Supplementary material

Enantioselective transfer hydrogenation, key step for the synthesis to 3-aminotetrahydroquinolines

Alexandre Aillerie, Vincent Lemau de Talencé, Clément Dumont, Sylvain Pellegrini, Till Bousquet* and Lydie Pélinski*

Univ. Lille, CNRS, Centrale Lille, ENSCL, Univ. Artois, UMR 8181 - UCCS - Unité de Catalyse et Chimie du Solide, F-59000 Lille, France.

till.bousquet@univ-lille1.fr and lydie.pelinski@univ-lille1.fr.

Table of content:

General Considerations

All reactions were carried out in oven-dried Schlenk tubes and under nitrogen atmosphere. Toluene, dichloromethane, tetrahydrofuran and acetonitrile were purified through a MBraun solvent purification system (MB SPS-800) prior to use. Methyl tert-butyl ether was dried over $CaSO_4$, passed through a column of activated alumina and distilled. Benzene was dried and distilled over CaH_2. Chloroform was dried over anhydrous K_2CO_3 and distilled. Dimethyl carbonate was purchased from Alfa-Aesar and used as received. VAPOL, BINOL and substituted BINOL phosphoric acids were purchased from commercial sources and used without further purification. Other common reagents were purchased from commercial sources and used without further purification unless noted otherwise. 3-Bromo-5-nitroquinoline,[1] 3-amino-7-trifluoromethylquinoline,[2] 3-amino-6-chloroquinoline,[3] 3-amino-6,7-dimethoxyquinoline,[4] 3-amino-7-methoxyquinoline,1 3-amino-6-bromoquinoline[5] and 3-amino-7-bromoquinoline[6] were prepared according to the reported

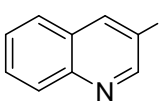
[1] J. D. Crowley, I. M. Steele, B. Bosnich, *Chem. Eur. J.*, 2006, **12**, 8935-8951.
[2] J.-C. Harmange, S. Booker, J. L. Buchanan, S. Chaffee, P. M. Novak, S. Van Der Plas, X. Zhu, *PCT Int. Appl.* WO 2003018021, A1, 2003.
[3] Y. Cheng, B. K. Albrecht, J. Brown, J. L. Buchanan, W. H. Buckner, E. F. DiMauro, R. Emkey, R. T. Fremeau, Jr., J.-C. Harmange, B. J. Hoffman, L. Huang, M. Huang, J. Han Lee, F.-F. Lin, M. W. Martin, H. Q. Nguyen, V. F. Patel, S. A. Tomlinson, R. D. White, X. Xia, S. A. Hitchcock, *J. Med. Chem.*, 2008, **51**, 5019-5034.
[4] F. Santangelo, C. Casagrande, G. Miragoli, V. Vecchietti, *Eur. J. Med. Chem.*, 1994, **29**, 877-882.

publications. Analytical thin layer chromatography was performed on Macherey-Nagel TLC plates (ALUGRAM® Xtra SIL G/UV254). Flash column chromatography was performed with Macherey-Nagel silica gel (230-400 mesh). Enantiomeric excesses were determined using a Hitachi Elite Lachrom HPLC with a binary pump and a diode array detector. Column conditions are reported in the experimental section below. The chiral HPLC method was calibrated with the corresponding racemic mixtures. Melting points were recorded on a Barnstead electrothermal 9300 apparatus and were uncorrected. Optical rotations were determined at 589 nm (sodium D line) by using a Perkin-Elmer-343 polarimeter. ^{1}H and ^{13}C-NMR spectra were recorded at room temperature on a Bruker Advance spectrometer (300 MHz for ^{1}H and 75 MHz for ^{13}C). ^{1}H and ^{13}C-NMR spectra were referenced to the residual solvent signals. High resolution mass spectra were measured on a Thermo Scientific Exactive Orbitrap mass spectrometer. Single-crystal X-rays measurements were performed at room temperature. Data were collected using an Apex II CCD 4K Bruker diffractometer (λ = 0.71073 Å). The structure was solved using SHELXT[7] and refined by least-squares procedures on F^2 using SHELXL.[8] Hydrogen atoms were placed in theoretical positions and refined riding on their parent atoms except for H atoms bonded to N atoms which were located from a difference Fourier map and refined freely.

Experimental Section

General procedure for the synthesis of *N*-protected 3-aminoquinoline:

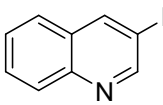
In a Schlenk tube under nitrogen atmosphere containing a mixture of toluenesulfonamide, benzyl carbamate or *tert*-butylcarbamate (1.5 mmol, 1.5 equiv.), potassium carbonate (3 mmol, 415 mg, 3 equiv.) and copper(I) iodide (0.05 mmol, 9.52 mg, 0.05 equiv.) was added the bromoquinoline (1 mmol, 136 µL, 1 equiv.), *N*,*N'*-dimethyl-1,2-ethanediamine (0.1 mmol, 11 µL, 0.1 equiv.) and 1,4-dioxane (3 mL). The reaction mixture was heated to 110 °C for 48 h. After cooling to room temperature and dilution in a mixture of 25% aqueous ammonia solution/water (1/1, 20 mL), the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (25 mL), dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified on silica gel column chromatography to afford the expected *N*-protected 3-aminoquinoline **1a-c**.



***N*-(quinolin-3-yl)-4-methylbenzenesulfonamide 1a:[9]**

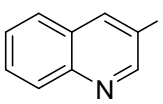
This compound was obtained from toluenesulfonamide (259 mg, 1.5 equiv.) and 3-bromoquinoline (136 µL, 1 equiv.) after purification on silica gel column chromatography (petroleum ether/ethyl acetate: 7/3 to 1/1) as a white solid with 47% yield. R_f 0.52 (petroleum ether/ethyl acetate: 1/1), mp 172-174 °C. ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.74 (brs, 1H), 8.62 (d, *J* = 2.6 Hz, 1H), 7.98 (d, *J* = 2.5 Hz, 1H), 7.92 (s, 1H), 7.89 (d, *J* = 1.4 Hz, 1H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.66-7.52 (m, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 2.30 (s, 3H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 145.0, 144.5, 143.6, 136.1, 131.5, 129.8, 128.5, 128.4, 127.6, 127.5, 127.3, 126.7, 123.3, 20.9; GC-MS: 298 , 233, 219, 207, 192, 178, 155, 143 (100), 116. HRMS m/z (ESI) calcd for $C_{16}H_{14}N_2O_2S$ [M+H]$^+$ 299.0849, found 299.0845.

[5] K. Wilson, M. Altman, K. Lipford, C. White, M. Daniels, *PCT Int. Appl.*, WO 2012009194 A1, 2012.
[6] M. L. Moore, C. A. Parrish, M. D. Squire, *PCT Int. Appl.*, WO 2013052716 A1, 2013.
[7] Sheldrick, G.M. *Acta Cryst.*, 2015, **A71**, 3-8.
[8] Sheldrick, G.M. *Acta Cryst.*, 2015, **C71**, 3-8.
[9] Y. Miura, S. Takaku, Y. Fujimura, M. Hamana, *Heterocycles*, 1992, **34**, 1055-1063.
[10] N. A. Isley, S. Dobarco, B. H. Lipshutz, *Green Chem.*,2014,**16**,1480–1488.



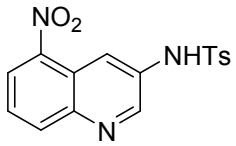
***tert*Butyl quinolin-3-yl carbamate 1b:** [10]

This compound was obtained from *tert*butyl carbamate (176 mg1.5 equiv.) and 3-bromoquinoline (136 µL, 1 equiv.) after purification on silica gel column chromatography (petroleum ether/ethyl acetate: 8/2 to 6/4) as a white solid with 64% yield. R_f: 0.14 (petroleum ether/ethyl acetate: 8/2), mp 151-153 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.66 (d, *J* = 2.5 Hz, 1H), 8.52 (brs, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.77 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.62-7.48 (m, 2H), 6.89 (brs, 1H), 1.56 (s, 9H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 152.8, 144.6, 143.4, 132.0, 128.9, 128.4, 127.8, 127.5, 127.2, 121.8, 81.4, 28.3. HRMS m/z (ESI) calcd for $C_{14}H_{16}N_2O_2$ $[M+H]^+$ 245.1285, found 245.1281.



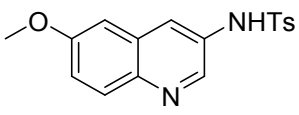
***N*-(quinolin-3-yl)-acetamide 1c:**[11]

This compound was obtained from acetamide (89 mg, 1.5 equiv.) and 3-bromoquinoline (136 µL, 1 equiv.) after purification on silica gel column chromatography (petroleum ether/ethyl acetate: 2/8) as an off-white solid with 75% yield. R_f: 0.33 (petroleum ether/ethyl acetate: 2/8), mp 159-161 °C. ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.40 (brs, 1H), 8.89 (d, *J* = 2.5 Hz, 1H), 8.68 (d, *J* = 2.3 Hz, 1H), 7.95-7.89 (m, 2H), 7.65-7.60 (m, 1H), 7.58-7.52 (m, 1H), 2.14 (s, 3H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 169.2, 144.4, 144.1, 133.0, 128.5, 127.9, 127.7, 127.6, 127.0, 121.7, 23.9. HRMS m/z (ESI) calcd for $C_{11}H_{10}N_2O$ $[M+H]^+$ 187.0866, found 187.0859.



***N*-(5-nitroquinolin-3-yl)- 4-methylbenzenesulfonamide 1h:**

This compound was obtained from toluenesulfonamide (259 mg, 1.5 equiv.) and 3-bromo-5-nitroquinoline (253 mg, 1 equiv.) after purification on silica gel column chromatography (petroleum ether/ethyl acetate: 6/4 to 5/5) as a yellow solid with 38% yield. R_f: 0.11 (petroleum ether/ethyl acetate: 8/2). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.85 (d, *J* = 2.1 Hz, 1H), 7.73 (dd, *J* = 2.5, 0.7 Hz, 1H), 8.41 (d, *J* = 7.8, 1.2 Hz, 1H), 8.34 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 2H), 7.72-7.67 (m, 1H), 7.64 (brs, 1H), 7.30 (dd, *J* = 8.5, 0.5 Hz, 2H), 2.38 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 145.3, 145.0, 145.0, 144.7, 136.4, 135.2, 133.5, 130.1, 127.6, 126.4, 126.0, 121.3, 118.7, 21.6. HRMS m/z (ESI) calcd for $C_{16}H_{13}N_3O_4S$ $[M+H]^+$ 344.0708, found 344.0700.



***N*-(6-methoxyquinolin-3-yl)-4-methylbenzenesulfonamide 1k:**

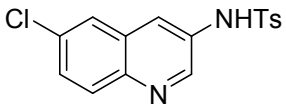
This compound was obtained from toluenesulfonamide (259 mg, 1.5 equiv.) and 3-bromo-6-methoxyquinoline (237 mg, 1 equiv) after purification on silica gel column chromatography (petroleum ether/ethyl acetate: 50/50) as a white solid with 74% yield. R_f: 0.25 (petroleum ether/ethyl acetate: 50/50). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.38 (d, *J* = 2.5 Hz, 1H), 7.98 (d, *J* = 2.5 Hz, 1H), 7.89 (d, *J* = 9.2 Hz, 1H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.27 (dd, *J* = 9.6, 2.4 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 2.7 Hz, 1H), 3.91 (s, 3H), 2.33 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 158.7, 144.5, 142.6, 141.8, 136.1, 131.0, 130.4, 130.0, 129.4, 127.3, 125.5, 122.1, 105.2, 55.7, 21.6. HRMS m/z (ESI) calcd for $C_{17}H_{17}O_3N_2S$ $[M+H]^+$ 329.0954, found 329.0949.

---

[11] K. A. Skupinska, E. J. McEachern, R. T. Skerlj, G. J. Bridger, *J.Org. Chem.*, 2002, **67**, 7890-7893.

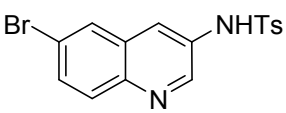
General procedure for the tosylation of 3-aminoquinolines:

The 3-aminoquinolines (1 mmole, 1 equiv.), 4-toluenesulfonyl chloride (1 mmole, 1 equiv.) and DMAP (0.15 mmol, 0.15 equiv.) were suspended in pyridine (10 mL/mmol) in a Schlenk tube under nitrogen atmosphere. The reaction was stirred at room temperature and the progress of the reaction was monitoring by TLC. After completion, the mixture was diluted in water (30 mL), extracted with DCM (5 × 10 mL) and the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography to give the desired quinoline 3-*N*H-Ts.



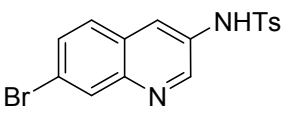
***N*-(6-Chloroquinolin-3-yl)-4-methylbenzenesulfonamide 1d:**

This compound was prepared from the 6-chloroquinolin-3-amine according to the general procedure and was purified by column chromatography (petroleum ether/ethyl acetate: 7/3 to 1/1) as a white solid with 79% yield. R_f: 0.49 (petroleum ether/ethyl acetate: 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.59 (d, *J* = 2.7 Hz, 1H), 7.96 (d, *J* = 8.1 Hz, 1H), 7.94 (s, 1H), 7.73-7.70 (m, 3H), 7.57 (dd, *J* = 8.9, 2.3 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 2.36 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 144.9, 144.7, 143.5, 135.6, 133.6, 131.3, 130.3, 130.0, 128.6, 127.2, 126.2, 124.6, 21.5. HRMS m/z (ESI) calcd for $C_{16}H_{14}O_2N_2ClS$ $[M+H]^+$ 333.0459, found 333.0453.



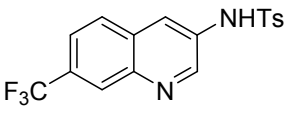
***N*-(6-bromoquinolin-3-yl)-4-methylbenzenesulfonamide 1e:**

This compound was prepared from 6-bromoquinolin-3-amine according to the general procedure and was purified by column chromatography (petroleum ether/ethyl acetate: 50/50) as a white solid with 75% yield. R_f: 0.29 (petroleum ether/ethyl acetate: 50/50). ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.85 (brs, 1H), 8.65 (d, *J* = 2.6 Hz, 1H), 8.25 (d, *J* = 2.1 Hz, 1H), 8.00 (d, *J* = 2.5 Hz, 1H), 7.83 (d, *J* = 8.9 Hz, 1H), 7.70-7.75 (m, 3H), 7.34 (d, *J* = 8.0 Hz, 2H), 2.30 (s, 3H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 145.2, 143.7, 142.9, 136.0, 132.3, 131.2, 130.6, 129.8, 129.5, 129.0, 126.8, 121.6, 120.4, 20.9. HRMS m/z (ESI) calcd for $C_{16}H_{14}O_2N_2BrS$ $[M+H]^+$ 376.9954, found 376.9948.



***N*-(7-bromoquinolin-3-yl)-4-methylbenzenesulfonamide 1f:**

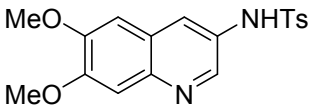
This compound was prepared from 7-bromoquinolin-3-amine according to the general procedure and was purified by column chromatography (petroleum ether/ethyl acetate: 50/50) as a white solid with 96% yield. R_f: 0.29 (petroleum ether/ethyl acetate: 50/50). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.45 (d, *J* = 1.7 Hz, 1H), 8.14 (s, 1H), 7.96 (d, *J* = 1.6 Hz, 1H), 7.59 (dd, *J* = 12.6, 4.6 Hz, 4H), 7.16 (d, *J* = 8.1 Hz, 2H), 2.30 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 146.2, 146.1, 144.8, 135.8, 131.4, 131.2, 130.9, 130.2, 129.0, 127.3, 126.7, 126.0, 123.1, 21.7. HRMS m/z (ESI) calcd for $C_{16}H_{14}O_2N_2BrS$ $[M+H]^+$ 376.9954, found 376.9947.



***N*-(7-(trifluoromethyl)quinolin-3-yl)-4-methylbenzenesulfonamide 1g:**

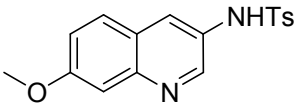
This compound was prepared from 7-trifluoromethylquinolin-3-amine according to the general procedure and was purified by column chromatography (petroleum ether/ethyl acetate: 70/30) as a white solid with 70% yield. R_f: 0.35

(petroleum ether/ethyl acetate: 70/30). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.65 (d, *J* = 2.6 Hz, 1H), 8.30 (s, 1H), 8.07 (d, *J* = 2.5 Hz, 1H), 7.88 (d, *J* = 8.6 Hz, 1H), 7.69-7.77 (m, 3H), 7.51 (s, 1H), 7.23 (s, 1H), 2.36 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 146.3, 145.0, 144.6, 135.7, 132.2, 131.0, 130.6, 130.2, 129.6, 128.9, 127.4, 127.3, 127.2, 127.1, 125.8, 124.4, 123.4, 122.2, 21.7. HRMS m/z (ESI) calcd for $C_{17}H_{14}O_2N_2F_3S$ $[M+H]^+$ 367.0723, found 367.0715.



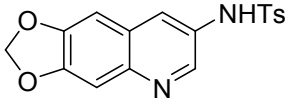
***N*-(6,7-dimethoxyquinolin-3-yl)-4-methylbenzenesulfonamide 1i:**

This compound was prepared from the 6,7-dimethoxyquinolin-3-amine according to the general procedure and was purified by column chromatography (petroleum ether/ethyl acetate: 1/1 to 2/8) as an orange solid with 79% yield. R_f: 0.17 (petroleum ether/ethyl acetate: 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.23 (d, *J* = 2.5 Hz, 1H), 7.95 (d, *J* = 2.4 Hz, 1H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.33 (s, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.00 (s, 1H), 6.75 (brs, 1H), 4.01 (s, 3H), 4.00 (s, 3H), 2.36 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 144.4, 143.6, 143.5, 136.0, 130.0, 128.8, 127.4, 127.2, 123.8, 107.9, 105.1, 56.3, 21.7. HRMS m/z (ESI) calcd for $C_{18}H_{19}O_4N_2S$ $[M+H]^+$ 359.1060, found 359.1054.



***N*-(7-methoxyquinolin-3-yl)-4-methylbenzenesulfonamide 1j:**

This compound was prepared from 7-methoxyquinolin-3-amine according to the general procedure and was purified by column chromatography (petroleum ether/ethyl acetate: 30/70) as a yellow solid with 99% yield. R_f: 0.40 (petroleum ether/ethyl acetate: 30/70). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.44 (d, *J* = 2.5 Hz, 1H), 7.98 (d, *J* = 2.4 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 3H), 7.36 (d, *J* = 2.4 Hz, 1H), 7.17-7.23 (m, 3H), 3.91 (s, 3H), 2.35 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 160.9, 147.5, 146.1, 144.4, 136.0, 130.0, 128.8, 128.6, 127.4, 123.3, 121.1, 106.9, 55.7, 21.6. HRMS m/z (ESI) calcd for $C_{17}H_{17}O_3N_2S$ $[M+H]^+$ 329.0954, found 329.0950.



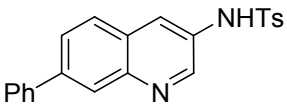
***N*-([1,3]dioxolo[4,5-*g*]quinolin-7-yl)-4-methylbenzenesulfonamide**

This compound was prepared from the [1,3]dioxolo[4,5-*g*]quinolin-7-amine according to the general procedure and was purified by column chromatography (petroleum ether/ethyl acetate: 8/2) as an orange solid with 81% yield. R_f: 0.25 (petroleum ether/ethyl acetate: 8/2). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.28 (d, *J* = 2.5 Hz, 1H), 7.87 (d, *J* = 2.5 Hz, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.29 (s, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 6.98 (s, 1H), 6.09 (s, 2H), 2.35 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 150.8, 148.8, 144.4, 144.4, 143.4, 136.0, 130.0, 129.2, 127.4, 127.4, 125.4, 105.6, 102.7, 102.1, 21.7. HRMS m/z (ESI) calcd for $C_{17}H_{15}O_4N_2S$ $[M+H]^+$ 343.0747, found 343.0741.

General procedure for the Suzuki cross coupling reaction

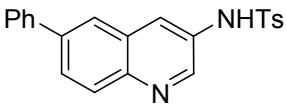
A degassed solution containing 1 equivalent of 6- or 7-bromoquinoline derivative (113 mg, 0.3 mmol, 1 equiv.), phenyl boronic acid (74 mg, 0.6 mmol, 2 equiv.) , 3 equivalents of K_2CO_3 (124 mg, 0.9 mmol, 3 equiv.) and 1.5 mol % of $Pd(OAc)_2$ (0.5 mg) in 6 mL of a mixture 50/50 of DMF/H_2O was heated at 50

°C overnight. Brine (8 mL) was then added to the reaction and the aqueous phase was extracted 4 times with 8 mL of diethyl ether. The organic phases were dried over $MgSO_4$ and evaporated under reduced pressure. The resulting residue was purified over silica gel chromatography (petroleum ether/ethyl acetate 50/50) affording thus the corresponding cross coupling product.



_N_-(7-phenylquinolin-3-yl)-4-methyl-benzenesulfonamide 1l:

This compound was prepared from *N*-(7-bromoquinolin-3-yl)-4-methylbenzenesulfonamide according to the general procedure. R_f: 0.40 (petroleum ether/ethyl acetate: 50/50). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.57 (brs, 1H), 8.26 (brs, 1H), 8.09 (brs, 1H), 7.84 (brs, 2H), 7.72-7.69 (m, 4H), 7.52-7.38 (m, 3H), 7.23 (d, *J* = 8.1 Hz, 2H), 2.36 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 144.6, 142.3, 140.0, 135.9, 130.1, 129.2, 128.2, 127.6, 127.5, 127.4, 129.6, 126.6, 21.7. HRMS m/z (ESI) calcd for $C_{16}H_{14}O_2N_2BrS$ $[M+H]^+$ 375.1162, found 375.1154.



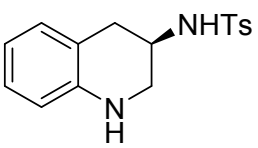
_N_-(6-phenylquinolin-3-yl)-4-methyl-benzenesulfonamide 1m:

This compound was prepared from *N*-(6-bromoquinolin-3-yl)-4-methylbenzenesulfonamide according to the general procedure. R_f: 0.45 (petroleum ether/ethyl acetate: 50/50). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.59 (d, *J* = 2.4 Hz, 1H), 8.10-8.06 (m, 2H), 7.92-7.87 (m, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.67 (d, *J* = 7.0 Hz, 2H), 7.51-7.38 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 2.33 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 145.3, 145.0, 144.6, 140.5, 140.1, 136.0, 131.0, 130.1, 129.4, 129.2, 129.0, 128.4, 128.1, 127.6, 127.4, 126.5, 125.4, 21.6. HRMS m/z (ESI) calcd for $C_{16}H_{14}O_2N_2BrS$ $[M+H]^+$ 375.1162, found 375.1156.

I. Reduction of aminoquinolines

General procedure for the reduction of quinolin-3-amines:

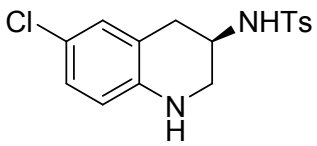
The quinolin-3-amine **1a**-**k** or **1m** (0.1 mmol, 1 equiv.), the Hantzsch dihydropyridine **4** (0.24 mmol, 60.8 mg, 2.4 equiv.) and the catalyst **3e** (5 µmol, 4 mg, 0.05 equiv.) were suspended in benzene (1 mL) in a screw-capped Schlenk tube under nitrogen atmosphere. The reaction was heated to 50 °C for 48 h. After dilution in CH_2Cl_2 (10 mL), the yellow solution was washed with a saturated sodium hydrogen carbonate solution (2 × 10 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on neutral alumina to afford the 3-aminotetrahydroquinoline **2a**-**k** or **2m**.



(*R*)-*N*-(1,2,3,4-tetrahydroquinolin-3-yl)-4-methylbenzenesulfonamide 2a:

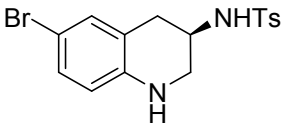
This compound was prepared from the quinoline **1a** (29.8 mg) according to the general procedure and was purified by column chromatography on neutral alumina (petroleum ether/ethyl acetate: 8/2 to 1/1) as a white solid with 96% yield. R_f: 0.47 (petroleum

ether/ethyl acetate: 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.02-6.97 (m, 1H), 6.81 (d, *J* = 7.5 Hz, 1H), 6.64 (td, *J* = 7.4, 1.1 Hz, 1H), 6.50 (dd, *J* = 8.0, 0.9 Hz, 1H), 4.99 (d, *J* = 8.7 Hz, 1H), 3.90-3.81 (m, 1H), 3.30-3.25 (m, 1H), 3.11-3.05 (m, 1H), 2.93-2.87 (m, 1H), 2.60-2.53 (m, 1H), 2.44 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 143.5, 143.3, 138.4, 130.5, 129.9, 127.6, 127.1, 118.4, 117.6, 114.5, 46.4, 46.2, 33.6, 29.8, 21.7. $[\alpha]_D^{20}$ -15.2 (c 0.3; $CHCl_3$). HPLC conditions: Chiracel® OJ-H (Hex/EtOH = 70/30, 0.9 mL.min^{-1}), major enantiomer: t_R = 72.67 min, minor enantiomer: t_R = 64.10 min, 90% ee. HRMS m/z (ESI) calcd for $C_{16}H_{19}O_2N_2S$ $[M+H]^+$ 303.1162, found 303.1146.



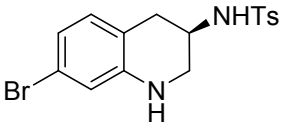
(*R*)-*N*-(6-Chloro-1,2,3,4-tetrahydroquinolin-3-yl)-4-methylbenzenesulfonamide 2d:

This compound was prepared from the quinoline **1d** (33.3 mg) according to the general procedure and was purified by column chromatography (petroleum ether/ethyl acetate: 8/2 to 7/3) as an off-white solid with 98% yield. R_f: 0.17 (petroleum ether/ethyl acetate: 8/2). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.94 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.73 (d, *J* = 2.3 Hz, 1H), 6.44 (d, *J* = 8.5 Hz, 1H), 5.00 (d, *J* = 8.4 Hz, 1H), 3.89-3.81 (m, 1H), 3.29-3.24 (m, 1H), 3.14-3.08 (m, 1H), 2.88-2.81 (m, 1H), 2.57-2.51 (m, 1H), 2.44 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 143.6, 141.3, 138.1, 129.8, 129.8, 127.4, 126.9, 123.0, 119.2, 115.6, 46.2, 45.5, 33.2, 21.5. $[\alpha]_D^{20}$ -12.3 (c 0.3; $CHCl_3$). HPLC conditions: Chiracel® OJ-H (Hex/EtOH = 70/30, 0.9 mL.min^{-1}), major enantiomer: t_R = 35.65 min, minor enantiomer: t_R = 54.21 min, 85% ee. HRMS m/z (ESI) calcd for $C_{16}H_{18}O_2N_2ClS$ $[M+H]^+$ 337.0772, found 337.0753.



(*R*)-*N*-(6-bromo-1,2,3,4-tetrahydroquinolin-3-yl)-4-methylbenzenesulfonamide 2e:

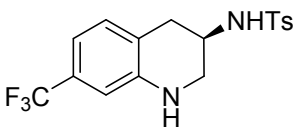
This compound was prepared from the quinoline **1e** (37 mg) according to the general procedure and was purified over silica gel column chromatography (petroleum ether/ethyl acetate/triethylamine: 6/3/1) as a white solid with 88% yield. R_f: 0.18 (petroleum ether/ethyl acetate/triethylamine: 6/3/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.06 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.85-6.86 (m, 1H), 6.36 (d, *J* = 8.5 Hz, 1H), 4.95 (d, *J* = 8.5 Hz, 1H), 3.80-3.88 (m, 1H), 3.26 (dd, *J* = 11.6, 1.2 Hz, 1H), 3.10 (ddd, *J* = 11.6, 4.6, 2.1 Hz, 1H), 2.84 (dd, *J* = 16.6, 4.3 Hz, 1H), 2.49-2.56 (m, 1H), 2.45 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 143.7, 142.4, 138.3, 132.8, 130.3, 129.9, 127.1, 119.5, 115.8, 109.7, 46.3, 45.7, 33.3, 21.7. $[\alpha]_D^{20}$ -8.5 (c 0.8; $CHCl_3$). HPLC conditions: Chiracel® OD (Hex/EtOH = 65/35, 0.3 mL.min^{-1}), major enantiomer: t_R = 53.89 min, minor enantiomer: t_R = 34.05 min, 60% ee. HRMS m/z (ESI) calcd for $C_{16}H_{16}O_2N_2BrS$ $[M-H]^-$ 379.0110, found 379.0093.



(*R*)-*N*-(7-bromo-1,2,3,4-tetrahydroquinolin-3-yl)-4-methylbenzenesulfonamide 2f:

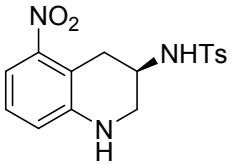
This compound was prepared from the quinoline **1f** (37 mg) according to the general procedure and was purified over silica gel column chromatography (petroleum ether/dichloromethane/triethylamine: 70/20/10) as a white solid with 87% yield. R_f: 0.52 (petroleum

ether/dichloromethane/methanol: 50/45/5). ^{1}H-NMR (300 MHz, CD_2Cl_2): δ = 7.72 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 7.9 Hz, 2H), 6.64-6.73 (m, 3H), 4.88 (d, *J* = 8.7 Hz, 1H), 3.93 (brs, 1H), 3.76-3.85 (m, 1H), 3.23-3.27 (m, 1H), 2.99-3.07 (m, 1H), 2.81 (dd, *J* = 16.4, 4.5 Hz, 1H), 2.50 (ddd, *J* = 16.5, 4.4, 2.2 Hz, 4H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 145.9, 142.7, 138.4, 131.0, 129.7, 126.5, 119.5, 117.7, 116.8, 114.8, 46.2, 45.3, 32.9, 20.9. $[\alpha]_D^{20}$ -8.5 (c 0.3; $CHCl_3$). HPLC conditions: Chiracel® OD (Hex/EtOH = 65/35, 0.3 mL.min^{-1}), major enantiomer: t_R = 26.13 min, minor enantiomer: t_R = 32.13 min, 87% ee. HRMS m/z (ESI) calcd for $C_{16}H_{16}O_2N_2BrS$ $[M-H]^-$ 379.0110, found 379.0097.



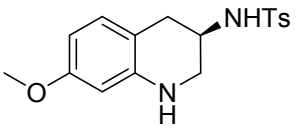
(*R*)-*N*-(7-(trifluoromethyl)-1,2,3,4-tetrahydroquinolin-3-yl)-4-methylbenzenesulfonamide 2g:

This compound was prepared from the quinoline **1g** (37 mg) according to the general procedure and was purified column chromatography on neutral alumina (petroleum ether/ethyl acetate: 8/2 to 1/1) as a white solid with 69% yield. R_f: 0.3 (petroleum ether/ethyl acetate: 80/20). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.84 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.70 (s, 1H), 4.93 (d, *J* = 8.0 Hz, 1H), 3.98 (brs, 1H), 3.84-3.88 (m, 1H), 3.31 (d, *J* = 12.2 Hz, 1H), 3.08-3.14 (m, 1H), 2.92 (dd, *J* = 16.8, 3.7 Hz, 1H), 2.60-2.67 (m, 1H), 2.44 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 143.7, 143.5, 138.2, 130.9, 130.3, 129.9, 127.1, 121.1,114.6, 114.5, 110.8, 110.7, 46.2, 45.7, 33.7, 21.7. $[\alpha]_D^{20}$ -7.5 (c 0.05; $CHCl_3$). HPLC conditions: Chiracel® OD (Hex/EtOH = 65/35, 0.3 mL.min^{-1}), major enantiomer: t_R = 19.50 min, minor enantiomer: t_R = 23.77 min, 75% ee. HRMS m/z (ESI) calcd for $C_{17}H_{18}O_2N_2F_3S$ $[M+H]^+$ 371.1036, found 371.1028.



(*R*)-*N*-(5-nitro-1,2,3,4-tetrahydroquinolin-3-yl)-4-methyl-benzenesulfonamide 2h:

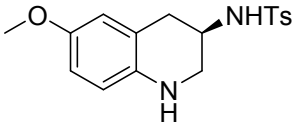
This compound was prepared from the quinoline **1h** (34.3 mg) according to the general procedure and was purified column chromatography on neutral alumina (petroleum ether/ethyl acetate: 8/2 to 1/1) as a yellow solid with 43% yield. R_f: 0.46 (petroleum ether/ethyl acetate: 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* =8.3 Hz, 2H), 7.22 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.09 (t, *J* = 8.0 Hz, 1H), 6.71 (dd, *J* = 8.0, 0.9 Hz, 1H), 4.86 (d, *J* = 8.5 Hz, 1H), 3.91-3.83 (m, 1H), 3.38-3.34 (m, 1H), 3.26-3.20 (m, 1H), 3.02-2.95 (m, 1H), 2.72-2.64 (m, 1H), 2.44 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 150.8, 144.8, 144.1, 137.8, 130.0, 127.6, 126.9, 118.9, 114.3, 112.0, 45.6, 45.2, 30.7, 21.7. $[\alpha]_D^{20}$ 39.5 (c 0.1; $CHCl_3$). HPLC conditions: Chiracel® OJ-H (Hex/EtOH = 70/30, 0.3 mL.min^{-1}), major enantiomer: t_R = 80.76 min, minor enantiomer: t_R = 71.79 min, 56% ee. HRMS m/z (ESI) calcd for $C_{16}H_{18}O_4N_3S$ $[M+H]^+$ 348.1013, found 348.0994.



(*R*)-*N*-(7-methoxy-1,2,3,4-tetrahydroquinolin-3-yl)-4-methylbenzenesulfonamide 2j:

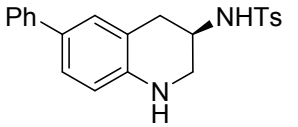
This compound was prepared from the quinoline **1j** (33 mg) according to the general procedure and was purified column chromatography on neutral alumina (petroleum ether/ethyl acetate: 8/2 to 1/1) as a white solid with 90% yield. R_f: 0.6 (petroleum ether/ethyl acetate: 8/2). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.70 (d, *J* = 8.3 Hz,

1H), 6.63 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.23 (d, *J* = 8.3, 2.5 Hz, 1H), 6.05 (d, *J* = 2.5 Hz, 1H), 4.95 (d, *J* = 8.8 Hz, 1H), 3.77-3.87 (m, 1H), 3.72 (s, 3H), 3.26 (dd, *J* = 11.5, 2.0 Hz, 1H), 3.07 (ddd, *J* = 11.5, 4.8, 2.0 Hz, 1H), 2.82 (dd, *J* = 16.0, 4.6 Hz, 1H), 2.44-2.52 (m, 4H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 159.5, 144.2, 143.5, 138.4, 131.2, 129.8, 127.1, 109.9, 104.5, 99.6, 55.3, 46.4, 46.3, 33.0, 21.7. $[\alpha]_D^{20}$ -11.5 (c 0.7; $CHCl_3$). HPLC conditions: Chiracel® OD (Hex/EtOH = 65/35, 0.3 mL.min^{-1}), major enantiomer: t_R = 36.68 min, minor enantiomer: t_R = 42.97 min, 84% ee. HRMS m/z (ESI) calcd for $C_{17}H_{21}O_3N_2S$ $[M+H]^+$ 333.1267, found 333.1263.



(*R*)-*N*-(6-methoxy-1,2,3,4-tetrahydroquinolin-3-yl)-4-methylbenzenesulfonamide 2k:

This compound was prepared from the quinoline **1k** (33 mg) according to the general procedure and was purified column chromatography on neutral alumina (petroleum ether/ethyl acetate: 8/2 to 1/1) as a brown solid with 30% yield. R_f: 0.48 (petroleum ether/ethyl acetate: 6/4). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.63 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.49 (d, *J* = 8.6 Hz, 1H), 6.40 (d, *J* = 2.7 Hz, 1H), 5.10 (d, *J* = 8.7 Hz, 1H), 3.81-3.89 (m, 1H), 3.70 (s, 3H), 3.21 (d, *J* = 11.4 Hz, 1H), 3.01-3.06 (m, 1H), 2.91 (dd, *J* = 16.5, 3.3 Hz, 1H), 2.58 (d, *J* = 15.3 Hz, 1H), 2.43 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.5, 153.4, 143.5, 138.4, 129.9, 127.3, 127.2, 119.9, 116.5, 115.4, 114.0, 55.9, 46.5, 46.3, 33.8, 21.7. $[\alpha]_D^{20}$ -16.2 (c 0.9; $CHCl_3$). HPLC conditions: Chiracel® OD (Hex/EtOH = 65/35, 0.3 mL.min^{-1}), major enantiomer: t_R = 71.99 min, minor enantiomer: t_R = 43.52 min, 87% ee. HRMS m/z (ESI) calcd for $C_{17}H_{21}O_3N_2S$ $[M+H]^+$ 333.1267, found 333.1261.

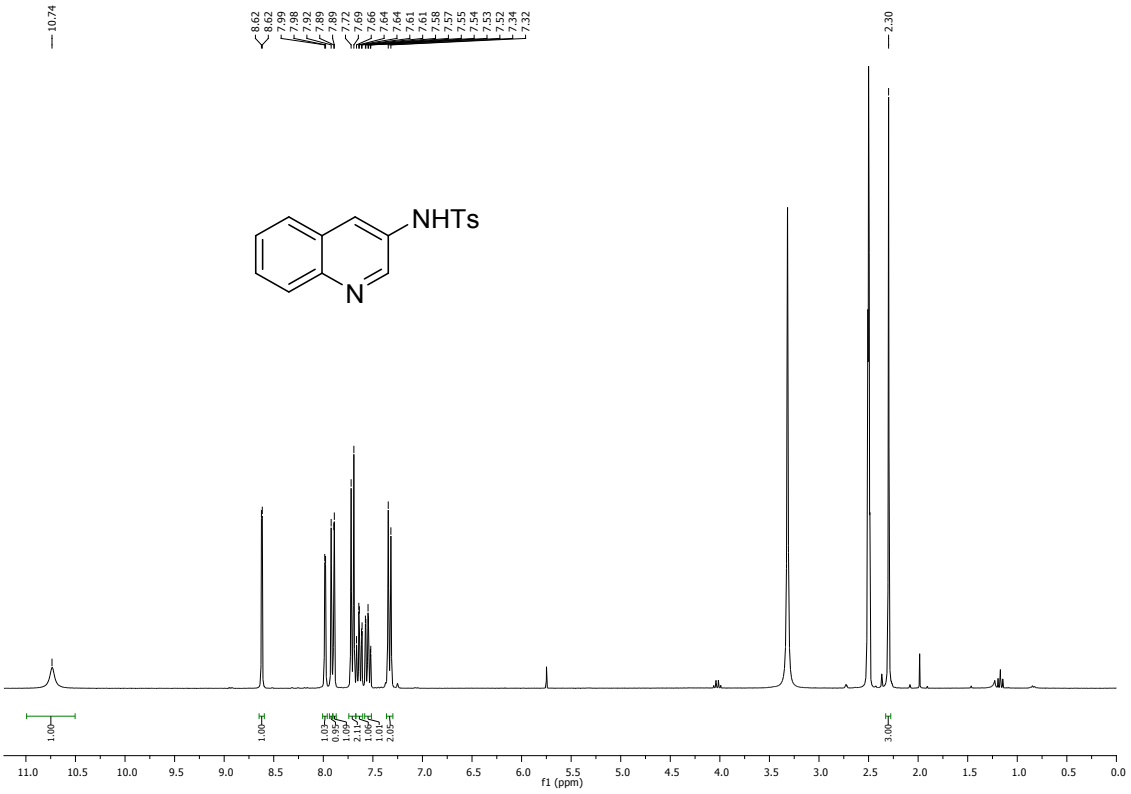


(*R*)-*N*-(6-phenyl-1,2,3,4-tetrahydroquinolin-3-yl)-4-methylbenzenesulfonamide 2m:

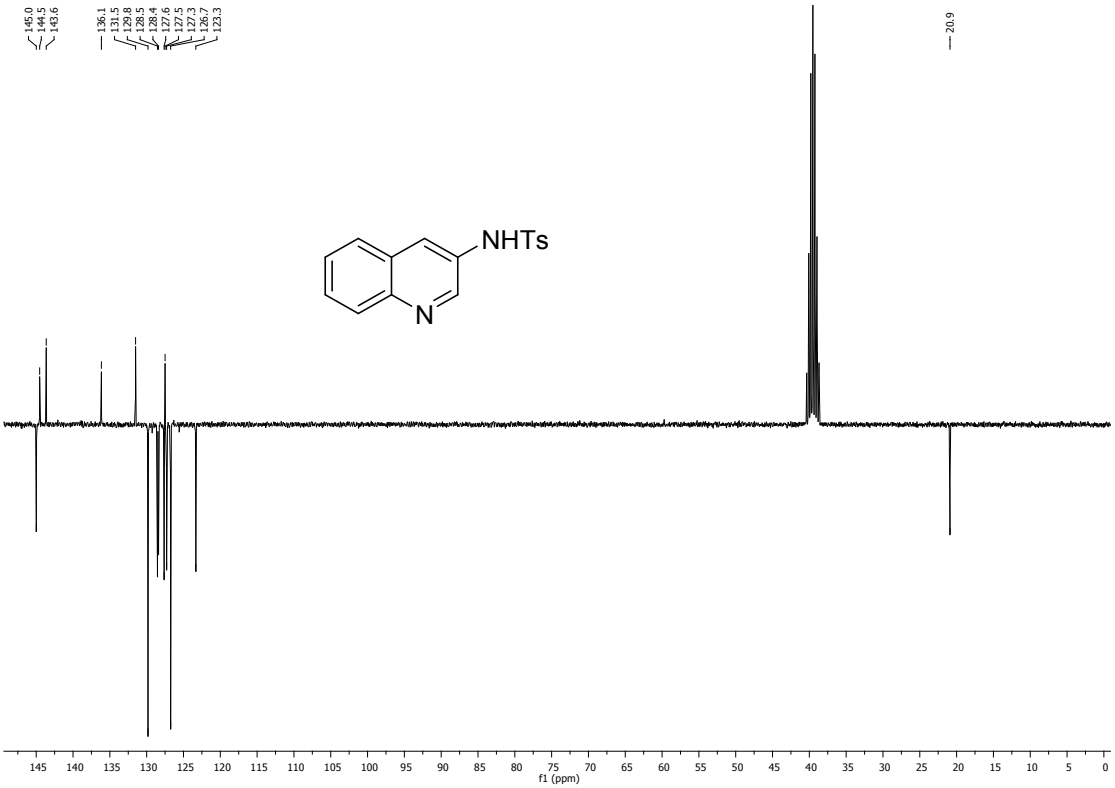
This compound was prepared from the quinoline **1m** (37 mg) according to the general procedure and was purified over silica gel column chromatography (chloroform/methanol 90/3) as an off-white solid with 87% yield. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.3 Hz, 2H), 7.48-7.45 (m, 2H), 7.40-7.35 (m, 2H), 7.29-7.24 (m,H), 7.01 (d, *J* = 1.9 Hz, 1H), 6.56 (d, *J* = 8.3 Hz, 1H), 5.03 (d, *J* = 8.7 Hz, 1H), 3.86-3.94 (m, 2H), 3.33 (dd, *J* = 11.1, 1.3 Hz, 1H), 3.13 (ddd, *J* = 11.5, 4.7, 2.0 Hz, 1H), 2.95 (dd, *J* = 16.3, 4.4 Hz, 1H), 2.60-2.66 (m, 1H), 2.40 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ = 143.6, 142.8, 141.1, 138.4, 131.3, 129.9, 129.1, 128.8, 127.1, 126.4, 117.7, 114.7, 46.5, 46.2, 33.7, 21.6. $[\alpha]_D^{20}$ -9.2 (c 0.07; $CHCl_3$). HPLC conditions: Chirapak® AD-H (Hex/EtOH = 80/20, 1 mL.min^{-1}), major enantiomer: t_R = 30.41 min, minor enantiomer: t_R = 33.45 min, 85% ee. HRMS m/z (ESI) calcd for $C_{22}H_{22}O_2N_2S$ $[M+H]^+$ 378.1402, found 378.1395.

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

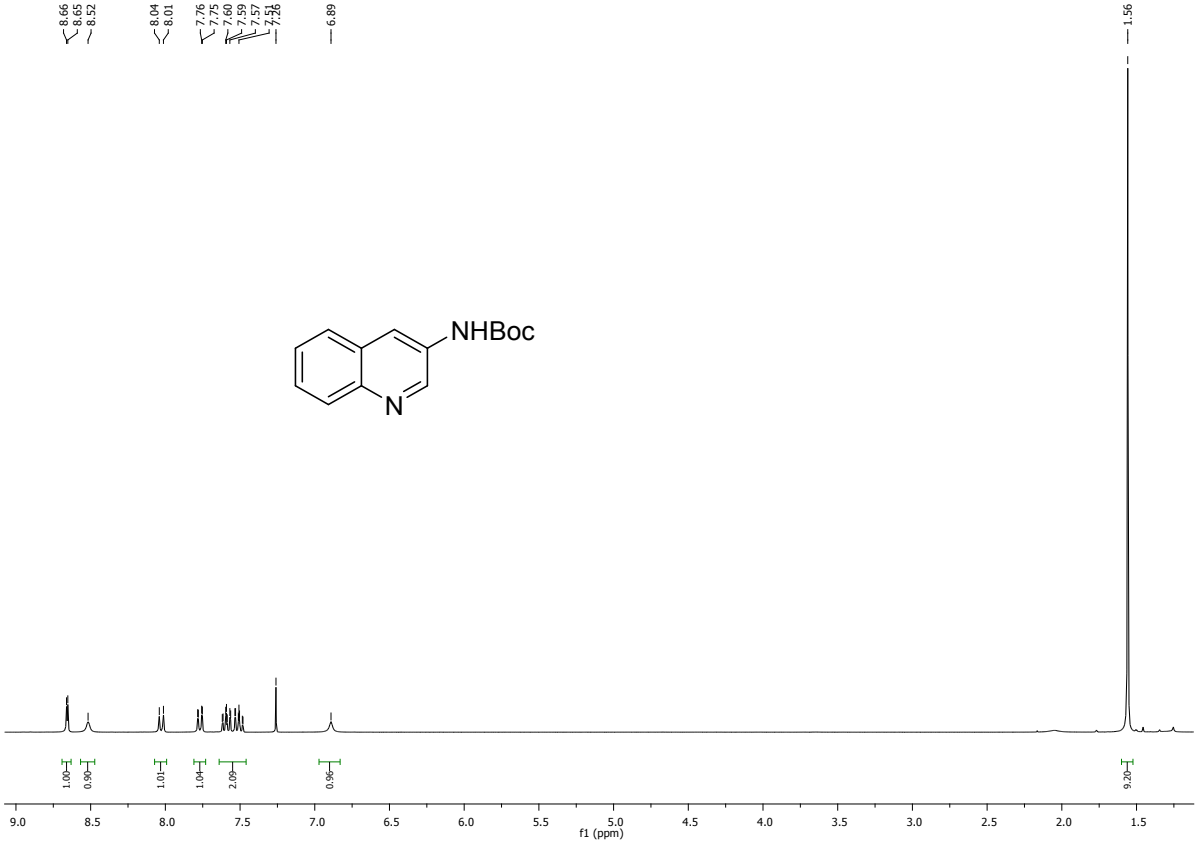
Compound **1a**: ^{1}H NMR



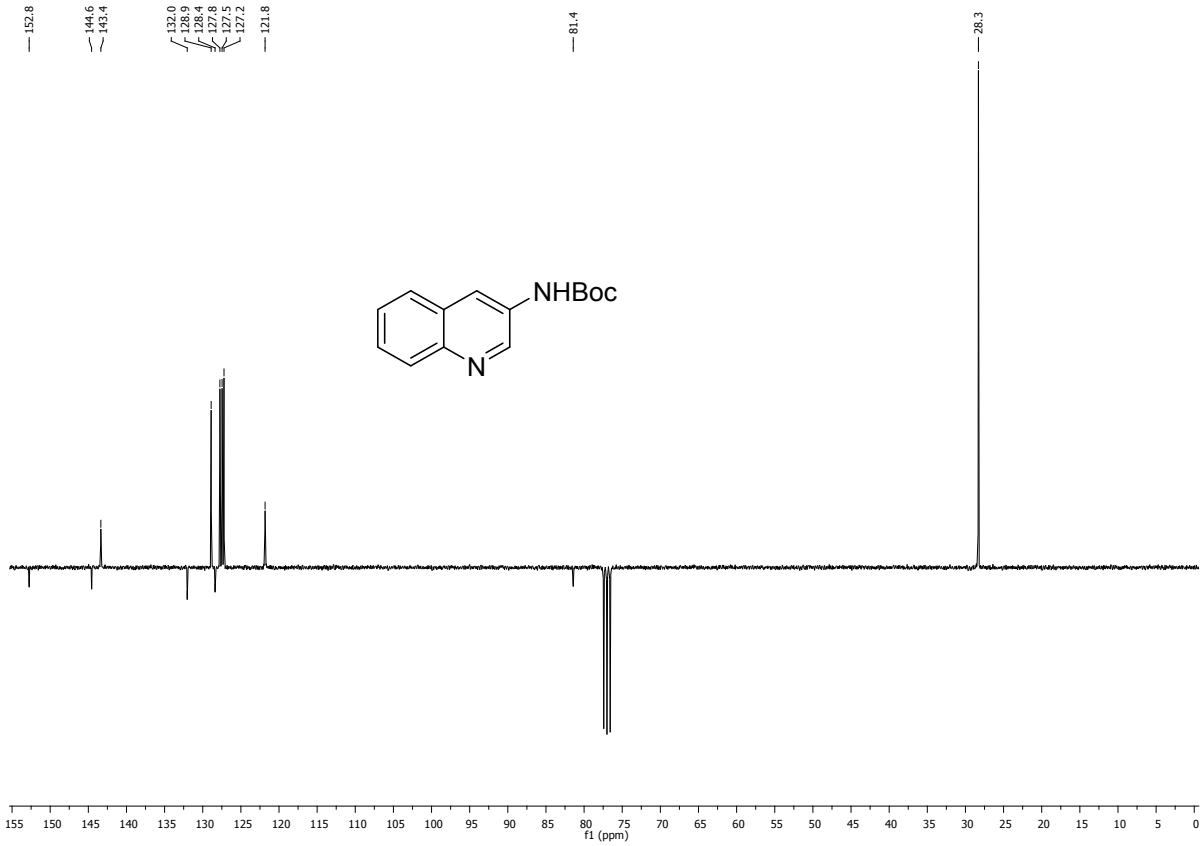
Compound **1a**: ^{13}C NMR



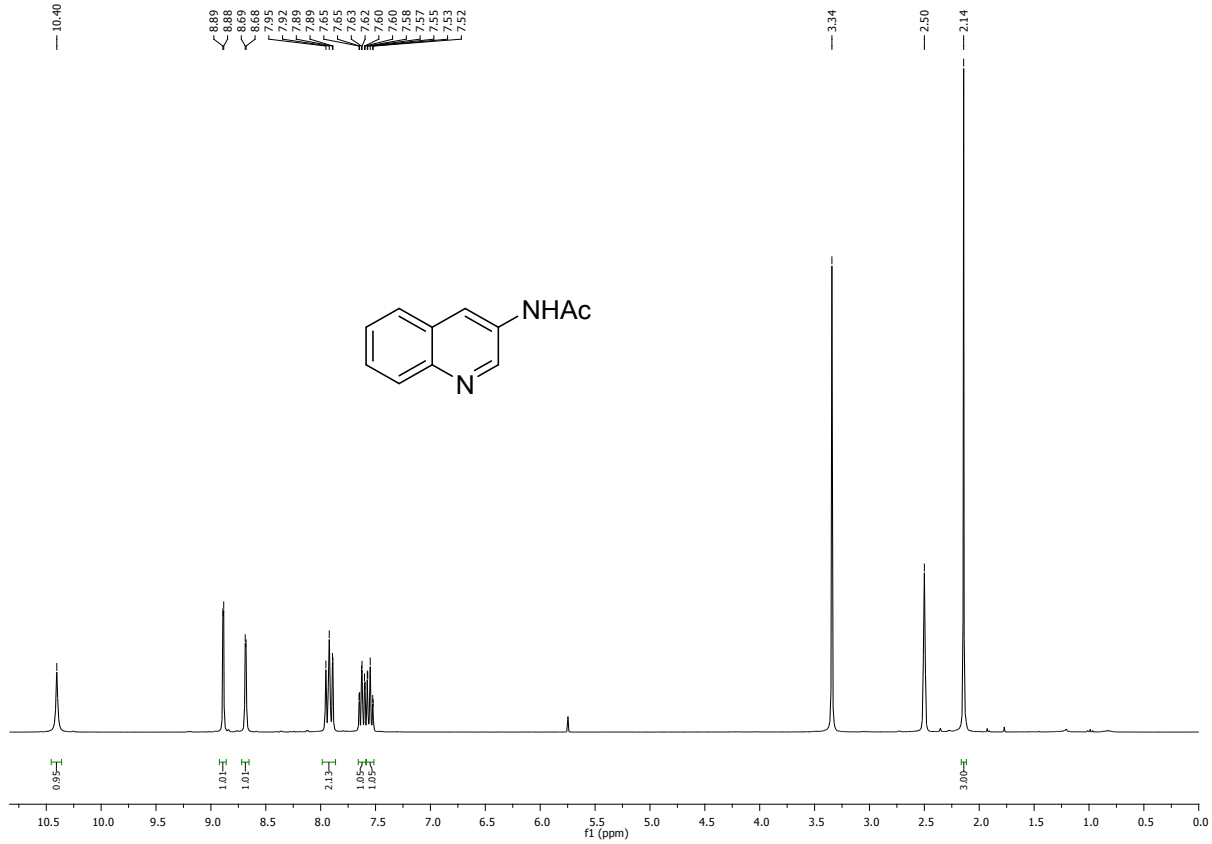
Compound **1b**: ^{1}H NMR



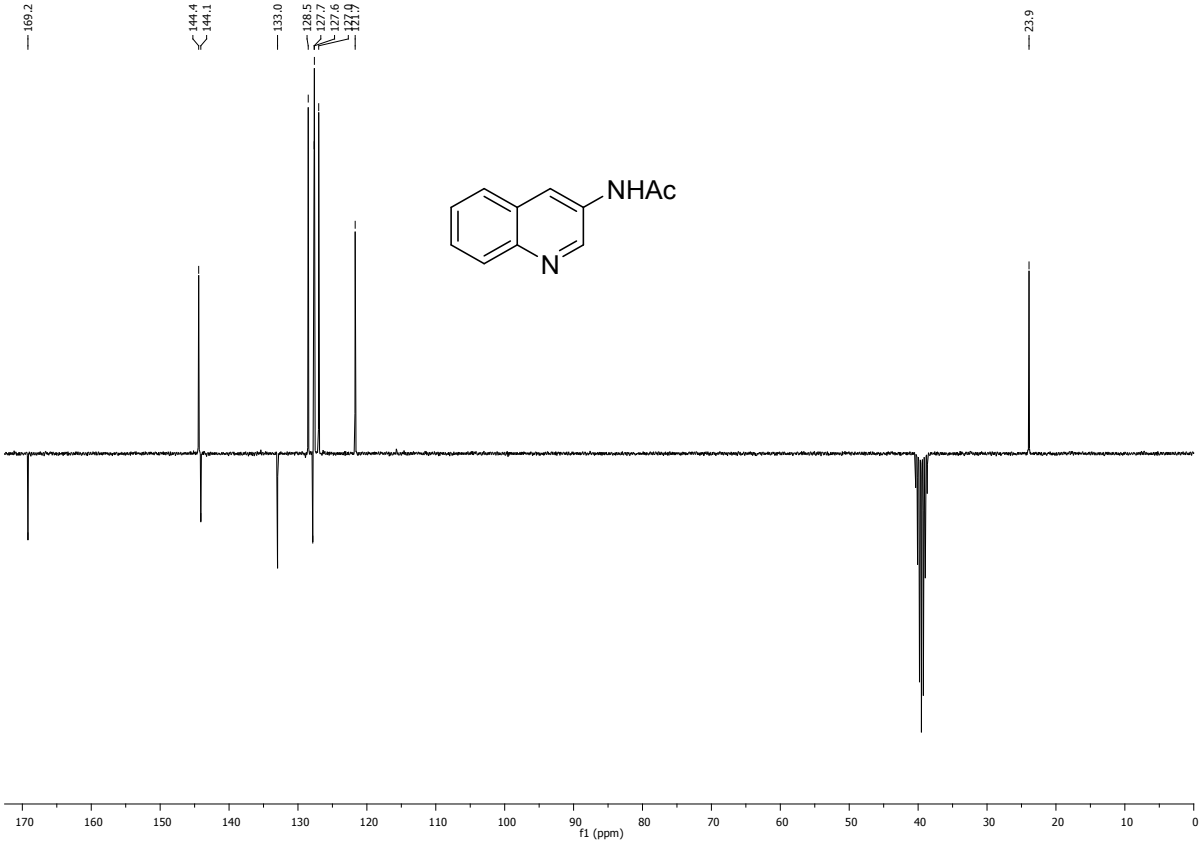
Compound **1b**: ^{13}C NMR



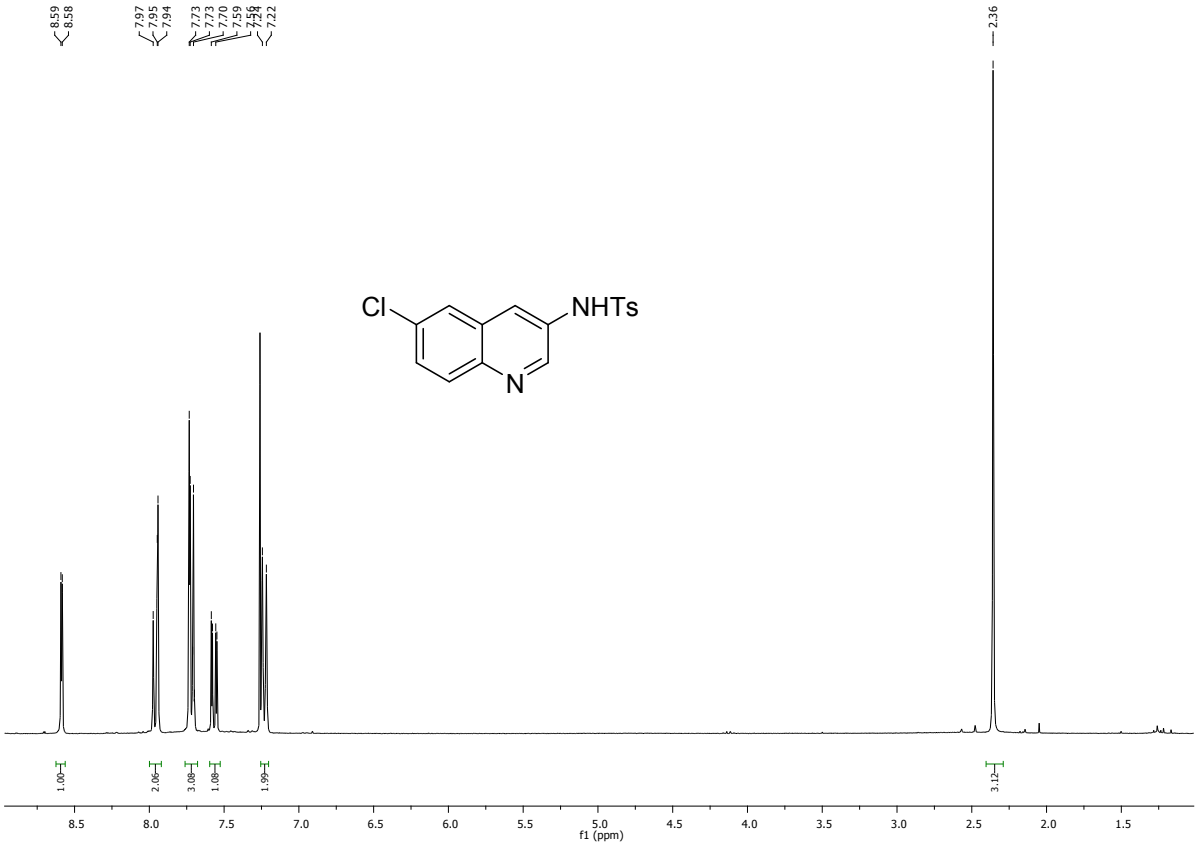
Compound **1c**: ^{1}H NMR



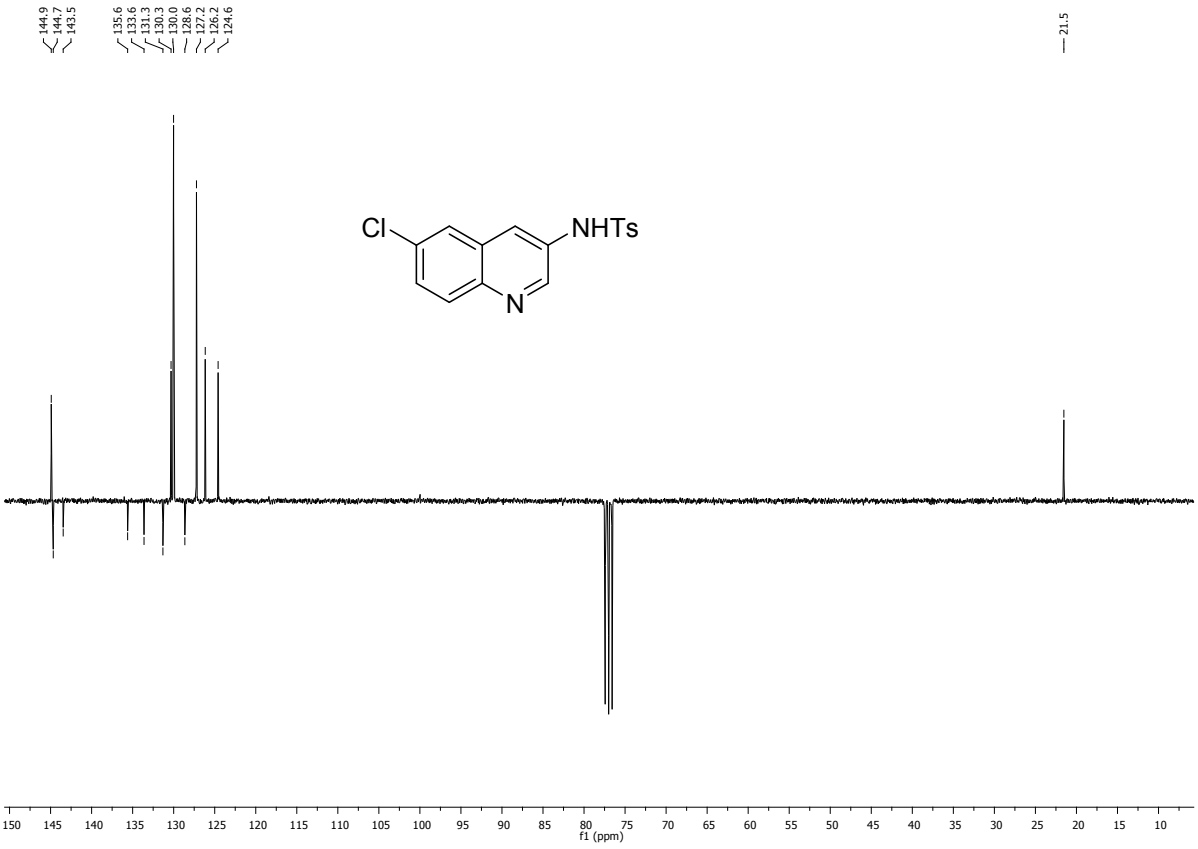
Compound **1c**: ^{13}C NMR



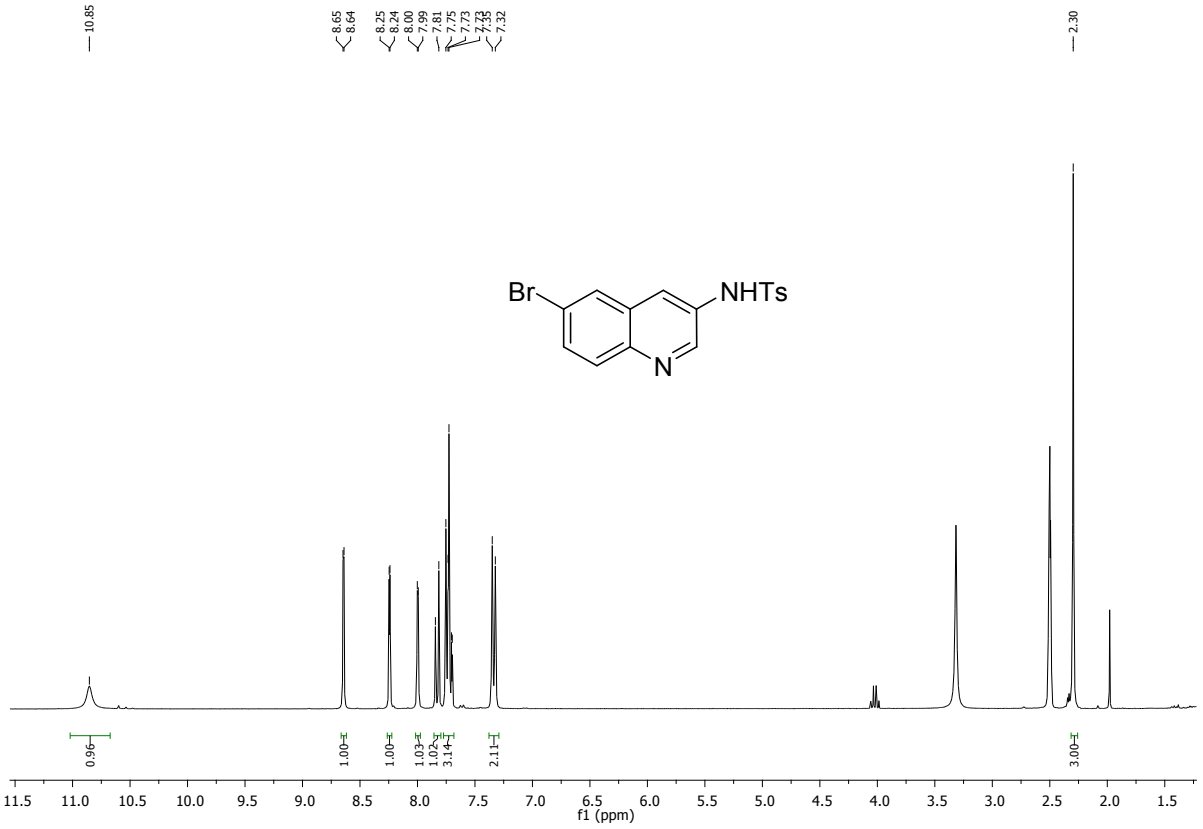
Compound **1d**: ^{1}H NMR



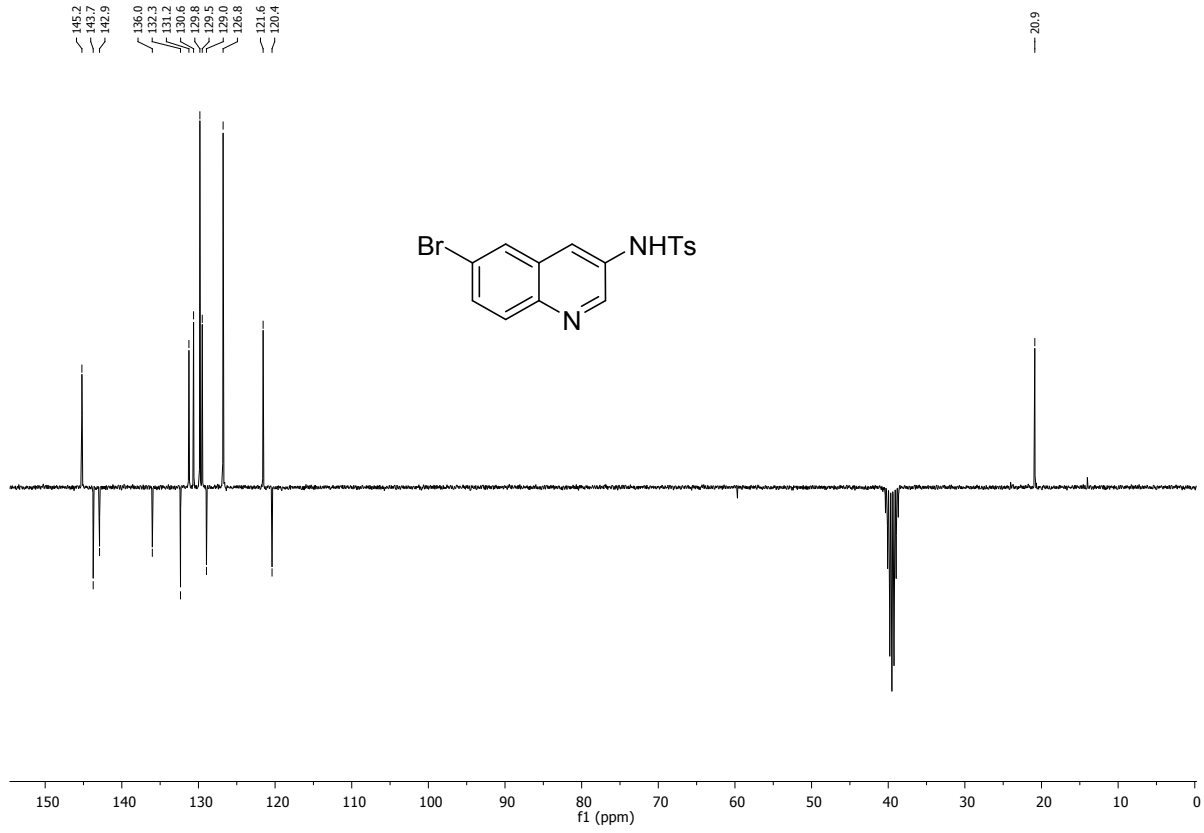
Compound **1d**: ^{13}C NMR



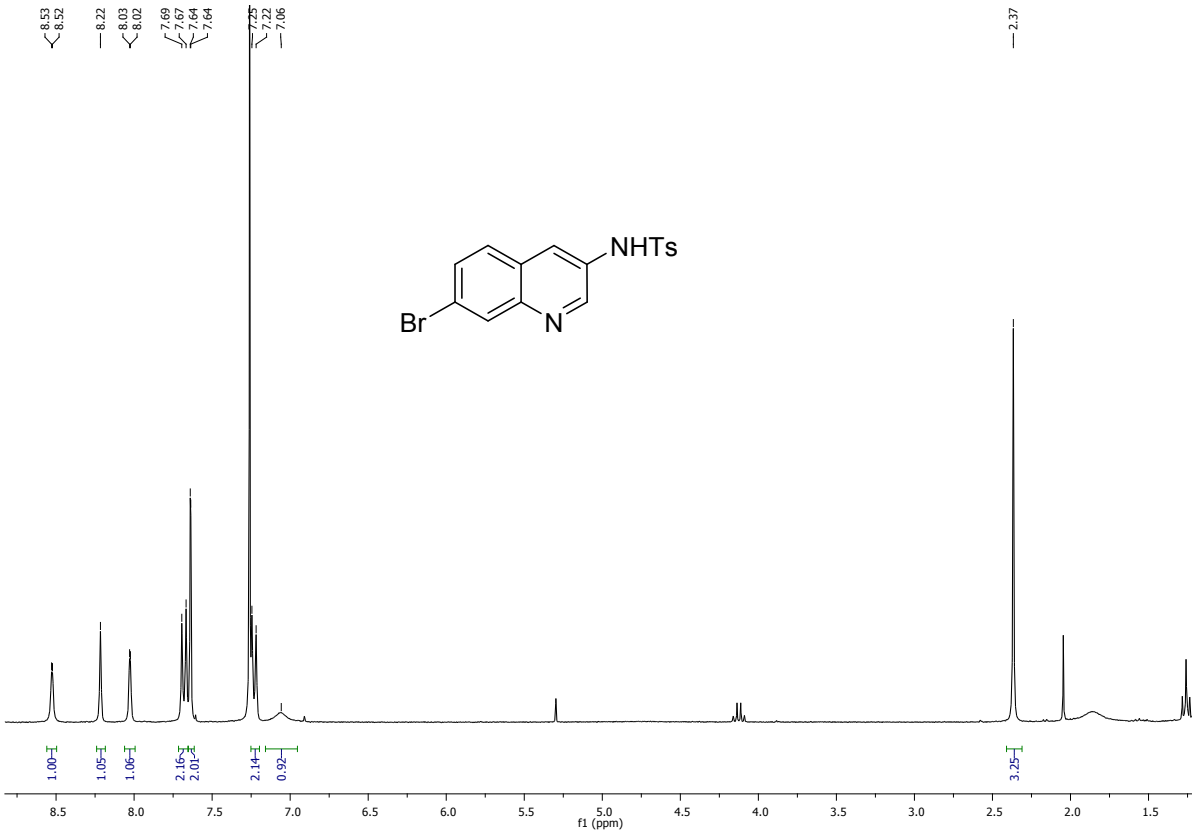
Compound **1e**: ^{1}H NMR



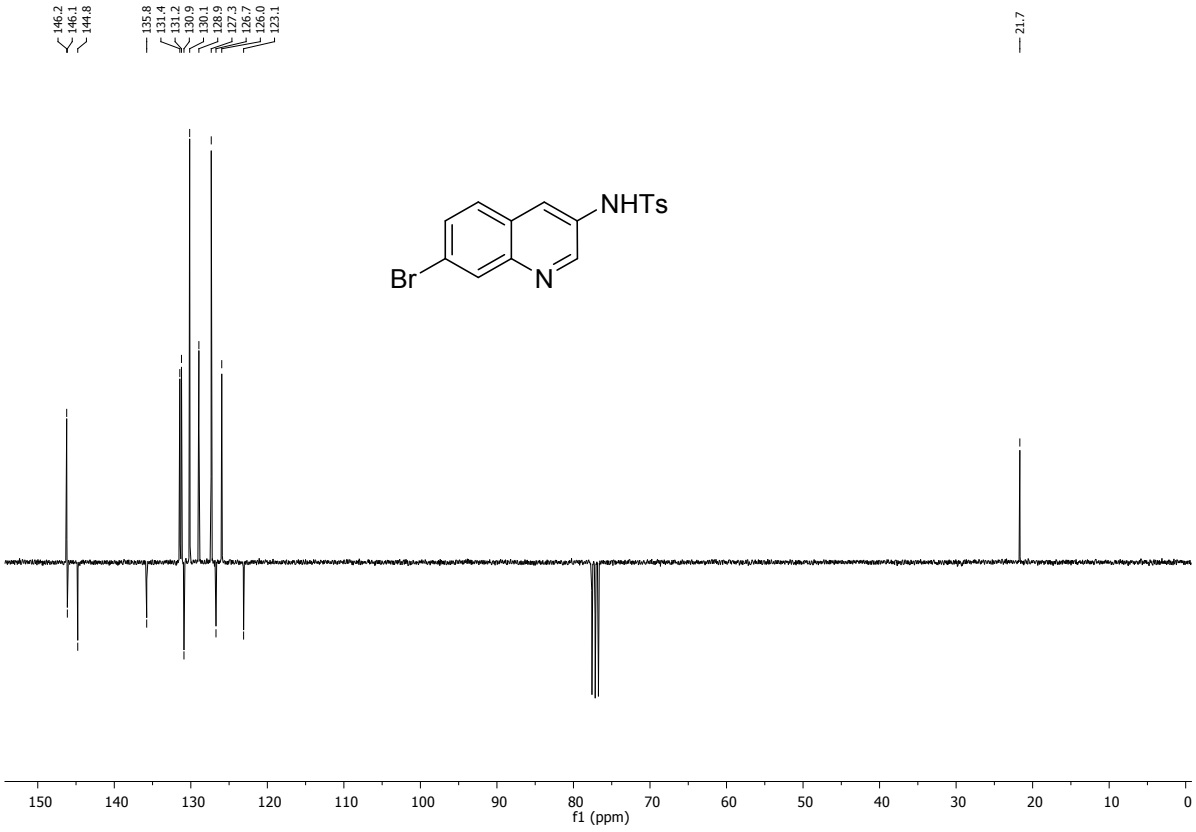
Compound **1e**: ^{13}C NMR



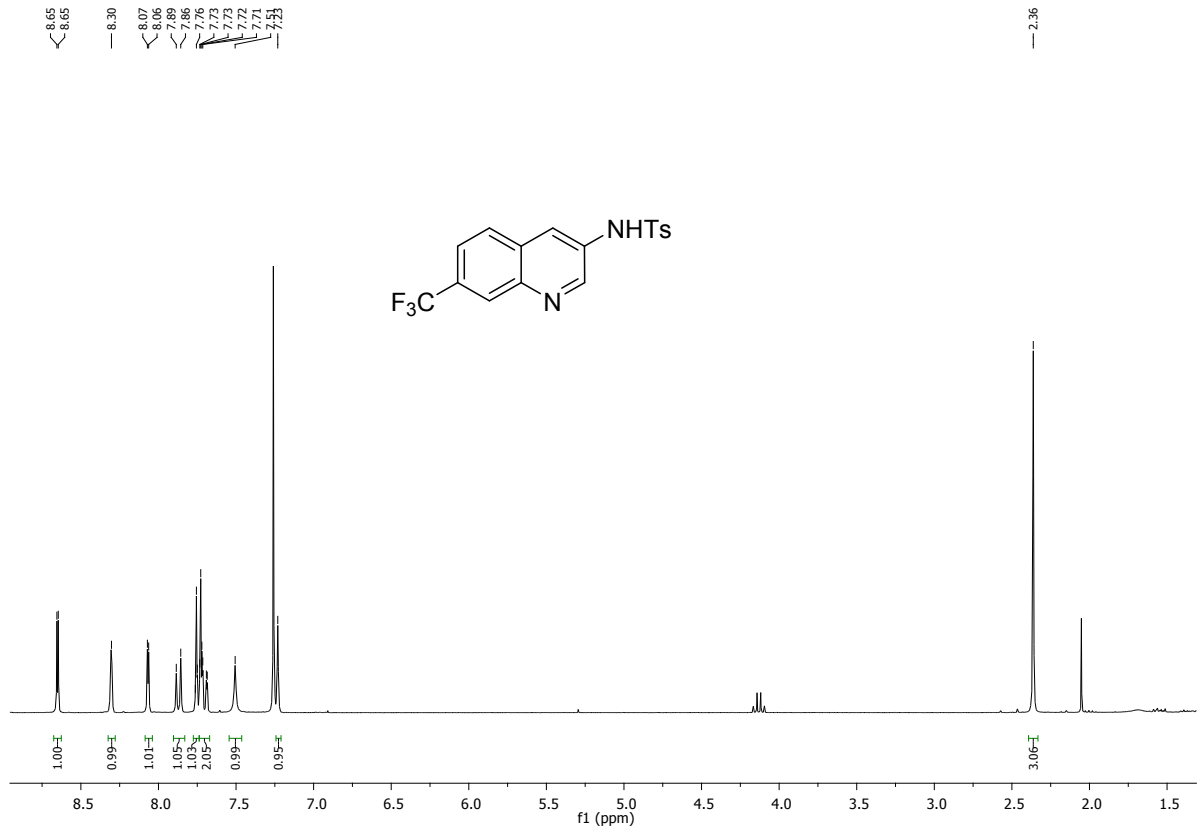
Compound **1f**: ^{1}H NMR



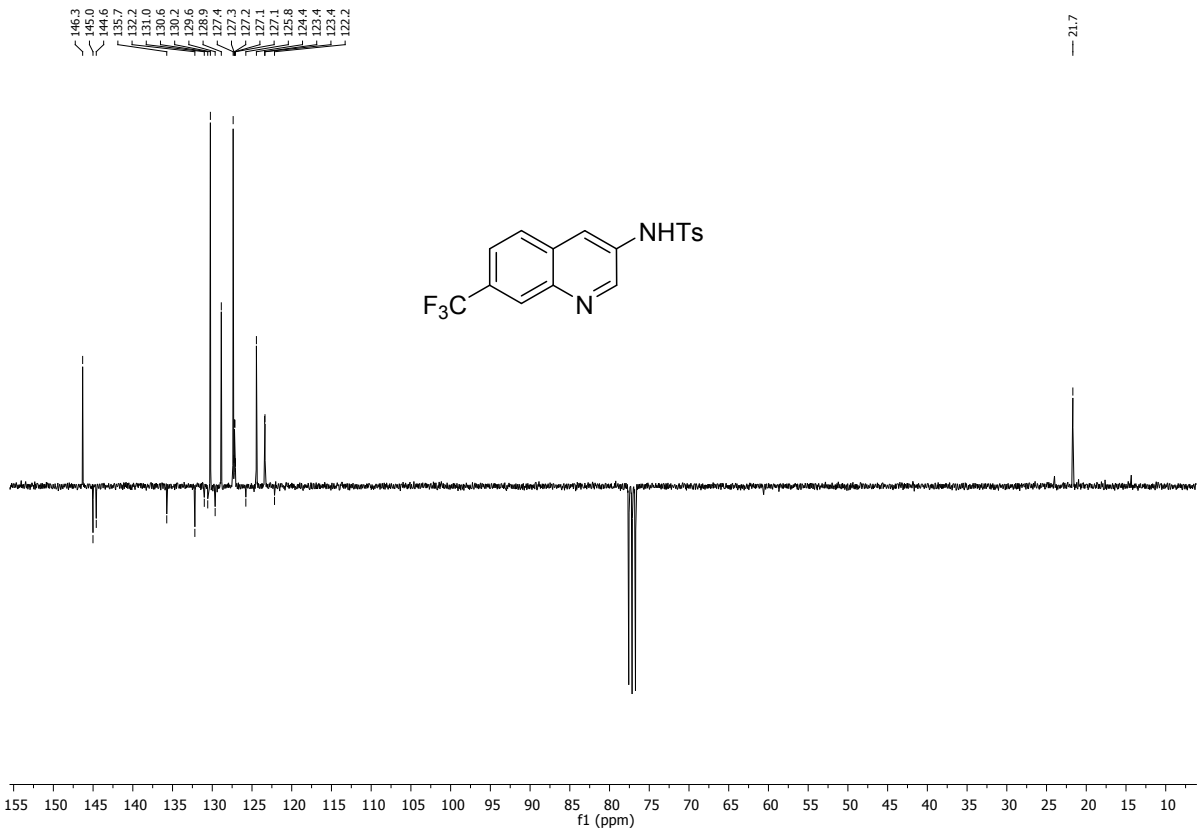
Compound **1f**: ^{13}C NMR



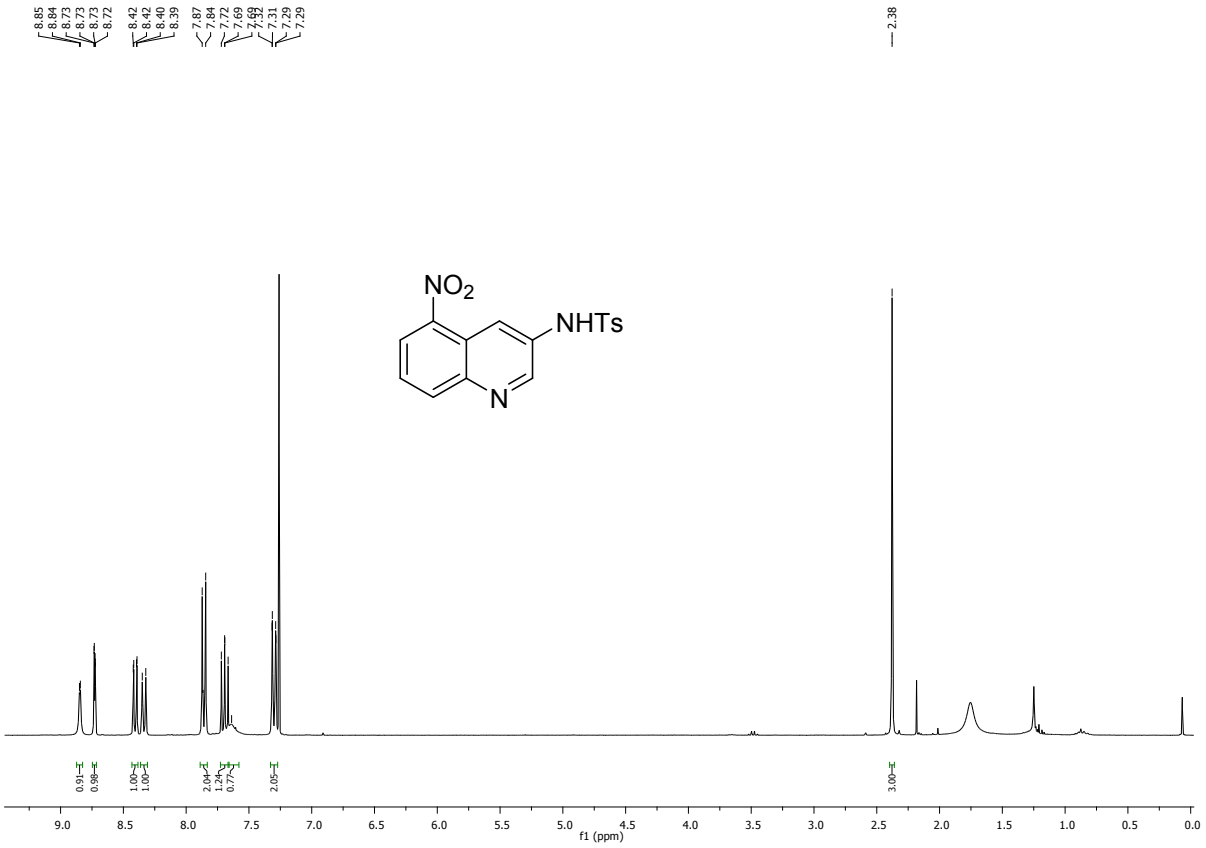
Compound **1g**: ^{1}H NMR



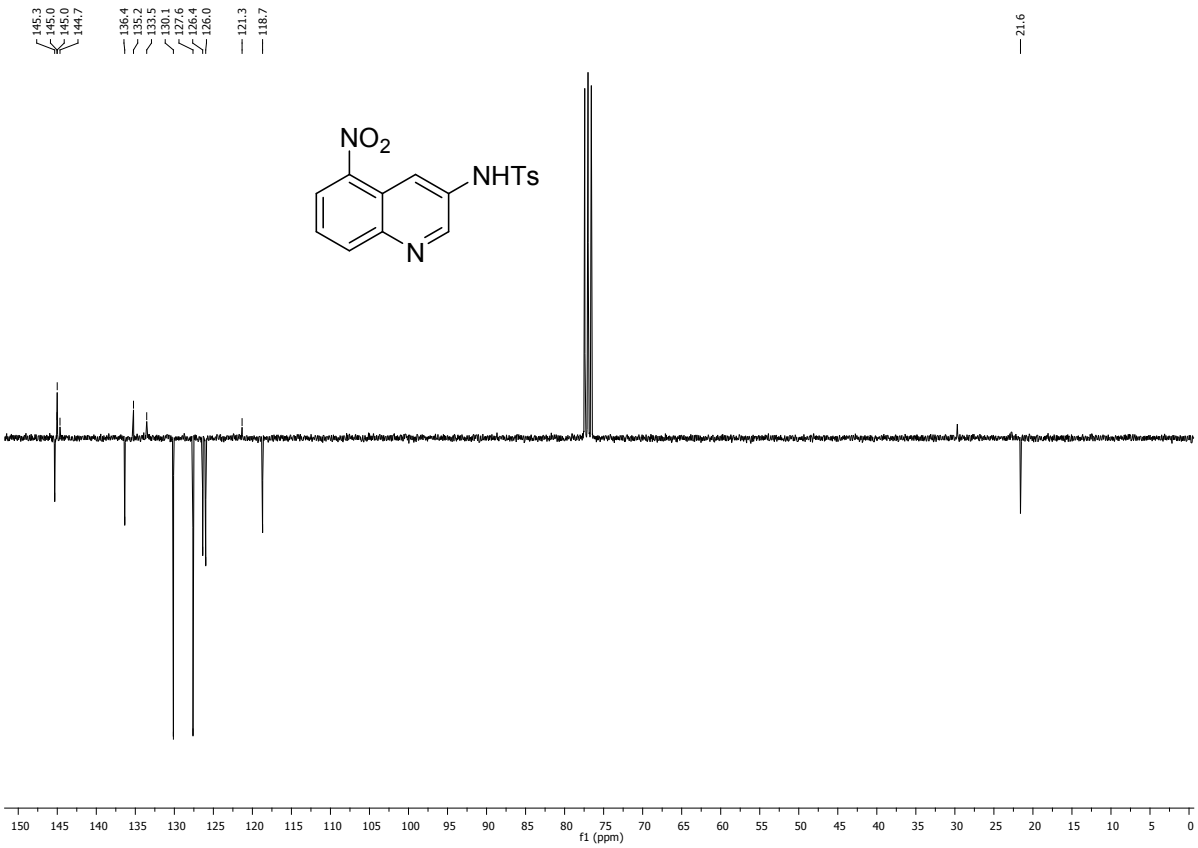
Compound **1g**: ^{13}C NMR



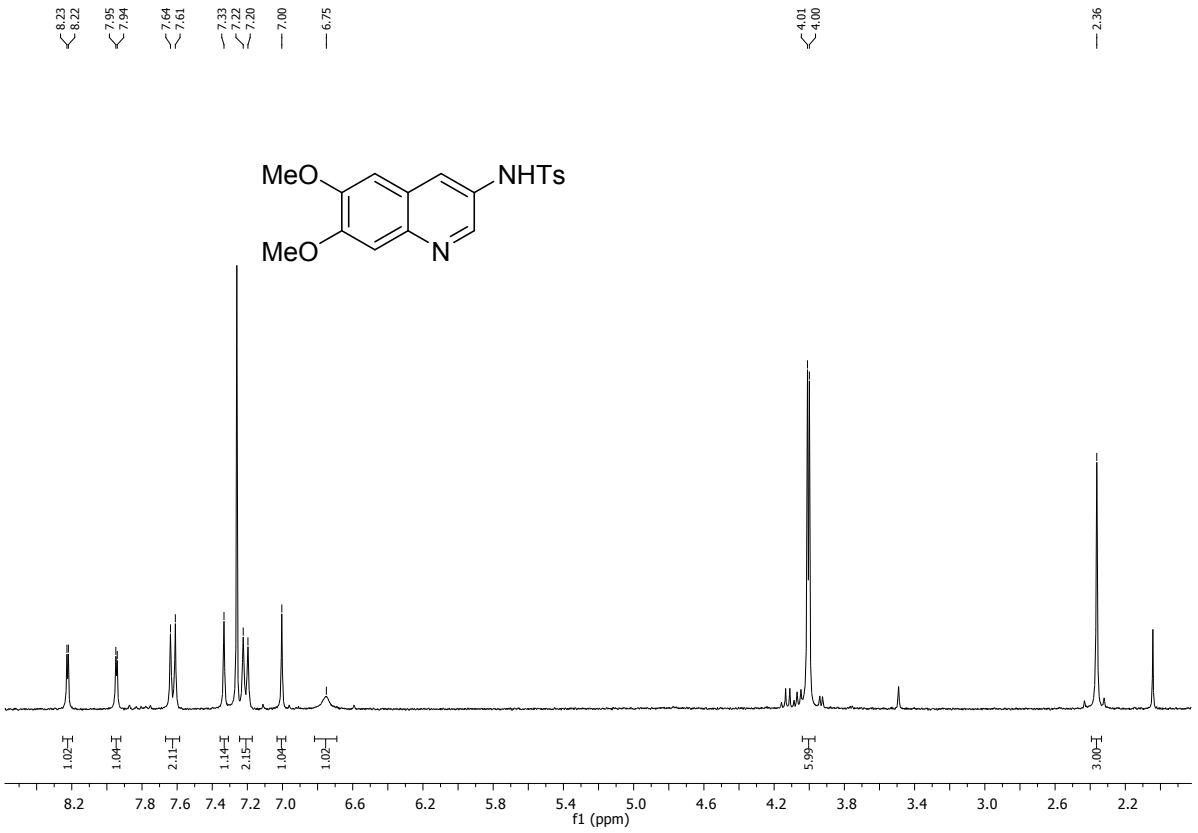
Compound **1h**: ^{1}H NMR



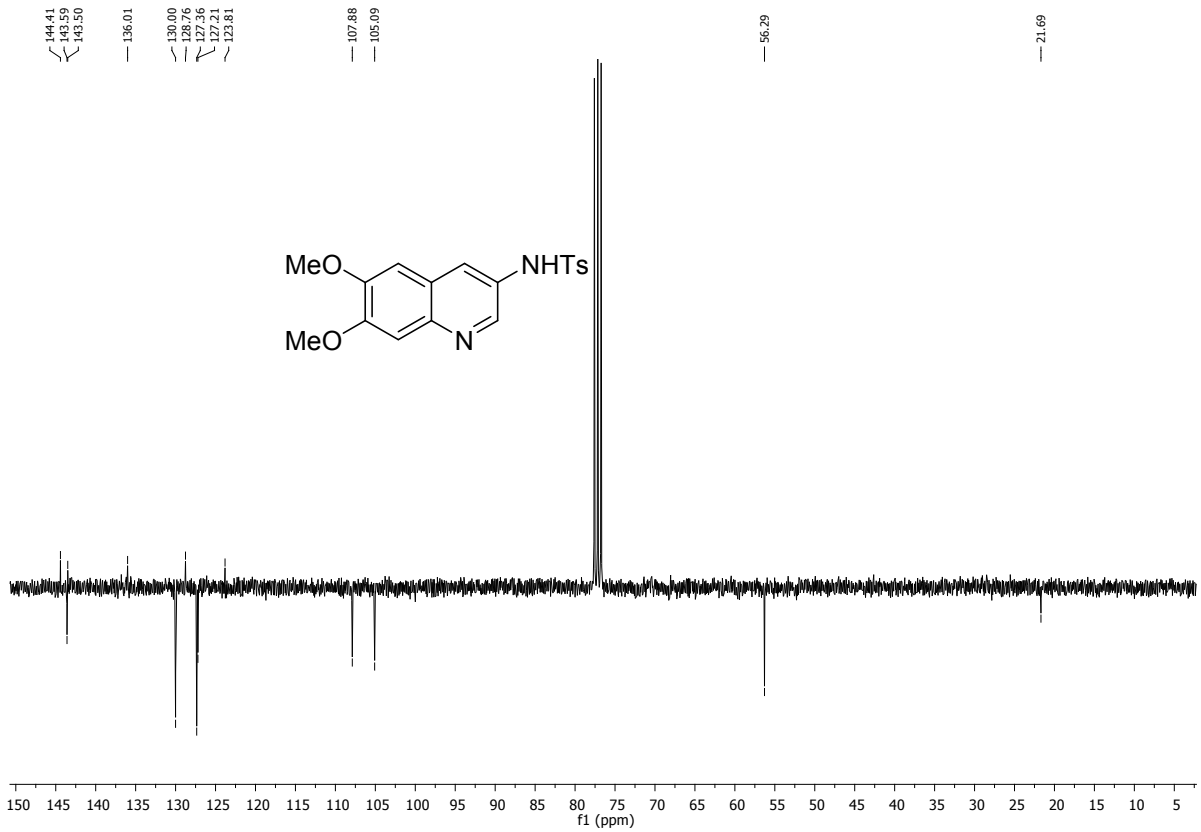
Compound **1h**: ^{13}C NMR



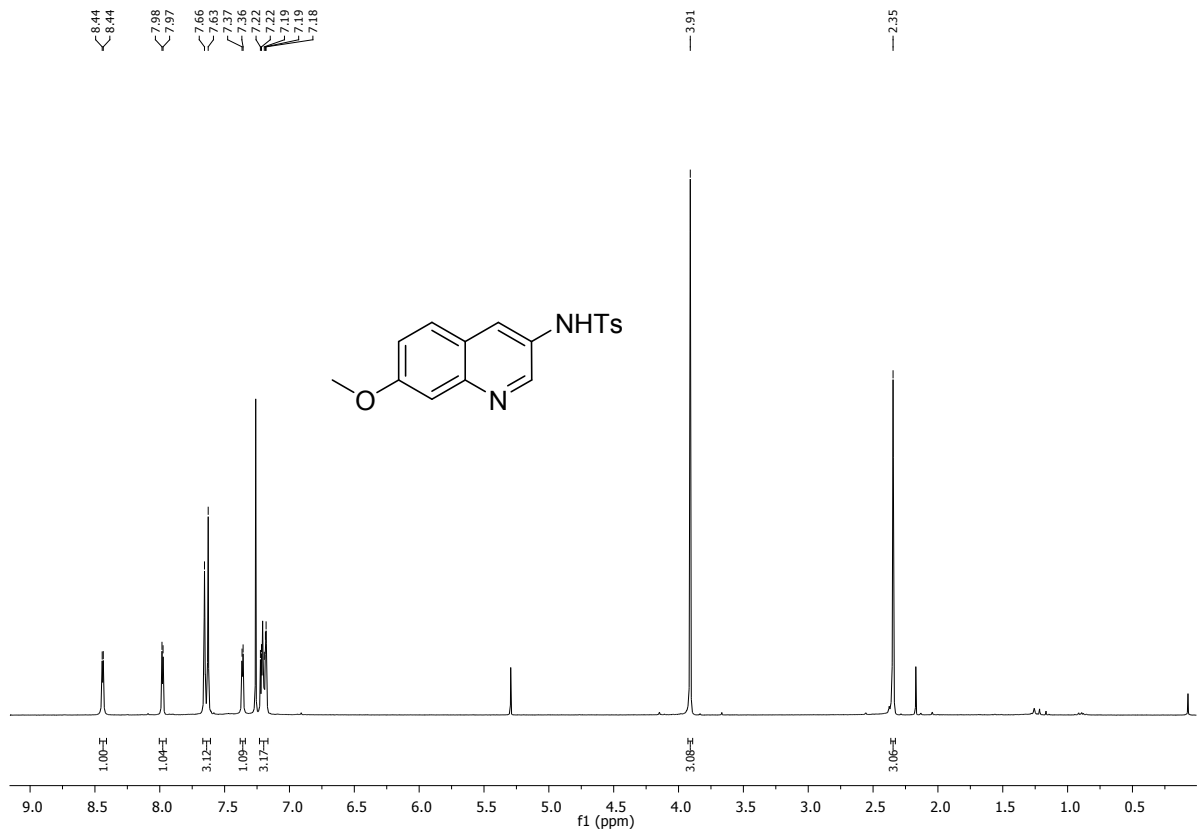
Compound **1i**: ^{1}H NMR



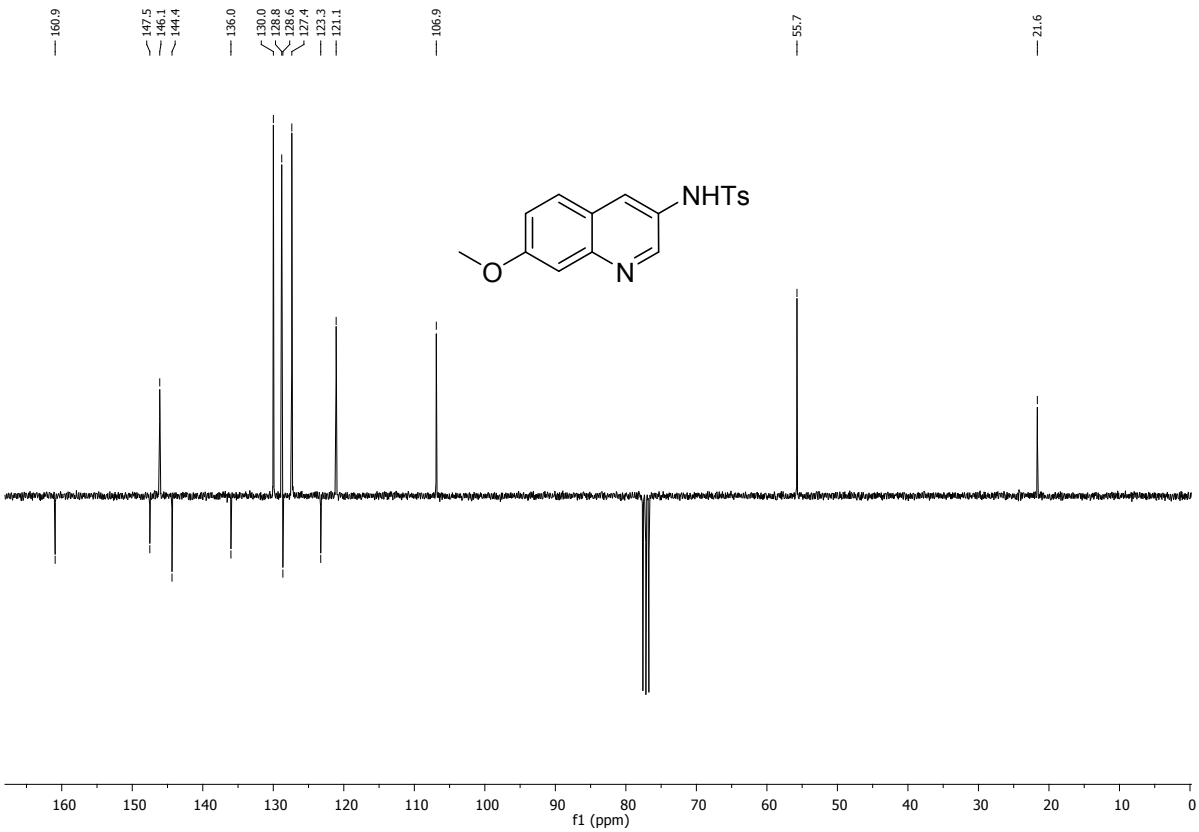
Compound **1i**: ^{13}C NMR



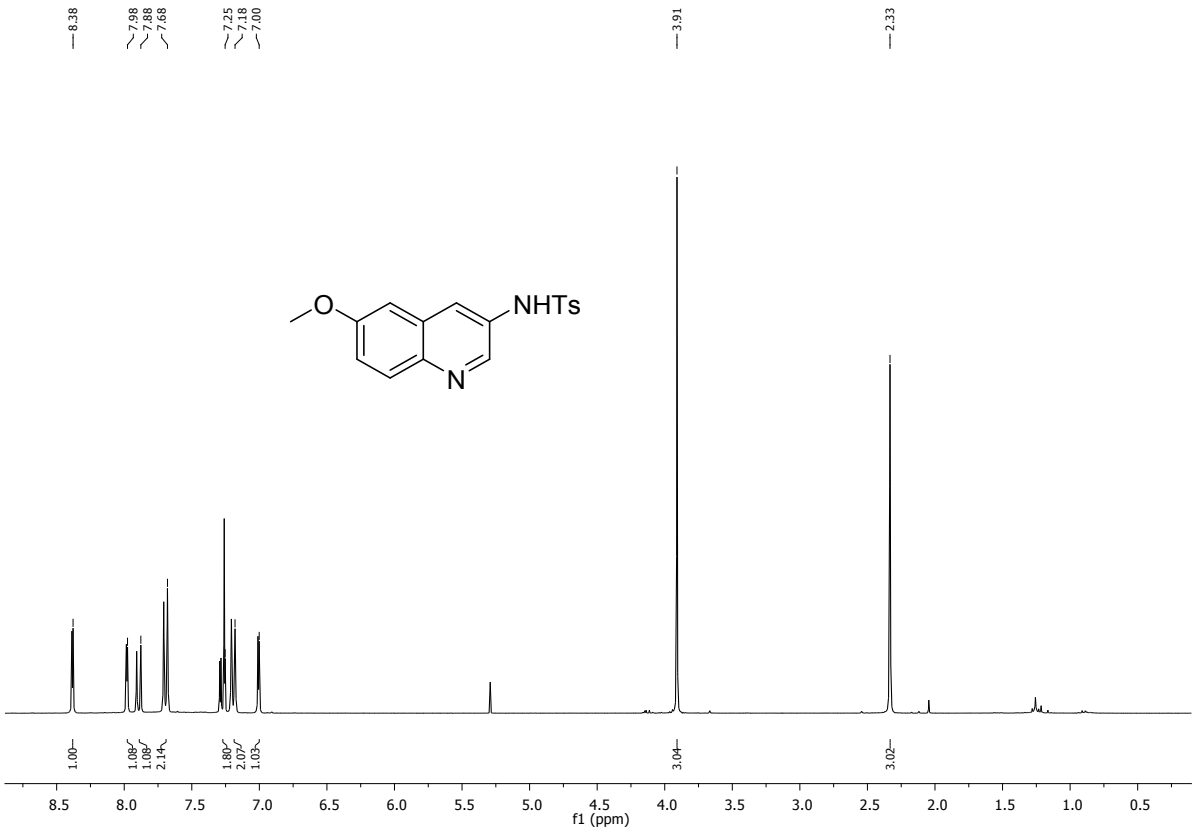
Compound **1j**: ^{1}H NMR



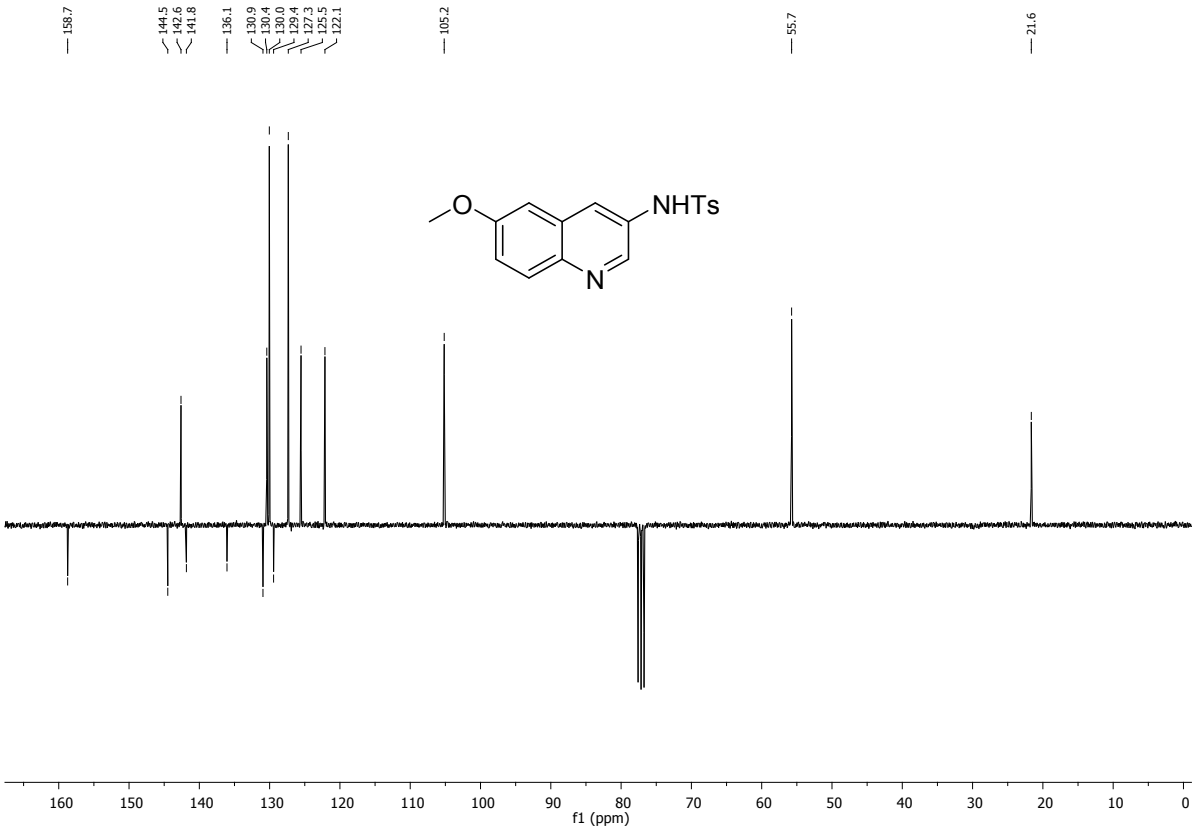
Compound **1j**: ^{13}C NMR



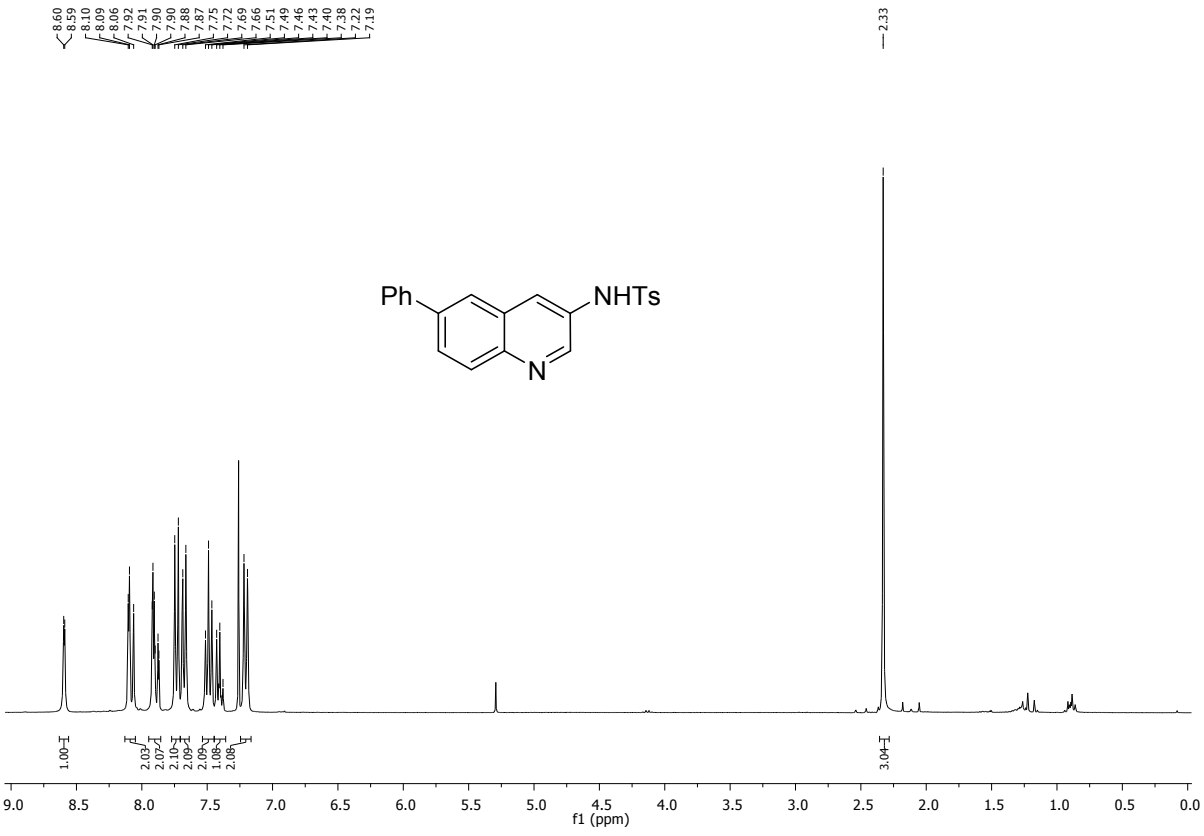
Compound **1k**: ^{1}H NMR



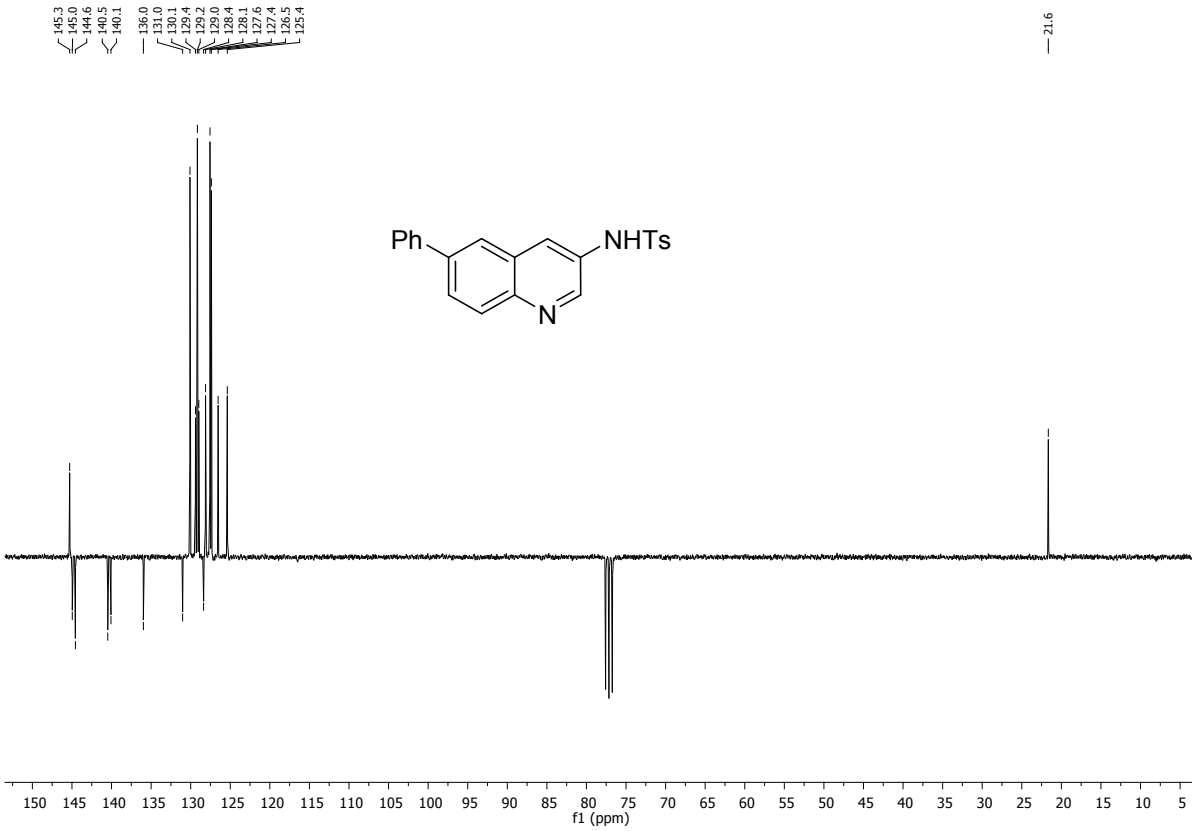
Compound **1k**: ^{13}C NMR



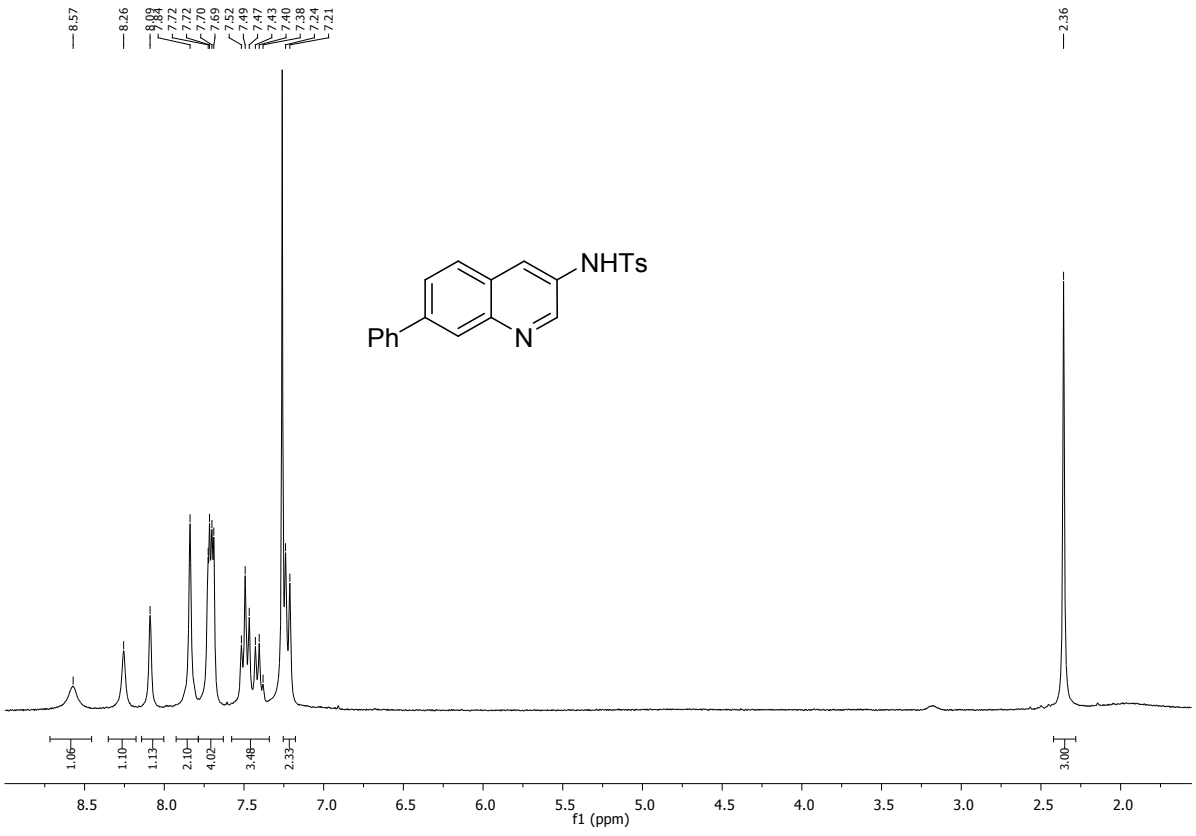
Compound **1l**: ^{1}H NMR



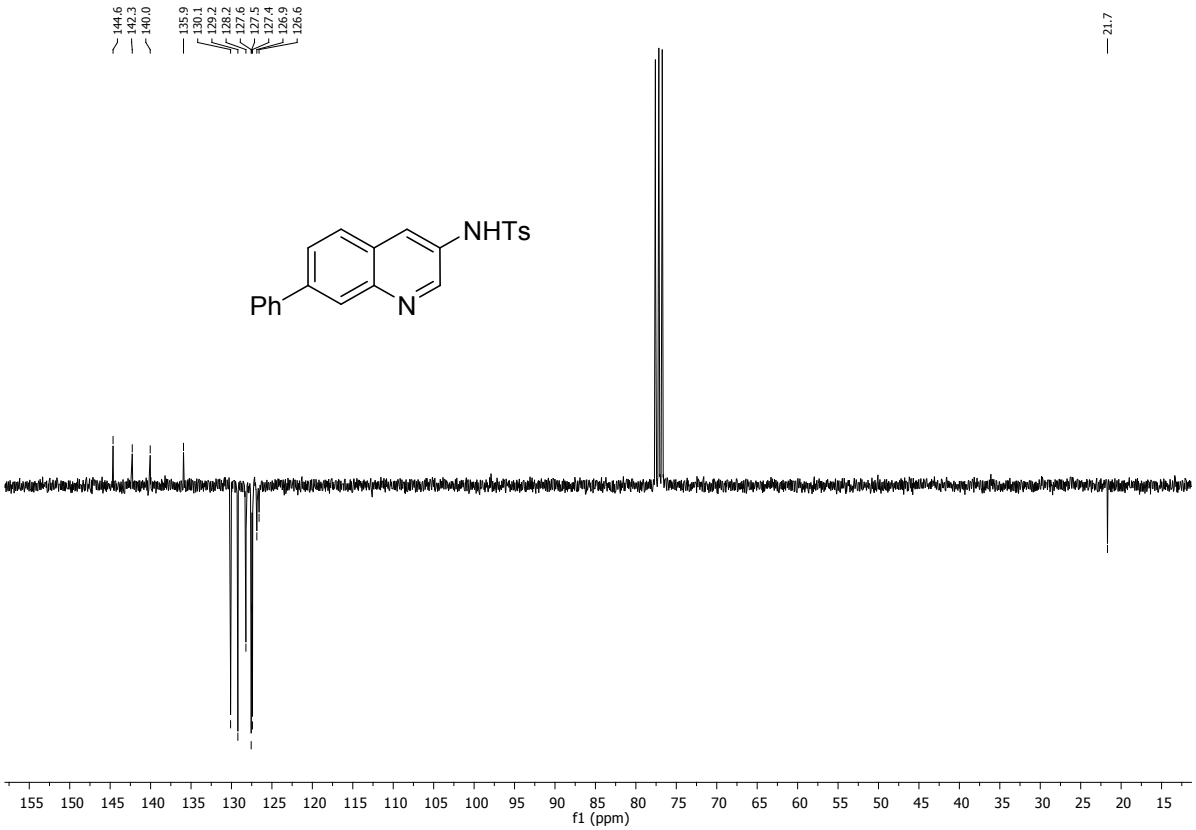
Compound **1l**: ^{13}C NMR



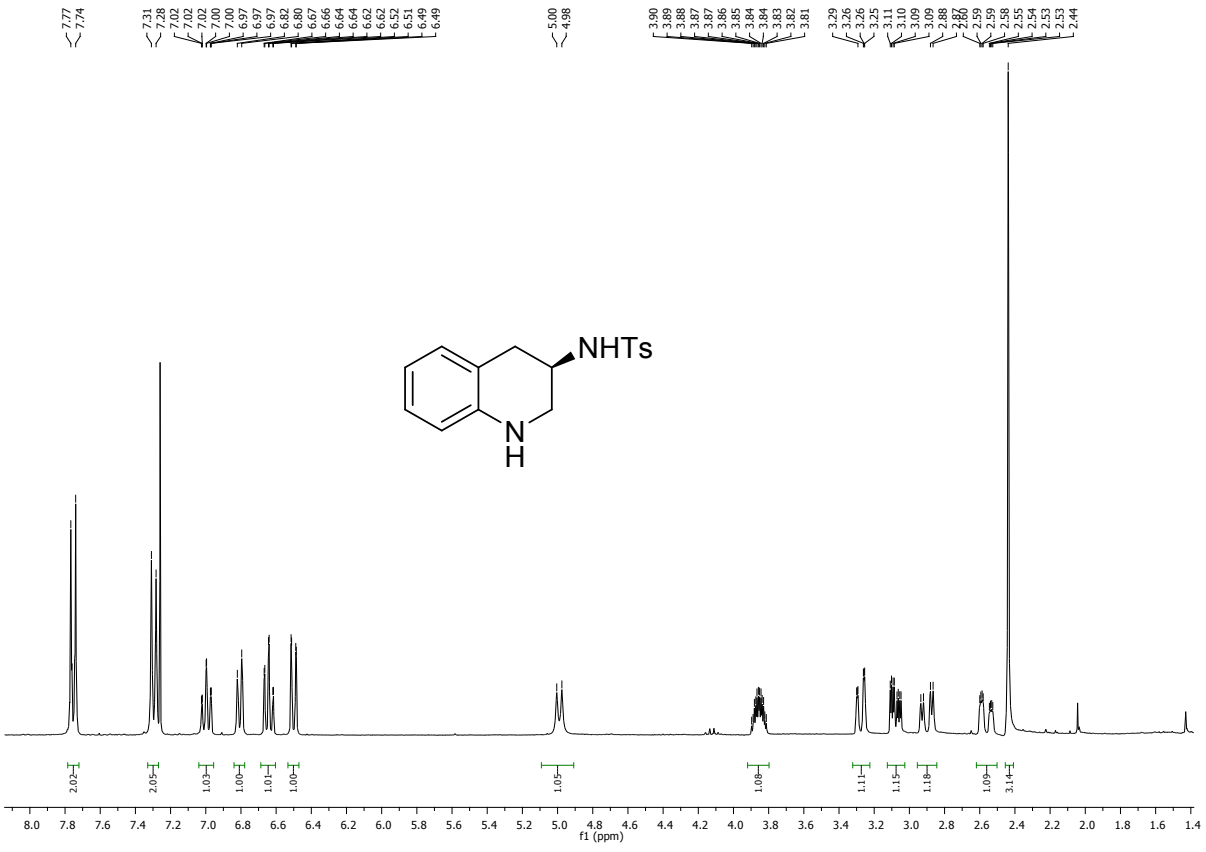
Compound **1m**: ^{1}H NMR



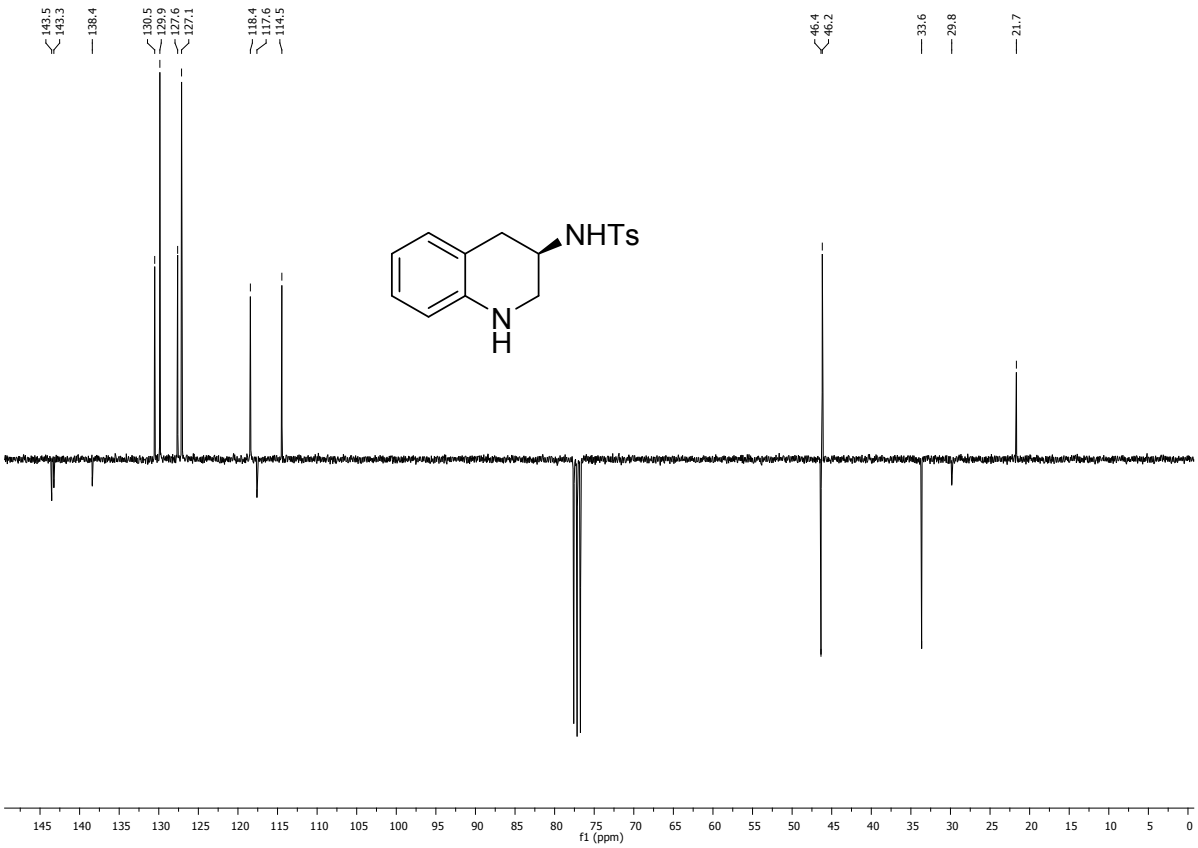
Compound **1m**: ^{13}C NMR



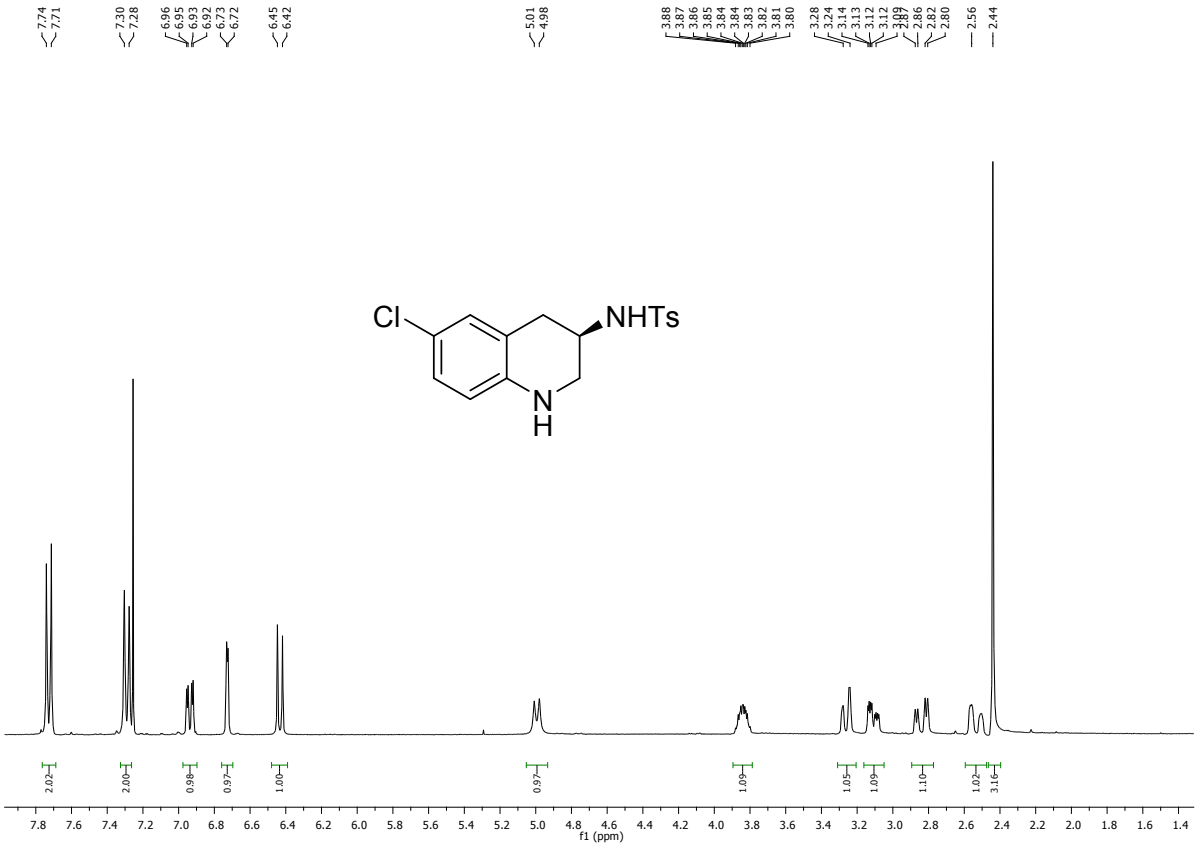
Compound **2a**: ^{1}H NMR



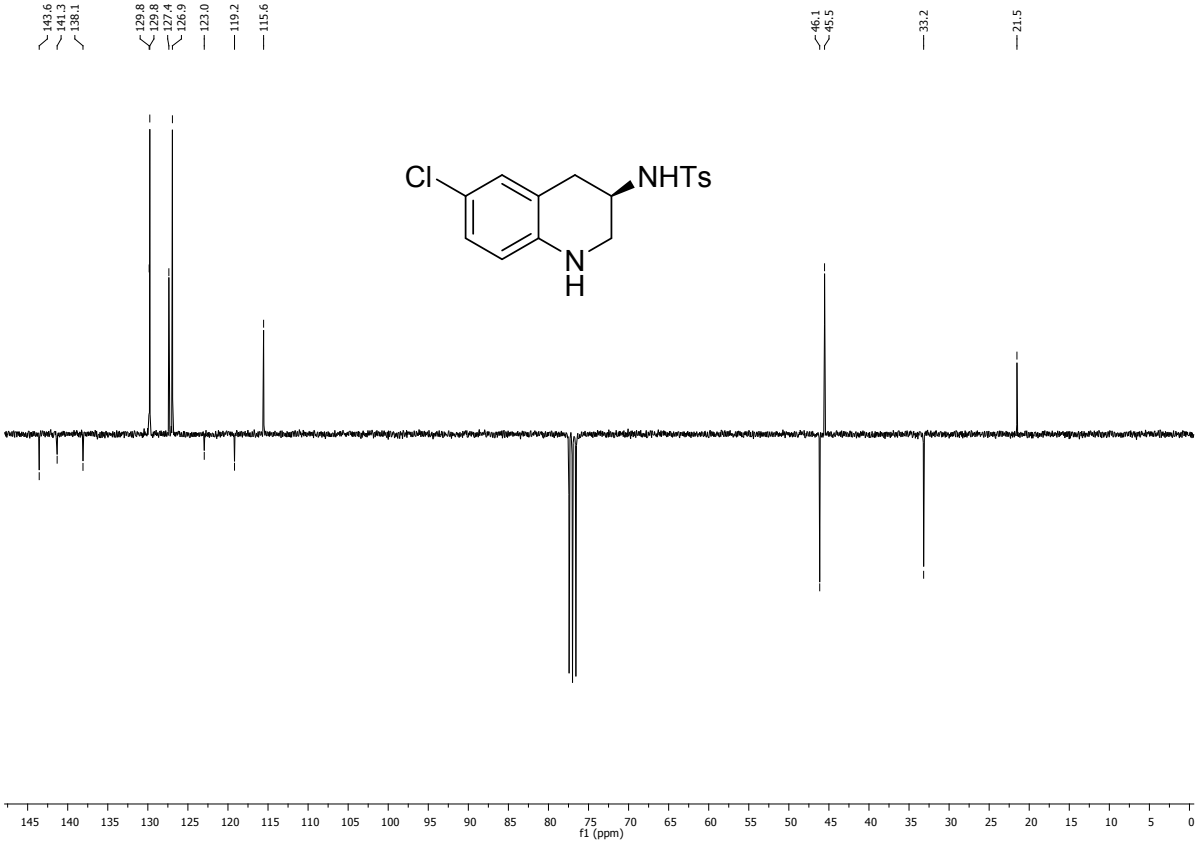
Compound **2a**: ^{13}C NMR



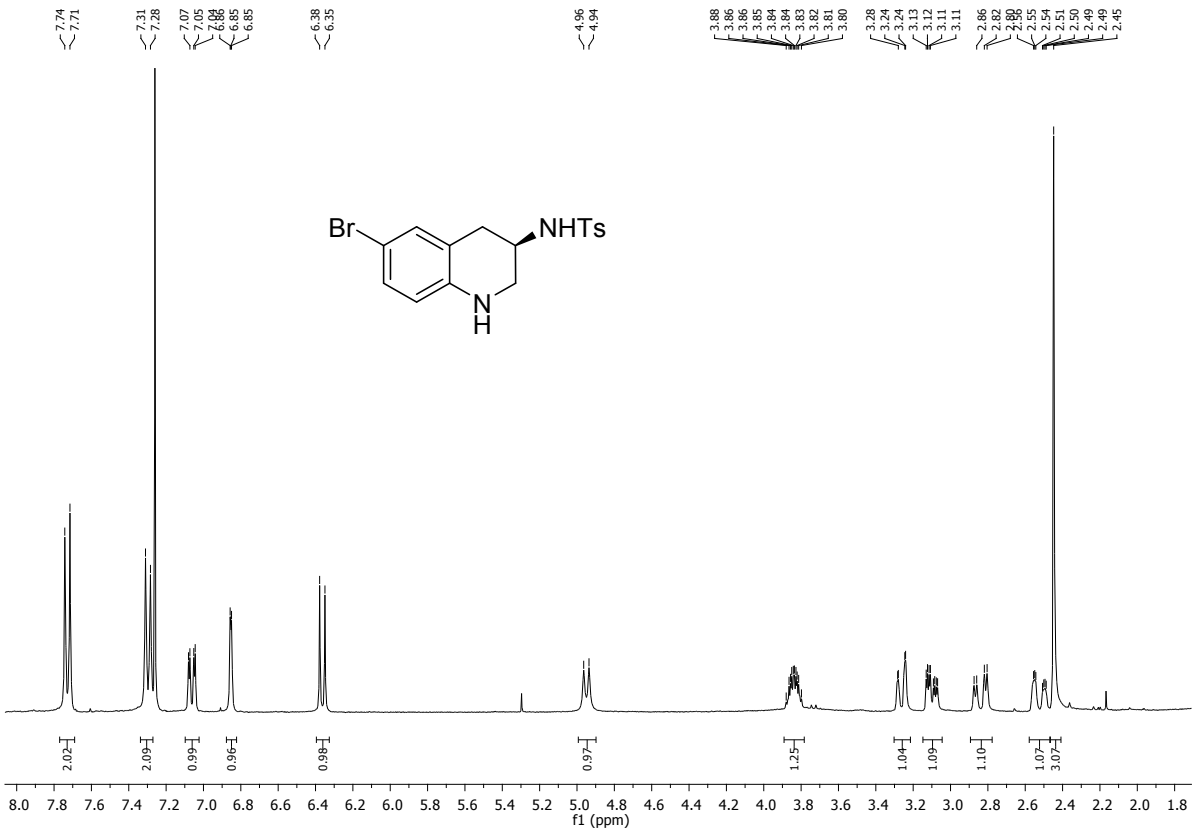
Compound **2d**: ^{1}H NMR



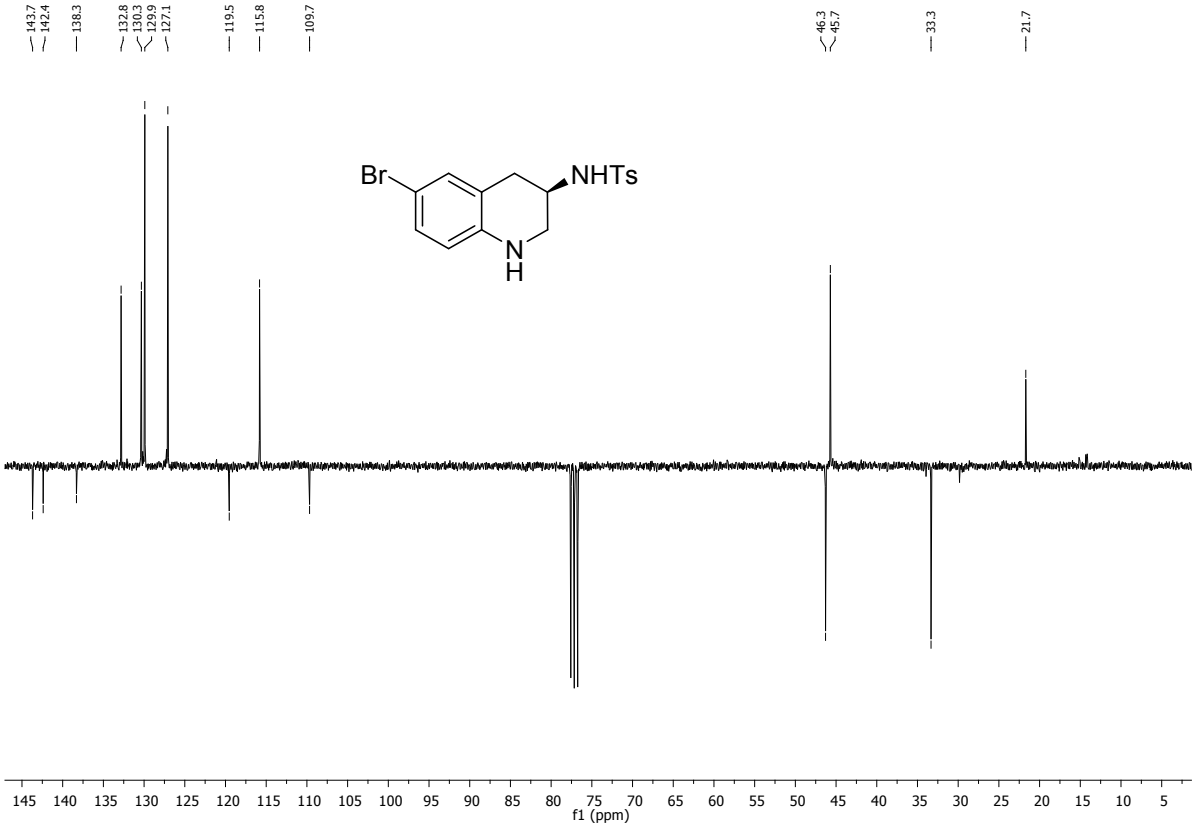
Compound **2d**: ^{13}C NMR



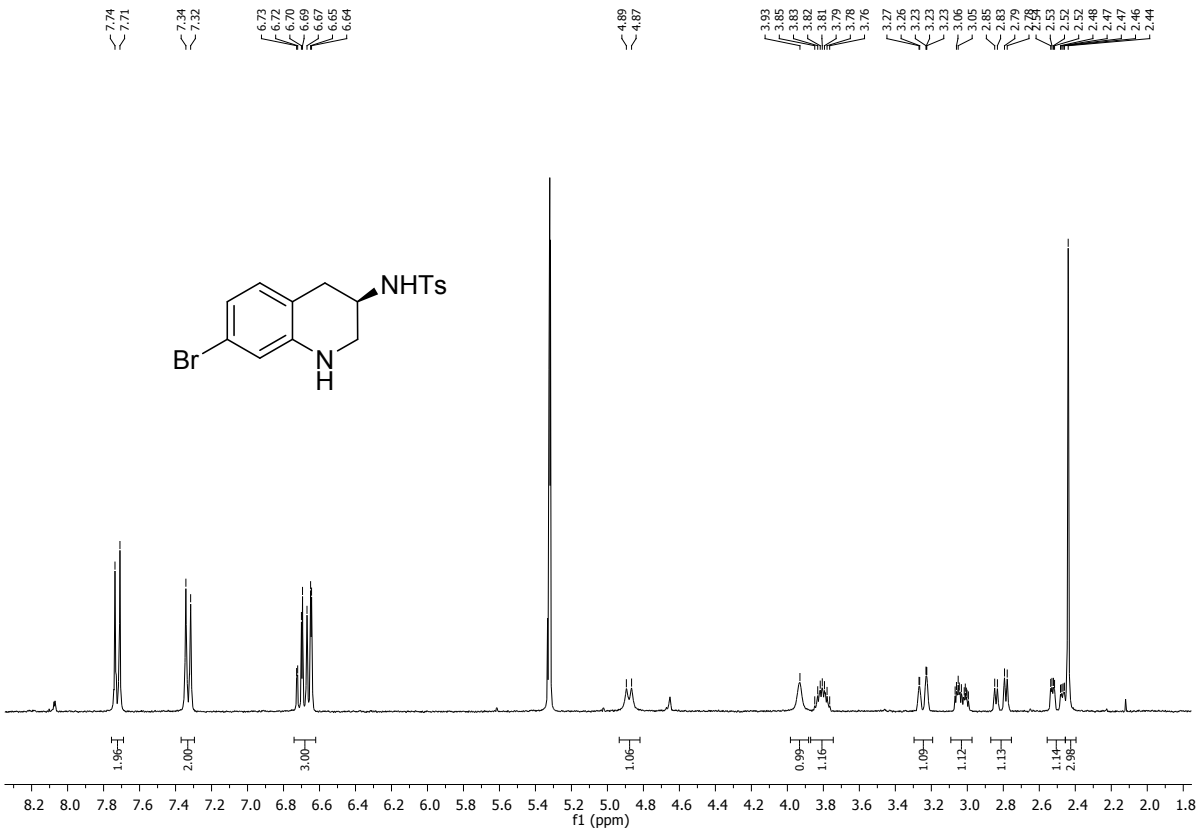
Compound **2e**: ^{1}H NMR



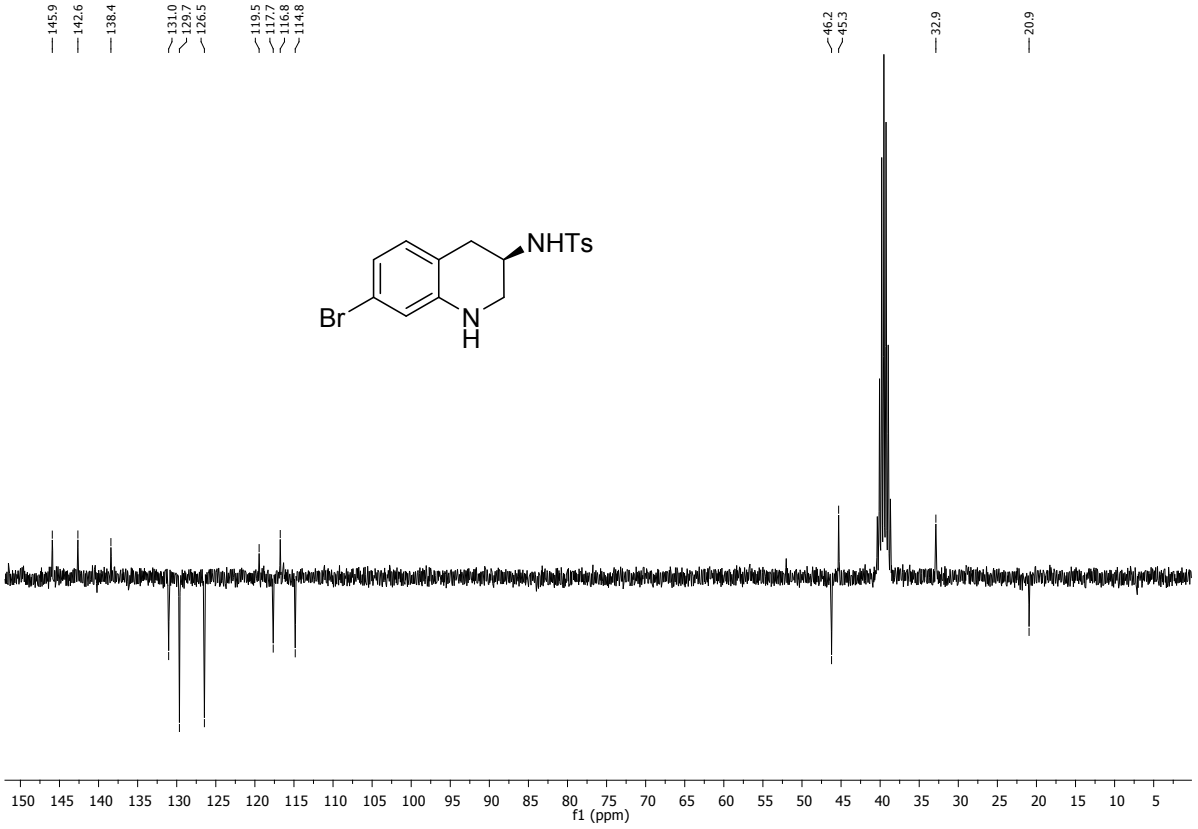
Compound **2e**: ^{13}C NMR



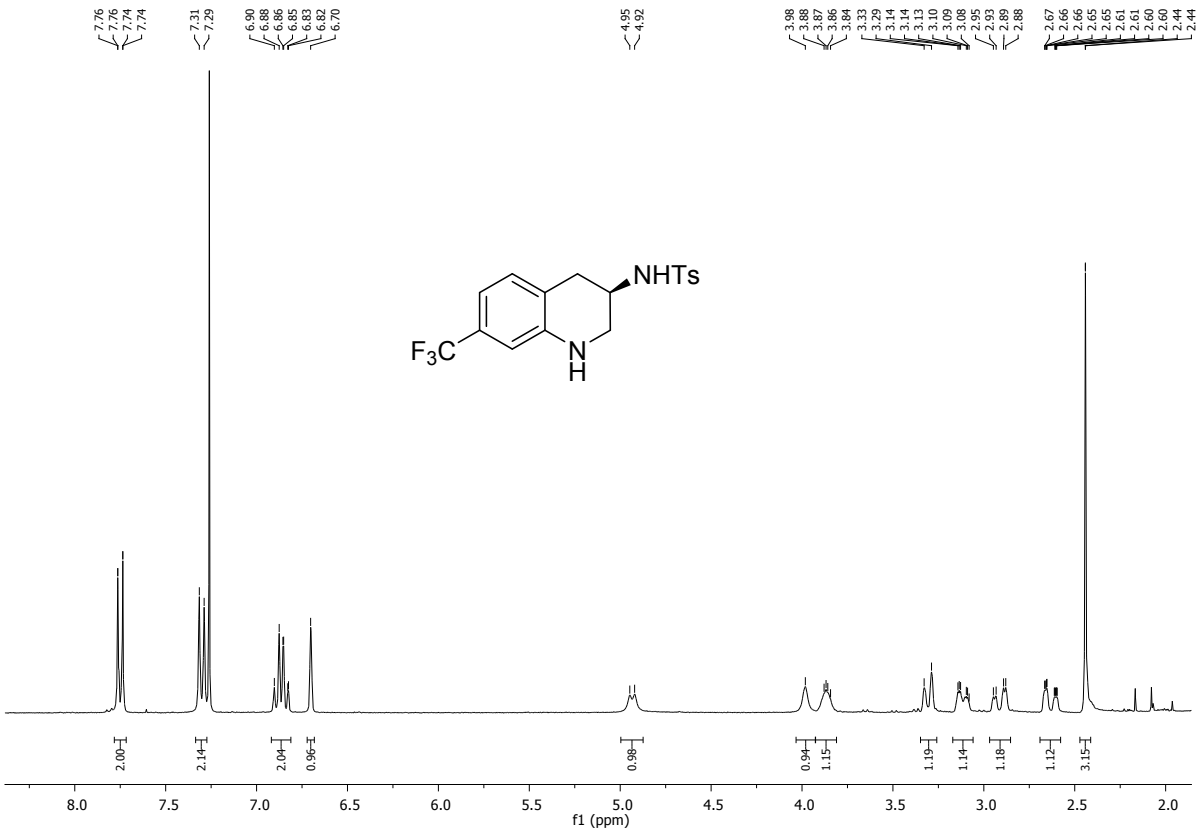
Compound **2f**: ^{1}H NMR



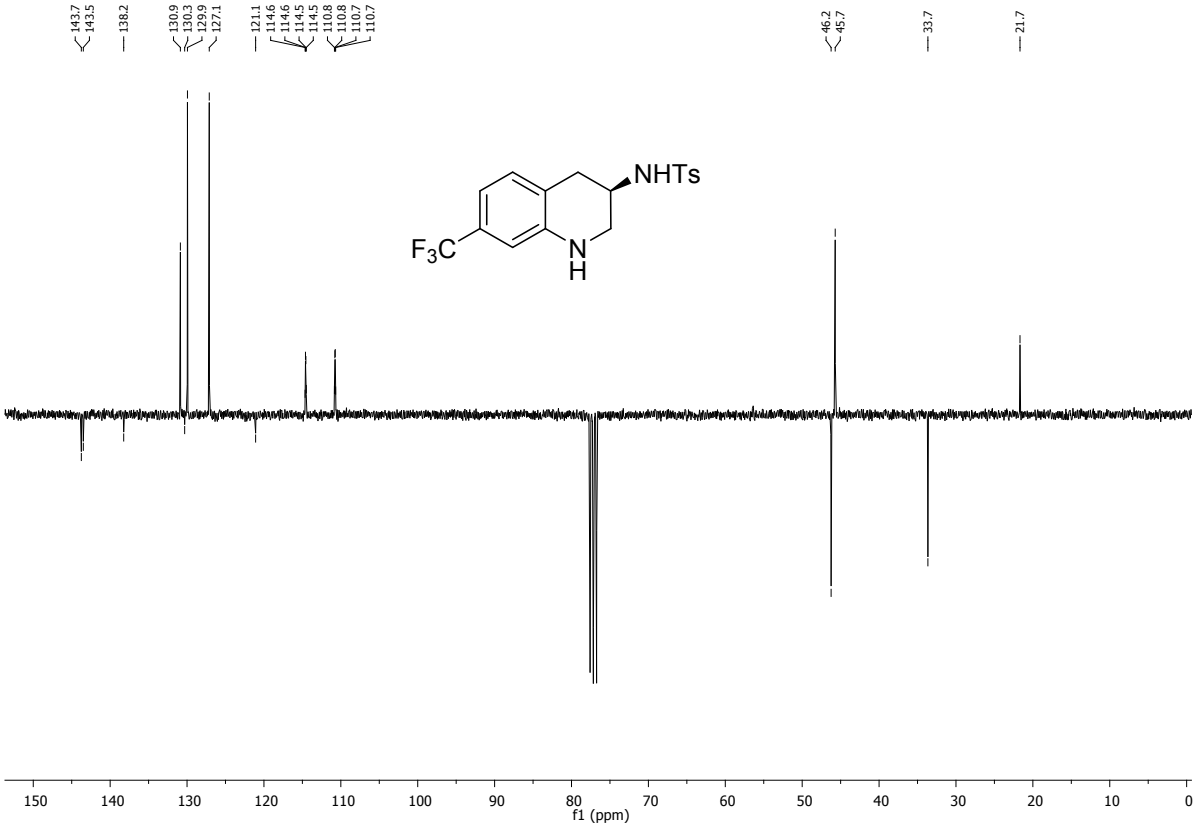
Compound **2f**: ^{13}C NMR



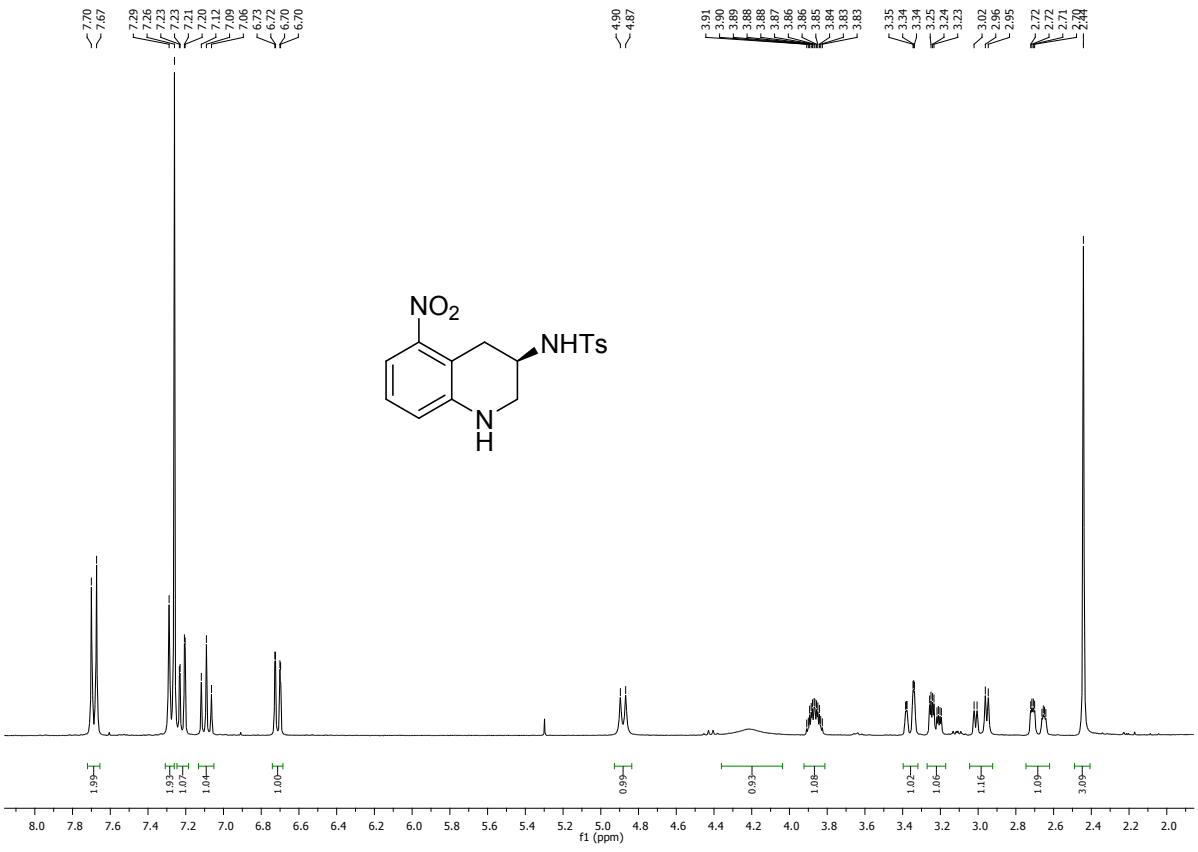
Compound **2g**: ^{1}H NMR



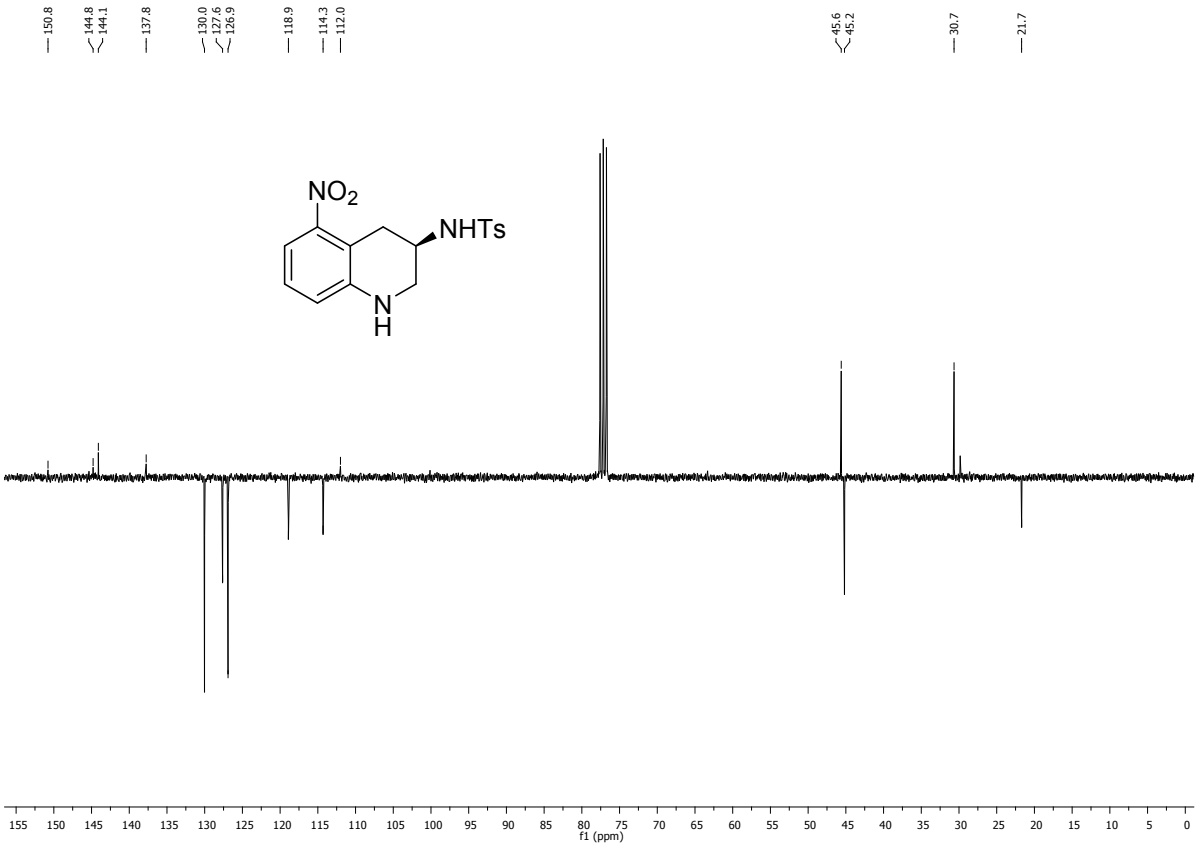
Compound **2g**: ^{13}C NMR



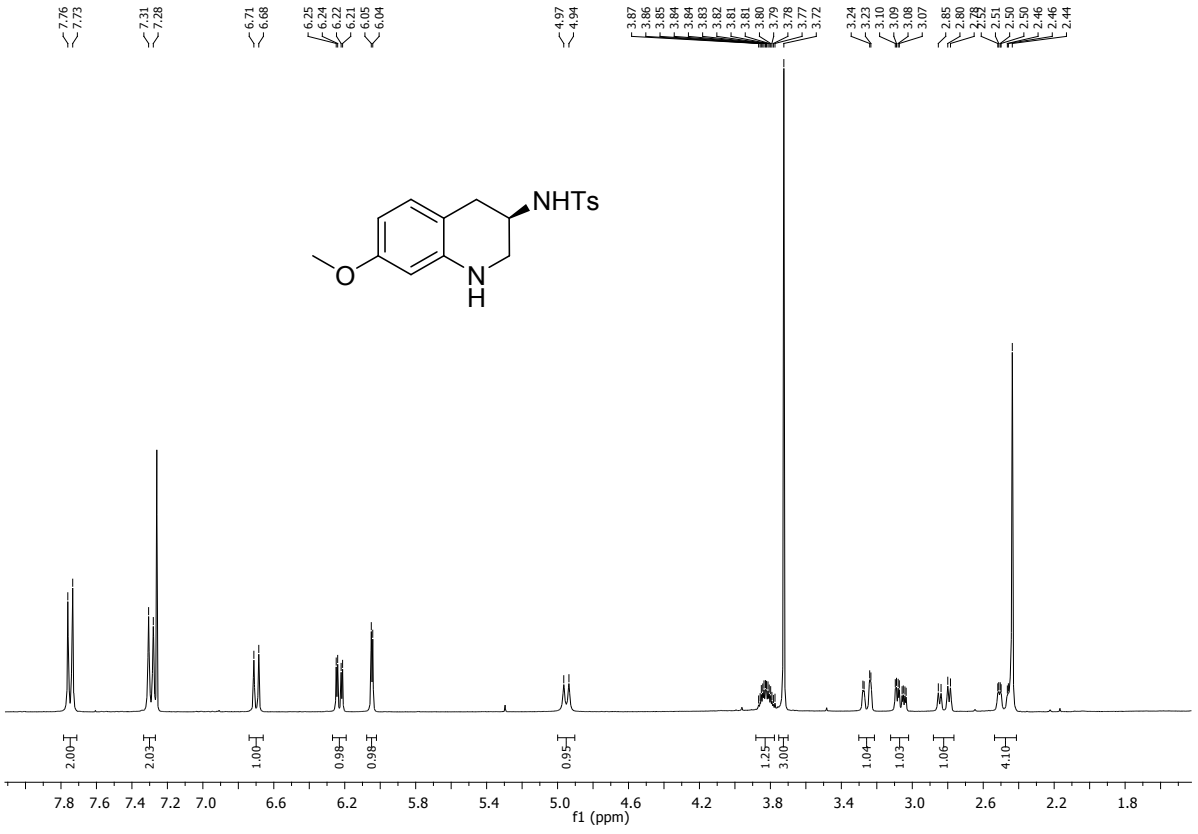
Compound **2h**: ^{1}H NMR



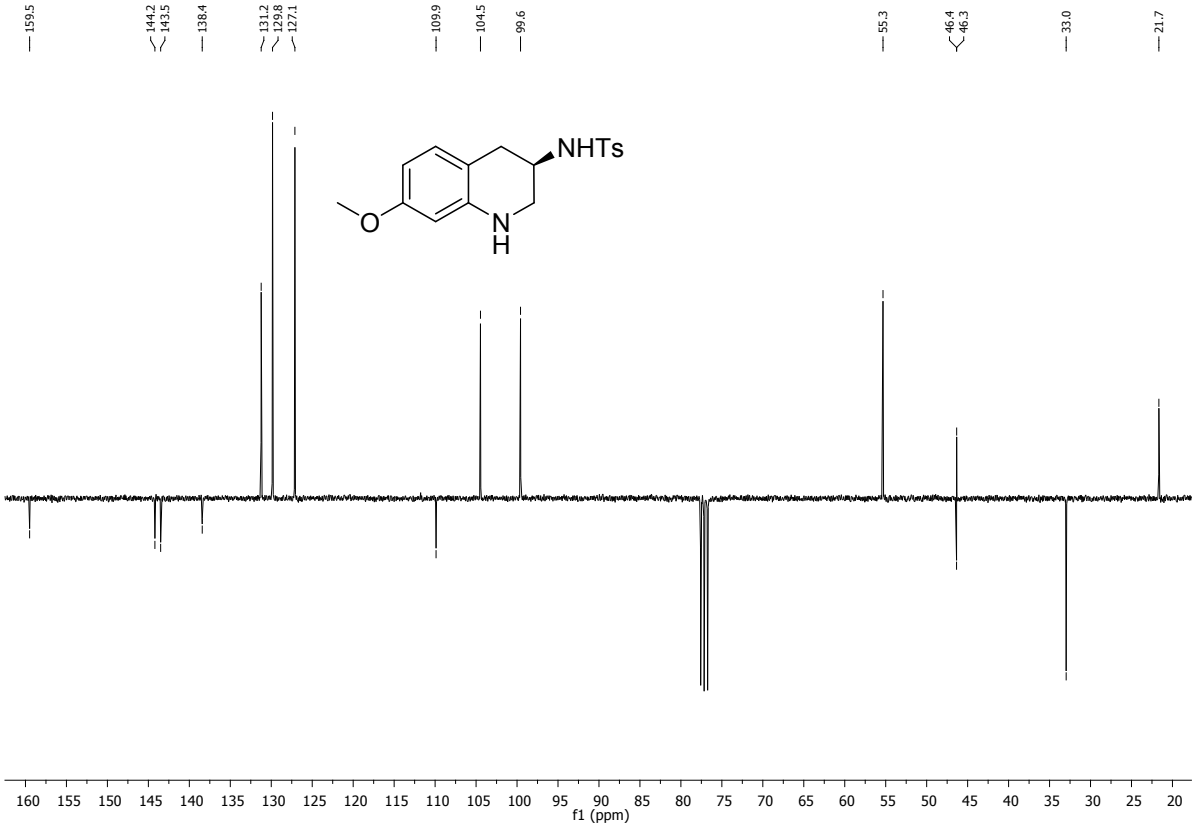
Compound **2h**: ^{13}C NMR



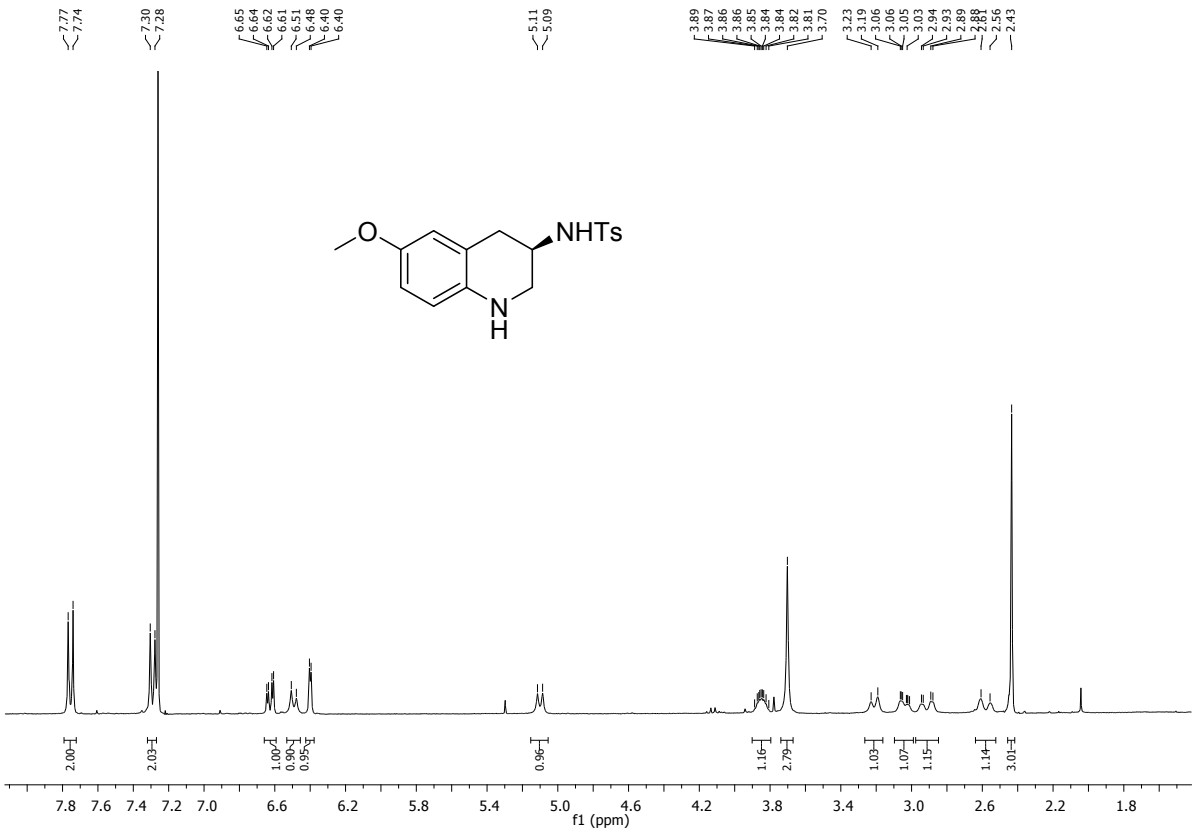
Compound **2j**: ^{1}H NMR



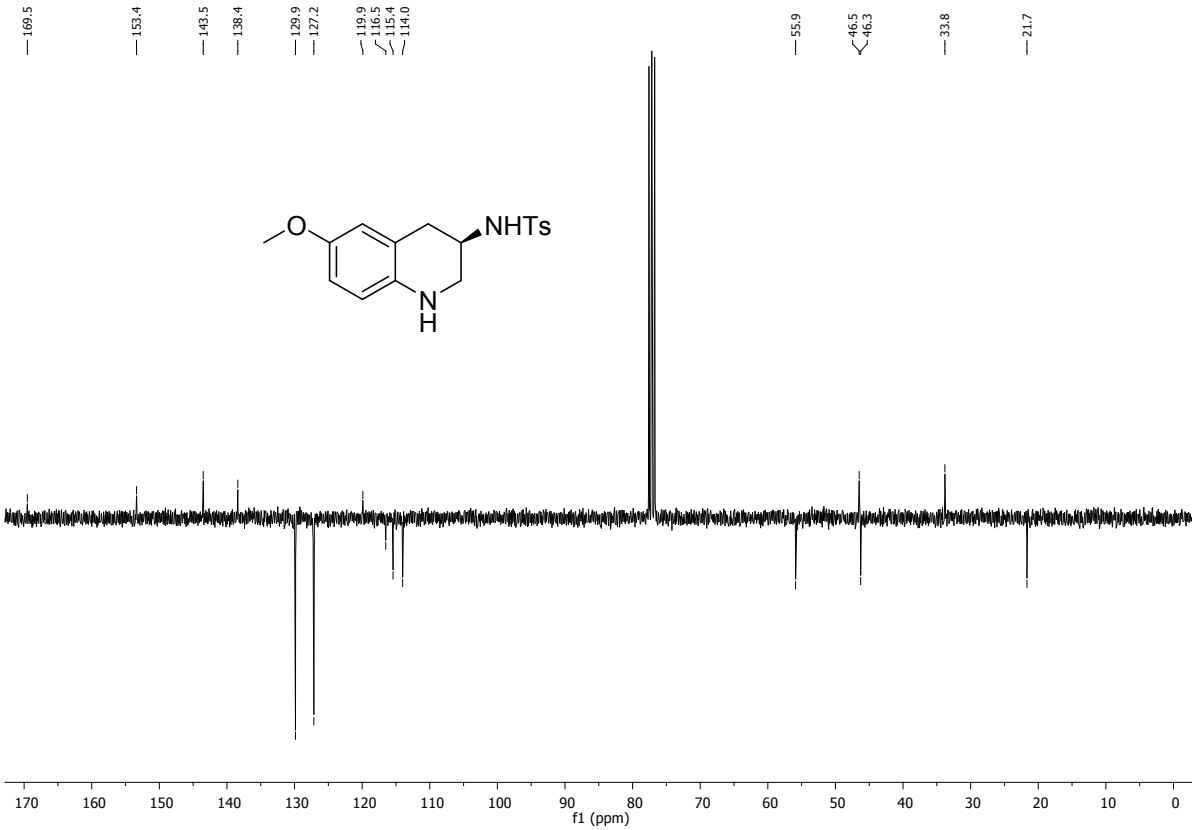
Compound **2j**: ^{13}C NMR



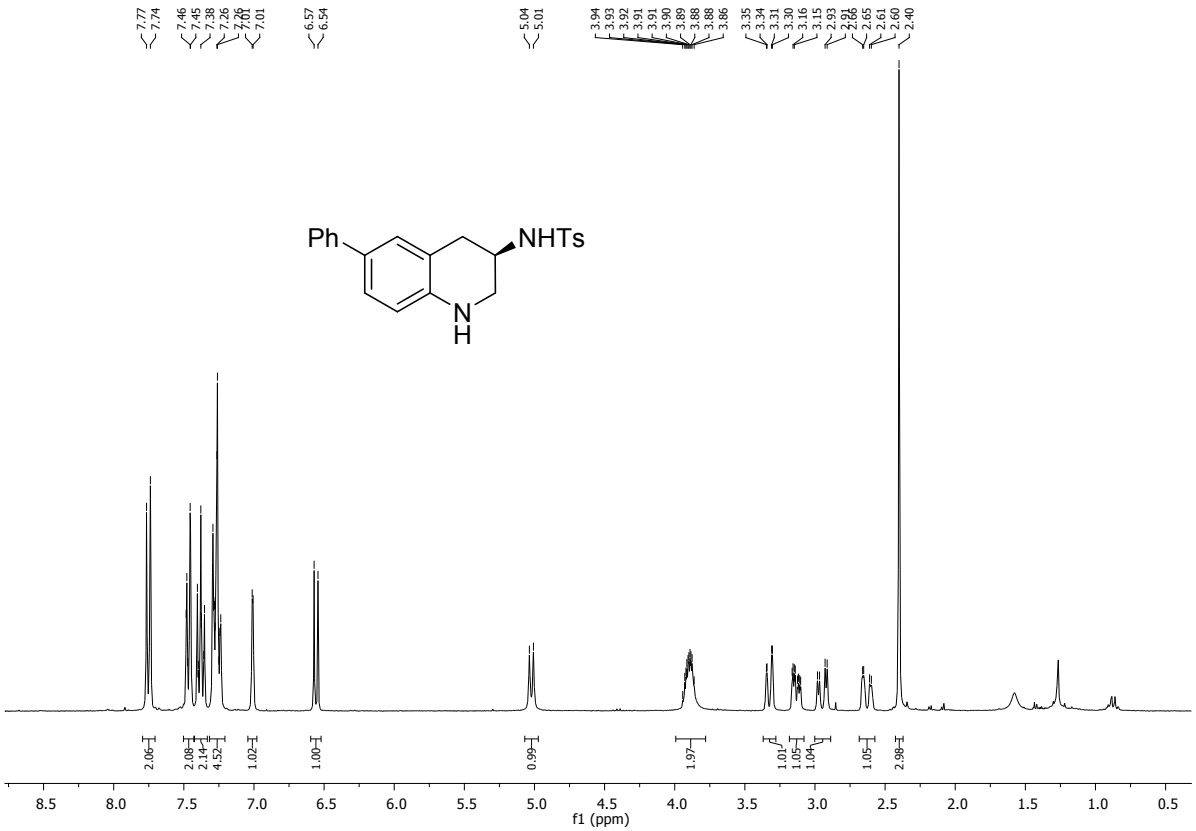
Compound **2k**: ^{1}H NMR



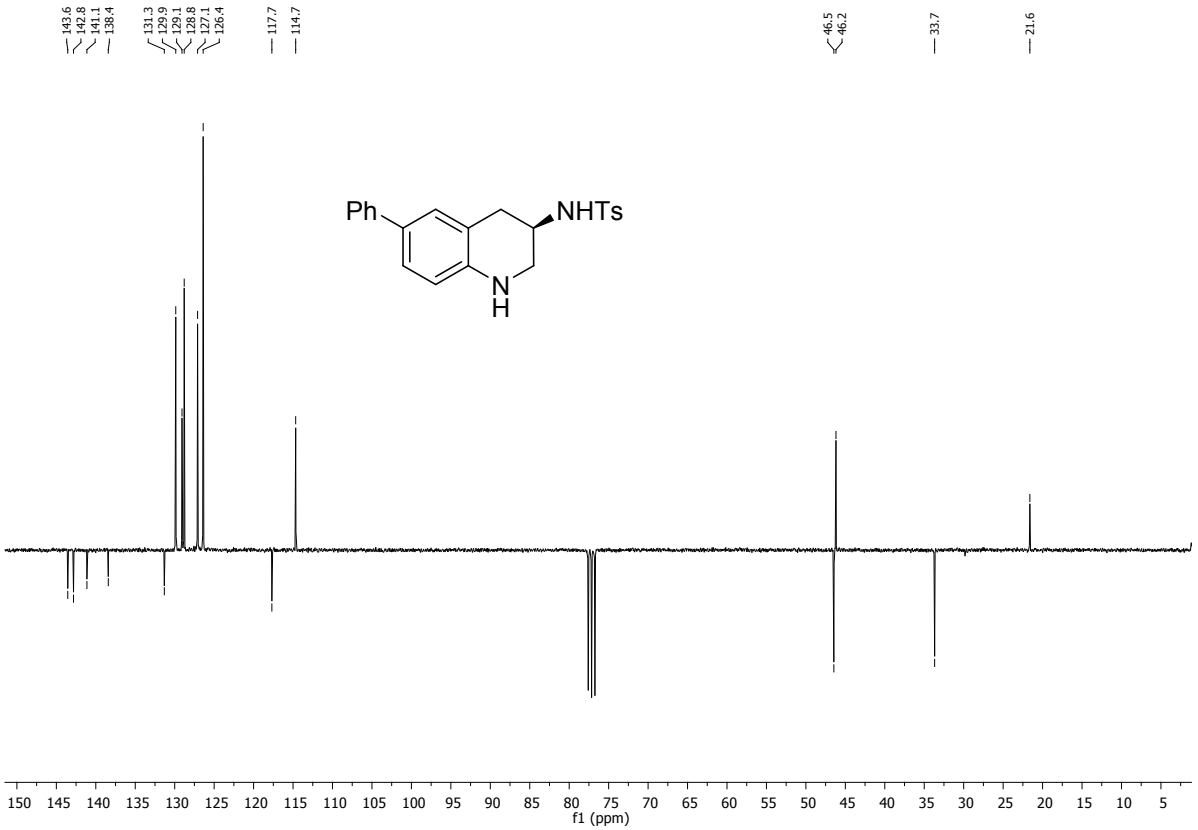
Compound **2k**: ^{13}C NMR



Compound **2m**: ^{1}H NMR

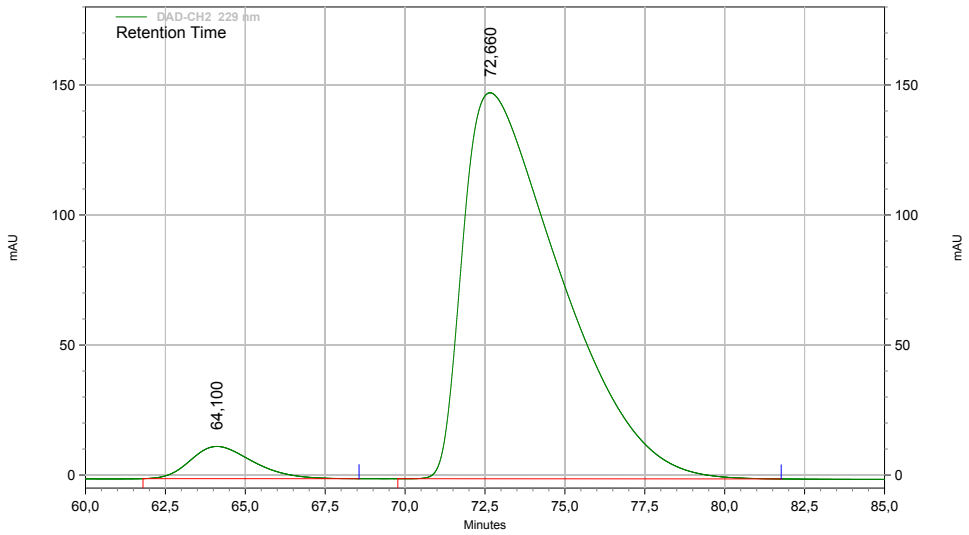


Compound **2m**: ^{13}C NMR


143.6
142.8
141.1
138.4
131.3
129.9
129.1
128.8
127.1
126.4
117.7
114.7
46.5
46.2
33.7
21.6
Ph
NHTs
N
H
150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5
f1 (ppm)

Chiral HPLC

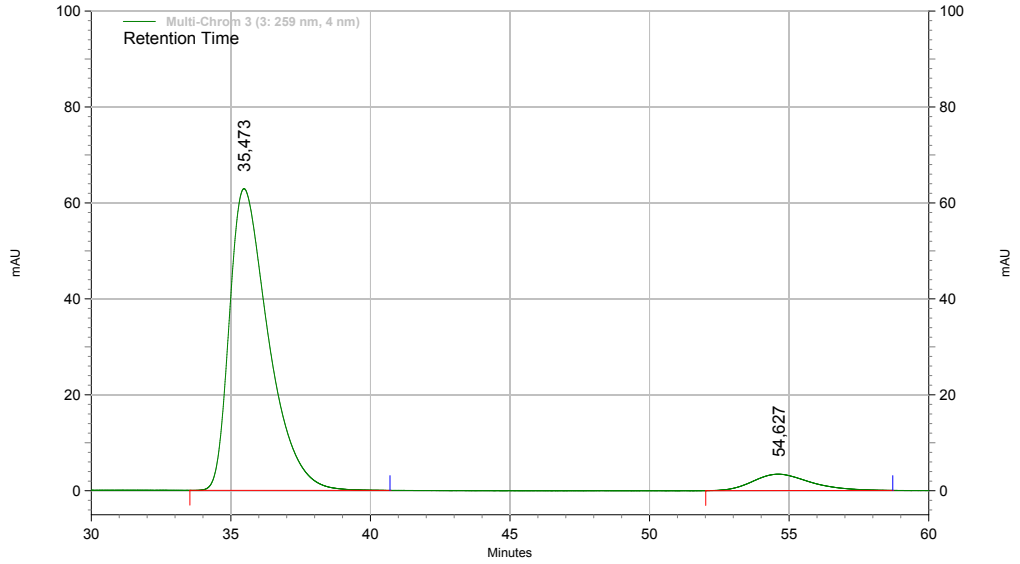
HPLC data compound **2a**: Chiralcel OJ-H, Hexane/iPrOH 70/30, 0.9 mL.min^{-1}, 20°C, 90% ee



229 nm

Retention Time	Area	Area %	Height	Height %
64.100	6750531	5.10	49567	7.71
72.660	125557631	94.90	593696	92.29
Totals	132308162	100.00	643263	100.00

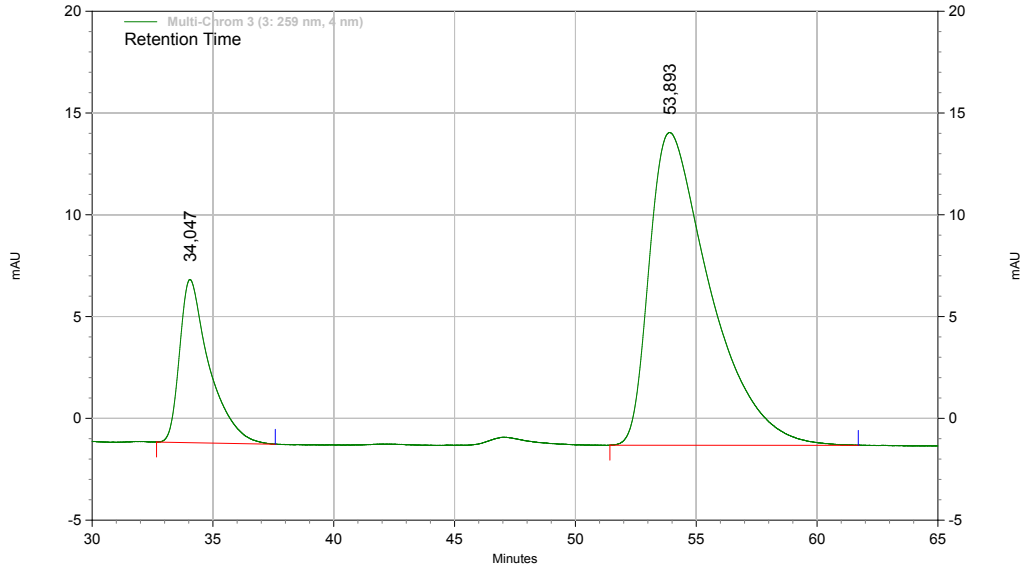
HPLC data compound **2d**: Chiralcel OJ-H, Hexane/iPrOH 70/30, 0.9 mL.min^{-1}, 20°C, 85% ee



259 nm

Retention Time	Area	Area %	Height	Height %
35.473	24402306	92.60	251577	94.84
54.627	1951144	7.40	13676	5.16
Totals	26353450	100.00	265253	100.00

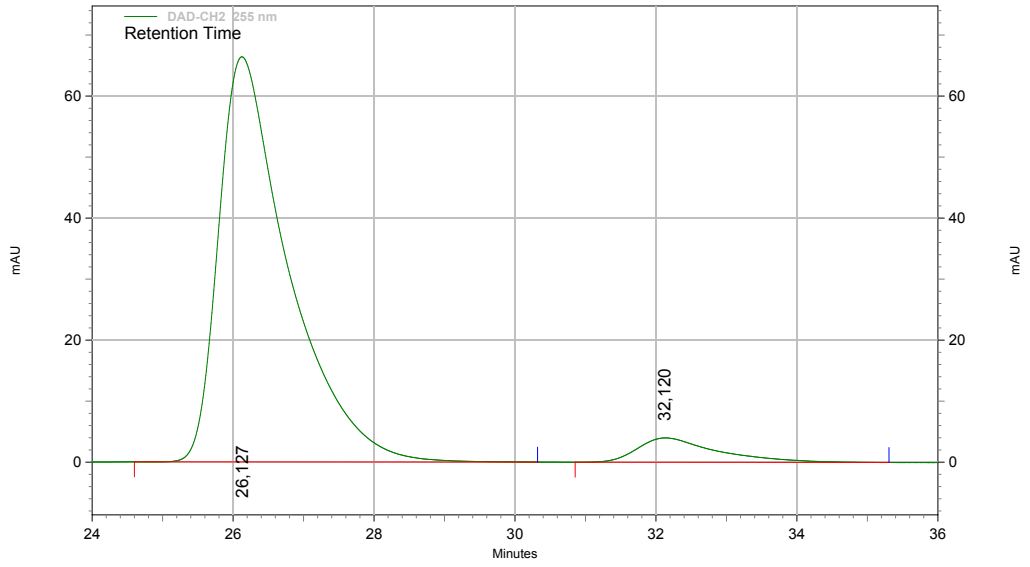
HPLC data compound **2e**: Chiralcel OD, Hexane/iPrOH 65/35, 0.3 mL.min^{-1}, 20°C, 60% ee



259 nm

Retention Time	Area	Area %	Height	Height %
34.047	2722866	20.21	32061	34.28
53.893	10749890	79.79	61456	65.72
Totals	13472756	100.00	93517	100.00

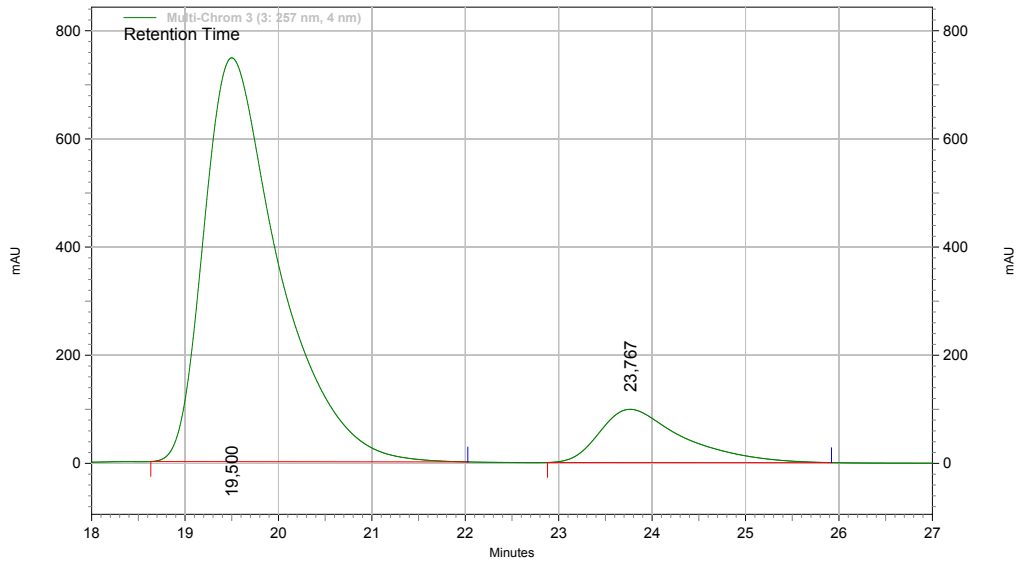
HPLC data compound **2f**: Chiralcel OD, Hexane/iPrOH 65/35, 0.3 mL.min^{-1}, 20°C, 87% ee



255 nm

Retention Time	Area	Area %	Height	Height %
26.127	18234993	93.60	265551	94.32
32.120	1246372	6.40	15993	5.68
Totals	19481365	100.00	281544	100.00

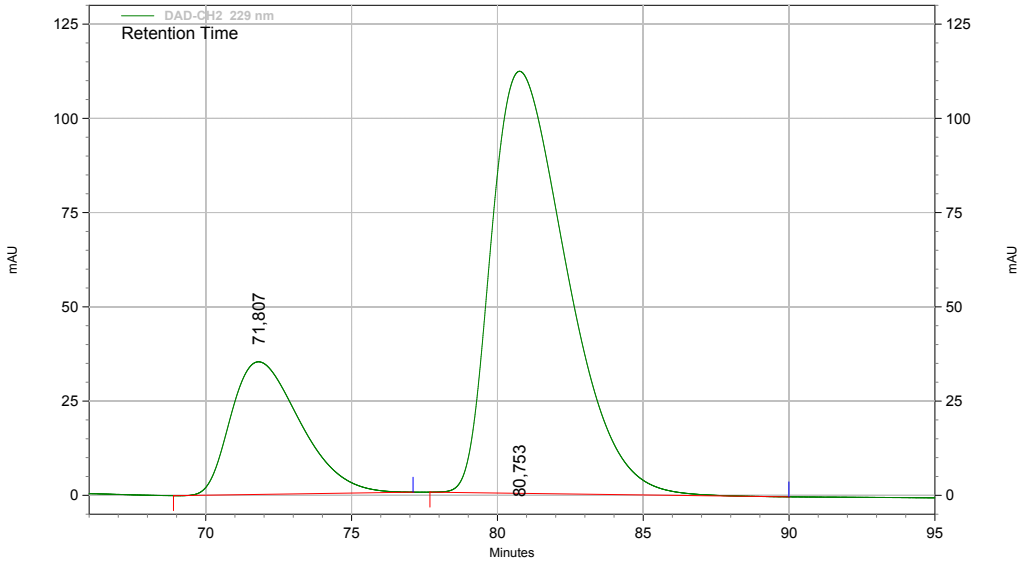
HPLC data compound **2g**: Chiralcel OD, Hexane/iPrOH 65/35, 0.3 mL.min^{-1}, 20°C, 75% ee



257 nm

Retention Time	Area	Area %	Height	Height %
19.500	166165048	87.27	2986966	88.35
23.767	24242067	12.73	393690	11.65
Totals	190407115	100.00	3380656	100.00

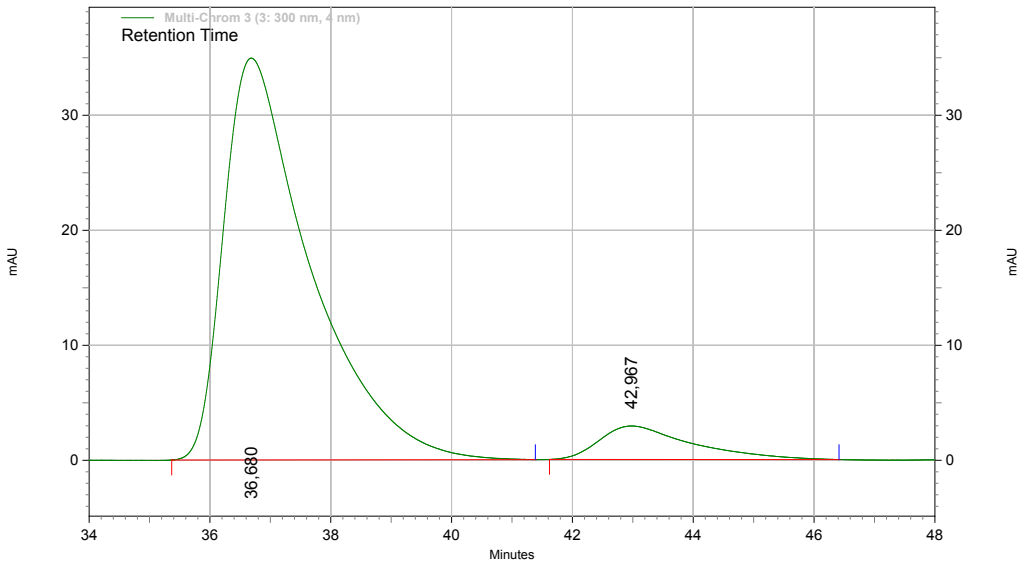
HPLC data compound **2h**: Chiralcel OJ-H, Hexane/iPrOH 70/30, 0.3 mL.min^{-1}, 20°C, 55% ee



229 nm

Retention Time	Area	Area %	Height	Height %
71.807	23222323	22.41	140735	23.91
80.753	80407380	77.59	447829	76.09
Totals	103629703	100.00	588564	100.00

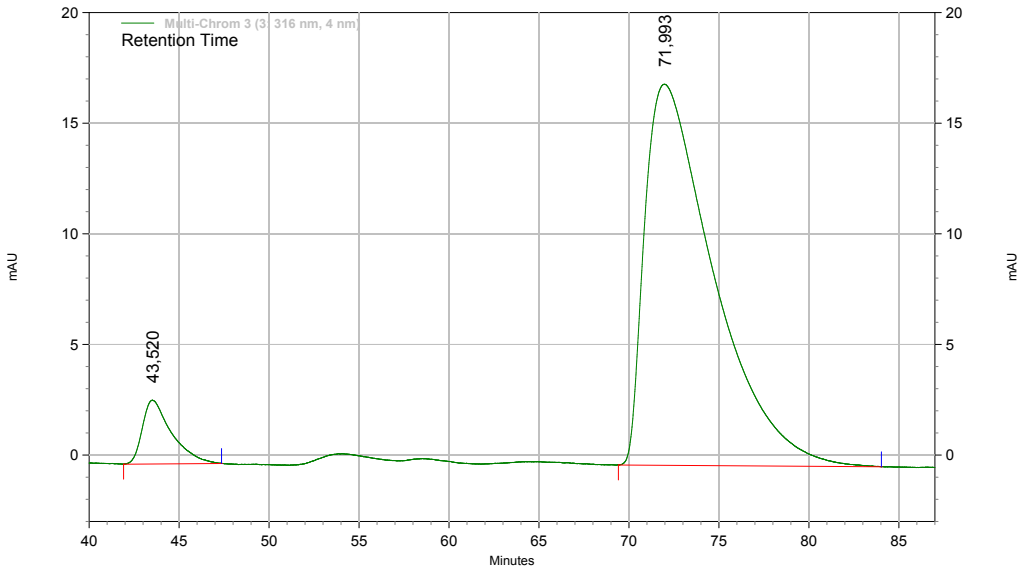
HPLC data compound **2j**: Chiralcel OD, Hexane/iPrOH 65/35, 0.3 mL.min^{-1}, 20°C, 84% ee



300 nm

Retention Time	Area	Area %	Height	Height %
36.680	13905213	91.87	139766	92.31
42.967	1230253	8.13	11651	7.69
Totals	15135466	100.00	151417	100.00

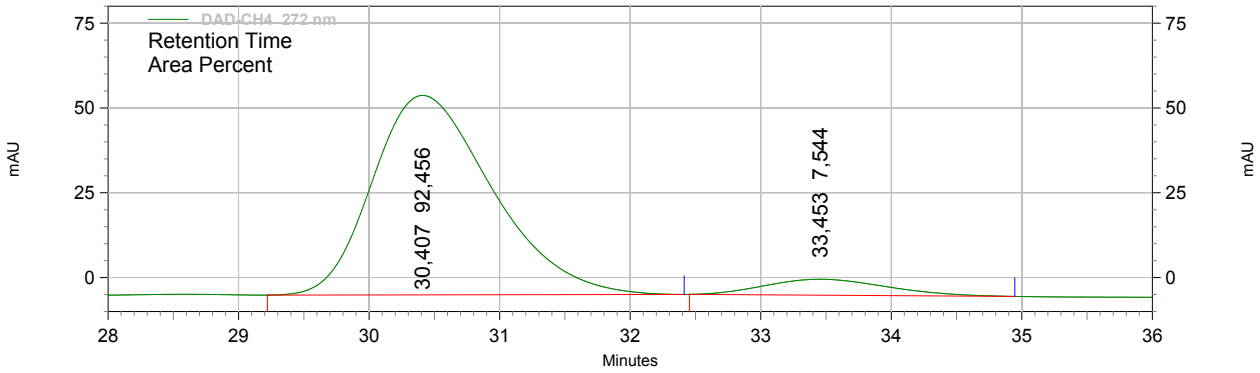
HPLC data compound **2k**: Chiralcel OD, Hexane/iPrOH 65/35, 0.3 mL.min^{-1}, 20°C, 87% ee



317 nm

Retention Time	Area	Area %	Height	Height %
43.520	1300328	6.62	11548	14.36
71.993	18343047	93.38	68897	85.64
Totals	19643375	100.00	80445	100.00

HPLC data compound **2m**: Chiralpak AD-H, Hexane/iPrOH 80/20, 1 mL.min^{-1}, 5°C, 85% ee



272 nm

Retention Time	Area	Area %	Height	Height %
30.407	14980019	92.46	235167	92.593
33.453	1222340	7.54	18812	7.407
Totals	16202359	100.00	253979	100.000

X-ray crystallography of compound (*R*)-2a

CCDC 1484089 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

Crystal data

$C_{16}H_{18}N_2O_2S$	D_x = 1.358 Mg m^{-3}
M_r = 302.38	Mo $K\alpha$ radiation, λ = 0.71073 Å
Monoclinic, $P2_1$	Cell parameters from 8629 reflections
a = 6.4138 (6) Å	θ = 2.7–29.8°
b = 7.6858 (7) Å	μ = 0.23 mm^{-1}
c = 15.2182 (14) Å	T = 299 K
β = 99.722 (3)°	Prism, colourless
V = 739.41 (12) Å^3	0.24 × 0.17 × 0.14 mm
Z = 2	
F(000) = 320	

Refinement

Refinement on F^2	Hydrogen site location: mixed
Least-squares matrix: full	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)]$ = 0.036	$w = 1/[\sigma^2(F_o^2) + (0.0459P)^2 + 0.098P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2)$ = 0.090	$(\Delta/\sigma)_{max} < 0.001$
S = 1.02	$\Delta\rho_{max}$ = 0.23 e Å^{-3}
4469 reflections	$\Delta\rho_{min}$ = −0.19 e Å^{-3}
199 parameters	Absolute structure: Flack x determined using 1634 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).
1 restraint	Absolute structure parameter: −0.02 (2)

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	y	z	U_{iso}*/U_{eq}
S1	0.64841 (8)	0.37546 (7)	0.70986 (3)	0.04180 (14)
O2	0.8270 (3)	0.4703 (3)	0.69166 (13)	0.0647 (6)
O1	0.6736 (4)	0.1966 (3)	0.73716 (13)	0.0667 (6)
N1	0.3765 (3)	0.6245 (3)	0.92402 (15)	0.0461 (5)
N2	0.5541 (3)	0.4723 (2)	0.78784 (12)	0.0400 (4)
C1	0.5691 (3)	0.6767 (3)	0.97111 (13)	0.0341 (4)
C8	0.4963 (4)	0.6568 (3)	0.78375 (14)	0.0402 (5)
H8	0.4532	0.6914	0.7214	0.048*
C6	0.7213 (3)	0.7512 (2)	0.92706 (14)	0.0344 (4)
C10	0.4539 (3)	0.3860 (3)	0.61262 (12)	0.0365 (4)
C15	0.2558 (4)	0.3193 (4)	0.61524 (16)	0.0506 (6)
H15	0.2220	0.2773	0.6684	0.061*
C7	0.6792 (4)	0.7715 (3)	0.82712 (15)	0.0427 (5)
H7A	0.8057	0.7409	0.8035	0.051*
H7B	0.6462	0.8922	0.8122	0.051*
C5	0.9136 (4)	0.8024 (3)	0.97706 (19)	0.0491 (6)
H5	1.0138	0.8554	0.9483	0.059*
C11	0.5024 (4)	0.4516 (3)	0.53392 (16)	0.0477 (5)
H11	0.6354	0.4987	0.5325	0.057*
C2	0.6175 (5)	0.6507 (3)	1.06375 (15)	0.0479 (6)
H2A	0.5182	0.6004	1.0940	0.057*
C13	0.1538 (4)	0.3764 (4)	0.45813 (13)	0.0485 (5)
C9	0.3110 (3)	0.6787 (3)	0.83306 (16)	0.0484 (5)
H9A	0.2667	0.7995	0.8312	0.058*
H9B	0.1925	0.6086	0.8050	0.058*
C14	0.1072 (4)	0.3155 (4)	0.53754 (18)	0.0556 (6)
H14	−0.0268	0.2709	0.5392	0.067*
C3	0.8139 (5)	0.7001 (4)	1.11000 (17)	0.0612 (8)
H3	0.8459	0.6803	1.1711	0.073*
C4	0.9599 (5)	0.7767 (4)	1.0679 (2)	0.0610 (7)
H4	1.0897	0.8116	1.0999	0.073*
C12	0.3518 (5)	0.4467 (4)	0.45730 (16)	0.0534 (6)
H12	0.3843	0.4913	0.4044	0.064*
C16	−0.0091 (5)	0.3685 (5)	0.37377 (18)	0.0727 (9)
H16A	−0.0027	0.2569	0.3461	0.109*

H16B	0.0198	0.4580	0.3335	0.109*
H16C	−0.1476	0.3858	0.3882	0.109*
H2	0.506 (5)	0.414 (4)	0.822 (2)	0.055 (9)*
H1	0.299 (5)	0.576 (5)	0.952 (2)	0.065 (10)*

S1—O2	1.424 (2)	C7—H7B	0.9700
S1—O1	1.437 (2)	C5—H5	0.9300
S1—N2	1.6034 (19)	C5—C4	1.378 (4)
S1—C10	1.7692 (19)	C11—H11	0.9300
N1—C1	1.379 (3)	C11—C12	1.383 (3)
N1—C9	1.439 (3)	C2—H2A	0.9300
N1—H1	0.80 (4)	C2—C3	1.389 (4)
N2—C8	1.464 (3)	C13—C14	1.375 (4)
N2—H2	0.78 (3)	C13—C12	1.382 (4)
C1—C6	1.397 (3)	C13—C16	1.513 (3)
C1—C2	1.406 (3)	C9—H9A	0.9700
C8—H8	0.9800	C9—H9B	0.9700
C8—C7	1.525 (3)	C14—H14	0.9300
C8—C9	1.518 (3)	C3—H3	0.9300
C6—C7	1.507 (3)	C3—C4	1.355 (5)
C6—C5	1.392 (3)	C4—H4	0.9300
C10—C15	1.377 (3)	C12—H12	0.9300
C10—C11	1.382 (3)	C16—H16A	0.9600
C15—H15	0.9300	C16—H16B	0.9600
C15—C14	1.388 (3)	C16—H16C	0.9600
C7—H7A	0.9700		
O2—S1—O1	119.40 (14)	C6—C5—H5	119.0
O2—S1—N2	108.83 (12)	C4—C5—C6	121.9 (3)
O2—S1—C10	106.90 (11)	C4—C5—H5	119.0
O1—S1—N2	105.55 (12)	C10—C11—H11	120.2
O1—S1—C10	108.35 (12)	C10—C11—C12	119.5 (2)
N2—S1—C10	107.27 (10)	C12—C11—H11	120.2
C1—N1—C9	120.4 (2)	C1—C2—H2A	120.1
C1—N1—H1	116 (3)	C3—C2—C1	119.8 (3)
C9—N1—H1	123 (3)	C3—C2—H2A	120.1

S1—N2—H2	117 (2)	C14—C13—C12	118.5 (2)
C8—N2—S1	122.85 (16)	C14—C13—C16	120.7 (3)
C8—N2—H2	117 (2)	C12—C13—C16	120.8 (2)
N1—C1—C6	120.47 (19)	N1—C9—C8	108.53 (18)
N1—C1—C2	120.4 (2)	N1—C9—H9A	110.0
C6—C1—C2	119.1 (2)	N1—C9—H9B	110.0
N2—C8—H8	109.4	C8—C9—H9A	110.0
N2—C8—C7	111.76 (18)	C8—C9—H9B	110.0
N2—C8—C9	107.5 (2)	H9A—C9—H9B	108.4
C7—C8—H8	109.4	C15—C14—H14	119.3
C9—C8—H8	109.4	C13—C14—C15	121.4 (2)
C9—C8—C7	109.31 (18)	C13—C14—H14	119.3
C1—C6—C7	120.40 (18)	C2—C3—H3	119.3
C5—C6—C1	118.7 (2)	C4—C3—C2	121.3 (2)
C5—C6—C7	120.9 (2)	C4—C3—H3	119.3
C15—C10—S1	118.85 (17)	C5—C4—H4	120.4
C15—C10—C11	120.3 (2)	C3—C4—C5	119.2 (2)
C11—C10—S1	120.74 (17)	C3—C4—H4	120.4
C10—C15—H15	120.4	C11—C12—H12	119.5
C10—C15—C14	119.2 (2)	C13—C12—C11	121.0 (2)
C14—C15—H15	120.4	C13—C12—H12	119.5
C8—C7—H7A	109.3	C13—C16—H16A	109.5
C8—C7—H7B	109.3	C13—C16—H16B	109.5
C6—C7—C8	111.75 (18)	C13—C16—H16C	109.5
C6—C7—H7A	109.3	H16A—C16—H16B	109.5
C6—C7—H7B	109.3	H16A—C16—H16C	109.5
H7A—C7—H7B	107.9	H16B—C16—H16C	109.5
S1—N2—C8—C7	−92.1 (2)	C6—C1—C2—C3	0.5 (3)
S1—N2—C8—C9	147.95 (16)	C6—C5—C4—C3	−0.3 (4)
S1—C10—C15—C14	−175.3 (2)	C10—S1—N2—C8	−61.8 (2)
S1—C10—C11—C12	175.3 (2)	C10—C15—C14—C13	0.2 (4)
O2—S1—N2—C8	53.5 (2)	C10—C11—C12—C13	−0.3 (4)
O2—S1—C10—C15	−173.5 (2)	C15—C10—C11—C12	−1.3 (4)
O2—S1—C10—C11	9.9 (2)	C7—C8—C9—N1	−61.1 (2)
O1—S1—N2—C8	−177.21 (19)	C7—C6—C5—C4	−176.5 (2)
O1—S1—C10—C15	56.6 (2)	C5—C6—C7—C8	161.3 (2)

O1—S1—C10—C11	−120.0 (2)	C11—C10—C15—C14	1.3 (4)
N1—C1—C6—C7	−1.5 (3)	C2—C1—C6—C7	176.5 (2)
N1—C1—C6—C5	179.9 (2)	C2—C1—C6—C5	−2.1 (3)
N1—C1—C2—C3	178.5 (2)	C2—C3—C4—C5	−1.4 (4)
N2—S1—C10—C15	−56.9 (2)	C9—N1—C1—C6	−13.4 (3)
N2—S1—C10—C11	126.5 (2)	C9—N1—C1—C2	168.6 (2)
N2—C8—C7—C6	−71.0 (2)	C9—C8—C7—C6	47.9 (2)
N2—C8—C9—N1	60.4 (2)	C14—C13—C12—C11	1.8 (4)
C1—N1—C9—C8	44.9 (3)	C12—C13—C14—C15	−1.7 (4)
C1—C6—C7—C8	−17.2 (3)	C16—C13—C14—C15	179.0 (3)
C1—C6—C5—C4	2.0 (3)	C16—C13—C12—C11	−178.9 (3)
C1—C2—C3—C4	1.3 (4)		

All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.