

Electronic Supporting Information

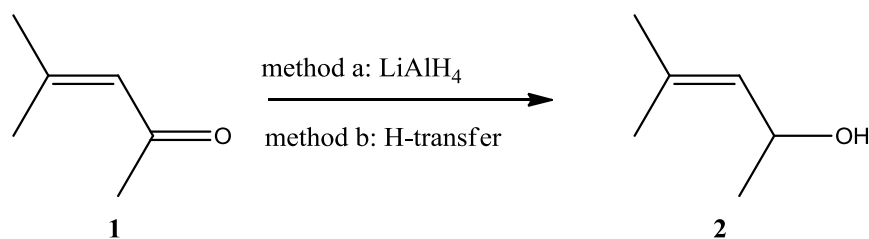
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General information:

^1H and ^{13}C NMR spectra were recorded on a Bruker dpx300, Bruker AV400 or Bruker AV(III)400 spectrometer. The chemical shifts and the coupling constants were obtained through analysis of the relevant spectra using ACD/SpecManager software version 12 and all spectra were referenced to CDCl_3 (7.28 ppm for ^1H -NMR, 77.00 ppm for ^{13}C -NMR). All GC data was obtained using a Shimadzu GC-2010 online GLC. All chemicals were purchased from Sigma Aldrich unless otherwise stated. FTIR spectra were recorded using a Nicolet 380 FT-IR spectrometer. BET surface area measurements were conducted using a Micrometrics ASAP 2020 Volumetric Sorptometer and analysed using ASAP 2020 V1.05 software. Powder X-ray diffraction patterns were obtained using a PANalytical multi-purpose diffractometer with a Cu source. Thermogravimetric analysis was conducted using a TA Instruments SDT Q600 Analyser and using TA Instruments Universal Analysis 2000 software. Photochemical experiments were irradiated using 4 x 5 x Citizen Electronics Co. Ltd 1000 lumen white light LEDs unless otherwise stated.

Synthesis of 4-methylpent-3-en-2-ol (**2**)



Method a: Reduction of mesityl oxide using LiAlH_4

Under an N_2 atmosphere, LiAlH_4 (4.9 g) was added to dry diethyl ether (75 mL) with stirring. The mixture was cooled (0 - 10 °C) and a solution of mesityl oxide (58.3 mL, 0.5 mol) in dry diethyl ether (75 mL) was added dropwise. After stirring (1 h), the reaction mixture was treated slowly with ice water (15 mL), NaOH solution (15 %, 15 mL) and finally water (50 mL). After extraction of the

organic phase, the aqueous layer was washed with diethyl ether (2 x 20 mL) and the combined ether extracts were dried over anhydrous Na_2SO_4 . Evaporation of the volatiles under reduced pressure afforded pure allylic alcohol (37.5 g, 0.37 mol, 75 %).¹

Method b: Continuous reduction of mesityl oxide *via* hydrogen transfer from IPA, over MgO

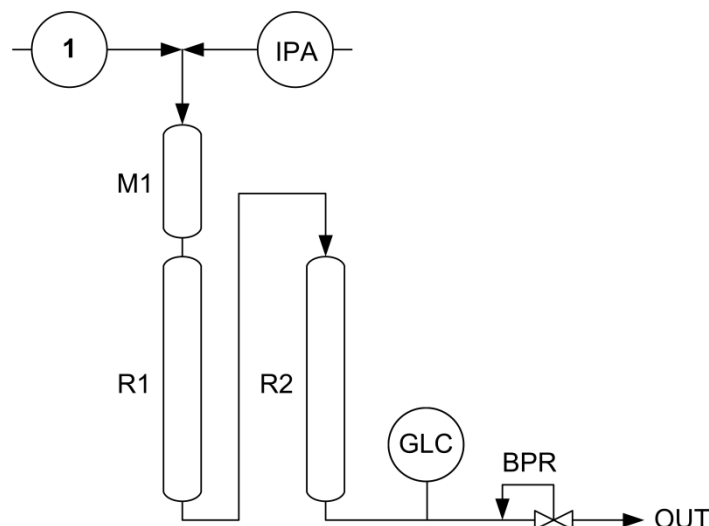


Fig. ESI-1: The flow reactor used for the reduction of **1** to **2**. **1** and IPA are pumped separately using Jasco PU-980 HPLC pumps. BPR: back-pressure regulator (Jasco BP-1580-81); M1: mixer filled with glass beads (1.5-2.0 mm) and maintained at 250°C; R1 & R2: ¼" stainless steel piping packed with MgO equipped with aluminium heating blocks. The reacting stream is monitored every 10 mins by online GLC: Shimadzu GC-2010.

IPA and **1** were pumped separately through a mixer (M1) at 250 °C and two ¼" o.d. stainless steel reactors filled with a total of 1 g high surface area MgO catalyst (see section "Synthesis of High Surface Area MgO"). The temperature of the reactors was controlled between 250 and 350 °C and the internal and external reactor temperatures were monitored using PicoLog software. The mixture was monitored by online gas-liquid chromatography (GLC) using a high pressure sample loop to study the effect of varying the reaction parameters and the activity of the catalyst. Typical experiments were conducted using an IPA:**1** molar ratio of 10:1.

Synthesis of High Surface Area MgO

Magnesium nitrate hexahydrate (80g) was dissolved in water (500mL) at 80 °C. K_2CO_3 (4 M) was then added dropwise until pH 10. The resulting mixture was then filtered and washed with water before the solid was dried overnight at 150 °C. The dry white solid was finally calcined in air at 400°C for 4h and was confirmed as MgO by powder X-ray diffraction.

Surface area (BET): 83.97 m²/g

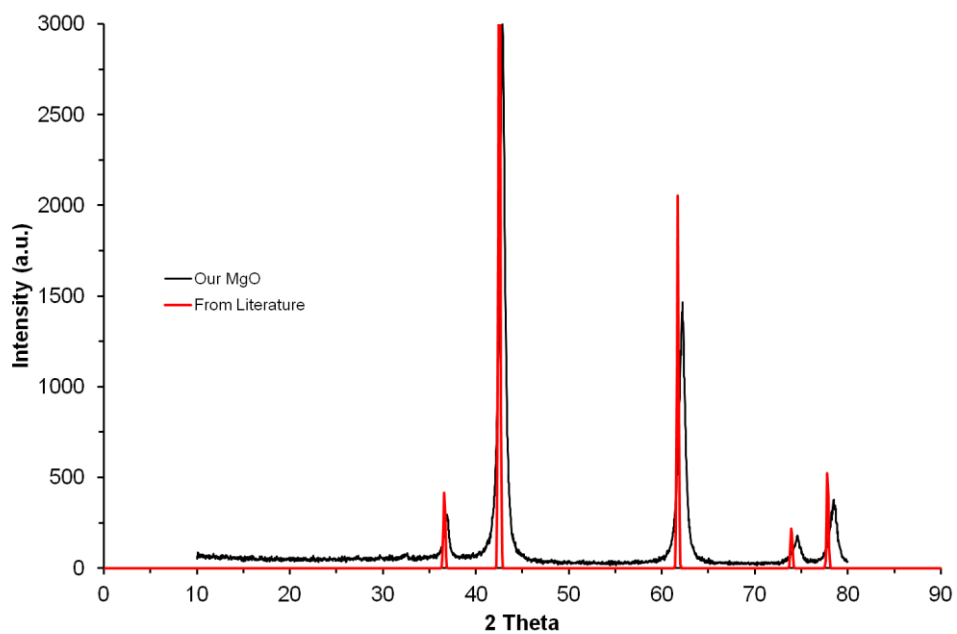


Fig. ESI-2: Powder X-ray diffraction pattern for our high surface area MgO compared with the literature.²

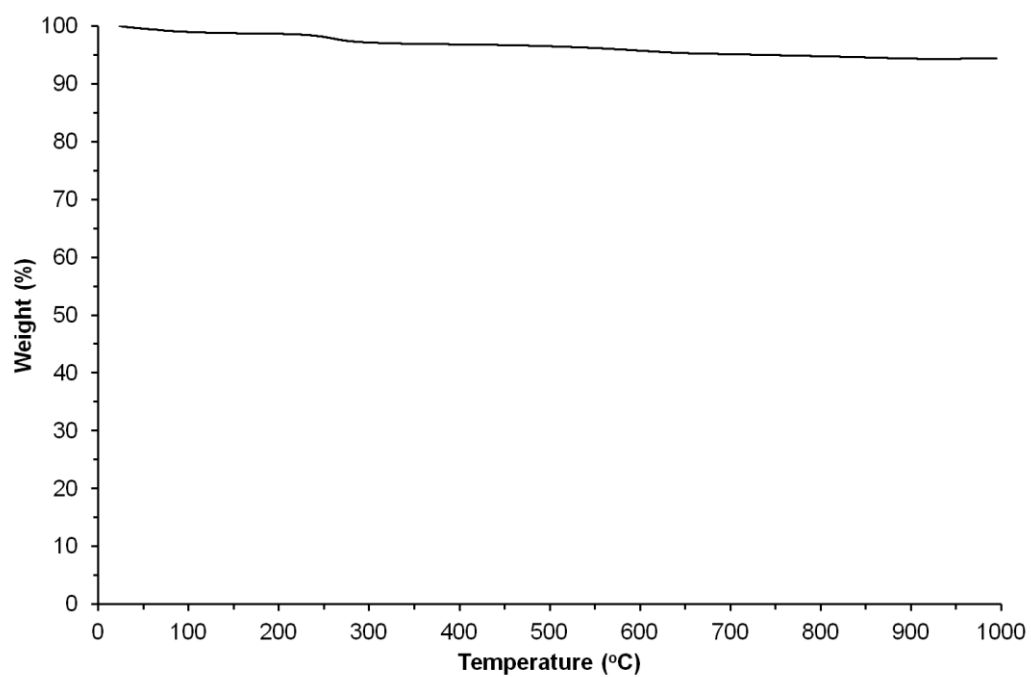


Fig. ESI-3: Thermogram of synthesised MgO.

Structure of 4-methylpent-3-en-2-ol^{1,3}:

¹H-NMR: (300 MHz, CDCl₃)

δ (ppm) = 1.19 (d, 3H, *J* = 6.1 Hz, CH₃CH), 1.65 (d, 3H, *J* = 1.3 Hz, CH₃C=C), 1.67 (d, 3H, *J* = 1.3 Hz, CH₃C=C), 4.47 (dq, 1H, *J* = 8.5, 6.3 Hz, CH-OH), 5.14 (dsep, 1H, *J* = 8.5, 1.4 Hz, CH=C)

¹³C-NMR: (75.5 MHz, CDCl₃)

δ (ppm) = 17.86 (CH₃CH), 23.48 (CH₃C=C), 25.53 (CH₃C=C), 64.53 (CH-OH), 129.45 (CH=C), 133.42 (C=CH)

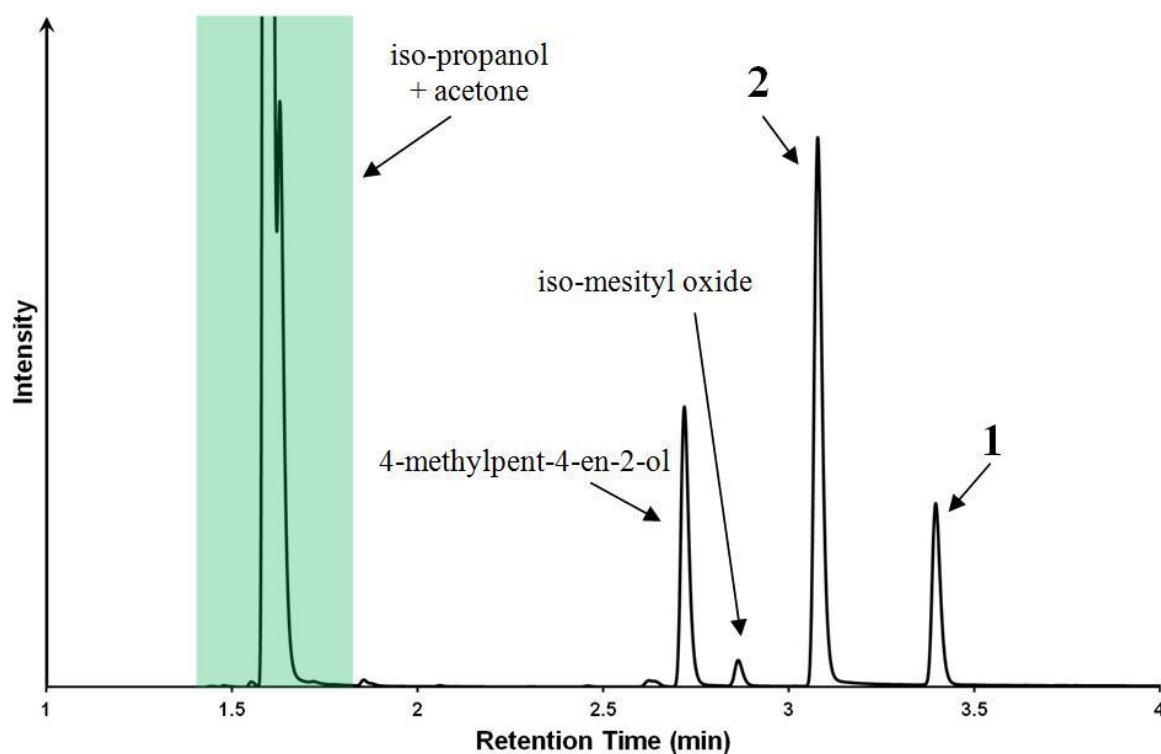


Fig. ESI-4: Representative GLC trace for the continuous flow hydrogen transfer reduction of **1** with IPA.

Retention times:

2: 3.077 min

1: 3.395 min

4-methylpent-4-en-2-ol: 2.718 min

Iso-mesityl oxide: 2.863 min

Effect of Pressure on H-transfer Reduction of **1** with IPA

Prior to further experimentation, the effect of pressure on the flow H-transfer reduction of **1** using IPA was examined. As can be seen in Fig. ESI-5, above 2 MPa the conversion to **2** only changed by *ca.* 2 %, between atmospheric pressure and 10 MPa, and so 2 MPa was the pressure used for all experiments, unless otherwise stated.

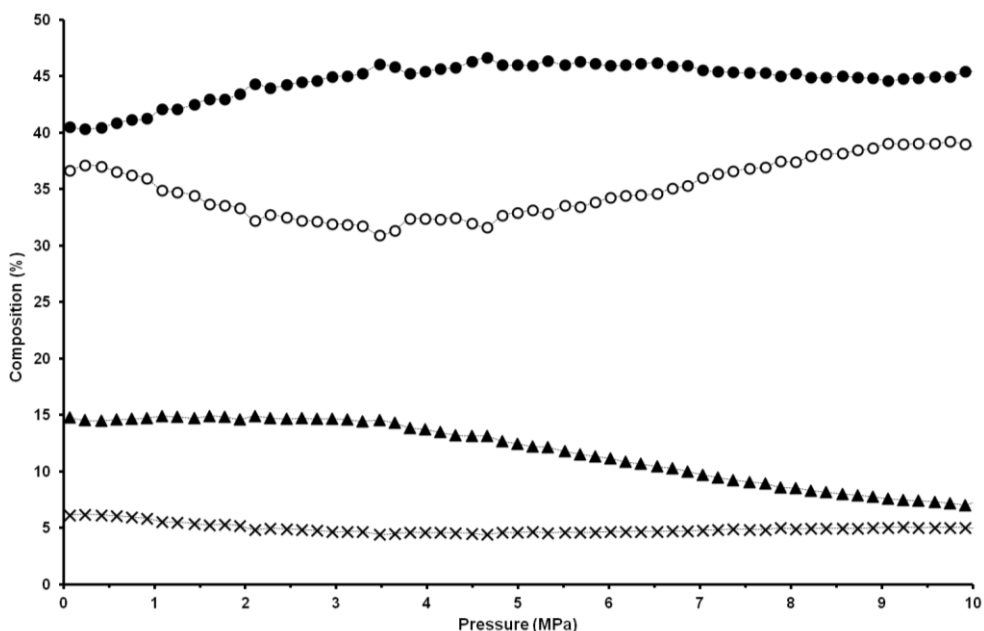
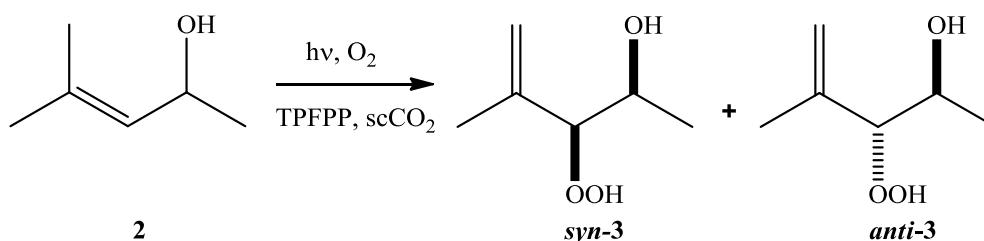


Fig. ESI-5: Effect of pressure on the conversion of **1** to **2** over 1 g MgO. The temperature remained constant at 350 °C with a total flow rate of 0.3 mLmin⁻¹ IPA + **1** in a 10:1 molar ratio. The pressure was gradually increased from atmospheric pressure to 10 MPa at a rate of 0.01 MPa/min over 600 min. The reacting stream was monitored by online GLC taken every 10 min. The traces are labelled as follows; ●: **2**; ○: **1**; ▲: 4-methylpent-4-en-2-ol; X: iso-mesityl oxide

Photo-oxidation of **2** with $^1\text{O}_2$ to give hydroperoxides (**3**)



Method a: Batch

The batch photo-oxidation of **2** in scCO_2 was performed in a high pressure batch cell (0.78 mL, 2 mm pathlength). 20 μL of a solution of **2** + TPFPP (2 mg mL^{-1}) and cyclopentanone or cyclohexanone (such that the molar ratio of ketone:**2** = 2:1) were injected into the cell, which was then filled with a CO_2/O_2 (O_2 : **2** molar ratio = 4:1) mixture to 18 MPa. The batch cell was irradiated with a single white 1000 lumen LED, and FTIR spectra were taken every 30 s to monitor the reaction.⁴ The hydroperoxides were isolated in *ca.* 80 % yield as a mixture of two isomers (*syn:anti* 85:15).

Method b: Flow

The continuous flow photo-oxidation of **2** in scCO_2 was performed in a custom built high pressure rig, consisting of two individual sapphire tube reactors for increased residence time.⁵ A solution of **2**, cyclopentanone or cyclohexanone (1:1 ketone:**2**, mol:mol) and TPFPP (2 mg mL^{-1} of **2**) was pumped into the rig at 0.03 mL min^{-1} , together with CO_2 (0.3 mL min^{-1}) and O_2 (6 % in CO_2 , molar ratio O_2 :**2** = 2:1) at a pressure of 18 MPa. The system was irradiated and the product stream was analysed by NMR. The maximum conversion to the hydroperoxides was 86 %, as a mixture of two isomers (*syn:anti* 85:15).

Syn-3-Hydroperoxy-4-methylpent-4-en-2-ol⁶:

$^1\text{H-NMR}$: (300 MHz, CDCl_3)

δ (ppm) = 1.08 (d, 3H, $J = 6.4$ Hz, CH_3CH), 1.72 (t, 3H, $J = 1.1$ Hz, $\text{CH}_3\text{C=}$), 3.83 (dq, 1H, $J = 8.4$, 6.4 Hz, CH-OH), 4.09 (d, 1H, $J = 8.4$ Hz, CH-OOH), 5.02 (m, 2H, $\text{CH}_2=\text{C}$)

$^{13}\text{C-NMR}$: (75.5 MHz, CDCl_3)

δ (ppm) = 17.94 ($\text{C-CH}_3\text{CH}$), 18.75 ($\text{C-CH}_3\text{C=}$), 67.23 (C-CH-OH), 94.82 (C-CH-OOH), 116.47 ($\text{C-CH}_2=\text{C}$), 141.43 ($\text{C}=\text{CH}_2$)

Anti-3-Hydroperoxy-4-methylpent-4-en-2-ol⁶:

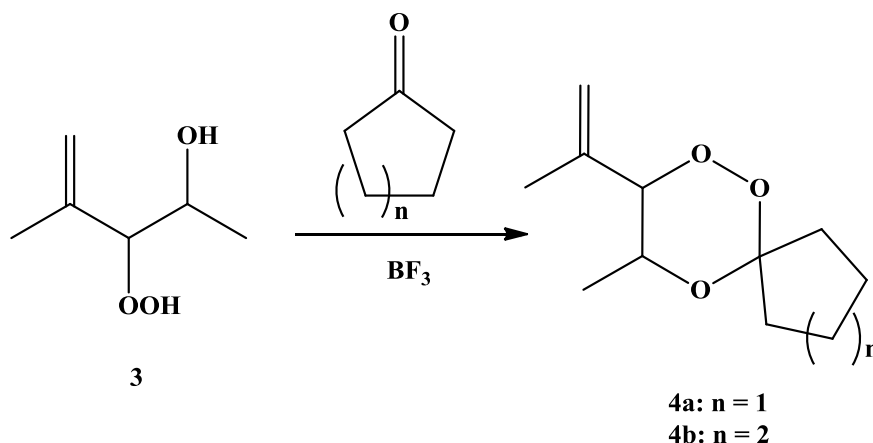
$^1\text{H-NMR}$: (300 MHz, CDCl_3)

δ (ppm) = 1.18 (d, 3H, $J = 6.4$ Hz, CH_3CH), 1.78 (t, 3H, $J = 1.2$ Hz, $\text{CH}_3\text{C=}$), 3.93 (m, 1H, CH-OH), 4.25 (d, 1H, $J = 4.9$ Hz, CH-OOH), 5.08 (m, 2H, $\text{CH}_2=\text{C}$)

$^{13}\text{C-NMR}$: (75.5 MHz, CDCl_3)

δ (ppm) = 18.06 ($\text{C-CH}_3\text{CH}$), 19.71 ($\text{C-CH}_3\text{C=}$), 66.89 (C-CH-OH), 92.26 (C-CH-OOH), 115.26 ($\text{C-CH}_2=\text{C}$), 141.34 ($\text{C}=\text{CH}_2$)

Condensation of hydroperoxides with cyclic ketone



Method a: using $\text{BF}_3 \cdot \text{Et}_2\text{O}$ ⁷

The product stream from the flow photo-oxidation of **2**, containing cyclohexanone, was collected in a flask containing $\text{BF}_3 \cdot \text{Et}_2\text{O}$ hydrate (0.2 mL) in dichloromethane (100 mL) at 0 – 10 °C. Once the photo-oxidation process was terminated, the mixture was slowly warmed to room temperature before stirring for 12 h. The desired product **4b** was isolated from the crude solution by thick layer silica gel chromatography (hexane:ethyl acetate 10:1) with an overall yield of *ca.* 25 %.

Method b: using Silica/ BF_3

The isomeric mixture of **2** was diluted in cyclopentanone and was pumped over 0.5 g silica/ BF_3 at 50 °C, 10 atm pressure at a total flow rate of 0.05 mLmin⁻¹. The product stream was collected periodically over 10 minutes and the resulting solutions were analysed by NMR. Trioxane **4a** was isolated in a pure form from the collected fractions after thick layer chromatography (hexane:ethyl acetate 10:1). The maximum conversion was found to be 60 %, and the overall yield of pure **4a** of was *ca.* 30 %.

4a - 8-Isopropenyl-9-methyl-6,7,10-trioxa-spiro[4.5]decane⁶

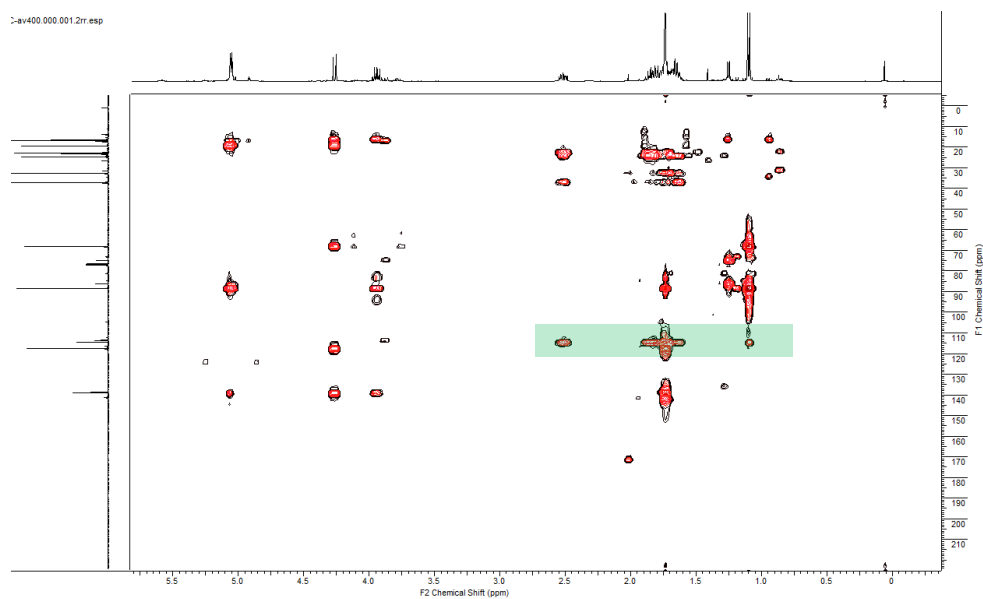
¹H-NMR: (400 MHz, CDCl_3)

δ (ppm) = 1.07 (d, 3H, $J = 6.2$ Hz, CH_3CH), 1.60 - 1.87 (m, 7H, CH_2), 1.72 (m, 3H, $\text{CH}_3\text{C}=\text{C}$), 2.47 (m, 1H, CH_2), 3.84 (dq, 1H, $J = 9.5, 6.3$ Hz, OCH), 4.24 (d, 1H, $J = 9.4$ Hz, OOCH), 5.05 (m, 2H, $\text{CH}_2=\text{C}$)

¹³C-NMR: (100 MHz, CDCl_3)

δ (ppm) = 16.72 (CH_3CH), 19.50 ($\text{CH}_3\text{C}=\text{C}$), 23.12 (CH_2), 24.73 (CH_2), 32.93 (CH_2), 37.32 (CH_2), 68.36 (OCH), 88.63 (OOCH), 114.64 (OCO), 117.63 ($\text{CH}_2=\text{C}$), 139.10 ($\text{C}=\text{CH}_2$)

HMBC – 400 MHz and 100 MHz



Green shading = quaternary carbon, indicating cyclopentane ring connected to trioxane core structure.

4b - 3-Isopropenyl-4-methyl-1,2,5-trioxa-spiro[5.5]undecane⁶

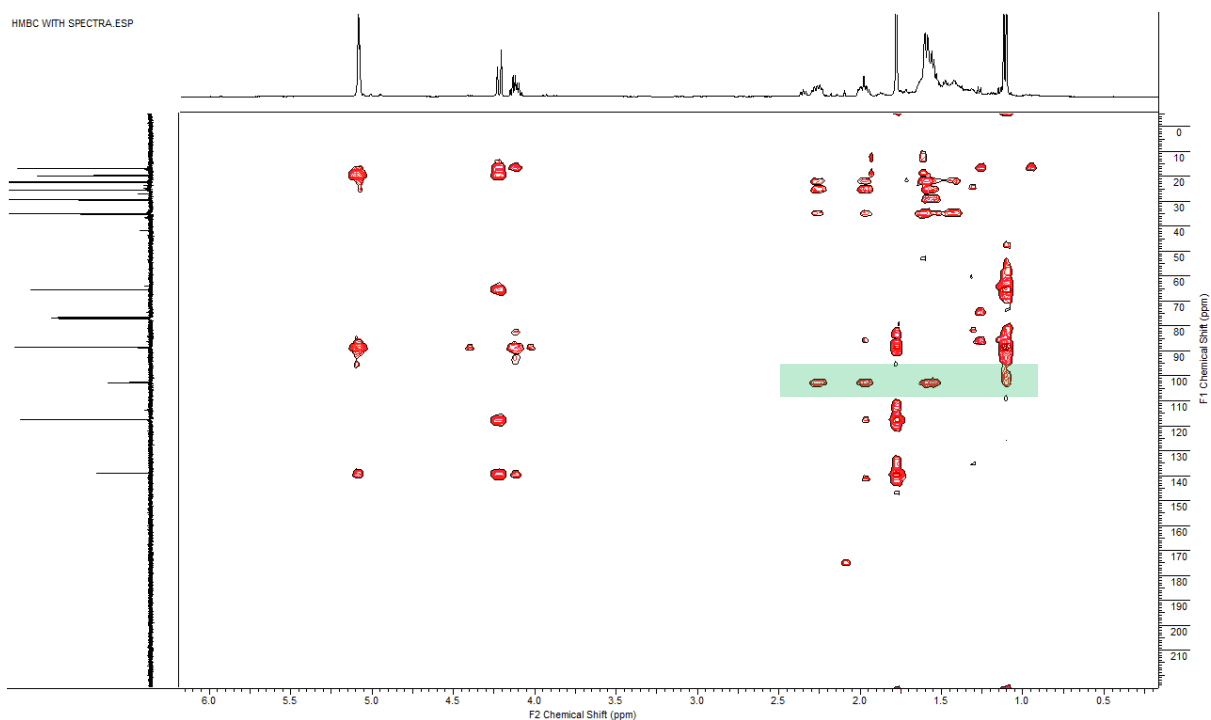
¹H-NMR: (400 MHz, CDCl₃)

δ (ppm) = 1.09 (d, 3H, J = 6.4 Hz, $\underline{\text{C}}\underline{\text{H}}_3\underline{\text{C}}\underline{\text{H}}$), 1.30 - 1.60 (m, 8H, 4 x $\underline{\text{C}}\underline{\text{H}}_2$), 1.77 (m, 3H, $\underline{\text{C}}\underline{\text{H}}_2\underline{\text{C}}=\underline{\text{C}}$), 1.93 (m, 1H, $\underline{\text{C}}\underline{\text{H}}_2$), 2.22 (m, 1H, $\underline{\text{C}}\underline{\text{H}}_2$), 4.08 (dq, 1H, J = 9.5, 6.1 Hz, $\underline{\text{O}}\underline{\text{C}}\underline{\text{H}}$), 4.20 (d, 1H, J = 9.7 Hz, $\underline{\text{O}}\underline{\text{O}}\underline{\text{C}}\underline{\text{H}}$), 5.07 (m, 2H, $\underline{\text{C}}\underline{\text{H}}_2=\underline{\text{C}}$)

¹³C-NMR: (100 MHz, CDCl₃)

δ (ppm) = 16.95 ($\underline{\text{C}}\underline{\text{H}}_3\underline{\text{C}}\underline{\text{H}}$), 19.69 ($\underline{\text{C}}\underline{\text{H}}_3\underline{\text{C}}=\underline{\text{C}}$), 22.22 ($\underline{\text{C}}\underline{\text{H}}_2$), 22.41 ($\underline{\text{C}}\underline{\text{H}}_2$), 25.57 ($\underline{\text{C}}\underline{\text{H}}_2$), 29.49 ($\underline{\text{C}}\underline{\text{H}}_2$), 35.51 ($\underline{\text{C}}\underline{\text{H}}_2$), 65.61 ($\underline{\text{O}}\underline{\text{C}}\underline{\text{H}}$), 88.76 ($\underline{\text{O}}\underline{\text{O}}\underline{\text{C}}\underline{\text{H}}$), 102.80 ($\underline{\text{O}}\underline{\text{C}}\underline{\text{O}}$), 117.61 ($\underline{\text{C}}\underline{\text{H}}_2=\underline{\text{C}}$), 139.24 ($\underline{\text{C}}=\underline{\text{C}}\underline{\text{H}}_2$)

HMBC – 400 MHz and 100 MHz



Green shading = quaternary carbon, indicating cyclohexane ring connected to trioxane core structure.

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