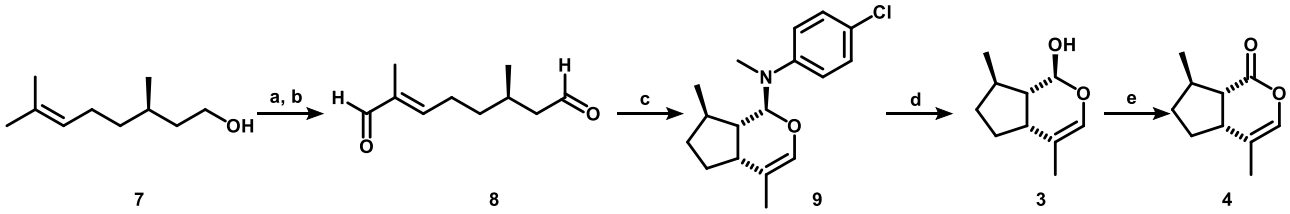
Appendix B. Synthetic chemistry & NMR data

Experimental Methods



Scheme 1: Synthesis of the non-natural sex pheromone components, (1*S*,4a*R*,7*R*,7a*S*)-nepetalactol **3** and (4a*R*,7*R*,7a*S*)-nepetalactone **4**, from enantiomerically pure (*R*)-citronellol **7**.[50,51] **a.** SeO_2, *t*-BuOOH, DCM, **36%**; **b.** i. $(COCl)_2$, DMSO, DCM, -78 ºC, ii. Et_3N, **77%**; **c.** *N*-Methyl-4-chloroanaline, Et_2O, **45%**; **d.** *p*-TsOH, THF, H_2O, **50%**; **e.** Ag_2CO_3, Tol, 120 ºC, **52%**.

Preparation of **1**

Nepeta cataria essential oil (1.00 g), prepared by steam distillation(Birkett and Pickett, 2003), was separated by flash column chromatography over silica gel (3:2 ethyl acetate (EtOAc): petroleum ether 40-60) to give a colourless oil containing (4a*S*,7*S*,7a*R*)-4,7-dimethyl-5,6,7,7a-tetrahydrocyclopenta[c]pyran-1(4aH)-one **1** (222 mg). Preparation of **2**: *N. cataria* essential oil (1.00g) was stirred in dry methanol (MeOH, 20 mL) at 0°C. Sodium borohydride ($NaBH_4$; 497.8 mg; 13.2 mmol) in dry MeOH (10 mL) was added carefully to the mixture and stirred for a further 16 hours at 0°C. Upon completion, the reaction was quenched with H_2O (10 mL), extracted with diethyl ether (2x10 mL), washed with H_2O (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*, giving a crude oil containing (1R,4aS,7S,7aR)-4,7-dimethyl-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-1-ol **2** (167 mg, 17% yield). Both **1** and **2** were purified further using high-pressure liquid-chromatography (HPLC). The HPLC (Shimadzu Prominence) was equipped with 2xLC-20ADxr pumps, SIL-20ac autosampler and SPD-M20A diode array. A water and acetonitrile (ACN) solvent system was used with a flow rate of 5.0 mL min^{-1}, a gradient of 5% to 100% ACN over 60 minutes and a semi-prep HPLC column (ACE 5 AQ V11-5053; 250 x 10 mm).

(E)-2,(6,R)-dimethylocta-2-ene-1,8-diol **7.**

Synthesis of **7** was achieved in 2 steps. Step 1: To a solution of (*R*)-citronellol (Sigma-Aldrich, 97 %) **6** (1.00 g; 6.40 mmol) in dichloromethane (DCM, 20 mL) under N_2 was added selenium dioxide (SeO_2; 71 mg; 0.64 mmol), followed by *tert*-butyl hydroperoxide (*t*-BuOOH; 5M nonane; 1.6 mL; 8.00 mmol). The reaction was stirred at ambient temperature under N_2 for 72 hours, after which an aqueous solution of $Na_2S_2O_3$ (15 mL) was added and stirred vigorously for 15 min. The organic layers were separated, washed with $NaHCO_3$ (15 mL), dried over $MgSO_4$ and concentrated *in vacuo* to yield a crude colourless oil. The crude product was separated by flash column chromatography over silica gel (2:3 to 3:2 EtOAc in pet. ether 40-60) to give **7** as a colourless oil (388 mg; 2.28 mmol; 36%). Step 2: Oxalyl chloride ($(COCl)_2$; 0.26 mL; 3.20 mmol) was stirred in DCM (10 mL) under N_2 and cooled to -78°C. Dimethyl sulphoxide (DMSO, 0.31 mL, 4.45 mmol) in DCM (5 mL) was added dropwise and the reaction stirred for a further 10 min. Compound **7** (333 mg; 1.78 mmol) was dissolved in DCM (5 mL) and added to the mixture and stirred for a further 45 min. Triethylamine (1.24 mL; 8.90 mmol)

was added and the reaction allowed to warm to ambient temperature over 20 min. The resulting white precipitate was dissolved in H_2O (approximately 10 mL), extracted with DCM (2x10 mL), washed with 2M HCl (10 mL) and brine (10mL), before being dried over $MgSO_4$ and concentrated *in vacuo* to yield a yellow oil containing *(E)*-2,(6*R*)-dimethylocta-2-enediol **8** (230 mg; 1.37 mmol; crude 77%)**.**

(1S,4aR,7R,7aS)-N,4,7-trimethyl-N-(4-chlorophenyl-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-1-amine **9.**
Compound **8** (950 mg; 5.64 mmol) and activated 4Å molecular sieves (200 mg) were stirred in diethyl ether (10 mL) under N_2 for 30 minutes, after which (*N*-methyl-4-chloroaniline (0.68 mL, 5.64 mmol) was added. The mixture was stirred for a further 16 hours at ambient temperature, then filtered over celite and concentrated *in vacuo* to yield a yellow oil. The crude oil was separated by chromatography over silica gel (1:20 EtOAc:Pet ether 40-60) to yield a yellow oil **9** (0.74 g, 2.54 mmol, 45 %, de 81%) containing *(1S,4aR,7R,7aS)-N,*4,7-trimethyl-N-(4-chlorophenyl-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-1-amine **9**. Diastereomeric excess was determined using NMR.

(4aS,7S,7aR)-4,7-dimethyl-5,6,7,7a-tetrahydrocyclopenta[c]pyran-1(4aH) **3**.
p-Toluensulfonic acid (25 mg; 0.13 mmol) was added to a solution of **9** (30 mg; 0.12 mmol) in tetrahydrofuran (THF, 2.5 mL) and H_2O (2.5 mL) and the reaction mixture stirred for 90 min at ambient temperature. $NaHCO_3$ was added (5 mL) and the organic layer extracted with EtOAc (2x5 mL) and 2M HCl (5 mL), dried over $MgSO_4$ and concentrated *in vacuo* to yield a crude yellow oil. The crude product was separated by chromatography over silica gel (9:1 pet. ether 40-60: EtOAc) to give *(1S,4aR,7R,7aS)-4,7-dimethyl-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-1-ol* **4** (10 mg; 0.06 mmol; 50 %) as a colourless oil. Compound **4** (43 mg, 0.26 mmol) was added to silver carbonate (347 mg, 1.26 mmol) and celite (240 mg) in toluene (5 mL) and the reaction refluxed at 120°C under N_2 for 1 hour. The final mixture was cooled to ambient temperature, filtered over celite and concentrated *in vacuo* to yield a colourless oil, which was separated by chromatography over silica gel (1:19 EtOAc in Pet. Ether 40-60) to give *(4aS,7S,7aR)*-4,7-dimethyl-5,6,7,7a-tetrahydrocyclopenta[c]pyran-1(4aH) **3** (23 mg, 52%) as a colourless oil.

NMR Data

(4aS,7S,7aR)-4,7-Dimethyl-5,6,7,7a-tetrahydrocyclopenta[c]pyran-1(4aH)-one **1**
$[\alpha]^{25}_D$ +6.70 (c 3.3, CH_3OH); δ_H (500 MHz; $CDCl_3$) 1.18 (3H, d, J = 6.62 Hz), 1.49-1.59 (1H, m), 1.60(3H, s), 1.82-1.91 (2H, m), 1.96-2.06 (2H, m), 2.30-2.39 (1H, m), 2.40-2.46 (1H, m), 6.13-6.18 (1H, m); δ_C (125 MHz; $CDCl_3$) 15.3, 20.1, 30.6, 32.9, 39.6, 40.6, 115.2, 133.4, 171.1; *m/z* HRMS calculated for $[C_{10}H_{15}O_2]^+$ ($M+H^+$) 167.1066, found 167.1079. Data consistent with literature[61,62].

(1R,4aS,7S,7aR)-4,7-Dimethyl-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-1-ol **2**
$[\alpha]^{25}_D$ -14.4 (c 2.2, CH_3OH); δ_H (500 MHz; $CDCl_3$) 1.10 (3H, d, J = 7.06 Hz), 1.31-1.40 (1H, m), 1.57 (3H, s), 1.61-1.73 (1H, m), 1.81-2.03 (4H, m), 2.47 (1H, q, J = 7.79 Hz, 10-H), 4.83-4.89 (1H, m), 6.03 (1H, s). δ_C (125 MHz; $CDCl_3$) 16.5, 20.9, 30.9, 33.4, 35.9, 38.7, 50.7, 94.5, 113.6, 134.3; *m/z* HRMS calculated for $[C_{10}H_{17}O_2]^+$ ($M+H^+$) 168.1145, found 169.1265. Data consistent with literature[61,62].

(E)-2,(6,R)-Dimethylocta-2-ene-1,8-diol ***7***
$[\alpha]^{25}_D$ +4.72 (c 1.8, CH_3OH); δ_H ($CDCl_3$, 500 MHz) 0.94 (3H, d, *J* = 6.45 Hz), 1.36-1.46 (2H, m), 1.58-1.67(2H, m), 1.69 (3H, s), 1.99-2.15 (1H, m), 3.64-3.77 (2H, m), 4.02 (2H, s), 5.42 (1H, t, *J* = 7.15 Hz); δc ($CDCl_3$, 125 MHz) 9.53, 19.51, 25.06, 36.83, 39.73, 60.92 61.33, 69.07, 126.54, 134.74; *m/z* HRMS calculated for $[C_{10}H_{20}O_2Na]^+$ ($M+Na^+$) 195.1356, found 195.1360. Data consistent with literature[62].

(E)-2,(6R)-Dimethylocta-2-enediol ***8***
δ_H (500 MHz; $CDCl_3$) 1.04 (3H, d, *J* = 6.80 Hz), 1.40-1.48 (1H, m), 1.54-1.62 (1H, m), 1.77 (3H, s), 2.12-2.18 (1H, m), 2.31-2.51 (4H, m), 6.49 (1H, t, *J* = 7.09 Hz), 9.42 (1H, s), 9.80 (1H, s); Full analysis including ^{13}C NMR, HRMS and $[\alpha]_D$ could not be performed due to the instability of the dialdehyde.

(1S,4aR,7R,7aS)-N,4,7-Trimethyl-N-(4-chlorophenyl-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-1-amine ***9***
$[[\alpha]^{25}_D$ – 17.7 (c 1.00, CH_3OH); δ_H ($CDCl_3$, 500 MHz) 1.09 (3H, d, *J* = 6.20), 1.64 (3H, s), 1.83-1.91 (2H, m), 2.06-2.19 (2H, m), 2.36-2.49 (1H, m), 2.97 (3H, s), 4.63 (1H, d, *J* = 10.34), 6.22 (1H, s), 6.53 (1H, d, *J* = 8.38), 6.89 (1H, d, *J* = 8.79), 7.15 (1H, d, *J* = 8.79), 7.21 (1H, d, *J* = 9.02). δ_C ($CDCl_3$, 125 MHz) 17.21, 21.86, 30.92, 33.15, 33.68, 36.51, 42.15, 45.51, 88.45, 113.31, 113.70, 117.19, 121.83, 124.08, 128.85, 129.09, 137.65; *m/z* HRMS calculated for $[C_{17}H_{23}ONCl]^+$ ($M+H^+$) 292.1463, found 292.1450.

(1S,4aR,7R,7aS)-4,7-Dimethyl-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-1-ol ***4***
$[\alpha]^{25}_D$ + 3.67 (c 0.31, CH_3OH); δ_H (500 MHz; $CDCl_3$) 1.10 (3H, d, *J* = 7.06 Hz), 1.31-1.40 (1H, m), 1.57 (3H, s), 1.61-1.73 (1H, m), 1.81-2.03 (4H, m), 2.47 (1H, q, *J* = 7.79 Hz, 10-H), 4.83-4.89 (1H, m), 6.03 (1H, s); δ_C (125 MHz; $CDCl_3$) 16.5, 20.9, 30.9, 33.4, 35.9, 38.7, 50.7, 94.5, 113.6, 134.3; *m/z* HRMS calculated for $[C_{10}H_{17}O_2]^+$ ($M+H^+$) 168.1145, found 169.1265. Data consistent with literature[61,62]

(4aS,7S,7aR)-4,7-Dimethyl-5,6,7,7a-tetrahydrocyclopenta[c]pyran-1(4aH)-one ***3***
$[\alpha]^{25}_D$ -17.10 (c 2.7, CH_3OH); δ_H (500 MHz; $CDCl_3$) 1.18 (3H, d, *J* = 6.62 Hz), 1.49-1.59 (1H, m), 1.60(3H, s), 1.82-1.91 (2H, m), 1.96-2.06 (2H, m), 2.30-2.39 (1H, m), 2.40-2.46 (1H, m), 6.13-6.18 (1H, m); δ_C (125 MHz; $CDCl_3$) 15.3, 20.1, 30.6, 32.9, 39.6, 40.6, 115.2, 133.4, 171.1; *m/z* HRMS calculated for $[C_{10}H_{15}O_2]^+$ ($M+H^+$) 167.1066, found 167.1079.

NMR Spectra

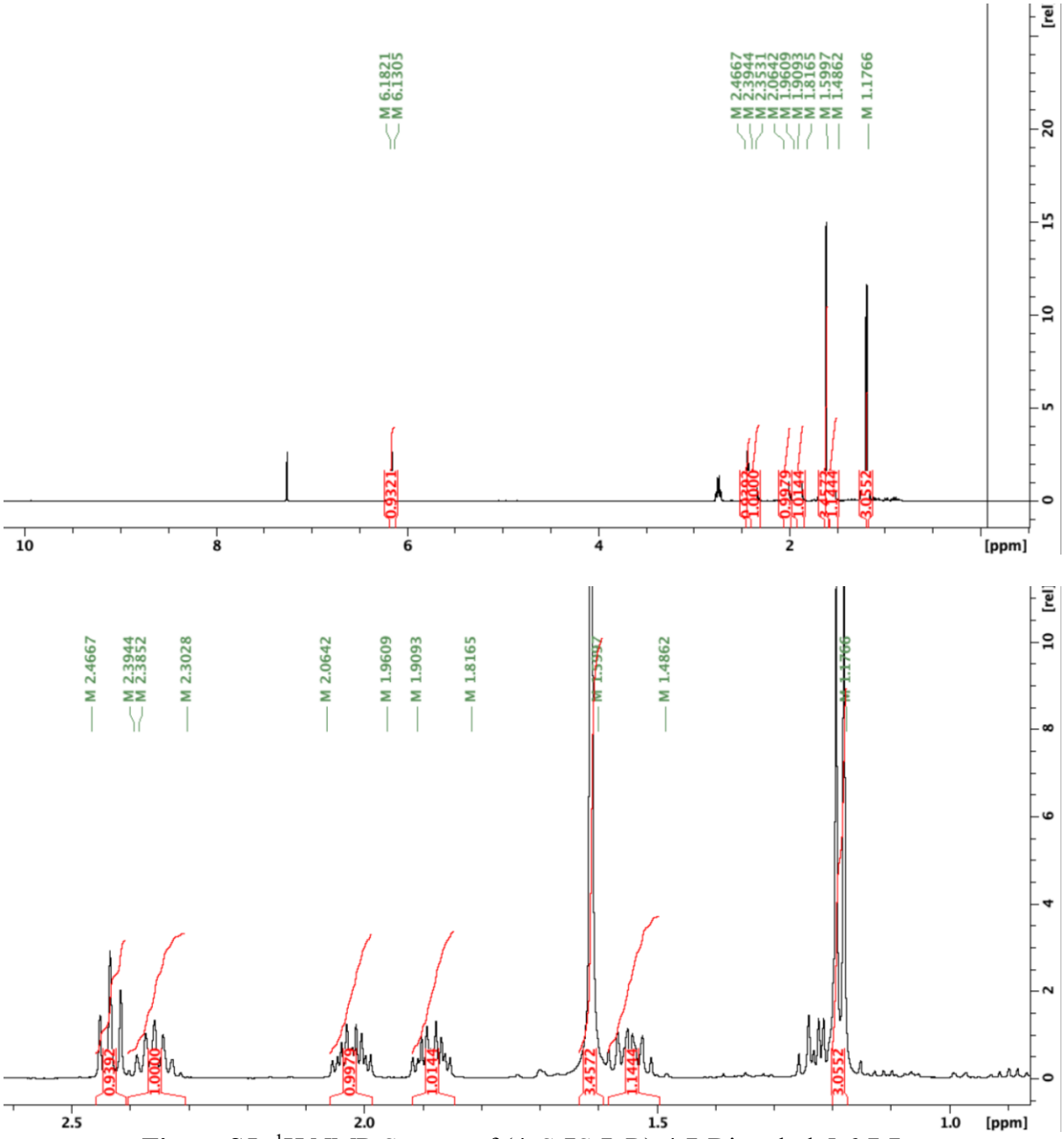


Figure S5: ^{1}H NMR Spectra of (4aS,7S,7aR)-4,7-Dimethyl-5,6,7,7a-tetrahydrocyclopenta[c]pyran-1(4aH)-one **1**

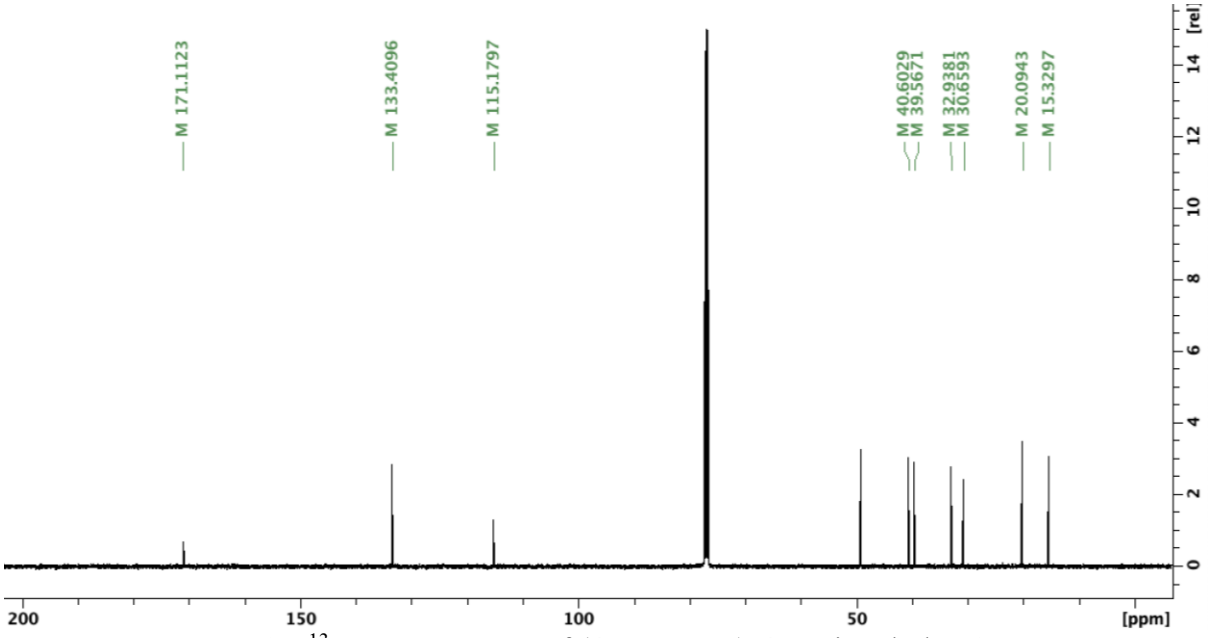


Figure S6: ^{13}C NMR Spectra of (4aS,7S,7aR)-4,7-Dimethyl-5,6,7,7a-tetrahydrocyclopenta[c]pyran-1(4aH)-one **1**

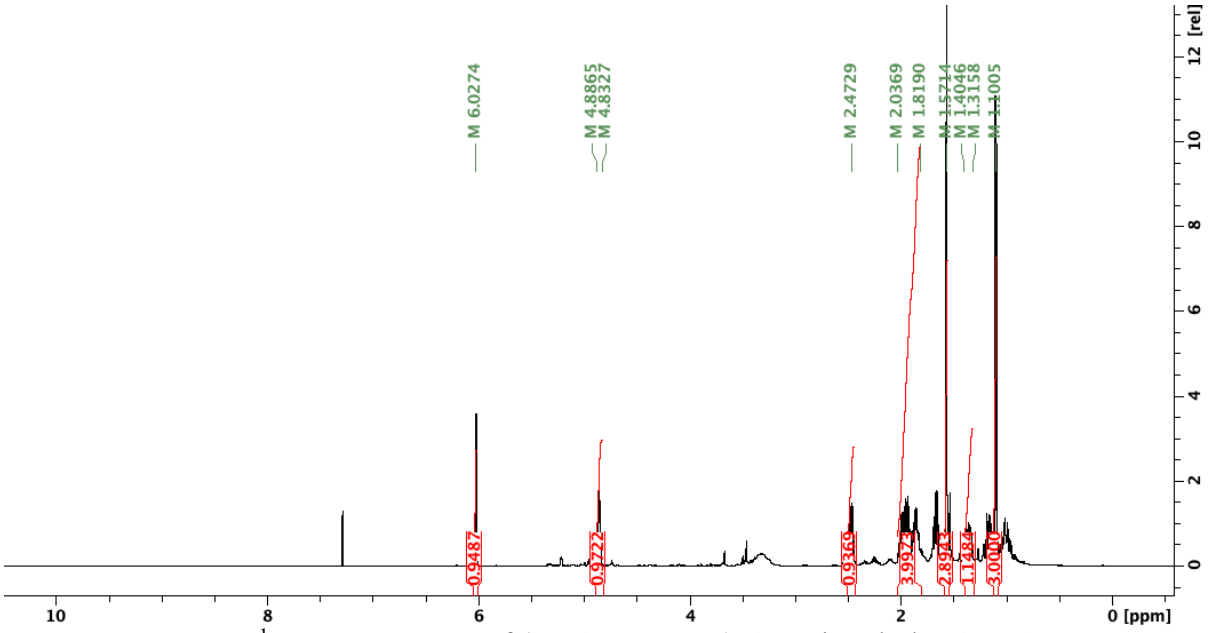


Figure S7: ^{1}H NMR Spectra of (1R,4aS,7S,7aR)-4,7-Dimethyl-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-1-ol **2**

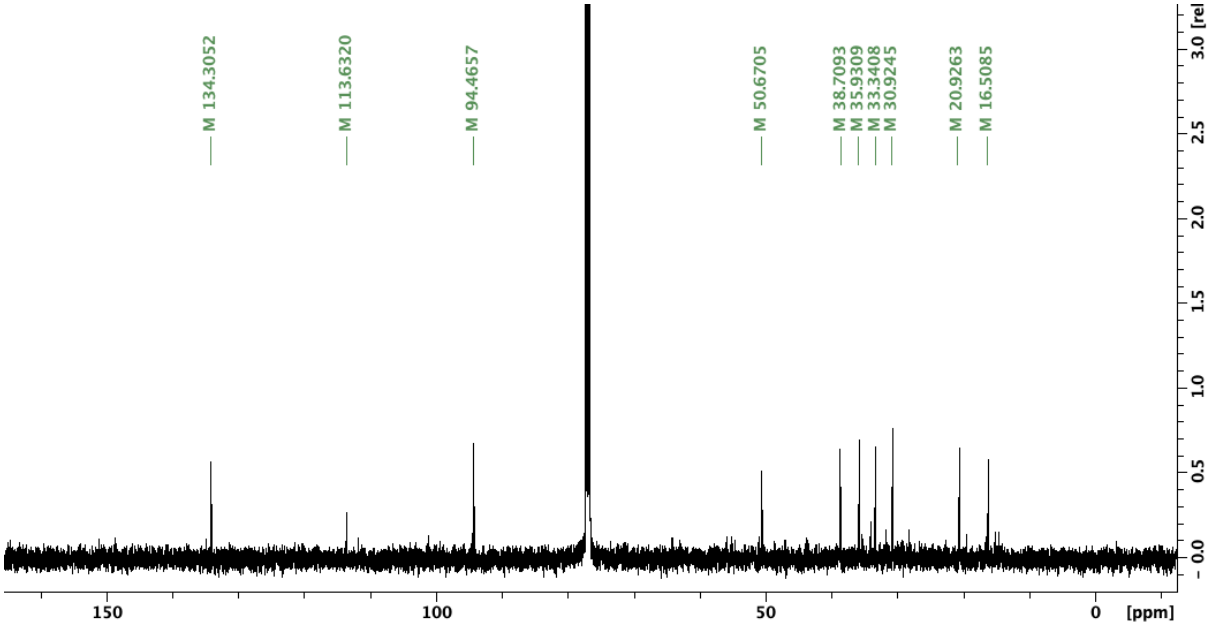


Figure S8: ^{13}C NMR Spectra of (1R,4aS,7S,7aR)-4,7-Dimethyl-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-1-ol **2**

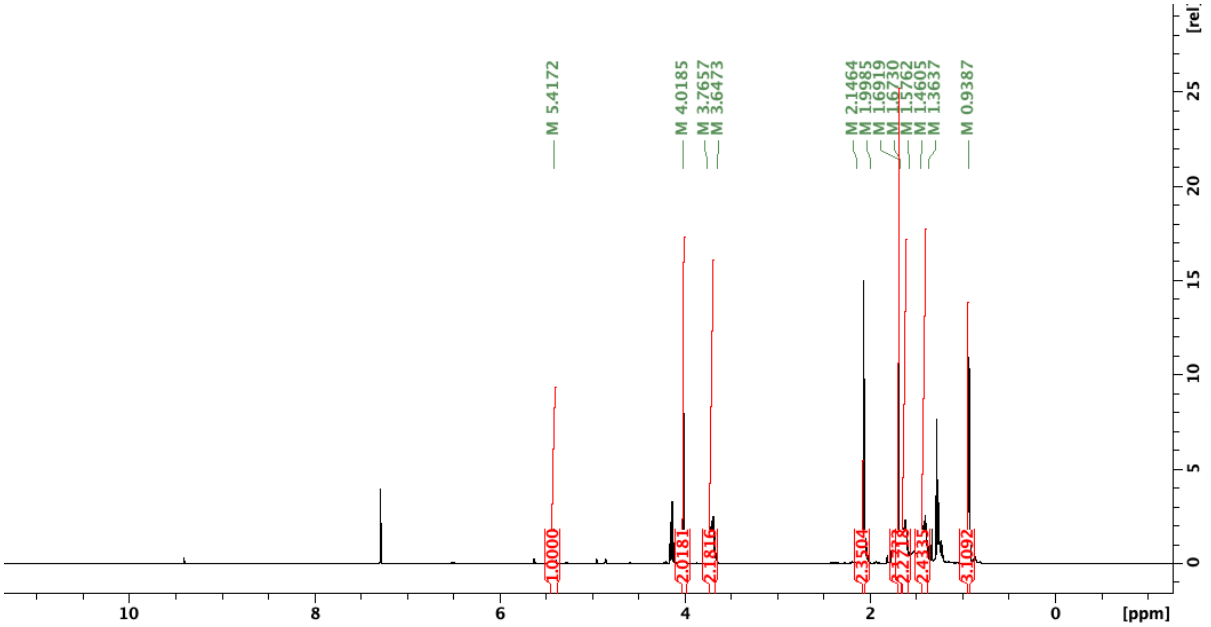


Figure S9: ^{1}H NMR Spectra of (E)-2,(6,R)-Dimethylocta-2-ene-1,8-diol **7**

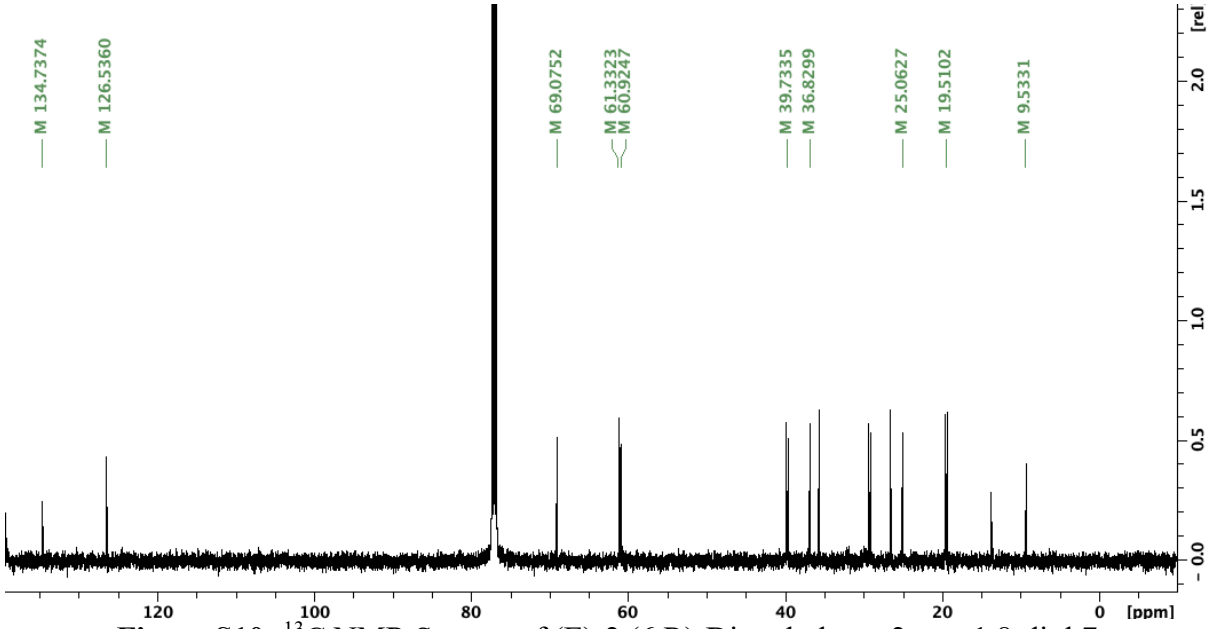


Figure S10: ^{13}C NMR Spectra of (E)-2,(6,R)-Dimethylocta-2-ene-1,8-diol **7**

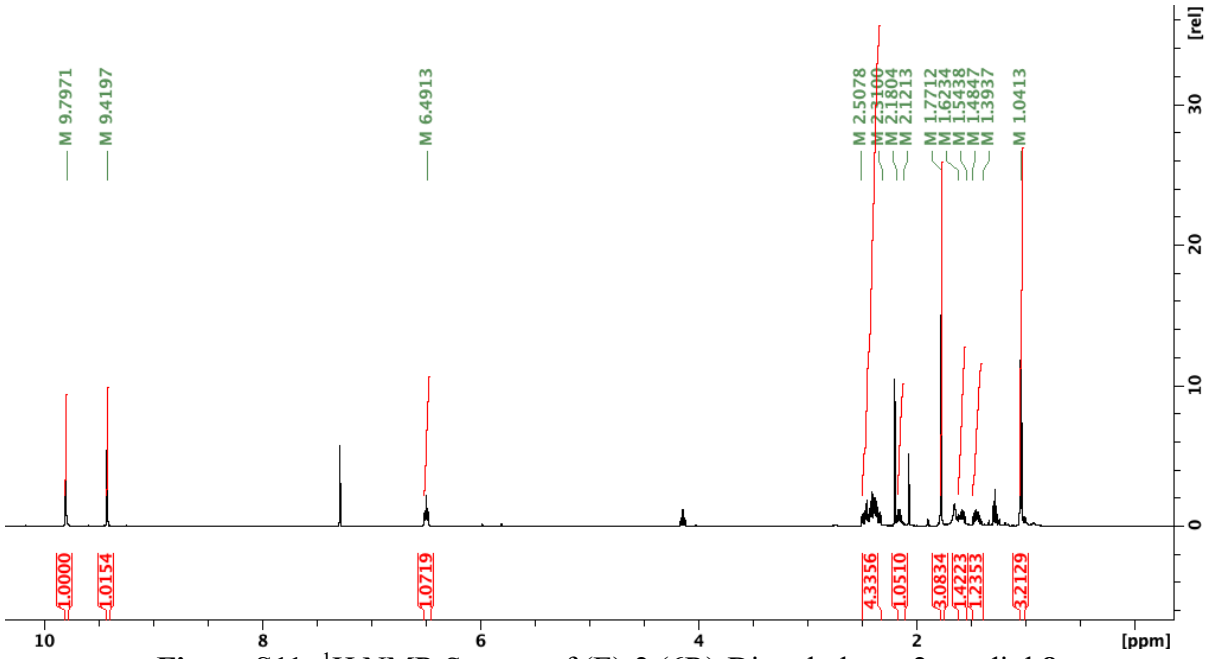


Figure S11: ^{1}H NMR Spectra of (E)-2,(6R)-Dimethylocta-2-enediol **8**

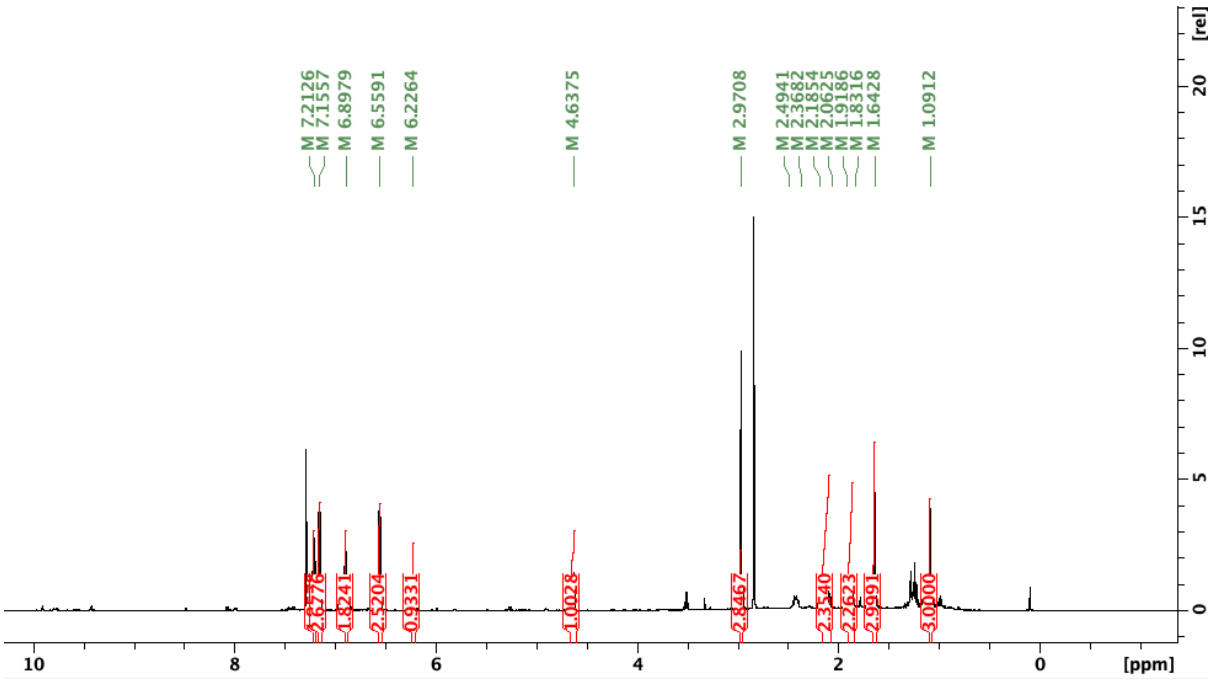


Figure S12: ^{1}H NMR Spectra of (1S,4aR,7R,7aS)-N,4,7-Trimethyl-N-(4-chlorophenyl-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-1-amine **9**

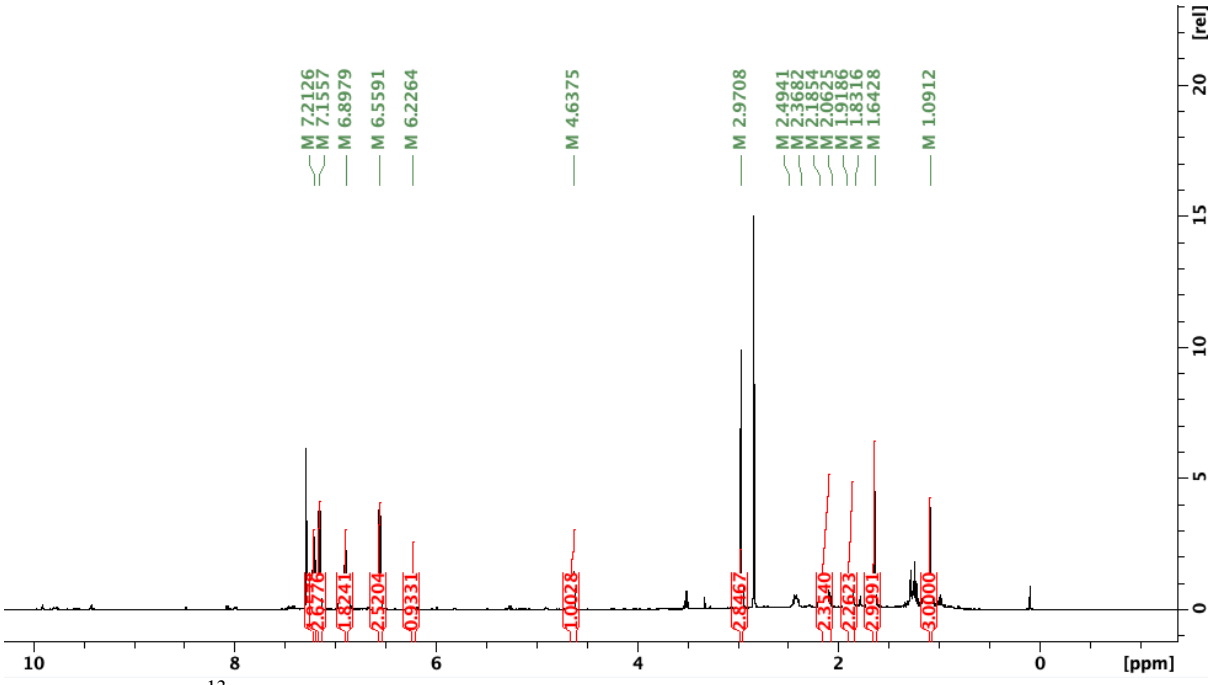


Figure S13: ^{13}C NMR Spectra of (1S,4aR,7R,7aS)-N,4,7-Trimethyl-N-(4-chlorophenyl-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-1-amine **9**

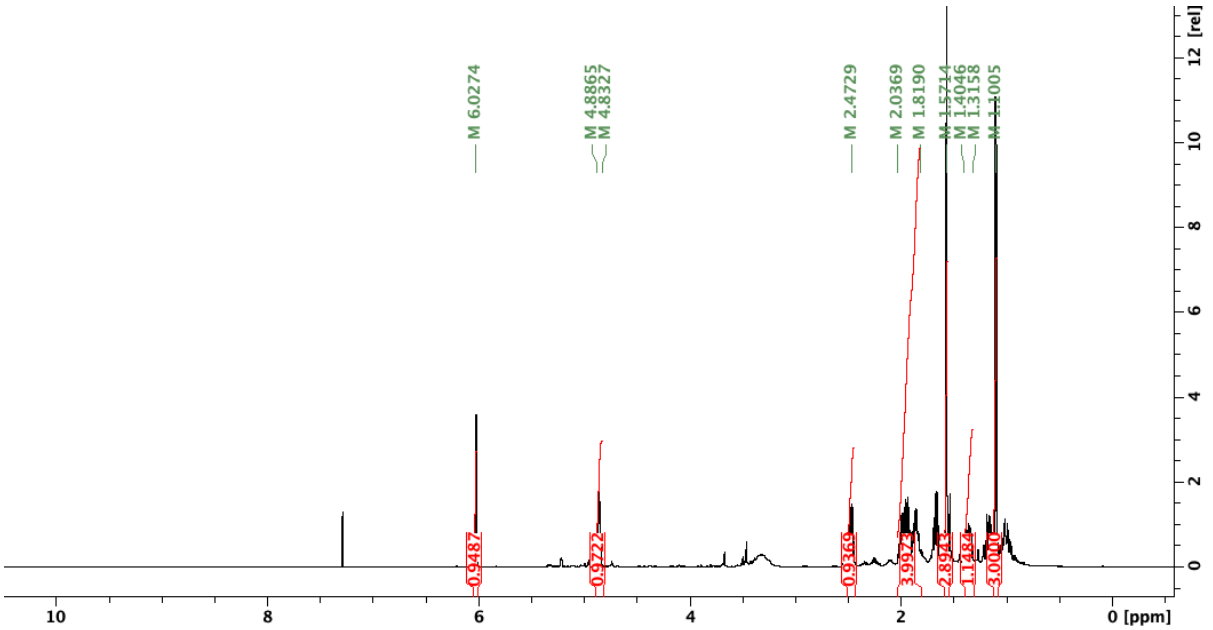


Figure S14: ^{1}H NMR Spectra of (1S,4aR,7R,7aS)-4,7-Dimethyl-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-1-ol **4**

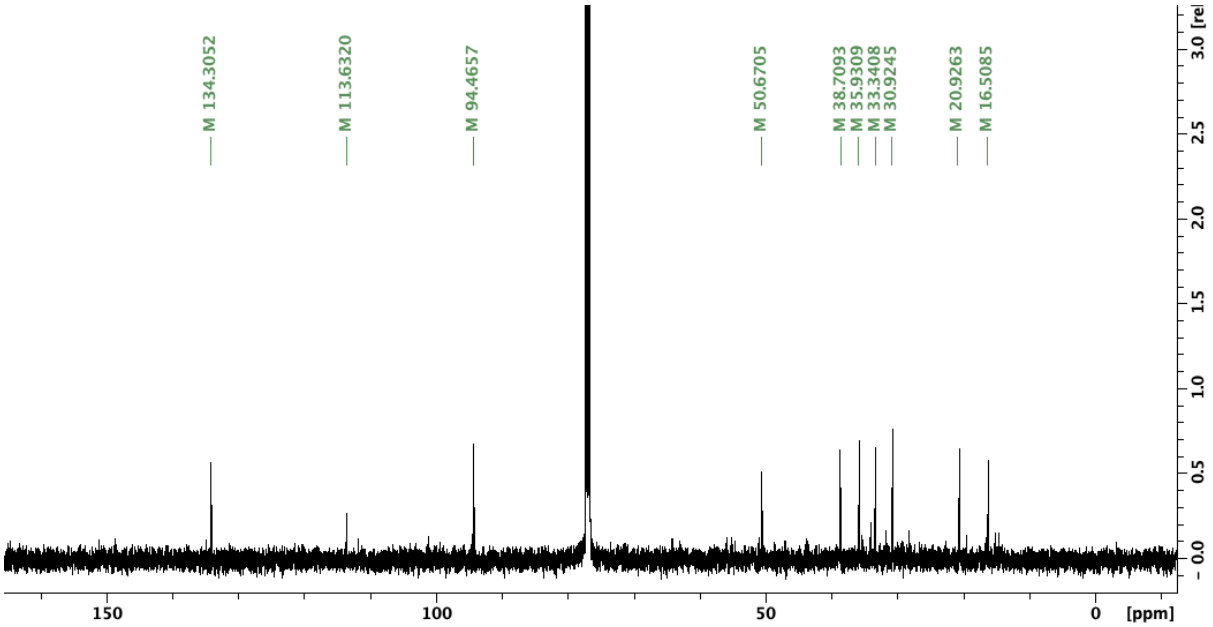


Figure S15: ^{13}C NMR Spectra of (1S,4aR,7R,7aS)-4,7-Dimethyl-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-1-ol **4**

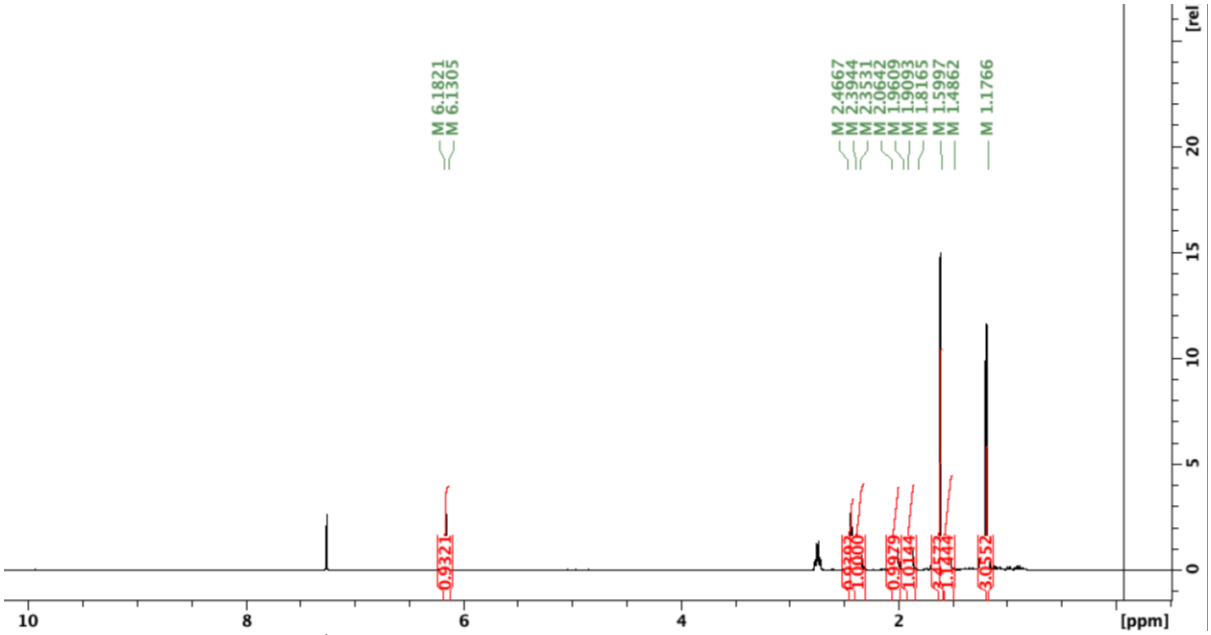


Figure S16: ^{1}H NMR Spectra of (4aS,7S,7aR)-4,7-Dimethyl-5,6,7,7a-tetrahydrocyclopenta[c]pyran-1(4aH)-one **3**

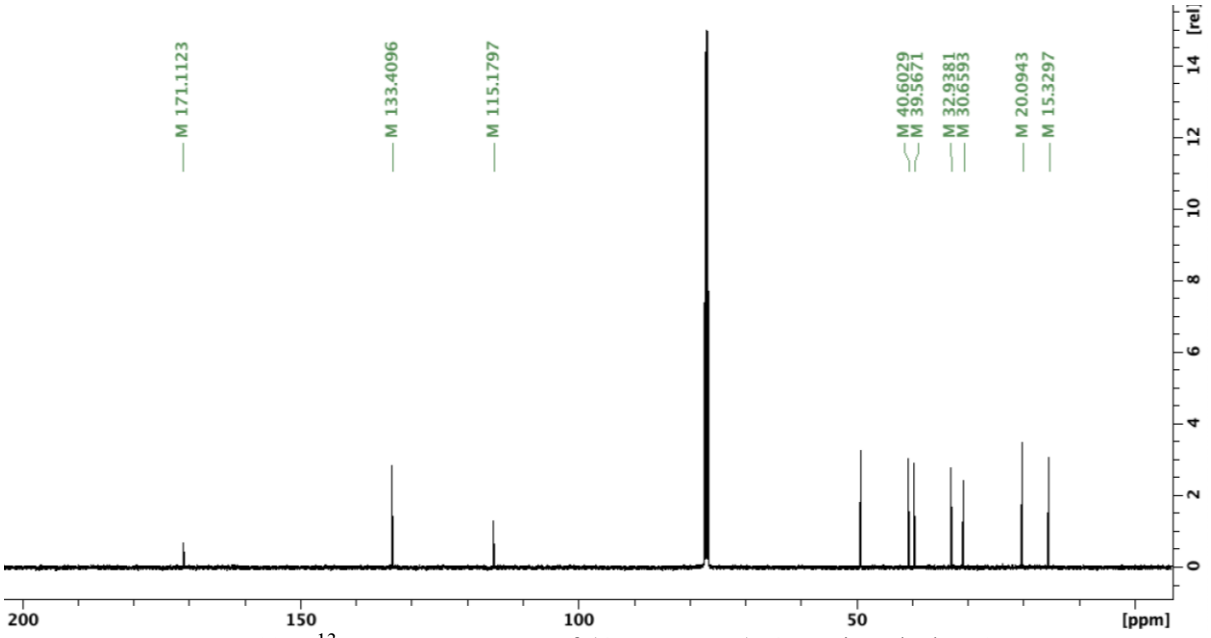


Figure S17: ^{13}C NMR Spectra of (4aS,7S,7aR)-4,7-Dimethyl-5,6,7,7a-tetrahydrocyclopenta[c]pyran-1(4aH)-one **3**