Reductive cyclization cascades of lactones using SmI_2-H_2O

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General experimental

All experiments were performed under an atmosphere of nitrogen, using anhydrous solvents, unless stated otherwise. THF was obtained from a solvent purification system, and when used in conjunction with SmI_2, deoxygenated by using freeze-pump-thaw. Dichloromethane was distilled from CaH_2. Water was distilled before being deoxygenated by bubbling with N_2.

^1H NMR and ^{13}C NMR were recorded using 300, 400 and 500 MHz spectrometers, with chemical shift values being reported in ppm relative to residual chloroform (δ_H = 7.27 or δ_C = 77.2) as internal standards. All coupling constants (*J*) are reported in Hertz (Hz).

Mass spectra were obtained using positive and negative electrospray (ES±) or gas chromatography (GC) methodology. Infra-red spectra were recorded as evaporated films or neat using a FT/IR spectrometer.

Column chromatography was carried out using 35 – 70 μ, 60A silica gel. Routine TLC analysis was carried out on aluminium sheets coated with silica gel 60 F254, 0.2 mm thickness. Plates were viewed using a 254 nm ultraviolet lamp and dipped in aqueous potassium permanganate, *p*-anisaldehyde or phosphomolybdic acid.

Preparation of samarium diiodide (SmI_2)

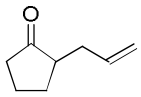
Samarium diiodide was prepared by a modification of the procedure of Imamoto and Ono.[1]

Samarium powder (2.00 g, 13.3 mmol, 1.2 eq) was added to an oven dried round-bottomed flask, the flask sealed, covered in aluminum foil and flushed with N_2 for 30 min. THF (110 ml) was added and the resulting suspension bubbled with N_2 for 15 min. Finally, iodine (2.80 g, 11.0 mmol, 1 eq) was added and the flask flushed again with N_2 for 10 min. The flask was heated at 60 ºC for 18 hours. The 0.1 M solution was allowed to cool to room temperature and then used directly.

[1] T. Imamoto, M. Ono, *Chem. Lett.* **1987**, 501.

Preparation of lactone substrates

2-Allylcyclopentanone S1[2]

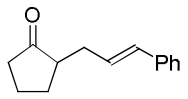


S1

To a stirred solution of $[(\eta^3\text{-allyl})PdCl]_2$ (157 mg, 0.43 mmol, 0.025 eq) and Xantphos (498 mg, 0.86 mmol, 0.05 eq) in DMSO (23 mL) was added allyl alcohol (1.00 g, 17 mmol, 1 eq), cyclopentanone (4.35 g, 52 mmol, 3 eq) and (*DL*)-proline (594 mg, 5.16 mmol, 0.30 eq). The resultant solution was heated to 70 ˚C for 18 hours, after which the reaction mixture was filtered through a pad of silica eluting with 20% EtOAc in petroleum ether (40 – 60 °C). The solvent was removed *in vacuo* to yield the crude product. Purification by column chromatography on silica gel eluting with 10% EtOAc in petroleum ether (40 – 60 °C) gave the title compound (1.53 g, 12.3 mmol, 73%) as a colourless oil; ν_{max} (neat)/cm^{-1} 3003, 2964, 2913, 1712 (C=O), 1432, 1364, 1222, 1094; δ_H (500 MHz, $CDCl_3$) 1.54-1.63 (1H, m, CH_aH$_b$CH), 1.77-1.85 (1H, m, CH_aH$_b$CH$_2$C(O)), 1.99-2.04 (1H, m, CH$_a$$H_bCH_2$C(O)), 2.05-2.08 (1H, m, CH_aH$_b$CH=CH$_2$), 2.09-2.16 (2H, m, CH + 1H from CH_aH$_b$C(O)), 2.17-2.24 (1H, m, CH$_a$$H_b$CH), 2.31-2.36 (1H, m, CH$_a$$H_b$C(O)), 2.50-2.55 (1H, m, CH$_a$$H_b$CH=CH$_2$), 5.04 (1H, dd, *J* 10.1, 1.6, CH=CH_aH$_b$), 5.08 (1H, dd, *J* 17.0, 1.6, CH=CH$_a$$H_b$), 5.74-5.82 (1H, m, C$H$=CH$_2$); δ_C (75 MHz, $CDCl_3$) 20.7 (*C*H$_2$), 29.0 (*C*H$_2$), 33.9 (*C*H$_2$CH=CH$_2$), 38.2 (*C*H$_2$C(O)), 48.6 (*C*H), 116.4 (CH=*C*H$_2$), 135.9 (*C*H=CH$_2$), 220.6 (*C*(O)); *m/z* (GC-MS) 124 (M, 40), 67 (100), 39 (57), 96 (49), 55 (37), 81 (26); (Found: (M), 124.0882. $C_8H_{12}O$ requires M, 124.0883).

[2] G. H. Posner, C. M. Lentz, *J. Am. Chem. Soc.* **1979**, *101*, 934.

2-Cinnamylcyclopentanone S2[3]

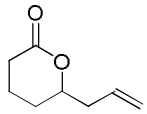


S2

To a stirred solution of $[(\eta^3\text{-allyl})PdCl]_2$ (0.137 g, 0.38 mmol, 0.025 eq) and Xantphos (0.434 g, 0.75 mmol, 0.05 eq) in DMSO (20 mL) was added (*E*)-3-phenylprop-2-en-1-ol (2.01 g, 15 mmol, 1 eq), cyclopentanone (3.79 g, 45 mmol, 3 eq) and (*DL*)-proline (0.518 g, 4.50 mmol, 0.30 eq). The resultant solution was heated to 70 ˚C for 18 hours, after which the reaction mixture was filtered through a pad of silica eluting with 20% EtOAc in petroleum ether (40 – 60 °C). The solvent was removed *in vacuo* to yield the crude product. Purification by column chromatography on silica gel eluting with 10% EtOAc in petroleum ether (40 – 60 °C) gave the title compound (2.00 g, 10 mmol, 66%) as a colourless oil; ν_{max} (neat)/cm^{-1} 2956, 1734 (C=O), 1491, 1448, 1152, 966, 692; δ_H (400 MHz, $CDCl_3$) 1.59-1.70 (1H, m, 1H from CH_2), 1.77-1.88 (1H, m, $CH_aH_bCH_2C(O)$), 1.99-2.06 (1H, m, $CH_aH_bCH_2C(O)$), 2.07-2.19 (1H, m, CH_aH$_b$C(O)), 2.21-2.28 (3H, m, CH_aH$_b$CH=CHPh + CH + 1H from CH_2), 2.36 (1H, ddt, *J* 18.4, 8.3, 1.3, $CH_aH_bC(O)$), 2.66-2.71 (1H, m, CH_aH_bCH=CHPh), 6.19 (1H, dt, *J* 15.6, 7.1, C*H*=CHPh), 6.45 (1H, d, *J* 15.6, CH=C*H*Ph), 7.21-7.38 (5H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 20.7 ($CH_2CH_2C(O)$), 29.0 (CH_2), 33.1 (CH_2CH=CHPh), 38.2 ($CH_2C(O)$), 49.1 (*C*H), 126.1 (Ar-*C*H), 127.2 (Ar-*C*H), 127.7 (*C*H=CHPh), 128.5 (Ar-*C*H), 131.8 (CH=*C*HPh), 137.4 (Ar-*C*), 220.6 (*C*(O)); *m/z* (ES+ mode) 218 ((M + NH_4), 100), 223 ((M + Na), 36); (Found: (M + Na), 223.1094. $C_{14}H_{16}ONa$ requires M, 223.1099).

[3] I. Usui, S. Schmidt, B. Breit, *Org. Lett.* **2009**, *11*, 1453.

6-Allyltetrahydro-2H-pyran-2-one S3[4]

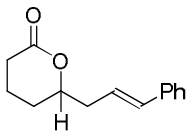


S3

To a stirred solution of 2-allylcyclopentanone (883 mg, 7.12 mmol, 1 eq) in CH_2Cl_2 (16 mL) was added anhydrous $NaHCO_3$ (1.20 g, 14.2 mmol, 2 eq) followed by dropwise addition of 77 % *m*-CPBA (1.76 g, 7.83 mmol, 1.1 eq). The reaction was stirred at room temperature for 18 hours. The reaction was quenched with saturated $NaHCO_3$ solution (10 mL), before being extracted with Et_2O (3 × 20 mL). The organic layers were combined and washed with H_2O (10 mL), then saturated $NaHCO_3$ (10 mL) before being dried (Na_2SO_4) and concentrated *in vacuo* to yield the crude product. Purification by column chromatography on silica gel eluting with 30% EtOAc in petroleum ether (40 – 60 °C) gave the title compound (647 mg, 4.62 mmol, 65%) as a colourless oil; ν_{max} (neat)/cm^{-1} 2936, 1734 (C=O), 1243, 1046, 920; δ_H (400 MHz, $CDCl_3$) 1.50-1.59 (2H, m, CH_2), 1.79-1.87 (1H, m, CH_aCH_bCH_2C(O)), 1.88-1.96 (1H, m, CH_aCH_bCH_2C(O)), 2.34-2.43 (1H, m, C$H_a$$H_b$CH=C$H_2$), 2.44-2.52 (2H, m, C$H_a$$H_b$C(O) + 1H from C$H_a$$H_b$CH=C$H_2$), 2.55-2.63 (1H, m, C$H_a$$H_b$C(O)), 4.31-4.38 (1H, m, CH), 5.12-5.18 (2H, m, CH=CH_2), 5.82 (1H, ddt, *J* 17.3, 10.2, 7.1, CH=CH_2); δ_C (100 MHz, $CDCl_3$) 18.4 (*C*H_2), 27.2 (*C*H_2), 29.5 (*C*H_2C(O)), 40.0 (*C*H_2CH=CH_2), 79.8 (*C*H), 118.6 (CH=*C*H_2), 132.6 (*C*H=CH_2), 171.7 (*C*(O)); *m/z* (GC mode) 158 (M + NH_4), 99 (100), 71 (63), 55 (29); (Found: (M + NH_4), 158.1175. $C_8H_{16}O_2N$ requires M, 158.1176).

[4] R. Zibuck, N. J. Liverton, A. B. Smith, *J. Am. Chem. Soc.* **1986**, *108*, 2451.

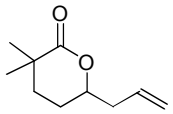
6-Cinnamyltetrahydro-2H-pyran-2-one 6a



6a

To a stirred solution of 2-cinnamylcyclopentanone (1.04 g, 5.18 mmol, 1 eq) in CH_2Cl_2 (11 mL) was added anhydrous $NaHCO_3$ (0.65 g, 7.76 mmol, 1.5 eq) followed by dropwise addition of 77 % *m*-CPBA (1.28 g, 5.70 mmol, 2.2 M solution in CH_2Cl_2, 1.1 eq). The reaction was stirred at room temperature for 18 hours. The reaction was quenched with saturated $NaHCO_3$ solution (10 mL), before being extracted with Et_2O (3 × 20 mL). The organic layers were combined and washed with H_2O (10 mL), then saturated $NaHCO_3$ (10 mL) before being dried (Na_2SO_4) and concentrated *in vacuo* to yield the crude product. Purification by column chromatography on silica gel eluting with 30% EtOAc in petroleum ether (40 – 60 °C) gave the title compound (0.32 g, 1.47 mmol, 29%) as a white solid; M.p. 87 ˚C recrystallised from pentane/Et_2O; ν_{max} (neat)/cm^{-1} 2924, 1733 (C=O), 1488, 1438, 1373, 1239, 1172, 1047, 962, 923; δ_H (500 MHz, $CDCl_3$) 1.59-1.67 (1H, m, CHCH_aH$_b$), 1.83-1.91 (2H, m, CH_2), 1.94-2.02 (1H, m, CHCH$_a$$H_b$), 2.46-2.52 (1H, m, C$H_aH_b$C(O)), 2.55-2.62 (2H, m, CH_aH$_b$CH=CHPh + 1H from CH$_a$$H_b$C(O)), 2.64-2.70 (1H, m, CH$_a$$H_b$CH=CHPh), 4.41-4.47 (1H, m, C*H*), 6.26 (1H, dt, *J* 16.1, 7.3, C*H*=CHPh), 6.51 (1H, d, *J* 16.1, CH=C*H*Ph), 7.24-7.39 (5H, m, Ar-*H*); δ_C (125 MHz, $CDCl_3$) 18.5 (*C*H$_2$), 27.3 (*C*H$_2$), 29.5 (*C*H$_2$C(O)), 39.3 (*C*H$_2$CH=CHPh), 80.1 (*C*H), 124.1 (*C*H=CHPh), 126.2 (Ar-*C*H), 127.5 (Ar-*C*H), 128.6 (Ar-*C*H), 133.6 (CH=*C*HPh), 137.0 (Ar-*C*), 171.7 (*C*(O)); *m/z* (ES+ mode) 239 ((M + Na), 100) 455 (31); (Found: (M + Na), 239.1051. $C_{14}H_{16}O_2Na$ requires M, 239.1043).

6-Allyl-3,3-dimethyltetrahydro-2H-pyran-2-one S4

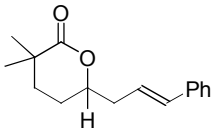


S4

A solution of LDA was prepared by adding *n*-butyllithium (5.9 mL, 9.44 mmol, 1.2 eq, 1.6 M solution in hexane) to diisopropylamine (955 mg, 9.44 mmol, 1.2 eq) in THF (25 mL) at -78 °C under N_2 and the solution stirred for 1 hour. To this solution was added 6-6-allyltetrahydro-2H-pyran-2-one (1.10 g, 7.87 mmol, 1 eq) dissolved in THF (10 mL) over 1 hour using a syringe pump and the resulting solution stirred for a further 1 hour. At this point, MeI (1.39 g, 9.44 mmol, 1.2 eq) was added and the reaction allowed to warm to room temperature over 18 hours. The reaction was quenched by the addition of aqueous saturated NH_4Cl (40 mL) and the aqueous layer was separated and extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (40 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was subsequently dissolved in THF (10 mL) and added over 1 hour using a syringe pump to a solution of LDA (8.23 mmol, 1.2 eq). MeI (1.17 g, 8.23 mmol, 1.2 eq) was subsequently added and the reaction allowed to warm to room temperature over 18 hours. The reaction was quenched by the addition of aqueous saturated NH_4Cl (40 mL) and worked up following the above procedure. Purification by column chromatography on silica gel eluting with 30% EtOAc in petroleum ether (40 – 60 °C) gave the title compound (1.02 g, 6.10 mmol, 76%) as a colourless oil; ν_{max} (neat)/cm^{-1} 2936, 1728 (C=O), 1472, 1385, 1287, 1138, 996, 920; δ_H (400 MHz, $CDCl_3$) 1.21 (3H, s, CH_3), 1.23 (3H, s, CH_3), 1.55-1.76 (4H, m, 2 × CH_2), 2.28-2.35 (1H, m, CH_aCH$_b$CH=CH$_2$), 2.37-2.44 (1H, m, CH$_a$CH_bCH=CH$_2$), 4.25-4.31 (1H, m,

C*H*), 5.05-5.10 (2H, m, CH=CH_2), 5.75 (1H, ddt, *J* 17.1, 10.3, 7.0, C*H*=CH_2); δ_C (100 MHz, $CDCl_3$) 25.3 (*C*H_2), 27.7 (*C*H_3), 27.8 (*C*H_3), 34.4 (*C*H_2), 38.0 (*C*), 40.3 (*C*H_2CH=CH_2), 80.7 (*C*H), 118.6 (CH=*C*H_2), 132.6 (*C*H=CH_2), 177.4 (*C*(O)); *m/z* (ES+ mode) 191 ((M + Na), 100), 223 (25); (found: (M + Na), 191.1049. $C_{10}H_{16}O_2Na$ requires M, 191.1043).

6-Cinnamyl-3,3-dimethyltetrahydro-2H-pyran-2-one 6b



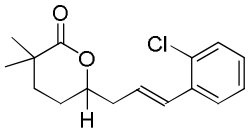
6b

A solution of LDA was prepared by adding *n*-butyllithium (0.21 mL, 0.49 mmol, 1.2 eq, 2.30 M solution in hexane) to diisopropylamine (51 mg, 0.49 mmol, 1.2 eq) in THF (1 mL) at -78 °C under N_2 and stirred for 1 hour. To this solution was added 6-cinnamyltetrahydro-2H-pyran-2-one (90 mg, 0.42 mmol, 1 eq) dissolved in THF (1 mL) over 1 hour using a syringe pump and the resulting solution stirred for a further 1 hour. At this point, MeI (106 mg, 0.75 mmol, 1.5 eq) was added and the reaction allowed to warm to room temperature over 18 hours. The reaction was quenched by the addition of aqueous saturated NH_4Cl (10 mL) and the aqueous layer was separated and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4) and concentrated *in vacuo* to yield the crude product. The crude product was subsequently dissolved in THF (1 mL) and added over 1 hour using a syringe pump to a solution of LDA (0.23 mmol, 1.2 eq). MeI (51 mg, 0.36 mmol, 1.5 eq) was subsequently added and the reaction allowed to warm to room temperature over 18 hours. The reaction was quenched by the addition of aqueous saturated NH_4Cl (10 mL) and worked up following the same procedure to

yield the crude product. Purification by column chromatography on silica gel eluting with 30% EtOAc in petroleum ether (40 – 60 °C) gave the title compound (25 mg, 0.10 mmol, 24%) as a colourless oil; ν_{max} (neat)/cm^{-1} 2928, 2843, 1724 (C=O), 1432, 1375, 1276, 1029, 987; δ_H (400 MHz, $CDCl_3$) 1.21 (3H, s, CH_3), 1.23 (3H, s, CH_3), 1.59-1.83 (4H, m, 2 × CH_2), 2.44-2.51 (1H, m, CH_aH$_b$CH=CHAr), 2.53-2.60 (1H, m, CH$_a$$H_b$CH=CHAr), 4.32-4.39 (1H, m, CH), 6.16 (1H, dt, *J* 15.9, 7.3, CH=CHAr), 6.42 (1H, d, *J* 15.9, CH=CHAr), 7.13-7.30 (5H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 25.5 (*C*H$_2$), 27.7 (*C*H$_3$), 27.8 (*C*H$_3$), 34.4 (*C*H$_2$), 38.1 (*C*), 39.6 (*C*H$_2$CH=CHAr), 81.0 (*C*H), 124.1 (*C*H=CHAr), 126.2 (Ar-*C*H), 127.4 (Ar-*C*H), 128.6 (Ar-*C*H), 133.6 (CH=*C*HAr), 137.1 (Ar-*C*), 177.5 (*C*(O)); *m/z* (ES+ mode) 267 ((M + Na), 100), 262 (13), 245 (11); (Found: (M + Na), 267.1367. $C_{16}H_{20}O_2Na_1$ requires M, 267.1356).

General procedure A: Olefin Cross Metathesis

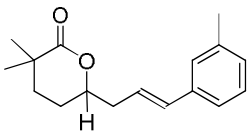
(*E*)-6-(3-(2-Chlorophenyl)allyl)-3,3-dimethyltetrahydro-2H-pyran-2-one 6c



6c

An oven-dried 1 piece flask and condenser was thoroughly flushed with N_2 before the addition of Grubbs 2nd generation catalyst (17 mg, 0.02 mmol, 1 mol%). To this was added 6-allyl-3,3-dimethyltetrahydro-2H-pyran-2-one (330 mg, 1.96 mmol, 1 eq) dissolved in CH_2Cl_2 (7 mL), followed by 1-chloro-2-vinylbenzene (545 mg, 3.93 mmol, 3 eq). The reaction mixture was refluxed at 40 °C for 24 hours, whilst periodically maintaining the solvent level. Once complete, the solvent was removed *in vacuo* to yield the crude product. Purification by flash chromatography on silica gel eluting with 10% EtOAc in petroleum ether (40 – 60 °C) gave the title compound (240 mg, 0.86 mmol, 44%) as an off-white solid. The product was dissolved in Et_2O with stirred with activated charcoal for 24 hours. The product was obtained was a white solid following filtration through celite; M.p. 81 ˚C recrystallised from pentane; ν_{max} (neat)/cm^{-1} 2977, 1731 (C=O), 1640, 1453, 1381, 1242, 1053, 999, 927; δ_H (400 MHz, $CDCl_3$) 1.22 (3H, s, CH_3), 1.24 (3H, s, CH_3), 1.64-1.85 (4H, m, 2 × CH_2), 2.40-2.57 (2H, m, CH_2CH=CHAr), 4.32-4.38 (1H, m, C*H*), 6.16 (1H, dt, *J* 15.9, 7.2, C*H*=CHAr), 6.39 (1H, d, *J* 15.9, CH=C*H*Ar), 7.05-7.27 (4H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 25.5 (*C*H_2), 27.7 (*C*H_3), 27.8 (*C*H_3), 34.4 (*C*H_2), 38.1 (*C*), 39.6 *C*H_2CH=CHAr), 81.1 (*C*H), 125.7 (*C*H=CHAr), 126.5 (Ar-*C*H), 127.2 (Ar-*C*H), 131.4 (Ar-CH), 132.1 (CH=*C*HAr), 132.9 (Ar-*C*H), 133.4 (Ar-*C*Cl) 136.9 (Ar-*C*), 177.5 (*C*(O)); *m/z* (ES+ mode) 301 ((M + Na), 100), 191 (10); (found: (M + Na), 301.0970. $C_{16}H_{19}ClO_2Na$ requires M, 301.0966).

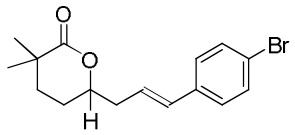
(*E*)-3,3-Dimethyl-6-(3-(*m*-tolyl)allyl)tetrahydro-2H-pyran-2-one 6d



6d

As for general procedure A, reaction of Grubbs 2nd generation catalyst (18 mg, 0.02 mmol, 1 mol%), 6-allyl-3,3-dimethyltetrahydro-2H-pyran-2-one (358 mg, 2.13 mmol, 1 eq), and 1-methyl-3-vinylbenzene (750 mg, 6.39 mmol, 3 eq), after workup and purification by flash chromatography on silica gel eluting with 10 % EtOAc in petroleum ether (40 – 60 °C), gave the title compound (205 mg, 0.79 mmol, 37%) as a yellow oil; ν_{max} (neat)/cm^{-1} 2961, 1721 (C=O), 1602, 1471, 1385, 1286, 1154, 1017, 968, 775, 694; δ_H (400 MHz, $CDCl_3$) 1.29 (3H, s, C*H*$_3$), 1.31 (3H, s, C*H*$_3$), 1.73-1.89 (4H, m, 2 × C*H*$_2$), 2.34 (3H, s, ArC*H*$_3$), 2.49-2.68 (2H, m, C*H*$_2$CH=CHAr), 4.35-4.44 (1H, m, C*H*), 6.24 (1H, dt, *J* 15.8, 7.2, C*H*=CHAr), 6.46 (1H, d, *J* 15.8, CH=C*H*Ar), 7.04-7.23 (4H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 21.4 (Ar-*C*H$_3$), 25.5 (*C*H$_2$), 27.8 (*C*H$_3$), 27.8 (*C*H$_3$), 34.4 (*C*H$_2$), 38.0 (*C*), 39.6 (*C*H$_2$CH=CHAr), 81.1 (*C*H), 123.4 (*C*H=CHAr), 126.9 (Ar-*C*H), 128.2 (Ar-*C*H), 128.5 (Ar-*C*H), 133.6 (CH=*C*HAr), 137.0 (Ar-*C*), 138.1 (2 × Ar-*C*), 177.4 (*C*(O)); *m/z* (ES+ mode) 281 ((M + Na), 100); (found: (M + Na), 281.1517. $C_{17}H_{22}O_2Na$ requires M, 281.1512).

(*E*)-6-(3-(4-Bromophenyl)allyl)-3,3-dimethyltetrahydro-2H-pyran-2-one 6e

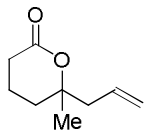


6e

As for general procedure A, reaction of Grubbs 2nd generation catalyst (17 mg, 0.02 mmol, 1 mol%), 6-allyl-3,3-dimethyltetrahydro-2H-pyran-2-one (330 mg, 1.96 mmol, 1 eq), and 1-bromo-4-vinylbenzene (720 mg, 3.93 mmol, 3 eq), after workup and

purification by flash chromatography on silica gel eluting with 10 % EtOAc in petroleum ether (40 – 60 °C) gave the title compound (184 mg, 0.57 mmol, 29%) as a yellow oil; ν_{max} (neat)/cm^{-1} 3461, 2076, 2977, 2956, 1732 (C=O), 1641, 1453, 1381, 1242, 1140, 1053, 999, 927; δ_H (400 MHz, $CDCl_3$) 1.20 (3H, s, C*H*$_3$), 1.23 (3H, s, C*H*$_3$), 1.61-1.81 (4H, m, 2 × C*H*$_2$), 2.40-2.59 (2H, m, C*H*$_2$CH=CHAr), 4.31-4.37 (1H, m, C*H*), 6.15 (1H, dt, *J* 15.8, 7.2, C*H*=CHAr), 6.36 (1H, d, *J* 15.8, CH=C*H*Ar), 7.12-7.36 (4H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 25.5 (*C*H$_2$), 27.7 (*C*H$_3$), 27.8 (*C*H$_3$), 34.4 (*C*H$_2$), 38.1 (*C*), 39.6 (*C*H$_2$CH=CHAr), 80.8 (*C*H), 121.4 (Ar-*C*Br), 125.1 (Ar-*C*H), 127.7 (*C*H=CHAr), 131.7 (CH=*C*HAr), 132.4 (Ar-*C*H), 136 (Ar-*C*), 177.3 (*C*(O)); *m/z* (ES+ mode) 345 ((M + Na), 60), 281 (25), 173 (100), 137 (55), 101 (70), 85 (25). Compound was unstable to accurate mass analysis.

6-Allyl-6-methyltetrahydro-2H-pyran-2-one 6f[5]



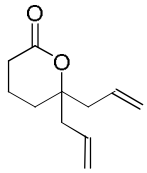
6f

To a flask, degassed with N_2, was added NiI_2 (48 mg, 0.15 mmol, 2 mol%) and the flask was cooled to 0 ˚C. SmI_2 (0.1 M in THF, 76 mL, 7.60 mmol, 4 eq) was added and the solution stirred for 5 minutes. Methyl 5-oxohexanoate (300 mg, 1.90 mmol, 1 eq) was then added, followed immediately by the dropwise addition of allyl bromide (1.1 M in THF, 19 mL, 2.09 mmol, 1.1 eq) over 30 minutes. The reaction was monitored by TLC and once complete the flask was opened to air till the reaction mixture decolourized. This was followed by the addition of a saturated solution of Rochelle salt (20 mL). The aqueous layer was separated and extracted with Et_2O (3 ×

[5] M. Wada, M. Honna, Y. Kuramoto, N. Miyoshi, *Bull. Chem. Soc. Jpn.* **1997**, *70*, 2265.

20 mL) and the combined organic layers were washed with brine (2 × 10 mL), dried (Na_2SO_4) and concentrated *in vacuo* to yield the crude product. Purification by flash chromatography on silica gel eluting with 30% EtOAc in petroleum ether (40 – 60 °C) gave the title compound (286 mg, 1.86 mmol, 98%) as a colourless oil; ν_{max} (neat)/cm^{-1} 3076, 2977, 2945, 1728 (C=O), 1640, 1453, 1380, 1359, 1328, 1298, 1242, 1173, 1140, 1096, 1053, 999, 927, 852; δ_H (400 MHz, $CDCl_3$) 1.39 (3H, s, C*H*$_3$), 1.65-1.71 (1H, m, 1H from C*H*$_2$), 1.79-1.84 (1H, m, 1H from C*H*$_2$), 1.87-1.93 (2H, m, C*H*$_2$CH$_2$C(O)), 22.44 (2H, d, *J* 7.3, C*H*$_2$CH=CH$_2$), 2.47-2.58 (2H, m, C*H*$_2$C(O)), 5.13-5.19 (2H, m, CH=C*H*$_2$), 5.82 (1H, ddd, *J* 14.6 10.1 7.3, C*H*=CH$_2$); δ_C (100 MHz, $CDCl_3$) 16.5 (*C*H$_2$), 26.3 (*C*H$_3$), 29.3 (*C*H$_2$C(O)), 31.4 (*C*H$_2$), 46.1 (*C*H$_2$CH=CH$_2$), 83.6 (*C*), 119.4 (CH=*C*H$_2$), 132.3 (*C*H=CH$_2$), 171.2 (*C*(O)); *m/z* (ES+ mode) 155 ((M + H), 100), 309 (41), 177 ((M + Na), 5); (Found: (M + Na), 177.0878. $C_9H_{14}O_2Na$ requires M, 177.0886).

6,6-Diallyltetrahydro-2H-pyran-2-one 6g[6]



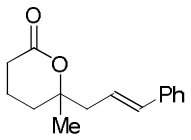
6g

Glutaric anhydride (1.00 g, 8.76 mmol, 1 eq) was dissolved in dry THF (13 mL) and cooled to 0 ˚C. Allyl magnesium chloride (8.80 mL, 8.80 mmol, 2 eq, 2 M solution in THF) was added over 10 mins and the reaction was stirred for a further 2 hours. The reaction was quenched with 1N HCl (20 mL) and heated to 40 ˚C for 30mins. The aqueous layer was separated and extracted with Et_2O (3 × 30 mL). The combined organic layers were washed with H_2O (10 mL), brine (10 mL), dried (Na_2SO_4) and

[6] J. Barluenga, J. R. Fernandez, J. Florez, M. Yus, *Synthesis* **1983**, 736.

concentrated *in vacuo* to yield the crude product. Purification by column chromatography on silica gel eluting with 5% Et_2O in $CHCl_3$ gave the title compound (0.14 g, 0.76 mmol, 9%) as a colourless oil; ν_{max} (neat)/cm^{-1} 2952, 1725 (C=O), 1640, 1445, 1333, 1235, 1188, 1031, 996, 923; δ_H (400 MHz, $CDCl_3$) 1.75 (2H, dt, *J* 6.6 3.8, CH_2), 1.84-1.91 (2H, m, CH_2), 2.43 (4H, tt, *J* 7.1 1.3, 2 × CH_2CH=CH_2) , 2.48 (2H, t, *J* 6.8, CH_2C(O)), 5.12-5.20 (4H, m, 2 × CH=CH_2), 5.81 (2H, dddd, *J* 17.7 10.3 7.3 7.3, 2 × C*H*=CH_2); δ_C (100 MHz, $CDCl_3$) 16.4 (*C*H_2), 29.0 (*C*H_2), 29.5 (*C*H_2C(O)), 43.5 (2 × *C*H_2CH=CH_2), 84.9 (*C*), 119.6 (2 × CH=*C*H_2), 132.1 (2 × *C*H=CH_2), 171.1 (*C*(O)); *m/z* (ES+ mode) 203 ((M + Na), 100); (Found: (M + Na), 203.1041. $C_{11}H_{16}O_2Na$ requires M, 203.1043).

(*E*)-6-Cinnamyl-6-methyltetrahydro-2H-pyran-2-one 6h

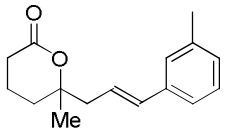


6h

As for general procedure A, reaction of Grubbs 2nd generation catalyst (37 mg, 0.044 mmol, 1 mol%), 6-allyl-6-methyltetrahydro-2H-pyran-2-one (670 mg, 4.35 mmol, 1 eq), and styrene (1.36 g, 13.05 mmol, 3 eq), after workup and purification by flash chromatography on silica gel eluting with 2% Et_2O in $CHCl_3$ gave the title compound (602 mg, 2.62 mmol, 60%) as a yellow oil; ν_{max} (neat)/cm^{-1} 3476, 2958, 1724 (C=O), 1496, 1450, 1379, 1325, 1233, 1090, 1052, 979, 923; δ_H (400 MHz, $CDCl_3$) 1.34 (3H, s, CH_3), 1.57-1.68 (2H, m, CH_2), 1.75-1.86 (2H, m, CH_2CH_2C(O)), 2.35-2.46 (2H, m, CH_2C(O)), 2.50 (2H, d, *J* 7.3, CH_2CH=CHPh), 6.13 (1H, dt, *J* 15.8 7.3, C*H*=CHPh), 6.39 (1H, d, *J* 15.8, CH=C*H*Ph), 7.09-7.30 (5H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 16.6 (*C*H_2), 26.5 (*C*H_3), 29.4 (*C*H_2C(O)), 31.7 (*C*H_2), 45.4 (*C*H_2CH=CHAr), 84.1 (*C*),

123.8 (C*H*=CHAr), 126.2 (Ar-*C*Br), 127.5 (Ar-*C*H), 128.6 (Ar-*C*H), 134.3 (CH=C*H*Ar), 137.0 (Ar-*C*), 171.3 (*C*(O)); *m/z* (ES+ mode) 253 ((M + Na), 100), 483 (44); (Found: (M + Na), 253.1211. $C_{15}H_{18}O_2Na$ requires M, 253.1199).

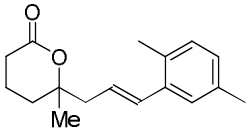
(*E*)-6-Methyl-6-(3-(m-tolyl)allyl)tetrahydro-2H-pyran-2-one 6i



6i

As for general procedure A, reaction of Grubbs 2nd generation catalyst (15 mg, 0.0175 mmol, 1 mol%), 6-allyl-6-methyltetrahydro-2H-pyran-2-one (270 mg, 1.75 mmol, 1 eq), and 3-methyl-1-vinylbenzene (414 mg, 3.51 mmol, 4 eq), after workup and purification by flash chromatography on silica gel eluting with 15% EtOAc in petroleum ether (40 – 60 °C), gave the title compound (207 mg, 0.84 mmol, 48%) as a colourless oil; ν_{max} (neat)/cm^{-1} 2950, 1723 (C=O), 1602, 1453, 1290, 1245, 1053; δ_H (400 MHz, $CDCl_3$) 1.33 (3H, s, CH_3), 1.59-1.65 (1H, m, CH_2), 1.73-1.85 (3H, m, 1H from CH_2 + 2H from CH_2), 2.26 (3H, s, ArCH_3), 2.31-2.45 (2*H*, m, CH_2C(O)), 2.48 (2H, d, *J* 7.8, CH_2CH=CHAr), 6.11 (1H, dt, *J* 15.9, 7.8 C*H*=CHAr), 6.35 (1H, d, *J* 15.9, CH=C*H*Ar), 6.97 (1H, d, *J* 7.31, Ar-*H*), 7.10 (3H, m, 3 × Ar-*H*); δ_C (100 MHz, $CDCl_3$) 16.6 (*C*H_2), 21.4 (Ar-*C*H_3), 26.5 (*C*H_3), 29.4 (*C*H_2), 31.7 (*C*H_2), 45.4 (*C*H_2CH=CHAr), 84.1 (*C*), 123.5 (*C*H=CHAr), 126.8 (2 × Ar-*C*H), 128.3 (2 × Ar-*C*H), 134.3 (CH=*C*HAr), 136.9 (Ar-*C*), 138.2 (Ar-*C*), 171.3 (*C*(O)); *m/z* (ES+ mode) 267 ((M + Na); (found: (M + Na), 267.1365. $C_{16}H_{20}O_2Na$ requires M, 267.1356).

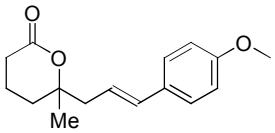
(*E*)-6-(3-(2,5-Dimethylphenyl)allyl)-6-methyltetrahydro-2H-pyran-2-one 6j



6j

As for general procedure A, reaction of Grubbs 2nd generation catalyst (17 mg, 0.02 mmol, 1 mol%), 6-allyl-6-methyltetrahydro-2H-pyran-2-one (310 mg, 2.01 mmol, 1 eq), and 1,4-dimethyl-2-vinylbenzene (664 mg, 5.03 mmol, 3 eq), after workup and purification by flash chromatography on silica gel eluting with 30% EtOAc in petroleum ether (40 – 60 °C), gave the title compound (194 mg, 0.74 mmol, 37%) as a colourless oil; ν_{max} (neat)/cm^{-1} 2920, 2851, 1729 (C=O), 1455, 1378, 1239, 1132, 1089, 1052, 971, 808; δ_H (400 MHz, $CDCl_3$) 1.35 (3H, s, C*H*$_3$), 1.62-1.68 (2H, m, C*H*$_2$), 1.76-1.88 (2H, m, C*H*$_2$CH$_2$C(O)), 2.22 (3H, s, Ar-C*H*$_3$), 2.24 (3H, s, Ar-C*H*$_3$), 2.35-2.48 (2H, m, C*H*$_2$C(O)), 2.52 (2H, d, *J* 8.6, C*H*$_2$CH=CHAr), 5.98 (1H, dt, *J* 15.6 7.6, C*H*=CHAr), 6.58 (1H, d, *J* 15.6, CH=C*H*Ar), 6.89 (1H, d, *J* 8.9, Ar-*H*), 6.96 (1H, d, *J* 7.8, Ar-*H*), 7.16 (1H, s, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 16.6 (*C*H$_2$), 19.4 (*C*H$_3$), 21.0 (*C*H$_3$), 26.5 (*C*H$_3$), 29.4 (*C*H$_2$C(O)), 31.7 (CH$_2$), 45.7 (*C*H$_2$CH=CHAr), 84.1 (*C*), 124.9 (*C*H=CHAr), 126.2 (Ar-*C*H), 128.2 (Ar-*C*H), 130.0 (Ar-*C*), 130.2 (Ar-*C*H), 132.0 (CH=*C*HAr), 135.5 (Ar-*C*), 135.9 (Ar-*C*), 171.3 (*C*(O)); *m/z* (ES+ mode) 281 ((M + Na), 100), 313 (28), 282 (19); (Found: (M + Na), 281.1512. $C_{17}H_{22}O_2Na$ requires M, 281.1512).

(*E*)-6-(3-(4-Methoxyphenyl)allyl)-6-methyltetrahydro-2H-pyran-2-one 6k

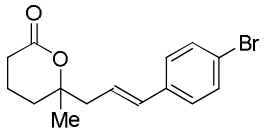


6k

As for general procedure A, reaction of Grubbs 2nd generation catalyst (5 mg, 0.0062 mmol, 1 mol%), 6-allyl-6-methyltetrahydro-2H-pyran-2-one (95 mg, 0.62 mmol, 1 eq), and 1-methoxy-4-vinylbenzene (248 mg, 1.85 mmol, 3 eq), after workup and

purification by flash chromatography on silica gel eluting with 30% EtOAc in petroleum ether (40 – 60 °C), gave the title compound (92 mg, 0.35 mmol, 57%) as a colourless oil; ν_{max} (neat)/cm^{-1} 2925, 1733 (C=O), 1605, 1504, 1243, 1173, 1088, 1049, 1028; δ_H (400 MHz, $CDCl_3$) 1.41 (3H, s, CH_3), 1.67-1.73 (1H, m, 1H from CH_2), 1.82-1.94 (3H, m, 3H from CH_2), 2.42-2.52 (2H, m, CH_2C(O)), 2.55 (1H, d, *J* 7.6, CH_aH$_b$CH=CHAr), 2.56 (1H, d, *J* 7.6, CH$_a$$H_b$CH=CHAr), 3.81 (3H, s, OCH_3), 6.05 (1H, dt, *J* 15.9 7.6, C*H*=CHAr), 6.41 (1H, d, *J* 15.9, CH=C*H*Ar), 6.85 (2H, d, *J* 8.8, Ar-*H*), 7.30 (2H, d, *J* 8.8, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 16.6 (*C*H$_2$), 26.5 (*C*H$_3$), 29.3 (*C*H$_2$C(O)), 31.6 (*C*H$_2$), 45.4 (*C*H$_2$CH=CHAr), 55.3 (O*C*H$_3$), 84.1 (*C*), 113.9 (Ar-*C*H), 121.5 (C*H*=CHAr), 127.3 (Ar-*C*H), 129.8 (Ar-*C*), 133.6 (CH=C*H*Ar), 159.1 (Ar-*C*OMe), 171.6 (*C*(O)); *m/z* (ES+ mode) 283 ((M + Na), 100), 543 (15), 299 (9); (Found: (M + Na), 283.1296. $C_{16}H_{20}O_3Na$ requires M, 283.1305).

(*E*)-6-(3-(4-Bromophenyl)allyl)-6-methyltetrahydro-2H-pyran-2-one 6l

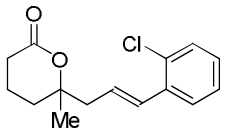


6l

As for general procedure A, reaction of Grubbs 2nd generation catalyst (7 mg, 0.0085 mmol, 0.5 mol%), 6-allyl-6-methyltetrahydro-2H-pyran-2-one (261 mg, 1.69 mmol, 1 eq), and 1-bromo-4-vinylbenzene (950 mg, 5.19 mmol, 3 eq), after workup and purification by flash chromatography on silica gel eluting with 5% Et_2O in $CHCl_3$, gave the title compound (186 mg, 0.60 mmol, 36%) as a colourless oil; ν_{max} (neat)/cm^{-1} 2935, 1726 (C=O), 1489, 1359, 1290, 1230, 1068, 1006; δ_H (400 MHz, $CDCl_3$) 1.41 (3H, s, CH_3), 1.69-1.75 (1H, m, CCH_aH$_b$), 1.81-1.85 (1H, m, CCH$_a$$H_b$), 1.86-1.95 (2H, m, C$H_2$), 2.42-2.53 (2H, m, C$H_2$C(O)), 2.55-2.61 (2H, m, CH_2CH=CHAr), 6.21 (1H,

dt, *J* 15.9 7.6, C*H*=CHAr), 6.41 (1H, d, *J* 15.9, CH=C*H*Ar), 7.23 (2H, d, *J* 8.3, Ar-*H*), 7.43 (2H, d, *J* 8.3, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 16.9 (*C*H_2), 26.8 (*C*H_3), 29.6 (*C*H_2C(O)), 32.1 (*C*H_2), 45.7 (*C*H_2CH=CHAr), 84.1 (*C*), 121.5 (Ar-*C*Br), 125.0 (*C*H=CHAr), 128.0 (Ar-*C*H), 131.9 (Ar-*C*H), 133.4 (CH=*C*HAr), 136.2 (Ar-*C*), 171.4 (*C*(O)); *m/z* (ES+ mode) 331 ((M_{Br79} + Na), 100), 333 ((M_{Br81} + Na), 100), 349 (16), 347 (13), 233 (13), 235 (9); (Found: (M + Na), 331.0302. $C_{15}H_{17}O_2BrNa$ requires M, 331.0304).

(*E*)-6-(3-(2-Chlorophenyl)allyl)-6-methyltetrahydro-2H-pyran-2-one 6m

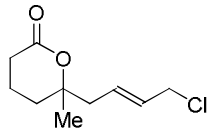


6m

As for general procedure A, reaction of Grubbs 2nd generation catalyst (9.6 mg, 0.0113 mmol, 1 mol%), 6-allyl-6-methyltetrahydro-2H-pyran-2-one (174 mg, 1.13 mmol, 1 eq), and 1-chloro-2-vinylbenzene (313 mg, 2.23 mmol, 2 eq), after workup and purification by flash chromatography on silica gel eluting with 30% EtOAc in petroleum ether (40 – 60 °C), gave the title compound (216 mg, 0.82 mmol, 72%) as a white powder; ν_{max} (neat)/cm^{-1} 2936, 2881, 1707 (C=O), 1587, 1467, 1384, 1325, 1301, 1286, 1237, 1090, 967, 802, 689; δ_H (400 MHz, $CDCl_3$) 1.45 (1H, s, CH_3), 1.72-1.78 (2H, m, C*H*$_2$), 1.85-1.98 (2H, m, C*H*$_2$CH$_2$C(O)), 2.45-2.61 (2H, m, C*H*$_2$C(O)), 2.64 (1H, d, *J* 8.8, C*H*$_2$CH=CHAr), 6.22 (1H, dt, *J* 15.9, 7.6, C*H*=CHAr), 6.87 (1H, d, *J* 15.9 CH=C*H*Ar), 7.37 (1H, dd, *J* 7.8 1.5, Ar-*H*), 7.53 (1H, dd, *J* 7.6 1.8, Ar-*H*), 7.17-7.26 (2H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 16.6 (*C*H_2), 26.5 (*C*H_3), 29.4 (*C*H_2C(O)), 31.8 (*C*H_2), 45.5 (*C*H_2CH=CHAr), 83.9 (*C*), 126.9 (*C*H=CHAr), 127.0 (Ar-*C*H), 127.0 (Ar-*C*H), 128.5 (Ar-*C*H), 129.6 (Ar-*C*H), 130.5 (CH=*C*HAr), 132.7

(Ar-*C*Cl) 135.2 (Ar-*C*), 171.1 (*C*(O)); *m/z* (ES+ mode) 287 (M + Na), 90), 196 (100), 289 (28), 204 (13), 194 (9); (Found: (M + Na), 287.0812. $C_{15}H_{17}O_2Cl_1Na_1$ requires M, 287.0809).

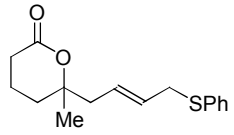
(*E*)-6-(4-Chlorobut-2-en-1-yl)-6-methyltetrahydro-2*H*-pyran-2-one S5



S5

As for general procedure A, reaction of Grubbs 2nd generation catalyst (27 mg, 0.33 mmol, 5 mol%), 6-allyl-6-methyltetrahydro-2*H*-pyran-2-one (100 mg, 0.65 mmol, 1 eq) and allyl chloride (0.22 ml, 2.60 mmol, 4 eq), after workup and purification by flash chromatography on silica gel with 20% EtOAc in petroleum ether (40 – 60 °C), gave the title compound (47 mg, 23.2 mmol, 36%) as a yellow oil and as a 6:1 *E*:*Z* mixture of geometric isomers; ν_{max} (neat)/cm^{-1} 2923, 2360, 2340, 1725 (C=O), 1236, 1092, 1053, 926, 668; δ_H (400 MHz, $CDCl_3$) 1.38 (3H, s, C*H*$_3$ from major isomer), 1.40 (3H, s, C*H*$_3$ from minor isomer), 1.65-1.83 (2H, m, C*H*$_2$CH$_2$CH$_2$C(O)), 1.84-1.95 (2H, m, C*H*$_2$CH$_2$C(O)), 2.39-2.47 (2H, m, C*H*$_2$CH=CHCH$_2$Cl), 2.47-2.59 (2H, m, C*H*$_2$C(O)), 4.06 (2H, d, *J* 6.3, C*H*$_2$Cl from major isomer), 4.10 (2H, d, *J* 8.1, C*H*$_2$Cl from minor isomer), 5.74 (1H, dt, *J* 15.4, 6.3, CH=C*H*CH$_2$Cl), 5.80 (1H, dt, *J* 15.4, 6.8, C*H*=CHCH$_2$Cl); δ_C (100 MHz, $CDCl_3$) 16.5 (*C*H$_2$CH$_2$C(O)), 26.3 (*C*H$_3$), 29.3 (*C*H$_2$C(O)), 31.7 (*C*H$_2$CH$_2$CH$_2$C(O)), 44.3 (*C*H$_2$CH=CHCH$_2$Cl), 44.7 (*C*H$_2$Cl), 83.6 (*C*), 129.1 (*C*H=CHCH$_2$Cl), 130.6 (CH=*C*HCH$_2$Cl), 171.0 (*C*(O)); m/z (ES+ mode) 225 ((M+Na), 100); (Found: (M + Na), 203.0828. $C_{10}H_{16}O_2ClNa$ requires M, 203.0833).

(*E*)-6-Methyl-6-(4-(phenylthio)but-2-en-1-yl)tetrahydro-2*H*-pyran-2-one 6n



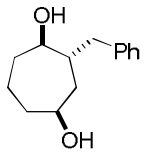
6n

To a stirred solution of (*E*)-6-(4-chlorobut-2-en-1-yl)-6-methyltetrahydro-2*H*-pyran-2-one (63 mg, 0.31 mmol, 1 eq) in acetone (2 ml) was added K_2CO_3 (52 mg, 0.37 mmol, 1.2 eq), NaI (12 mg, 0.08 mmol, 25 mol%) and thiophenol (0.44 ml, 0.37 mmol, 1.2 eq). The reaction was stirred at room temperature for 18 hours. The crude reaction mixture was concentrated *in vacuo* to yield the crude product as a 6:1 *E*:*Z* mixture of geometric isomers. Purification by column chromatography on silica gel with 30% EtOAc in petroleum ether (40 – 60 ^oC), gave the title compound (56 mg, 0.20 mmol, 68 %) as a yellow oil and as a 13:1 *E*:*Z* mixture of geometric isomers; ν_{max} (neat)/cm^{-1} 2922, 2360, 2340, 1719 (C=O), 1437, 1235, 1088, 1052, 969, 741, 690, 668; δ_H (400 MHz, $CDCl_3$) 1.14 (3H, s, C*H*$_3$ from major isomer), 1.25 (3H, s, C*H*$_3$ from minor isomer), 1.32-1.49 (2H, m, C*H*$_2$CH$_2$C(O)), 1.59-1.80 (2H, m, C*H*$_2$), 2.19-2.32 (1H, m, 1H from C*H*$_a$H$_b$C(O)), 2.25 (2H, d, *J* 7.3, C*H*$_2$CH=CHCH$_2$SPh), 2.39 (1H, dt, *J* 18.4, 6.6, 1H from CH$_a$*H*$_b$C(O)), 3.46 (2H, d, *J* 6.8, C*H*$_2$SPh, from major isomer), 3.49 (2H, d, *J* 7.4, C*H*$_2$SPh from minor isomer), 5.41 (1H, dt, *J* 15.1, 7.3, CH=C*H*CH$_2$SPh from major isomer), 5.51 (1H, dt, *J* 15.4, 6.8, C*H*=CHCH$_2$SPh from major isomer), 5.62-5.66 (1H, m, CH=C*H*CH$_2$SPh from minor isomer), 5.66-5.71 (1H, m, C*H*=CHCH$_2$SPh from minor isomer), 7.08-7.17 (1H, m, Ar-C*H*), 7.17-7.23 (2H, m, Ar-C*H*), 7.23-7.32 (2H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 16.5 (*C*H$_2$), 26.2 (*C*H$_3$), 29.2 (*C*H$_2$C(O)), 31.1 (*C*H$_2$CH$_2$C(O)), 31.6 (CH=CH*C*H$_2$SPh from minor isomer), 36.3 (CH=CH*C*H$_2$SPh from major isomer), 44.6 (*C*H$_2$CH=CHCH$_2$SPh), 83.7 (*C*), 126.4 (Ar-C*H*), 127.4 (CH=*C*HCH$_2$SPh), 128.9 (Ar-*C*H), 130.3 (*C*H=CHCH$_2$SPh

from major isomer), 130.5 (Ar-*C*H), 135.5 (Ar-*C*), 171.2 (*C*(O)); *m/z* (ES+ mode) 299 (M + Na), 100), (Found: (M 299.1079. $C_{16}H_{20}O_2SNa$ requires M, 299.107880).

General procedure B: SmI_2-H_2O mediated cyclization

***rac*-(1*R*, 2*R* ,4*S*)-2-Benzylcycloheptane-1,4-diol 8a**

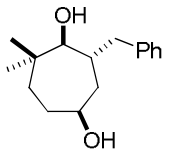


8a

To a stirred solution of SmI_2 (0.1 M in THF, 21 mL, 2.14 mmol, 7 eq) under N_2 at room temperature was added distilled H_2O (5.30 mL). This resulted in a colour change from blue to red at which point a solution of 6-cinnamyltetrahydro-2H-pyran-2-one (66 mg, 0.31 mmol, 1 eq) in THF (4 mL) was added quickly and the flask was sealed under N_2. The reaction was left to stir until decolourization had occurred. The reaction was quenched by opening the flask to air and by adding aqueous saturated sodium potassium tartrate (15 mL). The aqueous layer was extracted with Et_2O (3 × 15 mL), and the organic extracts combined, dried (Na_2SO_4) and concentrated in *vacuo* to yield the crude product. Purification by column chromatography on silica gel eluting with 60% EtOAc in petroleum ether (40 – 60 °C), gave the title compound (37 mg, 0.17 mmol, 55%) as a colourless oil; ν_{max} (neat)/cm^{-1} 3360 (OH), 2925, 2852, 1491, 1453, 1320, 1026, 984, 747, 699; δ_H (400 MHz, $CDCl_3$) 1.31 (1H, br dd, *J* 15.1 4.3, CHC*H*$_a$H$_b$CHOH), 1.42-1.48 (1H, m, 1H from C*H*$_a$CH$_b$CHOHCH$_2$), 1.62-1.71 (4H, m, 4H from 2 × C*H*$_2$), 1.81-1.92 (1H, m, CH$_a$C*H*$_b$CHOHCH$_2$), 2.05 (1H, ddd, *J* 14.9, 5.6, 4.3, CHCH$_a$*H*$_b$CHOH), 2.15-2.22 (1H, m, C*H* from major diastereoisomer), 2.32-2.43 (1H, m, C*H* from minor diastereoisomer), 2.52 (1H, dd, *J* 13.6, 8.3, C*H*$_a$H$_b$Ar from major diastereoisomer), 2.70 (1H, dd, *J* 13.6, 7.3, CH$_a$*H*$_b$Ar from major diastereoisomer), 2.84 (1H, dd, *J* 13.4, 5.8, C*H*$_a$H$_b$Ar from minor diastereoisomer), 3.01 (1H, dd, *J* 13.4, 4.5, CH$_a$*H*$_b$Ar from minor diastereoisomer), 3.82 (1H, dt, *J* 4.8, 1.5, CHC*H*OH from major diastereoisomer), 3.86 (1H, dt, *J* 4.5,

1.3, CHC*H*OH from minor diastereoisomer), 3.95-4.00 (1H, m, CH_2C*H*OH), 7.11-7.24 (5H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) for major diastereoisomer: 18.3 (*C*H_2), 34.5 (*C*H_2CHCHOH), 36.9 (*C*H_2), 37.8 (*C*H_2), 38.5 (*C*H), 40.2 (*C*H_2Ar), 69.3 (*C*HOH), 71.1 (*C*HOH), 126.0 (Ar-*C*H), 128.4 (Ar-*C*H), 129.2 (Ar-*C*H), 140.9 (Ar-*C*); *m/z* (ES+ mode) 243 ((M + Na), 100), 238 (21); (Found: (M + Na), 243.1354. $C_{14}H_{20}O_2Na$ requires M, 243.1356).

***rac*-(1*S*,2*R*,4*S*)-2-Benzyl-7,7-dimethylcycloheptane-1,4-diol 8b**

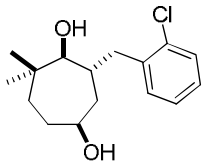


8b

As for general procedure B, reaction of 6-cinnamyl-3,3-dimethyltetrahydro-2H-pyran-2-one (25 mg, 0.10 mmol, 1 eq) with SmI_2 (0.1 M in THF, 8.2 mL, 0.82 mmol, 8 eq) and H_2O (1.50 mL) after workup and purification by column chromatography on silica gel eluting with 30% EtOAc in petroleum ether (40 – 60 °C) gave the title compound (21 mg, 0.085 mmol, 83%) as a colourless oil and as a 9:2 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3418 (OH), 2925, 2863, 1453, 1359, 1285, 1029, 987, 700; Major Diastereoisomer: δ_H (400 MHz, $CDCl_3$) 0.74 (3H, s, C*H*$_3$), 0.84 (3H, s, C*H*$_3$), 1.18 (1H, dd, J 14.4, 8.1, CC*H*$_a$H$_b$), 1.29 (1H, dt, *J* 14.9, 4.3, CHC*H*$_a$H$_b$), 1.43 (1H, dd, J 14.4, 12.1, CCH$_a$*H*$_b$), 1.50-1.57 (1H, m, C*H*$_a$H$_b$CHOH), 1.68-1.75 (1H, m, CH$_a$*H*$_b$CHOH), 2.09 (1H, ddd, *J* 14.9, 10.6, 5.8, CHCH$_a$*H*$_b$), 2.22-2.30 (1H, m, C*H*), 2.59 (2H, d, *J* 7.6, C*H*$_2$Ar), 3.13 (1H, s, CHC*H*OH), 3.92-3.98 (1H, m, CH_2C*H*OH), 7.10-7.23 (5H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 25.6 (*C*H$_3$), 28.9 (*C*H$_3$), 31.2 (*C*H_2CHOH), 32.4 (*C*H_2C), 35.0 (*C*H), 36.3 (CH*C*H_2), 37.5 (*C*), 42.1 (*C*H_2Ar), 70.6 (CH*C*HOH), 79.8 (CH_2*C*HOH), 126.0 (Ar-*C*H), 128.4 (Ar-*C*H), 129.1 (Ar-*C*H),

140.9 (Ar*C*); *m/z* (ES+ mode) 271 ((M + Na), 100), 269 (49); (Found: (M + H), 249.1850. $C_{16}H_{25}O_2$ requires M, 249.1849).

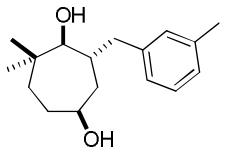
***rac*-(1*S*, 2*R*, 4*S*)-2-(2-Chlorobenzyl)-7,7-dimethylcycloheptane-1,4-diol 8c**



8c

As for general procedure B, reaction of (*E*)-6-(3-(2-chlorophenyl)allyl)-3,3-dimethyltetrahydro-2H-pyran-2-one (29 mg, 0.105 mmol, 1 eq) with SmI_2 (0.1 M in THF, 8.40 mL, 0.84 mmol, 8 eq) and H_2O (1.50 mL), after purification by column chromatography on silica gel eluting with 5 % Et_2O in $CHCl_3$ gave the title compound (24 mg, 0.086 mmol, 82%) as a colourless oil and as a 5:3 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3393 (OH), 2928, 1474, 1388, 992, 943, 754, 680; For major diastereoisomer: δ_H (400 MHz, $CDCl_3$) 0.71 (3H, s, CH_3), 0.85 (3H, s, CH_3), 1.14 (2H, m, CH_2CH$_2$CHOH), 1.29 (1H, dt, *J* 14.6, 4.5, CH$_2$CH_aCH$_b$CHOH), 1.45 (1H, dd, *J* 14.6, 12.3, CH$_2$CH$_a$CH_bCHOH), 1.50- 1.56 (1H, m, CHOHCH_aCH$_b$CH), 2.08 (1H, ddd, *J* 14.6, 10.6, 5.8, CHOHCH$_a$CH_bCH), 2.32-2.39 (1H, m, C*H*CH$_2$Ar), 2.64 (1H, dd, *J* 13.4, 7.3, CH_aCH$_b$Ar), 2.75 (1H, dd, *J* 13.4, 7.8 CH$_a$CH_bAr), 3.11 (1H, s, CHC*H*OH), 3.93- 3.99 (1H, m, CH$_2$C*H*OH), 7.05-7.27 (4H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 25.5 (*C*H$_3$), 28.9 (CH$_3$), 31.2 (*C*H$_2$CHOH), 32.6 (*C*H$_2$C), 33.6 (*C*H), 36.4 (CH*C*H$_2$) 37.4 (*C*), 39.8 (*C*H$_2$Ar), 70.7 (CH*C*HOH), 80.2 (CH$_2$*C*HOH), 126.6 (Ar-*C*H), 127.5 (Ar- *C*H), 129.6 (Ar-*C*H), 131.5 (Ar-*C*H), 134.4 (Ar-*C*Cl) 138.5 (Ar-*C*); *m/z* (ES+ mode) 305 ((M + Na), 90), 255 (40), 193 (50); (found: (M + Na), 305.1287. $C_{16}H_{23}ClO_2$ requires M, 305.1279).

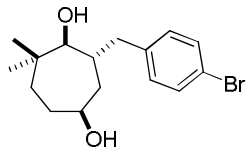
***rac*-(1*S*, 2*R*, 4*S*)-7,7-Dimethyl-2-(3-methylbenzyl)cycloheptane-1,4-diol 8d**



8d

As for general procedure B, reaction of (*E*)-3,3-dimethyl-6-(3-(*m*-tolyl)allyl)tetrahydro-2H-pyran-2-one (48 mg, 0.186 mmol, 1 eq) with SmI_2 (0.1 M in THF, 14.80 mL, 1.49 mmol, 8 eq) and H_2O (2.65 mL), purification by column chromatography on silica gel eluting with 5 % Et_2O in $CHCl_3$, gave the title compound (33 mg, 0.129 mmol, 69%) as a colourless oil and as a 4:3 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3428 (OH), 2959, 2868, 1704 (C=O), 1468, 1446, 1384, 1083, 1049, 781, 702, 665; For major diastereoisomer: δ_H (400 MHz, $CDCl_3$) 0.64 (3H, s, CH_3), 0.96 (3H, s, CH_3), 1.16-1.23 (2H, m, CH_2CH$_2$CHOH), 1.26-1.35 (2H, m, CH$_2$CH_2CHOH), 1.45 (1H, apparent dt, *J* 14.8, 3.2, CHCH_aCH$_b$CHOH), 1.74 (1H, d, *J* 14.8, CHCH$_a$CH_bCHOH), 2.22 (Ar-CH_3), 2.24-2.30 (1H, m, C*H*), 2.43 (1H, dd, *J* 13.4, 6.0, CH_aCH$_b$Ar), 2.94 (1H, dd, *J* 13.4, 8.6, CH_aCH$_b$Ar), 3.44-3.53 (1H, m, C*H*OH), 3.98-4.01 (1H, m, C*H*OH), 6.87-7.07 (4H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 21.4 (Ar-*C*H$_3$), 22.8 (*C*H$_3$), 26.4 (*C*H$_3$), 29.6 (*C*H$_2$CHOH), 30.8 (CH$_2$*C*H$_2$CHOH), 37.5 (*C*), 38.0 (*C*H$_2$Ar), 40.9 (CH*C*H$_2$CHOH), 43.6 (*C*HOH), 47.3 (*C*(CH$_3$)$_2$), 66.9 (*C*OH), 126.3 (Ar-*C*H), 126.8 (Ar-*C*H), 128.1 (Ar-*C*H), 130.1 (Ar-*C*H), 137.7 (Ar-*C*), 140.2 (Ar-*C*); *m/z* (ES+ mode) 285 ((M + Na), 30), 283 (100); (found: M + Na), 285.1821. $C_{17}H_{26}O_2Na$ requires M, 285.1826).

***rac*-(1*S*,2*R*,4*S*)-2-(4-Bromobenzyl)-7,7-dimethylcycloheptane-1,4-diol 8e**

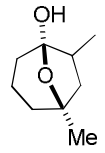


8e

As for general procedure B, reaction of (*E*)-6-(3-(4-bromophenyl)allyl)-3,3-dimethyltetrahydro-2H-pyran-2-one (25 mg, 0.08 mmol, 1 eq) with SmI_2 (0.1 M in THF, 6.10 mL, 0.62 mmol, 8 eq) and H_2O (1.10 mL), purification by column chromatography on silica gel eluting with 5 % Et_2O in $CHCl_3$, gave the title compound (19 mg, 0.059 mmol, 78%) as a colourless oil and as a 11:7 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3379 (OH), 2930, 2852, 1700, 1558, 1485, 1454, 1287, 1021; For major diastereoisomer: δ_H (400 MHz, $CDCl_3$) 0.73 (3H, s, C*H*$_3$), 0.84 (3H, s, C*H*$_3$), 1.25 (2H, m, C*H*$_2$), 1.44 (1H, m, CHC*H*$_a$CH$_b$), 1.49-1.54 (1H, m, C*H*$_a$H$_b$CHOH), 1.68-1.75 (1H, m, CH$_a$C*H*$_b$CHOH), 2.03-2.11 (1H, m, CHCH$_a$C*H*$_b$), 2.18-2.25 (1H, m, C*H*), 2.54 (2H, m, C*H*$_2$Ar), 3.08 (1H, s, CHC*H*OH), 3.92-3.98 (1H, m, CH$_2$C*H*OH), 6.99-7.32 (4H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 25.5 (*C*H$_3$), 28.3 (*C*H$_3$), 31.1 (*C*H$_2$), 32.2 (*C*H$_2$), 34.8 (*C*H), 36.1 (CH*C*H$_2$), 37.5 (*C*), 41.4 (*C*H$_2$Ar), 70.4 (CH*C*HOH), 79.6 (CH$_2$*C*HOH), 119.7 (Ar-*C*Br), 130.9 (Ar-*C*H), 131.4 (Ar-*C*H), 139.9 (Ar-*C*); Mass spectra data could not be obtained for the molecular ion.

General procedure C: SmI_2-H_2O mediated cyclization followed by DMP oxidation

rac-(1*R*,5*S*)-5,7-Dimethyl-8-oxabicyclo[3.2.1]octan-1-ol 9f

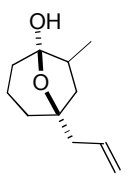


9f

To a stirred solution of SmI_2 (0.1 M in THF, 13.0 mL, 1.30 mmol, 8 eq) under N_2 at room temperature was added distilled H_2O (2.30 mL). This resulted in a colour change from blue to red at which point a solution of 6-allyl-6-methyltetrahydro-2H-pyran-2-one (25 mg, 0.16 mmol, 1 eq) in THF (2 mL) was added quickly and the flask was sealed under N_2. The reaction was left to stir until decolourization had occurred. The reaction was quenched by opening the flask to air and by adding aqueous saturated sodium potassium tartrate (15 mL). The aqueous layer was extracted with Et_2O (3 × 15 mL), and the organic extracts combined, dried (Na_2SO_4) and concentrated in *vacuo* to yield the crude diol. The crude diol was dissolved in dry CH_2Cl_2 (2 mL), cooled to 0 ˚C and Dess-Martin Periodinane (103 mg, 0.24 mmol, 1.5 eq) was added. The reaction was stirred for 3 hours whilst allowing to warm to room temperature. The reaction was then quenched by the addition of a saturated solution of $Na_2S_2O_3$ (2 mL) and $NaHCO_3$ (2 mL), whilst stirring for 30 min. The aqueous layer was extracted with Et_2O (3 × 20 mL), washed with brine and the organic extracts combined, dried (Na_2SO_4) and concentrated in *vacuo* to yield the crude product. Purification by column chromatography on silica gel eluting with 30% Et_2O in $CHCl_3$ gave the title compound (19 mg, 0.12 mmol, 75%) as a colourless oil and as a 1:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3397 (OH), 2961, 2873, 1450, 1376, 1227, 1205, 1112, 1030, 952, 922, 872, 792; δ_H (400 MHz, $CDCl_3$) 0.93 (3H, d, *J* 6.8,

CHCH_3 from 1 diastereoisomer), 1.03 (3H, d, *J* 7.1, CHCH_3 from 1 diastereoisomer), 1.20-1.26 (1H, m, CH_aH$_b$CO(OH) from 1 diastereoisomer), 1.29 (3H, s, CH_3 from 1 diastereoisomer), 1.32 (3H, s, CH_3 from 1 diastereoisomer), 1.34-1.35 (1H, m, CHCH_aH$_b$ from 1 diastereoisomer), 1.35-1.43 (1H, m, CH_aH$_b$CO(OH) from 1 diastereoisomer), 1.40-1.45 (2H, m, CHCH$_a$$H_b$ from 1 diastereoisomer and CHCH_aH$_b$ from 1 diastereoisomer), 1.51-1.60 (1H, m, CHCH$_a$$H_b$ from 1 diastereoisomer), 1.63-1.69 (2H, m, CH_2COMe from 1 diastereoisomer), 1.72-1.76 (2H, m, CH_2), 1.85-1.88 (CH_2COMe from 1 diastereoisomer), 1.97-2.02 (1H, m, C*H* from 1 diastereoisomer), 2.05-2.13 (2H, m, 1H from C*H* from 1 diastereoisomer + 1H from CH$_a$$H_b$CO(OH) from 1 diastereoisomer), 2.12-2.19 (1H, m, 1H from CH$_a$$H_b$CO(OH) from 1 diastereoisomer); δ_C (100 MHz, $CDCl_3$) 13.0 (CH*C*H$_3$ from 1 diastereoisomer), 17.4 (CH*C*H$_3$ from 1 diastereoisomer), 18.7 (*C*H$_2$ from 1 diastereoisomer), 18.8 (*C*H$_2$ from 1 diastereoisomer), 27.2 (*C*H$_3$), 30.3 (CH*C*H$_2$ from 1 diastereoisomer), 30.9 (*C*H$_2$COMe from 1 diastereoisomer), 35.4 (CH*C*H$_2$ from 1 diastereoisomer), 35.7 (*C*H$_2$COMe from 1 diastereoisomer), 38.5 (*C*H from 1 diastereoisomer), 41.5 (*C*H$_2$CO(OH) from 1 diastereoisomer), 43.4 (*C*H from 1 diastereoisomer), 44.3 (*C*H$_2$CO(OH) from 1 diastereoisomer), 65.8 (*C*OMe from 1 diastereoisomer), 79.2 (*C*OMe from 1 diastereoisomer), 104.1 (*C*O(OH) from 1 diastereoisomer), 105.1 (*C*O(OH) from 1 diastereoisomer); *m/z* (ES+ mode) 179 ((M + Na), 100), 195 (28); (Found: (M + Na), 179.1039. $C_9H_{16}O_2Na$ requires M, 179.1043).

rac-(1*R*, 5*R*)-5-Allyl-7-methyl-8-oxabicyclo[3.2.1]octan-1-ol 9g

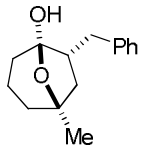


9g

As for general procedure C, reaction of 6,6-diallyltetrahydro-2H-pyran-2-one (26 mg, 0.14 mmol, 1 eq) with SmI_2 (0.1 M in THF, 12.0 mL, 1.16 mmol, 8 eq) and H_2O (2.10 mL) after workup gave the crude diol. Following oxidation of the crude reaction mixture using Dess-Martin Periodinane (89 mg, 0.21 mmol, 1.5 eq) gave after workup and purification by column chromatography on silica gel eluting with 30% Et_2O in $CHCl_3$ gave the title compound (24 mg, 0.13 mmol, 93%) as a colourless oil and as a 1:1 mixture of diastereoisomers; (neat)/cm^{-1} 3391 (OH), 2943, 1640, 1446, 1356, 1221, 1089, 1047, 975, 912; δ_H (400 MHz, $CDCl_3$) 0.98 (3H, d, *J* 7.1, C*H*$_3$ from 1 diastereoisomer), 1.11 (3H, d, *J* 6.8, C*H*$_3$ from 1 diastereoisomer), 1.28 (1H, dd, *J* 12.9, 7.1, CHC*H*$_a$H$_b$ from 1 diastereoisomer), 1.32-1.37 (1H, m, CHC*H*$_a$H$_b$ from 1 diastereoisomer), 1.39-1.51 (2H, m, 2H from C*H*$_2$ from both diastereoisomers), 1.58-1.69 (2H, m, 2H from C*H*$_2$ from both diastereoisomers), 1.71-1.78 (2H, m, 2H from C*H*$_2$ from both diastereoisomers), 1.96 (1H, dd, *J* 12.9, 9.1, CHCH$_a$*H*$_b$ from 1 diastereoisomer), 2.04 (2H, m, 1H from C*H* from 1 diastereoisomer + 1H from CHCH$_a$*H*$_b$ from 1 diastereoisomer), 2.09 (1H, m, C*H* from 1 diastereoisomer), 2.33 (2H, dd, *J* 7.3, 3.3, C*H*$_2$CH=CH$_2$ from 1 diastereoisomer), 2.36 (2H, dd, *J* 7.3, 4.0, C*H*$_2$CH=CH$_2$ from 1 diastereoisomer), 2.63 (1H, s, O*H* from 1 diastereoisomer), 2.74 (1H, s, O*H* from 1 diastereoisomer), 5.05-5.12 (2H, m, CH=C*H*$_2$ from both diastereoisomers), 5.84 (1H, ddt, *J* 15.6, 10.9, 7.3, C*H*=CH$_2$ from both diastereoisomers); δ_C (100 MHz, $CDCl_3$) 13.0 (*C*H$_3$ from 1 diastereoisomer), 17.1 (*C*H$_3$ from 1 diastereoisomer), 18.4 (*C*H$_2$ from 1 diastereoisomer), 18.6 (*C*H$_2$ from 1 diastereoisomer), 31.2 (*C*H$_2$ from 1 diastereoisomer), 33.6 (*C*H$_2$ from 1 diastereoisomer), 33.7 (*C*H$_2$ from 1 diastereoisomer), 35.8 (*C*H$_2$ from 1 diastereoisomer), 38.0 (*C*H from 1 diastereoisomer), 39.1 (CH*C*H$_2$ from 1 diastereoisomer), 41.7 (CH*C*H$_2$ from 1 diastereoisomer), 43.1 (*C*H from 1

diastereoisomer), 44.8 (CH$_2$CH=CH$_2$ from 1 diastereoisomer), 44.9 (CH$_2$CH=CH$_2$ from 1 diastereoisomer), 79.9 (COCH$_2$ from 1 diastereoisomer), 80.8 (COCH$_2$ from 1 diastereoisomer), 104.0 (COOH from 1 diastereoisomer), 104.9 (COOH from 1 diastereoisomer), 117.7 (CH=CH$_2$ from 1 diastereoisomer), 117.8 (CH=CH$_2$ from 1 diastereoisomer), 133.7 (CH=CH$_2$ from 1 diastereoisomer), 133.8 (CH=CH$_2$ from 1 diastereoisomer); *m/z* (ES+ mode) 205 ((M + Na), 100); (Found: (M + Na), 205.1195. $C_{11}H_{18}O_2Na$ requires M, 205.1199).

***rac*-(1*R*, 5*S*, 7*R*)-7-Benzyl-5-methyl-8-oxabicyclo[3.2.1]octan-1-ol 9h**

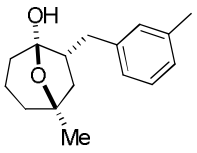


9h

As for general procedure C, reaction of 6-cinnamyl-6-methyltetrahydro-2H-pyran-2-one (25 mg, 0.11 mmol, 1 eq) with SmI_2 (0.1 M in THF, 8.70 mL, 0.87 mmol, 8 eq) and H_2O (1.50 mL), following oxidation of the crude reaction mixture using Dess-Martin Periodinane (72 mg, 0.17 mmol, 1.5 eq), after workup and purification by column chromatography on silica gel eluting with 30% Et_2O in $CHCl_3$ gave the title compound (23 mg, 0.099 mmol, 91%) as a colourless oil and as a 4:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3380 (OH), 2928, 1601, 1494, 1452, 1355, 1274, 1199, 1029, 974, 897, 721, 698; δ_H (400 MHz, $CDCl_3$) 1.22 (3H, s, CH_3), 1.27-1.34 (1H, m, CH_aH$_b$CO(OH)), 1.42 (1H, dd, *J* 12.9, 7.6, CHCH_aH$_b$), 1.54-1.62 (1H, m, CH_aCH$_b$CMe), 1.64-1.67 (1H, m, 1H from CH_2), 1.68-1.77 (3H, m, 1H from CHCH$_a$$H_b$ and 1H from CH$_a$$H_b$CO(OH)) and 1H from C$H_2$), 1.80-1.91 (1H, m, CH$_aCH_b$CMe), 2.24-2.31 (1H, m, CHCH$_2$Ar), 2.58 (1H, apparent t, *J* 13.4, CH_aH$_b$Ar from major diastereoisomer), 2.87 (1H, dd, *J* 13.4 3.8, CH$_a$$H_b$Ar from major

diastereoisomer), 3.06 (1H, dd, *J* 12.6 3.3, CH_aH_bAr from minor diastereoisomer), 7.11-7.24 (5H, m, Ph-*H*); δ_C (100 MHz, $CDCl_3$) 18.9 (*C*H_2), 27.2 (*C*H_3), 31.4 (*C*H_2CO(OH)), 34.8 (*C*H_2Ar), 35.6 (*C*H_2CMe), 39.4 (CH*C*H_2), 50.7 (*C*H), 79.4 (*C*OMe), 104.6 (*C*O(OH)), 126.0 (Ar-*C*H), 128.4 (Ar-*C*H), 129.1 (Ar-*C*H), 140.9 (Ar-*C*); *m/z* (ES+ mode) 255 ((M + Na), 100), 287 (20); (Found: (M + Na), 255.1350. $C_{15}H_{20}O_2Na$ requires M, 255.1356).

(1*R*, 5*S*, 7*R*)-5-Methyl-7-(3-methylbenzyl)-8-oxabicyclo[3.2.1]octan-1-ol 9i



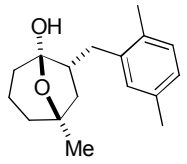
9i

As for general procedure C, reaction of (*E*)-6-methyl-6-(3-(*m*-tolyl)allyl)tetrahydro-2H-pyran-2-one (40 mg, 0.16 mmol, 1 eq) with SmI_2 (0.1 M in THF, 13.0 mL, 1.13 mmol, 8 eq) and H_2O (2.30 mL) after workup gave the crude diol. Oxidation of the crude reaction mixture using the Dess-Martin periodinane (103 mg, 0.24 mmol, 1.5 eq), after workup and purification by column chromatography on silica gel eluting with 5 % Et_2O in $CHCl_3$, gave the title compound (28 mg, 0.12 mmol, 72%) as a colourless oil and as a 4:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3378 (OH), 2930, 1703, 1608, 1451, 1274, 1103, 940, 780, 697; δ_H (400 MHz, $CDCl_3$) 1.22 (3H, s, C*H*$_3$), 1.26-1.33 (2H, m, C*H*$_2$), 1.40-1.48 (2H, m, 1H from C*H*$_2$ and 1H from *CH*$_2$COH), 1.54-1.58 (1H, m, C*H*$_2$), 1.65-1.77 (3H, m, 1H from C*H*$_2$COH and 2H from C*H*$_2$), 2.23-2.28 (1H, m, C*H*CH$_2$Ar), 2.25 (3H, s, ArC*H*$_3$), 2.50-2.57 (1H, m, C*H*$_a$CH$_b$Ar from major diastereoisomer), 2.85 (1H, dd, *J* 13.6, 4.29, CH_aH_bAr from major diastereoisomer), 3.02 (1H, dd, *J* 13.1, 3.8, CH_aCH_bAr from minor diastereoisomer), 6.93-7.12 (4H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 19.0 (*C*H_2), 21.4

(CH$_3$Ar), 27.3 (CH$_3$), 31.5 (CH$_2$), 34.7 (CH$_2$), 35.4 (CH$_2$Ar), 39.5 (CHCH$_2$), 50.8 (CH), 79.4 (COMe), 104.7 (CO(OH)), 125.5 (Ar-CH), 126.1 (Ar-CH), 128.3 (Ar-CH), 129.4 (Ar-CH), 138.0 (Ar-C), 140.8 (Ar-C); *m/z* (ES+ mode) 269 ((M + Na), 100); (Found: (M + Na), 269.1511. $C_{16}H_{22}O_2Na$ requires M, 269.1512).

rac-(1_R_, 5_S_, 7_R_)-7-(2,5-Dimethylbenzyl)-5-methyl-8-oxabicyclo[3.2.1]octan-1-ol

9j

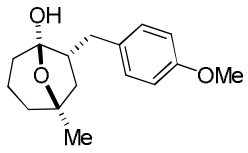


9j

As for general procedure C, reaction of (*E*)-6-(3-(2,5-dimethylphenyl)allyl)-6-methyltetrahydro-2H-pyran-2-one (53 mg, 0.22 mmol, 1 eq) with SmI_2 (0.1 M in THF, 17.6 ml, 1.76 mmol, 8 eq) and H_2O (3.10 mL) after workup gave the crude diol. Oxidation of the crude reaction mixture using the Dess-Martin periodinane (180 mg, 0.46 mmol, 1.5 eq), after workup and purification by column chromatography on silica gel eluting with 50 % Et_2O in $CHCl_3$, gave the title compound (39 mg, 0.68 mmol, 68%) as a colourless solid and as a 3:1 mixture of diastereoisomers; M.p. 106 $^{\circ}$C recrystallised from pentane/Et_2O; ν_{max} (neat)/cm^{-1} 3368 (OH), 2924, 2859, 1615, 1501, 1376, 1273, 1099, 1027, 939, 855, 734; δ_H (400 MHz, $CDCl_3$) 1.23 (3H, s, CH_3), 1.31 (1H, ddd, *J* 12.0, 8.8, 4.0, CH_aCH$_b$CMe), 1.46-1.56 (2H, m, 1H from CH$_a$CH_bCMe + 1H from CHCH_aH$_b$), 1.57-.1.66 (3H, m, CH_aH$_b$CO(OH) and 2H from CH_2), 1.71-1.78 (1H, m, CHCH$_a$$H_b$), 1.94-1.95 (1H, dd, CH$_a$$H_b$CO(OH)), 2.21-2.24 (1H, m, CHCH$_2$Ar), 2.22 (3H, s, Ar-CH_3), 2.23 (3H, s, Ar-CH_3), 2.53 (1H, dd, *J* 11.9, 1.8, CH_aH$_b$Ar from major diastereoisomer), 2.66 (1H, br s, OH), 2.83 (1H, dd, *J* 11.9, 3.5, CH$_a$$H_b$Ar from major diastereoisomer), 6.85 (1H, d, *J* 7.8, Ar-H), 6.89 (1H, s, Ar-

H), 6.97 (1H, d, *J* 7.6, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 19.0 (*C*H_2), 19.1 (Ar-*C*H_3) 21.0 (Ar-*C*H_3), 27.2 (*C*H_3), 31.4 (*C*H_2CO(OH)), 31.9 (*C*H_2Ar), 35.7 (*C*H_2COMe), 39.4 (CH*C*H_2), 49.3 (*C*H), 79.5 (*C*OMe), 104.7 (*C*O(OH)), 126.8 (Ar- *C*H), 129.7 (Ar-*C*H), 130.3 (Ar-*C*H), 132.8 (Ar-*C*), 135.3 (Ar-*C*), 138.8 (Ar-*C*); *m/z* (ES+ mode) 283 ((M + Na), 100), 315 (20); Found: (M + Na), 283.1669. $C_{17}H_{24}O_2Na$ requires M, 283.1669).

***rac*-(1*R*, 5*S*, 7*R*)-7-(4-Methoxybenzyl)-5-methyl-8-oxabicyclo[3.2.1]octan-1-ol 9k**

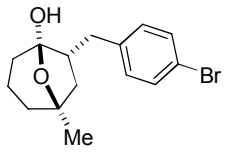


9k

As for general procedure C, reaction of (*E*)-6-(3-(4-methoxyphenyl)allyl)-6-methyltetrahydro-2H-pyran-2-one (30 mg, 0.14 mmol, 1 eq) with SmI_2 (0.1 M in THF, 11.1 mL, 0.11 mmol, 8 eq) and H_2O (1.90 mL) after workup gave the crude diol. Oxidation of the crude reaction mixture using Dess-Martin Periodinane (86 mg, 0.20 mmol, 1.5 eq), after workup and purification by column chromatography on silica gel eluting with 30% Et_2O in $CHCl_3$, gave the title compound (27 mg, 0.10 mmol, 89%) as a colourless oil and as a 4:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3389 (OH), 2929, 1611, 1506, 1453, 1246, 1177, 1103, 1032, 940, 802; δ_H (400 MHz, $CDCl_3$) 1.20-1.26 (1H, m, CH_aCH_bCMe), 1.30 (3H, s, CH_3), 1.37 (1H, dd, *J* 13.1 4.8, CH_aH$_b$CH), 1.53-1.58 (2H, m, 1H from CH_aH$_b$CO(OH) + 1H from CH$_a$CH_bCMe), 1.62-1.69 (2H, m, CH_2), 1.74 (1H, dd, *J* 13.1 4.5, CH$_a$$H_b$CH),1.83-1.89 (1H, m, CH$_a$$H_b$CO(OH), 2.27-2.33 (1H, m, C*H*), 2.60 (1H, dd, *J* 13.6 11.1, CH_aH$_b$Ar from major diastereoisomer), 2.89 (1H, dd, *J* 13.6 4.3, CH$_a$$H_b$Ar from major diastereoisomer), 3.07 (1H, dd, *J* 12.9 3.5, CH$_a$$H_b$Ar from minor diastereoisomer),

3.80 (3H, s, OCH_3), 6.84 (2H, d, *J* 8.6, Ar-C*H*), 7.14 (2H, d, *J* 8.6, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 27.2 (*C*H_3), 31.5 (*C*H_2CO(OH)), 33.9 (*C*H_2Ar), 35.7 (*C*H_2COMe), 36.5 (*C*H_2), 39.5 (CH*C*H_2), 51.0 (*C*H), 55.3 (ArO*C*H_3), 79.4 (*C*OMe), 104.6 (*C*O(OH)), 113.8 (Ar-*C*H), 129.4 (Ar-*C*H), 129.9 (Ar-*C*OMe), 133.0 (Ar-*C*); *m/z* (ES+ mode) 285 ((M + Na), 100), 286 (15); (Found: (M + Na), 285.1471. $C_{16}H_{22}O_3Na$ requires M, 285.1461).

***rac*-(1*R*, 5*S*, 7*R*)-7-(4-Bromobenzyl)-5-methyl-8-oxabicyclo[3.2.1]octan-1-ol 9l**

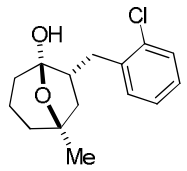


9l

As for general procedure C, reaction of (*E*)-6-(3-(4-bromophenyl)allyl)-6-methyltetrahydro-2H-pyran-2-one (40 mg, 0.13 mmol, 1 eq) with SmI_2 (0.1 M in THF, 10 mL, 1.0 mmol, 8 eq) and H_2O (2.50 mL) after workup gave the crude diol. Oxidation of the crude reaction mixture using Dess-Martin Periodinane (82 mg, 0.19 mmol, 1.5 eq), after workup and purification by column chromatography on silica gel eluting with 50% Et_2O in $CHCl_3$, gave the title compound (33 mg, 0.11 mmol, 82%) as a white solid; M.p. 105 ˚C recrystallised from pentane/Et_2O; ν_{max} (neat)/cm^{-1} 3370 (OH), 2929, 1486, 1452, 1351, 1274, 1204, 1104, 1011, 796; δ_H (400 MHz, $CDCl_3$) 1.30 (3H, s, CH_3), 1.33-1.39 (1H, m, C$H_a$$CH_b$CMe), 1.47 (1H, dd, *J* 12.9 7.6, CHC$H_a$$H_b$), 1.52-1.58 (1H, m, CH_aCH_bCMe), 1.61-1.69 (1H, m, C$H_a$$H_b$CO(OH)), 1.75-1.87 (3H, m, 1H from CHC$H_a$$H_b$ + 2H from CH_2), 1.92-1.96 (1H, m, $CH_a$$H_b$CO(OH)), 2.26-2.35 (1H, m, C*H*CH_2Ar), 2.61 (1H, dd, *J* 13.6 11.6, C$H_a$$H_b$Ar from major diastereoisomer), 2.89 (1H, dd, *J* 13.6 4.0, $CH_a$$H_b$Ar from major diastereoisomer), 3.00 (1H, br s, O-*H*), 3.07 (1H, dd, *J* 12.1 2.8, $CH_a$$H_b$Ar from minor

diastereoisomer), 7.09 (2H, d, *J* 8.3, Ar-*H*), 7.41 (2H, d, *J* 8.3, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 18.9 (*C*H_2), 27.1 (*C*H_3), 31.5 (*C*H_2CO(OH)), 34.2 (*C*H_2Ar), 35.6 (*C*H_2CMe), 39.3 (CH*C*H_2), 50.5 (*C*H), 79.5 (*C*OMe), 104.5 (*C*O(OH)), 119.8 (Ar-*C*Br), 130.2 (Ar-*C*H), 131.5 (Ar-*C*H), 139.8 (Ar-*C*); *m/z* (ES+ mode) 333 ((M_{Br79} + Na), 100), 335 ((M_{Br81} + Na), 100), 177 (26), 255 (24), 301 (22), 253 (15); (Found: (M_{Br79}+ Na), 333.0461. $C_{15}H_{19}O_2BrNa$ requires M, 333.0461).

***rac*-(1*R*, 5*S*, 7*R*)-7-(2-Chlorobenzyl)-5-methyl-8-oxabicyclo[3.2.1]octan-1-ol 9m**

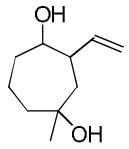


9m

As for general procedure C, reaction of (*E*)-6-(3-(2-chlorophenyl)allyl)-6-methyltetrahydro-2H-pyran-2-one (33 mg, 0.123 mmol, 1 eq) in THF (2 ml) with SmI_2 (0.1 M in THF, 9.95 ml, 0.10 mmol, 8 eq) and distilled H_2O (1.80 ml) after workup gave the crude diol. Oxidation of the crude reaction mixture using Dess-Martin Periodinane (79 mg, 0.19 mmol, 1.5 eq), after workup and purification by column chromatography on silica gel eluting with 50% Et_2O in $CHCl_3$, gave the title compound (25 mg, 0.09 mmol, 75%) as an off white solid and as a 6:1 mixture of diastereoisomers; M.p. 72 ˚C recrystallised from pentane/Et_2O; ν_{max} (neat)/cm^{-1}; 3367 (OH), 2926, 2872, 1699, 1570, 1473, 1440, 1375, 1354, 1273, 1201, 854, 806; δ_H (400 MHz, $CDCl_3$) 1.22 (3H, s, C*H*$_3$), 1.28-1.33 (1H, m, C*H*$_a$H$_b$CO(OH)), 1.43-1.46 (1H, m, CH$_a$*H*$_b$CO(OH)), 1.50 (1H, dd, *J* 12.9, 7.8, C*H*$_a$H$_b$CH), 1.59-1.61 (1H, m, C*H*$_a$H$_b$CMe), 1.69 (1H, apparent t, *J* 12.1, CH$_a$*H*$_b$CH), 1.74-1.79 (1H, m, C*H*$_a$H$_b$), 1.82-1.88 (1H, m, CH$_a$*H*$_b$), 1.89-1.94 (1H, m CH$_a$*H*$_b$CMe), 2.30-2.40 (1H, m, C*H*), 2.80 (1H, dd, *J* 13.9, 11.6, C*H*$_a$H$_b$Ar from major diastereoisomer), 2.94 (1H, dd, *J*

13.9, 4.3, CH_aH_bAr from major diastereoisomer), 2.97 (1H, s, O*H*), 7.05-7.29 (4H, m, ArC-*H*); δ_C (100 MHz, $CDCl_3$) 18.9 (*C*H_2), 27.2 (*C*H_3), 31.3 (*C*H_2COMe), 31.9 (*C*H_2Ar), 35.7 (*C*H_2CO(OH)), 38.9 (*C*H_2CH), 49.3 (*C*H), 79.4 (*C*Me), 104.7(*C*O(OH)), 126.8 (Ar-*C*H), 127.5 (Ar-*C*H), 129.6 (Ar-*C*H), 130.4 (Ar-*C*H), 133.9 (Ar-*C*), 138.4 (Ar-*C*Cl); *m/z* (ES+ mode) 289 ((M + Na), 100), 291 (35), 284 (18) 264 (22); (Found: (M + Na), 289.0963. $C_{15}H_{19}O_2Cl_1Na_1$ requires M, 289.0966).

1-Methyl-3-vinylcycloheptane-1,4-diol 8n



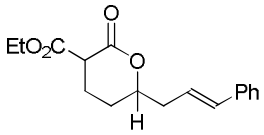
8n

As for general procedure B, reaction of (*E*)-6-methyl-6-(4-(phenylthio)but-2-en-1-yl)tetrahydro-2*H*-pyran-2-one (23 mg, 0.083 mmol, 1 eq) in THF (3 mL) with SmI_2 (6.7 ml, 0.1 M solution in THF, 0.69 mmol, 8 eq) and H_2O (1.24 ml, 68.6 mmol, 800 eq), after workup and purification by column chromatography on silica gel, eluting with 30% EtOAc in petroleum ether (40 – 60 °C), gave the title compound as a colourless oil; ν_{max} (neat)/cm^{-1} 3659 (br, OH), 3075, 2923, 2854, 1714, 1633, 1456, 1373, 1091, 1018, 962, 908, 758, 690; δ_H (400 MHz, $CDCl_3$) 1.37-1.83 (6H, m, 6H from 3 × CH_2 from four diastereoisomers), 1.83-2.05 (2H, m, 2H from CH_2 from four diastereoisomers), 2.10-2.21 (2H, m, C*H*$_2$CHCH=CH_2, from one diasteroisomer), 2.30-2.38 (1H, m, C*H*CH=CH_2, 1H from one diastereoisomer), 2.55 (1 H, dtd, *J* 8.7, 8.7, 3.5, C*H*CH=CH_2, 1H from one diastereoisomer), 2.73-2.79 (1H, m, C*H*CH=CH_2 from 2 diastereoisomers), 3.44 (1H, m, C*H*(OH) 1H from one diasteroisomer), 3.50-3.57 (1H, m, C*H*(OH) 1H from one diastereoisomer), 3.95-4.00 (1H, m, C*H*(OH), 1H from 2 diastereoisomers), 5.00-5.20 (2H, CH=C*H*$_2$ from four diastereoisomers), 5.69

(1H, ddd, *J* 17.3, 9.5, 9.5 C*H*=CH_2 from two diastereoisomers), 5.89-6.00 (1H, m, C*H*=CH_2, 1H from two diastereoisomers); δ_C (100 MHz, $CDCl_3$) 17.7 (*C*H_2 from one diastereoisomer), 18.4 (*C*H_2 from one diastereoisomer), 18.5 (*C*H_2 from two diastereoisomers), 29.4 (*C*H_3 from one diastereoisomer), 29.7 (*C*H_2 from one diastereoisomer), 30.4 (*C*H_3 from one diastereoisomer), 32.1 (*C*H_3 from one diastereoisomer), 32.6 (*C*H_3 from one diastereoisomer), 36.1 (*C*H_2 from one diastereoisomer), 37.0 (*C*H_2 from one diastereoisomer), 37.2 (*C*H_2 from one diastereoisomer), 38.2 (*C*H_2 from one diastereoisomer), 41.2 (C*H*CH=CH_2 from one diastereoisomer), 41.7 (*C*H_2 from one diastereoisomer), 42.6 (*C*H_2 from one diastereoisomer), 43.2 (*C*H_2 from one diastereoisomer), 45.5 (C*H*CH=CH_2 from one diastereoisomer), 45.6 (C*H*CH=CH_2 from one diastereoisomer), 47.6 (C*H*CH=CH_2 from one diastereoisomer), 71.3 (*C*HC(OH) from one diastereoisomer), 72.5 (*C*(OH)), 72.6 (*C*(OH)), 72.8 (*C*HC(OH), from one diastereoisomer), 74.3 (*C*HC(OH), from one diastereoisomer), 74.8 (*C*HC(OH), from one diastereoisomer), 114.0 (CH=*C*H_2 from one diastereoisomer), 114.9 (CH=*C*H_2 from one diastereoisomer), 115.9 (CH=*C*H_2 from one diastereoisomer), 116.3 (CH=*C*H_2 from one diastereoisomer), 141.3 (*C*H=CH_2 from one diastereoisomer), 141.6 (*C*H=CH_2 from one diastereoisomer), 142.1 (*C*H=CH_2 from one diastereoisomer), 142.3 (*C*H=CH_2 from one diastereoisomer); m/z (ES+ mode) 193 ((M+Na), 100), (Found: (M 171.1379. $C_{10}H_{19}O_2$ requires M, 171.1380).

General procedure D: Claisen condensation

Ethyl 6-cinnamyl-2-oxotetrahydro-2H-pyran-3-carboxylate S6



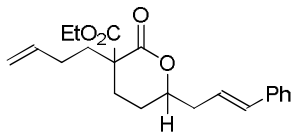
S6

A solution of LDA was prepared by adding *n*-butyllithium (0.18 mL, 0.39 mmol, 1.2 eq, 2.2 M solution in hexane) to diisopropylamine (39 mg, 0.39 mmol, 1.2 eq) in THF (1 mL) at -78 °C under N_2 and stirred for 1 hour. To this solution was added 6-cinnamyltetrahydro-2H-pyran-2-one (70 mg, 0.32 mmol, 1 eq) dissolved in THF (1 mL) over 30 min via syringe pump and the resulting solution stirred for 1 hour. The reaction was warmed to 0 °C for 10 min then cooled back to -78 °C before the addition of ethyl cyanoformate (48 mg, 0.49 mmol, 1.5 eq) and the resulting solution allowed to warm to room temperature over 18 hours. The reaction was quenched by the addition of aqueous saturated NH_4Cl (10 mL) and the aqueous layer was separated and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4) and concentrated *in vacuo* to yield the crude product. Purification by column chromatography on silica gel eluting with 20% EtOAc in petroleum ether (40 – 60 °C) gave the title compound (69 mg, 0.24 mmol, 74%) as a yellow oil and as a 1:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 2956, 1726 (C=O), 1602, 1444, 1305, 1256, 1177, 1051, 964; δ_H (400 MHz, $CDCl_3$) 1.10 (3H, apparent q, *J* 7.1, CH_3), 1.64-1.71 (2H, m, CH_2 from 1 diastereoisomer), 1.77-1.84 (2H, m, CH_2 from 1 diastereoisomer), 1.93-2.09 (2H, m, CH(O)CH_2 from 1 diastereoisomer), 2.11-2.34 (2H, m, CHC(O)CH_2 from 1 diastereoisomer), 2.53-2.62 (1H, m, PhCH=CHCH_aH$_b$), 2.64-2.71 (1H, m, PhCH=CHCH$_a$$H_b$), 3.50 (1H, t, *J* 7.3, C*H*C(O) from 1 diastereoisomer), 3.58 (1H, t, *J* 7.3, C*H*C(O) from 1 diastereoisomer),

4.20-4.28 (2H, m, C*H*$_2$O), 4.42-4.53 (1H, m, C*H*O), 6.17-6.26 (1H, m, PhCH=C*H*), 6.50 (1H, d, *J* 15.9, PhC*H*=CH), 7.22-7.38 (5H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 14.1 (*C*H$_3$), 21.6 (CHC(O)*C*H$_2$ from 1 diastereoisomer), 22.9 (CHC(O)*C*H$_2$ from 1 diastereoisomer), 25.2 (CHO*C*H$_2$ from 1 diastereoisomer), 26.6 (CHO*C*H$_2$ from 1 diastereoisomer), 38.9 (PhCH=CH*C*H$_2$ from 1 diastereoisomer), 39.1 (PhCH=CH*C*H$_2$ from 1 diastereoisomer), 46.1 (*C*HC(O) from 1 diastereoisomer), 47.9 (*C*HC(O) from 1 diastereoisomer), 62.0 (CH$_3$C*H*$_2$O), 80.0 (*C*H$_2$O from 1 diastereoisomer), 80.6 (*C*H$_2$O from 1 diastereoisomer), 123.5 (PhCH=*C*H from 1 diastereoisomer), 123.6 (PhCH=*C*H from 1 diastereoisomer), 126.2 (Ar*C*H), 127.5 (Ar*C*H), 128.6 (Ar*C*H), 133.8 (Ph*C*H=CH from 1 diastereoisomer), 133.9 (Ph*C*H=CH from 1 diastereoisomer), 137.0 (Ar*C*), 167.2 (*C*(O)), 169.3 (*C*(O)); *m/z* (ES+ mode) 311 ((M + Na), 34), 599 (100); (Found: (M + Na), 311.1270. $C_{17}H_{20}O_4Na$ requires M, 311.1254).

General procedure E: Alkylation

Ethyl 3-(but-3-enyl)-6-cinnamyl-2-oxotetrahydro-2H-pyran-3-carboxylate S7

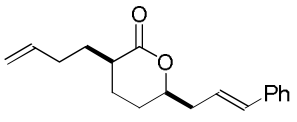


S7

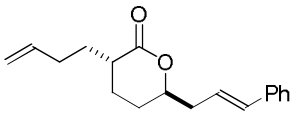
Ethyl 6-cinnamyl-2-oxotetrahydro-2H-pyran-3-carboxylate (164 mg, 0.57 mmol, 1 eq) was dissolved in DMF (4 mL) and cooled to 0 °C. NaH (60% in mineral oil, 27 mg, 0.68 mmol, 1.2 eq) was added slowly and the reaction allowed to warm up to room temperature. When the initial fizzing had subsided, the reaction was heated to 35 °C for 10 min then allowed to cool to room temperature before adding 4-bromobut-1-ene (92 mg, 0.68 mmol, 1.2 eq). The reaction mixture was heated to 60 °C for 18 hours then quenched with H_2O (10 mL) and extracted with Et_2O (3 × 15 mL). The organic layers were combined, washed with H_2O (3 × 10 mL), dried (Na_2SO_4) and concentrated *in vacuo* to yield the crude product. Purification by flash chromatography on silica gel eluting with 40% Et_2O in petroleum ether (40 – 60 °C) gave the title compound (167 mg, 0.49 mmol, 86%) as a yellow oil and as a 1:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 2935, 1728 (C=O), 1739 (C=O), 1640, 1449, 1366, 1176, 1094, 1024, 968, 914; δ_H (300 MHz, $CDCl_3$) 1.22 (3H, t, *J* 7.2, OCH_2CH_3 from 1 diastereoisomer), 1.28 (3H, t, *J* 7.2, OCH_2CH_3 from 1 diastereoisomer), 1.68-1.99 (4H, m, 2 × CH_2), 2.02-2.11 (2H, m, $CH_2CH{=}CH_2$), 2.13-2.28 (2H, m, CH_2), 2.47-2.69 (2H, m, $CH_2CH{=}CHAr$), 4.18 (2H, q, *J* 7.2, OCH_2 from 1 diastereoisomer), 4.24 (2H, q, *J* 7.2, OCH_2 from 1 diastereoisomer), 4.29-4.36 (1H, m, C*H* from 1 diastereoisomer), 4.40-4.49 (1H, m, C*H* from 1 diastereoisomer), 4.97-4.09 (2H, m, $CH{=}CH_2$), 5.73-5.86 (1H, m, $CH{=}CH_2$), 6.21 (1H, dt, *J* 15.8 7.2, C*H*=CHAr), 6.49 (1H, d, *J* 15.8, CH=C*H*Ar), 7.20-7.38 (5H, m, Ar-C*H*); δ_C (75 MHz,

$CDCl_3$) 14.0 (*C*H_3 from 1 diastereoisomer), 15.2 (*C*H_3 from 1 diastereoisomer), 25.5 (*C*H_2 from 1 diastereoisomer), 25.9 (*C*H_2 from 1 diastereoisomer), 26.8 (*C*H_2), 28.6 (*C*H_2CH=CH_2 from 1 diastereoisomer), 28.9 (*C*H_2CH=CH_2 from 1 diastereoisomer), 35.3 (*C*H_2 from 1 diastereoisomer), 35.6 (*C*H_2 from 1 diastereoisomer), 38.9 (*C*H_2CH=CHAr 1 diastereoisomer), 39.4 (*C*H_2CH=CHAr 1 diastereoisomer), 61.9 (O*C*H_2 from 1 diastereoisomer), 62.1 (O*C*H_2 from 1 diastereoisomer), 53.1 ((*C*) from 1 diastereoisomer), 53.9 ((*C*) from 1 diastereoisomer), 77.8 (*C*H from 1 diastereoisomer), 81.3 (*C*H from 1 diastereoisomer), 115.2 (CH=*C*H_2 from 1 diastereoisomer), 115.3 (CH=*C*H_2 from 1 diastereoisomer), 123.7 (*C*H=CHAr from 1 diastereoisomer), 123.8 (*C*H=CHAr from 1 diastereoisomer), 126.2 (Ar-*C*H), 127.4 (Ar-*C*H from 1 diastereoisomer), 127.5 (Ar-*C*H from 1 diastereoisomer), 128.5 (Ar-*C*H), 133.7 (CH=*C*HAr), 137.0 (Ar-*C*), 137.4 (*C*H=CH_2), 169.7 (*C*(O) from 1 diastereoisomer), 170.7 (*C*(O) from 1 diastereoisomer), 171.1 (*C*(O) from 1 diastereoisomer), 171.5 (*C*(O) from 1 diastereoisomer); *m/z* (ES+ mode) 365 ((M + Na), 100), 381 (15); (Found: (M + Na), 365.1723. $C_{21}H_{26}O_4Na$ requires M, 365.1723).

rac-(3_R_,6_R_)-3-(But-3-en-1-yl)-6-cinnamyltetrahydro-2H-pyran-2-one 11-_cis_ and _rac_-(3_S_,6_R_)-3-(but-3-en-1-yl)-6-cinnamyltetrahydro-2H-pyran-2-one 11-_trans_



11-*cis*



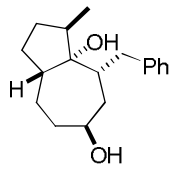
11-*trans*

Ethyl-3-(but-3-enyl)-6-cinnamyl-2-oxotetrahydro-2H-pyran-3-carboxylate (115 mg, 0.34 mmol, 1 eq) was dissolved in DMSO (1 mL) and placed under N_2. To this was added LiCl (24 mg, 0.57 mmol, 1.7 eq) and H_2O (19 µL) and the reaction mixture was heated to 180 °C for 12 hours. After cooling to room temperature, saturated $NaHCO_3$ (5 mL) was added and the reaction diluted with H_2O (5 mL). The aqueous layer was

extracted with Et_2O (3 × 10 mL) and the combined organic layers were washed with brine (10 mL) and dried (Na_2SO_4) followed by concentration *in vacuo* to yield the crude product. Purification by flash column chromatography on silica gel eluting with 30% Et_2O in hexane gave the title compound (44 mg, 0.16 mmol, 49%) as a yellow oil and as a 1:1 mixture of diastereoisomers. The diastereoisomers could be separated by HPLC eluting with 5% Et_2O in hexane; ν_{max} (neat)/cm^{-1} 2924, 2360, 1732 (C=O), 1448, 1379, 1244, 1176, 1062, 963; For the *cis*-lactone: δ_H (400 MHz, $CDCl_3$) 1.46-1.57 (2H, m, 2H from CH_2), 1.65-1.75 (1H from CH_aH$_b$CHOC(O)), 1.94-2.13 (3H, m, 2H from CH_2 + 1H from CH$_a$$H_b$ CHOC(O)), 2.15-2.22 (2H, m, CH_2CH=CH$_2$), 2.45-2.55 (2H, m, 1H for CH_aH$_b$CH=CHPh + 1H from C*H*), 2.61-2.68 (1H, m, CH$_a$$H_b$CH=CHPh), 4.37-4.44 (1H, m, C*H*OC(O)), 5.00 (1H, dd, *J* 10.1, 1.5, CH=CH_aH$_b$), 5.06 (1H, ddd, *J* 17.2, 3.3, 1.5, CH=CH$_a$$H_b$), 5.75-5.85 (1H, m, C*H*=CH$_2$), 6.25 (1H, dt, *J* 15.9, 7.3, C*H*=CHAr), 6.49 (1H, d, *J* 15.9, CH=C*H*Ar), 7.21-7.37 (5H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 23.1 (*C*H$_2$), 26.2 (*C*H$_2$), 29.7 (*C*H$_2$), 30.9 (*C*H$_2$CH=CH$_2$), 37.2 (*C*H), 38.7 (*C*H$_2$CH=CHAr), 77.4 (*C*HOC(O)), 115.4 (CH=*C*H$_2$), 124.2 (*C*H=CHAr), 126.1 (Ar-*C*H), 127.4 (Ar-*C*H), 128.5 (Ar-*C*H), 133.4 (CH=*C*HAr), 137.0 (*C*H=CH$_2$), 175.4 (*C*(O)); *m/z* (ES+ mode) 293 ((M + Na), 100), 271 (23); (Found: (M), 270.1618. $C_{18}H_{22}O_2$ requires M, 270.1614); For the *trans*-lactone: δ_H (400 MHz, $CDCl_3$) 1.42-1.50 (1H, m, 1H from CH_2), 1.54-1.62 (2H, m, 1H from CH_2 + 1H from CH_aH$_b$CHOC(O)), 1.90-2.06 (4H, m, 2H from CH_2 + 1H from CH$_a$$H_b$CHOC(O) + 1H from C$H_aH_b$CH=CH$_2$), 2.08-2.18 (1H, m, 1H from CH$_a$$H_b$CH=CH$_2$), 2.30-2.38 (1H, m, 1H from C*H*), 2.43-2.51 (1H, m, CH_aH$_b$CH=CHAr), 2.52-2.59 (1H, m, CH$_a$$H_b$CH=CHAr), 4.29-4.35 (1H, m, C*H*OC(O)), 4.92 (1H, dd, *J* 10.1, 1.5, CH=CH_aH$_b$), 4.98 (1H, dd, *J* 17.2, 1.5, CH=CH$_a$$H_b$), 5.67-5.77 (1H, m, C*H*=CH$_2$), 6.16 (1H, dt, *J* 15.9, 7.3, C*H*=CHAr), 6.41

(1H, d, *J* 15.9, CH=C*H*Ar), 7.13-7.30 (5H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 25.3 (*C*H_2), 28.3 (*C*H_2), 30.7 (*C*H_2), 30.9 (*C*H_2CH=CH_2), 39.6 (*C*H), 40.0 (*C*H_2CH=CHAr), 80.7 (*C*HOC(O)), 115.4 (CH=*C*H_2), 124.0 (*C*H=CHAr), 126.1 (Ar-*C*H), 127.4 (Ar-*C*H), 128.5 (Ar-*C*H), 133.5 (CH=*C*HAr), 137.0 (Ar-*C*), 137.6 (*C*H=CH_2), 173.7 (*C*(O)).

***rac*-(3*R*, 3a*S*, 4*R*, 6*S*, 8a*S*)-4-Benzyl-3-methyldecahydroazulene-3a,6-diol 12**

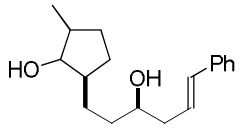


12

As for general procedure B, reaction of *rac*-(3S,6S)-3-(but-3-enyl)-6-cinnamyltetrahydro-2H-pyran-2-one (8 mg, 0.023 mmol, 1 eq) with SmI_2 (0.1 M in THF, 1.80 mL, 0.18 mmol, 8 eq) and H_2O (0.30 mL) after workup and purification by column chromatography on silica gel eluting with 30% Et_2O in hexane gave the title compound (5 mg, 0.016 mmol, 71%) as a white solid and as a 3:1 mixture of diastereoisomers; M.p. 110 ˚C recrystallised from pentane; For major diastereoisomer: ν_{max} (neat)/cm^{-1} 3379, 2919, 2360, 1449, 1115, 1027, 963; δ_H (400 MHz, $CDCl_3$) 1.08 (3H, d, *J* 7.1, C*H*$_3$), 1.26-1.30 (1H, m, 1H from C*H*$_2$), 1.38-1.42 (2H, m, 2H from C*H*$_2$), 1.45-1.49 (2H, m, C*H*$_2$), 1.51 (1H, dd, *J* 9.1 3.0, C*H*$_a$H$_b$CHCH$_2$Ar), 1.83 (1H, dd, *J* 9.1 2.5, CH$_a$*H*$_b$CHCH$_2$Ar), 1.87-1.96 (2H, m, 2H from C*H*$_2$), 1.99-2.05 (1H, m, C*H*), 2.07-2.10 (1H, m, 1H from C*H*$_2$), 2.14 (1H, q, *J* 6.6, C*H*CH$_3$), 2.22-2.28 (1H, m, C*H*CH$_2$Ar), 2.45 (1H, dd, *J* 13.6, 11.9, C*H*$_a$H$_b$Ar), 2.98 (1H, dd, *J* 13.6, 2.3, CH$_a$*H*$_b$Ar), 4.08 (1H, dq, *J* 6.3, 2.3, C*H*OH) 7.18-7.32 (5H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 18.6 (*C*H$_3$), 24.0 (*C*H$_2$), 29.6 (*C*H$_2$), 29.7 (*C*H$_2$), 34.9 (*C*H$_2$CHCH$_2$Ar), 36.2 (*C*H$_2$), 37.0 (*C*H$_2$Ar), 37.8 (CHCH$_2$Ar), 44.6 (*C*HCH$_3$),

45.7 (*C*H), 69.2 (*C*HOH), 85.2 (*C*OH), 125.9 (Ar-*C*H), 128.4 (Ar-*C*H), 129.2 (Ar-*C*H), 141.3 (Ar-*C*); *m/z* (ES+ mode) 297 ((M + Na), 100), 295 (68); (Found: (M + Na), 297.1822. $C_{18}H_{26}O_2Na$ requires M, 297.1825).

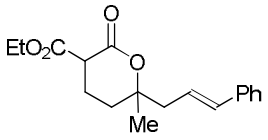
(2*S*)-2-((*R*, *E*)-3-Hydroxy-6-phenylhex-5-enyl)-5-methylcyclopentanol 13



13

As for general procedure B, reaction of *rac*-(3*S*, 6*R*)-3-(but-3-enyl)-6-cinnamyltetrahydro-2H-pyran-2-one (8 mg, 0.030 mmol, 1 eq) with SmI_2 (0.1 M in THF, 2.40 mL, 0.24 mmol, 8 eq) and H_2O (0.43 mL) after workup and purification by column chromatography on silica gel eluting with 30% Et_2O in hexane gave the title compound (6 mg, 0.022 mmol, 75%) as a colourless oil and as a 7:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3369 (OH), 2927, 1455, 1329, 1289, 1135, 1061, 965, 743, 692; For major diastereoisomer: δ_H (400 MHz, $CDCl_3$) 1.04 (3H, d, *J* 6.8, C*H*$_3$), 1.46-1.54 (2H, m, C*H*$_2$CHOH), 1.64-1.72 (3H, m, 3H from 2 × C*H*$_2$), 1.76-1.85 (4H, m, 3H from 2 × C*H*$_2$ + 1H from C*H*CH$_2$), 1.92-2.00 (1H, m, C*H*CH$_3$), 2.34 (1H, ddd, *J* 13.9, 8.4, 7.7, C*H*$_a$H$_b$CH=CHAr), 2.43-2.52 (1H, m, CH$_a$*H*$_b$CH=CHAr), 3.74 (1H, tt, *J* 7.7, 4.3, CH$_2$C*H*OH), 3.88 (1H, dd, *J* 3.2, 3.2, CHC*H*OH), 6.25 (1H, dt, *J* 15.8, 7.72, C*H*=CHAr), 6.49 (1H, d, *J* 15.8, CH=C*H*Ar), 7.20-7.29 (5H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 14.2 (*C*H$_3$), 26.0 (*C*H$_2$), 28.9 (*C*H$_2$), 29.8 (*C*H$_2$), 30.3 (*C*H), 35.5 (*C*H$_2$CHOH), 39.7 (*C*H), 45.9 (*C*H$_2$CH=CHAr), 75.1 (CH$_2$*C*HOH), 77.2 (CH*C*HOH), 125.5 (*C*H=CHAr), 126.1 (Ar-*C*H), 126.3 (Ar-*C*H), 127.3 (CH=*C*HAr), 128.5 (Ar-*C*H), 133.2 (Ar-*C*); *m/z* (ES+ mode) 297 ((M + Na), 100); (Found: (M), 297.1825. $C_{18}H_{26}O_2Na$ requires M, 297.1826).

Ethyl 6-cinnamyl-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate S8

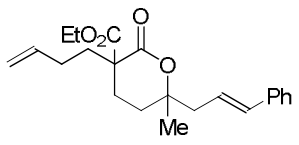


S8

As for general procedure D, 6-cinnamyl-6-methyltetrahydro-2H-pyran-2-one (600 mg, 2.61 mmol, 1 eq) was deprotonated using LDA and treated with Mander's reagent (310 mg, 3.13 mmol, 1.2 eq). After workup and purification by flash chromatography on silica gel eluting with 20% EtOAc in petroleum ether (40 – 60 °C) gave the title compound (346 mg, 1.15 mmol, 44%) as a yellow oil; ν_{max} (neat)/cm^{-1} 2979, 1742 (C=O), 1720 (C=O), 1450, 1370, 1320, 1259, 1176, 1098, 1032, 970, 928; δ_H (400 MHz, $CDCl_3$) 1.27 (3H, t, *J* 7.3, OCH_2CH_3 from 1 diastereoisomer), 1.31 (3H, t, *J* 7.3, OCH_2CH_3 from 1 diastereoisomer), 1.44 (3H, s, CH_3 from 1 diastereoisomer), 1.49 (3H, s, CH_3 from 1 diastereoisomer), 1.67-1.75 (1H, m, CH_aH_b from 1 diastereoisomer), 1.80-1.90 (1H, m, CH_aH_b), 2.00-2.04 (1H, m, CH_aH_b from 1 diastereoisomer), 2.11-2.20 (1H, m, $CHCH_aH_b$), 2.24-2.34 (1H, m, $CHCH_aH_b$), 2.59 (1H, dd, *J* 7.6, 3.5, CH_aH_bCH=CHAr), 2.64 (1H, d, *J* 7.6, CH_aH_bCH=CHAr), 3.44 (1H, dd, *J* 9.6, 7.1, CH from 1 diastereoisomer), 3.51 (1H, t, *J* 7.1, CH from 1 diastereoisomer), 4.20 (2H, q, *J* 7.3, OCH_2CH_3 from 1 diastereoisomer), 4.26 (2H, q, *J* 7.3, OCH_2CH_3 from 1 diastereoisomer), 6.20 (1H, dt, *J* 15.9, 7.6, CH=CHAr), 6.48 (1H, d, *J* 15.9, CH=CHAr), 7.22-7.39 (5H, m, Ar-CH); δ_C (100 MHz, $CDCl_3$) 14.0 (OCH_2CH_3), 20.9 ($CHCH_2$ from 1 diastereoisomer), 21.0 ($CHCH_2$ from 1 diastereoisomer), 26.3 (CH_3 from 1 diastereoisomer), 26.8 (CH_3 from 1 diastereoisomer), 29.7 (CH_2 from 1 diastereoisomer), 30.2 (CH_2 from 1 diastereoisomer), 44.9 (CH_2CH=CHAr from 1 diastereoisomer), 45.7 (CH_2CH=CHAr

from 1 diastereoisomer), 46.9 (*C*H from 1 diastereoisomer), 47.4 (*C*H from 1 diastereoisomer), 61.8 (O*C*H_2CH$_3$ from 1 diastereoisomer), 61.9 (O*C*H_2CH$_3$ from 1 diastereoisomer), 85.1 (*C*), 123.3 (*C*H=CHAr from 1 diastereoisomer), 123.5 (*C*H=CHAr from 1 diastereoisomer), 126.2 (Ar-*C*H), 127.5 (Ar-*C*H from 1 diastereoisomer), 127.6 (Ar-*C*H from 1 diastereoisomer), 128.5 (Ar-*C*H from 1 diastereoisomer), 128.6 (Ar-*C*H from 1 diastereoisomer), 134.4 (CH=*C*HAr from 1 diastereoisomer), 134.6 (CH=*C*HAr from 1 diastereoisomer), 136.8 (Ar-*C* from 1 diastereoisomer), 136.9 (Ar-*C* from 1 diastereoisomer), 166.9 (*C*(O) from 1 diastereoisomer), 167.0 (*C*(O) from 1 diastereoisomer), 169.3 (*C*(O) from 1 diastereoisomer), 169.4 (*C*(O) from 1 diastereoisomer); *m/z* (ES+ mode) 303 ((M + H), 100), 285 (23), 325 (19), 239 (19), 171 (18); (Found: (M + H), 303.1592. $C_{18}H_{23}O_4$ requires M, 303.1591).

Ethyl 3-(but-3-enyl)-6-cinnamyl-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate S9

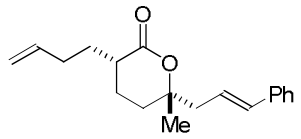


S9

As for general procedure E, reaction of ethyl 6-cinnamyl-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate (329 mg, 1.09 mmol, 1 eq) with NaH (97%, 33 mg, 1.31 mmol, 1.2 eq) and 4-bromobut-1-ene (177 mg, 1.31 mmol, 1.2 eq), after workup and purification by flash column chromatography on silica gel eluting with 10% EtOAc in petroleum ether (40 – 60 °C), gave the title compound (178 mg, 0.50 mmol, 46%) as a yellow oil; ν_{max} (neat)/cm^{-1} 2981, 1739 (C=O), 1720, 1640, 1446, 1379, 1287, 1209, 1152, 1109, 965, 918; δ_H (400 MHz, $CDCl_3$) 1.19 (3H, t, *J* 7.1, OCH$_2$C*H*$_3$ from 1

diastereoisomer), 1.30 (3H, t, *J* 7.3, OCH_2CH_3 from 1 diastereoisomer), 1.42 (3H, s, CH_3 from 1 diastereoisomer), 1.46 (3H, s, CH_3 from 1 diastereoisomer), 1.67-1.82 (2H, m, CH_2), 1.92-2.03 (2H, m, CH_2), 2.06-2.14 (2H, m, CH_2), 2.16-2.28 (2H, m, $CH_2CH=CH_2$), 2.52-2.66 (2H, m, $CH_2CH=CHAr$), 4.06-4.16 (2H, m, OCH_2CH_3 from 1 diastereoisomer), 4.17-4.29 (2H, m, OCH_2CH_3 from 1 diastereoisomer), 4.95-5.09 (2H, m, $CH=CH_2$), 5.73-5.86 (1H, m, $CH=CH_2$), 6.20 (1H, dt, *J* 15.6, 7.6, $CH=CHAr$), 6.46 (1H, d, *J* 15.6, $CH=CHAr$ from 1 diastereoisomer), 6.48 (1H, d, *J* 15.6, $CH=CHAr$ from 1 diastereoisomer), 7.23-7.28 (5H, m, Ar-CH); δ_C (100 MHz, $CDCl_3$) 14.0 (OCH_2CH_3), 26.0 (CH_2), 26.2 ($CH_2CH=CH_2$), 26.4 (CH_3 from 1 diastereoisomer), 27.5 (CH_3 from 1 diastereoisomer), 29.0 (CH_2 from 1 diastereoisomer), 29.4 (CH_2 from 1 diastereoisomer), 35.0 (CH_2 from 1 diastereoisomer), 35.2 (CH_2 from 1 diastereoisomer), 44.8 ($CH_2CH=CHAr$ from 1 diastereoisomer), 46.1 ($CH_2CH=CHAr$ from 1 diastereoisomer), 53.2 (CC(O) from 1 diastereoisomer), 53.5 (CC(O) from 1 diastereoisomer), 61.9 (OCH_2CH_3), 84.9 (CCH_3), 115.3 ($CH=CH_2$), 123.6 ($CH=CHAr$ from 1 diastereoisomer), 123.8 ($CH=CHAr$ from 1 diastereoisomer), 126.2 (Ar-CH), 127.5 (Ar-CH from 1 diastereoisomer), 127.6 (Ar-CH from 1 diastereoisomer), 128.5 (Ar-CH from 1 diastereoisomer), 128.6 (Ar-CH from 1 diastereoisomer), 134.3 ($CH=CHAr$ from 1 diastereoisomer), 134.5 ($CH=CHAr$ from 1 diastereoisomer), 136.8 (Ar-C from 1 diastereoisomer), 137.0 (Ar-C from 1 diastereoisomer), 137.4 ($CH=CH_2$), 169.7 (C(O)), 171.5 (C(O)); *m/z* (ES+ mode) 379 ((M + Na), 100), 395 (15), 357 (9); (Found: (M), 379.1895. $C_{22}H_{28}O_4Na$ requires M, 379.1880).

rac-(3*S*, 6*S*)-3-(But-3-enyl)-6-cinnamyl-6-methyltetrahydro-2H-pyran-2-one 14

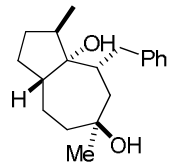


14

Ethyl-3-(but-3-enyl)-6-cinnamyl-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate (160 mg, 0.45 mmol, 1 eq) was dissolved in DMSO (5 mL) and placed under N_2. NaCl (39 mg, 0.67 mmol, 1.1 eq) and H_2O (0.016 mL, 0.90 mmol, 2 eq) were added and the reaction mixture was heated to 180 °C for 12 hours. After cooling to room temperature, saturated $NaHCO_3$ (5 mL) was added and the reaction diluted with H_2O (5 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic layers were washed with brine (10 mL), dried (Na_2SO_4) and concentrated *in vacuo* to give a 1:1 mixture of lactone diastereoisomers. Purification by flash column chromatography on silica gel eluting with 10% EtOAc in petroleum ether (40 – 60 °C) gave the title compound (18 mg, 0.063 mmol, 14%) as a yellow oil; ν_{max} (neat)/cm^{-1} 2920, 1720, 1643, 1545, 1450, 1378, 1356, 1297, 1259, 1200, 1101, 963, 920; δ_H (400 MHz, $CDCl_3$) 1.40 (3H, s, C*H*$_3$), 1.61-1.72 (2H, m, 2H from C*H*$_2$), 1.74-1.81 (1H, m, 1H from C*H*$_2$), 1.85-1.89 (1H, m, 1H from C*H*$_2$), 1.92-2.00 (1H, m, 1H from C*H*$_2$), 2.05-2.15 (2H, m, 1H from C*H*$_a$H$_b$CH=CH$_2$ + 1H from C*H*$_2$), 2.16-2.26 (1H, m, CH$_a$*H*$_b$CH=CH$_2$), 2.31-2.39 (1H, m, C*H*), 2.54 (1H, ddd, *J* 13.9, 7.6, 1.0, C*H*$_a$H$_b$CH=CHAr), 2.60 (1H, ddd, *J* 13.9, 7.3, 1.3, CH$_a$*H*$_b$CH=CHAr), 4.98-5.08 (2H, m, CH=C*H*$_2$), 5.60 (1H, ddt, *J* 16.7, 10.1, 6.3, C*H*=CH$_2$), 6.22 (1H, dt, *J* 15.9, 7.3, C*H*=CHAr), 6.47 (1H, d, *J* 15.9, CH=C*H*Ar), 7.22-7.38 (5H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 22.3 (*C*H$_2$), 26.3 (*C*H$_3$), 30.7 (*C*H$_2$), 30.8 (*C*H$_2$CH=CH$_2$), 31.8 (*C*H$_2$), 39.4 (*C*H), 46.3 (*C*H$_2$CH=CHAr), 83.8 (*C*), 115.4 (CH=*C*H$_2$), 123.9 (*C*H=CHAr), 126.2 (Ar-*C*H), 127.5 (Ar-*C*H), 128.6 (Ar-*C*H), 134.3 (CH=*C*HAr), 137.0 (Ar-*C*),

137.7 (*C*H=CH_2), 173.9 (*C*(O)); *m/z* (ES+ mode) 307 ((M + Na), 100); (Found: (M), 307.1665. $C_{19}H_{24}O_2Na$ requires M, 307.1669).

***rac*-(3*R*, 3a*S*, 4*R*, 6*S*, 8a*S*)-4-Benzyl-3,6-dimethyldecahydroazulene-3a,6-diol 19**

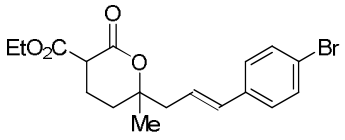


19

As for general procedure B, reaction of *rac*-(3*S*, 6*S*)-3-(but-3-enyl)-6-cinnamyl-6-methyltetrahydro-2H-pyran-2-one (11 mg, 0.039 mmol, 1 eq) with SmI_2 (0.1 M in THF, 3.1 mL, 0.31 mmol, 8 eq) and H_2O (0.60 mL), after workup and purification by flash column chromatography on silica gel eluting with 50% Et_2O in petroleum ether (40 – 60 °C), gave the title compound (10 mg, 0.035 mmol, 90%) as a colourless oil and a 4:1:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3459 (OH), 2935, 1602, 1495, 1453, 1371, 1323, 1142, 1093, 1025, 936, 743, 699, 665; For the major diastereoisomer: δ_H (400 MHz, $CDCl_3$) 1.04 (3H, s, CH_3), 1.11 (3H, d, *J* 7.6, CHCH_3), 1.19 (1H, dd, *J* 15.1, 2.5, C$H_a$$H_bCHCH_2$Ar), 1.26-1.29 (2H, m, 2H from CH_2), 1.35-1.39 (1H, m, C$H_a$$H_bCHCH_3$), 1.67-1.76 (2H, m, 2H from CH_2), 1.77-1.82 (1H, m, C*H*), 1.94 (1H, dd, *J* 15.1, 9.3, C$H_a$$H_bCHCH_2$Ar), 2.01-2.04 (1H, m, C$H_a$$H_bCHCH_3$), 2.07-2.10 (2H, m, 2H from CH_2), 2.12 (1H, dq, *J* 7.6, 5.8, C*H*CH_3), 2.35 (1H, dd, *J* 13.6, 11.9, C$H_a$$H_b$Ar from major diastereoisomer), 2.62 (1H, ddd, *J* 11.9, 9.4, 2.4, C*H*CH_2Ar), 2.91 (1H, dd, *J* 13.6, 1.8, C$H_a$$H_b$Ar from major diastereoisomer), 3.05 (1H, dd, *J* 13.1, 1.5, C$H_a$$H_b$Ar from minor diastereoisomer), 7.20-7.34 (5H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 15.6 (CH*C*H_3), 29.9 (*C*H_2), 31.4 (*C*H_2CHCH_3), 32.5 (*C*H_2), 33.2 (*C*H_3), 36.1 (*C*HCH_2Ar), 37.1 (*C*H_2Ar), 39.9 (*C*H_2CHCH_2Ar), 43.6 (*C*H_2), 45.1 (*C*HCH_3), 53.2 (*C*H), 70.8 (Me*C*OH), 88.2 (*C*OH), 126.0 (Ar-*C*H), 128.4 (Ar-

*C*H), 129.3 (Ar-*C*H), 141.0 (Ar-*C*); *m/z* (ES+ mode) 311 ((M + Na), 100), 253 (51), 271 (38), 414 (17), 289 (11); (Found: (M + Na), 311.1987. $C_{19}H_{28}O_2Na$ requires M, 311.1982).

(*E*)-Ethyl-6-(3-(4-bromophenyl)allyl)-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate S10

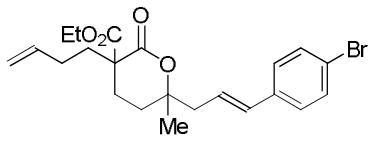


S10

As for general procedure D, 6-(*E*)-6-(3-(4-bromophenyl)allyl)-6-methyltetrahydro-2H-pyran-2-one (475 mg, 1.52 mmol, 1 eq) was deprotonated using LDA and treated with Mander's reagent (221 mg, 2.28 mmol, 1.6 eq). Workup and purification by column chromatography on silica gel, eluting with 20% EtOAc in petroleum ether (40 – 60 °C), gave the title compound (246 mg, 0.65 mmol, 43%) as a yellow oil and as a 1:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 2977, 1740 (C=O), 1486, 1370, 1257, 1178, 1071, 1007; δ_H (400 MHz, $CDCl_3$) 1.17-1.24 (3H, m, C*H*$_3$CH$_2$O), 1.35 (3H, s, C*H*$_3$ from 1 diastereoisomer), 1.40 (3H, s, C*H*$_3$ from 1 diastereoisomer), 1.59-1.66 (1H, m, from C*H*$_2$CCH$_3$), 1.75-180 (1H, m, from C*H*$_2$CCH$_3$), 2.03-2.12 (1H, m, from CHC*H*$_2$CH$_2$), 2.16-2.26 (1H, m, 1H from CHC*H*$_2$CH$_2$), 2.49 (2H, d, *J* 7.31, C*H*$_2$CH=CH from 1 diastereoisomer), 2.51 (2H, d, *J* 7.31, C*H*$_2$CH=CH from 1 diastereoisomer), 3.35 (1H, dd, *J* 7.1, 2.5, C*H*CH$_2$CH$_2$ from 1 diastereoisomer), 3.43 (1H, t, *J* 7.1, C*H*CH$_2$CH$_2$ from 1 diastereoisomer), 4.10-4.18 (2H, m, CH$_3$C*H*$_2$O), 6.11 (1H, ddt, *J* 15.6, 7.31, 3.0, CH$_2$C*H*=CH), 6.34 (1H, d, *J* 15.6, CH$_2$CH=C*H*), 7.13-7.37 (4H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 14.1 (*C*H$_3$CH$_2$O), 20.9 (*C*H$_2$CCH$_3$), 25.8 (*C*H$_3$ from 1 diastereoisomer), 26.3 (*C*H$_3$ from 1 diastereoisomer), 28.1

(CH*C*H$_2$CH$_2$ from 1 diastereoisomer), 28.6 (CH*C*H$_2$CH$_2$ from 1 diastereoisomer), 44.9 (*C*H$_2$CH=CH from 1 diastereoisomer), 45.5 (*C*H$_2$CH=CH from 1 diastereoisomer), 46.8 (*C*HCH$_2$CH$_2$ from 1 diastereoisomer), 47.4 (*C*HCH$_2$CH$_2$ from 1 diastereoisomer), 61.9 (CH$_3$*C*H$_2$O), 85.0 (*C*CH$_3$), 121.3 (Ar-*C*Br), 124.3 (*C*H=CHAr from 1 diastereoisomer), 124.5 (*C*H=CHAr from 1 diastereoisomer), 127.8 (Ar-*C*H), 131.7 (Ar-*C*H), 133.2 (CH=*C*HAr from 1 diastereoisomer) 133.4 (CH=*C*HAr from 1 diastereoisomer), 166.9 (*C*(O)), 167.0 (*C*(O)); *m/z* (ES+ mode) 403 ((M + Na), 95); found: (M + Na), 403.0511. $C_{18}H_{21}BrO_4Na$ requires M, 403.0515.

(*E*)-Ethyl-6-(3-(4-bromophenyl)allyl)-3-(but-3-en-1-yl)-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate S11

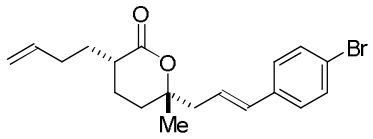


S11

As for general procedure E, reaction of (*E*)-ethyl-6-(3-(4-bromophenyl)allyl)-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate (246 mg, 0.65 mmol, 1 eq) with NaH (60%, 32 mg, 1.29 mmol, 2 eq) and 4-bromobut-1-ene (131 mg, 0.97 mmol, 1.5 eq), after workup and purification by flash chromatography on silica gel eluting with 40% Et$_2$O in petroleum ether (40 – 60 °C), gave the title compound (151 mg, 0.35 mmol, 54%) as a yellow oil as a 1:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 2975, 1723 (C=O), 1486, 1211, 1110, 1008; δ_H (400 MHz, $CDCl_3$) 1.10 (3H, t, *J* 7.3, OCH$_2$C*H*$_3$ from 1 diastereoisomer), 1.19 (3H, t, *J* 7.3, OCH$_2$C*H*$_3$ from 1 diastereoisomer), 1.33 (3H, s, C*H*$_3$ from 1 diastereoisomer), 1.37 (3H, s, C*H*$_3$ from 1 diastereoisomer), 1.58-1.63 (1H, m, 1H from C*H*$_2$ from 1 diastereoisomer), 1.68-1.74

(1H, m, 1H from CH_2 from 1 diastereoisomer), 1.82-1.93 (2H, m, CH_2), 1.82-1.96 (4H, m, 2 × CH_2), 2.08-2.20 (2H, m, CH_2CH=CH$_2$), 2.41-2.46 (1H, m, CH_aCH$_b$CH=CHAr from 1 diastereoisomer), 2.49-2.55 (1H, m, CH$_a$CH_bCH=CHAr from 1 diastereoisomer), 4.04 (2H, q, *J* 7.3, OCH_2 from 1 diastereoisomer), 4.15 (2H, q, *J* 7.3, OCH_2 from 1 diastereoisomer), 4.87-4.99 (2H, m, CH=CH_2), 5.65-5.76 (1H, m, CH=CH$_2$), 6.07-6.17 (1H, dt, *J* 15.8, 7.6, CH=CHAr), 6.32 (1H, d, *J* 15.8, CH=CHAr from 1 diastereoisomer), 6.33 (1H, d, *J* 15.8, CH=CHAr from 1 diastereoisomer), 7.13-7.35 (4H, m, Ar-CH); δ_C (100 MHz, CDCl$_3$) 14.0 (OCH$_2$*C*H$_3$ from 1 diastereoisomer), 14.2 (OCH$_2$*C*H$_3$ from 1 diastereoisomer), 21.0 (*C*H$_3$), 25.9 (*C*H$_2$CH=CH$_2$ from 1 diastereoisomer), 26.2 (*C*H$_2$CH=CH$_2$ from 1 diastereoisomer), 26.4 (*C*H$_2$), 29.0 (*C*H$_2$), 29.5 (CH$_2$ from 1 diastereoisomer), 34.9 (*C*H$_2$), 44.8 (*C*H$_a$CH$_b$CH=CHAr), 46.0 (*C*H$_a$CH$_b$CH=CHAr), 53.2 (*C* from 1 diastereoisomer), 53.5 (*C* from 1 diastereoisomer), 60.4 (CH$_3$*C*H$_2$O from 1 diastereoisomer), 61.9 (CH$_3$*C*H$_2$O from 1 diastereoisomer), 84.7 (*C*CH$_3$) 115.3 (CH=*C*H$_2$), 121.2 (Ar-*C*Br from 1 diastereoisomer), 121.3 (Ar-*C*Br from 1 diastereoisomer), 124.6 (*C*H=CHAr from 1 diastereoisomer), 124.8 (*C*H=CHAr from 1 diastereoisomer), 127.7 (Ar-*C*H), 127.8 (Ar-*C*H), 132.5 (CH=*C*HAr from 1 diastereoisomer), 133.1 (CH=*C*HAr from 1 diastereoisomer), 137.4 (*C*H=CH$_2$), 137.4 (Ar-*C*), 169.6 (*C*(O) from 1 diastereoisomer), 169.7 (*C*(O) from 1 diastereoisomer), 171.1 (*C*(O) from 1 diastereoisomer), 171.4 (*C*(O) from 1 diastereoisomer); *m/z* (ES+ mode) 457 ((M + Na), 100); found: (M + Na), 435.1187. $C_{19}H_{23}BrO_2Na$ requires 435.1166.

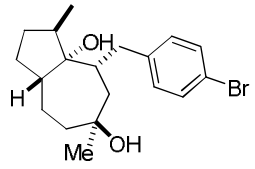
rac-(3*S*, 6*S*)-6-((*E*)-3-(4-Bromophenyl)allyl)-3-(but-3-enyl)-6-methyltetrahydro-2H-pyran-2-one 15



15

(*E*)-Ethyl-6-(3-(4-bromophenyl)allyl)-3-(but-3-en-1-yl)-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate (151 mg, 0.35 mmol, 1 eq) was dissolved in DMSO (4 mL) and placed under N_2. NaCl (31 mg, 0.52 mmol, 1.5 eq) and H_2O (12 μL) were added and the reaction mixture was heated to 165 °C for 12 hours. After cooling to room temperature, H_2O (10 mL) was added and the reaction diluted with Et_2O (15 mL). The aqueous layer was extracted with Et_2O (3 × 30 mL) and the combined organic layers were washed with brine (10 mL), dried (Na_2SO_4) and concentrated *in vacuo* to give a 1:1 crude mixture of lactone diastereoisomers. Purification by flash column chromatography on silica gel eluting with 30% Et_2O in hexane gave the title compound (42 mg, 0.16 mmol, 45%) as a yellow oil; ν_{max} (neat)/cm^{-1} 2945, 1723 (C=O), 1486, 1450, 1380, 1251, 1113, 1007, 971; δ_H (400 MHz, $CDCl_3$); 1.31 (3H, s, C*H*$_3$), 1.54-1.64 (2H, m, C*H*$_2$CH$_2$CH=CH$_2$), 1.68-1.91 (4H, m, 2 × C*H*$_2$), 2.02-2.10 (2H, m, C*H*$_2$CH=CH$_2$), 2.22-2.32 (1H, m, CH$_2$C*H*CH$_2$), 2.45-2.49 (2H, m, C*H*$_2$CH=CHAr), 4.95 (2H, m, CH=*CH*$_2$), 5.66-5.79 (1H, m, C*H*=CH$_2$), 6.14 (1H, m, C*H*=CHAr), 6.33 (1H, d, *J* 15.8, CH=C*H*Ar), 7.13-7.37 (4H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 22.4 (*C*H$_2$), 26.3 (*C*H$_3$), 30.7 (*C*H$_2$), 30.8 (*C*H$_2$), 31.9 (*C*H$_2$), 39.4 (CH$_2$*C*HCH$_2$), 46.3 (*C*H$_2$CH=CHAr), 83.5 (*C*), 115.4 (CH=*C*H$_2$), 121.2 (Ar-*C*Br), 124.9 (*C*H=CHAr), 127.6 (Ar-*C*H), 131.7 (Ar-*C*H) 133.1 (CH=*C*HAr), 136.0 (Ar-*C*), 137.7 (*C*H=CH$_2$), 173.8 (*C*(O)); *m/z* (ES+ mode) 385 ((M + Na), 100), 303 (10); found: (M + Na), 385.0786. $C_{19}H_{23}BrO_2Na$ requires 385.0774.

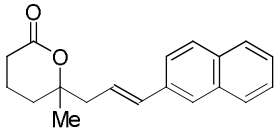
***rac*-(3*R*, 3a*S*, 4*R*, 6*S*, 8a*S*)-4-(4-Bromobenzyl)-3,6-dimethyldecahydroazulene-3a,6-diol 20**



20

As for general procedure B, reaction of (3*S*, 6*S*)-6-((*E*)-3-(4-bromophenyl)allyl)-3-(but-3-en-1-yl)-6-methyltetrahydro-2H-pyran-2-one (12 mg, 0.034 mmol, 1 eq) in THF (3 mL) with SmI_2 (0.1 M in THF, 2.7 mL, 0.27 mmol, 8 eq) and H_2O (0.5 mL), after workup and purification by column chromatography on silica gel eluting with 70% EtOAc in hexane, gave the title compound (9 mg, 0.024 mmol, 71%) as a colourless oil and as a 4:1:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3458 (OH), 2927, 2347, 1487, 1372, 1072, 1010; For major diastereoisomer: δ_H (400 MHz, $CDCl_3$) 0.98 (3H, s, CH_3), 1.01 (3H, d, *J* 7.8, CH_3), 1.03 (2H, m, 2H from CH_2), 1.10-1.13 (1H, dd, *J* 14.8, 2.5, CH_aCH_bCHCH_2Ar), 1.18 (2H, d, *J* 5.4, CH_2), 1.24-1.31 (2H, m, 2H from CH_2), 1.34-1.39 (2H, m, $CH_2CH_2CHCH_3$), 1.68-1.76 (1H, m, CH_2CHCH_2), 1.83 (1H, dd, *J* 14.8, 9.4, $CH_aCH_bCHCH_2Ar$), 1.99-2.05 (1H, m, C*H*CH_3), 2.26 (1H, dd, *J* 12.3, 1.3, CH_aCH_bAr), 2.50-2.54 (1H, m, C*H*CH_2Ar), 2.75 (1H, d, *J* 12.3, CH_aCH_bAr), 7.06-7.25 (4H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 15.6 (*C*H_3CH), 29.8 (*C*H_2), 30.3 (*C*H_2), 31.4 (*C*H_2), 33.3 (*C*H_3), 35.8 (*C*HCH_2Ar), 36.7 (CH*C*H_2Ar), 39.9 (*C*H_2CHCH_2Ar), 43.9 (*C*H_2), 45.1 (*C*HCH_3), 53.5 (CH_2*C*HCH_2), 70.9 (*C*OHCH_3), 88.2 (*C*OH), 119.8 (Ar-*C*Br), 131.1 (Ar-*C*H), 131.5 (Ar-*C*H), 140.1 (Ar-*C*); *m/z* (ES+ mode) 389 ((M + Na), 90), 309 (100), 173 (50). Compound was unstable to accurate mass analysis;

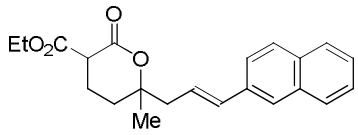
(*E*)-6-Methyl-6-(3-(naphthalen-2-yl)allyl)tetrahydro-2H-pyran-2-one S12



S12

As for general procedure A, reaction of Grubbs 2nd generation catalyst (57 mg, 0.068 mmol, 1 mol%), 6-allyl-6-methyltetrahydro-2H-pyran-2-one (1.04 g, 6.75 mmol, 1 eq), and 2-vinylnaphthalene (3.12 g, 20.3 mmol, 3 eq), after workup and purification by flash chromatography on silica gel eluting with 2% Et_2O in $CHCl_3$, gave the title compound (499 mg, 1.78 mmol, 26%) as a yellow oil; ν_{max} (neat)/cm^{-1} 2976, 1726 (C=O), 1595, 1505, 1450, 1379, 1326, 1232, 1131, 1090, 1052, 969, 925, 862, 817, 746; δ_H (400 MHz, $CDCl_3$) 1.45 (3H, s, C*H*$_3$), 1.71-1.77 (1H, m, 1H from C*H*$_2$), 1.86-1.96 (3H, m, 3H from 2 × C*H*$_2$), 2.44-2.59 (2H, m, C*H*$_2$C(O)), 2.64 (2H, d, *J* 7.6, C*H*$_2$CH=CHAr), 6.34 (1H, dt, *J* 15.9, 7.6, C*H*=CHAr), 6.64 (1H, d, *J* 15.9, CH=C*H*Ar), 7.42-7.49 (2H, m, Ar-C*H*), 7.60 (1H, dd, *J* 8.6, 1.8, Ar-C*H*), 7.72 (1H, s, Ar-C*H*), 7.78-7,82 (3H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 16.6 (*C*H_2), 26.5 (*C*H_3), 29.3 (*C*H_2C(O)), 31.7 (*C*H_2), 45.5 (*C*H_2CH=CHAr), 84.0 (*C*), 123.4 (Ar-*C*H), 124.2 (*C*H=CHAr), 125.8 (Ar-*C*H), 125.9 (Ar-*C*H), 126.2 (Ar-*C*H), 127.6 (Ar-*C*H), 127.9 (Ar-*C*H), 128.2 (Ar-*C*H), 132.8 (Ar-*C*), 133.5 (Ar-*C*), 134.3 (CH=*C*HAr), 134.4 (Ar-*C*), 171.2 (*C*(O)); *m/z* (ES+ mode) 303 ((M + Na), 100), 177 (40); found: (M + Na), 303.1357. $C_{19}H_{20}O_2Na$ requires 303.1356.

(*E*)-Ethyl-6-methyl-6-(3-(naphthalen-2-yl)allyl)-2-oxotetrahydro-2H-pyran-3-carboxylate S13

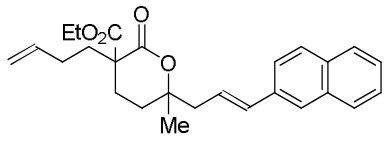


S13

As for general procedure D, (*E*)-6-methyl-6-(3-(naphthalen-2-yl)allyl)tetrahydro-2H-pyran-2-one (583 mg, 2.08 mmol, 1 eq) was deprotonated using LDA and treated with Mander's reagent (248 mg, 2.50 mmol, 1.2 eq). Workup and purification by column chromatography on silica gel, eluting with 25% EtOAc in petroleum ether (40 – 60 °C), gave the title compound (478 mg, 1.36 mmol, 65%) as a yellow oil and as a 1:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 2978, 1741, 1721, 1596, 1507, 1463, 1452, 1381, 1370, 1320, 1255, 1177, 1100, 1032, 971, 928, 862, 812, 748, 622; δ_H (400 MHz, $CDCl_3$) 1.26 (3H, t, *J* 7.1, OCH_2CH_3 from 1 diastereoisomer), 1.31 (3H, t, *J* 7.1, OCH_2CH_3 from 1 diastereoisomer), 1.47 (3H, s, CH_3 from 1 diastereoisomer), 1.52 (3H, s, CH_3 from 1 diastereoisomer), 1.70-1.76 (1H, m, 1H from CH_2 from 1 diastereoisomer), 1.83-1.96 (1H, m, 1H from CH_2), 2.02-2.09 (1H, m, 1H from CH_2 from 1 diastereoisomer), 2.12-2.21 (1H, m, $CHCH_aH_b$), 2.25-2.36 (1H, m, $CHCH_aH_b$), 2.64 (2H, d, *J* 7.6, CH_2CH=CHAr from 1 diastereoisomer), 2.70 (2H, d, *J* 7.6, CH_2CH=CHAr from 1 diastereoisomer), 3.46 (1H, dd, *J* 9.6, 6.8, C*H* from 1 diastereoisomer), 3.53 (1H, t, *J* 7.1, C*H* from 1 diastereoisomer), 4.21 (2H, q, *J* 7.1, OCH_2CH_3 from 1 diastereoisomer), 4.23-4.29 (2H, m, OCH_2CH_3 from 1 diastereoisomer), 6.32 (1H, dt, *J* 15.6, 7.6, C*H*=CHAr from 1 diastereoisomer), 6.33 (1H, dt, *J* 15.6, 7.6, C*H*=CHAr from 1 diastereoisomer), 6.64 (1H, d, *J* 15.6, CH=C*H*Ar from 1 diastereoisomer), 6.65 (1H, d, *J* 15.6, CH=C*H*Ar from 1 diastereoisomer), 7.42-7.49 (2H, m, Ar-C*H*), 7.60 (1H, dd, *J* 7.8, 1.8, Ar-C*H* from 1 diastereoisomer), 7.61 (1H, dd, *J* 7.8, 1.8, Ar-C*H* from 1 diastereoisomer), 7.72 (1H, s, Ar-C*H*), 7.78-7.82 (3H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 14.0 (OCH_2CH_3), 20.9

(CH*C*H$_2$ from 1 diastereoisomer), 21.0 (CH*C*H$_2$ from 1 diastereoisomer), 26.3 (*C*H$_3$ from 1 diastereoisomer), 26.8 (*C*H$_3$ from 1 diastereoisomer), 29.7 (*C*H$_2$ from 1 diastereoisomer), 30.3 (*C*H$_2$ from 1 diastereoisomer), 45.0 (*C*H$_2$CH=CHAr from 1 diastereoisomer), 45.7 (*C*H$_2$CH=CHAr from 1 diastereoisomer), 46.9 (*C*H from 1 diastereoisomer), 47.4 (*C*H from 1 diastereoisomer), 61.8 (O*C*H$_2$CH$_3$ from 1 diastereoisomer), 61.9 (O*C*H$_2$CH$_3$ from 1 diastereoisomer), 85.2 (*C*), 123.4 (Ar-*C*H), 123.7 (*C*H=CHAr from 1 diastereoisomer), 123.9 (*C*H=CHAr from 1 diastereoisomer), 125.8 (Ar-*C*H), 126.0 (Ar-*C*H), 126.3 (Ar-*C*H), 127.6 (Ar-*C*H), 127.9 (Ar-*C*H), 128.1 (Ar-*C*H from 1 diastereoisomer), 128.2 (Ar-*C*H from 1 diastereoisomer), 132.8 (Ar-*C*), 133.5 (Ar-*C*), 134.2 (Ar-*C* from 1 diastereoisomer), 134.3 (Ar-*C* from 1 diastereoisomer), 134.4 (CH=*C*HAr from 1 diastereoisomer), 134.6 (CH=*C*HAr from 1 diastereoisomer), 166.9 (*C*(O) from 1 diastereoisomer), 167.0 (*C*(O) from 1 diastereoisomer), 169.3 (*C*(O) from 1 diastereoisomer), 169.4 (*C*(O) from 1 diastereoisomer); *m/z* (ES+ mode) 375 ((M + Na), 100); found: (M + Na), 353.1743 $C_{22}H_{25}O_4$ requires 353.1748.

(*E*)-Ethyl-3-(but-3-enyl)-6-methyl-6-(3-(naphthalen-2-yl)allyl)-2-oxotetrahydro-2H-pyran-3-carboxylate S14



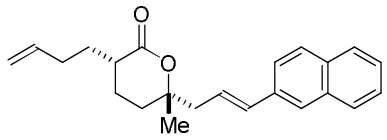
S14

As for general procedure E, reaction of (*E*)-ethyl-6-methyl-6-(3-(naphthalen-2-yl)allyl)-2-oxotetrahydro-2H-pyran-3-carboxylate (400 mg, 1.14 mmol, 1 eq) with NaH (60%, 55 mg, 1.37 mmol, 1.2 eq) and 4-bromobut-1-ene (185 mg, 1.37 mmol, 1.2 eq), after workup and purification by flash column chromatography on silica gel

eluting with 20% EtOAc in petroleum ether (40 – 60 °C), gave the title compound (319 mg, 0.79 mmol, 69%) as a yellow oil and as a 1:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 2976, 1739 (C=O), 1723 (C=O), 1640, 1596, 1506, 1448, 1381, 1219, 1153, 1108, 971, 927, 860, 746; δ_H (400 MHz, $CDCl_3$) 1.17 (3H, t, *J* 7.1, OCH_2CH_3 from 1 diastereoisomer), 1.30 (3H, t, *J* 7.1, OCH_2CH_3 from 1 diastereoisomer), 1.45 (3H, s, CH_3 from 1 diastereoisomer), 1.49 (3H, s, CH_3 from 1 diastereoisomer), 1.70-1.85 (1H, m, 1H from CH_2), 1.95-2.15 (5H, m, 5H from 3 × CH_2), 2.17-2.30 (2H, m, $CH_2CH=CH_2$), 2.57-2.72 (2H, m, $CH_2CH=CHAr$), 4.06-4.15 (2H, m, OCH_2CH_3 from 1 diastereoisomer), 4.20-4.30 (2H, m, OCH_2CH_3 from 1 diastereoisomer), 4.94-5.10 (2H, m, $CH=CH_2$), 5.73-5.86 (1H, m, $CH=CH_2$), 6.31 (1H, dt, *J* 15.9, 7.6, $CH=CHAr$ from 1 diastereoisomer), 6.35 (1H, dt, *J* 15.9, 7.6, $CH=CHAr$ from 1 diastereoisomer), 6.63 (1H, d, *J* 15.9, $CH=CHAr$ from 1 diastereoisomer), 6.64 (1H, d, *J* 15.9, $CH=CHAr$ from 1 diastereoisomer), 7.42-7.49 (2H, m, Ar-CH), 7.58 (1H, dd, *J* 7.8, 1.8, Ar-CH from 1 diastereoisomer), 7.60 (1H, dd, *J* 7.8, 1.8, Ar-CH from 1 diastereoisomer), 7.72 (1H, s, Ar-CH), 7.77-7.82 (3H, m, Ar-CH); δ_C (100 MHz, $CDCl_3$) 14.0 (OCH_2CH_3 from 1 diastereoisomer), 14.1 (OCH_2CH_3 from 1 diastereoisomer), 26.0 (CH_2), 26.2 ($CH_2CH=CH_2$), 26.5 (CH_3 from 1 diastereoisomer), 27.6 (CH_3 from 1 diastereoisomer), 29.0 (CH_2 from 1 diastereoisomer), 29.5 (CH_2 from 1 diastereoisomer), 35.0 (CH_2 from 1 diastereoisomer), 35.2 (CH_2 from 1 diastereoisomer), 44.9 ($CH_2CH=CHAr$ from 1 diastereoisomer), 46.2 ($CH_2CH=CHAr$ from 1 diastereoisomer), 53.2 (*C*C(O) from 1 diastereoisomer), 53.5 (*C*C(O) from 1 diastereoisomer), 61.9 (OCH_2CH_3 from 1 diastereoisomer), 62.0 (OCH_2CH_3 from 1 diastereoisomer), 84.9 (CCH_3), 115.2 ($CH=CH_2$), 123.4 (*C*H=CHAr from 1 diastereoisomer), 123.5 (*C*H=CHAr from 1 diastereoisomer), 124.0 (Ar-*C*H from 1 diastereoisomer), 124.2 (Ar-*C*H from 1 diastereoisomer), 125.8 (Ar-*C*H from 1

diastereoisomer), 125.9 (Ar-*C*H from 1 diastereoisomer), 126.0 (Ar-*C*H), 126.3 (Ar-*C*H), 127.6 (Ar-*C*H), 127.9 (Ar-*C*H), 128.2 (Ar-*C*H), 132.9 (Ar-*C*), 133.5 (Ar-*C*), 134.2 (CH=*C*HAr from 1 diastereoisomer), 134.3 (CH=*C*HAr from 1 diastereoisomer), 134.5 (Ar-*C*), 137.4 (*C*H=CH_2), 169.8 (*C*(O)), 171.5 (*C*(O)); *m/z* (ES+ mode) 429 ((M + Na), 100), 508 (48); found: (M + Na), 407.2201 $C_{26}H_{31}O_4$ requires 407.2217.

rac-(3*S*,6*S*)-3-(But-3-enyl)-6-methyl-6-((*E*)-3-(naphthalen-2-yl)allyl)tetrahydro-2H-pyran-2-one 16

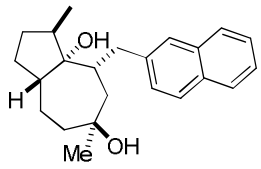


16

(*E*)-Ethyl-3-(but-3-enyl)-6-methyl-6-(3-(naphthalen-2-yl)allyl)-2-oxotetrahydro-2H-pyran-3-carboxylate (300 mg, 0.74 mmol, 1 eq) was dissolved in MeOH (3 mL) and THF (3 mL) before being warmed to 50 ˚C. At this point, LiOH (4.44 mL, 4.44 mmol, 1N solution in H_2O, 6 eq) was added and the reaction left to stir for 18 hours. The reaction mixture was acidified to pH 2 using 1N HCl and extracted with Et_2O (3 × 15 mL). The organic layers were combined, washed with brine (10 mL), dried (Na_2SO_4) and the solvent removed *in vacuo*. The crude acid was dissolved in toluene (6 mL) and heated to reflux for 1 hour then concentrated *in vacuo* to give a crude 1:1 mixture of lactone diastereoisomers. Purification by flash chromatography on silica gel eluting with 10% EtOAc in petroleum ether (40 – 60 °C), gave the title compound (69 mg, 0.21 mmol, 28% over 2 steps) as a yellow oil; ν_{max} (neat)/cm^{-1} 2974, 2947, 1719 (C=O), 1639, 1506, 1451, 1359, 1251, 1113, 970, 913, 815, 747; δ_H (400 MHz, $CDCl_3$) 1.43 (3H, s, CH_3), 1.61-1.84 (3H, m, 3H from CH_2), 1.87-2.00 (2H, m, 2H

from CH_2), 2.06-2.15 (2H, m, 1H from CH_aH$_b$CH=CH$_2$ + 1H from CH_2), 2.17-2.27 (1H, m, CH$_a$$H_b$CH=CH$_2$), 2.33-2.40 (1H, m, C$H$), 2.57-2.68 (2H, m, C$H_2$CH=CHAr), 4.99-5.09 (2H, m, CH=CH_2), 5.81 (1H, ddt, *J* 16.7, 10.1, 6.3, CH=CH$_2$), 6.36 (1H, dt, *J* 15.9, 7.6, CH=CHAr), 6.63 (1H, d, *J* 15.9, CH=CHAr), 7.42-7.49 (2H, m, Ar-CH), 7.60 (1H, dd, *J* 8.6, 1.8, Ar-CH), 7.72 (1H, s, Ar-CH), 7.78-7.82 (3H, m, Ar-CH); δ_C (100 MHz, CDCl$_3$) 22.3 (*C*H$_2$), 26.3 (*C*H$_3$), 30.6 (*C*H$_2$), 30.7 (*C*H$_2$CH=CH$_2$), 31.8 (*C*H$_2$), 39.3 (*C*H), 46.3 (*C*H$_2$CH=CHAr), 83.7 (*C*), 115.4 (CH=*C*H$_2$), 123.5 (*C*H=CHAr), 124.3 (Ar-*C*H), 125.8 (Ar-*C*H), 125.9 (Ar-*C*H), 126.2 (Ar-*C*H), 127.6 (Ar-*C*H), 127.9 (Ar-*C*H), 128.1 (Ar-*C*H), 132.8 (Ar-*C*), 133.5 (Ar-*C*), 134.3 (CH=*C*HAr), 134.4 (Ar-*C*), 137.6 (*C*H=CH$_2$), 173.9 (*C*(O)); *m/z* (ES+ mode) 357 ((M + Na), 100); found: (M + Na), 335.2005. $C_{23}H_{27}O_2Na$ requires 335.2006.

rac-(3_R_,3a_S_,4_R_,6_S_,8a_S_)-3,6-Dimethyl-4-(naphthalen-2-ylmethyl)decahydro-azulene-3a,6-diol 21

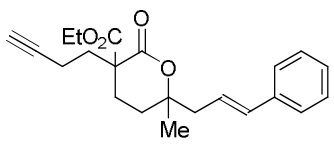


21

As for general procedure X, reaction of *rac*-(3*S*, 6*S*)-3-(but-3-enyl)-6-methyl-6-((*E*)-3-(naphthalen-2-yl)allyl)tetrahydro-2H-pyran-2-one (20 mg, 0.060 mmol, 1 eq) in THF (3 mL) with SmI_2 (0.1 M in THF, 4.80 mL, 0.48 mmol, 8 eq) and H_2O (0.86 mL) after workup and purification by column chromatography on silica gel eluting with 40% Et_2O in hexane gave the title compound (16 mg, 0.047 mmol, 79%) as a colourless oil and as a 3:1:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3445 (OH), 2921, 1493, 1452, 1370, 1314, 1229, 1151, 1104, 1018, 927, 868, 791, 755, 732; δ_H (400 MHz, CDCl$_3$) 0.98 (3H, s, CH_3 from minor diastereoisomer), 0.99 (3H, s, CH_3),

1.17 (3H, d, *J* 7.3, CHC*H*$_3$), 1.26-1.32 (1H, m, C*H*$_a$H$_b$CHCH$_2$Ar), 1.36-1.56 (3H, m, 3H from C*H*$_2$), 1.68-1.93 (4H, m, 1H from C*H* + 3H from C*H*$_2$), 1.99 (1H, dd, *J* 15.1, 9.6, CH$_a$*H*$_b$CHCH$_2$Ar), 2.04-2.25 (3H, m, 1H from C*H*CH$_3$ + 2H from C*H*$_2$), 2.16-2.23 (1H, m, C*H*CH$_3$ from minor diastereoisomer), 2.42 (1H, dd, *J* 12.6, 9.3, C*H*$_a$H$_b$Ar from minor diastereoisomer), 2.54 (1H, dd, *J* 13.4, 12.1, C*H*$_a$H$_b$Ar), 2.78 (1H, ddd, *J* 12.6, 9.3, 2.8, C*H*CH$_2$Ar), 3.06 (1H, d, *J* 12.6, CH$_a$*H*$_b$Ar from minor diastereoisomer), 3.21 (1H, d, *J* 13.4, CH$_a$*H*$_b$Ar); 7.38-7.50 (3H, m, Ar-C*H*), 7.66 (1H, s, Ar-C*H* from minor diastereoisomer), 7.69 (1H, s, Ar-C*H*), 7.80-7.84 (3H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 15.7 (CH*C*H$_3$), 16.6 (CH*C*H$_3$ from minor diastereoisomer), 27.6 (*C*H$_2$ from minor diastereoisomer), 30.0 (*C*H$_2$), 31.5 (*C*H$_2$), 32.5 (*C*H$_2$), 32.8 (*C*H$_2$ from minor diastereoisomer), 33.2 (*C*H$_3$), 33.7 (*C*H$_2$ from minor diastereoisomer), 35.8 (*C*HCH$_2$Ar), 37.2 (*C*H$_2$Ar from minor diastereoisomer), 37.3 (*C*H$_2$Ar), 40.0 (*C*H$_2$CHCH$_2$Ar), 40.4 (*C*H$_2$CHCH$_2$Ar from minor diastereoisomer), 41.9 (*C*H$_2$ from minor diastereoisomer), 43.7 (*C*H$_2$), 45.1 (*C*HCH$_3$), 53.3 (*C*H), 55.6 (*C*H from minor diastereoisomer), 70.9 (Me*C*OH), 71.0 (Me*C*OH from minor diastereoisomer), 85.2 (*C*OH from minor diastereoisomer), 88.3 (*C*OH), 125.3 (Ar-*C*H), 126.0 (Ar-*C*H), 127.5 (Ar-*C*H), 127.6 (2 × Ar-*C*H), 127.7 (Ar-*C*H), 128.1 (Ar-*C*H), 132.1 (Ar-*C*), 133.5 (Ar-*C*), 138.5 (Ar-*C*); *m/z* (ES+ mode) 361 ((M + Na); found: (M + Na), 361.2137. $C_{23}H_{30}O_2Na$ requires 361.2139.

Ethyl-3-(but-3-yn-1-yl)-6-cinnamyl-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate S15

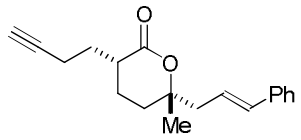


S15

As for general procedure E, reaction of ethyl 6-cinnamyl-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate (584 mg, 1.93 mmol, 1 eq) with NaH (60%, 93 mg, 2.32 mmol, 1.2 eq) and 4-bromobut-1-yne (309 mg, 2.32 mmol, 1.2 eq), after workup and purification by flash column chromatography on silica gel eluting with 20% EtOAc in petroleum ether (40 – 60 °C), gave the title compound (354 mg, 0.72 mmol, 37%) as a yellow oil and as a 1:1 mixture of diastereoisomers; ν_{max} (neat)/cm-1 3281, 2979, 1733 (C=O), 1717 (C=O), 1449, 1233, 1106, 969, 928; δ_H (400 MHz, $CDCl_3$) 1.18 (3H, t, *J* 7.3, OCH_2CH_3 from 1 diastereoisomer), 1.22-1.26 (1H, m, 1H from CH_2), 1.30 (3H, t, *J* 7.3, OCH_2CH_3 from 1 diastereoisomer), 1.43 (3H, s, CH_3 from 1 diastereoisomer), 1.46 (3H, s, CH_3 from 1 diastereoisomer), 1.68-1.81 (1H, m, 1H from CH_2), 1.97 (1H, t, *J* 2.5, C≡C*H* from 1 diastereoisomer), 1.98 (1H, t, *J* 2.5, C≡C*H* from 1 diastereoisomer), 2.04-2.14 (2H, m, CH_2), 2.19-2.29 (2H, m, CH_2), 2.33-2.47 (2H, m, CH_2), 2.55 (1H, dd, *J* 14.1, 7.6, CH_aH_bCH=CHAr), 2.63 (1H, dd, *J* 14.1, 7.6, CH_aH_bCH=CHAr), 4.06-4.16 (2H, m, OCH_2CH_3 from 1 diastereoisomer), 4.17-4.31 (2H, m, OCH_2CH_3 from 1 diastereoisomer), 6.15 (1H, dt, *J* 15.6, 7.6, C*H*=CHAr from 1 diastereoisomer), 6.20 (1H, dt, *J* 15.9, 7.6, C*H*=CHAr from 1 diastereoisomer), 6.47 (1H, d, *J* 15.6, CH=C*H*Ar from 1 diastereoisomer), 6.49 (1H, d, *J* 15.9, CH=C*H*Ar from 1 diastereoisomer), 7.23-7.38 (5H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 14.0 (OCH_2CH_3), 14.5 (CH_2), 26.2 (CH_2), 26.4 (CH_3 from 1 diastereoisomer), 27.4 (CH_3 from 1 diastereoisomer), 29.2 (CH_2), 34.4 (CH_2 from 1 diastereoisomer), 34.7 (CH_2 from 1 diastereoisomer), 44.8 (CH_2CH=CHAr from 1 diastereoisomer), 45.9 (CH_2CH=CHAr from 1 diastereoisomer), 52.9 (*C*C(O) from 1 diastereoisomer), 53.1 (*C*C(O) from 1 diastereoisomer), 62.1 (OCH_2CH_3), 69.0 (C≡*C*H from 1 diastereoisomer), 69.1 (C≡*C*H from 1 diastereoisomer), 83.3 (*C*≡CH), 85.1 (CCH_3), 123.4 (*C*H=CHAr from 1 diastereoisomer), 123.6 (*C*H=CHAr from 1

diastereoisomer), 126.2 (Ar-*C*H), 127.5 (Ar-*C*H from 1 diastereoisomer), 127.6 (Ar-*C*H from 1 diastereoisomer), 128.5 (Ar-*C*H from 1 diastereoisomer), 128.6 (Ar-*C*H from 1 diastereoisomer), 134.3 (CH=*C*HAr from 1 diastereoisomer), 134.5 (CH=*C*HAr from 1 diastereoisomer), 136.8 (Ar-*C* from 1 diastereoisomer), 136.9 (Ar-*C* from 1 diastereoisomer), 169.3 (*C*(O)), 171.0 (*C*(O) from 1 diastereoisomer), 171.1 (*C*(O) from 1 diastereoisomer); *m/z* (ES+ mode) 471 (100), 377 ((M + Na), 89), 562 (42); (Found: (M), 355.1899. $C_{22}H_{27}O_4$ requires M, 355.1904).

***rac*-(3*S*, 6*S*)-3-(But-3-ynyl)-6-cinnamyl-6-methyltetrahydro-2H-pyran-2-one 17**

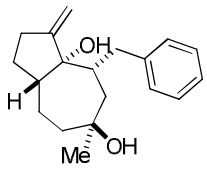


17

Ethyl-3-(but-3-yn-1-yl)-6-cinnamyl-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate (89 mg, 0.25 mmol, 1 eq) was dissolved in MeOH (2 mL) and THF (2 mL) before being warmed to 50 ˚C. LiOH (1.50 mL, 1.50 mmol, 1 N solution in H_2O, 6 eq) was added and the reaction left to stir for 5 hours. The reaction mixture was acidified to pH 2 using 1N HCl and extracted with Et_2O (3 × 15 mL). The organic layers were combined, washed with brine (10 mL), dried (Na_2SO_4) and the solvent removed *in vacuo*. The crude acid was dissolved in toluene (6 mL) and heated to reflux for 1 hour then concentrated in *vacuo* to give a 1:1 crude mixture of lactone diastereoisomers. Purification by flash chromatography on silica gel eluting with 10% EtOAc in petroleum ether (40 – 60 °C) gave the title compound (42 mg, 0.15 mmol, 59% over 2 steps) as a yellow oil; ν_{max} (neat)/cm^{-1} 3289, 2941, 1717 (C=O), 1446, 1102, 967, 744; δ_H (400 MHz, $CDCl_3$) 1.41 (3H, s, CH_3), 1.66-1.83 (3H, m, 3H from CH_2), 1.98-2.04 (2H, m, 2H from CH_2), 2.18-2.25 (1H, m, 1H from CH_2), 1.96 (1H, t, *J* 2.5, C≡C*H*),

2.32 (1H, ddt, *J* 9.3, 7.1, 2.5, C*H*$_a$H$_b$C≡CH), 2.43 (1H, ddt, *J* 9.3, 6.8, 2.5, CH$_a$*H*$_b$C≡CH), 2.51-2.54 (1H, m, C*H*), 2.58 (1H, dd, *J* 13.1, 7.3, C*H*$_a$H$_b$CH=CHAr), 2.59 (1H, dd, *J* 13.1, 7.3, CH$_a$*H*$_b$CH=CHAr), 6.22 (1H, dt, *J* 15.9, 7.3, C*H*=CHAr), 6.48 (1H, d, *J* 15.9, CH=C*H*Ar), 7.22-7.35 (5H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 16.1 (*C*H$_2$CCH), 22.5 (*C*H$_2$), 26.3 (*C*H$_3$), 30.2 (*C*H$_2$), 31.9 (*C*H$_2$), 38.9 (*C*H), 46.3 (*C*H$_2$CH=CHAr), 69.3 (CH$_2$CC≡*C*H), 83.1 (*C*≡CH), 83.9 (*C*), 123.8 (*C*H=CHAr), 126.2 (Ar-*C*H), 127.5 (Ar-*C*H), 128.6 (Ar-*C*H), 134.3 (CH=*C*HAr), 137.0 (Ar-*C*), 173.5 (*C*(O)); *m/z* (ES+ mode) 305 ((M + Na), 100), 587 (70), 358 (27), 133(27); (Found: (M + Na), 305.1515. $C_{19}H_{22}O_2Na$ requires M, 305.1512).

rac-(3a*S*, 4*R*, 6*S*, 8a*S*)-4-Benzyl-6-methyl-3-methylenedecahydroazulene-3a,6-diol 22

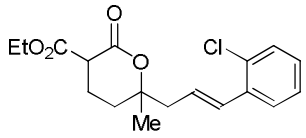


22

As for general procedure B, reaction of *rac*-(3*S*, 6*S*)-3-(but-3-ynyl)-6-cinnamyl-6-methyltetrahydro-2H-pyran-2-one (13 mg, 0.046 mmol, 1 eq) in THF (2 mL) with SmI_2 (0.1 M in THF, 3.70 mL, 3.70 mmol, 8 eq) and H_2O (1.0 mL), after workup and purification by column chromatography on silica gel eluting with 60% EtOAc in hexane, gave the title compound (7 mg, 0.024 mmol, 50%) as a colourless oil and as a 10:2:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3442 (OH), 2950, 2915, 2858, 1648, 1597, 1499, 1454, 1369, 1130, 1106, 1065, 1028, 1010, 943, 891, 739, 692; for the major diastereoisomer: δ_H (400 MHz, $CDCl_3$) 1.02 (3H, s, C*H*$_3$), 1.15 (1H, dd, *J* 14.6, 6.6, C*H*$_a$H$_b$CHCH$_2$Ar), 1.43-1.61 (4H, m, 4H from 2 × C*H*$_2$), 1.63-1.70 (1H, m, 1H from C*H*$_2$), 1.75-1.85 (1H, m, 1H from C*H*$_2$), 1.91 (1H, ddd, *J* 15.1, 8.3, 3.5, C*H*),

2.09 (1H, dd, *J* 14.6, 8.1, $CH_aH_bCHCH_2Ar$), 2.16 (1H, dd, *J* 8.1, 6.6, $CHCH_2Ar$), 2.23 (1H, d, *J* 12.6, CH_aH_bAr), 2.40 (2H, dt, *J* 7.1, 2.0, $CH_2C{=}CH_2$), 2.99 (1H, d, *J* 12.6, CH_aH_bAr), 4.97 (1H, t, *J* 2.0, $C{=}CH_aH_b$), 5.05 (1H, t, *J* 2.0, $C{=}CH_aH_b$), 7.09-7.23 (5H, m, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 24.9 (CH_2), 26.2 (CH_2), 28.8 ($CH_2C{=}CH_2$), 32.0 (CH_3), 36.5 ($CHCH_2Ar$), 37.2 (CH_2), 37.3 (CH_2Ar), 39.9 (CH_2CHCH_2Ar), 51.2 (*C*H), 72.1 (Me*C*OH), 83.7 (*C*OH), 107.5 ($C{=}CH_2$), 125.8 (Ar-*C*H), 128.3 (Ar-*C*H), 129.3 (Ar-*C*H), 141.5 (Ar-*C*), 157.4 ($C{=}CH_2$); *m/z* (ES+ mode) 309 ((M + Na), 100), 369 (90), 251 (85); (Found: (M + Na), 309.1823. $C_{19}H_{26}O_2Na$ requires M, 309.1826).

Ethyl-6-(3-(2-chlorophenyl)allyl)-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate S16

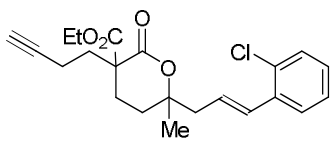


S16

As for general procedure D, 6-(3-(2-chlorophenyl)allyl)-6-methyltetrahydro-2H-pyran-2-one (830 mg, 2.99 mmol, 1 eq) was deprotonated using LDA and treated with Mander's reagent (356 mg, 3.59 mmol, 1.2 eq). Workup and purification by flash chromatography on silica gel, eluting with a 20% EtOAc in petroleum ether (40 – 60 °C), gave the title compound (675 mg, 1.93 mmol, 65%) as a yellow oil; ν_{max} (neat)/cm^{-1} 2977, 1741 (C=O), 1723 (C=O), 1470, 1370, 1319, 1256, 1178, 1101, 1032, 970, 929, 753; δ_H (400 MHz, $CDCl_3$) 1.26 (3H, t, *J* 7.1, OCH_2CH_3 from 1 diastereoisomer), 1.31 (3H, t, *J* 7.1, OCH_2CH_3 from 1 diastereoisomer), 1.45 (3H, s, CH_3 from 1 diastereoisomer), 1.50 (3H, s, CH_3 from 1 diastereoisomer), 1.69-1.75 (1H, m, 1H from CH_2 from 1 diastereoisomer), 1.81-1.95 (1H, m, 1H from CH_2 from 1 diastereoisomer), 2.00-2.07 (1H, m, 1H from CH_2), 2.12-2.21 (1H, m, $CHCH_aH_b$),

2.25-2.35 (1H, m, $CHCH_aH_b$), 2.66 (2H, dd, *J* 19.4, 7.3, CH_2CH=CHAr), 3.44 (1H, dd, *J* 9.6 7.1, C*H* from 1 diastereoisomer), 3.61 (1H, t, *J* 6.8, C*H* from 1 diastereoisomer), 4.20 (2H, q, *J* 7.3, OCH_2CH_3 from 1 diastereoisomer), 4.23-4.29 (2H, m, OCH_2CH_3 from 1 diastereoisomer), 6.19 (1H, ddd, *J* 15.9, 7.3, 4.3, C*H*=CHAr), 6.86 (1H, d, *J* 15.6, CH=C*H*Ar), 7.15-7.25 (2H, m, Ar-C*H*), 7.35 (1H, dt, *J* 7.6, 1.8, Ar-C*H*), 7.52 (1H, dt, *J* 7.6, 1.8, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 14.0 (OCH_2CH_3), 20.9 ($CHCH_2$ from 1 diastereoisomer), 21.0 ($CHCH_2$ from 1 diastereoisomer), 26.3 (CH_3 from 1 diastereoisomer), 26.8 (CH_3 from 1 diastereoisomer), 29.8 (CH_2 from 1 diastereoisomer), 30.3 (CH_2 from 1 diastereoisomer), 45.0 (CH_2CH=CHAr from 1 diastereoisomer), 45.7 (CH_2CH=CHAr from 1 diastereoisomer), 46.8 (*C*H from 1 diastereoisomer), 47.4 (*C*H from 1 diastereoisomer), 61.8 (OCH_2CH_3 from 1 diastereoisomer), 61.9 (OCH_2CH_3 from 1 diastereoisomer), 85.0 (*C*), 126.4 (Ar-*C*H), 126.6 (Ar-*C*H from 1 diastereoisomer), 126.8 (Ar-*C*H from 1 diastereoisomer), 126.9 (*C*H=CHAr), 128.5 (Ar-*C*H from 1 diastereoisomer), 128.6 (Ar-*C*H from 1 diastereoisomer), 129.6 (Ar-*C*H), 130.6 (CH=*C*HAr from 1 diastereoisomer), 130.8 (CH=*C*HAr from 1 diastereoisomer), 132.7 (Ar-*C*Cl), 135.0 (Ar-*C* from 1 diastereoisomer), 135.1 (Ar-*C* from 1 diastereoisomer), 166.9 (*C*(O)), 169.3 (*C*(O)); *m/z* (ES+ mode) 359 ((M + Na), 100), 361 (35), 337 (34); (Found: (M), 337.1202. $C_{18}H_{22}O_4Cl$ requires M, 337.1202).

(*E*)-Ethyl-3-(but-3-ynyl)-6-(3-(2-chlorophenyl)allyl)-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate S17

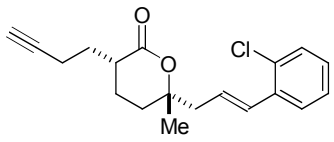


S17

As for general procedure E, reaction of ethyl 6-(3-(2-chlorophenyl)allyl)-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate (750 mg, 2.14 mmol, 1 eq) with NaH (60%, 103 mg, 2.57 mmol, 1.2 eq) and 4-bromobut-1-yne (342 mg, 2.57 mmol, 1.2 eq) after workup and purification by flash column chromatography on silica gel, eluting with 20% EtOAc in petroleum ether (40 – 60 °C), gave the title compound (324 mg, 0.84 mmol, 39%) as a yellow oil and as a 1:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3283, 2974, 2924, 1737 (C=O), 1717 (C=O), 1469, 1443, 1379, 1298, 1236, 1208, 1102, 973, 926, 750, 629; δ_H (400 MHz, $CDCl_3$) 1.18 (3H, t, *J* 7.3, OCH_2CH_3 from 1 diastereoisomer), 1.30 (3H, t, *J* 7.3, OCH_2CH_3 from 1 diastereoisomer), 1.44 (3H, s, CH_3 from 1 diastereoisomer), 1.47 (3H, s, CH_3 from 1 diastereoisomer), 1.70-1.82 (1H, m, 1H from CH_2), 1.97 (1H, t, *J* 2.8, $CH_2C{\equiv}CH$ from 1 diastereoisomer), 1.99 (1H, t, *J* 2.5, $CH_2CC{\equiv}CH$ from 1 diastereoisomer), 1.96-2.02 (1H, m, 1H from CH_2), 2.07-2.19 (2H, m, CH_2), 2.22-2.28 (2H, m, CH_2), 2.29-2.48 (2H, m, CH_2), 2.57-2.61 (1H, m, $CH_aH_bCH{=}CHAr$), 2.65-2.70 (1H, m, $CH_aH_bCH{=}CHAr$), 4.08-4.17 (2H, m, OCH_2CH_3 from 1 diastereoisomer), 4.20-4.29 (2H, m, OCH_2CH_3 from 1 diastereoisomer), 6.15 (1H, dt, *J* 15.6, 7.6, $CH{=}CHAr$ from 1 diastereoisomer), 6.20 (1H, dt, *J* 15.6, 7.6, $CH{=}CHAr$ from 1 diastereoisomer), 6.83 (1H, d, *J* 15.6, $CH{=}CHAr$ from 1 diastereoisomer), 6.86 (1H, d, *J* 15.6, $CH{=}CHAr$ from 1 diastereoisomer), 7.19 (1H, td, *J* 7.6, 1.6, Ar-CH), 7.23 (1H, dd, *J* 7.6, 1.6, Ar-CH), 7.35 (1H, td, *J* 7.6, 1.6, Ar-CH), 7.52 (1H, dd, *J* 7.6, 1.6, Ar-CH from 1 diastereoisomer), 7.51 (1H, dd, *J* 7.6, 1.6, Ar-CH from 1 diastereoisomer); δ_C (100 MHz, $CDCl_3$) 13.9 (OCH_2CH_3 from 1 diastereoisomer), 14.0 (OCH_2CH_3 from 1 diastereoisomer), 14.5 (CH_2), 26.3 (CH_2 from 1 diastereoisomer), 26.4 (CH_2 from 1 diastereoisomer), 26.5 (CH_3 from 1 diastereoisomer), 27.3 (CH_3 from 1 diastereoisomer), 29.3 (CH_2), 34.4 (CH_2 from 1 diastereoisomer), 34.7 (CH_2 from 1

diastereoisomer), 44.9 (*C*H_2CH=CHAr from 1 diastereoisomer), 46.0 (*C*H_2CH=CHAr from 1 diastereoisomer), 53.0 (*C*C(O) from 1 diastereoisomer), 53.2 (*C*C(O) from 1 diastereoisomer), 62.1 (CH_2*C*CH), 69.1 (O*C*H_2CH_3), 83.3 (CH_2C*C*H), 84.9 (*C*CH_3), 126.6 (Ar-*C*H), 126.8 (*C*H=CHAr from 1 diastereoisomer), 126.9 (*C*H=CHAr from 1 diastereoisomer), 128.5 (Ar-*C*H), 128.6 (Ar-*C*H), 129.6 (Ar-*C*H), 130.5 (CH=*C*HAr from 1 diastereoisomer), 130.8 (CH=*C*HAr from 1 diastereoisomer), 132.7 (Ar-*C*Cl), 135.0 (Ar-*C* from 1 diastereoisomer), 135.1 (Ar-*C* from 1 diastereoisomer), 169.3 (*C*(O)), 170.9 (*C*(O) from 1 diastereoisomer), 171.0 (*C*(O) from 1 diastereoisomer); *m/z* (ES+ mode) 411 ((M + Na), 100), 413 (34), 389 (27); (Found: (M), 389.1519. $C_{22}H_{26}O_4Cl$ requires M, 389.1514).

rac-(3_S_, 6_S_)-3-(But-3-ynyl)-6-((_E_)-3-(2-chlorophenyl)allyl)-6-methyltetrahydro-2H-pyran-2-one 18

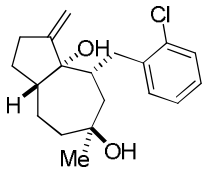


18

(*E*)-Ethyl-3-(but-3-ynyl)-6-(3-(2-chlorophenyl)allyl)-6-methyl-2-oxotetrahydro-2H-pyran-3-carboxylate (325 mg, 0.84 mmol, 1 eq) was dissolved in MeOH (3 mL) and THF (3 mL) before being warmed to 50 ˚C. At this point, LiOH (5 mL, 5.03 mmol, 1 N solution in H_2O, 6 eq) was added and the reaction left to stir for 4 hours. The reaction mixture was acidified to pH 2 using 1 N HCl and extracted with Et_2O (3 × 15 mL). The organic layers were combined, washed with brine (10 mL), dried (Na_2SO_4) and the solvent removed *in vacuo*. The crude acid was dissolved in toluene (6 mL) and heated to reflux for 1 hour then concentrated in *vacuo* to give a 1:1 crude mixture of lactone diastereoisomers. Purification by flash chromatography on silica gel eluting

with 2% Et_2O in $CHCl_3$ gave the title compound (44 mg, 0.14 mmol, 17% over 2 steps) as a colourless oil; ν_{max} (neat)/cm^{-1} 3300, 2924, 1717 (C=O), 1471, 1437, 1376, 1245, 1108, 1032, 976, 744; δ_H (400 MHz, $CDCl_3$) 1.41 (3H, s, C*H*$_3$), 1.68-1.75 (1H, m, 1H from C*H*$_2$), 1.77-1.84 (1H, m, 1H from C*H*$_2$), 1.97 (1H, t, *J* 2.8, CH_2CCH), 1.98-2.04 (2H, m, 2H from C*H*$_2$), 2.18-2.30 (2H, m, 2H from C*H*$_2$), 2.31-2.35 (1H, m, C*H*$_a$H$_b$C≡CH), 2.40-2.48 (1H, m, CH$_a$*H*$_b$C≡CH), 2.46-2.54 (1H, m, C*H*), 2.59 (1H, ddd, *J* 14.1, 7.8, 1.3, C*H*$_a$H$_b$CH=CHAr), 2.65 (1H, ddd, *J* 14.1, 7.8, 1.3, CH$_a$*H*$_b$CH=CHAr), 6.21 (1H, dt, *J* 15.9, 7.6, C*H*=CHAr), 6.35 (1H, d, *J* 15.9, CH=C*H*Ar), 7.21 (1H, td, *J* 7.3, 2.0, Ar-C*H*), 7.19 (1H, dd, *J* 7.3, 1.3, Ar-C*H*), 7.35 (1H, td, *J* 7.8, 1.3, Ar-C*H*), 7.52 (1H, dd, *J* 7.8, 2.0, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 16.1 (*C*H_2CCH), 22.5 (*C*H_2), 26.3 (*C*H_3), 30.2 (*C*H_2), 31.9 (*C*H_2), 38.9 (*C*H), 46.3 (*C*H_2CH=CHAr), 69.3 (CH_2C≡*C*H), 83.1 (*C*), 83.8 (CH_2*C*≡CH), 126.8 (Ar-*C*H + *C*H=CHAr), 126.9 (Ar-*C*H), 128.5 (Ar-*C*H), 129.6 (Ar-*C*H), 130.5 (CH=*C*HAr), 132.7 (Ar-*C*), 135.1 (Ar-*C*Cl), 173.4 (*C*(O)); *m/z* (ES+ mode) 339 ((M + Na), 100), (Found: (M), 339.1130. $C_{19}H_{21}O_2ClNa$ requires M, 339.1122).

rac-(3a*S*, 4*R*, 6*S*, 8a*S*)-4-(2-Chlorobenzyl)-6-methyl-3-methylenedecahydro-azulene-3a,6-diol 23



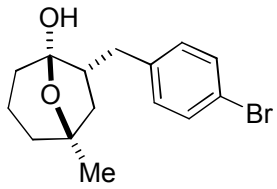
23

As for general procedure B, reaction of *rac*-(3*S*, 6*S*)-3-(but-3-ynyl)-6-((*E*)-3-(2-chlorophenyl)allyl)-6-methyltetrahydro-2H-pyran-2-one (12 mg, 0.038 mmol, 1 eq) in THF (3 mL) with SmI_2 (0.1 M in THF, 3.0 mL, 0.30 mmol, 8 eq) and H_2O (0.55 mL), after workup and purification by column chromatography on silica gel, eluting with

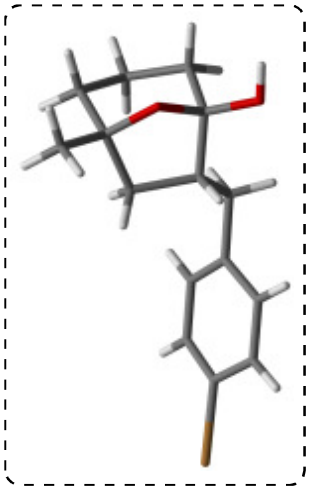
40% Et_2O in hexane, gave the title compound (6 mg, 0.019 mmol, 50%) as a colourless oil and as a 8:1 mixture of diastereoisomers; ν_{max} (neat)/cm^{-1} 3445 (OH), 2952, 2929, 2857, 1471, 1440, 1370, 1127, 1062, 939, 889, 746; For major diastereoiosmer: δ_H (400 MHz, $CDCl_3$) 1.13 (3H, s, C*H*$_3$), 1.21 (2H, d, *J* 9.6, C*H*$_2$CHCH$_2$Ar), 1.61-1.75 (5H, m, 5H from 3 × C*H*$_2$), 1.77-1.85 (1H, m, 1H from C*H*$_2$), 1.98 (1H, q, *J* 5.6, C*H*COH), 2.27 (1H, ddt, J 9.6, 7.3, 1.8, C*H*CH$_2$Ar), 2.40-2.60 (2H, m, C*H*$_2$C=CH$_2$), 2.48 (1H, dd, *J* 13.4, 7.3, C*H*$_a$H$_b$Ar), 3.09 (1H, dd, *J* 13.4, 1.8, CH$_a$*H*$_b$Ar), 5.06 (1H, t, *J* 1.8, C=C*H*$_a$H$_b$), 5.10 (1H, t, *J* 1.8, C=CH$_a$*H*$_b$), 7.13 (1H, dt, *J* 7.6, 1.8, Ar-C*H*), 7.20 (1H, dt, *J* 7.6, 1.3, Ar-C*H*), 7.25 (1H, dd, *J* 7.6, 1.8, Ar-C*H*), 7.34 (1H, dd, *J* 7.6, 1.3, Ar-C*H*); δ_C (100 MHz, $CDCl_3$) 24.3 (*C*H$_2$), 25.5 (*C*H$_2$), 28.2 (*C*H$_2$), 28.5 (*C*H$_2$C=CH$_2$), 31.8 (*C*H$_3$), 34.4 (*C*H$_2$Ar), 34.9 (*C*HCH$_2$Ar), 39.4 (*C*H$_2$CHCH$_2$Ar), 51.2 (*C*H), 72.5 (Me*C*OH), 88.3 (*C*OH), 107.4 (C=*C*H$_2$), 125.3 (Ar-*C*H), 127.3 (2 × Ar-*C*H), 129.6 (Ar-*C*H), 131.7 (Ar-*C*Cl), 139.1 (Ar-*C*), 145.3 (*C*=CH$_2$); *m/z* (ES+ mode) 343 ((M + Na), 100), (Found: (M), 343.1433. $C_{19}H_{25}O_2ClNa$ requires M, 343.1435).

X-ray structure of major diastereoisomer: 9l

CCDC = 804694



Major diastereoisomer
9l



X-ray structure of major diastereoisomer: 9j

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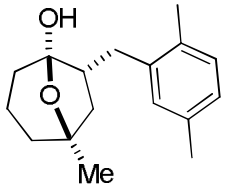
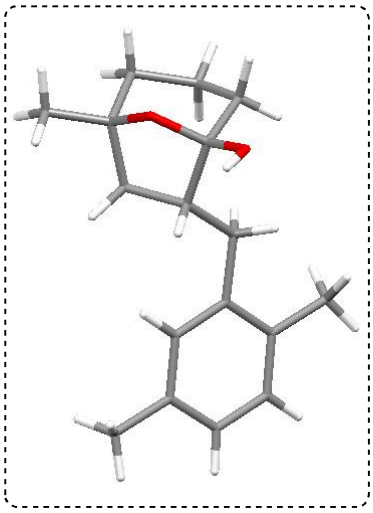
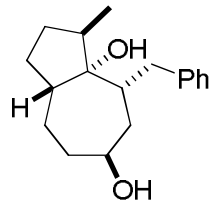


Major diastereoisomer
9j

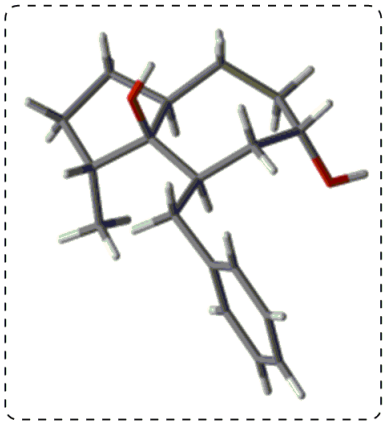


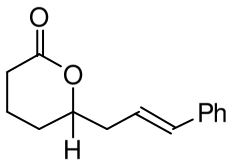
X-ray structure of major diastereoisomer: 12

CCDC = 804696

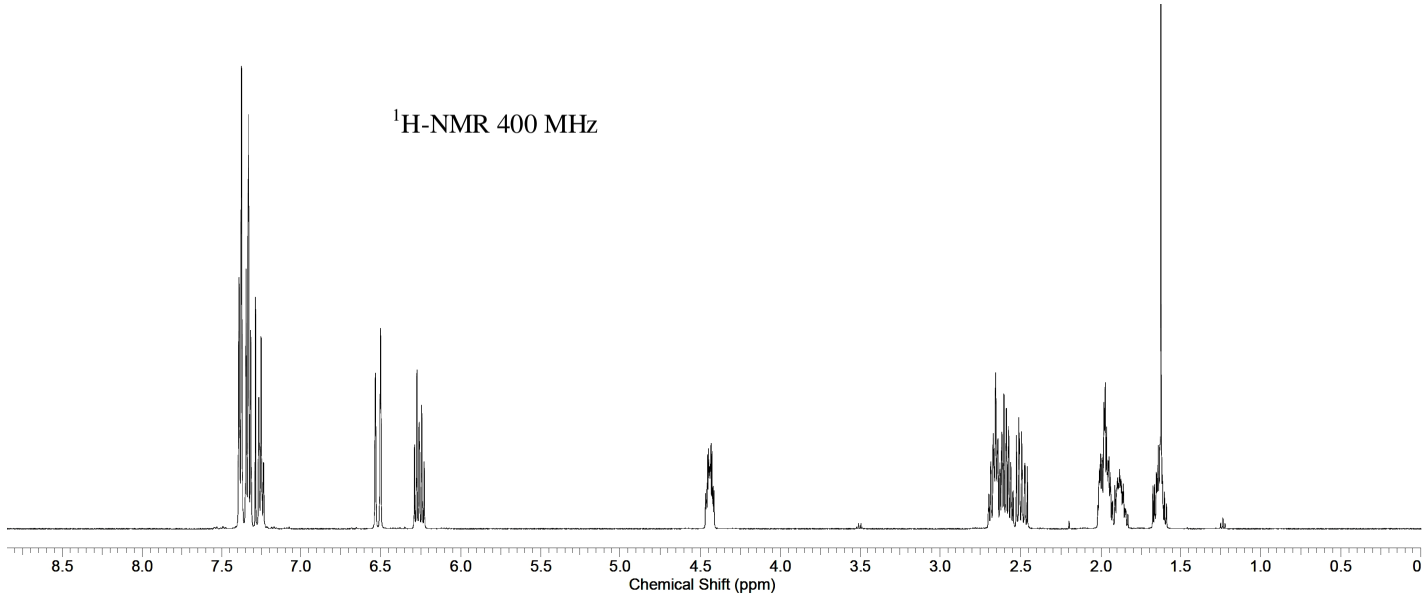


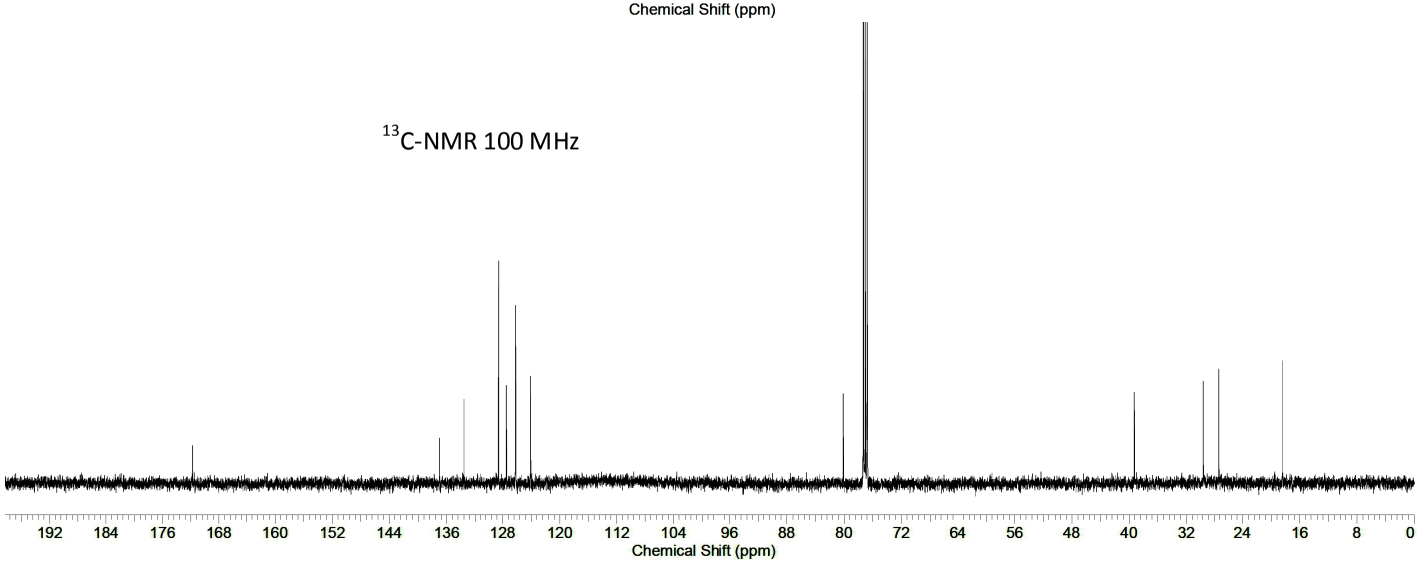
Major diastereoisomer
12

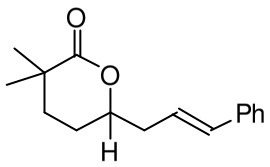



O
O
Ph
H

6a

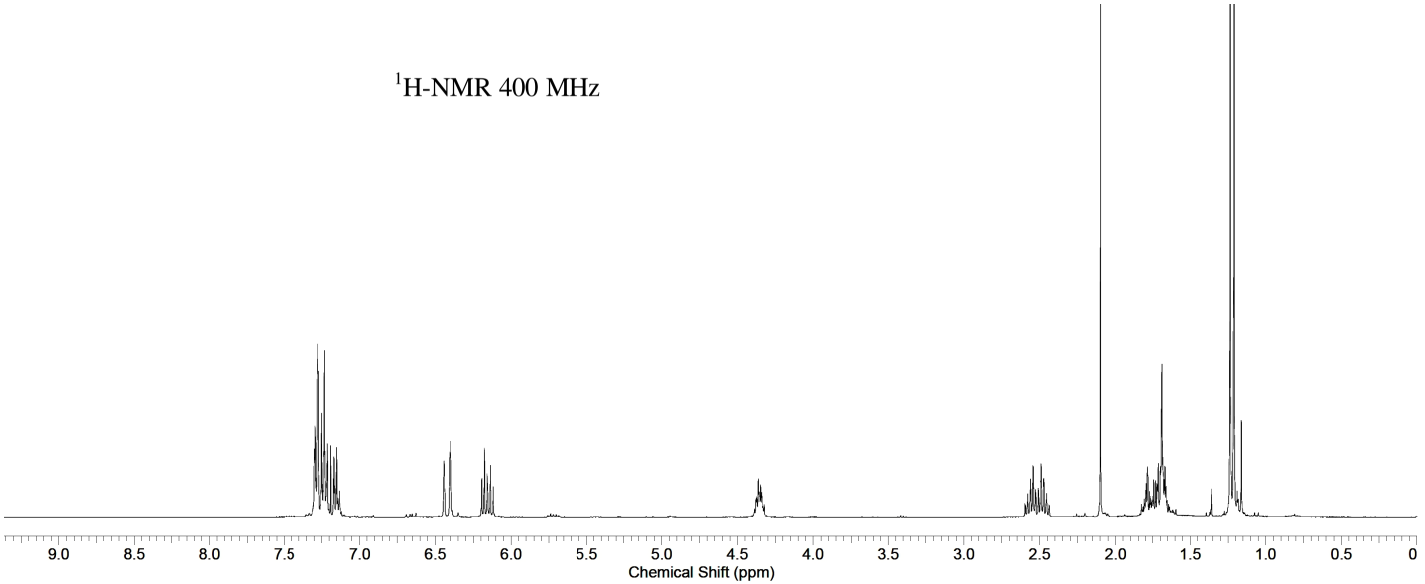

^{1}H-NMR 400 MHz
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


^{13}C-NMR 100 MHz
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)



6b

^{1}H-NMR 400 MHz



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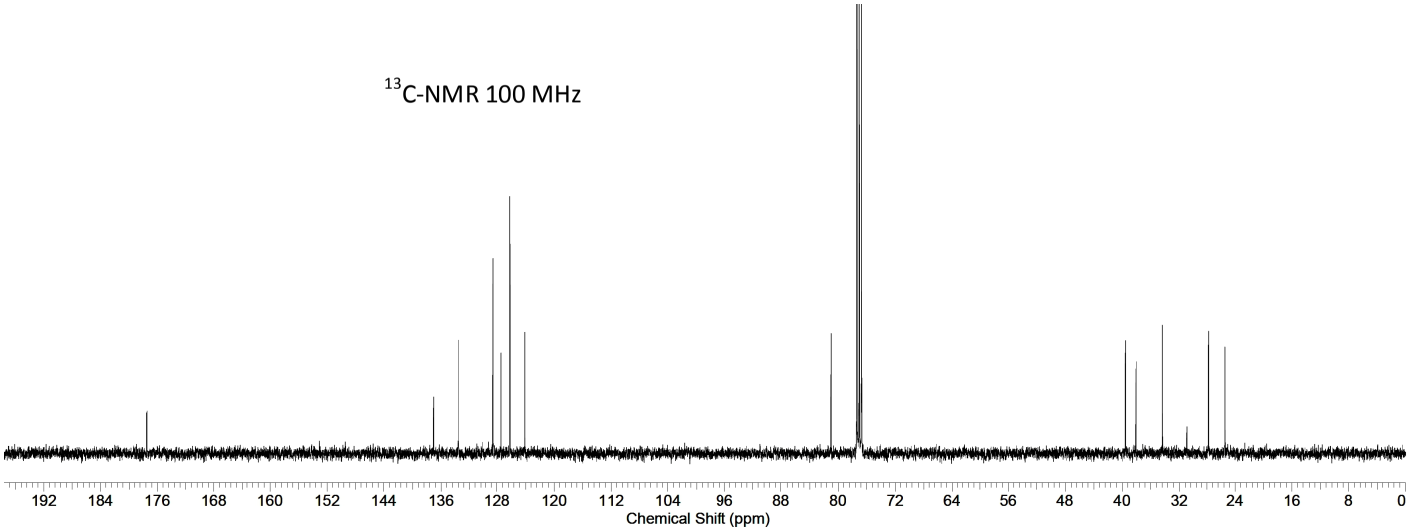

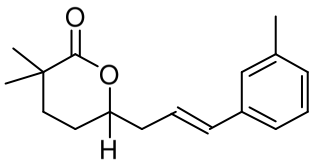

6d

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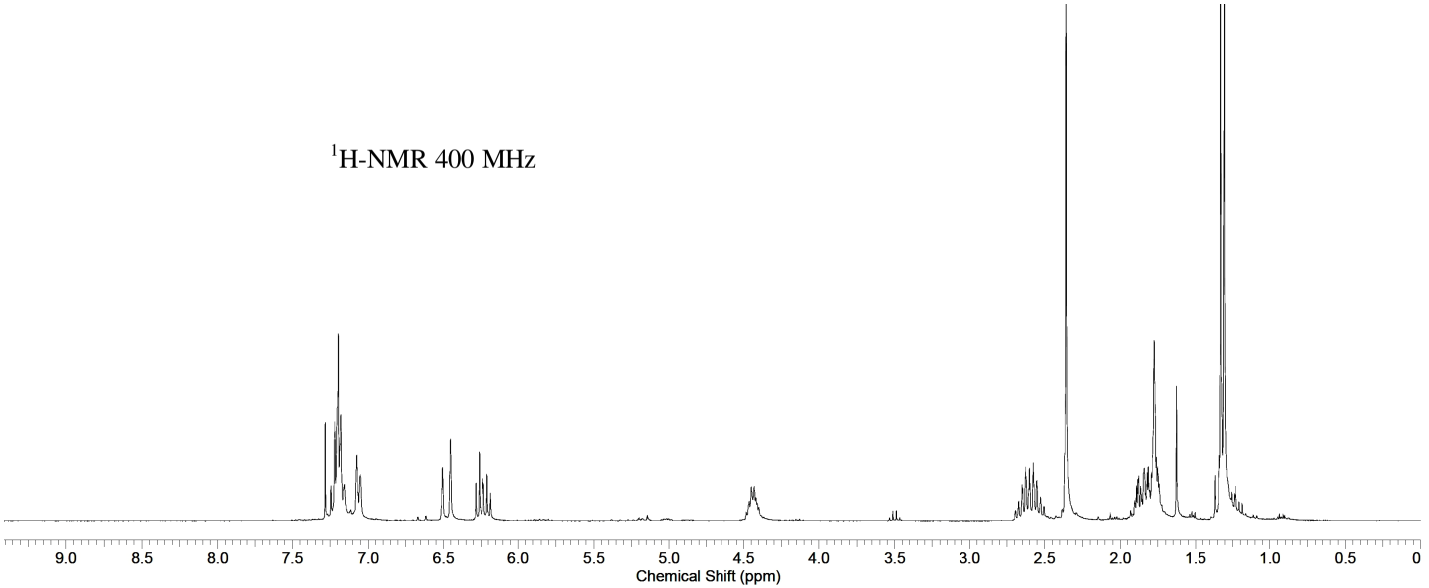
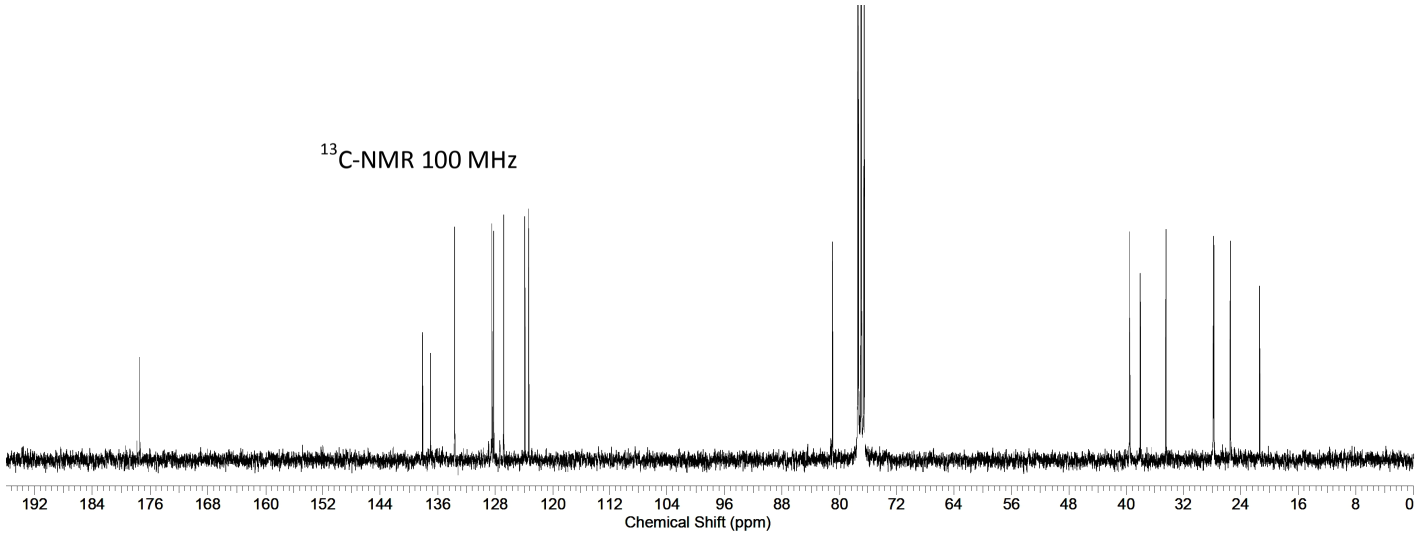
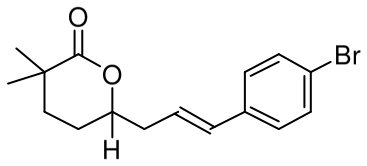


^{13}C-NMR 100 MHz





6e

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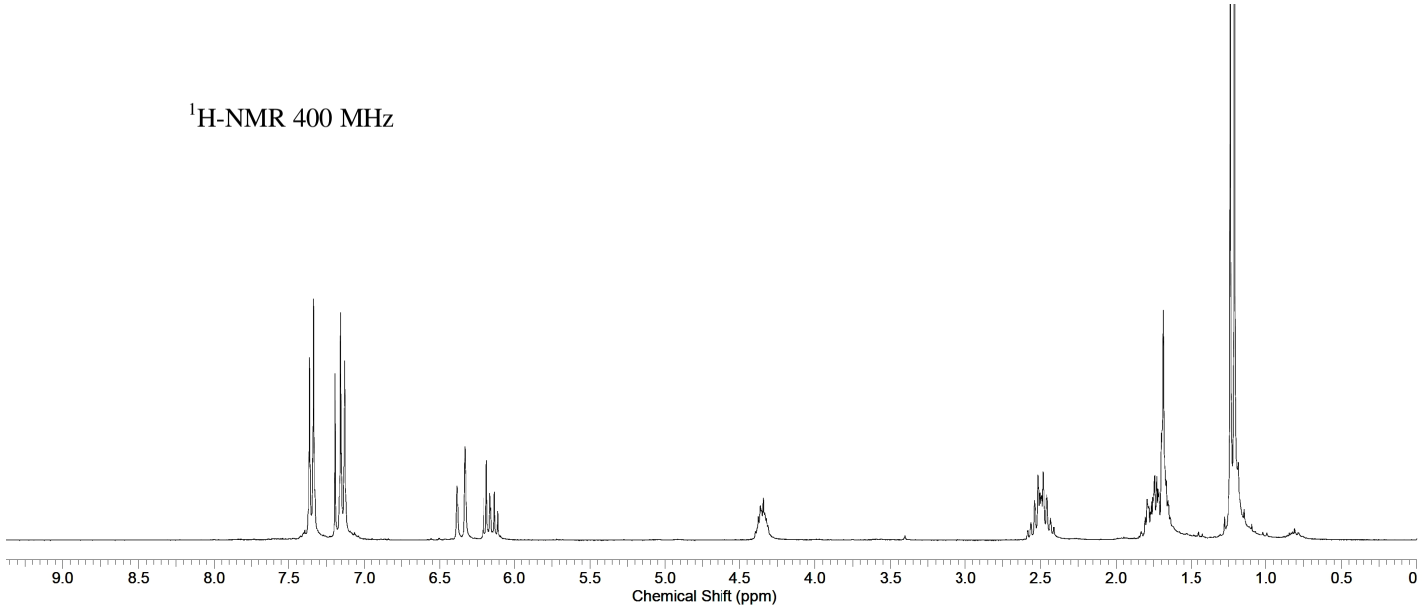

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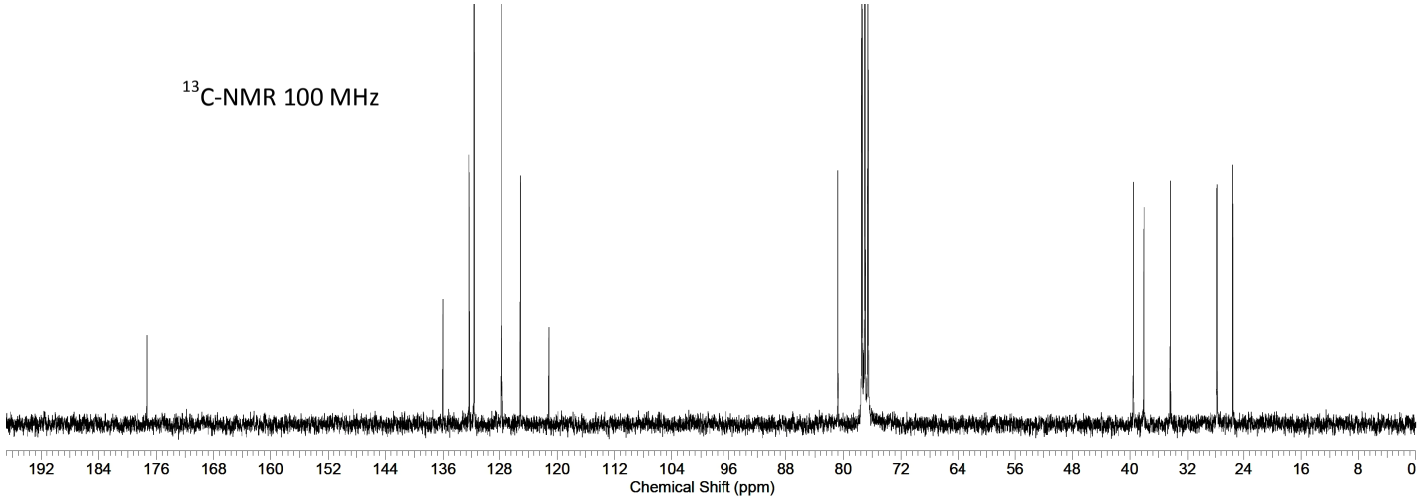

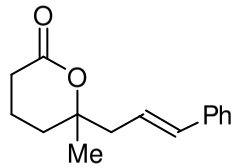

6h

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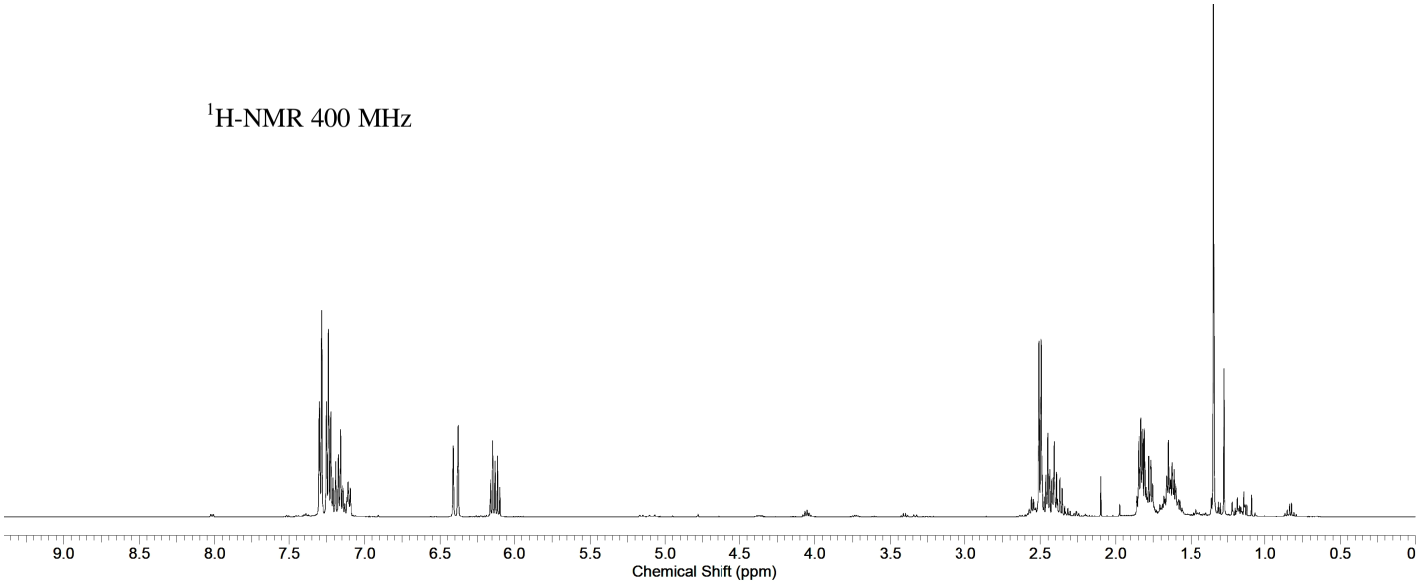

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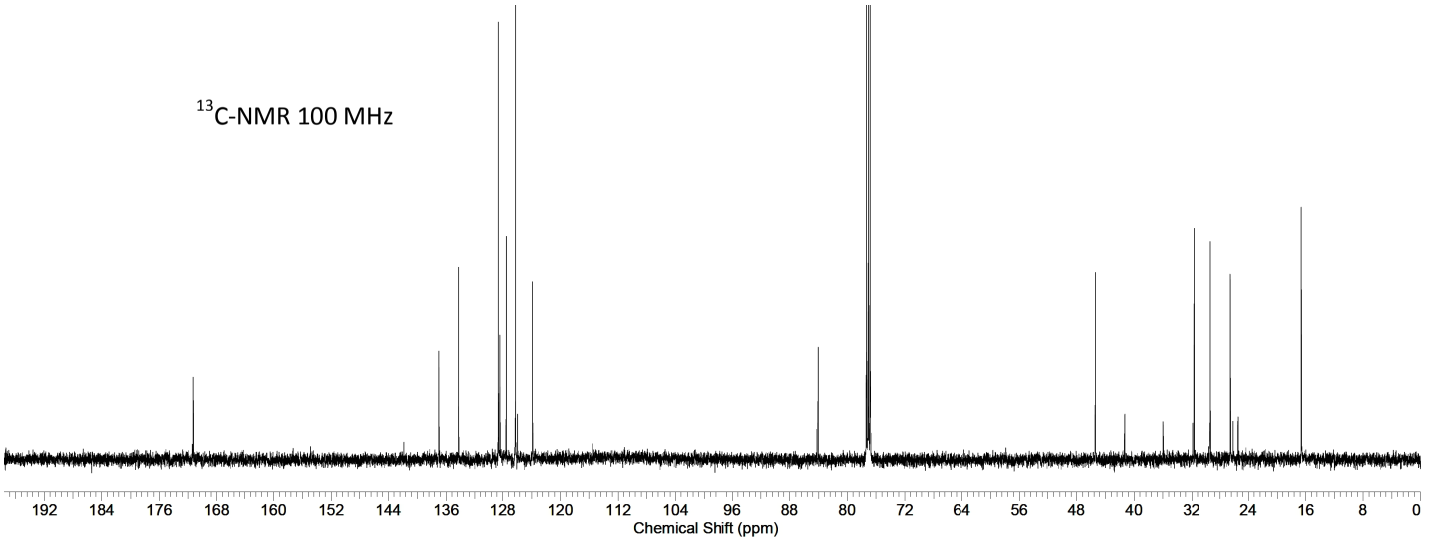
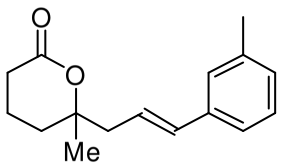
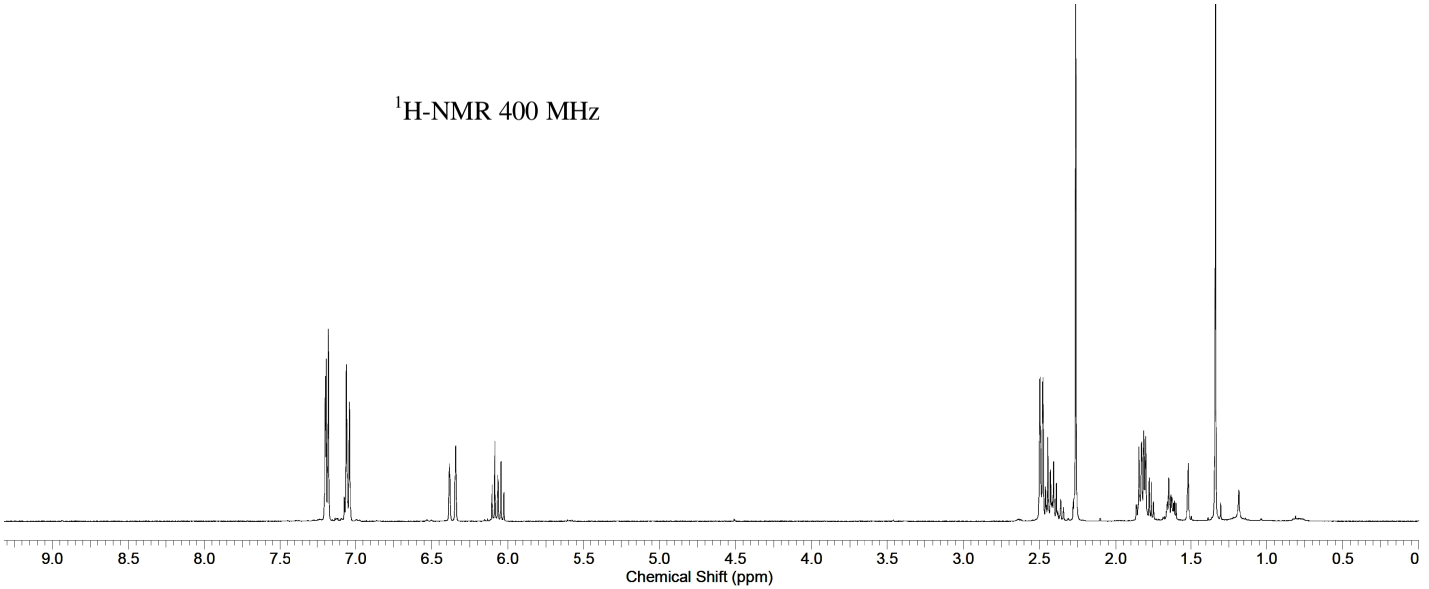




6i

^{1}H-NMR 400 MHz



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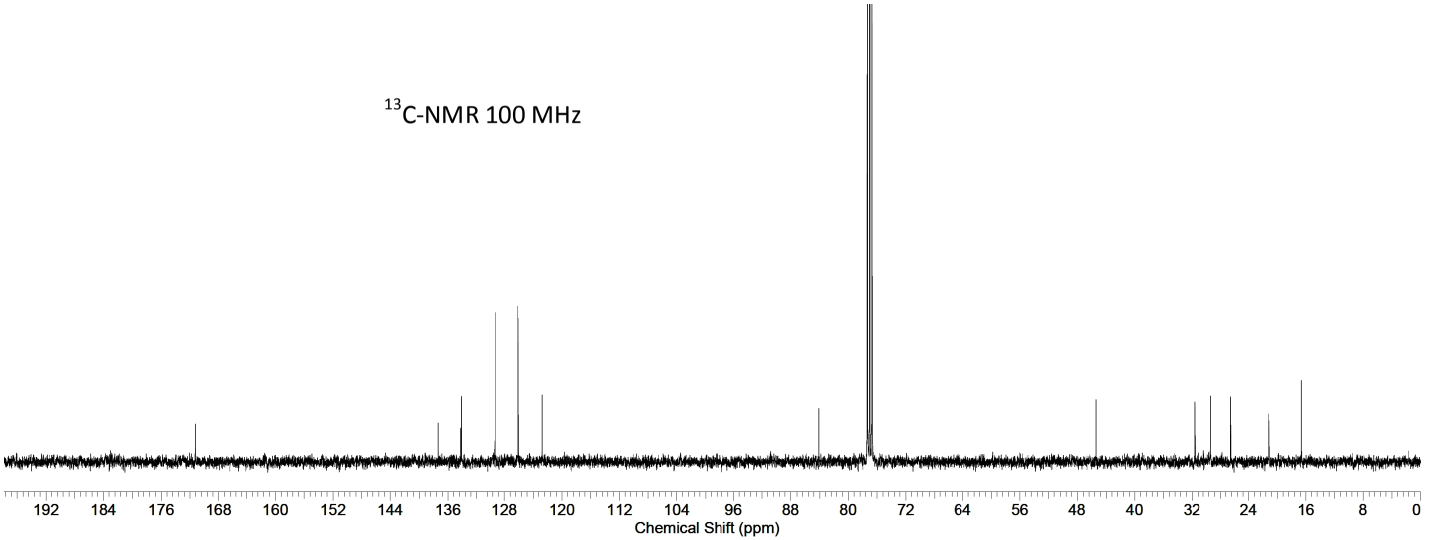

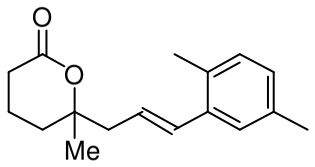

6j

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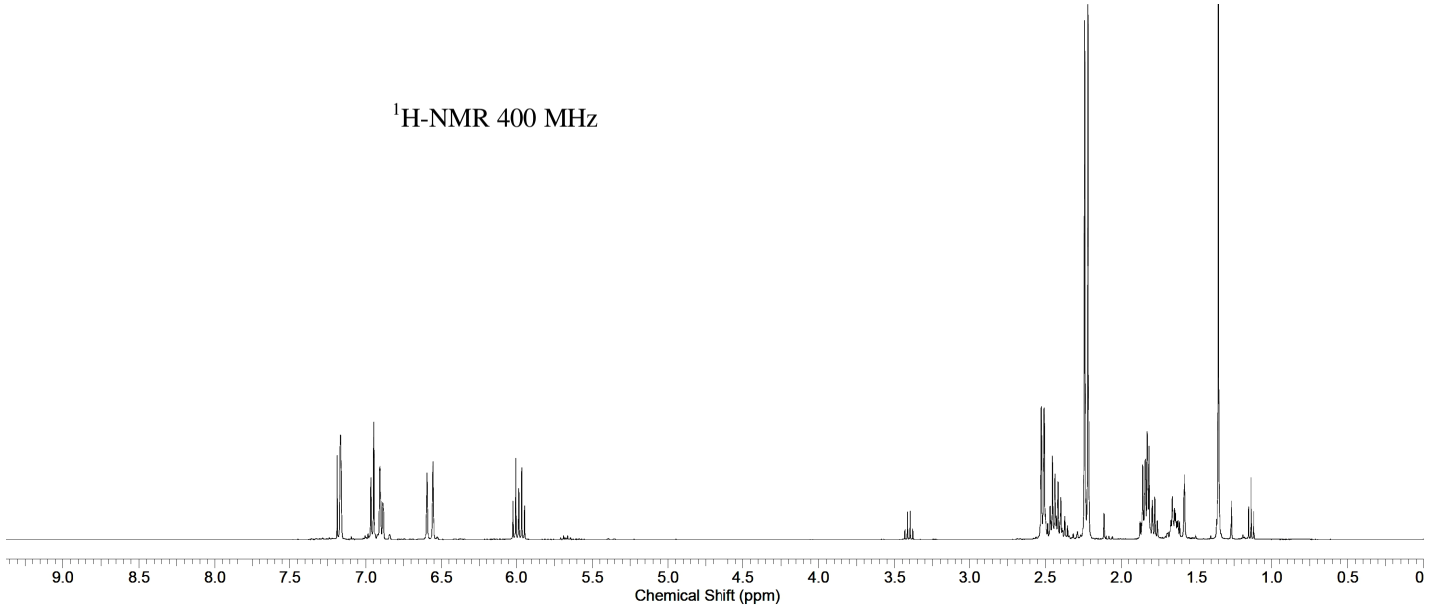

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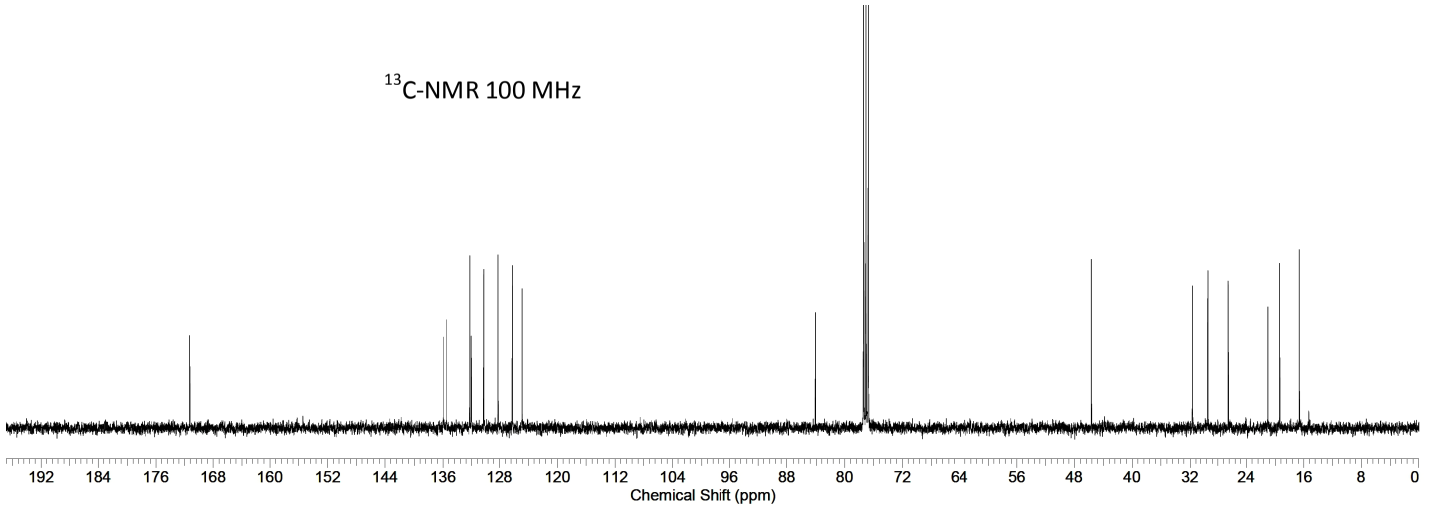
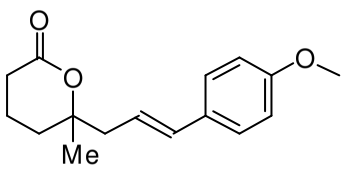
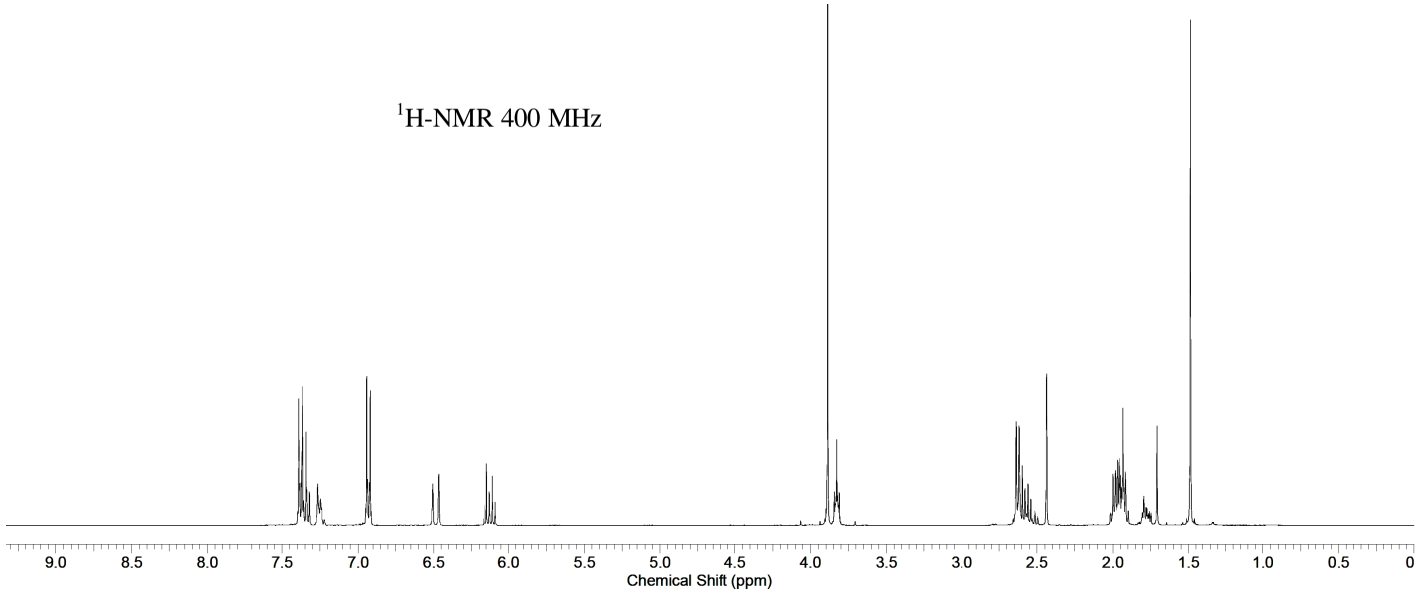


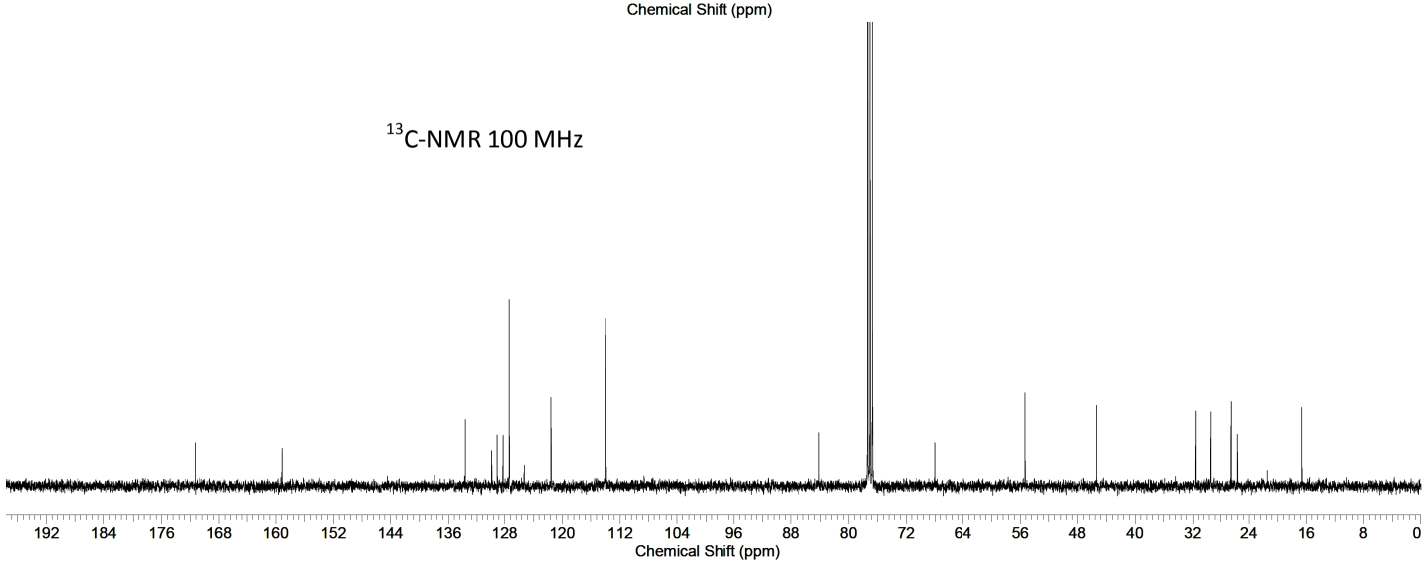


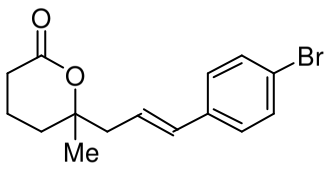
6k

^{1}H-NMR 400 MHz



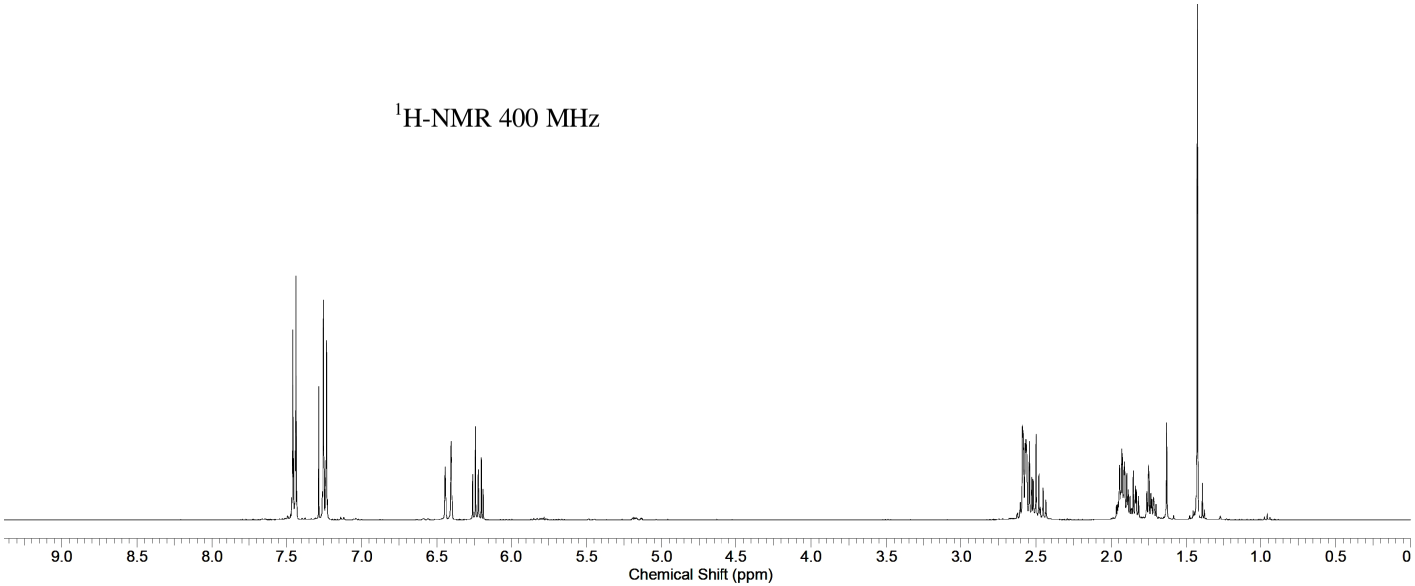
^{13}C-NMR 100 MHz





6l

^{1}H-NMR 400 MHz



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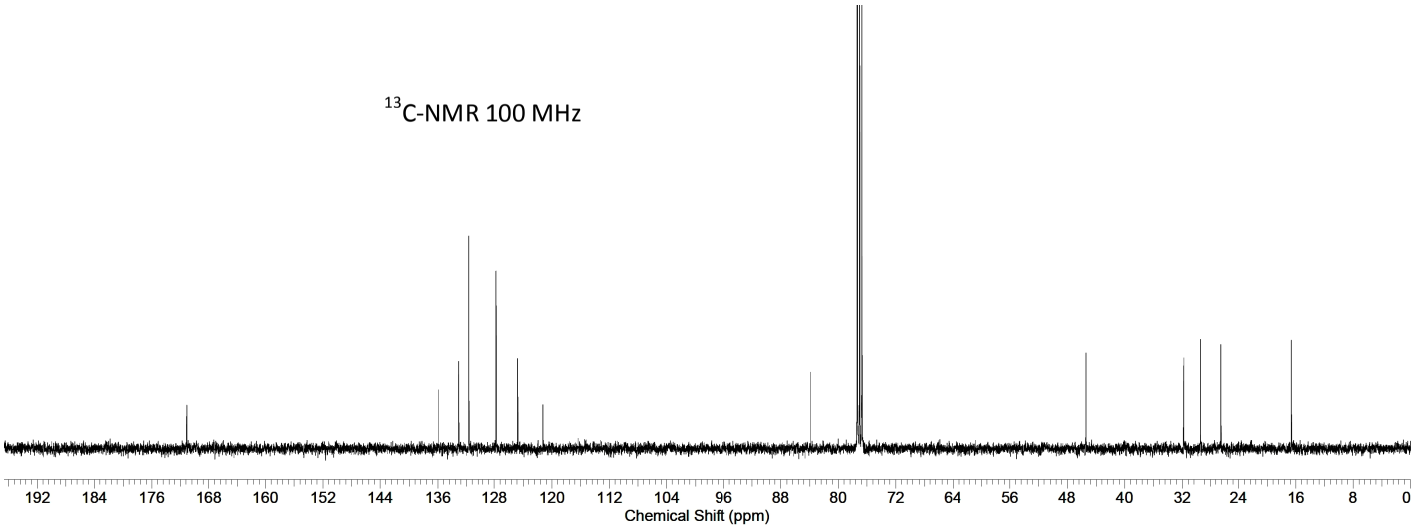
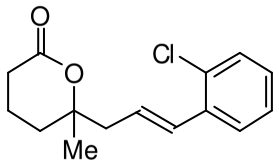
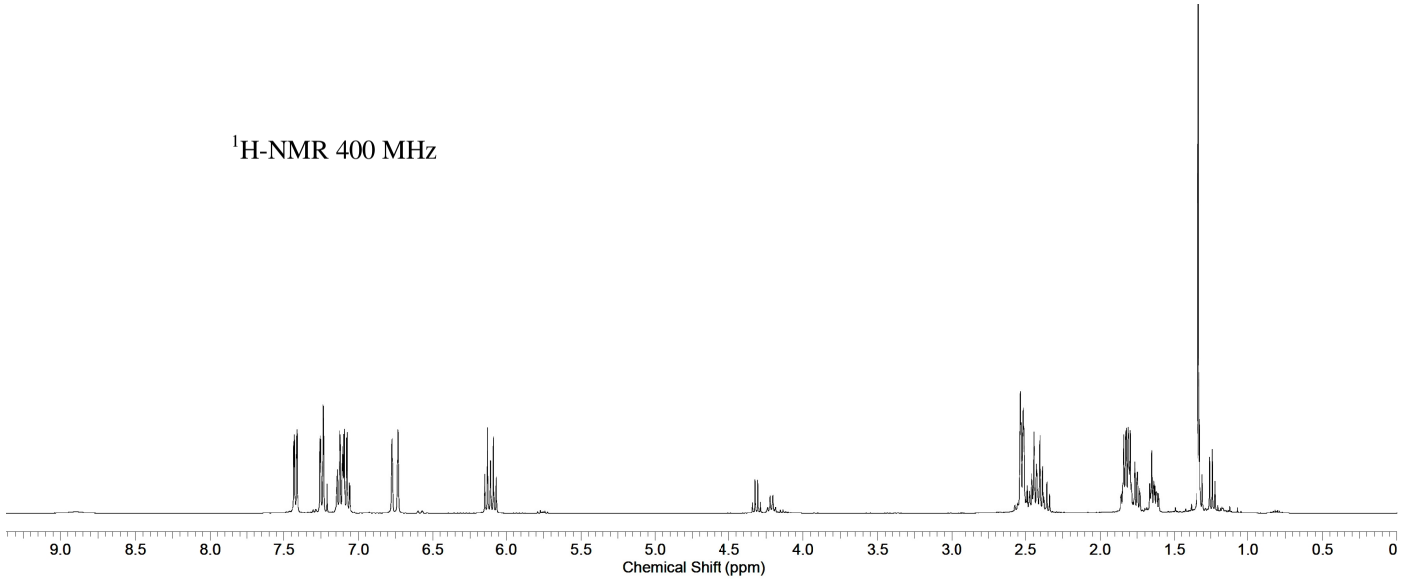




6m

^{1}H-NMR 400 MHz



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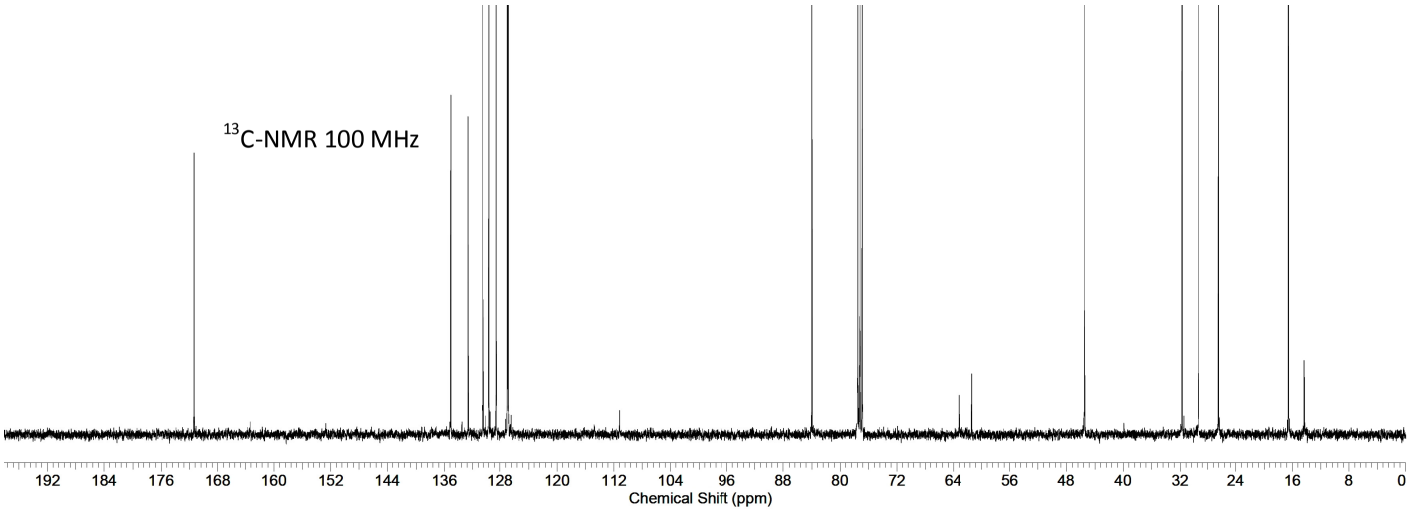
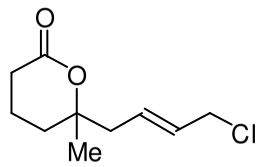
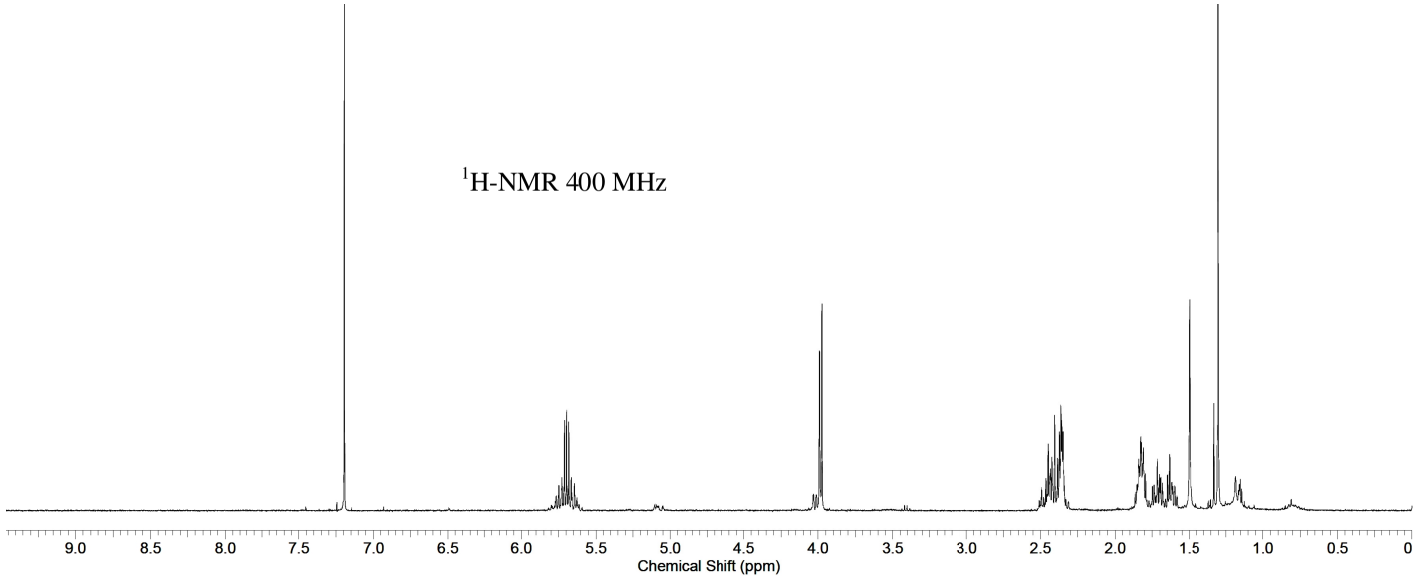




S5

^{1}H-NMR 400 MHz



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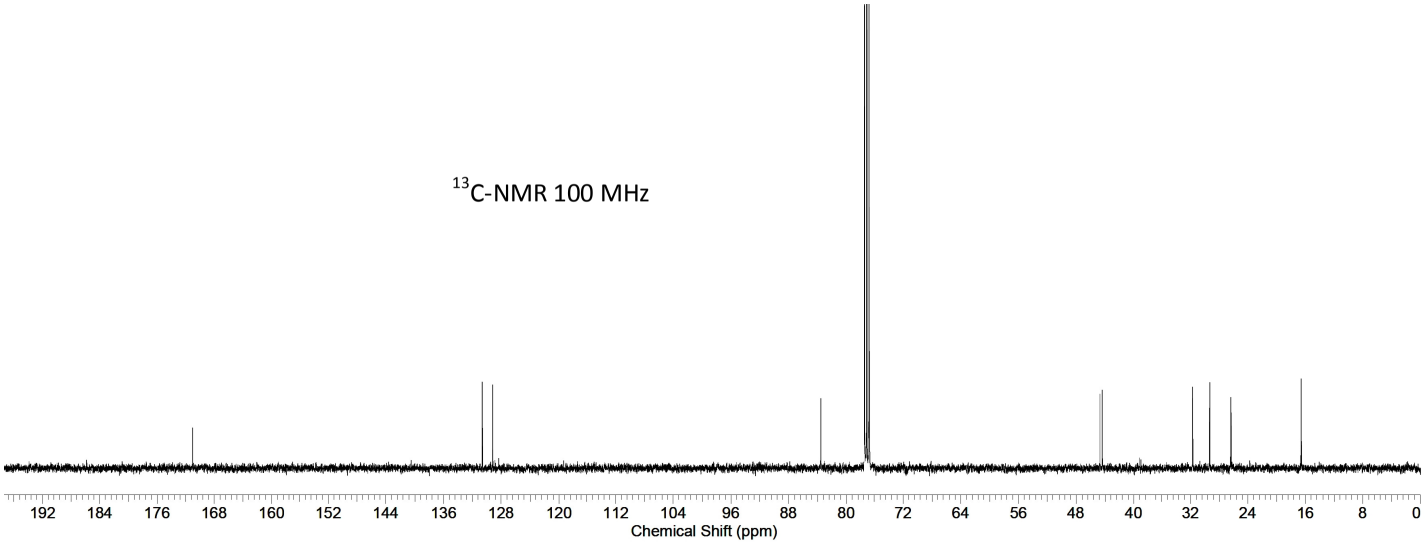
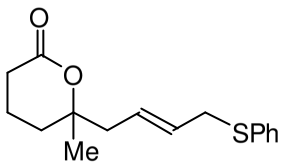
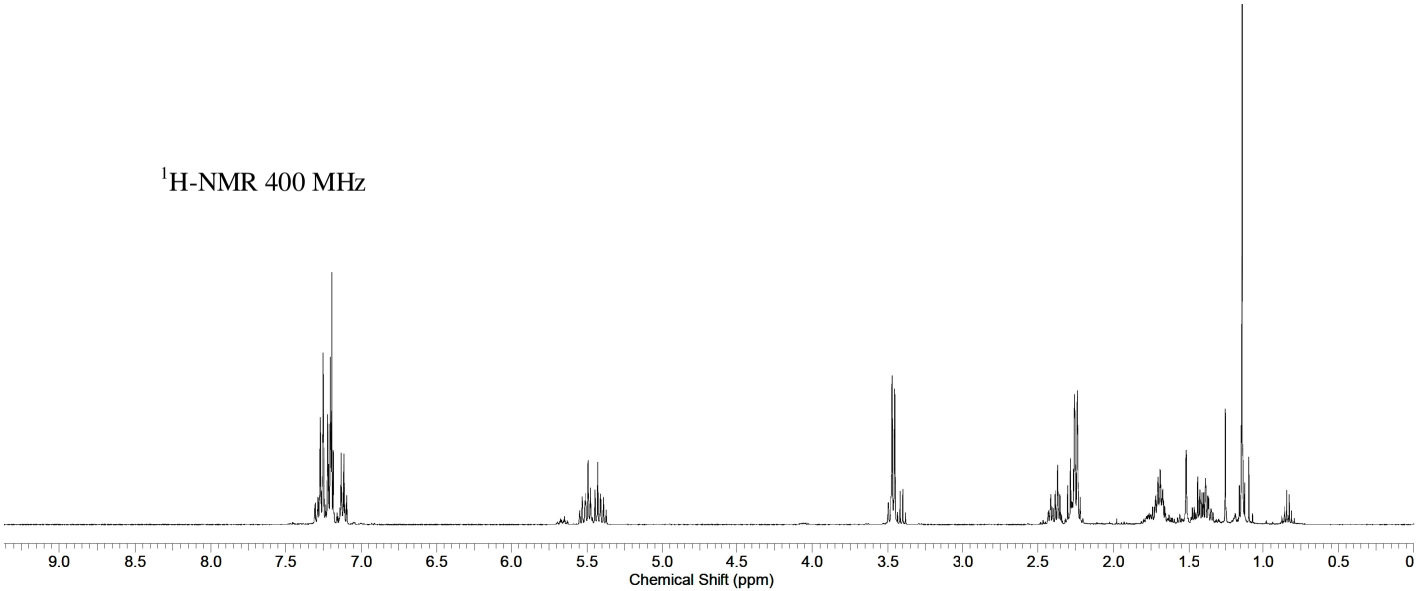




6n

^{1}H-NMR 400 MHz



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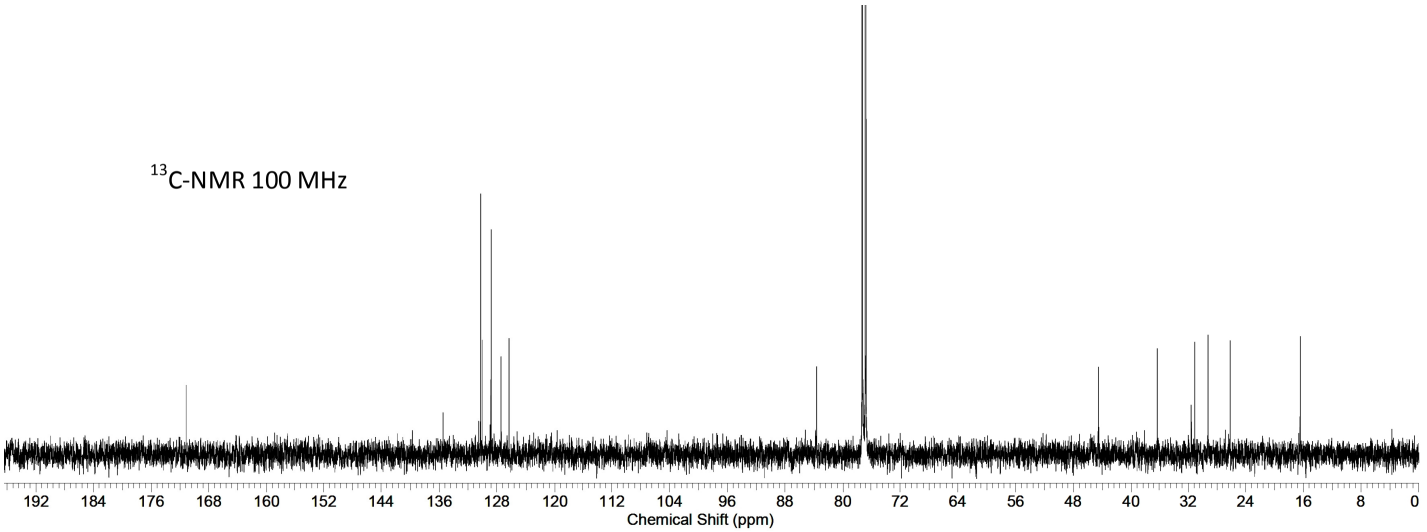
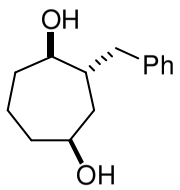
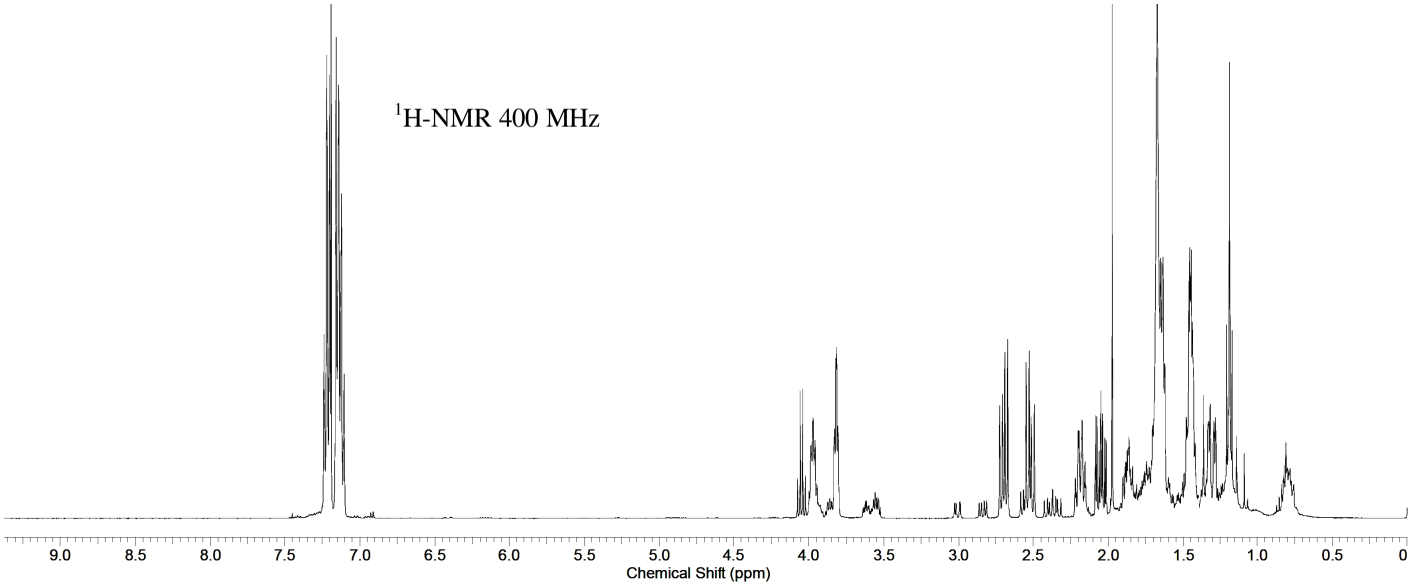




8a
Major
+
Minor diastereoisomers

^{1}H-NMR 400 MHz



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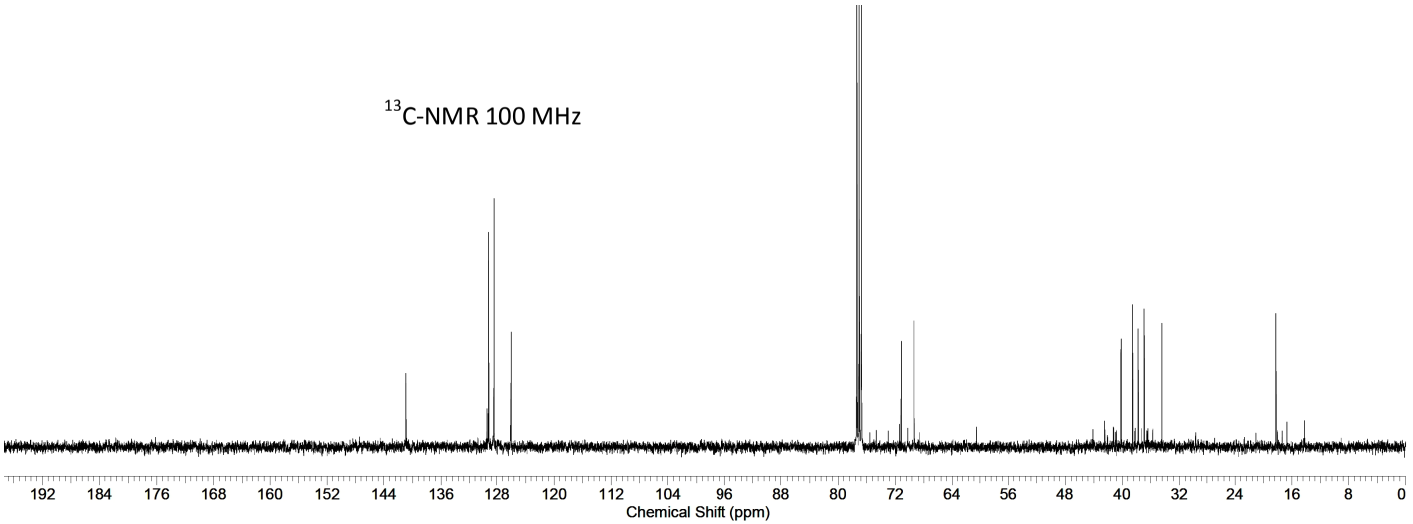
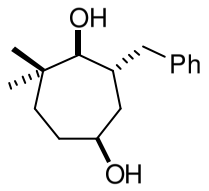
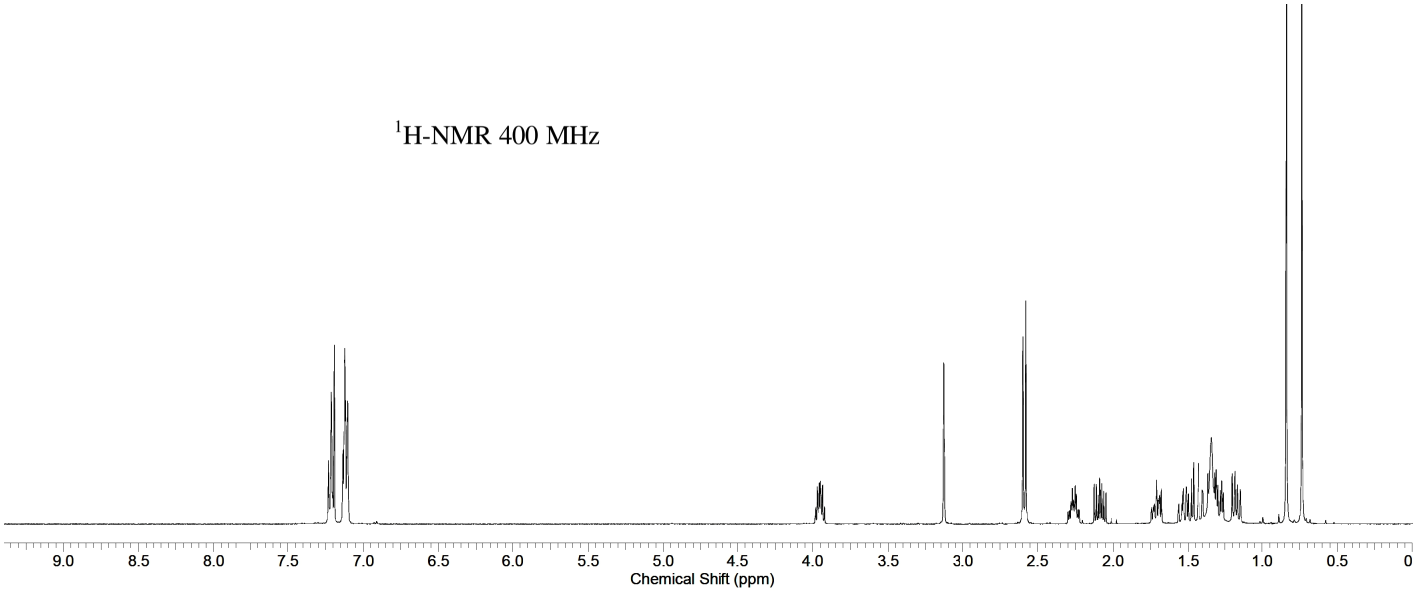




8b
Major Diastereoisomer

^{1}H-NMR 400 MHz



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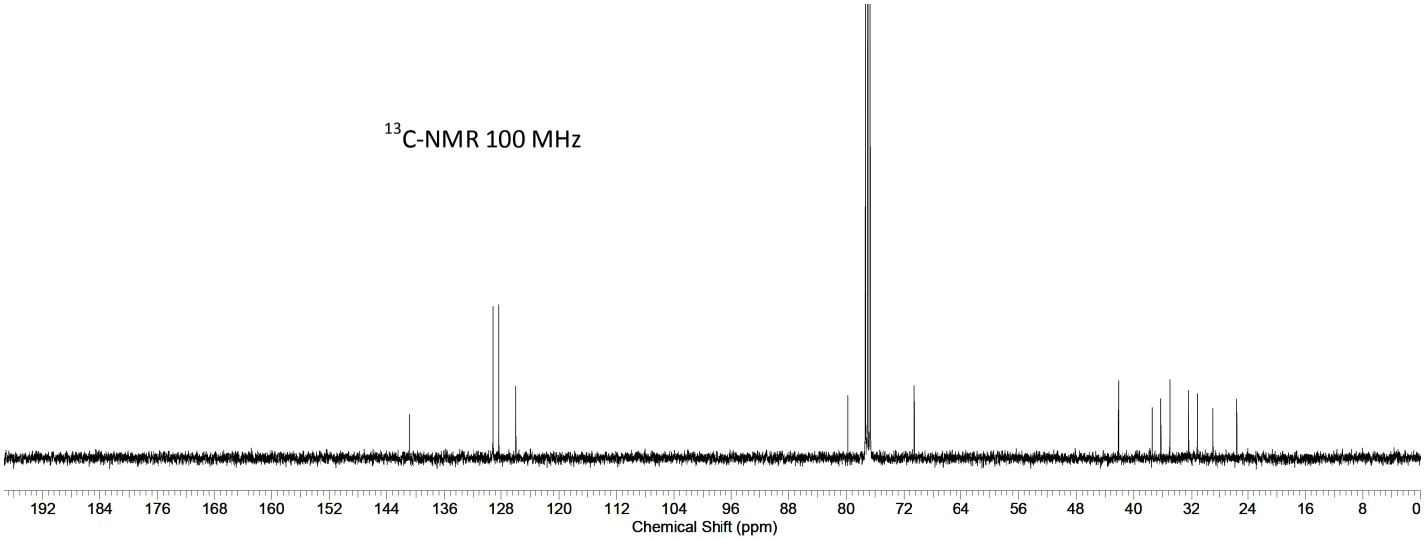
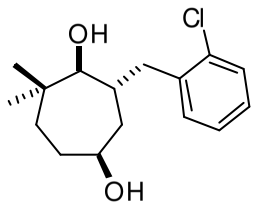
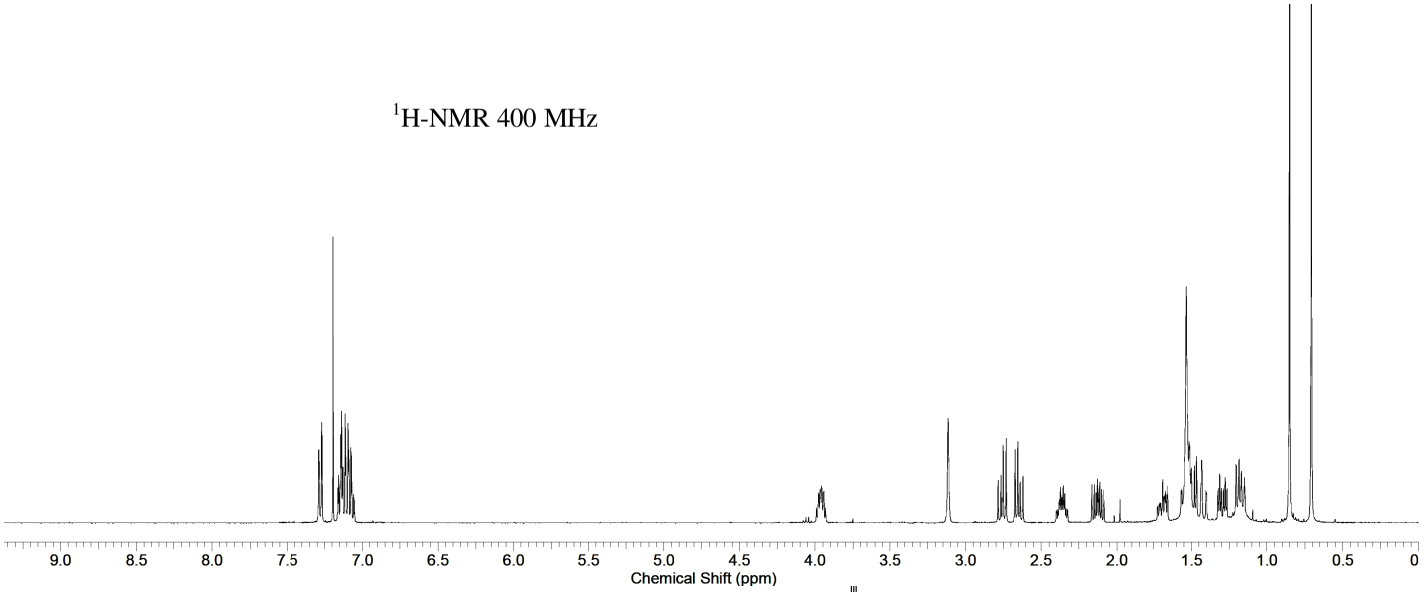


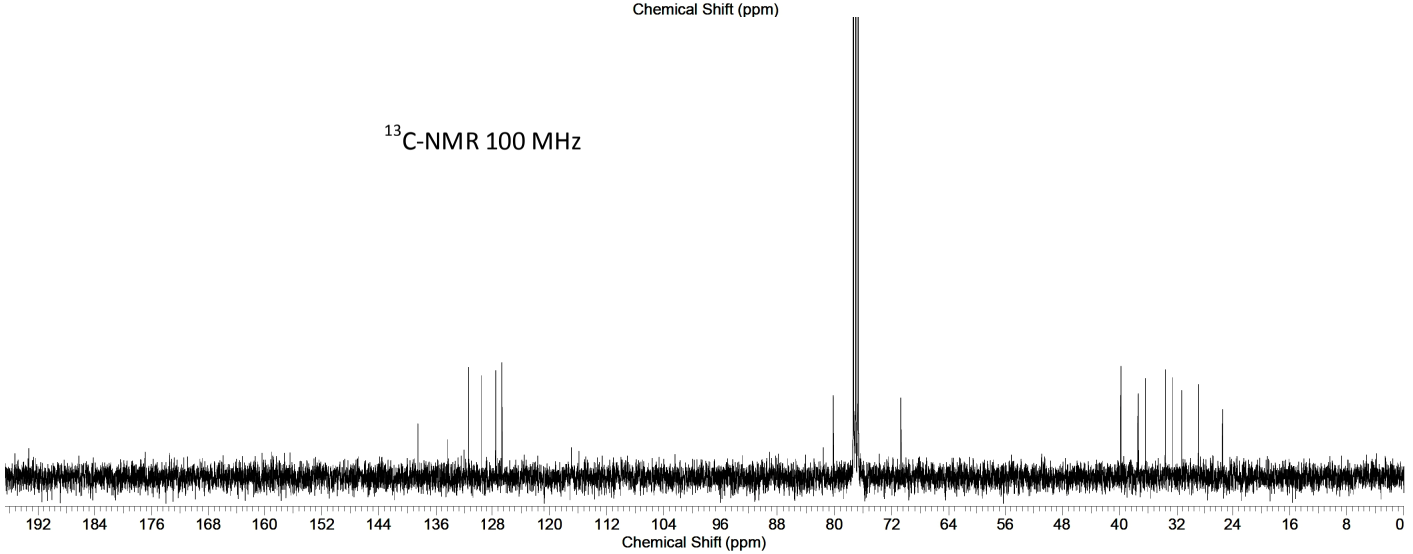


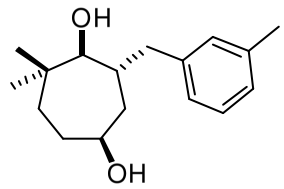
8c

^{1}H-NMR 400 MHz



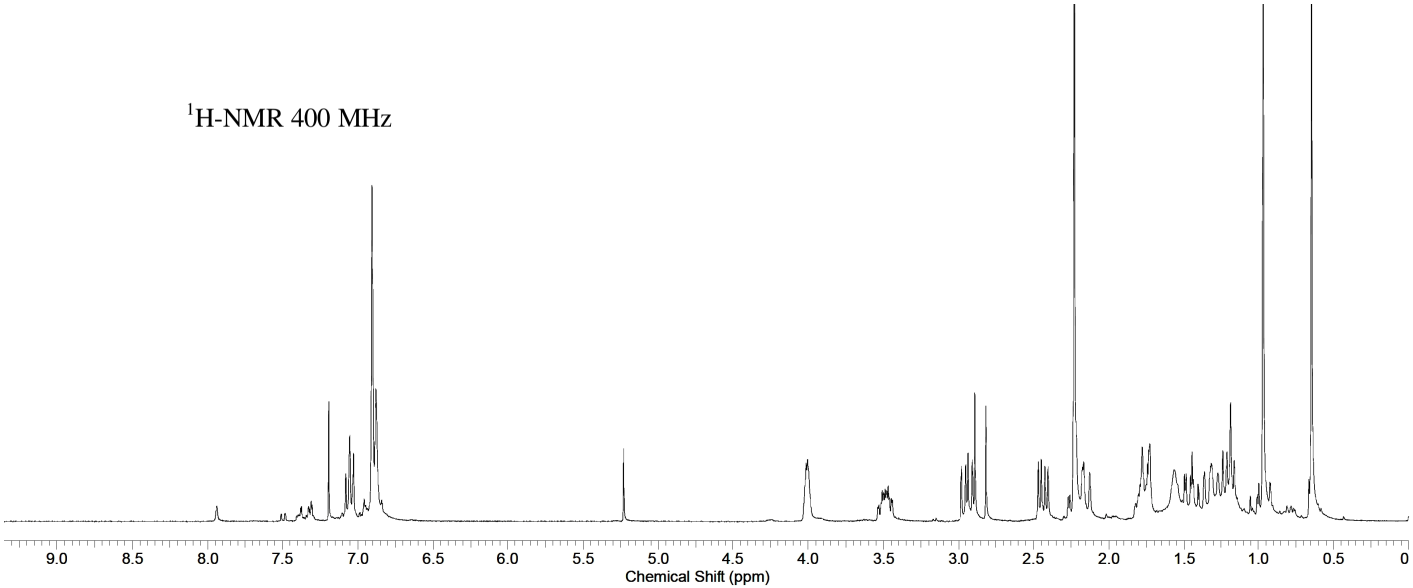
^{13}C-NMR 100 MHz



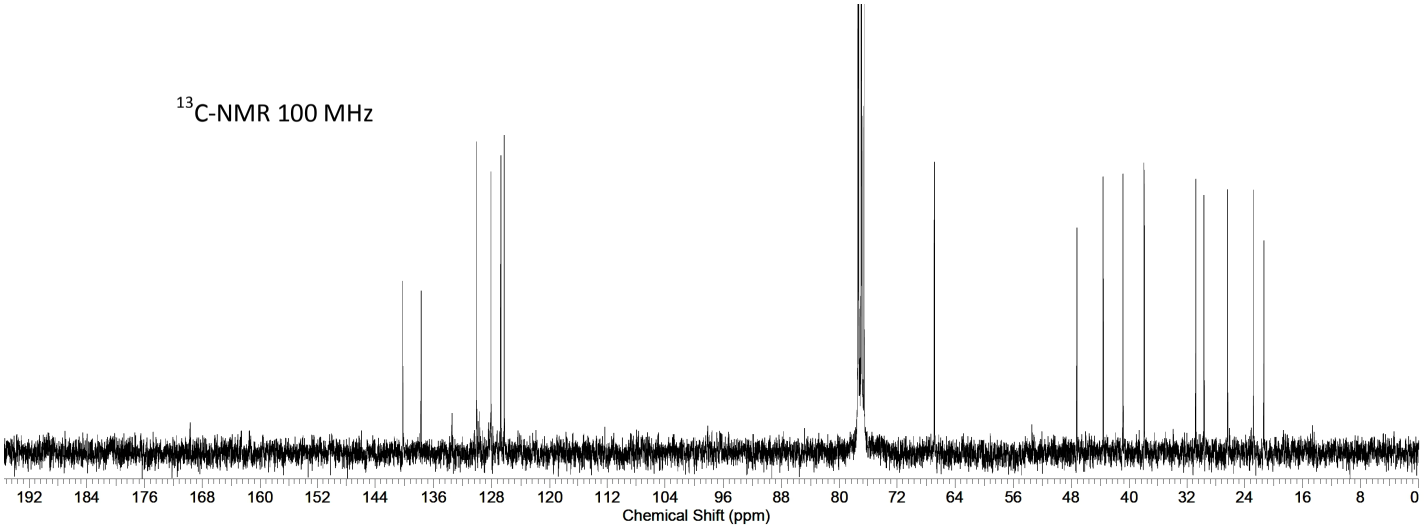


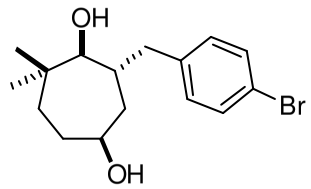
8d

^{1}H-NMR 400 MHz



^{13}C-NMR 100 MHz





8e

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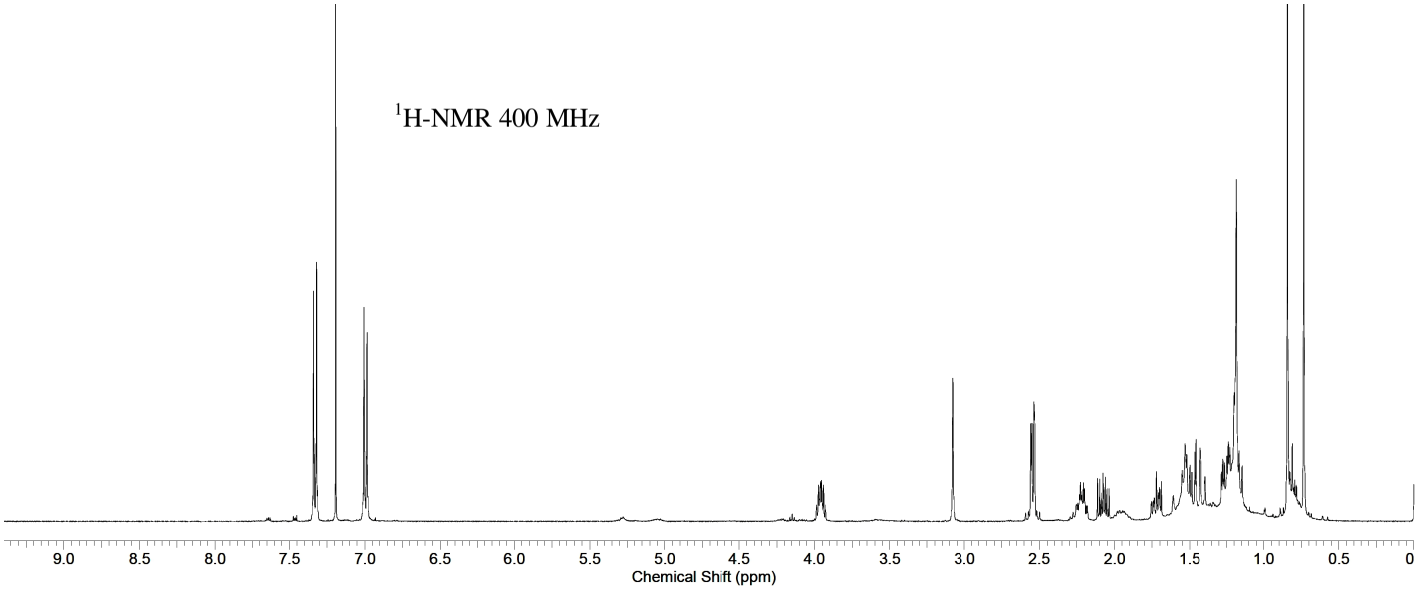
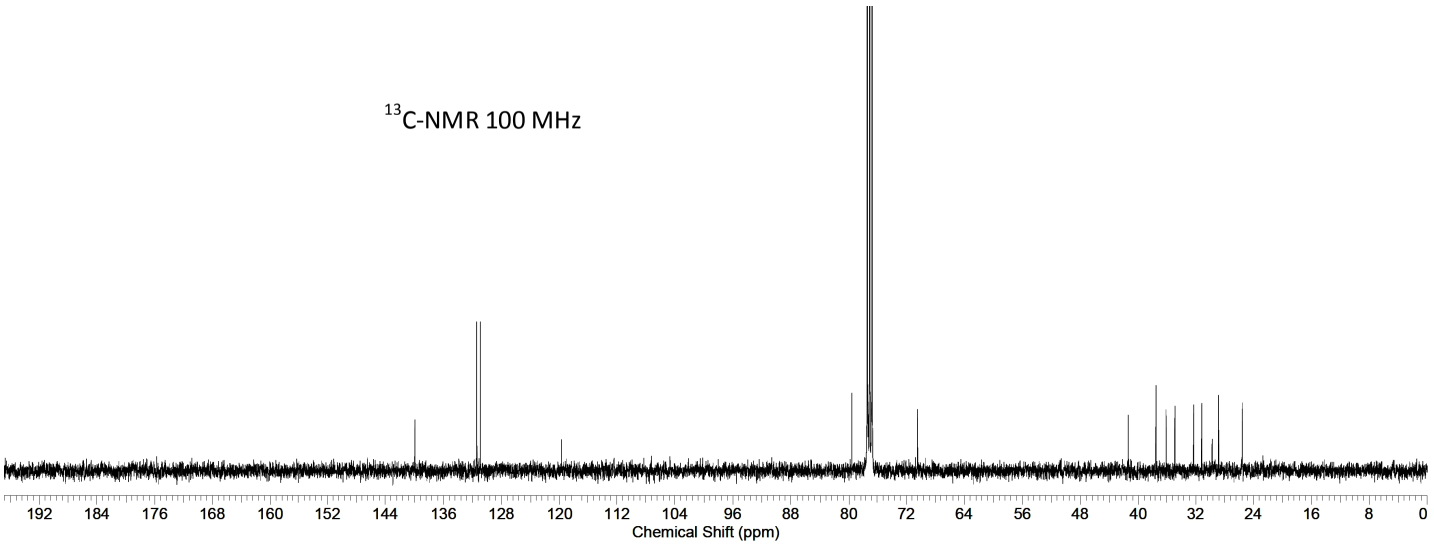
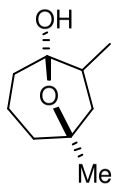


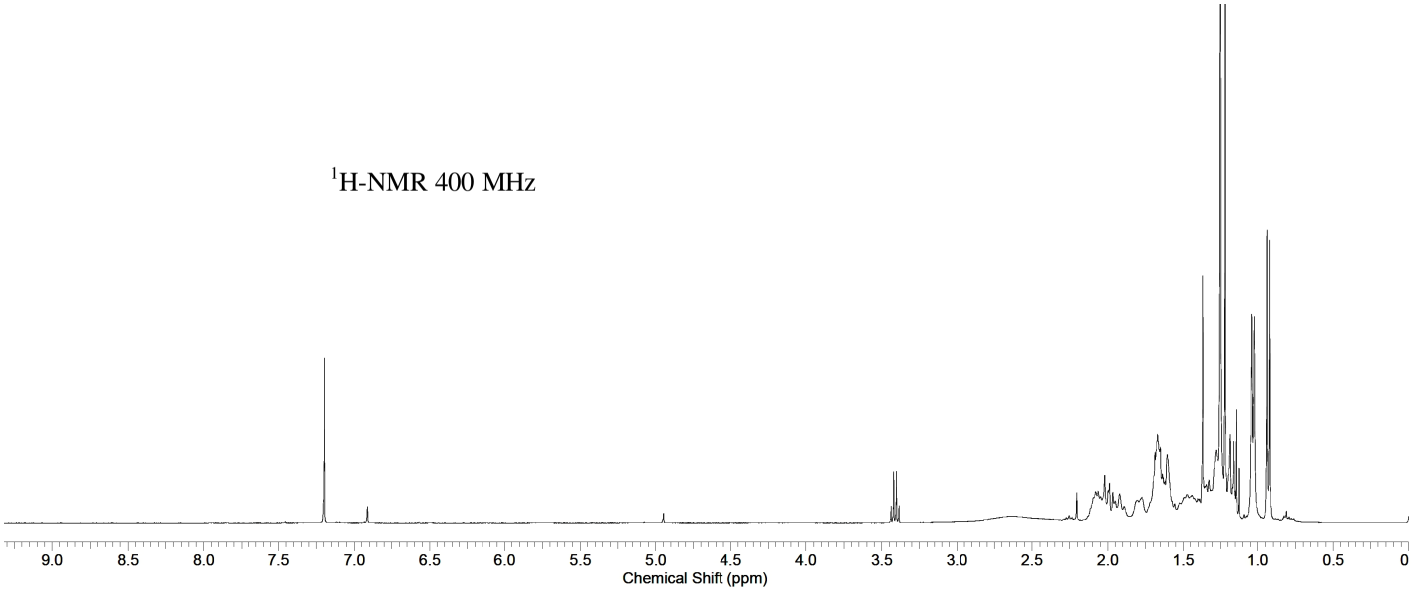
^{13}C-NMR 100 MHz





9f

^{1}H-NMR 400 MHz



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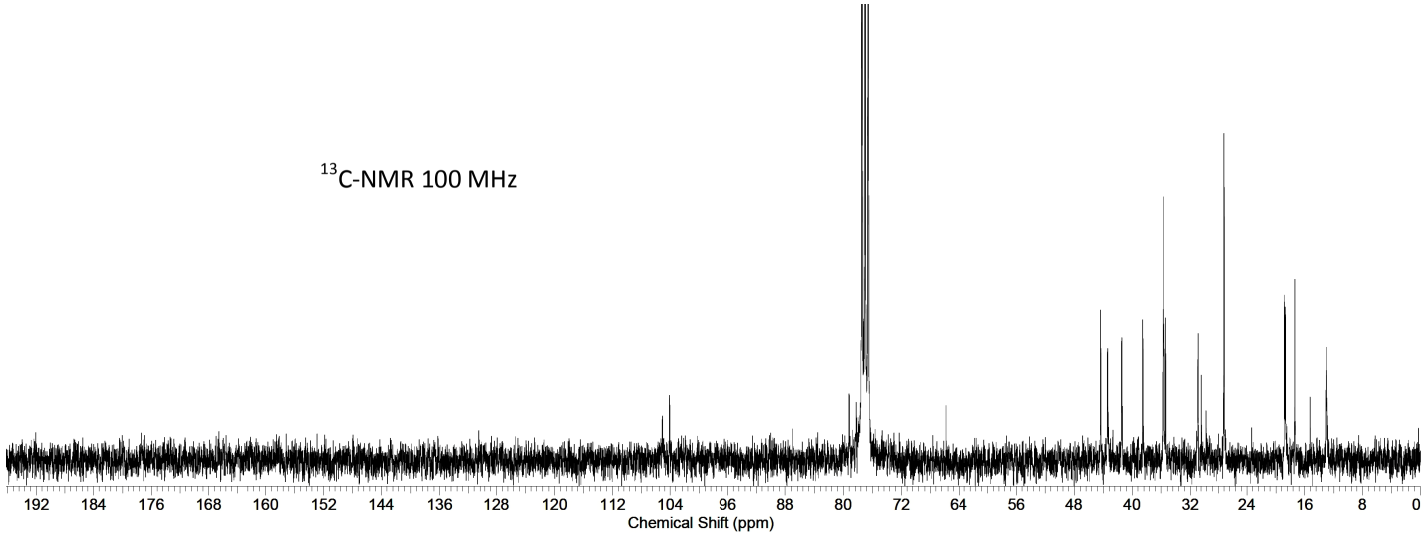
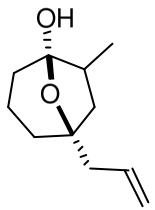
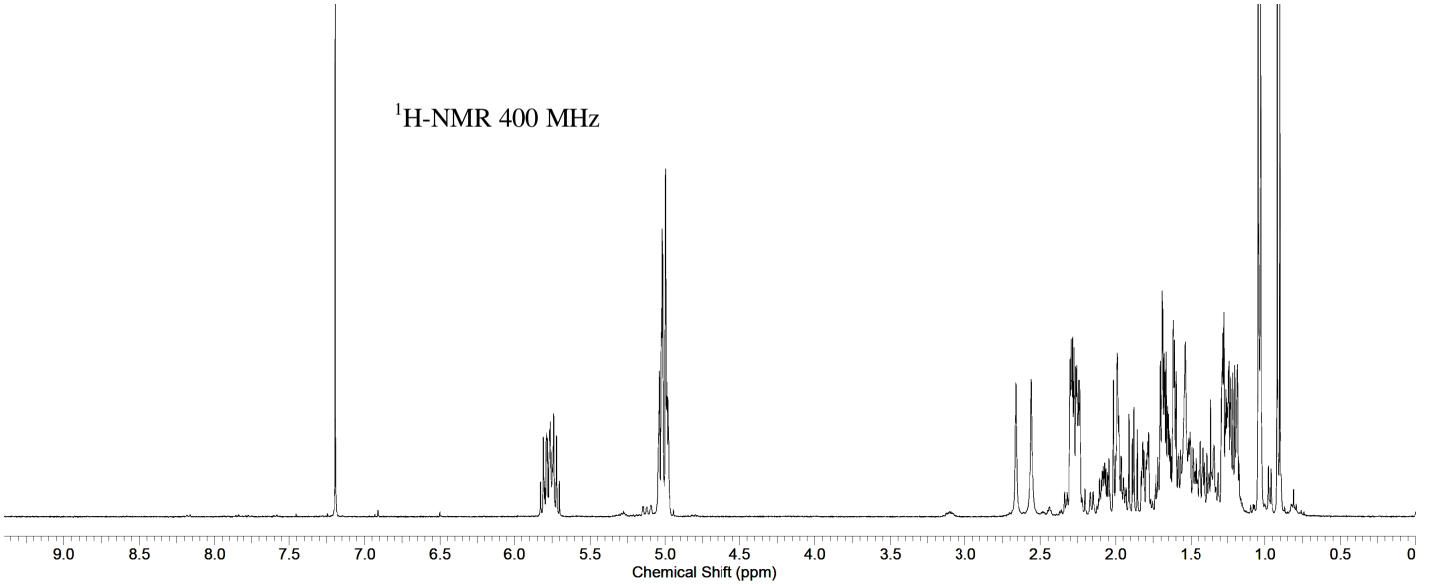
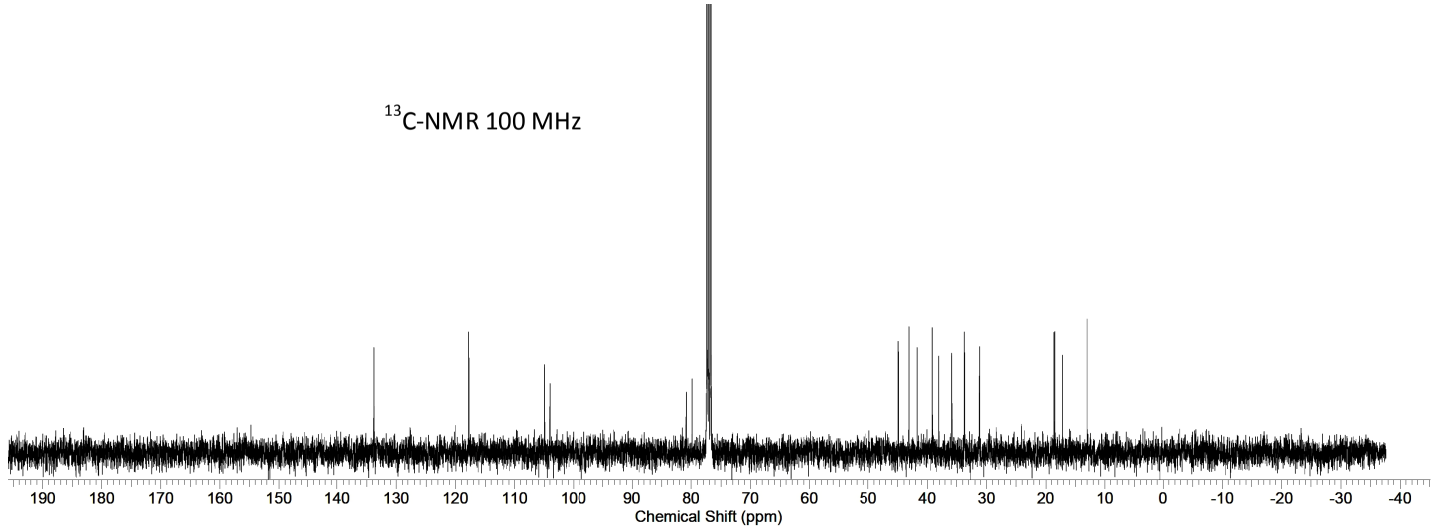
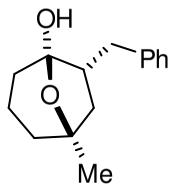



OH
O

9g

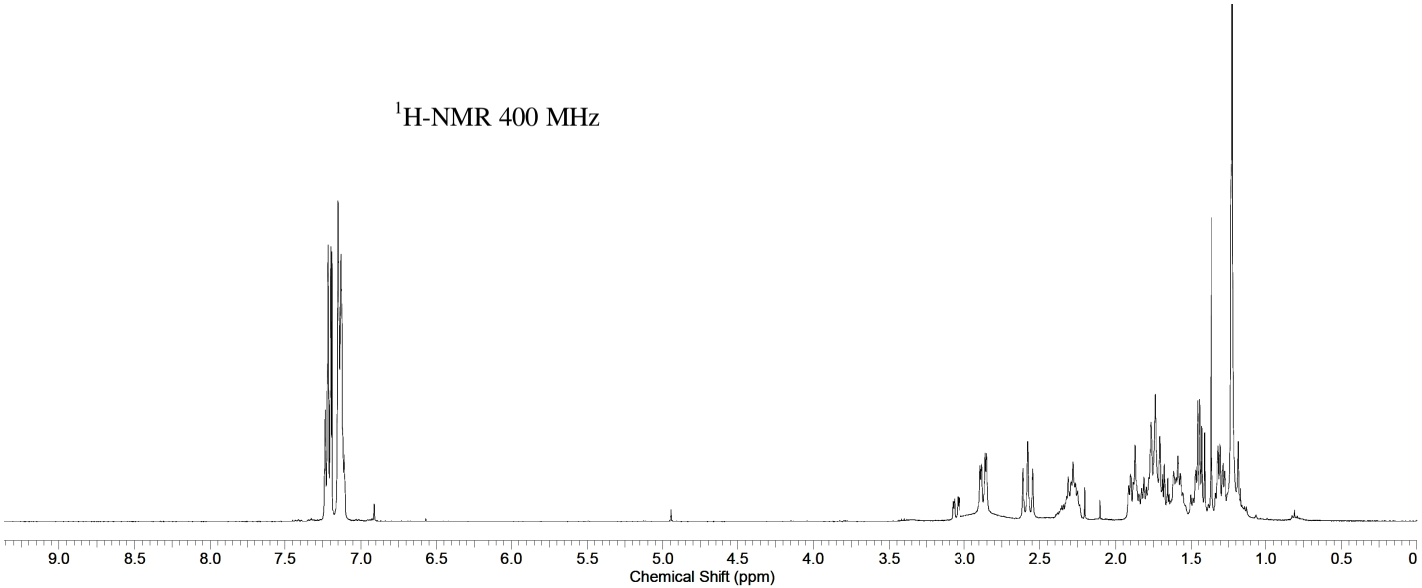

^{1}H-NMR 400 MHz
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


^{13}C-NMR 100 MHz
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
Chemical Shift (ppm)

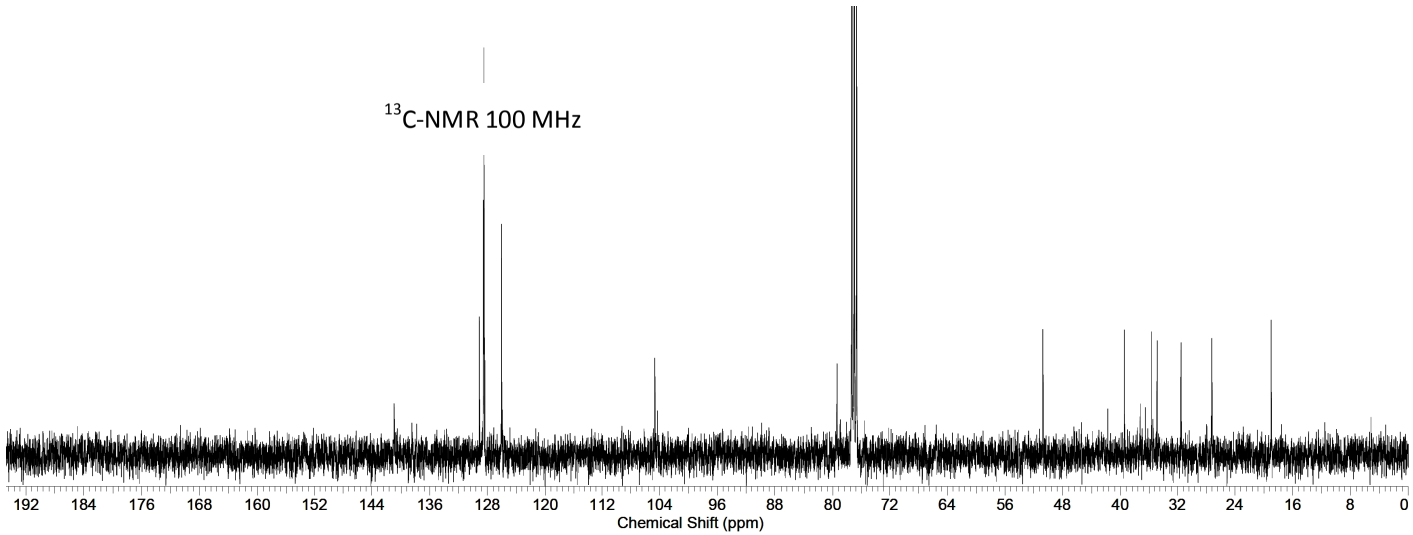


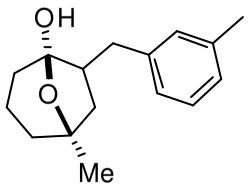
9h

^{1}H-NMR 400 MHz



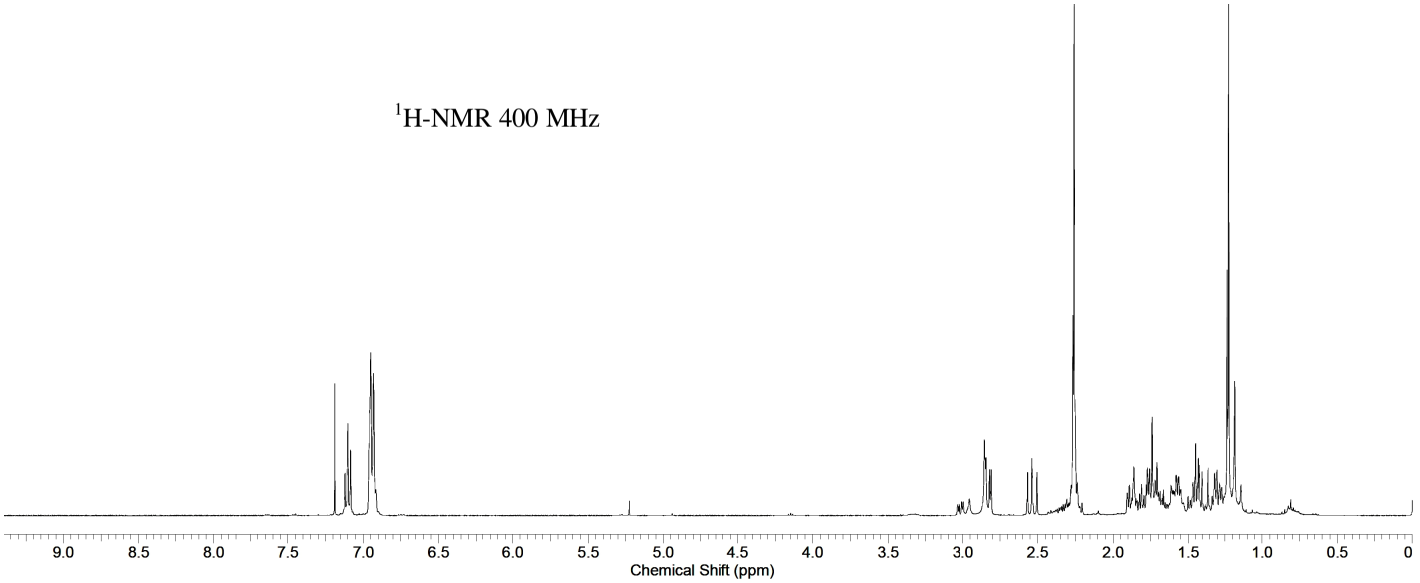
^{13}C-NMR 100 MHz



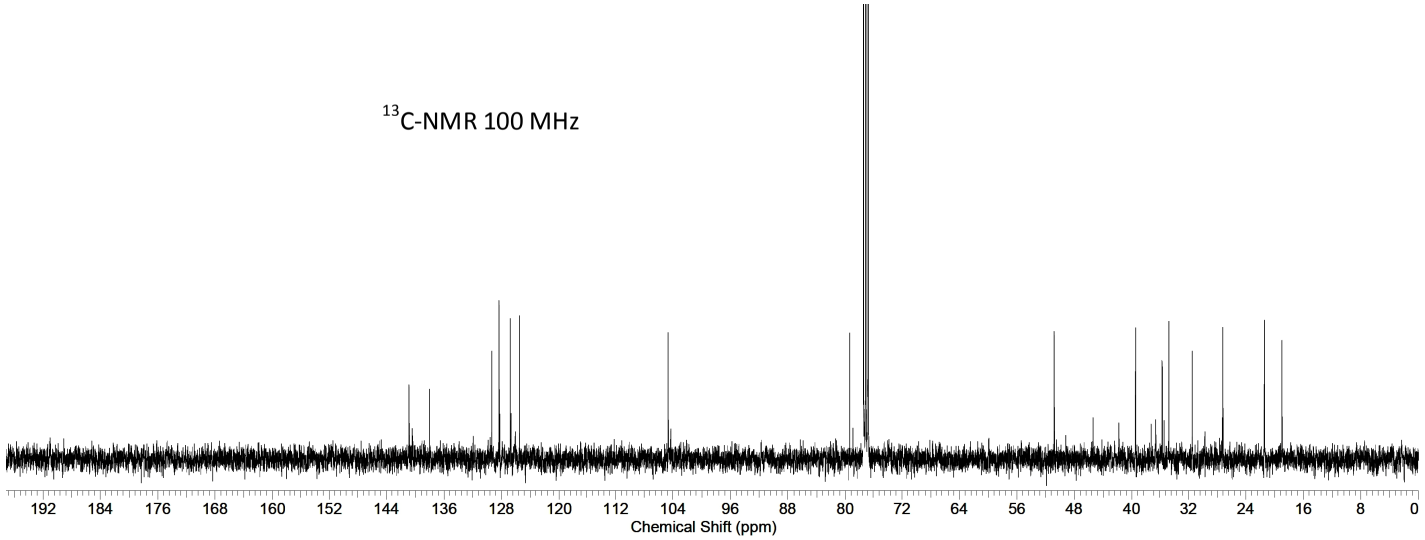


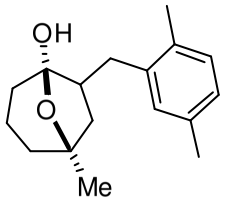
9i

^{1}H-NMR 400 MHz



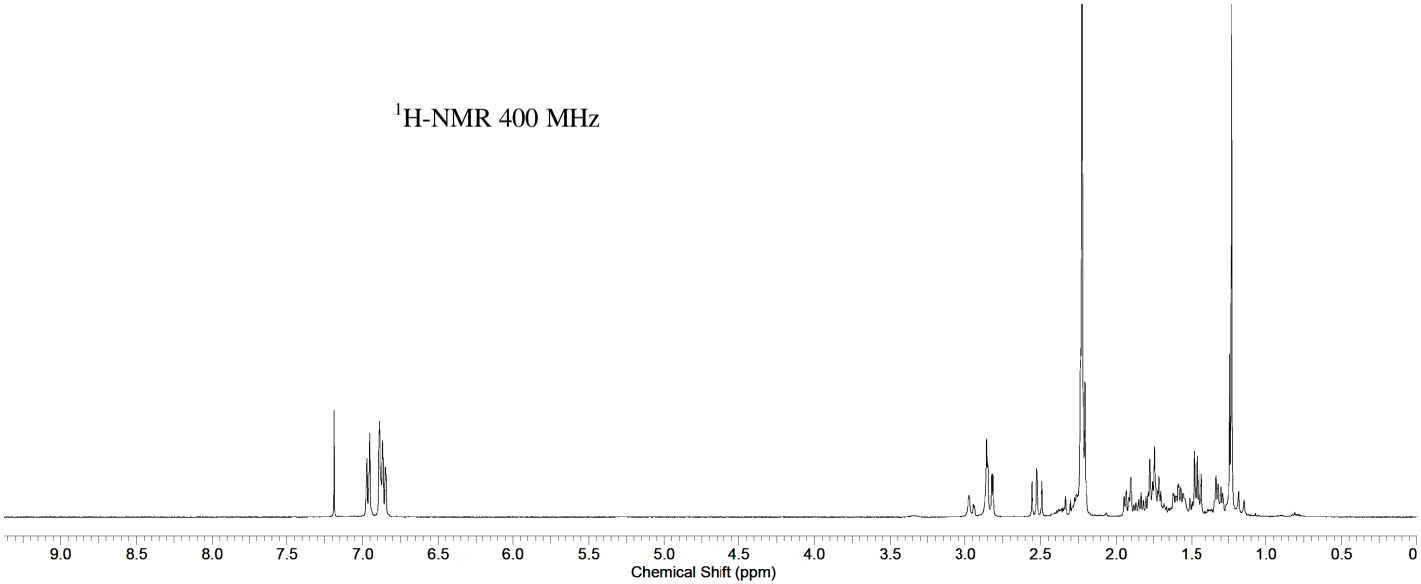
^{13}C-NMR 100 MHz



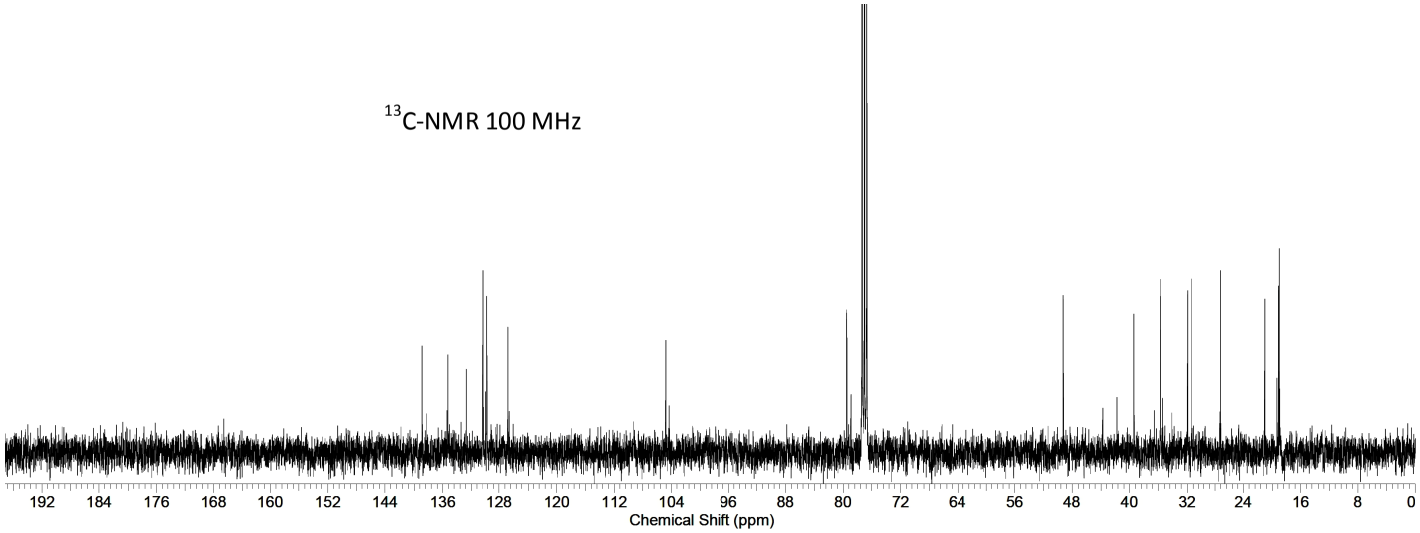


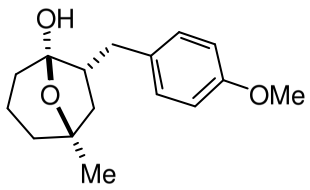
9j

^{1}H-NMR 400 MHz



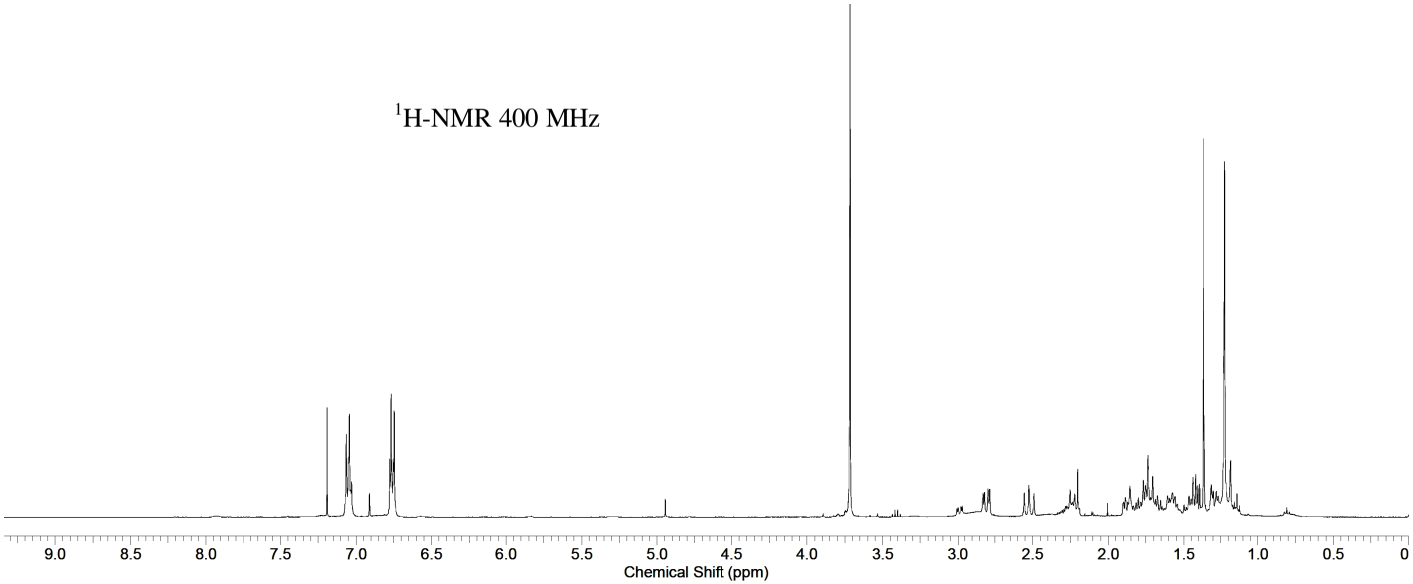
^{13}C-NMR 100 MHz



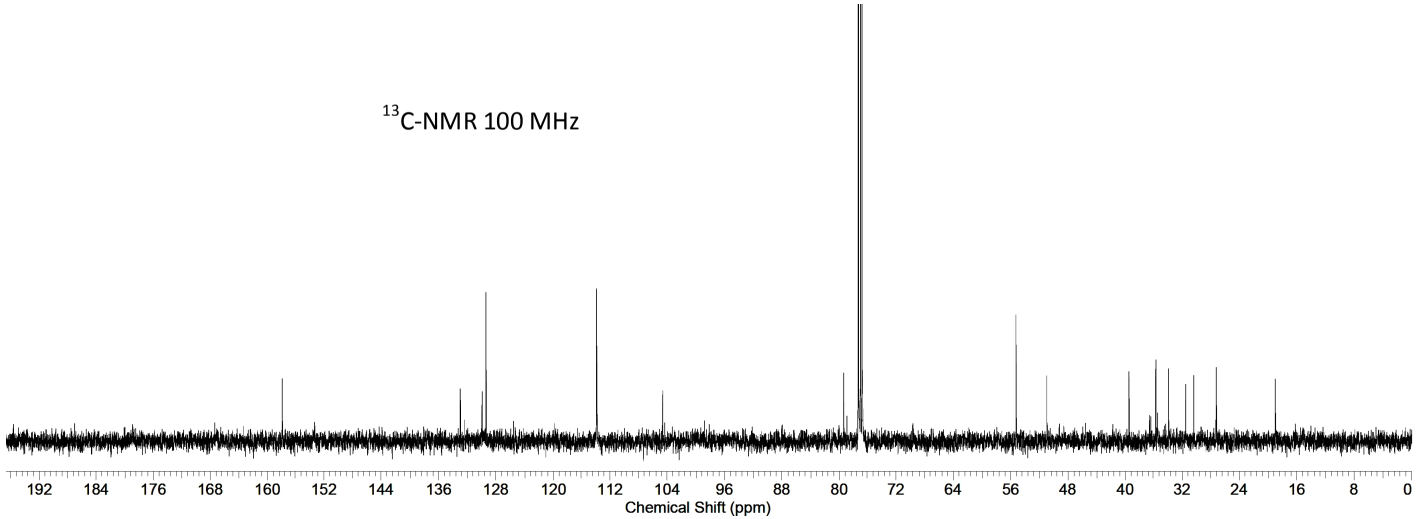


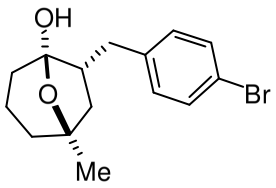
9k

^{1}H-NMR 400 MHz



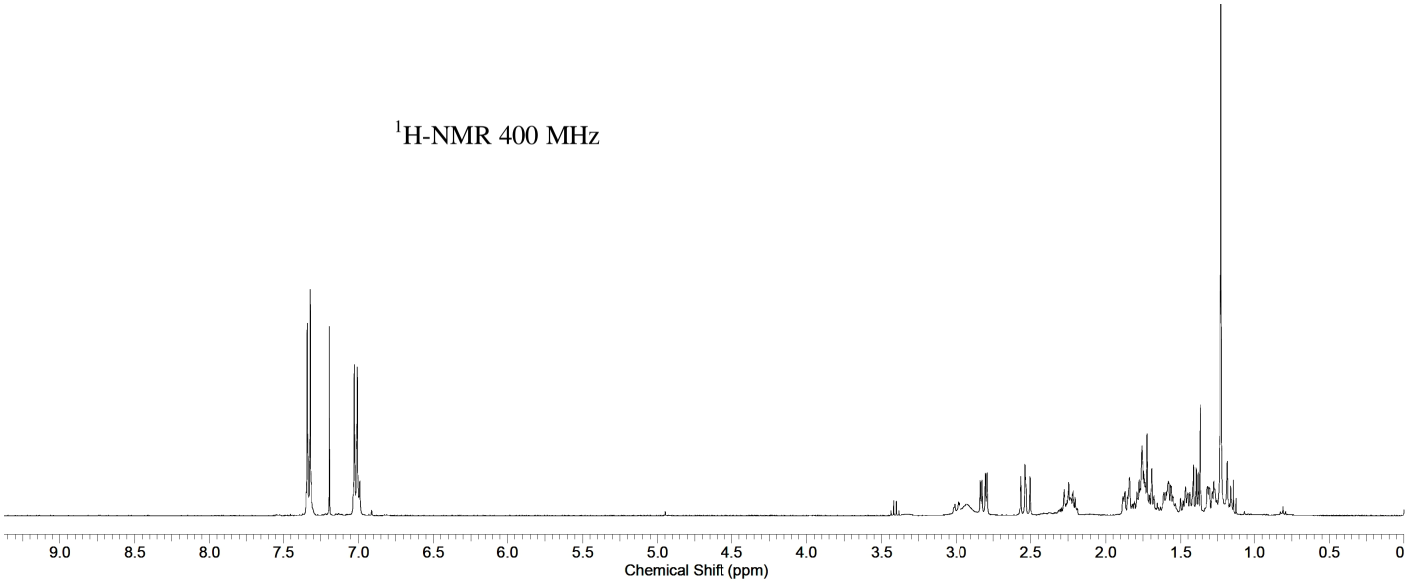
^{13}C-NMR 100 MHz



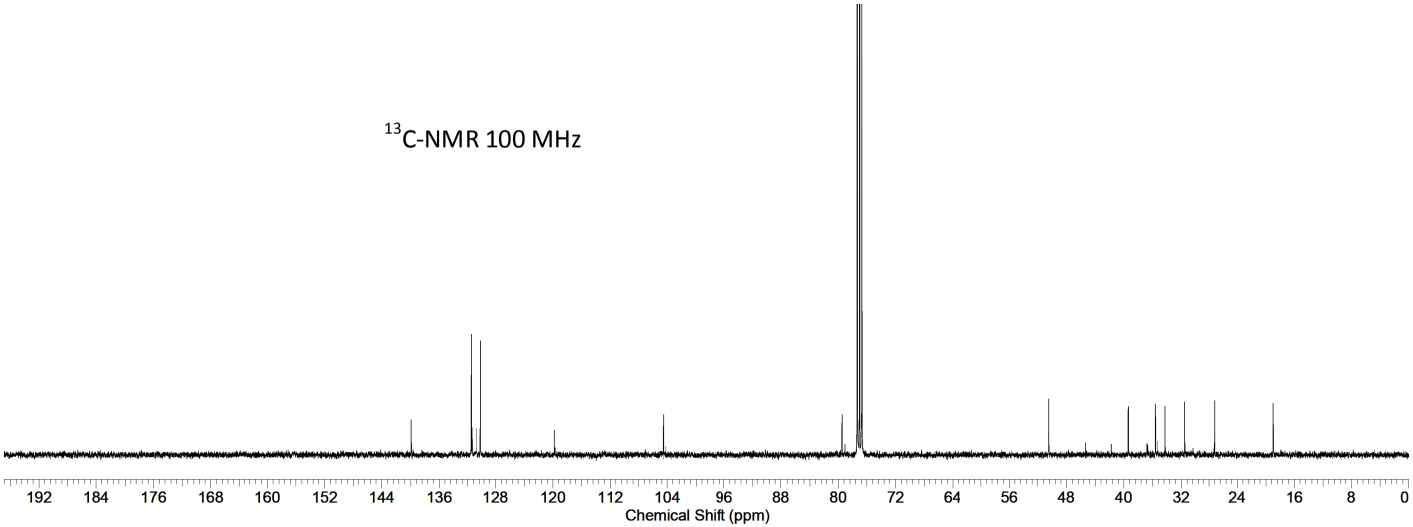


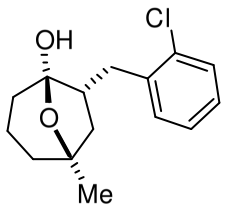
9l

^{1}H-NMR 400 MHz



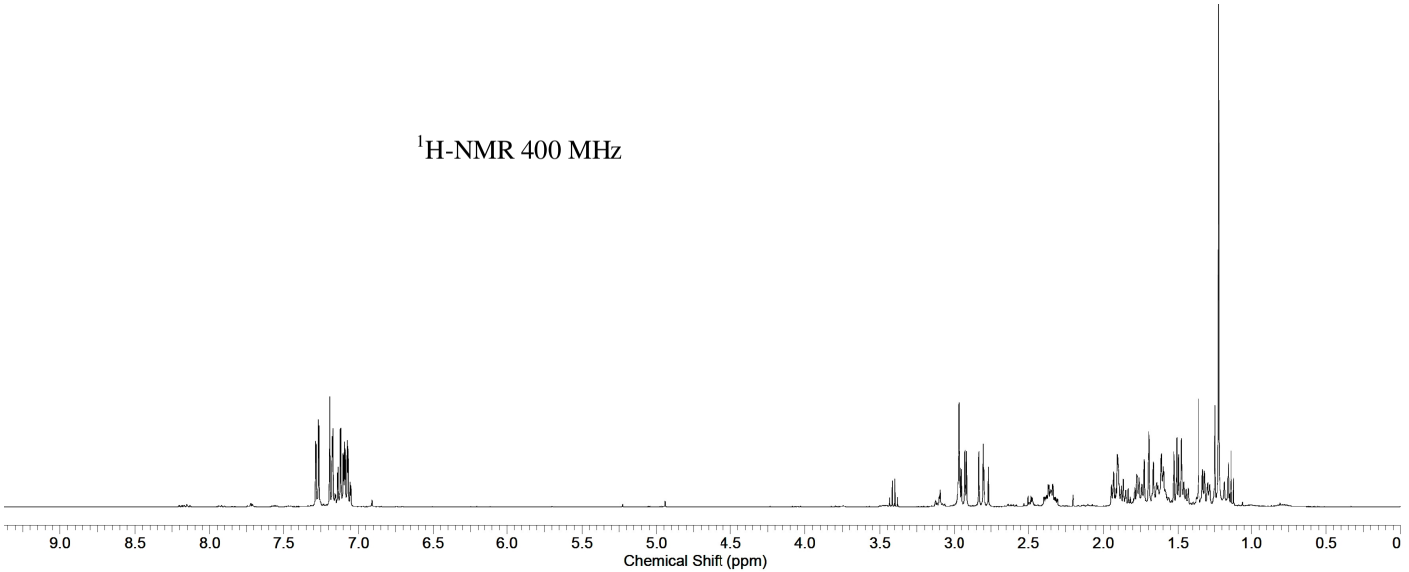
^{13}C-NMR 100 MHz



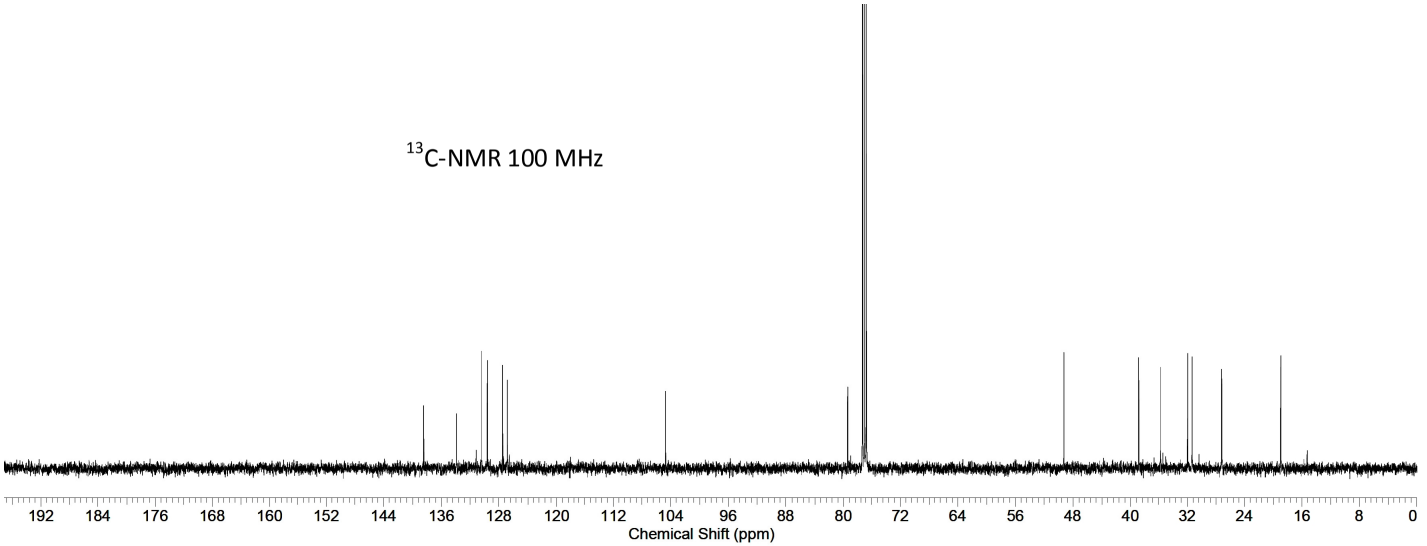


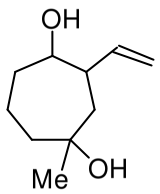
9m

^{1}H-NMR 400 MHz



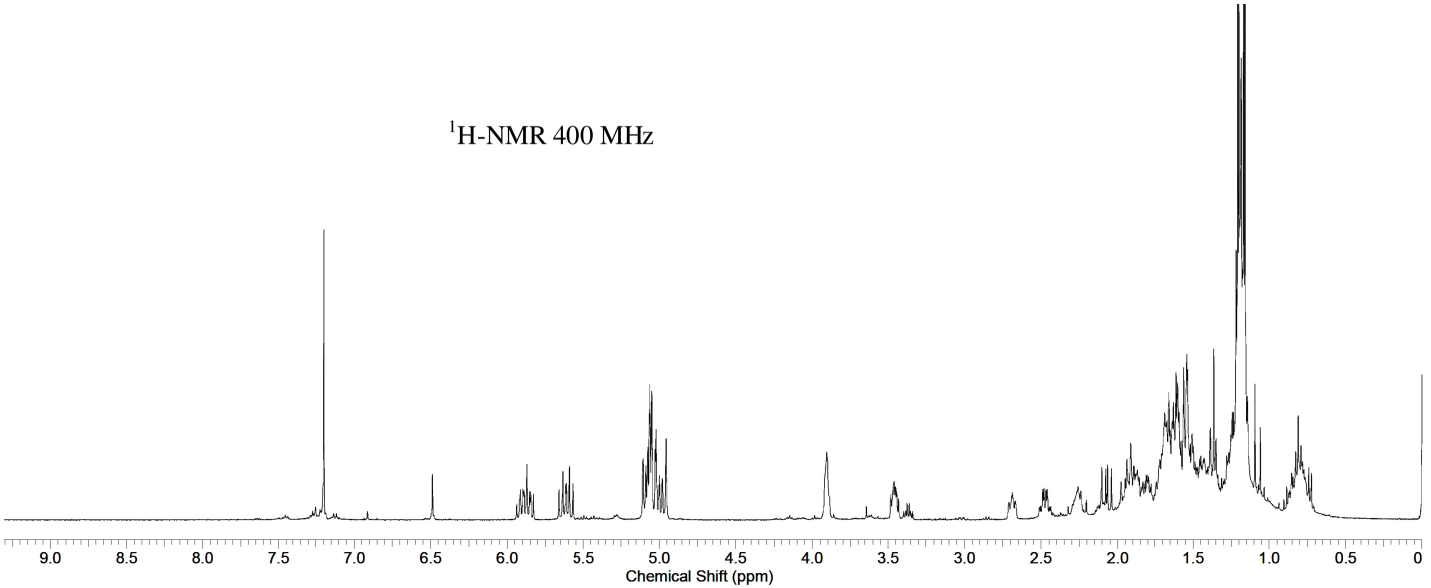
^{13}C-NMR 100 MHz



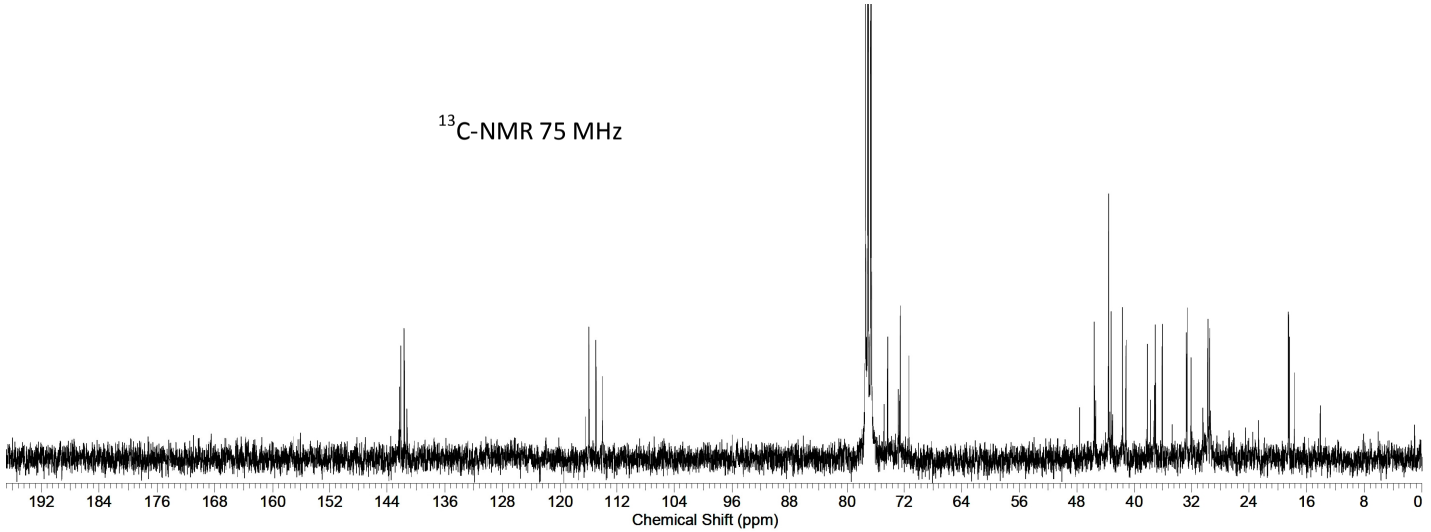


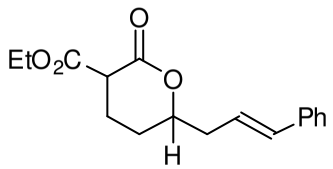
8f

^{1}H-NMR 400 MHz

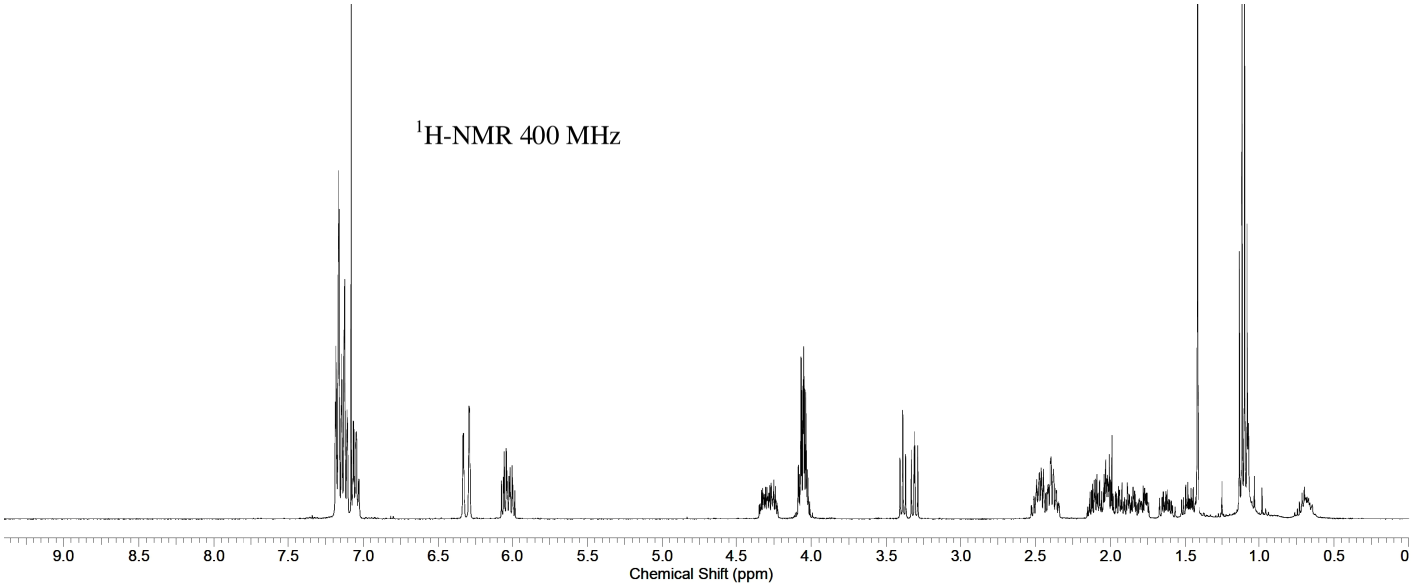


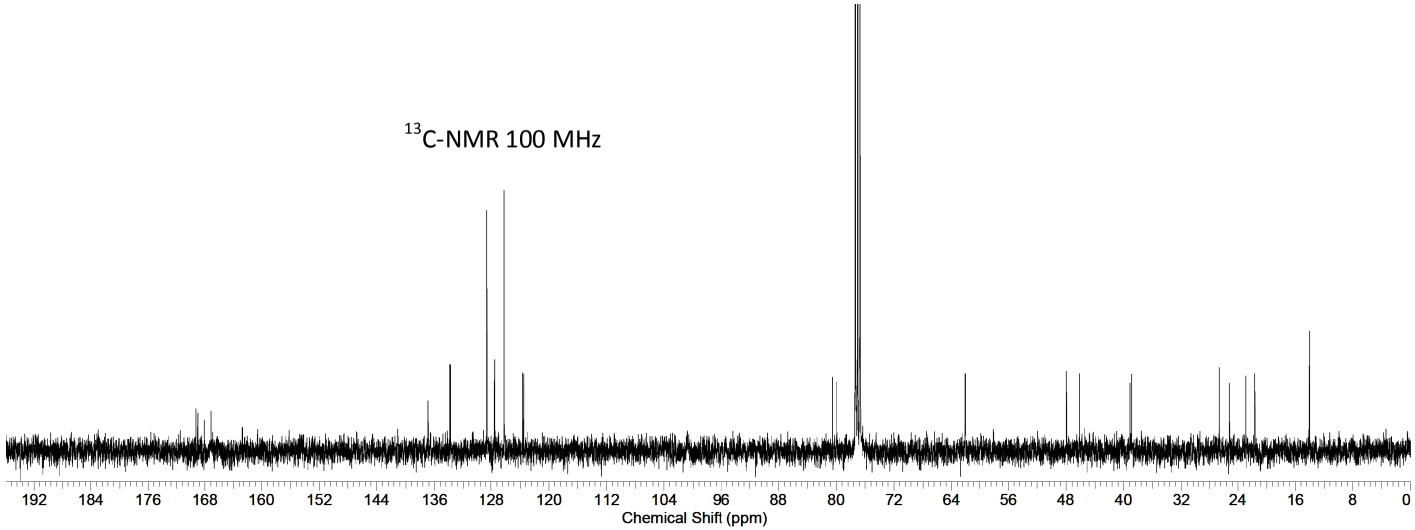
^{13}C-NMR 75 MHz

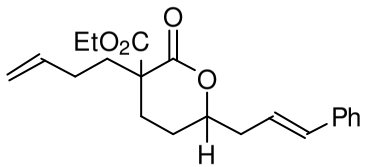



O
EtO2C
O
Ph
H

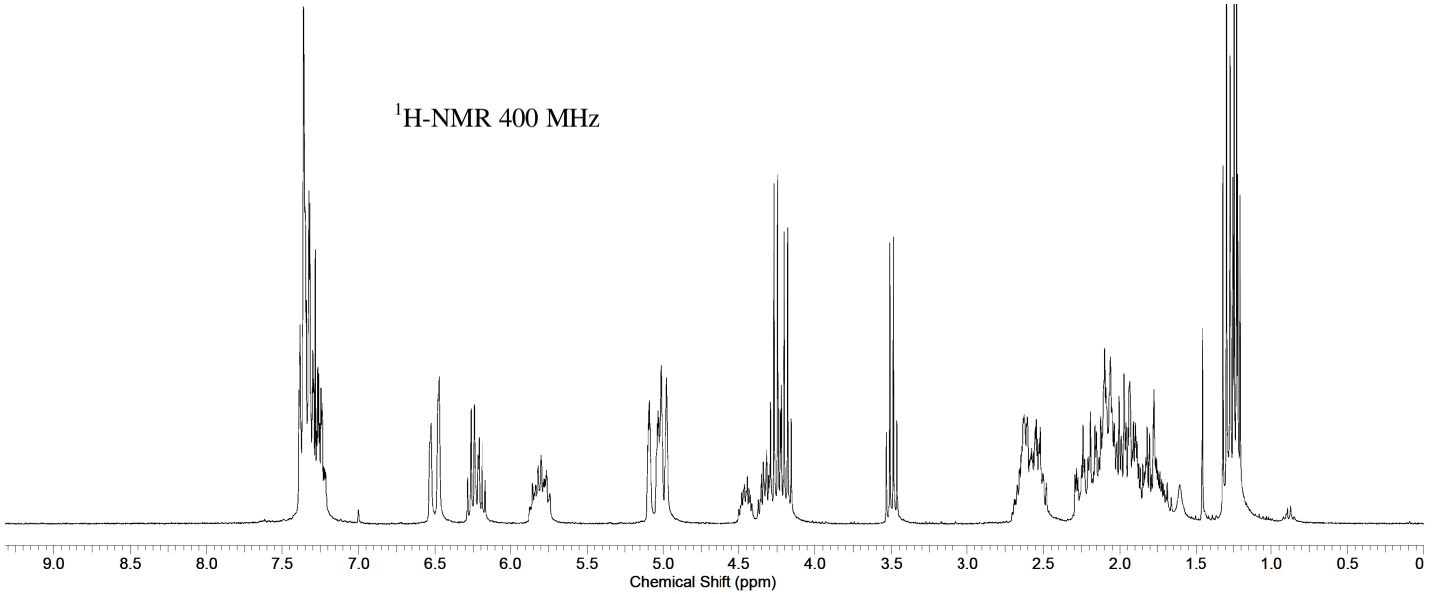
S6

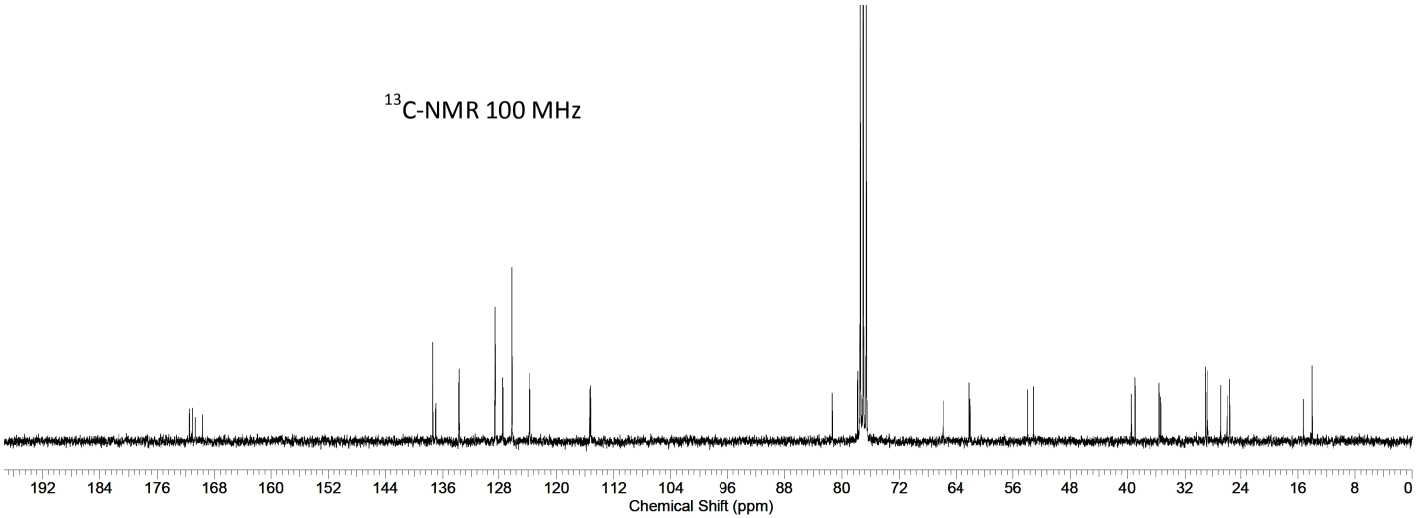

1H-NMR 400 MHz
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)

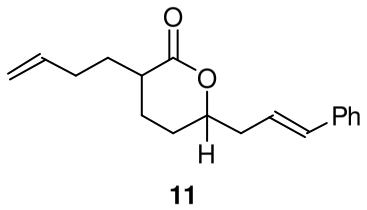

13C-NMR 100 MHz
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)


EtO2C
O
O
Ph
H

S7

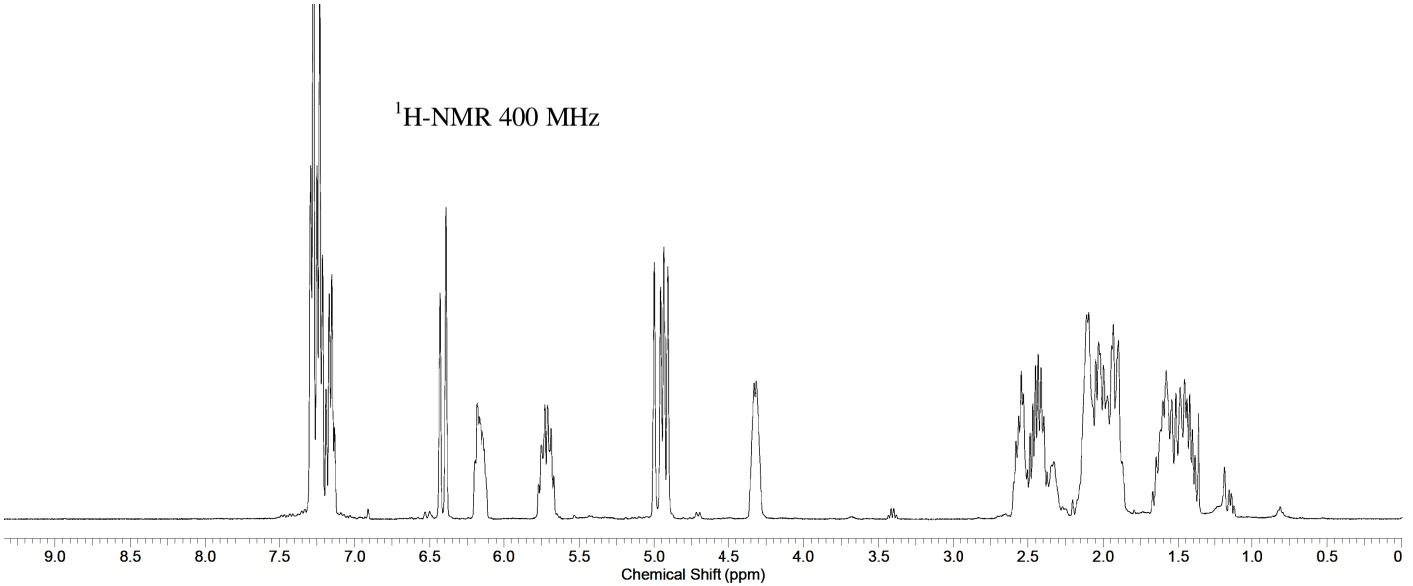

1H-NMR 400 MHz
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


13C-NMR 100 MHz
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

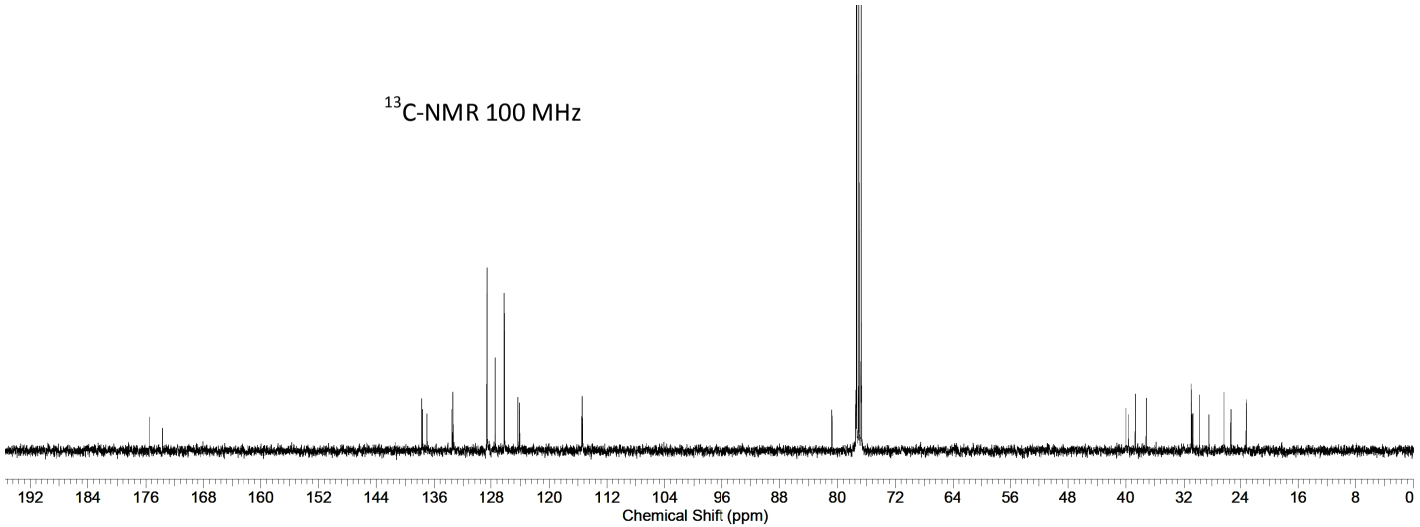


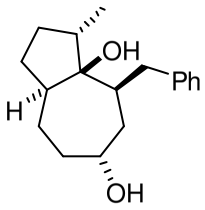
11

^{1}H-NMR 400 MHz

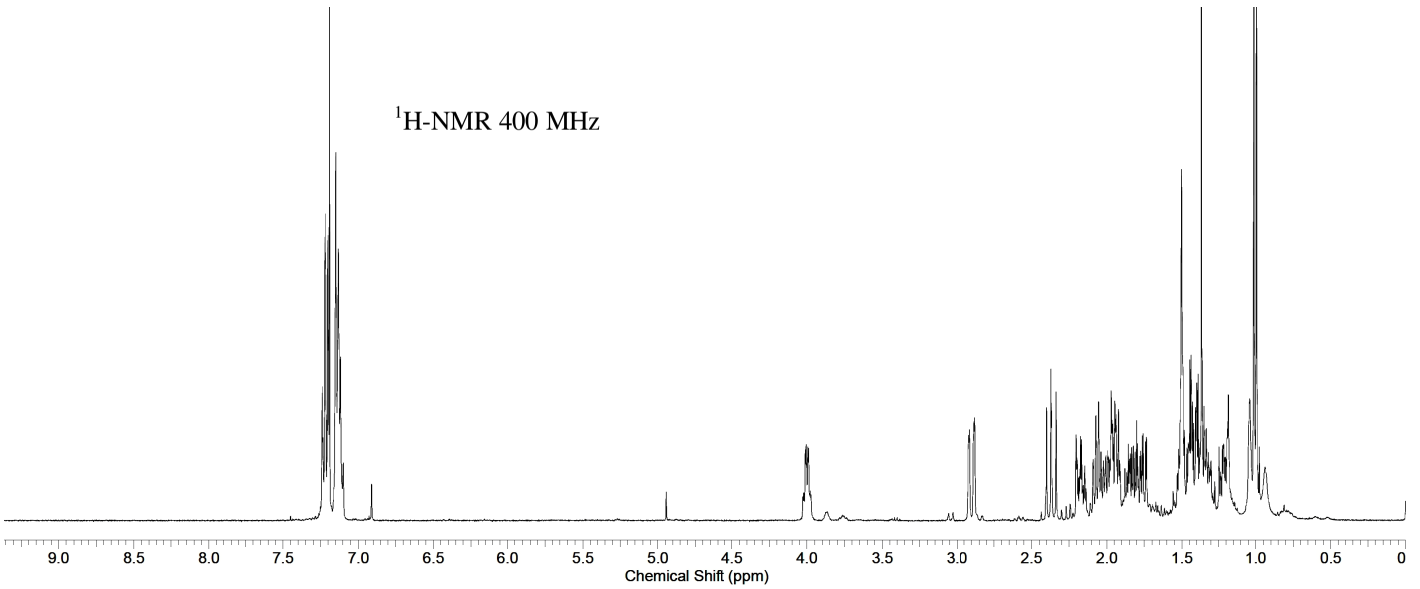


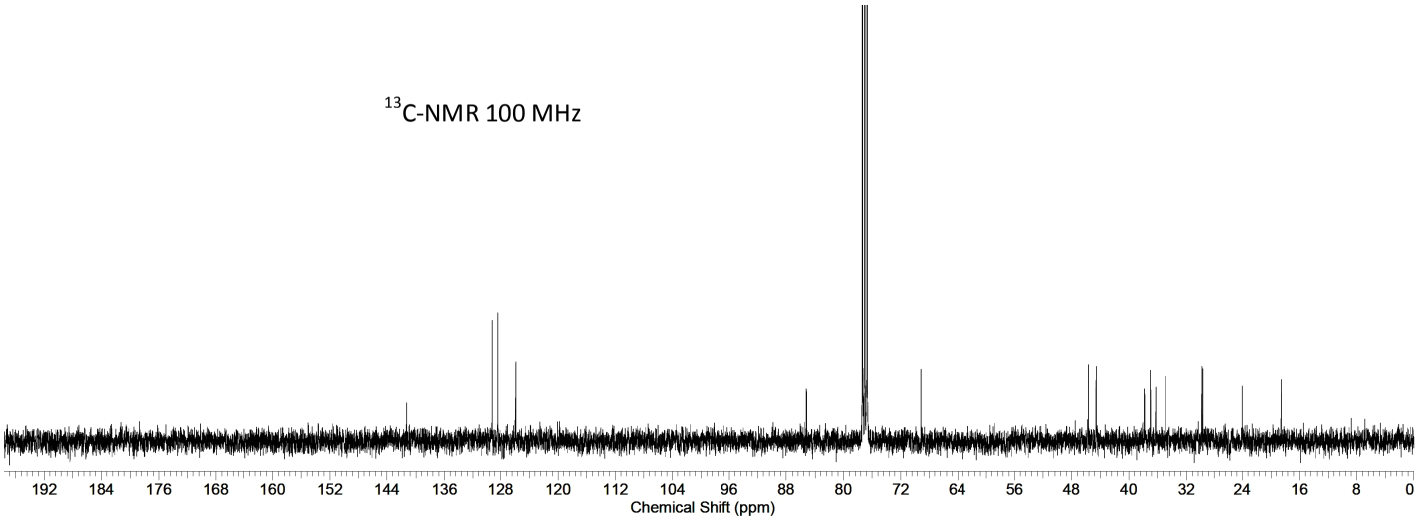
^{13}C-NMR 100 MHz

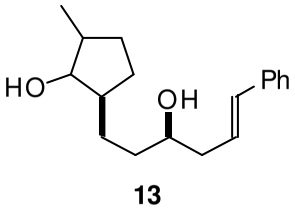



OH
Ph
H
OH

12

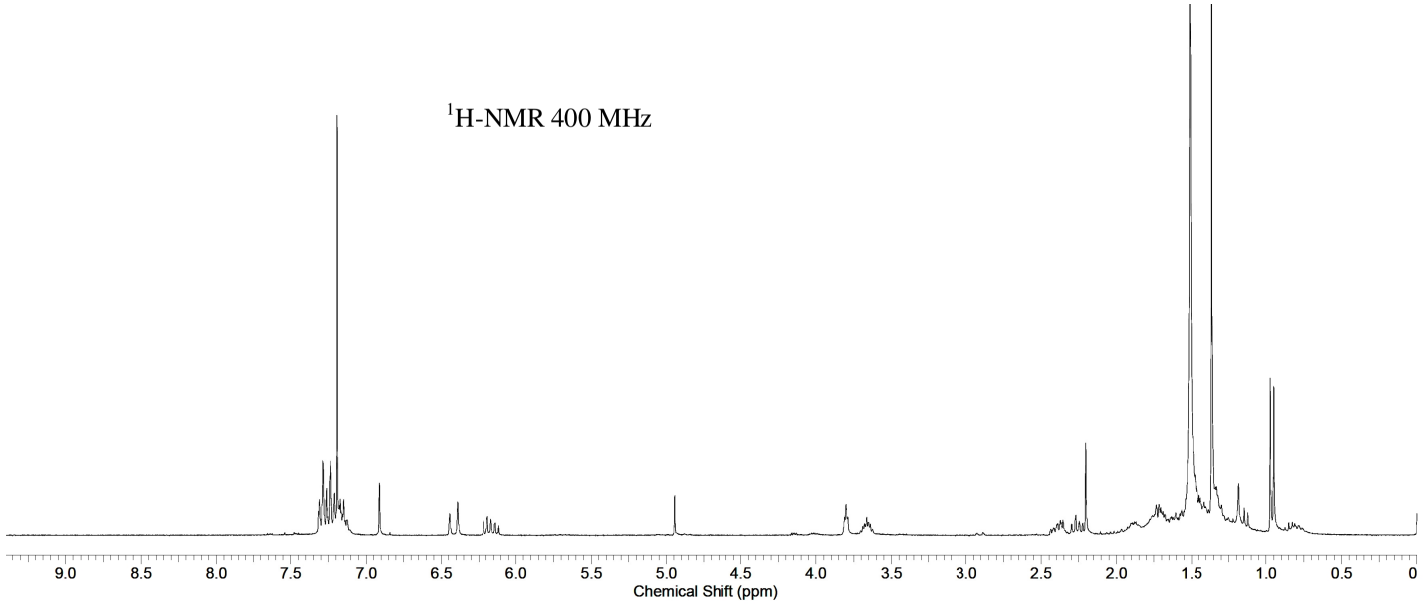

^{1}H-NMR 400 MHz
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


^{13}C-NMR 100 MHz
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

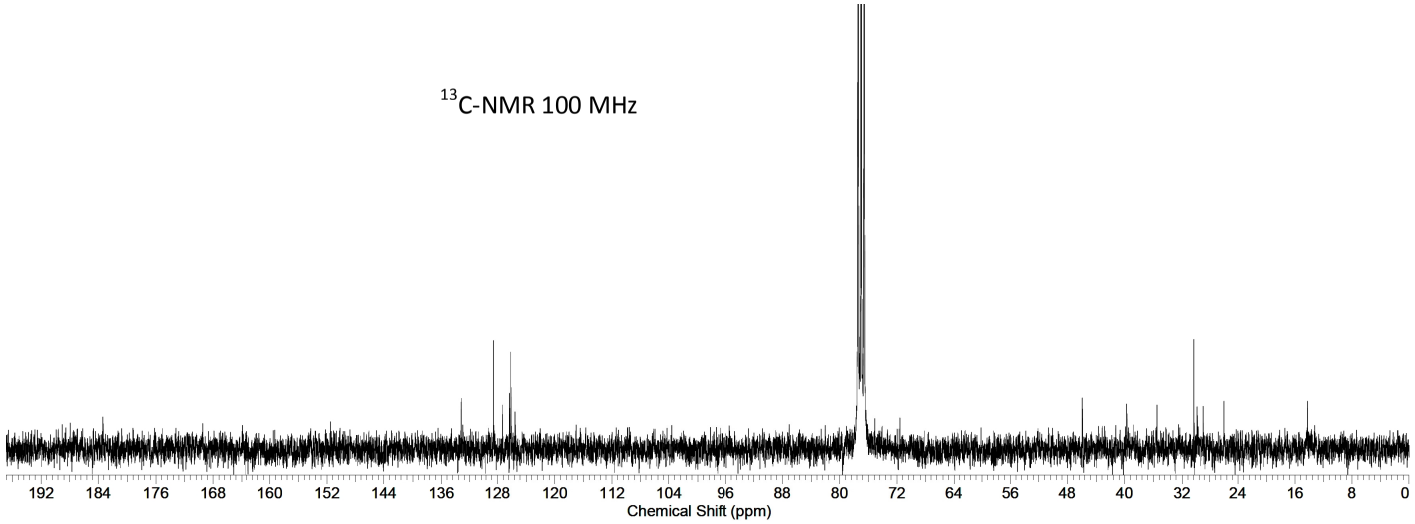


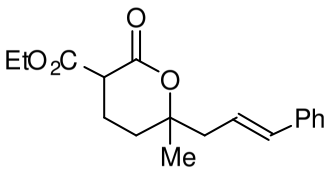
13

^{1}H-NMR 400 MHz



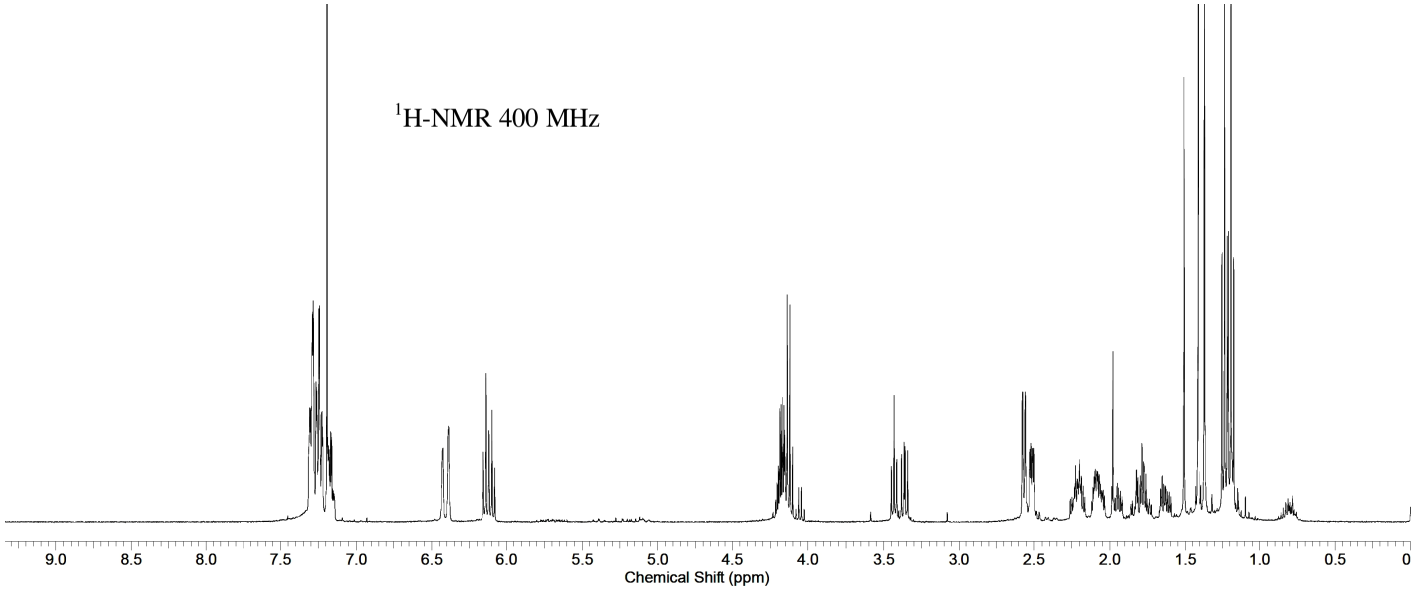
^{13}C-NMR 100 MHz



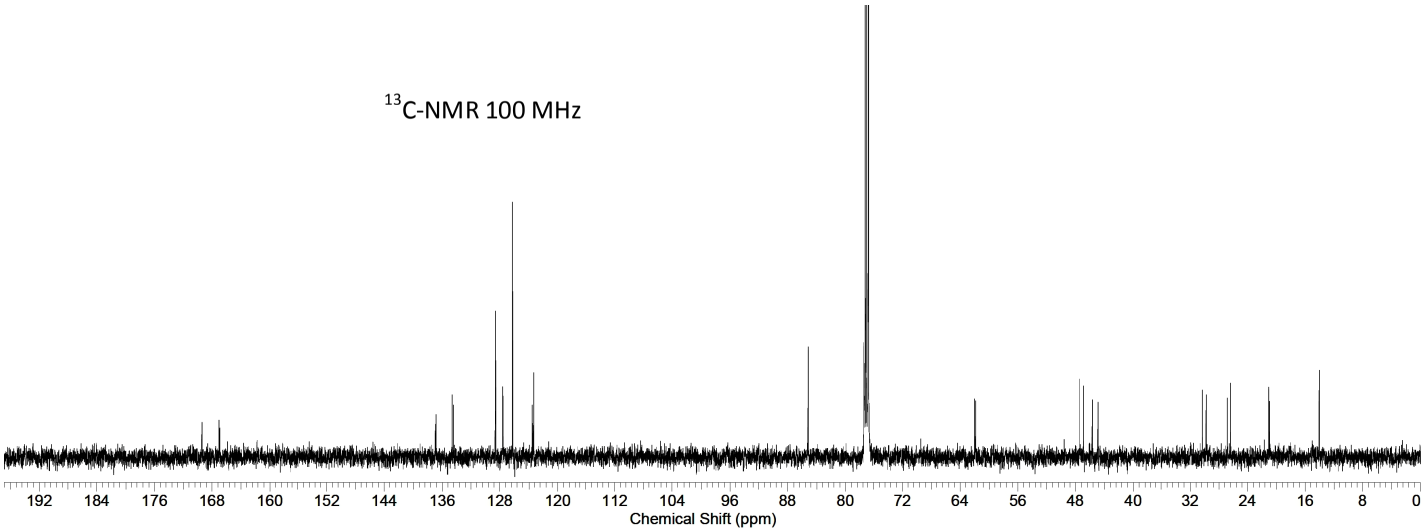


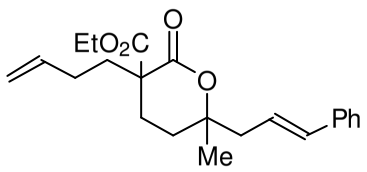
S8

^{1}H-NMR 400 MHz



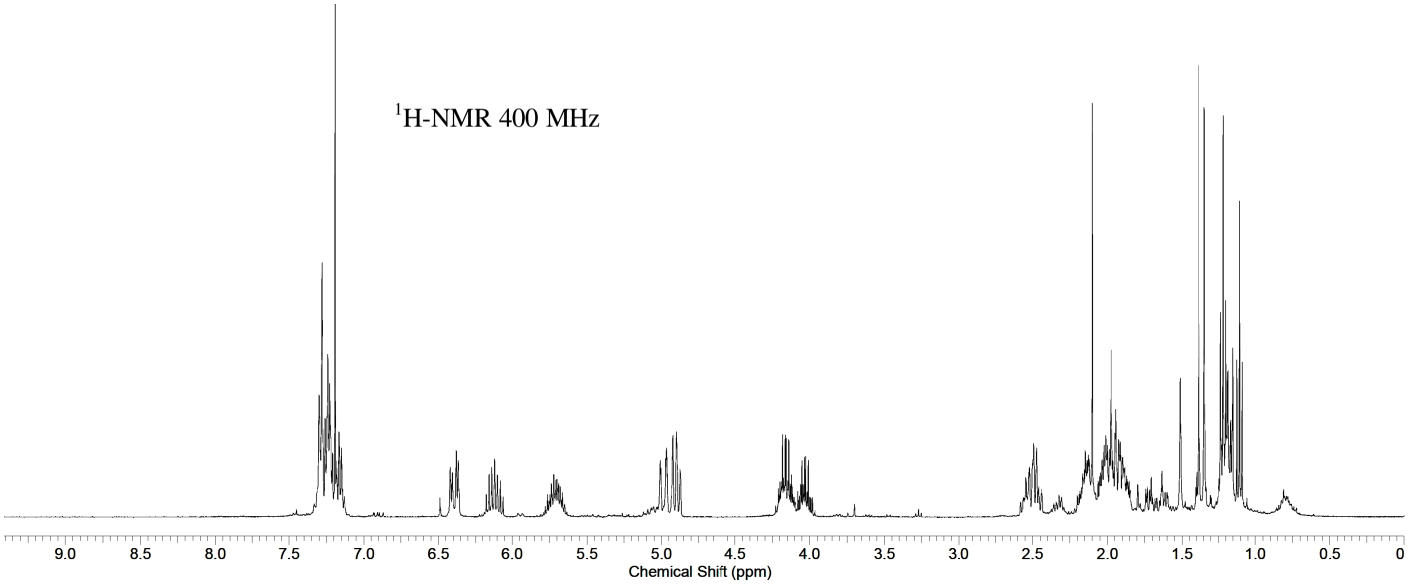
^{13}C-NMR 100 MHz



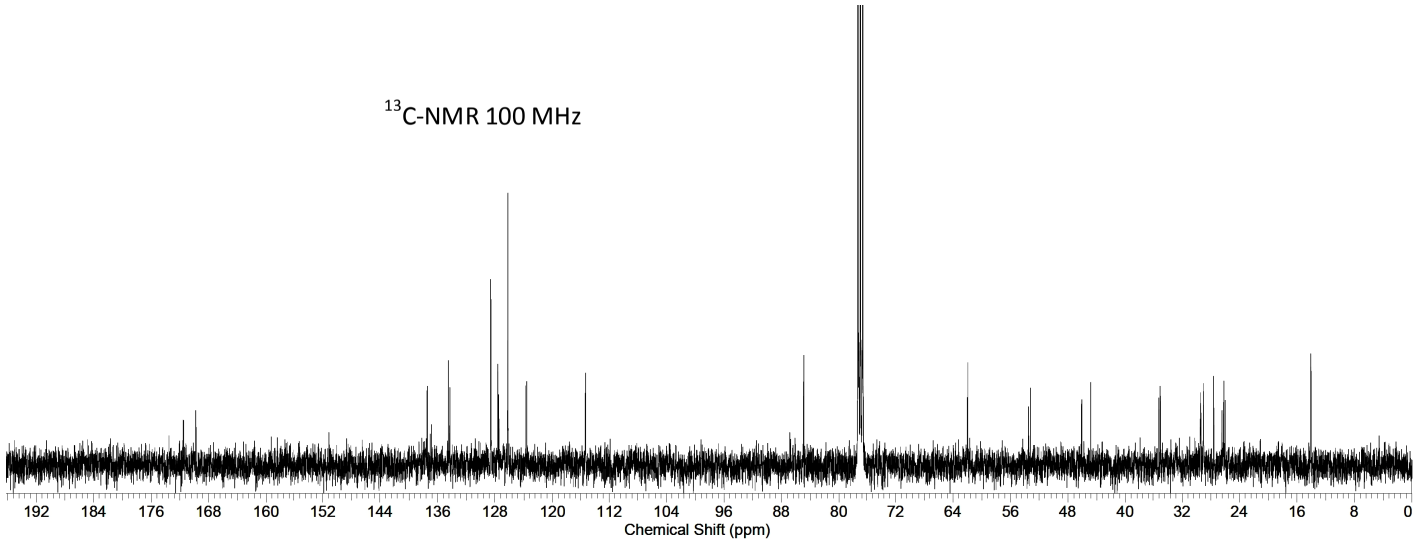


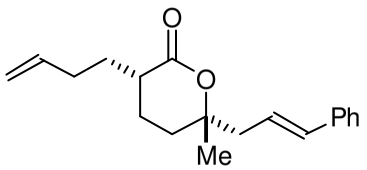
S9

^{1}H-NMR 400 MHz



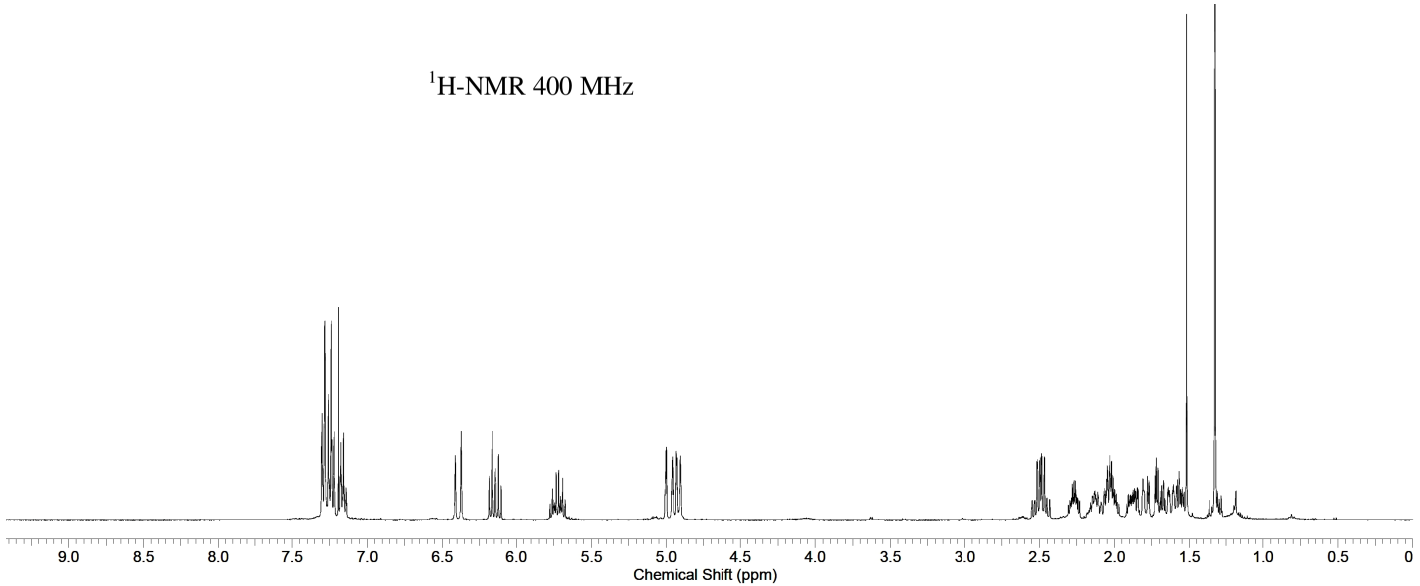
^{13}C-NMR 100 MHz



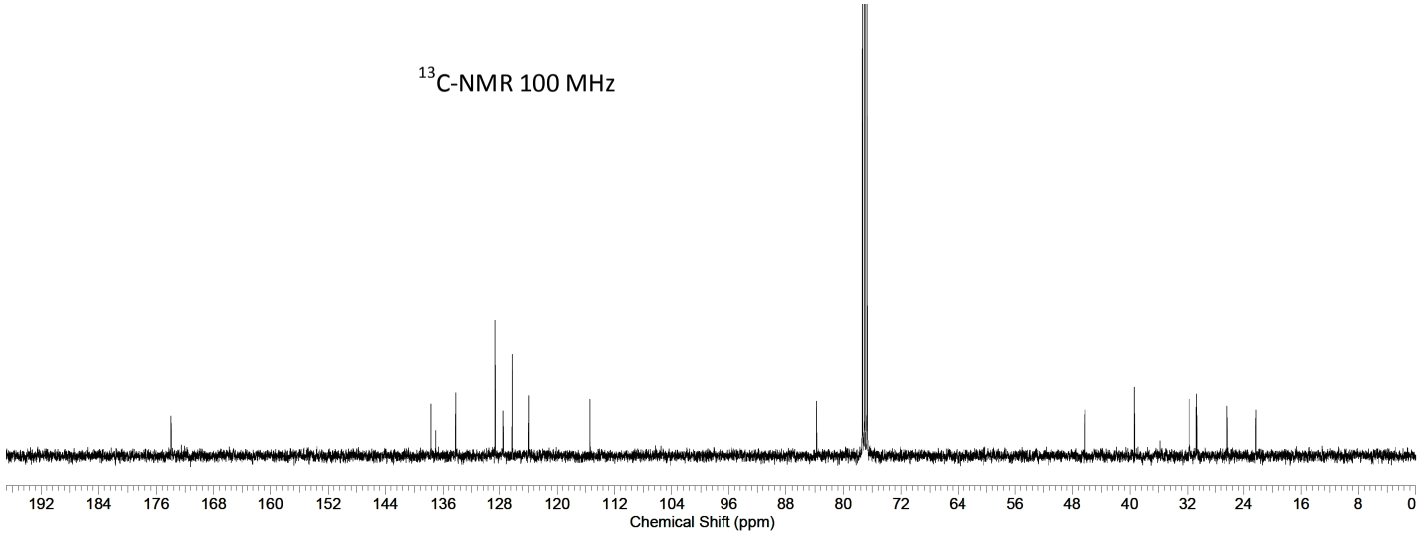


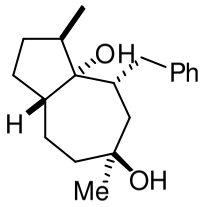
14

^{1}H-NMR 400 MHz



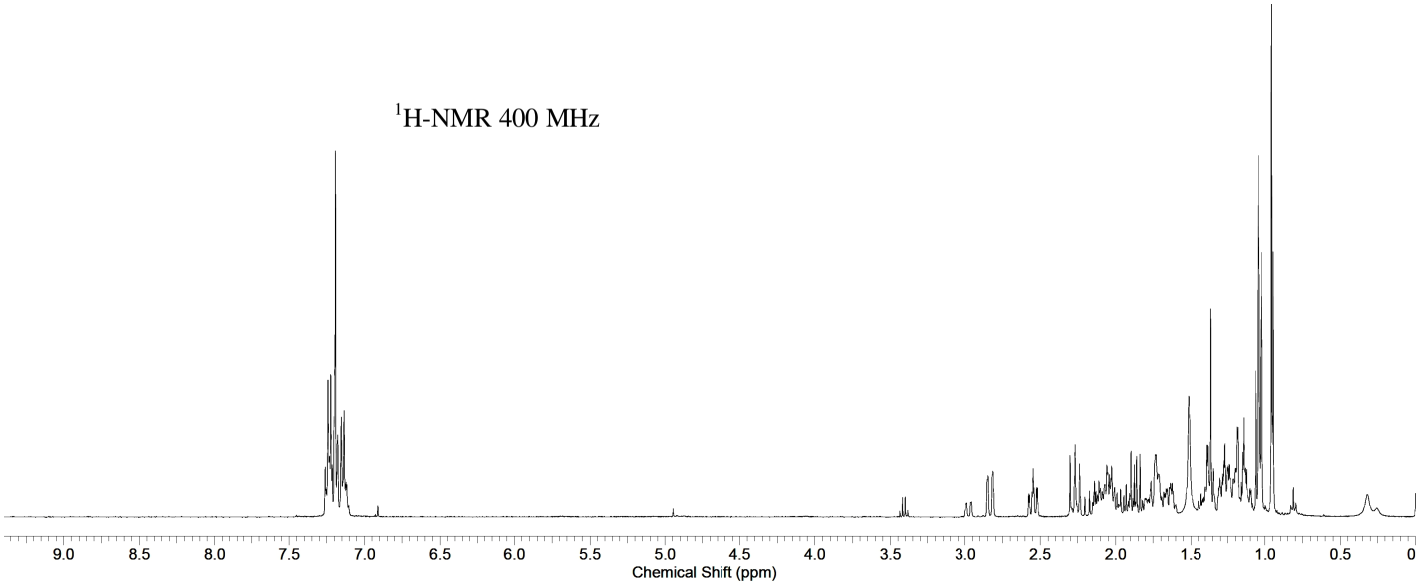
^{13}C-NMR 100 MHz



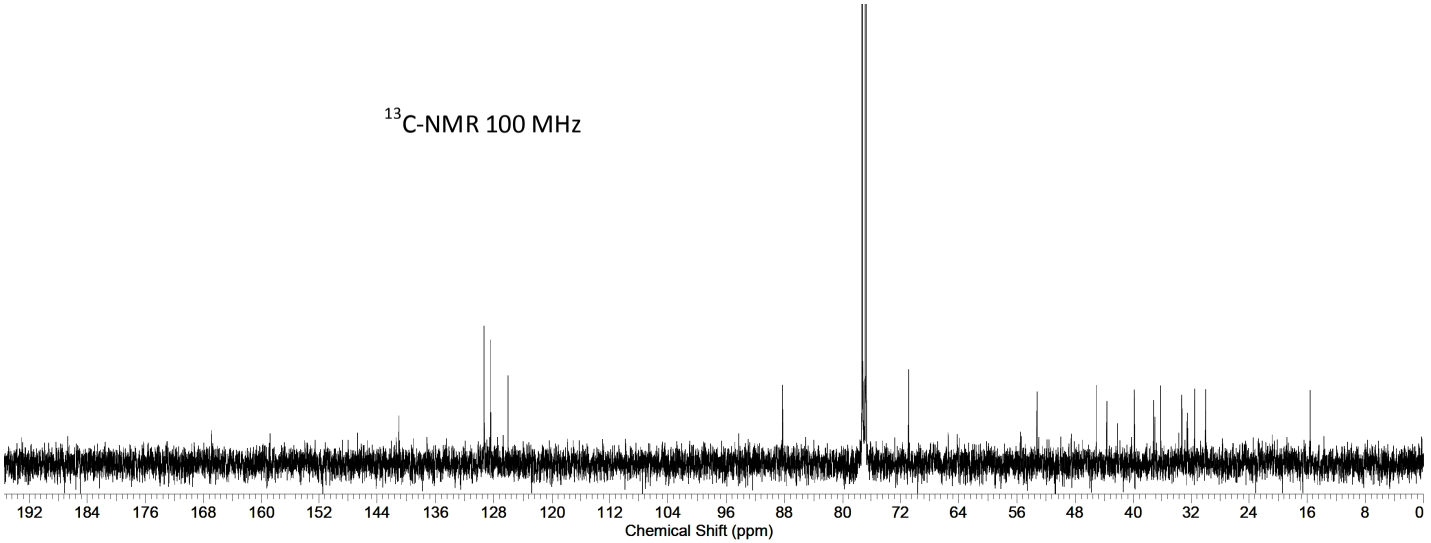


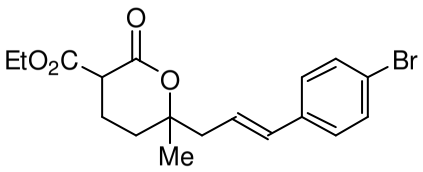
19

^{1}H-NMR 400 MHz



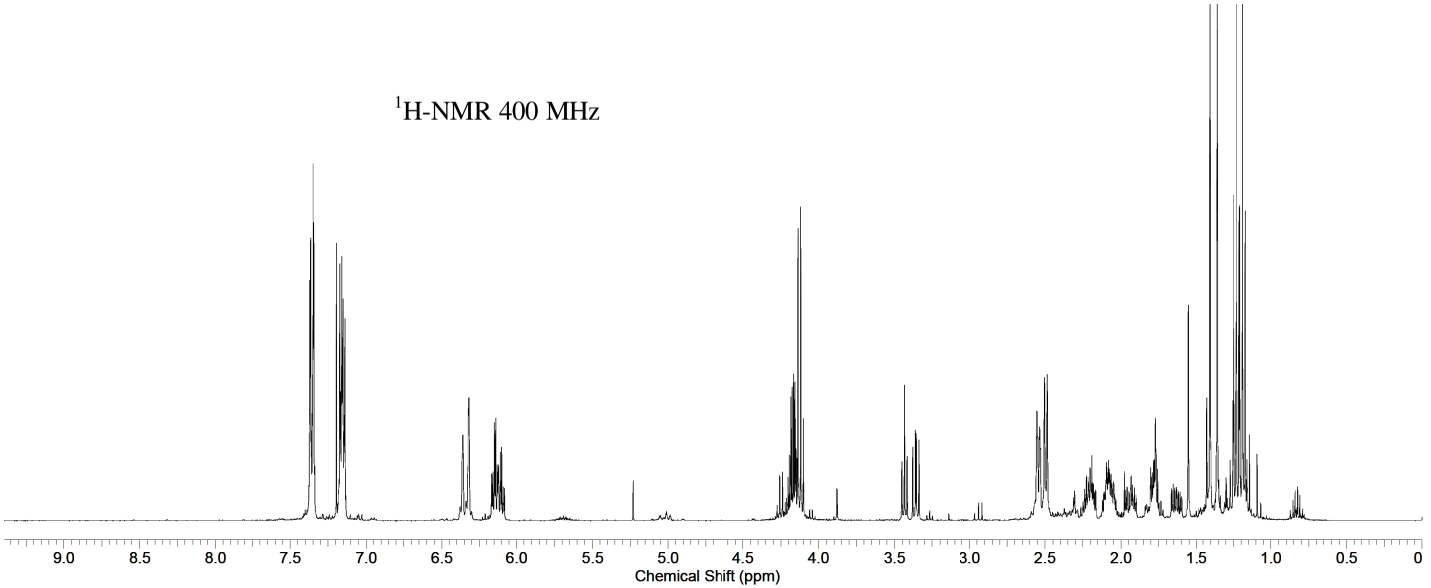
^{13}C-NMR 100 MHz



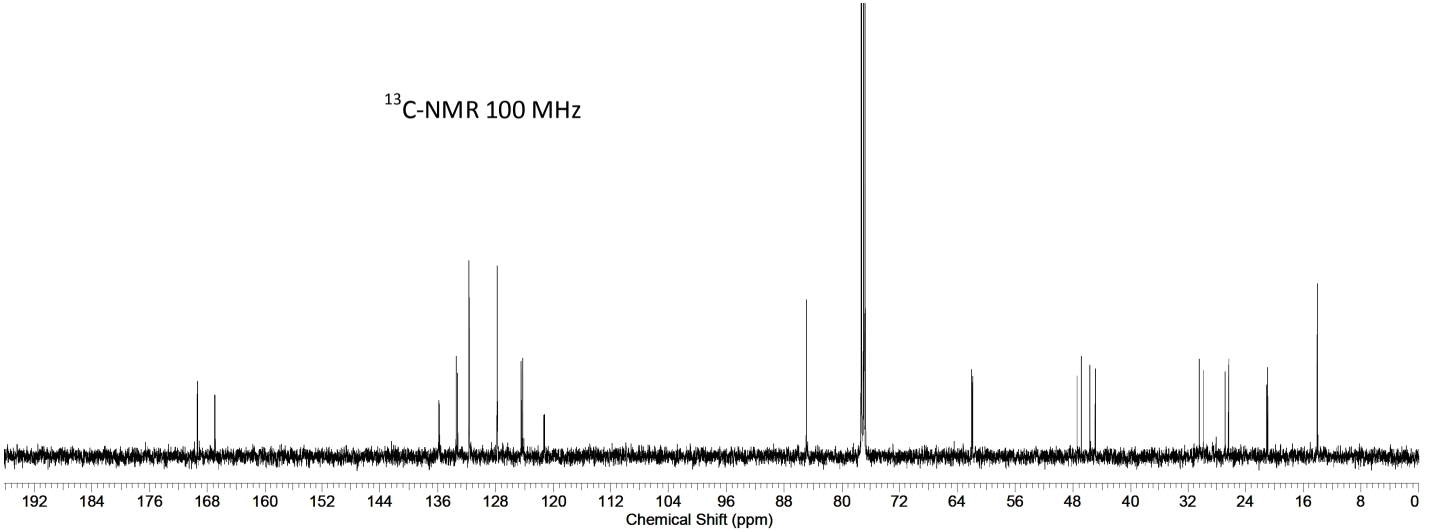


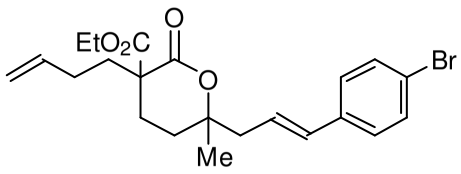
S10

^{1}H-NMR 400 MHz



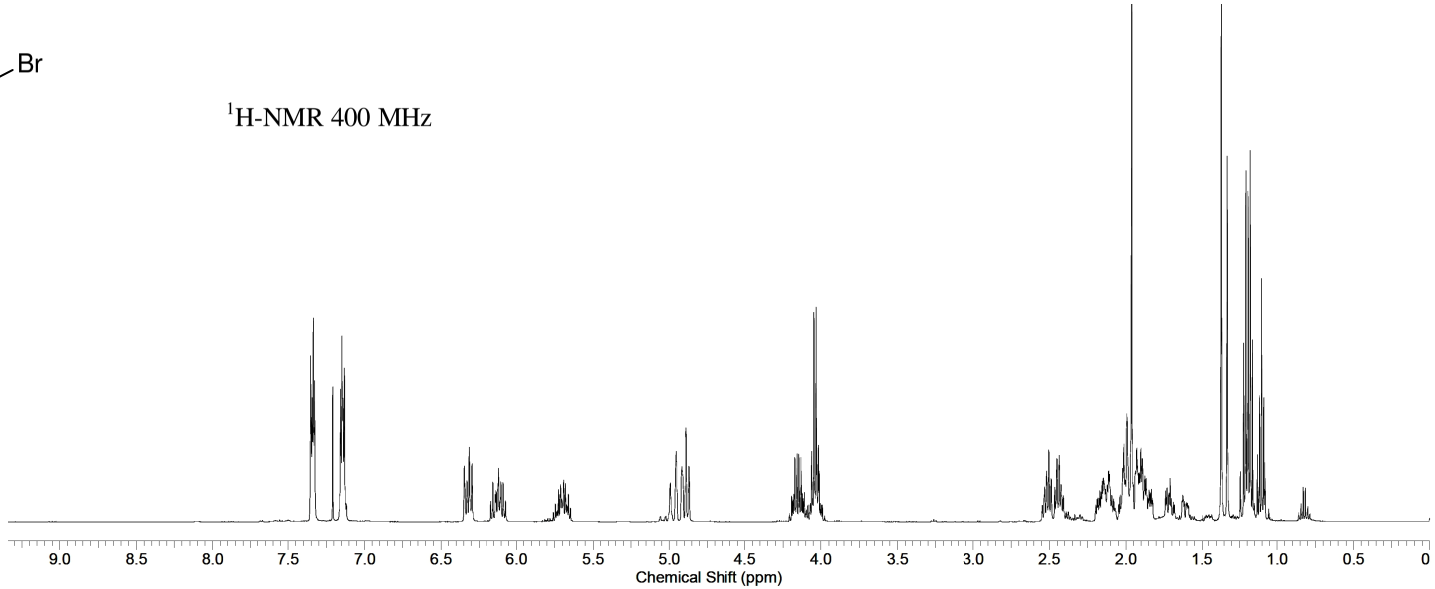
^{13}C-NMR 100 MHz



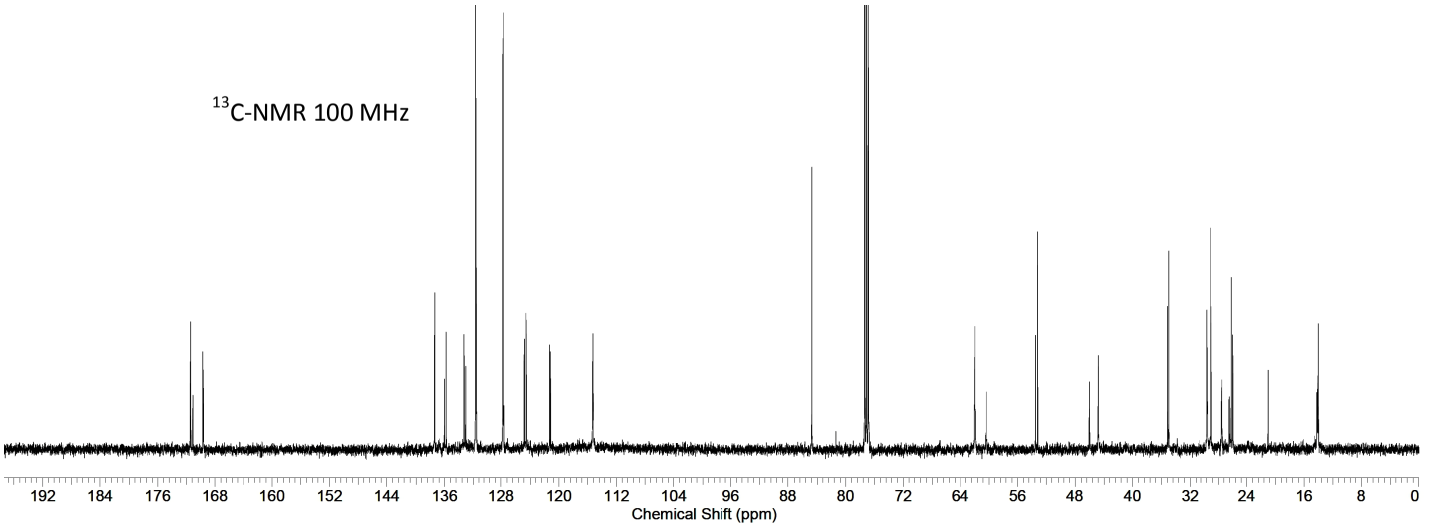


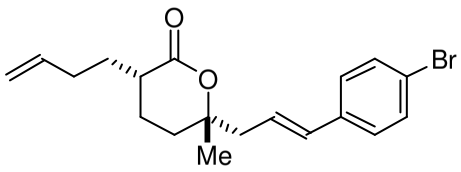
S11

^{1}H-NMR 400 MHz



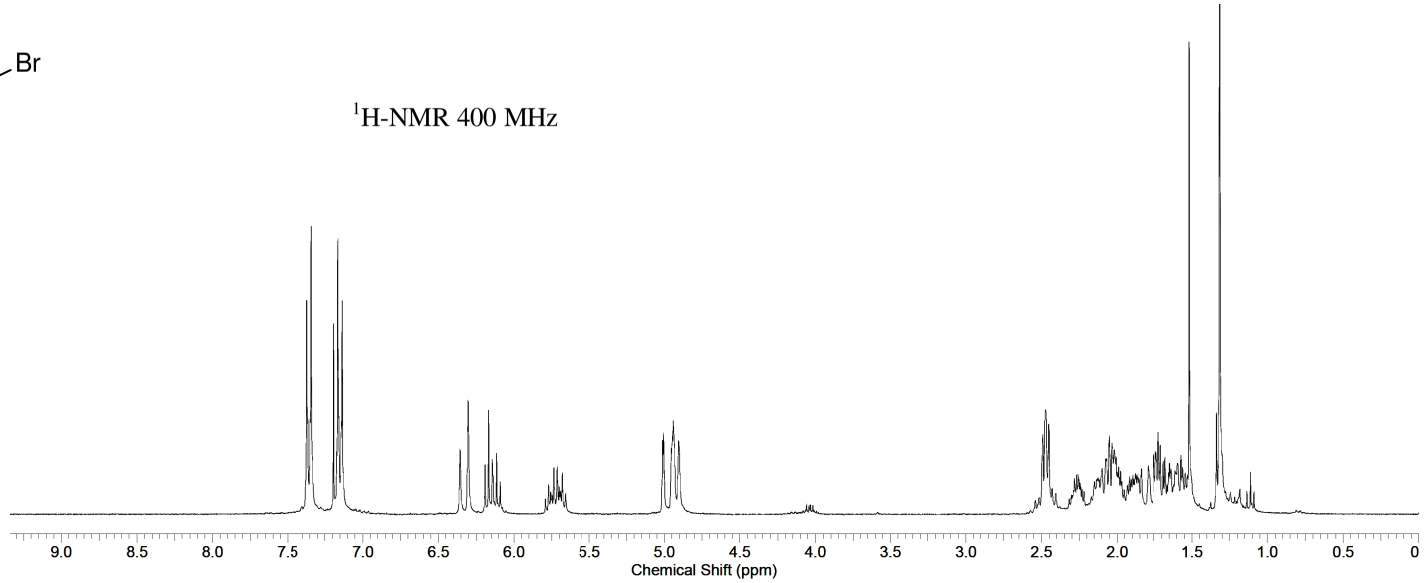
^{13}C-NMR 100 MHz



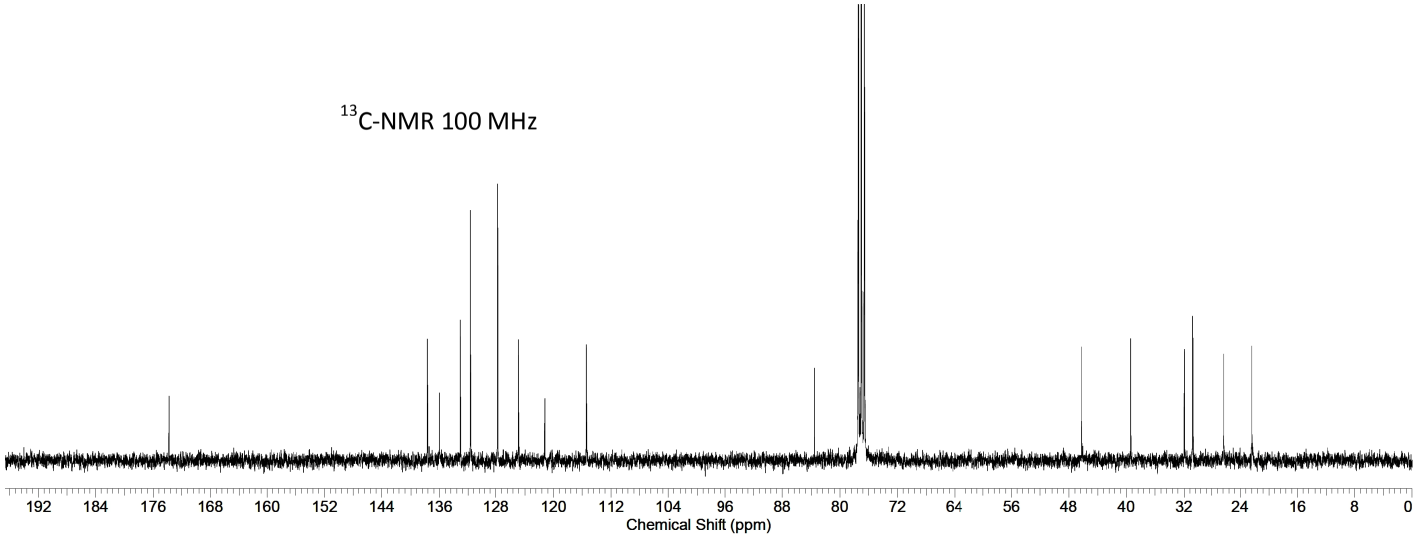


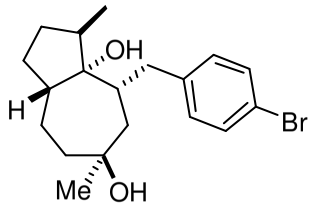
15

^{1}H-NMR 400 MHz

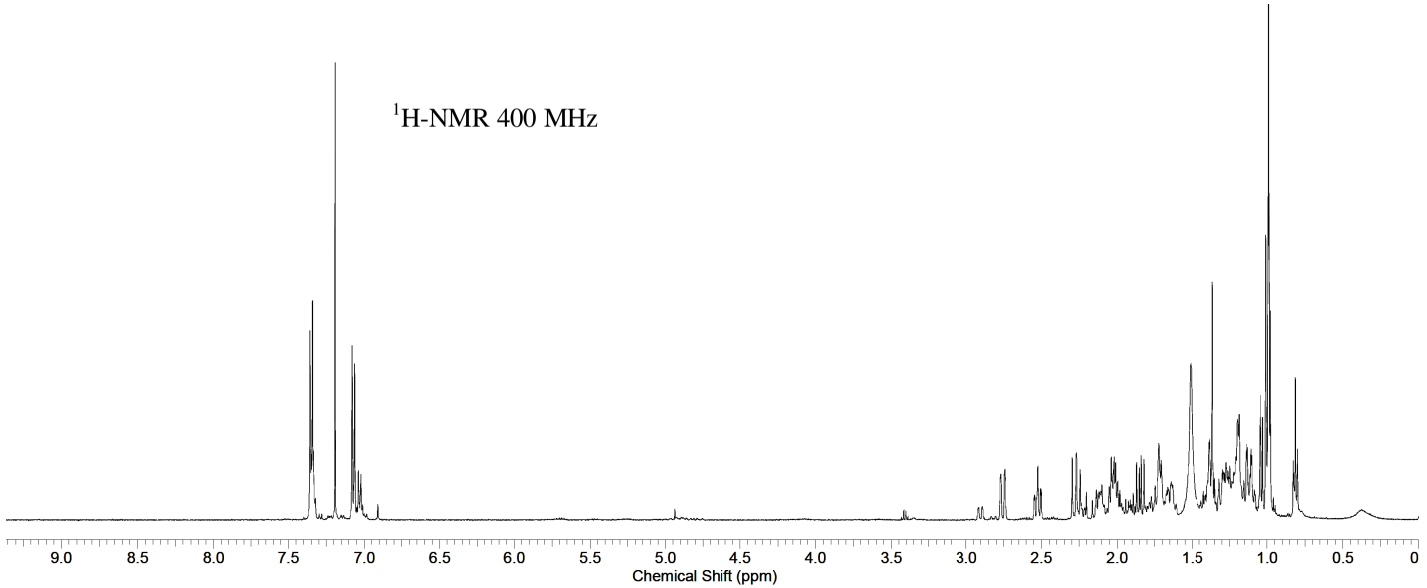


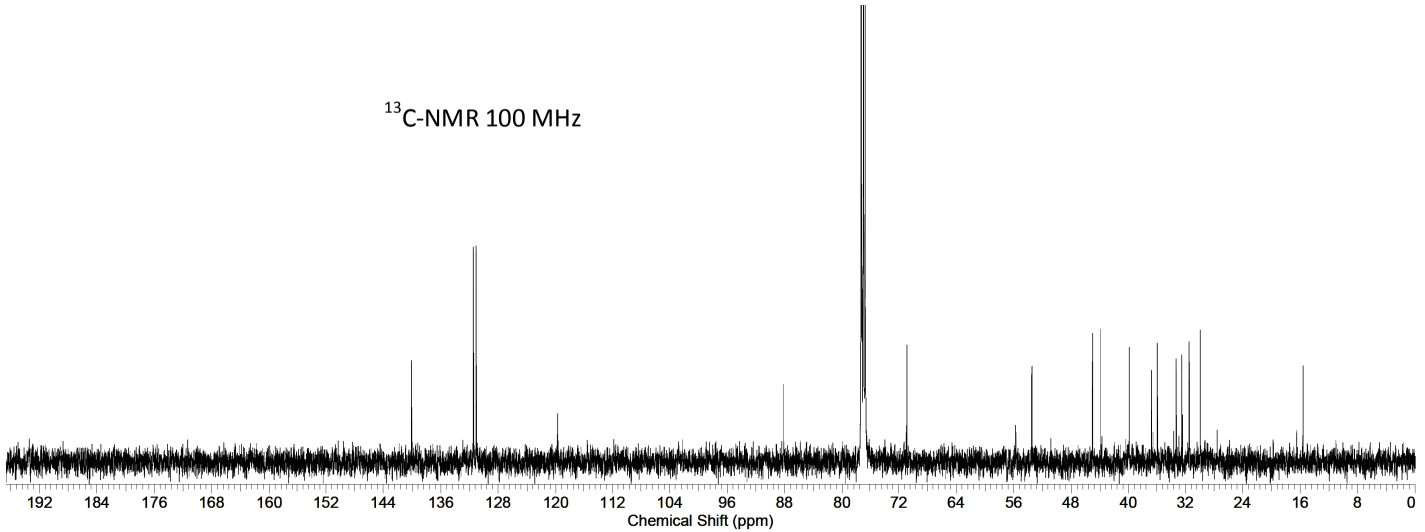
^{13}C-NMR 100 MHz

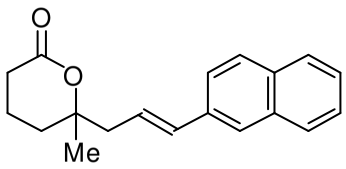



OH
H
Br
Me
OH

20

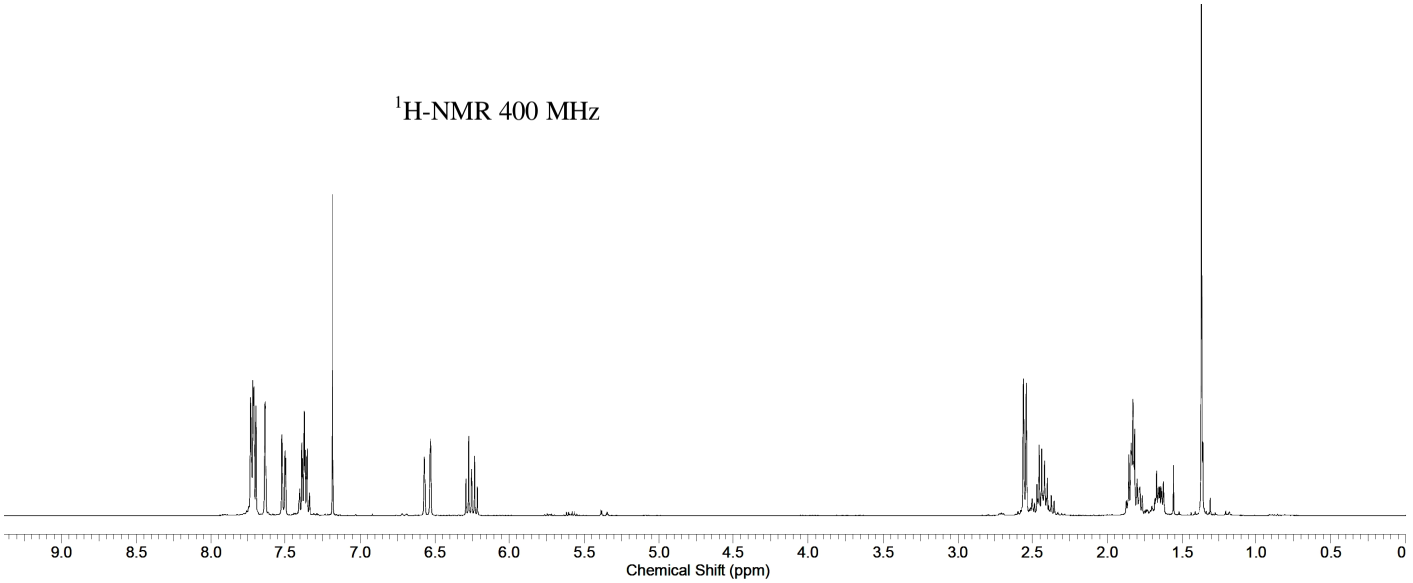

^{1}H-NMR 400 MHz
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


^{13}C-NMR 100 MHz
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

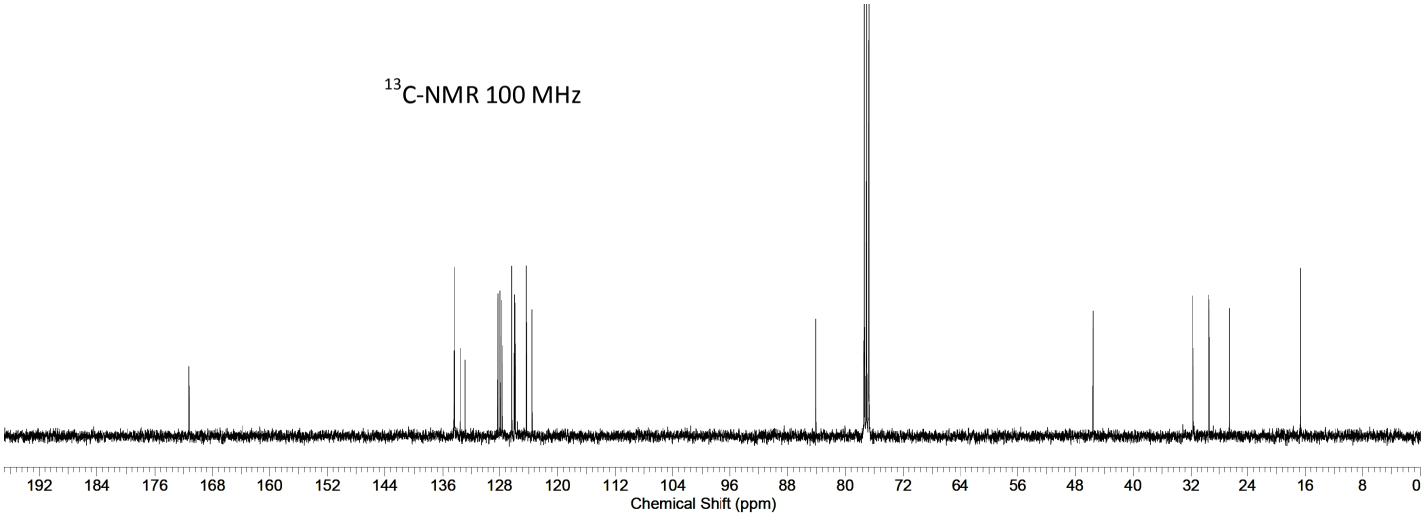


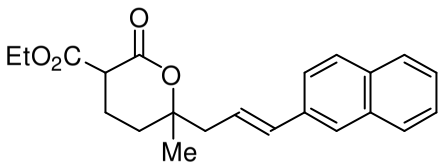
S12

^{1}H-NMR 400 MHz



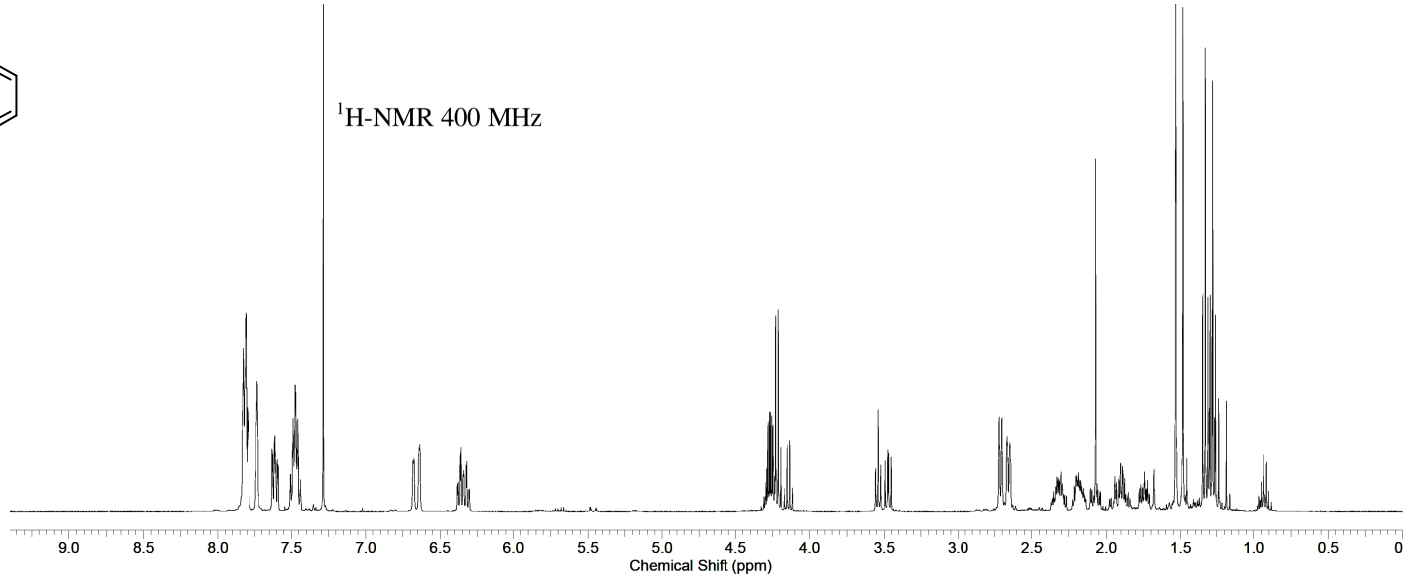
^{13}C-NMR 100 MHz



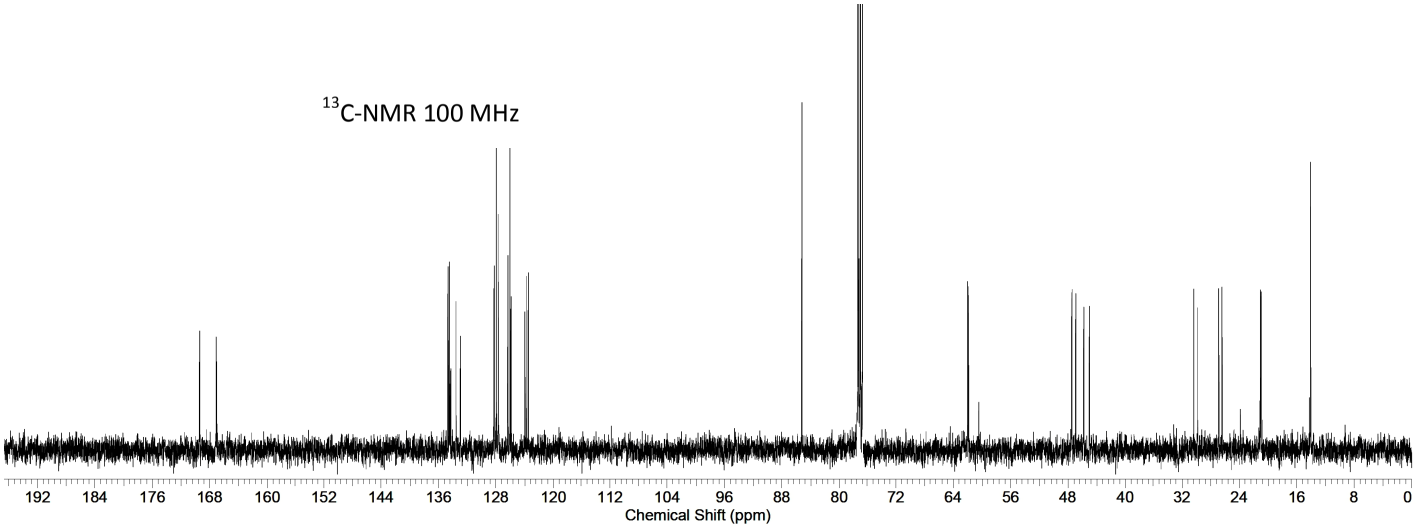


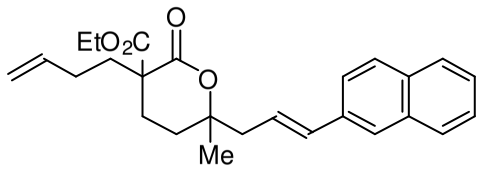
S13

^{1}H-NMR 400 MHz



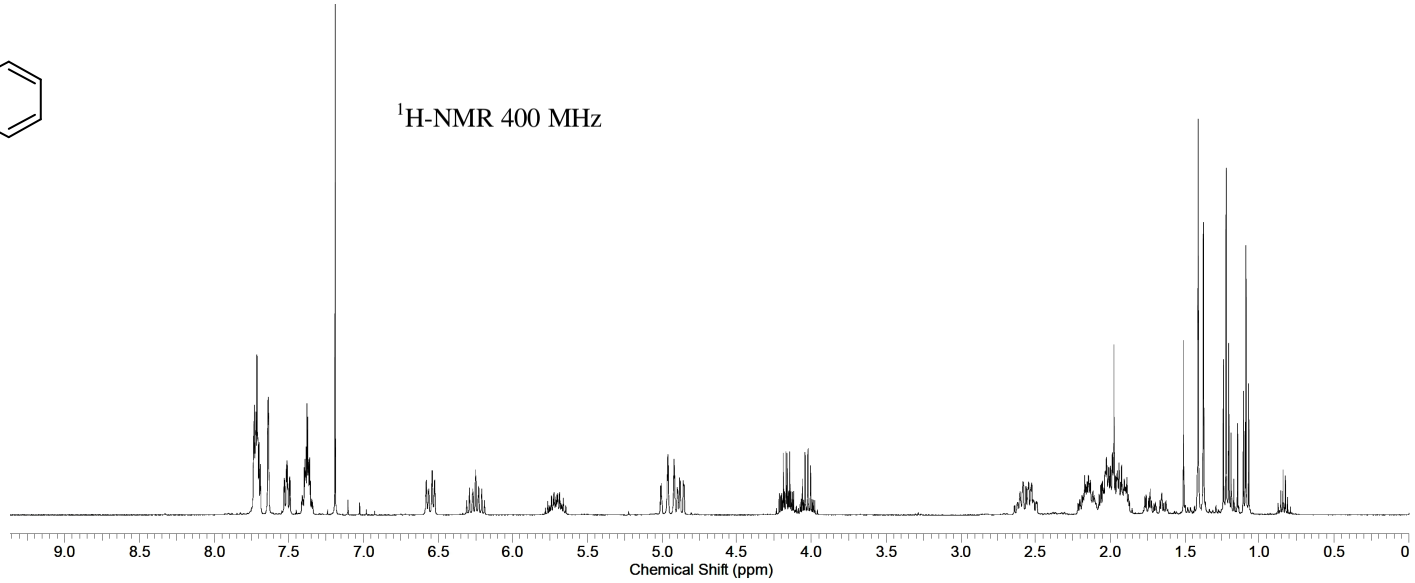
^{13}C-NMR 100 MHz



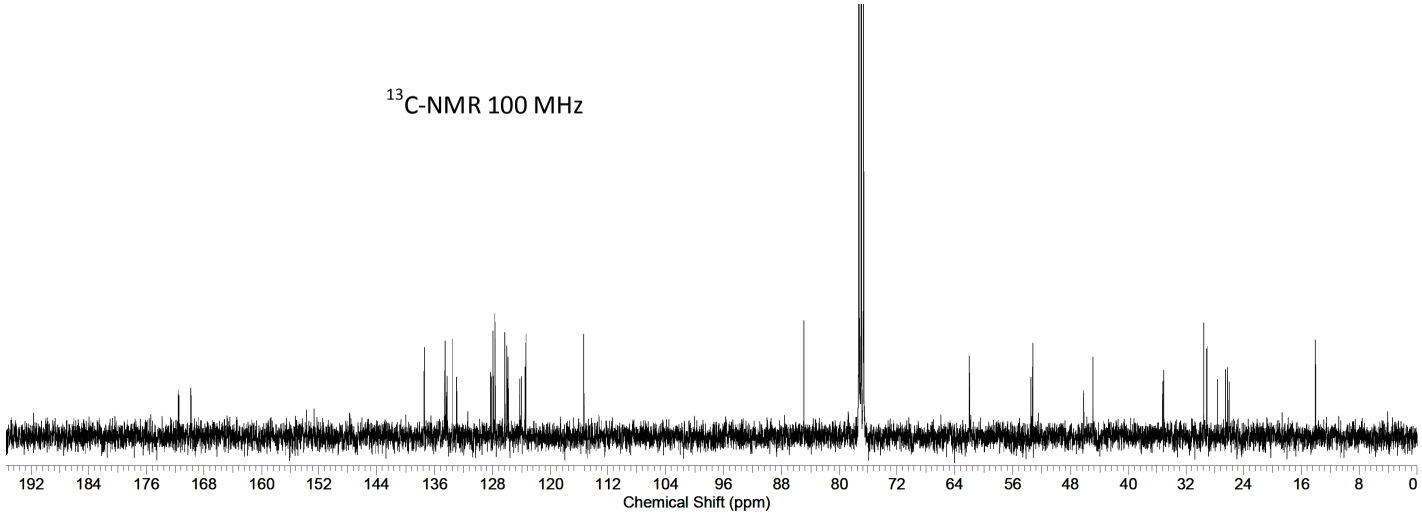


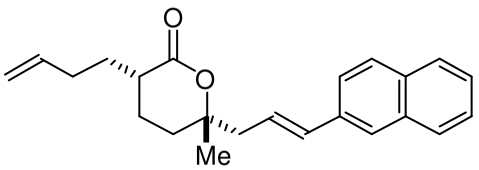
S14

^{1}H-NMR 400 MHz



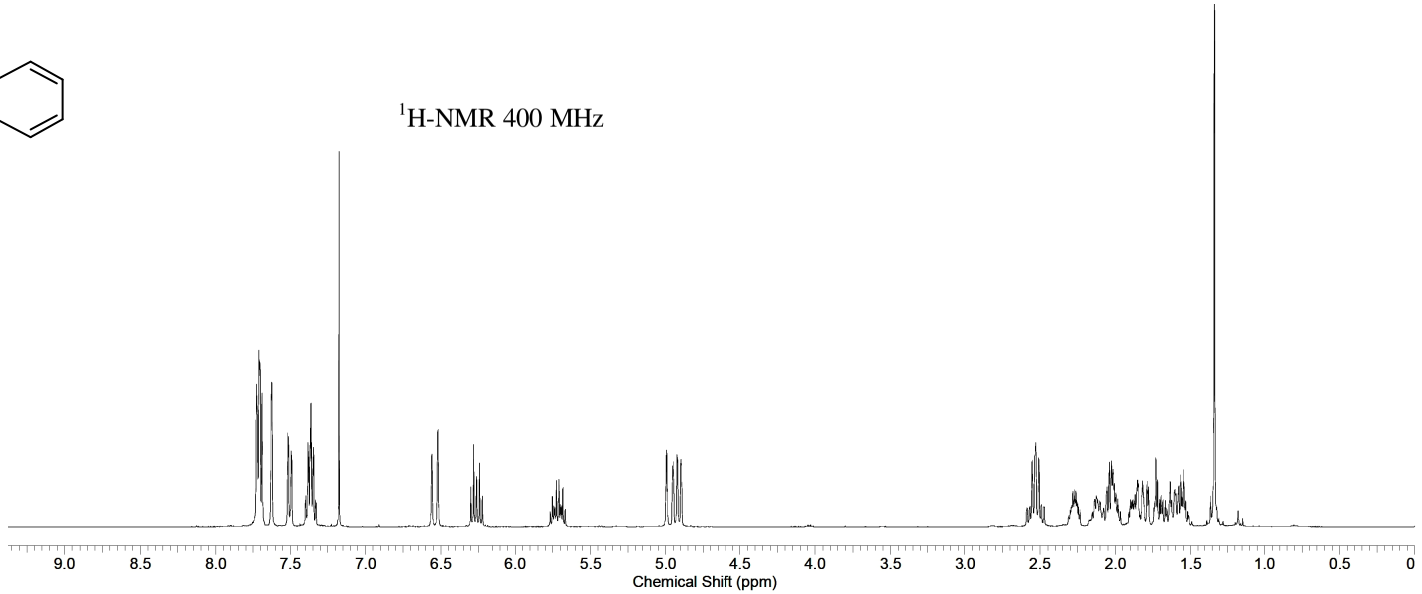
^{13}C-NMR 100 MHz



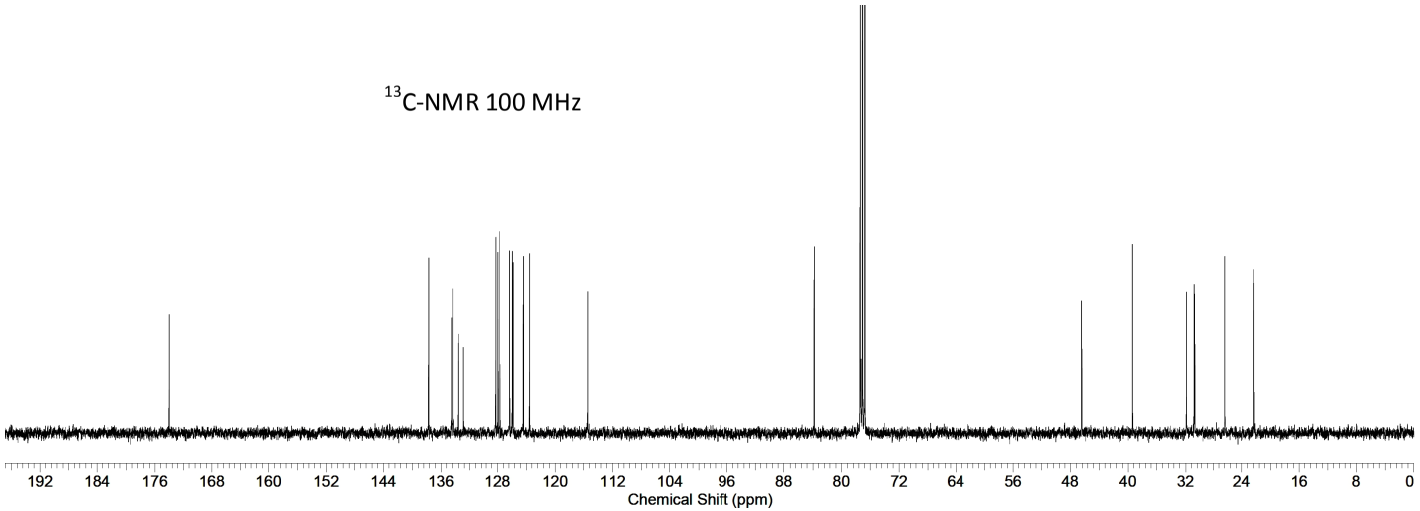


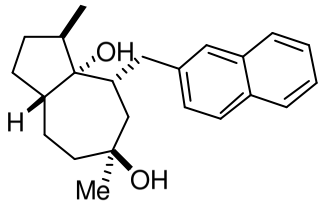
16

^{1}H-NMR 400 MHz

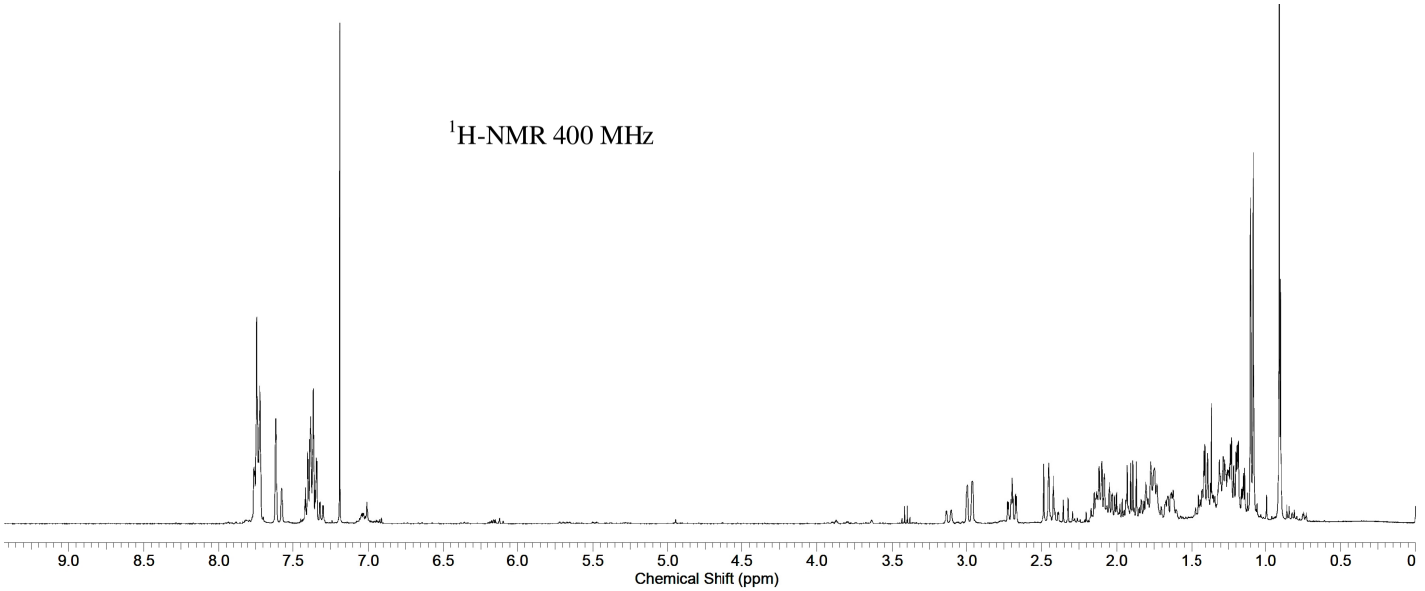


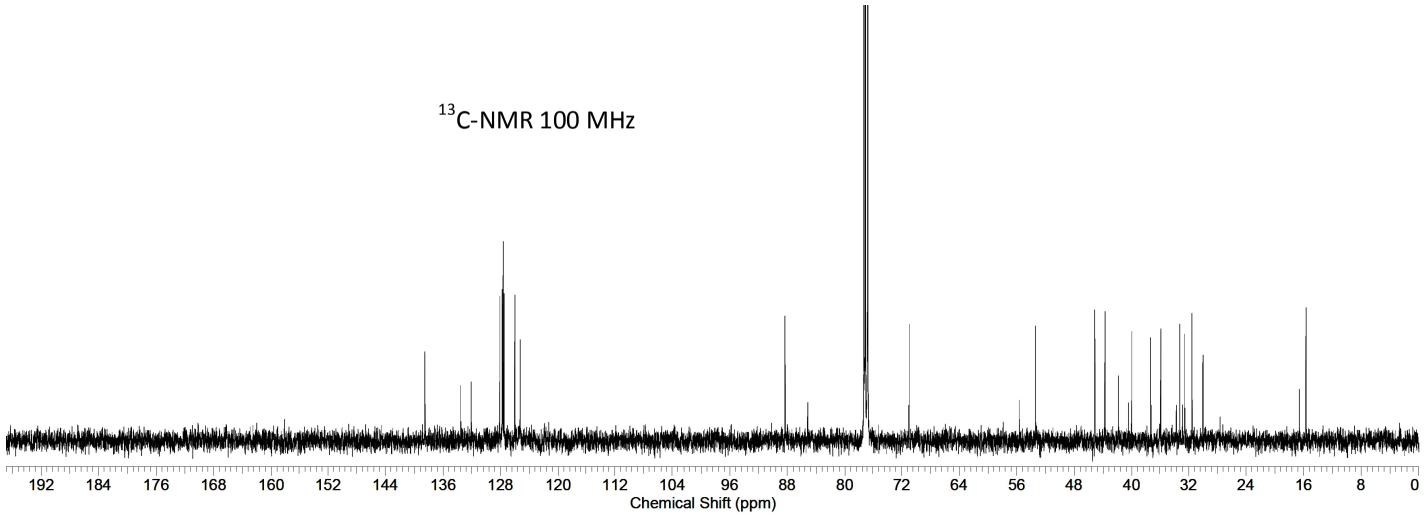
^{13}C-NMR 100 MHz

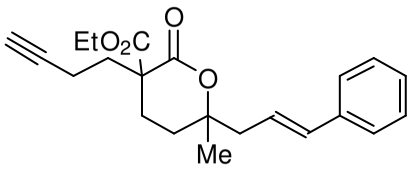



OH
H
Me
OH

21

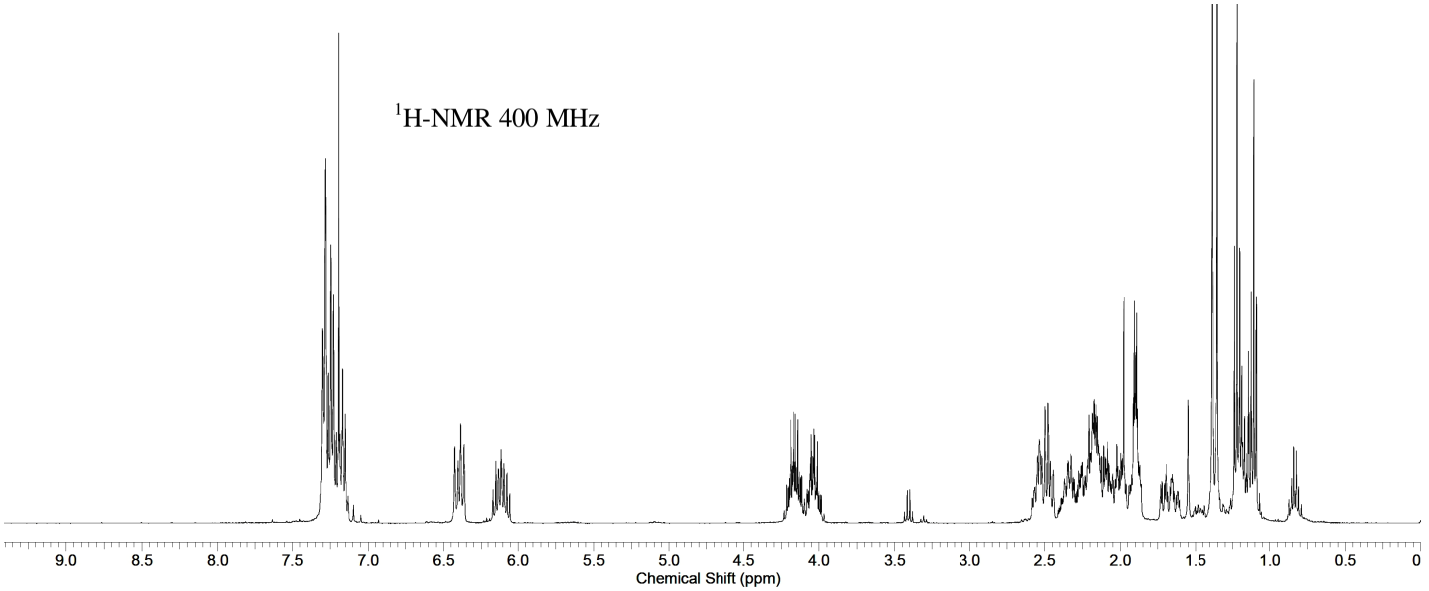

^{1}H-NMR 400 MHz
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
Chemical Shift (ppm)


^{13}C-NMR 100 MHz
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)

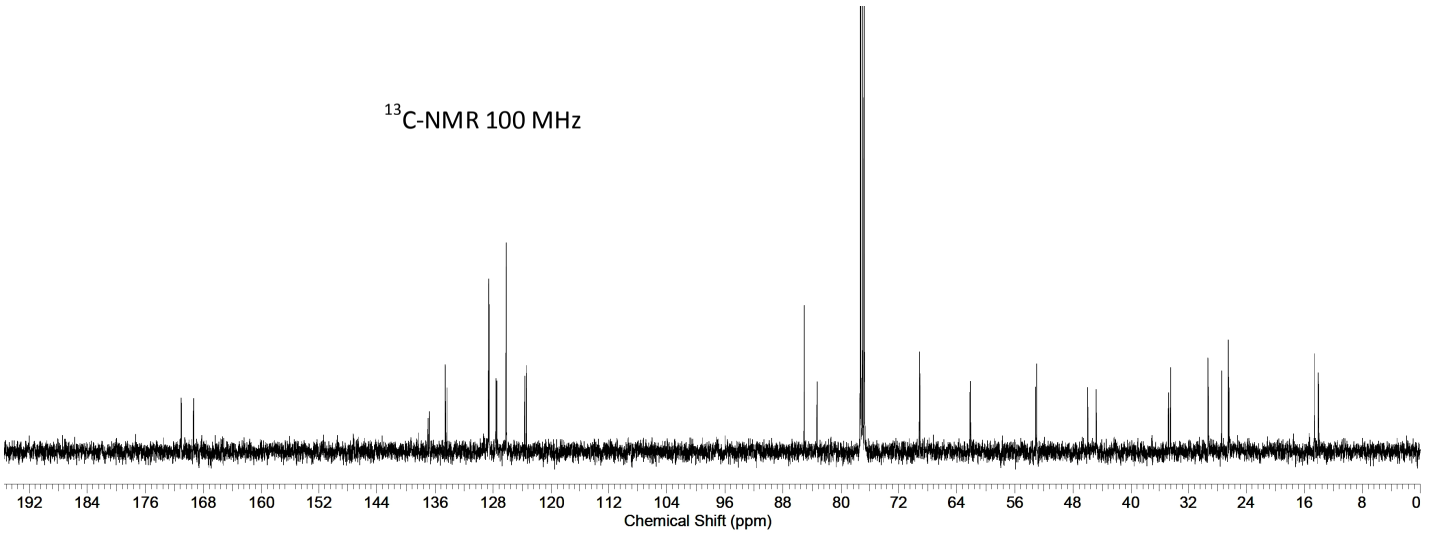


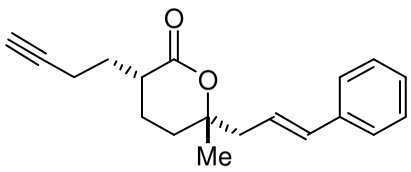
S15

^{1}H-NMR 400 MHz



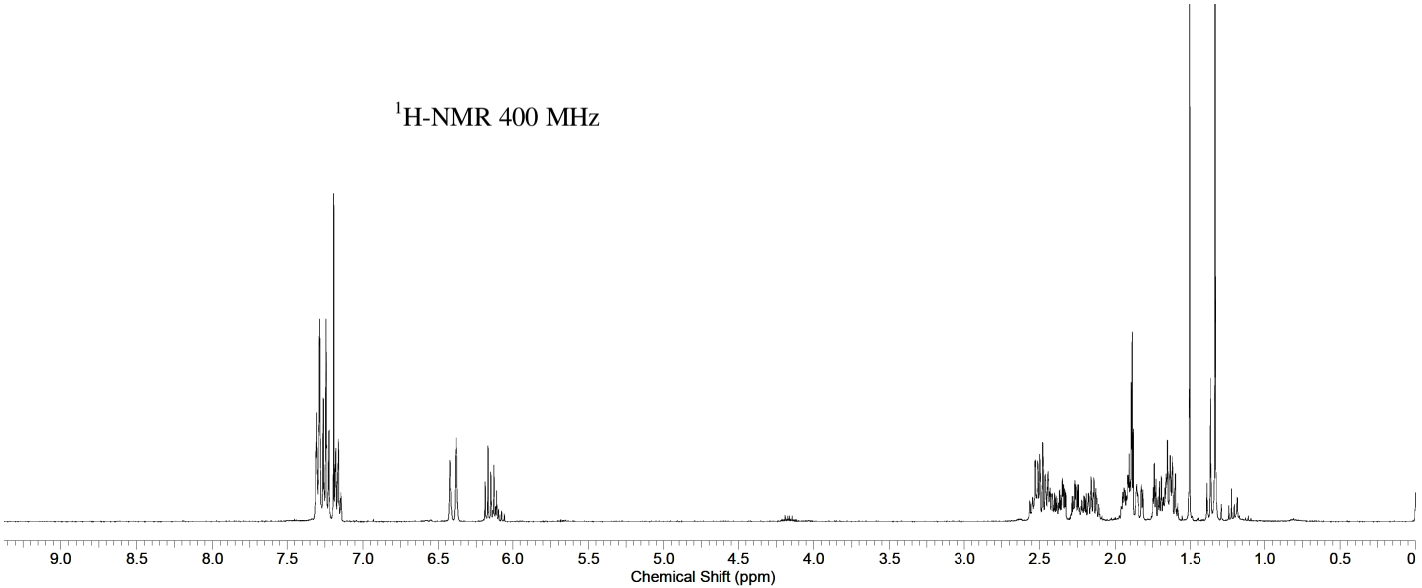
^{13}C-NMR 100 MHz



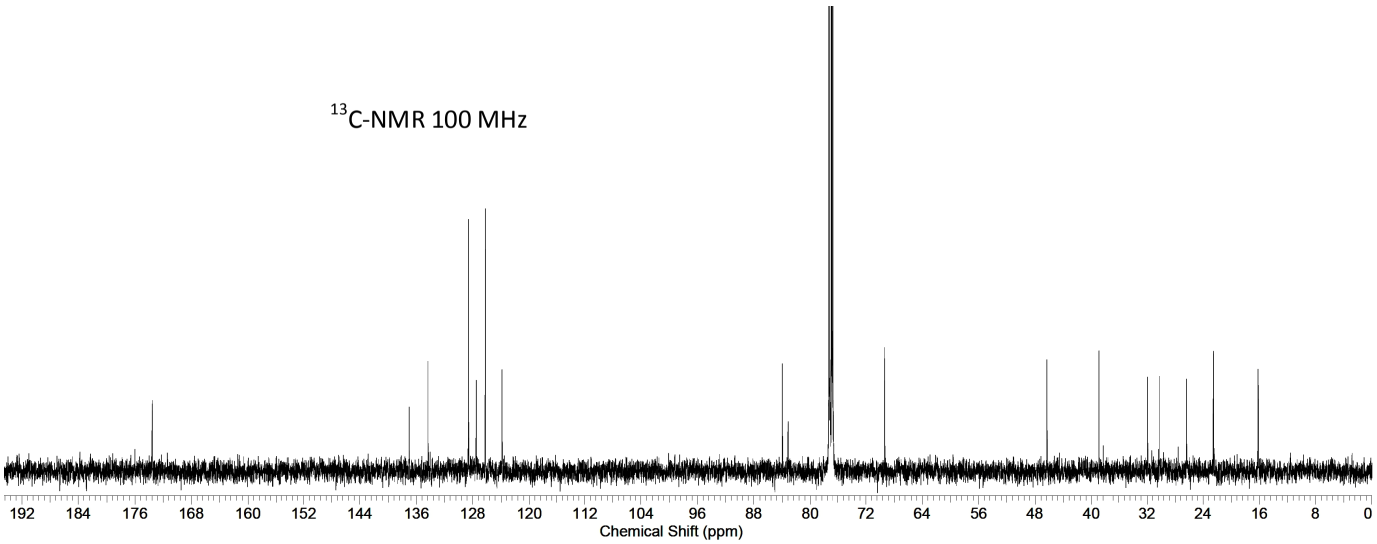


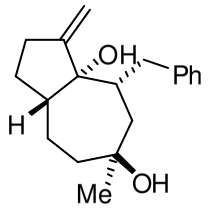
17

^{1}H-NMR 400 MHz



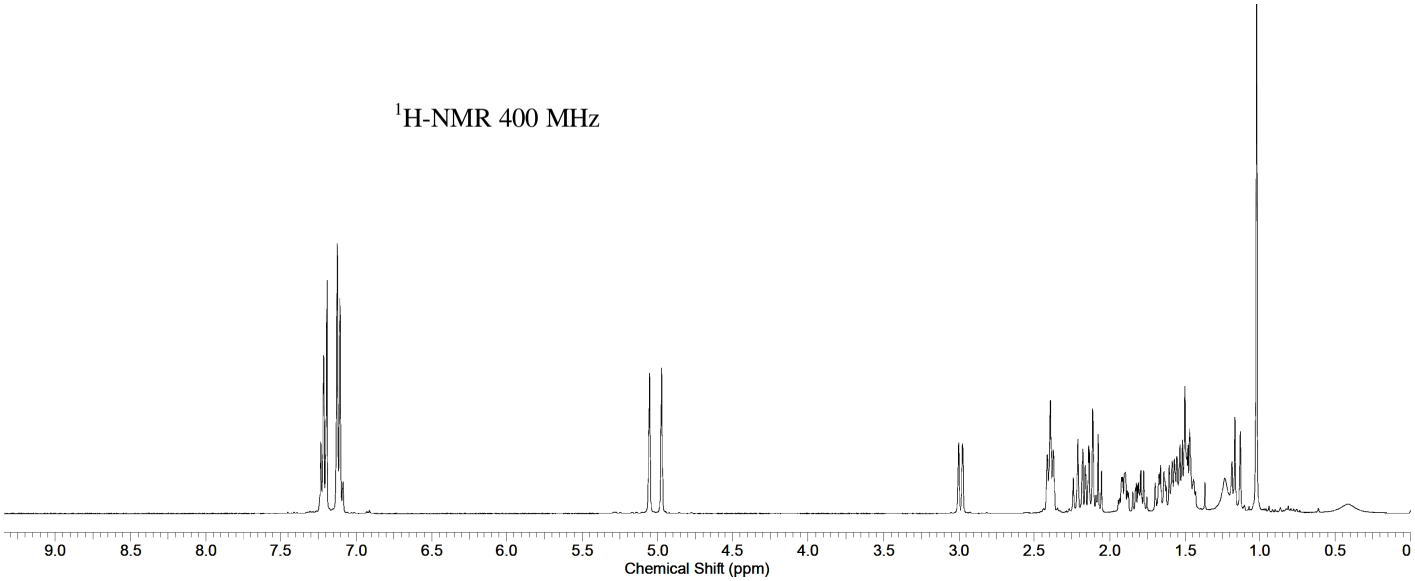
^{13}C-NMR 100 MHz





22

^{1}H-NMR 400 MHz



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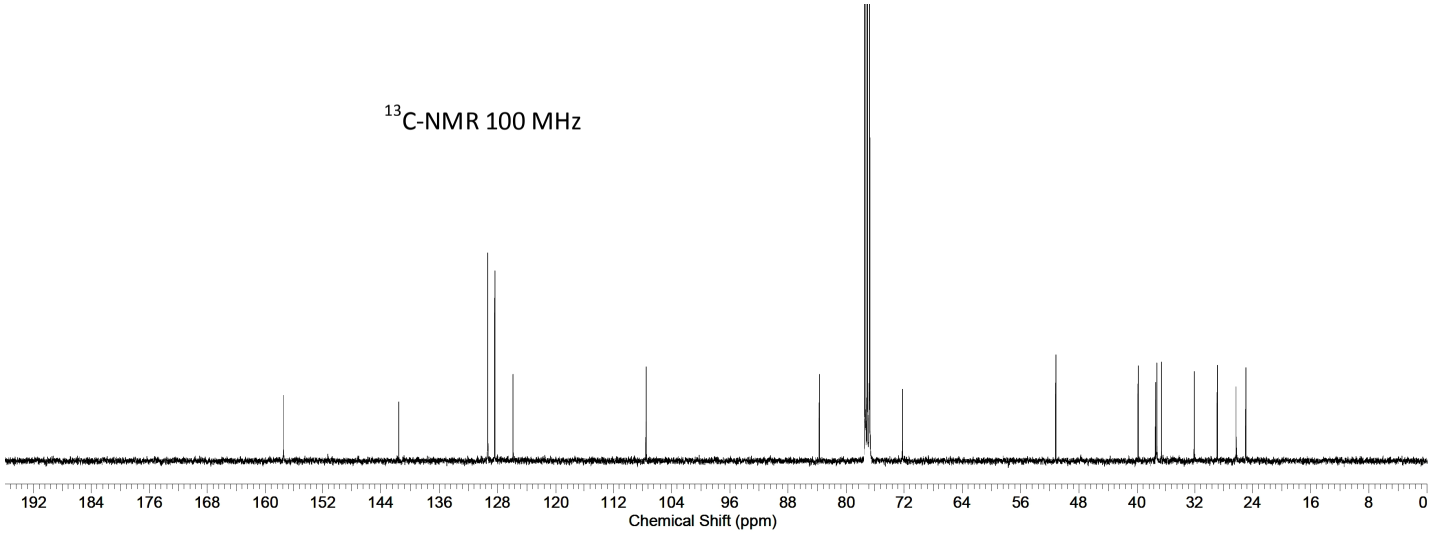
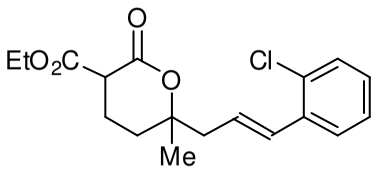
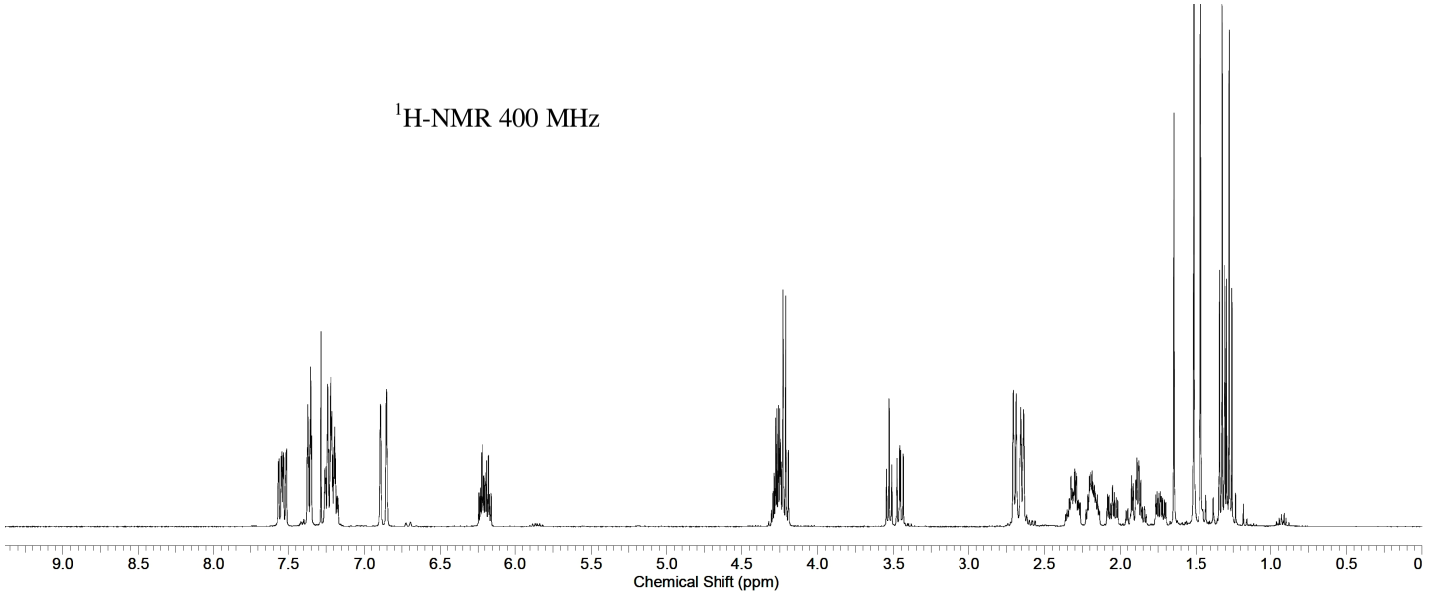


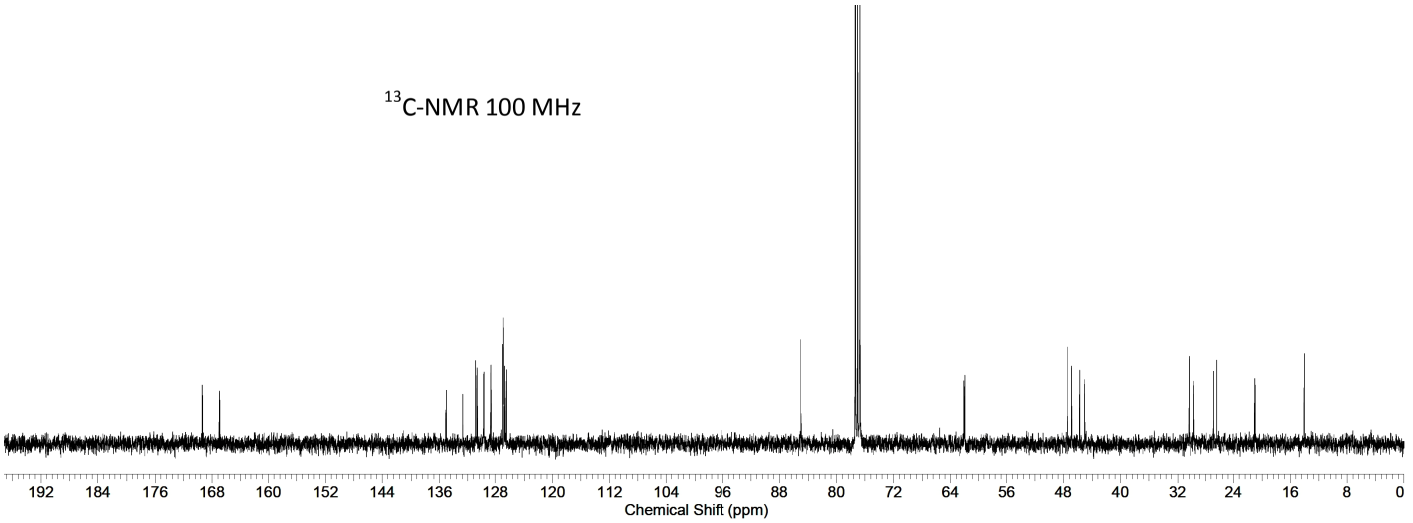


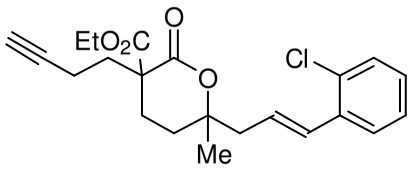
S16

^{1}H-NMR 400 MHz



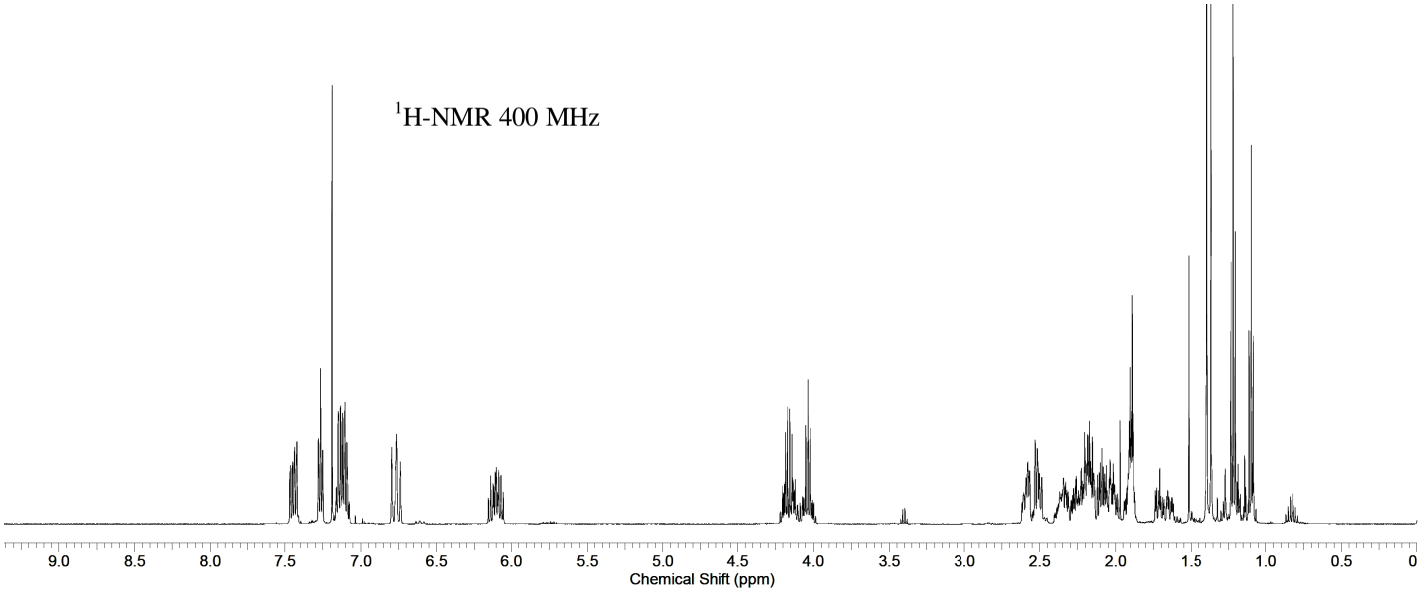
^{13}C-NMR 100 MHz



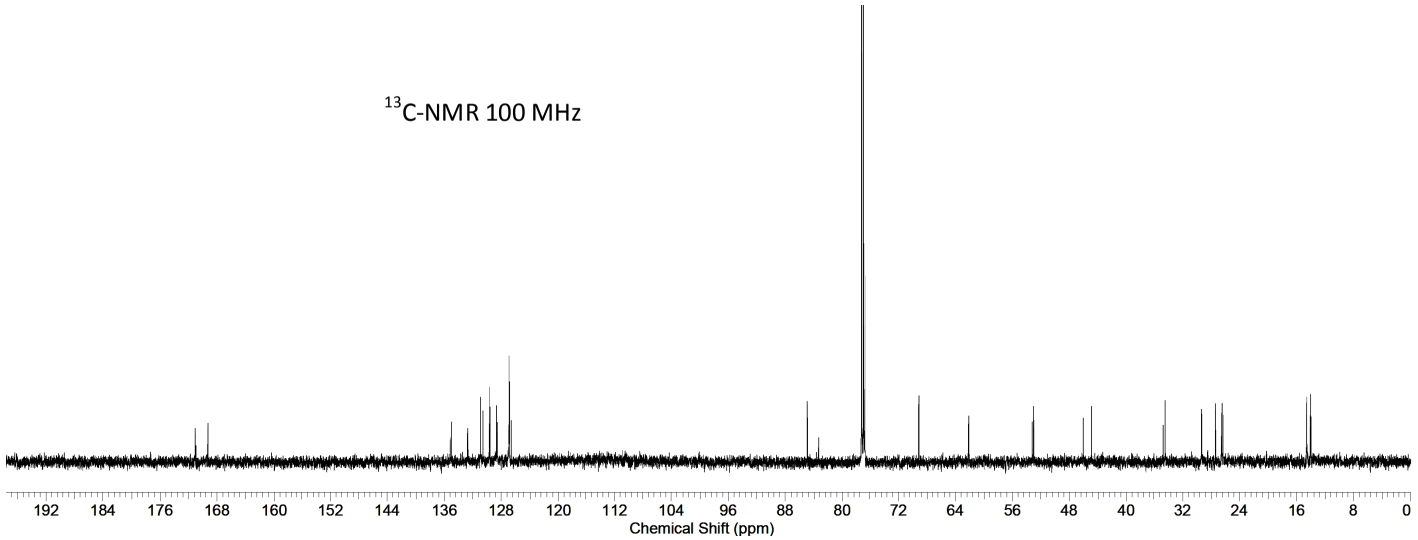


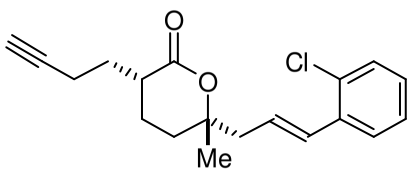
S17

^{1}H-NMR 400 MHz



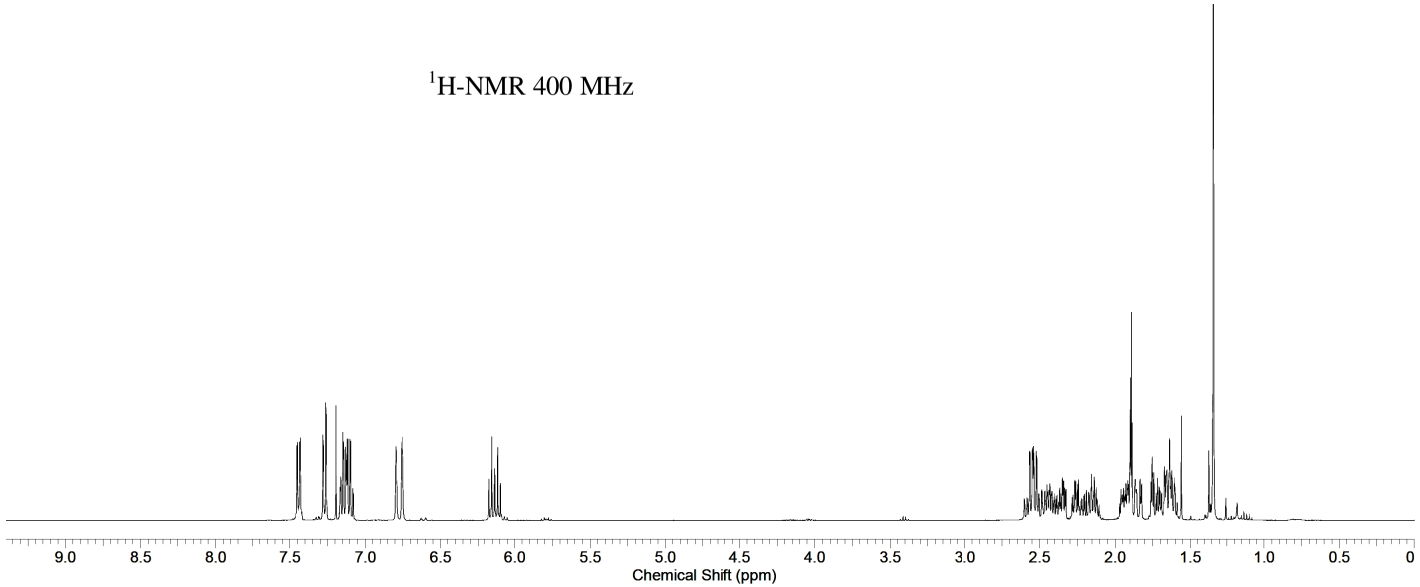
^{13}C-NMR 100 MHz



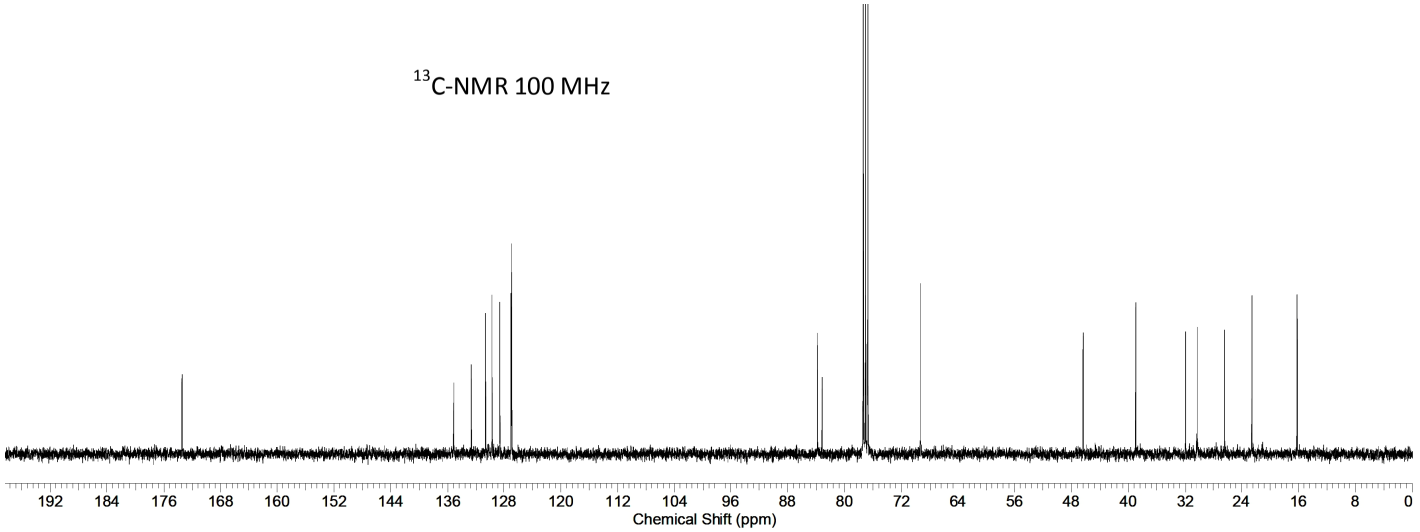


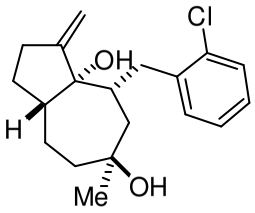
18

^{1}H-NMR 400 MHz



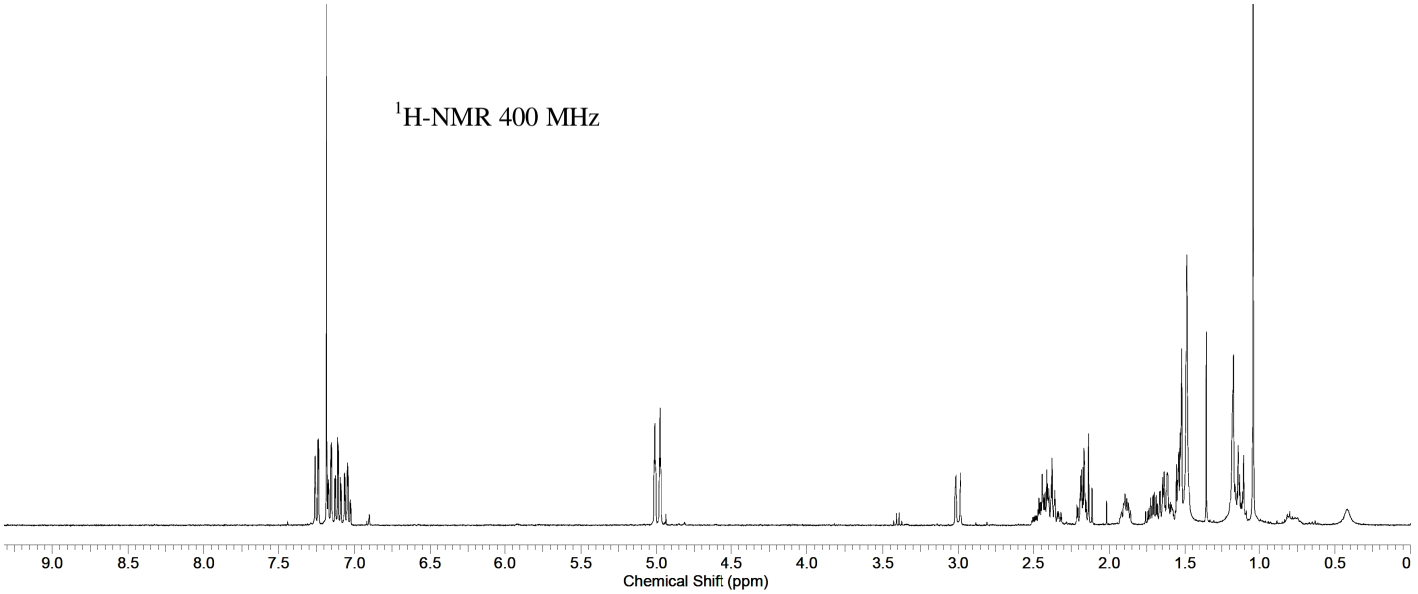
^{13}C-NMR 100 MHz



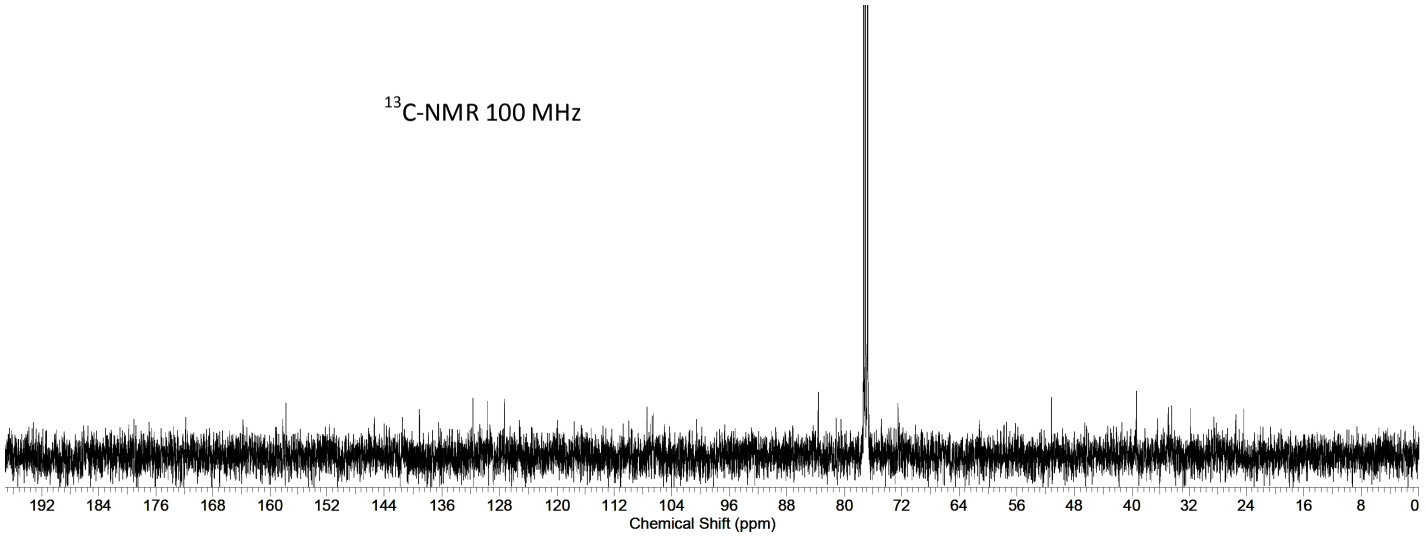


23

^{1}H-NMR 400 MHz



^{13}C-NMR 100 MHz



Details of calculations and additional discussion

(a) Calculations to assess the feasibility of reductive cyclization cascades of lactones

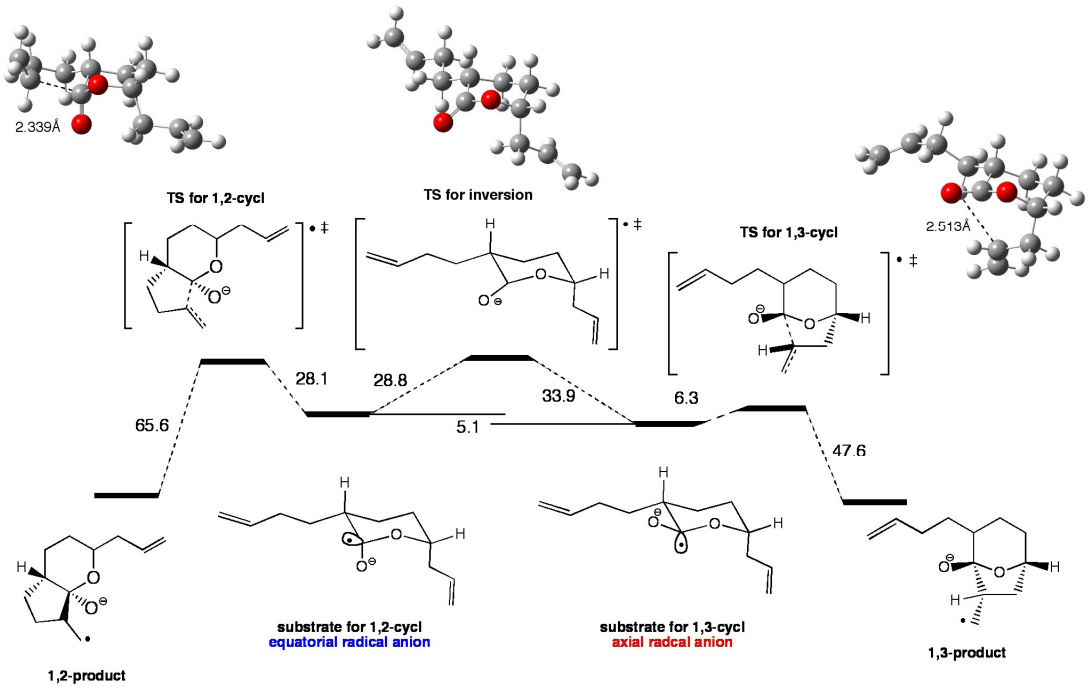


Figure S1. Reaction profile of reductive cyclization of lactone **10**. Energies (in kJ/mol) were calculated on the MP2/aug-cc-pVDZ//MP2/cc-pVDZ level of theory.

(b) Calculations on the diastereoselectivity of lactone cyclizations to form cycloheptandiols

(i) Unselective cyclization of terminal alkenes

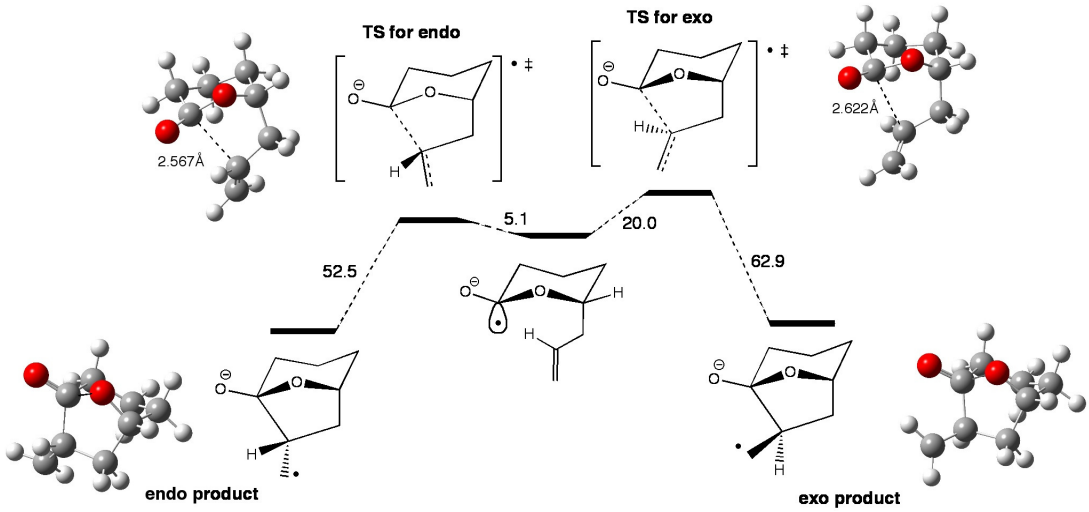


Figure S2. Reaction profile of reductive cyclization of lactone bearing non-substituted alkene tether. Energies (in kJ/mol) were calculated on the MP2/aug-cc-pVDZ//MP2/cc-pVDZ level of theory.

(ii) Selective cyclization of aryl-substituted alkenes

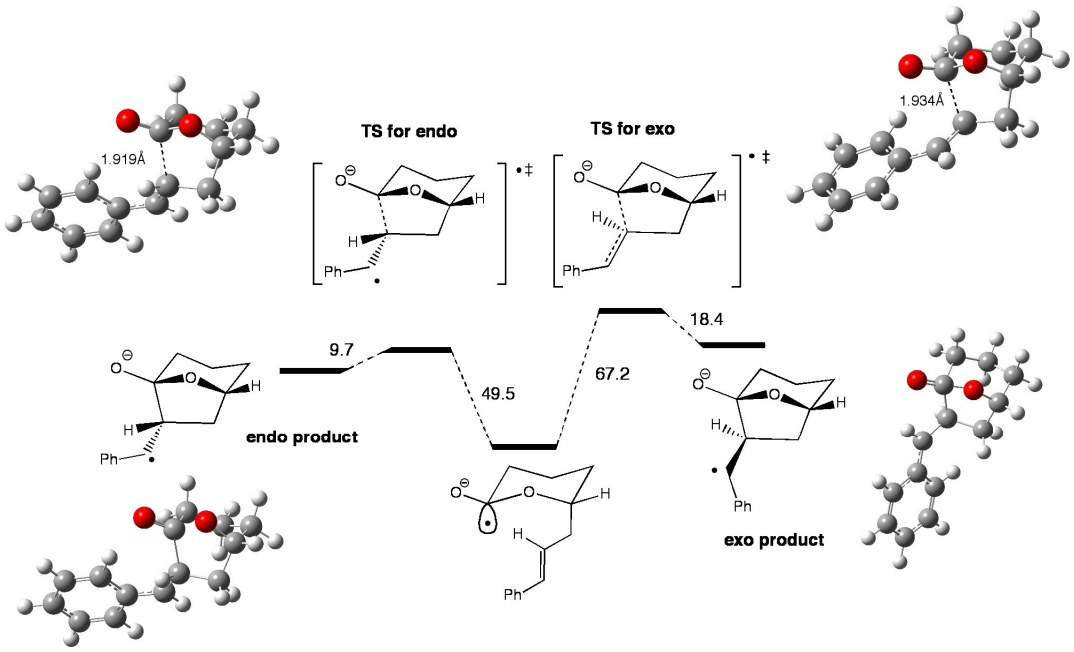


Figure S3. Reaction profile of reductive cyclization of lactone bearing phenyl-substituted alkene tether. Energies (in kJ/mol) were calculated on the MP2/aug-cc-pVDZ//MP2/cc-pVDZ level of theory.

(iii) Discussion of calculations

Inspection of Figures S2 and S3 reveals that calculated energies barriers for a terminal alkene are relatively small (<20 kJ/mol) while those for a phenyl substituted alkene are significantly larger (>50 kJ/mol). Therefore, the terminal alkene molecules have enough energy to cyclize through either cyclization mode. In contrast, few of the phenyl-substituted alkene molecules have energies to cyclize. Therefore, cyclization of the phenyl-substituted alkene takes place *via* the favourable endo mode predominantly.

(c) Calculations – general considerations

MO Calculations All MO calculations were carried out using the Gaussian 03 program [1]. Geometry optimizations were performed using standard gradient techniques at the MP2 level of theory using unrestricted (UMP2) method [2].[3] All ground and transition states were verified by vibrational frequency analysis. Standard basis sets were used throughout this work.

References

[1] Gaussian 03, Revision E.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A. Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.: Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. Gaussian, Inc., Wallingford CT, 2004.

[2] Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, P. A. *Ab Initio Molecular Orbital Theory,* Wiley, New York, 1986.

MP2/cc-pVDZ Gaussian Archive entries for the optimized structures in this study and single point energies using the MP2/aug-cc-pVDZ level.

Substrate of the "right" cyclization (1,3-cyclization): axial radical anion

MP2/cc-pVDZ
1\1\GINC-I7\FOpt\UMP2-FC\CC-pVDZ\C12H18O2(1-,2)\HIROSHI\08-Oct-2010\0\\#MP2/cc-pVDZ scf=(xqc,MaxConventionalCycles=35) OPT=(ReadFC,Maxcycle=100) Nosymm geom=check guess=read\\subst 1,3\\-1,2\C,-0.6775493753,-0.9761585739,-0.3140872762\O,-0.3341587492,-2.0400051647,-0.9019479391\O,-1.0012967368,0.1753282725,-1.2789997984\C,-1.6995378944,1.2161262363,-0.6529297586\C,-0.8595183257,1.8434726104,0.4747563805\C,0.2418214807,-0.3951831801,0.7884801722\C,-0.422950533,0.7917980803,1.4989344204\H,-1.8692018563,2.004003988,-1.420130441\C,-3.9046578546,1.8036626571,0.5116972912\C,-3.1079611069,0.7465760559,-0.1915926897\C,-4.931847026,2.4819838566,-0.0187928102\H,0.0468079814,2.2634542145,-0.0019868667\H,-1.3970695968,2.6849523012,0.9545021737\H,0.2541001646,1.2577647721,2.2435640013\H,-1.3028728201,0.4171754647,2.0611358224\H,-3.5980623707,2.051988039,1.5390730882\H,-2.9518847528,-0.1379826133,0.4487760504\H,-3.6387507019,0.401091189,-1.0971533398\H,-5.2758885745,2.2728106622,-1.0390605515\H,-5.4604789541,3.2605856543,0.542567524\C,0.6207072412,-1.5319335999,1.7417698843\H,1.0008879089,-2.360854011,1.1207465898\H,1.179659041,-0.025961125,0.299091157\H,-0.3060274368,-1.9053343811,2.2241078427\C,1.6481812125,-1.1593076498,2.8235892422\H,1.2443066918,-0.341824548,3.4520484838\H,2.5711385709,-0.7737773477,2.3502939752\C,1.9879379493,-2.3242637037,3.7118163523\H,1.1453191871,-2.778657467,4.2554070367\C,3.2137984146,-2.8609321406,3.8618158769\H,3.3859943537,-3.7275121126,4.5093017743\H,4.0779287183,-2.4479631554,3.3282021916\\Version=EM64L-G03RevE.01\HF=-614.5591767\MP2=-616.5804603\PUHF=-614.5631209\PMP2-0=-616.5831095\S2=0.768346\S2-1=0.756213\S2A=0.750219\RMSD=8.820e-09\RMSF=5.081e-06\Thermal=0.\Dipole=0.00815,1.4884783,2.3018824\PG=C01 [X(C12H18O2)]\\@

No imaginary frequencies.

MP2/aug-cc-pVDZ//MP2/cc-pVDZ
MP2=-616.7282919

Substrate of the “left” cyclization (1,2-cyclization): equatorial radical anion

MP2/cc-pVDZ
1\1\GINC-QUAD\FOpt\UMP2-FC\CC-pVDZ\C12H18O2(1-,2)\HIROSHI\16-Oct-2010\0\\#MP2/cc-pVDZ scf=(xqc,MaxConventionalCycles=35) freq=Noraman OPT=(ReadFC,Maxcycle=100) Nosymm geom=check\\subst 1,2\\-1,2\C,-0.7636898919,-1.0309207541,-0.2341718206\O,-1.7474277379,-1.7105545231,0.222254483\O,-1.0799958833,0.0858594555,-1.207449241\C,-1.7429985731,1.1756054264,-0.5986872652\C,-0.8835324081,1.7760179784,0.5306583118\C,0.2359077056,-0.4513137371,0.7975399045\C,-0.4480674307,0.7103129813,1.5445198835\H,-1.8554886706,1.9578703902,-1.3829812696\C,-3.939137087,1.9380257608,0.4551506834\C,-3.1807580817,0.7944431037,-0.1491778755\C,-4.9084843472,2.6410887739,-0.1630996931\H,0.0253951845,2.1974813853,0.0581682536\H,-1.4109735893,2.6166697183,1.02210899\H,0.2075899149,1.1757761744,2.3097349581\H,-1.3294768365,0.2961720845,2.0738594382\H,-3.6637772549,2.2350799083,1.4785577429\H,-3.0941068225,-0.0649847898,0.5360820061\H,-3.7011177237,0.4211990099,-1.0494679705\H,-5.2229207179,2.3849648665,-1.182234343\H,-5.4143632752,3.4814728016,0.3258600063\C,0.6765305038,-1.580144347,1.732584889\H,1.1394950451,-2.3760276172,1.1184289657\H,1.1197857332,-0.0423956105,0.2630528962\H,-0.2402572999,-2.0221474481,2.1645516271\C,1.658536444,-1.1687216305,2.8426263748\H,1.1807030209,-0.4111247972,3.4926055667\H,2.5569978057,-0.693962052,2.4025060756\C,2.0742584936,-2.3375933869,3.6918621693\H,1.2594263014,-2.8778833673,4.1975080655\C,3.3369939483,-2.7826799586,3.8465385365\H,3.5657290475,-3.658457664,4.4634225866\H,4.1755375926,-2.2806623959,3.349506104\\Version=EM64L-G03RevE.01\HF=-614.5599477\MP2=-616.5810639\PUHF=-614.563531\PMP2-0=-616.5833164\S2=0.764404\S2-1=0.75366\S2A=0.7501\RMSD=6.83e-09\RMSF=2.056e-06\Thermal=0.\Dipole=0.7768879,1.3297568,1.7607315\PG=C01 [X(C12H18O2)]\\@

No imaginary frequencies.

MP2/aug-cc-pVDZ//MP2/cc-pVDZ

MP2=-616.7263607

Transision state involved in the “right” cyclization (1,3-cyclization)

MP2/cc-pVDZ

1\1\GINC-I7\FTS\UMP2-FC\CC-pVDZ\C12H18O2(1-,2)\HIROSHI\10-Oct-2010\1\\#MP2/cc-pVDZ geom=check guess=read scf=(NoVarAcc,xqc,MaxConventionalCycles=32) OPT=(TS,z-matrix,NoEigenTest,ReadFC,Maxcycle=100,Maxstep=10) Nosymm\\TS 1,3\\-1,2\C\O,1,r2\O,1,r3,2,a3\C,3,r4,1,a4,2,d4,0\C,4,r5,3,a5,1,d5,0\C,1,r6,3,a6,4,d6,0\C,6,r7,1,a7,3,d7,0\H,4,r8,3,a8,1,d8,0\C,1,r9,3,a9,4,d9,0\C,9,r10,1,a10,3,d10,0\C,9,r11,1,a11,3,d11,0\H,5,r12,4,a12,3,d12,0\H,5,r13,4,a13,3,d13,0\H,6,r14,1,a14,3,d14,0\C,6,r15,1,a15,3,d15,0\H,7,r16,6,a16,1,d16,0\H,7,r17,6,a17,1,d17,0\H,9,r18,10,a18,11,d18,0\H,10,r19,9,a19,18,d19,0\H,10,r20,9,a20,18,d20,0\H,11,r21,9,a21,18,d21,0\H,11,r22,9,a22,18,d22,0\C,15,r23,6,a23,1,d23,0\C,23,r24,15,a24,6,d24,0\C,24,r25,23,a25,15,d25,0\H,15,r26,6,a26,1,d26,0\H,15,r27,6,a27,1,d27,0\H,23,r28,15,a28,6,d28,0\H,23,r29,15,a29,6,d29,0\H,24,r30,23,a30,15,d30,0\H,25,r31,24,a31,23,d31,0\H,25,r32,24,a32,23,d32,0\\r2=1.25823265\r3=1.46651143\a3=115.61964405\r4=1.41213443\a4=109.32225699\d4=148.28784243\r5=1.5382466\a5=110.5707538\d5=64.06479417\r6=1.52907433\a6=110.34363013\d6=-65.91852041\r7=1.53721577\a7=110.13988224\d7=57.8976352\r8=1.11036823\a8=106.08046739\d8=-179.75567451\r9=2.51265728\a9=88.32108693\d9=43.53917047\r10=1.51229429\a10=86.98486665\d10=-18.85810484\r11=1.34280335\a11=127.993679\d11=-148.53399604\r12=1.10814666\r13=1.10829097\a12=106.80293551\a13=110.13476842\d12=62.86954193\d13=179.21187749\r14=1.12441549\r15=1.53339882\a14=109.23465289\a15=110.4796 7546\d14=-60.30923762\d15=180.74453739\r16=1.11029152\r17=1.10305147\a16=110.20244872\a17=108.20972018\d16=-171.29323598\d17=71.26743726\r181.09564029\a18=116.26853282\d18=165.48186853\r19=1.10859108\r20=1.10826048\a19=108.15346096\a20=109.71454128\d19=48.75418764\d20=165.07953818\r21=1.09815479\r22=1.09559368\a21=121.26319068\a22=121.30434582\d21=-176.41066192\d22=8.91367076\r23=1.53732587\r24=1.50280379\r25=1.34718128\a23=113.0303216\a24=112.44878871\a25=124.85802474\d23=74.57147036\d24=179.87145209\d25=116.77312171\r26=1.10580244\r27=1.11095642\a26=108.13986787\a27=109.48087609\d26=-46.53920964\d27=-163.17044584\r28=1.10895589\r29=1.10218401\a28=108.22319709\a29=107.35176275\d28=59.18057757\d29=-57.1884256\r30=1.10241922\a30=116.76176859\d30=-61.45297356\r31=1.09593519\r32=1.09598693\a31=120.54824512\a32=121.66077733\d31=0.88465888\d32=181.53663514\\Version=EM64L-G03RevE.01\HF=-614.5527649\MP2=-616.5778077\PUHF=-614.5624623\PMP2-0=-616.5860232\S2=0.875512\S2-1=0.836435\S2A=0.753945\RMSD=9.629e-09\RMSF=2.490e-05\Thermal=0.\Dipole=-0.9011462,0.6567278,-1.0933856\PG=C01 [X(C12H18O2)]\\@

Imaginary frequency: 181.5968i

MP2/aug-cc-pVDZ//MP2/cc-pVDZ

MP2=-616.7258928

Transision state involved in the “left” cyclization (1,2-cyclization)

MP2/cc-pVDZ

1\1\GINC-I7\FTS\UMP2-FC\CC-pVDZ\C12H18O2(1-,2)\HIROSHI\17-Oct-2010\1\\#MP2/cc-pVDZ scf=(xqc,MaxConventionalCycles=36) geom=check guess=read OPT=(TS,z-matrix,NoEigenTest,ReadFC,Maxcycle=100,Maxstep=15) Nosymm\\TS 1,2 new\\-1,2\C\O,1,r2\O,1,r3,2,a3\C,3,r4,1,a4,2,d4,0\C,4,r5,3,a5,1,d5,0\C,1,r6,3,a6,4,d6,0\C,6,r7,1,a7,3,d7,0\H,4,r8,3,a8,1,d8,0\C,4,r9,3,a9,1,d9,0\H,5,r10,4,a10,3,d10,0\H,5,r11,4,a11,3,d11,0\C,6,r12,1,a12,3,d12,0\H,6,r13,1,a13,3,d13,0\H,7,r14,6,a14,1,d14,0\H,7,r15,6,a15,1,d15,0\H,12,r16,6,a16,1,d16,0\H,12,r17,6,a17,1,d17,0\C,1,r18,3,a18,4,d18,0\C,18,r19,1,a19,3,d19,0\C,18,r20,1,a20,3,d20,0\H,18,r21,19,a21,20,d21,0\H,19,r22,18,a22,21,d22,0\H,19,r23,18,a23,21,d23,0\H,20,r24,18,a24,21,d24,0\H,20,r25,18,a25,21,d25,0\C,9,r26,4,a26,3,d26,0\C,26,r27,9,a27,4,d27,0\H,9,r28,4,a28,3,d28,0\H,9,r29,4,a29,3,d29,0\H,26,r30,9,a30,4,d30,0\H,27,r31,26,a31,9,d31,0\H,27,r32,26,a32,9,d32,0\\r2=1.26589654\r3=1.46081368\a3=118.57565586\r4=1.4276386\a4=110.16057688\d4=76.43138806\r5=1.54622344\a5=111.82338438\d5=56.59483204\r6=1.5245174\a6=108.61558897\d6=-66.193761\r7=1.53297927\a7=107.35845282\d7=68.42313894\r8=1.11037965\a8=105.66731612\d8=173.26885861\r9=1.55099012\a9=111.08783924\d9=-71.39260989\r10=1.10731247\a10=107.1761209\d10=67.30764506\r11=1.10669913\a11=109.83689375\d11=-177.00167979\r12=1.5194216\r

13=1.11003292\a12=105.20219795\a13=107.92117116\d12=-164.23932583\d13=-47.95578885\r14=1
.11051659\r15=1.10705861\a14=113.03625595\a15=108.46033935\d14=-181.31560568\d15=59.4646
2399\r16=1.1081169\r17=1.10378015\a16=113.18301628\a17=107.63300179\d16=185.57959468\d17
=-53.95531993\r18=2.33873456a18=114.12329786\d18=196.33296673\r19=1.52403534\r20=1.35205
809\a19=91.36682499\a20=119.80598679\d19=135.97690373\d20=9.73240817\r21=1.09633699\r22=
1.10764977\a21=116.08233209\a22=107.39989739\d21=-201.04571872\d22=170.80966297\r23=1.10
851372\r24=1.09746394\r25=1.09544046\a23=109.22606948\a24=120.84440826\a25=121.3353734\d
23=55.60760881\d24=185.35985441\d25=14.69700255\r26=1.50103354\r27=1.34706246\a26=113.19
295463\a27=124.93146905\d26=-173.68139369\d27=103.61188654\r28=1.10221641\r29=1.1044006\
a28=108.08744153\a29=106.43005182\d28=61.55360273\d29=-52.30503642\r30=1.10029505\a30=11
7.17441118\d30=-75.21931551\r31=1.09576703\r32=1.09670189\a31=121.7701324\a32=120.736062
15\d31=-178.83175796\d32=1.40700273\\Version=EM64L-G03RevE.01\HF=-614.5428147\MP2=-61
6.5693569\PUHF=-614.5551976\PMP2-0=-616.5798873\S2=0.912918\S2-1=0.863194\S2A=0.755507
\RMSD=2.340e-09\RMSF=4.143e-05\Thermal=0.\Dipole=0.5744315,-2.1687909,-0.3724562\PG=C01
[X(C12H18O2)]\\@

Imaginary frequency: 238.8663i

MP2/aug-cc-pVDZ//MP2/cc-pVDZ
MP2=-616.7156579

Product of the “right” cyclization (1,3-cyclization)

MP2/cc-pVDZ
1\1\GINC-QUAD\FOpt\UMP2-FC\CC-pVDZ\C12H18O2(1-,2)\HIROSHI\08-Oct-2010\0\\#MP2/cc-p
VDZ freq=Noraman OPT=(ReadFC,Maxcycle=100) Nosymm geom=check guess=read\\product 1,3\\-
1,2\C,0.2984118362,-0.4373285396,0.5309380112\C,-0.33617057,0.3922223117,2.8143103734\C,0.8
396735272,0.0503994122,1.8812452272\O,-1.1034384333,1.4292784737,2.2672504609\C,-0.837116
28,0.4654095733,0.0312436648\H,-0.0867850068,-1.4709083183,0.6342902938\H,1.4311882755,0.9
738142421,1.7337226293\H,1.122474209,-0.4935001189,-0.2097584077\H,1.504923714,-0.70950358
85,2.3413724971\H,0.0631611785,0.7205338062,3.7975529224\C,-1.2827179904,-0.8328424796,2.9
787228732\H,-1.6762800571,-0.8788721981,4.010148792\H,-0.7595622601,-1.7901416251,2.787489
6282\C,-1.9601379269,0.7585531569,1.1004513718\O,-2.9129651444,1.4814651649,0.6839976989\
C,-2.4059280637,-0.5584282327,1.9679765007\H,-3.2713067301,-0.095398889,2.4757701911\C,-2.8
66709025,-1.7100102233,1.1644867654\H,-2.1959703619,-2.5481299703,0.9376225128\H,-3.733087
9022,-1.5772104613,0.5072905867\C,-1.4553858197,-0.0135296002,-1.285160509\H,-2.3810400656,
0.5720617886,-1.4234524463\H,-1.7448442904,-1.0799686521,-1.2017341889\C,-0.5345660168,0.16
38643117,-2.5055894937\H,-0.278253529,1.2337956958,-2.6235048943\H,0.4164021429,-0.3783352
433,-2.3345789038\C,-1.1591005369,-0.3479849726,-3.7739291927\H,-1.4217130669,-1.417126856,-
3.7868295445\C,-1.447389354,0.3982250061,-4.8594270389\H,-1.2164869963,1.4696666673,-4.8826
877118\H,-1.9283758332,-0.0354734084,-5.7429137399\H,-0.4291865926,1.4824223869,-0.1436973
992\\Version=EM64L-G03RevE.01\HF=-614.563831\MP2=-616.5955491\PUHF=-614.5673747\PMP
2-0=-616.5978795\S2=0.765545\S2-1=0.754825\S2A=0.750185\RMSD=5.924e-09\RMF=7.451e-07\
Thermal=0.\Dipole=1.5807708,-1.5169404,-1.2453021\PG=C01 [X(C12H18O2)]\\@

No imaginary frequencies.

MP2/aug-cc-pVDZ//MP2/cc-pVDZ
MP2=-616.7440275

Product of the “left” cyclization (1,2-cyclization)

MP2/cc-pVDZ
1\1\GINC-QUAD\FOpt\UMP2-FC\CC-pVDZ\C12H18O2(1-,2)\HIROSHI\07-Oct-2010\0\\#MP2/cc-p
VDZ freq=Noraman OPT=(ReadFC,Maxcycle=100) Nosymm geom=check guess=read\\product 1,2\\-
1,2\C,0.1334572587,-0.0161658251,0.0922068112\C,0.035053214,0.0908137931,1.5687990168\C,1.5
978569339,0.0819285404,-0.4376021712\C,1.6832038751,1.33344303,-1.3605383036\C,-0.58801165

59,1.1603676028,-0.7423116377\C,0.5688396974,2.2142820507,-0.8089106844\C,0.0447766034,3.403969914,-1.596563664\C,-1.1349941854,3.9847634061,-0.7944973614\O,-1.6352917314,1.7644617605,0.1768249414\C,-2.1969546143,2.9255464139,-0.4066852573\O,-1.0168159982,0.7745613013,-1.8983554129\H,-0.3736096862,-0.9251781619,-0.2736959373\H,-0.9274669537,-0.1124803416,2.0509047466\H,0.7014881365,0.7816600043,2.1026117294\H,1.914300921,-0.8371211386,-0.9627887386\H,2.2878363665,0.2125907888,0.4185624907\H,1.4135538153,1.0588074389,-2.3936858114\H,2.6907318293,1.7916785047,-1.3497274049\H,0.8289904844,2.5366729354,0.2218342265\H,-0.2984082808,3.0268675733,-2.5762544544\H,0.8100407166,4.1876983837,-1.7707859988\H,-1.6316809985,4.8090724399,-1.3415553183\H,-0.7317986901,4.4116688415,0.1451948038\C,-3.1681029434,2.6062675926,-1.5740737774\H,-2.591692817,2.2639438282,-2.4465028242\H,-3.7615961841,1.7368682993,-1.235720988\C,-4.073737543,3.7592896095,-1.8925643049\H,-4.709477001,4.133106529,-1.0722202563\C,-4.1525854021,4.3810686807,-3.0887739458\H,-3.5330235014,4.0491337091,-3.9300292197\H,-4.8290486848,5.2271772982,-3.2564793602\H,-2.8194636809,3.3779755772,0.3978320863\\Version=EM64L-G03RevE.01\HF=-614.5644533\MP2=-616.5956152\PUHF=-614.5677416\PMP2-0=-616.5977738\S2=0.764185\S2-1=0.754375\S2A=0.750153\RMSD=4.710e-09\RMSF=1.11e-06\Thermal=0.\Dipole=-0.1388669,1.4383434,0.1484129\PG=C01 [X(C12H18O2)]\\@

No imaginary frequencies.

MP2/aug-cc-pVDZ//MP2/cc-pVDZ
MP2=-616.7406373

Transision state involved in the transformation between the axial and equatorial radical anions

MP2/cc-pVDZ
1\1\GINC-I7\FTS\UMP2-FC\CC-pVDZ\C12H18O2(1-,2)\HIROSHI\13-Oct-2010\0\\#MP2/cc-pVDZ freq=Noraman scf=(xqc,MaxConventionalCycles=35) OPT=(TS,NoEigenTest,ReadFC,Maxcycle=100,Maxstep=15) Nosymm geom=check guess=read\\TS inversion\\-1,2\C,-0.6412530315,-0.8531833595,-0.3700170895\O,-1.1516288009,-2.0216280413,-0.4959885972\O,-0.9473359089,0.1868882545,-1.3498275315\C,-1.6746535272,1.2296929927,-0.7242880355\C,-0.8072903456,1.8857235803,0.3655048252\C,0.2826434166,-0.3628938042,0.6923377216\C,-0.3267587385,0.8725832583,1.4110132658\H,-1.8730541973,1.9975818402,-1.5047222788\C,-3.8046014495,1.6610146952,0.6294372128\C,-3.0461778325,0.7000705723,-0.2352372952\C,-4.9050195047,2.3410784915,0.2586932818\H,0.083353111,2.2939679188,-0.1526150713\H,-1.3344470007,2.7405361473,0.8318102761\H,0.4057214044,1.3702123388,2.0868309069\H,-1.1751994108,0.526126211,2.0365414755\H,-3.4104403682,1.8278892996,1.6431644185\H,-2.8435986112,-0.2471933296,0.2973093415\H,-3.639658266,0.4447369775,-1.1325638329\H,-5.3359115897,2.210245214,-0.7413621841\H,-5.4060023949,3.0403081102,0.9375235059\C,0.576813021,-1.5058712559,1.6717685593\H,0.9930237925,-2.3533814335,1.1000339422\H,1.2765747051,0.007906142,0.2890003247\H,-0.3862557534,-1.8684966958,2.0780537318\C,1.5299337701,-1.1344503161,2.820025216\H,1.0776898174,-0.3256123569,3.4256347771\H,2.4785157732,-0.7365446028,2.412192439\C,1.819162927,-2.3052445713,3.71776417\H,0.9458309195,-2.7741567339,4.1966136241\C,3.0394429873,-2.8316685951,3.9472721699\H,3.1760913481,-3.7030305321,4.596838414\H,3.9337885682,-2.4031183164,3.4797807162\\Version=EM64L-G03RevE.01\HF=-614.544838\MP2=-616.565936\PUHF=-614.5473873\PMP2-0=-616.5691057\S2=0.770758\S2-1=0.755931\S2A=0.750347\RMSD=8.124e-09\RMSF=7.553e-06\Thermal=0.\Dipole=0.2285722,1.3843344,2.0068787\PG=C01 [X(C12H18O2)]\\@

Imaginary frequency: 460.1294i

MP2/aug-cc-pVDZ//MP2/cc-pVDZ
MP2=-616.7153826

Substrate of 1,3-cyclization of lactone bearing non-substituted alkene tether

MP2/cc-pVDZ

1\1\GINC-GOMBERG01\FOpt\UMP2-FC\CC-pVDZ\C8H12O2(1-,2)\HIROSHI\08-Sep-2010\1\\#MP2/cc-pVDZ freq=noraman opt=(z-matrix,calchffc,maxcycle=100) Nosymm geom=check guess=read\\radical anion non-subst\\-1,2\C\C,1,B1\C,1,B2,2,A1\O,2,B3,1,A2,3,D1,0\C,1,B4,3,A3,2,D2,0\H,1,B5,5,A4,4,D3,0\H,3,B6,1,A5,5,D4,0\H,5,B7,1,A6,3,D5,0\H,1,B8,5,A7,4,D6,0\H,3,B9,1,A8,5,D7,0\H,5,B10,1,A9,3,D8,0\C,4,B11,2,A10,1,D9,0\O,12,B12,4,A11,2,D10,0\C,2,B13,1,A12,5,D11,0\H,14,B14,2,A13,1,D12,0\H,14,B15,2,A14,1,D13,0\C,14,B16,2,A15,1,D14,0\H,17,B17,14,A16,2,D15,0\C,17,B18,14,A17,2,D16,0\H,19,B19,17,A18,14,D17,0\H,19,B20,17,A19,14,D18,0\H,2,B21,1,A20,5,D 19,0\\B1=2.57037981\B2=1.53387998\B3=1.39719623\B4=1.53280588\B5=1.10380076\B6=1.10812059\B7=1.11808021\B8=1.10978951\B9=1.1093365\B10=1.10612846\B11=1.56130768\B12=1.25848518\B13=1.55756058\B14=1.1071587\B15=1.11007438\B16=1.50218891\B17=1.09907563\B18=1.34765947\B19=1.09594592\B20=1.098102\B21=1.11476959\A1=33.51218247\A2=89.31105548\A3=110.04580638\A4=109.19512927\A5=107.90179987\A6=109.6003426\A7=111.57749125\A8=111.28363989\A9=110.92142717\A10=114.73664069\A11=112.72059134\A12=106.00342145\A13=104.41551011\A14=109.13478884\A15=117.30009066\A16=114.6566168\A17=124.24870956\A18=121.45691077\A19=121.25472458\A20=137.71320075\D1=136.60869231\D2=47.58640297\D3=96.14113272\D4=-70.34911851\D5=64.99260654\D6=-146.0666181\D7=172.29209778\D8=-176.82759923\D9=31.59247897\D10=166.55644775\D11=115.02102058\D12=-140.60675895\D13=104.33315722\D14=-20.40687346\D15=-52.45432795\D16=126.54742187\D17=179.86200803\D18=-0.85620807\D19=-112.51150142\\Version=AM64L-G03RevE.01\HF=-459.5935508\MP2=-461.0636049\PUHF=-459.5974187\PMP2-0=-461.0660562\S2=0.765796\S2-1=0.754169\S2A=0.750129\RMSD=4.690e-09\RMSF=1.018e-05\Thermal=0.\Dipole=1.9998569,-1.8657924,-0.1340545\PG=C01 [X(C8H12O2)]\\@

No imaginary frequencies.

MP2/aug-cc-pVDZ//MP2/cc-pVDZ
MP2=-461.1838736

Transition state involved in exo 1,3-cyclization of lactone bearing non-substituted alkene tether

MP2/cc-pVDZ
1\1\GINC-I7\FTS\UMP2-FC\CC-pVDZ\C8H12O2(1-,2)\HIROSHI\11-Jun-2010\1\\#MP2/cc-pVDZ geom=check guess=read OPT=(TS,z-matrix,NoEigenTest,ReadFC,Maxcycle=100) Nosymm\\TS 1,3-cycl exo\\-1,2\C\C,1,B1\C,1,B2,2,A1\O,2,B3,1,A2,3,D1,0\C,1,B4,3,A3,2,D2,0\H,1,B5,3,A4,2,D3,0\H,3,B6,1,A5,5,D4,0\H,5,B7,1,A6,3,D5,0\H,1,B8,3,A7,2,D6,0\H,3,B9,1,A8,5,D7,0\H,5,B10,1,A9,3,D8,0\H,2,B11,1,A10,3,D9,0\C,2,B12,1,A11,3,D10,0\H,13,B13,2,A12,1,D11,0\H,13,B14,2,A13,1,D12,0\C,4,B15,2,A14,1,D13,0\O,16,B16,4,A15,2,D14,0\C,13,B17,2,A16,1,D15,0\H,18,B18,13,A17,2,D16,0\C,18,B19,13,A18,2,D17,0\H,20,B20,18,A19,13,D18,0\H,20,B21,18,A20,13,D19,0\\B1=2.55841186\B2=1.53200316\B3=1.40417099\B4=1.53576406\B5=1.10468368\B6=1.10805358\B7=1.12123542\B8=1.10940876\B9=1.10879344\B10=1.10504161\B11=1.11249315\B12=1.54916066\B13=1.10606438\B14=1.11160359\B15=1.49789757\B16=1.25035861\B17=1.50958011\B18=1.09473401\B19=1.32995609\B20=1.0964706\B21=1.09495208\A1=33.80582829\A2=90.36631789\A3=109.62894542\A4=109.84907357\A5=108.30817814\A6=108.84070799\A7=109.93171221\A8=111.58556536\A9=111.10768282\A10=139.37149501\A11=101.22757294\A12=107.16524423\A13=108.2156202\A14=108.96136446\A15=115.88285048\A16=117.46128679\A17=117.66651993\A18=122.51707739\A19=121.00342509\A20=121.39239338\D1=129.51455247\D2=45.71008976\D3=-74.98576785\D4=-71.45948105\D5=72.64080124\D6=168.42837621\D7=170.6084599\D8=-169.8565179\D9=13.11541139\D10=-118.30187501\D11=193.20101284\D12=78.32737273\D13=38.32192329\D14=153.26142276\D15=-46.33261766\D16=66.03923447\D17=-126.71072391\D18=11.61064403\D19=184.26508479\\Version=EM64L-G03RevE.01\HF=-459.5843124\MP2=-461.0523961\PUHF=-459.594096\PMP2-0=-461.06072\S2=0.876839\S2-1=0.838257\S2A=0.754132\RMSD=5.981e-09\RMSF=2.688e-05\Thermal=0.\Dipole=1.9372539,-1.1698193,-0.4035987\PG=C01 [X(C8H12O2)]\\@

Imaginary frequency: 169.9281i

MP2/aug-cc-pVDZ//MP2/cc-pVDZ
MP2=-461.1762588

Transition state involved in endo 1,3-cyclization of lactone bearing non-substituted alkene tether

MP2/cc-pVDZ

1\1\GINC-I7\FTS\UMP2-FC\CC-pVDZ\C8H12O2(1-,2)\HIROSHI\04-Jul-2010\1\\#MP2/cc-pVDZ geom=check guess=read OPT=(TS,z-matrix,NoEigenTest,ReadFC,Maxcycle=100) Nosymm\\TS 1,3-cycl endo\\-1,2\C\C,1,B1\C,1,B2,2,A1\O,2,B3,1,A2,3,D1,0\C,1,B4,3,A3,2,D2,0\H,1,B5,3,A4,2,D3,0\H,3,B6,1,A5,5,D4,0\H,5,B7,1,A6,3,D5,0\H,1,B8,3,A7,2,D6,0\H,3,B9,1,A8,5,D7,0\H,5,B10,1,A9,3,D8,0\H,2,B11,1,A10,3,D9,0\C,2,B12,1,A11,3,D10,0\H,13,B13,2,A12,1,D11,0\H,13,B14,2,A13,1,D12,0\C,4,B15,2,A14,1,D13,0\O,16,B16,4,A15,2,D14,0\C,13,B17,2,A16,1,D15,0\H,18,B18,13,A17,2,D16,0\C,18,B19,13,A18,2,D17,0\H,20,B20,18,A19,13,D18,0\H,20,B21,18,A20,13,D19,0\\B1=2.55333778\B2=1.53151044\B3=1.40909125\B4=1.53482527\B5=1.10247515\B6=1.10872681\B7=1.12222724\B8=1.10991545\B9=1.10859754\B10=1.10438531\B11=1.11160623\B12=1.55023609\B13=1.10886352\B14=1.10861724\B15=1.48189581\B16=1.25402166\B17=1.51094879\B18=1.09555049\B19=1.34069956\B20=1.09821133\B21=1.09565564\A1=33.90111301\A2=90.38130204\A3=109.37099634\A4=109.66237105\A5=108.79163215\A6=109.5145792\A7=109.8935265\A8=111.49338221\A9=111.03415341\A10=140.00542958\A11=100.07811066\A12=106.55021449\A13=109.54303797\A14=109.19857408\A15=115.82066374\A16=115.70463336\A17=116.26491216\A18=122.39274182\A19=121.21407495\A20=121.37567823\D1=129.70260172\D2=48.0197633\D3=-71.09753977\D4=-69.74264415\D5=71.61973409\D6=170.66535582\D7=172.11139255\D8=-170.30918763\D9=13.42011349\D10=-118.84311732\D11=190.41636232\D12=75.04347182\D13=35.82856034\D14=149.53186918\D15=-49.5320826\D16=-68.46915352\D17=124.0643718\D18=-10.39708727\D19=174.70054917\\Version=EM64L-G03RevE.01\HF=-459.5889288\MP2=-461.0592118\PUHF=-459.5978298\PMP2-0=-461.066722\S2=0.861569\S2-1=0.826063\S2A=0.753432\RMSD=9.209e-09\RMSF=1.428e-05\Thermal=0.\Dipole=1.8166949,-0.8938888,-0.1361332\PG=C01 [X(C8H12O2)]\\@

Imaginary frequency: 173.5680i

MP2/aug-cc-pVDZ//MP2/cc-pVDZ

MP2=-461.1819442

Exo product of 1,3-cyclization of lactone bearing non-substituted alkene tether

MP2/cc-pVDZ

1\1\GINC-I7\FOpt\UMP2-FC\CC-pVDZ\C8H12O2(1-,2)\HIROSHI\13-Jun-2010\1\\#MP2/cc-pVDZ freq=Noraman geom=check guess=read OPT=(z-matrix,ReadFC,Maxcycle=100,Maxstep=15) Nosymm\\product 1,3-cycl exo\\-1,2\C\C,1,B1\C,1,B2,2,A1\O,2,B3,1,A2,3,D1,0\C,1,B4,3,A3,2,D2,0\H,1,B5,3,A4,2,D3,0\H,3,B6,1,A5,5,D4,0\H,5,B7,1,A6,3,D5,0\H,1,B8,3,A7,2,D6,0\H,3,B9,1,A8,5,D7,0\H,5,B10,1,A9,3,D8,0\H,2,B11,1,A10,3,D9,0\C,2,B12,1,A11,3,D10,0\H,13,B13,2,A12,1,D11,0\H,13,B14,2,A13,1,D12,0\C,13,B15,2,A14,1,D13,0\H,16,B16,13,A15,2,D14,0\H,16,B17,13,A16,2,D15,0\C,4,B18,2,A17,1,D16,0\O,19,B19,4,A18,2,D17,0\C,16,B20,13,A19,2,D18,0\H,21,B21,16,A20,13,D19,0\\B1=2.5127243\B2=1.53396255\B3=1.39437452\B4=1.53702533\B5=1.10811301\B6=1.10700002\B7=1.10553064\B8=1.10927483\B9=1.11003434\B10=1.10822348\B11=1.11284596\B12=1.55542807\B13=1.1049791\B14=1.10783454\B15=2.54615619\B16=1.09364956\B17=1.0965777\B18=1.61904044\B19=1.26911238\B20=1.49070864\B21=1.1137827\A1=35.30338305\A2=92.11731455\A3=110.81471176\A4=108.97636843\A5=109.76521767\A6=110.58896913\A7=110.62045023\A8=111.09582621\A9=110.49552849\A10=143.80608186\A11=89.67435612\A12=109.04250716\A13=112.42566203\A14=117.6804027\A15=134.9207288\A16=97.76216239\A17=105.0972936\A18=112.86493214\A19=33.75631807\A20=109.78941442\D1=123.59075054\D2=44.65984277\D3=-75.64891527\D4=-72.77029875\D5=70.18581216\D6=168.48303898\D7=168.0096411\D8=-171.005373\D9=-4.56970891\D10=-130.0087483\D11=179.11871073\D12=59.85878452\D13=-95.19770435\D14=1.76853339\D15=-150.3905134\D16=45.41654638\D17=166.64229477\D18=71.34275367\D19=123.67038213\\Version=EM64L-G03RevE.01\HF=-459.6058462\MP2=-461.0810106\PUHF=-459.609176\PMP2-0=-461.0831543\S2=0.763239\S2-1=0.753757\S2A=0.750116\RMSD=6.439e-09\RMSF=6.471e-06\Thermal=0.\Dipole=1.399075,-1.7014696,-0.4544961\PG=C01 [X(C8H12O2)]\\@

No imaginary frequencies.

MP2/aug-cc-pVDZ//MP2/cc-pVDZ

MP2=-461.2001978

Endo product of 1,3-cyclization of lactone bearing non-substituted alkene tether

MP2/cc-pVDZ
1\1\GINC-I7\FOpt\UMP2-FC\CC-pVDZ\C8H12O2(1-,2)\HIROSHI\15-Sep-2010\1\\#MP2/cc-pVDZ s
cf=direct freq=noraman geom=check guess=read OPT=(z-matrix,ReadFC,Maxcycle=100) Nosymm\\pr
o 1,3-cycl endo\\-1,2\C\C,1,B1\C,2,B2,1,A1\O,2,B3,1,A2,3,D1,0\C,1,B4,3,A3,2,D2,0\H,1,B5,3,A4,2,D
3,0\H,3,B6,2,A5,1,D4,0\H,5,B7,1,A6,3,D5,0\H,1,B8,3,A7,2,D6,0\H,3,B9,2,A8,1,D7,0\H,5,B10,1,A9,3
,D8,0\H,2,B11,1,A10,3,D9,0\C,2,B12,1,A11,3,D10,0\H,13,B13,2,A12,1,D11,0\H,13,B14,2,A13,1,D12
,0\C,4,B15,2,A14,1,D13,0\O,16,B16,4,A15,2,D14,0\C,16,B17,4,A16,2,D15,0\H,18,B18,16,A17,4,D16
,0\C,18,B19,16,A18,4,D17,0\H,20,B20,18,A19,16,D18,0\H,20,B21,18,A20,16,D19,0\\B1=2.5095788\
B2=1.54069136\B3=1.39831602\B4=1.53629423\B5=1.10637337\B6=1.10674947\B7=1.10606608\B
8=1.10929213\B9=1.11015685\B10=1.10709683\B11=1.11187647\B12=1.55985431\B13=1.1051036
6\B14=1.10770465\B15=1.60863971\B16=1.2622955\B17=1.63971729\B18=1.1045646\B19=1.4772
9485\B20=1.09763309\B21=1.09628511\A1=35.20639848\A2=92.11666609\A3=111.15881647\A4=1
0 9.02699263\A5=107.29911472\A6=110.54456091\A7=110.5345658\A8=111.21097818\A9=110.45
205143\A10=144.09685608\A11=89.05291443\A12=110.11137154\A13=112.11415994\A14=105.50
634417\A15=113.80862152\A16=95.45935476\A17=97.51662478\A18=113.14926245\A19=120.900
84898\A20=117.9801268\D1=122.82461618\D2=44.2956226\D3=-76.13699858\D4=119.27749514\D
5=71.96534393\D6=168.02701795\D7=-122.94965921\D8=-169.38141029\D9=-4.88154188\D10=-13
0.18852459\D11=171.620583\D12=52.64167667\D13=45.5763823\D14=166.20183916\D15=44.8214
8568\D16=84.58478844\D17=-159.99569834\D18=96.77452285\D19=-58.94442315\\Version=EM64
L-G03RevE.01\HF=-459.6042355\MP2=-461.0809983\PUHF=-459.6077119\PMP2-0=-461.0832805\
S2=0.765184\S2-1=0.75468\S2A=0.750175\RMSD=5.482e-09\RMSF=1.421e-05\Thermal=0.\Dipole=
1.4599532,-1.6268305,-0.5306905\PG=C01 [X(C8H12O2)]\\@

No imaginary frequencies.

MP2/aug-cc-pVDZ//MP2/cc-pVDZ
MP2=-461.2019408

Substrate of 1,3-cyclization of lactone bearing phenyl-substituted alkene tether

MP2/cc-pVDZ
1\1\GINC-I7\FOpt\UMP2-FC\CC-pVDZ\C14H16O2(1-,2)\HIROSHI\19-Sep-2010\0\\#MP2/cc-pVDZ
geom=check guess=read OPT=(ReadFC,Maxcycle=100) Nosymm\\ph 1,3 sub\\-1,2\C,0.1267351617,2.
6278932381,0.0142619508\C,1.3778000904,1.5757255631,1.9009397235\C,1.4026991968,2.6801744
716,0.8500791271\O,0.2010865493,1.6704149621,2.7692593646\C,-1.0691253269,2.7905261867,0.9
544866309\H,0.0699671787,1.6643464617,-0.5209339107\H,1.478818491,3.6627677537,1.35319816
35\H,-1.13692138,3.8493739456,1.2724916762\H,0.1150599623,3.4204129177,-0.7540986497\H,2.3
073620453,2.5368181143,0.236895574\H,-2.0334880401,2.5452800741,0.4817233745\C,-1.0095057
159,2.005974138,2.2647667917\O,-2.0152646032,1.7770778904,2.9104991822\C,1.4634317212,0.15
09598817,1.3202967037\H,0.5323131748,-0.0552117428,0.7557133194\H,1.4607809784,-0.5403494
176,2.1847441683\C,2.6879741636,-0.0506702247,0.473658391\H,2.6188900673,0.1891994469,-0.5
924745384\C,3.9047836883,-0.4470462128,1.0196694625\H,3.9105072989,-0.7183081571,2.088409
2745\H,2.2228365813,1.7087029191,2.5959905717\C,5.1548552374,-0.5494476051,0.3456749472\C,
5.3645370442,-0.183401578,-1.0378548163\C,6.3184113055,-1.03525805,1.0393214532\C,6.600933
3474,-0.3169247355,-1.6085058326\H,4.5300434131,0.2138526698,-1.6264749854\C,7.5260801807,-
1.1482119551,0.425332445\H,6.2075651181,-1.3207158543,2.0956059924\C,7.7294237922,-0.79697
70431,-0.9358636623\H,6.7035984074,-0.0215818501,-2.665497013\H,8.3732102278,-1.5283187414
,1.0169092639\H,8.7025789431,-0.8946047468,-1.4233617535\\Version=EM64L-G03RevE.01\HF=-
689.2056375\MP2=-691.4357722\PUHF=-689.2240266\PMP2-0=-691.4515798\S2=1.015687\S2-1=0.
931963\S2A=0.806299\RMSD=6.391e-09\RMSF=3.152e-05\Thermal=0.\Dipole=-3.4961659,2.27746
47,0.3637087\PG=C01 [X(C14H16O2)]\\@

No imaginary frequencies.

MP2/aug-cc-pVDZ//MP2/cc-pVDZ
MP2=-691.5847025

Transition state involved in exo 1,3-cyclization of lactone bearing phenyl-substituted alkene tether

MP2/cc-pVDZ
1\1\GINC-I7\FTS\UMP2-FC\CC-pVDZ\C14H16O2(1-,2)\HIROSHI\13-Sep-2010\1\\#MP2/cc-pVDZ geom=check guess=read OPT=(TS,z-matrix,NoEigenTest,ReadFC,Maxcycle=100) Nosymm\\ph TS 1, 3-cycl exo\\-1,2\C\O,1,r2\O,1,r3,2,a3\C,3,r4,1,a4,2,d4,0\C,4,r5,3,a5,1,d5,0\C,1,r6,3,a6,4,d6,0\C,6,r7,1,a7,3,d7,0\H,4,r8,3,a8,1,d8,0\C,1,r9,3,a9,4,d9,0\C,9,r10,1,a10,3,d10,0\C,9,r11,1,a11,3,d11,0\H,5,r12,4,a12,3,d12,0\H,5,r13,4,a13,3,d13,0\H,6,r14,1,a14,3,d14,0\H,6,r15,1,a15,3,d15,0\H,7,r16,6,a16,1,d16,0\H,7,r17,6,a17,1,d17,0\H,9,r18,10,a18,11,d18,0\H,10,r19,9,a19,18,d19,0\H,10,r20,9,a20,18,d20,0\H,11,r21,9,a21,18,d21,0\C,11,r22,9,a22,18,d22,0\C,22,r23,11,a23,9,d23,0\C,23,r24,22,a24,11,d24,0\C,24,r25,23,a25,22,d25,0\C,22,r26,11,a26,9,d26,0\C,26,r27,22,a27,11,d27,0\H,23,r28,22,a28,11,d28,0\H,24,r29,23,a29,22,d29,0\H,25,r30,24,a30,23,d30,0\H,26,r31,22,a31,11,d31,0\H,27,r32,26,a32,22,d32,0\\r2=1.23707579\r3=1.4848832\a3=116.25159686\r4=1.41047648\a4=109.32505762\d4=164.51295743\r5=1.53627103\a5=110.4927943\d5 =71.14163543\r6=1.55818646\a6=107.64991954\d6=-61.08965815\r7=1.53486124\a7=116.42628457\d7=48.91927602\r8=1.10790054\a8=107.10169891\d8=-169.90885416\r9=1.93398889\a9=94.46611172\d9=42.54623147\r10=1.52104404\a10=100.22993466\d10=-21.456212\r11=1.43091185\a11=106.8863806\d11=100.40330409\r12=1.10676413\r13=1.10800821\a12=107.80965\a13=110.47274417\d12=56.03576596\d13=173.66846501\r14=1.1087865\r15=1.1049605\a14=104.13181926\a15=107.56945874\d14=-72.00736521\d15=174.63254367\r16=1.10774025\r17=1.10567317\a16=110.75777009\a17=109.8809674\d16=-166.51153276\d17=76.54737664\r18=1.1022511\a18=115.426319\d18=-137.84479257\r19=1.10802566\r20=1.10569146\a19=113.75824723\a20=109.62320451\d19=-19.14825247\d20=-139.05133359\r21=1.09940155\r22=1.41951823\a21=117.9940967\a22=125.81550217\d21=152.61542674\d22=-34.74769569\r23=1.41728371\r24=1.37193347\r25=1.39579599\a23=122.70105885\a24=121.20808549\a25=121.51313594\d23=-2.39237794\d24=176.12750916\d25=0.74993297\r26=1.41688338\r27=1.37247633\a26=120.95170107\a27=121.8869579\d26=-184.61047998\d27=183.51730039\r28=1.091924\r29=1.09702627\r30=1.09464267\r31=1.09701572\r32=1.09715873\a28=118.54782401\a29=118.98145937\a30=120.87189327\a31=118.1815472\a32=119.36005523\d28=-6.05124009\d29=179.65411397\d30=179.63474796\d31=3.11643284\d32=179.76192376\\Version=EM64L-G03RevE.01\HF=-689.187233\MP2=-691.4064701\PUHF=-689.2250048\PMP2-0=-691.4402849\S2=1.277048\S2-1=1.135521\S2A=1.013781\RMSD=3.680e-09\RMSF=8.917e-06\Thermal=0.\Dipole=-0.5769076,-0.3234514,-1.4171909\PG=C01 [X(C14H16O2)]\\@

Imaginary frequency: 321.3193i

MP2/aug-cc-pVDZ//MP2/cc-pVDZ
MP2=-691.5591132

Transition state involved in endo 1,3-cyclization of lactone bearing phenyl-substituted alkene tether

MP2/cc-pVDZ
1\1\GINC-I7\FTS\UMP2-FC\CC-pVDZ\C14H16O2(1-,2)\HIROSHI\05-Oct-2010\1\\#MP2/cc-pVDZ geom=check guess=read OPT=(TS,z-matrix,NoEigenTest,ReadFC,Maxcycle=100) Nosymm\\TS ph 1, 3 endo\\-1,2\C\O,1,r2\O,1,r3,2,a3\C,3,r4,1,a4,2,d4,0\C,4,r5,3,a5,1,d5,0\C,1,r6,3,a6,4,d6,0\C,6,r7,1,a7,3,d7,0\H,4,r8,3,a8,1,d8,0\C,1,r9,3,a9,4,d9,0\C,9,r10,1,a10,3,d10,0\C,9,r11,1,a11,3,d11,0\H,5,r12,4,a12,3,d12,0\H,5,r13,4,a13,3,d13,0\H,6,r14,1,a14,3,d14,0\H,6,r15,1,a15,3,d15,0\H,7,r16,6,a16,1,d16,0\H,7,r17,6,a17,1,d17,0\H,9,r18,10,a18,11,d18,0\H,10,r19,9,a19,18,d19,0\H,10,r20,9,a20,18,d20,0\H,11,r21,9,a21,18,d21,0\C,11,r22,9,a22,18,d22,0\C,22,r23,11,a23,9,d23,0\C,23,r24,22,a24,11,d24,0\C,24,r25,23,a25,22,d25,0\C,22,r26,11,a26,9,d26,0\C,26,r27,22,a27,11,d27,0\H,23,r28,22,a28,11,d28,0\H,24,r29,23,a29,22,d29,0\H,25,r30,24,a30,23,d30,0\H,26,r31,22,a31,11,d31,0\H,27,r32,26,a32,22,d32,0\\r2=1.24538899\r3=1.47520756\a3=114.94334071\r4=1.41451576\a4=109.35400627\d4=162.23781334\r5=1.53576456\a5=109.99047968\d5=70.32873764\r6=1.54593812\a6=109.03598015\d6=-61.69731219\r7=1.53421077\a7=115.3449467\d7=48.64788083\r8=1.10724684\a8=106.84164636\d8=-170.99484816\r9=

1.91877882\a9=93.30819391\d9=45.19233441\r10=1.52344978\a10=100.97805046\d10=-25.2088414
1\r11=1.42961387\a11=116.32723351\d11=-154.86523338\r12=1.10682271\r13=1.10814656\a12=107
.6006562\a13=110.41525486\d12=57.43041319\d13=174.74894186\r14=1.1088647\r15=1.10348063\
a14=104.78644259\a15=107.10848087\d14=-72.83298146\d15=172.86955396\r16=1.10749054\r17=1
.10342665\a16=110.63689385\a17=109.08993671\d16=-165.67267378\d17=77.80081998\r18=1.0999
4601\a18=113.01533889\d18=137.7117.67267378\d17=77.80081998\r18=1.09994601\a18=113.01533
889\d18=137.7117772\r19=1.1058701\r20=1.10746518\a19=111.29430972\a20=111.99670509\d19=2
4.3255121\d20=144.20737525\r21=1.1005938\r22=1.42876875\a21=118.76216529\a22=125.5067673
\d21=-150.38755287\d22=31.51995403\r23=1.41608187\r24=1.37399496\r25=1.39365271\a23=122.0
040037\a24=120.59504174\a25=121.76419215\d23=7.8917897\d24=181.39004485\d25=-0.28346504\
r26=1.41354666\r27=1.37300829\a26=121.13489747\a27=121.72145001\d26=-172.03785031\d27=17
8.57657101\r28=1.09587738\r29=1.09706893\r30=1.09490313\r31=1.09745867\r32=1.09729786\a28
=118.54079371\a29=118.72588691\a30=120.87100583\a31=118.4030909\a32=119.40231183\d28=4.
91839709\d29=180.5012395\d30=180.07276441\d31=-0.92999947\d32=180.3817433\\Version=EM64
L-G03RevE.01\HF=-689.1936707\MP2=-691.4149517\PUHF=-689.2309059\PMP2-0=-691.448272\S
2=1.271791\S2-1=1.131284\S2A=1.010877\RMSD=5.506e-09\RMSF=1.474e-05\Thermal=0.\Dipole=
-0.6114781,-0.1832352,-1.563763\PG=C01 [X(C14H16O2)]\\@

Imaginary frequency: 335.9856i

MP2/aug-cc-pVDZ//MP2/cc-pVDZ
MP2=-691.5658504

Exo product of 1,3-cyclization of lactone bearing phenyl-substituted alkene tether

MP2/cc-pVDZ
1\1\GINC-I7\FOpt\UMP2-FC\CC-pVDZ\C14H16O2(1-,2)\HIROSHI\18-Sep-2010\1\\#MP2/cc-pVDZ
scf=direct freq=Noraman geom=check guess=read OPT=(z-matrix,ReadFC,Maxcycle=100) Nosymm\\
ph pro exo\\-1,2\C\O,1,r2\O,1,r3,2,a3\C,3,r4,1,a4,2,d4,0\C,4,r5,3,a5,1,d5,0\C,1,r6,3,a6,4,d6,0\C,6,r7,1,
a7,3,d7,0\H,4,r8,3,a8,1,d8,0\C,1,r9,3,a9,4,d9,0\C,9,r10,1,a10,3,d10,0\C,9,r11,1,a11,3,d11,0\H,5,r12,4,a
12,3,d12,0\H,5,r13,4,a13,3,d13,0\H,6,r14,1,a14,3,d14,0\H,6,r15,1,a15,3,d15,0\H,7,r16,6,a16,1,d16,0\H
,7,r17,6,a17,1,d17,0\H,9,r18,10,a18,11,d18,0\H,10,r19,9,a19,18,d19,0\H,10,r20,9,a20,18,d20,0\H,11,r2
1,9,a21,18,d21,0\C,11,r22,9,a22,18,d22,0\C,22,r23,11,a23,9,d23,0\C,23,r24,22,a24,11,d24,0\C,24,r25,
23,a25,22,d25,0\C,22,r26,11,a26,9,d26,0\C,26,r27,22,a27,11,d27,0\H,23,r28,22,a28,11,d28,0\H,24,r29,
23,a29,22,d29,0\H,25,r30,24,a30,23,d30,0\H,26,r31,22,a31,11,d31,0\H,27,r32,26,a32,22,d32,0\\r2=1.2
7257582\r3=1.59247528\a3=112.69822657\r4=1.39748668\a4=105.45772458\d4=165.94167265\r5=1.
53998922\a5=110.44840892\d5=75.24825495\r6=1.55970262\a6=101.97500755\d6=-69.81828917\r7
=1.537049\a7=115.07270016\d7=57.78659131\r8=1.11110093\a8=109.2781611\d 8=-164.84960762\r
9=1.61773319\a9=97. 83987042\d9=41.8686949\r10=1.54874988\a10=106.80709174\d10=-22.18394
444\r11=1.48989441\a11=106.90531754\d11=100.5577413\r12=1.10676972\r13=1.10938534\a12=10
7.16433947\a13=111.11858404\d12=57.04191417\d13=174.62244649\r14=1.1054037\r15=1.1074913
9\a14=105.15657804\a15=107.46246644\d14=-64.17336455\d15=181.56177443\r16=1.10856567\r17
=1.10811721\a16=111.21351238\a17=109.37834265\d16=-171.93255235\d17=71.63298778\r18=1.11
095104\a18=110.66839805\d18=-123.99654559\r19=1.10767191\r20=1.10413238\a19=113.63732729
\a20=110.22614559\d19=-6.07630574\d20=-126.96711428\r21=1.09981415\r22=1.41704059\a21=113
.17914625\a22=126.0108128\d21=244.27496279\d22=62.10954659\r23=1.42018627\r24=1.37192427
\r25=1.39799627\a23=120.47722679\a24=121.65408047\a25=120.74947999\d23=-180.88396168\d24
=179.59425506\d25=-0.09402386\r26=1.41948929\r27=1.37589581\a26=122.95740401\a27=121.221
01661\d26=-1.44979495\d27=180.56005236\r28=1.09550945\r29=1.09624469\r30=1.094375\r31=1.0
935996\r32=1.09635617\a28=117.90148389\a29=119.54092005\a30=120.63671996\a31=118.582254
21\a32=119.29895643\d28=-0.4091752\d29=179.98517784\d30=179.99754617\d31=0.14738731\d32
=179.82725433\\Version=EM64L-G03RevE.01\HF=-689.2064782\MP2=-691.4128645\PUHF=-689.2
441883\PMP2-0=-691.4466525\S2=1.278874\S2-1=1.139167\S2A=0.999689\RMSD=6.897e-09\RMS
F=2.296e-05\Thermal=0.\Dipole=-0.9157543,-2.017477,-1.7397946\PG=C01 [X(C14H16O2)]\\@

No imaginary frequencies.

MP2/aug-cc-pVDZ//MP2/cc-pVDZ

MP2=-691.5661391

Endo product of 1,3-cyclization of lactone bearing phenyl-substituted alkene tether

MP2/cc-pVDZ

1\1\GINC-I7\FOpt\UMP2-FC\CC-pVDZ\C14H16O2(1-,2)\HIROSHI\13-Sep-2010\1\\#MP2/cc-pVDZ scf=direct geom=check guess=read OPT=(z-matrix,ReadFC,Maxcycle=100) Nosymm\\ph 1,2 pro endo \\-1,2\C\C,1,B1\C,1,B2,2,A1\O,2,B3,1,A2,3,D1,0\C,1,B4,3,A3,2,D2,0\H,1,B5,5,A4,4,D3,0\H,3,B6,1,A5,5,D4,0\H,5,B7,1,A6,3,D5,0\H,1,B8,5,A7,4,D6,0\H,3,B9,1,A8,5,D7,0\H,5,B10,1,A9,3,D8,0\C,4,B11,2,A10,1,D9,0\O,12,B12,4,A11,2,D10,0\C,2,B13,1,A12,5,D11,0\H,14,B14,2,A13,1,D12,0\H,14,B15,2,A14,1,D13,0\C,14,B16,2,A15,1,D14,0\H,17,B17,14,A16,2,D15,0\C,17,B18,14,A17,2,D16,0\H,19,B19,17,A18,14,D17,0\H,2,B20,1,A19,5,D18,0\C,19,B21,17,A20,14,D19,0\C,22,B22,19,A21,17,D20,0\C,22,B23,19,A22,17,D21,0\C,23,B24,22,A23,19,D22,0\H,23,B25,22,A24,19,D23,0\C,24,B26,22,A25,19,D24,0\H,24,B27,22,A26,19,D25,0\C,27,B28,24,A27,22,D26,0\H,25,B29,23,A28,22,D27,0\H,27,B30,24,A29,22,D28,0\H,29,B31,27,A30,24,D29,0\\B1=2.51137613\B2=1.53412423\B3=1.40419283\B4=1.53625195\B5=1.10647406\B6=1.10658058\B7=1.10609952\B8=1.10840708\B9=1.10933082\B10=1.10609611\B11=1.55562874\B12=1.2746367\B13=1.55492138\B14=1.10427287\B15=1.10737618\B16=1.5389059\B17=1.10510802\B18=1.47814613\B19=1.09944481\B20=1.10960885\B21=1.42770875\B22=1.41694378\B23=1.41380892\B24=1.3761392\B25=1.1019497\B26=1.37488141\B27=1.09693156\B28=1.39346981\B29=1.0963217\B30=1.09641701\B31=1.09513713\A1=35.24770838\A2=91.74883975\A3=110.95983966\A4=109.18839189\A5=109.95454547\A6=110.74189073\A7=111.09476641\A8=111.08896961\A9=110.64525544\A10=106.21396829\A11=112.77488422\A12=89.80241845\A13=109.91325759\A14=112.10458197\A15=103.83540407\A16=110.35844892\A17=115.07687672\A18=118.8500798\A19=144.41236462\A20=125.01083039\A21=121.45145544\A22=120.72927819\A23=119.92195622\A24=117.81566192\A25=121.34981109\A26=118.60155788\A27=120.30799503\A28=118.91226221\A29=119.74025514\A30=120.43034406\D1=123.67304532\D2=44.87079413\D3=104.67255067\D4=-72.89126729\D5=72.36277956\D6=-139.07767683\D7=167.83910891\D8=-168.43133984\D9=44.30337747\D10=166.00107135\D11=91.17660391\D12=-185.25307589\D13=55.5780093\D14=-66.45618691\D15=-101.72744298\D16=132.99370608\D17=-12.37534709\D18=-141.04862685\D19=166.38807913\D20=8.55448527\D21=188.87810047\D22=-178.5176999\D23=5.63182399\D24=-181.59515593\D25=-1.13379992\D26=0.37141177\D27=180.54443809\D28=180.39429034\D29=-180.0699652\\Version=EM64L-G03RevE.01\HF=-689.2069351\MP2=-691.4170814\PUHF=-689.2445567\PMP2-0=-691.4508056\S2=1.279237\S2-1=1.139815\S2A=1.001766\RMSD=9.227e-09\RMSF=2.460e-05\Thermal=0.\Dipole=-0.021965,-2.0365122,-0.8914526\PG=C01 [X(C14H16O2)]\\@

No imaginary frequencies.

MP2/aug-cc-pVDZ//MP2/cc-pVDZ

MP2=-691.5695386