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Supporting Information

for

Pyridinium 1,4-Zwitterionic Thiolates as a Useful Class of Sulfur-containing Synthons: Application to the Synthesis of 2,5-Dihydro-1,4,5-thiadiazepines

Bin Cheng,[*ab] Yuntong Li,[b]† Taimin Wang,[a]† Xinping Zhang,[ab] Hui Li,[ab] Yun Li,[b] and Hongbin Zhai[*abc]

[a] Institute of Marine Biomedicine, Shenzhen Polytechnic, Shenzhen 518055, China; e-mail: chengbin@szpt.edu.cn

[b] State Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou 730000, China

[c] State Key Laboratory of Chemical Oncogenomics, Shenzhen Engineering Laboratory of Nano Drug Slow-Release, Peking University Shenzhen Graduate School, Shenzhen 518055, China; e-mail: zhaihb@pkusz.edu.cn

† These authors contributed equally to this work

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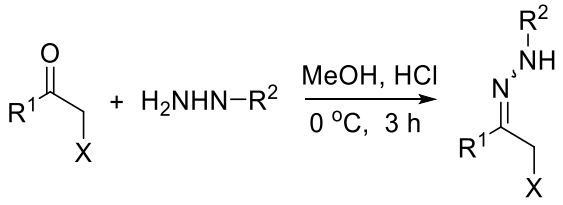
1. General information

All isolated compounds were characterized on Varian 300, Bruker 400, and JEOL 400 MHz spectrometers in $CDCl_3$ or $(CD_3)_2CO$ or $(CD_3)_2SO$. Chemical shifts were reported as δ values relative to internal chloroform (δ 7.26 for ^1H NMR and 77.00 for ^{13}C NMR), acetone (δ 2.05 for ^1H NMR and 29.84 for ^{13}C NMR) and dimethyl sulfoxide (δ 2.50 for ^1H NMR and 39.52 for ^{13}C NMR). ^{19}F NMR chemical shifts were determined as δ values relative to external standard $PhCF_3$ at −63.00. High-resolution mass spectra (HRMS) were obtained on a 4G mass spectrometer by using electrospray ionization (ESI) analyzed by quadrupole time-of-flight (QTof). All melting points were measured with the samples after column chromatography and uncorrected. Column chromatography was performed on silica gel. All other solvents and reagents were used as obtained from commercial sources without further purification.

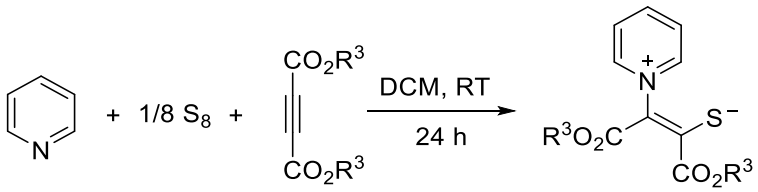
2. General experimental procedures

2.1 General procedure for the preparation of α-halo hydrazones[1]



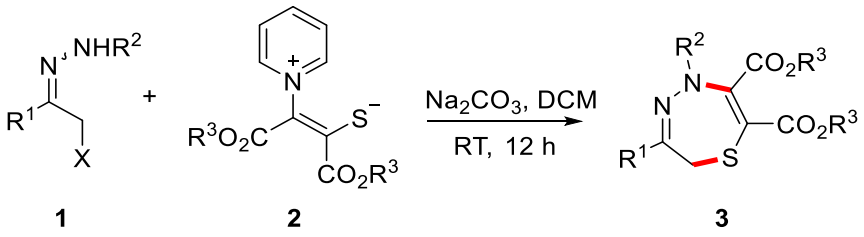
To a solution of α-halo ketone (20 mmol, 1.0 equiv) in methanol (10 mL) were added acylhydrazide (30 mmol, 1.5 equiv) and HCl (conc., 0.5 mL) at 0 ℃. The mixture was stirred at the same temperature for 3 h, then filtered and washed with Et_2O (15 mL). The crude product was directly used without further purification.

2.2 General procedure for the preparation of pyridinium 1,4-diionic organosulfurs[2]



To a solution of pyridine (1 mmol) and S_8 (1/8 mmol) in DCM (5 mL) was added the electron-poor internal alkyne (1 mmol) dropwise at 0 ℃. The mixture was stirred for 24 h at room temperature. Then, the mixture was filtered and the precipitate was washed with Et_2O (2 × 5 mL) to afford pure product as a yellow powder, which was pure enough to use for the next step.

2.3 General procedure for the synthesis of 2,5-dihydro-1,4,5-thiadiazepines

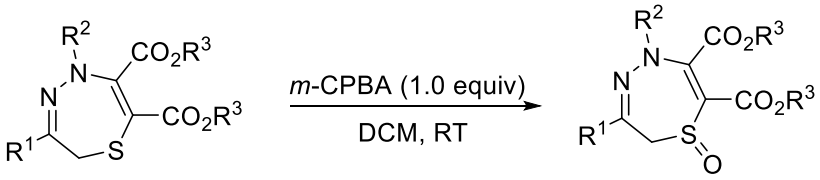


1 **2** **3**

To a solution of α-halo hydrazone **1** (0.3 mmol, 1.0 equiv) in DCM (3 mL) were added pyridinium 1,4-diionic organosulfur **2** (0.45 mmol, 1.5 equiv) and Na_2CO_3 (0.6 mmol, 2.0 equiv) at room temperature, then the mixture was stirred at the same temperature for 12 h. The solvent was evaporated and the resulting crude product was purified by silica gel column chromatography to give the corresponding 2,5-dihydro-1,4,5-thiadiazepine derivative **3**.

Scaled-up experiment for the synthesis of 3a: To a solution of **1a** (1.51 g, 1.0 equiv) in DCM (60 mL) were added **2a** (2.25 g, 1.5 equiv) and Na_2CO_3 (1.25 g, 2.0 equiv) at room temperature, then the mixture was stirred at the same temperature for 24 h. The solvent was evaporated and the resulting crude product was purified by silica gel column chromatography to give **3a** (1.88 g, 91%) as a yellow solid.

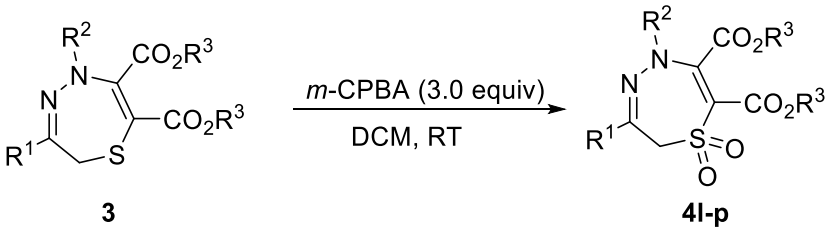
2.4 General procedure for the synthesis of sulfoxides



3 **4a-k**

To a solution of 2,5-dihydro-1,4,5-thiadiazepine derivative **3** (0.3 mmol) in DCM (3 mL) was added *m*-CPBA (0.3 mmol, 1.0 equiv) at 0 ℃, then the mixture was stirred at the room temperature. After completion as monitored by TLC, the crude reaction mixture was purified by silica gel column chromatography to get the corresponding sulfoxide.

2.5 General procedure for the synthesis of sulfones



3 **4l-p**

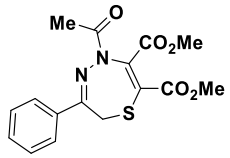
To a solution of 2,5-dihydro-1,4,5-thiadiazepine derivative **3** (0.3 mmol) in DCM (2 mL) was added *m*-CPBA (0.9 mmol, 3.0 equiv) at 0 ℃, Then the mixture was stirred at the room temperature. After

completion as monitored by TLC, the mixture was diluted with DCM and washed with saturated solution of $NaHSO_3$, then the aqueous layer was extracted with DCM twice. The combined organic layers were washed with saturated brine solution and dried over anhydrous Na_2SO_4. After evaporation of solvent, the residue was purified by silica gel column chromatography to get the corresponding sulfone.

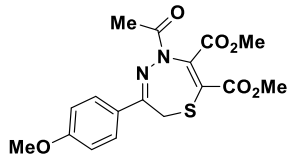
3. References

[1] Hu, X.; Chen, J.; Gao, S.; Feng, B.; Lua, L.; Xiao, W. *Chem. Commun*. **2013**, *49*, 7905.
[2] Moafi, L.; Ahadi, S.; Khavasi, H. R.; Bazgir, A. Synthesis **2011**, *9*, 1399.

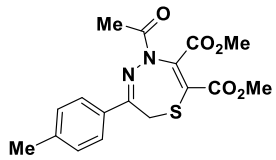
4. Characterization data of products



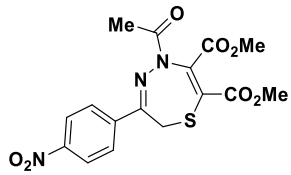
Dimethyl 4-acetyl-6-phenyl-4,7-dihydro-1,4,5-thiadiazepine-2,3-dicarboxylate. Compound **3a** (103 mg, Yield = 98%, R_f = 0.33 (PE:EA = 1:1)) was isolated as a yellow solid; mp 192.8−193.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.6 Hz, 2H), 7.56 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.2 Hz, 2H), 4.27 (s, 2H), 3.74 (s, 3H), 3.73 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 170.8, 163.9, 162.9, 132.6, 132.2, 129.9, 129.8, 128.9, 127.4, 53.2, 52.7, 25.5, 21.6; ESI-HRMS m/z calcd for $C_{16}H_{16}N_2O_5S$ + H^+ 349.0853, found 349.0855.



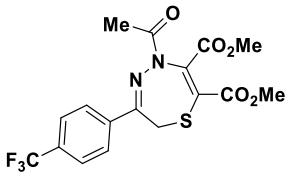
Dimethyl 4-acetyl-6-(4-methoxyphenyl)-4,7-dihydro-1,4,5- thiadiazepine-2,3-dicarboxylate. Compound **3b** (102 mg, Yield = 89%, R_f = 0.41 (PE:EA = 1:1)) was isolated as a yellow solid; mp 71.8−72.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.8 Hz, 2H), 6.95 (d, J = 8.8 Hz, 2H), 4.24 (s, 2H), 3.84 (s, 3H), 3.73 (s, 3H), 3.71 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 170.7, 163.9, 163.0, 162.9, 129.8, 129.7, 129.2, 124.4, 114.2, 55.4, 53.2, 52.7, 25.1, 21.5; ESI-HRMS m/z calcd for $C_{17}H_{18}N_2O_6S$ + Na^+ 401.0787, found 401.0784.



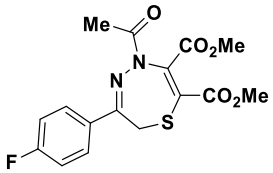
Dimethyl 4-acetyl-6-(*p*-tolyl)-4,7-dihydro-1,4,5-thiadiazepine-2,3-dicarboxylate. Compound **3c** (94 mg, Yield = 86%, R_f = 0.42 (PE:EA = 1:1)) was isolated as a yellow solid; mp 151.7−152.5°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 7.6 Hz, 2H), 4.28 (s, 2H), 3.77 (s, 3H), 3.75 (s, 3H), 2.43 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 170.8, 163.9, 162.9, 143.0, 129.8, 129.7, 129.6, 129.6, 127.4, 53.2, 52.7, 25.3, 21.6, 21.4. ESI-HRMS m/z calcd for $C_{17}H_{18}N_2O_5S$ + Na^+ 385.0829, found 385.0831.



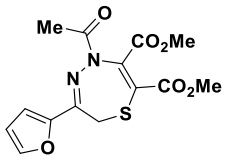
Dimethyl 4-acetyl-6-(4-nitrophenyl)-4,7-dihydro-1,4,5-thiadiazepine-2,3-dicarboxylate. **3d** (96 mg, Yield = 81%, R_f = 0.36 (PE:EA = 1:1)) was isolated as a yellow solid; mp 206.7−207.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 8.8 Hz, 2H), 8.08 (d, J = 9.2 Hz, 2H), 4.26 (s, 2H), 3.79 (s, 6H), 2.20 (s, 3H). ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 171.2, 170.0, 164.1, 162.6, 149.6, 138.6, 130.8, 129.2, 128.5, 124.0, 53.6, 52.8, 25.2, 21.6; ESI-HRMS m/z calcd for $C_{16}H_{15}N_3O_7S + Na^+$ 416.0523, found 416.0526.



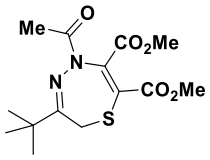
Dimethyl 4-acetyl-6-(4-(trifluoromethyl)phenyl)-4,7-dihydro-1,4,5-thiadiazepine-2,3-dicarboxylate. Compound **3e** (114 mg, Yield = 91%, R_f = 0.49 (PE:EA = 1:1)) was isolated as a yellow solid; mp 173.2−173.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 4.28 (s, 2H), 3.75 (s, 6H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 169.0, 163.9, 162.8, 136.3, 133.7 (q, J = 32.7 Hz), 130.4, 129.8, 127.8, 125.9 (q, J = 3.7 Hz), 123.5 (q, J = 271.2 Hz), 53.3, 52.8, 25.8, 21.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.10 (s, 3F); ESI-HRMS m/z calcd for $C_{17}H_{15}F_3N_2O_5S + Na^+$ 439.0546, found 439.0548.



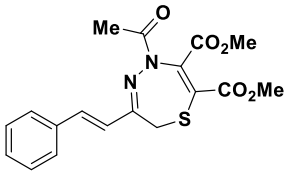
Dimethyl 4-acetyl-6-(4-fluorophenyl)-4,7-dihydro-1,4,5-thiadiazepine-2,3-dicarboxylate. Compound **3f** (101 mg, Yield = 92%, R_f = 0.47 (PE:EA = 1:1)) was isolated as a yellow solid; mp 151.9−152.3°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96–7.90 (m, 2H), 7.15 (t, J = 8.4 Hz, 2H), 4.26 (s, 2H), 3.72 (s, 6H), 2.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 170.1, 165.2 (d, J = 252.6 Hz), 163.8 162.9, 129.8, 129.8 (d, J = 8.6 Hz), 128.6, 128.6, 116.0 (d, J = 21.8 Hz), 53.2, 52.7, 25.4, 21.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.28 (s, F); ESI-HRMS m/z calcd for $C_{16}H_{15}FN_2O_5S + Na^+$ 389.0578, found 389.0574.



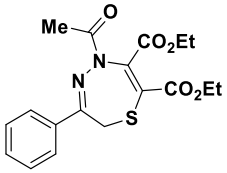
Dimethyl 4-acetyl-6-(furan-2-yl)-4,7-dihydro-1,4,5-thiadiazepine-2,3-dicarboxylate. Compound **3g** (56 mg, Yield = 55%, R_f = 0.28 (PE:EA = 1:1)) was isolated as a yellow solid; mp 134.6−135.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 1.2 Hz, 1H), 7.26 (d, J = 3.6 Hz, 1H), 6.63 (dd, J = 3.6, 1.6 Hz, 1H), 4.23 (s, 2H), 3.77 (s, 6H), 2.13 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 164.0, 162.8, 161.8, 146.9, 146.6, 130.7, 129.8, 115.8, 112.9, 53.3, 52.8, 24.8, 21.6; ESI-HRMS m/z calcd for $C_{14}H_{14}N_2O_6S + Na^+$ 361.0465, found 361.0464.



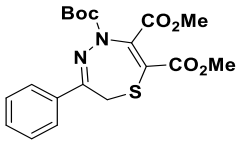
Dimethyl 4-acetyl-6-(*tert*-butyl)-4,7-dihydro-1,4,5-thiadiazepine-2,3-dicarboxylate. Compound **3h** (90 mg, Yield = 91%, R_f = 0.38 (PE:EA = 1:1)) was isolated as a yellow solid; mp 186.8−187.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (s, 2H), 3.74 (s, 3H), 3.72 (s, 3H), 1.97 (s, 3H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.6, 170.3, 163.9, 162.9, 129.5, 129.1, 53.2, 52.6, 39.2, 27.6, 23.9, 21.4; ESI-HRMS m/z calcd for $C_{14}H_{20}N_2O_5S + Na^+$ 351.0985, found 351.0984.



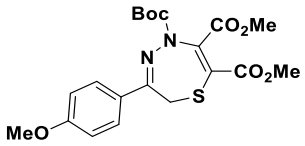
Dimethyl (*E*)-4-acetyl-6-styryl-4,7-dihydro-1,4,5-thiadiazepine-2,3-dicarboxylate. Compound **3i** (72 mg, Yield = 64%, R_f = 0.44 (PE:EA = 1:1)) was isolated as a yellow solid; mp 212.3−212.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.53 (m, 2H), 7.46–7.39 (m, 3H), 7.30 (d, *J* = 16.4 Hz, 1H), 7.00 (d, *J* = 16.4 Hz, 1H), 4.13 (s, 2H), 3.77 (s, 6H), 2.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 170.9, 164.0, 162.9, 141.1, 134.5, 130.6, 130.3, 129.8, 129.0, 127.8, 122.4, 53.3, 52.8, 23.8, 21.6; ESI-HRMS m/z calcd for $C_{18}H_{18}N_2O_5S + Na^+$ 397.0829, found 397.0827.



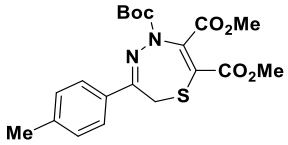
Diethyl 4-acetyl-6-phenyl-4,7-dihydro-1,4,5-thiadiazepine-2,3-dicarboxylate. Compound **3j** (101 mg, Yield = 89%, R_f = 0.43 (PE:EA = 1:1)) was isolated as a yellow solid; mp 150.2−150.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.2 Hz, 2H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 4.25 (s, 2 H), 4.23–4.14 (m, 4H), 2.11 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.24 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.8, 163.5, 162.3, 132.7, 132.2, 130.0, 129.9, 128.8, 127.4, 62.5, 61.9, 25.5, 21.6, 13.8, 13.7; ESI-HRMS m/z calcd for $C_{18}H_{20}N_2O_5S + H^+$ 377.1166, found 377.1164.



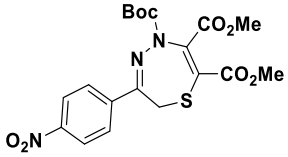
4-(*tert*-Butyl) 2,3-dimethyl 6-phenyl-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate. Compound **3k** (114 mg, Yield = 93%, R_f = 0.44 (PE:EA = 1:1)) was isolated as a yellow solid; mp 135.3−136.7 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.0 Hz, 2H), 7.52–7.45 (m, 1H), 7.44–7.46 (m, 2H), 3.75 (s, 3H), 3.72 (s, 3H), 1.46 (s, 9H), (2H missing); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 164.0, 163.1, 151.4, 133.0, 131.8, 128.6, 127.6, 83.0, 53.2, 52.5, 28.0, 26.1, (2C missing)； ESI-HRMS m/z calcd for $C_{19}H_{22}N_2O_6S$ + Na^+ 429.1091, found 429.1089.



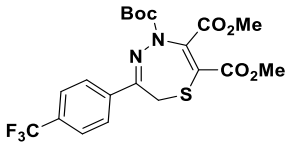
4-(*tert*-Butyl) 2,3-dimethyl 6-(4-methoxyphenyl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate. Compound **3l** (81 mg, Yield = 62%, R_f = 0.35 (PE:EA = 2:1)) was isolated as a yellow solid; mp 57−58 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 9.2 Hz, 2H), 3.83 (s, 3H), 3.77 (s, 3H), 3.73 (s, 3H), 1.47 (s, 9H), (2H missing); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 164.2, 163.2, 162.7, 129.5, 125.2, 114.1, 83.0, 55.4, 53.2, 52.5, 28.1, 26.0, (3C missing); ESI-HRMS m/z calcd for $C_{20}H_{24}N_2O_7S$ + H^+ 437.1377, found 437.1371.



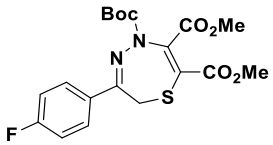
4-(*tert*-Butyl) 2,3-dimethyl 6-(*p*-tolyl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate. Compound **3m** (105 mg, Yield = 83%, R_f = 0.46 (PE:EA = 2:1)) was isolated as a yellow solid; mp 62−63 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 3.76 (s, 3H), 3.72 (s, 3H), 2.37 (s, 3H), 1.46 (s, 9H), (2H missing); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 164.1, 163.1, 151.4, 142.4, 130.0, 129.3, 127.6, 82.9, 53.1, 52.4, 28.0, 26.0, 21.3, (2C missing); ESI-HRMS m/z calcd for $C_{20}H_{24}N_2O_6S$ + H^+ 421.1428, found 421.1427.



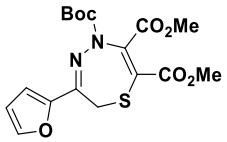
4-(*tert*-Butyl) 2,3-dimethyl 6-(4-nitrophenyl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate. Compound **3n** (131 mg, Yield = 97%, R_f = 0.41 (PE:EA = 2:1)) was isolated as a yellow solid; mp 74−75 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.8 Hz, 2H), 8.06 (d, J = 8.8 Hz, 2H) , 3.74 (s, 3H), 3.71 (s, 3H), 1.44 (s, 9H), (2H missing); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 163.8, 162.9, 151.2, 149.5, 139.0, 130.8, 128.8, 128.6, 123.7, 83.5, 53.2, 52.6, 27.9, 26.0; ESI-HRMS m/z calcd for $C_{19}H_{21}N_3O_8S$ + Na^+ 474.0942, found 474.0941.



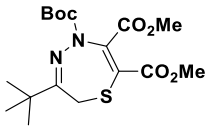
4-(*tert*-Butyl) 2,3-dimethyl 6-(4-(trifluoromethyl)phenyl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate. Compound **3o** (135 mg, Yield = 95%, R_f = 0.47 (PE:EA = 2:1)) was isolated as a yellow solid; mp 64−65 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.0 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H), 3.77 (s, 3H), 3.74 (s, 3H), 1.47 (s, 9H), (2H missing); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 164.0, 163.0, 151.4, 136.6, 133.3 (q, J = 32.6 Hz), 131.0, 128.8, 128.0, 125.6 (q, J = 3.7 Hz), 123.6 (q, J = 270.9 Hz), 83.4, 53.3, 52.6, 28.0, 26.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.03 (s, 3F); ESI-HRMS m/z calcd for $C_{20}H_{21}F_3N_2O_6S$ + Na^+ 497.0965, found 497.0966.



4-(*tert*-Butyl) 2,3-dimethyl 6-(4-fluorophenyl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate. Compound **3p** (117 mg, Yield = 92%, R_f = 0.51 (PE:EA = 2:1)) was isolated as a yellow solid; mp 74−75 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92–7.82 (m, 2H), 7.10–6.99 (m, 4H), 3.72 (s, 3H), 3.68 (s, 3H), 1.42 (s, 9H), (2H missing); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 164.8 (d, J = 251.6 Hz), 163.9, 163.0, 151.3, 130.9, 129.8 (d, J = 8.8 Hz), 129.0 (d, J = 2.5 Hz), 128.4, 115.7 (d, J = 21.8 Hz), 83.0, 53.1, 52.4, 27.8, 25.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -107.11 (s, F); ESI-HRMS m/z calcd for $C_{19}H_{21}FN_2O_6S$ + Na^+ 447.0997, found 447.0995.

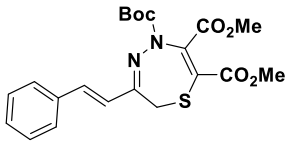


4-(*tert*-Butyl) 2,3-dimethyl 6-(furan-2-yl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate. Compound **3q** (100 mg, Yield = 84%, R_f = 0.49 (PE:EA = 2:1)) was isolated as a yellow solid; mp 144−145 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 1.2 Hz, 1H), 7.22 (d, J = 3.2 Hz, 1H), 6.54 (dd, J = 3.6, 1.6 Hz, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 1.44 (s, 9H), (2H missing); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 162.9, 162.0, 151.5, 147.0, 146.0, 131.9, 128.2, 115.4, 112.6, 83.0, 53.2, 52.4, 27.9, 25.0; ESI-HRMS m/z calcd for $C_{17}H_{20}N_2O_7S$ + Na^+ 419.0883, found 419.0885.

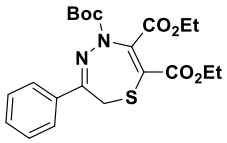


4-(*tert*-Butyl) 2,3-dimethyl 6-(*tert*-butyl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate. Compound **3r**

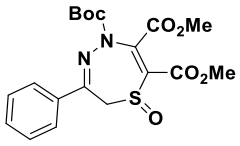
(59 mg, Yield = 51%, R_f = 0.39 (PE:EA = 2:1)) was isolated as a yellow solid; mp 130−131 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.74 (s, 3H), 3.73 (s, 3H), 1.41 (s, 9H), 1.28 (s, 9H), (2H missing); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.2, 164.1, 163.1, 151.0, 82.5, 53.2, 52.4, 39.0, 28.0, 27.8, 24.4, (2C missing); ESI-HRMS m/z calcd for $C_{17}H_{26}N_2O_6S + Na^+$ 409.1404, found 409.1403.



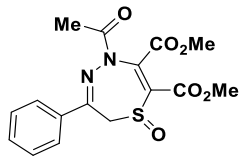
4-(*tert*-Butyl) 2,3-dimethyl (*E*)-6-styryl-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate. Compound **3s** (67 mg, Yield = 52%, R_f = 0.41 (PE:EA = 2:1)) was isolated as a yellow solid; mp 88−89 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.46 (m, 2H), 7.40–7.31 (m, 3H), 7.21 (d, J = 16.4 Hz, 1H), 7.01 (d, J = 16.4 Hz, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 1.45 (s, 9H), (2H missing); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 164.1, 163.0, 151.6 , 140.3, 134.7, 131.8, 129.8, 128.8, 128.6, 127.5, 122.8, 83.0, 53.2, 52.4, 27.9, 24.1; ESI-HRMS m/z calcd for $C_{21}H_{24}N_2O_6S + Na^+$ 455.1247, found 455.1248.



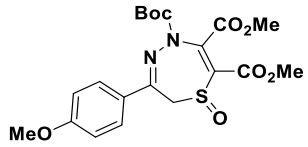
4-(*tert*-Butyl) 2,3-diethyl 6-phenyl-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate. Compound **3t** (120 mg, Yield = 92%, R_f = 0.57 (PE:EA = 2:1)) was isolated as a yellow solid; mp 56−57 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 7.6 Hz, 2H), 7.47 (t, J = 7.6 Hz, 1H), 7.40 (t, J = 7.6 Hz, 2H), 4.22–4.12 (m, 4H), 1.46 (s, 9H), 1.27 (t, J = 7.2 Hz, 3H), 1.22 (t, J = 7.2 Hz, 3H), (2H missing); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 163.6, 162.6, 151.3, 133.1, 131.6, 128.5, 127.5, 82.8, 62.4, 61.7, 28.0, 26.0, 13.8, 13.6, (2C missing); ESI-HRMS m/z calcd for $C_{21}H_{26}N_2O_6S + Na^+$ 457.1404, found 457.1407.



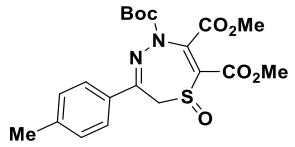
4-(*tert*-Butyl) 2,3-dimethyl 6-phenyl-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate 1-oxide. Compound **4a** (91 mg, Yield = 72%, R_f = 0.62 (PE:EA = 1:1)) was isolated as a yellow solid; mp 72.0−73.0 °C. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.96–7.92 (m, 2H), 7.61–7.56 (m, 1H), 7.54–7.49 (m, 2H), 5.01 (d, J = 14.0 Hz, 1H), 4.76 (d, J = 14.0 Hz, 1H), 3.79 (s, 3H), 3.75 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 170.9, 164.1, 163.1, 149.7, 140.0, 134.8, 132.1, 128.7, 128.3, 126.0, 84.8, 53.6, 47.2, 27.5, (1C missing); ESI-HRMS m/z calcd for $C_{19}H_{22}N_2O_7S + Na^+$ 445.1040, found 445.1039.



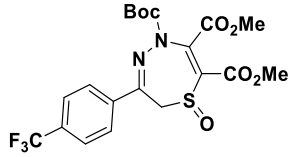
Dimethyl 4-acetyl-6-phenyl-4,7-dihydro-1,4,5-thiadiazepine-2,3-dicarboxylate 1-oxide. Compound **4b** (81 mg, Yield = 74%, R_f = 0.22 (PE:EA = 1:1)) was isolated as a white solid; mp 123.9−124.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.2 Hz, 1H), 7.48 (t, J = 7.2 Hz, 2H), 4.49 (d, J = 13.6 Hz, 1H), 4.30 (d, J = 13.2 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 166.0, 163.0, 162.3, 140.3, 134.3, 132.5, 129.0, 127.8, 53.5, 48.0, 22.3, (2C missing); ESI-HRMS m/z calcd for $C_{16}H_{16}N_2O_6S$ + Na^+ 387.0621, found 387.0620.



4-(*tert*-Butyl) 2,3-dimethyl 6-(4-methoxyphenyl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate 1-oxide. Compound **4c** (94 mg, Yield = 69%, R_f = 0.37 (PE:EA = 1:1)) was isolated as a yellow solid; mp 75−76 °C. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.90 (d, J = 8.8 Hz, 2H), 7.05 (d, J = 8.8 Hz, 2H), 4.95 (d, J = 14.0 Hz, 1H), 4.66 (d, J = 13.6 Hz, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 3.74 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 169.9, 164.1, 163.1, 162.5, 149.8, 140.5, 130.2, 127.3, 125.6, 114.1, 84.6, 55.6, 54.9, 53.5, 46.9, 27.5; ESI-HRMS m/z calcd for $C_{20}H_{24}N_2O_8S$ + Na^+ 475.1146, found 475.1148.

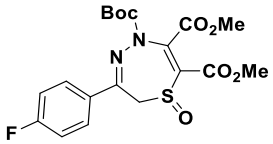


4-(*tert*-Butyl) 2,3-dimethyl 6-(*p*-tolyl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate 1-oxide. Compound **4d** (81 mg, Yield = 62%, R_f = 0.13 (PE:EA = 2:1)) was isolated as a yellow solid; mp 69−70 °C. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.84 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 4.94 (d, J = 14.0 Hz, 1H), 4.68 (d, J = 14.0 Hz, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 2.36 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 170.5, 164.1, 163.1, 149.7, 142.4, 140.2, 132.2, 129.2, 128.2, 125.9, 84.7, 53.5 (2C), 47.1, 27.5, 21.0; ESI-HRMS m/z calcd for $C_{20}H_{24}N_2O_7S$ + Na^+ 459.1196, found 459.1197.

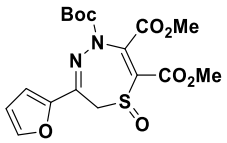


4-(*tert*-Butyl)2,3-dimethyl6-(4-(trifluoromethyl)phenyl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate 1-oxide. Compound **4e** (104 mg, Yield = 71%, R_f = 0.2 (PE:EA = 2:1)) was isolated as a yellow solid; mp 78−79 °C. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.13 (d, J = 8.4 Hz, 2H), 7.87 (d, J = 8.4 Hz, 2H), 5.05

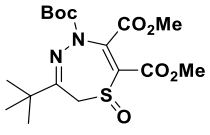
(d, *J* = 14.0 Hz, 1H), 4.79 (d, *J* = 14.0 Hz, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 170.1, 164.0, 163.0, 149.7, 139.8, 138.7, 131.8 (q, *J* = 31.9 Hz), 129.1, 126.6, 125.6 (q, *J* = 3.6 Hz), 123.9 (q, *J* = 270.8 Hz), 85.2, 53.7, 47.5, 27.5, (1C missing); ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.06 (s, 3F); ESI-HRMS m/z calcd for $C_{20}H_{21}F_3N_2O_7S + Na^+$ 513.0914, found 513.0915.



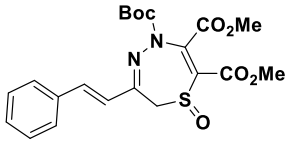
4-(*tert*-Butyl) 2,3-dimethyl 6-(4-fluorophenyl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate 1-oxide. Compound **4f** (95 mg, Yield = 72%, R_f = 0.39 (PE:EA = 1:1)) was isolated as a yellow solid; mp 67−68 °C. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.00 (dd, *J* = 8.8, 5.6 Hz, 2H), 7.34 (t, *J* = 8.8 Hz, 2H), 4.99 (d, *J* = 13.6 Hz, 1H), 4.73 (d, *J* = 14.0 Hz, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 170.0, 164.5 (d, *J* = 249.6 Hz), 164.0, 163.0, 149.7, 140.1, 131.5 (d, *J* = 2.9 Hz), 131.0 (d, *J* = 9.0 Hz), 126.0, 115.8 (d, *J* = 21.8 Hz), 84.9, 53.6, 47.2, 27.5, (1C missing); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.74 (s, F); ESI-HRMS m/z calcd for $C_{19}H_{21}FN_2O_7S + Na^+$ 463.0946, found 463.0949.



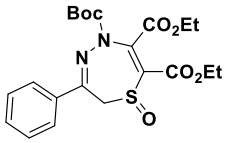
4-(*tert*-Butyl) 2,3-dimethyl 6-(furan-2-yl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate 1-oxide. Compound **4g** (97 mg, Yield = 78%, R_f = 0.23 (PE:EA = 1:1)) was isolated as a yellow solid; mp 77−78 °C. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.98 (d, *J* = 0.8 Hz, 1H), 7.41 (d, *J* = 3.6 Hz, 1H), 6.72 (dd, *J* = 3.2, 1.6 Hz, 1H), 4.76 (d, *J* = 14.0 Hz, 1H), 4.69 (d, *J* = 13.6 Hz, 1H), 3.78 (s, 3H), 3.74 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 164.1, 163.1, 160.0, 149.8, 149.2, 147.8, 140.5, 126.3, 119.8, 113.0, 84.9, 53.6, 47.0, 27.5, (1C missing); ESI-HRMS m/z calcd for $C_{17}H_{20}N_2O_8S + Na^+$ 435.0833, found 435.0832.



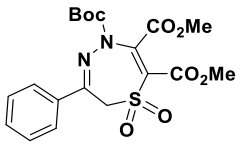
4-(*tert*-Butyl) 2,3-dimethyl 6-(*tert*-butyl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate 1-oxide. Compound **4h** (94 mg, Yield = 78%, R_f = 0.19 (PE:EA = 2:1)) was isolated as a white solid; mp 58−59 °C. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 4.46 (d, *J* = 13.2 Hz, 1H), 4.37 (d, *J* = 13.6 Hz, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 1.41 (s, 9H), 1.16 (s, 9H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 180.2, 164.0, 163.0, 149.5, 140.0, 124.7, 84.4, 53.4, 46.6, 38.5, 27.5, 27.1, (1C missing); ESI-HRMS m/z calcd for $C_{17}H_{26}N_2O_7S + Na^+$ 425.1353, found 425.1354.



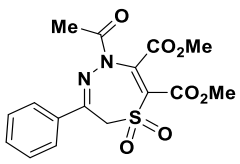
4-(*tert*-Butyl) 2,3-dimethyl *(E)*-6-styryl-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate 1-oxide. Compound **4i** (100 mg, Yield = 74%, R_f = 0.25 (PE:EA = 2:1)) was isolated as a yellow solid; mp 87−88 °C. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.67 (d, J = 6.4 Hz, 2H), 7.56 (d, J = 16.4 Hz, 1H), 7.47–7.40 (m, 3H), 7.15 (d, J = 16.4 Hz, 1H), 4.84 (d, J = 13.6 Hz, 1H), 4.57 (d, J = 14.0 Hz, 1H), 3.78 (s, 3H), 3.74 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 170.1, 164.1, 163.1, 149.9, 143.2, 140.2, 135.1, 130.3, 129.1, 128.1, 126.7, 125.6, 84.9, 53.6, 45.7, 27.6, (1C missing); ESI-HRMS m/z calcd for $C_{21}H_{24}N_2O_7S + Na^+$ 471.1196, found 471.1196.



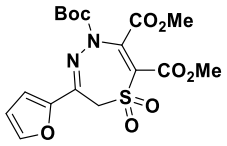
4-(*tert*-Butyl) 2,3-diethyl 6-phenyl-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate 1-oxide. Compound **4j** (93 mg, Yield = 69%, R_f = 0.39 (PE:EA = 2:1)) was isolated as a yellow solid; mp 62−63 °C. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 7.94 (d, J = 7.2 Hz, 2H), 7.58 (t, J = 7.2 Hz, 1H), 7.51 (t, J = 7.2 Hz, 2H), 4.96 (d, J = 14.0 Hz, 1H), 4.71 (d, J = 14.0 Hz, 1H), 4.32–4.12 (m, 4H), 1.46 (s, 9H), 1.26 (t, J = 7.2 Hz, 3H), 1.20 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 170.9, 163.6, 162.4, 149.9, 140.0, 134.9, 132.1, 128.7, 128.3, 126.6, 84.7, 62.8, 62.6, 47.3, 27.6, 13.7, 13.6; ESI-HRMS m/z calcd for $C_{21}H_{26}N_2O_7S + Na^+$ 473.1353, found 473.1353.



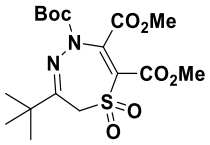
4-(*tert*-Butyl) 2,3-dimethyl 6-phenyl-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate 1,1-dioxide. Compound **4k** (92 mg, Yield = 70%, R_f = 0.77 (PE:EA = 1:1)) was isolated as a white solid; mp 80.2−80.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.2 Hz, 2H), 4.76 (s, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 1.52 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 162.1, 160.4, 150.1, 142.7, 132.7, 132.1, 128.9, 128.4, 125.5, 86.5, 55.1, 53.7, 53.6, 27.7; ESI-HRMS m/z calcd for $C_{19}H_{22}N_2O_8S + Na^+$ 461.0989, found 461.0985.



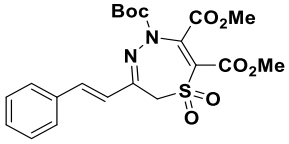
Dimethyl 4-acetyl-6-phenyl-4,7-dihydro-1,4,5-thiadiazepine-2,3-dicarboxylate 1,1-dioxide. Compound **4l** (75 mg, Yield = 66%, R_f = 0.48 (PE:EA = 1:1)) was isolated as a white solid; mp 185.3−185.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 7.2 Hz, 2H), 7.62 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 7.2 Hz, 2H), 4.74 (s, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 163.0, 161.8, 160.4, 142.6, 133.2, 131.8, 129.2, 128.3, 54.5, 53.8, 53.7, 22.4, (1C missing); ESI-HRMS m/z calcd for $C_{16}H_{16}N_2O_7S + Na^+$ 403.0570, found 403.0565.



4-(*tert*-Butyl) 2,3-dimethyl 6-(furan-2-yl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate 1,1-dioxide. Compound **4m** (89 mg, Yield = 69%, R_f = 0.26 (PE:EA = 2:1)) was isolated as a yellow solid; mp 153−154 °C. ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 7.95 (s, 1H), 7.59 (d, J = 3.6 Hz, 1H), 6.78 (dd, J = 3.6, 1.6 Hz, 1H), 5.16 (s, 2H), 3.86 (s, 3H), 3.79 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 163.3, 161.4, 155.9, 151.1, 149.1, 148.3, 142.8, 128.3, 120.1, 113.9, 86.1, 55.2, 54.1, 53.9, 28.0; ESI-HRMS m/z calcd for $C_{17}H_{20}N_2O_9S + Na^+$ 451.0782, found 451.0781.



4-(*tert*-Butyl) 2,3-dimethyl 6-(*tert*-butyl)-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate 1,1-dioxide. Compound **4n** (86 mg, Yield = 68%, R_f = 0.37 (PE:EA = 2:1)) was isolated as a yellow solid; mp 78−79 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.34 (s, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 1.47 (s, 9H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 162.1, 160.5, 150.0, 141.8, 125.6, 85.9, 54.3, 53.7, 53.5, 39.4, 27.8, 27.7; ESI-HRMS m/z calcd for $C_{17}H_{26}N_2O_8S + Na^+$ 441.1302, found 441.1299.



4-(*tert*-Butyl) 2,3-dimethyl (*E*)-6-styryl-1,4,5-thiadiazepine-2,3,4(7*H*)-tricarboxylate 1,1-dioxide. Compound **4o** (99 mg, Yield = 71%, R_f = 0.37 (PE:EA = 2:1)) was isolated as a yellow solid; mp 136−137 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57–7.53 (m, 2H), 7.45–7.38 (m, 4H), 7.11 (d, J = 16.4 Hz, 1H), 4.62 (s, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 1.52 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 162.1, 160.4, 150.3, 143.8, 142.9, 134.4, 130.6, 129.0, 128.2, 128.1, 126.5, 122.4, 86.6, 53.8, 53.7, 27.8; ESI-HRMS m/z calcd for $C_{21}H_{24}N_2O_8S + Na^+$ 487.1146, found 487.1144.

5. NMR spectra

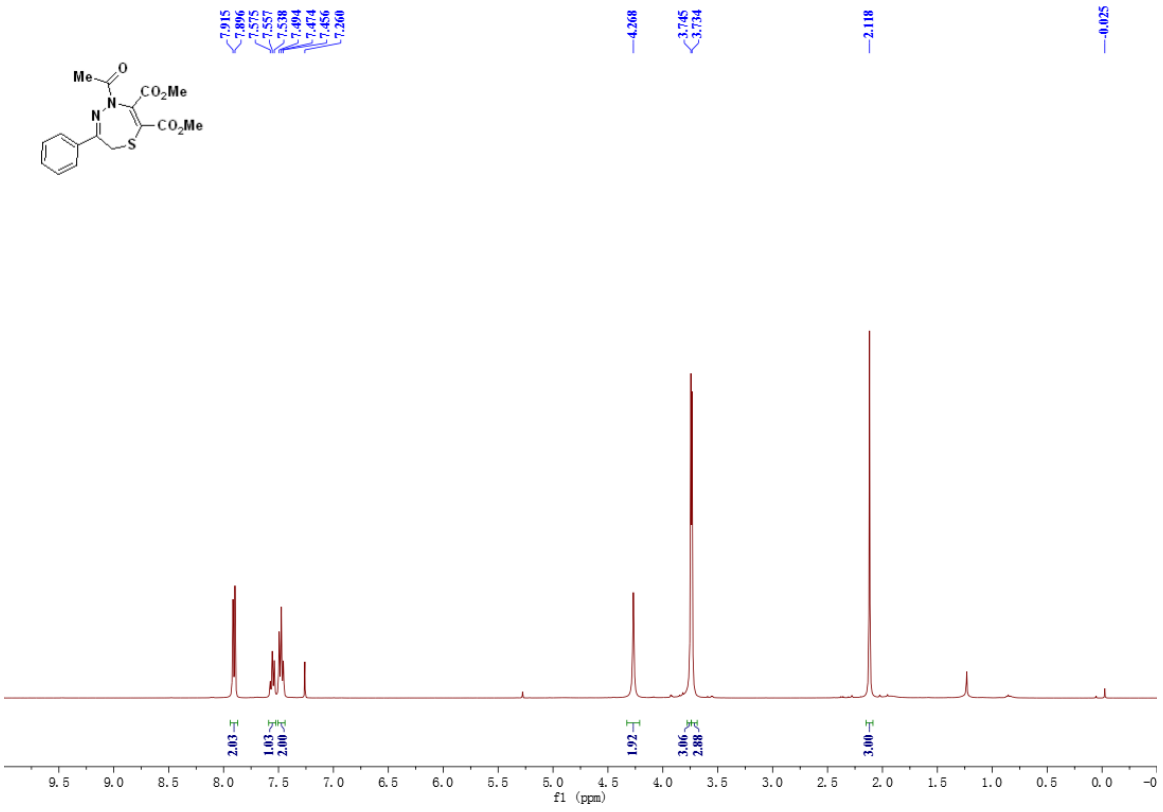


Fig. S1 ^{1}H NMR of compound **3a** (400 MHz, $CDCl_3$).

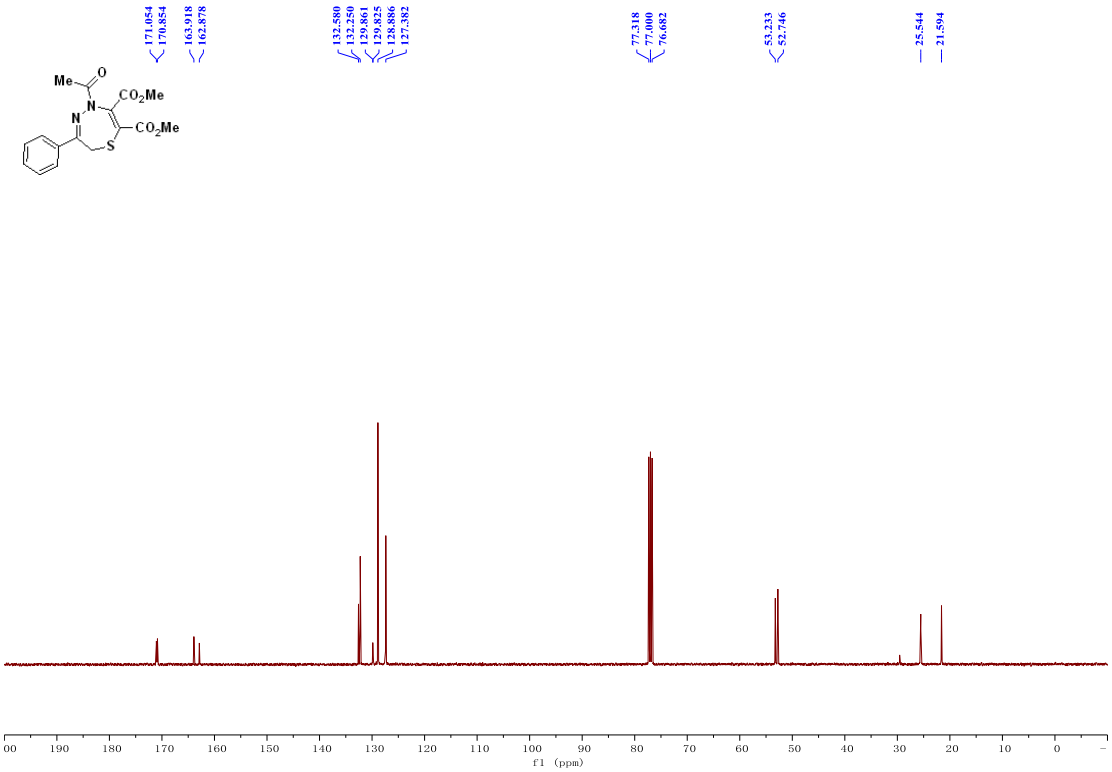


Fig. S2 ^{13}C NMR of compound **3a** (100 MHz, $CDCl_3$).

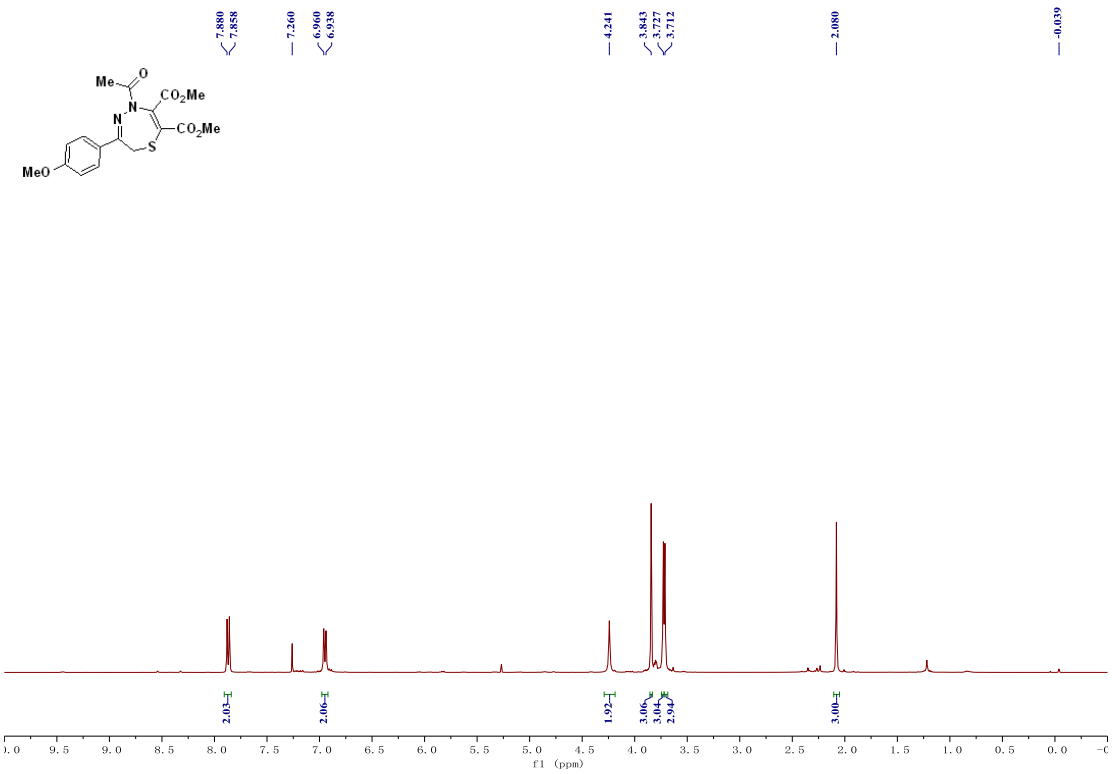


Fig. S3 ^{1}H NMR of compound **3b** (400 MHz, $CDCl_3$).

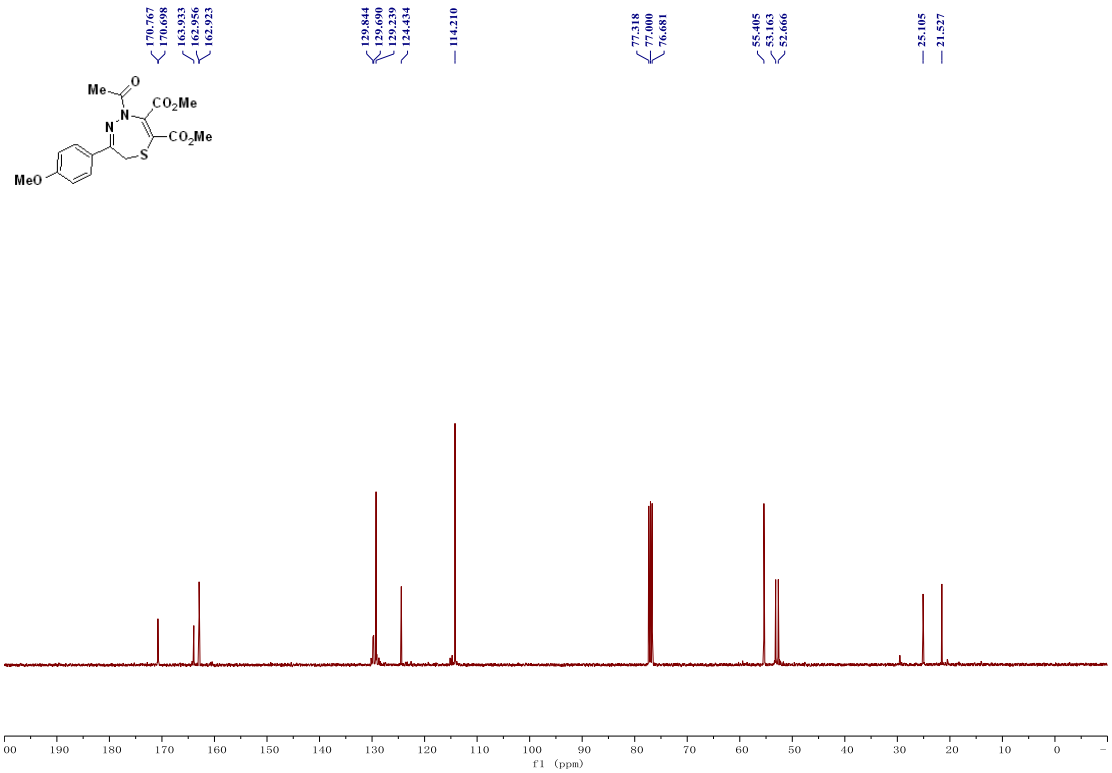


Fig. S4 ^{13}C NMR of compound **3b** (100 MHz, $CDCl_3$).

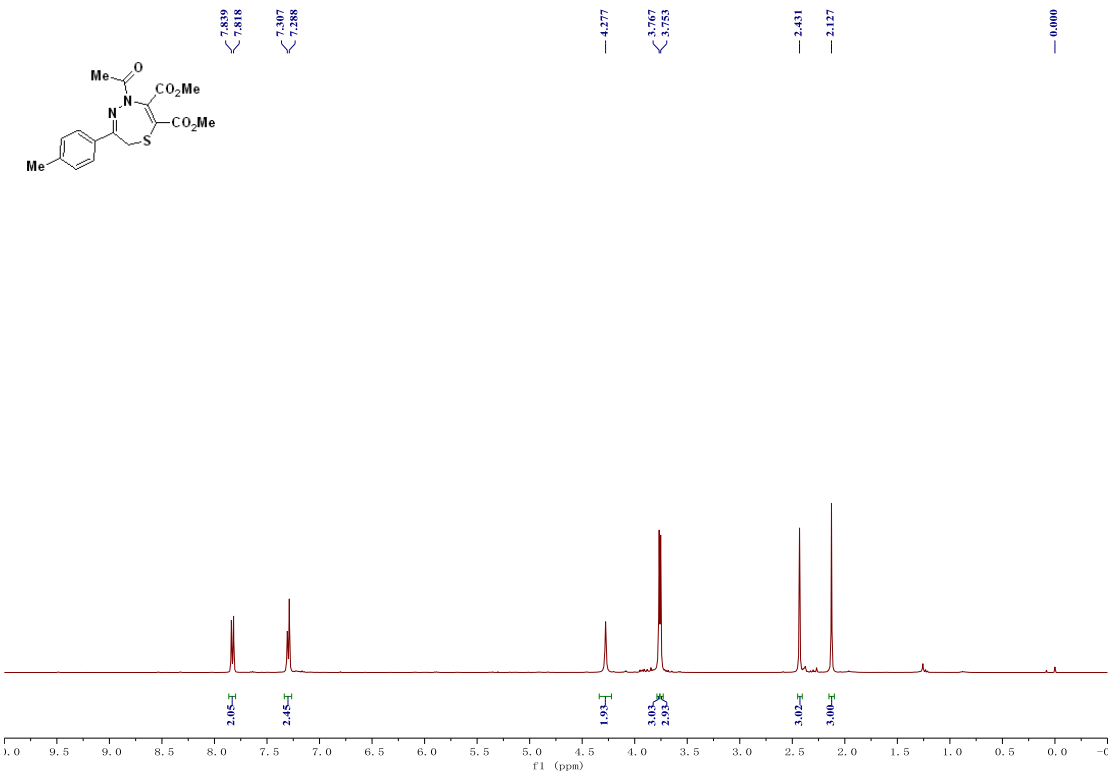


Fig. S5 ^{1}H NMR of compound **3c** (400 MHz, $CDCl_3$).

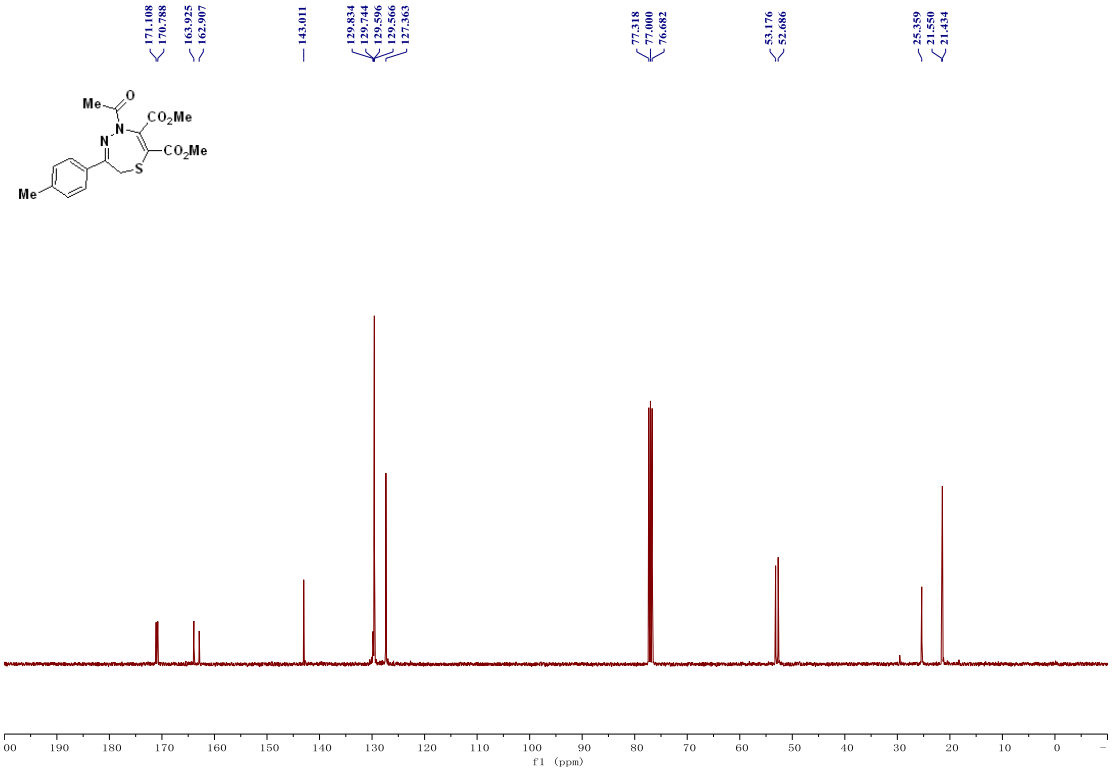


Fig. S6 ^{13}C NMR of compound **3c** (100 MHz, $CDCl_3$).

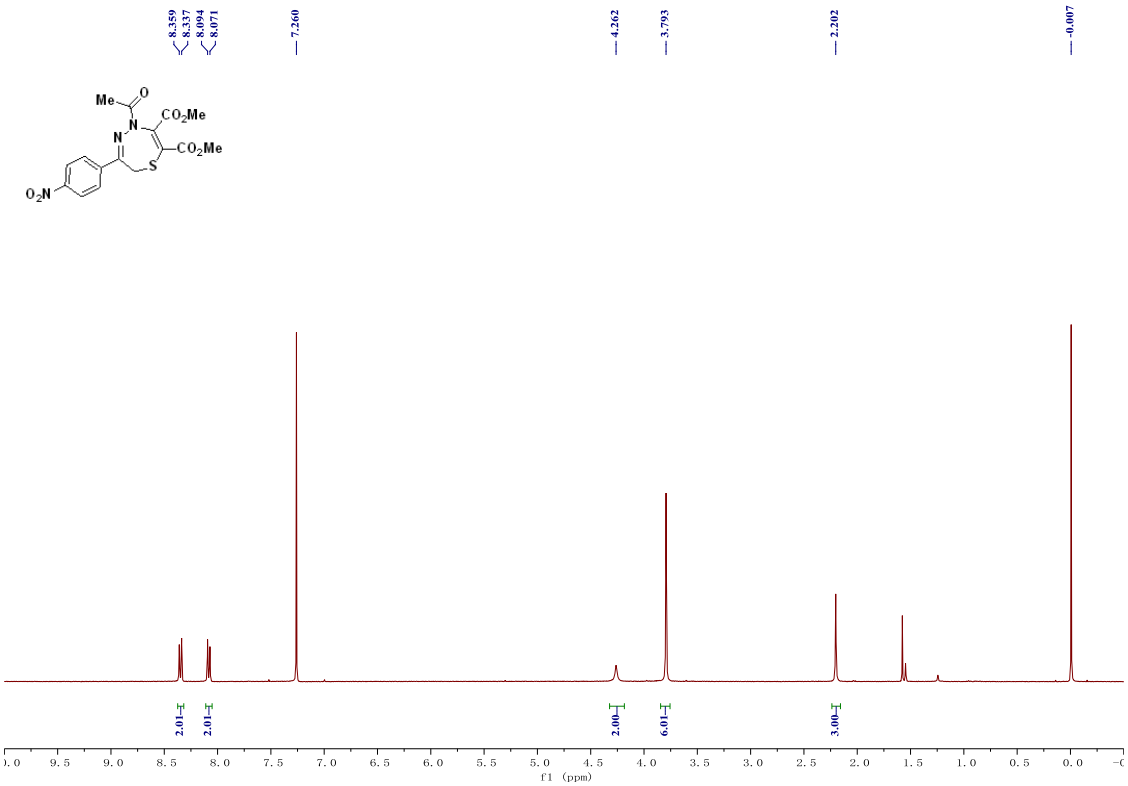


Fig. S7 ^{1}H NMR of compound **3d** (400 MHz, $CDCl_3$).

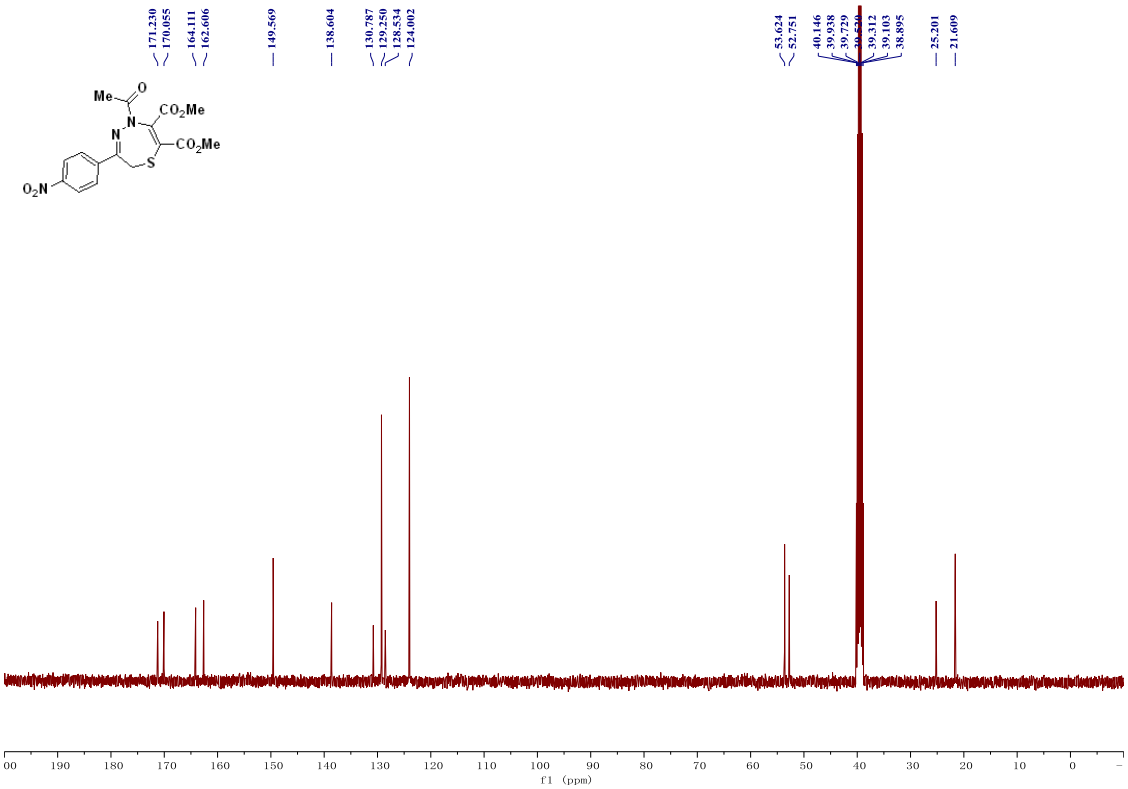


Fig. S8 ^{13}C NMR of compound **3d** (100 MHz, $(CD_3)_2SO$).

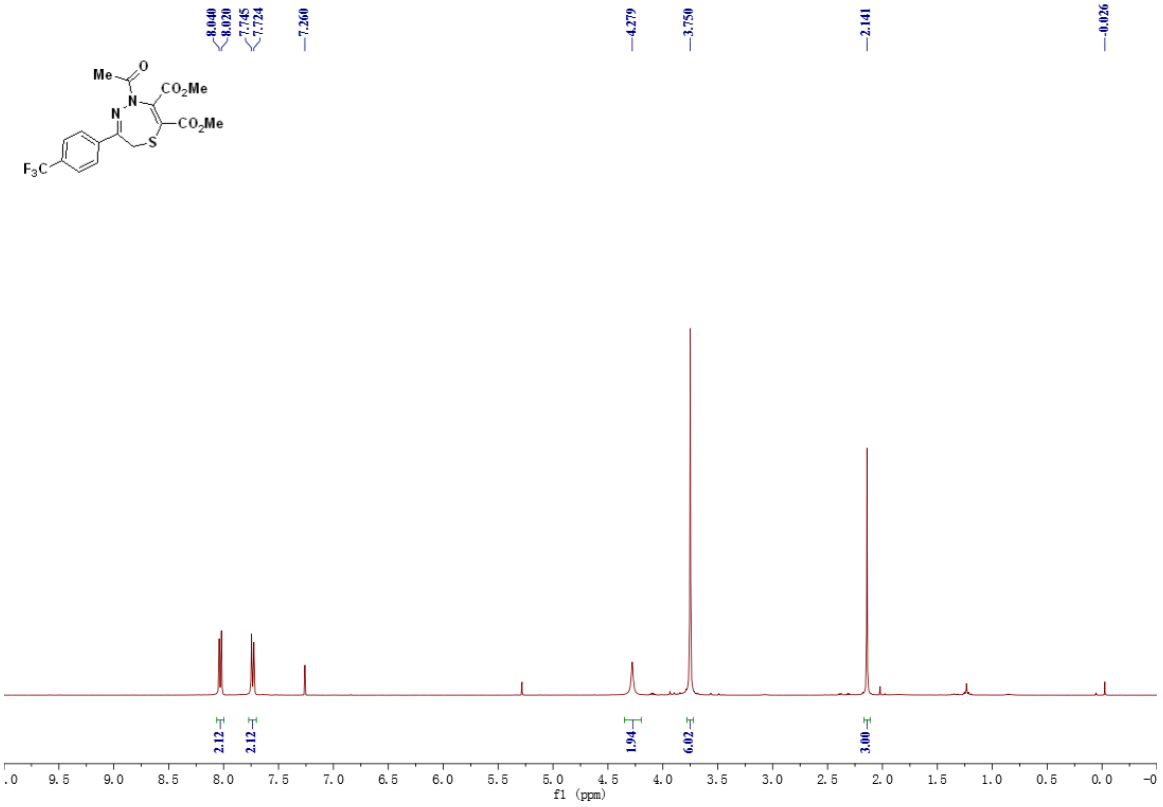


Fig. S9 ^{1}H NMR of compound **3e** (400 MHz, $CDCl_3$).

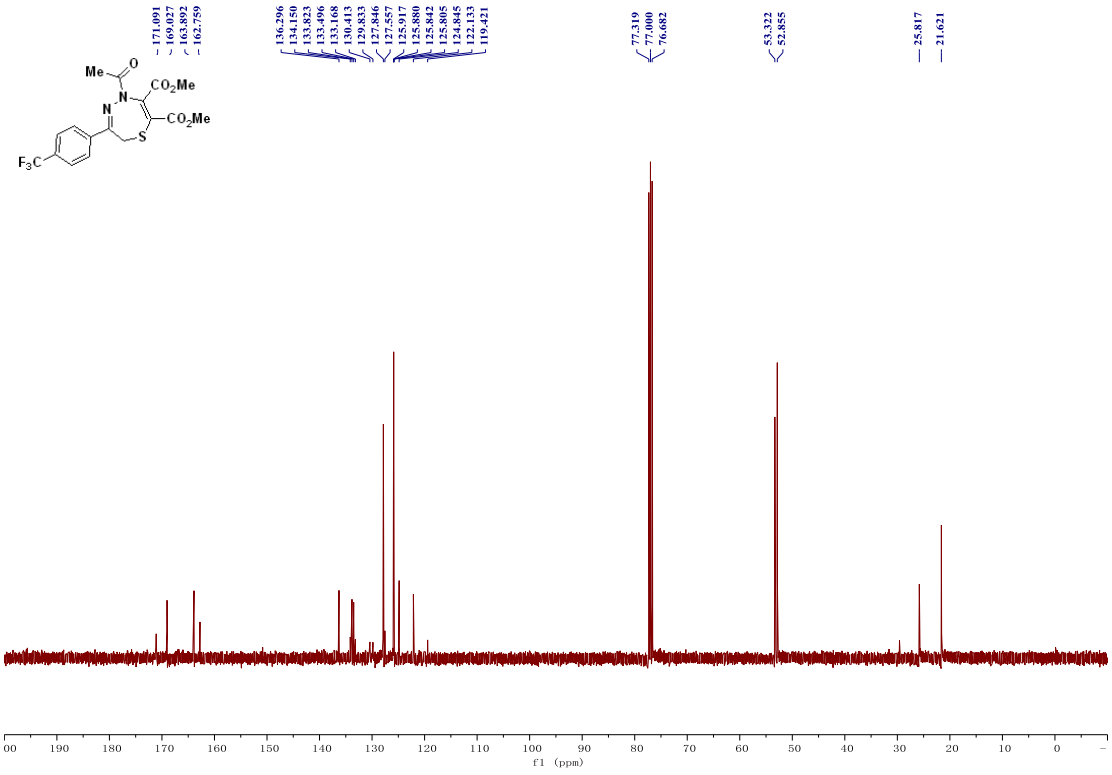


Fig. S10 ^{13}C NMR of compound **3e** (100 MHz, $CDCl_3$).

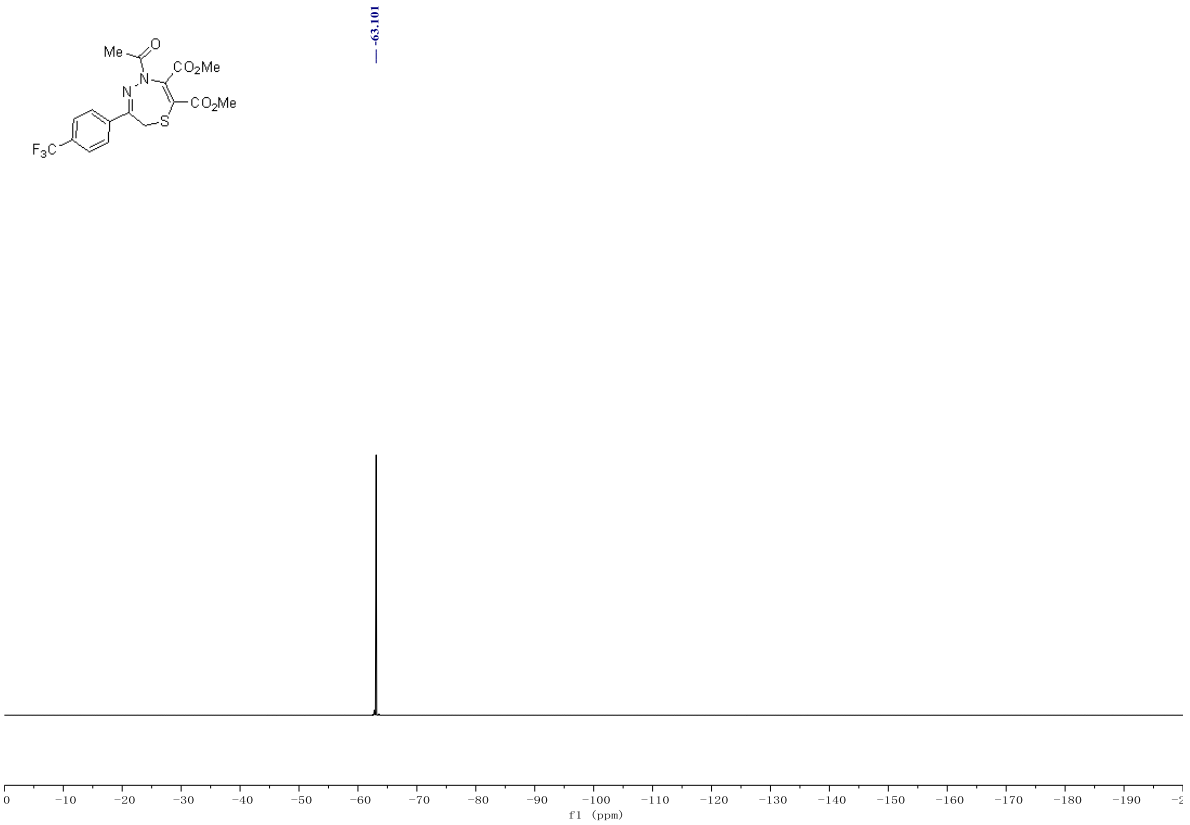


Fig. S11 ^{19}F NMR of compound **3e** (376 MHz, $CDCl_3$).

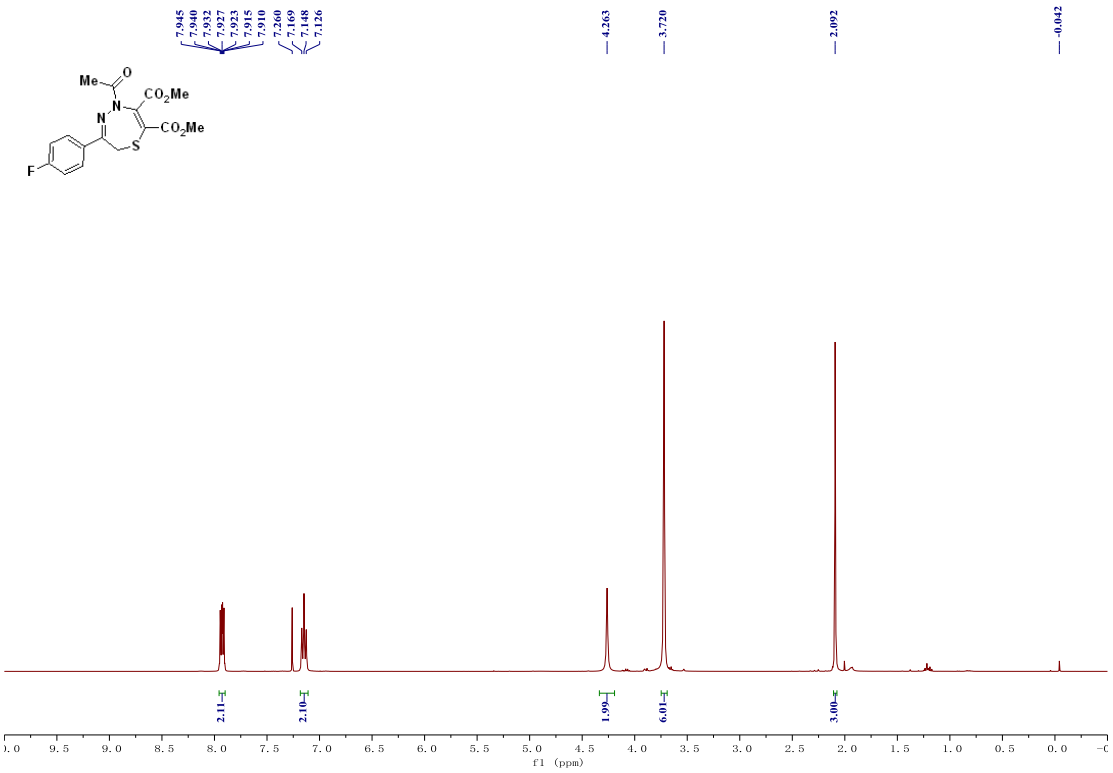


Fig. S12 ^{1}H NMR of compound **3f** (400 MHz, $CDCl_3$).

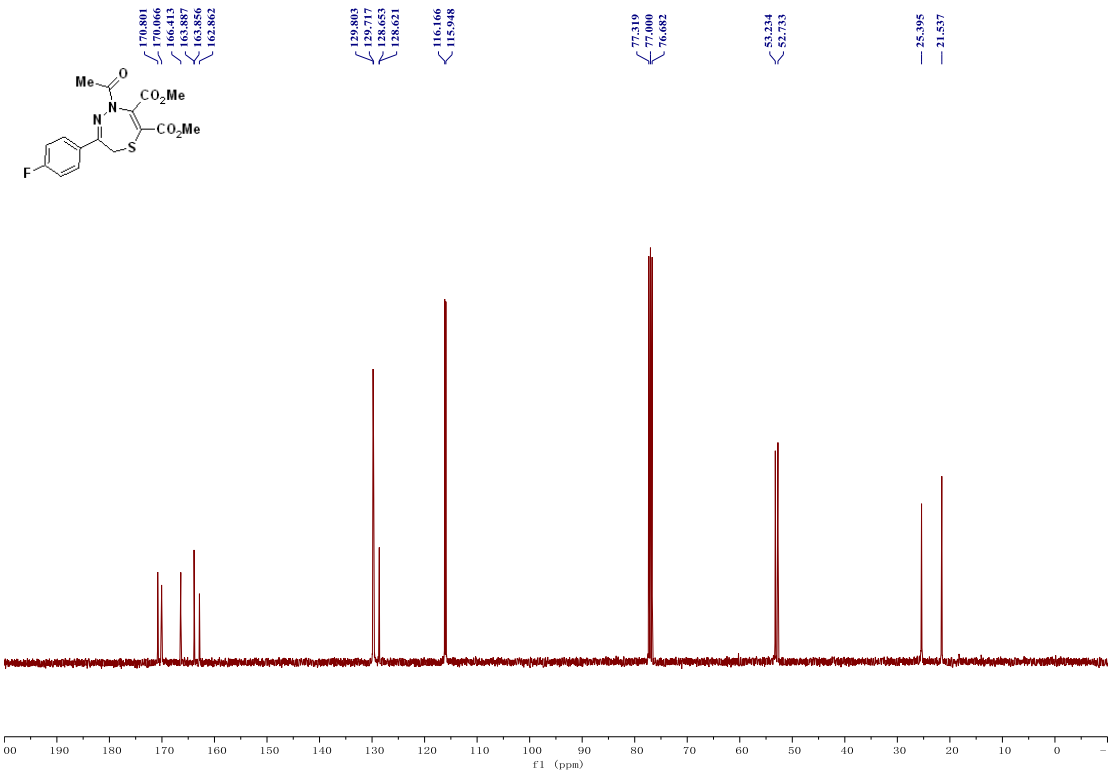


Fig. S13 ^{13}C NMR of compound **3f** (100 MHz, $CDCl_3$).

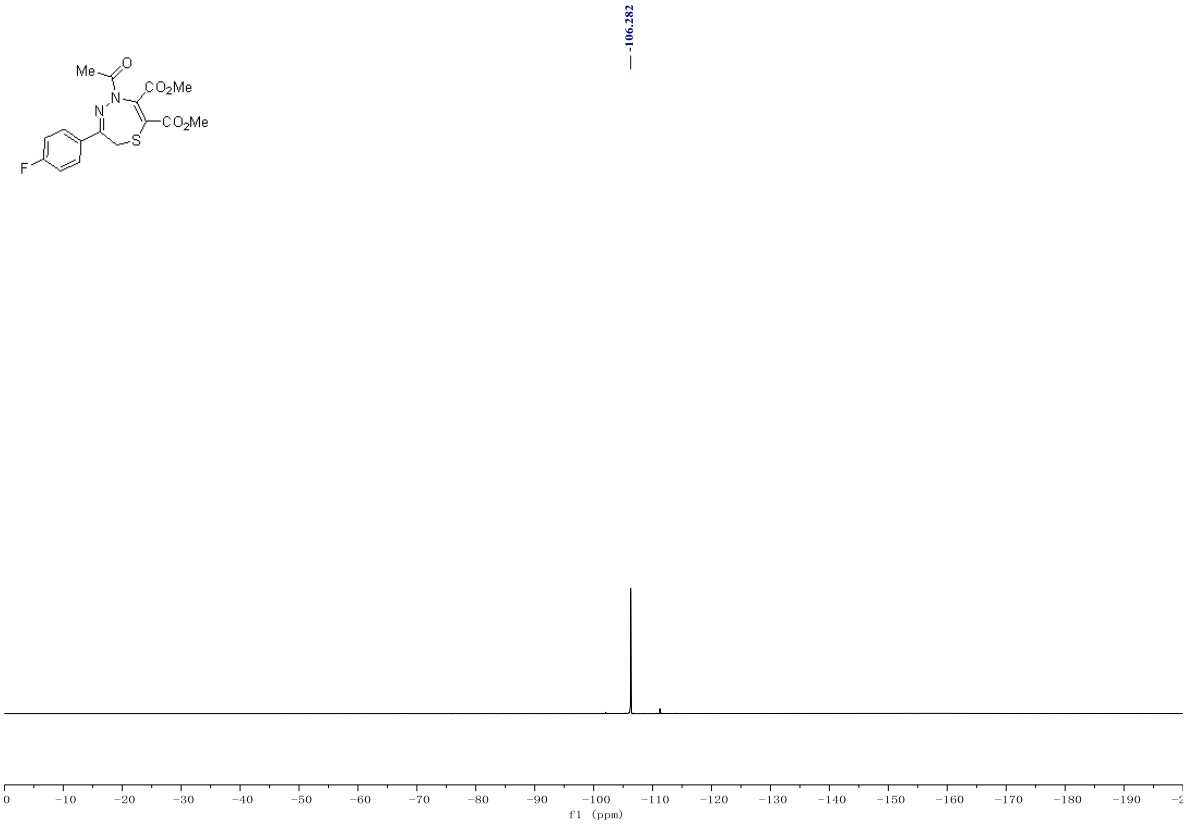


Fig. S14 ^{19}F NMR of compound **3f** (376 MHz, $CDCl_3$).

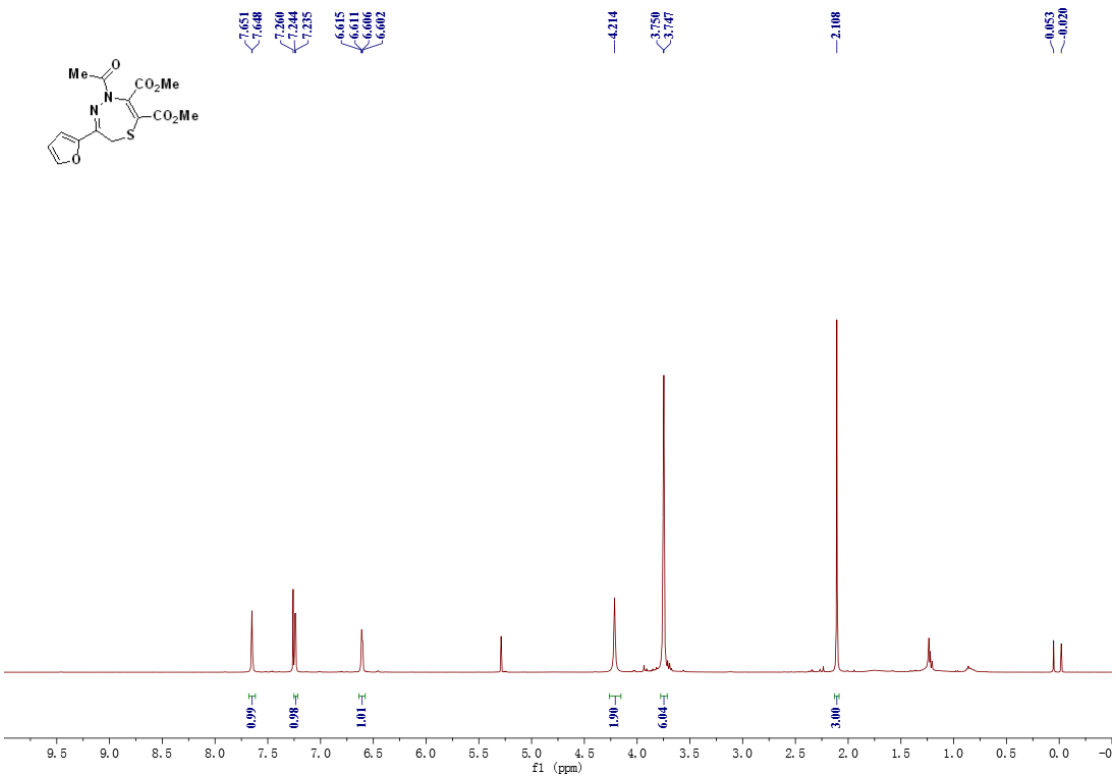


Fig. S15 ^{1}H NMR of compound **3g** (400 MHz, $CDCl_3$).

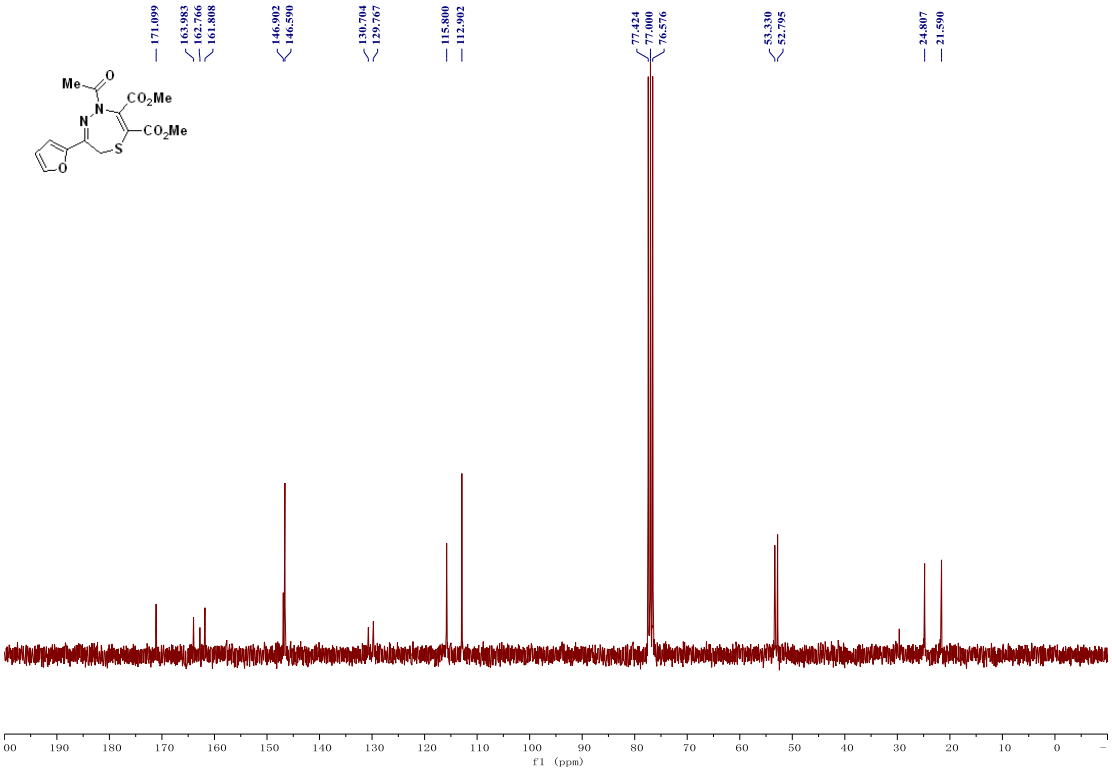


Fig. S16 ^{13}C NMR of compound **3g** (75 MHz, $CDCl_3$).

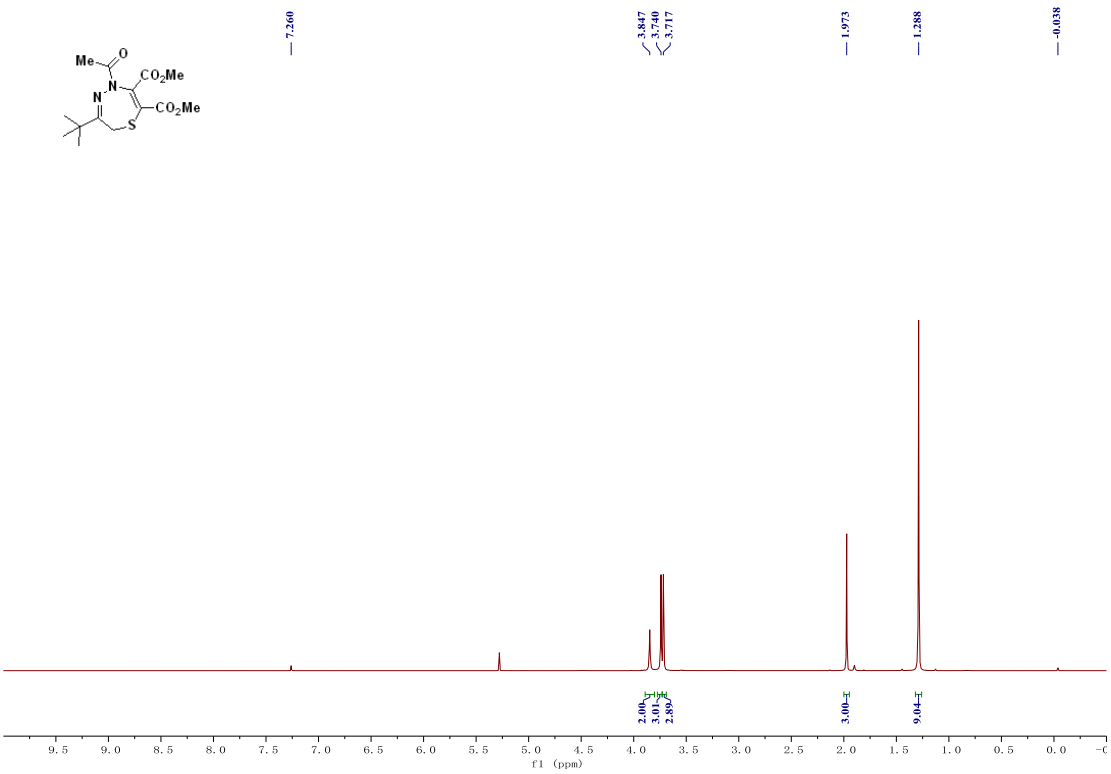


Fig. S17 ^{1}H NMR of compound **3h** (400 MHz, $CDCl_3$).

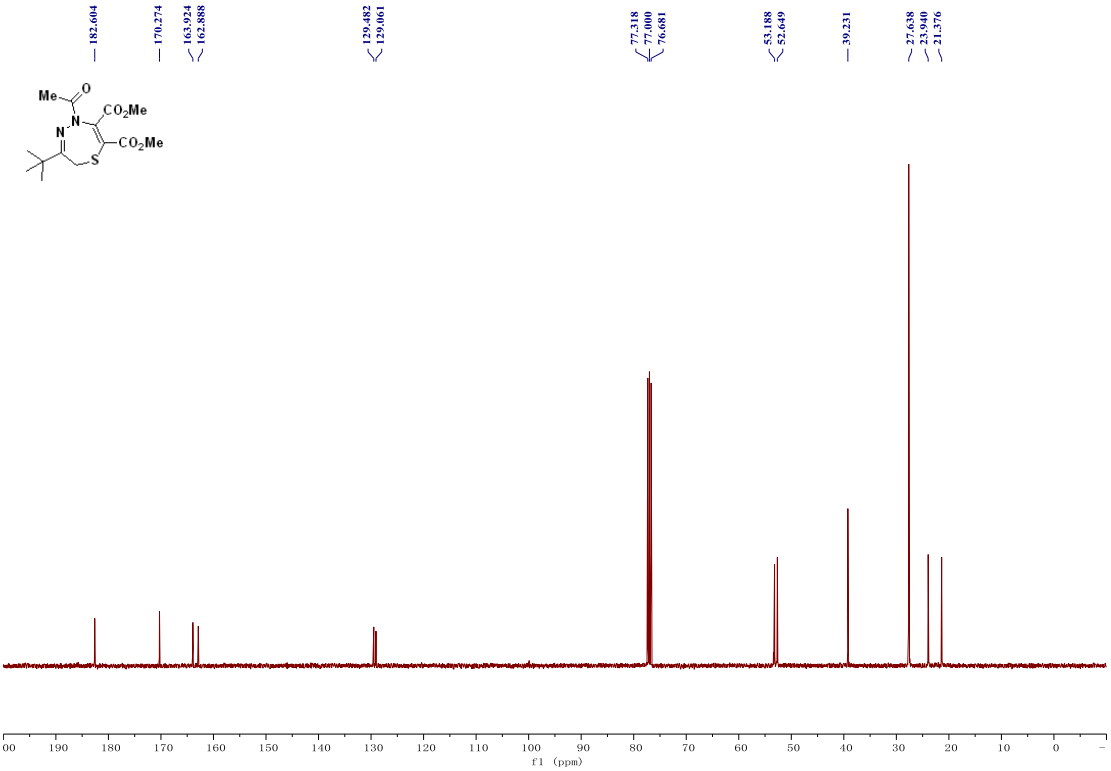


Fig. S18 ^{13}C NMR of compound **3h** (100 MHz, $CDCl_3$).

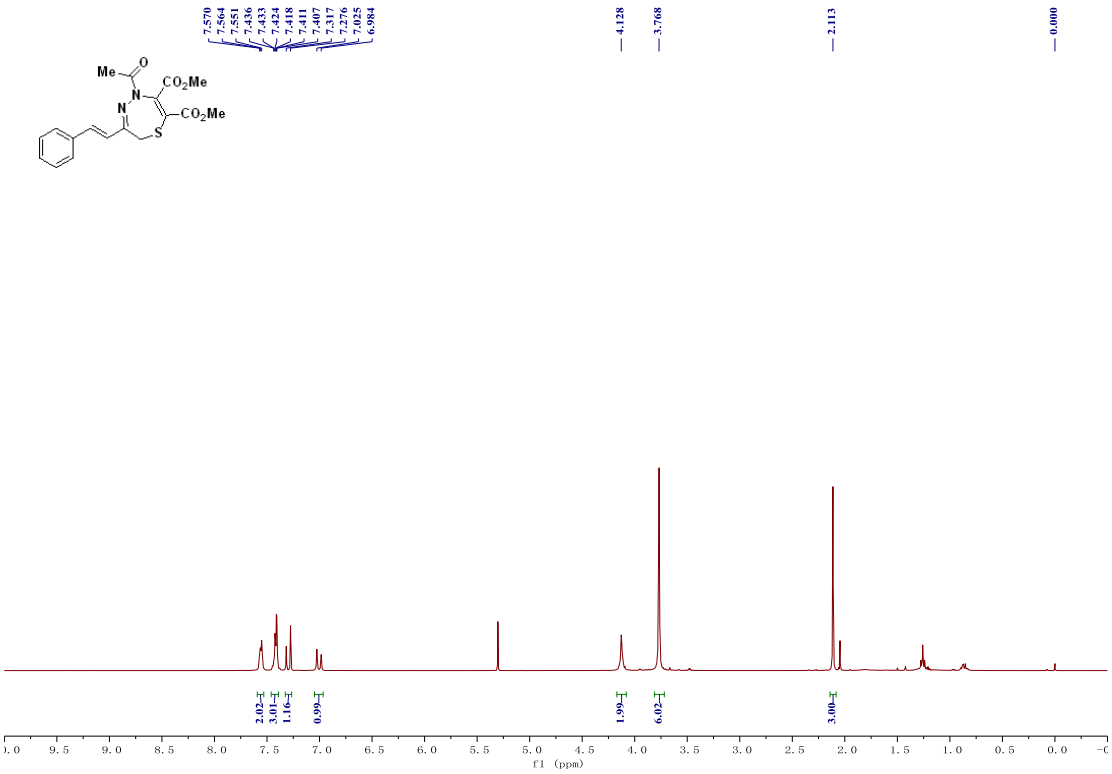


Fig. S19 ^{1}H NMR of compound **3i** (400 MHz, $CDCl_3$).

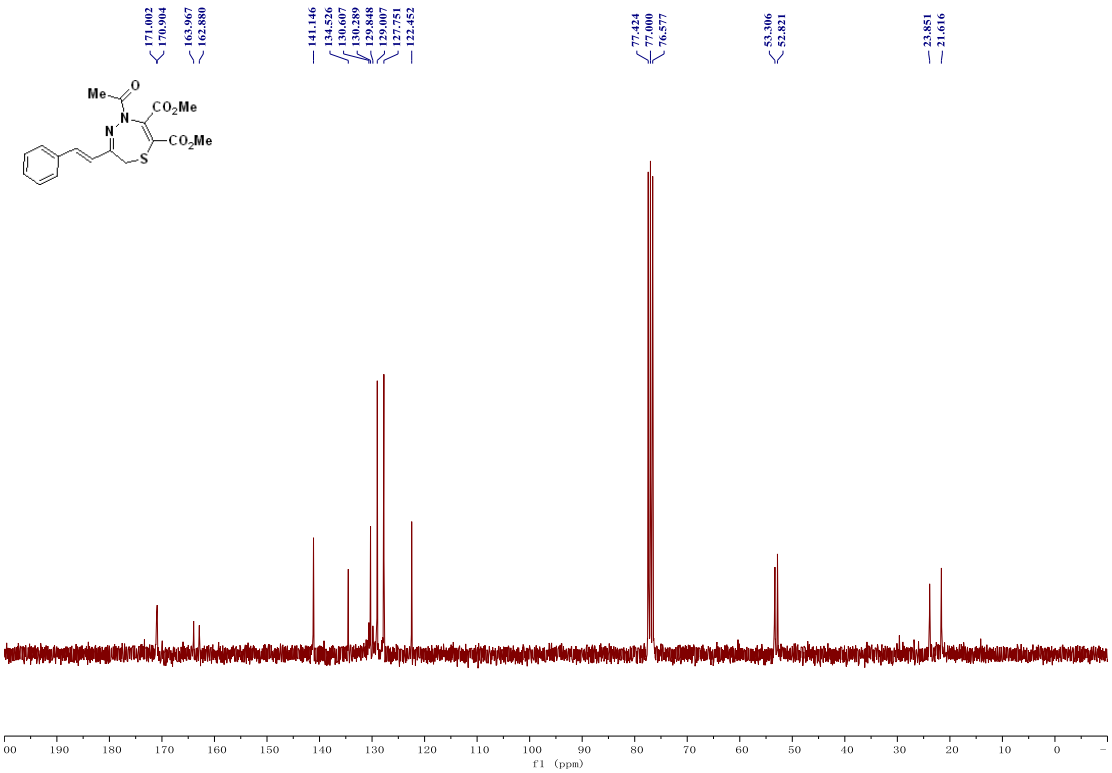


Fig. S20 ^{13}C NMR of compound **3i** (75 MHz, $CDCl_3$).

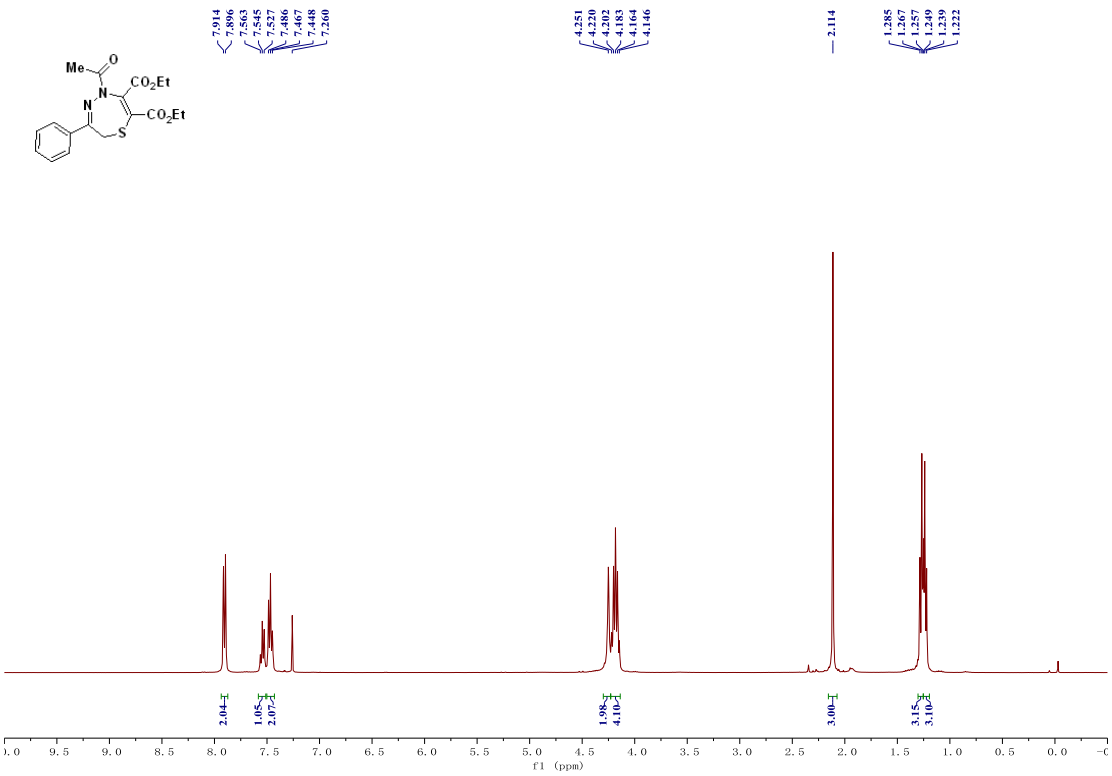


Fig. S21 ^{1}H NMR of compound **3j** (400 MHz, $CDCl_3$).

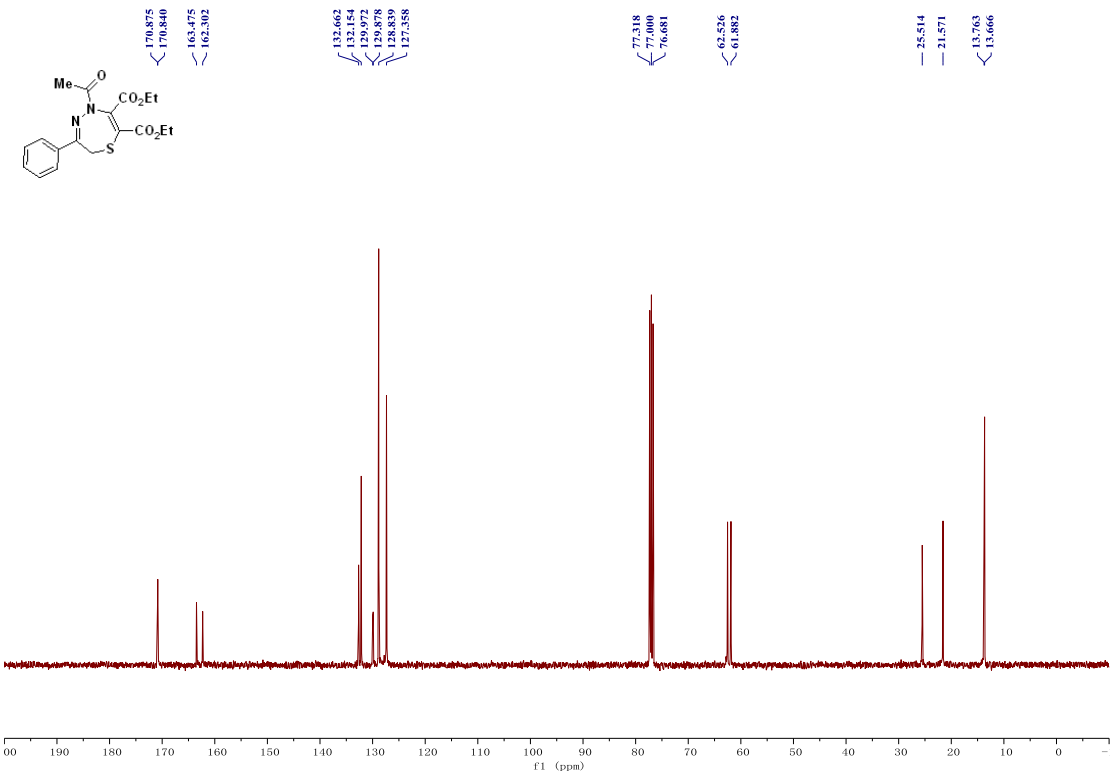


Fig. S22 ^{13}C NMR of compound **3j** (100 MHz, $CDCl_3$).

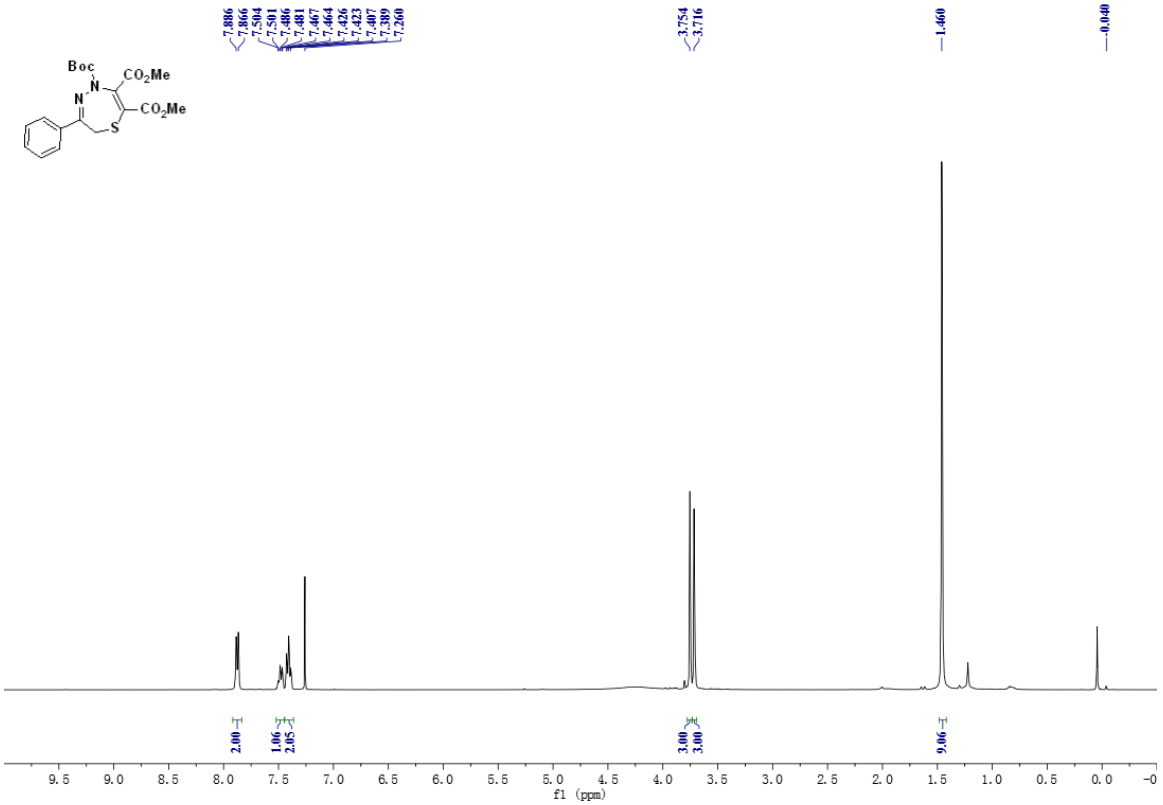


Fig. S23 ^{1}H NMR of compound **3k** (400 MHz, $CDCl_3$).

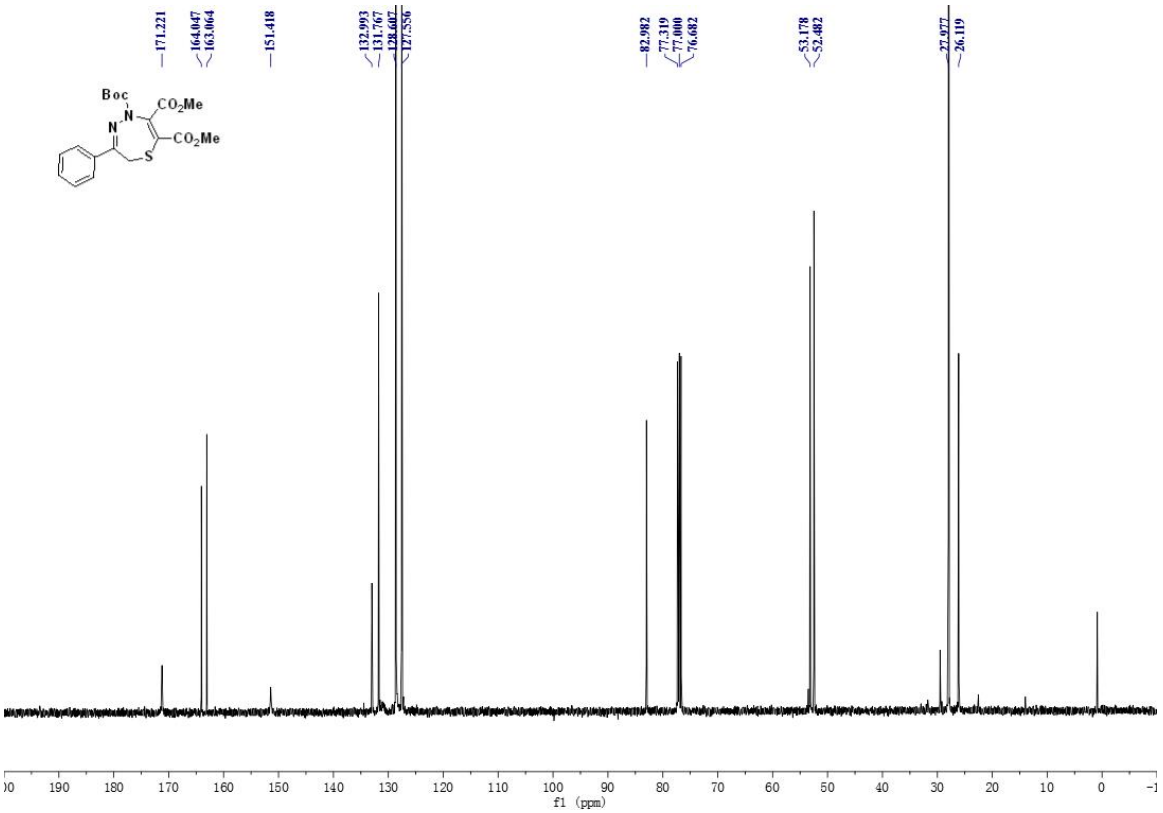


Fig. S24 ^{13}C NMR of compound **3k** (100 MHz, $CDCl_3$).

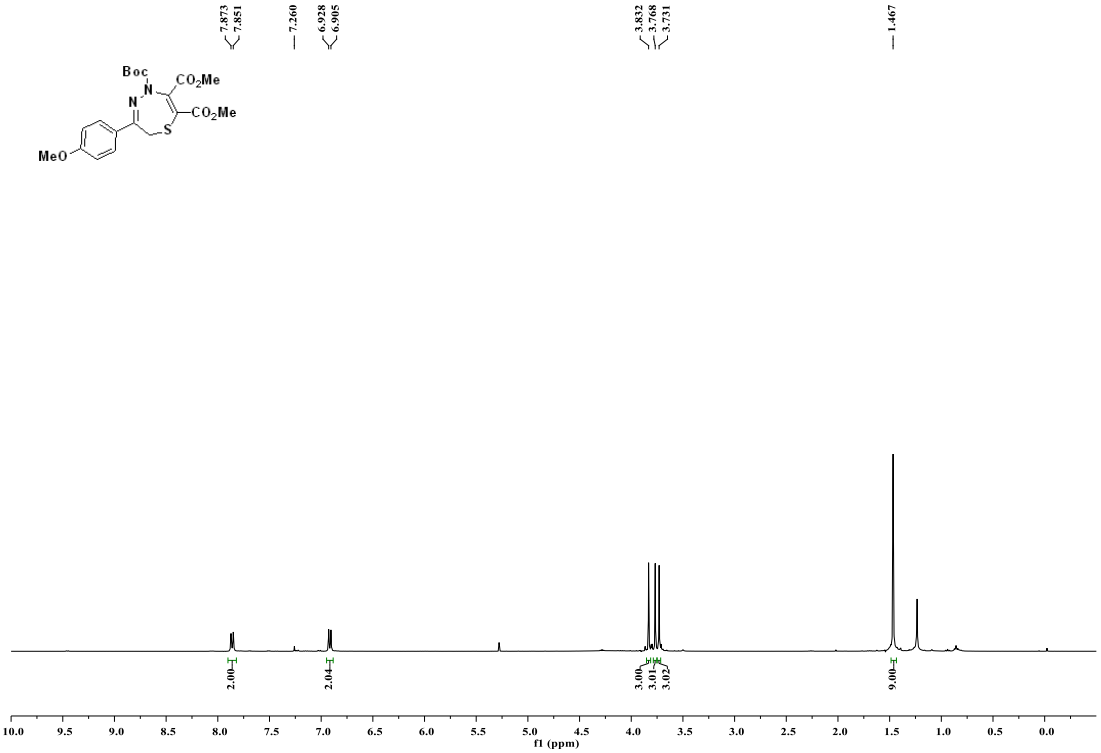


Fig. S25 ^{1}H NMR of compound **3l** (400 MHz, $CDCl_3$).

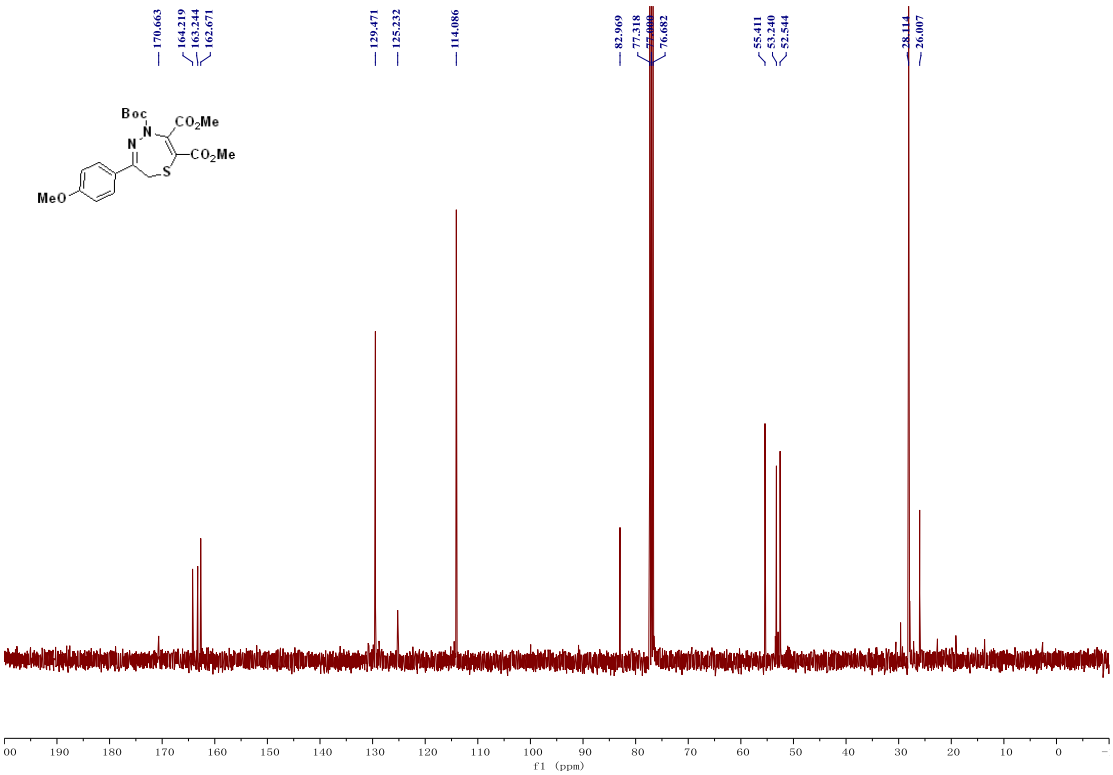


Fig. S26^{13}C NMR of compound **3l** (100 MHz, $CDCl_3$).

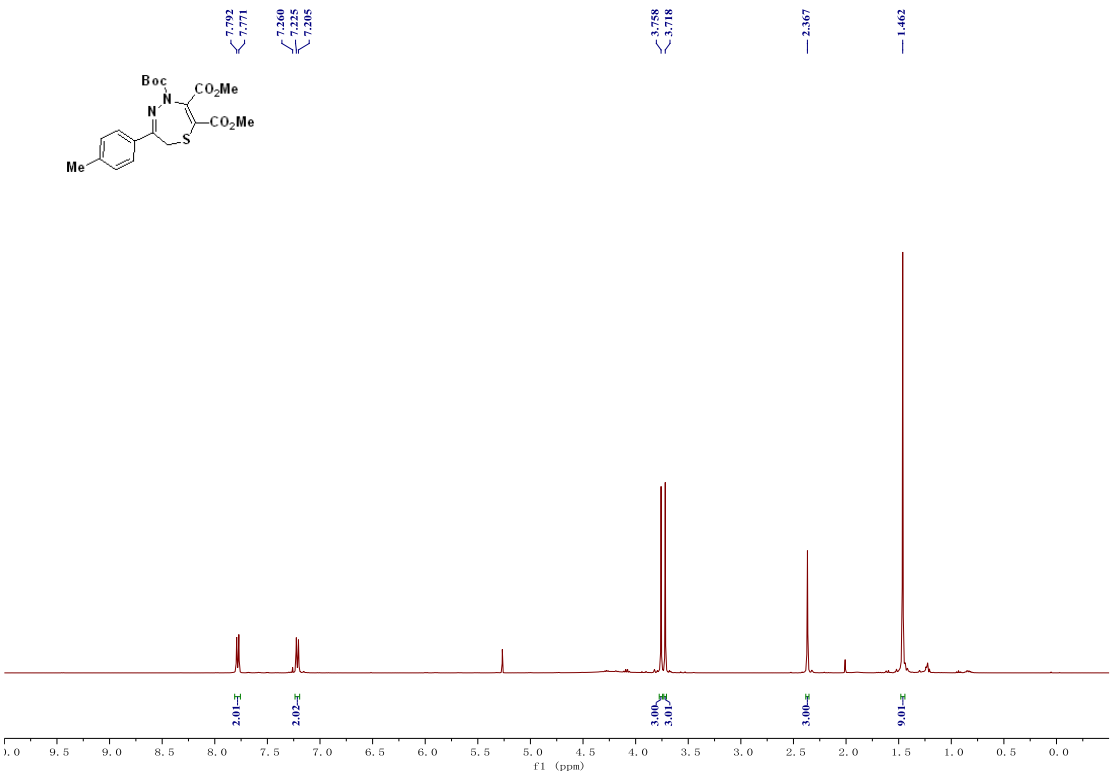


Fig. S27 ^{1}H NMR of compound **3m** (400 MHz, $CDCl_3$).

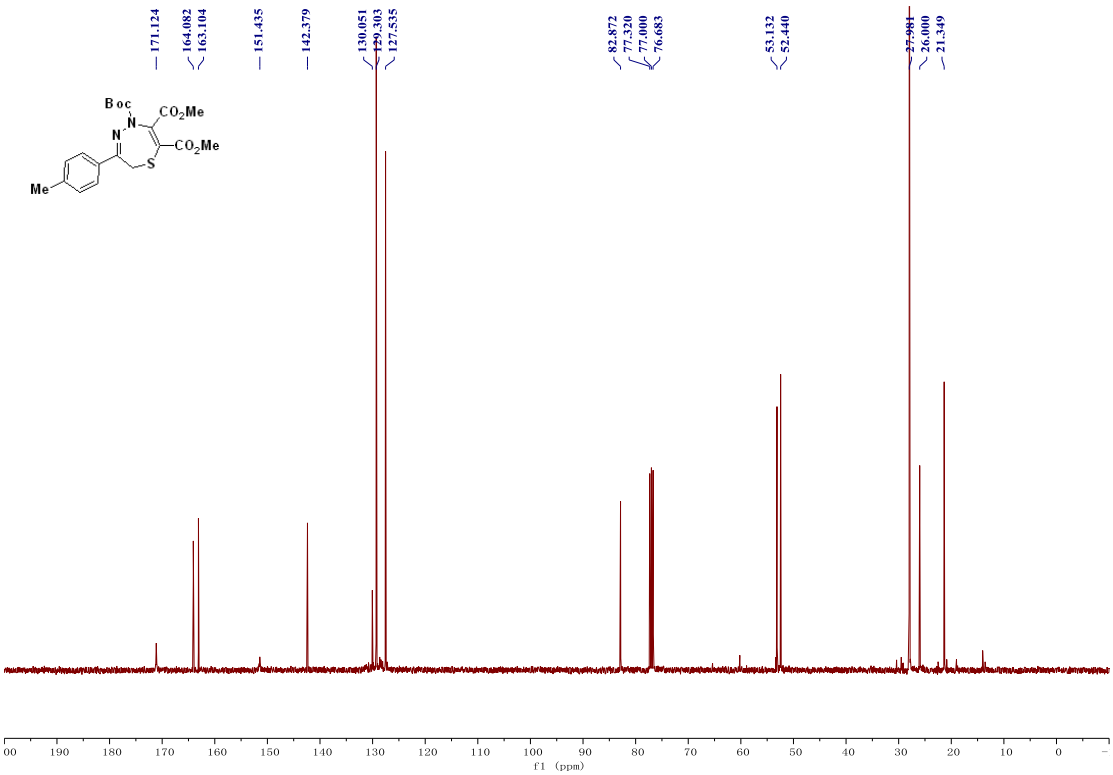


Fig. S28 ^{13}C NMR of compound **3m** (100 MHz, $CDCl_3$).

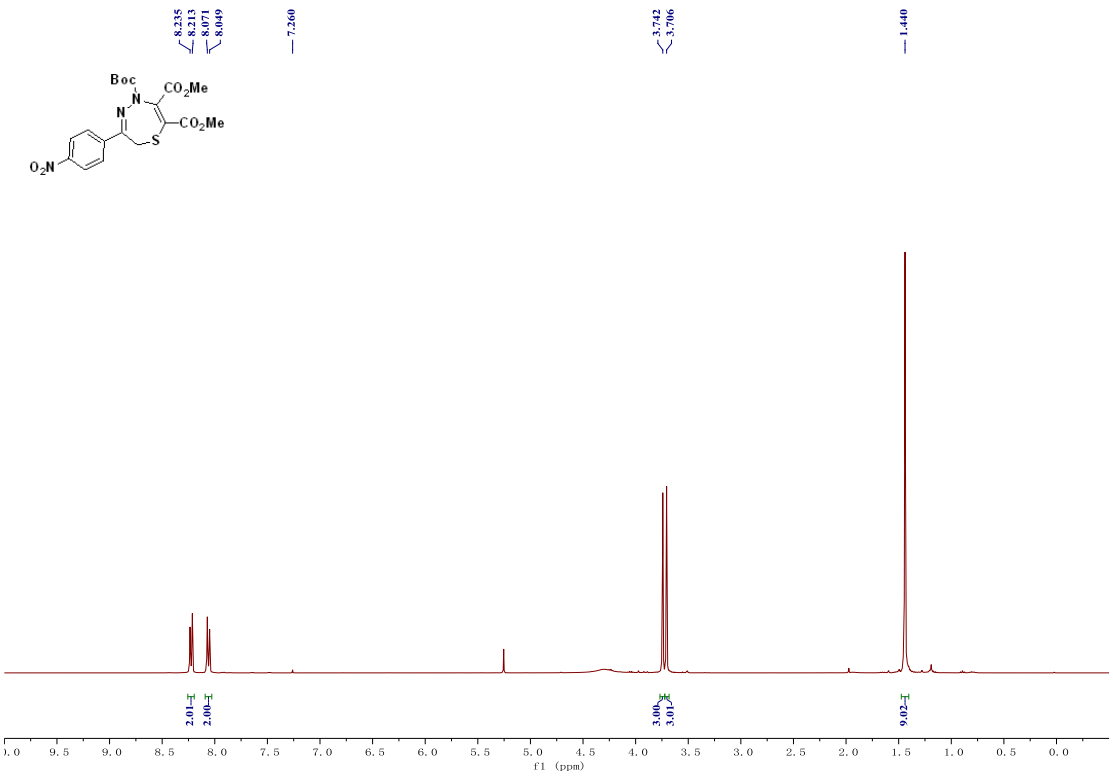


Fig. S29 ^{1}H NMR of compound **3n** (400 MHz, $CDCl_3$).

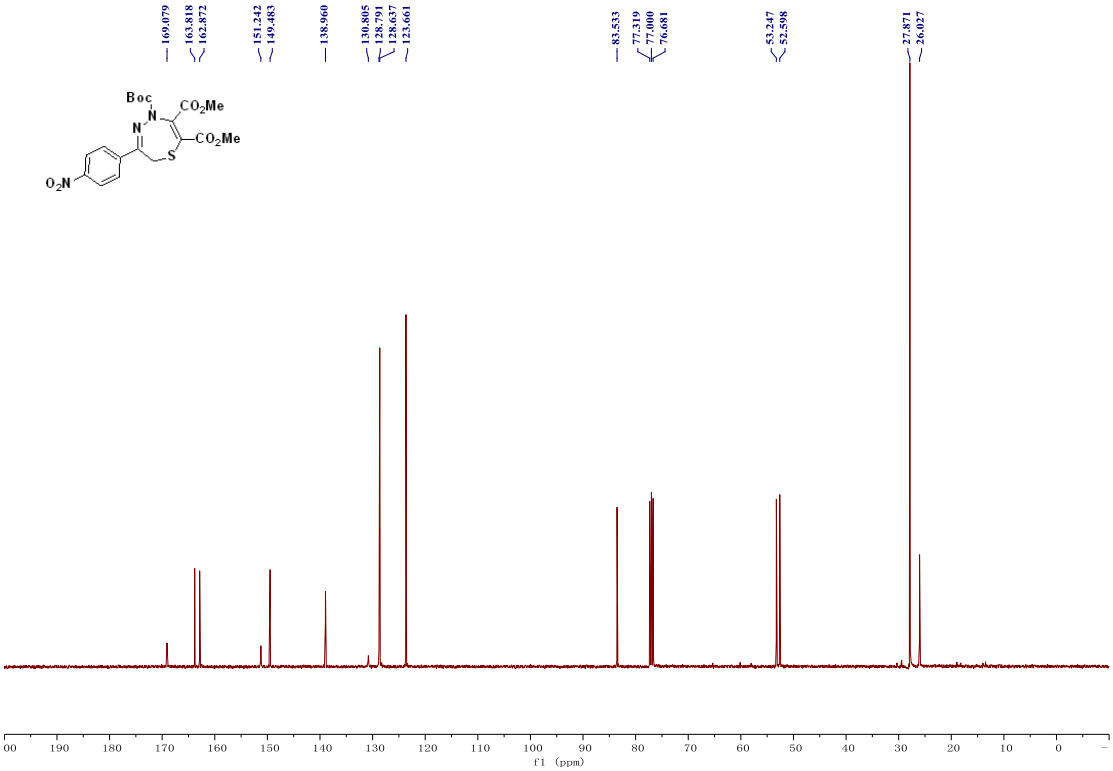


Fig. S30 ^{13}C NMR of compound **3n** (100 MHz, $CDCl_3$).

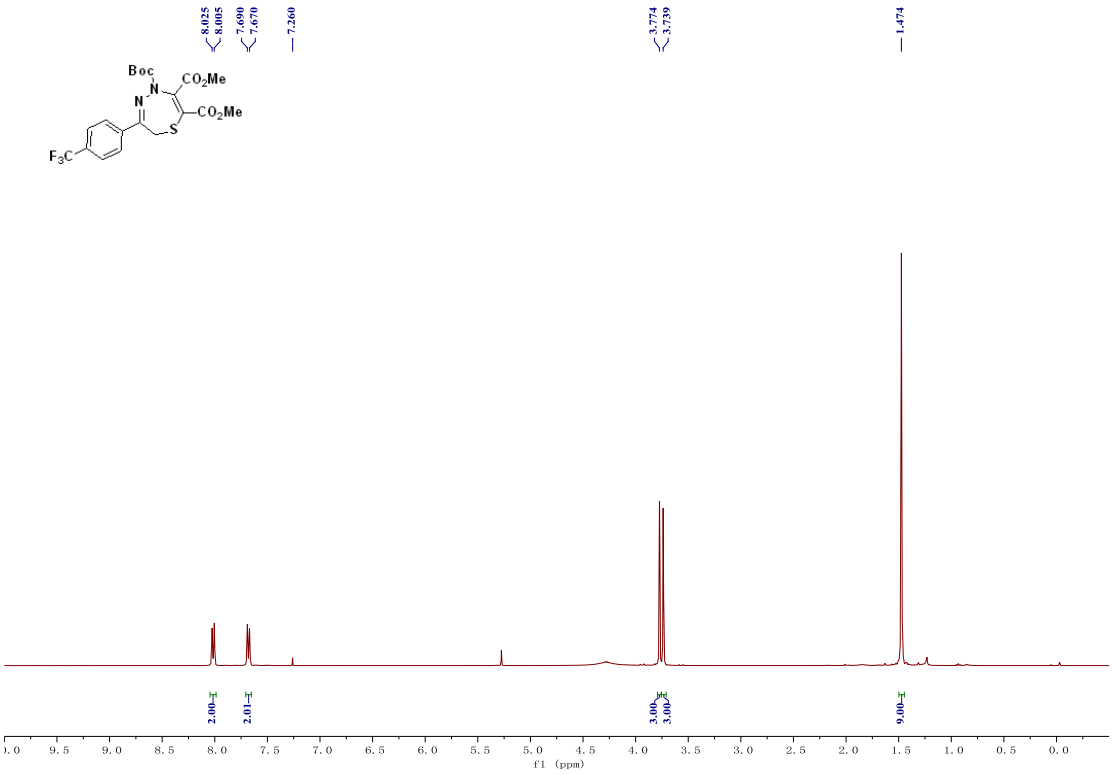


Fig. S31 ^{1}H NMR of compound **3o** (400 MHz, $CDCl_3$).

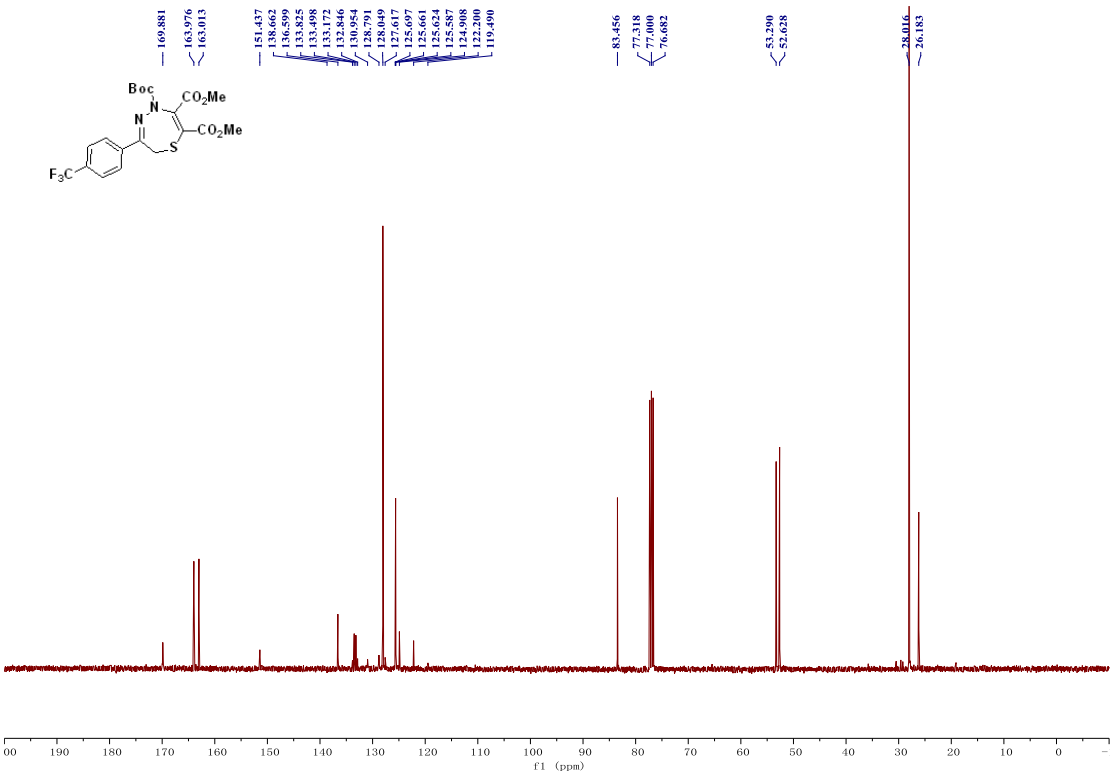


Fig. S32 ^{13}C NMR of compound **3o** (100 MHz, $CDCl_3$).

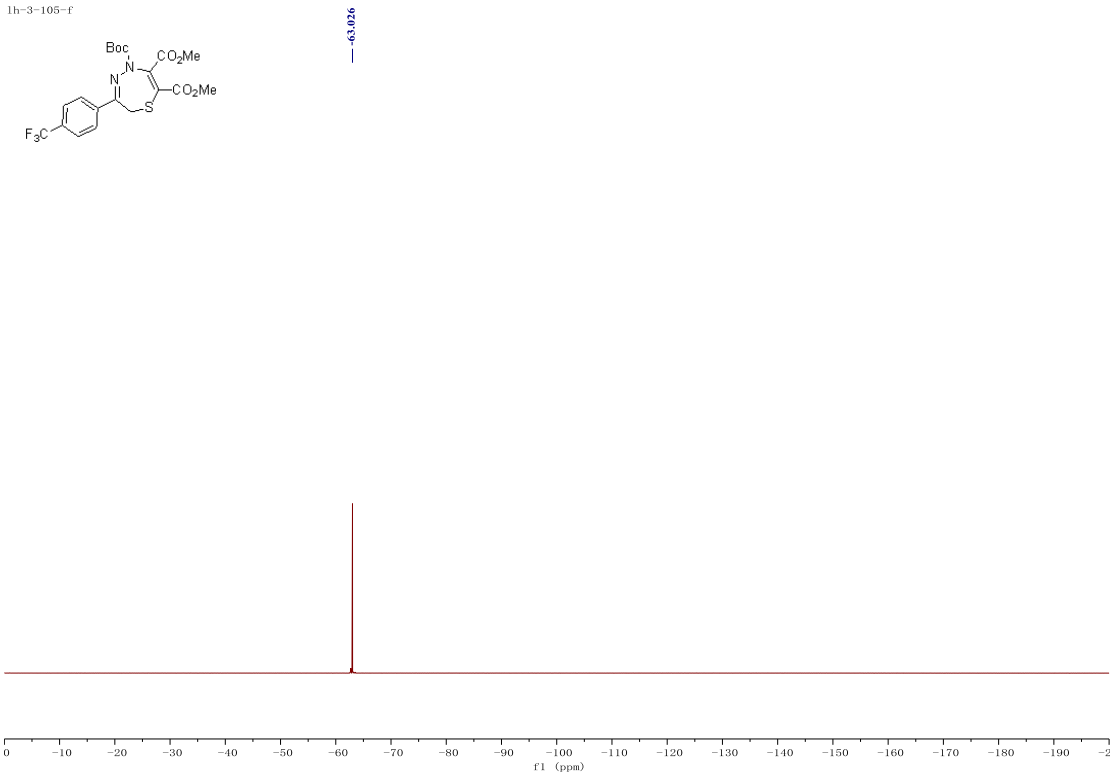


Fig. S33 ^{10}F NMR of compound **3o** (376 MHz, $CDCl_3$).

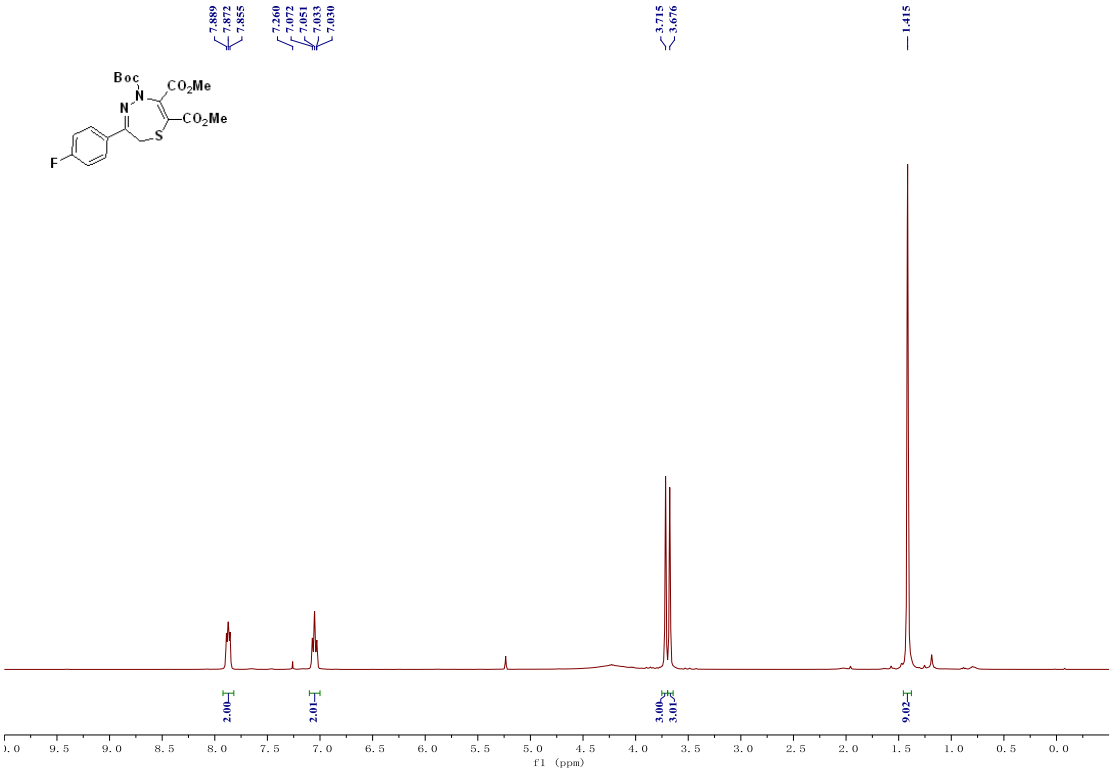


Fig. S34 ^{1}H NMR of compound **3p** (400 MHz, $CDCl_3$).

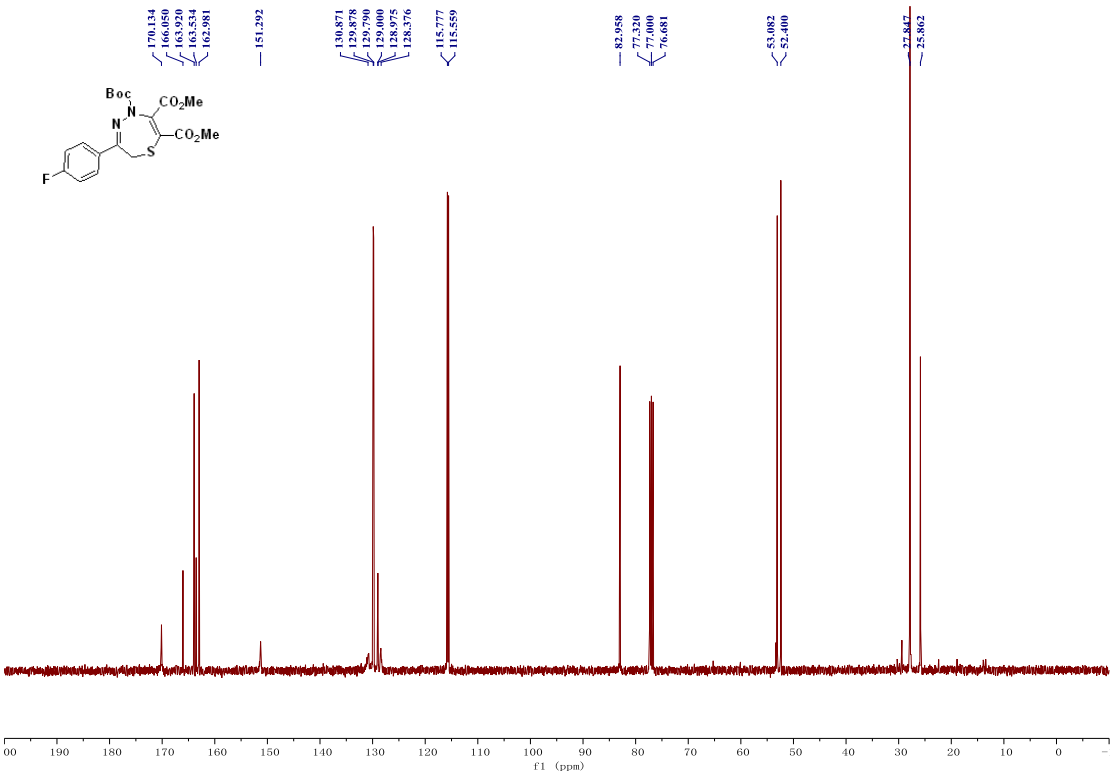


Fig. S35 ^{13}C NMR of compound **3p** (100 MHz, $CDCl_3$).

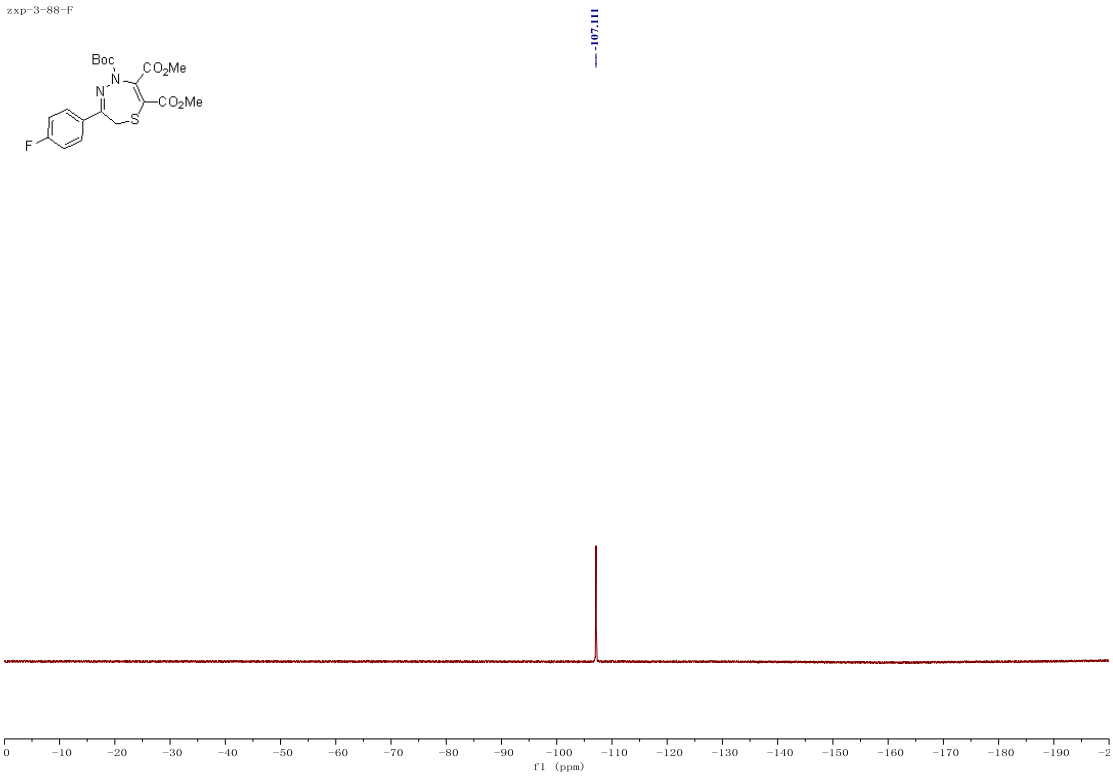


Fig. S36 ^{19}F NMR of compound **3p** (376 MHz, $CDCl_3$).

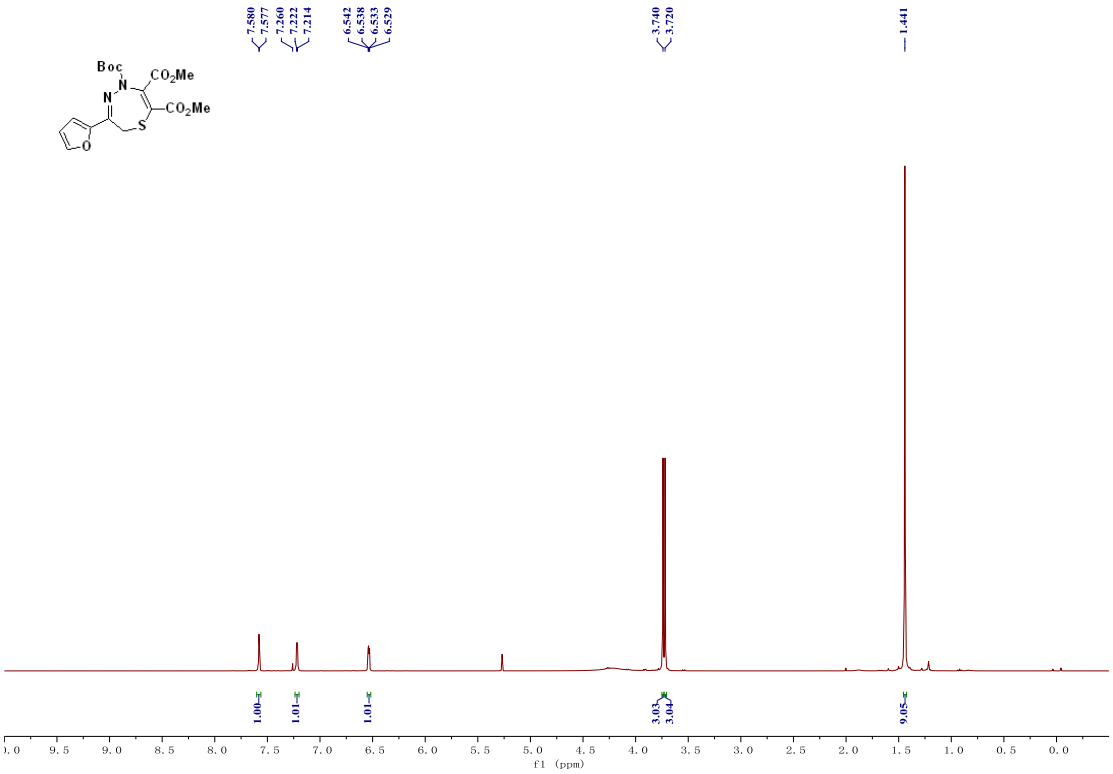


Fig. S37 ^{1}H NMR of compound **3q** (400 MHz, $CDCl_3$).

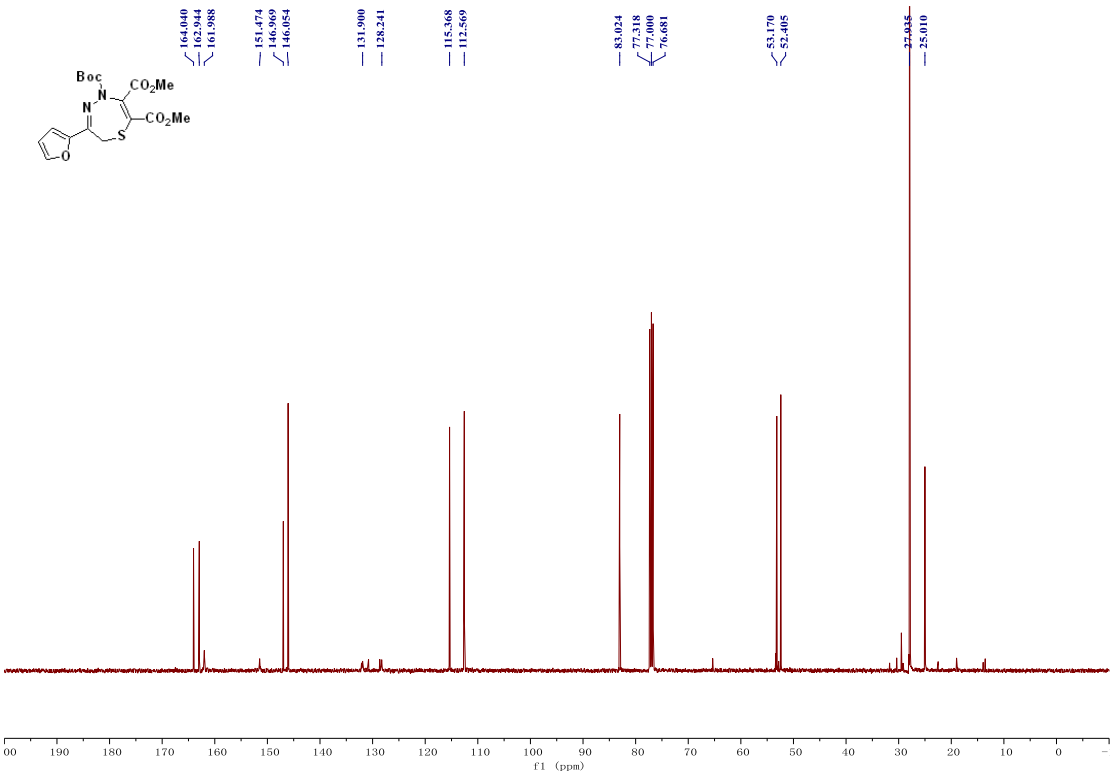


Fig. S38 ^{13}C NMR of compound **3q** (100 MHz, $CDCl_3$).

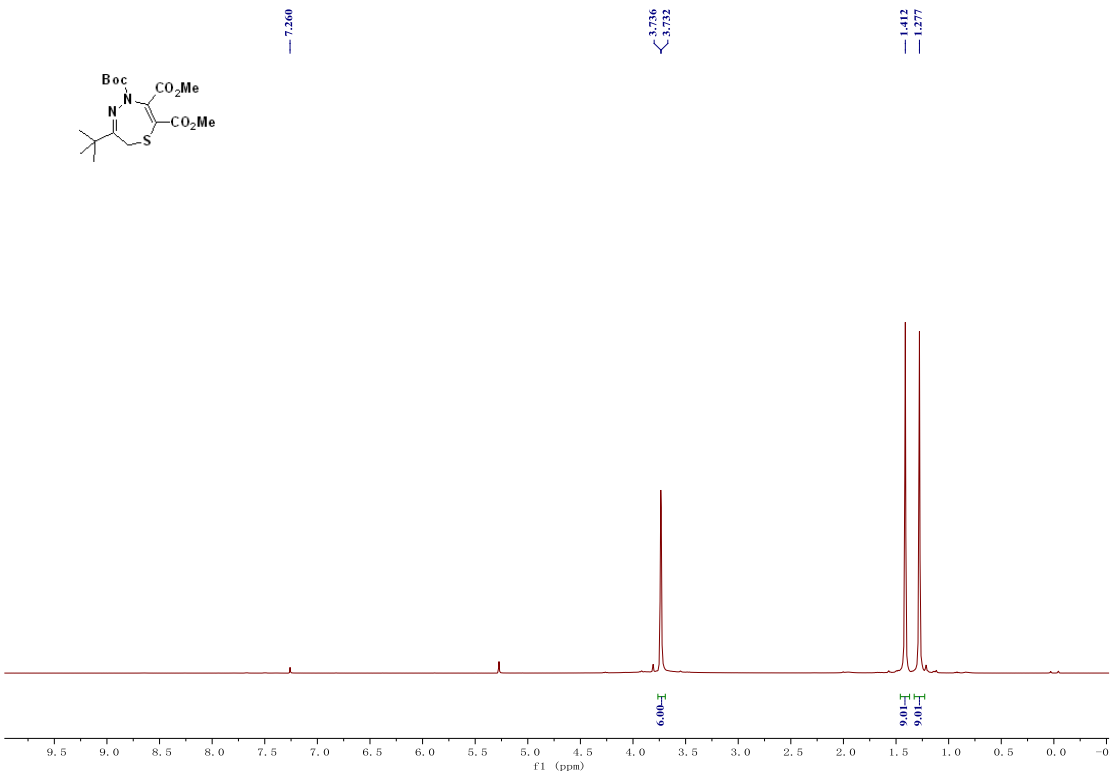


Fig. S39 ^{1}H NMR of compound **3r** (400 MHz, $CDCl_3$).

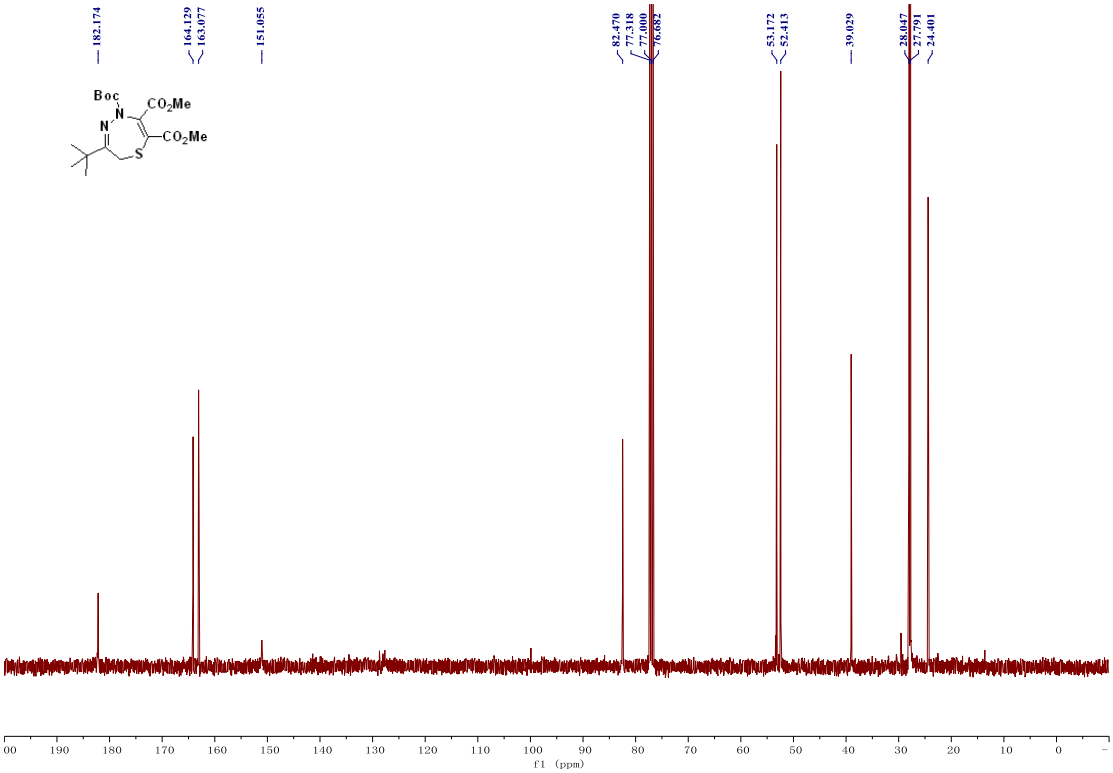


Fig. S40 ^{13}C NMR of compound **3r** (100 MHz, $CDCl_3$).

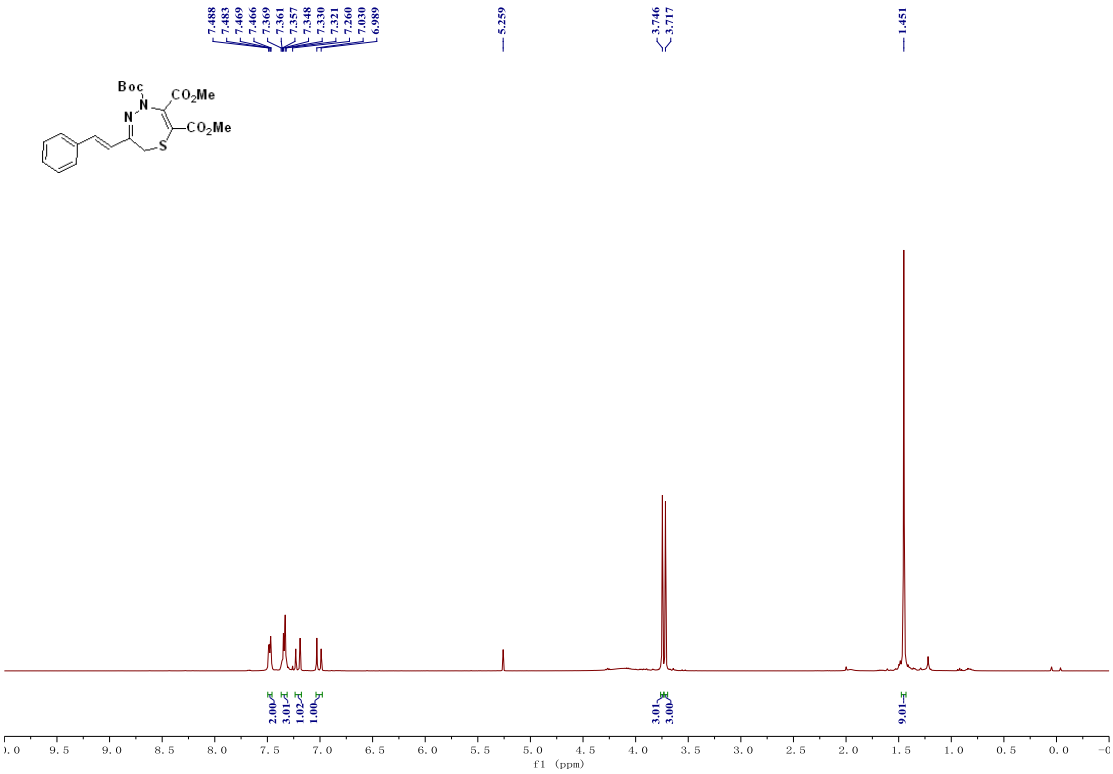


Fig. S41 ^{1}H NMR of compound **3s** (400 MHz, $CDCl_3$).

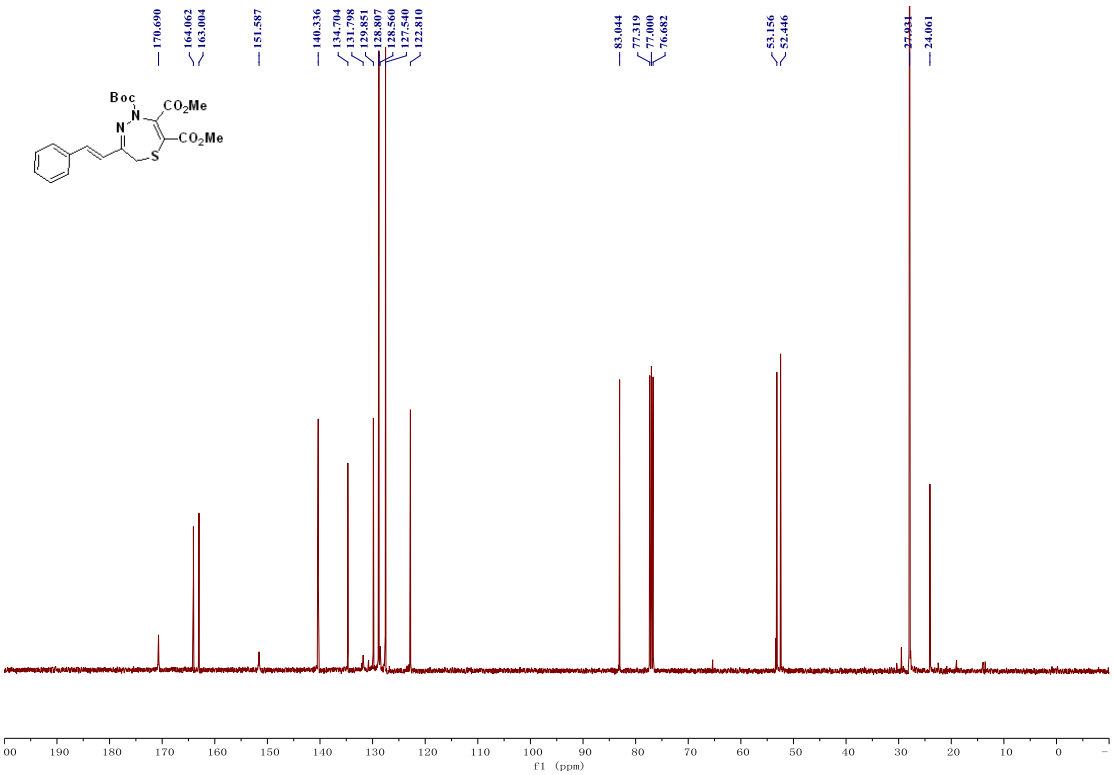


Fig. S42 ^{13}C NMR of compound **3s** (100 MHz, $CDCl_3$).

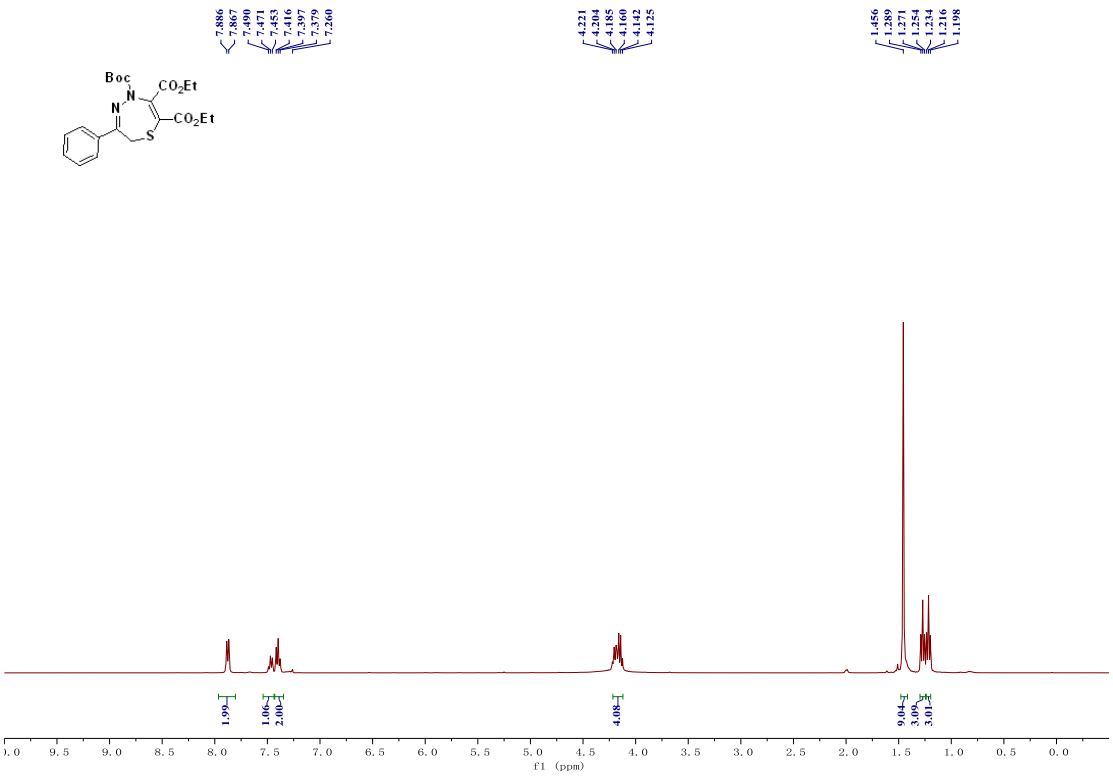


Fig. S43 ^{1}H NMR of compound **3t** (400 MHz, $CDCl_3$).

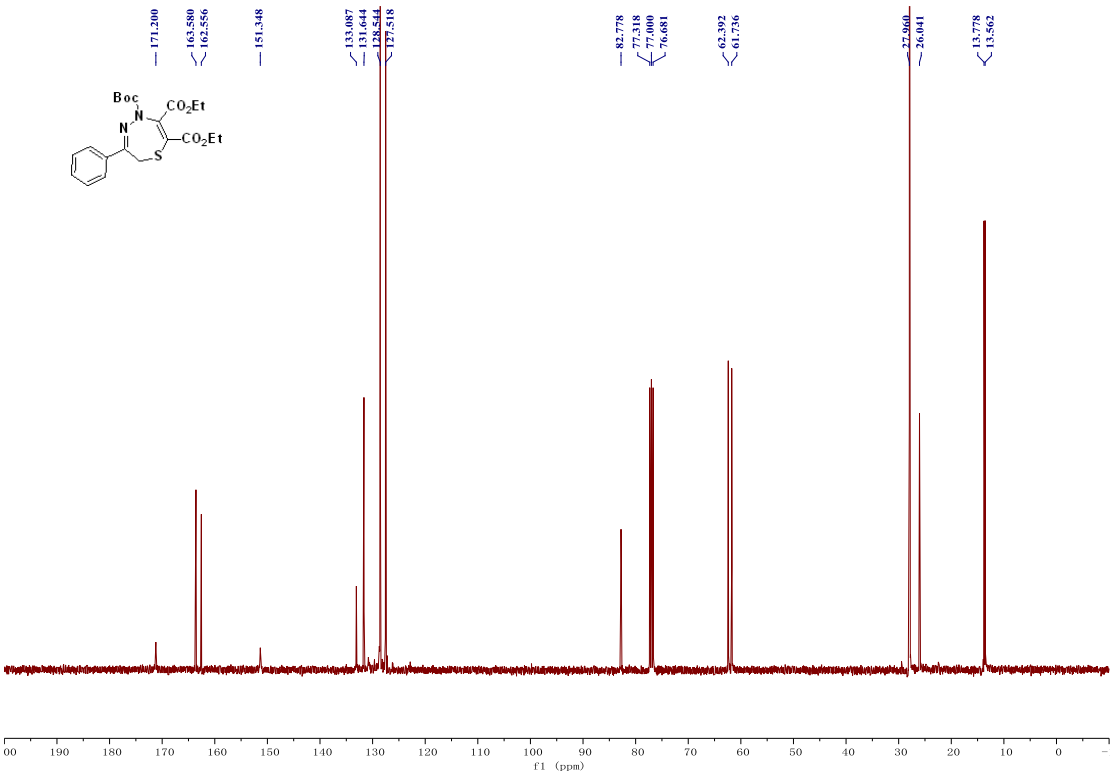


Fig. S44 ^{13}C NMR of compound **3t** (100 MHz, $CDCl_3$).

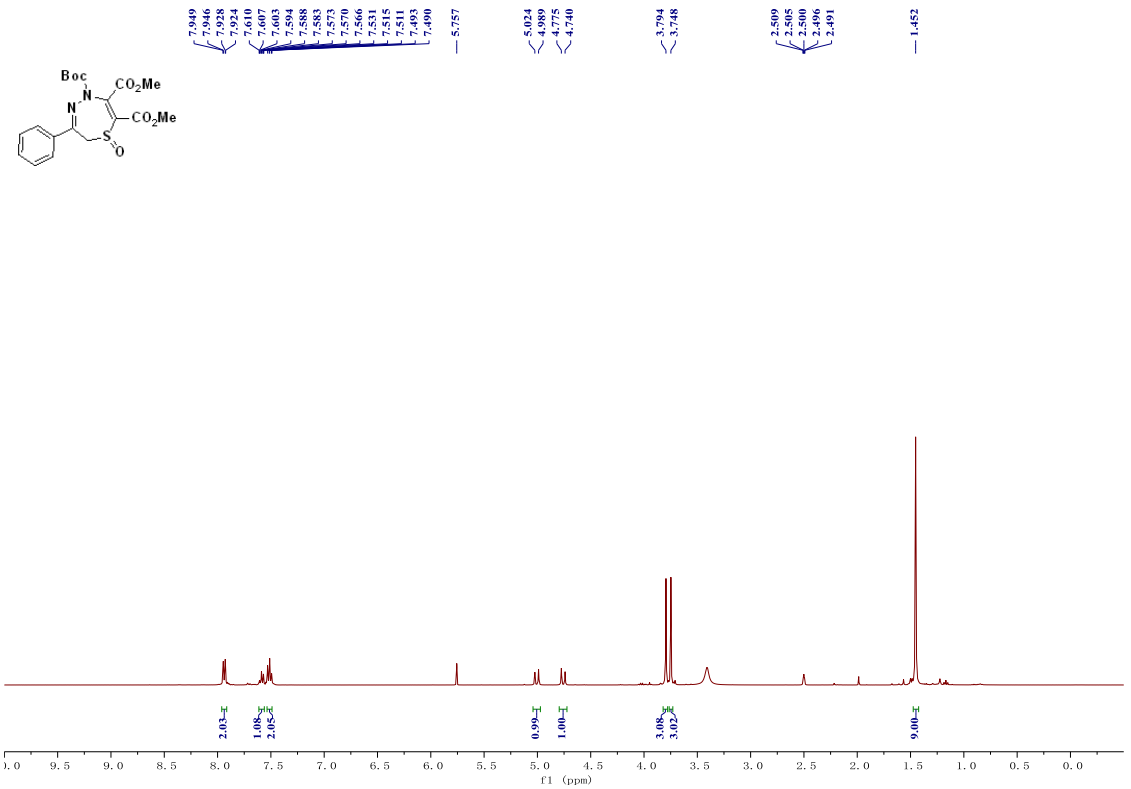


Fig. S45 ^{1}H NMR of compound **4a** (400 MHz, $(CD_3)_2SO$).

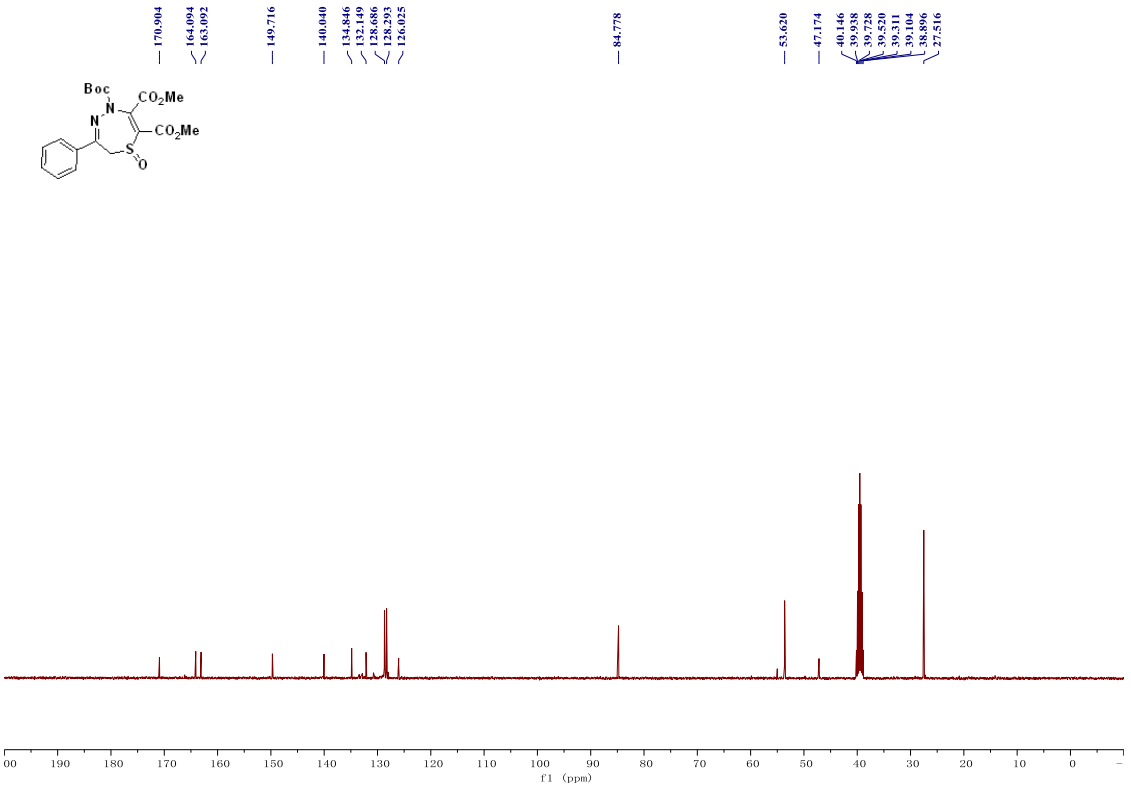


Fig. S46 ^{13}C NMR of compound **4a** (100 MHz, $(CD_3)_2SO$).

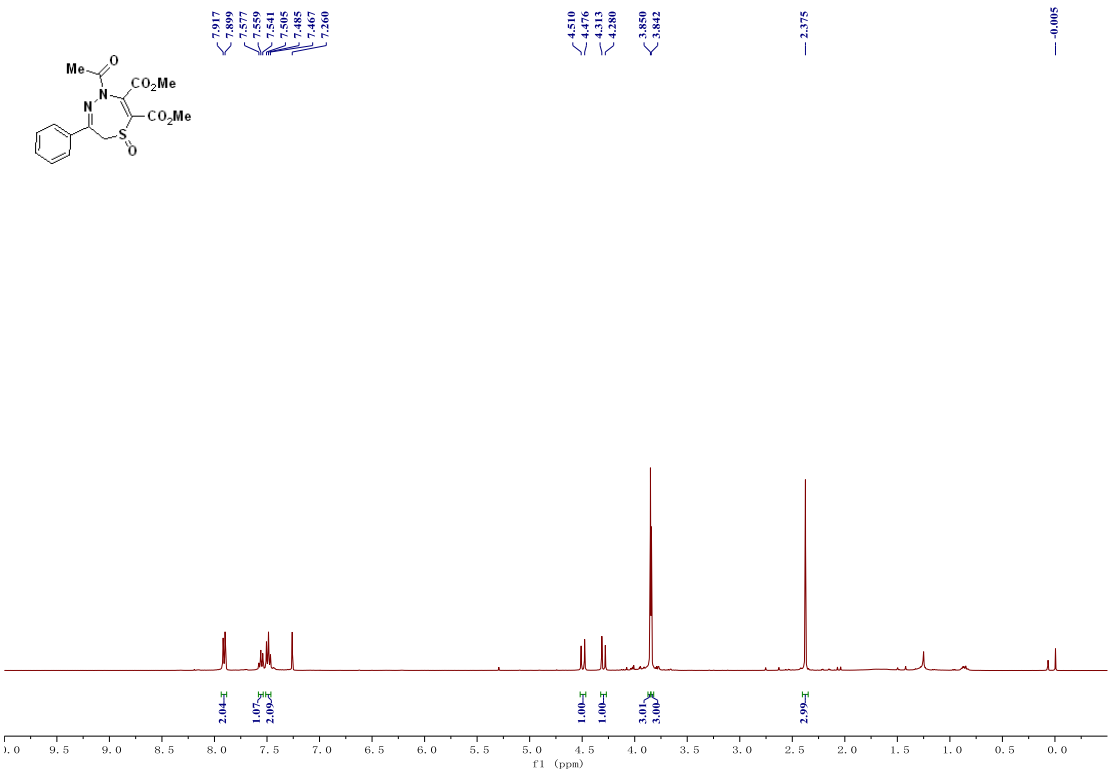


Fig. S47 ^{1}H NMR of compound **4b** (400 MHz, $CDCl_3$).

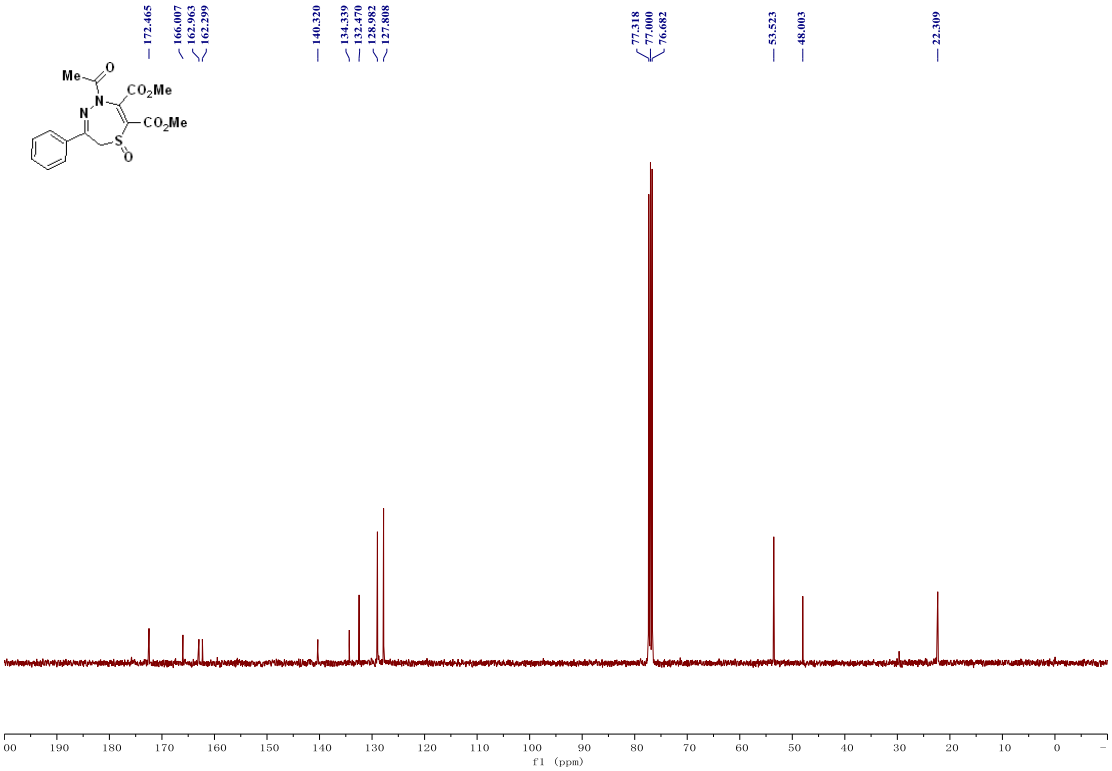


Fig. S48 ^{13}C NMR of compound **4b** (100 MHz, $CDCl_3$).

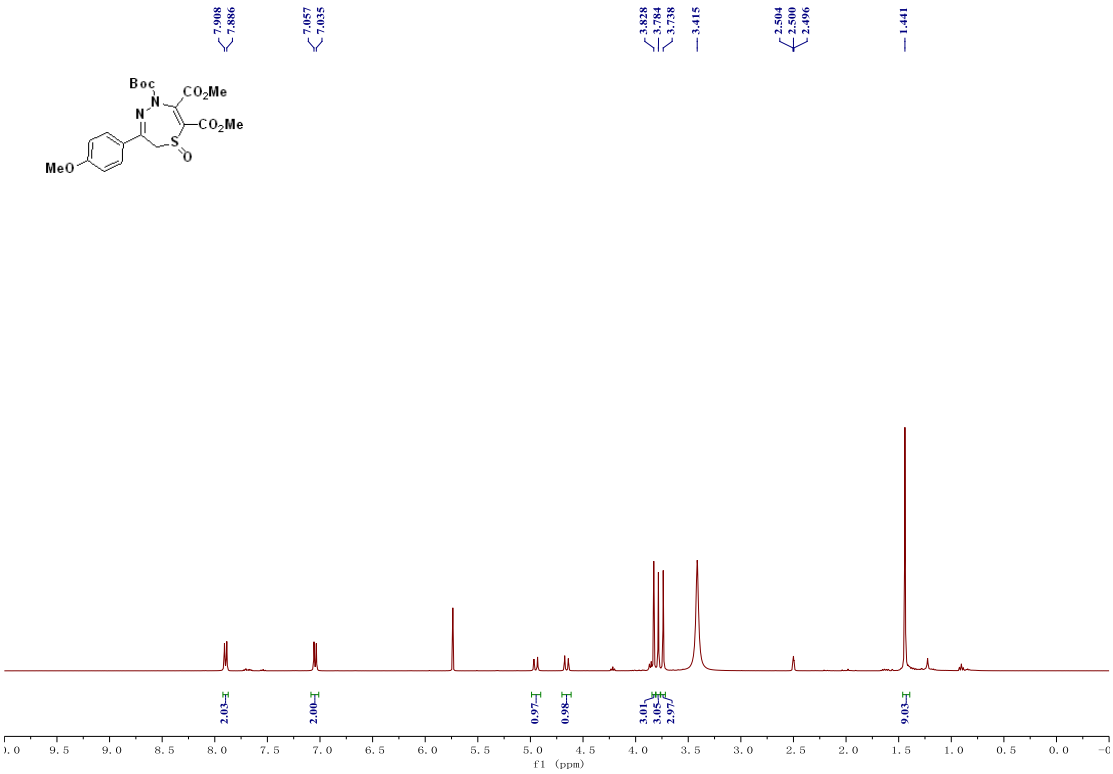


Fig. S49 ^{1}H NMR of compound **4c** (400 MHz, $(CD_3)_2SO$).

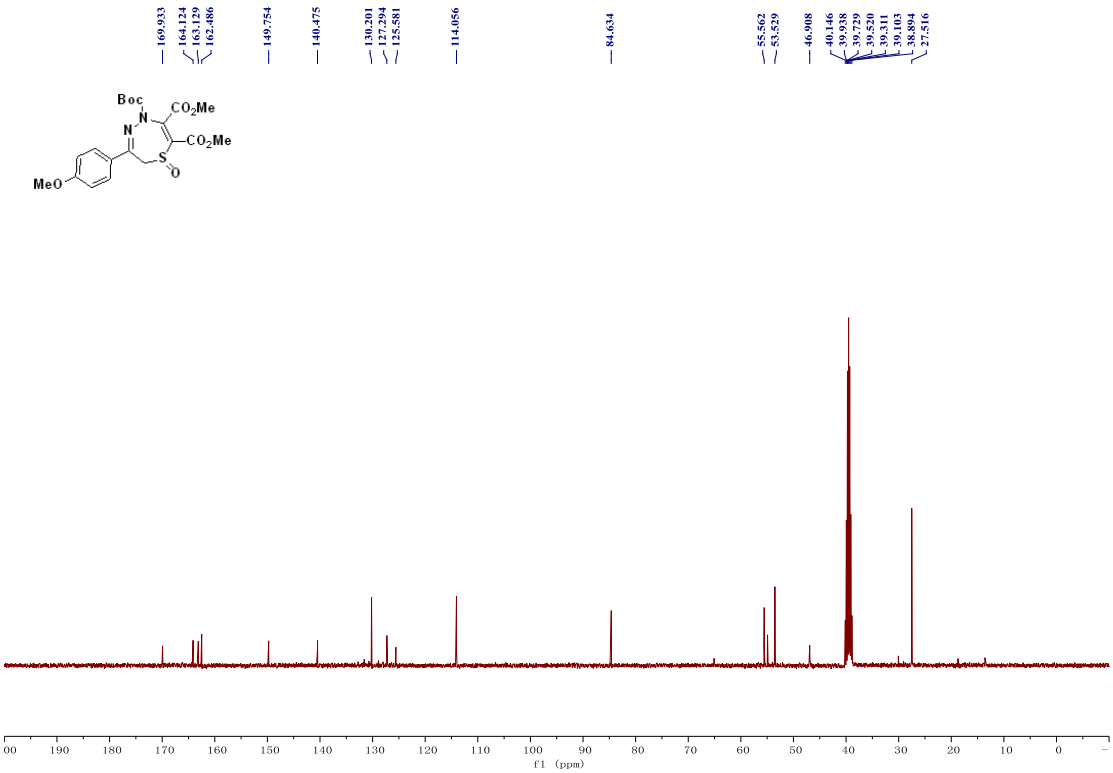


Fig. S50 ^{13}C NMR of compound **4c** (100 MHz, $(CD_3)_2SO$).

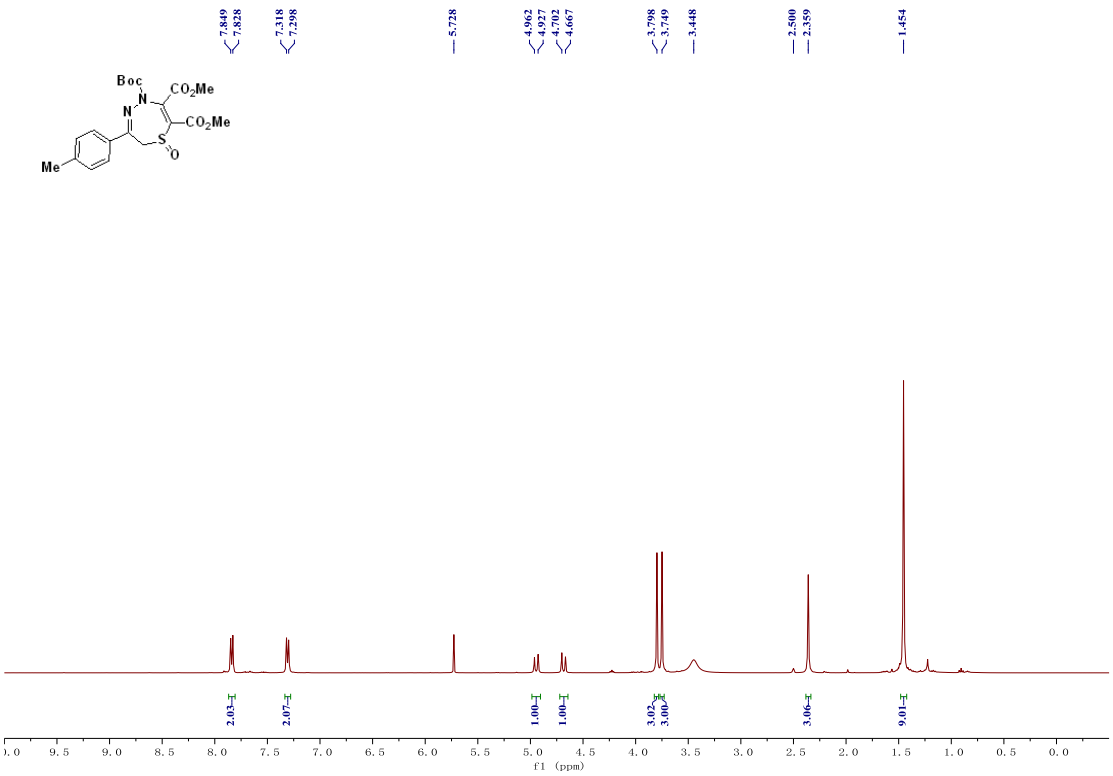


Fig. S51 ^{1}H NMR of compound **4d** (400 MHz, $(CD_3)_2SO$).

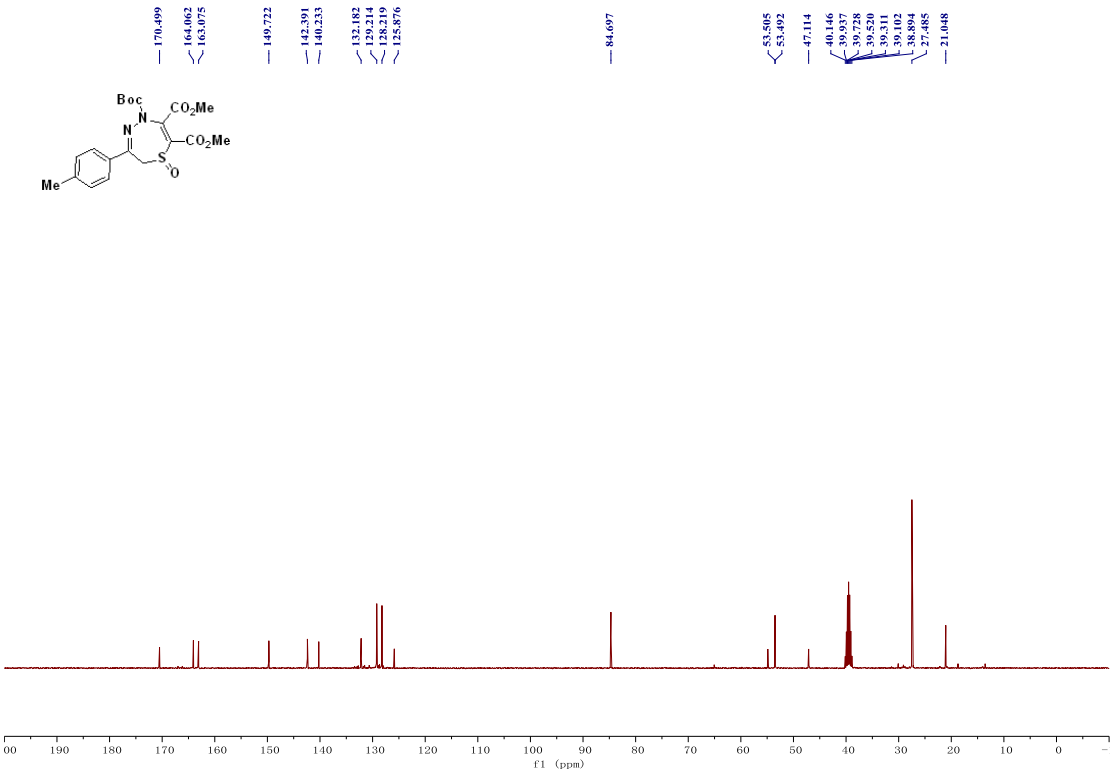


Fig. S52 ^{13}C NMR of compound **4d** (100 MHz, $(CD_3)_2SO$).

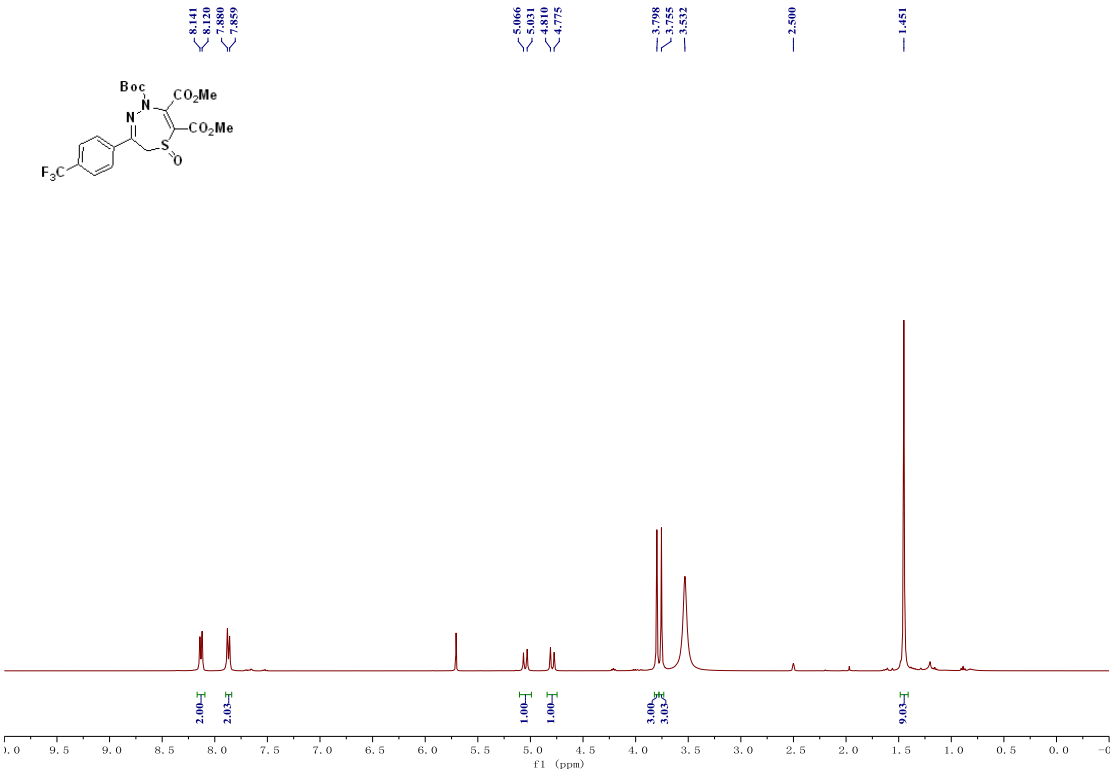


Fig. S53 ^{1}H NMR of compound **4e** (400 MHz, $(CD_3)_2SO$).

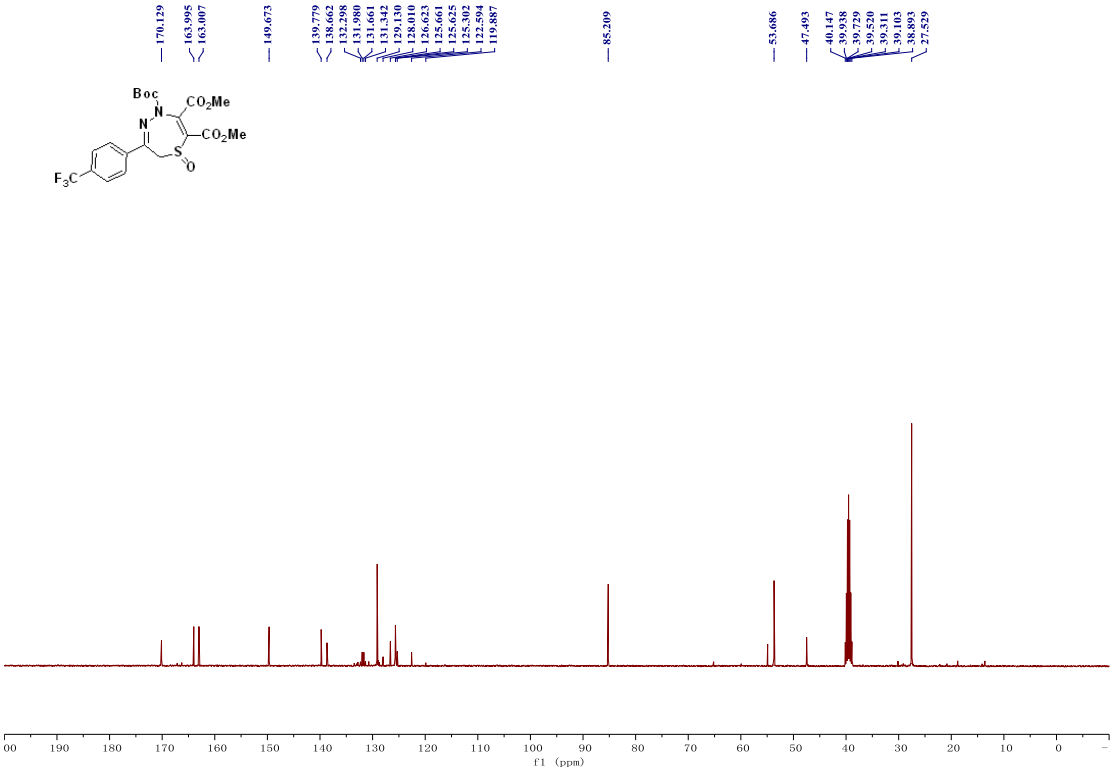


Fig. S54 ^{13}C NMR of compound **4e** (100 MHz, $(CD_3)_2SO$).

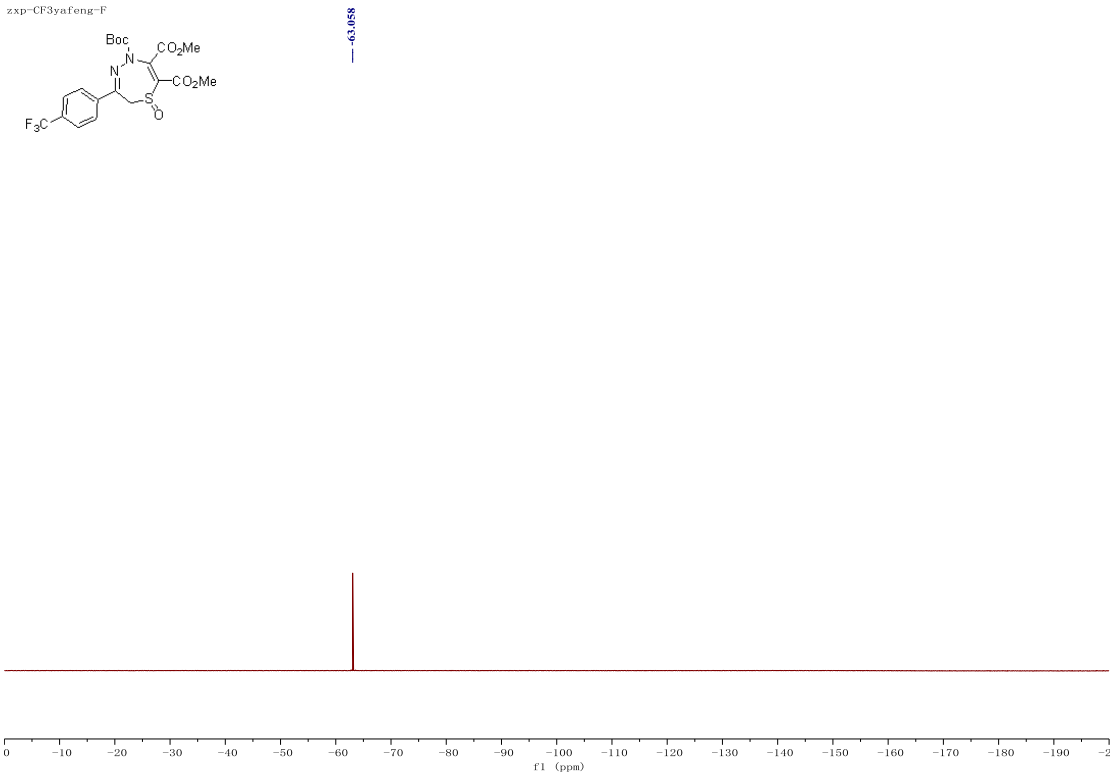


Fig. S55 ^{19}F NMR of compound **4e** (376 MHz, $CDCl_3$).

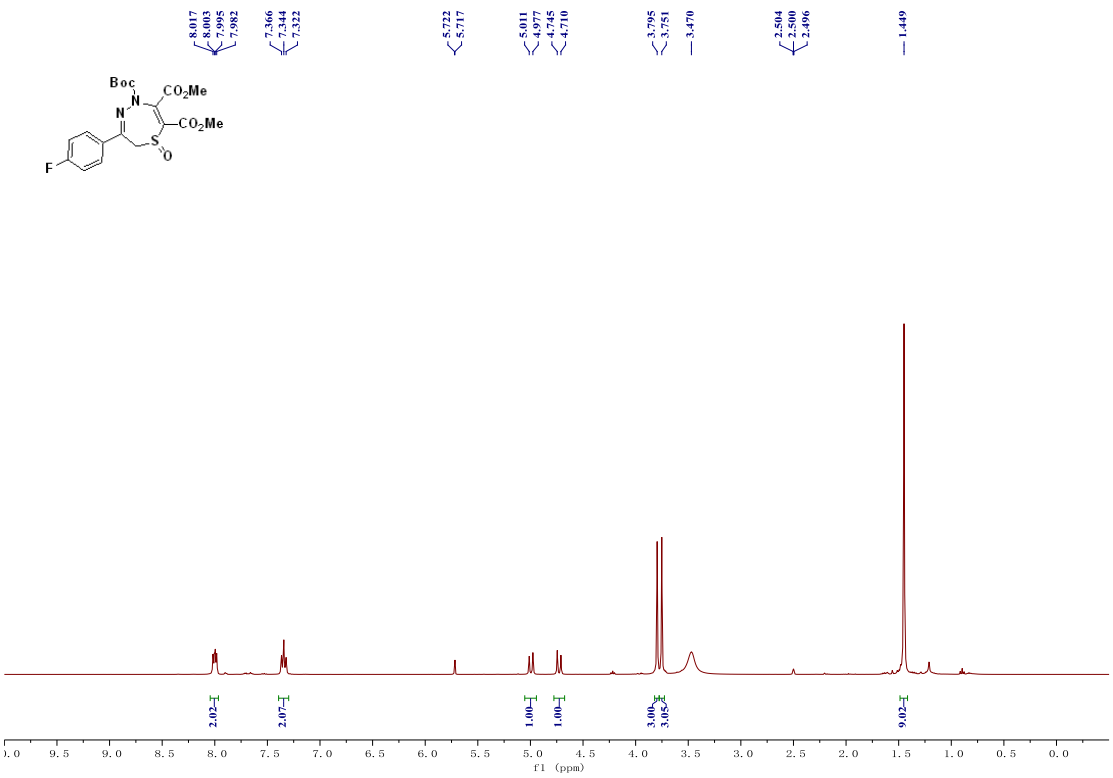


Fig. S56 ^{1}H NMR of compound **4f** (400 MHz, $(CD_3)_2SO$).

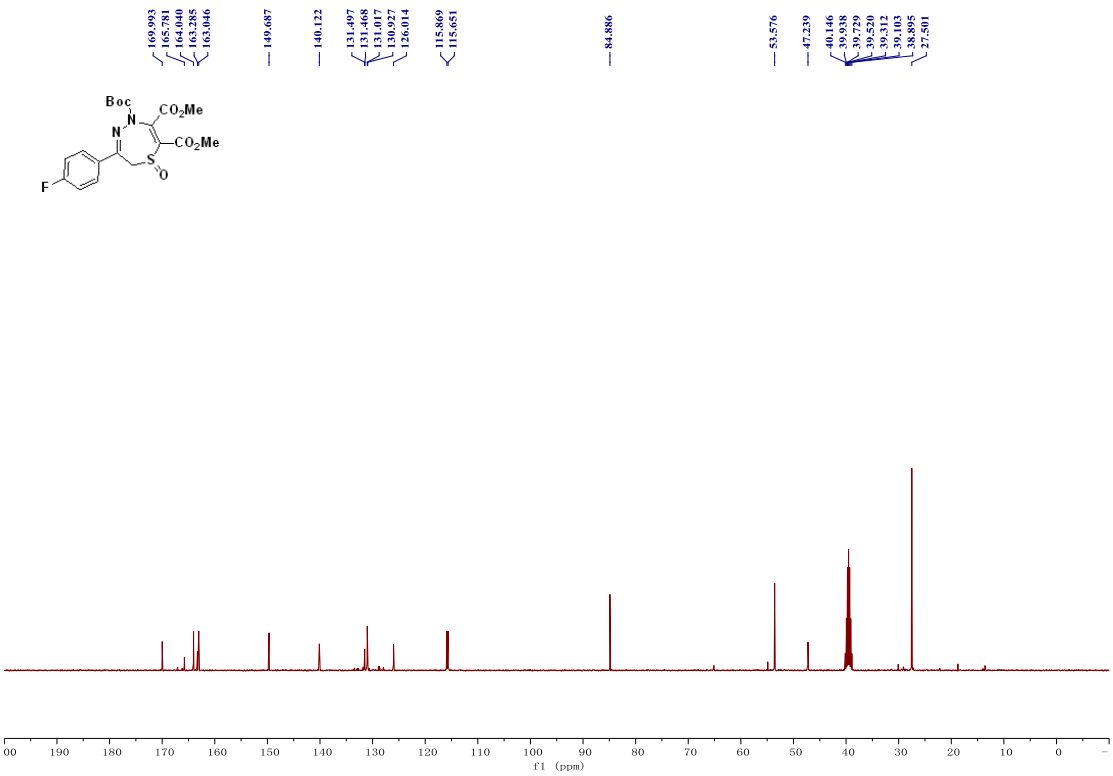


Fig. S57 ^{13}C NMR of compound **4f** (100 MHz, $(CD_3)_2SO$).

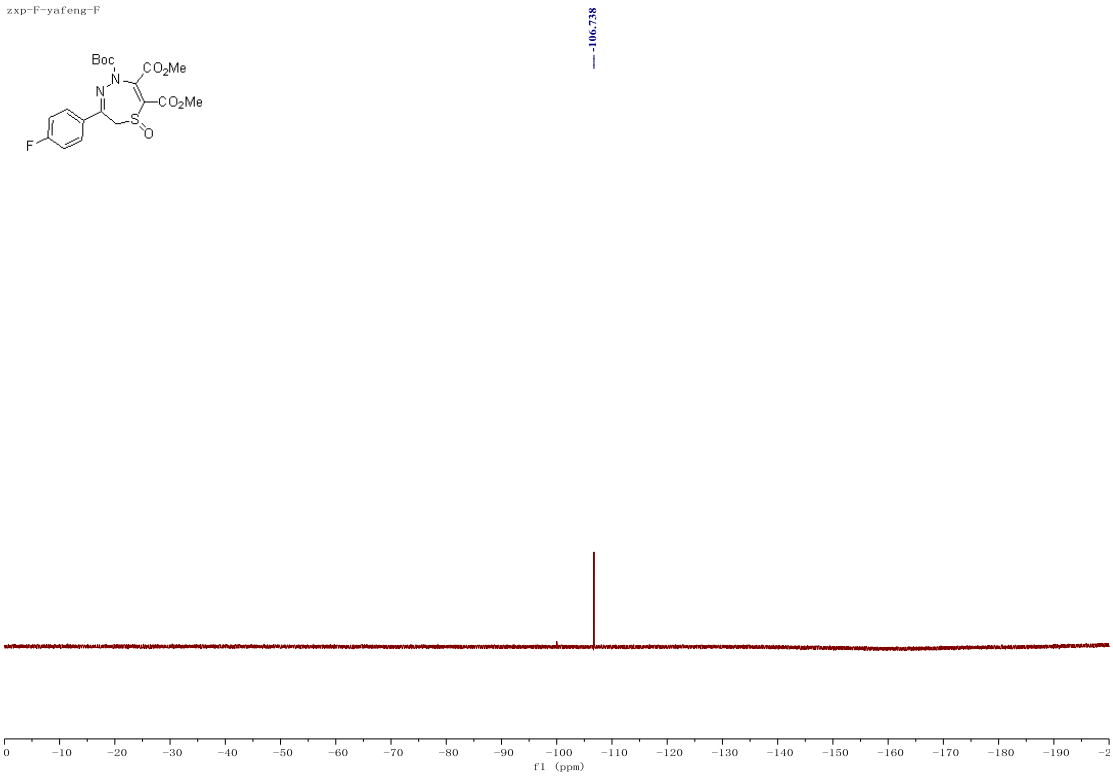


Fig. S58 ^{19}F NMR of compound **4f** (376 MHz, $CDCl_3$).

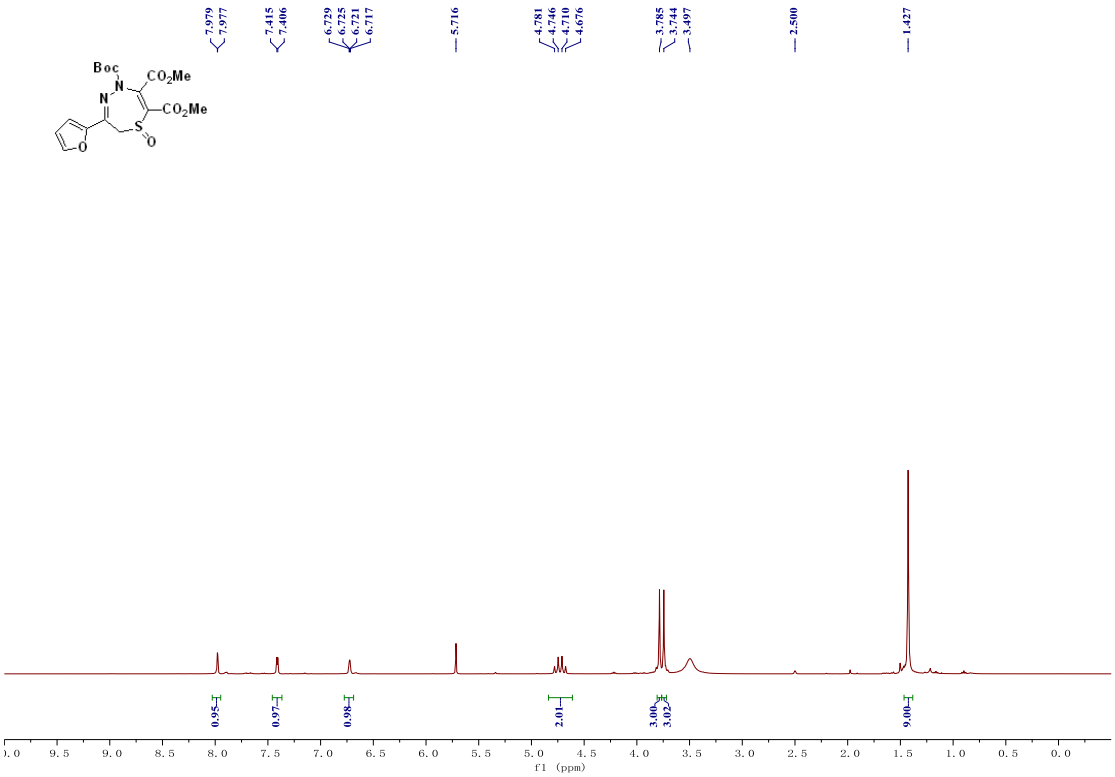


Fig. S59 ^{1}H NMR of compound **4g** (400 MHz, $(CD_3)_2SO$).

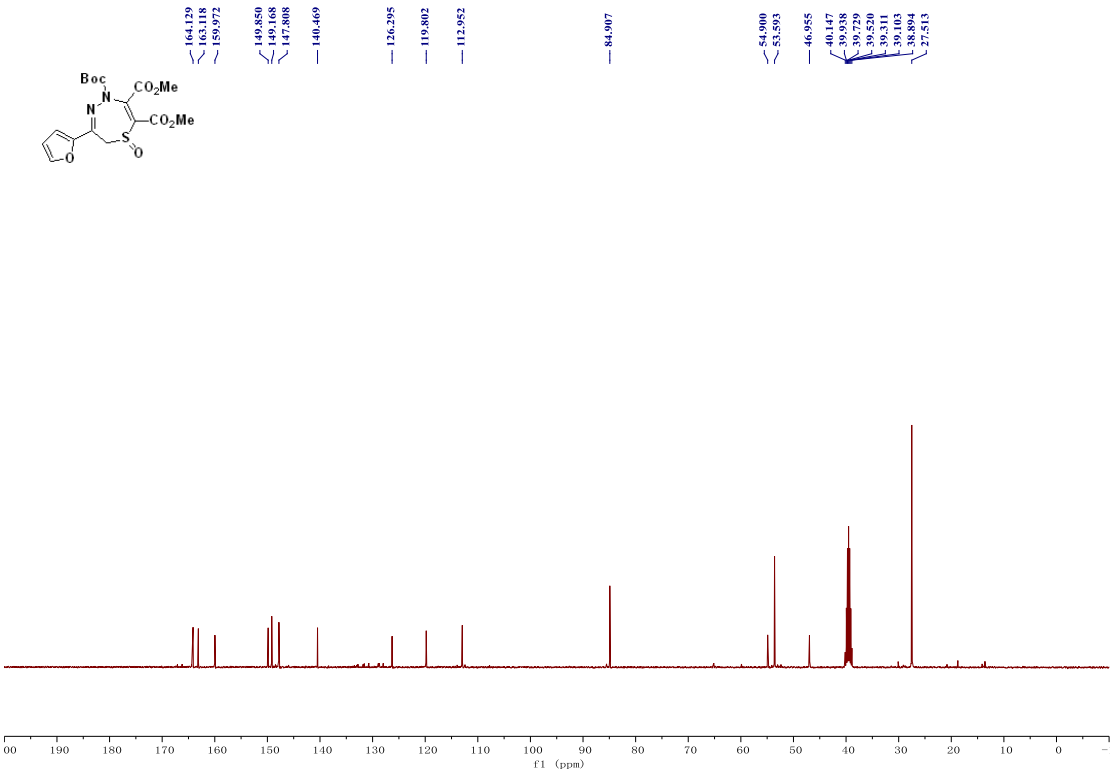


Fig. S60 ^{13}C NMR of compound **4g** (100 MHz, $(CD_3)_2SO$).

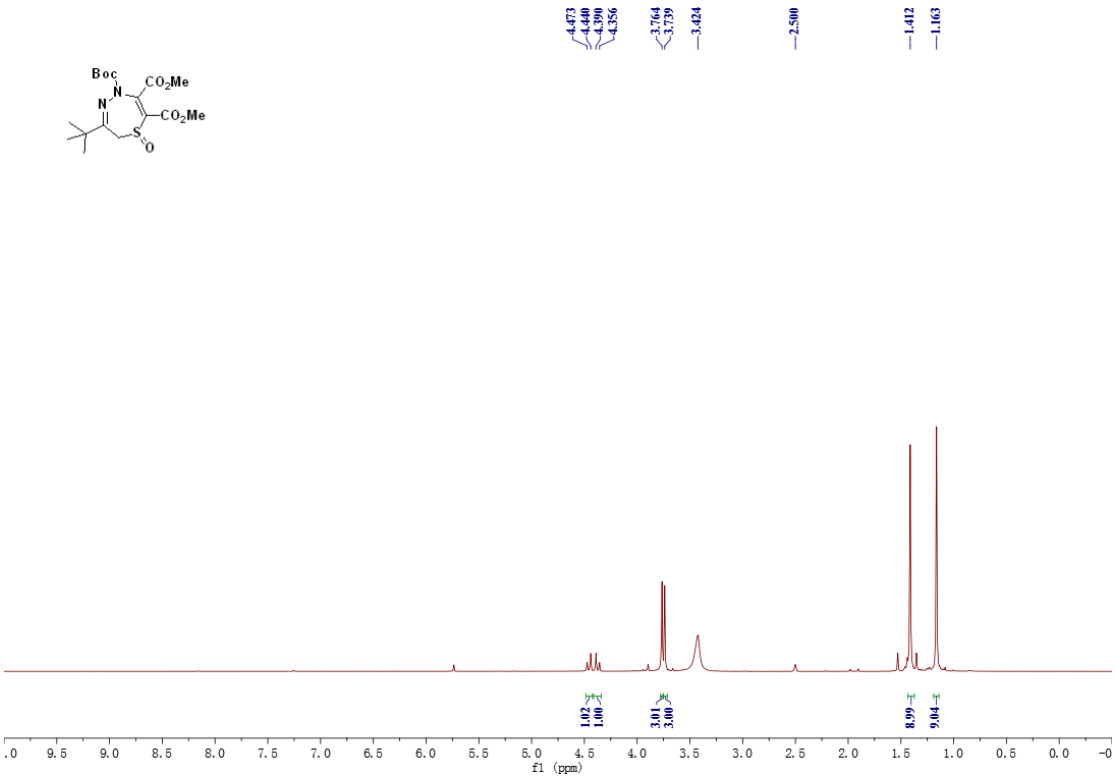


Fig. S61 ^{1}H NMR of compound **4h** (400 MHz, $(CD_3)_2SO$).

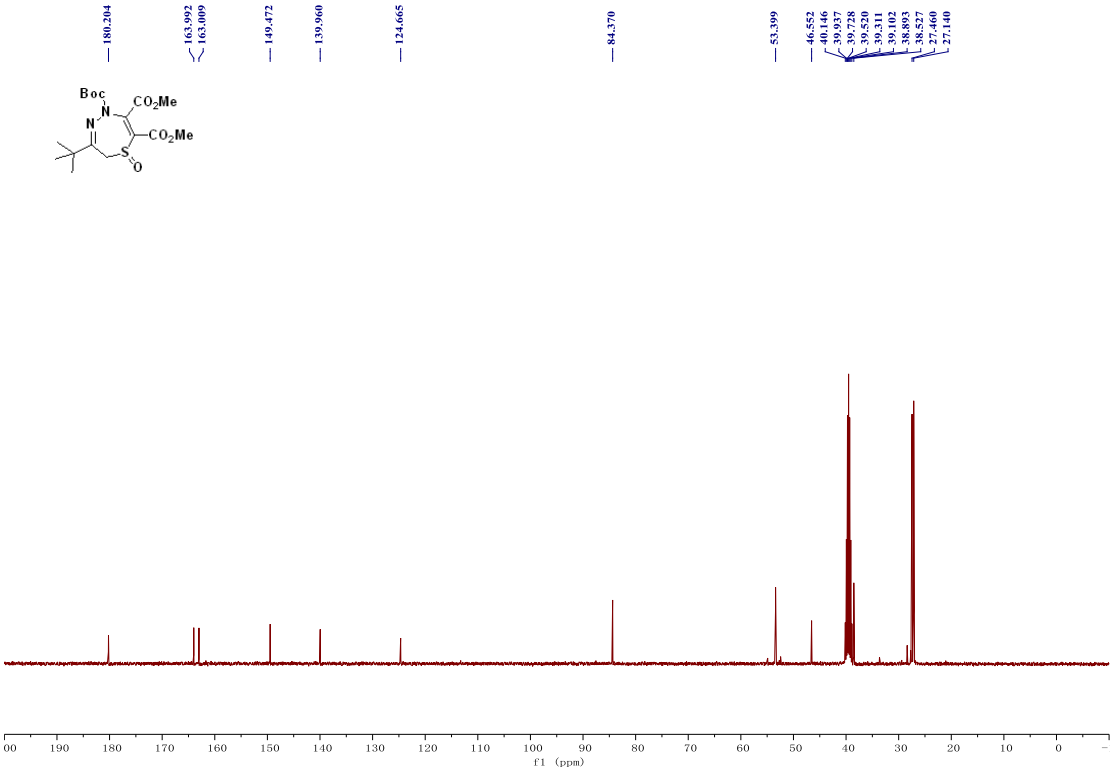


Fig. S62 ^{13}C NMR of compound **4h** (100 MHz, $(CD_3)_2SO$).

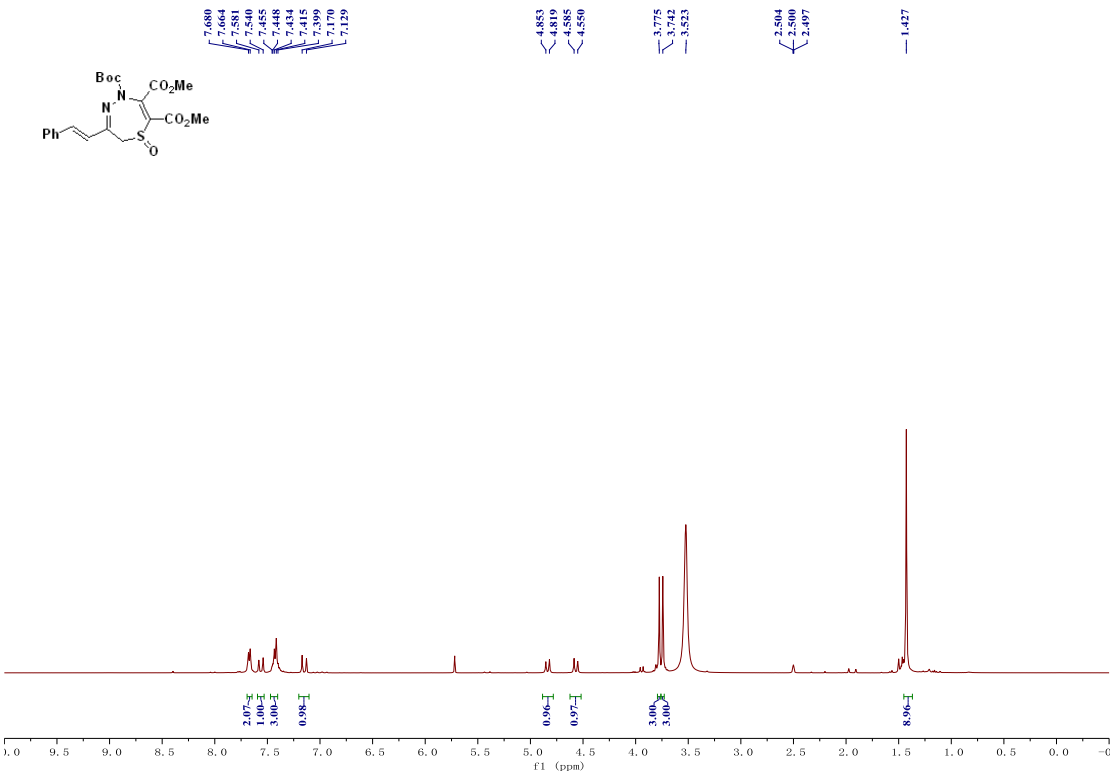


Fig. S63 ^{1}H NMR of compound **4i** (400 MHz, $(CD_3)_2SO$).

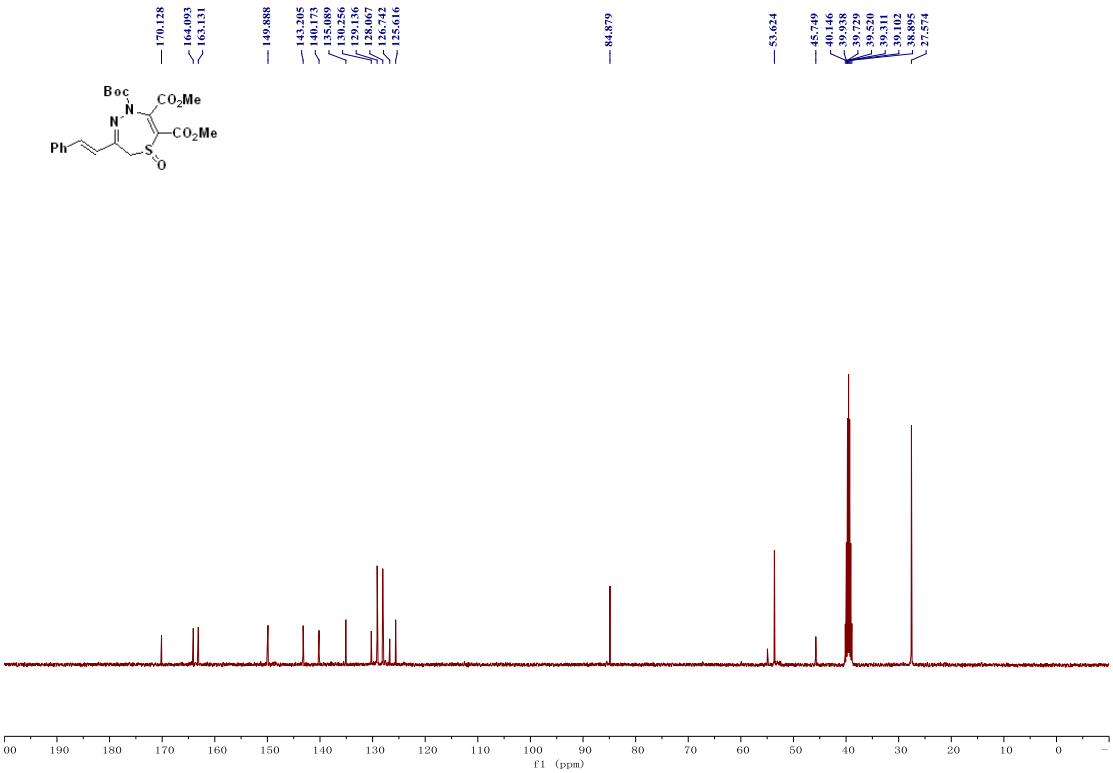


Fig. S64 ^{13}C NMR of compound **4i** (100 MHz, $(CD_3)_2SO$).

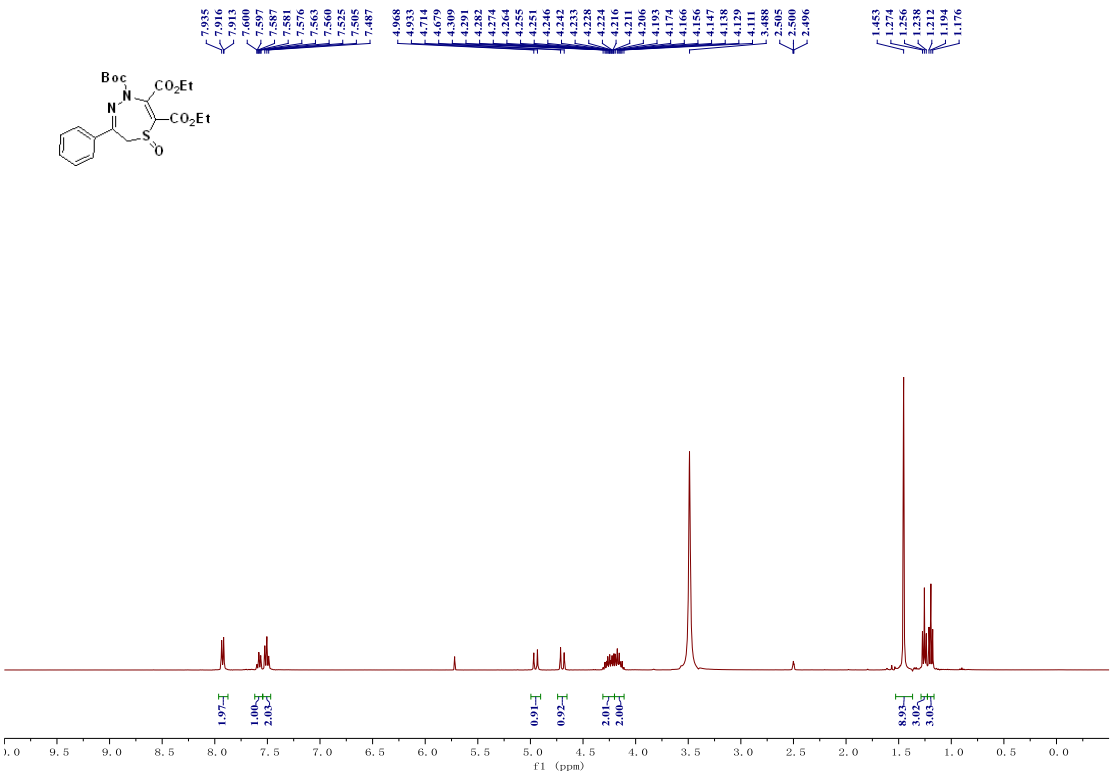


Fig. S65 ^{1}H NMR of compound **4j** (400 MHz, $(CD_3)_2SO$).

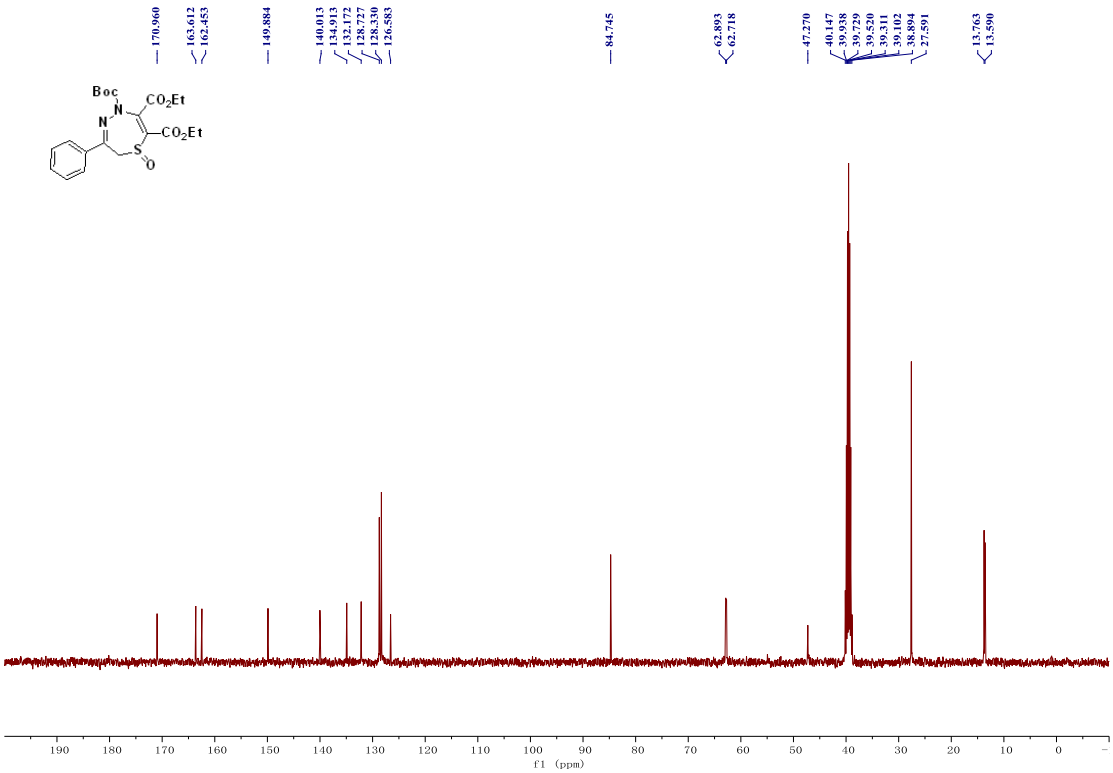


Fig. S66 ^{13}C NMR of compound **4j** (100 MHz, $(CD_3)_2SO$).

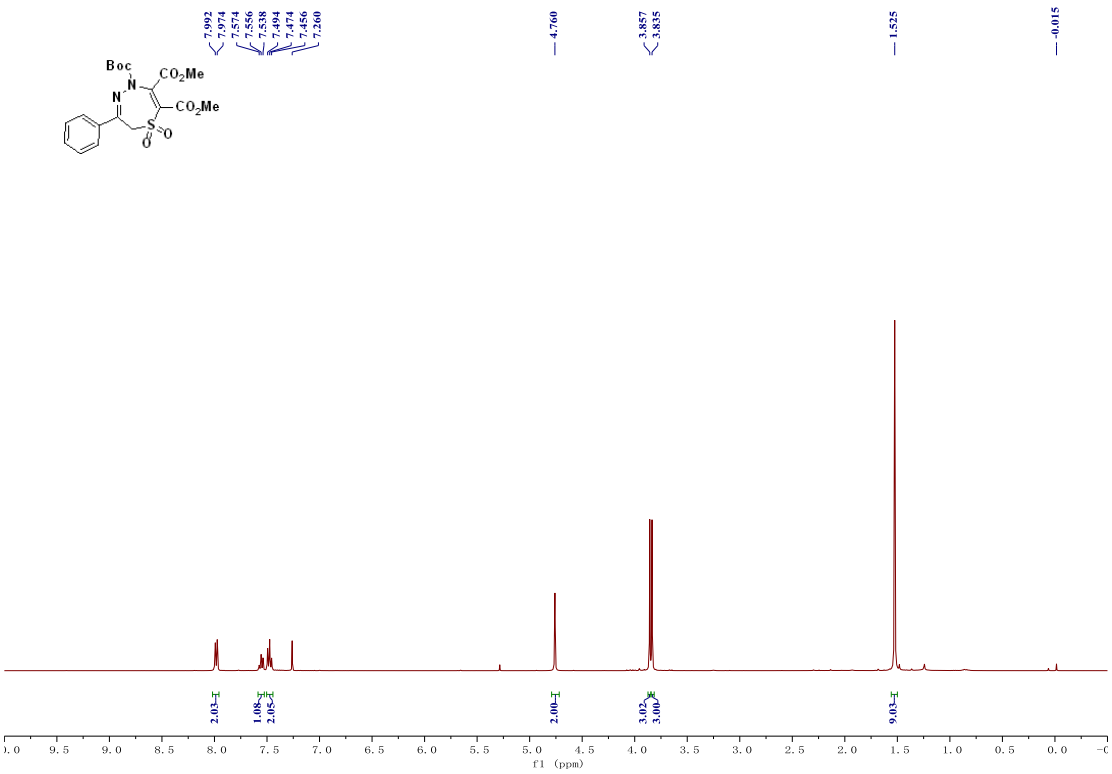


Fig. S67 ^{1}H NMR of compound **4k** (400 MHz, $CDCl_3$).

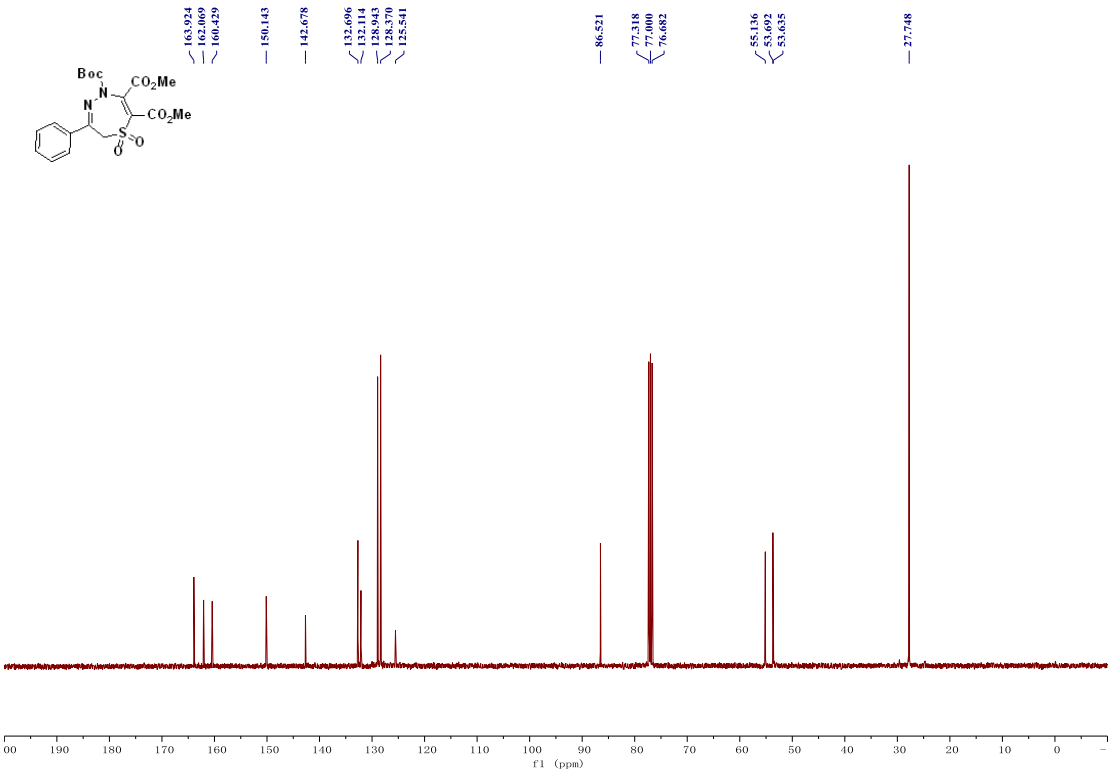


Fig. S68 ^{13}C NMR of compound **4k** (100 MHz, $CDCl_3$).

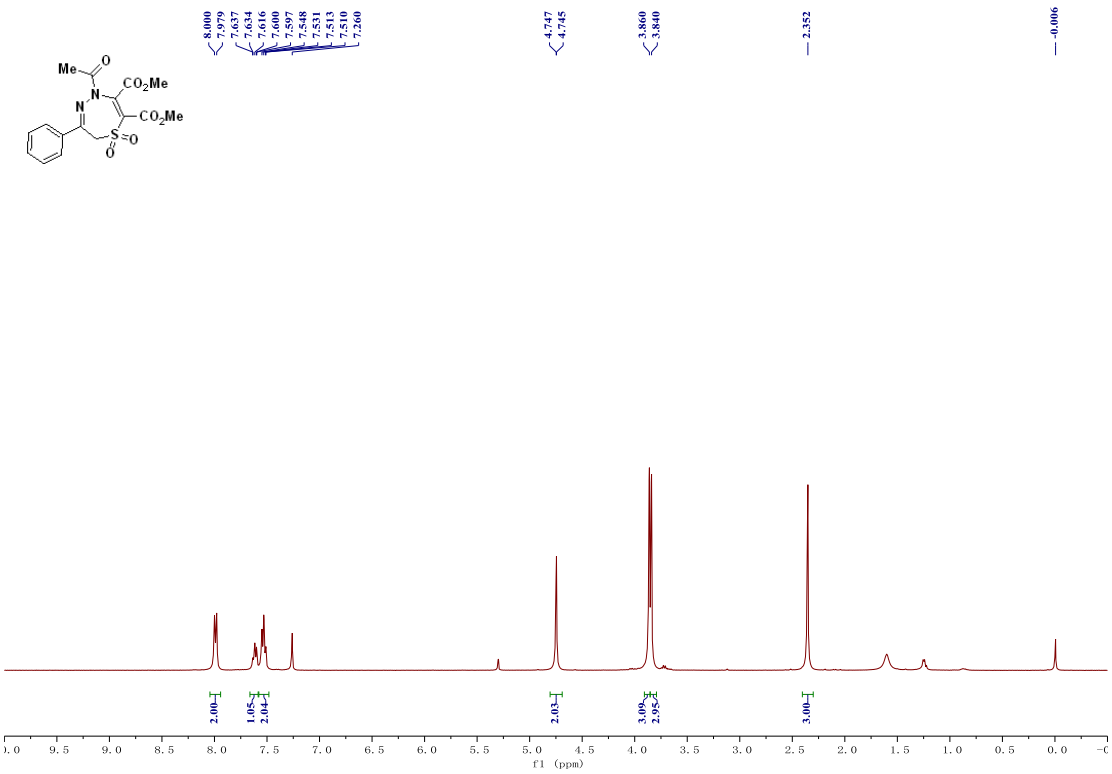


Fig. S69 ^{1}H NMR of compound **4l** (400 MHz, $CDCl_3$).

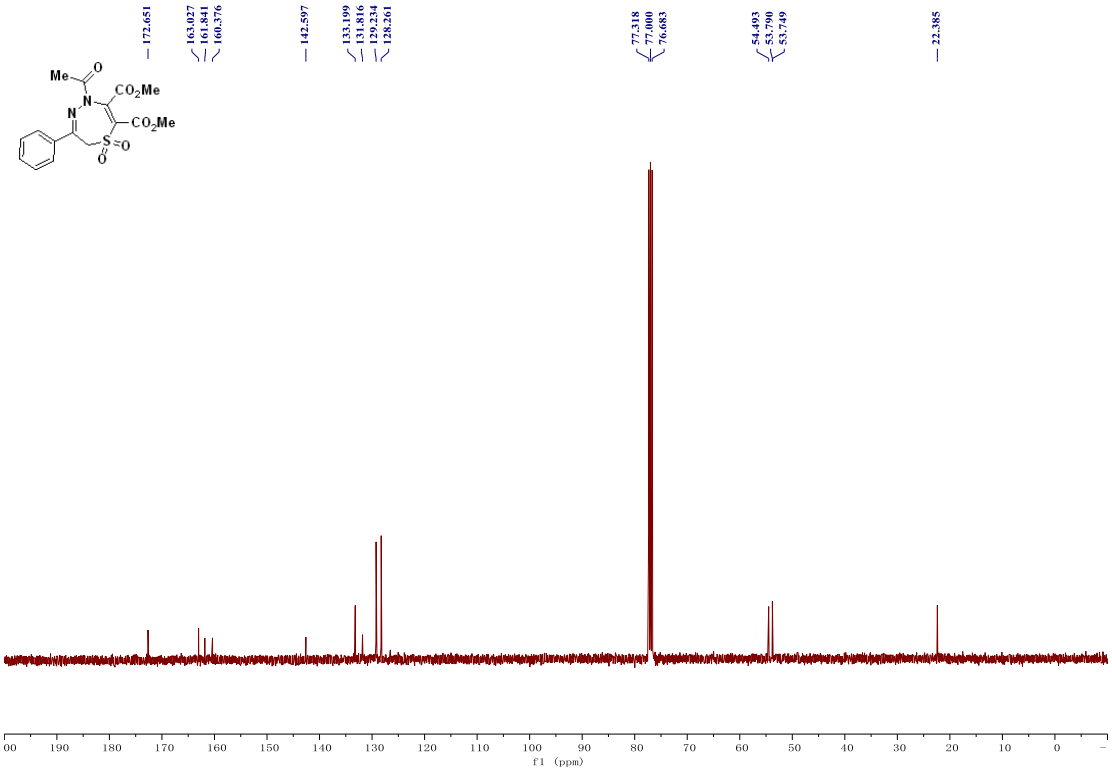


Fig. S70 ^{13}C NMR of compound **4l** (100 MHz, $CDCl_3$).

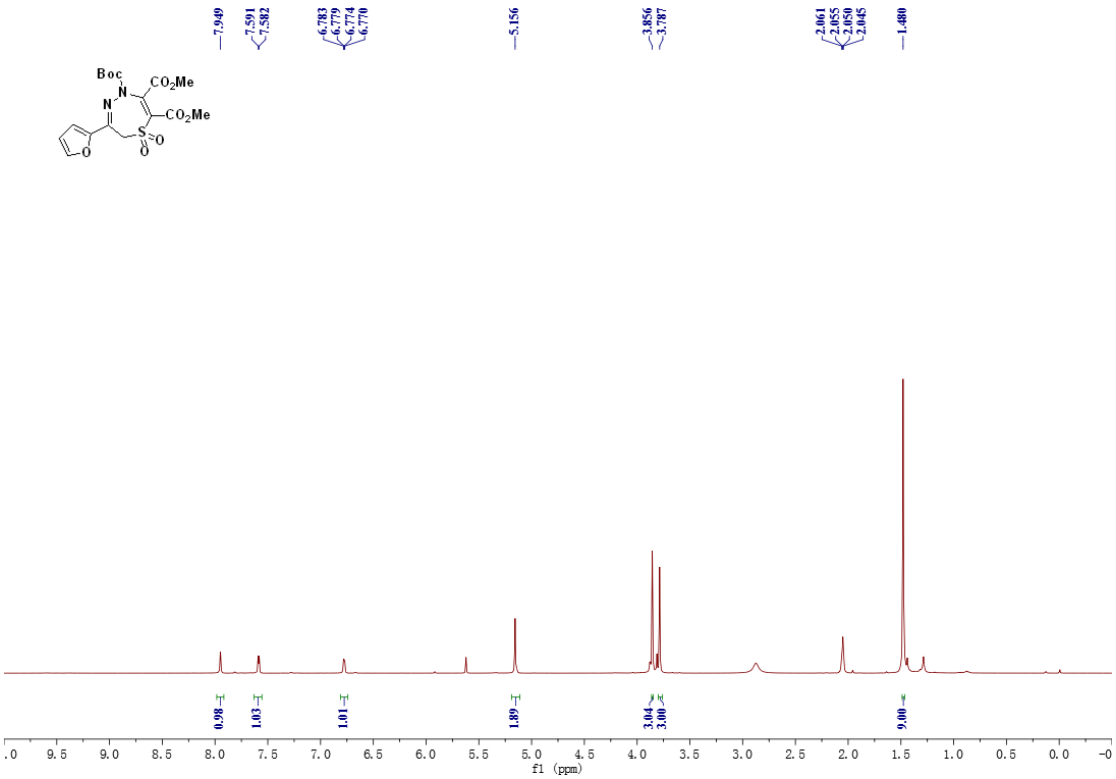


Fig. S71 ^{1}H NMR of compound **4m** (400 MHz, $(CD_3)_2CO$).

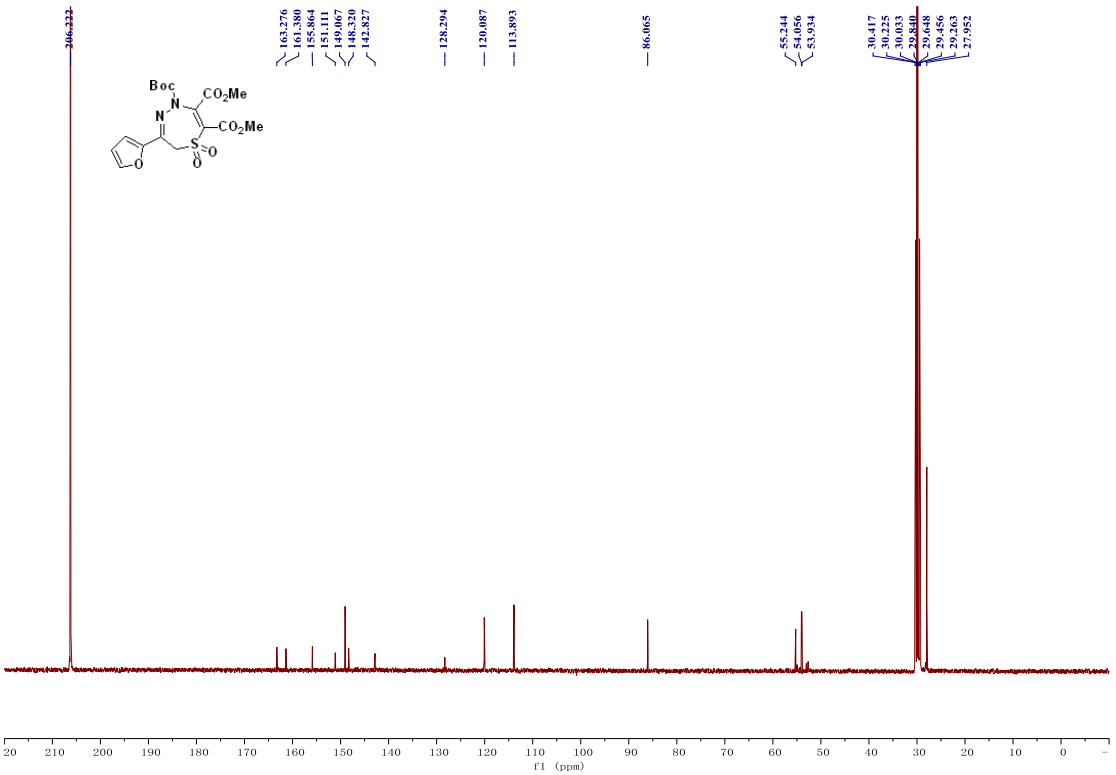


Fig. S72 ^{13}C NMR of compound **4m** (100 MHz, $(CD_3)_2CO$).

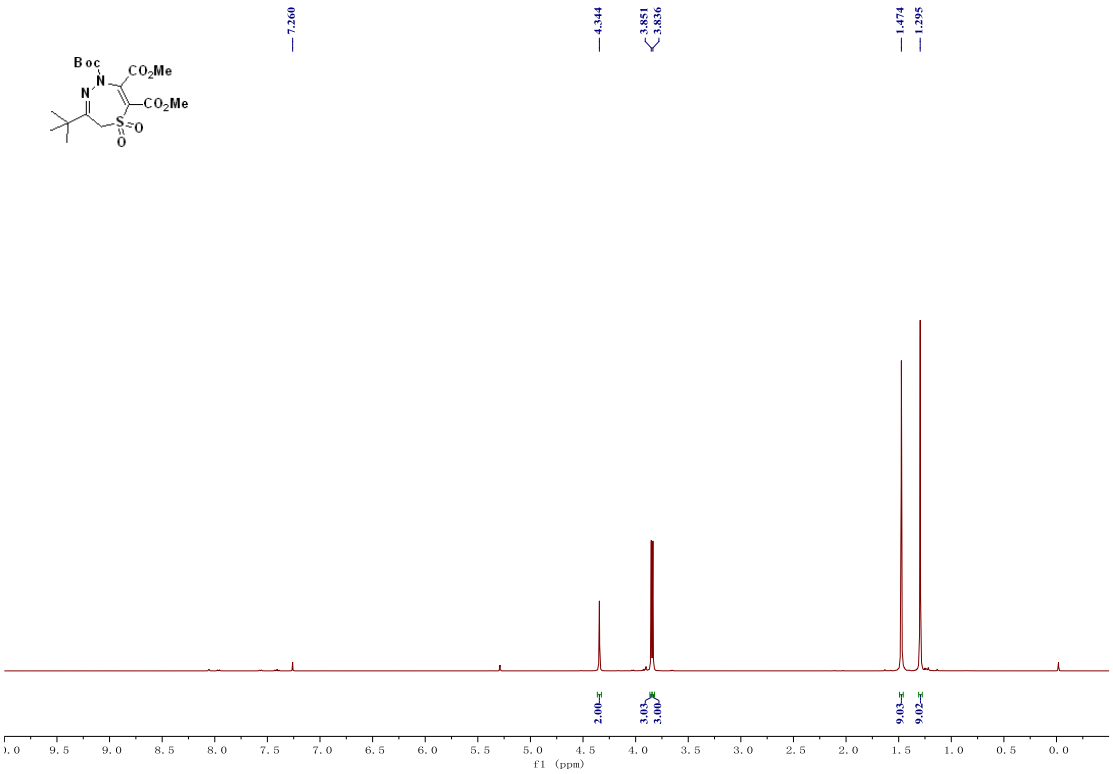


Fig. S73 ^{1}H NMR of compound **4n** (400 MHz, $CDCl_3$).

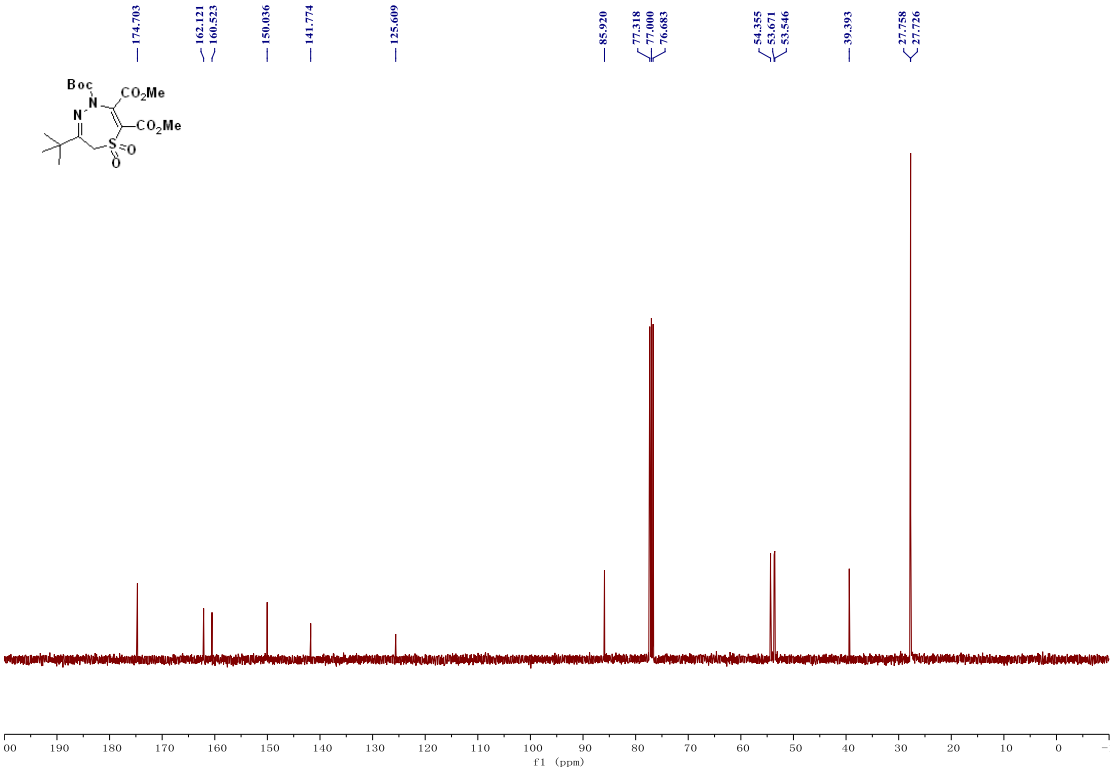


Fig. S74 ^{13}C NMR of compound **4n** (100 MHz, $CDCl_3$).

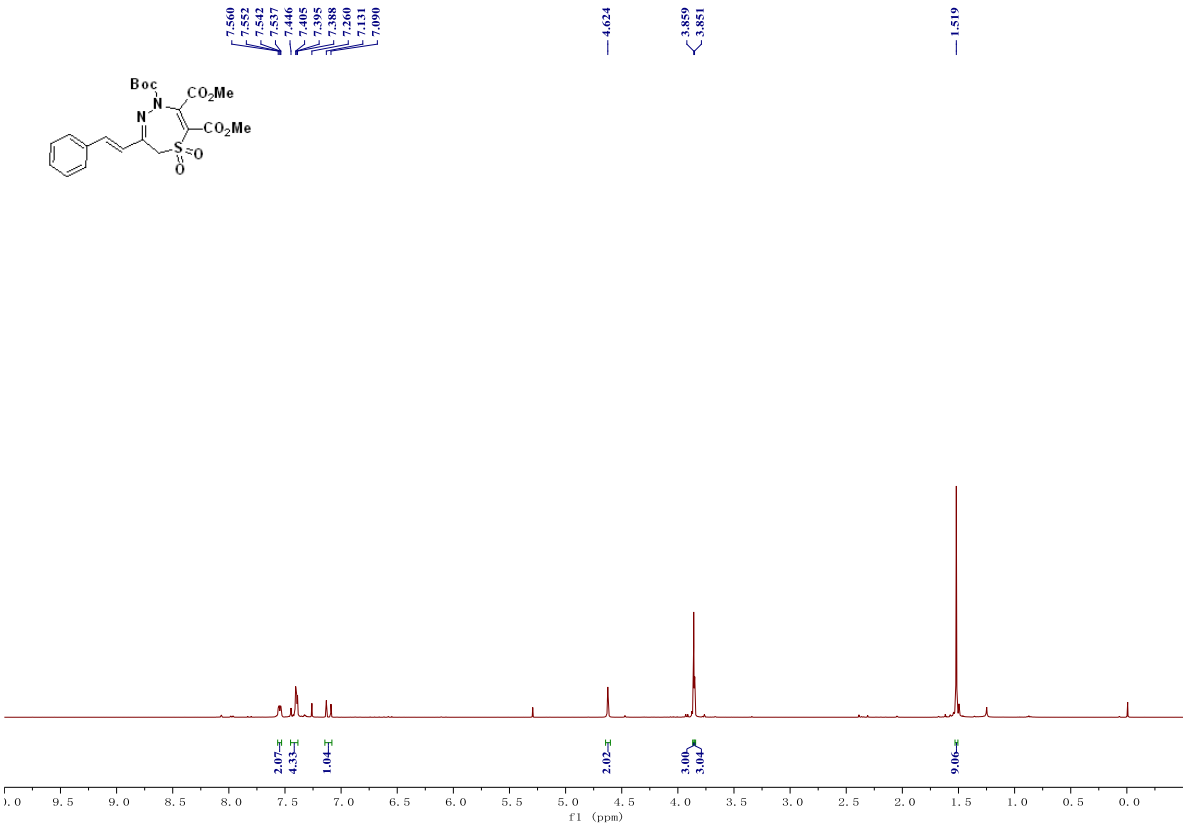


Fig. S75 ^{1}H NMR of compound **4o** (400 MHz, $CDCl_3$).

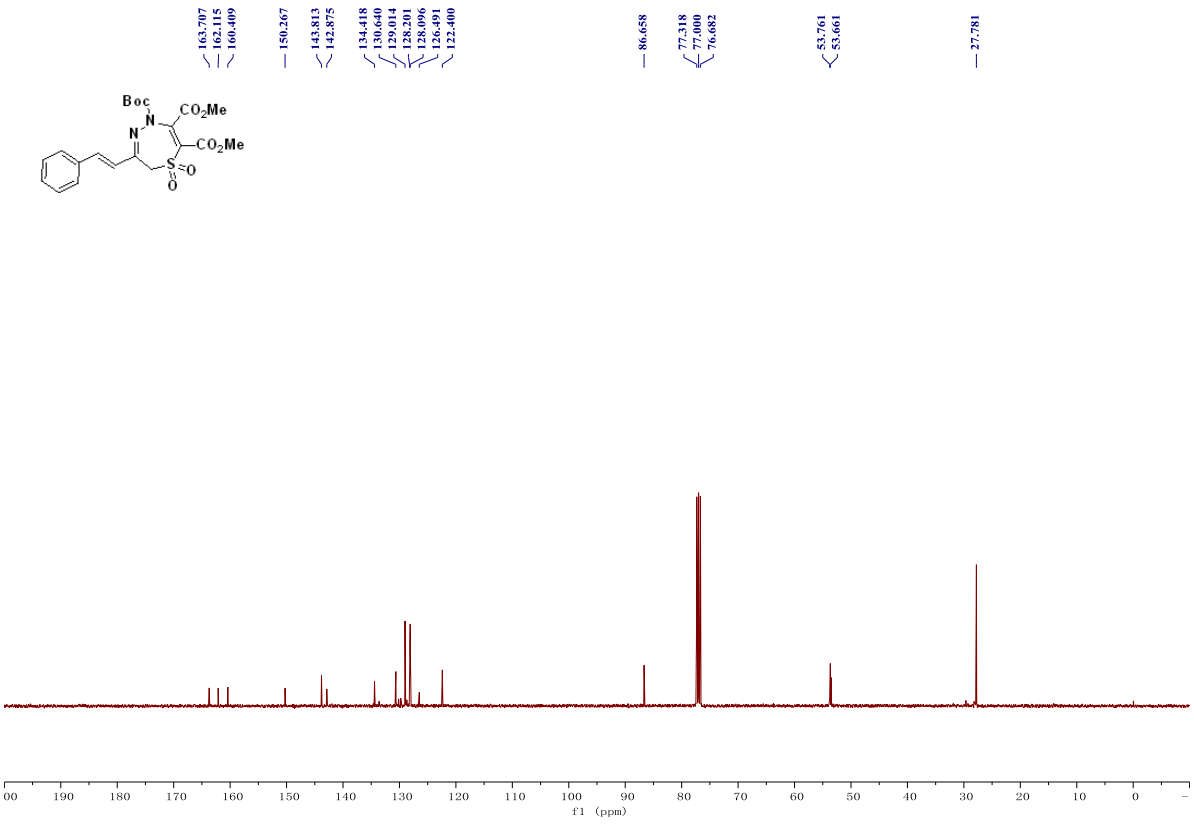


Fig. S76 ^{13}C NMR of compound **4o** (100 MHz, $CDCl_3$).