Facile Synthesis of Quinoxaline Annulated Perfluoroalkylated Benzoazepine Derivatives

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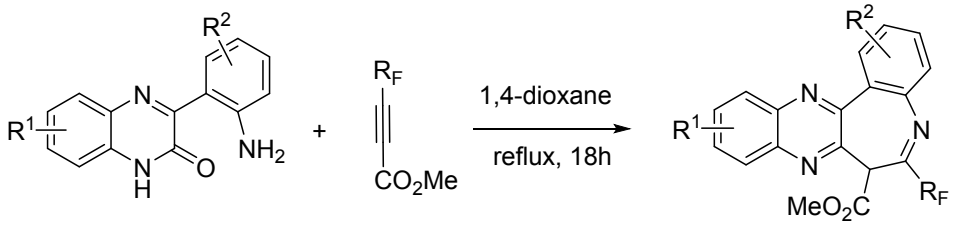
1. General information

Reagents and solvents were purchased from commercially sources and used without further purification. Methyl perfluoroalk-2-ynoates were prepared according to the known literature. Melting points were recorded on a WRS-1 instrument and are uncorrected. ^{1}H, ^{19}F and ^{13}C NMR spectra were recorded on a Bruker DRX- 500 MHz spectrometer. All chemical shifts are reported in parts per million downfield (positive) of the standard: C_6F_6 for ^{19}F, TMS for ^{1}H and ^{13}C NMR spectra. IR spectra were obtained on an AVATAR370 FTIR spectrometer. LR-MS (lower resolution mass spectra) and HR-MS (high resolution mass spectra) were obtained on LCMS 2020 and Bruker Daltonics APEXIII 7.0 TESALA FTMS instruments, respectively. X-ray analysis was performed on a Bruker Smart Apex2 CCD spectrometer. Yields reported in this publication refer to isolated ones of compounds and their purity was determined by ^{1}H NMR.

2. General procedure for the preparation of 3-(2-aminophenyl)quinoxalin-2(1*H*)-ones *1*

A mixture of o-phenylenediamine (5.0 mmol), isatin (5.0 mmol), and PhCOOH (5.0 mmol) was stirred in 1,4-dioxane (10 mL) at room temperature. Progress of the reaction was monitored by thin-layer chromatography. After completion of the reaction, the precipitate was filtered, washed with 1,4-dioxane and dried to give pure compound **1**.

3. General procedure for the preparation of 6-perfluoroalkylated benzoazepinoquinoxalines *3*



1 **2** **3**

A yellow suspension of 3-(2-aminophenyl)quinoxalin-2(1*H*)-ones **1** (1.0 mmol) and methyl perfluoroalk-2-ynoates **2** (1.2 mmol) in 1,4-dioxane (10.0 mL) was stirred under reflux. After 18 h, a deep yellow solution was obtained. The solvent was removed under vacuum, and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate) to give **3**.

4. Characterization of products

3-(2-Aminophenyl)quinoxalin-2(1*H*)-one *1a*[12]: yellow solid; m.p.: 205.2-206.5 °C; yield: 80% ; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 6.45 (s, 2H), 6.56-6.59 (m, 1H), 6.80-6.82 (m, 1H), 7.13-7.16 (m, 1H), 7.29-7.32 (m, 2H), 7.49-7.53 (m, 1H), 7.80-7.81 (m, 1H), 8.08-8.10 (m, 1H), 12.48 (s, 1H) ppm;

3-(2-Amino-5-chlorophenyl)quinoxalin-2(1*H*)-one *1b*[13]: white solid; m.p.: 276.4-277.8 °C; yield: 62%; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 6.74 (s, 2H), 6.84 (d, J = 8.8 Hz, 1H), 7.17-7.19 (m, 1H), 7.30-7.34 (m, 2H), 7.51-7.54 (m, 1H), 7.83-7.85 (m, 1H), 8.25 (d, J = 2.6 Hz, 1H), 12.57 (s, 1H) ppm;

3-(2-Amino-5-methylphenyl)quinoxalin-2(1*H*)-one *1c*: yellow solid; m.p.: 214.6-216.0 °C; yield: 31%; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.19 (s, 3H), 6.17 (brs, 2H), 6.72-6.74 (m, 1H), 6.97-6.99 (m, 1H), 7.29-7.33 (m, 2H), 7.49-7.52 (m, 1H), 7.79-7.80 (m, 1H), 7.86 (s, 1H), 12.47 (brs, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 20.7, 115.4, 116.9, 118.3, 123.3, 123.7, 128.5, 130.1, 131.7, 131.8, 132.0, 132.1, 146.8, 155.1, 156.6 ppm; IR (KBr): υ 3418, 1628, 1432, 1381, 1030, 881 cm^{-1}; MS (ESI) m/z (%): 251 [M]$^{+}$. HRMS (ESI) calcd. for $C_{15}H_{13}N_3O$ [M]$^{+}$: 251.1059, found: 251.1053.

3-(2-Amino-5-methoxyphenyl)quinoxalin-2(1*H*)-one *1d*: orange solid; m.p.: 226.8-228.1 °C; yield: 41%; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 3.68 (s, 3H), 6.03 (brs, 2H), 6.77-6.79 (m, 1H), 6.86-6.88 (m, 1H), 7.30-7.34 (m, 2H), 7.50-7.53 (m, 1H), 7.73-7.74 (m, 1H), 7.80-7.82 (m, 1H), 12.45 (brs, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 55.9, 115.4, 116.1, 117.8, 118.7, 118.8, 123.8, 128.5, 130.2, 131.8, 132.0, 143.4, 149.7, 155.1, 156.1 ppm; IR (KBr): υ 3423, 2897, 1629, 1432, 1382, 1043, 896 cm^{-1}; MS (ESI) m/z (%): 267 [M]$^{+}$. HRMS (ESI) calcd. for $C_{15}H_{13}N_3O_2$ [M]$^{+}$: 267.1008, found: 267.1024.

3-(2-Amino-3-bromophenyl)quinoxalin-2(1*H*)-one *1e*: pale yellow solid; m.p.: 240.9-241.5 °C; yield: 89%; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 6.17 (brs, 2H), 6.58-6.61 (m, 1H), 7.32-7.35 (m, 2H), 7.52-7.57 (m, 2H), 7.78-7.80 (m, 1H), 7.86-7.88 (m, 1H), 12.57 (brs, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 109.7, 115.5, 116.5, 120.5, 123.8, 128.7, 130.7, 131.3, 131.8, 132.5, 134.3, 145.0, 154.9, 156.2 ppm; IR (KBr): υ 3415, 1659, 1452, 1253, 1072, 771 cm^{-1}; MS (ESI) m/z (%): 315 [M]$^{+}$. HRMS (ESI) calcd. for $C_{14}H_{10}BrN_3O$ [M]$^{+}$: 315.0007, found: 315.0025.

3-(2-Amino-4-bromophenyl)quinoxalin-2(1*H*)-one *1f*: yellow solid; m.p.: 230.5-231.0 °C; yield: 69%; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 6.71- 6.73 (m, 1H), 6.82 (brs, 2H),7.04 (s, 1H), 7.29-7.32 (m, 2H), 7.50-7.53 (m, 1H), 7.82-7.84 (m, 1H), 8.14-8.16 (m, 1H), 12.53 (brs, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 115.4, 116.6, 117.5, 118.4, 123.7, 124.5, 128.5, 130.3, 131.6, 132.0, 133.7, 150.8, 155.1, 155.3 ppm; IR (KBr): υ 3419, 1653, 1490, 1295, 1003, 750 cm^{-1}; MS (ESI) m/z (%): 315 [M]$^{+}$. HRMS (ESI) calcd. for $C_{14}H_{10}BrN_3O$ [M]$^{+}$: 315.0007, found: 315.0025.

3-(2-Amino-5-bromophenyl)quinoxalin-2(1*H*)-one *1g*[13]: yellow solid; m.p.: 287.3-289.1; yield: 43%; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 6.75- 6.80 (m, 3H), 7.27-7.33 (m, 3H), 7.51-7.54 (m, 1H), 7.84 (d, J = 7.8 Hz, 1H), 8.36 (s, 1H), 12.56 (s, 1H) ppm;

3-(2-Aminophenyl)-7-chloroquinoxalin-2(1*H*)-one *1h*: yellow solid; m.p.: 245.3-245.9 °C; yield: 27%; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 6.58 (brs, 3H), 6.81-6.82 (m, 1H), 7.15 (s, 1H), 7.29-7.31 (m, 1H), 7.53-7.54 (m, 1H), 7.94 (s, 1H), 8.15-8.17 (m, 1H), 12.55 (brs, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 114.9, 116.8, 116.9, 117.2, 127.3, 127.5, 129.8, 130.9, 131.6, 132.0, 132.4, 149.5, 155.0, 157.4 ppm; IR (KBr): υ 3459, 1656, 1481, 1247, 996, 751 cm^{-1}; MS (ESI) m/z (%): 271 [M]$^{+}$. HRMS (ESI) calcd. for $C_{14}H_{10}ClN_3O$ [M]$^{+}$: 271.0512, found: 271.0522.

3-(2-Aminophenyl)-6,7-dimethylquinoxalin-2(1*H*)-one *1i*: yellow solid; m.p.: 237.8-239.5 °C; yield: 62%; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.30 (s, 3H), 2.33 (s, 3H), 6.43 (s, 2H), 6.56-6.59 (m, 1H), 6.79-6.81 (m, 1H), 7.08 (s, 1H), 7.11-7.15 (m, 1H), 7.58 (s, 1H), 8.09-8.10

(m, 1H), 12.37 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 19.4, 20.2, 115.1, 115.4, 116.7, 118.2, 128.3, 130.0, 130.2, 131.0, 131.8, 132.5, 139.8, 149.0, 155.1, 155.2 ppm; IR (KBr): υ 3428, 1642, 1388, 1262, 1115, 741 cm^{-1}; MS (ESI) m/z (%): 265 $[M]^+$. HRMS (ESI) calcd. for $C_{14}H_{10}BrN_3O$ $[M]^+$: 265.1213, found: 265.1215.

3-(2-Aminophenyl)-7-methoxyquinoxalin-2(1*H*)-one *1j*: yellowish brown solid; m.p.: 224.0-224.5 °C; yield: 30%; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 3.84 (s, 3H), 6.54-6.60 (m, 3H), 6.81-6.83 (m, 1H), 7.13-7.17 (m, 2H), 7.24-7.26 (m, 1H), 7.36 (s, 1H), 8.14-8.16 (m, 1H), 12.42 (brs, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 56.1, 110.0, 115.0, 116.2, 116.7, 118.1, 119.4, 126.1, 131.2, 132.0, 132.4, 149.2, 154.8, 155.9, 156.5 ppm; IR (KBr): υ 3485, 2952, 1613, 1493, 1279, 1161, 1036, 749 cm^{-1}; MS (ESI) m/z (%): 267 $[M]^+$. HRMS (ESI) calcd. for $C_{15}H_{13}N_3O_2$ $[M]^+$: 267.1008, found: 267.1024.

Methyl 6-(trifluoromethyl)-7*H*-benzo[2,3]azepino[4,5-*b*]quinoxaline-7-carboxylate *3a*: white solid; m.p.: 162.0-163.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.30 (s, 3H), 5.57 (s, 1H), 7.52-7.57 (m, 2H), 7.63-7.66 (m, 1H), 7.83-7.90 (m, 2H), 8.18-8.20 (m, 1H), 8.24-8.26 (m, 1H), 8.30-8.31 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 53.1, 53.4, 119.2 (q, $^1J_{C\text{-}F}$ = 276.0 Hz, CF_3), 127.2, 128.1, 129.1, 129.6, 130.7, 130.9, 131.0, 131.1, 142.1, 142.5, 142.6, 147.8, 148.2, 150.4 (q, $^2J_{C\text{-}F}$ = 35.7 Hz, CF_3), 165.7 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ: -72.6 (s, CF_3) ppm; IR (KBr): υ 2948, 1741, 1630, 1443, 1377, 1356, 1284, 1211, 1188, 1127, 760 cm^{-1}; MS (DART) m/z (%): 372 $[(M+H)]^+$. HRMS (DART) calcd. for $C_{19}H_{13}F_3N_3O_2$ $[(M+H)]^+$: 372.0954; found: 372.0951.

Methyl 2-chloro-6-(trifluoromethyl)-7*H*-benzo[2,3]azepino[4,5-*b*]quinoxaline-7-carboxylate *3b*: yellow solid; m.p.: 162.2-163.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.38 (s, 3H), 5.59 (s, 1H), 7.51-7.52 (m, 1H), 7.59-7.61 (m, 1H), 7.86-7.92 (m, 2H), 8.19-8.20 (m, 1H), 8.25-8.27 (m, 1H), 8.32-8.33 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 53.3, 53.4, 119.1 (q, $^1J_{C\text{-}F}$ = 276.2 Hz, CF_3), 128.9, 129.1, 129.5, 129.6, 130.6, 131.1, 131.2, 134.0, 140.9, 142.3, 142.5, 146.8, 147.1, 150.6 (q, $^2J_{C\text{-}F}$ = 35.8 Hz, CF_3), 165.6 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ: -72.6 (s, CF_3) ppm; IR (KBr): υ 2918, 1744, 1635, 1436, 1361, 1252, 1201, 1143, 772 cm^{-1}; MS (DART) m/z (%): 406 $[(M+H)]^+$. HRMS (DART) calcd. for $C_{19}H_{12}ClF_3N_3O_2$ $[(M+H)]^+$: 406.0565, found: 406.0560.

Methyl 2-methyl-6-(trifluoromethyl)-7*H*-benzo[2,3]azepino[4,5-*b*]quinoxaline-7-carboxylate *3c*: yellow solid; m.p.: 150.8-152.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.53 (s, 3H), 3.33 (s, 3H), 5.55 (s, 1H), 7.45 (s, 2H), 7.83-7.89 (m, 2H), 8.10 (s, 1H), 8.18-8.19 (m, 1H), 8.25-8.26 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 21.3, 53.1, 53.3, 119.3 (q, $^1J_{C\text{-}F}$ = 276.0 Hz, CF_3), 127.4, 127.9, 129.1, 129.5, 130.6, 130.9, 131.2, 132.1, 138.4, 140.3, 142.1, 142.6, 147.8, 148.3, 149.5 (q, $^2J_{C\text{-}F}$ = 35.5 Hz, CF_3), 165.9 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ: -72.5 (s, CF_3) ppm; IR (KBr): υ 2927, 1747, 1606, 1435, 1360, 1331, 1283, 1223, 1191, 1141, 766 cm^{-1}; MS (DART) m/z (%): 386 $[(M+H)]^+$. HRMS (DART) calcd. for $C_{20}H_{15}F_3N_3O_2$ $[(M+H)]^+$: 386.1111, found: 386.1105.

Methyl 2-methoxy-6-(trifluoromethyl)-7*H*-benzo[2,3]azepino[4,5-*b*]quinoxaline-7-carboxylate *3d*: yellow solid; m.p.: 166.3-167.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.36 (s, 3H), 3.97 (s, 3H), 5.55 (s, 1H), 7.18-7.21 (m, 1H), 7.50-7.52 (m, 1H), 7.79 (s, 1H), 7.83-7.89 (m, 2H), 8.18-8.20 (m, 1H), 8.24-8.25 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 53.1,

53.3, 55.7, 114.0, 118.4, 119.4 (q, $^{1}J_{C\text{-}F}$ = 275.8 Hz, CF_3), 129.1, 129.6, 130.7, 130.9, 136.3, 142.3, 142.5, 147.5, 148.0, 148.2 (q, $^{2}J_{C\text{-}F}$ = 35.4 Hz, CF_3), 159.0, 166.1 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ: -72.3 (s, CF_3) ppm; IR (KBr): υ 2958, 1744, 1631, 1484, 1339, 1254, 1229, 1192, 1131, 773 cm^{-1}; MS (DART) m/z (%): 402 $[(M+H)]^+$. HRMS (DART) calcd. for $C_{20}H_{15}F_3N_3O_3$ $[(M+H)]^+$: 402.1060, found: 420.1056.

Methyl 4-bromo-6-(trifluoromethyl)-7*H*-benzo[2,3]azepino[4,5-*b*]quinoxaline-7-carboxylate *3e*: yellow solid; m.p.: 161.1-162.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.36 (s, 3H), 5.60 (s, 1H), 7.36-7.39 (m, 1H), 7.85-7.92 (m, 3H), 8.19-8.21 (m, 1H), 8.24-8.28 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 53.2, 53.5, 119.0 (q, $^{1}J_{C\text{-}F}$ = 276.4 Hz, CF_3), 121.4, 128.5, 129.1, 129.7, 130.4, 131.0, 131.2, 134.9, 140.7, 142.2, 142.4, 147.2, 147.3, 151.0 (q, $^{2}J_{C\text{-}F}$ = 36.2 Hz, CF_3), 165.4 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ: -72.3 (s, CF_3) ppm; IR (KBr): υ 2922, 1747, 1640, 1426, 1354, 1261, 1196, 1130, 779 cm^{-1}; MS (DART) m/z (%): 450 $[(M+H)]^+$. HRMS (DART) calcd. for $C_{19}H_{12}BrF_3N_3O_2$ $[(M+H)]^+$: 450.0060, found: 450.0052.

Methyl 3-bromo-6-(trifluoromethyl)-7*H*-benzo[2,3]azepino[4,5-*b*]quinoxaline-7-carboxylate *3f*: yellow solid; m.p.: 182.5-184.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.38 (s, 3H), 5.59 (s, 1H), 7.64-7.67 (m, 1H), 7.76 (s, 1H), 7.84-7.90 (m, 2H), 8.18-8.25 (m, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 53.3, 53.5, 119.1 (q, $^{1}J_{C\text{-}F}$ = 276.3 Hz, CF_3), 124.9, 127.1, 129.1, 129.6, 129.9, 130.9, 131.1, 131.3, 132.4, 142.2, 142.6, 143.3, 147.2, 147.3, 151.5 (q, $^{2}J_{C\text{-}F}$ = 36.0 Hz, CF_3), 165.5 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ: -72.7 (s, CF_3) ppm; IR (KBr): υ 2927, 1740, 1667, 1479, 1329, 1285, 1210, 1137, 765 cm^{-1}; MS (DART) m/z (%): 450 $[(M+H)]^+$. HRMS (DART) calcd. for $C_{19}H_{12}BrF_3N_3O_2$ $[(M+H)]^+$: 450.0060, found: 450.0054.

Methyl 2-bromo-6-(trifluoromethyl)-7*H*-benzo[2,3]azepino[4,5-*b*]quinoxaline-7-carboxylate *3g*: yellow solid; m.p.: 170.3-171.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.38 (s, 3H), 5.59 (s, 1H), 7.43-7.45 (m, 1H), 7.73-7.76 (m, 1H), 7.86-7.92 (m, 2H), 8.18-8.20 (m, 1H), 8.25-8.27 (m, 1H), 8.48 (s, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 53.3, 53.4, 119.2 (q, $^{1}J_{C\text{-}F}$ = 276.2 Hz, CF_3), 120.0, 129.0, 129.1, 129.7, 131.1, 131.2, 133.6, 134.0, 141.4, 142.3, 142.5, 146.7, 147.1, 150.7 (q, $^{2}J_{C\text{-}F}$ = 35.9 Hz, CF_3), 165.5 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ: -72.6 (s, CF_3) ppm; IR (KBr): υ 2945, 1749, 1356, 1326, 1131, 889, 826, 766 cm^{-1}; MS (DART) m/z (%): 450 $[(M+H)]^+$. HRMS (DART) calcd. for $C_{19}H_{12}BrF_3N_3O_2$ $[(M+H)]^+$: 450.0060, found: 450.0059.

Methyl 10-chloro-6-(trifluoromethyl)-7*H*-benzo[2,3]azepino[4,5-*b*]quinoxaline-7-carboxylate *3h*: white solid; m.p.: 104.5-105.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.31 (s, 3H), 5.54 (s, 1H), 7.52-7.57 (m, 2H), 7.64-7.68 (m, 1H), 7.77-7.79 (m, 1H), 8.11-8.13 (m, 1H), 8.24-8.25 (m, 1H), 8.27-8.28 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 53.1, 53.3, 119.2 (q, $^{1}J_{C\text{-}F}$ = 276.0 Hz, CF_3), 127.2, 127.7, 128.2, 128.4, 130.3, 131.2, 131.3, 131.7, 136.9, 140.5, 142.6, 142.9, 147.9, 149.0, 150.3 (q, $^{2}J_{C\text{-}F}$ = 35.8 Hz, CF_3), 165.6 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ: -72.6 (s, CF_3) ppm; IR (KBr): υ 2953, 1743, 1636, 1480, 1334, 1286, 1195, 1127, 765 cm-^{1}; MS (DART) m/z (%): 406 $[(M+H)]^+$. HRMS (DART) calcd. for $C_{19}H_{12}ClF_3N_3O_2$ $[(M+H)]^+$: 406.0565, found: 406.0561.

Methyl 10,11-dimethyl-6-(trifluoromethyl)-7*H*-benzo[2,3]azepino[4,5-*b*]quinoxaline-7-

carboxylate *3i*: pale white solid; m.p.: 164.6-166.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.55 (s, 6H), 3.29 (s, 3H), 5.52 (s, 1H), 7.50-7.55 (m, 2H), 7.60-7.63 (m, 1H), 7.92 (s, 1H), 7.99 (s, 1H), 8.26-8.28 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 20.5, 53.0, 53.3, 119.3 (q, $^{1}J_{C\text{-}F}$ = 276.0 Hz, CF_3), 127.1, 127.9, 128.0, 128.4, 130.6, 130.9, 141.1, 141.7, 141.8, 142.5, 146.8, 147.2, 150.4 (q, $^{2}J_{C\text{-}F}$ = 35.5 Hz, CF_3), 165.9 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ: -72.6 (s, CF_3) ppm; IR (KBr): υ 2946, 1744, 1630, 1482, 1346, 1284, 1199, 1128, 766 cm^{-1}; MS (DART) m/z (%): 400 $[(M+H)]^+$. HRMS (DART) calcd. for $C_{21}H_{17}F_3N_3O_2$ $[(M+H)]^+$: 400.1267, found: 400.1263.

Methyl 10-methoxy-6-(trifluoromethyl)-7*H*-benzo[2,3]azepino[4,5-*b*]quinoxaline-7-carboxylate *3l*: pale yellow solid; m.p.: 165.7-166.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.30 (s, 3H), 4.01 (s, 3H), 5.51 (s, 1H), 7.47-7.56 (m, 4H), 7.61-7.65 (m, 1H), 8.04-8.06 (m, 1H), 8.28-8.29 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 53.0, 55.9, 106.4, 119.3 (q, $^{1}J_{C\text{-}F}$ = 276.0 Hz, CF_3), 124.5, 127.2, 128.0, 128.3, 130.0, 130.8, 130.9, 142.5, 144.4, 145.2, 148.0, 150.6 (q, $^{2}J_{C\text{-}F}$ = 35.6 Hz, CF_3), 161.6, 166.0 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ: -72.6 (s, CF_3) ppm; IR (KBr): υ 2964, 1741, 1621, 1442, 1343, 1285, 1229, 1194, 1123, 766 cm^{-1}; MS (DART) m/z (%): 402 $[(M+H)]^+$. HRMS (DART) calcd. for $C_{20}H_{15}F_3N_3O_3$ $[(M+H)]^+$: 402.1060, found: 402.1053.

Methyl 6-(pentafluoroethyl)-7*H*-benzo[2,3]azepino[4,5-*b*]quinoxaline-7-carboxylate *3k*: pale yellow solid; m.p.: 144.6-145.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.29 (s, 3H), 5.65 (s, 1H), 7.52-7.56 (m, 2H), 7.63-7.66 (m, 1H), 7.83-7.90 (m, 2H), 8.18-8.20 (m, 1H), 8.25-8.26 (m, 1H), 8.30-8.32 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 53.1, 53.4, 109.9 (tq,$^{1}J_{C\text{-}F}$ = 255.0 Hz, $^{2}J_{C\text{-}F}$ = 37.5 Hz, CF_2), 118.4 (qt, $^{1}J_{C\text{-}F}$ = 285.0 Hz, $^{2}J_{C\text{-}F}$ = 35.4 Hz, CF_3), 127.3, 127.9, 128.2, 129.1, 129.6, 130.7, 130.9, 131.0, 131.1, 142.1, 142.6, 142.8, 147.8, 148.1, 151.3 (t, $^{2}J_{C\text{-}F}$ = 27.3 Hz, CF_2), 165.8 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ: -117.3- -115.7 (m, CF_2), -81.2 (s, CF_3) ppm; IR (KBr): υ 2957, 1751, 1631, 1484, 1332, 1269, 1203, 1159, 1117, 766 cm^{-1}; MS (DART) m/z (%): 422 $[(M+H)]^+$. HRMS (DART) calcd. for $C_{20}H_{13}F_5N_3O_2$ $[(M+H)]^+$: 422.0922, found: 422.0914.

Methyl 2-methoxy-6-(pentafluoroethyl)-7*H*-benzo[2,3]azepino[4,5-*b*]quinoxaline-7-carboxylate *3l*: yellow solid; m.p.: 127.6-128.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.35 (s, 3H), 3.98 (s, 3H), 5.62 (s, 1H), 7.18-7.20 (m, 1H), 7.48-7.50 (m, 1H), 7.79 (s, 1H), 7.83-7.90 (m, 2H), 8.18-8.20 (m, 1H), 8.25-8.27 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 53.1, 53.3, 55.7, 110.0 (tq,$^{1}J_{C\text{-}F}$ = 254.6 Hz, $^{2}J_{C\text{-}F}$ = 37.5 Hz, CF_2), 114.0, 118.4, 118.5 (qt, $^{1}J_{C\text{-}F}$ = 285.1 Hz, $^{2}J_{C\text{-}F}$ = 35.5 Hz, CF_3), 129.1, 129.5, 129.6, 129.8, 130.7, 130.9, 136.6, 142.4, 142.5, 147.5, 147.9, 148.9 (t, $^{2}J_{C\text{-}F}$ = 27.3 Hz, CF_2), 159.0, 166.2 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ: -117.1- -115.3 (m, CF_2), -81.2 (s, CF_3) ppm; IR (KBr): υ 2954, 1745, 1604, 1490, 1338, 1273, 1225, 1192, 1107, 767cm^{-1}; MS (DART) m/z (%): 452 $[(M+H)]^+$. HRMS (DART) calcd. for $C_{21}H_{15}F_5N_3O_3$ $[(M+H)]^+$: 452.1028, found: 452.1021.

Methyl 6-(*n*-heptafluoropropyl)-7*H*-benzo[2,3]azepino[4,5-*b*]quinoxaline-7-carboxylate *3m*: yellow solid; m.p.: 102.6-103.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.29 (s, 3H), 5.65 (s, 1H), 7.52-7.56 (m, 2H), 7.63-7.67 (m, 1H), 7.84-7.90 (m, 2H), 8.18-8.20 (m, 1H), 8.24-8.26 (m, 1H), 8.30-8.32 (m, 1H) ppm; δ: 53.0, 53.8, 109.2 (m, CF_2), 111.4 (tt, $^{1}J_{C\text{-}F}$ = 257.4 Hz, $^{2}J_{C\text{-}F}$ = 31.0 Hz, CF_2), 117.7 (qt, $^{1}J_{C\text{-}F}$ = 286.3 Hz, $^{2}J_{C\text{-}F}$ = 33.4 Hz, CF_3), 127.3, 127.8, 128.2,

129.1, 129.6, 130.7, 130.9, 131.0, 131.1, 142.1, 142.6, 142.9, 147.8, 148.1, 151.5 (t, $^{2}J_{C\text{-}F}$ = 26.0 Hz, CF_2), 165.8 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ: -125.1 (s, CF_2), -114.4 (s, CF_2), -79.9 (s, CF_3) ppm; IR (KBr): υ 2950, 1755, 1632, 1484, 1444, 1331, 1222, 1190, 1118, 769 cm^{-1}; MS (DART) m/z (%): 472 $[(M+H)]^+$. HRMS (DART) calcd. for $C_{21}H_{13}F_7N_3O_2$ $[(M+H)]^+$: 472.0891, found: 472.0883.

Methyl 6-(*n*-heptafluoropropyl)-2-methoxy-7*H*-benzo[2,3]azepino[4,5-*b*]quinoxaline-7-carboxylate *3n*: yellow solid; m.p.: 93.4-95.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.35 (s, 3H), 3.97 (s, 3H), 5.64 (s, 1H), 7.19-7.21 (m, 1H), 7.50-7.51 (m, 1H), 7.79-7.80 (m, 1H), 7.83-7.89 (m, 2H), 8.18-8.20 (m, 1H), 8.24-8.25 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 53.1, 53.7, 55.7, 109.2 (m, CF_2), 111.5 (tt, $^{1}J_{C\text{-}F}$ = 256.9 Hz, $^{2}J_{C\text{-}F}$ = 31.1 Hz, CF_2), 114.0, 117.7 (qt, $^{1}J_{C\text{-}F}$ = 286.3 Hz, $^{2}J_{C\text{-}F}$ = 33.4 Hz, CF_3), 118.4, 129.1, 129.4, 129.6, 129.7, 130.7, 130.9, 136.7, 142.4, 142.5, 147.5, 147.9, 149.1 (t, $^{2}J_{C\text{-}F}$ = 26.0 Hz, CF_2), 159.1, 166.1 ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ: -125.2 (s, CF_2), -114.2 (s, CF_2), -79.9 (s, CF_3) ppm; IR (KBr): υ 2947, 1740, 1606, 1489, 1435, 1329, 1267, 1230, 1118, 757 cm^{-1}; MS (DART) m/z (%): 502 $[(M+H)]^+$. HRMS (DART) calcd. for $C_{22}H_{15}F_7N_3O_3$ $[(M+H)]^+$: 502.0996, found: 502.0985.

References:

12. B. Jan, E. Robert, S. Claes and W. Hans, *Tetrahedron*, 2003, **59**, 1033.

13. F. Iveta and S. Jan, *Acta Universitatis Palackianae Olomucensis, Facultas Rerum Naturalium, Chemica.*, 2003, **42**, 61.

5. NMR spectra of products

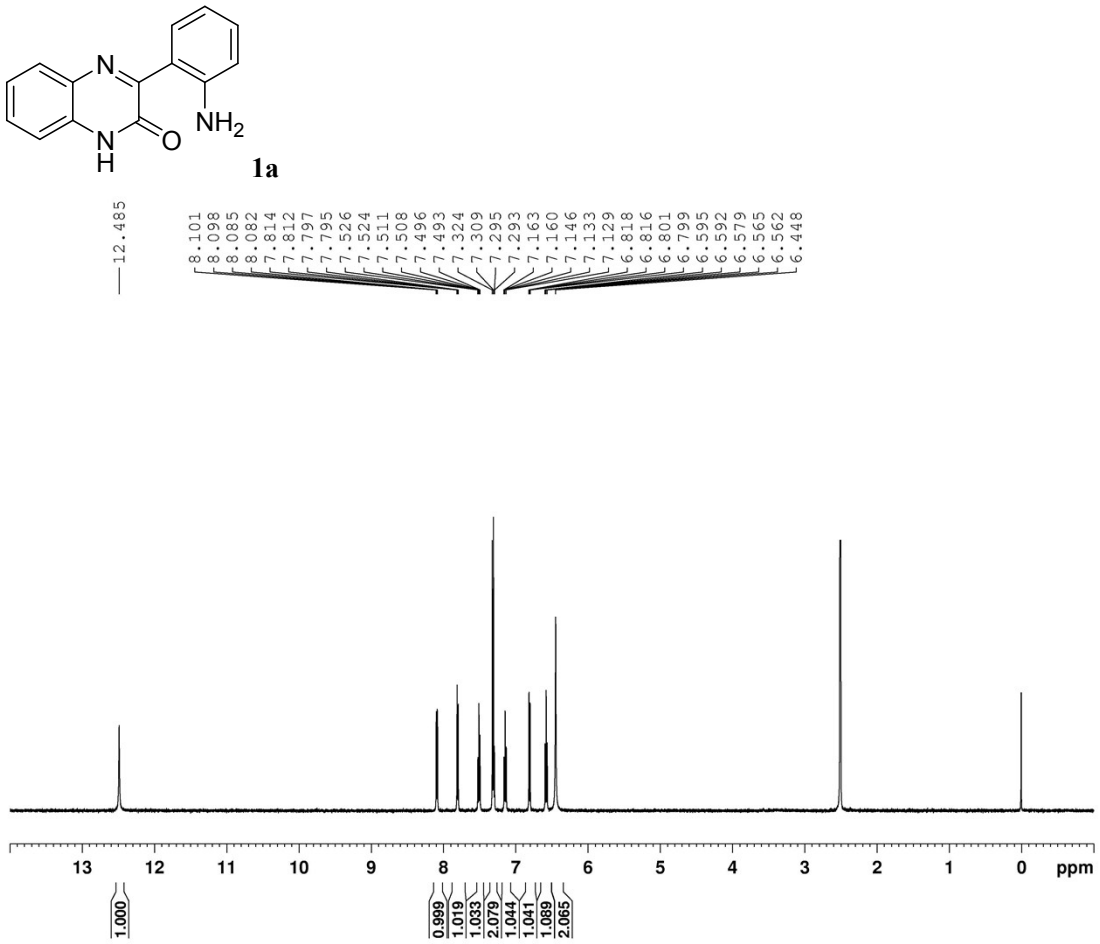


Fig S1. ^{1}H NMR of **1a** in DMSO-d_6

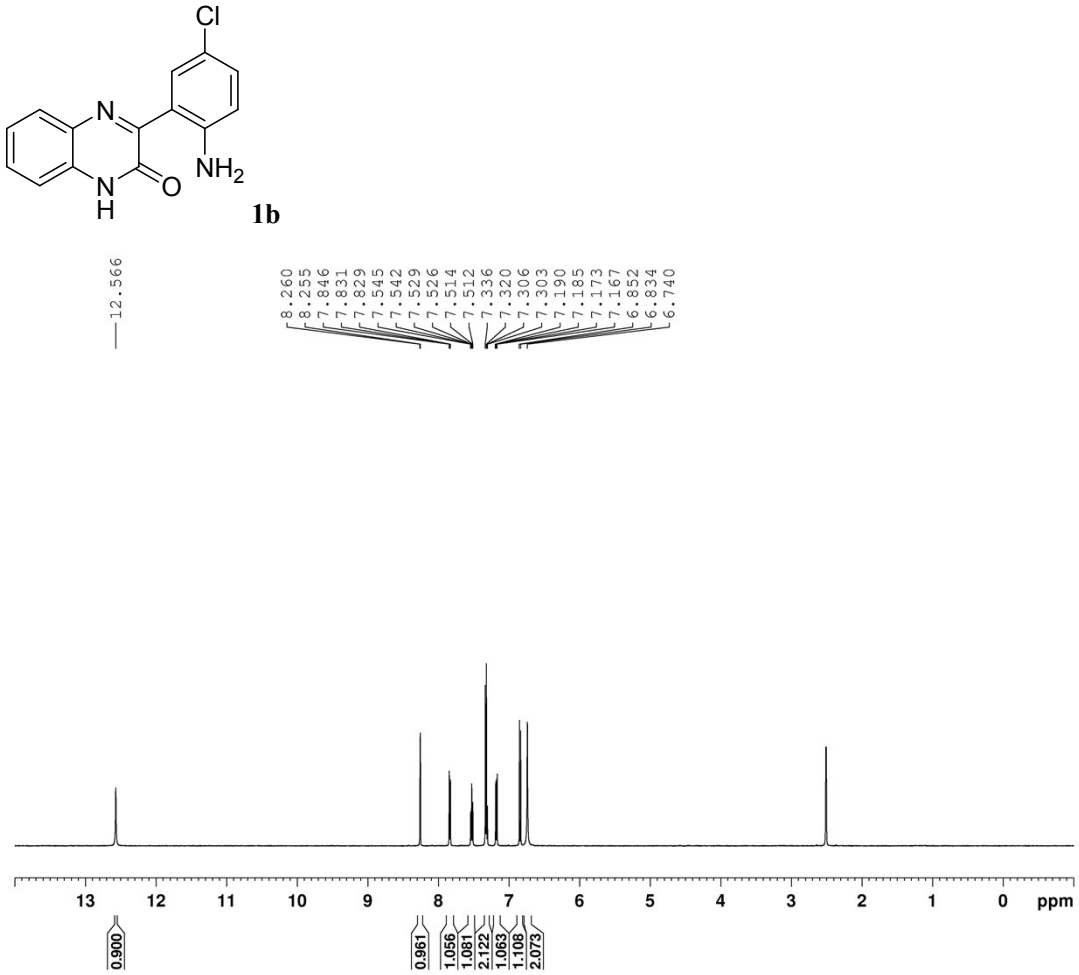


Fig S2. ^{1}H NMR of **1b** in DMSO-d_6

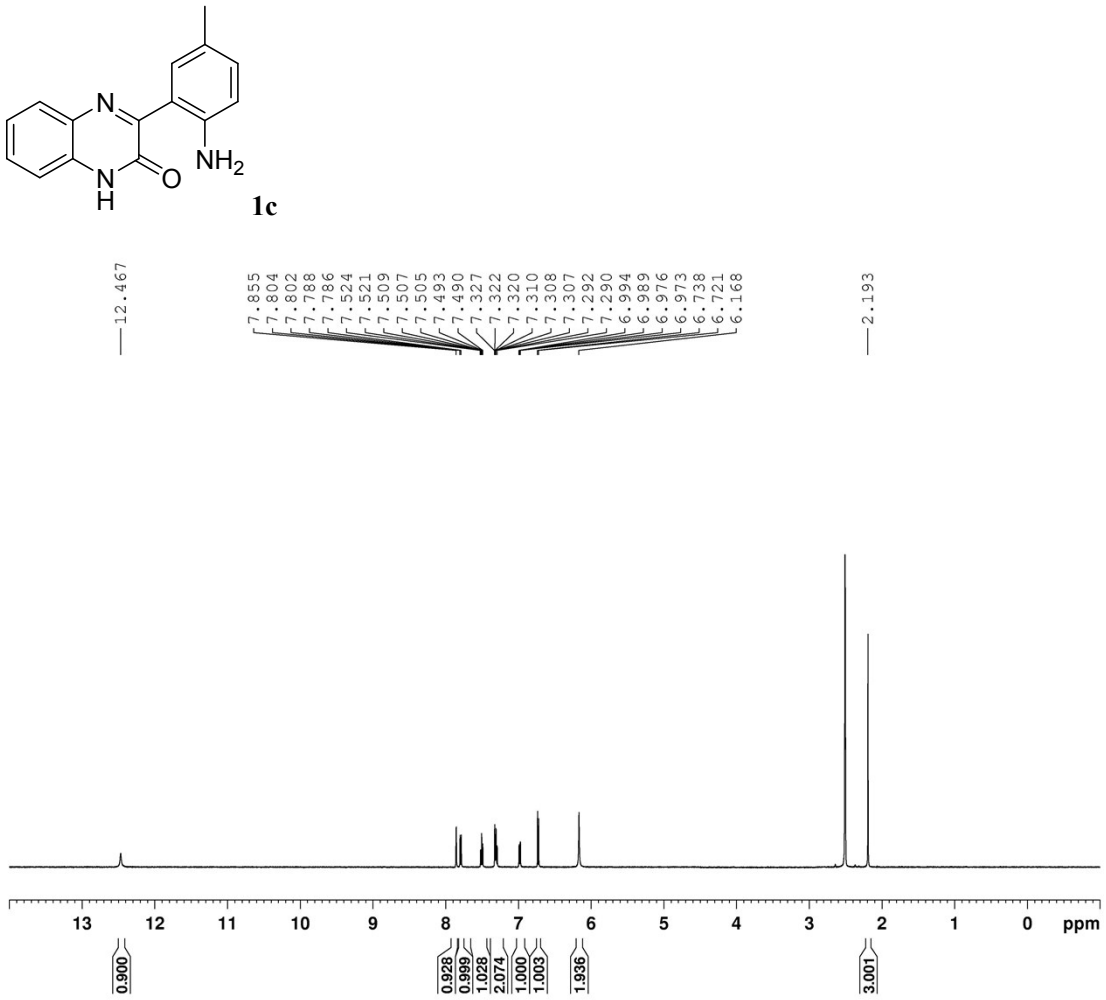


Fig S3. ^{1}H NMR of **1c** in DMSO-d_6

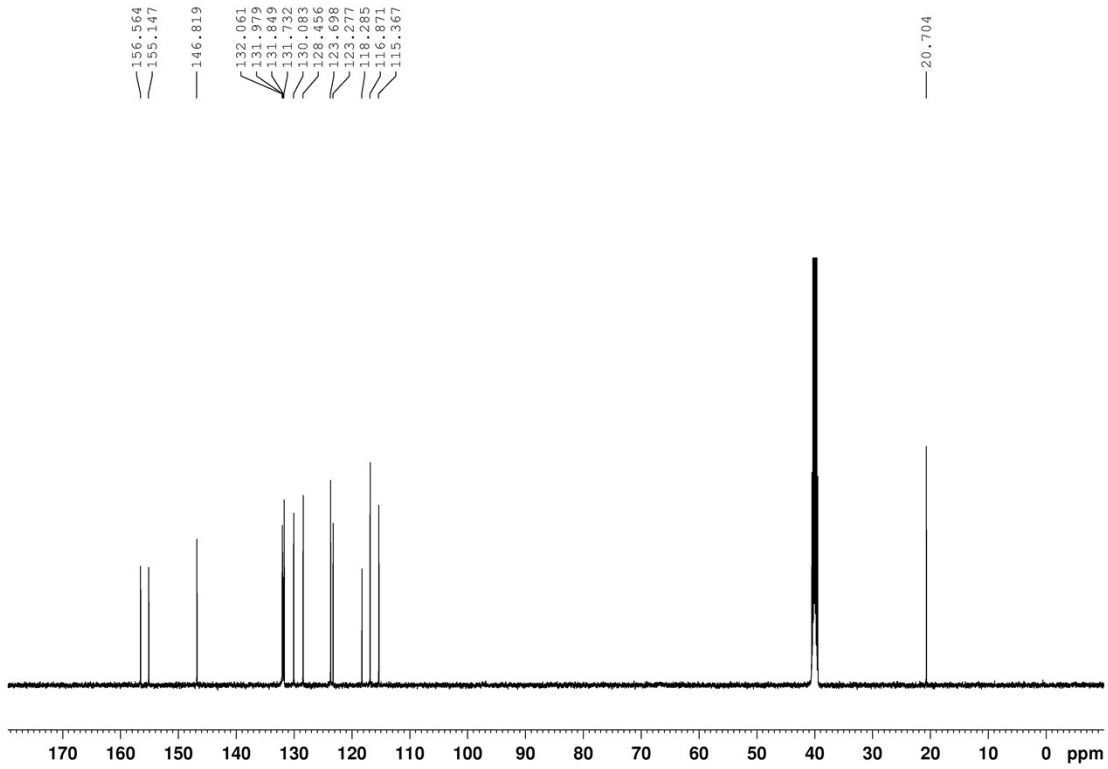


Fig S4. ^{13}C NMR of **1c** in DMSO-d_6

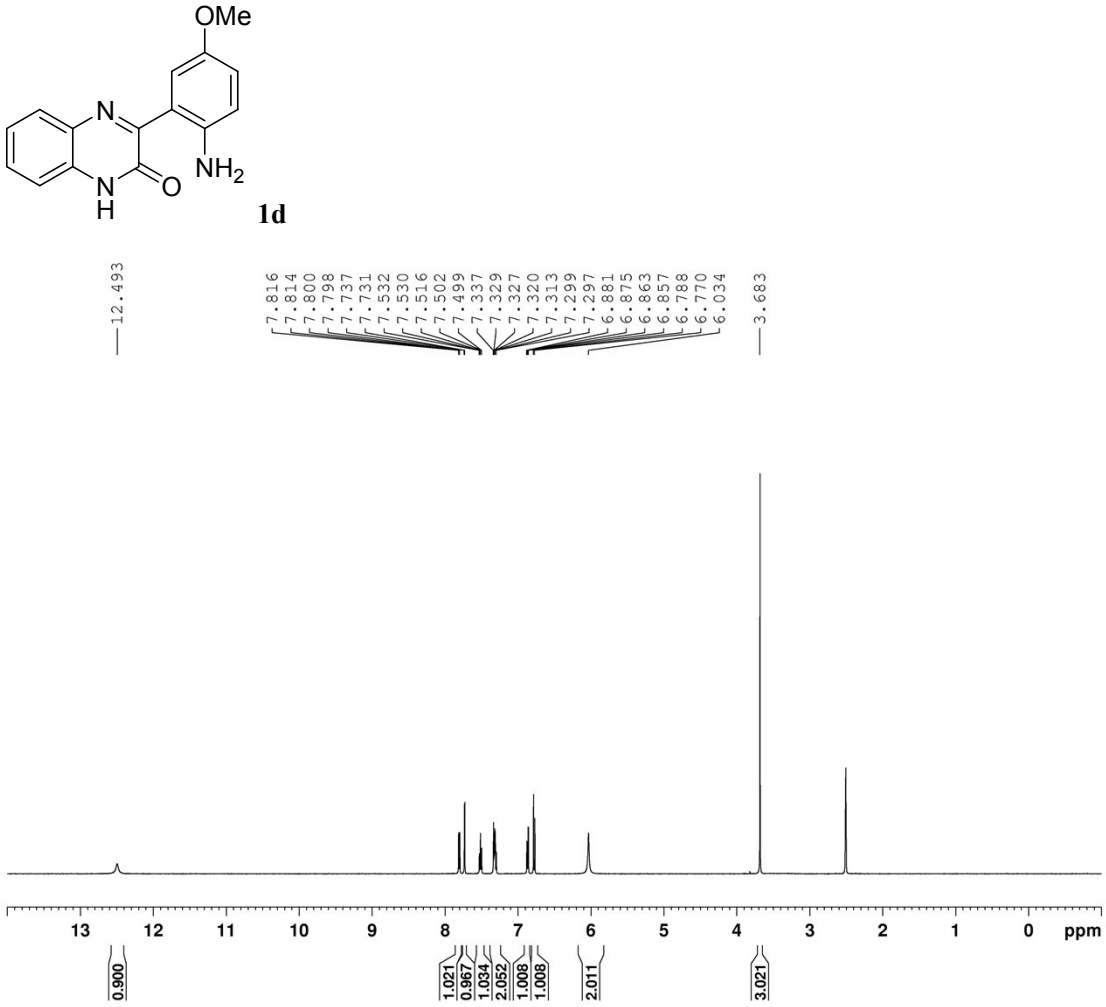


Fig S5. ^{1}H NMR of **1d** in DMSO-d_6

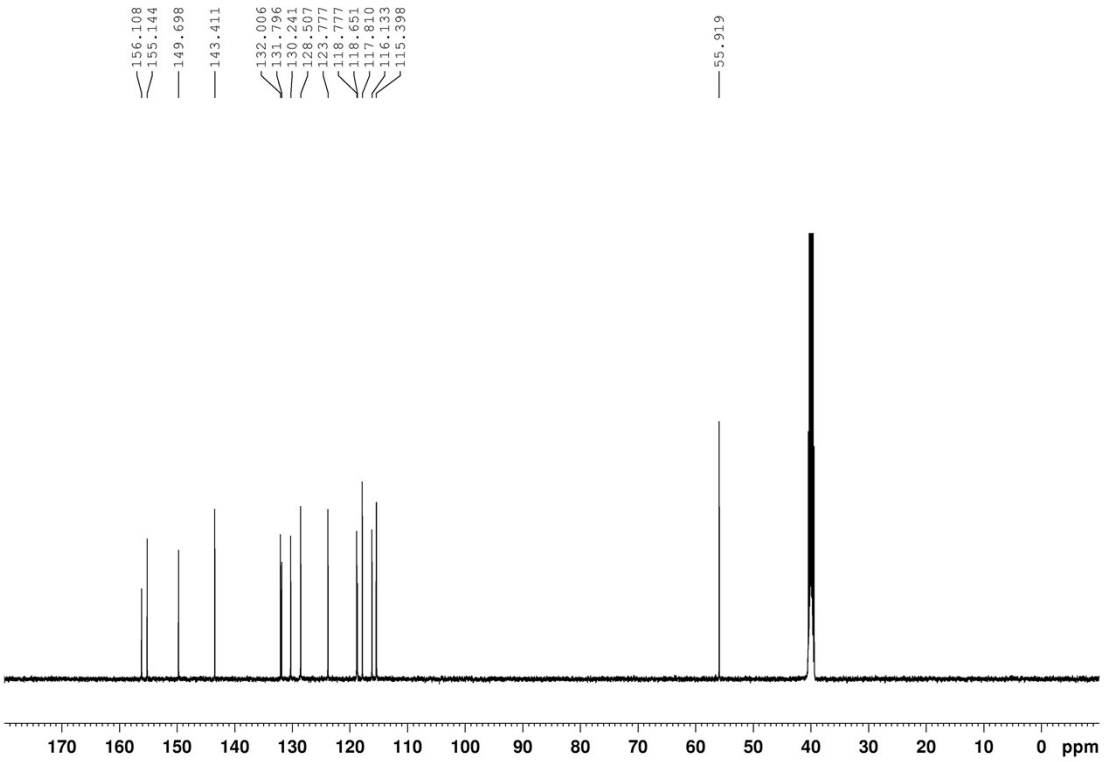
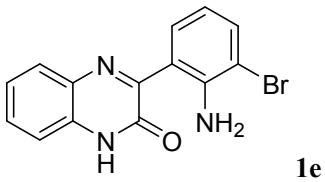


Fig S6. ^{13}CNMR of **1d** in DMSO-d_6



1e

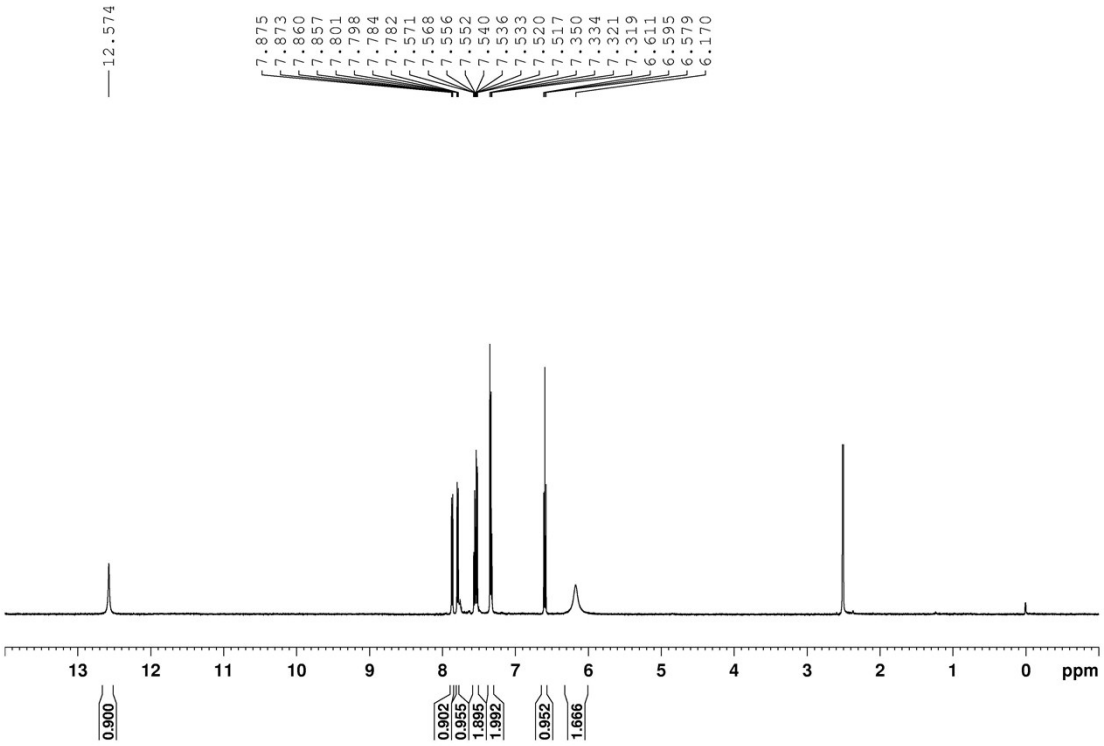


Fig S7. [1]H NMR of **1e** in DMSO-d_6

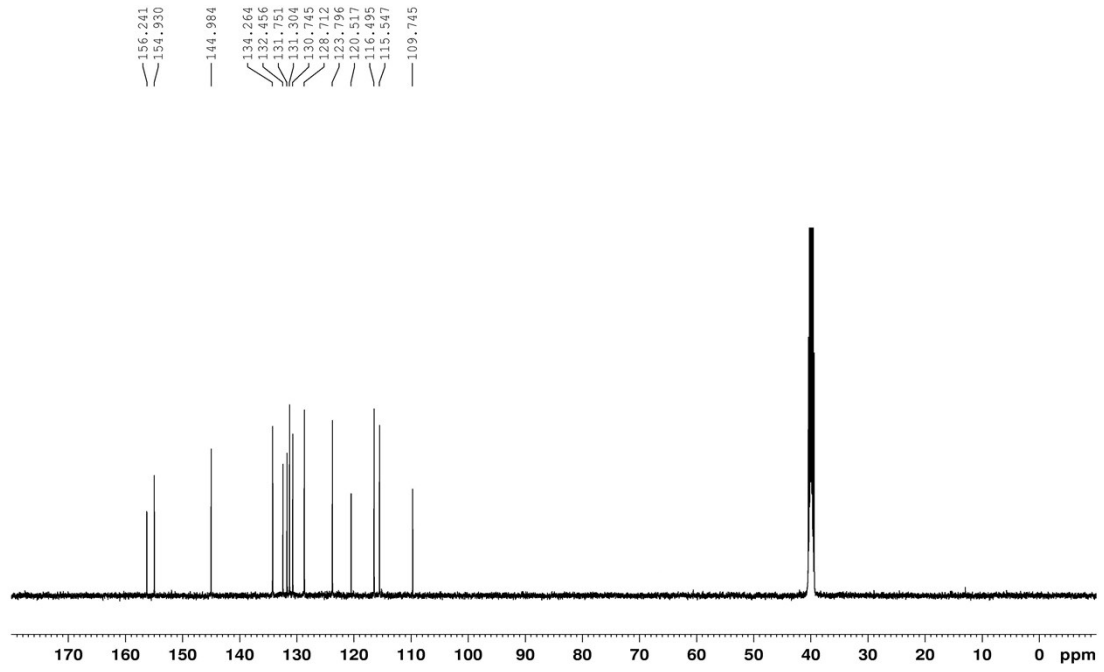
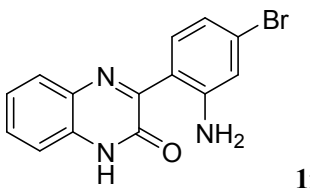
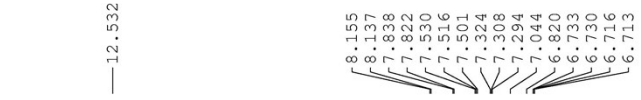


Fig S8. [13]C NMR of **1e** in DMSO-d_6



1f



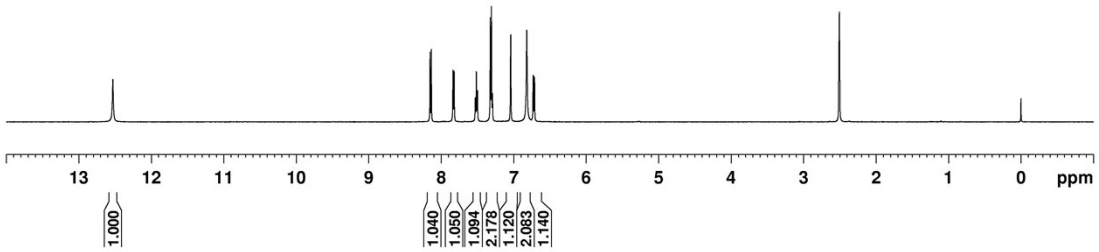
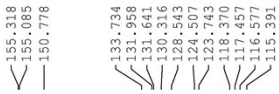


Fig S9. ^{1}H NMR of **1f** in DMSO-d_6



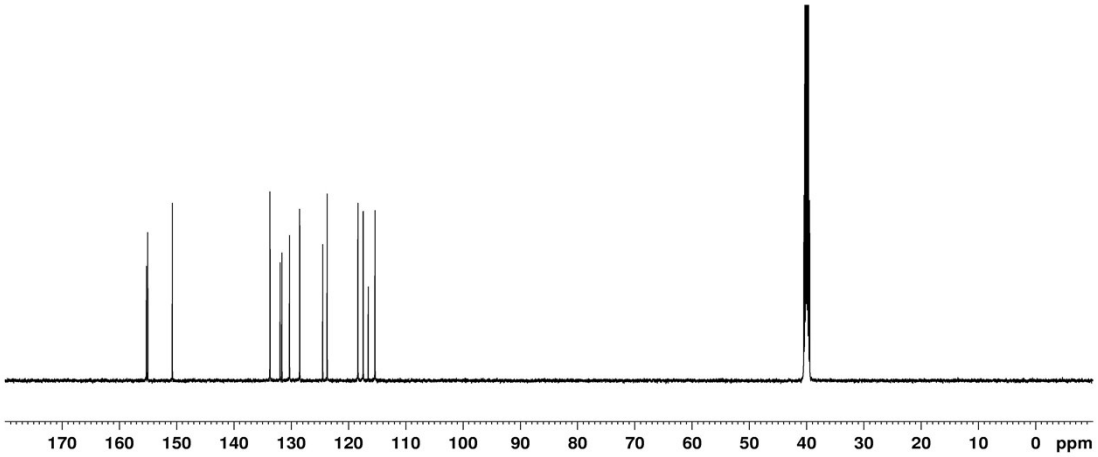
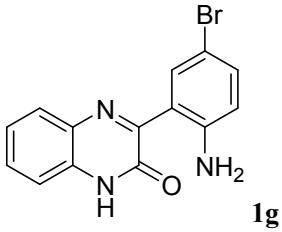


Fig S10. ^{13}C NMR of **1f** in DMSO-d_6



1g

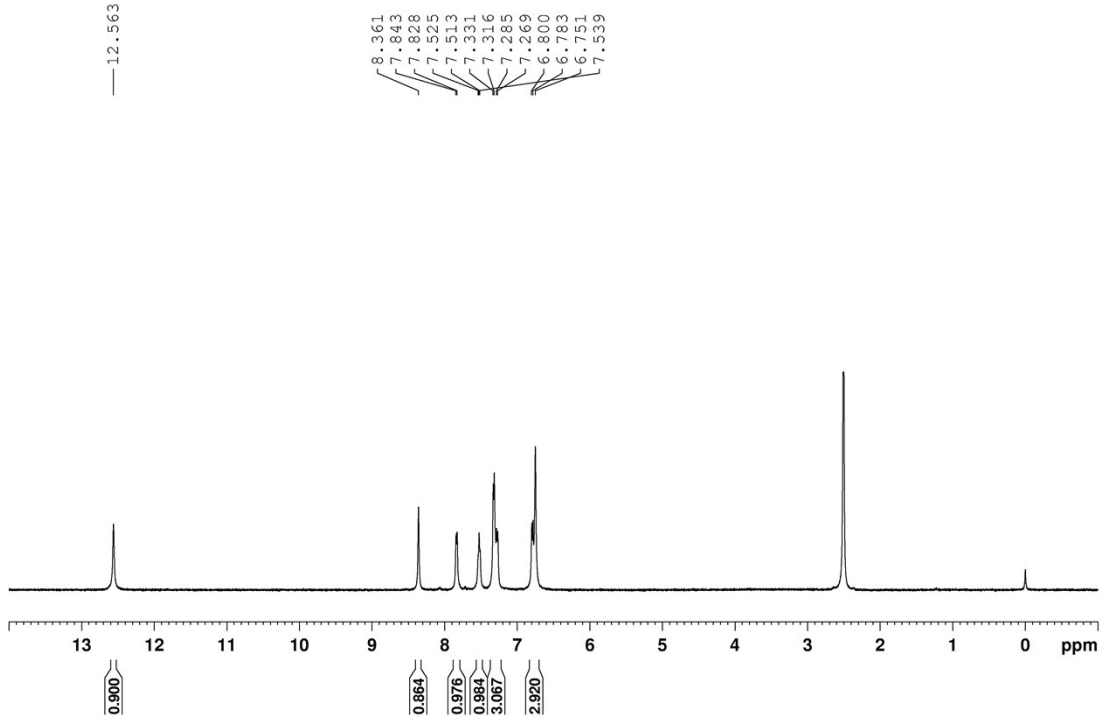
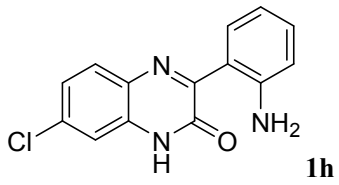


Fig S11. ^{1}H NMR of **1g** in DMSO-d_6



1h

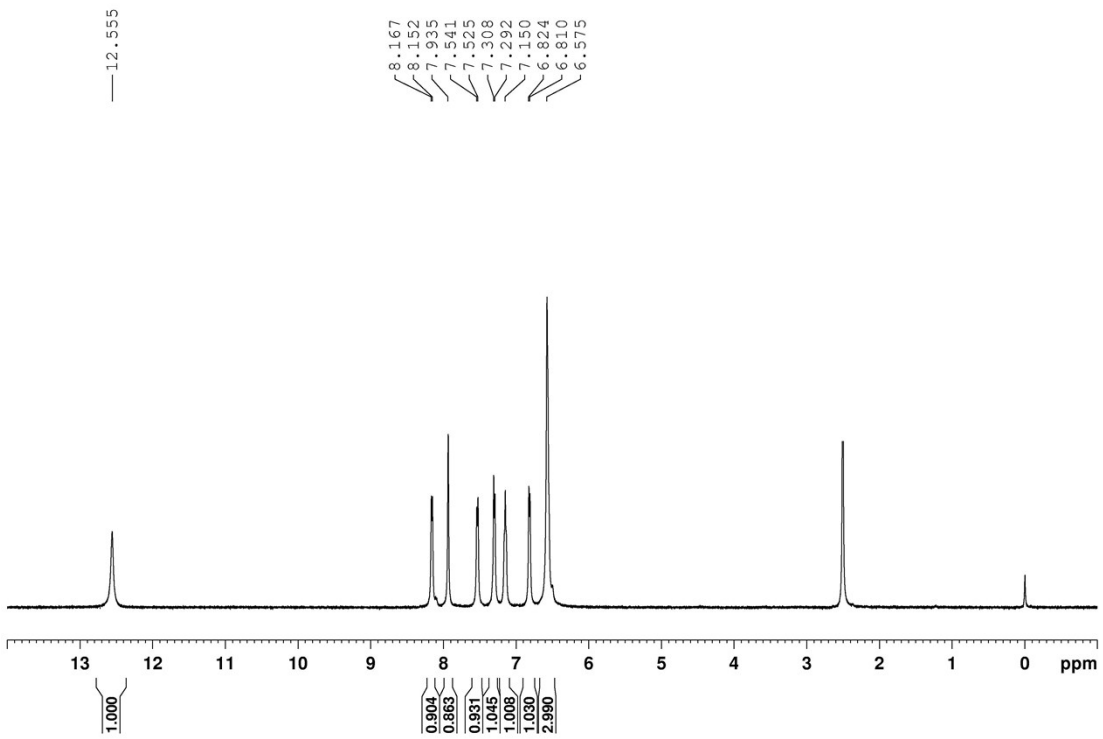


Fig S12. ^{1}H NMR of **1h** in DMSO-d_6

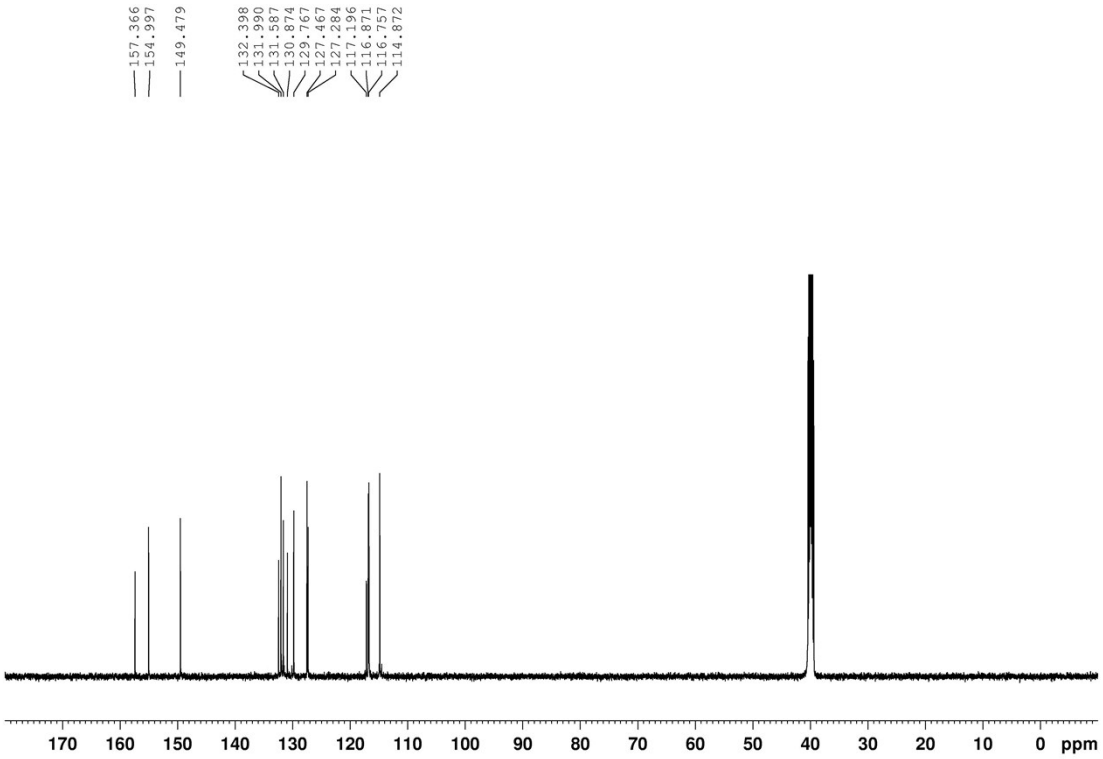


Fig S13. ^{13}C NMR of **1h** in DMSO-d_6

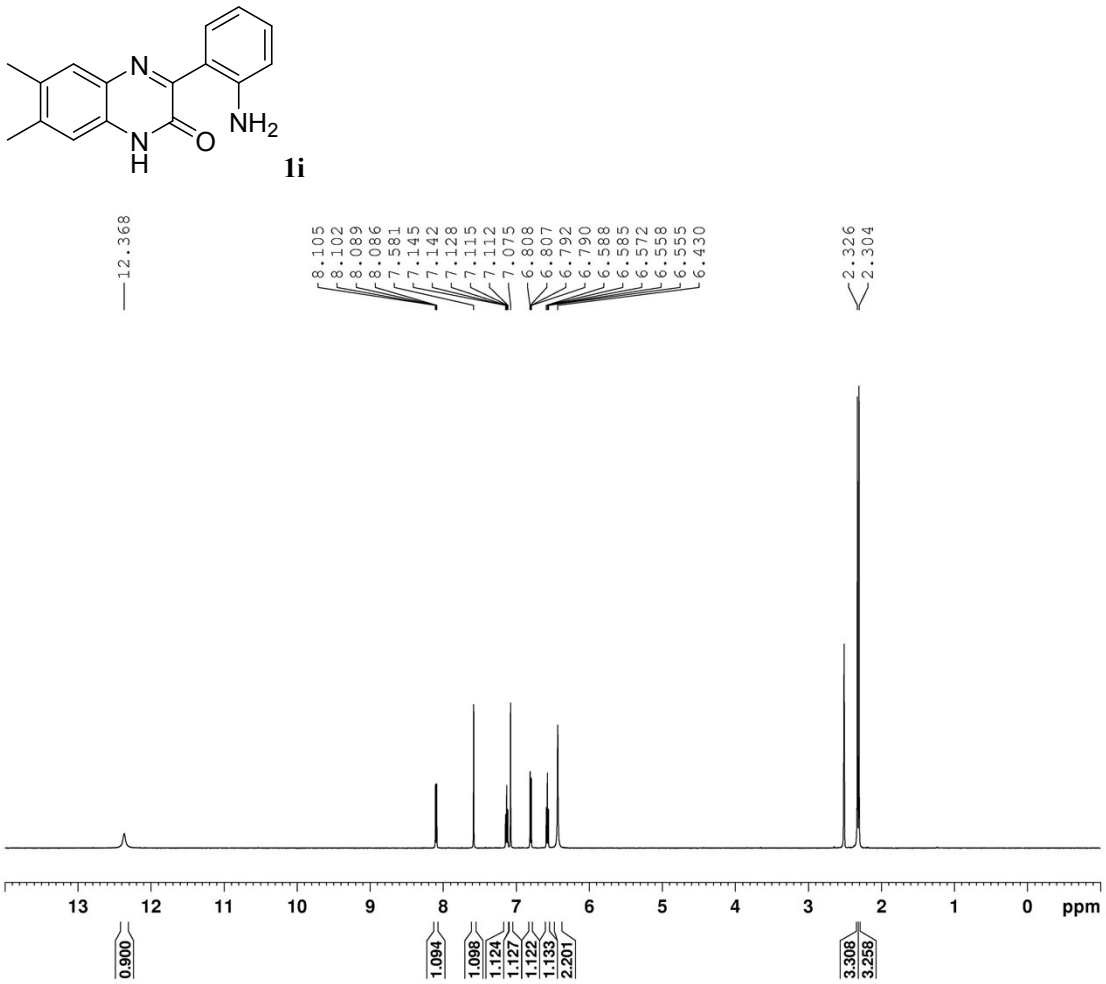


Fig S14. ^{1}H NMR of **1i** in DMSO-d_6

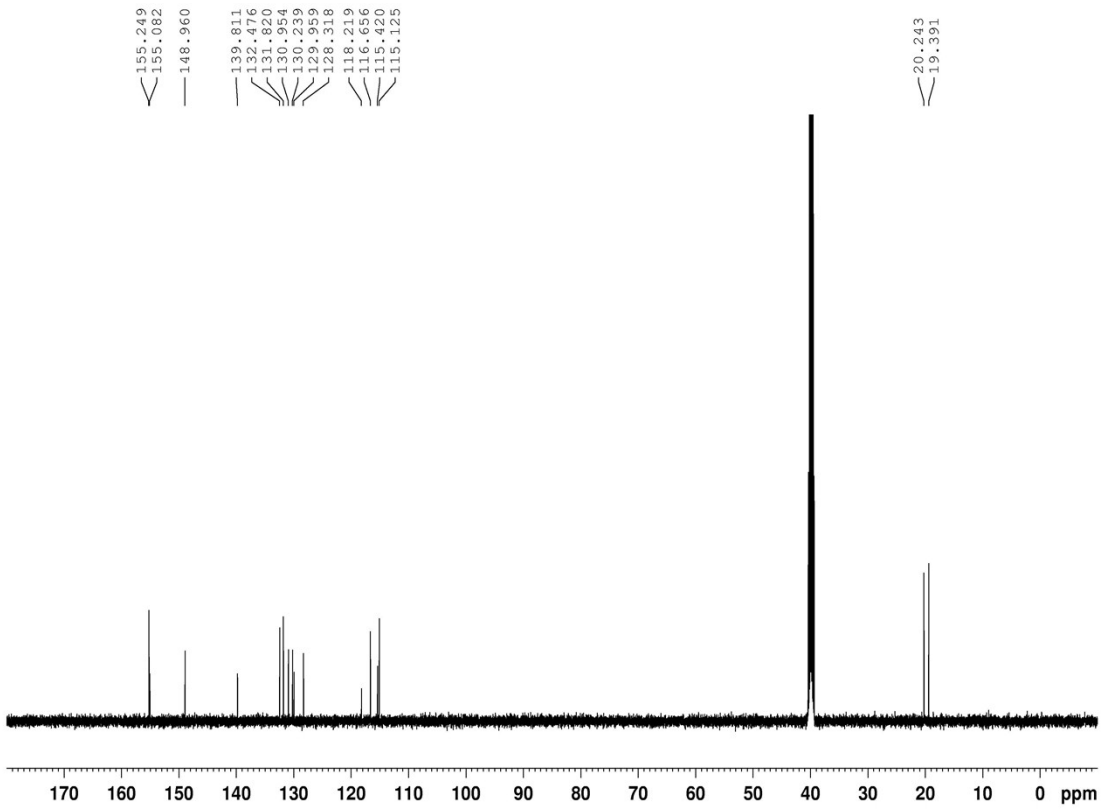


Fig S15. ^{13}C NMR of **1i** in DMSO-d_6

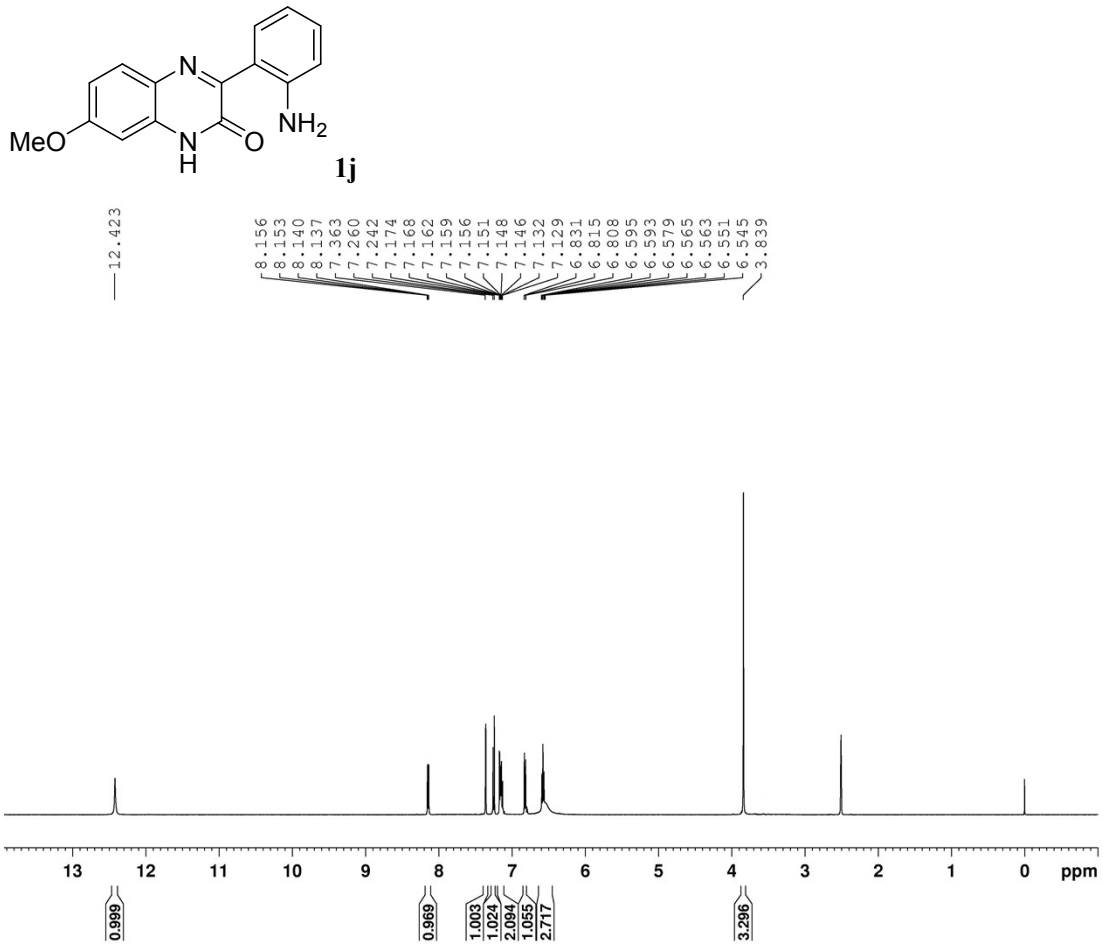


Fig S16. ^{1}H NMR of **1j** in DMSO-d_6

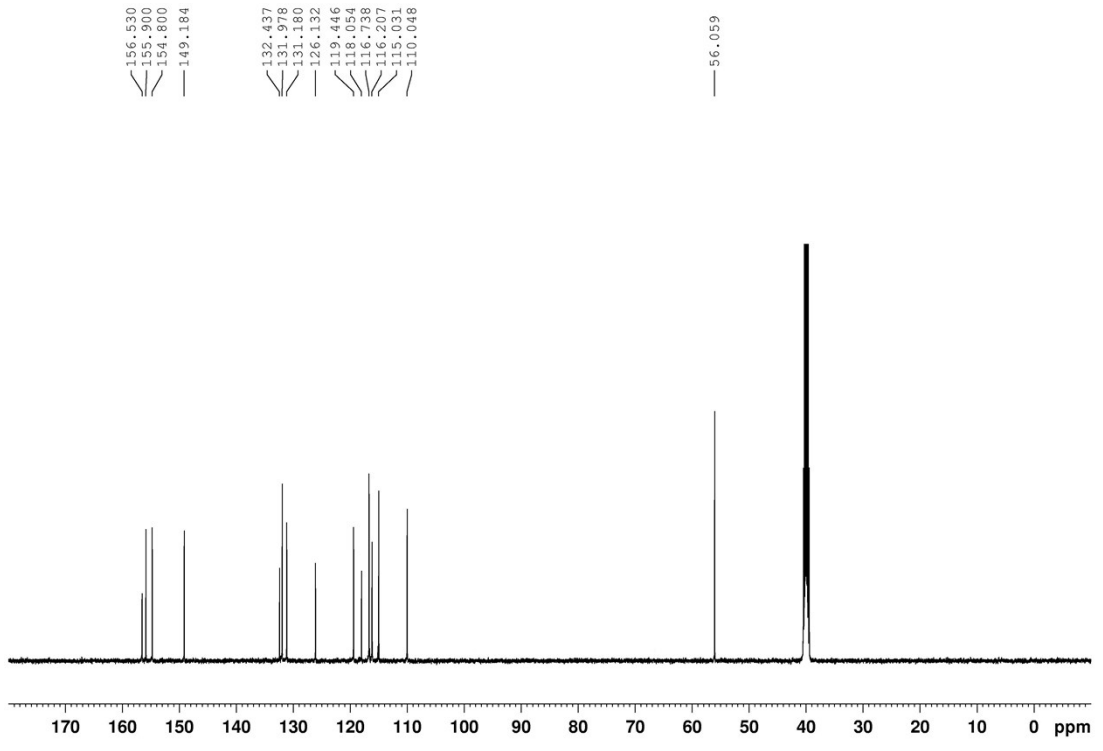


Fig S17. ^{13}C NMR of **1j** in DMSO-d_6

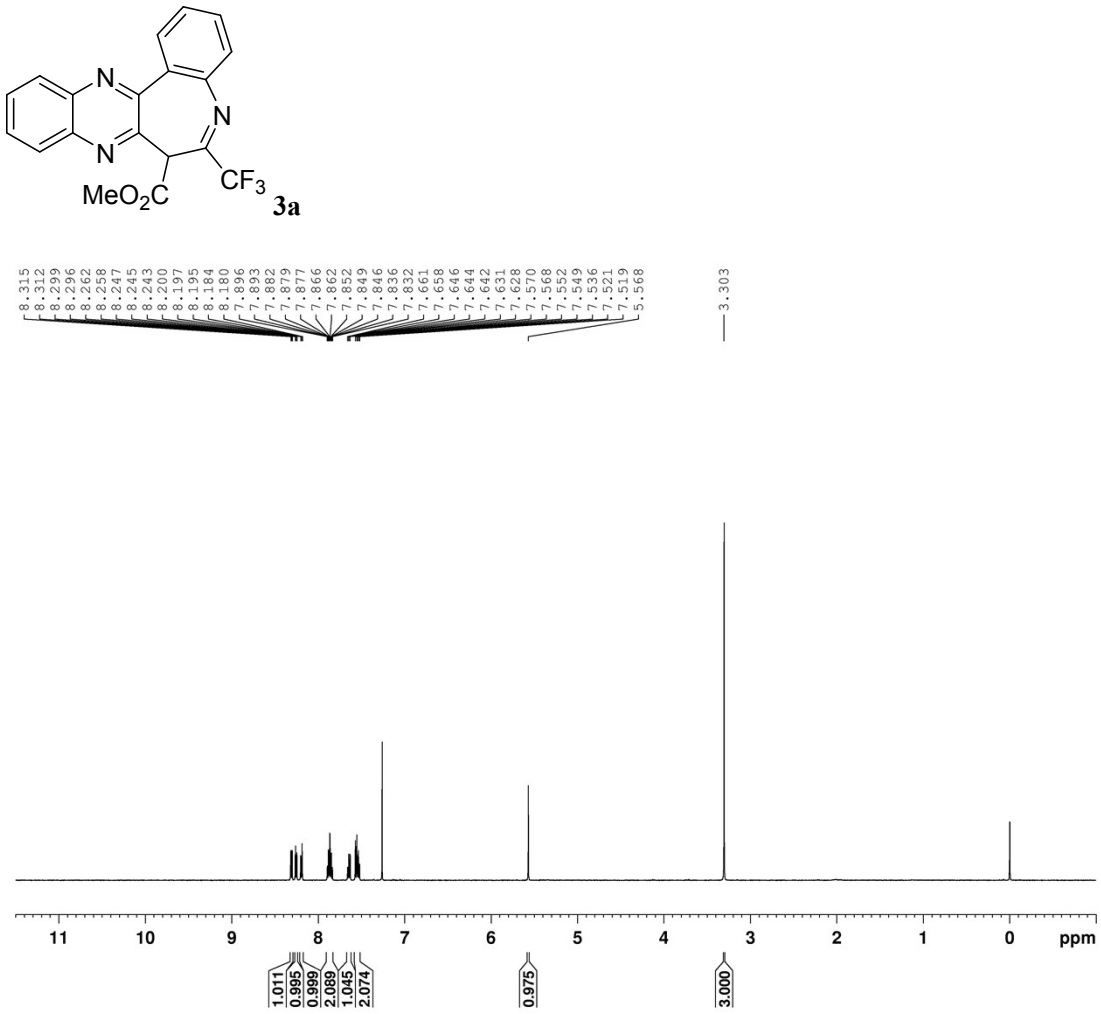


Fig S18. ^{1}H NMR of **3a** in $CDCl_3$

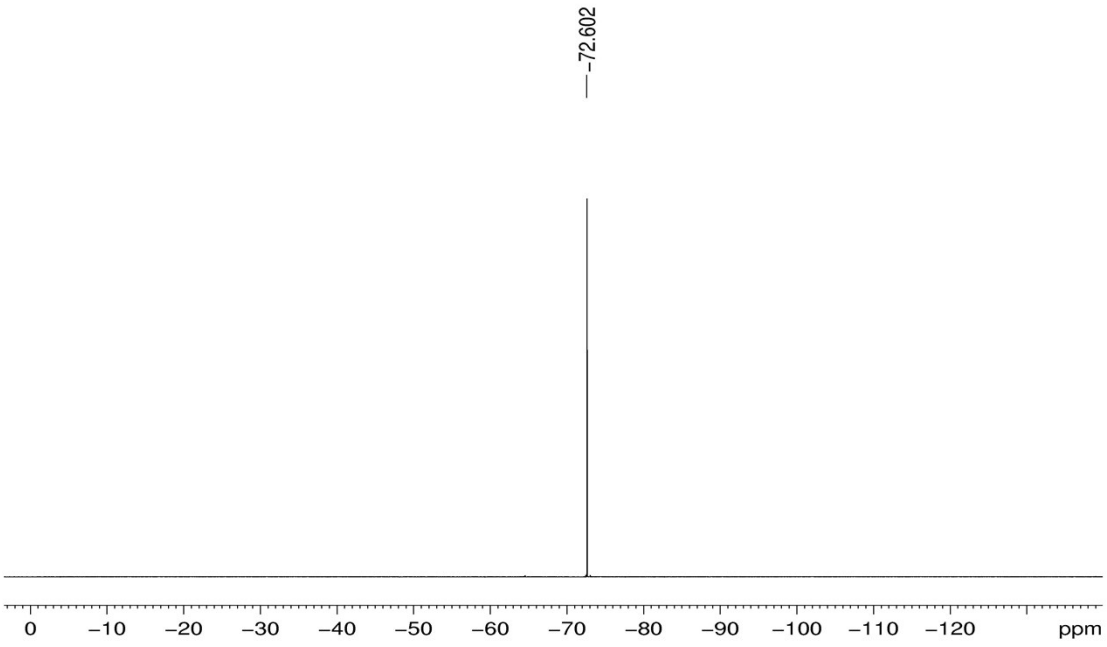


Fig S19. ^{19}F NMR of **3a** in $CDCl_3$

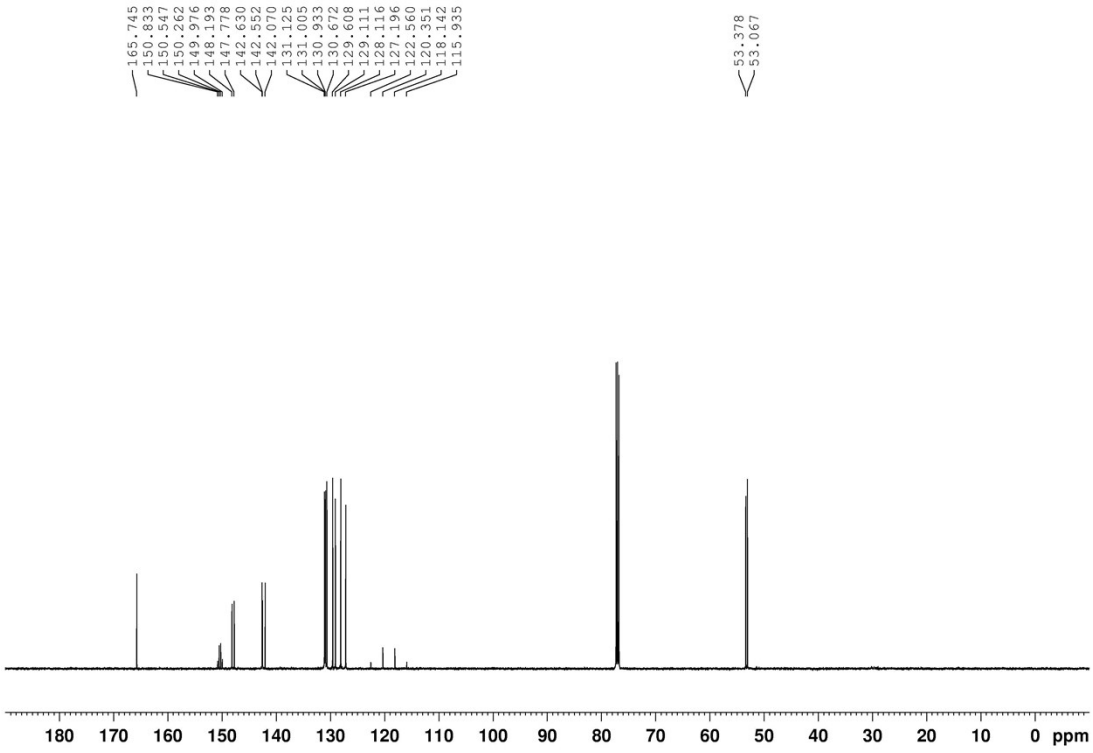


Fig S20. ^{13}C NMR of **3a** in $CDCl_3$

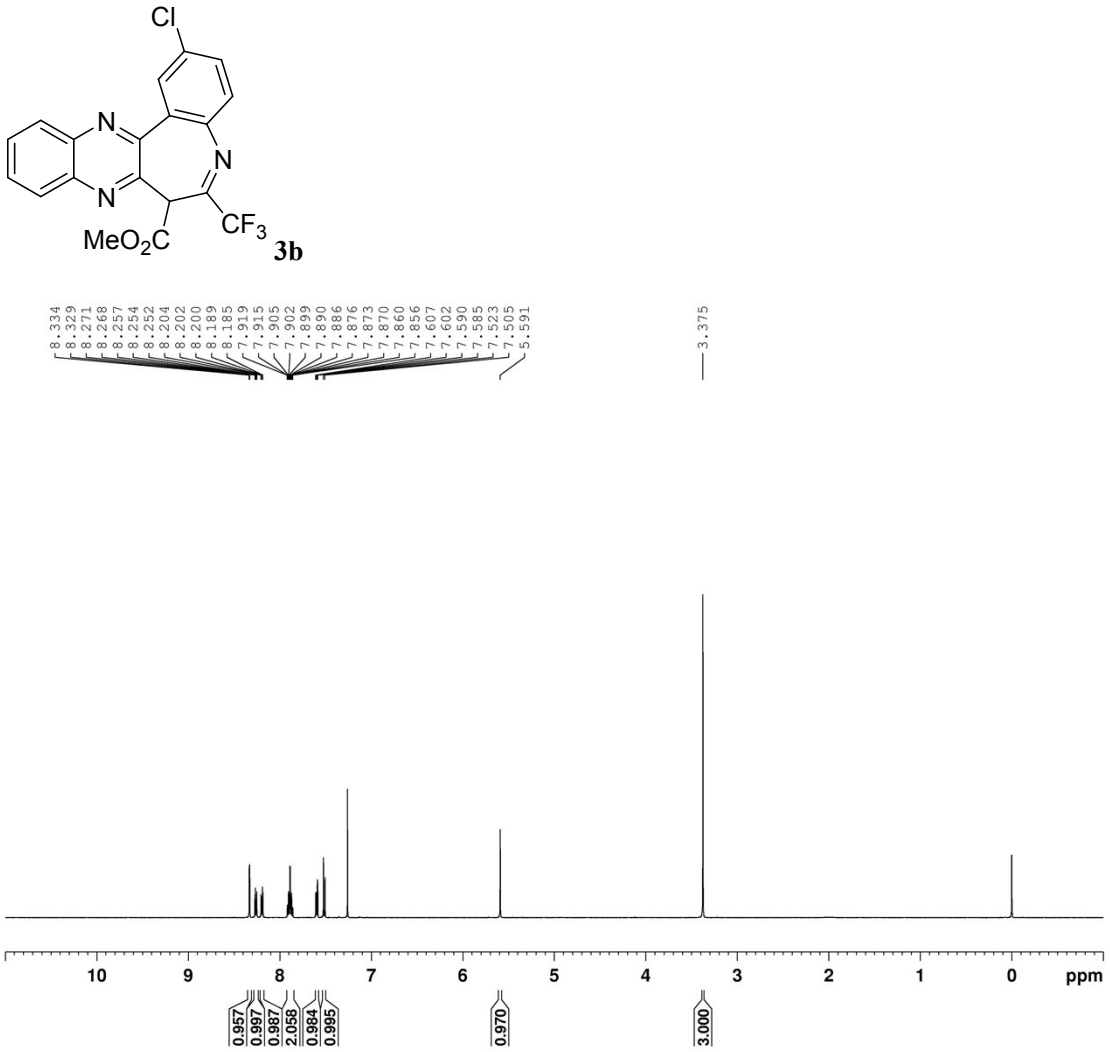


Fig S21. ^{1}H NMR of **3b** in $CDCl_3$

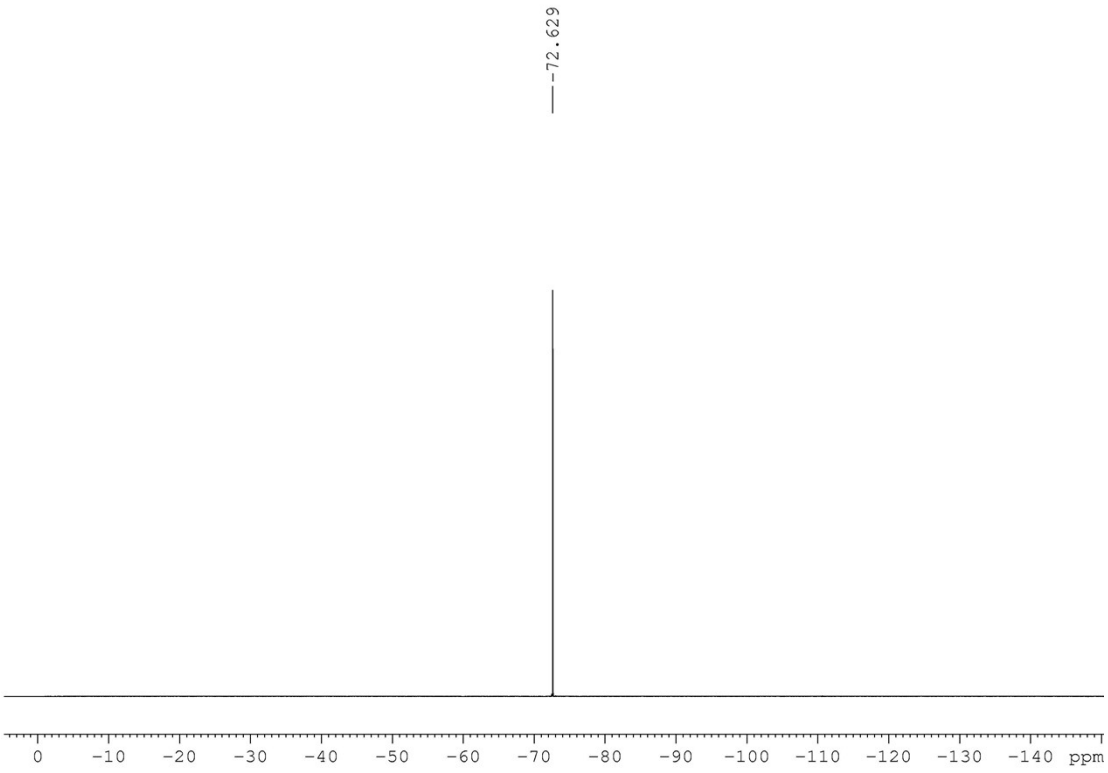


Fig S22. ^{19}F NMR of **3b** in $CDCl_3$

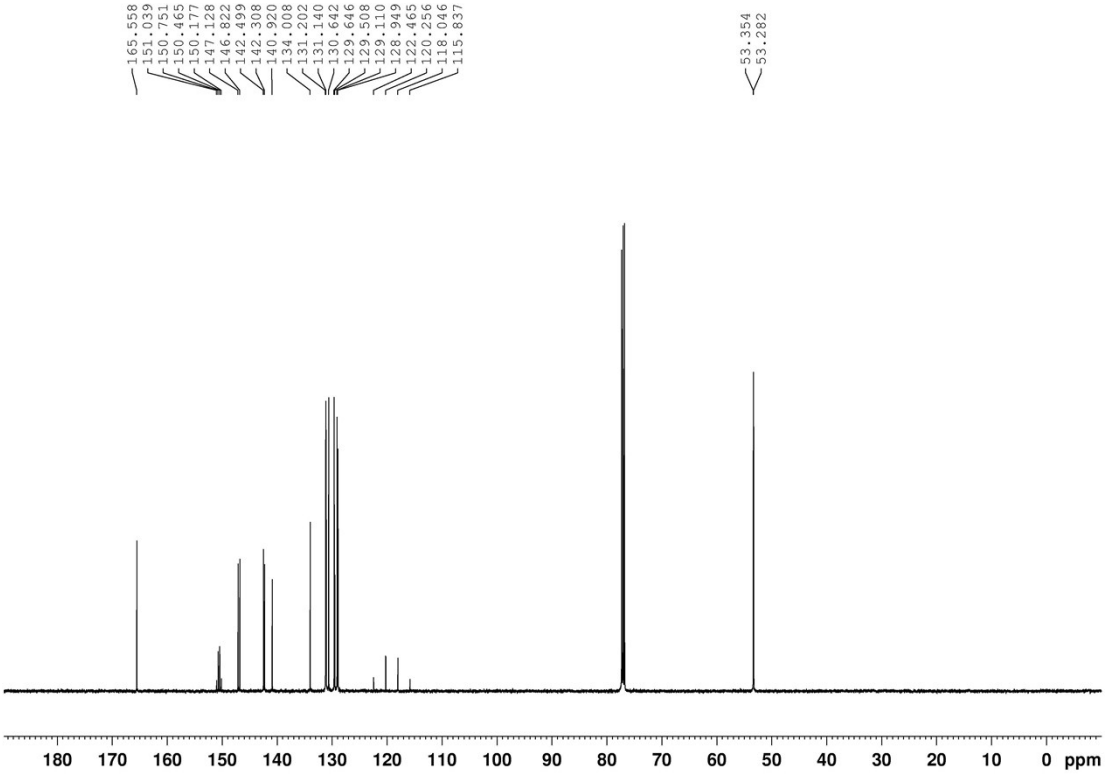


Fig S23. ^{13}C NMR of **3b** in $CDCl_3$

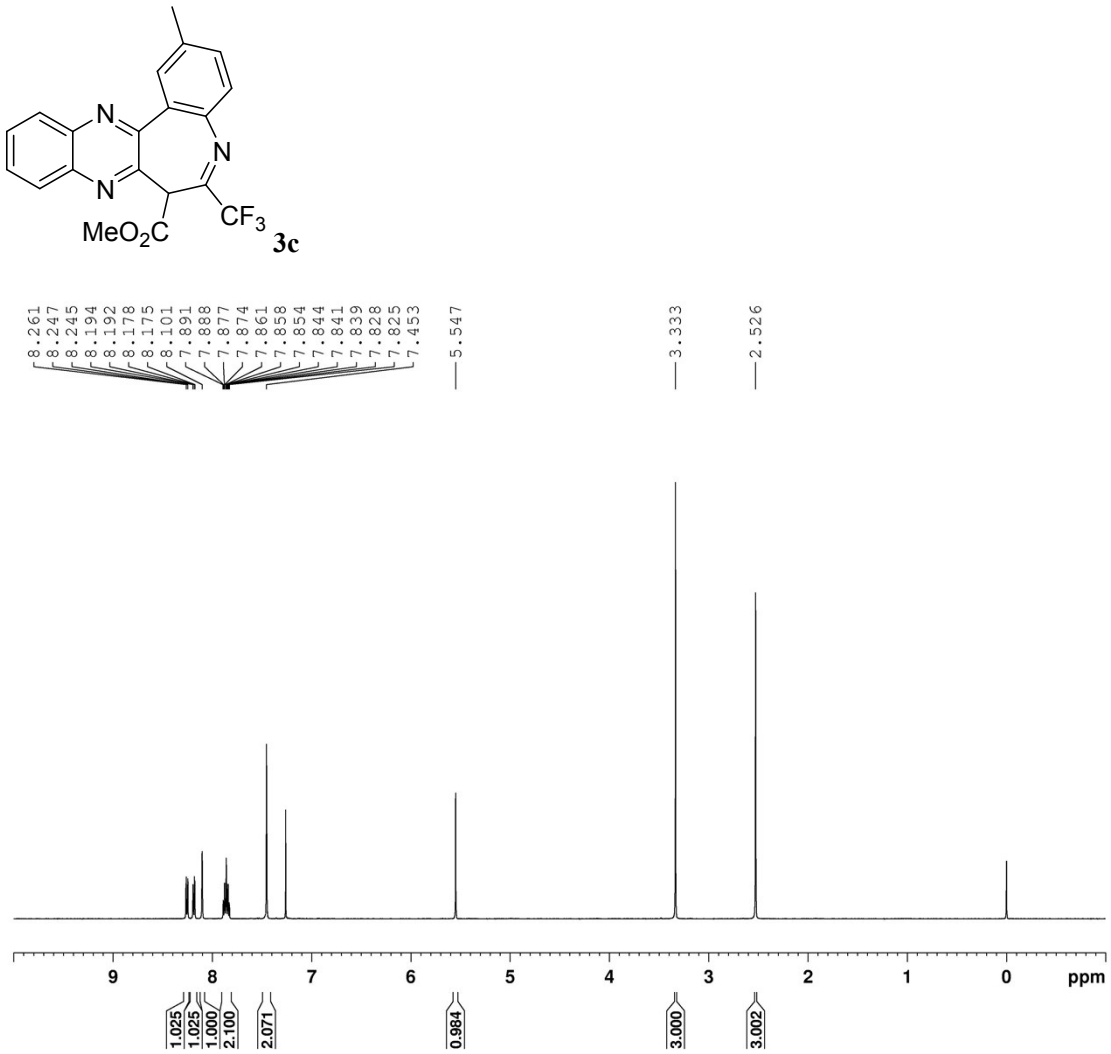


Fig S24. ^{1}H NMR of **3c** in $CDCl_3$

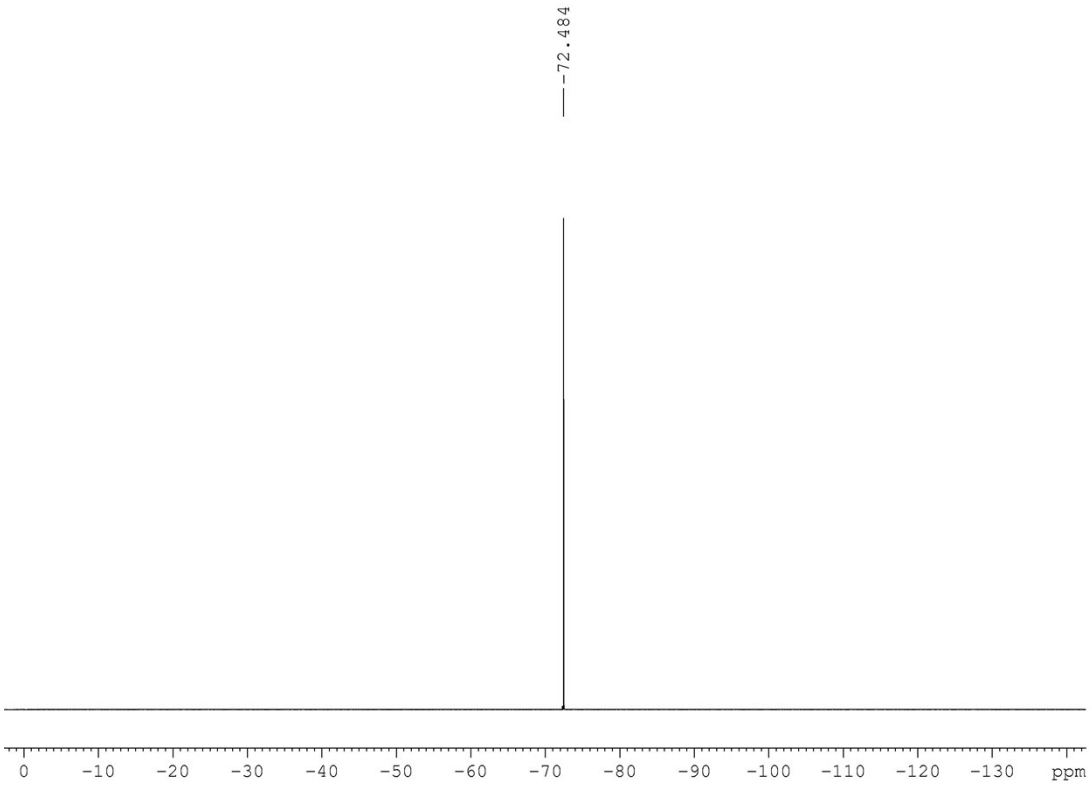


Fig S25. ^{19}F NMR of **3c** in $CDCl_3$

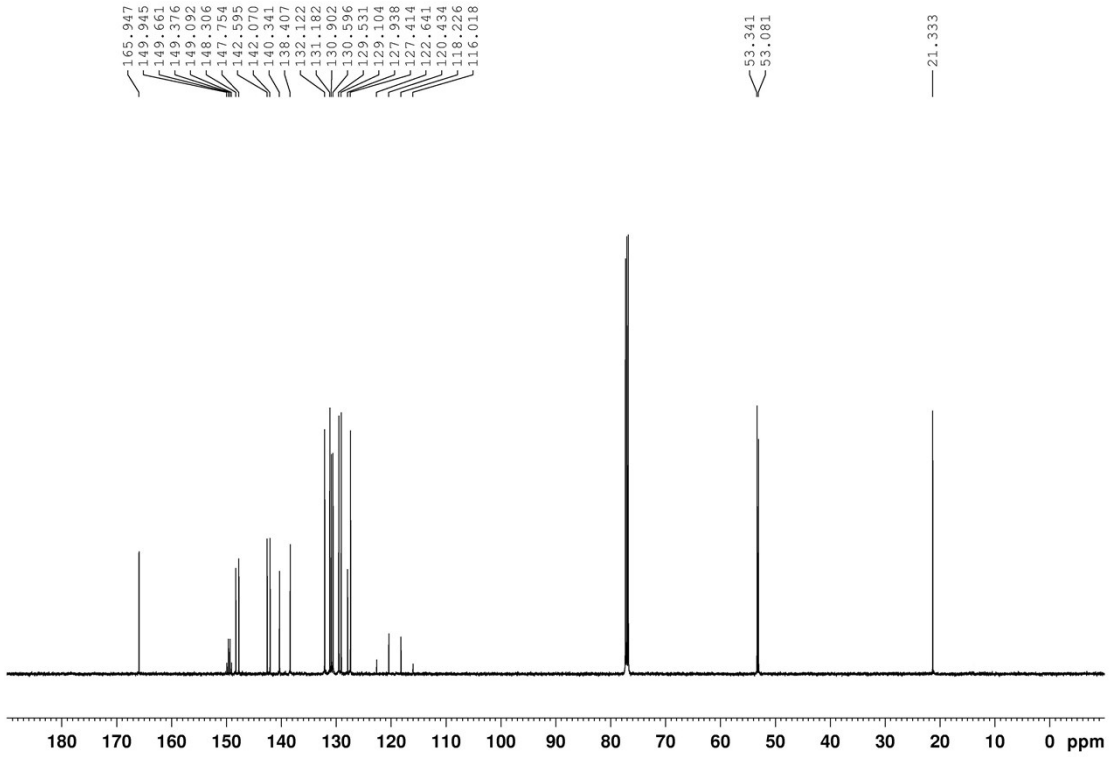


Fig S26. ^{13}C NMR of **3c** in $CDCl_3$

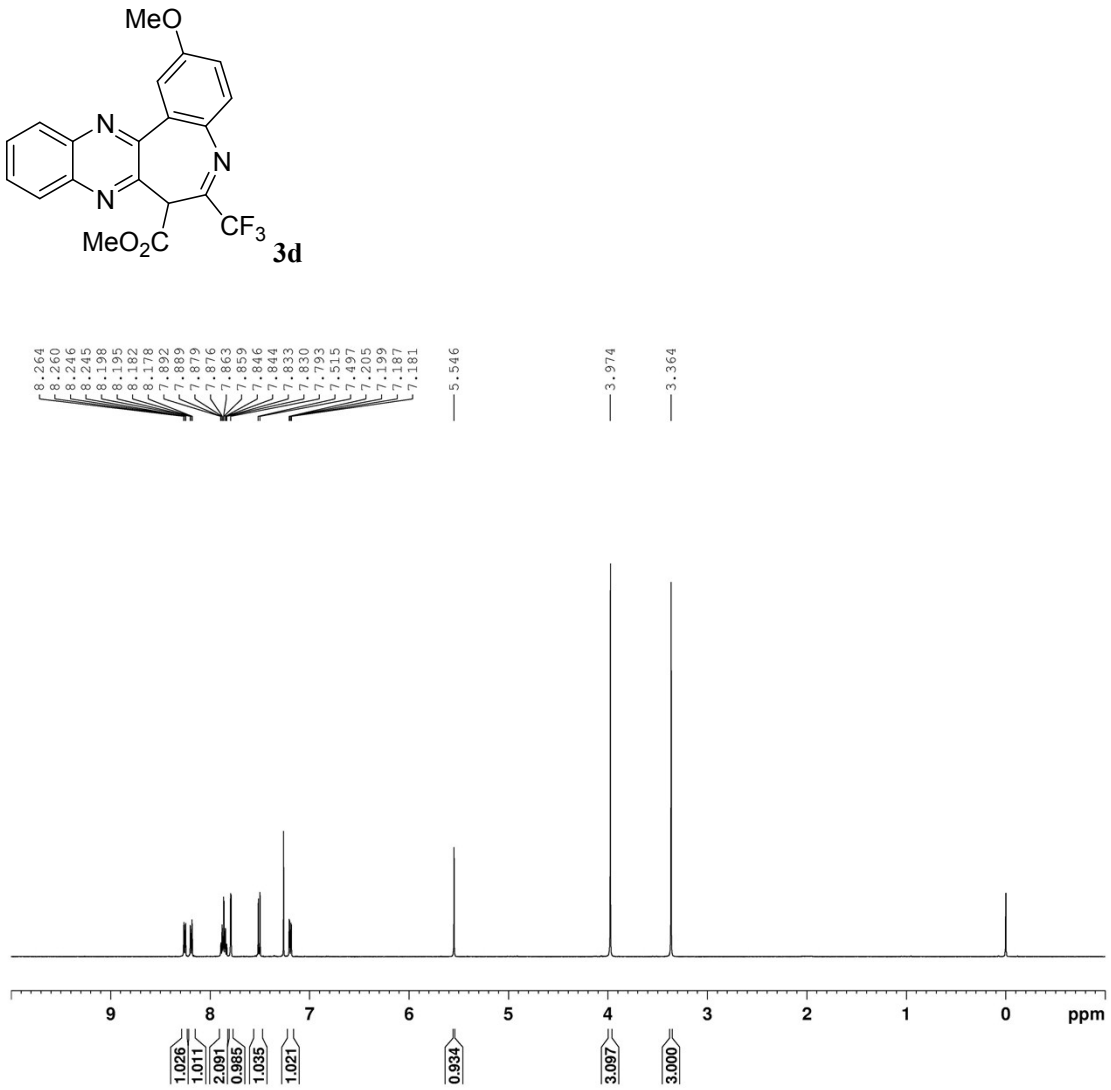


Fig S27. ^{1}H NMR of **3d** in $CDCl_3$

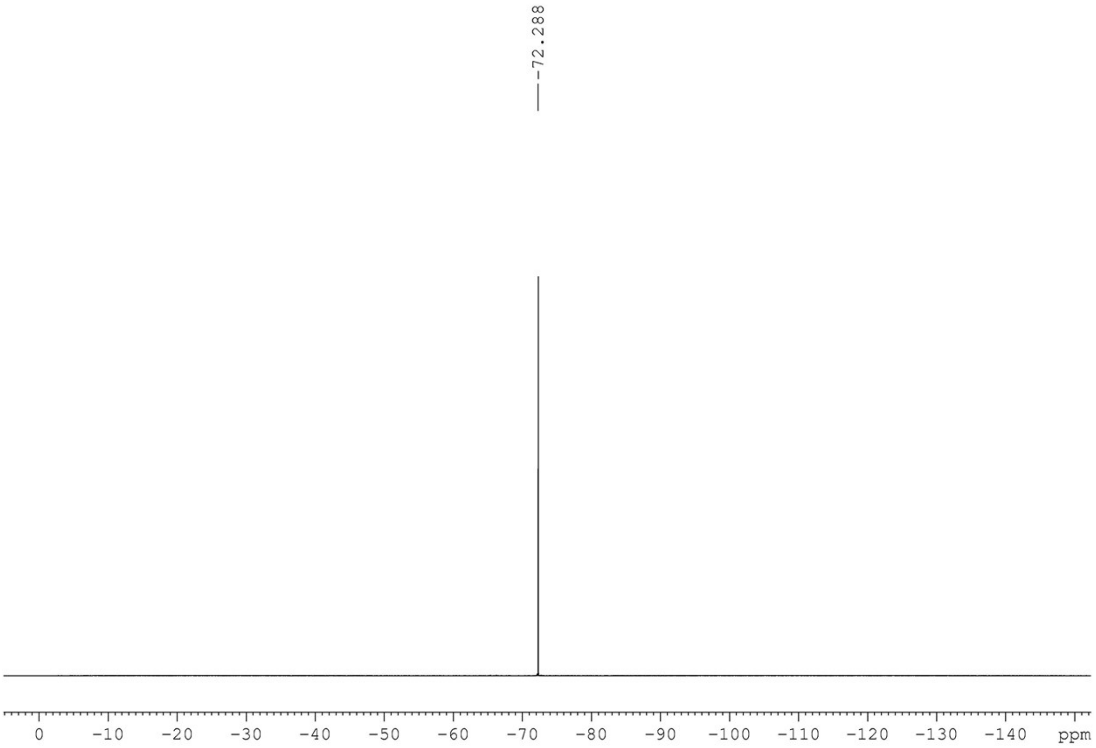


Fig S28. ^{19}F NMR of **3d** in $CDCl_3$

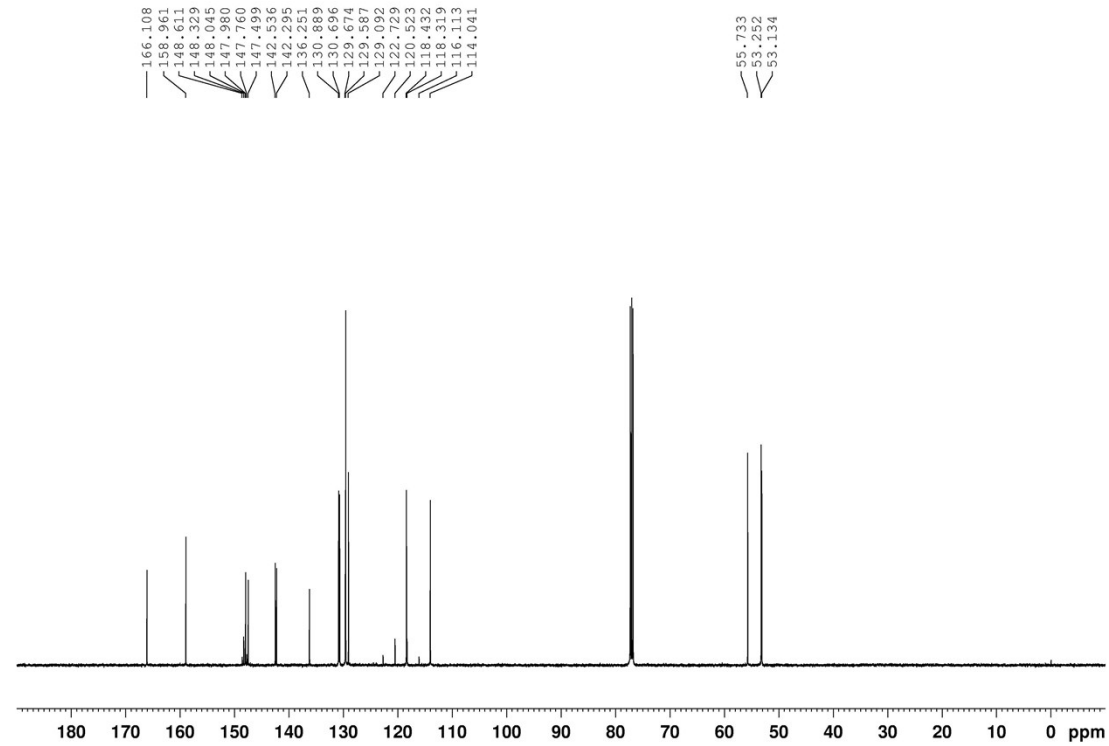


Fig S29. ^{13}C NMR of **3d** in $CDCl_3$

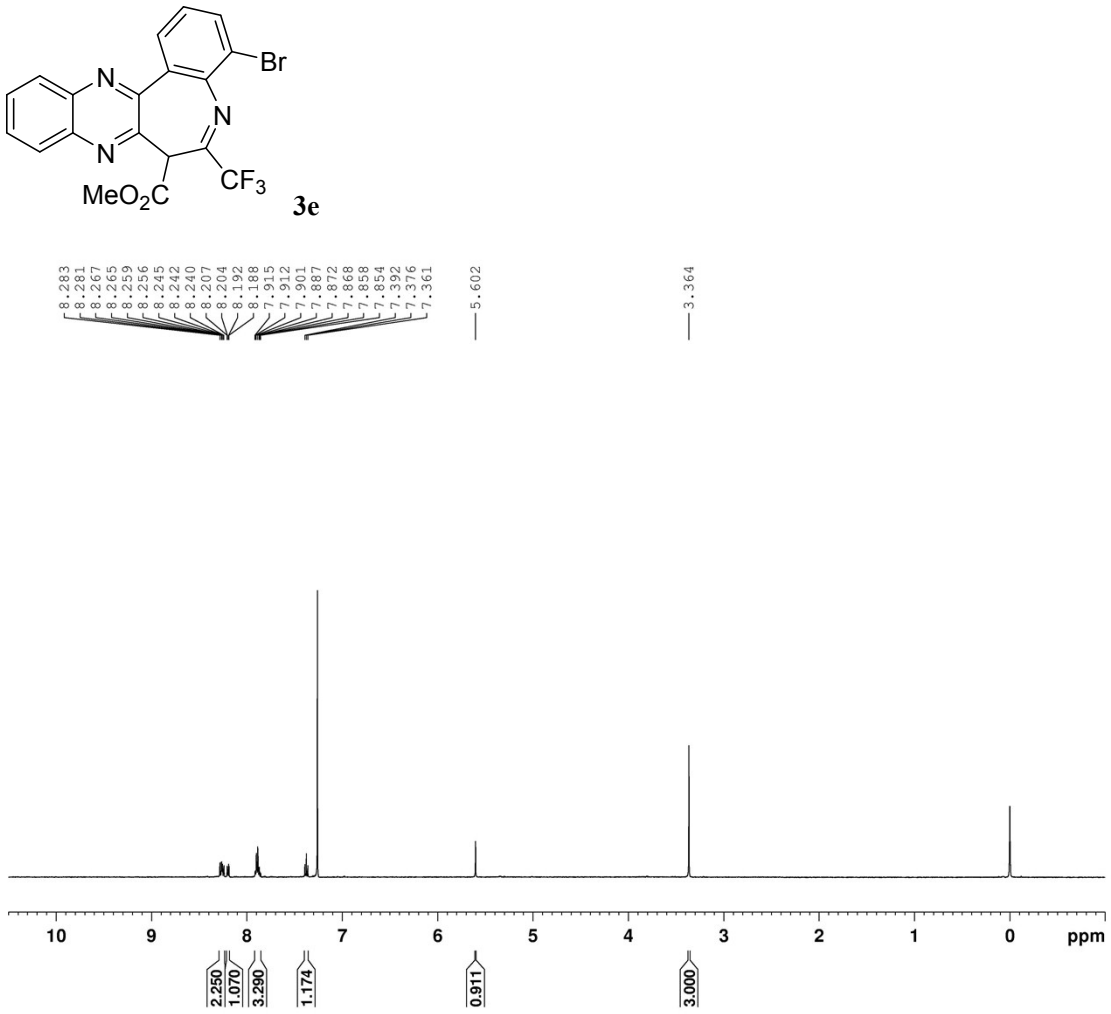


Fig S30. ^{1}H NMR of **3e** in $CDCl_3$

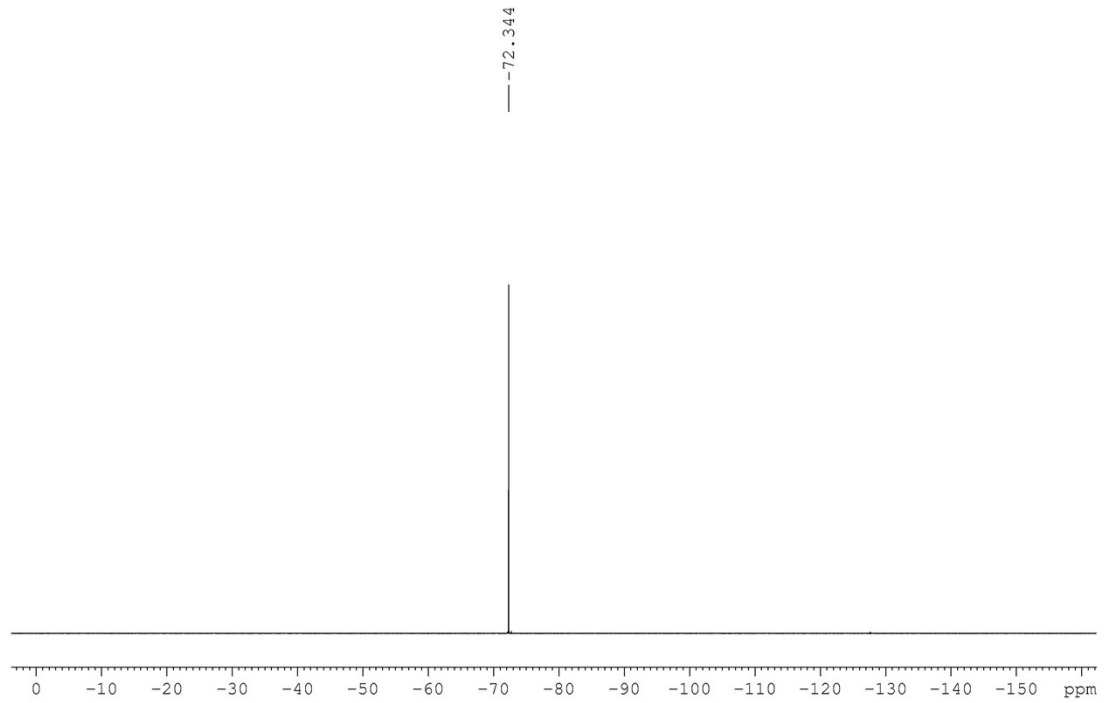


Fig S31. ^{19}F NMR of **3e** in $CDCl_3$

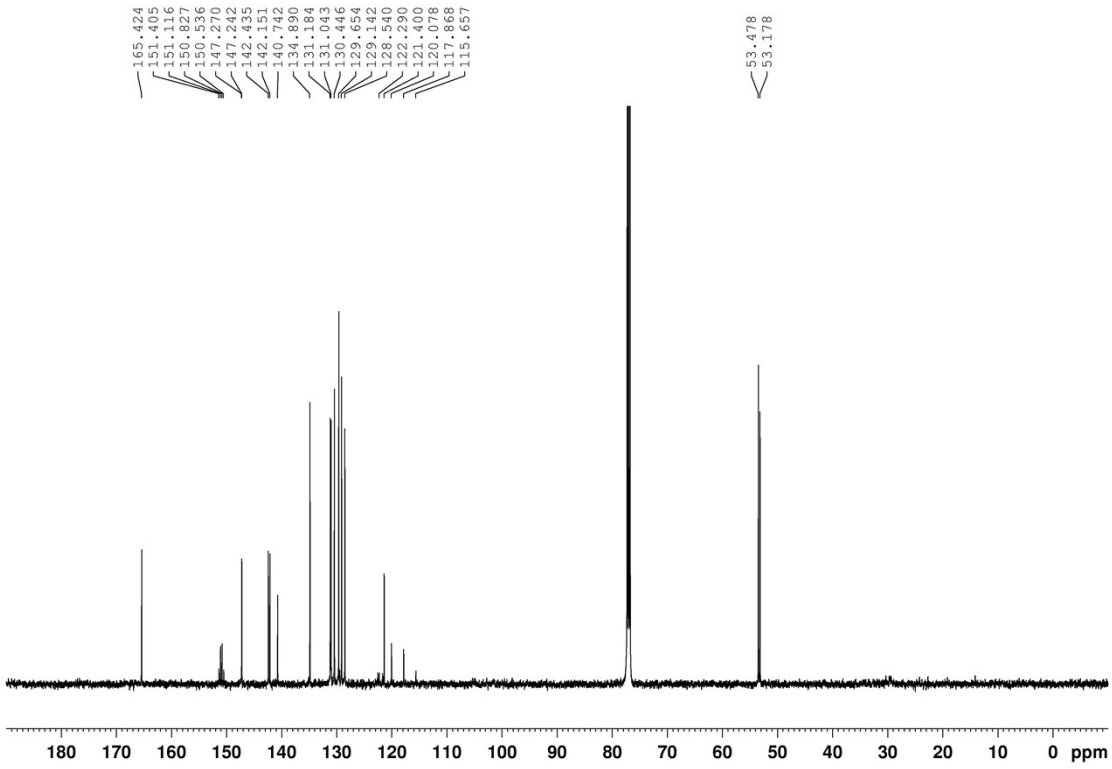


Fig S32. ^{13}C NMR of **3e** in $CDCl_3$

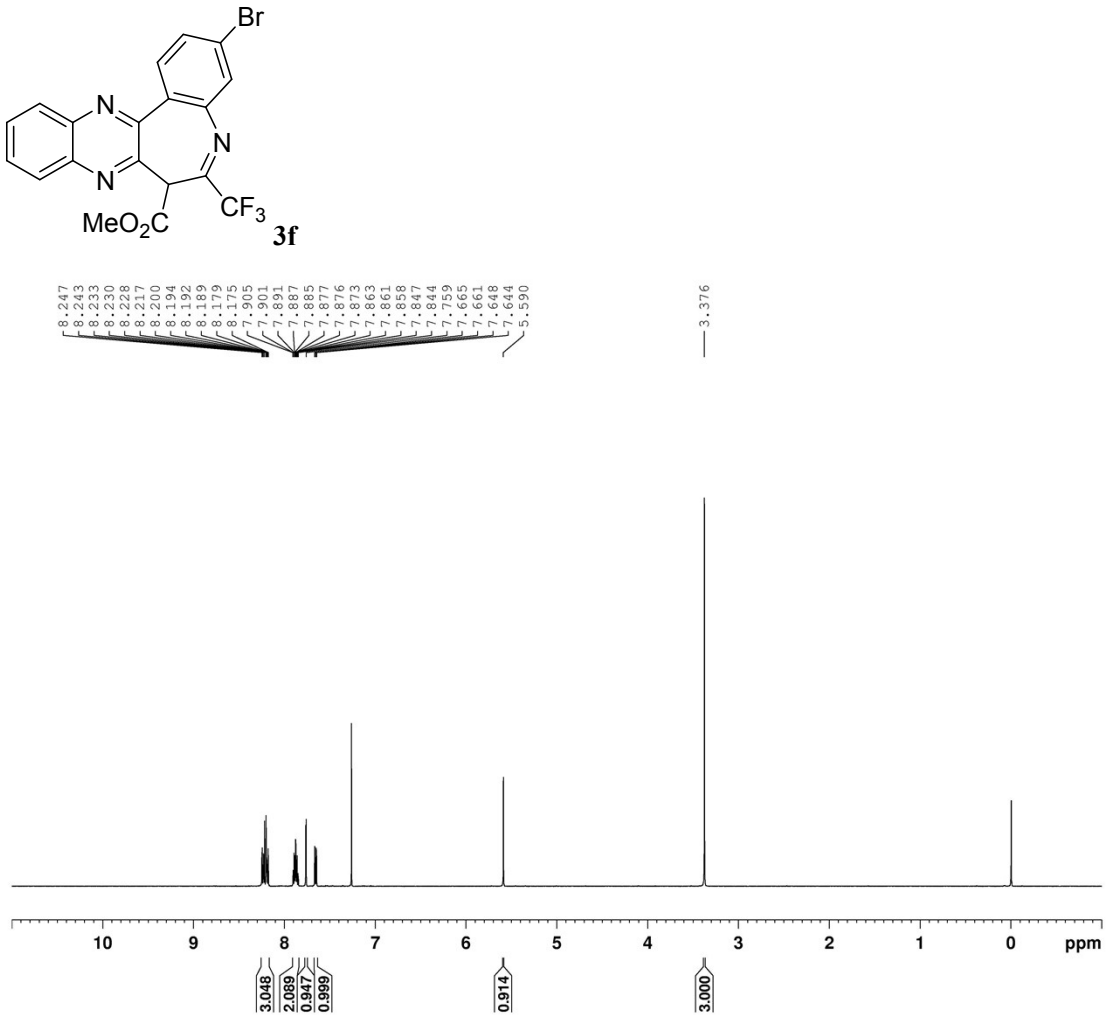


Fig S33. ^{1}H NMR of **3f** in $CDCl_3$

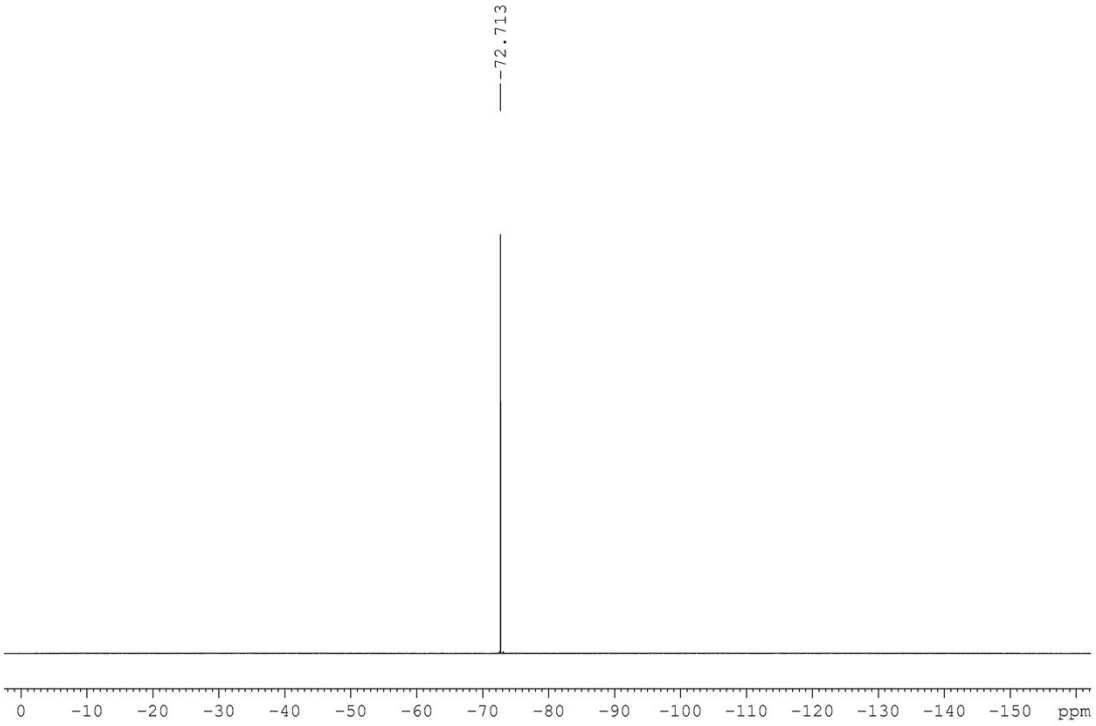


Fig S34. ^{19}F NMR of **3f** in $CDCl_3$

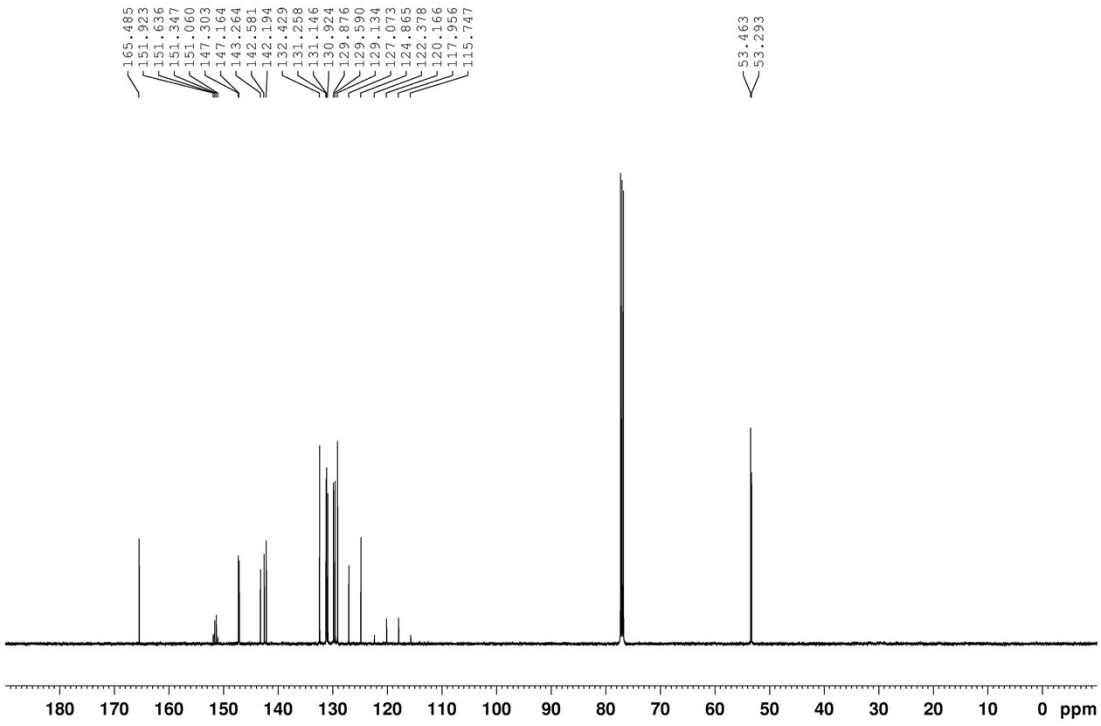


Fig S35. ^{13}C NMR of **3f** in $CDCl_3$

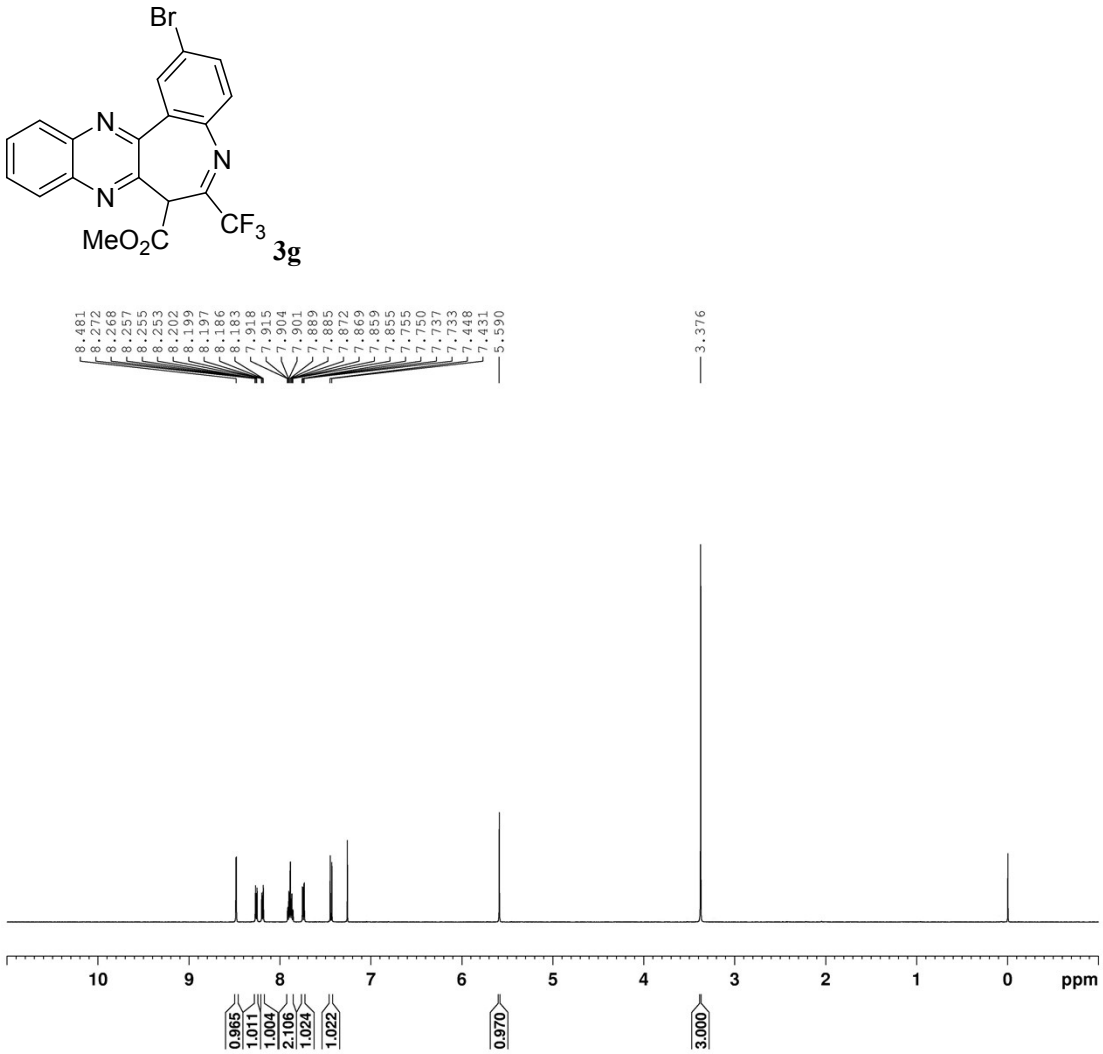


Fig S36. ^{1}H NMR of **3g** in $CDCl_3$

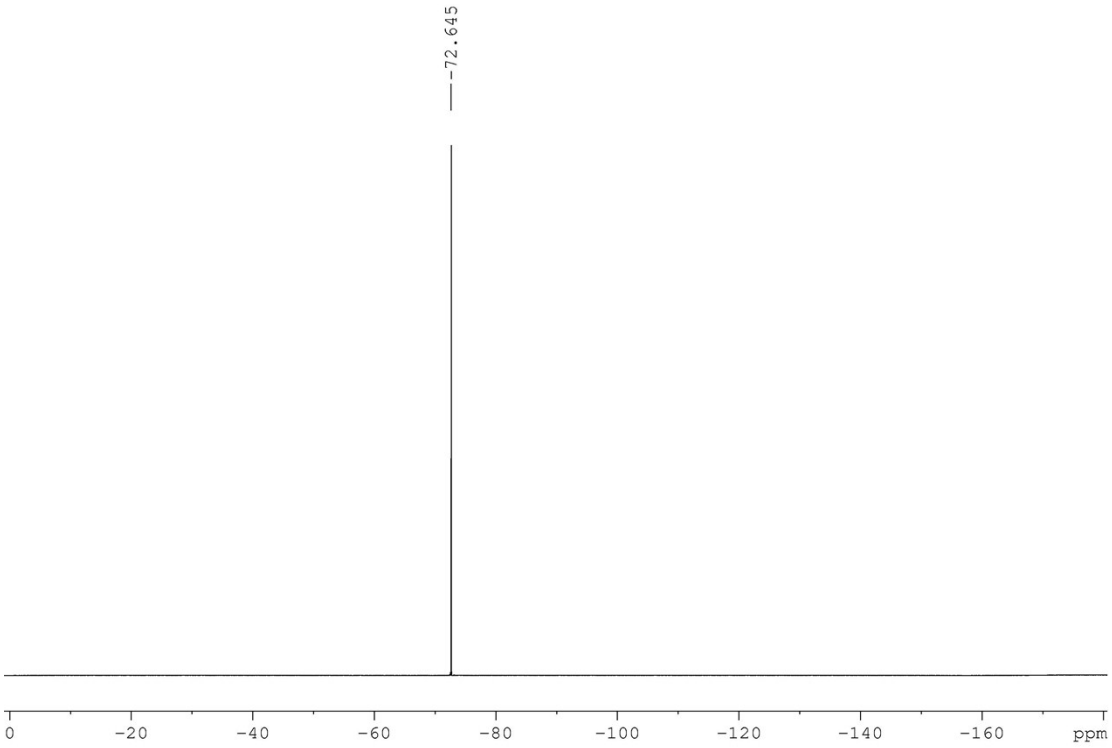


Fig S37. ^{19}F NMR of **3g** in $CDCl_3$

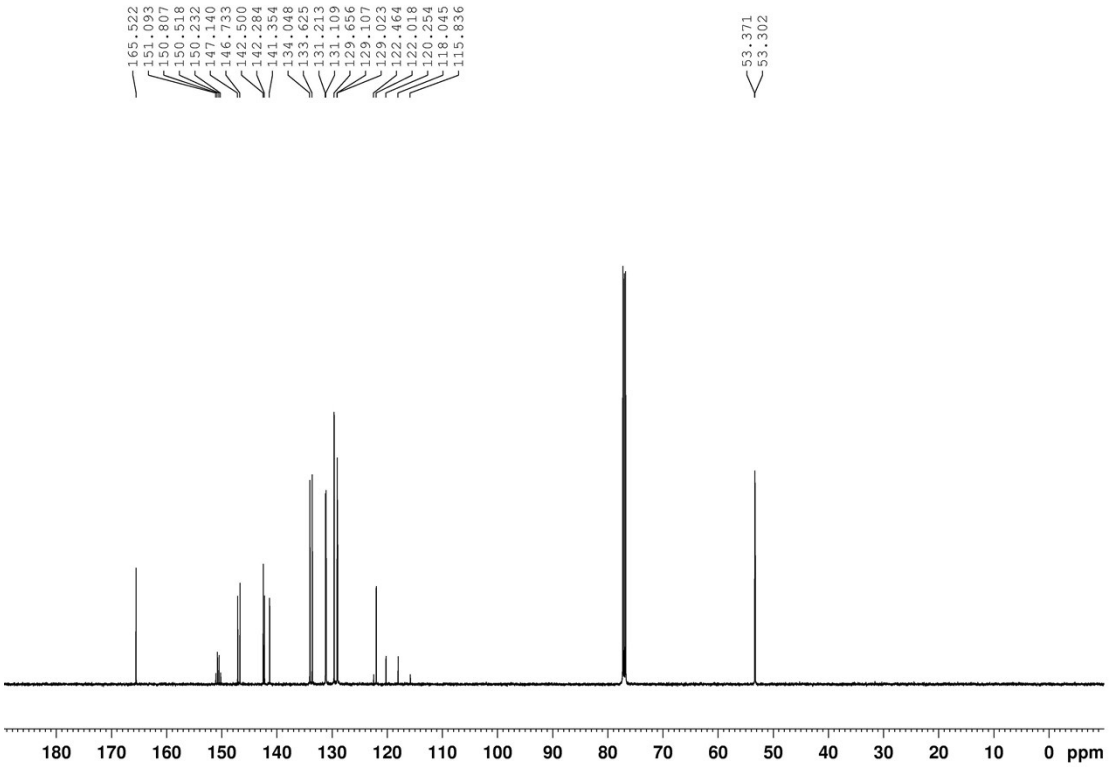


Fig S38. ^{13}C NMR of **3g** in $CDCl_3$

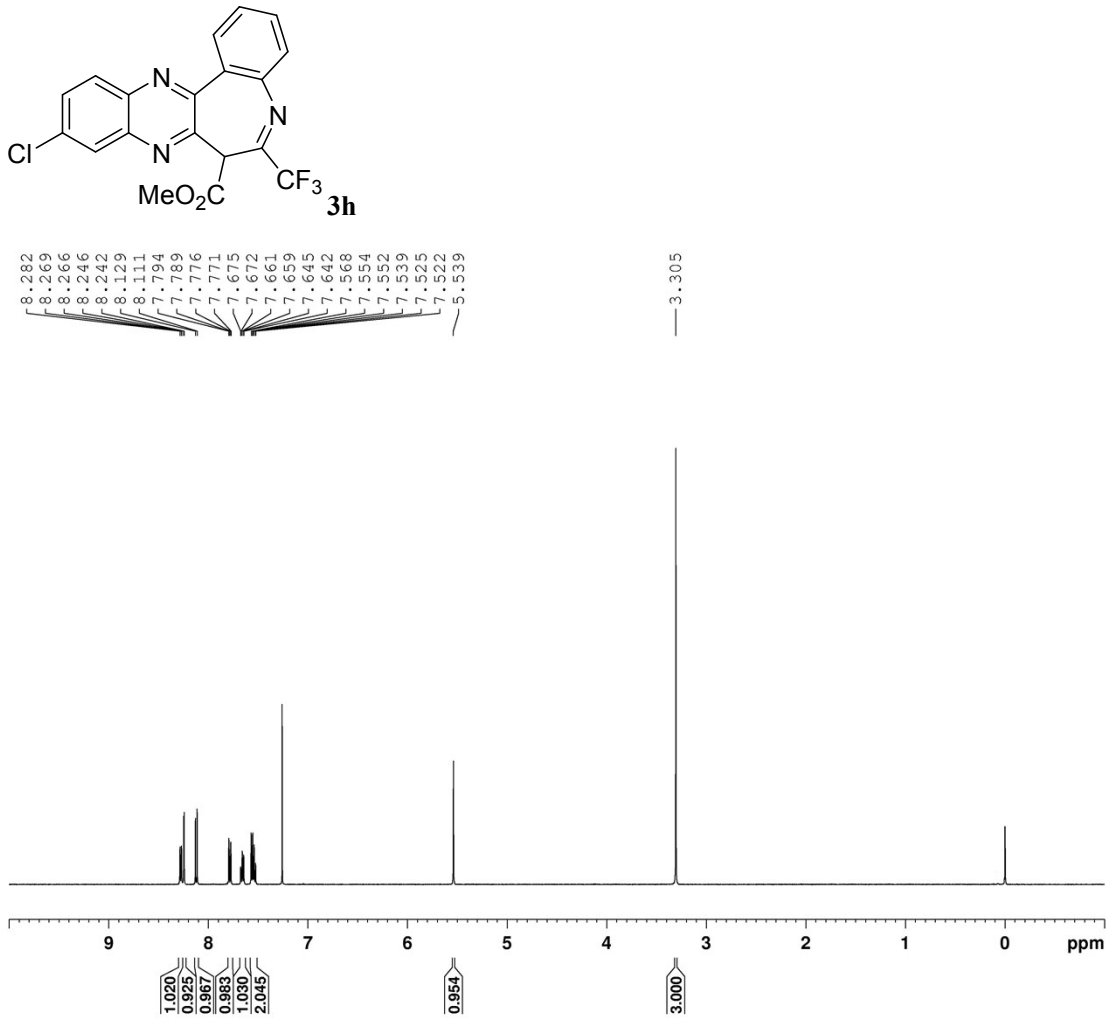


Fig S39. ^{1}H NMR of **3h** in $CDCl_3$

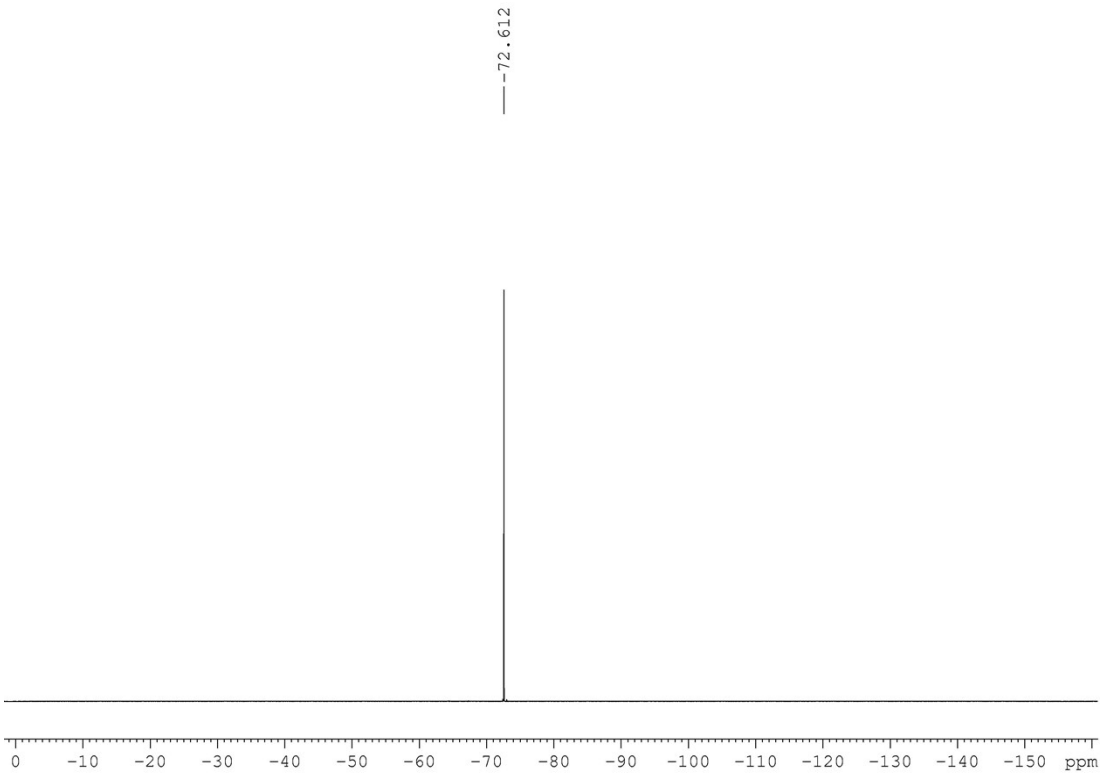


Fig S40. ^{19}F NMR of **3h** in $CDCl_3$

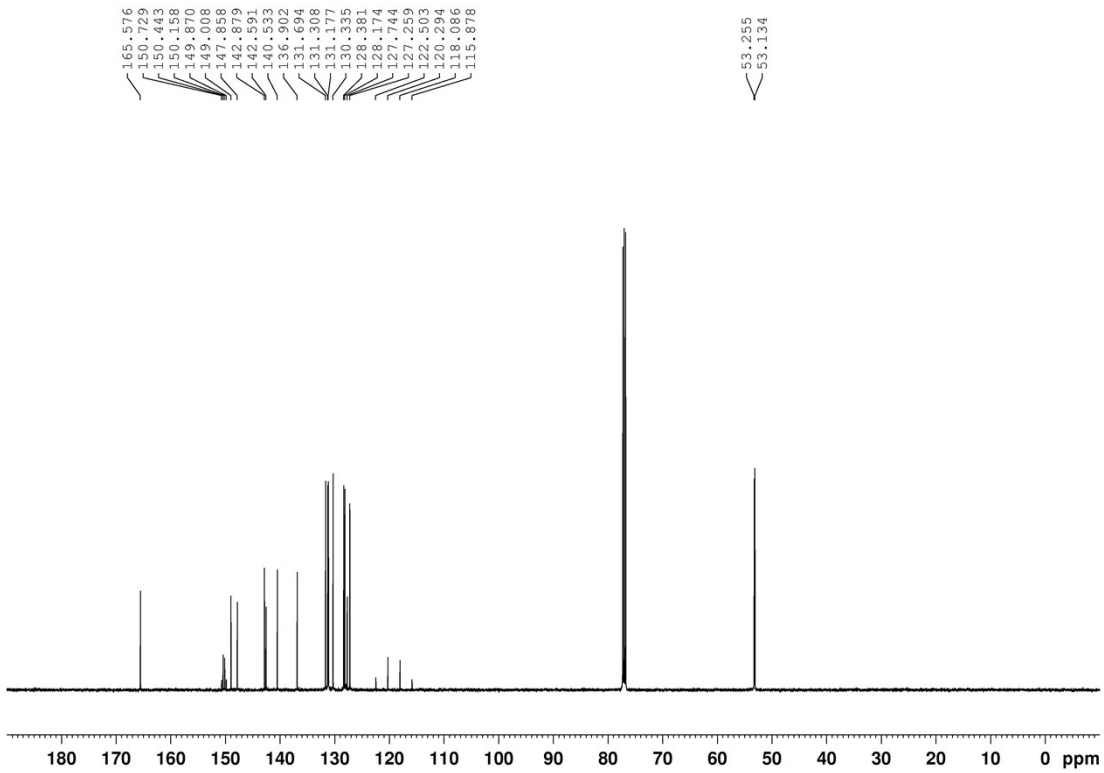


Fig S41. ^{13}C NMR of **3h** in $CDCl_3$

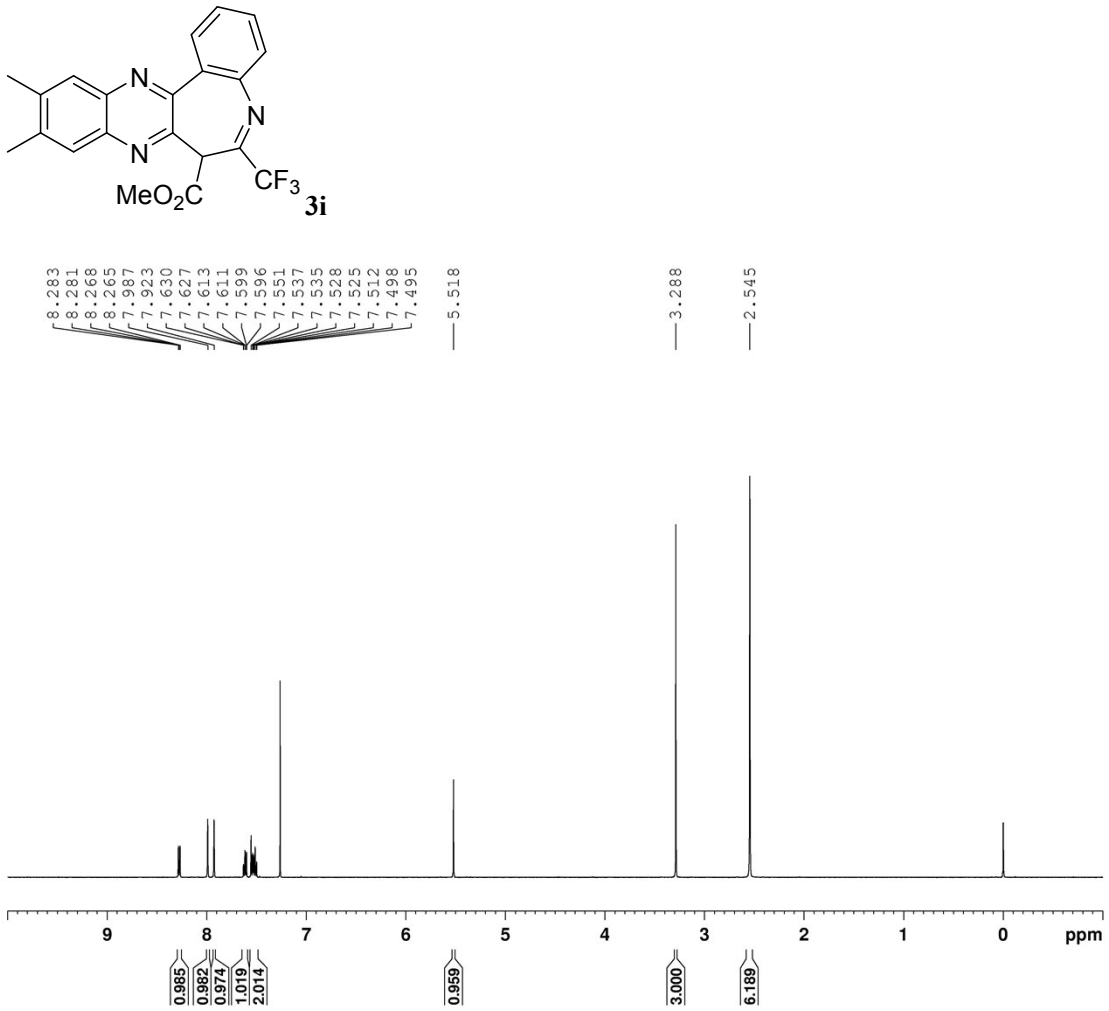


Fig S42. ^{1}H NMR of **3i** in $CDCl_3$

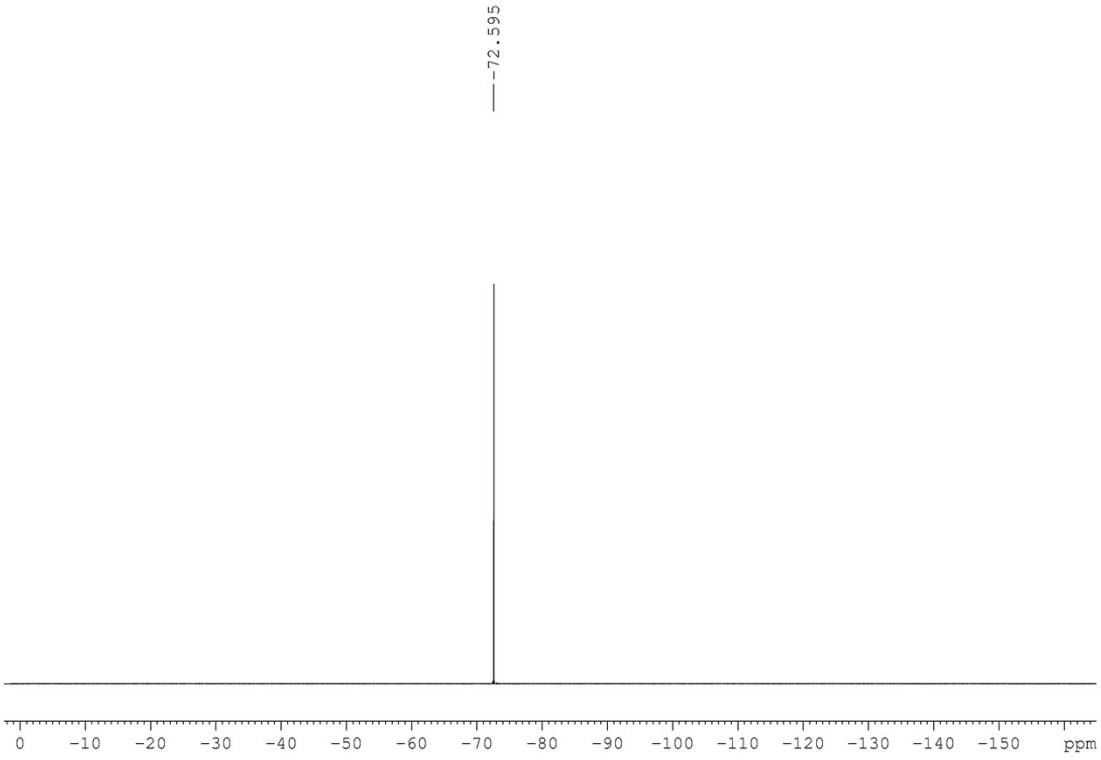


Fig S43. ^{19}F NMR of **3i** in $CDCl_3$

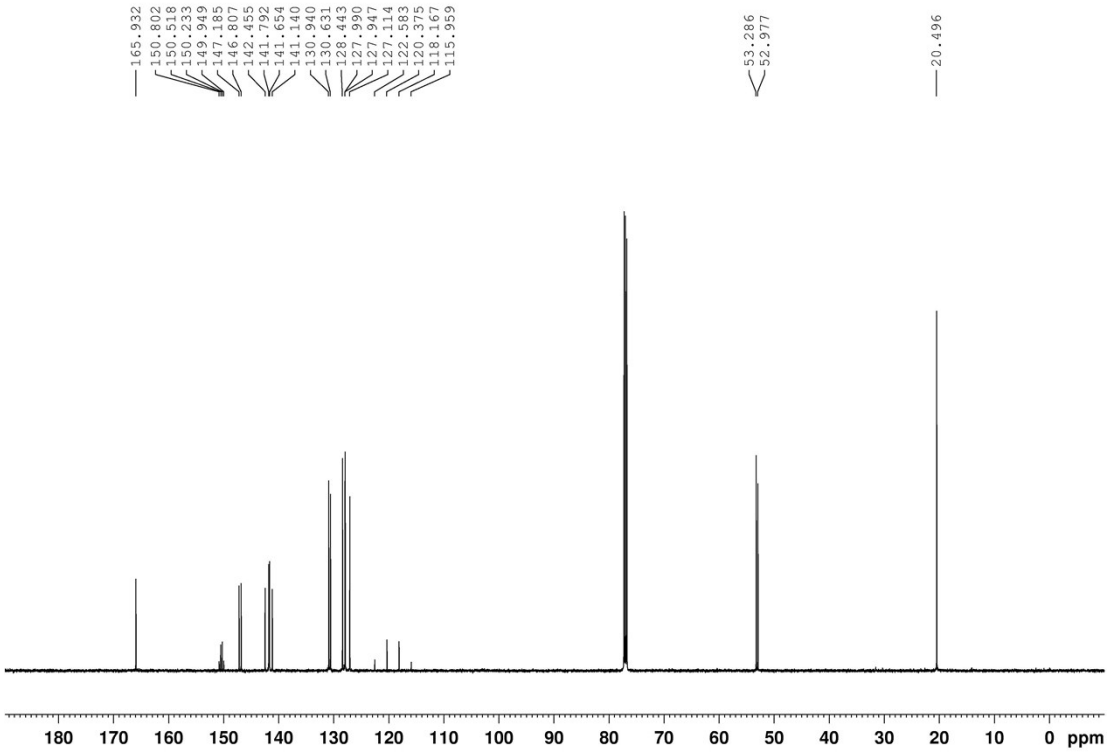


Fig S44. ^{13}C NMR of **3i** in $CDCl_3$

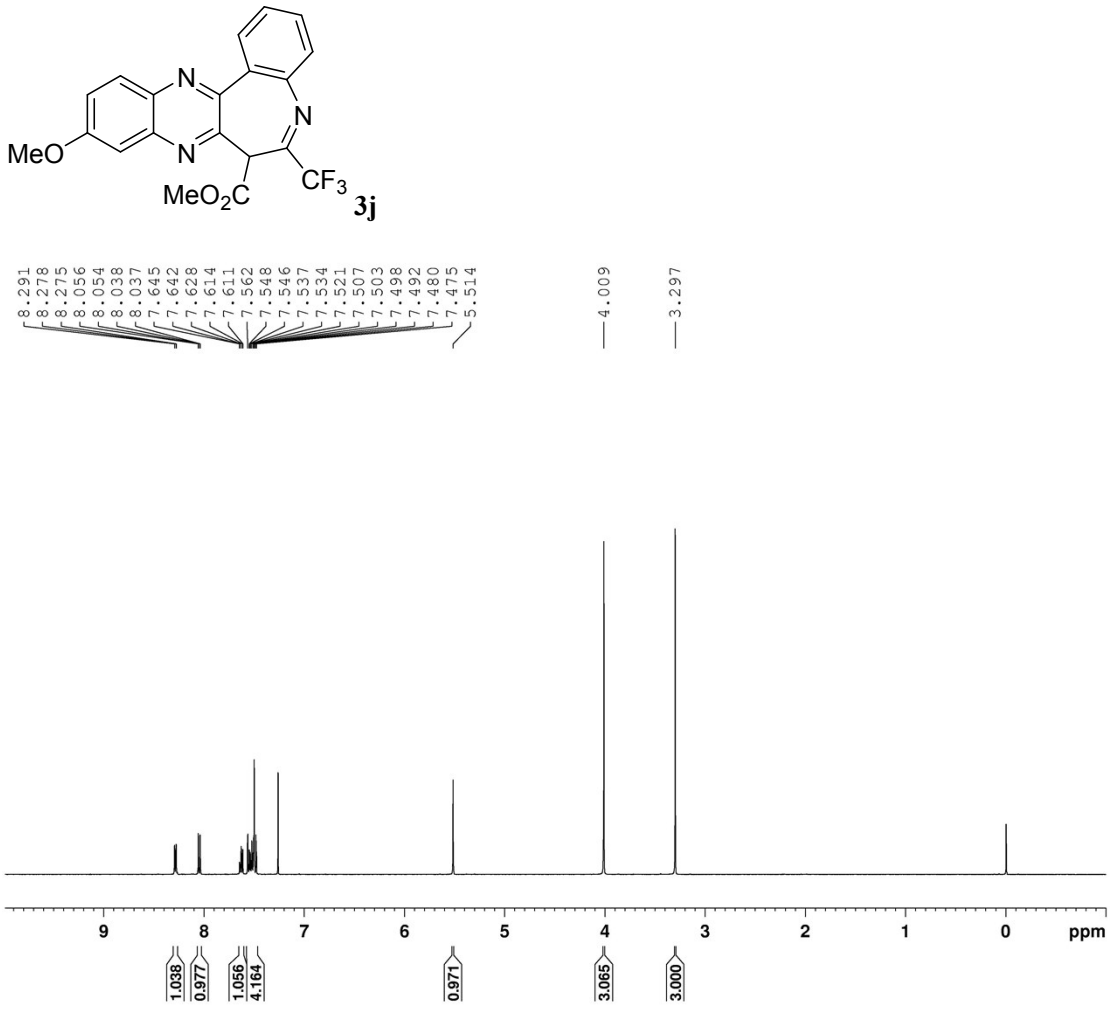


Fig S45. ^{1}H NMR of **3j** in $CDCl_3$

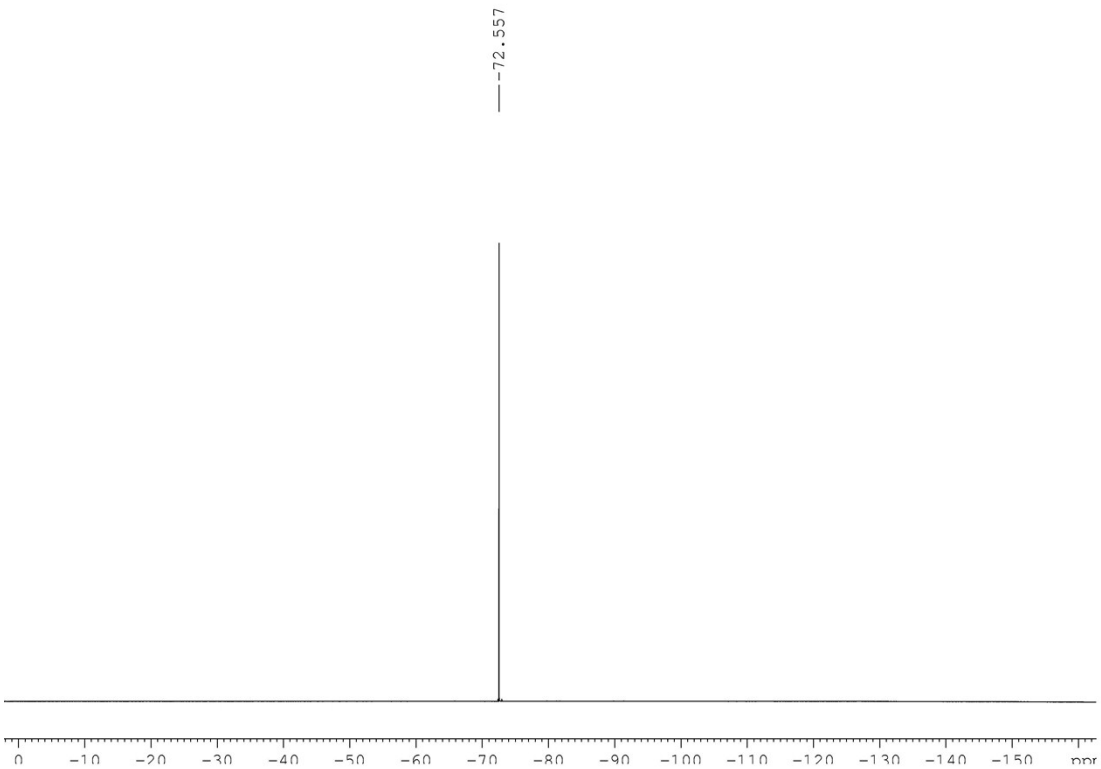


Fig S46. ^{19}F NMR of **3j** in CDCl

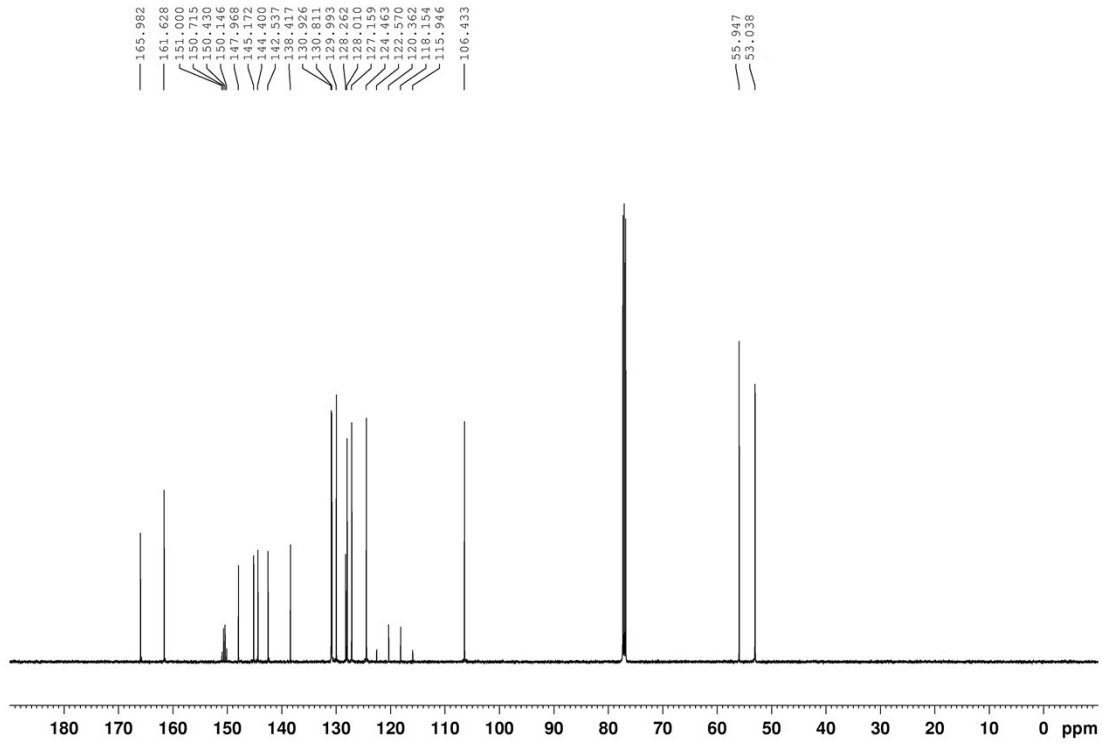


Fig S47. ^{13}C NMR of **3j** in $CDCl_3$

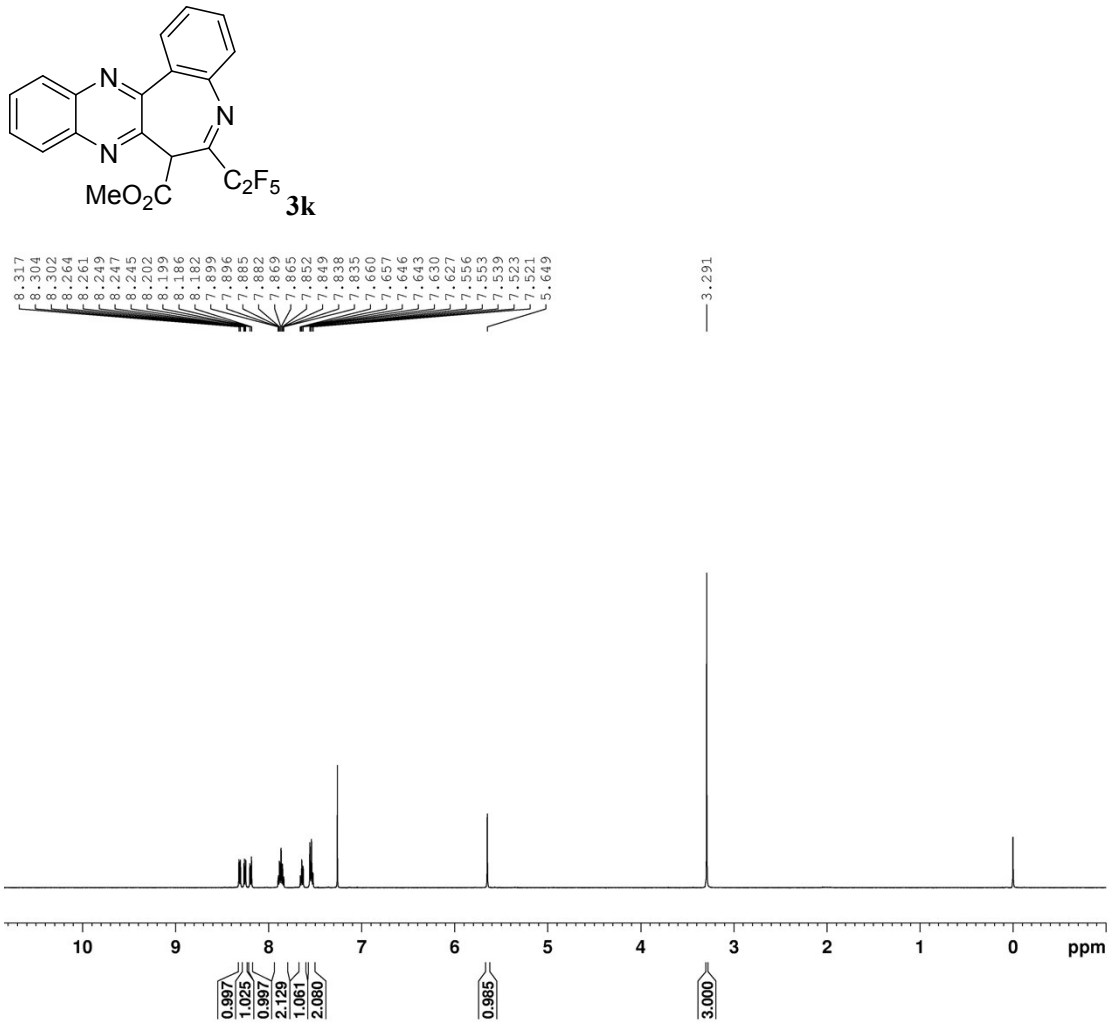


Fig S48. ^{1}H NMR of **3k** in $CDCl_3$

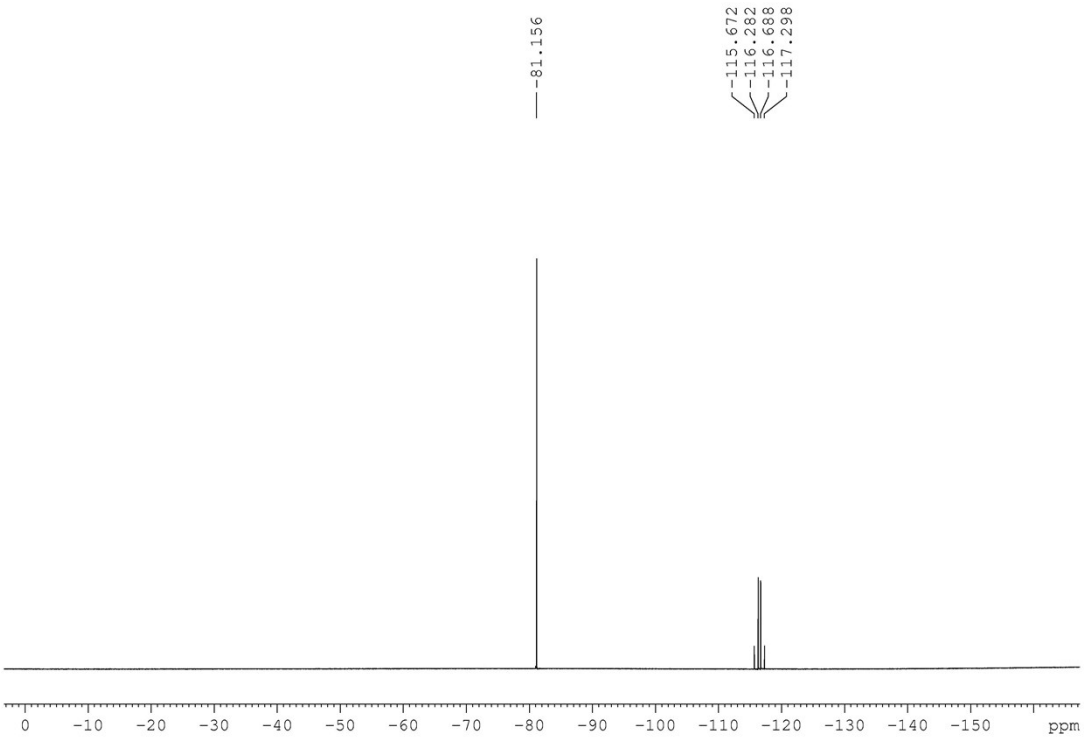


Fig S49. ^{19}F NMR of **3k** in $CDCl_3$

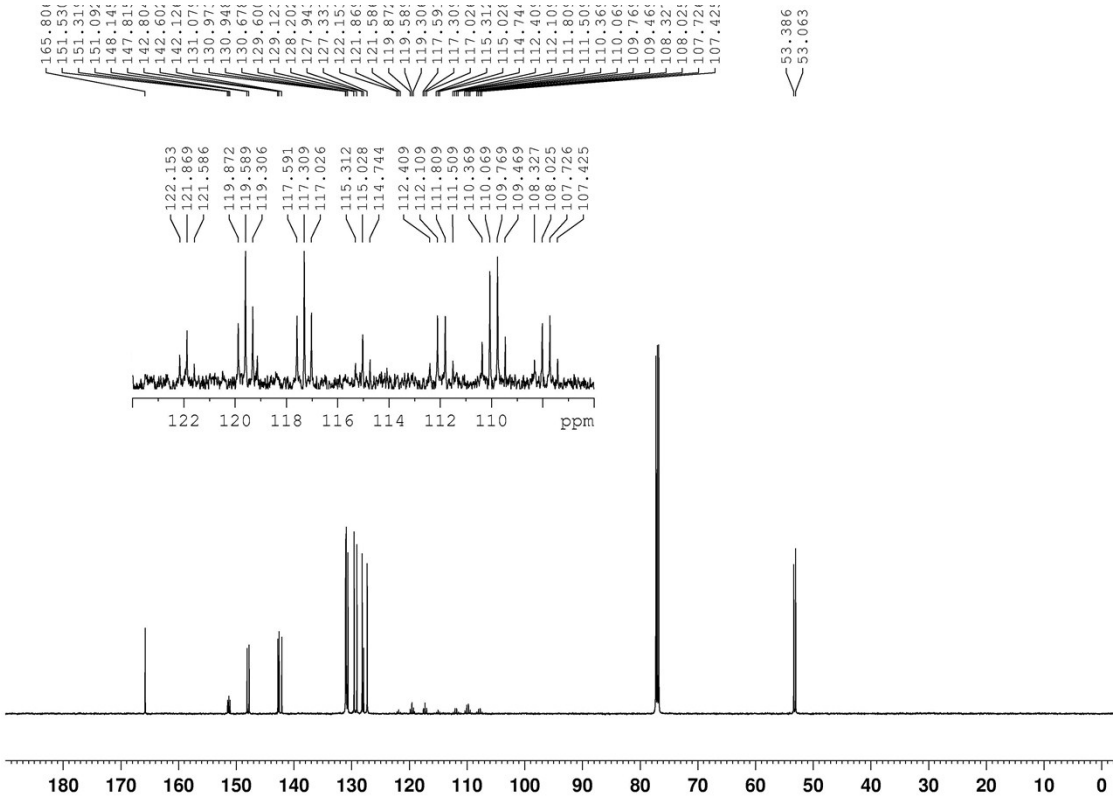


Fig S50. ^{13}C NMR of **3k** in $CDCl_3$

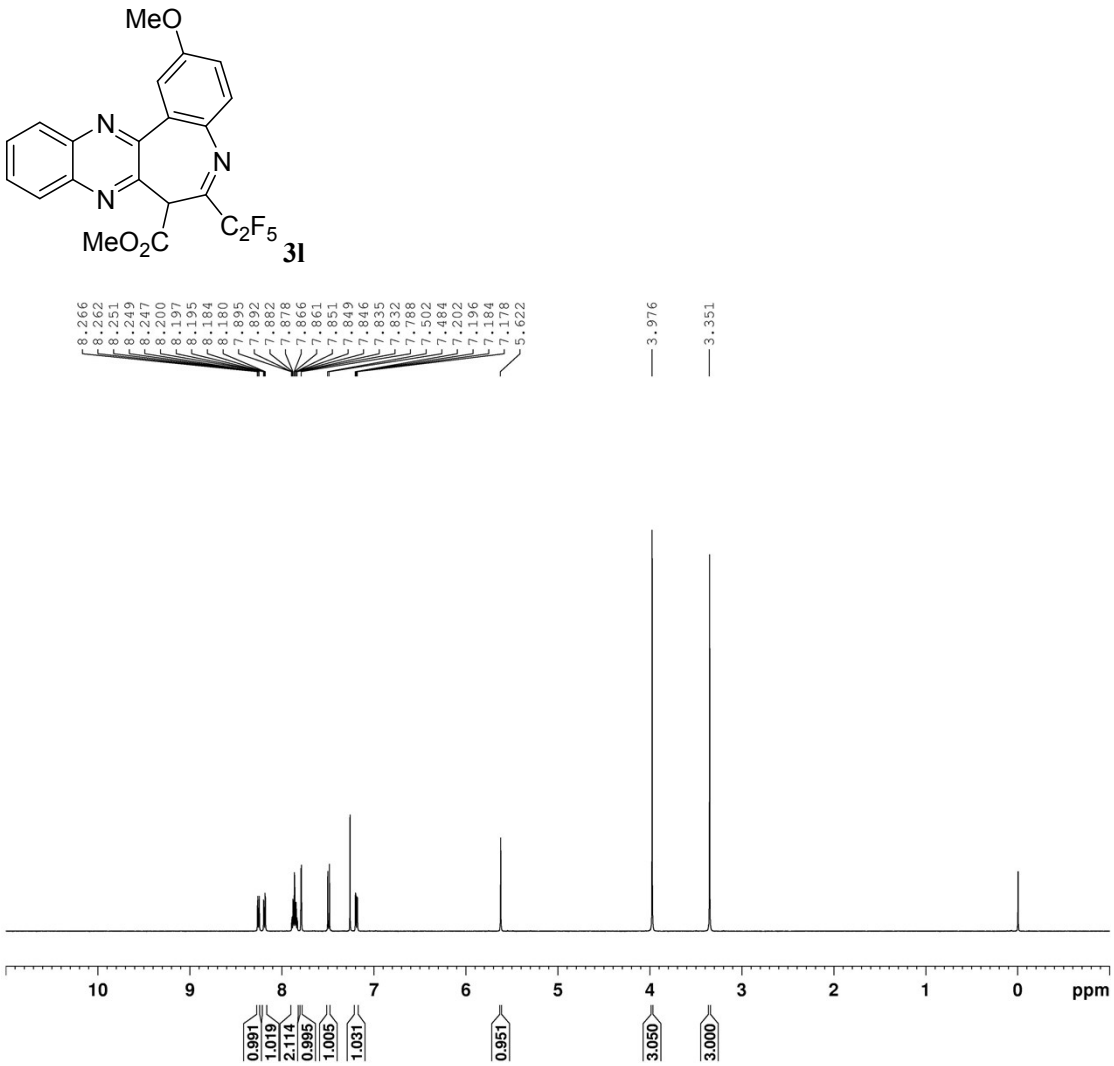


Fig S51. ^{1}H NMR of **3l** in $CDCl_3$

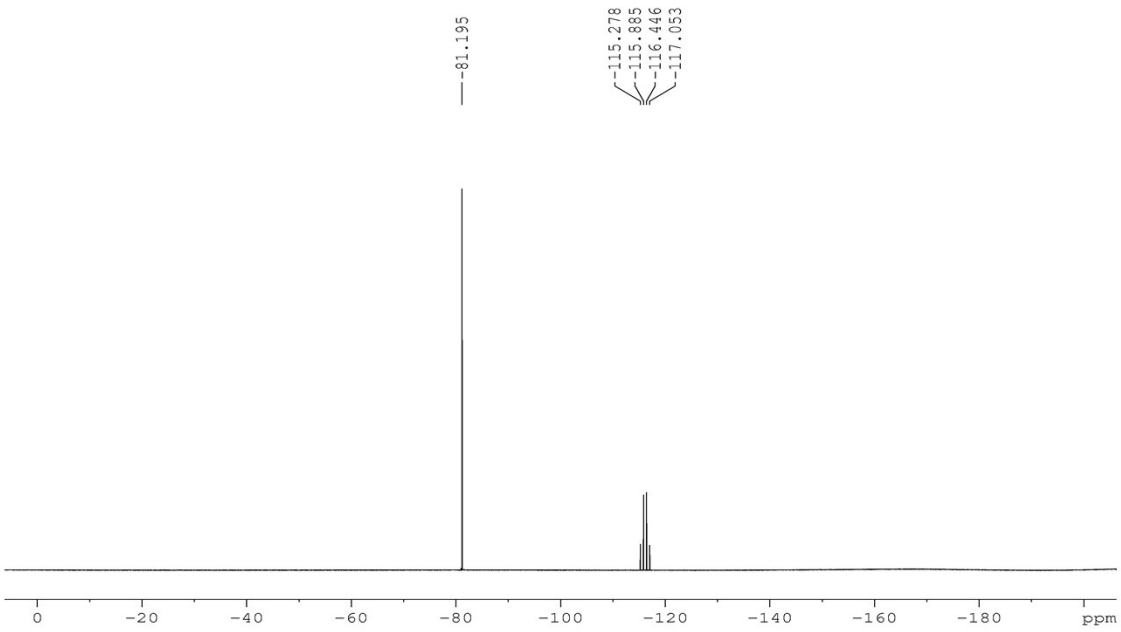


Fig S52. ^{19}F NMR of **3l** in $CDCl_3$

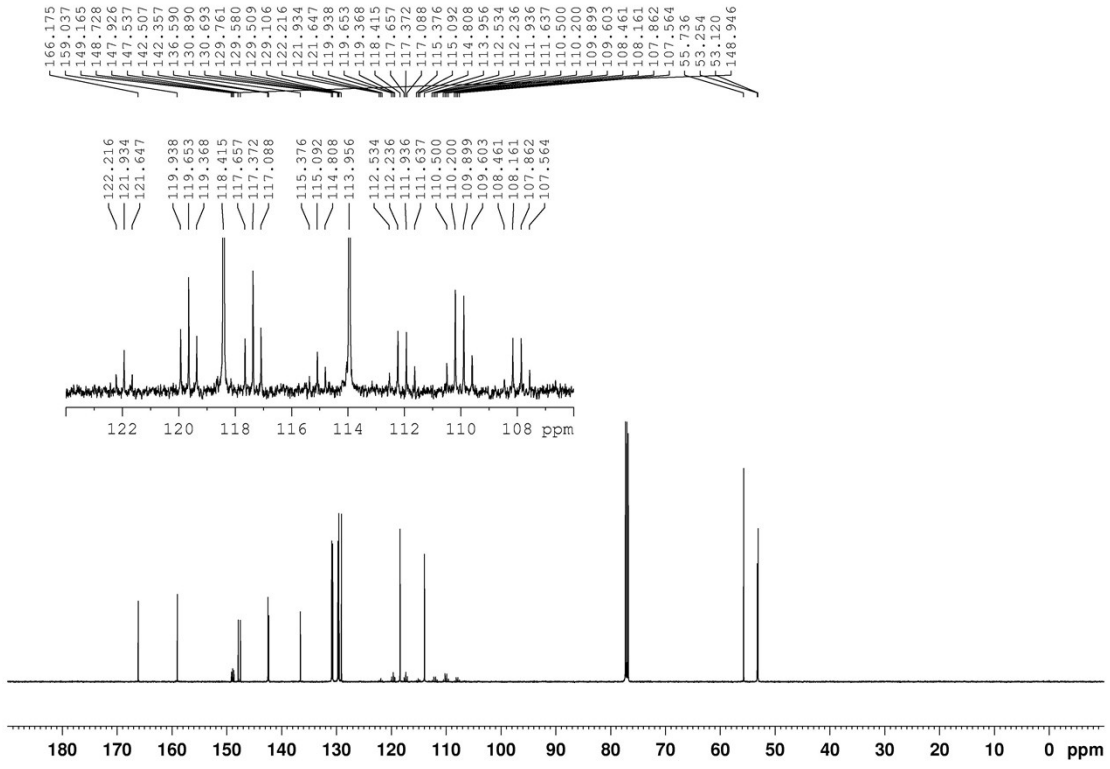


Fig S53. ^{13}C NMR of **3l** in $CDCl_3$

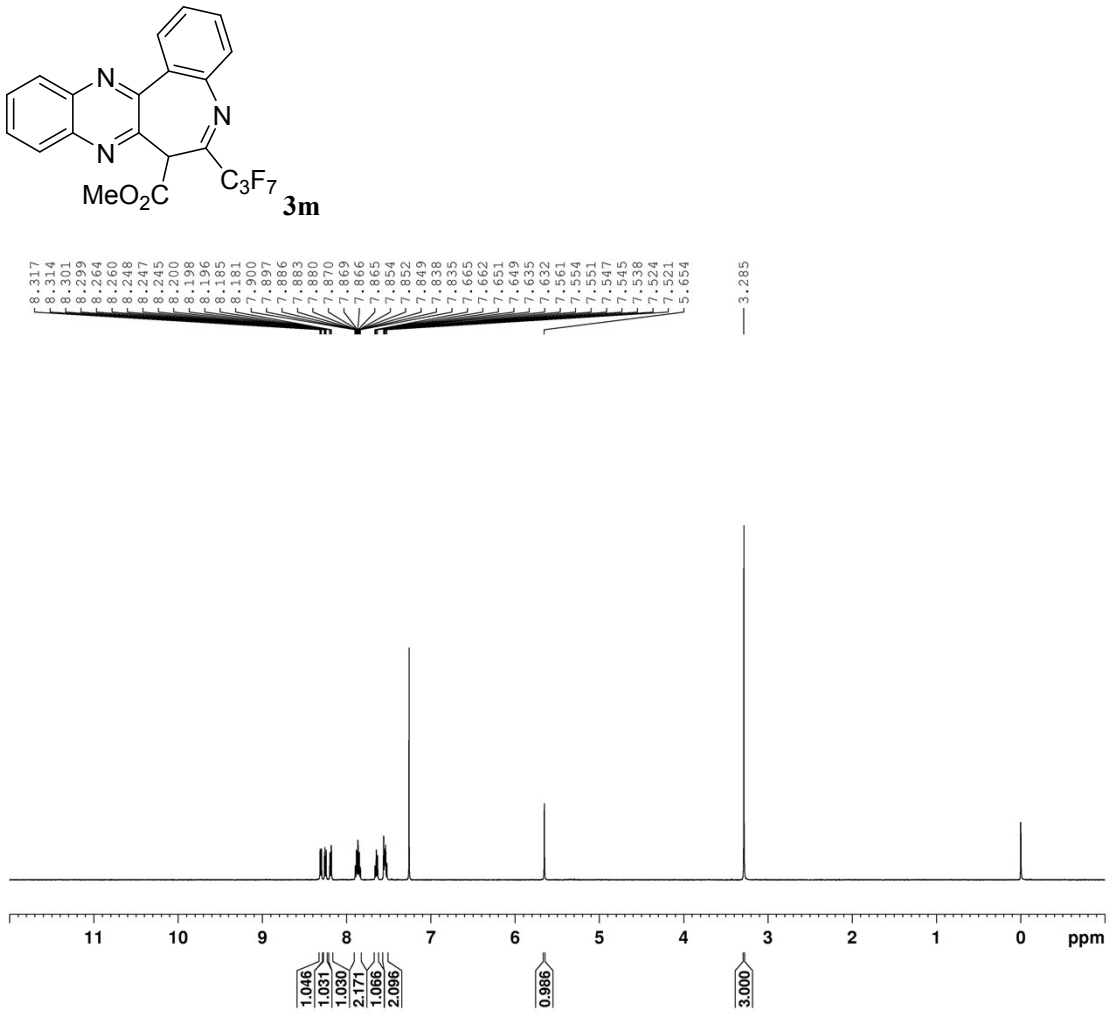


Fig S54. ^{1}H NMR of **3m** in $CDCl_3$

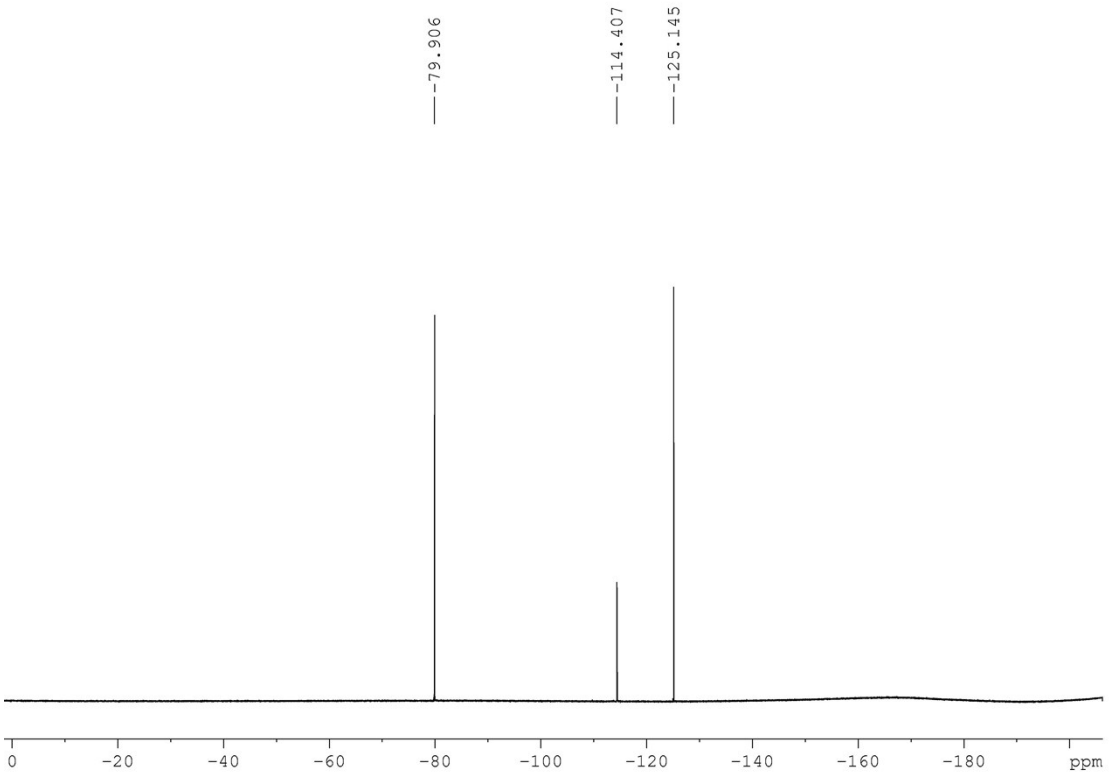


Fig S55. ^{19}F NMR of **3m** in $CDCl_3$

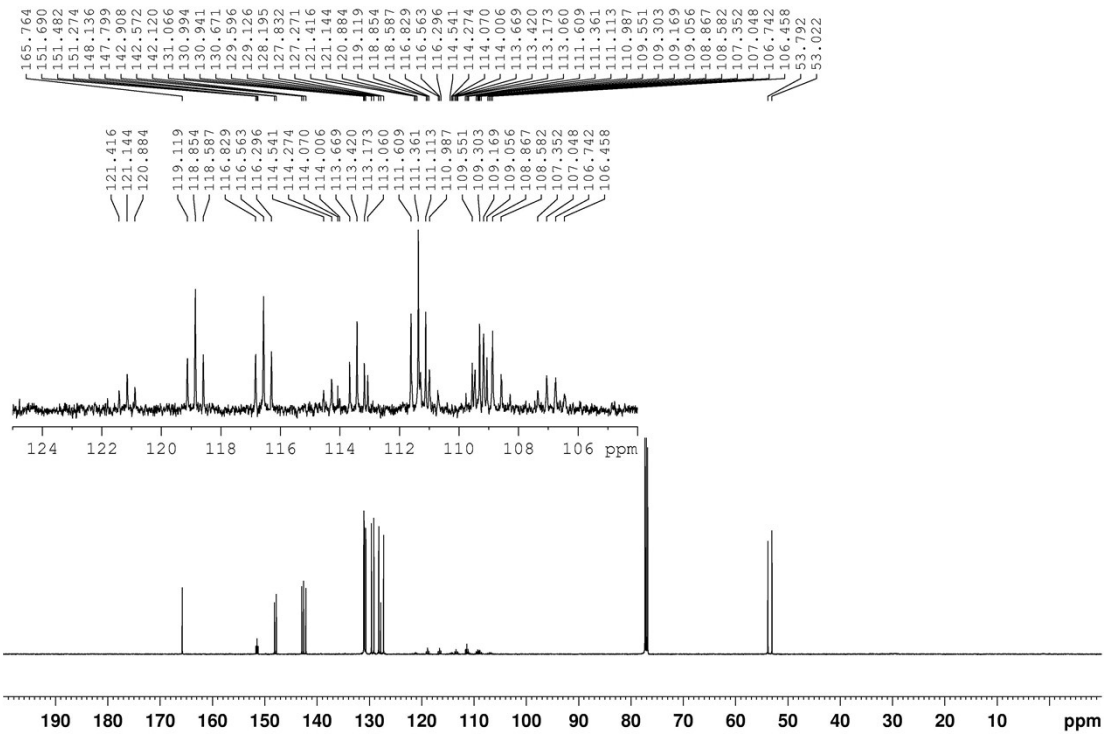


Fig S56. ^{13}C NMR of **3m** in $CDCl_3$

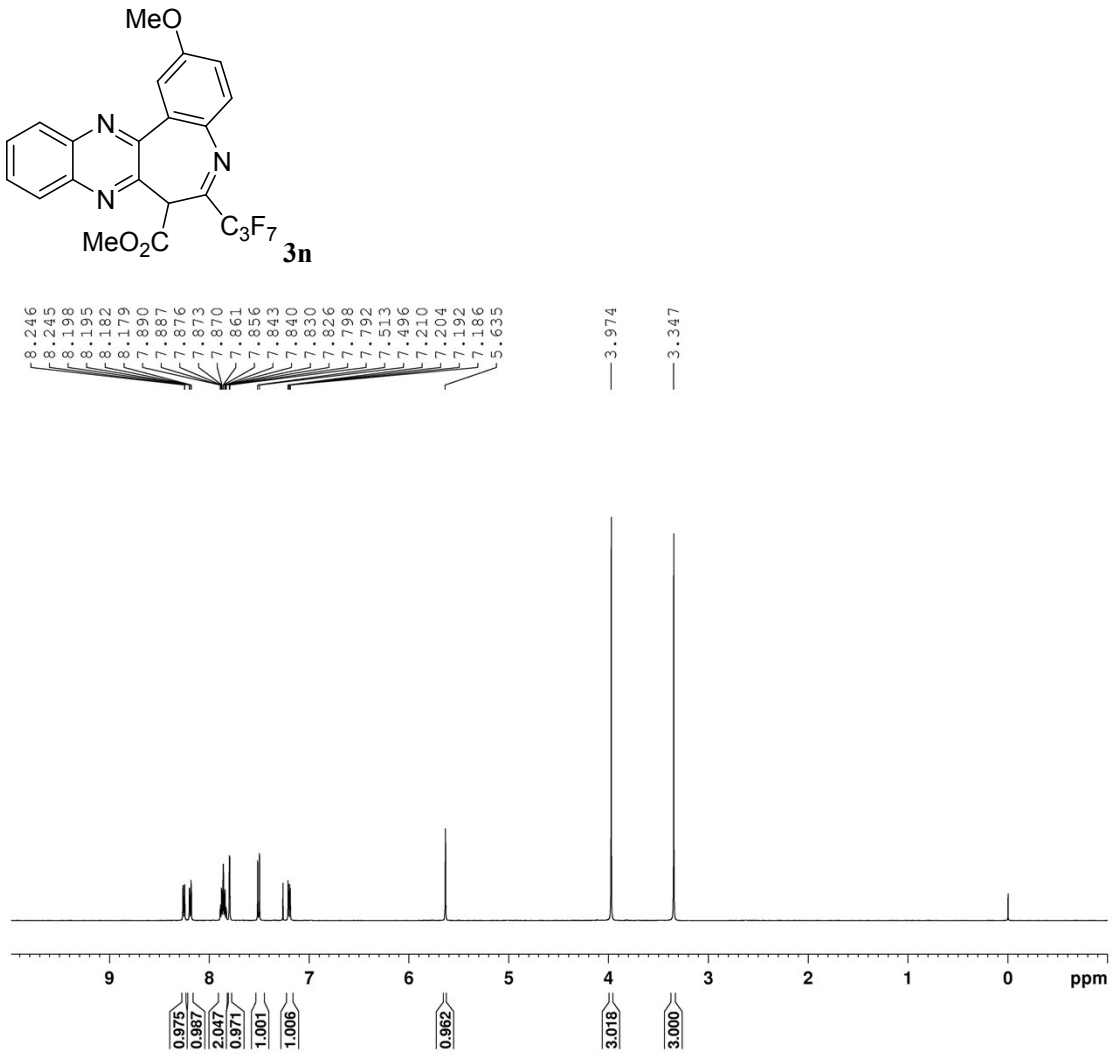


Fig S57. ^{1}H NMR of **3n** in $CDCl_3$

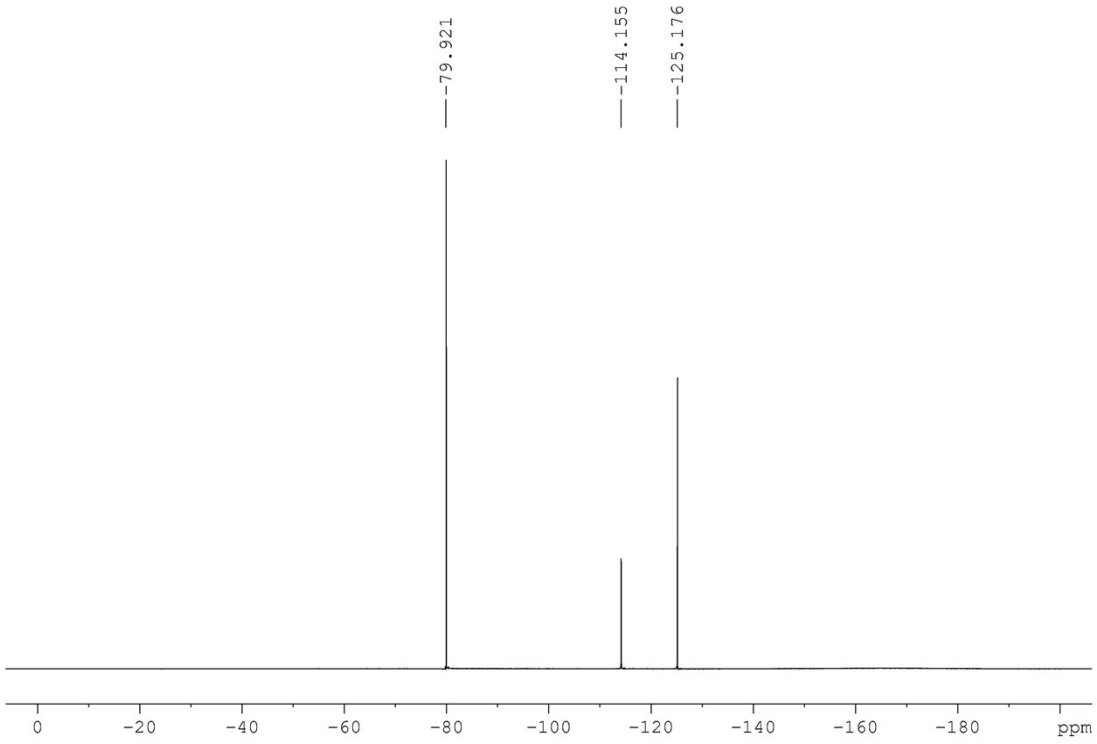


Fig S58. ^{19}F NMR of **3n** in $CDCl_3$

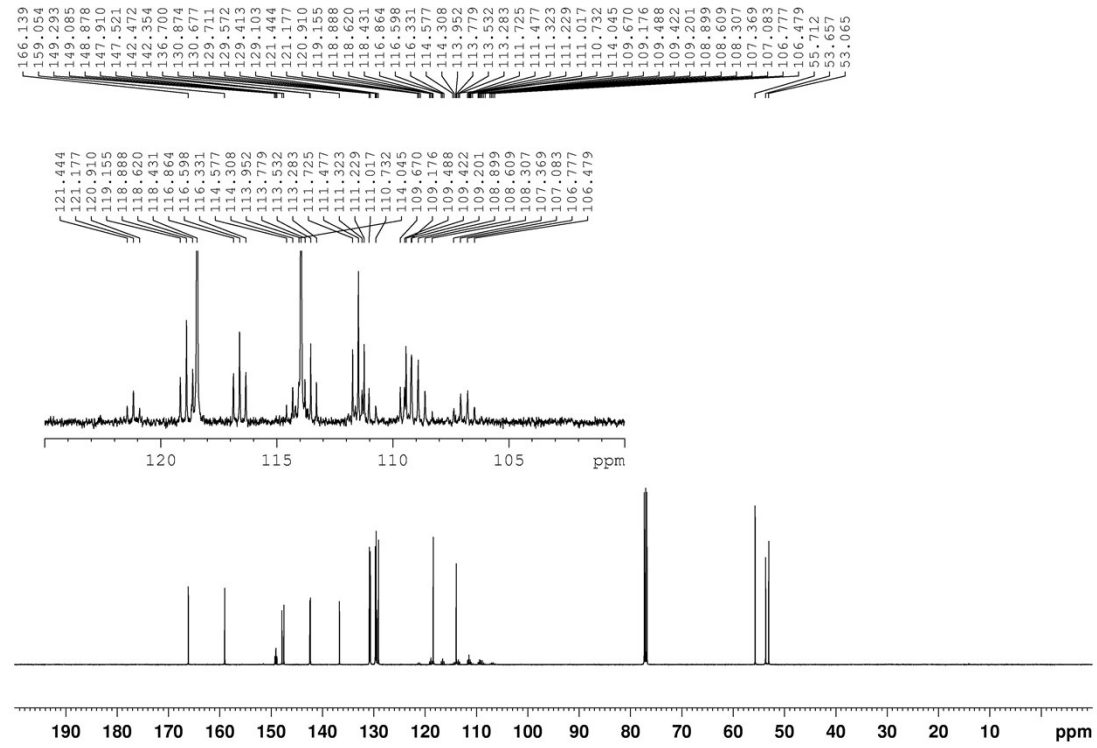


Fig S59. ^{13}C NMR of **3n** in $CDCl_3$