Electronic Supplementary Material (ESI) for Chemical Communications

Supplementary Information:

Hydrometallation – asymmetric conjugate addition: application to complex molecule synthesis

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General Information

Procedures using oxygen- and/or moisture-sensitive materials were performed with anhydrous solvents (*vide infra*) under an atmosphere of anhydrous argon in flame-dried flasks, using standard Schlenk techniques. Analytical thin-layer chromatography was performed on precoated glass-backed plates (Silica Gel 60 F_{254}; Merck), and visualised using a combination of UV light (254 nm) and aqueous ceric ammonium molybdate (CAM), aqueous basic potassium permanganate stains or vanillin solution. Flash column chromatography was carried out using Apollo Scientific silica gel 60 (0.040 – 0.063 nm), Merck 60 Å silica gel, VWR (40-63 μm) silica gel and Sigma Aldrich silica gel. Pressure was applied at the column head via hand bellows or a flow of nitrogen with the solvent system used in parentheses.

Cooling of reaction mixtures to 0 °C was achieved using an ice-water bath. Unless stated otherwise, solution NMR spectra were recorded at room temperature; ^{1}H and ^{13}C nuclear magnetic resonance experiments were carried out using Bruker DPX-200 (200/50 MHz), DPX-400 (400/100 MHz), DQX-400 (400/100 MHz) or AVC-500 (500/125 MHz) spectrometers. Chemical shifts are reported in ppm from the residual solvent peak. Chemical shifts (δ) are given in ppm and coupling constants (*J*) are quoted in hertz (Hz). Resonances are described as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Labels H and H' refer to diastereotopic protons attached to the same carbon and impart no stereochemical information. Assignments were made with the assistance of gCOSY, DEPT-135, gHSQC, gHMBC, NOESY, TOCSY, or NOE NMR spectra.

Numbering and names of structures accompanying reported data is non-IUPAC, and solely for reference.

Low-resolution mass spectra were recorded using a Walters LCT premier XE. High-resolution mass spectra (EI and ESI) were recorded using a Bruker MicroTOF spectrometer by the internal service at the University of Oxford.

Chiral HPLC separations were achieved using an Agilent 1230 Infinity series normal phase HPLC unit and HP Chemstation software. Chiralpak® columns (250 × 4.6 mm), fitted with matching Chiralpak® Guard Cartridges (10 × 4 mm), were used as specified in the text. Solvents used were of HPLC grade (Fisher Scientific, Sigma Aldrich or Rathburn); all eluent systems were isocratic.

Infrared measurements (neat, thin film) were carried out using a Bruker Tensor 27 FT-IR with internal calibration in the range 4000-600 cm^{-1}.

Optical rotations were recorded using a Perkin-Elmer 241 Polarimeter. CD spectra were recorded using an Applied Photophysics ChiraScan CD/Fluorometer.

Chemicals

Dry CH_2Cl_2, Et_2O and benzene were collected fresh from an mBraun SPS-800 solvent purification system having been passed through anhydrous alumina columns. All other solvents were used as purchased from Sigma Aldrich, Rathburn or Fisher Scientific.

Unless stated otherwise, commercially available reagents were purchased from Sigma-Aldrich, Fisher Scientific, Apollo Scientific, Acros Organics, Strem Chemicals, Alfa Aesar, AK Scientific or TCI UK and were used without purification. Petroleum ether refers to light petroleum boiling in the range 40–60 °C. Deuterated solvents were purchased from Sigma-Aldrich (C_6D_6, $CDCl_3$). Schwartz reagent was prepared according to the literature procedure[1] from Cp_2ZrCl_2 provided by Alfa Aesar or Strem Chemicals. $(CuOTf)_2.C_6H_6$ was synthesised using a modified literature procedure[2] and carefully maintained under an inert atmosphere. $(CuOTf)_2.C_6H_6$ should be a white or off-white powder, not green or brown. The phosphoramidite ligand was synthesised according to the literature procedure.[3]

Synthesis of racemic products:

Using a modified procedure of Wipf *et al*.,[4] Cp_2ZrHCl (206 mg, 0.80 mmol, 2.0 eq) was added to a stirred, room temperature, solution of alkene (1.0 mmol, 2.5 eq) in CH_2Cl_2 (2.0 mL) under an argon atmosphere. After stirring for about 40 min, $CuBr \cdot Me_2S$ (82 mg, 0.40 mmol 1.0 eq), was added to the reaction mixture and the resulting black mixture was allowed to stir for an additional 10 min before a cyclic enone (0.40 mmol, 1.0 eq) was added via syringe over about 1 min. Stirring at room temperature was continued arbitrarily for 15 h before the reaction was quenched by the addition of Et_2O (*ca* 3 mL) and then NH_4Cl (1 M aq., *ca* 1.5 mL). The mixture was partitioned between water and Et_2O and the aqueous phase extracted with Et_2O (3 × 10 mL). The combined organic phase was washed with $NaHCO_3$ (aq. sat., *ca* 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give an oil. Flash column chromatography of the residue (EtOAc/petrol; SiO_2) gave the desired cyclic ketone.

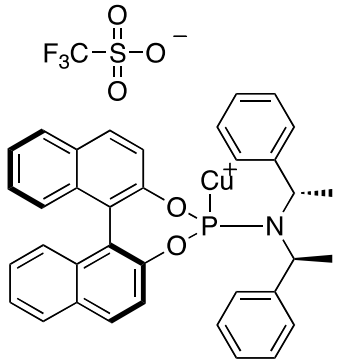
Procedure A: Catalytic asymmetric conjugate addition with copper-ligand complex formed in situ:

$(CuOTf)_2.(C_6H_6)$ (10.1 mg, 0.02 mmol, 0.05 eq.) and the phosphoramidite ligand (21.6 mg, 0.04 mmol, 0.1 eq.) were dissolved in Et_2O (2.0 mL) under an argon atmosphere and allowed to stir for 1 h at room temperature. In another flask, Cp_2ZrHCl (206.0 mg, 0.80 mmol, 2.0 eq.) was added to a stirred, room temperature, solution of alkene (1.0 mmol, 2.5 eq.) in CH_2Cl_2 (0.40 mL) under an argon atmosphere. After stirring for 40 min, the resulting clear yellow solution was transferred *via* syringe over about 1 min to the stirred solution containing the copper and ligand under an argon atmosphere. The resulting dark mixture was allowed to stir for an additional 10 min before cyclic enone (0.40 mmol, 1.0 eq.) and then TMSCl (0.26 mL, 2.0 mmol, 5.0 eq.) were added dropwise *via* syringe. The reaction was stirred until complete (TLC control (EtOAc/Petrol 1:2.5)). The reaction was quenched by the addition of Et_2O (*ca* 3 mL) and then NH_4Cl (1 M aq., *ca* 1.5 mL). The mixture was partitioned between water and Et_2O and the aqueous phase extracted with Et_2O (3 × 10 mL). The combined organic phase was washed with $NaHCO_3$ (aq. sat., *ca* 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give an oil. Flash column chromatography of the residue (SiO_2) gave the desired steroid product.

Procedure B: Catalytic asymmetric conjugate addition with premade copper-ligand complex:

Cp_2ZrHCl (206 mg, 0.80 mmol, 2.0 eq.) was added to a stirred, room temperature, solution of alkene (1.0 mmol, 2.5 eq.) in CH_2Cl_2 (0.40 mL) under an argon atmosphere. After stirring for about 40 min, the resulting clear yellow solution was transferred *via* syringe over about 1 min to a clear colourless stirred solution of CuOTf-ligand complex (30.0 mg, 0.040 mmol, 0.10 eq.) in Et_2O (2.0 mL) under an argon atmosphere. The resulting dark mixture was allowed to stir for an additional 10 min before cyclic enone (0.40 mmol, 1.0 eq.) and then TMSCl (0.26 mL, 2.0 mmol, 5.0 eq.) were added dropwise *via* syringe. The reaction was stirred until complete (TLC control (EtOAc/Petrol 1:2.5)). The reaction was quenched by the addition of Et_2O (*ca* 3 mL) and then NH_4Cl (1 M. aq., *ca* 1.5 mL). The mixture was partitioned between water and Et_2O and the aqueous phase extracted with Et_2O (3 × 10 mL). The combined organic phase was washed with $NaHCO_3$ (aq. sat., *ca* 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give an oil. Flash column chromatography of the residue (SiO_2) gave the desired steroid product.

Preparation of copper-ligand complex A:



To a flame dried Schlenk flask containing $(CuOTf)_2.(C_6H_6)$ (239 mg, 0.48 mmol, 0.5 eq.) at room temperature under an argon atmosphere was added the phosphoramidite ligand (513 mg, 0.95 mmol, 1.0 eq.) and then CH_2Cl_2 (10 mL). This mixture was stirred for 1 h before the resulting clear colourless solution was cannula filtrated into another Schlenk flask. The solvent was then gently removed by use of an oil-pump vacuum (with liquid nitrogen trapping). The resulting off-white solid was dried for at least one extra hour under oil-pump vacuum before storing the catalyst complex under argon.

^{1}H NMR (500 MHz, CD_2Cl_2) δ_H /ppm 1.89 (d, *J*=6.7 Hz, 6 H) 4.59 - 4.71 (m, 2 H) 7.19 - 7.44 (m, 6 H) 7.45 - 7.61 (m, 10 H) 7.69 (d, *J*=8.8 Hz, 2 H) 7.94 - 8.07 (m, 3 H) 8.14 (d, *J*=8.8 Hz, 1 H)

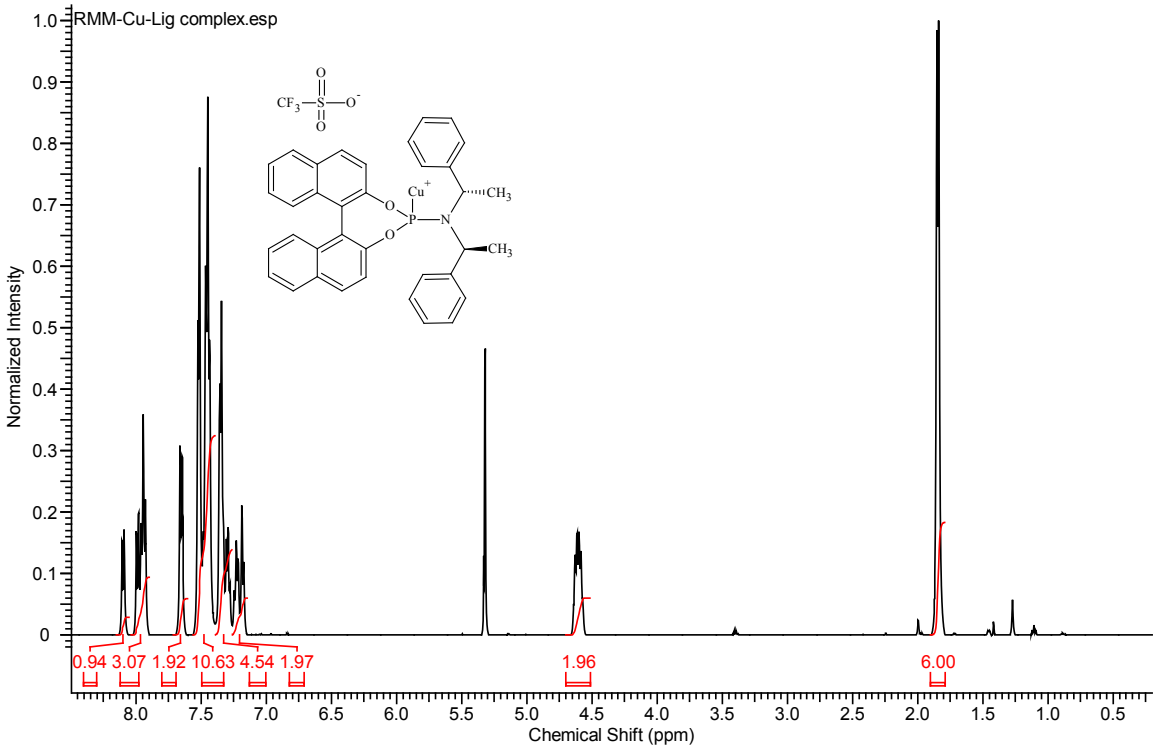
^{13}C NMR (125 MHz, CD_2Cl_2) δ_C /ppm 22.0 (2 C), 53.8 (2C under solvent peak), 121.1, 121.2, 122.1, 123.60, 123.64, 125.90, 125.97, 126.9, 127.1, 127.2, 127.7, 127.8 (4 C), 128.5 (2 C), 128.7, 129.0, 129.6 (4 C), 131.2, 131.5, 132.5, 132.80, 133.0, 141.37, 141.41, 148.2 (d, *J*=3.9 Hz), 149.4 (d, *J*=14.2 Hz).

^{31}P NMR (200 MHz, CD_2Cl_2) δ_P /ppm 124.1 (br, s).

^{19}F NMR (500 MHz, CD_2Cl_2) δ_F /ppm –78.2 (s).

HRMS (EI) *m*/*z* calcd for $C_{36}H_{30}CuNO_2P$ $[M - CF_3O_3S]^+$: 602.1310, found: 602.1319. Also found: CuL_2 cald for $C_{72}H_{60}CuN_2O_4P_2$ $[M]^+$: 1141.3324, found: 1141.3325.

IR (ν_{max} /cm^{-1}): 633, 670, 748, 827, 949, 1025, 1223.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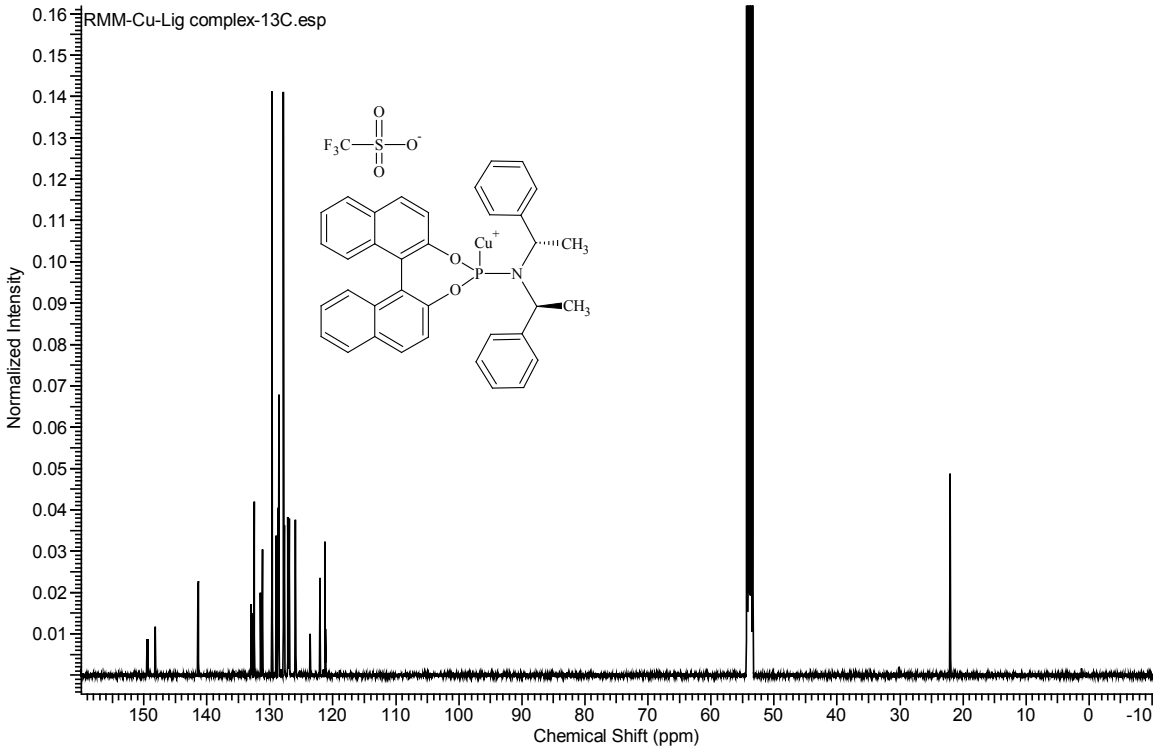
1.96
6.00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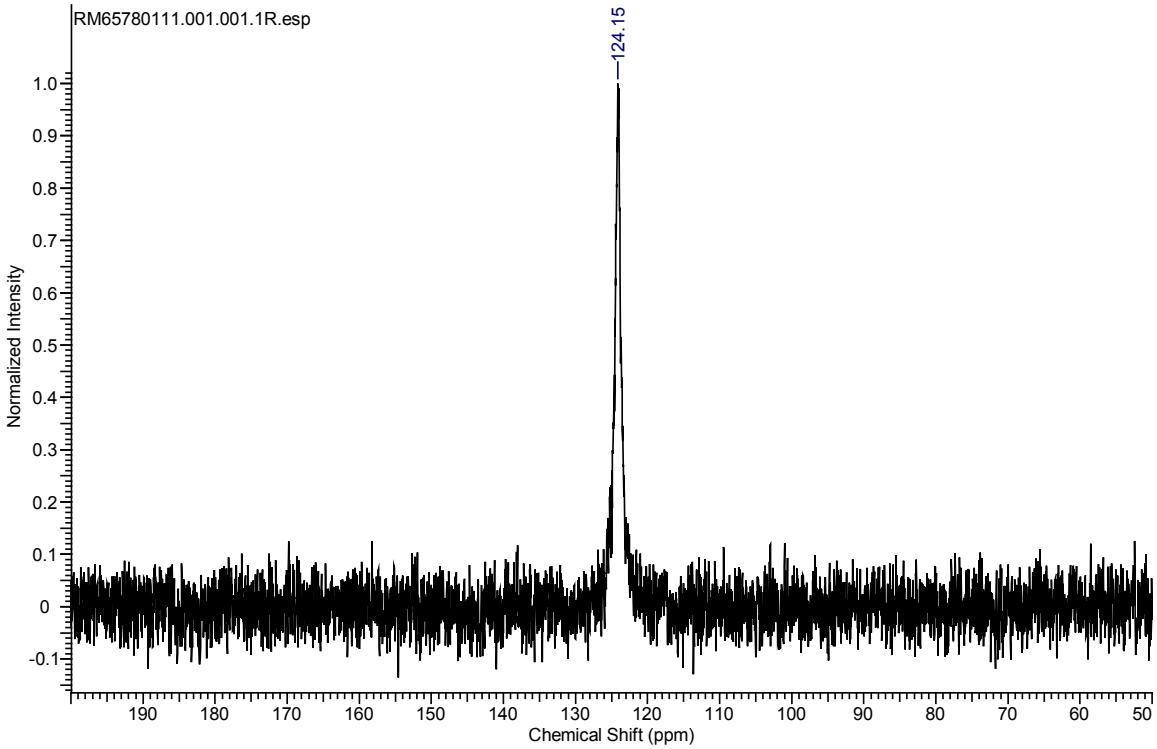
Chemical Shift (ppm)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0.6
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0.3
0.2
0.1
0
-0.1
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170
160
150
140
130
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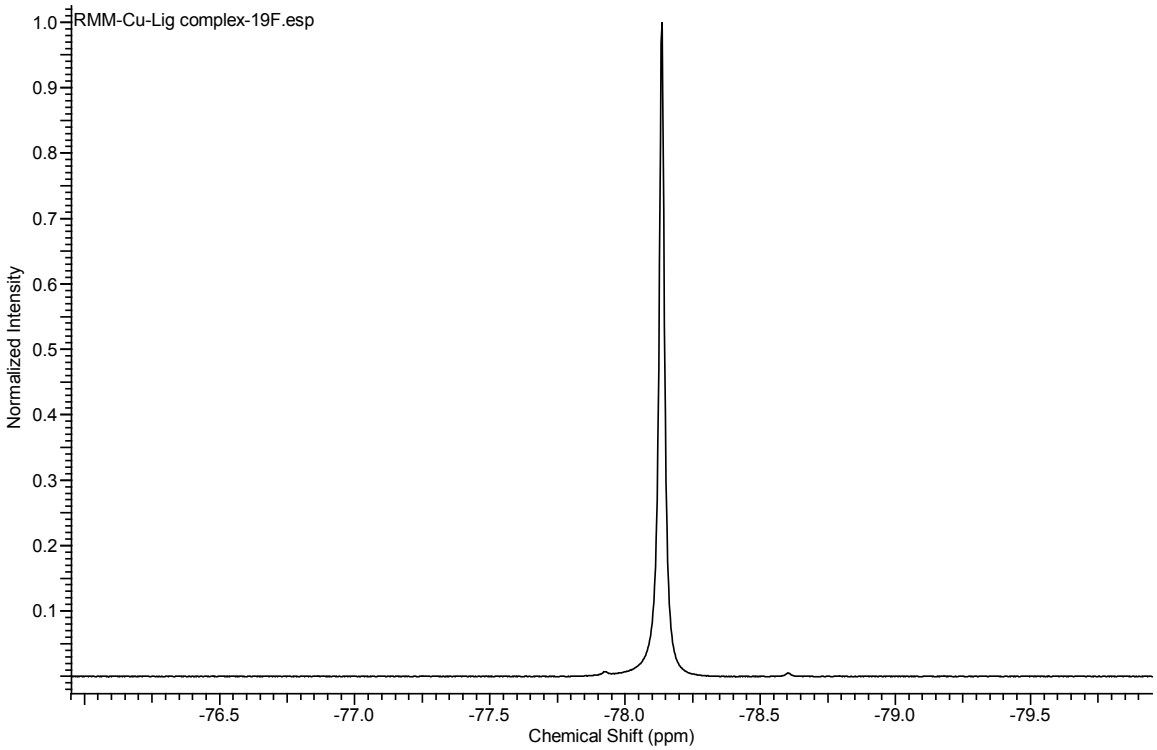
110
100
90
80
70
60
50
Chemical Shift (ppm)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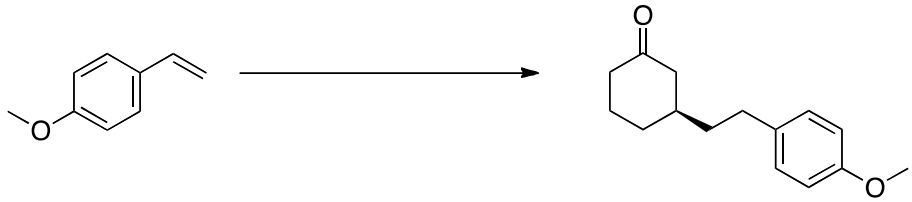
Chemical Shift (ppm)

(−)-(*S*)-4-(4-methoxyphenethyl)cyclohexanone ((−)-1)



Procedure A: $(CuOTf)_2.(C_6H_6)$ (10.1 mg, 0.02 mmol, 0.05 eq.) and the (*S,S,S*)-phosphoramidite ligand (21.6 mg, 0.040 mmol, 0.10 eq.) were dissolved in Et_2O (2.0 mL) under an argon atmosphere and allowed to stir for 1 h at room temperature before cooling to 0 °C. In another flask, Cp_2ZrHCl (206.0 mg, 0.80 mmol, 2.0 eq.) was added to a stirred, room temperature, solution of 4-methoxystyrene (0.13 mL, 1.0 mmol, 2.5 eq.) in CH_2Cl_2 (0.40 mL) under an argon atmosphere. After stirring for 15 min, the resulting clear red/orange solution was transferred *via* syringe over about 1 min to the stirred solution containing the copper and ligand under an argon atmosphere at 0 °C. The resulting black mixture was allowed to stir for an additional 10 minutes before cyclohexenone (39 µL, 0.40 mmol, 1.0 eq) and then TMSCl (0.26 mL, 2.0 mmol, 5.0 eq.) were added dropwise *via* syringe. Stirring continued at 0 °C for 6 h before the reaction was quenched by the addition of Et_2O (*ca* 3mL) and then NH_4Cl (1M aq., *ca* 1.5mL). The mixture was partitioned between the aqueous and Et_2O layers and the aqueous phase extracted with Et_2O (3 × 10 mL). The combined organic phase was washed with $NaHCO_3$ (aq. sat., *ca* 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Flash column chromatography of the yellow residue (5:95 → 1:9 EtOAc/petrol; SiO_2) gave (*S*)-3-(4-methoxyphenethyl)cyclohexanone (49 mg, 0.21 mmol, 53%) as a colourless oil.
HPLC analysis indicated an enantiomeric excess of 95% [Chiralpak® IB; flow: 1 mL/min; hexane/i-PrOH: 98:2; λ = 210 nm; minor enantiomer (*R*)-3-(4-methoxyphenethyl)cyclohexanone, t_R = 11.4 minutes; major enantiomer (*S*)-3-(4-methoxyphenethyl)cyclohexanone, t_R = 12.2 minutes]

Data in accordance with published literature.[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ_H /ppm 1.32 - 1.45 (m, 1 H), 1.55 - 1.73 (m, 3 H), 1.75 - 1.87 (m, 1 H), 1.91 - 2.00 (m, 1 H), 2.01 - 2.11 (m, 2 H), 2.28 (dddd, *J*=14.2, 12.0, 6.0, 1.0 Hz, 1 H), 2.33 - 2.41 (m, 1 H), 2.49 (ddt, *J*=13.8, 4.0, 1.9, 1.9 Hz, 1 H), 2.58 (t, *J*=8.0 Hz, 2 H), 3.79 (s, 3 H), 6.83 (d, *J*=8.7 Hz, 2 H), 7.09 (d, *J*=8.7 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$) δ_C /ppm 25.1, 31.2, 32.0, 38.4, 38.6, 41.5, 48.0, 55.2, 113.8 (2 C), 129.1 (2 C), 134.0, 157.7, 211.8.

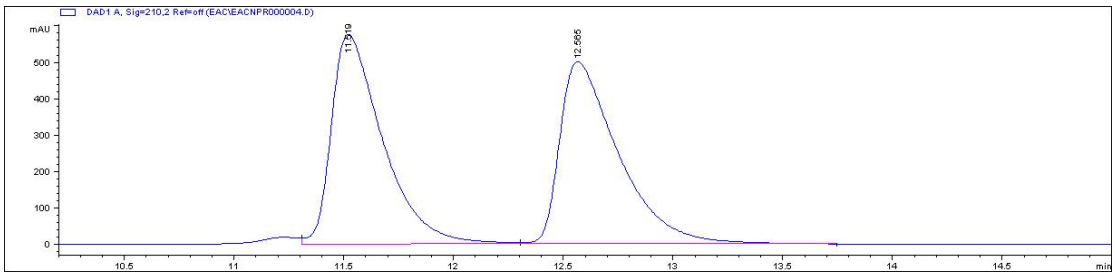
HRMS (ESI) *m/z* calcd for $C_{15}H_{20}NaO_2$ $[M+Na]^+$: 255.1356 found: 255.1349.

$[\alpha]^{20}_{589}$ = −19.8 (*c* 0.43, $CHCl_3$).

IR (ν_{max} /cm^{-1}): 1034, 1245, 1512, 1710, 2933.

CD: Θ (γ) = –2.94 (290 nm), (c = 0.17 mg/ml in EtOH).

Absolute configuration assigned by analysis of optical rotation and circular dichroism spectra.[6 7]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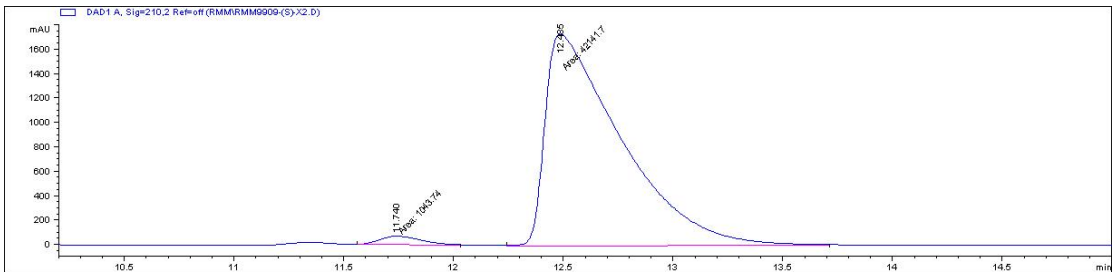
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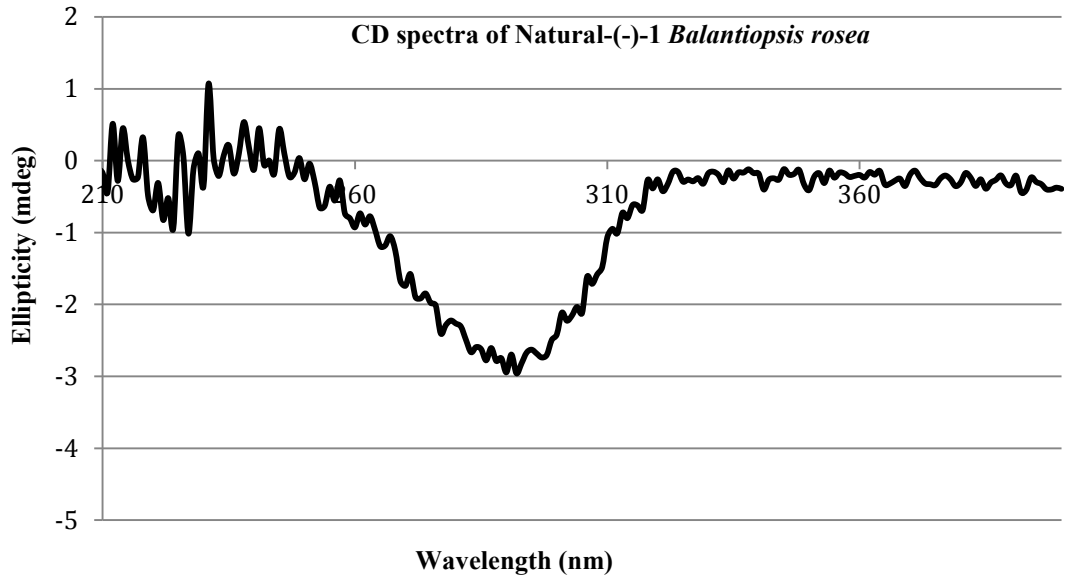
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Wavelength (nm)
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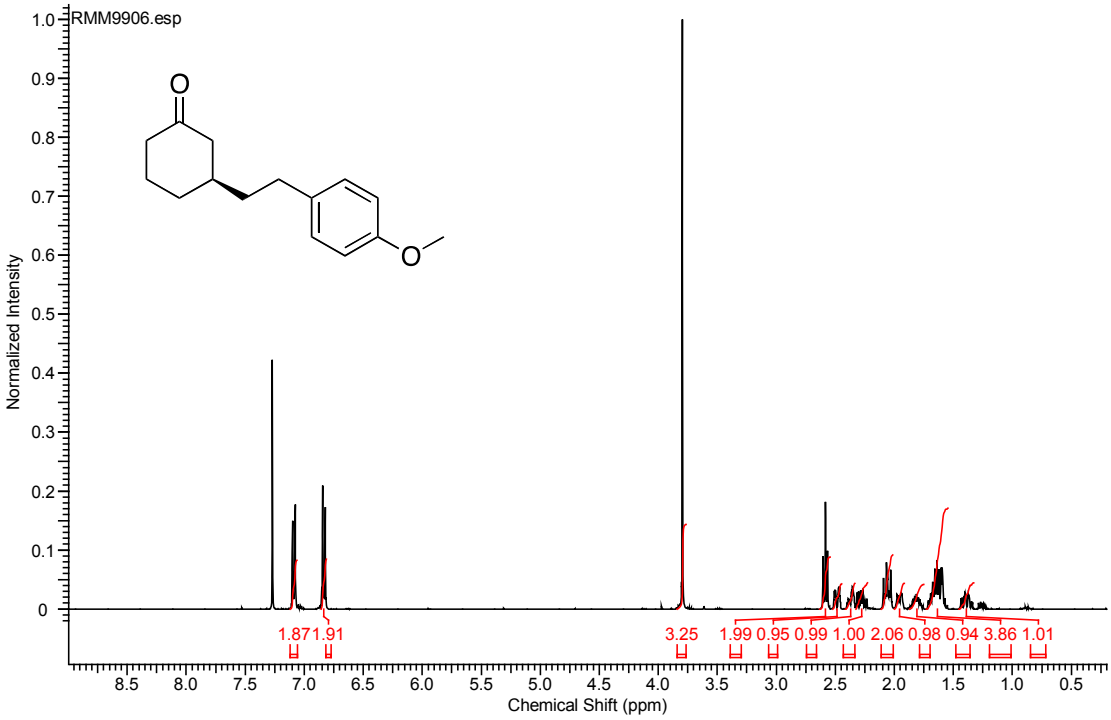
-1
-2
-3
-4
-5
210
260
310
360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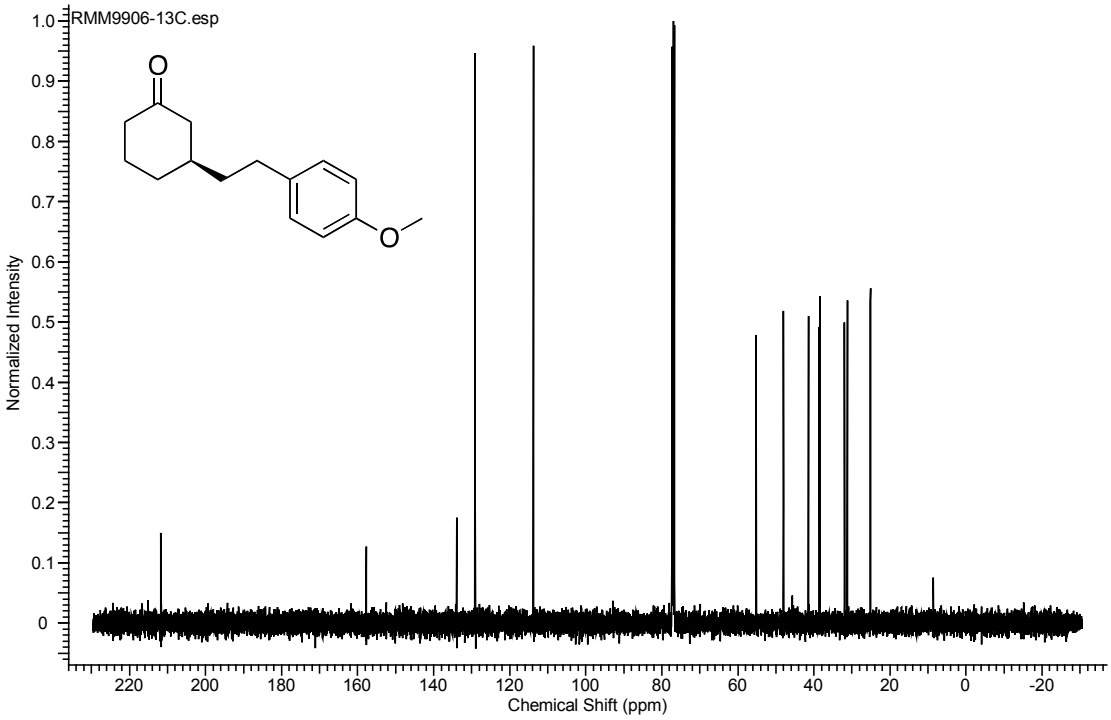
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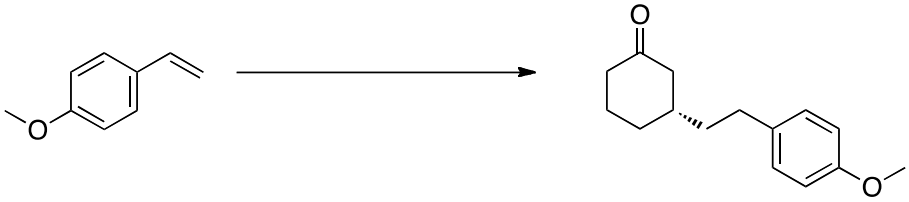
Chemical Shift (ppm)

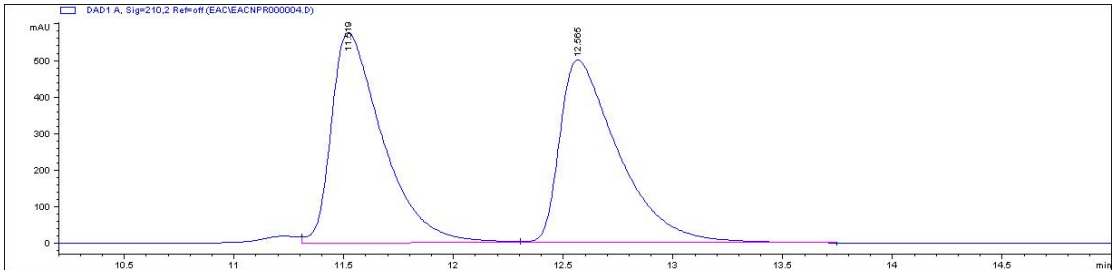
(+)-(*R*)-4-(4-methoxyphenethyl)cyclohexanone ((+)-1)

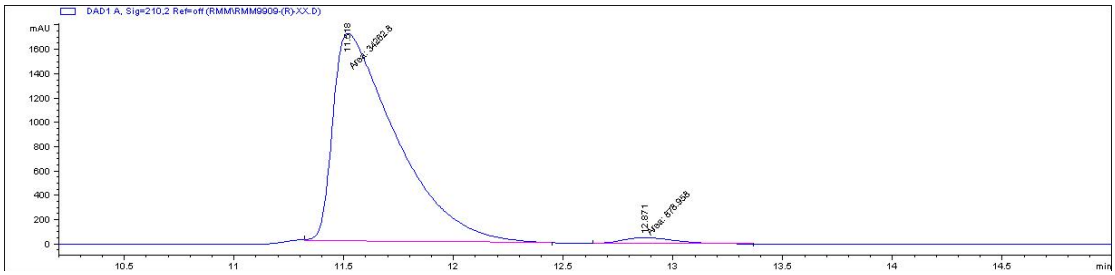


Procedure A: $(CuOTf)_2.(C_6H_6)$ (10.1 mg, 0.02 mmol, 0.05 eq.) and the (*R,R,R*)-phosphoramidite ligand (21.6 mg, 0.040 mmol, 0.10 eq.) were dissolved in Et_2O (2.0 mL) under an argon atmosphere and allowed to stir for 1 h at room temperature before cooling to 0 °C. In another flask, Cp_2ZrHCl (206.0 mg, 0.80 mmol, 2.0 eq.) was added to a stirred, room temperature, solution of 4-methoxystyrene (0.13 mL, 1.0 mmol, 2.5 eq.) in CH_2Cl_2 (0.40 mL) under an argon atmosphere. After stirring for 15 min, the resulting clear red/orange solution was transferred *via* syringe over about 1 min to the stirred solution containing the copper and ligand under an argon atmosphere at 0 °C. The resulting black mixture was allowed to stir for an additional 10 minutes before cyclohexenone (39 µL, 0.40 mmol, 1.0 eq) and then TMSCl (0.26 mL, 2.0 mmol, 5.0 eq.) were added dropwise via syringe. Stirring continued at 0 °C for 6 h before the reaction was quenched by the addition of Et_2O (*ca* 3mL) and then NH_4Cl (1M aq., *ca* 1.5mL). The mixture was partitioned between the aqueous and Et_2O layers and the aqueous phase extracted with Et_2O (3 × 10 mL). The combined organic phase was washed with $NaHCO_3$ (aq. sat., *ca* 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Flash column chromatography of the yellow residue (5:95 → 1:9 EtOAc/petrol; SiO_2) gave (*R*)-3-(4-methoxyphenethyl)cyclohexanone (42 mg, 0.18 mmol, 45%) as a colourless oil.
HPLC analysis indicated an enantiomeric excess of 94% [Chiralpak® IB; flow: 1 mL/min; hexane/i-PrOH: 98:2; λ = 210 nm; major enantiomer (*R*)-3-(4-methoxyphenethyl)cyclohexanone, t_R = 11.4 minutes; minor enantiomer (*S*)-3-(4-methoxyphenethyl)cyclohexanone, t_R = 12.2 minutes].

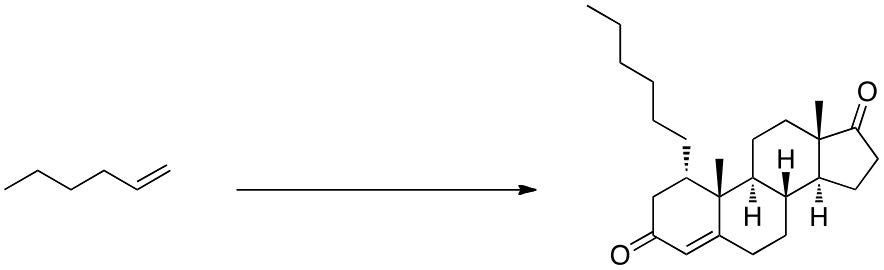
$[\alpha]^{20}_{589}$ = +14.9 (*c* 0.42, $CHCl_3$).

IR (ν_{max} /cm^{-1}): 1036, 1245, 1512, 1710, 2933.





(+)-1α-Hexyl-4-androstene-3,17-dione (4α)



Procedure A: $(CuOTf)_2.(C_6H_6)$ (10.1 mg, 0.02 mmol, 0.05 eq.) and the (*S,S,S*)-phosphoramidite ligand (21.6 mg, 0.040 mmol, 0.10 eq.) were dissolved in Et_2O (2.0 mL) under an argon atmosphere and allowed to stir for 1 h at room temperature. In another flask, Cp_2ZrHCl (206.0 mg, 0.80 mmol, 2.0 eq.) was added to a stirred, room temperature, solution of 1-hexene (0.13 mL, 1.0 mmol, 2.5 eq.) in CH_2Cl_2 (0.40 mL) under an argon atmosphere. After stirring for 40 min, the resulting clear yellow solution was transferred *via* syringe over about 1 min to the stirred solution containing the copper and ligand under an argon atmosphere. The resulting dark mixture was allowed to stir for an additional 10 min before 1,4-androstadiene-3,17-dione (114.0 mg, 0.40 mmol, 1.0 eq.) and TMSCl (0.26 mL, 2.00 mmol, 5.0 eq.) were added sequentially dropwise *via* syringe. Stirring at room temperature was continued arbitrarily for 15 h before the reaction was quenched by the addition of Et_2O (*ca* 3 mL) and NH_4Cl (1 M aq., *ca* 1.5 mL). The mixture was partitioned between the aqueous and Et_2O layers and the former phase was extracted with Et_2O (3 × 10 mL). The combined organic phase was washed with $NaHCO_3$ (sat. aq., *ca* 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give an oil. Diastereomeric ratio of the crude product (~3.5:1) was determined by integration of ^1H NMR spectra. Flash column chromatography of the yellow residue (5:30:65 EtOAc/DCM/petrol; SiO_2) gave first the major diastereomer (4α) (+)-1α-hexyl-4-androstene-3,17-dione (75 mg, 0.20 mmol, 50%) and then the minor diastereomer (4β) (+)-1β-hexyl-4-androstene-3,17-dione (24 mg, 0.064 mmol, 16%).

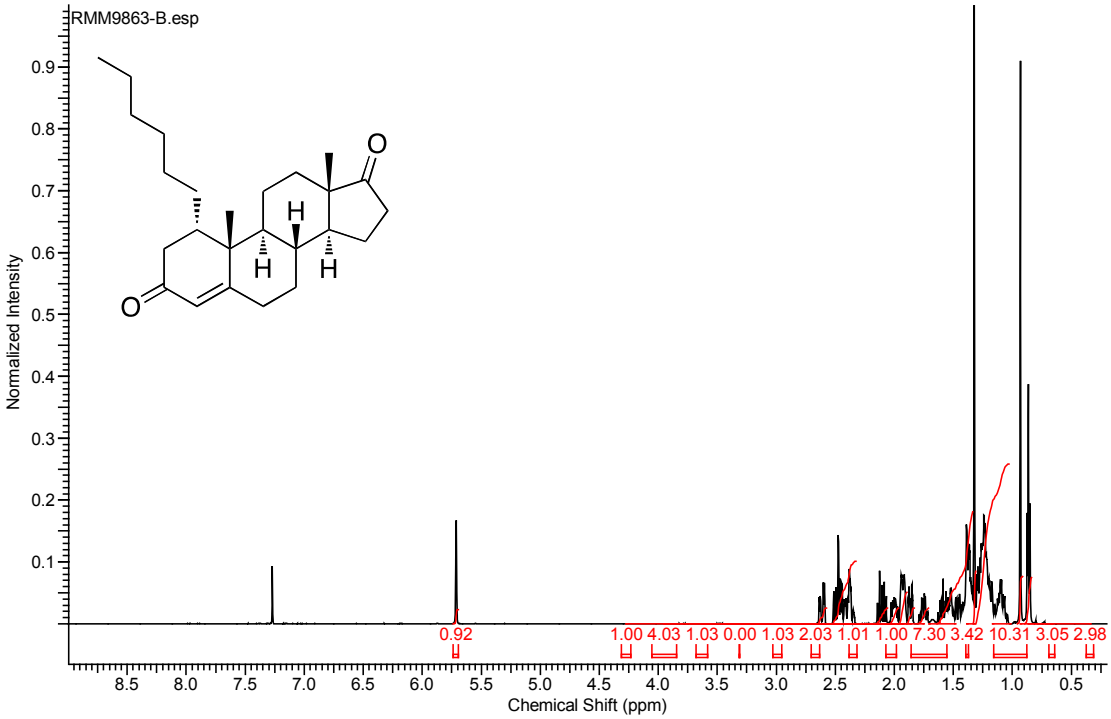
^1H NMR (500 MHz, $CDCl_3$) δ_H /ppm 0.86 (t, *J*=7.0 Hz, 3 H), 0.93 (s, 3 H), 1.03 - 1.31 (m, 10 H), 1.32 (s, 3 H), 1.33 - 1.64 (m, 7 H), 1.75 (qd, *J*=10.9, 3.3 Hz, 1 H), 1.86 (dt, *J*=12.9, 3.1 Hz, 1 H), 1.89 - 1.96 (m, 2 H), 1.96 - 2.04 (m, 1 H), 2.11 (dt, *J*=17.6, 9.0 Hz, 1 H), 2.33 - 2.53 (m, 4 H), 2.61 (dd, *J*=16.6, 4.5 Hz, 1 H), 5.71 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$) δ_C /ppm 13.7, 14.1, 19.5, 20.5, 21.7, 22.6, 27.1, 27.4, 29.4, 29.8, 31.2, 31.7, 32.7, 35.0, 35.7, 37.9, 41.7, 41.8, 46.3, 47.5, 51.0, 124.0, 167.8, 199.0, 220.5.

HRMS (ESI) *m/z* calcd for $C_{25}H_{38}NaO_2$ $[M+Na]^+$: 393.2764, found: 393.2748.

$[\alpha]^{20}_{589}$ = +140.9 (*c* 1.12, $CHCl_3$).

IR (ν_{max} /cm^{-1}): 1455, 1671, 1738, 2926.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Normalized Intensity
Chemical Shift (ppm)
0.92
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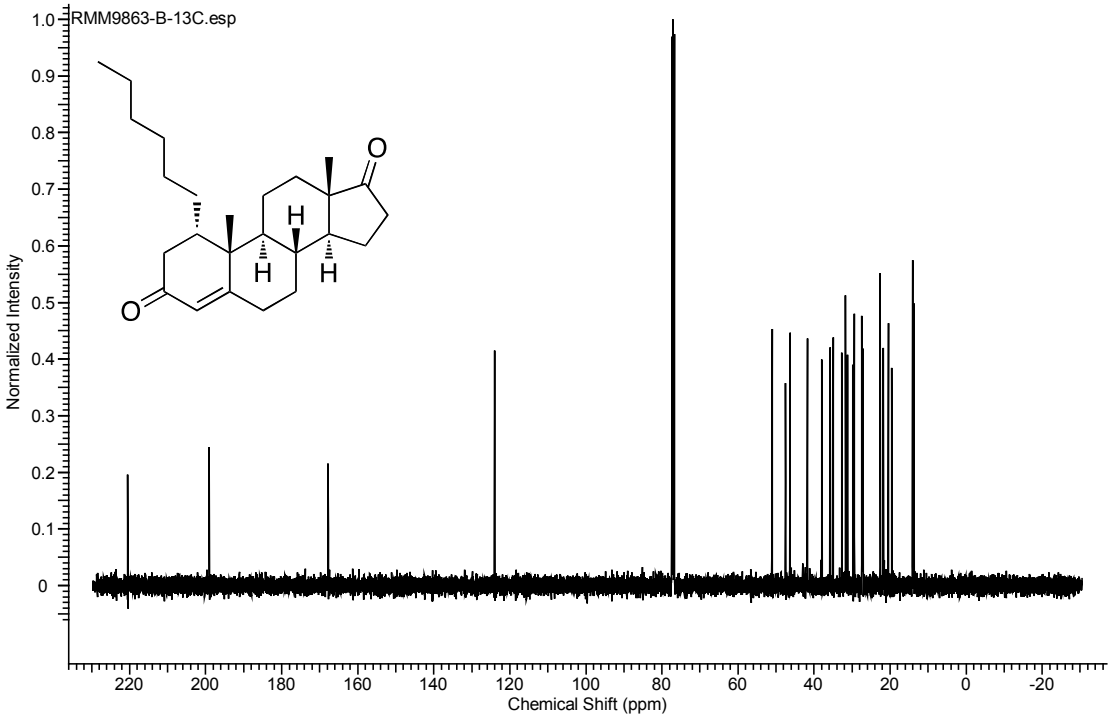
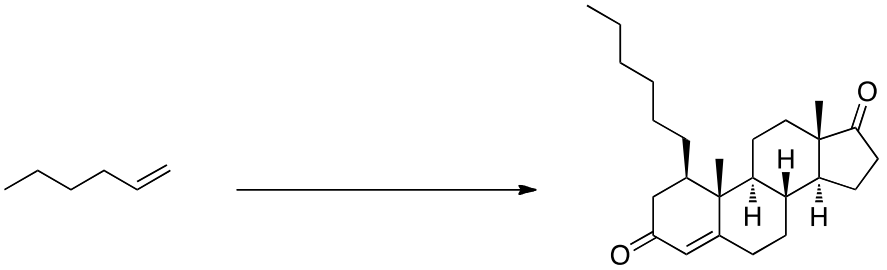
O
H
H
H
O


RMM9863-B-13C.esp
Normalized Intensity
Chemical Shift (ppm)
O
H
H
H
O

(+)-1β-hexyl-4-androstene-3,17-dione (4β)



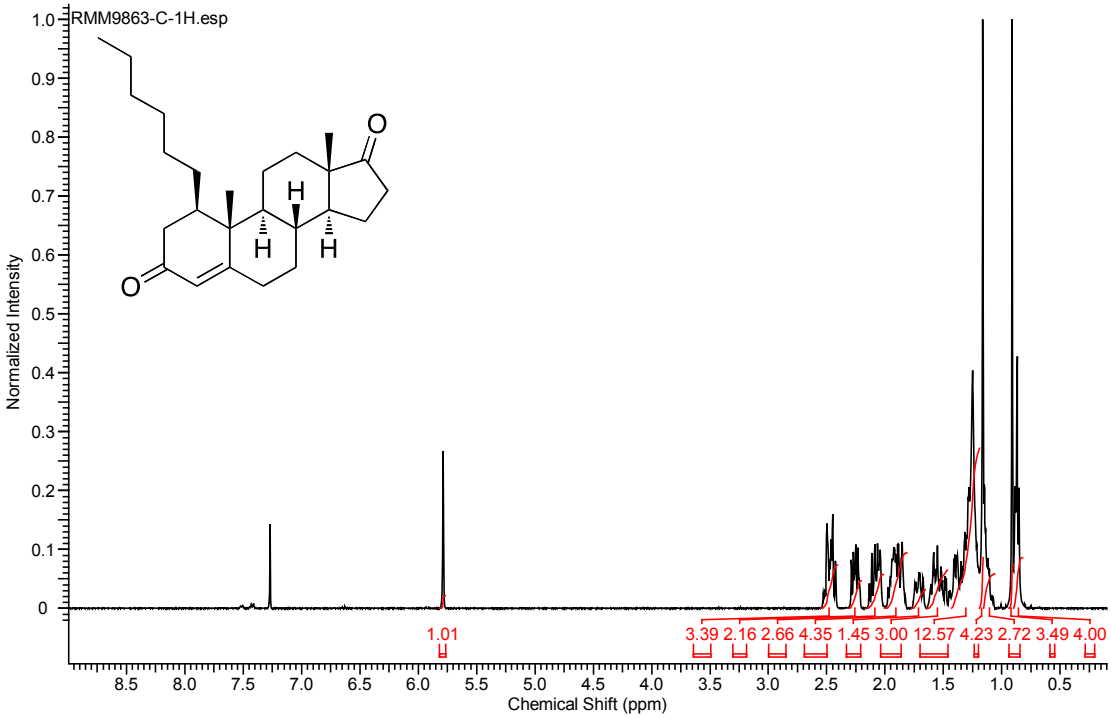
^{1}H NMR (400 MHz, $CDCl_3$) δ_H /ppm 0.87 (t, *J*=6.8 Hz, 3 H), 0.91 (s, 3 H), 1.06 - 1.15 (m, 2 H), 1.16 (s, 3 H), 1.19 - 1.43 (m, 11 H), 1.46 - 1.64 (m, 3 H), 1.65 - 1.77 (m, 1 H), 1.81 - 2.00 (m, 4 H), 2.01 - 2.16 (m, 2 H), 2.20 - 2.31 (m, 2 H), 2.40 - 2.55 (m, 3 H), 5.79 (br. s, 1 H).

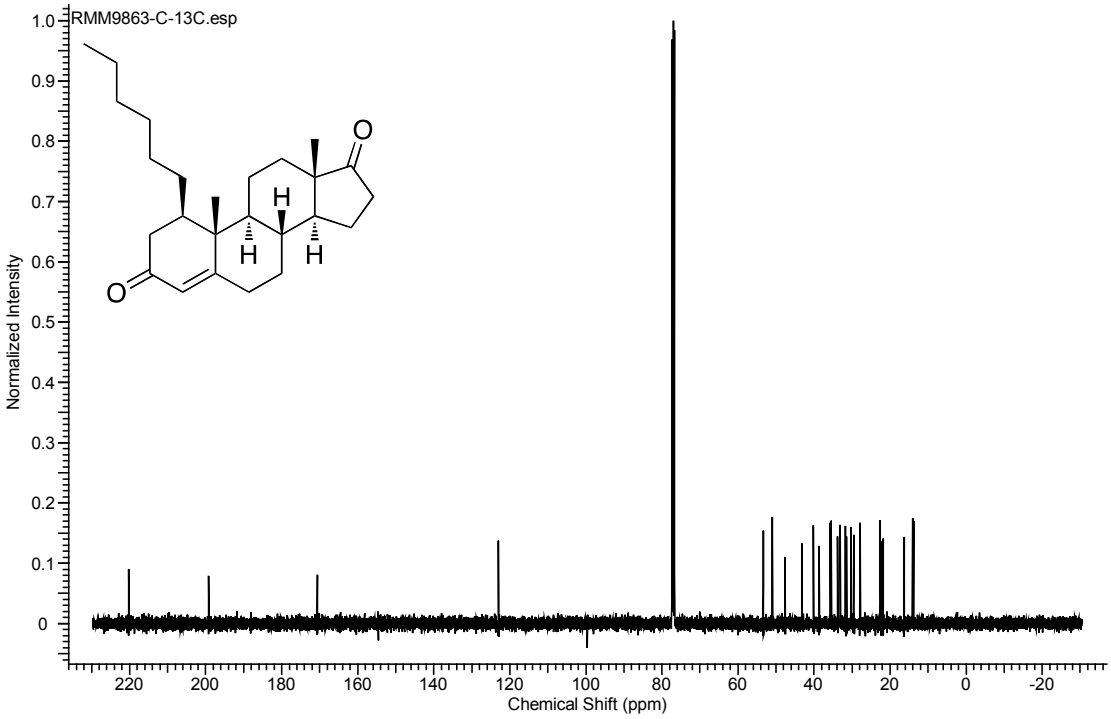
^{13}C NMR (100 MHz, $CDCl_3$) δ_C /ppm 13.8, 14.1, 16.3, 21.9, 22.3, 22.6, 27.8, 29.5, 30.1, 31.4, 31.7, 33.1, 33.8, 35.5, 35.7, 38.6, 40.1, 43.2, 47.6, 50.9, 53.4, 123.0, 170.7, 199.2, 220.3.

HRMS (ESI) *m*/*z* calcd for $C_{25}H_{38}NaO_2$ $[M+Na]^+$: 393.2764 found: 393.2753.

$[\alpha]^{20}_{589}$ = +14.7 (*c* 1.05, $CHCl_3$).

IR (ν_{max} /cm^{-1}): 1454, 1673, 1738, 2926.


RMM9863-C-1H.esp
Normalized Intensity
Chemical Shift (ppm)
1.01
3.39 2.16 2.66 4.35 1.45 3.00 12.57 4.23 2.72 3.49 4.00


RMM9863-C-13C.esp
Normalized Intensity
Chemical Shift (ppm)

(+)-1α-(5-Bromopentyl)-4-androstene-3,17-dione (5α)

Procedure B: Cp_2ZrHCl (206 mg, 0.80 mmol, 2.0 eq.) was added to a stirred, room temperature, solution of 5-bromo-1-pentene (0.12 mL, 1.0 mmol, 2.5 eq.) in CH_2Cl_2 (0.40 mL) under an argon atmosphere. After stirring for about 15 min, the resulting clear yellow solution was transferred *via* syringe over about 1 min to a clear colourless stirred solution of CuOTf-ligand complex (30.0 mg, 0.040 mmol, 0.10 eq.) in Et_2O (2.0 mL) under an argon atmosphere. The resulting dark mixture was allowed to stir for an additional 10 min before 1,4-androstadiene-3,17-dione (114.0 mg, 0.40 mmol, 1.0 eq.) and TMSCl (0.26 mL, 2.00 mmol, 5.0 eq.) were added sequentially dropwise *via* syringe. Stirring at room temperature was continued arbitrarily for 15 h before the reaction was quenched by the addition of Et_2O (*ca* 3 mL) and NH_4Cl (1 M aq., *ca* 1.5 mL). The mixture was partitioned between the aqueous and Et_2O layers and the former phase was extracted with Et_2O (3 × 10 mL). The combined organic phase was washed with $NaHCO_3$ (sat. aq., *ca* 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give an oil. Diastereomeric ratio of the crude product (~4.8:1) was determined by integration of ^{1}H NMR spectra. Flash column chromatography of the yellow residue (10:30:60 EtOAc/DCM/petrol; SiO_2) gave first the major diastereomer (5α) (+)-1α-(5-bromopentyl)-4-androstene-3,17-dione (107 mg, 0.24 mmol, 60%) and then the minor diastereomer (5β) (+)-1β-(5-bromopentyl)-4-androstene-3,17-dione (14 mg, 0.032 mmol, 8%).

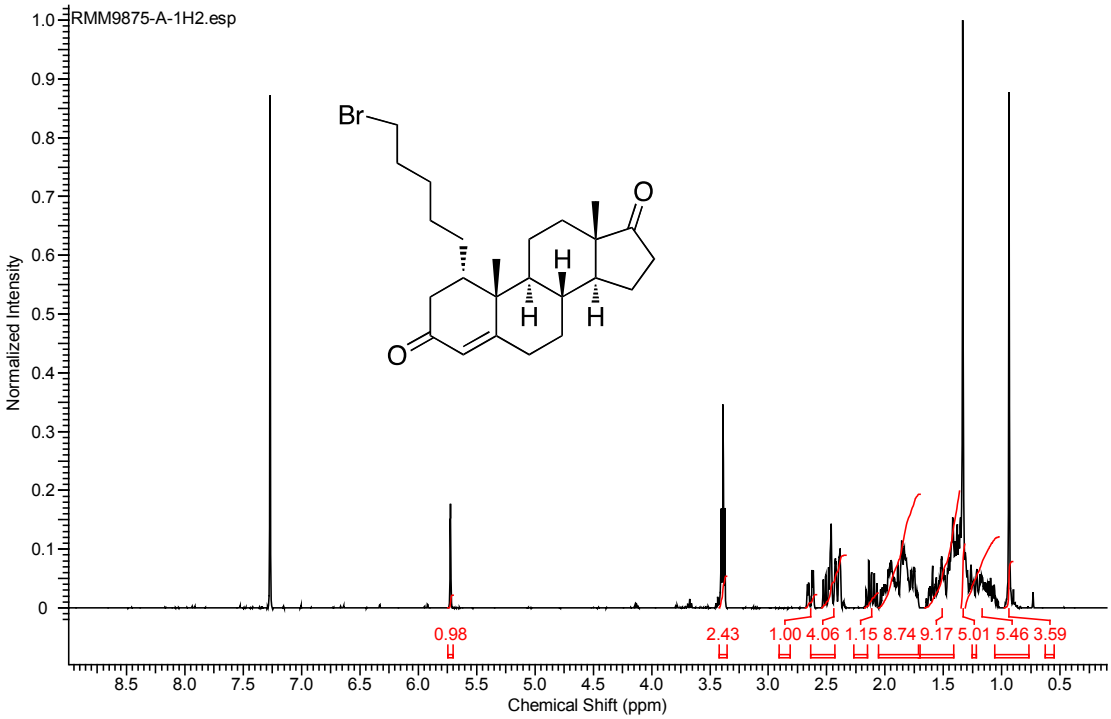
^{1}H NMR (400 MHz, $CDCl_3$) δ_H /ppm 0.92 (s, 3 H), 1.01 - 1.28 (m, 4 H), 1.31 (s, 3 H), 1.36 - 1.66 (m, 9 H), 1.69 - 2.04 (m, 7 H), 2.11 (dt, *J*=19.2, 9.0 Hz, 1 H), 2.32 - 2.54 (m, 4 H), 2.63 (dd, *J*=16.5, 4.4 Hz, 1 H), 3.38 (t, *J*=6.7 Hz, 2 H), 5.71 (br. s, 1 H).

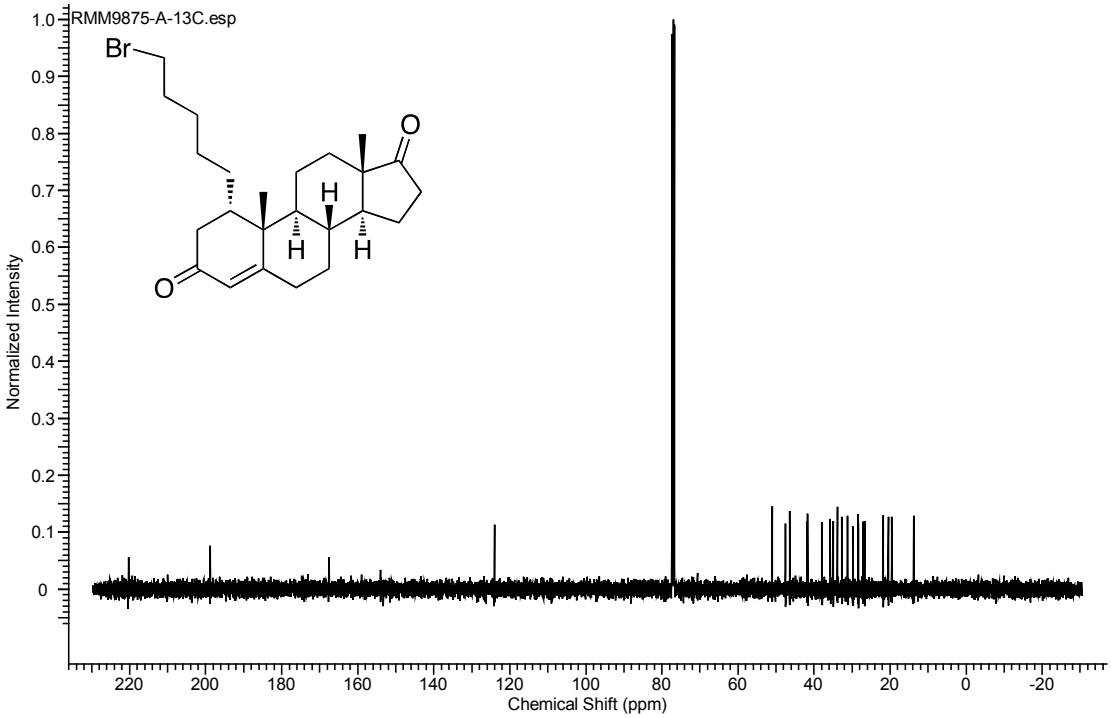
^{13}C NMR (100 MHz, $CDCl_3$) δ_C /ppm 13.7, 19.6, 20.5, 21.8, 26.6, 27.1, 28.4, 29.8, 31.2, 32.6, 32.7, 33.8, 35.0, 35.7, 37.9, 41.7, 41.8, 46.3, 47.5, 51.0, 124.0, 167.6, 198.8, 220.3.

HRMS (ESI) *m/z* calcd for $C_{24}H_{35}BrNaO_2$ $[M+Na]^+$: 457.1713 found: 457.1705.

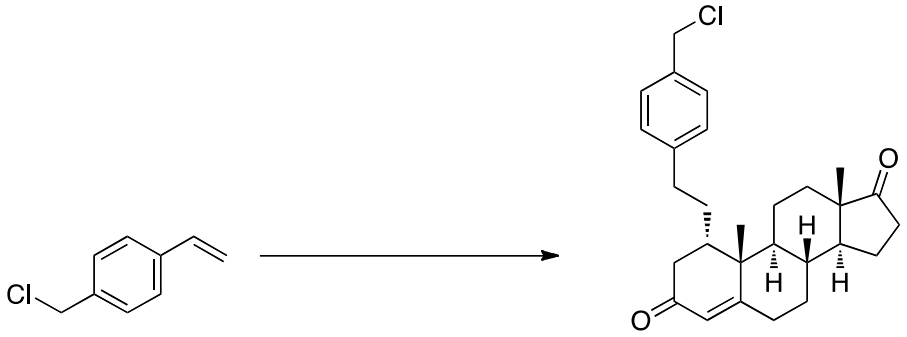
$[\alpha]^{20}_{589}$ = +122.4 (*c* 1.055, $CHCl_3$).

IR (ν_{max} /cm^{-1}): 703, 1051, 1669, 1737, 2934.


RMM9875-A-1H2.esp
Br
O
H
H
H
O
Normalized Intensity
0.98
2.43
1.00 4.06 1.15 8.74 9.17 5.01 5.46 3.59
Chemical Shift (ppm)


RMM9875-A-13C.esp
Br
O
H
H
H
O
Normalized Intensity
Chemical Shift (ppm)

(+)-1α-(4-(Chloromethyl)phenethyl)-4-androstene-3,17-dione (6α)



Procedure B: Cp_2ZrHCl (206 mg, 0.80 mmol, 2.0 eq.) was added to a stirred, room temperature, solution of 4-vinylbenzyl chloride (0.14 mL, 1.0 mmol, 2.5 eq.) in CH_2Cl_2 (0.40 mL) under an argon atmosphere. After stirring for about 15 min, the resulting clear yellow solution was transferred *via* syringe over about 1 min to a clear colourless stirred solution of CuOTf-ligand complex (30.0 mg, 0.040 mmol, 0.10 eq.) in Et_2O (2.0 mL) under an argon atmosphere. The resulting dark mixture was allowed to stir for an additional 10 min before 1,4-androstadiene-3,17-dione (114.0 mg, 0.40 mmol, 1.0 eq.) and TMSCl (0.26 mL, 2.00 mmol, 5.0 eq.) were added sequentially dropwise *via* syringe. Stirring at room temperature was continued arbitrarily for 15 h before the reaction was quenched by the addition of Et_2O (*ca* 3 mL) and NH_4Cl (1 M aq., *ca* 1.5 mL). The mixture was partitioned between the aqueous and Et_2O layers and the former phase was extracted with Et_2O (3 × 10 mL). The combined organic phase was washed with $NaHCO_3$ (sat. aq., *ca* 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give an oil. Flash column chromatography of the yellow residue (5:35:60 → 10:30:60 EtOAc/DCM/petrol; SiO_2) gave major diastereomer (6α) (+)-1α-(4-(chloromethyl)phenethyl))-4-androstene-3,17-dione (54 mg, 0.12 mmol, 30%), minor diastereomer (+)-1β-(4-(chloromethyl)phenethyl))-4-androstene-3,17-dione was not seen.

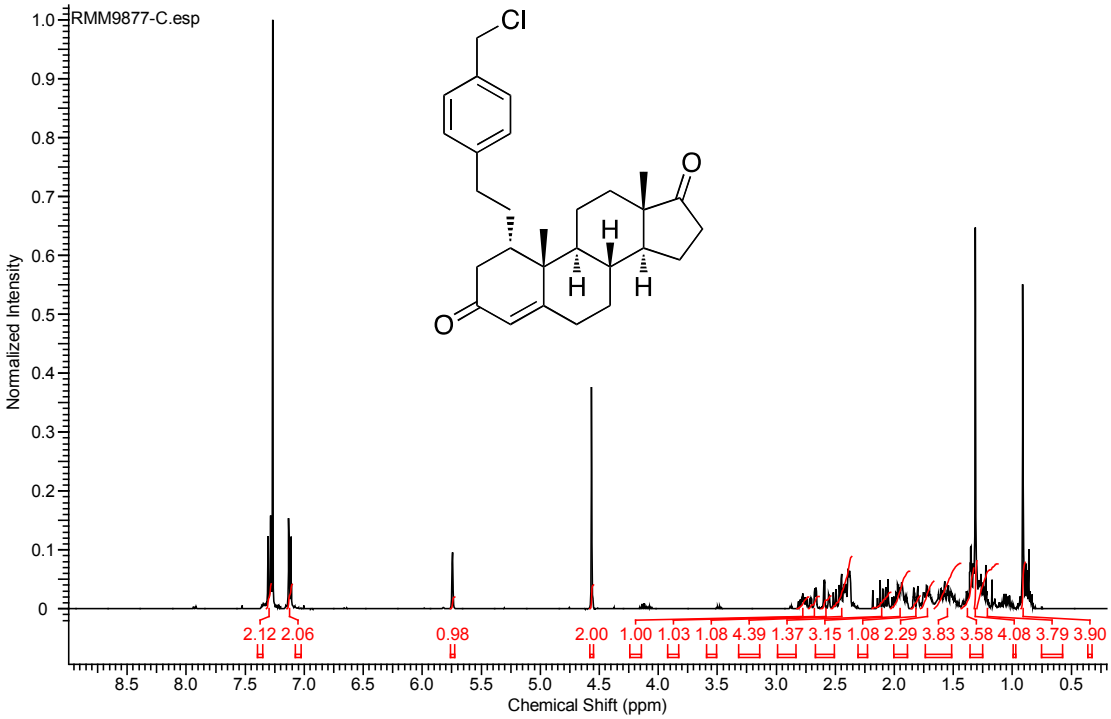
^{1}H NMR (400 MHz, $CDCl_3$) δ_H /ppm 0.90 (s, 3 H), 0.98 - 1.28 (m, 3 H), 1.29 (s, 3 H), 1.33 - 1.43 (m, 3 H), 1.43 - 1.64 (m, 2 H), 1.64 - 1.77 (m, 2 H), 1.81 (dt, *J*=12.9, 3.1 Hz, 1 H), 1.86 - 2.03 (m, 3 H), 2.09 (dt, *J*=19.2, 9.0 Hz, 1 H), 2.32 - 2.52 (m, 4 H), 2.57 (dd, *J*=16.6, 1.6 Hz, 1 H), 2.68 (dd, *J*=16.6, 3.3 Hz, 1 H), 2.73 - 2.82 (m, 1 H), 4.56 (br. s, 2 H), 5.74 (br. s, 1 H), 7.12 (d, *J*=8.2 Hz, 2 H), 7.29 (d, *J*=8.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$) δ_C /ppm 13.7, 19.4, 20.4, 21.7, 29.4, 29.8, 31.1, 32.6, 33.2, 35.0, 35.7, 37.9, 41.1, 41.8, 46.1, 46.4, 47.5, 51.0, 124.0, 128.7 (2 C), 128.8 (2 C), 135.2, 142.2, 167.6, 198.5, 220.2.

HRMS (ESI) *m/z* calcd for $C_{28}H_{35}ClNaO_2$ $[M+Na]^+$: 461.2218 found: 461.2204.

$[\alpha]^{20}_{589}$ = +125.0 (*c* 0.28, $CHCl_3$).

IR (ν_{max} /cm^{-1}): 730, 1667, 1737, 2934.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Cl
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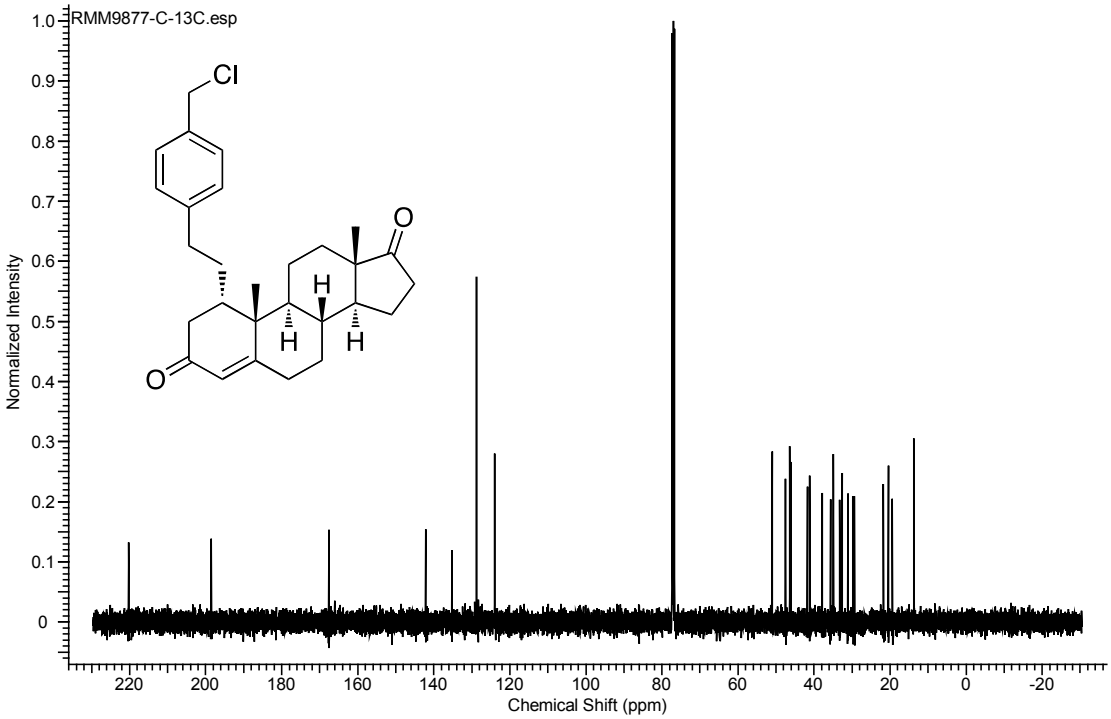
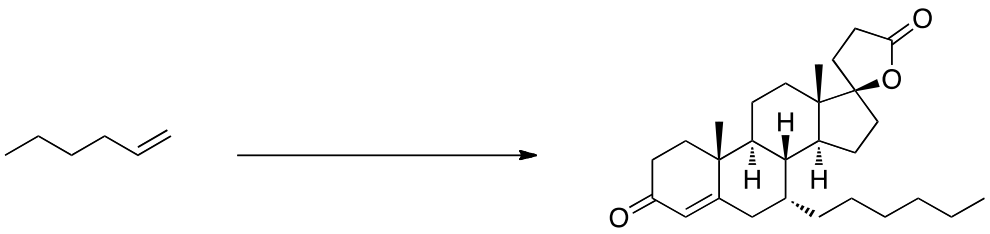
H
H
H
O
Normalized Intensity
2.12 2.06
0.98
2.00
1.00 1.03 1.08 4.39 1.37 3.15 1.08 2.29 3.83 3.58 4.08 3.79 3.90
Chemical Shift (ppm)


RMM9877-C-13C.esp
Cl
O
H
H
H
O
Normalized Intensity
Chemical Shift (ppm)

(+)-7α-Hexyl-17α-hydroxy-3-oxo-pregn-4-ene-21-carboxylic acid γ-lactone (7α)



Procedure A: $(CuOTf)_2.(C_6H_6)$ (10.1 mg, 0.02 mmol, 0.05 eq.) and the (*S,S,S*)-phosphoramidite ligand (21.6 mg, 0.040 mmol, 0.10 eq.) were dissolved in Et_2O (2.0 mL) under an argon atmosphere and allowed to stir for 1 h at room temperature. In another flask, Cp_2ZrHCl (206.0 mg, 0.80 mmol, 2.0 eq.) was added to a stirred, room temperature, solution of 1-hexene (0.13 mL, 1.0 mmol, 2.5 eq.) in CH_2Cl_2 (0.40 mL) under an argon atmosphere. After stirring for 40 min, the resulting clear yellow solution was transferred *via* syringe over about 1 min to the stirred solution containing the copper and ligand under an argon atmosphere. The resulting dark mixture was allowed to stir for an additional 10 min before canrenone (136.0 mg, 0.40 mmol, 1.0 eq.) and TMSCl (0.26 mL, 2.00 mmol, 5.0 eq.) were added sequentially dropwise *via* syringe. Stirring at room temperature was continued arbitrarily for 15 h before the reaction was quenched by the addition of Et_2O (*ca* 3 mL) and NH_4Cl (1 M aq., *ca* 1.5 mL). The mixture was partitioned between the aqueous and Et_2O layers and the former phase was extracted with Et_2O (3 × 10 mL). The combined organic phase was washed with $NaHCO_3$ (sat. aq., *ca* 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give an oil. Diastereomeric ratio of the crude product (~4.8:1) was determined by integration of ^1H NMR spectra. Flash column chromatography of the yellow residue (30:70 EtOAc/petrol; SiO_2) gave first the major diastereomer (7α) (+)-7α-hexyl-17α-hydroxy-3-oxo-pregn-4-ene-21-carboxylic acid γ-lactone (101 mg, 0.24 mmol, 59%) and then the minor diastereomer (7β) (+)-1β-hexyl-4-androstene-3,17-dione (35 mg, 0.082 mmol, 21%).

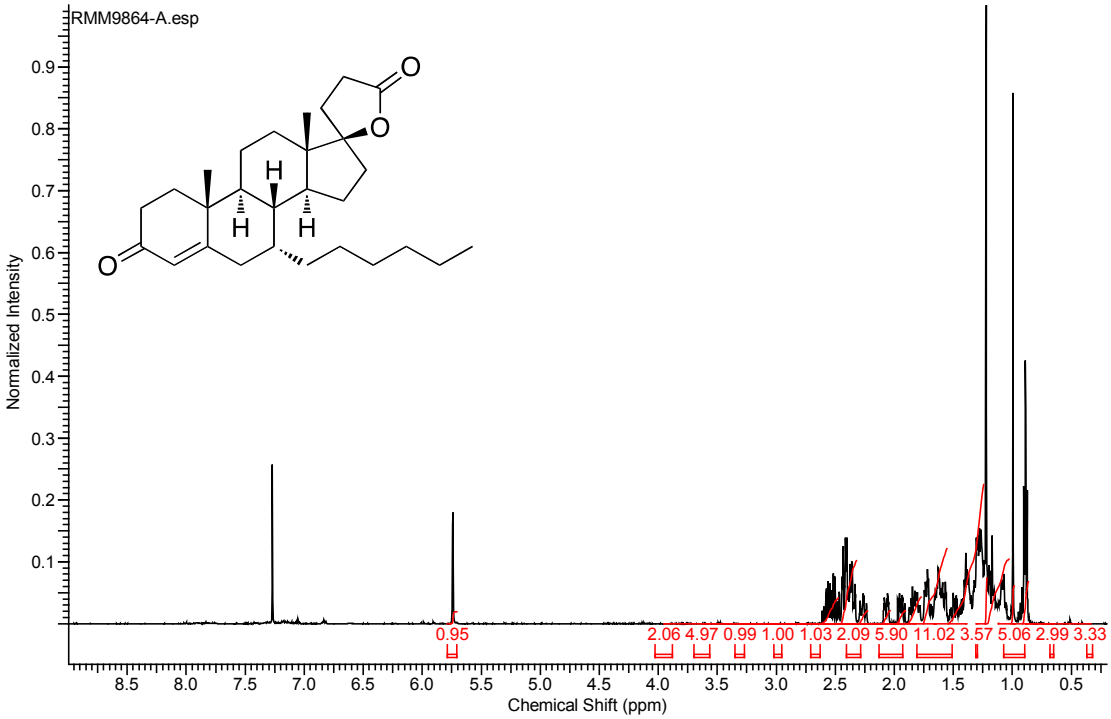
^1H NMR (500 MHz, $CDCl_3$) δ_H /ppm 0.89 (t, *J*=7.1 Hz, 3 H), 0.99 (s, 3 H), 1.04 - 1.20 (m, 5 H), 1.22 (s, 3 H), 1.24 - 1.53 (m, 11 H), 1.55 - 1.76 (m, 5 H), 1.77 - 1.89 (m, 2 H), 1.90 - 1.98 (m, 1 H), 2.03 - 2.10 (m, 1 H), 2.22 - 2.31 (m, 1 H), 2.32 - 2.45 (m, 4 H), 2.47 - 2.62 (m, 2 H), 5.74 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$) δ_C /ppm 14.1, 14.4, 18.1, 20.7, 22.4, 22.6, 25.2, 27.3, 29.3, 29.5, 31.2, 31.5, 31.9, 34.0, 35.3, 36.0, 36.1, 36.6, 38.6, 39.3, 44.8, 45.6, 46.9, 95.8, 125.9, 169.5, 176.7, 199.1.

HRMS (ESI) *m/z* calcd for $C_{28}H_{42}NaO_3$ $[M+Na]^+$: 449.3026 found: 449.3017.

$[\alpha]^{20}_{589}$ = +37.3 (*c* 1.00, $CHCl_3$).

IR (ν_{max} /cm^{-1}): 1192, 1669, 1769, 2927.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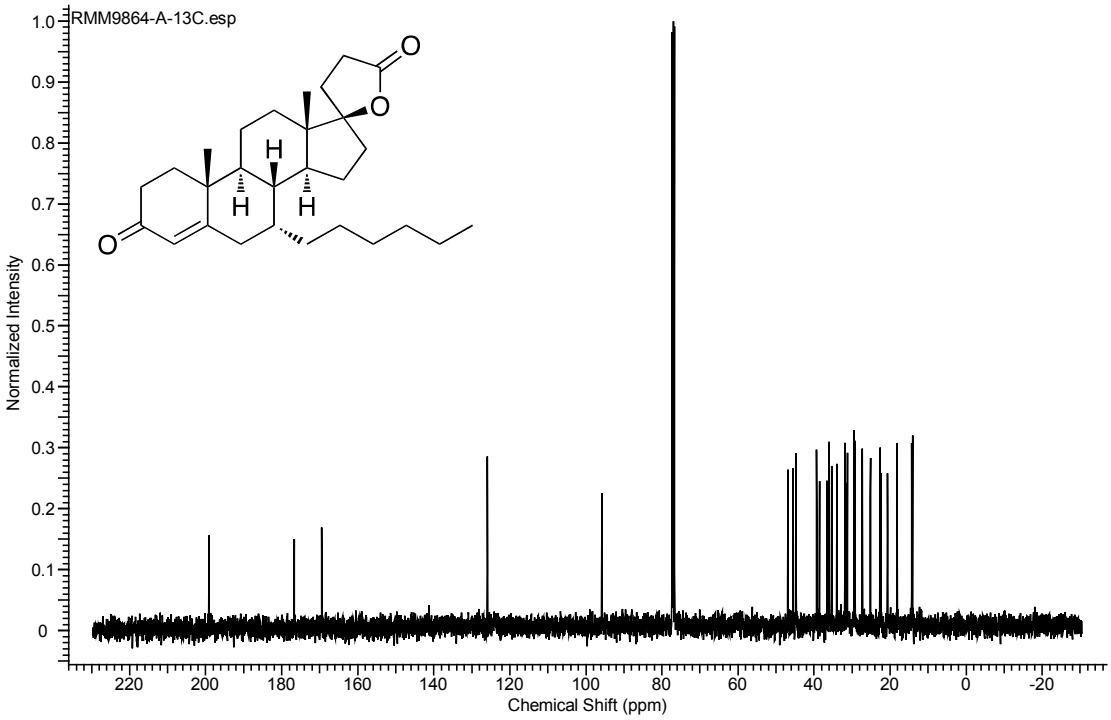
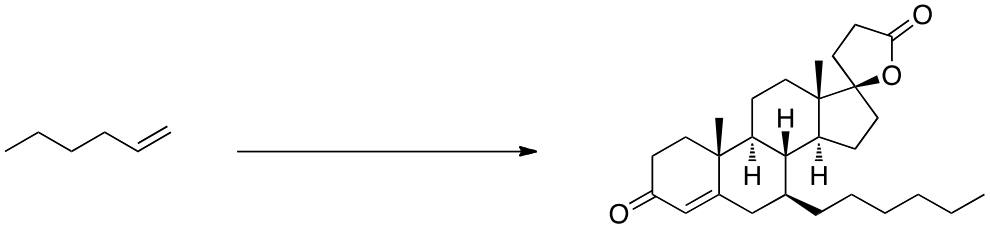
Normalized Intensity
Chemical Shift (ppm)
0.95
2.06 4.97 0.99 1.00 1.03 2.09 5.90 11.02 3.57 5.06 2.99 3.33


RMM9864-A-13C.esp
Normalized Intensity
Chemical Shift (ppm)

(+)-7β-Hexyl-17α-hydroxy-3-oxo-pregn-4-ene-21-carboxylic acid γ-lactone (7β)



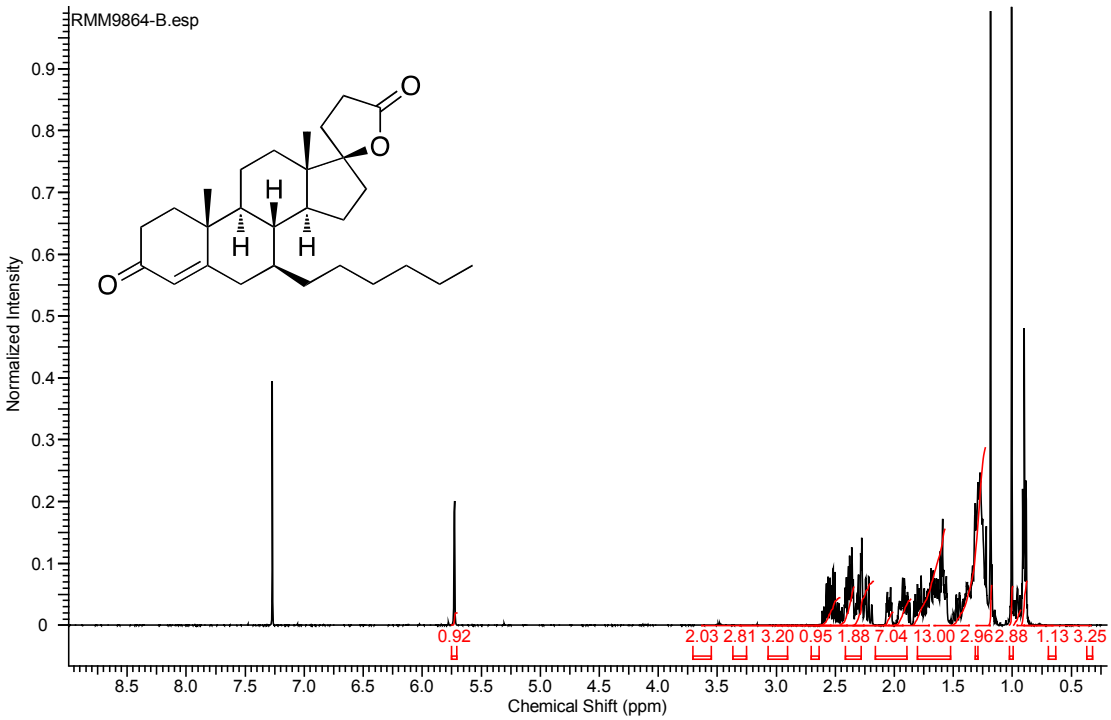
^{1}H NMR (500 MHz, $CDCl_3$) δ_H /ppm 0.90 (t, *J*=6.9 Hz, 3 H), 0.92 - 0.99 (m, 1 H), 1.01 (s, 3 H), 1.18 (s, 3 H), 1.23 - 1.51 (m, 13 H), 1.57 - 1.84 (m, 7 H), 1.86 - 2.00 (m, 2 H), 2.05 (dt, *J*=13.3, 4.3 Hz, 1 H), 2.18 - 2.34 (m, 3 H), 2.34 - 2.46 (m, 3 H), 2.46 - 2.62 (m, 2 H), 5.73 (br. s, 1 H).

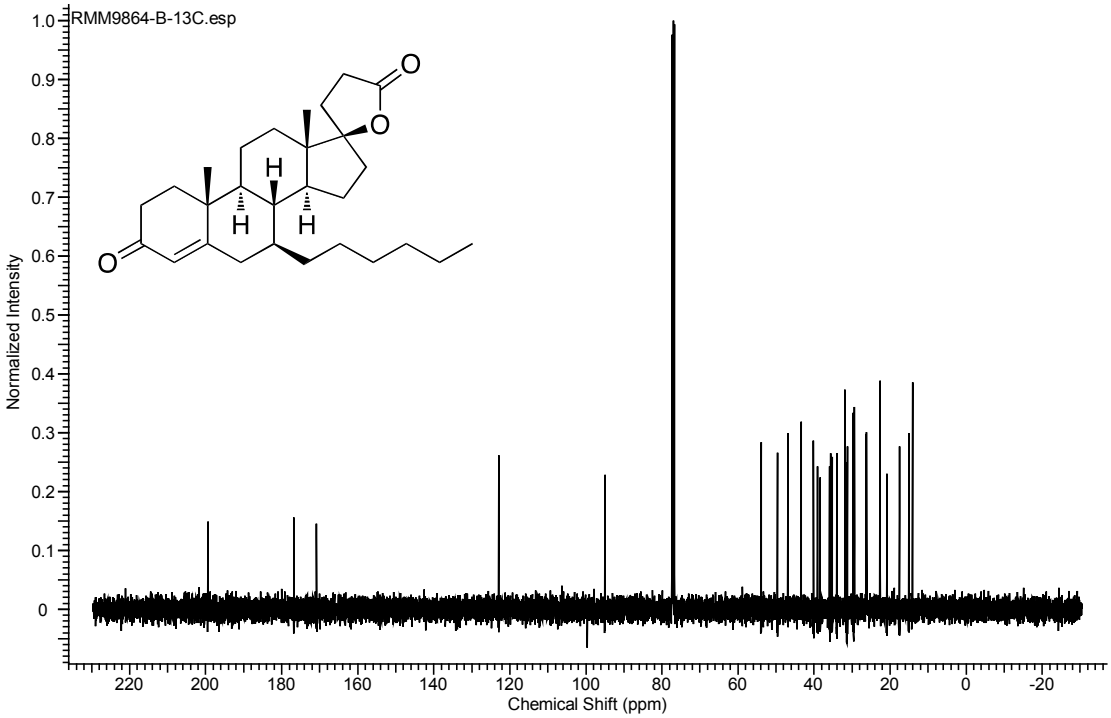
^{13}C NMR (100 MHz, $CDCl_3$) δ_C /ppm 14.1, 15.1, 17.5, 20.8, 22.7, 26.2, 26.3, 29.4, 29.7, 31.2, 31.5, 31.8, 34.0, 35.2, 35.7, 35.9, 38.4, 39.1, 40.1, 43.4, 46.9, 49.6, 53.9, 95.0, 122.9, 170.8, 176.8, 199.4.

HRMS (ESI) *m*/*z* calcd for $C_{28}H_{42}NaO_3$ $[M+Na]^+$: 449.3026 found: 449.3009.

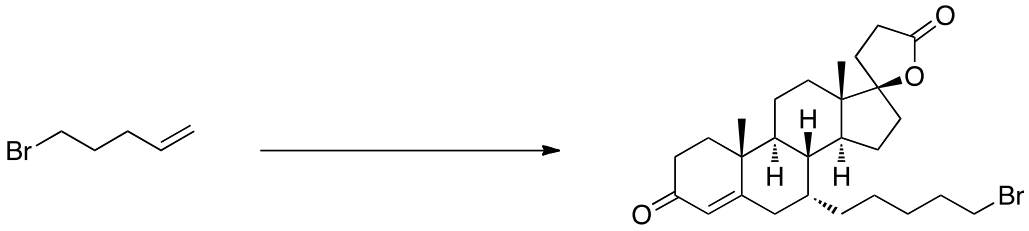
$[\alpha]^{20}_{589}$ = +34.6 (*c* 0.55, $CHCl_3$).

IR (ν_{max} /cm^{-1}): 1174, 1675, 1770, 2925.


RMM9864-B.esp
Normalized Intensity
Chemical Shift (ppm)
0.92
2.03 2.81 3.20 0.95 1.88 7.04 13.00 2.96 2.88 1.13 3.25


RMM9864-B-13C.esp
Normalized Intensity
Chemical Shift (ppm)

(+)-7α-(5-Bromopentyl)-17α-hydroxy-3-oxo-pregn-4-ene-21-carboxylic acid γ-lactone (8α)



Procedure B: Cp_2ZrHCl (206 mg, 0.80 mmol, 2.0 eq.) was added to a stirred, room temperature, solution of 5-bromo-1-pentene (0.12 mL, 1.0 mmol, 2.5 eq.) in CH_2Cl_2 (0.40 mL) under an argon atmosphere. After stirring for about 15 min, the resulting clear yellow solution was transferred *via* syringe over about 1 min to a clear colourless stirred solution of CuOTf-ligand complex (30.0 mg, 0.040 mmol, 0.10 eq.) in Et_2O (2.0 mL) under an argon atmosphere. The resulting dark mixture was allowed to stir for an additional 10 min before canrenone (136.0 mg, 0.40 mmol, 1.0 eq.) and TMSCl (0.26 mL, 2.00 mmol, 5.0 eq.) were added sequentially dropwise *via* syringe. Stirring at room temperature was continued arbitrarily for 15 h before the reaction was quenched by the addition of Et_2O (*ca* 3 mL) and NH_4Cl (1 M aq., *ca* 1.5 mL). The mixture was partitioned between the aqueous and Et_2O layers and the former phase was extracted with Et_2O (3 × 10 mL). The combined organic phase was washed with $NaHCO_3$ (sat. aq., *ca* 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give an oil. Flash column chromatography of the yellow residue (30:70 EtOAc/petrol; SiO_2) gave first the major diastereomer (8α) (+)-7α-(5-bromopentyl)-17α-hydroxy-3-oxo-pregn-4-ene-21-carboxylic acid γ-lactone (64 mg, 0.13 mmol, 33%) and then the minor diastereomer (8β) (+)-1β-(5-bromopentyl)-4-androstene-3,17-dione (14 mg, 0.028 mmol, 7%).

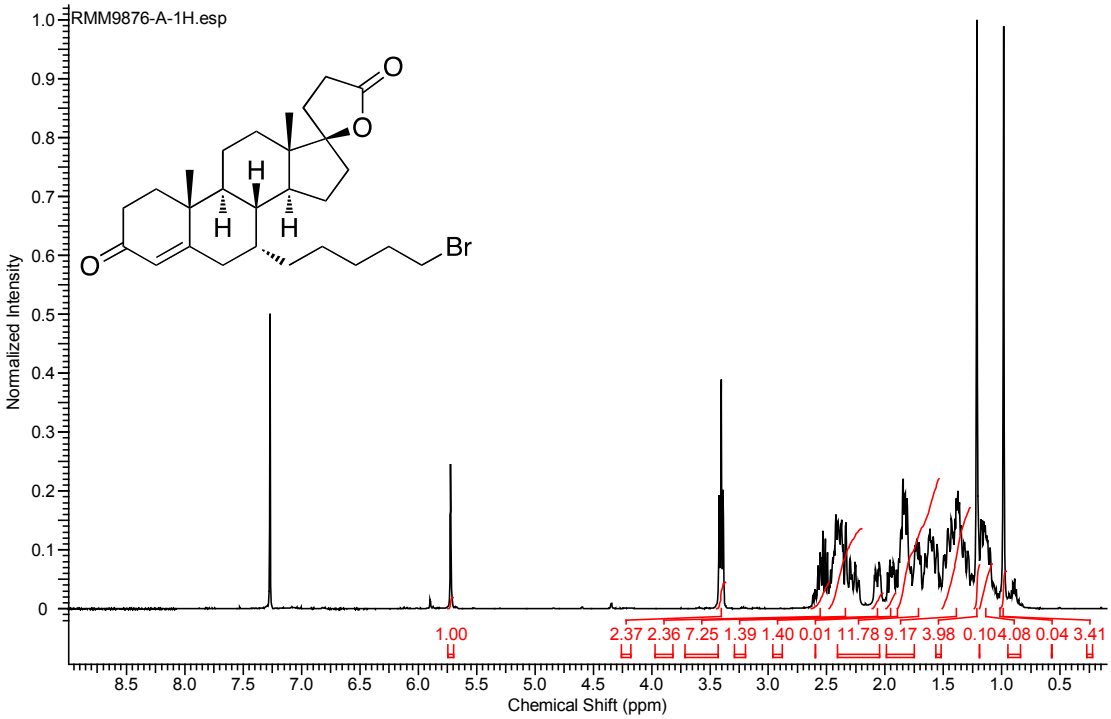
^{1}H NMR (400 MHz, $CDCl_3$) δ_H /ppm 0.98 (s, 3 H), 1.08 - 1.19 (m, 3 H), 1.21 (s, 3 H), 1.27 - 1.52 (m, 7 H), 1.53 - 1.89 (m, 10 H), 1.91 - 2.00 (m, 1 H), 2.02 - 2.11 (m, 1 H), 2.20 - 2.48 (m, 6 H), 2.48 - 2.63 (m, 2 H), 3.40 (t, *J*=6.7 Hz, 2 H), 5.72 (br. s, 1 H).

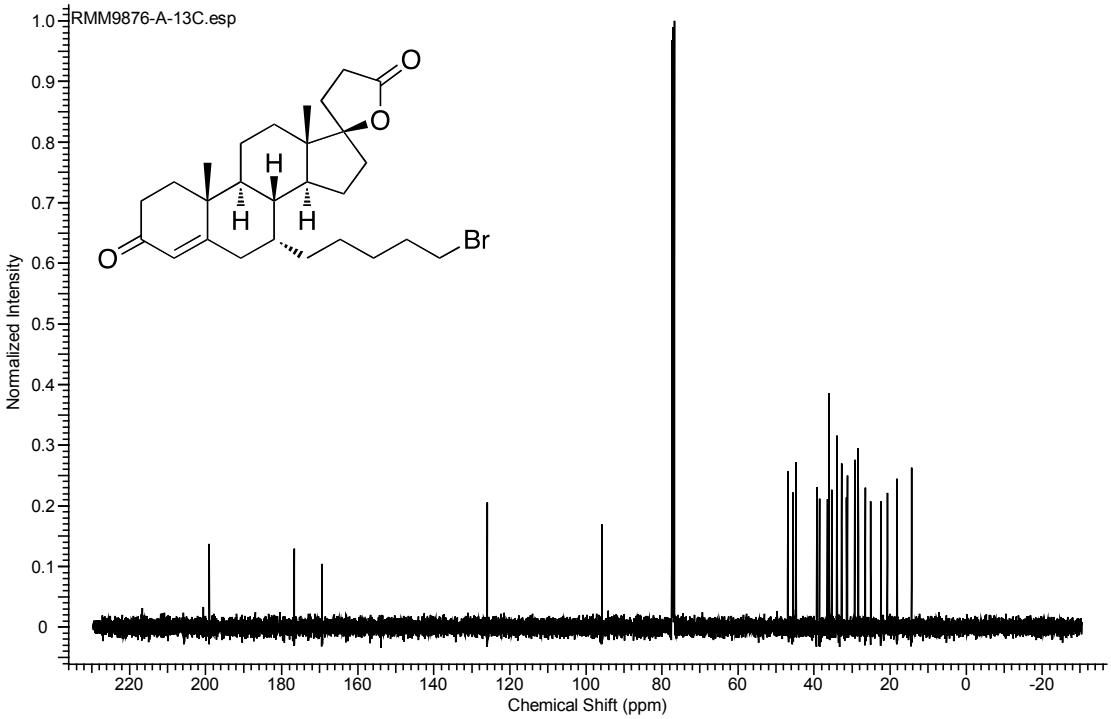
^{13}C NMR (100 MHz, $CDCl_3$) δ_C /ppm 14.4, 18.1, 20.7, 22.4, 25.1, 26.5, 28.4, 29.3, 31.2, 31.5, 32.7, 33.95, 33.99, 35.3, 36.0 (2 C), 36.5, 38.6, 39.3, 44.8, 45.6, 46.9, 95.8, 125.9, 169.3, 176.7, 199.1.

HRMS (ESI) *m/z* calcd for $C_{27}H_{39}BrNaO_3$ $[M+Na]^+$: 513.1975 found: 513.1961.

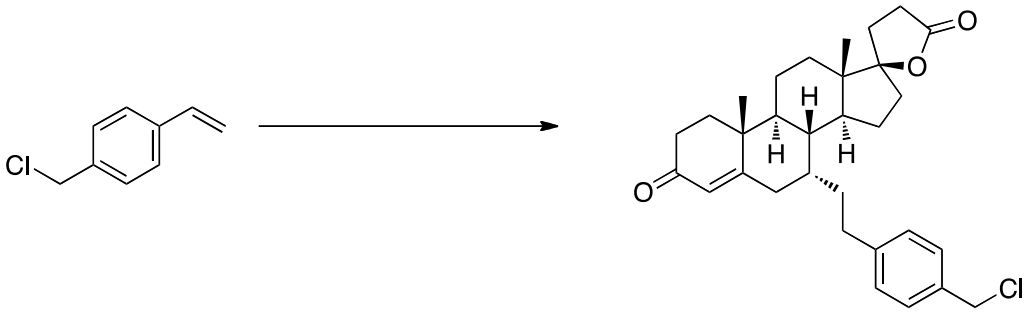
$[\alpha]^{20}_{589}$ = +32.1 (*c* 0.80, $CHCl_3$).

IR (ν_{max} /cm^{-1}): 728, 913, 1663, 1767, 2939.


RMM9876-A-1H.esp
Normalized Intensity
Chemical Shift (ppm)
1.00
2.37 2.36 7.25 1.39 1.40 0.01 11.78 9.17 3.98 0.10 4.08 0.04 3.41
O
O
H
H
H
O
Br


RMM9876-A-13C.esp
Normalized Intensity
Chemical Shift (ppm)
O
O
H
H
H
O
Br

(+)-7α-(4-(Chloromethyl)phenethyl)-17α-hydroxy-3-oxo-pregn-4-ene-21-carboxylic acid γ-lactone (9α)



Procedure B: Cp_2ZrHCl (206 mg, 0.80 mmol, 2.0 eq.) was added to a stirred, room temperature, solution of 4-vinylbenzyl chloride (0.14 mL, 1.0 mmol, 2.5 eq.) in CH_2Cl_2 (0.40 mL) under an argon atmosphere. After stirring for about 15 min, the resulting clear yellow solution was transferred *via* syringe over about 1 min to a clear colourless stirred solution of CuOTf-ligand complex (30.0 mg, 0.040 mmol, 0.10 eq.) in Et_2O (2.0 mL) under an argon atmosphere. The resulting dark mixture was allowed to stir for an additional 10 min before canrenone (136.0 mg, 0.40 mmol, 1.0 eq.) and TMSCl (0.26 mL, 2.00 mmol, 5.0 eq.) were added sequentially dropwise *via* syringe. Stirring at room temperature was continued arbitrarily for 15 h before the reaction was quenched by the addition of Et_2O (*ca* 3 mL) and NH_4Cl (1 M aq., *ca* 1.5 mL). The mixture was partitioned between the aqueous and Et_2O layers and the former phase was extracted with Et_2O (3 × 10 mL). The combined organic phase was washed with $NaHCO_3$ (sat. aq., *ca* 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give an oil. Flash column chromatography of the yellow residue (35:65 EtOAc/petrol; SiO_2) gave major diastereomer (9α) (+)-7α-(4-(chloromethyl)phenethyl)-17α-hydroxy-3-oxo-pregn-4-ene-21-carboxylic acid γ-lactone (68 mg, 0.14 mmol, 35%), minor diastereomer (+)-7β-(4-(chloromethyl)phenethyl)-17α-hydroxy-3-oxo-pregn-4-ene-21-carboxylic acid γ-lactone was not seen.

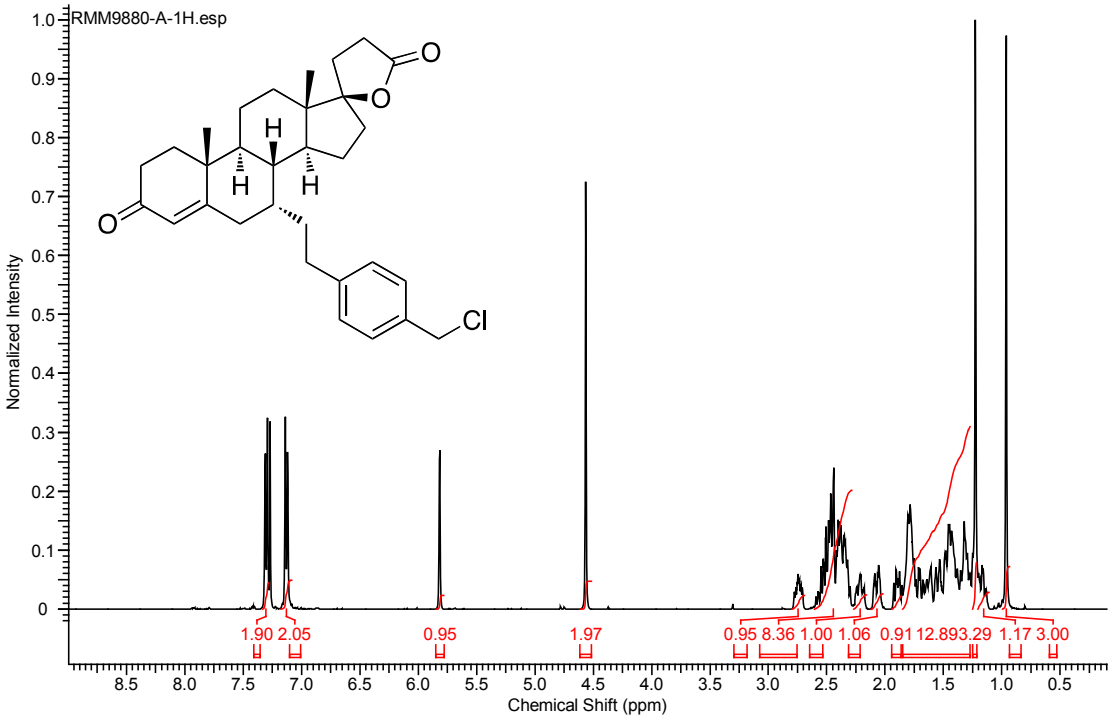
^{1}H NMR (400 MHz, $CDCl_3$) δ_H /ppm 0.97 (s, 3 H), 1.10 - 1.21 (m, 1 H), 1.24 (br. s., 3 H), 1.27 - 1.85 (m, 13 H), 1.86 - 1.94 (m, 1 H), 2.01 - 2.12 (m, 1 H), 2.16 - 2.27 (m, 1 H), 2.28 - 2.60 (m, 8 H), 2.69 - 2.79 (m, 1 H), 4.56 (s, 2 H), 5.82 (br. s, 1 H), 7.13 (d, *J*=8.1 Hz, 2 H), 7.30 (d, *J*=8.1 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$) δ_C /ppm 14.3, 18.2, 20.7, 22.2, 27.7, 29.2, 31.2, 31.4, 33.3, 34.0, 35.3, 35.7, 36.0, 36.4, 38.6, 39.3, 44.7, 45.6, 46.1, 47.0, 95.7, 126.0, 128.77 (2 C), 128.81 (2 C), 135.3, 142.5, 169.1, 176.7, 199.0.

HRMS (ESI) *m/z* calcd for $C_{31}H_{39}ClNaO_3$ $[M+Na]^+$: 517.2480 found: 517.2463.

$[\alpha]^{20}_{589}$ = +64.0 (*c* 0.88, $CHCl_3$).

IR (ν_{max} /cm^{-1}): 727, 1663, 1765, 2945.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1.97
0.95 8.36 1.00 1.06 0.91 12.89 3.29 1.17 3.00
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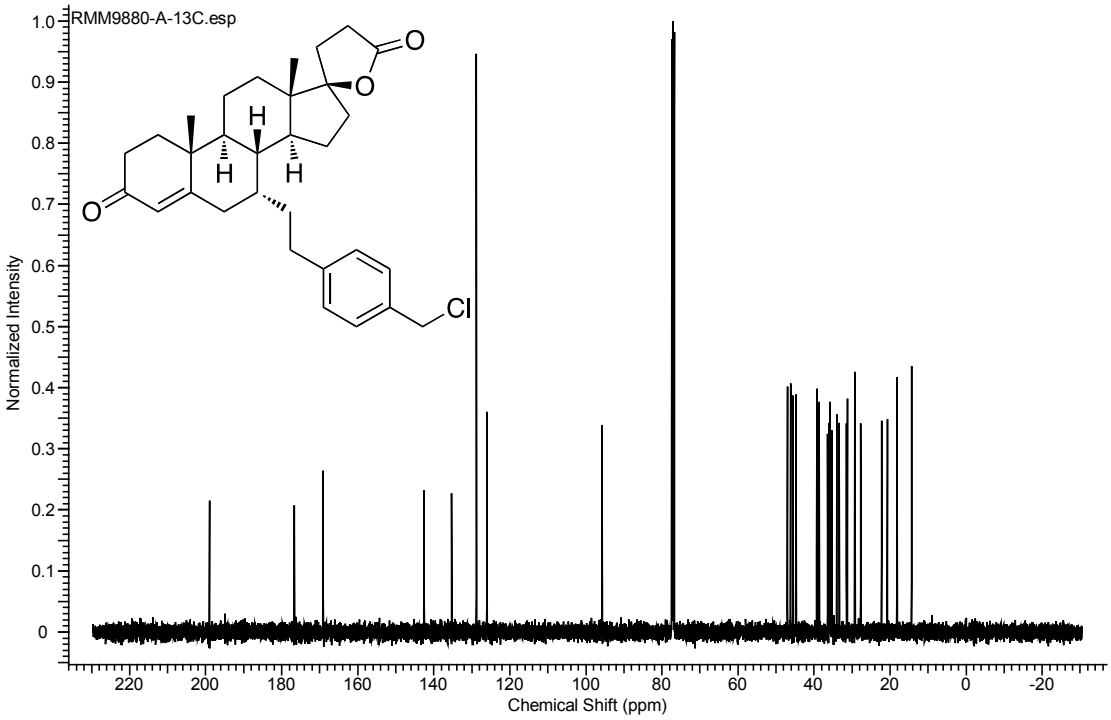
O
H
H
H
O
Cl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Normalized Intensity
Chemical Shift (ppm)
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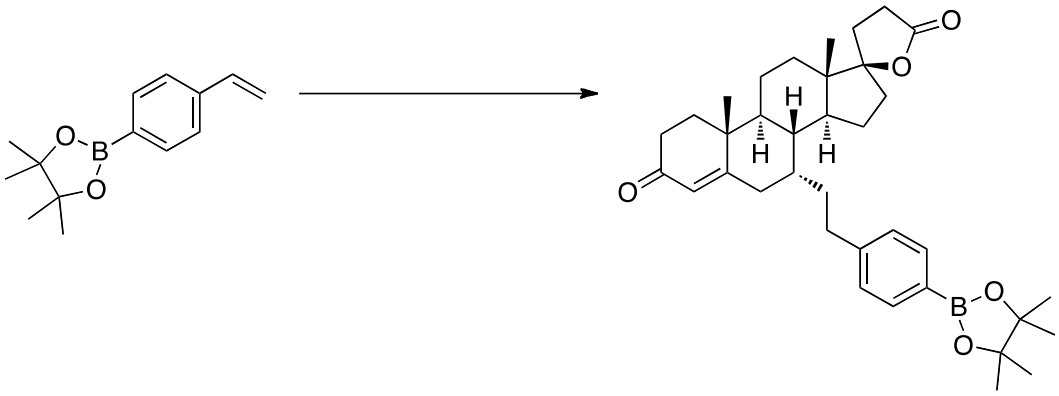
O
H
H
H
O
Cl

(+)-7α-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenethyl)-17α-hydroxy-3-oxo-pregn-4-ene-21-carboxylic acid γ-lactone (10α)



Procedure B: Cp_2ZrHCl (206 mg, 0.80 mmol, 2.0 eq.) was added to a stirred, room temperature, solution of 4-vinylphenylpinacol-boronic ester (230.0 mg, 1.0 mmol, 2.5 eq.) in CH_2Cl_2 (0.40 mL) under an argon atmosphere. After stirring for about 15 min, the resulting clear yellow solution was transferred *via* syringe over about 1 min to a clear colourless stirred solution of CuOTf-ligand complex (30.0 mg, 0.040 mmol, 0.10 eq.) in Et_2O (2.0 mL) under an argon atmosphere. The resulting dark mixture was allowed to stir for an additional 10 min before canrenone (136.0 mg, 0.40 mmol, 1.0 eq.) and TMSCl (0.26 mL, 2.0 mmol, 5.0 eq.) were added sequentially dropwise *via* syringe. Stirring at room temperature was continued arbitrarily for 15 h before the reaction was quenched by the addition of Et_2O (*ca* 3 mL) and NH_4Cl (1 M aq., *ca* 1.5 mL). The mixture was partitioned between the aqueous and Et_2O layers and the former phase was extracted with Et_2O (3 × 10 mL). The combined organic phase was washed with $NaHCO_3$ (sat. aq., *ca* 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give an oil. Flash column chromatography of the yellow residue (30:70 EtOAc/petrol; SiO_2) gave major diastereomer (10α) (+)-7α-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenethyl)-17α-hydroxy-3-oxo-pregn-4-ene-21-carboxylic acid γ-lactone (104 mg, 0.18 mmol, 45%), minor diastereomer (+)-7β-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenethyl)-17α-hydroxy-3-oxo-pregn-4-ene-21-carboxylic acid γ-lactone was not seen.

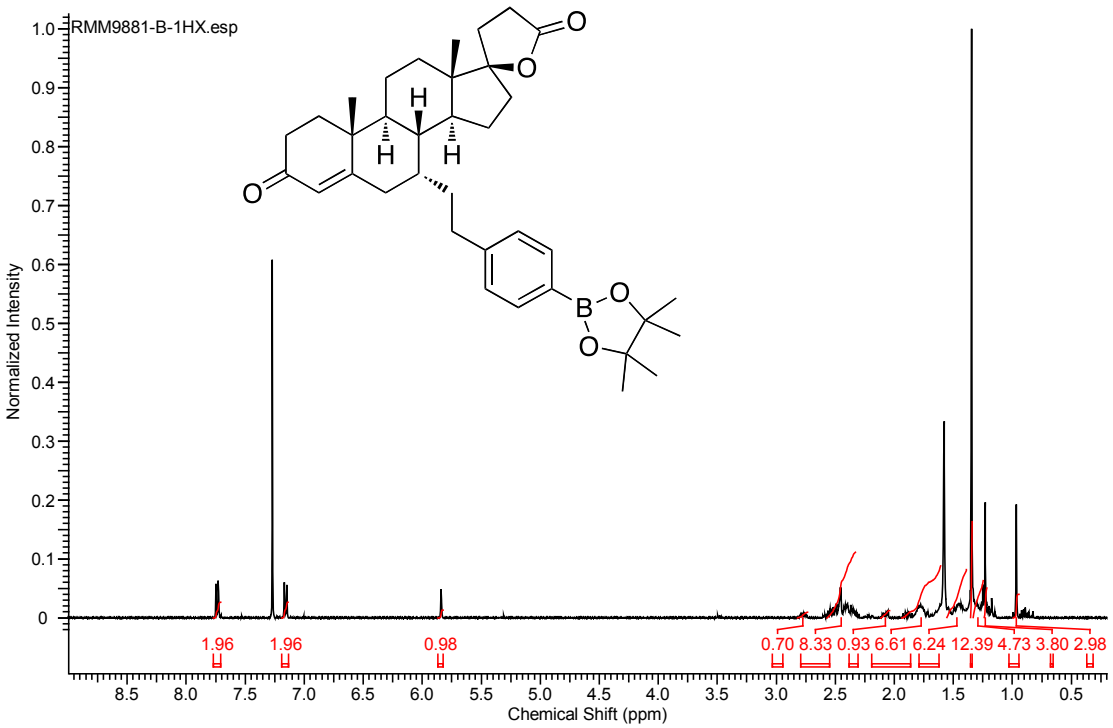
^{1}H NMR (400 MHz, $CDCl_3$) δ_H /ppm 0.97 (s, 3 H), 1.23 (s, 3 H), 1.25 - 1.33 (m, 4 H), 1.35 (br. s, 12 H), 1.38 - 1.56 (m, 6 H), 1.60 - 1.94 (m, 6 H), 2.04 - 2.12 (m, 1 H), 2.31 - 2.58 (m, 8 H), 2.73 - 2.83 (m, 1 H), 5.84 (s, 1 H), 7.16 (d, *J*=7.9 Hz, 2 H), 7.74 (d, *J*=7.9 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$) δ_C /ppm 14.3, 18.1, 20.7, 22.2, 24.8 (5 C), 27.5, 29.3, 31.2, 31.4, 33.7, 34.0, 35.3, 35.6, 36.0, 36.4, 38.6, 39.2, 44.7, 45.6, 46.9, 83.7 (2 C), 95.8, 126.0, 127.9 (2 C), 135.0 (2 C), 145.4, 169.2, 176.8, 199.1.

HRMS (ESI) *m/z* calcd for $C_{36}H_{49}BNaO_5$ $[M+Na]^+$: 595.3565 found: 595.3562.

$[\alpha]^{20}_{589}$ = +50.4 (*c* 0.51, $CHCl_3$).

IR (ν_{max} /cm^{-1}): 1360, 1666, 1769, 2976.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Normalized Intensity
Chemical Shift (ppm)
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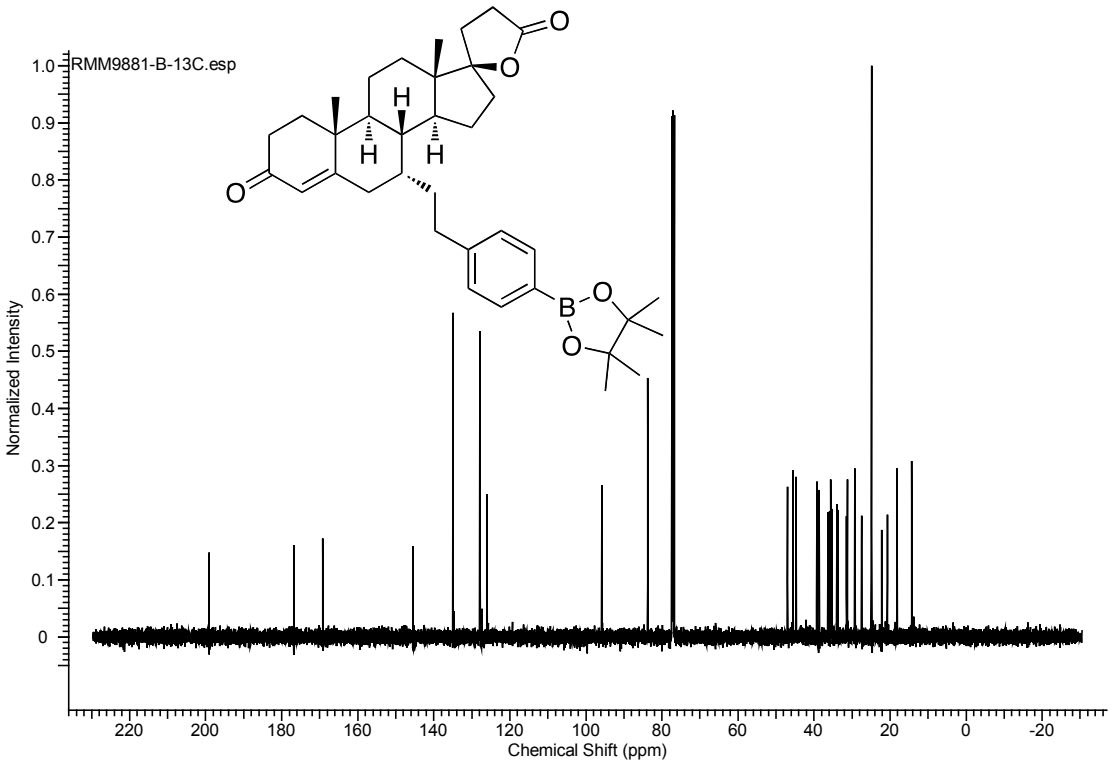
1.96
0.98
0.70 8.33 0.93 6.61 6.24 12.39 4.73 3.80 2.98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Normalized Intensity
Chemical Shift (ppm)

References

1. Buchwald, S. L.; LaMaire, S. J.; Nielsen, R. B., *Org. Synth.* **1993,** *71*, 77–82.
2. Salomon, R. G.; Kochi, J. K., *J. Am. Chem. Soc.* **1973,** *95* (6), 1889-1897.
3. Arnold, L. A.; Imbos, R.; Mandoli, A.; de Vries, A. H. M.; Naasz, R.; Feringa, B. L., *Tetrahedron* **2000,** *56* (18), 2865-2878.
4. Wipf, P.; Smitrovich, J. H., *J. Org. Chem.* **1991,** *56* (23), 6494-6496.
5. Nagashima, F.; Kuba, Y.; Asakawa, Y., *Chem. Pharm. Bull.* **2006,** *54* (6), 902-906.
6. Robert, T.; Velder, J.; Schmalz, H. G., *Angew. Chem. Int. Ed.* **2008,** *47* (40), 7718-7721.
7. Kirk, D. N., *Tetrahedron* **1986,** *42* (3), 777-818.