Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Enantioselective one-pot synthesis of dihydroquinolones *via* BINOL-derived Lewis acid catalysis

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1. GENERAL INFORMATION

Unless otherwise indicated, all reactions were carried out under a positive pressure of argon or nitrogen (balloon pressure) in washed and oven-dried glassware.

1.1 Solvents and Reagents

Tetrahydrofuran, dichloromethane, diethyl ether, methanol, toluene and acetonitrile were purified by pressurized filtration through activated silica columns, employing the method of Grubbs *et al.*[1] Unless otherwise indicated, solvents were used as supplied (analytical or HPLC grade) without further purification. "Petrol" or "petroleum ether" refers to the fraction of petroleum ether boiling in the range 40−60 °C. Where mixtures of solvents are specified, the stated ratios are volume:volume. Triethylamine was distilled over calcium hydride and stored over potassium hydroxide under an inert argon atmosphere. Unless otherwise indicated, all aqueous solutions used were saturated. Reagents were used directly as supplied by major chemical suppliers, or purified by procedures described by Perrin and Armarego.[2] (*R*)-TRIP (**6**) , (+)-2,2'-Isopropylidenebis[(4R)-4-benzyl-2-oxazoline] (**5**) and 2,6-bis[(3*aS*,8*aR*)-3*a*,8*a*-dihydro-8*H*-indeno[1,2-*d*]oxazolin-2-yl]pyridine (**4**) were purchased from the Sigma Aldrich® chemical company.

1.2 Chromatography

Flash column chromatography was carried out using VWR silica gel (40−63 μm particle size). Analytical thin-layer chromatography was carried out on Merck Kieselgel 60 F_{254} 0.25 mm precoated aluminium plates. Visualization was carried out under ultra-violet irradiation (254 nm) and by appropriate heating with potassium permanganate, ammonium molybdate or ninhydrin. Potassium permanganate solution was prepared by dissolving potassium permanganate (2.5 g), potassium carbonate (13 g) and sodium hydroxide (0.63 g) in water (250 mL). Ammonium

molybdate solution was prepared by dissolving ammonium molybdate (5 g) and ceric sulfate (0.2 g) in 5% aqueous sulfuric acid (100 mL). Ninhydrin solution was prepared by dissolving ninhydrin (0.3 g) in *n*-butanol (100 mL) and adding acetic acid (3 mL).

1.3 NMR Spectroscopy

NMR spectra were recorded on a Bruker AV400 (^{1}H: 400 MHz, ^{13}C: 101 MHz, ^{19}F: 377 MHz), Bruker AVII Cryo 500 (^{1}H: 500 MHz, ^{13}C: 126 MHz), Bruker AVII 500 (^{1}H: 500 MHz, ^{13}C: 126 MHz, ^{19}F: 470 MHz), Bruker DRX500 (^{1}H: 500 MHz, ^{13}C: 126 MHz, ^{31}P: 202 MHz) or Bruker DPX300 (^{1}H: 300 MHz, ^{13}C: 75 MHz) spectrometer. Chemical shifts are quoted in ppm, and are referenced to the residual non-deuterated solvent peak. ^{1}H spectra are reported as follows: *^{1}H NMR* (*spectrometer frequency, solvent*): *δ chemical shift/ppm* (*multiplicity, number of protons, J-coupling constant(s), assignment*). ^{13}C spectra are reported as follows: *^{13}C NMR* (*spectrometer frequency, solvent*): *δ chemical shift/ppm* (*assignment*). Multiplets are abbreviated as follows: br – *broad*; s – *singlet*; d – *doublet*; t – *triplet*; q – *quartet*; hept – *heptet*; m – *multiplet*, and are reported based on appearance rather than interpretation. Compound multiplets are reported in the order of decreasing coupling constant magnitude. Spectral assignment was aided by the results of DEPT, COSY, HMBC, HSQC and NOESY experiments where appropriate. Unless otherwise indicated, spectra were acquired at 298 K.

1.4 IR Spectroscopy

Infra-red spectra were recorded on a Bruker Tensor 27 FTIR spectrometer equipped with an attenuated total reflectance attachment with internal calibration. Absorbtion maxima (ν_{max}) are reported in wavenumbers (cm^{-1}).

1.5 Mass Spectrometry

Mass spectra were recorded on a Micromass LCT Premier spectrometer under conditions of electrospray ionization (ESI). Accurate masses (HRMS) were recorded on Bruker MicroTOF and Micromass GCT spectrometers under conditions of ESI and field ionization (FI) respectively. Masses are reported in daltons (Da).

1.6 Melting Points

All melting points were measured on a Reichert melting point stage, and are uncorrected. Solvents are reported in parentheses where solids were purified by recrystallization. Temperatures are reported in °C.

1.7 HPLC

Analytical chiral HPLC was performed on a Dionex Ultimate 3000 HPLC system comprising a Dionex LPG-3400A pump, WPS-3000SL autosampler, TCC-3000SD column compartment and DAD-3000 diode-array detector, equipped with the appropriate Daicel Chiralpak column (dimensions: 0.46 cm ø x 25 cm) and corresponding guard column (0.4 cm ø x 1 cm). Wavelengths (λ) are reported in nm, retention times (t_R) are reported in minutes and solvent flow rates are reported in mL/min.

1.8 Naming, Numbering and Depiction of Compounds

Where given, systematic compound names are those generated by ChemBioDraw Ultra 12.0 following IUPAC conventions. The numbering of atoms for discussion and spectral assignment purposes is arbitrary and not necessarily consistent with the IUPAC names.

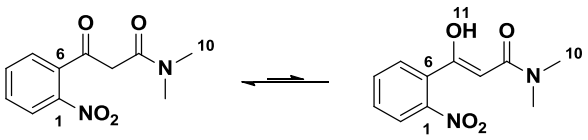
1.9 X-ray Crystallography

Crystals were mounted using the oil technique, in perfluoropolyether oil at 150(2) K with a Cryostream N_2 open-flow cooling device. Single crystal X-ray diffraction data were collected using graphite monochromated Mo-Ka radiation (λ = 0.71073 Å) using a Nonius KappaCCD diffractometer. Series of μ-scans were performed to provide sufficient data to a maximum resolution of 0.77 Å. Data collection and cell refinement were carried out using DENZO-SMN Intensity data were processed and corrected for absorption effects by the multi-scan method, based on multiple scans of identical and Laue equivalent reflections using SCALEPACK (within DENZO-SMN). Structure solution was carried out with direct methods using SuperFlip within the CRYSTALS software suite. Refinement was carried out using full-matrix least-squares within the CRYSTALS suite, on either F2. In general, all non-hydrogen atoms were refined with anisotropic displacement parameters.

2. EXPERIMENTAL PROCEDURES AND DATA

2.1 Substrate Synthesis

_N_,_N_-Dimethyl-3-(2-nitrophenyl)-3-oxopropanamide (S1)



This compound was prepared by analogy to a literature procedure.[3] A solution of 2-nitrobenzoic acid (1.67 g, 10 mmol) in thionyl chloride (3 mL) was heated to reflux for two hours. The resulting brown solution was cooled to RT and the solvent removed *in vacuo* to afford the crude acid chloride. *n*-Butyllithium (1.6 M in hexanes, 12.5 mL, 20 mmol) was added dropwise to a solution of diisopropylamine (2.82 mL, 20 mmol) in diethyl ether (25 mL) at −78 °C and the mixture allowed to warm to 0 °C for 15 min before cooling back to −78 °C. *N*,*N*-Dimethyl acetamide (1.20 mL, 13 mmol) was added dropwise to the reaction mixture, and after 20 min a solution of the crude 2-nitrobenzoyl chloride in diethyl ether (10 mL) was added over 5 min. After a further 30 min the reaction mixture was quenched cautiously with hydrochloric acid (1 *N*, 30 mL) and the organic layer extracted with diethyl ether (2 x 10 mL), dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (silica gel, petrol:ethyl acetate, 2:1 → 1:1) to afford **S1** (870 mg, 38%, 10:7, *ketone*:*enol*) as a yellow amorphous solid.

Integrals are reported relative to the doublet corresponding to $H2_{ketone}$ at 8.11 ppm.

δ_H (400 MHz, $CDCl_3$) 15.42 (0.70 H, s, $H11_{enol}$), 8.11 (1.00 H, d, *J* 8.2, $H2_{ketone}$), 7.82 (0.79 H, d, *J* 7.8, $H2_{enol}$), 7.75 (1.04 H, t, *J* 7.3, $H4_{ketone}$), 7.68 (0.98 H, d, *J* 7.3, $H5_{ketone}$), 7.66 – 7.51 (3.34 H, m,

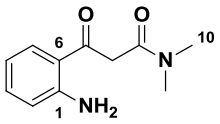
$H3_{ketone}$, $H3_{enol}$, $H4_{enol}$ & $H5_{enol}$), 5.54 (0.72 H, s, $H8_{enol}$), 4.00 (2.00 H, s, $H8_{ketone}$), 3.10 (3.01 H, s, $H10_{ketone}$), 3.04 (4.54 H, s, $H10_{ketone}$), 2.97 (2.97 H, s, $H10'_{ketone}$).

δ_C (101 MHz, $CDCl_3$) 196.3 ($C7_{ketone}$), 171.6 ($C9_{ketone}$), 170.1 ($C9_{enol}$), 148.6 ($C1_{enol}$), 145.4 ($C1_{ketone}$), 137.2 ($C6_{ketone}$), 134.6 ($C4_{ketone}$), 132.5 ($C3_{enol}$), 130.9 ($C6_{enol}$), 130.8 ($C3_{ketone}$), 130.6 ($C4_{enol}$/$C5_{enol}$), 130.0 ($C4_{enol}$/$C5_{enol}$), 128.7 ($C5_{ketone}$), 124.1 ($C2_{ketone}$ & $C2_{enol}$), 88.6 ($C8_{enol}$), 48.7 ($C8_{ketone}$), 37.9 (C10), 35.5 (C10').

ν_{max} (neat): 2937 , 1720, 1636, 1526, 1360, 1163, 800, 779 cm^{-1}.

HRMS (ESI+): found 259.0697; $C_{11}H_{12}N_2NaO_4$, $[M+Na]^+$ requires 259.0689.

3-(2-Aminophenyl)-*N*,*N*-dimethyl-3-oxopropanamide (1)



Palladium on activated carbon (10 wt%, 50 mg) was added to a stirred RT solution of nitroarene **S1** (500 mg, 2.43 mmol) in methanol (10 mL). The reaction mixture was purged under vacuum and placed under an atmosphere of hydrogen (balloon pressure). The resulting mixture was stirred vigorously for 30 min, filtered over Celite® and the solvent removed *in vacuo*. The crude residue was purified by single recrystallization from hot toluene to afford **1** as a yellow crystalline solid (394 mg, 79%).

δ_H ($CDCl_3$, 400 MHz): 7.76 (1H, dd, *J* 8.4, 1.4, H5), 7.28 (1H, ddd, *J* 8.3, 7.0, 1.4, H3), 6.69−6.64 (2H, m, H2 & H4), 6.30 (2H, br s, NH_2), 4.10 (2H, s, H8), 3.04 (3H, s, H10), 3.02 (3H, s, H10').

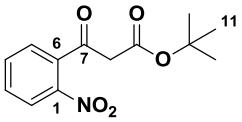
δ_C ($CDCl_3$, 101 MHz):* 195.8 (C7), 167.7 (C9), 150.8 (C1), 134.9 (C3), 131.7 (C5), 117.3 & 116.0 (C2 & C4), 46.6 (C8), 38.1 (C10), 35.6 (C10').

HRMS (ESI+): found 229.0954; $C_{11}H_{14}N_2NaO_2$, $[M+Na]^+$ requires 229.0947.

ν_{max} (neat): 3440 (NH_2), 3329 (NH_2), 3071 (CH), 2975 (CH), 2933 (CH), 1647 (ketone), 1614 (amide), 1393, 1145, 756 cm^{-1}.

MP: 126−128 °C (toluene).

tert-Butyl 3-(2-nitrophenyl)-3-oxopropanoate (S2)



This compound was prepared by analogy to a literature procedure.[3] *n*-Butyllithium (1.6 M in hexanes, 30.3 mL, 48.5 mmol) was added to a stirred solution of diisopropylamine (6.84 mL, 48.5 mmol) in diethyl ether (60 mL) at −78 °C. The stirring solution was allowed to warm to 0 °C and was cooled to −78 °C after 15 min. *tert*-Butyl acetate (5.6 mL, 42 mmol) was added and the mixture was stirred for a further 20 min before adding 2-nitrobenzoyl chloride (4.29 mL, 32.3 mmol). The resulting turbid mixture was stirred for 30 min, hydrochloric acid (1 M aq., 100 mL) was added and the aqueous layer extracted with diethyl ether (3 x 50 mL), dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography (silica gel, petrol:ethyl acetate, 20:1) to afford **S2** (4.55 g, 53%) as a viscous orange oil composed of a 7:1 mixture of ketone:enol tautomeric forms.†

* *The ^{13}C peak corresponding to C6 was not observed, and is presumed to coincide with another peak.*

† *The ^1H and ^{13}C data presented is for the major (ketone) tautomer. The presence of the enol as a minor component is asserted on the basis of characteristic OH (12.45 ppm) and C=CH (5.33) peaks in the ^1H spectrum.*

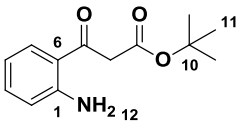
δ_H (400 MHz, $CDCl_3$): 8.15 (1H, dd, *J* 8.2, 0.9, H2), 7.75 (1H, td, *J* 7.5, 1.1, H4), 7.63 (1H, ddd, *J* 8.2, 7.5, 1.3, H3), 7.51 (1H, dd, *J* 7.6, 1.3, H5), 3.79 (2H, s, H8), 1.37 (9H, s, H11).

δ_C (101 MHz, $CDCl_3$): 195.2 (C7), 165.7 (C9), 145.5 (C1), 136.9 (C6), 134.4 (C4), 130.8 (C3), 128.3 (C5), 124.2 (C2), 82.4 (C10), 50.4 (C8), 27.8 (C11).

ν_{max} (neat): 2980 (CH), 2935 (CH), 1731 (ketone), 1703 (ester), 1574 (NO_2), 1346 (NO_2), 1150, 853, 748 cm^{-1}.

HRMS (ESI+): found 288.0843; $C_{13}H_{15}NO_5Na$, $[M+Na]^+$ requires 288.0842.

tert-Butyl 3-(2-aminophenyl)-3-oxopropanoate (S3)



Palladium on activated carbon (10 wt%, 100 mg) was added to a stirred RT solution of nitroarene **S2** (1.0 g, 3.8 mmol) in methanol (20 mL). The reaction mixture was purged under vacuum and placed under an atmosphere of hydrogen (balloon pressure). The resulting mixture was stirred vigorously for 2.5 h, filtered over Celite® and the solvent removed *in vacuo*. The crude residue was purified flash column chromatography (silica gel, petrol:ethyl acetate, 8:2) to afford aniline **S3** (681 mg, 77%) as a pale yellow oil.*

δ_H ($CDCl_3$, 400 MHz): 7.61 (1H, d, *J* 7.3, H5), 7.28 (1H, td, *J* 7.7, 0.5, H3), 6.68−6.62 (2H, m, H2 & H4), 6.28 (2H, br s, H12), 3.87 (2H, s, H8), 1.47 (9H, s, H11).

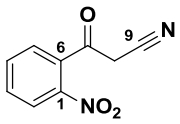
* *This compound is prone to RT decomposition to 4-hydroxyquinolin-2(1H)-one, and must be stored at −18 °C under argon.*

δ_C ($CDCl_3$, 101 MHz):* 195.0 (C7), 167.3 (C9), 150.7 (C1), 134.8 (C3), 131.4 (C5), 117.3 & 115.8 (C2 & C4), 81.7 (C10), 48.2 (C8), 28.0 (C11).

HRMS (ESI+): found 258.1106; $C_{13}H_{17}NNaO_3$, $[M+Na]^+$ requires 258.1101.

ν_{max} (film): 3468 (NH_2), 3351 (NH_2), 2979 (CH), 1724 (C=O), 1646 (ester), 1616, 1368, 1138, 947, 748 cm^{-1}.

3-(2-Nitrophenyl)-3-oxopropanenitrile (S4)



This compound was prepared according to a literature procedure.[4] Acetonitrile (1.74 mL, 33.1 mmol) was added dropwise to a stirred −78 °C solution of *n*-butyllithium (1.49 M in hexanes, 22 mL, 33.1 mmol) in tetrahydrofuran (20 mL). After 1 h methyl-2-nitrobenzoate (2.34 mL, 16.6 mmol) was added dropwise over 15 min, and the resulting mixture was stirred for a further 1 h before warming to −45 °C. After 2 h the reaction mixture was warmed to 0 °C and ammonium chloride (aq., 50 mL) was added. The aqueous layer was extracted with ethyl acetate (3 x 50 mL), dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo.* The crude residue was purified by flash column chromatography (silica gel, petrol:ethyl acetate, 5:1 → 1:1) to afford nitroarene **S4** (1.34 g, 43%) as a red crystalline solid. *Data is consistent with that reported in the literature.*[5]

δ_H ($CDCl_3$, 400 MHz): 8.26 (1H, d, *J* 8.3, H2), 7.85 (1H, td, *J* 7.5, 0.8, H4), 7.74 (1H, td, *J* 7.9, 1.9, H3), 7.48 (1H, dd, *J* 7.5, 0.9, H5), 3.91 (2H, s, H8).

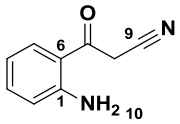
* *The ^{13}C peak corresponding to C6 was not observed.*

δ_C ($CDCl_3$, 101 MHz): 190.0 (C7), 145.1 (C1), 135.2 (C4), 134.7 (C6), 131.9 (C3), 127.6 (C5), 124.7 (C2), 113.3 (C9), 32.5 (C8).

ν_{max} (neat): 2971 (CH), 2908 (CH), 2268 (C≡N), 1718 (C=O), 1524 (NO_2), 1340 (NO_2), 1216, 1004, 743, 702 cm^{-1}.

MP: 88−90 °C (ethyl acetate).

3-(2-Aminophenyl)-3-oxopropanenitrile (S5)



Palladium on activated carbon (10 wt%, 30 mg) was added to a stirred RT solution of nitroarene **S4** (300 mg, 1.58 mmol) in methanol (6 mL). The reaction mixture was purged under vacuum and placed under an atmosphere of hydrogen (balloon pressure). After 45 min the reaction mixture was filtered over Celite® and concentrated *in vacuo*. The crude residue was purified by passing over a short pad of silica gel, eluting with copious amounts of 1:1 petrol:ethyl acetate, and concentrated *in vacuo* to afford aniline **S5** (199 mg, 79%) as a white crystalline solid. *Data is consistent with that reported in the literature.*[6]

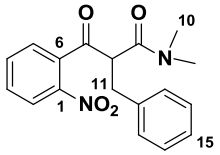
δ_H ($CDCl_3$, 400 MHz): 7.46 (1H, d, *J* 8.2, H5), 7.34 (1H, t, *J* 7.7, H3), 6.72−6.64 (2H, m, H2 & H4) 6.34 (2H, br s, H10), 4.07 (2H, s, H8).

δ_C ($CDCl_3$, 101 MHz): 188.1 (C7), 151.2 (C1), 135.9 (C3), 130.4 (C5), 117.7 (C2/C4), 116.2 (C2/C4), 115.2 (C6/C9), 114.4 (C6/C9), 30.1 (C8).

ν_{max} (neat): 3476 (NH_2), 3364 (NH_2), 2945 (CH), 2258 (C≡N), 1647 (C=O), 1617, 1544, 1451, 1208, 1158, 742 cm^{-1}.

MP: 78−81 °C (dichloromethane).

(±)-2-Benzyl-*N*,*N*-dimethyl-3-(2-nitrophenyl)-3-oxopropanamide (S6)



This compound was prepared according to a modified literature procedure.[7] Caesium carbonate (0.759 g, 2.66 mmol) was added to a stirred solution of nitroarene **S1** (550 mg, 2.66 mmol) in acetone (5 mL) at 0 °C and the resulting mixture allowed to warm to RT. Benzyl bromide (275 μL, 2.66 mmol) was added dropwise and the reaction was stirred for 16 h. The reaction mixture was diluted with dichloromethane (25 mL) and ammonium chloride (aq., 15 mL) was added, and the aqueous layer was extracted with dichloromethane (3 x 10 mL). The combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (silica gel, petrol:ethyl acetate, 3:1) to afford **S6** (587 mg, 77%) as a viscous yellow oil, which crystallized upon prolonged standing to a yellow solid.

δ_H ($CDCl_3$, 400 MHz): 8.16 (1H, dd, *J* 8.3, 0.8, H2), 7.73 (1H, dt, *J* 7.5, 1.1, H4), 7.60 (1H, ddd, *J* 8.2, 7.5, 1.3, H3), 7.53 (1H, dd, *J* 7.6, 1.3, H5), 7.36−7.16 (5H, m, H13-H15), 4.50−4.44 (1H, m, H8), 3.31 (2H, d, *J* 7.8, H11), 2.75 (3H, s, H10), 2.44 (3H, s, H10').

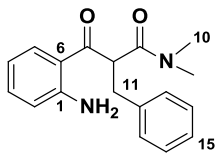
δ_C ($CDCl_3$, 101 MHz): 198.2 (C7), 168.8 (C9), 145.1 (C1), 138.1 (C12), 136.9 (C6), 134.6 (C4), 130.3 (C3), 129.0 (C5), 129.0 & 128.5 (C13 & C14), 126.8 (C15), 124.1 (C2), 57.3 (C8), 37.4 (C10), 35.8 (C11), 35.7 (C10').

HRMS (ESI+): found 349.1159; $C_{18}H_{18}N_2NaO_4$, $[M+Na]^+$ requires 349.1159.

ν_{max} (neat): 3062 (CH), 3030 (CH), 2930 (CH), 1719 (ketone) 1626 (amide), 1526 (NO_2), 1343 (NO_2), 750, 692 cm^{-1}.

MP: 62−66 °C (chloroform).

(±)-3-(2-Aminophenyl)-2-benzyl-*N*,*N*-dimethyl-3-oxopropanamide (28)



Palladium on activated carbon (10 wt%, 28 mg) was added to a stirred RT solution of nitroarene **S6** (280 mg, 0.86 mmol) in methanol (5 mL). The reaction mixture was purged under vacuum and placed under an atmosphere of hydrogen (balloon pressure). The resulting mixture was stirred vigorously for two hours, filtered over Celite® and the solvent removed *in vacuo*. The crude residue was purified by flash column chromatography (silica gel, petrol:ethyl acetate, 3:2) to afford **28** as a yellow crystalline solid (180 mg, 71%).

δ_H ($CDCl_3$, 400 MHz): 7.58 (1H, d, *J* 8.2, H5), 7.30−7.18 (6H, m, H3, H13-H15), 6.67 (1H, d, *J* 8.3, H2), 6.60 (1H, t, *J* 7.5, H4), 6.33 (2H, br s, NH_2), 4.68 (1H, dd, *J* 8.6, 5.3, H8), 3.45 (1H, dd, *J* 13.9, 8.5, H11), 3.22 (1H, dd, *J* 13.9, 5.2, H11'), 2.93 (3H, s, H10), 2.78 (3H, s, H10').

δ_C ($CDCl_3$, 101 MHz): 197.4 (C7), 169.6 (C9), 151.3 (C1), 139.6 (C12), 134.6 (C3), 130.0 (C5), 129.1 & 129.1 (C13 & C14), 126.5 (C15), 117.7 (C2), 116.6 (C6), 115.8 (C4), 54.5 (C8), 37.1 (C10), 35.9 (C10'), 35.8 (C11).

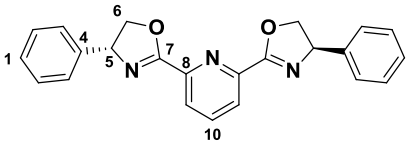
HRMS (ESI+): found 319.1413; $C_{18}H_{20}N_2NaO_2$, $[M+Na]^+$ requires 319.1417.

ν_{max} (neat): 3433 (NH_2), 3314 (NH_2), 3032 (CH), 2934 (CH), 1651 (ketone), 1614 (amide), 1484, 1257, 749, 696 cm^{-1}.

MP: 103−109 °C (chloroform).

2.2 Synthesis of Catalysts

2,6-Bis(4-(*R*)-phenyloxazolin-2-yl)pyridine (3)



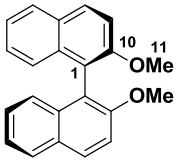
This compound was prepared according to a literature procedure.[8] A stirred neat mixture of (*R*)-phenylglycinol (4.85 g, 35.4 mmol) and dimethyl-2,6-pyridine dicarboxylate (3.45 g, 17.7 mmol) was heated to 120 °C. After 16 h the crude mixture was allowed to cool to RT and dissolved in dichloromethane (20 mL). Triethylamine (10 mL) and *para*-toluenesulfonyl chloride (6.80 g, 35.4 mmol) were added, and the mixture was heated to reflux. After 20 h the reaction mixture was allowed to cool to RT, and water (20 mL) was added. The aqueous layer was extracted with dichloromethane (3 x 10 mL) and the combined organic extracts dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo*. The crude solid residue obtained was purified by single recrystallization (ethanol) to afford (*R*)-phenyl PyBOX **3** (4.63 g, 71%) as a white crystalline solid. *Data is consistent with that reported in the literature.*[9]

δ_H (400 MHz, $CDCl_3$): 8.36 (2H, d, *J* 7.9, H9), 7.93 (1H, t, *J* 7.8, H10), 7.41−7.28 (10H, m, H1, H2 & H3), 5.47 (2H, dd, *J* 10.3, 8.6, H5), 4.94 (2H, dd, *J* 10.3, 8.7, H6), 4.44 (2H, t, *J* 8.6, H6').

δ_C (101 MHz, $CDCl_3$): 163.5 (C7), 146.8 (C8), 141.7 (C4), 137.5 (C10), 128.8 (C2/C3), 127.8 (C1), 126.8 (C2/C3), 126.3 (C9), 75.5 (C6), 70.4 (C5).

MP: 153−156 °C (ethanol).

(*R*)-Dimethyl BINOL (S7)



This compound was prepared according to a literature procedure.[10] Acetone (200 mL) was added to a flask containing (*R*)-BINOL* (14 g, 49 mmol) and warmed until all of the diol was dissolved. Potassium carbonate (22.8 g, 166 mmol) and iodomethane (18.4 mL, 293 mmol) were added, and the resulting mixture was heated under reflux for 24 h. The mixture was allowed to cool to RT and concentrated *in vacuo* to a volume of approximately 50 mL. Water (500 mL) was added, and the mixture stirred for 8 h at RT. The solid residue was obtained by filtration, and washed with water (3 x 200 mL) to afford **S7** (15.3 g, 99%) as a white powder. *Data is consistent with that reported in the literature.*[10]

δ_H (400 MHz, $CDCl_3$): 8.00 (2H, d, *J* 9.0, H8), 7.89 (2H, d, *J* 8.1, H3), 7.48 (2H, d, *J* 9.1, H9), 7.34 (2H, ddd, *J* 8.1, 6.8, 1.2, H4), 7.23 (2H, ddd, *J* 8.4, 6.8, 1.4, H5), 7.13 (2H, d, *J* 8.2, H6), 3.78 (6H, s, H11).

δ_C (101 MHz, $CDCl_3$): 155.0 (C10), 134.0 (C2), 129.4 (C8), 129.2 (C7), 127.9 (C3), 126.3 (C5), 125.3 (C6), 123.5 (C4), 119.6 (C1), 114.3 (C9), 56.9 (C11).

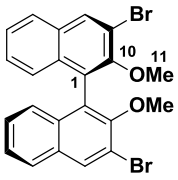
MP = 230−235 °C (diethyl ether/petrol).

$[\alpha]_D^{20.0}$ +56.6 (*c* = 1.0, $CHCl_3$).

ν_{max} (neat): 3048 (CH), 3021 (CH), 2956 (CH), 2933 (CH), 1619, 1591, 1250, 1065, 811 cm^{-1}.

* *(R)-BINOL was purchased from AK Scientific, Union City, CA, USA.*

(*R*)-3,3-Dibromo-dimethyl BINOL (S8)



This compound was prepared according to a literature procedure.[10] *n*-Butyllithium (1.6 M in hexanes, 35 mL, 56 mmol) was slowly added to a stirred RT solution of tetramethylenediamine (5.21 mL, 35 mmol) in diethyl ether (250 mL). After 1 h (*R*)-dimethyl BINOL **S7** (5.0 g, 16 mmol) was added, and the mixture was stirred for a further 3.5 h before cooling to −78 °C. Bromine (4.1 mL, 80 mmol) was added, and the mixture was allowed to warm to RT and stirred for a further 20 h. Sodium sulfite (aq., 80 mL) was added, and the biphasic mixture stirred for 1 h, before the aqueous phase was extracted with diethyl ether (3 x 100 mL). The combined organic extracts were washed with brine (100 mL), dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (silica gel, petrol:ethyl acetate, 1:0 → 20:1) and subsequent recrystallization (dichloromethane/petrol), affording (*R*)-3,3'-dibromo-dimethyl BINOL **S8** as a white crystalline solid (3.33 g, 44%). *Data is consistent with that reported in the literature.*[10]

δ_H (400 MHz, $CDCl_3$): 8.28 (2H, s, H8), 7.83 (2H, d, *J* 8.2, H3), 7.43 (2H, ddd, *J* 8.0, 7.1, 1.0, H4), 7.28 (2H, ddd, *J* 8.4, 7.0, 1.3, H5), 7.09 (2H, d, *J* 8.5, H6), 3.52 (6H, s, H11).

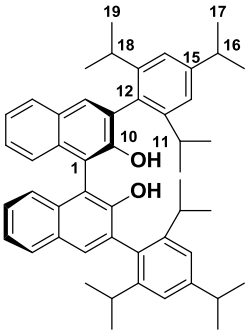
δ_C (101 MHz, $CDCl_3$): 152.5 (C10), 133.1 (C2), 133.0 (C8), 131.4 (C7), 127.1 (C3), 126.9 (C5), 126.5 (C1), 125.9 (C4), 125.8 (C6), 117.5 (C9), 61.1 (C11).

MP: 182-187 °C (dichloromethane/petrol).

$[\alpha]_D^{20.0}$ -14.0 (*c* = 1.0, $CHCl_3$).

ν_{max} (neat): 3056 (CH), 1575, 1493, 1328, 1043, 750 cm^{-1}.

(*R*)-3,3'-Bis(2,4,6-triisopropylphenyl)-BINOL (S9)



This compound was prepared according to a literature procedure.[11] Mechanically-activated magnesium turnings (1.26 g, 52 mmol) were covered with diethyl ether (~ 3 mL) and further activated by the addition of a single crystal of iodine. 2-Bromo-1,3,5-triisopropylbenzene (6.86 mL, 26 mmol), diethyl ether (35 mL) and 1,2-dibromoethane (0.1 mL) were added separately and simultaneously *via* syringe in a manner that maintained the exothermic reaction, and the grey solution was heated to reflux for a further 24 h. The resulting Grignard solution was filtered over a pad of cotton wool and used without further purification in the subsequent step.

In a separate flask, dibromoarene **S8** (2.00 g, 4.26 mmol) and bis(triphenylphosphine)nickel(II) chloride* (277 mg, 0.42 mmol) were suspended in diethyl ether (25 mL). The Grignard solution was added dropwise to the suspension, and the mixture heated to reflux for 6 h. The resulting brown solution was allowed to cool to RT and hydrochloric acid (1.0 M aq., 30 mL), and the aqueous layer was extracted with diethyl ether (3 x 25 mL), dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo*.

The crude product of the Kumada coupling was dissolved in anhydrous dichloromethane (100 mL) and cooled to 0 °C. Boron tribromide (1.0 M in dichloromethane, 29.7 mL,

* *This compound was prepared according to* L. M. Venanzi, *J. Chem. Soc.,* **1958***, 719.*

29.7 mmol) was added dropwise, and the resulting clear solution allowed to warm to RT and stirred for a further 24 h. Water (40 mL) was added, and the aqueous layer extracted with dichloromethane (3 x 25 mL). The combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo*. The crude brown residue was purified by flash column chromatography (silica gel, petrol:ethyl acetate, 100:1), and the resulting yellow solid was triturated with hexanes, affording diol **S9** (1.26 g, 43% over two steps) as a white powder. *Data is consistent with that reported in the literature.*[11]

δ_H (400 MHz, $CDCl_3$): 7.89 (2H, d, *J* 7.9, H3), 7.79 (2H, s, H8), 7.42−7.37 (2H, m, H4), 7.36−7.29 (4H, m, H5 & H6), 7.16 (2H, s, H14), 7.14 (2H, s, H14'), 4.94 (2H, s, H11), 2.98 (2H, septet, *J* 6.9, H16), 2.86 (2H, septet, *J* 6.8, H18), 2.71 (2H, septet, *J* 6.8, H18'), 1.33 (12H, d, *J* 6.9, H17), 1.22 (6H, d, *J* 6.8, H19) 1.13 (6H, d, *J* 7.0, H19), 1.11 (6H, d, *J* 7.0, H19'), 1.05 (6H, d, *J* 6.8, H19').

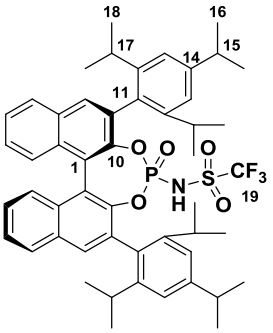
δ_C (101 MHz, $CDCl_3$): 150.6 (C10), 149.1 (C15), 147.8 (C13), 147.7 (C13'), 133.4 (Ar C), 130.6 (C8), 130.4 (Ar C), 129.1 (Ar C), 129.0 (Ar C), 128.2 (C3), 126.6 (C5/C6), 124.5 (C5/C6), 123.8 (C4), 121.2 (C14), 121.2 (C14'), 113.1 (C1), 34.3 (C16), 30.9 (C18), 30.8 (C18'), 24.3 (C17/C19), 24.3 (C17/C19), 24.1 (C17/C19), 24.0 (C17/C19), 23.9 (C17/C19), 23.7 (C17/C19).

MP: 268−274 °C (ethyl acetate/hexanes).

$[\alpha]_D^{20.0}$ +68.9 (*c* = 1.0, $CHCl_3$).

ν_{max} (neat): 3524 (OH), 2960 (CH), 2928 (CH), 2869 (CH), 1739, 1364, 1230, 1217, 749 cm^{-1}.

N-Trifylphosphoramide S10



This compound was prepared according to a literature procedure.[12] Triethylamine (707 μL, 5.07 mmol), phosphoryl chloride (81 μL, 0.87 mmol) and 4-dimethylaminopyridine (177 mg, 1.45 mmol) were added to a stirred RT solution of bis(aryl) BINOL **S9** (500 mg, 0.72 mmol) in dichloromethane (3.5 mL). After 1 h propionitrile (3.5 mL) and trifluoromethanesulfonamide (216 mg, 1.45 mmol) were added, and the mixture heated to 100 °C. After 12 h water (5 mL) was added, and the aqueous layer extracted with diethyl ether (3 x 5 mL). The combined organic extracts were washed with sodium bicarbonate solution (aq., 5 mL) and hydrochloric acid (4 M, 2 x 5 mL), dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The solid residue was purified by flash column chromatography (silica gel, hexanes: dichloromethane:diethyl ether, 1:1:1), to afford the product as a mixture of the free acid and calcium salt. This residue was dissolved in dichloromethane (25 mL), washed with hydrochloric acid (4.0 M aq., 2 x 10 mL), dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to afford triflamide **S10** (545 mg, 86%) as a pale orange powder. *Data is consistent with that reported in the literature*.[12] *This compound was obtained as a 10:1 inseperable mixture of the desired NTPA and phosphoric acid TRIP.*

δ_H (500 MHz, $CDCl_3$): 8.00−7.95 (4H, m, H3 & H8), 7.57 (2H, t, *J* 7.4, H4), 7.39−7.27 (4H, m, H5 & H6), 7.18 (1H, d, *J* 1.6, H13), 7.13 (2H, d, *J* 0.9, 2 x H13), 7.06 (1H, d, *J* 1.6, H13), 3.00−2.90 (2H, m, 2 x H15), 2.80−2.69 (2H, m, 2 x H17), 2.66 (1H, septet, *J* 6.9, H17), 2.58 (1H,

septet, *J* 6.7, H17), 1.32−1.24 (15H, m, 12 x H16 & 3 x H18), 1.24−1.13 (12H, m, 12 x H18), 1.11 (3H, d, *J* 6.8, 3 x H18), 1.00 (3H, d, *J* 6.8, 3 x H18), 0.96 (3H, d, *J* 6.8, 3 x H18).

δ_C (126 MHz, $CDCl_3$): 149.7 (C14), 149.1 (C14'), 147.9 (C12), 147.8 (C12), 147.1 (C12), 146.6 (C12), 145.4 (d, *J* 11.0, C10), 144.7 (d, *J* 9.0, C10'), 133.2 (C8), 133.0 (C8'), 132.3 (d, *J* 2.9, C9), 132.1 (C7), 131.6 (C2), 131.2 (C2'), 130.5 (d, *J* 4.4, C9'), 130.1 (C11), 129.9 (C11), 128.4(1) (C3), 128.3(6) (C3'), 127.3 (C6), 126.8 (C5), 126.7 (C5'), 126.4(0) (C4), 126.3(5) (C4'), 121.8 (C13), 121.2 (2 x C13), 121.1 (C1), 120.4 (C13), 118.8 (q, *J* 322, C19), 34.5 (C15), 34.3 (C15'), 31.4 (C17), 31.0(4) (C17), 30.9(7) (C17), 30.5 (C17), 26.9 (C16/C18), 26.7 (C16/C18), 25.4 (C16/C18), 25.1 (C16/C18), 24.1 (C16/C18), 24.0 (C16/C18), 23.9(1) (C16/C18), 23.8(7) (C16/C18), 23.0 (C16/C18), 22.9 (C16/C18), 22.8 (C16/C18), 22.6 (C16/C18).

δ_F (470 MHz, $CDCl_3$): 77.4.

δ_P (202 MHz, $CDCl_3$): -1.98.

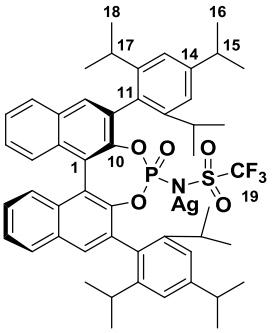
MP: 170−175 °C (dichloromethane).

$[\alpha]_D^{20.0}$ -24.1 (c = 1.0, $CHCl_3$).

ν_{max} (neat): 2961 (CH), 2870 (CH), 1738, 1364, 1227, 975, 751 cm^{-1}.

HRMS (ES-): found 882.3572; $C_{51}H_{56}F_3NO_5PS$, $[M-H]^-$ requires 882.3574.

Silver(I) NTPA (S11)



This compound was prepared by analogy to a literature procedure.[13] *Where possible, all steps of this procedure were carried out in the dark.* Silver(I) carbonate (31.2 mg, 0.113 mmol) and water (2 mL) were added to a stirred solution of triflamide **S10** (200 mg, 0.226 mmol) in dichloromethane (2 mL). The resulting biphasic solution was stirred vigorously for 1 h, diluted with dichloromethane (5 mL) and water (5 mL) and the organic layer extracted with dichloromethane (3 x 5 mL). The organic extracts were filtered over Celite® and concentrated *in vacuo* to afford silver salt **S11** (214 mg, 96%) as a pale grey powder which was stored in the dark.

δ_H (500 MHz, $CDCl_3$): 7.97 (1H, d, *J* 8.3, H3), 7.95 (1H, s, H8), 7.91 (1H, d, *J* 7.9, H3'), 7.90 (1H, s, H8'), 7.53 (1H, t, *J* 7.4, H4), 7.49 (1H, ddd, *J* 8.0, 5.8, 2.2, H4'), 7.36−7.27 (5H, m, 2 x H5, 2 x H6, H13), 7.14 (1H, s, H13), 7.06 (1H, s, H13), 7.03 (1H, s, H13), 3.04−2.94 (1H, m, H15), 2.94−2.85 (2H, m, 2 x H15/H17), 2.85−2.77 (2H, m, 2 x H15/H17), 2.67 (1H, septet, *J* 6.7, H15/H17), 1.34−1.22 (24H, m, 24 x H16/H18), 1.20 (3H, d, *J* 6.7, 3 x H16/H18), 1.15 (3H, d, *J* 6.8, 3 x H16/H18), 1.02 (3H, d, *J* 6.7, 3 x H16/H18), 0.91 (3H, d, *J* 6.8, 3 x H16/H18).

δ_C (126 MHz, $CDCl_3$): 151.4 (C14), 148.5 (C14'), 148.4 (C12), 147.6 (2 x C12), 147.2 (C12), 146.9 (d, *J* 11.0, C10), 145.4 (d, *J* 9.0, C10'), 132.9 (C8), 132.7 (Ar C), 132.3 (Ar C), 132.1 (Ar C), 132.1 (C11), 131.5 (C8'), 131.3 (Ar C), 131.3 (C11'), 130.8 (Ar C), 130.7 (Ar C), 128.3 (C3), 128.1 (C3'), 127.5 (C5), 127.4 (C5'), 126.4 (C6), 126.0 (C6'), 125.8 (C4), 125.5 (C4'), 123.0 (C1), 121.7(3) (C13), 121.6(6) (C13), 121.2 (C1'), 120.4 (2 x C13'), 34.3 (C15), 34.2 (C15'), 31.6 (C17), 31.0

(C17), 30.8 (2 x C17), 26.9 (C16/C18), 26.6 (C16/C18), 25.2 (C16/C18), 25.2 (2 x C16/C18), 24.8 (C16/C18), 24.3 (C16/C18), 24.1 (C16/C18), 24.8 (C16/C18), 23.3 (2 x C16/C18), 22.2 (C16/C18).

δ_P (202 MHz, $CDCl_3$): 6.81.

δ_F (470 MHz, $CDCl_3$): -77.87.

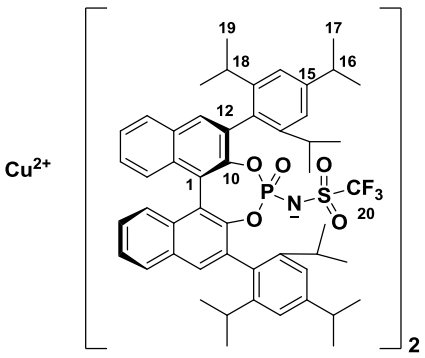
MP: 236−242 °C (dichloromethane).

$[\alpha]_D^{20.0}$ -38.9 (c = 0.61, $CHCl_3$).

ν_{max} (neat): 2962 (CH), 1364, 1314, 1194, 974 cm^{-1}.

HRMS (MALDI+): found 1010.12; $C_{51}H_{58}AgF_3NO_6PS$, $[M+H_3O]^+$ requires 1010.28; *isotope pattern consistent with Ag(I) salt.*

Copper(II) NTPA Salt (7)



This compound was prepared by analogy to a literature procedure.[14] *Where possible, all steps of this procedure were carried out in the dark.* Copper(II) chloride dihydrate (9.5 mg, 0.056 mmol) was added to a stirred RT solution of silver salt **S11** (100 mg, 0.101 mmol) in acetonitrile:dichloromethane (1:1 v/v, 2 mL). After 16 h the reaction mixture was filtered over Celite® and concentrated *in vacuo.* The solid residue was redissolved in dichloromethane (5 mL) and filtered over Celite®, washing

with dichloromethane (1 mL), and the solvent removed *in vacuo* to afford **7** (72 mg, 78%) as a green/grey solid. *Note that due to the paramagnetic nature of the copper(II) ion it was not possible to carry out NMR analysis of this compound.*

MP: 241−244 °C (dichloromethane).

$[\alpha]_D^{20.0}$ -33.8 (c = 0.29, $CHCl_3$).

ν_{max} (neat): 2961 (CH), 2871 (CH), 1196, 1146, 999, 751 cm^{-1}.

m/*z* (ESI$^+$):* 1850 ($[M+Na]^+$, 71%), 1828 ($[M+H]^+$, 53%), 928.3 ($[NTPA^-+2Na]^+$, 100%).

2.3 Synthesis of Dihydroquinolones

General Procedure 1 – Asymmetric Synthesis of Dihydroquinolones

The appropriate aldehyde (2.0 eq.) was added to a stirred -30 °C suspension of *the appropriate aniline (1.0 eq.)*, oven-dried 4 Å molecular sieves (*1 mg / 1 mg aniline*) and copper catalyst **7** (*0.01 eq.*) in 1:1 tetrahydrofuran:toluene (v:v, *0.2 M concentration of aniline*). After 48 h the product dihydroquinolone was obtained by work-up procedure A or B.†

Work-up procedure A. The solvent was removed *in vacuo*, and the residue purified by flash column chromatography on silica gel.

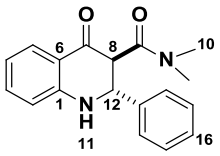
Work-up procedure B. The reaction mixture was poured into dichloromethane (200 mL / mmol aniline) and passed over a short plug of silica gel to remove the catalyst. The solvent was removed *in vacuo*, and the residue purified by flash column chromatography on silica gel.

General Procedure 2– Racemic Synthesis of Dihydroquinolones

* *"$NTPA^-$" refers to the conjugate base anion of the neutral N-trifylphosphoramide* ***S10****.*

† *Work-up procedure A should be employed where TLC and MS indicate that the reaction has gone to completion, with no residual aniline remaining. Otherwise, work-up procedure B is necessary to prevent further reaction at RT, which would give mis-representative yields and enantioselectivities. Quenching these reactions with acid or base is not possible, since both the free acid and salt forms of the catalyst are active.*

***N,N*-Dimethyl-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxamide (2)**



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), benzaldehyde (49 μL, 0.48 mmol). *Work-up procedure A* was employed: chromatography (silica gel, dichloromethane:methanol, 100:1). The product dihydroquinolone **2** (64 mg, 90%, 83:17 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 2***.

δ_H ($CDCl_3$, 400 MHz): 7.89 (1H, dd, *J* 7.9, 1.5, H5), 7.55 (2H, dd, *J* 7.7, 1.7, H14), 7.39−7.33 (4H, m, H3, H15, H16), 6.79 (1H, t, *J* 7.5, H4), 6.70 (1H, d, *J* 8.2, H2), 5.25 (1H, d, *J* 12.9, H12), 4.50 (1H, br s, H11), 4.15 (1H, d, *J* 13.1, H8), 2.87 (3H, s, H10), 2.85 (3H, s, H10').

δ_C ($CDCl_3$, 101 MHz): 189.6 (C7), 167.9 (C9), 151.2 (C1), 139.7 (C13), 135.7 (C3), 128.7 (C14), 128.6 (C16), 128.0 (C5), 127.6 (C15), 118.6 (C6), 118.5 (C4), 115.8 (C2), 60.7 (C12), 57.6 (C8), 37.5 (C10), 35.5 (C10').

HRMS (ESI+): found 317.1261; $C_{18}H_{18}N_2NaO_2$, $[M+Na]^+$ requires 317.1260.

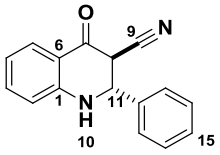
ν_{max} (neat): 3282 (NH), 3034 (CH), 2940 (CH), 1659 (ketone), 1632 (amide), 1510, 1481, 1331, 1303, 760, 662 cm^{-1}.

MP: 203−208 °C (dichloromethane).

HPLC (Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min^{-1}, λ = 245): t_R (major) = 8.1, t_R (minor) = 14.4.

$[\alpha]_D^{20.0}$ +60.4 (c = 1, $CHCl_3$).

4-Oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carbonitrile (8)



Attempted asymmetric synthesis: prepared according to ***general procedure 1***. Aniline **S5** (50 mg, 0.31 mmol), benzaldehyde (64 μL, 0.62 mmol). *Work-up procedure B* was employed: chromatography (silica gel, petrol:ethyl acetate, 4:1). The product dihydroquinolone **8** (49 mg, 63%, *racemic*, 4:1 dr) was obtained as a yellow crystalline solid. *Although the diastereomers were inseparable by column chromatography, a pure sample of the major diastereomer was obtained by single recrystallization (dichloromethane/petrol).*

Major (as drawn): δ_H (400 MHz, d6-acetone): 7.78 (1H, d, *J* 7.6, H5), 7.68 (2H, d, *J* 6.5, H13), 7.52−7.41 (4H, m, H3, H14, H15), 7.02 (1H, d, *J* 8.3, H2), 6.81 (1H, t, *J* 7.6, H4), 6.59 (1H, br s, H10), 4.99 (1H, d, *J* 13.1, H11), 4.55 (1H, d, *J* 13.2, H8).

δ_C (101 MHz, d6-acetone): 184.4 (C7), 152.2 (C1), 138.6 (C12), 136.5 (C3), 129.6 (C15), 129.2 (C14), 128.3 (C13), 127.8 (C5), 118.5 (C4), 117.0 (C6/C9), 116.9 (C2), 115.5 (C6/C9), 60.9 (C11), 48.1 (C8).

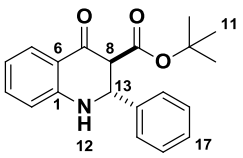
HRMS (ESI+): found 271.0839; $C_{16}H_{12}N_2NaO$, $[M+Na]^+$ requires 271.0842.

ν_{max} (film): 3350 (NH), 2891 (CH), 2252 (C≡N), 1661, 1609, 1481, 1455, 1335, 752, 705 cm^{-1}.

MP: 164−168 °C (dichloromethane/petrol).

HPLC (Chiralpak AS, 50% IPA, 50% hexane, 1.0 $mL.min^{-1}$, λ = 245): $t_R(1)$ = 8.6, $t_R(2)$ = 11.4.

tert-Butyl 4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (9)



Asymmetric: prepared according to ***general procedure 5***. Aniline **S3** (100 mg, 0.42 mmol), benzaldehyde (86 μL, 0.84 mmol). *Work-up procedure B* was employed: chromatography (silica gel, petrol:ethyl acetate, 20:1). The product dihydroquinolone **9** (47 mg, 34%, 32:68 e.r., >20:1 dr, ~10:1 *ketone*:*enol*) was obtained as a yellow oil.

Racemic: prepared according to ***general procedure 2***.

δ_H (400 MHz, $CDCl_3$): 7.88 (1H, d, *J* 8.0, 1.2, H5), 7.51 (2H, dd, *J* 7.6, 1.7, H15), 7.42−7.31 (4H, m, H3, H16 & H17), 6.80 (1H, td, *J* 7.2, 0.7, H4), 6.69 (1H, d, *J* 8.1, H2), 4.97 (1H, d, *J* 13.1, H13), 4.54 (1H, br s, H12), 3.76 (1H, d, *J* 13.1, H8), 1.29 (9H, s, H11).

δ_C (101 MHz, $CDCl_3$): 189.2 (C7), 167.2 (C9), 150.8 (C1), 138.5 (C14), 135.7 (C3), 128.9 (C17), 128.7 (C16), 127.9 (C5), 127.8 (C15), 118.6 (C4), 118.4 (C6), 115.7 (C2), 81.8 (C10), 61.8 (C8), 60.6 (C13), 27.8 (C11).

HRMS (ESI+): found 346.1402; $C_{20}H_{21}NNaO_3$, $[M+Na]^+$ requires 346.1414.

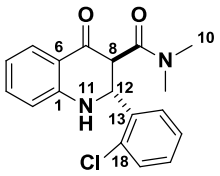
ν_{max} (film): 3342 (NH), 2979 (CH), 2932 (CH), 1725 (C=O), 1665, 1611, 1482, 1334, 1296, 1148, 910, 730 cm^{-1}.

$[\alpha]_D^{20.0}$ +35.4 (*c* = 1, $CHCl_3$).

HPLC (Chiralpak ADH, 5% IPA, 95% hexane, 1.0 mL.min^{-1}, λ = 245): t_R(minor) = 8.2, t_R(major) = 15.4.

2-(2-Chlorophenyl)-*N,N*-dimethyl-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide

(10)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), 2-chlorobenzaldehyde (54 μL, 0.48 mmol). *After 48 h incomplete conversion was observed by TLC analysis. An additional aliquot of o-chlorobenzaldehyde (54 μL, 0.48 mmol) and catalyst* ***7*** *(4.4 mg, 2.4 μmol) was added, and the reaction stirred for a further 24 h. Work-up procedure A* was employed: chromatography (silica gel, dichloromethane:methanol, 100:1). The product dihydroquinolone **10** (71 mg, 90%, 61:38 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: Scandium(III) triflate (6 mg, 0.012 mmol) was added to a stirred RT solution of aniline **1** (25 mg, 0.12 mmol) and 2-chlorobenzaldehyde (27 μL, 0.24 mmol) in dichloromethane (1 mL). After 1 h the solvent was removed *in vacuo* and the crude product purified by flash column chromatography (silica gel, petrol:ethyl acetate, 1:1) to afford **10** (34 mg, 86%) as a yellow foam.

δ_H (400 MHz, $CDCl_3$): 7.85 (1H, dd, *J* 8.0, 1.0, H5), 7.48−7.43 (1H, m, H15), 7.43−7.38 (1H, m, H16), 7.34 (1H, ddd, *J* 8.3, 7.1, 1.4, H3), 7.29−7.23 (2H, m, H14 & H17), 6.77 (1H, t, *J* 7.6, H4), 6.69 (1H, d, *J* 8.3, H2), 5.63 (1H, d, *J* 11.6, H12), 4.58 (1H, s, H11), 4.44 (1H, d, *J* 11.6, H8), 3.07 (3H, s, H10), 2.89 (3H, s, H10').

δ_C (101 MHz, $CDCl_3$):* 189.4 (C7), 167.4 (C9), 150.9 (C1), 136.6 (C13), 135.8 (C3), 133.9 (C18), 130.6 (C16), 129.6 (C17), 128.7 (C15), 128.0 (C5), 127.2 (C14), 118.3 (C4), 115.8 (C2), 56.5 (C12), 54.5 (C8), 37.7 (C10), 35.7 (C10').

HRMS (ESI+): found 351.0874; $C_{18}H_{17}{}^{35}ClN_2NaO_2$, $[M(^{35}Cl)+Na]^+$ requires 351.0871.

ν_{max} (neat): 3328 (NH), 2924 (CH), 2854 (CH), 1639 (ketone), 1608 (amide), 1479, 1324, 1057, 757 cm^{-1}.

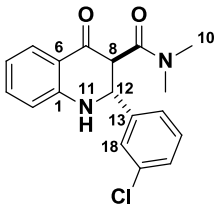
MP: 173-175 °C (dichloromethane).

HPLC (Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 $mL.min^{-1}$, λ = 245): t_R (major) = 7.1, t_R (minor) = 11.0.

$[\alpha]_D^{20.0}$ +69.2 (c = 1, $CHCl_3$).

2-(3-Chlorophenyl)-*N*,*N*-dimethyl-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide

(11)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), 3-chlorobenzaldehyde (54 μL, 0.48 mmol). *Work-up procedure A* was employed: chromatography (silica gel, 0.75% methanol in dichloromethane). The product dihydroquinolone **11** (66 mg, 83%, 78:22 e.r., >20:1 dr) was obtained as a yellow foam.

* *The ^{13}C peak corresponding to C6 was not observed.*

Racemic: Scandium(III) triflate (6 mg, 0.012 mmol) was added to a stirred RT solution of aniline **1** (25 mg, 0.12 mmol) and 3-chlorobenzaldehyde (27 μL, 0.24 mmol) in dichloromethane (1 mL). After 1 h the solvent was removed *in vacuo* and the crude product purified by flash column chromatography (silica gel, petrol:ethyl acetate, 1:1) to afford **11** (28 mg, 71%) as a yellow crystalline solid.

δ_H (400 MHz, $CDCl_3$): 7.87 (1H, dd, *J* 8.0, 1.1, H5), 7.59 (1H, s, H18), 7.42 (1H, dt, *J* 6.7, 1.7, H16), 7.36 (1H, ddd, *J* 8.3, 7.0, 1.4, H3), 7.33−7.28 (2H, m, H14 & H15), 6.80 (1H, t, *J* 7.5, H4), 6.72 (1H, d, *J* 8.4, H2), 5.23 (1H, d, *J* 13.0, H12), 4.51 (1H, s, H11), 4.10 (1H, d, *J* 12.9, H8), 2.87 (6H, s, H10).

δ_C (101 MHz, $CDCl_3$): 189.2 (C7), 167.6 (C9), 150.9 (C1), 141.9 (C13), 135.8 (C3), 134.5 (C17), 130.0 (C14/C15), 128.8 (C14/C15), 128.0 (C5), 127.5 (C18), 126.3 (C16), 118.7 (C4), 118.6 (C6), 115.9 (C2), 60.1 (C12), 57.4 (C8), 37.6 (C10), 35.6 (C10').

HRMS (ESI+): found 351.0871; $C_{18}H_{17}{}^{35}ClN_2NaO_2$, $[M(^{35}Cl)+Na]^+$ requires 351.0871.

ν_{max} (neat): 3282 (NH), 2924 (CH), 2854 (CH), 1632 (ketone), 1608 (amide), 1327, 1162, 747 cm^{-1}.

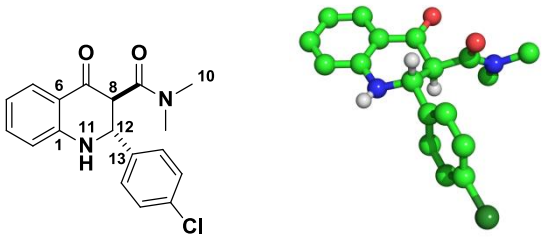
MP: 232−235 °C (dichloromethane).

HPLC (Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 $mL.min^{-1}$, λ = 245): t_R (major) = 7.9, t_R (minor) = 14.2.

$[\alpha]_D^{20.0}$ +80.0 (*c* = 1, $CHCl_3$).

2-(4-Chlorophenyl)-*N*,*N*-dimethyl-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide

(12)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), 4-chlorobenzaldehyde (72 mg, 0.48 mmol). *Work-up procedure A* was employed: chromatography (silica gel, 0.75% methanol in dichloromethane). The product dihydroquinolone **12** (71 mg, 90%, 68:32 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: Scandium(III) triflate (6 mg, 0.012 mmol) was added to a stirred RT solution of aniline **1** (25 mg, 0.12 mmol) and 4-chlorobenzaldehyde (27 μL, 0.24 mmol) in dichloromethane (1 mL). After 1 h the solvent was removed *in vacuo* and the crude product purified by flash column chromatography (silica gel, petrol:ethyl acetate, 1:1) to afford **12** (31 mg, 79%) as a yellow crystalline solid.

δ_H (400 MHz, $CDCl_3$): 7.86 (1H, d, *J* 8.0, H5), 7.49 (2H, d, *J* 7.8, H14), 7.35 (1H, t, *J* 7.7, H3), 7.32 (2H, d, *J* 7.8, H15), 6.80 (1H, t, *J* 7.6, H4), 6.72 (1H, d, *J* 8.2, H2), 5.20 (1H, d, *J* 12.9, H12), 4.53 (1H, s, H11), 4.07 (1H, d, *J* 13.1, H8), 2.86 (6H, s, H10).

δ_C (101 MHz, $CDCl_3$): 189.3 (C7), 167.6 (C9), 151.1 (C1), 138.4 (C13), 135.8 (C3), 134.3 (C16), 129.1 (C14), 128.8 (C15), 128.0 (C5), 118.7 (C4), 118.6 (C6), 115.9 (C2), 60.0 (C12), 57.6 (C8), 37.5 (C10), 35.6 (C10').

HRMS (ESI+): found 351.0866; $C_{18}H_{17}{}^{35}ClN_2NaO_2$, $[M(^{35}Cl)+Na]^+$ requires 351.0871.

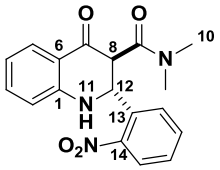
ν_{max} (neat): 3328 (NH), 2924 (CH), 2855 (CH), 1662 (ketone), 1628 , 1607 (amide), 1507, 1484, 1134, 1107, 765 cm^{-1}.

MP: 198−200 °C (dichloromethane).

HPLC (Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 $mL.min^{-1}$, λ = 245): t_R (major) = 7.5, t_R (minor) = 17.8.

$[\alpha]_D^{20.0}$ +51.4 (c = 0.5, $CHCl_3$).

_N,N_-Dimethyl-2-(2-nitrophenyl)-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide (13)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), 2-nitrobenzaldehyde (72 mg, 0.48 mmol). *Work-up procedure B* was employed: chromatography (silica gel, 0.5% methanol in dichloromethane). The product dihydroquinolone **13** (14 mg, 17%, 71:29 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 6***.

δ_H (400 MHz, $CDCl_3$): 7.85 (1H, d, *J* 8.0, H5), 7.80 (1H, d, *J* 8.1, H15), 7.71 (1H, d, *J* 7.8, H18), 7.59 (1H, t, *J* 7.6, H17), 7.47 (1H, t, *J* 7.7, H16), 7.38 (1H, t, *J* 7.8, H3), 6.82 (1H, t, *J* 7.6, H4), 6.75 (1H, d, *J* 8.2, H2), 5.66 (1H, d, *J* 11.6, H12), 4.80 (1H, d, *J* 11.4, H8), 3.05 (3H, s, H10), 2.88 (3H, s, H10').

δ_C (101 MHz, $CDCl_3$): 188.6 (C7), 167.0 (C9), 150.8 & 150.4 (C1 & C14), 135.9 (C3), 133.8 (C13), 132.7 (C17), 129.2 (C18), 129.0 (C16), 127.9 (C5), 124.6 (C15), 119.0 (C4), 118.5 (C6), 116.1 (C2), 55.6 (C8), 55.1 (C12), 37.6 (C10), 35.7 (C10').

HRMS (ESI+): found 362.1120; $C_{18}H_{17}N_3NaO_4$, $[M+Na]^+$ requires 362.1111.

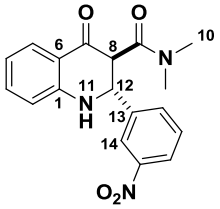
ν_{max} (neat): 3361 (NH), 2930 (CH), 1640 (ketone), 1611 (amide), 1528 (NO_2), 1355 (NO_2), 1155, 762 cm^{-1}.

MP: 202−204 °C (dichloromethane).

$[\alpha]_D^{20.0}$ +61.8 (c = 1, $CHCl_3$).

HPLC (Chiralpak ODH, 30% IPA, 70% hexane, 1.0 mL.min^{-1}, λ = 246): t_R(major) = 9.5, t_R(minor) = 13.7.

_N,N_-Dimethyl-2-(3-nitrophenyl)-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide (14)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), 3-nitrobenzaldehyde (72 mg, 0.48 mmol). *Work-up procedure A* was employed: chromatography (silica gel, 0.5% methanol in dichloromethane). The product dihydroquinolone **14** (53 mg, 64%, 71:29 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 2***.

δ_H (400 MHz, d_6-DMSO): 8.43 (1H, t, *J* 1.9, H14), 8.20 (1H, ddd, *J* 8.3, 2.3, 0.9, H16), 8.00 (1H, d, *J* 7.7, H18), 7.71−7.63 (2H, m, H5 & H17), 7.37 (1H, ddd, *J* 8.4, 7.0, 1.5, H3), 7.22 (1H, br s, H11), 6.87 (1H, d, *J* 8.3, H2), 6.70 (1H, t, *J* 7.6, H4), 5.13 (1H, d, *J* 13.2, H12), 4.70 (1H, d, *J* 13.3, H8), 2.84 (3H, s, H10), 2.67 (3H, s, H10').

δ_C (101 MHz, d_6-DMSO): 190.2 (C7), 168.4 (C9), 152.7 (C1), 148.4 (C15), 143.3 (C13), 136.3 (C3), 136.0 (C18), 130.7 (C17), 127.6 (C5), 123.9 (C16), 123.9 (C14), 118.2 (C6), 117.8 (C4), 117.1 (C2), 59.8 (C12), 56.2 (C8), 37.8 (C10), 35.7 (C10').

HRMS (ESI+): found 362.1107; $C_{18}H_{17}N_3NaO_4$, $[M+Na]^+$ requires 362.1111.

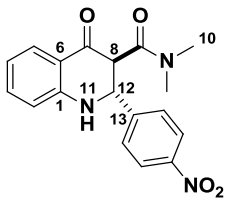
ν_{max} (neat): 3262 (NH), 2922 (CH), 2853 (CH), 1664 (ketone), 1625 (amide), 1531 (NO_2), 1347 (NO_2), 766, 731, 705 cm^{-1}.

MP: 231−234 °C (dichloromethane).

$[\alpha]_D^{20.0}$ +65.5 (c = 1, $CHCl_3$).

HPLC (Chiralpak ODH, 30% IPA, 70% hexane, 1.0 mL.min^{-1}, λ = 245): t_R(major) = 12.9, t_R(minor) = 21.2.

_N,N_-Dimethyl-2-(4-nitrophenyl)-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide (15)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), 4-nitrobenzaldehyde (72 mg, 0.48 mmol). *Work-up procedure A* was employed: chromatography

(silica gel, 0.5% methanol in dichloromethane). The product dihydroquinolone **15** (60 mg, 73%, 62:38 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 2***.

δ_H (400 MHz, $CDCl_3$): 8.21 (2H, d, *J* 8.8, H15), 7.89 (1H, dd, *J* 8.0, 1.4, H5), 7.78 (2H, d, *J* 8.7, H14), 7.40 (1H, ddd, *J* 8.2, 7.2, 1.5, H3), 6.85 (1H, t, *J* 7.2, H4), 6.75 (1H, d, *J* 8.2, H2), 5.39 (1H, d, *J* 12.9, H12), 4.51 (1H, br s, H11), 4.11 (1H, d, *J* 12.9, H8), 2.89 (3H, s, H10), 2.87 (3H, s, H10').

δ_C (101 MHz, $CDCl_3$): 188.5 (C7), 167.1 (C9), 150.7 (C1), 148.0 (C16), 147.1 (C13), 136.0 (C3), 128.9 (C14), 128.0 (C5), 123.9 (C15), 119.2 (C4), 118.7 (C6), 116.0 (C2), 60.0 (C12), 57.5 (C8), 37.6 (C10), 35.6 (C10').

HRMS (ESI+): found 362.1115; $C_{18}H_{17}N_3NaO_4$, $[M+Na]^+$ requires 362.1111.

ν_{max} (neat): 3245 (NH), 3058 (CH), 2923 (CH), 2854 (CH), 1665 (ketone), 1630 (amide), 1513 (NO_2), 1480, 1344 (NO_2), 858, 745, 662 cm^{-1}.

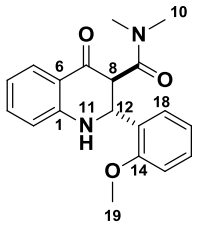
MP: 248−253 °C (dichloromethane).

$[\alpha]_D^{20.0}$ +30.3 (c = 1, $CHCl_3$).

HPLC (Chiralpak ODH, 30% IPA, 70% hexane, 1.0 mL.min^{-1}, λ = 245): t_R(major) = 12.3, t_R(minor) = 31.6.

2-(2-Methoxyphenyl)-*N*,*N*-dimethyl-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide

(16)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), 2-methoxybenzaldehyde (65 mg, 0.48 mmol). *Work-up procedure B* was employed: chromatography (silica gel, 0.5% methanol in dichloromethane). The product dihydroquinolone **16** (56 mg, 72%, 56:44 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 2***.

δ_H (400 MHz, $CDCl_3$) 7.78 (1 H, dd, *J* 8.0, 1.4, H5), 7.28 – 7.18 (3 H, m, H3, H16 & H18), 6.91 – 6.83 (2 H, m, H15 & H17), 6.67 (1 H, t, *J* 7.5, H4), 6.59 (1 H, d, *J* 8.2, H2), 5.42 (1 H, d, *J* 11.5, H12), 4.50 (1 H, s, H11), 4.43 (1 H, d, *J* 11.5, H8), 3.79 (3 H, s, H19), 3.01 (3 H, s, H10), 2.83 (3 H, s, H10').

δ_C (101 MHz, $CDCl_3$) 190.3 (C7), 168.3 (C9), 157.5 (C14), 151.3 (C1), 135.5 (C3), 129.6 (C16/C18), 128.3 (C16/C18), 127.9 (C5), 127.1 (C12), 120.9 (C17), 118.6 (C6), 117.9 (C4), 115.8 (C2) 111.5 (C15), 55.6 (C19), 54.8 (C12), 53.9 (C8), 37.6 (C10), 35.6 (C10).

ν_{max} (neat): 3312, 2933, 1634, 1610, 1494, 1483, 1248, 756, 731 cm^{-1}.

HRMS (ESI): found 347.1354; $C_{19}H_{20}N_2NaO_3$ $[M+Na]^+$ requires 347.1366.

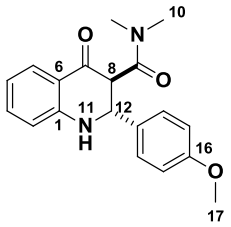
MP: 214–216 °C (dichloromethane).

HPLC (Chiralpak OD-H, 50% IPA, 50% hexane, 1.0 mL.min^{-1}, λ = 245): t_R (major) = 5.5, t_R (minor) = 9.5.

$[\alpha]_D^{20.0}$ +38.4 (c = 1, $CHCl_3$).

2-(4-Methoxyphenyl)-*N*,*N*-dimethyl-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide

(17)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), 4-methoxybenzaldehyde (65 mg, 0.48 mmol). *Work-up procedure B* was employed: chromatography (silica gel, 0.5% methanol in dichloromethane). The product dihydroquinolone **17** (66 mg, 85%, 59:41 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 2***.

δ_H (400 MHz, $CDCl_3$) 7.87 (1 H, dd, *J* 8.0, 1.3, H5), 7.49 – 7.43 (2 H, m, H14), 7.35 (1 H, ddd, *J* 8.5, 7.1, 1.6, H3), 6.92 – 6.84 (2 H, m, H15), 6.78 (1 H, t, *J* 7.5, H4), 6.69 (1 H, d, *J* 8.2, H2), 5.18 (1 H, d, *J* 13.0, H12), 4.48 (1 H, br s, H11), 4.11 (1 H, d, *J* 13.0, H8), 3.82 (3 H, s, H17), 2.85 (6 H, s, H10).

δ_C (101 MHz, $CDCl_3$) 189.9 (C7), 168.1 (C9), 159.6 (C16), 151.3 (C1), 135.7 (C3), 131.8 (C13), 128.8 (C14), 128.0 (C5), 118.6 (C6), 118.3 (C4), 115.8 (C2), 114.0 (C15), 60.1 (C12), 57.7 (C8), 55.3 (C17), 37.6 (C10), 35.6 (C10').

ν_{max} (neat): 2206, 2934, 1634, 1610, 1509, 1248, 762, 735 cm^{-1}.

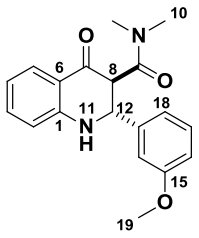
HRMS (ESI): found 347.1356; $C_{19}H_{20}N_2NaO_3$ $[M+Na]^+$ requires 347.1366.

MP: 160–164 °C (dichloromethane).

HPLC (Chiralpak OD-H, 50% IPA, 50% hexane, 1.0 mL.min^{-1}, λ = 245): t_R (major) = 6.1, t_R (minor) = 11.1.

$[\alpha]_D^{20.0}$ +19.0 (c = 1, $CHCl_3$).

2-(3-Methoxyphenyl)-*N*,*N*-dimethyl-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide (18)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), 3-methoxybenzaldehyde (65 mg, 0.48 mmol). *Work-up procedure B* was employed: chromatography (silica gel, 0.5% methanol in dichloromethane). The product dihydroquinolone **18** (58 mg, 75%, 63:37 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 2***.

δ_H (400 MHz, $CDCl_3$) 7.89 (1 H, dd, *J* 8.0, 1.2, H5), 7.37 (1 H, ddd, *J* 8.5, 7.2, 1.6, H3), 7.32 – 7.26 (1 H, m, H17), 7.16 – 7.08 (2 H, m, H, H14 & H18), 6.89 (1 H, dd, *J* 7.9, 2.2, H16), 6.80 (1 H, t, *J* 7.5, H4), 6.72 (1 H, d, *J* 8.2, H2), 5.23 (1 H, d, *J* 13.0, H12), 4.54 (1 H, s, H11), 4.16 (1 H, d, *J* 13.0, H8), 3.83 (3 H, s, H19), 2.88 (3 H, s, H10), 2.86 (3 H, s, H10').

δ_C (101 MHz, $CDCl_3$) 189.7 (C5), 168.0 (C9), 159.8 (C15), 151.1 (C1), 141.4 (C13), 135.7 (C3), 129.8 (C17), 128.0 (C5), 120.0 (C18), 118.5 (C4), 118.5 (C4), 115.8 (C2), 114.1 (C16), 113.0 (C14), 60.6 (C12), 57.5 (C8), 55.3 (C19), 37.6 (C10), 35.6 (C10').

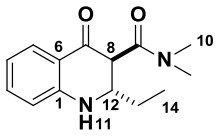
ν_{max} (neat): 3305, 2936, 1633, 1609, 1484, 1260, 1156, 1041, 760, 729 cm^{-1}.

HRMS (ESI): found 347.1355; $C_{19}H_{20}N_2NaO_3$ $[M+Na]^+$ requires 347.1366.

HPLC (Chiralpak OD-H, 50% IPA, 50% hexane, 1.0 mL.min^{-1}, λ = 245): t_R (major) = 6.5, t_R (minor) = 12.1.

$[\alpha]_D^{20.0}$ +31.1 (*c* = 1, $CHCl_3$).

2-Ethyl-*N*,*N*-dimethyl-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide (19)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), *n*-butyraldehyde (34 μL, 0.48 mmol). *Work-up procedure A* was employed: chromatography (silica gel, 1% methanol in dichloromethane). The product dihydroquinolone **19** (60 mg, 100%, 82:18 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 2.***.

δ_H (400 MHz, $CDCl_3$) 7.85 – 7.73 (1 H, dd, *J* 7.9, 1.4, H5), 7.33 – 7.27 (1 H, ddd, *J* 8.3, 7.1, 1.4, H3), 6.75 – 6.67 (2 H, m, H2 & H4), 4.44 (1 H, s, H11), 4.09 (1 H, ddd, *J* 12.6, 7.3, 3.1, H12), 3.73 (1 H, d, *J* 12.7, H8), 3.07 (3 H, s, H10), 3.06 (3 H, s, H10'), 1.75 (1 H, dqd, *J* 15.2, 7.6, 3.1, H 13), 1.62 (1 H, dp, *J* 14.6, 7.4, H13'), 1.03 (3 H, t, *J* 7.5, H14).

δ_H (400 MHz, $CDCl_3$): 7.80 (1H, dd, *J* 7.9, 1.4, H5), 7.30 (1H, ddd, *J* 8.3, 7.1, 1.4, H3), 6.74−6.68 (2H, m, H2 & H4), 4.44 (1H, br s, H11), 4.09 (1H, ddd, *J* 12.6, 7.3, 3.1, H12), 3.73 (1H, d, *J* 12.6, H8), 3.07 (3H, s, H10), 3.06 (3H, s, H10'), 1.75 (1H, dqd, *J* 14.7, 7.3, 3.2, H13), 1.62 (1H, ddq, *J* 14.4, 7.2, 7.2, H13'), 1.03 (3H, t, *J* 7.5, H14). δ_C (101 MHz, $CDCl_3$):

ν_{max} (neat): 3288, 2970, 2875, 1660, 1625, 1610, 1517, 1483, 1155, 1046, 767 cm^{-1}.

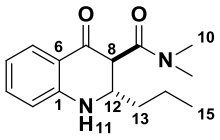
MP: 124−128 °C (dichloromethane).

HRMS (ESI+): found 269.1262; $C_{14}H_{18}N_2NaO_2$, $[M+Na]^+$ requires 269.1260.

HPLC (Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min^{-1}, λ = 245): t_R (major) = 5.7, t_R (minor) = 9.8.

$[\alpha]_D^{20.0}$ +278.8 (c = 1, $CHCl_3$).

N,N-Dimethyl-4-oxo-2-propyl-1,2,3,4-tetrahydroquinoline-3-carboxamide (20)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), *n*-butyraldehyde (43 μL, 0.48 mmol). *Work-up procedure A* was employed: chromatography (silica gel, 1% methanol in dichloromethane). The product dihydroquinolone **20** (64 mg, 100%, 88:12 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 2***.

δ_H (400 MHz, $CDCl_3$) 7.82 (1 H, dd, *J* 8.0, 1.2, H5), 7.35 – 7.28 (1 H, m, H3), 6.73 (1 H, t, *J* 7.5, H4), 6.69 (1 H, d, *J* 8.3, H2), 4.39 (1 H, s, H11), 4.13 (1 H, ddd, *J* 12.5, 7.7, 3.9, H12), 3.72 (1 H,

d, *J* 12.6, H8), 3.08(4) (3 H, s, H10), 3.07(6) (3 H, s, H10'), 1.70 – 1.54 (2 H, m, H13), 1.54 – 1.42 (2 H, m, H14), 0.99 (3 H, t, *J* 7.2, H15).

δ_C (101 MHz, $CDCl_3$) 190.2 (C7), 168.6 (C9), 151.1 (C1), 135.5 (C3), 127.9 (C5), 118.6 (C6), 118.0 (C4), 115.9 (C2), 55.4 (C8), 55.1 (C12), 37.7 (C10), 35.7 (C10' & C11), 18.4 (C13), 14.0 (C14).

ν_{max} (neat): 3284, 2959, 2873, 1664, 1611, 1519, 1484, 1198, 1154, 772 cm^{-1}.

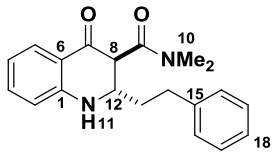
HRMS (ESI+): found 283.1416; $C_{15}H_{20}N_2NaO_2$, $[M+Na]^+$ requires 283.1417.

MP: 106−108 °C (dichloromethane).

HPLC (Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min^{-1}, λ = 237): t_R (major) = 5.4, t_R (minor) = 10.0.

$[\alpha]_D^{20.0}$ +280.3 (c = 1, $CHCl_3$).

N,N-Dimethyl-4-oxo-2-phenethyl-1,2,3,4-tetrahydroquinoline-3-carboxamide (21)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), 3-phenypropionaldehyde (64 μL, 0.48 mmol). *Work-up procedure A* was employed: chromatography (silica gel, 1% methanol in dichloromethane). The product dihydroquinolone **21** (72 mg, 92%, 79:21 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 2***.

δ_H (400 MHz, $CDCl_3$): 7.81 (1H, dd, *J* 8.0, 1.4, H5), 7.28−7.37 (3H, m, H3 & H17), 7.27−7.22 (3H, m, H16 & H18), 6.73 (1H, t, *J* 7.5, H4), 6.55 (1H, d, *J* 8.3, H2), 4.32−4.19 (2H, m, H11 & H12, *H12 appears as a ddd, J 12.4, 7.8, 3.0*), 3.74 (1H, d, *J* 12.5, H8), 3.06 (3H, s, H10'), 3.03 (3H, s, H10'), 2.85 (1H, ddd, *J* 14.0, 8.8, 5.5, H14), 2.79 (1H, ddd, *J* 13.8, 9.0, 7.2, H14'), 2.09−1.90 (2H, m, H13 & H13').

δ_C (101 MHz, $CDCl_3$): 190.0 (C7), 168.4 (C9), 151.0 (C1), 141.0 (C15), 135.5 (C3), 128.7 (C16), 128.4 (C17), 127.8 (C5), 126.4 (C18), 118.6 (C6), 118.1 (C4), 115.7 (C2), 55.6 (C12), 55.4 (C8), 37.6 (C10), 35.7 (C10'), 35.0 (C13), 32.1 (C14).

ν_{max} (neat): 3325 (NH), 3026 (CH), 2929 (CH), 1629, 1609 (amide), 1483, 1343, 1153, 1114, 754, 699 cm^{-1}.

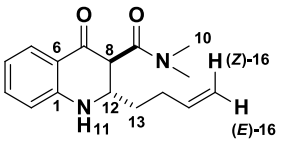
HRMS (ESI+): found 345.1573; $C_{20}H_{22}N_2NaO_2$, $[M+Na]^+$ requires 345.1573.

MP: 54−56 °C (dichloromethane).

HPLC (Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min^{-1}, λ = 245): t_R (major) = 27.4, t_R (minor) = 18.0.

$[\alpha]_D^{20.0}$ +187.7 (c = 1, $CHCl_3$).

2-(But-3-en-1-yl)-*N*,*N*-dimethyl-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide (22)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), 4-pentenal (57 μL, 0.48 mmol). *Work-up procedure A* was employed: chromatography (silica gel,

0.5% methanol in dichloromethane). The product dihydroquinolone **22** (65 mg, 98%, 68:32 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 2***.

δ_H (400 MHz, $CDCl_3$): 7.82 (1H, d, *J* 8.0, H5), 73 (1H, ddd, *J* 8.9, 6.6, 1.2, H3), 6.73 (1H, ddt, *J* 8.9, 6.6, 1.2, H3), 6.73 (1H, ddt, *J* 8.0, 7.2, 0.7, H4), 6.78 (1H, d, *J* 8.3, H2), 5.86 (1H, ddt, *J* 17.0, 10.3, 6.7, H15), 5.12 (1H, d, *J* 17.1, (*Z*)-H16), 5.04 (1H, d, *J* 10.1, (*E*)-H16), 4.50 (1H, br s, H11), 4.17 (1H, ddd, *J* 12.1, 8.5, 3.3, H12), 3.73 (1H, d, *J* 12.5, H8), 3.08 (3H, s, H10), 3.07 (3H, s, H10'), 2.31−2.19 (2H, m, H14), 1.86−1.77 (1H, m, H13), 1.76−1.65 (1H, m, H13').

δ_C (101 MHz, $CDCl_3$): 190.0 (C7), 168.5 (C9), 151.1 (C1), 137.6 (C15), 135.5 (C3), 127.9 (C5), 118.6 (C6), 118.1 (C4), 115.8 (C2/C16), 115.7 (C2/C16), 55.3 (C8), 55.2 (C12), 37.7 (C10), 35.7 (C10'), 32.4 (C13), 29.7 (C14).

HRMS (ESI+): found 295.1412; $C_{16}H_{20}N_2NaO_2$, $[M+Na]^+$ requires 295.1417.

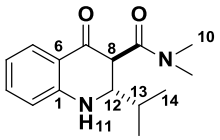
MP: 146−150 °C (dichloromethane).

ν_{max} (neat): 3325 (NH), 3075 (CH), 2927 (CH), 1631, 1610 (amide), 1483, 1346, 1154, 912, 759 cm^{-1}.

$[\alpha]_D^{20.0}$ +143.7 (c = 1, $CHCl_3$).

HPLC (Chiralpak ODH, 30% IPA, 70% hexane, 1.0 mL.min^{-1}, λ = 245): t_R(major) = 5.5, t_R(minor) = 9.6.

2-i*so*-Propyl-*N*,*N*-dimethyl-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide (23)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), *n*-butyraldehyde (44 μL, 0.48 mmol). *Work-up procedure A* was employed: chromatography (silica gel, 0.5% methanol in dichloromethane). The product dihydroquinolone **23** (64 mg, 100%, 59:41 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 2***.

δ_H (400 MHz, $CDCl_3$): 7.81 (1H, d, *J* 7.9, H5), 7.31 (1H, t, *J* 8.1, H3), 6.74−6.68 (2H, m, H2 & H4), 4.26 (1H, br s, H11), 4.07 (1H, dd, *J* 12.5, 2.8, H12), 3.84 (1H, d, *J* 12.4, H8), 3.10 (3H, s, H10), 3.07 (3H, s, H10'), 2.04 (1H, septet of doublets, *J* 6.9, 2.8, H13), 1.10 (3H, d, *J* 7.1, H14), 0.95 (3H, d, *J* 6.9, H14').

δ_C (101 MHz, $CDCl_3$): 190.5 (C7), 168.6 (C9), 151.4 (C1), 135.5 (C3), 127.8 (C5), 118.4 (C6), 117.8 (C4), 115.9 (C2), 59.7 (C12), 53.2 (C8), 37.6 (C10), 35.7 (C10'), 28.9 (C13), 19.7 (C14), 15.7 (C14').

ν_{max} (neat): 3319 (NH), 2959 (CH), 2934 (CH), 1663 (ketone), 1631 (amide), 1514, 1484, 1302, 1146, 1094, 769, 755 cm^{-1}.

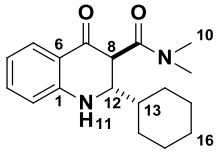
HRMS (ESI+): found 283.1418; $C_{15}H_{20}N_2NaO_2$, $[M+Na]^+$ requires 283.1417.

MP: 130−136 °C (dichloromethane).

HPLC (Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min^{-1}, λ = 245): t_R (major) = 5.5, t_R (minor) = 9.7.

$[\alpha]_D^{20.0}$ +36.5 (c = 1, $CHCl_3$).

2-Cyclohexyl-*N*,*N*-dimethyl-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide (24)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), cyclohexanecarboxaldehyde (58 μL, 0.48 mmol). *Work-up procedure A* was employed: chromatography (silica gel, 0.5% methanol in dichloromethane). The product dihydroquinolone **24** (63 mg, 87%, 90:10 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 2***.

δ_H (400 MHz, $CDCl_3$): 7.81 (1H, dd, *J* 7.9, 1.1, H5), 7.31 (1H, t, *J* 7.6, H3), 6.74−6.66 (2H, m, H2 & H4), 4.31 (1H, br s, H11), 4.03 (1H, d, *J* 11.1, H12), 3.89 (1H, d, *J* 11.9, H8), 3.10 (3H, s, H10), 3.07 (3H, s, H10'), 1.90−1.57 (6H, m, H13 & 5 x H14/H15/H16), 1.41−1.11 (5H, m, 5 x H14/H15/H16).

δ_C (126 MHz, $CDCl_3$): 190.7 (C7), 168.7 (C9), 151.2 (C1), 135.4 (C3), 127.7 (C5), 118.4 (C6), 117.8 (C4), 115.8 (C2), 59.5 (C12), 52.5 (C8), 39.2 (C13), 37.7 (C10), 35.7 (C10'), 30.4 (C14/C15/C16), 26.7 (C14/C15/C16), 26.4 (C14/C15/C16), 26.3(5) (C14/C15/C16), 26.2(9) (C14/C15/C16).

ν_{max} (neat): 3339 (NH), 2927 (CH), 2853 (CH), 1634, 1612 (amide), 1484, 1398, 759, 731 cm^{-1}.

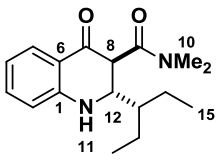
HRMS (ESI+): found 323.1731; $C_{18}H_{24}N_2NaO_2$, $[M+Na]^+$ requires 323.1731.

MP: 140−142 °C (dichloromethane).

$[\alpha]_D^{20.0}$ +334.0 (c = 1, $CHCl_3$).

HPLC (Chiralpak ODH, 30% IPA, 70% hexane, 1.0 mL.min^{-1}, λ = 245): t_R(major) = 5.3, t_R(minor) = 9.8.

_N,N_-Dimethyl-4-oxo-2-(pentan-3-yl)-1,2,3,4-tetrahydroquinoline-3-carboxamide (25)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), cyclohexanecarboxaldehyde (59 μL, 0.48 mmol). *Work-up procedure A* was employed: chromatography (silica gel, 0.5% methanol in dichloromethane). The product dihydroquinolone **25** (69 mg, 99%, 77% ee, >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 2***.

δ_H (400 MHz, $CDCl_3$) 7.81 (1 H, dd, *J* 7.9, 1.3, H5), 7.30 (1 H, ddd, *J* 8.4, 7.0, 1.5, H3), 6.74 – 6.66 (2 H, m, H2 & H4), 4.26 (1 H, dd, *J* 12.8, 2.1, H12), 4.22 (1 H, br s, H11), 3.93 (1 H, d, *J* 12.7, H8), 3.09 (3 H, s, H10), 3.07 (3 H, s, H10'), 1.69 – 1.44 (3 H, m, H13 & 2 x H14), 1.40 – 1.15 (2 H, m, 2 x H14), 1.01 (3 H, t, *J* 7.4, H15), 0.95 (3 H, t, *J* 7.4, H15').

δ_C (101 MHz, $CDCl_3$) 190.7 (C7), 168.6 (C9), 151.4 (C1), 135.4 (C3), 127.9 (C5), 118.3 (C6), 117.7 (C4), 115.8 (C2), 56.5 (C12), 52.8 (C8), 42.2 (C13), 37.7 (C10), 35.7 (C10'), 23.4 (C14), 21.7 (C14'), 12.7 (C15), 11.8 (C15').

ν_{max} (neat): 3339, 2961, 2874, 1634, 1612, 1509, 1484, 1259, 1150, 758 cm^{-1}.

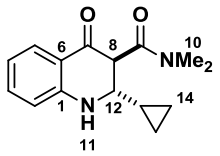
HRMS (ESI): found 311.1721; $C_{17}H_{14}N_2NaO_2$ $[M+Na]^+$ requires 311.1730.

MP: 96–98 °C (dichloromethane).

HPLC (Chiralpak IC, 50% IPA, 50% hexane, 1.0 mL.min^{-1}, λ = 245): t_R (major) = 10.0, t_R (minor) = 13.6.

$[\alpha]_D^{20.0}$ +219.8 (c = 1, $CHCl_3$).

2-Cyclopropyl-*N*,*N*-dimethyl-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide (26)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), cyclopropanecarboxaldehyde (36 μL, 0.48 mmol). *Work-up procedure A* was employed: chromatography (silica gel, 0.5% methanol in dichloromethane). The product dihydroquinolone **26** (60 mg, 97%, 65:35 e.r., >20:1 dr) was obtained as a yellow foam.

Racemic: prepared according to ***general procedure 2***.

δ_H (400 MHz, $CDCl_3$) 7.81 (1 H, dd, *J* 8.0, 1.6, H5), 7.30 (1 H, ddd, *J* 8.3, 7.0, 1.5, H3), 6.77 – 6.55 (2 H, m, H2 & H4), 4.48 (1 H, s, H11), 3.92 (1 H, d, *J* 12.4, H8), 3.38 (1 H, dd, *J* 12.3, 9.0, H12), 3.14 (3 H, s, H10), 3.07 (3 H, s, H10'), 1.09 – 0.89 (1 H, m, H13), 0.64 – 0.51 (3 H, m 3 x H14), 0.39 – 0.26 (1 H, m, H14).

δ_C (101 MHz, $CDCl_3$) 188.3 (C7), 166.6 (C9), 148.9 (C1), 133.4 (C5), 125.8 (C3), 116.3 (C6), 115.8 (C4), 113.5 (C2), 58.0 (C12), 54.3 (C8), 35.8 (C10), 33.6 (C10'), 13.7 (C13), 1.1 (C14), 0.0 (C14').

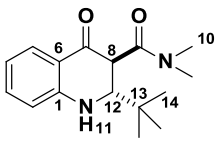
HRMS (ESI+): found 281.1266; $C_{15}H_{18}N_2NaO_2$, $[M+Na]^+$ requires 281.1260.

ν_{max} (neat): 3324, 3005, 1637, 1612, 1505, 1483, 757 cm^{-1}.

HPLC (Chiralpak IC, 50% IPA, 50% hexane, 1.0 $mL.min^{-1}$, λ = 245): t_R (major) = 14.2, t_R (minor) = 18.5.

$[\alpha]_D^{20.0}$ +88.8 (c = 1, $CHCl_3$).

2-(*Tert*-butyl)-*N*,*N*-dimethyl-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide (27)



Asymmetric: prepared according to ***general procedure 1***. Aniline **1** (50 mg, 0.24 mmol), pivaldehyde (52 μL, 0.48 mmol). *Work-up procedure A* was employed: chromatography (silica gel, 1% methanol in dichloromethane). The product dihydroquinolone **27** (62 mg, 94%, 90:10 e.r., >20:1 dr) was obtained as a yellow solid.

Racemic: prepared according to ***general procedure 2***.

δ_H (400 MHz, $CDCl_3$): 7.67 (1H, dd, *J* 8.3, 1.4, H5), 7.24 (1H, ddd, *J* 8.2, 7.2, 1.3, H3), 6.62−6.56 (2H, m, H2 & H4), 4.60 (1H, br s, H11), 3.96 (1H, d, *J* 5.4, H8), 3.76 (1H, dd, *J* 5.2, 2.1, H12), 3.25 (3H, s, H10), 2.97 (3H, s, H10'), 0.98 (9H, s, H14).

δ_C (101 MHz, $CDCl_3$): 190.1 (C7), 169.4 (C9), 150.9 (C1), 135.9 (C3), 127.4 (C5), 116.7 (C4), 116.5 (C6), 115.2 (C2), 62.3 (C12), 49.6 (C8), 38.1 (C10), 36.2 (C10'), 29.7 (C13), 26.4 (C14).

ν_{max} (neat): 3343 (NH), 2918 (CH), 1613 (amide), 1529, 1485, 1445, 1143, 1054, 906, 758 cm^{-1}.

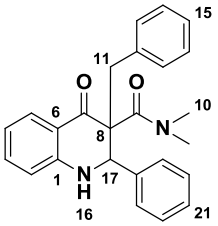
HRMS (ESI+): found 297.1572; $C_{16}H_{22}N_2NaO_2$, $[M+Na]^+$ requires 297.1573.

MP: 124−128 °C (dichloromethane).

HPLC (Chiralpak IA, 30% IPA, 70% hexane, 1.0 mL.min^{-1}, λ = 245): t_R (major) = 7.7, t_R (minor) = 5.6.

$[\alpha]_D^{20.0}$ +616.6 (c = 0.11, $CHCl_3$).

(±)-3-Benzyl-*N*,*N*-dimethyl-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxamide (29)



Benzaldehyde (7 μL, 0.07 mmol) was added to a stirred RT solution of aniline **28** (10 mg, 0.033 mmol) and scandium(III) trifluoromethanesulfonate (2 mg, 4 μmol) in dichloromethane (0.5 mL). After 16 h the solvent was removed *in vacuo* and the residue was purified by flash column chromatography (silica gel, petrol:ethyl acetate, 4:1) to afford dihydroquinolone **29** (9 mg, 69%) as a yellow solid.

δ_H ($CDCl_3$, 500 MHz): 7.74 (1H, dd, *J* 7.9, 1.3, H5), 7.40−7.34 (4H, m, H3, H13 & H21), 7.34-7.30 (2H, m, H14), 7.16−7.10 (5H, m, H15, H19, H20), 6.79 (1H, t, *J* 7.6, H4), 6.71 (1H, d, *J* 8.2, H2), 5.37 (1H, s, H17), 4.72 (1H, br s, H16), 3.21 (1H, d, *J* 13.3, H11), 3.14 (1H, d, *J* 13.2 H11'), 2.88 (3H, br s, H10), 2.68 (3H, br s, H10).

δ_C ($CDCl_3$, 126 MHz):* 168.5 (C9), 149.7 (C1), 137.2 (C12/C18), 137.1 (C12/C18), 135.5 (C3), 131.4 (C19), 128.9 (C21), 128.7 (C13), 128.2 (C5), 127.9 (C14), 127.5 (C20), 126.4 (C15), 118.8 (C6), 118.3 (C4), 115.4 (C2), 63.9 (C8), 63.7 (C17), 38.6 (C10), 37.6 (C10'), 34.8 (C11).

MP: 214−220 °C (ethyl acetate/petrol).

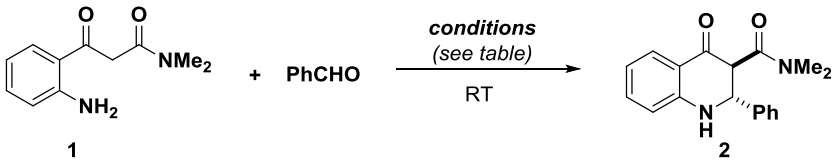
* *The ^{13}C peak corresponding to C7 was not observed.*

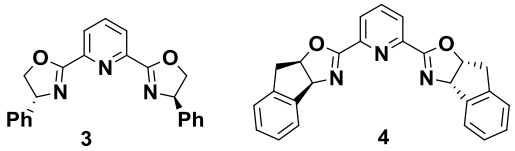
HRMS (ESI+): found 407.1714; $C_{25}H_{24}N_2NaO_2$, $[M+Na]^+$ requires 407.1730.

ν_{max} (neat): 3328 (NH), 2924 (CH), 2853 (CH), 1738, 1636, 1609, 1154, 728, 697 cm^{-1}.

3. SCREENING ASYMMETRIC CONDITIONS

3.1 Asymmetric Lewis Acidic Conditions





Entry[i]	Solvent[ii]	Catalyst[iii]	Ligand (eq.)	Conversion (time) [iv]	e.r. [v]
1[15]	1:1 THF:PhMe	$Sc(OTf)_3$	**5** (0.11)	100% (2 h)	50:50
2[15]	1:1 THF:PhMe	$Sc(OTf)_3$	**3** (0.11)	100% (2 h)	50:50
3[15]	1:1 THF:PhMe	$Cu(OTf)_2$	**5** (0.11)	56% (16 h)	50:50
4[15]	1:1 THF:PhMe	$Cu(OTf)_2$	**3** (0.11)	49% (16 h)	50:50
5[15]	1:1 THF:PhMe	$Zn(OTf)_2$	**5** (0.11	0% (16 h)	-
6[15]	1:1 THF:PhMe	$Zn(OTf)_2$	**3** (0.11)	0% (16 h)	-
7[16]	MeCN	$Sc(OTf)_3$	**3** (0.2)	100% (20 min)	54:46
8[17]	CH_2Cl_2	$Sc(OTf)_3$ (0.01 eq.)	**3** (0.025)	100% (3 h)	50:50
9[17]	CH_2Cl_2	$Sc(OTf)_3$ (0.01 eq.)	**4** (0.025)	100% (3 h)	52:48

[i] *References given where literature procedures were followed.* [ii] *All reactions were carried out on 25−50 mg scale (aniline) with 2.0 eq. aldehyde at RT. Unless stated otherwise, all reactions were carried out using 0.1 eq. catalyst.* [iii] *In all cases the catalyst and ligand were stirred for 1−3 h in the presence of powdered 3 or 4 Å molecular sieves prior to adding the aniline and aldehyde.* [iv] *Values determined by ^{1}H NMR analysis after reaction reached completeness (TLC) or after 16 h.* [v] *Determined by chiral HPLC.*

Entries 1−6. These reactions were carried out by analogy to a literature protocol, according to the following general procedure:[15]

A suspension of *the appropriate metal triflate* (0.012 mmol), *the appropriate ligand* (0.013 mmol) and 4 Å powdered molecular sieves (30 mg) in tetrahydrofuran (1 mL) was stirred for 2 h at RT. Amine **1** (25 mg, 0.12 mmol) in toluene (1 mL) and benzaldehyde (24 μL, 0.24 mmol) were added. *Reaction completeness was monitored approximately by TLC and conversion was determined by ^{1}H NMR analysis. HPLC analysis was carried out on pure samples of the product **2** isolated by small-scale preparative TLC.*

Entry 7. This reaction was carried out by analogy to a literature procedure.[16]

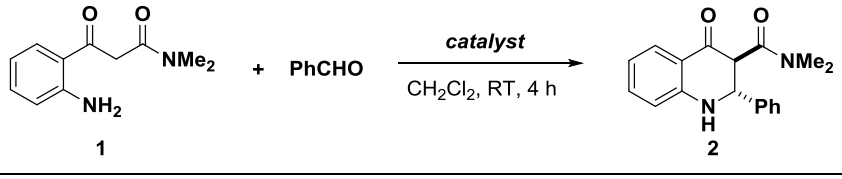
A suspension of scandium(III) triflate (12 mg, 0.024 mmol), (*R*)-phenylpybox **3** (18 mg, 0.049 mmol) and 3 Å powdered molecular sieves (150 mg) in acetonitrile (3 mL) was stirred vigorously for 80 min. Aniline **1** (50 mg, 0.24 mmol) and benzaldehyde (49 μL, 0.48 mmol) were added, and the reaction was monitored by TLC. After 20 min TLC indicated consumption of the starting material; the reaction mixture was concentrated *in vacuo* and ^{1}H NMR analysis of the crude material indicated complete conversion to the product. The crude residue was purified by column chromatography (silica gel, 99:1, dichloromethane:methanol) to afford dihydroquinolone **2** (66 mg, 93%, 54:46 e.r.) as a yellow crystalline solid.

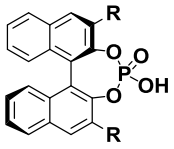
Entries 8 & 9. These reactions were carried out by analogy to a literature protocol, according to the following general procedure:[17]

A suspension of scandium(III) triflate (1.2 mg, 0.0024 mmol), *the appropriate ligand* (0.060 mmol) and 4 Å powdered molecular sieves (25 mg) in dichloromethane (1 mL) was stirred for 3 h at RT. Aniline **1** (50 mg, 0.24 mmol) and benzaldehyde (49 μL, 0.48 mmol) were added. *Reaction completeness was monitored approximately by TLC and conversion was determined by ^{1}H NMR analysis.. HPLC analysis was carried out on pure samples of the product **2** isolated by small-scale preparative TLC.*

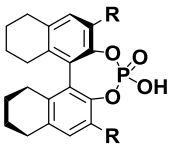
3.2 Asymmetric Brønsted Acidic Conditions

3.2.1 Catalyst Screening

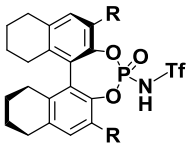




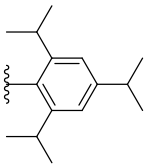
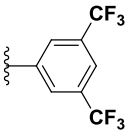
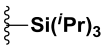
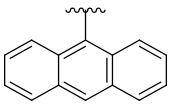
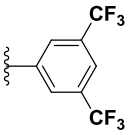
entries 1-5



entry 6

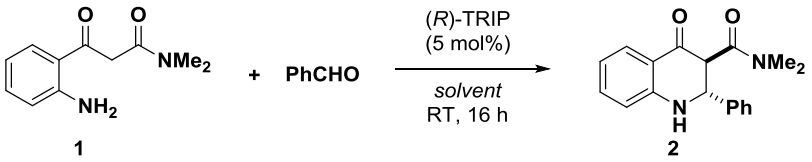


entry 7

Entry	R	e.r. [ii]
1		67:33
2		47:53
3		46:54
4		53:47
5		54:46
6		41:59
7		51:49

[i] *All reactions were carried out at RT on a 10 mg scale (aniline) with 2.0 eq. benzaldehyde and 5 mol% catalyst in dichloromethane at an aniline concentration of 0.1 M. All reactions went to completion (TLC) after 4 h. Yields not determined.* [ii] *Determined by chiral HPLC.*

3.2.2 Solvent Screen

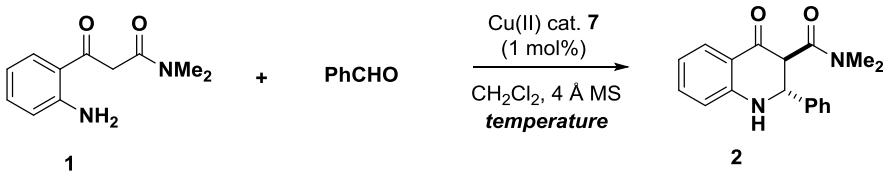


Entry[i]	Solvent	Aniline conc. / M	e.r. [ii]
1	CH_2Cl_2	0.05	57:43
2	CH_2Cl_2	0.10	67:33
3	CH_2Cl_2	0.20	56:44
4	MeCN	0.10	54:46
5	MeOH	0.10	47:53[iii]
6	THF	0.10	51:49
7	Et_2O	0.10	64:46
8	iPr_2O	0.10	~60:40[iv]
9	PhMe	0.10	70:30
10	PhCl	0.10	70:30

[i] *All reactions were carried out at RT on a 10 mg scale (aniline) with 2.0 eq. benzaldehyde and 5 mol% catalyst, and were analysed after 16 h. Yields not determined.* [ii] *Determined by chiral HPLC.* [iii] *Unidentified contaminant present in HPLC trace; ee value may be inaccurate.* [iv] *ee value approximate due to poor conversion leading to high noise/signal ratio in HPLC trace.*

3.3 Optimization of Reaction Conditions for use of Catalyst 7

3.3.1 Temperature Screen



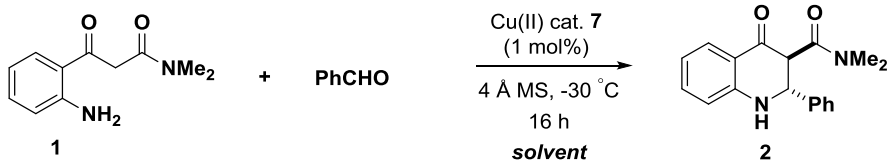
Entry[i]	Temp. / °C	Conv. / % (time) [ii]	e.r. [iii]
1	RT	100 (1 h)	70:30
2	−30	84 (16 h)	70:30
3	−50	25 (16 h)	69:31
4	−78	~5 (48 h)	63:37

[i] *All reactions were carried out on a 25 mg scale (aniline) with 2.0 eq. aldehyde and 1 mol% catalyst* ***7*** *at an aniline concentration of 0.1 M. Yields not determined.* [ii] *Determined by* ^{1}*H NMR analysis of the crude reaction mixture.* [iii] *Determined by chiral HPLC.*

Procedure:

Benzaldehyde (25 μL, 0.25 mmol) was added to a stirred suspension of aniline **1** (25 mg, 0.12 mmol), oven-dried 4 Å molecular sieves (25 mg) and copper catalyst **7** (2.2 mg, 1.2 μmol) in dichloromethane (1.25 mL) at *the appropriate temperature*. After *the indicated time period* the reaction was diluted with dichloromethane (100 mL) and filtered over a short plug of silica to remove the catalyst, and the solvents removed *in vacuo*. ^{1}*H NMR analysis was carried out on the crude material. HPLC analysis was carried out on pure samples of the product* ***2*** *isolated by small-scale preparative TLC.*

3.3.2 Solvent Screen



Entry[i]	Solvent	Conv. / % [ii]	e.r. [iii]
1	CH_2Cl_2	84	70:30
2	MeCN	NR	-
3	PhCl	55	52:48
4	MeOH	NR	-
5	THF	70	76:24

[i] *All reactions were carried out on a 25 mg scale (aniline) with 2.0 eq. aldehyde and 1 mol% catalyst* ***7*** *at an aniline concentration of 0.1 M in the presence of 4 Å MS, and were analysed after 16 h. Yields not determined.* [ii] *Determined by ^{1}H NMR analysis of the crude reaction mixture.* [iii] *Determined by chiral HPLC.*

Entry[i]	Solvent ratio THF:PhMe v/v	Aniline conc. / M	e.r. [iii]
1	1:0	0.1	76:24
2	10:1	0.1	77:23
3	1:1	0.1	80:20
4	1:10	0.1	64:36
5	1:0	0.05	76:24

[i] *All reactions were carried out on a 25 mg (aniline) scale with 2.0 eq. aldehyde and 1 mol% catalyst* ***7*** *in the presence of 4 Å MS, and were analysed after 48 h. Yields not determined. All reactions went to completion (TLC, ^{1}H NMR).* [iii] *Determined by chiral HPLC.*

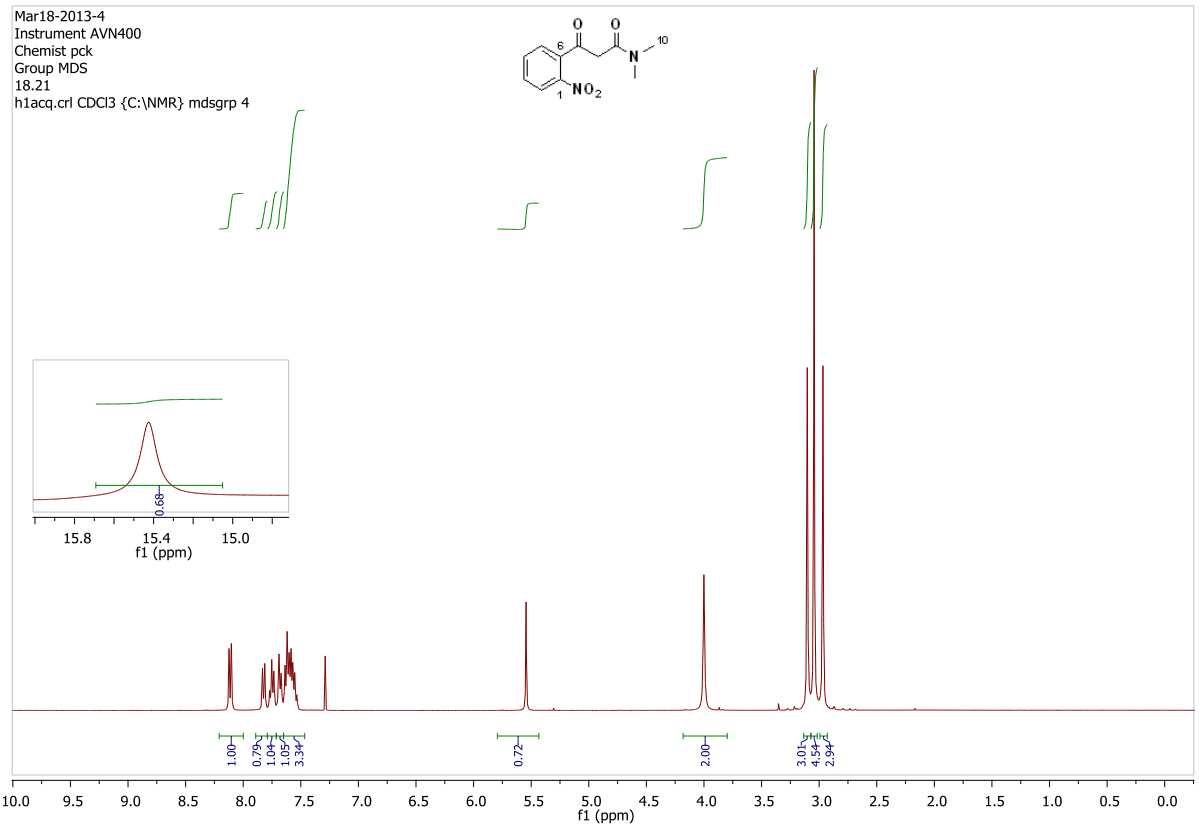
Procedure

Benzaldehyde (25 μL, 0.25 mmol) was added to a stirred −30 °C suspension of aniline **1** (25 mg, 0.12 mmol), oven-dried 4 Å molecular sieves (25 mg) and copper catalyst **7** (2.2 mg, 1.2 μmol) in *the appropriate solvent* at *the indicated concentration*. After *the indicated time period* the reaction was diluted with dichloromethane (100 mL) and filtered over a short plug of silica to remove the catalyst, and the solvents removed *in vacuo*. *^{1}H NMR analysis was carried out on the crude material. HPLC analysis was carried out on pure samples of the product **2** isolated by small-scale preparative TLC.*

4. NMR SPECTRA

4.1 Substrates and Precursors

S1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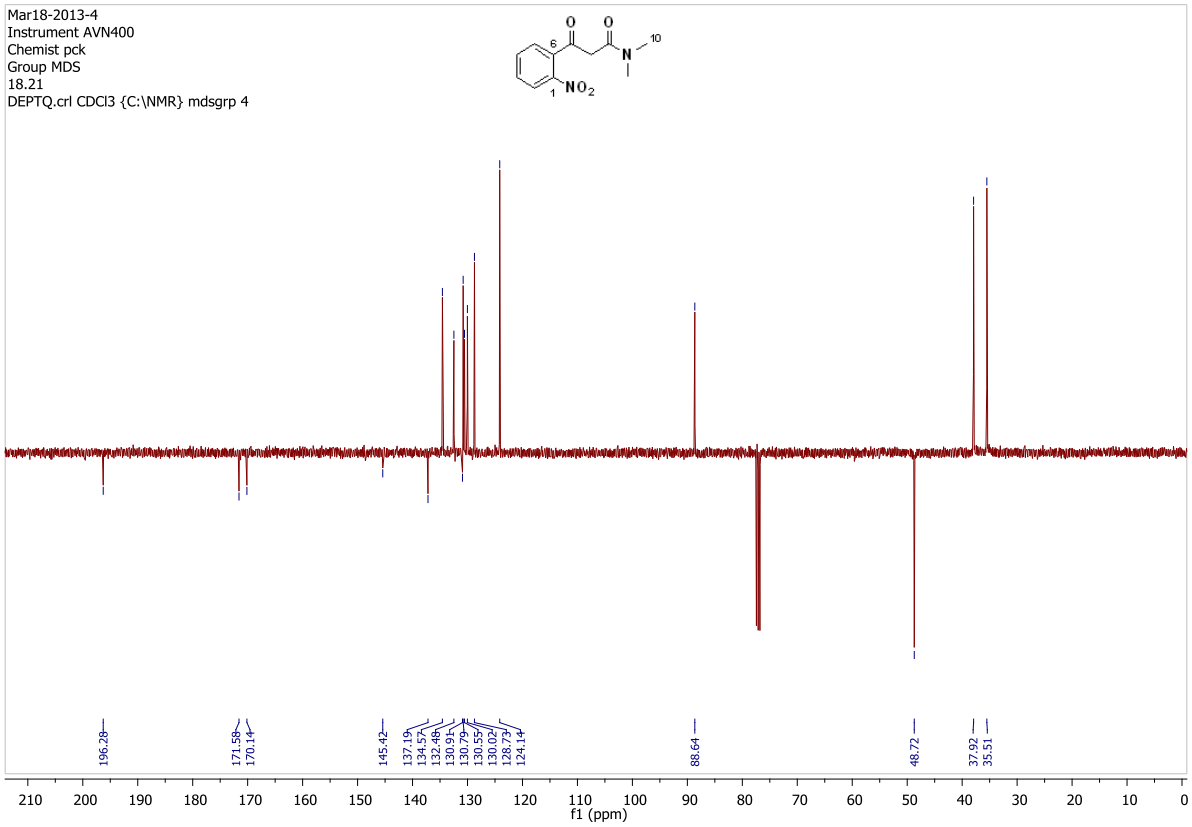
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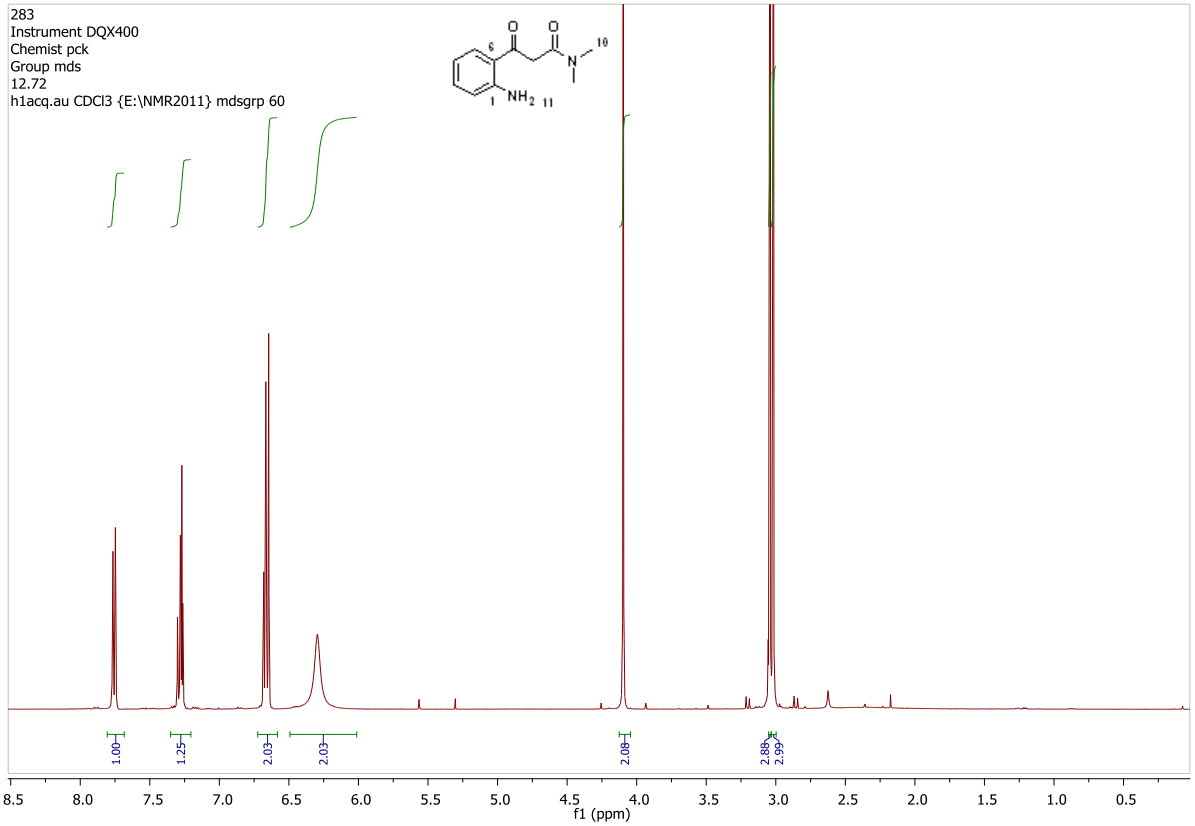
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2.88
2.99
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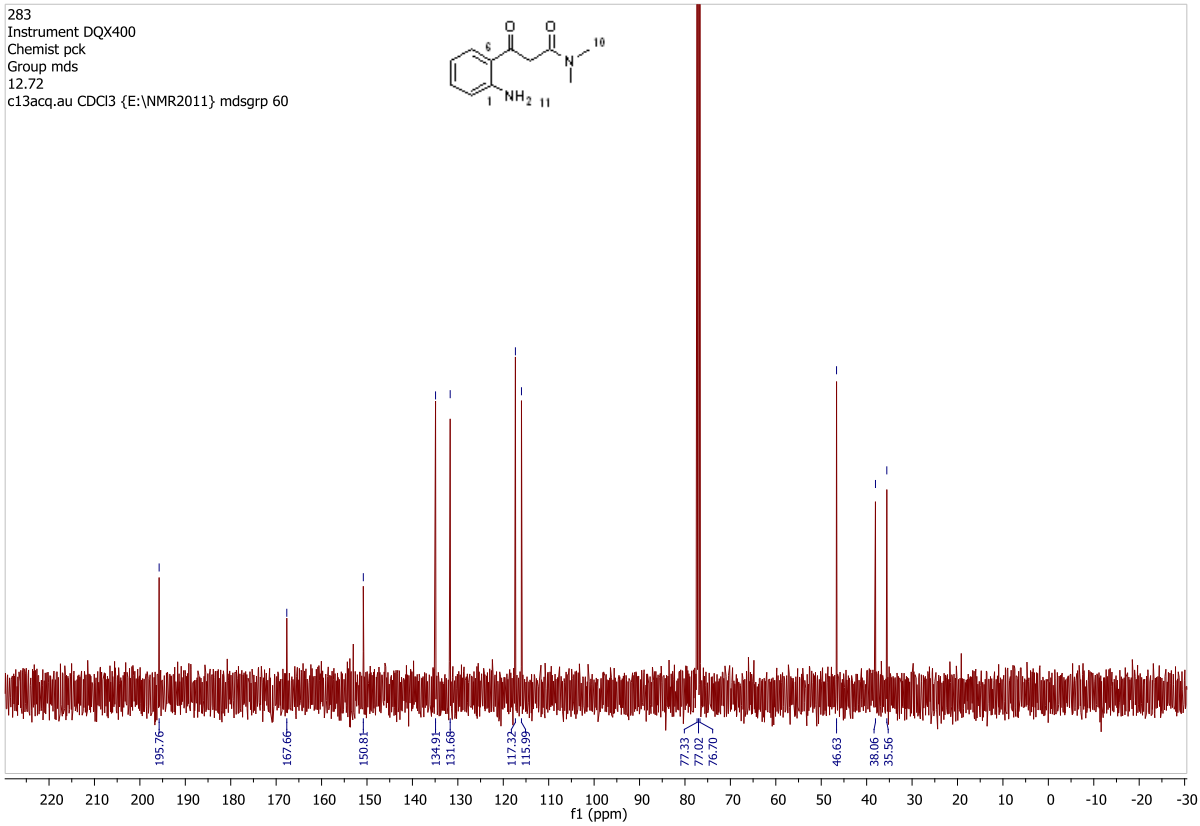
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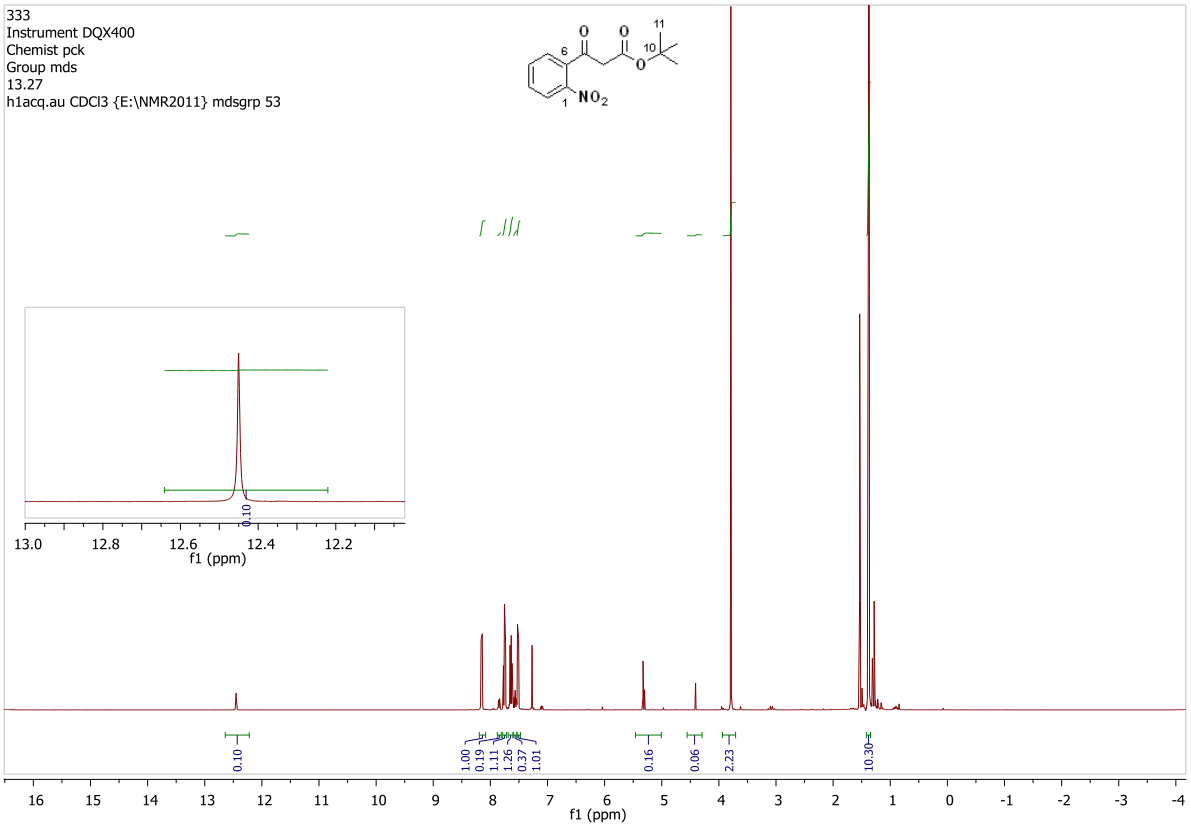
38.06
35.56
f1 (ppm)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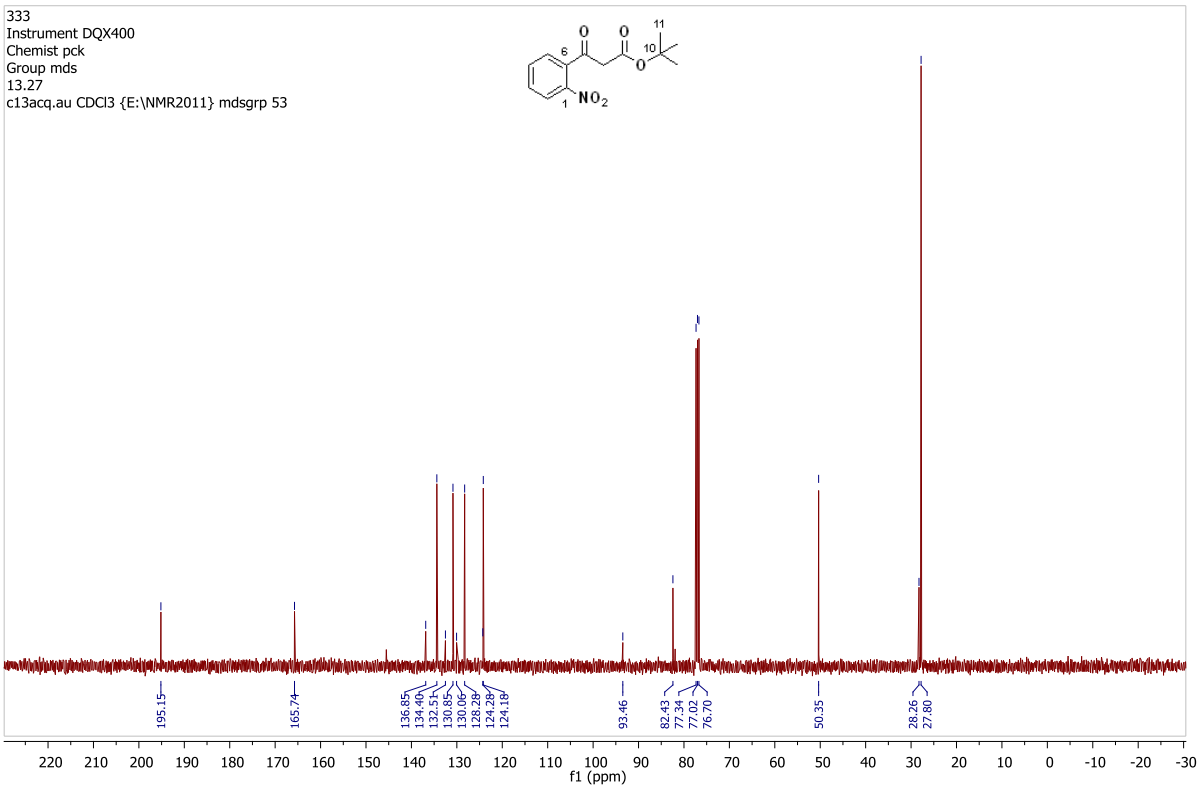
f1 (ppm)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Group mds
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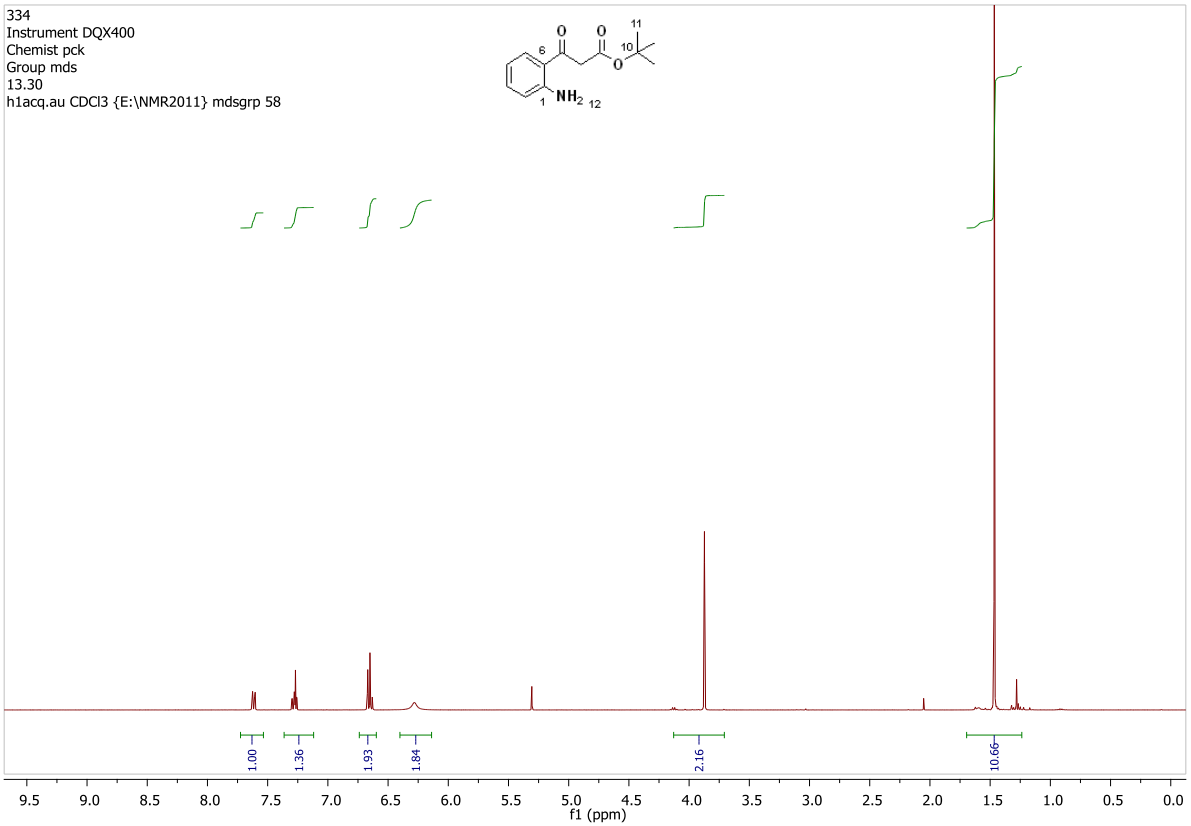
f1 (ppm)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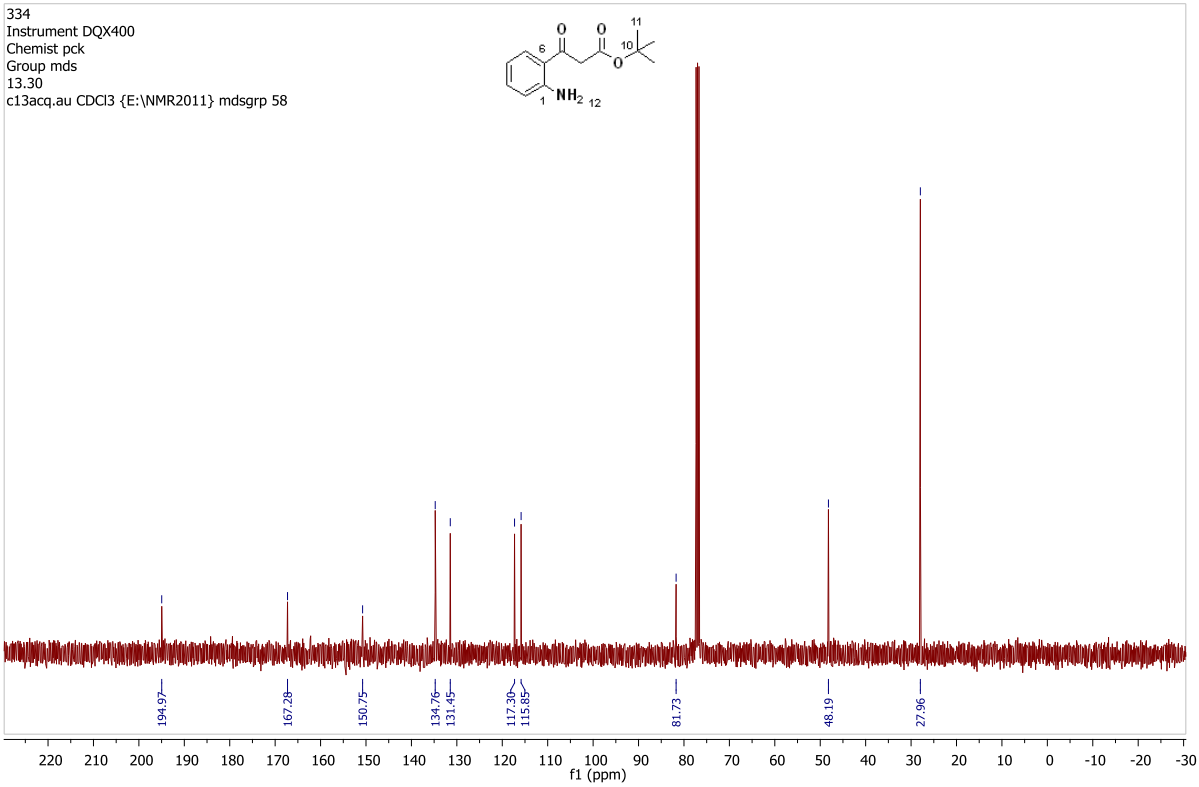
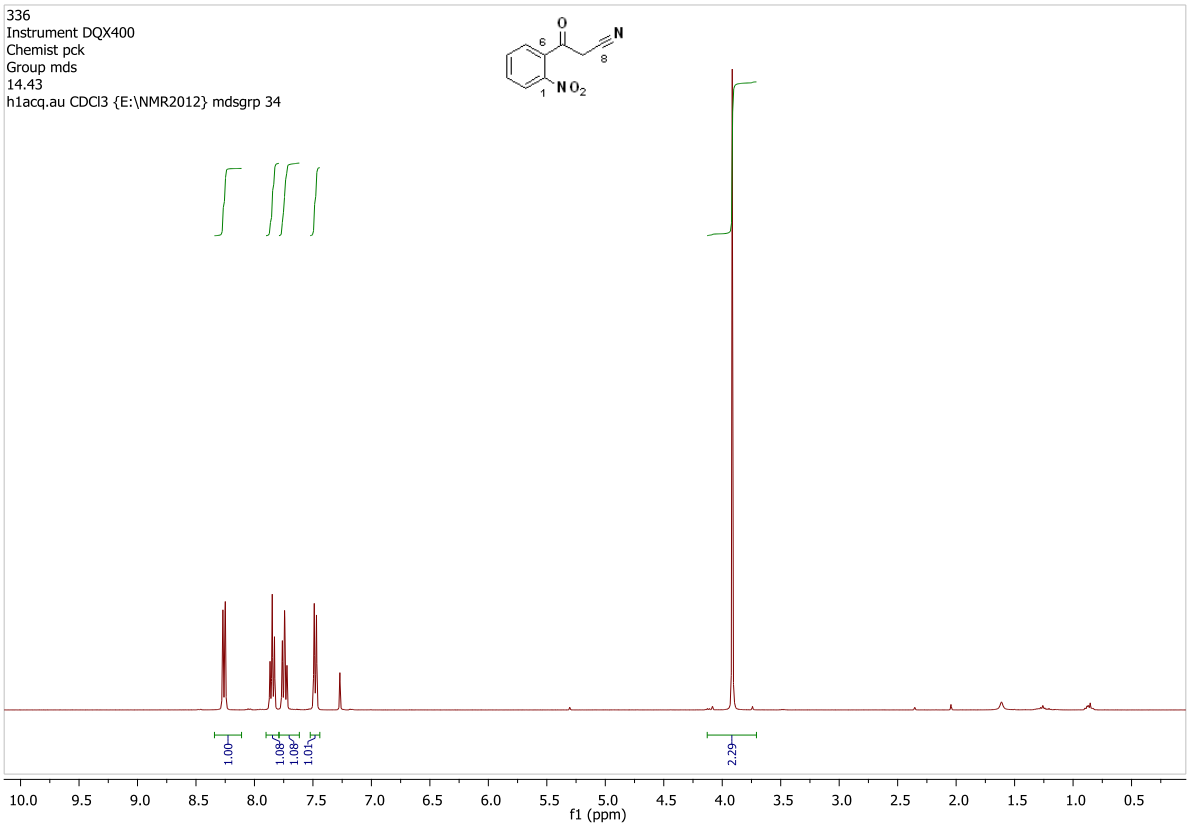
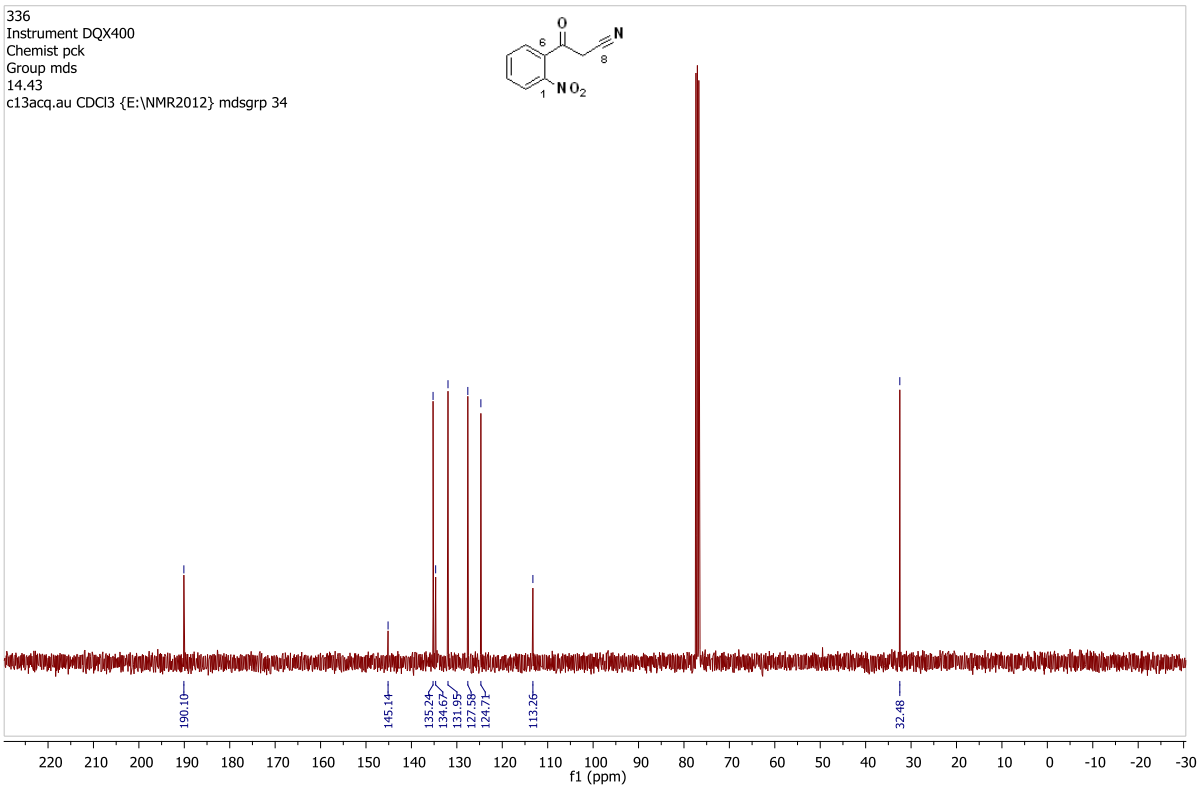
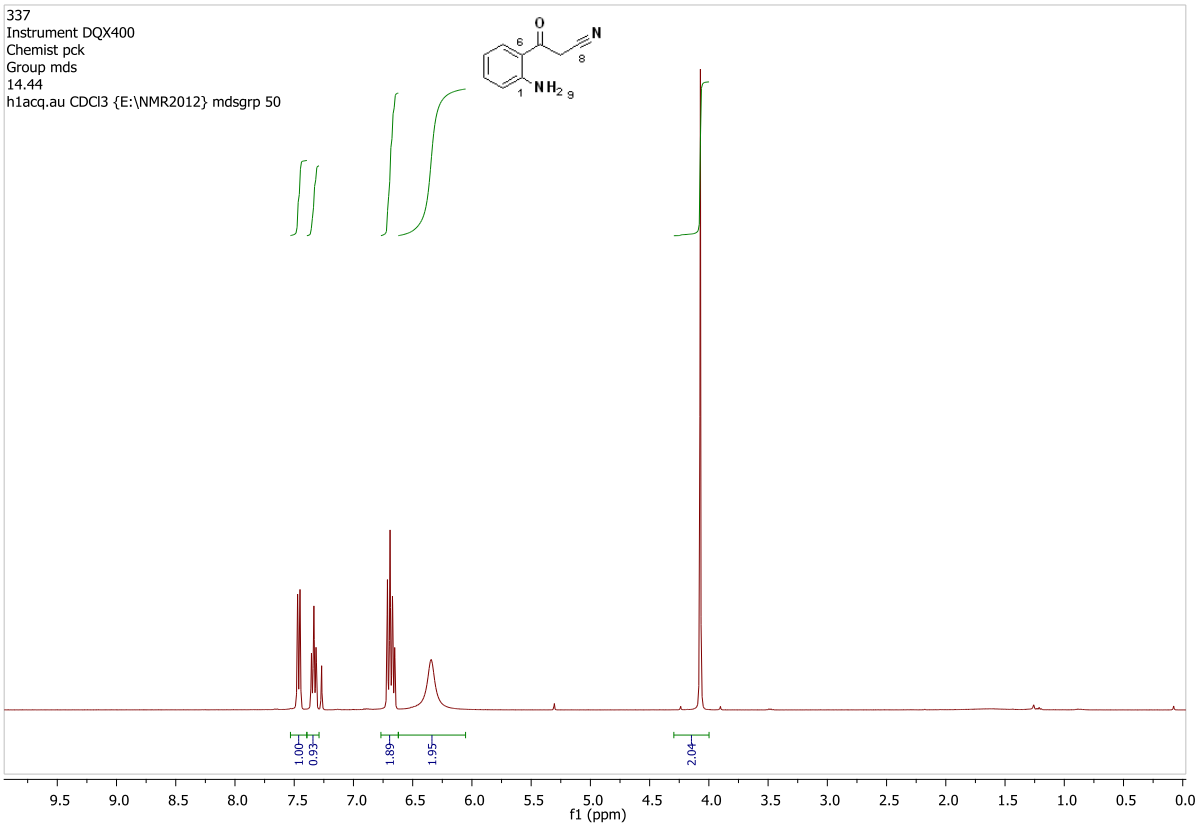
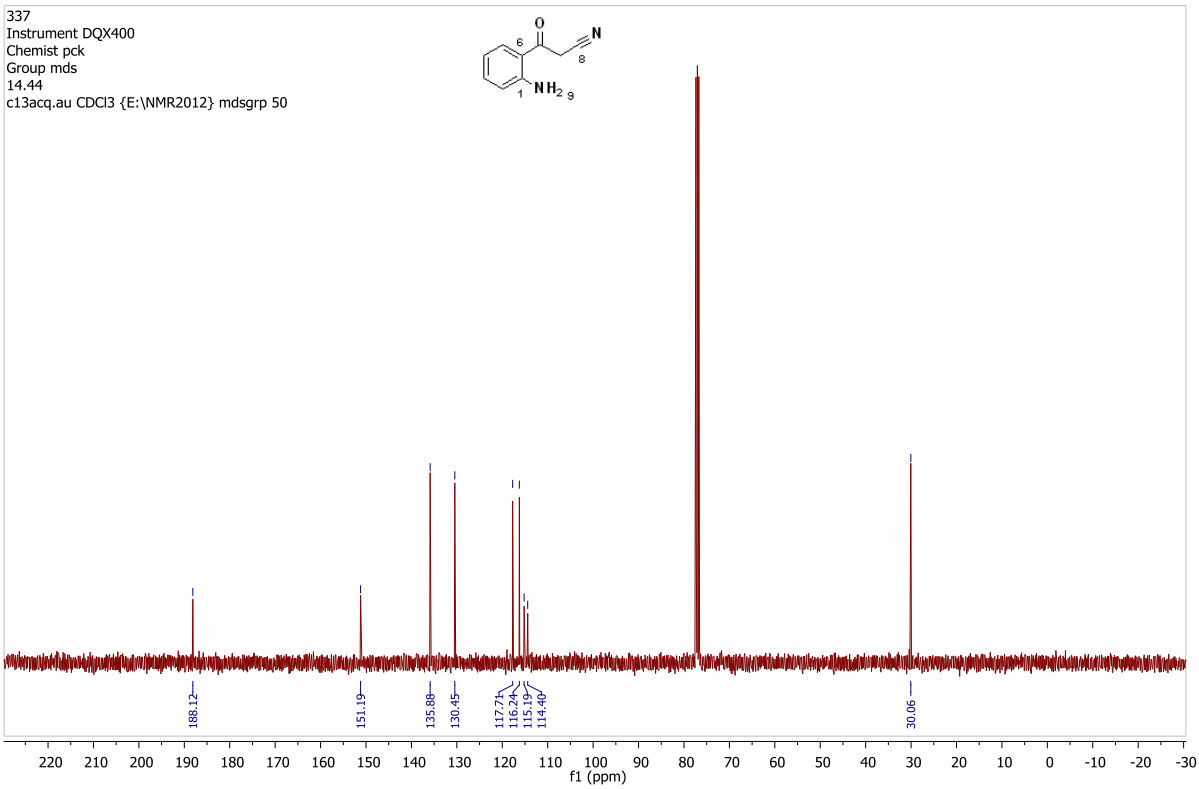
1.93
1.84
2.16
10.66
f1 (ppm)

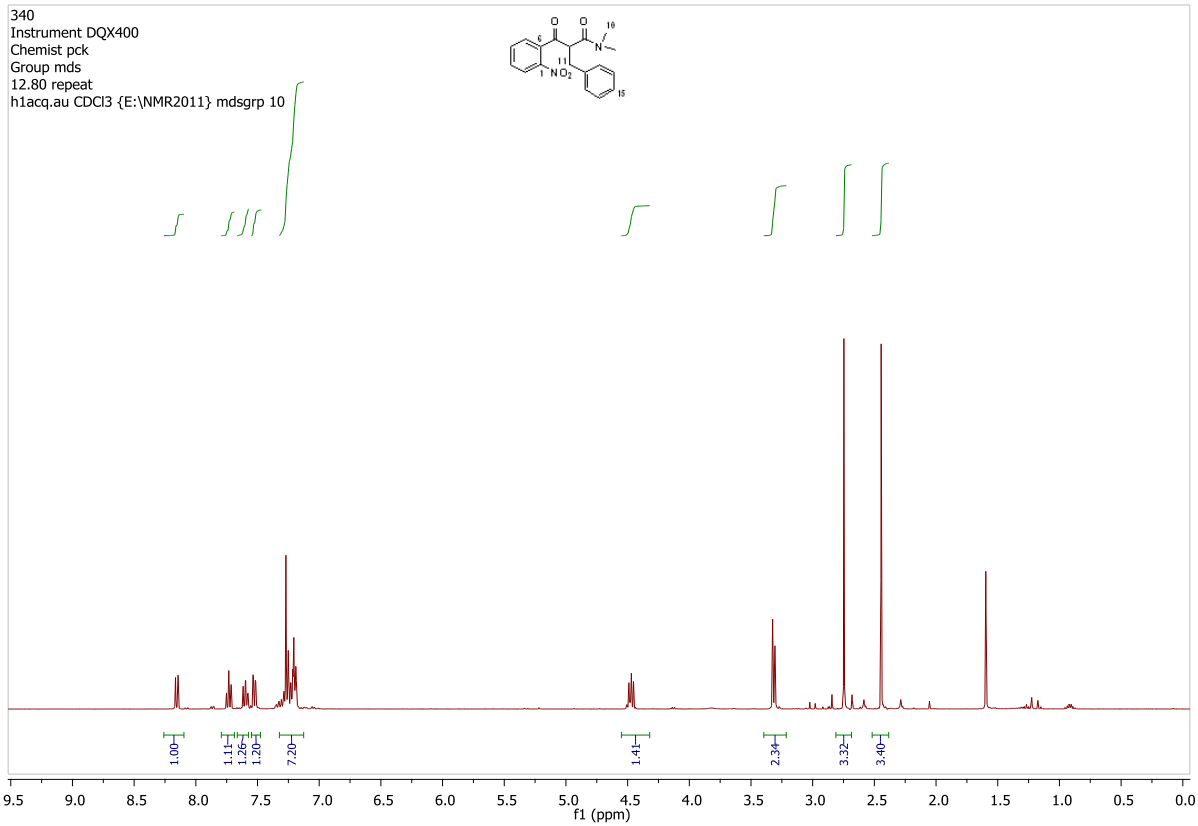

334
Instrument DQX400
Chemist pck
Group mds
13.30
c13acq.au CDCl3 {E:\NMR2011} mdsgrp 58
194.97
167.28
150.75
134.76
131.45
117.30
115.85
81.73
48.19
27.96
f1 (ppm)

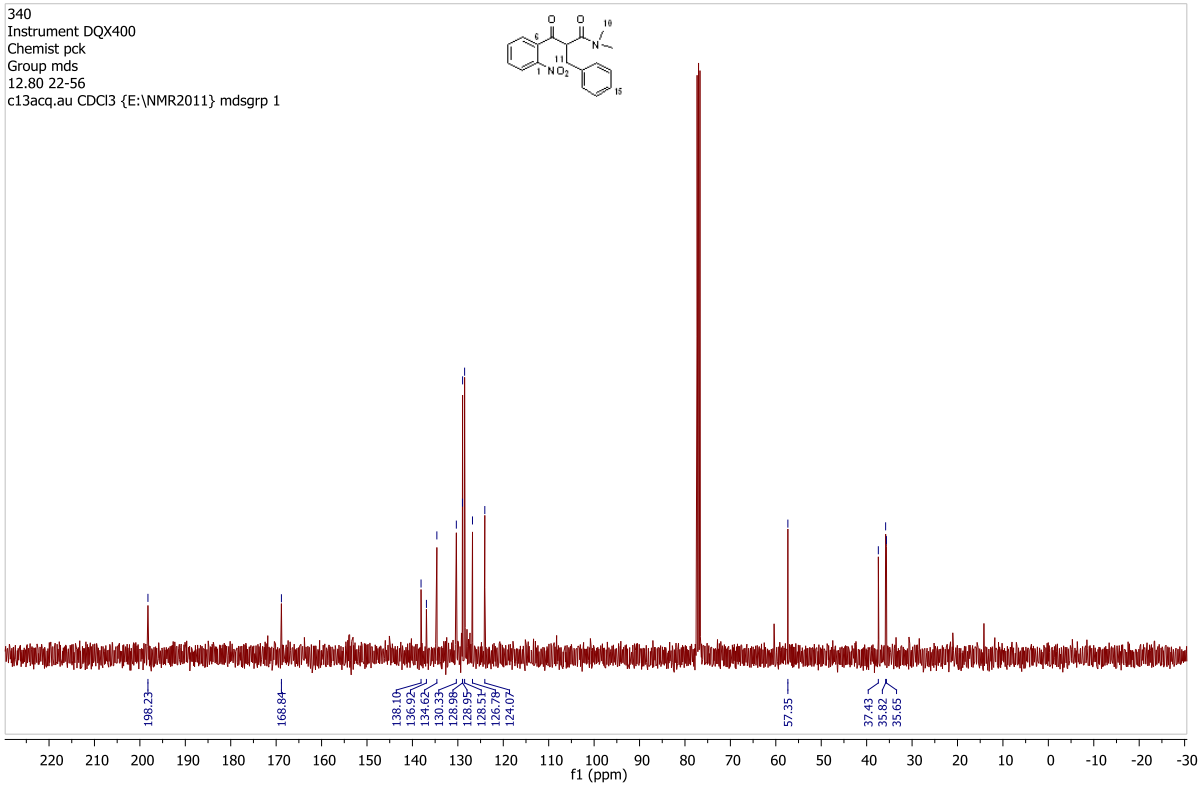

336
Instrument DQX400
Chemist pck
Group mds
14.43
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 34
1.00
1.08
1.08
1.01
2.29
f1 (ppm)

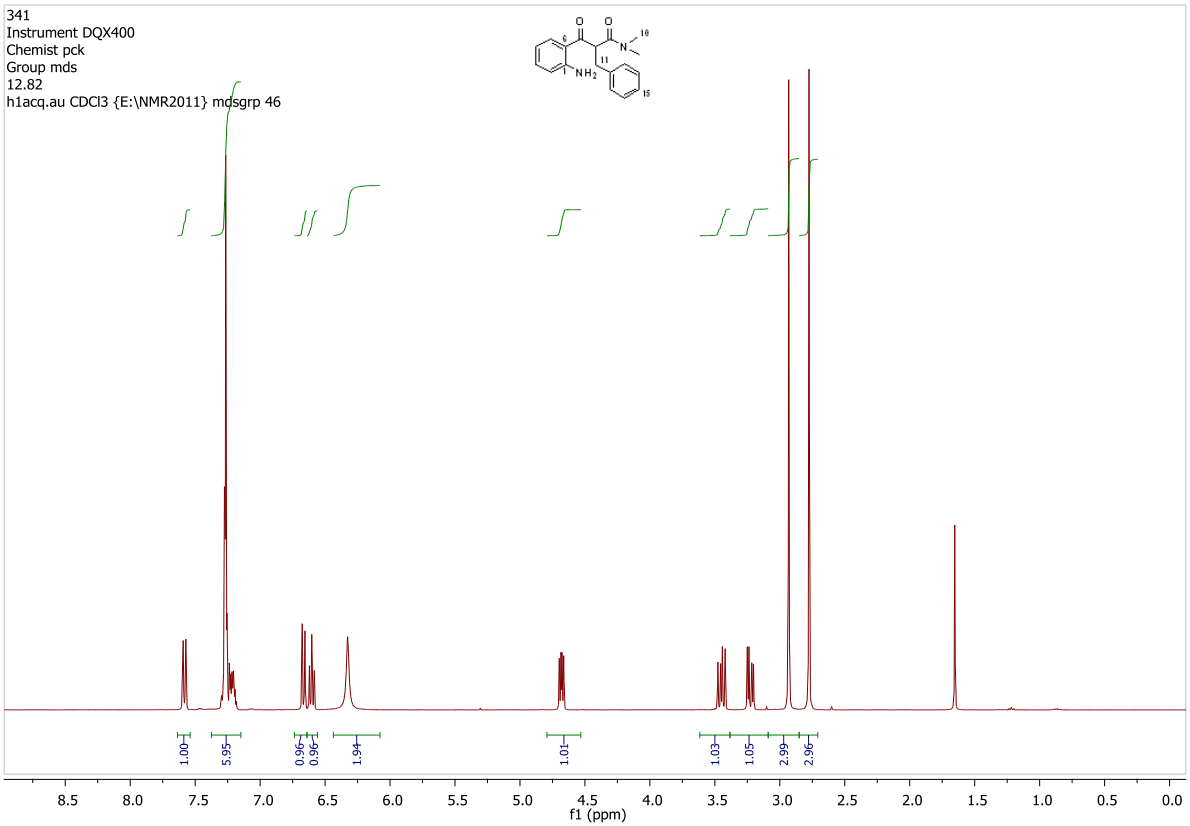

336
Instrument DQX400
Chemist pck
Group mds
14.43
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 34
190.10
145.14
135.24
134.67
131.95
127.58
124.71
113.26
32.48
f1 (ppm)

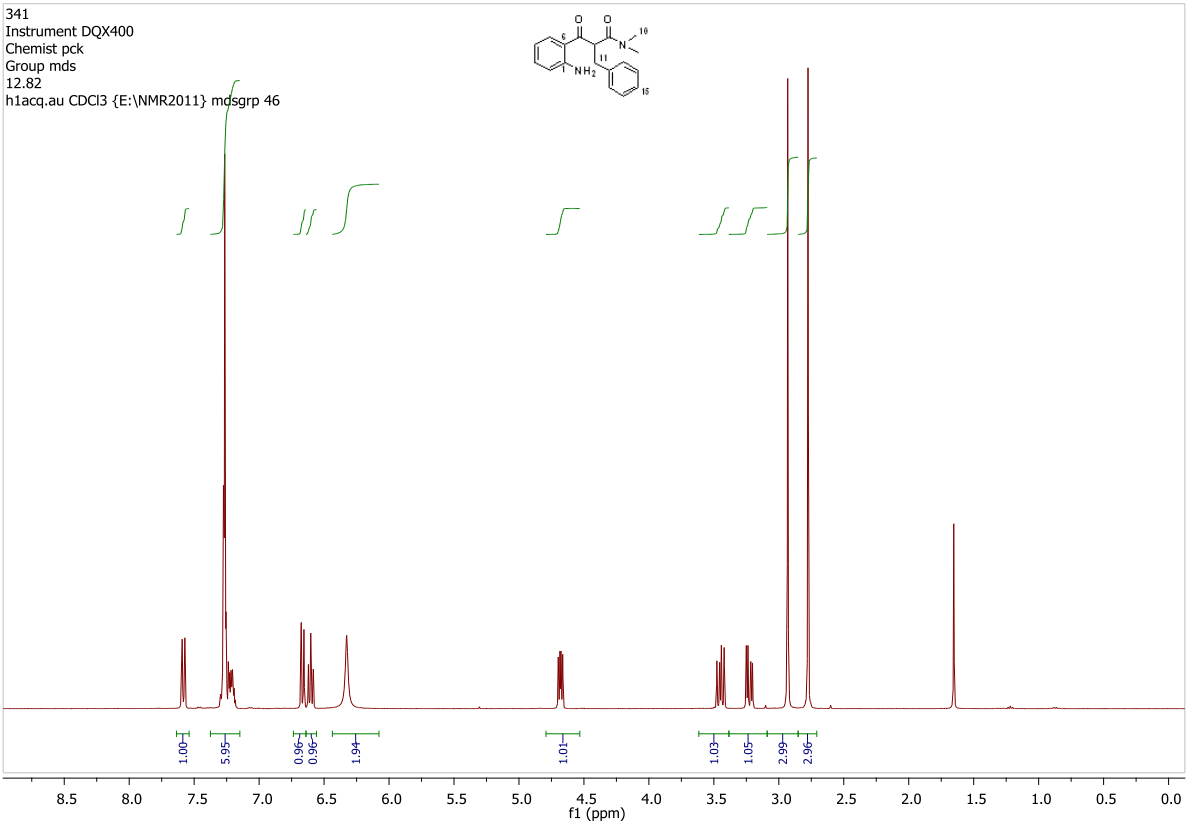

337
Instrument DQX400
Chemist pck
Group mds
14.44
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 50
1.00
0.93
1.89
1.95
2.04
f1 (ppm)


337
Instrument DQX400
Chemist pck
Group mds
14.44
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 50
188.12
151.19
135.88
130.45
117.71
116.24
115.19
114.40
30.06
f1 (ppm)


340
Instrument DQX400
Chemist pck
Group mds
12.80 repeat
h1acq.au CDCl3 {E:\NMR2011} mdsgrp 10
1.00
1.11
1.26
1.20
7.20
1.41
2.34
3.32
3.40
f1 (ppm)

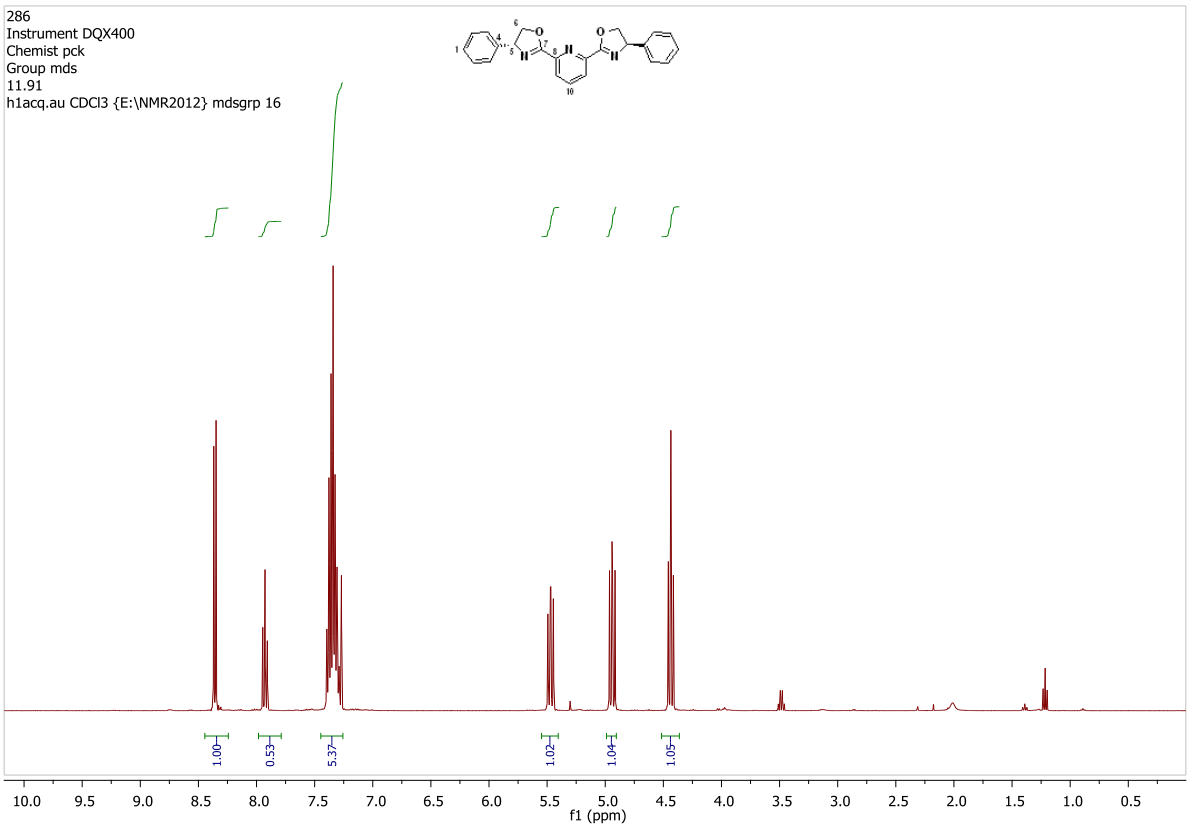

340
Instrument DQX400
Chemist pck
Group mds
12.80 22-56
c13acq.au CDCl3 {E:\NMR2011} mdsgrp 1
198.23
168.84
138.10
136.92
134.62
130.33
128.98
128.95
128.51
126.78
124.07
57.35
37.43
35.82
35.65
f1 (ppm)

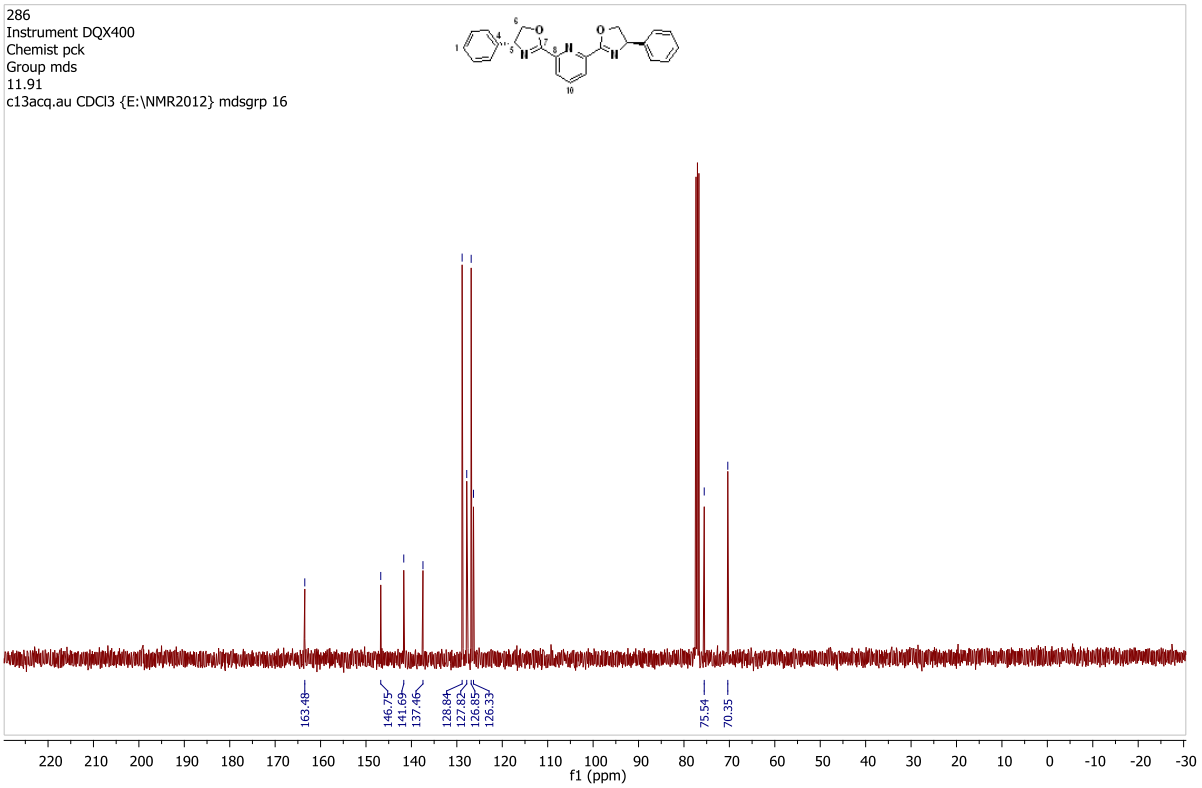

341
Instrument DQX400
Chemist pck
Group mds
12.82
h1acq.au CDCl3 {E:\NMR2011} mdsgrp 46
1.00
5.95
0.96
0.96
1.94
1.01
1.03
1.05
2.99
2.96
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

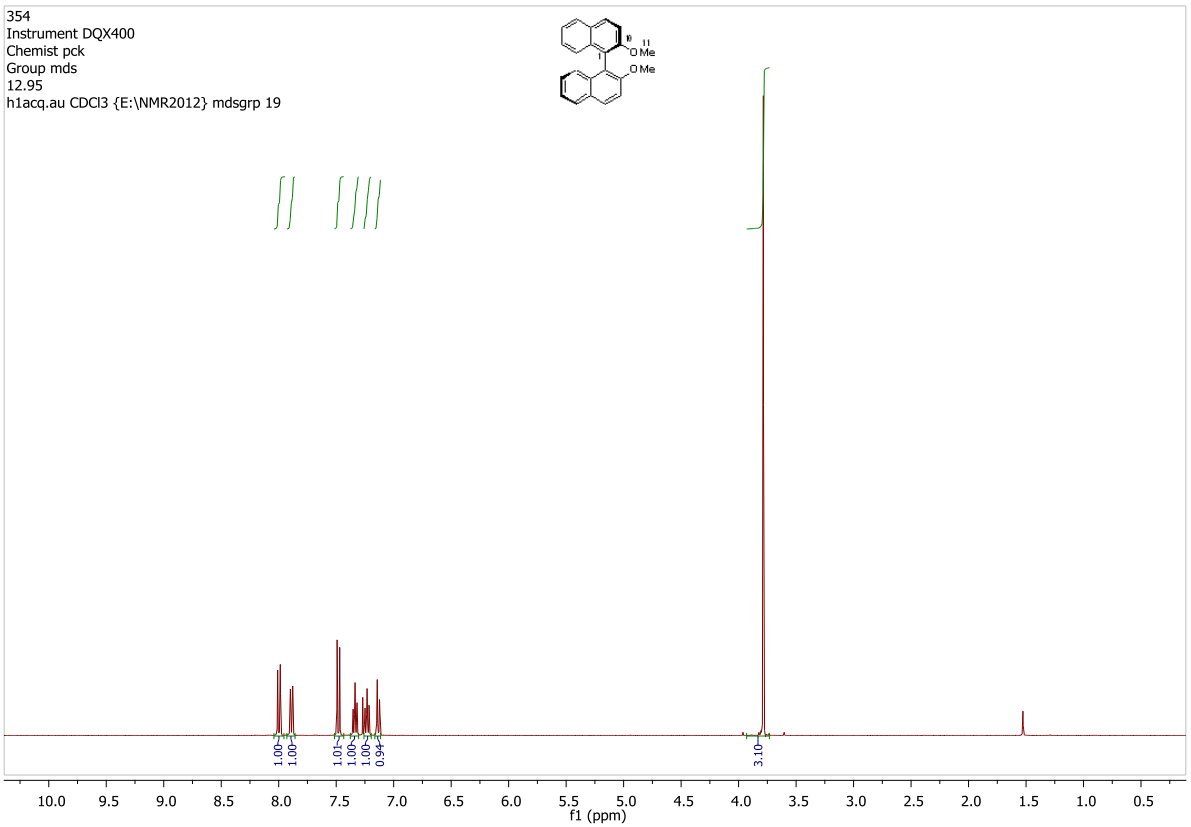

341
Instrument DQX400
Chemist pck
Group mds
12.82
h1acq.au CDCl3 {E:\NMR2011} mdsgrp 46
1.00
5.95
0.96
0.96
1.94
1.01
1.03
1.05
2.99
2.96
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

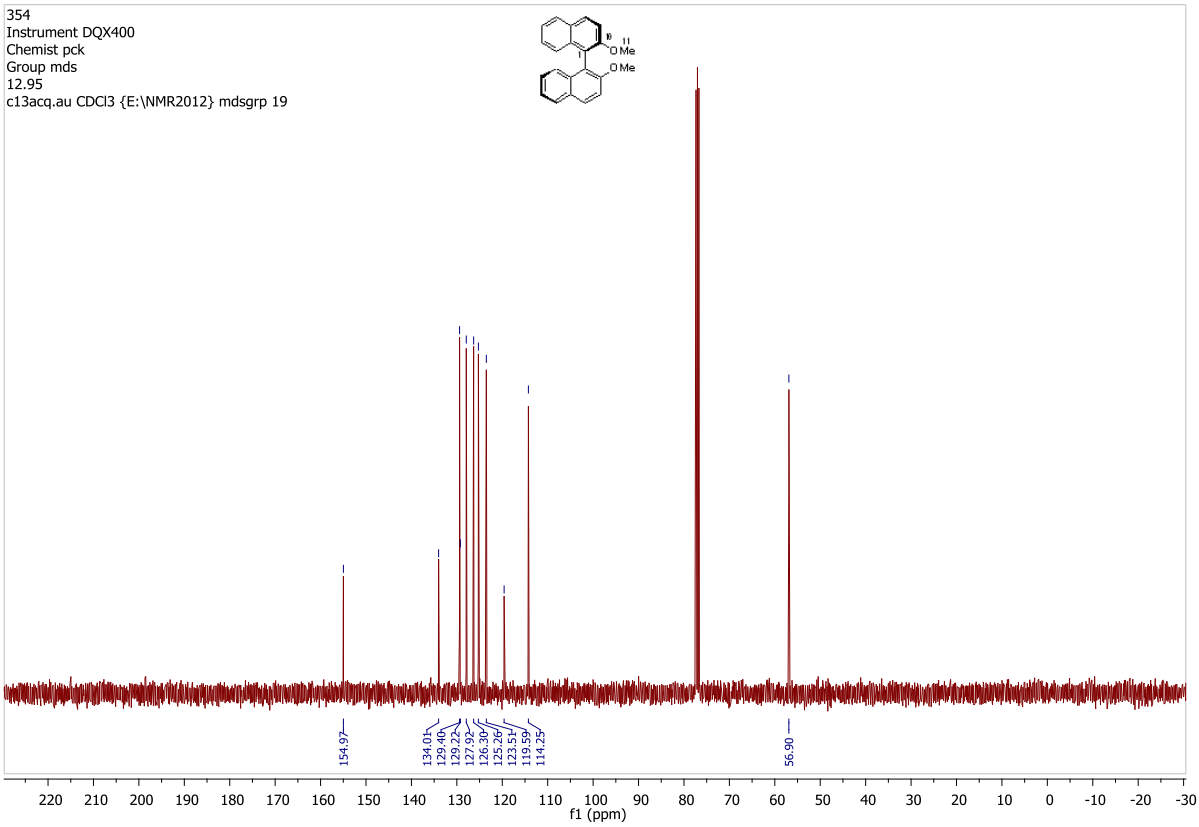
4.2 Catalysts and Precursors

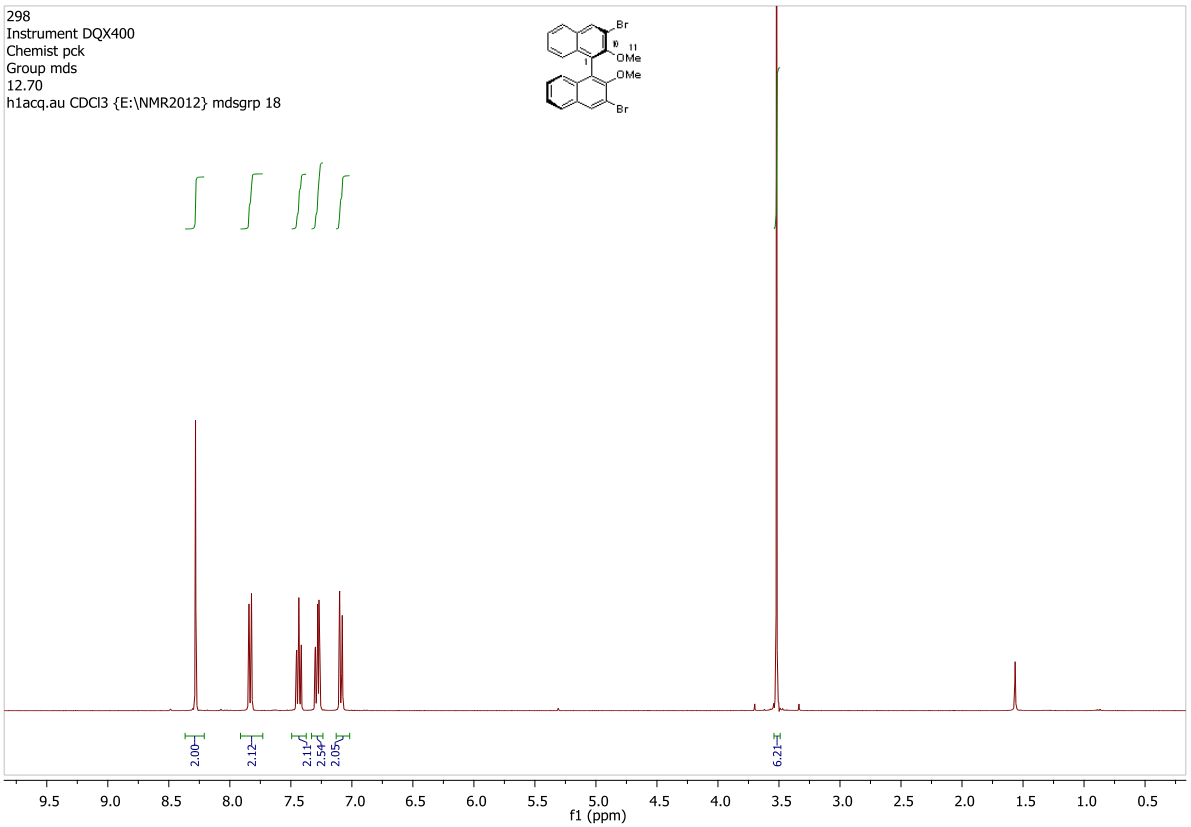
3

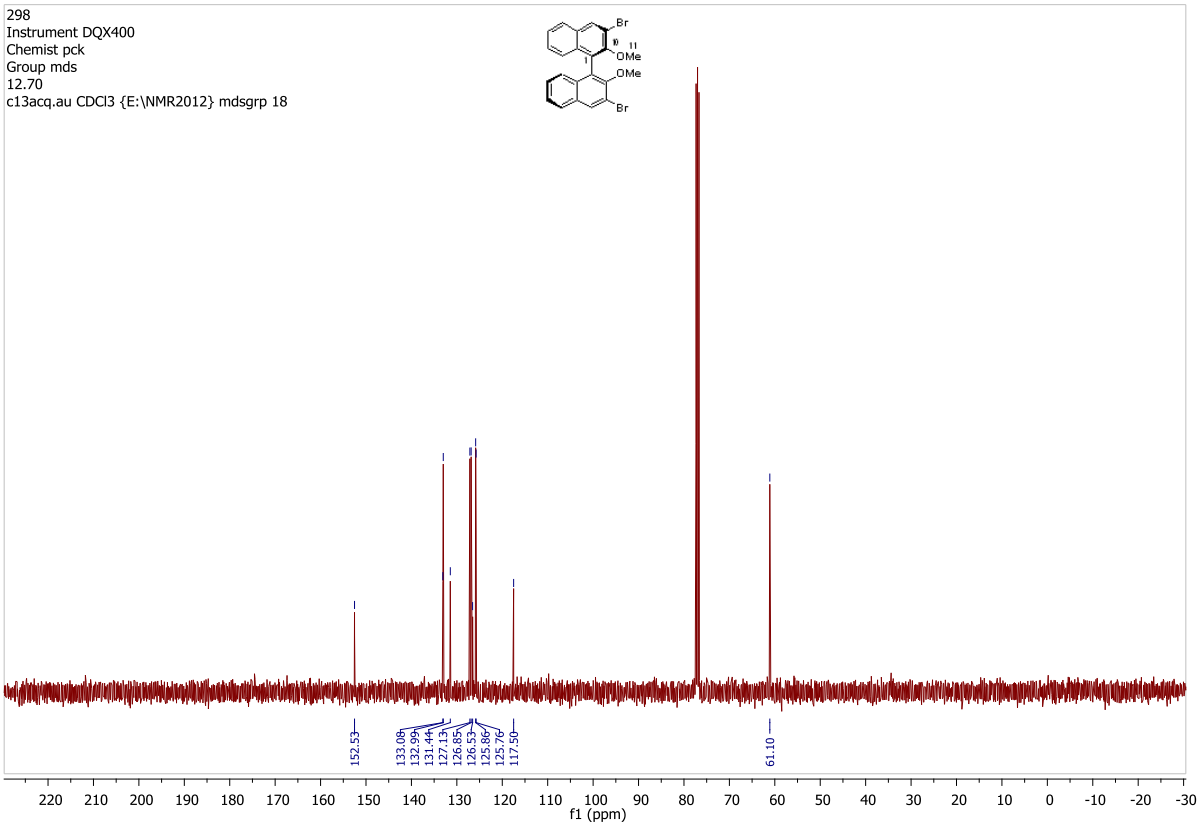

286
Instrument DQX400
Chemist pck
Group mds
11.91
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 16
1.00
0.53
5.37
1.02
1.04
1.05
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

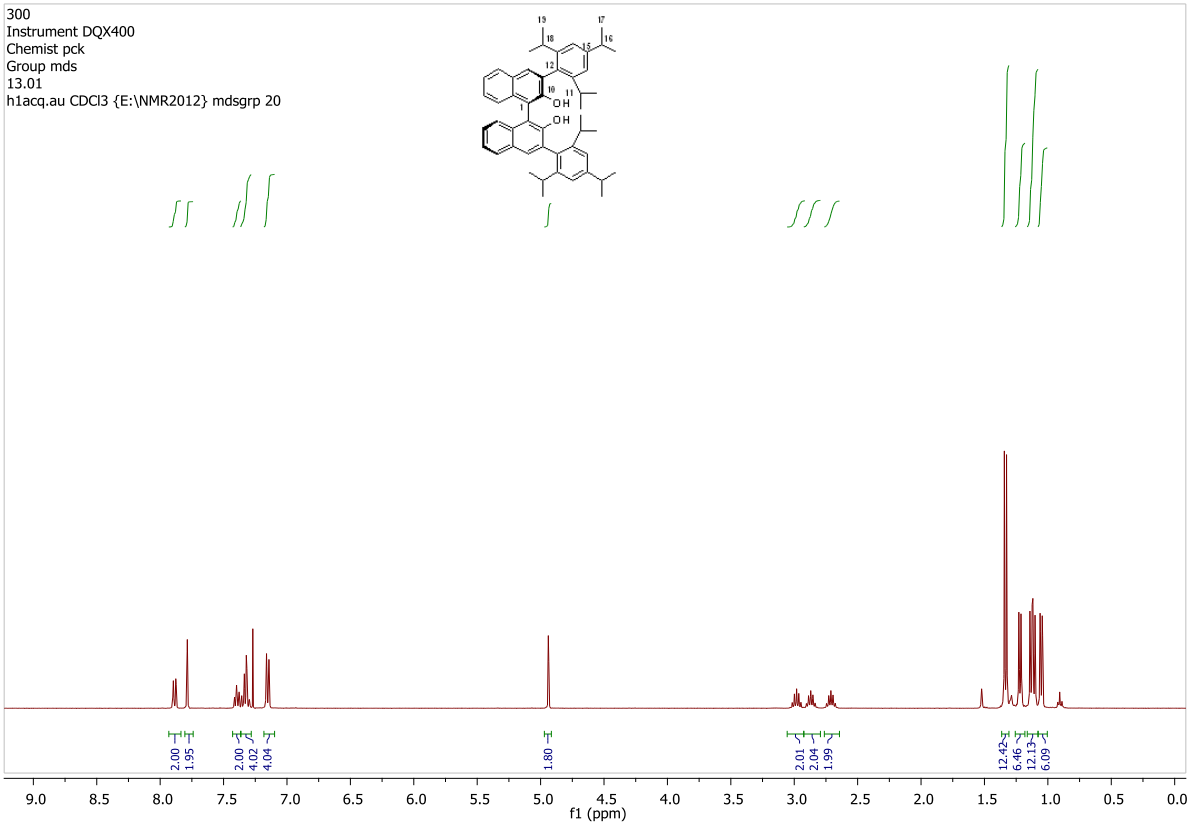

286
Instrument DQX400
Chemist pck
Group mds
11.91
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 16
163.48
146.75
141.69
137.46
128.84
127.82
126.85
126.33
75.54
70.35
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

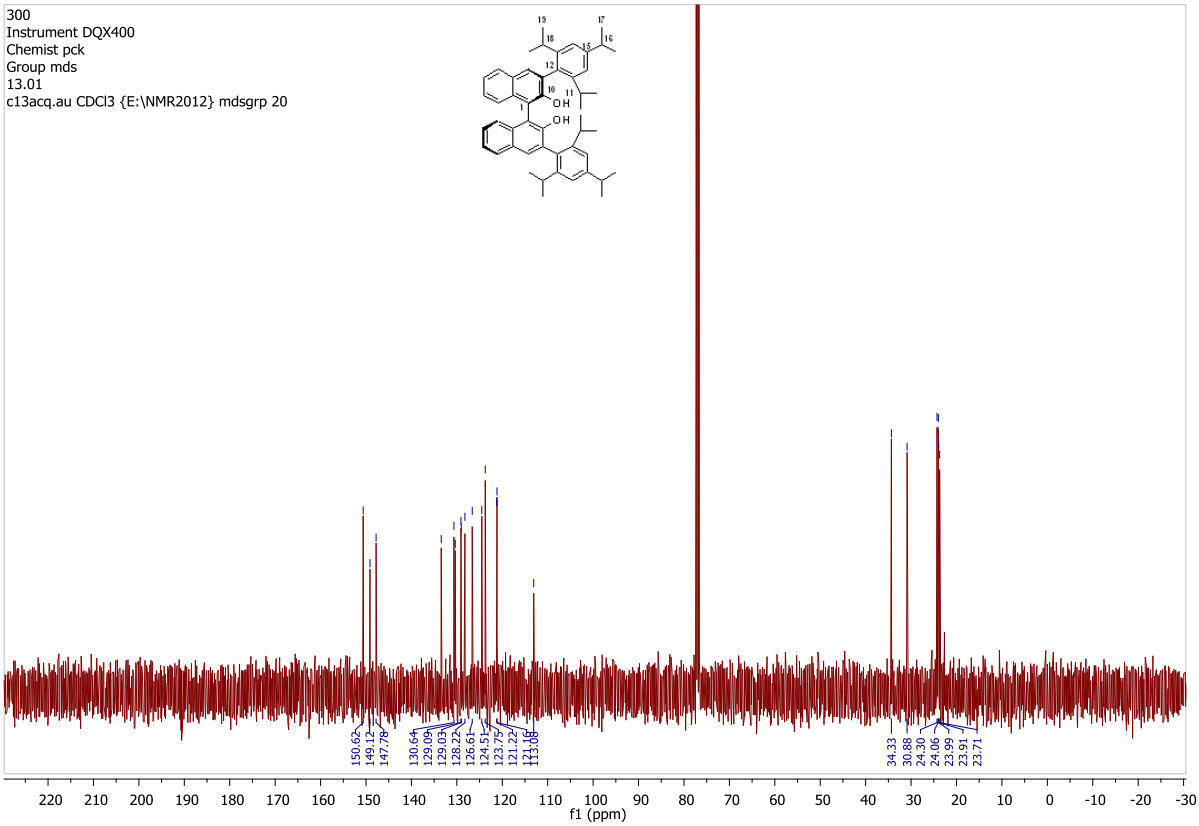

354
Instrument DQX400
Chemist pck
Group mds
12.95
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 19
OMe
OMe
1.00
1.00
1.01
1.00
1.00
0.94
3.10
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

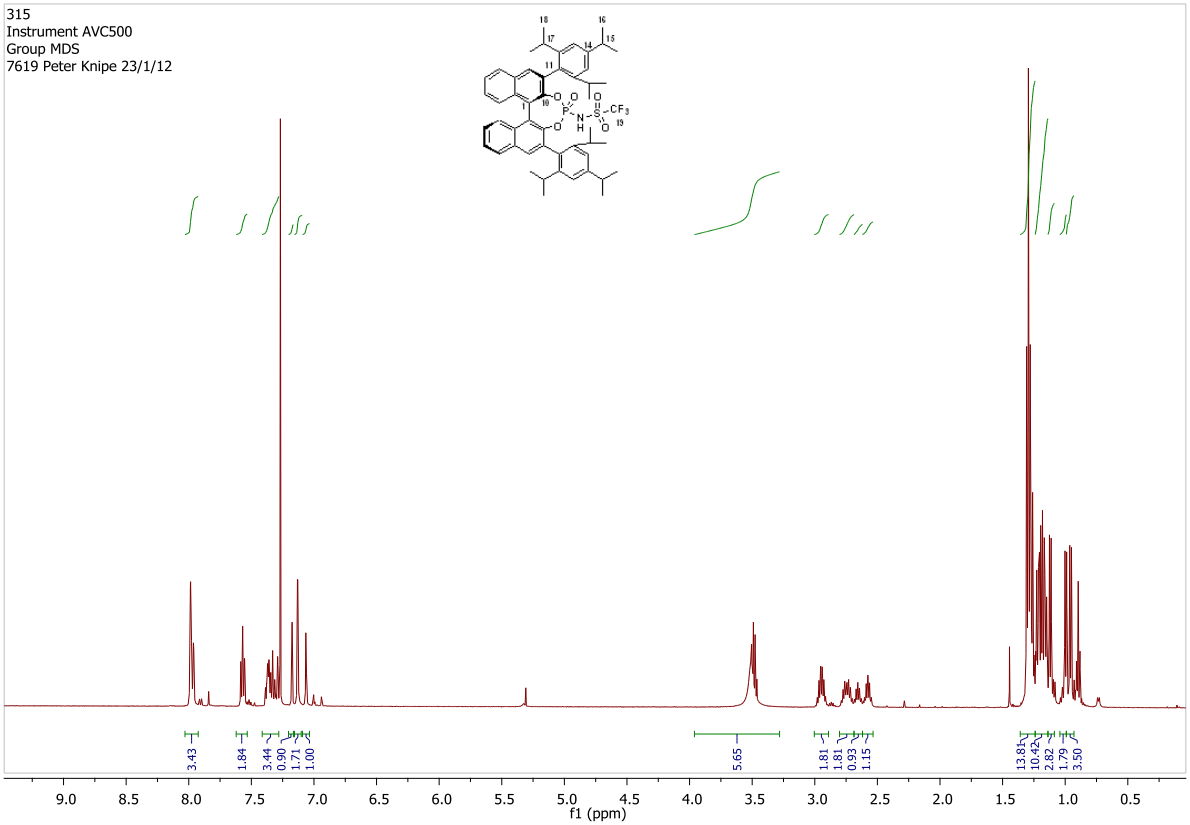

354
Instrument DQX400
Chemist pck
Group mds
12.95
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 19
OMe
OMe
154.97
134.01
129.40
129.22
127.92
126.30
125.26
123.51
119.59
114.25
56.90
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

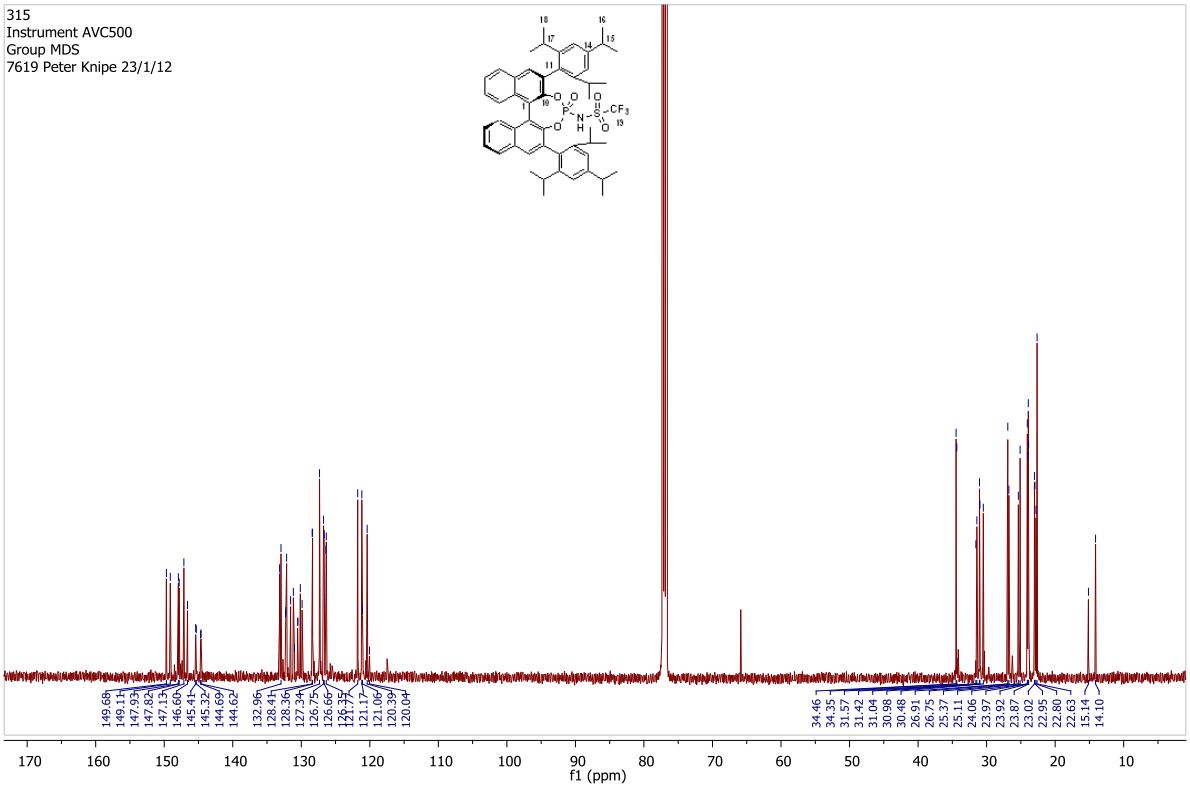

298
Instrument DQX400
Chemist pck
Group mds
12.70
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 18
Br
OMe
OMe
Br
2.00
2.12
2.11
2.54
2.05
6.21
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

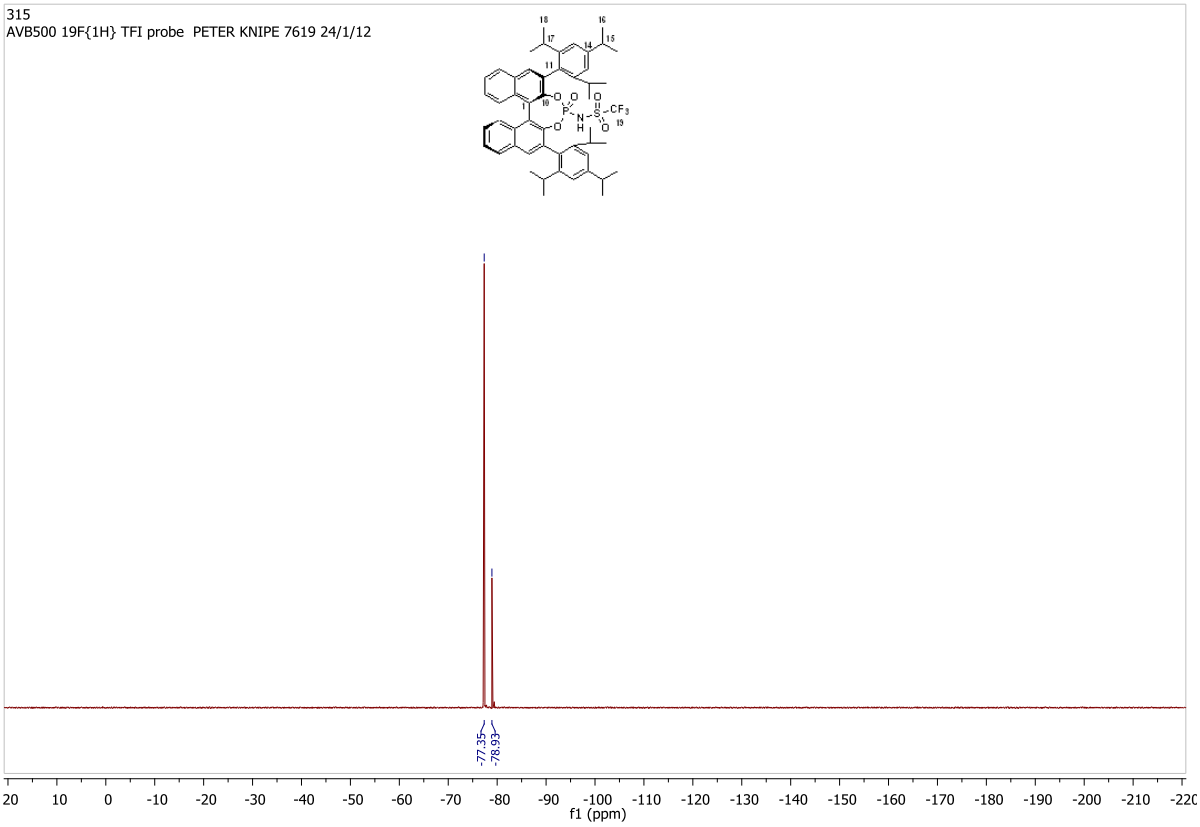

298
Instrument DQX400
Chemist pck
Group mds
12.70
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 18
Br
OMe
OMe
Br
152.53
133.08
132.99
131.44
127.13
126.85
126.53
125.86
125.76
117.50
61.10
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

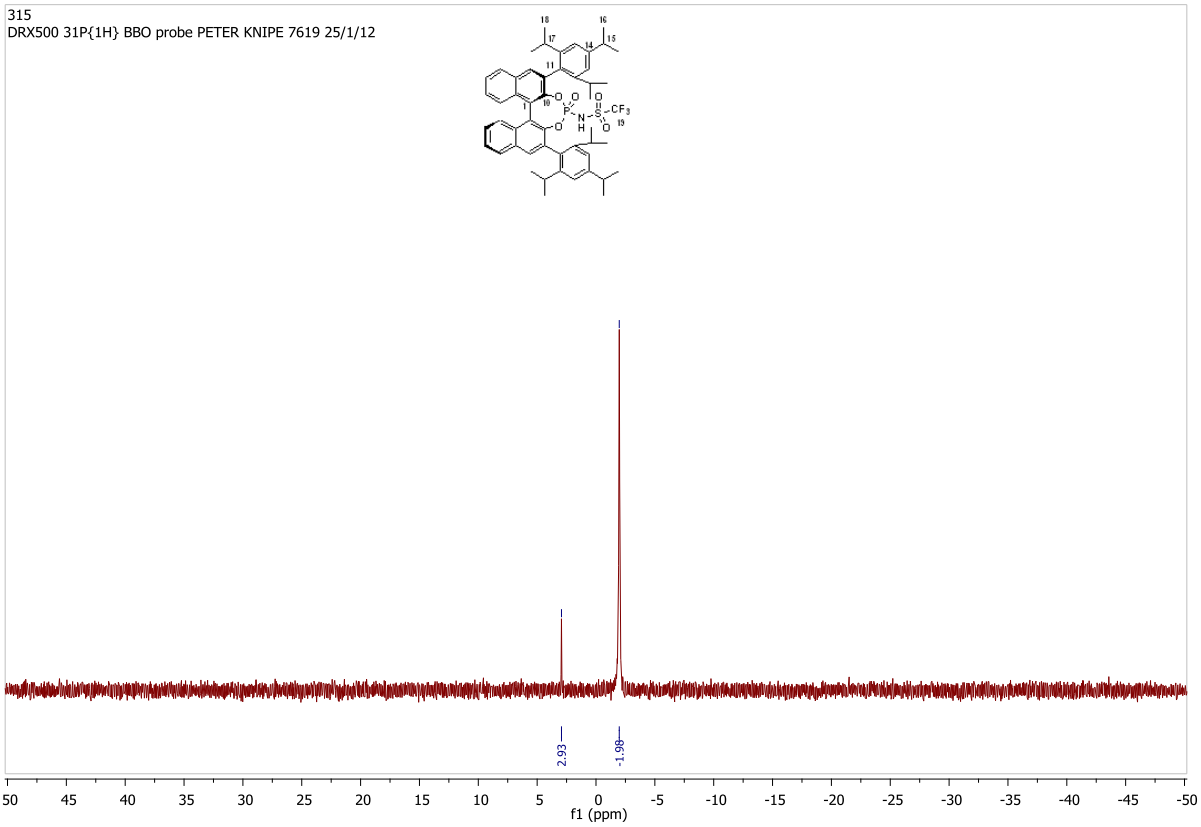

300
Instrument DQX400
Chemist pck
Group mds
13.01
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 20
2.00
1.95
2.00
4.02
4.04
1.80
2.01
2.04
1.99
12.42
6.46
12.13
6.09
f1 (ppm)

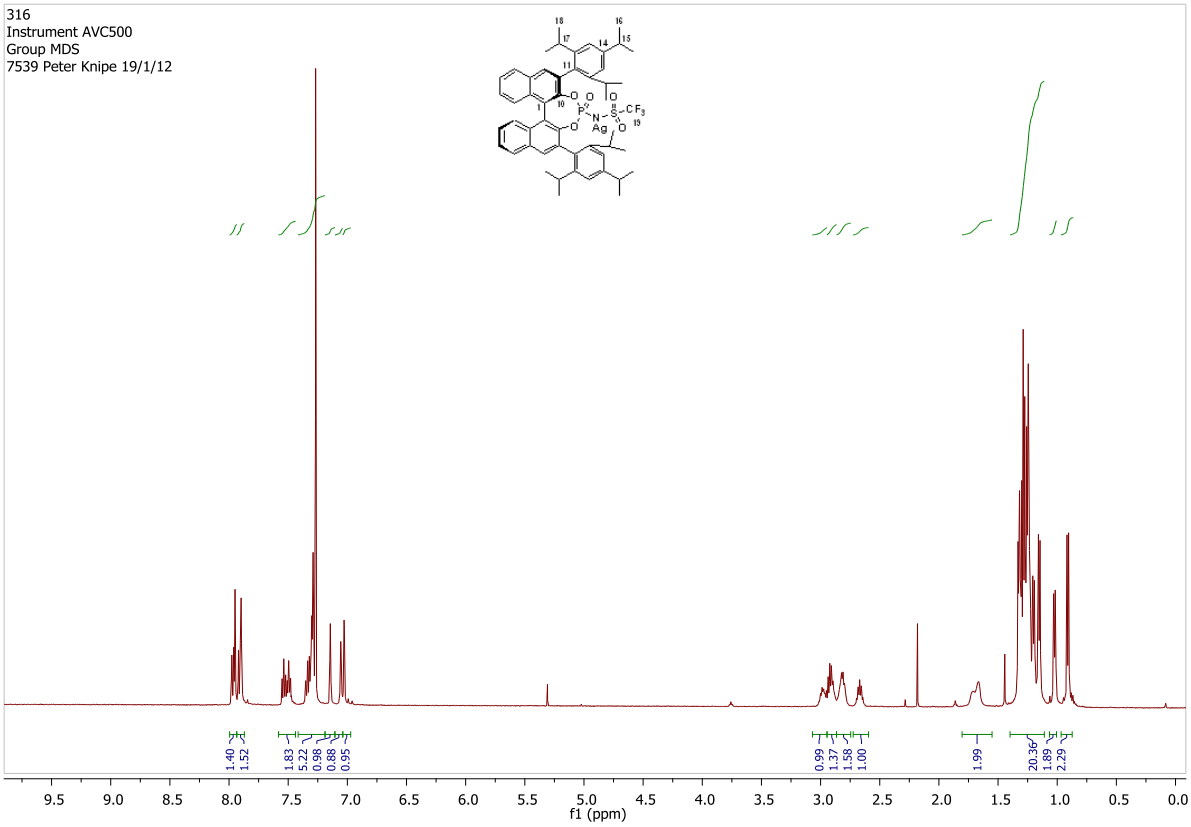

300
Instrument DQX400
Chemist pck
Group mds
13.01
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 20
150.62
149.12
147.78
130.64
129.09
129.03
128.22
126.61
124.51
123.75
121.22
121.16
113.08
34.33
30.88
24.38
24.06
23.99
23.91
23.71
f1 (ppm)

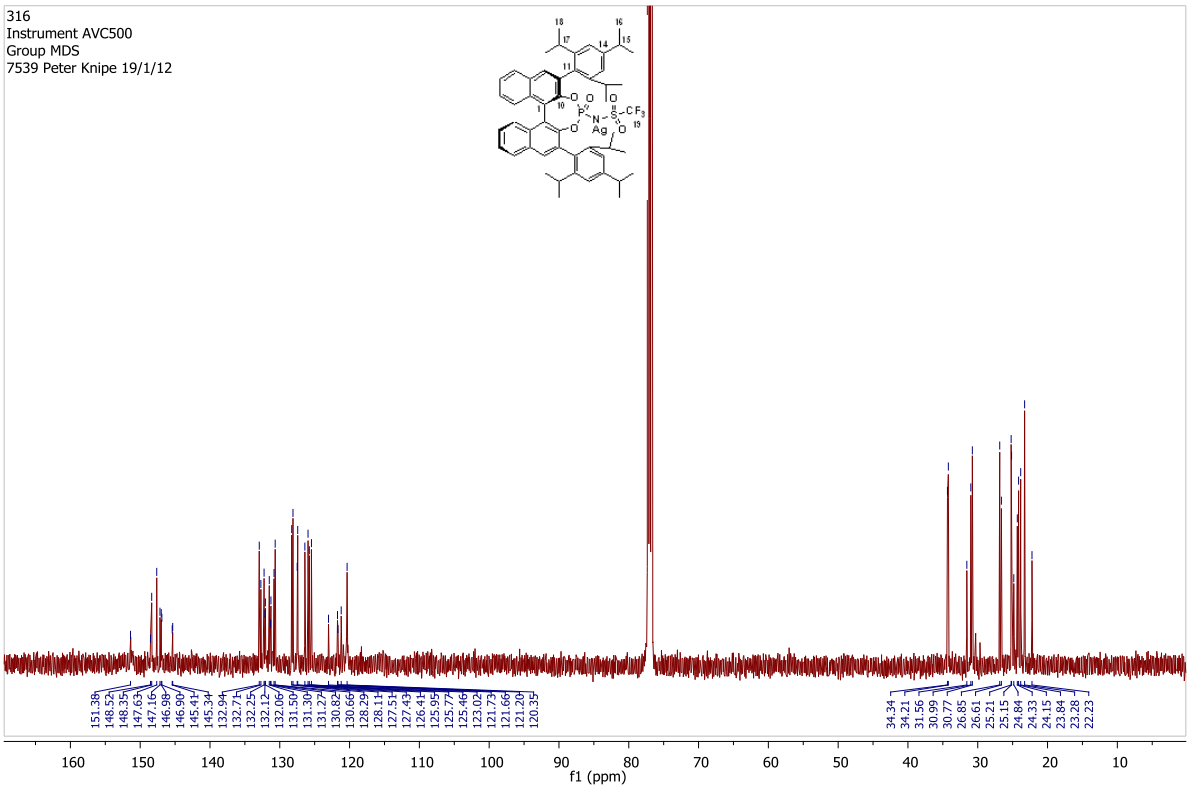

315
Instrument AVC500
Group MDS
7619 Peter Knipe 23/1/12
3.43
1.84
3.44
0.90
1.71
1.00
5.65
1.81
1.81
0.93
1.15
13.81
10.42
2.82
1.79
3.50
f1 (ppm)


315
Instrument AVC500
Group MDS
7619 Peter Knipe 23/1/12
f1 (ppm)

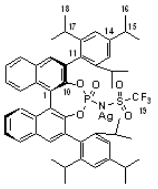

315
AVB500 19F{1H} TFI probe PETER KNIPE 7619 24/1/12
-77.35
-78.93
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

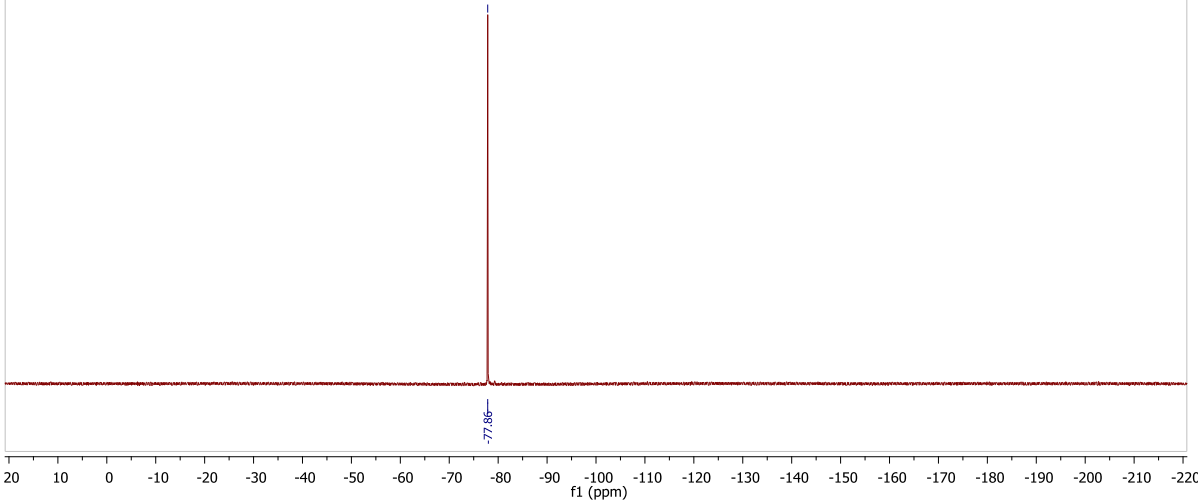

315
DRX500 31P{1H} BBO probe PETER KNIPE 7619 25/1/12
2.93
-1.98
50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50
f1 (ppm)


316
Instrument AVC500
Group MDS
7539 Peter Knipe 19/1/12
1.40
1.52
1.83
5.22
0.98
0.88
0.95
0.99
1.37
1.58
1.00
1.99
20.36
1.89
2.29
f1 (ppm)

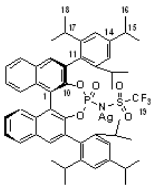

316
Instrument AVC500
Group MDS
7539 Peter Knipe 19/1/12
151.38
148.52
148.35
147.63
147.16
146.99
146.90
145.41
145.34
132.94
132.71
132.25
132.12
132.06
131.50
131.30
131.27
130.82
130.66
128.29
128.11
127.51
127.43
126.41
125.95
125.77
125.46
123.02
121.73
121.66
121.20
120.35
34.34
34.21
31.56
30.99
30.77
26.85
26.61
25.21
25.15
24.84
24.33
24.15
23.84
23.28
22.23
f1 (ppm)

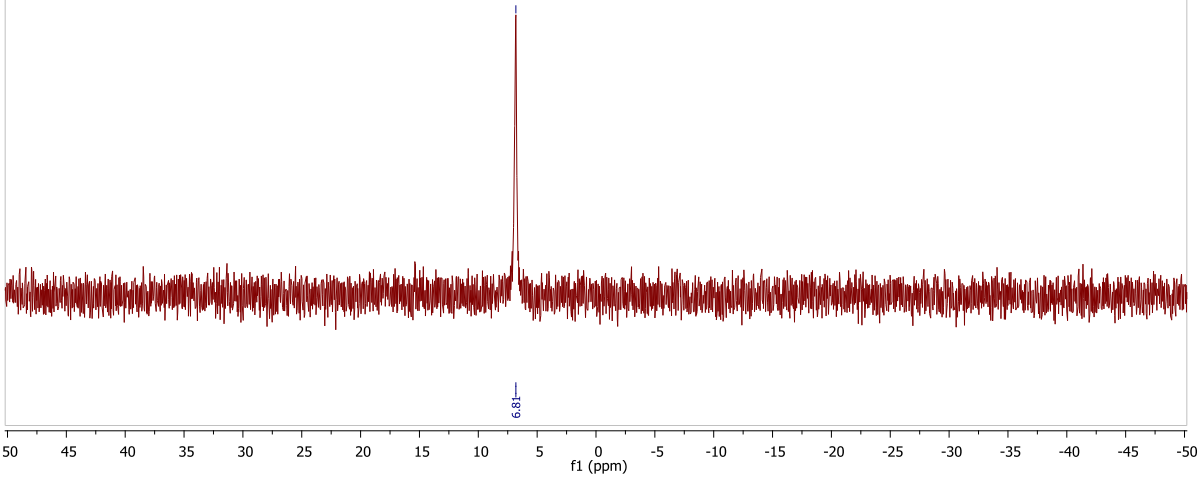
316
AVB500 19F{1H} TFI probe
PETER KNIPE 7534 19/1/12





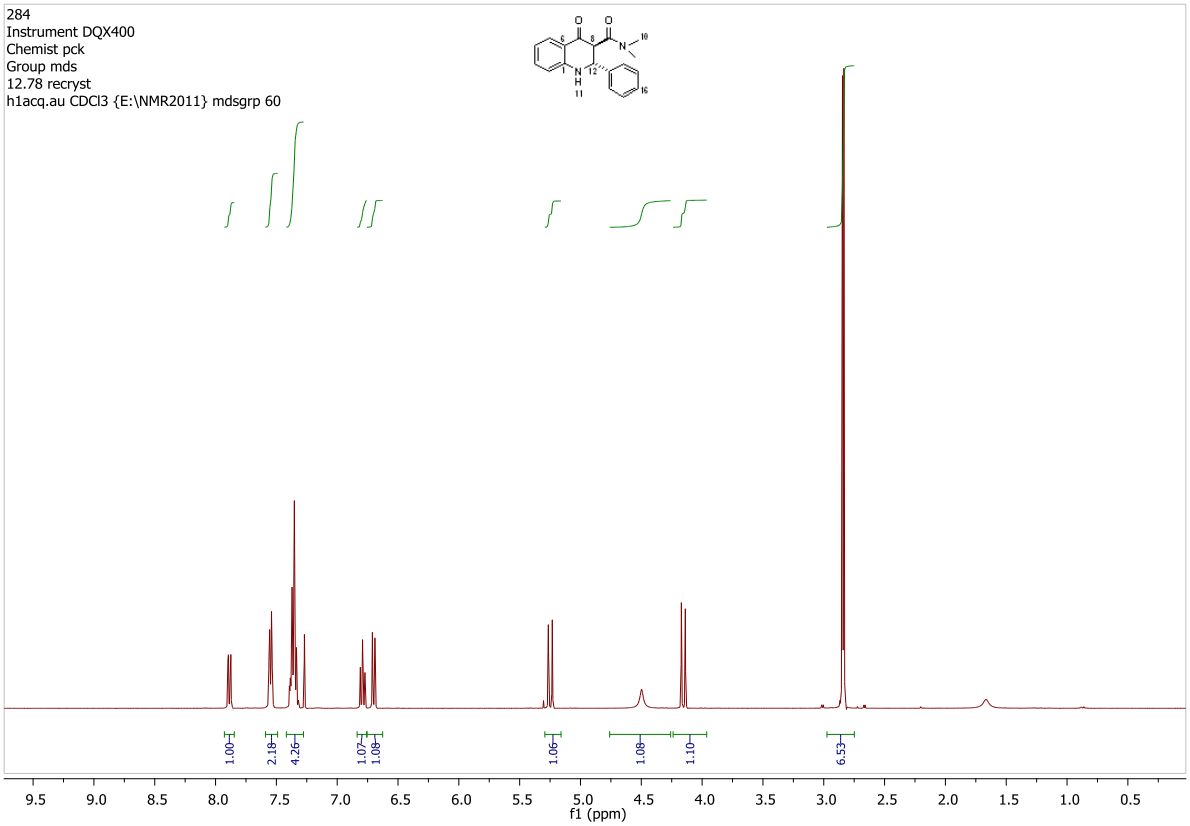
316
DRX500 31P{1H} BBO probe PETER KNIPE 7534 19/1/12

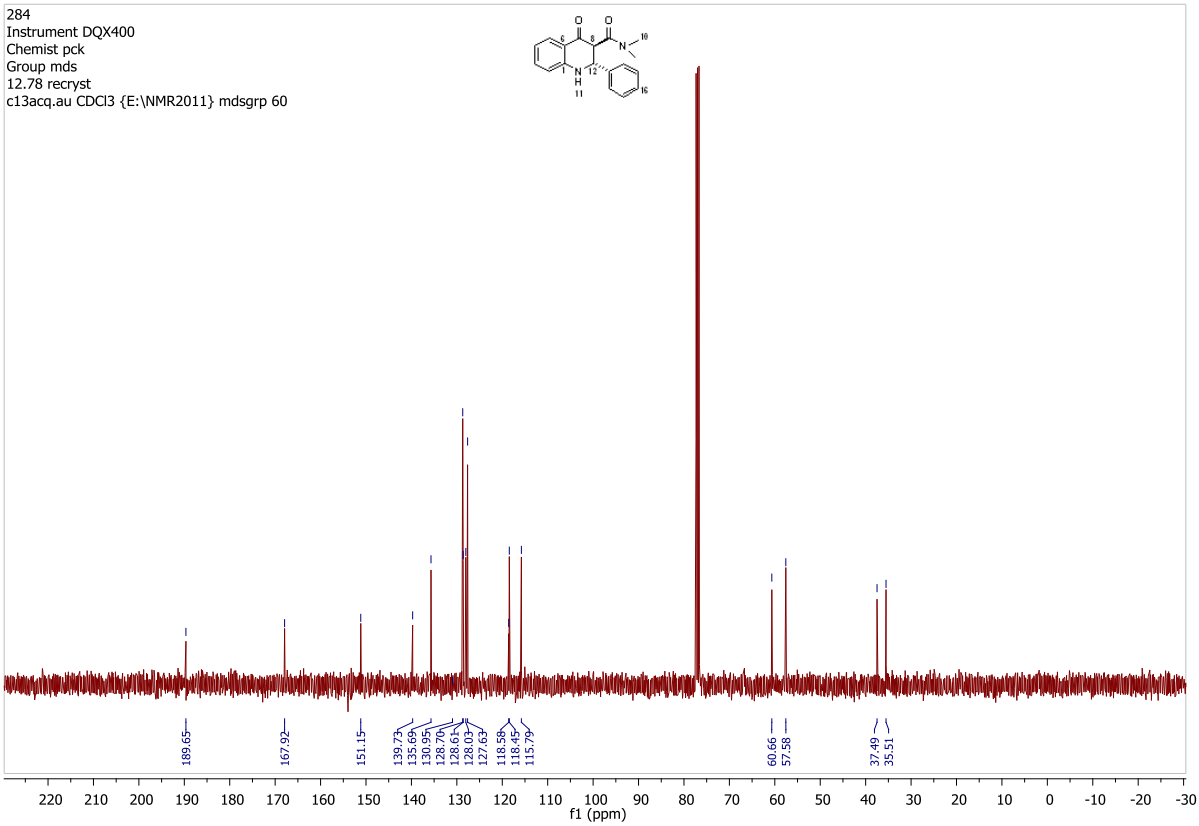




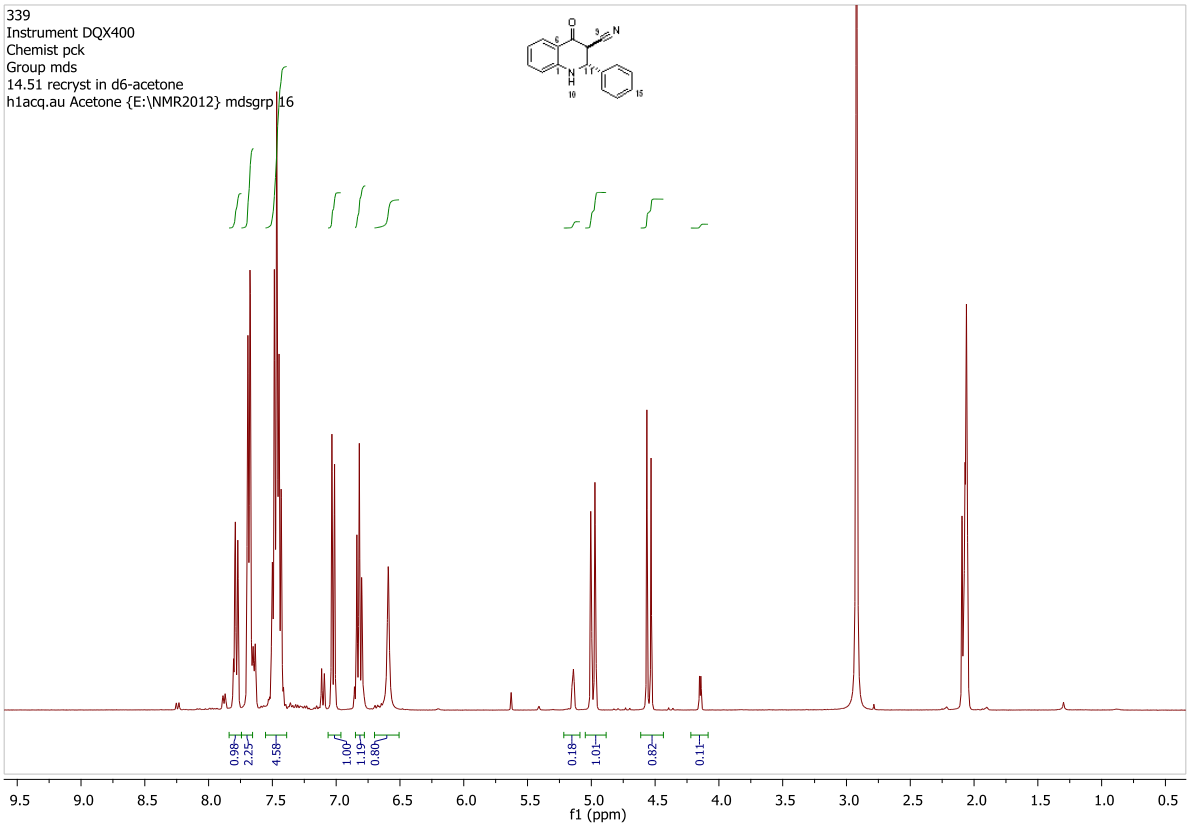
4.3 Dihydroquinolones

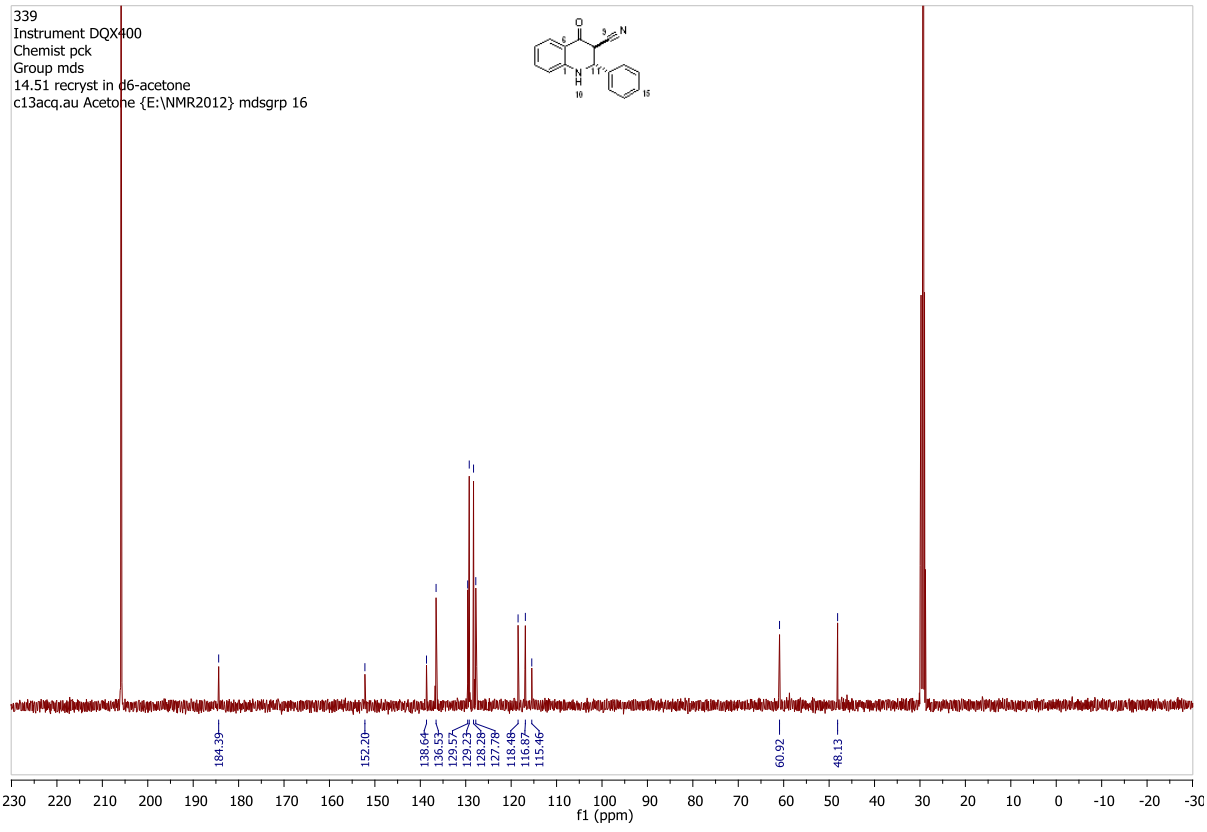
2


284
Instrument DQX400
Chemist pck
Group mds
12.78 recryst
h1acq.au CDCl3 {E:\NMR2011} mdsgrp 60
1.00
2.18
4.26
1.07
1.08
1.06
1.08
1.10
6.53
f1 (ppm)

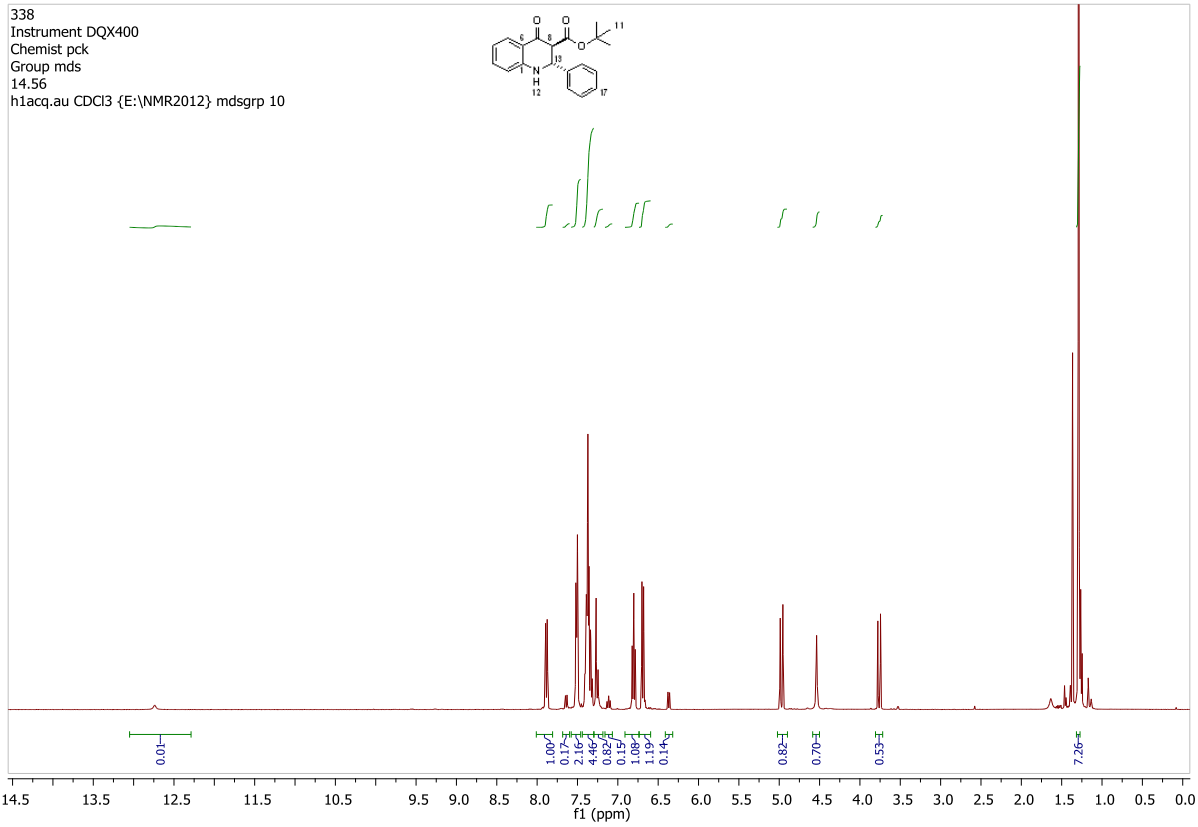

284
Instrument DQX400
Chemist pck
Group mds
12.78 recryst
c13acq.au CDCl3 {E:\NMR2011} mdsgrp 60
189.65
167.92
151.15
139.73
135.69
130.95
128.70
128.61
128.03
127.63
118.58
118.45
115.79
60.66
57.58
37.49
35.51
f1 (ppm)

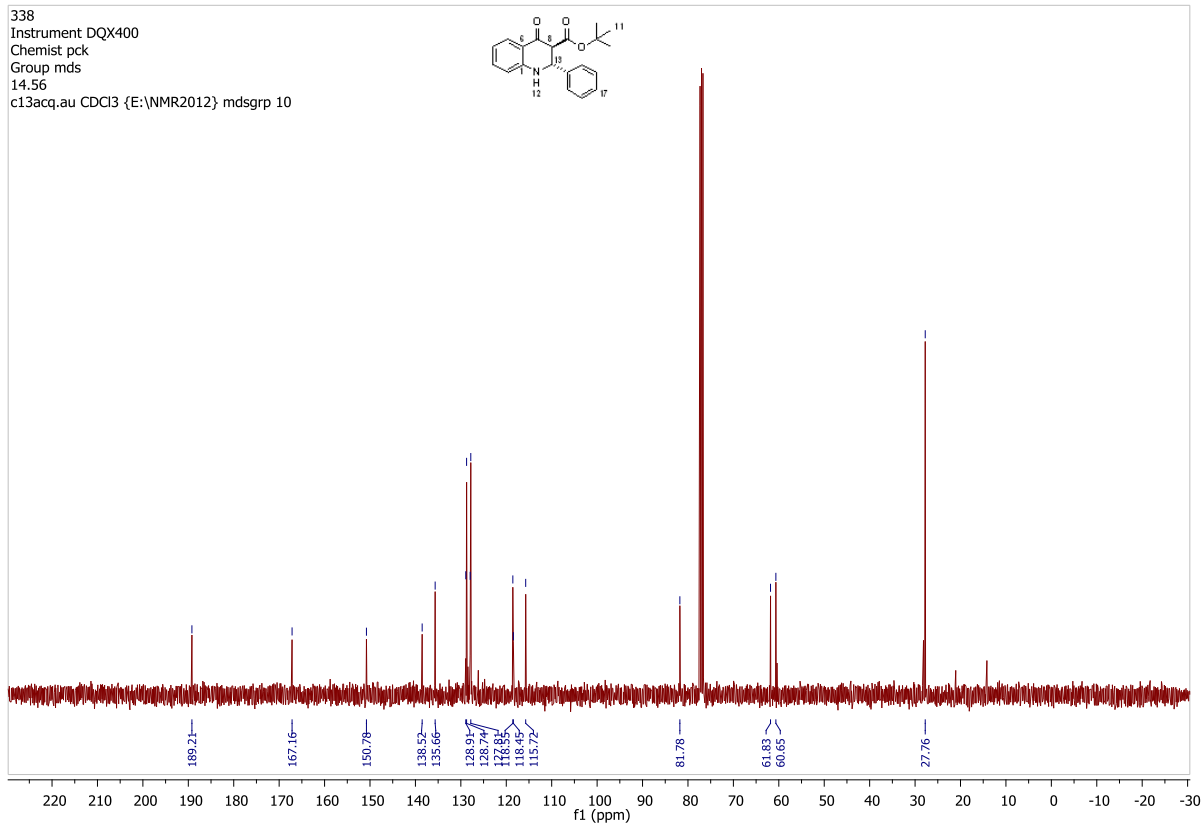
8


339
Instrument DQX400
Chemist pck
Group mds
14.51 recryst in d6-acetone
h1acq.au Acetone {E:\NMR2012} mdsgrp 16
0.98
2.25
4.58
1.00
1.19
0.80
0.18
1.01
0.82
0.11
f1 (ppm)

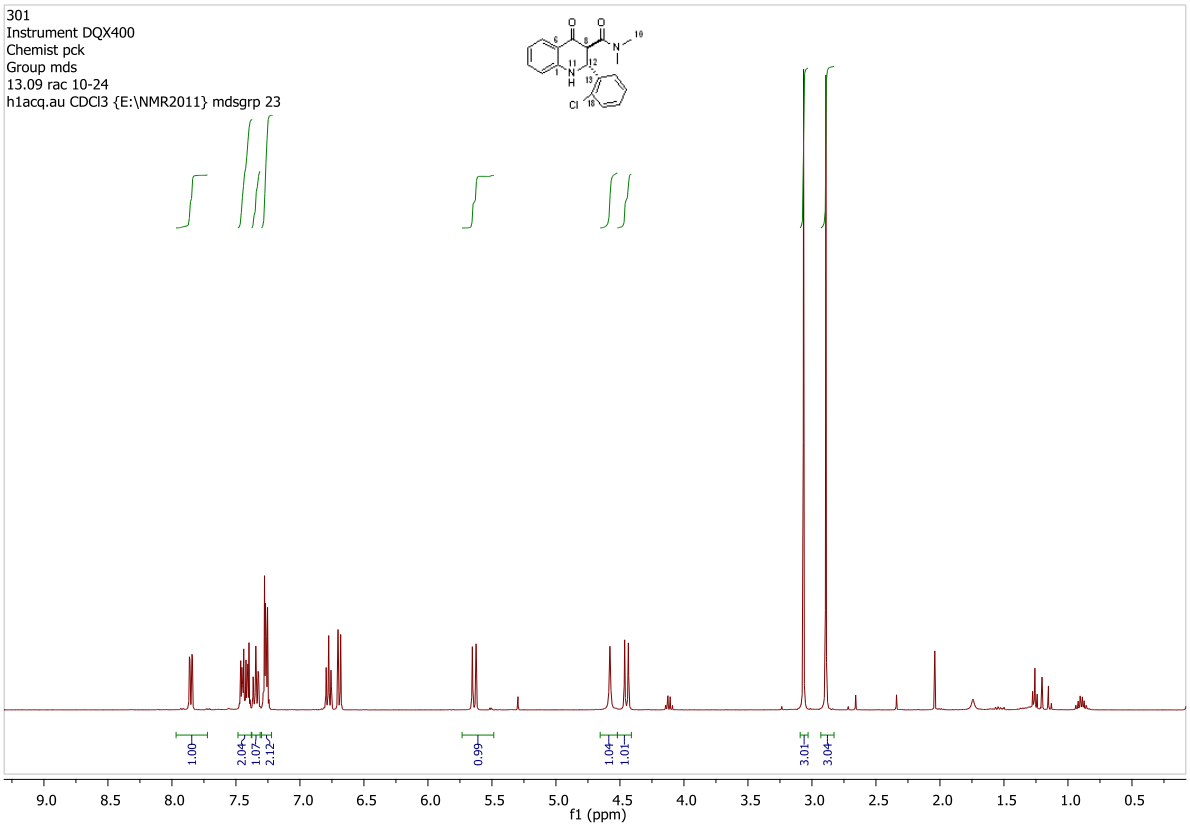

339
Instrument DQX400
Chemist pck
Group mds
14.51 recryst in d6-acetone
c13acq.au Acetone {E:\NMR2012} mdsgrp 16
184.39
152.20
138.64
136.53
129.57
129.23
128.28
127.78
118.48
116.87
115.46
60.92
48.13
f1 (ppm)

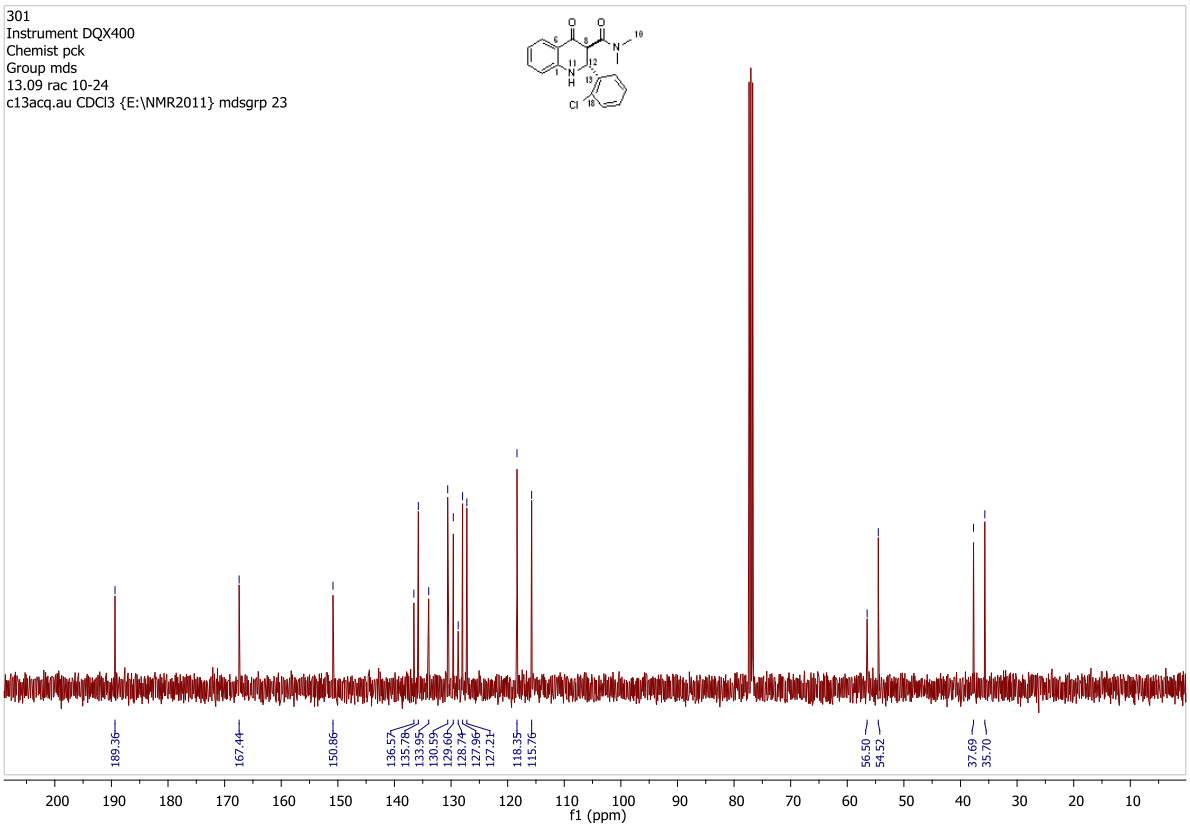
9


338
Instrument DQX400
Chemist pck
Group mds
14.56
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 10
0.01
1.00
0.17
2.16
4.46
0.82
0.15
1.08
1.19
0.14
0.82
0.70
0.53
7.26
f1 (ppm)

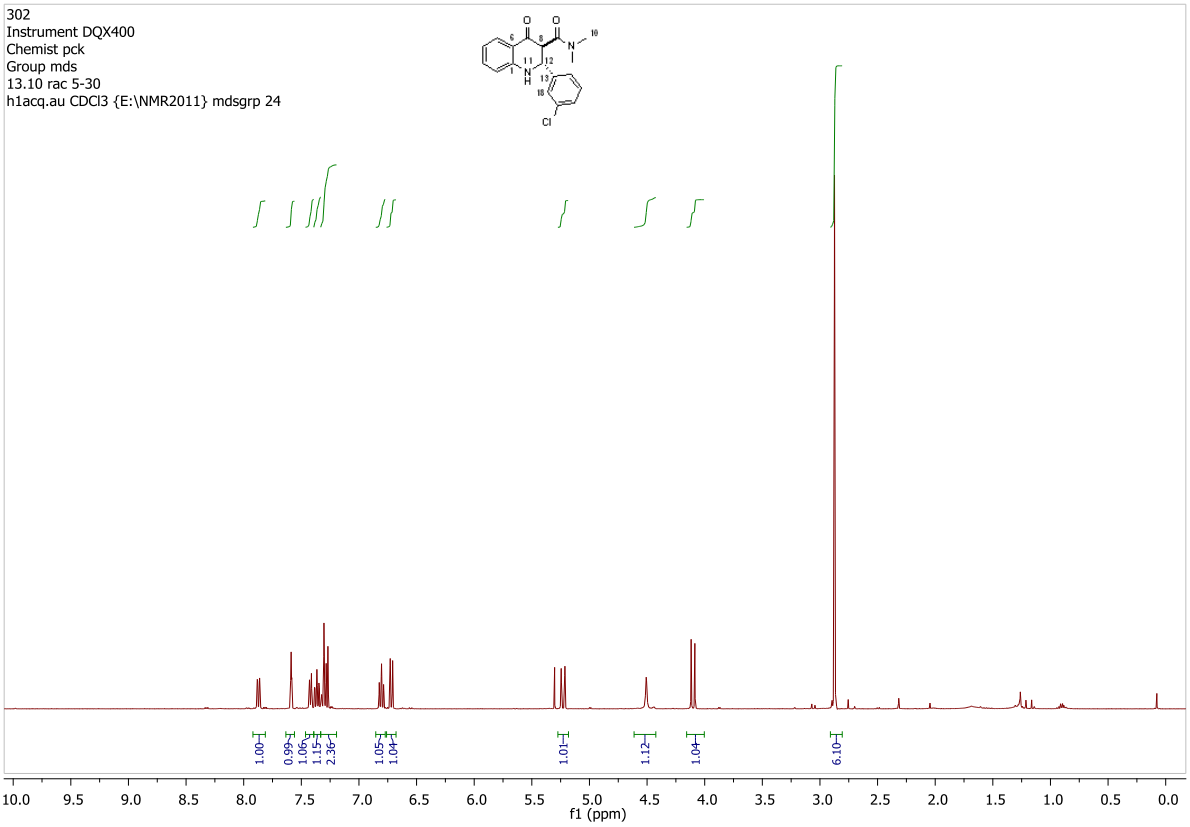

338
Instrument DQX400
Chemist pck
Group mds
14.56
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 10
189.21
167.16
150.78
138.52
135.66
128.91
128.74
118.55
118.45
115.72
81.78
61.83
60.65
27.76
f1 (ppm)

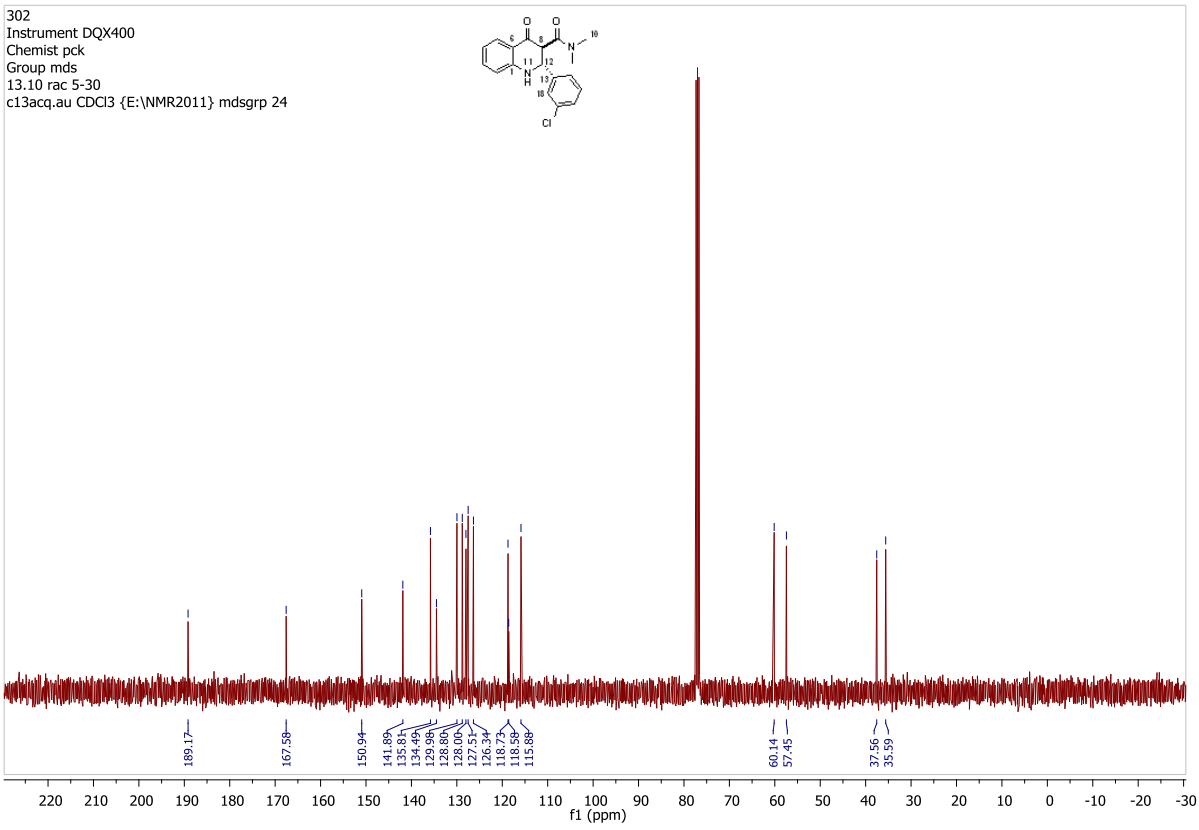
10


301
Instrument DQX400
Chemist pck
Group mds
13.09 rac 10-24
h1acq.au CDCl3 {E:\NMR2011} mdsgrp 23
1.00
2.04
1.07
2.12
0.99
1.04
1.01
3.01
3.04
f1 (ppm)

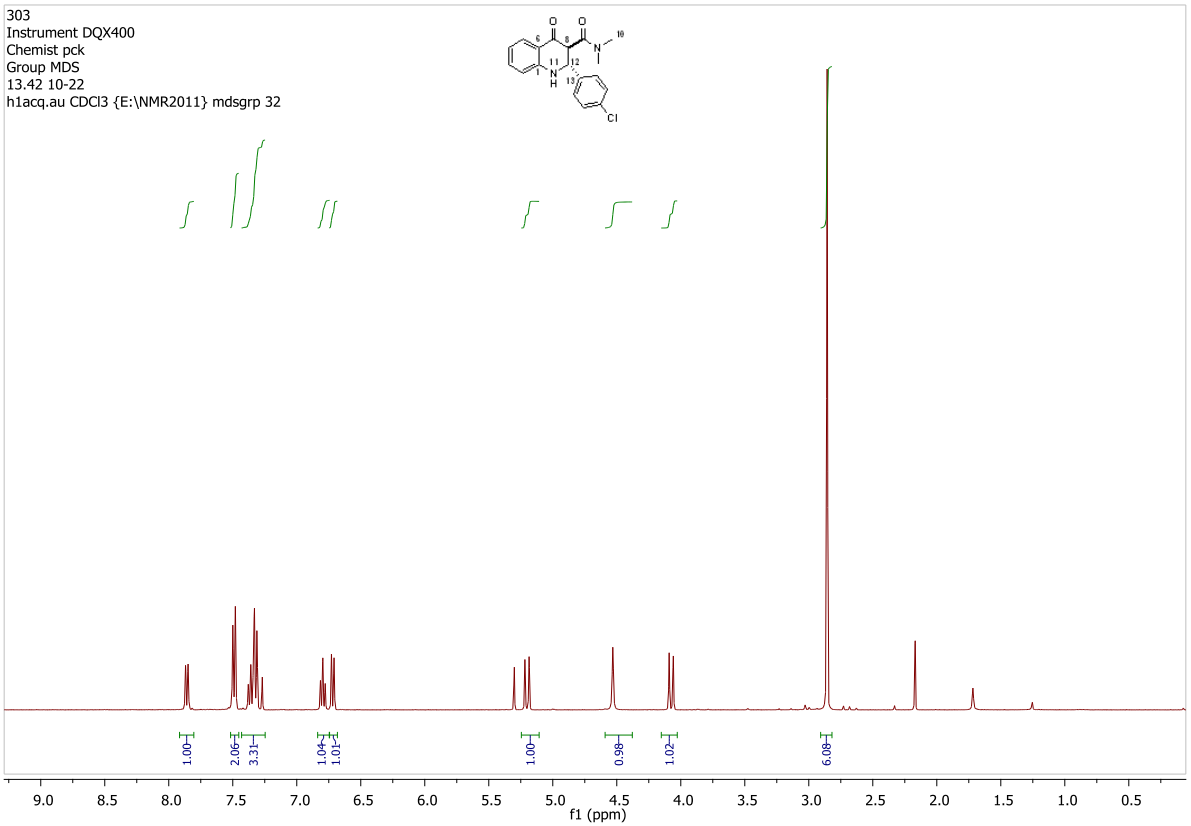

301
Instrument DQX400
Chemist pck
Group mds
13.09 rac 10-24
c13acq.au CDCl3 {E:\NMR2011} mdsgrp 23
189.36
167.44
150.86
136.57
135.78
133.95
130.59
129.60
128.74
127.96
127.21
118.35
115.76
56.50
54.52
37.69
35.70
f1 (ppm)

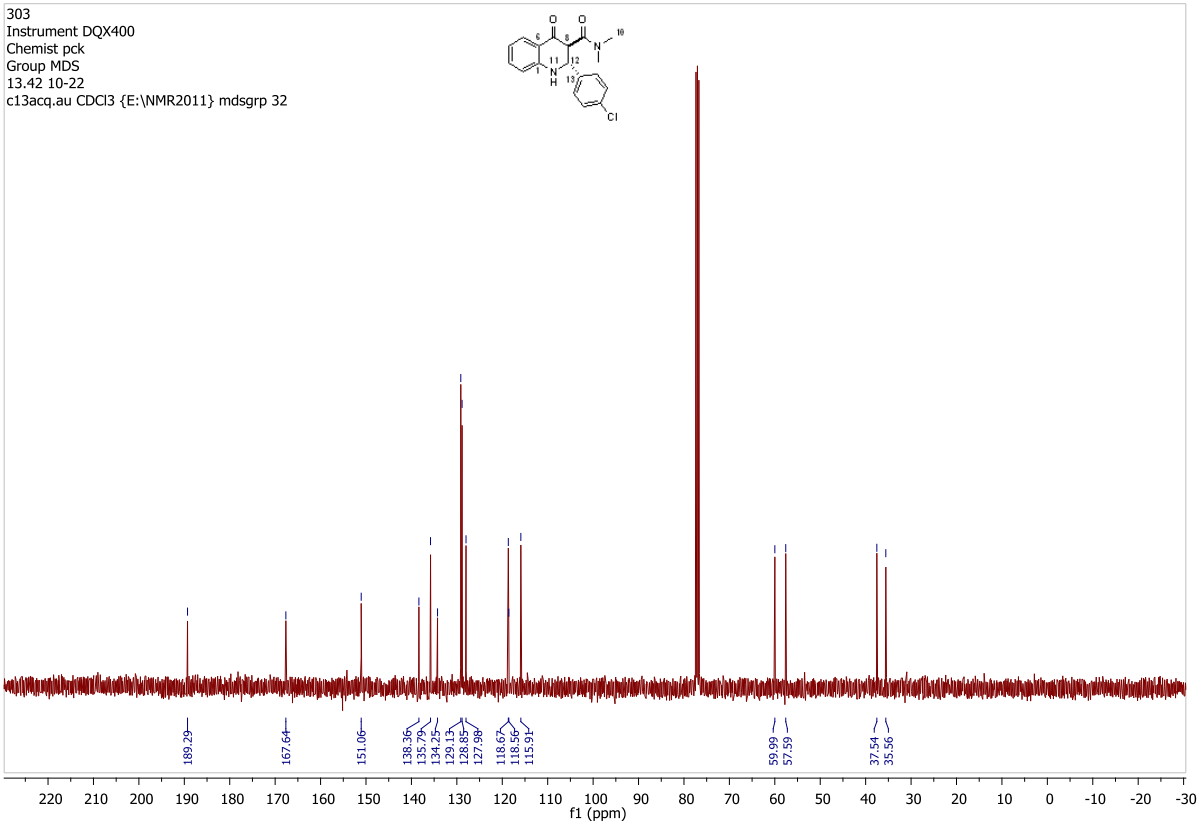
11


302
Instrument DQX400
Chemist pck
Group mds
13.10 rac 5-30
h1acq.au CDCl3 {E:\NMR2011} mdsgrp 24
1.00
0.99
1.06
1.15
2.36
1.05
1.04
1.01
1.12
1.04
6.10
f1 (ppm)

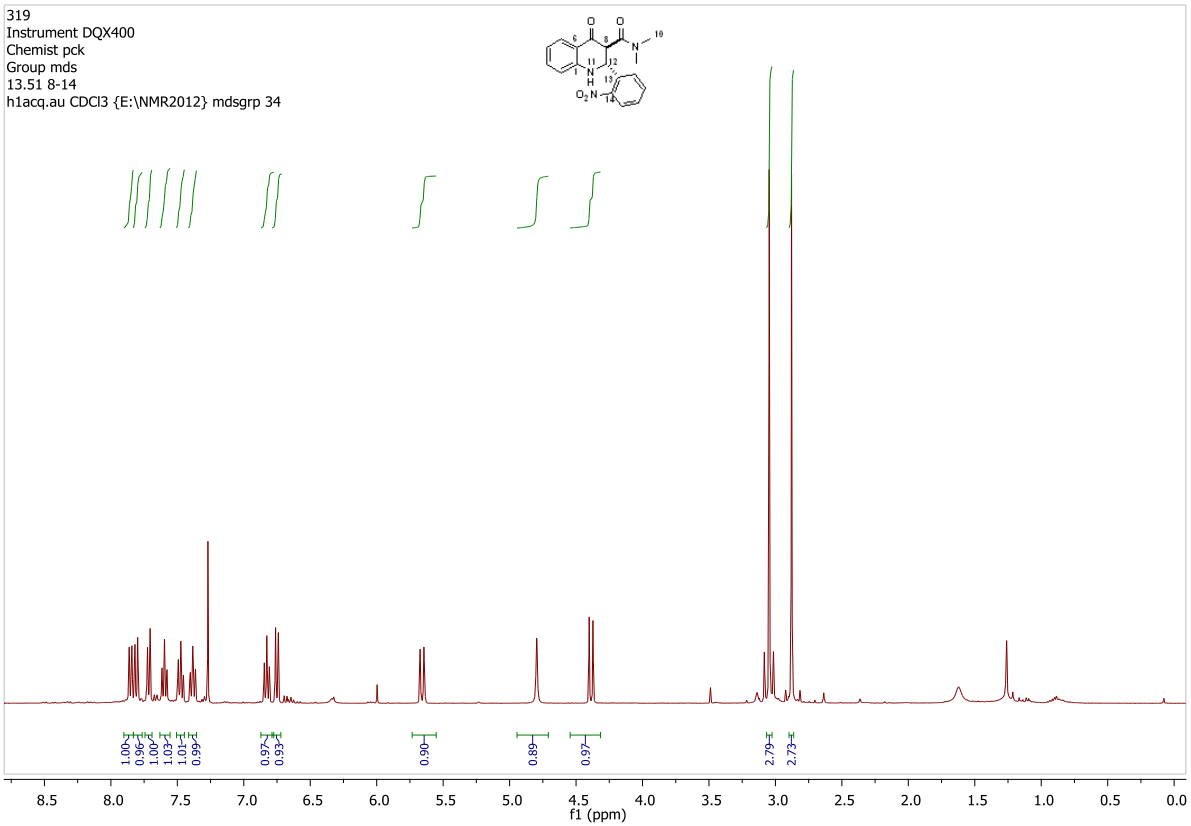

302
Instrument DQX400
Chemist pck
Group mds
13.10 rac 5-30
c13acq.au CDCl3 {E:\NMR2011} mdsgrp 24
189.17
167.58
150.94
141.89
135.81
134.49
129.98
128.86
128.06
127.51
126.34
118.73
118.58
115.88
60.14
57.45
37.56
35.59
f1 (ppm)

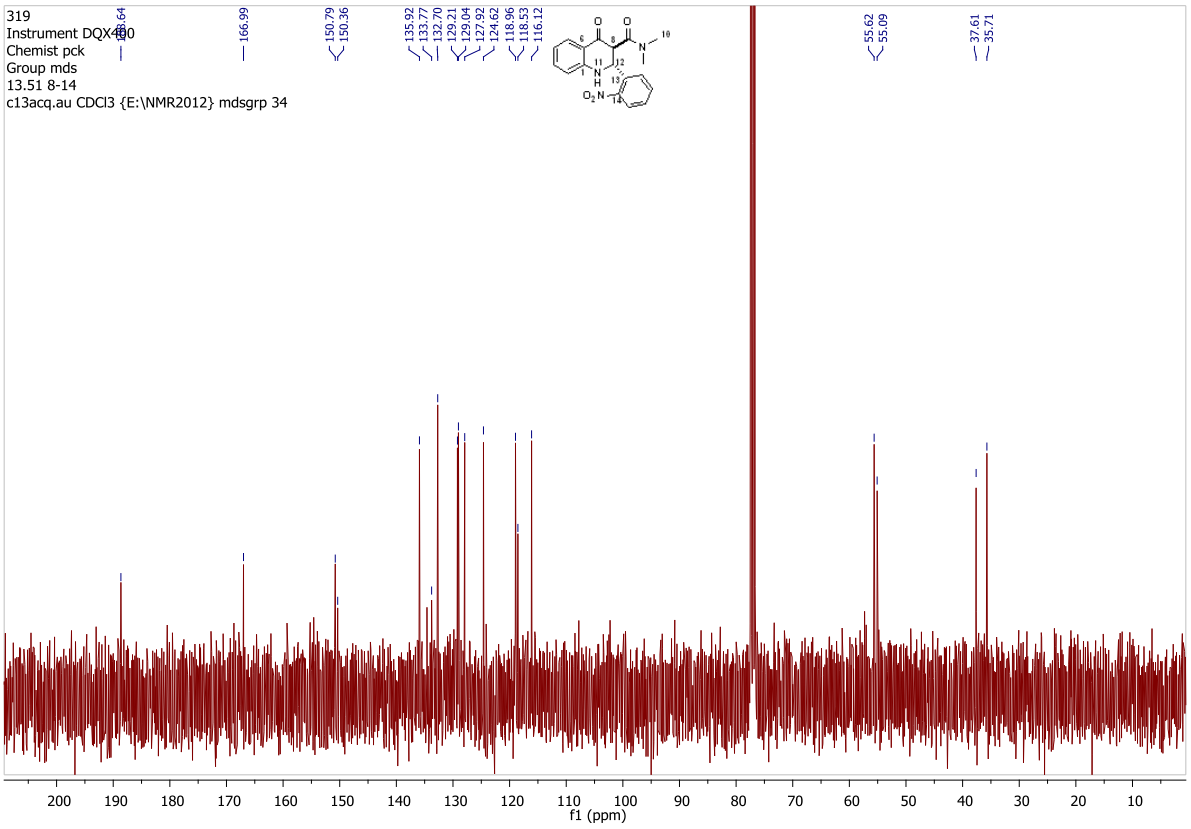
12


303
Instrument DQX400
Chemist pck
Group MDS
13.42 10-22
h1acq.au CDCl3 {E:\NMR2011} mdsgrp 32
1.00
2.06
3.31
1.04
1.01
1.00
0.98
1.02
6.08
f1 (ppm)

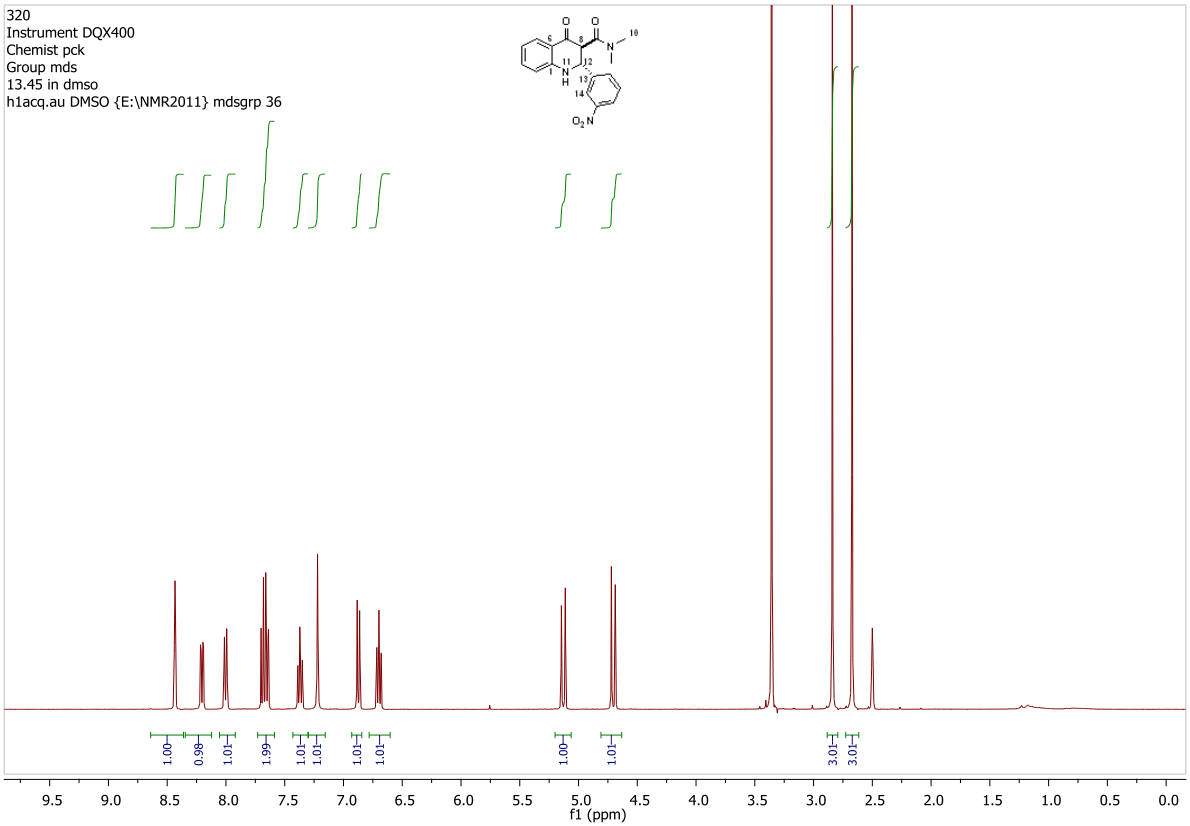

303
Instrument DQX400
Chemist pck
Group MDS
13.42 10-22
c13acq.au CDCl3 {E:\NMR2011} mdsgrp 32
189.29
167.64
151.06
138.36
135.79
134.25
129.13
128.85
127.98
118.67
118.56
115.91
59.99
57.59
37.54
35.56
f1 (ppm)

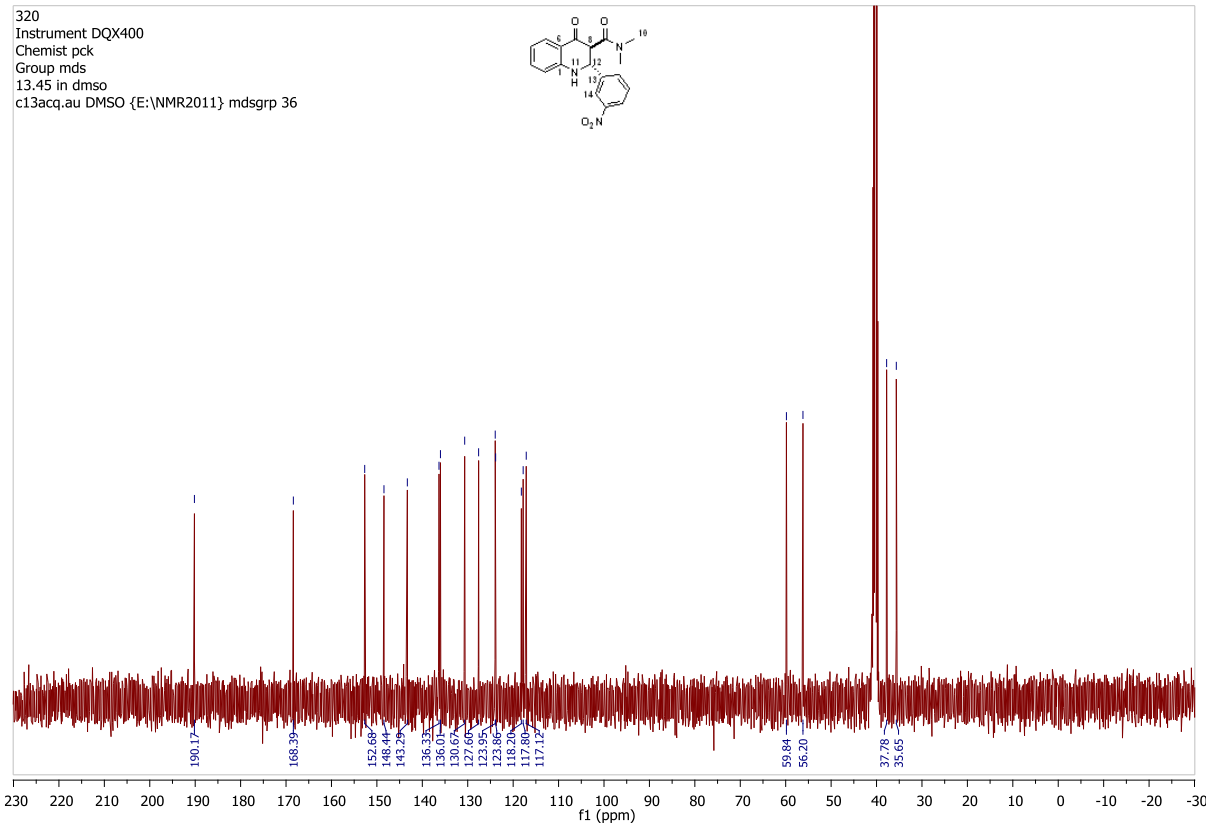
13


319
Instrument DQX400
Chemist pck
Group mds
13.51 8-14
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 34
1.00
0.96
1.00
1.03
1.01
0.99
0.97
0.93
0.90
0.89
0.97
2.79
2.73
f1 (ppm)

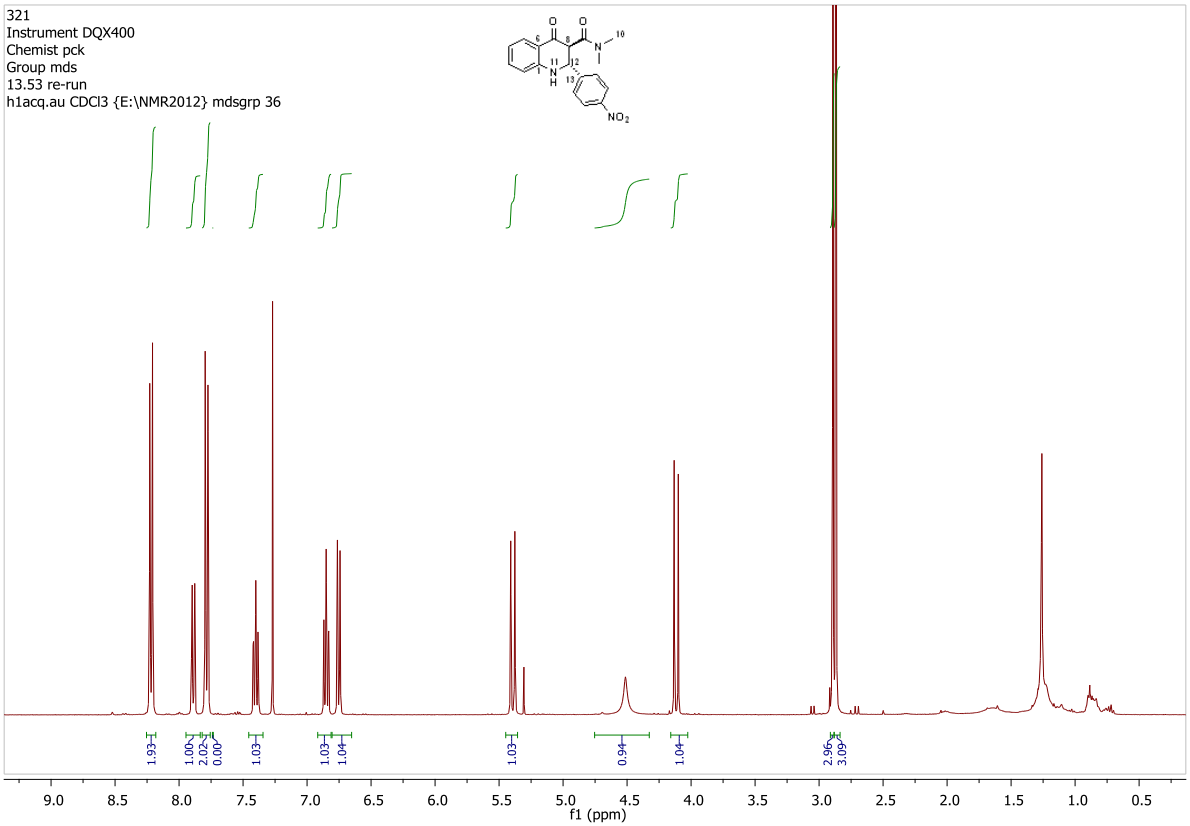

319
Instrument DQX400
Chemist pck
Group mds
13.51 8-14
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 34
166.99
150.79
150.36
135.92
133.77
132.70
129.21
129.04
127.92
124.62
118.96
118.53
116.12
55.62
55.09
37.61
35.71
f1 (ppm)

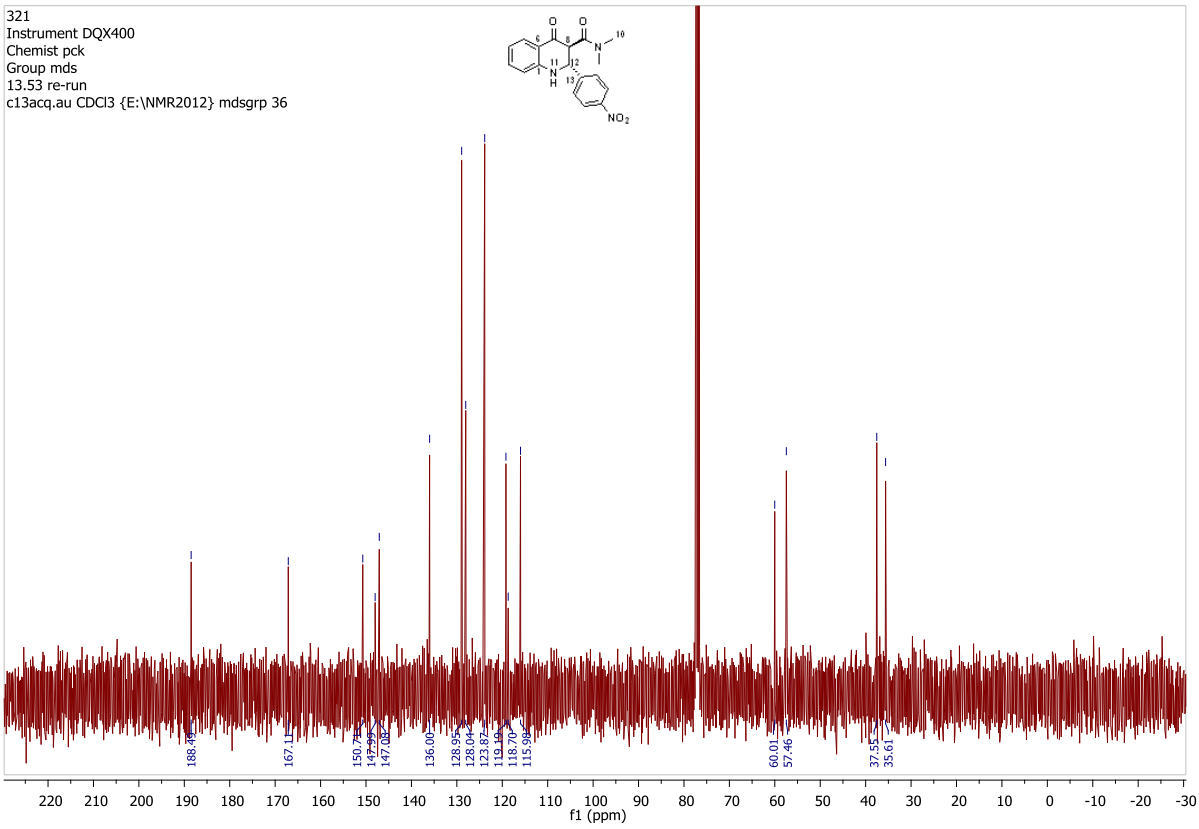
14


320
Instrument DQX400
Chemist pck
Group mds
13.45 in dmso
h1acq.au DMSO {E:\NMR2011} mdsgrp 36
1.00
0.98
1.01
1.99
1.01
1.01
1.01
1.01
1.00
1.01
3.01
3.01
f1 (ppm)

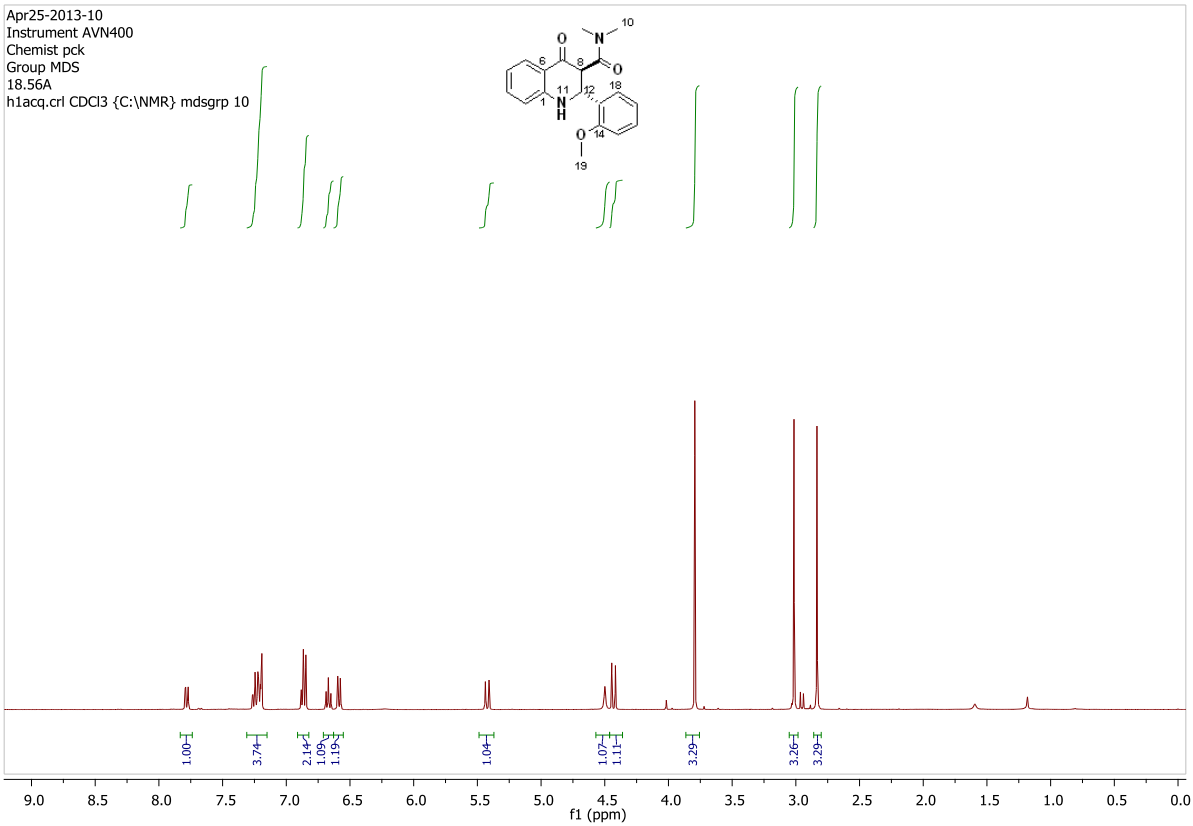

320
Instrument DQX400
Chemist pck
Group mds
13.45 in dmso
c13acq.au DMSO {E:\NMR2011} mdsgrp 36
190.17
168.39
152.68
148.44
143.29
136.33
136.01
130.67
127.66
123.95
123.96
118.20
117.80
117.12
59.84
56.20
37.78
35.65
f1 (ppm)

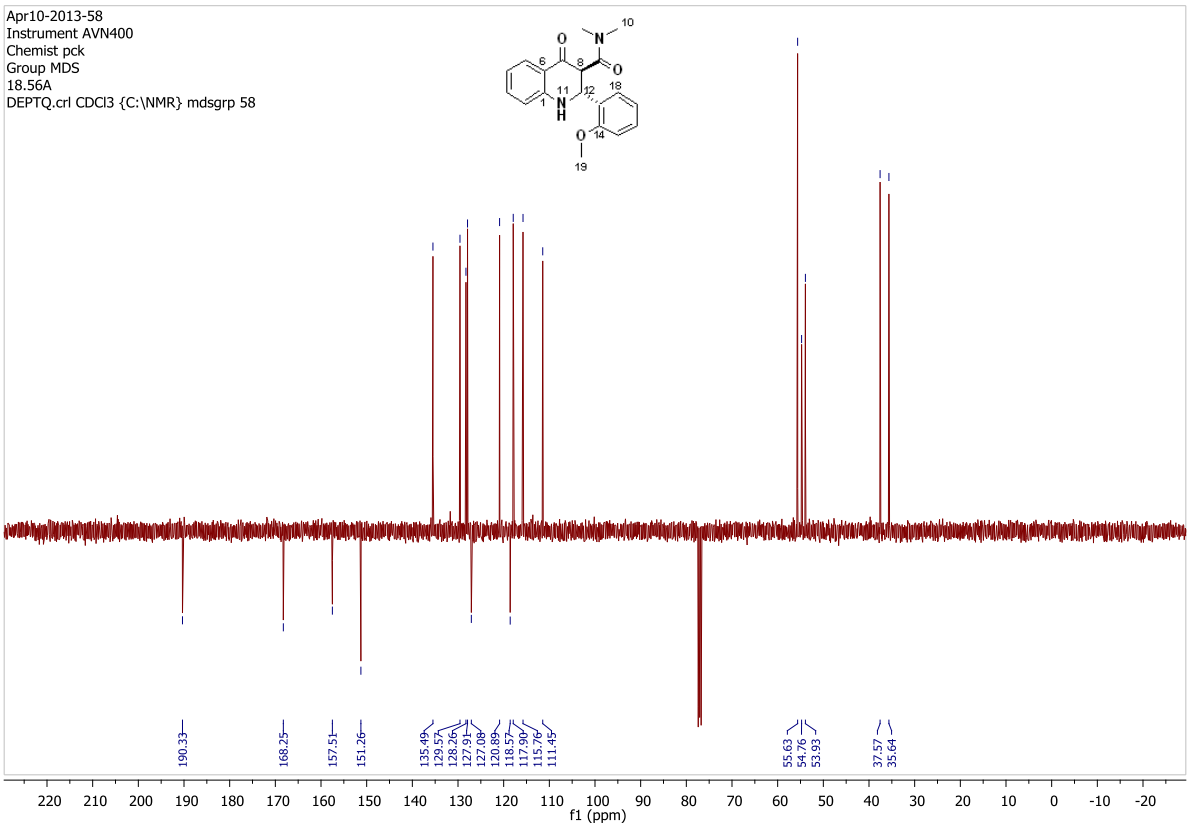
15


321
Instrument DQX400
Chemist pck
Group mds
13.53 re-run
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 36
1.93
1.00
2.02
0.00
1.03
1.03
1.04
1.03
0.94
1.04
2.96
3.09
f1 (ppm)

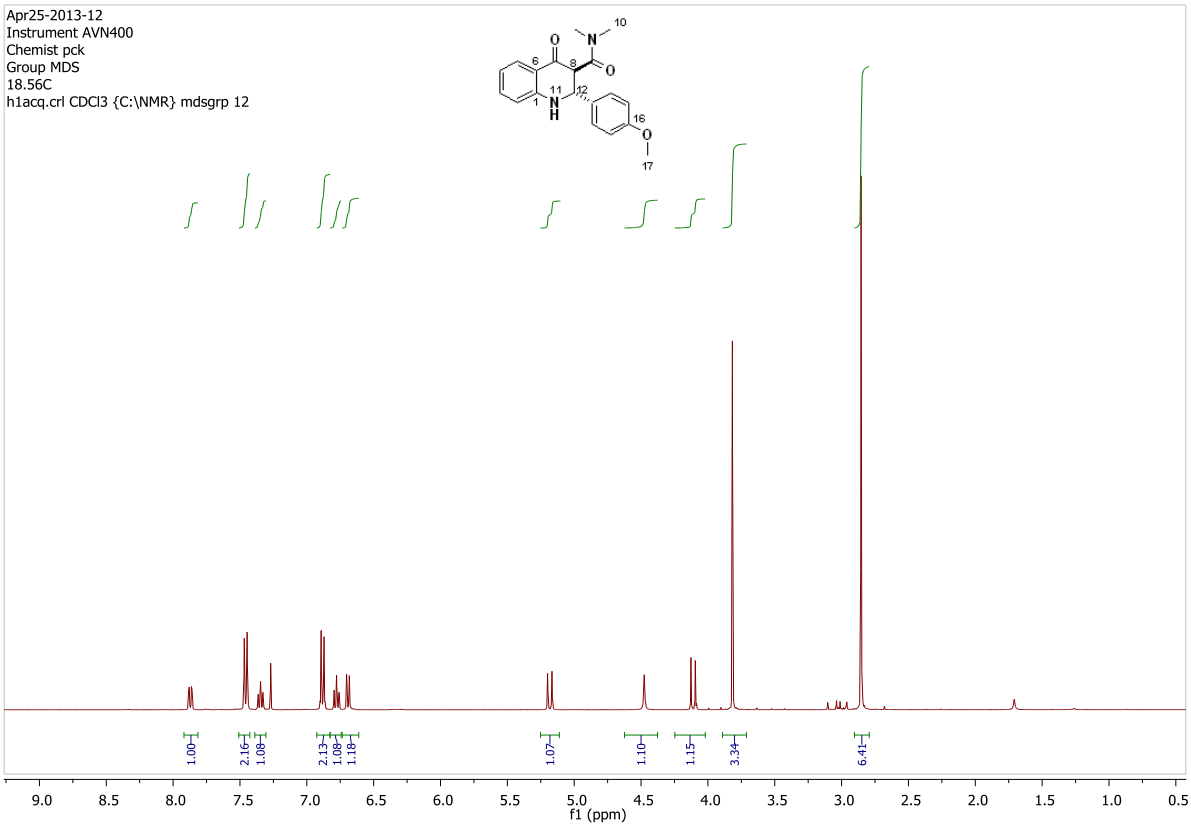

321
Instrument DQX400
Chemist pck
Group mds
13.53 re-run
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 36
188.46
167.11
150.78
147.99
147.08
136.00
128.95
128.04
123.87
119.19
118.70
115.98
60.01
57.46
37.55
35.61
f1 (ppm)

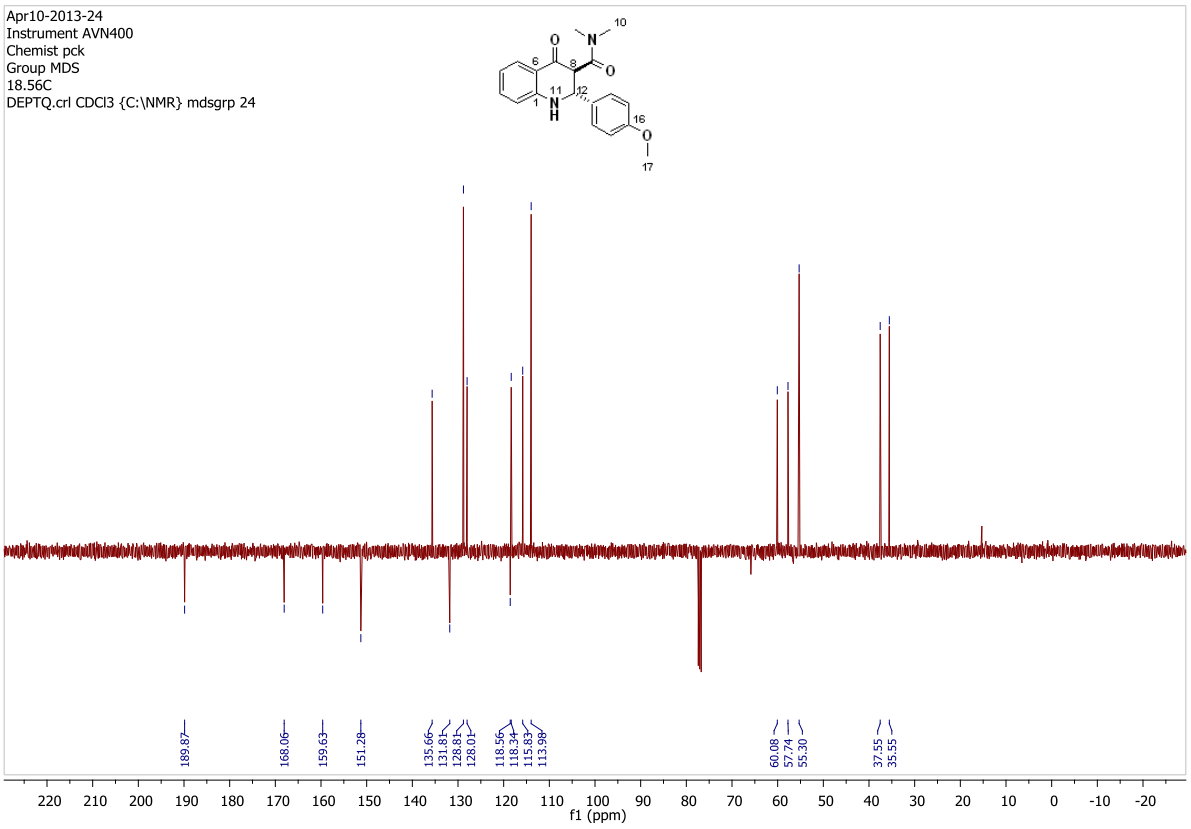
16


Apr25-2013-10
Instrument AVN400
Chemist pck
Group MDS
18.56A
h1acq.crl CDCl3 {C:\NMR} mdsgrp 10
1.00
3.74
2.14
1.09
1.19
1.04
1.07
1.11
3.29
3.26
3.29
f1 (ppm)

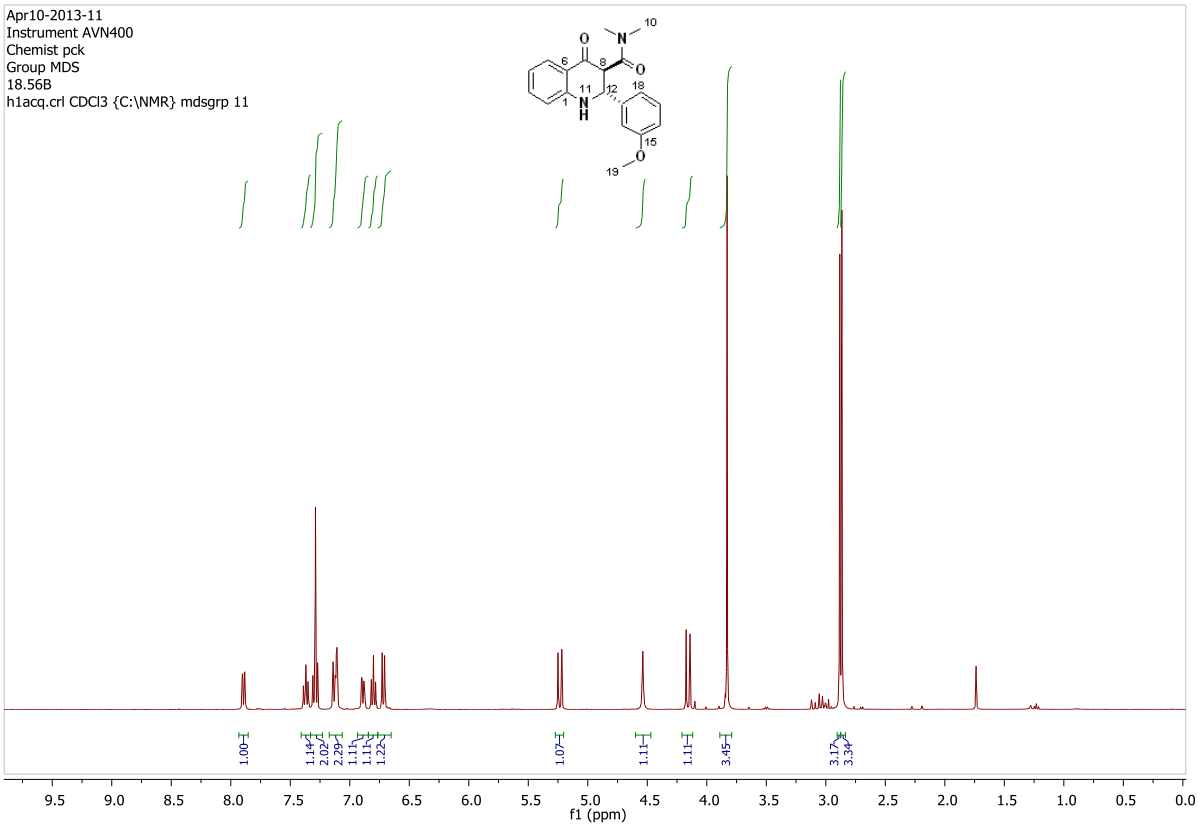

Apr10-2013-58
Instrument AVN400
Chemist pck
Group MDS
18.56A
DEPTQ.crl CDCl3 {C:\NMR} mdsgrp 58
190.33
168.25
157.51
151.26
135.49
129.57
128.26
127.91
127.08
120.89
118.57
117.90
115.76
111.45
55.63
54.76
53.93
37.57
35.64
f1 (ppm)

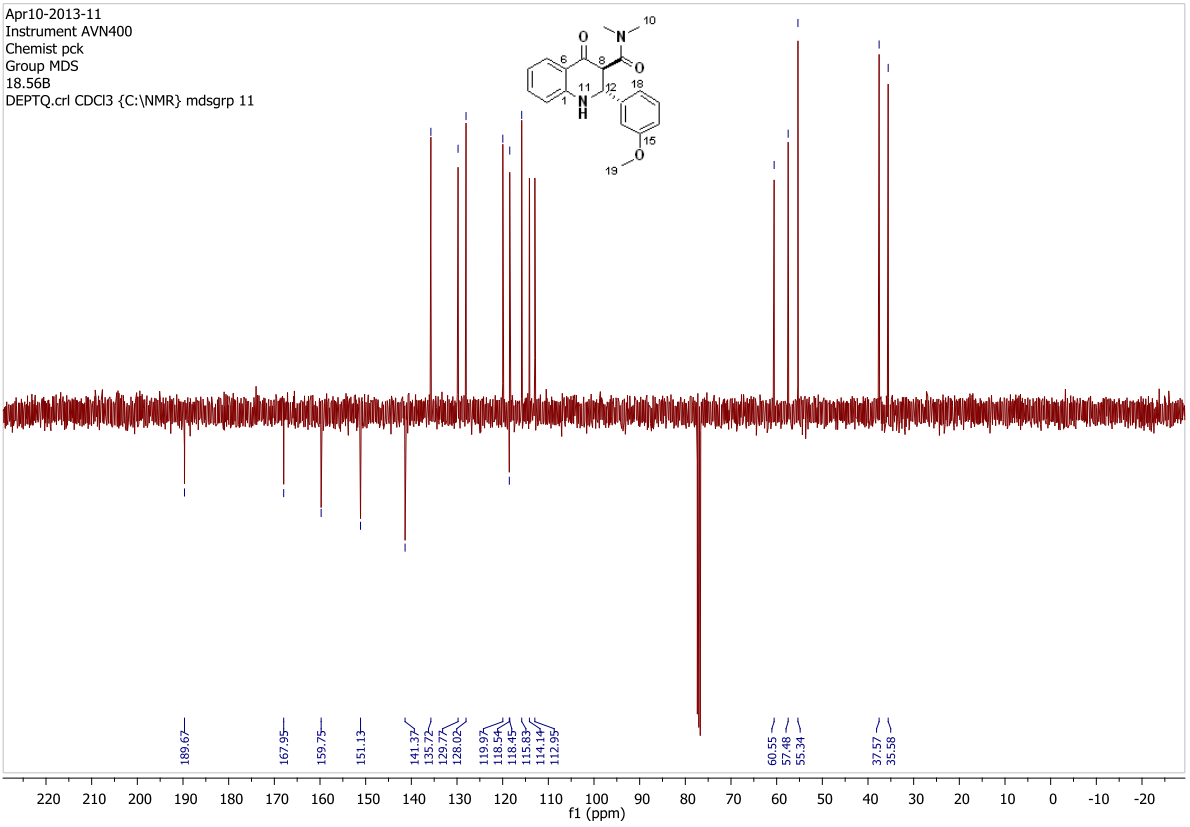
17


Apr25-2013-12
Instrument AVN400
Chemist pck
Group MDS
18.56C
h1acq.crl CDCl3 {C:\NMR} mdsgrp 12
1.00
2.16
1.08
2.13
1.08
1.18
1.07
1.10
1.15
3.34
6.41
f1 (ppm)

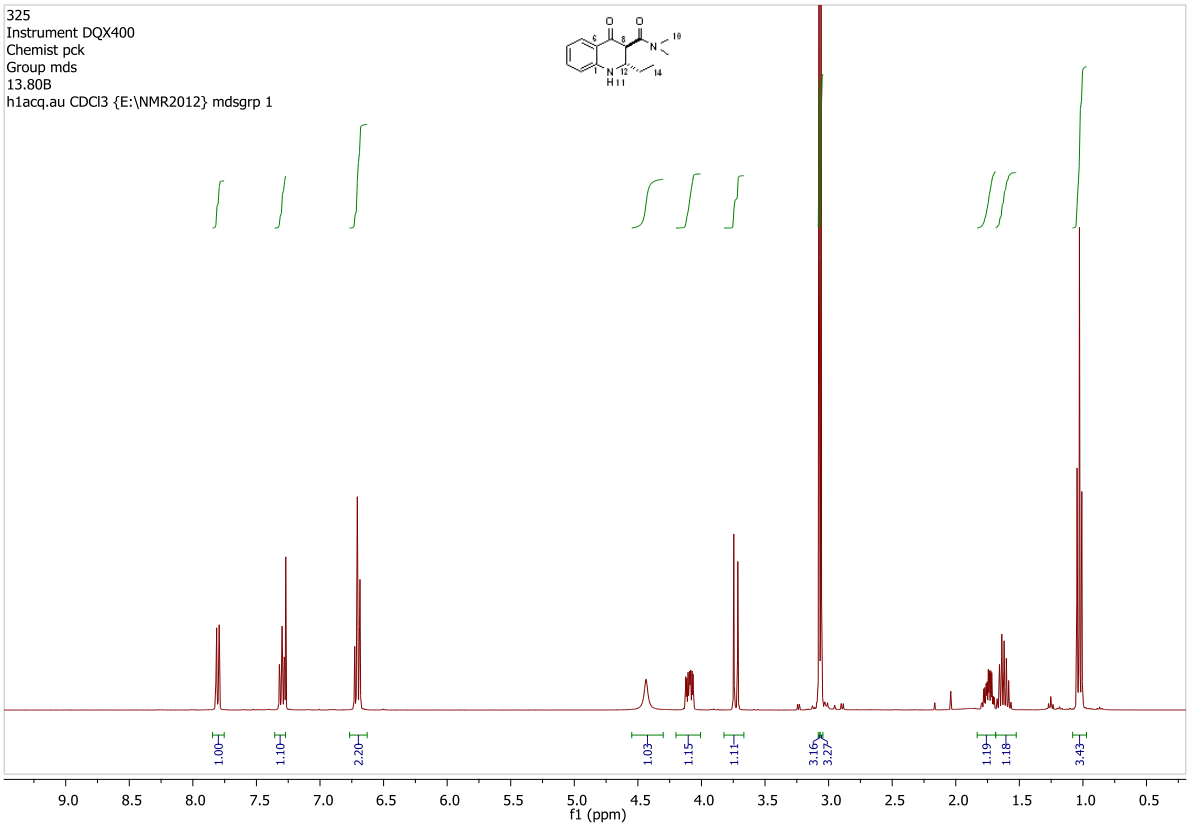

Apr10-2013-24
Instrument AVN400
Chemist pck
Group MDS
18.56C
DEPTQ.crl CDCl3 {C:\NMR} mdsgrp 24
189.87
168.06
159.63
151.28
135.66
131.81
128.81
128.01
118.56
118.34
115.83
113.98
60.08
57.74
55.30
37.55
35.55
f1 (ppm)

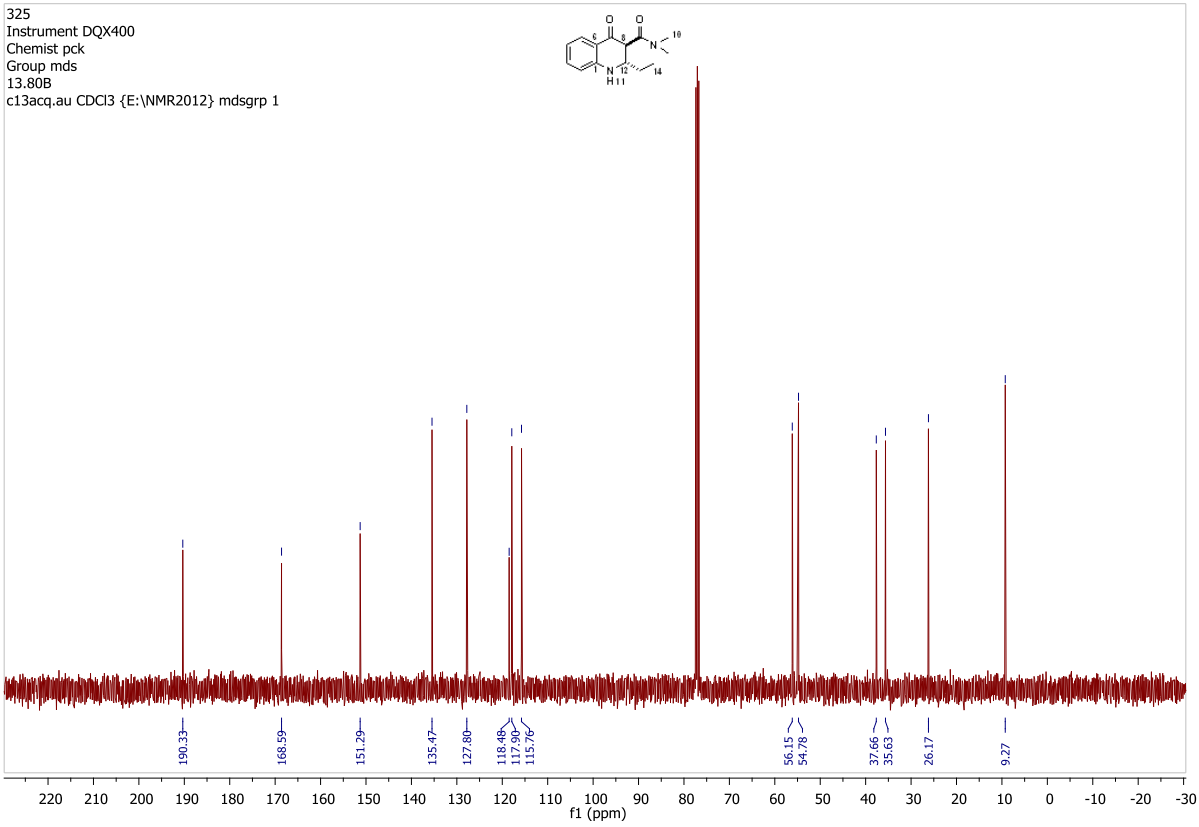
18


Apr10-2013-11
Instrument AVN400
Chemist pck
Group MDS
18.56B
h1acq.crl CDCl3 {C:\NMR} mdsgrp 11
1.00
1.14
2.02
2.29
1.11
1.11
1.22
1.07
1.11
1.11
3.45
3.17
3.34
f1 (ppm)

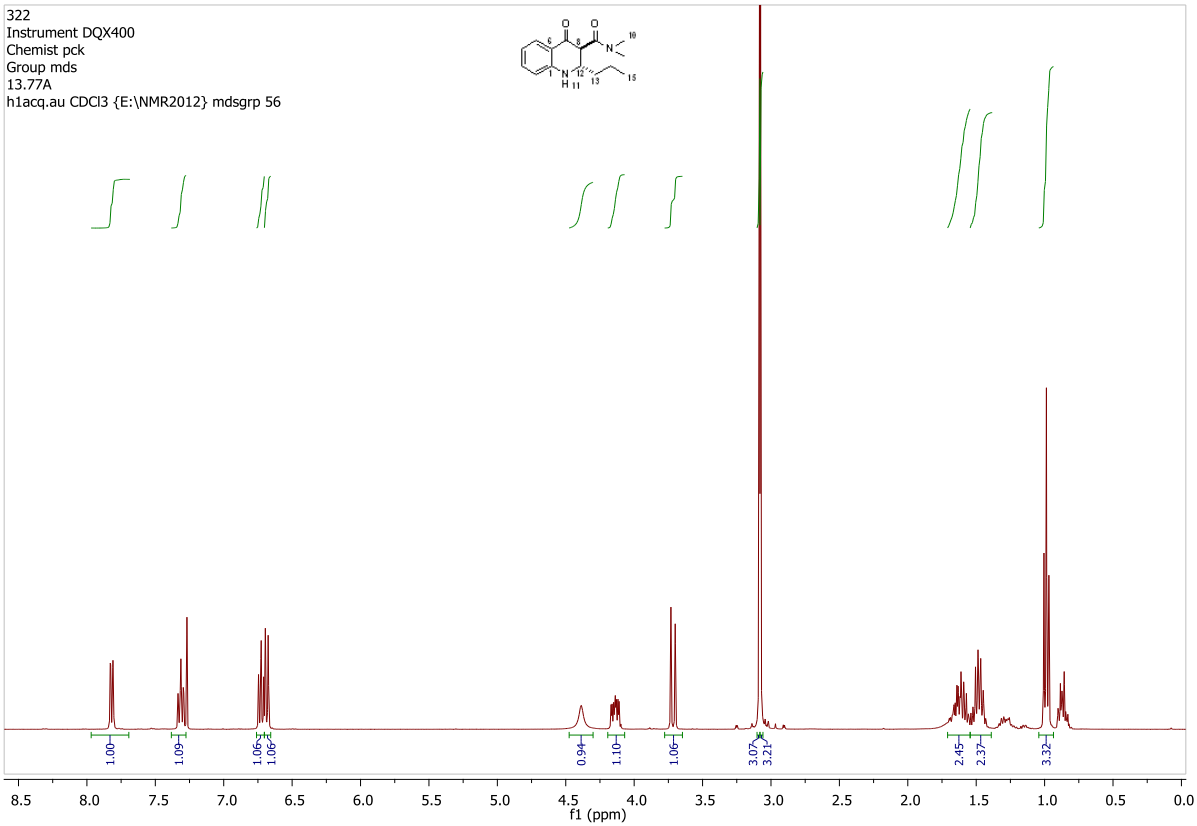

Apr10-2013-11
Instrument AVN400
Chemist pck
Group MDS
18.56B
DEPTQ.crl CDCl3 {C:\NMR} mdsgrp 11
189.67
167.95
159.75
151.13
141.37
135.72
129.75
128.02
119.97
118.54
118.45
115.83
114.14
112.95
60.55
57.48
55.34
37.57
35.58
f1 (ppm)

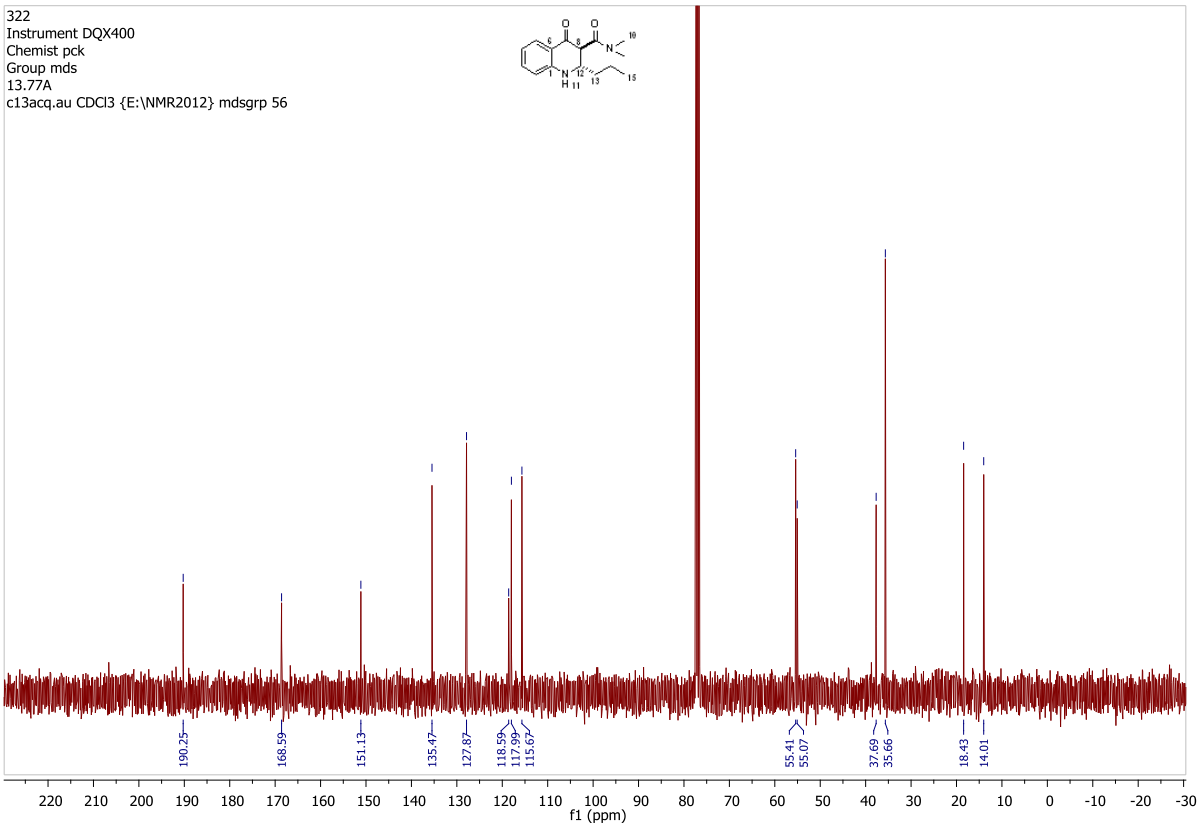
19


325
Instrument DQX400
Chemist pck
Group mds
13.80B
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 1
1.00
1.10
2.20
1.03
1.15
1.11
3.16
3.27
1.19
1.18
3.43
f1 (ppm)


325
Instrument DQX400
Chemist pck
Group mds
13.80B
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 1
190.33
168.59
151.29
135.47
127.80
118.48
117.90
115.76
56.15
54.78
37.66
35.63
26.17
9.27
f1 (ppm)

20


322
Instrument DQX400
Chemist pck
Group mds
13.77A
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 56
1.00
1.09
1.06
1.06
0.94
1.10
1.06
3.07
3.21
2.45
2.37
3.32
f1 (ppm)


322
Instrument DQX400
Chemist pck
Group mds
13.77A
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 56
190.25
168.59
151.13
135.47
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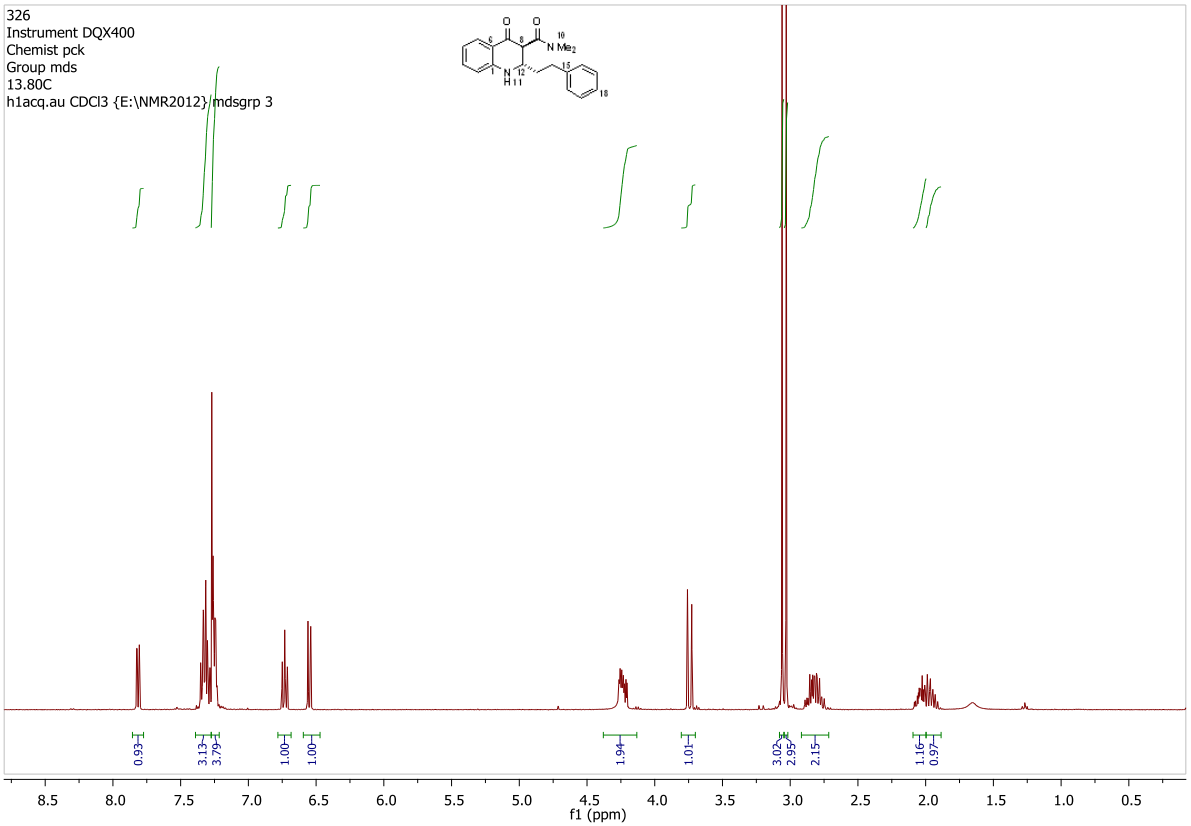
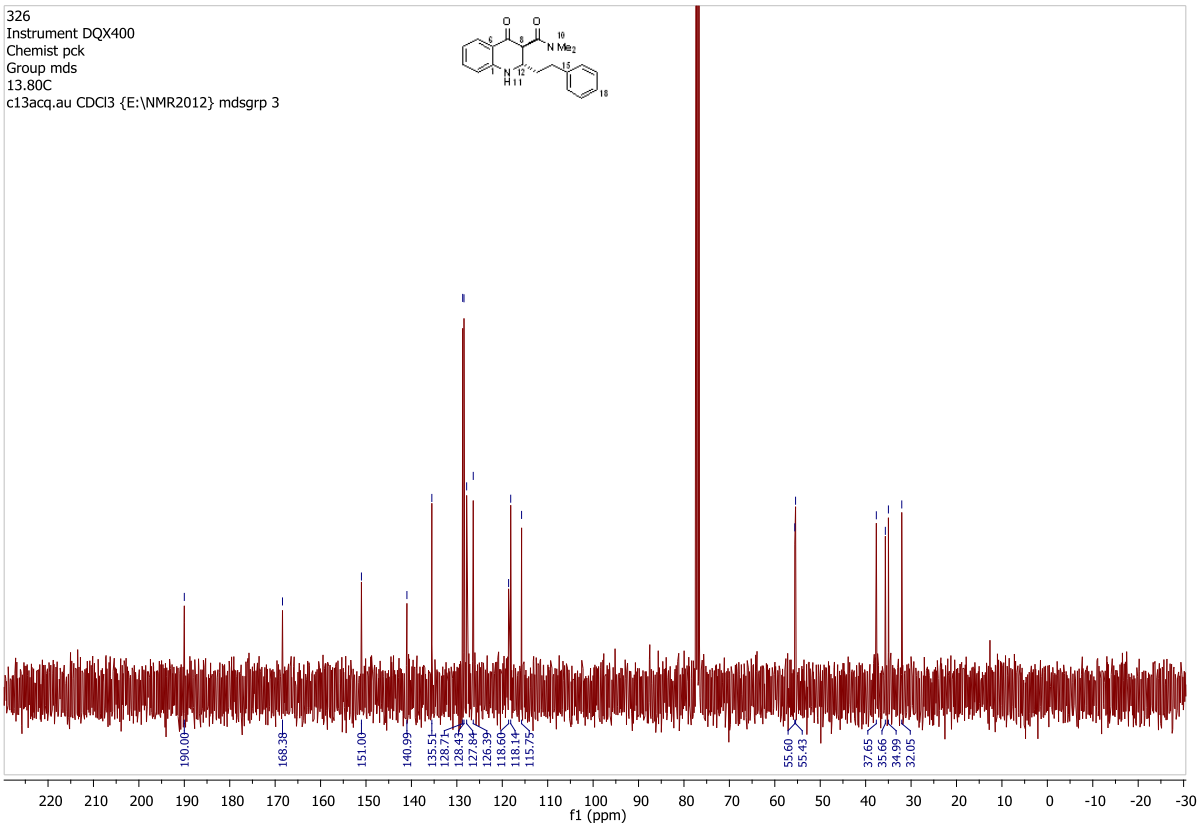
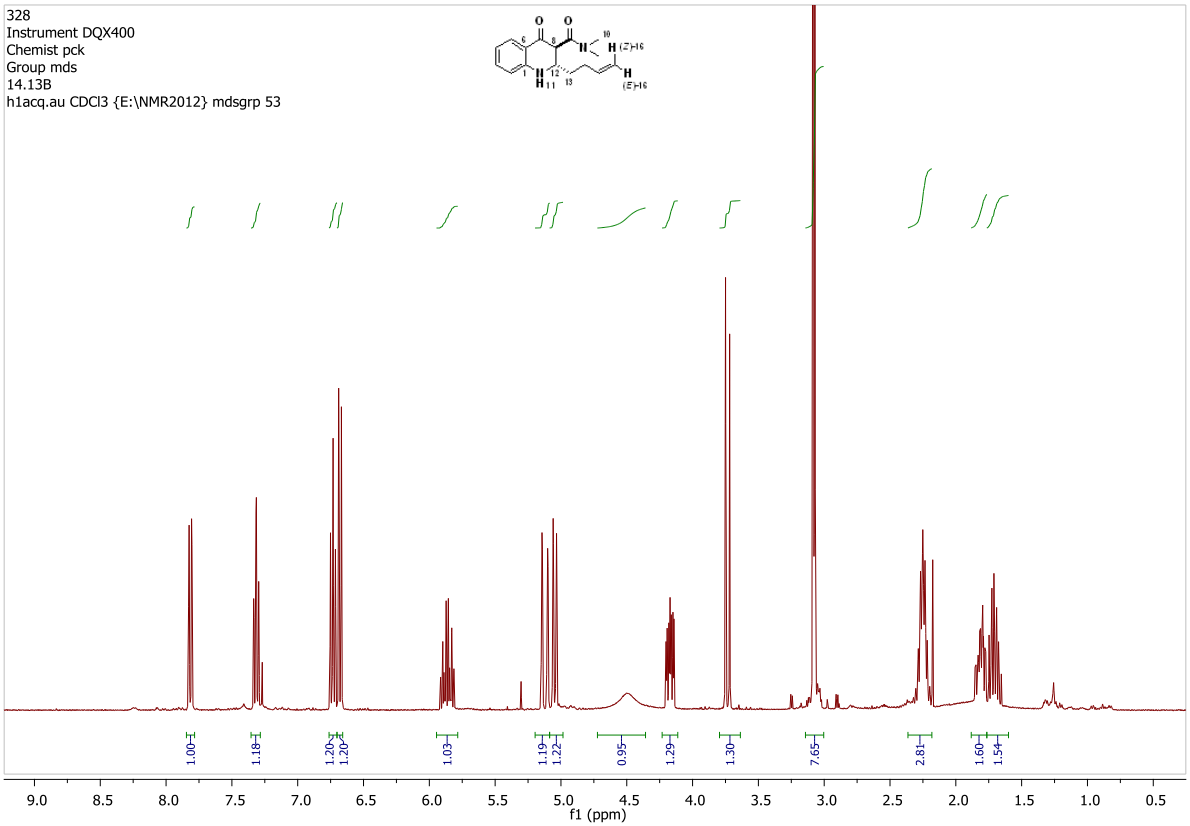
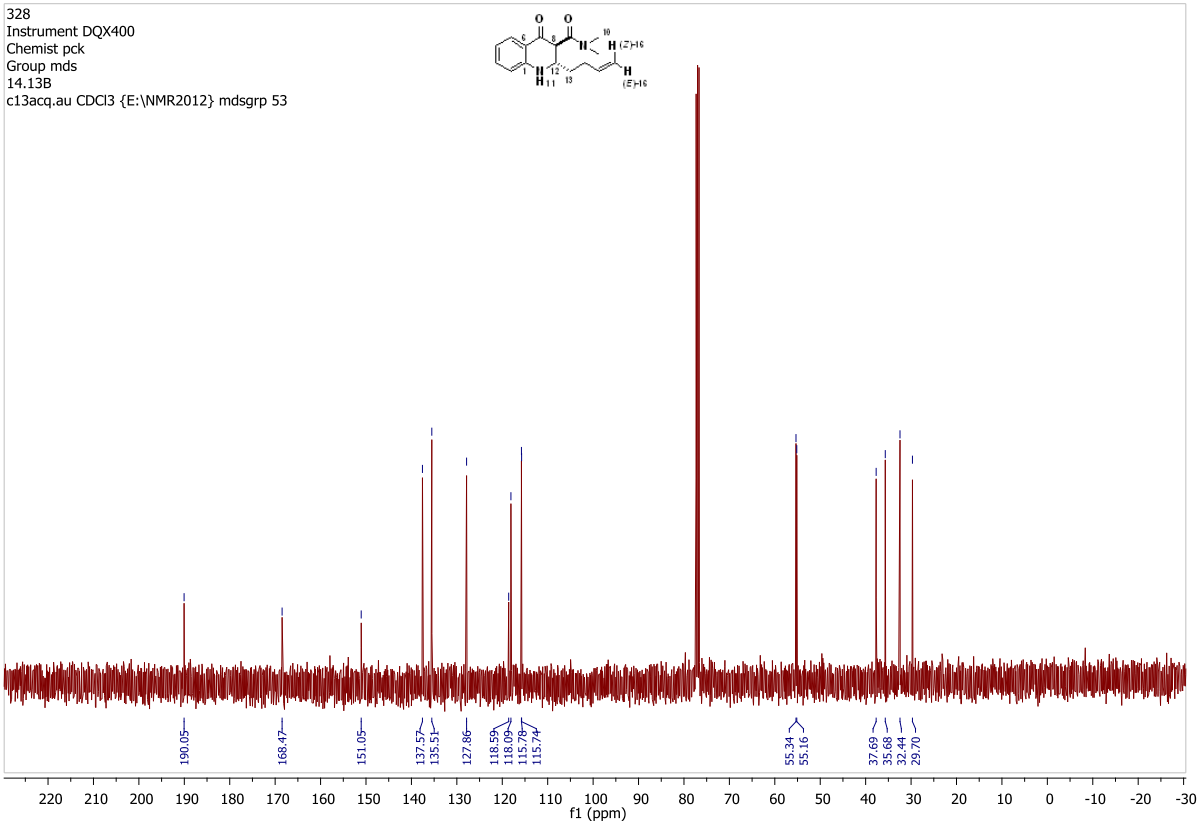
37.69
35.66
18.43
14.01
f1 (ppm)

21

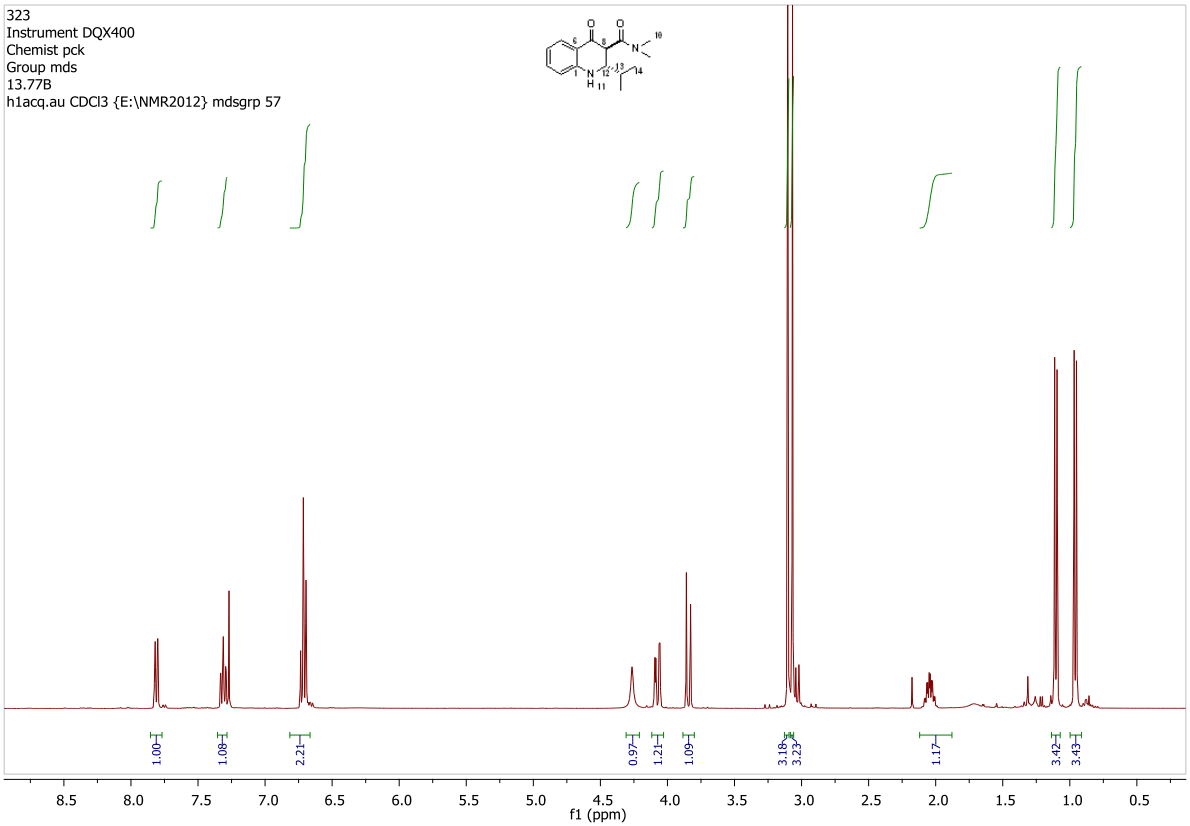

326
Instrument DQX400
Chemist pck
Group mds
13.80C
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 3
0.93
3.13
3.79
1.00
1.00
1.94
1.01
3.02
2.95
2.15
1.16
0.97
f1 (ppm)


326
Instrument DQX400
Chemist pck
Group mds
13.80C
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 3
190.00
168.38
151.00
140.99
135.51
128.71
128.49
127.94
126.39
118.60
118.14
115.75
55.60
55.43
37.65
35.66
34.99
32.05
f1 (ppm)


328
Instrument DQX400
Chemist pck
Group mds
14.13B
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 53
1.00
1.18
1.20
1.20
1.03
1.19
1.22
0.95
1.29
1.30
7.65
2.81
1.60
1.54
f1 (ppm)


328
Instrument DQX400
Chemist pck
Group mds
14.13B
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 53
190.05
168.47
151.05
137.57
135.51
127.86
118.59
118.09
115.78
115.74
55.34
55.16
37.69
35.68
32.44
29.70
f1 (ppm)

23


323
Instrument DQX400
Chemist pck
Group mds
13.77B
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 57
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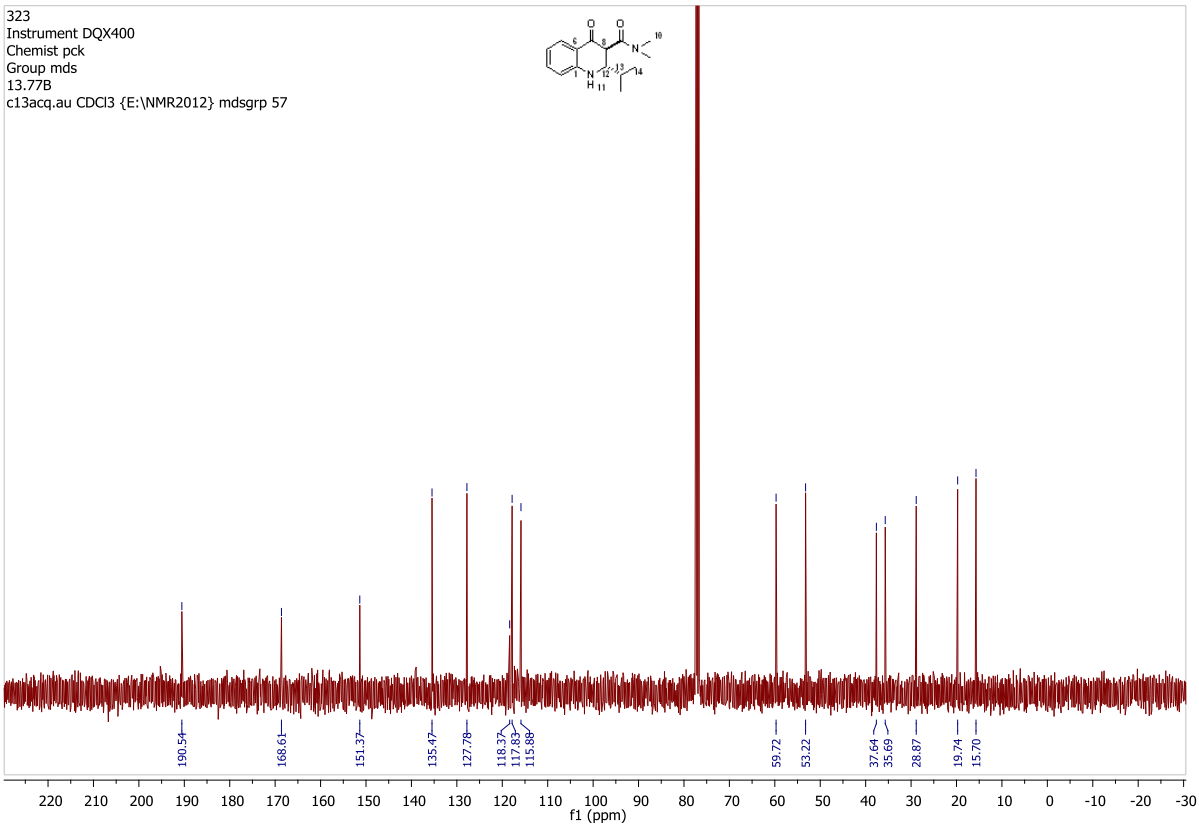
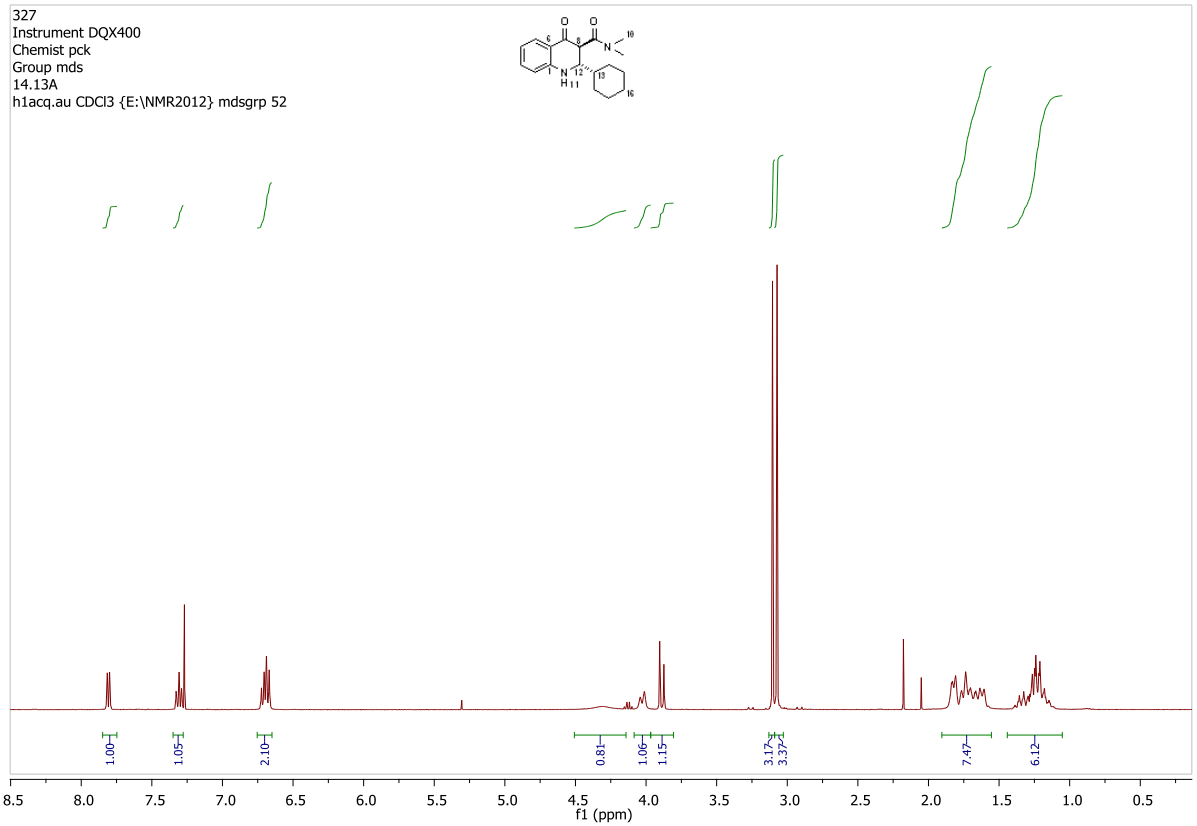
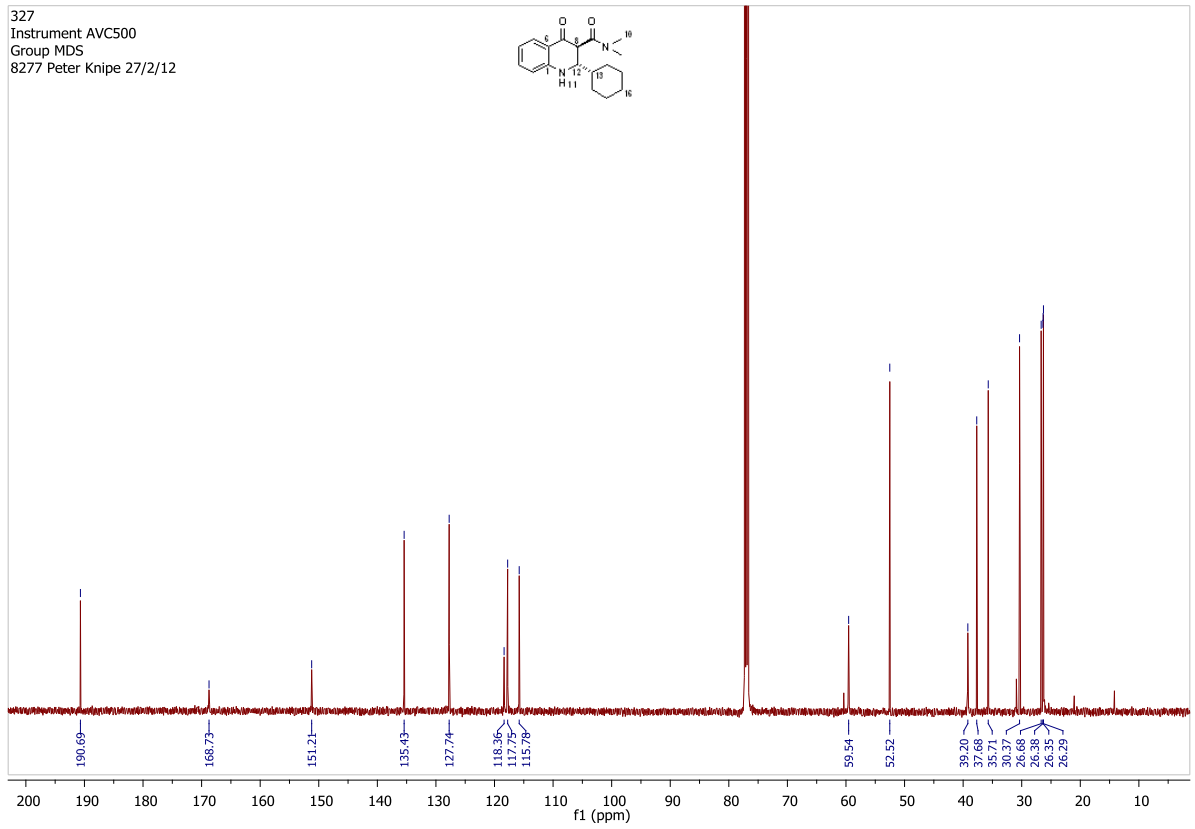
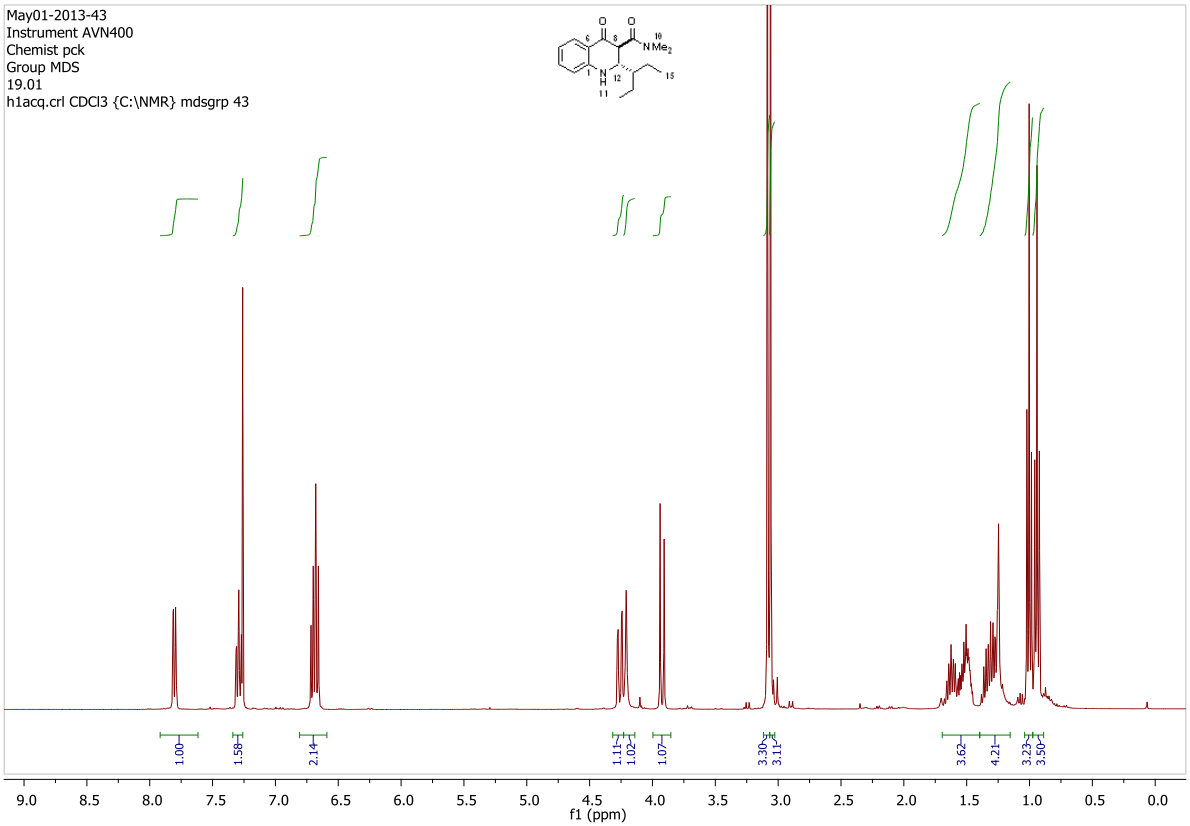
1.08
2.21
0.97
1.21
1.09
3.18
3.23
1.17
3.42
3.43
f1 (ppm)

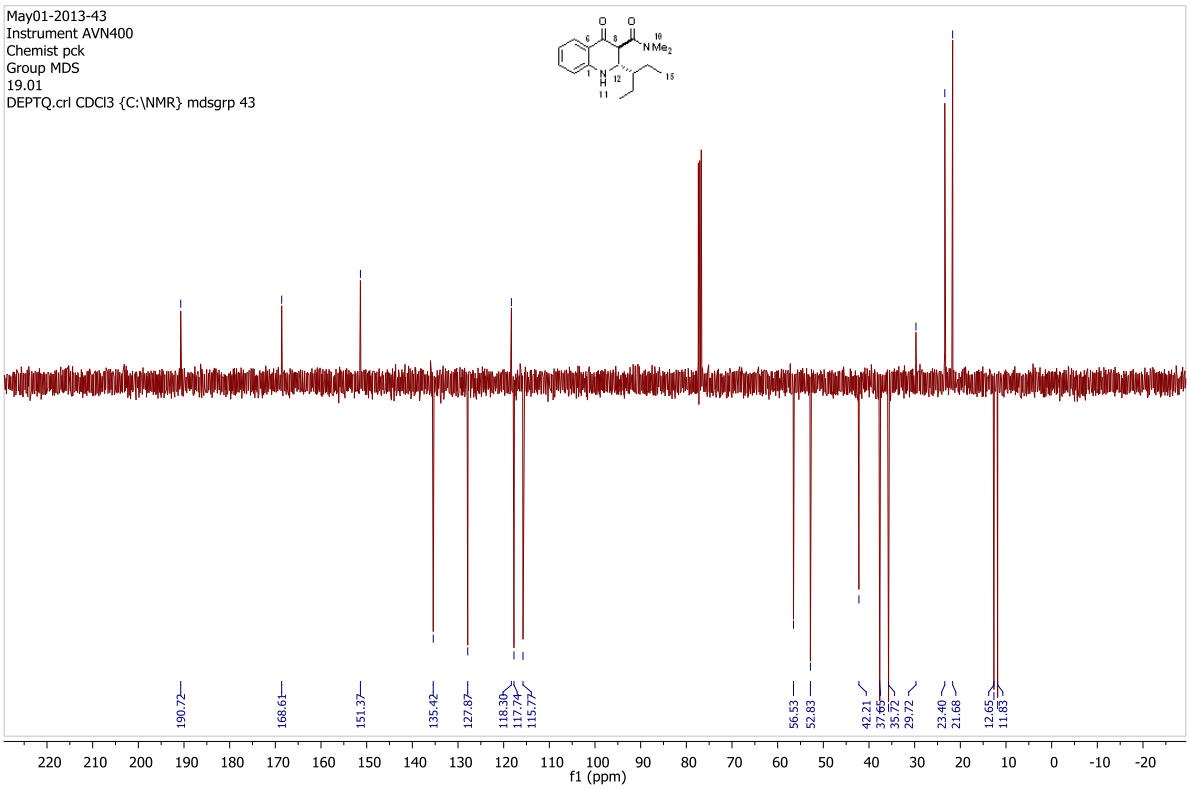

323
Instrument DQX400
Chemist pck
Group mds
13.77B
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 57
190.54
168.61
151.37
135.47
127.78
118.37
117.83
115.88
59.72
53.22
37.64
35.69
28.87
19.74
15.70
f1 (ppm)


327
Instrument DQX400
Chemist pck
Group mds
14.13A
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 52
1.00
1.05
2.10
0.81
1.06
1.15
3.17
3.37
7.47
6.12
f1 (ppm)

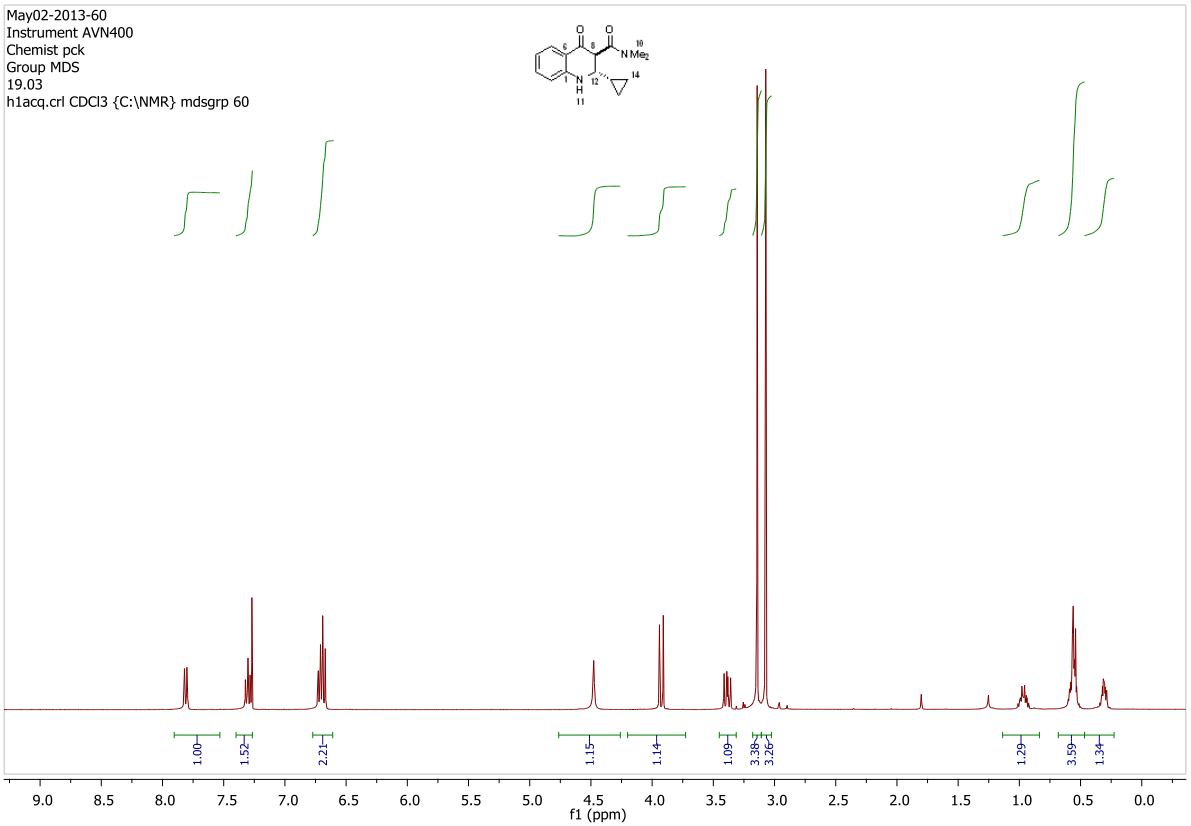

327
Instrument AVC500
Group MDS
8277 Peter Knipe 27/2/12
190.69
168.73
151.21
135.43
127.74
118.36
117.75
115.78
59.54
52.52
39.20
37.68
35.71
30.37
26.68
26.38
26.35
26.29
f1 (ppm)

25


May01-2013-43
Instrument AVN400
Chemist pck
Group MDS
19.01
h1acq.crl CDCl3 {C:\NMR} mdsgrp 43
1.00
1.58
2.14
1.15
1.02
1.07
3.30
3.11
3.62
4.21
3.23
3.50
f1 (ppm)


May01-2013-43
Instrument AVN400
Chemist pck
Group MDS
19.01
DEPTQ.crl CDCl3 {C:\NMR} mdsgrp 43
190.72
168.61
151.37
135.42
127.87
118.30
117.74
115.77
56.53
52.83
42.21
37.65
35.72
29.72
23.40
21.68
12.65
11.83
f1 (ppm)

26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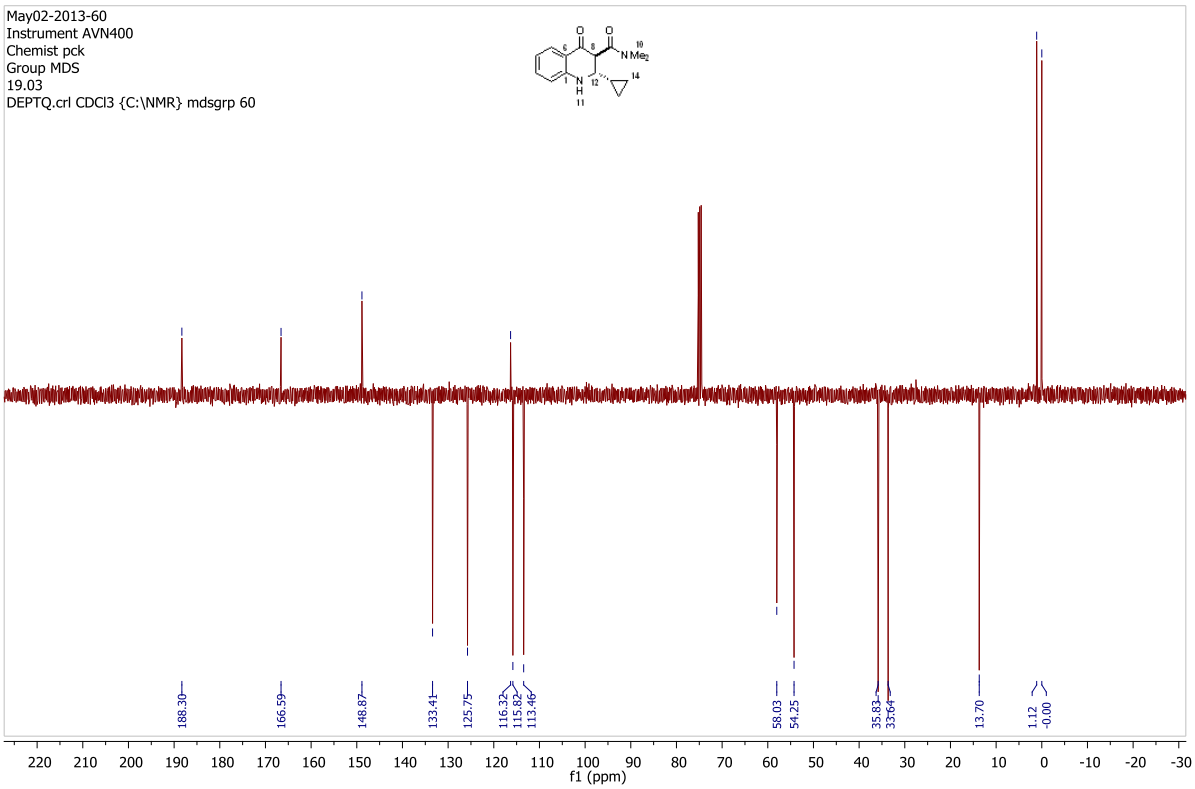
Instrument AVN400
Chemist pck
Group MDS
19.03
h1acq.crl CDCl3 {C:\NMR} mdsgrp 60
1.00
1.52
2.21
1.15
1.14
1.09
3.38
3.26
1.29
3.59
1.34
f1 (ppm)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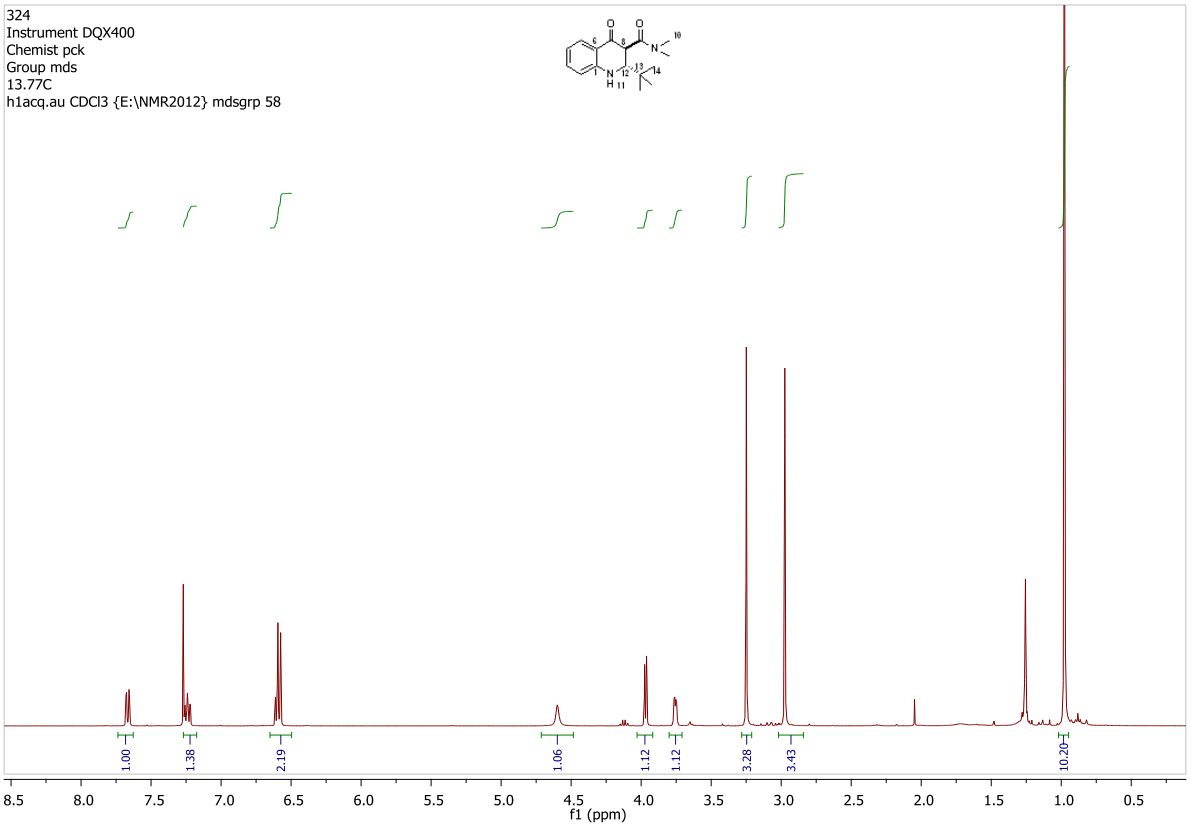
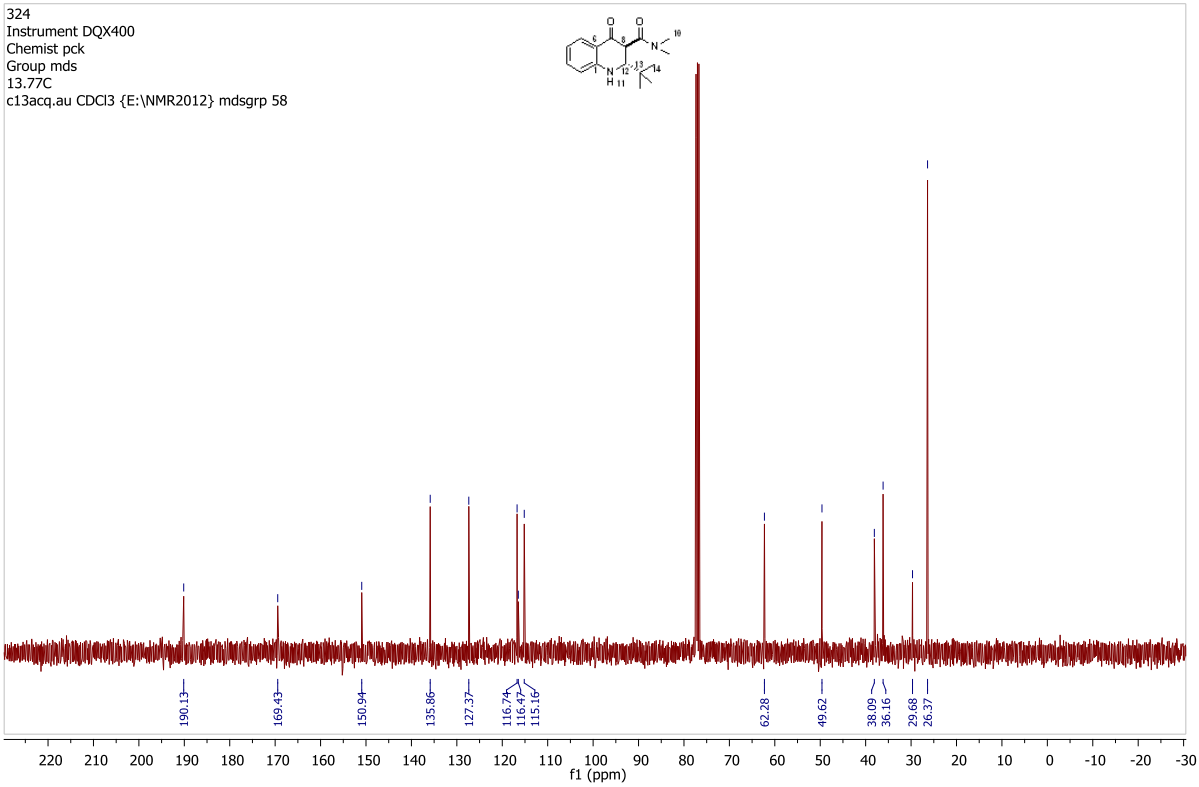
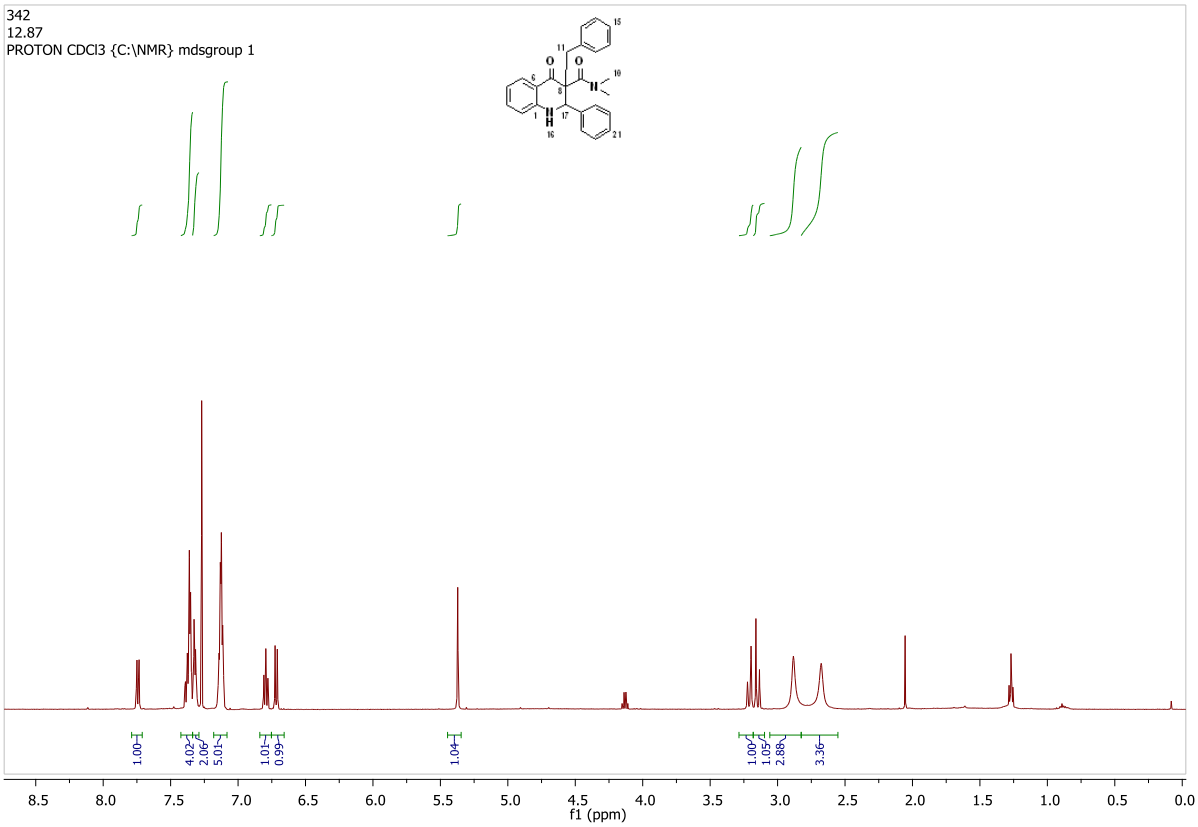
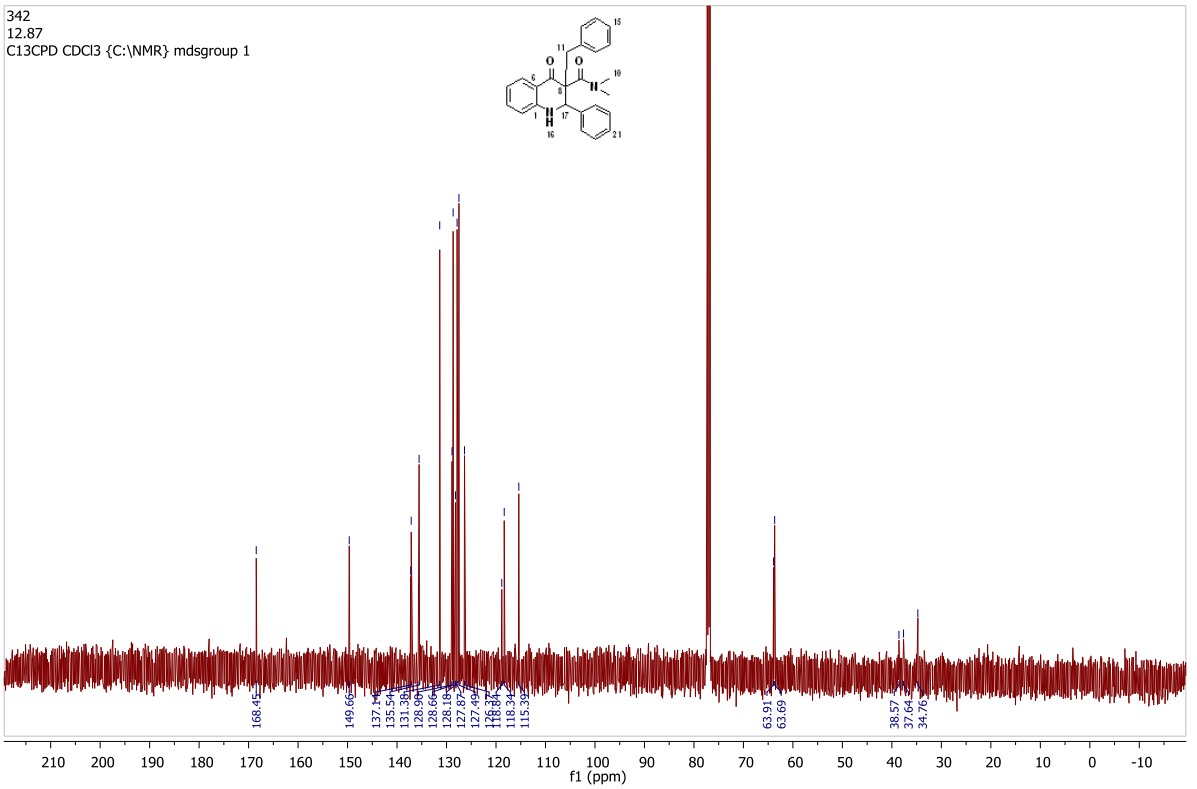
Instrument AVN400
Chemist pck
Group MDS
19.03
DEPTQ.crl CDCl3 {C:\NMR} mdsgrp 60
188.30
166.59
148.87
133.41
125.75
116.32
115.82
113.46
58.03
54.25
35.83
33.64
13.70
1.12
-0.00
f1 (ppm)


324
Instrument DQX400
Chemist pck
Group mds
13.77C
h1acq.au CDCl3 {E:\NMR2012} mdsgrp 58
1.00
1.38
2.19
1.06
1.12
1.12
3.28
3.43
10.20
f1 (ppm)


324
Instrument DQX400
Chemist pck
Group mds
13.77C
c13acq.au CDCl3 {E:\NMR2012} mdsgrp 58
190.13
169.43
150.94
135.86
127.37
116.74
116.47
115.16
62.28
49.62
38.09
36.16
29.68
26.37
f1 (ppm)

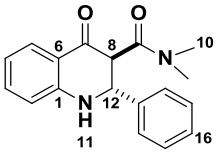
29


342
12.87
PROTON CDCl3 {C:\NMR} mdsgroup 1
1.00
4.02
2.06
5.01
1.01
0.99
1.04
1.00
1.05
2.88
3.36
f1 (ppm)

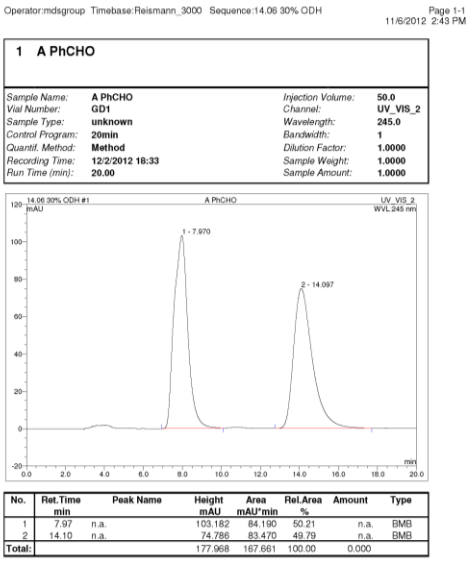

342
12.87
C13CPD CDCl3 {C:\NMR} mdsgroup 1
168.45
149.66
137.14
135.54
131.38
128.96
128.66
128.18
127.87
127.49
118.34
115.39
63.91
63.69
38.57
37.64
34.76
f1 (ppm)

5. HPLC TRACES

2



Conditions: Daicel Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 8.1 min, t_R(minor) = 14.4 min



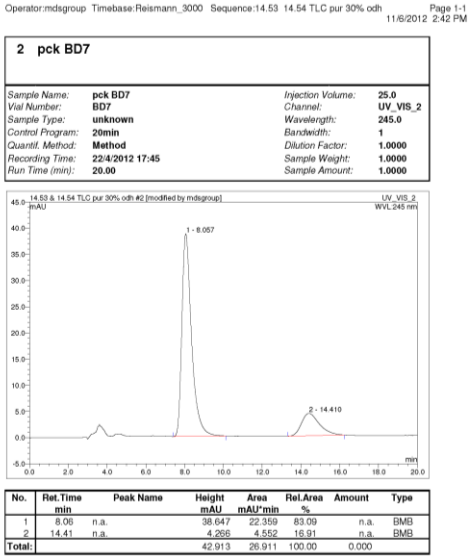
Operator:mdsgroup Timebase:Reismann_3000 Sequence:14.06 30% ODH Page 1-1
11/5/2012 2:43 PM

1 A PhCHO

Sample Name:	A PhCHO	Injection Volume:	50.0
Vial Number:	GD1	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	20min	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	12/2/2012 18:33	Sample Weight:	1.0000
Run Time (min):	20.00	Sample Amount:	1.0000

14.06 30% ODH #1 A PhCHO UV_VIS_2 WVL:245 nm
mAU
1 - 7.970
2 - 14.097
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.97	n.a.	103.182	84.190	50.21	n.a.	BMB
2	14.10	n.a.	74.786	83.470	49.79	n.a.	BMB
Total:			177.968	167.661	100.00	0.000	



Operator:mdsgroup Timebase:Reismann_3000 Sequence:14.53 14.54 TLC pur 30% odh Page 1-1
11/5/2012 2:42 PM

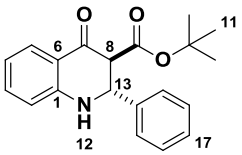
2 pck BD7

Sample Name:	pck BD7	Injection Volume:	25.0
Vial Number:	BD7	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	20min	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	22/4/2012 17:45	Sample Weight:	1.0000
Run Time (min):	20.00	Sample Amount:	1.0000

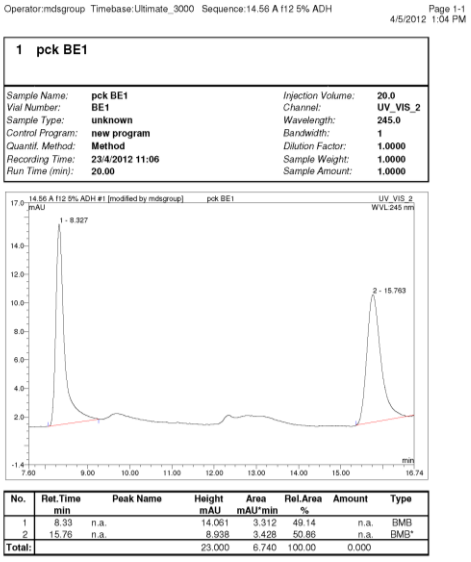
14.53 & 14.54 TLC pur 30% odh #2 [modified by mdsgroup] UV_VIS_2 WVL:245 nm
mAU
1 - 8.057
2 - 14.410
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	8.06	n.a.	38.647	22.359	83.09	n.a.	BMB
2	14.41	n.a.	4.266	4.552	16.91	n.a.	BMB
Total:			42.913	26.911	100.00	0.000	

9



Conditions: Daicel Chiralpak OD-H, 5% IPA, 95% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 8.2 min, t_R(minor) = 15.4 min



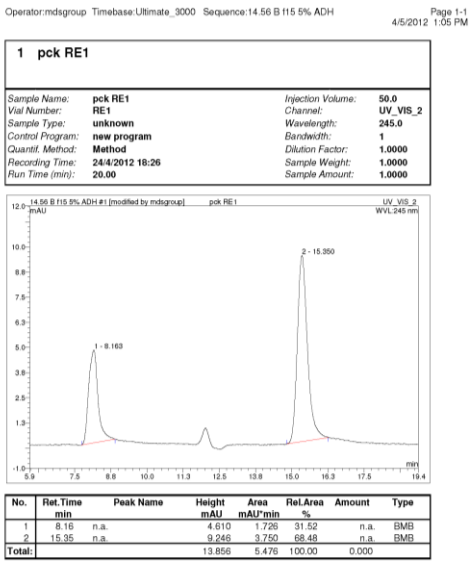
Operator:mdsgroup Timebase:Ultimate_3000 Sequence:14.56 A f12 5% ADH Page 1-1
4/5/2012 1:04 PM

1 pck BE1

Sample Name:	pck BE1	Injection Volume:	20.0
Vial Number:	BE1	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	new program	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	23/4/2012 11:06	Sample Weight:	1.0000
Run Time (min):	20.00	Sample Amount:	1.0000

14.56 A f12 5% ADH #1 [modified by mdsgroup] pck BE1 UV_VIS_2 WVL:245 nm
mAU
1 - 8.327
2 - 15.763
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	8.33	n.a.	14.061	3.312	49.14	n.a.	BMB
2	15.76	n.a.	8.938	3.428	50.86	n.a.	BMB*
Total:			23.000	6.740	100.00	0.000	



Operator:mdsgroup Timebase:Ultimate_3000 Sequence:14.56 B f15 5% ADH Page 1-1
4/5/2012 1:05 PM

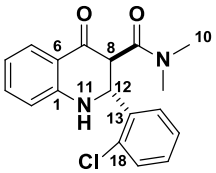
1 pck RE1

Sample Name:	pck RE1	Injection Volume:	50.0
Vial Number:	RE1	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	new program	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	24/4/2012 18:26	Sample Weight:	1.0000
Run Time (min):	20.00	Sample Amount:	1.0000

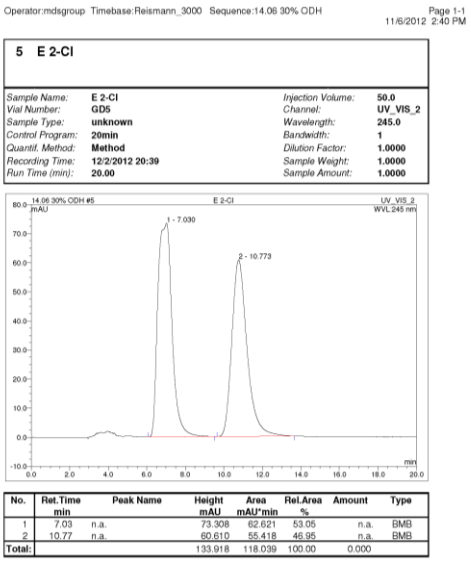
14.56 B f15 5% ADH #1 [modified by mdsgroup] pck RE1 UV_VIS_2 WVL:245 nm
mAU
1 - 8.169
2 - 15.350
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	8.16	n.a.	4.610	1.726	31.52	n.a.	BMB
2	15.35	n.a.	9.246	3.750	68.48	n.a.	BMB
Total:			13.856	5.476	100.00	0.000	

10



Conditions: Daicel Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 7.1 min, t_R(minor) = 11.0 min



Operator:mdsgroup Timebase:Reismann_3000 Sequence:14.06 30% ODH Page 1-1 11/6/2012 2:40 PM

5 E 2-Cl

Sample Name:	E 2-Cl	Injection Volume:	50.0
Vial Number:	GD5	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	20min	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	12/2/2012 20:39	Sample Weight:	1.0000
Run Time (min):	20.00	Sample Amount:	1.0000

14.06 30% ODH #5 E 2-Cl UV_VIS_2 WVL:245 nm

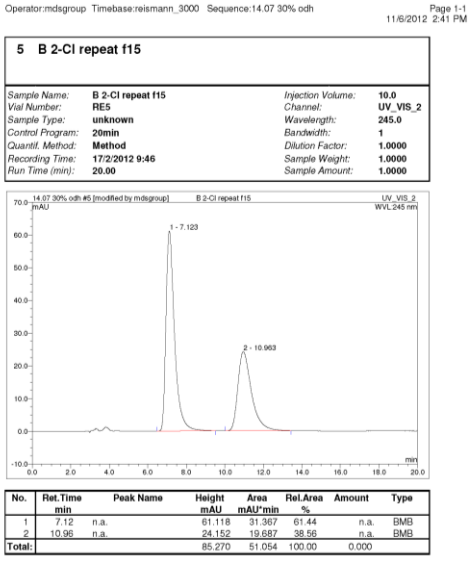
mAU

1 - 7.030

2 - 10.773

min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.09	n.a.	73.308	62.621	53.05	n.a.	BMB
2	10.77	n.a.	60.610	55.418	46.95	n.a.	BMB
Total:			133.918	118.039	100.00	0.000	



Operator:mdsgroup Timebase:reismann_3000 Sequence:14.07 30% odh Page 1-1 11/6/2012 2:41 PM

5 B 2-Cl repeat f15

Sample Name:	B 2-Cl repeat f15	Injection Volume:	10.0
Vial Number:	RE5	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	20min	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	17/2/2012 9:46	Sample Weight:	1.0000
Run Time (min):	20.00	Sample Amount:	1.0000

14.07 30% odh #5 [modified by mdsgroup] B 2-Cl repeat f15 UV_VIS_2 WVL:245 nm

mAU

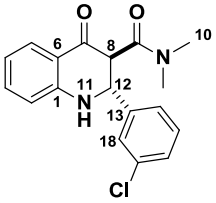
1 - 7.123

2 - 10.963

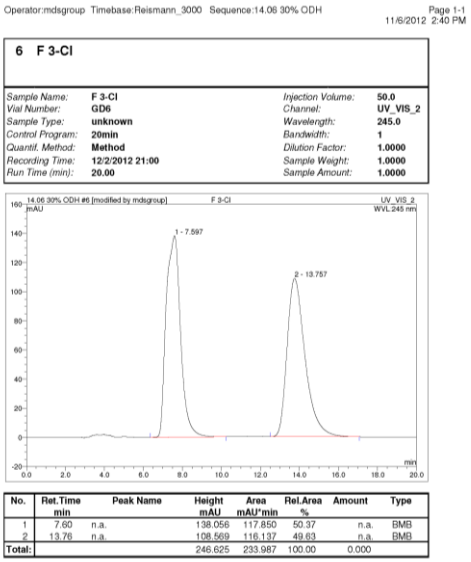
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.12	n.a.	61.118	31.367	61.44	n.a.	BMB
2	10.96	n.a.	24.152	19.687	38.56	n.a.	BMB
Total:			85.270	51.054	100.00	0.000	

11



Conditions: Daicel Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 7.9 min, t_R(minor) = 14.2 min



Operator:mdsgroup Timebase:Reismann_3000 Sequence:14.06 30% ODH Page 1-1 11/6/2012 2:40 PM

6 F 3-Cl

Sample Name:	F 3-Cl	Injection Volume:	50.0
Vial Number:	GD6	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	20min	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	12/2/2012 21:00	Sample Weight:	1.0000
Run Time (min):	20.00	Sample Amount:	1.0000

14.06 30% ODH #6 [modified by mdsgroup] F 3-Cl UV_VIS_2 WVL:245 nm

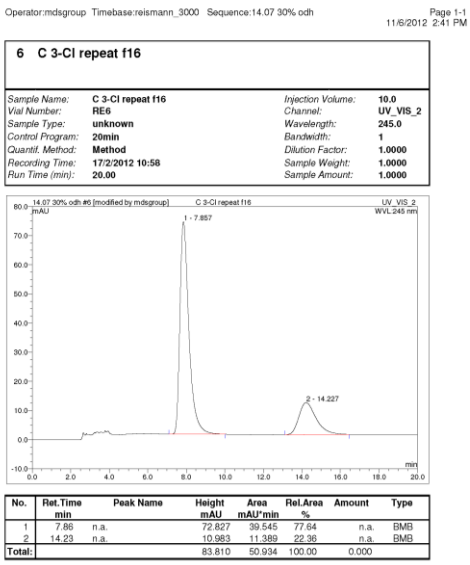
mAU

1 - 7.597

2 - 13.757

min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.60	n.a.	138.056	117.850	50.37	n.a.	BMB
2	13.76	n.a.	108.569	116.137	49.63	n.a.	BMB
Total:			246.625	233.987	100.00	0.000	



Operator:mdsgroup Timebase:reismann_3000 Sequence:14.07 30% odh Page 1-1 11/6/2012 2:41 PM

6 C 3-Cl repeat f16

Sample Name:	C 3-Cl repeat f16	Injection Volume:	10.0
Vial Number:	RE6	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	20min	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	17/2/2012 10:58	Sample Weight:	1.0000
Run Time (min):	20.00	Sample Amount:	1.0000

14.07 30% odh #6 [modified by mdsgroup] C 3-Cl repeat f16 UV_VIS_2 WVL:245 nm

mAU

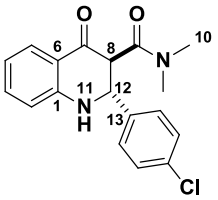
1 - 7.857

2 - 14.227

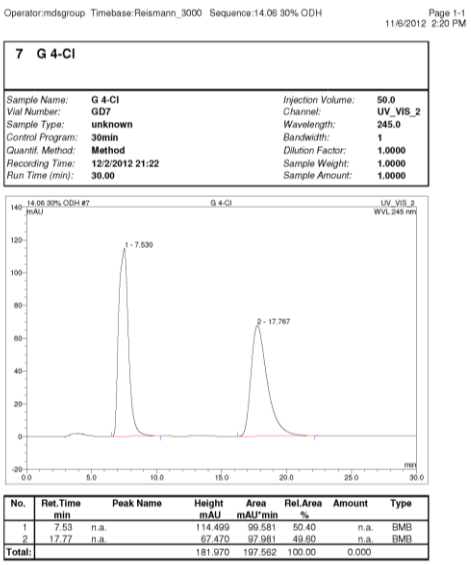
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.86	n.a.	72.827	39.545	77.64	n.a.	BMB
2	14.23	n.a.	10.983	11.389	22.36	n.a.	BMB
Total:			83.810	50.934	100.00	0.000	

12



Conditions: Daicel Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 7.5 min, t_R(minor) = 17.8 min



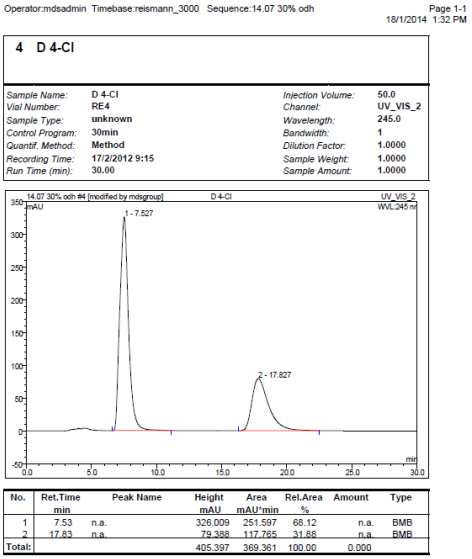
Operator:mdsgroup Timebase:Reismann_3000 Sequence:14.06 30% ODH Page 1-1
11/6/2012 2:20 PM

7 G 4-Cl

Sample Name:	G 4-Cl	Injection Volume:	50.0
Vial Number:	GD7	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	30min	Bandwidth:	1
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	12/2/2012 21:22	Sample Weight:	1.0000
Run Time (min):	30.00	Sample Amount:	1.0000

14.06 30% ODH #7 G 4-Cl UV_VIS_2 WVL:245 nm
mAU
1 - 7.530
2 - 17.767
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.53	n.a.	114.499	99.581	50.40	n.a.	BMB
2	17.77	n.a.	67.470	97.981	49.60	n.a.	BMB
Total:			181.970	197.562	100.00	0.000	



Operator:mdsadmin Timebase:reismann_3000 Sequence:14.07 30% odh Page 1-1
18/1/2014 1:32 PM

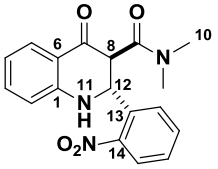
4 D 4-Cl

Sample Name:	D 4-Cl	Injection Volume:	50.0
Vial Number:	RE4	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	30min	Bandwidth:	1
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	17/2/2012 9:15	Sample Weight:	1.0000
Run Time (min):	30.00	Sample Amount:	1.0000

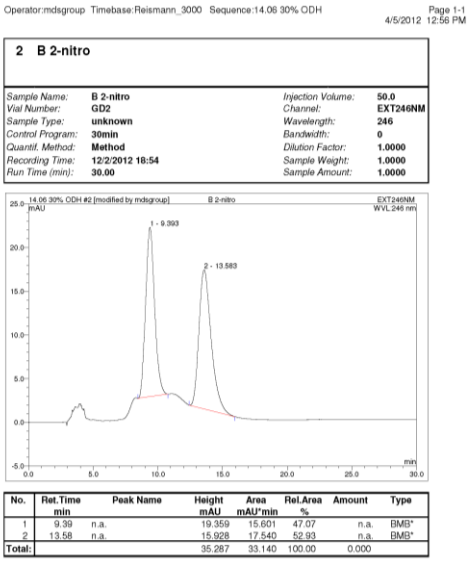
14.07 30% odh #4 [modified by mdsgroup] D 4-Cl UV_VIS_2 WVL:245 nm
mAU
1 - 7.527
2 - 17.827
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.53	n.a.	326.009	251.597	68.12	n.a.	BMB
2	17.83	n.a.	79.388	117.765	31.88	n.a.	BMB
Total:			405.397	369.361	100.00	0.000	

13



Conditions: Daicel Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 9.5 min, t_R(minor) = 13.7 min



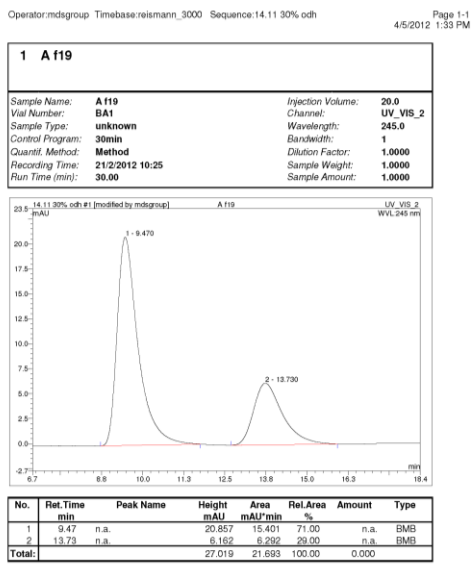
Operator:mdsgroup Timebase:Reismann_3000 Sequence:14.06 30% ODH Page 1-1
4/5/2012 12:56 PM

2 B 2-nitro

Sample Name:	B 2-nitro	Injection Volume:	50.0
Vial Number:	GD2	Channel:	EXT246NM
Sample Type:	unknown	Wavelength:	246
Control Program:	30min	Bandwidth:	0
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	12/2/2012 18:54	Sample Weight:	1.0000
Run Time (min):	30.00	Sample Amount:	1.0000

14.06 30% ODH #2 [modified by mdsgroup] B 2-nitro EXT246NM WVL:246 nm
mAU
1 - 9.393
2 - 13.583
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9.39	n.a.	19.359	15.601	47.07	n.a.	BMB*
2	13.58	n.a.	15.928	17.540	52.93	n.a.	BMB*
Total:			35.287	33.140	100.00	0.000	



Operator:mdsgroup Timebase:reismann_3000 Sequence:14.11 30% odh Page 1-1
4/5/2012 1:33 PM

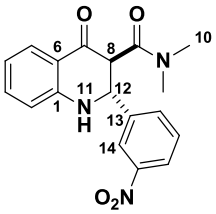
1 A f19

Sample Name:	A f19	Injection Volume:	20.0
Vial Number:	BA1	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	30min	Bandwidth:	1
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	21/2/2012 10:25	Sample Weight:	1.0000
Run Time (min):	30.00	Sample Amount:	1.0000

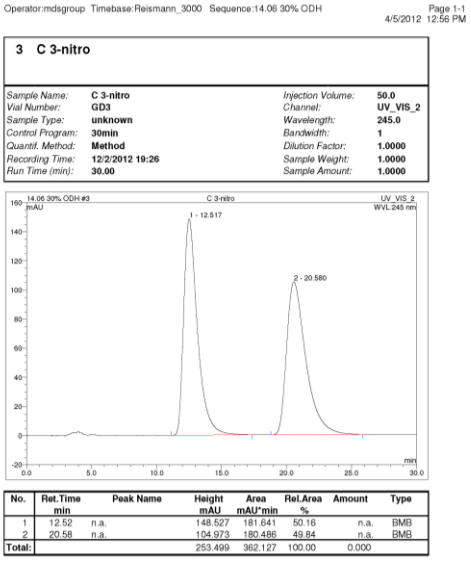
14.11 30% odh #1 [modified by mdsgroup] A f19 UV_VIS_2 WVL:245 nm
mAU
1 - 9.470
2 - 13.730
min

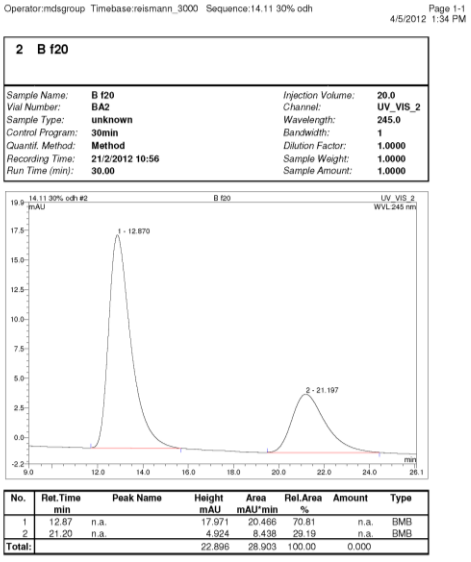
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9.47	n.a.	20.857	15.401	71.00	n.a.	BMB
2	13.73	n.a.	6.162	6.292	29.00	n.a.	BMB
Total:			27.019	21.693	100.00	0.000	

14

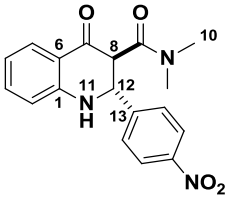


Conditions: Daicel Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 12.9 min, t_R(minor) = 21.2 min

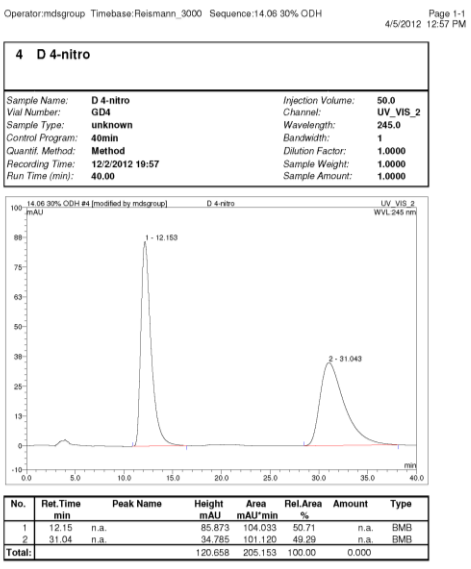


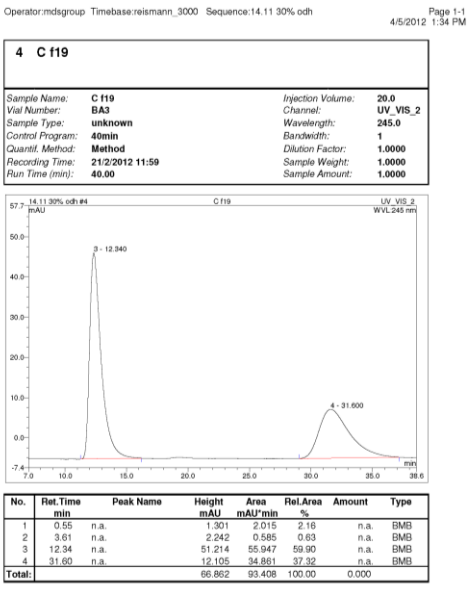


15

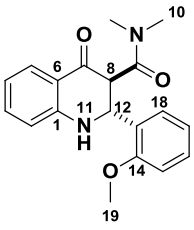


Conditions: Daicel Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 12.3 min, t_R(minor) = 31.6 min

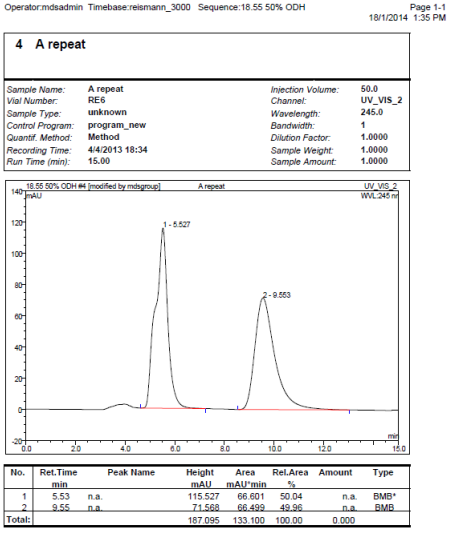




16



Conditions: Daicel Chiralpak OD-H, 50% IPA, 50% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 5.5 min, t_R(minor) = 9.5 min



Operator:mdsadmin Timebase:reismann_3000 Sequence:18.55 50% ODH

Page 1-1
18/1/2014 1:35 PM

4 A repeat

Sample Name:	A repeat	Injection Volume:	50.0
Vial Number:	RE6	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	4/4/2013 18:34	Sample Weight:	1.0000
Run Time (min):	15.00	Sample Amount:	1.0000

18.55 50% ODH #4 [modified by mdsgroup] A repeat UV_VIS_2 WVL:245 nm

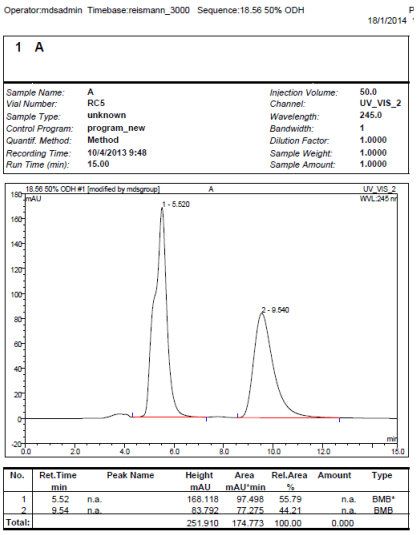
mAU

1 - 5.527

2 - 9.553

min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.53	n.a.	115.527	66.601	50.04	n.a.	BMB*
2	9.55	n.a.	71.568	66.499	49.96	n.a.	BMB
Total:			187.095	133.100	100.00	0.000	



Operator:mdsadmin Timebase:reismann_3000 Sequence:18.56 50% ODH

1 A

Sample Name:	A	Injection Volume:	50.0
Vial Number:	RC5	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	10/4/2013 9:48	Sample Weight:	1.0000
Run Time (min):	15.00	Sample Amount:	1.0000

18.56 50% ODH #1 [modified by mdsgroup] A UV_VIS_2 WVL:245 nm

mAU

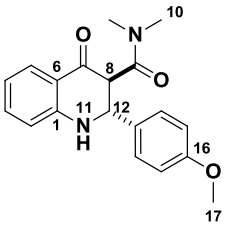
1 - 5.520

2 - 9.540

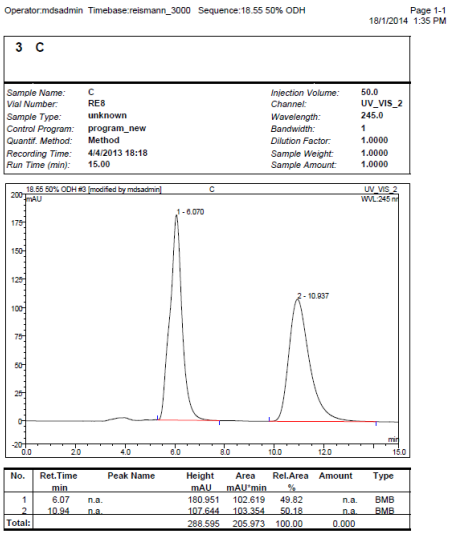
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.52	n.a.	168.118	97.498	55.79	n.a.	BMB*
2	9.54	n.a.	83.792	77.275	44.21	n.a.	BMB
Total:			251.910	174.773	100.00	0.000	

17



Conditions: Daicel Chiralpak OD-H, 50% IPA, 50% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 6.1 min, t_R(minor) = 11.1 min



Operator:mdsadmin Timebase:reismann_3000 Sequence:18.55 50% ODH

Page 1-1
18/1/2014 1:35 PM

3 C

Sample Name:	C	Injection Volume:	50.0
Vial Number:	RE8	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	4/4/2013 18:18	Sample Weight:	1.0000
Run Time (min):	15.00	Sample Amount:	1.0000

18.55 50% ODH #3 [modified by mdsadmin] C UV_VIS_2 WVL:245 nm

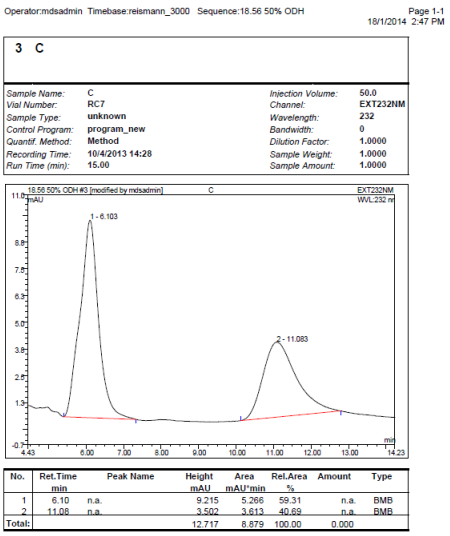
mAU

1 - 6.070

2 - 10.937

min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.07	n.a.	180.951	102.619	49.82	n.a.	BMB
2	10.94	n.a.	107.644	103.354	50.18	n.a.	BMB
Total:			288.595	205.973	100.00	0.000	



Operator:mdsadmin Timebase:reismann_3000 Sequence:18.56 50% ODH

Page 1-1
18/1/2014 2:47 PM

3 C

Sample Name:	C	Injection Volume:	50.0
Vial Number:	RC7	Channel:	EXT232NM
Sample Type:	unknown	Wavelength:	232
Control Program:	program_new	Bandwidth:	0
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	10/4/2013 14:28	Sample Weight:	1.0000
Run Time (min):	15.00	Sample Amount:	1.0000

18.56 50% ODH #3 [modified by mdsadmin] C EXT232NM WVL:232 nm

mAU

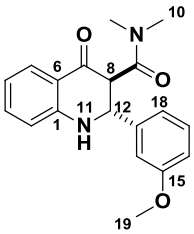
1 - 6.103

2 - 11.083

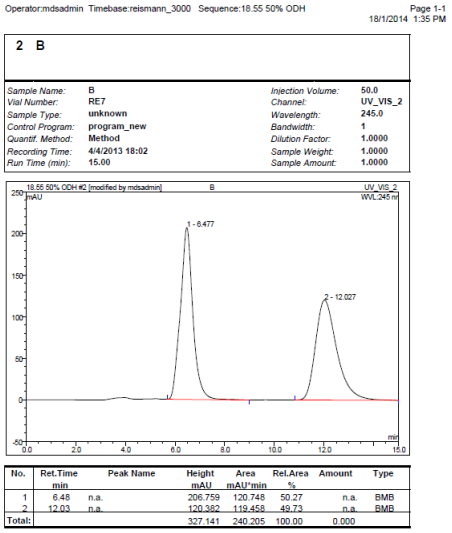
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.10	n.a.	9.215	5.266	59.31	n.a.	BMB
2	11.08	n.a.	3.502	3.613	40.69	n.a.	BMB
Total:			12.717	8.879	100.00	0.000	

18



Conditions: Daicel Chiralpak OD-H, 50% IPA, 50% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 6.5 min, t_R(minor) = 12.1 min



Operator:mdsadmin Timebase:reismann_3000 Sequence:18.55 50% ODH Page 1-1 18/1/2014 1:35 PM

2 B

Sample Name:	B	Injection Volume:	50.0
Vial Number:	RE7	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	4/4/2013 18:02	Sample Weight:	1.0000
Run Time (min):	15.00	Sample Amount:	1.0000

18.55 50% ODH #2 [modified by mdsadmin] B UV_VIS_2 WVL:245 nm

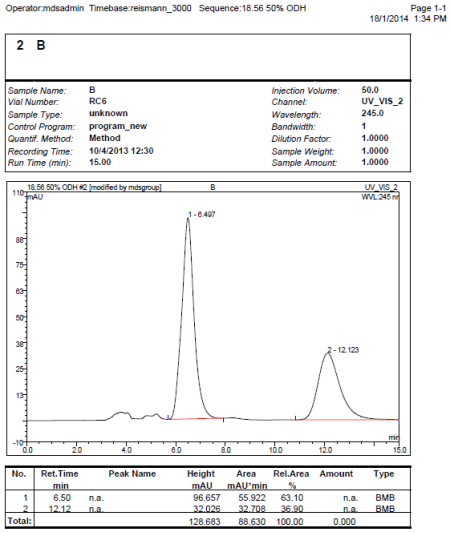
mAU

1 - 6.477

2 - 12.027

min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.48	n.a.	206.759	120.748	50.27	n.a.	BMB
2	12.03	n.a.	120.382	119.458	49.73	n.a.	BMB
Total:			327.141	240.205	100.00	0.000	



Operator:mdsadmin Timebase:reismann_3000 Sequence:18.56 50% ODH Page 1-1 18/1/2014 1:34 PM

2 B

Sample Name:	B	Injection Volume:	50.0
Vial Number:	RC6	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	10/4/2013 12:30	Sample Weight:	1.0000
Run Time (min):	15.00	Sample Amount:	1.0000

18.56 50% ODH #2 [modified by mdsgroup] B UV_VIS_2 WVL:245 nm

mAU

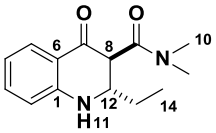
1 - 6.497

2 - 12.123

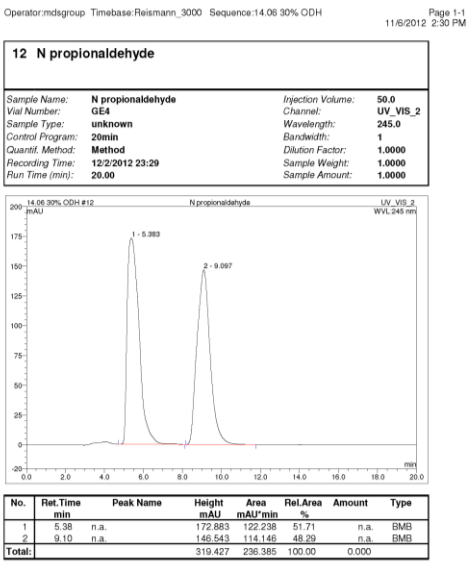
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.50	n.a.	96.657	55.922	63.10	n.a.	BMB
2	12.12	n.a.	32.026	32.708	36.90	n.a.	BMB
Total:			128.683	88.630	100.00	0.000	

19



Conditions: Daicel Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 5.7 min, t_R(minor) = 9.8 min



Operator:mdsgroup Timebase:Reismann_3000 Sequence:14.06 30% ODH Page 1-1 11/6/2012 2:30 PM

12 N propionaldehyde

Sample Name:	N propionaldehyde	Injection Volume:	50.0
Vial Number:	GE4	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	20min	Bandwidth:	1
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	12/2/2012 23:29	Sample Weight:	1.0000
Run Time (min):	20.00	Sample Amount:	1.0000

14.06 30% ODH #12 N propionaldehyde UV_VIS_2 WVL:245 nm

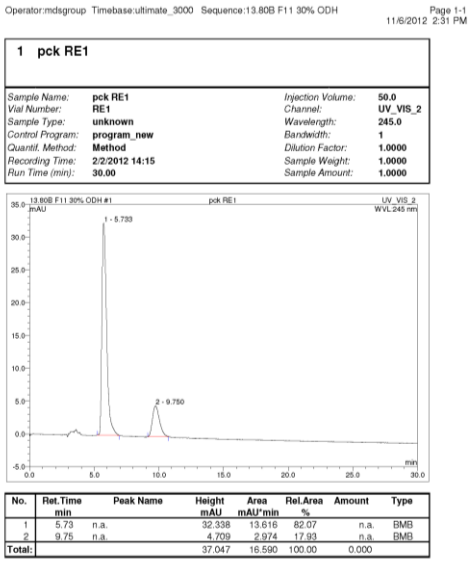
mAU

1 - 5.383

2 - 9.097

min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.38	n.a.	172.883	122.238	51.71	n.a.	BMB
2	9.10	n.a.	146.543	114.146	48.29	n.a.	BMB
Total:			319.427	236.385	100.00	0.000	



Operator:mdsgroup Timebase:ultimate_3000 Sequence:13.80B F11 30% ODH Page 1-1 11/6/2012 2:31 PM

1 pck RE1

Sample Name:	pck RE1	Injection Volume:	50.0
Vial Number:	RE1	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	2/2/2012 14:15	Sample Weight:	1.0000
Run Time (min):	30.00	Sample Amount:	1.0000

13.80B F11 30% ODH #1 pck RE1 UV_VIS_2 WVL:245 nm

mAU

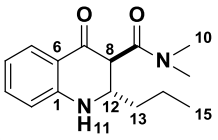
1 - 5.733

2 - 9.750

min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.73	n.a.	32.338	13.616	82.07	n.a.	BMB
2	9.75	n.a.	4.709	2.974	17.93	n.a.	BMB
Total:			37.047	16.590	100.00	0.000	

20

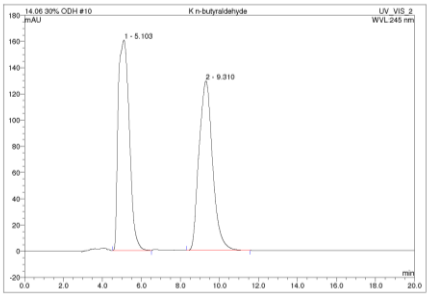


Conditions: Daicel Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 5.4 min, t_R(minor) = 10.0 min

Operator:mdsgroup Timebase:Reismann_3000 Sequence:14.06 30% ODH Page 1-1
11/6/2012 2:36 PM

10 K n-butyraldehyde

Sample Name:	K n-butyraldehyde	Injection Volume:	50.0
Vial Number:	GE2	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	20min	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	12/2/2012 22:46	Sample Weight:	1.0000
Run Time (min):	20.00	Sample Amount:	1.0000

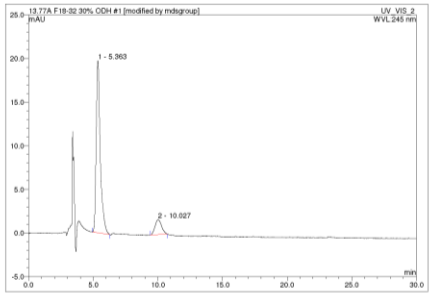


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.10	n.a.	160.409	105.852	50.45	n.a.	BMB
2	9.31	n.a.	129.184	103.960	49.55	n.a.	BMB
Total:			289.594	209.812	100.00	0.000	

Operator:mdsgroup Timebase:ultimate_3000 Sequence:13.77A F18-32 30% ODH Page 1-1
11/6/2012 2:37 PM

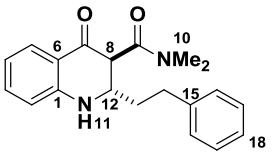
1 pck RD2

Sample Name:	pck RD2	Injection Volume:	20.0
Vial Number:	RD2	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	30/1/2012 15:07	Sample Weight:	1.0000
Run Time (min):	30.00	Sample Amount:	1.0000



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.36	n.a.	19.723	7.200	87.78	n.a.	BMB*
2	10.03	n.a.	1.726	1.003	12.22	n.a.	BMB
Total:			21.449	8.203	100.00	0.000	

21

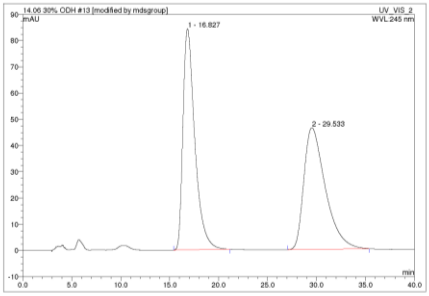


Conditions: Daicel Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(minor) = 18.0 min, t_R(minor) = 27.4 min

Operator:mdsgroup Timebase:Reismann_3000 Sequence:14.06 30% ODH Page 1-1
11/6/2012 2:29 PM

13 O 3-phenyl propionaldehyde

Sample Name:	O 3-phenyl propionaldehyde	Injection Volume:	50.0
Vial Number:	GE5	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	40min	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	12/2/2012 23:50	Sample Weight:	1.0000
Run Time (min):	40.00	Sample Amount:	1.0000

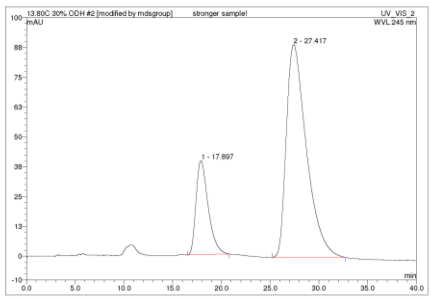


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	16.83	n.a.	84.185	118.382	50.16	n.a.	BMB
2	29.53	n.a.	46.354	117.620	49.84	n.a.	BMB
Total:			130.539	236.001	100.00	0.000	

Operator:mdsgroup Timebase:ultimate_3000 Sequence:13.80C 30% ODH Page 1-1
11/6/2012 2:28 PM

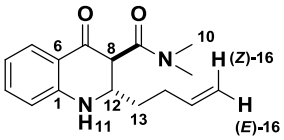
2 stronger sample!

Sample Name:	stronger sample!	Injection Volume:	50.0
Vial Number:	RD7	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	1/2/2012 18:14	Sample Weight:	1.0000
Run Time (min):	40.00	Sample Amount:	1.0000

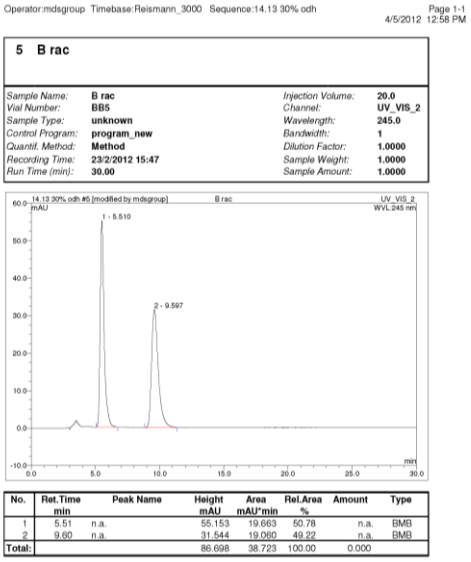


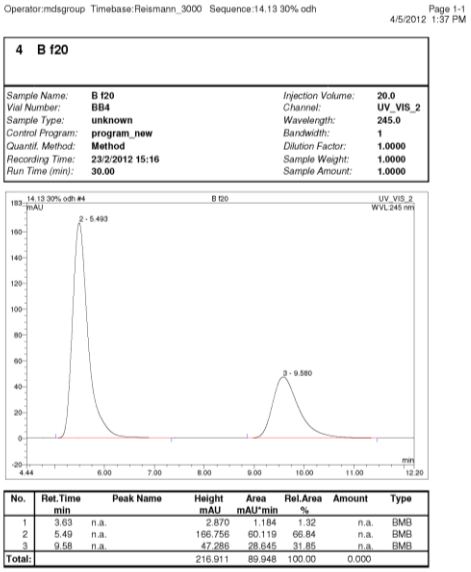
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	17.90	n.a.	39.420	56.963	21.07	n.a.	BMB
2	27.42	n.a.	89.122	213.409	78.93	n.a.	BMB
Total:			128.543	270.372	100.00	0.000	

22



Conditions: Daicel Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) =5.5 min, t_R(minor) = 9.6 min





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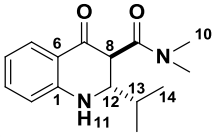
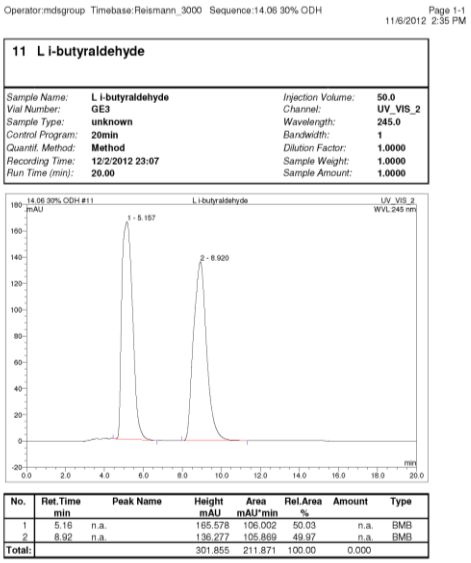
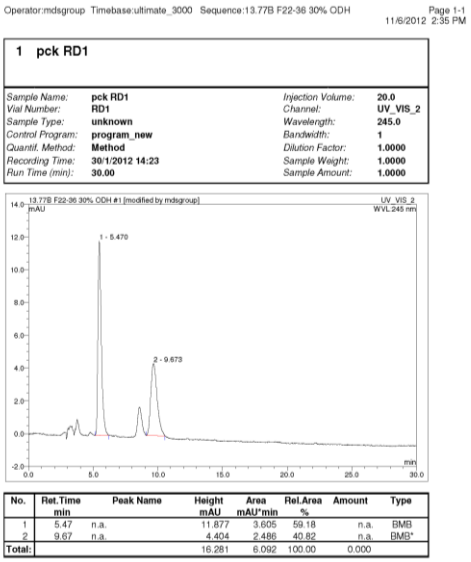
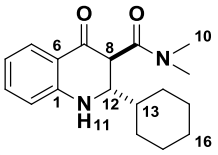


Conditions: Daicel Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) =5.5 min, t_R(minor) = 9.7 min

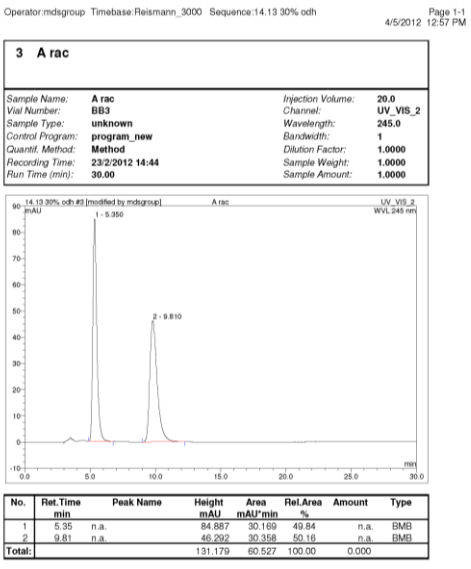




24



Conditions: Daicel Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) =5.3 min, t_R(minor) = 9.8 min



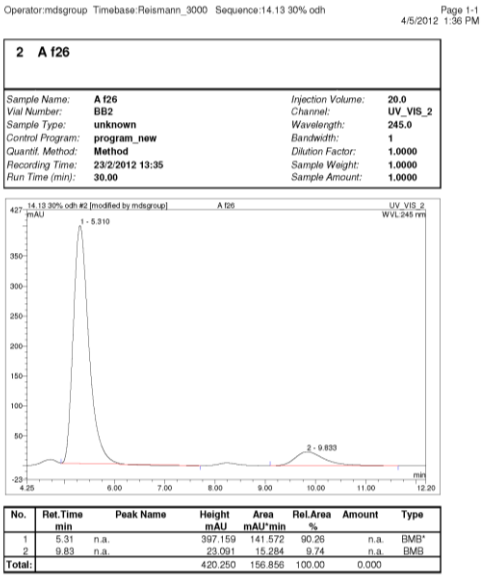
Operator:mdsgroup Timebase:Reismann_3000 Sequence:14.13 30% odh Page 1-1
4/5/2012 12:57 PM

3 A rac

Sample Name:	A rac	Injection Volume:	20.0
Vial Number:	BB3	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	23/2/2012 14:44	Sample Weight:	1.0000
Run Time (min):	30.00	Sample Amount:	1.0000

14.13 30% odh #3 [modified by mdsgroup] A rac UV_VIS_2 WVL:245 nm
mAU
1 - 5.350
2 - 9.810
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.35	n.a.	84.887	30.169	49.84	n.a.	BMB
2	9.81	n.a.	46.292	30.358	50.16	n.a.	BMB
Total:			131.179	60.527	100.00	0.000	



Operator:mdsgroup Timebase:Reismann_3000 Sequence:14.13 30% odh Page 1-1
4/5/2012 1:36 PM

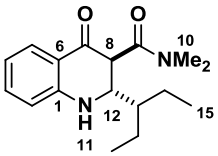
2 A f26

Sample Name:	A f26	Injection Volume:	20.0
Vial Number:	BB2	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	23/2/2012 13:35	Sample Weight:	1.0000
Run Time (min):	30.00	Sample Amount:	1.0000

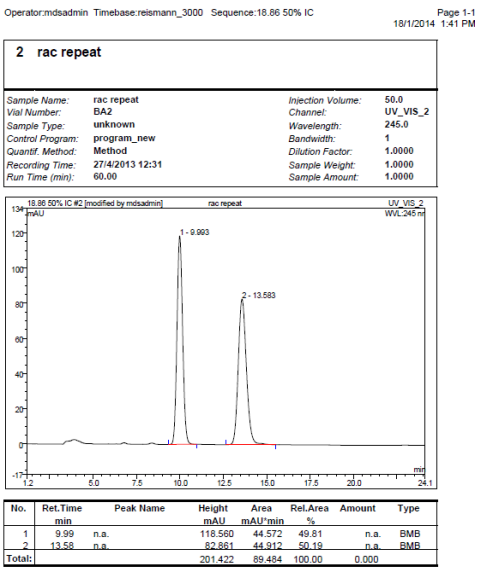
14.13 30% odh #2 [modified by mdsgroup] A f26 UV_VIS_2 WVL:245 nm
mAU
1 - 5.310
2 - 9.833
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.31	n.a.	397.159	141.572	90.26	n.a.	BMB*
2	9.83	n.a.	23.091	15.284	9.74	n.a.	BMB
Total:			420.250	156.856	100.00	0.000	

25



Conditions: Daicel Chiralpak IC, 50% IPA, 50% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 10.0 min, t_R(minor) = 13.6 min



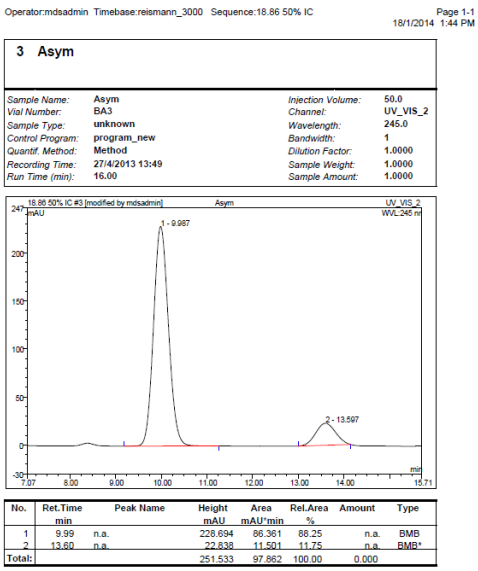
Operator:mdsadmin Timebase:reismann_3000 Sequence:18.86 50% IC Page 1-1
18/1/2014 1:41 PM

2 rac repeat

Sample Name:	rac repeat	Injection Volume:	50.0
Vial Number:	BA2	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	27/4/2013 12:31	Sample Weight:	1.0000
Run Time (min):	60.00	Sample Amount:	1.0000

18.86 50% IC #2 [modified by mdsadmin] rac repeat UV_VIS_2 WVL:245 nm
mAU
1 - 9.993
2 - 13.583
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9.99	n.a.	118.560	44.572	49.81	n.a.	BMB
2	13.58	n.a.	82.861	44.912	50.19	n.a.	BMB
Total:			201.422	89.484	100.00	0.000	



Operator:mdsadmin Timebase:reismann_3000 Sequence:18.86 50% IC Page 1-1
18/1/2014 1:44 PM

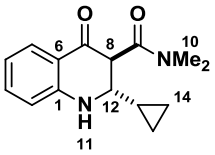
3 Asym

Sample Name:	Asym	Injection Volume:	50.0
Vial Number:	BA3	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantit. Method:	Method	Dilution Factor:	1.0000
Recording Time:	27/4/2013 13:49	Sample Weight:	1.0000
Run Time (min):	16.00	Sample Amount:	1.0000

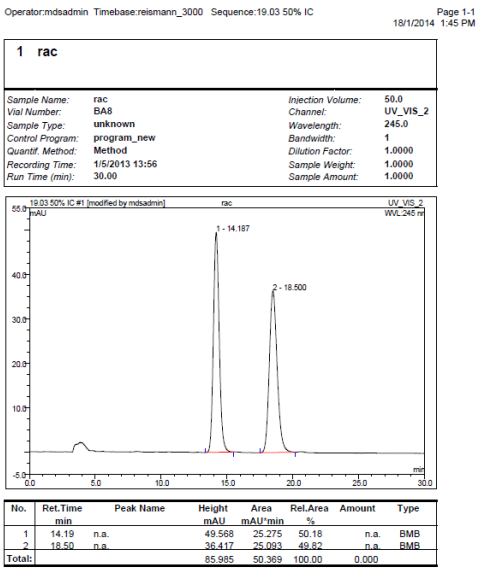
18.86 50% IC #3 [modified by mdsadmin] Asym UV_VIS_2 WVL:245 nm
mAU
1 - 9.987
2 - 13.597
min

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9.99	n.a.	228.694	86.361	88.25	n.a.	BMB
2	13.60	n.a.	22.838	11.501	11.75	n.a.	BMB*
Total:			251.533	97.862	100.00	0.000	

26



Conditions: Daicel Chiralpak IC, 50% IPA, 50% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) = 14.2 min, t_R(minor) = 18.5 min



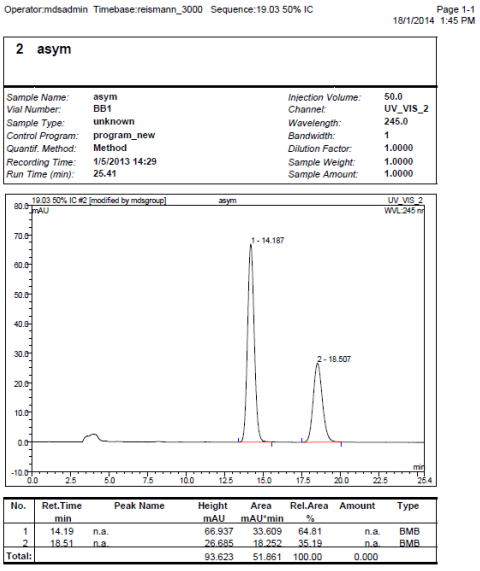
Operator:mdsadmin Timebase:reismann_3000 Sequence:19.03 50% IC

Page 1-1
18/1/2014 1:45 PM

1 rac

Sample Name:	rac	Injection Volume:	50.0
Vial Number:	BA8	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	1/5/2013 13:56	Sample Weight:	1.0000
Run Time (min):	30.00	Sample Amount:	1.0000

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	14.19	n.a.	49.568	25.275	50.18	n.a.	BMB
2	18.50	n.a.	36.417	25.093	49.82	n.a.	BMB
Total:			85.985	50.369	100.00	0.000	



Operator:mdsadmin Timebase:reismann_3000 Sequence:19.03 50% IC

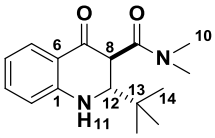
Page 1-1
18/1/2014 1:45 PM

2 asym

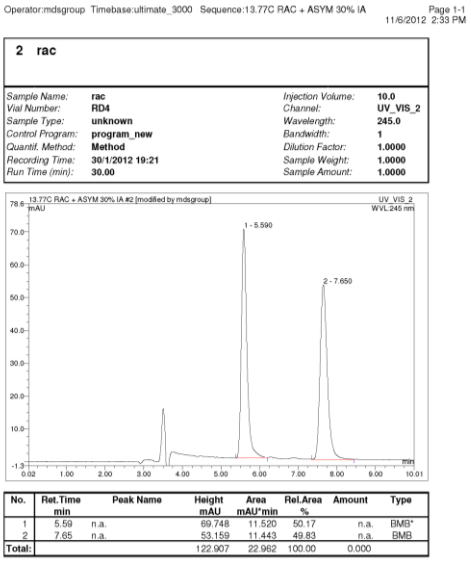
Sample Name:	asym	Injection Volume:	50.0
Vial Number:	BB1	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	1/5/2013 14:29	Sample Weight:	1.0000
Run Time (min):	25.41	Sample Amount:	1.0000

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	14.19	n.a.	66.937	33.609	64.81	n.a.	BMB
2	18.51	n.a.	26.685	18.252	35.19	n.a.	BMB
Total:			93.623	51.861	100.00	0.000	

27



Conditions: Daicel Chiralpak OD-H, 30% IPA, 70% hexane, 1.0 mL.min–1, λ = 245 nm; t_R(major) =5.6 min, t_R(minor) = 7.7 min



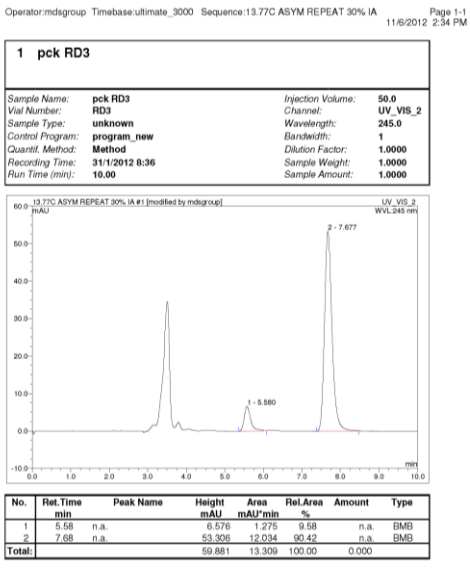
Operator:mdsgroup Timebase:ultimate_3000 Sequence:13.77C RAC + ASYM 30% IA

Page 1-1
11/6/2012 2:33 PM

2 rac

Sample Name:	rac	Injection Volume:	10.0
Vial Number:	RD4	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	30/1/2012 19:21	Sample Weight:	1.0000
Run Time (min):	30.00	Sample Amount:	1.0000

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.59	n.a.	69.748	11.520	50.17	n.a.	BMB*
2	7.65	n.a.	53.159	11.443	49.83	n.a.	BMB
Total:			122.907	22.962	100.00	0.000	



Operator:mdsgroup Timebase:ultimate_3000 Sequence:13.77C ASYM REPEAT 30% IA

Page 1-1
11/6/2012 2:34 PM

1 pck RD3

Sample Name:	pck RD3	Injection Volume:	50.0
Vial Number:	RD3	Channel:	UV_VIS_2
Sample Type:	unknown	Wavelength:	245.0
Control Program:	program_new	Bandwidth:	1
Quantif. Method:	Method	Dilution Factor:	1.0000
Recording Time:	31/1/2012 8:36	Sample Weight:	1.0000
Run Time (min):	10.00	Sample Amount:	1.0000

No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5.58	n.a.	6.576	1.275	9.58	n.a.	BMB
2	7.68	n.a.	53.306	12.034	90.42	n.a.	BMB
Total:			59.881	13.309	100.00	0.000	

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