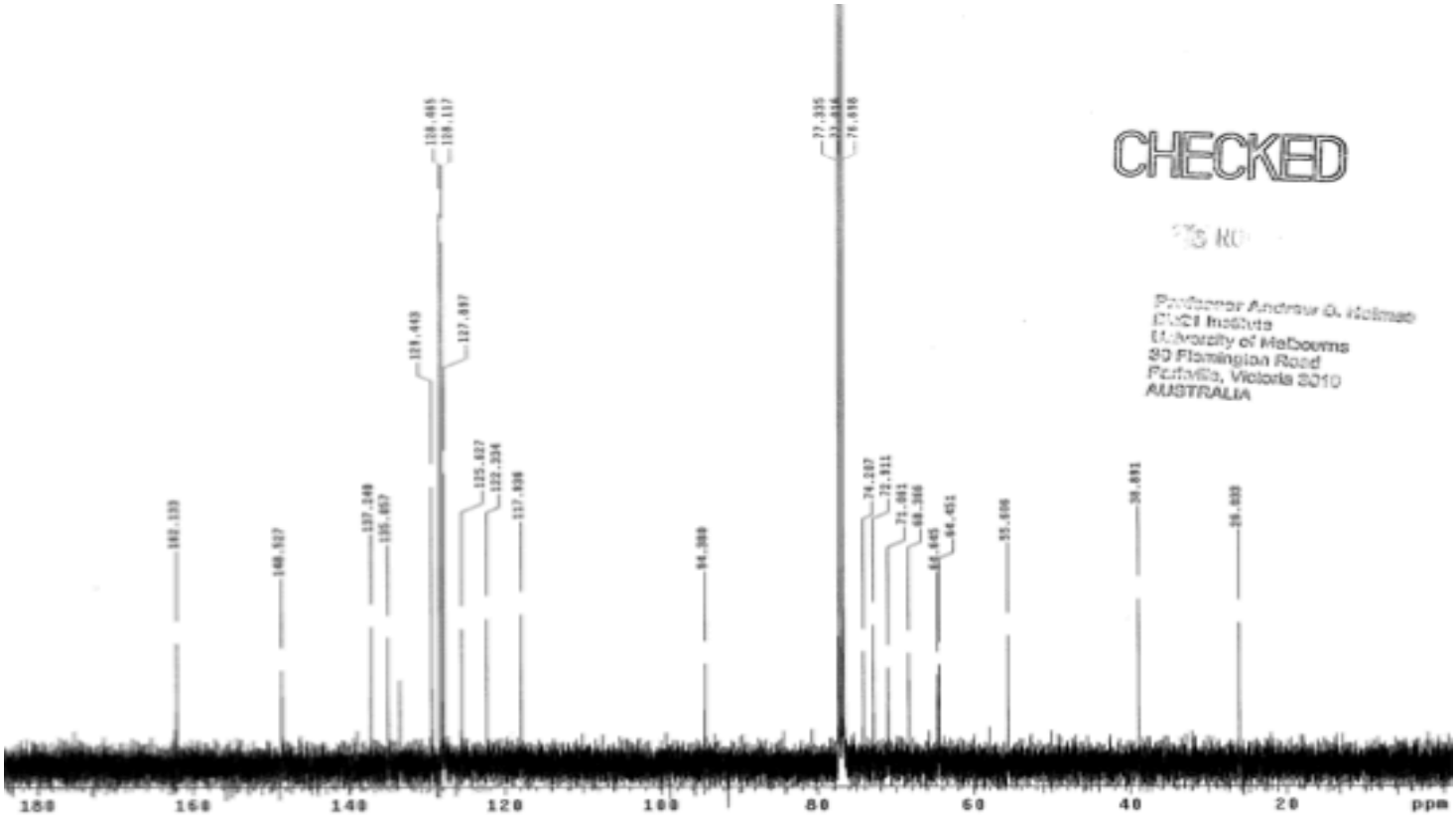


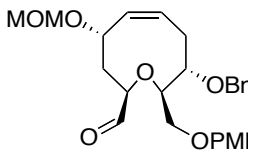
(2R,4S,8S,9R,Z)-8-(Benzyloxy)-9-((4-methoxybenzyloxy)methyl)-4-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonine-2-carbonitrile (32)

^{1}H NMR (500 MHz, $CDCl_3$)



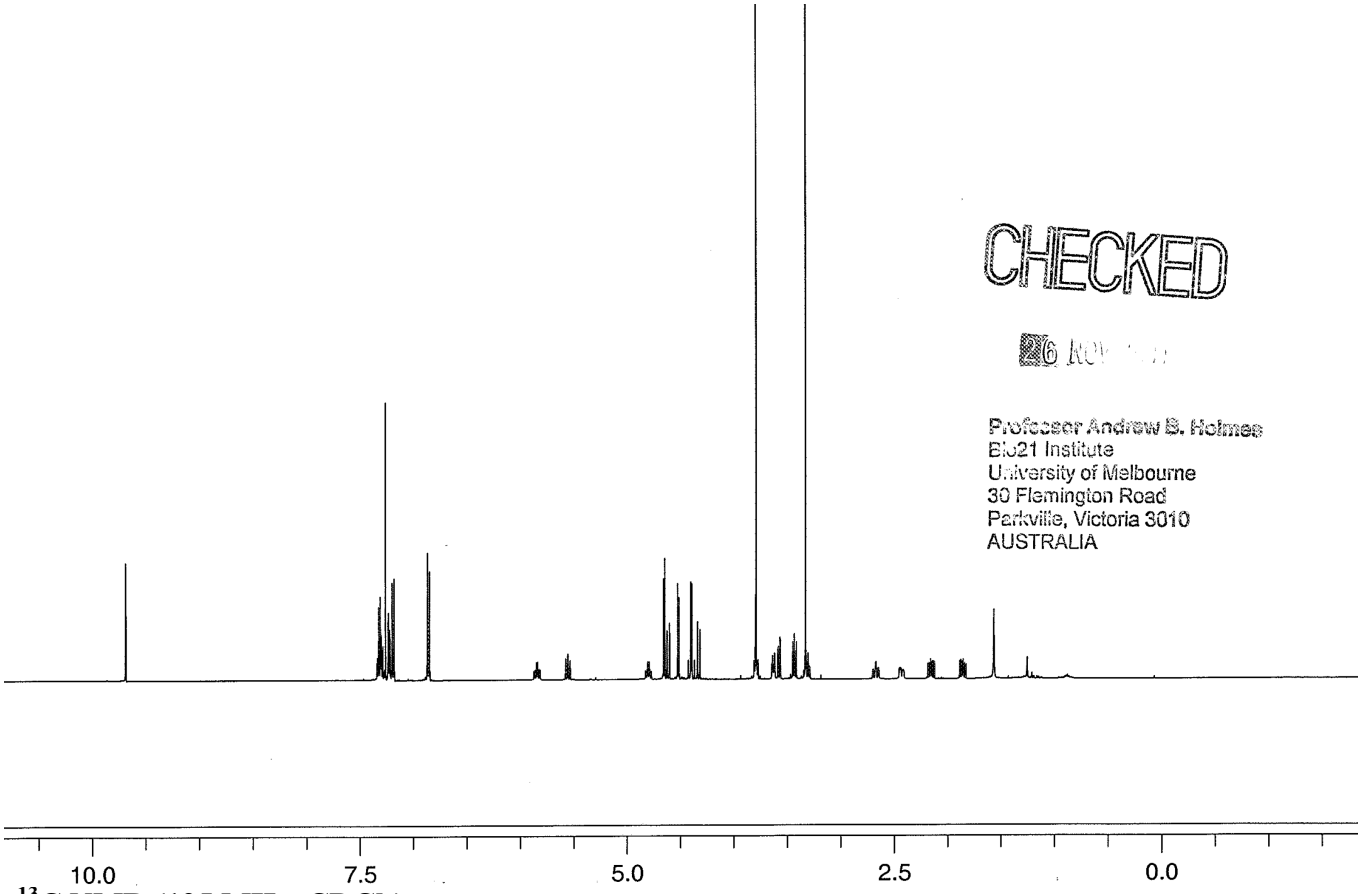
^{13}C NMR (125 MHz, $CDCl_3$)



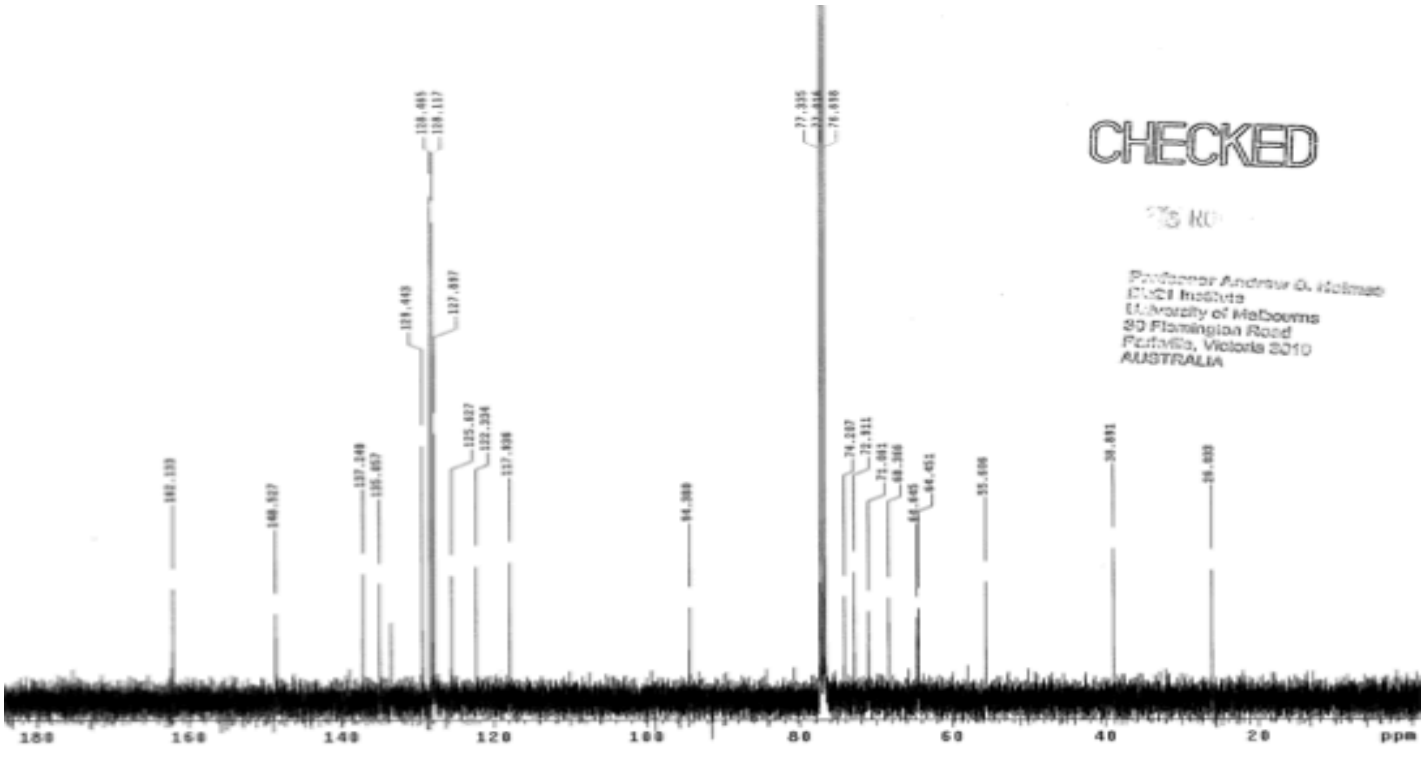


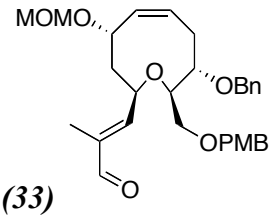
(2S,4S,8S,9R,Z)-8-(Benzyloxy)-9-((4-methoxybenzyloxy)methyl)-4-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonine-2-carbaldehyde (32a)

^{1}H NMR (500 MHz, $CDCl_3$)



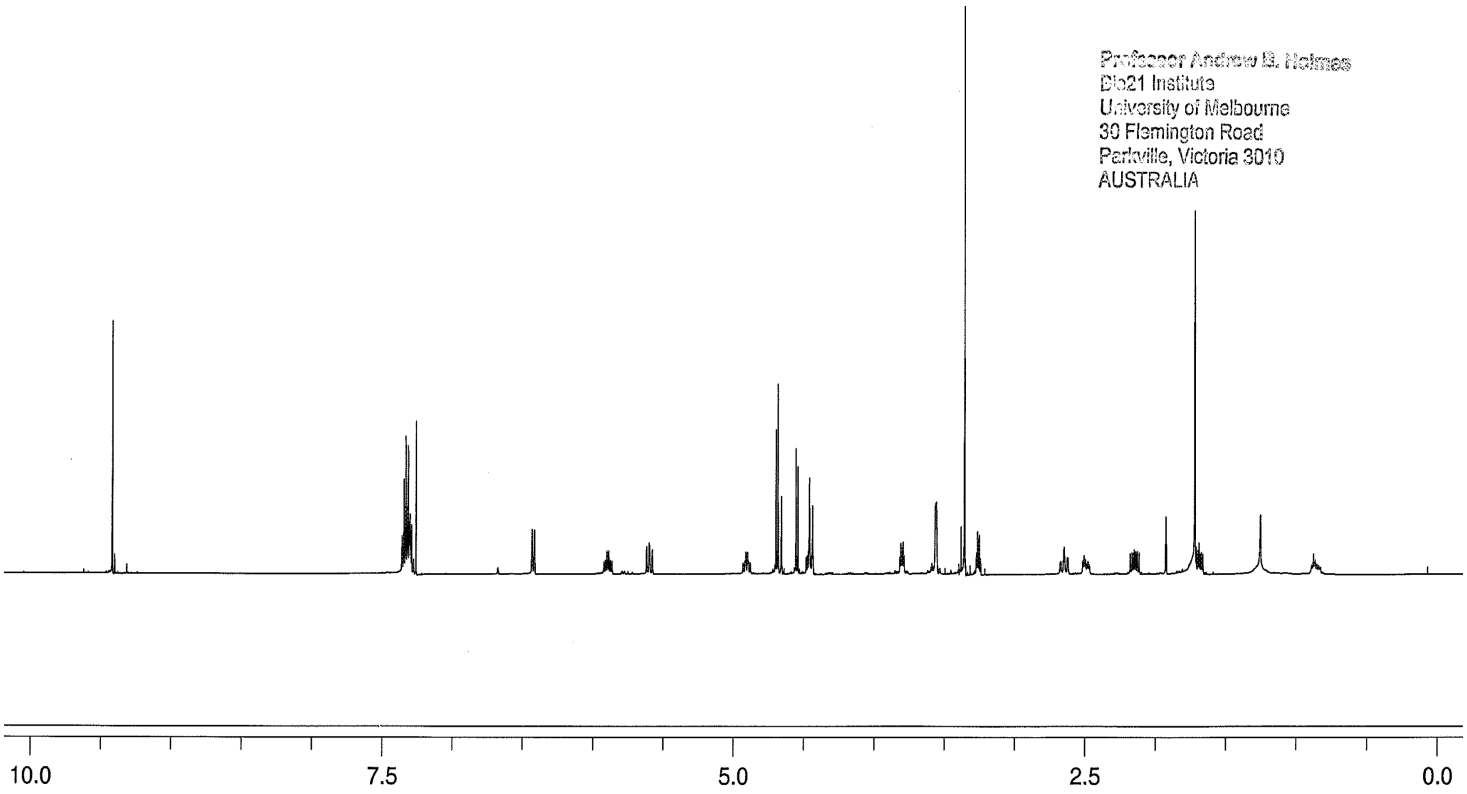
^{13}C NMR (125 MHz, $CDCl_3$)



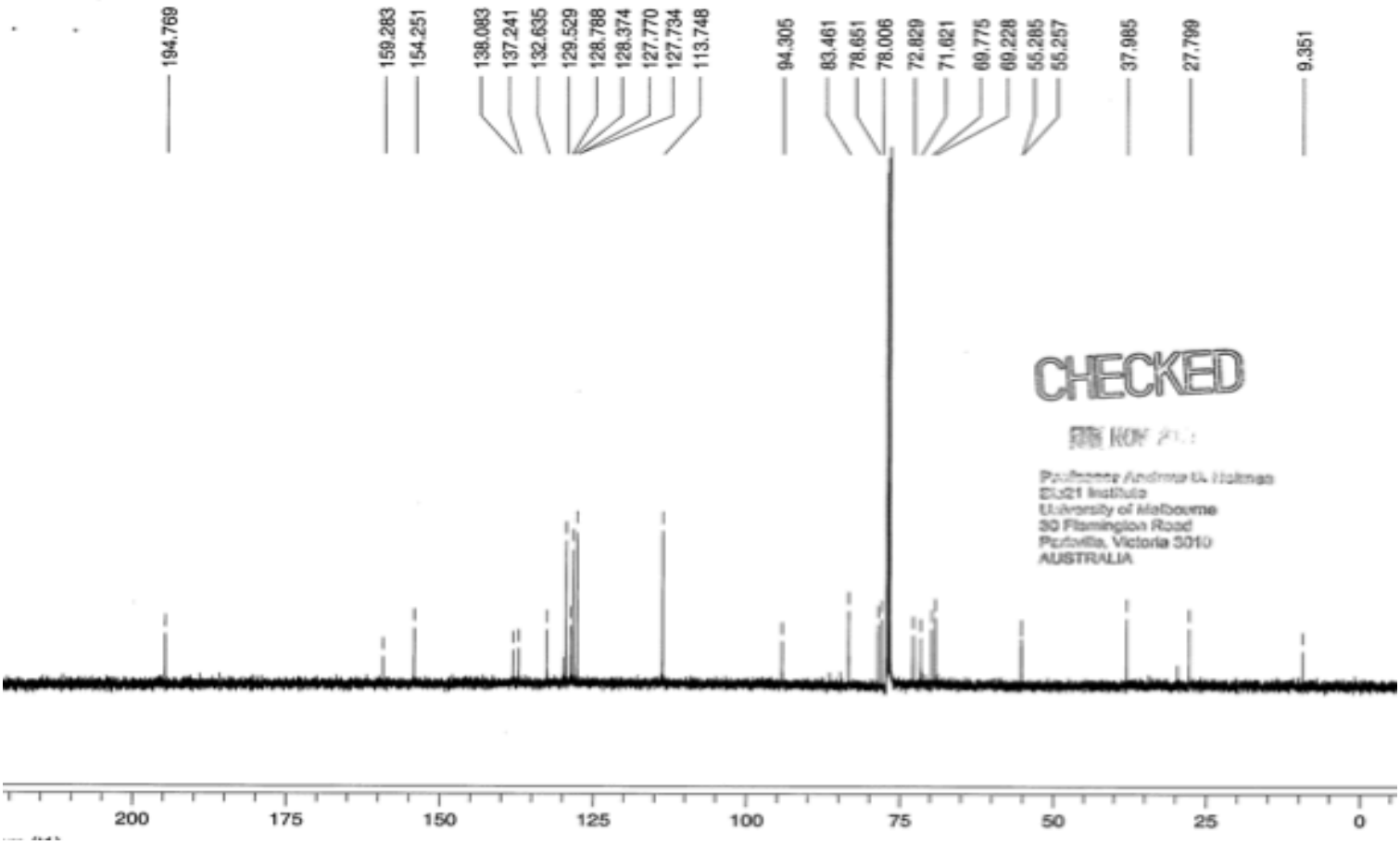


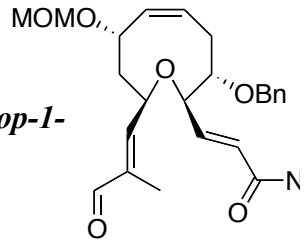
(E)-3-((2R,4S,8S,9R,Z)-8-(Benzyloxy)-9-((4-methoxybenzyloxy)methyl)-4-(methoxymethoxy)-2,3,4,7,8,9-hexahydrooxonin-2-yl)-2-methylacrylaldehyde (33)

^{1}H NMR (500 MHz, $CDCl_3$)



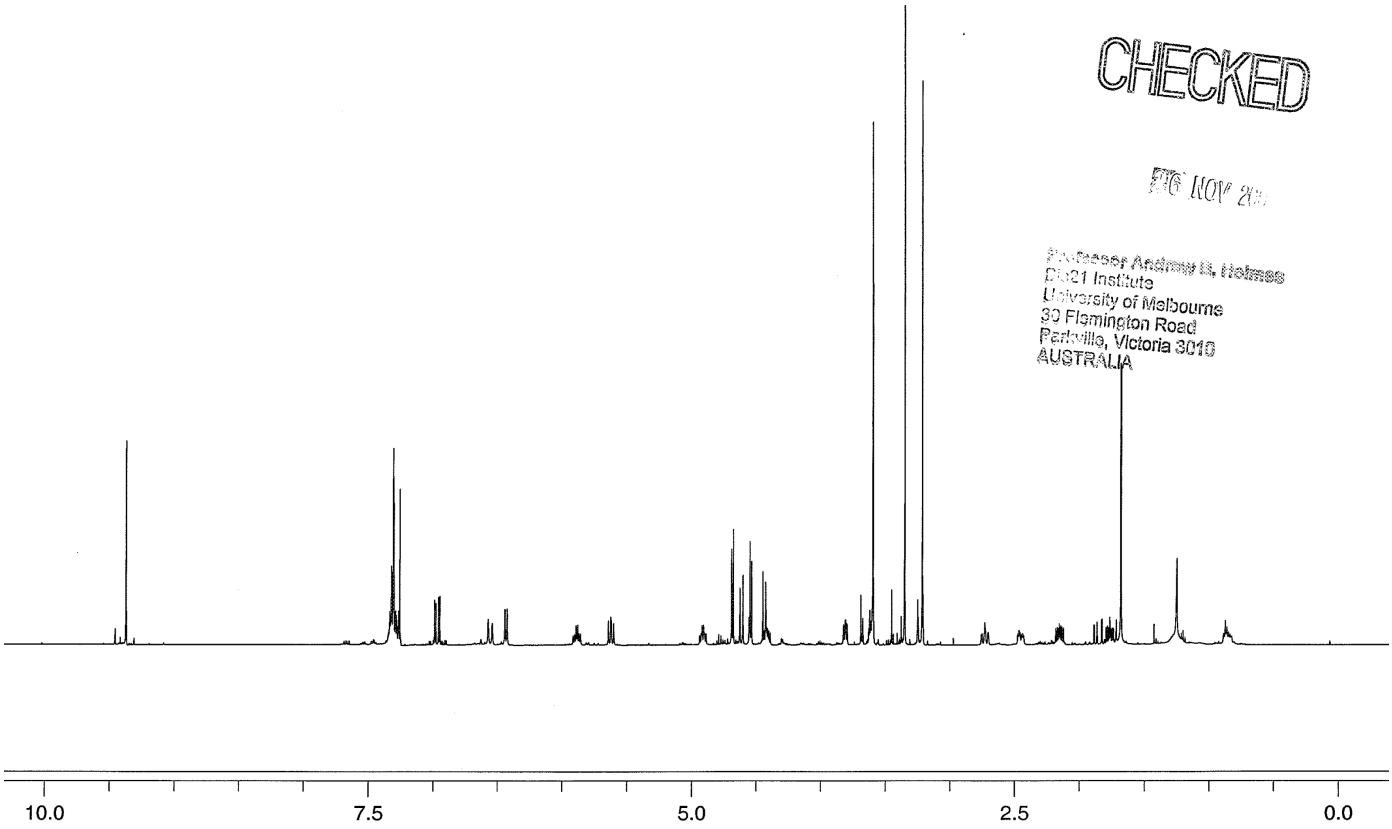
^{13}C NMR (125 MHz, $CDCl_3$)



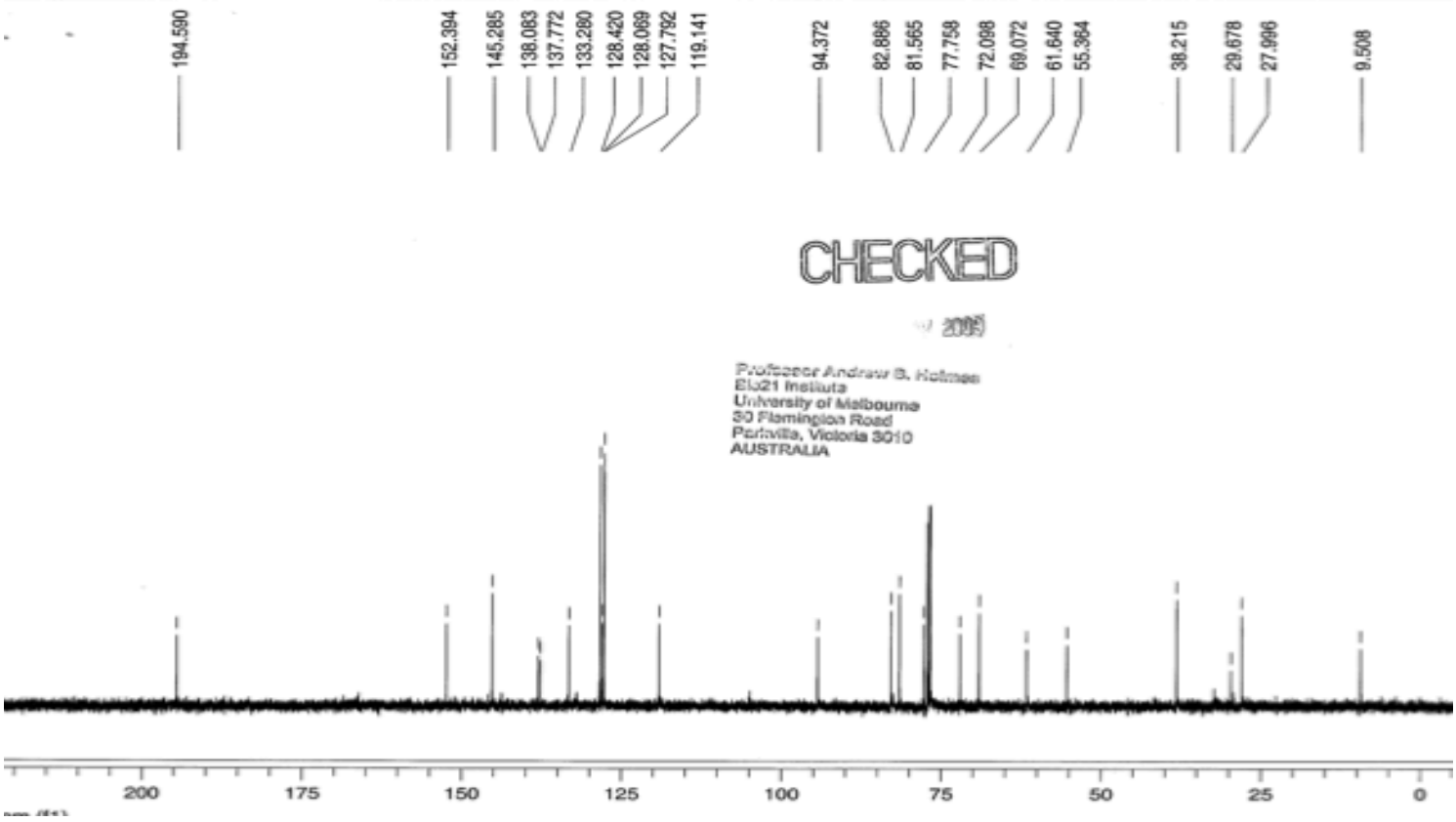


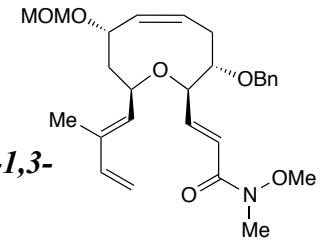
(E)-3-((2R,3S,7S,9R,Z)-3-(Benzyloxy)-7-(methoxymethoxy)-9-((E)-2-methyl-3-oxoprop-1-enyl)-2,3,4,7,8,9-hexahydrooxonin-2-yl)-N-methoxy-N-methylacrylamide (34)

^{1}H NMR (500 MHz, $CDCl_3$)



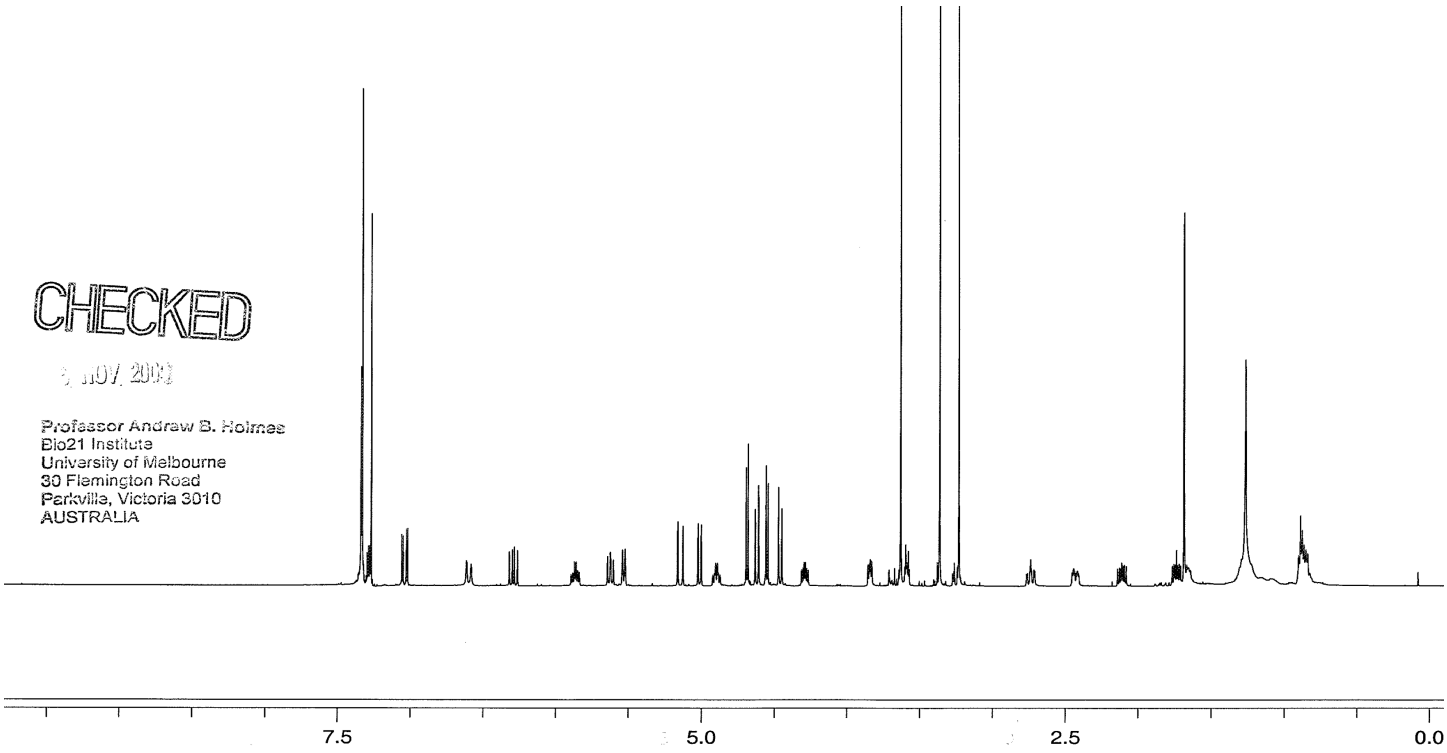
^{13}C NMR (125 MHz, $CDCl_3$)



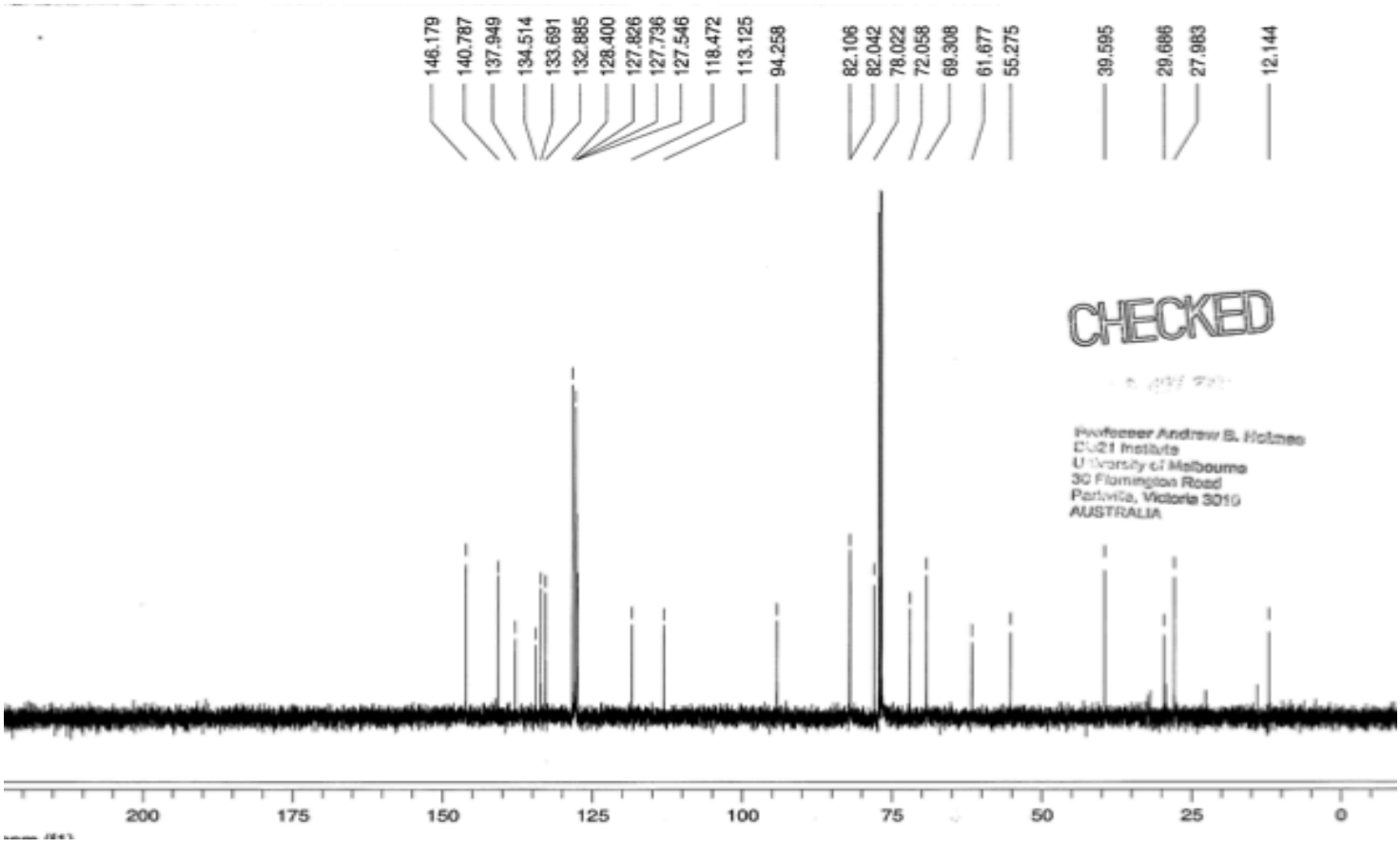


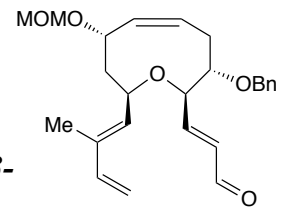
(E)-3-((2R,3S,7S,9R,Z)-3-(Benzyloxy)-7-(methoxymethoxy)-9-((E)-2-methylbuta-1,3-dienyl)-2,3,4,7,8,9-hexahydrooxonin-2-yl)-N-methoxy-N-methylacrylamide (35)

^{1}H NMR (500 MHz, $CDCl_3$)



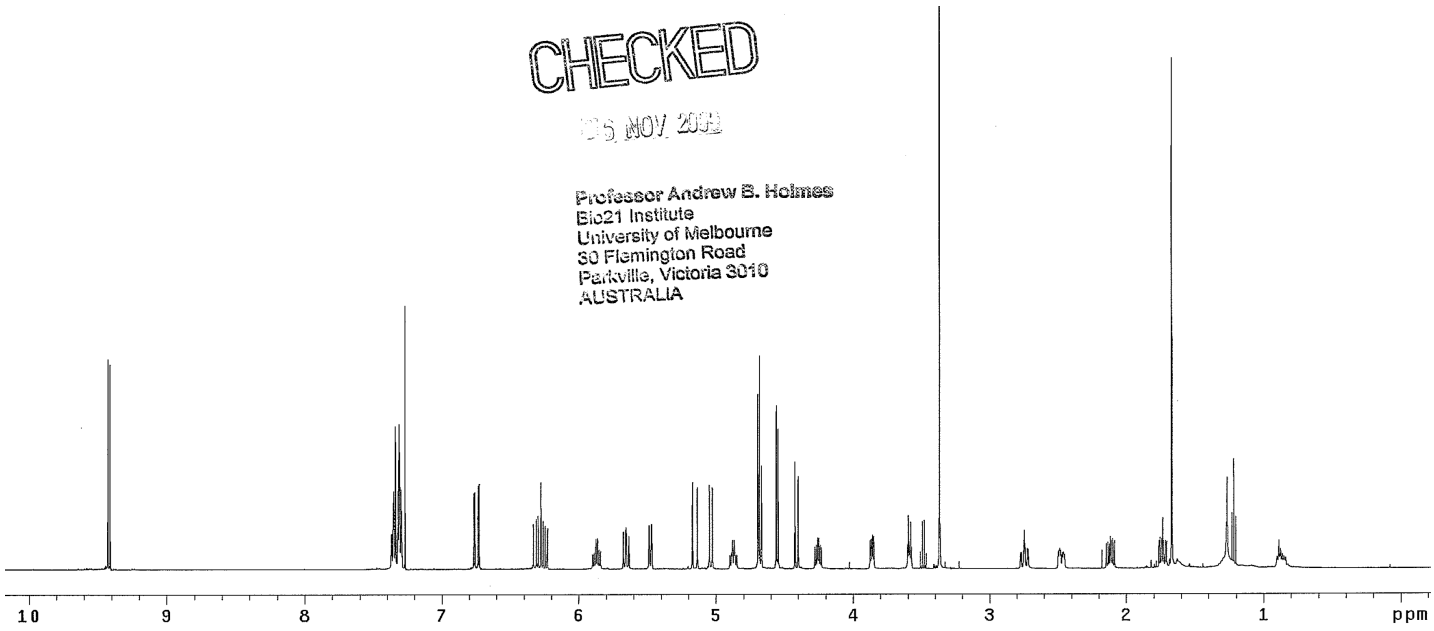
^{13}C NMR (125 MHz, $CDCl_3$)



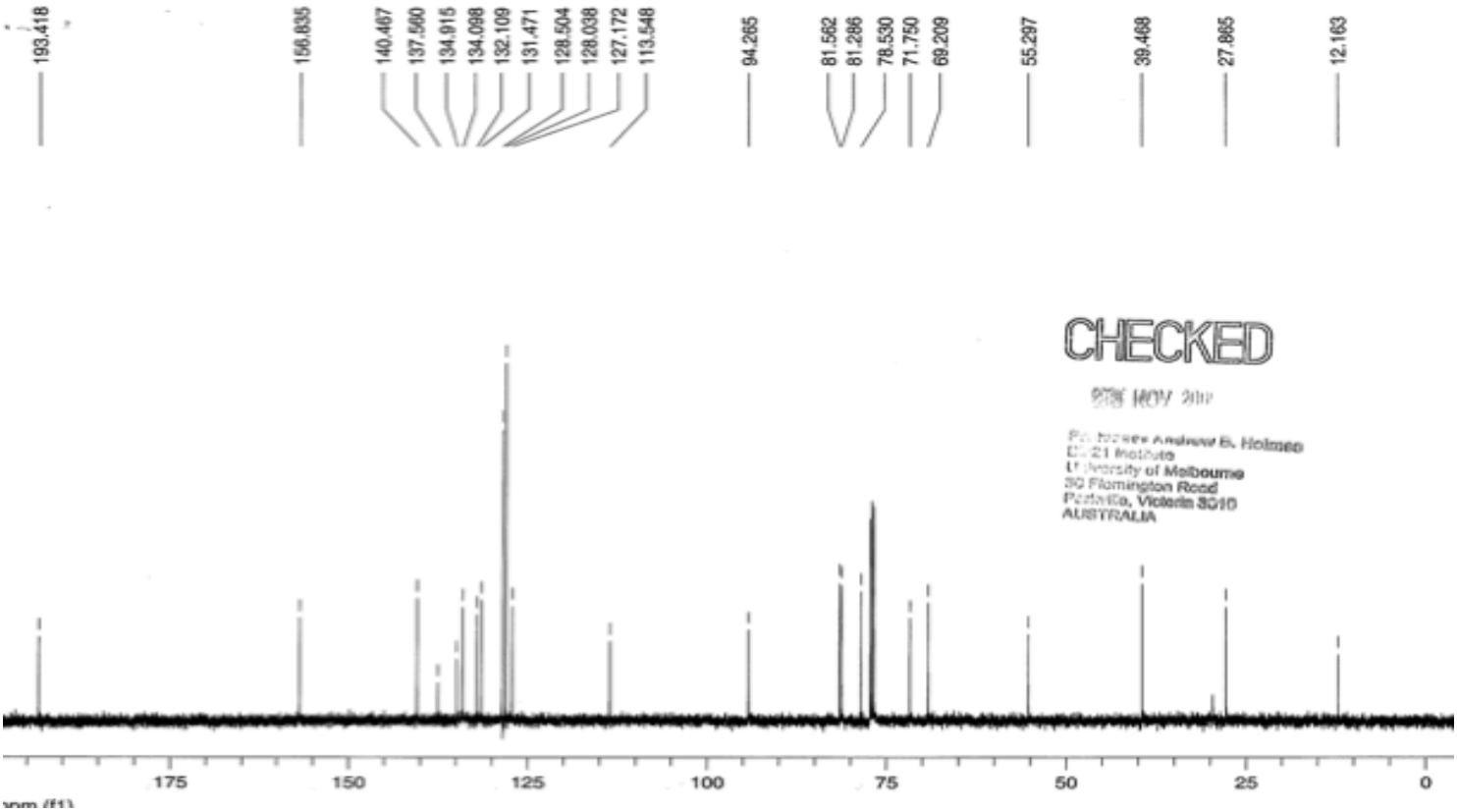


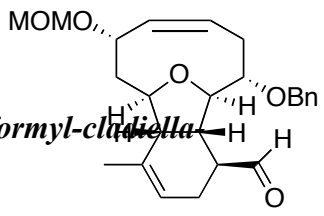
(E*)-3-((2*R*,3*S*,7*S*,9*R*,Z)-3-(Benzyloxy)-7-(methoxymethoxy)-9-((E)-2-methylbuta-1,3-dienyl)-2,3,4,7,8,9-hexahydrooxonin-2-yl)acrylaldehyde (36)*

^{1}H NMR (500 MHz, $CDCl_3$)



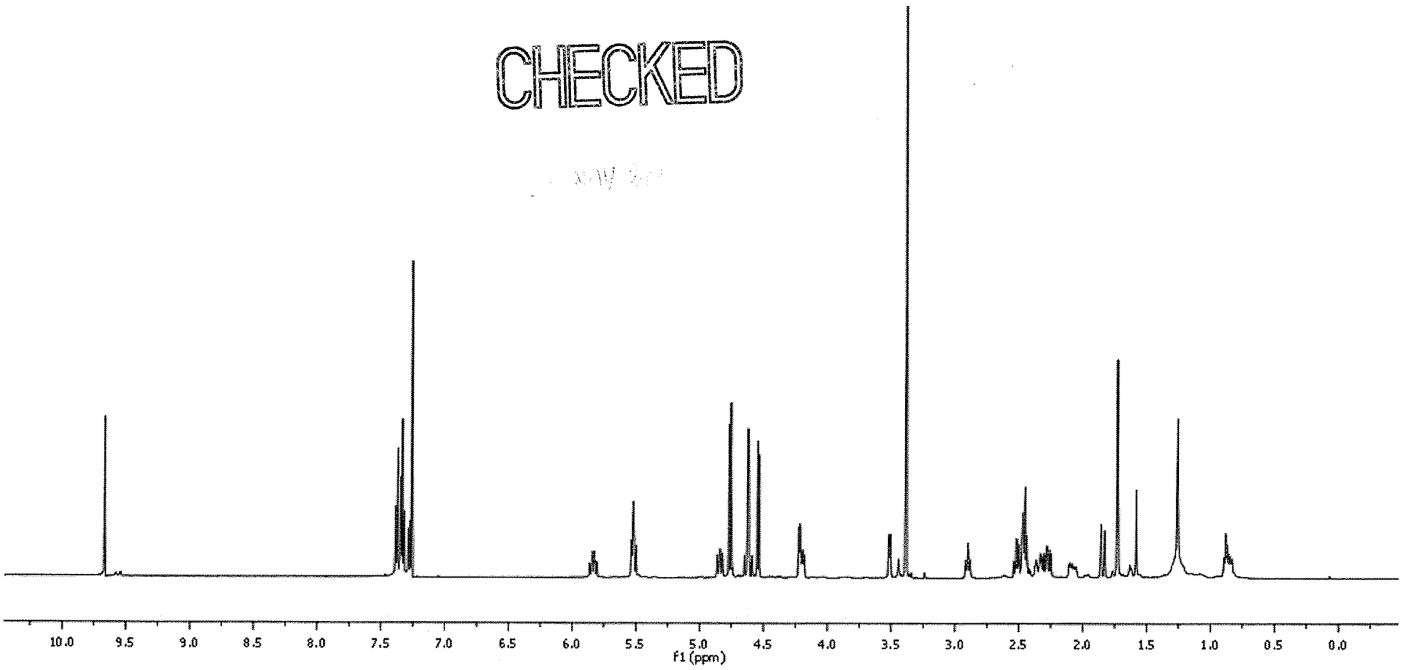
^{13}C NMR (125 MHz, $CDCl_3$)



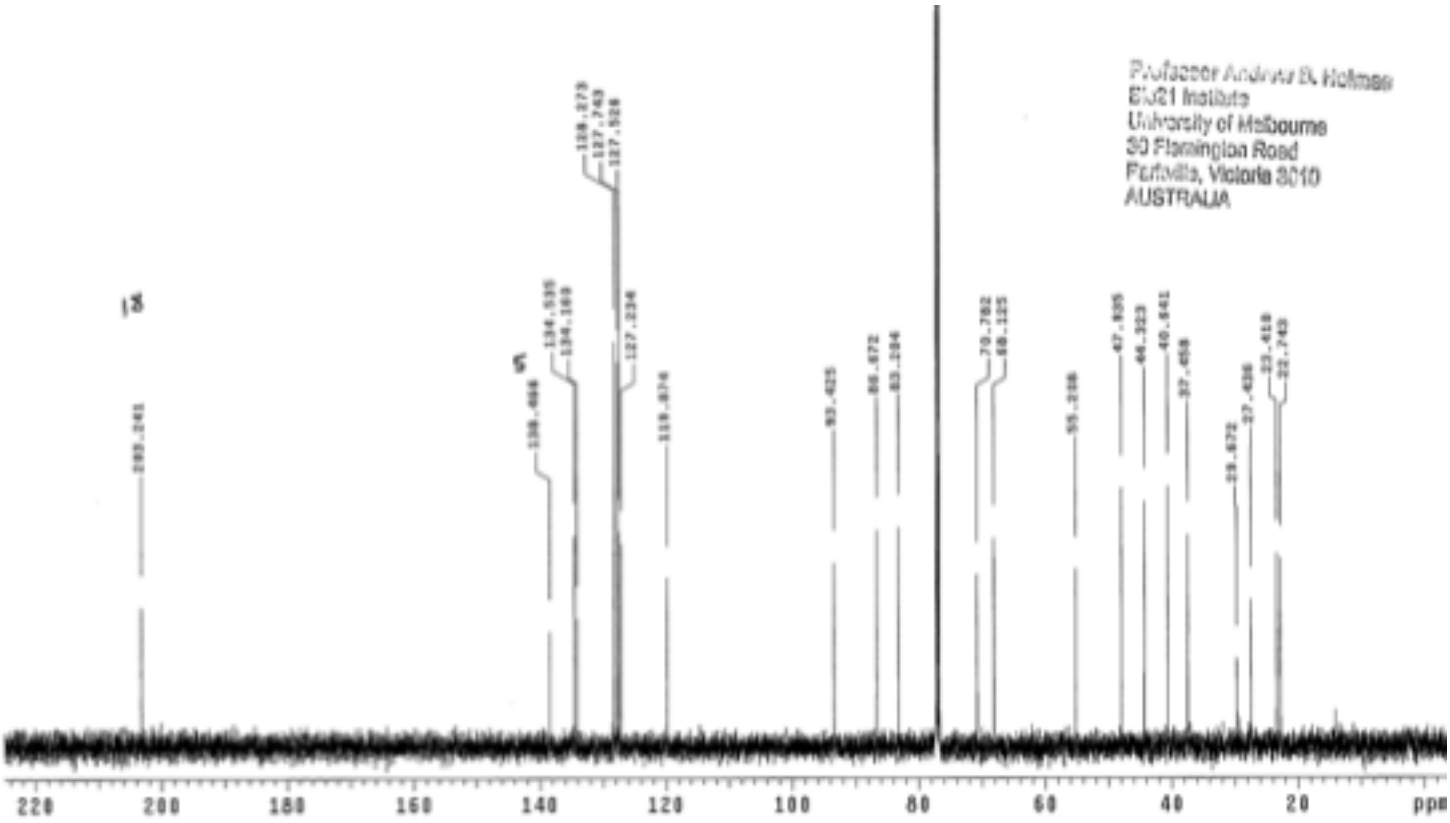


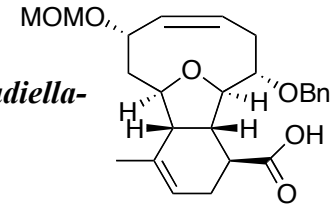
(*1*S,*2*R,*3*S,*5*Z,*7*S,*9*R,*10*R,*11*Z,*14*S)-*3-(Benzyloxy)-7-(methoxymethoxy)-14-formyl-cladiella-5(6),11(12)-diene (37)

^{1}H NMR (500 MHz, $CDCl_3$)



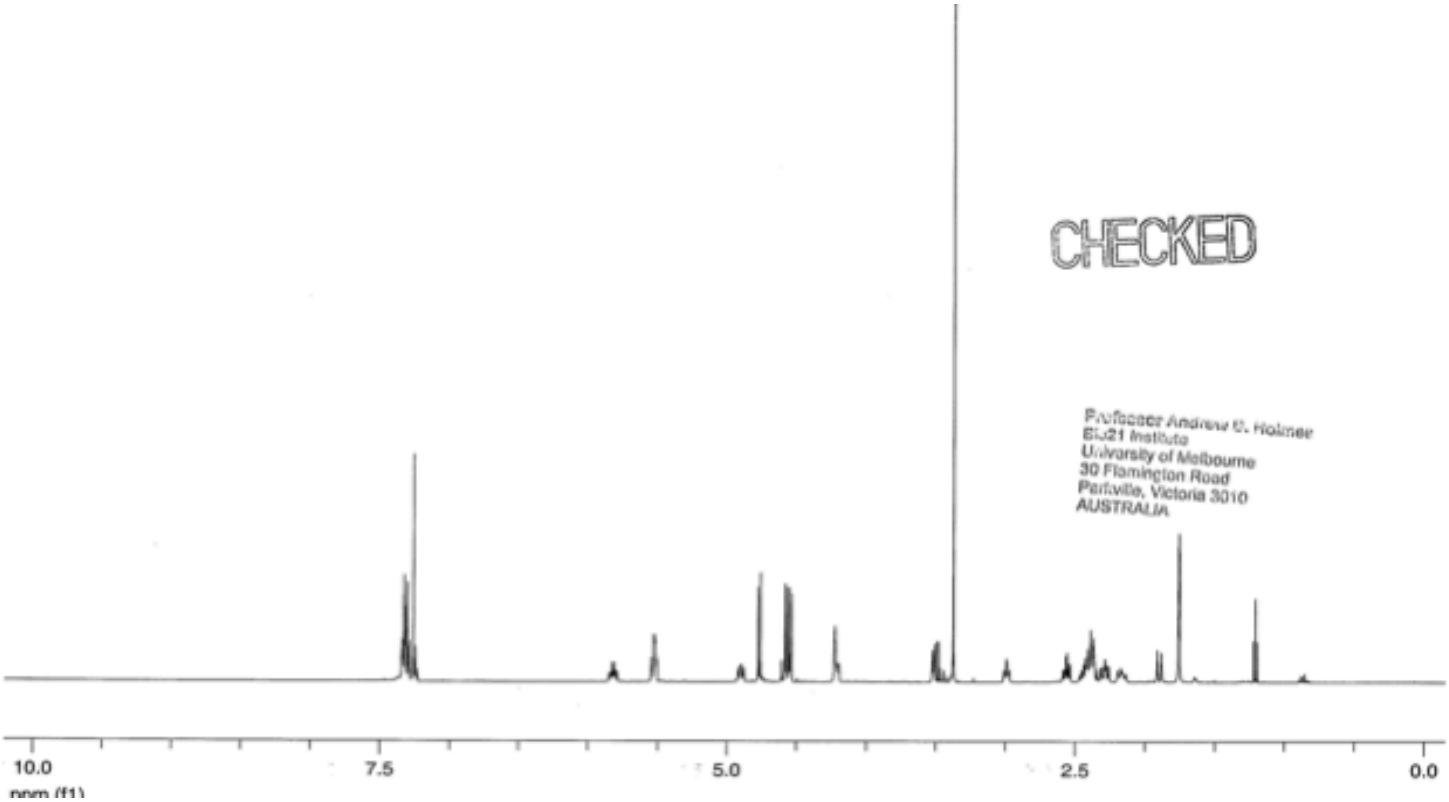
^{13}C NMR (125 MHz, $CDCl_3$)



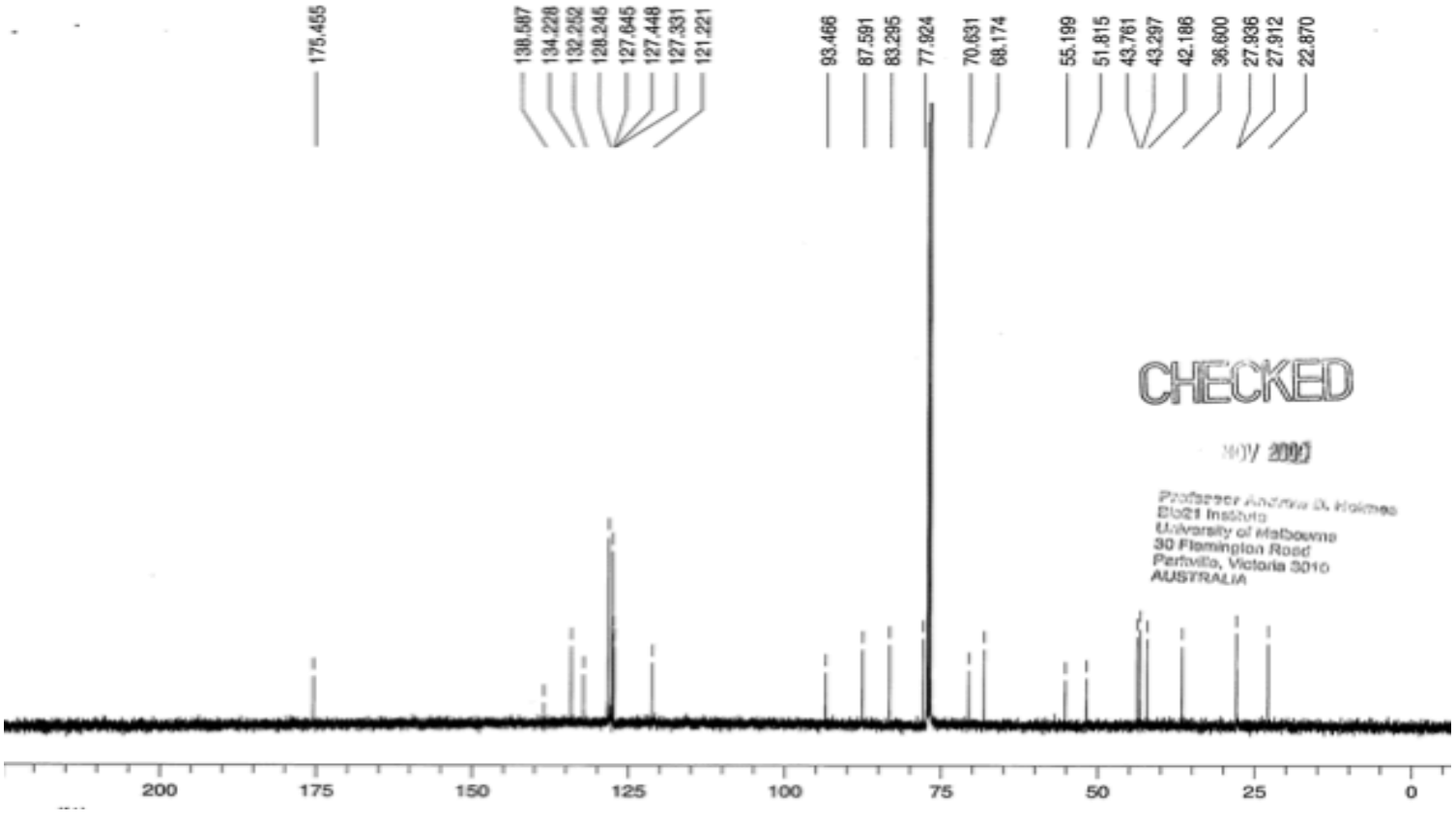


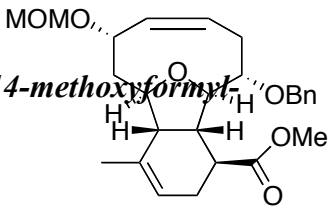
(*1*S,*2*R,*3*S,*5*Z,*7*S,*9*R,*10*R,*11*Z,*14*S)-*3-(Benzyloxy)-7-(methoxymethoxy)-cladiella-5(6),11(12)-dienyl-14-methanoic acid (37a)

^{1}H NMR (500 MHz, $CDCl_3$)



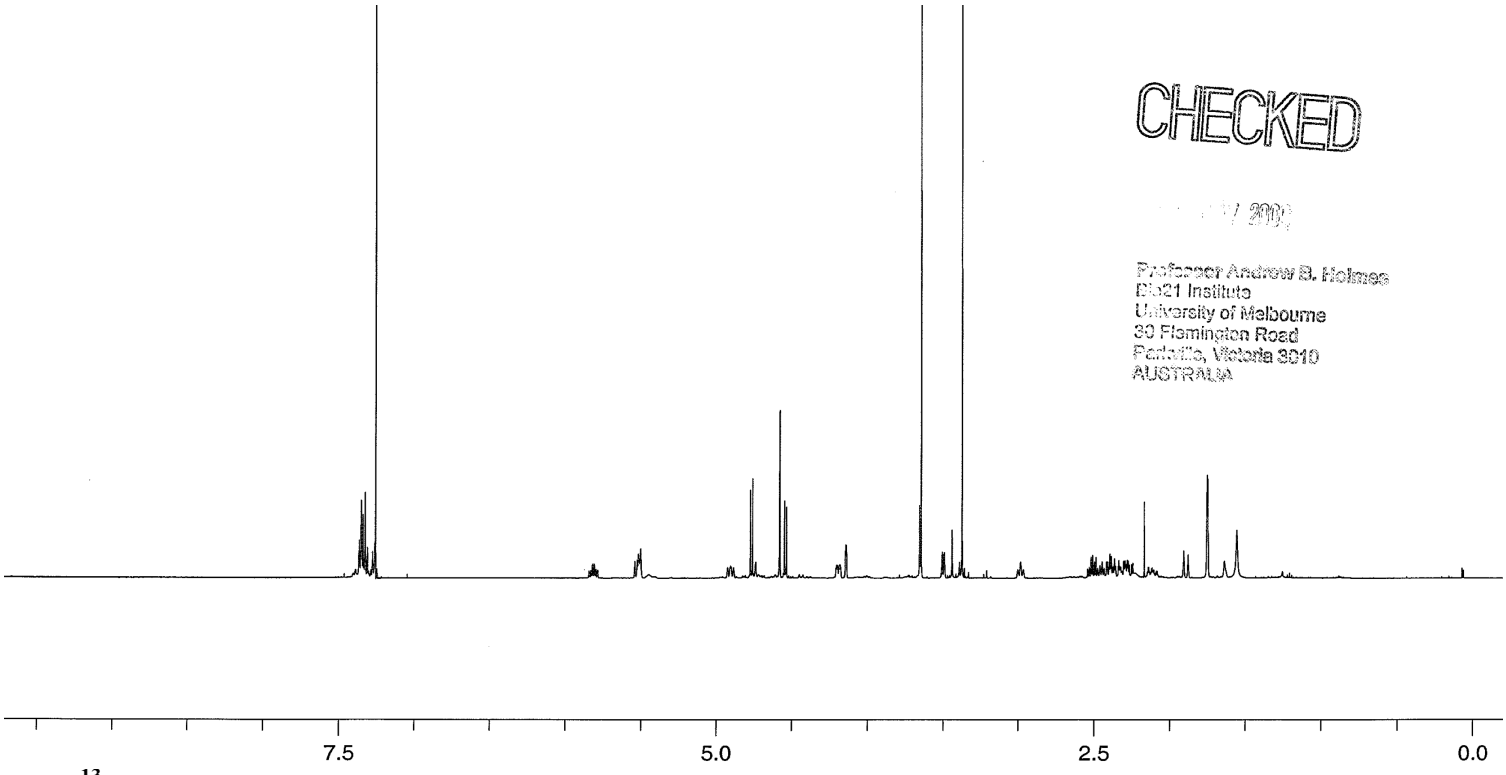
^{13}C NMR (125 MHz, $CDCl_3$)



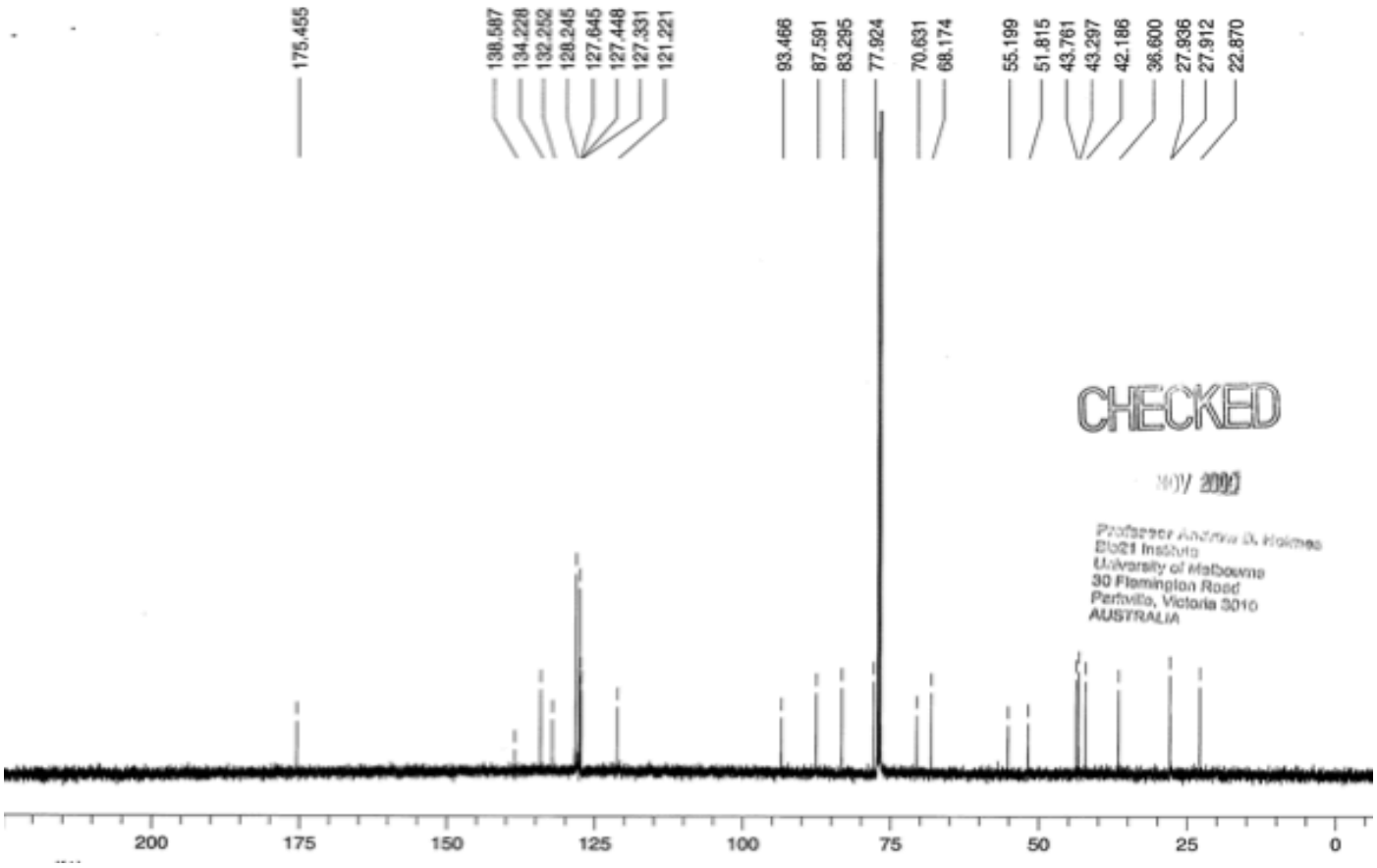


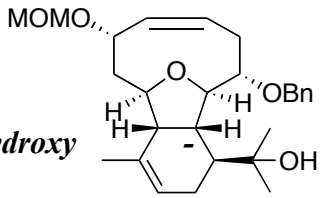
(*1*S,*2*R,*3*S,*5*Z,*7*S,*9*R,*10*R,*11*Z,*14*S)-*3-(Benzyloxy)-7-(methoxymethoxy)-14-methoxyformyl-cladiella-5(6),11(12)-diene (38)

^{1}H NMR (500 MHz, $CDCl_3$)



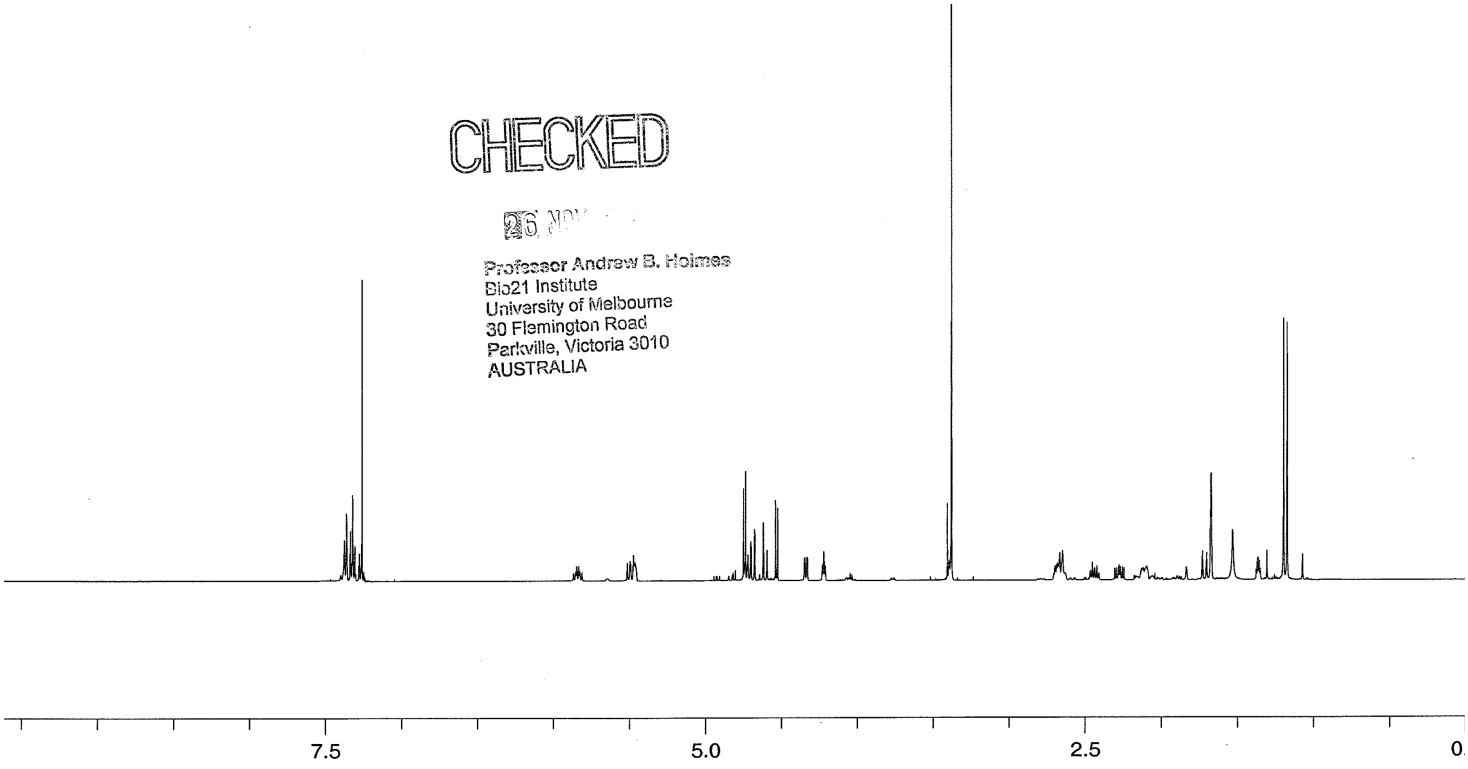
^{13}C NMR (125 MHz, $CDCl_3$)



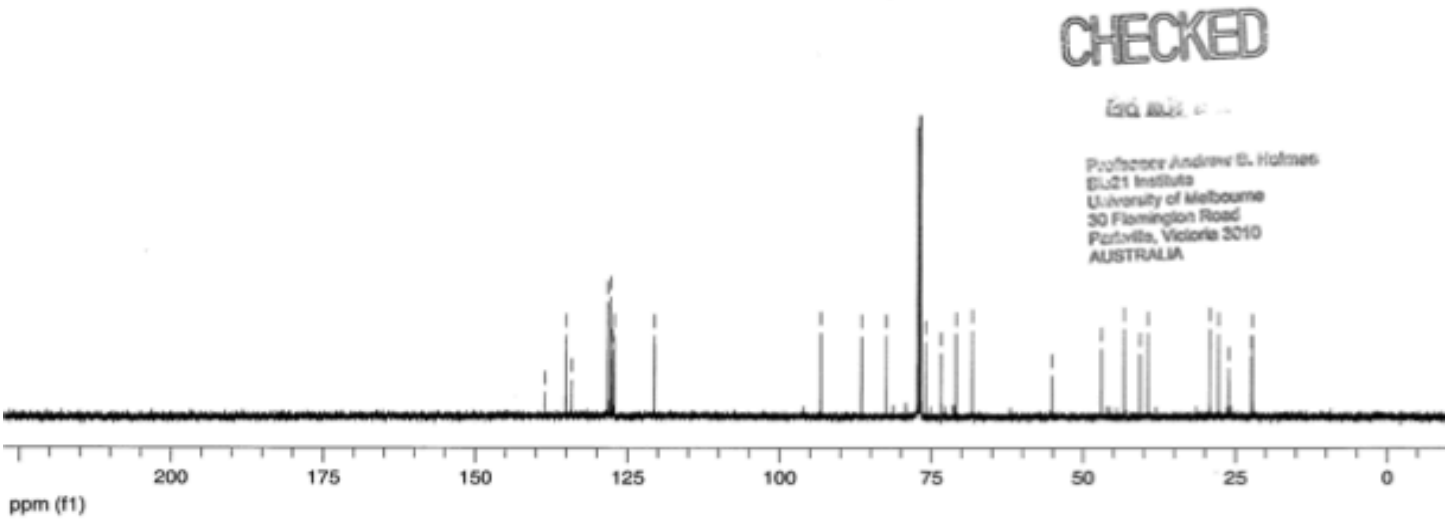


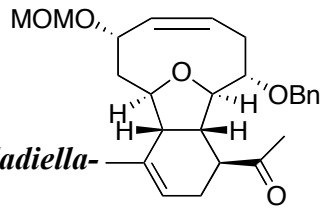
(*1*S,*2*R,*3*S,*5*Z,*7*S,*9*R,*10*R,*11*Z,*14*S)-*3-(Benzyloxy)-7-(methoxymethoxy)-18-hydroxy cladiella-5(6),11(12)-diene (39)

^{1}H NMR (500 MHz, $CDCl_3$)



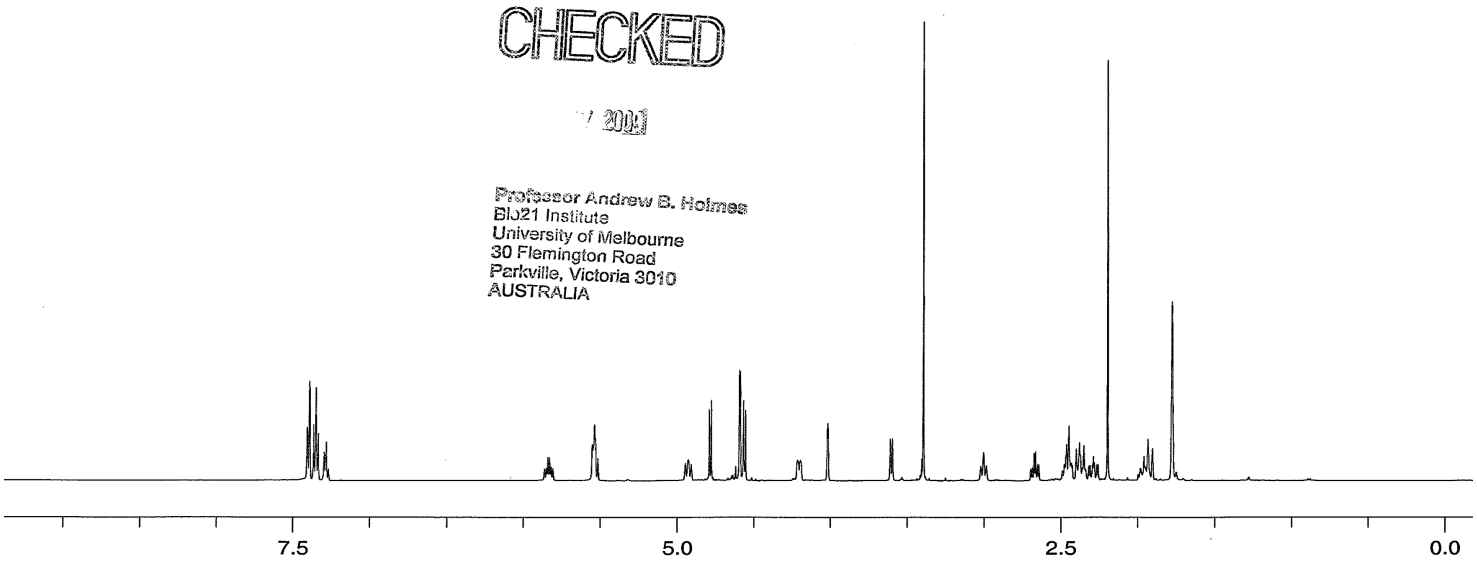
^{13}C NMR (125 MHz, $CDCl_3$)



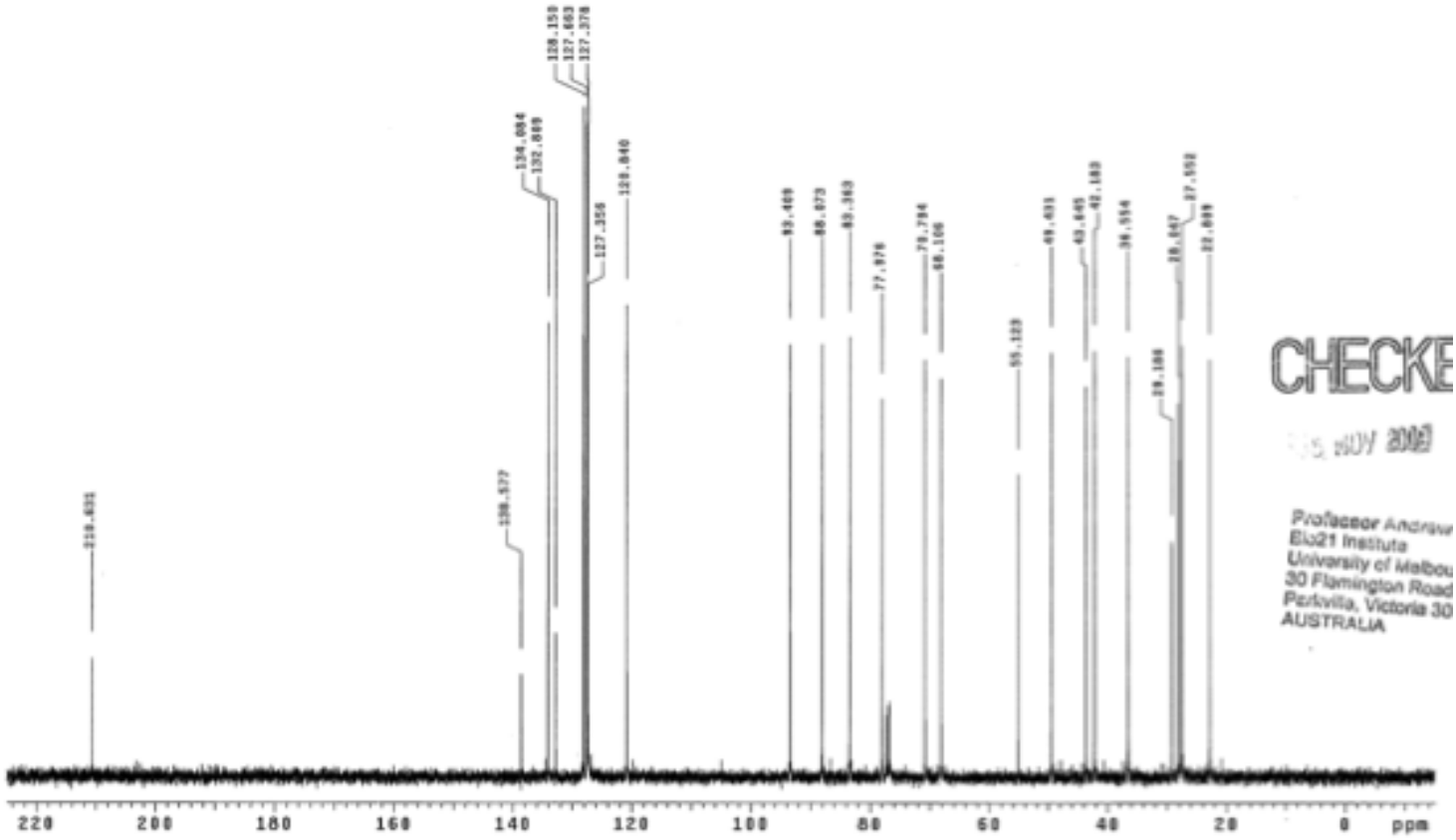


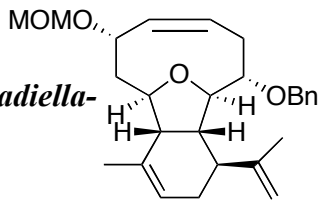
(1S,2R,3S,5Z,7S,9R,10R,11Z,14S)-3-(Benzyloxy)-7-(methoxymethoxy) -cladiella-5(6),11(12)-dienyl-18-one (41)

^{1}H NMR (500 MHz, $CDCl_3$)



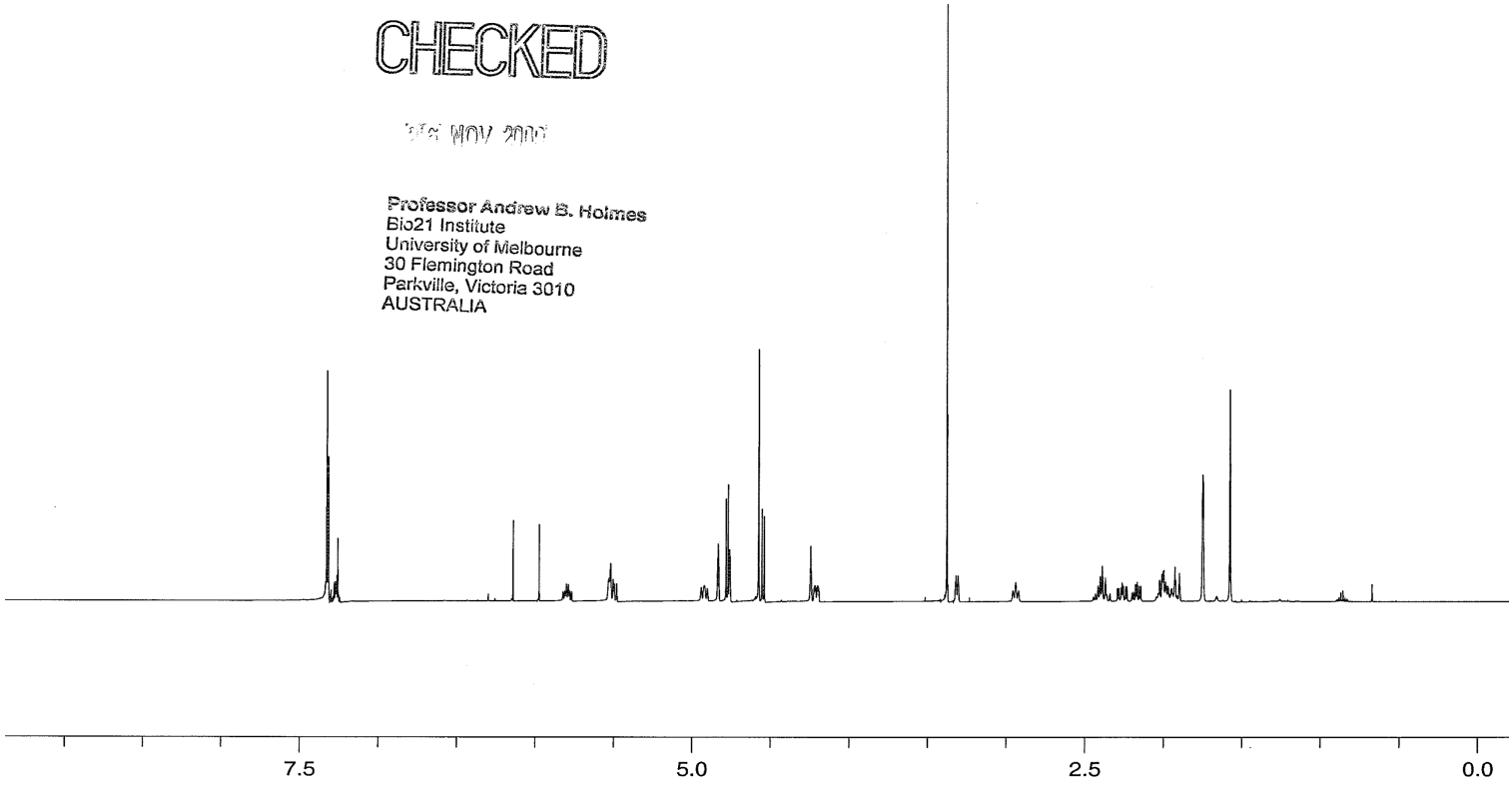
^{13}C NMR (125 MHz, $CDCl_3$)



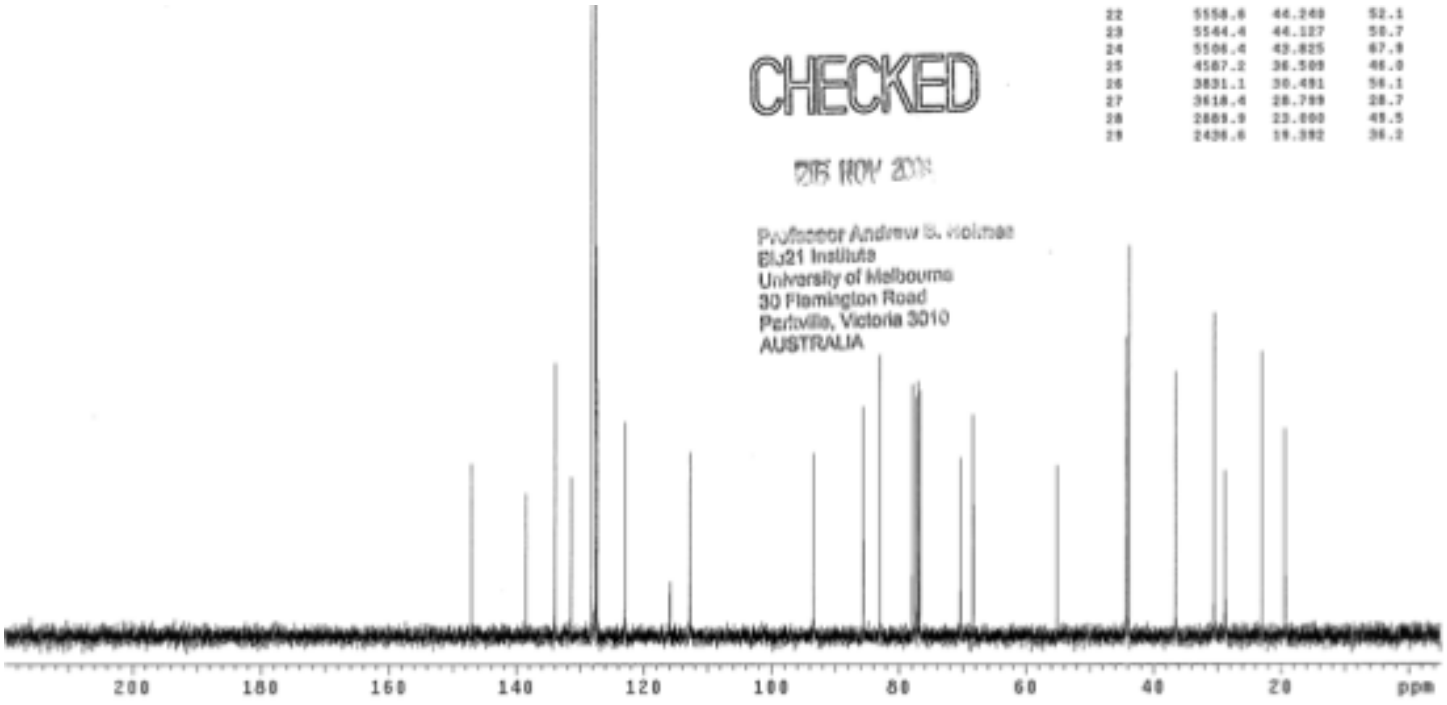


(*1*S,*2*R,*3*S,*5*Z,*7*S,*9*R,*10*R,*11*Z,*14*S)-*3-(Benzyloxy)-7-(methoxymethoxy) -cladiella-5(6),11(12),14(15)-triene (42)

^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (125 MHz, $CDCl_3$)



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1) Pangborn, A.B., Giardello, M.A., Grubbs, R.H., et al; *Organometallics*, **1996**, *5*, 1518-1520,

2) Gilmour, R.; Prior, T. J.; Burton, J. W.; Holmes, A. B. *Chem. Commun.* **2007**, 3954.