Supporting Information for

Asymmetric Synthesis of QUINAP via Dynamic Kinetic Resolution

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General Information

Unless stated otherwise, reactions were performed with dry, deoxygenated solvents (distilled over sodium or passed over a column of activated alumina). Commercially available chemicals were used as received. High-throughput reaction screens were carried out inside a nitrogen-filled glovebox on Freeslate Core Module 2. The reactions were monitored by UHPLC-MS analysis of reaction aliquots. IKAmag temperature modulators were used to control reaction temperature for reactions performed outside the glovebox at higher than ambient temperature (24 ºC). All other reactions were monitored by thin-layer chromatography (TLC) and Agilent 1290 UHPLC-MS analysis. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching. Silicycle Silia*Flash*® P60 Academic Silica gel (particle size 40–63 nm) was used for flash chromatography. ^{1}H NMR spectra were recorded on Varian Inova 500 MHz spectrometer and are reported relative to residual $CHCl_3$ (δ 7.26 ppm). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet, br d = broad doublet, app = apparent. ^{13}C NMR spectra were recorded on a Varian Inova 500 MHz spectrometer (125 MHz) and are reported relative to $CHCl_3$ (δ 77.16 ppm). Data for ^{13}C NMR are reported in terms of chemical shifts (δ ppm) (multiplicity, coupling constant ($J_{P,C}$), if any). Optical rotations were measured with a Jasco P-2000 polarimeter operating on the sodium D-line (589 nm), using a 100 mm path-length cell and are reported as: $[\alpha]_D^T$ (concentration in g/100 mL, solvent). Enantiomeric ratios were determined by SFC analysis with 20% isopropyl alcohol (IPA) or 35% IPA in CO_2 using 4.6 × 250 mm Daicel® AD-H column. High-resolution mass spectra (HRMS) were obtained on Agilent 6200 Series TOF with an Agilent G1978A Multimode source for electrospray ionization (ESI+).

Procedure A: synthesis of (*S*)-QUINAP [(*S*)-1a] from bromide 2a via kinetic resolution:

(Manuscript Table 2, entry 1) To an oven-dried 100 mL round-bottom flask was added bromide **2a** (1.003 g, 3.0 mmol, 1.0 equiv.) followed by, under nitrogen, dioxane (30 mL) and diisopropylethylamine (DIPEA, 2.1 mL, 12.0 mmol, 4.0 equiv.). Inside a nitrogen filled glovebox, a glass vial was charged with $^{n}Bu_4NHSO_4$ (1.037 g, 3.0 mmol, 1.0 equiv.), Pd(*o*-tol$_3$P)$_2$ (10.8 mg, 0.015 mmol, 0.005 equiv.), and (*S*,*S*)-**4** (9.3 mg, 0.0225 mmol, 0.0075 equiv.). The vial was brought out of the glovebox and its contents were rapidly transferred to the 100 mL round-bottom flask. Ph_2PH (0.42 mL, 2.4 mmol, 0.8 equiv.) was added to the mixture via syringe. The flask was evacuated and back-filled with nitrogen (× 3). The flask was then placed into an oil-bath preheated to 70 °C and the reaction was stirred under nitrogen at that temperature. The reaction was followed by UHPLC-MS and after 20 hours, approximately 50% conversion was observed. At this point, the homogenous reaction mixture was allowed to cool to ambient temperature and was poured into a separatory funnel containing 100 mL water and 40 mL toluene:ethyl acetate (5:1). The flask was rinsed with 10 mL water (× 2) and 10 mL toluene:ethyl acetate (5:1) (× 2) and poured into the separatory funnel. Layers were separated and the aqueous layer was extracted with 30 mL toluene:ethyl acetate (5:1) (× 2). The combined organic layers were washed with brine (40 mL), dried ($MgSO_4$) and concentrated to obtain yellow oil. QUINAP (**1a**) and bromide **2a** were found to have very similar R_f value on silica (0.3, 5:1 toluene:ethyl acetate). The crude was loaded on a silica gel column and eluted with 5:1 toluene:ethyl acetate (N_2 was used to perform flash chromatography). Fractions containing QUINAP **1a** and bromide **2a** were combined and concentrated to a yellow solid.

The mixture of QUINAP **1a** and bromide **2a** was dissolved in about 5 mL toluene and was left undisturbed for 14–20 hours at ambient temperature. Over this time period, (*S*)-QUINAP crystallized out and the mother liquor was carefully removed using a pipet. The crystals were washed with 2 mL toluene (× 2) and the washings were combined with the mother liquor. Pure (*S*)-QUINAP crystals were found to be white prisms (595 mg, 45% yield, >99.5% ee). SFC conditions: 35% IPA, 3.5 mL/min, λ = 280 nm, t_R (min): 3.67 [minor], 4.73 [major]. $[\alpha]_D^{25}$ −170.5 (*c* 1.0, $CHCl_3$); Lit. $[\alpha]_D^{21}$ −153.0 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.64 (d, *J* = 5.7 Hz, 1H), 7.94–7.87 (m, 3H), 7.75 (d, *J* = 5.7 Hz, 1H), 7.61 (ddd, *J* = 8.2, 6.7, 1.3 Hz, 1H), 7.48 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.44 (dd, *J* = 8.6, 3.1 Hz, 1H), 7.32–7.14 (m, 13H), 7.11 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 160.6 (d, *J* = 6.7 Hz), 144.4 (d, *J* = 33.2 Hz), 142.4, 137.5 (d, *J* = 12.0 Hz), 137.4 (d, *J* = 12.0 Hz), 136.0, 134.9 (d, *J* = 13.2 Hz), 133.8 (d, 20.1 Hz), 133.7, 133.3 (d, *J* = 18.5 Hz), 132.7 (d, *J* = 7.7 Hz), 131.0–

126.0 (Ar-C), 120.5. ^{31}P NMR (300 MHz, Chloroform-*d*) δ –14.3. HRMS (ESI+) *m/z* calc'd for $C_{31}H_{23}NP$ $[M+H]^+$: 440.1563, found 440.1566.

Note: We have observed that scalemic QUINAP crystallizes with enrichment whereas scalemic bromide **2a** crystallizes as a racemate leaving enriched bromide **2a** in the mother liquor.

Purity of the mother liquor was determined through UHPLC-MS analysis. Up to 3% QUINAP, nearly racemic, was found remaining in the mother liquor. The mother liquor was diluted with toluene (10 mL) and poured into a separatory funnel containing 20 mL water and 1 mL of H_2O_2 (33% aqueous solution). Contents of the funnel were vigorously shaken and the layers were allowed to separate. The process was repeated if QUINAP was not completely removed through oxidation (as judged by UHPLC-MS analysis of the organic layer). The oxide of QUINAP was found to be water-soluble and thus conveniently removed from the organic layer. The organic layer was washed with brine (10 mL), dried ($MgSO_4$) and concentrated to a yellow solid (475 mg, 47% yield), which was found to be 96% ee. Bromide **2a** was then dissolved in diethyl ether (approx. 8 mL) and left overnight at ambient temperature to deposit the racemic component of the mixture. The mother liquor was pipetted out and separated from the nearly racemic bromide crystals. Mother liquor was concentrated to afford 442 mg (44% yield), 99.7% ee bromide (*R*)-**2a**. SFC conditions: 35% IPA, 2.5 mL/min, λ = 310 nm, t_R (min): 2.99 (major), 3.51 (minor). $[\alpha]_D^{25}$ 72.0 (*c* 1.2, $CHCl_3$).

Note: Racemic bromide **2a** was prepared by following reported procedure (Thaler, T.; Geittner, F.; Knochel, P. *Synlett* **2007**, 2655). Samples of bromide **2a** were found to be contaminated with up to 5% chloride (as judged by mass spectrometry), which could not be removed via chromatographic separation. The chloride impurity was unreactive in the phosphination reactions described in this study.

(*S*)-1b (Manuscript Table 2, entry 2) Synthesized in a manner similar to **Procedure A** except $(p\text{-tol})_2PH$ (514 mg, 2.4 mmol, 0.8 equiv.) was used and the reaction was stopped at ~50% conversion after 14 hours. Product (*S*)-**1b** and the remaining enriched starting material [(*R*)-**2a**] were found to be inseparable by column chromatography. Moreover the product was found to be highly susceptible to oxidation under ambient conditions. Prep HPLC was used for the separation to give (*S*)-**1b** in 42% yield (595 mg, white foam) and 92% ee. SFC conditions: 35% IPA, 3.5 mL/min, λ = 280 nm, t_R (min): 4.46 (major), 4.96 (minor). $[\alpha]_D^{25}$ –86.1 (*c* 2.0, $CHCl_3$). ^{1}H NMR (500 MHz, Methylene Chloride-d_2) δ 8.59 (d, *J* = 5.7 Hz, 1H), 7.95–7.92 (m, 3H), 7.81–7.74 (m, 1H), 7.69–7.63 (m, 1H), 7.50 (ddd, *J* = 8.3, 6.7, 1.2 Hz, 1H), 7.42 (dd, *J* = 8.6, 3.1 Hz, 1H), 7.32–7.25 (m, 3H), 7.12 (app. d, *J* = 4.3 Hz, 4H), 7.06–6.99

(m, 5H), 2.33 (s, 3H), 2.30 (s, 3H). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.65 (d, *J* = 5.7 Hz, 1H), 7.93–7.86 (m, 3H), 7.75 (dd, *J* = 5.8, 0.9 Hz, 1H), 7.61 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.50–7.45 (m, 2H), 7.33–7.27 (m, 2H), 7.26–7.21 (m, 2H), 7.20–7.14 (m, 2H), 7.13–7.05 (m, 4H), 7.02 (ddt, *J* = 7.6, 1.5, 0.8 Hz, 2H), 2.33 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 160.7 (d, *J* = 6.4 Hz), 144.0 (d, *J* = 32.6 Hz), 142.3, 138.4, 138.0, 136.0, 135.6 (d, *J* = 13.8 Hz), 134.1 (d, *J* = 12.6 Hz), 134.0 (d, *J* = 12.0 Hz), 133.8 (d, *J* = 20.4 Hz), 133.6, 133.3 (d, *J* = 18.7 Hz), 132.7 (d, *J* = 7.6 Hz), 131.0–126.0 (Ar-C), 120.4, 21.40, 21.38. ^{31}P NMR (300 MHz, Chloroform-*d*) δ –15.7. HRMS (ESI+) *m/z* calc'd for $C_{33}H_{27}NP$ $[M+H]^+$: 468.1876, found 468.1884. (*R*)-**2a** was obtained in 44% yield (460 mg, off white solid) and 96% ee and was further enriched to >99% ee by recrystallization from toluene or ether.

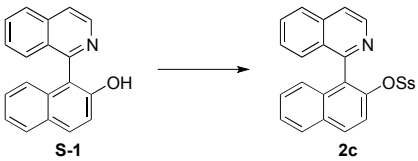
(*S*)-1c (Manuscript Table 2, entry 3) Synthesized in a manner similar to **Procedure A** except (p-CF_3-Ph)$_2$PH (580 mg, 1.8 mmol, 0.6 equiv.) was used and the reaction was stopped at 45% conversion after 26 hours. Product (*S*)-**1c** and the remaining enriched starting material [(*R*)-**2a**] were separated by column chromatography (4:1 hexane:ethyl acetate, N_2 was used to perform flash chromatography) to give (*S*)-**1c** in 41% yield (700 mg, white foam) and 63% ee. SFC conditions: 25% IPA, 2.5 mL/min, λ = 310 nm, t_R (min): 2.49 (major), 3.02 (minor). $[\alpha]_D^{25}$ –61.7 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.63 (d, *J* = 5.7 Hz, 1H), 7.98–7.91 (m, 3H), 7.78 (d, *J* = 5.7 Hz, 1H), 7.65 (dt, *J* = 8.2, 4.0 Hz, 1H), 7.56–7.51 (m, 3H), 7.47 (ddt, *J* = 7.3, 1.4, 0.8 Hz, 2H), 7.39–7.34 (m, 3H), 7.32 (ddd, *J* = 8.3, 6.8, 1.3 Hz, 1H), 7.29–7.24 (m, 4H), 7.14 (dq, *J* = 8.6, 0.9 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 160.1 (d, *J* = 6.9 Hz), 145.1 (d, *J* = 33.5), 142.4, 141.9 (d, *J* = 15.3 Hz), 141.7 (d, *J* = 16.0 Hz), 136.1, 134.0 (d, *J* = 20.5 Hz), 133.9, 133.4 (d, *J* = 18.9 Hz), 132.8 (d, *J* = 11.4 Hz), 132.7 (d, *J* = 7.9 Hz), 131.0–121.0 (Ar-C), 120.8. ^{31}P NMR (300 MHz, Chloroform-*d*) δ –13.8. HRMS (ESI+) *m/z* calc'd for $C_{33}H_{21}F_6NP$ $[M+H]^+$: 576.1310, found 576.1309. (*R*)-**2a** was obtained in 51% yield (510 mg, off white solid) and 75% ee and was further enriched to >99% ee by recrystallization from toluene or ether.

(*R*)-1c (Manuscript Table 3, entry 4): Carried out in a manner similar to that described above with resolved bromide (*R*)-**2a** (100 mg, 0.3 mmol, 1.0 equiv, 99% ee) as the starting material, (*R*,*R*)-**4** as the ligand and (p-CF_3-Ph)$_2$PH (97 mg, 0.3 mmol, 1.0 equiv.) in dioxane (3 mL) to afford (*R*)-**1c** in 98% yield (170 mg, white foam) and 86% ee. $[\alpha]_D^{25}$ 98.8 (*c* 1.1, $CHCl_3$).

(*S*)-1d (Manuscript Table 2, entry 4) Synthesized in a manner similar to **Procedure A** except (*o*-tol)$_2$PH (448 mg, 2.09 mmol, 0.7 equiv.) was used and the reaction was stopped at 30% conversion after 48 hours. The reaction required 3.0 mol% Pd[(*o*-tol)$_3$P]$_2$ and 4.5 mol% (*R*,*R*)-**4**. Product (*S*)-**1d** and remaining enriched starting material [(*R*)-**2a**] were found to be inseparable by column chromatography and crystallization methods.

(*R*)-1d (Manuscript Table 3, entry 5): Carried out in a manner similar to that described above with resolved bromide (*R*)-**2a** (33.4 mg, 0.1 mmol, 1.0 equiv, 99% ee) as the starting material, (*R*,*R*)-**4** as the ligand and (*o*-tol)$_2$PH (32 mg, 0.15 mmol, 1.5 equiv.) in dioxane (1 mL). The crude material was purified via silica gel column chromatography (4:1 hexane:ethyl acetate, N_2 was used to perform flash chromatography) to afford (*R*)-**1d** in 85% yield (40 mg, white solid) and 82% ee. $[\alpha]_D^{25}$ 143.3 (*c* 1.0, $CHCl_3$). SFC conditions: 23% IPA, 3.5 mL/min, λ = 310 nm, t_R (min): 2.98 (minor), 3.57 (major). ^{1}H NMR (500 MHz, Methylene Chloride-*d*$_2$) δ 8.52 (d, *J* = 5.7 Hz, 1H), 7.99–7.89 (m, 3H), 7.75 (d, *J* = 6.3 Hz, 1H), 7.62 (app. t, *J* = 7.6 Hz, 1H), 7.51 (ddd, *J* = 8.2, 6.7, 1.2 Hz, 1H), 7.33–7.13 (m, 8H), 7.12–7.02 (m, 4H), 6.95–6.87 (m, 2H), 2.09 (s, 3H), 1.93 (s, 3H). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.56 (d, *J* = 5.7 Hz, 1H), 7.89 (app. q, *J* = 8.3 Hz, 3H), 7.71 (dd, *J* = 5.8, 0.9 Hz, 1H), 7.57 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.48 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.33–6.95 (m, 12H), 6.90 (ddd, *J* = 7.6, 4.3, 1.4 Hz, 1H), 2.11 (s, 3H), 1.91 (s, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 160.6 (d, *J* = 6.8 Hz), 144.2 (d, *J* = 33.1 Hz), 142.8 (d, *J* = 27.1 Hz), 142.4, 142.2 (d, *J* = 26.0 Hz), 136.0, 135.7 (d, *J* = 12.1 Hz), 135.2 (d, *J* = 12.6 Hz), 134.0 (d, *J* = 12.2 Hz), 133.8, 133.7 (d, *J* = 19.0 Hz), 132.9 (d, *J* = 7.8 Hz), 131.0–126.0 (Ar-C), 120.2, 21.5 (d, *J* = 21.0 Hz), 21.3 (d, *J* = 22.5 Hz). ^{31}P NMR (300 MHz, Chloroform-*d*) δ –30.5. HRMS (ESI+) *m/z* calc'd for $C_{33}H_{27}NP$ $[M+H]^+$: 468.1876, found 468.1890.

Synthesis of sosylate 2c



To a solution of phenol **S-1** (Alcock, N. W.; Brown, J. M.; Hulmes, D. I. *Tetrahedron: Asymmetry* **1993**, *4*, 743) (420 mg, 1.55 mmol, 1.0 equiv.) in DCM (8 mL) was added *N*,*N*-dimethylaminopyridine (DMAP, 568 mg, 4.65 mmol, 3.0 equiv.) and 4-methanesulfonylbenzenesulfonyl chloride (394 mg, 1.55 mmol, 1.0 equiv.) at ambient temperature and stirred at that temperature. The reaction was followed by TLC (R_f value of **2c** on silica = 0.3, 1:1

hexane:ethyl acetate), which indicated complete consumption of starting material after 3 hours. The reaction mixture was concentrated to about half its initial volume and loaded on a silica gel column and eluted with 1:1 hexane:ethyl acetate. Fractions containing **2c** were combined and concentrated to give the title compound as a white solid (482 mg, 64%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.40 (d, *J* = 5.7 Hz, 1H), 8.08 (d, *J* = 9.0 Hz, 1H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 9.0 Hz, 1H), 7.70–7.66 (m, 3H), 7.62 (dd, *J* = 5.7, 0.9 Hz, 1H), 7.50 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.43–7.27 (m, 5H), 7.07 (dq, *J* = 8.6, 0.9 Hz, 1H), 3.02 (s, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 154.8, 145.1, 144.7, 142.5, 141.0, 135.9, 133.2, 132.4, 131.0, 130.8, 128.4, 128.3, 128.3, 128.2, 127.9, 127.6, 127.2, 127.1, 126.8, 126.3, 121.7, 120.9, 44.4. HRMS (MM: ESI+) *m/z* calc'd for $C_{26}H_{20}NO_5S_2$ $[M+H]^+$: 490.0777, found 490.0786.

Asymmetric synthesis of QUINAP (1a) from sosylate 2c:

Kinetic Resolution: (Manuscript Table 5, entry 1) This reaction was performed inside a nitrogen-filled glovebox. To a solution of sosylate **2c** (20 mg, 0.04 mmol, 1.0 equiv.) in distilled dioxane (0.4 mL) was added $Pd[(o\text{-tol})_3P]_2$ (0.6 mg, 0.8 μmol, 0.02 equiv.), (*R*,*R*)-**4** (0.5 mg, 1.22 μmol, 0.03 equiv.), Ph_2PH (7.0 μL, 0.04 mmol, 1.0 equiv.), and DMAP (20 mg, 0.16 mmol, 4.0 equiv.) and was heated to 80 ºC. The reaction was approximately 55% complete in 8 hours. The reaction was cooled, removed from the glovebox and poured into 2 mL water in a separatory funnel and extracted with 1:1 hexane:ethyl acetate (× 3). The combined organic extracts were dried ($MgSO_4$) and concentrated. Column chromatography (3:1 hexane:ethyl acetate then 1:1 hexane:ethyl acetate, N_2 was used to perform flash chromatography) afforded product (*R*)-QUINAP [(*R*)-**1a**] (39% yield, 82% ee) and recovered sosylate (*S*)-**2c** (41% yield, 96% ee). SFC conditions for **2c**: 35% IPA, 2.5 mL/min, λ = 310 nm, t_R (min): 3.50 (major), 4.46 (minor). $[\alpha]_D^{25}$ 24.0 (*c* 1.5, $CHCl_3$). QUINAP was recrystallized from toluene to >99% ee.

Dynamic Kinetic Resolution: (Manuscript Table 5, entry 2) This reaction was performed inside a nitrogen-filled glovebox. To a solution of sosylate **2c** (100.0 mg, 0.2 mmol, 1.0 equiv.) in distilled dioxane (2.1 mL) was added $Pd[(o\text{-tol})_3P]_2$ (5.7 mg, 8.0 μmol, 0.04 equiv.), (*R*,*R*)-**4** (5.1 mg, 12.2 μmol, 0.06 equiv.), Ph_2PH (52.0 μL, 0.3 mmol, 1.5 equiv.), and DMAP (99.0 mg, 0.8 mmol, 4.0 equiv.) and was heated to 90 ºC. The reaction was followed by UHPLC-MS. After 48 hours, the reaction was found to have stalled at ~70% conversion (~10% **S-1** was present in the reaction mixture) when 5.7 mg Pd(0) and 5.1 mg (*R*,*R*)-**4** were added to the reaction. After 4 days, the starting material **2c** was nearly consumed (~15% **S-1** was present in the reaction mixture). The reaction was cooled, removed from the

glovebox and poured into 10 mL water in a separatory funnel and extracted with 1:1 hexane:ethyl acetate (× 3). The combined organic extracts were dried ($MgSO_4$) and concentrated. Column chromatography (3:1 hexane:ethyl acetate, N_2 was used to perform flash chromatography) afforded product (*R*)-QUINAP [(*R*)-**1a**] (43% yield, 56% ee) as a white solid.

Data for Resolved triflate 2b:

(*R*)-**2b** (>99% ee): SFC conditions: 20% IPA, 3.5 mL/min, λ = 280 nm, t_R (min): 2.69. $[\alpha]_D^{25}$ –33.6 (*c* 1.0, $CHCl_3$). (*S*)-**2b** (>99% ee): SFC conditions: 20% IPA, 3.5 mL/min, λ = 280 nm, t_R (min): 2.95. $[\alpha]_D^{25}$ 30.3 (*c* 1.2, $CHCl_3$).

Asymmetric synthesis of QUINAP (1a) from triflate 2b via dynamic kinetic resolution:

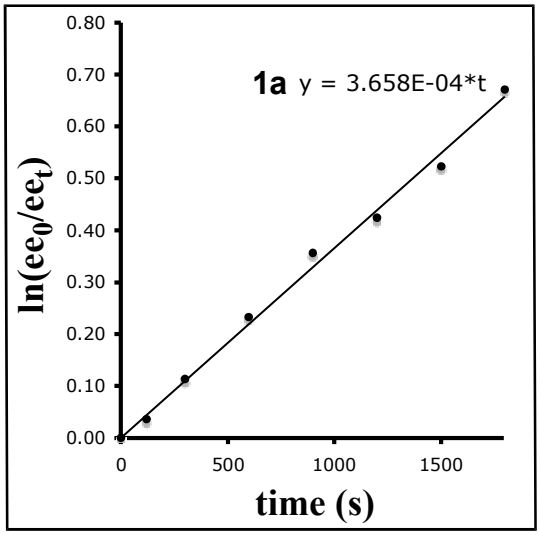
This reaction was performed inside a nitrogen-filled glovebox. To a solution of triflate **2c** (350.0 mg, 0.86 mmol, 1.0 equiv.) in 3.5 mL dioxane was added DMAP (420.0 mg, 3.44 mmol, 4.0 equiv.), Pd[(*o*-tol)$_3$P]$_2$ (18.5 mg, 0.026 mmol, 0.03 equiv.) and (*R*, S_{Fc})-**5** (23.5 mg, 0.039 mmol, 0.03 equiv.). The mixture was placed in a reaction well preheated to 80 ºC. A solution of Ph_2PH (150.0 µL, 0.86 mmol, 1.0 equiv.) in 750 µL dioxane was added to the reaction mixture in 30 µL portions every 8 minutes using robotic syringe dispensing (Freeslate Core Module 2). Manual addition could be employed to obtain similar results. **Note:** Observed trend for % ee of QUINAP (**1a**) with addition time of Ph_2Ph: T = 0, 60% ee; T = 30 min, 81% ee; T = 90 min, 86% ee; T = 180 min, 90% ee; T = 240 min, 90% ee. After completion of the addition (4 hours) about 95% triflate was consumed as determined by UHPLC-MS analysis. The reaction was stirred for further 2 hours at which point complete consumption of the starting material was observed. The reaction was cooled, removed from the glovebox and poured into 20 mL water in a separatory funnel and extracted with 1:1 hexane:ethyl acetate (× 3). The combined organic extracts were dried ($MgSO_4$) and concentrated. The crude material was loaded on a silica gel column and eluted with 4:1 hexane:ethyl acetate (N_2 was used to perform flash chromatography). Fractions containing QUINAP (**1a**) were combined and concentrated to obtain 330 mg (86%) of white solid that was found to be 90% ee by SFC analysis.

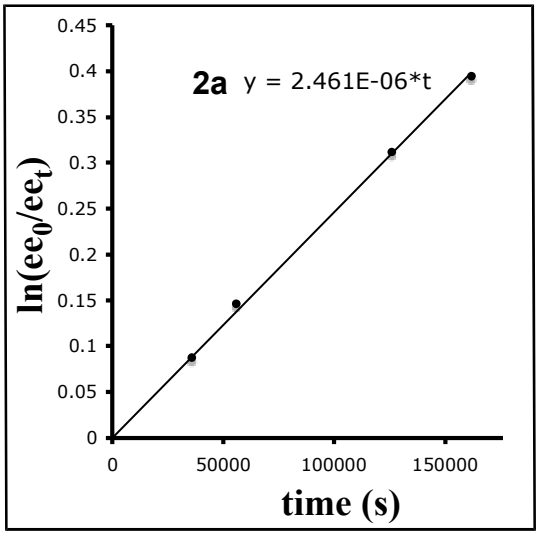
Toluene was the preferred solvent for recrystallization of QUINAP **1a**. The 90% ee material was dissolved in CH_2Cl_2 and transferred to a tared 25 mL round-bottom flask. The solution was concentrated to dryness to once again obtain the white solid. Warm toluene (about 10 mL at approx. 50 ºC) was added to the solid and dissolution was aided by sonication in a water bath at 50 ºC. We found

that the amount of toluene used to dissolve the solid to be critical to the efficiency of recrystallization (less the better). Once the entire solid had dissolved, the flask was left in the oil bath with heating turned off to allow gradual cooling of the solution. The solution was left undisturbed under nitrogen. After 16 hours, mother liquor was carefully removed with a pipette leaving behind prismatic white crystals of QUINAP (*S*)-**1a** (271 mg, 99.5% ee). A second crop could be obtained from the mother liquor using the method described above.

Racemization Data

Racemization of 1a and 2a in Mesitylene at 150 °C[a,b,c]

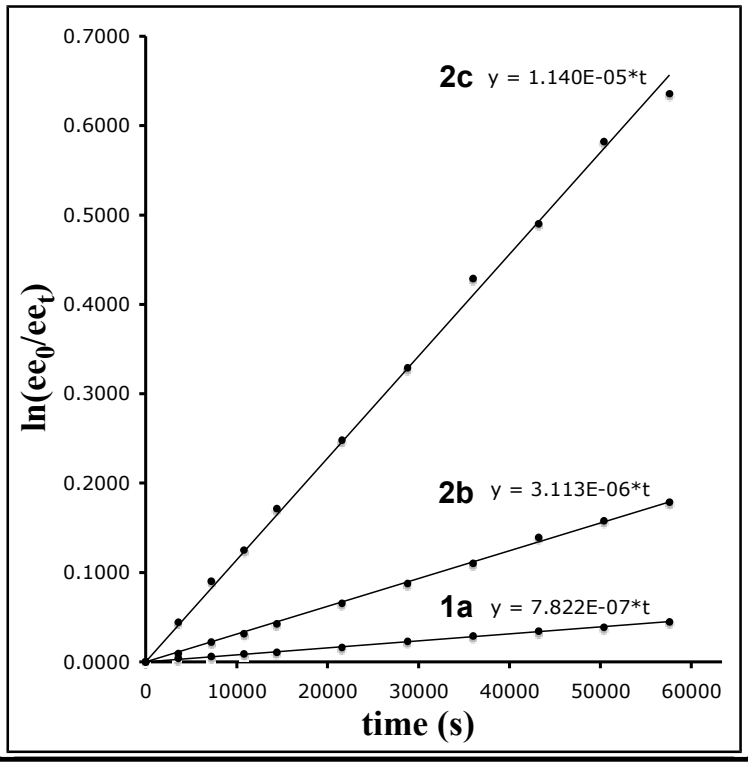




Time	$QPPh_2$ (1a) *R*:*S*	Time	QBr (2a) *R*:*S*
0	0:100.0	0	99.02:0.98
2 min	1.79:98.21	10 h	94.91:5.09
5 min	5.33:94.67	15.5 h	92.33:7.67
10 min	10.40:89.60	35 h	85.86:14.14
15 min	14.98:85.02	45 h	83.03:16.97
20 min	17.30:82.70		
25 min	20.35:79.65		
30 min	24.46:75.54		
	$k_{epi} = 1.83 \times 10^{-4}$ s^{-1}		$k_{epi} = 1.23 \times 10^{-6}$ s^{-1}
	$t_{1/2}^{rac} = 0.53$ h		$t_{1/2}^{rac} = 78.2$ h

[a]Reactions were conducted at 1 mg/mL concentration. The experiment with **1a** was performed in separate N_2-filled reaction vessels to minimize air oxidation. Enantiomeric ratios were determined by SFC with 35% IPA in CO_2 using 4.6 x 250mm Daicel® AD-H column. [b]Rate constants for epimerization were obtained from the equation: $\ln(ee_0/ee_t) = 2 * k_{epi} * t$. [c]Half-life for racemization were obtained from the equation: $t_{1/2}^{rac} = 0.5 * \ln 2/k_{epi}$.

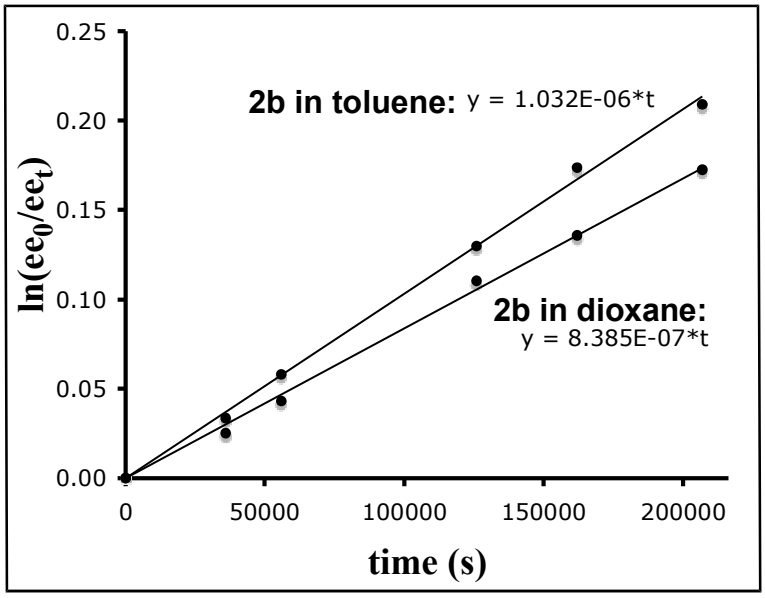
Racemization of 1a, 2b and 2c in Toluene at 90 °C[a,b,c]



Time (h)	$QPPh_2$ (1a) *R*:*S*	QOTf (2b) *R*:*S*	QOSs (2c) *R*:*S*
0	0:100.0	0.48:99.52	3.52:96.48
0.5	0.13:99.87	0.68:99.32	4.18:95.82
1	0.20:99.80	0.95:99.05	5.53:94.47
2	0.30:99.70	1.57:98.43	7.53:92.47
3	0.44:99.56	2.02:97.98	8.98:91.02
4	0.52:99.48	2.55:97.45	10.83:89.17
6	0.81:99.19	3.62:96.38	13.72:86.28
8	1.14:98.86	4.64:95.36	16.54:83.46
10	1.43:98.57	5.66:94.34	19.72:80.28
12	1.70:98.30	6.90:93.10	21.53:78.47
14	1.90:98.10	7.72:92.28	24.03:75.97
16	2.18:97.82	8.58:91.42	25.38:74.62
	k_{epi} = 3.91 x 10^{-7} s^{-1}	k_{epi} = 1.56 x 10^{-6} s^{-1}	k_{epi} = 5.70 x 10^{-6} s^{-1}
	$t_{1/2}^{rac}$ = 246 h	$t_{1/2}^{rac}$ = 62 h	$t_{1/2}^{rac}$ = 17 h

[a]Reactions at 1 mg/mL concentration. Enantiomeric ratios determined by SFC with 20% IPA (**2b**) or 35% IPA in CO_2 using 4.6 x 250mm Daicel® AD-H column.
[b]Rate constants for epimerization obtained from the equation: $\ln(ee_0/ee_t) = 2 * k_{epi} * t$.
[c]Half-life for racemization obtained from the equation: $t_{1/2}^{rac} = 0.5 * \ln 2/k_{epi}$.

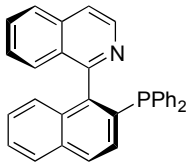
Racemization of 2b in Toluene and Dioxane at 80 °C[a,b,c]



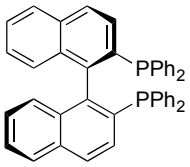
Time (h)	QOTf (2b) in toluene *R*:*S*	QOTf (2b) in dioxane *R*:*S*
0	0:100	0:100
10	1.99:98.01	1.59:98.41
15.5	3.14:96.86	2.45:97.55
35	6.40:93.60	5.54:94.46
45	8.27:91.73	6.66:93.34
57.5	9.72:90.28	8.21:91.79
	k_{epi} = 5.16 x 10^{-7} s^{-1}	k_{epi} = 4.19 x 10^{-7} s^{-1}
	$t_{1/2}^{rac}$ = 187 h	$t_{1/2}^{rac}$ = 230 h

[a]Reactions were conducted at 1 mg/mL concentration. Enantiomeric ratios were determined by SFC with 35% IPA in CO_2 using 4.6 x 250mm Daicel® AD-H column. [b]Rate constants for epimerization were obtained from the equation: $\ln(ee_0/ee_t) = 2 * k_{epi} * t$. [c]Half-life for racemization were obtained from the equation: $t_{1/2}^{rac} = 0.5 * \ln 2/k_{epi}$.

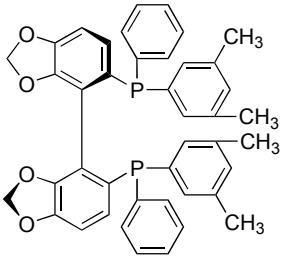
Ligands used in the Present Study



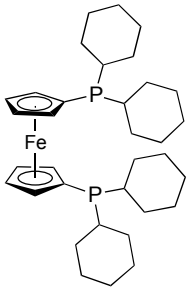
(*S*)-QUINAP (**1a**)



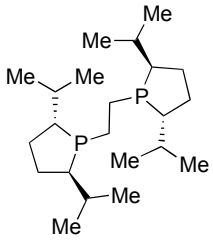
(*R*)-BINAP



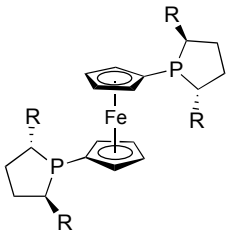
(*R*)-DM-SEGPHOS



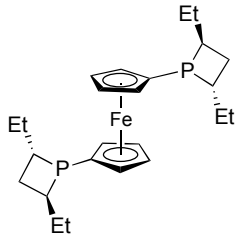
1,1'-Bis(dicyclohexylphosphino)ferrocene (dcypf)



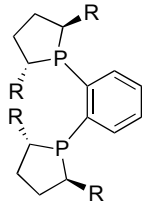
(*S*,*S*)-^{i}Pr-BPE



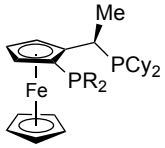
R = Me (*S*,*S*)-Me-Ferrocelane [(*S*,*S*)-**4**]
R = Et (*S*,*S*)-Et-Ferrocelane
R = CH(CH$_3$)$_2$ (*S*,*S*)-^{i}Pr-Ferrocelane



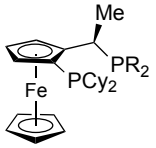
(*S*,*S*)-Et-Ferrotane



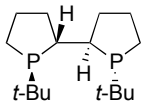
R = Me (*S*,*S*)-Me-DuPhos [(*S*,*S*)-**6**]
R = Et (*S*,*S*)-Et-DuPhos [(*S*,*S*)-**7**]
R = CH(CH$_3$)$_2$ (*S*,*S*)-^{i}Pr-DuPhos [(*S*,*S*)-**8**]



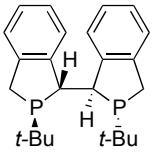
R = Cy (*R*,*S*$_{Fc}$)-Josiphos SL-J003-1 [(*R*,*S*$_{Fc}$)-**5**]
R = Ph (*R*,*S*$_{Fc}$)-Josiphos SL-J001-1



R = Ph (*R*,*S*$_{Fc}$)-Josiphos SL-J004-1
R = C(CH$_3$)$_3$ (*R*,*S*$_{Fc}$)-Josiphos SL-J009-1

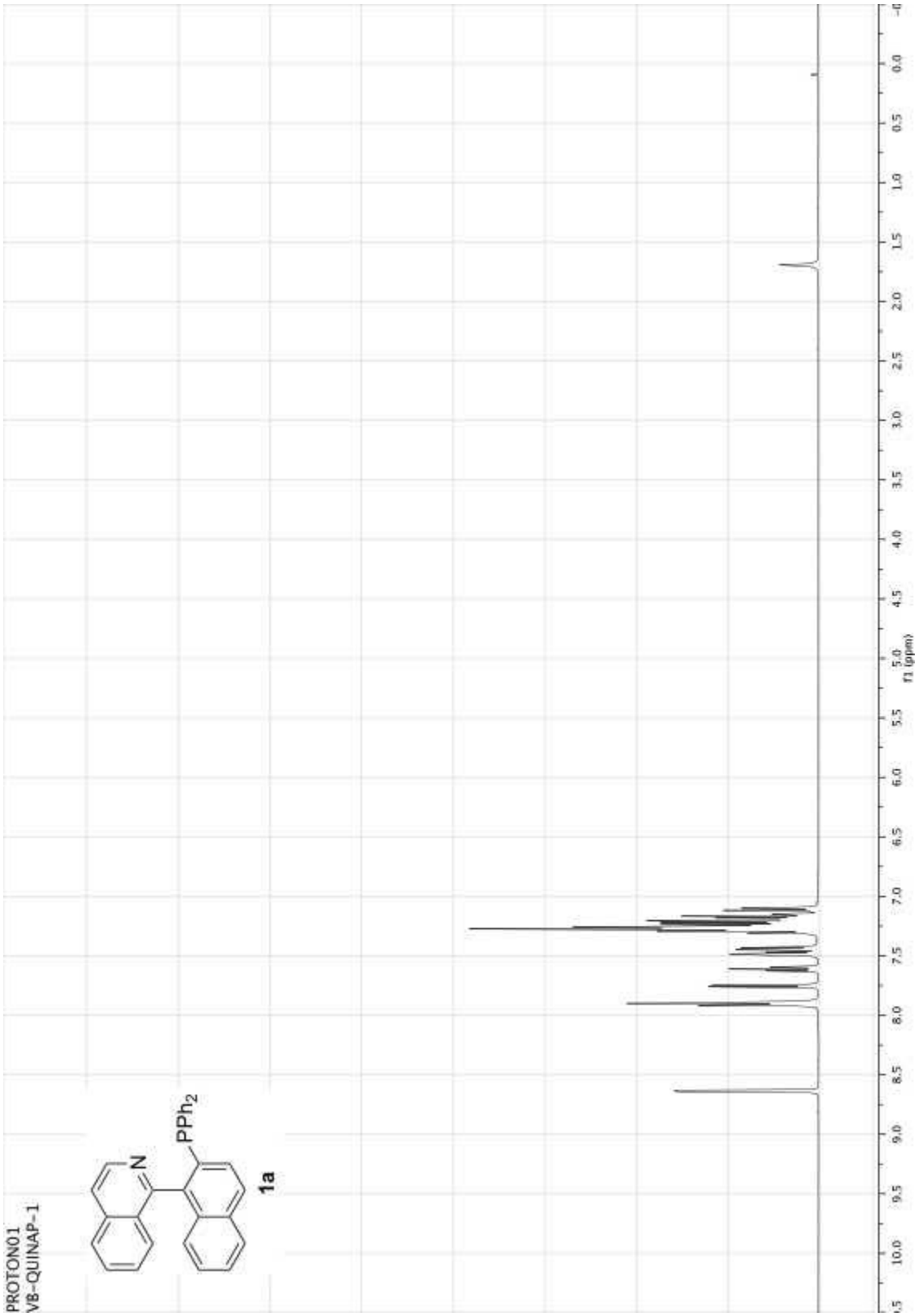


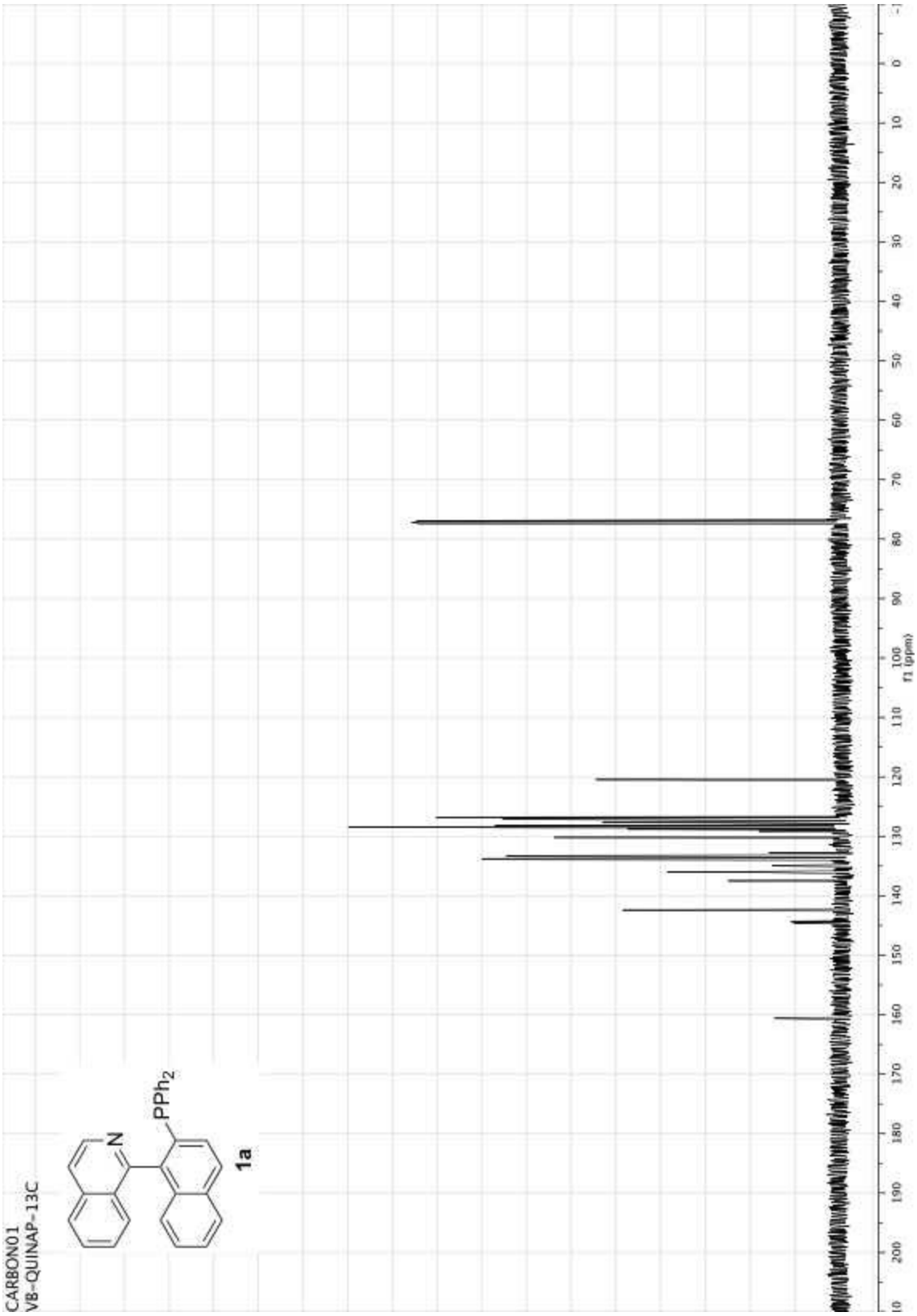
(*S*,*S*,*R*,*R*)-TangPhos

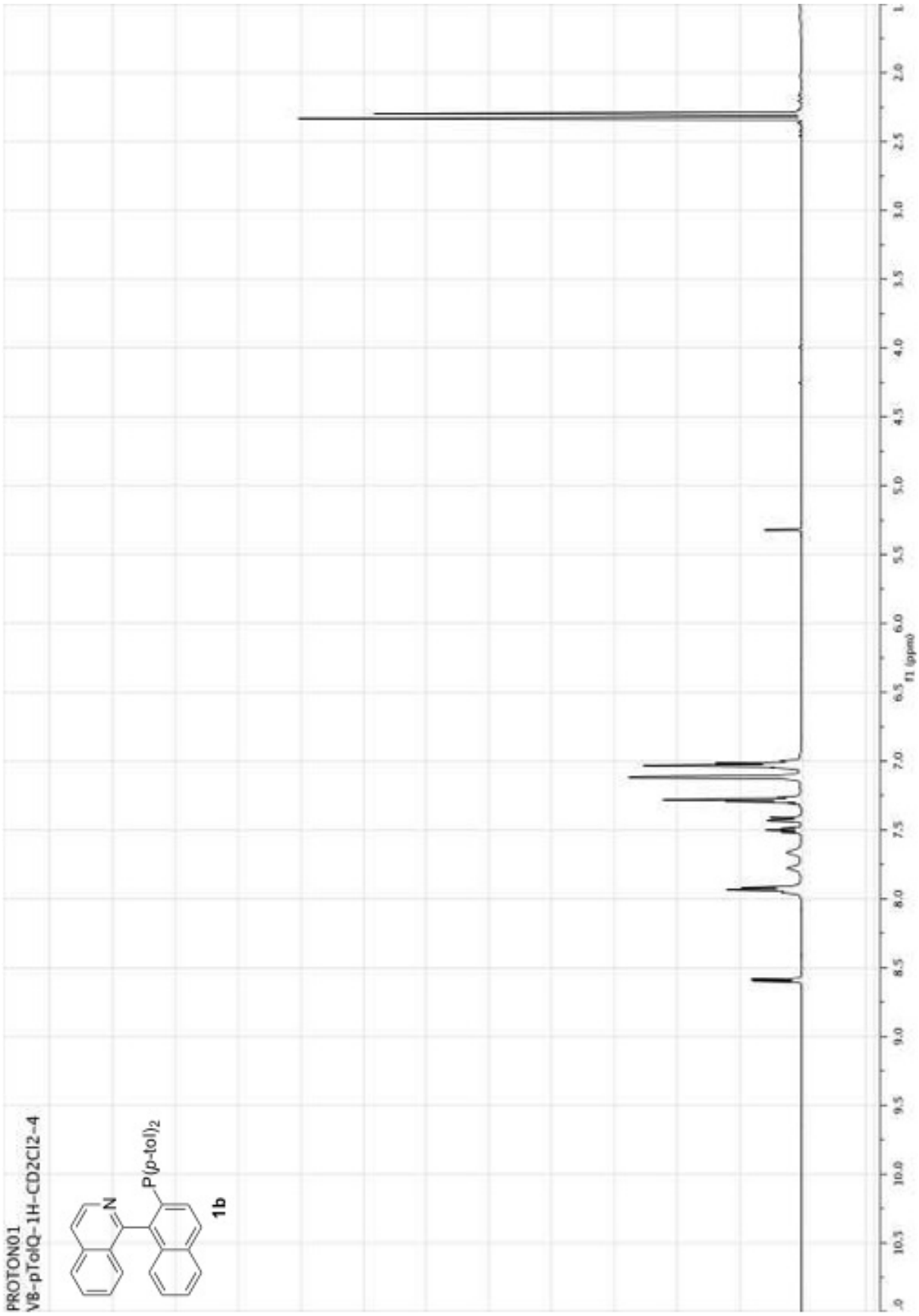


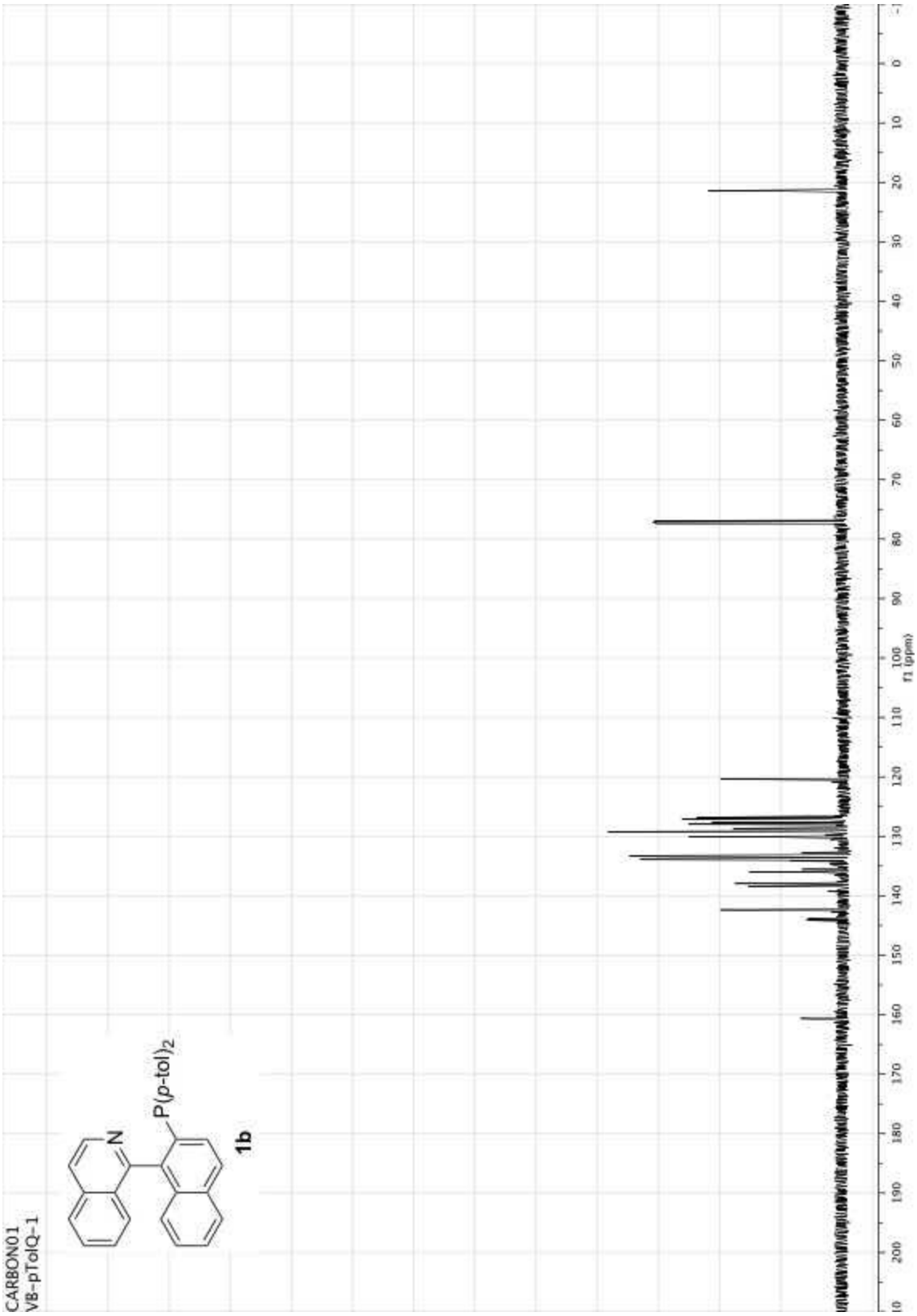
(*R*,*R*,*S*,*S*)-DuanPhos

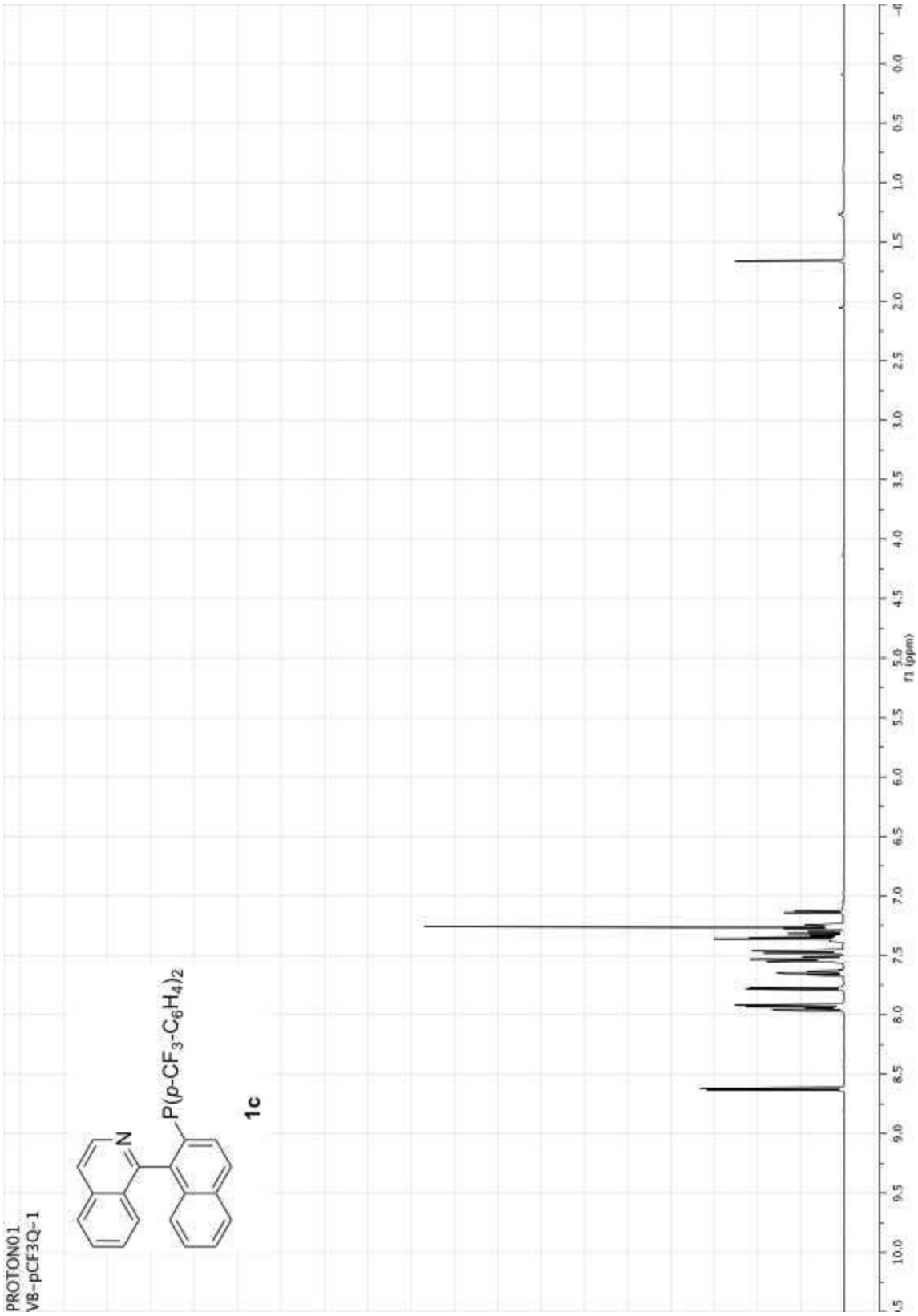
^{1}H and ^{13}C NMR Spectra

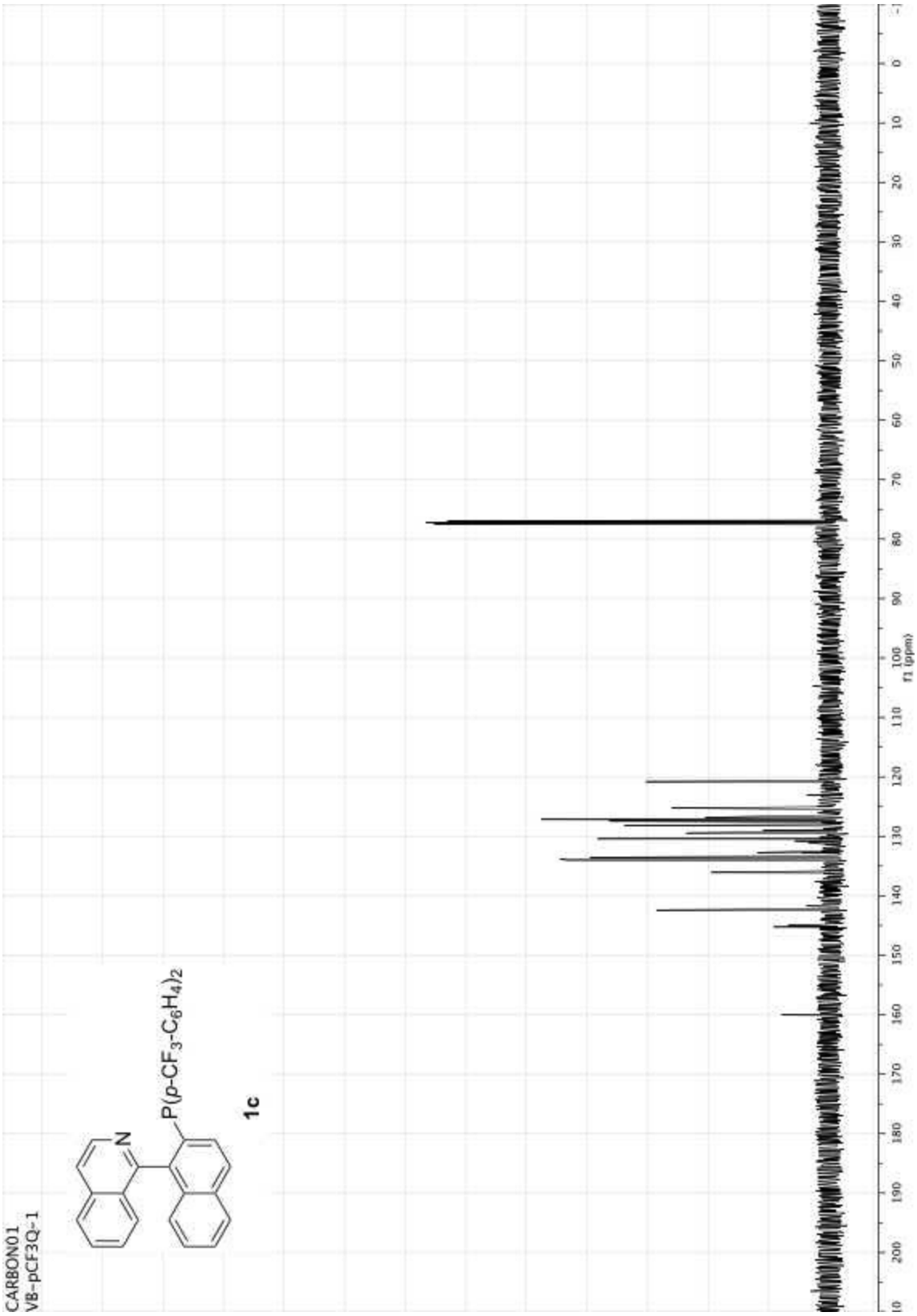



CARBON01
VB-QUINAP-13C
PPh2
N
1a
f1 (ppm)


PROTON01
V8-pTolQ-1H-CD2Cl2-4
N
P(p-tol)2
1b
f1 (ppm)


CARBON01
VB-pTolQ-1
P(p-tol)2
N
1b
f1 (ppm)


PROTON01
VB-pCF3Q-1
N
P(p-CF3-C6H4)2
1c
f1 (ppm)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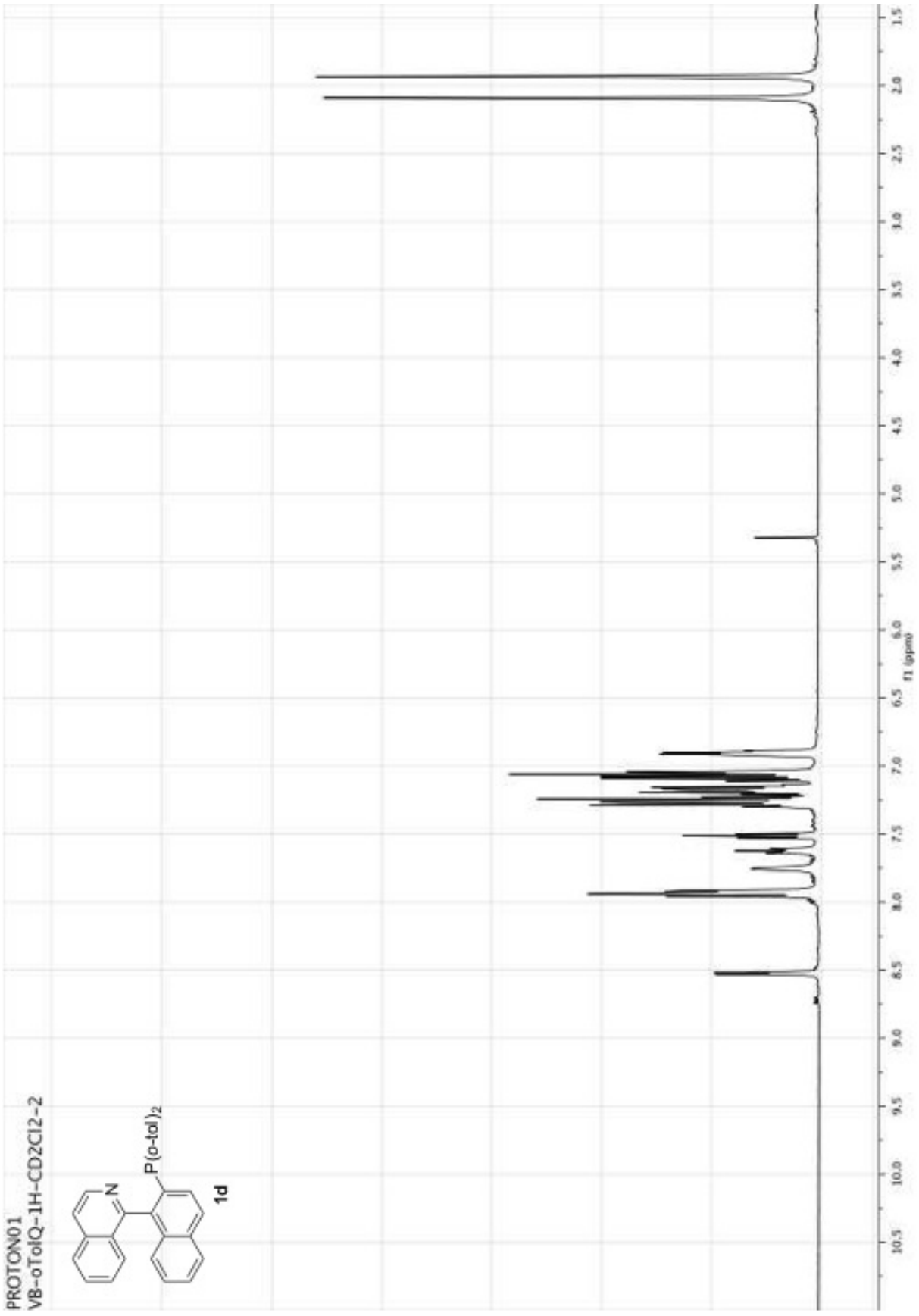
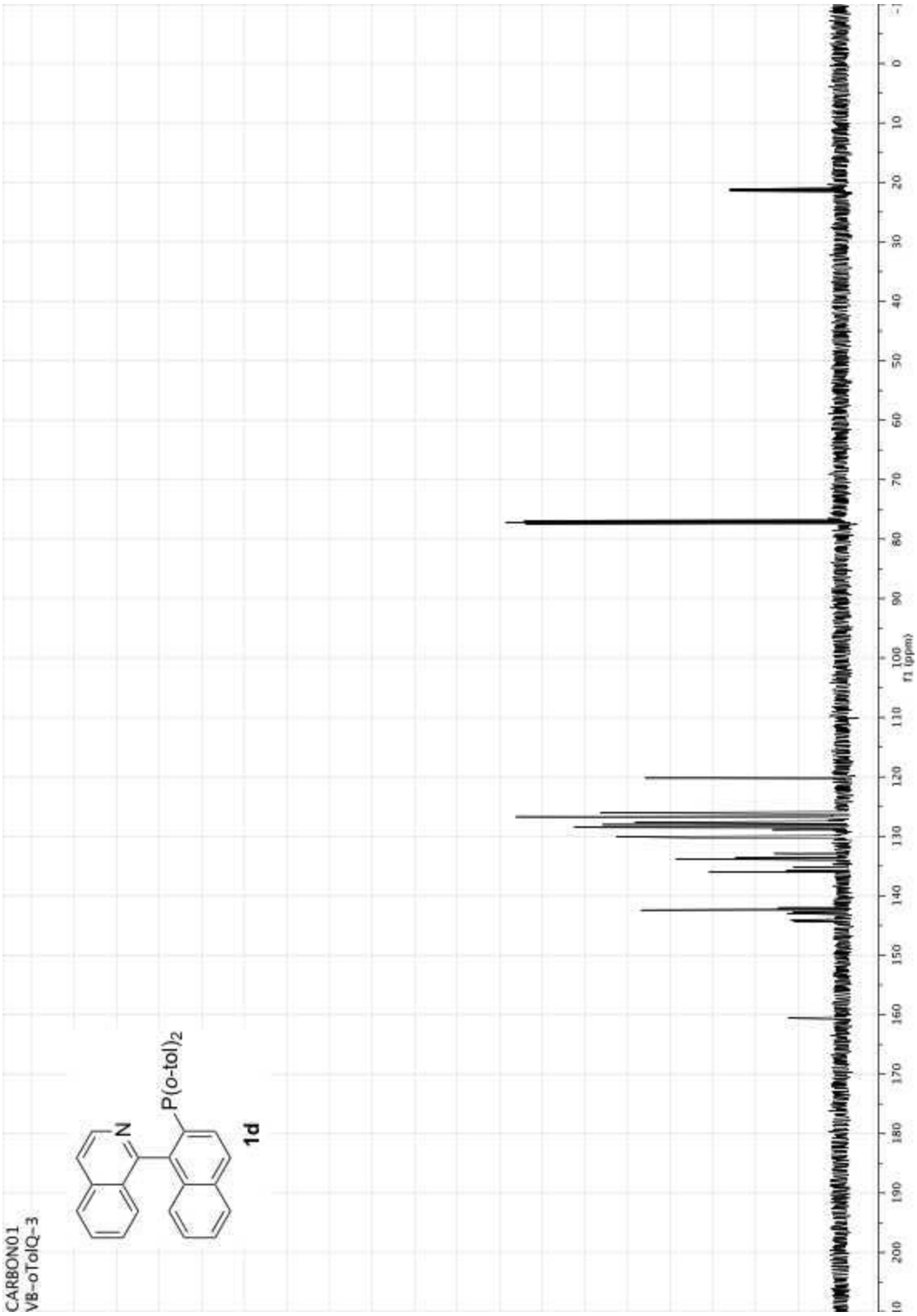
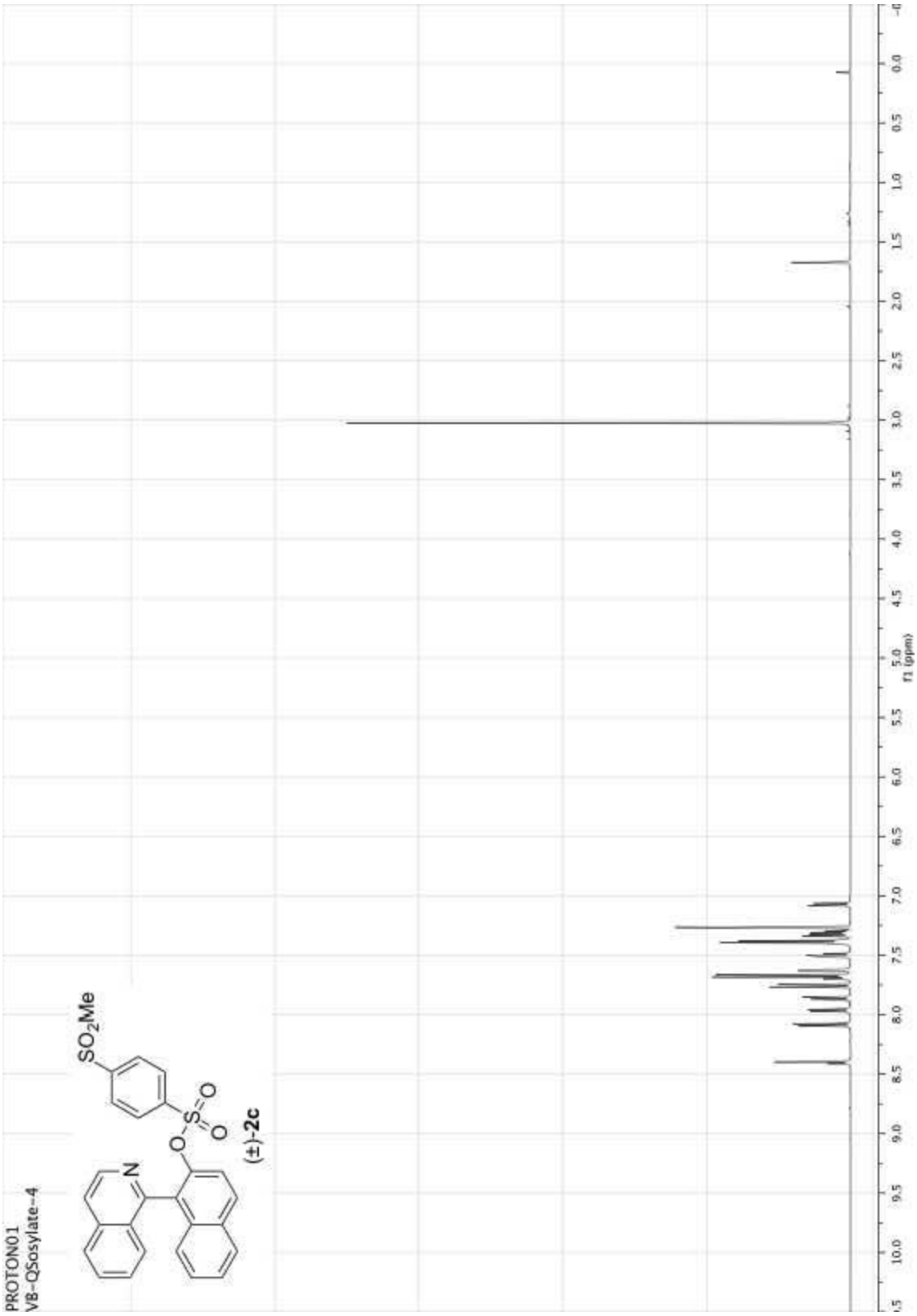
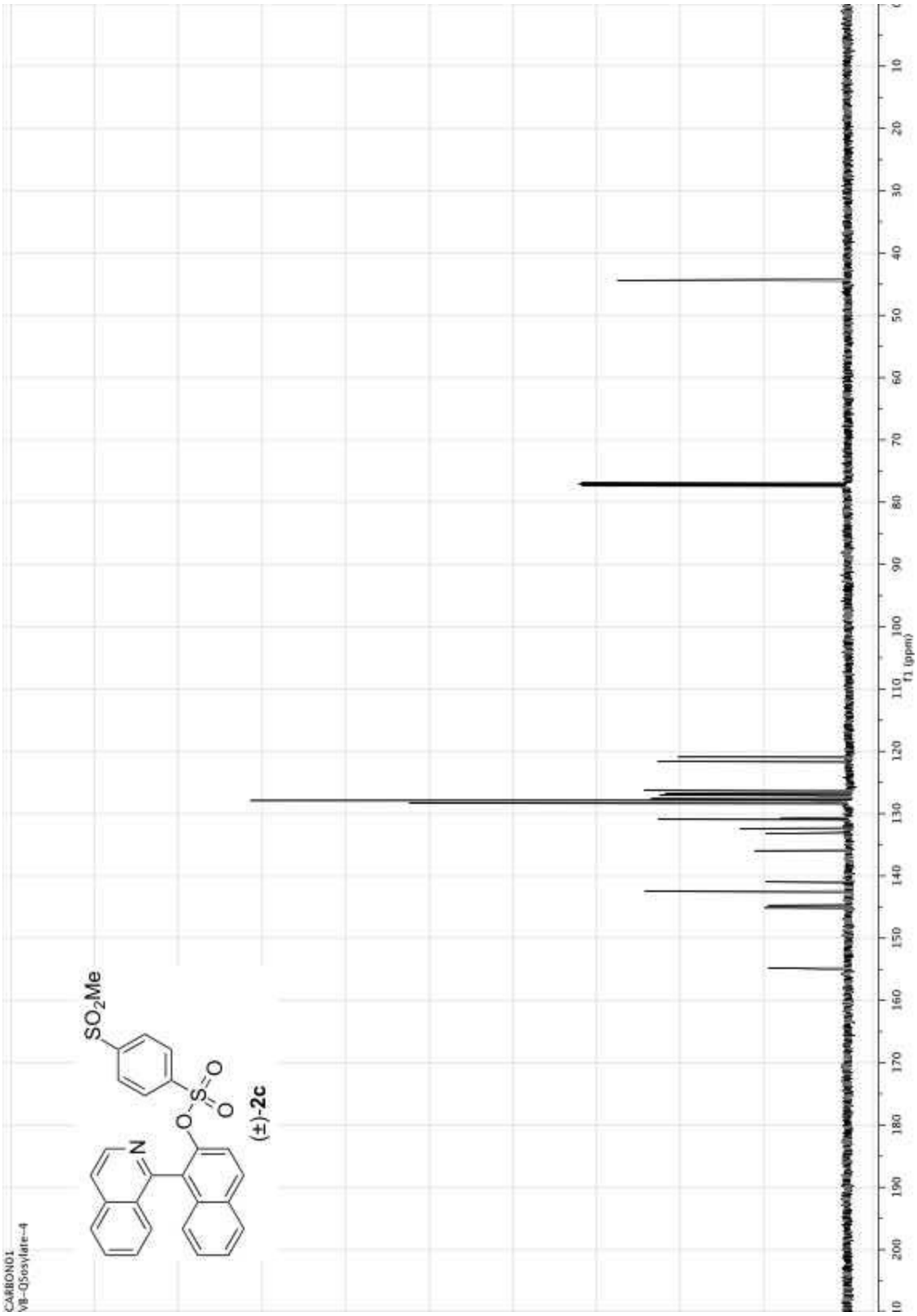
N
P(p-CF3-C6H4)2
1c
f1 (ppm)


PROTON01
VB-oTolQ-1H-CD2Cl2-2
P(o-tol)2
N
1d
f1 (ppm)


CARBON01
VB--oTolQ--3
N
P(o-tol)2
1d
f1 (ppm)


PROTON01
VB-QSosylate-4
SO2Me
(±)-2c
f1 (ppm)


CA8BON01
VB-Qtosylate-4
f1 (ppm)
SO2Me
(±)-2c