Electronic Supplementary Material (ESI) for ChemComm.

Electronic Supporting Information

Continuous-Flow Synthesis of Alkyl Zinc Sulfinates for the Direct Photofunctionalization of Heterocycles

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Summary:

General information

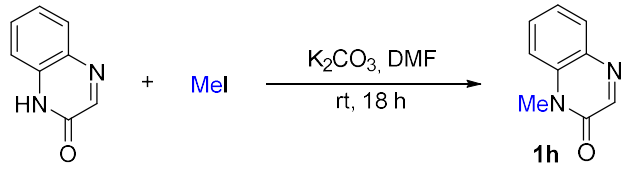
NMR spectra were acquired on a BRUKER AVANCE 300 or 500 MHz spectrometer running at 300 MHz for ^{1}H, 75 MHz for ^{13}C and 282 MHz for ^{19}F, and were internally referenced to residual solvent signals ($CDCl_3$ referenced at δ 7.26 ppm for ^{1}H-NMR and δ 77.2 ppm for ^{13}C-NMR and DMSO-d_6 referenced at δ 2.50 ppm for ^{1}H-NMR). Data for ^{1}H-NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, sext = sextuplet, hept = heptuplet, m = multiplet, br = broad), coupling constant (Hz) and integration. Data for ^{13}C-NMR and ^{19}F-NMR are reported in terms of chemical shift.

High-Resolution Mass Spectra (HRMS) were obtained on an Agilent Technologies 6120 Quadrupole LC/MS coupled with an SFC Agilent Technologies 1260 Infinity Series instrument for the MS (ESI) (Electrospray Ionization). MassWorks software version 4.0.0.0 (Cerno Bioscience) was used for the formula identification. MassWorks is an MS calibration software which calibrates isotope profiles to achieve high mass accuracy and enables elemental composition determination on conventional mass spectrometers of unit mass resolution, allowing highly accurate comparisons between calibrated and theoretical spectra. Obtained data are expressed in mass/charge (m/z) units.

All continuous-flow experiments were carried out using a commercially available Vapourtec UV-150 photoreactor fixed on an E-series Vapourtec equipment. This module consists of a temperature-controlled irradiation chamber where a transparent perfluoroalcoxy (PFA) capillary tube reactor (7.83 mL, 1/8" OD, 1.60 mm ID) is coiled around a blue LED assembly (emitting at 450 nm with a total output power of 24W). Temperature-controlled fixed bed reactor including an adjustable Omnifit® column (6.6 mm bore x 150 mm length) was also purchased from Vapourtec.

All reagents and materials were purchased from commercial sources and used without further purification, except compound **1h** and heterocycles **1k-1q**, which were synthesized as described below. Zinc granules were purchased from Alfa Aesar (zinc granules, ACS, -20 mesh, 99.8% min.). Chromatographic purification of products was accomplished by flash column chromatography using silica gel (Merck Geduran® Si 60 0.040-0.063 nm).

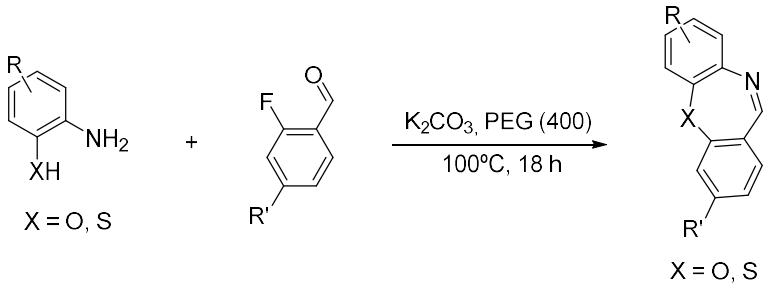
Synthesis of starting material 1h[1]



Following a reported procedure,[1] quinoxalin-2(1*H*)-one (730.8 mg, 5.0 mmol, 1.0 equiv.) and K_2CO_3 (829.2 mg, 6.0 mmol, 1.2 equiv.) were added to a 50 mL round-bottomed flask equipped with a magnetic stir bar and dissolved in DMF (20 mL). MeI (500 µL, 8.0 mmol, 1.6 equiv.) was added, and the reaction was stirred overnight at room temperature. Then, the mixture was quenched with water (20 mL) and extracted with EtOAc (40 mL). The organic layer was washed with water (2 x 20 mL), a saturated aqueous solution of NH_4Cl (20 mL) and brine (20 mL). Then, the organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford 700 mg (87%, pale yellow solid) of pure 1-methylquinoxalin-2(1*H*)-one **1h**.

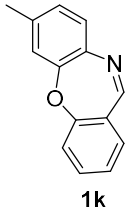
^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.89 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.61 (td, *J* =8.0, 1.4 Hz, 1H), 7.41-7.32 (m, 2H), 3.70 (s, 3H).

General procedure for the synthesis of dibenzothia/oxazepines 1k-1q



Following a described method[1], the corresponding 2-aminophenol or 2-aminotiophenol (1.1 equiv.) and the subsequent fluorobenzaldehyde (1.0 equiv.) were added to an oven-dried sealed tube equipped with a magnetic stir bar and dissolved in poly(ethylene glycol) (0.5 M, PEG, average M_n 400). K_2CO_3 (1.1 equiv.) was added, and the reaction was heated at 100 °C and stirred overnight. Then, the mixture was allowed to cool to room temperature and water (10 mL) was added. The resulting suspension was extracted with EtOAc (3 x 20 mL), and the combined organic layers were washed with brine (20 mL), dried over anhydrous $MgSO_4$, and filtered. Solvent was removed under reduced pressure, and the resulting crude mixture was purified by flash column chromatography (silica gel) to provide the corresponding compound (**1k-1q**).

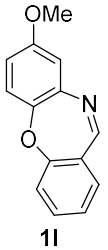
7-Methyldibenzo[*b,f*][1,4]oxazepine (1k)[1]



Compound prepared following general procedure and starting from 2-fluorobenzaldehyde (526.8 µL, 5.0 mmol, 1.0 equiv.) and 2-amino-5-methylphenol (677.3 mg, 5.5 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, Cyhex:EtOAc 90:10) afforded 705 mg (67% yield, pale orange solid) of compound **1k.**

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.47 (s, 1H), 7.49-7.40 (m, 1H), 7.34 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.25-7.16 (m, 2H), 7.14 (d, *J* = 8.1 Hz, 1H), 7.01-6.97 (m, 1H), 6.95 (s, 1H), 2.33 (s, 3H).

8-Methoxydibenzo[*b,f*][1,4]oxazepine (1l)[1]

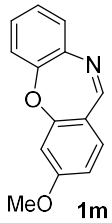


1l

Compound prepared following general procedure and starting from 2-fluorobenzaldehyde (210.7 µL, 2.0 mmol, 1.0 equiv.) and 2-amino-4-methoxyphenol (306.1 mg, 2.2 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, Cyhex:EtOAc 75:25) afforded 330 mg (73% yield, brown solid) of **1l**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.53 (s, 1H), 7.45 (ddd, *J* = 8.1, 7.5, 1.7 Hz, 1H), 7.35 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.21 (td, *J* = 7.5, 1.1 Hz, 1H), 7.14 (br d, *J* = 8.1 Hz, 1H), 7.05 (d, *J* = 8.8 Hz, 1H), 6.89 (d, *J* = 3.1 Hz, 1H), 6.77 (dd, *J* = 8.8, 3.1 Hz, 1H), 3.78 (s, 3H).

3-Methoxydibenzo[*b,f*][1,4]oxazepine (1m)[1]

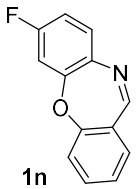


1m

Compound prepared following general procedure and starting from 2-fluoro-4-methoxybenzaldehyde (770.7 mg, 5.0 mmol, 1.0 equiv.) and 2-aminophenol (600.2 mg, 5.5 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, Cyhex:EtOAc 80:20) afforded 890 mg (79% yield, orange solid) of dibenzoxazepine **1m**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.40 (s, 1H), 7.36-7.32 (m, 1H), 7.25 (d, *J* = 8.5 Hz, 1H), 7.19 (ddd, *J* = 6.7, 5.3, 2.1 Hz, 2H), 7.12-7.07 (m, 1H), 6.72 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.67 (d, *J* = 2.5 Hz, 1H), 3.83 (s, 3H).

7-Fluorodibenzo[*b,f*][1,4]oxazepine (1n)[1]

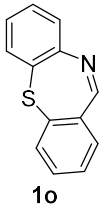


1n

Compound prepared following general procedure and starting from 2-fluorobenzaldehyde (526.8 µL, 5.0 mmol, 1.0 equiv.) and 2-amino-5-fluorophenol (699.2 mg, 5.5 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, Cyhex:EtOAc 90:10) afforded 323 mg (30% yield, pale orange solid) of the title compound **1n**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.46 (s, 1H), 7.51-7.44 (m, 1H), 7.37-7.29 (m, 2H), 7.24-7.21 (m, 1H), 7.13 (br d, *J* = 8.1 Hz, 1H), 6.94-6.83 (m, 2H).

Dibenzo[*b,f*][1,4]thiazepine (1o)[1]

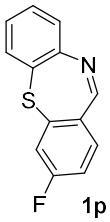


1o

Compound prepared following general procedure and starting from 2-fluorobenzaldehyde (526.8 µL, 5.0 mmol, 1.0 equiv.) and 2-aminothiophenol (588.5 µL, 5.5 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, Cyhex:EtOAc 95:5) afforded 434 mg (41% yield, pale yellow solid) of the title dibenzothiazepine **1o**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.90 (s, 1H), 7.45-7.31 (m, 7H), 7.21-7.15 (m, 1H).

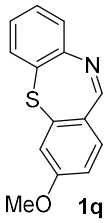
3-Fluorodibenzo[*b,f*][1,4]thiazepine (1p)[1]



Compound prepared following general procedure and starting from 2,4-difluorobenzaldehyde (547.0 µL, 5.0 mmol, 1.0 equiv.) and 2-aminothiophenol (588.5 µL, 5.5 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, Cyhex:EtOAc 92:8) afforded 609 mg (53% yield, yellow solid) of compound **1p**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.84 (s, 1H), 7.43-7.28 (m, 4H), 7.22-7.14 (m, 2H), 7.05 (td, *J* = 8.3, 2.5 Hz, 1H).

3-Methoxydibenzo[*b,f*][1,4]thiazepine (1q)[1]



Compound prepared following general procedure and starting from 2-fluoro-4-methoxybenzaldehyde (770.7 mg, 5.0 mmol, 1.0 equiv.) and 2-aminothiophenol (588.5 µL, 5.5 mmol, 1.1 equiv.). Purification by column chromatography (silica gel, Cyhex:EtOAc 85:15) afforded 1.038 g (86% yield, yellow solid) of the title compound **1q**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.79 (s, 1H), 7.42-7.39 (m, 1H), 7.36-7.28 (m, 3H), 7.17 (ddd, *J* = 7.6, 6.6, 2.5 Hz, 1H), 6.96 (d, *J* = 2.5 Hz, 1H), 6.86 (dd, *J* = 8.5, 2.5 Hz, 1H), 3.82 (s, 3H).

Assembly of reactor used for the alkylation of heterocycles

All continuous-flow experiments were carried out using a commercially available Vapourtec UV-150 photoreactor fixed on an E-series Vapourtec equipment[2]. The system, represented in **figure S1a**, consisted of two pumps, a temperature-controlled adjustable Omnifit® column filled with zinc granules (6.6 mm bore x 150 mm length, 10 g Zn, 2 mL) (**figure S1b**), and a coil reactor (7.83 mL, perfluoroalcoxy (PFA) capillary tube, 1/8" OD, 1.60 mm ID, 3.9 m length) inside the temperature-controlled UV-150 photoreactor chamber.

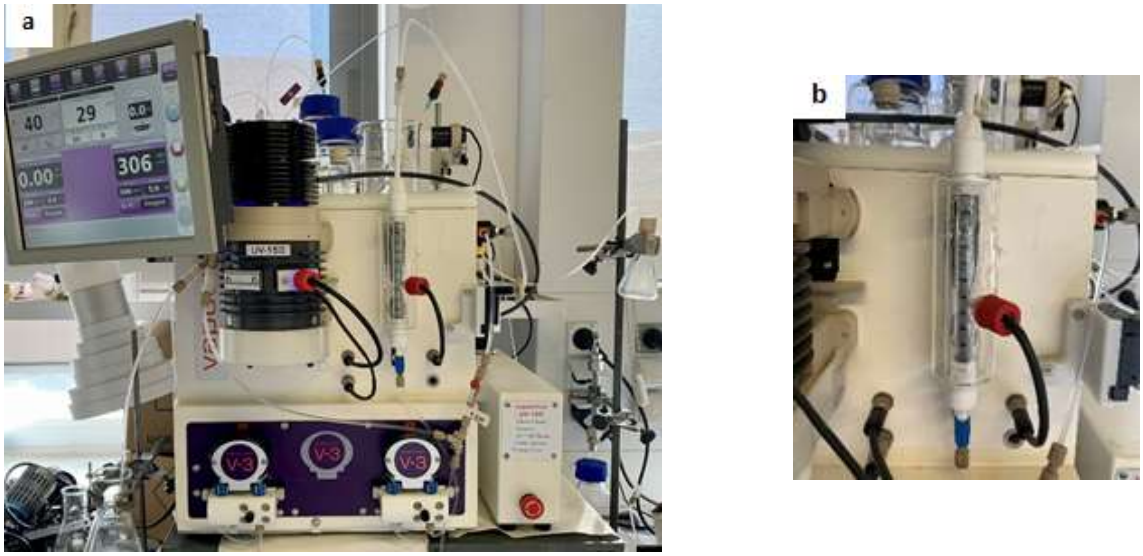
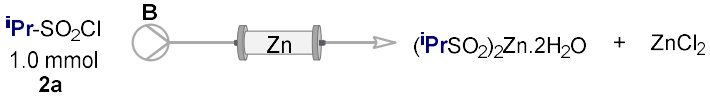


Figure S1 a. Flow system assembly for the alkylation of heterocycles. **b.** Temperature-controlled Omnifit® column.

Proof of concept for the zinc sulfinate formation



Activating solution:[3] 1,2-dibromoethane (227.6 µL, 2.4 mmol, 0.24 M) and chlorotrimethylsilane (837.6 µL, 6.0 mmol, 0.6 M) were dissolved in an oven-dried vial equipped with a septum using 10 mL of acetone. Solution was bubbled with nitrogen for 10 minutes.

Solvent was pumped through using pump B at a flow rate of 1 mL min^{-1} in order to purge the whole system (approximately 10 minutes). Then, activating solution was pumped through the zinc column at a flow rate of 1 mL min^{-1}. Ethylene gas evolution is observed due to zinc activation. Once the addition is finished, solvent is pumped through the column at 1 mL min^{-1} to homogenize the system and avoid ethylene bubbles during reaction (approximately 3-5 minutes).

Isopropylsulfonyl chloride **2a** (112.3 µL, 1.0 mmol) was dissolved in an oven-dried vial equipped with a septum with an acetone/water 1/1 mixture (5 mL). The solution was homogenized by sonication in an ultrasound bath and pumped through pump B at 398 µL min^{-1} (5 min Zn column residence time). Solvents from the reaction mixture collected were removed under reduced pressure. The resulting white solid was analyzed by ^{1}H-NMR spectroscopy, giving a 100% conversion of the isopropyl zinc sulfinate.[4]

^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.12-1.99 (m, 1H), 0.96 (d, *J* = 6.9 Hz, 6H).

General procedure for the alkylation of heterocycles

Activating solution:[3] 1,2-dibromoethane (227.6 µL, 2.4 mmol, 0.24 M) and chlorotrimethylsilane (837.6 µL, 6.0 mmol, 0.6 M) were dissolved in an oven-dried vial equipped with a septum using 10 mL of acetone. Solution was bubbled with nitrogen for 10 minutes.

Solution A: the corresponding heterocycle **1** (0.125 mmol, 1.0 equiv.) and **$(NH_4)_2S_2O_8$** (85.6 mg, 0.375 mmol, 3.0 equiv.) were added to an oven-dried vial equipped with a septum. An acetone/water 1/1 mixture was added (5 mL), and the solution was homogenized by sonication in an ultrasound bath.

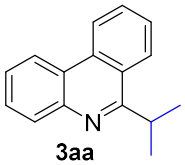
Solution B: the corresponding sulfonyl chloride **2** (0.5 mmol, 4.0 equiv.) was dissolved in an oven-dried vial equipped with a septum with an acetone/water 1/1 mixture (5 mL). The solution was homogenized by sonication in an ultrasound bath.

Due to their poor solubility, for starting dibenzothiazepines and dibenzoxazepines **1k-1q**, solutions A and B were prepared using 10 mL of acetone/water 1/1 instead of the volume reported above.

Solvent was pumped through using both pumps at a flow rate of 1 mL min^{-1} in order to purge the whole system (approximately 10 minutes). Then, activating solution was pumped through the zinc column at a flow rate of 1 mL min^{-1}. Ethylene gas evolution is observed due to zinc activation. Once the addition is finished, solvent is pumped through the column at 1 mL min^{-1} to homogenize the system and avoid ethylene bubbles during reaction (approximately 3-5 minutes).

The reaction was performed, if not otherwise stated, by setting column temperature at 30 °C and reactor temperature at 40 °C. Then, solutions A and B were pumped through the system at 306 µL min^{-1} (6.5 minutes Zn column residence time and 13 minutes photoreactor residence time), and the reactor was irradiated with blue LEDs (450 nm, 24 W total power). Solvents from the reaction mixture collected were removed under reduced pressure. The resulting crude was redissolved in EtOAc (15 mL) and 1 mL NH_3 7N in MeOH was added. The solution was stirred for 10 minutes and then filtered through a plug of Celite®. Solvent was evaporated *in vacuo* and the residue was purified by flash column chromatography to obtain functionalized heterocycles **3**.

6-Isopropylphenanthridine (3aa)[5]

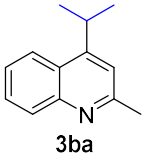


3aa

Following general procedure with phenanthridine **1a** (22.4 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.), compound **3aa** was obtained after column chromatography purification (silica gel, Cyhex:EtOAc 85:15) in a 94% yield (26.0 mg, white solid).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.66 (d, *J* = 8.0 Hz, 1H), 8.55 (dd, *J* = 8.1, 1.3 Hz, 1H), 8.33 (d, *J* = 8.2 Hz, 1H), 8.16 (d, *J* = 8.1 Hz, 1H), 7.86-7.78 (m, 1H), 7.74-7.66 (m, 2H), 7.65-7.58 (m, 1H), 4.02 (hept, *J* = 6.8 Hz, 1H), 1.53 (d, *J* = 6.8 Hz, 6H).

4-Isopropyl-2-methylquinoline (3ba)[6]

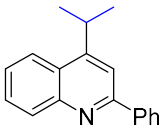


3ba

General procedure with 2-methylquinoline **1b** (16.9 µL, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.) afforded compound **3ba** after column chromatography purification (silica gel, Cyhex:EtOAc 83:17) in 61% yield (14.1 mg, brownish oil).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.03 (br d, *J* = 8.5 Hz, 2H), 7.69-7.61 (m, 1H), 7.52-7.45 (m, 1H), 7.18 (s, 1H), 3.70 (hept, *J* = 6.8 Hz, 1H), 2.72 (s, 3H), 1.39 (d, *J* = 6.9 Hz, 6H).

4-Isopropyl-2-phenylquinoline (3ca)[7]

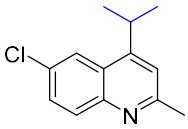


3ca

General procedure was followed using 2-phenylquinoline **1c** (25.7 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.). After column chromatography purification (silica gel, Cyhex:DCM 70:30), quinoline **3ca** was obtained in 59% yield (18.3 mg, pale yellow solid).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.24-8.08 (m, 4H), 7.78 (s, 1H), 7.75-7.67 (m, 1H), 7.59-7.43 (m, 4H), 3.80 (m, 1H), 1.47 (d, *J* = 6.9 Hz, 1H).

6-Chloro-4-isopropyl-2-methylquinoline (3da)



3da

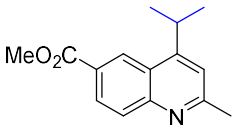
Following general procedure with 6-chloro-2-methylquinoline **1d** (22.2 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.), compound **3da** was obtained after column chromatography purification (silica gel, Cyhex:EtOAc 90:10) in a 44% yield (12.1 mg, brown oil).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.06-7.96 (m, 1H), 7.61 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.22 (s, 1H), 3.61 (hept, *J* = 6.9 Hz, 1H), 2.74 (s, 2H), 1.39 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 159.2, 131.7, 130.9, 130.0, 126.1, 122.3 (2C), 118.8 (2C), 28.5, 25.3, 23.0 (2C).

HRMS (ESI$^+$): Calculated for $C_{13}H_{14}ClN$ $[M + H]^+$: 220.0815, found: 220.0888

Methyl 4-isopropyl-2-methylquinoline-6-carboxylate (3ea)



3ea

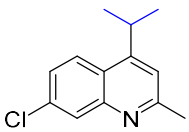
General procedure with methyl 2-methylquinoline-6-carboxylate **1e** (25.2 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.) afforded compound **3ea** after column chromatography purification (silica gel, Cyhex:EtOAc 90:10) in 50% yield (15.2 mg, brown solid).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.82 (d, *J* = 1.8 Hz, 1H), 8.24 (dd, *J* = 8.8, 1.8 Hz, 1H), 8.07 (br d, *J* = 8.8 Hz, 1H), 7.25 (br s, 1H), 3.98 (s, 3H), 3.87-3.73 (m, 1H), 2.75 (s, 3H), 1.41 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 167.1, 161.5, 156.3, 150.0, 129.7, 128.7, 127.1, 126.4, 124.6, 118.8, 52.5, 28.4, 25.7, 23.2 (2C).

HRMS (ESI$^+$): Calculated for $C_{15}H_{17}NO_2$ $[M + H]^+$: 244.1259, found: 244.1332

7-Chloro-4-isopropyl-2-methylquinoline (3fa)[5]

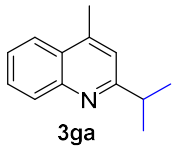


3fa

General procedure with 7-chloro-2-methylquinoline **1f** (22.2 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.) afforded compound **3fa** after column chromatography purification (silica gel, Cyhex:EtOAc 90:10) in 65% yield (17.9 mg, orange oil).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.02 (d, *J* = 2.1 Hz, 1H), 7.96 (d, *J* = 9.0 Hz, 1H), 7.43 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.17 (s, 1H), 3.63 (hept, *J* = 6.8 Hz, 1H), 2.71 (s, 3H), 1.37 (d, *J* = 6.8 Hz, 6H).

2-Isopropyl-4-methylquinoline (3ga)[5]

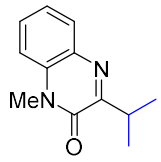


3ga

General procedure was followed using 4-methylquinoline **1g** (16.5 µL, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.). After column chromatography purification (silica gel, Cyhex:EtOAc 88:12), quinoline **3ga** was obtained in 57% yield (13.2 mg, yellow oil).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.18 (s, 1H), 3.22 (hept, *J* = 7.0 Hz, 1H), 2.69 (s, 3H), 1.39 (d, *J* = 7.0 Hz, 6H).

3-Isopropyl-1-methylquinoxalin-2(1*H*)-one (3ha)[8]

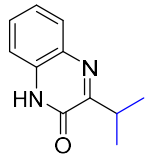


3ha

General procedure was followed using 1-methylquinoxalin-2(1*H*)-one **1h** (20.0 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.). After column chromatography purification (silica gel, Cyhex:EtOAc 82:18), quinoxalinone **3ha** was obtained in 70% yield (17.7 mg, white solid).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.85 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.55-7.48 (m, 1H), 7.32 (m, 2H), 3.70 (s, 3H), 3.63 (hept, *J* = 6.8 Hz, 1H), 1.31 (d, *J* = 6.9 Hz, 6H).

3-Isopropylquinoxalin-2(1*H*)-one (3ia)[9]

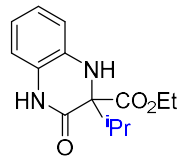


3ia

Following general procedure with quinoxaline-2(1*H*)-one **1i** (18.3 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.), compound **3ia** was obtained after column chromatography purification (silica gel, Cyhex:EtOAc 75:25) in a 93% yield (21.9 mg, white solid).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 11.57 (br s, 1H, NH), 7.85 (d, *J* = 7.8 Hz, 1H), 7.51-7.44 (m, 1H), 7.37-7.28 (m, 2H), 3.65 (m, 1H), 1.36 (d, *J* = 6.7 Hz, 6H).

Ethyl 2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (3ja)



3ja

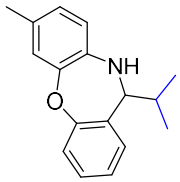
General procedure with ethyl 3-oxo-1,2,3,4-tetrahydroquinoxaline-2-carboxylate **1j** (27.3 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.) afforded compound **3ja** after column chromatography purification (silica gel, Cyhex:EtOAc 78:22) in 69% yield (22.6 mg, white solid).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.88 (br s, 1H, NH), 6.98-6.86 (m, 1H), 6.86-6.68 (m, 3H), 4.47 (br s, 1H, NH), 4.29-4.01 (m, 2H), 2.87 (hept, *J* = 6.8 Hz, 1H), 1.24-1.11 (m, 6H), 1.00 (d, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 171.3, 164.6, 133.3, 124.4, 124.2, 119.8, 115.3, 114.8, 69.8, 62.3, 33.0, 17.9, 16.5, 14.2.

HRMS (ESI$^+$): Calculated for $C_{14}H_{18}N_2O_3$ $[M + H]^+$: 263.1317, found: 263.1390

11-Isopropyl-7-methyl-10,11-dihydrodibenzo[*b,f*][1,4]oxazepine (3ka)



3ka

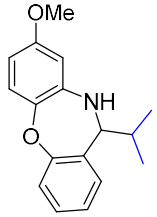
General procedure was followed using 7-methyl-10,11-dihydrodibenzo[*b,f*][1,4]oxazepine **1k** (26.2 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.). After column chromatography purification (silica gel, Cyhex:EtOAc 97:3), dihydrodibenzoxazepine **3ka** was obtained in 58% yield (18.4 mg, orange solid).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.26-7.19 (m, 1H), 7.16-6.99 (m, 3H), 6.89 (d, *J* = 1.3 Hz, 1H), 6.67 (dd, *J* = 8.0, 1.3 Hz, 1H), 6.48 (d, *J* = 8.0 Hz, 1H), 4.18 (br s, 1H, NH), 3.51 (d, *J* = 10.2 Hz, 1H), 2.75-2.63 (m, 1H), 2.23 (s, 3H), 1.09 (d, *J* = 6.6 Hz, 3H), 0.76 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 156.6, 143.3, 134.4, 133.8, 129.4, 128.8, 128.4, 124.9, 123.9, 122.1, 121.3, 118.6, 67.0, 31.8, 20.8, 20.5, 20.3.

HRMS (ESI$^+$): Calculated for $C_{17}H_{19}NO$ $[M + H]^+$: 254.1467, found: 254.1539

11-Isopropyl-8-methoxy-10,11-dihydrodibenzo[*b,f*][1,4]oxazepine (3la)



3la

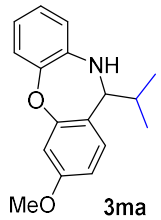
Following general procedure with 8-methoxy-10,11-dihydrodibenzo [*b,f*][1,4]oxazepine **1l** (28.2 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.), compound **3la** was obtained after column chromatography purification (silica gel, Cyhex:EtOAc 93:7) in a 46% yield (15.5 mg, white solid).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.26-7.19 (m, 1H), 7.15-7.00 (m, 3H), 6.98 (d, *J* = 8.7 Hz, 1H), 6.19 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.10 (d, *J* = 2.9 Hz, 1H), 4.32 (br s, 1H, NH), 3.71 (s, 3H), 3.51 (d, *J* = 10.2 Hz, 1H), 2.79-2.67 (m, 1H), 1.12 (d, *J* = 6.6 Hz, 3H), 0.75 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 156.9, 156.5, 138.0, 137.8, 133.6, 129.2, 128.8, 123.9, 122.2, 121.1, 103.2, 103.0, 66.5, 55.5, 32.2, 20.7, 20.4.

HRMS (ESI$^+$): Calculated for $C_{17}H_{19}NO_2$ $[M + H]^+$: 270.1416, found: 270.1489

11-Isopropyl-3-methoxy-10,11-dihydrodibenzo[*b,f*][1,4]oxazepine (3ma)



3ma

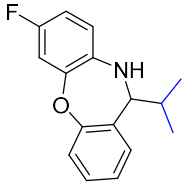
General procedure with 3-methoxy-10,11-dihydrodibenzo[*b,f*][1,4] oxazepine **1m** (28.2 mg, 0.25 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.) afforded compound **3ma** after column chromatography purification (silica gel, Cyhex:EtOAc 95:5) in 54% yield (18.2 mg, brown solid).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.05 (dd, *J* = 7.9, 1.4 Hz, 1H), 6.98 (d, *J* = 8.3 Hz, 1H), 6.85 (td, *J* = 7.8, 1.4 Hz, 1H), 6.72 (d, *J* = 2.5 Hz, 1H), 6.68-6.53 (m, 3H), 4.31 (br s, 1H, NH), 3.79 (s, 3H), 3.48 (d, *J* = 10.2 Hz, 1H), 2.65 (m, 1H), 1.09 (d, *J* = 6.6 Hz, 3H), 0.76 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 160.1, 157.4, 143.4, 137.3, 129.9, 125.9, 124.5, 121.8, 118.4, 118.4, 109.7, 106.9, 66.2, 55.6, 32.3, 20.8, 20.5.

HRMS (ESI$^+$): Calculated for $C_{17}H_{19}NO_2$ $[M + H]^+$: 270.1416, found: 270.1489

7-Fluoro-11-isopropyl-10,11-dihydrodibenzo[*b,f*][1,4]oxazepine (3na)



3na

General procedure was followed using 7-fluoro-10,11-dihydro dibenzo[*b,f*][1,4]oxazepine **1n** (26.7 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.). After column chromatography purification (silica gel, Cyhex:EtOAc 95:5), dihydrodibenzoxazepine **3na** was obtained in 75% yield (24.1 mg, yellow pale solid).

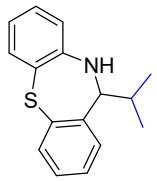
^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.10-7.01 (m, 2H), 6.93-6.84 (m, 2H), 6.75 (td, *J* = 8.3, 2.6 Hz, 1H), 6.66 (td, *J* = 7.4, 1.5 Hz, 1H), 6.57 (dd, *J* = 7.9, 1.5 Hz, 1H), 4.31 (br s, 1H, NH), 3.52 (d, *J* = 10.3 Hz, 1H), 2.74-2.59 (m, 1H), 1.10 (d, *J* = 6.5 Hz, 3H), 0.76 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 162.6 (d, J_{C-F} = 246.7 Hz), 157.2 (d, J_{C-F} = 10.9 Hz), 143.0, 136.9, 130.0 (d, J_{C-F} = 9.4 Hz), 129.6 (d, J_{C-F} = 3.6 Hz), 124.6, 121.6, 118.7, 118.5, 110.5 (d, J_{C-F} = 21.0 Hz), 109.0 (d, J_{C-F} = 23.1 Hz), 66.2, 31.9, 20.6, 20.3.

^{19}F-NMR (282 MHz, $CDCl_3$): δ -113.39

HRMS (ESI$^+$): Calculated for $C_{16}H_{16}FNO$ $[M + H]^+$: 258.1216, found: 258.1289

11-Isopropyl-10,11-dihydrodibenzo[*b,f*][1,4]thiazepine (3oa)



3oa

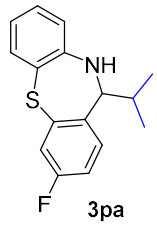
Following general procedure with 10,11-dihydrodibenzo[*b,f*][1,4]thiazepine **1o** (26.4 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.), compound **3oa** was obtained after column chromatography purification (silica gel, Cyhex:EtOAc 98:2) in a 76% yield (24.3 mg, dark green oil).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.53-7.46 (m, 1H), 7.26-7.18 (m, 2H), 7.16-7.13 (m, 2H), 6.93-6.88 (m, 1H), 6.59-6.54 (m, 1H), 6.42 (d, *J* = 8.1 Hz, 1H), 4.65 (d, *J* = 10.1 Hz, 1H), 4.04 (br s, 1H), 2.95-2.70 (m, 1H), 1.21 (d, *J* = 6.5 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 146.6, 144.2, 135.0, 132.2, 131.6, 128.2, 127.9 (2C), 127.6, 118.4, 118.3, 116.7, 77.2, 65.5, 31.0, 21.0, 20.5.

HRMS (ESI$^+$): Calculated for $C_{16}H_{17}NS$ $[M + H]^+$: 256.1082, found: 256.1154

3-Fluoro-11-isopropyl-10,11-dihydrodibenzo[*b,f*][1,4]thiazepine (3pa)



3pa

General procedure with 3-fluoro-10,11-dihydrodibenzo[*b,f*][1,4]thiazepine **1p** (28.7 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.) afforded compound **3pa** after column chromatography purification (silica gel, Cyhex:EtOAc 98:2) in 57% yield (19.5 mg, dark green oil).

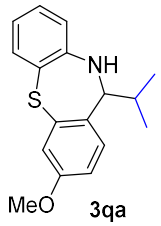
^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.22 (dd, *J* = 8.5, 2.7 Hz, 1H), 7.15-7.07 (m, 2H), 6.93 (ddd, *J* = 8.6, 3.8, 2.2 Hz, 2H), 6.57 (td, *J* = 7.7, 1.3 Hz, 1H), 6.42 (dd, *J* = 8.1, 1.2 Hz, 1H), 4.62 (d, *J* = 10.1 Hz, 1H), 4.04 (br s, 1H), 2.76 (qd, *J* = 13.1, 6.5 Hz, 1H), 1.20 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 161.6 (d, J_{C-F} = 248.7 Hz), 146.4, 140.1 (d, J_{C-F} = 3.6 Hz), 136.7 (d, J_{C-F} = 7.6 Hz), 131.7, 129.0 (d, J_{C-F} = 8.1 Hz), 128.3, 119.0 (d, J_{C-F} = 21.9 Hz), 118.5, 118.4, 116.0, 114.9 (d, J_{C-F} = 20.8 Hz), 64.8, 31.1, 21.0, 20.4.

^{19}F-NMR (282 MHz, $CDCl_3$): δ -114.79

HRMS (ESI$^+$): Calculated for $C_{16}H_{16}FNS$ [M + H]$^+$: 274.0987, found: 274.1060

11-Isopropyl-3-methoxy-10,11-dihydrodibenzo[*b,f*][1,4]thiazepine (3qa)



3qa

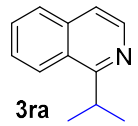
General procedure was followed using 3-methoxy-10,11-dihydro dibenzo[*b,f*][1,4]thiazepine **1q** (30.2 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.). After column chromatography purification (silica gel, Cyhex:EtOAc 93:7), dihydrodibenzothiazepine **3qa** was obtained in 65% yield (23.2 mg, white solid).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.15 (d, *J* = 7.8 Hz, 1H), 7.08-7.03 (m, 2H), 6.95-6.88 (m, 1H), 6.78 (dd, *J* = 8.4, 2.7 Hz, 1H), 6.56 (t, *J* = 7.5 Hz, 1H), 6.42 (d, *J* = 8.1 Hz, 1H), 4.56 (d, *J* = 10.1 Hz, 1H), 4.07 (br s, 1H, NH), 3.79 (s, 3H), 2.79 (m, 1H), 1.20 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 6.5 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 158.8, 146.7, 136.4, 135.8, 131.7, 128.7, 128.1, 118.3, 118.1, 117.0, 116.4, 114.0, 64.9, 55.5, 31.3, 21.0, 20.5.

HRMS (ESI$^+$): Calculated for $C_{17}H_{19}NOS$ [M + H]$^+$: 286.1187, found: 286.1260

1-Isopropylisoquinoline (3ra)[6]

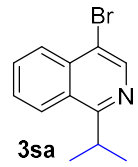


3ra

General procedure with isoquinoline **1r** (16.1 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.) afforded compound **3ra** after column chromatography purification (silica gel, Cyhex:EtOAc 88:12) in 24% yield (5.1 mg, white solid).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.49 (d, *J* = 5.7 Hz, 1H), 8.23 (d, *J* = 8.3 Hz, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.70-7.63 (m, 1H), 7.63-7.56 (m, 1H), 7.50 (d, *J* = 5.7 Hz, 1H), 3.97 (hept, *J* = 6.7 Hz, 1H), 1.45 (d, *J* = 6.8 Hz, 6H).

4-Bromo-1-isopropylisoquinoline (3sa)[5]

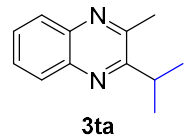


3sa

General procedure was followed using 4-bromoisoquinoline **1s** (26.0 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.). After column chromatography purification (silica gel, Cyhex:EtOAc 90:10), 4-bromo-1-isopropylisoquinoline **3sa** was obtained in 24% yield (7.5 mg, white solid).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.67 (s, 1H), 8.21 (t, *J* = 8.6 Hz, 2H), 7.82-7.74 (m, 1H), 7.70-7.61 (m, 1H), 3.92 (hept, *J* = 6.8 Hz, 1H), 1.43 (d, *J* = 6.8 Hz, 6H).

2-Isopropyl-3-methylquinoxaline (3ta)[10]

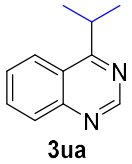


3ta

Following general procedure with 2-methylquinoxaline **1s** (16.1 µL, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.), compound **3ta** was obtained after column chromatography purification (silica gel, Cyhex:EtOAc 90:10) in a 22% yield (5.2 mg, white solid).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.05-7.94 (m, 1H), 7.68-7.63 (m, 1H), 3.44 (m, 1H), 2.80 (s, 3H), 1.40 (d, *J* = 6.8 Hz, 6H).

4-Isopropylquinazoline (3ua)[5]

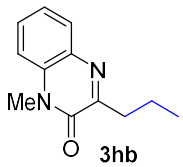


3ua

General procedure with quinazoline **1u** (16.3 mg, 0.125 mmol, 1.0 equiv.) and isopropylsulfonyl chloride **2a** (56.2 µL, 0.5 mmol, 4.0 equiv.) afforded compound **3ua** after column chromatography purification (silica gel, Cyhex:EtOAc 50:50) in 17% yield (3.7 mg, white solid).

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.28 (s, 1H), 8.20 (br d, *J* = 8.6 Hz, 1H), 8.07 (br d, *J* = 8.4 Hz, 1H), 7.89 (t, *J* = 7.0 Hz, 1H), 7.65 (t, *J* = 8.2 Hz, 1H), 3.95 (m, 1H), 1.45 (d, *J* = 6.8 Hz, 6H).

1-Methyl-3-propylquinoxalin-2(1*H*)-one (3hb)[11]

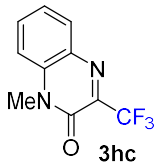


3hb

General procedure was followed using 1-methylquinoxalin-2(1*H*)-one **1h** (20.0 mg, 0.125 mmol, 1.0 equiv.) and propylsulfonyl chloride **2b** (56.3 µL, 0.5 mmol, 4.0 equiv.). Quinoxalinone **3hb** was obtained in 16% yield (4.1 mg, white solid) after column chromatography purification (silica gel, Cyhex:EtOAc 85:15).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.83 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.56-7.49 (m, 1H), 7.37-7.27 (m, 2H), 3.70 (s, 3H), 2.93 (t, *J* = 7.4 Hz, 2H), 1.83 (sext, *J* = 7.4 Hz, 2H), 1.05 (t, *J* = 7.4 Hz, 3H).

3-(Trifluoromethyl)-1-methylquinoxalin-2(1*H*)-one (3hc)[12]

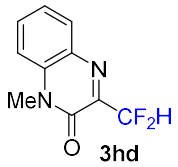


3hc

Following general procedure (including in this case the addition of 1 equivalent of trifluoroacetic acid in pump A) with 1-methylquinoxalin-2(1*H*)-one **1h** (20.0 mg, 0.125 mmol, 1.0 equiv.) and (trifluoromethyl)sulfonyl chloride **2c** (53.2 µL, 0.5 mmol, 4.0 equiv.), compound **3hc** was obtained after column chromatography purification (silica gel, Cyhex:EtOAc 80:20) in a 45% yield (12.8 mg, yellow solid).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.00 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.78-7.70 (m, 1H), 7.49-7.42 (m, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 3.76 (s, 3H).

3-(Difluoromethyl)-1-methylquinoxalin-2(1*H*)-one (3hd)[1]

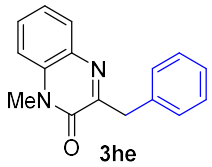


3hd

General procedure with 1-methylquinoxalin-2(1*H*)-one **1h** (20.0 mg, 0.125 mmol, 1.0 equiv.) and difluoromethylsulfonyl chloride **2d** (44.4 µL, 0.5 mmol, 4.0 equiv.) afforded compound **3hd** after column chromatography purification (silica gel, Cyhex:EtOAc 75:25) in 27% yield (7.5 mg, white solid).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.01 (d, *J* = 8.2 Hz, 1H), 7.70 (t, *J* = 7.9 Hz, 1H), 7.42 (m, 2H), 6.97 (t, *J* = 53.7 Hz, 1H), 3.75 (s, 3H).

3-Benzyl-1-methylquinoxalin-2(1*H*)-one (3he)[8]

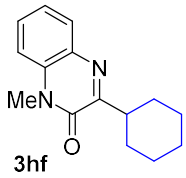


3he

General procedure was followed using 1-methylquinoxalin-2(1*H*)-one **1h** (20.0 mg, 0.125 mmol, 1.0 equiv.) and benzylsulfonyl chloride **2e** (95.3 mg, 0.5 mmol, 4.0 equiv.). After column chromatography purification (silica gel, Cyhex:EtOAc 85:15), quinoxalinone **3he** was obtained in 40% yield (12.5 mg, yellow solid) at a flow rate of 612 µL min^{-1} (3 minutes 15 seconds Zn column residence time and 6.5 minutes photoreactor residence time).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.1 Hz, 1H), 7.57-7.45 (m, 3H), 7.36-7.29 (m, 4H), 7.25-7.15 (m, 1H), 4.27 (s, 2H), 3.67 (s, 3H).

3-Cyclohexyl-1-methylquinoxalin-2(1*H*)-one (3hf)[13]



3hf

General procedure with 1-methylquinoxalin-2(1*H*)-one **1h** (20.0 mg, 0.125 mmol, 1.0 equiv.) and cyclohexylsulfonyl chloride **2f** (72.5 µL, 0.5 mmol, 4.0 equiv.) afforded compound **3hf** after column chromatography purification (silica gel, Cyhex:EtOAc 89:11) in 55% yield (16.7 mg, white solid).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.83 (d, *J* = 7.9 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.36-7.28 (m, 2H), 3.69 (s, 3H), 3.39-3.28 (m, 1H), 2.00-1.72 (m, 5H), 1.67-1.38 (m, 4H), 1.38-1.22 (m, 1H).

Continuous synthesis of heterocycle 3ia

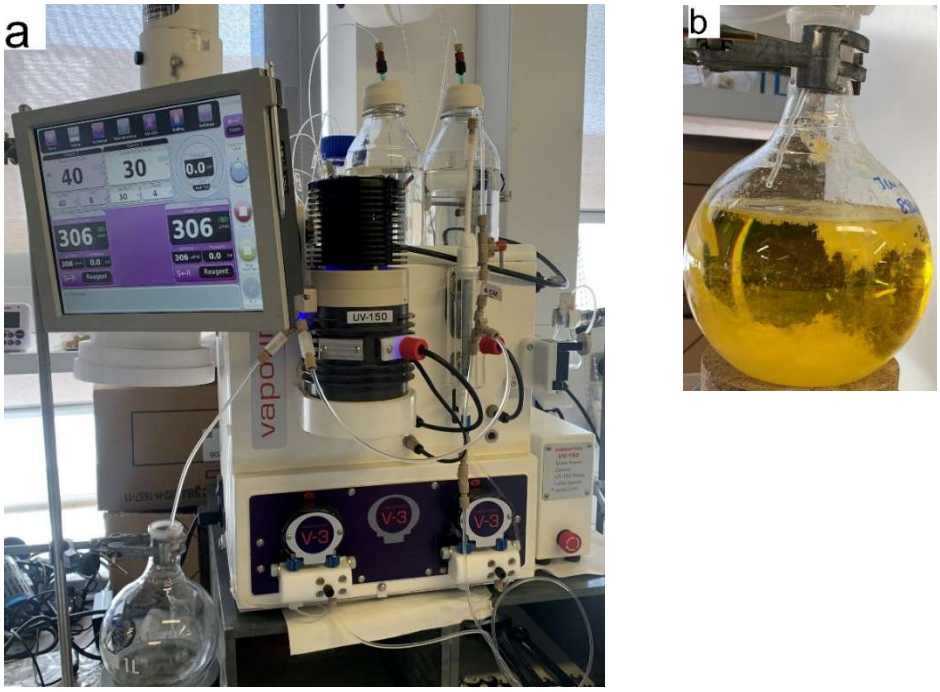


Figure S2 a. Flow system assembly for the 11.0 mmol reaction scale. **b.** Collector flask with product **3ia** during reaction course.

Activating solution:[3] 1,2-dibromoethane (227.6 µL, 2.4 mmol, 0.24 M) and chlorotrimethylsilane (837.6 µL, 6.0 mmol, 0.6 M) were dissolved in an oven-dried vial equipped with a septum using 10 mL of acetone. Solution was bubbled with nitrogen for 10 minutes.

Solution A: heterocycle **1i** (1605.7 mg, 11.0 mmol, 1.0 equiv.) and $(NH_4)_2S_2O_8$ (7530.6 mg, 33.0 mmol, 3.0 equiv.) were added to an oven-dried flask equipped with a septum. An acetone/water 1/1 mixture was added (440 mL), and the solution was homogenized by sonication in an ultrasound bath.

Solution B: isopropyl sulfonyl chloride **2a** (4940.5µL, 44.0 mmol, 4.0 equiv.) was dissolved in an oven-dried flask equipped with a septum with an acetone/water 1/1 mixture (440 mL). The solution was homogenized by sonication in an ultrasound bath.

Solvent was pumped through using both pumps at a flow rate of 1 mL min^{-1} in order to purge the whole system (approximately 10 minutes). Then, activating solution was pumped through the zinc column at a flow rate of 1 mL min^{-1}. Ethylene gas evolution is observed due to zinc

activation. Once the addition is finished, solvent is pumped through the column at 1 mL min^{-1} to homogenize the system and avoid ethylene bubbles during reaction (approximately 3-5 minutes).

The reaction was performed by setting column temperature at 30 °C and reactor temperature at 40 °C. Then, solutions A and B were pumped through the system for 24 hours at 306 µL min^{-1} (6.5 minutes Zn column residence time and 13 minutes photoreactor residence time), and the reactor was irradiated with blue LEDs (450 nm, 24 W total power). During crude collection, product **3ia** precipitates in the solvent media. After reaction completion, the solid was filtrated and washed with 2 x 5 mL of cold water, obtaining heterocycle **3ia** in a 75% yield (1552.9 mg, white solid, 8.25 mmol day^{-1} production).

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NMR spectra

1-Methylquinoxalin-2(1*H*)-one (1h)

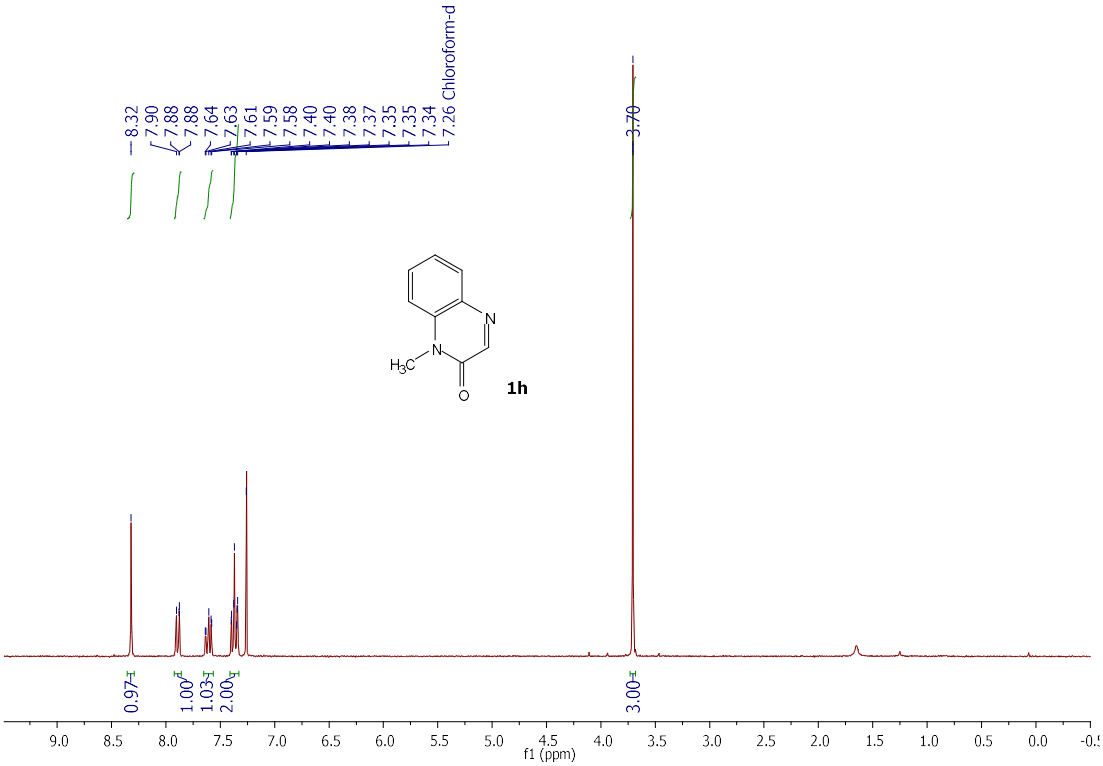

Figure S3. ^{1}H-NMR spectrum of **1h**

7-Methyldibenzo[*b,f*][1,4]oxazepine (1k)

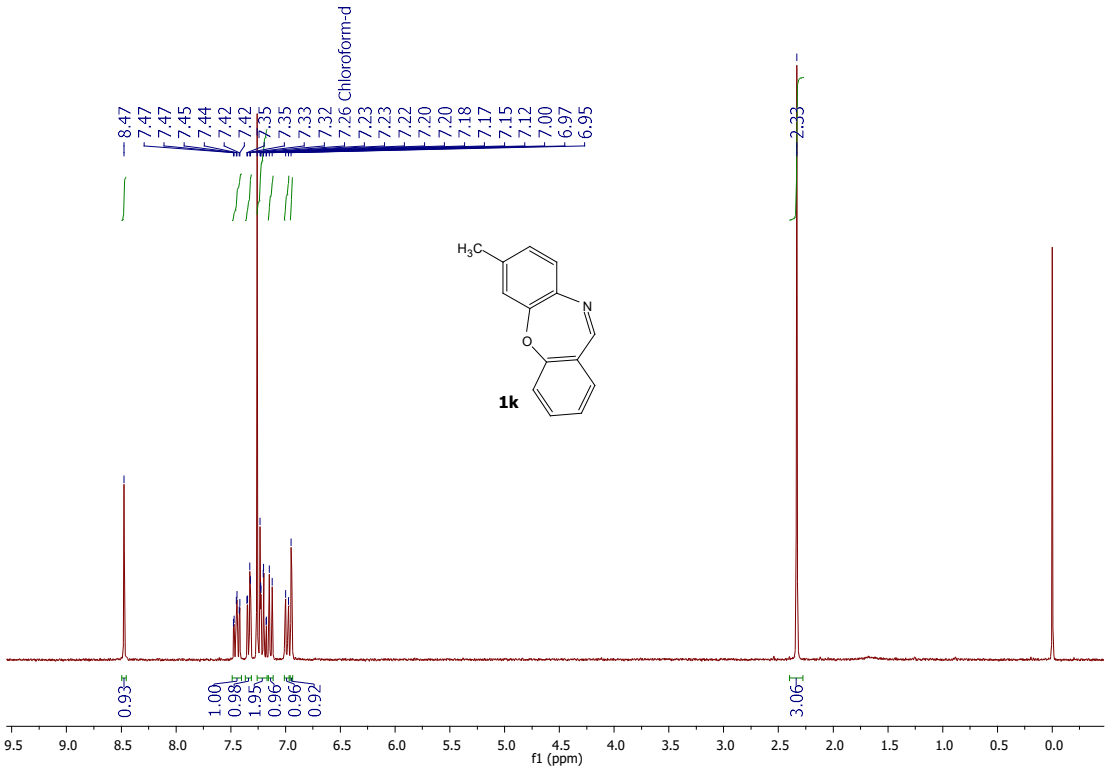

Figure S4 ^{1}H-NMR spectrum of **1k**

8-Methoxydibenzo[*b,f*][1,4]oxazepine (1l)

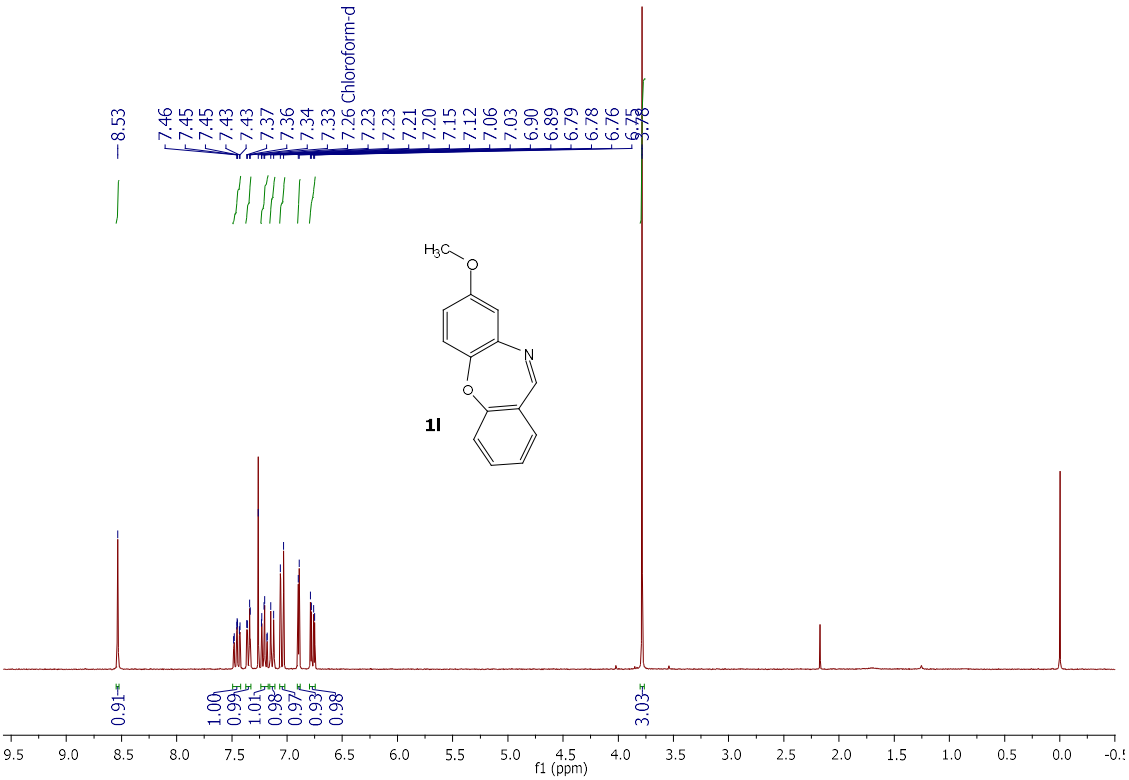

Figure S5. ^{1}H-NMR spectrum of **1l**

3-Methoxydibenzo[*b,f*][1,4]oxazepine (1m)

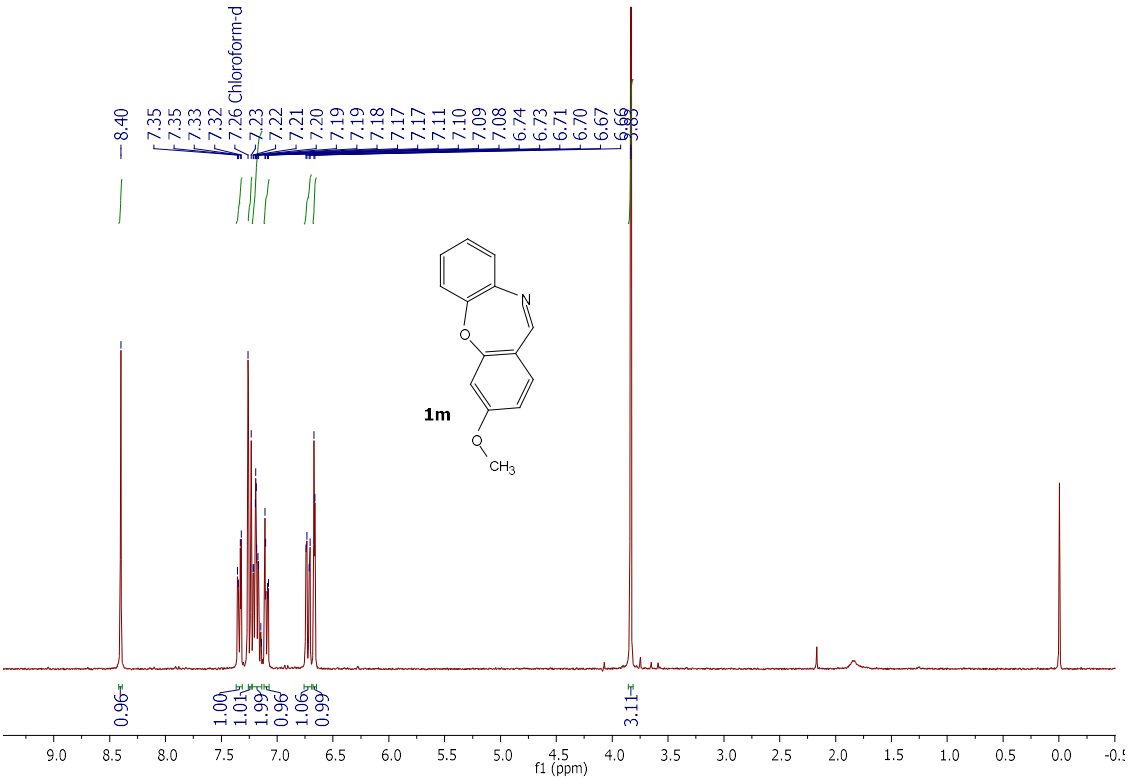

Figure S6. ^{1}H-NMR spectrum of **1m**

7-Fluorodibenzo[*b,f*][1,4]oxazepine (1n)

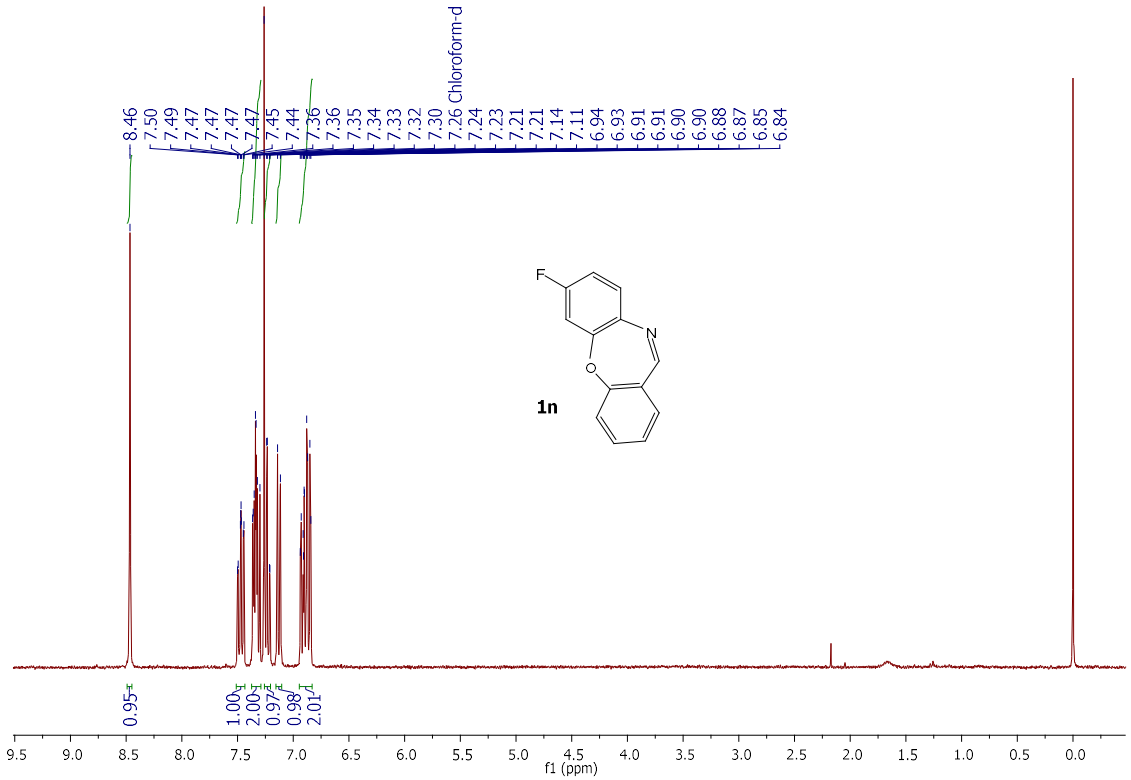

Figure S7. ^{1}H-NMR spectrum of **1n**

Dibenzo[*b,f*][1,4]thiazepine (1o)

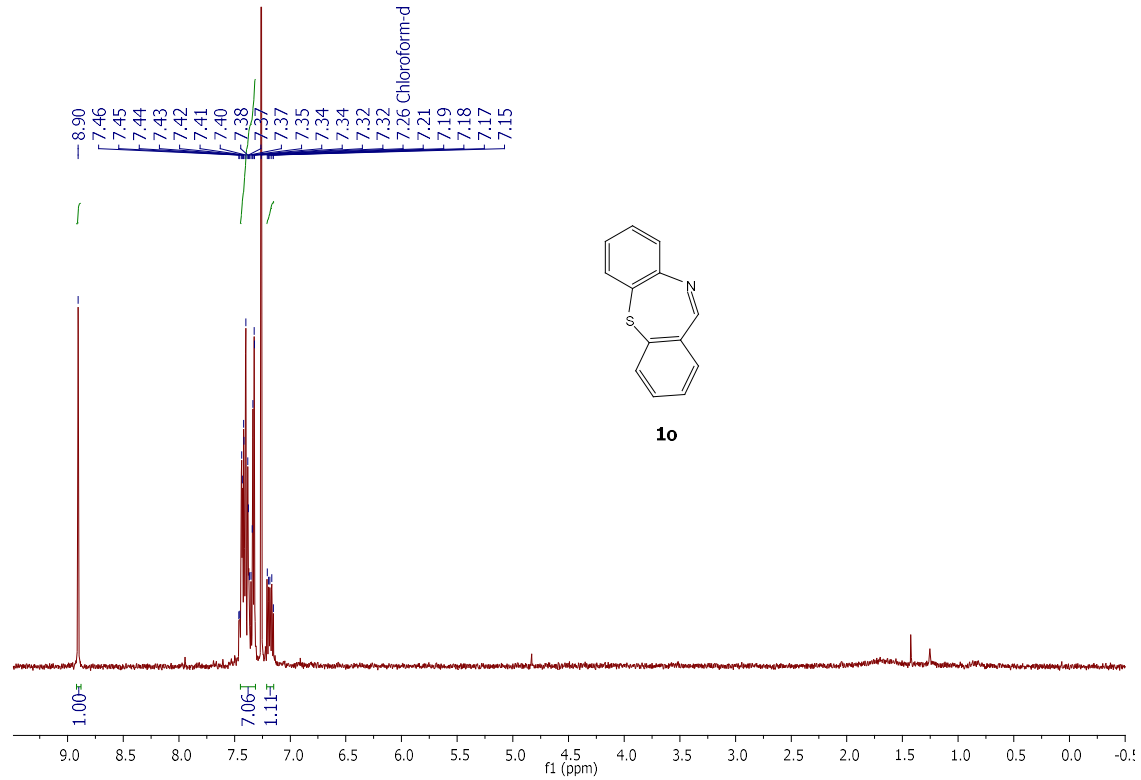

Figure S8. ^{1}H-NMR spectrum of **1o**

3-Fluorodibenzo[*b,f*][1,4]thiazepine (1p)

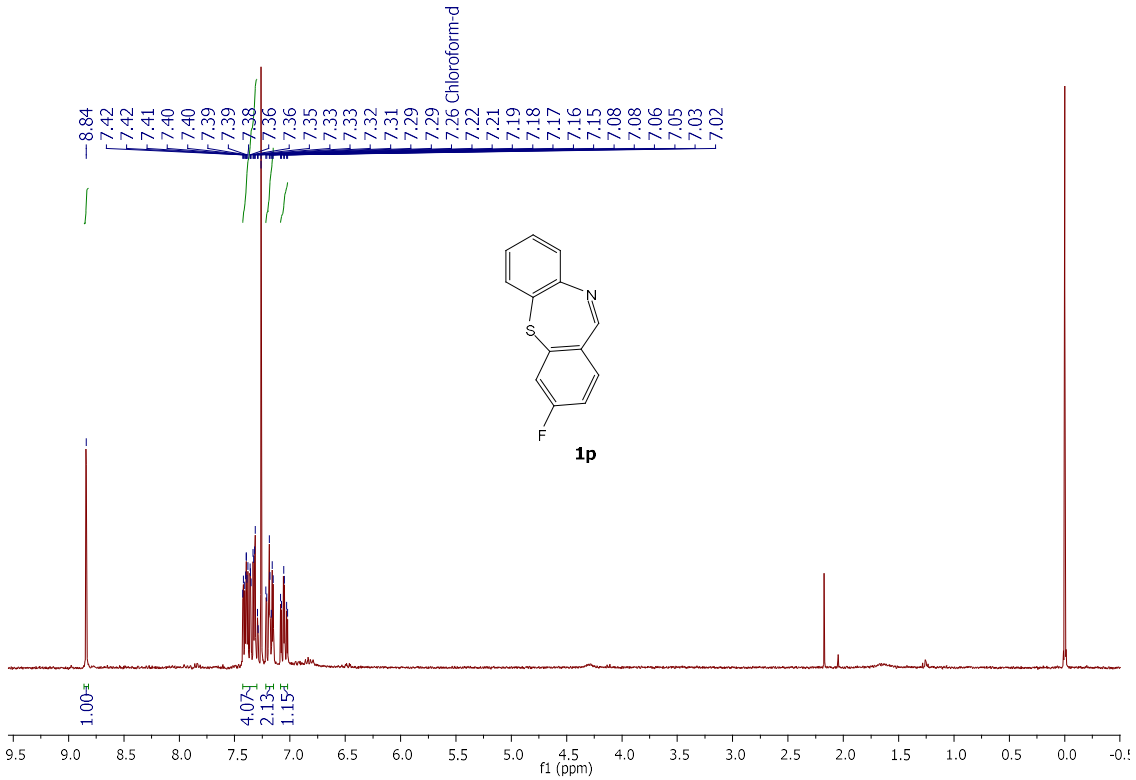

Figure S9. ^{1}H-NMR spectrum of **1p**

3-Methoxydibenzo[*b,f*][1,4]thiazepine (1q)

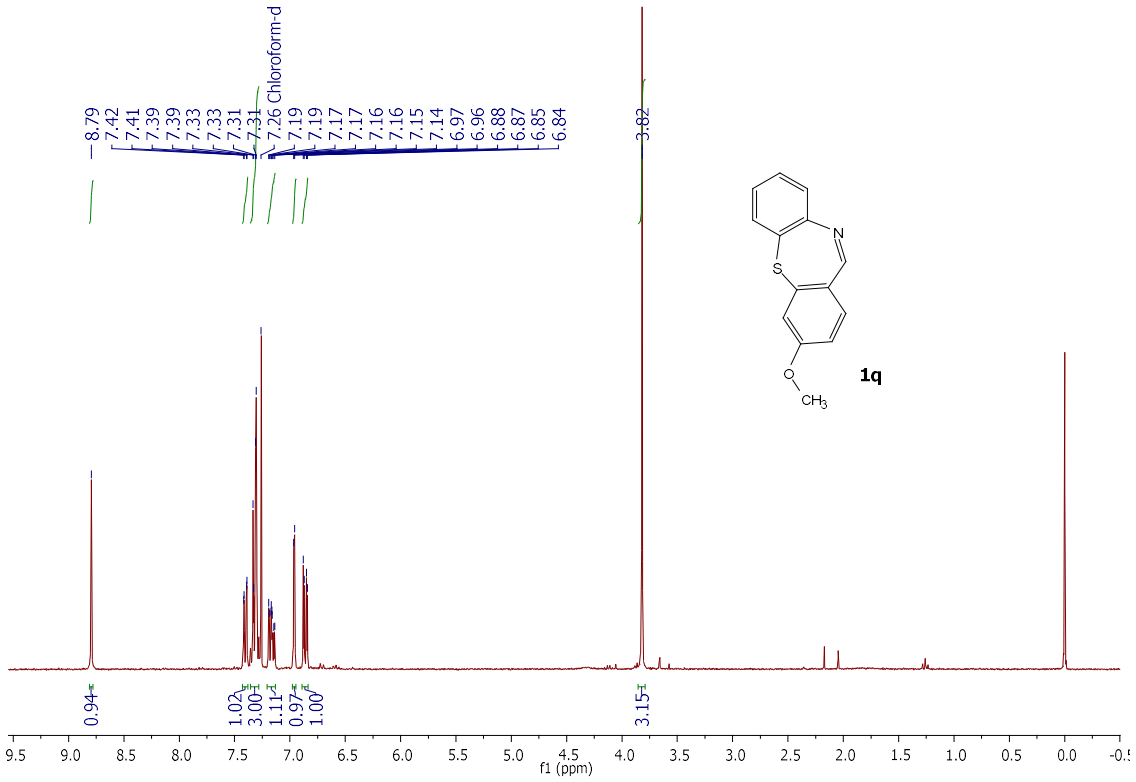

Figure S10. ^{1}H-NMR spectrum of **1q**

Isopropyl zinc sulfinate

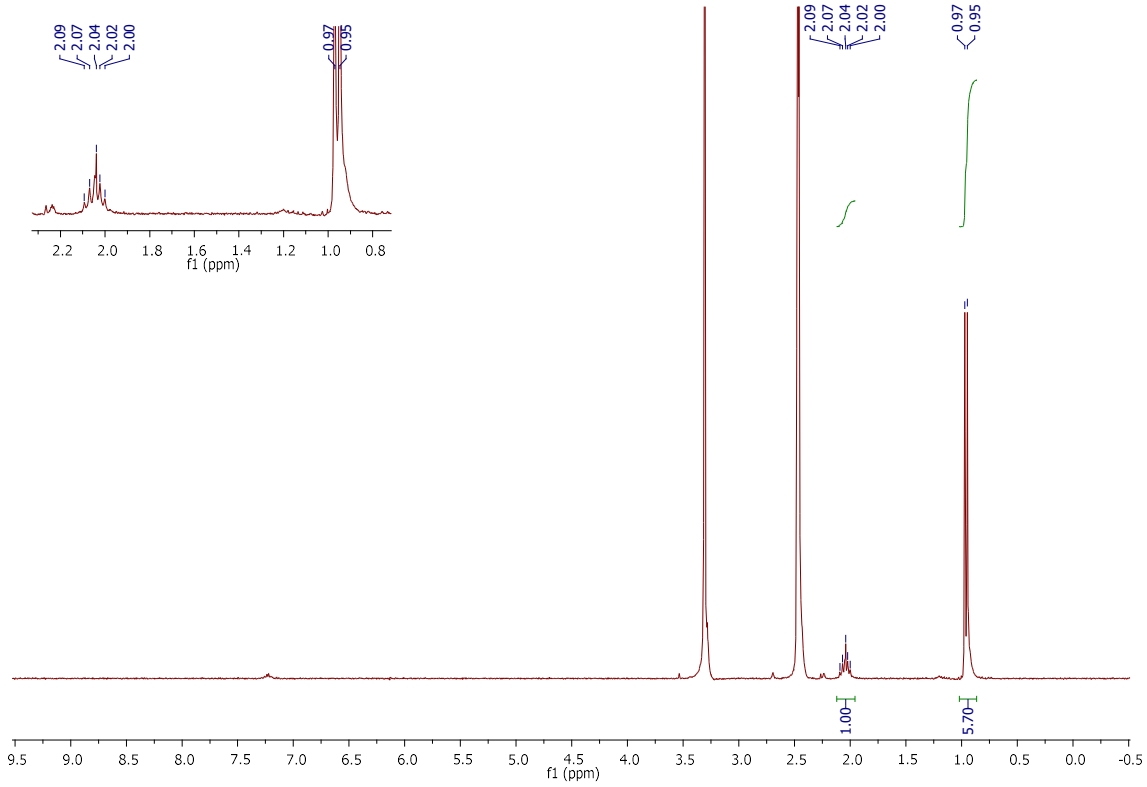

Figure S11. ^{1}H-NMR spectrum of isopropyl zinc sulfinate

6-Isopropylphenanthridine (3aa)

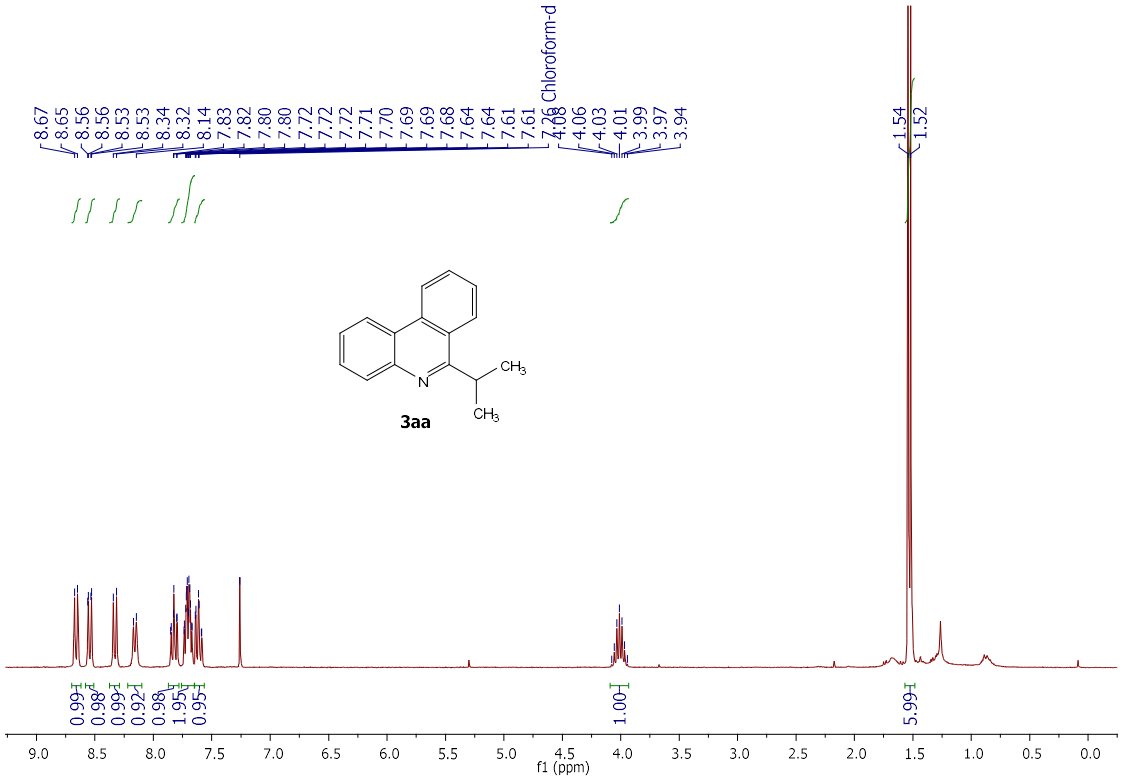

Figure S12. ^{1}H-NMR spectrum of **3aa**

4-Isopropyl-2-methylquinoline (3ba)

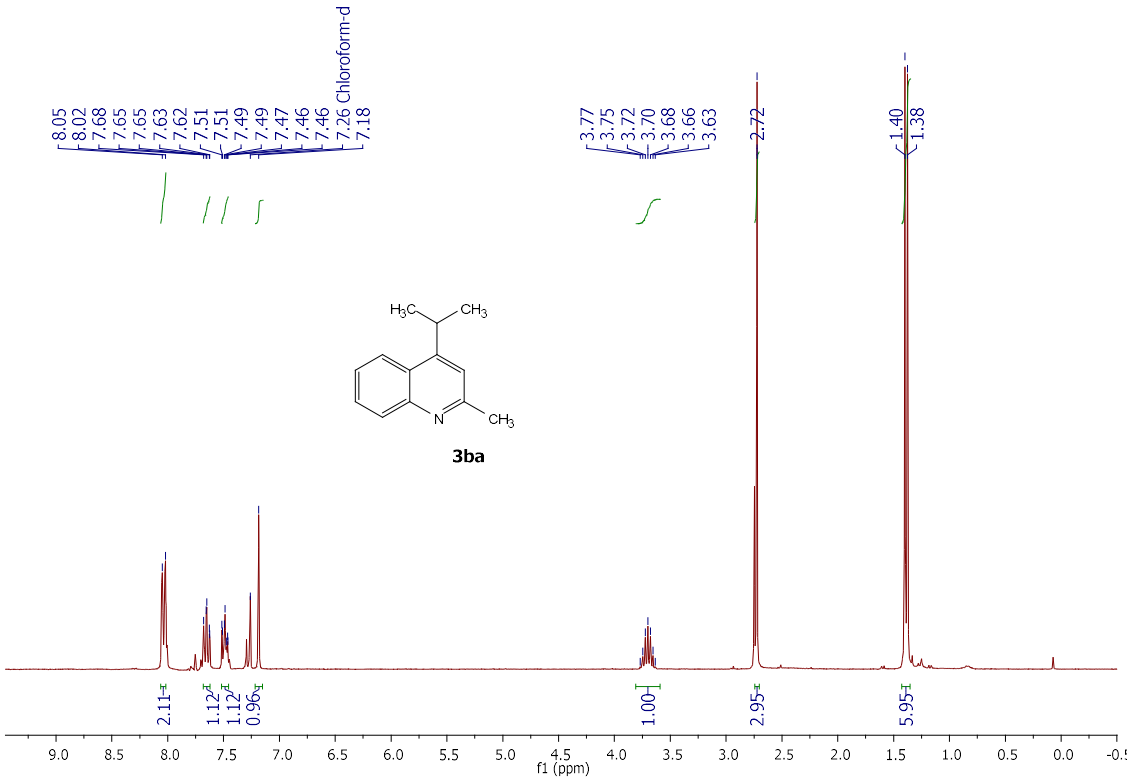

Figure S13. ^{1}H-NMR spectrum of **3ba**

4-Isopropyl-2-phenylquinoline (3ca)

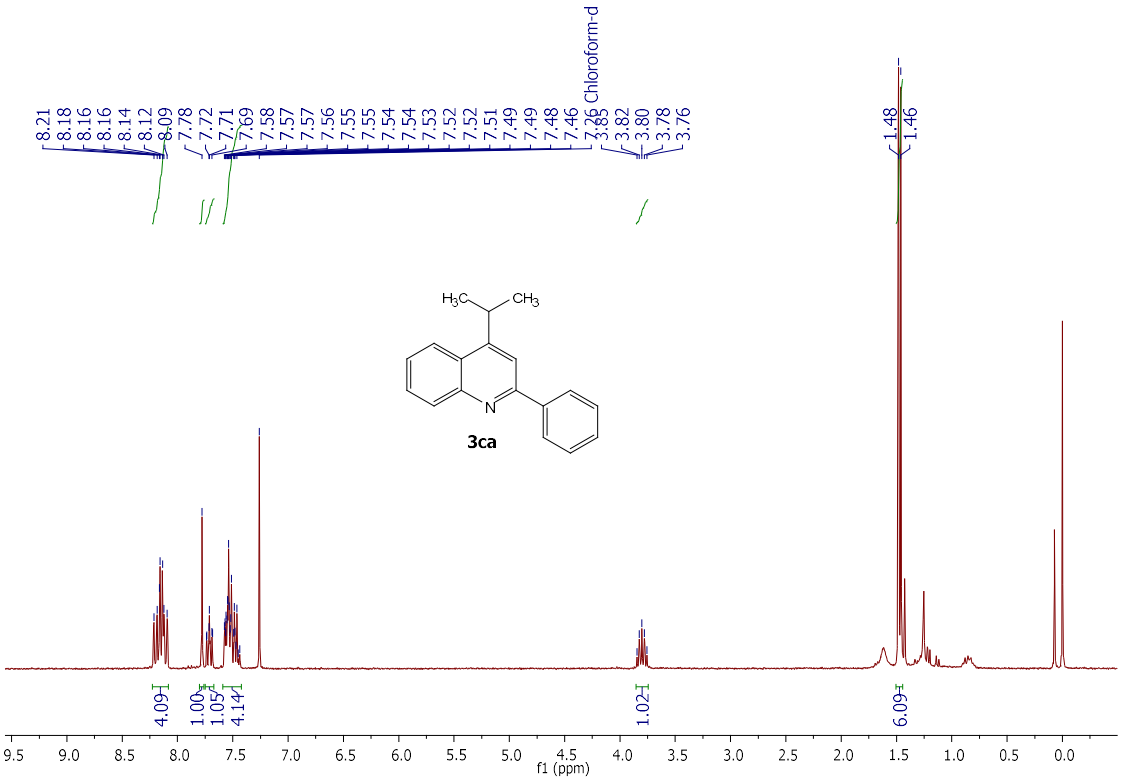

Figure S14. ^{1}H-NMR spectrum of **3ca**

6-Chloro-4-isopropyl-2-methylquinoline (3da)

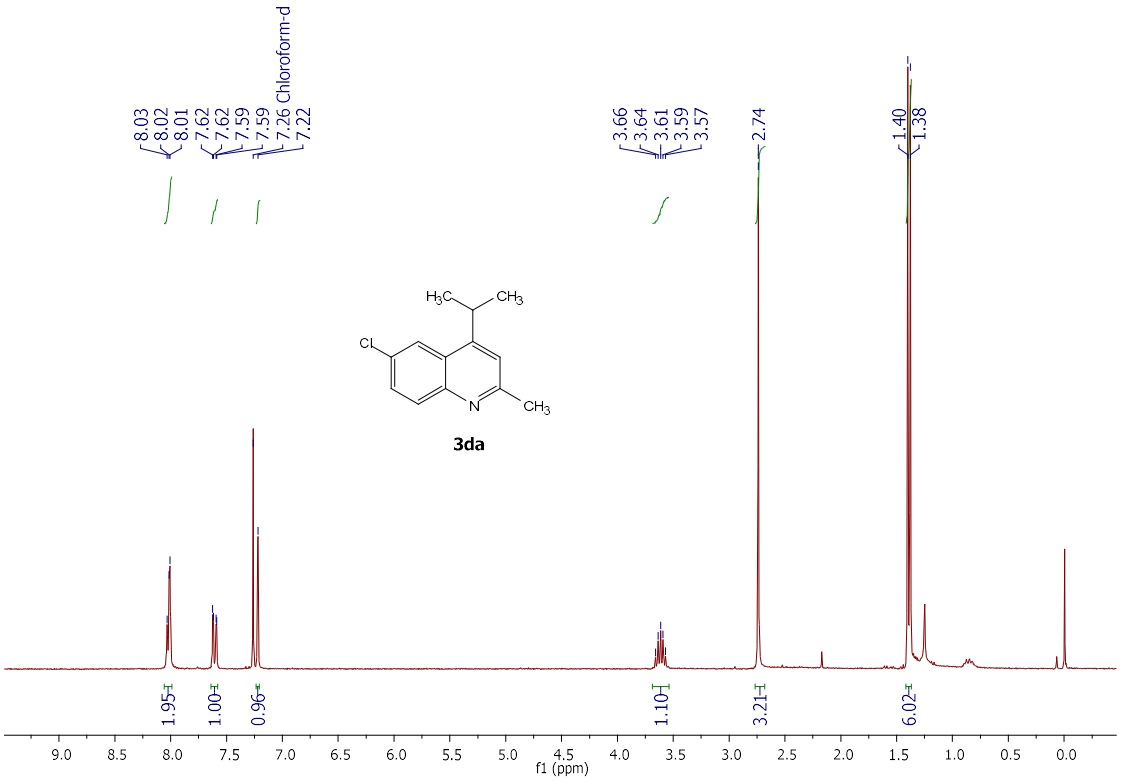

Figure S15. ^{1}H-NMR spectrum of **3da**

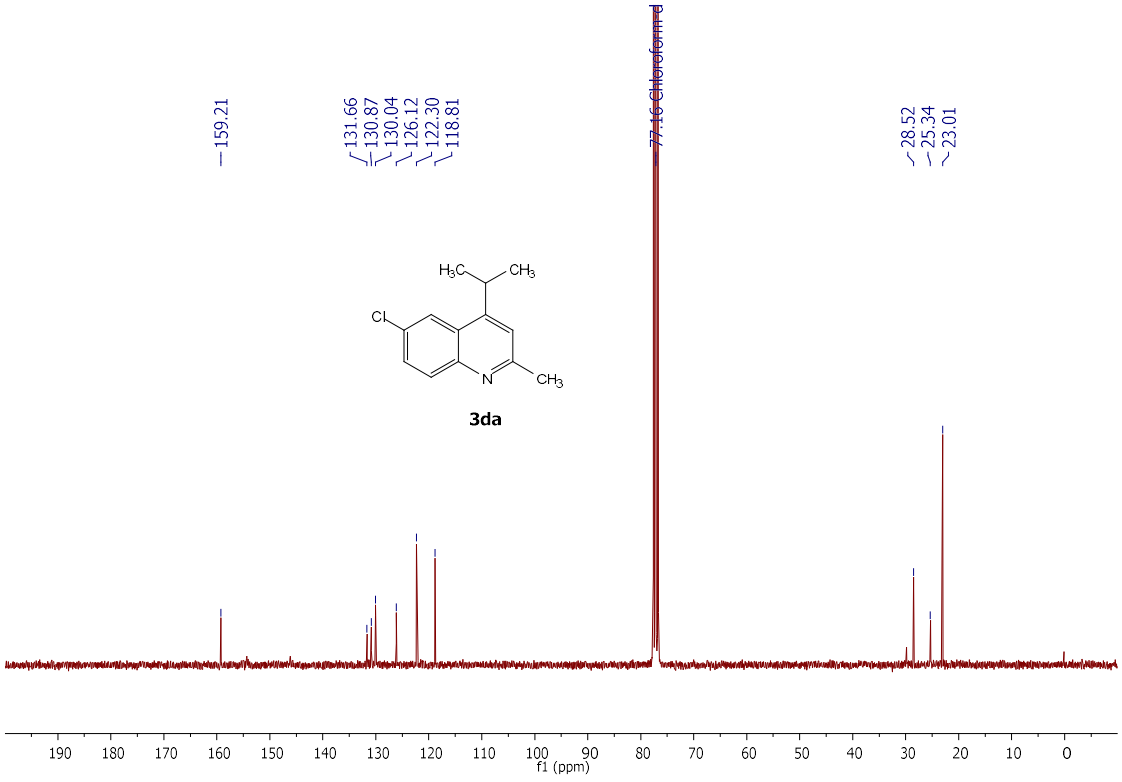

Figure S16. ^{13}C-NMR spectrum of **3da**

Methyl 4-isopropyl-2-methylquinoline-6-carboxylate (3ea)

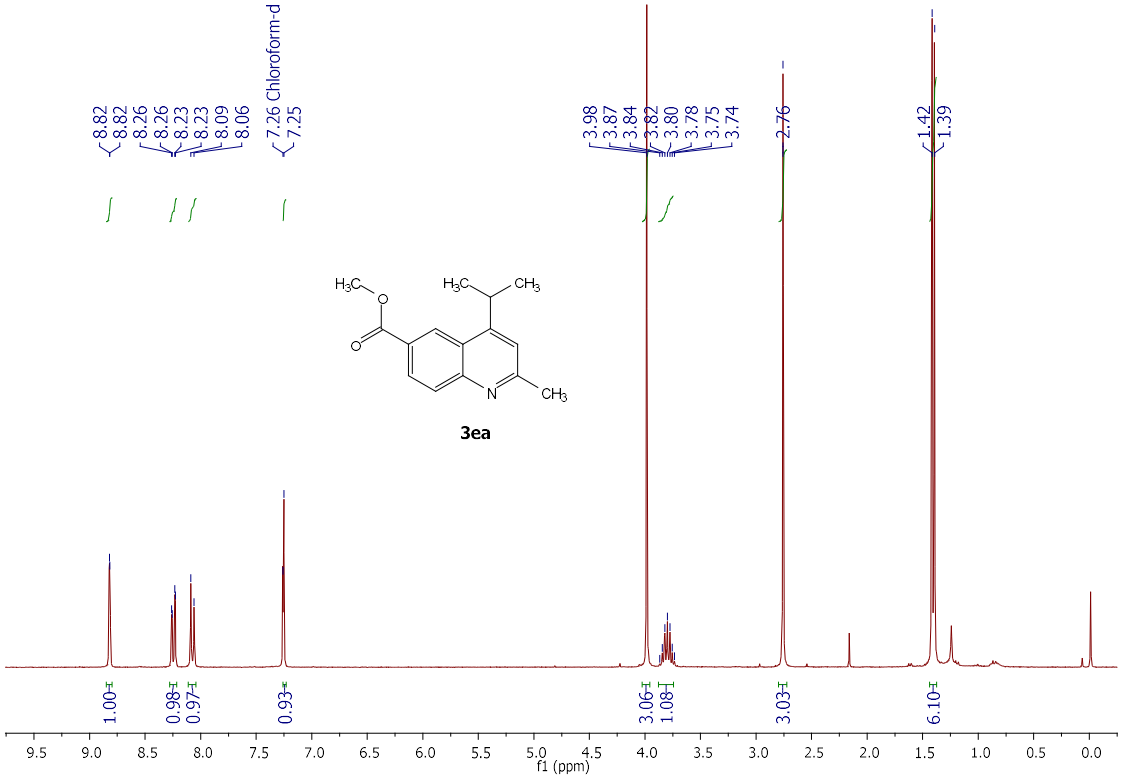

Figure S17. ^{1}H-NMR spectrum of **3ea**

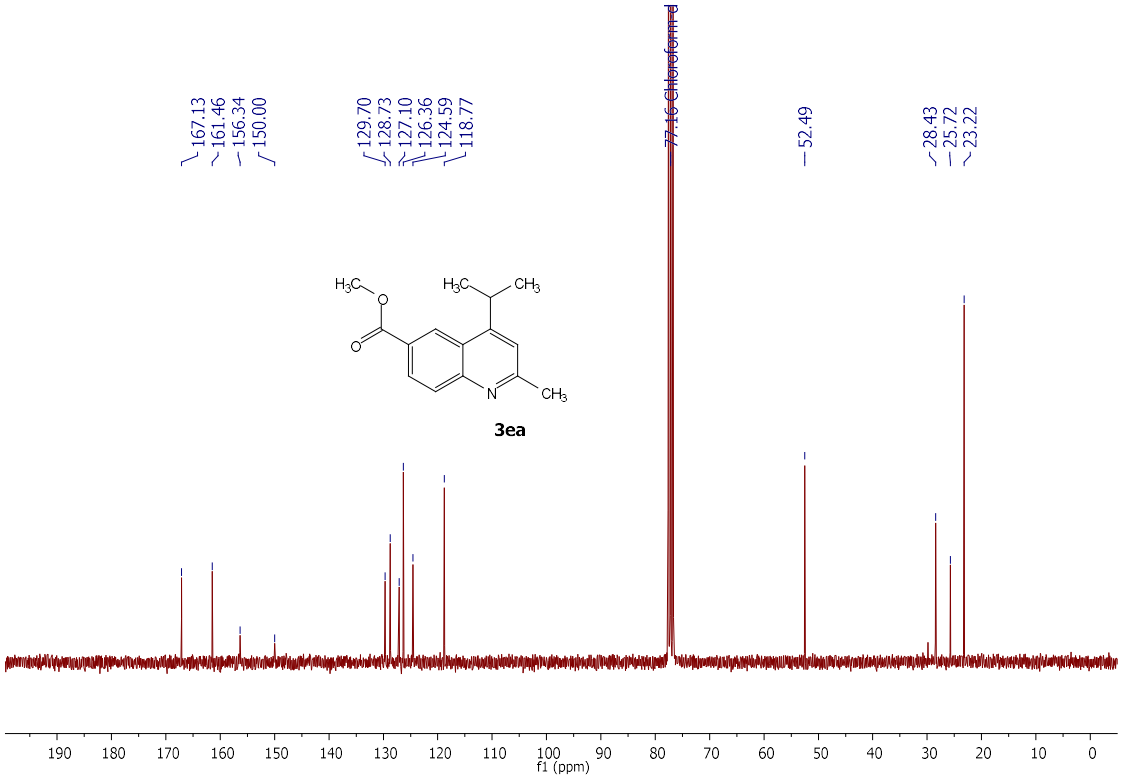

Figure S18. ^{13}C-NMR spectrum of **3ea**

2-Isopropyl-4-methylquinoline (3fa)

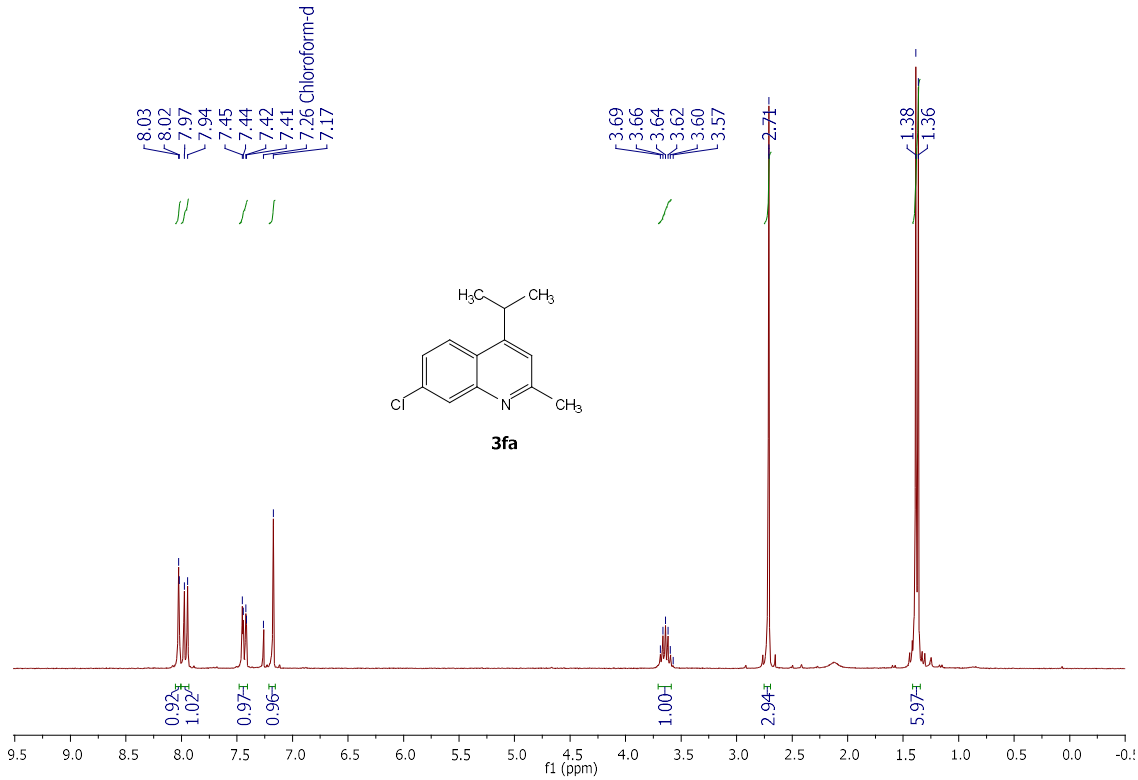

Figure S19. ^{1}H-NMR spectrum of **3fa**

7-Chloro-4-isopropyl-2-methylquinoline (3ga)

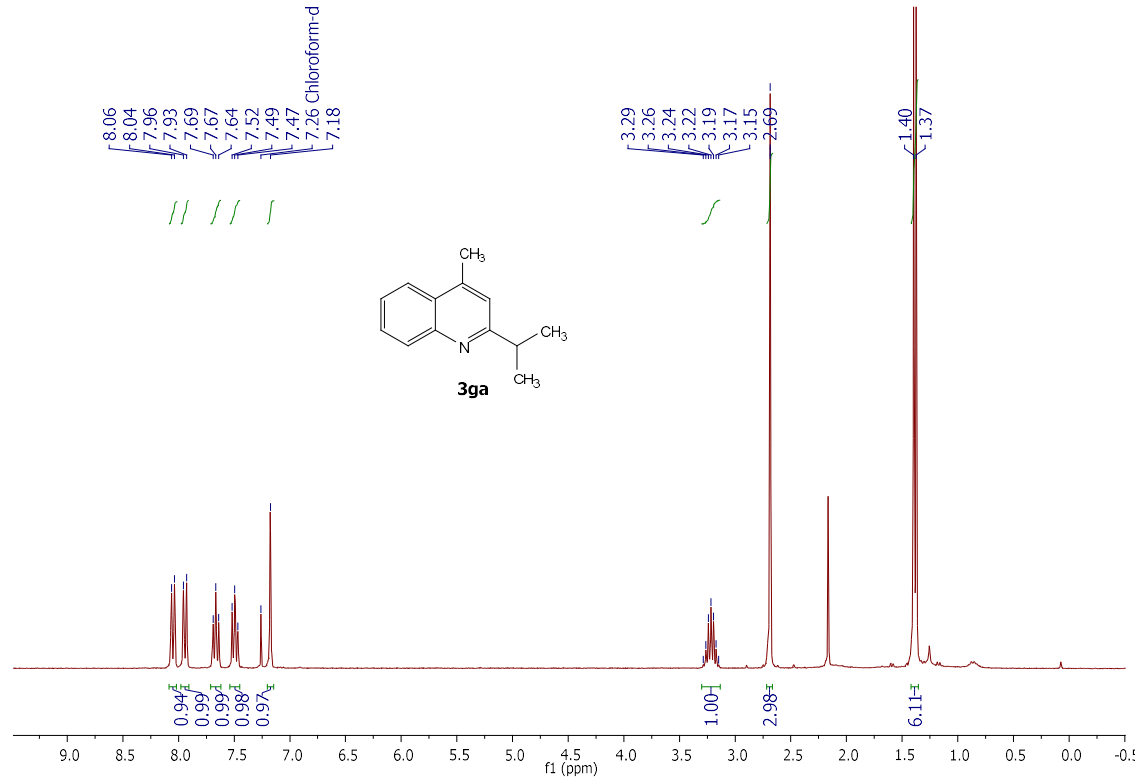

Figure S20. ^{1}H-NMR spectrum of **3ga**

3-Isopropyl-1-methylquinoxalin-2(1*H*)-one (3ha)

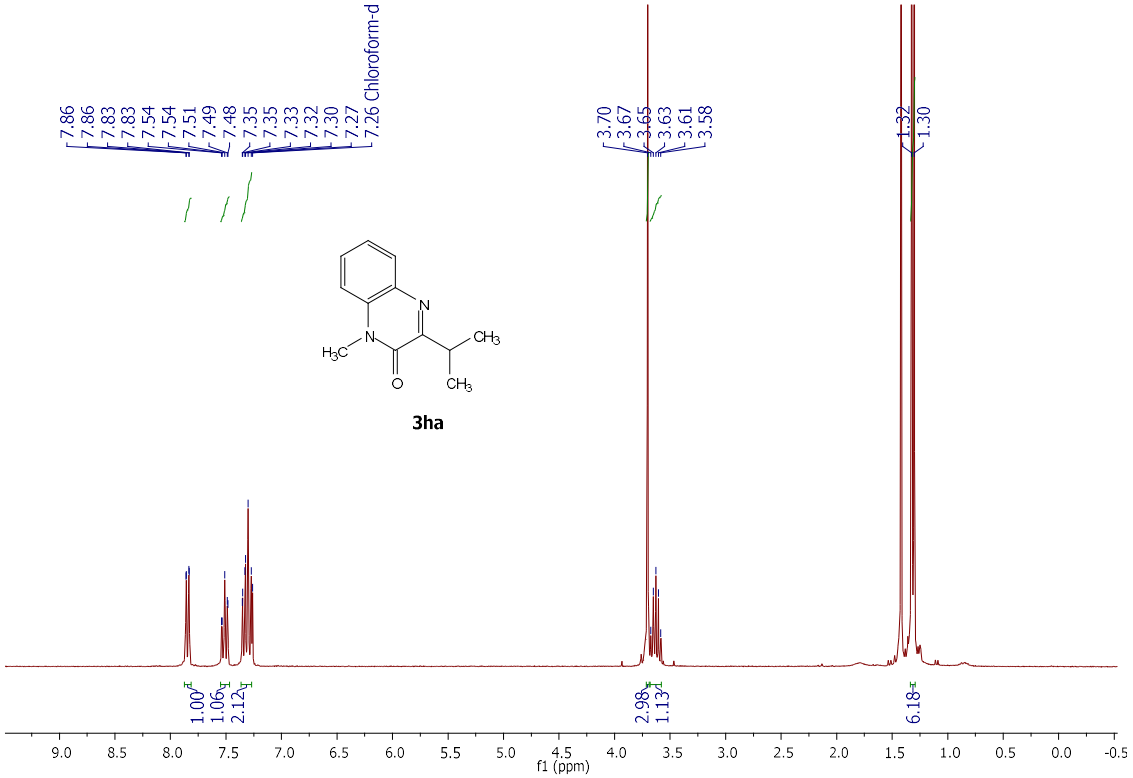

Figure S21. ^{1}H-NMR spectrum of **3ha**

3-Isopropylquinoxalin-2(1*H*)-one (3ia)

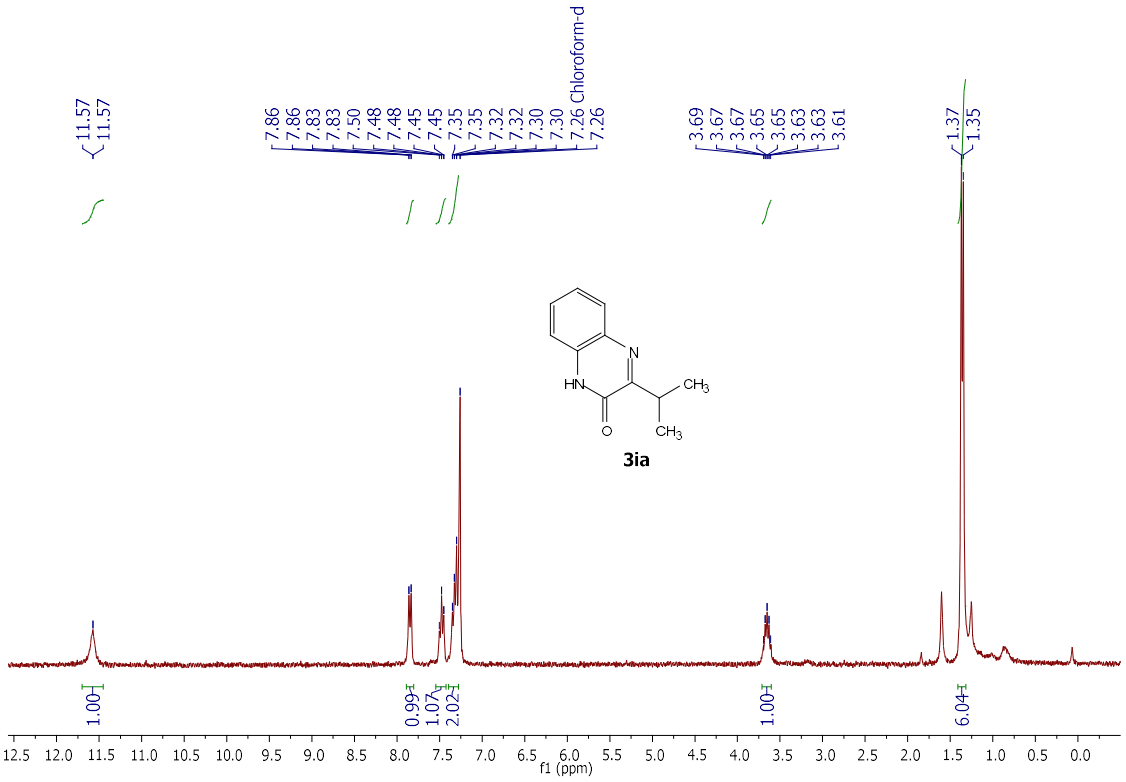

Figure S22. ^{1}H-NMR spectrum of **3ia**

Ethyl 2-isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (3ja)

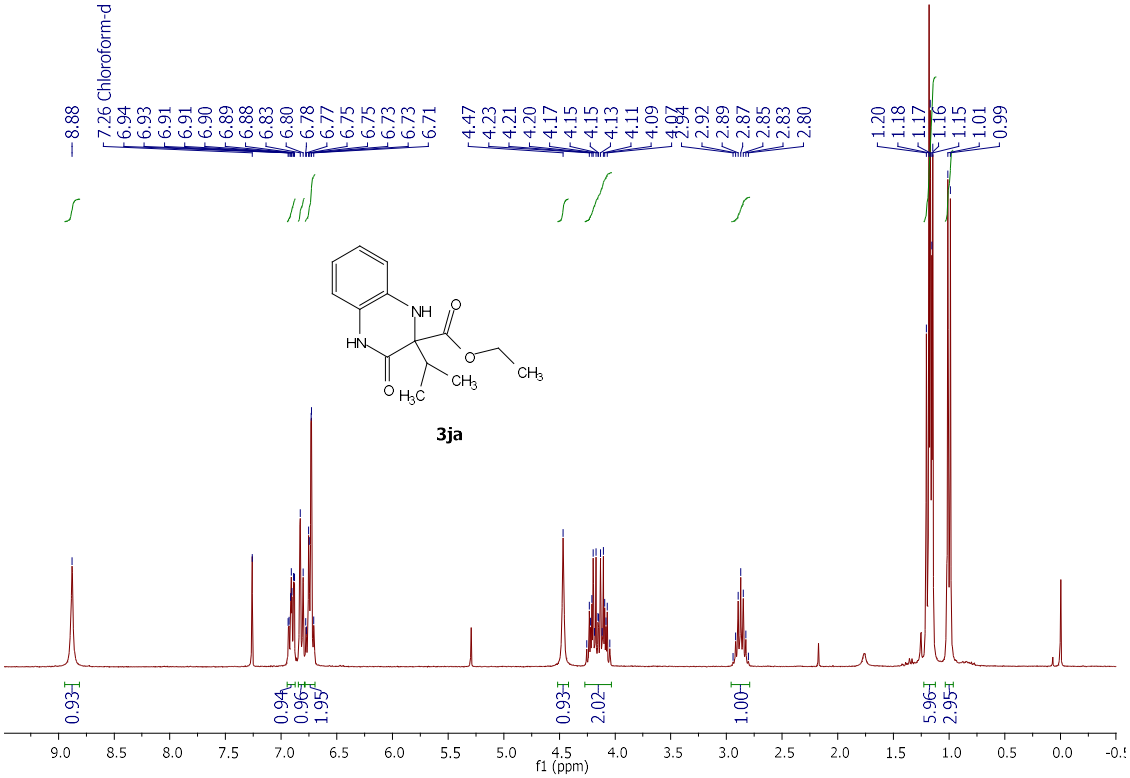

Figure S23. ^{1}H-NMR spectrum of **3ja**

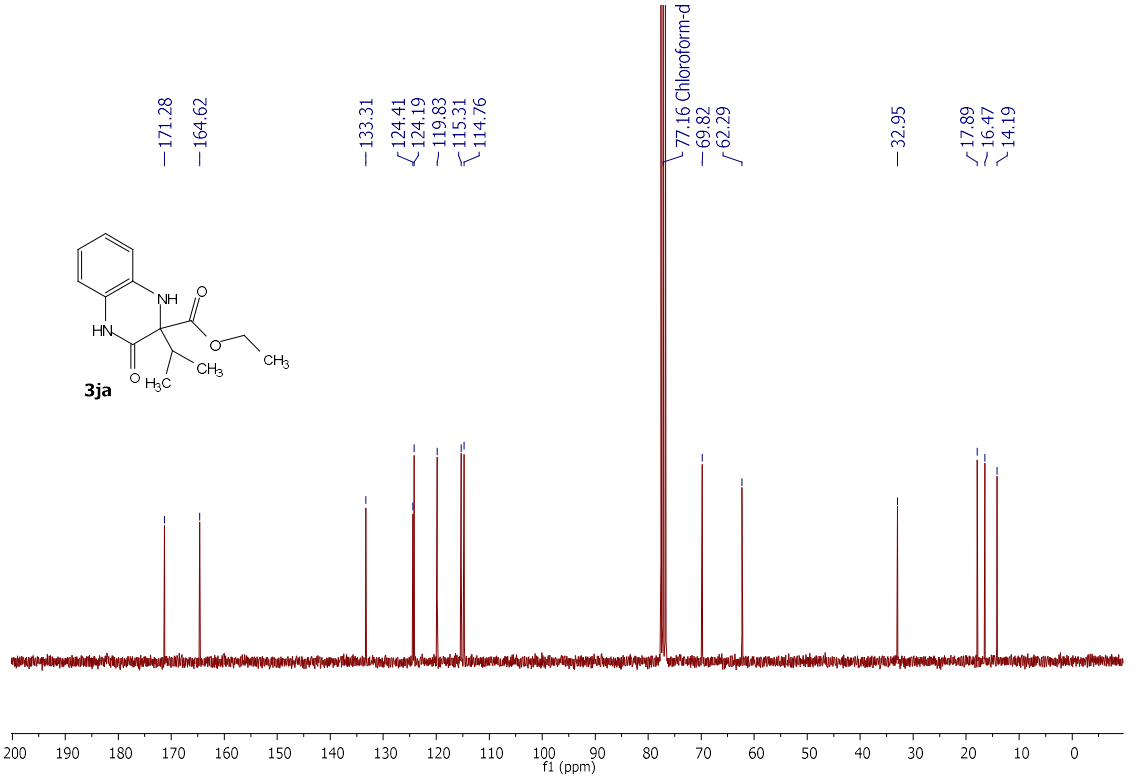

Figure S24. ^{13}C-NMR spectrum of **3ja**

11-Isopropyl-7-methyl-10,11-dihydrodibenzo[*b,f*][1,4]oxazepine (3ka)

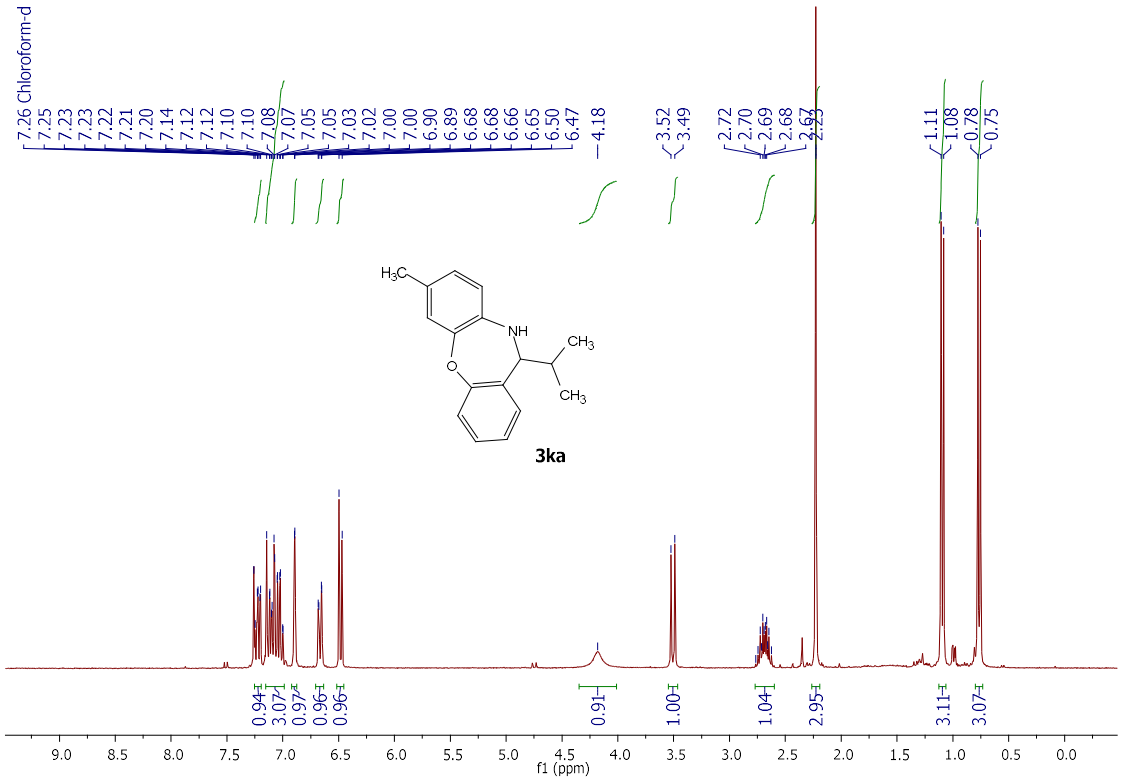

Figure S25. ^{1}H-NMR spectrum of **3ka**

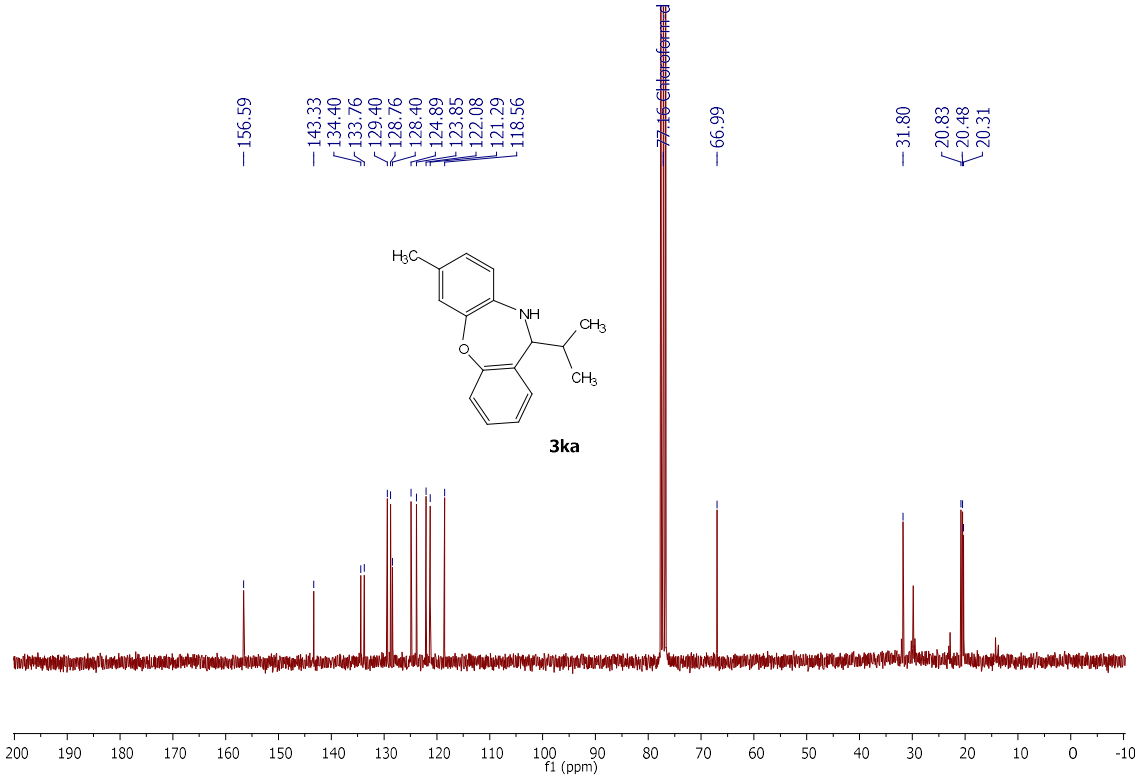

Figure S26. ^{13}C-NMR spectrum of **3ka**

11-Isopropyl-8-methoxy-10,11-dihydrodibenzo[*b,f*][1,4]oxazepine (3la)

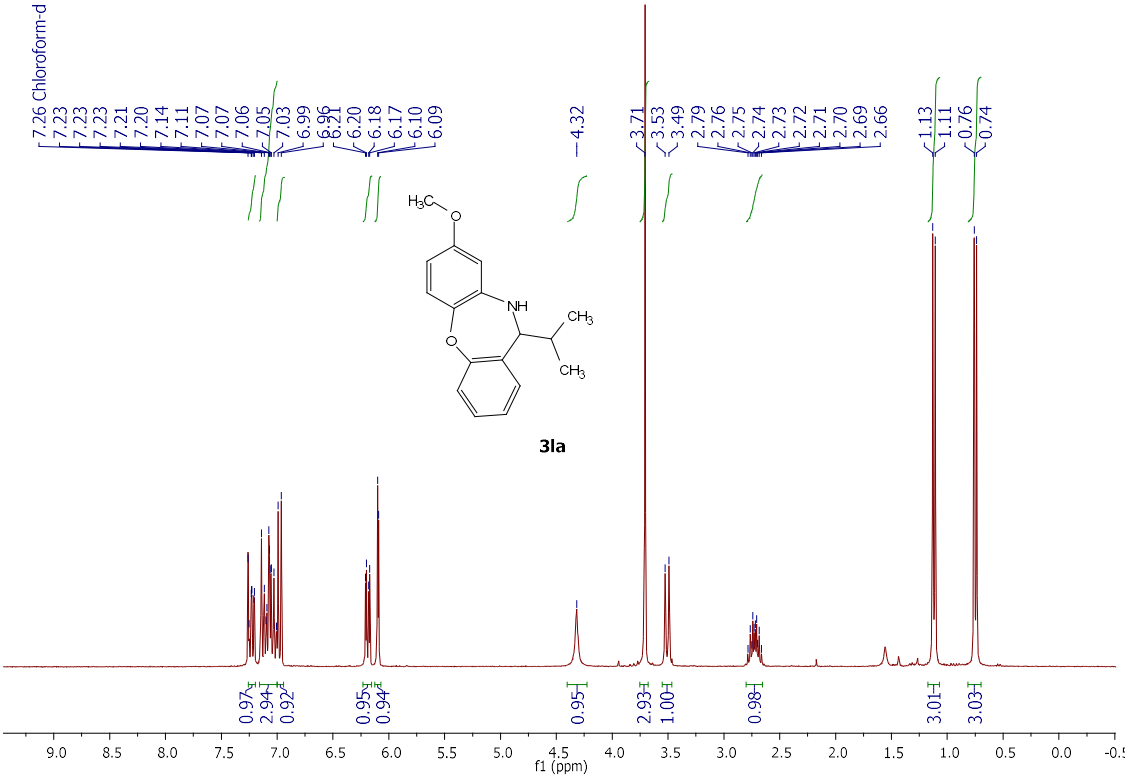

Figure S27. ^{1}H-NMR spectrum of **3la**

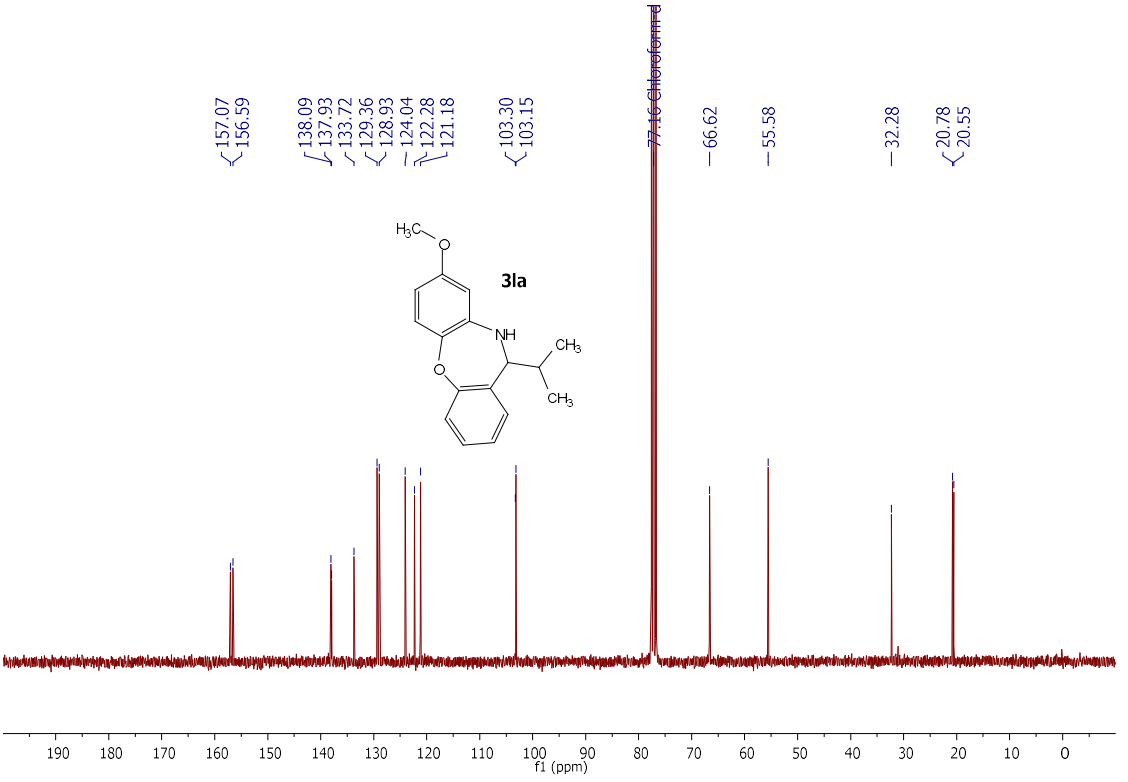

Figure S28. ^{13}C-NMR spectrum of **3la**

11-Isopropyl-3-methoxy-10,11-dihydrodibenzo[*b,f*][1,4]oxazepine (3ma)

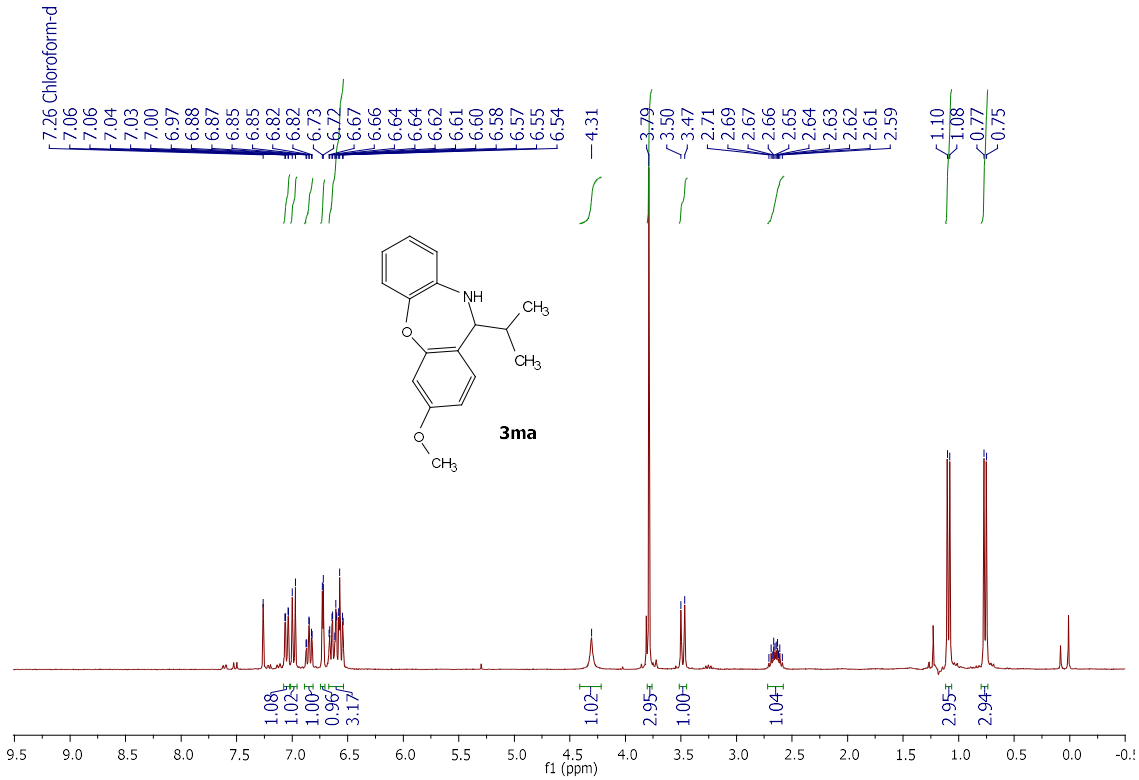

Figure S29. ^{1}H-NMR spectrum of **3ma**

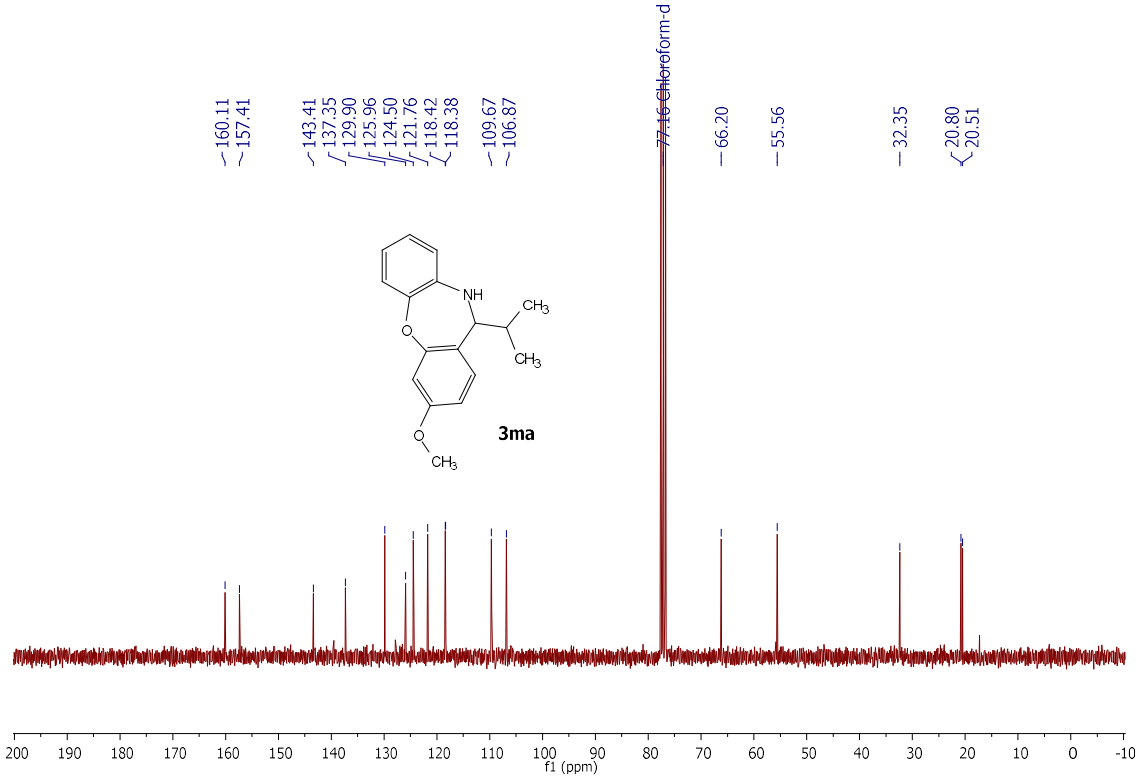

Figure S30. ^{13}C-NMR spectrum of **3ma**

7-Fluoro-11-isopropyl-10,11-dihydrodibenzo[*b,f*][1,4]oxazepine (3na)

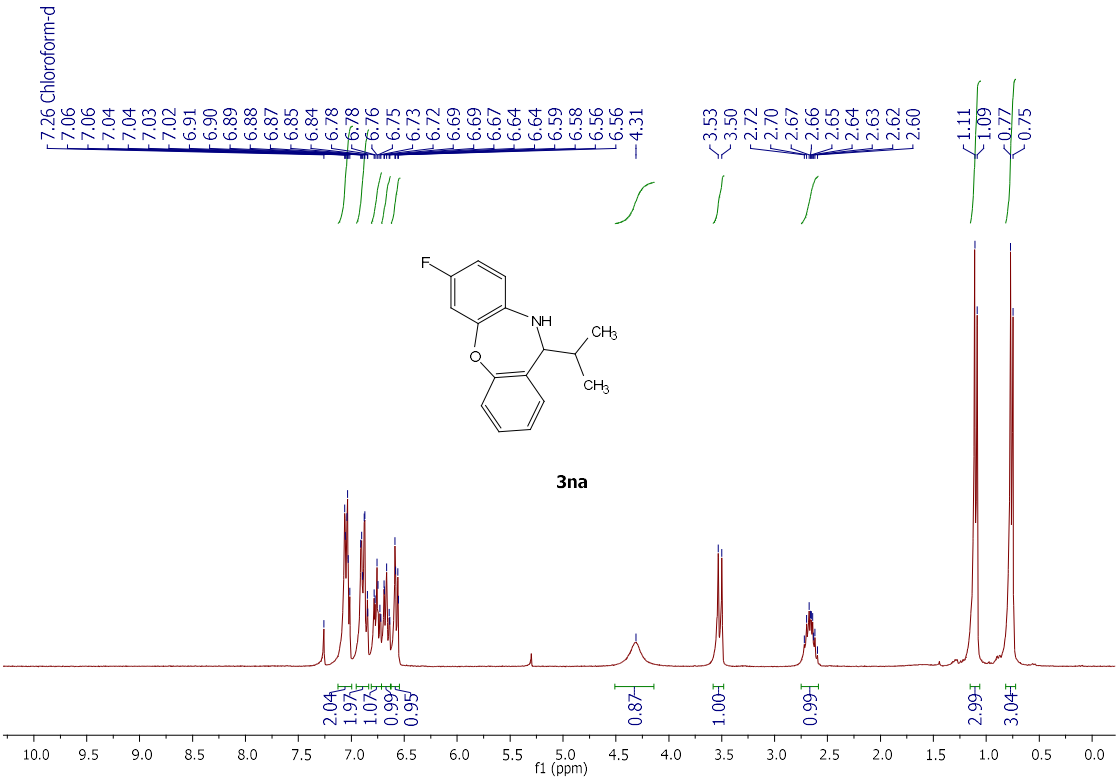

Figure S31. ^{1}H-NMR spectrum of **3na**

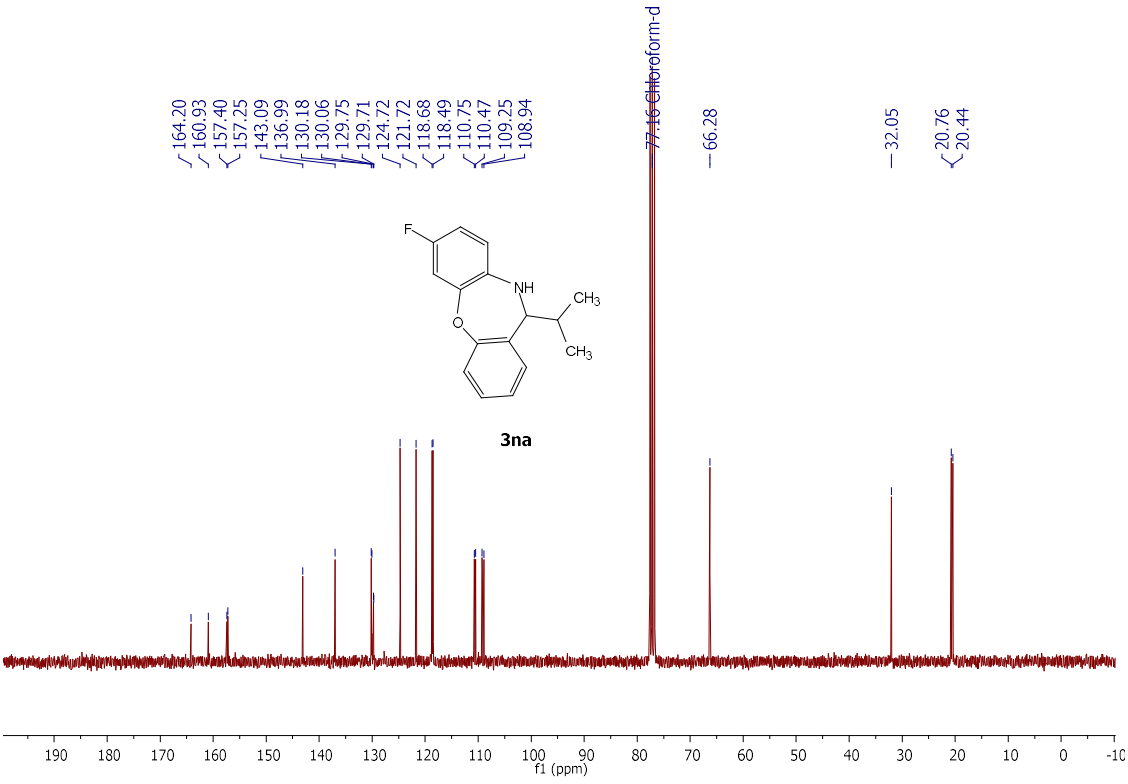

Figure S32. ^{13}C-NMR spectrum of **3na**

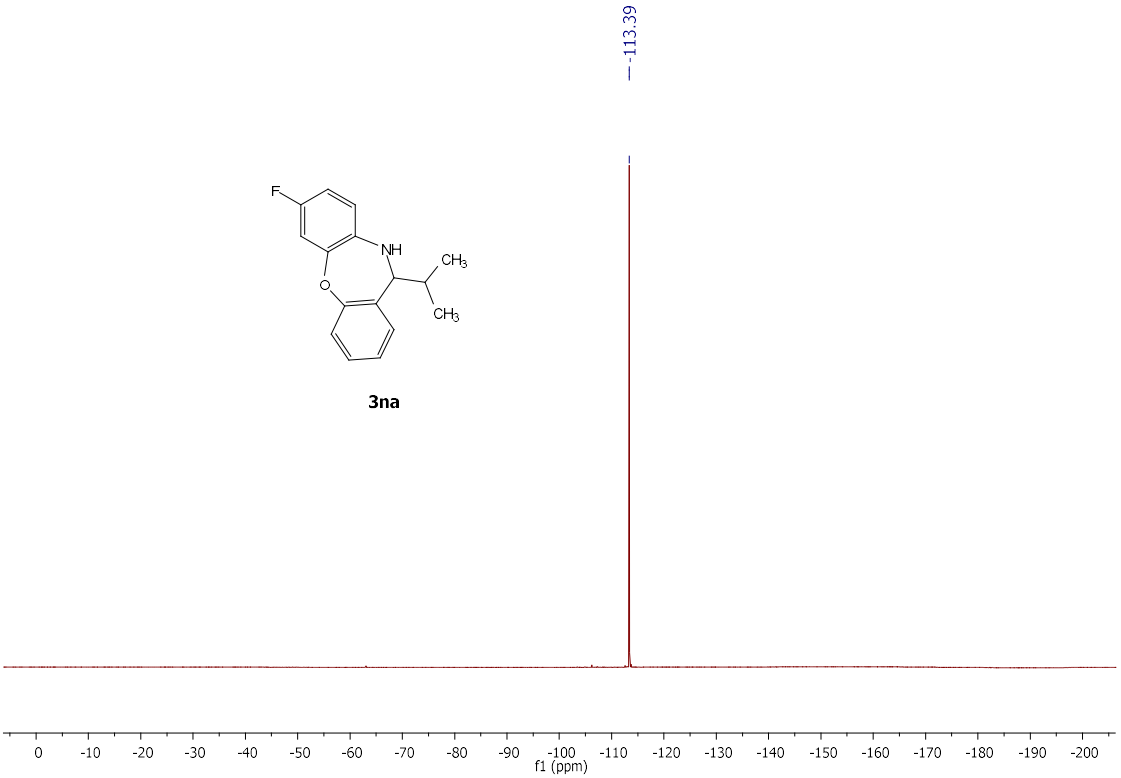

Figure S33. ^{19}F-NMR spectrum of **3na**

11-Isopropyl-10,11-dihydrodibenzo[*b,f*][1,4]thiazepine (3oa)

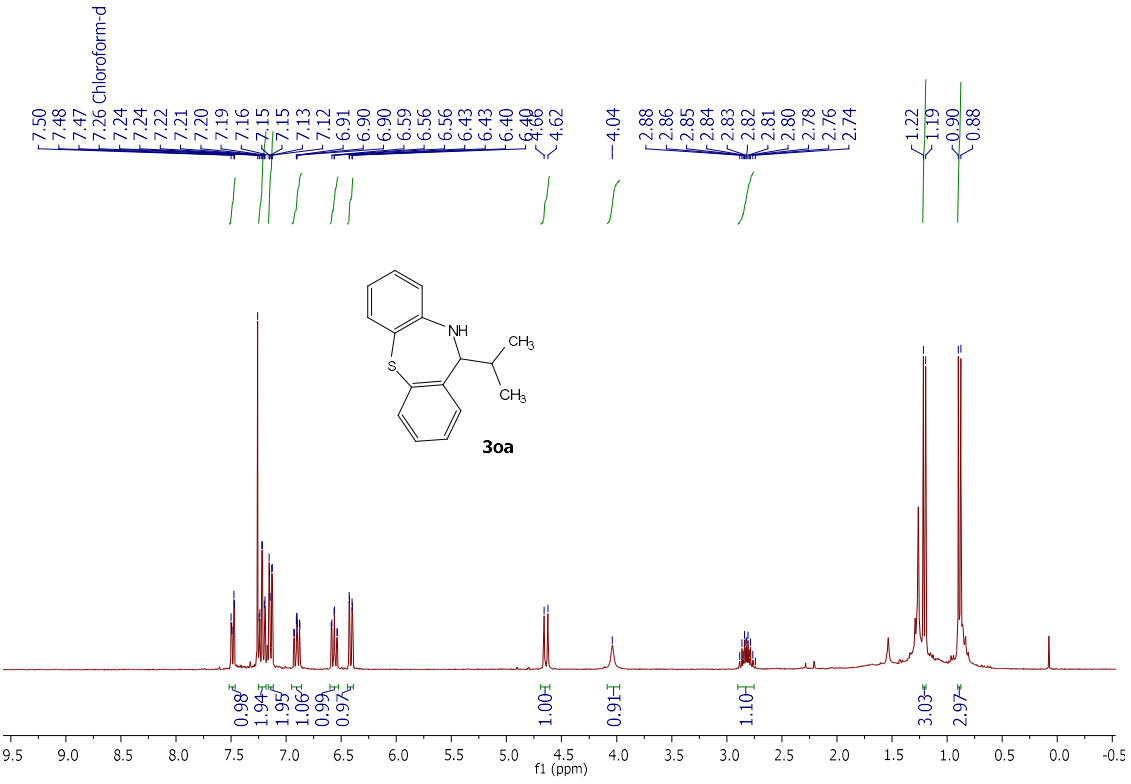

Figure S34. ^{1}H-NMR spectrum of **3oa**

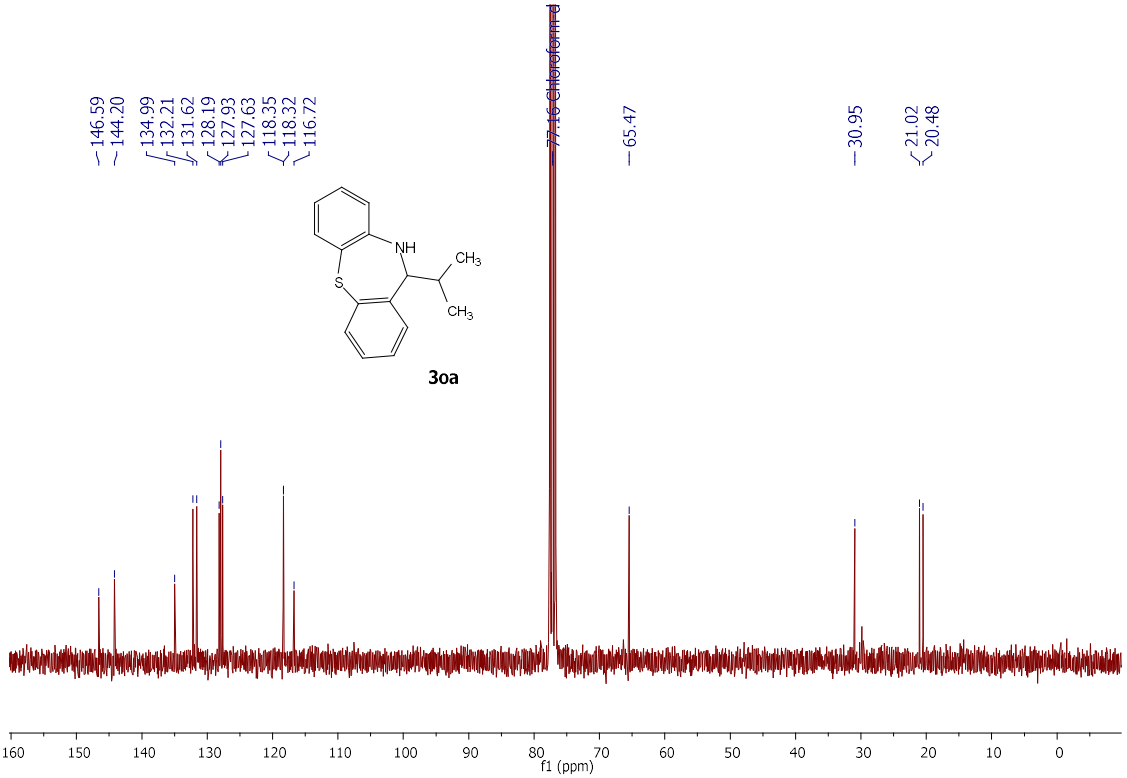

Figure S35. ^{13}C-NMR spectrum of **3oa**

3-Fluoro-11-isopropyl-10,11-dihydrodibenzo[*b,f*][1,4]thiazepine (3pa)

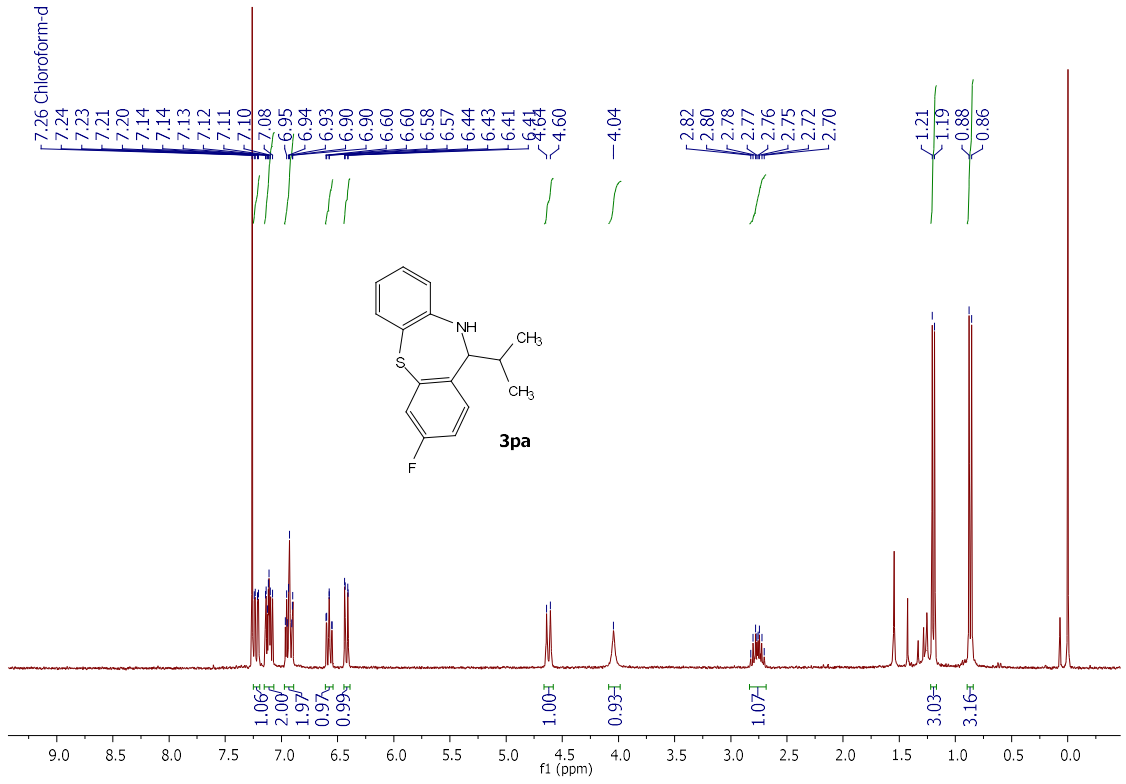

Figure S36. ^{1}H-NMR spectrum of **3pa**

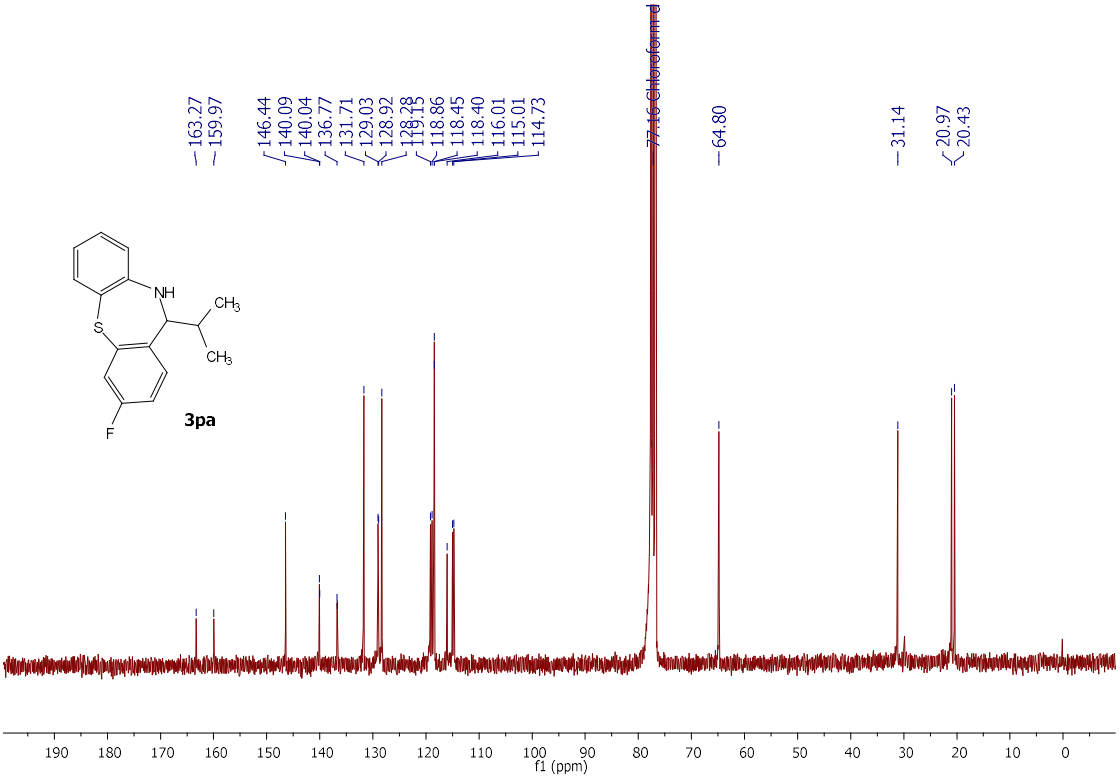

Figure S37. ^{13}C-NMR spectrum of **3pa**

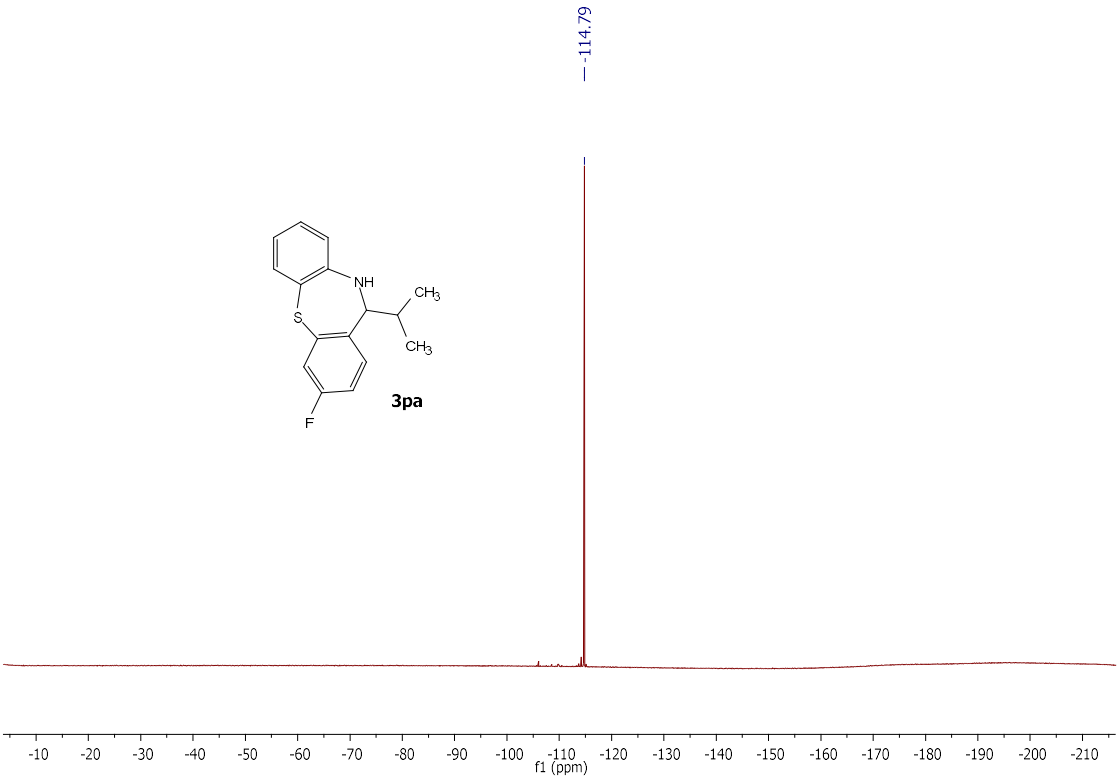

Figure S38. ^{19}F-NMR spectrum of **3pa**

11-Isopropyl-3-methoxy-10,11-dihydrodibenzo[*b,f*][1,4]thiazepine (3qa)

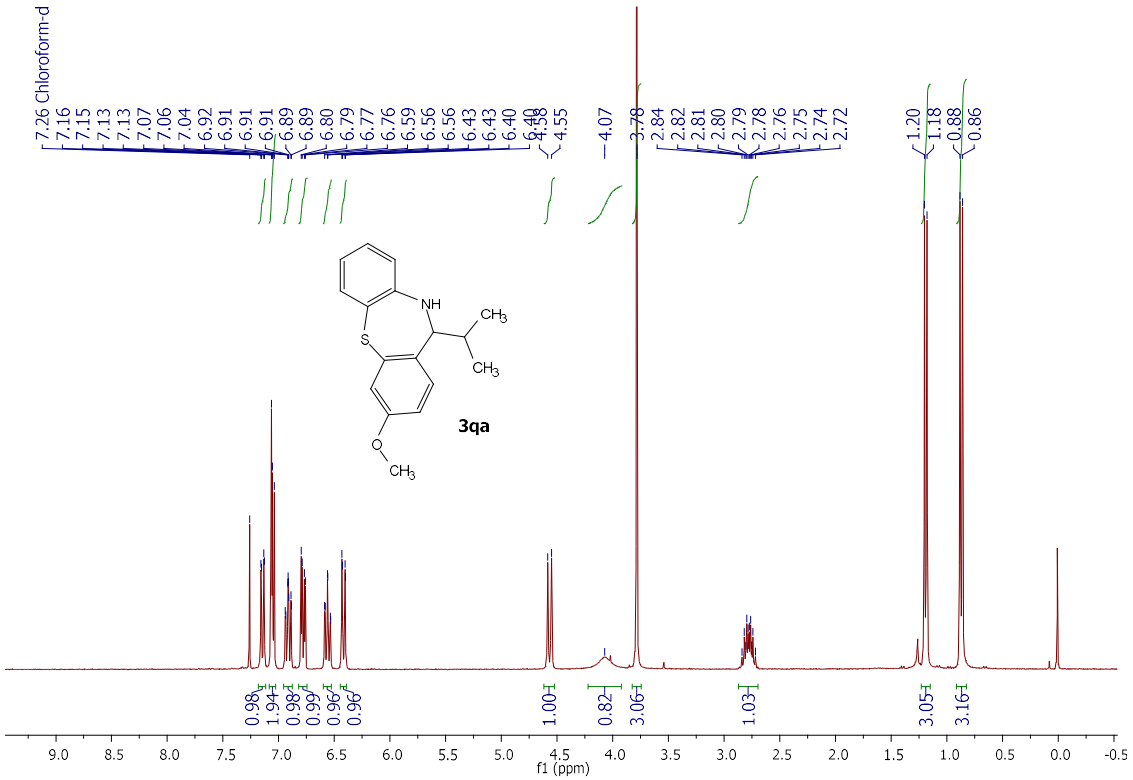

Figure S39. ^{1}H-NMR spectrum of **3qa**

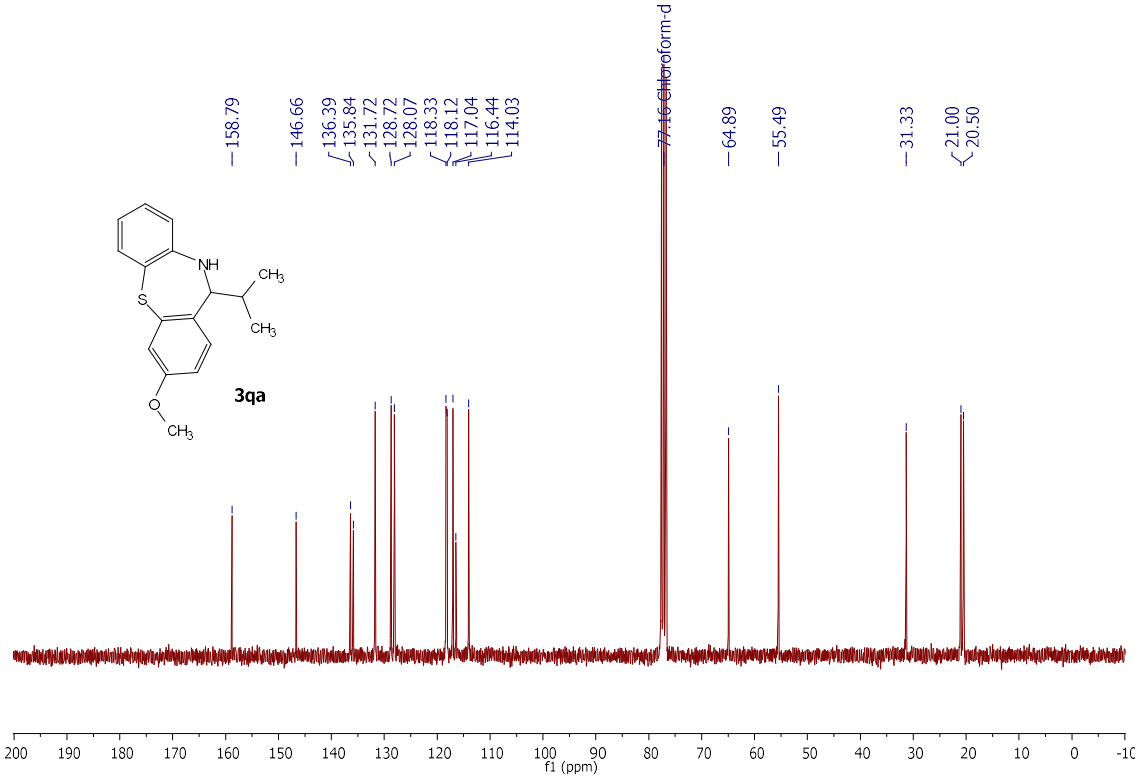

Figure S40. ^{13}C-NMR spectrum of **3qa**

1-Isopropylisoquinoline (3ra)

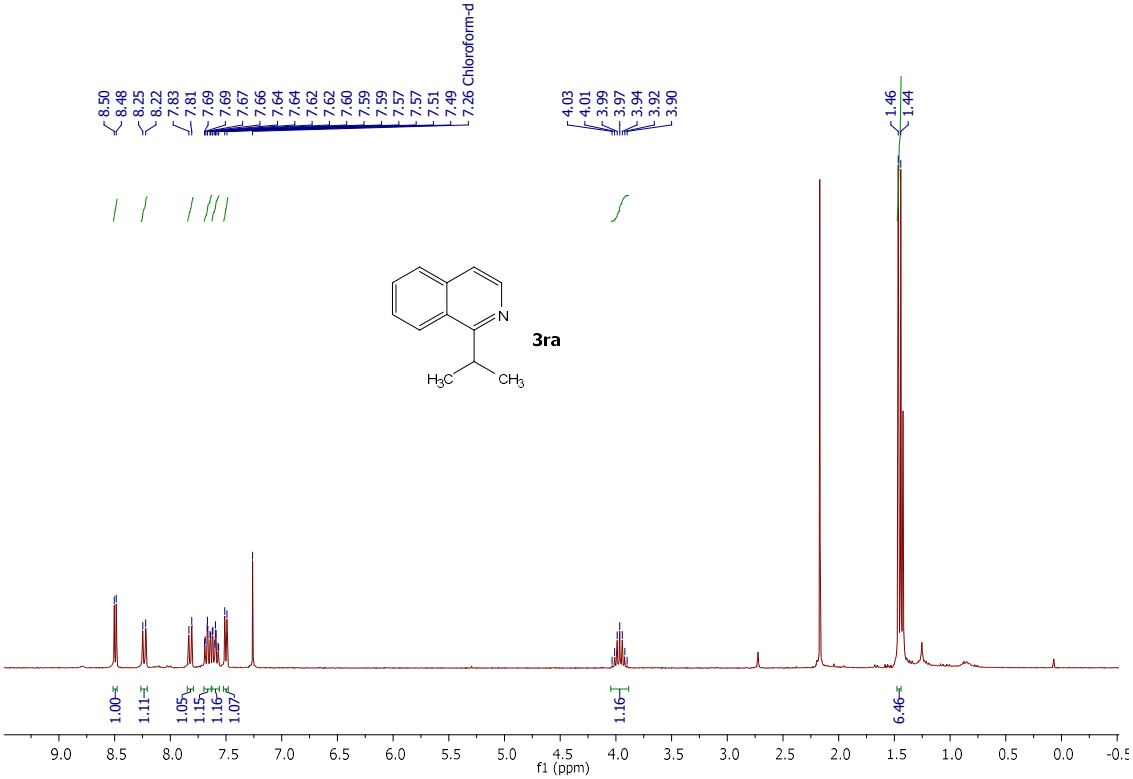

Figure S41. ^{1}H-NMR spectrum of **3ra**

4-Bromo-1-isopropylisoquinoline (3sa)

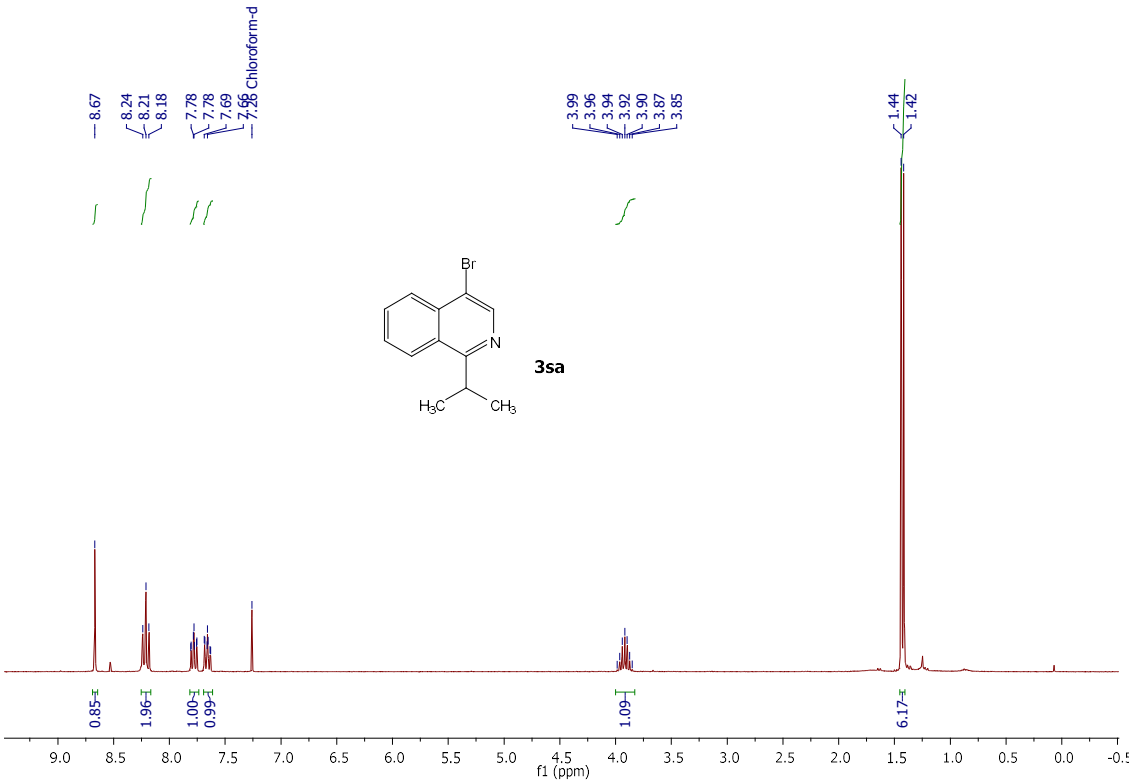

Figure S42. ^{1}H-NMR spectrum of **3sa**

2-Isopropyl-3-Methylquinoxaline (3ta)

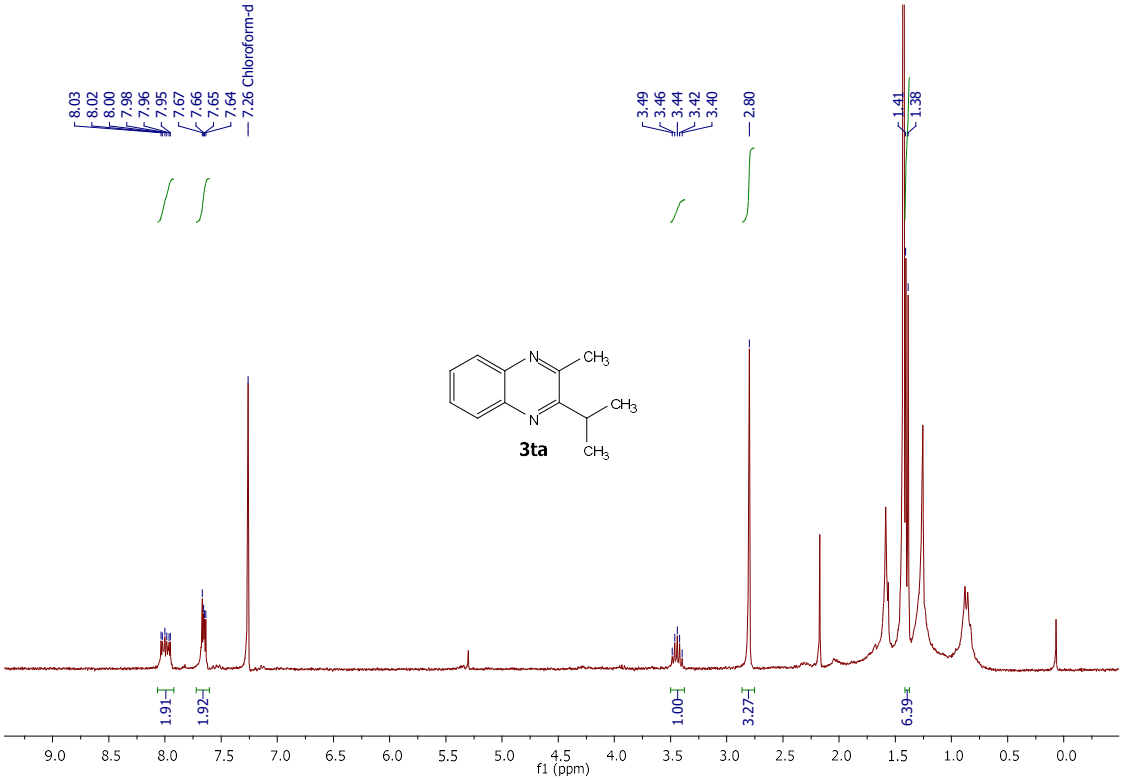

Figure S43. ^{1}H-NMR spectrum of **3ta**

4-Isopropylquinazoline (3ua)

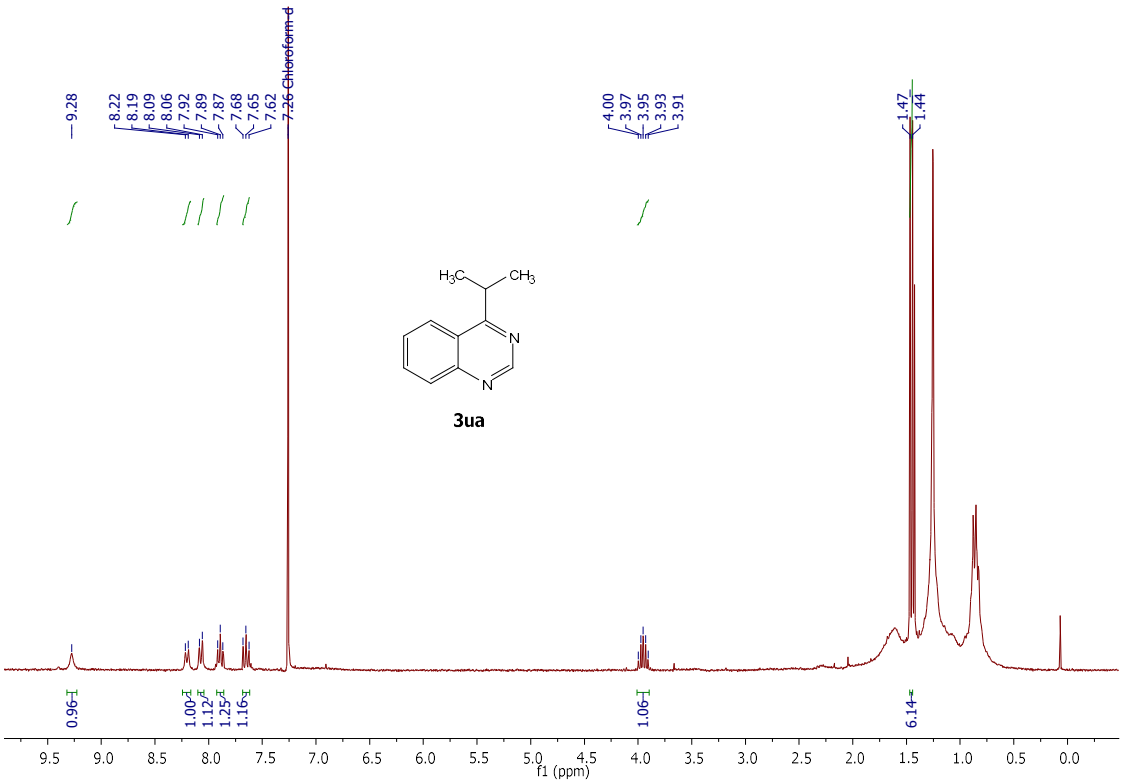

Figure S44. ^{1}H-NMR spectrum of **3ua**

1-Methyl-3-propylquinoxalin-2(1*H*)-one (3hb)

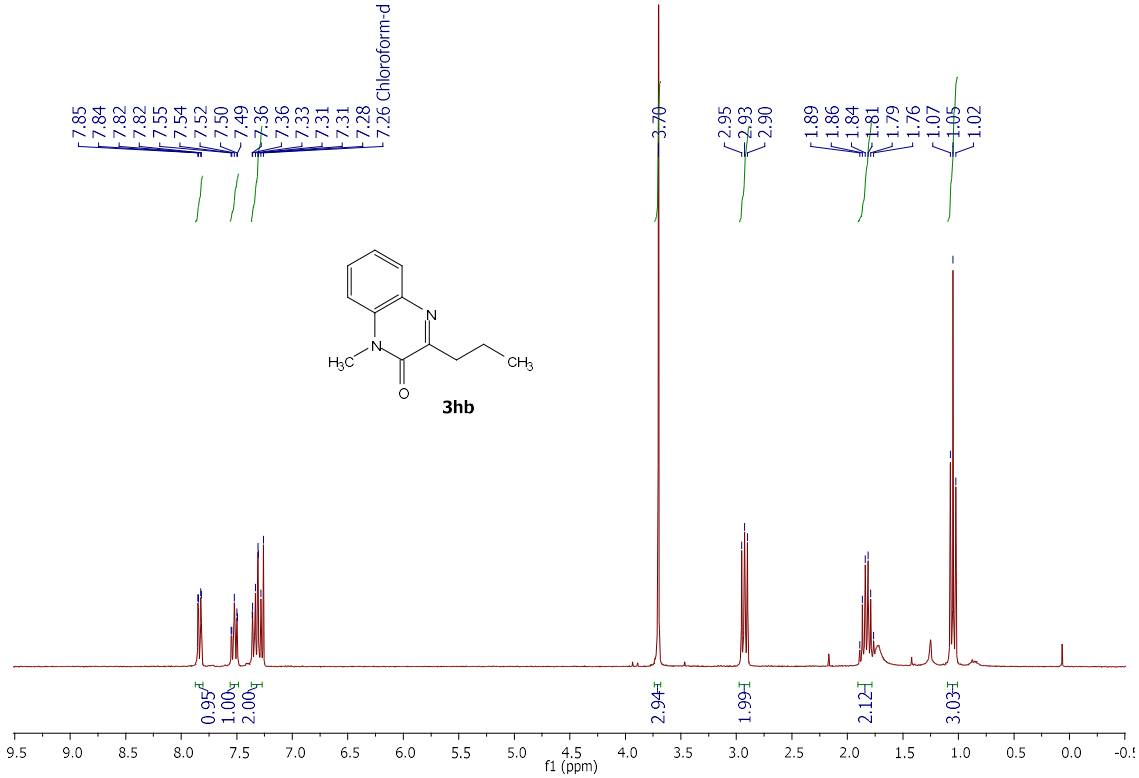

Figure S45. ^{1}H-NMR spectrum of **3hb**

3-(trifluoromethyl)-1-methylquinoxalin-2(1*H*)-one (3hc)

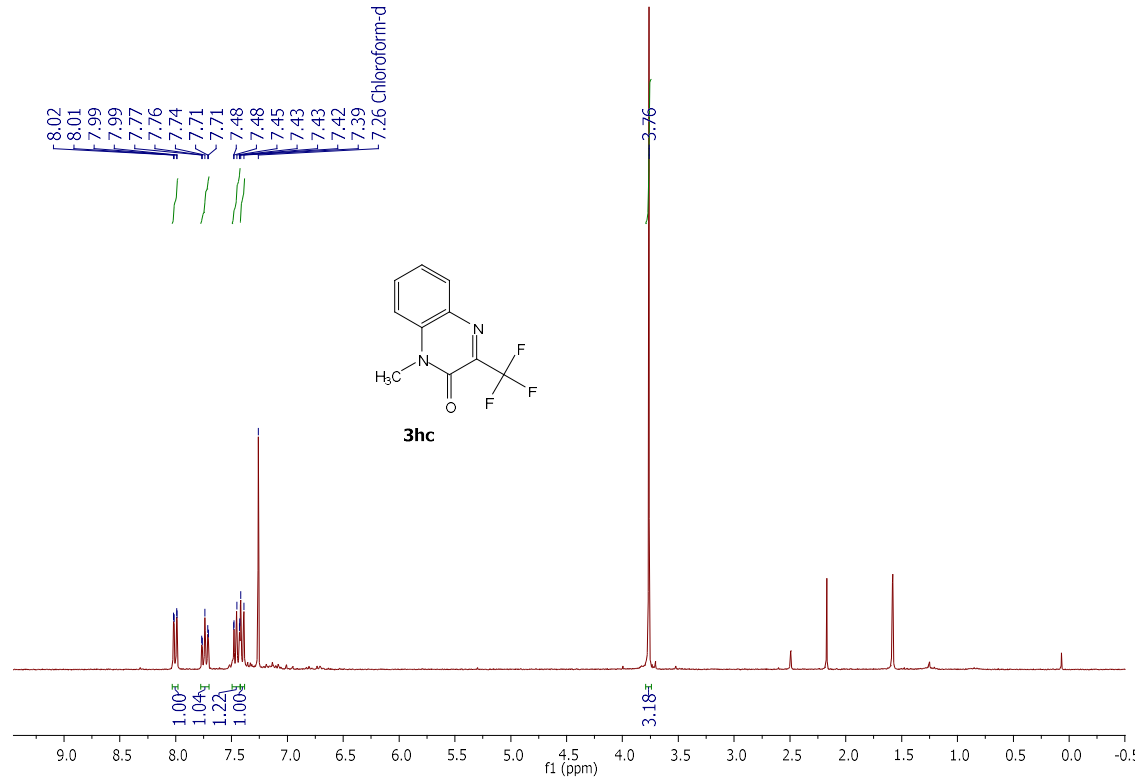

Figure S46. ^{1}H-NMR spectrum of **3hc**

3-(Difluoromethyl)-1-methylquinoxalin-2(1*H*)-one (3hd)

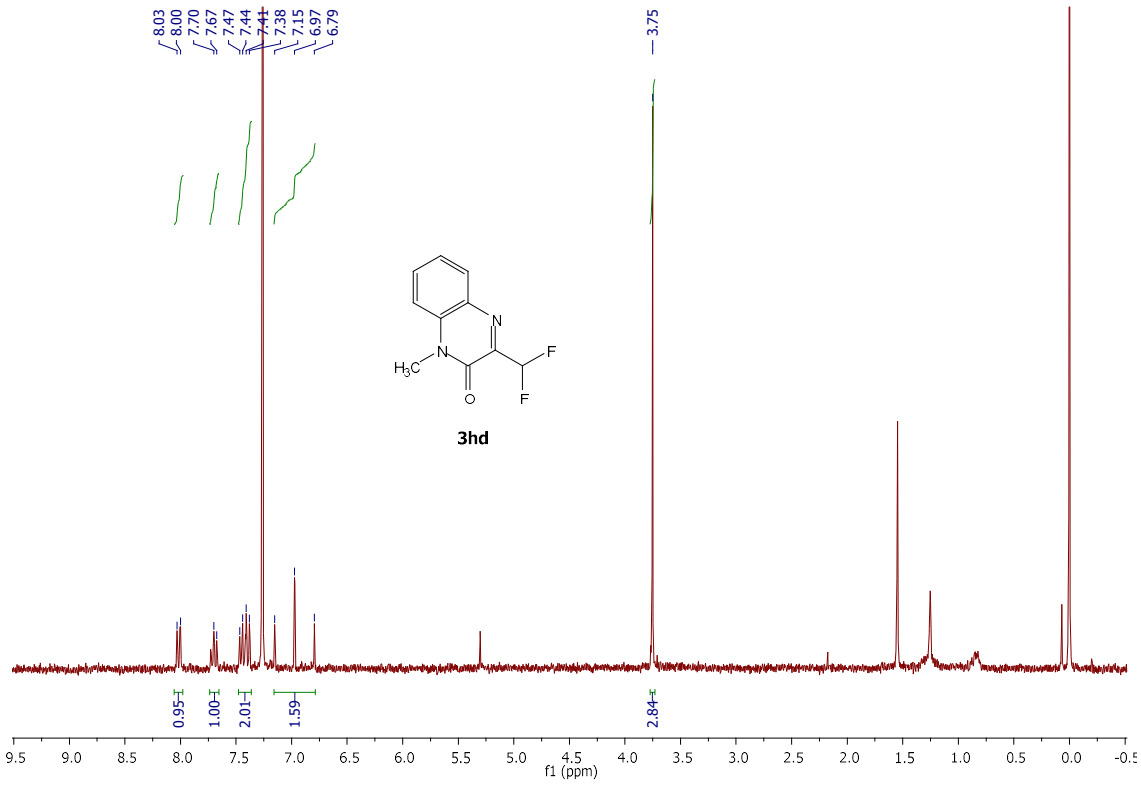

Figure S47. ^{1}H-NMR spectrum of **3hd**

3-Benzyl-1-methylquinoxalin-2(1*H*)-one (3he)

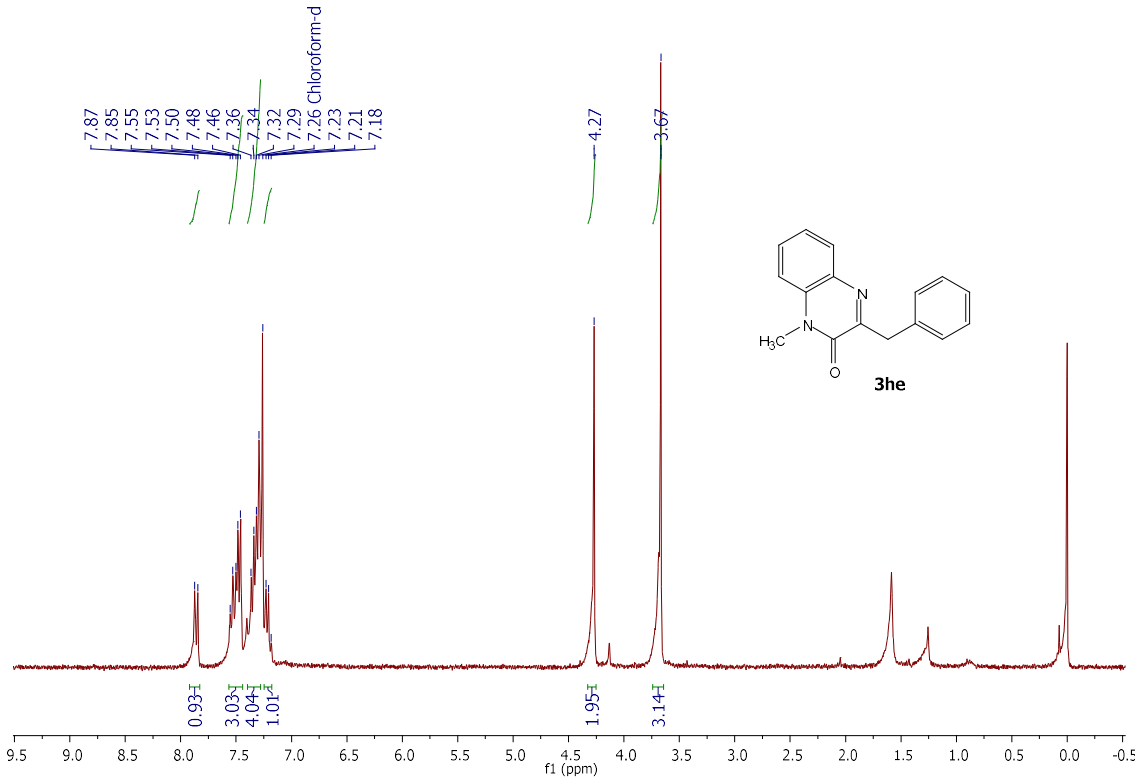

Figure S48. ^{1}H-NMR spectrum of **3he**

3-Cyclohexyl-1-methylquinoxalin-2(1*H*)-one (3hf)

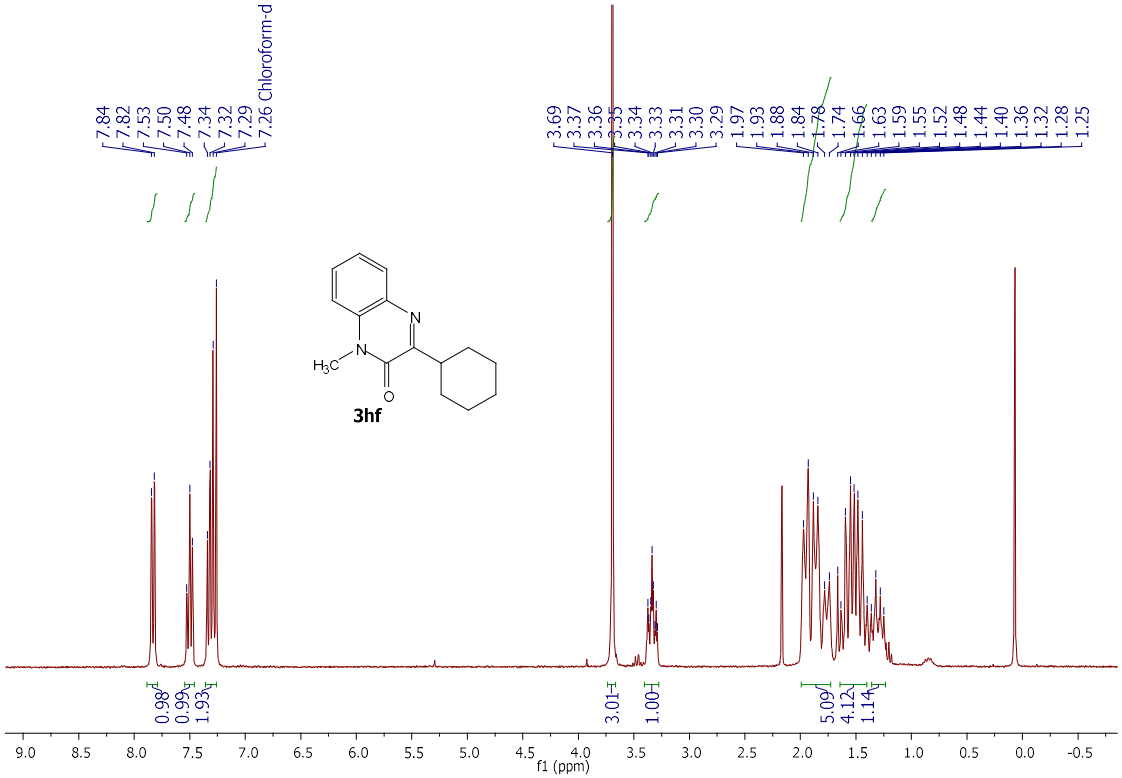

Figure S49. ^{1}H-NMR spectrum of **3hf**