Electronic Supplementary Material (ESI) for Reaction Chemistry & Engineering.

Supporting Information

Integrating Reactive Distillation with Continuous Flow Processing

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Materials and methods:

Unless otherwise stated, all solvents were purchased from Fisher Scientific and used without further purification. Substrates and reagents were purchased from Fluorochem or Sigma Aldrich and used as received.

^{1}H-NMR spectra were recorded on 400 MHz instruments and are reported relative to residual solvent: $CHCl_3$ (δ 7.26 ppm). ^{13}C-NMR spectra were recorded on the same instruments (100 MHz) and are reported relative to $CHCl_3$ (δ 77.16 ppm). Data for ^{1}H-NMR are reported as follows: chemical shift (δ/ ppm) (integration, multiplicity, coupling constant (Hz)). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br. s = broad singlet, app = apparent. Data for ^{13}C-NMR are reported in terms of chemical shift (δ/ ppm) and multiplicity (C, CH, CH_2 or CH_3). DEPT-135, COSY, HSQC, HMBC and NOESY experiments were used in the structural assignment.

IR spectra were obtained by use of a Bruker Platinum spectrometer (neat, ATR sampling) with the intensities of the characteristic signals being reported as weak (w, <20% of tallest signal), medium (m, 21-70% of tallest signal) or strong (s, >71% of tallest signal).

High-resolution mass spectrometry was performed using the indicated techniques on a micromass LCT orthogonal time-of-flight mass spectrometer with leucine-enkephalin (Tyr-Gly-Phe-Leu) as an internal lock mass.

Continuous flow experiments were performed on a Vapourtec E-series system in conjunction with Omnifit glass columns.

General experimental procedures and spectroscopic data

Synthesis of imines 1: A solution of the aniline (10 mmol) and benzaldehyde (10 mmol) components was prepared in MeCN (5 M) and stirred in an open flask at 45 °C overnight. The reaction progress was monitored by ^{1}H-NMR and once complete conversion was realised the imine products were used after evaporation of the solvent directly in the next step.

Synthesis of Povarov products 3a-3i: In a 50 mL round bottom flask dicyclopentadiene (ca. 30 mL) was heated at 200 °C using a hot plate stirrer for about 30 minutes. After that time the distillate (cyclopentadiene) started to condense in the Hickman still head that was placed on top of a 10 cm long air-cooled spiral condenser. Using a peristaltic pump of the Vapourtec E-series flow reactor, the distillate was continuously withdrawn at a rate of 0.1 mL/min from the rim of the Hickman still head via a threaded cannula placed at the side port. The distillate was united with a solution of the respective imine substrate (2 M, MeCN, 0.2 mL/min) in a T-piece and directed into an Omnifit glas column (10 cm length, 0.6 cm i.d.). This column was mounted within a heating mantle on the Vapourtec reactor and maintained at 40 °C. The column was filled with a mixture of $InCl_3$ and silica gel (ca. 2-5 weight% $InCl_3$) acting as a heterogeneous catalyst bed for the Povarov reaction. As the material passed through this column a colour change to orange was noticed. The resulting material passed a back-pressure regulator before collection in a round bottom flask. After evaporation of the volatiles the crude product was purified by silica column chromatography (5-15% EtOAc in hexanes).

Rac. (3a*S*,4*R*,9b*R*)-4-(benzo[*d*][1,3]dioxol-5-yl)-8-(trifluoromethoxy)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[c]quinoline, 3a:

Appearance: Colourless solid. Yield: 867 mg (2.3 mmol, 77%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ/ppm 6.95 – 6.87 (m, 3H), 6.85 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.82 (d, *J* = 8.1 Hz, 1H), 6.58 (d, *J* = 8.6 Hz, 1H), 5.97 (s, 2H), 5.79-5.83 (m, 1H), 5.67-5.71 (m, 1H), 4.55 (d, *J* = 3.5 Hz, 1H), 4.07 (d, *J* = 7.0 Hz, 1H), 3.75 (s, 1H), 2.95 (qd, *J* = 8.9, 3.2 Hz, 1H), 2.60 (ddq, *J* = 16.6, 9.5, 2.4 Hz, 1H), 1.88 (dddd, *J* = 16.4, 8.7, 2.7, 1.5 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ/ppm 147.8 (C), 146.7 (C), 144.3 (C), 141.5 (C, q, *J* = 3 Hz), 136.4 (C), 133.3 (CH), 131.0 (CH), 127.0 (C), 121.8 (CH), 120.7 (CF_3, q, *J* = 254 Hz), 119.5 (CH), 119.4 (CH), 116.2 (CH), 108.3 (CH), 106.9 (CH), 101.0 (CH_2), 57.8 (CH), 46.3 (CH), 45.8 (CH), 31.4 (CH_2). ^{19}F-NMR ($CDCl_3$, 376 MHz) δ/ppm -58.3 (s). IR (neat, ν/cm^{-1}) 3369 (w), 2876 (w), 1400 (m), 1471 (m), 1438 (m), 1219 (s), 1204 (s), 1161 (s), 1036 (s), 932 (s), 814 (s), 729 (m), 583 (m). HRMS (TOF+) calculated for $C_{20}H_{17}NO_3F_3$ (M+H) 376.1161, found 376.1160 (Δ 0.1 ppm). Crystal data CCDC1869606: P-1; a = 9.3037(2), b = 9.9178(2), c = 10.0419(2), α = 99.975(2), β = 110.641(2), γ = 102.404(2).

Rac. (3a*S*,4*R*,9b*R*)-4-(pyridin-3-yl)-8-(trifluoromethoxy)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta-[c]quinoline, 3b:

Appearance: Brown solid. Yield: 545 mg (1.6 mmol, 82%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ/ppm 8.67 (d, *J* = 2.3 Hz, 1H), 8.56 (dd, *J* = 4.7, 1.8 Hz, 1H), 7.76 (dt, *J* = 7.9, 2.1 Hz, 1H), 7.31 (dd, *J* = 7.9, 4.8 Hz, 1H), 6.92 (d, *J* = 2.6 Hz, 1H), 6.86 (dd, *J* = 8.5, 2.7 Hz, 1H), 6.61 (d, *J* = 8.6 Hz, 1H), 5.84 – 5.79 (m, 1H), 5.71 – 5.66 (m, 1H), 4.67 (d, *J* = 3.4 Hz, 1H), 4.11 (dd, *J* = 8.8, 2.1 Hz, 1H), 3.81 (d, *J* = 1.9 Hz, 1H), 3.05 – 2.94 (m, 1H), 2.61 (ddq, *J* = 16.5, 9.5, 2.4 Hz, 1H), 1.88 – 1.80 (m, 1H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ/ppm 148.9 (br CH), 148.4 (br CH), 143.8 (C), 141.9 (C, q, *J* = 3 Hz), 138.0 (br C), 134.0 (CH), 133.3 (CH), 130.7 (CH), 126.9 (C), 123.8 (br CH), 121.8 (CH), 120.6 (CF_3, q, *J* = 254 Hz), 119.5 (CH), 116.5 (CH), 56.1 (CH), 46.2 (CH), 45.4 (CH), 31.3 (CH_2). IR (neat, ν/cm^{-1}) 3218 (m), 2905 (w), 1496 (m), 1249 (s), 1200 (s), 1147 (s), 905 (m), 813 (m), 713 (s), 690 (m), 599 (m). HRMS (TOF+) calculated for $C_{18}H_{16}N_2OF_3$ (M+H) 333.1215, found 333.1212 (Δ 0.8 ppm).

Rac. (3a*S*,4*R*,9b*R*)-4-(3,5-dichlorophenyl)-8-(trifluoromethoxy)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[c]quinoline, 3c:

Appearance: Colourless solid. Yield: 898 mg (2.3 mmol, 75%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ/ppm 7.31 (d, *J* = 1.9 Hz, 2H), 7.29 (app t, *J* = 1.9 Hz, 1H), 6.90 (s, 1H), 6.86 (d, *J* = 8.6 Hz, 1H), 6.60 (d, *J* = 8.6 Hz, 1H), 5.84 – 5.78 (m, 1H), 5.70 – 5.64 (m, 1H), 4.57 (d, *J* = 3.3 Hz, 1H), 4.07 (dd, *J* = 8.8, 2.2 Hz, 1H), 3.73 (s, 1H), 2.96 (qd, *J* = 9.1, 3.2 Hz, 1H), 2.53 (ddq, *J* = 16.4, 9.4, 2.4 Hz, 1H), 1.82 (ddt, *J* = 16.1, 8.7, 2.0 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ/ppm 145.9 (C), 143.4 (C), 141.9 (C, q, *J* = 2 Hz), 135.2 (2C), 133.2 (CH), 130.7 (CH), 127.6 (CH), 126.8 (C), 125.0 (2CH), 121.8 (CH), 120.6 (CF_3, q, *J* = 254 Hz), 119.6 (CH), 116.6 (CH), 57.3 (CH), 46.1 (CH), 45.3 (CH), 31.3 (CH_2). ^{19}F-NMR ($CDCl_3$, 376 MHz) δ/ppm -58.3 (s). IR (neat, ν/cm^{-1}) 3365 (w), 2918 (w), 2848 (w), 1591 (m), 1568 (m), 1502 (m), 1474 (m), 1430 (m), 1345 (s), 1206 (s), 1144 (s), 859 (s), 800 (s), 718 (m), 698 (s), 606 (m). HRMS (TOF+) calculated for $C_{19}H_{15}NOF_3Cl_2$ (M+H) 400.0483, found 400.0489 (Δ 1.6 ppm).

Rac. (3a*S*,4*R*,9b*R*)-4-(4-bromophenyl)-8-(trifluoromethoxy)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[c]quinoline, 3d:

Appearance: Colourless solid. Yield: 1067 mg (2.6 mmol, 87%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ/ppm 7.50 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 6.91 (d, *J* = 2.5 Hz, 1H), 6.89 – 6.80 (m, 1H), 6.59 (d, *J* = 8.7 Hz, 1H), 5.79-5.83 (m, 1H), 5.67-5.71 (m, 1H), 4.58 (d, *J* = 3.3 Hz, 1H), 4.08 (dd, *J* = 8.8, 2.3 Hz, 1H), 3.75 (s, 1H), 2.96 (qdd, *J* = 8.8, 3.4, 1.8 Hz, 1H), 2.56 (ddq, *J* = 16.5, 9.4, 2.4 Hz, 1H), 1.80 (dddd, *J* = 16.4, 8.7, 2.7, 1.5 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ/ppm 144.0 (C), 141.7 (C, q, *J* = 2 Hz), 141.4 (C), 133.3 (CH), 131.7 (2CH), 130.8 (CH), 128.1 (2CH), 127.0 (C), 121.8 (CH), 121.1 (C), 120.7 (CF_3, q, *J* = 254 Hz), 119.5 (CH), 116.4 (CH), 57.5 (CH), 46.2 (CH), 45.5 (CH), 31.3 (CH_2). ^{19}F-NMR ($CDCl_3$, 376 MHz) δ/ppm -58.3 (s). IR (neat, ν/cm^{-1}) 3367 (w), 3052 (w), 2929 (w), 1501 (m), 1470 (m), 1242 (s), 1222 (s), 1208 (s), 1151 (s), 1072 (m), 815 (m), 700 (m), 601 (w), 504 (w). HRMS (TOF+) calculated for $C_{19}H_{16}NOBrF_3$ (M+H) 410.0367, found 410.0358 (Δ 2.3 ppm).

Rac. (3a*S*,4*R*,9b*R*)-8-isopropyl-4-phenyl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[c]quinoline, 3e:

Appearance: Yellow oil. Yield: 722 mg (2.5 mmol, 83%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ/ppm 7.47 – 7.42 (m, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.32 – 7.27 (m, 1H), 6.93 (d, *J* = 2.1 Hz, 1H), 6.87 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.58 (d, *J* = 8.2 Hz, 1H), 5.89 – 5.83 (m, 1H), 5.68 – 5.64 (m, 1H), 4.63 (d, *J* = 3.3 Hz, 1H), 4.11 (d, *J* = 8.8 Hz, 1H), 3.67 (s, 1H), 3.01 (qd, *J* = 9.0, 3.3 Hz, 1H), 2.81 (hept, *J* = 6.8 Hz, 1H), 2.65 (ddq, *J* = 16.6, 9.4, 2.5 Hz, 1H), 1.81 (dddd, *J* = 16.4, 8.7, 2.7, 1.5 Hz, 1H), 1.23 (d, *J* = 1.9 Hz, 3H), 1.21 (d, *J* = 1.8 Hz, 3H). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ/ppm 143.4 (C), 143.0 (C), 139.6 (C), 134.0 (CH), 130.3 (CH), 128.4 (2CH), 127.1 (CH), 126.8 (CH), 126.5 (2CH), 125.8 (C), 124.3 (CH), 115.8 (CH), 58.2 (CH), 46.5 (CH), 46.0 (CH), 33.3 (CH), 31.4 (CH_2), 24.3 (CH_3), 24.2 (CH_3). IR (neat, ν/cm^{-1}) 3354 (w), 3049 (w), 2956 (m), 2925 (m), 1614 (m), 1506 (s), 1460 (s), 1334 (m), 1261 (m), 1229 (m), 816 (s), 739 (m), 701 (s), 603 (m). HRMS (EI+) calculated for $C_{21}H_{23}N$ (M+H) 289.1830, found 289.1831 (Δ 0.3 ppm).

Rac. (3a*S*,4*R*,9b*R*)-4-(3,5-dichlorophenyl)-8-isopropyl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta-[c]quinoline, 3f:

Appearance: Light yellow solid. Yield: 858 mg (2.4 mmol, 80%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ/ppm 7.35 (d, *J* = 1.8 Hz, 2H), 7.30 (t, *J* = 1.9 Hz, 1H), 6.93 (d, *J* = 2.1 Hz, 1H), 6.90 (dd, *J* = 8.1, 2.1 Hz, 1H), 6.61 (d, *J* = 8.1 Hz, 1H), 5.91 – 5.85 (m, 1H), 5.69 – 5.64 (m, 1H), 4.58 (d, *J* = 3.4 Hz, 1H), 4.13 – 4.05 (m, 1H), 3.60 (s, 1H), 2.97 (qd, *J* = 9.0, 3.3 Hz, 1H), 2.82 (hept, *J* = 7.0 Hz, 1H), 2.58 (ddq, *J* = 16.5, 9.6, 2.4 Hz, 1H), 1.82 (ddt, *J* = 16.0, 8.7, 2.2 Hz, 1H), 1.24 (d, *J* = 2.0 Hz, 3H), 1.22 (d, *J* = 1.9 Hz, 3H). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ/ppm 146.6 (C), 142.5 (C), 140.2 (C), 135.1 (2C), 134.0 (CH), 130.1 (CH), 127.4 (CH), 126.8 (CH), 125.6 (C), 125.0 (2CH), 124.4 (CH), 116.1 (CH), 57.4 (CH), 46.3 (CH), 45.7 (CH), 33.3 (CH), 31.2 (CH_2), 24.3 (CH_3), 24.1 (CH_3). IR (neat, ν/cm^{-1}) 3362 (w), 3051 (w), 2956 (m), 2926 (w), 1590 (m), 1567 (s), 1507 (s), 1461 (m), 1407 (s), 1320 (m), 1285 (m), 859 (m),

801 (m), 744 (s). HRMS (TOF+) calculated for $C_{21}H_{22}NCl_2$ (M+H) 358.1129, found 358.1126 (Δ 0.9 ppm).

Rac. (3a*S*,4*R*,9b*R*)-4-(4-bromophenyl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[c]quinoline, 3g:

Appearance: Colourless solid. Yield: 1010 mg (3.1 mmol, 78%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ/ppm 7.52 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.08 (d, *J* = 7.5 Hz, 1H), 7.01 (td, *J* = 7.6, 1.5 Hz, 1H), 6.79 (td, *J* = 7.5, 1.4 Hz, 1H), 6.64 (dd, *J* = 7.8, 1.2 Hz, 1H), 5.90 – 5.84 (m, 1H), 5.69 – 5.64 (m, 1H), 4.61 (d, *J* = 3.4 Hz, 1H), 4.12 (dd, *J* = 8.8, 2.1 Hz, 1H), 3.70 (s, 1H), 2.98 (qd, *J* = 9.0, 3.4 Hz, 1H), 2.61 (ddq, *J* = 16.5, 9.4, 2.4 Hz, 1H), 1.81 (ddt, *J* = 16.2, 8.8, 2.1 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ/ppm 145.2 (C), 141.9 (C), 134.0 (CH), 131.6 (2CH), 130.2 (CH), 129.0 (CH), 128.2 (2CH), 126.4 (CH), 126.0 (C), 120.9 (C), 119.4 (CH), 116.0 (CH), 57.5 (CH), 46.2 (CH), 45.9 (CH), 31.4 (CH_2). IR (neat, ν/cm^{-1}) 3360 (w), 3038 (w), 2927 (w), 1603 (w), 1588 (m), 1471 (s), 1264 (m), 1069 (m), 1010 (m), 808 (s), 752 (s), 691 (s), 503 (s). HRMS (TOF+) calculated for $C_{18}H_{17}NBr$ (M+H) 326.0544, found 326.0543 (Δ 0.4 ppm).

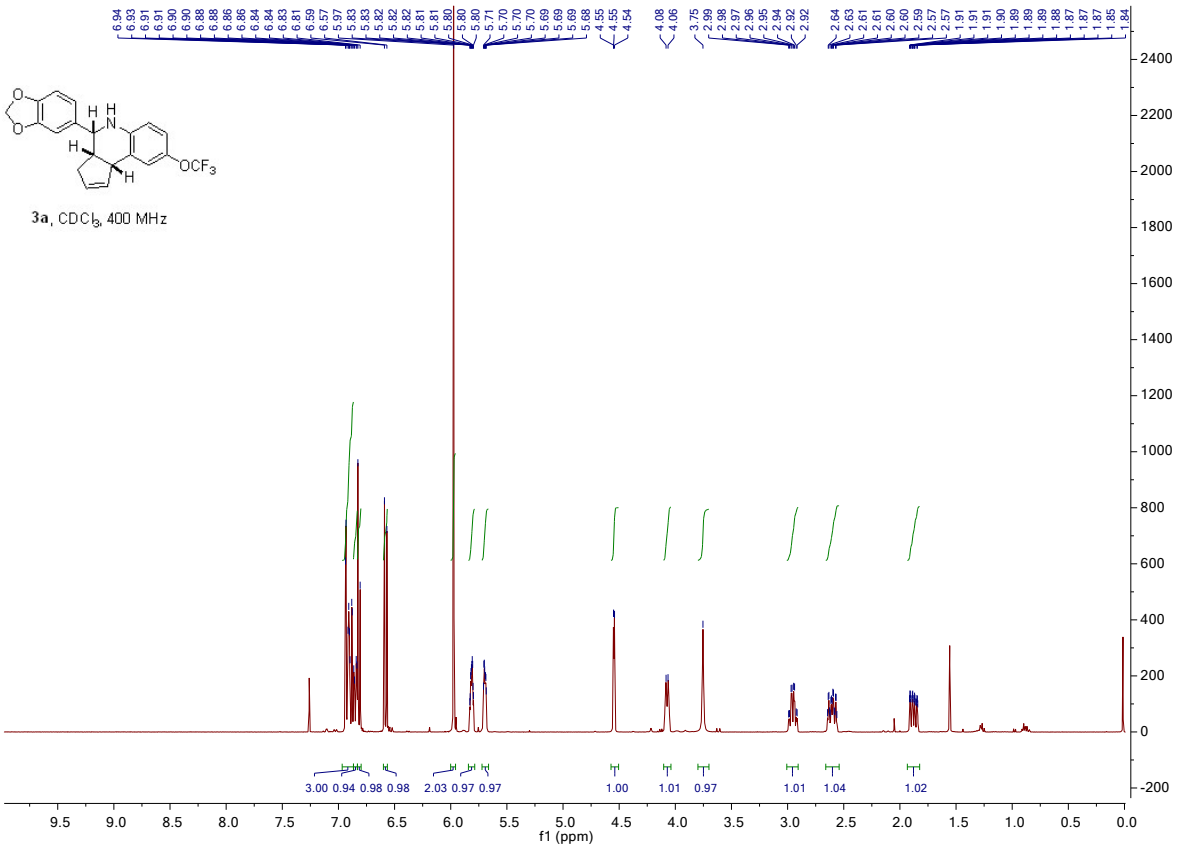
Rac. (3a*S*,4*R*,9b*R*)-4-(2-chlorophenyl)-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[c]quinoline, 3h:

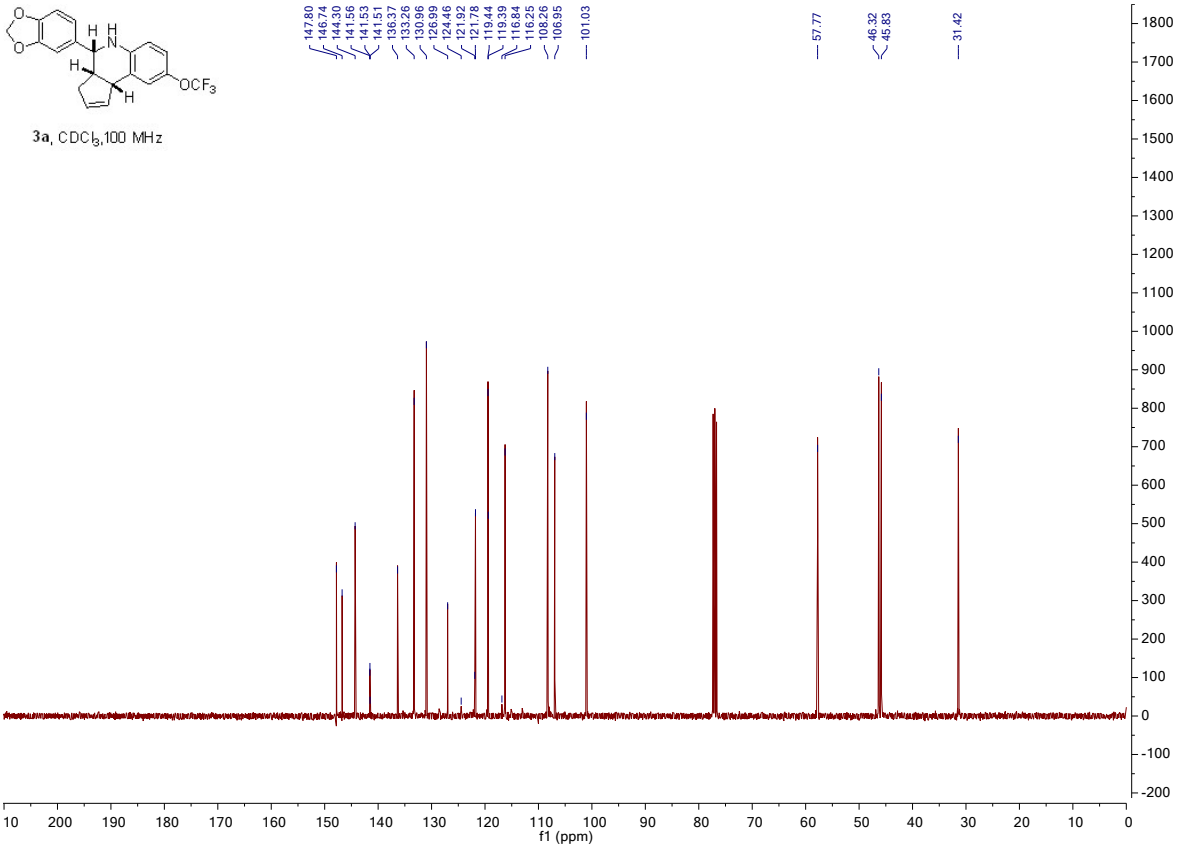
Appearance: Off-white solid. Yield: 760 mg (2.7 mmol, 90%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ/ppm 7.69 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.40 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.33 (td, *J* = 7.6, 1.4 Hz, 1H), 7.28 – 7.22 (m, 1H), 7.10 (d, *J* = 7.5 Hz, 1H), 7.02 (td, *J* = 7.6, 1.6 Hz, 1H), 6.79 (td, *J* = 7.4, 1.2 Hz, 1H), 6.65 (dd, *J* = 7.9, 1.2 Hz, 1H), 5.91 – 5.85 (m, 1H), 5.67 (dd, *J* = 5.4, 2.3 Hz, 1H), 5.06 (d, *J* = 3.4 Hz, 1H), 4.17 (dd, *J* = 9.0, 2.3 Hz, 1H), 3.60 (s, 1H), 3.29 (qd, *J* = 9.1, 3.2 Hz, 1H), 2.63 (ddq, *J* = 16.4, 9.3, 2.5 Hz, 1H), 1.77 (ddt, *J* = 16.1, 8.6, 2.1 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ/ppm 145.5 (C), 139.9 (C), 134.1 (CH), 132.8 (C), 130.2 (CH), 129.6 (CH), 129.0 (CH), 128.2 (CH), 127.7 (CH), 126.9 (CH), 126.33 (CH), 126.28 (C), 119.4 (CH), 116.1 (CH), 54.5 (CH), 46.2 (CH), 41.9 (CH), 31.5 (CH_2). IR (neat, ν/cm^{-1}) 3362 (w), 3052 (w), 2933 (w), 1588 (w), 1474 (m), 1262 (m), 1032 (m), 1004 (m), 748 (s), 720 (m), 705 (s), 613 (m), 466 (m). HRMS (TOF+) calculated for $C_{18}H_{17}NCl$ (M+H) 282.1050, found 282.1051 (Δ 0.5 ppm).

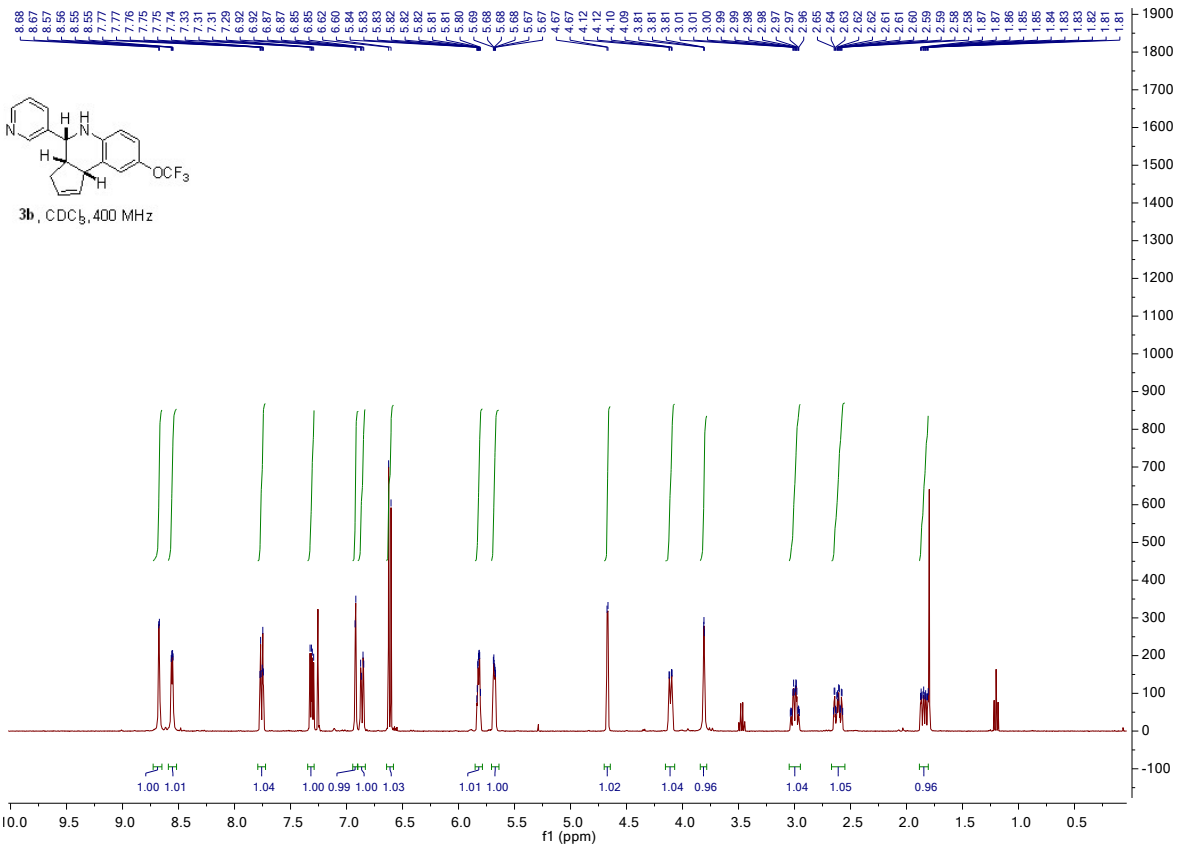
Rac. (3a*S*,4*R*,9b*R*)-4-(2-chlorophenyl)-8-isopropyl-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[c]-quinoline, 3i:

Appearance: Yellow oil. Yield: 833 mg (2.6 mmol, 86%). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ/ppm 7.69 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.39 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.32 (td, *J* = 7.6, 1.4 Hz, 1H), 7.23 (td, *J* = 7.7, 1.8 Hz, 1H), 6.95 (d, *J* = 2.1 Hz, 1H), 6.89 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 5.91 – 5.84 (m, 1H), 5.68 – 5.63 (m, 1H), 5.03 (d, *J* = 3.1 Hz, 1H), 4.14 (dd, *J* = 9.0, 2.3 Hz, 1H), 3.51 (s, 1H), 3.26 (qd, *J* = 9.1, 3.2 Hz, 1H), 2.82 (hept, *J* = 6.9 Hz, 1H), 2.63 (ddq, *J* = 16.5, 9.5, 2.4 Hz, 1H), 1.75 (ddt, *J* = 16.1, 8.8, 2.1 Hz, 1H), 1.24 (d, *J* = 2.0 Hz, 3H), 1.23 (d, *J* = 2.0 Hz, 3H). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ/ppm 143.3 (C), 140.0 (C), 139.9 (C), 134.1 (CH), 132.8 (C), 130.2 (CH), 129.6 (CH), 128.1 (CH), 127.7 (CH), 126.9 (CH), 126.8 (CH), 126.0 (C), 124.3 (CH), 116.0 (CH), 54.6 (CH), 46.3 (CH), 41.9 (CH), 33.4 (CH), 31.4 (CH_2), 24.3 (CH_3), 24.2 (CH_3). IR (neat, ν/cm^{-1}) 3359 (w), 3052 (w), 2957 (m), 1614 (w), 1571 (s), 1504 (m), 1290 (m), 1051 (m), 1036 (m), 906 (s), 817 (s), 726 (s), 693 (s), 602 (m). HRMS (TOF+) calculated for $C_{21}H_{23}NCl$ (M+H) 324.1519, found 324.1512 (Δ 2.2 ppm).

Copies of NMR spectra



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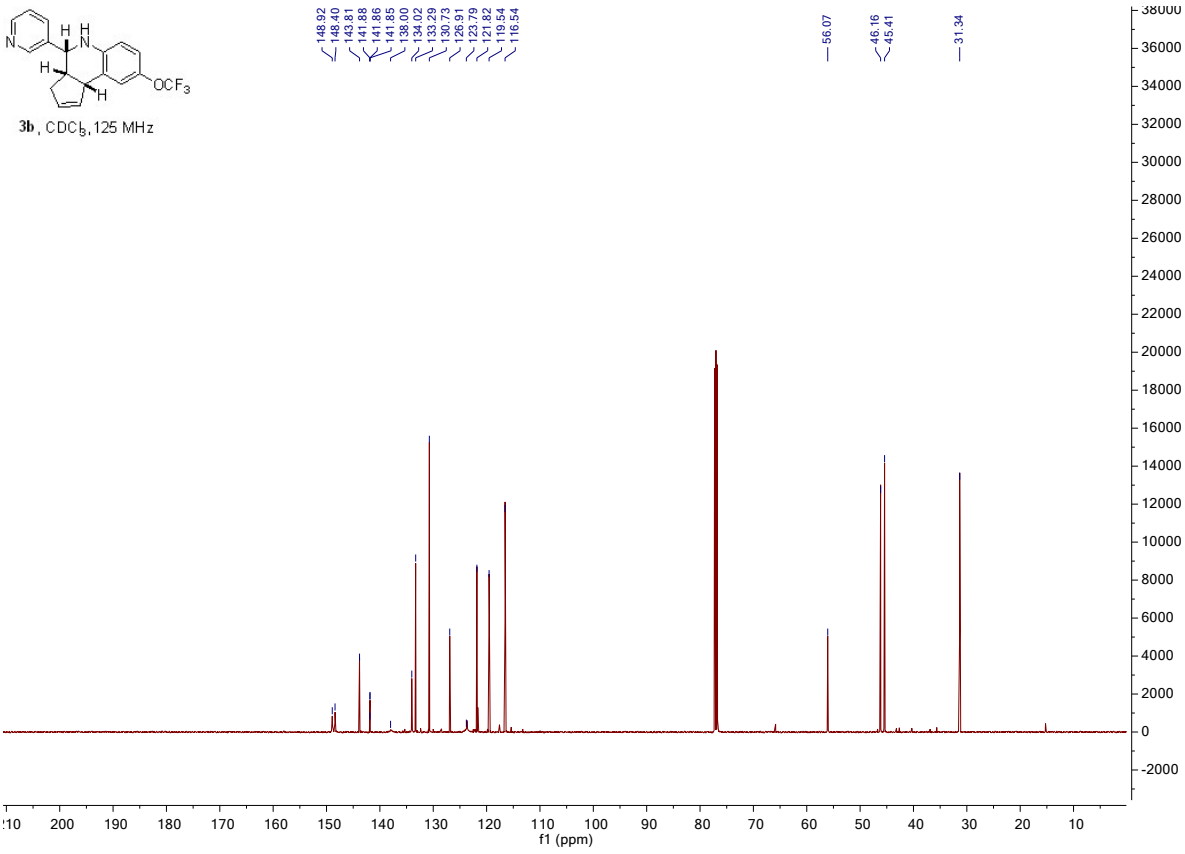
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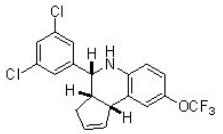

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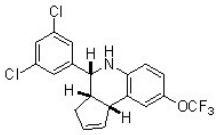

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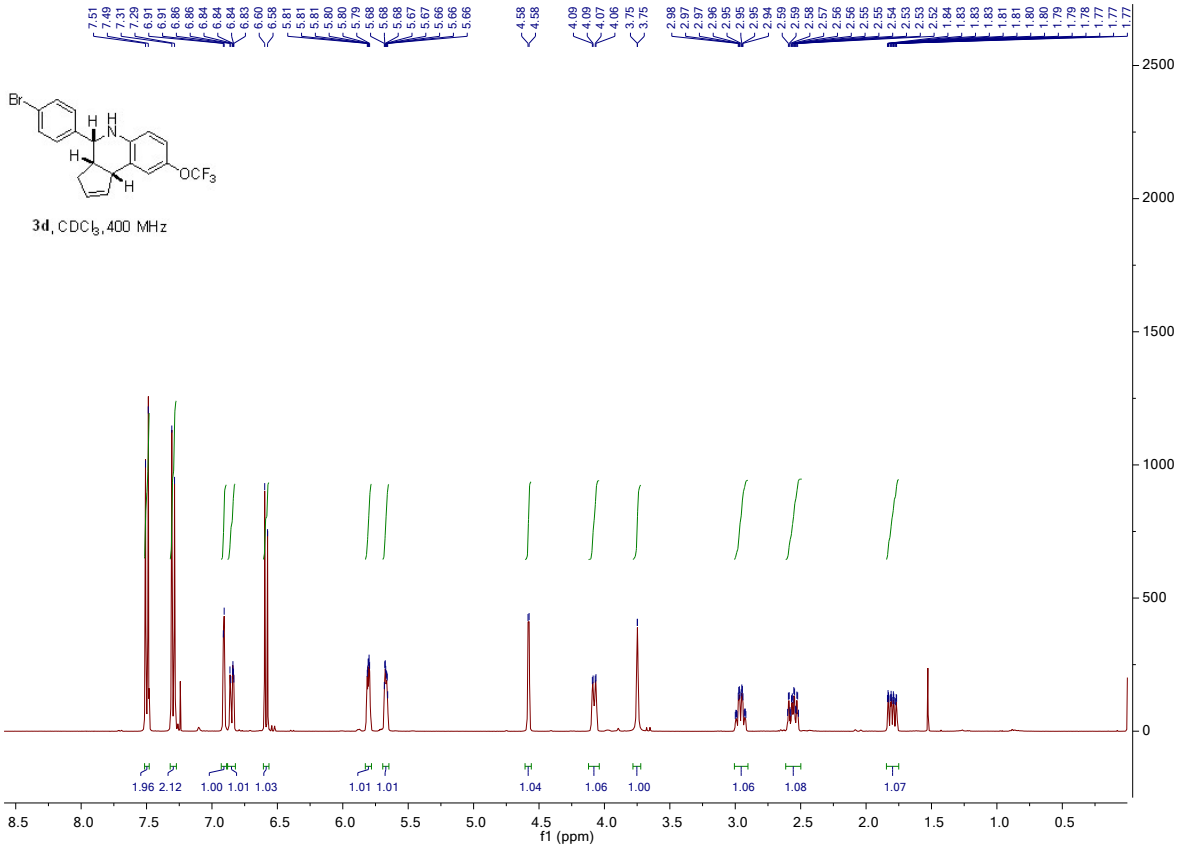
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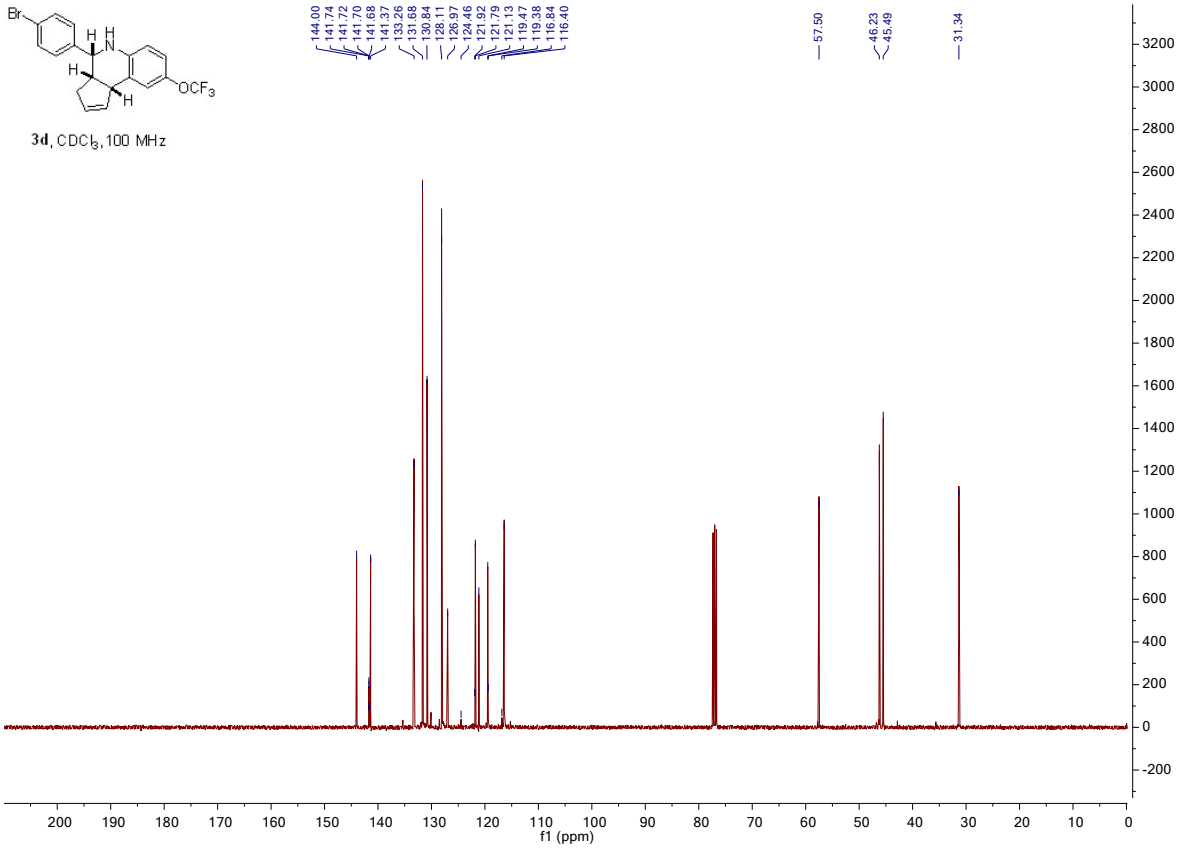
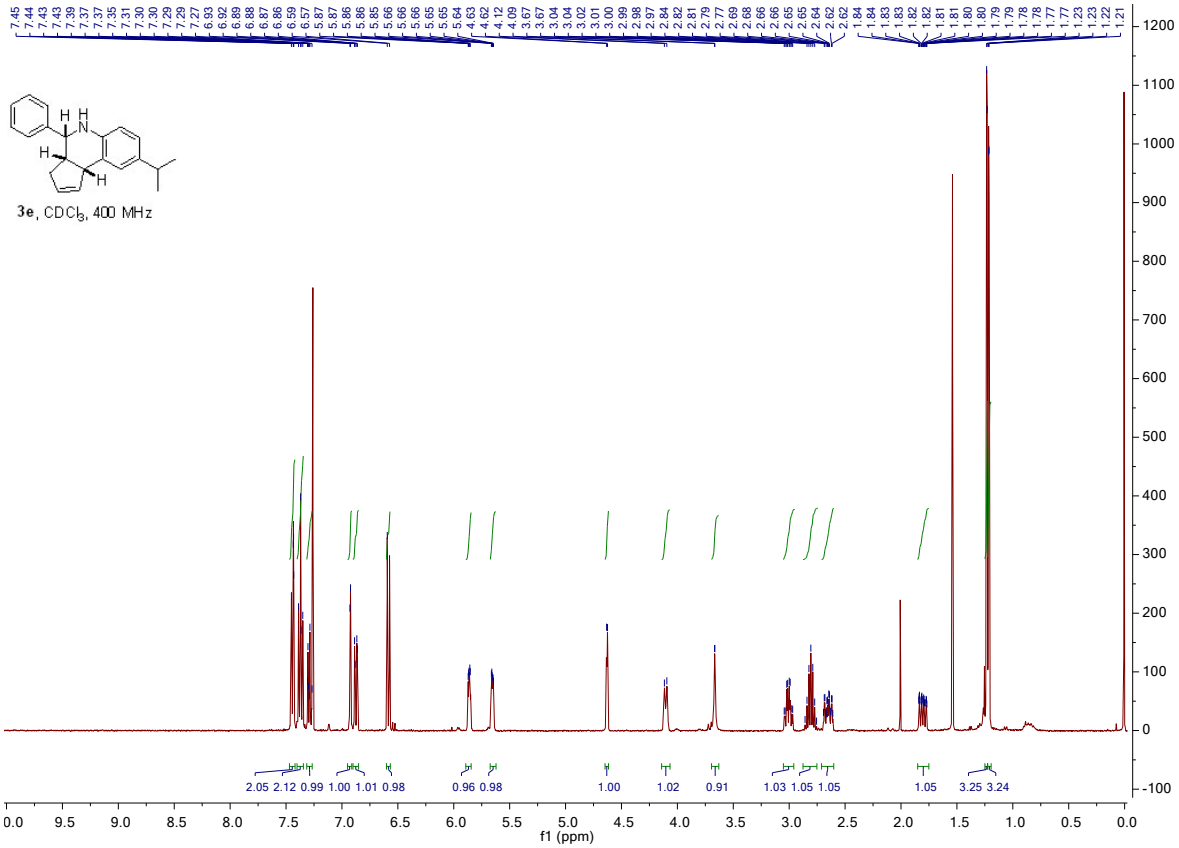
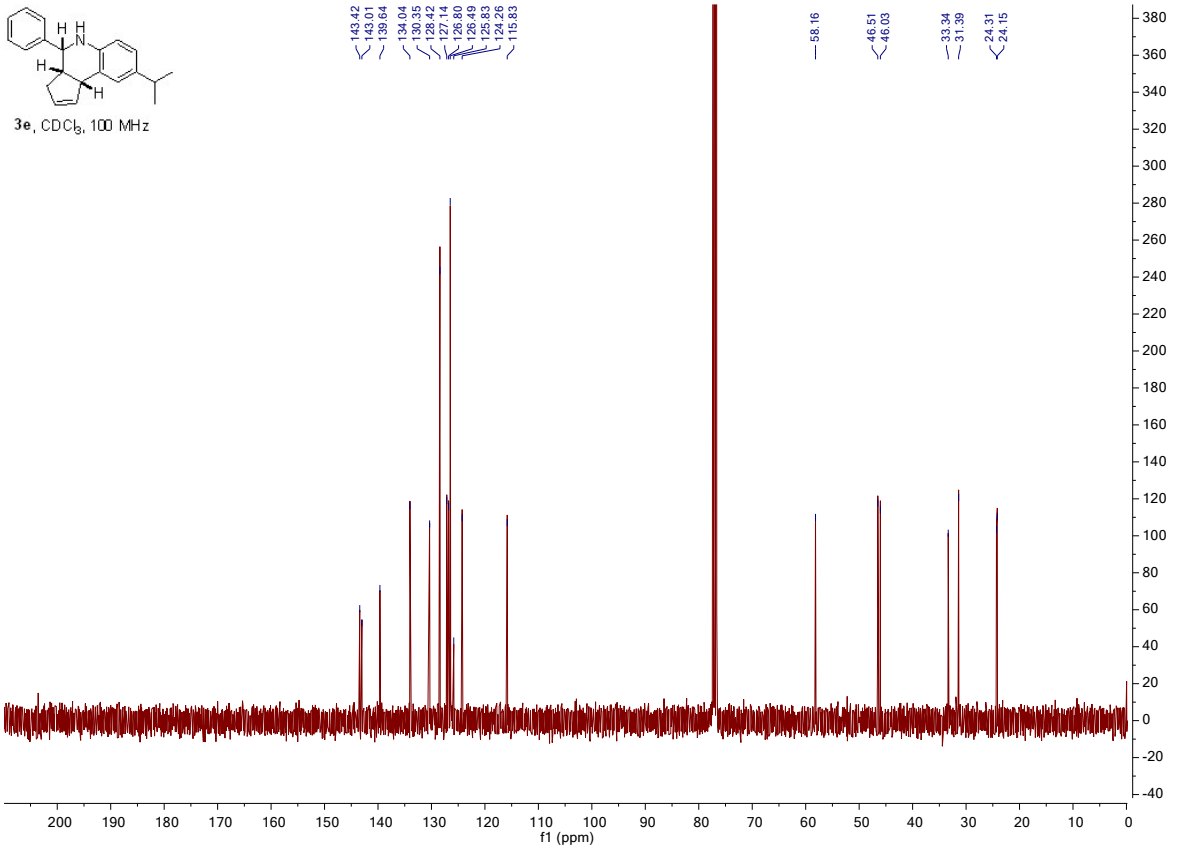
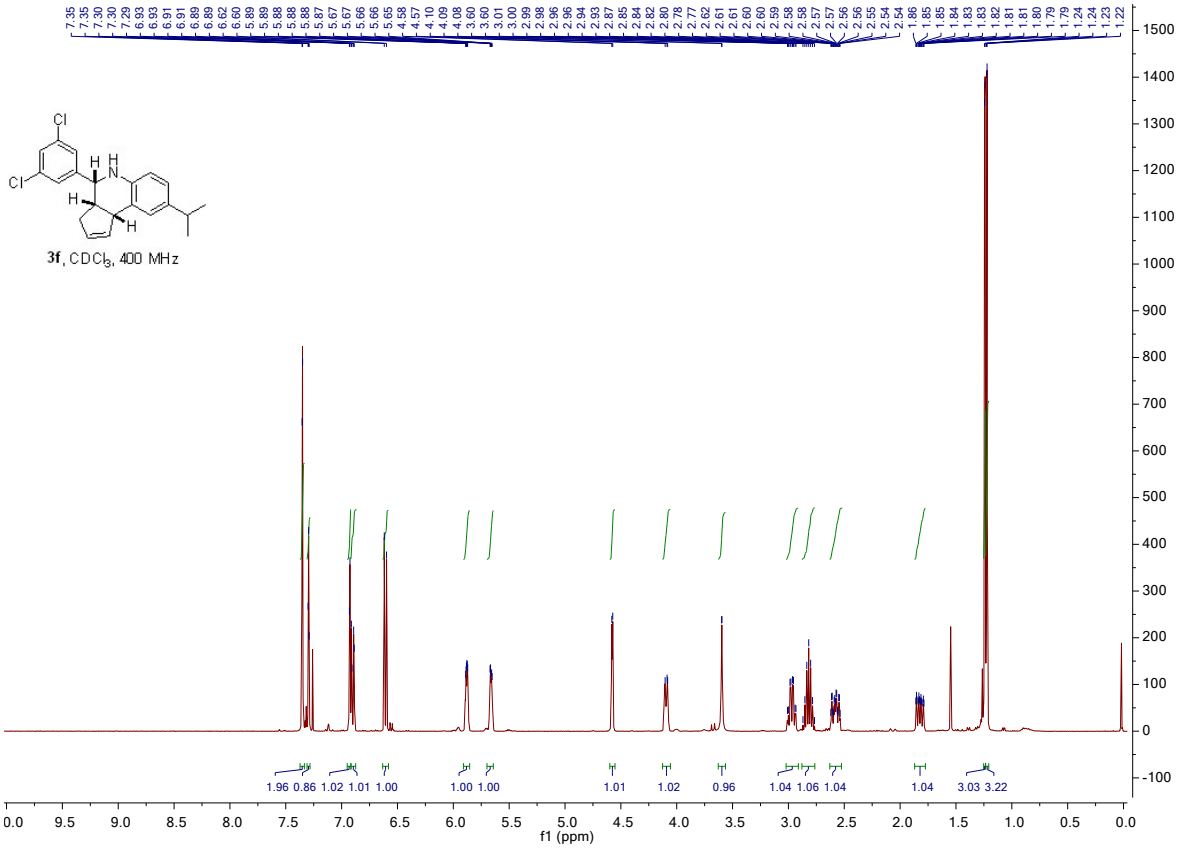
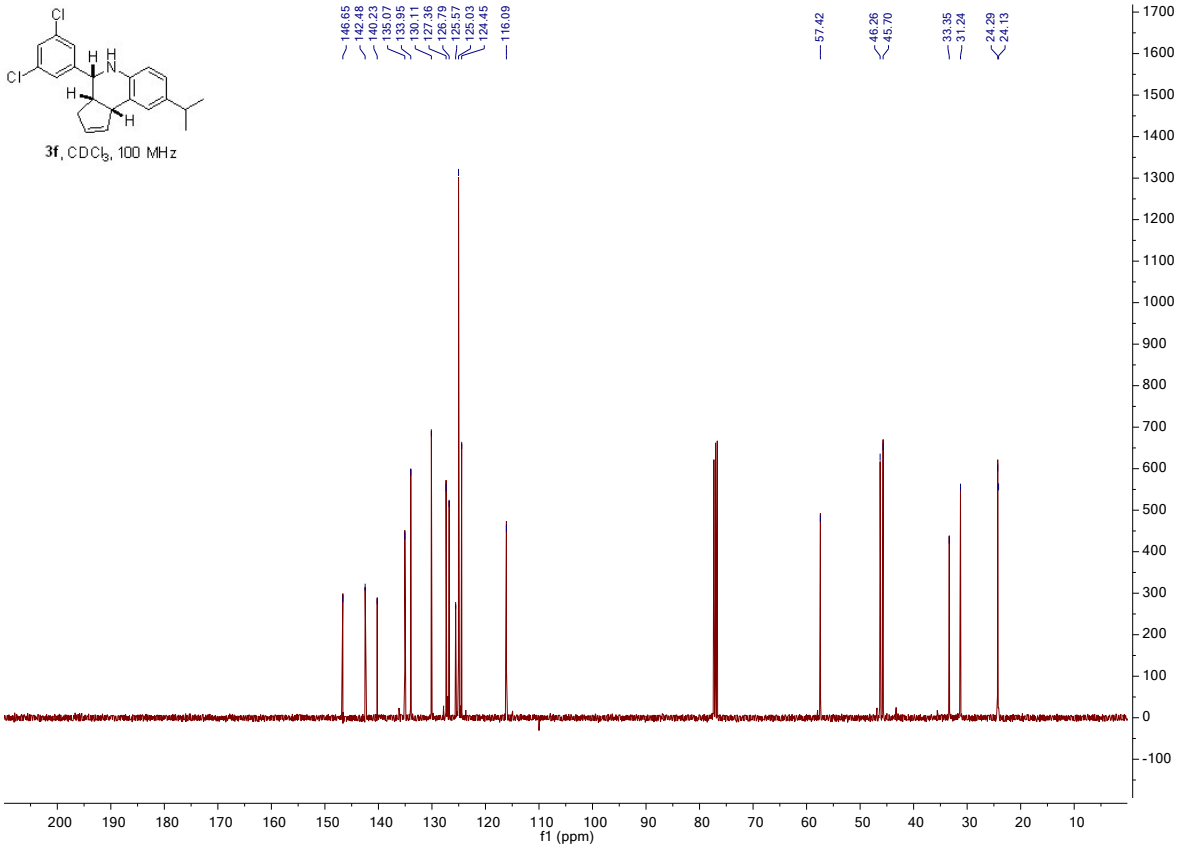
1.96 2.12 1.00 1.01 1.03 1.01 1.01 1.04 1.06 1.00 1.06 1.08 1.07
f1 (ppm)

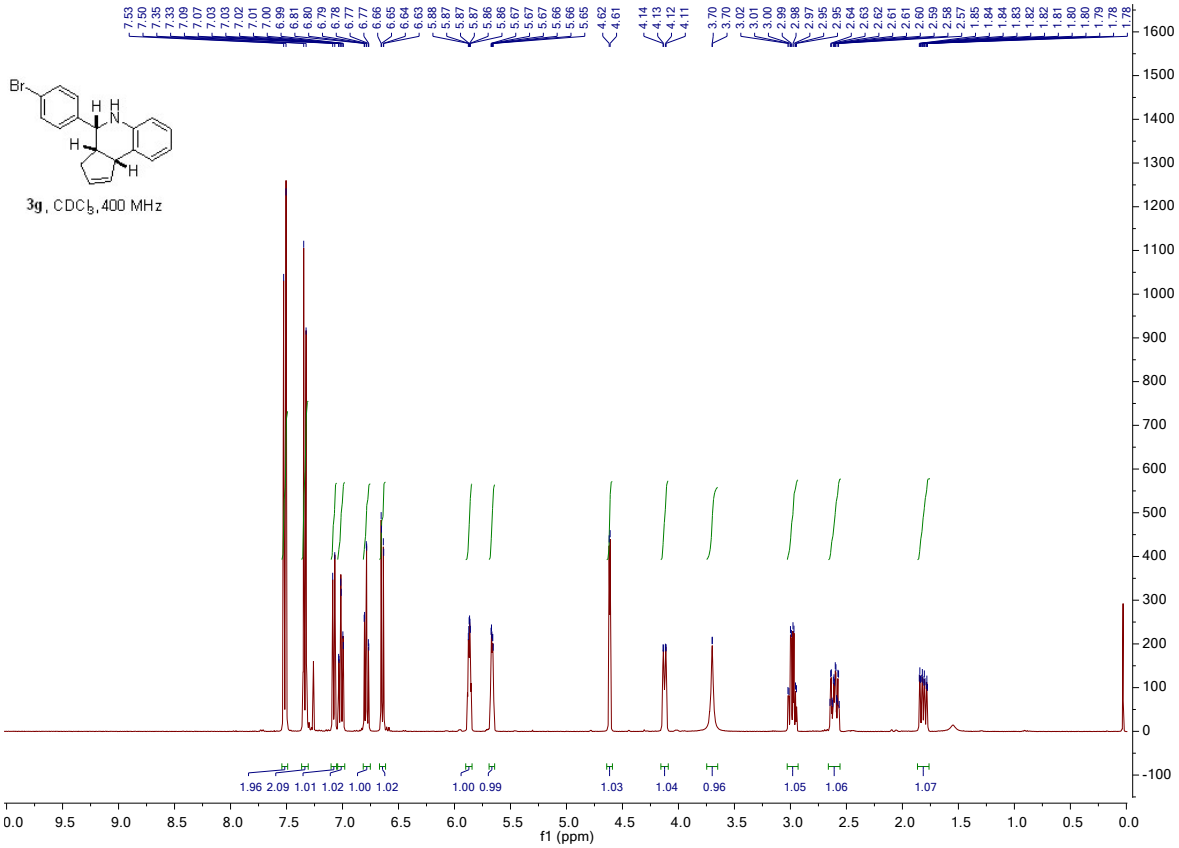

144.00 141.74 141.72 141.70 141.68 141.37 133.26 131.68 130.84 128.11 126.97 124.46 121.92 121.79 121.13 119.47 119.38 116.84 116.40 57.50 46.23 45.49 31.34
Br
H
H
N
H
H
OCF3
3d, CDCl3, 100 MHz
f1 (ppm)

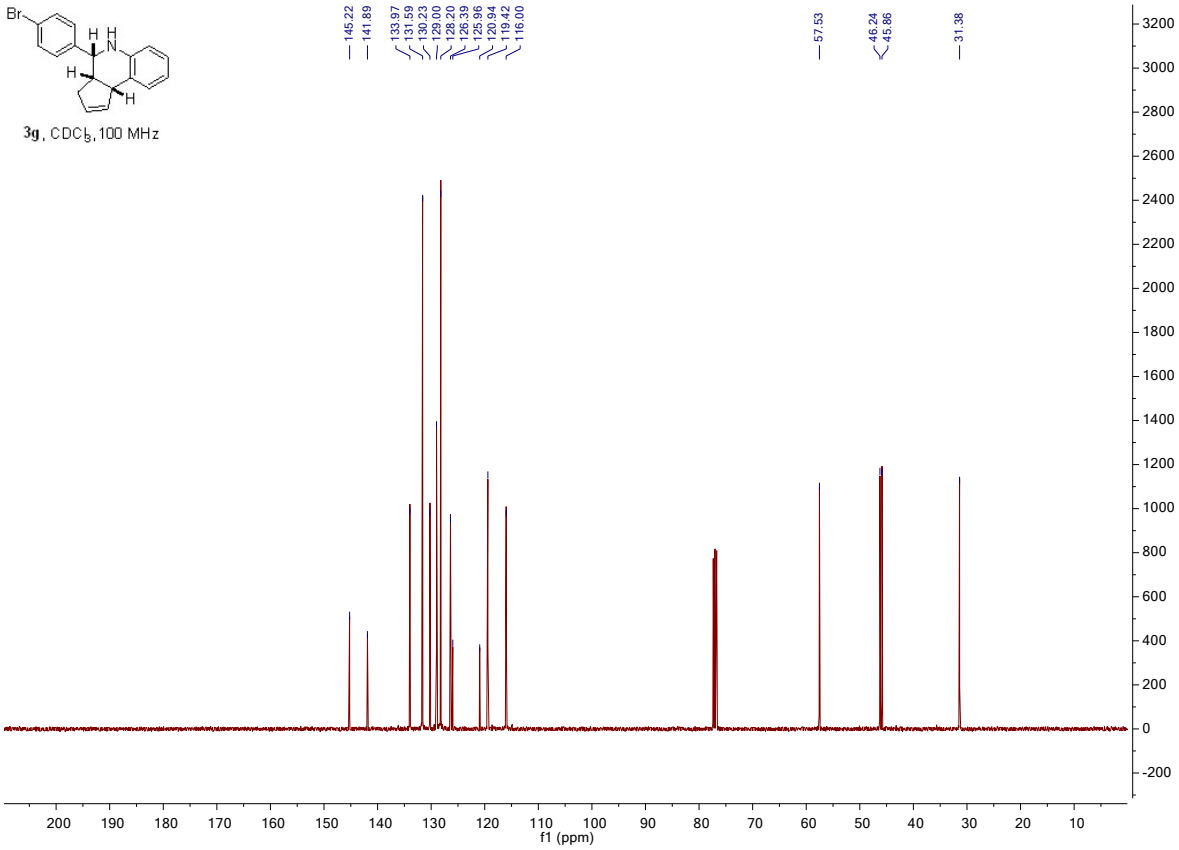

3e, CDCl3, 400 MHz
2.05 2.12 0.99 1.00 1.01 0.98 0.96 0.98 1.00 1.02 0.91 1.03 1.05 1.05 1.05 3.25 3.24
f1 (ppm)

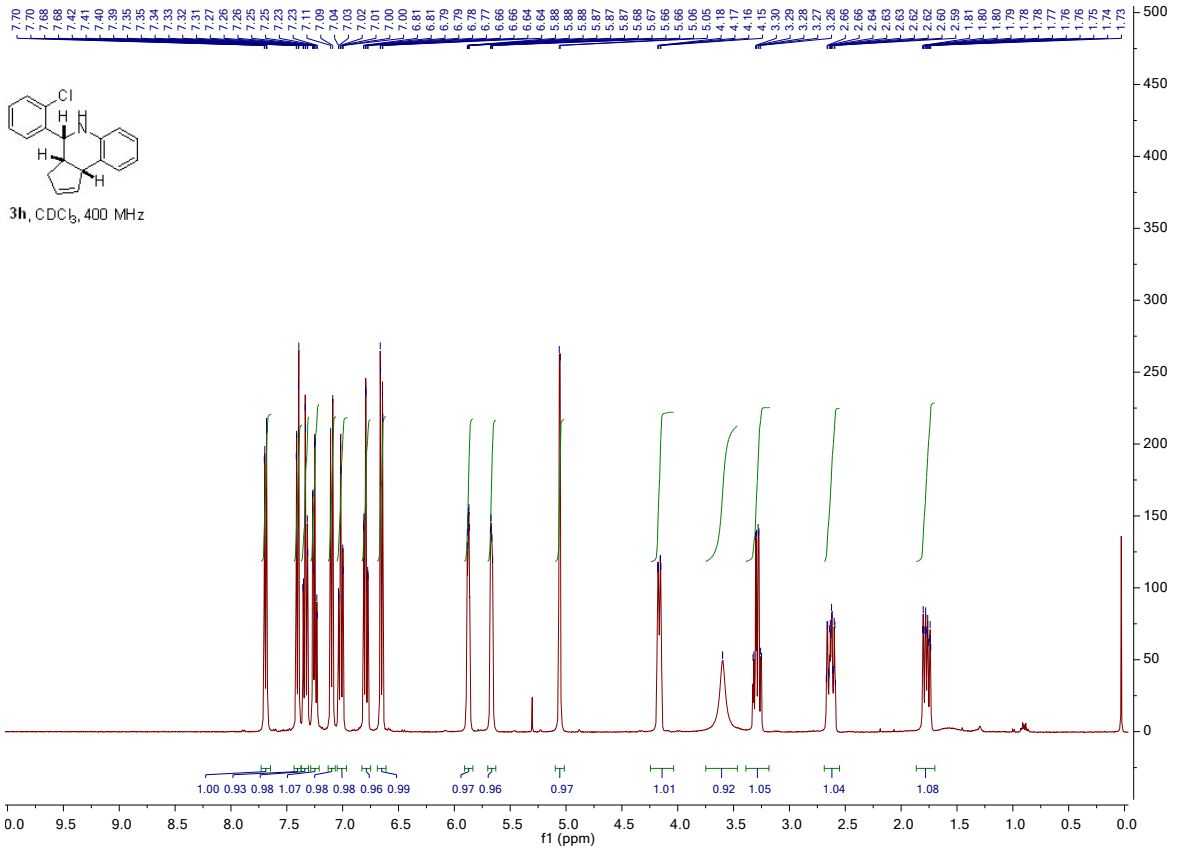

3e, CDCl3, 100 MHz
143.42
143.01
139.64
134.04
130.35
128.42
127.14
126.80
126.49
125.83
124.26
115.83
58.16
46.51
46.03
33.34
31.39
24.31
24.15
f1 (ppm)

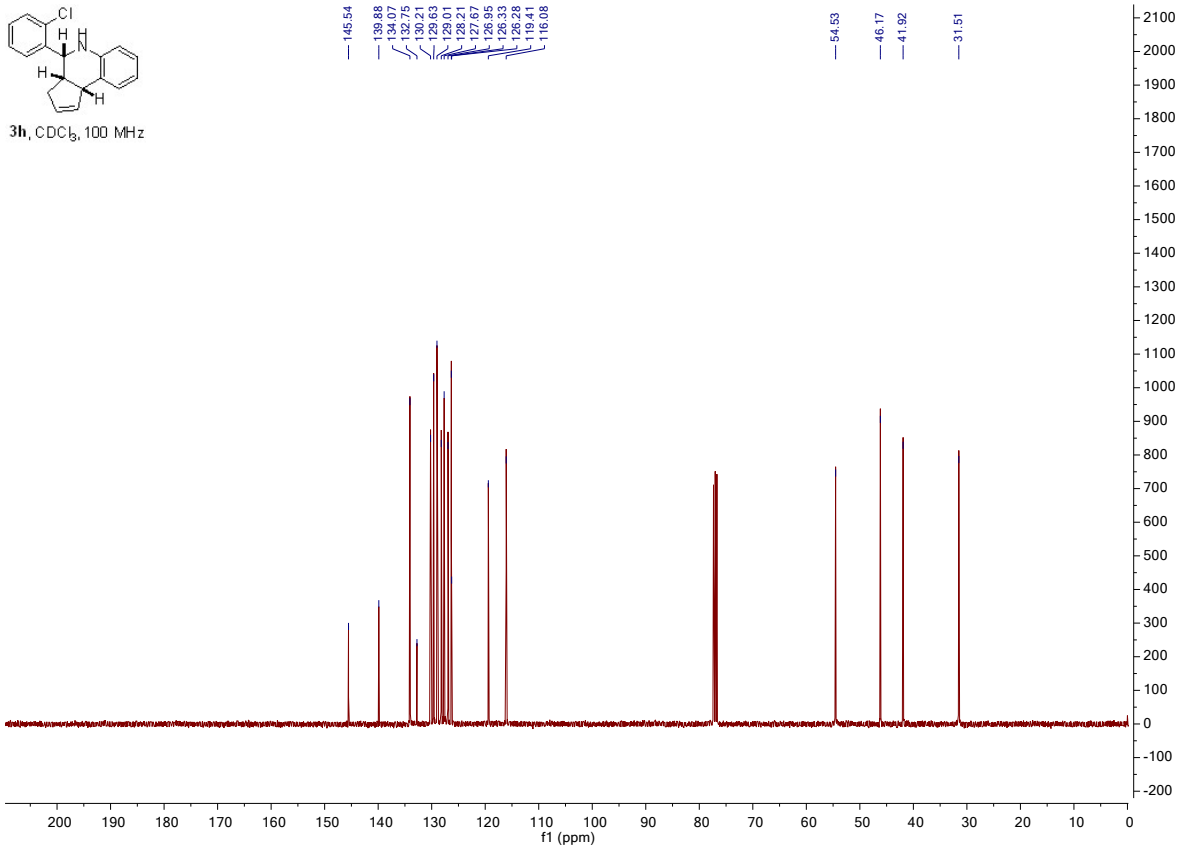

Cl
Cl
H
H
N
H
H
3f, CDCl3, 400 MHz
7.35 7.35 7.30 7.30 7.29 6.93 6.93 6.91 6.91 6.89 6.89 6.62 6.60 5.89 5.89 5.88 5.88 5.87 5.67 5.66 5.66 5.65 4.58 4.57 4.10 4.09 4.08 3.60 3.60 3.01 3.00 2.99 2.98 2.96 2.94 2.93 2.87 2.85 2.84 2.82 2.80 2.78 2.77 2.62 2.61 2.61 2.60 2.60 2.59 2.58 2.58 2.57 2.57 2.56 2.56 2.55 2.54 2.54 1.86 1.85 1.85 1.84 1.83 1.83 1.82 1.81 1.81 1.80 1.79 1.79 1.24 1.24 1.23 1.22
1.96 0.86 1.02 1.01 1.00 1.00 1.00 1.01 1.02 0.96 1.04 1.06 1.04 1.04 3.03 3.22
f1 (ppm)

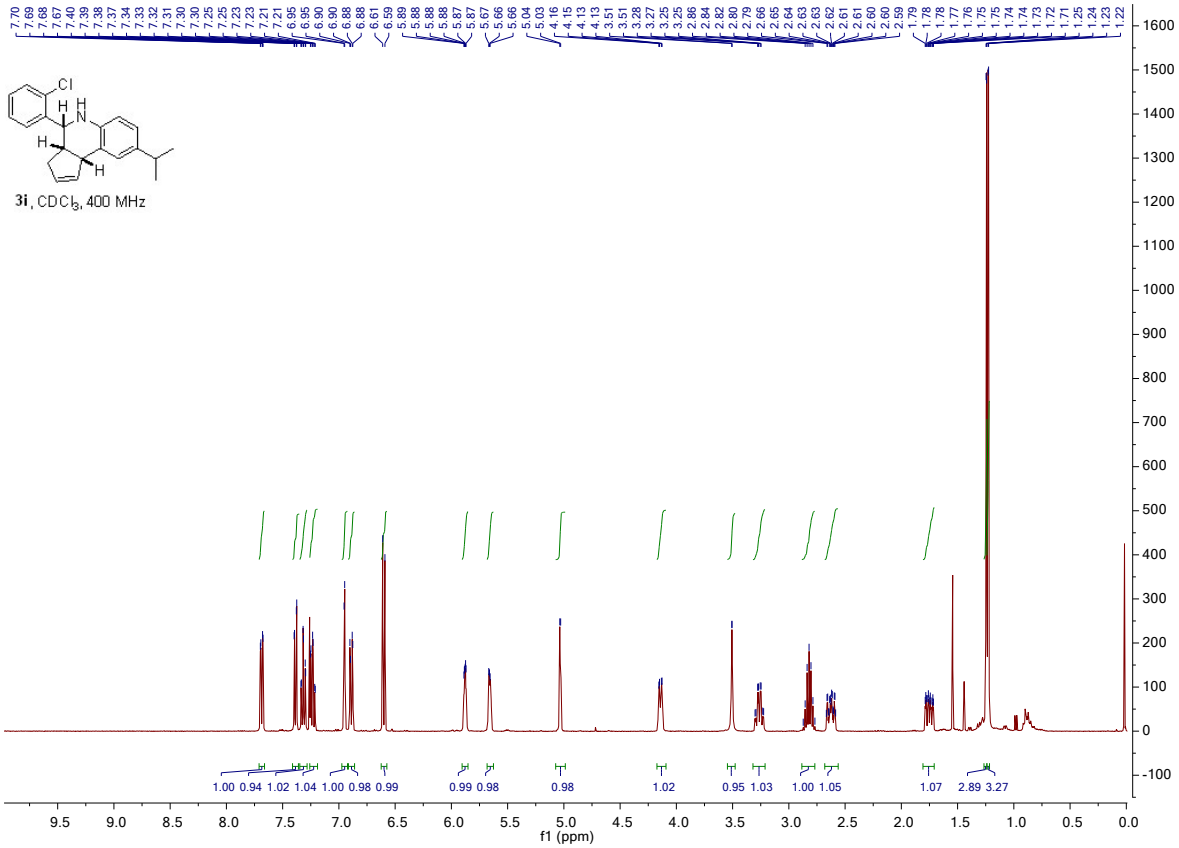

Cl
Cl
H
H
N
H
H
3f, CDCl3, 100 MHz
146.65 142.48 140.23 135.07 133.95 130.11 127.36 126.79 125.77 125.03 124.45 116.09 57.42 46.26 45.70 33.35 31.24 24.29 24.13
f1 (ppm)

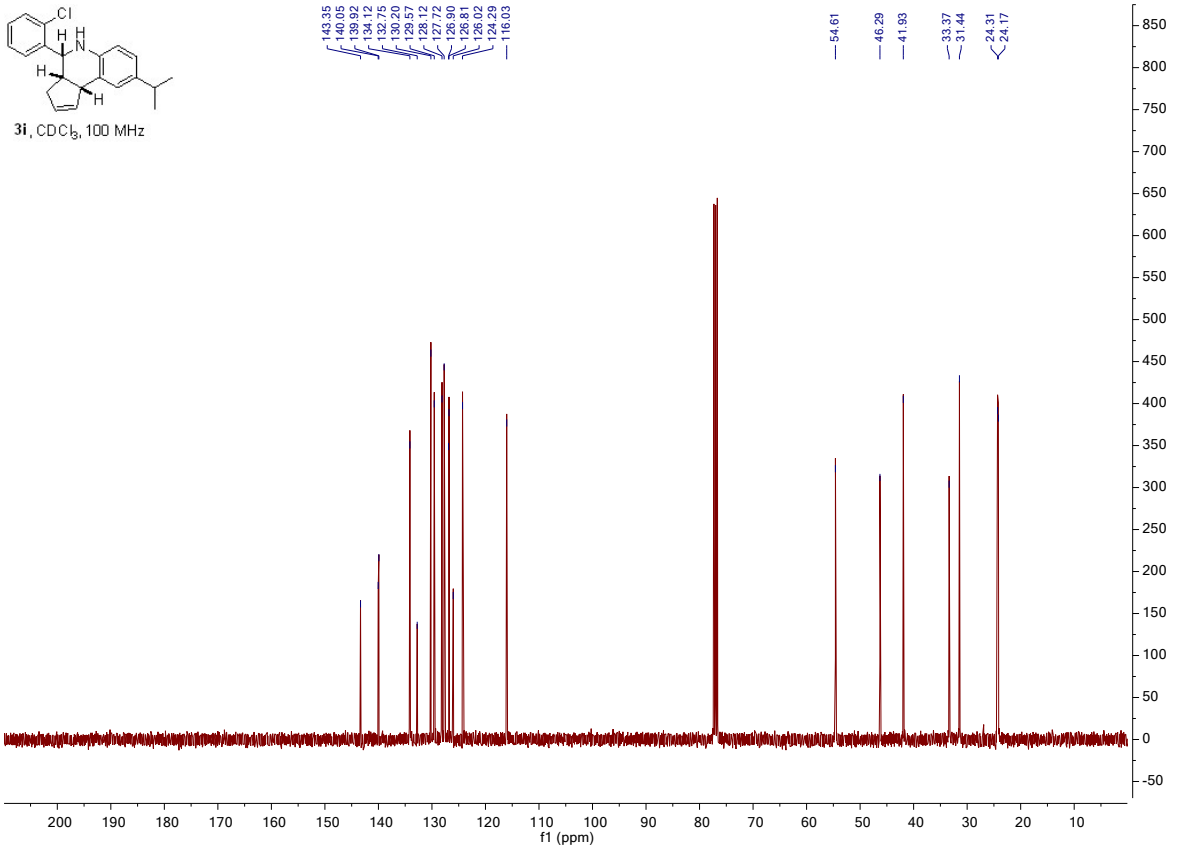

7.53 7.50 7.35 7.33 7.09 7.07 7.03 7.03 7.02 7.01 7.00 6.99 6.81 6.80 6.79 6.78 6.77 6.77 6.66 6.65 6.64 6.63 5.88 5.87 5.87 5.87 5.86 5.86 5.67 5.67 5.66 5.66 5.65 4.62 4.61 4.14 4.13 4.12 4.11 3.70 3.70 3.02 3.01 3.00 2.99 2.98 2.97 2.95 2.95 2.64 2.63 2.62 2.61 2.61 2.60 2.59 2.58 2.57 1.85 1.84 1.84 1.83 1.82 1.81 1.81 1.80 1.80 1.79 1.78 1.78
Br
H H
N
H
H
3g, CDCl3, 400 MHz
1.96 2.09 1.01 1.02 1.00 1.02 1.00 0.99 1.03 1.04 0.96 1.05 1.06 1.07
f1 (ppm)


Br
H H
N
H
H
3g, CDCl3, 100 MHz
145.22 141.89 133.97 131.59 130.23 129.00 128.20 126.39 125.96 120.94 119.42 116.00 57.53 46.24 45.86 31.38
f1 (ppm)


7.70 7.70 7.68 7.68 7.42 7.41 7.40 7.39 7.35 7.35 7.34 7.33 7.32 7.31 7.27 7.26 7.26 7.25 7.25 7.23 7.23 7.11 7.09 7.04 7.03 7.02 7.01 7.00 7.00 6.81 6.81 6.79 6.79 6.78 6.77 6.66 6.66 6.64 6.64 5.88 5.88 5.87 5.87 5.68 5.67 5.66 5.66 5.06 5.05 4.18 4.17 4.16 4.15 3.30 3.29 3.28 3.27 3.26 2.66 2.66 2.64 2.63 2.63 2.62 2.62 2.60 2.59 1.81 1.80 1.80 1.79 1.78 1.78 1.77 1.76 1.76 1.75 1.74 1.73
Cl
H
H
N
H
H
3h, CDCl3, 400 MHz
1.00 0.93 0.98 1.07 0.98 0.98 0.96 0.99 0.97 0.96 0.97 1.01 0.92 1.05 1.04 1.08
f1 (ppm)


Cl
H
H
N
H
H
3h, CDCl3, 100 MHz
145.54 139.88 134.07 132.75 130.21 129.63 129.01 128.21 127.67 126.95 126.33 126.28 119.41 116.08
54.53 46.17 41.92 31.51
f1 (ppm)


7.70 7.69 7.68 7.67 7.40 7.39 7.38 7.37 7.34 7.33 7.32 7.31 7.30 7.30 7.25 7.25 7.23 7.23 7.21 7.21 6.95 6.90 6.90 6.88 6.88 6.61 6.59 5.89 5.88 5.88 5.87 5.87 5.67 5.66 5.04 5.03 4.16 4.15 4.13 3.51 3.51 3.28 3.27 3.25 3.25 2.86 2.84 2.82 2.80 2.79 2.66 2.65 2.64 2.63 2.63 2.62 2.61 2.61 2.60 2.60 2.59 1.79 1.78 1.78 1.77 1.76 1.75 1.75 1.74 1.74 1.73 1.72 1.71 1.25 1.24 1.23 1.22
Cl
H
H
N
H
H
3i, CDCl3, 400 MHz
1.00 0.94 1.02 1.04 1.00 0.98 0.99 0.99 0.98 0.98 1.02 0.95 1.03 1.00 1.05 1.07 2.89 3.27
f1 (ppm)


Cl
H
H
N
H
H
3i, CDCl3, 100 MHz
143.35 140.05 139.92 134.12 132.75 130.20 129.57 128.12 127.72 126.90 126.81 126.02 124.29 116.03
54.61 46.29 41.93 33.37 31.44 24.31 24.17
f1 (ppm)