

Effect of tether length on endo/exo stereoselectivity in alkene–arene meta-photocycloaddition reactions towards the Aphidocolin/Stemodin scaffolds

Article

Supplemental Material

SI with experimental procedures and spectra

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SUPPLEMENTARY INFORMATION

Effect of Tether Length on *endo/exo* Stereoselectivity in Alkene–Arene *meta*-Photocycloaddition Reactions towards the Aphidocolin/Stemodin Scaffolds

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EXPERIMENTAL

Materials Used

All chemicals and solvents were supplied by Sigma-Aldrich (Merck), Avocado, Acros, Fluka, Lancaster Synthesis, VWR or Fluorochem. The solvents used in anhydrous reactions were distilled before use in the following manners: tetrahydrofuran (THF) and diethyl ether (sodium/benzophenone); dichloromethane and toluene (calcium hydride); methanol (magnesium methoxide); 1,3-dimethyl-3,4,5,6-tetrahydro-2-(1*H*)pyrimidone and acetone (calcium sulphate/magnesium sulphate). An MBRAUN SPS 7 solvent purifier was also used to dry THF.

The following reagents were dried by distillation from the drying agent calcium hydride; chlorotrimethylsilane, diisopropylamine, and 2,6-lutidine.

The moisture/air sensitive reagents 9-borabicyclo[3.3.1]nonane, boron trifluoride diethyl etherate, *n*-butyllithium, lithium-tri-*sec*-butylborohydride, methyllithium, methyl magnesium bromide and phosphorous tribromide were purchased in sureseal® bottles and kept under an inert atmosphere in a refrigerator.

Finally, magnesium turnings were activated by stirring vigorously under argon overnight,^[1] and allyl iodide was purified by filtration through a short plug of alumina.

Separation techniques

Thin Layer Chromatography

All thin layer chromatography was carried out on Merck silica gel 60 F₂₅₄ aluminium backed plates. The plates were visualised by the quenching of Ultra Violet fluorescence ($\lambda_{\text{max}}=254\text{ nm}$) and then permanent staining by iodine on silica and solutions of vanillin, potassium permanganate or phosphomolybdic acid.

Flash Column Chromatography

Silica gel (particle size 40-63 μm) was used for all flash column chromatography.

Analytical techniques

Ultra-Violet/Visible Spectroscopy

All UV/VIS spectra were recorded between 190 and 300 nm wavelength on a Kontron Uvikon 860 Spectrophotometer or a Perkin Elmer Lambda 25 UV/VIS Spectrometer using two-way quartz cuvettes with a 1 cm path length.

Fluorescence Spectrophotometry

A Shimadzu Spectrofluorophotometer RF-540 and a Varian Eclipse Fluorescence Spectrophotometer were used to record all fluorescence quenching data using four-way quartz cells with a 1 cm path length.

Infrared Spectroscopy

A Perkin Elmer 1720-X Infrared Fourier Transform Spectrometer or a Perkin Elmer Paragon 1000 FT-IR Spectrometer were used to record all IR spectra of samples either as a thin film or in a KBr disk.

Nuclear Magnetic Resonance Spectroscopy

Unless stated otherwise, all ^1H and ^{13}C NMR spectra were recorded at either 250 MHz and 63 MHz respectively using a Bruker DPX250 spectrometer or at 400 MHz and 100 MHz respectively on Bruker AMX400, Bruker DPX-400 or Bruker Nanobay spectrometers. All COSY, DEPT, C-H correlation, nOeSY and nOe irradiation techniques were carried out on Bruker AMX400, Bruker DPX-400 or Bruker Nanobay spectrometers. Deuterated chloroform (CDCl_3), deuterated benzene (C_6D_6), dimethylsulphoxide- d_6 ($\text{DMSO-}d_6$) and methanol- d_4 (CD_3OD) were all used as solvents. Chemical shifts (δ values) were reported in parts per million (ppm) and referenced to the residual solvent peak or tetramethylsilane. All coupling constants (J) were quoted in hertz.

Mass Spectrometry

Low resolution and Accurate mass data was recorded on a V.G. Micromass 70-70F machine under chemical ionisation (CI) or under electrospray conditions on a Thermo Scientific LTQ Orbitrap XL instrument.

Melting Points

A Gallenkamp melting point detector was used to record all melting points. All values were rounded to the nearest whole degree centigrade and are uncorrected.

Finally, concentrated *in vacuo* refers to the evaporation of solvents under water aspirator vacuum on a Buchi or IKA Rotavapor at 30-40 °C.

Experimental Description for Single Crystal X-ray

Colourless plate-shaped crystals were mounted on a thin glass fibre using silicon grease and cooled on the diffractometer to 100 K using an Oxford Cryostream cooler. A total of 80 and 287 oscillation frames of 10 and 7.5 s exposure time with 2° rotation in ϕ were recorded using a Nonius KappaCCD diffractometer, with a detector to crystal distance of 30 mm. The crystal was indexed from ten preliminary frames using the Collect + DENZO package and positional data were refined along with diffractometer constants to give the final unit cell parameters. Integration and scaling of the whole dataset resulted in complete data to $2\theta \leq 55^\circ$ (Mo-K α radiation, $\lambda = 0.71073 \text{ \AA}$) which were corrected for Lorentz and polarisation effects and for absorption and were used in subsequent refinement. The structures were solved using direct methods and developed *via* alternating least squares cycles and difference Fourier synthesis with the aid of the Maxus package. All non-hydrogen atoms were modelled anisotropically. For CCDC-246802 (ketone of **16**) all hydrogen atom parameters were allowed to refine freely because of the strained nature of portions of the molecule. This resulted in an excellent model for H atom positions, clearly showing CH...O interactions. Compound CCDC-246802 (ketone of **16**) has two unique molecules in the asymmetric unit, which are not significantly chemically different, but appear to be diastereomeric. The configuration shown in the diagrams is the most likely.

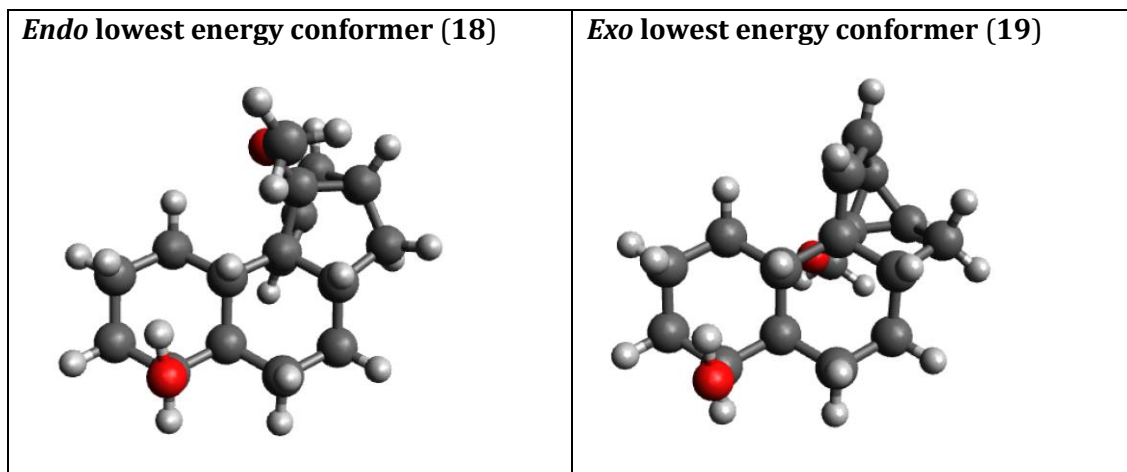
Crystal data for ketone **17** **CCDC-246801**: C₁₆H₂₀O₂, $M = 244.32$, colourless block, $0.60 \times 0.30 \times 0.20 \text{ mm}^3$, monoclinic, space group $P2_1/n$ (No. 14), $a = 10.0994(3)$, $b = 9.8419(4)$, $c = 13.8692(4) \text{ \AA}$, $\beta = 108.588(2)^\circ$, $V = 1306.65(8) \text{ \AA}^3$, $Z = 4$, $D_c = 1.242 \text{ g/cm}^3$, $F_{000} = 528$, KappaCCD, MoK α radiation, $\lambda = 0.71070 \text{ \AA}$, $T = 100(2)\text{K}$, $2\theta_{\max} = 55.0^\circ$, 9726 reflections collected, 3004 unique ($R_{\text{int}} = 0.0432$). Final $Goof = 1.030$, $R1 = 0.0427$, $wR2 = 0.1063$, R indices based on 2500 reflections with $I > 2\sigma(I)$ (refinement on F^2), 165 parameters, 0 restraints. Lp and absorption corrections applied, $\mu = 0.080 \text{ mm}^{-1}$.

Crystal data for **ketone of 16** **CCDC-246802**: C₃₂H₄₀O₄, $M = 488.64$, colourless plate, $0.30 \times 0.10 \times 0.10 \text{ mm}^3$, triclinic, space group $P-1$ (No. 2), $a = 9.7193(4)$, $b = 11.0209(5)$, $c = 12.6844(7) \text{ \AA}$, $\alpha = 96.475(3)$, $\beta = 92.135(3)$, $\gamma = 102.443(3)^\circ$, $V = 1315.66(11) \text{ \AA}^3$, $Z = 2$, $D_c = 1.233 \text{ g/cm}^3$, $F_{000} = 528$, KappaCCD, MoK α radiation, $\lambda = 0.71070 \text{ \AA}$, $T = 100(2)\text{K}$, $2\theta_{\max} = 55.0^\circ$, 10806 reflections collected, 6012 unique ($R_{\text{int}} = 0.0617$). Final $Goof = 1.026$, $R1 = 0.0577$, $wR2 = 0.1188$, R indices based on 3620 reflections with $I > 2\sigma(I)$ (refinement on F^2), 486 parameters, 0 restraints. Lp and absorption corrections applied, $\mu = 0.079 \text{ mm}^{-1}$.

Crystal data for **20 CCDC-246803**: $C_{17}H_{22}O_2$, $M = 258.35$, colourless prism, $0.80 \times 0.60 \times 0.60$ mm³, monoclinic, space group $P2_1/c$ (No. 14), $a = 14.0686(3)$, $b = 7.5569(2)$, $c = 12.8458(6)$ Å, $\beta = 102.310(2)^\circ$, $V = 1334.30(8)$ Å³, $Z = 4$, $D_c = 1.286$ g/cm³, $F_{000} = 560$, Nonis KappaCCD CCD diffractometer, MoK α radiation, $\lambda = 0.71070$ Å, $T = 100(2)$ K, $2\theta_{max} = 55.0^\circ$, 9005 reflections collected, 3053 unique ($R_{int} = 0.0372$). Final $Goof = 1.030$, $R1 = 0.0389$, $wR2 = 0.0978$, R indices based on 2681 reflections with $I > 2\sigma(I)$ (refinement on F^2), 174 parameters, 0 restraints. Lp and absorption corrections applied, $\mu = 0.082$ mm⁻¹.

Calculations of Lowest Energy Isomer of 4-Unit Tether: *endo* (**18**) versus *exo* (**19**)

All calculations were performed using the conformer-rotamer ensemble sampling tool (CREST),^[2] and the ORCA 5.0.3 electronic structure program.^[3] Cartesian coordinates for all complexes were built using Avogadro.^[4] Conformational sampling was performed at the extended tight-binding level GFN2-xTB.^[5] GBSA implicit solvation^[6] for toluene was applied during conformational sampling. The lowest energy conformers were refined further at the DFT level using ORCA 5.0.3. Geometry optimisations were performed with tight convergence without symmetry constraints using the B3LYP/G hybrid functional,^[7,8] with a def2-TZVPP basis set,^[9] and def2/J auxiliary basis set.^[10] The RIJCOSX approximation was implemented to speed up optimisations.^[11] Dispersion effects were taken into account using the atom-pairwise dispersion correction with the Becke-Jonson damping scheme.^[12,13] The solvent environment was modelled using the Conductor-like Polarizable Continuum Model (CPCM),^[14] via the PCM implicit solvent model for toluene. Frequency calculations were taken on the optimised geometries to identify if the molecule is in a true energy minima. Avogadro was used as an aid in the quantitative analysis of ORCA output files and the visualisation of molecular orbitals (isosurface: 0.03).



$\Delta E(\text{B3LYP/G}) = \text{Single point calculation energy/Electronic energy}$. The more negative, the more stable the configuration.

Hence, *endo* structure (18) is more stable, wrt *exo* (19).

Compounds	$E_{\text{HOMO}} / \text{eV}$	$E_{\text{LUMO}} / \text{eV}$	$E_{\text{gap}} / \text{eV}$	$E(\text{B3LYP/G}) / \text{Eh}$	$E(\text{B3LYP/G}) / \text{kJ/mol}$	E_G / Eh	$E_G / \text{kJ/mol}$	$\Delta E(\text{B3LYP}) / \text{kJ/mol}$	$\Delta G / \text{kJ/mol}$
<i>Endo</i> (18)	-6.34	-0.02	6.32	-813.054496023433	-2134674.579	-812.7143418	-2133781.504	4.07 Endo favoured	2.78
<i>Exo</i> (19)	-6.12	0.04	6.16	-813.052943961402	-2134670.504	-812.7132841	-2133778.727		

E_G = Final Gibbs free energy (from thermodynamics calculation).

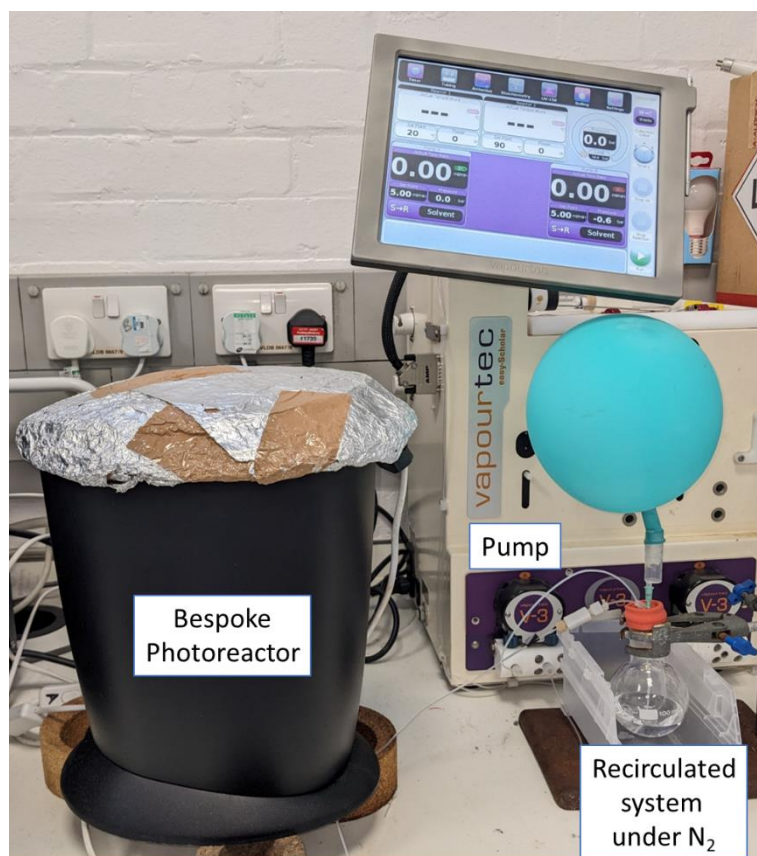
Photochemical Apparatus

Falling film photochemical reactions

Falling film photochemical reactions were carried out using a Photochemical Reactors Ltd. Thin Film Photochemical Reactor containing a low-pressure mercury arc lamp. This apparatus has the advantage of subjecting the reactants to high light exposure, as a thin film of reaction solution is kept constantly flowing over the lamp. The low-pressure mercury arc lamp was employed as it emits over 90% of its Ultra Violet light at a wavelength of 254 nm, which is sufficient to excite benzenoid arenes to their first excited state without producing many reaction by-products that can form as a result of emissions at lower wavelengths.

Continuous Flow Photochemical Reactions

Continuous flow photochemical reactions were performed using a bespoke flow photochemical system. The flask was connected to the flow system by threading the input tube through a red rubber septa and the output into the collection flask. The flow system using consists of a Vapourtec E-Scholar peristaltic pump, and a 10 mL or 3 mL FEP (1/16" o.d., 0.5 mm i.d.) reactor placed around a 25 W germicide lamp inside a light box with a gentle flow of compressed air for cooling (not essential). The reaction mixture was degassed by bubbling N₂ for 20 minutes and then a balloon was used to keep the flask under a positive pressure of N₂. The reaction mixture was then pumped at the requisite flow rate for the desired residence time.



Initial optimisation was performed by using the reactor in recirculatory mode. The **Actual Time Of Irradiation (ATOI) ratio** for the reaction was calculated as below in equation (1). The **Actual Time Of Irradiation (ATOI) / Residence Time** by multiplying the ATOI ratio by the time required to reach a satisfactory result, equation (2).

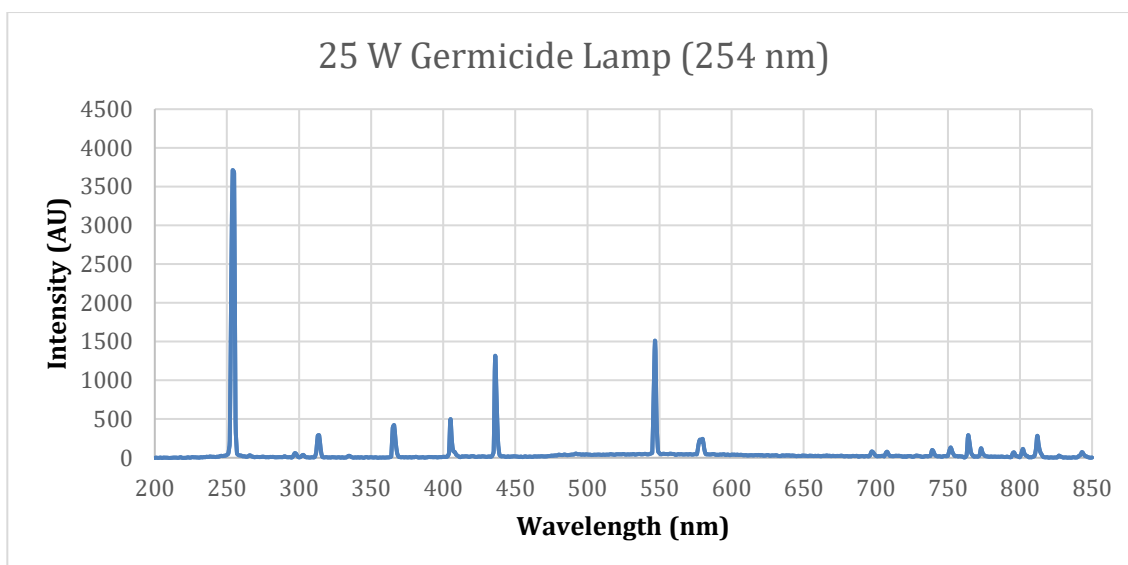
This **ATOI** is thus the residence time required in continuous mode.

$$(1) \text{ ATOI ratio} = \frac{\text{Reactor Vol}}{\text{Reactor Vol} + \text{Vol solvent in flask}} = \frac{\text{Reactor Vol}}{\text{Total Solvent Vol}}$$

$$(2) \text{ ATOI} = \text{Residence Time (continuous flow)} = \text{Recirculatory Time} \times \text{ATOI ratio}$$

Emission Spectra of the 25 W Germicidal Lamp

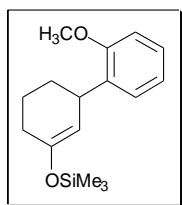
The emission spectrum from the 25 W germicidal lamp was measured using an Ocean Optics Red Tide USB650 fibre optic spectrometer.



CHARACTERISATION

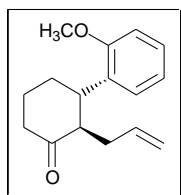
Synthesis of the 3-carbon tether substrate (7)

a. [3-(2'-Methoxyphenyl)cyclohex-1-enyloxy]trimethylsilane (10)^[15]



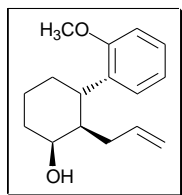
To a vigorously stirred suspension of activated magnesium turnings (1.550g, 63.80mmol) in anhydrous THF (10ml) was added 2-bromoanisole (93) (2.50ml, 20.10mmol) under nitrogen. Once the initial reaction had subsided, a solution of 2-bromoanisole (4.90ml, 39.30mmol) in dry THF (15ml) was added to the reaction mixture drop-wise over a period of 10 minutes. TLC indicated completion of the reaction after 1.5 hours. The reaction mixture was then added *via* syringe to a solution of copper cyanide (0.200g, 2.20mmol) and DMPU (12.05ml, 99.60mmol) in THF (10ml) under nitrogen at -78°C. After 10 minutes, a solution of 2-cyclohexen-1-one (4.800g, 50.00mmol) and chlorotrimethylsilane (12.55ml, 98.90mmol) in THF (15ml) was added drop-wise to the reaction mixture. TLC indicated completion after 3 hours so triethylamine (15ml) and hexane (150ml) was added to the reaction mixture. The organics were separated from the precipitated solids then washed with water (2x150ml) before being dried over MgSO₄, filtered and concentrated *in vacuo* to give a crude yellow oil. The crude product was purified using flash column chromatography (95:5 petroleum ether [40-60]/ ethyl acetate) to afford the pure oil [3-(2'-methoxyphenyl)cyclohex-1-enyloxy]trimethylsilane (10) (11.130g, 68%).

R_f = 0.70 (95:5 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 279nm. ν_{max} (thin film, cm⁻¹) 1599 (aromatic stretch), 1411 (SiCH₃), 844 (Si(CH₃)₃). δ_H (250MHz, CDCl₃) 0.03 (9H, s, OSi(CH₃)₃), 1.11- 1.26 (1H, m, one of CH₂CH(Ar)), 1.36- 1.59 (2H, m, CH₂CH₂COSi), 1.66- 1.78 (1H, m, one of CH₂CH(Ar)), 1.83- 1.95 (2H, m, CH₂COSi), 3.63 (3H, s, OCH₃), 3.69- 3.80 (1H, m, CH(Ar)), 4.67- 4.69 (1H, m, CH=COSi), 6.65 (1H, dd, *J* 1.0 and 7.5Hz, CH=COCH₃), 6.72 (1H, app. dt, *J* 1.0 and 7.5Hz, CHCHCH=COCH₃), 6.98 (1H, app. dt, *J* 1.5 and 7.5Hz, CHCH=COCH₃), 7.02 (1H, dd, *J* 1.5 and 7.5Hz, CHC(CH)=COCH₃). δ_C (63MHz, CDCl₃) 0.0 ((CH₃)₃), 20.7 (CH₂CH₂COSi), 29.5 (CH₂CH(Ar)) and (CH₂COSi), 33.1 (CH(Ar)), 54.9 (OCH₃), 107.3 (CH=COSi), 109.7 (CH=COCH₃), 119.8 (CHCHCH=COCH₃), 126.4 (CHCH=COCH₃), 128.1 (CHC(CH)=COCH₃), 134.6 (C(CH)=COCH₃), 151.4 (COSi), 156.4 (COCH₃). *m/z* (CI, NH₃, high resolution) found 277.1623 [C₁₆H₂₄O₂Si] ((MH)⁺, 100%) [requires 277.1625], 276 (33), 248.1183 (14), 217.1042 (18), 73.0480 (23).

b. (\pm) (2*R*, 3*S*)-2-Allyl-3-(2'-methoxyphenyl)cyclohexanone (**11**)^[15]

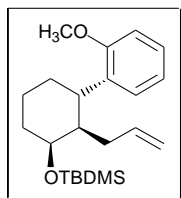
To a stirred solution of the silyl enol ether [*3*-(2'-methoxyphenyl)cyclohex-1-enyloxy]trimethylsilane (**10**) (1.510g, 5.48mmol) in anhydrous THF (32ml) was added a 1.5M solution of methyllithium in Et₂O (4.00ml, 6.00mmol). TLC confirmed cleavage of the silyl enol ether after 5 minutes. The reaction flask was then cooled to -78°C before a solution of allyl iodide (4.90ml, 5.40mmol) in THF (11ml) was added drop-wise. The reaction was then allowed to warm to room temperature over 3 hours. TLC indicated completion of the reaction after 6 hours and the mixture was quenched with ethyl acetate (100ml) and water (100ml). The aqueous layer was extracted with ethyl acetate (3x50ml). The combined extracts were washed with saturated NaCl solution (150ml), dried over MgSO₄, filtered and concentrated *in vacuo* to afford a pale yellow crude oil. Pure (\pm) (2*R*, 3*S*)-2-allyl-3-(2'-methoxyphenyl)cyclohexanone (**11**) (1.058g, 79%) was obtained using flash column chromatography (95:5 petroleum ether [40-60]/ ethyl acetate) as a pale yellow oil.

R_f = 0.21 (95:5 petroleum ether [40-60]/ ethyl acetate). λ_{\max} (cyclohexane) 231 and 265nm. ν_{\max} (thin film, cm⁻¹) 1710 (C=O), 1599 (aromatic stretch). δ_{H} (400MHz, CDCl₃) 1.60- 1.78 (1H, m, one of CH₂CH₂CO), 1.79- 1.95 (3H, m, one of CH₂CH=CH₂ and CH₂CH₂CH₂CO), 1.96- 2.07 (1H, m, one of CH₂CH₂CO), 2.10- 2.22 (1H, m, one of CH₂CH=CH₂), 2.35- 2.44 (2H, m, CH₂C=O), 2.79 (1H, ddd, *J* 11.5, 8.5 and 3.0Hz, CH(C₃H₅)), 3.15 (1H, ddd, *J* 11.5, 11.0 and 5.0Hz, CH(Ar)), 3.74 (3H, s, OCH₃), 4.68 (1H, app. ddt, *J* 17.0, 2.0 and 1.5Hz, CH=CH₂ (*trans*-H)), 4.76 (1H, app. ddt, *J* 10.0, 2.0 and 1.0Hz, CH=CH₂ (*cis*-H)), 5.65 (1H, app. ddt, *J* 17.0, 10.0 and 7.0Hz, CH=CH₂), 6.80 (1H, dd, *J* 1.0 and 8.0Hz, CH=COCH₃), 6.88 (1H, app. dt, *J* 1.0 and 7.5Hz, CHCHCH=COCH₃), 7.10 (1H, dd, *J* 1.5 and 7.5Hz, CHC(CH)=COCH₃), 7.14 (1H, ddd, *J* 1.5, 7.5 and 8.0Hz, CHCH=COCH₃). δ_{C} (100MHz, CDCl₃) 26.9 (CH₂CH₂CO), 31.4 (CH₂CH=CH₂), 33.2 (CH₂CH₂CH₂CO), 42.7 (CH₂CO), 44.4 (CH(Ar)), 55.0 (CH(C₃H₅)), 55.7 (OCH₃), 111.2 (CH=COCH₃), 115.8 (CH=CH₂), 121.1 (CHCHCH=COCH₃), 127.9 (CHCH=COCH₃), 128.2 (CHC(CH)=COCH₃), 131.9 (C(CH)=COCH₃), 137.4 (CH=CH₂), 157.5 (COCH₃), 212.5 (C=O). *m/z* (CI, NH₃, high resolution) found 245.1539 [C₁₆H₂₀O₂] ((MH)⁺, 100%) [requires 245.1542], 147 (16).

c. (\pm) (1*S*, 2*R*, 3*S*)-2-Allyl-3-(2'-methoxyphenyl)cyclohexanol (**7**)^[15]

To a stirred solution of (\pm) (2*R*, 3*S*)-2-allyl-3-(2'-methoxyphenyl)cyclohexanone (**11**) (1.803g, 7.38mmol) in anhydrous THF (35ml) was added a 1M solution of lithium tri-*sec*-butylborohydride in THF (8.20ml, 8.20mmol) drop-wise at -78°C under nitrogen. The reaction was allowed to warm to room temperature over 3 hours and stirred at that temperature for a further 23 hours until TLC confirmed completion. The reaction was then quenched by the addition of ethanol (15ml) and water (25ml). After 50 minutes, 6N NaOH solution (25ml) was added followed by careful drop-wise addition of aqueous hydrogen peroxide solution (25ml, 30% w/v in water). After 35 minutes, the evolution of oxygen had ceased and the mixture was transferred to a separating funnel where it was extracted with diethyl ether (3x75ml). The organic layer was back extracted with water (2x75ml), dried over MgSO₄, filtered and concentrated under vacuum to give a colourless oil. Pure (\pm) (1*S*, 2*R*, 3*S*)-2-allyl-3-(2'-methoxyphenyl)cyclohexanol (**7**) (1.769g, 97%) was obtained by flash column chromatography (95:5 petroleum ether [40-60]/ ethyl acetate) as a white crystalline solid.

Mp. 60-62 °C. R_f = 0.23 (90:10 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 228 and 267nm (225 M⁻¹cm⁻¹). ν_{max} (thin film, cm⁻¹) 3302 (OH), 1599 (aromatic stretch). δ_H (400MHz, C₆D₆ at 70°C) 0.98 (1H, bs, CHOH), 1.36- 1.58 (3H, m, one of CH₂CH₂CHOH), one of CH₂CH(Ar) and one of CH₂CHOH), 1.74- 1.95 (4H, m, one of CH₂CH(Ar), one of CH₂CHOH), one of CH₂CH₂CHOH) and CH(C₃H₅)), 1.95- 2.04 (1H, m, one of CH₂CH=CH₂), 2.12- 2.22 (1H, m, one of CH₂CH=CH₂), 3.42 (3H, s, OCH₃), 3.52 (1H, app. dt, *J* 3.5 and 12.0Hz, CH(Ar)), 4.00 (1H, app. bd, *J* 2.5Hz, CHOH), 4.87- 4.95 (2H, m, CH=CH₂), 5.66- 5.78 (1H, m, CH=CH₂), 6.64 (1H, d, *J* 7.5Hz, CH=COCH₃), 6.89 (1H, app. t, *J* 7.5Hz, CHCHCH=COCH₃), 7.06 (1H, app. dt, *J* 1.5 and 7.5Hz, CHCH=COCH₃), 7.13 (1H, d, *J* 7.5Hz, CHC(CH)=COCH₃). δ_C (100MHz, C₆D₆ at 70°C) 20.8 (CH₂CH₂CHOH), 34.2, 34.6 and 34.8 (CH₂CHOH, CH₂CH(Ar) and CH₂CH=CH₂), 36.6 (CH(Ar)), 46.3 (CH(C₃H₅)), 55.2 (OCH₃), 67.5 (CHOH), 111.5 (CH=COCH₃), 115.3 (CH=CH₂), 121.3 (CHCHCH=COCH₃), 127.0 (CHCH=COCH₃), 128.6 (CHC(CH)=COCH₃), 134.8 (C(CH)=COCH₃), 138.2 (CH=CH₂), 158.3 (COCH₃). *m/z* (EI, high resolution) found 246.1619 [C₁₆H₂₂O₂] [(M)⁺, 100%] [requires 246.1620], 280.9820 (42), 230.9853 (96).

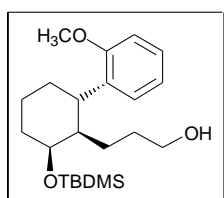
Synthesis of the 4-carbon tether substrate (**8**) Route Aa. (\pm) [(1*S*, 2*R*, 3*S*)-2-Allyl-3-(2'-methoxyphenyl)cyclohexyloxy-*tert*-butyldimethylsilane]^[15]

To a stirred solution of (\pm) (1*S*, 2*R*, 3*S*)-2-allyl-3-(2'-methoxyphenyl)cyclohexanol (**7**) (0.256g, 1.04mmol) in dry DCM (5ml) was added 2,6-lutidine (0.24ml, 2.06mmol) under a nitrogen atmosphere. The mixture was cooled to 0°C and *tert*-butyldimethylsilyl triflate (0.35ml, 1.52mmol) was added drop-wise *via* syringe. After 30 minutes, TLC indicated that the reaction was complete and it was subsequently quenched with saturated sodium bicarbonate solution (15ml). The reaction mixture was transferred to a separating funnel where the aqueous phase was extracted with dichloromethane (3x30ml). The combined organic extracts were then washed with 0.73M hydrochloric acid (30ml) and then saturated sodium bicarbonate solution (30ml) and water (30ml). The organic layer was dried over MgSO₄, filtered and concentrated *in vacuo* to give a colourless crude oil. Pure (\pm) [(1*S*, 2*R*, 3*S*)-2-allyl-3-(2'-methoxyphenyl)cyclohexyloxy-*tert*-butyldimethylsilane (0.366g, 98%) was obtained by flash column chromatography (95:5 petroleum ether [40-60]/ ethyl acetate) as a colourless oil.

R_f = 0.70 (95:5 petroleum ether [40-60]/ ethyl acetate). λ_{\max} (cyclohexane) 232 and 257nm. ν_{\max} (thin film, cm⁻¹) 3074 (H₂C=), 3026 (HC=), 1600 (aromatic stretch). δ_{H} (400MHz, C₆D₆) 0.11 (3H, s, OSiCH₃), 0.12 (3H, s, OSiCH₃), 1.09 (9H, s, OSiC(CH₃)₃), 1.32- 1.44 (2H, m, one of CH₂CH(Ar) and one of CH₂CHOTBDMS), 1.44- 1.53 (1H, m, one of CH₂CH₂CHOTBDMS), 1.57 (1H, app. bs, CH(C₃H₅)), 1.79- 1.94 (2H, m, one of CH₂CH(Ar) and one of CH₂CHOTBDMS), 1.94- 2.07 (2H, m, one of CH₂CH=CH₂ and one of CH₂CH₂CHOTBDMS), 2.20- 2.32 (1H, m, one of CH₂CH=CH₂), 3.36 (3H, s, OCH₃), 3.67 (1H, app. bs, CH(Ar)), 4.12 (1H, app. t, *J* 1.5Hz, CHOTBDMS), 4.93- 5.03 (2H, m, CH=CH₂), 5.65- 5.78 (1H, m, CH=CH₂), 6.58 (1H, dd, *J* 1.0 and 7.5Hz, CH=COCH₃), 6.93 (1H, app. t, *J* 7.5Hz, CHCHCH=COCH₃), 7.03 (1H, dt, *J* 1.5 and 7.5Hz, CHCH=COCH₃), 7.17 (1H, dd, *J* 1.5 and 7.5Hz, CHC(CH)=COCH₃). δ_{C} (100MHz, C₆D₆) - 4.8 and -3.6 (OSiCH₃ and OSiCH₃), 18.6 (OSiC(CH₃)₃), 20.9 (CH₂CH₂CHOTBDMS), 26.2 (OSiC(CH₃)₃), 33.8 (CH₂CH=CH₂), 34.4 (CH₂CHOTBDMS and CH₂CH(Ar)), 34.5 (CH(Ar)), 47.0 (CH(C₃H₅)), 55.0 (OCH₃), 68.4 (CHOTBDMS), 110.9 (CH=COCH₃), 115.3 (CH=CH₂), 121.1 (CHCHCH=COCH₃), 126.9 (CHCH=COCH₃), 128.2 (CHC(CH)=COCH₃), 134.6 (C(CH)=COCH₃), 138.5 (CH=CH₂), 158.0 (COCH₃). *m/z* (CI, NH₃, high resolution) found 361.2599 [C₂₂H₃₆O₂Si]

((MH)⁺, 54%) [requires 361.2564], 303.1541 (100), 229.1533 (41), 147.0784 (24), 121.0648 (29), 82.9509 (56).

b. (±) 3-[(1*R*, 2*S*, 6*S*)-2'-(*tert*-Butyldimethylsilyloxy)-6'-(2''-methoxyphenyl)cyclohexyl]propan-1-ol^[15]

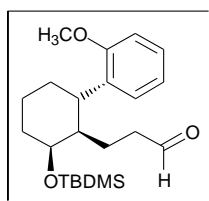


To a stirred solution of (±) [(1*S*, 2*R*, 3*S*)-2-allyl-3-(2'-methoxyphenyl)cyclohexyloxy-*tert*-butyldimethylsilane (0.366g, 1.00mmol) in dry THF (7ml) under nitrogen was added 0.5M 9-borabicyclo[3.3.1]nonane solution in THF (3.00ml, 1.50mmol) *via* syringe. After 45 minutes, TLC indicated that the reaction had run to completion, so the mixture was quenched with 3M NaOH solution (0.5ml). This was followed by careful, drop-wise addition of hydrogen peroxide 27.5% wt. solution in water (0.50ml, 4.10mmol). The mixture was left stirring for 10 minutes after which time the THF was removed *in vacuo*. The remaining mixture was transferred to a separating funnel where the aqueous layer was extracted with ethyl acetate (2x30ml). The combined organic washings were collected and washed with saturated sodium hydrogen carbonate solution (2x20ml) and then water (20ml). The organic layer was dried over MgSO₄, filtered and concentrated *in vacuo* to give a colourless, crude oil. Pure (±) 3-[(1*R*, 2*S*, 6*S*)-2'-(*tert*-butyldimethylsilyloxy)-6'-(2''-methoxyphenyl)cyclohexyl]propan-1-ol (0.363g, 94%) was obtained by flash column chromatography (90:10 petroleum ether [40-60]/ ethyl acetate) as a colourless oil.

R_f = 0.31 (85:15 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 231 and 267nm. ν_{max} (thin film, cm⁻¹) 3384 (OH), 1600 (aromatic stretch). δ_H (400MHz, C₆D₆) 0.10 (3H, s, OSiCH₃), 0.11 (3H, s, OSiCH₃), 1.09 (9H, s, OSiC(CH₃)₃), 1.15- 1.80 (8H, m, one of CH₂CHOTBDMS, one of CH₂CH₂CHOTBDMS, one of CH₂CH(Ar), CH(C₃H₆OH), CH₂(CH₂)₂OH, CH₂CH₂OH), 1.80- 1.87 (1H, m, one of CH₂CHOTBDMS), 1.89- 1.95 (1H, m, one of CH₂CH(Ar)), 1.95- 2.08 (1H, m, one of CH₂CH₂CHOTBDMS), 3.36 (3H, s, OCH₃), 3.66 (1H, app. bs, CH(Ar)), 3.87- 3.99 (2H, m, CH₂OH), 4.07 (1H, app. bs, CHOTBDMS), 6.60 (1H, d, *J* 8.0Hz, CH=COCH₃), 6.95 (1H, t, *J* 8.0Hz, CHCHCH=COCH₃), 7.08 (1H, dt, *J* 1.5 and 8.0Hz, CHCH=COCH₃), 7.18 (1H, d, *J* 8.0Hz, CHC(CH)=COCH₃). δ_C (100MHz, C₆D₆) -4.9 and -3.8 (OSiCH₃ and OSiCH₃), 18.5 (OSiC(CH₃)₃), 20.9 (CH₂CH₂CHOTBDMS), 26.2 (OSiC(CH₃)₃), 30.2

and 30.7 ($\underline{\text{C}}\text{H}_2(\text{C}\text{H}_2)_2\text{OH}$ and $\underline{\text{C}}\text{H}_2\text{CH}_2\text{OH}$), 34.5 ($\underline{\text{C}}\text{H}_2\text{CH}(\text{Ar})$ and $\underline{\text{C}}\text{H}_2\text{CHOTBDMS}$), 34.7 ($\underline{\text{C}}\text{H}(\text{Ar})$), 46.4 ($\underline{\text{C}}\text{H}(\text{C}_3\text{H}_6\text{OH})$), 55.0 ($\text{O}\underline{\text{C}}\text{H}_3$), 62.9 ($\underline{\text{C}}\text{H}_2\text{OH}$), 68.3 ($\underline{\text{C}}\text{HOTBDMS}$), 111.0 ($\underline{\text{C}}\text{H}=\text{COCH}_3$), 121.1 ($\underline{\text{C}}\text{HCHCH}=\text{COCH}_3$), 126.8 ($\underline{\text{C}}\text{HCH}=\text{COCH}_3$), 128.6 ($\underline{\text{C}}\text{HC}(\text{CH})=\text{COCH}_3$), 135.1 ($\underline{\text{C}}(\text{CH})=\text{COCH}_3$), 158.0 ($\underline{\text{C}}\text{OCH}_3$).). m/z (CI, NH_3 , high resolution) found 379.2773 [$\text{C}_{22}\text{H}_{38}\text{O}_3\text{Si}$] ($(\text{MH})^+$, 100%) [requires 379.2769].

c. (\pm) 3-[(1*R*, 2*S*, 6*S*)-2'-(*tert*-Butyldimethylsilyloxy)-6'-(2''-methoxyphenyl)cyclohexyl]propionaldehyde (**12**)^[15]

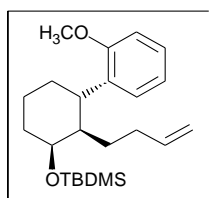


To a stirred solution of (\pm) 3-[(1*R*, 2*S*, 6*S*)-2'-(*tert*-butyldimethylsilyloxy)-6'-(2''-methoxyphenyl)-cyclohexyl]-propan-1-ol (0.343g, 0.90mmol) in dry DCM (2.5ml) under a nitrogen atmosphere was added the Dess-Martin periodinane (102) (0.499g, 1.18mmol) in dry DCM (2.5ml) *via* syringe. The reaction mixture was left stirring for 1.75 hours at which time TLC indicated that the reaction had run to completion. The mixture was diluted with diethyl ether (20ml) before a 1M solution of NaOH (20ml) was added. The reaction mixture was left to stir for 10 minutes and was then transferred to a separating funnel where the aqueous layer was extracted with diethyl ether (2x30ml). The organic extracts were collected together and washed with 1M NaOH solution (30ml) and then water (30ml). The organic layer was dried over MgSO_4 , filtered and concentrated *in vacuo* to give the colourless pure oil of (\pm) 3-[(1*R*, 2*S*, 6*S*)-2'-(*tert*-butyldimethylsilyloxy)-6'-(2''-methoxyphenyl)-cyclohexyl]propionaldehyde (**12**) (0.337g, 99%).

R_f = 0.26 (95:5 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 228 and 270nm. ν_{max} (thin film, cm^{-1}) 1727 (C=O), 1599 (aromatic stretch). δ_{H} (400MHz, C_6D_6) 0.02 (3H, s, OSiCH_3), 0.06 (3H, s, OSiCH_3), 1.02 (9H, s, $\text{OSiC}(\text{CH}_3)_3$), 1.26- 1.65 (6H, m, one of $\underline{\text{C}}\text{H}_2\text{CH}(\text{Ar})$, one of $\underline{\text{C}}\text{H}_2\text{CHOTBDMS}$, $\underline{\text{C}}\text{H}_2\text{CH}_2\text{CHO}$, one of $\underline{\text{C}}\text{H}_2\text{CH}_2\text{CH}(\text{Ar})$ and $\underline{\text{C}}\text{H}(\text{CH}_2)_2\text{CHO}$), 1.72- 1.97 (5H, m, one of $\underline{\text{C}}\text{H}_2\text{CH}(\text{Ar})$, one of $\underline{\text{C}}\text{H}_2\text{CHOTBDMS}$, one of $\underline{\text{C}}\text{H}_2\text{CH}_2\text{CH}(\text{Ar})$ and $\underline{\text{C}}\text{H}_2\text{CHO}$), 3.38 (3H, s, OCH_3), 3.52 (1H, app. bs, $\underline{\text{C}}\text{H}(\text{Ar})$), 3.90 (1H, app. s, $\underline{\text{C}}\text{HOTBDMS}$), 6.59 (1H, d, J 7.5Hz, $\underline{\text{C}}\text{H}=\text{COCH}_3$), 6.90 (1H, app. t, J 7.5Hz, $\underline{\text{C}}\text{HCHCH}=\text{COCH}_3$), 7.06 (1H, app. dt, J 1.5 and 7.5Hz, $\underline{\text{C}}\text{HCH}=\text{COCH}_3$), 7.10 (1H, dd, J 1.5 and 7.5Hz, $\underline{\text{C}}\text{HC}(\text{CH})=\text{COCH}_3$), 9.20 (1H, t, J 2.0Hz, $\underline{\text{C}}\text{HO}$). δ_{C} (100MHz, C_6D_6) -5.0 and -3.8 (OSiCH_3 and OSiCH_3), 18.5 ($\text{OSiC}(\text{CH}_3)_3$), 20.7

($\underline{\text{C}}\text{H}_2\text{CH}_2\text{CHOTBDMS}$), 22.4 ($\underline{\text{C}}\text{H}_2\text{CH}_2\text{CHO}$), 26.1 ($\text{OSiC}(\underline{\text{C}}\text{H}_3)_3$), 34.2 ($\underline{\text{C}}\text{H}(\text{Ar})$, $\underline{\text{C}}\text{H}_2\text{CH}(\text{Ar})$ and $\underline{\text{C}}\text{H}_2\text{CHOTBDMS}$), 41.5 ($\underline{\text{C}}\text{H}_2\text{CHO}$), 46.0 ($\underline{\text{C}}\text{H}(\text{CH}_2)_2\text{CHO}$), 55.0 ($\text{O}\underline{\text{C}}\text{H}_3$), 68.4 ($\underline{\text{C}}\text{HOTBDMS}$), 111.0 ($\underline{\text{C}}\text{H}=\text{COCH}_3$), 121.1 ($\underline{\text{C}}\text{HCHCH}=\text{COCH}_3$), 127.1 ($\underline{\text{C}}\text{HCH}=\text{COCH}_3$), 128.2 ($\underline{\text{C}}\text{HC}(\text{CH})=\text{COCH}_3$), 134.4 ($\underline{\text{C}}(\text{CH})=\text{COCH}_3$), 157.9 ($\underline{\text{C}}\text{OCH}_3$), 201.1 ($\underline{\text{C}}\text{HO}$). m/z (CI, NH_3 , high resolution) found 377.2497 [$\text{C}_{22}\text{H}_{36}\text{O}_3\text{Si}$] ($(\text{MH})^+$, 27%) [requires 377.2513], 319.1723 (93), 245.2347 (74), 227.1139 (100), 147.0804 (81), 121.0650 (44), 75.0267 (27).

d. (\pm) [(1*S*, 2*R*, 3*S*)-2-But-3'-enyl-3-(2''-methoxyphenyl)cyclohexyloxy]-*tert*-butyldimethylsilane^[15]



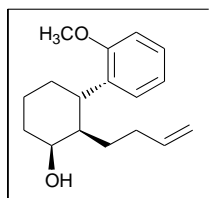
General Procedure A

To a stirred solution of methyltriphenylphosphonium bromide (0.272g, 0.76mmol) in anhydrous THF (5ml) was added a 1.6M solution of methyllithium in hexanes (0.43ml, 0.70mmol) at 0°C under nitrogen. The reaction mixture changed to a bright yellow colour almost immediately and was left to stir at 0°C for 45 minutes. After this time, a solution of (\pm) 3-[(1*R*,2*S*,6*S*)-2'-(*tert*-butyldimethyl-silyloxy)-6'-(2''-methoxyphenyl)-cyclohexyl]propionaldehyde (**12**) (0.191g, 0.51mmol) in dry THF (5ml) was added to the reaction mixture *via* syringe. The mixture was then left stirring at 0°C for another hour until TLC confirmed that no more starting material was being consumed. The reaction was quenched with saturated NH_4Cl solution (20ml) before being transferred to a separating funnel where the aqueous layer was extracted with ethyl acetate (2x30ml). The combined organic extracts were washed with saturated NaCl solution (30ml) and then water (30ml). The organic layer was dried over MgSO_4 , filtered and concentrated *in vacuo* to give a colourless crude oil. Pure (\pm) [(1*S*, 2*R*, 3*S*)-2-but-3'-enyl-3-(2''-methoxyphenyl)cyclo-hexyloxy]*tert*-butyldimethylsilane (0.163g, 86%) was obtained by flash column chromatography (petroleum ether [40-60]) as a colourless oil.

R_f = 0.23 (petroleum ether [40-60]). λ_{max} (cyclohexane) 235 and 265nm. ν_{max} (thin film, cm^{-1}) 3075 ($\text{H}_2\text{C}=\text{}$), 3027 ($\text{HC}=\text{}$), 1600 (aromatic stretch). δ_{H} (400MHz, C_6D_6) 0.09 (3H, s, OSiCH_3), 0.11 (3H, s, OSiCH_3), 1.07 (9H, s, $\text{OSiC}(\text{CH}_3)_3$), 1.22- 1.33 (1H, m, one of

CH₂CH₂CH=CH₂), 1.33- 1.46 (2H, m, one of CH₂CH(Ar) and one of CH₂CHOTBDMS), 1.45- 1.53 (1H, m, one of CH₂CH₂CH(Ar)), 1.52- 1.63 (1H, m, one of CH₂CH₂CH=CH₂), 1.65 (1H, app. bs, CH(C₄H₇)), 1.78- 1.93 (3H, m, one of CH₂CH=CH₂, one of CH₂CH(Ar) and one of CH₂CHOTBDMS), 1.93-2.11 (2H, m, one of CH₂CH₂CH(Ar) and one of CH₂CH=CH₂), 3.36 (3H, s, OCH₃), 3.63 (1H, app. bs, CH(Ar)), 4.07- 4.10 (1H, m, CHOTBDMS), 4.88 (1H, app. ddt, *J* 10.5, 2.0 and 1.0Hz, CH=CH₂ (*cis*-H)), 4.95 (1H, app. dq, *J* 17.0 and 2.0Hz, CH=CH₂ (*trans*-H)), 5.64 (1H, app. ddt, *J* 17.0, 10.5 and 6.5Hz, CH=CH₂), 6.59 (1H, dd, *J* 1.0 and 8.0Hz, CH=COCH₃), 6.93 (1H, app. t, *J* 7.5Hz, CHCHCH=COCH₃), 7.07 (1H, ddd, *J* 2.0, 7.5 and 8.0Hz, CHCH=COCH₃), 7.17 (1H, dd, *J* 2.0 and 7.5Hz, CHC(CH)=COCH₃). δ_c (100MHz, C₆D₆) -4.9 and -3.8 (OSiCH₃ and OSiCH₃), 18.5 (OSiC(CH₃)₃), 20.9 (CH₂CH₂CHOTBDMS), 26.2 (OSiC(CH₃)₃), 28.0 (CH₂CH₂CH=CH₂), 31.6 (CH₂CH=CH₂), 34.5 (CH₂CH(Ar) and CH₂CHOTBDMS), 34.6 (CH(Ar)), 46.0 CH(CH₂)₂CH=CH₂), 55.0 (OCH₃), 68.3 (CHOTBDMS), 110.9 (CH=COCH₃), 114.3 (CH=CH₂), 121.1 (CHCHCH=COCH₃), 126.8 (CHCH=COCH₃), 128.2 (CHC(CH)=COCH₃), 134.9 (C(CH)=COCH₃), 139.3 (CH=CH₂), 158.0 (COCH₃). *m/z* (CI, NH₃, high resolution) found 375.2730 [C₂₃H₃₈O₂ Si] ((MH)⁺, 17%) [requires 375.2720], 317.1927 (100), 243.1993 (56), 201.1372 (15), 147.0193 (34), 121.0662 (58), 74.9939 (40).

e. (±) (1*S*, 2*R*, 3*S*)-2-But-3'-enyl-3-(2''-methoxyphenyl)cyclohexanol (**8**)^[15]



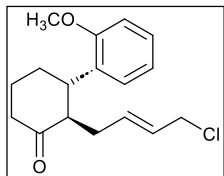
General Procedure B

To a stirred solution of the protected alkene (±) [(1*S*, 2*R*, 3*S*)-2-but-3'-enyl-3-(2''-methoxyphenyl)cyclohexyloxy]tert-butyl-dimethylsilane (0.045g, 0.12mmol) in anhydrous THF (2ml) was added tetrabutylammonium fluoride 1M solution in THF (0.40ml, 0.40mmol) drop-wise, under nitrogen. The reaction mixture was heated to 50°C and left to stir for 146 hours until TLC indicated that no more starting material was being consumed. The reaction mixture was quenched with water (20ml) before being transferred to a separating funnel where the aqueous layer was extracted with diethyl ether (3x20ml). The combined organic extracts were washed with saturated NaCl solution (20ml) and then water (20ml). The organic layer was dried over MgSO₄, filtered and concentrated *in vacuo* to give a crude oil. Pure (±) (1*S*, 2*R*, 3*S*)-2-but-3'-enyl-3-(2''-methoxyphenyl)cyclohexanol (**8**) (0.030g, 94%) was obtained by flash column chromatography (90:10 petroleum ether [40-60]/ ethyl acetate) as a colourless oil.

$R_f = 0.23$ (90:10 petroleum ether [40-60]/ ethyl acetate). λ_{\max} (cyclohexane) 228 and 272nm ($48 \text{ M}^{-1}\text{cm}^{-1}$). ν_{\max} (thin film, cm^{-1}) 3422 (OH), 3072 ($\text{H}_2\text{C}=\text{C}$), 1598 (aromatic stretch). δ_{H} (400MHz, C_6D_6) 0.90 (1H, bs, CHOH), 1.28- 1.48 (4H, m, one of $\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$, one of CH_2CHOH , one of $\text{CH}_2\text{CH}(\text{Ar})$ and one of $\text{CH}_2\text{CH}_2\text{CHOH}$), 1.52- 1.63 (1H, m, one of $\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$), 1.63- 1.77 (2H, m, $\text{CH}(\text{C}_4\text{H}_7)$ and one of CH_2CHOH), 1.81- 1.95 (3H, m, one of $\text{CH}_2\text{CH}(\text{Ar})$, one of $\text{CH}_2\text{CH}=\text{CH}_2$ and one of $\text{CH}_2\text{CH}_2\text{CHOH}$), 2.01- 2.11 (1H, m, one of $\text{CH}_2\text{CH}=\text{CH}_2$), 3.33 (3H, s, OCH_3), 3.60 (1H, app. bs, $\text{CH}(\text{Ar})$), 3.92 (1H, app. bd, J 2.0Hz, CHOH), 4.86- 4.97 (2H, m, $\text{CH}=\text{CH}_2$), 5.58- 5.69 (1H, m, $\text{CH}=\text{CH}_2$), 6.59 (1H, dd, J 1.0 and 7.5Hz, $\text{CH}=\text{COCH}_3$), 6.93 (1H, dt, J 1.0 and 7.5Hz, $\text{CHCHCH}=\text{COCH}_3$), 7.07 (1H, dt, J 2.0 and 7.5Hz, $\text{CHCH}=\text{COCH}_3$), 7.15 (1H, dd, J 2.0 and 7.5Hz, $\text{CHC}(\text{CH})=\text{COCH}_3$). δ_{C} (100MHz, C_6D_6) 20.6 ($\text{CH}_2\text{CH}_2\text{CHOH}$), 28.7 ($\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$), 31.3 ($\text{CH}_2\text{CH}=\text{CH}_2$), 34.1 (CH_2CHOH and $\text{CH}_2\text{CH}(\text{Ar})$), 35.0 ($\text{CH}(\text{Ar})$), 45.0 ($\text{CH}(\text{C}_4\text{H}_7)$), 54.9 (OCH_3), 66.7 (CHOH), 110.9 ($\text{CH}=\text{COCH}_3$), 114.3 ($\text{CH}=\text{CH}_2$), 121.0 ($\text{CHCHCH}=\text{COCH}_3$), 126.8 ($\text{CHCH}=\text{COCH}_3$), 128.6 ($\text{CHC}(\text{CH})=\text{COCH}_3$), 134.7 ($\text{C}(\text{CH})=\text{COCH}_3$), 139.4 ($\text{CH}=\text{CH}_2$), 157.9 (COCH_3). m/z (CI, NH_3 , high resolution) found 260.1787 [$\text{C}_{17}\text{H}_{24}\text{O}_2$] ($(\text{M})^+$, 63%) requires [260.1776], 201.1253 (37), 134.0834 (32), 121.0822 (100).

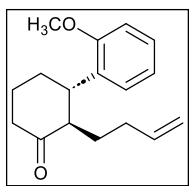
Synthesis of the 4-carbon tether substrate (**8**) Route B

- a. (\pm) (2*R*,3*S*)-2-((*E*)-4-chlorobut-2-en-1-yl)-3-(2-methoxyphenyl)cyclohexan-1-one
– novel



To a stirred solution of the [*3*-(2'-methoxyphenyl)cyclohex-1-enyloxy]trimethylsilane (**10**) (0.70 g, 2.53 mmol) in anhydrous THF (30 ml) was added a 1.6 M solution of methyllithium in Et₂O (1.70 ml, 2.79 mmol). TLC confirmed cleavage of the silyl enol ether after 5 minutes. The reaction flask was then cooled to -78 °C before a solution of 1-chloro-4-iodobut-2-ene (2.2 g, 10.13 mmol) in THF (10ml) was added drop-wise. The reaction was then allowed to warm to room temperature over 3 hours. TLC indicated completion of the reaction after 15 hours and the mixture was quenched with ethyl acetate (50 ml) and water (50 ml). The aqueous layer was extracted with ethyl acetate (3×50ml) then the combined extracts were washed with saturated NaCl solution (50 ml), dried over anhydrous MgSO₄, filtered and concentrated *in vacuo* to afford a pale brown oil. The crude product was purified using flash column chromatography (80%:20%) petroleum ether [40-60]/ ethyl acetate) to afford (\pm) (2*R*,3*S*)-2-((*E*)-4-chlorobut-2-en-1-yl)-3-(2-methoxyphenyl)cyclohexan-1-one as a pale-brown oil (0.40g, 58%).

R_f = 0.45 (80%:20%) petroleum ether [40-60]/ ethyl acetate). IR (thin film) ν_{\max} / cm⁻¹ = 2936 brm, 2863w, 1705s (CO), 1599w, 1586w, 1492m, 1463m, 1438m, 1344w, 1290w, 1241s, 1175w, 1118w 1051m, 1027m, 972m, 751s, 737m, 674m; ¹H NMR (400 MHz, CDCl₃) δ 7.21 (td, J = 8.2, 1.1 Hz, 1H, Ar-H), 7.16 (dd, J = 7.6, 1.7 Hz, 1H, Ar-H), 6.95 (td, J = 7.5, 1.1 Hz, 1H, Ar-H), 6.87 (dd, J = 8.2, 1.2 Hz, 1H, Ar-H), 5.66 (m, 1H, CH₂CH=), 5.30 (m, , 1H, ClCH₂CH=), 3.90 (dd, J = 7.2, 1.0 Hz, 2H, CH₂Cl), 3.81 (s, 3H, CH₃O), 3.17 (td, J = 11.7, 4.1 Hz, 1H, CH-Ar), 2.87 (td, J = 11.0, 2.8 Hz, 1H, CHCO), 2.51 – 2.42 (m, 2H, CH₂CO), 2.20 (app dt, J = 14.8, 7.4 Hz, 1H, 1 of CH₂-CH=), 2.11 (m, 1H, CH₂), 2.02 – 1.89 (m, 3H), 1.75 (m, 1H, CH₂CH₂C=O); ¹³C NMR (101 MHz, CDCl₃) δ 211.90 (CO), 157.22 (COCH₃), 134.18 (CH₂CH=), 131.25 (C), 128.0 (Ar-H), 127.74 (Ar-H), 127.15 (ClCH₂CH=), 120.90 (Ar-H), 110.93 (Ar-H), 55.42 (CH₃O), 54.51 (COCH), 45.58 (CH₂Cl), 44.41 (CH-Ar), 42.43 (CH₂C=O), 32.96 (CH₂CH₂CH₂C=O), 29.46 (CH₂-CH=), 26.59 (CH₂CH₂C=O); HRMS ([M + H]⁺, +ESI) m/z C₁₇H₂₂O₂³⁵Cl = calculated 293.1303, found 293.1304; HRMS ([M + H]⁺, +ESI) m/z C₁₇H₂₂O₂³⁷Cl = calculated 295.1273, found 295.1275;

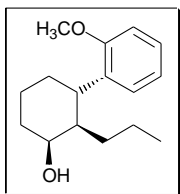
b. (\pm) (2*R*,3*S*)-2-(But-3-en-1-yl)-3-(2-methoxyphenyl)cyclohexan-1-one (**13**) – novel

To palladium (II) acetate (0.026g, 0.115 mmol) and HCO₂NH₄ (0.266g, 4.21 mmol) in toluene (25 mL), *n*-Bu₃P (1.6 ml, 0.860 mmol) was added at 23 °C. The light-yellow solution turned to dark yellow over the course of 10 minutes at which point a solution of (\pm) (2*R*,3*S*)-2-((*Z*)-4-chlorobut-2-en-1-yl)-3-(2-methoxyphenyl)cyclohexan-1-one (0.57g, 1.91 mmol) in toluene (10 mL) was added *via* cannula. The resulting suspension was heated at 105 °C until TLC analysis revealed consumption of the allyl chloride after 18 hours and the mixture was quenched with ethyl acetate (50 ml) and water (50 ml). The aqueous layer was extracted with ethyl acetate (2×50 ml). The combined extracts were dried over anhydrous MgSO₄, filtered and concentrated *in vacuo* to afford a yellow oil. The crude product was purified using flash column chromatography (70:30 petroleum ether [40-60]/ ethyl acetate) to afford (\pm) (2*R*,3*S*)-2-(but-3-en-1-yl)-3-(2-methoxyphenyl)cyclohexan-1-one (**13**) as a pale-yellow oil (0.30g, 60%).

R_f = 0.80 (70:30 petroleum ether [40-60]/ ethyl acetate). IR (thin film) ν_{\max} / cm⁻¹ = 2931brm, 1708s (CO), 1597w, 1493m, 1463m, 1290w, 1242s, 1174w, 1053w, 1029m, 909w, 753m; ¹H NMR (400 MHz, CDCl₃) δ 7.24 – 7.16 (m, 2H, Ar-H), 6.95 (td, J = 7.5, 1.2 Hz, 1H, Ar-H), 6.87 (dd, J = 8.2, 1.1 Hz, 1H, Ar-H), 5.73 (ddt, J = 17.1, 10.2, 6.9 Hz, 1H, CH=CH₂), 4.83 (ddt, J = 10.1, 2.2, 1.1 Hz, 1H, C=CH₂), 4.75 (app. dq, J = 17.2, 1.6 Hz, 1H, C=CH₂), 3.80 (s, 3H, OCH₃), 3.21 (app. td, J = 11.7, 4.7 Hz, 1H, CH-Ar), 2.87 (ddd, J = 11.6, 8.1, 3.1 Hz, 1H, CHC=O), 2.50 – 2.44 (m, 2H, CH₂C=O), 2.23 (dddd, J = 14.2, 8.1, 6.9, 1.2 Hz, 1H, CH₂), 2.12 – 2.04 (m, 1H, CH₂), 1.99 – 1.89 (m, 3H, 3 of 2 x CH₂), 1.75 (m, 1H, 1 of 2 x CH₂); ¹³C NMR (101 MHz, CDCl₃) δ 212.73 (CO), 157.14 (C-OMe), 139.05 (vinyl-CH), 131.92 (C), 127.79 (Ar-H), 127.51 (Ar-H), 120.86 (Ar-H), 114.44 (vinyl-CH₂), 110.89 (Ar-H), 55.43 (CH₃O), 53.91 (CHC=O), 44.33 (br, CH-Ar), 42.63 (CH₂C=O), 33.10 (CH₂), 31.90 (CH₂), 26.80 (CH₂), 25.89 (CH₂); HRMS ([M + H]⁺, +ESI) m/z C₁₇H₂₃O₂ = calculated 259.1693, found 259.1694.

Synthesis of substrates for fluorescence comparison

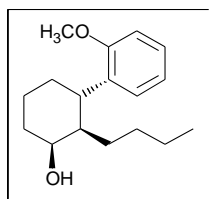
a. (\pm) (1*S*, 2*R*, 3*S*)-3-(2'-Methoxyphenyl)-2-propylcyclohexanol – novel



General Procedure C

To a round-bottomed flask was added (\pm) (1*S*, 2*R*, 3*S*)-2-allyl-3-(2'-methoxyphenyl)cyclohexanol (**8**) (0.043g, 0.17mmol) in anhydrous methanol (2ml) under argon. To the stirred solution was added a catalytic amount of 10% palladium on carbon. The flask was then evacuated before being filled with hydrogen. The reaction mixture was vigorously stirred under a positive pressure of hydrogen for 70 minutes until TLC indicated that the reaction had run to completion. The reaction mixture was filtered through celite and the filtrate concentrated *in vacuo* to give white star crystals of pure (\pm) (1*S*, 2*R*, 3*S*)-3-(2'-methoxyphenyl)-2-propylcyclohexanol (0.043g, 99%).

Mp. 65-67 °C. R_f = 0.64 (70:30 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 227 and 272nm. ν_{max} (KBr disc, cm^{-1}) 3268 (OH), 1599 (aromatic stretch). δ_H (400MHz, C_6D_6) 0.74 (3H, t, J 7.0Hz, CH_2CH_3), 0.99 (1H, bs, $CHOH$), 1.02- 1.14 (1H, m, one of CH_2CH_3), 1.14- 1.25 (1H, m, one of $CH_2CH_2CH_3$), 1.28- 1.52 (6H, m, one of CH_2CH_3 , $CH_2CH(Ar)$, one of CH_2CHOH , one of $CH_2CH_2CH_3$ and one of CH_2CH_2CHOH), 1.73- 1.81 (1H, m, one of CH_2CHOH), 1.85- 1.98 (2H, m, one of CH_2CH_2CHOH and $CH(C_3H_7)$), 3.35 (3H, s, OCH_3), 3.60 (1H, app. bs, $CH(Ar)$), 3.95 (1H, app. bd, J 2.5Hz, $CHOH$), 6.60 (1H, d, J 8.0Hz, $CH=COCH_3$), 6.95 (1H, t, J 8.0Hz, $CHCHCH=COCH_3$), 7.08 (1H, dt, J 1.5 and 8.0Hz, $CHCH=COCH_3$), 7.16 (1H, dd, J 1.5 and 8.0Hz, $CHC(CH)=COCH_3$). δ_C (100MHz, C_6D_6) 14.4 (CH_2CH_3), 20.2 (CH_2CH_3), 20.7 (CH_2CH_2CHOH), 30.2 ($CH_2CH(Ar)$), 31.7 ($CH_2CH_2CH_3$), 34.1 (CH_2CHOH), 35.0 ($CH(Ar)$), 45.6 ($CH(C_3H_7)$), 54.9 (OCH_3), 66.9 ($CHOH$), 110.9 ($CH=COCH_3$), 121.0 ($CHCHCH=COCH_3$), 126.8 ($CHCH=COCH_3$), 128.2 ($CHC(CH)=COCH_3$), 134.9 ($C(CH)=COCH_3$), 157.9 ($COCH_3$). m/z (EI, high resolution) found 248.1775 [$C_{16}H_{24}O_2$] ($(M)^+$, 66%) [requires 248.1776], 280.9819 (44), 230.9854 (100).

b. (\pm) (1*S*, 2*R*, 3*S*)-2-Butyl-3-(2'-methoxyphenyl)cyclohexanol^[15]

Substrate was synthesised according to general procedure C using (\pm) (1*S*, 2*R*, 3*S*)-2-but-3'-enyl-3-(2''-methoxyphenyl)cyclohexanol (**8**) (0.030g, 0.12mmol) in anhydrous methanol (2ml), a catalytic amount of 10% palladium on carbon and excess hydrogen. After 70 minutes of reaction the mixture was filtered through celite and the filtrate concentrated *in vacuo* to afford the pure (\pm) (1*S*, 2*R*, 3*S*)-2-butyl-3-(2'-methoxyphenyl)cyclohexanol (0.028g, 91%) as a yellow oil.

R_f = 0.64 (70:30 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 222 and 273nm. ν_{max} (thin film, cm^{-1}) 3417 (OH), 1599 (aromatic stretch). δ_H (400MHz, C_6D_6) 0.78 (3H, t, J 7.0Hz, CH_2CH_3), 1.00- 1.17 (3H, m, CH_2CH_3 and one of $CH_2CH_2CH_3$), 1.17- 1.52 (7H, m, $CH_2(CH_2)_2CH_3$, one of $CH_2CH_2CH_3$, $CH_2CH(Ar)$, one of CH_2CHOH , and one of CH_2CH_2CHOH), 1.74- 1.81 (1H, m, one of CH_2CHOH), 1.85- 1.95 (2H, m, one of CH_2CH_2CHOH and $CH(C_4H_9)$), 3.34 (3H, s, OCH_3), 3.60 (1H, app. bs, $CH(Ar)$), 3.96 (1H, app. bd, J 2.5Hz, $CHOH$), 6.60 (1H, d, J 8.0Hz, $CH=COCH_3$), 6.95 (1H, t, J 8.0Hz, $CHCHCH=COCH_3$), 7.08 (1H, dt, J 1.5 and 8.0Hz, $CHCH=COCH_3$), 7.16 (1H, dd, J 1.5 and 8.0Hz, $CHC(CH)=COCH_3$). δ_C (100MHz, C_6D_6) 14.3 (CH_2CH_3), 20.7 (CH_2CH_2CHOH), 23.1 (CH_2CH_3), 29.0 ($CH_2(CH_2)_2CH_3$), 29.4 ($CH_2CH_2CH_3$), 30.2 ($CH_2CH(Ar)$), 34.1 (CH_2CHOH), 35.0 ($CH(Ar)$), 45.6 ($CH(C_4H_9)$), 54.9 (OCH_3), 66.9 ($CHOH$), 110.9 ($CH=COCH_3$), 121.0 ($CHCHCH=COCH_3$), 126.8 ($CHCH=COCH_3$), 128.6 ($CHC(CH)=COCH_3$), 134.9 ($C(CH)=COCH_3$), 157.9 ($COCH_3$). m/z (EI, high resolution) found 262.1933 [$C_{17}H_{26}O_2$] ($(M)^+$, 26%) [requires 262.1933], 280.9818 (45), 242.9861 (50), 230.9860 (100).

Photolysis of the 3-carbon tether substrate (7)

1) Falling film

General Procedure D

A 8.3mM solution of (\pm) (1*S*, 2*R*, 3*S*)-2-allyl-3-(2'-methoxyphenyl)cyclo-hexanol (7) was prepared by dissolving 0.204g (0.83mmol) of the substrate in 100ml of cyclohexane. The flask was connected to a condenser and placed inside a thin-film photoreactor containing a low-pressure mercury arc lamp. The photoreactor pump was initiated and the system was completely de-gassed by bubbling nitrogen through the solution for 1 hour. After this time the flow of nitrogen was stopped and the lamp was switched on. After 1 hour of photoreaction TLC and NMR indicated that no more starting material remained and that four major photoproducts appeared to have formed. The reaction mixture was transferred to a separate flask before the system was thoroughly washed through with cyclohexane (4x50ml). All the washings were collected together and concentrated *in vacuo* to give a crude yellow oil. The three major products were separated from all the reaction by-products and then purified using flash column chromatography by gradually increasing the solvent polarity (95:5→90:10→85:15 petroleum ether [40-60]/ ethyl acetate).

2) Flow Photochemistry Recirculation Optimisation

A 4 mM solution of (\pm) (1*S*, 2*R*, 3*S*)-2-allyl-3-(2'-methoxyphenyl)cyclo-hexanol (7) was prepared by dissolving (0.020 g, 0.081mmol) of the substrate in 20 ml of cyclohexane. The flask was connected to the flow system by threading the input and output tubes through a red rubber septa. The flow system using consists of a Vapourtec peristaltic pump, a cyclohexane-filled 10 mL reactor placed around a 25 W germicide lamp inside a light box with a gentle flow of compressed air for cooling (not essential). The pump flow rate was set to recirculate at 5 mL and the solvent was degassed by bubbling N₂ for 20 minutes. A balloon was then used to keep the flask under a positive pressure of N₂. The lamp was switched on and the reaction was analysed periodically. After 1h30, TLC and NMR indicated that no more starting material remained. The reactor was flushed with cyclohexane, concentrated *in vacuo* and then purified using flash column chromatography.

The ATOI ratio for this experiment was 0.33

$$ATOI\ ratio = \frac{Vol\ reactor}{Vol\ solvent\ used} = \frac{10}{10 + 20} = 1/3 \approx 0.33$$

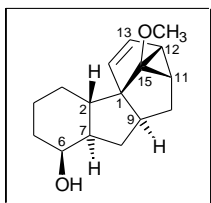
Hence **ATOI / Actual Time Of Irradiation = 30 minutes.**

3) Flow Photochemistry Continuous Flow / One Pass Manner

The flask containing a 4mM solution of (\pm) (1*S*, 2*R*, 3*S*)-2-allyl-3-(2'-methoxyphenyl)cyclohexanol (**7**) in cyclohexane was connected to the flow system by threading the input tube through a red rubber septa and the output went into the collection flask. The flow system using consists of a Vapourtec peristaltic pump, and a 10 mL reactor placed around a 25 W germicide lamp inside a light box with a gentle flow of compressed air for cooling (not essential). The reaction mixture was degassed by bubbling N₂ for 20 minutes and then a balloon was used to keep the flask under a positive pressure of N₂. As the **ATOI / Actual Time Of Irradiation** for this 10 mL reactor system was known (30 minutes), the reaction was then performed in a continuous manner with a residence time of 30 minutes by flowing at 0.3 mL/min (10 mL / 30 minutes).

a. (\pm) (1*S*, 2*S*, 6*S*, 7*R*, 9*S*, 11*S*, 12*R*, 15*R*)-15-Methoxypentacyclo[10.2.1.0^{1,9}.0^{2,7}.0^{11,15}]pentadec-13-en-6-ol (**14**) – novel

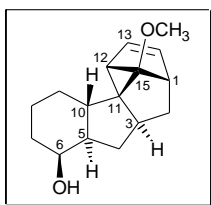
Fraction 3 was identified as the pure colourless oil (0.044g, 21%)



$R_f = 0.15$ (85:15 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 196, 222 and 274nm. ν_{max} (thin film, cm⁻¹) 3445 (OH). δ_H (400MHz, CDCl₃) 1.26- 1.37 (1H, m, one of CH₂CHCHOH), 1.38- 1.59 (3H, m, one of CH₂CHOH, one of CH₂CHCHOH and CHCHCHOH), 1.62- 1.88 (7H, m, CH₂CHCHCHOH, CH₂CHCHCH=CH, CH₂CH₂CHOH and one of CH₂CHOH), 2.03 (1H, ddd, J 1.0, 2.5 and 8.5Hz, CHCH=CH), 2.05- 2.14 (1H, m, CHCH₂CHCHOH), 2.21 (1H, app. dd, J 8.5 and 6.0Hz, CHCHCH=CH), 2.40 (1H, app. dt, J 3.0 and 12.5Hz, CHCHOH), 3.27 (3H, s, OCH₃), 4.15 (1H, app. bs, CHOH), 5.52 (1H, dd, J 2.5 and 5.5Hz, CHCH=CH), 5.66 (1H, app. d, J 5.5Hz, CHCH=CH). δ_C (100MHz, CDCl₃) 22.0 (CH₂CH₂CHOH), 27.0 (CH₂CHCHCH=CH), 29.5 (CH₂CHCHCHOH), 32.3 (CH₂CHCHOH), 33.2 (CH₂CHOH), 34.7 (CHCHOH), 35.1 (CHCH=CH), 41.0 (CHCHCH=CH), 54.2 (CHCHCHOH), 56.5 (OCH₃), 60.1 (CHCH₂CHCHOH), 67.9 (COCH₃), 68.5 (CHOH), 91.5 (COCH₃), 124.2 (CHCH=CH), 136.2 (CHCH=CH). m/z (EI, high resolution) found 246.1617 [C₁₆H₂₂O₂] ((M)⁺, 46%) [requires 246.1620], 280.9817 (47), 230.9854 (100).

b. (±) (1*S*, 3*S*, 5*R*, 6*S*, 10*S*, 11*S*, 12*R*, 15*R*)-15-Methoxypentacyclo[10.2.1.0^{3,11}.0^{5,10}.0^{11,15}]pentadec-13-en-6-ol (**15**) – novel

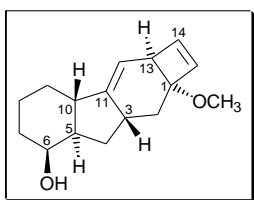
Fraction 2 contained the pure colourless oil (0.063g, 31%).



$R_f = 0.20$ (85:15 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 196 and 218nm. ν_{max} (thin film, cm^{-1}) 3422 (OH). δ_H (400MHz, CD_3OD) 1.09- 1.20 (1H, m, one of $\underline{CH_2}CHCHOH$), 1.42- 1.52 (1H, m, one of $\underline{CH_2}CHCHCHOH$), 1.55- 1.65 (1H, m, one of $\underline{CH_2}CHOH$), 1.65- 1.86 (4H, m, $\underline{CH_2}CH_2CHOH$, one of $\underline{CH_2}CHCHOH$ and $\underline{CH}CHCHOH$), 1.86- 1.98 (4H, m, $\underline{CH}CH_2CHCH=CH$, one of $\underline{CH_2}CHCH=CH$, one of $\underline{CH_2}CHOH$ and one of $\underline{CH_2}CHCHCHOH$), 2.19- 2.29 (2H, m, one of $\underline{CH_2}CHCH=CH$ and $\underline{C}CHCH=CH$), 2.35 (1H, app. dt, J 12.0 and 3.0Hz, one of $\underline{CH}CHOH$), 3.43- 3.47 (1H, m, $\underline{CH_2}CHCH=CH$), 3.53 (3H, s, $\underline{OCH_3}$), 4.14- 4.18 (1H, m, \underline{CHOH}), 5.70 (1H, ddd, J 1.5, 2.5 and 5.5Hz, $\underline{CH_2}CHCH=CH$), 5.74 (1H, dd, J 2.5 and 5.5Hz, $\underline{CH_2}CHCH=CH$). δ_C (100MHz, CD_3OD) 22.5 ($\underline{CH_2}CH_2CHOH$), 31.9 ($\underline{CH_2}CHCHOH$), 35.3 ($\underline{CH_2}CHOH$), 36.1 ($\underline{CH}CHOH$), 36.4 ($\underline{CH_2}CHCHCHOH$), 39.2 ($\underline{C}CHCH=CH$), 45.4 ($\underline{CH}CH_2CHCH=CH$), 45.5 ($\underline{CH_2}CHCH=CH$), 56.6 ($\underline{CH_2}CHCH=CH$ and $\underline{COCH_3}$), 57.4 ($\underline{CH}CHCHOH$), 57.8 ($\underline{OCH_3}$), 69.8 (\underline{CHOH}), 89.2 ($\underline{COCH_3}$), 129.5 ($\underline{CH_2}CHCH=CH$), 134.5 ($\underline{CH_2}CHCH=CH$). m/z (CI, NH_3 , high resolution) found 247.1704 [$C_{16}H_{22}O_2$] ($(MH)^+$, 22%) [requires 247.1698], 215.1396 (100), 197.1553 (49).

c. (±) (1*S*, 3*S*, 5*R*, 6*S*, 10*S*, 13*R*)-1-Methoxytetracyclo[11.2.0^{1,13}.0^{3,11}.0^{5,10}]pentadec-11,14-dien-6-ol (**16**) – novel

Fraction 1 was found to contain the pure cream coloured solid (0.044g, 22%).

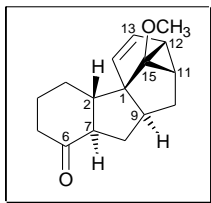


Mp. 83-86 °C. $R_f = 0.24$ (85:15 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 197 and 275nm. ν_{max} (KBr disc, cm^{-1}) 3322 (OH). δ_H (400MHz, $CDCl_3$) 0.99- 1.10 (1H, m, one of $\underline{CH_2}CHCHCHOH$), 1.18- 1.26 (1H, m, one of $\underline{CH_2}COCH_3$), 1.32- 1.48 (3H, m, $\underline{CH}CHOH$, one of $\underline{CH_2}CHCHOH$ and one of $\underline{CH_2}CHOH$), 1.56- 1.64 (2H, m, $\underline{CH_2}CH_2CHOH$), 1.81- 1.93 (2H, m, one of $\underline{CH_2}CHOH$ and one of $\underline{CH_2}CHCHOH$), 1.96- 2.03 (1H, m, one of $\underline{CH_2}CHCHCHOH$), 2.05 (1H, dd, J 5.0 and 12.0Hz, one of $\underline{CH_2}COCH_3$), 2.16- 2.26 (1H, m, $\underline{CH}CHCHOH$), 2.28- 2.38 (1H, m, $\underline{CH}CH_2COCH_3$), 3.28- 3.31 (1H, m, $\underline{CH}CH=CH$), 3.33 (3H, s, $\underline{OCH_3}$), 4.08- 4.11 (1H, m, \underline{CHOH}), 5.33- 5.37 (1H, m,

$\text{CH}=\text{C}(\text{CH})_2$), 6.09 (1H, dd, J 0.5 and 3.0Hz, $\text{CHCH}=\text{CH}$), 6.11 (1H, app. dt, J 3.0 and 1.0Hz, $\text{CHCH}=\text{CH}$). δ_c (100MHz, CDCl_3) 19.5 ($\text{CH}_2\text{CH}_2\text{CHOH}$), 28.2 ($\text{CH}_2\text{CHCHCHOH}$), 30.7 (CH_2CHCHOH), 33.2 ($\text{CHCH}_2\text{COCH}_3$), 33.6 (CH_2CHOH), 37.6 (CH_2COCH_3), 41.9 (CHCHCHOH), 46.4 ($\text{CHCH}=\text{CH}$), 48.5 (CHCHOH), 51.7 (OCH_3), 67.5 (CHOH), 84.8 (COCH_3), 113.4 ($\text{CH}=\text{C}(\text{CH})_2$), 136.0 ($\text{CHCH}=\text{CH}$), 139.3 ($\text{CHCH}=\text{CH}$), 154.1 ($\text{CH}=\text{C}(\text{CH})_2$). m/z (CI, NH_3 , high resolution) found 247.1702 [$\text{C}_{16}\text{H}_{22}\text{O}_2$] ($(\text{MH})^+$, 12%) [requires 247.1698], 232.2001 (52), 215.1418 (100).

Identification of 3-carbon tether cycloadducts

- a. (\pm) (1*S*, 2*S*, 7*R*, 9*S*, 11*S*, 12*R*, 15*R*)-15-Methoxypentacyclo-[10.2.1.0^{1,9}.0^{2,7}.0^{11,15}]pentadec-13-en-6-one (**17**)^[15]

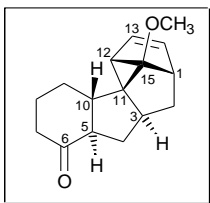


Cycloadduct (**17**) was synthesised according to general procedure E from a solution of the compound (\pm) (1*S*, 2*S*, 6*S*, 7*R*, 9*S*, 11*S*, 12*R*, 15*R*)-15-methoxypentacyclo-[10.2.1.0^{1,9}.0^{2,7}.0^{11,15}]pentadec-13-en-6-ol (**14**) (0.064g, 0.26mmol) in dry DCM (2ml) and pyridinium chlorochromate (0.100g, 0.55mmol) in anhydrous DCM (2x1ml).

The reaction mixture was stirred for 1 hour under argon until TLC indicated that no more starting material remained. Flash column chromatography (80:20 petroleum ether [40-60]/ ethyl acetate) yielded the pure semi-solid *meta* cycloadduct ketone (\pm) (1*S*, 2*S*, 7*R*, 9*S*, 11*S*, 12*R*, 15*R*)-15-methoxypenta-cyclo[10.2.1.0^{1,9}.0^{2,7}.0^{11,15}]pentadec-13-en-6-one (**17**) (0.028g, 44%).

Mp. 85-88 °C. R_f = 0.22 (80:20 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 194, 216 and 282nm. ν_{max} (KBr disc, cm⁻¹) 1712 (C=O). δ_H (400MHz, CDCl₃) 1.55- 1.74 (4H, m, CH₂CHC=O, one of CH₂CHCHC=O and one of CH₂CHCHCH=CH), 1.74- 1.85 (1H, m, one of CH₂CH₂C=O), 1.87 (1H, ddd, *J* 1.0, 6.0 and 14.0Hz, one of CH₂CHCHCH=CH), 1.92- 1.99 (1H, m, one of CH₂CHCHC=O), 2.05 (1H, dd, *J* 2.5 and 8.5Hz, CHCH=CH), 2.10- 2.28 (3H, m, CHCH₂CHC=O, one of CH₂CH₂C=O and CHCHCH=CH), 2.28- 2.40 (3H, m, CH₂C=O and CHCHC=O), 2.44 (1H, dt, *J* 4.5 and 12.0Hz, CHC=O), 3.21 (3H, s, OCH₃), 5.58 (1H, dd, *J* 2.5 and 5.5Hz, CHCH=CH), 5.71 (1H, d, *J* 5.5Hz, CHCH=CH). δ_C (100MHz, CDCl₃) 26.8 (CH₂CHCHCH=CH), 27.9 (CH₂CH₂C=O), 28.6 (CH₂CHCHC=O), 29.3 (CH₂CHC=O), 35.2 (CHCH=CH), 40.7 (CHCHCH=CH), 40.9 (CH₂C=O), 45.1 (CHCHC=O), 56.4 (OCH₃), 59.6 (CHCH₂CHC=O), 61.4 (CHC=O), 68.0 (C=O), 91.3 (COCH₃), 125.1 (CHCH=CH), 135.0 (CHCH=CH), 210.7 (C=O). *m/z* (CI, NH₃, high resolution) found 245.1552 [C₁₆H₂₀O₂] ((MH)⁺, 16%) [requires 245.1542], 212.9707 (100), 146.9782 (43).

b. (\pm) (1*S*, 3*S*, 5*R*, 10*S*, 11*S*, 12*R*, 15*R*)-15-Methoxypentacyclo[10.2.1.0^{3,11}.0^{5,10}.0^{11,15}]pentadec-13-en-6-one – novel

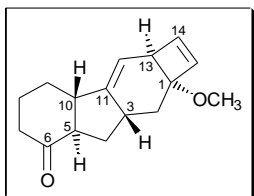


Prepared according to general procedure E from a solution of cycloadduct (\pm) (1*S*, 3*S*, 5*R*, 6*S*, 10*S*, 11*S*, 12*R*, 15*R*)-15-methoxypentacyclo[10.2.1.0^{3,11}.0^{5,10}.0^{11,15}]-pentadec-13-en-6-ol (**15**) (0.050g, 0.20mmol) in anhydrous DCM (1ml) and pyridinium chlorochromate (0.112g, 0.61mmol) in anhydrous DCM (2x1ml).

After 1.5 hours of stirring under argon, TLC indicated that the reaction had run to completion. Pure *meta* cycloadduct ketone (\pm) (1*S*, 3*S*, 5*R*, 10*S*, 11*S*, 12*R*, 15*R*)-15-methoxypentacyclo[10.2.1.0^{3,11}.0^{5,10}.0^{11,15}]-pentadec-13-en-6-one was obtained by flash column chromatography (90:10 petroleum ether [40-60]/ ethyl acetate) as a yellow coloured crystalline solid (0.039g, 77%).

Mp. 62-64 °C. R_f = 0.22 (90:10 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 198, 218 and 275nm. ν_{max} (KBr disc, cm^{-1}) 1717 (C=O). δ_H (400MHz, CD₃OD) 1.53 (1H, app. dt, J 10.0 and 12.0Hz, one of $\underline{CH}_2CHC=O$), 1.67 (1H, app. dt, J 4.0 and 12.0Hz, one of $\underline{CH}_2CHCH=CH$), 1.79- 1.90 (1H, m, one of $\underline{CH}_2CH_2C=O$), 1.90- 2.02 (3H, m, one of $\underline{CH}_2CHCH=CH$ and $\underline{CH}_2CHCHC=O$), 2.19 (1H, ddd, J 5.0, 7.5 and 12.0Hz, one of $\underline{CH}_2CHC=O$), 2.30 (1H, app. dt, J 3.0 and 13.0Hz, $\underline{CH}CHC=O$), 2.31- 2.40 (2H, m, one of $\underline{CH}_2CH_2C=O$ and $\underline{CH}CH_2CHC=O$), 2.40- 2.47 (2H, m, $\underline{C}CHCH=CH$ and one of $\underline{CH}_2C=O$), 2.58 (1H, ddt, J 1.5, 7.0 and 14.0Hz, one of $\underline{CH}_2C=O$), 2.96 (1H, dddd, J 1.5, 5.0, 12.0 and 13.0Hz, $\underline{CH}C=O$), 3.50- 3.53 (1H, m, $\underline{CH}_2CHCH=CH$), 3.57 (3H, s, \underline{OCH}_3), 5.79 (1H, ddd, J 1.5, 2.5 and 5.5Hz, $\underline{CH}_2CHCH=CH$), 5.83 (1H, dd, J 2.5 and 5.5Hz, $\underline{C}CHCH=CH$). δ_C (100MHz, CD₃OD) 28.5 ($\underline{CH}_2CH_2C=O$), 29.8 ($\underline{CH}_2CHCH=CH$), 32.3 ($\underline{CH}_2CHC=O$), 38.8 ($\underline{C}CHCH=CH$), 41.9 ($\underline{CH}_2C=O$), 44.1 ($\underline{CH}CH_2CHC=O$), 44.7 ($\underline{CH}_2CHCHC=O$), 46.5 ($\underline{CH}CHC=O$), 54.8 ($\underline{C}CHCH=CH$), 55.5 ($\underline{CH}_2CHCH=CH$), 57.1 (\underline{OCH}_3), 62.8 ($\underline{CH}C=O$), 87.8 (\underline{COCH}_3), 128.2 ($\underline{C}CHCH=CH$), 134.0 ($\underline{CH}_2CHCH=CH$), 213.5 ($\underline{C}C=O$). m/z (CI, NH₃, high resolution) found 245.1537 [C₁₆H₂₀O₂] ((MH)⁺, 100%) [requires 245.1542], 207.0275 (24), 147.0860 (43), 56.0610 (33).

c. (±) (1*S*, 3*S*, 5*R*, 10*S*, 13*R*)-1-Methoxytetracyclo[11.2.0^{1,13}.0^{3,11}.0^{5,10}]-pentadec-11,14-dien-6-one – novel



General Procedure E

To an argon flushed round-bottomed flask containing a solution of cycloadduct alcohol (±) (1*S*, 3*S*, 5*R*, 6*S*, 10*S*, 13*R*)-1-methoxytetracyclo[11.2.0^{1,13}.0^{3,11}.0^{5,10}]pentadec-11,14-dien-6-ol (16) (0.089g, 0.36mmol) in anhydrous DCM (5ml) was added a solution of pyridinium chlorochromate (0.134g, 0.73mmol) in dry DCM (2x2ml) *via* syringe. On stirring, the reaction mixture turned dark brown as the insoluble reduced reagent was deposited. After 2 hours of stirring under argon, TLC indicated that no more starting material remained. The mixture was diluted with diethyl ether (15 ml), the solvent decanted, and the black solid washed with diethyl ether (3x20ml). The crude product was isolated simply by filtration of the combined organic washings through Florisil and evaporation of the solvent *in vacuo*. Flash column chromatography (95:5 petroleum ether [40-60]/ ethyl acetate) afforded the pure cycloadduct ketone (±) (1*S*, 3*S*, 5*R*, 10*S*, 13*R*)-1-methoxytetracyclo[11.2.0^{1,13}.0^{3,11}.0^{5,10}]pentadec-11,14-dien-6-one as a cream coloured crystalline solid (0.033g, 37%).

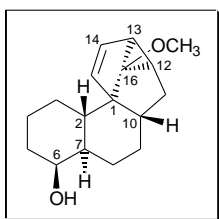
Mp. 66-68 °C. R_f = 0.24 (95:5 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 203nm. ν_{max} (KBr disc, cm^{-1}) 1710 (C=O). δ_H (400MHz, $CDCl_3$) 1.20 (1H, app. t, J 12.5Hz, one of CH_2COCH_3), 1.40- 1.52 (1H, m, one of $CH_2CHCHC=O$), 1.53 (1H, ddd, J 2.0, 6.0 and 13.0Hz, one of $CH_2CHC=O$), 1.65- 1.78 (1H, m, one of $CH_2CH_2C=O$), 2.05- 2.22 (4H, m, one of CH_2COCH_3 , one of $CH_2CHC=O$, one of $CH_2CHCHC=O$ and one of $CH_2CH_2C=O$), 2.23- 2.41 (5H, m, $CHCHC=O$, $CH_2C=O$, $CHC=O$ and $CHCH_2COCH_3$), 3.28- 3.33 (1H, m, $CHCH=CHCOCH_3$), 3.33 (3H, s, OCH_3), 5.45- 5.49 ($CH=C(CH)_2$), 6.08 (1H, dd, J 1.0 and 3.0Hz, $CH=CHCOCH_3$), 6.13 (1H, app. dt, J 3.0 and 1.0Hz, $CH=CHCOCH_3$). δ_C (100MHz, $CDCl_3$) 27.2 ($CH_2CH_2C=O$), 27.4 ($CH_2CHCHC=O$), 27.9 ($CH_2CHC=O$), 33.0 ($CHCH_2CHC=O$), 37.5 (CH_2COCH_3), 41.7 ($CH_2C=O$), 46.2 ($CHCH=CHCOCH_3$), 51.7 (OCH_3), 52.2 ($CHCHC=O$), 55.9 ($CHC=O$), 84.4 ($COCH_3$), 114.7 ($CH=C(CH)_2$), 136.2 ($CH=CHCOCH_3$), 139.0 ($CH=CHCOCH_3$), 151.7 ($CH=C(CH)_2$), 211.3 ($C=O$). m/z (EI, high resolution) found 244.1470 [$C_{16}H_{20}O_2$] ($(M)^+$, 2%) [requires 244.1463], 254.9849 (17), 230.9858 (100).

Photolysis of the 4-carbon tether substrate (**8**)

Photolysis of substrate (**8**) was carried out according to general procedure D. A 4.5mM solution of (\pm) (1*S*, 2*R*, 3*S*)-2-but-3'-enyl-3-(2''-methoxyphenyl)cyclo-hexanol (**8**) (0.118g, 0.45mmol) in cyclohexane (100ml) was irradiated for 1.5 hours until TLC and NMR spectroscopy indicated that no more starting material remained. Analysis also suggested that two major products had formed. All the washings from the thin film photoreactor were collected together and concentrated *in vacuo* to give a crude yellow oil. The two main photoproducts were separated from all the reaction by-products and then purified using flash column chromatography by gradually increasing the solvent polarity (95:5→90:10→85:15 petroleum ether [40-60]/ diethyl ether).

a. (\pm) (1*R*, 2*S*, 6*S*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-16-Methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-ol (**19**)^[15]

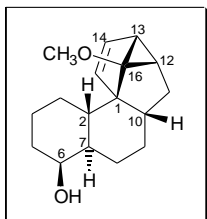
Fraction 1 was found to contain the pure colourless oil (0.048g, 40%).



$R_f = 0.27$ (90:10 dichloromethane/ petroleum ether [40-60]). λ_{\max} (cyclohexane) 224 and 287nm. ν_{\max} (thin film, cm^{-1}) 3432 (OH). δ_H (400MHz, CD_3OD) 1.34 (1H, dd, J 6.5 and 13.0Hz, one of $\text{CH}_2\text{CHCHCH}=\text{CH}$), 1.42- 1.56 (6H, m, CH_2CHCHOH , one of $\text{CH}_2\text{CH}_2\text{CHOH}$, one of $\text{CH}_2\text{CHCHCH}=\text{CH}$, one of CH_2CHOH and one of $\text{CH}_2\text{CH}_2\text{CHCHOH}$), 1.58- 1.78 (7H, m, $\text{CHCH}_2\text{CHCHCH}=\text{CH}$, $\text{CH}_2\text{CHCHCHOH}$, one of $\text{CH}_2\text{CH}_2\text{CHOH}$, one of $\text{CH}_2\text{CH}_2\text{CHCHOH}$, CHCHCHOH and CHCHOH), 1.80- 1.87 (1H, m, one of CH_2CHOH), 2.14- 2.19 (1H, m, $\text{CHCHCH}=\text{CH}$), 2.34 (1H, app. dt, J 8.5 and 2.0Hz, $\text{CHCH}=\text{CH}$), 3.25 (3H, s, OCH_3), 3.77- 3.80 (1H, m, CHOH), 5.31 (1H, dd, J 2.0 and 5.5Hz, $\text{CHCH}=\text{CH}$), 5.54 (1H, dd, J 2.0 and 5.5Hz, $\text{CHCH}=\text{CH}$). δ_C (100MHz, CD_3OD) 21.6 ($\text{CH}_2\text{CH}_2\text{CHOH}$), 28.5 ($\text{CH}_2\text{CHCHCHOH}$), 29.3 ($\text{CH}_2\text{CHCHCH}=\text{CH}$), 29.8 ($\text{CH}_2\text{CH}_2\text{CHCHOH}$), 29.9 (CH_2CHCHOH), 31.3 ($\text{CHCHCH}=\text{CH}$), 34.8 (CH_2CHOH), 37.3 ($\text{CHCH}=\text{CH}$), 39.3 (CHCHCHOH), 43.0 (CHCHOH), 53.2 ($\text{CHCH}_2\text{CHCHCH}=\text{CH}$), 55.0 (OCH_3), 66.1 ($\text{CCH}=\text{CH}$), 71.4 (CHOH), 90.6 (COCH_3), 125.0 ($\text{CHCH}=\text{CH}$), 139.5 ($\text{CHCH}=\text{CH}$). m/z (CI, NH_3 , high resolution) found 261.1856 [$\text{C}_{17}\text{H}_{24}\text{O}_2$] ($(\text{MH})^+$, 26%) [requires 261.1855], 211.1435 (100), 146.0965 (20).

b. (\pm) (1*S*, 2*S*, 6*S*, 7*R*, 10*S*, 12*S*, 13*R*, 16*R*)-16-Methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-ol (**18**)^[15]

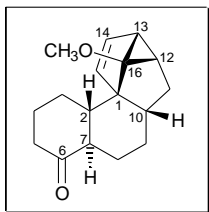
Fraction 2 contained the pure solid (0.059g, 50%).



Mp. 62-64 °C. R_f = 0.15 (dichloromethane). λ_{\max} (cyclohexane) 231 and 276nm. ν_{\max} (thin film, cm^{-1}) 3448 (OH). δ_H (400MHz, CD_3OD) 0.98- 1.15 (2H, m, one of $\text{CH}_2\text{CHCHCH}=\text{CH}$ and one of CH_2CHCHOH), 1.15- 1.25 (1H, m, one of $\text{CH}_2\text{CH}_2\text{CHCHOH}$), 1.40- 1.60 (6H, m, one of $\text{CH}_2\text{CH}_2\text{CHOH}$, $\text{CH}_2\text{CHCHCHOH}$, CHCHOH , one of CH_2CHOH and one of $\text{CH}_2\text{CH}_2\text{CHCHOH}$), 1.71- 1.81 (1H, m, one of $\text{CH}_2\text{CH}_2\text{CHOH}$), 1.81- 1.90 (2H, m, one of CH_2CHOH and one of $\text{CH}_2\text{CHCHCH}=\text{CH}$), 1.95- 2.11 (4H, m, one of CH_2CHCHOH , $\text{CHCH}_2\text{CHCHCH}=\text{CH}$, $\text{CHCHCH}=\text{CH}$ and CHCHCHOH), 2.21 (1H, dt, J 8.5 and 2.0Hz, $\text{CHCH}=\text{CH}$), 3.51 (3H, s, OCH_3), 3.84 (1H, app. bq, J 2.5Hz, CHOH), 5.63- 5.68 (2H, m, $\text{CHCH}=\text{CH}$ and $\text{CHCH}=\text{CH}$). δ_C (100MHz, CD_3OD) 21.0 ($\text{CH}_2\text{CH}_2\text{CHOH}$), 27.7 ($\text{CH}_2\text{CH}_2\text{CHCHOH}$ and $\text{CH}_2\text{CHCHCH}=\text{CH}$), 30.0 (CH_2CHCHOH), 30.4 ($\text{CHCHCH}=\text{CH}$), 31.1 ($\text{CH}_2\text{CHCHCHOH}$), 35.0 (CH_2CHOH), 39.0 (CHCHOH), 39.7 ($\text{CHCH}=\text{CH}$), 44.2 (CHCHCHOH), 57.9 (OCH_3), 60.5 ($\text{CHCH}_2\text{CHCHCH}=\text{CH}$), 65.1 ($\text{CCH}=\text{CH}$), 71.1 (CHOH), 91.9 (COCH_3), 127.2 and 132.4 ($\text{CHCH}=\text{CH}$ and $\text{CHCH}=\text{CH}$). m/z (EI, high resolution) found 260.1778 [$\text{C}_{17}\text{H}_{24}\text{O}_2$] ($(\text{M})^+$, 9%) [requires 260.1776], 280.9822 (44), 242.9863 (49), 230.9862 (100).

Identification of 4-carbon tether cycloadducts

a. (\pm) (1*S*, 2*S*, 7*R*, 10*S*, 12*S*, 13*R*, 16*R*)-16-Methoxypentacyclo-[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-one (**20**)^[15]

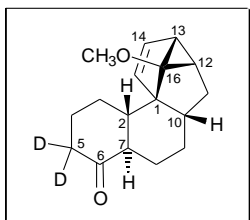


Compound (**20**) was prepared according to general procedure E using solutions of cycloadduct (\pm) (1*S*, 2*S*, 6*S*, 7*R*, 10*S*, 12*S*, 13*R*, 16*R*)-16-methoxypentacyclo-[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]-hexadec-14-en-6-ol (**18**) (0.020g, 0.08mmol) in anhydrous DCM (2ml) and pyridinium chlorochromate (0.023g, 0.12mmol) in anhydrous DCM (2x1ml). After 30 minutes of stirring under nitrogen, TLC indicated that no more starting material remained. Pure ketone cycloadduct (\pm) (1*S*, 2*S*, 7*R*, 10*S*, 12*S*, 13*R*, 16*R*)-16-methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]-hexadec-14-en-6-one (**20**) (0.016g, 81%) was obtained by flash column chromatography (90:10 petroleum ether [40-60]/ ethyl acetate) as a cream coloured solid.

Mp. 102-105 °C. R_f = 0.22 (90:10 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 209 and 275nm. ν_{max} (thin film, cm^{-1}) 1713 (C=O). δ_H (400MHz, CD₃OD) 1.06 (1H, app. ddd, J 1.5, 11.5 and 13.0Hz, one of $\underline{CH}_2CHCHCH=CH$), 1.15 (1H, dt, J 3.5 and 13.0Hz, one of $\underline{CH}_2CH_2CHC=O$), 1.33- 1.46 (1H, m, one of $\underline{CH}_2CHC=O$), 1.51- 1.63 (2H, m, one of $\underline{CH}_2CH_2CHC=O$ and one of $\underline{CH}_2(CH_2)_2C=O$), 1.64- 1.77 (1H, m, one of $\underline{CH}_2CH_2C=O$), 1.85- 1.95 (3H, m, one of $\underline{CH}_2CHC=O$, one of $\underline{CH}_2CHCHCH=CH$ and $\underline{CH}CHC=O$), 1.99- 2.09 (1H, m, $\underline{CH}CH_2CH_2CHC=O$), 2.09- 2.22 (3H, m, $\underline{CH}CHCH=CH$, one of $\underline{CH}_2CH_2C=O$ and one of $\underline{CH}_2(CH_2)_2C=O$), 2.28 (1H, dt, J 8.5 and 2.0Hz, $\underline{CH}CH=CH$), 2.34 (1H, app. quintet, J 13.5 and 2.0Hz, one of $\underline{CH}_2C=O$), 2.46 (1H, app. tdd, J 13.5, 6.0 and 1.5Hz, one of $\underline{CH}_2C=O$), 2.50 (1H, app. ddt, J 1.5, 4.0 and 12.0Hz, $\underline{CH}C=O$), 3.45 (3H, s, OCH_3), 5.75- 5.79 (2H, m, $CHCH=CH$ and $CHCH=CH$). δ_C (100MHz, CDCl₃) 25.4 ($\underline{CH}_2CHC=O$), 25.5 ($\underline{CH}_2CH_2CHC=O$), 26.6 ($\underline{CH}_2CHCHCH=CH$), 26.7 ($\underline{CH}_2CH_2C=O$), 28.3 ($\underline{CH}_2(CH_2)_2C=O$), 29.5 ($\underline{CH}CHCH=CH$), 38.5 ($\underline{CH}CH=CH$), 42.3 ($\underline{CH}_2C=O$), 47.2 ($\underline{CH}CHC=O$), 51.4 ($\underline{CH}C=O$), 57.5 (OCH_3), 58.7 ($\underline{CH}CH_2CH_2CHC=O$), 63.9 ($\underline{C}CH=CH$), 90.8 ($\underline{C}OCH_3$), 127.6 ($CH\underline{C}H=CH$), 129.5 ($CHCH=\underline{C}H$), 213.0 ($\underline{C}=O$). m/z (CI, NH₃, high resolution) found 259.1699 [C₁₇H₂₂O₂] ((MH)⁺, 100%) [requires 259.1699], 204.1044 (72), 84.0956 (14).

Deuteration and desaturation for identification of 4-carbon tether cycloadduct

- a. (\pm) (1*S*, 2*S*, 7*R*, 10*S*, 12*S*, 13*R*, 16*R*)-5,5-Dideutero-16-methoxypentacyclo-[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-one – novel



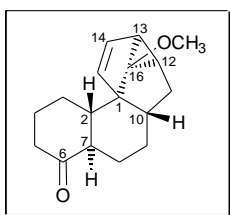
General Procedure F

To a vial containing a small volume of methanol-*d*₄ was added a tiny piece of sodium metal. After 10 minutes, the sodium had completely dissolved to form a solution of sodium methoxide-*d*₃. Two drops of this mixture were added to a vial containing a solution of the cycloadduct ketone (\pm) (1*S*, 2*S*, 7*R*, 10*S*, 12*S*, 13*R*, 16*R*)-16-methoxypentacyclo-[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-one (**18**) (0.016g, 0.06mmol) dissolved in methanol-*d*₄. The vial was shaken vigorously and within 15-20 minutes the two most acidic protons (α to the carbonyl) had become fully deuterated. The contents of the vial containing the deuterated product were then transferred to a tube containing a mixture of NH₄Cl solution and ethyl acetate. The tube was shaken vigorously before the mixture was transferred to a small separating funnel. The organic product was separated and the aqueous layer washed with ethyl acetate (3x10ml). The combined organic extracts were washed with NH₄Cl solution (10ml) and water (10ml). The organic layer was then dried over MgSO₄, filtered and concentrated *in vacuo* to afford the pure deuterated cycloadduct ketone (\pm) (1*S*, 2*S*, 7*R*, 10*S*, 12*S*, 13*R*, 16*R*)-5,5-dideutero-16-methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]-hexadec-14-en-6-one (quantitative).

Mp. 101-103 °C. *R*_f = 0.22 (90:10 petroleum ether [40-60]/ ethyl acetate). λ_{\max} (cyclohexane) 219 and 274nm. ν_{\max} (thin film, cm⁻¹) 1709 (C=O). δ_{H} (400MHz, CD₃OD) 1.06 (1H, ddd, *J* 1.5, 11.5 and 13.0Hz, one of $\text{CH}_2\text{CHCHCH}=\text{CH}$), 1.15 (1H, dt, *J* 3.5 and 13.0Hz, one of $\text{CH}_2\text{CH}_2\text{CHC}=\text{O}$), 1.33- 1.46 (1H, m, one of $\text{CH}_2\text{CHC}=\text{O}$), 1.51- 1.63 (2H, m, one of $\text{CH}_2\text{CH}_2\text{CD}_2$ and one of $\text{CH}_2\text{CH}_2\text{CHC}=\text{O}$), 1.63- 1.76 (1H, m, one of CH_2CD_2), 1.84- 1.94 (3H, m, one of $\text{CH}_2\text{CHCHCH}=\text{CH}$, one of $\text{CH}_2\text{CHC}=\text{O}$ and $\text{CHCHC}=\text{O}$), 1.98- 2.08 (1H, m, $\text{CHCH}_2\text{CH}_2\text{CHC}=\text{O}$), 2.08- 2.14 (2H, m, one of CH_2CD_2 and $\text{CHCHCH}=\text{CH}$), 2.14- 2.22 (1H, m, one of $\text{CH}_2\text{CH}_2\text{CD}_2$), 2.27 (1H, dt, *J* 8.5 and 2.0Hz, $\text{CHCH}=\text{CH}$), 2.50 (1H, app. dt, *J* 4.0 and 12.0Hz, $\text{CHC}=\text{O}$), 3.45 (3H, s, OCH₃), 5.75- 5.79 (2H, m, $\text{CHCH}=\text{CH}$ and $\text{CHCH}=\text{CH}$). δ_{C} (100MHz, CD₃OD) 26.5 ($\text{CH}_2\text{CH}_2\text{CHC}=\text{O}$), 26.6 ($\text{CH}_2\text{CHC}=\text{O}$), 27.5 ($\text{CH}_2\text{CHCHCH}=\text{CH}$), 27.7 (CH_2CD_2), 29.2 ($\text{CH}_2\text{CH}_2\text{CD}_2$), 30.3 ($\text{CHCHCH}=\text{CH}$), 39.5 ($\text{CHCH}=\text{CH}$), 42.6 (biquintet, CD_2),

48.8 ($\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{O}}$), 52.3 ($\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{O}}$), 57.7 ($\underline{\text{O}}\underline{\text{C}}\underline{\text{H}}_3$), 60.0 ($\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{O}}$), 65.2 ($\underline{\text{C}}\underline{\text{C}}\underline{\text{H}}=\underline{\text{C}}\underline{\text{H}}$), 92.1 ($\underline{\text{C}}\underline{\text{O}}\underline{\text{C}}\underline{\text{H}}_3$), 128.3 and 131.0 ($\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}=\underline{\text{C}}\underline{\text{H}}$ and $\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}=\underline{\text{C}}\underline{\text{H}}$), 215.5 ($\underline{\text{C}}=\underline{\text{O}}$). m/z (CI, NH_3 , high resolution) found 260.1761 [$\text{C}_{17}\text{H}_{20}\text{D}_2\text{O}_2$] ($(\text{M})^+$, 100%) [requires 260.1743], 205.1155 (41), 147.0861 (26), 121.0670 (17), 96.0557 (21).

b. (\pm) (1*R*, 2*S*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-16-Methoxypentacyclo-[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-one – novel

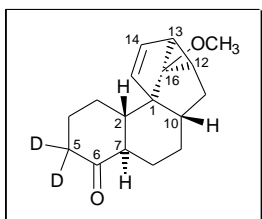


Cycloadduct was synthesised according to general procedure E from a solution of the cycloadduct alcohol (\pm) (1*R*, 2*S*, 6*S*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-16-methoxypentacyclo-[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-ol (**19**) (0.027g, 0.10mmol) in dry DCM (2ml) and a solution of pyridinium chlorochromate (0.057g, 0.31mmol) in anhydrous DCM (2x1ml). After 1 hour of stirring under argon, TLC indicated that the reaction had run to completion. The pure semi-solid cycloadduct ketone (\pm) (1*R*, 2*S*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-16-methoxypentacyclo-[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-one (**123**) was obtained by flash column chromatography (90:10 petroleum ether [40-60]/ ethyl acetate) (0.021g, 78%). Slow re-crystallisation of the product from cyclohexane afforded a cream/yellow crystalline solid.

Mp. 58-61 °C. R_f = 0.23 (90:10 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 207 and 267nm. ν_{max} (thin film, cm^{-1}) 1710 ($\text{C}=\text{O}$). δ_{H} (400MHz, CD_3OD) 1.17- 1.29 (1H, m, one of $\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{O}}$), 1.38 (1H, dd, J 6.5 and 13.0Hz, one of $\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}=\underline{\text{C}}\underline{\text{H}}$), 1.50- 1.68 (5H, m, one of $\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}=\underline{\text{C}}\underline{\text{H}}$, $\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{O}}$, one of $\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}=\underline{\text{O}}$ and $\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{O}}$), 1.71 (1H, app. dt, J 3.5 and 12.0Hz, $\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{O}}$), 1.82- 1.89 (1H, m, one of $\underline{\text{C}}\underline{\text{H}}_2(\underline{\text{C}}\underline{\text{H}}_2)_2\underline{\text{C}}=\underline{\text{O}}$), 1.96 (1H, app. dq, J 13.5 and 3.0Hz, one of $\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{O}}$), 2.07- 2.23 (2H, m, one of $\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}=\underline{\text{O}}$ and one of $\underline{\text{C}}\underline{\text{H}}_2(\underline{\text{C}}\underline{\text{H}}_2)_2\underline{\text{C}}=\underline{\text{O}}$), 2.22- 2.27 (1H, m, $\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{C}}\underline{\text{H}}$), 2.28- 2.34 (1H, m, one of $\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}=\underline{\text{O}}$), 2.41- 2.44 (1H, m, $\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}=\underline{\text{C}}\underline{\text{H}}$), 2.45 (1H, ddt, J 1.5, 6.0 and 13.5Hz, one of $\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}=\underline{\text{O}}$), 2.80 (1H, ddt, J 1.5, 3.5 and 12.0Hz, $\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{O}}$), 3.27 (3H, s, $\underline{\text{O}}\underline{\text{C}}\underline{\text{H}}_3$), 5.33 (1H, dd, J 1.5 and 5.5Hz, $\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}=\underline{\text{C}}\underline{\text{H}}$), 5.60 (1H, dd, J 2.5 and 5.5Hz, $\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}=\underline{\text{C}}\underline{\text{H}}$). δ_{C} (100MHz, CDCl_3) 25.4 ($\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{O}}$), 25.5 ($\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{O}}$), 26.6 ($\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{C}}\underline{\text{H}}$), 26.7 ($\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}=\underline{\text{O}}$), 28.3 ($\underline{\text{C}}\underline{\text{H}}_2(\underline{\text{C}}\underline{\text{H}}_2)_2\underline{\text{C}}=\underline{\text{O}}$), 29.5 ($\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{C}}\underline{\text{H}}$), 38.5 ($\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}=\underline{\text{C}}\underline{\text{H}}$), 42.3 ($\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}=\underline{\text{O}}$), 47.2 ($\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{O}}$), 51.4 ($\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}=\underline{\text{O}}$), 57.5 ($\underline{\text{O}}\underline{\text{C}}\underline{\text{H}}_3$), 58.7 ($\underline{\text{C}}\underline{\text{H}}\underline{\text{C}}\underline{\text{C}}\underline{\text{H}}=\underline{\text{C}}\underline{\text{H}}$), 63.9 ($\underline{\text{C}}\underline{\text{C}}\underline{\text{O}}\underline{\text{C}}\underline{\text{H}}_3$), 90.8 ($\underline{\text{C}}\underline{\text{O}}\underline{\text{C}}\underline{\text{H}}_3$), 127.6

(CH \underline{C} H=CH), 129.5 (CHCH= \underline{C} H), 213.0 (C=O). m/z (CI, NH₃, high resolution) found 259.1701 [C₁₇H₂₂O₂] ((MH)⁺, 100%) [requires 259.1699], 227.1478 (14), 205.2420 (17), 181.1893 (11).

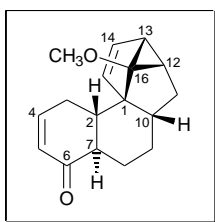
c. (±) (1*R*, 2*S*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-5,5-Dideutero-16-methoxypentacyclo-[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-one – novel



Deuterated cycloadduct was obtained from the cycloadduct ketone (±) (1*R*, 2*S*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-16-methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-one (123) (0.021g, 0.08mmol) by following general procedure F. Slow re-crystallisation of the semi-solid from cyclohexane afforded a yellow solid of pure (±) (1*R*, 2*S*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-5,5-dideutero-16-methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-one in a quantitative yield.

Mp. 57-59 °C. R_f = 0.23 (90:10 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 209 and 273nm. ν_{max} (thin film, cm⁻¹) 1721 (C=O). δ_H (400MHz, CD₃OD) 1.17- 1.29 (1H, m, one of CH₂CHC=O), 1.38 (1H, dd, *J* 6.5 and 13.0Hz, one of CH₂CHCHCH=CH), 1.50- 1.68 (5H, m, one of CH₂CHCHCH=CH, CH₂CH₂CHC=O, one of CH₂CD₂ and CHCH₂CH₂CHC=O), 1.71 (1H, app. dt, *J* 3.5 and 12.0Hz, CHCHC=O), 1.86 (1H, app. dq, *J* 13.5 and 3.5Hz, one of CH₂CH₂CD₂), 1.96 (1H, app. dq, *J* 13.5 and 3.0Hz, one of CH₂CHC=O), 2.07- 2.14 (1H, m, one of CH₂CD₂), 2.14- 2.23 (1H, m, one of CH₂CH₂CD₂), 2.22- 2.27 (1H, m, CHCHCH=CH), 2.44 (1H, app. dt, *J* 8.5 and 2.0Hz, CHCH=CH), 2.80 (1H, dt, *J* 3.0 and 12.0Hz, CHC=O), 3.27 (3H, s, OCH₃), 5.33 (1H, dd, *J* 1.5 and 5.5Hz, CHCH=CH), 5.60 (1H, dd, *J* 2.5 and 5.5Hz, CHCH=CH). δ_C (100MHz, CD₃OD) 25.7 (CH₂CHC=O), 27.7 (CH₂CD₂), 27.9 (CH₂CH₂CD₂), 28.5 (CH₂CH₂CHC=O), 29.3 (CH₂CHCHCH=CH), 30.8 (CHCHCH=CH), 36.6 (CHCH=CH), 42.5 (CD₂), 48.6 (CHCHC=O), 51.8 (CHC=O), 52.6 (CHCH₂CH₂CHC=O), 54.7 (OCH₃), 65.8 (CCH=CH), 90.8 (COCH₃), 125.8 (CHCH=CH), 138.3 (CHCH=CH), 216.1 (C=O). m/z (EI, high resolution) found 260.1747 [C₁₇H₂₀D₂O₂] ((M)⁺, 1%) [requires 260.1743], 268.9826 (23), 242.9862 (50), 230.9865 (100).

d. (\pm) (1*S*, 2*S*, 7*R*, 10*S*, 12*S*, 13*R*, 16*R*)-16-Methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-4,14-dien-6-one – novel



General Procedure G

To prepare a 0.2M solution of lithium diisopropylamide an oven dried round-bottomed flask was evacuated and flushed with argon before anhydrous diisopropylamine (distilled from calcium hydride) (0.46ml, 3.28mmol) was added *via* syringe. To the flask was also added anhydrous THF (15ml) and the mixture was stirred under argon whilst being cooled to -78°C using an acetone/dry ice bath. To the cold, stirred solution was slowly added 1.6M *n*-butyllithium solution (1.88ml, 3.00mmol) drop-wise *via* syringe, over a period of 20 minutes. The newly formed 0.2M LDA solution was left stirring at -78°C for a further 15-20 minutes whilst the other reaction vessel containing the cycloadduct was prepared.

General Procedure H

Into a reaction tube was placed the *meta* cycloadduct ketone (\pm) (1*S*, 2*S*, 7*R*, 10*S*, 12*S*, 13*R*, 16*R*)-16-methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-one (121) (0.029g, 0.11mmol) and anhydrous THF (1ml). The stirred solution was cooled to -78°C using an acetone/dry ice bath and then the cold LDA solution (0.2M, 0.62ml, 0.12mmol) was added drop-wise, down the inside of the tube, over a period of 15 minutes. After leaving to stir under argon at -78°C for a further 15 minutes to ensure complete formation of the enolate, a solution of phenylselenenyl chloride (0.028g, 0.15mmol) in THF (2x1ml) was added rapidly to the reaction mixture. The mixture was left to stir at -78°C for 45 minutes after which time TLC indicated that no more starting material remained so the reaction was quenched by the addition of saturated NH₄Cl solution (15ml). The mixture was transferred to a separating funnel where the aqueous layer was extracted and washed with diethyl ether (3x15ml). The combined organic extracts were collected together and washed with saturated NH₄Cl solution (15ml) and then water (15ml). The organic layer was dried over MgSO₄, filtered and concentrated *in vacuo* to give a clear oil. Purification using silica gel flash column chromatography (dichloromethane) afforded the two separate diastereoisomers of the pure α -phenylseleno ketone derivative (\pm) (1*S*, 2*S*, 5*RS*, 7*R*, 10*S*, 12*S*, 13*R*, 16*R*)-5-phenylselenanyl-16-methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-one, one as a colourless oil and the other as a white crystalline solid (Mp. 125-127 °C). The overall yield

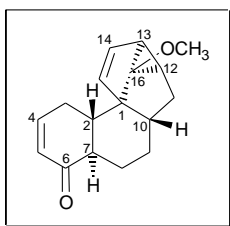
of the two diastereoisomers was 71% (0.033 g). The two isomers were collected together and directly reacted on to give the desired α,β -unsaturated ketone in the following manner.

To the α -phenylseleno ketone (0.033g, 0.08mmol) was added THF (1ml). The flask was then cooled to 0°C before 27.5% wt. hydrogen peroxide solution in water (0.03ml, 0.24mmol) was added drop-wise, *via* syringe, over a period of 5 minutes. The reaction mixture was stirred at 0°C for 30 minutes and then the flask was allowed to warm up to room temperature, with stirring, for a further 30 minutes. After this time, TLC indicated that the reaction had run to completion and was therefore terminated by quenching with saturated sodium bicarbonate solution (15ml). The mixture was transferred to a separating funnel where the organic layer was separated and the aqueous layer washed with a 1:1 mixture of ether and pentane (3x15ml). All the organic extracts were collected together and washed with saturated sodium bicarbonate solution (15ml) and then water (15ml). The organic layer was dried over MgSO₄, filtered and concentrated *in vacuo* to give a barely solid crude product. The desired α,β -unsaturated ketone cycloadduct (\pm) (1*S*, 2*S*, 7*R*, 10*S*, 12*S*, 13*R*, 16*R*)-16-methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-4,14-dien-6-one was obtained by purification of the crude product using flash column chromatography (80:20 petroleum ether [40-60]/ ethyl acetate) as cream coloured, fine needle crystals (0.017g, 83%). The overall yield for the process of converting the cycloadduct ketone to its α,β -unsaturated derivative (126) was 59%.

Mp. 120-121 °C. R_f = 0.31 (80:20 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 223 and 275nm. ν_{max} (thin film, cm⁻¹) 1670 (α,β -unsaturated C=O). δ_H (400MHz, CD₃OD) 1.04- 1.12 (1H, m, one of CH₂CHCHCH=CH), 1.15- 1.38 (2H, m, one of CH₂CH₂CHC=O and one of CH₂CHC=O), 1.61- 1.67 (1H, m, one of CH₂CH₂CHC=O), 1.92 (1H, ddd, *J* 6.5, 7.5 and 12.5Hz, one of CH₂CHCHCH=CH), 2.05- 2.13 (1H, m, CHCH₂CH₂CHC=O), 2.13- 2.18 (1H, m, CHCHCH=CH), 2.22- 2.40 (4H, m, CCHCHC=O, one of CH₂CHC=O, CHCH=CH and one of CH₂CH=CHC=O), 2.45- 2.55 (1H, m, CH₂CHC=O), 2.70- 2.82 (1H, m, one of CH₂CH=CHC=O), 3.47 (3H, s, OCH₃), 5.75- 5.80 (2H, m, CHCH=CH and CHCH=CH), 5.94- 5.99 (1H, m, CH=CHC=O), 7.07- 7.12 (1H, m, CH=CHC=O). δ_C (100MHz, CD₃OD) 26.6 (CH₂CH₂CHC=O), 26.8 (CH₂CHC=O), 27.6 (CH₂CHCHCH=CH), 30.2 (CH₂CH=CHC=O), 30.3 (CHCHCH=CH), 39.4 (CCHCHC=O), 44.2 (CHCH=CH), 48.4 (CH₂CHC=O), 57.8 (OCH₃), 59.7 (CHCH₂CH₂CHC=O), 64.6 (CCH=CH), 91.8 (COCH₃), 128.7 (CHCH=CH or CHCH=CH), 129.3 (CH=CHC=O), 131.0 (CHCH=CH or CHCH=CH), 152.3 (CH=CHC=O), 203.9 (C=O). *m/z* (CI,

NH₃, high resolution) found 257.1534 [C₁₇H₂₀O₂] ((MH)⁺, 100%) [requires 257.1542], 202.1075 (30).

e. (±) (1*R*, 2*S*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-16-Methoxypentacyclo-[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-4,14-dien-6-one – novel



Firstly, a 0.2M solution of lithium diisopropylamide was prepared according to general procedure G. Cycloadduct enone was then synthesised according to general procedure H from a solution of the ketone (±) (1*R*, 2*S*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-16-methoxypentacyclo-[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-one (0.019g, 0.07mmol) in anhydrous THF (1ml), and the 0.2M LDA solution (0.41ml, 0.08mmol). A solution of phenylselenenyl chloride (0.017g, 0.09mmol) in THF (2x1ml) was added rapidly to the reaction mixture at -78°C and left to stir under argon for 45 minutes after which time TLC indicated that the reaction had run to completion. The pure α-phenylseleno ketone derivative (±) (1*R*, 2*S*, 5*RS*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-5-phenylselanyl-16-methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]-hexadec-14-en-6-one was obtained as a mixture of two diastereoisomers by purification using silica-gel flash column chromatography (90:10 dichloromethane/ petroleum ether [40-60]) in an overall yield of 73% (0.022g).

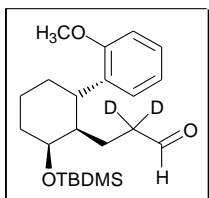
The pure, clear oil was then directly reacted on to give the desired α,β-unsaturated ketone by following general procedure H from the α-phenylseleno cycloadduct ketone (0.022g, 0.05mmol), anhydrous THF (1ml) and 27.5% wt. hydrogen peroxide solution in water (0.02ml, 0.16mmol). The reaction mixture was left to stir at 0°C for 30 minutes and room temperature for a further 30 minutes. After this time, TLC indicated that the reaction had run to completion. Purification of the crude oil using flash column chromatography (85:15 petroleum ether [40-60]/ ethyl acetate) afforded the desired α,β-unsaturated ketone cycloadduct (±) (1*R*, 2*S*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-16-methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-4,14-dien-6-one as a colourless oil (0.010g, 75%). The overall yield for the process of converting the cycloadduct ketone to its α,β-unsaturated derivative was calculated to be 55%.

R_f = 0.27 (85:15 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 218 and 276nm. ν_{max} (thin film, cm⁻¹) 1669 (α,β-unsaturated C=O). δ_H (400MHz, CD₃OD) 1.07- 1.18

(1H, m, one of $\text{CH}_2\text{CHC}=\text{O}$), 1.42 (1H, dd, J 6.5 and 13.0Hz, one of $\text{CH}_2\text{CHCHCH}=\text{CH}$), 1.54-1.77 (4H, m, one of $\text{CH}_2\text{CHCHCH}=\text{CH}$, $\text{CH}_2\text{CH}_2\text{CHC}=\text{O}$ and $\text{CHCH}_2\text{CH}_2\text{CHC}=\text{O}$), 2.11 (1H, ddd, J 4.5, 11.5 and 13.5Hz, $\text{CCHCHC}=\text{O}$), 2.25- 2.33 (2H, m, one of $\text{CH}_2\text{CHC}=\text{O}$ and $\text{CHCHCH}=\text{CH}$), 2.37- 2.46 (2H, m, one of $\text{CH}_2\text{CHCHC}=\text{O}$ and $\text{CHCH}=\text{CH}$), 2.71 (1H, ddd, J 4.0, 11.5 and 13.5Hz, $\text{CH}_2\text{CHC}=\text{O}$), 2.92 (1H, dddd, J 2.0, 3.0, 11.5 and 19.5Hz, one of $\text{CH}_2\text{CHCHC}=\text{O}$), 3.22 (3H, s, OCH_3), 5.35 (1H, dd, J 1.5 and 5.5Hz, $\text{CHCH}=\text{CH}$), 5.65 (1H, dd, J 2.5 and 5.5Hz, $\text{CHCH}=\text{CH}$), 5.96 (1H, ddd, J 1.0, 3.0 and 10.0Hz, $\text{CH}=\text{CHC}=\text{O}$), 7.12 (1H, ddd, J 2.0, 6.0 and 10.0Hz, $\text{CH}=\text{CHC}=\text{O}$). δ_c (100MHz, CD_3OD) 25.9 ($\text{CH}_2\text{CHC}=\text{O}$), 28.7 ($\text{CH}_2\text{CH}_2\text{CHC}=\text{O}$), 29.3 ($\text{CH}_2\text{CHCHCH}=\text{CH}$), 29.6 ($\text{CH}_2\text{CHCHC}=\text{O}$), 29.9 ($\text{CHCHCH}=\text{CH}$), 36.3 ($\text{CHCH}=\text{CH}$), 42.9 ($\text{CCHCHC}=\text{O}$), 47.9 ($\text{CH}_2\text{CHC}=\text{O}$), 52.3 ($\text{CHCH}_2\text{CH}_2\text{CHC}=\text{O}$), 54.1 (OCH_3), 65.2 ($\text{CCH}=\text{CH}$), 90.9 (COCH_3), 126.6 ($\text{CHCH}=\text{CH}$), 129.3 ($\text{CH}=\text{CHC}=\text{O}$), 137.5 ($\text{CHCH}=\text{CH}$), 153.2 ($\text{CH}=\text{CHC}=\text{O}$), 204.3 ($\text{C}=\text{O}$). m/z (CI, NH_3 , high resolution) found 257.1544 [$\text{C}_{17}\text{H}_{20}\text{O}_2$] ($(\text{MH})^+$, 100%) [requires 257.1542], 202.1012 (63), 121.0640 (28), 55.0382 (32).

Synthesis of the deuterated 4-carbon tether substrate (**23**)

- a. (\pm) 3-[(1*R*, 2*S*, 6*S*)-2'-(*tert*-Butyldimethylsilyloxy)-6'-(2''-methoxyphenyl)cyclohexyl]-2,2-dideuteropropionaldehyde^[15]



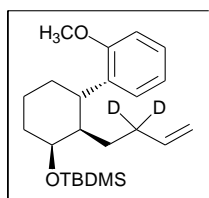
In a reaction tube was placed a solution of the aldehyde (\pm) 3-[(1*R*, 2*S*, 6*S*)-2'-(*tert*-butyldimethylsilyloxy)-6'-(2''-methoxyphenyl)cyclohexyl]propionaldehyde (**12**) (0.104g, 0.28mmol) in methanol-*d* (5ml). To a separate vial containing methanol-*d*₄ (0.5ml) was added 3 small lumps of sodium metal.

Once the sodium had completely dissolved, the newly formed solution of sodium methoxide was transferred *via* syringe to the reaction tube containing the aldehyde. The tube was shaken vigorously before being left to stand for 1.5 hours. After this time, ¹H NMR spectroscopy indicated that the two most acidic protons (α to the carbonyl) had become fully exchanged with deuterium. The reaction mixture was then transferred to a separating funnel where it was diluted with ethyl acetate and saturated NH₄Cl solution. The organic layer was separated and the aqueous layer washed with ethyl acetate (3x15ml). The combined organic extracts were washed with sat. NH₄Cl solution (15ml) and water (15ml). The organic product was then dried over MgSO₄, filtered and concentrated *in vacuo* to afford the pure deuterated aldehyde (\pm) 3-[(1*R*, 2*S*, 6*S*)-2'-(*tert*-butyldimethylsilyloxy)-6'-(2''-methoxyphenyl)cyclohexyl]-2,2-dideuteropropionaldehyde (quantative).

R_f = 0.26 (95:5 petroleum ether [40-60]/ ethyl acetate). λ_{max} (cyclohexane) 227 and 272nm. ν_{max} (thin film, cm⁻¹) 1726 (C=O), 1599 (aromatic stretch). δ_H (400MHz, CDCl₃) 0.06 (3H, s, OSiCH₃), 0.11 (3H, s, OSiCH₃), 0.96 (9H, s, OSiC(CH₃)₃), 1.19- 1.34 (1H, m, one of CH₂CD₂CHO), 1.42- 1.65 (5H, m, one of CH₂CH₂CH(Ar), one of CH₂CH(Ar), one of CH₂CHOTBDMS, CHCH₂CD₂CHO and one of CH₂CD₂CHO), 1.65- 1.73 (1H, m, one of CH₂CH₂CH(Ar)), 1.77- 1.90 (2H, m, one of CH₂CH(Ar) and one of CH₂CHOTBDMS), 3.33 (1H, app. bs, CH(Ar)), 3.79 (3H, s, OCH₃), 4.05 (1H, app. s, CHOTBDMS), 6.84 (1H, dd, *J* 0.5 and 8.0Hz, CH=COCH₃), 6.91 (1H, dt, *J* 0.5 and 7.5Hz, CHCHCH=COCH₃), 7.10- 7.18 (2H, m, CHCH=COCH₃ and CHC(CH)=COCH₃), 9.50 (1H, s, CHO). δ_C (100MHz, CDCl₃) -5.0 and -3.8 (OSiCH₃ and OSiCH₃), 18.3 (OSiC(CH₃)₃), 20.3 (CH₂CH₂CH(Ar)), 22.0 (CH₂CD₂CHO), 25.9 (OSiC(CH₃)₃), 33.9 (CH(Ar)), 34.0 (CH₂CH(Ar) and CH₂CHOTBDMS), 41.4 (bquintet, CD₂), 45.7 (CHCH₂CD₂), 55.0 (OCH₃), 68.0 (CHOTBDMS), 110.9 (CH=COCH₃), 120.8 (CHCHCH=COCH₃), 126.7 (CHCH=COCH₃), 127.9 (CHC(CH)=COCH₃), 133.6 (C(CH)=COCH₃),

157.6 (COCH_3), 203.5 (CHO). m/z (CI, NH_3 , high resolution) found 379.2649 [$\text{C}_{22}\text{H}_{34}\text{D}_2\text{O}_3\text{Si}$] ($(\text{MH})^+$, 18%) [requires 379.2635], 321.1857 (43), 246.8471 (100).

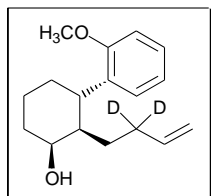
b. (\pm) *tert*-Butyl-[(1*S*, 2*R*, 3*S*)-2-(2',2'-dideuterobut-3'-enyl)-3-(2''-methoxyphenyl)cyclohexyloxy]dimethylsilane^[15]



The substrate was prepared according to general procedure A using methyltriphenylphosphonium bromide (0.462g, 1.29mmol), anhydrous THF (5ml), 1.6M methyllithium solution in hexanes (0.74ml, 1.18mmol) and a solution of the deuterated aldehyde (\pm) 3-[(1*R*, 2*S*, 6*S*)-2'-(*tert*-butyldimethylsilyloxy)-6'-(2''-methoxyphenyl)cyclohexyl]-2,2-dideuteropropionaldehyde (0.326g, 0.86mmol) in dry THF (2x5ml). Pure (\pm) *tert*-butyl-[(1*S*, 2*R*, 3*S*)-2-(2',2'-dideuterobut-3'-enyl)-3-(2''-methoxyphenyl)cyclohexyloxy]-dimethylsilane (0.249g, 77%) was obtained by flash column chromatography (petroleum ether [40-60]) as a colourless oil.

R_f = 0.22 (petroleum ether [40-60]). λ_{max} (cyclohexane) 228 and 267nm. ν_{max} (thin film, cm^{-1}) 1600 (aromatic stretch). δ_{H} (400MHz, C_6D_6) 0.09 (3H, s, OSiCH_3), 0.11 (3H, s, OSiCH_3), 1.07 (9H, s, $\text{OSiC}(\text{CH}_3)_3$), 1.22- 1.29 (1H, m, one of CH_2CD_2), 1.34- 1.78 (5H, m, one of $\text{CH}_2\text{CH}(\text{Ar})$, one of $\text{CH}_2\text{CHOTBDMS}$, one of $\text{CH}_2\text{CH}_2\text{CH}(\text{Ar})$, one of CH_2CD_2 and CHCH_2CD_2), 1.80- 1.93 (2H, m, one of $\text{CH}_2\text{CH}(\text{Ar})$ and one of $\text{CH}_2\text{CHOTBDMS}$), 2.00 (1H, app. qt, J 13.0 and 3.5Hz, one of $\text{CH}_2\text{CH}_2\text{CH}(\text{Ar})$), 3.36 (3H, s, OCH_3), 3.63 (1H, app. bs, $\text{CH}(\text{Ar})$), 4.09 (1H, app. s, CHOTBDMS), 4.90 (1H, dd, J 2.0 and 10.0Hz, $\text{CH}=\text{CH}_2$ (*cis*-H)), 4.94 (1H, dd, J 2.0 and 17.0Hz, $\text{CH}=\text{CH}_2$ (*trans*-H)), 5.63 (1H, dd, J 10.0 and 17.0Hz, $\text{CH}=\text{CH}_2$), 6.59 (1H, dd, J 1.0 and 8.0Hz, $\text{CH}=\text{COCH}_3$), 6.93 (1H, app. t, J 7.5Hz, $\text{CHCHCH}=\text{COCH}_3$), 7.07 (1H, ddd, J 2.0, 7.5 and 8.0Hz, $\text{CHCH}=\text{COCH}_3$), 7.17 (1H, dd, J 2.0 and 7.5Hz, $\text{CHC}(\text{CH})=\text{COCH}_3$). δ_{C} (100MHz, C_6D_6) -4.9 (OSiCH_3), -3.8 (OSiCH_3), 18.5 ($\text{OSiC}(\text{CH}_3)_3$), 20.9 ($\text{CH}_2\text{CH}_2\text{CH}(\text{Ar})$), 26.2 ($\text{OSiC}(\text{CH}_3)_3$), 28.4 (CH_2CD_2), 30.5 (biquintet, CD_2), 34.5 ($\text{CH}_2\text{CH}(\text{Ar})$ and $\text{CH}_2\text{CHOTBDMS}$), 34.6 ($\text{CH}(\text{Ar})$), 46.0 (CHCH_2CD_2), 55.0 (OCH_3), 68.3 (CHOTBDMS), 110.9 ($\text{CH}=\text{COCH}_3$), 114.3 ($\text{CH}=\text{CH}_2$), 121.1 ($\text{CHCHCH}=\text{COCH}_3$), 126.8 ($\text{CHCH}=\text{COCH}_3$), 128.2 ($\text{CHC}(\text{CH})=\text{COCH}_3$), 135.0 ($\text{C}(\text{CH})=\text{COCH}_3$), 139.2 ($\text{CH}=\text{CH}_2$), 158.0 (COCH_3). m/z (CI, NH_3 , high resolution) found 377.2853 [$\text{C}_{23}\text{H}_{36}\text{D}_2\text{O}_2\text{Si}$] ($(\text{MH})^+$, 25%) [requires 377.2843], 319.2086 (68), 245.1884 (100), 121.0638 (50).

c. (\pm) (1*S*, 2*R*, 3*S*)-2-(2',2'-Dideuterobut-3'-enyl)-3-(2''-methoxyphenyl)-cyclohexanol (**21**)^[15]



Compound (**134**) was synthesised according to general procedure B from a solution of the deuterated alkene (\pm) *tert*-butyl-[(1*S*, 2*R*, 3*S*)-2-(2',2'-dideuterobut-3'-enyl)-3-(2''-methoxyphenyl)cyclohexyloxy]dimethylsilane (0.236g, 0.63mmol) in anhydrous THF (15ml) and 1M tetrabutylammonium fluoride solution in THF (2.10ml, 2.10mmol). The reaction mixture was heated to 50°C and left to stir for 119 hours until TLC indicated that no more starting material was being consumed. Flash column chromatography (90:10 petroleum ether [40-60]/ ethyl acetate) afforded the pure deuterated 4-carbon tether substrate (\pm) (1*S*, 2*R*, 3*S*)-2-(2',2'-dideuterobut-3'-enyl)-3-(2''-methoxyphenyl)cyclohexanol (**21**) (0.158g, 96%) as a white solid.

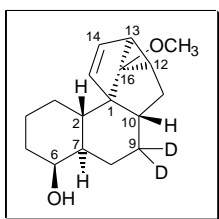
Mp. 63-65 °C. R_f = 0.13 (90:10 petroleum ether [40-60]/ ethyl acetate). λ_{\max} (cyclohexane) 220 and 273nm. ν_{\max} (KBr disc, cm^{-1}) 3267 (OH). δ_H (400MHz, C_6D_6) 0.96 (1H, bs, CHOH), 1.29- 1.48 (4H, m, one of CH_2CD_2 , one of CH_2CHOH , one of $\text{CH}_2\text{CH}(\text{Ar})$ and one of $\text{CH}_2\text{CH}_2\text{CHOH}$), 1.52- 1.60 (1H, m, one of CH_2CD_2), 1.70- 1.77 (1H, m, one of CH_2CHOH), 1.81- 1.95 (2H, m, one of $\text{CH}_2\text{CH}(\text{Ar})$ and one of $\text{CH}_2\text{CH}_2\text{CHOH}$), 3.34 (3H, s, OCH_3), 3.59 (1H, app. bs, $\text{CH}(\text{Ar})$), 3.93 (1H, app. bs, CHOH), 4.89 (1H, dd, J 2.0 and 10.0Hz, $\text{CH}=\text{CH}_2$ (*cis*-H)), 4.94 (1H, dd, J 2.0 and 17.0Hz, $\text{CH}=\text{CH}_2$ (*trans*-H)), 5.62 (1H, dd, J 10.0 and 17.0Hz, $\text{CH}=\text{CH}_2$), 6.59 (1H, dd, J 1.0 and 7.5Hz, $\text{CH}=\text{COCH}_3$), 6.93 (1H, app. t, J 7.5Hz, $\text{CHCHCH}=\text{COCH}_3$), 7.07 (1H, dt, J 2.0 and 7.5Hz, $\text{CHC}(\text{CH})=\text{COCH}_3$), 7.15 (1H, dd, J 2.0 and 7.5Hz, $\text{CHC}(\text{CH})=\text{COCH}_3$). δ_C (100MHz, C_6D_6) 20.6 ($\text{CH}_2\text{CH}_2\text{CHOH}$ and $\text{CH}_2\text{CH}(\text{Ar})$), 28.5 (CH_2CD_2), 31.3 (bqintet, CD_2), 34.1 (CH_2CHOH), 35.0 ($\text{CH}(\text{Ar})$), 45.0 (CHCHOH), 54.9 (OCH_3), 66.7 (CHOH), 110.9 ($\text{CH}=\text{COCH}_3$), 114.4 ($\text{CH}=\text{CH}_2$), 121.0 ($\text{CHCHCH}=\text{COCH}_3$), 126.8 ($\text{CHCH}=\text{COCH}_3$), 128.2 ($\text{CHC}(\text{CH})=\text{COCH}_3$), 134.7 ($\text{C}(\text{CH})=\text{COCH}_3$), 139.4 ($\text{CH}=\text{CH}_2$), 157.9 (COCH_3). m/z (EI, high resolution) found 262.1901 [$\text{C}_{17}\text{H}_{22}\text{D}_2\text{O}_2$] ($(\text{M})^+$, 26%) [requires 262.1900], 203.1075 (84), 180.9882 (100).

Photolysis of the deuterated 4-carbon tether substrate (**21**)

Photolysis of substrate (**21**) was carried out according to general procedure D. A 6.0mM solution of (\pm) (1*S*, 2*R*, 3*S*)-2-(2',2'-dideuterobut-3'-enyl)-3-(2''-methoxyphenyl)cyclohexanol (**21**) (0.158g, 0.60mmol) in cyclohexane (100ml) was irradiated for 3 hours until TLC and NMR spectroscopy indicated that no more starting material remained and that two major products had formed. All the washings from the thin film photoreactor were collected together and concentrated *in vacuo* to give a crude yellow oil. The two main photoproducts were separated from all the reaction by-products and then purified using flash column chromatography by gradually increasing the solvent polarity (90:10→85:15→80:20 petroleum ether [40-60]/ diethyl ether).

a. (\pm) (1*R*, 2*S*, 6*S*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-9,9-Dideutero-16-methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]-hexadec-14-en-6-ol^[15]

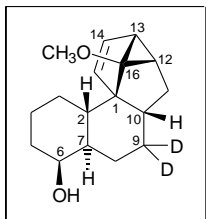
Fraction 1 was found to contain the cycloadduct alcohol as a pure colourless oil (0.055g, 35%).



R_f = 0.22 (80:20 petroleum ether [40-60]/ diethyl ether). λ_{max} (cyclohexane) 218 and 275nm. ν_{max} (thin film, cm^{-1}) 3439 (OH). δ_H (400MHz, CD_3OD) 1.34 (1H, dd, J 6.5 and 13.0Hz, one of CD_2CHCH_2), 1.44- 1.57 (5H, m, CH_2CD_2 , one of CD_2CHCH_2 , one of CH_2CH_2CHOH and one of CH_2CHOH), 1.58- 1.80 (6H, m, $CHCD_2$, $CH_2CHCHCHOH$, one of CH_2CH_2CHOH , $CHCHOH$ and $CHCHCHOH$), 1.80- 1.87 (1H, m, one of CH_2CHOH), 2.13- 2.19 (1H, m, $CHCHCH=CH$), 2.32- 2.36 (1H, m, $CHCH=CH$), 3.24 (3H, s, OCH_3), 3.77- 3.80 (1H, m, $CHOH$), 5.31 (1H, dd, J 1.5 and 5.5Hz, $CHCH=CH$), 5.54 (1H, dd, J 2.5 and 5.5Hz, $CHCH=CH$). δ_C (100MHz, CD_3OD) 21.6 (CH_2CH_2CHOH), 28.5 ($CH_2CHCHCHOH$), 29.3 (CD_2CHCH_2), 29.7 (CH_2CD_2), 29.8 (bquintet, CD_2), 31.3 ($CHCHCH=CH$), 34.8 (CH_2CHOH), 37.3 ($CHCH=CH$), 39.3 ($CHCHCHOH$), 42.9 ($CHCHOH$), 53.0 ($CHCD_2$), 55.0 (OCH_3), 66.1 ($CCH=CH$), 71.4 ($CHOH$), 90.6 ($COCH_3$), 125.0 ($CHCH=CH$), 139.5 ($CHCH=CH$). m/z (CI, NH_3 , high resolution) found 262.1911 [$C_{17}H_{22}D_2O_2$] ($(M)^+$, 21%) [requires 262.1900], 213.1669 (100), 148.0052 (24), 96.0563 (27).

b. (\pm) (1*S*, 2*S*, 6*S*, 7*R*, 10*S*, 12*S*, 13*R*, 16*R*)-9,9-Dideutero-16-methoxypentacyclo-[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-ol – novel

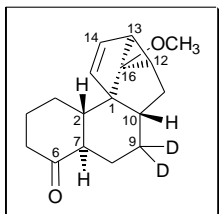
Fraction 2 contained the pure known deuterated cycloadduct alcohol (0.071g, 45%).



Mp. 42-44 °C. R_f = 0.15 (60:40 petroleum ether [40-60]/ diethyl ether). λ_{max} (cyclohexane) 209 and 278nm. ν_{max} (thin film, cm^{-1}) 3441 (OH). δ_H (400MHz, CD_3OD) 0.98- 1.14 (2H, m, one of CD_2CHCH_2 and one of CH_2CD_2), 1.40- 1.59 (5H, m, $CHCHCHOH$, $CH_2CHCHCHOH$, one of CH_2CH_2CHOH and one of CH_2CHOH), 1.71- 1.80 (1H, m, one of CH_2CH_2CHOH), 1.81- 1.89 (2H, m, one of CD_2CHCH_2 and one of CH_2CHOH), 1.95- 2.08 (4H, m, one of CH_2CD_2 , $CHCHCH=CH$, $CHCHOH$ and $CHCD_2$), 2.21 (1H, dt, J 8.5 and 2.0Hz, $CHCH=CH$), 3.50 (3H, s, OCH_3), 3.84 (1H, app. bq, J 2.5Hz, $CHOH$), 5.62- 5.67 (2H, m, $CHCH=CH$ and $CHCH=CH$). δ_C (100MHz, CD_3OD) 21.0 (CH_2CH_2CHOH), 27.1 (bqintet, CD_2), 27.6 (CD_2CHCH_2), 30.0 (CH_2CD_2), 30.4 ($CHCHCH=CH$), 30.9 ($CH_2CHCHCHOH$), 35.0 (CH_2CHOH), 39.0 ($CHCHOH$), 39.7 ($CHCH=CH$), 44.2 ($CHCHCHOH$), 57.9 (OCH_3), 60.3 ($CHCD_2$), 65.0 ($CCH=CH$), 71.1 ($CHOH$), 91.9 ($COCH_3$), 127.2 and 132.4 ($CHCH=CH$ and $CHCH=CH$). m/z (EI, high resolution) found 262.1898 [$C_{17}H_{22}D_2O_2$] ($(M)^+$, 35%) [requires 262.1900], 230.1655 (71), 203.1078 (98), 180.9884 (100).

Identification of the deuterated analogues of cycloadducts (**18**) and (**19**)

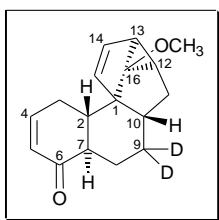
- a. (\pm) (*1R, 2S, 7R, 10S, 12R, 13S, 16S*)-9,9-Dideutero-16-methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-one (**22**)^[15]



Compound (**22**) was synthesised according to general procedure E from a solution of the deuterated cycloadduct alcohol (\pm) (*1R, 2S, 6S, 7R, 10S, 12R, 13S, 16S*)-9,9-dideutero-16-methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]-hexadec-14-en-6-ol (0.029g, 0.11mmol) in dry DCM (2ml), and a solution of pyridinium chlorochromate (0.045g, 0.24mmol) in anhydrous DCM (2x1ml). After 1.5 hours of stirring under argon, TLC indicated that no more starting material remained. Flash column chromatography (70:30 dichloromethane/ petroleum ether [40-60]) afforded the pure deuterated cycloadduct ketone (\pm) (*1R, 2S, 7R, 10S, 12R, 13S, 16S*)-9,9-dideutero-16-methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]-hexadec-14-en-6-one (**22**) as a colourless oil (0.021g, 73%).

R_f = 0.20 (70:30 dichloromethane/ petroleum ether [40-60]). λ_{max} (cyclohexane) 213 and 277nm. ν_{max} (thin film, cm^{-1}) 1706 (C=O). δ_H (400MHz, CD_3OD) 1.17- 1.25 (1H, m, one of CH_2CD_2), 1.38 (1H, dd, J 6.5 and 13.0Hz, one of CD_2CHCH_2), 1.49- 1.65 (3H, m, one of CD_2CHCH_2 , one of $CH_2CH_2C=O$ and CD_2CH), 1.71 (1H, dt, J 3.5 and 12.0Hz, $CHCHC=O$), 1.82- 1.90 (1H, m, one of $CH_2CHCHC=O$), 1.92- 1.98 (1H, m, one of CH_2CD_2), 2.08- 2.22 (2H, m, one of $CH_2CH_2C=O$ and one of $CH_2CHCHC=O$), 2.22- 2.27 (1H, m, $CHCHCH=CH$), 2.29- 2.35 (1H, m, one of $CH_2C=O$), 2.41- 2.50 (2H, m, $CHCH=CH$ and one of $CH_2C=O$), 2.80 (1H, app. ddt, J 1.5, 3.5 and 12.0Hz, $CHC=O$), 3.28 (3H, s, OCH_3), 5.33 (1H, dd, J 1.5 and 5.5Hz, $CHCH=CH$), 5.60 (1H, dd, J 2.5 and 5.5Hz, $CHCH=CH$). δ_C (100MHz, CD_3OD) 26.5 ($CH_2CHC=O$), 28.8 (biquintet, CD_2), 28.9 ($CH_2CH_2C=O$ and $CH_2CHCHC=O$), 30.2 (CH_2CHCD_2), 31.7 ($CHCHCH=CH$), 37.6 ($CHCH=CH$), 43.9 ($CH_2C=O$), 49.4 ($CHCHC=O$), 52.8 ($CHC=O$), 53.5 ($CHCD_2$), 55.7 (OCH_3), 66.7 ($CCH=CH$), 91.8 ($COCH_3$), 126.8 ($CHCH=CH$), 139.3 ($CHCH=CH$), 217.0 ($C=O$). m/z (EI, high resolution) found 260.1748 [$C_{17}H_{20}D_2O_2$] ($(M)^+$, 11%) [requires 260.1743], 205.1206 (100), 180.9890 (74), 168.9882 (75).

b. (\pm) (1*R*, 2*S*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-9,9-Dideutero-16-methoxypentacyclo-[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-4,14-dien-6-one (**23**)^[15]



Firstly, a 0.2M solution of lithium diisopropylamide was prepared according to general procedure G. Deuterated cycloadduct enone (**22**) was then synthesised according to general procedure H from a solution of the ketone (\pm) (1*R*, 2*S*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-9,9-dideutero-16-methoxypentacyclo-[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-one (**22**) (0.020g, 0.08mmol) in anhydrous THF (1ml), and the 0.2M LDA solution (0.41ml, 0.08mmol). A solution of phenylselenenyl chloride (0.016g, 0.09mmol) in THF (2x1ml) was added rapidly to the reaction mixture and left to stir under argon at -78°C for 1.5 hours after which time TLC indicated that the reaction had run to completion. The pure α -phenylseleno ketone intermediate (\pm) (1*R*, 2*S*, 5*RS*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-9,9-dideutero-5-phenylselenanyl-16-methoxypentacyclo-[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]hexadec-14-en-6-one was obtained as a mixture of two diastereoisomers by purification using silica gel flash column chromatography (50:50 dichloromethane/ petroleum ether [30-40]) in an overall yield of 61% (0.019g).

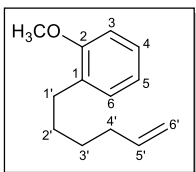
The pure, clear oil was then directly reacted on to give the desired α,β -unsaturated ketone (**23**) by following procedure H from the α -phenylseleno ketone (0.019g, 0.05mmol), anhydrous THF (1ml) and 27.5% wt. hydrogen peroxide solution in water (0.02ml, 0.14mmol). The reaction mixture was left to stir at 0°C for 30 minutes and room temperature for a further 30 minutes, after which time TLC indicated that the reaction had run to completion. Purification of the crude oil using flash column chromatography (70:30 dichloromethane/ petroleum ether [30-40]) afforded the desired α,β -unsaturated ketone cycloadduct (\pm) (1*R*, 2*S*, 7*R*, 10*S*, 12*R*, 13*S*, 16*S*)-9,9-dideutero-16-methoxypentacyclo[11.2.1.0^{1,10}.0^{2,7}.0^{12,16}]-hexadec-4,14-dien-6-one (**23**) as a colourless oil (0.011g, 94%). The overall yield for the process of converting the cycloadduct ketone (**22**) to its α,β -unsaturated derivative (**23**) was calculated to be 57%.

R_f = 0.20 (70:30 dichloromethane/ petroleum ether [30-40]). λ_{max} (cyclohexane) 220nm. ν_{max} (thin film, cm⁻¹) 1671 (α,β -unsaturated C=O). δ_H (400MHz, CD₃OD) 1.06- 1.14 (1H, m, one of CH₂CD₂), 1.41 (1H, dd, J 6.5 and 13.0Hz, one of CD₂CHCH₂), 1.56 (1H, ddd, J 1.5, 5.5 and 13.0Hz, one of CD₂CHCH₂), 1.67 (1H, app. bd, J 5.5Hz, CD₂CH), 2.10 (1H, ddd, J 4.5, 11.5

and 13.5Hz, CCHCHC=O), 2.24- 2.32 (2H, m, one of CH₂CD₂ and CHCHCH=CH), 2.36- 2.45 (2H, m, one of CH₂CHCHC=O and CHCH=CH), 2.70 (1H, ddd, *J* 4.0, 11.5 and 13.5Hz, CH₂CHC=O), 2.91 (1H, app. ddt, *J* 2.0, 11.5 and 19.5Hz, one of CH₂CH=CHC=O), 3.22 (3H, s, OCH₃), 5.34 (1H, dd, *J* 1.5 and 5.5Hz, CHCH=CH), 5.64 (1H, dd, *J* 2.5 and 5.5Hz, CHCH=CH), 5.95 (1H, ddd, *J* 1.0, 3.0 and 10.0Hz, CH=CHC=O), 7.12 (1H, ddd, *J* 2.0, 6.0 and 10.0Hz, CH=CHC=O). δ_c (100MHz, CD₃OD) 26.6 (CH₂CD₂), 28.7 (CD₂), 30.1 (CD₂CHCH₂), 30.4 (CH₂CH=CHC=O), 30.8 (CHCHCH=CH), 37.1 (CHCH=CH), 43.8 (CCHCHC=O), 48.7 (CH₂CHC=O), 53.0 (CD₂CH), 55.0 (OCH₃), 66.1 (CCOCH₃), 91.8 (COCH₃), 127.4 (CHCH=CH), 130.1 (CH=CHC=O), 138.4 (CHCH=CH), 154.1 (CH=CHC=O), 205.2 (C=O). *m/z* (CI, NH₃, high resolution) found 259.1675 [C₁₇H₁₈D₂O₂] ((MH)⁺, 100%) [requires 259.1665], 227.1395 (17), 202.1081 (31).

Synthesis of the control substrate

a. 1-(Hex-5-en-1-yl)-2-methoxybenzene (**9**)^[16]

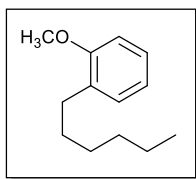


2-Methoxybenzyl alcohol (1.90ml, 14.47mmol) in anhydrous toluene (20ml) was warmed to 50°C before phosphorous tribromide (0.48ml, 5.06mmol) was added drop-wise *via* syringe. The oil bath was then heated to 100°C and the mixture stirred at this temperature, under argon, for 1.5 hours. After this time, TLC indicated that no more starting material remained and the reaction was terminated by the addition of water and saturated NaCl solution. The mixture was transferred to a separating funnel where the aqueous layer was extracted with diethyl ether (3x20ml). The combined organic extracts were then washed with saturated NaCl solution (2x20ml) and water (2x20ml). The organic layer was dried over MgSO₄, filtered and concentrated *in vacuo* to give a golden yellow crude oil of 2-methoxybenzyl bromide (3.215g), which was directly reacted on.

To activated magnesium turnings (0.490g, 20.16mmol) under argon was added dry THF (1.5ml) followed shortly by neat 5-bromopent-1-ene (0.21ml, 1.76mmol). After 10 minutes the mixture began to exotherm as the reaction initiated. At this stage, a solution of the remaining 5-bromopent-1-ene (1.87ml, 15.83mmol) in dry THF (5ml) was added to the reaction mixture drop-wise over a period of 15 minutes. The solution was then stirred under argon for 45 minutes to ensure complete formation of the Grignard reagent (139). At this stage, 2-methoxybenzyl bromide (3.215g, 15.99mmol) was added drop-wise, *via* syringe, to the reaction mixture, which was then heated to 60°C and stirred under argon for 20 hours. After this time TLC indicated that the reaction had run to completion and was quenched with water and 1M HCl solution. The mixture was transferred to a separating funnel where the aqueous layer was extracted with diethyl ether (3x30ml). The organic washings were then collected together and washed with 1M HCl solution and water (2x30ml). The organic layer was dried over MgSO₄, filtered and concentrated *in vacuo* to give a crude oil. The majority of the by-products formed were removed using flash column chromatography (pentane) and then purified further using Kugelrohr distillation. The oil was initially heated to 170°C to remove any remaining impurities and then heated further to 180°C to afford a pure fraction of the desired 1-hex-5'-enyl-2-methoxybenzene (**9**) (0.313g, 10%).

Bp. 178-179°C. $R_f = 0.27$ (pentane). λ_{\max} (cyclohexane) 223 and 272nm. ν_{\max} (thin film, cm^{-1}) 1601 (aromatic stretch). δ_{H} (400MHz, CDCl_3) 1.43- 1.52 (2H, m, $\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$), 1.59- 1.68 (2H, m, $\text{CH}_2\text{CH}_2\text{Ar}$), 2.09- 2.16 (2H, m, $\text{CH}_2\text{CH}=\text{CH}_2$), 2.65 (2H, t, J 7.5Hz, CH_2Ar), 3.84 (3H, s, OCH_3), 4.96 (1H, ddt, $J_{\text{H6cis-H5}}$ 10.0, J_{gem} 2.0 and $J_{\text{H6-H4}}$ 1.0Hz, $\text{CH}=\text{CH}_2$ (*cis*-H5)), 5.03 (1H, app. dq, $J_{\text{H6trans-H5}}$ 17.0 and $J_{\text{gem/H6-H4}}$ 2.0Hz, $\text{CH}=\text{CH}_2$ (*trans*-H5)), 5.85 (1H, ddt, J 17.0, 10.0 and 6.5Hz, $\text{CH}=\text{CH}_2$), 6.87 (1H, app. d, J 7.5Hz, $\text{CH}=\text{COCH}_3$), 6.91 (1H, app. dt, J 1.0 and 7.5Hz, $\text{CHCHCH}=\text{COCH}_3$), 7.16 (1H, dd, J 1.5 and 7.5Hz, $\text{CHC}(\text{C}_6\text{H}_{11})=\text{COCH}_3$), 7.20 (1H, dt, J 1.5 and 7.5Hz, $\text{CHCH}=\text{COCH}_3$). δ_{C} (63MHz, CDCl_3) 29.3 ($\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$), 30.0 ($\text{CH}_2\text{CH}_2\text{Ar}$), 30.4 (CH_2Ar), 34.1 ($\text{CH}_2\text{CH}=\text{CH}_2$), 55.6 (OCH_3), 110.6 ($\text{CH}=\text{COCH}_3$), 114.6 ($\text{CH}=\text{CH}_2$), 120.7 ($\text{CHCHCH}=\text{COCH}_3$), 127.2 ($\text{CHCH}=\text{COCH}_3$), 130.2 ($\text{CHC}(\text{C}_6\text{H}_{11})=\text{COCH}_3$), 131.5 ($\text{C}(\text{C}_6\text{H}_{11})=\text{COCH}_3$), 139.5 ($\text{CH}=\text{CH}_2$), 157.8 (COCH_3). m/z (CI, NH_3 , high resolution) found 190.1358 [$\text{C}_{13}\text{H}_{18}\text{O}$] ($[\text{M}]^+$, 76%) [requires 190.1358], 147.0863 (35), 121.0636 (100), 91.0545 (39).

b. 1-Hexyl-2-methoxybenzene^[17]



The substrate was prepared according to general procedure C using 1-hex-5'-enyl-2-methoxybenzene (**9**) (0.026g, 0.14mmol) in anhydrous methanol (2ml), a catalytic amount of 10% palladium on carbon and excess hydrogen. After 1 hour of vigorous stirring TLC indicated that the reaction had run to completion, so the mixture was filtered through celite and the filtrate concentrated *in vacuo* to afford the pure oil 1-hexyl-2-methoxybenzene in a quantitative yield.

$R_f = 0.53$ (95:5 petroleum ether [40-60]/ diethyl ether). λ_{\max} (cyclohexane) 198, 222 and 273nm. ν_{\max} (thin film, cm^{-1}) 1601 (aromatic stretch), 1242 ($_{\text{ar}}\text{C}-\text{O}-\text{C}_{\text{al}}$). δ_{H} (250MHz, CDCl_3) 0.77- 0.85 (3H, m, CH_2CH_3), 1.15- 1.34 (6H, m, $\text{CH}_2(\text{CH}_2)_2\text{CH}_3$, $\text{CH}_2\text{CH}_2\text{CH}_3$ and CH_2CH_3), 1.43- 1.57 (2H, m, $\text{CH}_2\text{CH}_2\text{Ar}$), 2.52 (2H, t, J 7.5Hz, CH_2Ar), 3.73 (3H, s, OCH_3), 6.75 (1H, app. d, J 7.5Hz, $\text{CH}=\text{COCH}_3$), 6.79 (1H, app. dt, J 1.0 and 7.5Hz, $\text{CHCHCH}=\text{COCH}_3$), 7.02- 7.13 (2H, m, $\text{CHCH}=\text{COCH}_3$ and $\text{CHC}(\text{C}_6\text{H}_{13})=\text{COCH}_3$). δ_{C} (63MHz, CDCl_3) 14.6 (CH_2CH_3), 23.1 (CH_2CH_3), 29.7 ($\text{CH}_2\text{CH}_2\text{CH}_3$ or $\text{CH}_2(\text{CH}_2)_2\text{CH}_3$), 30.3 ($\text{CH}_2\text{CH}_2\text{Ar}$), 30.7 (CH_2Ar), 32.2 ($\text{CH}_2\text{CH}_2\text{CH}_3$ or $\text{CH}_2(\text{CH}_2)_2\text{CH}_3$), 55.6 (OCH_3), 110.6 ($\text{CH}=\text{COCH}_3$), 120.7 ($\text{CHCHCH}=\text{COCH}_3$), 127.1 ($\text{CHCH}=\text{COCH}_3$), 130.1 ($\text{CHC}(\text{C}_6\text{H}_{13})=\text{COCH}_3$), 131.8 ($\text{C}(\text{C}_6\text{H}_{13})=\text{COCH}_3$), 157.8 (COCH_3). m/z

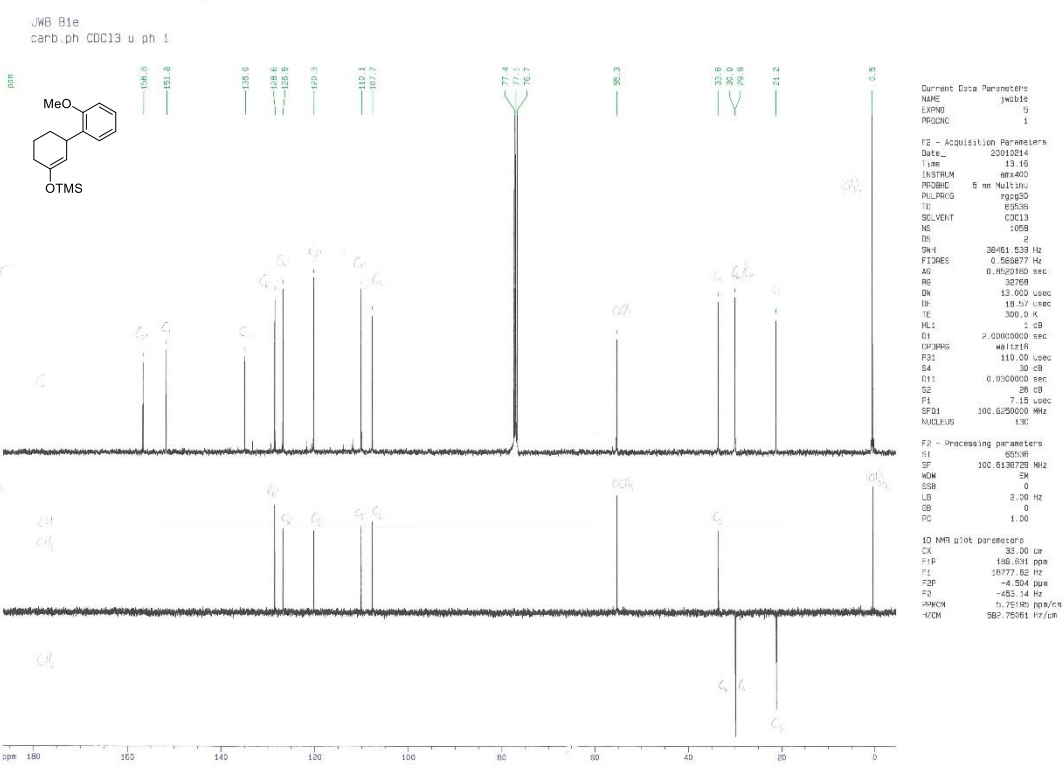
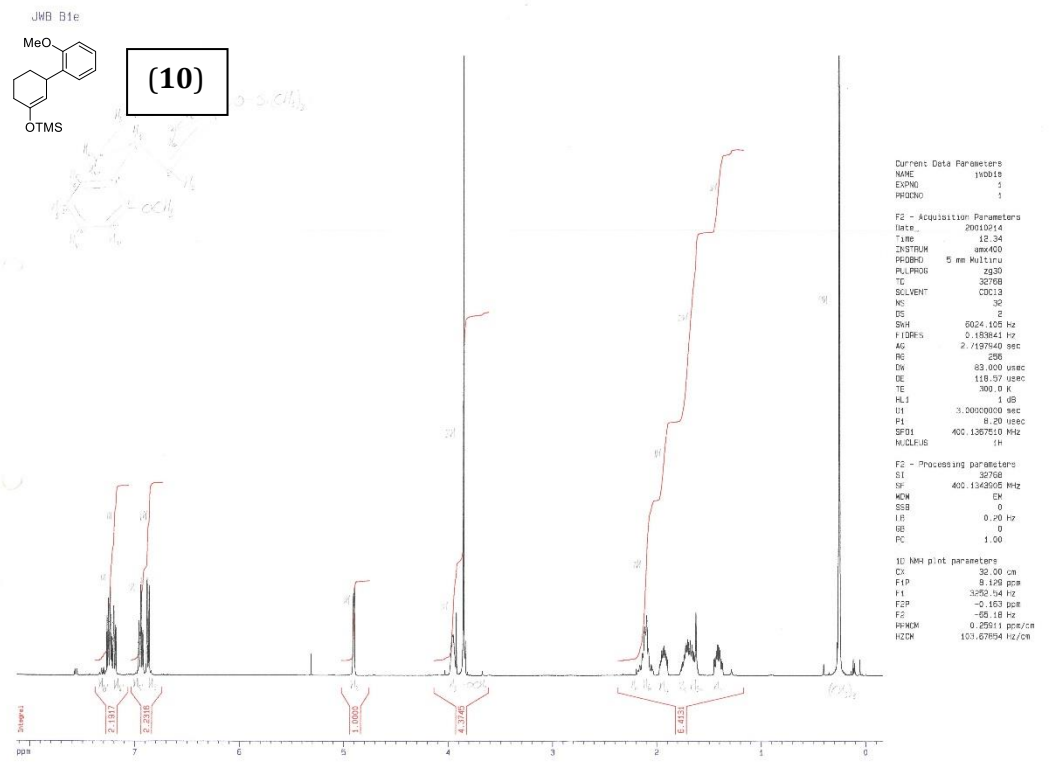
(CI, NH₃, high resolution) found 192.1512 [C₁₃H₂₀O] ((M)⁺, 35%) [requires 192.1514], 121.0647 (100).

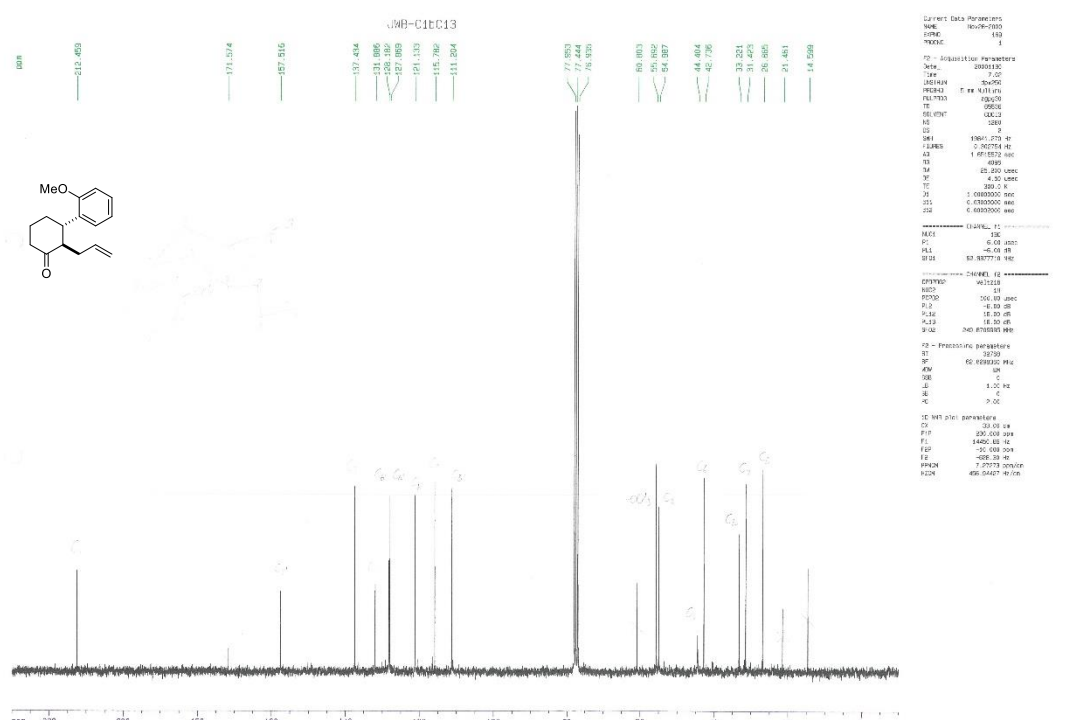
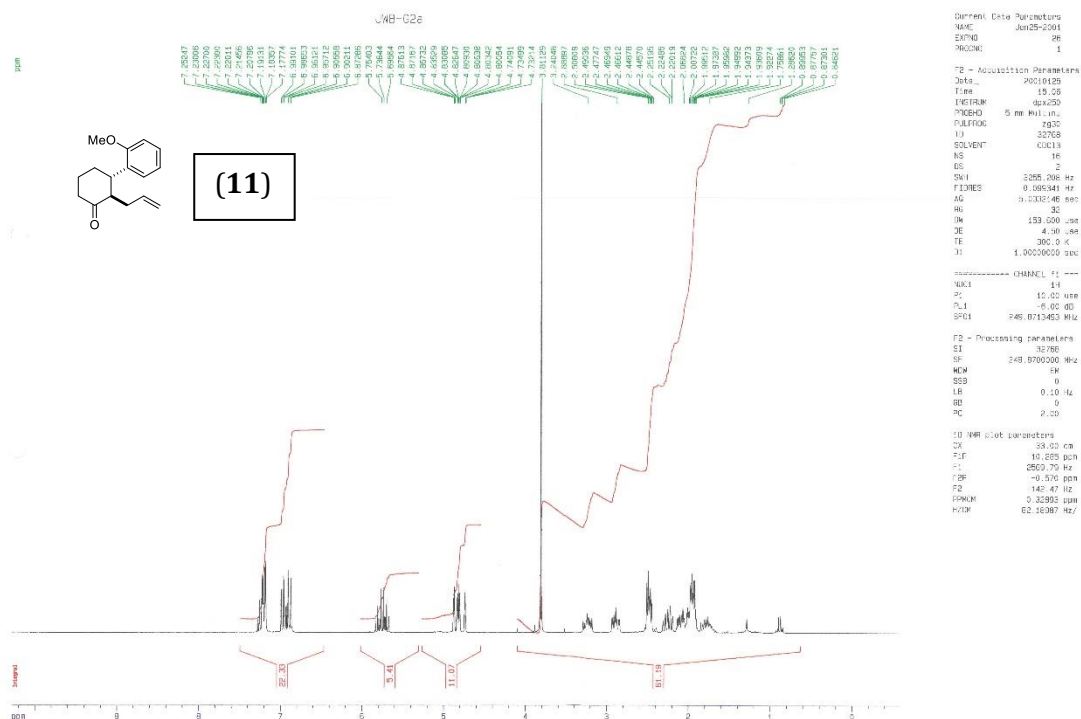
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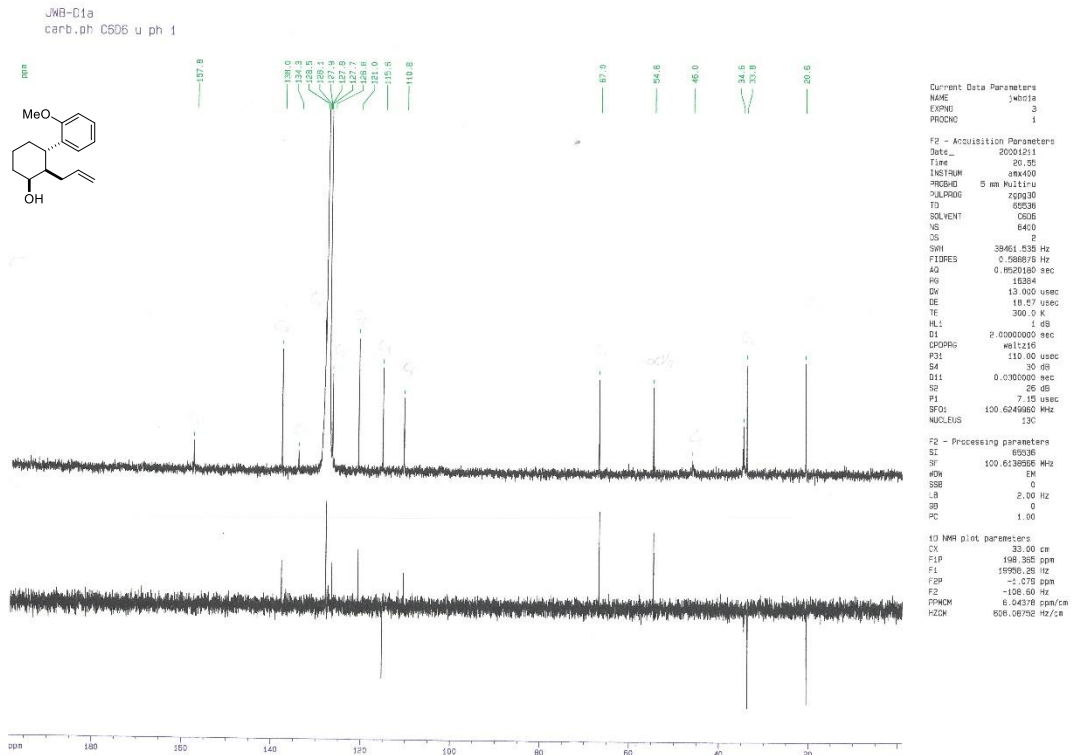
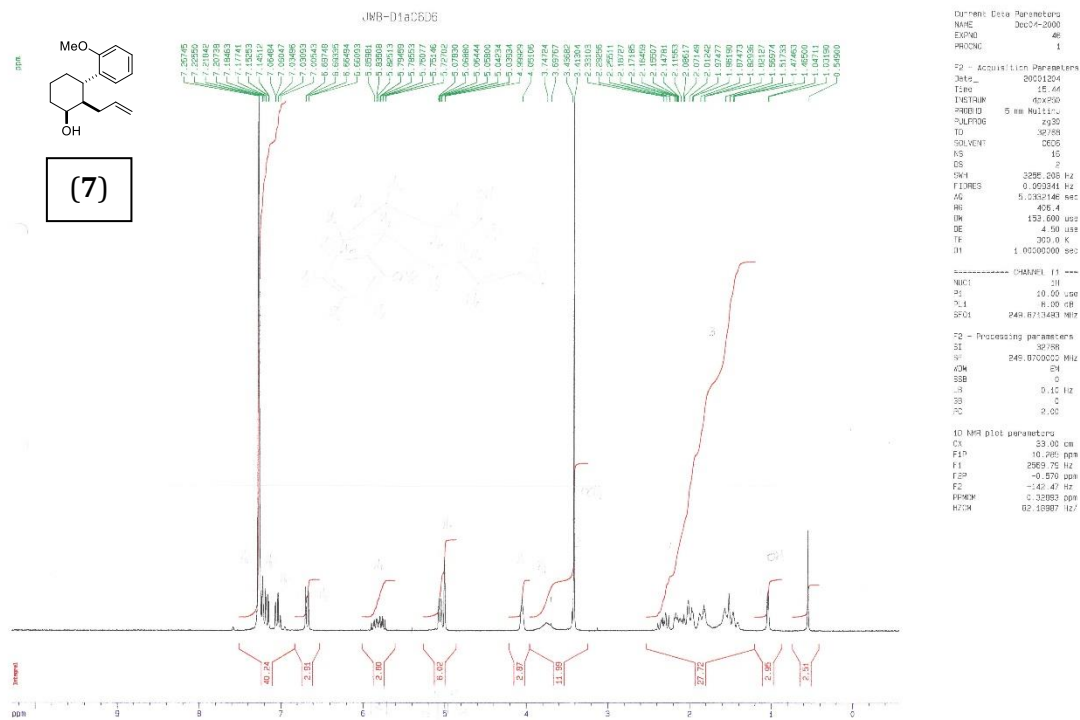
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NMR SPECTRA

Synthesis of the 3-carbon tether substrate

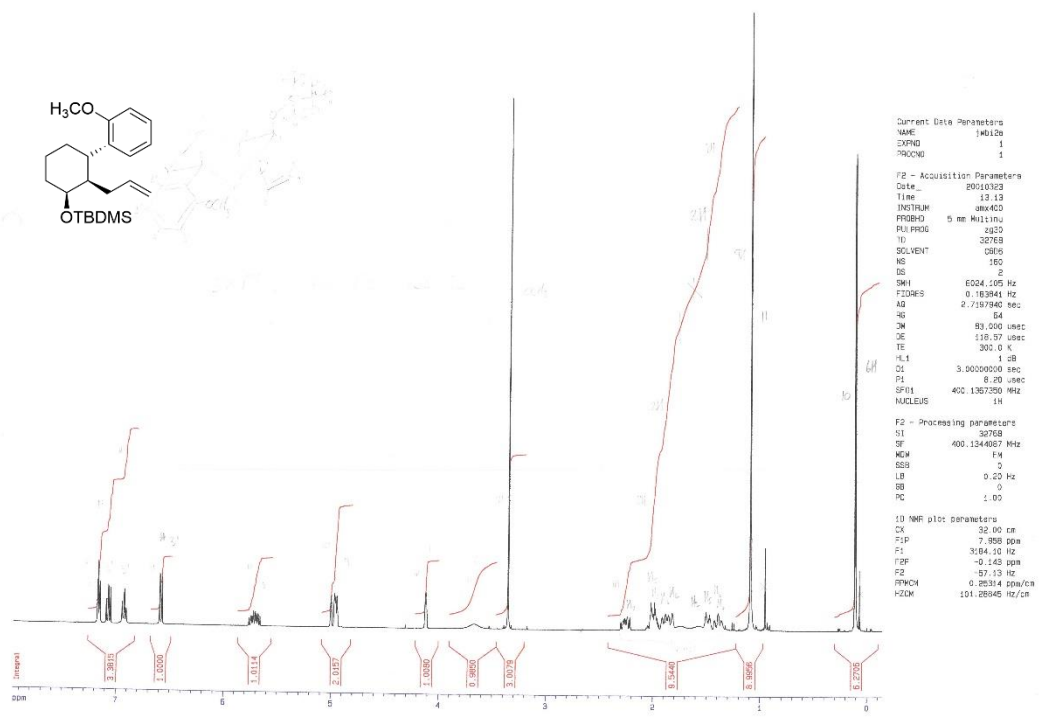




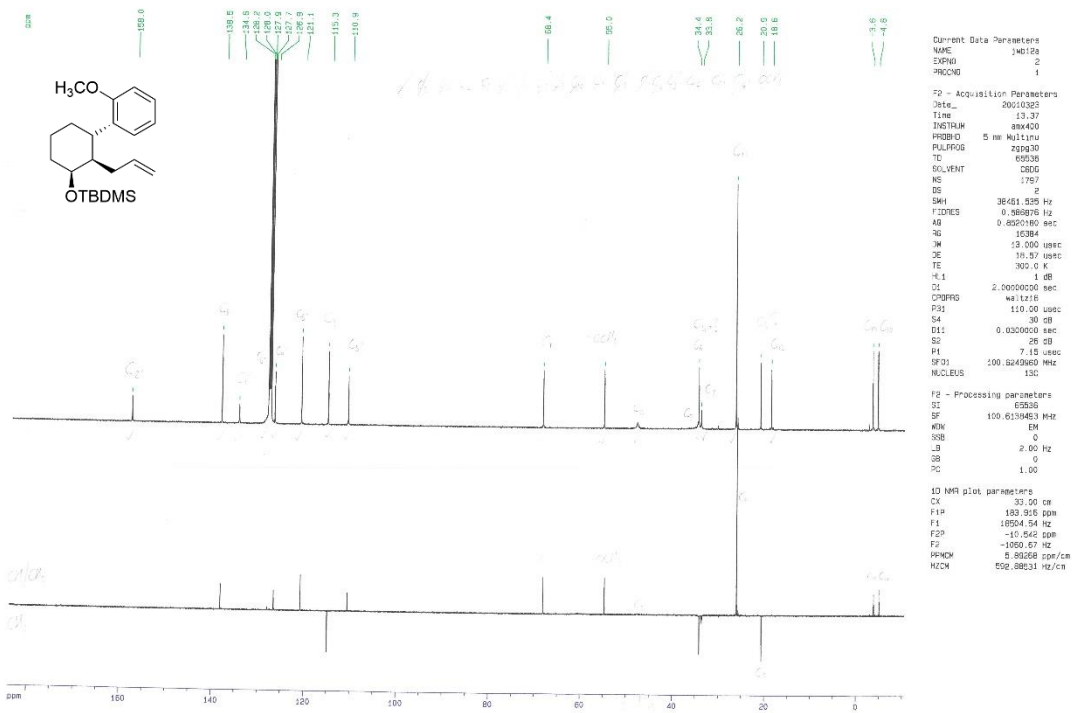


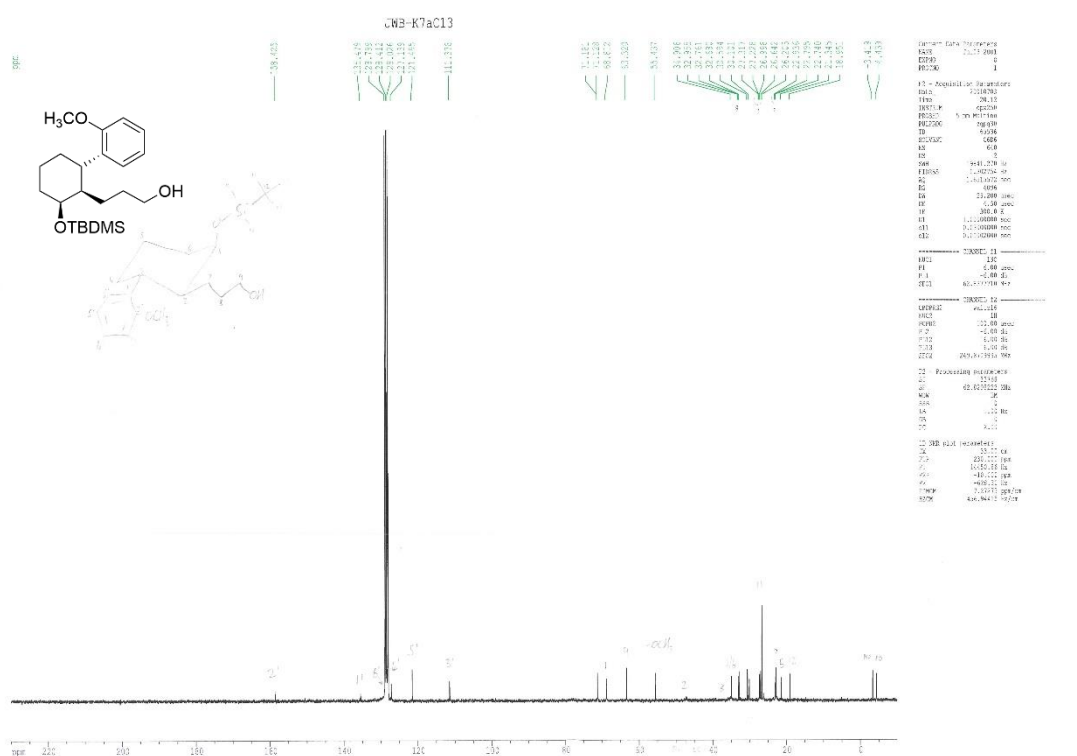
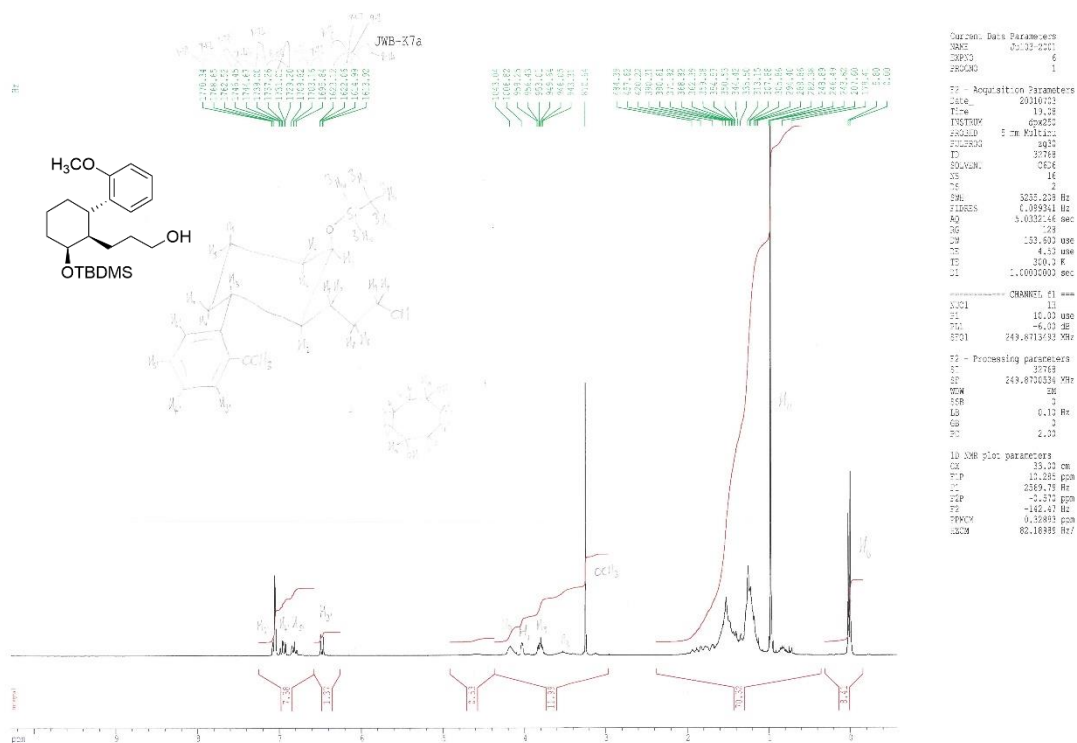
Synthesis of the 4-carbon tether substrate: Route A

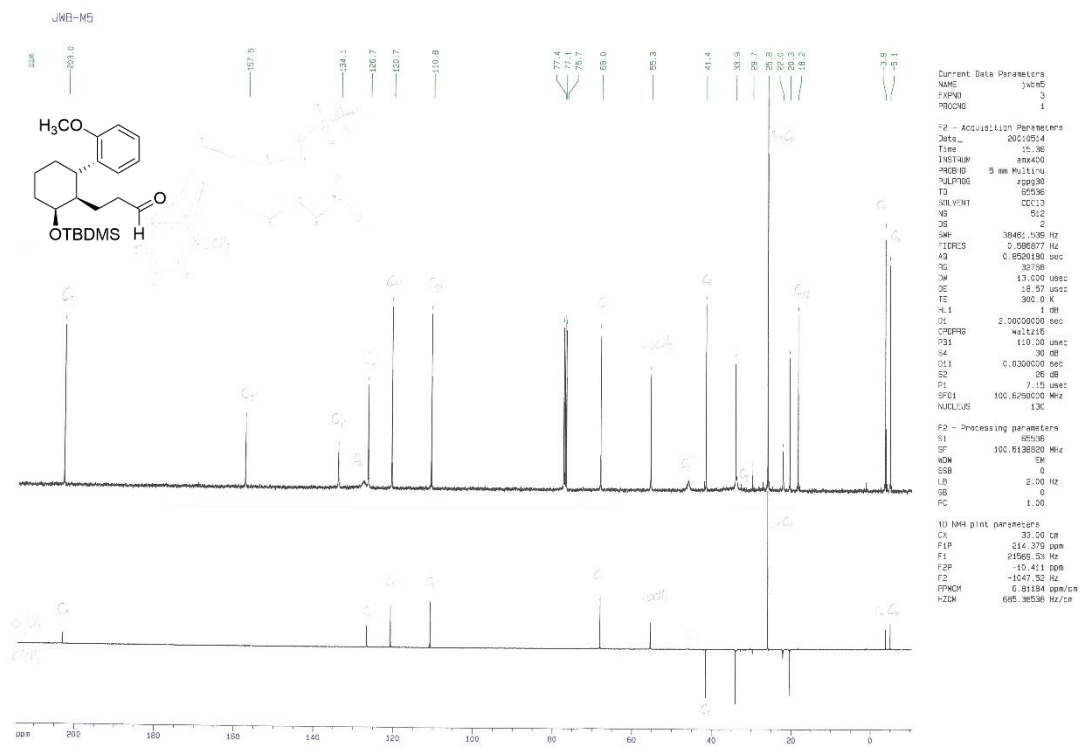
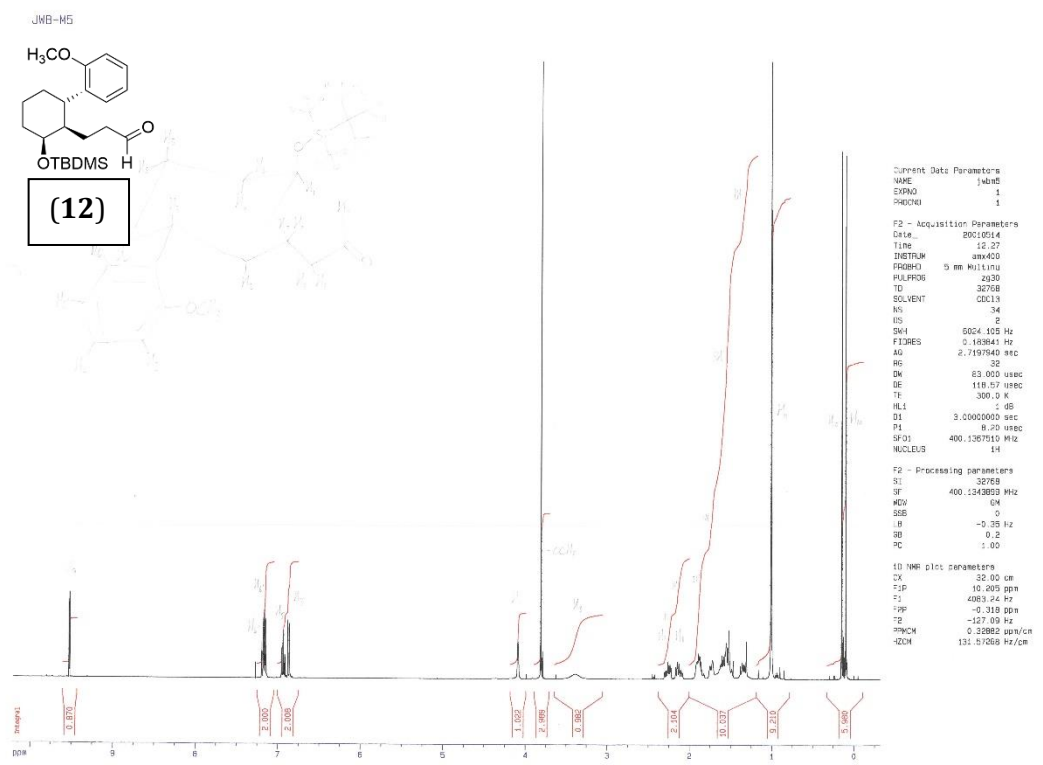
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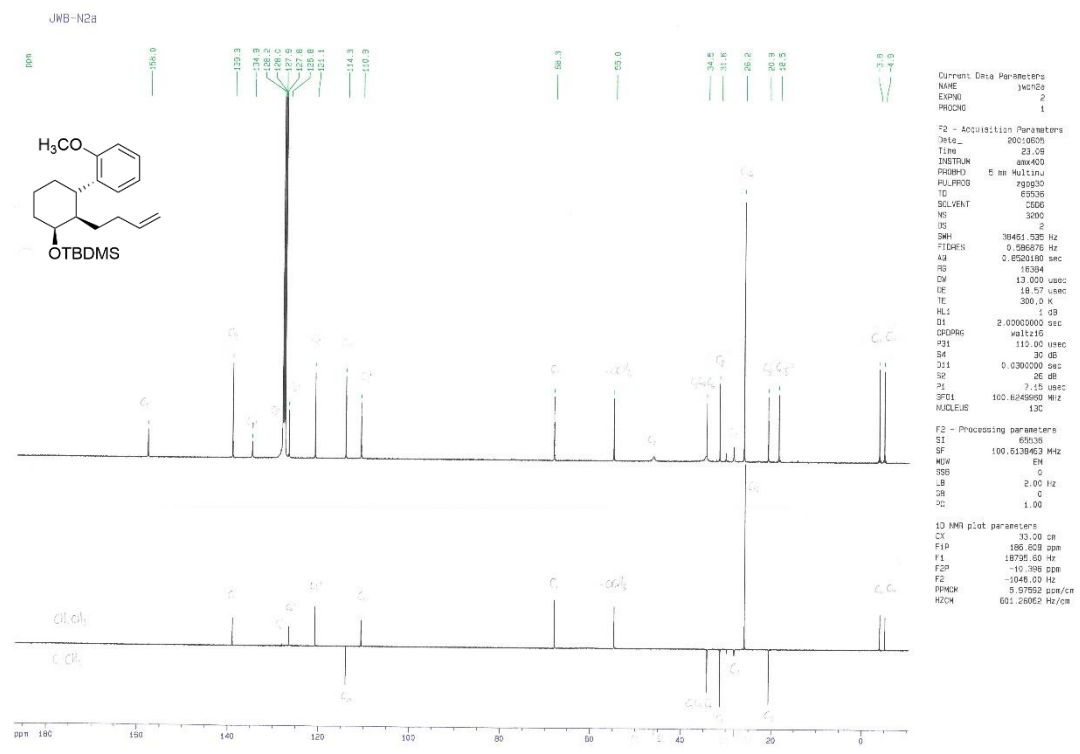
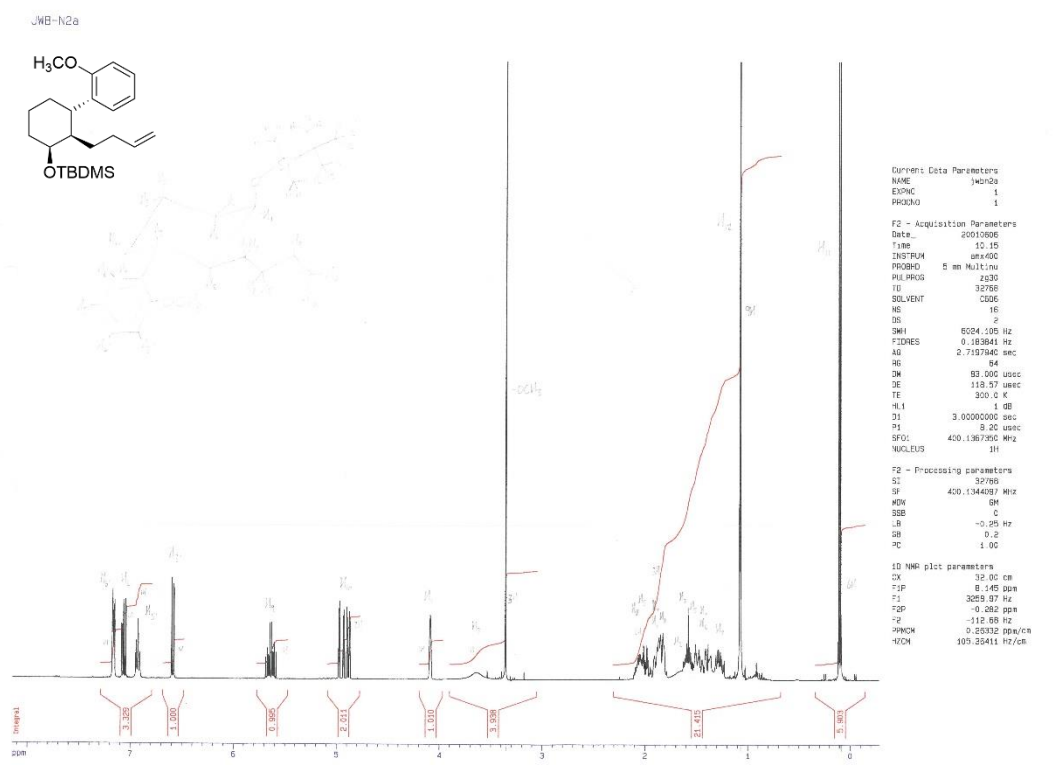


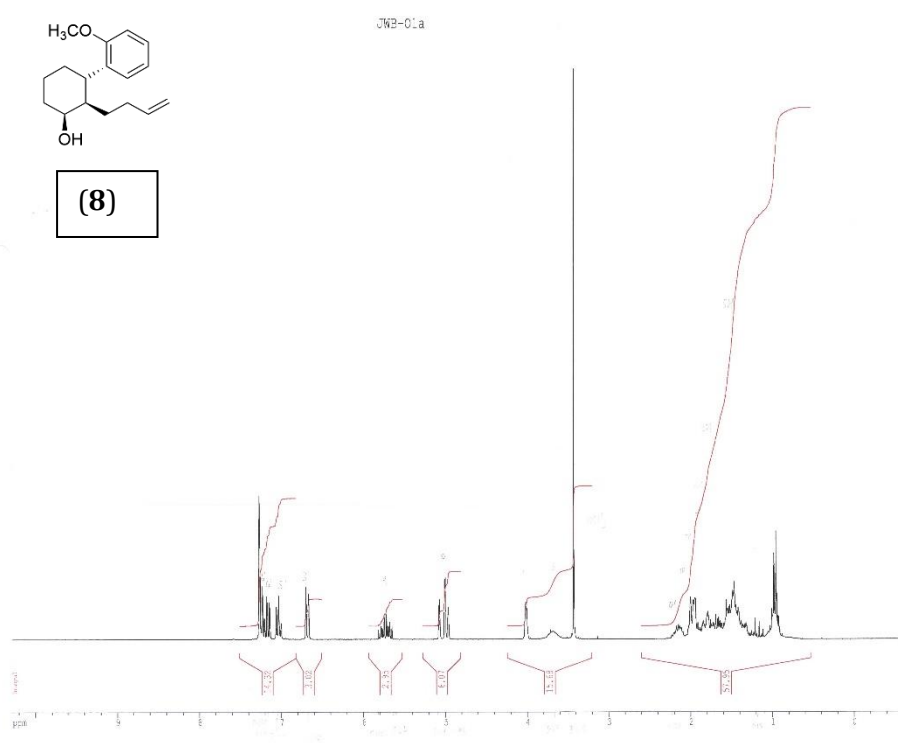
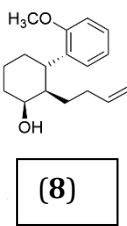
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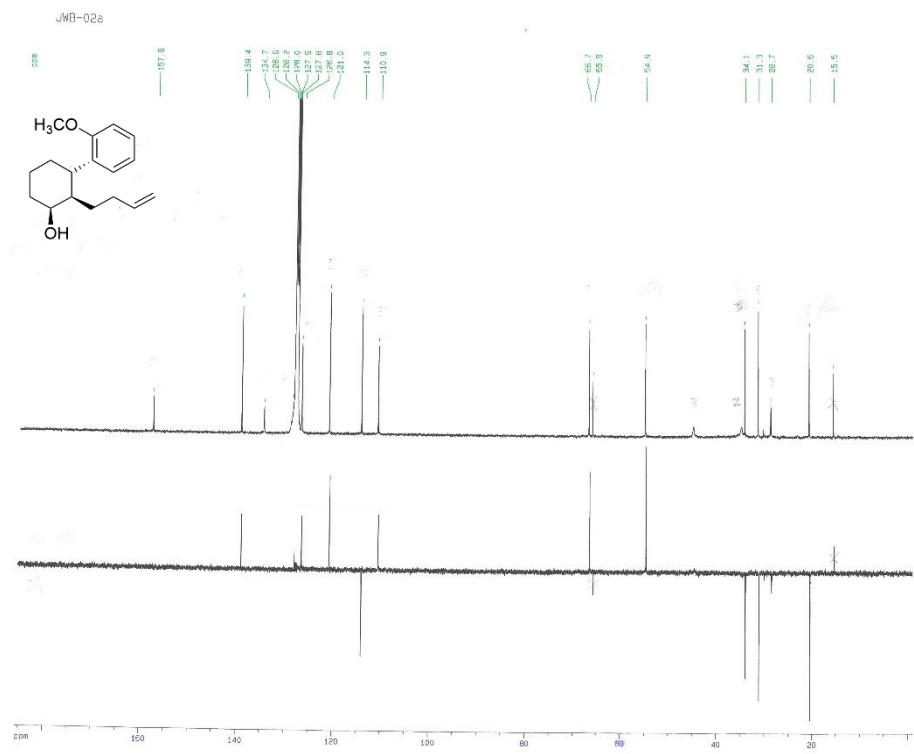
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PROCNO   1

F2 - Acquisition Parameters
Date_    20161226
Time     21.46
INSTRUM  spect
PROBHD   5 mm Multic
PULPROG  zgpg30
TD        65536
SOLVENT  CDCl3
VS        32768
DS        2
SWH       32768.000 Hz
FIDRES    0.885916 Hz
AQ         0.4925160 sec
RG         32768
DM         13.200 sec
DE         18.57 usec
TE         300.2 K
H1        1 dB
D1         2.0000000 sec
CDEPRG    waltz16
P31        110.00 usec
S4         30 dB
D11        0.0300000 sec
S2         0 dB
P1         7.15 usec
SFO1      100.6249960 MHz
NUC1       13C

F2 - Processing parameters
SI        65536
SF        100.6196433 MHz
WDW        EM
SSB        0
LB         2.00 Hz
GB         0
PC         1.00

1D NMR plot parameters
CX         33.00 cm
F1P        17.235 ppm
F1         2569.15 Hz
F2P        -1.510 ppm
F2         -147.17 Hz
F2MIN      0.32893 ppm
F2MAX      82.16381 Hz
    
```



```

Current Data Parameters
NAME      JWB02a
EXPNO    2
PROCNO   1

F2 - Acquisition Parameters
Date_    20160903
Time     15.26
INSTRUM  spect
PROBHD   5 mm Multic
PULPROG  zgpg30
TD        65536
SOLVENT  CDCl3
VS        32768
DS        2
SWH       30461.530 Hz
FIDRES    0.885916 Hz
AQ         0.4925160 sec
RG         32768
DM         13.200 sec
DE         18.57 usec
TE         300.2 K
H1        1 dB
D1         2.0000000 sec
CDEPRG    waltz16
P31        110.00 usec
S4         30 dB
D11        0.0300000 sec
S2         0 dB
P1         7.15 usec
SFO1      100.6249960 MHz
NUC1       13C

F2 - Processing parameters
SI        65536
SF        100.6196433 MHz
WDW        EM
SSB        0
LB         2.00 Hz
GB         0
PC         1.00

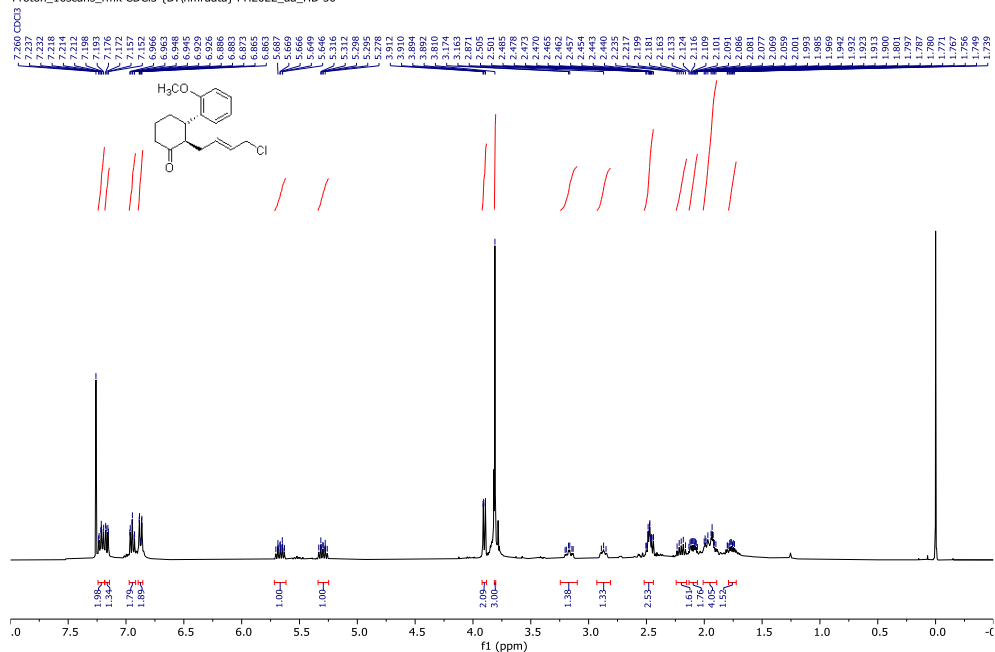
1D NMR plot parameters
CX         33.00 cm
F1P        185.677 ppm
F1         18681.66 Hz
F2P        -1.086 ppm
F2         -109.48 Hz
F2MIN      5.95995 ppm/cm
F2MAX      95.42892 Hz/cm
    
```

Synthesis of the 4-carbon tether substrate: Route B

Jun19-2023-PH2022_aa_HD.20.fid

SampleNumber 2.01 12 may

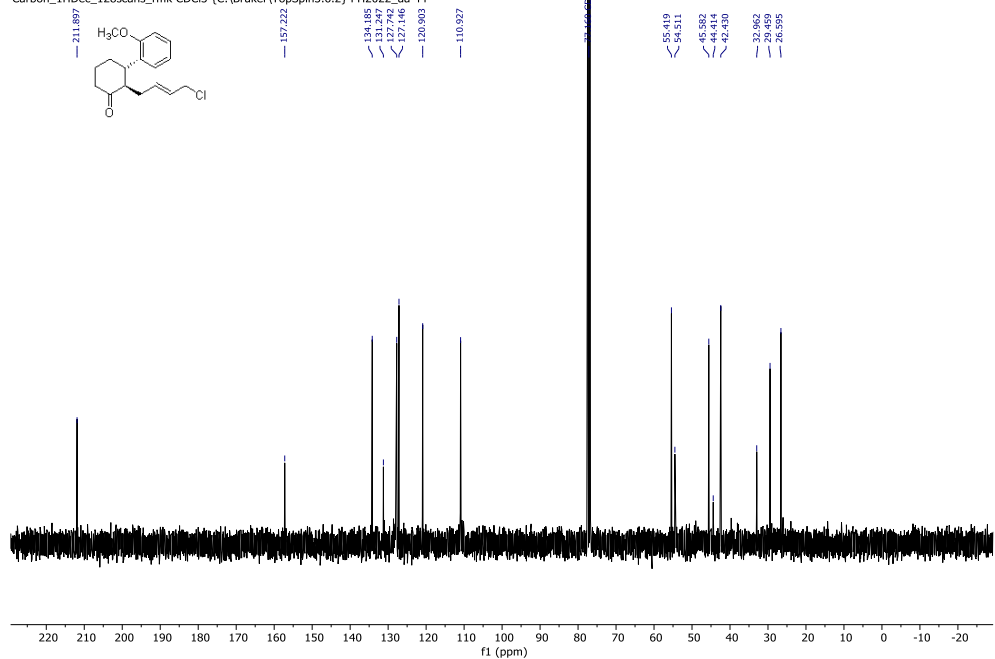
Proton_16scans_rmk CDCl3 {D:\nmrdata} PH2022_aa_HD 50

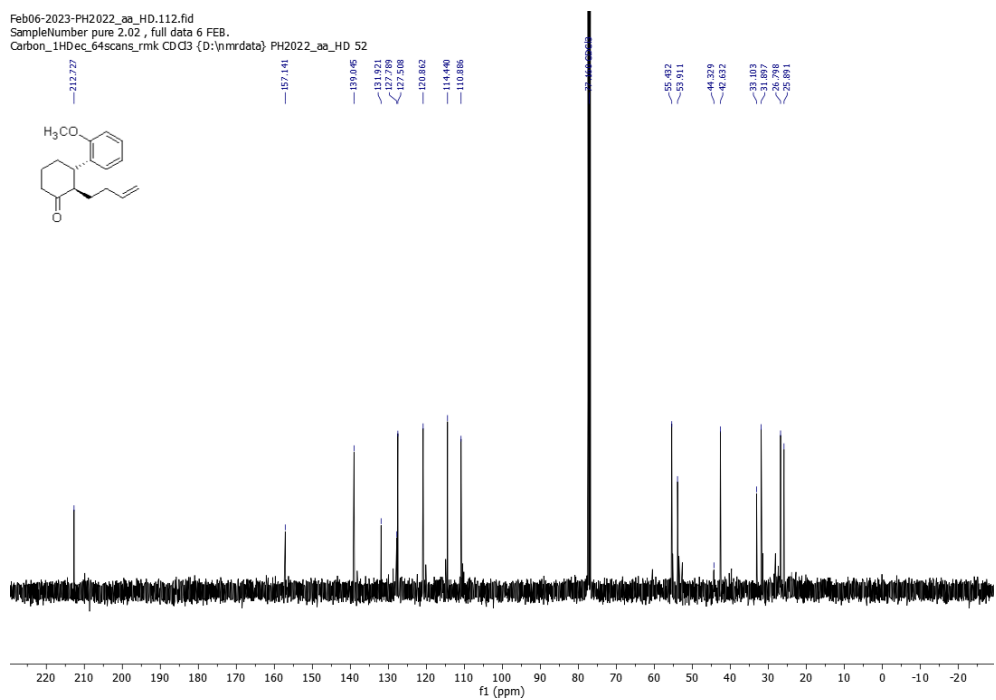
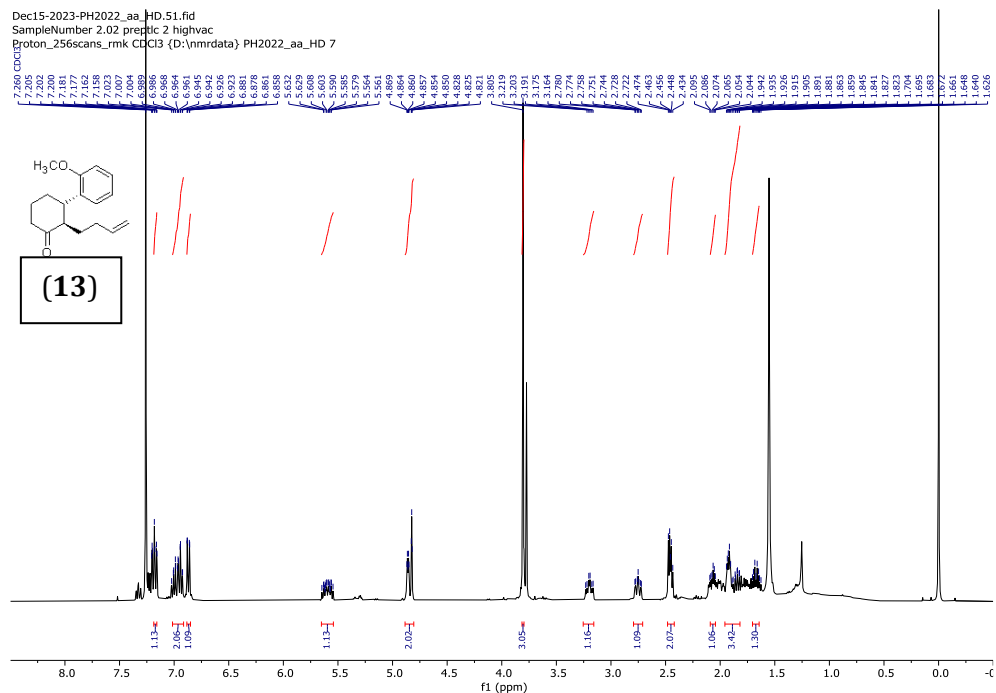


Jan19-2023-PH2022_aa.42.fid

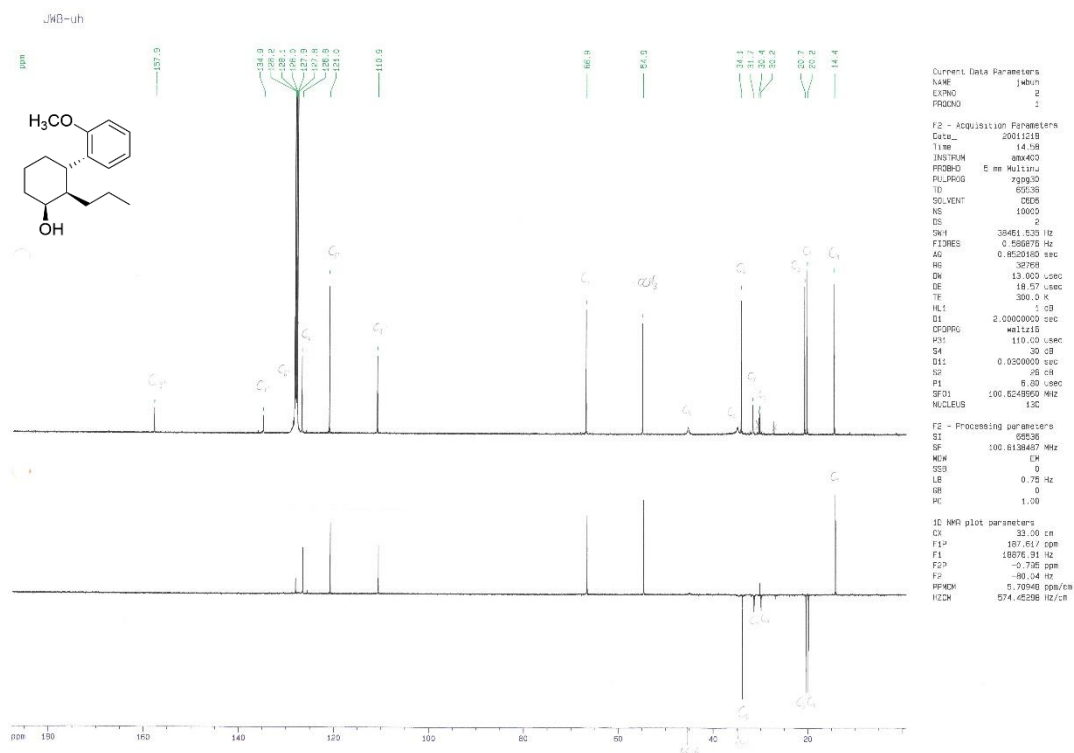
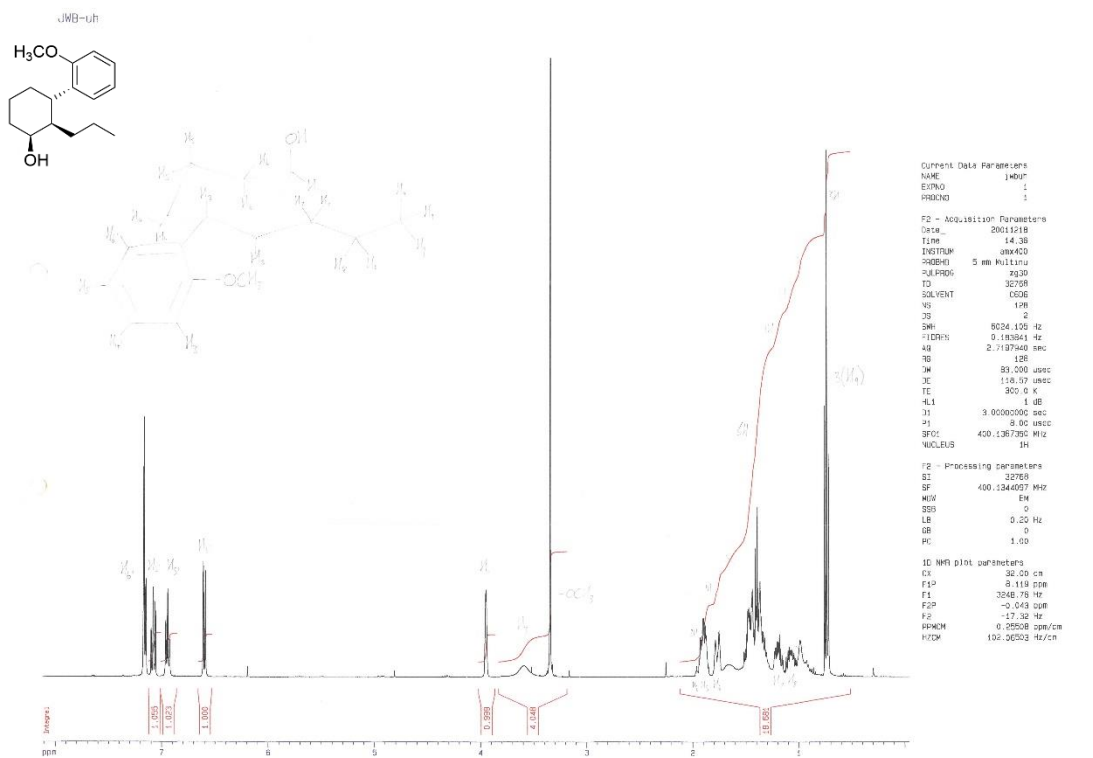
2.01 pure full data, alkylation silyl with iodo chloro but.

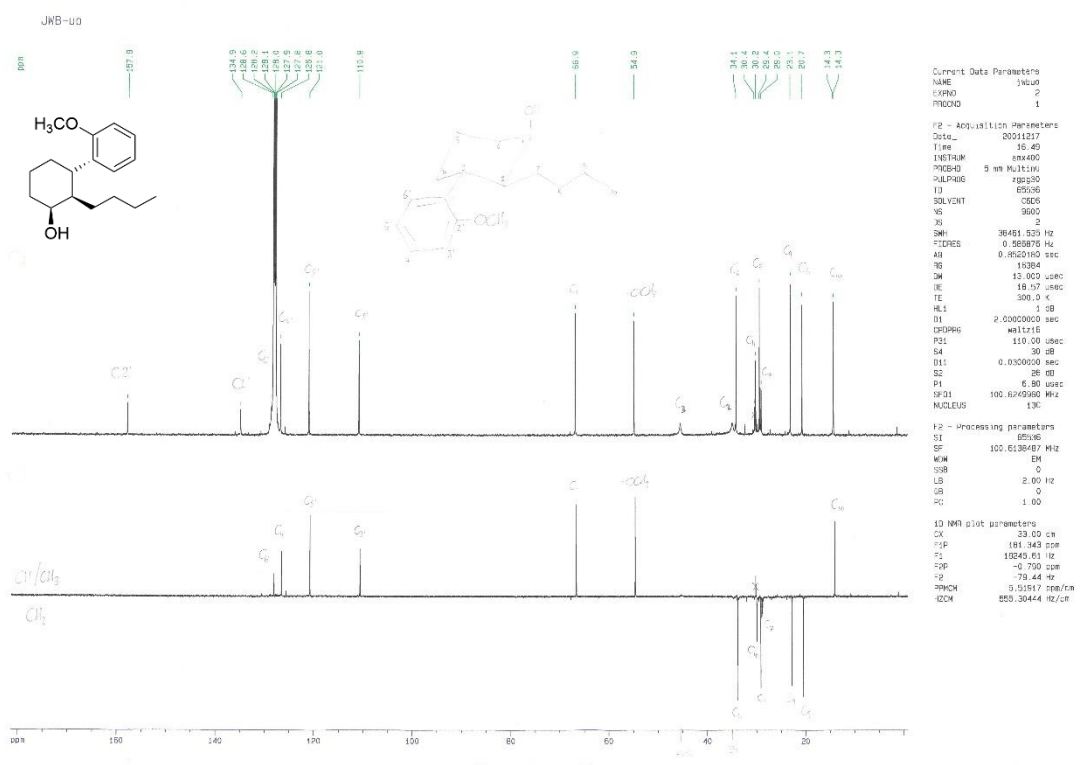
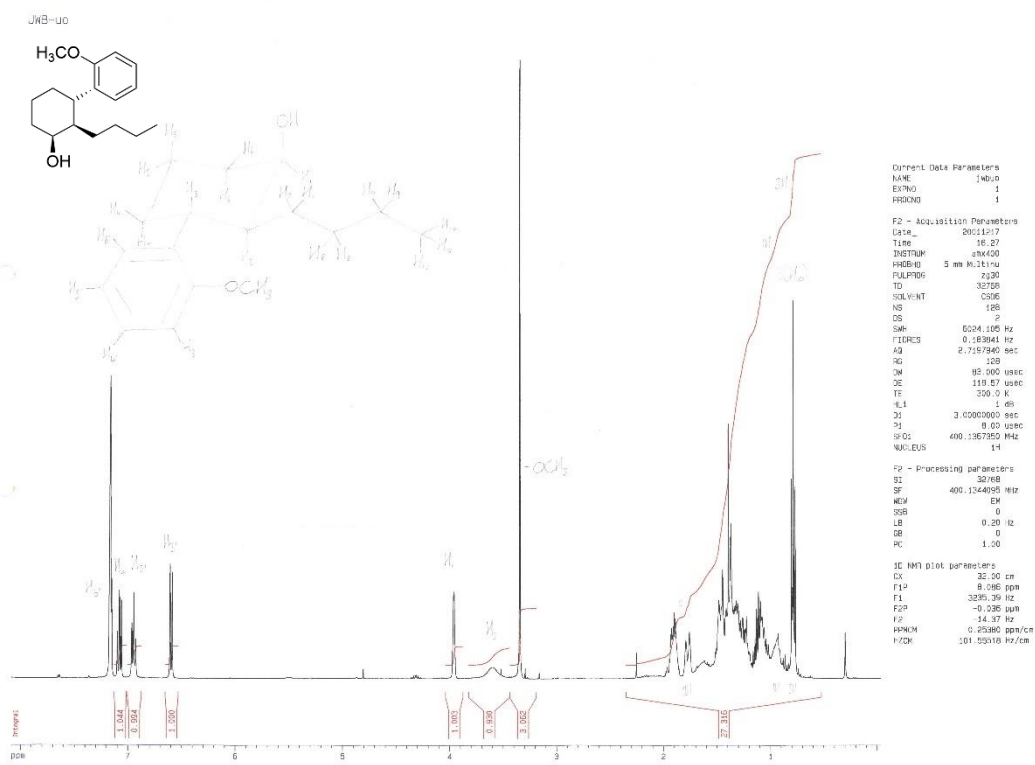
Carbon_1HDec_128scans_rmk CDCl3 {C:\Bruker\TopSpin3.6.2} PH2022_aa 44



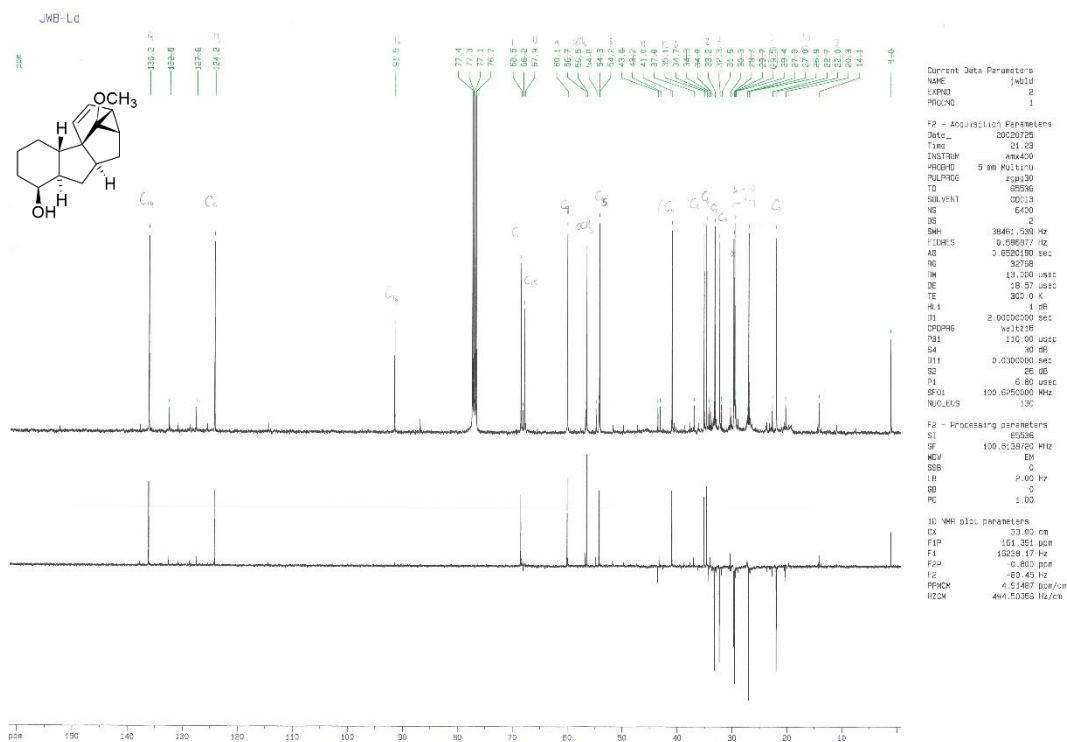
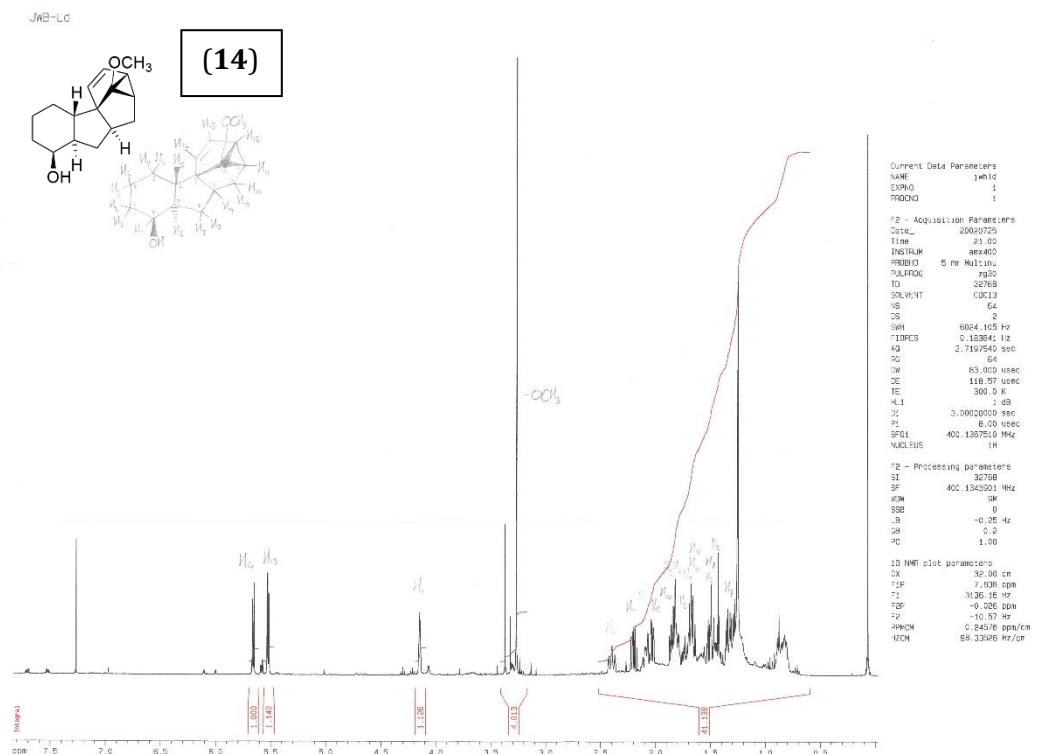


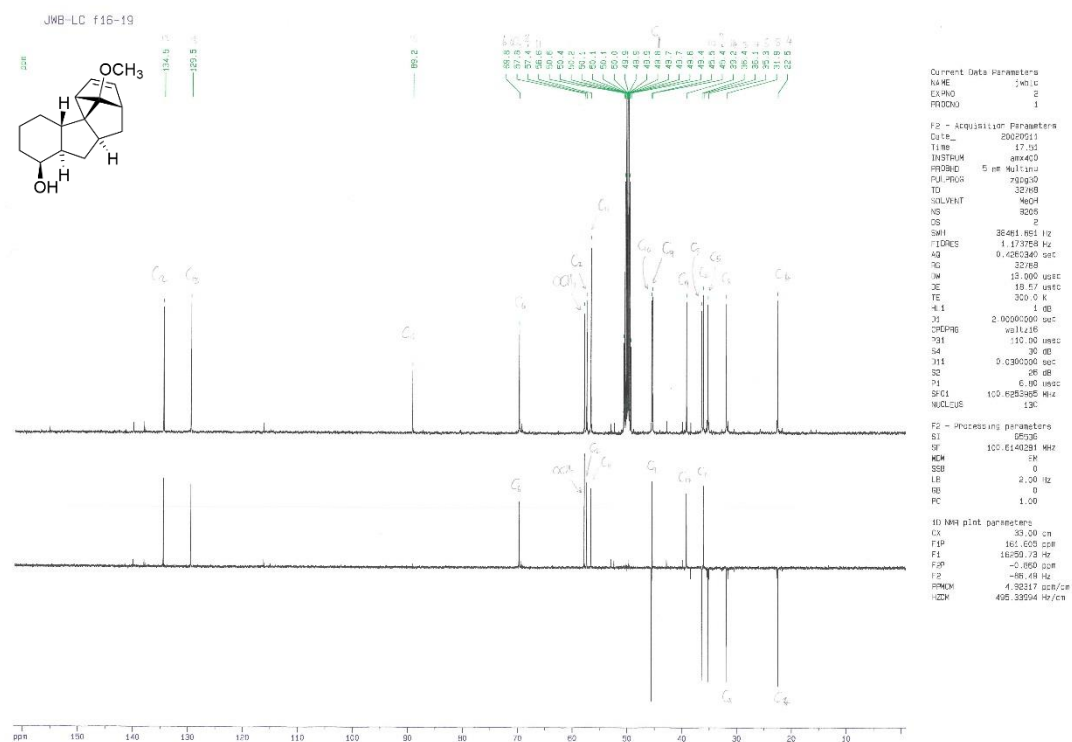
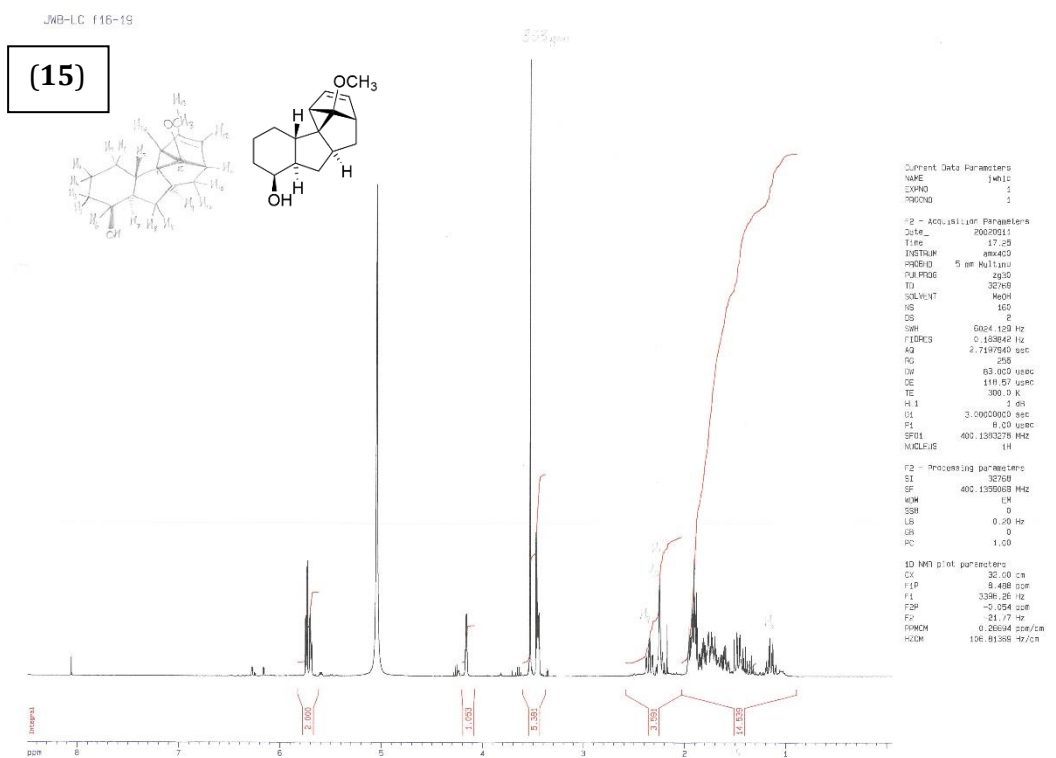
Synthesis of substrates for fluorescence comparison

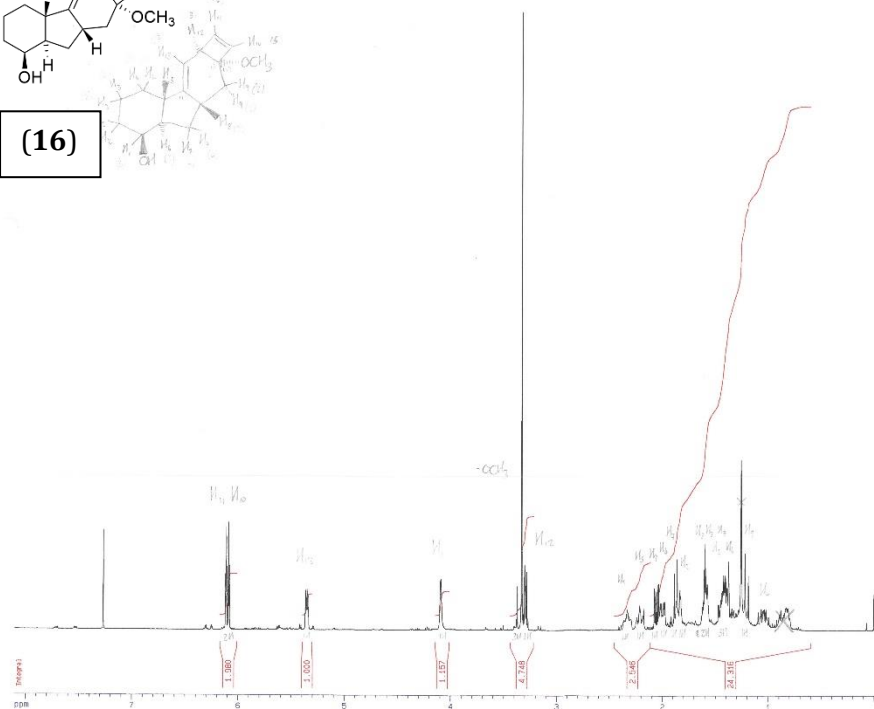
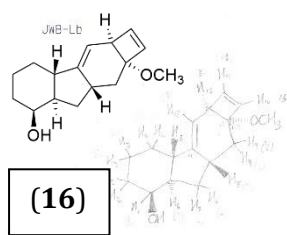




Photolysis of the 3-carbon





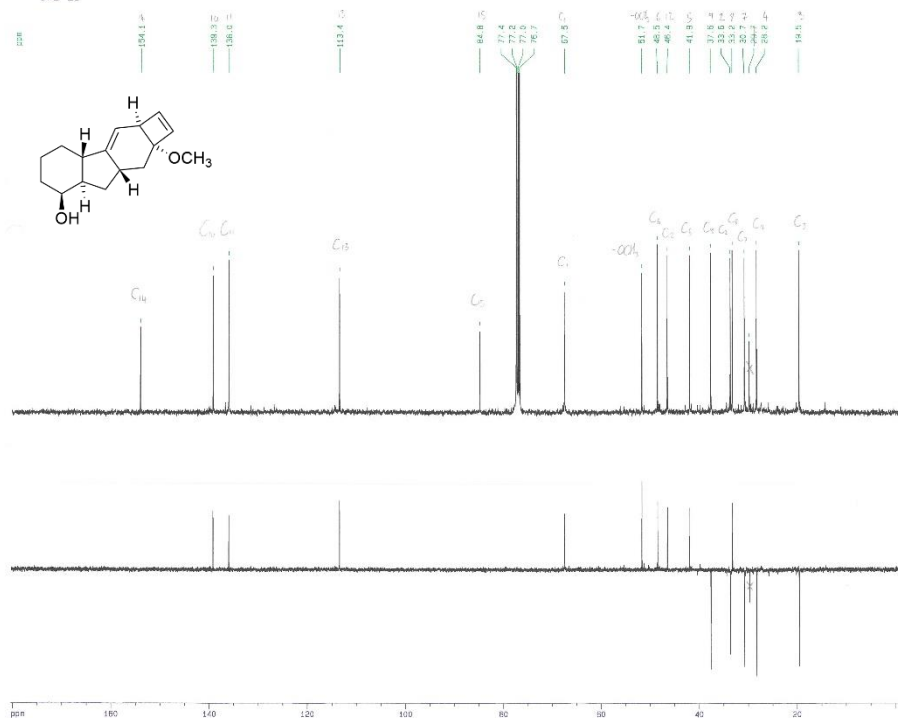
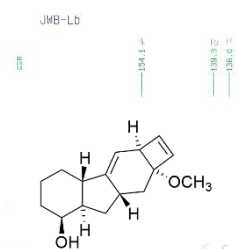


Current Data Parameters
 NAME: jwb1c
 EXPNO: 1
 PROCNO: 1

F2 - Acquisition Parameters
 Date_: 2023012
 Time: 0.03
 INSTRUM: smx400
 PULPROG: 5 mm Multis
 TD: 32768
 SOLVENT: CDCl3
 NS: 15
 DS: 2
 SWH: 5024.103 Hz
 FIDRES: 0.183841 Hz
 AQ: 2.7197540 sec
 RG: 128
 CW: 83.000 usec
 DE: 118.57 usec
 TE: 300.2 K
 HL1: 1.00
 D1: 3.0000000 sec
 P1: 8.00 usec
 SFO1: 400.1367510 MHz
 NUCLEUS: 1H

F2 - Processing parameters
 SI: 32768
 SF: 400.1343906 MHz
 WDM: CM
 SSB: 0
 LB: 0.00 Hz
 GB: 0
 PC: 1.00

1D NMR plot parameters
 CX: 32.00 cm
 F1P: 0.000 ppm
 F1: 3240.89 Hz
 F2P: -0.053 ppm
 F2: -25.50 Hz
 SFO1: 0.25508 ppm/cm
 HZ/CM: 107.06303 Hz/cm



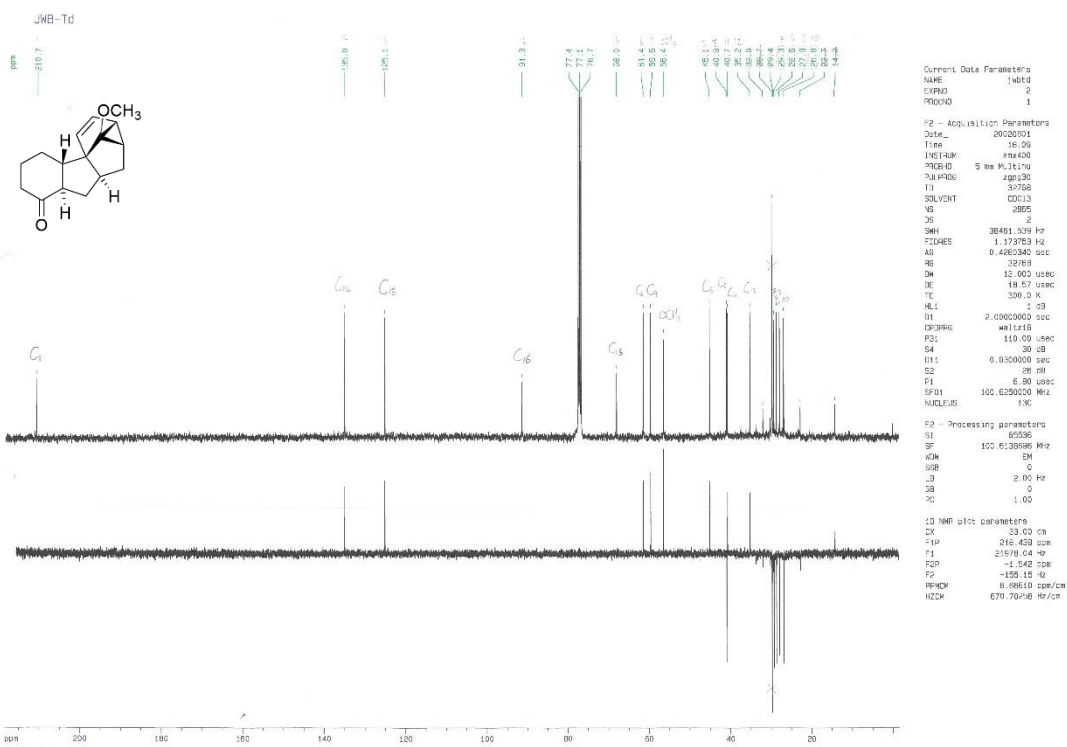
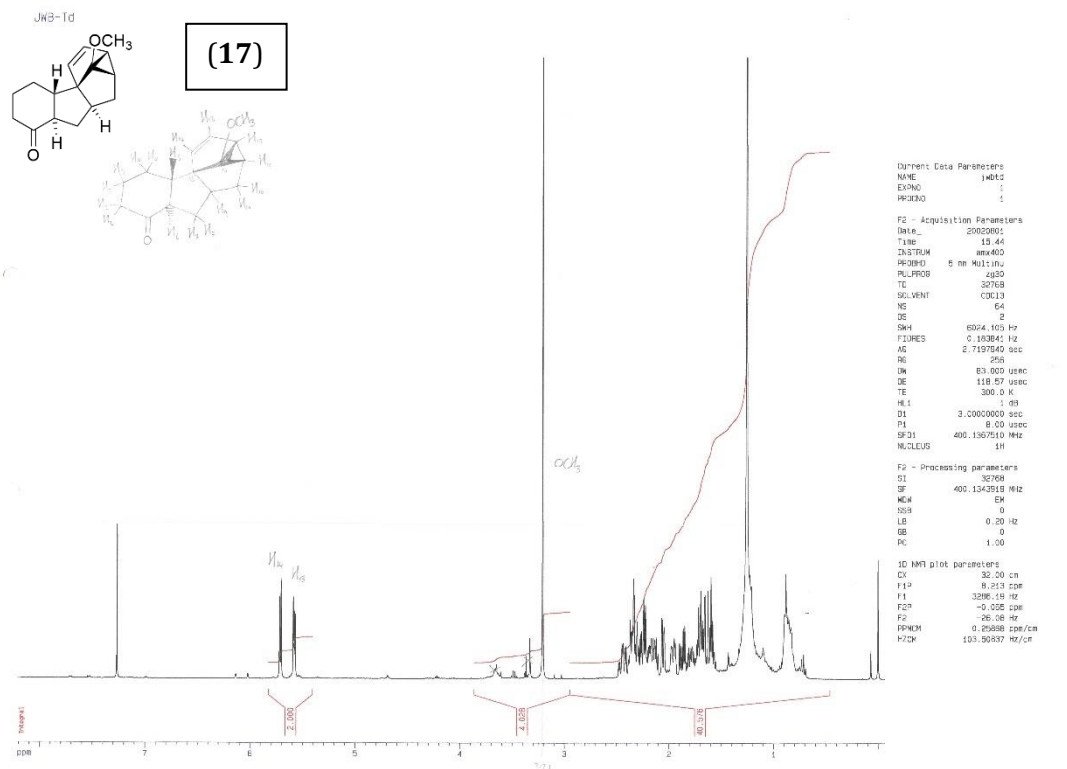
Current Data Parameters
 NAME: jwb1b
 EXPNO: 2
 PROCNO: 1

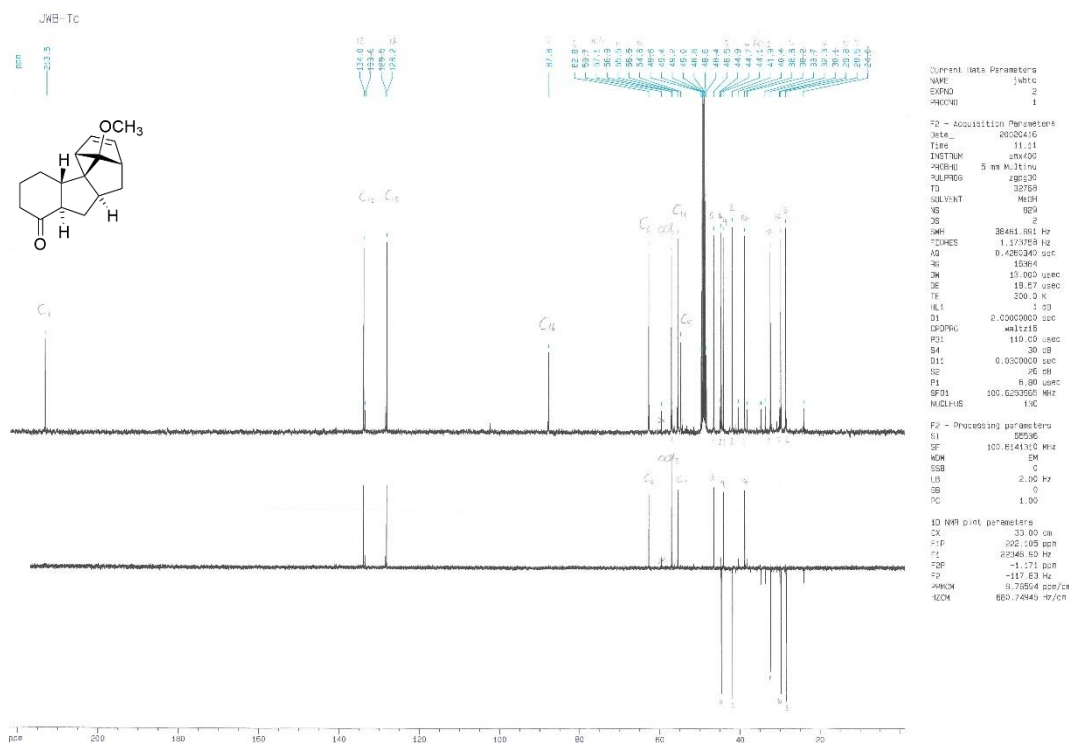
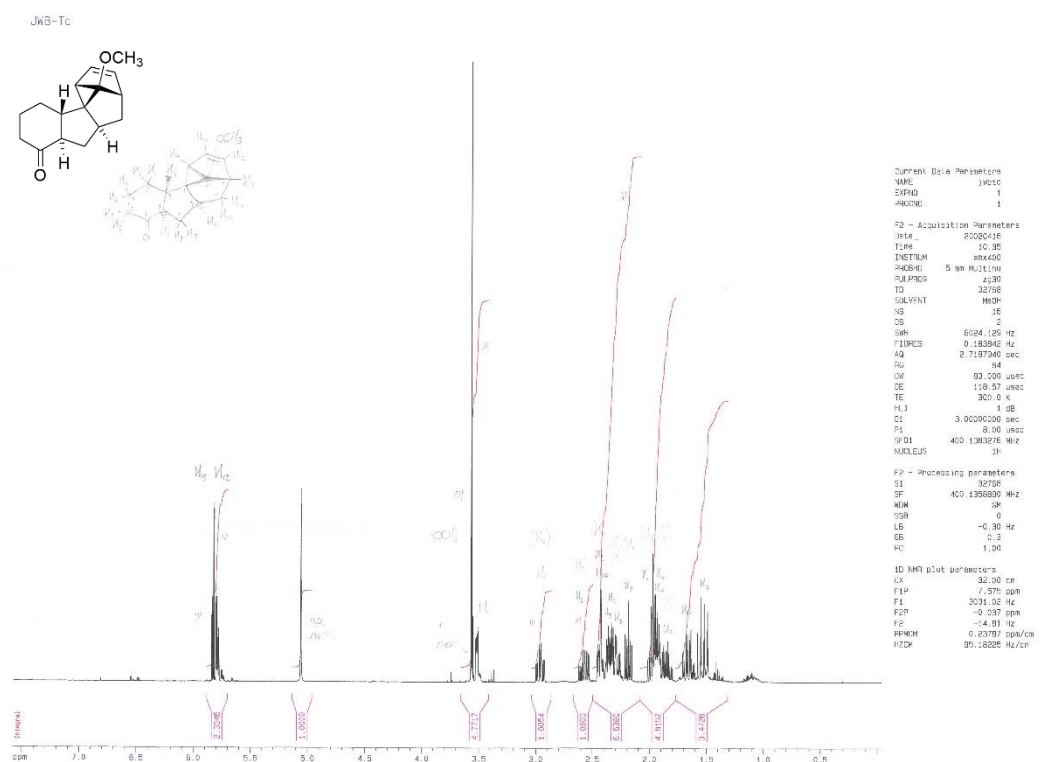
F2 - Acquisition Parameters
 Date_: 20230120
 Time: 0.27
 INSTRUM: smx400
 PULPROG: 5 mm Multis
 TD: 32768
 SOLVENT: CDCl3
 NS: 3000
 DS: 2
 SWH: 30461.833 Hz
 FIDRES: 1.173753 Hz
 AQ: 0.4282340 sec
 RG: 32768
 CW: 13.000 usec
 DE: 10.57 usec
 TE: 300.2 K
 HL1: 1.00
 D1: 2.0000000 sec
 P1: 110.00 usec
 SFO1: 101.6252000 MHz
 NUCLEUS: 13C

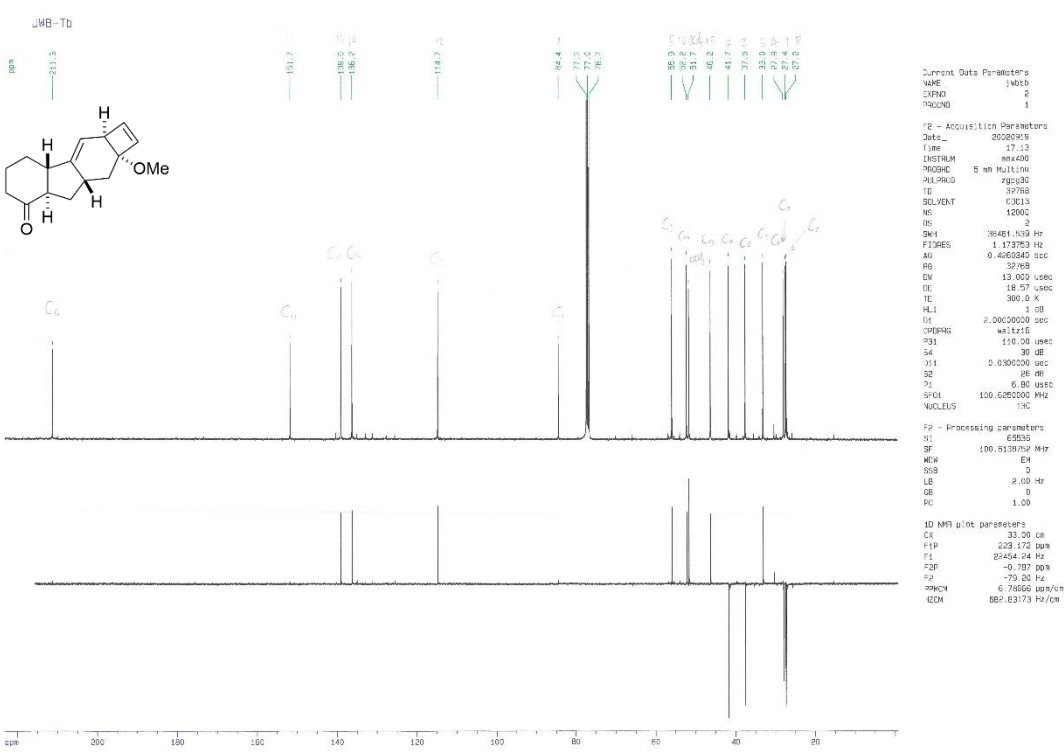
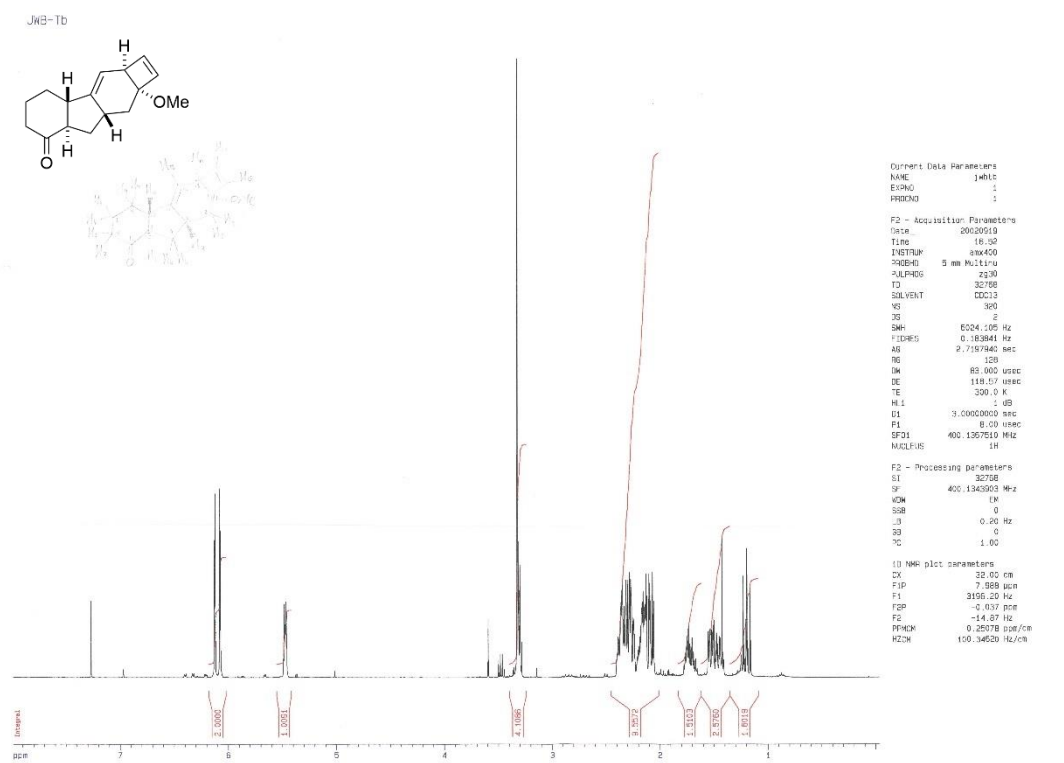
F2 - Processing parameters
 SI: 65536
 SF: 100.6137003 MHz
 WDM: CM
 SSB: 0
 LB: 2.00 Hz
 GB: 0
 PC: 1.00

1D NMR plot parameters
 CX: 33.00 cm
 F1P: 180.326 ppm
 F1: 18141.25 Hz
 F2P: -1.827 ppm
 F2: -181.70 Hz
 SFO1: 5.51525 ppm/cm
 HZ/CM: 305.31444 Hz/cm

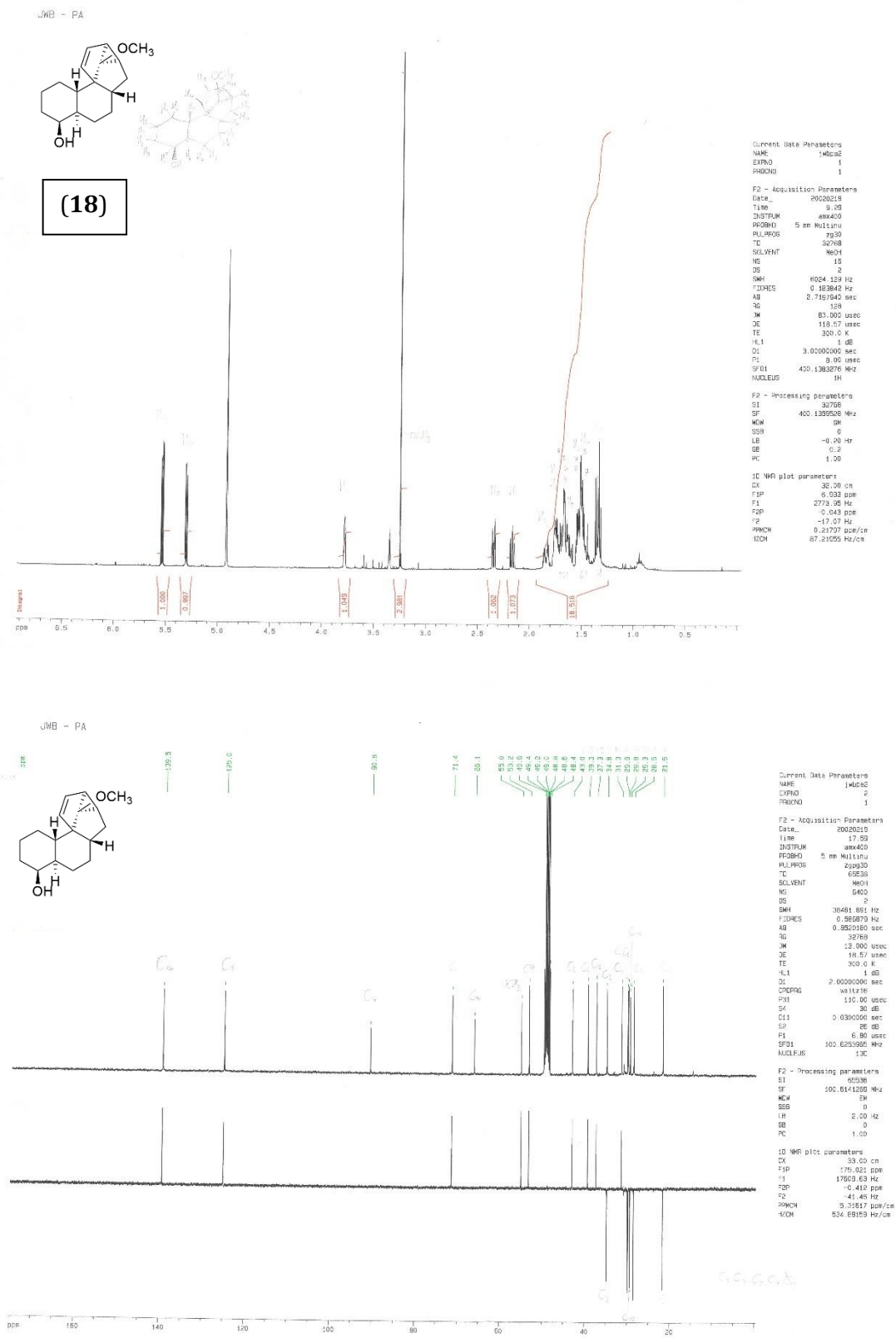
Identification of 3-carbon tether cycloadducts

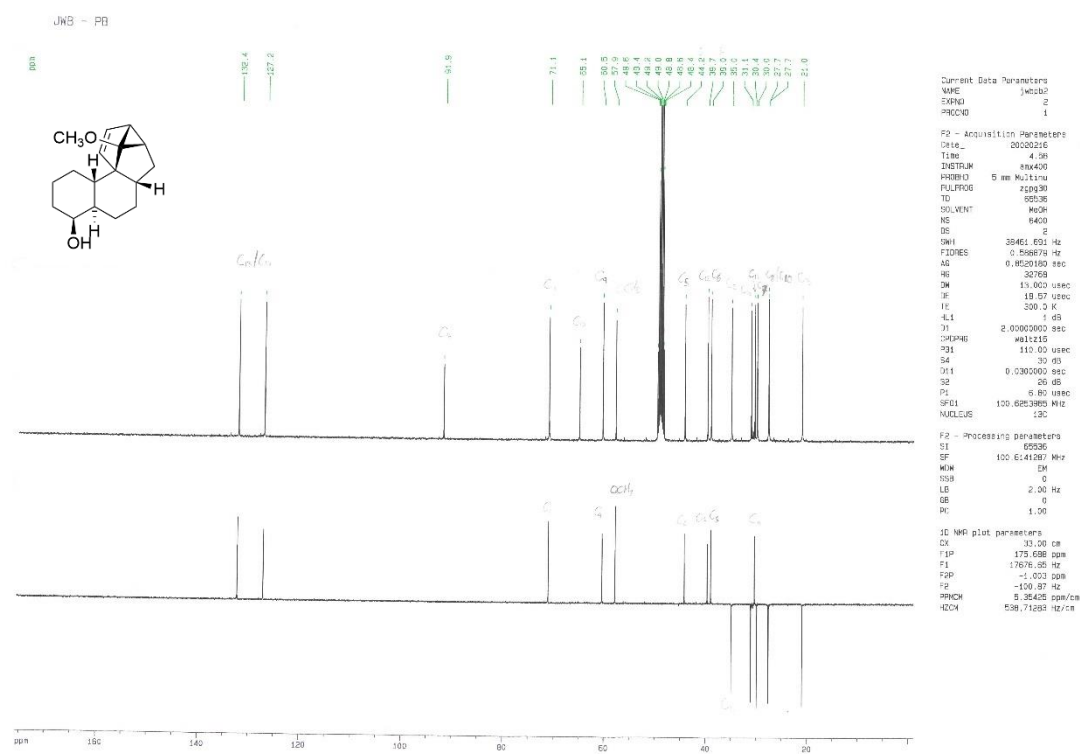
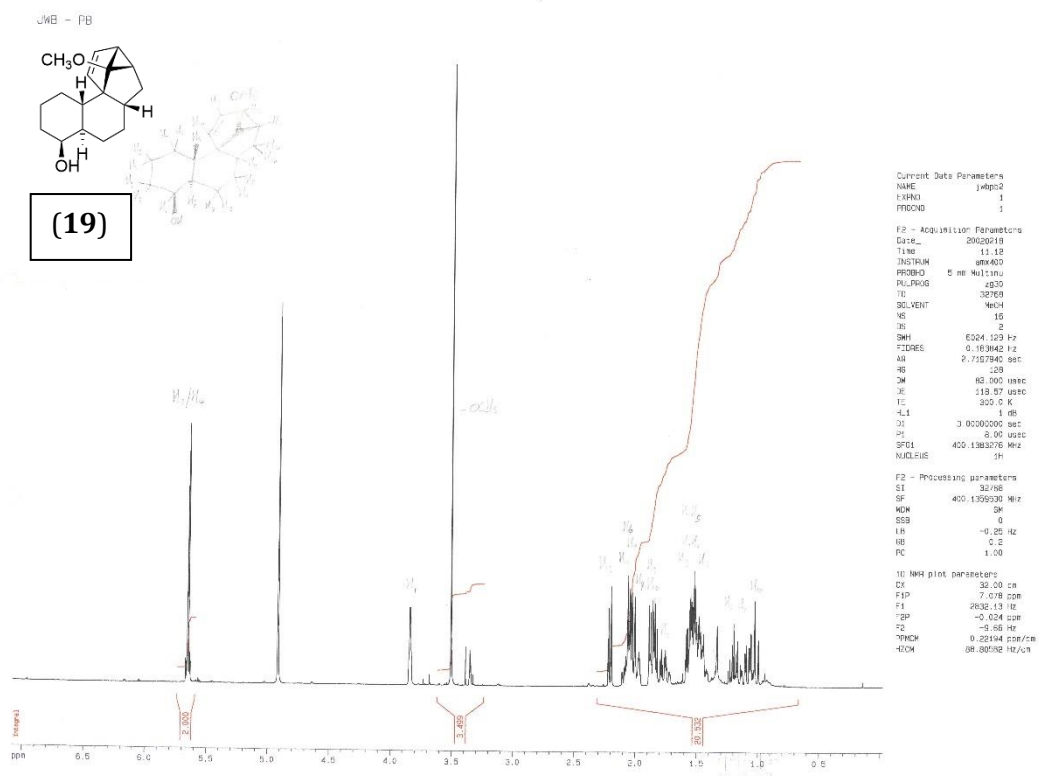




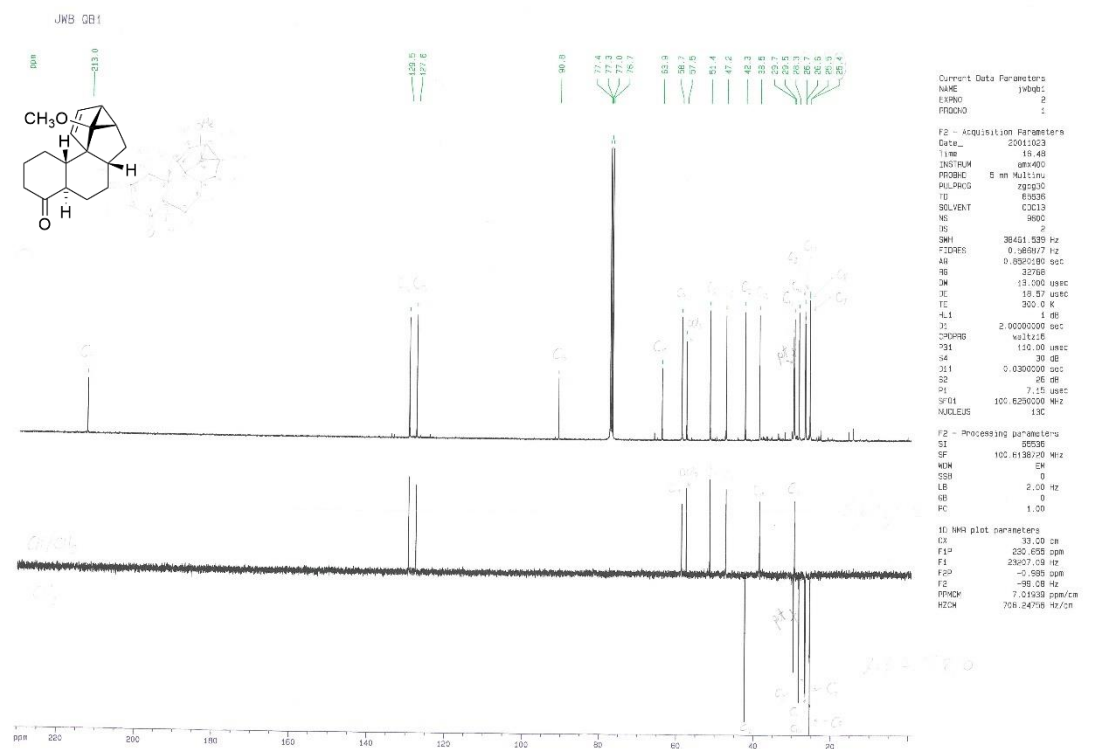
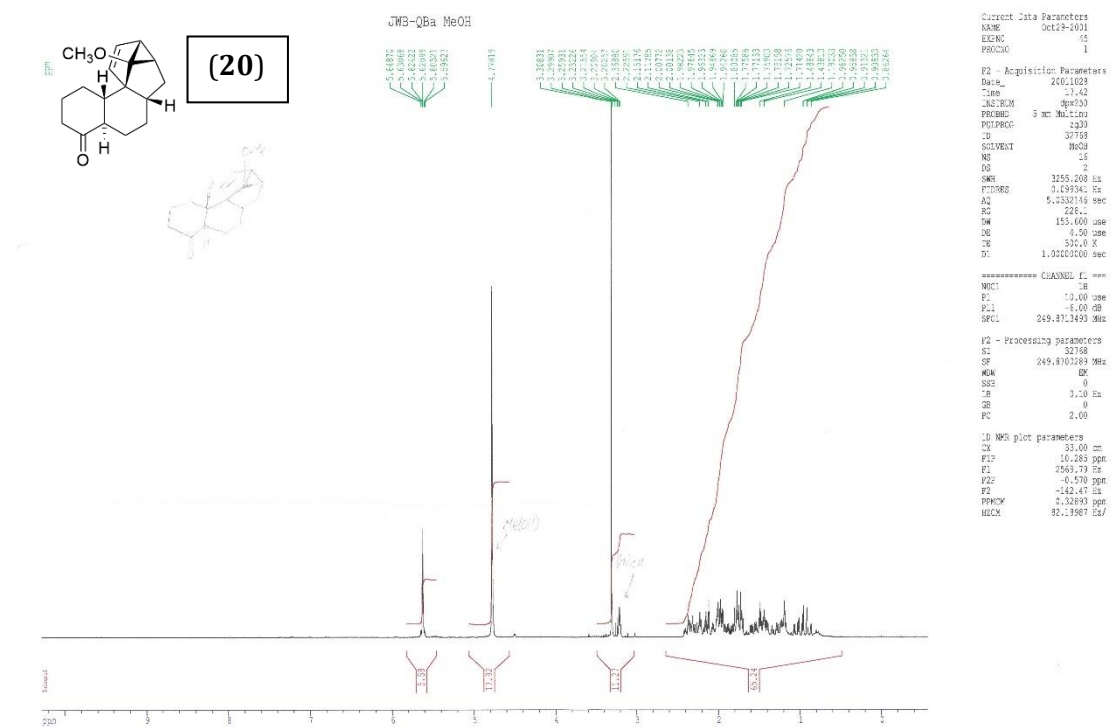


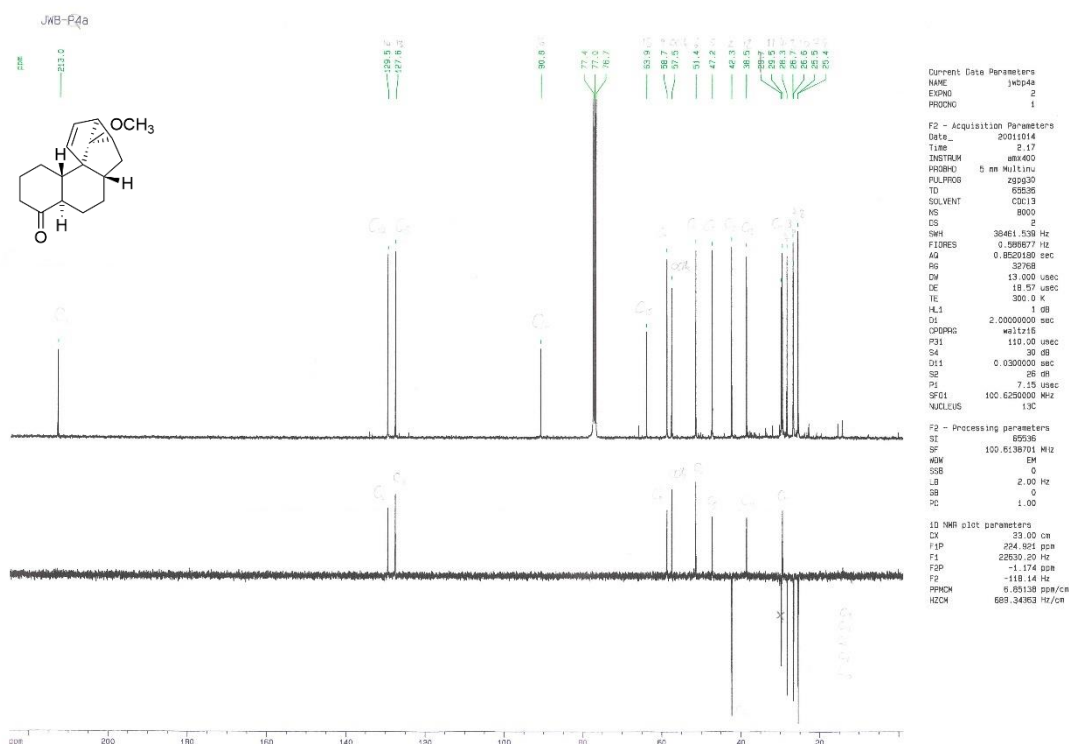
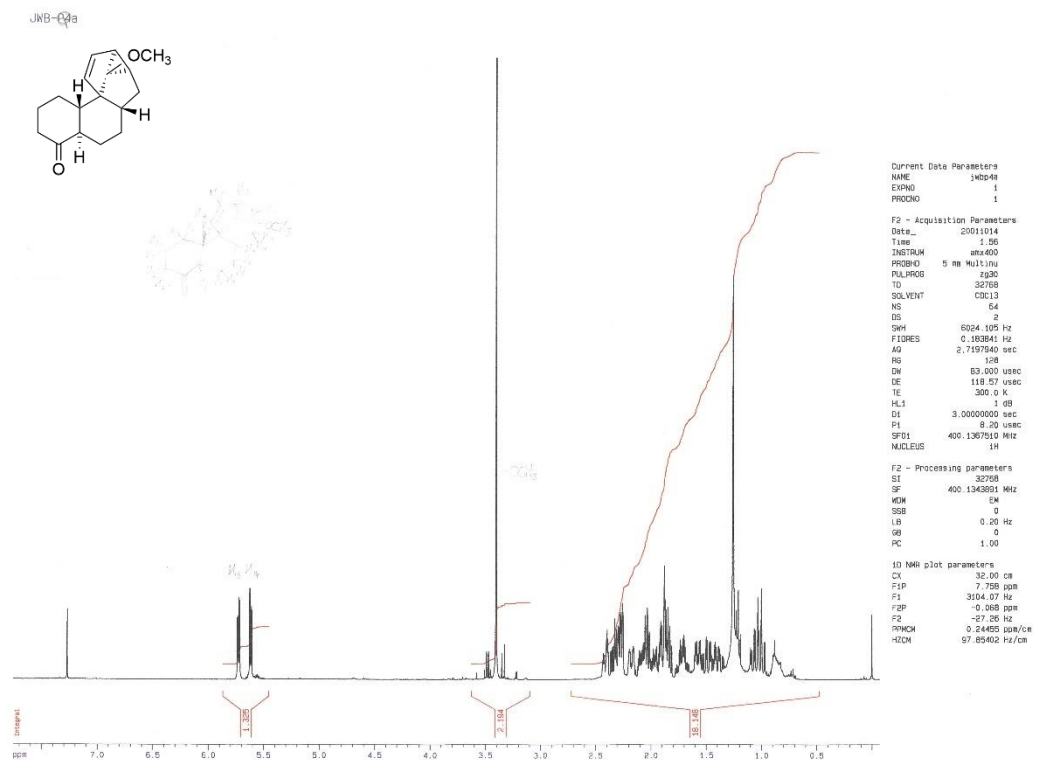
Photolysis of the 4-carbon tether substrate (8)





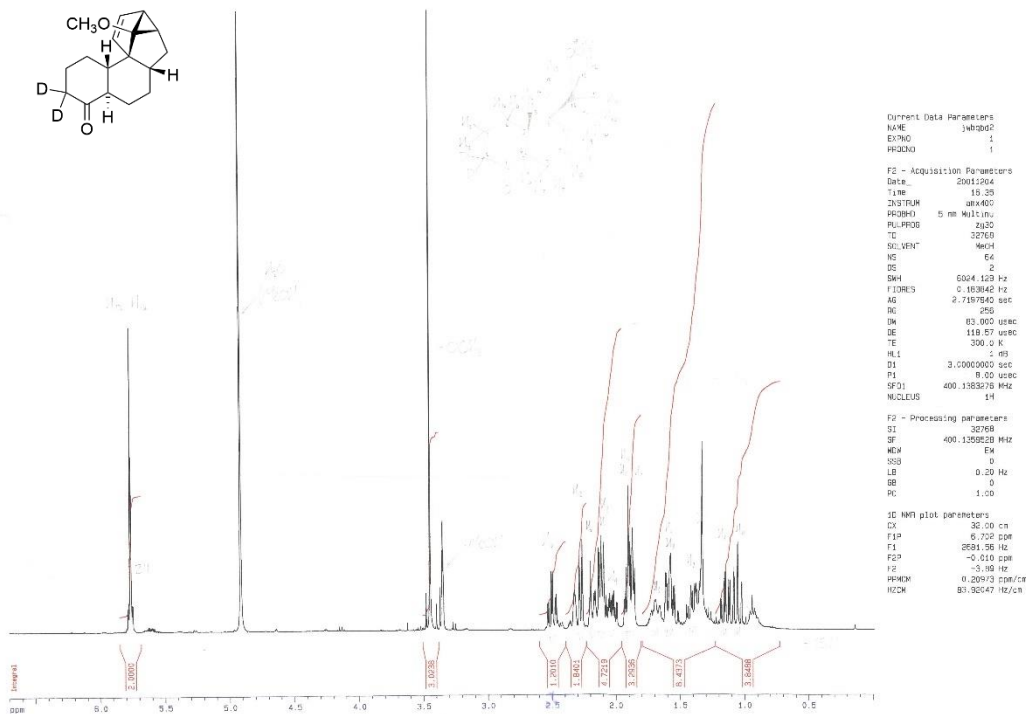
Identification of 4-carbon tether cycloadducts



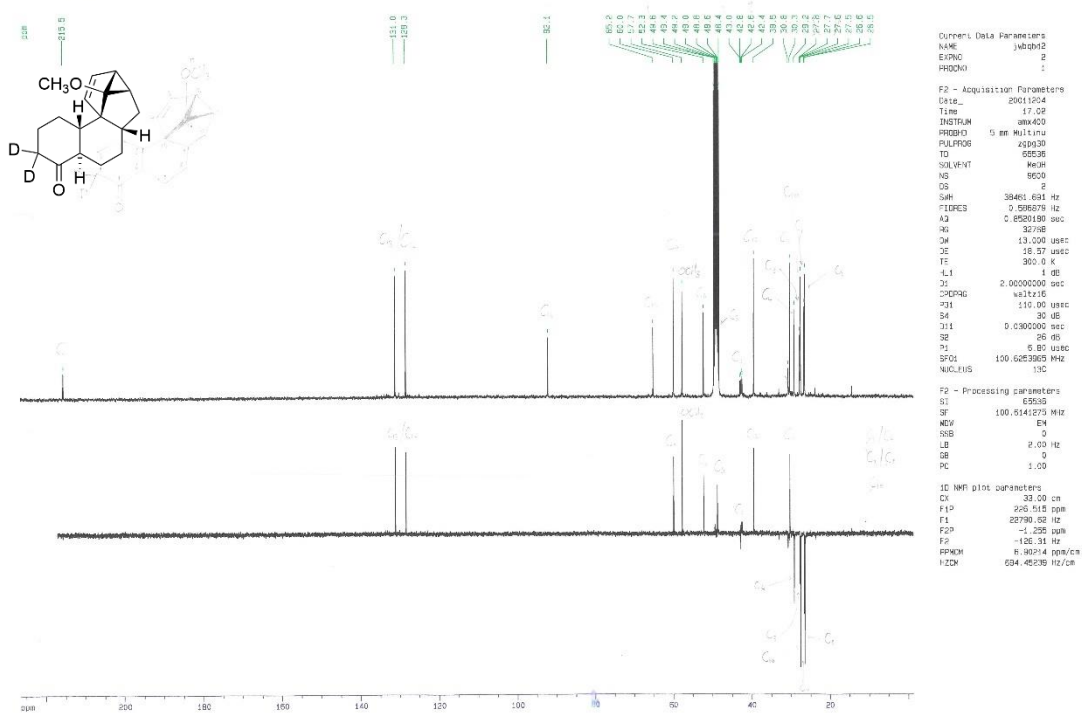


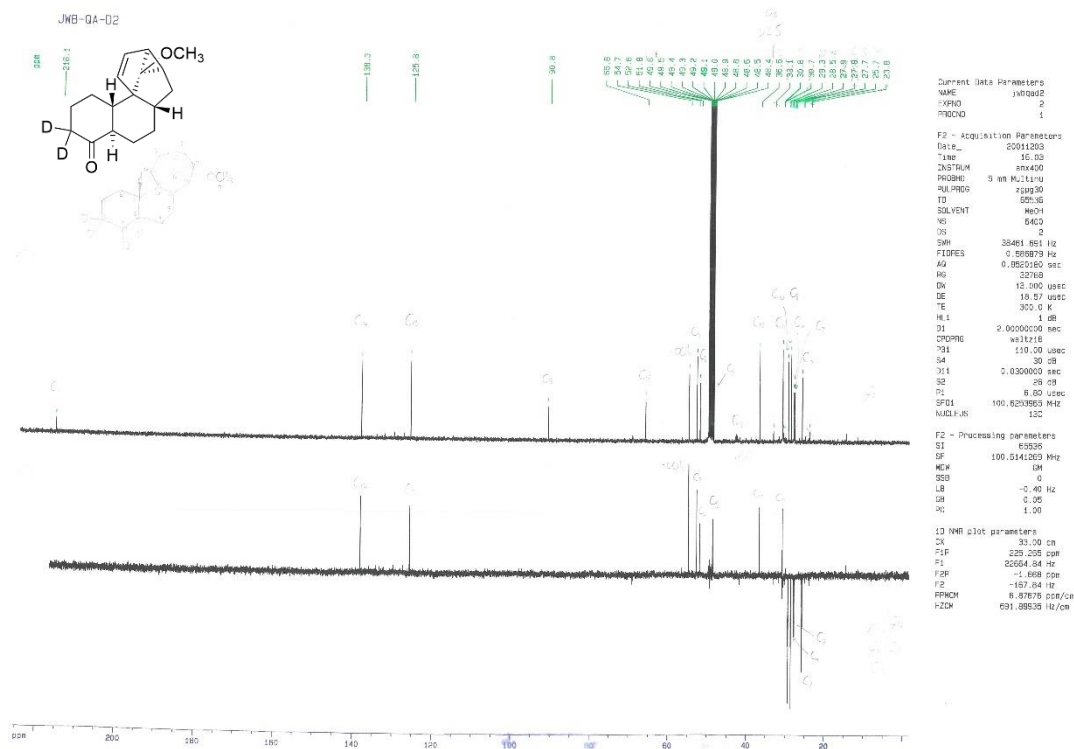
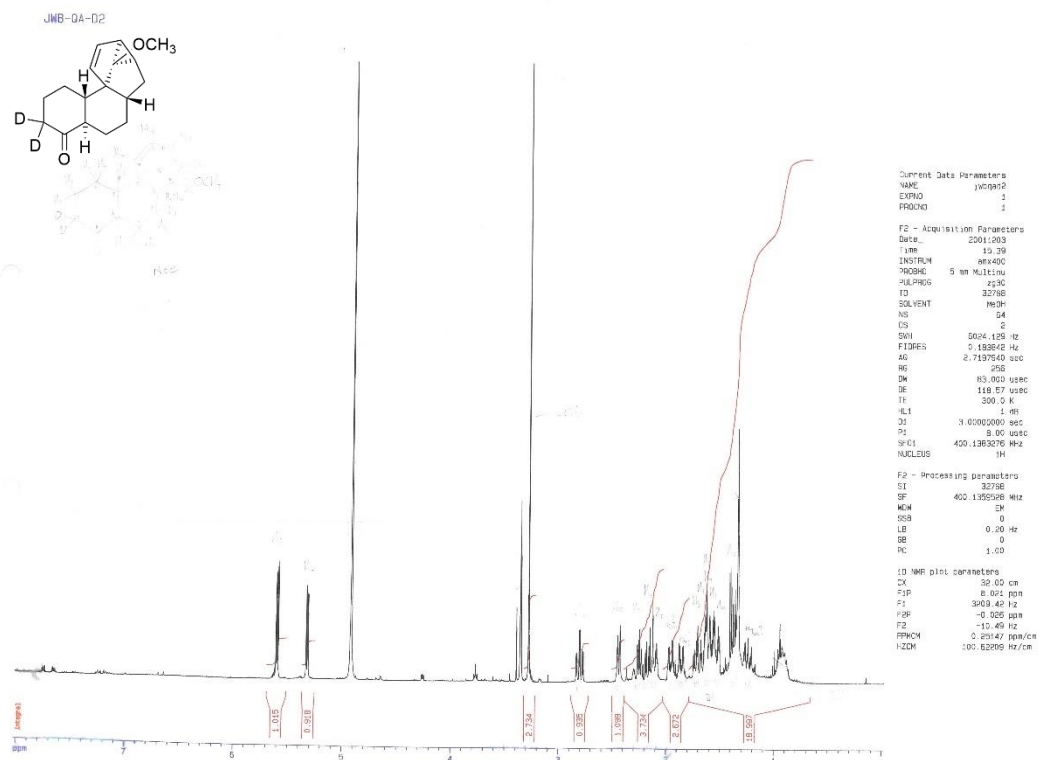
Deuteration and desaturation for identification of 4-carbon tether cycloadduct

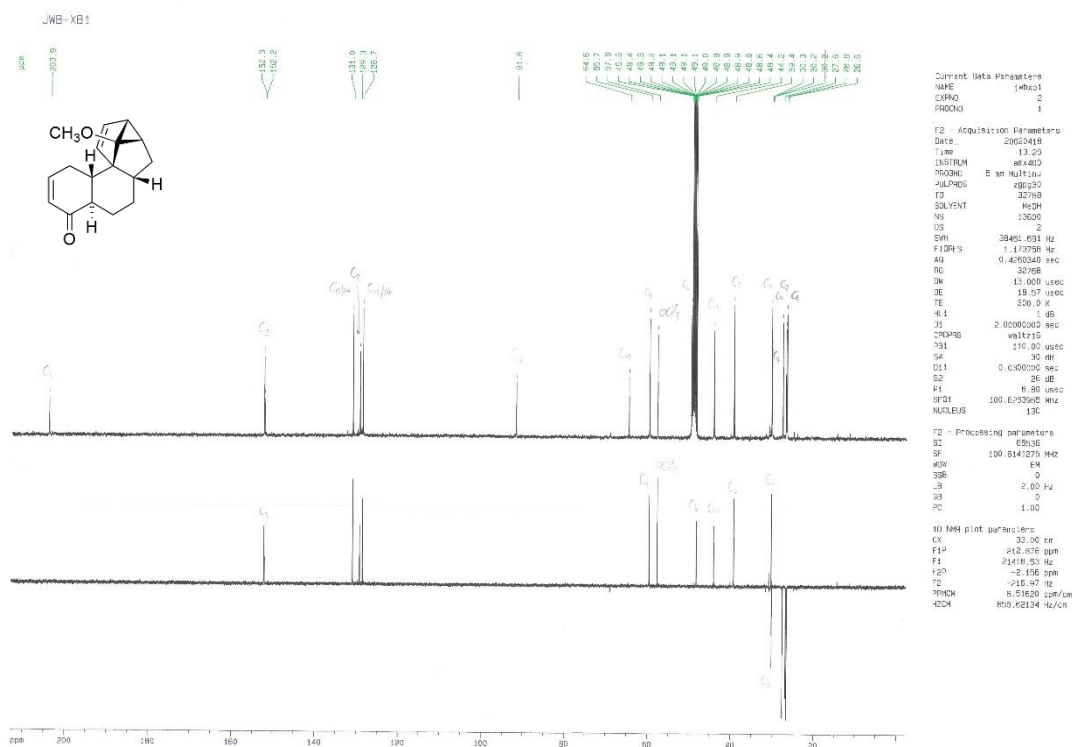
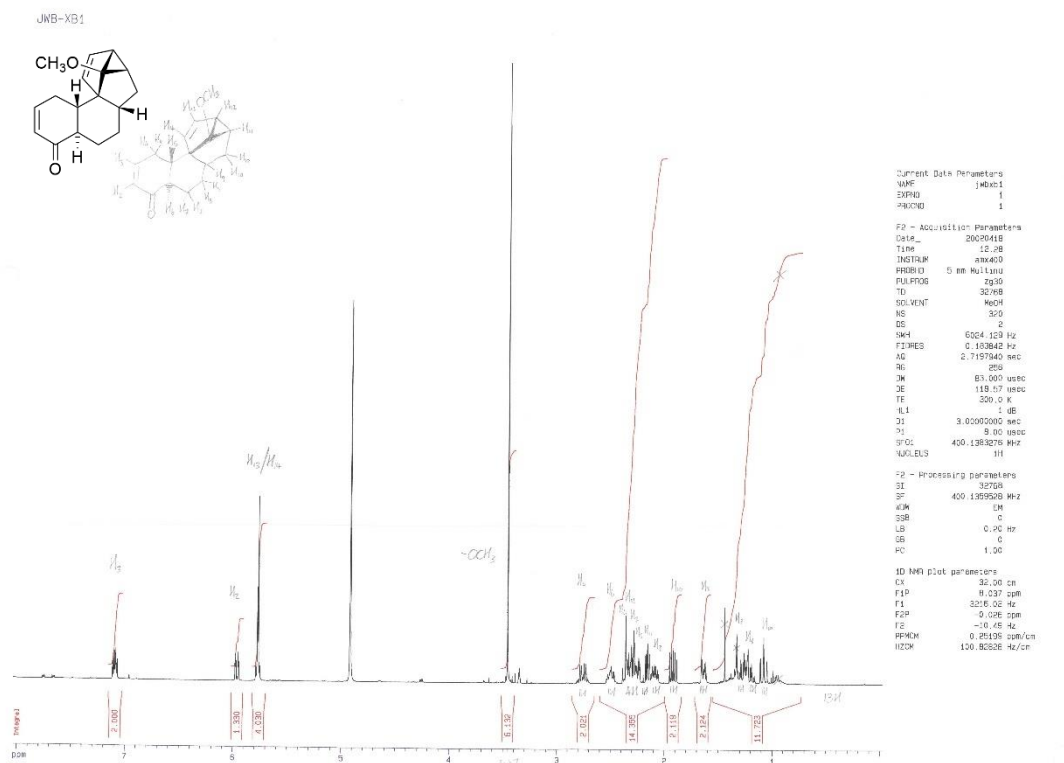
JWB-08-D2

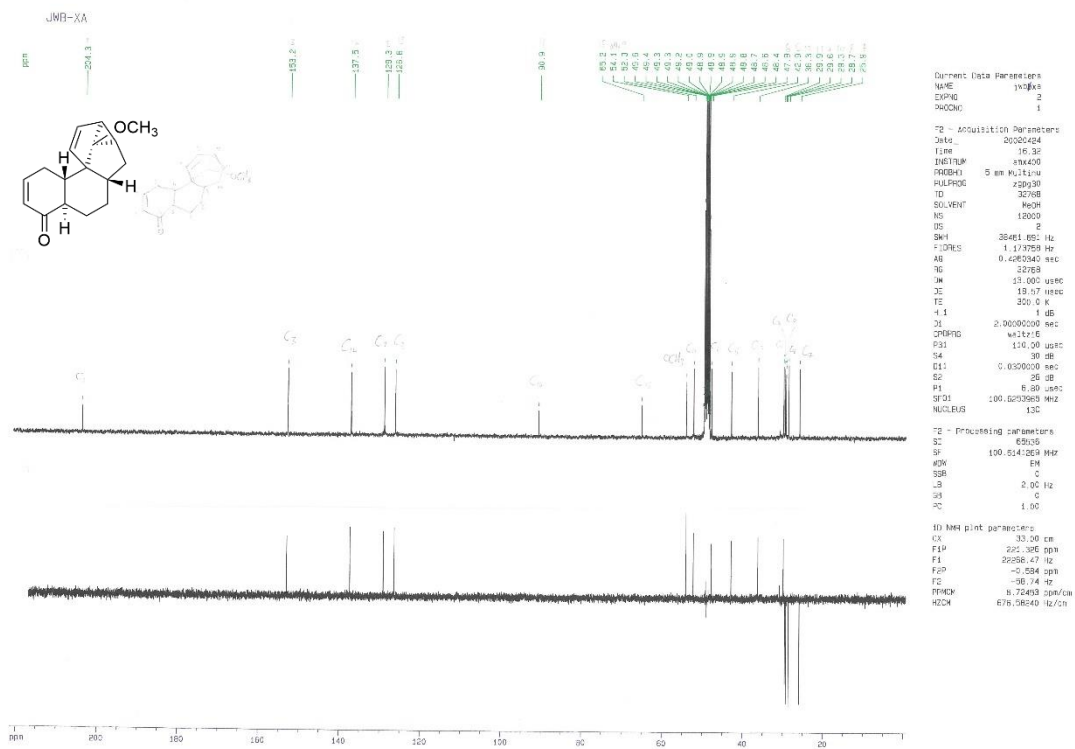
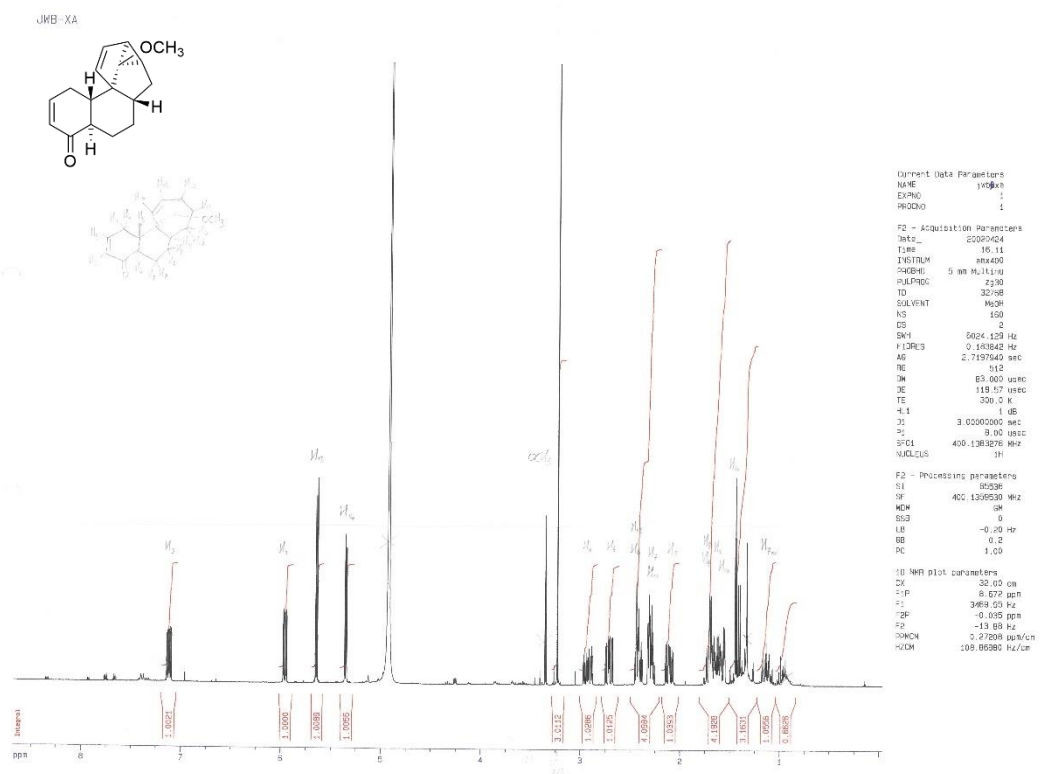


JWB-08-D2

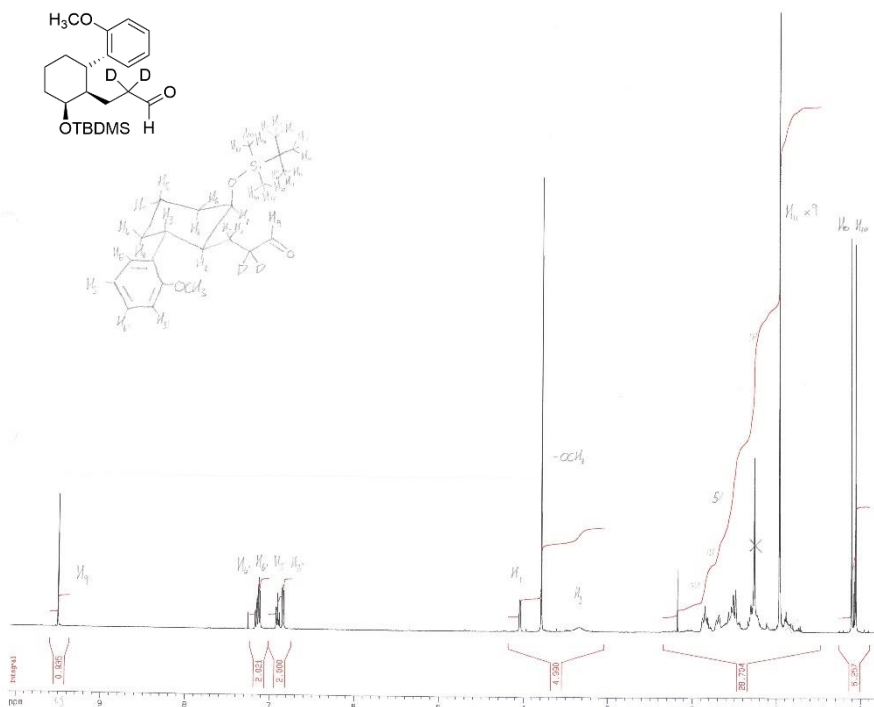
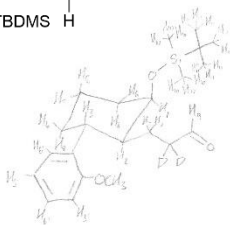
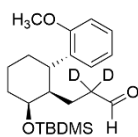








JMB-M-02



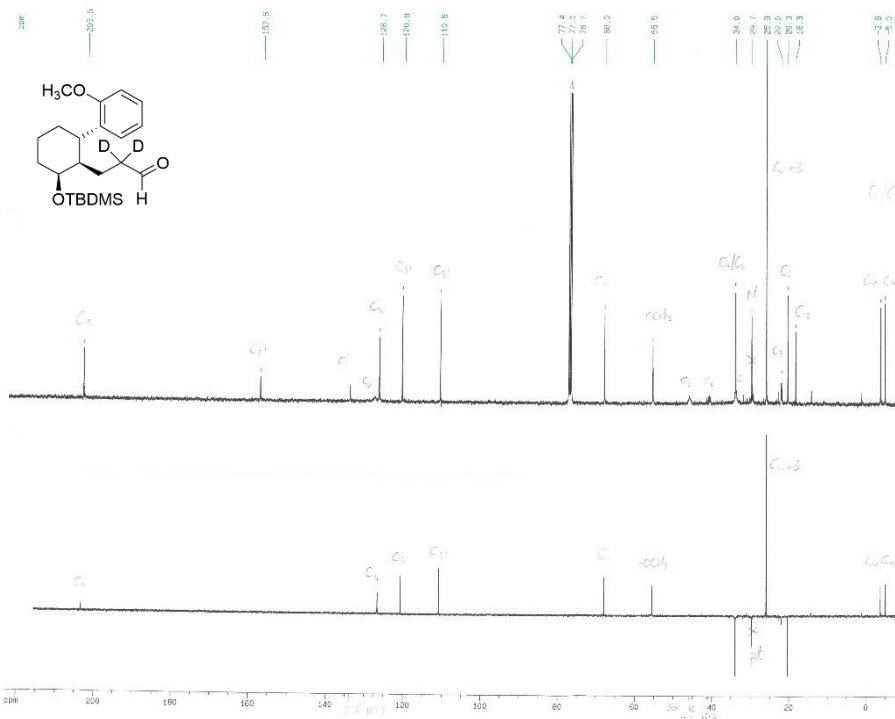
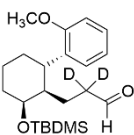
Current Data Parameters
 NAME jmb02
 EXNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20020411
 Time 9:36
 INSTRUM mxa400
 PROBHD 5 mm Multis
 PULPROG zgpg30
 TD 32768
 SOLVENT CDCl3
 NS 160
 DS 2
 SWH 8024.150 Hz
 FIDRES 0.182841 Hz
 AQ 2.7197640 sec
 RG 128
 DW 83.000 usec
 DE 118.07 usec
 TE 300.0 K
 HL1 1.00
 D1 5.0000000 sec
 P1 8.00 usec
 SFO1 400.130750 MHz
 NUCLEUS 1H

F2 - Processing parameters
 SI 32768
 SF 400.130750 MHz
 MHZ 0
 SSB 0
 LB 0.20 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
 CX 30.00 cm
 FIP 10.076 ucm
 F1 4031.63 Hz
 F2P -0.220 ppm
 F3 -88.00 Hz
 PPHC1 0.32174 ucm/cm
 IZCM 128.73624 Hz/cm

JMB-M-02

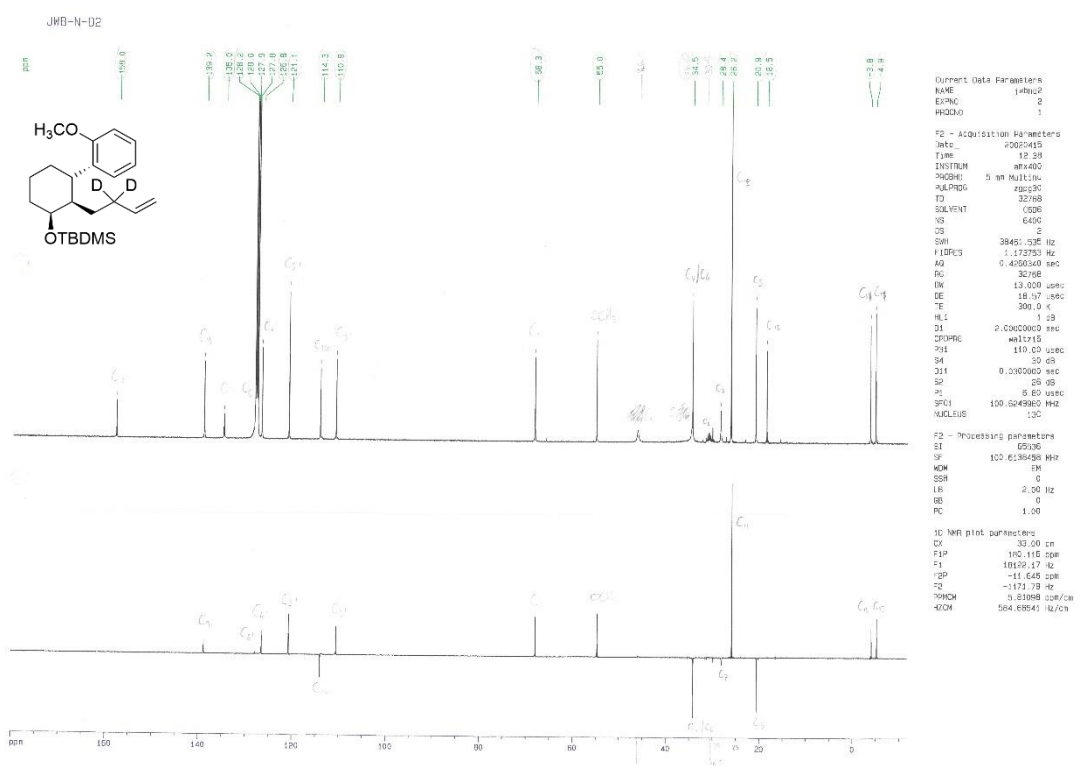
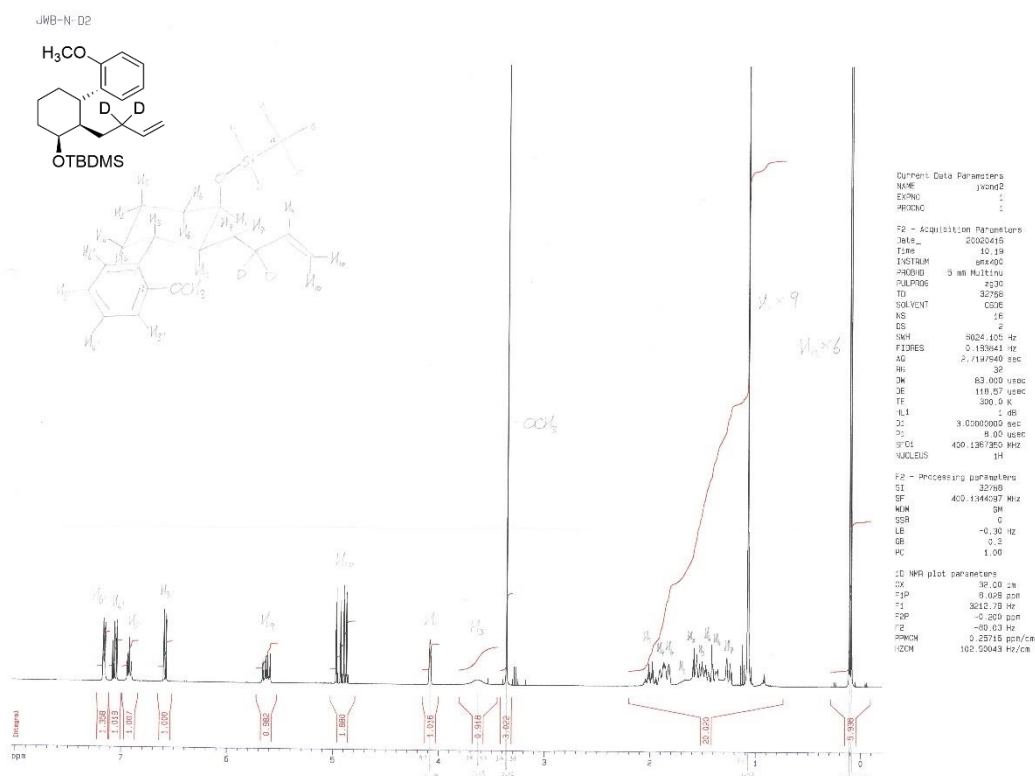


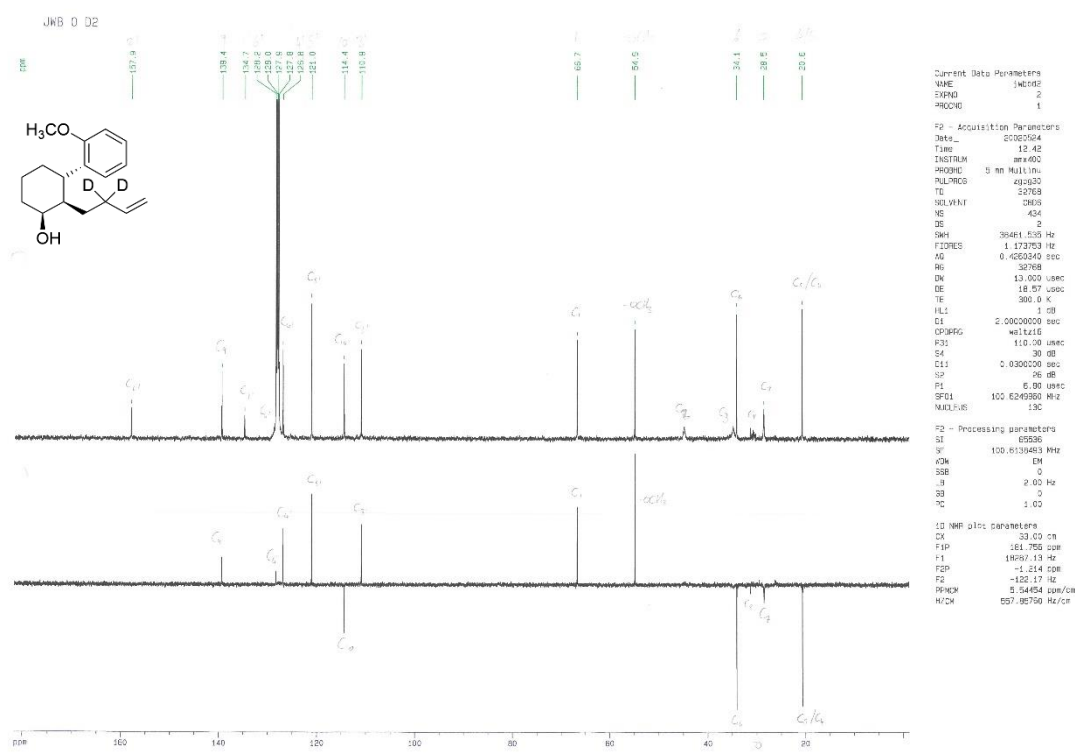
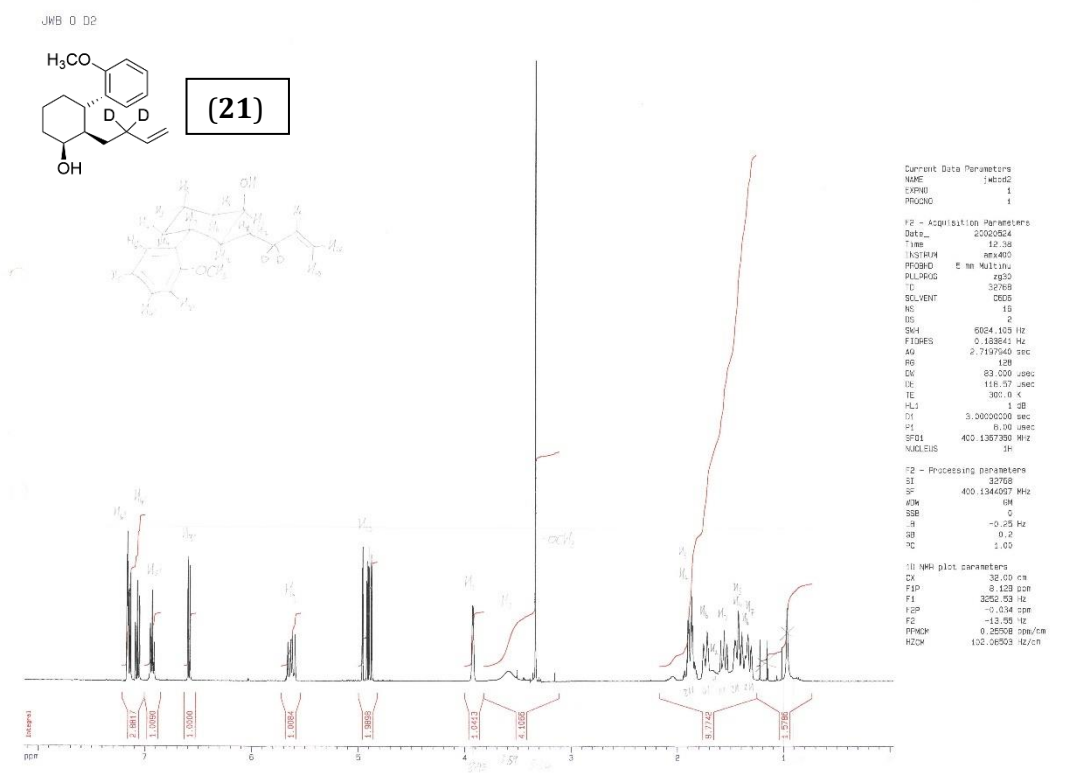
Current Data Parameters
 NAME jmb02
 EXNO 2
 PROCNO 5

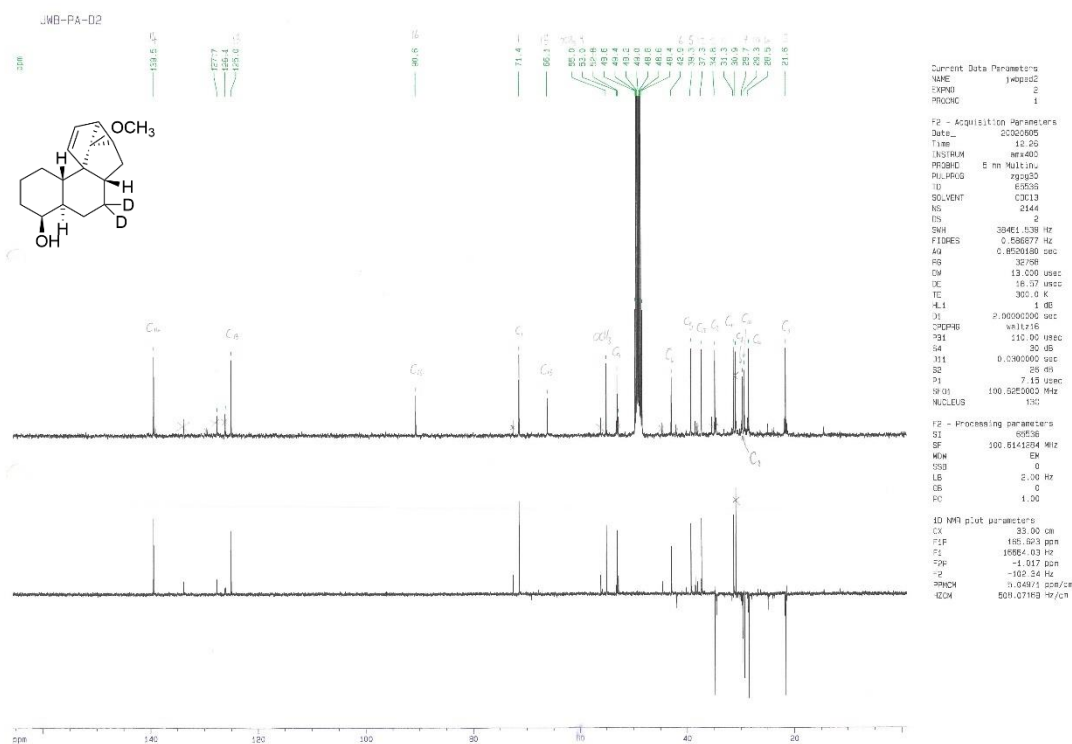
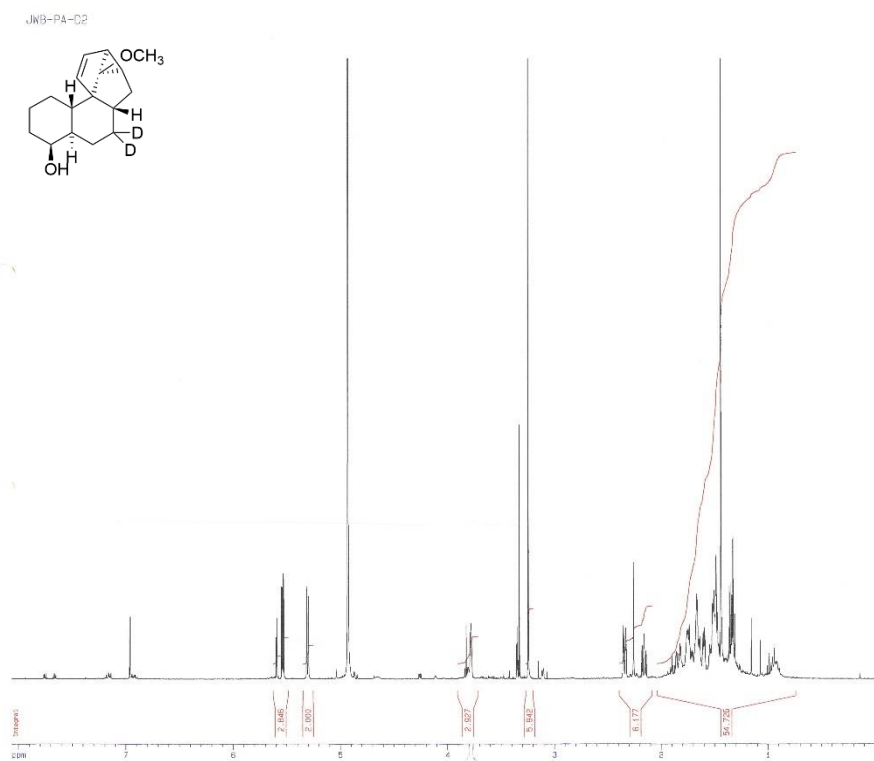
F2 - Acquisition Parameters
 Date_ 20020411
 Time 12:23
 INSTRUM mxa400
 PROBHD 5 mm Multis
 PULPROG zgpg30
 TD 32768
 SOLVENT CDCl3
 NS 160
 DS 2
 SWH 80481.530 Hz
 FIDRES 1.173783 Hz
 AQ 0.4262340 sec
 RG 128
 DW 13.000 usec
 DE 19.57 usec
 TE 300.0 K
 HL1 1.00
 D1 1.0000000 sec
 CPDPRG waltz16
 P1 110.00 usec
 S1 20 dB
 D11 0.0300000 sec
 S2 20 dB
 P2 8.00 usec
 SFO1 100.626000 MHz
 NUCLEUS 13C

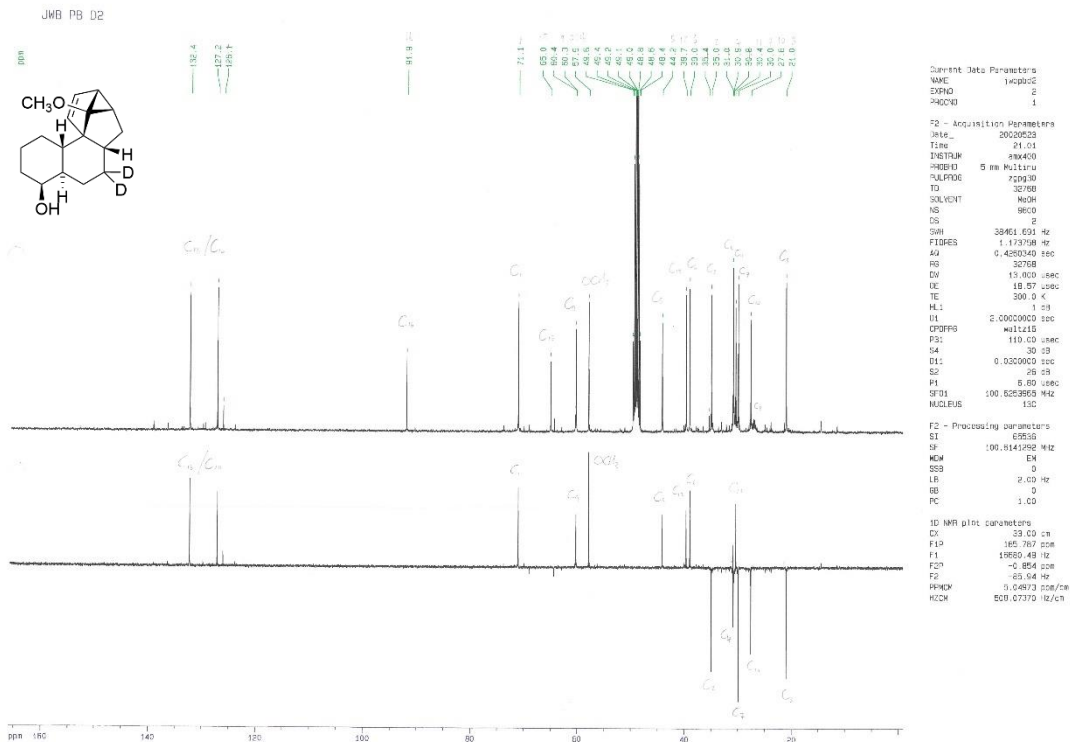
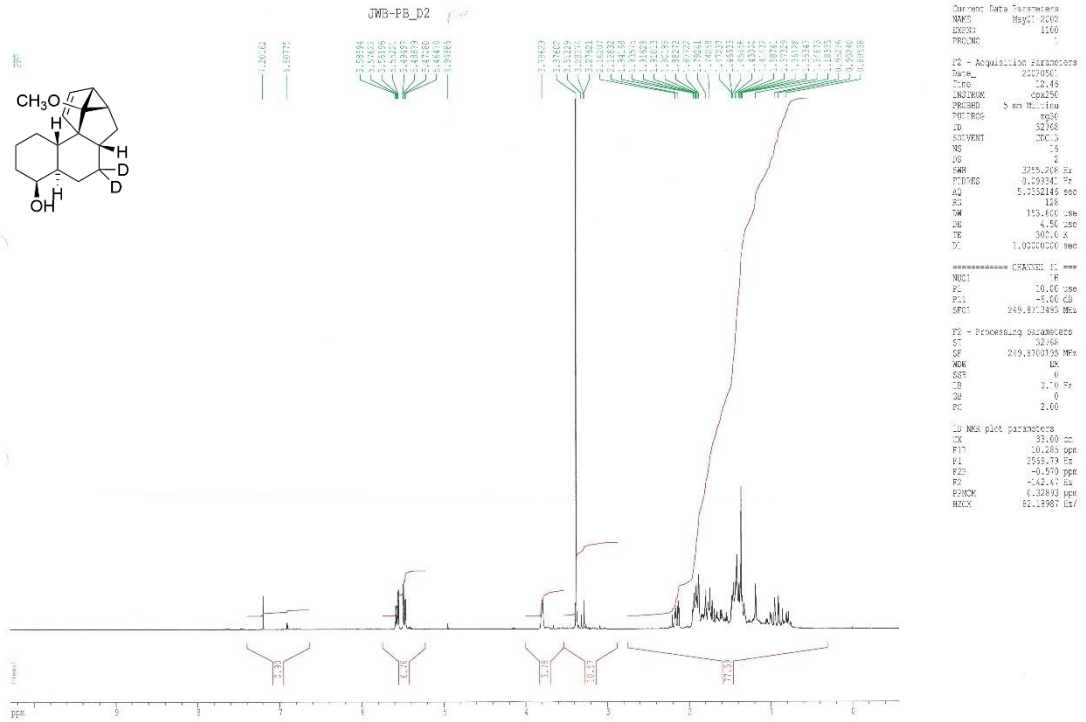
F2 - Processing parameters
 SI 32768
 SF 100.626000 MHz
 MHZ 0
 SSB 0
 LB 2.00 Hz
 GB 0
 PC 1.00

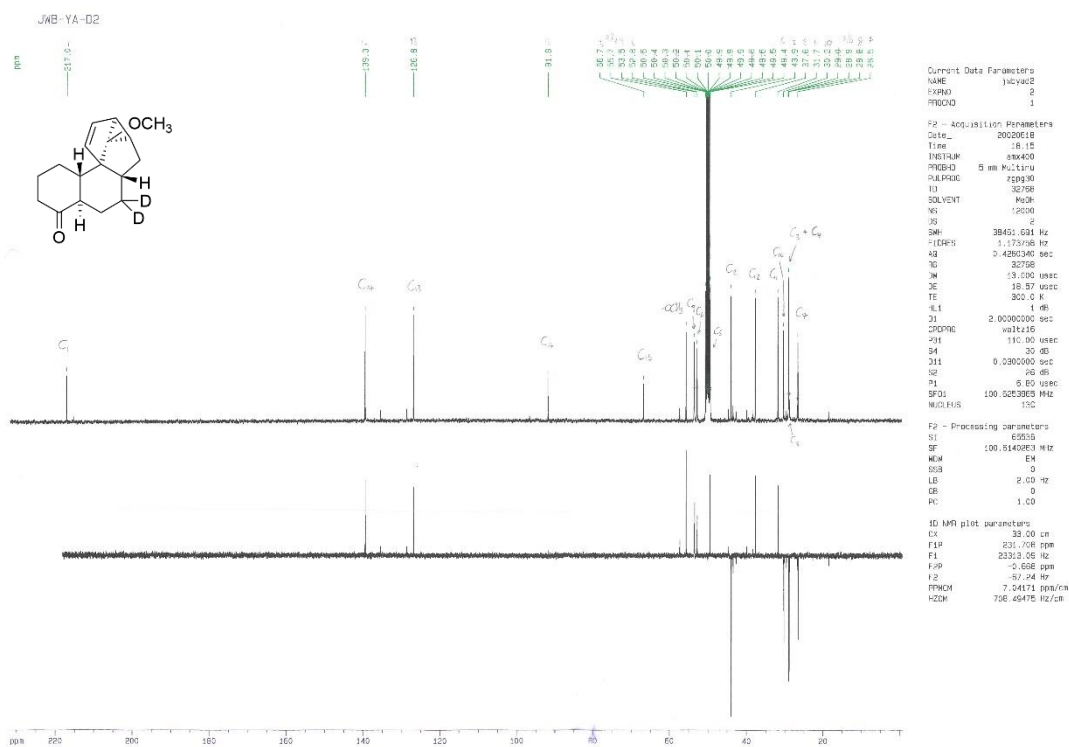
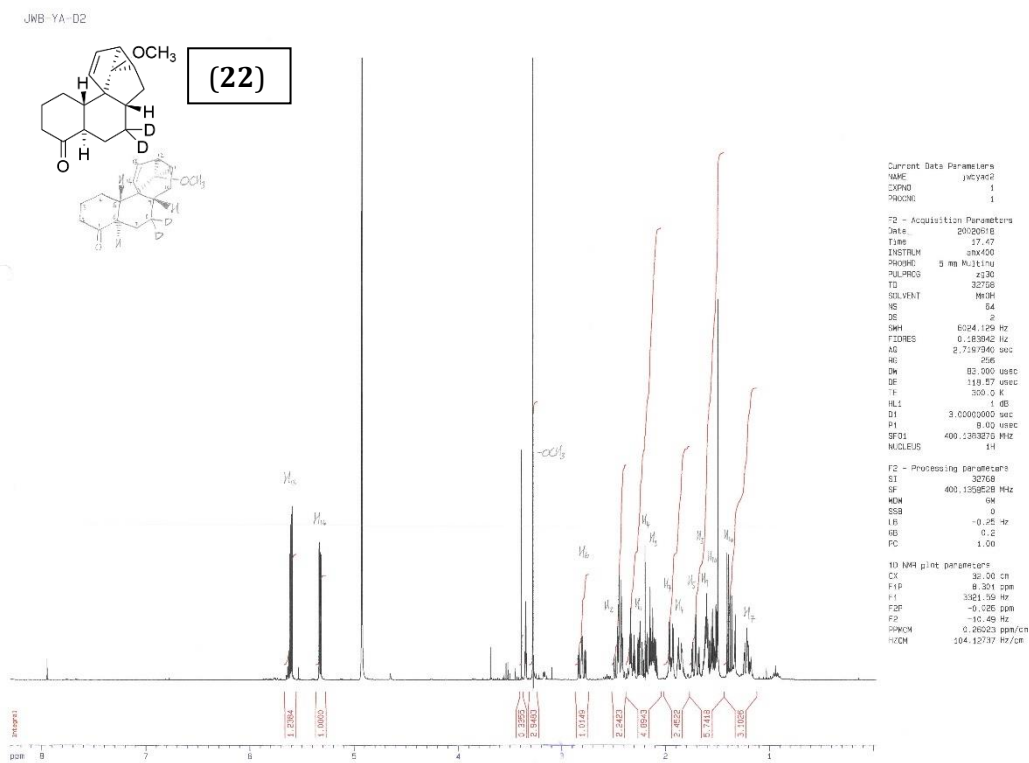
1D NMR plot parameters
 CX 30.00 cm
 FIP 225.864 ppm
 F1 82425.10 Hz
 F2P -0.282 ucm
 F3 -843.50 Hz
 PPHC1 7.03869 ppm/cm
 IZCM 705.19667 Hz/cm

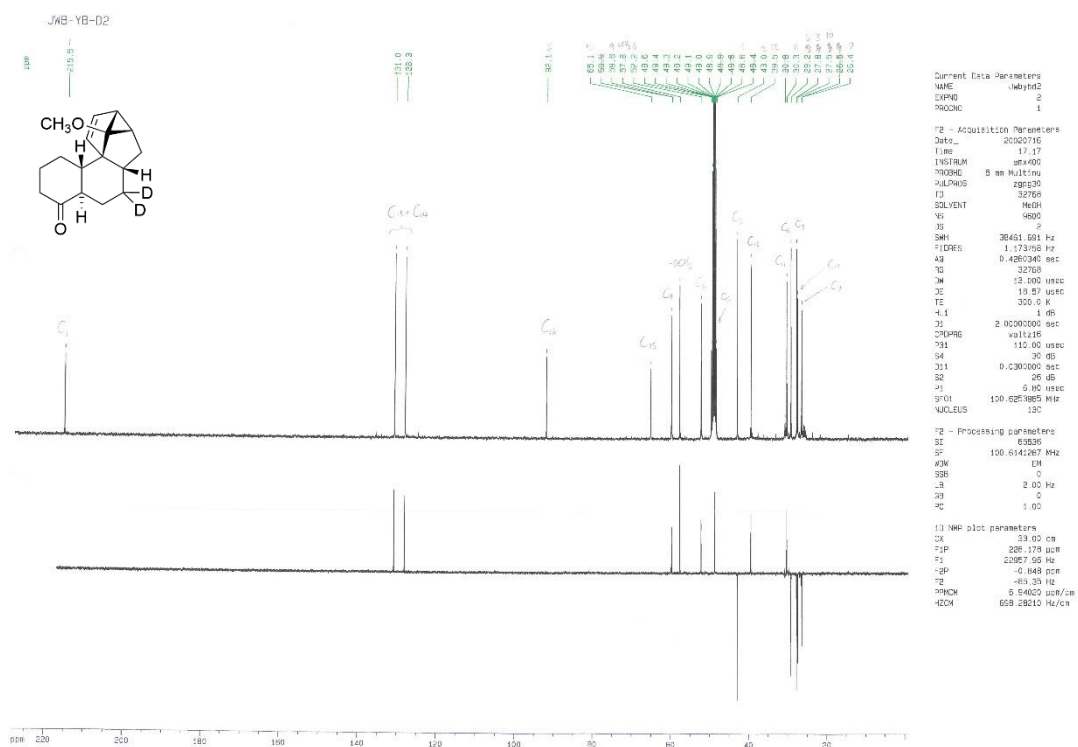
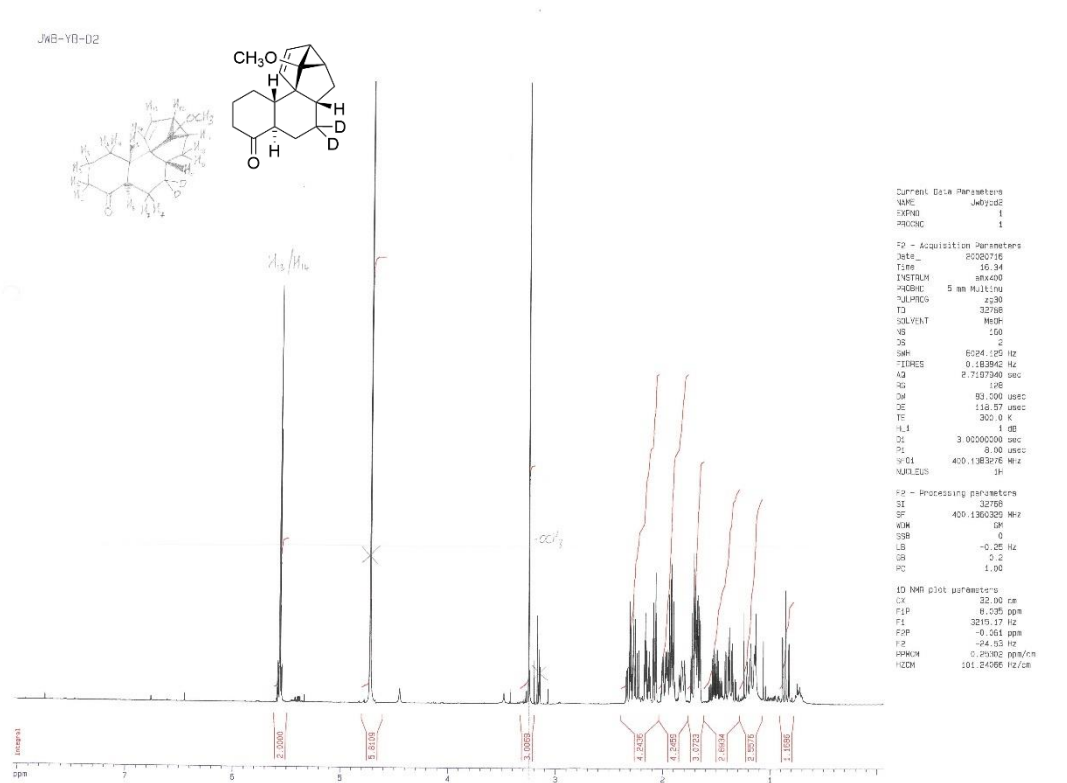


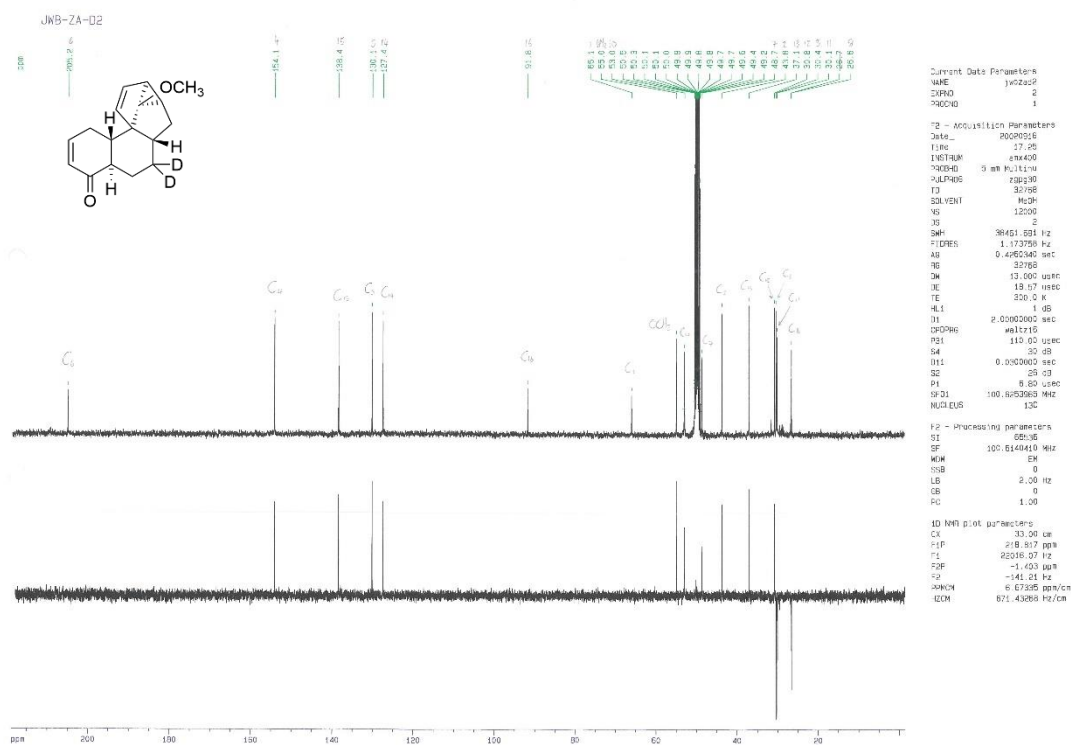
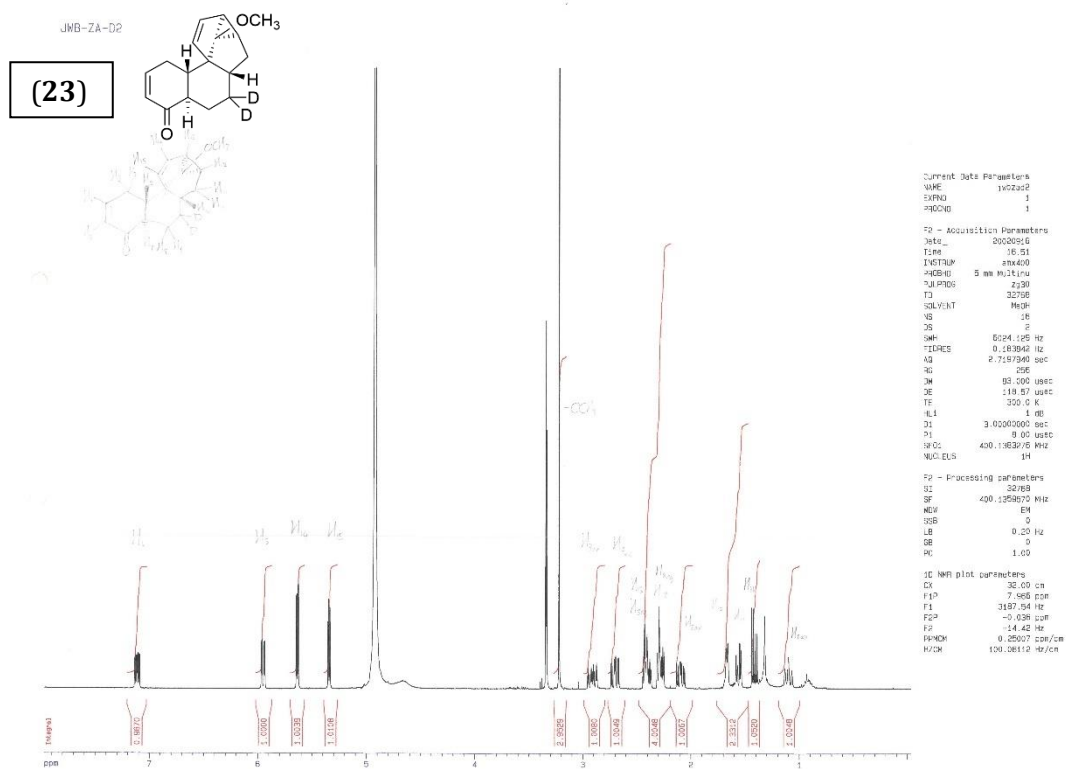


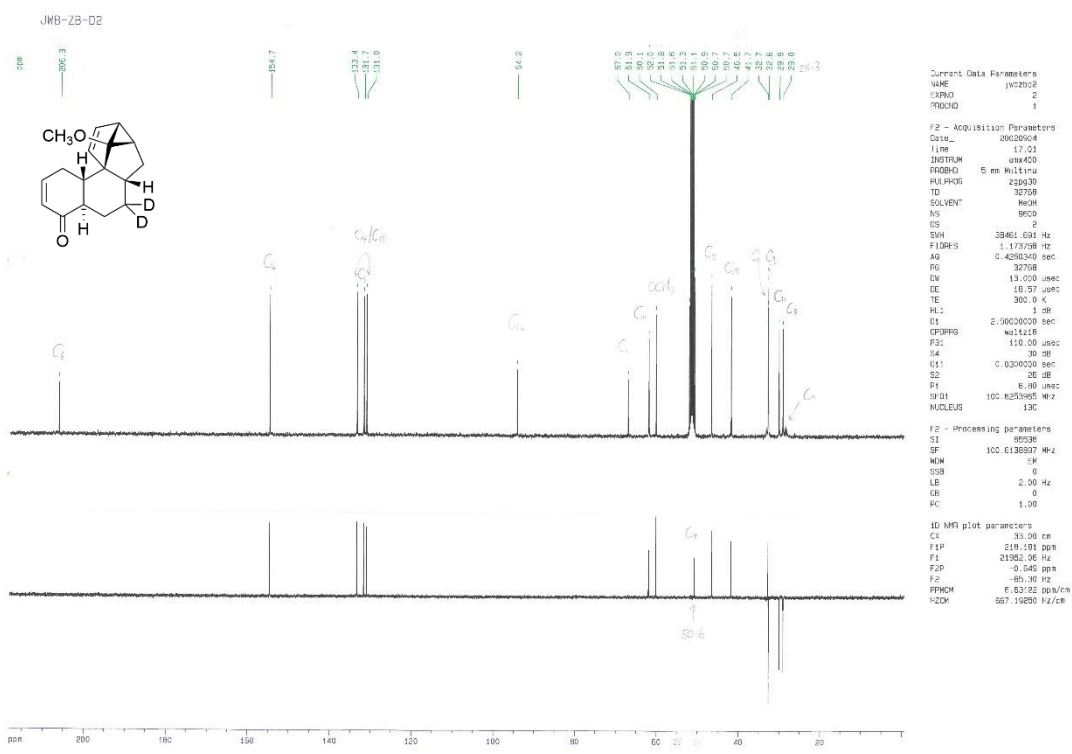
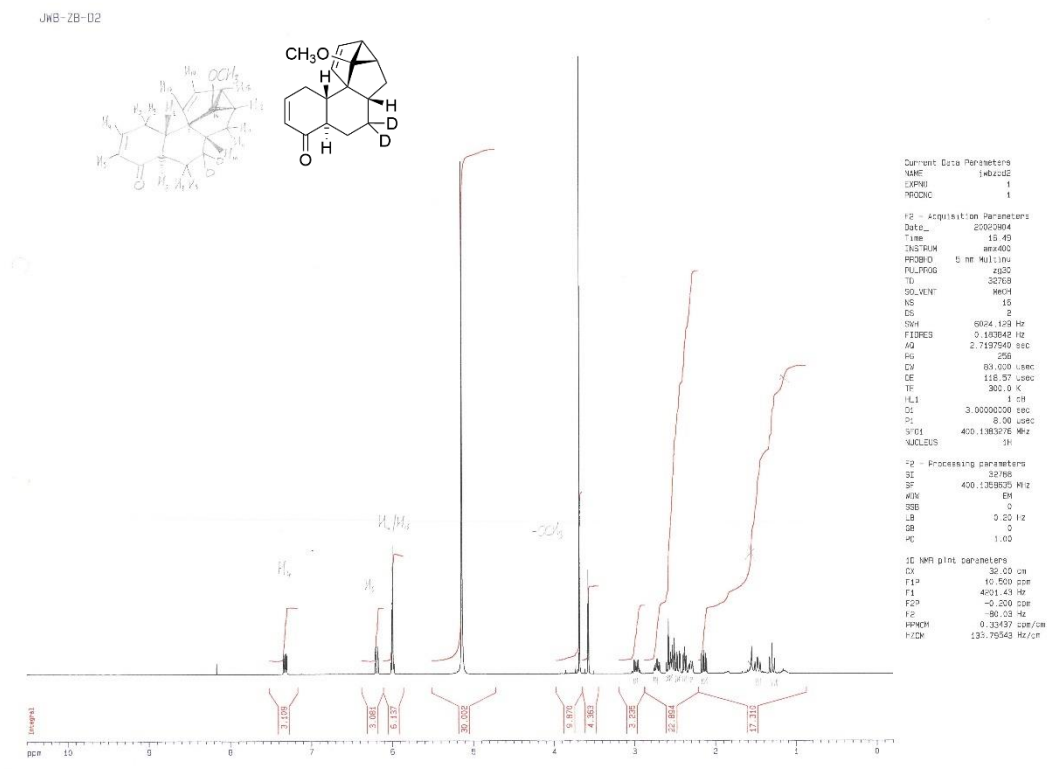












Synthesis of the control substrate (9)

