The Silver(I)-catalyzed Cascade Bicyclization Strategy for Synthesis of 5*H*-benzo[*d*]tetrazolo[5,1-*b*][1,3] thiazines

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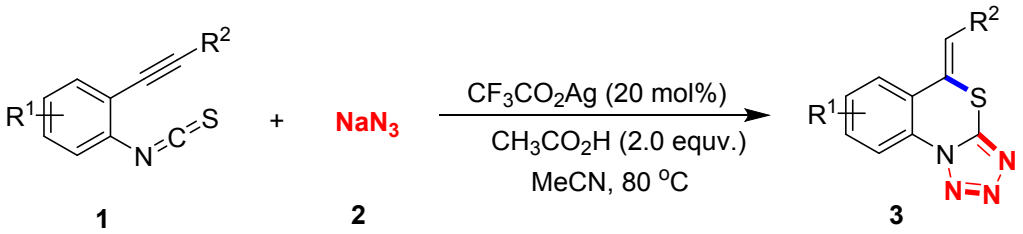
Support Information

CONTENTS:

1. General Information

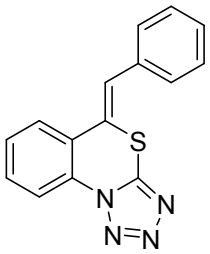
All reagents and metal catalysts were obtained from commercial sources without further purification, and commercially available solvents were purified before use. All reactions were performed in reaction tubes. All new compounds were fully characterized. Silica gel plate GF254 were used for thin layer chromatography (TLC) and silica gel H or 300-400 mesh were used for flash column chromatography. Thin layer chromatography plates were visualized by exposure to ultraviolet light. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale. The mass analyzer type used for the HRMS measurements is micro TOF. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise indicated.

2. Synthesis and Characterization for Compounds 3a-3p, 4 and 3a':



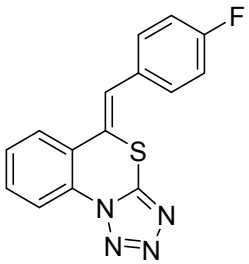
1 2 3

A mixture of *o*-alkynylphenyl isothiocyanate **1** (0.20 mmol) and sodium azide **2** (2.0 equiv.) was added into a tube. Subsequently MeCN (2 mL), CH_3COOH (2.0 equiv.) was added. Then, the sealed tube was heated at 80 °C for 20 hours. After completion of reaction as indicated by TLC, the mixture was concentrated and directly purified by flash column chromatography (EtOAc/petroleum ether, 1:5) to give the desired product **3.**



(Z)-5-benzylidene-5H-benzo[d]tetrazolo[5,1-b][1,3]thiazine (3a)

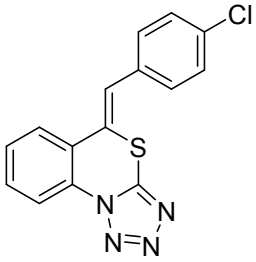
white solid; (46.8 mg, 84%); δ 8.16 (dd, *J* = 1.2, 8.0 Hz, 1H), 7.77 (dd, *J* = 1.2, 8.0 Hz, 1H), 7.59 (td, *J* = 1.2, *J* =7.6 Hz, 1H), 7.53 (dd, *J* = 1.2, 8.0 Hz, 1H), 7.40-7.50 (m, 5H),7.36 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 134.2, 133.5, 130.8, 130.4, 129.5, 129.3, 129.1, 128.7, 126.7, 124.4, 120.8, 118.4; HRMS calcd for $C_{15}H_{11}N_4S^+$ ($M + H^+$): 279.0699; Found: 279.0699.



(Z)-5-(4-fluorobenzylidene)-5H-benzo[d]tetrazolo[5,1-b][1,3]thiazine (3b)

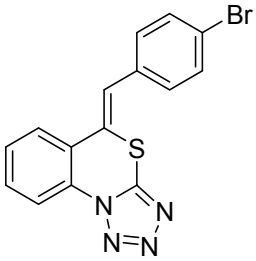
white solid; (40.9 mg, 69%); δ 8.10 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 7.2 Hz, 1H), 7.54 (td, *J* = 0.8, *J* =7.6 Hz, 1H), 7.46 (td, *J* = 0.8, *J* =7.6 Hz, 1H), 7.35-7.38 (m, 2H), 7.24

(s, 1H), 7.09 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8 (d, $^1J_{CF}$ = 249 Hz), 158.2, 148.5, 132.3, 131.3 (d, $^3J_{CF}$ = 8 Hz), 130.9, 130.4, 129.5, 126.1, 124.3, 120.8, 118.5, 115.9 (d, $^2J_{CF}$ = 21 Hz); HRMS calcd for $C_{15}H_{10}FN_4S^+$ (M + H^+): 297.0605; Found: 297.0595.



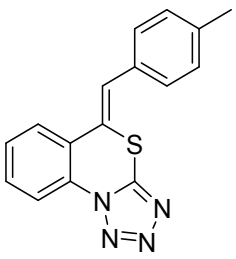
(Z)-5-(4-chlorobenzylidene)-5H-benzo[d]tetrazolo[5,1-b][1,3]thiazine(3c)

white solid; (44.4 mg, 71%); δ 8.12 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.35 (dd, J = 8.0, 23.2 Hz, 4H),7.23 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.4, 135.1, 132.6, 132.0, 131.0, 130.6, 130.4, 129.5, 129.0, 126.7, 124.2, 121.6, 118.5; HRMS calcd for $C_{15}H_{10}ClN_4S^+$ (M + H^+): 313.0309; Found: 313.0302.



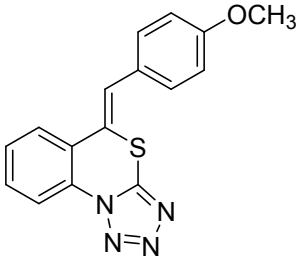
(Z)-5-(4-bromobenzylidene)-5H-benzo[d]tetrazolo[5,1-b][1,3]thiazine (3d)

Yellow solid; (47.9 mg, 67%); δ 8.10 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 7.6 Hz, 1H), 7.51-7.58 (m, 3H), 7.46 (t, J = 7.6 Hz, 1H), 7.25 (d, J = 8.4 Hz, 2H),7.20 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 133.1, 132.0, 131.9, 131.0, 130.8, 130.4, 129.5, 126.6, 124.2, 123.3, 121.7, 118.5; HRMS calcd for $C_{15}H_{10}BrN_4S^+$ (M + H^+): 356.9804; Found: 356.9796.



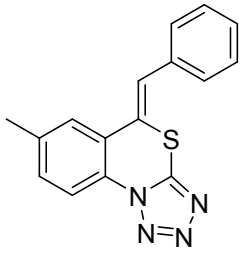
(Z)-5-(4-methylbenzylidene)-5H-benzo[d]tetrazolo[5,1-b][1,3]thiazine (3e)

white solid; (49.7 mg, 85%); δ 8.05 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.35-7.50 (m, 3H), 7.24 (t, *J* = 6.8 Hz, 3H), 7.19 (s, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 139.4, 133.6, 131.4, 130.6, 130.3, 129.4, 129.4, 129.3, 126.7, 124.6, 119.6, 118.3, 21.5; HRMS calcd for $C_{16}H_{13}N_4S^+$ (M + H^+): 293.0855; Found: 293.0850.



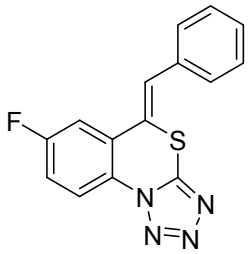
(Z)-5-(4-methoxybenzylidene)-5H-benzo[d]tetrazolo[5,1-b][1,3]thiazine (3f)

white solid; (53.7 mg, 87%); δ 8.06 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.45 (t, *J* =7.8 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.19 (s, 1H), 6.90 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 148.9, 133.4, 131.0, 130.4, 130.3, 129.4, 129.1, 126.9, 126.7, 124.9, 118.3, 114.1, 55.4. HRMS calcd for $C_{16}H_{13}N_4OS^+$ (M + H^+): 309.0805; Found: 309.0801.



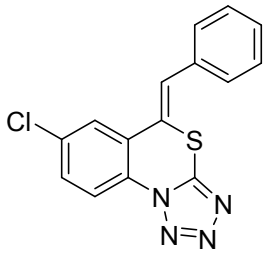
(Z)-5-benzylidene-7-methyl-5H-benzo[d]tetrazolo[5,1-b][1,3]thiazine (3g)

Yellow solid; (50.9 mg, 87%); δ 8.03 (d, *J* =8.4 Hz, 1H), 7.56 (s, 1H), 7.41-7.48 (m, 4H), 7.38 (d, *J* =6.8 Hz, 2H), 7.35 (s, 1H), 2.48 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.4, 139.7, 134.3, 132.9, 131.5, 129.3, 129.0, 128.7, 128.2, 126.9 124.2, 121.0, 118.3, 21.4; HRMS calcd for $C_{16}H_{13}N_4S^+$ (M + H^+): 293.0855; Found: 293.0861.



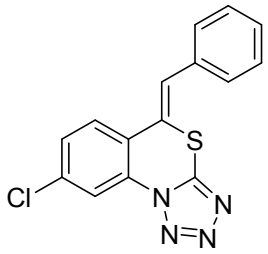
(Z)-5-benzylidene-7-fluoro-5H-benzo[d]tetrazolo[5,1-b][1,3]thiazine (3h)

Yellow solid; (44.4 mg, 75%); δ 8.17 (q, J = 4.8 Hz, 1H), 7.42-7.50 (m, 6H), 7.36 (s, 1H), 7.30 (dt, J = 2.8, 9.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5 (d, $^1J_{CF}$ = 249 Hz), 148.3, 134.4, 133.8, 129.5, 129.4, 129.0, 128.8, 127.7, 126.6 (d, $^3J_{CF}$ = 8 Hz), 120.6 (d, $^3J_{CF}$ = 9 Hz), 118.0 (d, $^2J_{CF}$ = 24 Hz), 113.5 (d, $^2J_{CF}$ = 25 Hz); HRMS calcd for $C_{15}H_{10}FN_4S^+$ (M + H^+): 297.0605; Found: 297.0607.



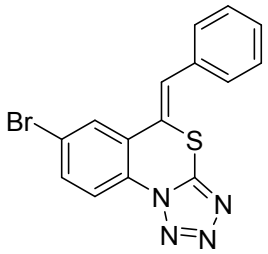
(Z)-5-benzylidene-7-chloro-5H-benzo[d]tetrazolo[5,1-b][1,3]thiazine (3i)

Yellow solid; (47.5mg, 76%); δ 8.01 (q, J = 8.8 Hz, 1H), 7.67 (s, 1H), 7.46 (dd, J = 1.6, J = 8.8 Hz, 1H), 7.30-7.39 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 135.3, 134.6, 133.8, 130.7, 129.4, 129.3, 129.0, 128.8, 127.7, 126.6, 126.0, 119.8. HRMS calcd for $C_{15}H_{10}ClN_4S^+$ (M + H^+): 313.0309; Found: 313.0307.



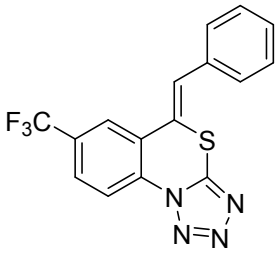
(Z)-5-benzylidene-8-chloro-5H-benzo[d]tetrazolo[5,1-b][1,3]thiazine (3j)

Yellow solid; (46.9 mg, 75%); δ 8.10 (d, J = 2.8 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.34-7.43 (m, 6H), 7.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 136.9, 133.9, 129.6, 129.4, 129.3, 128.9, 128.8, 128.0, 127.7, 122.9, 119.9, 118.6. HRMS calcd for $C_{15}H_{10}ClN_4S^+$ (M + H^+): 313.0309; Found: 313.0307.



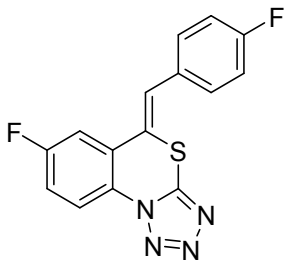
(Z)-5-benzylidene-7-bromo-5H-benzo[d]tetrazolo[5,1-b][1,3]thiazine (3k)

Yellow solid; (52.9 mg, 74%); δ 8.02 (d, J = 8.8 Hz, 1H), 7.90 (d, J = 1.6 Hz, 1H), 7.70 (dd, J = 2.0, J = 8.8 Hz, 1H), 7.39-7.49 (m, 5H), 7.36 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 134.7, 133.8, 133.6, 129.5, 129.4, 129.3, 129.0, 128.8, 127.7, 126.2, 123.1, 120.1, 119.3; HRMS calcd for $C_{15}H_{10}BrN_4S^+$ (M + H^+): 356.9804; Found: 356.9806.



(Z)-5-benzylidene-7-(trifluoromethyl)-5H-benzo[d]tetrazolo[5,1-b][1,3]thiazine (3l)

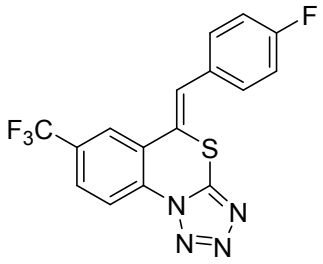
Yellow solid; (45.7 mg, 66%); δ 8.30 (d, J = 8.4 Hz, 1H), 8.03 (s, 1H), 7.85 (d, J = 8.8 Hz, 1H), 7.42-7.51 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.4, 135.6, 133.7, 132.6, 131.8, 131.5, 129.6, 129.4, 128.8, 127.5 (q, J_{CF3} = 12 Hz), 125.2, 124.2 (q, J_{CF3} = 12 Hz), 119.4, 119.2; HRMS calcd for $C_{16}H_{10}F_3N_4S^+$ (M + H^+): 347.0573; Found: 347.0580.



(Z)-7-fluoro-5-(4-fluorobenzylidene)-5H-benzo[d]tetrazolo[5,1-b][1,3]thiazine(3m)

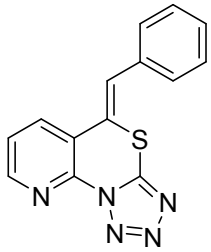
white solid; (44.0 mg, 70%); δ 8.08 (q, J = 4.0 Hz, 1H), 7.92 (dd, J = 2.8, 10.0 Hz, 1H), 7.69 (s, 1H), 7.48-7.57 (m, 3H), 7.29 (t, J = 8.8 Hz, 2H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5 (d, $^1J_{CF}$ = 247 Hz), 162.3 (d, $^1J_{CF}$ = 245 Hz), 148.0, 133.8, 132.2 (d,

$^{3}J_{CF}$ = 8 Hz), 131.1 (d, $^{4}J_{CF}$ = 3 Hz), 130.2 (d, $^{3}J_{CF}$ = 8 Hz), 126.8 (d, $^{4}J_{CF}$ = 3 Hz), 126.5 (d, $^{3}J_{CF}$ = 9 Hz), 121.0 (d, $^{3}J_{CF}$ = 10 Hz), 118.6 (d, $^{2}J_{CF}$ = 24 Hz), 116.2 (d, $^{2}J_{CF}$ = 21 Hz), 114.3 (d, $^{2}J_{CF}$ = 26 Hz); HRMS calcd for $C_{15}H_9F_2N_4S^+$ (M + H^+): 315.0510; Found: 315.0515.



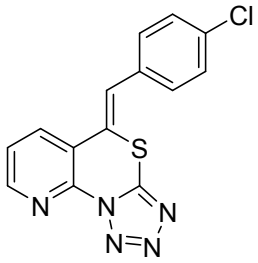
(Z)-5-(4-fluorobenzylidene)-7-(trifluoromethyl)-5H-benzo[d]tetrazolo[5,1-b][1,3]thiazine(3n)

Yellow solid; (48.8 mg, 67%); δ 8.35 (s, 1H), 8.24 (d, *J* = 8.8 Hz, 1H), 7.99 (dd, *J* = 1.2, 8.4 Hz, 1H), 7.81 (s, 1H), 7.56-7.60 (m, 2H), 7.27-7.34 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, (d, $^{1}J_{CF}$ = 246 Hz), 149.2, 135.0, 132.9, 132.3 (d, $^{3}J_{CF}$ = 8 Hz), 131.1 (d, $^{3}J_{CF}$ = 8 Hz), 130.4, 130.2 (d, $^{2}J_{CF}$ = 24 Hz), 128.1 (q, J_{CF3} = 4 Hz), 126.3, 125.1 (q, J_{CF3} = 4 Hz), 119.7, 118.2, 116.1 (d,$^{2}J_{CF}$ = 24 Hz); HRMS calcd for $C_{16}H_9F_4N_4S^+$ (M + H^+): 365.0479; Found: 365.0482.



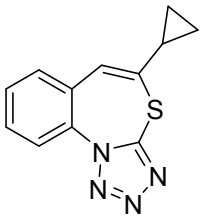
(Z)-5-benzylidene-5H-pyrido[2,3-d]tetrazolo[5,1-b][1,3]thiazine(3o)

Yellow solid; (43.6 mg, 78%); δ 8.47 (dd, *J* = 1.6, 4.8 Hz, 1H), 7.94 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.76 (dd, *J* = 1.6, 8.0 Hz, 2H), 7.48-7.56 (m, 3H), 7.31 (q, *J* = 4.8 Hz, 1H), 6.75 (s, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 145.5, 139.7, 130.1, 129.8, 129.3, 128.6, 127.7, 121.3, 120.5, 105.8, 104.8. HRMS calcd for $C_{14}H_{10}N_5S^+$ (M + H^+): 280.0651; Found: 280.0655.



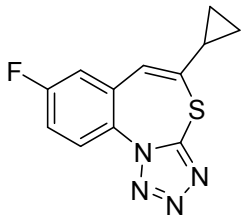
(Z)-5-(4-chlorobenzylidene)-5H-pyrido[2,3-d]tetrazolo[5,1-b][1,3]thiazine(3p)

Yellow solid; (44.6 mg, 71%); δ 8.48 (dd, *J* = 1.2, 4.8 Hz, 1H), 7.95 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.33 (q, *J* = 5.2 Hz, 1H), 6.76 (s, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.3, 144.8, 137.4, 135.3, 128.9, 128.5, 127.8, 126.0, 120.1, 119.6, 104.6, 104.2. HRMS calcd for $C_{14}H_9ClN_5S^+$ (M + H^+): 314.0262; Found: 314.0272.



5-cyclopropylbenzo[d]tetrazolo[5,1-b][1,3]thiazepine (4a)

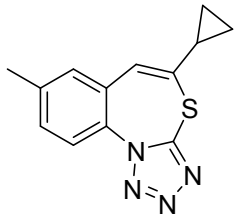
white solid; (33.9 mg, 70%); δ 8.10 (d, *J* = 8.4 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 7.47-7.41 (m, 1H), 5.73 (d, *J* = 9.6 Hz, 1H), 1.94-1.85 (m, 1H), 1.08 (q, *J* = 8.0 Hz, 2H), 0.68 (q, *J* = 4.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.4, 139.5 129.9, 129.3, 129.2, 128.7, 125.6, 124.2, 118.5, 12.7, 8.5. HRMS calcd for $C_{14}H_{11}N_4S^+$ (M + H^+): 243.0699; Found: 243.0700.



5-cyclopropyl-8-fluorobenzo[d]tetrazolo[5,1-b][1,3]thiazepine (4b)

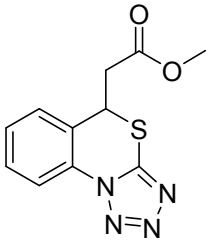
white solid; (39.0 mg, 75%); δ 7.86 (q, *J* = 5.2 Hz, 1H), 7.51 (dt, *J* = 2.0, 9.2 Hz, 1H), 7.06 (dd, *J* = 2.0, 8.8 Hz, 1H), 6.82 (s, 1H), 1.92-1.85 (m, 1H), 0.98-0.89 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3 (d, $^1J_{CF}$ = 250 Hz), 152.3, 143.6, 131.7 (d, $^3J_{CF}$ = 9 Hz), 128.5, 127.8, 126.6 (d, $^3J_{CF}$ = 9 Hz), 116.6 (d, $^2J_{CF}$ = 23 Hz), 100.0, 19.6, 6.5.

HRMS calcd for $C_{12}H_{10}FN_4S^+$ (M + H^+): 261.0605; Found: 261.0606.



5-cyclopropyl-8-methylbenzo[d]tetrazolo[5,1-b][1,3]thiazepine（4c）

white solid; (30.8 mg, 60%); δ 7.96 (d, *J* = 8.4 Hz, 1H), 7.30-7.27 (m, 2H), 5.73 (d, *J* = 9.6 Hz, 1H), 2.42 (s, 3H), 1.83-1.92 (m, 1H), 1.04-1.09 (m, 2H), 0.67-0.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ149.0, 139.5 130.6, 130.0, 129.0, 127.7, 125.8, 124.0, 118.3, 21.3, 12.7, 8.4. HRMS calcd for $C_{13}H_{13}N_4S^+$ (M + H^+): 257.0855; Found: 257.0850.



methyl 2-(5H-benzo[d]tetrazolo[5,1-b][1,3]thiazin-5-yl)acetate (3a')

Red-brown solid; (28.9 mg, 55%);δ 8.0 (d, *J* = 8.0 Hz, 1H), 7.47-7.52 (m, 1H), 7.40 (d, *J* = 4.0 Hz, 2H), 4.71 (d, *J* = 8.4 Hz, 1H), 3.60 (s, 3H), 2.61-2.75 (dq, *J* = 8.8, 16.8 Hz, 2H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 148.9, 130.9, 130.2, 129.4, 128.0, 124.9, 119.2, 52.3, 42.2, 39.8. HRMS calcd for $C_{11}H_{11}N_4O_2S^+$ (M + H^+): 263.0597; Found: 263.0600.

3. X-Ray Crystal Structure for Compound 3n

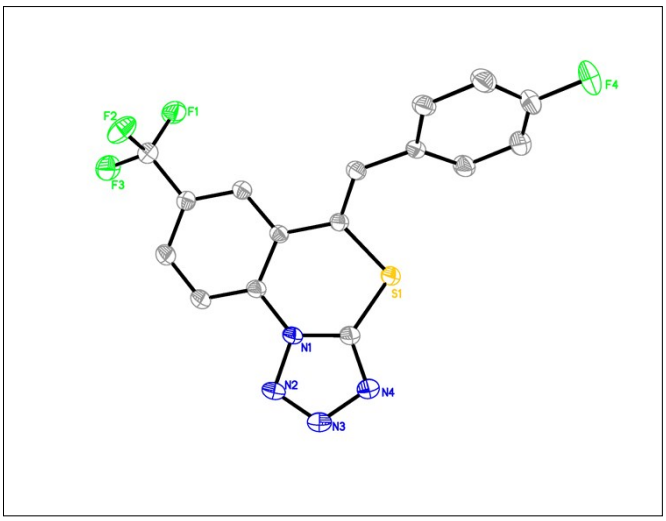


Figure 1. Single-crystal X-ray diffraction structure of **3n,** the thermal ellipsoids are at the 30% probability level

CCDC: 1858182

X-Ray Crystal Structure for Compound 4a

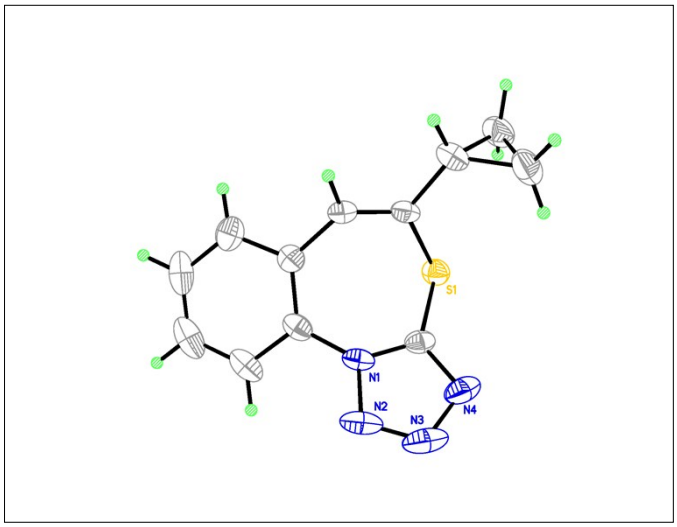
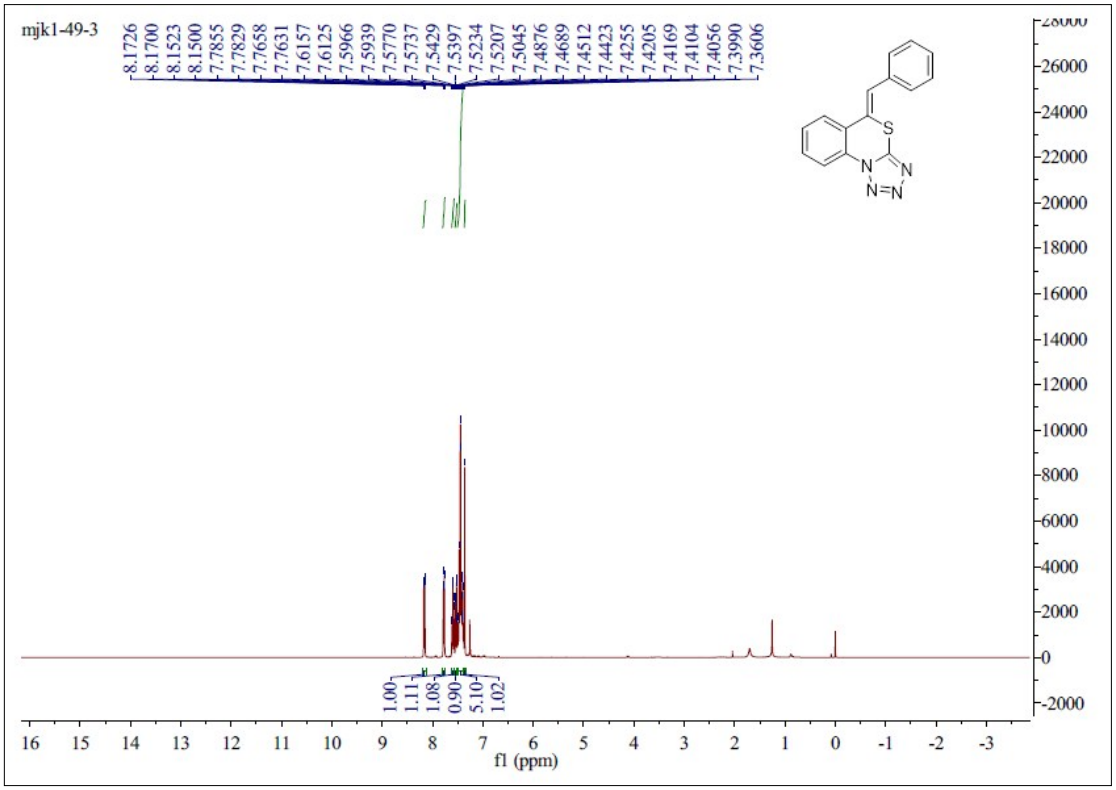


Figure 2. Single-crystal X-ray diffraction structure of **4a,** the thermal ellipsoids are at the 30% probability level

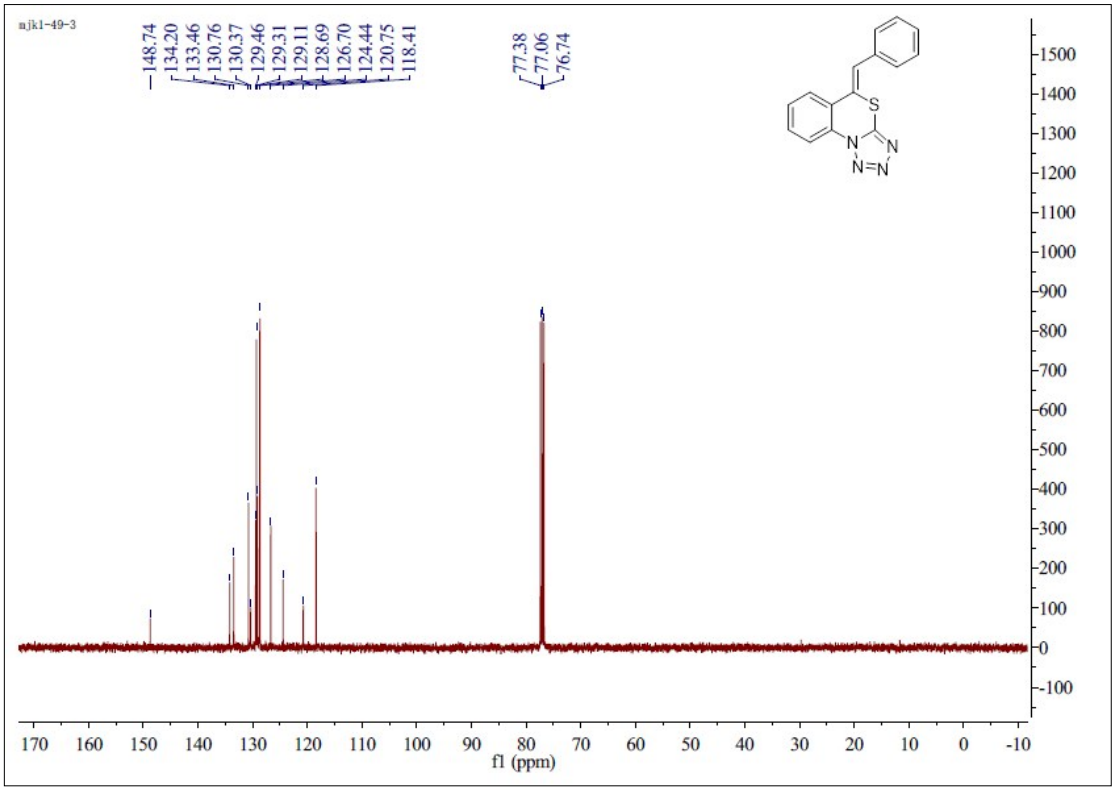
CCDC: 1882658

4. Copies of ^{1}H NMR, ^{13}C NMR Spectra for compounds 3a-3p, 4a-4c and 3a'

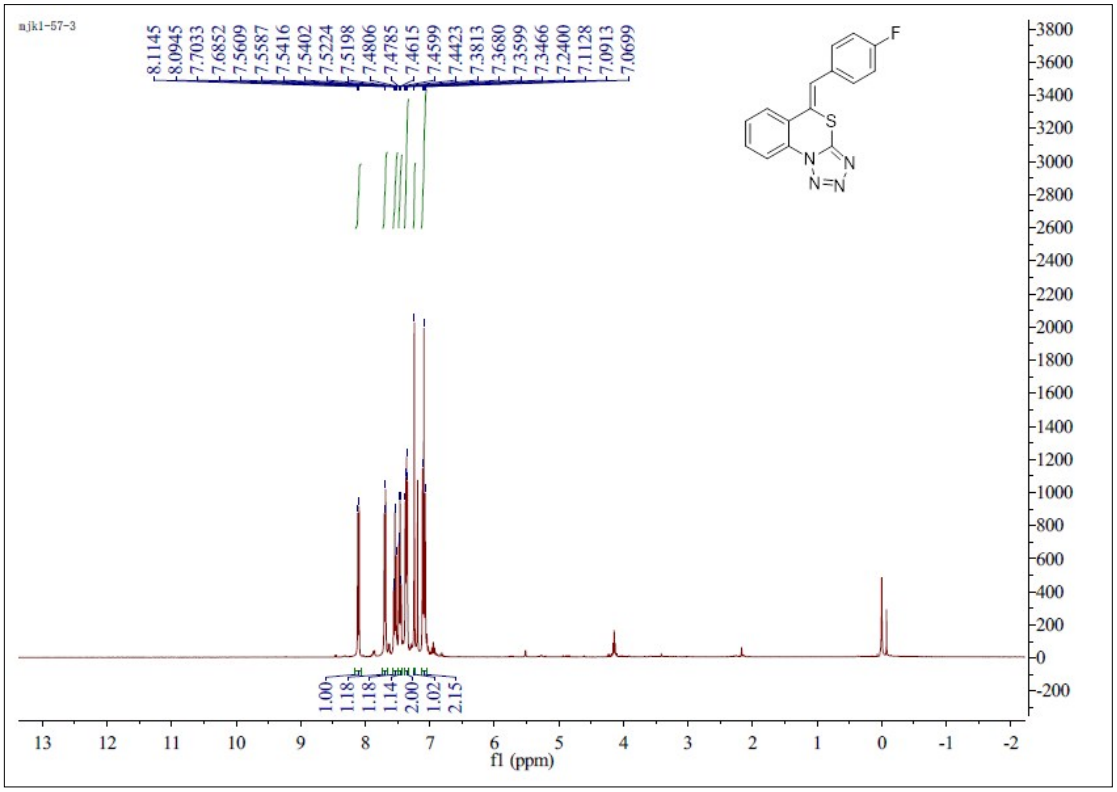
^{1}H NMR of **3a**



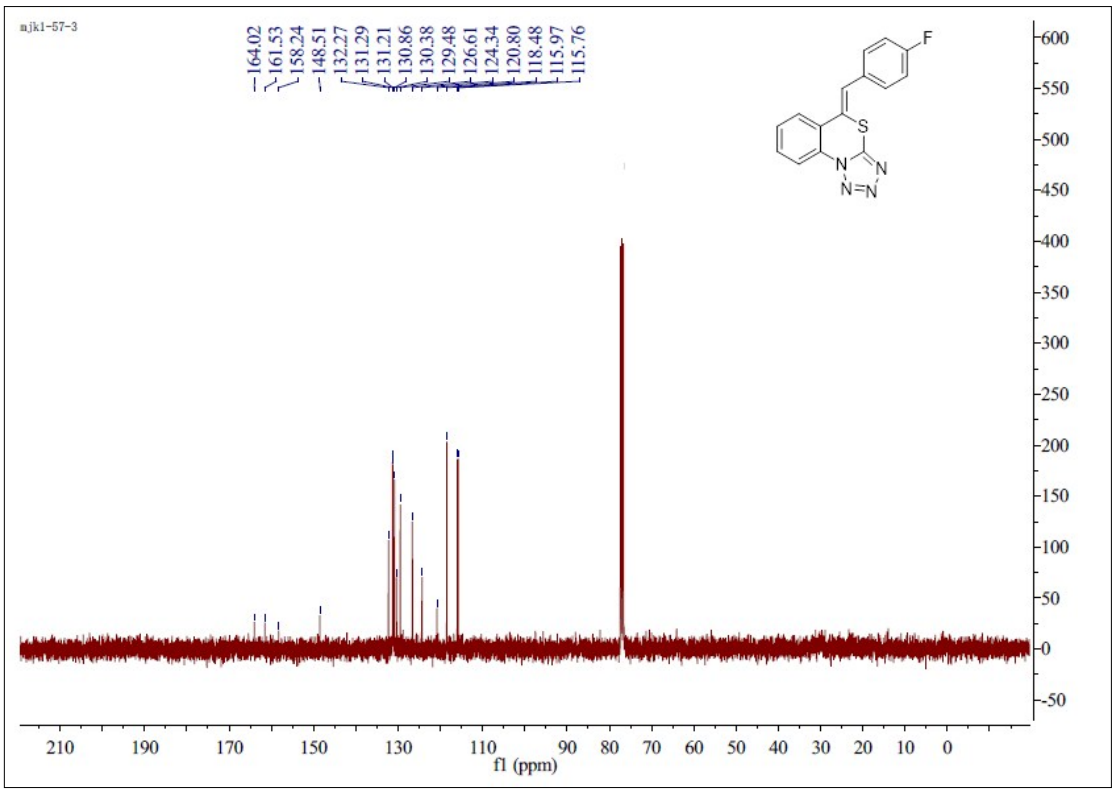
^{13}C NMR of **3a**



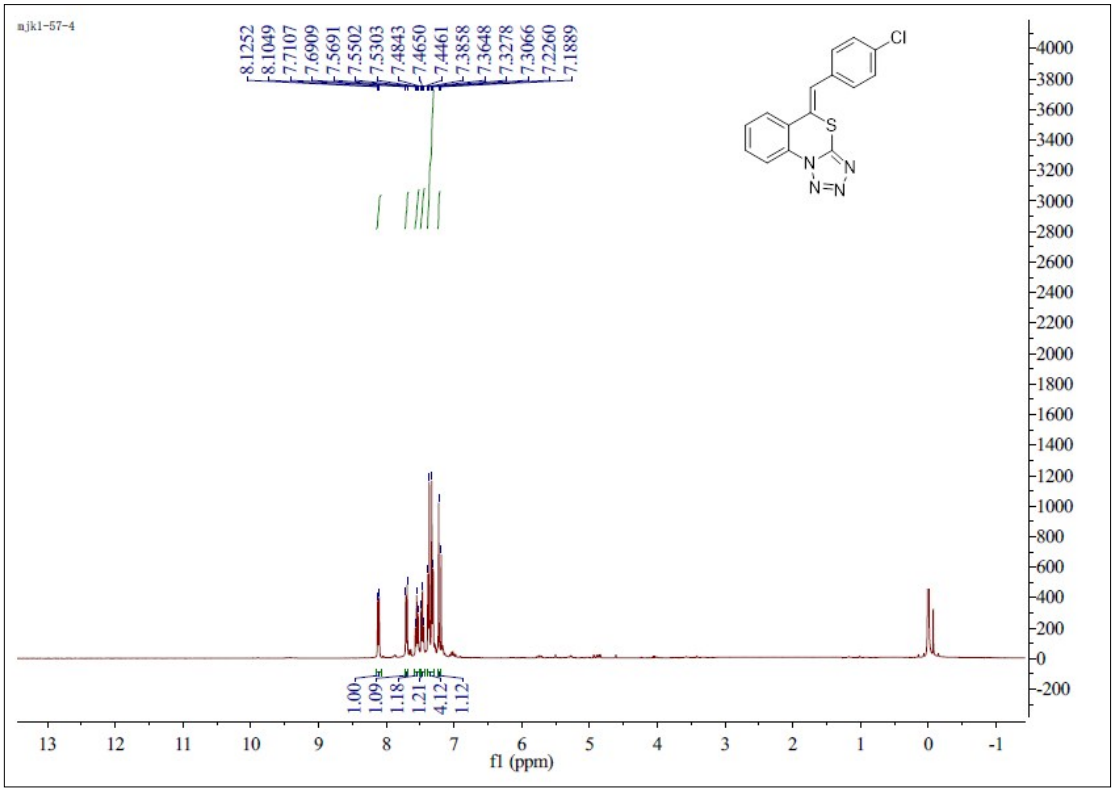
^{1}H NMR of **3b**



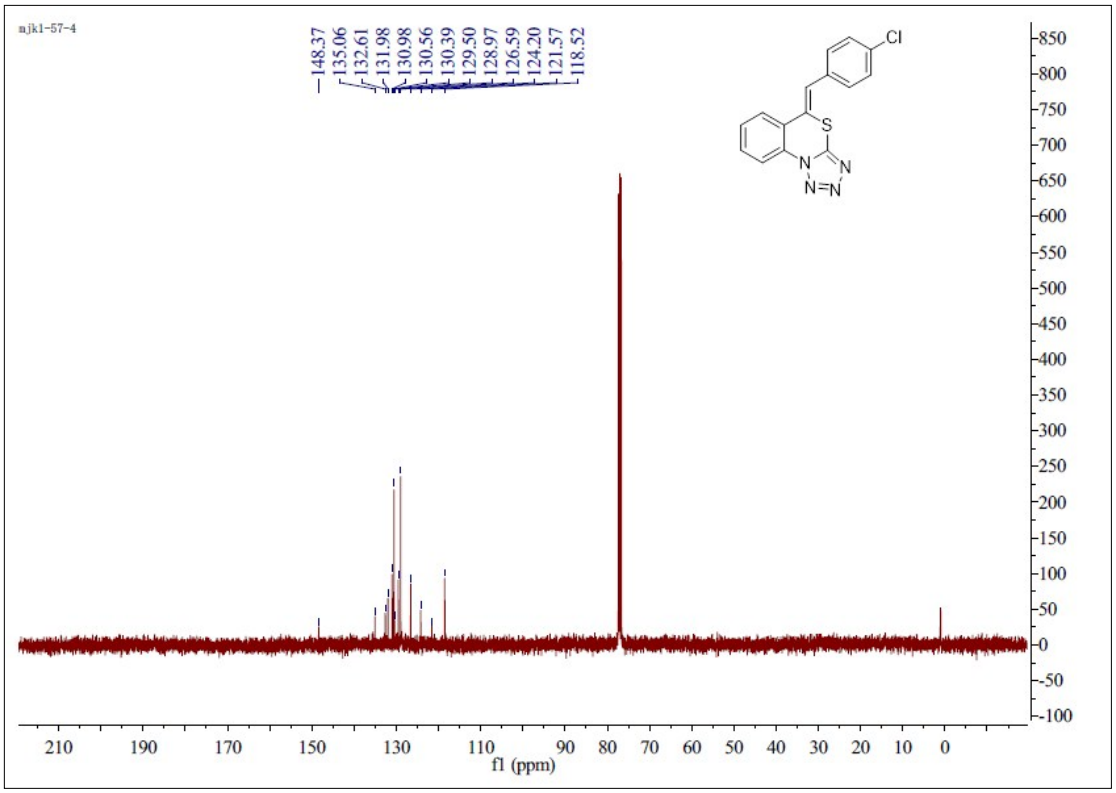
^{13}C NMR of **3b**



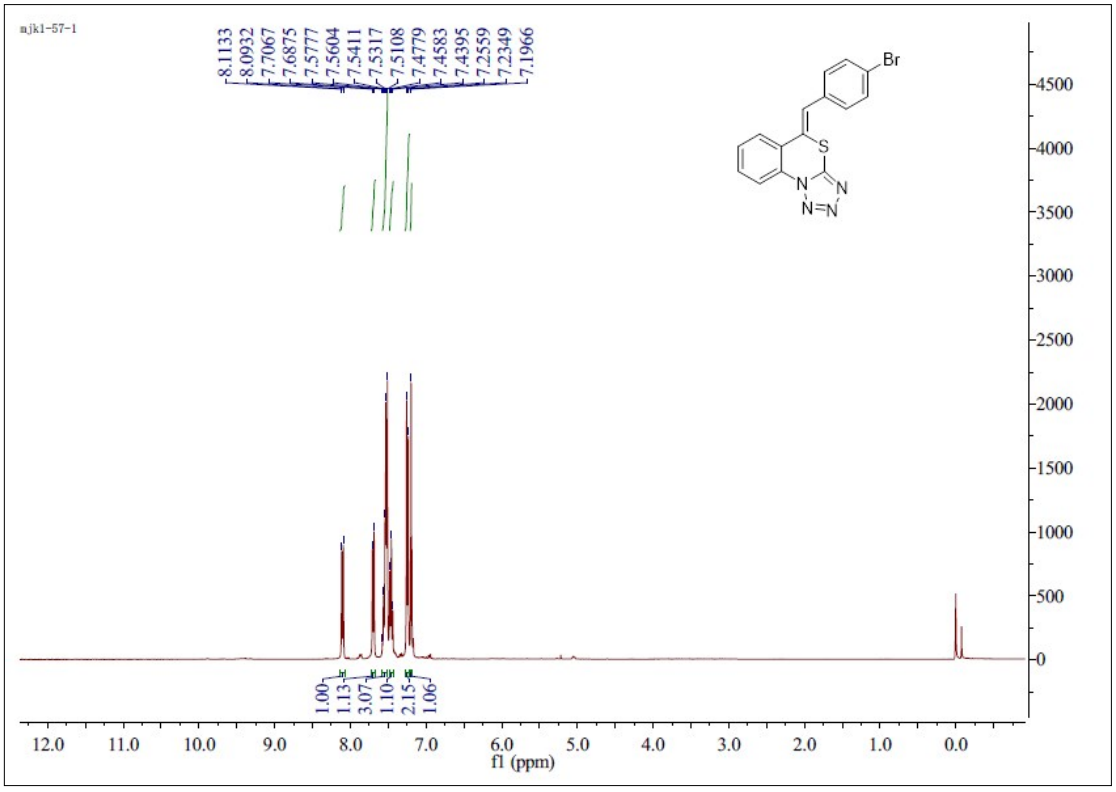
^{1}H NMR of **3c**



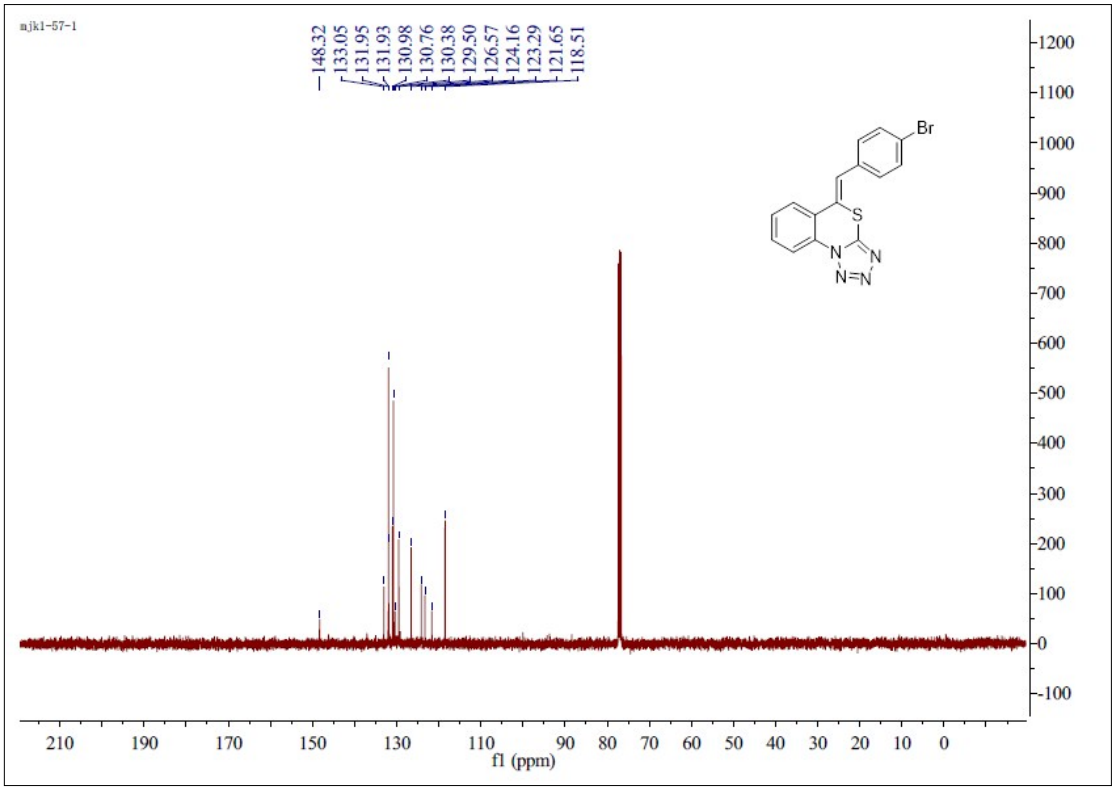
^{13}C NMR of **3c**



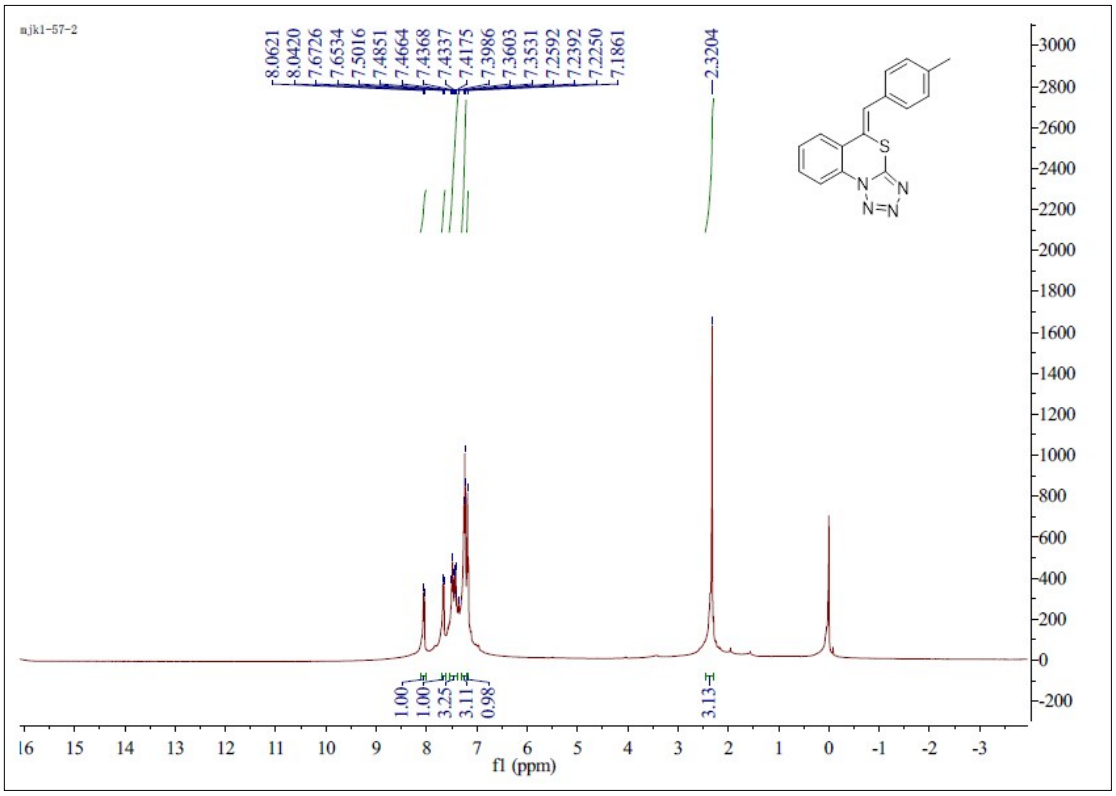
^{1}H NMR of **3d**



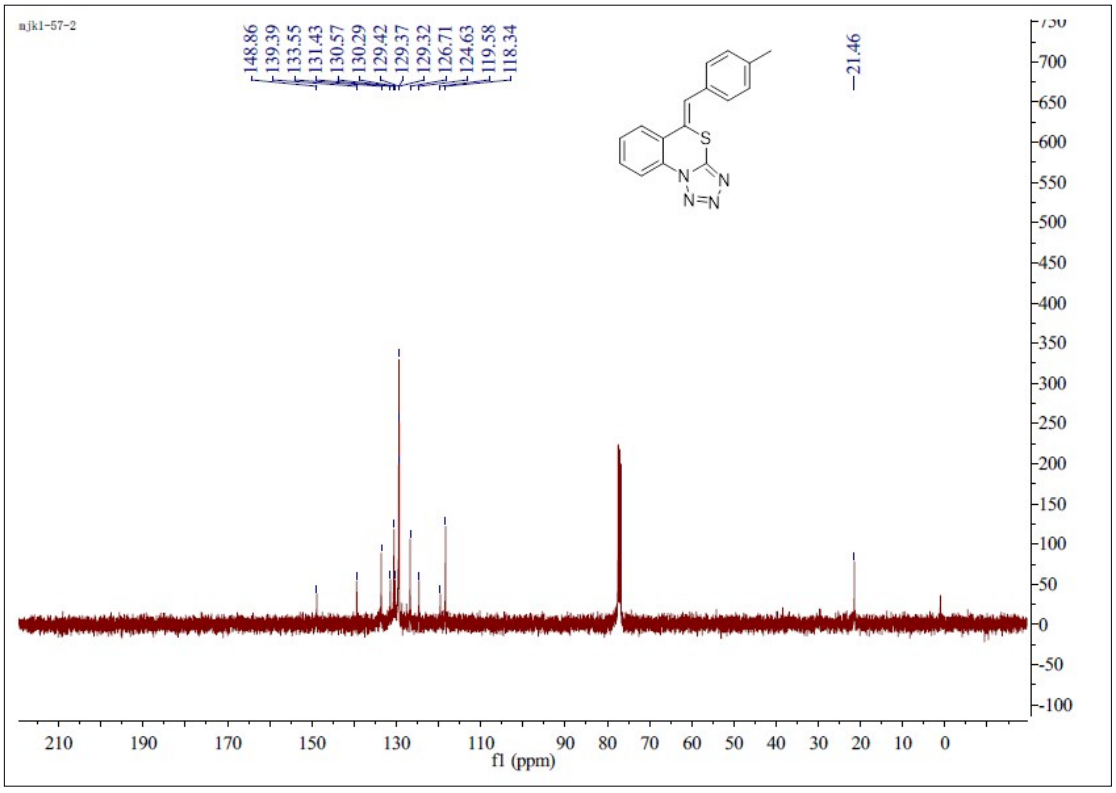
^{13}C NMR of **3d**



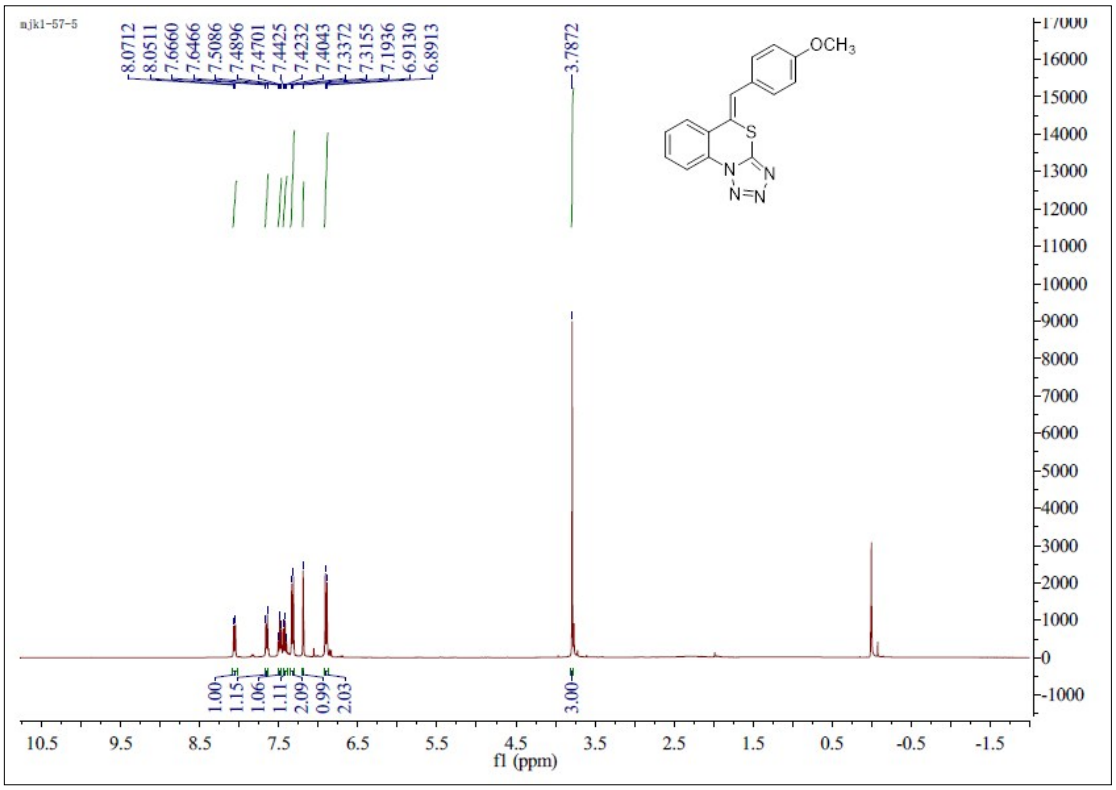
^{1}H NMR of **3e**



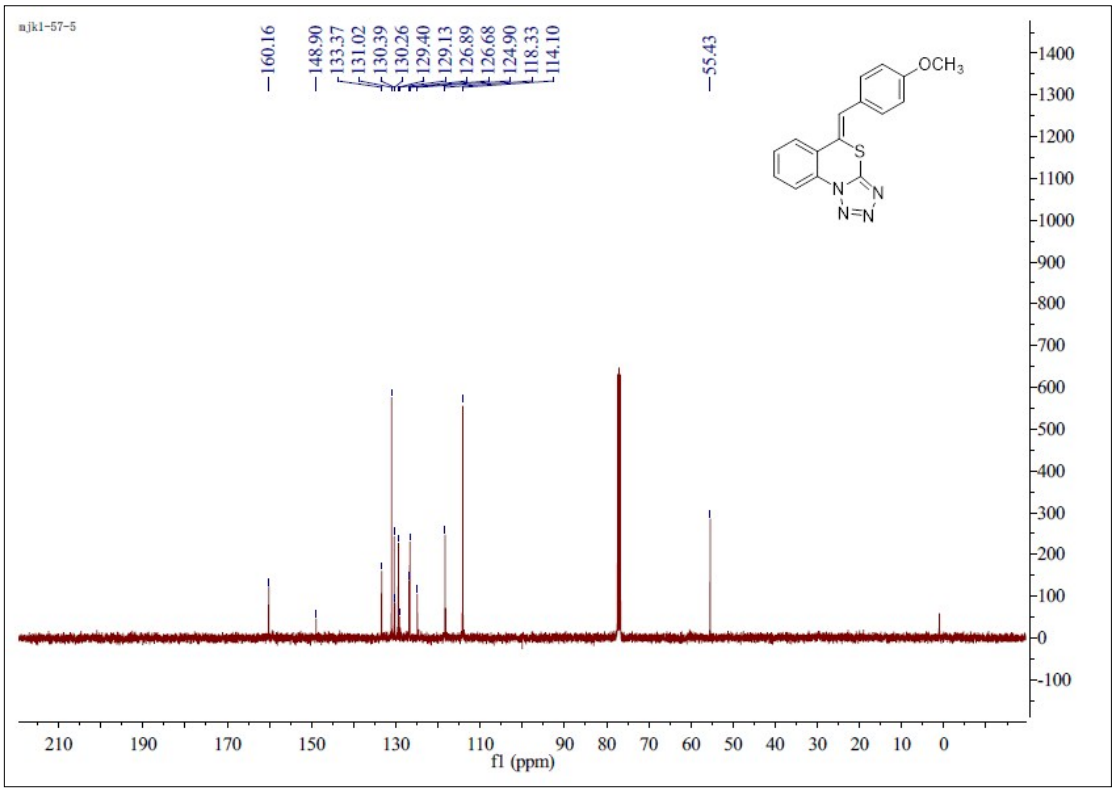
^{13}C NMR of **3e**



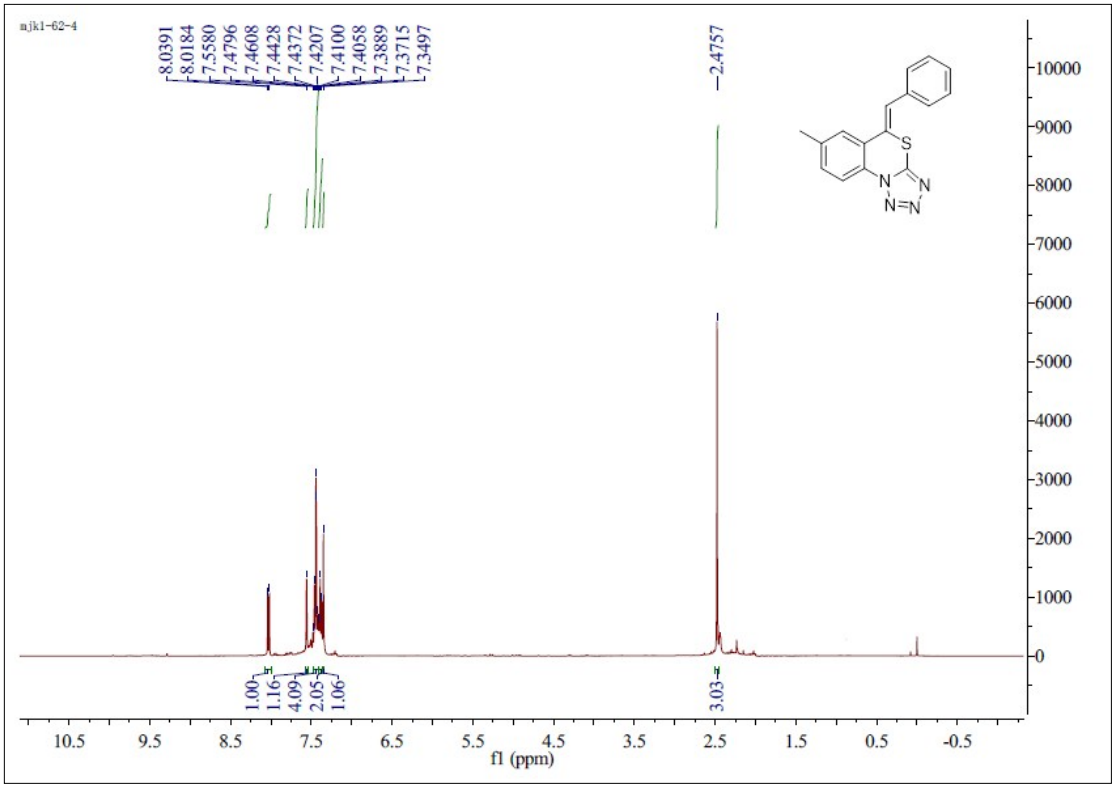
^{1}H NMR of **3f**



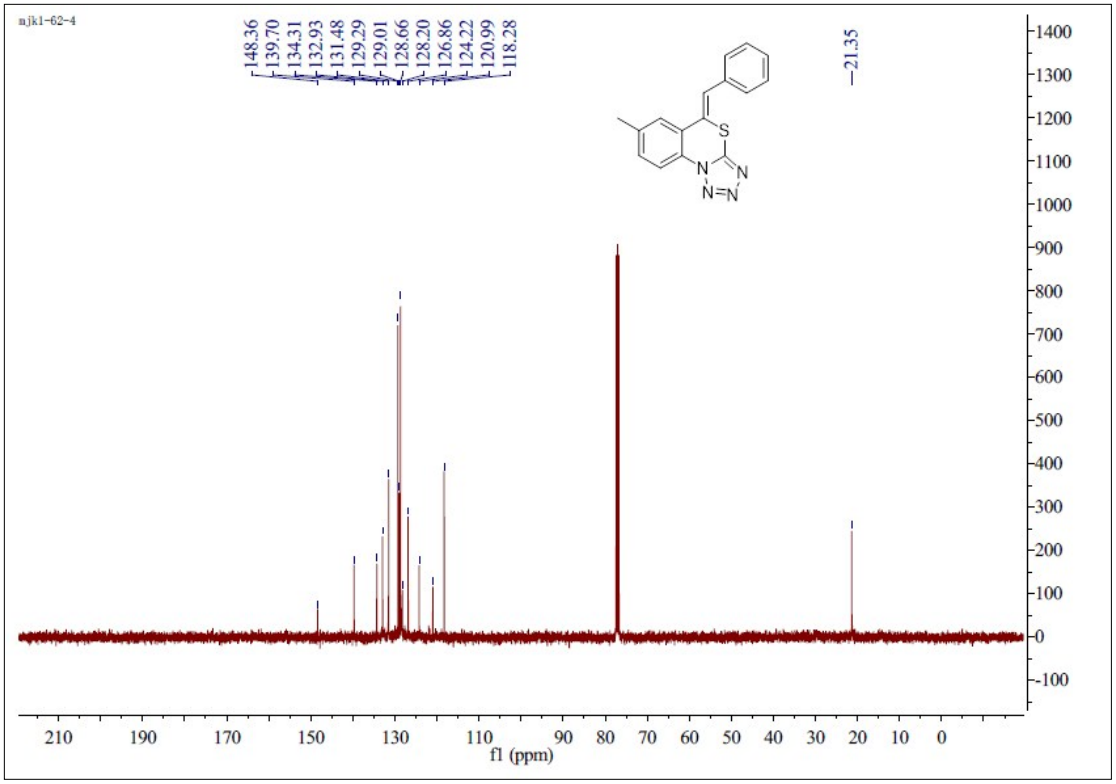
^{13}C NMR of **3f**



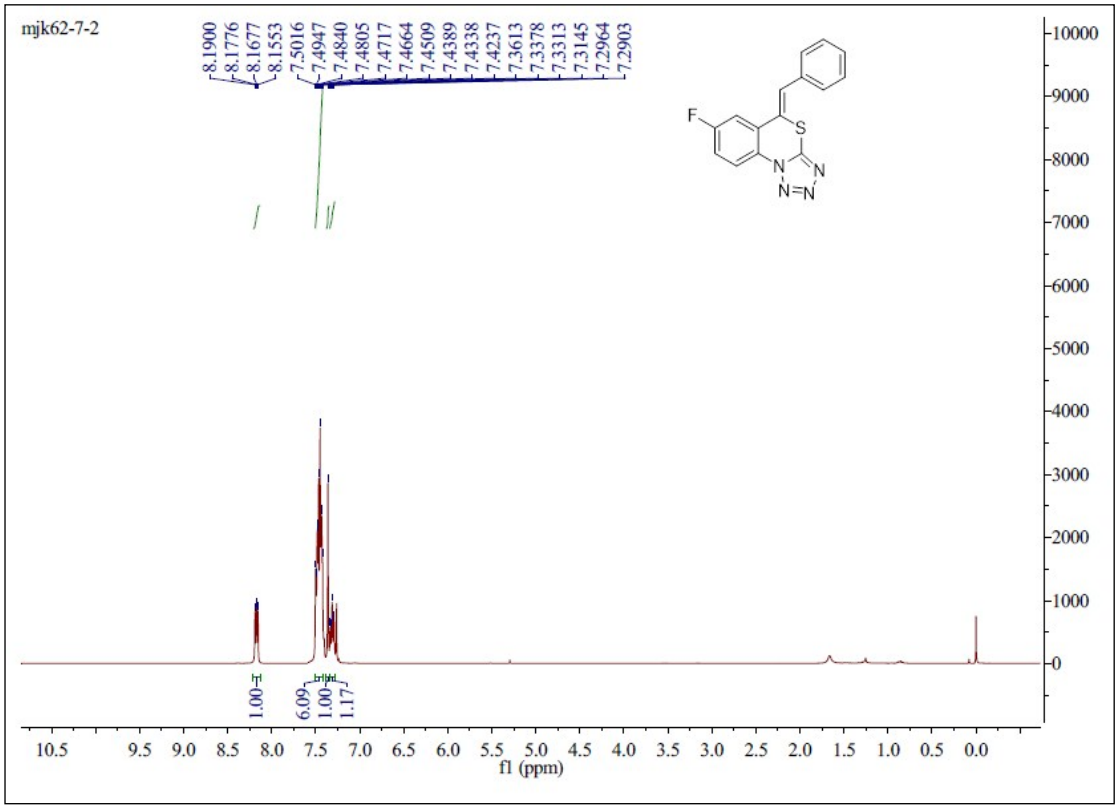
^{1}H NMR of **3g**



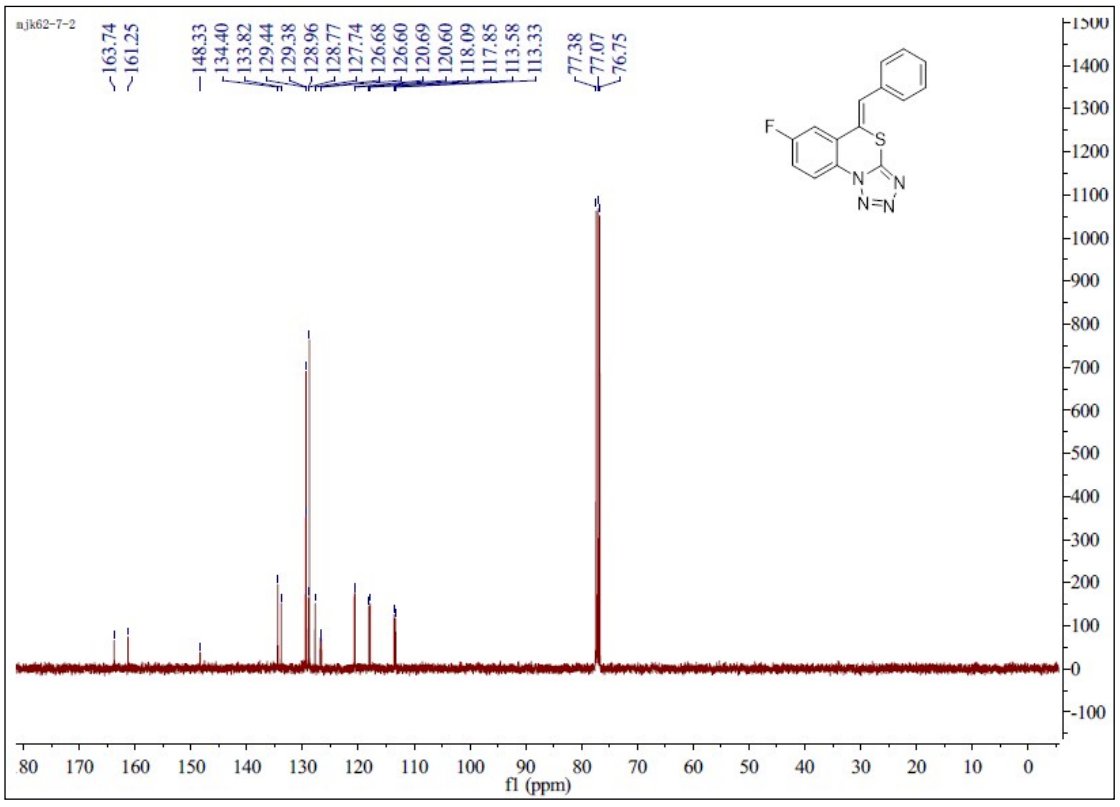
^{13}C NMR of **3g**



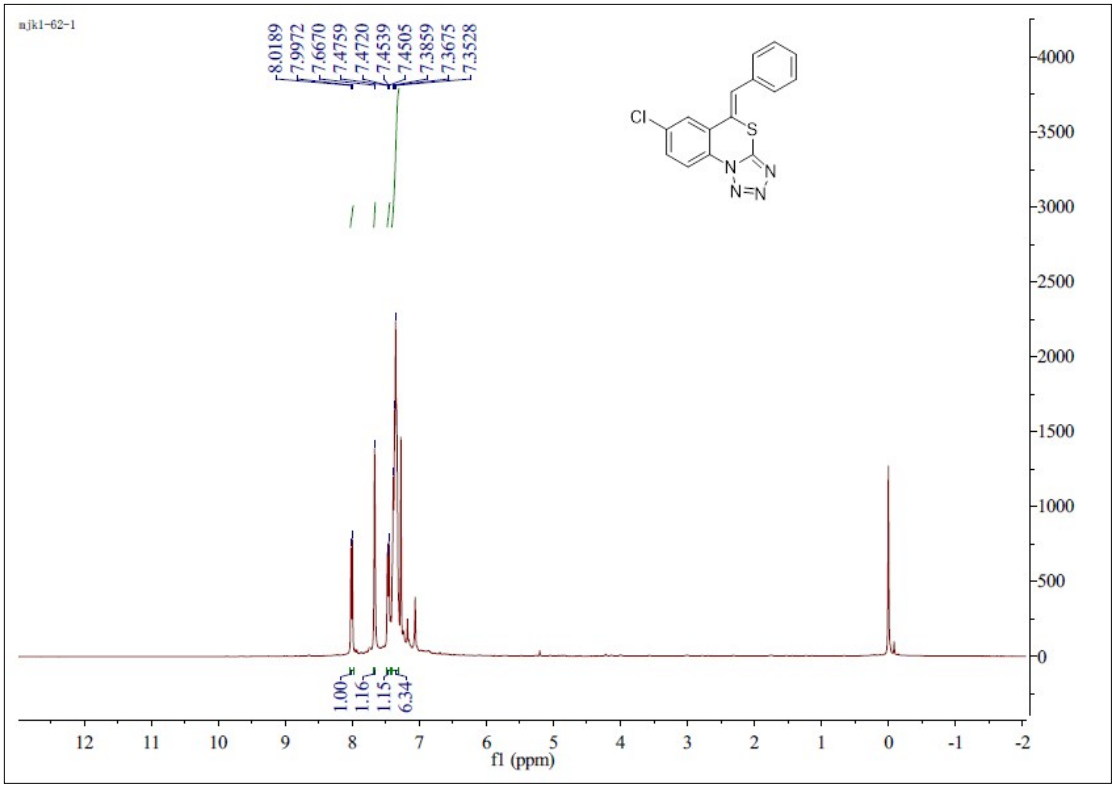
^{1}H NMR of **3h**



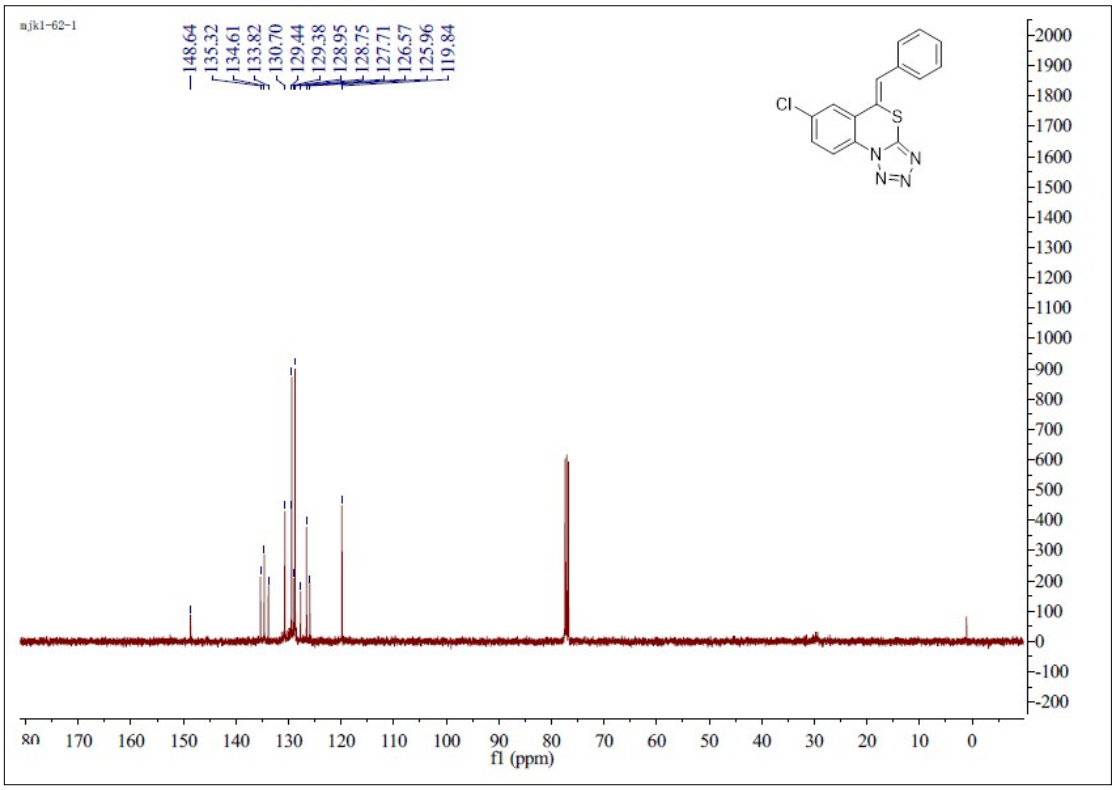
^{13}C NMR of **3h**



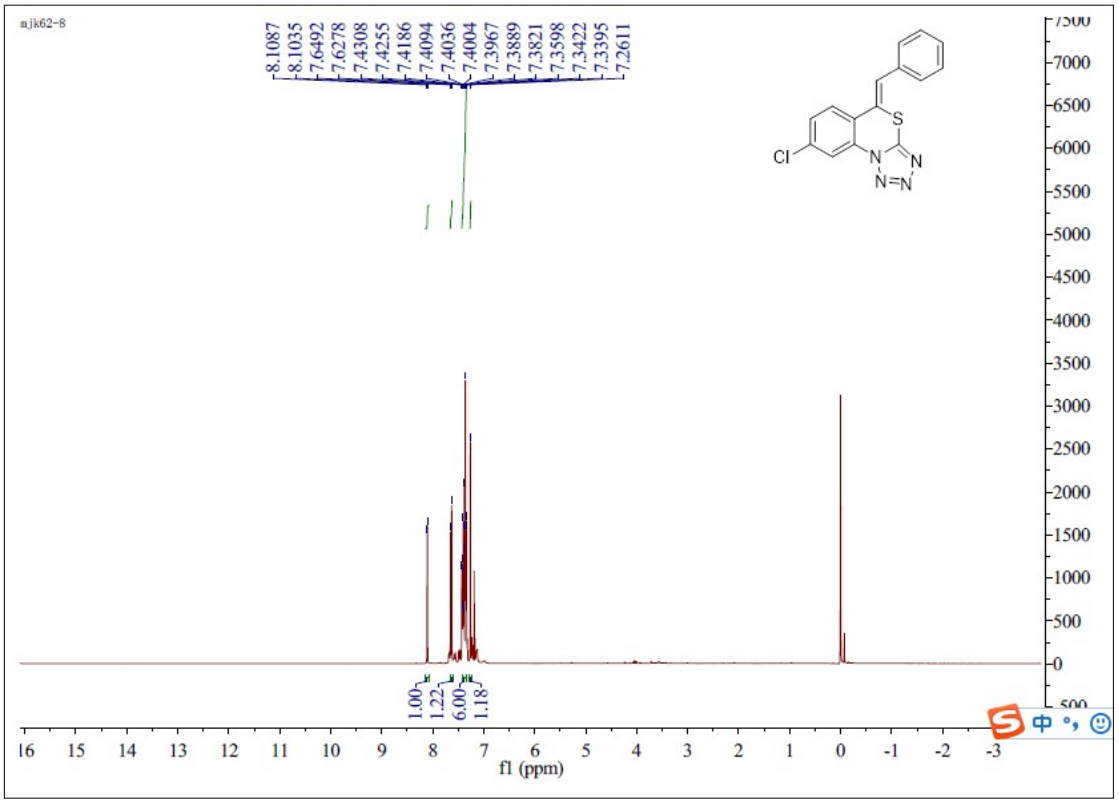
^{1}H NMR of **3i**



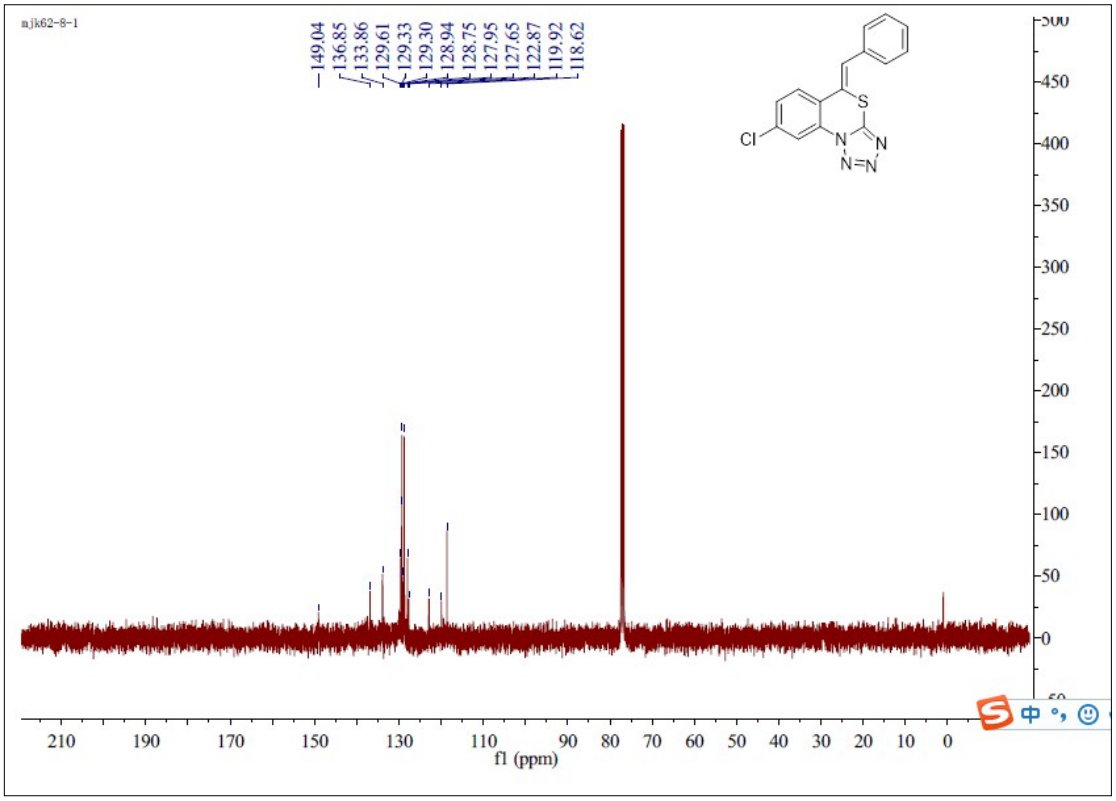
^{13}C NMR of **3i**



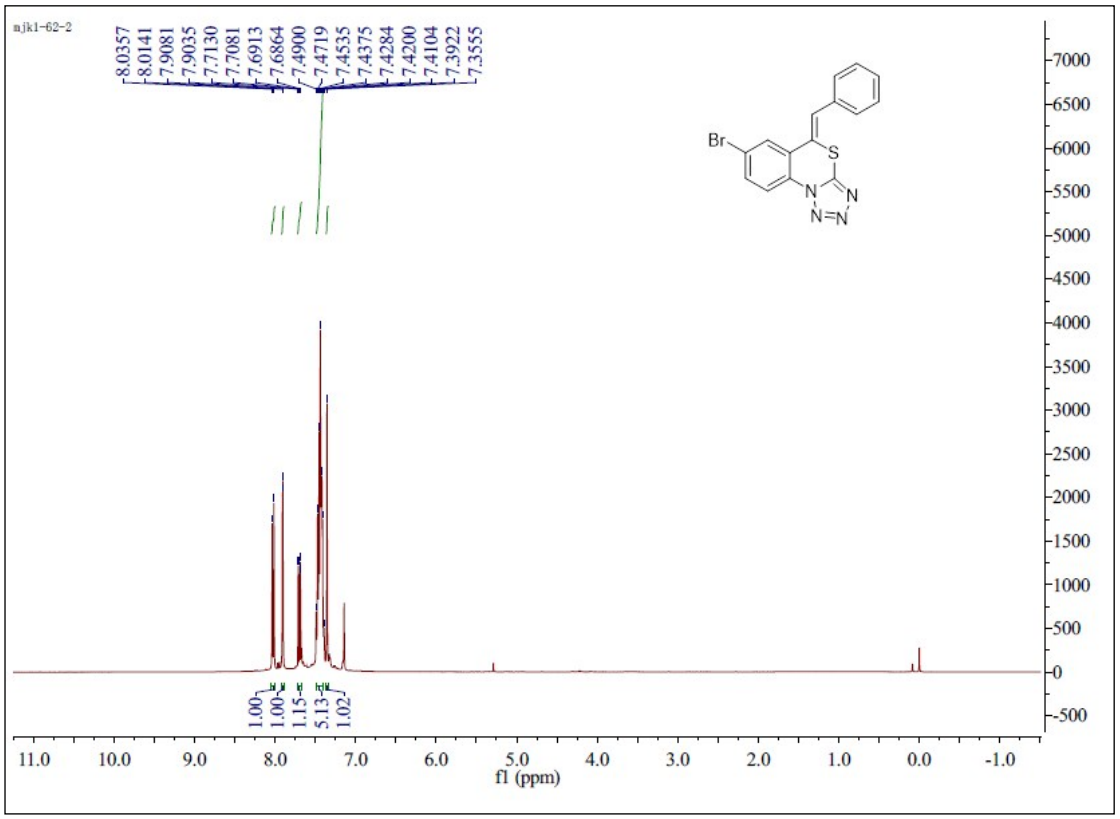
^{1}H NMR of **3j**



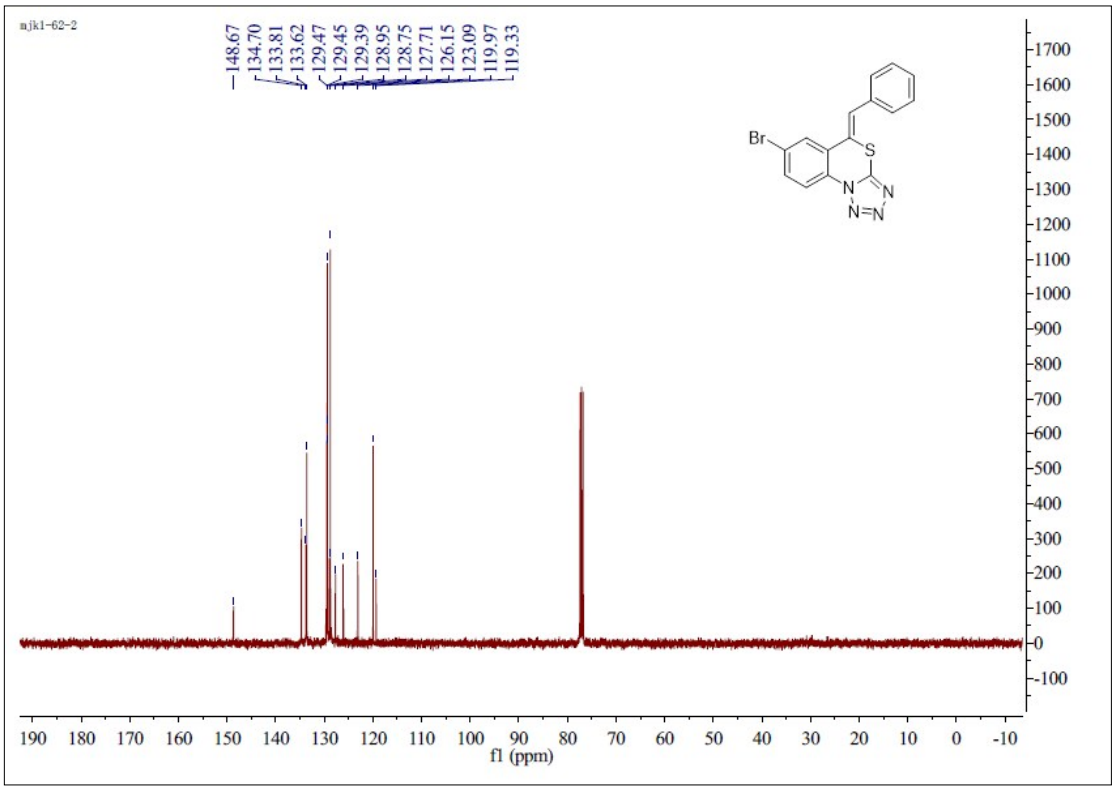
^{13}C NMR of **3j**



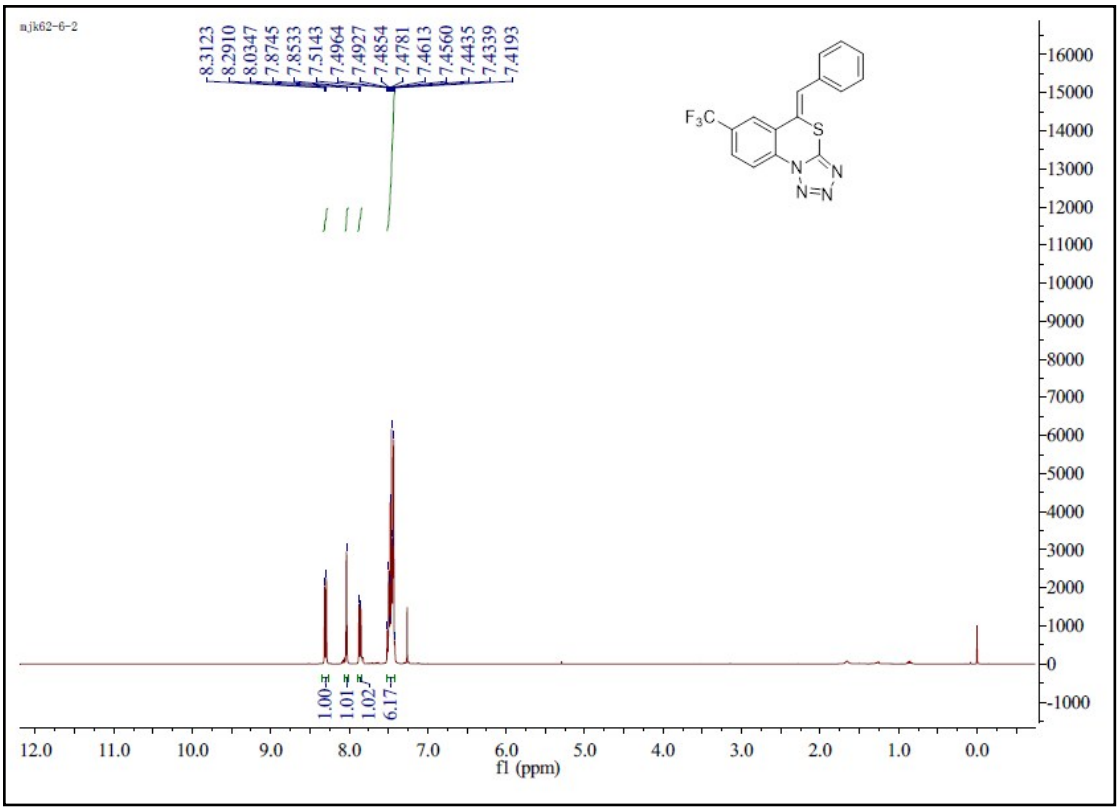
^{1}H NMR of **3k**



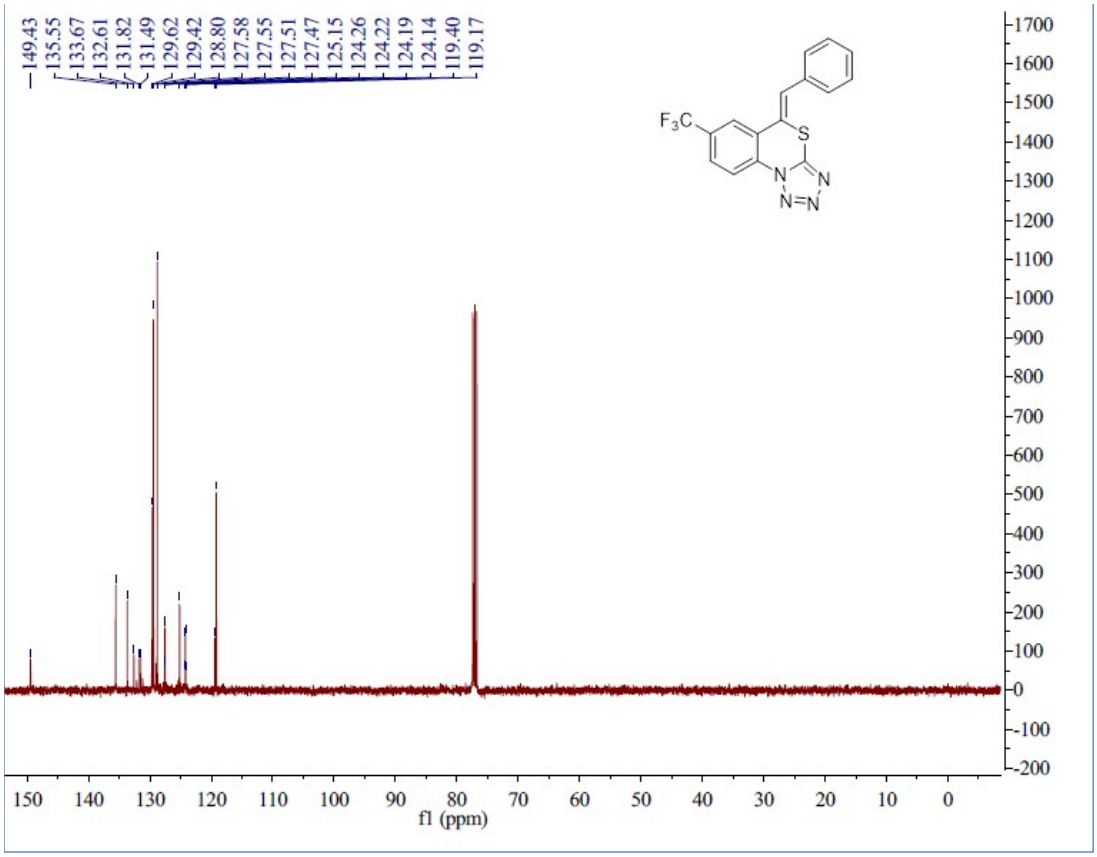
^{13}C NMR of **3k**



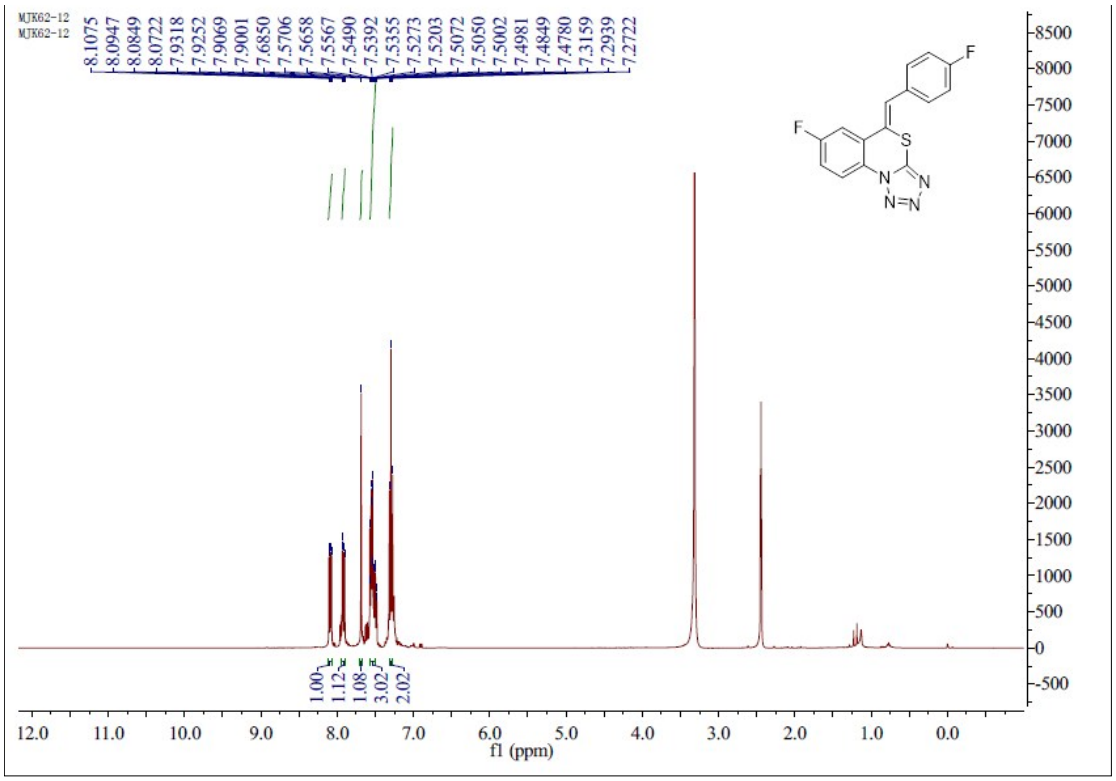
^{1}H NMR of **3l**



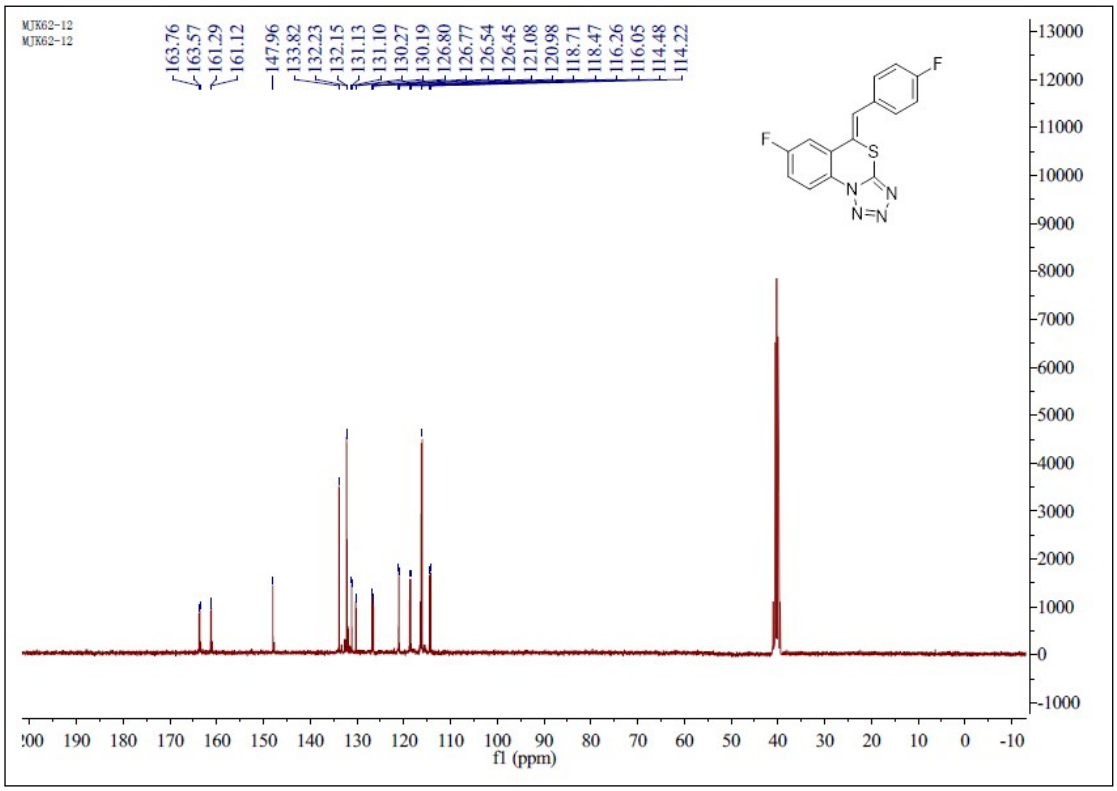
^{13}C NMR of **3l**



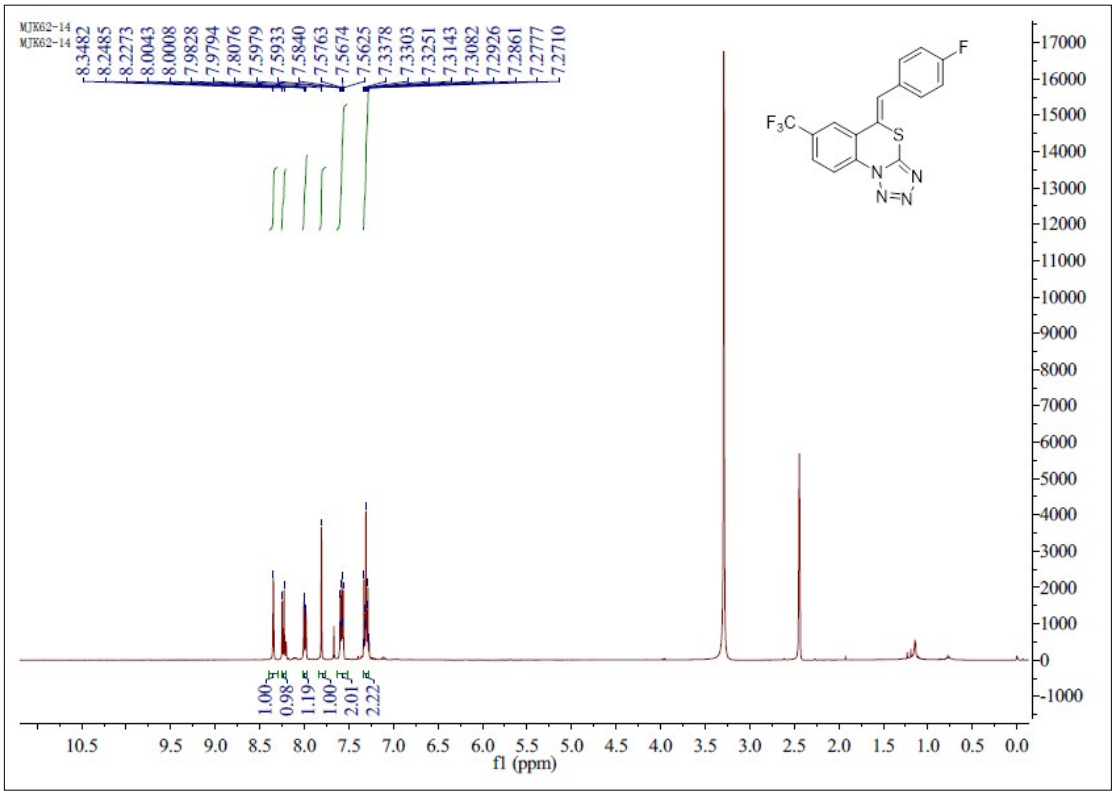
^{1}H NMR of **3m**



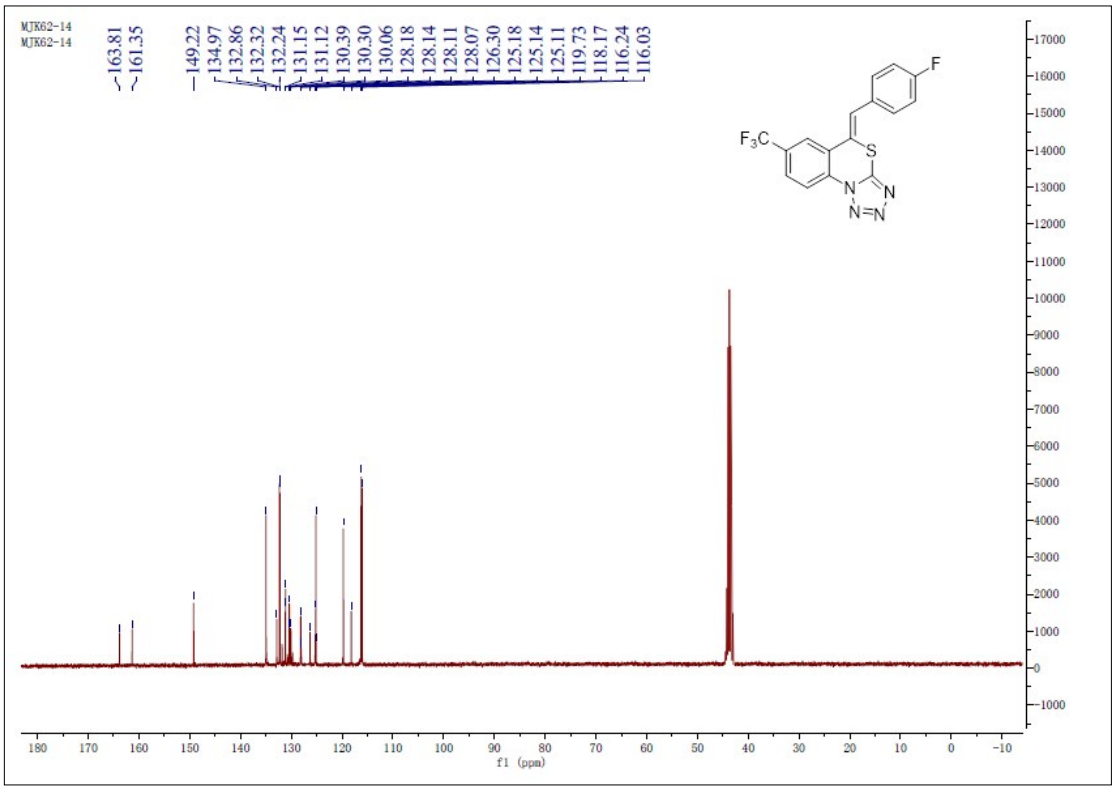
^{13}C NMR of **3m**



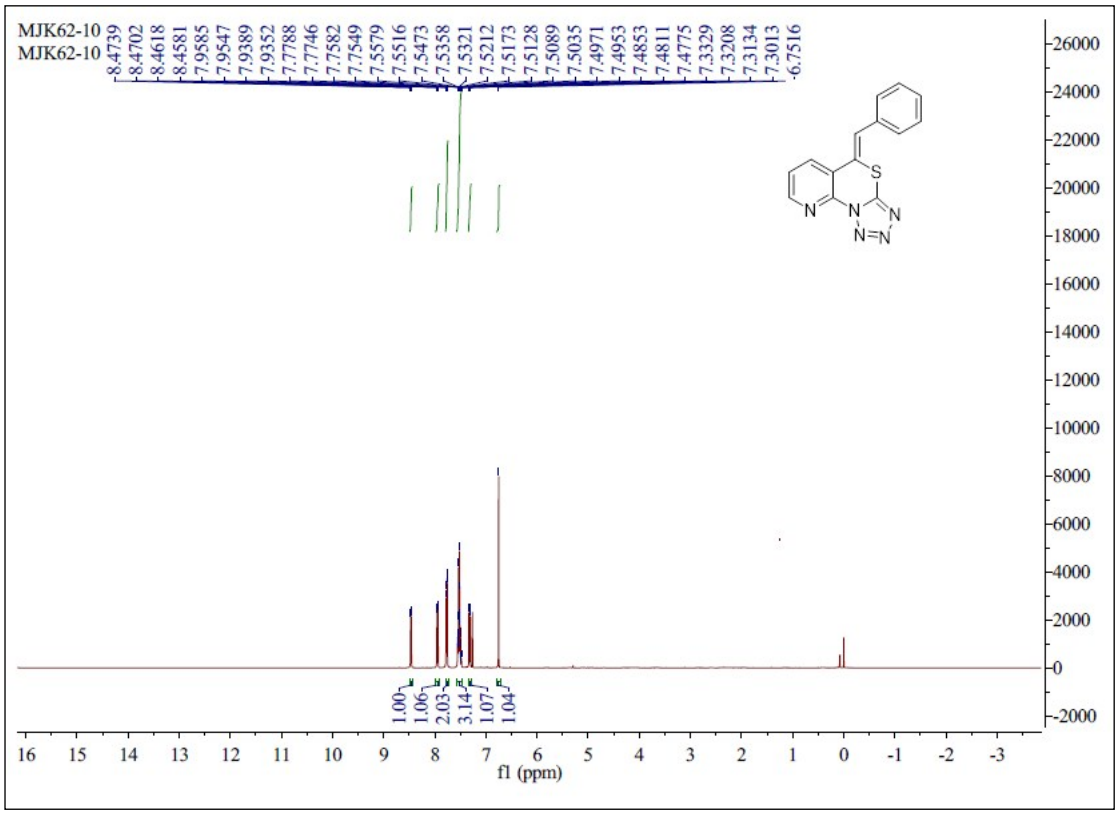
^{1}H NMR of **3n**



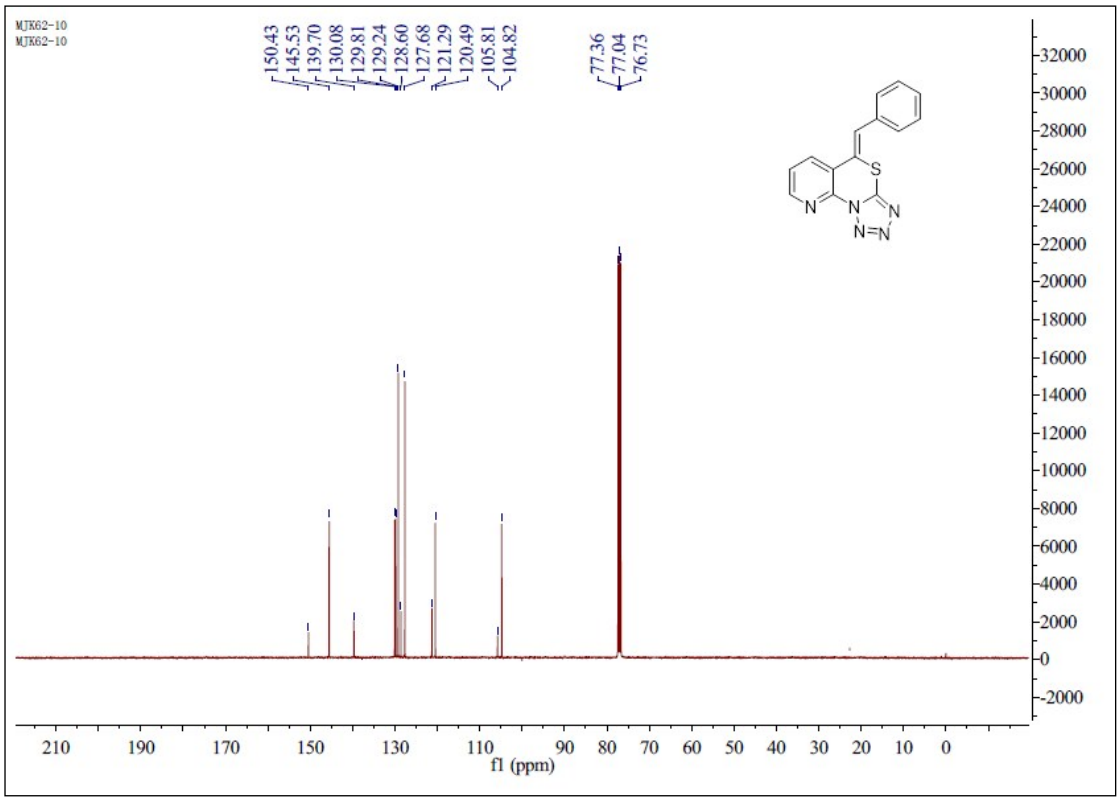
^{13}C NMR of **3n**



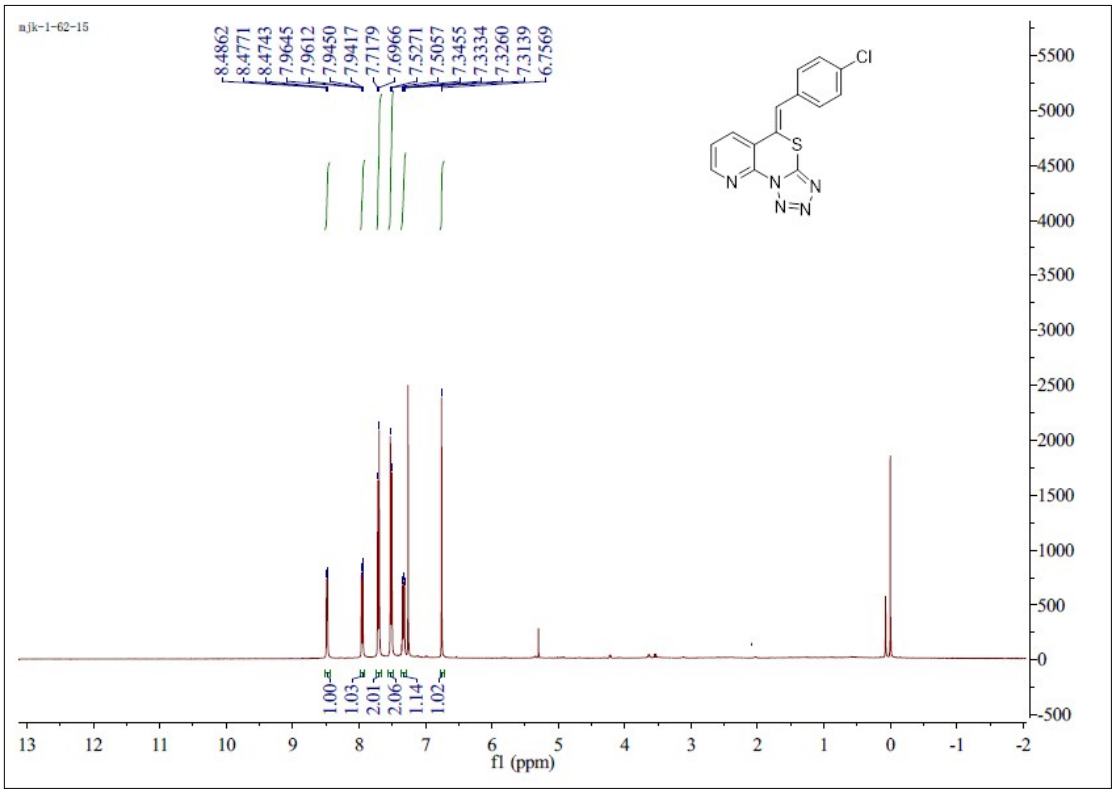
^{1}H NMR of **3o**



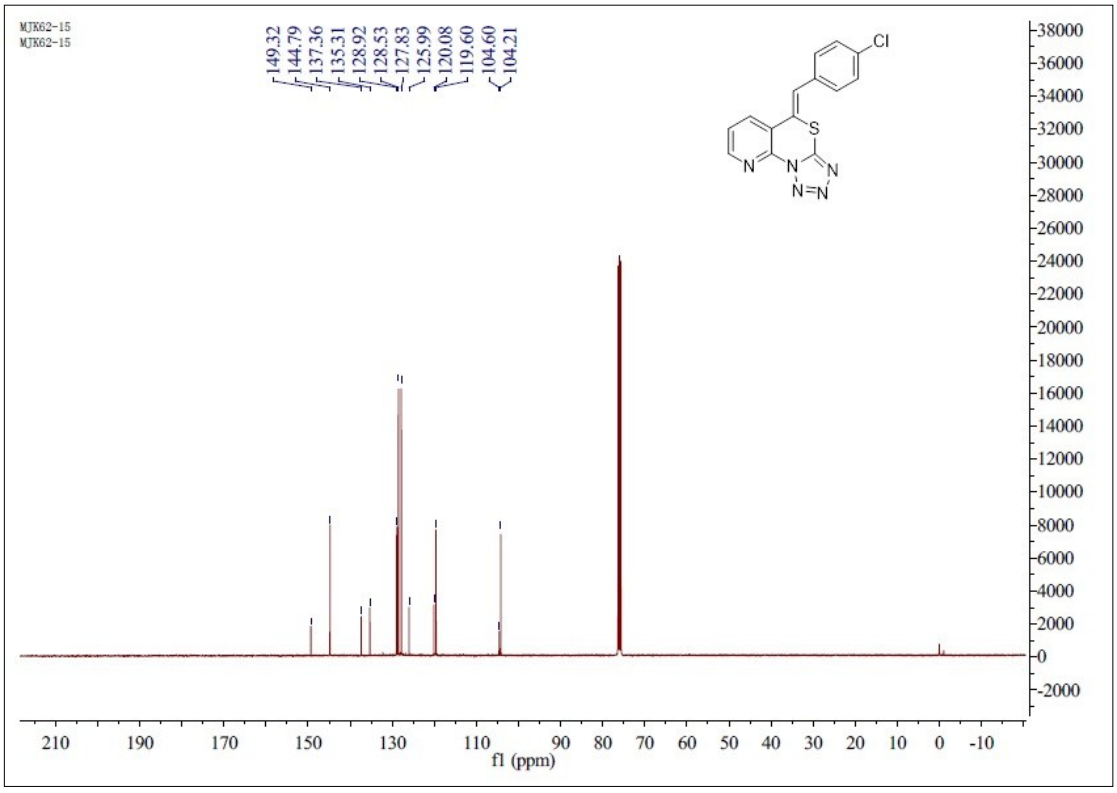
^{13}C NMR of **3o**



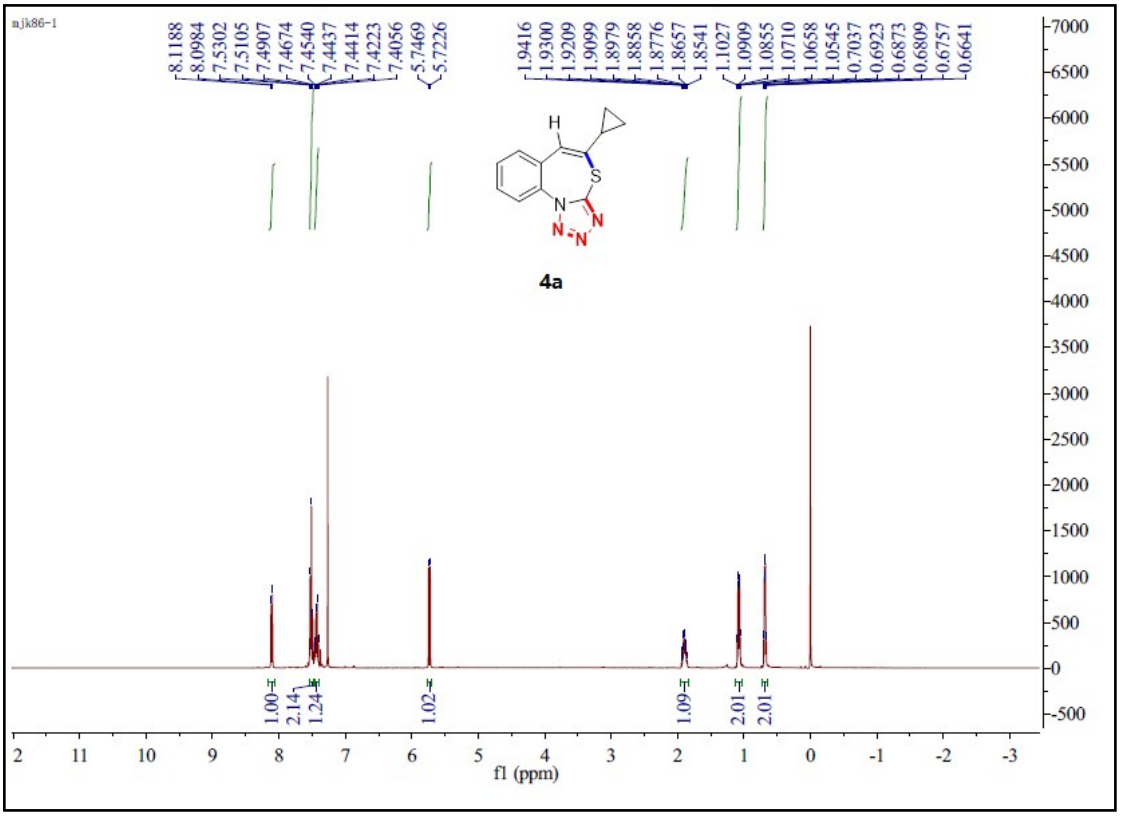
^{1}H NMR of **3p**



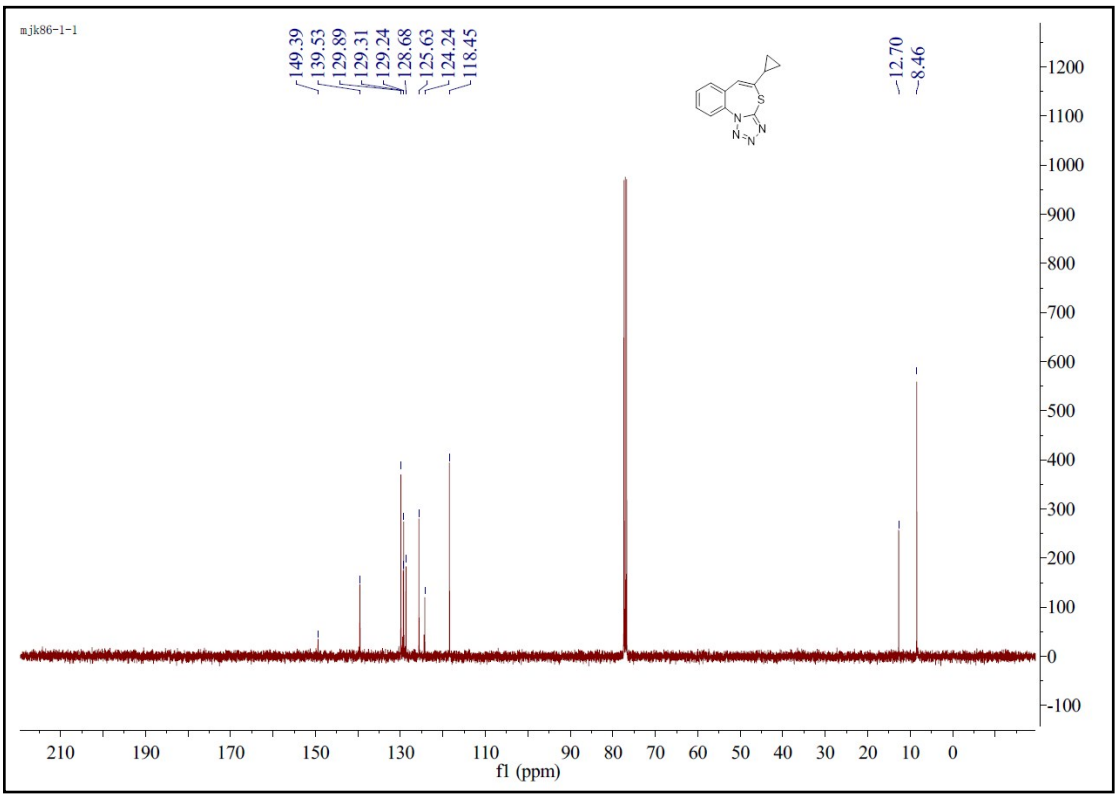
^{13}C NMR of **3p**



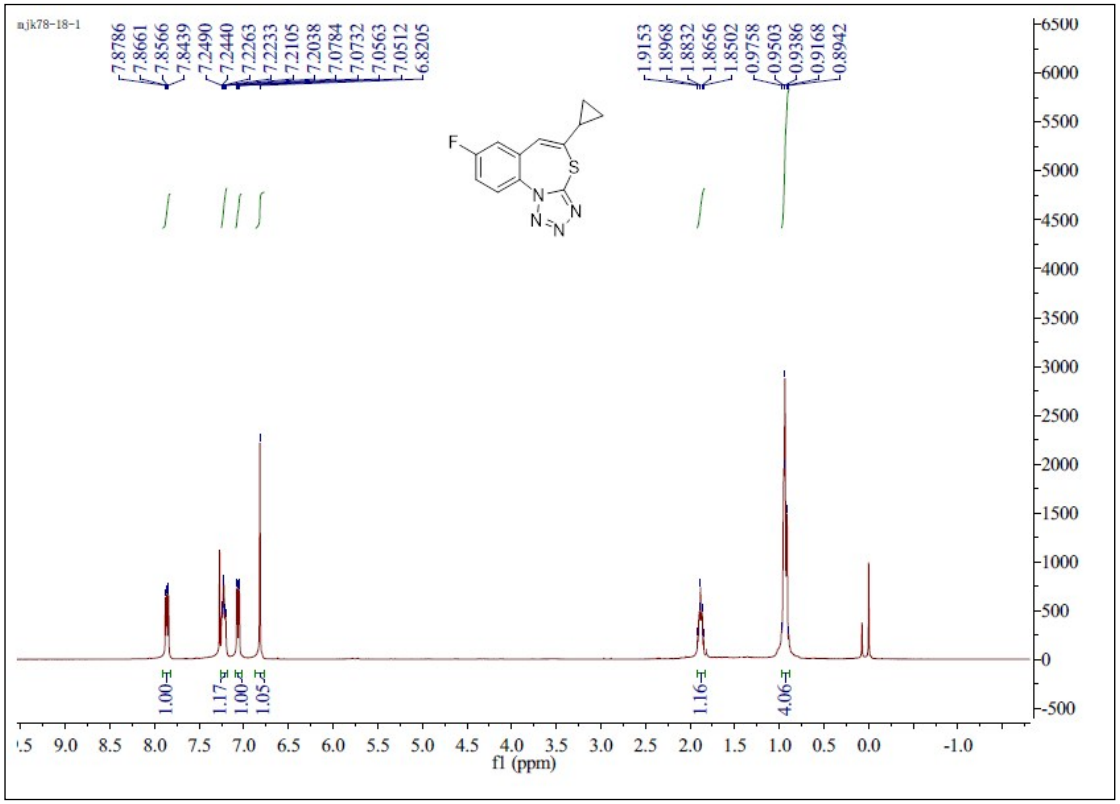
^{1}H NMR of **4a**



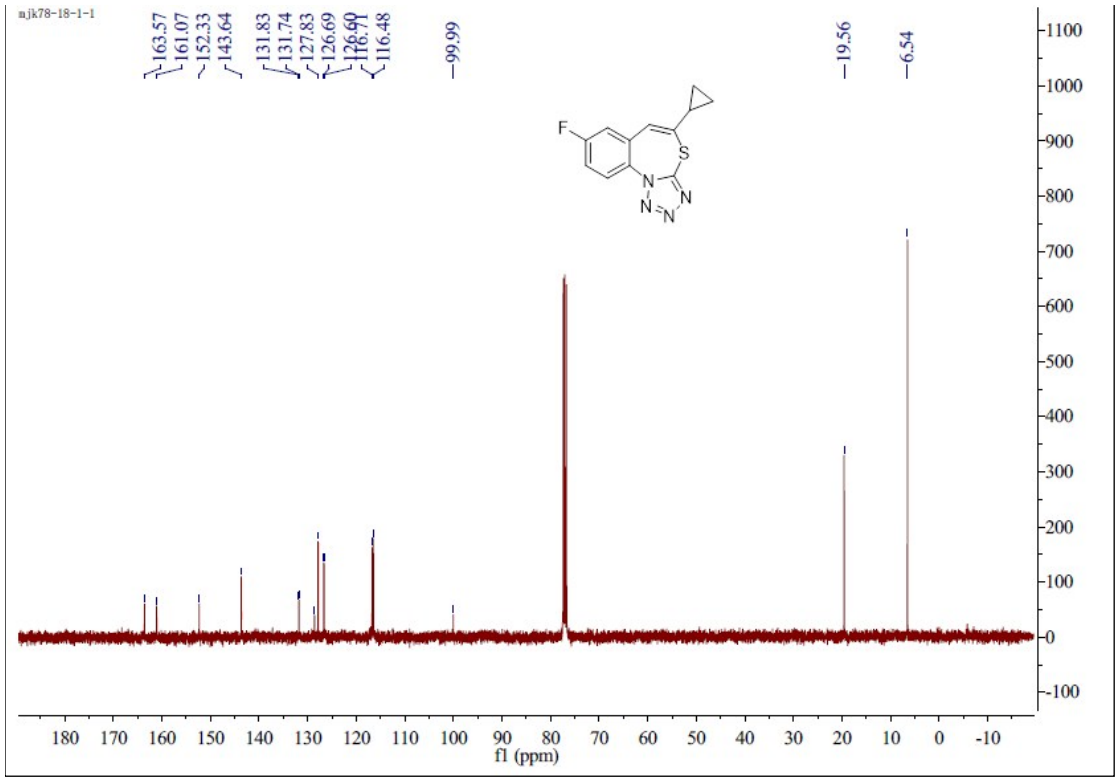
^{13}C NMR of **4a**



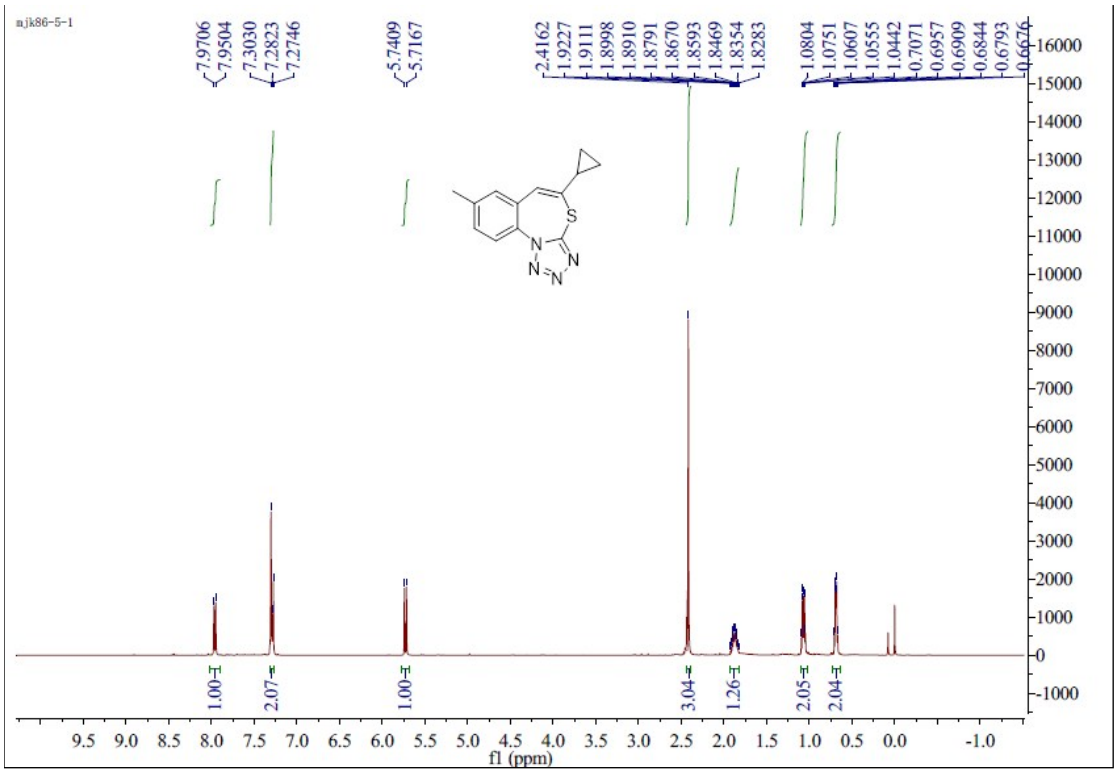
^{1}H NMR of **4b**



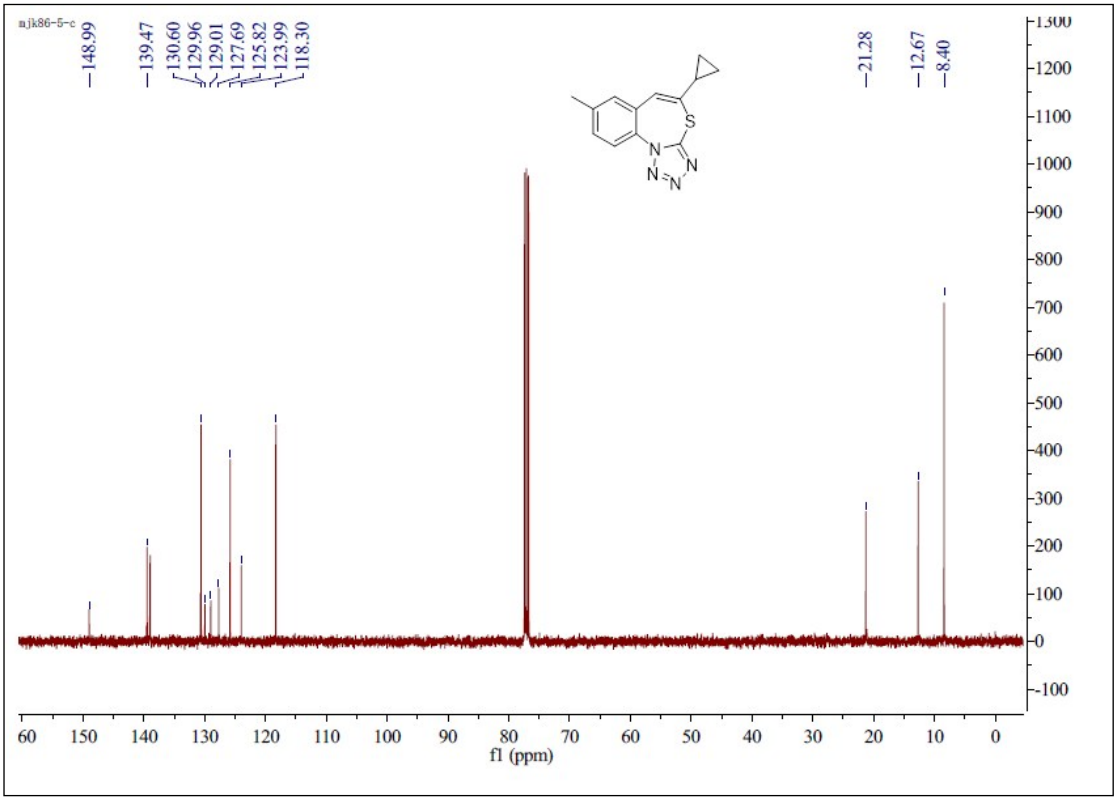
^{13}C NMR of **4b**



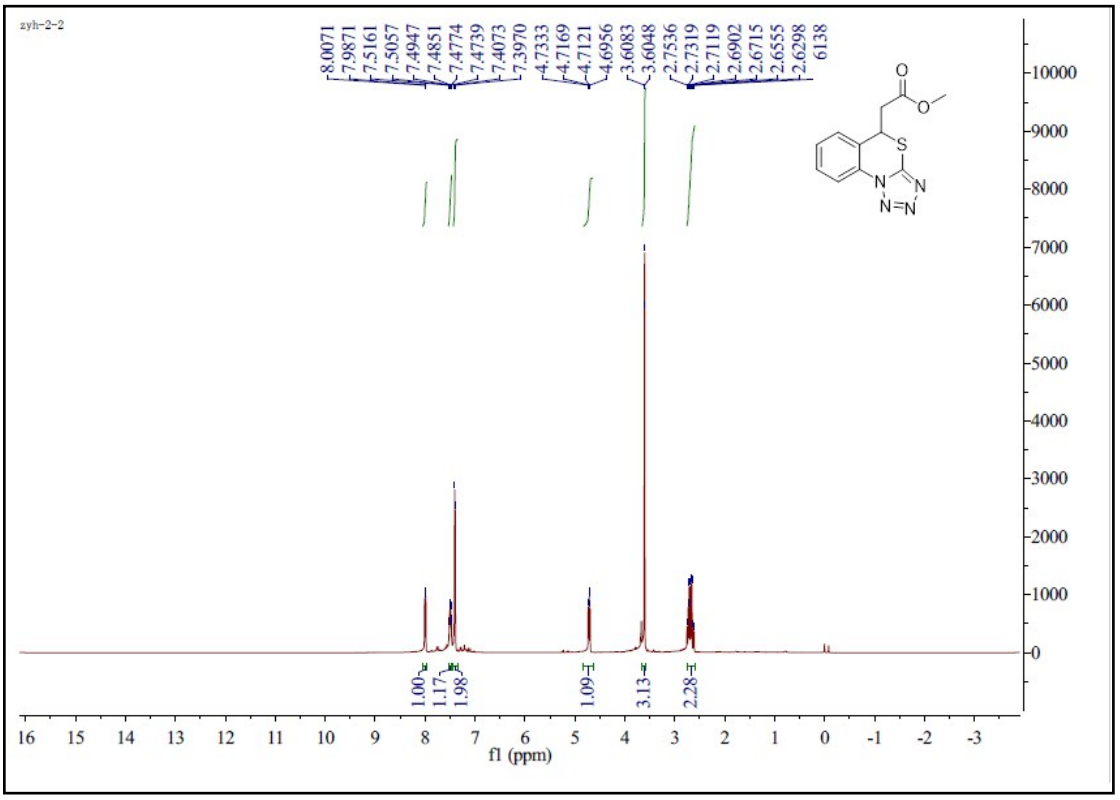
^{1}H NMR of **4c**



^{13}C NMR of **4c**



^{1}H NMR of **3a'**



^{13}C NMR of **3a'**