Electronic Supplementary Material (ESI) for ChemComm.

Convergent and Stereoselective Synthesis of Tetrahydroquinolines

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Supporting Information

Contents:

General experimental methods

All experiments were conducted under an atmosphere of nitrogen using anhydrous solvents unless otherwise stated. The racemic tetrahydroquinoline syntheses were carried out in 25 mL Schlenk tubes. The asymmetric tetrahydroquinoline syntheses were carried out in 25 mL round bottom flasks.

Sure seal toluene and DCM were purchased from Aldrich. Pinacol boronates were synthesised according to published procedures[1] or, in the case of 2-aminophenyl boronic acid pinacol ester and *N*-Boc-2-amino-phenylboronic acid pinacol ester, purchased from Alfa Aesar. *N*-Boc-2-amino-5-trifluoromethylphenylboronic acid pinacol ester was synthesised from the corresponding 2-amino-5-trifluoromethylphenylboronic acid pinacol ester by reacting with di-*tert*-butyl dicarbonate. (*R,R,S,S*)- and (*S,S,R,R*)-Duanphos were purchased from Sigma Aldrich. [((*R,R,S,S*)-Duanphos)Rh(nbd)][BF_4] complex was supplied by Chiral Quest. All reagents were used without further purification.

Column chromatography was carried out using Fisher Matrix silica gel 60 or Biotage® SNAP KP-Sil flash cartridges. Ion-exchange chromatography was carried out using Biotage® ISOLUTE® SCX-2 columns. Glass-backed plates, pre-coated with silica gel 60 (UV_{254}), were used for thin layer chromatography and were visualized by UV and staining either with anisaldehyde or $KMnO_4$.

The chemical shifts for ^1H and ^{13}C NMR spectra are reported in ppm relative to residual protic solvent as internal standards unless otherwise stated. Infra-red spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrometer, with absorption reported in wavenumbers (cm^{-1}). Optical rotations were measured on an Optical Activity AA-1000 polarimemter (using 10 cm cell) or a Jason P1030 polarimeter (using 0.2 mm or 2 mm cell) at the sodium D-line (589 nm) and are reported as follows: $[\alpha]_D^T$, concentration (c in g/100 mL, T in degrees Celsius) and solvent.

Diastereomeric ratios were determined by ^1H NMR analysis of the purified products. The relative configuration of the products was determined by analysis of the coupling constants of H_3^{ax} proton; nOe studies were also performed for compounds **7f** and **7l**.

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[1] Horn, J.; Marsden, S. P.; Nelson, A.; House, D.; Weingarten, G.G. *Org. Lett.* **2008**, *10*, 4117-4120.

The absolute configuration of compounds **7c** and **7l** was determined by comparison of their experimental and simulated vibrational circular dichroism spectra.[2] The experimental data was acquired using a BioTools Chiral*IR* VCD spectrometer. Molecular modelling was carried out using DGDZVP basis set at B3LYP level of theory and conformers were generated using MOE (MMFF94x forcefield). The calculated and experimental IR and VCD spectra were compared to determine the absolute configuration. Enantiomeric excesses were determined by chiral analytical HPLC by comparison with racemic standards.

[2] (a) Stephens, P. J. in *Computational Medicinal Chemistry for Drug Discovery*, eds. Bultinick, P.; de Winter, H.; Langenaeker, W.; Tollenare, J. P. Marcel Dekker, New York, 2004, pp 699-725; (b) Kuppens, T.; Bultinick, P.; Langenaeker, W. *Drug. Discov. Today Tech.* 2004, **1**, 269-275.

General procedure A: Synthesis of tetrahydroquinolines from boronic acids

To a suspension of chloro(1,5-cyclooctadiene)rhodium(I) dimer (3.4 mg, 6.9 μmol, 0.03 equiv), 2-aminophenylboronic acid (63 mg, 0.46 mmol, 2 equiv) and enone (0.23 mmol, 1 equiv) in toluene (1.2 mL, *ca* 0.19 M) under nitrogen was added 3.8 M aqueous potassium hydroxide solution (0.12 ml). The mixture was stirred vigorously at rt for 24 hr. To the mixture was added toluene (4 mL) and sodium triacetoxyborohydride (585 mg, 2.76 mmol, 12 equiv). The resulting suspension was stirred under nitrogen at rt until TLC indicated complete formation of the product. The reaction was then quenched with water (1 mL) and the aqueous phase extracted with toluene (2 × 2 mL). The combined organic phases were concentrated under reduced pressure to give the crude product.

General procedure B: Synthesis of tetrahydroquinolines from pinacolboronates

To a solution of chloro(1,5-cyclooctadiene)rhodium(I) dimer (6.8 mg, 13.8 μmol, 0.06 equiv), pinacolboronate (0.46 mmol, 2 equiv) and enone (0.23 mmol, 1 equiv) in toluene (1.2 mL, *ca* 0.19 M) was added 3.8 M aqueous potassium hydroxide solution (150 μl). The mixture was stirred vigorously at rt for 24 hr. To the mixture was added toluene (4 mL) and sodium triacetoxyborohydride (585 mg, 2.76 mmol, 12 equiv). The resulting suspension was stirred under nitrogen at rt until TLC indicated complete formation of the product. The reaction was then quenched with water (1 mL) and the aq. phase extracted with toluene (2 × 2 mL). The combined organic phases were concentrated under reduced pressure to give the crude product which.

General procedure C: Asymmetric synthesis of tetrahydroquinolines from pinacolboronates using a preformed catalyst

To a solution of [((*R,R,S,S*)-Duanphos)Rh(nbd)][BF_4] (19.9 mg, 30.0 μmol, 0.06 equiv), pinacolboronate (1.0 mmol, 2 equiv) and enone (0.5 mmol, 1 equiv) in toluene (1.3 mL, *ca* 0.38 M) was added 3.8 M aqueous potassium hydroxide solution (260 μl, 2 equiv). The reaction mixture was stirred vigorously at rt for 24 hr. The reaction mixture was diluted with DCM (20 mL), dried (Na_2SO_4), filtered and then

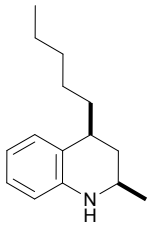
concentrated under reduced pressure. The crude product was dissolved in DCM (1.6 mL) and TFA (0.8 mL, 10.7 mmol) was added. The reaction mixture was stirred vigorously at rt for 30 min, Et_3SiH (0.8 mL, 5.0 mmol) added, stirred for 2 hr, basified with 3.8 M aq. KOH (5 mL), and extracted with diethyl ether (30 mL). The organic layer was washed with water (10 mL), and extracted with 1 M aq. HCl (2 × 10 mL). The aqueous layer was basified with 2.5 M aq. KOH (15 mL) and then extracted with diethyl ether (5 x 10 mL). The combined organic layer was dried ($MgSO_4$), filtered and then concentrated under reduced pressure to give the crude product which was purified by flash column chromatography.

General procedure D: Asymmetric synthesis of tetrahydroquinolines from pinacolboronates with in situ formation of the chiral catalyst

To a solution of chloro(norbornadiene)rhodium(I) dimer (6.9 mg, 15.0 μmol, 0.03 equiv), (*R,R,S,S*)- or (*S,S,R,R*)-Dunaphos (11.5 mg, 30.0 μmol, 0.06 equiv), pinacolboronate (1.0 mmol, 2 equiv) and enone (0.5 mmol, 1 equiv) in toluene (1.3 mL, *ca* 0.38 M) was added 3.8 M aqueous potassium hydroxide solution (260 μl, 2 equiv). The reaction mixture was stirred vigorously at rt for 24 hr. The reaction mixture was diluted with DCM (20 mL), dried (Na_2SO_4), filtered and then concentrated under reduced pressure. The intermediate was dissolved in DCM (1.6 mL) and TFA (0.8 mL, 10.7 mmol) was added. The reaction mixture was stirred vigorously at rt for 30 min, Et_3SiH (0.8 mL, 5.0 mmol) added, stirred for 2 hr, basified with 3.8 M aq. KOH (5 mL), and extracted with diethyl ether (30 mL). The organic layer was washed with water (10 mL), and then extracted with 1 M aq. HCl (2 × 10 mL). The aqueous layer was basified with 2.5 M aq. KOH (15 mL) and extracted with diethyl ether (5 × 10 mL). The combined organic layer was dried ($MgSO_4$), filtered and then concentrated under reduced pressure to give the crude product which was purified by flash column chromatography.

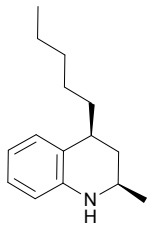
Compound data

(2RS,4SR)-2-Methyl-4-pentyl-1,2,3,4-tetrahydroquinoline, *rac*-7a



Novel compound. (Table 1, entry 1) Synthesis according to general procedure **A** using 0.23 mmol of enone gave the crude product as a brown oil, which was purified by column chromatography (9:1 petrol/ethyl acetate, column pre-conditioned with 1% Et_3N) to give **7a** as a pale yellow oil (47 mg, yield 94%, d.r. = 88:12 *cis:trans*). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.15 (d, J = 7.7 Hz, 1H, H_5), 6.96 (t, J = 7.9 Hz, 1H, H_7), 6.65 (t, J = 7.6 Hz, 1H, H_6), 6.47 (dd, J = 7.8 and 1.2 Hz, 1H, H_8), 3.64 (br s, 1H, NH), 3.39 (dqd, J = 12.3, 6.4 and 2.3 Hz, 1H, H_2), 2.83-2.93 (m, 1H, H_4), 2.01 (ddd, J = 12.8, 5.9 and 2.6 Hz, 1H, H_3^{eq}), 1.89-1.96 (m, 1H, 4-$CH_A$$H_B$), 1.26-1.54 (m, 8H, 3 pentyl-CH_2, 4-C$H_A$$H_B$ and H_3^{ax}), 1.20 (d, J = 6.1 Hz, 3H, 2-CH_3), 0.90 (t, J = 6.7 Hz, 3H, pentyl-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 144.3 (C_{8a}), 126.0 (C_5), 125.5 (C_7), 124.5 (C_{4a}), 116.4 (C_6), 113.3 (C_8), 46.4 (C_2), 36.3 (C_3), 34.5 (C_4), 33.6 (alkyl-CH_2), 31.2 (alkyl-CH_2), 25.0 (alkyl-CH_2), 21.8 (2-Me), 21.7 (alkyl-CH_2), 13.1 (alkyl-CH_3); ESI-HRMS for $C_{15}H_{24}N$ ($[M+H]^+$): cald. 218.1903; found 218.1908; IR (neat, cm^{-1}) 3389 (br), 3020 (w), 2955 (m), 2926 (m), 2856 (m), 1605 (m), 1583 (m), 1483 (s), 1454 (m), 1376 (m), 1341 (m), 1306 (m), 1255 (m), 1168 (w), 1136 (w), 1043 (w), 970 (w), 927 (w), 843 (w), 743 (s). Diagnostic 300 MHz ^{1}H NMR signals for the *trans* isomer: 2.65-2.72 (m, 1H, H_4).

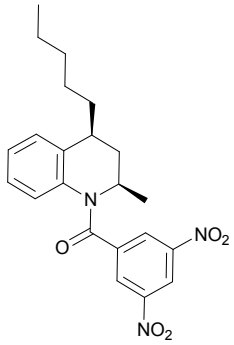
(2*R*,4*S*)-2-Methyl-4-pentyl-1,2,3,4-tetrahydroquinoline, 7a



Novel compound. (Table 3, entry 1) Asymmetric synthesis according to general procedure **C** using 0.5 mmol of enone gave the crude product as a brown oil, which

was purified by column chromatography (100% DCM) to give **7a** as a yellow oil (82 mg, yield 76%, d.r. = 94:6 *cis:trans*), $[\alpha]_D^{19}$ –36.1 (c = 1.94, CH_2Cl_2), spectroscopically identical to the racemic material obtained previously. The enantiomeric excess was determined by chiral analytical HPLC analysis of the derivative **S1**.

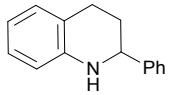
(3,5-Dinitrophenyl)((2*R*,4*S*)-2-methyl-4-pentyl-3,4-dihydroquinolin-1(2*H*)-yl)methanone, S1



Novel compound. To a solution of **7a** (20 mg, 0.09 mmol, 1 equiv) and Et_3N (14 µl, 0.10 mmol, 1.1 equiv) in $CHCl_3$ (2 mL, ca. 0.05M) was added 3,5-dinitrobenzoyl chloride (23 mg, 0.10 mmol, 1.1 equiv). The reaction mixture was stirred at rt for 4 h. The reaction was quenched with H_2O (5 mL) and then extracted with $CHCl_3$ (2 × 10 mL), dried (Na_2SO_4), filtered and then concentrated under reduced pressure. The crude product was purified column chromatography (100% DCM) to give **S1** as a yellow solid (32 mg, yield 78%, d.r. = >95:<5 *cis:trans,* ee = >98%). mp 101-104°C ($CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.93 (t, *J* = 2.1 Hz, 1 H, ArH_4), 8.30 (d, *J* = 2.0 Hz, 2 H, ArH_2), 7.36 (d, *J* = 7.6 Hz, 1 H, H_8), 7.19 (t, *J* = 7.6 Hz, 1 H, H_7), 6.90 (t, *J* = 7.6 Hz, 1 H, H_6), 6.43 (d, *J* = 7.8 Hz, 1 H, H_5), 4.86 - 4.80 (m, 1 H, H_2), 2.72 - 2.61 (m, 2 H, H_3), 2.21 - 2.07 (m, 1 H. H_4), 1.75 - 1.38 (m, 8 H, 4 pentyl CH_2), 1.29 (d, *J* = 6.4 Hz, 3 H, 2-CH_3), 0.97 (t, *J* = 4.0 Hz, 3 H, pentyl CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 164.6 (C=O), 148.3 (q), 140.2 (q), 137.0 (q), 129.3 (2C, CH), 127.5 (q), 127.2 (CH), 126.7 (CH), 124.8 (CH), 120.0 (CH), 51.5 (CH), 39.7 (CH_2), 35.9 (CH), 32.6 (CH_2), 30.8 (CH_2), 27.2 (CH_2), 23.1 (CH_2), 21.4 (CH_3), 14.5 (CH_3); ESI-HRMS for $C_{22}H26N_3O_5$ ($[M+H]^+$): cald. 412.1867; found 412.1861; $[\alpha]_D^{25}$ +39.13 (c = 0.23, $CHCl_3$); HPLC: CHIRALPAK® AS-RH 250 mm x 4.6 mm, detection wavelength = 230 nm, 60% to 100% MeCN/H_2O over 30 min, 1 mL/min) t_1 = 25.1 min (minor), t_2 = 27.3 min (major). IR (neat, cm^{-1}) 3090 (w), 2961 (w), 2923 (m), 2857 (w), 1644 (s),

1584 (w), 1539 (s), 1490 (m), 1457 (m), 1396 (m), 1339 (s), 1293 (w), 1193 (w), 1151 (w), 1128 (w), 1111 (m), 958 (w), 911 (m), 826 (w), 763 (m), 715 (s), 677 (m). Signals corresponding to the *trans* isomer were not observed in the 300 MHz ^{1}H NMR spectrum.

2-Phenyl-1,2,3,4-tetrahydroquinoline, 7b

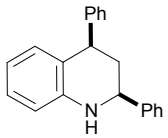


Known compound.[3] (Table 1, entry 2) Synthesis according to general procedure **A** using 0.23 mmol of enone gave crude product as a black oil, which was purified by column chromatography (gradient of pure cyclohexane to 20% ethyl acetate within 15 column volumes, column pre-conditioned with 1% Et_3N) followed by acidic ion-exchange chromatography on an Isolute SPX-cartridge (washing with dichloromethane and MeOH, elution with 2N NH_3 in MeOH) to give **7b** as yellow oil (16 mg, yield 33%).

(Table 2, entry 2) Synthesis according to general procedure **B** using 0.23 mmol of enone gave crude product as a black oil, which was purified by column chromatography (gradient of pure cyclohexane to 20% ethyl acetate within 15 column volumes, column pre-conditioned with 1% Et_3N) followed by acidic ion-exchange chromatography on an Isolute SPX-cartridge (washing with dichloromethane and MeOH, elution with 2N NH_3 in MeOH) to give **7b** as yellow oil (37 mg, yield 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.29-7.40 (m, 5H, 2-Ph), 6.95-7.04 (m, 2H, H_7 and H_5), 6.64 (t, J = 7.0 Hz, 1H, H_6), 6.53 (d, J = 7.6 Hz, 1H, H_8), 4.43 (dd, J = 9.4 and 3.3, 1H, H_2), 4.01 (br s, 1H, NH), 2.92 (m, 1H, H_{4B}), 2.73 (dt, J = 16.4 and 4.8 Hz, 1H, H_{4A}), 2.08-2.14 (m, 1H, H_{3B}), 1.96-2.03 (m, 1H, H_{3A}); UPLC/MS (BEH C18 column, I.D. 50 mm x 2.1 mm, 1.7 μm, 40 ^{o}C, 1% 10 mM NH_4CO_3 in H_2O adjusted to pH 10 with NH_4OH to 100% MeCN over 2 min) for $C_{15}H_{15}N$ ($[M]^+$): cald. 210.13; found 210.14; t_1 = 1.35 min.

***(2RS,4SR)*-2,4-Diphenyl-1,2,3,4-tetrahydroquinoline, *rac*-7c**

[3] Pitts, M. R.; Harrison, J. R.; Moody, C. J. *J. Chem. Soc., Perkin Trans. 1*, **2001**, 955-977.

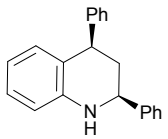


Known compound.[4] (Table 1, entry 3) Synthesis according to general procedure **A** using 0.23 mmol of enone gave the crude product as a brown oil, which was purified by column chromatography (9:1 petrol/ethyl acetate, column pre-conditioned with 1% NEt_3) to give **7c** as colourless crystals (63 mg, yield 96%, dr = >95:<5 *cis:trans*).

(Table 2, entry 1) Synthesis according to general procedure **B** using 0.23 mmol of enone gave the crude product as a brown oil, which was purified by column chromatography (9:1 petrol/ethyl acetate, column pre-conditioned with 1% NEt_3) to give **7c** as colourless crystals (62 mg, yield 95%, dr = >95:<5 *cis:trans*).

mp 86 °C (from hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.43-7.47 (m, 2H, Ph-H), 7.19-7.38 (m, 8H, Ph-H), 7.00 (t, J = 7.0 Hz, 1H, H_5), 6.62-6.66 (m, 1H, H_7), 6.53-6.58 (m, 2H, H_8 and H_6), 4.60 (dd, J = 10.6 and 3.2 Hz, 1H, H_2), 4.31 (dd, J = 11.8 and 5.9 Hz, 1H, H_4), 4.06 (s, 1H, NH), 2.29 (ddd, J = 13.1, 6.1 and 3.3 Hz, 1H, H_3^{eq}), 2.22 (q, J = 13.0 Hz, 1H, H_3^{ax}); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 145.5 (C_{Ph}), 145.3 (C_{Ph}), 143.9 (C_{8a}), 129.7 (C_7), 128.7 (2C, C_{Ph}), 128.5 (C_{Ph}), 127.7 (C_{Ph}), 127.2 (C_5), 126.6 (C_{Ph}), 126.5 (C_{Ph}), 124.7 (C_{4a}), 117.6 (C_6), 114.3 (C_8), 57.3 (C_2), 45.0 (C_4), 42.1 (C_3); ESI-HRMS for $C_{21}H_{20}N$ ($[M+H]^+$): cald. 286.1590; found 286.1597; IR (neat, cm^{-1}) 3379 (br), 3058 (w), 3025 (w), 2949, (w), 2918 (w), 2854 (w), 1603 (m), 1584 (m), 1477 (s), 1453 (m), 1312 (m), 1254 (m), 1172 (w), 1156 (w), 1107 (m), 1078 (m), 1029 (m), 908 (w), 803 (w), 747 (s), 698 (s). Signals corresponding to the *trans* isomer were not observed in the 300 MHz ^{1}H NMR spectrum.

(2*S*,4*R*)-2,4-Diphenyl-1,2,3,4-tetrahydroquinoline, 7c

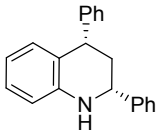


(Table 3, entry 2) Asymmetric synthesis according to general procedure **C** using 0.5 mmol of enone gave the crude product as a brown oil, which was purified by column chromatography (100% DCM) to give **7c** as a yellow solid (85 mg, yield 60%, dr = >95:<5 *cis:trans*, ee = >98 %).

[4] no NMR data reported in the literature

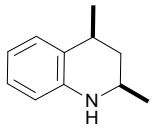
(Table 3, entry 8) Asymmetric synthesis according to general procedure **D** using 0.5 mmol of enone and (*R,R,S,S*)-Duanphos gave the crude product as a brown oil, which was purified by column chromatography (100% DCM) to give **7c** as a yellow solid (115 mg, yield 81%, >95:<5 *cis:trans*, ee = >98 %), $[\alpha]_D^{25}$ +102.8 (c = 0.24, $CHCl_3$), spectroscopically identical in both cases to the racemic material obtained previously. HPLC: CHIRALPAK® AS-RH 250 mm x 4.6 mm, detection wavelength = 210 nm, 80% to 100% MeCN/H_2O over 30 min, 1 mL/min) t_1 = 15.7 min (minor), t_2 = 16.9 min (major); also resolved on CHIRALPAK® AD 250 mm x 4.6 mm, detection wavelength = 215 nm, 10% EtOH/ heptane, 1 mL/min) t_1 = 5.6 min (major), t_2 = 7.3 min (minor). The absolute configuration of the product was determined by VCD analysis.

(2*R*,4*S*)-2,4-Diphenyl-1,2,3,4-tetrahydroquinoline, *ent*-7c



The enantiomeric tetrahydroquinoline ***ent*-7c** was prepared for the use in VCD analysis according to general procedure **D** using 0.5 mmol of enone and (*S,S,R,R*)-Duanphos to give a crude product as a brown oil, which was purified by column chromatography (100% DCM) to give *ent*-**7c** as a colourless solid (111 mg, yield 78%, d.r. = >95:<5 *cis:trans*, ee = >98 %), $[\alpha]_D^{25}$ −111.2 (c = 0.52, $CHCl_3$), spectroscopically identical to the racemic material previously obtained. HPLC: CHIRALPAK® AD 250 mm x 4.6 mm, detection wavelength = 215 nm, 10% EtOH/ heptane, 1 mL/min) t_1 = 5.6 min (minor), t_2 = 7.3 min (major).

(2*RS*,4*SR*)-2,4-Dimethyl-1,2,3,4-tetrahydroquinoline, *rac*-7d

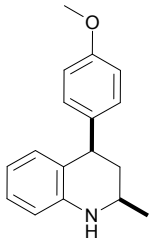


Known compound.[5] (Table 1, entry 4) Synthesis according to general procedure **A** using 0.23 mmol of enone gave the crude product as a brown oil, which was purified by column chromatography (9:1 petrol/ethyl acetate, column pre-conditioned with 1%

[5] Shaw, J. E.; Stapp, P.R. *J. Het. Chem.* **1987**, *24*, 1477-1483.
Murahashi, S.-I.; Imada, Y.; Hirai, Y. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2968-2976.

Et_3N) to give **7d** as yellow oil (20 mg, yield 54%, d.r. = 88:12 *cis:trans*). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.13 (d, *J* = 7.7 Hz, 1H, H_5), 6.96 (t, *J* = 7.6 Hz, 1H, H_7), 6.65 (td, *J* = 7.4 and 1.3 Hz, 1H, H_6), 6.46 (dd, *J* = 7.9 and 1.0 Hz, 1H, H_8), 3.66 (br s, 1H, NH), 3.46 (dqd, *J* = 11.0, 6.4 and 2.6 Hz, 1H, H_2), 2.88-3.03 (m, 1H, H_4), 1.93 (ddd, *J* = 12.8, 5.4 and 2.6 Hz, 1H, H_3^{eq}), 1.34 (dt, *J* = 12.0 and 11.3 Hz, 1H, H_3^{ax}), 1.31 (d, *J* = 6.9 Hz, 3H, 4-CH_3), 1.19 (d, *J* = 6.1 Hz, 3H, 2-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 143.6 (C_{8a}), 125.7 (2C, C_5 and C_7), 125.3 (C_{4a}), 116.3 (C_6), 113.0 (C_8), 46.4 (C_2), 39.6 (C_3), 29.8 (C_4), 21.7 (2-Me), 19.3 (4-Me); ESI-HRMS for $C_{11}H_{16}N$ ($[M+H]^+$): cald. 162.1277; found 162.1270; IR (neat, cm^{-1}) 3422 (br), 2979 (m), 1675 (w), 1605 (w), 1472 (m), 1448 (m), 1371 (s), 1340 (m), 1271 (w), 1142 (s), 1008 (w), 982 (w), 949 (s), 833 (m), 851 (m), 828 (m), 747(w), 672 (m). Diagnostic signals for the *trans* isomer in the 300 MHz ^1H NMR spectrum: 1.63-1.67 (m, 2H, H_3^{eq+ax}), 1.26 (d, *J* = 7.2 Hz, 3H, 4-Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 143.0 (C_{8a}), 128.1 (C_5), 116.0 (C_6), 113.1 (C_8), 41.4 (C_2), 36.1 (C_3), 29.1 (C_4), 28.7 (2-Me), 23.7 (4-Me).

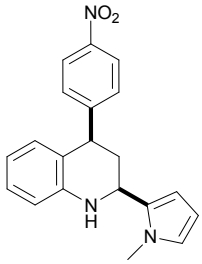
(2*RS*,4*RS*)-4-(4-Methoxyphenyl)-2-methyl-1,2,3,4-tetrahydroquinoline, *rac*-7e



Novel compound. (Table 1, entry 5) Synthesis according to general procedure **A** using 0.23 mmol of enone gave the crude product as a brown oil, which was purified by column chromatography (8:1 petrol/ethyl acetate, column pre-conditioned with 1% Et_3N) to give **7e** as yellow oil, that crystallised eventually (53 mg, yield 91%, d.r. = 95:5 *cis:trans*). mp 76°C (hexanes); ^1H NMR (300 MHz, $CDCl_3$,) δ: 7.13 (d, *J* = 8.7 Hz, 2H, MeOPh-H_2), 6.96 (t, *J* = 7.6 Hz, 1H, H_5), 6.86 (d, *J* = 8.7 Hz, 2H, MeOPh-H_3), 6.57-6.61 (m, 1H, H_7), 6.48-6.53 (m, 2H, H_8 and H_6), 4.09 (dd, *J* = 12.5 and 5.4 Hz, 1H, H_4), 3.81 (s, 3H, OCH_3), 3.77 (br s, 1H, NH), 3.60 (dqd, *J* = 12.3, 6.1 and 2.3 Hz, 1H, H_2), 2.10 (ddd, *J* = 12.9, 5.4 and 2.4 Hz, 1H, H_3^{eq}), 1.80 (q, *J* = 12.5 Hz, 1H, H_3^{ax}), 1.22 (d, *J* = 6.4 Hz, 3H, 2-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 157.1 (MeOPh-C_4), 144.2 (C_{8a}), 136.9 (MeOPh-C_1), 128.6 (2C, C_7 and MeOPh-C_2), 126.0 (C_5), 124.2 (C_{4a}), 116.3 (C_6), 113.0 (C_8), 112.9 (MeOPh-C_3), 54.2 (OCH_3), 46.7 (C_2), 42.7 (C_4),

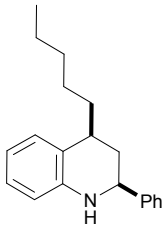
40.3 (C_3), 21.6 (2-CH_3); ESI-HRMS for $C_{17}H_{20}NO$ ($[M+H]^+$): cald. 254.1539; found 254.1529; IR (neat, cm^{-1}) 3427 (br), 2980 (m), 1670 (s), 1512 (m), 1453 (m), 1359 (m), 1254 (m), 1200 (s), 1180 (s), 1139 (s), 1034 (m), 833 (m), 798 (w), 751 (w), 722 (w). Diagnostic signals for the *trans* isomer in the 300 MHz ^1H NMR spectrum: 3.25-3.33 (m, 1H, H_2), 1.88-1.92 (m, 2H, H_3^{eq+ax}).

(2*RS*,4*SR*)-2-(1-Methyl-1*H*-pyrrol-2-yl)-4-(4-nitrophenyl)-1,2,3,4-tetrahydroquinoline, *rac*-7f



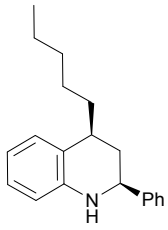
Novel compound. (Table 1, entry 6) Synthesis according to general procedure **A** using 0.23 mmol of enone gave the crude product as an orange oil, which was purified by column chromatography (7:1 petrol/ethyl acetate, column pre-conditioned with 1% Et_3N) to give **7f** as a yellow oil (61 mg, yield 80%, d.r. = >95:<5 *cis:trans*). ^1H NMR (300 MHz, $CDCl_3$) δ: 8.18 (d, *J* = 8.7 Hz, 2H, $NO_2C_6H_4$-H_3), 7.41 (d, *J* =8.7 Hz, 2H, NO_2 C_6H_4-H_2), 7.02 (t, *J* = 7.1 Hz, 1H, C_5), 6.50-6.61 (m, 4H, pyrrol-H, C_8, C_6 and C_7), 6.17 (dd, *J* = 3.6 and 1.8 Hz, 1H, pyrrol-H), 6.17-6.10 (m, 1H, pyrrol-H), 4.69 (dd, *J* = 11.0 and 2.6 Hz, 1H, H_2), 4.43 (dd, *J* =12.0 and 5.9 Hz, 1H, H_4), 4.02 (br s, 1H, NH), 3.70 (s, 3H, CH_3), 2.35 (ddd, *J* =12.8, 5.6 and 2.8 Hz, 1H, H_{3eq}), 2.24 (q, *J* = 12.5 Hz, 1H, H_{3ax}); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 153.3 (NO_2Ph-C_4), 146.8 ($C_{pyrrol\text{-}2}$ or C_8), 145.0 ($C_{pyrrol\text{-}2}$ or C_8), 133.4 (NO_2Ph-C_1), 129.5 ((NO_2Ph-C_2), 127.8 (C_5), 123.9 (NO_2Ph-C_3), 122.9 (2C, C_7 and C_{pyrrol}), 118.0 (C_6), 114.9 (C_8), 107.2 (C_{pyrrol}), 106.3 (C_{pyrrol}), 49.4 (C_2), 44.8 (C_4), 39.4 (C_3), 34.1 (NCH_3); ESI-HRMS for $C_{20}H_{20}N_3O_2$ ($[M+H]^+$): cald. 334.1550; found 334.1535. IR (neat, cm^{-1}) 3301 (br), 2928 (w), 1717 (w), 1649 (m), 1602 (m), 1517 (s), 1405 (m), 1343 (s), 1158 (s), 1065 (w), 987 (w), 846 (m), 746 (m), 697 (w). Minor *trans*-isomer was not observed.

(2*RS*,4*RS*)-4-Pentyl-2-phenyl-1,2,3,4-tetrahydroquinoline, *rac*-7g



Novel compound. (Table 2, entry 3) Synthesis according to general procedure **B** using 0.23 mmol of enone at 50 °C gave the crude product as a black oil, which was purified by column chromatography (gradient of pure cyclohexane to 10% ethyl acetate within 15 column volumes, column pre-conditioned with 1% Et_3N) to give **7g** as a yellow oil (61 mg, yield 76%, d.r. = 95:5 *cis:trans*). ^{1}H NMR (300 MHz, $CDCl_3$,) δ: 7.28-7.46 (m, 5H, Ph), 7.20 (d, *J* = 7.6 Hz, 1H, H_5), 7.00 (t, *J* = 7.5 Hz, 1H, H_7), 6.71 (t, *J* = 7.5 Hz, 1H, H_6), 6.54 (d, *J* = 7.8 Hz, 1H, H_8), 4.41 (dd, *J* = 11.2 and 2.7 Hz, 1H, H_2), 3.94 (br s, 1H, NH), 3.01-3.08 (m, 1H, H_4), 2.19 (ddd, *J* = 12.9, 5.6 and 2.5 Hz, 1H, H_{3eq}), 1.93-2.05 (m, 1H, 4-$CH_A\mathit{H_B}$), 1.72 (dt, *J* = 12.6 and 11.6 Hz, 1H, H_3^{ax}), 1.26-1.56 (m, 7H, 3 pentyl-CH_2 and 4-C$\mathit{H_A}H_B$), 0.88 (t, *J* = 6.4 Hz, 3H, pentyl-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 145.4 (PhC_1 or C_{8a}), 144.7 (C_{8a} or PhC_1), 128.7 (Ph), 127.6 (Ph), 127.0 (C_5), 126.7 (2C, C_7 and Ph), 125.3 (C_{4a}), 117.7 (C_6), 114.5 (C_8), 57.1 (C_2), 38.5 (C_3), 36.0 (C_4), 34.5 (pentyl-CH_2), 32.3 (pentyl-CH_2), 26.1 (pentyl-CH_2), 22.7 (pentyl-CH_2), 14.2 (pentyl-CH_3); LC-ESI-HRMS for $C_{20}H_{26}N$ ($[M+H]^+$): cald 280.2065; found 280.2052; IR (neat, cm^{-1}) 3406 (br), 2980 (m), 1673 (m), 1473 (m), 1447 (m), 1372 (m), 1340 (m), 1140 (s), 1008(m), 982 (m), 949 (m), 883 (m), 829 (m), 673 (m).

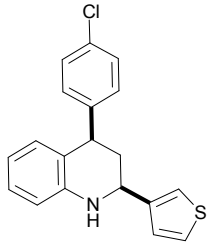
(2*S*,4*S*)-4-Pentyl-2-phenyl-1,2,3,4-tetrahydroquinoline, 7g



(Table 3, entry 9) Asymmetric synthesis according to general procedure **D** using 0.5 mmol of enone and (*R,R,S,S*)-Duanphos gave the crude product as a brown oil, which was purified by column chromatography (10% 40-60 petrol in DCM) to give **7g** as a yellow oil (86 mg, yield 62%, d.r. = >95:<5 *cis:trans*, ee = 87%); $[\alpha]_D^{19}$ -123.3 (c = 1.52, CH_2Cl_2); HPLC: CHIRALCEL® 250 mm x 4.6 mm, detection wavelength =

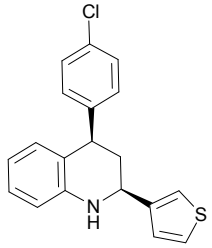
215 nm, 1% EtOH/heptane, 0.5 mL/min) t_1 = 10.8 min (major), t_2 = 12.2 min (minor). Spectroscopically identical to the racemic material obtained previously. Minor *trans*-isomer was not observed.

(2*RS*,4*SR*)-4-(4-Chlorophenyl)-2-(thiophen-3-yl)-1,2,3,4-tetrahydroquinoline, *rac*-7h



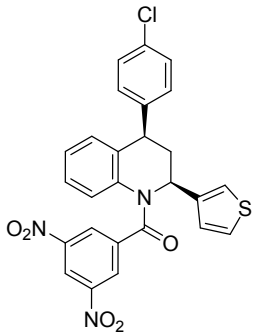
Novel compound. (Table 2, entry 4) Synthesis according to general procedure **B** using 0.23 mmol of enone gave the crude product as a black oil, which was purified by column chromatography (gradient of pure cyclohexane to 10% ethyl acetate within 15 column volumes, column pre-conditioned with 1% Et_3N) to give **7h** as a yellow solid (61 mg, yield 81%, d.r. = >95:<5 *cis:trans*). mp 118-122°C (DCM); ^{1}H NMR (300 MHz, $CDCl_3$,) δ: 7.27-7.33 (m, 4H, ClPh-H_3 , thienyl-H_2 and thienyl-$H_{4\ or\ 5}$), 7.17 (d, J = 8.6 Hz, 2H, ClPh- H_2), 7.15 (dd, J = 4.8 and 1.0 Hz, 1H, H_5), 7.02 (m, 1H, H_7), 6.56-6.61 (m, 3H, H_8, H_6 and thienyl- $H_{4\ or\ 5}$), 4.73 (dd, J = 11.2 and 2.4 Hz, 1H, H_2), 4.28 (dd, J = 12.3 and 5.4 Hz, 1H, H_4), 4.10 (br s, 1H, NH), 2.31 (ddd, J = 12.8, 5.6 and 2.8 Hz, 1H, H_3^{eq}), 2.17 (q, J = 12.0 Hz, 1H, H_3^{ax}); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.1 (ClPh-C_4), 144.9 (ClPh-C_1), 143.9 (C_{8a}), 132.2 ($C_{thienyl\text{-}1}$), 130.0 (ClPh-C_3), 129.6 ($C_{thienyl}$), 128.7 (ClPh-C_2), 127.5 (C_7), 126.3 ($C_{Thienyl}$ or C_5), 126.0 ($C_{Thienyl}$ or C_5), 124.2 (C_{4a}), 121.0 ($C_{thienyl}$), 117.9 (C_6), 114.5 (C_8), 52.8 (C_2), 44.2 (C_4), 41.4 (C_3); LC-ESI-HRMS for $C_{19}H_{15}ClNS$ ($[M-H]^+$): cald. 324.0614; found 324.0602. IR (neat, cm^{-1}) 3383 (br), 3016 (w), 2962 (w), 2926 (w), 2867 (w), 1600 (m), 1580 (m), 1472 (s), 1426 (m), 1308 (m), 1293 (m), 1248 (m), 1186 (w) 1087 (m), 1013 (m), 964 (w), 936 (w), 885 (w), 832 (s), 789 (s), 750 (s). Signals corresponding to the *trans* isomer were not observed in the 300 MHz ^{1}N NMR spectrum. The relative configuration was determined by nOe analysis.

(2*S*,4*R*)-4-(4-Chlorophenyl)-2-(thiophen-3-yl)-1,2,3,4-tetrahydroquinoline, 7h



(Table 3, entry 3) Asymmetric synthesis according to general procedure **C** using 0.43 mmol of enone gave the crude product as a brown oil, which was purified by column chromatography (100% DCM) to give **7h** as a yellow solid (62 mg, yield 45%, >95:<5 *cis:trans*), $[\alpha]_D^{19}$ +78.60 (c = 0.70, CH_2Cl_2), spectroscopically identical to the racemic material obtained previously. The enantiomeric excess was determined by chiral analytical HPLC analysis of the derivative **S2**.

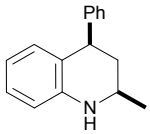
((2*S*,4*R*)-4-(4-Chlorophenyl)-2-(thiophen-3-yl)-3,4-dihydroquinolin-1(2*H*)-yl)(3,5-dinitrophenyl)methanone, S2



Novel compound. To a solution of **7h** (10 mg, 0.03 mmol, 1 equiv) and triethylamine (4 µl, 0.03 mmol, 1 equiv) in $CHCl_3$ (2 ml, ca. 0.02M) was added 3,5-dinitrobenzoyl chloride (7 mg, 0.03 mmol, 1 equiv). The reaction mixture was stirred at rt for 15 min. The reaction was quenched with 2.5 M aq. KOH (2 mL) and then extracted with DCM (2 x 10 mL), washed with brine (10 mL), dried (Na_2SO_4), filtered and then concentrated under reduced pressure. The crude product was purified column chromatography (25% to 100% DCM in petrol) to give **S2** as a yellow oil (12 mg, yield 77%, d.r. = >95:<5 *cis:trans,* ee = >98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.96 (t, *J* = 2.1 Hz, 1 H, 3,5- NO_2Ph-H_4), 8.34 (d, *J* = 2.0 Hz, 2 H, 3,5-NO_2Ph-H_2), 7.45 (d, *J* = 8.3 Hz, 2 H, ClPh-H_3), 7.33 - 7.25 (m, 3 H ClPh-H_2 and thienyl-$H_{4\text{ or }5}$), 7.21 (d, *J* = 1.7 Hz, 1 H, thienyl-H_2), 7.14 - 7.07 (m, 1 H, H_8), 6.99 - 6.89 (m, 2 H, H_5 and thienyl-$H_{4\text{ or }5}$), 6.78 (d, *J* = 7.6 Hz, 1 H, H_7), 6.55 (d, *J* = 7.8 Hz, 1 H, H_6), 5.98 (t, *J* =

9.0 Hz, 1 H, H_2), 4.12 (dd, *J* = 3.1, 12.8 Hz, 1 H, H_4), 2.98 (ddd, *J* = 3.7, 9.0, 13.0 Hz, 1 H, H_{3eq}), 2.25 (td, *J* = 7.8, 13.0 Hz 1 H, H_{3ax}); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.0 (q), 142.7 (q), 139.3 (q), 139.2 (q), 137.7 (q), 136.6 (q), 133.5 (q), 130.1 (Ar), 129.2 (Ar), 128.9 (Ar), 127.3 (q), 127.2 (Ar), 126.6 (Ar), 126.6 (Ar), 125.8 (Ar), 12 2.1 (q), 121.9 (Ar), 119.9 (Ar), 53.4 (CH), 42.3 (CH), 41.2 (CH_2), C=O signal not observed due to low intensity. ESI-HRMS for $C_{26}H_{19}ClN_3O_{5S}$ ([M+H]$^+$): cald. 520.0728; found 520.0750; $[\alpha]_D^{19}$ +60.00 (c = 0.50, CH_2Cl_3); HPLC: CHIRALPAK® AD-RH 250 mm x 4.6 mm, detection wavelength = 210 nm, 93% to 97% MeCN/H_2O over 30 min, 1 mL/min) t_1 = 12.5 min (major), t_2 = 17.2 min (minor). IR (neat, cm^{-1}) 3400 (w), 3103 (w), 2961 (w), 2924 (w), 2865 (w), 1721 (m), 1630 (s), 1539 (s), 1484 (s), 1339 (s), 1256 (s), 1091 (s), 1015 (s), 923 (w), 833 (w), 793 (s), 723 (s). Signals corresponding to the *trans* isomer were not observed in the 400 MHz ^{1}H NMR spectrum.

***(2RS,4RS)*-2-Methyl-4-phenyl-1,2,3,4-tetrahydroquinoline, *rac*-7i**

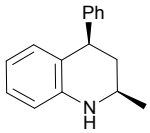


Known compound.[6] (Table 2, entry 5) Synthesis according to general procedure **B** using 1 mmol of enone gave the crude product as a brown oil which was purified by column chromatography (10% ethyl acetate in petrol) to give **7i** as a colourless oil (202 mg, yield 91%, d.r. = >95:<5 cis:trans). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.20-7.34 (m, 5H, Ph), 6.96 (t, *J* = 7.5 Hz, 1H, H_5), 6.48-6.59 (m, 3H, H_6, H_7 and H_8), 4.13 (dd, *J* = 12.3, 5.4 Hz, 1H, H_2), 3.77 (br s, 1H, NH), 3.60 (ddt, *J* = 2.7, 6.3, 12.6 Hz, 1H, H_4), 2.12 (ddd, *J* = 12.9, 5.4, 2.4 Hz, 1H, H_{3eq}), 1.83 (q, *J* = 12.6 Hz, 1H, H_{3ax}), 1.22 (d, *J* = 6.0 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 144.9 (C_{8a}), 144.3 (C_{Ph}), 128.7 (Ar), 127.7 (Ar), 127.5 (Ar), 126.1 (Ar), 125.4 (Ar), 123.9 (q), 116.3 (Ar), 113.0 (Ar), 46.7 (CH), 43.6 (CH_2), 40.2 (CH), 21.6 (CH_3); ESIHRMS for $C_{16}H_{18}N$ ([M+H]): calcd. 224.1434; found 224.1439); IR (neat, cm^{-1}) 3389 (br), 3025 (w), 2961 (w), 2859 (w), 1721 (w), 1603 (m), 1484 (s), 1451 (s), 1377 (w), 1339 (w), 1310 (m), 1256 (m), 1163 (w), 1121 (w), 1099 (w), 1062 (w), 1029 (w), 908 (m), 867 (w),

[6] no NMR data reported in the literature

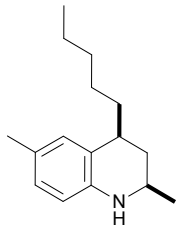
846 (w), 746 (s), 731 (s), 698 (s). Signals corresponding to the *trans* isomer were not observed in the 300 MHz ^{1}H NMR spectrum.

***(2R,4R)*-2-Methyl-4-phenyl-1,2,3,4-tetrahydroquinoline, 7i**



Asymmetric synthesis according to general procedure **C** using 0.5 mmol of enone gave the crude product as a brown oil which was purified by column chromatography (10% ethyl acetate in petrol) to give **7i** as a colourless oil (72 mg, yield 65%, dr = >95:<5 *cis:trans*, ee = >98%), $[\alpha]_D^{25}$ +3.92 (c = 0.51, $CHCl_3$), spectroscopically identical to the racemic material obtained previously. HPLC (CHIRALPAK® AD-RH 250 mm x 4.6 mm, detection wavelength = 210 nm, 65% to 70% MeCN/H_2O over 30 min, 1 mL/min) t_1 = 21.8 min (minor), t_2 = 23.9 min (major).

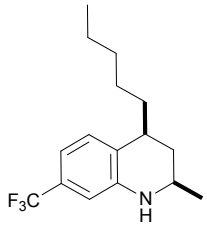
***(2RS,4SR)*-2,6-Dimethyl-4-pentyl-1,2,3,4-tetrahydroquinoline, *rac*-7j**



Novel compound. (Table 2, entry 6) Synthesis according to general procedure **B** using 0.23 mmol of enone gave the crude product as a brown oil, which was purified by column chromatography (12:1 petrol/ethyl acetate, column pre-conditioned with 1% Et_3N) to give **7j** as a brownish oil (37 mg, yield 70%, 90:10 *cis:trans*). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.96 (s, 1H, H_5), 6.77 (d, *J* = 8.0 Hz, 1H, H_7), 6.41 (d, *J* = 8.2, 1H, H_8), 3.52 (br s, 1H, NH), 3.34 (dqd, *J* = 12.5, 6.4 and 2.3 Hz, 1H, H_2), 2.80-2.91 (m, 1H, H_4), 2.22 (s, 3H, 6-CH_3), 2.01 (ddd, *J* = 12.9, 6.0 and 2.4 Hz, 1H, H_3^{eq}), 1.87-1.96 (m, 1H, 4-CH_AH_B), 1.23-1.57 (m, 8H, 3 pentyl-CH_2, H_3^{ax} and 4-CH_AH_B), 1.19 (d, *J* = 6.1 Hz, 3H, 2-Me), 0.90 (*J* = 6.4 Hz, 3H, pentyl-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 134.0 (C_{8a}), 127.6 (C_5), 127.0 (C_7), 126.6 (C_{4a} or C_6), 125.7 (C_{4a} or C_6), 114.5 (C_8), 47.6 (C_2), 37.6 (C_3), 35.5 (C_4), 34.9 (pentyl-CH_2), 32.2 (pentyl-CH_2), 26.1 (pentyl-CH_2), 22.9 (2-CH_3), 22.7 (pentyl-CH_2), 20.7 (6-Me), 14.1 (pentyl-CH_3); ESI-HRMS for $C_{16}H_{26}N$ ($[M+H]^+$): cald. 232.2060; found 232.2063; IR (neat, cm^{-1}) 3391 (br),

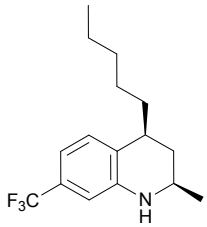
3018 (w), 2954 (m), 2921 (m), 1609 (m), 1581 (m), 1485 (s), 1455 (m), 1377 (m), 1341 (m), 1307 (m), 1251 (m), 1168 (w), 1132 (w), 1043 (w), 971 (w), 933 (w), 740 (s). Signals of the *trans*-isomer visible at ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.13 (q, *J* = 7.1 Hz, 1H, H_2), 2.60-2.69 (m, 1H, H_4), 1.76-1.82 (m, 2H, H_{3ax+eq}).

***(2RS,4SR)*-2-Methyl-4-pentyl-7-(trifluoromethyl)-1,2,3,4-tetrahydroquinoline, *rac*-7k**



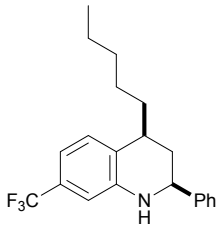
Novel compound. (Table 2, entry 7) Synthesis according to general procedure **B** using 0.23 mmol of enone gave the crude product as a black oil, which was purified by column chromatography (gradient of pure cyclohexane to 5% ethyl acetate within 15 column volumes, column pre-conditioned with 1% Et_3N) to give **7k** as a colourless oil (48 mg, yield 73%, 90:10 *cis:trans*). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.21 (d, *J* = 8.1 Hz, 1H, H_5), 6.85 (d, *J* = 7.8 Hz, 1H, H_6), 6.67 (s, 1H, H_8), 3.83 (br s, 1H, NH), 3.43 (dqd, *J* = 12.4, 6.3 and 2.5 Hz, 1H, H_2), 2.83-2.93 (m, 1H, H_{3ax}), 2.03 (ddd, *J* = 12.8, 5.4 and 2.8 Hz, 1H, H_{3eq}), 1.90-1.99 (m, 1H, 4-CH_AH_B), 1.27-1.56 (m, 8H, 3 pentyl-CH_2, H_3^{ax} and 4-CH_AH_B), 1.22 (d, *J* =6.1 Hz, 3H, 2-Me), 0.91 (t, *J* = 6.6 Hz, 3H, pentyl-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.9 (C_{8a}), 129.4 (m, C_7), 129.2 (m, CF_3), 127.6 (C_5), 126.1 (C_{4a}), 113.8 (q, *J* 4.0, C_6), 110.7 q, *J* 4.0, C_8), 47.8 (C_2), 36.9 (C_3), 35.9 (C_4), 34.5 (pentyl-CH_2), 32.6 (pentyl-CH_2), 26.3 (pentyl-CH_2), 23.1 (2C, (pentyl-CH_2 and CH_3), 14.5 (pentyl-CH_3); LC-ESI-HRMS for $C_{16}H_{23}NF_3$ ($[M+H]^+$): cald. 286.1783; found 286.1779. IR (neat, cm^{-1}) 3414 (br), 2958 (w), 2930 (w), 2859 (w), 1782 (w), 1619 (w), 1583 (w), 1485 (m), 1453 (w), 1325 (s), 1244 (w), 1163 (s), 1115 (s), 1378 (s), 979 (m), 947 (w), 903 (w), 861 (m), 807 (m), 723 (w), 665 (w). Signals of the *trans*-isomer visible at δ: 7.04 (d, *J* = 7.8 Hz, 1H, H_5), 6.80 (d, *J* = 7.6 Hz, 1H, H_6), 2.70-2.76 (m, 1H, H_4), 1.81-1.86 (m, 2H, H_{3eq+ax}).

(2*R*,4*S*)-2-Methyl-4-pentyl-7-(trifluoromethyl)-1,2,3,4-tetrahydroquinoline, 7k



(Table 3, entry 6) Asymmetric synthesis according to general procedure **C** using 0.5 mmol of enone gave the crude product as a brown oil, which was purified by column chromatography (gradient of 10% to 33% DCM in 40-60 petrol) to give **7k** as a yellow oil (103 mg, yield 72%, >95:<5 *cis:trans*, ee = >98%), $[\alpha]_D^{25}$ -34.62 (c = 0.39, $CHCl_3$), spectroscopically identical to the racemic material obtained previously. HPLC (CHIRALPAK® AS-RH, detection wavelength = 210 nm, 60% to 90% MeCN/H_2O over 30 min, 1 ml/min) t_1 = 23.8 min (major), t_2 = 24.4 min (minor). Minor *trans*-isomer was not observed.

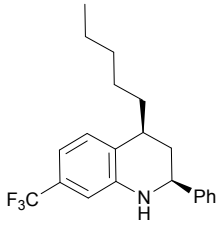
***(2RS,4RS)*-4-Pentyl-2-phenyl-7-(trifluoromethyl)-1,2,3,4-tetrahydroquinoline, *rac*-7l**



Novel compound. (Table 2, entry 8) Synthesis according to general procedure **B** at 50°C using 0.23 mmol of enone gave the crude product as a red-brown oil, which was purified by column chromatography (gradient of pure cyclohexane to 10% ethyl acetate within 15 column volumes, column pre-conditioned with 1 % NEt_3) followed by an acidic ion-exchange chromatography on an Isolute SPX-cartridge (washing with dichloromethane, elution with MeOH) to give **7l** as a yellow oil (61 mg, yield 81%, dr = 95:5 *cis:trans*). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.30-7.45 (m, 5H, Ph), 7.27 (d, *J* = 7.9 Hz, 1H, H_5), 6.91 (d, *J* = 8.1 Hz, 1H, H_6), 6.74 (s, 1H, H_8), 4.44 (dd, *J* = 11.1 and 2.8, 1H, H_2), 4.14 (br s, 1H, NH), 3.00-3.10 (m, 1H, H_4), 2.20 (ddd, *J* = 12.9, 5.3 and 2.8 Hz, 1H, H_{3eq}), 1.94-2.04 (m, 1H, 4-CH_AH_B), 1.71 (dt, *J* = 13.0 and 11.5 Hz, 1H, H_{3ax}), 1.49-1.58 (m, 1H, 4-CH_AH_B), 1.24-1.45 (m, 6H, 3 pentyl-CH_2), 0.89 (t, *J* = 6.1 Hz, 3H, pentyl-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.9 (C_{8a} or Ph), 144.4 (C_{8a} or Ph), 129.6 (C_{4a}), 129.2 (2C, m, Ph and CF_3), 129.1 (m, C_7), 128.3 (Ph), 127.7 (C_5),

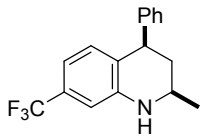
127.0 (Ph), 114.2 (q, *J* 4.0, C_6), 111.1 (q, *J* 4.0, C_8), 57.3 (C_2), 36.1 (C_3), 36.4 (C_4), 34.4 (4-CH_2), 32.6 (pentyl-CH_2), 26.3 (pentyl-CH_2), 23.1 (pentyl-CH_2), 14.5 (pentyl-CH_3); LC-ESI-HRMS for $C_{21}H_{25}NF_3$ ($[M+H]^+$): cald. 348.1939; found 348.1931. IR (neat, cm^{-1}) 3399 (br), 3032 (w), 2930 (w), 2859 (w), 1617 (w), 1583 (w), 1478 (m), 1326 (s), 1240 (w), 1216 (w), 1163 (m), 1118 (s), 1074 (m), 1029 (w), 907 (w), 864 (w), 810 (w), 756 (s), 698 (s), 665 (m). Diagnostic signal in the 400 MHz ^{1}H NMR spectrum of the *trans* isomer: 2.76-2.81 (m, 1H, H_4). The relative configuration was confirmed by 1D nOe studies.

***(2S,4S)*-4-Pentyl-2-phenyl-7-(trifluoromethyl)-1,2,3,4-tetrahydroquinoline, 7l**



(Table 3, entry 6) Asymmetric synthesis according to general procedure **C** using 0.5 mmol of enone gave the crude product as a brown oil, which was purified by column chromatography (gradient of 10% to 50% DCM in 40-60 petrol) to give **7l** as a yellow oil (112 mg, yield 65%, 92:8 *cis:trans*, ee = 92%), $[\alpha]_D^{25}$ +42.59 (c = 0.54, $CHCl_3$), spectroscopically identical to the racemic material obtained previously. HPLC: CHIRALCEL® OJ 250 mm x 4.6 mm, detection wavelength = 215 nm, 20% EtOH/heptane, 1 ml/min) t_1 = 5.8 min (minor), t_2 = 7.8 min (major). The absolute configuration of the product was determined by VCD analysis.

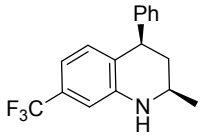
***(2RS,4RS)*-2-Methyl-4-phenyl-7-(trifluoromethyl)-1,2,3,4-tetrahydroquinoline, *rac*-7m**



Novel compound. (Table 2, entry 9) Synthesis according to general procedure **B** using 1 mmol of enone gave the crude product as a brown oil which was purified by column chromatography (25% DCM in petrol) to give **7m** as a colourless oil (252 mg, yield 87%, >95:<5 cis:trans). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.18-7.36 (m, 5H, Ph), 6.30-6.72 (m, 3H, H_5, H_6 and H_8), 4.11 (dd, *J* = 12.6, 5.4 Hz, 1H, H_2), 3.97 (br s, 1H, NH),

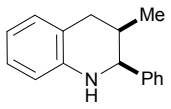
3.63 (ddt, *J* = 12.3, 6.0, 2.4 Hz, 1H, H_4), 2.15 (ddd, *J* = 13.2, 5.4, 2.4 Hz, 1H, H_{3eq}), 1.83 (q, *J* = 12.6 Hz, 1H, H_{3ax}), 1.24 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl3) δ: 145.1 (q), 130.5 (q), 129.9 (q, *J* = 32 Hz, C7), 129.8 (Ar), 129.7 (Ar), 129.2 (Ar), 129.1 (Ar), 127.2 (q), 126.6 (q, *J* = 242 Hz, CF_3), 114.3 (d, J = 12 Hz, C6), 111.2 (d, J = 12 Hz, C8), 48.3 (CH), 44.8 (CH_2), 40.7 (CH), 22.7 (CH_3); ESIHRMS for $C_{17}H_{17}NF_3$ ($[M+H]^+$): calcd. 292.1308; found 292.1313); IR (neat, cm^{-1}) 3407 (br), 3029 (w), 2958 (w), 2875 (w), 1618 (w), 1583 (w), 1487 (m), 1452 (w), 1404 (w), 1379 (w), 1325 (s), 1240 (m), 1161 (s), 1116 (s), 1076 (s) 1015 (w), 975 (m), 917 (m), 861 (m), 811 (m), 744 (m), 719 (m), 699 (s). Signals corresponding to the *trans* isomer were not observed in the 300 MHz ^1H NMR spectrum.

***(2R,4R)*-2-Methyl-4-phenyl-7-(trifluoromethyl)-1,2,3,4-tetrahydroquinoline, 7m**



(Table 3, entry 2) Asymmetric synthesis according to general procedure **C** using 0.5 mmol of enone gave the crude product as a brown oil which was purified by column chromatography (25% DCM in petrol) to give **7m** as a colourless oil (105 mg, yield 72%, >95:<5 *cis:trans*, ee = >98%), $[\alpha]_D^{25}$ +14.89 (c = 0.47, $CHCl_3$), spectroscopically identical to the racemic material obtained previously. HPLC (CHIRALPAK® AD-RH 250 mm x 4.6 mm, detection wavelength = 210 nm, 60% to 100% MeCN/H_2O over 30 min, 1 ml/min) t_1 = 21.0 min (major), t_2 = 22.3 min (minor).

***(2RS,3SR)*-3-Methyl-2-phenyl-1,2,3,4-tetrahydroquinoline, *rac*-9**

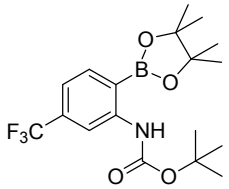


Known compound.[7] Synthesis according to general procedure **B** at 40°C using 0.23 mmol of enone gave the crude product as a black oil, which was purified by column chromatography (gradient of pure cyclohexane to 15% ethyl acetate within 15 column volumes, column pre-conditioned with 1% Et_3N) followed by an acidic ion-exchange chromatography on an Isolute SCX-cartridge (washing with dichloromethane and

[7] Guo, Q.-S.; Du, D.-M.; Xu, J. *Angew. Chem. Int. Ed.*, **2008**, *47*, 759-762.

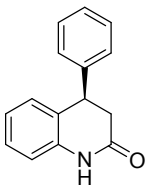
MeOH, elution with 2N NH_3 in MeOH) to give **9** as yellow oil (35 mg, yield 67%, >95:<5 *cis:trans*). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.24-7.35 (m, 5H, Ph), 6.99-7.04 (m, 2H, H_7 and H_5), 6.65 (td, J = 7.3 and 1.0 Hz, 1H, H_6), 6.55 (d, J = 7.8 Hz, 1H, H_8), 4.51 (d, J = 3.5 Hz, 1H, H_2), 4.12 (br s, 1H, NH), 2.97 (dd, J = 16.2 and 4.8 Hz, 1H, H_{4B}), 2.50 (dd, J = 16.0 and 6.7 Hz, 1H, H_{4A}), 2.26-2.35 (m, 1H, H_3), 0.82 (d, J = 6.8 Hz, 3H, 3-CH_3). UPLC/MS (BEH C18 column, I.D. 50 mm x 2.1 mm, 1.7 μm, 40 ^{o}C, 1% 10 mM NH_4CO_3 in H_2O adjusted to pH 10 with NH_4OH to 100% MeCN over 2 min) for $C_{16}H_{18}N$ ([M+H]$^+$): cald. 224.14; found 224.17; t_1 = 1.42 min. Signals corresponding to the *trans* isomer were not observed in the 400 MHz ^{1}H NMR spectrum.

***tert*-Butyl-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trifluoromethyl)phenyl)carbamate, 10** (R^3 = CF_3)



The boronate **8** (R^3 = CF_3) (3.53 g, 12.3 mmol, 1 equiv.), di-tert-butyl dicarbonate (4.03g, 18.4 mmol, 1.5 equiv.) and triethylamine (2.59 ml, 18.4 mmol, 1.5 equiv.) was heated in toluene (50 ml, *ca.* 0.25 M) for 3 h. The reaction mixture was concentrated and the residues oil was purified by flash chromatography (4% ethyl acetate/petrol) to give **10** (R^3 = CF_3) as a yellow oil which solidified after standing to give an orange solid (2.66 g, 56%). mp 80-83°C (40-60 petrol); 1H NMR (300 MHz, $CDCl_3$) δ: 8.79 (s, 1H, NH), 8.52 (s, 1H, H_6), 7.81 (d, J = 7.8 Hz, 1H), 7.21 (d, J = 8.1 Hz, 1H), 1.53 (s, 9H, ^{t}Bu), 1.37 (s, 12H, pinacol CH_3). 13C NMR (75 MHz, $CDCl_3$) δ: 153.3, 147.2, 146.1, 137.0, 134.9, 134.7 (q, J = 32 Hz), 124,4 (q, J = 271 Hz), 118.2, 114.6, 85.6, 85.1, 28.7, 25.3. ESIHRMS for $C_{18}H_{26}BNF_3O_4$ ([M+H]): calcd. 388.1907; found 388.1901; IR (neat, cm^{-1}) 3376 (w), 2978 (w), 2934 (w), 1805 (w), 1757 (w), 1727 (m), 1612 (w), 1583 (m), 1533 (m), 1476 (w), 1449 (m), 1352 (s), 1234 (m), 1143 (s), 1120 (s), 1077 (s), 1045 (s), 1024 (m), 961 (m), 901 (w), 857 (m), 839 (m), 766 (m), 750 (m), 659 (s).

(*R*)-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one, S3

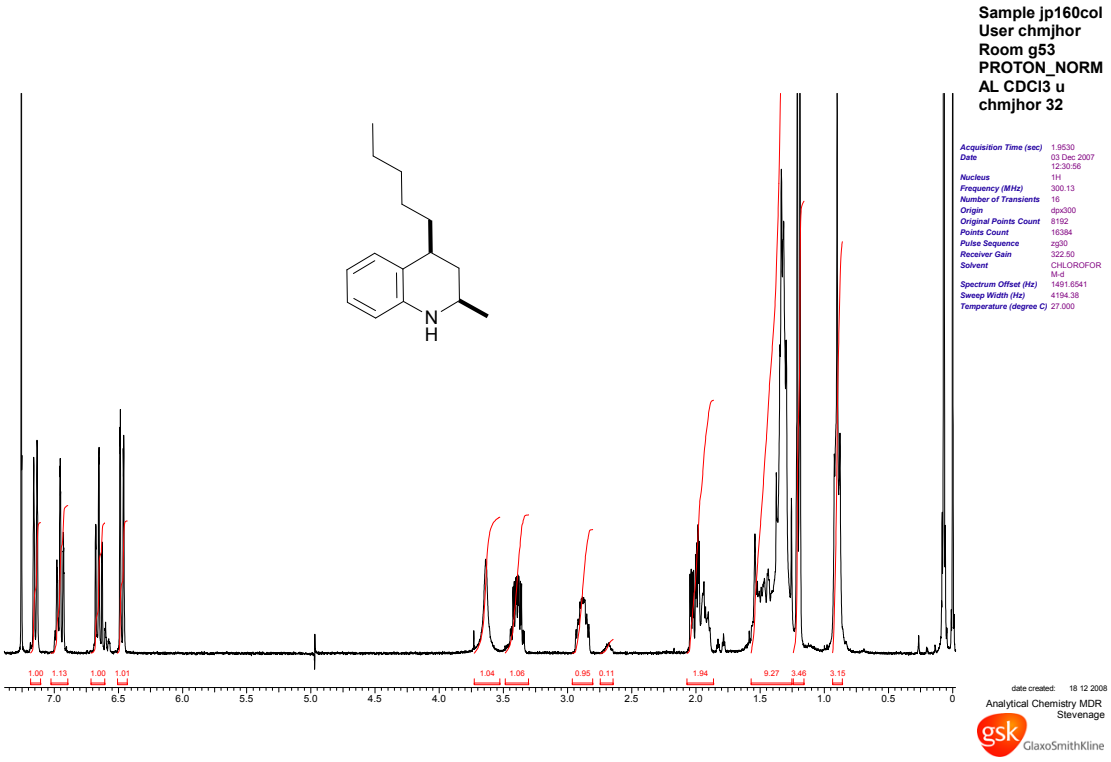


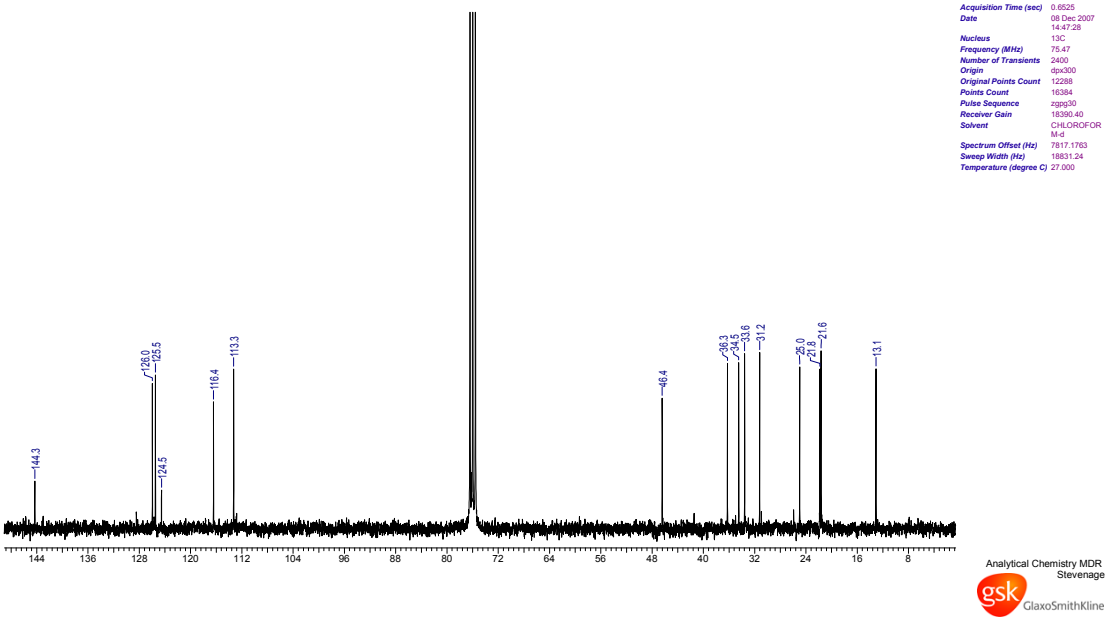
Known compound.[8] To a solution of [((*R,R,S,S*)-Duanphos)Rh(nbd)][BF_4] (20 mg, 0.03 mmol, 0.06 equiv), 10 M aq. KOH (0.1 mL, 1.00 mmol, 2.00 equiv) and *tert*-butyl (2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)carbamate (319 mg, 1.00 mmol, 2.00 equiv) in dioxane (1.4 mL, *ca.* 0.33 M), was added methyl cinnamte (82 mg, 0.50 mmol, 1.00 equiv). The reaction mixture was heated at reflux temperature for 4 hr. After cooling to rt, TFA (0.33 mL, 3.00 mmol, 6.00 equiv) was added to the mixture and then stirred for 3 days. Then the reaction mixture was concentrated, residue was dissolved in EtOAc, washed with 1 M aq. HCl twice, 2.5 M aq. KOH twice, brine, dried (Na_2SO_4), filtered and then concentrated to give the crude product which was purified by flash chromatography (3:2 petrol/EtOAc) to give **S3** as a yellow solid (18 mg, 16% yield, ee = >98%), $[\alpha]_D^{28}$ +51.8 (c = 0.05, $CHCl_3$); mp 181-182°C (DCM/MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.43 (br s, 1H, NH), 7.18-7.37 (m, 6H, Ph-H), 6.84-6.99 (m, 3H, Ph-H), 4.30 (t, *J* = 7.5 Hz, 1H, H_4), 2.92-2.96 (app. dd, *J* = 8.5, 6.0 Hz, 2H, H_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.6 (C=O), 141.5 (q), 137.1 (q), 128.9 (C_{Ph}), 128.4 (C_{Ph}), 128.0 (C_{Ph}), 127.8 (C_{Ph}), 127.2 (C_{Ph}), 126.8 (q), 123.4 (C_{Ph}), 115.6 (C_{Ph}), 42.1 (C_4), 38.4 (C_3); ESI-HRMS for $C_{15}H_{14}NO$ ($[M+H]^+$): cald. 224.1070; found 224.1061; IR (neat, cm^{-1}) 3429 (m), 1648 (s), 1485 (m), 1376, (m); HPLC: CHIRALPAK® AS-RH 250 mm x 4.6 mm, detection wavelength = 250 nm, 30% to 100% MeCN/H_2O over 30 min, 1 mL/min) t_1 = 24.1 min (minor), t_2 = 26.0 min (major). The absolute configuration was determined by comparing the optical rotation to that previously reported.[8] The racemic standard was prepared according to the literature procedure.[9]

[8] Dong, C.; Alper, H. *Tetrahedron: Asymmetry*, **2004**, *15*, 35-40.
[9] Horn, J.; Li, H. Y.; Marsden, S. P.; Nelson, A.; Shearer, R. J.; Campbell, A. J.; House, D.; Weingarten, G. G. *Tetrahedron* **2009**, *65,* 9002-9007.

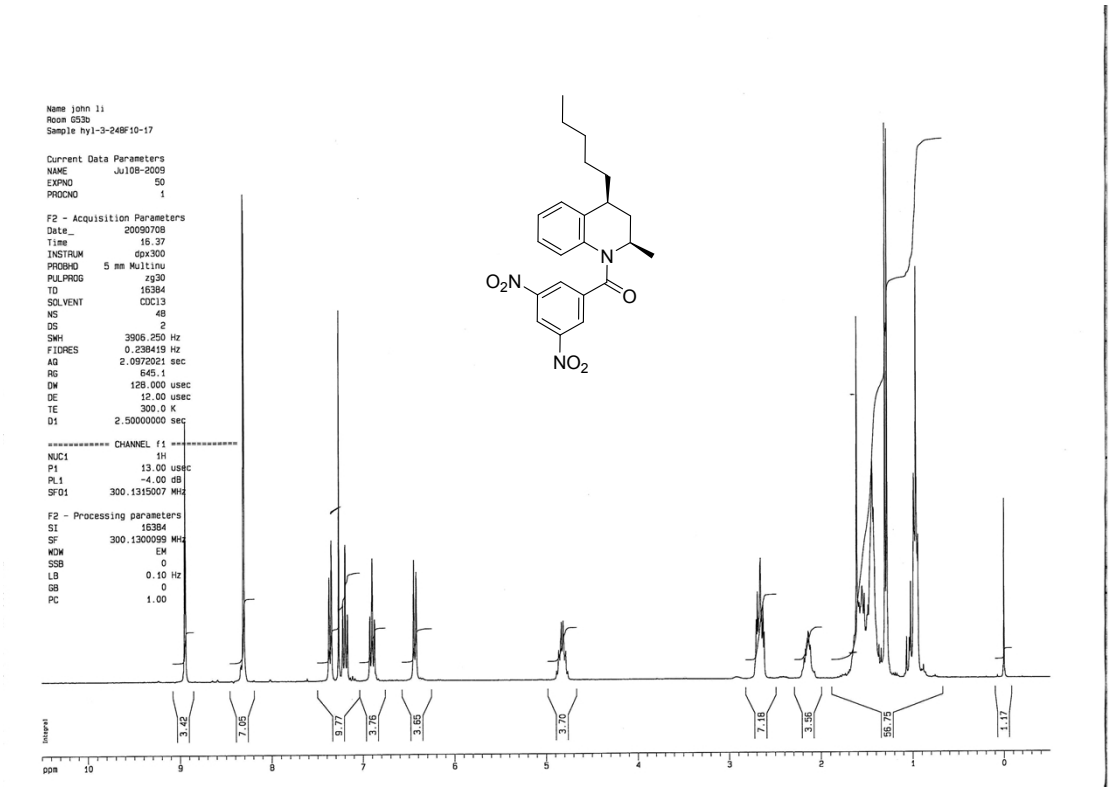
NMR and HPLC data

Compound 7a





Compound S1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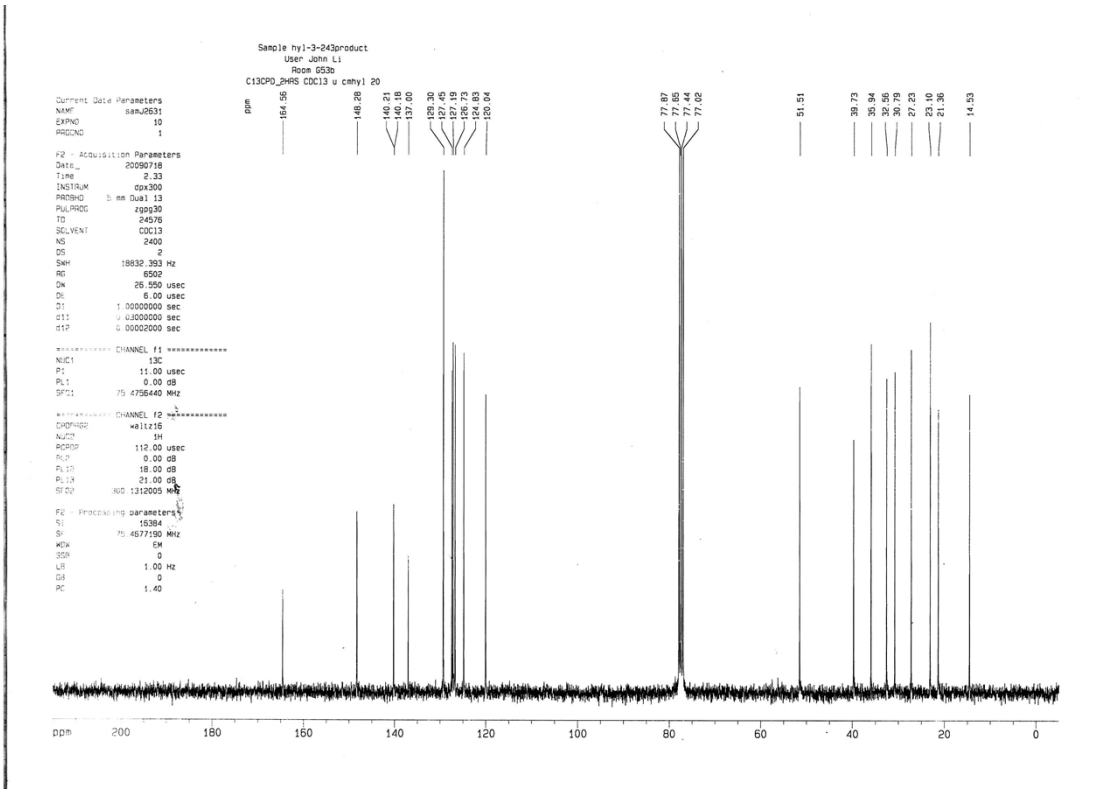
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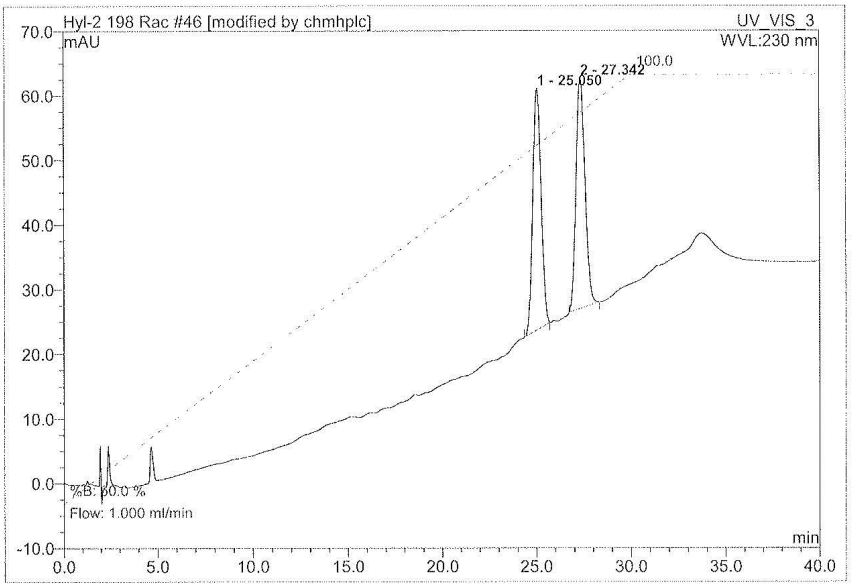
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090718
Time 2.33
INSTRUM dpx300
PROBHD 5 mm Dual 13
PULPROG zgpg30
TD 24576
SOLVENT CDCl3
NS 2400
DS 2
SWH 18832.393 Hz
RG 6502
DW 26.550 usec
DE 6.00 usec
D1 1.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
CHANNEL f1
NUC1 13C
P1 11.00 usec
PL1 0.00 dB
SFO1 75.4756440 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 112.00 usec
PL2 0.00 dB
PL12 18.00 dB
PL13 21.00 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 16384
SF 75.4577190 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
ppm
164.56
148.28
140.21
140.18
137.00
128.30
127.45
127.19
126.73
124.83
120.04
77.87
77.65
77.44
77.02
51.51
39.73
35.94
32.56
30.79
27.23
23.10
21.36
14.53
ppm

Compound *rac*-S1

46 HYL-3-234 RAC AS-RH

Sample Name:	HYL-3-234 RAC AS-RH	*Injection Volume:*	10.0
Vial Number:	BB1	*Channel:*	UV_VIS_3
Sample Type:	unknown	*Wavelength:*	n.a.
Control Program:	RP (60-100) 30 mins	*Bandwidth:*	n.a.
Quantif. Method:	Default	*Dilution Factor:*	1.0000
Recording Time:	7/7/2009 10:22	*Sample Weight:*	1.0000
Run Time (min):	40.00	*Sample Amount:*	1.0000

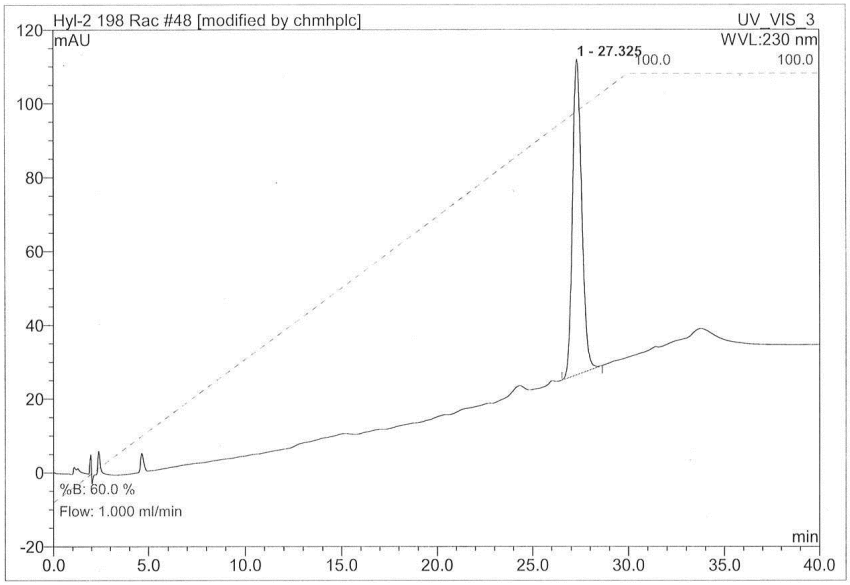


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	25.05	n.a.	37.284	19.170	49.40	n.a.	BMB*
2	27.34	n.a.	35.576	19.633	50.60	n.a.	BMB*
Total:			72.860	38.802	100.00	0.000	

Compound S1 (Table 3, entry 1)

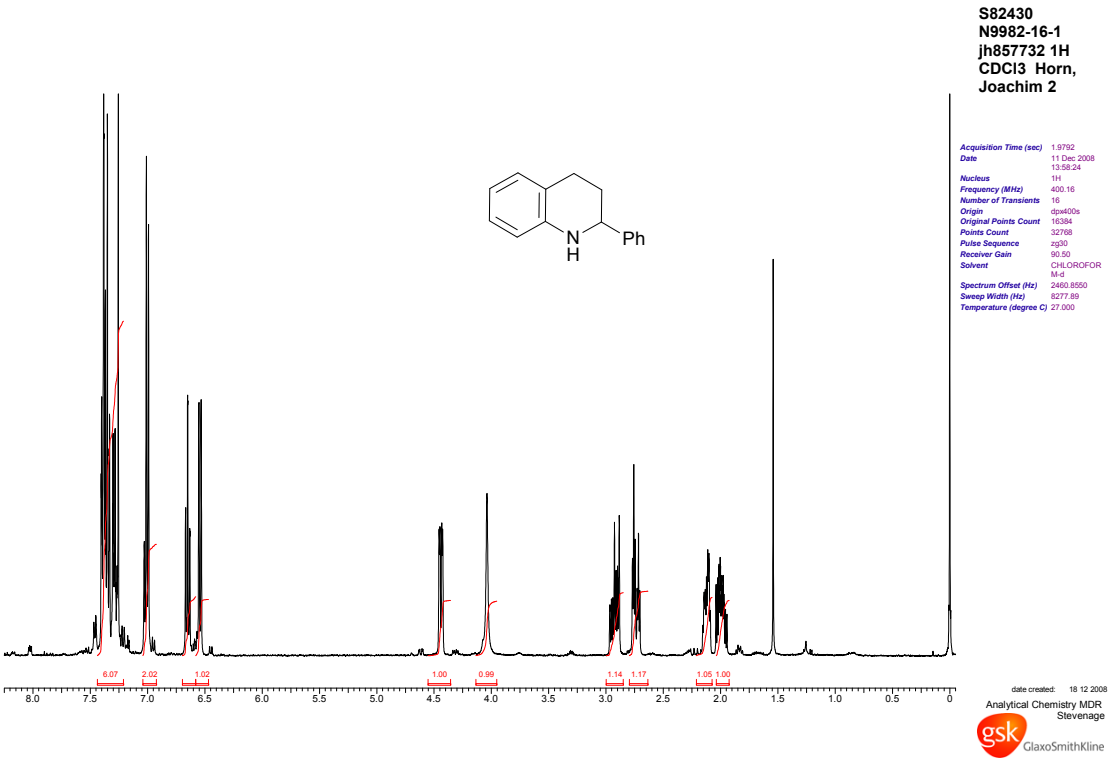
48 HYL-3-243 Chiral AS-RH

Sample Name:	**HYL-3-243 Chiral AS-RH**	*Injection Volume:*	**10.0**
Vial Number:	**BB2**	*Channel:*	**UV_VIS_3**
Sample Type:	**unknown**	*Wavelength:*	**n.a.**
Control Program:	**RP (60-100) 30 mins**	*Bandwidth:*	**n.a.**
Quantif. Method:	**Default**	*Dilution Factor:*	**1.0000**
Recording Time:	**9/7/2009 8:29**	*Sample Weight:*	**1.0000**
Run Time (min):	**40.00**	*Sample Amount:*	**1.0000**

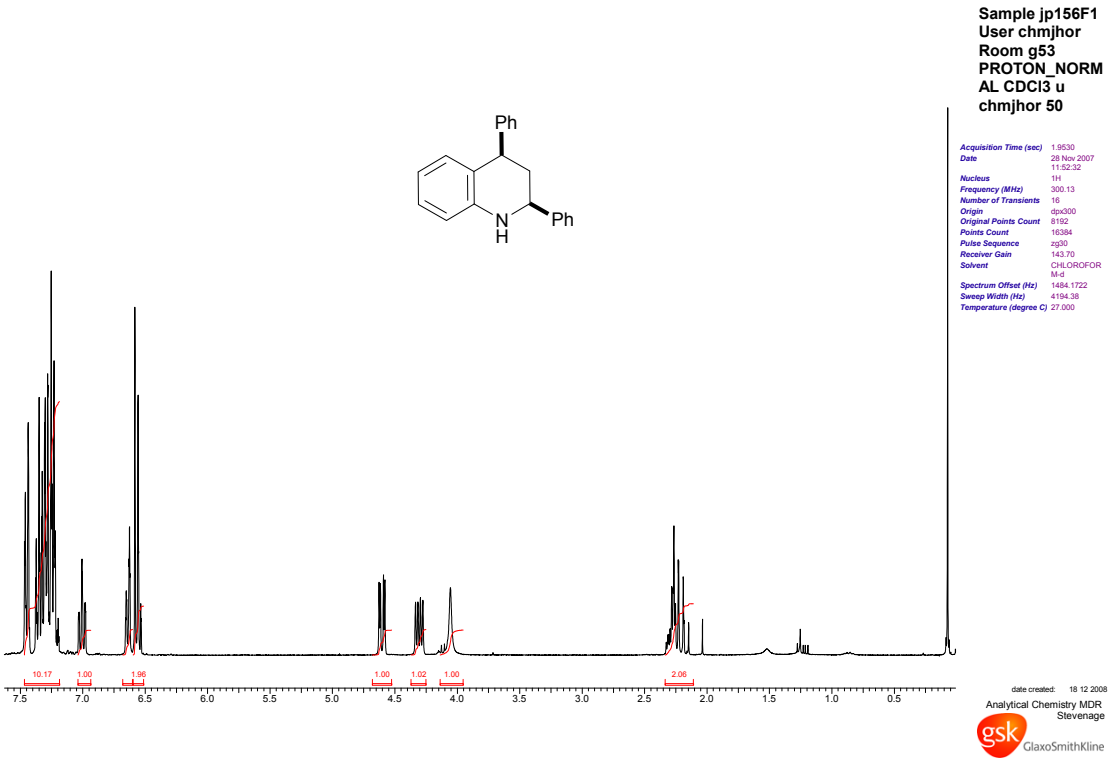


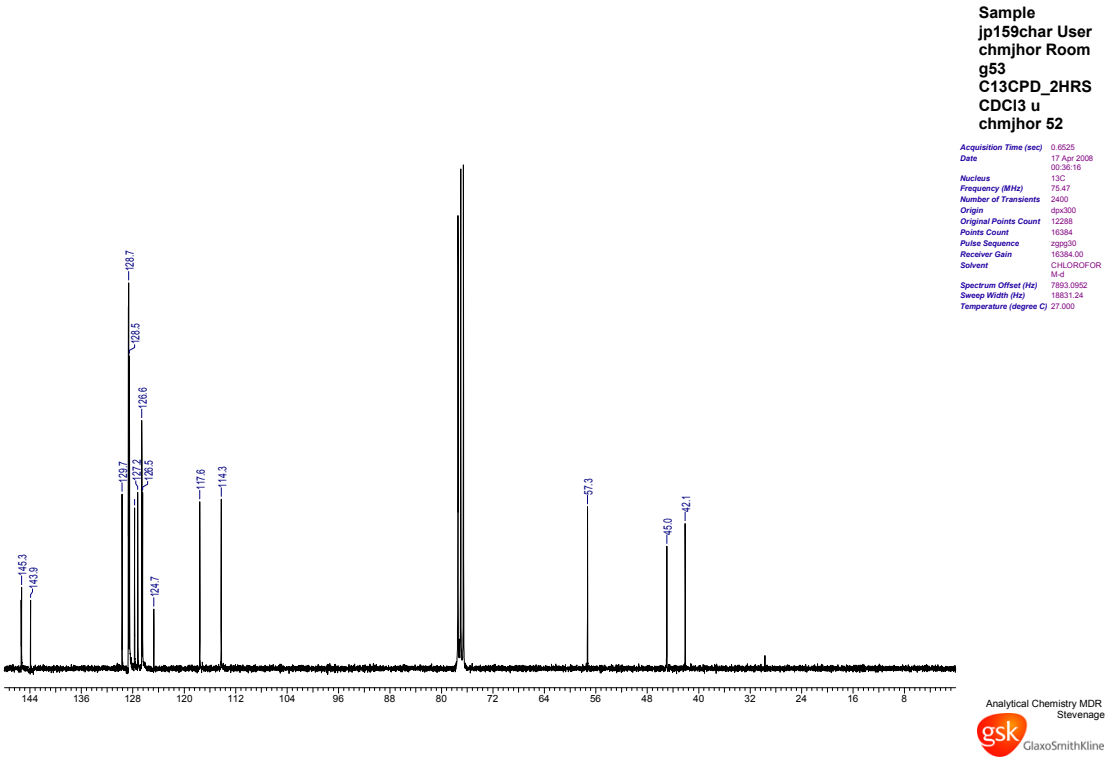
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	27.33	n.a.	85.334	47.691	100.00	n.a.	BMB
Total:			85.334	47.691	100.00	0.000	

Compound 7b


S82430
N9982-16-1
jh857732 1H
CDCl3 Horn, Joachim 2
Acquisition Time (sec) 1.9792
Date 11 Dec 2008 13:58:24
Nucleus 1H
Frequency (MHz) 400.16
Number of Transients 16
Origin dpx400s
Original Points Count 16384
Points Count 32768
Pulse Sequence zg30
Receiver Gain 90.50
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 2460.8550
Sweep Width (Hz) 8277.89
Temperature (degree C) 27.000
N
H
Ph
6.07
2.02
1.02
1.00
0.99
1.14
1.17
1.05
1.00
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
date created: 18 12 2008
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline

Compound 7c

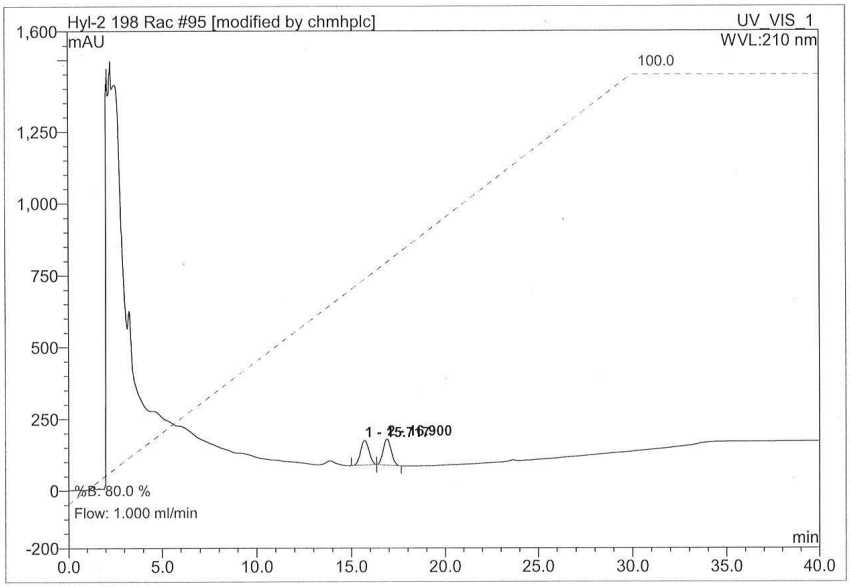

Ph
N
H
Ph
Sample jp156F1
User chmjhor
Room g53
PROTON_NORMAL CDCl3 u
chmjhor 50
Acquisition Time (sec) 1.9530
Date 28 Nov 2007 11:52:32
Nucleus 1H
Frequency (MHz) 300.13
Number of Transients 16
Origin dpx300
Original Points Count 8192
Points Count 16384
Pulse Sequence zg30
Receiver Gain 143.70
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 1484.1722
Sweep Width (Hz) 4194.38
Temperature (degree C) 27.000
10.17
1.00
1.96
1.00
1.02
1.00
2.06
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
date created: 18 12 2008
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline


Sample jp159char User chmjhor Room g53
C13CPD_2HRS CDCl3 u
chmjhor 52
Acquisition Time (sec) 0.6525
Date 17 Apr 2008 00:36:16
Nucleus 13C
Frequency (MHz) 75.47
Number of Transients 2400
Origin dpx300
Original Points Count 12288
Points Count 16384
Pulse Sequence zgpg30
Receiver Gain 16384.00
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 7893.0952
Sweep Width (Hz) 18831.24
Temperature (degree C) 27.000
146.3
143.9
129.7
128.5
128.6
127.2
126.5
124.7
117.6
114.3
57.3
45.0
42.1
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline

Compound *rac*-7c (resolved on AS-RH column)

95 HYL-3-267 RAC AS-RH

Sample Name:	**HYL-3-267 RAC AS-RH**	*Injection Volume:*	**20.0**
Vial Number:	**RC2**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**n.a.**
Control Program:	**RP (80-100) 30 mins**	*Bandwidth:*	**n.a.**
Quantif. Method:	**Default**	*Dilution Factor:*	**1.0000**
Recording Time:	**7/9/2009 12:12**	*Sample Weight:*	**1.0000**
Run Time (min):	**40.00**	*Sample Amount:*	**1.0000**

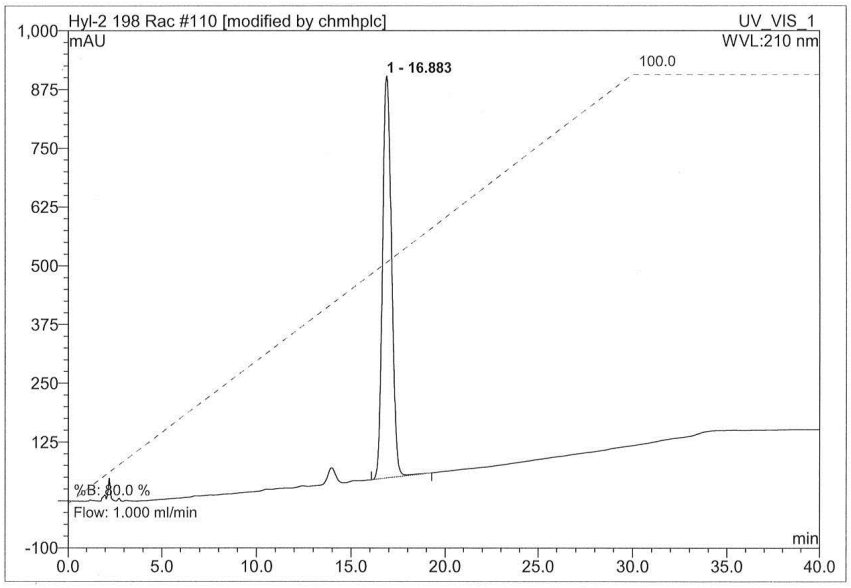


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	15.72	n.a.	85.957	44.264	49.66	n.a.	BMb
2	16.90	n.a.	90.843	44.871	50.34	n.a.	bMB
Total:			176.800	89.136	100.00	0.000	

Compound 7c (resolved on AS-RH column) (Table, entry 2)

110 HYL-3-276 chiral AS-RH

Sample Name:	**HYL-3-276 chiral AS-RH**	*Injection Volume:*	**20.0**
Vial Number:	**RA4**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**n.a.**
Control Program:	**RP (80-100) 30 mins**	*Bandwidth:*	**n.a.**
Quantif. Method:	**Default**	*Dilution Factor:*	**1.0000**
Recording Time:	**22/9/2009 14:33**	*Sample Weight:*	**1.0000**
Run Time (min):	**40.00**	*Sample Amount:*	**1.0000**

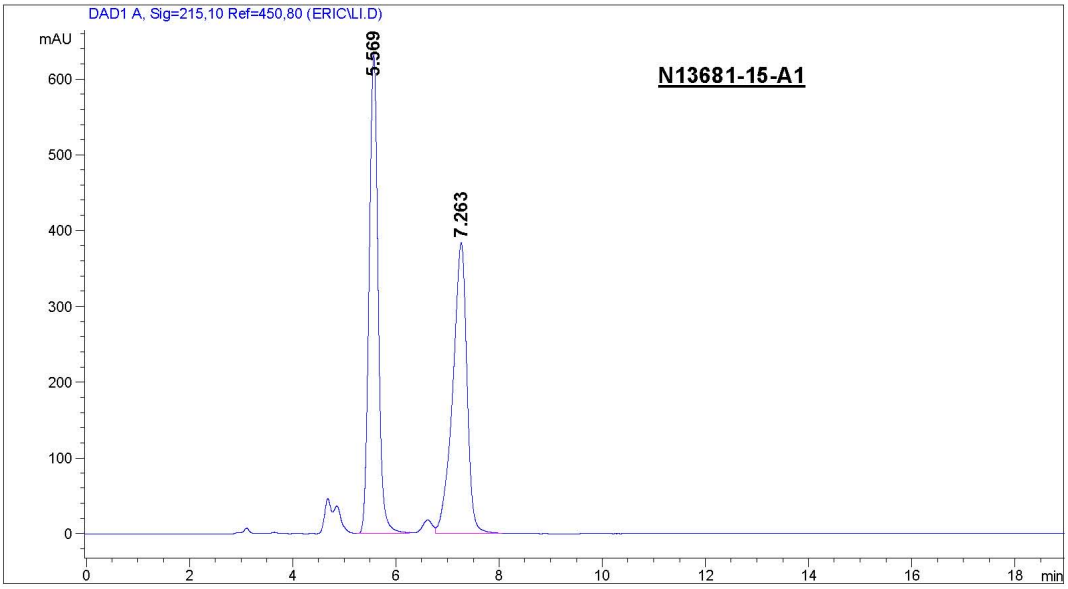


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	16.88	n.a.	855.401	474.277	100.00	n.a.	BMB
Total:			855.401	474.277	100.00	0.000	

Compound *rac*-7c (resolved on AD column)

Data File K:\HOYTEN\HPCHEM\1\DATA\ERIC\LI.D
Sample Name: N13681-15-A1

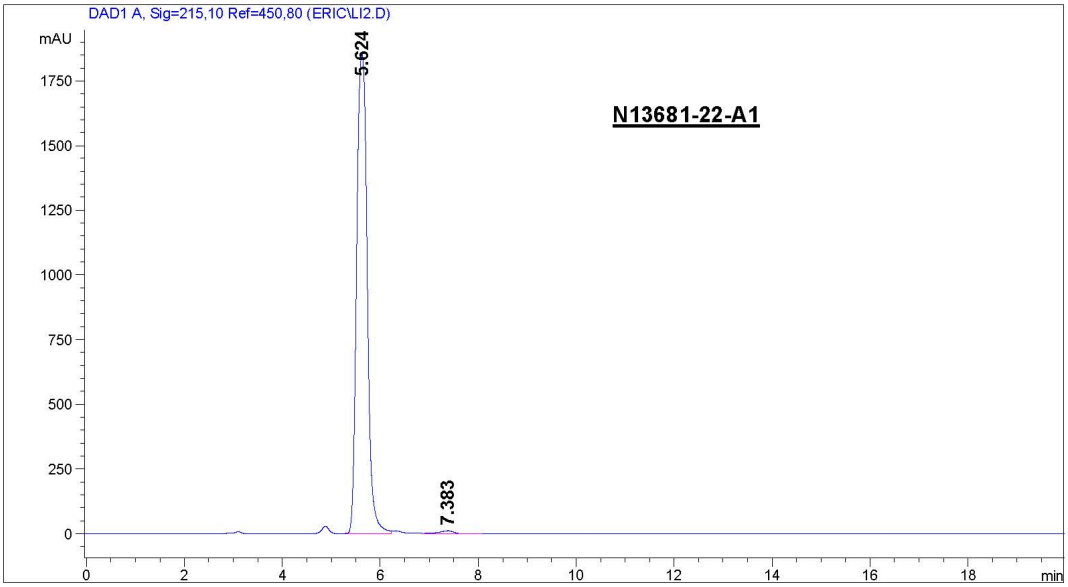
```
    ======================================================================
    Acq. Operator   : ERIC HORTENSE
    Acq. Instrument : HOYTEN                          Location : Vial 1
    Injection Date  : 09/11/2009 10:06:09
                                                     Inj Volume : 5 µl
    Acq. Method     : K:\HOYTEN\HOYTENS METHODS\CHIMETH1.M
    Last changed    : 09/11/2009 10:01:32  by ERIC HORTENSE
                      (modified after loading)
    Analysis Method : K:\HOYTEN\HOYTENS METHODS\CHIMETH1.M
    Last changed    : 09/11/2009 11:41:35  by ERIC HORTENSE
                      (modified after loading)
    Method Info     : Chiral Method 1.  Isocratic Analysis at 1.000 ml/min.

    Sample Info     : 25cm Chiralpak AD
                      ,col.no.ADOOCE-A1074,10%ETOH/C7,1ml/min,wavelength 215n
                      m,RT
```




```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=215,10 Ref=450,80

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   5.569 VB    0.1875 7669.32080  632.49847  51.1385
       2   7.263 VB    0.2849 7327.82910  383.52939  48.8615

    Totals :                  1.49971e4  1016.02786

    ======================================================================
                              *** End of Report ***
```

Compound 7c (resolved on AD column) (Table, entry 8)

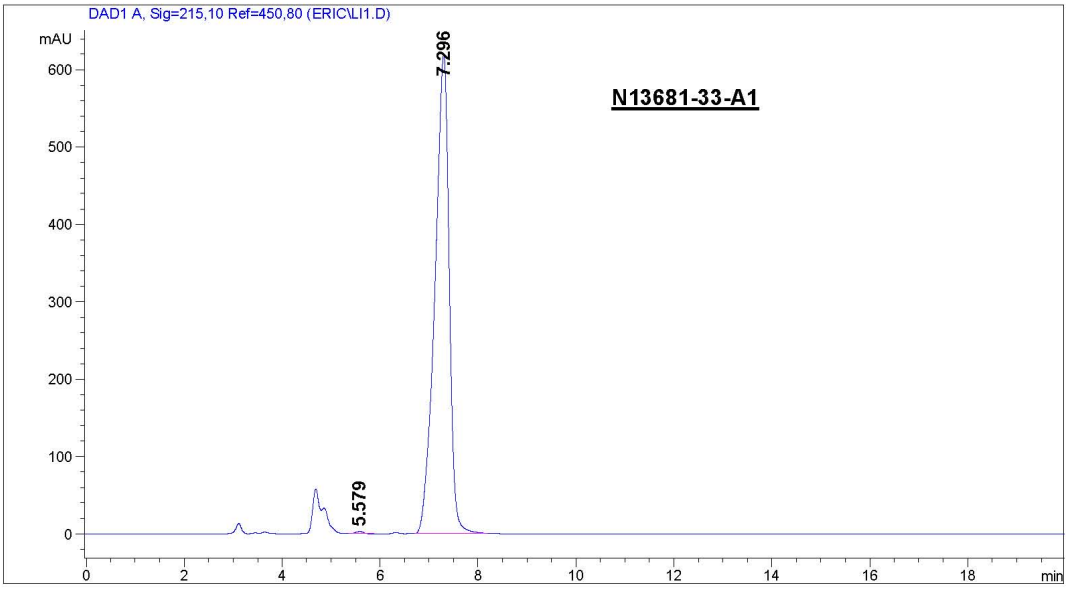
```
Data File K:\HOYTEN\HPCHEM\1\DATA\ERIC\LI2.D
Sample Name: N13681-22-A1

=====================================================================
Acq. Operator   : ERIC HORTENSE
Acq. Instrument : HOYTEN                        Location : Vial 1
Injection Date  : 09/11/2009 11:43:12
                                               Inj Volume : 5 µl
Method          : K:\HOYTEN\HOYTENS METHODS\CHIMETH1.M
Last changed    : 09/11/2009 11:41:35  by ERIC HORTENSE
                  (modified after loading)
Method Info     : Chiral Method 1.  Isocratic Analysis at 1.000 ml/min.

Sample Info     : 25cm Chiralpak AD
                  ,col.no.ADOOCE-A1074,10%ETOH/C7,1ml/min,wavelength 215n
                  m,RT
```




```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=215,10 Ref=450,80

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.624 BV    0.2405 2.77303e4  1853.98340  99.0244
   2   7.383 BB    0.3235  273.20352   12.18699   0.9756

Totals :                  2.80035e4  1866.17039


=====================================================================
                        *** End of Report ***
```

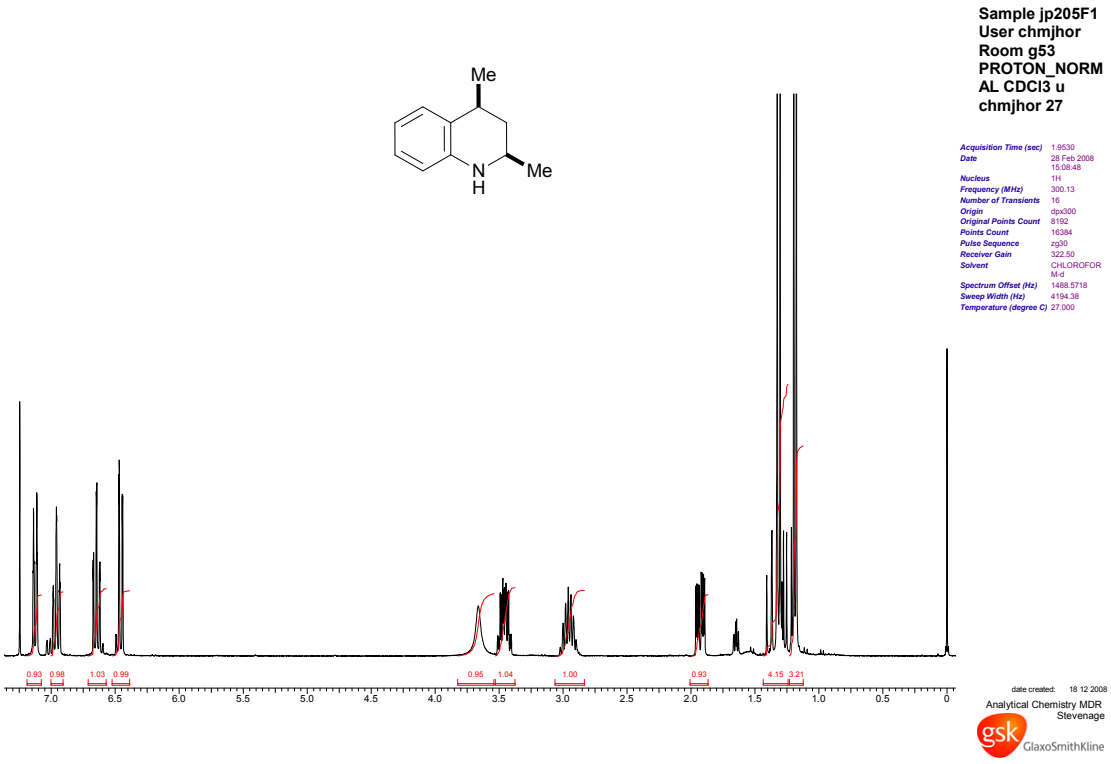
Compound *ent*-7c (resolved on AD column)

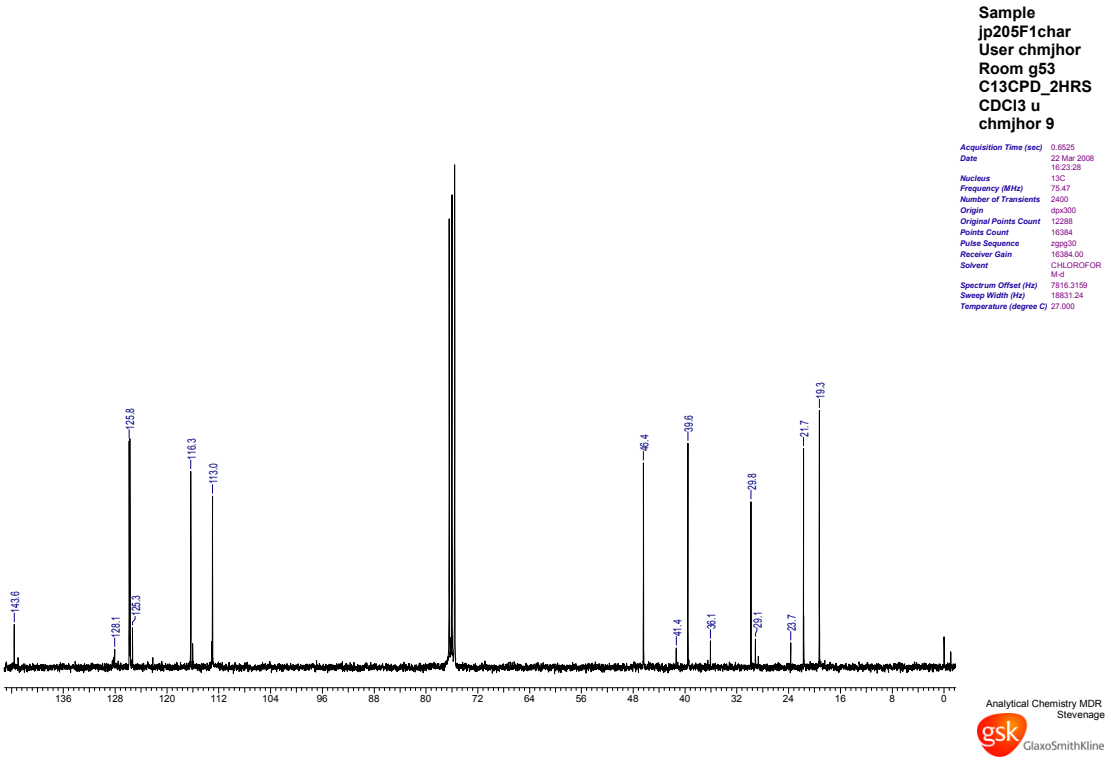
```
Data File K:\HOYTEN\HPCHEM\1\DATA\ERIC\LI1.D
Sample Name: N13681-33-A1

    ======================================================================
    Acq. Operator   : ERIC HORTENSE
    Acq. Instrument : HOYTEN                          Location : Vial 1
    Injection Date  : 09/11/2009 11:00:14
                                                     Inj Volume : 10 µl
    Acq. Method     : K:\HOYTEN\HOYTENS METHODS\CHIMETH1.M
    Last changed    : 09/11/2009 10:59:00  by ERIC HORTENSE
                      (modified after loading)
    Analysis Method : K:\HOYTEN\HOYTENS METHODS\CHIMETH1.M
    Last changed    : 09/11/2009 11:41:35  by ERIC HORTENSE
                      (modified after loading)
    Method Info     : Chiral Method 1.  Isocratic Analysis at 1.000 ml/min.

    Sample Info     : 25cm Chiralpak AD
                      ,col.no.ADOOCE-A1074,10%ETOH/C7,1ml/min,wavelength 215n
                      m,RT
```



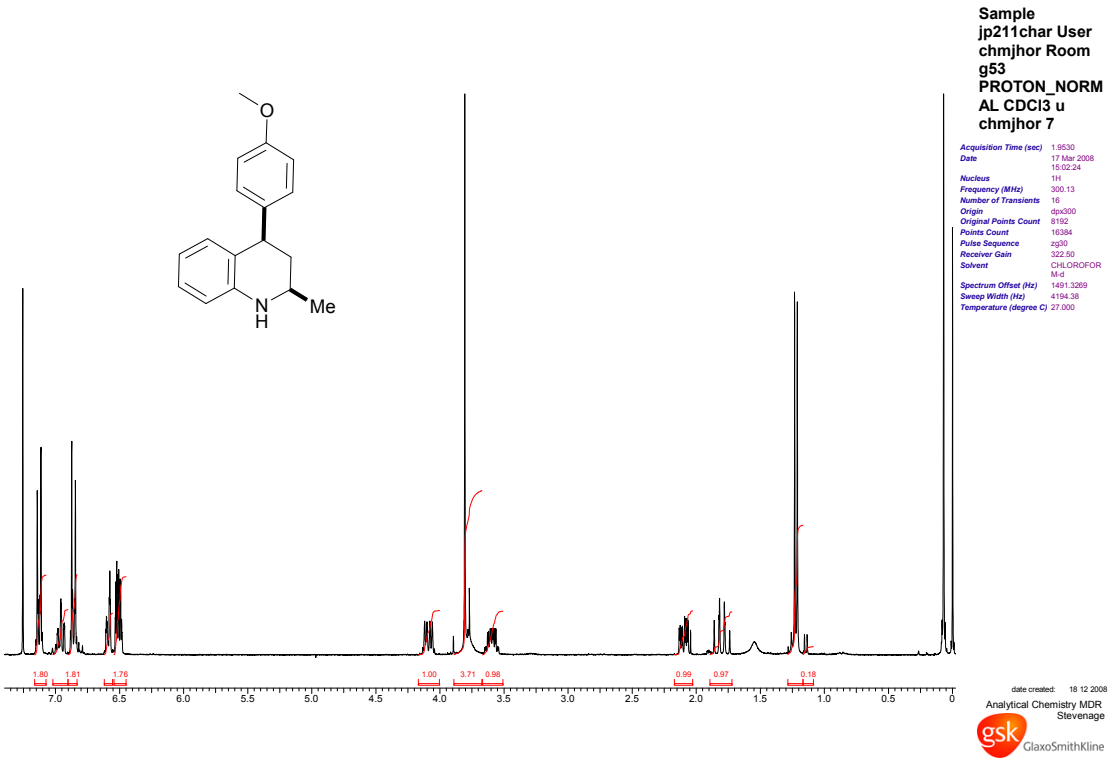

```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=215,10 Ref=450,80

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]    [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   5.579 BB    0.1861   37.63638    3.09016   0.2993
       2   7.296 BB    0.3001 1.25372e4   619.63239  99.7007

    Totals :                   1.25748e4   622.72254


    ======================================================================
                              *** End of Report ***

HOYTEN 09/11/2009 12:28:12  ERIC HORTENSE                          Page   1 of 1
```

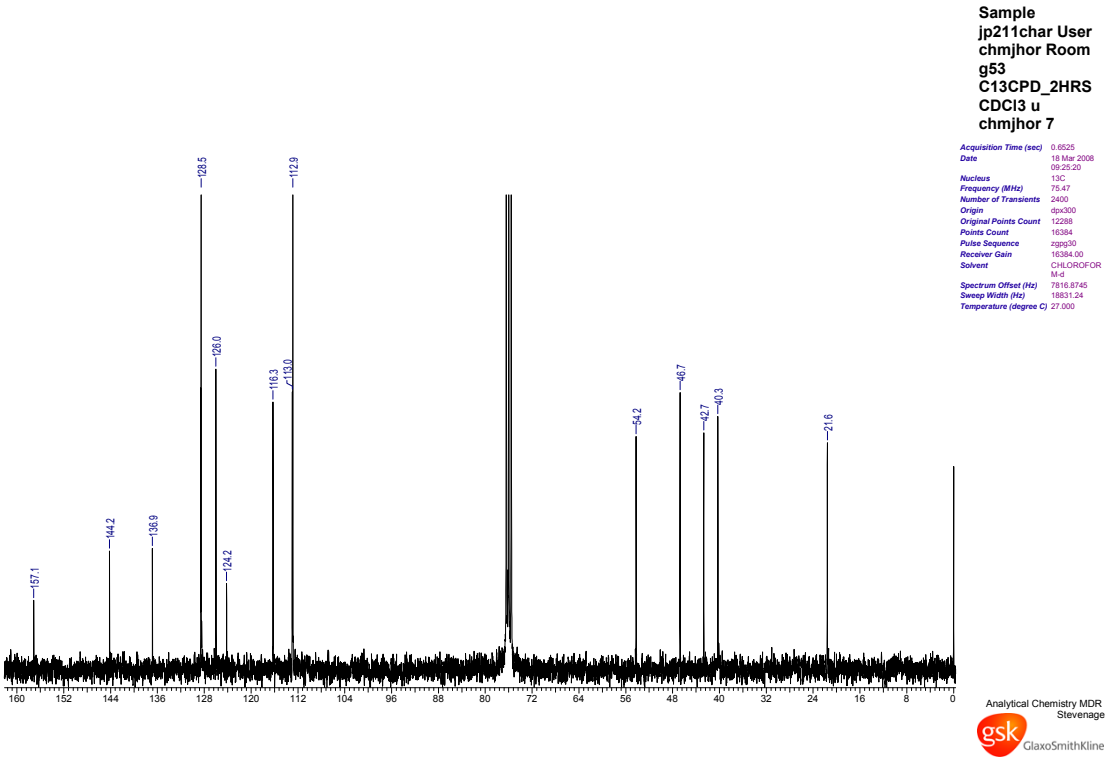
Compound 7d


Me
N
H
Me
Sample jp205F1
User chmjhor
Room g53
PROTON_NORMAL CDCl3 u
chmjhor 27
Acquisition Time (sec) 1.9530
Date 28 Feb 2008 15:08:48
Nucleus 1H
Frequency (MHz) 300.13
Number of Transients 16
Origin dpx300
Original Points Count 8192
Points Count 16384
Pulse Sequence zg30
Receiver Gain 322.50
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 1488.5718
Sweep Width (Hz) 4194.38
Temperature (degree C) 27.000
0.93 0.98 1.03 0.99 0.95 1.04 1.00 0.93 4.15 3.21
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
date created: 18 12 2008
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline

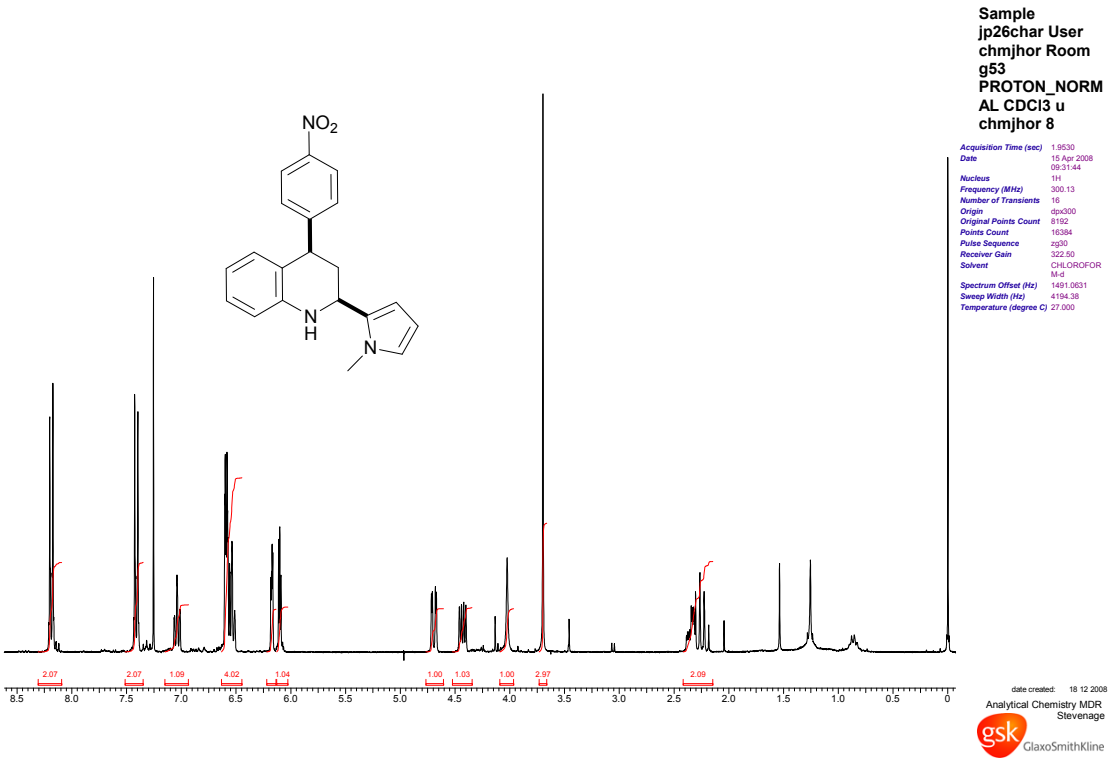

Sample jp205F1char
User chmjhor
Room g53
C13CPD_2HRS CDCl3 u
chmjhor 9
Acquisition Time (sec) 0.6525
Date 22 Mar 2008 16:23:28
Nucleus 13C
Frequency (MHz) 75.47
Number of Transients 2400
Origin dpx300
Original Points Count 12288
Points Count 16384
Pulse Sequence zgpg30
Receiver Gain 16384.00
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 7816.3159
Sweep Width (Hz) 18831.24
Temperature (degree C) 27.000
143.6
128.1
125.8
125.3
116.3
113.0
46.4
41.4
39.6
36.1
29.8
29.1
23.7
21.7
19.3
136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline

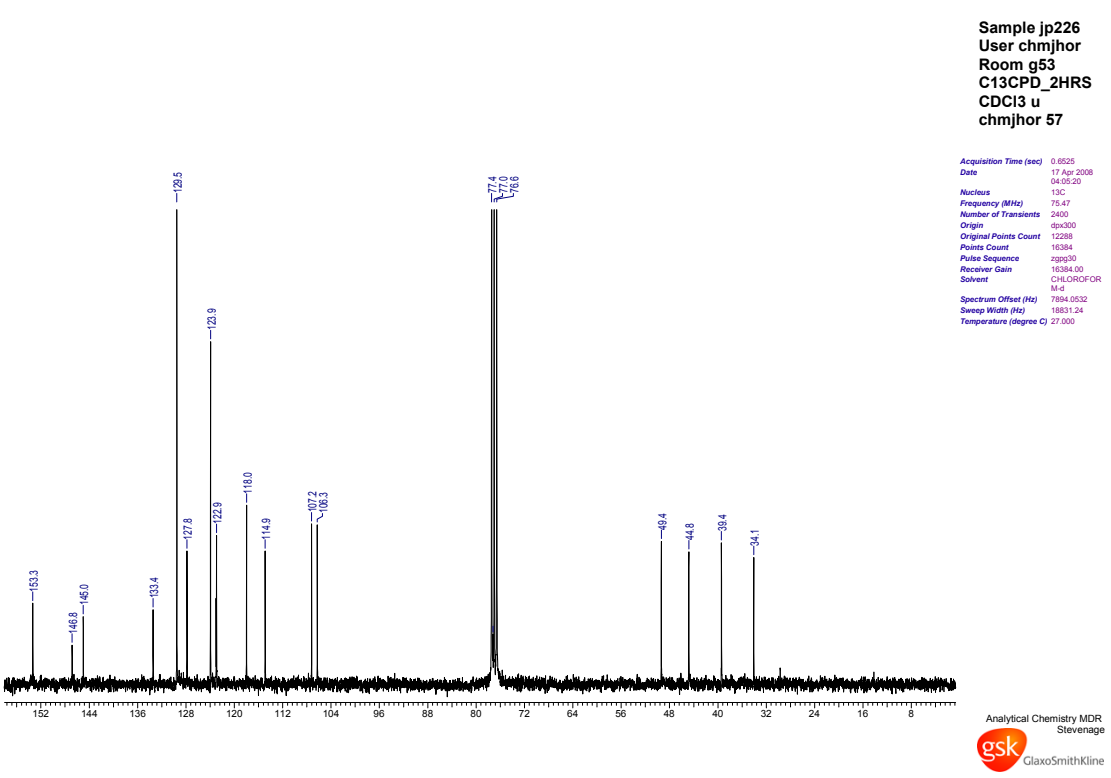
Compound 7e


Sample
jp211char User
chmjhor Room
g53
PROTON_NORM
AL CDCl3 u
chmjhor 7
Acquisition Time (sec) 1.9530
Date 17 Mar 2008 15:02:24
Nucleus 1H
Frequency (MHz) 300.13
Number of Transients 16
Origin dpx300
Original Points Count 8192
Points Count 16384
Pulse Sequence zg30
Receiver Gain 322.50
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 1491.3269
Sweep Width (Hz) 4194.38
Temperature (degree C) 27.000
O
N
H
Me
1.80 1.81 1.76 1.00 3.71 0.98 0.99 0.97 0.18
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
date created: 18 12 2008
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline


Sample
jp211char User
chmjhor Room
g53
C13CPD_2HRS
CDCl3 u
chmjhor 7
Acquisition Time (sec) 0.6525
Date 18 Mar 2008 09:25:20
Nucleus 13C
Frequency (MHz) 75.47
Number of Transients 2400
Origin dpx300
Original Points Count 12288
Points Count 16384
Pulse Sequence zgpg30
Receiver Gain 16384.00
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 7816.8745
Sweep Width (Hz) 18831.24
Temperature (degree C) 27.000
128.5
112.9
126.0
116.3
113.0
46.7
54.2
42.7
40.3
21.6
144.2
136.9
124.2
157.1
160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline

Compound 7f


Sample jp26char User chmjhor Room g53 PROTON_NORMAL CDCl3 u chmjhor 8
Acquisition Time (sec) 1.9530
Date 15 Apr 2008 09:31:44
Nucleus 1H
Frequency (MHz) 300.13
Number of Transients 16
Origin dpx300
Original Points Count 8192
Points Count 16384
Pulse Sequence zg30
Receiver Gain 322.50
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 1491.0631
Sweep Width (Hz) 4194.38
Temperature (degree C) 27.000
NO2
N
H
N
2.07
2.07
1.09
4.02
1.04
1.00
1.03
1.00
2.97
2.09
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
date created: 18 12 2008
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline


Sample jp226 User chmjhor Room g53 C13CPD_2HRS CDCl3 u chmjhor 57
Acquisition Time (sec) 0.6525
Date 17 Apr 2008 04:05:20
Nucleus 13C
Frequency (MHz) 75.47
Number of Transients 2400
Origin dpx300
Original Points Count 12288
Points Count 16384
Pulse Sequence zgpg30
Receiver Gain 16384.00
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 7894.0532
Sweep Width (Hz) 18831.24
Temperature (degree C) 27.000
153.3
146.8
145.0
133.4
129.5
127.8
122.9
121.9
118.0
114.9
107.2
106.3
77.4
77.0
76.6
49.4
44.8
39.4
34.1
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
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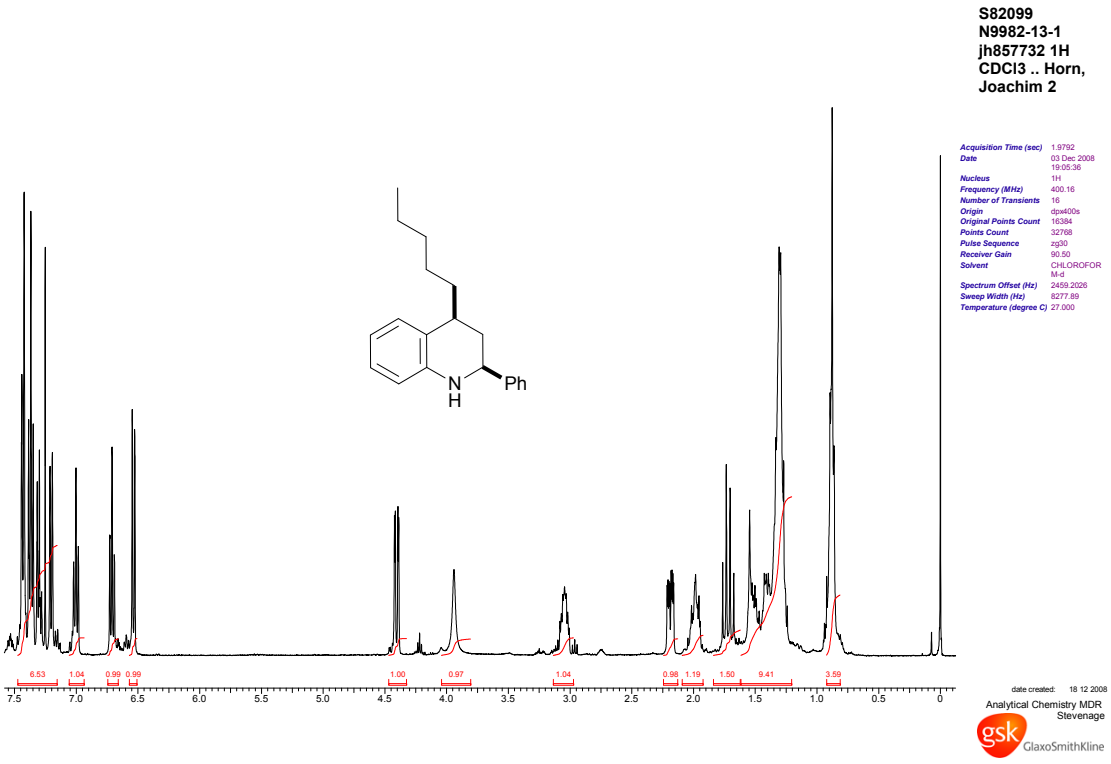
Stevenage
GlaxoSmithKline

Compound 7g


S82099
N9982-13-1
jh857732 1H
CDCl3 .. Horn, Joachim 2
Acquisition Time (sec) 1.9792
Date 03 Dec 2008 19:05:36
Nucleus 1H
Frequency (MHz) 400.16
Number of Transients 16
Origin dpx400s
Original Points Count 16384
Points Count 32768
Pulse Sequence zg30
Receiver Gain 90.50
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 2459.2026
Sweep Width (Hz) 8277.69
Temperature (degree C) 27.000
N
H
Ph
6.53 1.04 0.99 0.99 1.00 0.97 1.04 0.98 1.19 1.50 9.41 3.59
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
date created: 18 12 2008
Analytical Chemistry MDR
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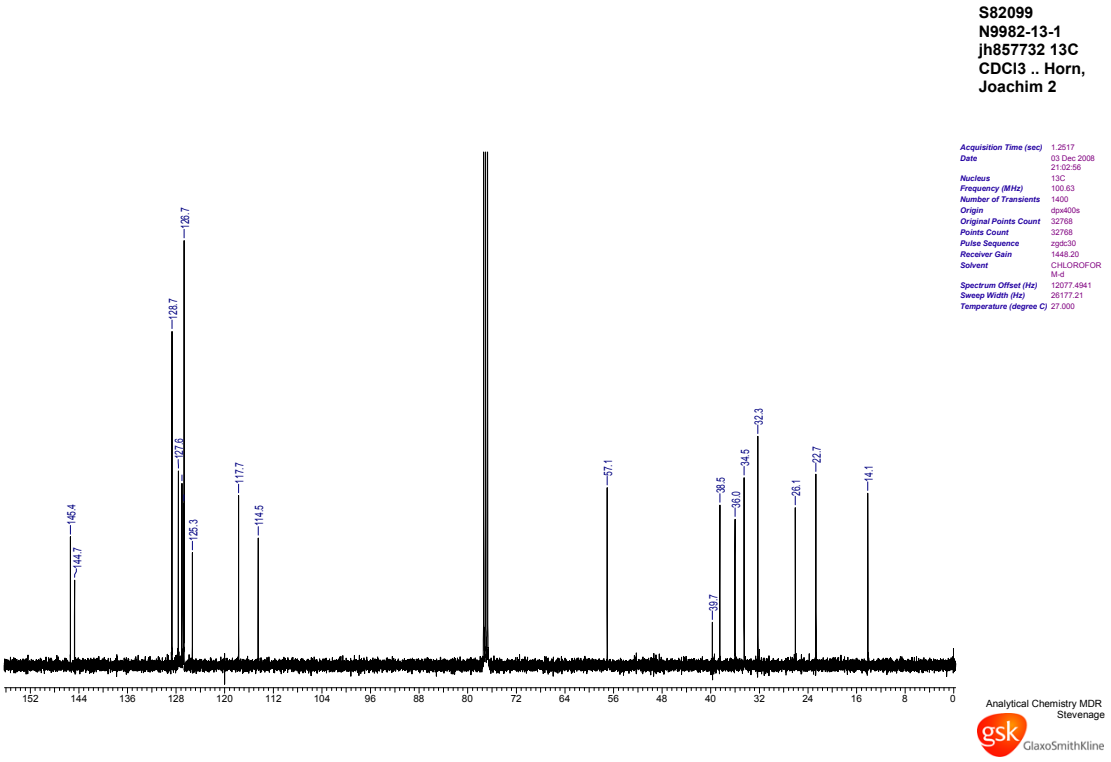
S82099
N9982-13-1
jh857732 13C
CDCl3 .. Horn, Joachim 2
Acquisition Time (sec) 1.2517
Date 03 Dec 2008 21:02:56
Nucleus 13C
Frequency (MHz) 100.63
Number of Transients 1400
Origin dpx400s
Original Points Count 32768
Points Count 32768
Pulse Sequence zgdc30
Receiver Gain 1448.20
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 12077.4941
Sweep Width (Hz) 26177.21
Temperature (degree C) 27.000
145.4
144.7
128.7
126.7
127.6
125.3
117.7
114.5
57.1
39.7
38.5
36.0
34.5
32.3
26.1
22.7
14.1
152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Analytical Chemistry MDR
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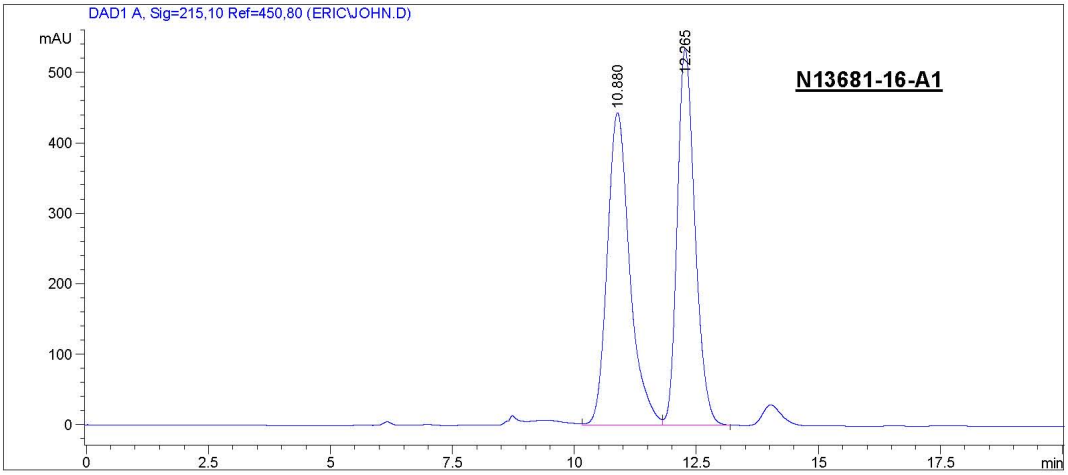
GlaxoSmithKline

Compound *rac*-7g

```
Data File K:\HPCHEM\1\DATA\ERIC\JOHN.D
Sample Name: N13681-16-A1
    ========================================================================
    Acq. Operator   : ERIC HORTENSE
    Acq. Instrument : LALANDRY                        Location : Vial 1
    Injection Date  : 19/11/2009 14:38:32
                                                     Inj Volume : 5 µl
    Method          : C:\CHEM32\1\METHODS\ERIC1.M
    Last changed    : 19/11/2009 14:20:34  by ERIC HORTENSE
                      (modified after loading)
    Sample Info     : 25cm Chiralcel OD-H ,col.no.ODHOCE-CG100,1%IETOH/C7,0.5
                      ml/min,wavelength 215nm,RT


    ========================================================================
```

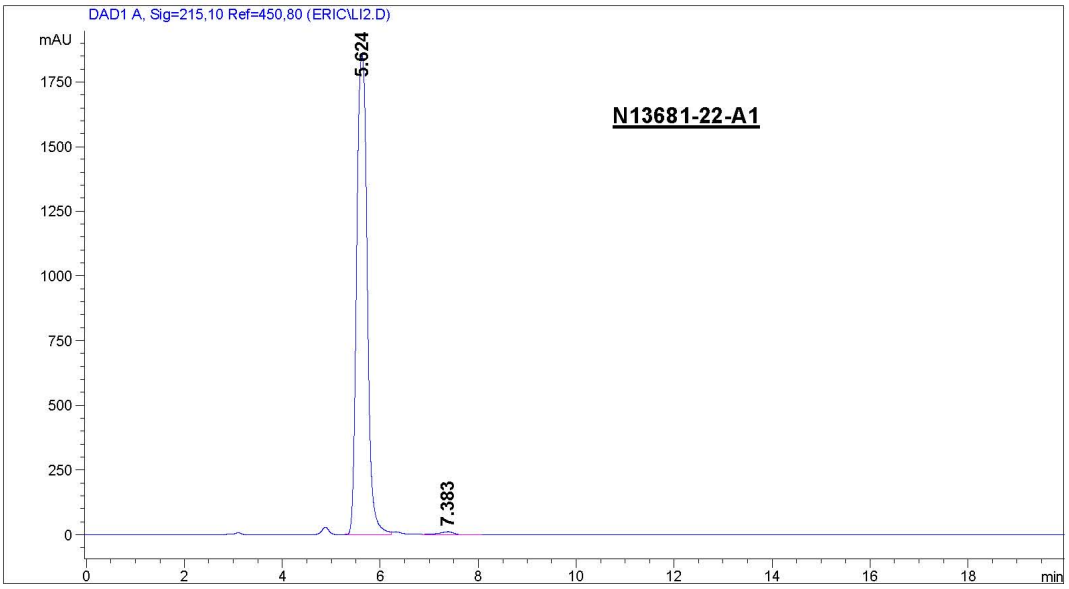



```
    ========================================================================
                              Area Percent Report
    ========================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=215,10 Ref=450,80

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  10.880 VV    0.4873 1.42736e4   443.70905  51.3587
       2  12.265 VB    0.3869 1.35184e4   534.73755  48.6413

    Totals :                  2.77920e4   978.44659


    ========================================================================
                              *** End of Report ***
```

Compound 7g (Table, entry 9)

Data File K:\HOYTEN\HPCHEM\1\DATA\ERIC\LI2.D
Sample Name: N13681-22-A1

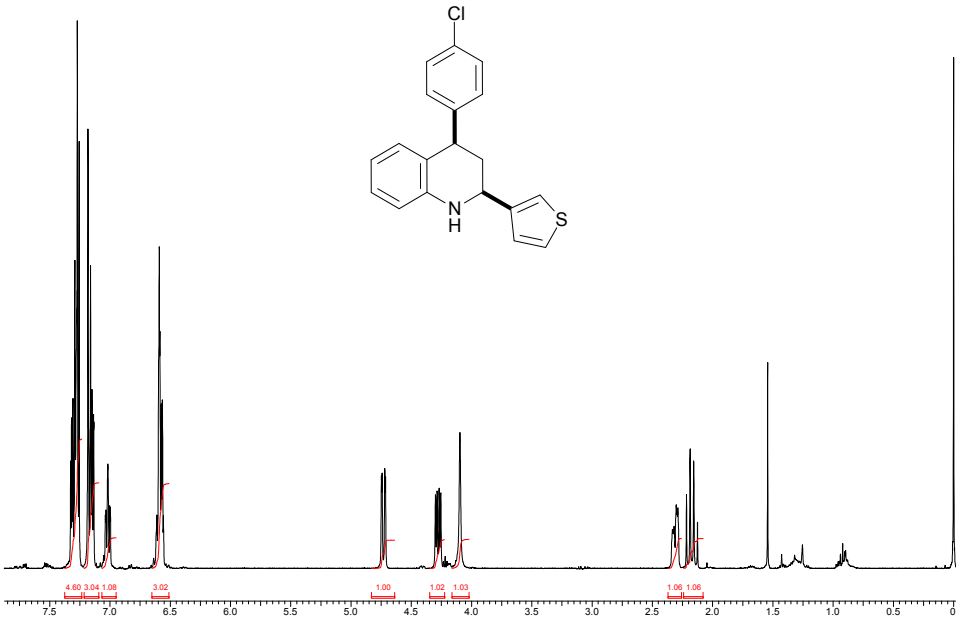
```
=====================================================================
Acq. Operator   : ERIC HORTENSE
Acq. Instrument : HOYTEN                          Location : Vial 1
Injection Date  : 09/11/2009 11:43:12
                                                  Inj Volume : 5 µl
Method          : K:\HOYTEN\HOYTENS METHODS\CHIMETH1.M
Last changed    : 09/11/2009 11:41:35  by ERIC HORTENSE
                  (modified after loading)
Method Info     : Chiral Method 1.  Isocratic Analysis at 1.000 ml/min.

Sample Info     : 25cm Chiralpak AD
                  ,col.no.ADOOCE-A1074,10%ETOH/C7,1ml/min,wavelength 215n
                  m,RT
```




```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=215,10 Ref=450,80

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.624 BV    0.2405 2.77303e4  1853.98340  99.0244
   2   7.383 BB    0.3235  273.20352   12.18699   0.9756

Totals :                  2.80035e4  1866.17039


=====================================================================
                        *** End of Report ***
```

Compound 7h

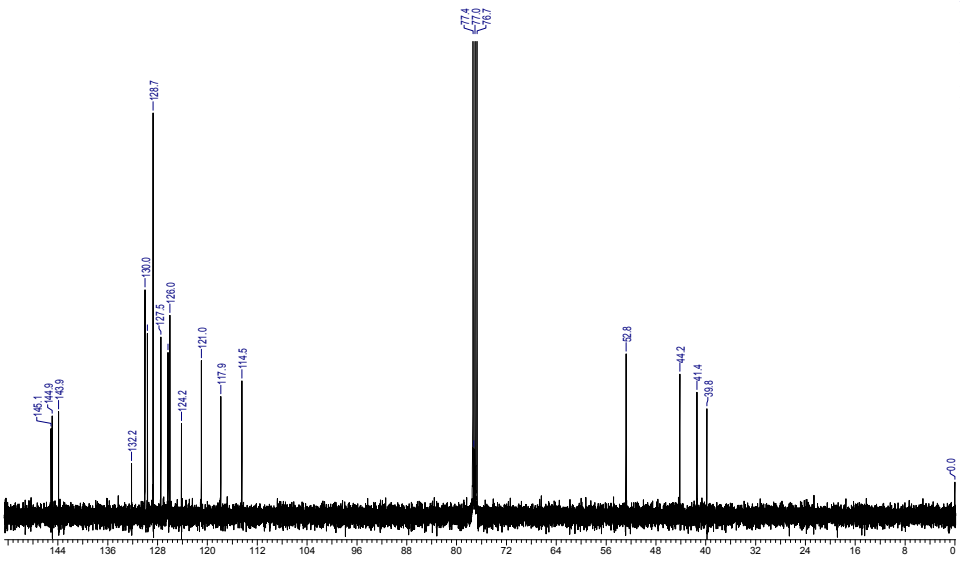
S82029
N9982-14-1
jh857732 1H
CDCl3 Horn, Joachim 2



Acquisition Time (sec)	1.9792
Date	01 Dec 2008 11:12:00
Nucleus	1H
Frequency (MHz)	400.16
Number of Transients	16
Origin	dpx400s
Original Points Count	16384
Points Count	32768
Pulse Sequence	zg30
Receiver Gain	90.50
Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	2461.1191
Sweep Width (Hz)	8277.89
Temperature (degree C)	27.000

date created: 18 12 2008
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline

S82017
N9982-14-1
jh857732 13C
CDCl3 .. Horn, Joachim 2



Acquisition Time (sec)	1.2517
Date	29 Nov 2008 05:52:00
Nucleus	13C
Frequency (MHz)	100.63
Number of Transients	1400
Origin	dpx400s
Original Points Count	32768
Points Count	32768
Pulse Sequence	zgdc30
Receiver Gain	1290.20
Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	12076.0039
Sweep Width (Hz)	26177.21
Temperature (degree C)	27.000

Analytical Chemistry MDR
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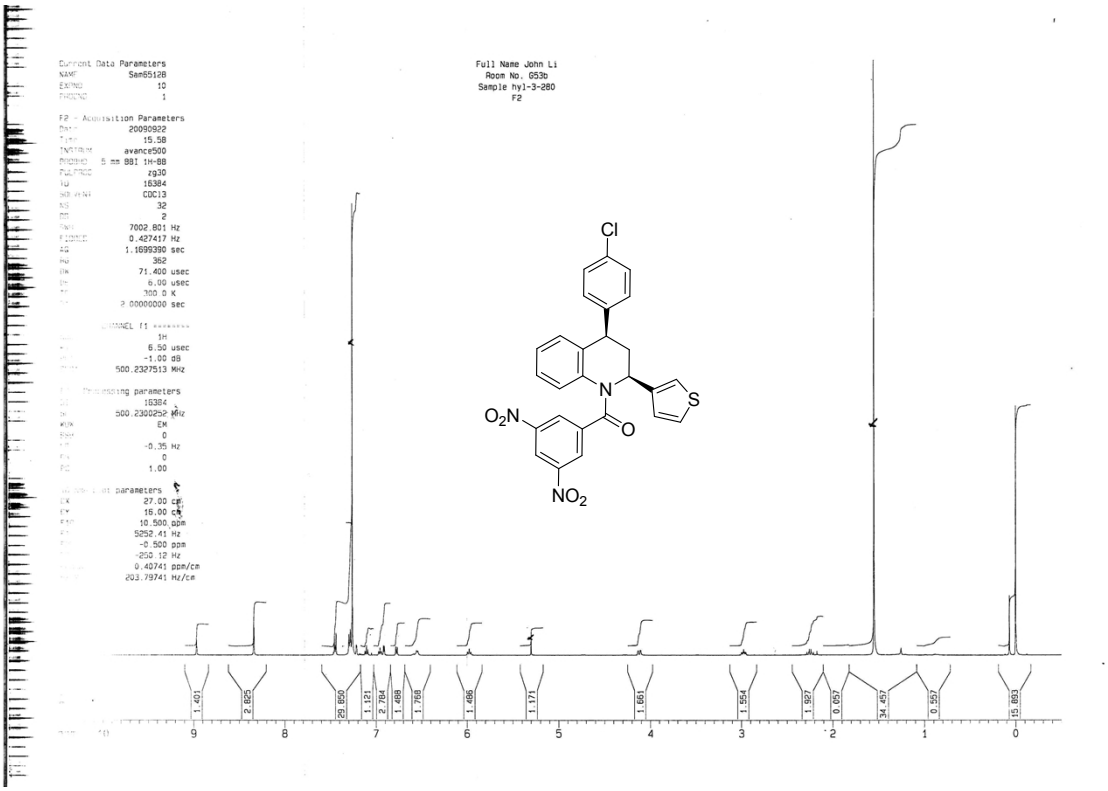
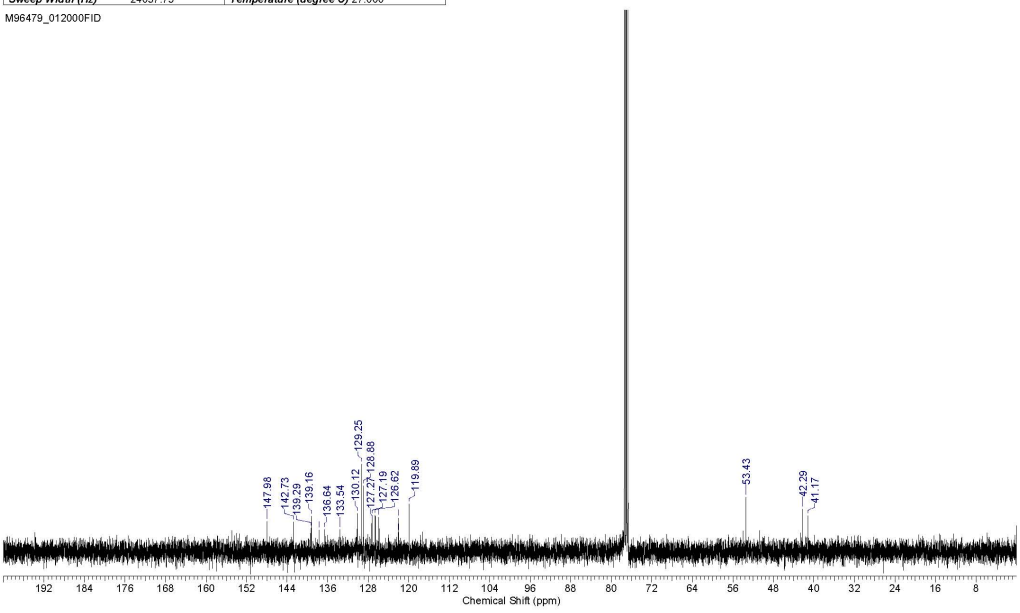
GlaxoSmithKline

Compound S2



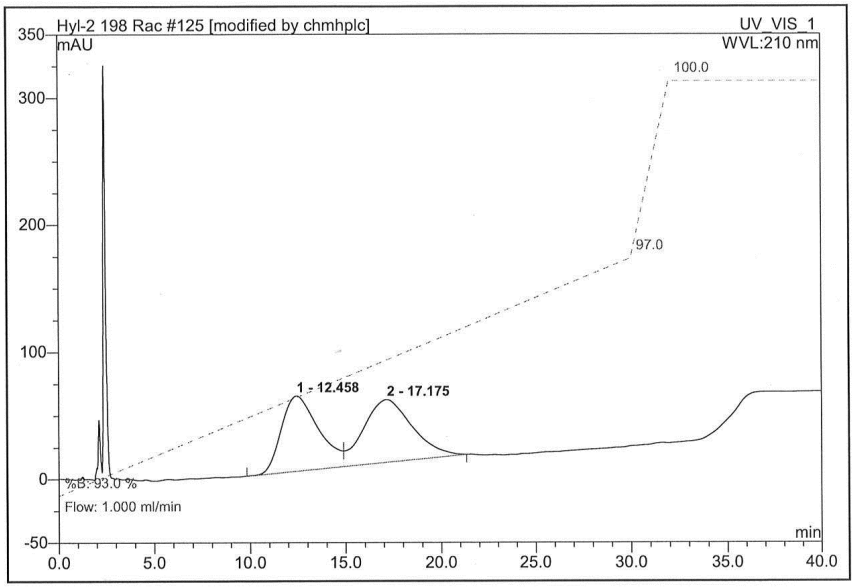
Acquisition Time (sec)	1.3631	***Comment***	M96479 N22359-52-R1 13C CDCl3 hyl90376 Li, Ho Y ...			***Date***	11 Feb 2012 01:57:20
Date Stamp	11 Feb 2012 01:57:20			***File Name***	C:\DOCUMENTS AND SETTINGS\HYL90376\LOCAL SETTINGS\TEMP\M96479\12\FID		
Frequency (MHz)	100.62	***Nucleus***	13C	***Number of Transients***	1024	***Origin***	M400
Original Points Count	32768	***Owner***	chemist	***Points Count***	32768	***Pulse Sequence***	zgpg30
Receiver Gain	118.17	***SW(cyclical) (Hz)***	24038.46	***Solvent***	CHLOROFORM-d	***Spectrum Offset (Hz)***	10062.5391
Sweep Width (Hz)	24037.73	***Temperature (degree C)***	27.000				



Compound *rac*-S2

125 HYL-3-278 rac AD-RH

Sample Name:	**HYL-3-278 rac AD-RH**	*Injection Volume:*	**20.0**
Vial Number:	**RA5**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**n.a.**
Control Program:	**RP (93-97) 30 mins**	*Bandwidth:*	**n.a.**
Quantif. Method:	**Default**	*Dilution Factor:*	**1.0000**
Recording Time:	**24/9/2009 15:06**	*Sample Weight:*	**1.0000**
Run Time (min):	**40.00**	*Sample Amount:*	**1.0000**

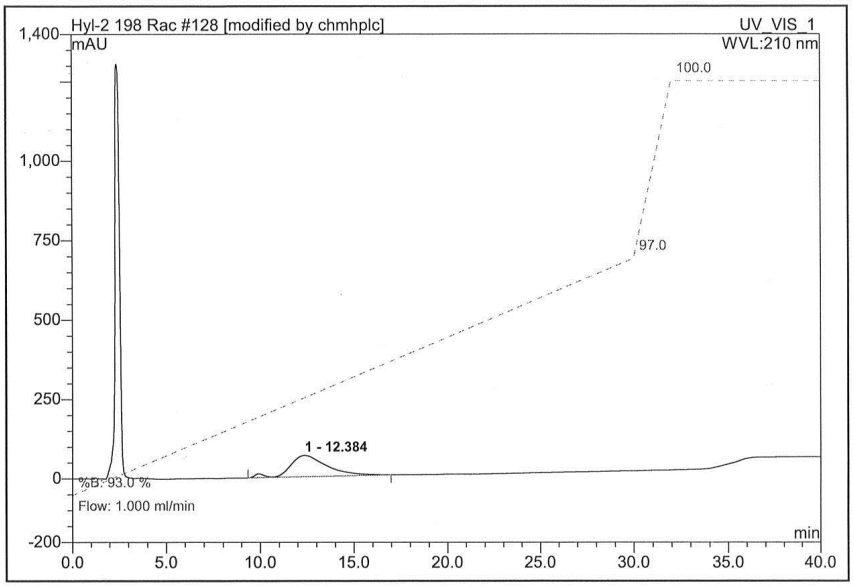


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	12.46	n.a.	59.182	134.350	47.84	n.a.	BM
2	17.18	n.a.	49.362	146.495	52.16	n.a.	MB
Total:			108.544	280.845	100.00	0.000	

Compound S2 (Table, entry 3)

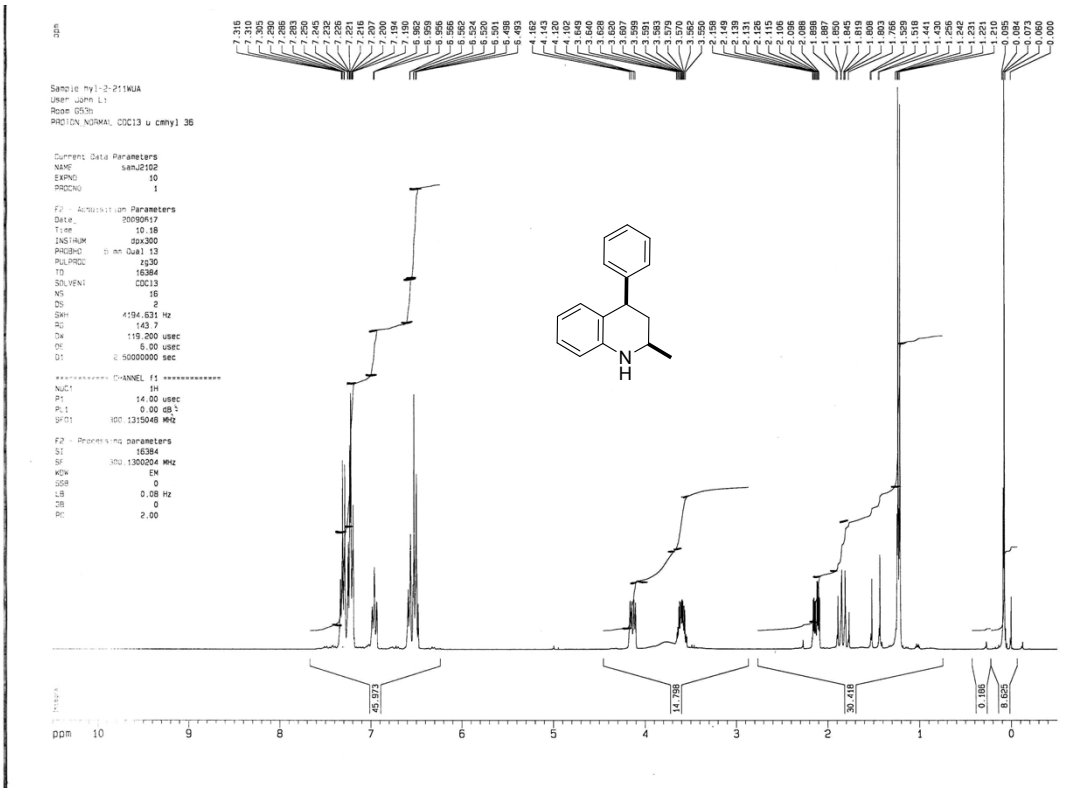
128 HYL-3-280 chiral AD-RH

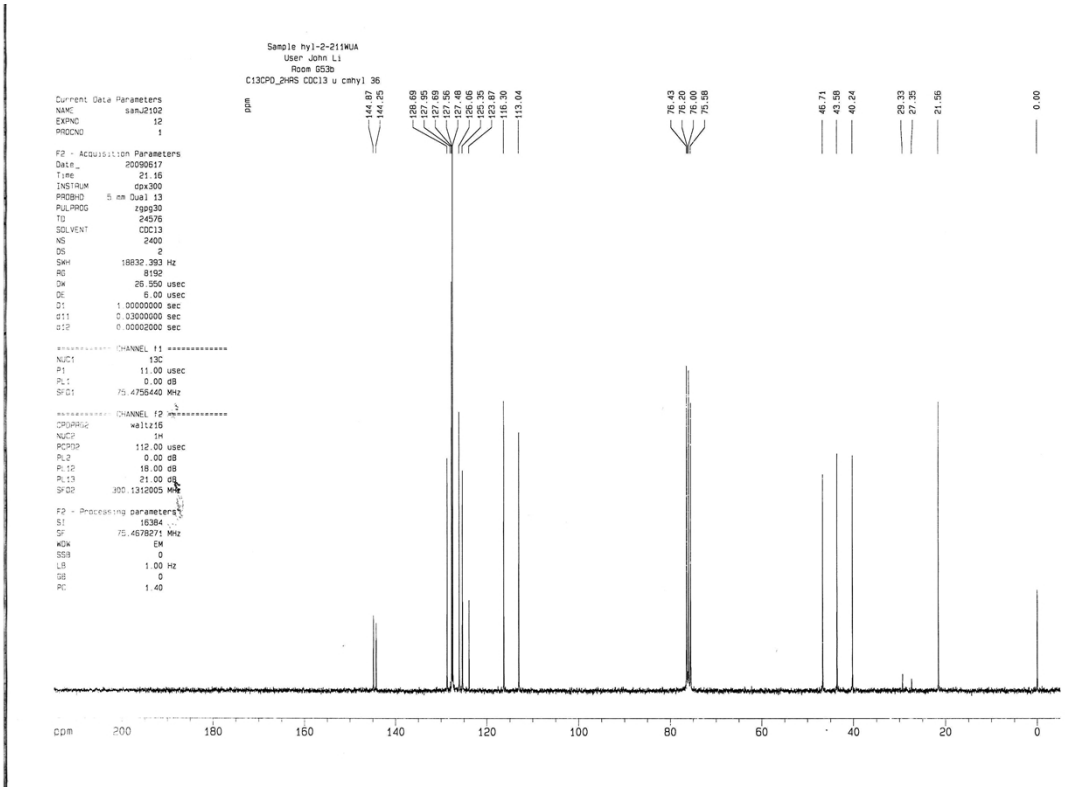
Sample Name:	**HYL-3-280 chiral AD-RH**	*Injection Volume:*	**50.0**
Vial Number:	**RA3**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**n.a.**
Control Program:	**RP (93-97) 30 mins**	*Bandwidth:*	**n.a.**
Quantif. Method:	**Default**	*Dilution Factor:*	**1.0000**
Recording Time:	**25/9/2009 9:57**	*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	12.38	n.a.	66.951	155.723	100.00	n.a.	BMB*
Total:			66.951	155.723	100.00	0.000	

Compound 7i

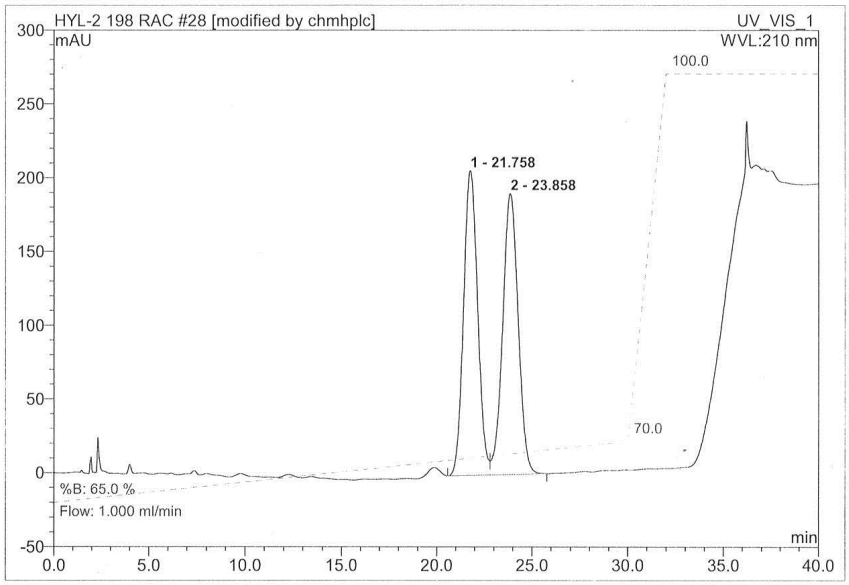

Sample hyl-2-211WUA
User John Li
Room G53b
PROTON_NORMAL CDCl3 u cmhyl 36
Current Data Parameters
NAME samJ2102
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090617
Time 10.18
INSTRUM dpx300
PROBHD 5 mm Dual 13
PULPROG zg30
TD 16384
SOLVENT CDCl3
NS 16
DS 2
SWH 4194.631 Hz
FIDRES 143.7
DW 119.200 usec
DE 6.00 usec
D1 2.50000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
SFO1 300.1315048 MHz
F2 - Processing parameters
SI 16384
SF 300.1300204 MHz
WDW EM
SSB 0
LB 0.08 Hz
GB 0
PC 2.00
45.973
14.798
30.418
0.186
8.625
ppm


Sample hyl-2-211WUA
User John Li
Room G53b
C13CPD_2HRS CDCl3 u cmhyl 36
Current Data Parameters
NAME samJ2102
EXPNO 12
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090617
Time 21.16
INSTRUM dpx300
PROBHD 5 mm Dual 13
PULPROG zgpg30
TD 24576
SOLVENT CDCl3
NS 2400
DS 2
SWH 18832.393 Hz
FIDRES 0.766
AQ 0.6529 sec
RG 8192
DW 26.550 usec
DE 6.00 usec
D1 1.00000000 sec
D11 0.03000000 sec
D12 0.00002000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 11.00 usec
PL1 0.00 dB
SFO1 75.4756440 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 112.00 usec
PL2 0.00 dB
PL12 18.00 dB
PL13 21.00 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 16384
SF 75.4678271 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
144.87
144.25
128.69
127.95
127.69
127.56
127.48
126.06
125.35
123.87
119.50
113.04
76.43
76.20
76.00
75.58
46.71
43.58
40.24
29.33
27.35
21.56
0.00
ppm

Compound *rac*-7i

28 Hyl-2-204 Rac AS-RH

Sample Name:	**Hyl-2-204 Rac AS-RH**	*Injection Volume:*	**10.0**
Vial Number:	**BB4**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**n.a.**
Control Program:	**RP (65-70) 30 mins**	*Bandwidth:*	**n.a.**
Quantif. Method:	**Default**	*Dilution Factor:*	**1.0000**
Recording Time:	**26/6/2009 11:34**	*Sample Weight:*	**1.0000**
Run Time (min):	**40.00**	*Sample Amount:*	**1.0000**

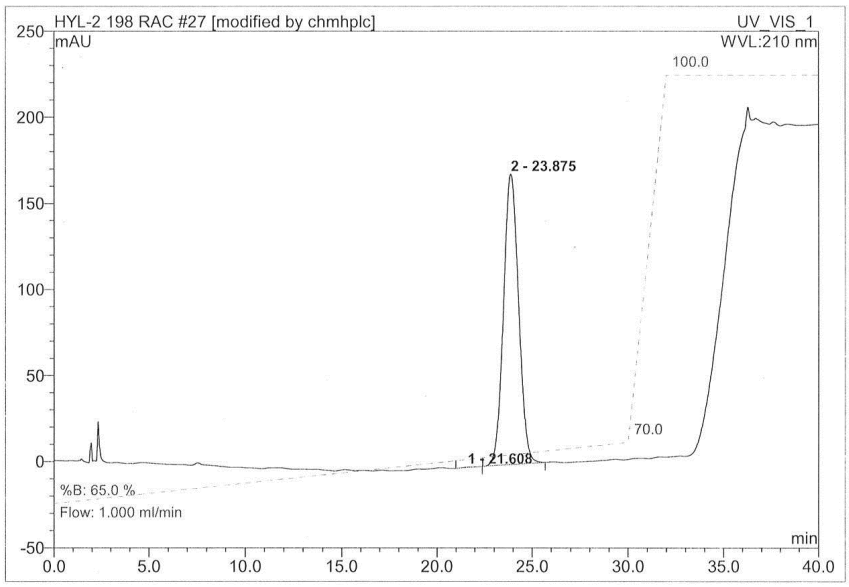


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	21.76	n.a.	206.584	176.915	49.59	n.a.	BM *
2	23.86	n.a.	190.432	179.823	50.41	n.a.	MB*
Total:			397.016	356.739	100.00	0.000	

Compound 7i (Table, entry 4)

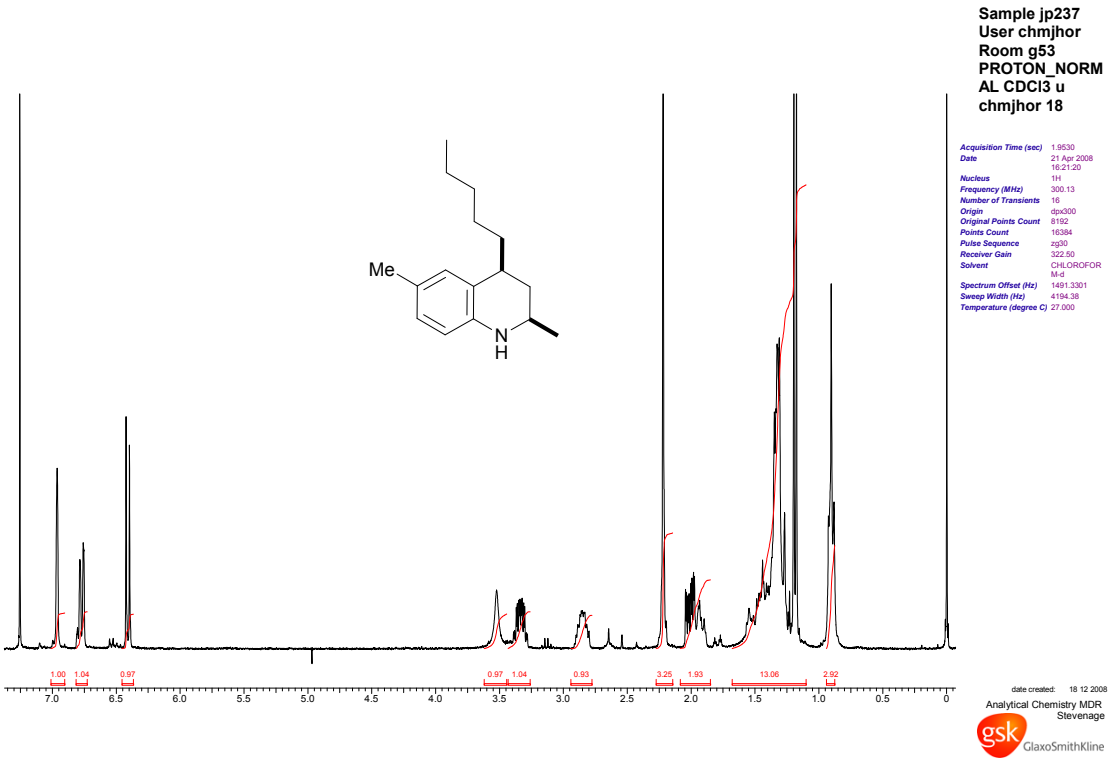
27 Hyl-2-211 AS-RH

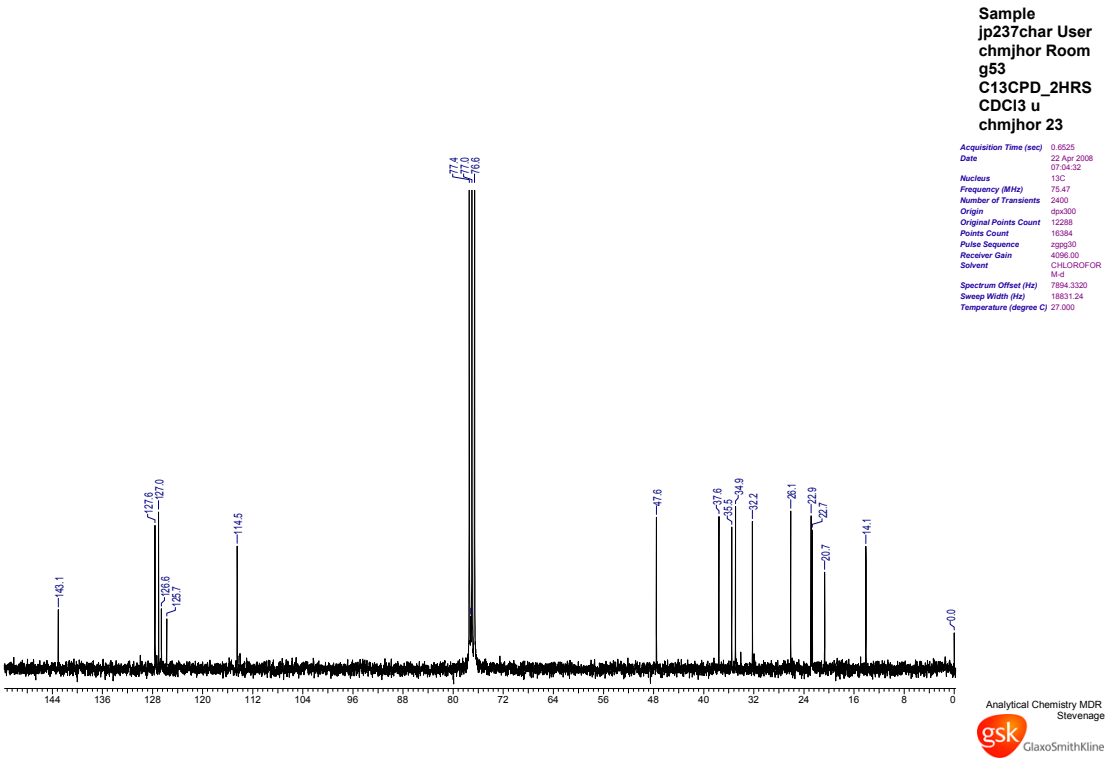
Sample Name:	**Hyl-2-211 AS-RH**	*Injection Volume:*	**10.0**
Vial Number:	**BB8**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**n.a.**
Control Program:	**RP (65-70) 30 mins**	*Bandwidth:*	**n.a.**
Quantif. Method:	**Default**	*Dilution Factor:*	**1.0000**
Recording Time:	**26/6/2009 10:47**	*Sample Weight:*	**1.0000**
Run Time (min):	**40.00**	*Sample Amount:*	**1.0000**



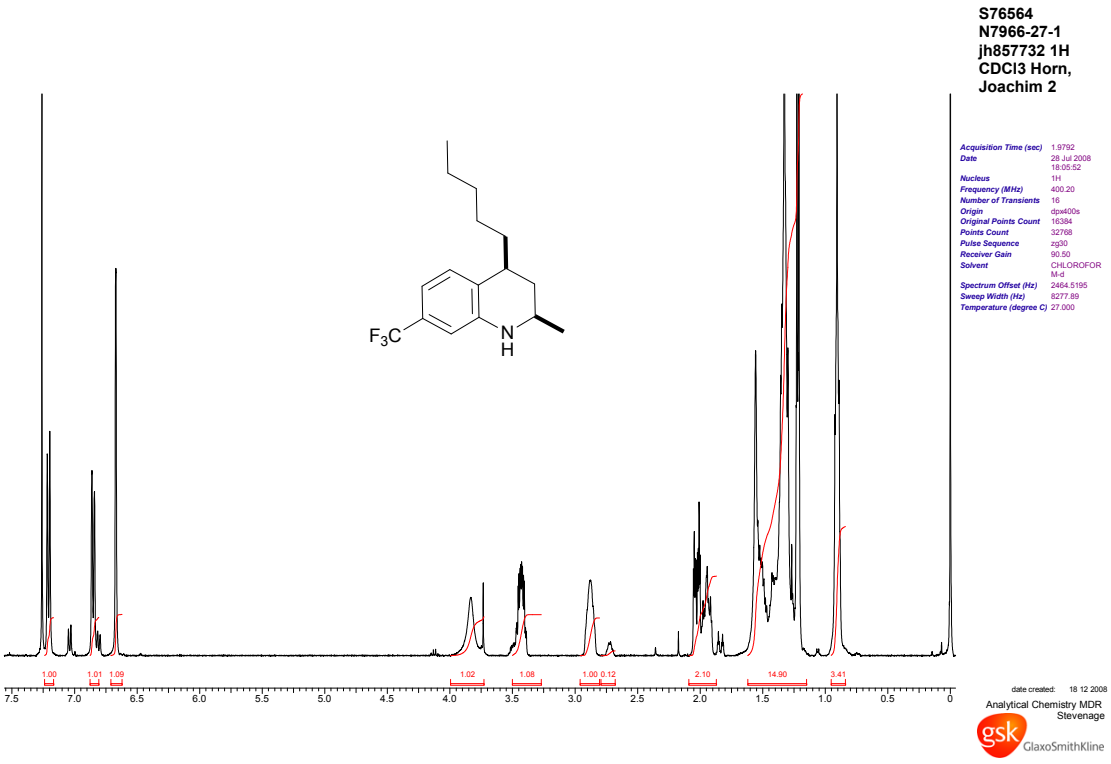
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	21.61	n.a.	0.253	0.147	0.09	n.a.	BMB*
2	23.88	n.a.	168.691	155.383	99.91	n.a.	BMB*
Total:			168.943	155.531	100.00	0.000	

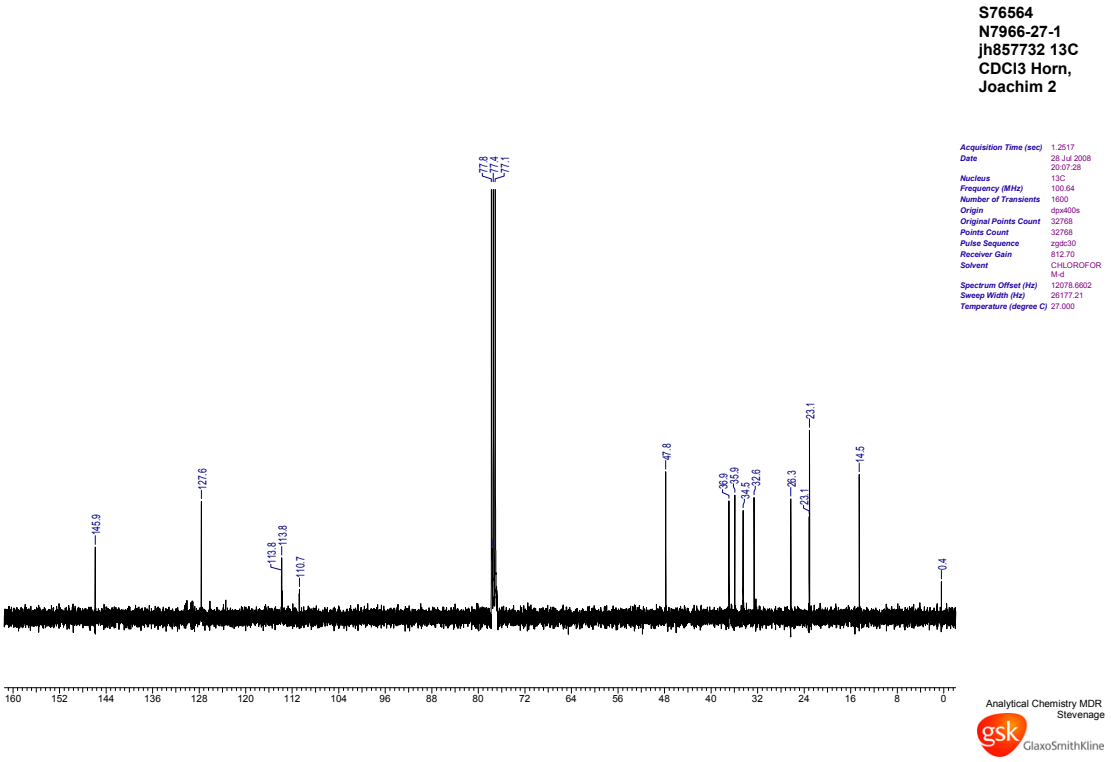
Compound 7j


Sample jp237
User chmjhor
Room g53
PROTON_NORMAL CDCl3 u
chmjhor 18
Acquisition Time (sec) 1.9530
Date 21 Apr 2008 16:21:20
Nucleus 1H
Frequency (MHz) 300.13
Number of Transients 16
Origin dpx300
Original Points Count 8192
Points Count 16384
Pulse Sequence zg30
Receiver Gain 322.50
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 1491.3301
Sweep Width (Hz) 4194.38
Temperature (degree C) 27.000
Me
N
H
1.00 1.04 0.97 0.97 1.04 0.93 3.25 1.93 13.06 2.92
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
date created: 18 12 2008
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline


Sample jp237char User chmjhor Room g53 C13CPD_2HRS CDCl3 u chmjhor 23
Acquisition Time (sec) 0.6525
Date 22 Apr 2008 07:04:32
Nucleus 13C
Frequency (MHz) 75.47
Number of Transients 2400
Origin dpx300
Original Points Count 12288
Points Count 16384
Pulse Sequence zgpg30
Receiver Gain 4096.00
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 7894.3320
Sweep Width (Hz) 18831.24
Temperature (degree C) 27.000
77.4
77.0
76.6
143.1
127.6
127.0
126.6
125.7
114.5
47.6
37.6
35.3
34.9
32.2
26.1
22.9
22.7
20.7
14.1
10.0
144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline

Compound 7k

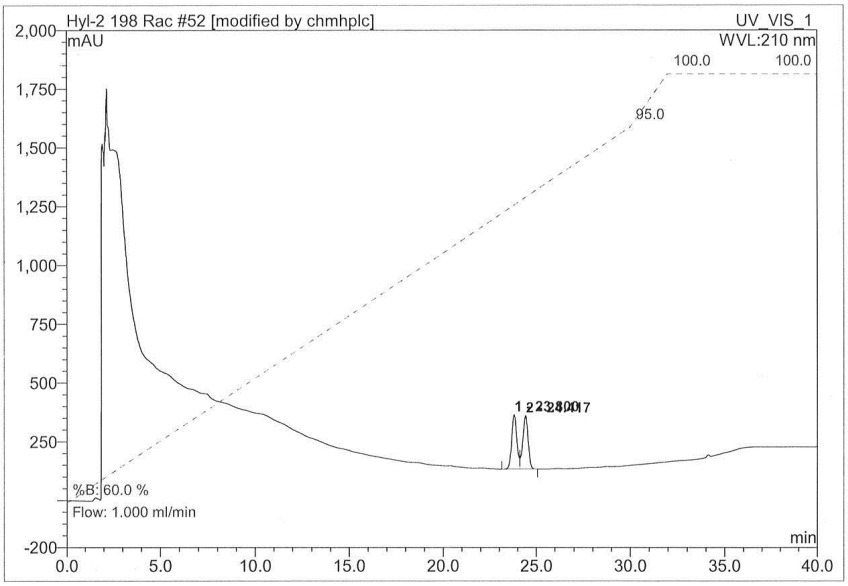

S76564
N7966-27-1
jh857732 1H
CDCl3 Horn, Joachim 2
Acquisition Time (sec) 1.9792
Date 28 Jul 2008 18:05:52
Nucleus 1H
Frequency (MHz) 400.20
Number of Transients 16
Origin dpx400s
Original Points Count 16384
Points Count 32768
Pulse Sequence zg30
Receiver Gain 90.50
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 2464.5195
Sweep Width (Hz) 8277.89
Temperature (degree C) 27.000
F3C
N
H
1.00 1.01 1.09 1.02 1.08 1.00 0.12 2.10 14.90 3.41
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
date created: 18 12 2008
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline


S76564
N7966-27-1
jh857732 13C
CDCl3 Horn, Joachim 2
Acquisition Time (sec) 1.2517
Date 28 Jul 2008 20:07:28
Nucleus 13C
Frequency (MHz) 100.64
Number of Transients 1600
Origin dpx400s
Original Points Count 32768
Points Count 32768
Pulse Sequence zgdc30
Receiver Gain 812.70
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 12078.6602
Sweep Width (Hz) 26177.21
Temperature (degree C) 27.000
77.8
77.4
77.1
145.9
127.6
113.8
113.8
110.7
47.8
36.9
35.9
34.3
32.6
28.3
23.1
23.1
14.5
0.4
160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Analytical Chemistry MDR
Stevenage
GlaxoSmithKline

Compound *rac*-7k

52 HYL-3-263 Rac AS-RH

Sample Name:	**HYL-3-263 Rac AS-RH**	*Injection Volume:*	**50.0**
Vial Number:	**BC1**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**n.a.**
Control Program:	**RP (60-95) 30 mins**	*Bandwidth:*	**n.a.**
Quantif. Method:	**Default**	*Dilution Factor:*	**1.0000**
Recording Time:	**18/8/2009 11:03**	*Sample Weight:*	**1.0000**
Run Time (min):	**40.00**	*Sample Amount:*	**1.0000**

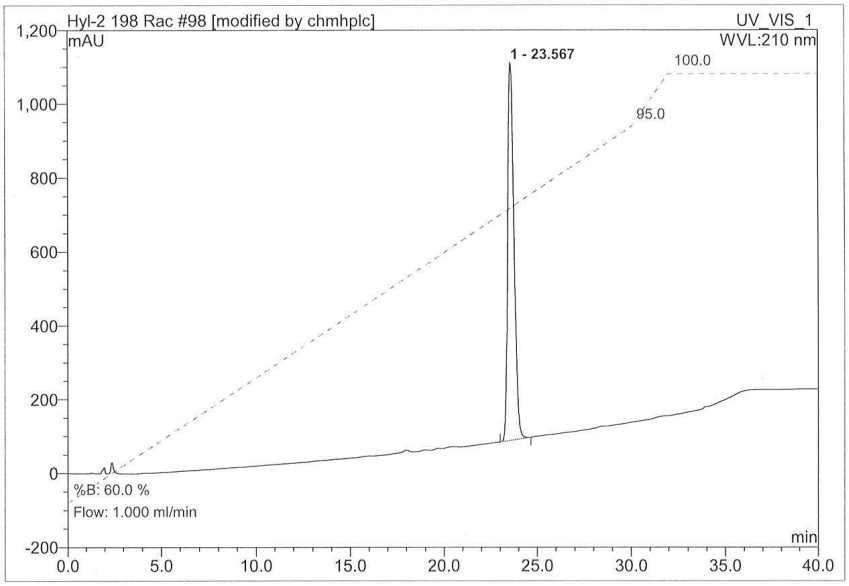


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	23.80	n.a.	231.906	74.515	49.57	n.a.	BM
2	24.42	n.a.	227.521	75.800	50.43	n.a.	MB
Total:			459.427	150.315	100.00	0.000	

Compound 7k (Table, entry 5)

98 HYL-3-258 Chiral AS-RH

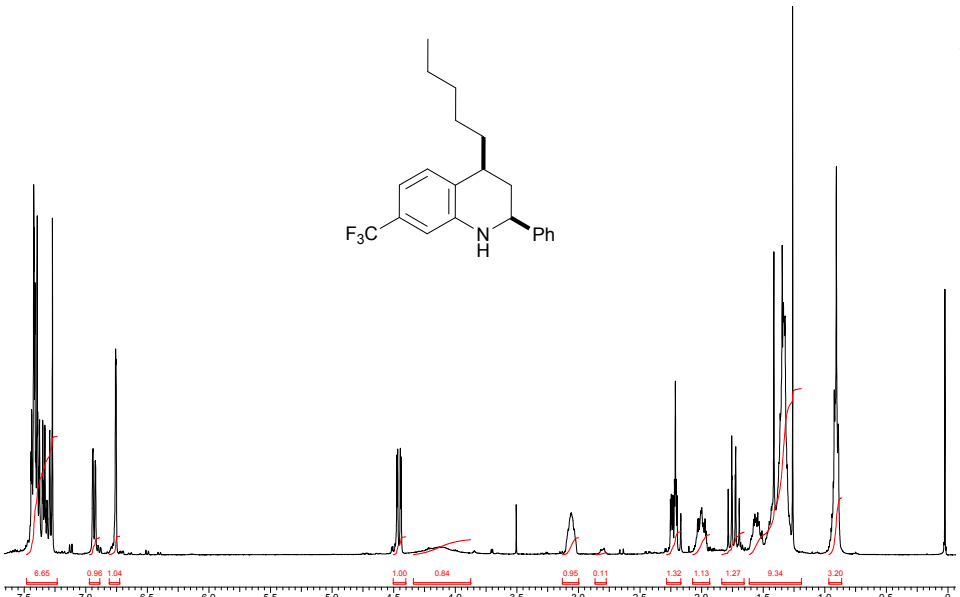
Sample Name:	**HYL-3-258 Chiral AS-RH**	*Injection Volume:*	**20.0**
Vial Number:	**RC5**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**n.a.**
Control Program:	**RP (60-95) 30 mins**	*Bandwidth:*	**n.a.**
Quantif. Method:	**Default**	*Dilution Factor:*	**1.0000**
Recording Time:	**8/9/2009 8:24**	*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	23.57	n.a.	1023.206	402.042	100.00	n.a.	BMB
Total:			1023.206	402.042	100.00	0.000	

Compound 7l

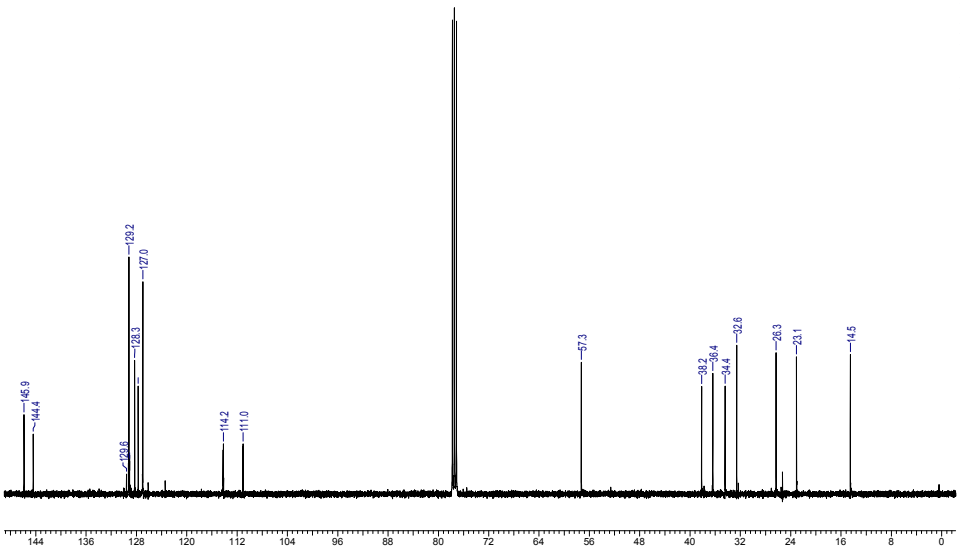
AG1912
N9982-10-2
jh857732 7198
1H CDCl3 Horn, Joachim 2



Acquisition Time (sec)	3.9846
Date	27 Nov 2008 12:09:36
Nucleus	1H
Frequency (MHz)	400.13
Number of Transients	16
Origin	ap400
Original Points Count	32768
Points Count	32768
Pulse Sequence	zg30
Receiver Gain	64.00
Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	2453.7112
Sweep Width (Hz)	8223.43
Temperature (degree C)	30.160

date created: 18 12 2008
Analytical Chemistry MDR
Stevenage

S81821
N9982-10-2
jh857732 13C CDCl3 DEPT & HMQC Horn, Joachim 2



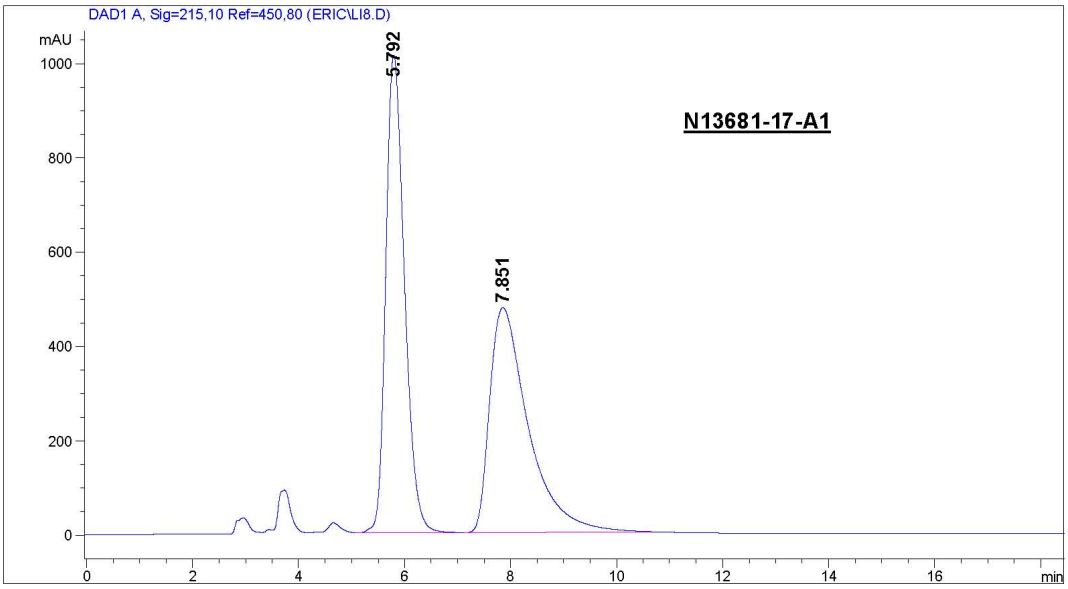
Acquisition Time (sec)	1.2517
Date	25 Nov 2008 21:11:28
Nucleus	13C
Frequency (MHz)	100.64
Number of Transients	1400
Origin	dpx400s
Original Points Count	32768
Points Count	32768
Pulse Sequence	zgdc30
Receiver Gain	812.70
Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	12078.6602
Sweep Width (Hz)	26177.21
Temperature (degree C)	27.000

Analytical Chemistry MDR
Stevenage

Compound *rac*-7l

Data File K:\HOYTEN\HPCHEM\1\DATA\ERIC\LI8.D
Sample Name: N13681-17-A1

```
=====================================================================
Acq. Operator   : ERIC HORTENSE
Acq. Instrument : HOYTEN                          Location : Vial 1
Injection Date  : 23/11/2009 14:04:45
                                                  Inj Volume : 10 µl
Method          : K:\HOYTEN\HOYTENS METHODS\CHIMETH1.M
Last changed    : 23/11/2009 13:37:38  by ERIC HORTENSE
                  (modified after loading)
Method Info     : Chiral Method 1.  Isocratic Analysis at 1.000 ml/min.

Sample Info     : 25cm Chiralcel OJ
                  ,col.no.OJOOCE-IF013,20%ETOH/C7,1ml/min,wavelength 215n
                  m,RT
```

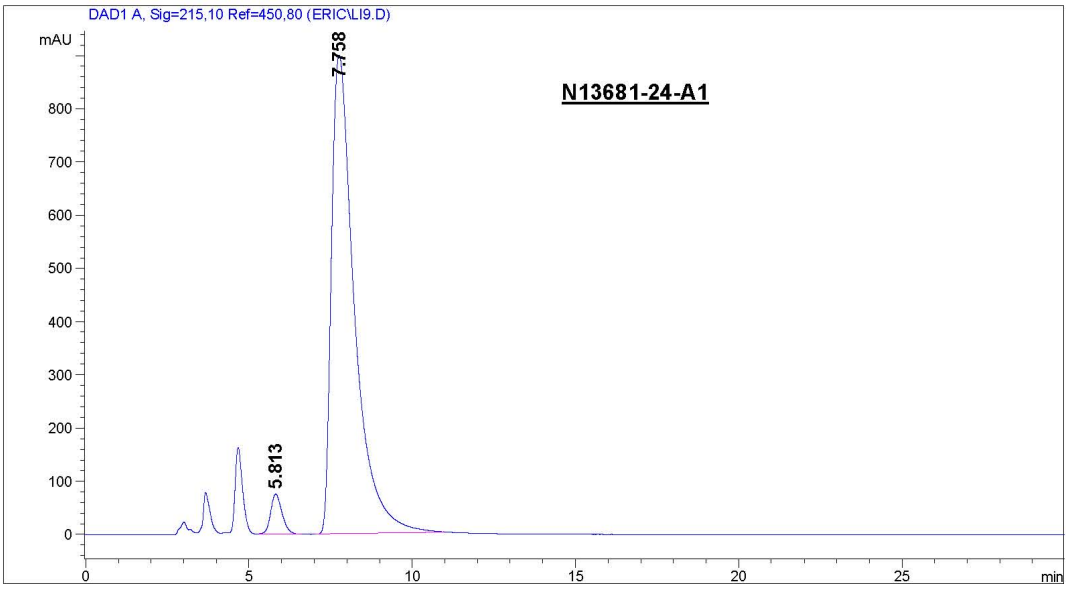



```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=215,10 Ref=450,80

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.792 VB    0.3798 2.48425e4  1014.04498  50.6233
   2   7.851 BB    0.7603 2.42307e4   477.28644  49.3767

Totals :                  4.90732e4  1491.33142


=====================================================================
                        *** End of Report ***
```

Compound 7l (Table, entry 6)

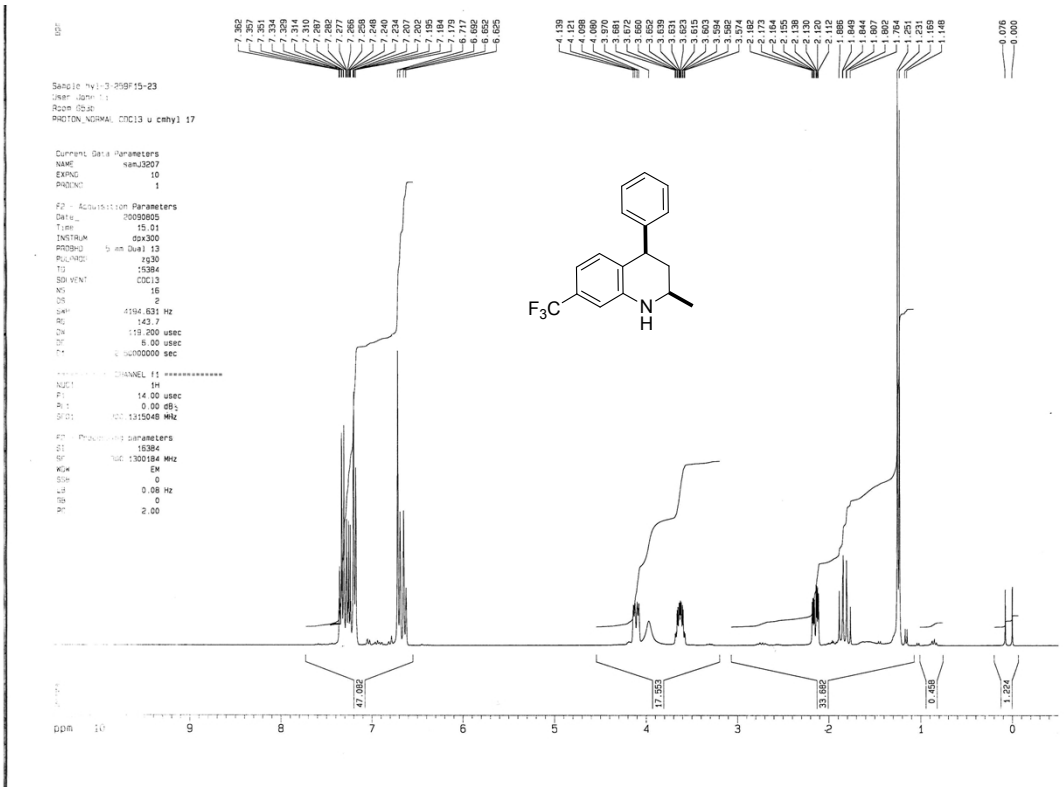
Data File K:\HOYTEN\HPCHEM\1\DATA\ERIC\LI9.D
Sample Name: N13681-24-A1

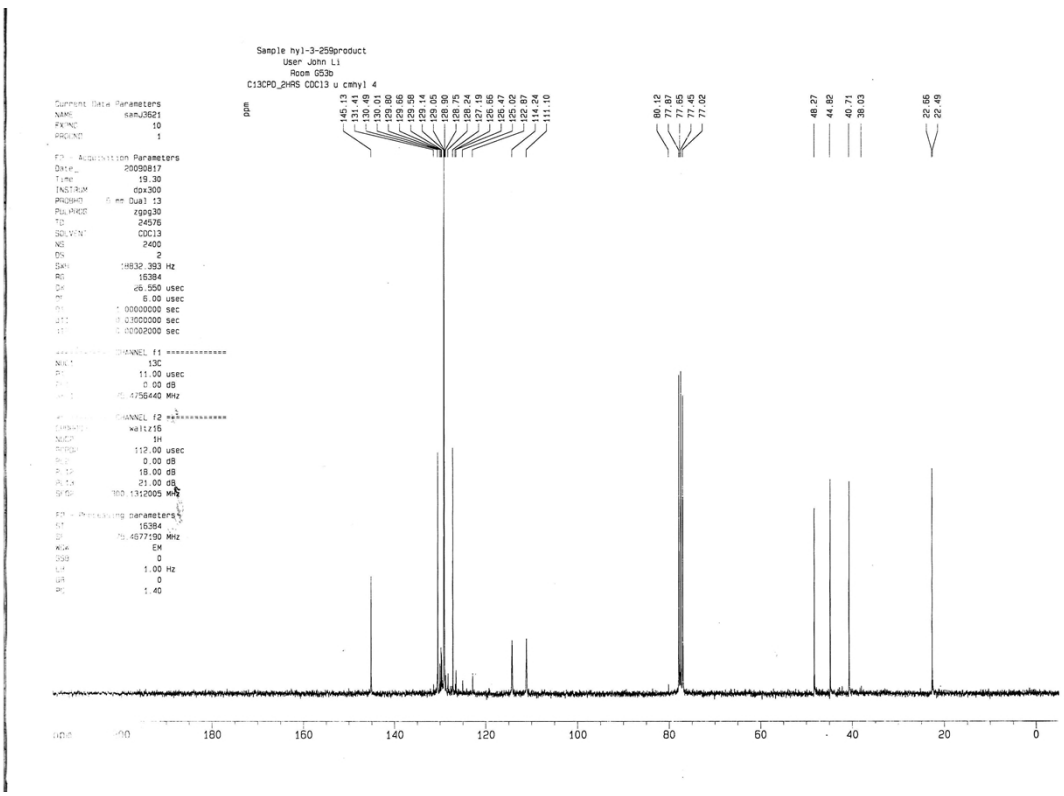
```
==================================================================
Acq. Operator   : ERIC HORTENSE
Acq. Instrument : HOYTEN                        Location : Vial 1
Injection Date  : 23/11/2009 14:32:18
                                               Inj Volume : 10 µl
Method          : K:\HOYTEN\HOYTENS METHODS\CHIMETH1.M
Last changed    : 23/11/2009 13:37:38  by ERIC HORTENSE
                  (modified after loading)
Method Info     : Chiral Method 1.  Isocratic Analysis at 1.000 ml/min.

Sample Info     : 25cm Chiralcel OJ
                  ,col.no.OJOOCE-IF013,20%ETOH/C7,1ml/min,wavelength 215n
                  m,RT
```




```
==================================================================
                        Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=215,10 Ref=450,80

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.813 BB    0.3741 1864.25513   76.03320   4.0483
   2   7.758 BB    0.7330 4.41862e4   899.70447  95.9517

Totals :                  4.60505e4   975.73766


==================================================================
                        *** End of Report ***
```

Compound 7m

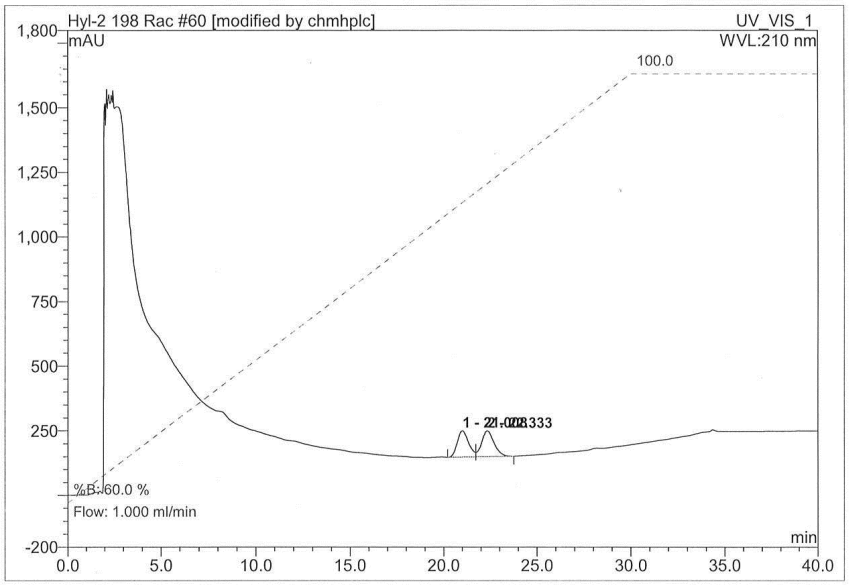




Compound *rac*-7m

60 HYL-3-264 rac AD-RH

Sample Name:	**HYL-3-264 rac AD-RH**	*Injection Volume:*	**50.0**
Vial Number:	**BC2**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**n.a.**
Control Program:	**RP (60-100) 30 mins**	*Bandwidth:*	**n.a.**
Quantif. Method:	**Default**	*Dilution Factor:*	**1.0000**
Recording Time:	**20/8/2009 14:39**	*Sample Weight:*	**1.0000**
Run Time (min):	**40.00**	*Sample Amount:*	**1.0000**

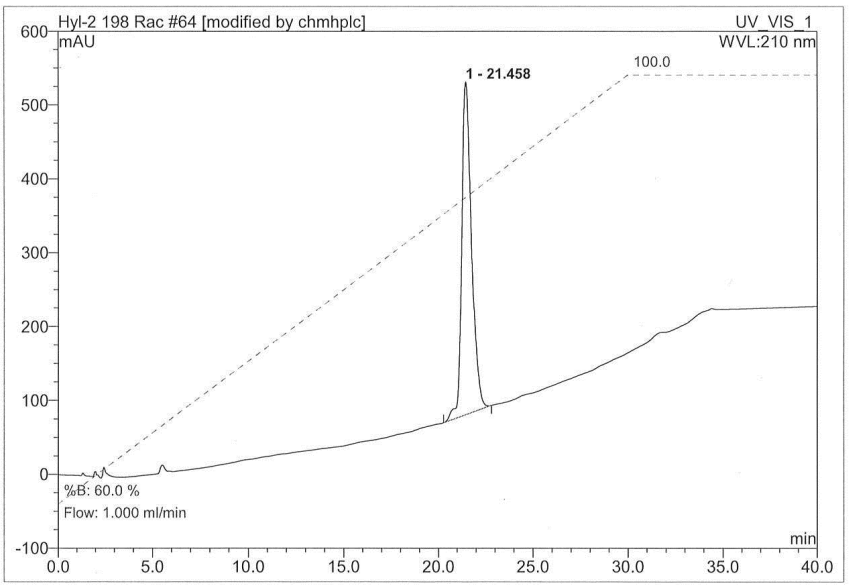


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	21.01	n.a.	101.393	70.650	48.16	n.a.	BM *
2	22.33	n.a.	99.285	76.034	51.84	n.a.	MB
Total:			200.678	146.684	100.00	0.000	

Compound 7m (Table, entry 7)

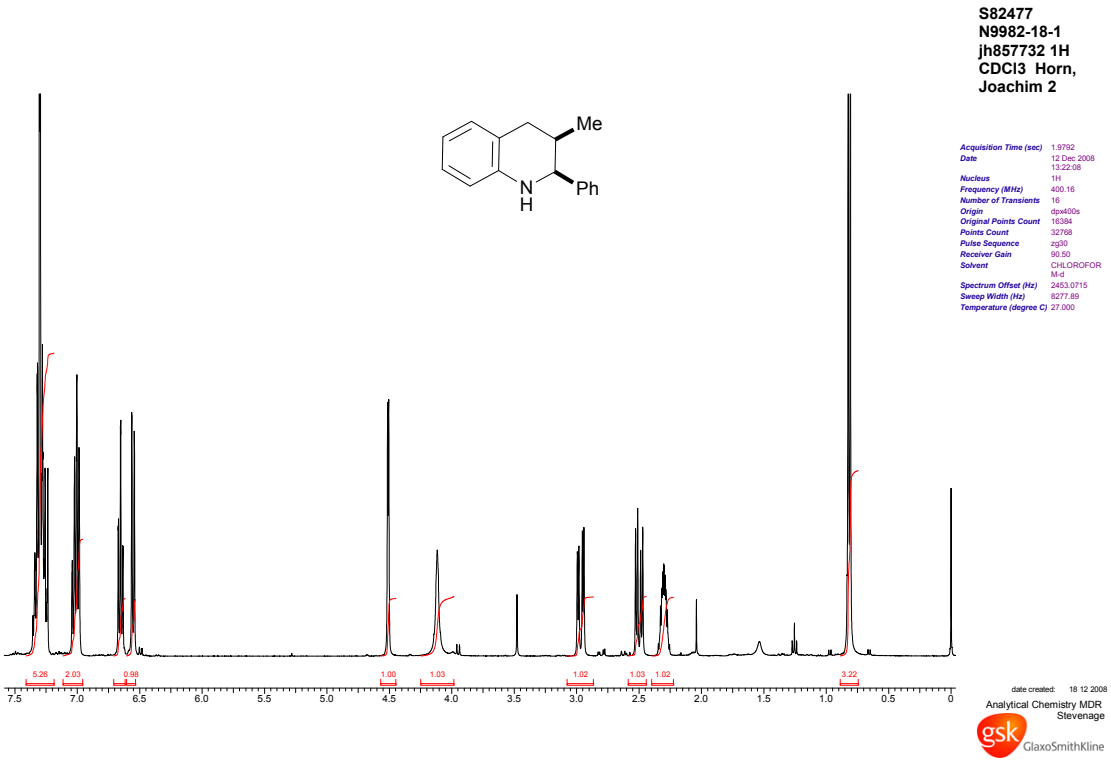
64 HYL-3-259 Chiral AD-RH

Sample Name:	**HYL-3-259 Chiral AD-RH**	*Injection Volume:*	**10.0**
Vial Number:	**BC4**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**n.a.**
Control Program:	**RP (60-100) 30 mins**	*Bandwidth:*	**n.a.**
Quantif. Method:	**Default**	*Dilution Factor:*	**1.0000**
Recording Time:	**27/8/2009 12:49**	*Sample Weight:*	**1.0000**
Run Time (min):	**40.00**	*Sample Amount:*	**1.0000**

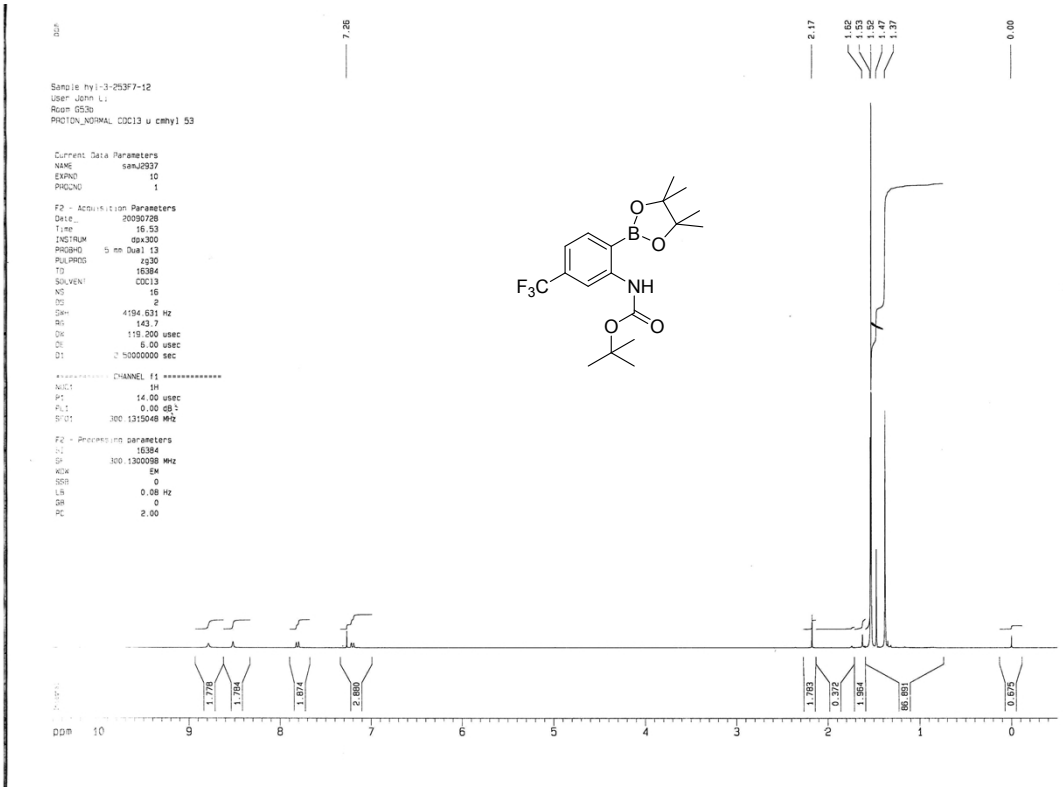


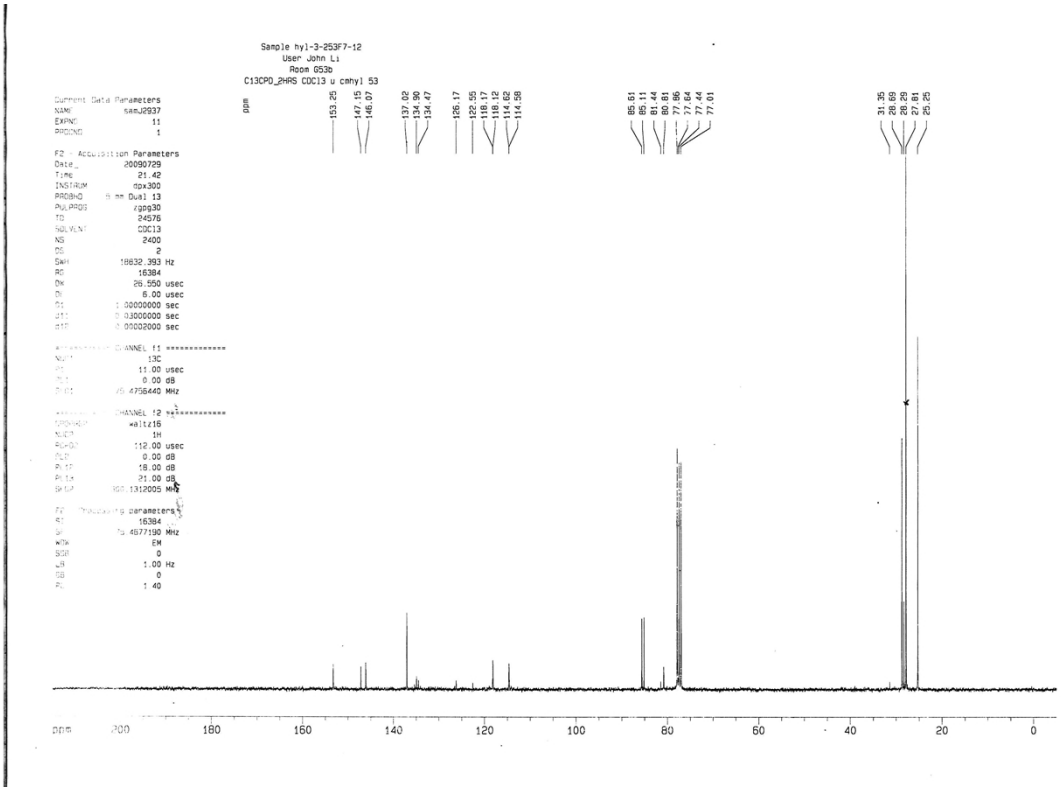
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	21.46	n.a.	449.895	268.819	100.00	n.a.	BMB*
Total:			449.895	268.819	100.00	0.000	

Compound *rac*-9

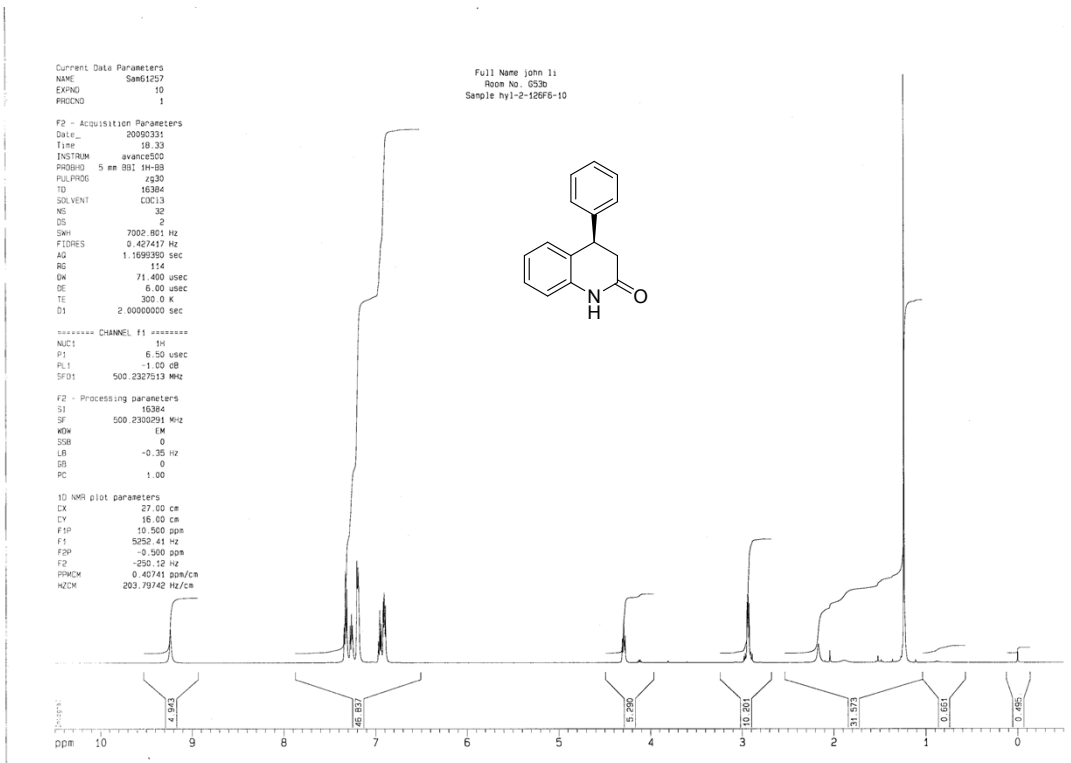


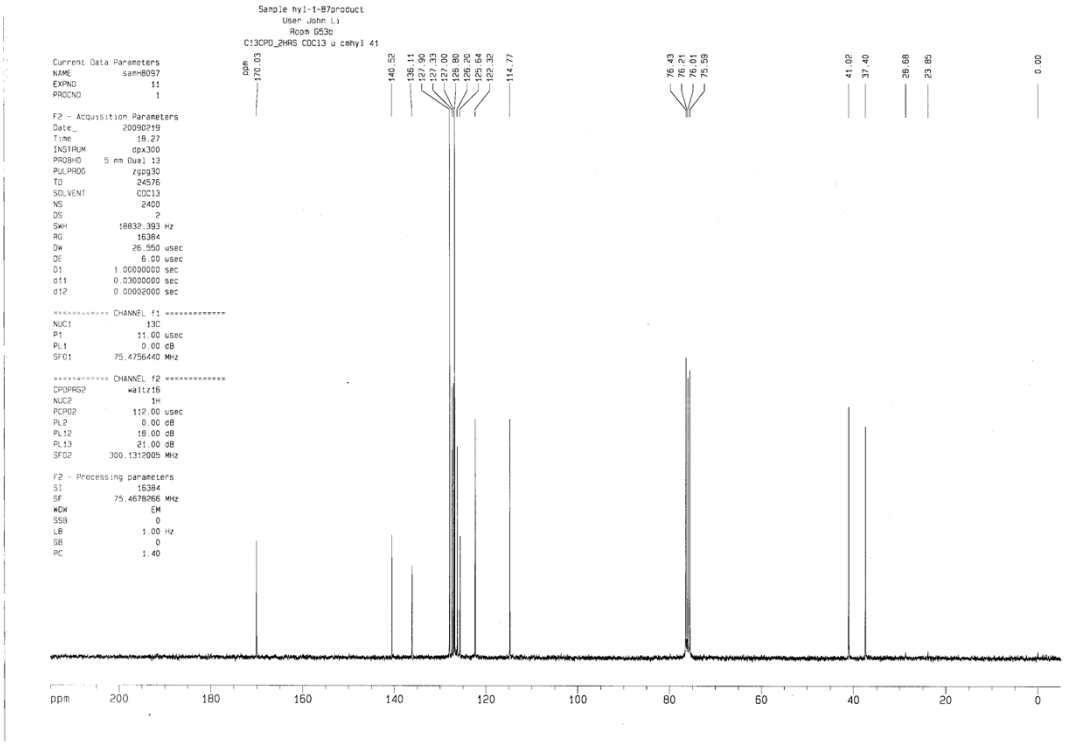
Compound 10 ($R^3 = CF_3$)





Compound S3

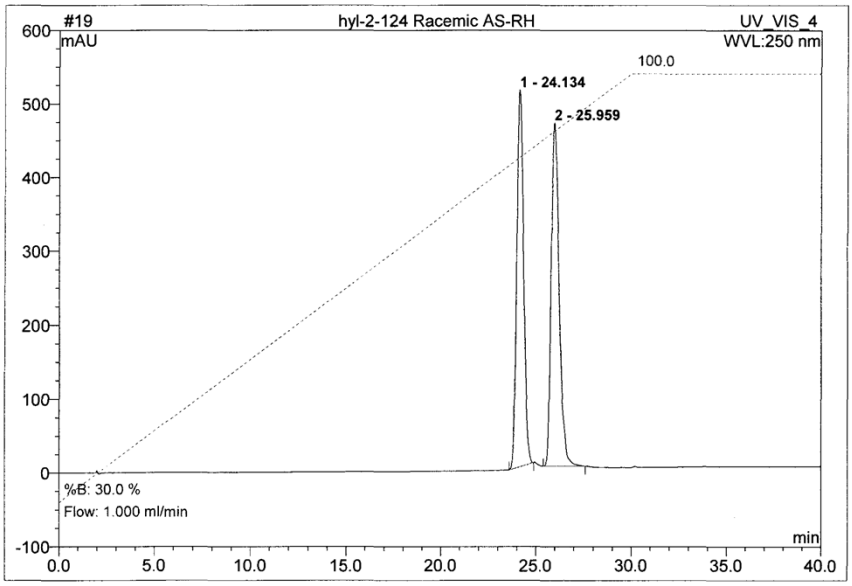

Current Data Parameters
NAME Sam61257
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090331
Time 18.33
INSTRUM avance500
PROBHD 5 mm BBI 1H-BB
PULPROG zg30
TD 16384
SOLVENT CDCl3
NS 32
DS 2
SWH 7002.801 Hz
FIDRES 0.427417 Hz
AQ 1.1699350 sec
RG 114
DW 71.400 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 6.50 usec
PL1 -1.00 dB
SFO1 500.2327513 MHz
F2 - Processing parameters
SI 16384
SF 500.2300291 MHz
WDW EM
SSB 0
LB -0.35 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 27.00 cm
CY 16.00 cm
F1P 10.500 ppm
F1 5252.41 Hz
F2P -0.500 ppm
F2 -250.12 Hz
PPMCM 0.40741 ppm/cm
HZCM 203.79742 Hz/cm
Full Name john li
Room No. G53b
Sample hyl-2-126F6-10
O
N
H
4.943
45.837
5.290
10.201
31.572
0.661
0.485
ppm 10 9 8 7 6 5 4 3 2 1 0


Sample hyl-1-87product
User John Li
Room G53b
C13CPD_2HRS CDCl3 u cmhyl 41
Current Data Parameters
NAME samH8057
EXPNO 11
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090219
Time 18.27
INSTRUM dpx300
PROBHD 5 mm Dual 13
PULPROG zgpg30
TD 24576
SOLVENT CDCl3
NS 2400
DS 2
SWH 18832.393 Hz
RG 16384
DW 26.550 usec
DE 6.00 usec
D1 1.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec
========== CHANNEL f1 ==========
NUC1 13C
P1 11.00 usec
PL1 0.00 dB
SFO1 75.4756440 MHz
========== CHANNEL f2 ==========
CPDPRG2 waltz16
NUC2 1H
PCPD2 112.00 usec
PL2 0.00 dB
PL12 18.00 dB
PL13 21.00 dB
SFO2 300.1312005 MHz
F2 - Processing parameters
SI 16384
SF 75.4678266 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
ppm
170.03
140.52
138.11
137.99
137.33
137.00
128.80
126.20
125.64
122.32
114.77
76.43
76.21
76.01
75.59
41.02
37.40
28.68
23.85
0.00
ppm 200 180 160 140 120 100 80 60 40 20 0

Compound *rac*-S3

19 hyl-2-124 Racemic AS-RH

Sample Name:	**hyl-2-124 Racemic AS-RH**	*Injection Volume:*	**10.0**
Vial Number:	**GC7**	*Channel:*	**UV_VIS_4**
Sample Type:	**unknown**	*Wavelength:*	**n.a.**
Control Program:	**RP (30-100) 30 mins**	*Bandwidth:*	**n.a.**
Quantif. Method:	**Default**	*Dilution Factor:*	**1.0000**
Recording Time:	**16/4/2009 12:39**	*Sample Weight:*	**1.0000**
Run Time (min):	**40.00**	*Sample Amount:*	**1.0000**

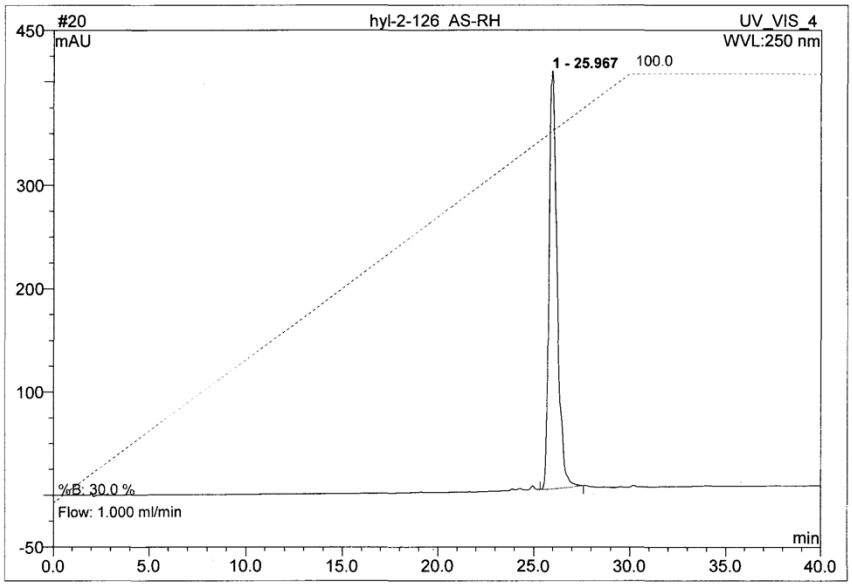


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	24.13	n.a.	510.568	212.655	48.61	n.a.	BMB
2	25.96	n.a.	464.819	224.782	51.39	n.a.	BMB
Total:			975.387	437.437	100.00	0.000	

Compound S3

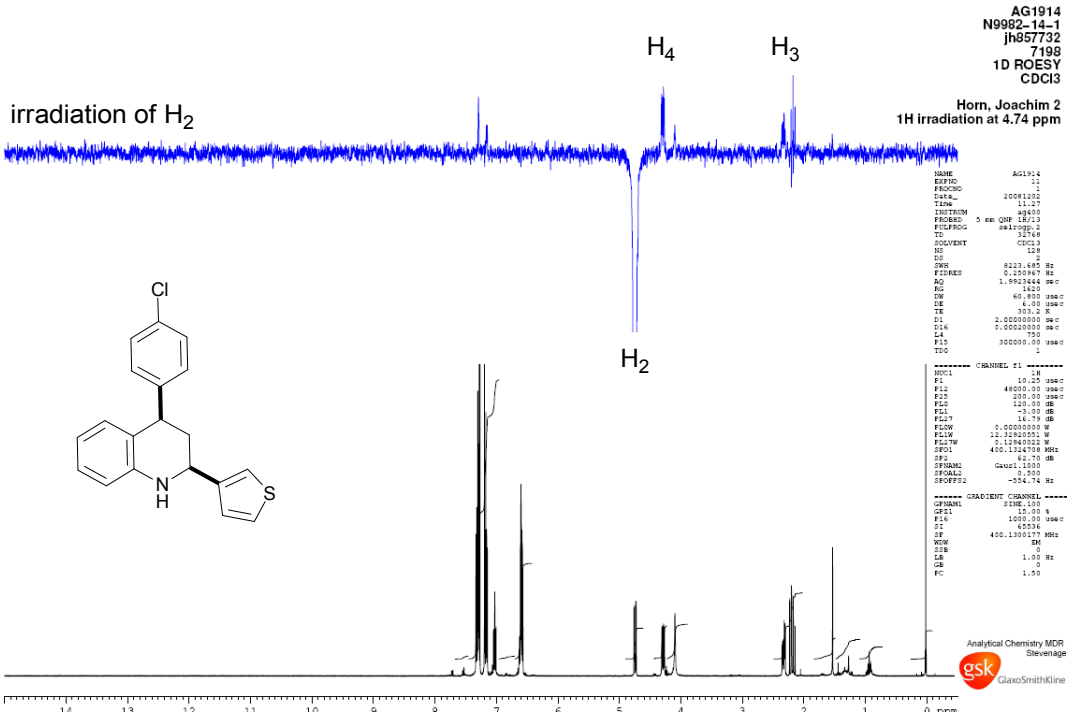
20 hyl-2-126 AS-RH

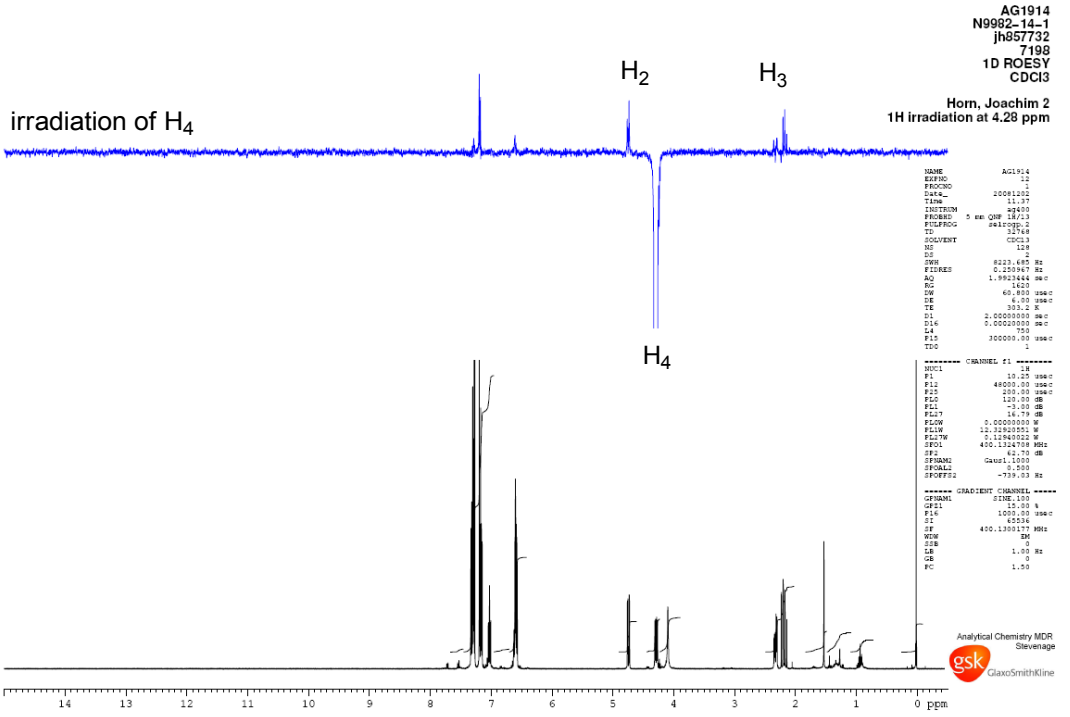
Sample Name:	**hyl-2-126 AS-RH**	*Injection Volume:*	**10.0**
Vial Number:	**GC8**	*Channel:*	**UV_VIS_4**
Sample Type:	**unknown**	*Wavelength:*	**n.a.**
Control Program:	**RP (30-100) 30 mins**	*Bandwidth:*	**n.a.**
Quantif. Method:	**Default**	*Dilution Factor:*	**1.0000**
Recording Time:	**16/4/2009 14:03**	*Sample Weight:*	**1.0000**
Run Time (min):	**40.00**	*Sample Amount:*	**1.0000**



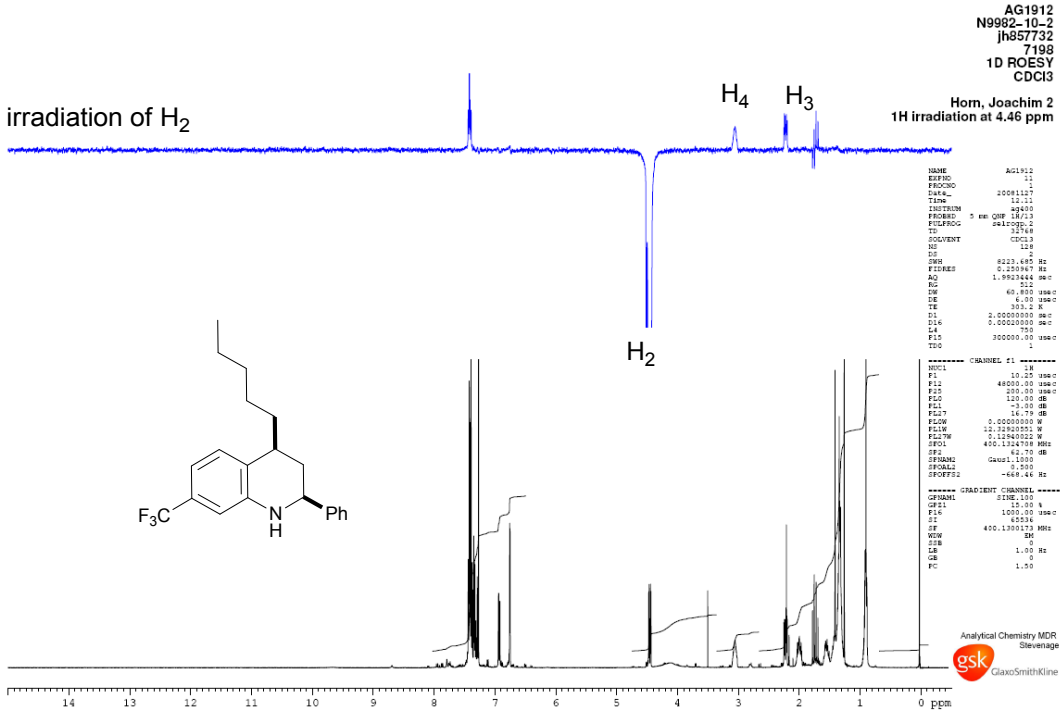
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	25.97	n.a.	404.220	197.625	100.00	n.a.	BMB
Total:			404.220	197.625	100.00	0.000	

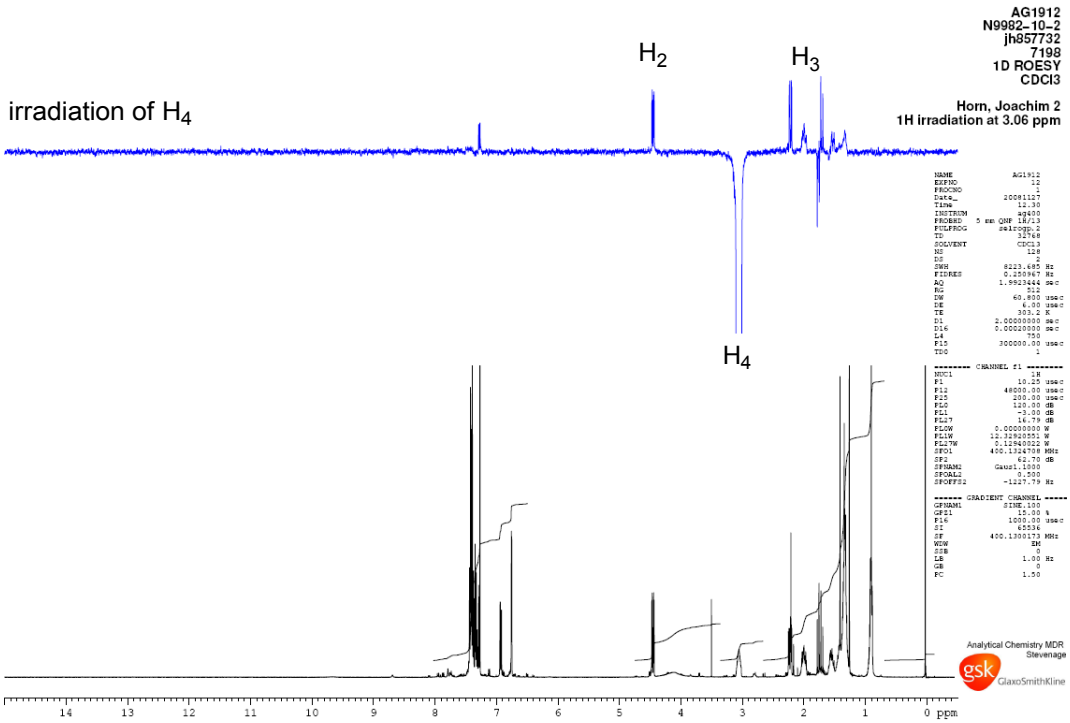
nOe for compound 7h





nOe for compound 7l





VCD for compound 7c

Ab Initio VCD Analysis of N13681-33-A1

I. Sample Information:

- Date: September 30, 2011
- Analyst: Doug Minick
- Analytical Reference: N21881-13

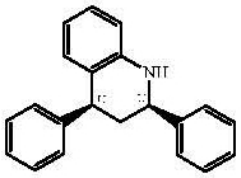
II. Technique: VCD

III. Experiment:

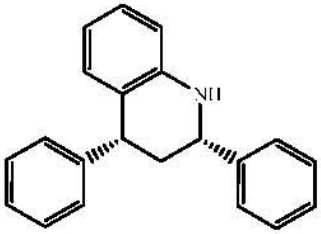
- Determination of absolute stereochemistry

IV. Objective:

- Assign the absolute configurations for a single enantiomer with the following general structure:



V. Assigned Structure:



N13681-33-A1

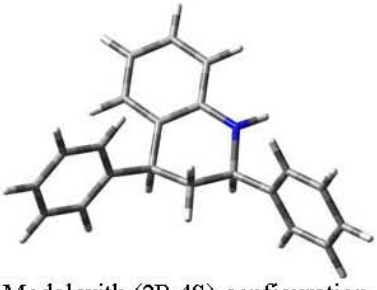
(2*S*,4*R*)-2,4-diphenyl-1,2,3,4-tetrahydroquinoline

VI. Comments:

- The relative stereochemistry was determined from NMR analysis.

VII. Theoretical Analysis:

- Model:



Model with (2R,4S)-configuration

- Conformational Search: MOE stochastic csearch using MMFF94x force field
- Model Chemistry: # opt freq=(noraman,vcd) b3lyp/dgdzvp
- Conformational Analysis: Fractional populations estimated using Boltzmann statistics
- Lorentzian band width: 6 cm^{-1}
- Frequency scale factor: 0.975
- Estimation of Confidence Limit: CompareVOA (BioTools, Inc.) analysis (Section IX)

VIII. Experimental:

- Spectrometer: BioTools Chiral*IR* VCD spectrometer operated at 4 cm^{-1}
- Frequency Range: 2000-800 cm^{-1}
- PEM Calibration: PEM calibrated at 1400 cm^{-1}
- PEM Retardation Settings: PEM1 = 0.250*λ; PEM2 = 0.260*λ
- Scan Method: single block scan [2 min. DC scan + 360 min. AC scan]
- Solvent: CCl_4
- Concentration: ~9mg/125ul
- Baseline Correction Method: modified half-difference (VCD_{E1} (corr'd) = VCD_{E1} minus VCD_{E2}; VCD_{E2} (corr'd) = VCD_{E2} minus VCD_{E1})
- Additional Processing: Savitsky-Golay 9-point smooth

IX. Results:

- Analysis of Experimental and Calculated Data:
  The experimental VCD and IR spectra of N13681-33-A1 are compared in Figure 1 with corresponding spectral data calculated for Model 1. The green box in each panel highlights the VCD spectral range used to assign the absolute configuration and estimate the level of reliability (Section X). The smaller green box designates the spectral range excluded from this VCD study.

  In the upper panel of Figure 1, the experimental VCD spectrum inside the highlighted box is the mirror image of the calculated VCD spectrum, indicating that the chiral centers in this molecule are inverted relative to the model. Therefore, N13681-33-A1 was assigned as the (2S,4R) enantiomer.

  Note: The IR spectrum calculated for the model is in very good overall agreement with experimental, indicating adequate coverage of the conformational space (required for a reliable VCD assignment)

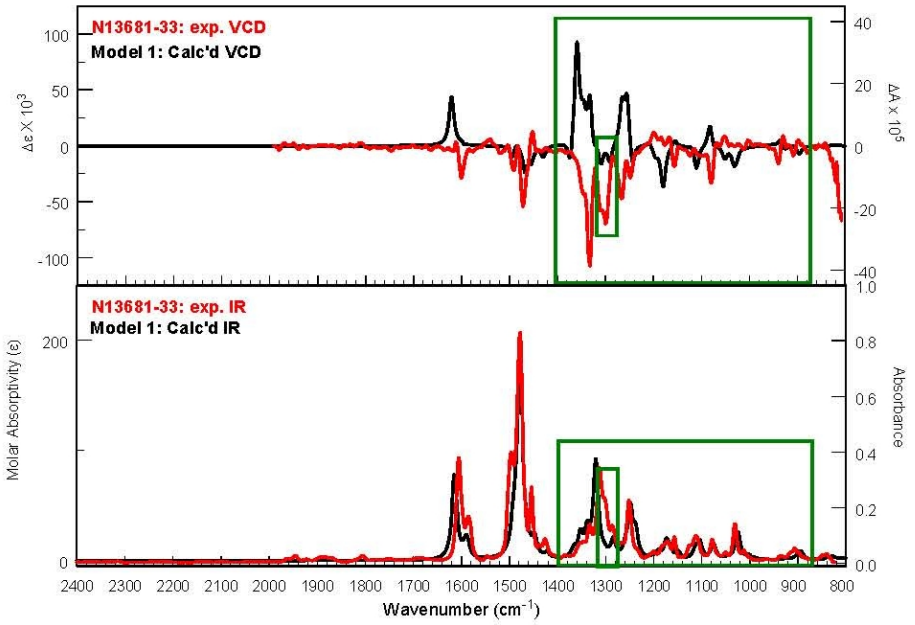


Figure 1. Upper panel: VCD spectrum of N13681-33-A1 (red trace) vs calculated VCD spectrum (black trace). Lower panel: IR spectrum of N13681-33-A1 (red) vs calculated IR spectrum (black).

X. Estimated Level of Reliability

- The confidence limit in this study was estimated using CompareVOA™ (BioTools, Inc.), an automated tool for quantifying the level of agreement between two sets of spectral data.
- The degree of reliability (the confidence limit) is assessed using the absolute values of two parameters: total neighborhood similarity for the VCD correlation (TNS (VCD)) and the enantiomeric similarity index (ESI).
- The degrees of reliability based on CompareVOA analysis are as follows:

Reliability	*TNS (VCD) (range)	*ESI (range)	Confidence Limit (CL) (range)
High	≥ 70	≥ 60	> 99 %
Medium	60 - 70	50 - 60	95 – 99 %
Low	50 - 60	40 – 50	90 – 95 %
Unreliable	< 50	< 40	< 90 %

*absolute value

- CompareVOA results for the current study:
  - Spectral range: 1400-850 cm^{-1}
  - Region omitted: 1320-1285
  - Range of statistical analysis (minimum 400 cm^{-1}): 660 cm^{-1}
  - Width of triangular weighting function: 20 cm^{-1}
  - TNS (VCD): 71.2 (absolute value)
  - ESI: 67.3 (absolute value)
  - Optimized scale factor: 0.980

- *Level of Reliability:* ***High (CL > 99%)***

XI. Optical Rotation Data:

- Not measured.

VCD for compound 7l

Ab Initio VCD Analysis of N13681-24-A1

I. Sample Information:

- Date: September 15, 2011
- Submitter: Paolo Tosatti
- Analyst: Doug Minick
- Analytical Reference: N21881-12

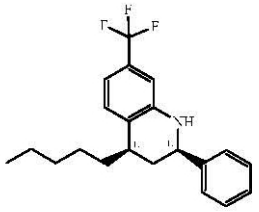
II. Technique: VCD

III. Experiment:

- Determination of absolute stereochemistry

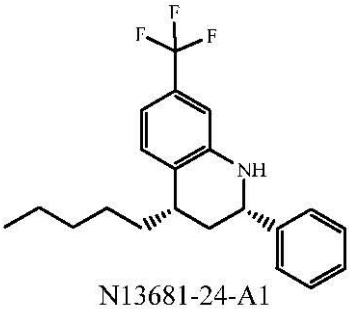
IV. Objective:

- Assign the absolute configurations for a single enantiomer with the following general structure:



cis-relative stereochemistry from NMR

V. Assigned Structure:



N13681-24-A1

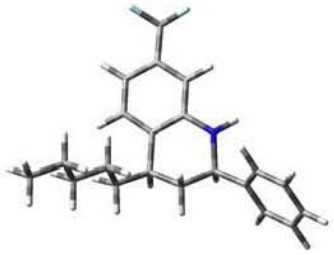
(2*S*,4*S*)-4-pentyl-2-phenyl-7-(trifluoromethyl)-1,2,3,4-tetrahydroquinoline

VI. Comments:

- The relative stereochemistry was determined from NMR analysis.
- The VCD analysis was performed using N-deuterium exchanged models and sample.

VII. Theoretical Analysis:

- Model:



Model with (2R,4R)-configuration
(VCD assignment based on N-deutereo model)

- Conformational Search: MOE stochastic csearch using MMFF94x force field
- Model Chemistry: # opt freq=(noraman,vcd) b3lyp/dgdzvp
- Conformational Analysis: Fractional populations estimated using Boltzmann statistics
- Lorentzian band width: 10 cm^{-1}
- Frequency scale factor: 0.975
- Estimation of Confidence Limit: CompareVOA (BioTools, Inc.) analysis (Section IX)

VIII. Experimental:

- Spectrometer: BioTools Chiral*IR* VCD spectrometer operated at 4 cm^{-1}
- Frequency Range: 2000-800 cm^{-1}
- PEM Calibration: PEM calibrated at 1400 cm^{-1}
- PEM Retardation Settings: PEM1 = 0.250*λ; PEM2 = 0.260*λ
- Scan Method: single block scan [2 min. DC scan + 360 min. AC scan]
- Solvent: $CDCl_3$ saturated with D_2O
- Concentration: ~16mg/300ul
- Baseline Correction Method: modified half-difference (VCD_{E1} (corr'd) = VCD_{E1} minus VCD_{E2}; VCD_{E2} (corr'd) = VCD_{E2} minus VCD_{E1})
- Additional Processing: Savitsky-Golay 9-point smooth

IX. Results:

- Analysis of Experimental and Calculated Data:
  The experimental VCD and IR spectra of N13681-24-A1 are compared in figure 1 with corresponding spectral data calculated for Model 1. The green box in each figure highlights the VCD spectral range used to assign the absolute configuration and estimate the level of reliability (Section X). The smaller green box designates the spectral range excluded from this VCD study.

  In the upper panel of Figure 1, the experimental VCD spectrum inside the highlighted box is the mirror image of the calculated VCD spectrum, indicating that the chiral centers in this molecule is inverted relative to the model. Therefore, N13681-24-A1 was assigned as the (2S,4S) enantiomer.

  Note: The IR spectrum calculated for the model is in good overall agreement with experimental, indicating adequate coverage of the conformational space (required for a reliable VCD assignment).

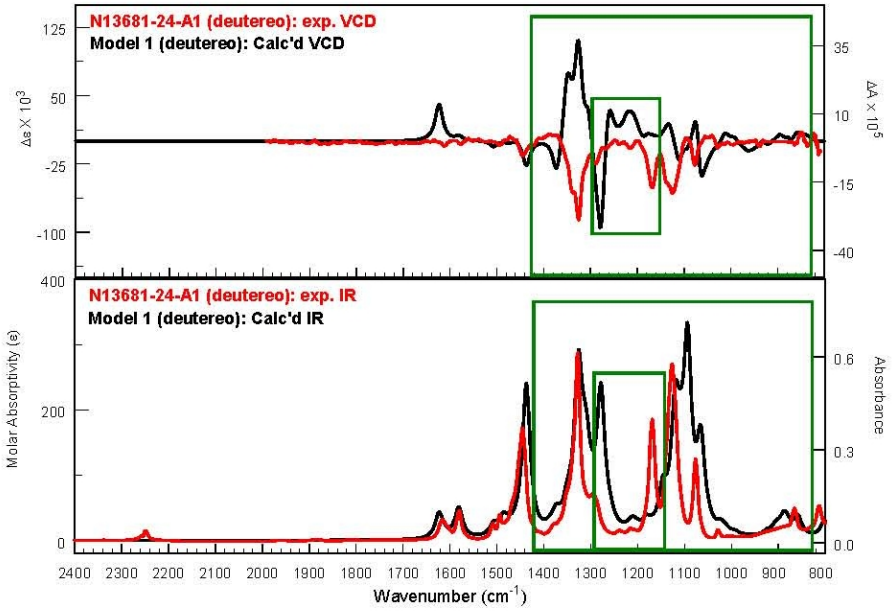


Figure 1. Upper panel: VCD spectrum of N13681-24-A1 (red trace) vs calculated VCD spectrum (black trace). Lower panel: IR spectrum of N13681-24-A1 (red) vs calculated IR spectrum (black).

X. Estimated Level of Reliability

- The confidence limit in this study was estimated using CompareVOA™ (BioTools, Inc.), an automated tool for quantifying the level of agreement between two sets of spectral data.
- The degree of reliability (the confidence limit) is assessed using the absolute values of two parameters: total neighborhood similarity for the VCD correlation (TNS (VCD)) and the enantiomeric similarity index (ESI).
- The degrees of reliability based on CompareVOA analysis are as follows:

Reliability	*TNS (VCD) (range)	*ESI (range)	Confidence Limit (CL) (range)
High	≥ 70	≥ 60	> 99 %
Medium	60 - 70	50 - 60	95 – 99 %
Low	50 - 60	40 – 50	90 – 95 %
Unreliable	< 50	< 40	< 90 %

*absolute value

- CompareVOA results for the current study:
  - Spectral range: 1420-820 cm^{-1}
  - Region omitted: 1295-1150
  - Range of statistical analysis (minimum 400 cm^{-1}): 455 cm^{-1}
  - Width of triangular weighting function: 20 cm^{-1}
  - TNS (VCD): 78.3 (absolute value)
  - ESI: 67.5 (absolute value)
  - Optimized scale factor: 0.972

- *Level of Reliability:* ***High (CL > 99%)***

XI. Optical Rotation Data:

- Not measured.