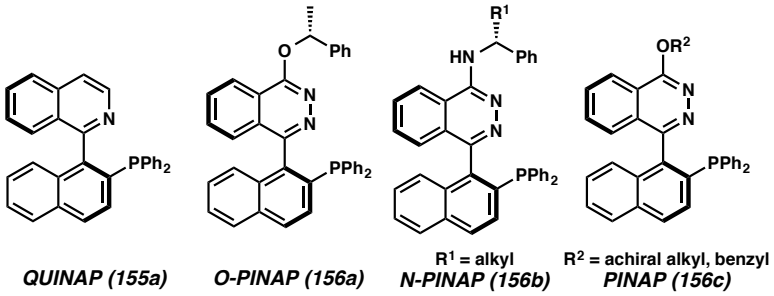
CHAPTER 3

Enantioselective Synthesis of PINAP via Dynamic Kinetic Resolution

3.1. Introduction

The unique properties of the axially chiral P,N ligand QUINAP (**155a**) have been employed widely for various transition metal catalyzed asymmetric reactions.[1] However, approaches to the synthesis of QUINAP ligands in high enantiomeric purity are limited.[2] In 2013, our laboratories explored the palladium-catalyzed atroposelective synthesis of QUINAP and its derivatives via kinetic resolution and dynamic kinetic resolution.[3] With a robust method for the synthesis of chiral QUINAP in hand, we turned our attention to the architecturally related PINAP ligands (**156**). PINAP ligands (**156a** and **156b**), which possess analogous ligation reactivity to QUINAP, were first developed by the Carreira group in 2004.[4] Carreira and co-workers separated the two atropoisomeric diastereomers through column chromatography by preparing chiral ether- or amine-substituted PINAP scaffolds. Herein, we disclose synthetic methods for accessing enantiomerically enriched PINAP ligands via dynamic kinetic resolution (**156a**, **156c**).

Figure 3.1.1. *QUINAP (**155**) and PINAP (**156**)*

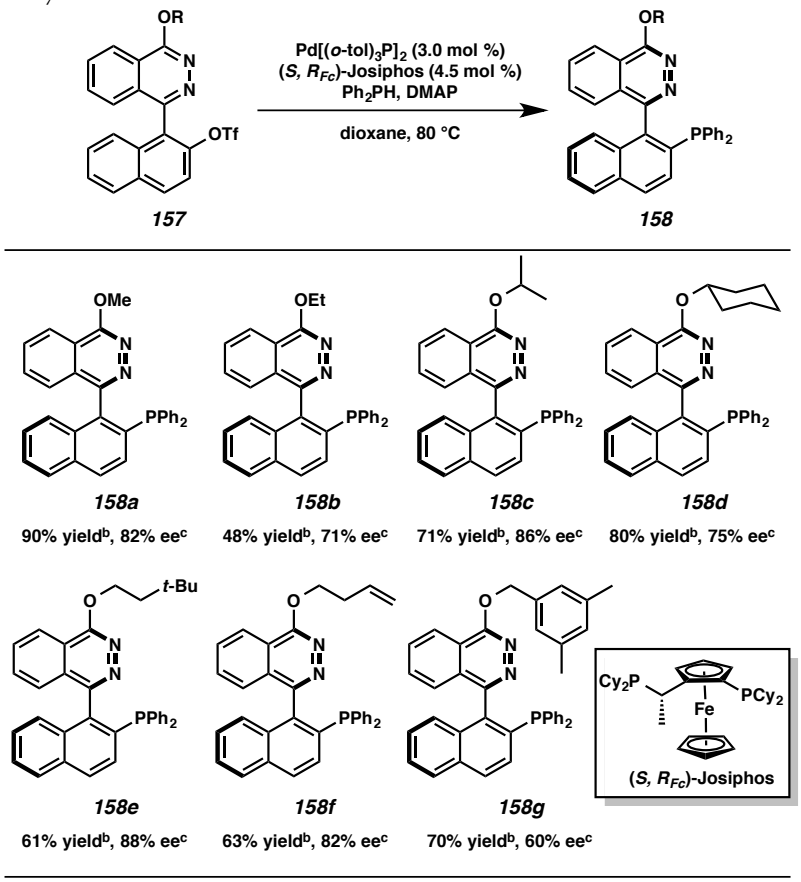


QUINAP (155a) ***O-PINAP (156a)*** ***N-PINAP (156b)*** ***PINAP (156c)***

3.2. Results and Discussion

Our initial attempts to apply the standard QUINAP dynamic kinetic resolution conditions,[3] 3.0 mol % of $Pd[(o\text{-tol})_3P]_2$ and 4.5 mol % of (S, R_{Fc})-Josiphos at 80 °C, to aryl triflate **157** afforded various alkyl- or benzyl-substituted PINAP ligands (Table 3.2.1). Asymmetric C–P couplings via dynamic kinetic resolution on substrates incorporating methoxy, ethoxy, and isopropoxy groups furnished the corresponding PINAP ligands in good yields and selectivities (**158a,b,c**). Cyclohexyl, 3,3-dimethyl-1-butyl, and homoallyl ether groups were also well tolerated under the reaction conditions to give the desired products. (**158d,e,f**). Additionally, 3,5-dimethyl benzyloxy-substituted PINAP was obtained in good yield and moderate selectivity (**158g**). Although these initial results were exciting, it was clear that additional optimization was needed to improve the enantioselectivities in the synthesis of these PINAP ligands.

Table 3.2.1. *Scope of dynamic kinetic resolution under initial standard conditions*

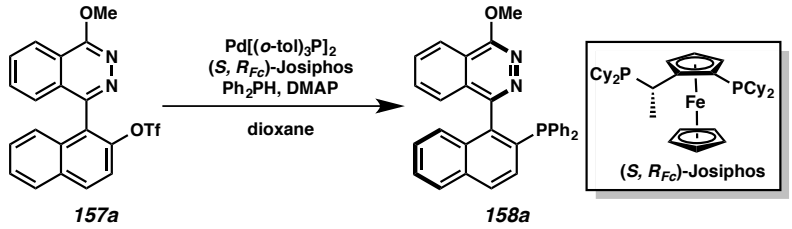


[a]Reactions performed with 1.0 equiv of triflate **157**, 4.0 equiv of DMAP, 3.0 mol % of Pd[(*o*-tol)$_3$P]$_2$, 4.5 mol % of (*S*, R_{Fc})-Josiphos, 1.05 equiv of Ph_2PH (1.0 M in dioxane) at 0.20 M in dioxane at 80 °C in a glovebox. Ph_2PH (1.0 M in dioxane) was added over 4 h.

In order to allow more time for the isomerization of the presumed arylpalladium complex before its subsequent phosphination, diphenylphosphine (1.0 M solution in dioxane) was added slowly.[5] In addition, we used pre-stirred 1.0 mol % of Pd[(*o*-tol)$_3$P]$_2$ and 1.5 mol % of (*S*, R_{Fc})-Josiphos solutions in dioxane. Interestingly, improved enantioselectivity was observed with reduced palladium and Josiphos ligand loadings (1.0 mol % and 1.5 mol %, respectively) (Table 3.2.2, entries 1 and 2). We were pleased to find that higher enantioselectivities were obtained at lower temperatures (Table 3.2.2,

entries 3 and 4). However, the conversion rate was dramatically diminished at 50 °C (Table 3.2.2, entry 5).

Table 3.2.2. *Optimization of reaction parameters*[a]



157a ***158a***

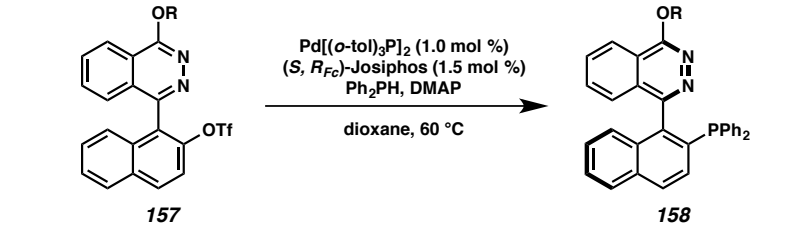
entry	$Pd[(o\text{-tol})_3P]_2$	(S, R_{Fc})-Josiphos	T (°C)	yield (%)[b]	ee (%)
1	3.0 mol %	4.5 mol %	80	90	82[c]
2	1.0 mol %	1.5 mol %	80	95	88[c]
3	1.0 mol %	1.5 mol %	70	75	92[c]
4	1.0 mol %	1.5 mol %	60	80	96[c]
5	1.0 mol %	1.5 mol %	50	–[d]	94[c]

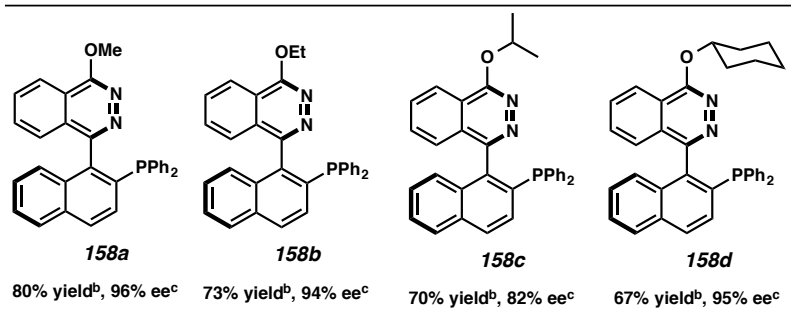
[a]Reactions performed with 1.0 equiv of **157a**, 4.0 equiv of DMAP, 1.0 mol % of $Pd[(o\text{-tol})_3P]_2$, 1.5 mol % of (S, R_{Fc})-Josiphos, 1.05 equiv of Ph_2PH (1.0 M in dioxane) at 0.20 M in dioxane in a glovebox. $Pd[(o\text{-tol})_3P]_2$ and (S, R_{Fc})-Josiphos in dioxane were pre-stirred before use. Ph_2PH (1.0 M in dioxane) was added over 8 h. [b]All yields are isolated yields. [c]Determined by chiral SFC analysis. [d]~50% conversion.

With the optimized conditions in hand, we investigated the substrate scope of the reaction (Table 3.2.3). Several alkoxy- and benzyloxy-substituted PINAP ligands were furnished in improved enantioselectivities under the optimized conditions (**158a**–**158h**, 57–80% yields and 82–96% ee). Applying our optimized conditions to a (*R*)-phenylethoxy-substituted substrate, which was previously prepared by the Carreira group by chromatographic separation, generated the corresponding PINAP product in 95% de (**158i**). Interestingly, diastereomeric PINAP **158j** was produced by our method with lower selectivity using the (R, S_{Fc})-Josiphos ligand indicating some balance between substitute and catalyst in the progress (e.g., mismatched pair). Thankfully, nearly enantiopure PINAP **158j** was obtained after recrystallization. Unfortunately, in the case of (*R*)-α-phenethylamine-substituted PINAP, only moderate selectivity was observed

(**158k**). Additionally, application of our conditions to the reaction of triflate **157a** with diphenylphosphine oxide or $(p\text{-}CF_3\text{-}C_6H_4)_2PH$ proved unsuccessful, and only low yield and selectivities were observed.[6,7]

Table 3.2.3. *Scope of dynamic kinetic resolution under optimized conditions*[a]



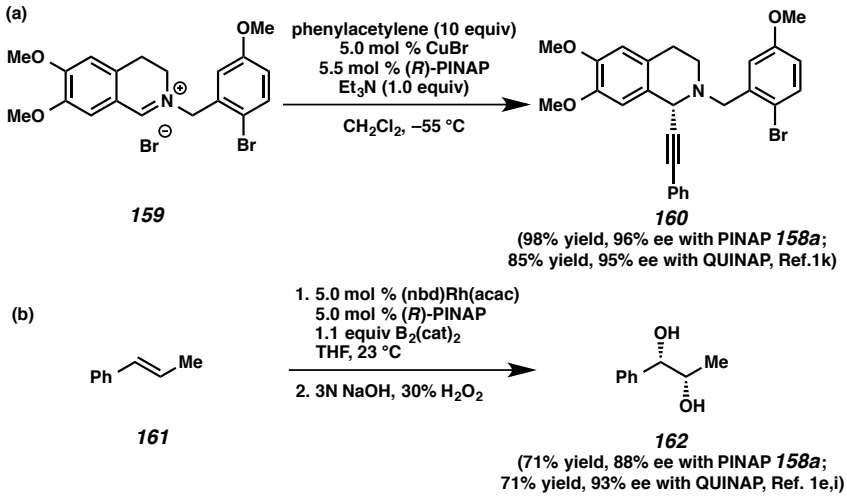


[a]Reactions performed with 1.0 equiv of **157a**, 4.0 equiv of DMAP, 1.0 mol % of $Pd[(o\text{-tol})_3P]_2$, 1.5 mol % of (S, R_{Fc})-Josiphos, 1.05 equiv of Ph_2PH (1.0 M in dioxane) at 0.20 M in dioxane at 60 °C in a glovebox. $Pd[(o\text{-tol})_3P]_2$ and (S, R_{Fc})-Josiphos in dioxane were pre-stirred before use. Ph_2PH (1.0 M in dioxane) was added over 8 h. [b]All yields are isolated yields. [c]Determined by chiral SFC analysis. [d]Determined by chiral

SFC analysis; SFC conditions: 40% IPA, 2.5 mL/min, Chiralpak OD-H column, t_R (min): major = 2.81, minor = 3.18. [e]Determined by chiral HPLC. [f](R, S_{Fc})-Josiphos was used. [g]Determined by ^{1}H NMR.

We applied PINAP ligand **158a** (96% ee) to two different reactions (Scheme 3.2.1).[8] Copper catalyzed asymmetric phenylacetylene addition to isoquinoline iminium **159** with PINAP ligand **158a** afforded propargylamine **160** in 98% yield and 96% ee (Scheme 3.2.1a).[1k,9] In addition, rhodium-catalyzed enantioselective diboration and oxidation of *trans*-b-methylstyrene **161** with PINAP **158a** produced diol **162** in 71% yield and 88% ee (Scheme 3.2.1b).[1e,i,10] The enantioselectivities and yields with PINAP **158a** ligand are parallel to those with QUINAP **155a**.

Scheme 3.2.1. *Applications*



3.3. Conclusion

In conclusion, the atroposelective synthesis of various achiral alkyl- or benzyloxy-substituted PINAP ligands via dynamic kinetic resolution has been developed. The asymmetric PINAP ligands formed in this communication are envisioned to be useful in several important asymmetric transformations.[4]

3.4. Experimental Methods and Analytical Data

3.4.1. Materials and Methods

Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Reaction progress was monitored by thin-layer chromatography (TLC). THF, Et_2O, CH_2Cl_2, toluene, benzene, CH_3CN, and dioxane were dried by passage through an activated alumina column under argon. Purified water was obtained using a Barnstead NANOpure Infinity UV/UF system. Brine solutions are saturated aqueous solutions of sodium chloride. Commercially available reagents were purchased from Sigma-Aldrich, Acros Organics, Strem, or Alfa Aesar and used as received unless otherwise stated. Reaction temperatures were controlled by an IKAmag temperature modulator unless otherwise indicated. Glove box manipulations were performed under a N_2 atmosphere. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, *p*-anisaldehyde, or PMA (phosphomolybdic acid) staining. Silicycle Silia*Flash* P60 Academic Silica gel (particle size 0.040-0.064 mm) was used for flash column chromatography. ^{1}H NMR spectra were recorded on a Varian Inova 500 MHz spectrometer and are reported relative to residual $CHCl_3$ (δ 7.26 ppm). ^{13}C NMR spectra are recorded on a Varian Inova 500 MHz spectrometer (125MHz) and are reported relative to $CHCl_3$ (δ 77.16 ppm). Data for ^{1}H NMR 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. Data for ^{13}C are reported in terms of chemical shifts (δ ppm). IR spectra were obtained using a

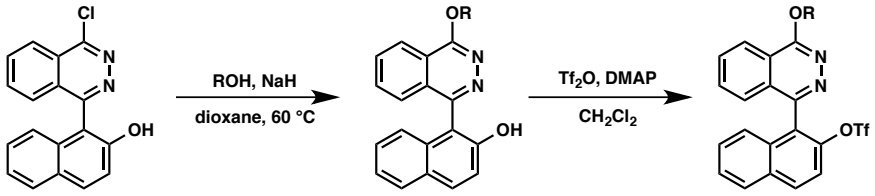
Perkin Elmer Paragon 1000 spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). Optical rotations were measured with a Jasco P-2000 polarimeter operating on the sodium D-line (589 nm), using a 100 mm path-length cell and are reported as: $[a]_D^T$ (concentration in g/100 mL, solvent). Analytical HPLC was performed with an Agilent 1100 Series HPLC utilizing Chiralpak (AD-H or AS) or Chiralcel (OD-H, OJ-H, or OB-H) columns (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. Analytical SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system utilizing Chiralpak (AD-H, AS-H or IC) or Chiralcel (OD-H, OJ-H, or OB-H) columns (4.5 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. High resolution mass spectra (HRMS) were obtained from the Caltech Mass Spectral Facility using a JEOL JMS-600H High Resolution Mass Spectrometer in fast atom bombardment (FAB+) or electron ionization (EI+) mode, or Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI+), or mixed ionization mode (MM: ESI-APCI+).

Triflate substrates **157i–157k** were prepared by known methods.[11] All the data from pinap **158i**–**158k** were confirmed by reported data.[1]

(1) (a) Knöpfel, T. F.; Aschwanden, P.; Ichikawa, T.; Watanabe, T.; Carreira, E. M. *Angew. Chem. Int., Ed.* **2004**, *43*, 5971–5973. (b) Fujimori, S.; Knöpfel, T. F.; Zarotti, P.; Ichikawa, T.; Boyall, D.; Carreira, E. M. *Bull. Chem. Soc. Jpn.* **2007**, *80*, 1635–1657.

3.4.2. Experimental Procedures

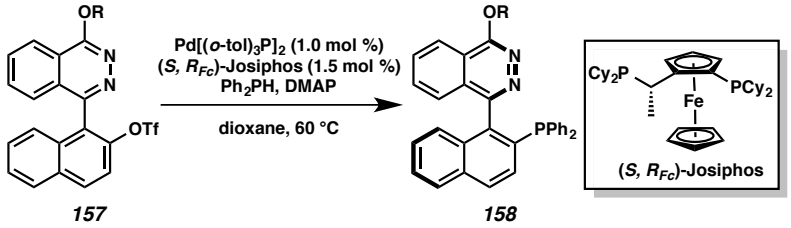
General Procedure for Synthesis of Triflate Substrates



SI-3-1 ***SI-3-2*** ***157***

To a solution of NaH (2.64 mmol, 2.00 equiv) in dioxane (5.60 mL) was added alcohol (1.39 mmol, 1.05 equiv) in dioxane (1.00 mL) dropwise. The reaction mixture was stirred for 15 min at 23 °C and then **SI-3-1** (1.32 mmol, 1.00 equiv) was added portionwise. The solution was stirred for 18 h at 60 °C then diluted with EtOAc (5.00 mL) and water (10.0 mL). The aqueous phase was extracted with EtOAc (3 x 5.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was used in the next step without further purification. To a solution of crude mixture of **SI-3-2** (1.32 mmol, 1.00 equiv) and DMAP (2.64 mmol, 2.00 equiv) in CH_2Cl_2 (13.2 mL) was added Tf_2O (1.32 mmol, 1.00 equiv) dropwise at 0 °C. The reaction mixture was stirred at 23 °C until **SI-3-2** was fully consumed by TLC analysis. The reaction mixture was diluted with CH_2Cl_2 (5.00 mL) and water (5.00 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 3.00 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography (1:4 EtOAc:hexanes) on silica gel to give the corresponding triflate substrates.

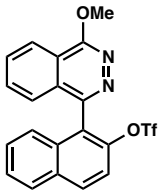
General Procedure of PINAP from Triflates via Dynamic Kinetic Resolution



157 ***158***

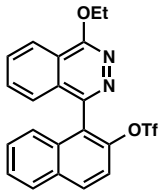
This reaction was performed in a nitrogen-filled glovebox. $Pd[(o\text{-tol})_3P]_2$ (10.8 mg, 0.0151 mmol) and (*S, R_{Fc}*)-Josiphos (13.7 mg, 0.0226 mmol) in dioxane (0.302 mL) were pre-stirred in a vial until all the solids were dissolved. To a solution of triflates **157** (0.211 mmol, 1.00 equiv) in dioxane (1.06 mL) was added DMAP (0.844 mmol, 4.00 equiv) and pre-stirred $Pd[(o\text{-tol})_3P]_2$ and (*S, R_{Fc}*)-Josiphos (0.05 M in dioxane; 0.00211 mmol, 0.01 equiv) at 23 °C. The mixture was placed in a reaction well preheated to 60 °C. A solution of Ph_2PH (1.00 M in dioxane; 0.317 mmol, 1.50 equiv) was added to the reaction mixture in 20 uL portions every 30 minutes manually. After completion of the addition (8 hours), the reaction was stirred for further 7 hours at which point complete consumption of the starting material was observed. The reaction was cooled, removed from the glovebox and dilulted with EtOAc (1.50 mL) and water (2.00 mL). The aqueous phase was extracted with EtOAc (3 x 1.50 mL). The combined organic phases were washed with brine, dried with $MgSO_4$ and concentrated. The crude material was purified by flash column chromatography on silica gel to afford the corresponding PINAP **158**.

3.4.3. Spectroscopic Data



157a

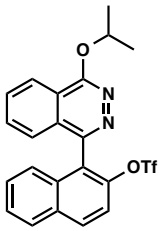
52% (2-step yield); R_f = 0.29 (1:4 EtOAc:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (dd, *J* = 8.2, 1.0 Hz, 1H), 8.12 (d, *J* = 9.1 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.87 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H), 7.70 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1H), 7.62 (d, *J* = 9.1 Hz, 1H), 7.58 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.42 (ddd, *J* = 8.2, 6.7, 1.3 Hz, 1H), 7.36 (d, *J* = 8.5 Hz, 1H), 7.31 (dt, *J* = 8.4, 1.0 Hz, 1H), 4.41 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.9, 151.1, 145.6, 133.6, 132.7, 132.6, 132.4, 131.9, 129.2, 128.4, 128.1, 127.4, 126.7, 126.6, 125.7, 123.5, 119.9, 119.6, 117.1, 55.3; IR (Neat Film NaCl) 3063, 2945, 1668, 1581, 1541, 1496, 1457, 1420, 1364, 1247, 1213, 1139, 952, 834 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{20}H_{14}F_3N_2O_4S$ $[M+H]^+$: 435.0621; found: 435.0625.



157b

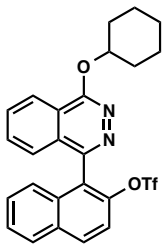
48% (2-step yield); R_f = 0.33 (1:4 EtOAc:hexanes); ^{1}H NMR (500 MHz, Chloroform-d) δ 8.38 (dd, *J* = 8.2, 1.2 Hz, 1H), 8.12 (d, *J* = 9.1 Hz, 1H), 7.99 (d, *J* = 8.3 Hz, 1H), 7.87 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.69 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1H), 7.61 (d, *J* = 9.0 Hz, 1H), 7.57 (ddd, *J* = 8.2, 6.7, 1.4 Hz, 1H), 7.42 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H), 7.37 (d, *J* = 8.5 Hz, 1H), 7.29 (dd, *J* = 8.3, 1.0 Hz, 1H), 4.88 (qd, *J* = 7.0, 3.9 Hz, 2H), 1.62 (td, *J* =

7.1, 1.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.6, 150.7, 145.6, 133.6, 132.7, 132.5, 132.3, 131.8, 129.2, 128.4, 128.1, 127.4, 126.7, 126.6, 125.6, 123.6, 120.0, 119.6, 117.1, 63.9, 14.7; IR (Neat Film NaCl) 3066, 2984, 1582, 1540, 1495, 1422, 1381, 1342, 1214, 1140, 1073, 1024, 956, 941, 834 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{21}H_{16}F_3N_2O_4S$ $[M+H]^+$: 449.0777; found: 449.0780.



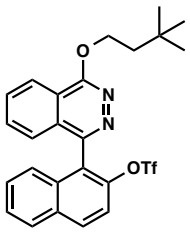
157c

37% (2-step yield); R_f = 0.35 (1:4 EtOAc:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (dd, *J* = 8.2, 1.0 Hz, 1H), 8.13 (d, *J* = 9.1 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.87 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.69 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1H), 7.62 (d, *J* = 9.1 Hz, 1H), 7.58 (ddd, *J* = 8.2, 6.7, 1.3 Hz, 1H), 7.43 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H), 7.40 – 7.35 (m, 1H), 7.30 (dt, *J* = 8.3, 0.9 Hz, 1H), 5.94 (hept, *J* = 6.2 Hz, 1H), 1.60 (d, *J* = 6.1 Hz, 3H), 1.58 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.3, 150.2, 145.7, 133.5, 132.7, 132.5, 132.4, 132.0, 129.3, 128.5, 128.2, 127.4, 126.6, 126.4, 125.7, 123.7, 120.4, 119.7, 71.1, 22.3, 22.1; IR (Neat Film NaCl) 2981, 1582, 1493, 1417, 1322, 1212, 1140, 1106, 958, 942, 833, 748 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{22}H_{17}F_3N_2O_4S$ $[M+H]^+$: 463.0934; found: 463.0964.



157d

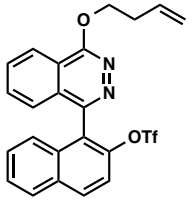
36% (2-step yield); R_f = 0.43 (1:4 EtOAc:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.2 Hz, 1H), 8.11 (dd, *J* = 9.1, 1.6 Hz, 1H), 7.99 (d, *J* = 8.3 Hz, 1H), 7.85 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1H), 7.67 (td, *J* = 7.7, 7.0, 1.4 Hz, 1H), 7.61 (dd, *J* = 9.1, 2.0 Hz, 1H), 7.57 (ddd, *J* = 8.2, 6.2, 1.9 Hz, 1H), 7.44 – 7.37 (m, 2H), 7.27 (d, *J* = 8.3 Hz, 1H), 5.72 (tt, *J* = 8.7, 3.7 Hz, 1H), 2.25 (d, *J* = 12.3 Hz, 2H), 1.90 (ddt, *J* = 13.9, 8.9, 4.5 Hz, 2H), 1.85 – 1.74 (m, 2H), 1.66 (td, *J* = 8.5, 7.7, 4.2 Hz, 1H), 1.57 (dtt, *J* = 13.5, 10.2, 3.4 Hz, 2H), 1.45 (ddt, *J* = 13.3, 10.1, 3.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.2, 150.3, 145.6, 133.6, 132.7, 132.3, 132.1, 131.7, 129.3, 128.4, 128.1, 127.3, 126.9, 126.7, 125.5, 123.7, 120.3, 119.7, 75.4, 32.0, 31.8, 25.9, 24.1; IR (Neat Film NaCl) 2937, 2858, 1582, 1537, 1493, 1418, 1362, 1342, 1214, 1140, 959, 944, 834 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{25}H_{22}F_3N_2O_4S$ $[M+H]^+$: 503.1247; found: 503.1248.



157e

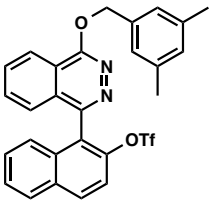
49% (2-step yield); R_f = 0.33 (1:4 EtOAc:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.2 Hz, 1H), 8.12 (d, *J* = 9.1 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.86 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H), 7.69 (ddd, *J* = 8.3, 7.1, 1.2 Hz, 1H), 7.62 (d, *J* = 9.1 Hz, 1H), 7.57 (ddd,

J = 8.2, 6.6, 1.3 Hz, 1H), 7.42 (ddd, *J* = 8.1, 6.6, 1.2 Hz, 1H), 7.39 – 7.35 (m, 1H), 7.29 (d, *J* = 8.3 Hz, 1H), 4.88 (t, *J* = 7.2 Hz, 2H), 1.96 (t, *J* = 7.2 Hz, 2H), 1.10 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.7, 150.7, 145.6, 133.6, 132.7, 132.4, 132.3, 131.8, 129.2, 128.4, 128.1, 127.4, 126.6, 125.6, 123.5, 120.0, 119.6, 117.1, 110.2, 65.8, 42.5, 30.0; IR (Neat Film NaCl) 2958, 1582, 1538, 1495, 1422, 1360, 1214, 1141, 1073, 953, 834, 620 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{25}H_{23}F_3N_2O_4S$ $[M+H]^+$: 505.1403; found: 505.1436.



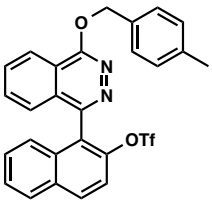
157f

52% (2-step yield); R_f = 0.33 (1:4 EtOAc:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 – 8.34 (m, 1H), 8.12 (d, *J* = 9.1 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.87 (ddd, *J* = 8.3, 7.0, 1.1 Hz, 1H), 7.69 (ddd, *J* = 8.4, 7.0, 1.3 Hz, 1H), 7.61 (d, *J* = 9.1 Hz, 1H), 7.57 (ddd, *J* = 8.2, 6.7, 1.3 Hz, 1H), 7.42 (ddd, *J* = 8.1, 6.7, 1.2 Hz, 1H), 7.38 – 7.35 (m, 1H), 7.30 (dd, *J* = 8.3, 1.1 Hz, 1H), 6.04 (ddt, *J* = 17.1, 10.3, 6.7 Hz, 1H), 5.28 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.17 (dq, *J* = 10.3, 1.4 Hz, 1H), 4.94 – 4.83 (m, 2H), 2.78 (dddd, *J* = 8.1, 6.6, 5.2, 1.4 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.6, 150.9, 145.6, 134.6, 133.6, 132.7, 132.5, 132.3, 131.8, 129.2, 128.4, 128.1, 127.4, 126.7, 126.6, 125.6, 123.5, 119.9, 119.6, 117.3, 117.1, 67.0, 33.6; IR (Neat Film NaCl) 1581, 1538, 1494, 1421, 1349, 1213, 1139, 954, 833 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{23}H_{18}F_3N_2O_4S$ $[M+H]^+$: 475.0934; found: 475.0956.



157g

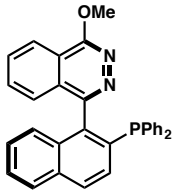
35% (2-step yield); R_f = 0.38 (1:4 EtOAc:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (dt, *J* = 8.2, 1.0 Hz, 1H), 8.13 (d, *J* = 9.1 Hz, 1H), 8.00 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.86 (ddd, *J* = 8.3, 7.1, 1.2 Hz, 1H), 7.70 (ddd, *J* = 8.3, 7.1, 1.2 Hz, 1H), 7.63 (d, *J* = 9.1 Hz, 1H), 7.58 (ddd, *J* = 8.2, 6.6, 1.3 Hz, 1H), 7.43 (ddd, *J* = 7.9, 6.6, 1.3 Hz, 1H), 7.39 (dd, *J* = 8.6, 1.2 Hz, 1H), 7.31 (dt, *J* = 8.4, 1.0 Hz, 1H), 7.04 (s, 1H), 5.80 (d, *J* = 2.3 Hz, 2H), 2.39 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.6, 151.1, 145.6, 138.3, 136.7, 133.6, 132.7, 132.6, 132.3, 131.8, 130.1, 129.3, 128.4, 128.1, 127.4, 126.7, 126.6, 126.6, 125.6, 123.7, 119.9, 119.7, 117.1, 69.8, 21.4; IR (Neat Film NaCl) 2917, 1581, 1494, 1418, 1343, 1213, 1140, 956, 835 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{28}H_{22}F_3N_2O_4S$ $[M+H]^+$: 539.1247; found: 539.1252.



157h

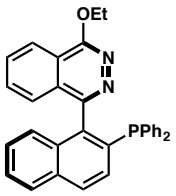
68% (2-step yield); R_f = 0.37 (1:4 EtOAc:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (dt, *J* = 8.2, 1.0 Hz, 1H), 8.13 (d, *J* = 9.1 Hz, 1H), 8.01 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.85 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.70 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1H), 7.62 (dd, *J* = 9.1, 1.1 Hz, 1H), 7.58 (ddd, *J* = 8.1, 6.8, 1.3 Hz, 1H), 7.57 – 7.52 (m, 2H), 7.43 (ddd, *J* = 8.1, 6.8, 1.3 Hz, 1H), 7.37 (dt, J = 8.6, 1.0 Hz, 1H), 7.31 (dt, *J* = 8.3, 1.0 Hz, 1H), 7.27 (d, *J* = 7.2

Hz, 2H), 5.81 (d, *J* = 7.1 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.5, 151.1, 145.5, 138.3, 133.7, 133.5, 132.6, 132.3, 131.9, 129.4, 129.2, 128.90, 128.4, 128.1, 127.4, 126.7, 126.6, 125.6, 123.6, 119.8, 119.6, 119.6, 117.0, 69.6, 21.4; IR (Neat Film NaCl) 3058, 1581, 1538, 1494, 1422, 1342, 1248, 1266, 1140, 1072, 953, 834, 776 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{27}H_{19}F_3N_2O_4S$ $[M+H]^+$: 525.1090; found: 525.1096.



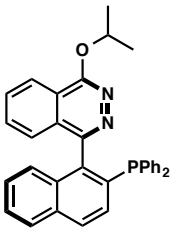
158a

$[a]_D^{25}$ +124.5 (*c* 0.51, $CHCl_3$); R_f = 0.42 (1:2 EtOAc:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (dt, *J* = 8.3, 1.0 Hz, 1H), 7.91 (dd, *J* = 8.6, 0.8 Hz, 1H), 7.90 – 7.87 (m, 1H), 7.74 (ddd, *J* = 8.2, 7.1, 1.1 Hz, 1H), 7.49 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.46 – 7.42 (m, 2H), 7.29 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.27 – 7.14 (m, 11H), 7.07 (dt, *J* = 8.2, 0.9 Hz, 1H), 4.36 (s, 3H); (due to the C–P coupling, the ^{13}C NMR contained extra peaks. See the attached spectrum); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.4, 156.8, 156.8, 141.5, 141.3, 137.5, 137.4, 137.3, 137.2, 136.0, 135.9, 134.0, 133.9, 133.7, 133.3, 133.2, 133.1, 131.8, 131.7, 130.3, 130.0, 129.9, 129.3, 128.7, 128.4, 128.4, 128.2, 128.1, 127.1, 126.9, 126.7, 126.7, 126.1, 123.2, 119.6, 55.1; ^{31}P NMR (121 MHz, $CDCl_3$) δ -14.3; IR (Neat Film NaCl) 3053, 1582, 1538, 1495, 1456, 1362, 1112, 1018, 744 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{31}H_{23}N_2OP$ $[M+H]^+$: 471.1621; found: 471.1674; SFC conditions: 35% IPA, 2.5mL/min, Chiralcel OD-H column, t_R (min): major = 5.81, minor = 5.16.



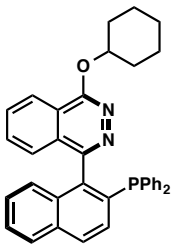
158b

$[a]_D^{25}$ +150.3 (*c* 0.47, $CHCl_3$); R_f = 0.54 (1:2 EtOAc:hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 8.30 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.91 (d, *J* = 8.6 Hz, 1H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.74 (ddd, *J* = 8.2, 7.1, 1.1 Hz, 1H), 7.49 (ddd, *J* = 8.1, 6.8, 1.3 Hz, 1H), 7.47 – 7.41 (m, 2H), 7.29 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.27 – 7.13 (m, 11H), 7.07 (d, *J* = 8.2 Hz, 1H), 4.83 (qt, *J* = 7.1, 2.1 Hz, 2H), 1.60 (t, *J* = 7.1 Hz, 3H); (due to the C–P coupling, the ^{13}C NMR contained extra peaks. See the attached spectrum); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.2, 156.5, 156.5, 141.6, 141.3, 137.6, 137.5, 137.3, 137.2, 136.0, 135.9, 134.0, 133.8, 133.7, 133.3, 133.2, 133.1, 131.8, 131.5, 130.3, 130.0, 129.9, 129.2, 128.6, 128.4, 128.4, 128.2, 128.1, 127.1, 126.8, 126.8, 126.7, 126.1, 123.3, 119.6, 63.5, 14.9; ^{31}P NMR (121 MHz, $CDCl_3$) δ -14.2; IR (Neat Film NaCl) 3053, 2980, 1583, 1538, 1494, 1418, 1378, 1342, 1165, 1110, 1023, 818, 744 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{32}H_{25}N_2OP$ $[M+H]^+$: 485.1777; found: 485.1800; SFC conditions: 30% MeOH, 2.5mL/min, Chiralpak AD-H column, t_R (min): major = 2.60, minor = 3.09.



158c

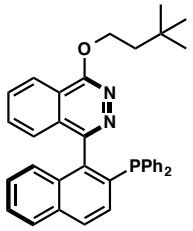
$[a]_D^{25}$ +131.7 (*c* 0.57, $CHCl_3$); R_f = 0.54 (1:2 EtOAc:hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 8.29 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.90 (t, *J* = 9.0 Hz, 2H), 7.73 (ddd, *J* = 8.2, 7.1, 1.1 Hz, 1H), 7.52 – 7.42 (m, 3H), 7.30 (ddd, *J* = 8.4, 6.6, 1.2 Hz, 1H), 7.28 – 7.15 (m, 11H), 7.08 (dt, *J* = 8.1, 0.9 Hz, 1H), 5.88 (p, *J* = 6.2 Hz, 1H), 1.58 (d, *J* = 5.7 Hz, 3H), 1.56 (d, *J* = 5.7 Hz, 3H); (due to the C–P coupling, the ^{13}C NMR contained extra peaks. See the attached spectrum); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.7, 156.0, 156.0, 141.6, 141.3, 137.6, 137.5, 137.3, 137.2, 136.0, 135.9, 134.0, 133.8, 133.7, 133.4, 133.2, 133.2, 133.1, 131.7, 131.4, 130.2, 130.0, 129.2, 128.6, 128.4, 128.4, 128.4, 128.4, 128.2, 128.1, 127.0, 126.8, 126.0, 123.4, 120.0, 70.1, 22.4, 22.3; ^{31}P NMR (121 MHz, $CDCl_3$) δ -13.9; IR (Neat Film NaCl) 3053, 2978, 1584, 1489, 1413, 1383, 1315, 1106, 744 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{33}H_{27}N_2OP$ $[M+H]^+$: 499.1934; found: 499.1960; SFC conditions: 40% MeOH, 2.5mL/min, Chiralpak AD-H column, t_R (min): major = 1.94, minor = 2.22.



158d

$[a]_D^{25}$ +91.0 (*c* 0.57, $CHCl_3$); R_f = 0.61 (1:2 EtOAc:hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 8.29 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.89 (ddd, *J* = 9.4, 8.2, 0.8 Hz, 2H), 7.73 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.49 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H), 7.46 – 7.41 (m, 2H), 7.29 (ddd, *J* = 8.2, 6.7, 1.3 Hz, 1H), 7.26 – 7.14 (m, 11H), 7.07 (dt, *J* = 8.3, 0.9 Hz, 1H), 5.67 (tt, *J* = 8.9, 3.8 Hz, 1H), 2.30 – 2.18 (m, 2H), 1.88 (ddtd, *J* = 9.3, 7.9, 5.4, 4.0 Hz, 2H), 1.76 (qdt,

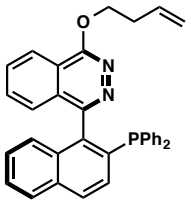
J = 9.9, 6.1, 3.7 Hz, 2H), 1.64 (tt, *J* = 9.1, 4.9 Hz, 1H), 1.54 (qq, *J* = 10.2, 3.5 Hz, 2H), 1.42 (ddt, *J* = 13.4, 10.2, 3.5 Hz, 1H); (due to the C–P coupling, the ^{13}C NMR contained extra peaks. See the attached spectrum); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.6, 156.0, 155.9, 141.6, 141.4, 137.6, 137.5, 137.3, 137.2, 136.0, 135.9, 134.0, 133.9, 133.7, 133.4, 133.2, 131.7, 131.4, 130.3, 130.0, 129.2, 128.6, 128.4, 128.4, 128.4, 128.4, 128.2, 128.1, 127.0, 126.8, 126.8, 126.8, 126.0, 123.4, 120.0, 74.8, 32.0, 31.9, 25.9, 24.1, 24.0; ^{31}P NMR (121 MHz, $CDCl_3$) δ -13.9; IR (Neat Film NaCl) 3051, 2933, 2856, 1582, 1538, 1490, 1432, 1413, 1361, 1341, 1311, 1263, 1215, 1165, 1113, 1068, 1046, 1019, 744 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{36}H_{31}N_2OP$ $[M+H]^+$: 539.2247; found: 539.2268; SFC conditions: 25% MeOH, 2.5mL/min, Chiralcel OD-H column, t_R (min): major = 7.58, minor = 8.13.



158e

$[a]_D^{25}$ +101.2 (*c* 0.42, $CHCl_3$); R_f = 0.62 (1:2 EtOAc:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.73 (ddt, *J* = 8.7, 7.1, 1.4 Hz, 1H), 7.49 (ddt, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.29 (ddd, *J* = 8.2, 6.7, 1.3 Hz, 1H), 7.27 – 7.14 (m, 11H), 7.06 (d, *J* = 8.2 Hz, 1H), 4.87 – 4.77 (m, 2H), 1.94 (td, *J* = 7.1, 1.9 Hz, 2H), 1.09 (s, 9H); (due to the C–P coupling, the ^{13}C NMR contained extra peaks. See the attached spectrum); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.3, 156.5, 156.4, 141.6, 141.3, 137.6, 137.5, 137.3, 137.2, 136.0,

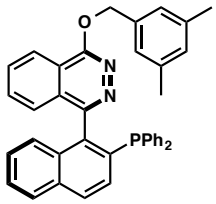
135.9, 134.0, 133.9, 133.7, 133.3, 133.2, 133.1, 131.7, 131.6, 130.3, 129.9, 129.2, 128.7, 128.4, 128.4, 128.2, 128.1, 127.1, 126.8, 126.8, 126.7, 126.1, 123.2, 119.7, 77.2, 65.4, 42.5, 30.1; ^{31}P NMR (121 MHz, $CDCl_3$) δ -14.2; IR (Neat Film NaCl) 3051, 2956, 1418, 1386, 1114, 743 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{36}H_{33}N_2OP$ $[M+H]^+$: 541.2403; found: 541.2409; SFC conditions: 35% IPA, 2.5mL/min, Chiralcel OD-H column, t_R (min): major = 4.33, minor = 4.84.



158f

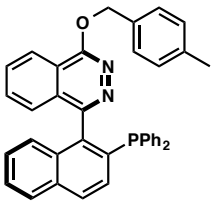
$[a]_D^{25}$ +117.9 (*c* 0.52, $CHCl_3$); R_f = 0.62 (1:2 EtOAc:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.2 Hz, 1H), 7.91 (d, *J* = 8.6 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.75 (ddd, *J* = 8.3, 7.1, 1.2 Hz, 1H), 7.52 – 7.41 (m, 3H), 7.30 (ddd, *J* = 8.3, 6.8, 1.3 Hz, 1H), 7.26 – 7.14 (m, 11H), 7.08 (dt, *J* = 8.4, 0.9 Hz, 1H), 6.04 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.28 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.17 (dt, *J* = 10.5, 1.6 Hz, 1H), 4.88 – 4.77 (m, 2H), 2.75 (qt, *J* = 6.8, 1.3 Hz, 2H); (due to the C–P coupling, the ^{13}C NMR contained extra peaks. See the attached spectrum); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.1, 156.7, 156.6, 141.5, 141.2, 137.6, 137.5, 137.2, 137.2, 136.0, 135.9, 134.9, 134.0, 133.8, 133.7, 133.3, 133.2, 133.2, 133.1, 131.9, 131.6, 130.3, 130.0, 130.0, 129.3, 128.7, 128.4, 128.4, 128.2, 128.1, 127.1, 126.9, 126.7, 126.7, 126.1, 123.2, 119.6, 117.2, 77.2, 66.7, 33.7; ^{31}P NMR (121 MHz, $CDCl_3$) δ -14.2; IR (Neat Film NaCl) 2096, 1642, 1417, 1348, 1113, 1020, 818, 744 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{34}H_{27}N_2OP$ $[M+H]^+$: 511.1934;

found: 511.1954; SFC conditions: 35% MeOH, 2.5mL/min, Chiralpak AD-H column, t_R (min): major = 3.00, minor = 3.66.



158g

$[a]_D^{25}$ +40.1 (*c* 0.31, $CHCl_3$); R_f = 0.56 (1:2 EtOAc:hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.2 Hz, 1H), 7.91 (t, *J* = 7.8 Hz, 2H), 7.73 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H), 7.54 – 7.41 (m, 3H), 7.35 – 7.13 (m, 14H), 7.12 – 7.03 (m, 2H), 5.74 (d, *J* = 5.4 Hz, 2H), 2.39 (s, 6H); (due to the C–P coupling, the ^{13}C NMR contained extra peaks. See the attached spectrum); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 156.9, 156.8, 141.5, 141.1, 138.3, 137.5, 137.4, 137.3, 137.1, 136.9, 136.0, 135.9, 134.1, 133.8, 133.7, 133.4, 133.2, 133.1, 133.1, 131.9, 131.6, 130.3, 130.0, 130.0, 129.3, 128.7, 128.5, 128.4, 128.4, 128.2, 128.1, 127.1, 126.9, 126.7, 126.7, 126.6, 126.6, 126.1, 123.4, 119.6, 69.5, 21.5; ^{31}P NMR (121 MHz, $CDCl_3$) δ -14.2; IR (Neat Film NaCl) 3052, 2917, 1608, 1582, 1538, 1492, 1480, 1432, 1414, 1386, 1345, 1264, 1165, 1113, 1019, 962, 851, 818, 777, 743 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{39}H_{31}N_2OP$ $[M+H]^+$: 575.2247; found: 575.2293; SFC conditions: 40% MeOH, 2.5mL/min, Chiralcel OD-H column, t_R (min): major = 5.77, minor = 6.82.



158h

$[a]_D^{25}$ +118.5 (*c* 0.33, $CHCl_3$); R_f = 0.61 (1:2 EtOAc:hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 8.29 (dt, *J* = 8.2, 1.7 Hz, 1H), 7.91 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.88 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.71 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.52 (dd, *J* = 8.2, 2.6 Hz, 2H), 7.48 (ddd, *J* = 8.2, 6.7, 1.3 Hz, 1H), 7.43 (dddd, *J* = 9.2, 6.0, 3.4, 1.8 Hz, 2H), 7.32 – 7.13 (m, 14H), 7.10 – 7.06 (m, 1H), 5.76 (q, *J* = 12.1 Hz, 2H), 2.40 (s, 3H); (due to the C–P coupling, the ^{13}C NMR contained extra peaks. See the attached spectrum); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.1, 156.9, 156.8, 141.4, 141.2, 138.1, 137.5, 137.4, 137.2, 137.1, 136.0, 135.9, 134.0, 133.9, 133.7, 133.4, 133.2, 133.1, 131.9, 131.6, 130.3, 130.0, 130.0, 129.4, 129.4, 129.3, 128.9, 128.7, 128.4, 128.4, 128.4, 128.4, 128.3, 128.1, 127.1, 126.9, 126.7, 126.7, 126.1, 123.3, 119.6, 69.3, 21.4; ^{31}P NMR (121 MHz, $CDCl_3$) δ -14.2; IR (Neat Film NaCl) 3051, 1583, 1492, 1416, 1345, 1163, 1112, 1019, 744 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{38}H_{29}N_2OP$ $[M+H]^+$: 561.2090; found: 561.2090; SFC conditions: 40% MeOH, 2.5mL/min, Chiralpak AD-H column, t_R (min): major = 3.43, minor = 5.21.

3.5. References and Notes

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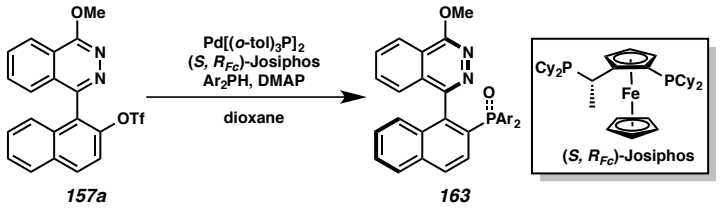
(2) (a) Alcock, N. W.; Brown, J. M.; Hulmes, D. I. *Tetrahedron: Asymmetry* **1993**, *4*, 743–756. (b) Lim, C. W.; Tissot, O.; Mattison, A. Hooper, M. W.; Brown, J. M.; Cowley, A. R.; Hulmes, D. I.; Blacker, A. J. *Org. Process Res. Dev.* **2003**, *7*, 379–384. (c) Thaler, T.; Geittner, F.; Knochel, P. *Synlett* **2007**, 2655–2658. (d) Clayden, J.; Fletcher, S. P.; McDouall, J. J. W.; Rowbottom, S. J. M. *J. Am. Chem. Soc.* **2009**, *131*, 5331–5343.

(3) Bhat, V.; Wang, S.; Stoltz, B. M.; Virgil, S. C. *J. Am. Chem. Soc.* **2013**, *135*, 16829–16832.

(4) (a) Knöpfel, T. F.; Aschwanden, P.; Ichikawa, T.; Watanabe, T.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 5971–5973. (b) Fujimori, S.; Knöpfel, T. F.; Zarotti, P.; Ichikawa, T.; Boyall, D.; Carreira, E. M. *Bull. Chem. Soc. Jpn.* **2007**, *80*, 1635–1657.

(5) See Ref. 3 for a plausible mechanism of this dynamic kinetic resolution.

(6) Attempts to produce PINAP derivatives with diphenylphosphine oxide and (p-CF_3-$C_6H_4)_2PH$ in high enantioselectivities under our dynamic kinetic resolution conditions were unsuccessful.

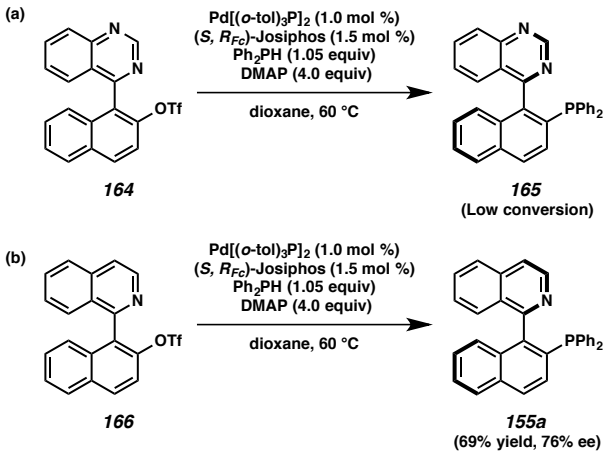


157a *163*

entry	$Ar_2\overset{O}{\overset{\|}{P}}H$	T (°C)	ee (%)
1	diphenylphosphine oxide	60	–[b]
2	(p-CF_3-$C_6H_4)_2PH$	60	–[c]
3	(p-CF_3-$C_6H_4)_2PH$	70	38[d]
4	(p-CF_3-$C_6H_4)_2PH$	80	50[d]

[a] Reactions performed with 1.0 equiv of **157a**, 4.0 equiv of DMAP, 1.0 mol % of $Pd[(o\text{-tol})_3P]_2$, 1.5 mol % of (S, R_{Fc})-Josiphos, 1.05 equiv of Ar_2PH (1.0 M in dioxane) at 0.20 M in dioxane in a glovebox. Ar_2PH (1.0 M in dioxane) was added over 8 h. [b] No reaction. [c] ~50% conversion. [d] Determined by chiral SFC analysis; SFC conditions: 35% IPA, 2.5 mL/min, Chiralpak IC column, t_R (min): major = 3.06, minor = 3.98.

(7) To demonstrate the scope of our methodology, the enantioselective synthesis of Quinazolinap from triflate **164** was attempted, but our reaction conditions led to poor conversion. Moreover, treatment of triflate **166** with the optimized conditions for PINAP provided the QUINAP ligand in diminished selectivity compared to that with the original reaction conditions[3].



(8) 96% ee (*R*)-PINAP **158a** was used for both applications.

(9) Determined by chiral HPLC analysis: conditions: 10% IPA 45 min, AD column, t_R: (min): minor = 10.5 min, major = 18.2 min. All the other spectra data were identical to the reported data. (ref. 1k)

(10) Determined by chiral SFC analysis: conditions: 20% MeOH, 2.5 mL/min, AD-H column, t_R (min): major = 2.46 min, minor = 2.92 min; $[a]_D^{25}$ +38.6 (*c* 0.19, $CHCl_3$)

APPENDIX 7

Spectra Relevant to Chapter 3:

Enantioselective Synthesis of PINAP via Dynamic Kinetic Resolution

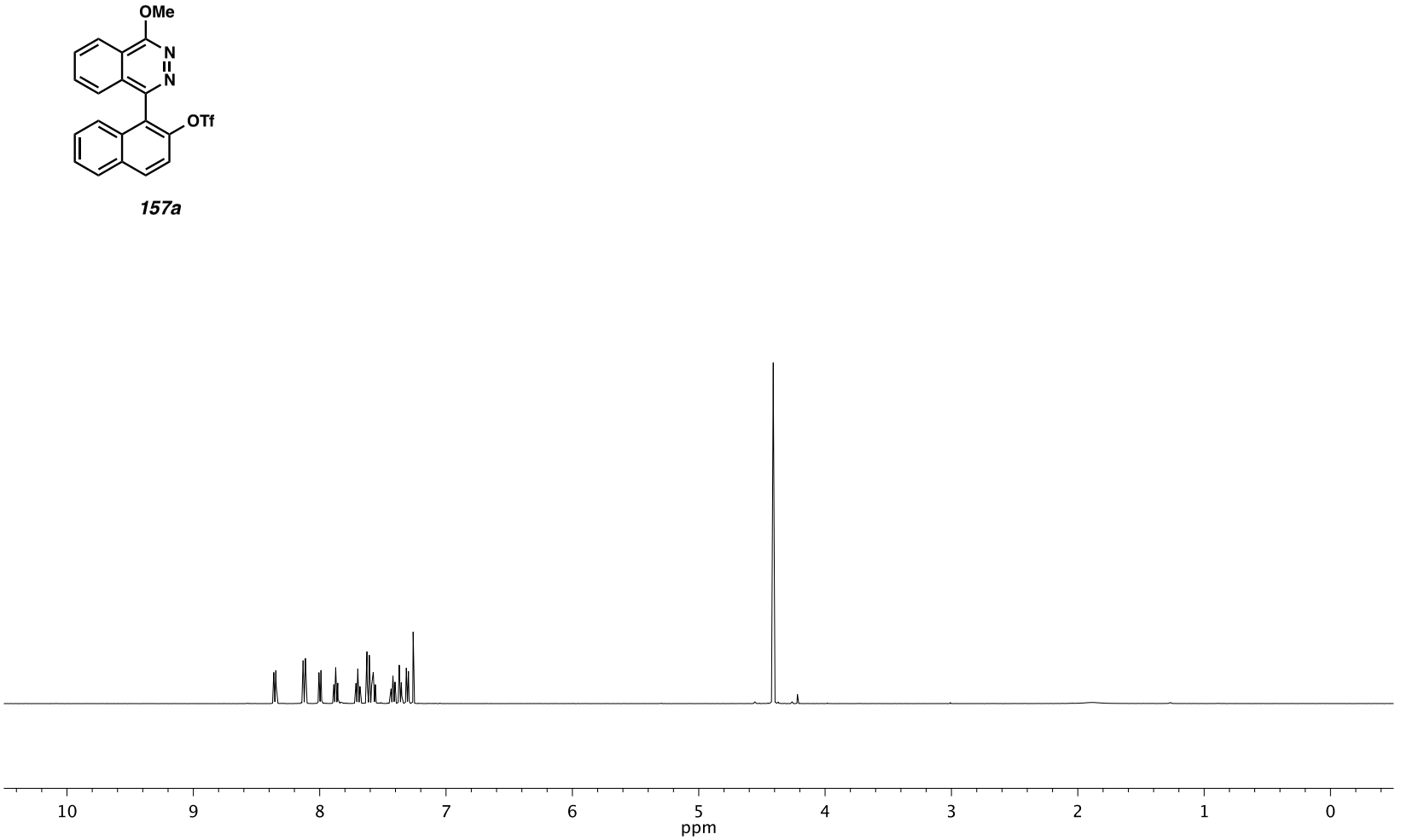


Figure A7.1. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **157a**.

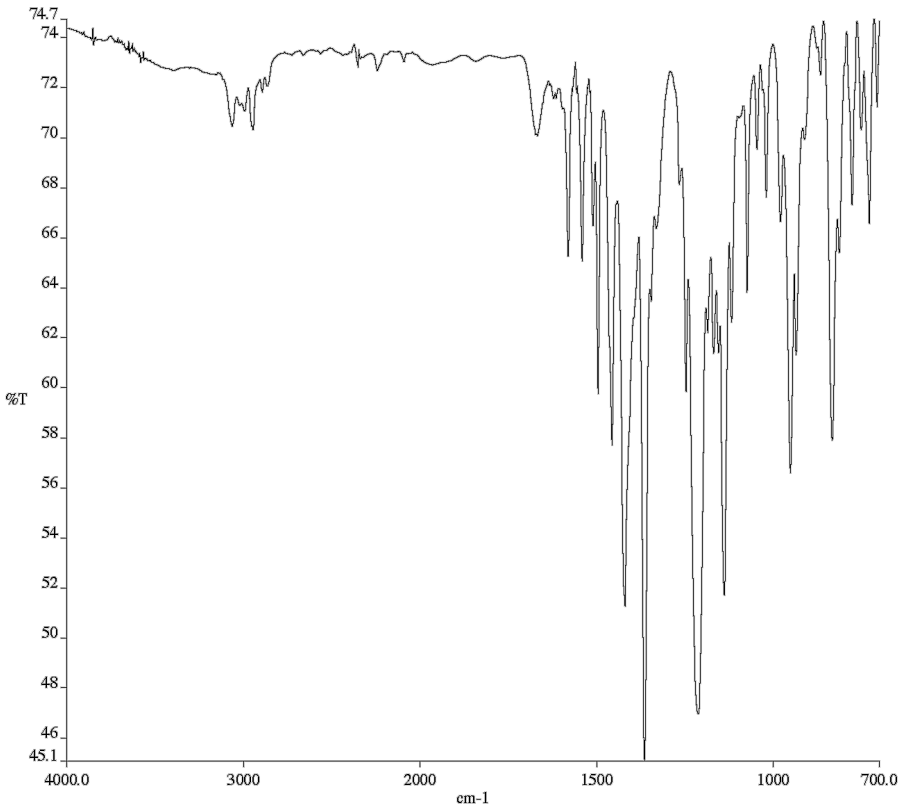


Figure A7.2. Infrared spectrum (Thin Film, NaCl) of compound **157a**.

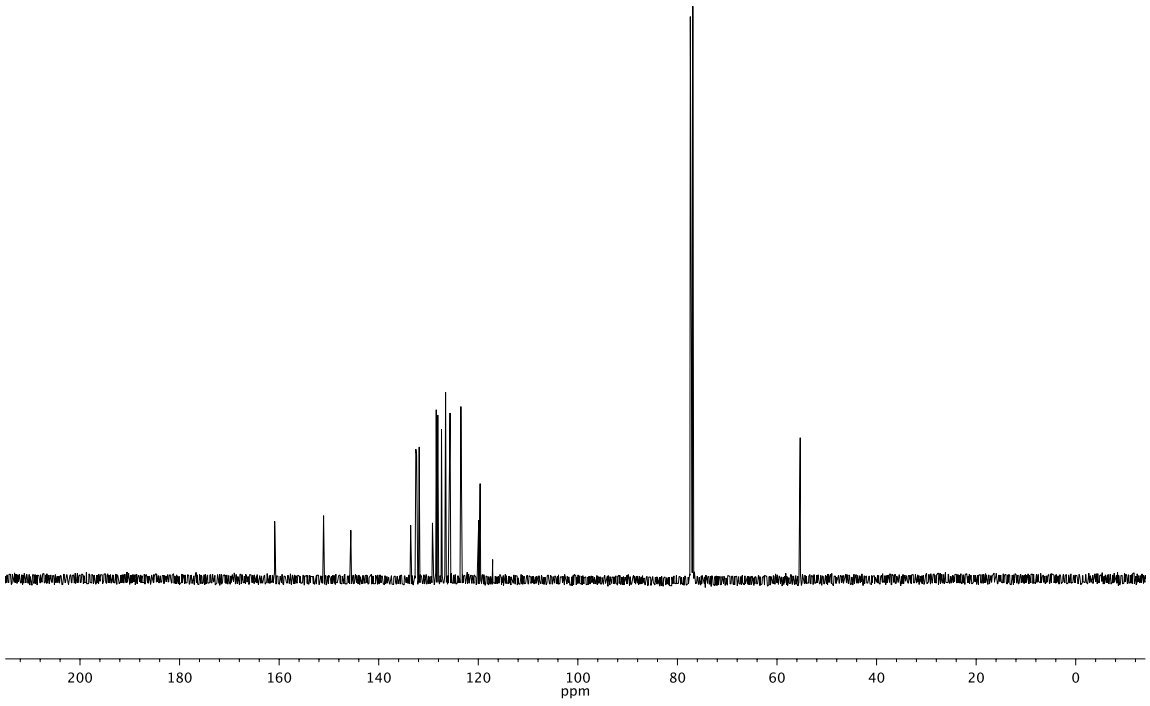


Figure A7.3. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **157a**.

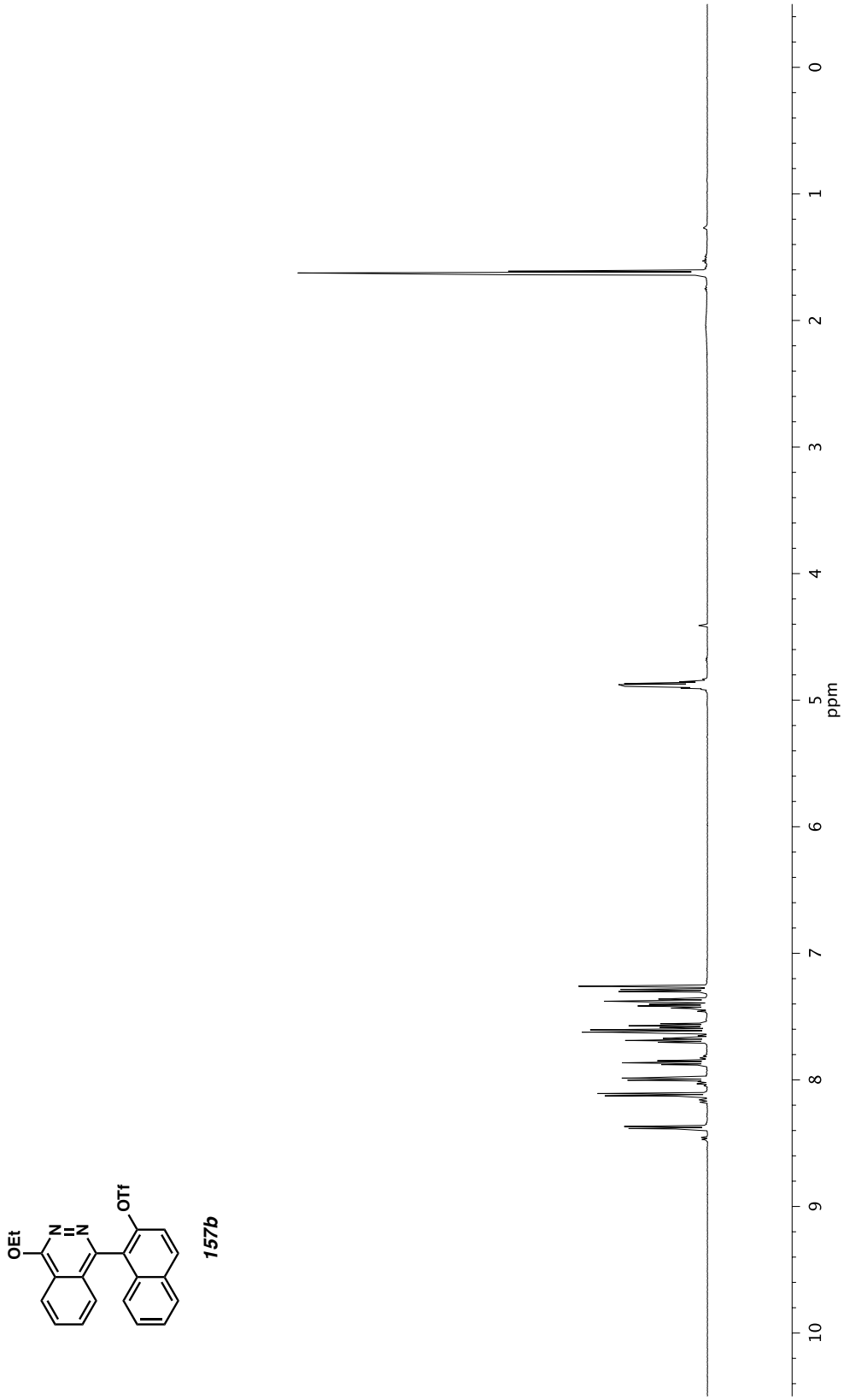


Figure A7.4. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **157b**.

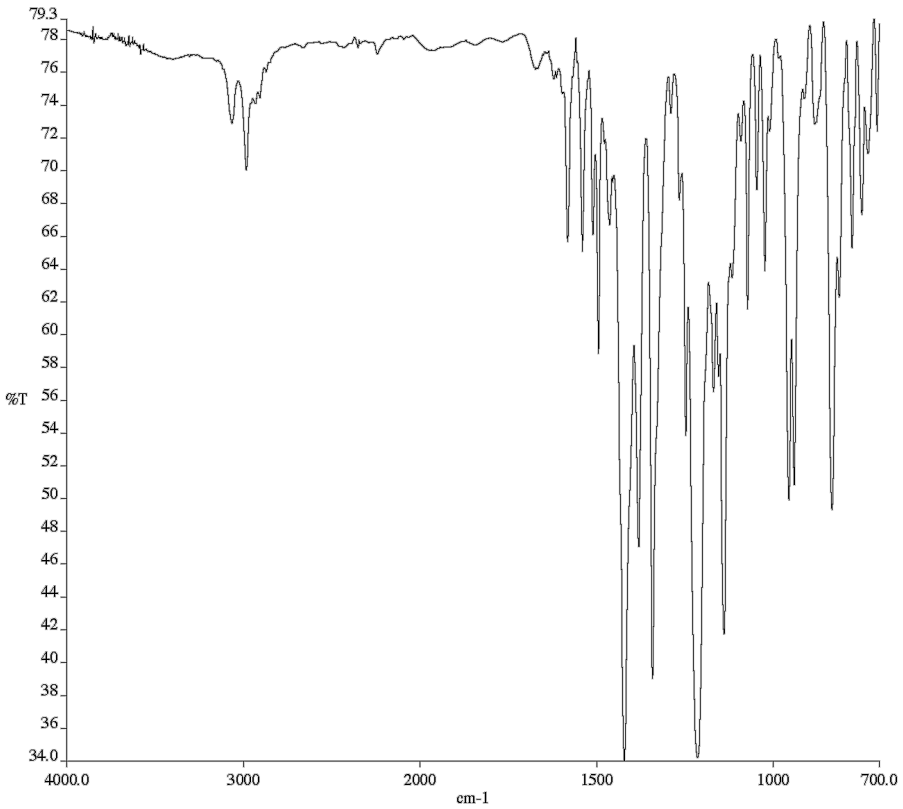


Figure A7.5. Infrared spectrum (Thin Film, NaCl) of compound **157b**.

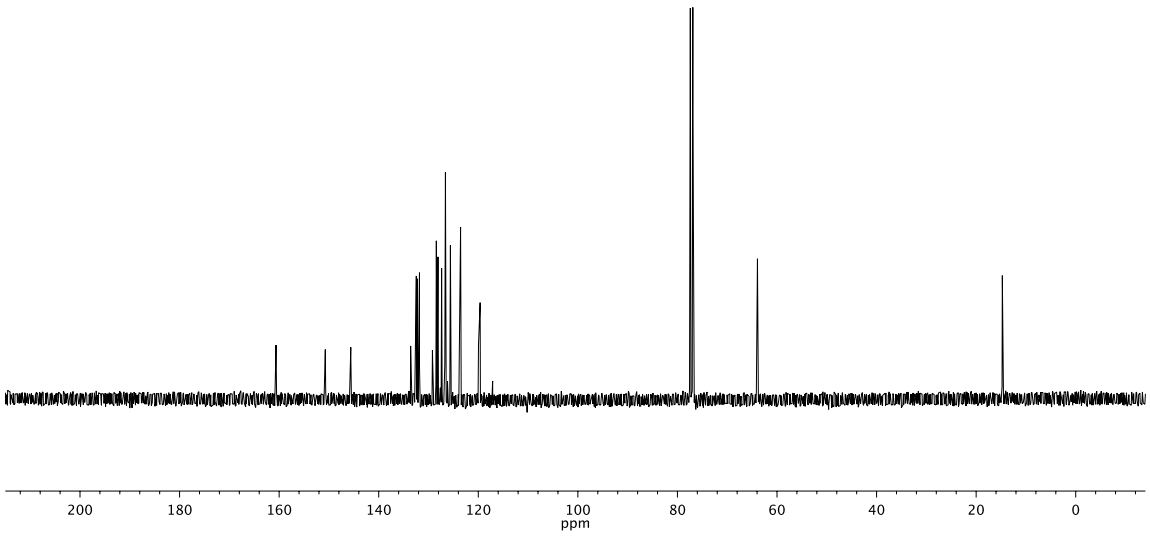


Figure A7.6. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **157b**.

Figure A7.7. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **157c**.

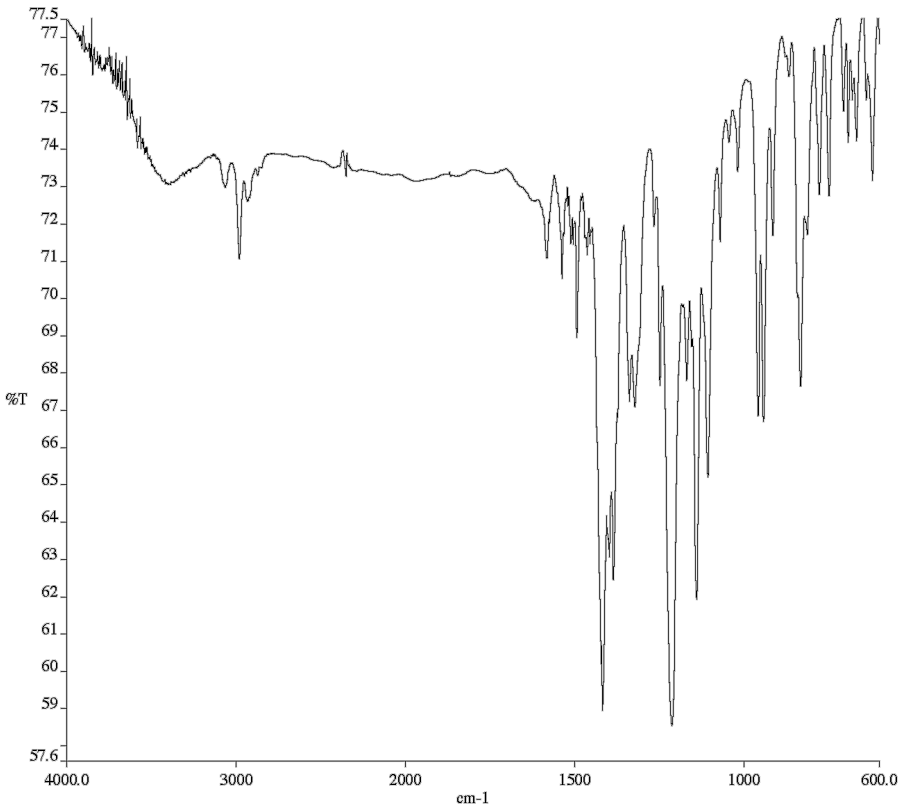


Figure A7.8. Infrared spectrum (Thin Film, NaCl) of compound **157c**.

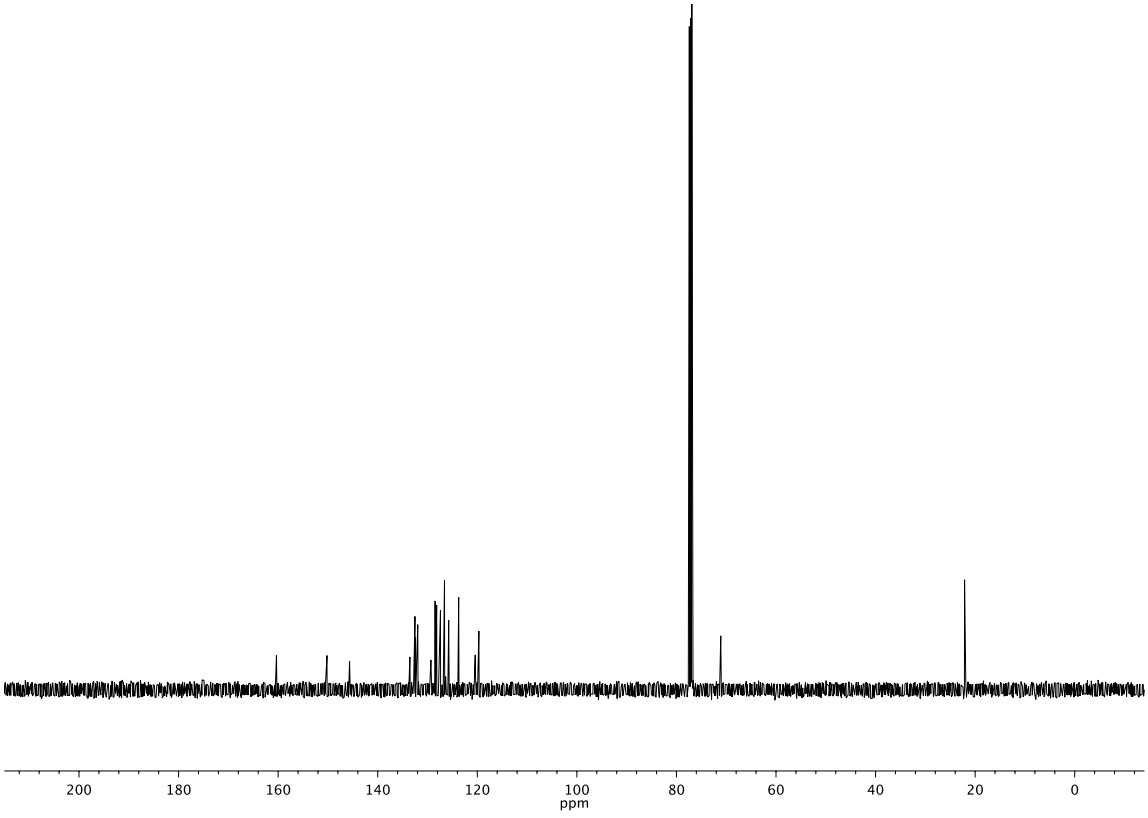


Figure A7.9. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **157c**.

Figure A7.10. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **157d**.

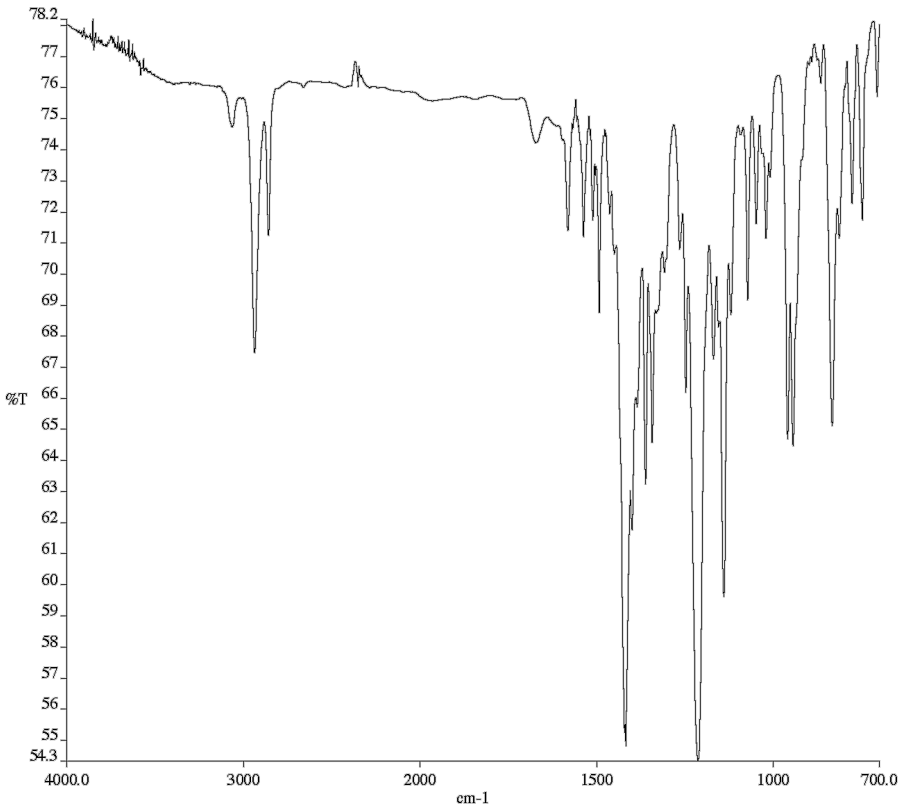


Figure A7.11. Infrared spectrum (Thin Film, NaCl) of compound **157d**.

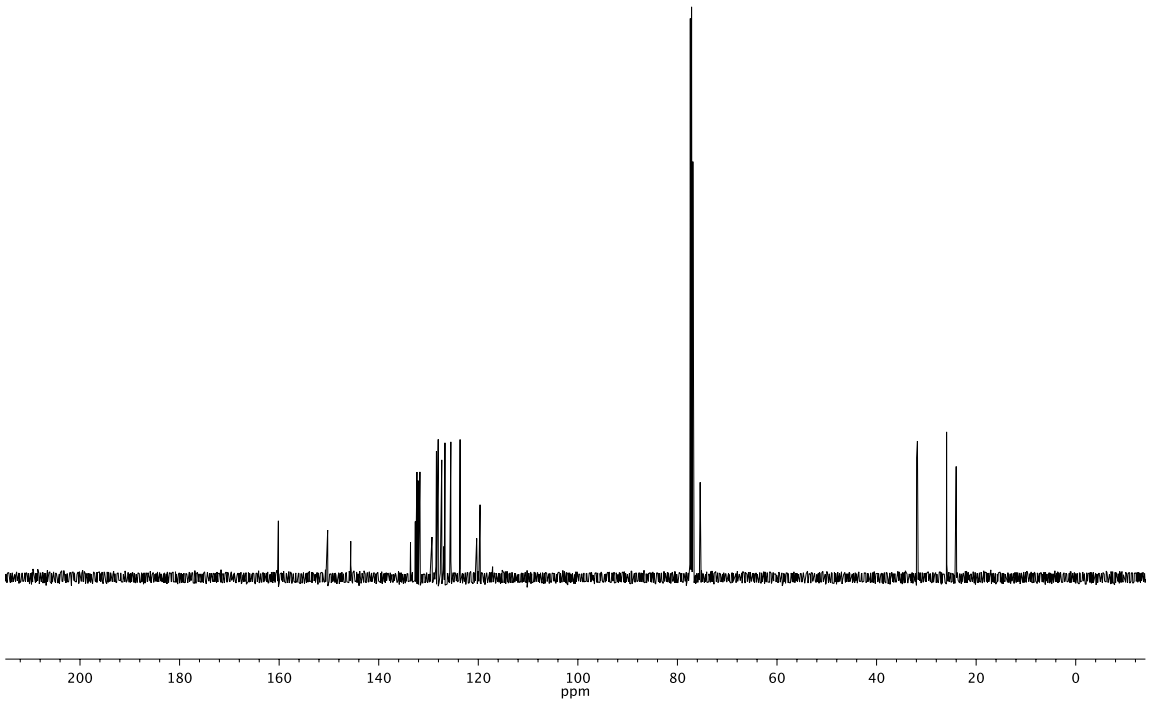


Figure A7.12. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **157d**.

Figure A7.13. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **157e**.

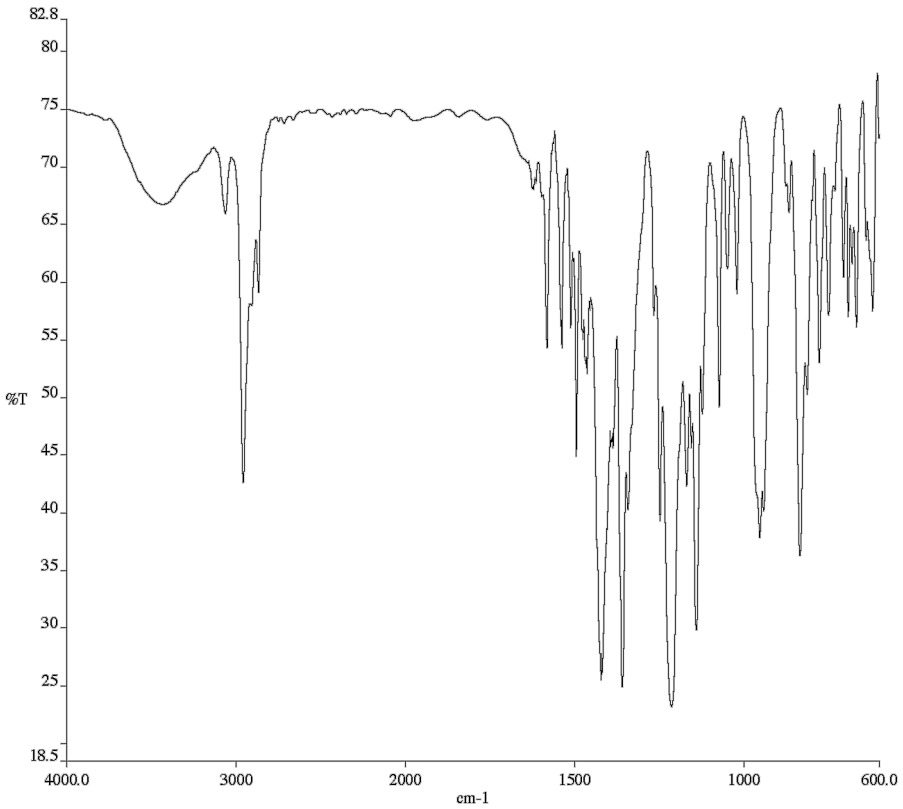


Figure A7.14. Infrared spectrum (Thin Film, NaCl) of compound **157e**.

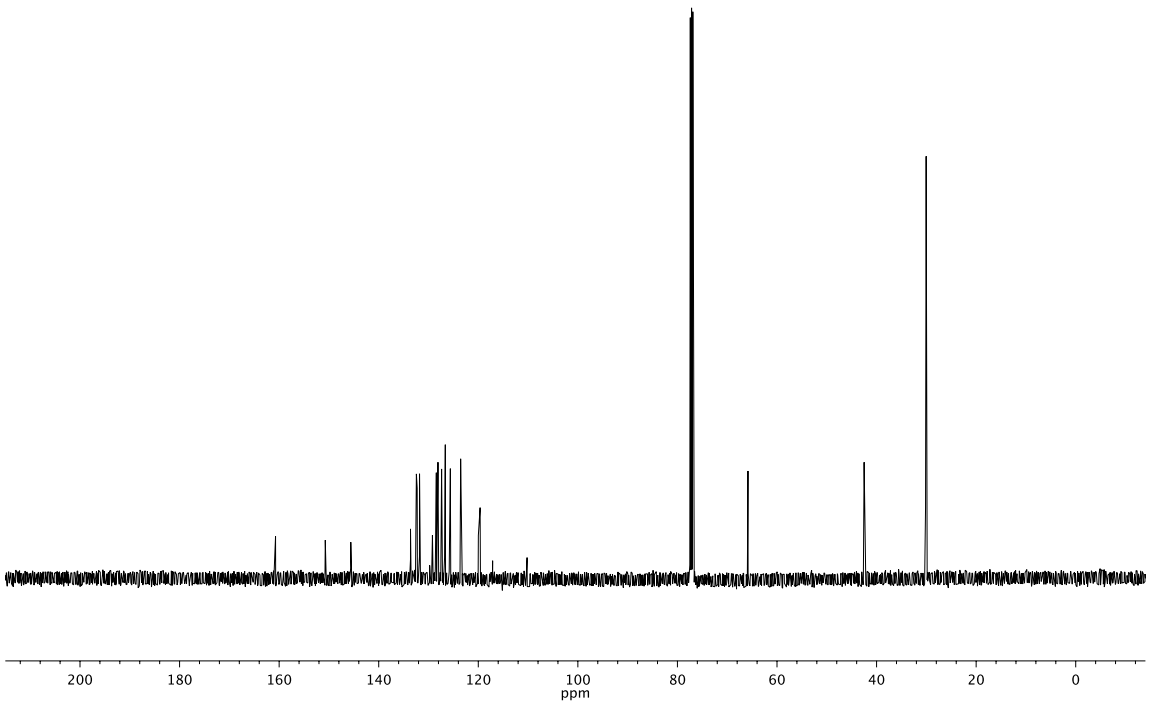


Figure A7.15. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **157e**.

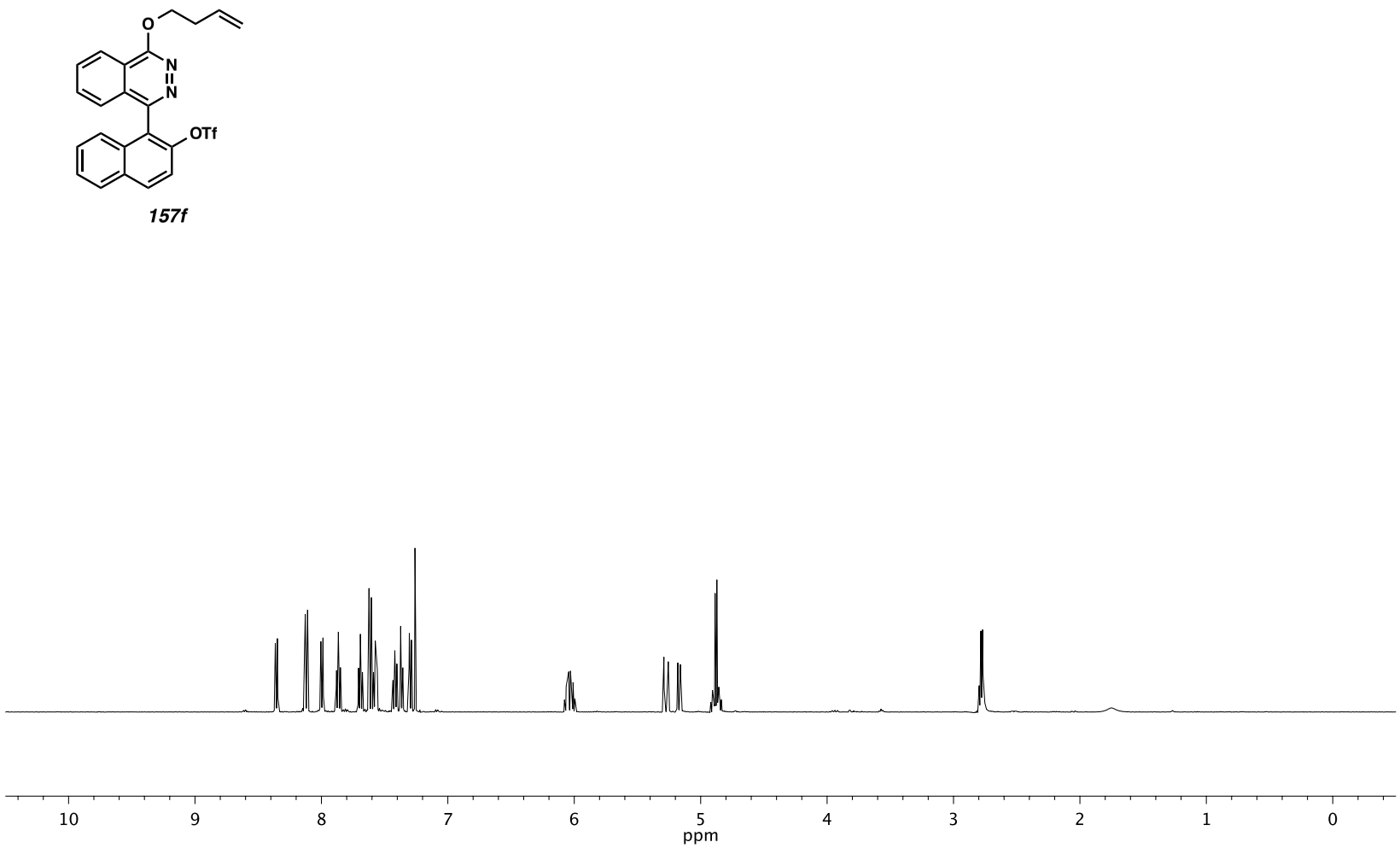


Figure A7.16. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **157f**.

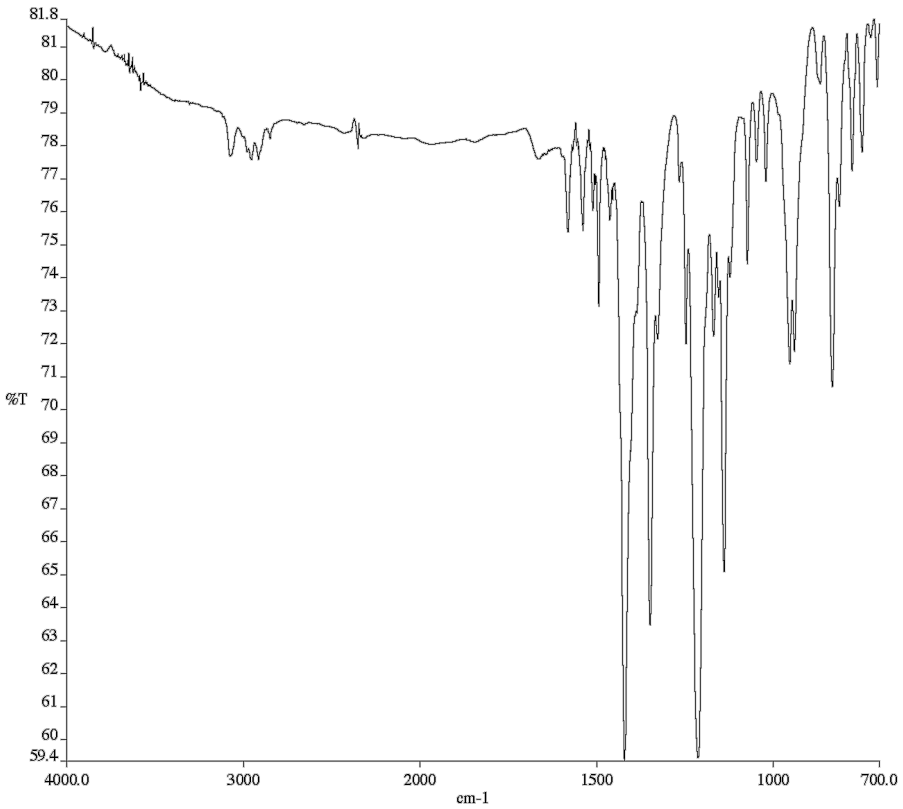


Figure A7.17. Infrared spectrum (Thin Film, NaCl) of compound **157f**.

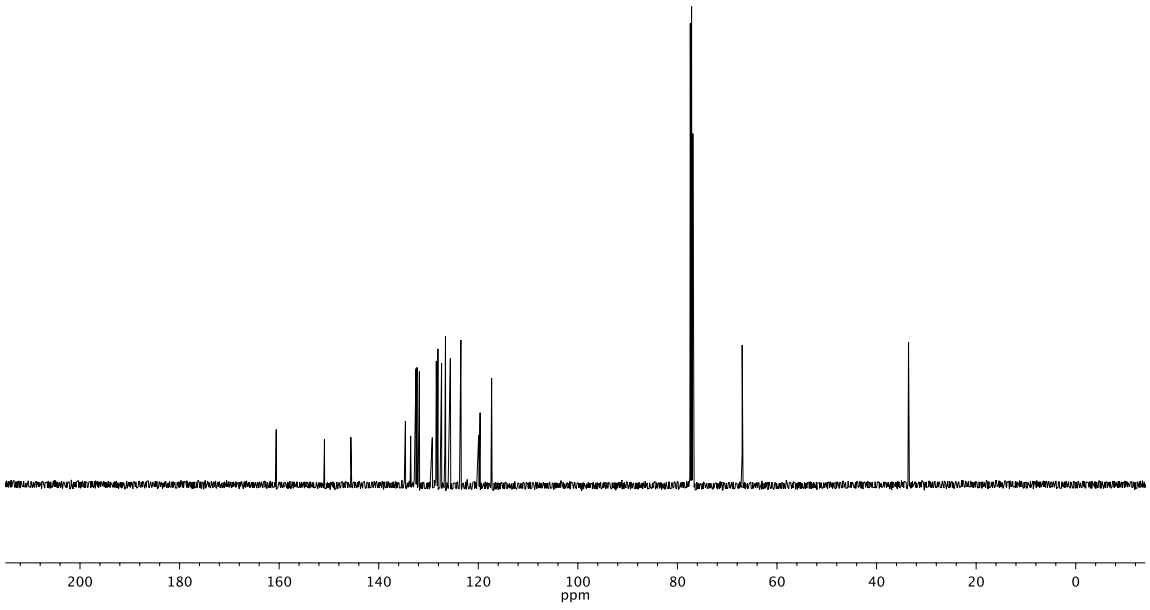


Figure A7.18. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **157f**.

Figure A7.19. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **157g**.

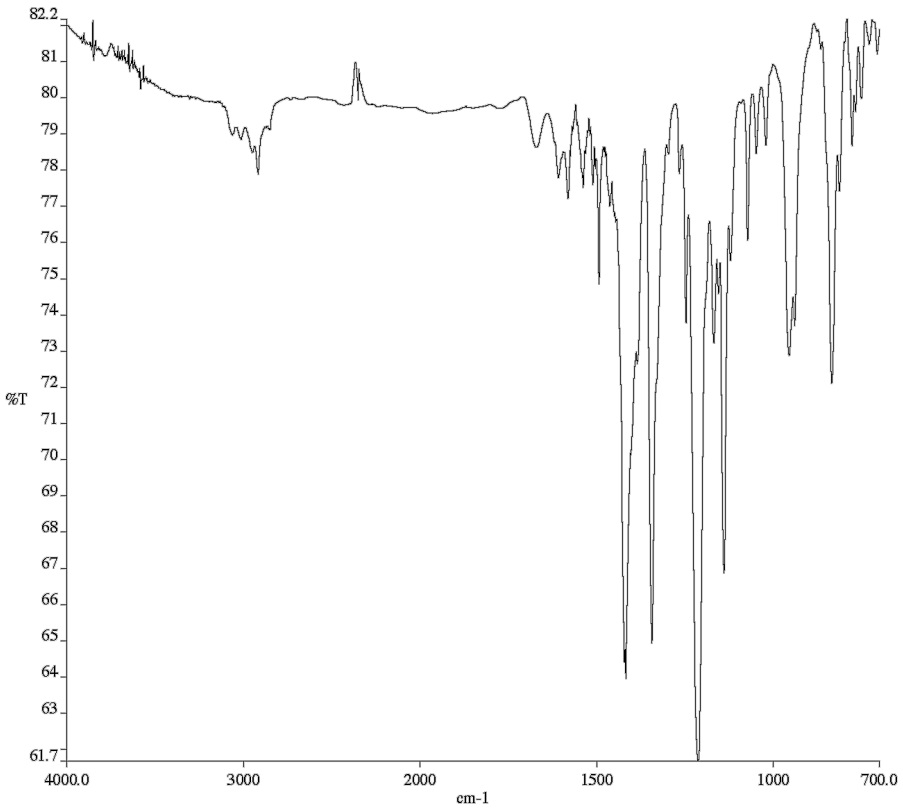


Figure A7.20. Infrared spectrum (Thin Film, NaCl) of compound **157g.**

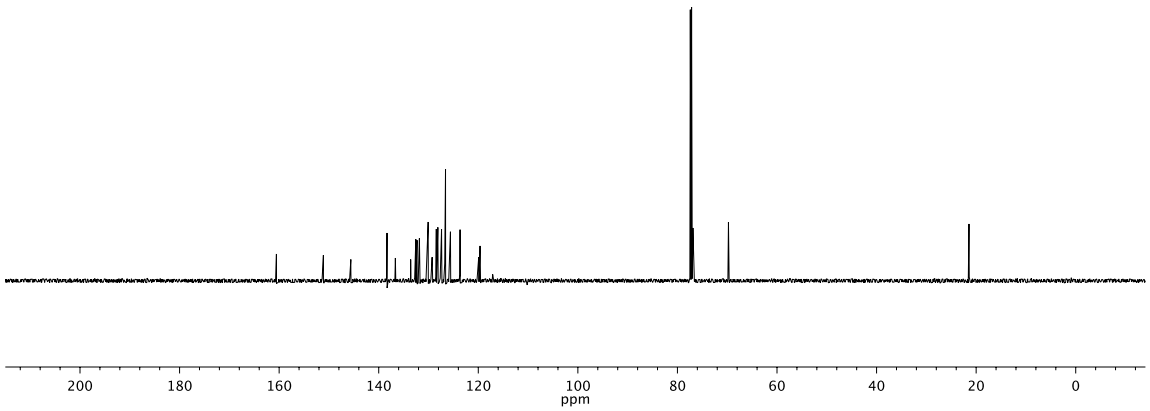


Figure A7.21. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **157g**.

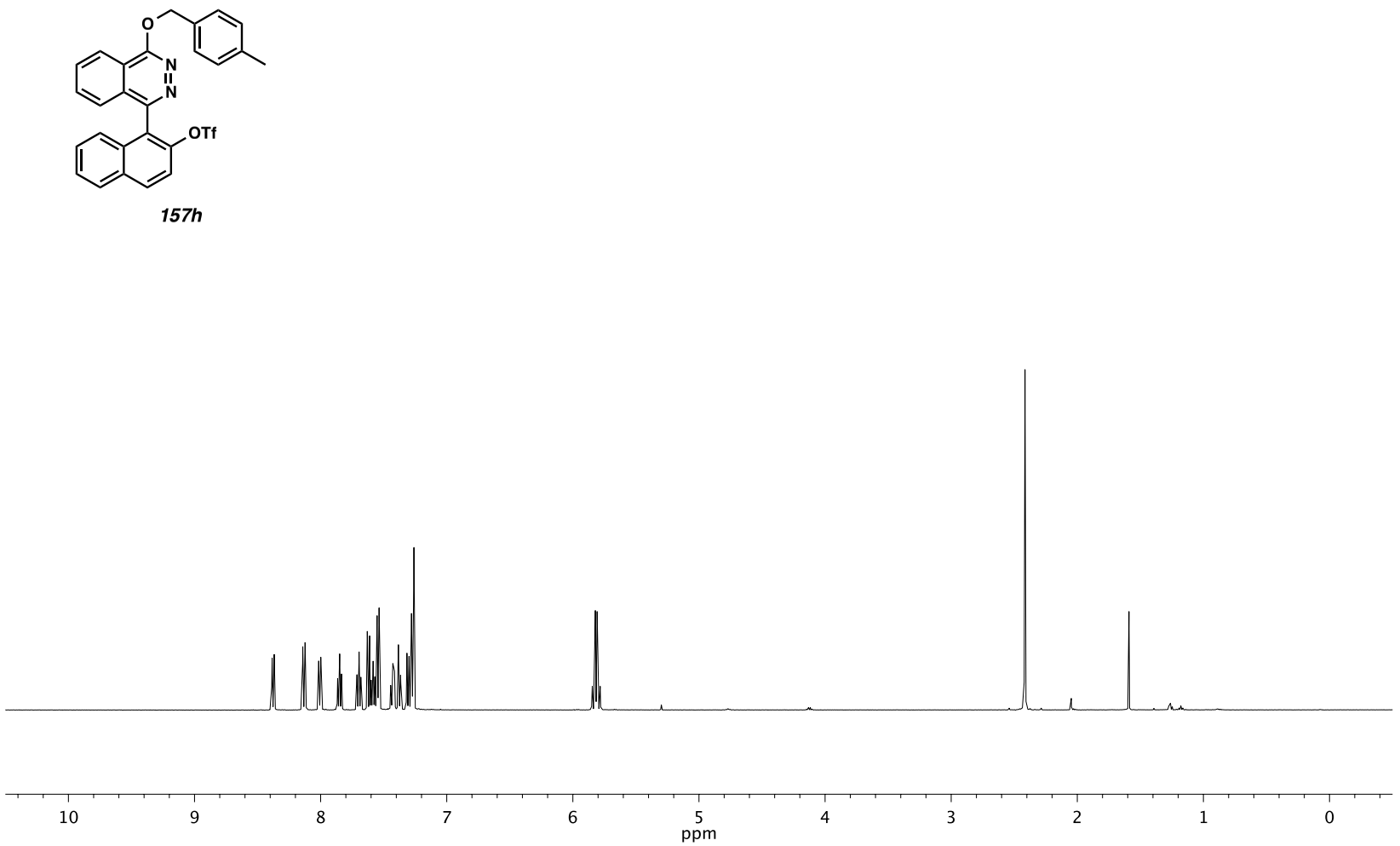


Figure A7.22. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **157h**.

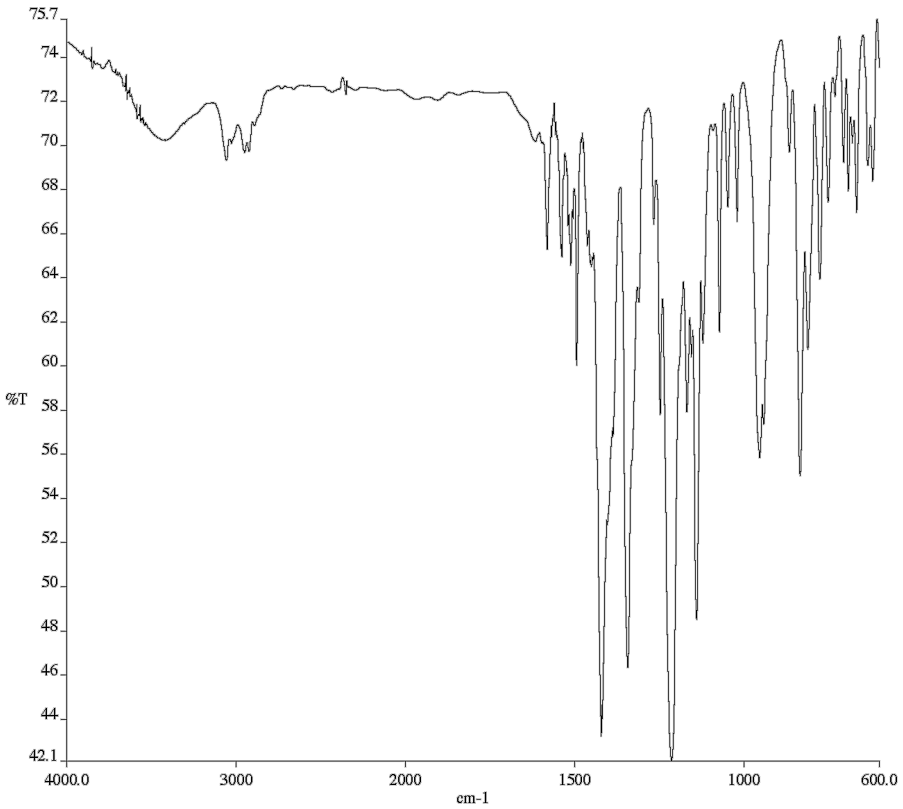


Figure A7.23. Infrared spectrum (Thin Film, NaCl) of compound **157h.**

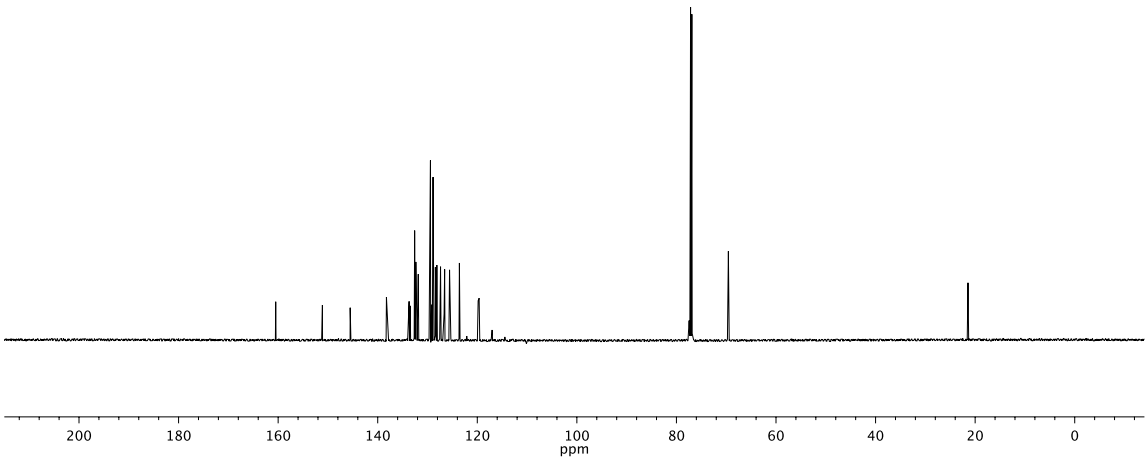


Figure A7.24. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **157h**.

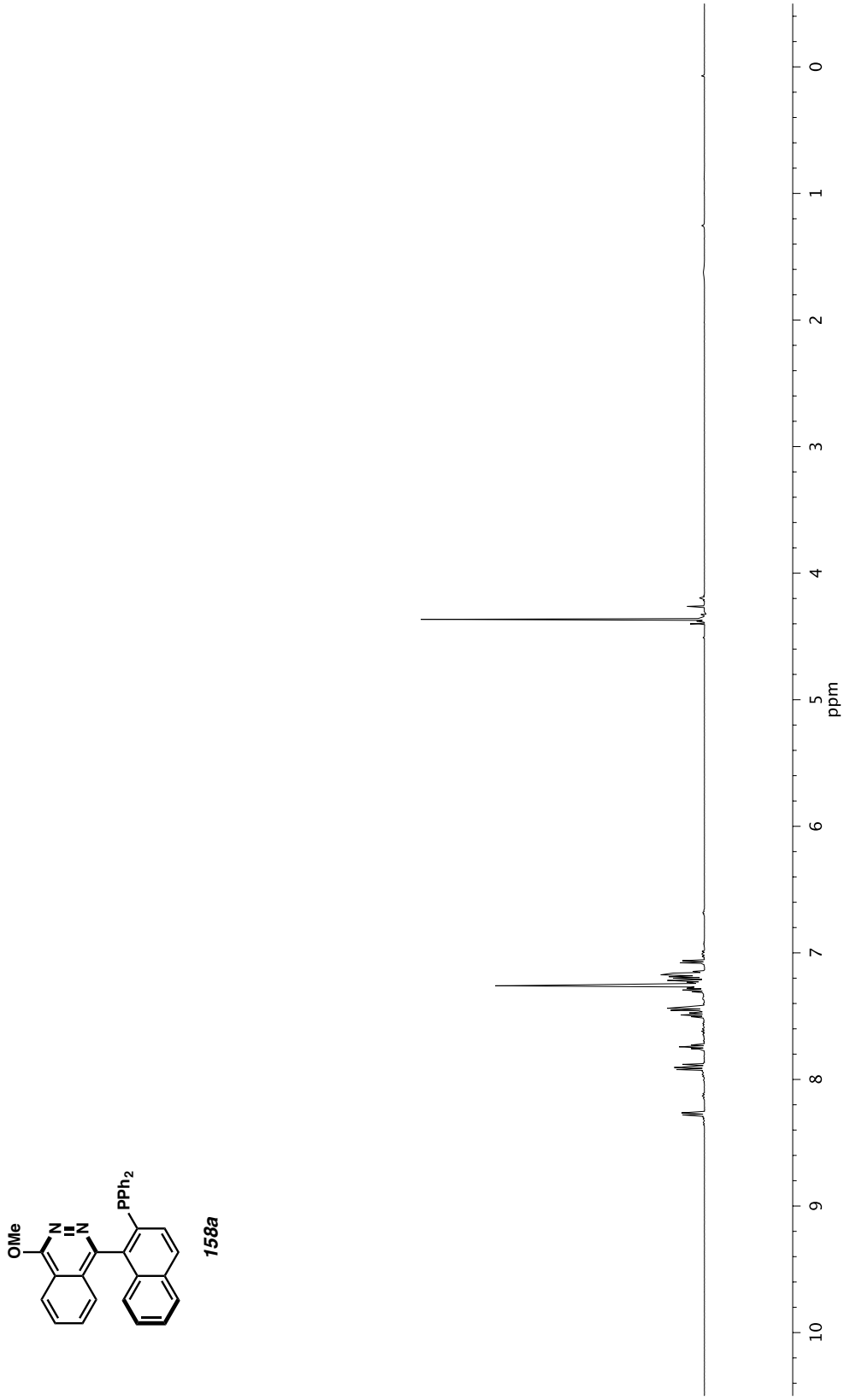


Figure A7.25. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **158a**.

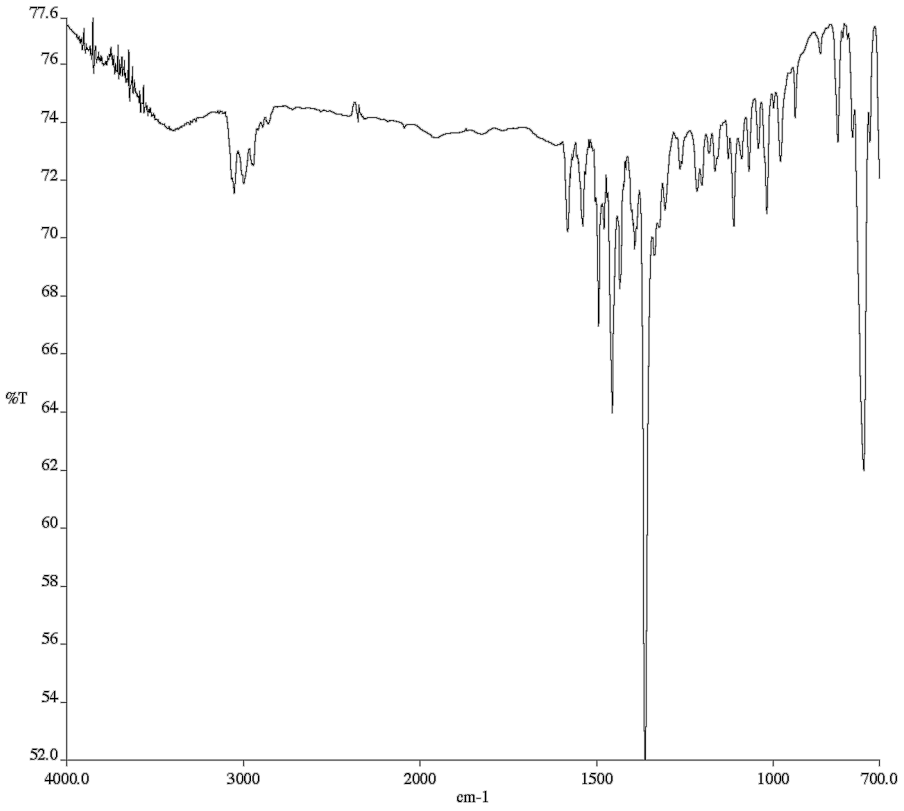


Figure A7.26. Infrared spectrum (Thin Film, NaCl) of compound **158a**.

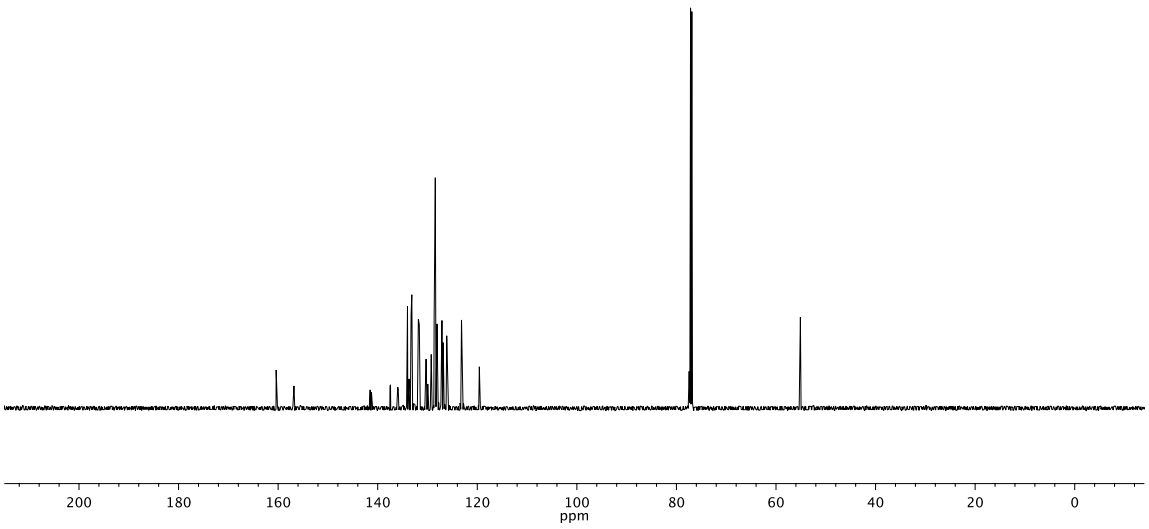


Figure A7.27. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **158a**.

Figure A7.28. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **158b**.

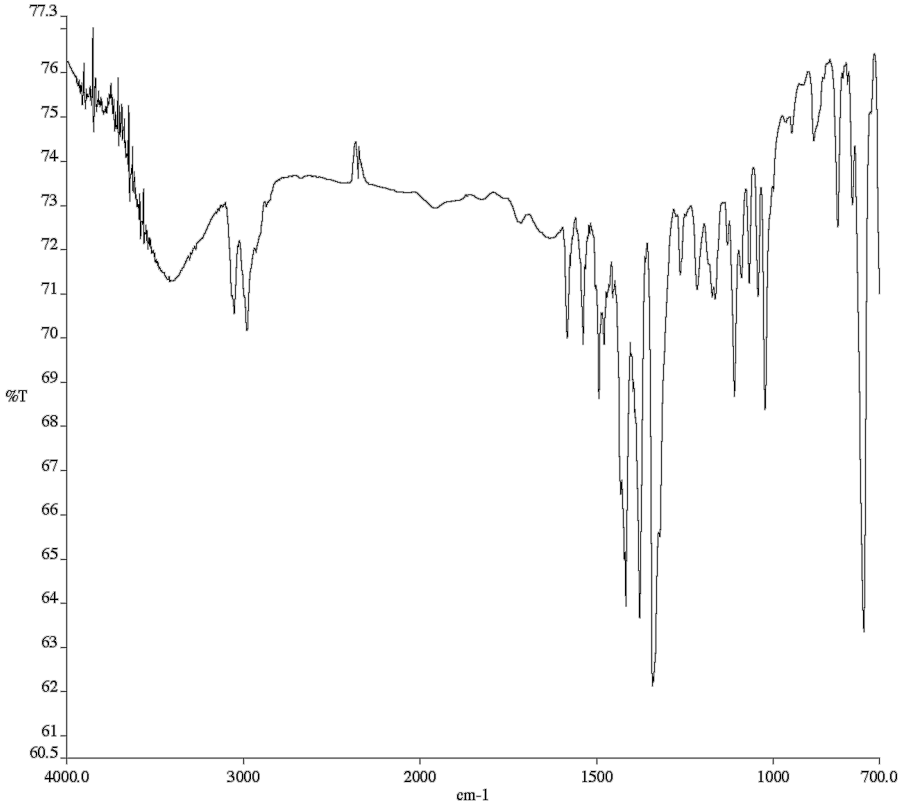


Figure A7.29. Infrared spectrum (Thin Film, NaCl) of compound **158b**.

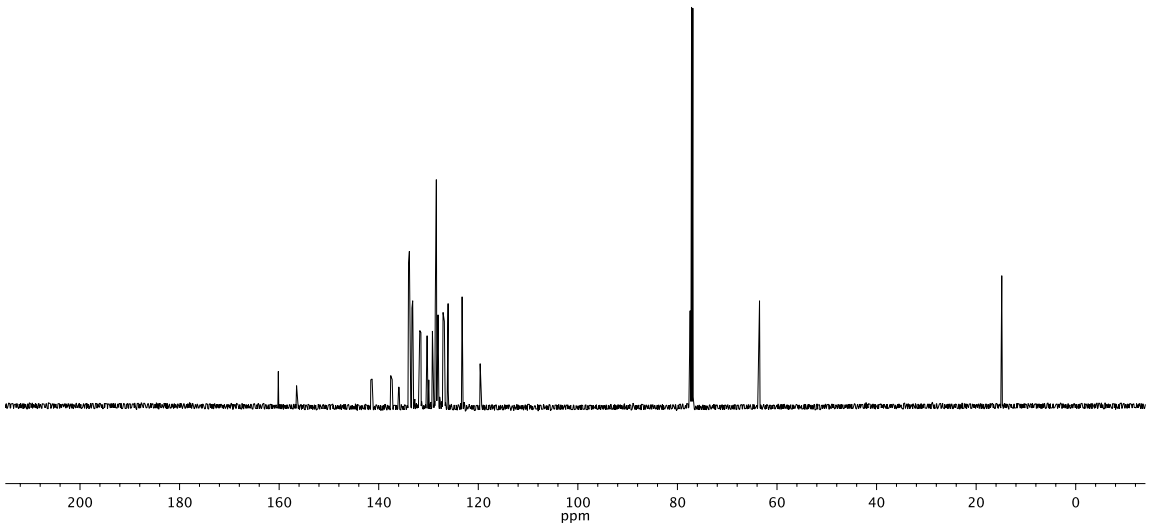


Figure A7.30. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **158b**.

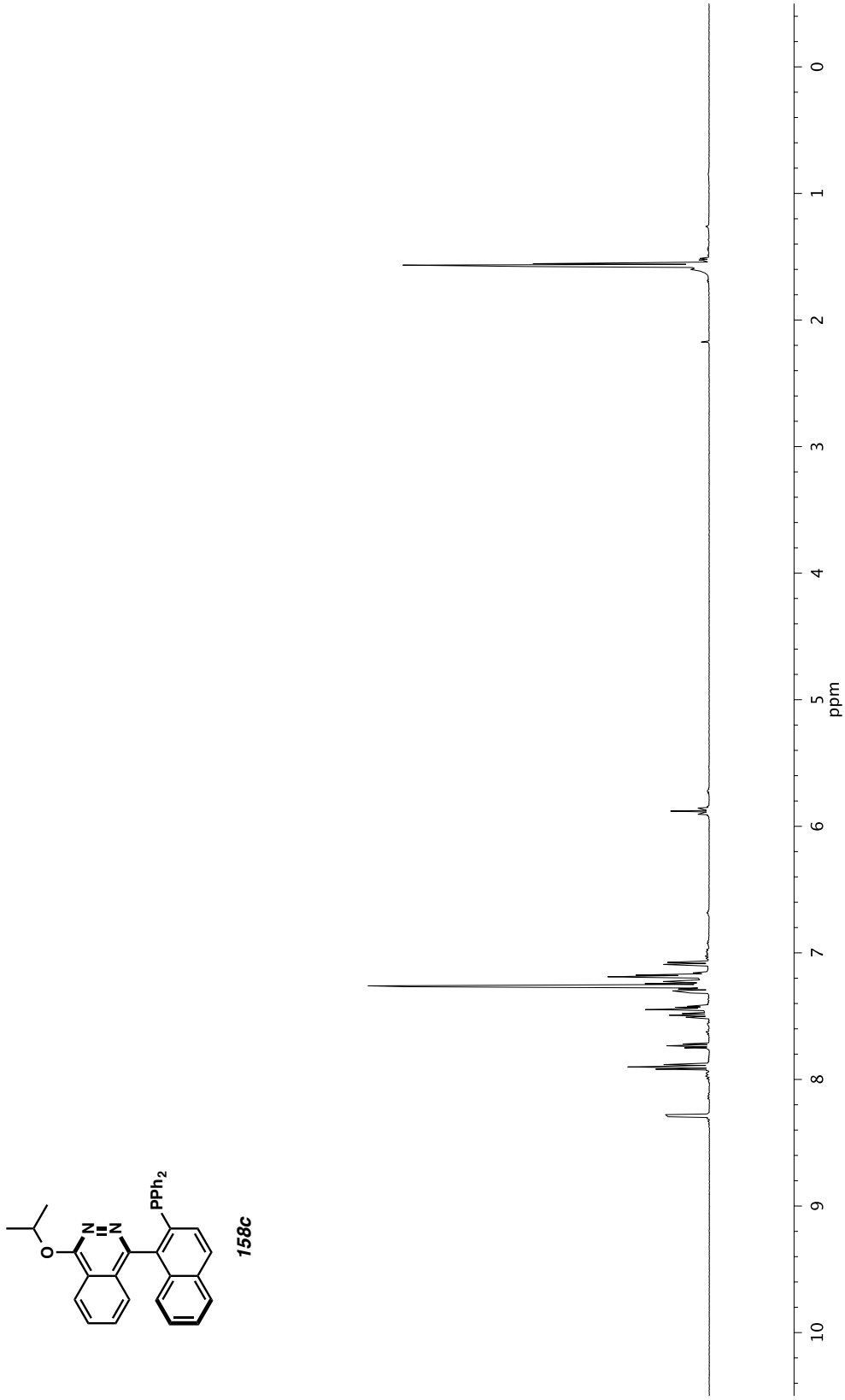


Figure A7.31. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **158c.**

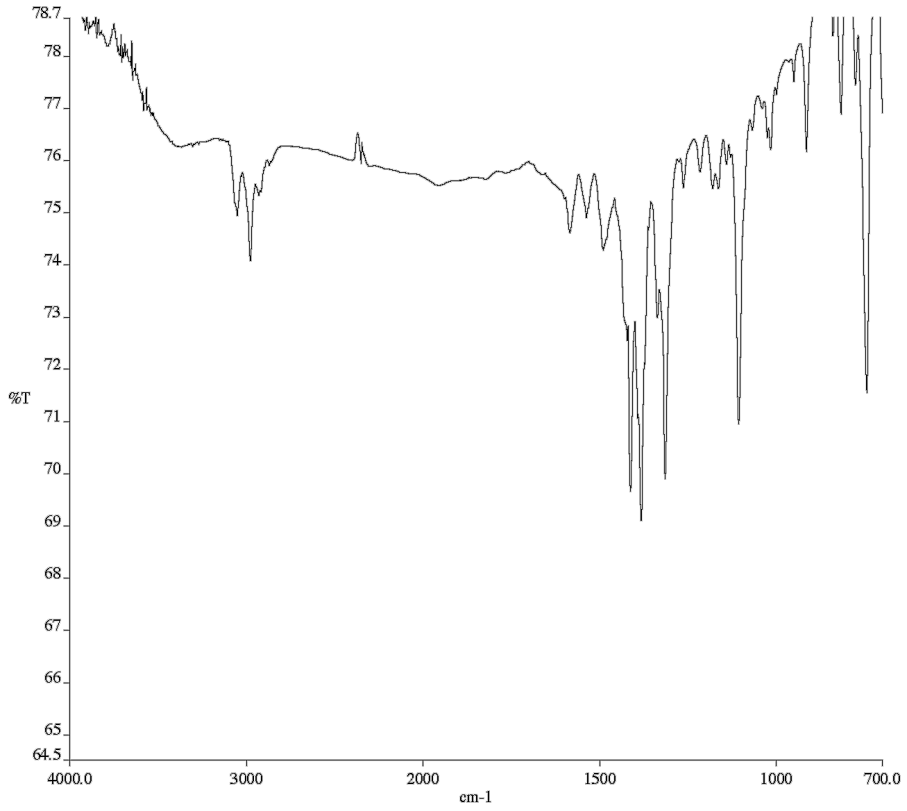


Figure A7.32. Infrared spectrum (Thin Film, NaCl) of compound **158c**.

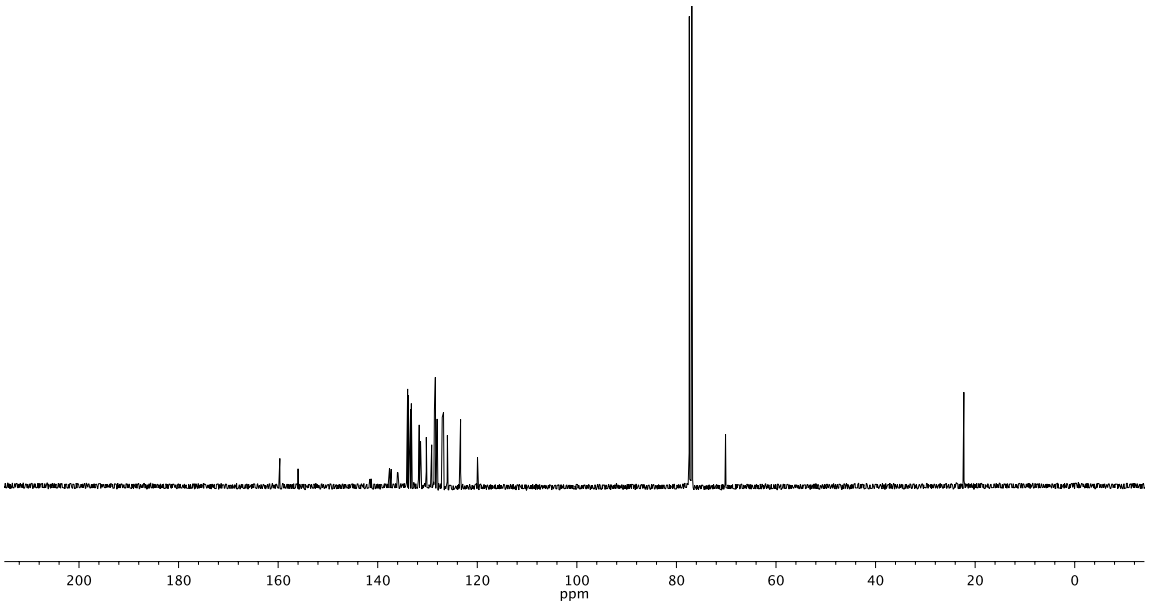


Figure A7.33. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **158c**.

Figure A7.34. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **158d.**

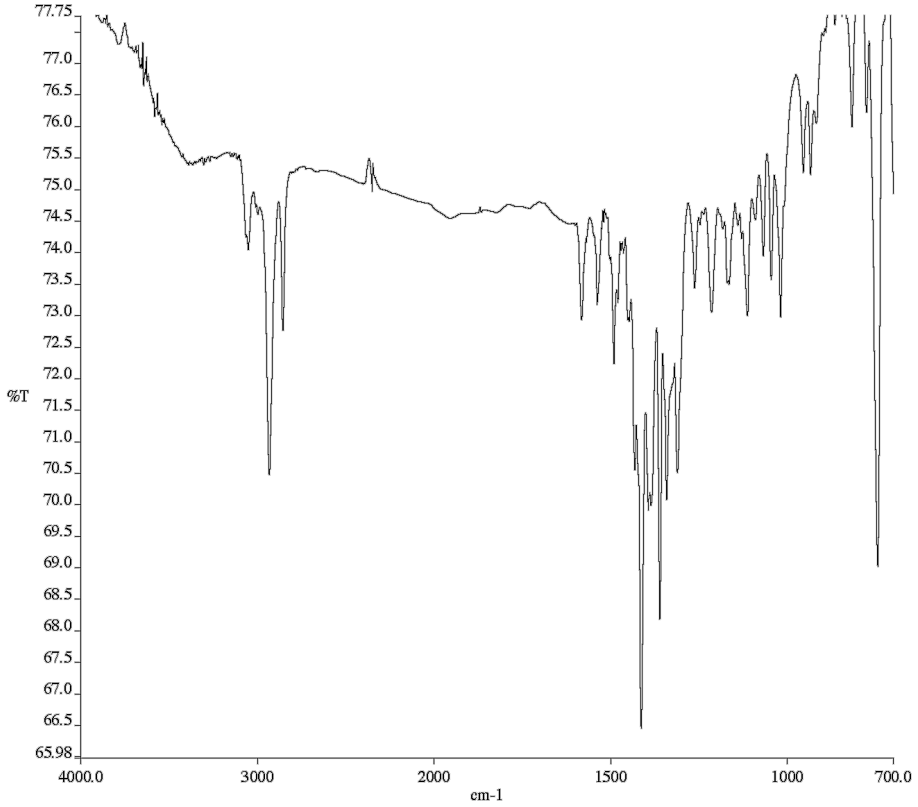


Figure A7.35. Infrared spectrum (Thin Film, NaCl) of compound **158d**.

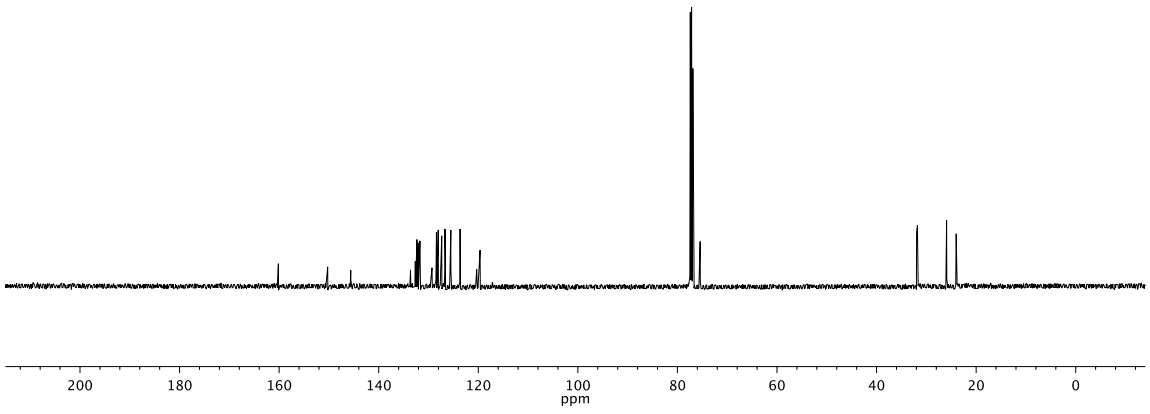


Figure A7.36. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **158d**.

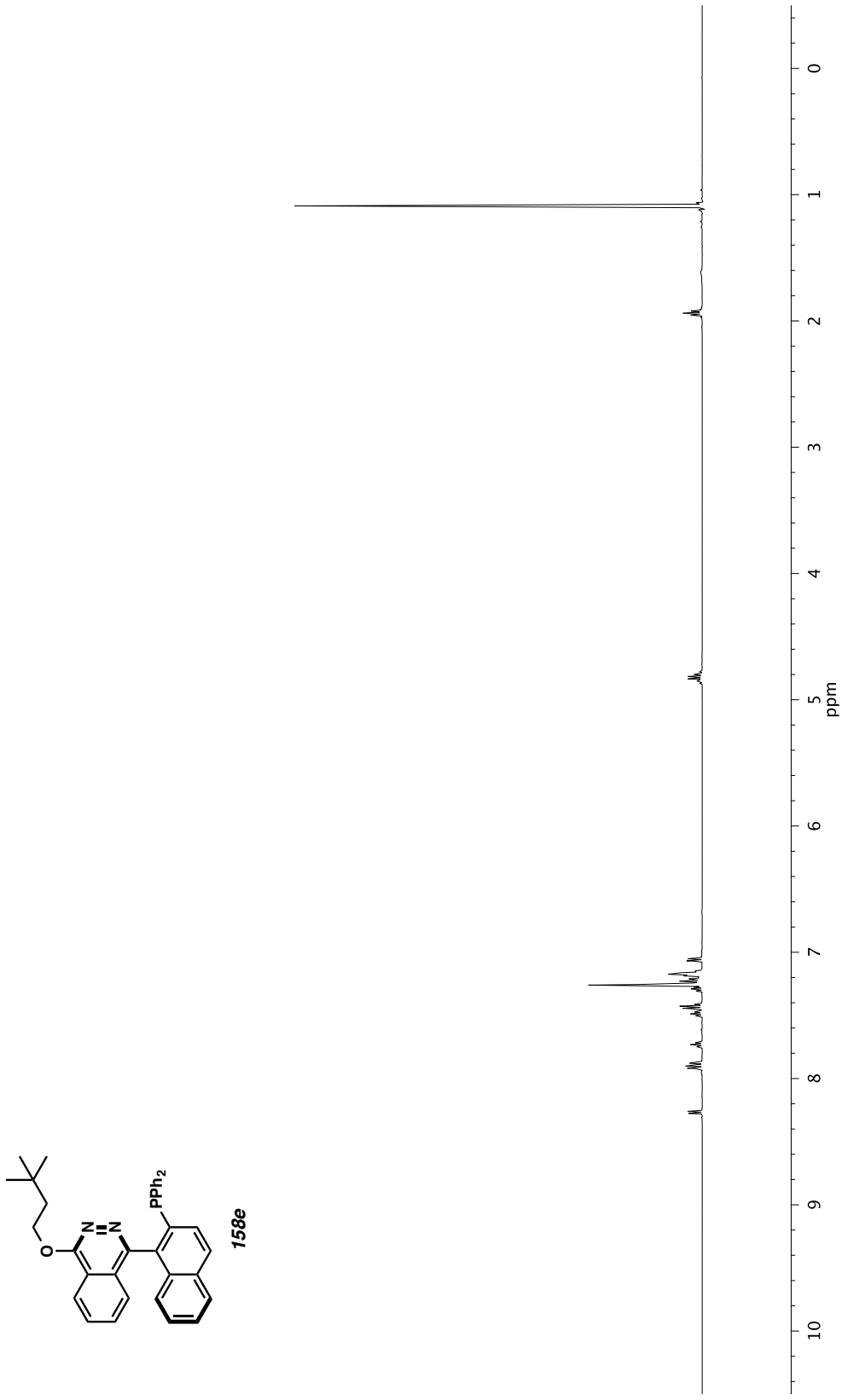


Figure A7.37. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **158e**.

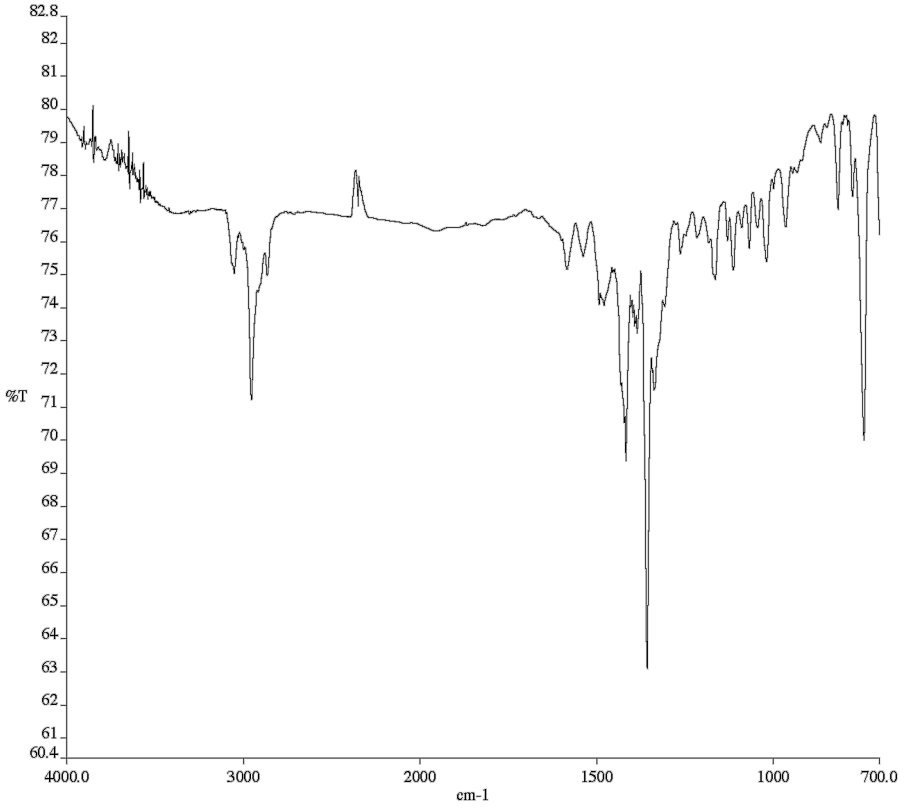


Figure A7.38. Infrared spectrum (Thin Film, NaCl) of compound **158e.**

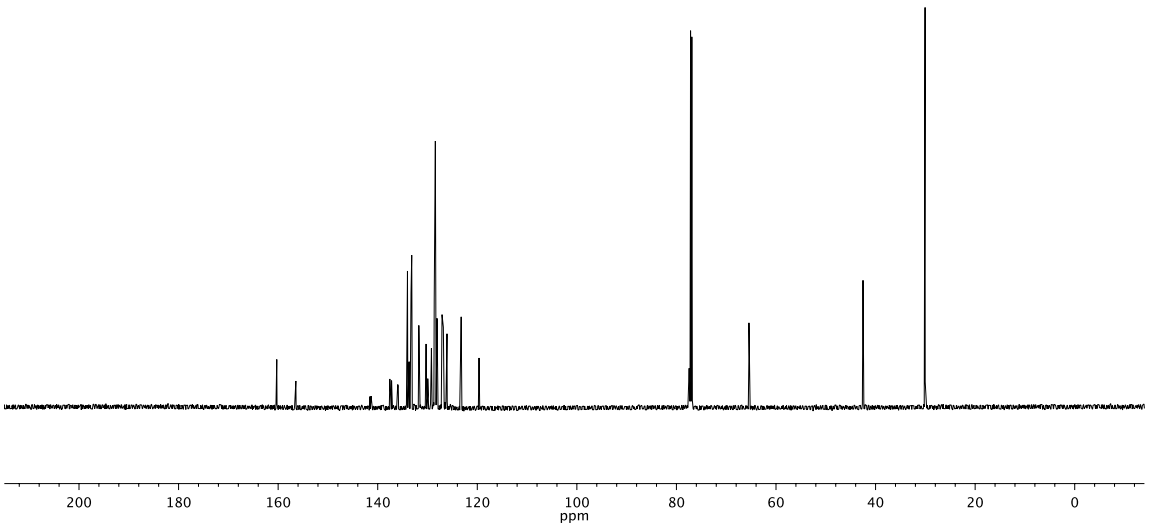


Figure A7.39. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **158e**.

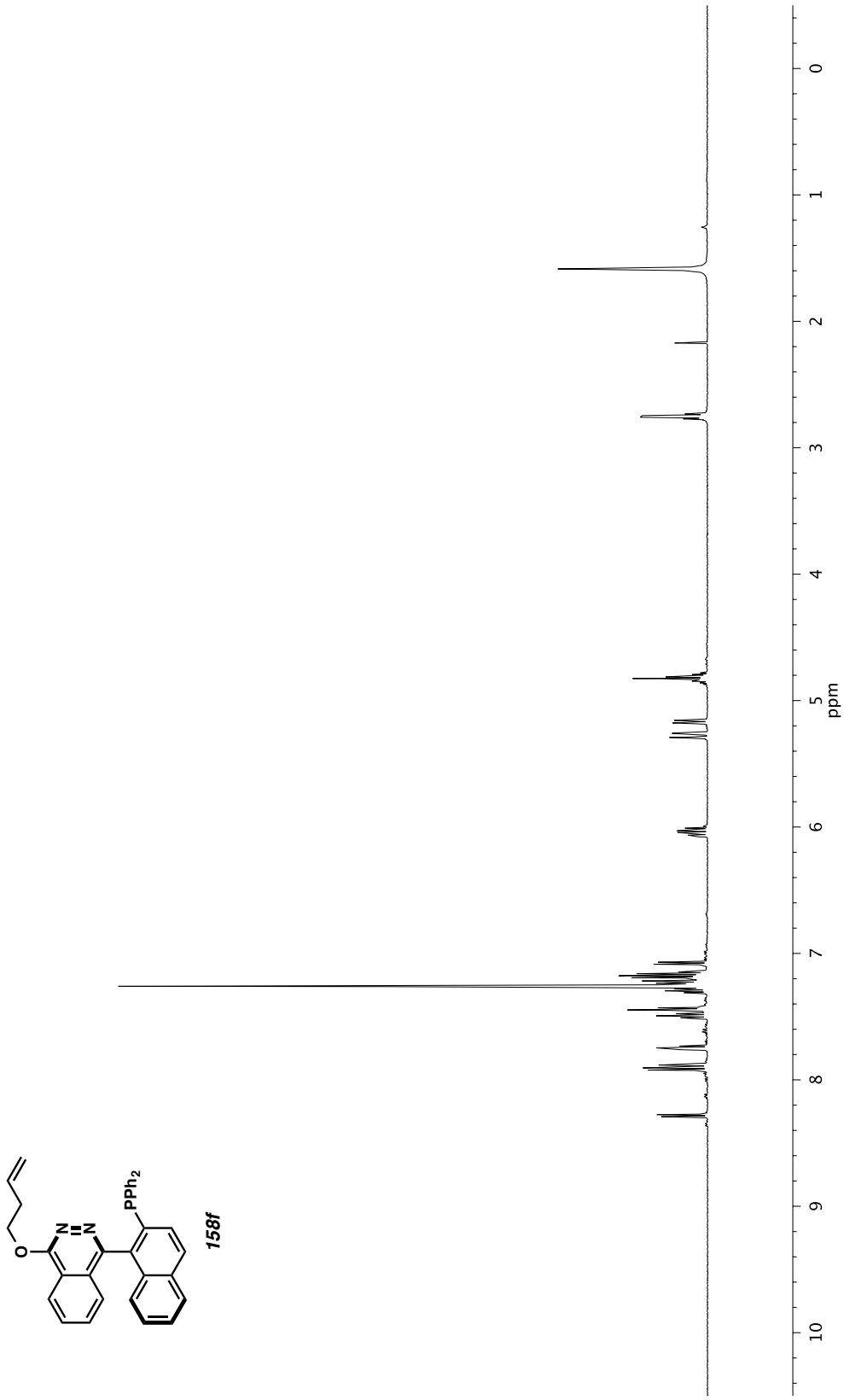


Figure A7.40. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **158f.**

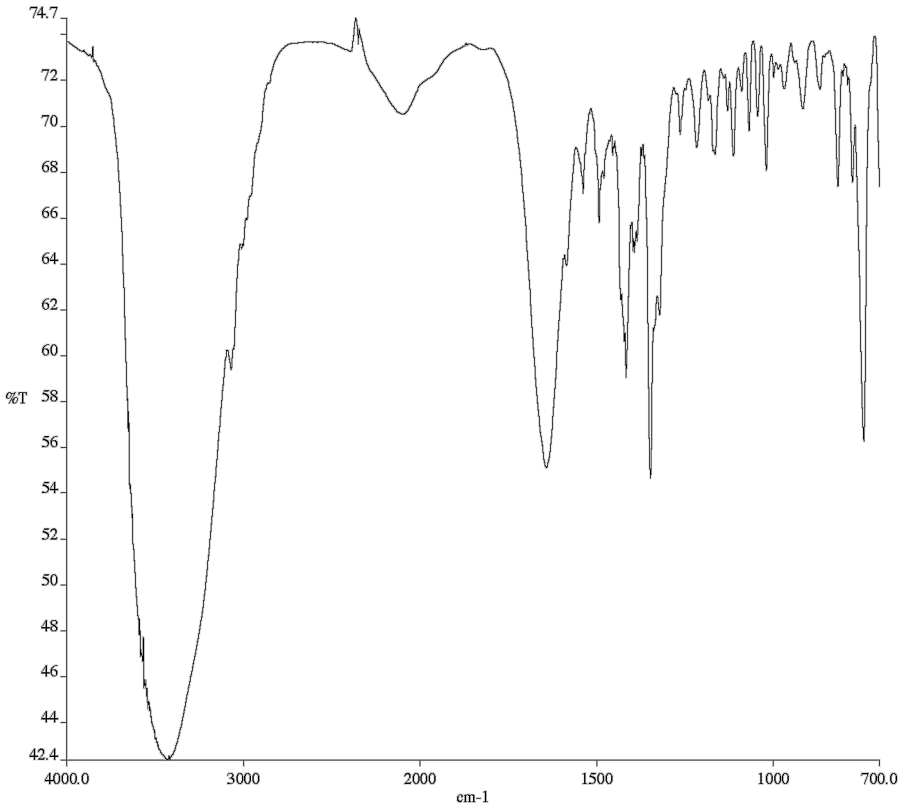


Figure A7.41. Infrared spectrum (Thin Film, NaCl) of compound **158f.**

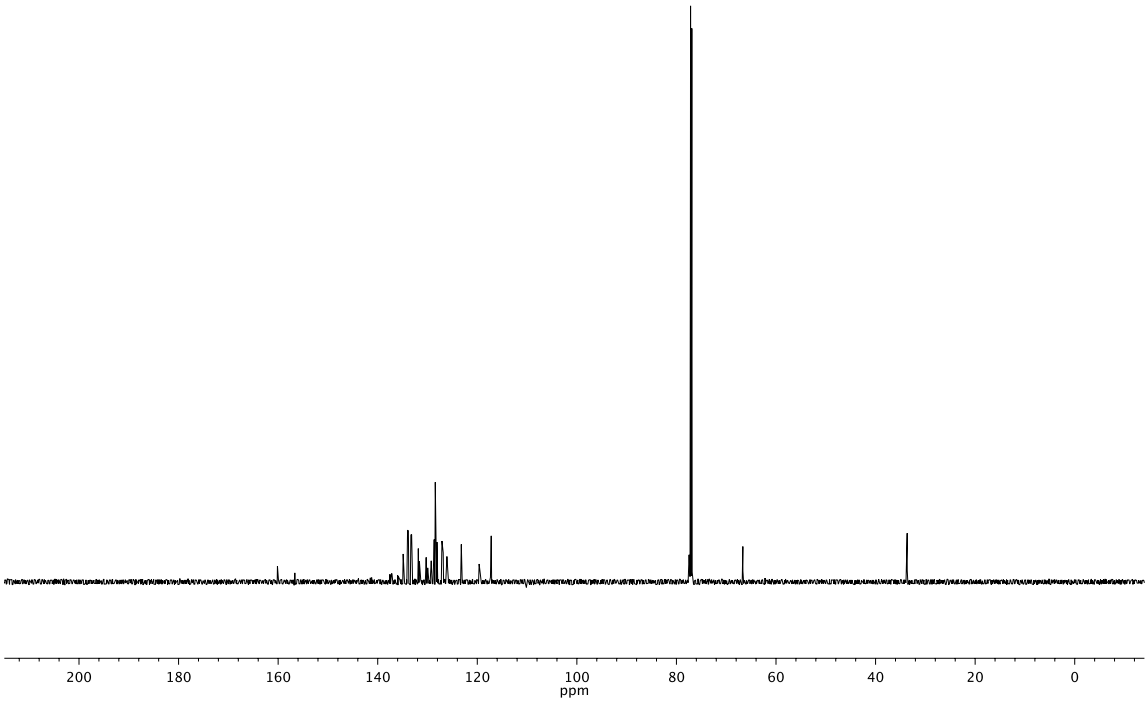


Figure A7.42. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **158f**.

Figure A7.43. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **158g**.

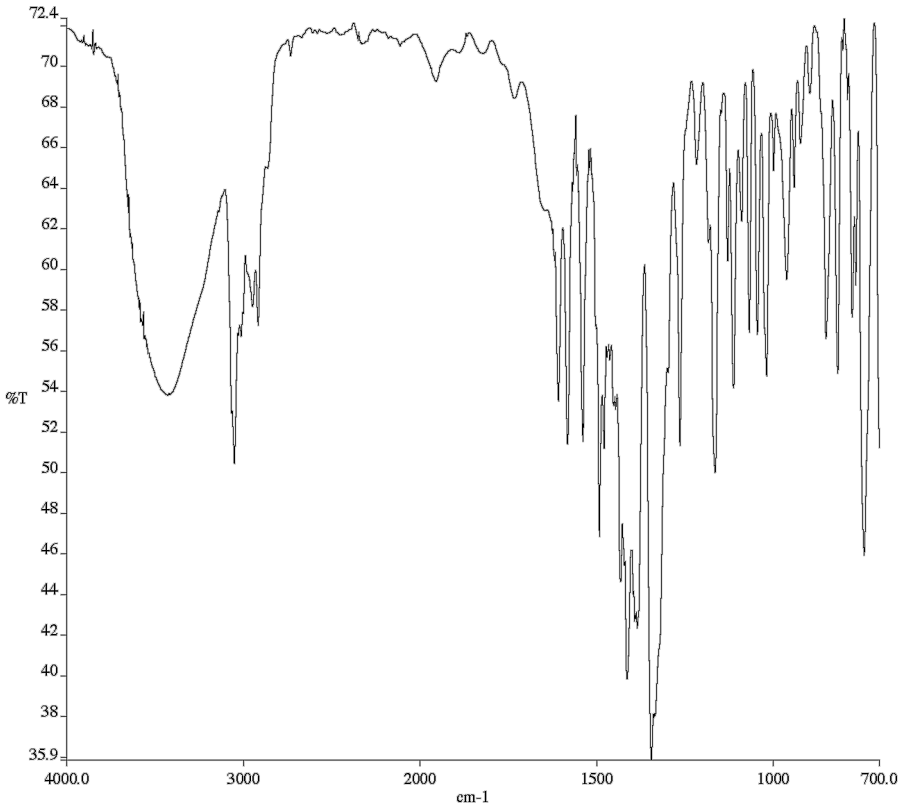


Figure A7.44. Infrared spectrum (Thin Film, NaCl) of compound **158g.**

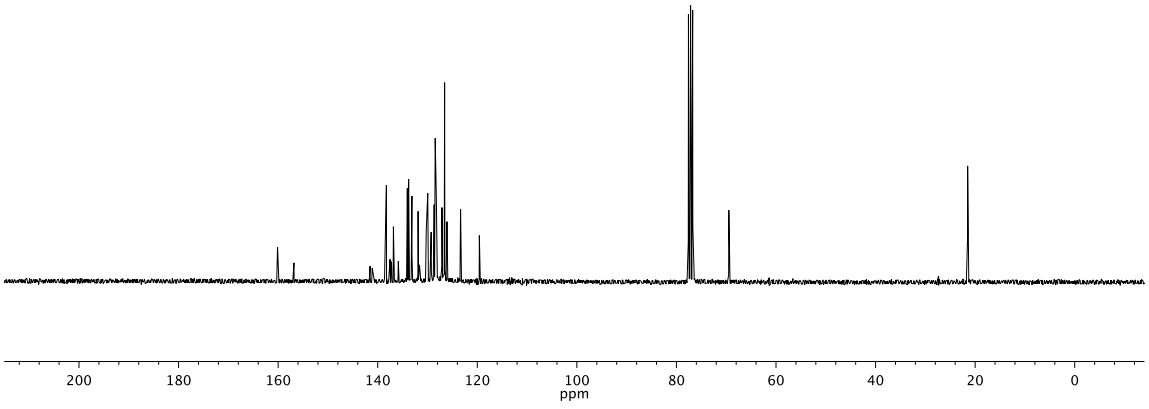


Figure A7.45. ^{13}C NMR (75 MHz, $CDCl_3$) of compound **158g**.

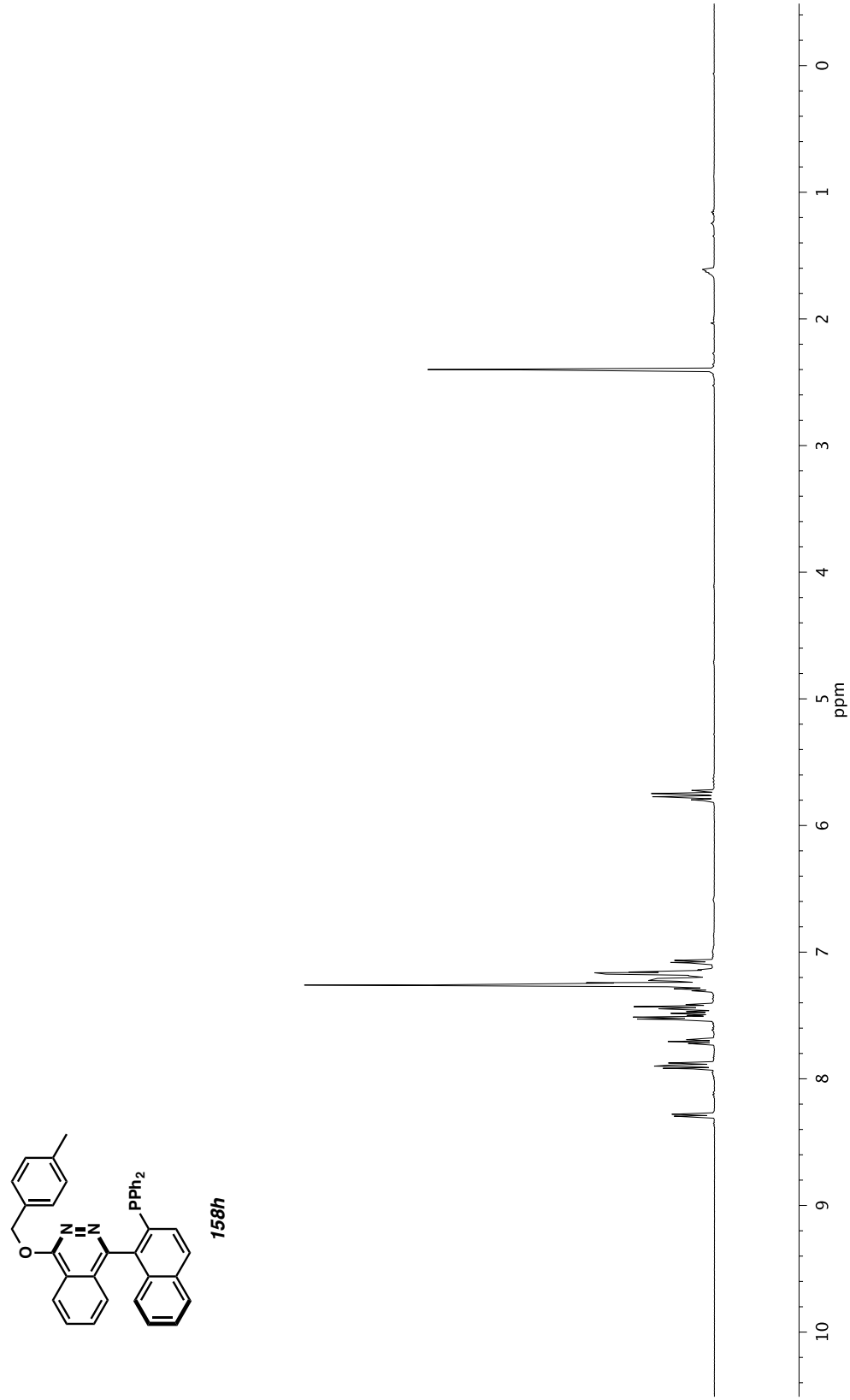


Figure A7.46. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **158h.**

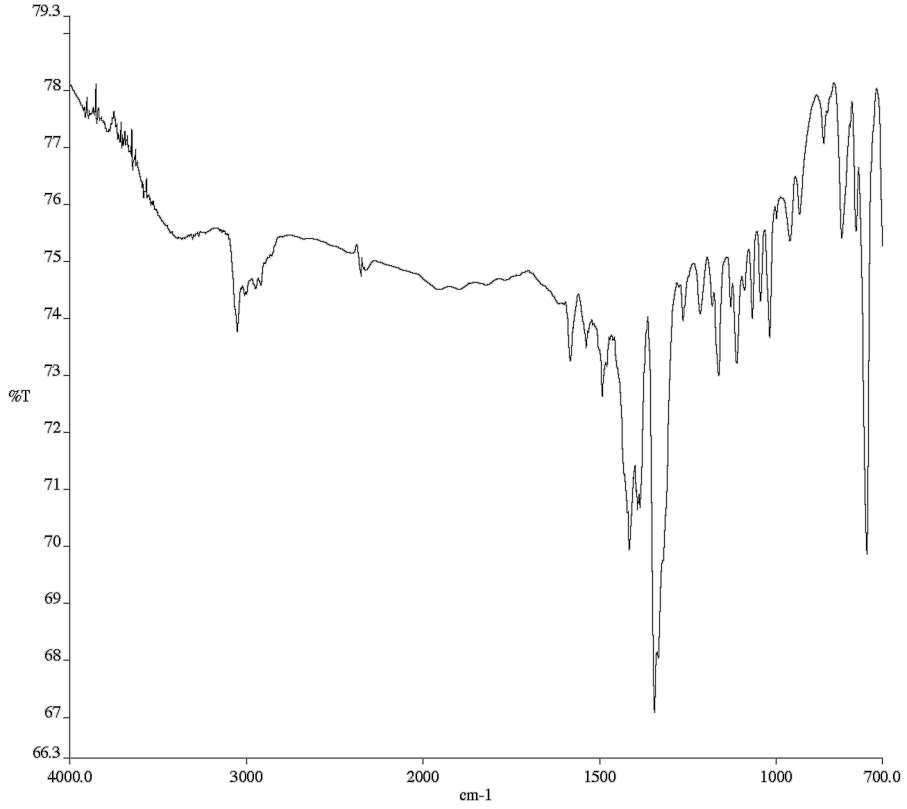


Figure A7.47. Infrared spectrum (Thin Film, NaCl) of compound **158h.**

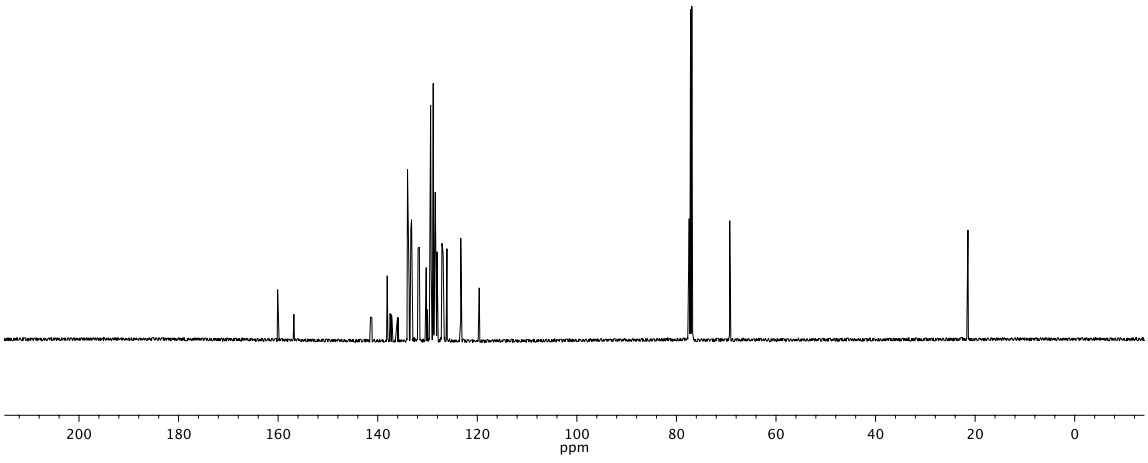


Figure A7.48. ^{13}C NMR (126 MHz, $CDCl_3$) of compound **158h**.