Supporting Information

Novel Synthesis of Thiazolo/thienoazepine-5,8-diones from Dihalo Cyclic 1,3-Diketones and Mercaptonitrile Salts

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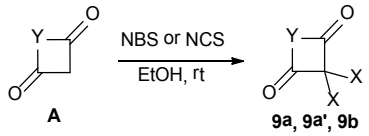
Content

1. General information

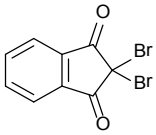
^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker AVIII-400 spectrometer at ambient temperature with $CDCl_3$ or DMSO-d_6 as the solvent. High-resolution mass spectra were recorded by Bruker Apex IV Fourier Transform Ion Cyclotron Resonance Mass Spectrometer spectrometer. All melting points were measured on a melting point apparatus with uncorrected thermometers. X-Ray crystallographic analysis was performed with a SuperNova, Dual, Cu at zero, Atlas diffractometer. The crystal was kept at 180.00(10) K during data collection. Using Olex2, the structure was solved with the Superflip structure solution program using Charge Flipping and refined with the XL refinement package using Least Squares minimization. Flash column chromatography was performed with 200-300 mesh silica gel.

2. Synthesis of dihalo cyclic 1,3-diketones 9a-f

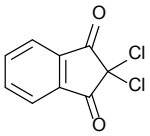


A **9a, 9a', 9b**

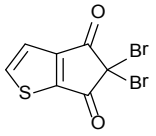
To the solution of 1,3-diketones **A** (5 mmol) in EtOH (10 mL) was added NBS or NCS (10 mmol). The mixture was stirred at room temperature for 10 min, then diluted with water (30.0 mL), and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried with anhydrous Na_2SO_4. The solvent was removed and the residue was recrystallized from EtOAc/petroleum ether.



2,2-Dibromoindane-1,3-dione (9a)[1]: Obtained in 95% yield, yellow solid; m.p. 180-181 °C (Lit.[1] 177-178 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14-8.10 (m, 2H), 8.06-8.01 (m, 2H).

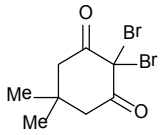


2,2-Dichloroindane-1,3-dione (9a')[2]: Obtained in 92% yield, yellow solid; m.p. 122-124 °C (Lit.[2] 125-126 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16-8.13 (m, 2H), 8.07-8.04 (m, 2H).

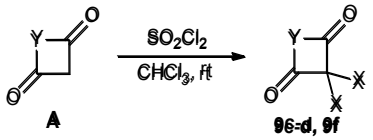


[1] R. Horcajada, B. Batanero, F. Barba and A. Martín, *Tetrahedron Lett.* 2007, **48**, 6437-6441.
[2] J.-J. Kim, D.-H. Kweon, S.-D. Cho, H.-K. Kim, S.-G. Lee and Y.-J. Yoon, *Synlett*. 2006, 194-200.

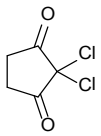
5,5-Dibromo-4H-cyclopenta[b]thiophene-4,6(5H)-dione (9b): Obtained in 87% yield from 4H-cyclopenta[b]thiophene-4,6(5H)-dione[3], yellow solid; m.p. 180-181 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 4.9 Hz, 1H), 7.53 (d, J = 4.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.5, 179.1, 149.8, 148.6, 144.9, 122.6, 55.4; IR (cm^{-1}):1754, 1712, 1376, 1269, 717, 664, 593; HRMS (ESI): *m/z* calcd for $C_7H_3Br_2O_2S$ $[M+H]^+$: 308.8215, found: 308.8217.



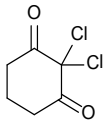
2,2-Dibromo-5,5-dimethylcyclohexane-1,3-dione (9e)[4-6]: Prepared from 5,5-dimethylcyclohexane-1,3-dione according to the literature procedure.[4] Obtained in 85% yield, white solid; m.p. 140-141 °C (Lit.[5] 140 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.02 (s, 4H), 1.02 (s, 6H).[6]



9c-d and **9f** were prepared according to the literature procedure[7]. To the solution of 1,3-diketones **A** (10 mmol) in $CHCl_3$ (20 mL) was added sulfuryl chloride (4.0 g, 30 mmol). The mixture was stirred at room temperature for 5 hours. The solvent was removed and the residue was recrystallized from EtOAc/petroleum ether.

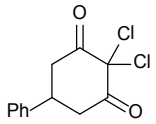


2,2-Dichlorocyclopentane-1,3-dione (9c)[7]: Obtained in 66% yield, yellow solid; m.p. 80-81 °C (Lit.[7a] 83.5 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.09 (s, 4H).



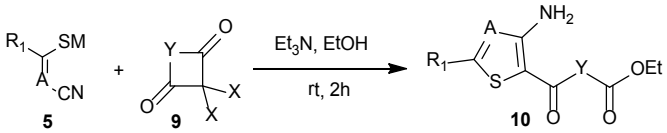
2,2-Dichlorocyclohexane-1,3-dione (9d)[8]: Obtained in 71% yield, yellow solid; m.p. 66-67 °C (Lit.[8] 68 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.05 (t, J = 6.8 Hz, 4H), 2.00 (quintet, J = 6.8 Hz, 2H).

[3] G. Sartori, F. Bigi, R. Maggi, D. Baraldi and G. Casnati, *J. Chem. Soc., Perkin Trans. 1* 1992, 2985-2988.
[4] P. Goswami, A. Baruah and B. Das, *Adv. Synth. Catal.* 2009, **351**, 1483-1487.
[5] V. V. Dabholkar and S. K. J. Mishra, *Heterocycl. Commun.* 2006, **12**, 241-246.
[6] K.-M. Kim and I.-H. Park, *Synthesis* 2004, 2641-2644.
[7] (a) J. R. Beckwith and L. P. Hager, *J. Org. Chem.* 1961, **26**, 5206-5208; (b) M. Vandewalle, N. Schamp and H. De Wilde, *Bulletin des Sociétés Chimiques Belges* 1966, **75**, 648-654.
[8] N. Schamp and M. Verzele, *Bulletin des Sociétés Chimiques Belges* 1964, **73**, 38-43.

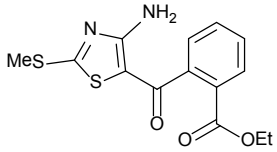


2,2-Dichloro-5-phenylcyclohexane-1,3-dione (9f)[9]: Obtained in 63% yield, yellow solid; m.p. 68-69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.21 (m, 5H), 3.51-3.44 (m, 2H), 3.26-3.18 (m, 1H), 3.14-3.10 (m, 2H).

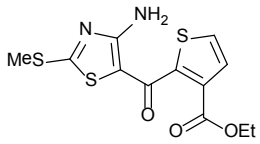
3. Preparation and characterisation data of multifunctionalized thiazoles and thiophenes 10a-l.



To the solution of dihalo cyclic 1,3-diketones **9** (0.5 mmol) in EtOH (2.0 mL) was added mercaptonitrile salt **5** (1 mmol) and Et_3N (0.5 mmol). The mixture was stirred at room temperature for 2 h, then diluted with water (20.0 mL), and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried with anhydrous Na_2SO_4. The solvent was removed and the residue was purified by a short silica gel column (EtOAc/petroleum ether, 1:5) to afford the desired product **10**.



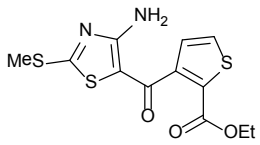
Ethyl 2-(4-amino-2-(methylthio)thiazole-5-carbonyl)benzoate (10a): Obtained in 75% yield, yellow solid; m.p. 129-130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, J = 7.7, 1.0 Hz, 1H), 7.58 (td, J = 7.5, 1.3 Hz, 1H), 7.51 (td, J = 7.6, 1.4 Hz, 1H), 7.42 (dd, J = 7.5, 1.0 Hz, 1H), 6.70 (s, 2H), 4.26 (q, J = 7.1 Hz, 2H), 2.58 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.8, 175.9, 166.1, 163.0, 142.9, 132.3, 130.5, 129.5, 128.3, 127.0, 104.1, 61.5, 16.0, 13.8; IR (cm^{-1}): 3412, 3262, 3158, 1719, 1609, 1483, 1379, 1268, 1078, 745; HRMS (ESI): *m/z* calcd for $C_{14}H_{15}N_2O_3S_2$ $[M+H]^+$: 323.0519, found: 323.0524.



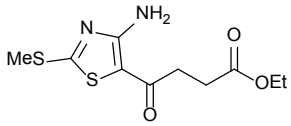
Ethyl 2-(4-amino-2-(methylthio)thiazole-5-carbonyl)thiophene-3-carboxylate (10b): Obtained in 34% yield, yellow solid; m.p. 114-115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 5.1 Hz, 1H), 7.34 (d, J = 5.1 Hz, 1H), 4.23 (q, J = 7.1 Hz, 2H), 2.61 (s, 3H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.8, 176.9, 163.4, 162.2, 147.3, 131.4, 128.7, 125.9, 105.3, 61.2, 16.0, 13.8; IR (cm^{-1}): 3422, 3317, 1713, 1600, 1474, 1377, 1262; HRMS (ESI): *m/z* calcd for $C_{12}H_{13}N_2O_3S_3$ $[M+H]^+$: 329.0083, found: 329.0089. The ^{1}H NMR spectrum of **10b** has shown

[9] E. Gudriniece, G. Vanags, A. Kurzemnieks and Z. Grants, *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.* 1960, **3**, 119-121.

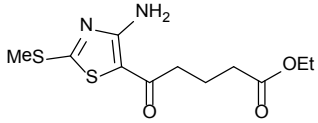
distinctive signals corresponding to 2-substituted alkyl 3-thiophenecarboxylates.[10]



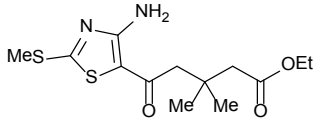
Ethyl 3-(4-amino-2-(methylthio)thiazole-5-carbonyl)thiophene-2-carboxylate (10b'): Obtained in 36% yield, yellow solid; m.p. 141-142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 5.0 Hz, 1H), 7.13 (d, J = 5.0 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 2.60 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.4, 176.4, 163.0, 161.1, 147.1, 131.6, 130.7, 127.7, 104.9, 61.6, 16.0, 13.9; IR (cm^{-1}): 3435, 3327, 1717, 1607, 1475, 1383, 1285, 1077; HRMS (ESI): *m/z* calcd for $C_{12}H_{13}N_2O_3S_3$ $[M+H]^+$: 329.0083, found: 329.0089. The ^{1}H NMR spectrum of **10b'** has shown distinctive signals corresponding to 3-substituted alkyl 2-thiophenecarboxylates.[11]



Ethyl 4-(4-amino-2-(methylthio)thiazol-5-yl)-4-oxobutanoate (10c): Obtained in 65% yield, yellow solid; m.p. 119-121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.57 (s, 2H), 4.15 (q, J = 7.0 Hz, 2H), 2.86 (t, J = 6.6 Hz, 2H), 2.69 (t, J = 6.7 Hz, 2H), 2.66 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.8, 173.6, 172.8, 162.7, 102.7, 60.7, 36.2, 28.6, 16.0, 14.2; IR (cm^{-1}): 3400, 3258, 3165, 1733, 1620, 1483, 1376, 1232; HRMS (ESI): *m/z* calcd for $C_{10}H_{15}N_2O_3S_2$ $[M+H]^+$: 275.0519, found: 275.0520.

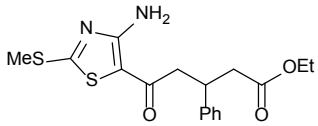


Ethyl 5-(4-amino-2-(methylthio)thiazol-5-yl)-5-oxopentanoate (10d): Obtained in 68% yield, pale yellow solid; m.p. 66-67 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (s, 2H), 4.11 (q, J = 7.1 Hz, 2H), 2.63 (s, 3H), 2.57 (t, J = 7.2 Hz, 2H), 2.37 (t, J = 7.2 Hz, 2H), 2.11-1.93 (m, 2H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.2, 173.3, 173.1, 162.8, 102.9, 60.3, 40.8, 33.4, 20.0, 15.9, 14.2; IR (cm^{-1}): 3416, 3278, 2982, 1727, 1625, 1493, 1384, 1292, 968. HRMS (ESI): *m/z* calcd for $C_{11}H_{17}N_2O_3S_2$ $[M+H]^+$: 289.0675, found: 289.0676.

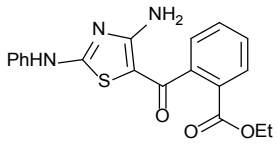


Ethyl 5-(4-amino-2-(methylthio)thiazol-5-yl)-3,3-dimethyl-5-oxopentanoate (10e): Obtained in 59% yield, pale yellow solid; m.p. 74-75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.68 (s, 2H), 4.12 (q, J = 7.1 Hz, 2H), 2.65 (s, 3H), 2.63 (s, 2H), 2.47 (s, 2H), 1.25 (t, J = 7.1 Hz, 3H), 1.20-1.08 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.4, 173.2, 172.1, 162.7, 104.6, 60.0, 52.0, 45.6, 33.8, 28.1, 16.0, 14.3; IR (cm^{-1}): 3405, 3296, 2973, 2956, 1736, 1610, 1482, 1385, 1164; HRMS (ESI): *m/z* calcd for $C_{13}H_{21}N_2O_3S_2$ $[M+H]^+$: 317.0988, found: 317.0995.

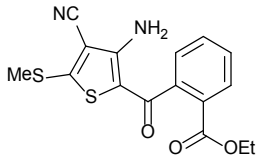
[10] H. Satonaka, *Bull. Chem. Soc. Jpn.* 1983, **56**, 3337-3342.
[11] H. Satonaka, *Bull. Chem. Soc. Jpn.* 1983, **56**, 2463-2468.



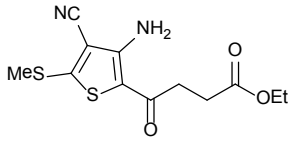
Ethyl 5-(4-amino-2-(methylthio)thiazol-5-yl)-5-oxo-3-phenylpentanoate (10f): Obtained in 52% yield, yellow solid; m.p. 61-62 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.16 (m, 5H), 6.54 (s, 2H), 4.06-3.97 (m, 2H), 3.85-3.76 (m, 1H), 2.94-2.61 (m, 7H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.6, 173.6, 171.7, 163.0, 143.1, 128.5, 127.3, 126.8, 103.1, 60.3, 48.1, 40.7, 38.2, 15.9, 14.1; IR (cm^{-1}): 3431, 3319, 2980, 2928, 1731, 1613, 1483, 1390, 701; HRMS (ESI): *m/z* calcd for $C_{17}H_{21}N_2O_3S_2$ $[M+H]^+$: 365.0988, found: 365.0992.



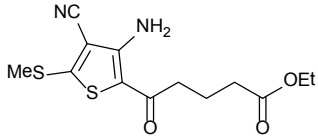
Ethyl 2-(4-amino-2-(phenylamino)thiazole-5-carbonyl)benzoate (10g): Obtained in 43% yield, yellow solid; m.p. 189-190 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.96 (d, J = 7.5 Hz, 1H), 7.54 (td, J = 7.5, 1.1 Hz, 1H), 7.48-7.40 (m, 2H), 7.36-7.31 (m, 2H), 7.30-7.24 (m, 2H), 7.14 (t, J = 7.3 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.8, 169.5, 166.4, 162.8, 143.2, 138.4, 132.2, 130.4, 129.7, 129.2, 128.4, 127.2, 125.1, 120.3, 96.2, 61.4, 13.8; IR (cm^{-1}): 3421, 3304, 1728, 1630, 1603, 1526, 1263, 749; HRMS (ESI): *m/z* calcd for $C_{19}H_{18}N_3O_3S$ $[M+H]^+$: 368.1063, found: 368.1069.



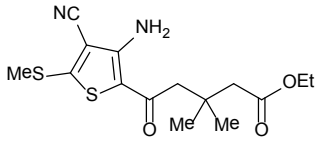
Ethyl 2-(3-amino-4-cyano-5-(methylthio)thiophene-2-carbonyl)benzoate (10h): Obtained in 82% yield, yellow solid; m.p. 169-170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, J = 7.7, 0.9 Hz, 1H), 7.65-7.52 (m, 2H), 7.41 (dd, J = 7.5, 0.9 Hz, 1H), 6.63 (s, 2H), 4.27 (q, J = 7.1 Hz, 2H), 2.54 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.6, 165.7, 161.1, 154.4, 141.8, 132.4, 130.6, 129.8, 128.5, 127.2, 112.3, 110.0, 98.6, 61.6, 17.4, 13.8.; IR (cm^{-1}): 3409, 3308, 2216, 1720, 1603, 1504, 1403, 1320, 1290, 1137, 753; HRMS (ESI): *m/z* calcd for $C_{19}H_{19}N_2O_3S$ $[M+H]^+$: 355.1111, found: 355.1117.



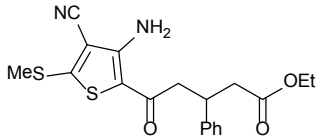
Ethyl 4-(3-amino-4-cyano-5-(methylthio)thiophen-2-yl)-4-oxobutanoate (10i): Obtained in 64% yield, yellow solid; m.p. 140-142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.53 (s, 2H), 4.16 (q, J =7.1 Hz, 2H), 2.91 (t, J = 6.5 Hz, 2H), 2.81-2.61 (m, 5H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.2, 172.9, 158.9, 154.2, 112.3, 108.6, 98.8, 60.8, 35.0, 28.3, 17.5, 14.2; IR (cm^{-1}): 3422, 3314, 2917, 2218, 1718, 1628, 1605, 1503, 1410, 1237, 1175; HRMS (ESI): *m/z* calcd for $C_{12}H_{15}N_2O_3S_2$ $[M+H]^+$: 299.0519, found: 299.0523.



Ethyl 5-(3-amino-4-cyano-5-(methylthio)thiophen-2-yl)-5-oxopentanoate (10j): Obtained in 71% yield, yellow solid; m.p. 101-102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.60 (s, 2H), 4.14 (q, J = 7.1 Hz, 2H), 2.72-2.44 (m, 5H), 2.40 (t, J = 7.2 Hz, 2H), 2.04 (m, 2H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.7, 173.1, 158.9, 154.2, 112.3, 108.8, 98.8, 60.4, 39.7, 33.3, 19.8, 17.6, 14.3; IR (cm^{-1}): 3410, 3301, 2986, 2923, 2215, 1721, 1630, 1602, 1507, 1411, 1182, 1027; HRMS (ESI): *m/z* calcd for $C_{13}H_{17}N_2O_3S_2$ $[M+H]^+$: 313.0675, found: 313.0682.

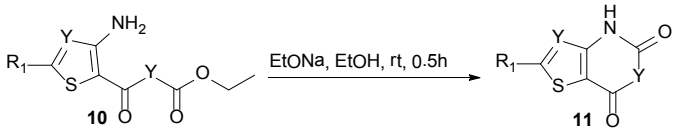


Ethyl 5-(3-amino-4-cyano-5-(methylthio)thiophen-2-yl)-3,3-dimethyl-5-oxopentanoate (10k): Obtained in 55% yield, yellow solid; m.p. 93-94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.60 (s, 2H), 4.12 (q, J = 7.1 Hz, 2H), 2.68 (m, 5H), 2.49 (s, 2H), 1.25 (t, J = 7.1 Hz, 3H), 1.16 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8, 172.1, 158.5, 154.2, 112.4, 110.2, 98. 9, 60.1, 50.4, 45.4, 33.74, 28.2, 17.5, 14.3; IR (cm^{-1}): 3418, 3312, 2971, 2211, 1701, 1633, 1600, 1506, 1412, 1363, 1301, 1239, 1041, 881; HRMS (ESI): *m/z* calcd for $C_{15}H_{21}N_2O_3S_2$ $[M+H]^+$: 341.0988, found: 341.0993.

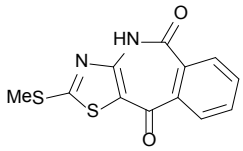


Ethyl 5-(3-amino-4-cyano-5-(methylthio)thiophen-2-yl)-5-oxo-3-phenylpentanoate (10l): Obtained in 57% yield, yellow solid; m.p. 93-94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.18 (m, 5H), 6.50 (s, 2H), 4.06-3.99 (m, 2H), 3.86-3.77 (m, 1H), 3.00-2.89 (m, 2H), 2.80-2.63 (m, 5H), 1.13 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.4, 171.8, 159.1, 154.4, 143.0, 128.7, 127.4, 127.0, 112.4, 109.2, 98.9, 50.6, 46.9, 30.7, 38.1, 17.6, 14.2; IR (cm^{-1}): 3418, 3307, 2920, 2210, 1732, 1716, 1604, 1504, 1408; HRMS (ESI): *m/z* calcd for $C_{19}H_{21}N_2O_3S_2$ $[M+H]^+$: 389.0988, found: 389.0995.

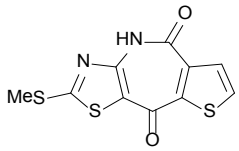
4. Preparation and characterisation data of thiazolo/thienoazepine-5,8-diones 11a-f



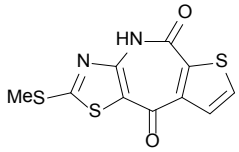
To the solution of **10** (0.2 mmol) in EtOH (2.0 mL) was added NaOEt (27 mg, 0.4 mmol). The mixture was stirred at room temperature for 0.5 h, then diluted with water and extracted with CH_2Cl_2 (3 × 8 mL). The combined organic layers were washed with brine, dried with anhydrous Na_2SO_4. Then the solvent was removed and crystallized from ethanol to afford the desired product **11**.



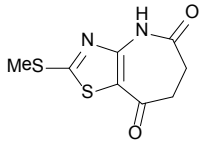
2-(Methylthio)-4H-benzo[e]thiazolo[4,5-b]azepine-5,10-dione (11a): Obtained in 93% yield, yellow solid; m.p. 224-225 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.32 (s, 1H), 8.60-8.51 (m, 1H), 8.40-8.32 (m, 1H), 8.96-7.86 (m, 2H), 2.80 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 177.4, 176.4, 163.9, 149.2, 133.5, 133.4, 133.3, 133.2, 130.9, 129.6, 118.5, 16.2; IR (cm^{-1}): 3424, 2921, 2852, 1649, 1566, 1377, 1261, 802; HRMS (ESI): *m/z* calcd for $C_{12}H_9N_2O_2S_2$ $[M+H]^+$: 277.0100, found: 277.0093.



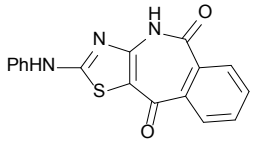
2-(Methylthio)-4H-thiazolo[4,5-b]thieno[2,3-e]azepine-5,9-dione (11b): Obtained in 95% yield, yellow solid; m.p. 185-187 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.48 (s, 1H), 8.12 (d, J = 5.2 Hz, 1H), 7.86 (d, J = 5.2 Hz, 1H), 2.78 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 177.6, 170.9, 159.6, 150.4, 146.2, 135.8, 134.2, 133.2, 117.3, 16.8; IR (cm^{-1}): 3425, 2921, 1714, 1605, 1374, 1262; HRMS (ESI): *m/z* calcd for $C_{10}H_7N_2O_2S_3$ $[M+H]^+$: 282.9664, found: 282.9668.



2-(Methylthio)-4H-thiazolo[4,5-b]thieno[3,2-e]azepine-5,9-dione (11b'): Obtained in 93% yield, pale yellow solid; m.p. 254-256 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.66 (s, 1H), 8.15 (d, J = 5.3 Hz, 1H), 7.76 (d, J = 5.3 Hz, 1H), 2.79 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 177.3, 172.0, 159.4, 149.3, 143.2, 139.2, 135.6, 130.1, 120.0, 16.7; IR (cm^{-1}): 3447, 2925, 1650, 1596, 1460, 1431, 1407; HRMS (ESI): *m/z* calcd for $C_{10}H_7N_2O_2S_3$ $[M+H]^+$: 282.9664, found: 282.9667.

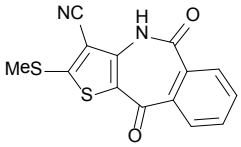


2-(Methylthio)-6,7-dihydro-4H-thiazolo[4,5-b]azepine-5,8-dione (11c): Obtained in 94% yield, white solid; m.p. 218-219 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.22 (s, 1H), 2.78 (m, 4H), 2.71 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 189.7, 175.4, 172.3, 151.3, 116.9, 34.5, 30.4, 16.2; IR (cm^{-1}): 3442, 3202, 3127, 2983, 2910, 1673, 1638, 1539, 1377, 1249; HRMS (ESI): *m/z* calcd for $C_8H_9N_2O_2S_2$ $[M+H]^+$: 229.0100, found: 229.0101.

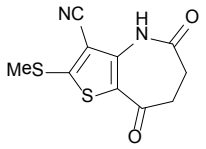


2-(Phenylamino)-4H-benzo[e]thiazolo[4,5-b]azepine-5,10-dione (11d): Obtained in 90% yield, yellow solid; m.p. > 300 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (s, 1H), 11.45 (s, 1H), 8.55 (d, J = 7.6 Hz, 1H), 8.41 (d, J = 7.8 Hz, 1H), 7.94-7.82 (m, 2H), 7.78 (d, J = 8.0 Hz, 2H), 7.39 (t, J = 7.9 Hz, 2H), 7.12 (t, J = 7.4 Hz, 1H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 175.2, 166.9, 164.3, 149.4, 139.5, 134.1, 133.6, 133.2, 132.8, 130.4, 129.5, 129.2, 123.6, 119.0, 109.8; IR (cm^{-1}): 3450, 2965, 1652, 1620, 1573, 1454, 1395; HRMS (ESI): *m/z* calcd for $C_{17}H_{11}N_3NaO_2S$ $[M+Na]^+$:

344.0464, found: 344.0465.

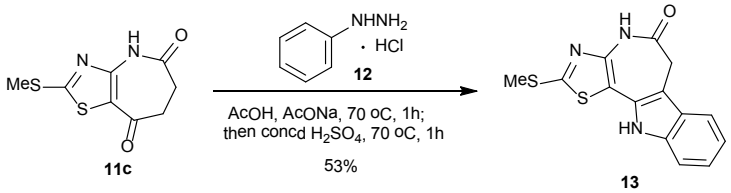


2-(Methylthio)-5,10-dioxo-5,10-dihydro-4H-benzo[e]thieno[3,2-b]azepine-3-carbonitrile (11e): Obtained in 96% yield, yellow solid; m.p. 240-242 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.56 (s, 1H), 8.46-8.39 (m, 1H), 8.32-8.26 (m, 1H), 7.96-7.87 (m, 2H), 2.83 (s, 3H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 177.9, 165.3, 165.1, 139.1, 133.8, 133.7, 133.5, 133.2, 131.0, 129.5, 123.7, 111.8, 98.9, 16.9; IR (cm^{-1}): 3433, 3212, 3128, 2220, 1661, 1583, 1561, 1526, 1393; HRMS (ESI): *m/z* calcd for $C_{14}H_9N_2O_2S_2$ $[M+H]^+$: 301.0100, found: 301.0104.



2-(Methylthio)-5,8-dioxo-5,6,7,8-tetrahydro-4H-thieno[3,2-b]azepine-3-carbonitrile (11f): Obtained in 96% yield, yellow solid; m.p. 203-204 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 2.98-2.88 (m, 4H), 2.72 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 188. 7, 172.0, 163. 8, 140.3, 122.7, 111.3, 100.2, 34.9, 30.2, 17.6; IR (cm^{-1}): 3270, 2923, 2213, 1718, 1639, 1537, 1505, 1367, 1201, 749; HRMS (ESI): *m/z* calcd for $C_{14}H_9N_2O_2S_2$ $[M+H]^+$: 301.0100, found: 301.0104.

5. Synthesis of 2-(methylthio)-6,11-dihydro-thiazolo[4',5':2,3]azepino[4,5-b]-indol- 5(4H)-one (13)



To the solution of **11c** (114 mg, 0.5 mmol) in glacial acetic acid (4 mL) was added phenylhydrazine hydrochloride (108 mg, 0.75 mmol) and sodium acetate (62 mg, 0.75 mmol). After being stirred at 70 °C for 1 h, the mixture was cooled to room temperature. Then 2 drops of concentrated sulfuric acid were added and the reaction mixture was stirred at 70 °C for another 1 h. After cooling to room temperature, the mixture was poured into a 5% aqueous sodium acetate solution (10 mL). A precipitate was formed, which was filtered off with suction and crystallized from ethanol to yield the desired product.

2-(Methylthio)-6,11-dihydro-thiazolo[4',5':2,3]azepino[4,5-b]indol-5(4H)-one (13): Obtained in 53% yield, yellow solid; m.p. 218-219 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.63 (s, 1H), 10.78 (s, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.38 (d, J = 8.1 Hz, 1H), 7.11 (m, 2H), 3.56 (s, 2H), 2.75 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.6, 164.3, 145.2, 138.5, 127.2, 126.7, 122.8, 120.0, 118.3, 111.9, 109.6, 106.0, 33.0, 16.5; IR (cm^{-1}): 3442, 3270, 1638, 1030, 742; HRMS (ESI): *m/z* calcd for $C_{14}H_{12}N_3OS_2$ $[M+H]^+$: 302.0416, found: 302.0419.

6. Crystal information of compounds 11c

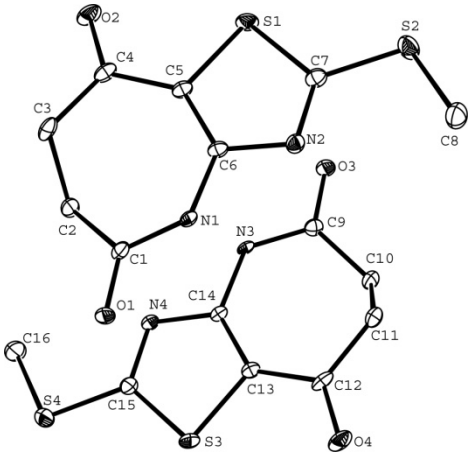


Table 1 Crystal data and structure refinement for

Identification code	
Empirical formula	$C_8H_8N_2O_2S_2$
Formula weight	228.28
Temperature/K	100.00(10)
Crystal system	triclinic
Space group	P-1
a/Å	10.3197(9)
b/Å	10.5653(9)
c/Å	10.8549(9)
α/°	117.738(9)
β/°	104.820(7)
γ/°	102.452(7)
Volume/Å^3	931.99(14)
Z	4
ρ_{calc}mg/mm^3	1.627
m/mm^{-1}	0.543
F(000)	472.0
Crystal size/mm^3	0.3 × 0.2 × 0.1
2Θ range for data collection	3.16 to 26.02°
Index ranges	$-10 \le h \le 12$, $-13 \le k \le 12$, $-11 \le l \le 13$
Reflections collected	5748
Independent reflections	3640[R(int) = 0.0559]
Data/restraints/parameters	3640/0/263
Goodness-of-fit on F^2	1.003
Final R indexes [I>=2σ (I)]	R_1 = 0.0506, wR_2 = 0.0941
Final R indexes [all data]	R_1 = 0.0785, wR_2 = 0.1109
Largest diff. peak/hole / e Å^{-3}	0.38/-0.55

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for . U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
C1	9019(3)	9492(3)	2771(4)	17.7(7)
C2	8176(4)	9157(3)	1236(4)	22.5(7)
C3	8757(4)	8453(3)	25(4)	23.1(7)
C4	8264(4)	6722(3)	-776(4)	21.0(7)
C5	8385(3)	6104(3)	173(4)	18.1(7)
C6	8840(3)	6774(3)	1707(4)	17.1(7)
C7	8464(4)	4382(3)	1041(4)	21.3(7)
C8	9362(4)	3752(4)	3170(4)	34.4(9)
C9	5487(3)	5391(3)	2194(4)	18.5(7)
C10	5696(4)	5599(3)	3700(4)	23.8(8)
C11	7177(4)	6747(3)	5005(4)	23.7(8)
C12	7321(4)	8411(3)	5783(4)	20.8(7)
C13	6736(4)	8921(3)	4806(4)	19.9(7)
C14	6067(3)	8200(3)	3262(4)	17.0(7)
C15	6227(4)	10541(3)	3920(4)	21.8(7)
C16	4939(4)	11081(4)	1793(4)	36.8(10)
N1	9278(3)	8316(3)	2870(3)	18.6(6)
N2	8902(3)	5806(2)	2219(3)	19.4(6)
N3	5688(3)	6667(3)	2111(3)	18.2(6)
N4	5774(3)	9117(2)	2743(3)	18.8(6)
O1	9452(2)	10776(2)	3954(2)	20.9(5)
O2	7816(3)	5850(2)	-2164(3)	30.5(6)
O3	5102(2)	4115(2)	1019(2)	24.2(5)
O4	7905(3)	9313(2)	7169(3)	29.0(6)
S1	7974.6(9)	4126.1(8)	-711.6(9)	24.2(2)
S2	8353.8(11)	2786.5(8)	1168.7(11)	31.8(2)
S3	6995.6(9)	10869.2(8)	5685.3(9)	22.6(2)
S4	6105.5(10)	12092.1(8)	3772.9(10)	28.1(2)

Table 3 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for . The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+...+2hka\times b\times U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	18.1(19)	20.1(15)	14.4(17)	10.0(14)	7.6(16)	4.1(13)
C2	30(2)	20.1(15)	13.1(17)	9.2(14)	4.1(17)	8.3(14)

C3	22(2)	30.7(16)	13.5(17)	15.0(15)	2.8(16)	4.2(14)
C4	15.8(19)	31.6(16)	13.4(17)	11.8(15)	4.8(16)	8.3(14)
C5	15.4(19)	21.2(15)	13.3(17)	7.4(14)	5.1(16)	5.5(13)
C6	14.6(19)	17.9(14)	12.6(17)	5.6(13)	4.7(15)	3.7(12)
C7	19(2)	21.4(15)	17.6(18)	8.6(14)	6.8(16)	4.8(13)
C8	44(3)	30.0(17)	26(2)	17.5(17)	9(2)	12.5(17)
C9	16.0(19)	20.7(15)	14.2(17)	8.2(14)	3.3(16)	6.5(13)
C10	32(2)	22.8(15)	16.2(18)	12.1(15)	8.3(18)	9.6(15)
C11	30(2)	27.1(16)	16.8(18)	14.9(15)	7.3(18)	12.3(15)
C12	15.8(19)	31.3(16)	10.7(17)	10.7(15)	4.5(16)	4.7(14)
C13	24(2)	19.4(15)	12.4(17)	7.3(14)	5.9(16)	7.6(14)
C14	19.2(19)	19.5(14)	12.8(16)	8.8(13)	7.8(16)	7.4(13)
C15	27(2)	20.2(15)	21.1(19)	11.6(15)	14.4(18)	8.7(14)
C16	57(3)	31.8(18)	20(2)	14.5(17)	10(2)	19.7(19)
N1	27.6(18)	17.4(13)	5.9(14)	5.7(12)	3.2(14)	7.1(11)
N2	20.3(17)	20.0(13)	15.8(15)	10.0(12)	5.2(14)	6.9(11)
N3	25.8(18)	18.4(13)	5.9(14)	5.1(12)	4.7(14)	7.1(11)
N4	23.5(17)	18.8(12)	11.2(14)	7.3(12)	5.5(13)	7.7(11)
O1	27.7(14)	15.6(10)	11.0(12)	4.2(9)	4.1(11)	6.1(9)
O2	35.6(17)	34.2(12)	12.8(13)	9.9(11)	7.5(13)	9.2(11)
O3	32.6(16)	20.5(10)	13.5(12)	6.9(10)	6.1(12)	10.2(10)
O4	30.2(16)	32.5(12)	11.4(13)	9.5(11)	1.9(12)	4.8(11)
S1	28.6(6)	19.6(4)	12.0(4)	2.8(3)	4.1(4)	7.9(4)
S2	41.4(6)	17.6(4)	25.2(5)	9.4(4)	5.4(5)	8.7(4)
S3	28.2(6)	18.6(4)	10.9(4)	3.7(3)	5.5(4)	6.0(3)
S4	38.5(6)	19.8(4)	21.7(5)	10.2(4)	9.4(5)	10.6(4)

Table 4 Bond Lengths for .

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C1	C2	1.495(4)	C9	C10	1.494(4)
C1	N1	1.371(3)	C9	N3	1.368(3)
C1	O1	1.230(3)	C9	O3	1.229(3)
C2	C3	1.525(4)	C10	C11	1.519(5)
C3	C4	1.501(4)	C11	C12	1.505(4)
C4	C5	1.448(4)	C12	C13	1.457(4)
C4	O2	1.225(4)	C12	O4	1.220(4)
C5	C6	1.362(4)	C13	C14	1.363(4)
C5	S1	1.735(3)	C13	S3	1.738(2)
C6	N1	1.388(3)	C14	N3	1.389(3)
C6	N2	1.379(3)	C14	N4	1.377(3)

C7	N2	1.312(4)	C15	N4	1.310(4)
C7	S1	1.708(3)	C15	S3	1.705(3)
C7	S2	1.737(3)	C15	S4	1.746(3)
C8	S2	1.779(4)	C16	S4	1.787(4)

Table 5 Bond Angles for .

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
N1	C1	C2	118.9(2)	C12	C11	C10	113.7(3)
O1	C1	C2	122.2(2)	C13	C12	C11	117.1(3)
O1	C1	N1	118.8(3)	O4	C12	C11	122.4(3)
C1	C2	C3	116.2(3)	O4	C12	C13	120.5(3)
C4	C3	C2	113.0(2)	C12	C13	S3	117.5(2)
C5	C4	C3	117.0(3)	C14	C13	C12	133.3(2)
O2	C4	C3	122.6(3)	C14	C13	S3	109.1(2)
O2	C4	C5	120.3(3)	C13	C14	N3	129.2(3)
C4	C5	S1	117.8(2)	C13	C14	N4	116.5(2)
C6	C5	C4	133.1(3)	N4	C14	N3	114.2(3)
C6	C5	S1	109.0(2)	N4	C15	S3	117.0(2)
C5	C6	N1	129.8(3)	N4	C15	S4	123.9(3)
C5	C6	N2	116.6(2)	S3	C15	S4	119.16(17)
N2	C6	N1	113.5(3)	C1	N1	C6	128.7(3)
N2	C7	S1	116.5(2)	C7	N2	C6	108.9(3)
N2	C7	S2	124.2(2)	C9	N3	C14	128.9(3)
S1	C7	S2	119.31(17)	C15	N4	C14	108.8(3)
N3	C9	C10	118.6(2)	C7	S1	C5	89.00(13)
O3	C9	C10	122.7(2)	C7	S2	C8	99.90(15)
O3	C9	N3	118.7(3)	C15	S3	C13	88.70(14)
C9	C10	C11	116.1(2)	C15	S4	C16	100.74(15)

Table 6 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for .

Atom	*x*	*y*	*z*	U(eq)
H2A	8139	10139	1368	27
H2B	7164	8438	847	27
H3A	8429	8707	-741	28
H3B	9834	8930	514	28
H8A	10339	4461	3476	52
H8B	9438	2982	3418	52
H8C	8863	4345	3719	52
H10A	5524	4575	3565	29
H10B	4944	5940	4000	29

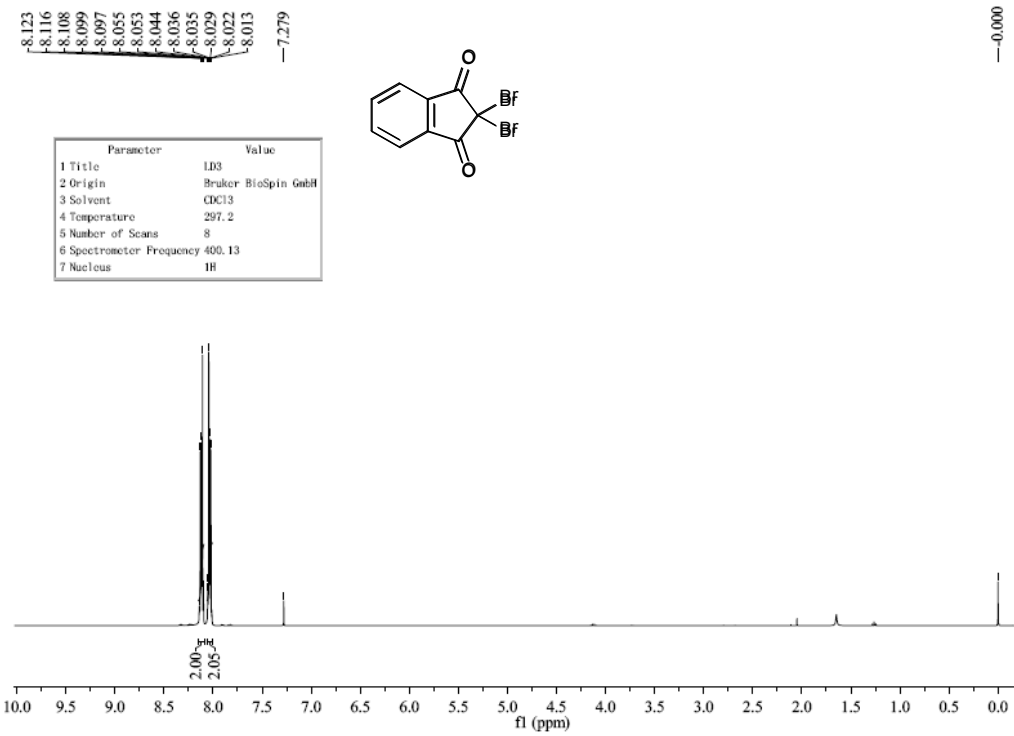
H11A	7356	6471	5771	28
H11B	7936	6651	4605	28
H16A	5277	10310	1184	55
H16B	4959	11823	1489	55
H16C	3941	10555	1619	55
H1	9610(30)	8490(30)	3700(40)	7(7)
H3	5570(40)	6530(30)	1310(40)	13(8)

Crystal Data for $C_8H_8N_2O_2S_2$ (M =228.28): triclinic, space group P-1 (no. 2), a = 10.3197(9) Å, b = 10.5653(9) Å, c = 10.8549(9) Å, α = 117.738(9)°, β = 104.820(7)°, γ = 102.452(7)°, V = 931.99(14) Å^3, Z = 4, T = 180.00(10) K, μ(Mo Kα) = 0.543 mm^{-1}, *Dcalc* = 1.627 g/mm^3, 5748 reflections measured (6.32 ≤ 2Θ ≤ 52.04), 3640 unique (R_{int} = 0.0559) which were used in all calculations. The final R_1 was 0.0506 (>2sigma(I)) and wR_2 was 0.1109 (all data).

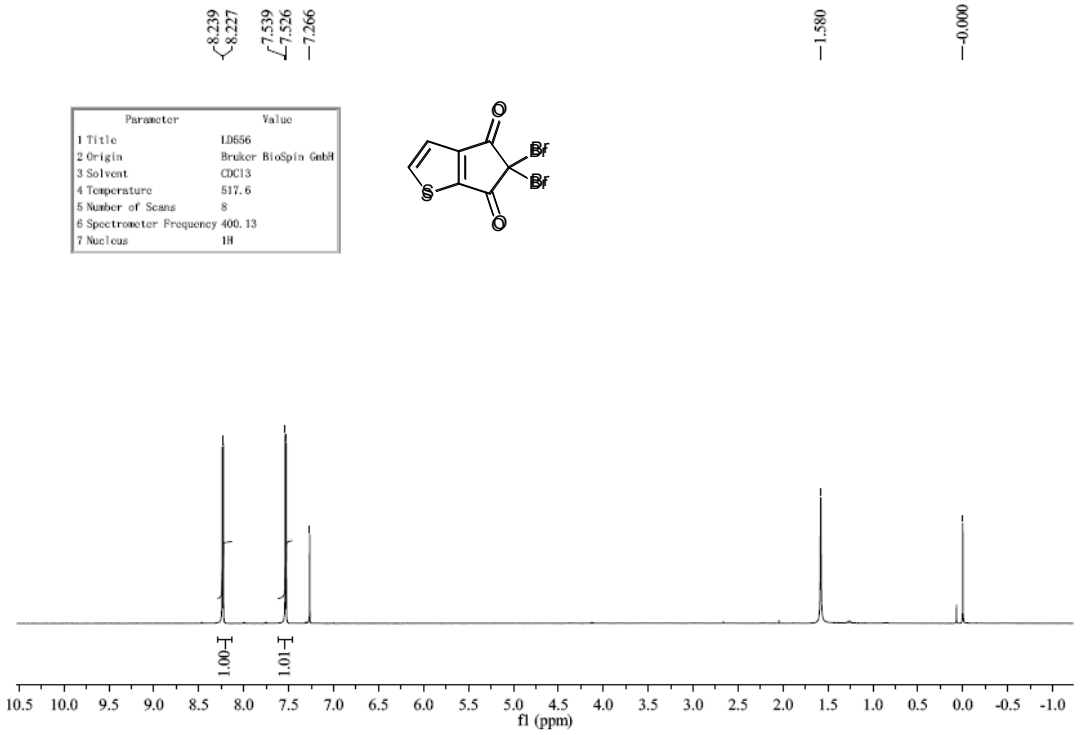
This report has been created with Olex2, compiled on Nov 5 2012 18:22:26. Please let us know if there are any errors or if you would like to have additional featrues.

7. ^{1}H NMR and ^{13}C NMR spectra

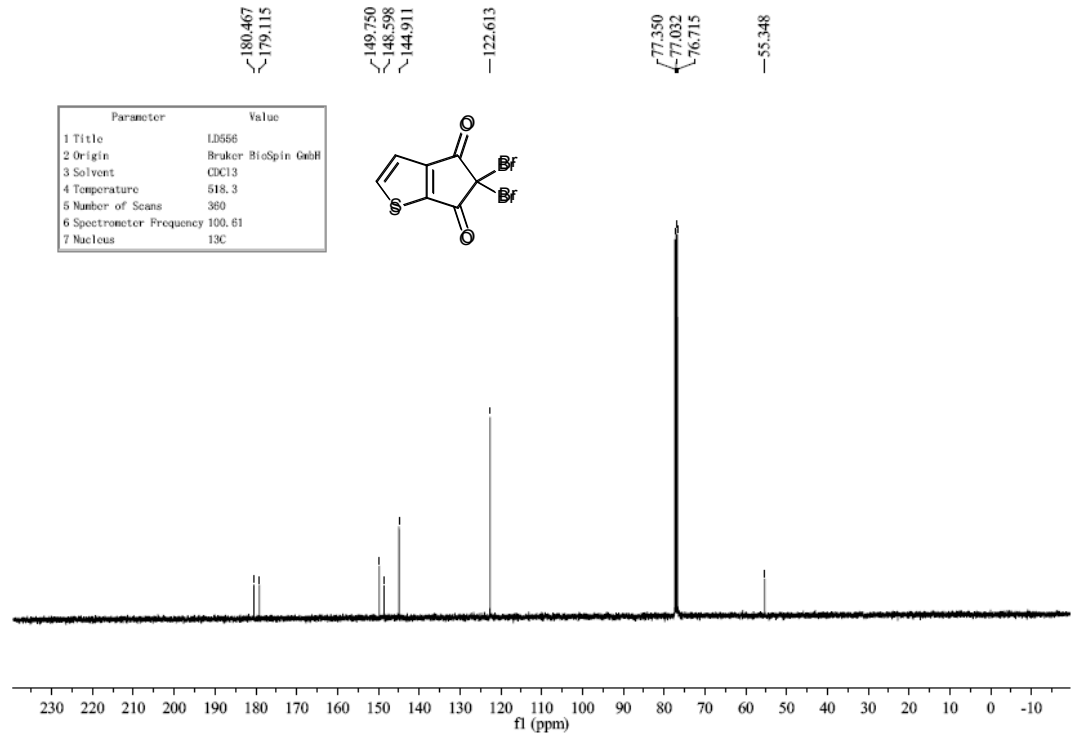
^{1}H NMR (400 MHz, $CDCl_3$) of **9a**



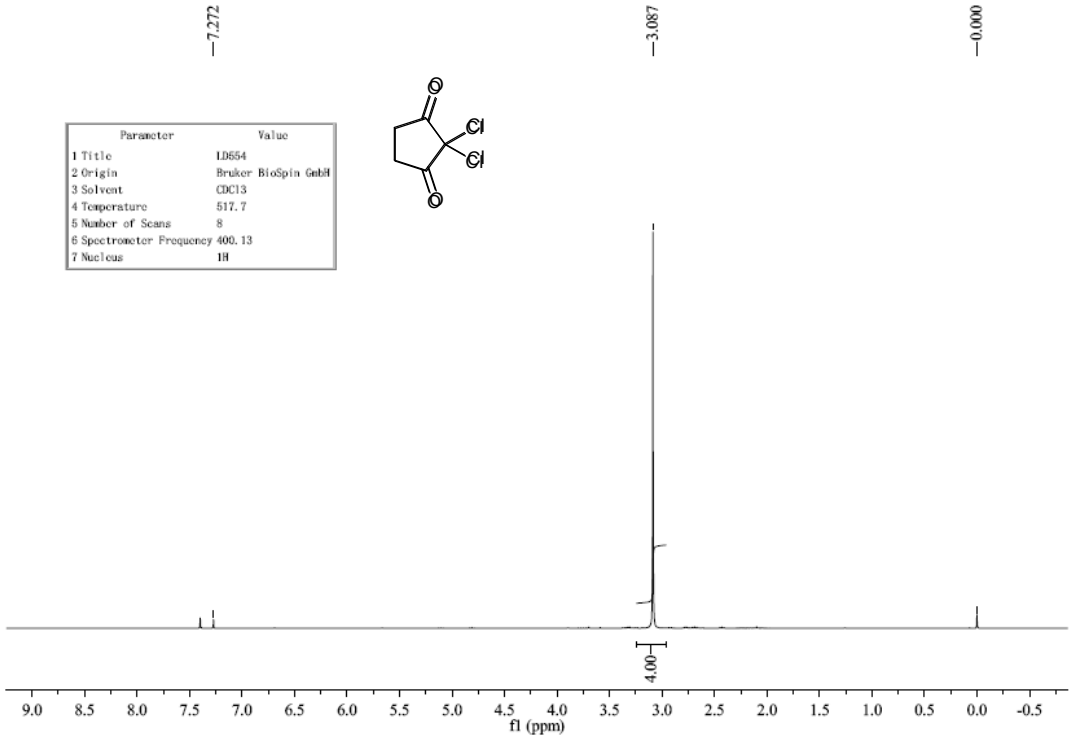
^{1}H NMR (400 MHz, $CDCl_3$) of **9b**



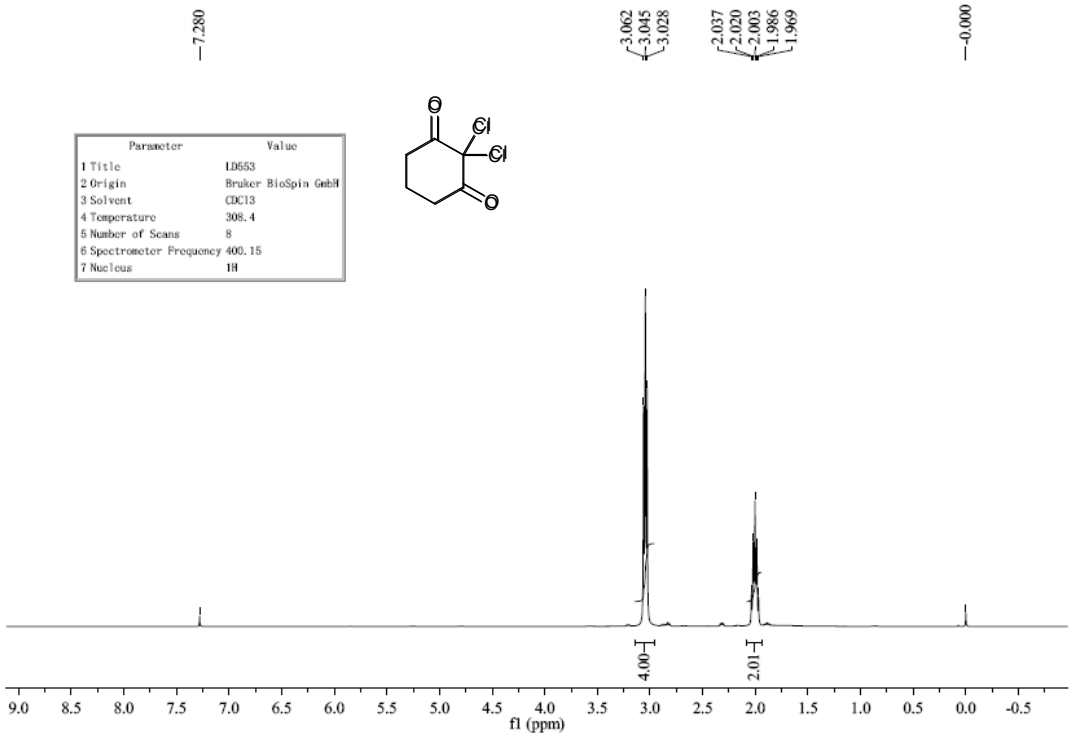
^{13}C NMR (101 MHz, $CDCl_3$) of **9b**



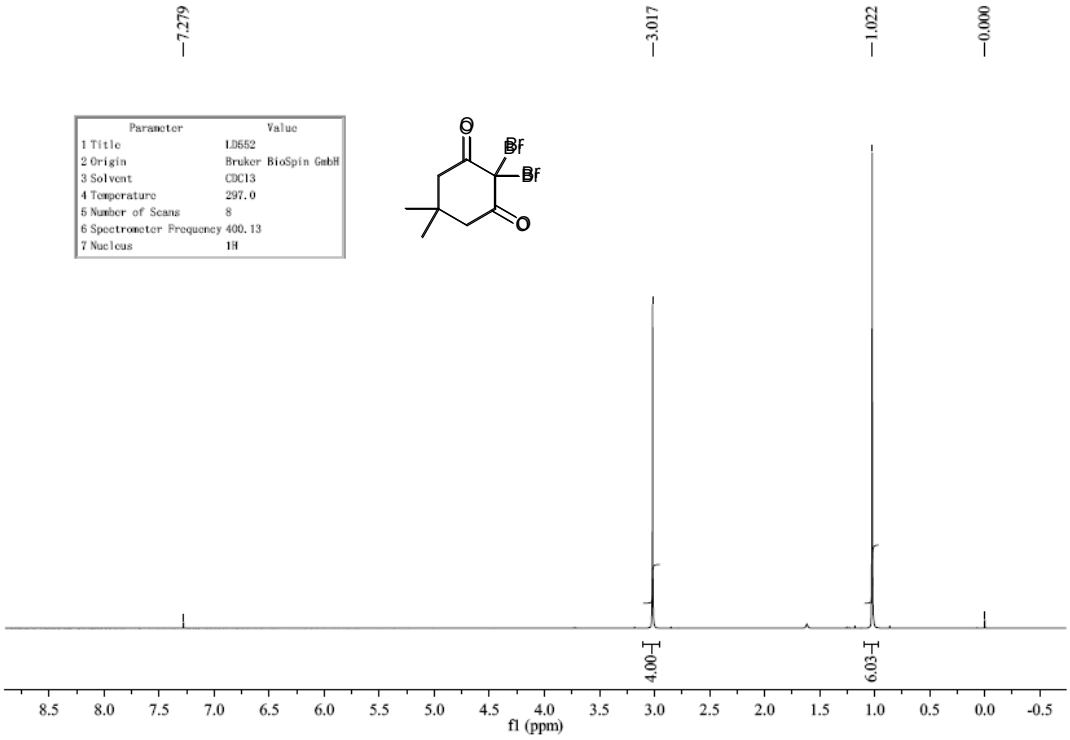
^{1}H NMR (400 MHz, $CDCl_3$) of **9c**



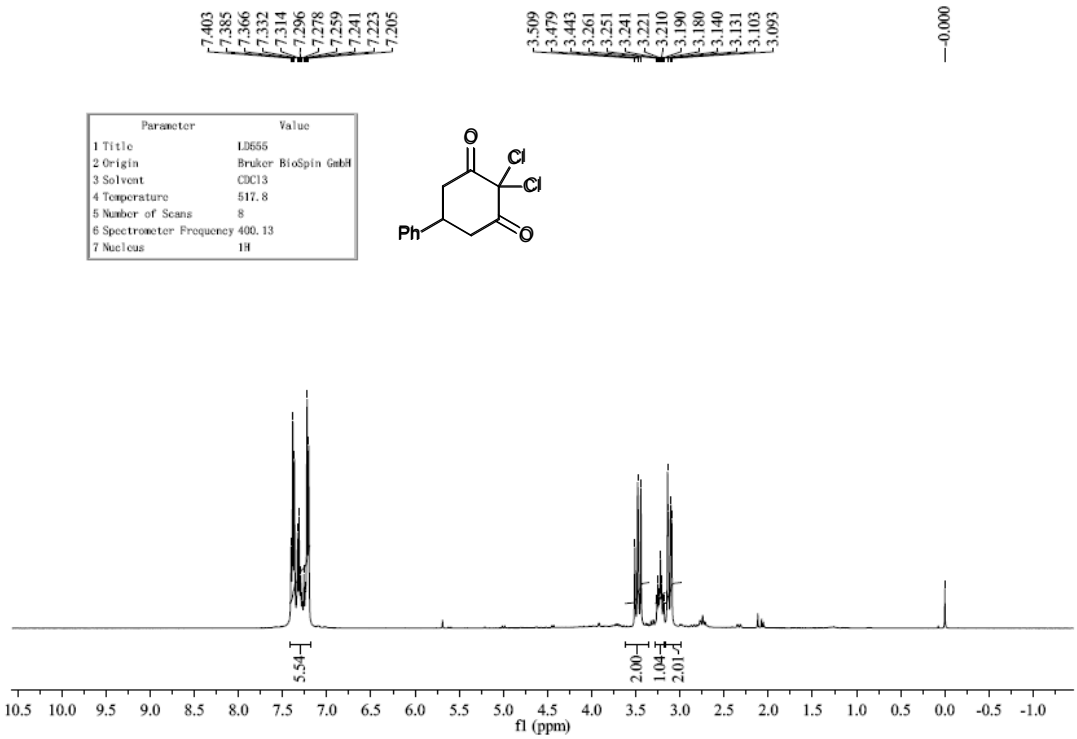
^{1}H NMR (400 MHz, $CDCl_3$) of **9d**



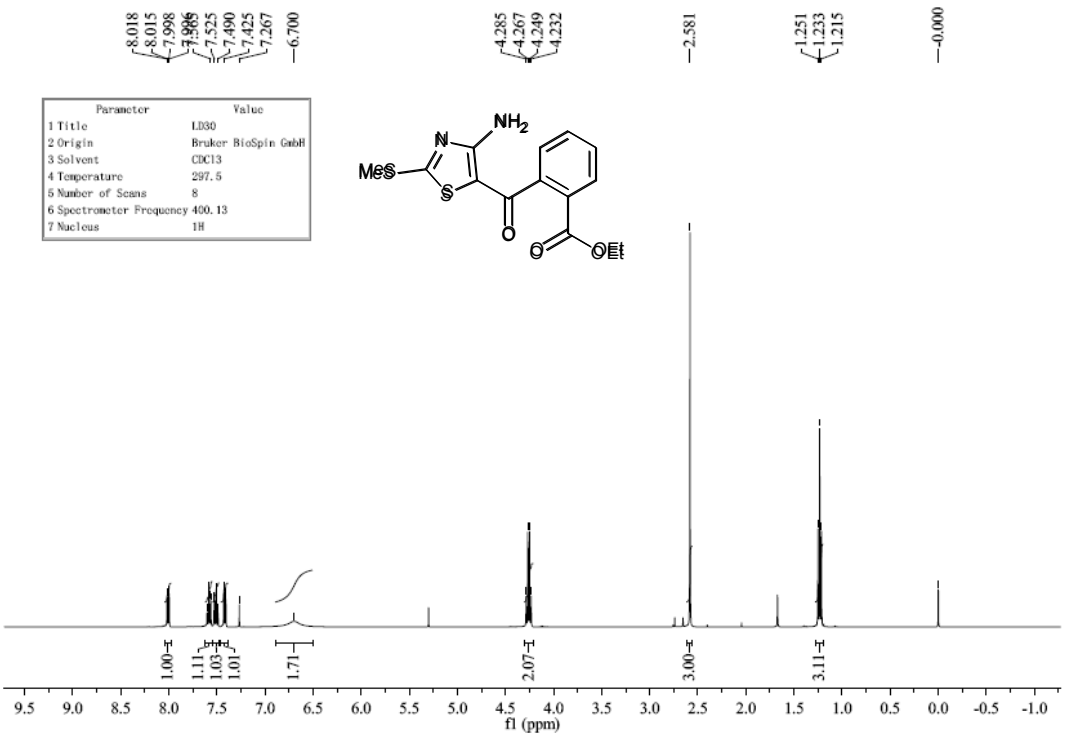
^{1}H NMR (400 MHz, $CDCl_3$) of **9e**



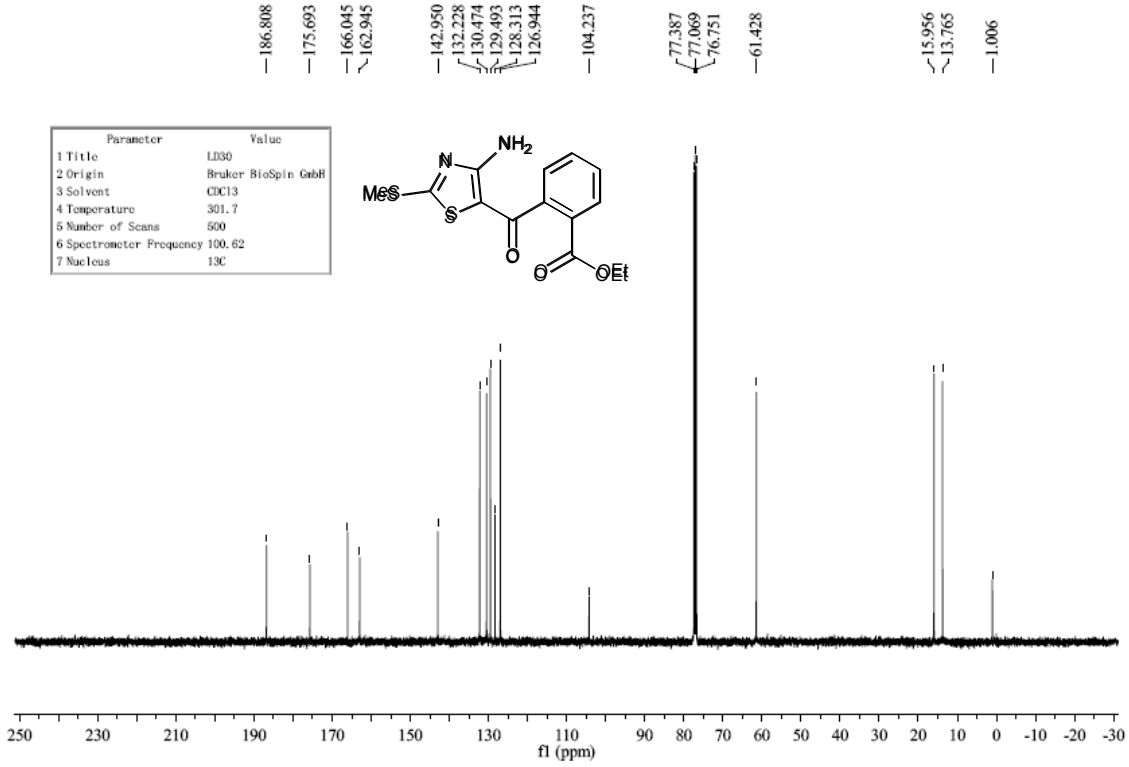
^{1}H NMR (400 MHz, $CDCl_3$) of **9f**



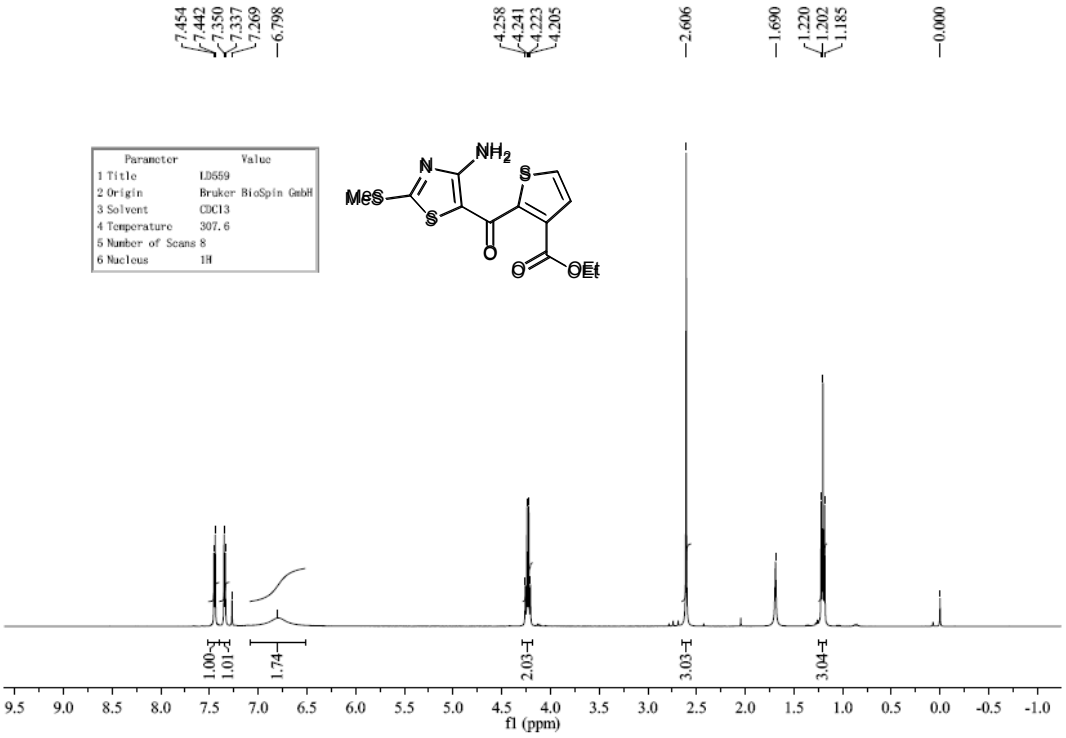
^{1}H NMR (400 MHz, $CDCl_3$) of **10a**



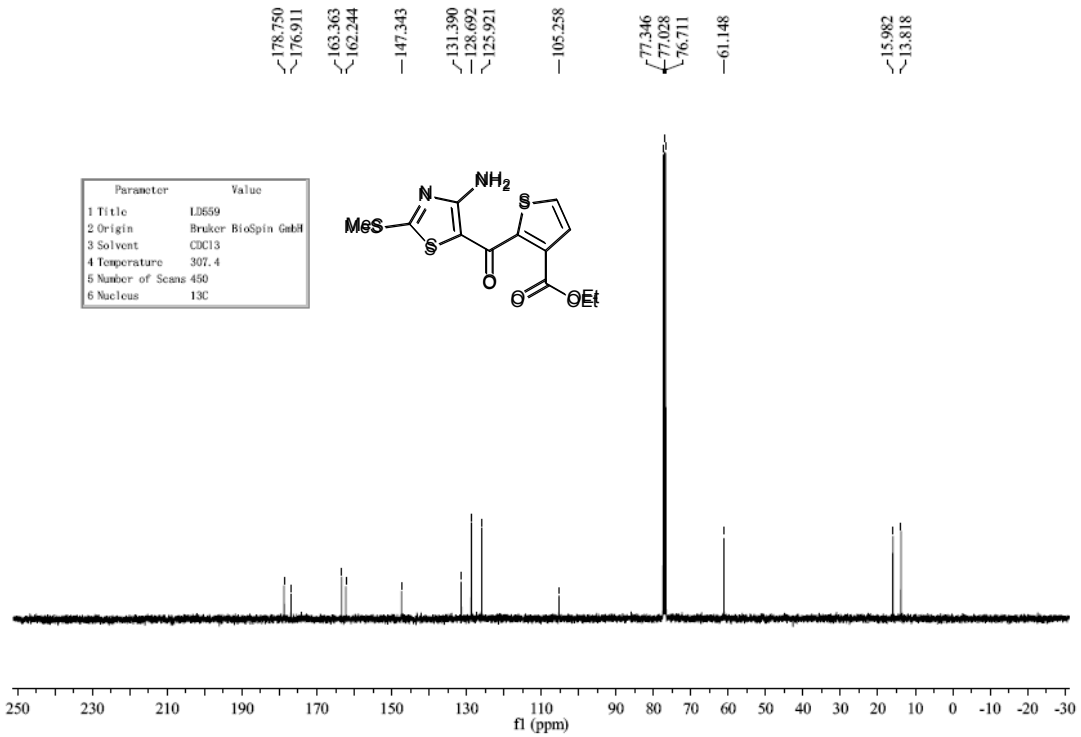
^{13}C NMR (101 MHz, $CDCl_3$) of **10a**



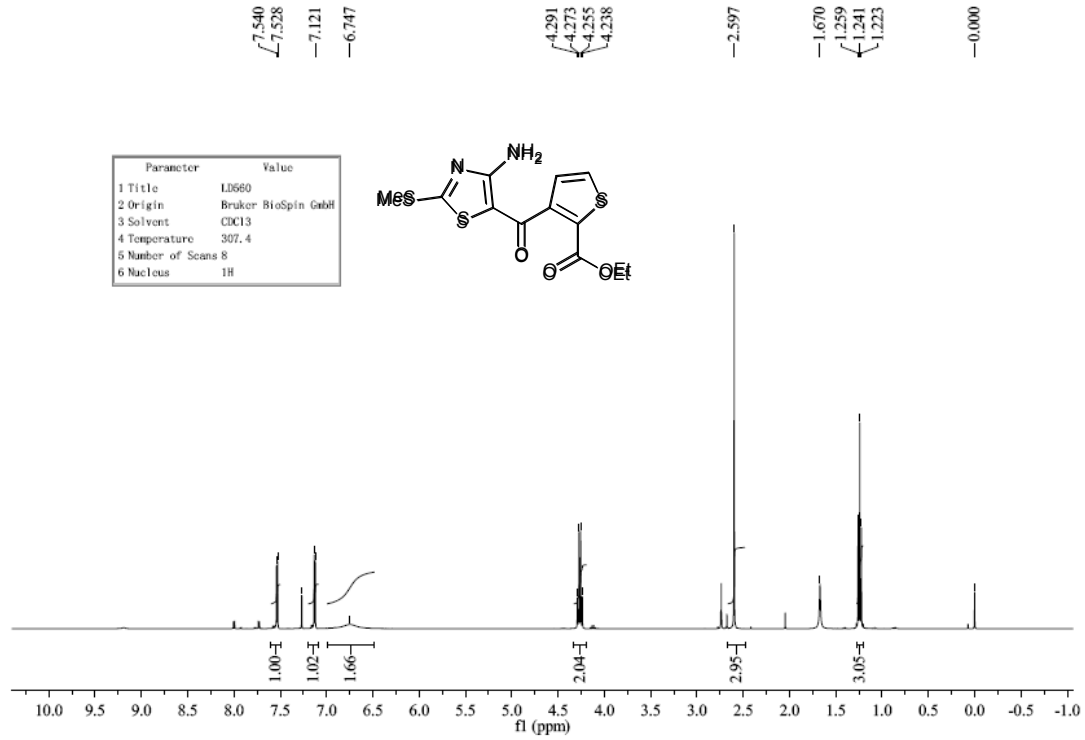
^{1}H NMR (400 MHz, $CDCl_3$) of **10b**



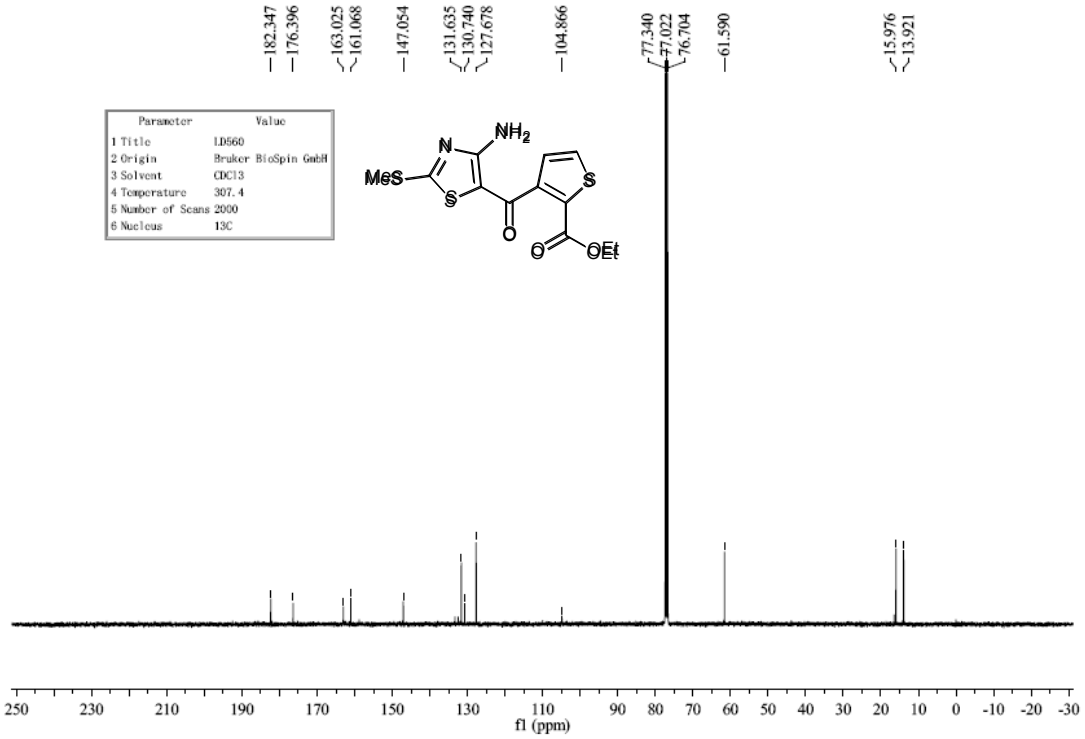
^{13}C NMR (101 MHz, $CDCl_3$) of **10b**



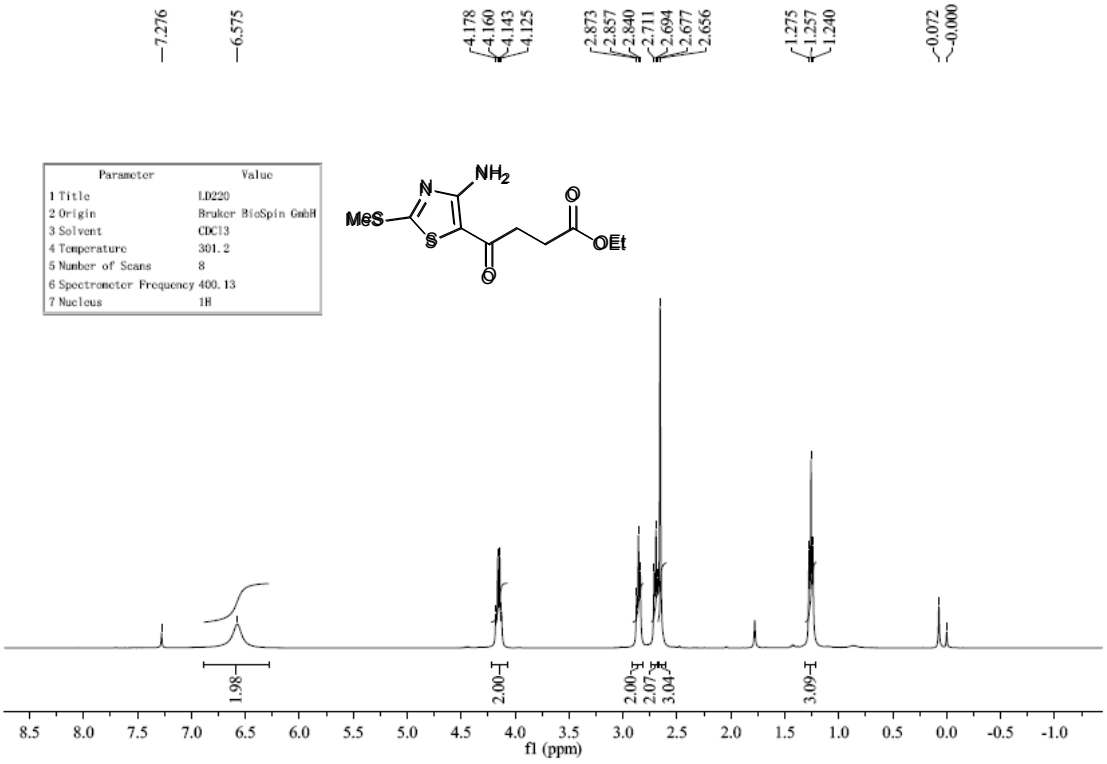
^{1}H NMR (400 MHz, $CDCl_3$) of **10b'**



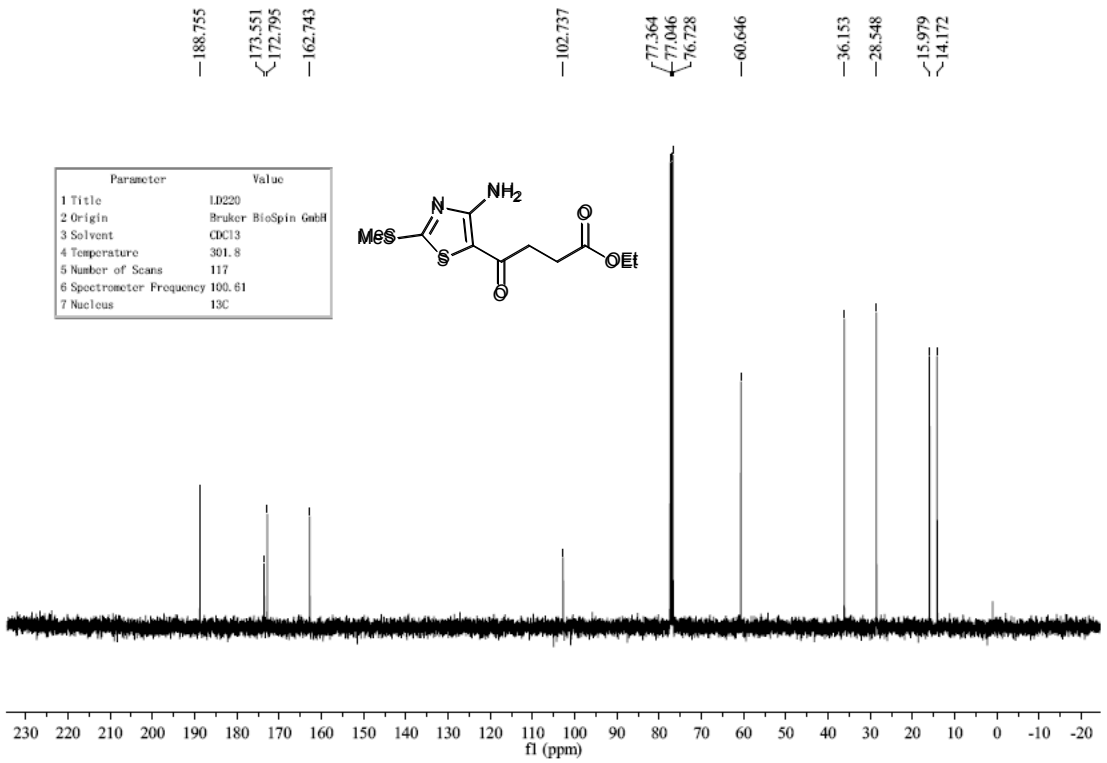
^{13}C NMR (101 MHz, $CDCl_3$) of **10b'**



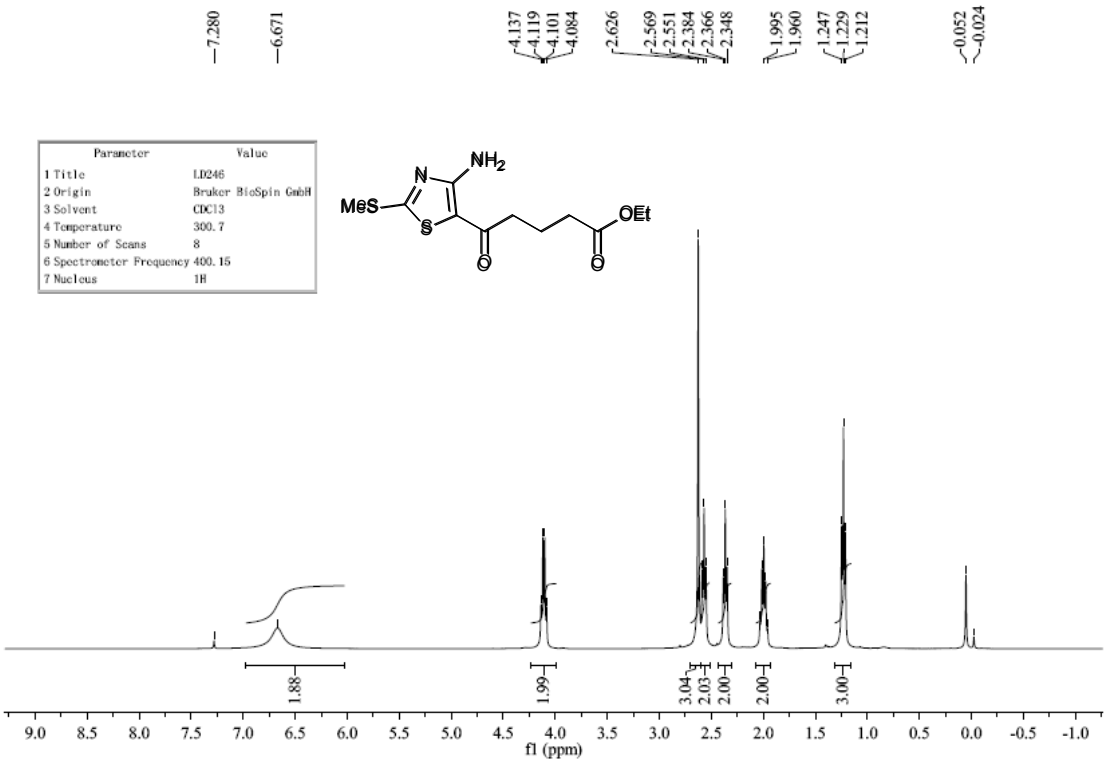
^{1}H NMR (400 MHz, $CDCl_3$) of **10c**



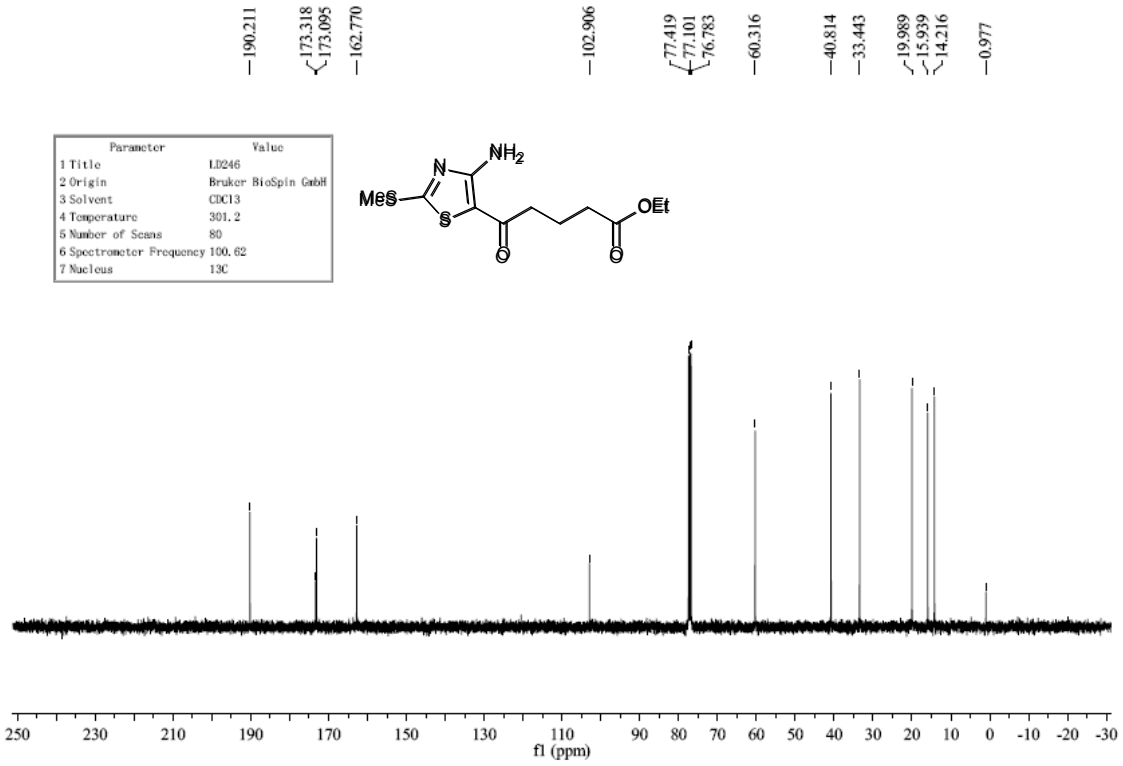
^{13}C NMR (101 MHz, $CDCl_3$) of **10c**



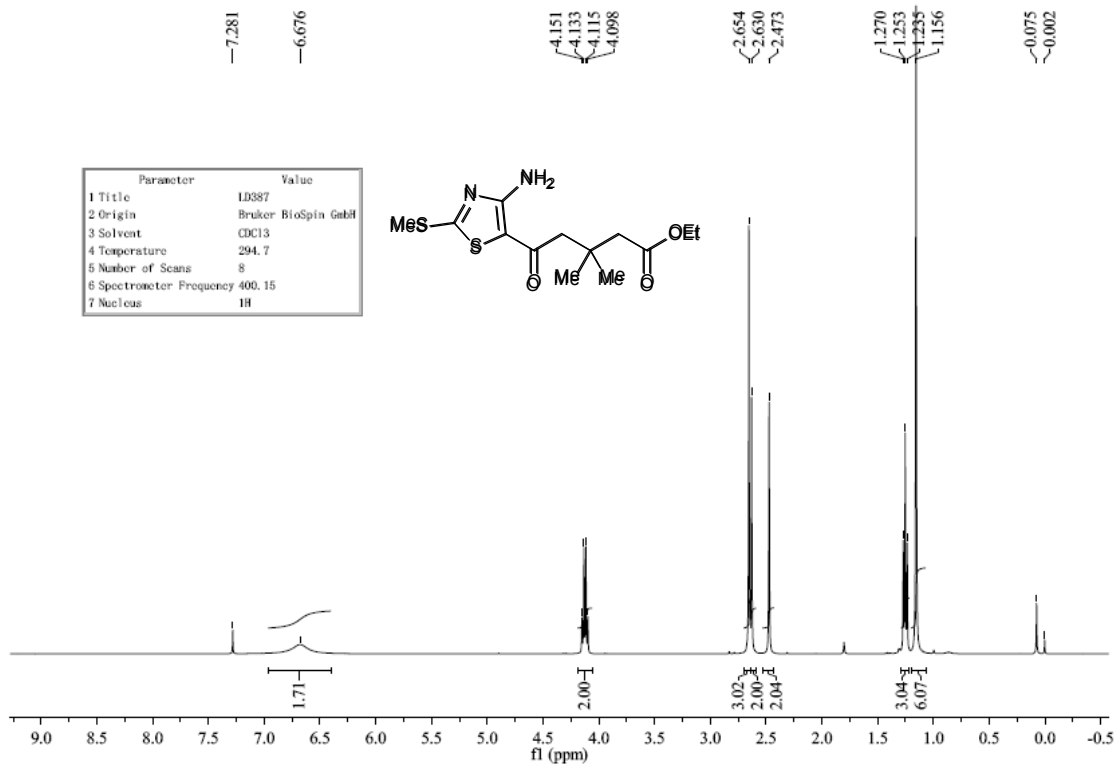
^{1}H NMR (400 MHz, $CDCl_3$) of **10d**



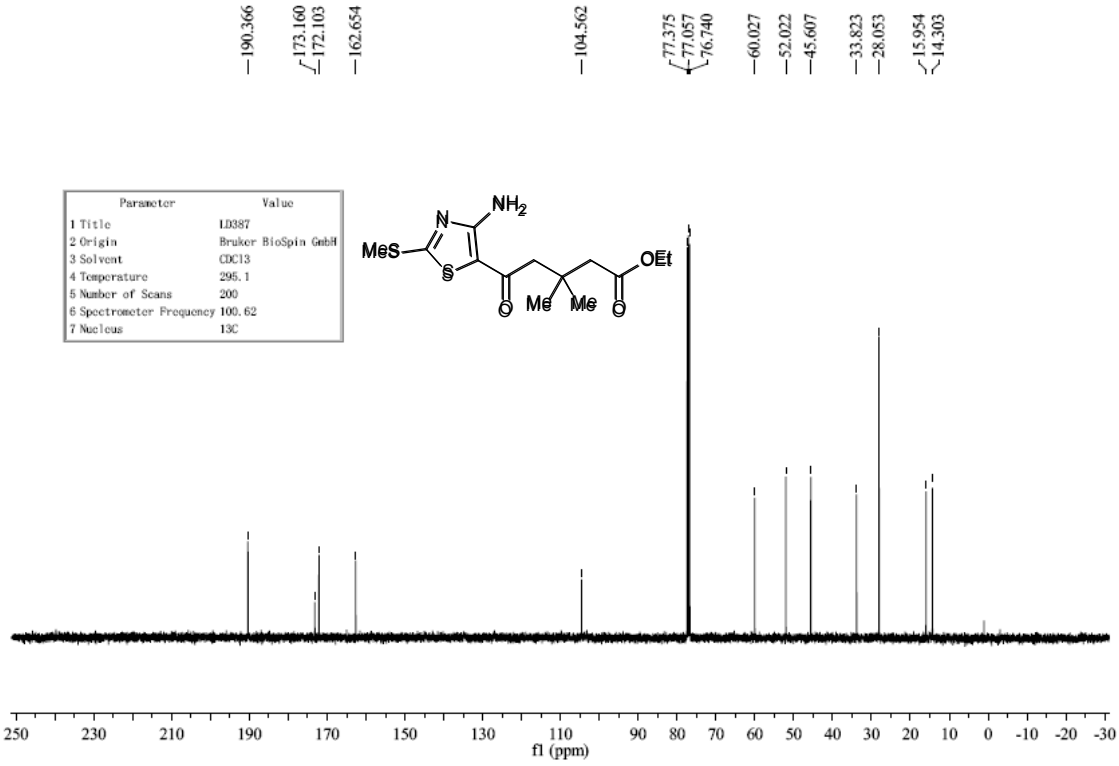
^{13}C NMR (101 MHz, $CDCl_3$) of **10d**



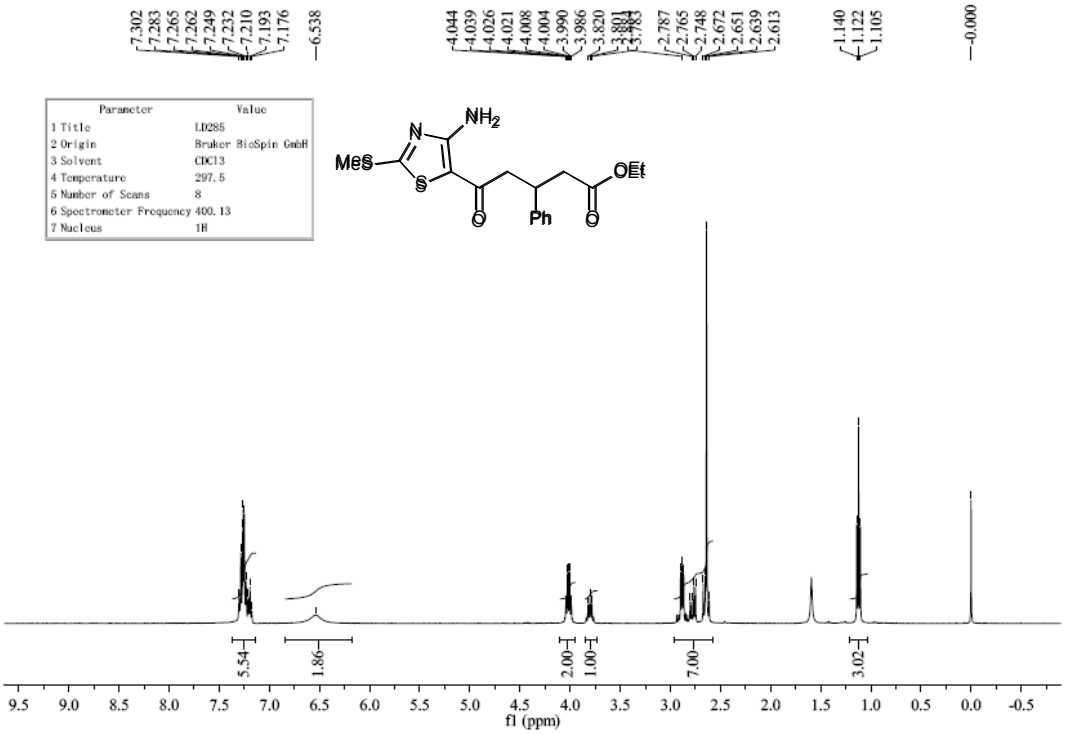
^{1}H NMR (400 MHz, $CDCl_3$) of **10e**



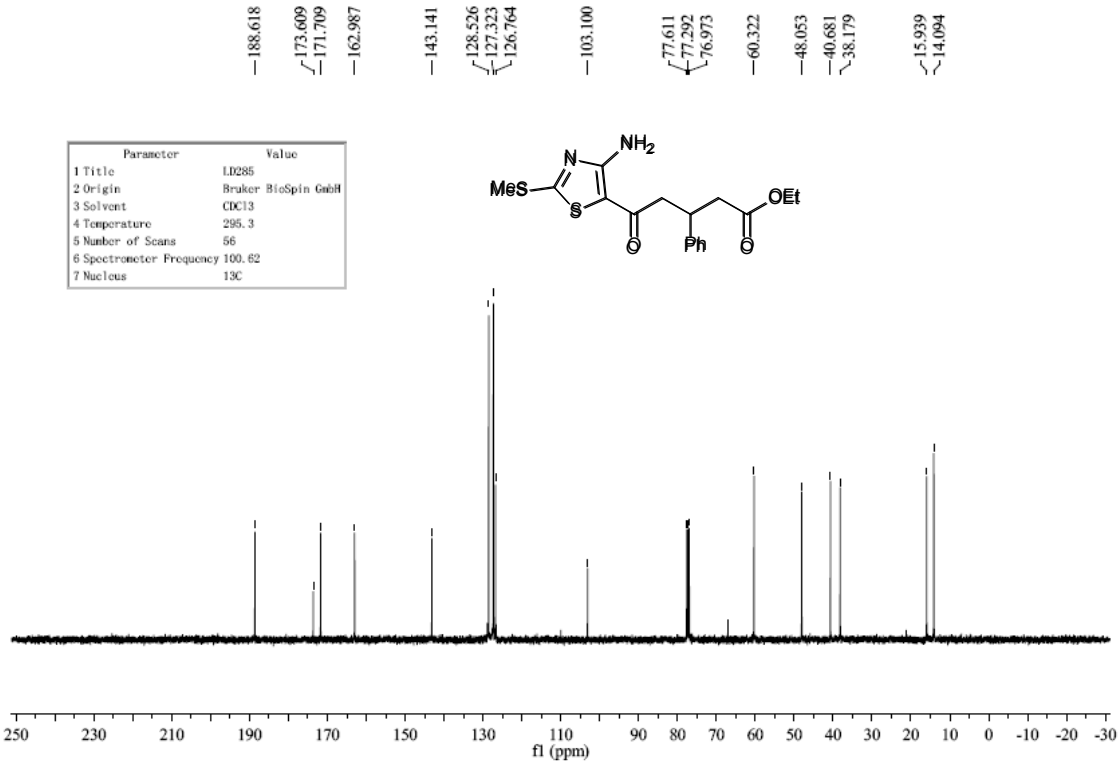
^{13}C NMR (101 MHz, $CDCl_3$) of **10e**



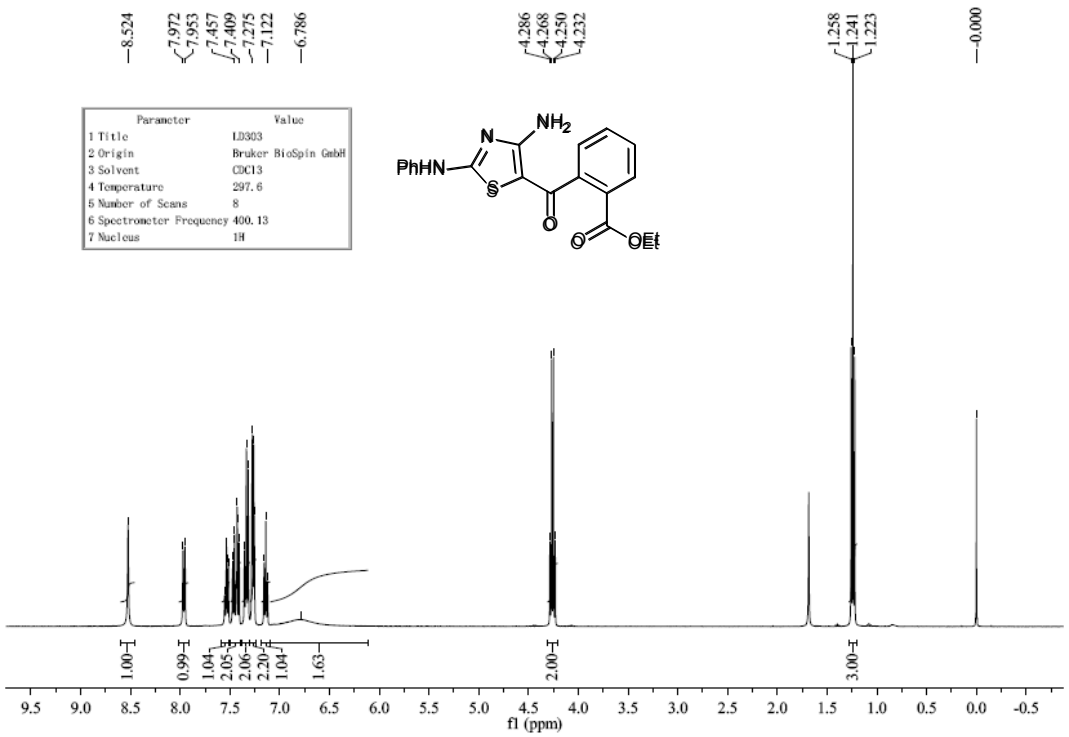
^{1}H NMR (400 MHz, $CDCl_3$) of **10f**



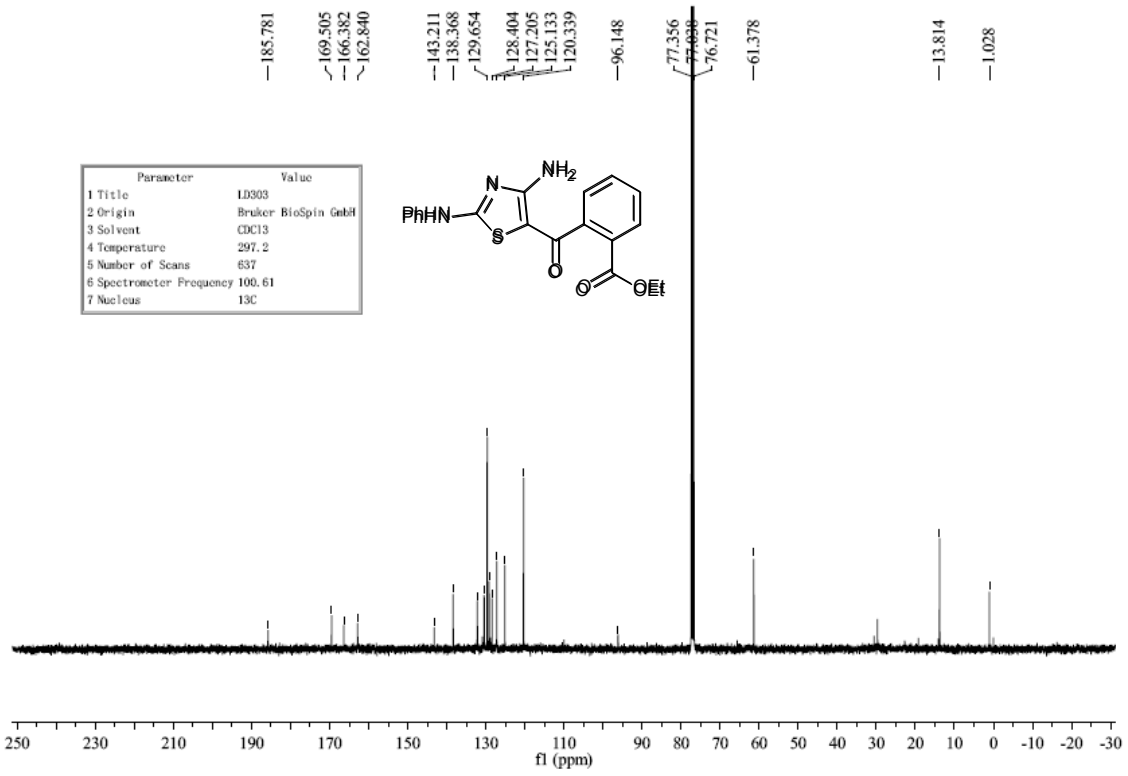
^{13}C NMR (101 MHz, $CDCl_3$) of **10f**



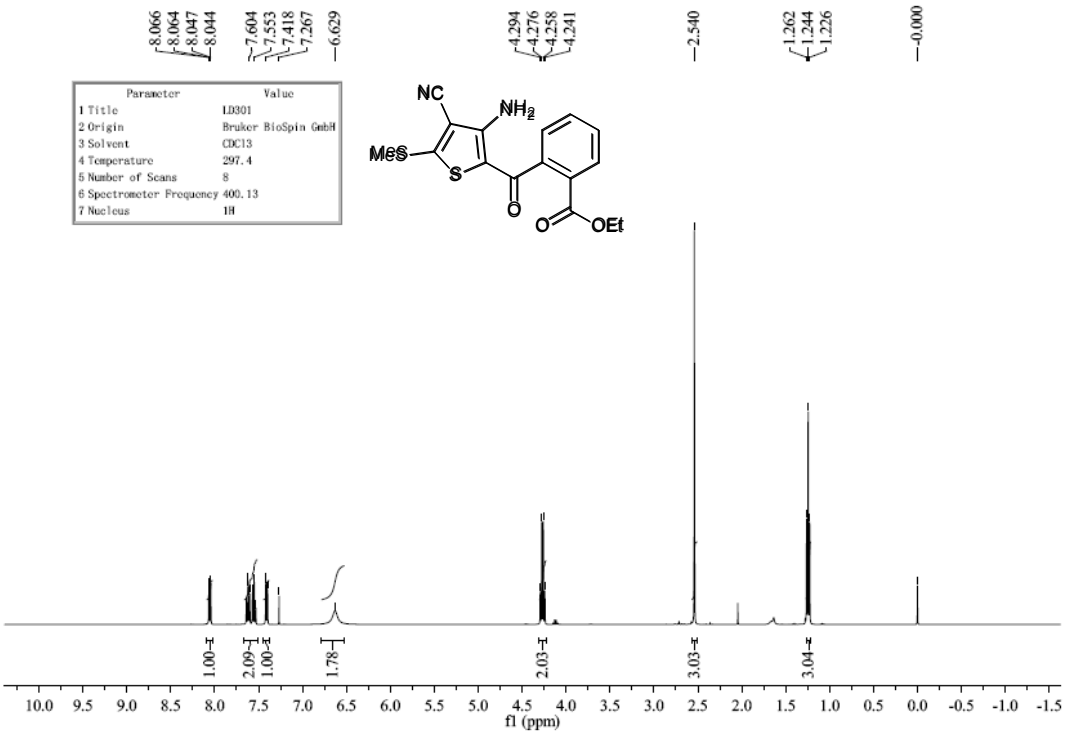
^{1}H NMR (400 MHz, $CDCl_3$) of **10g**



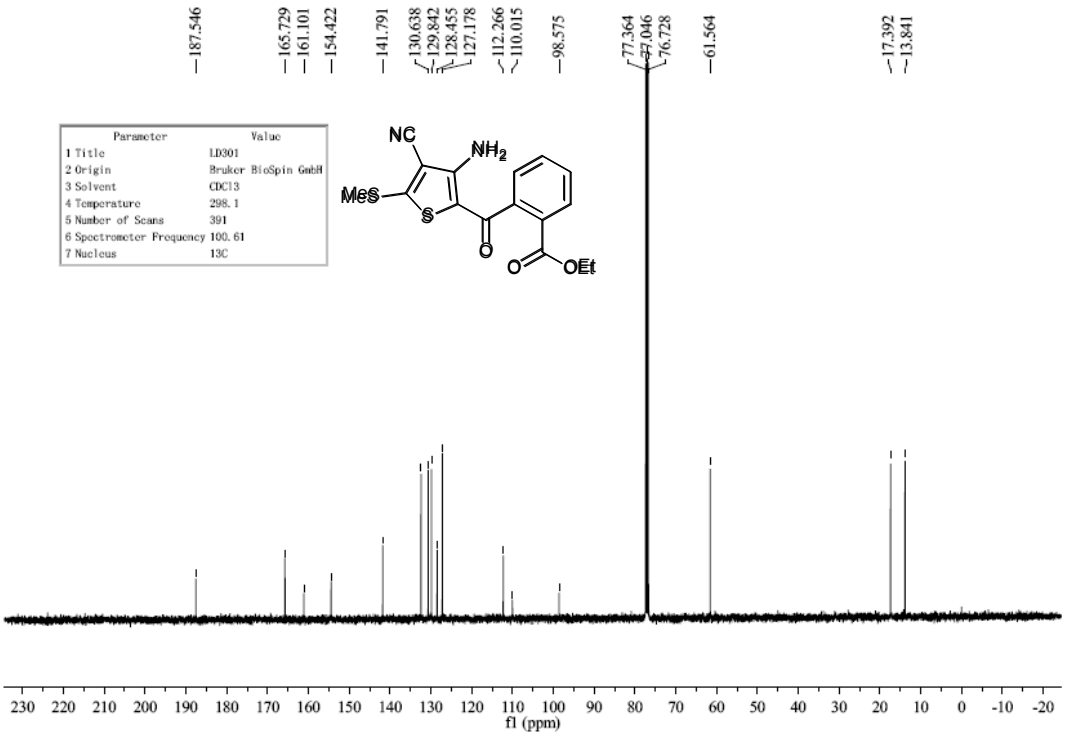
^{13}C NMR (101 MHz, $CDCl_3$) of **10g**



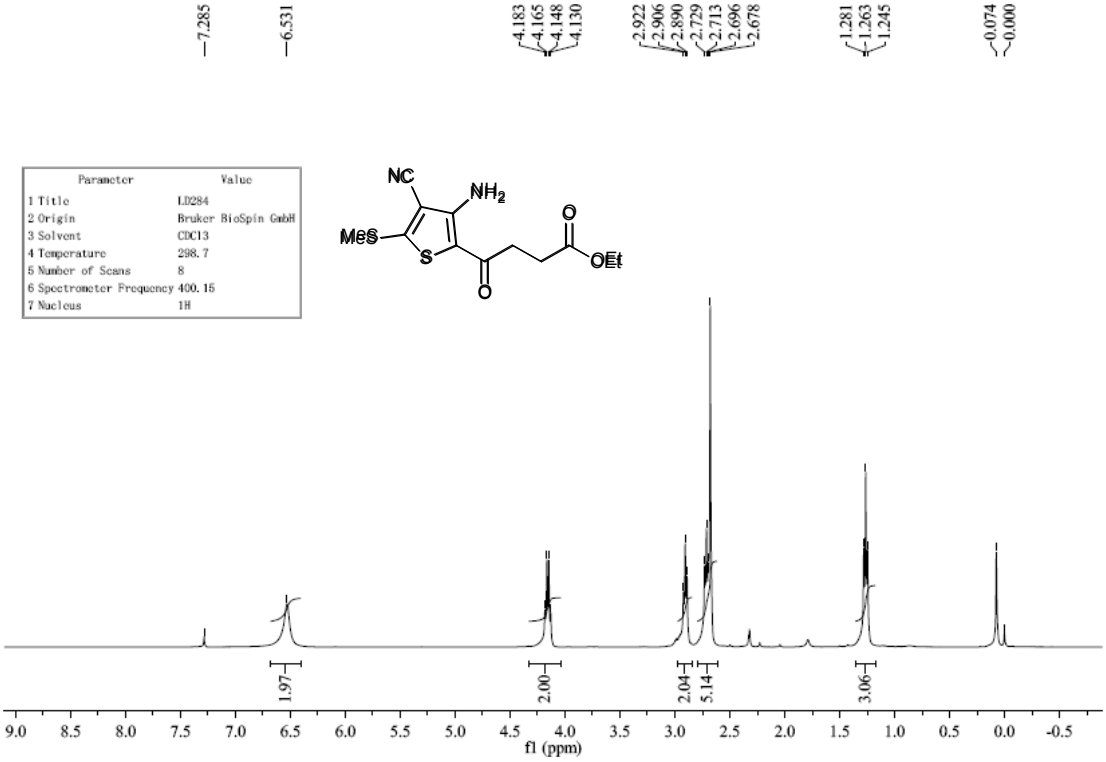
^{1}H NMR (400 MHz, $CDCl_3$) of **10h**



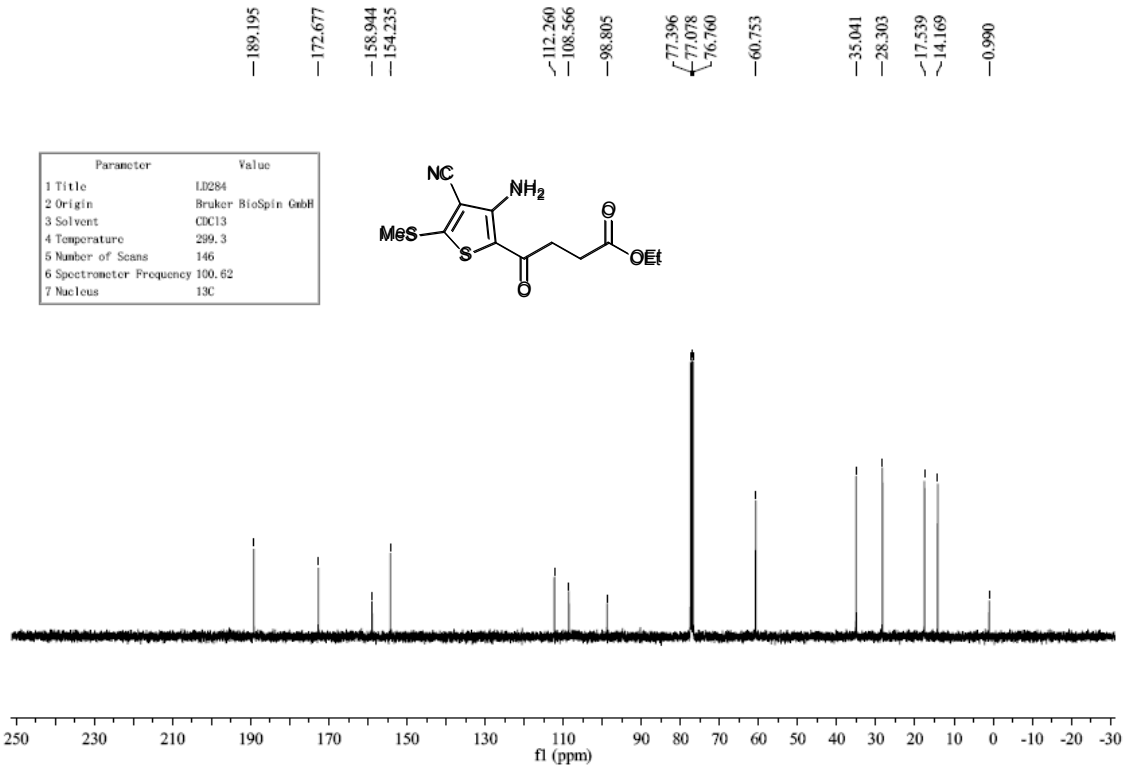
^{13}C NMR (101 MHz, $CDCl_3$) of **10h**



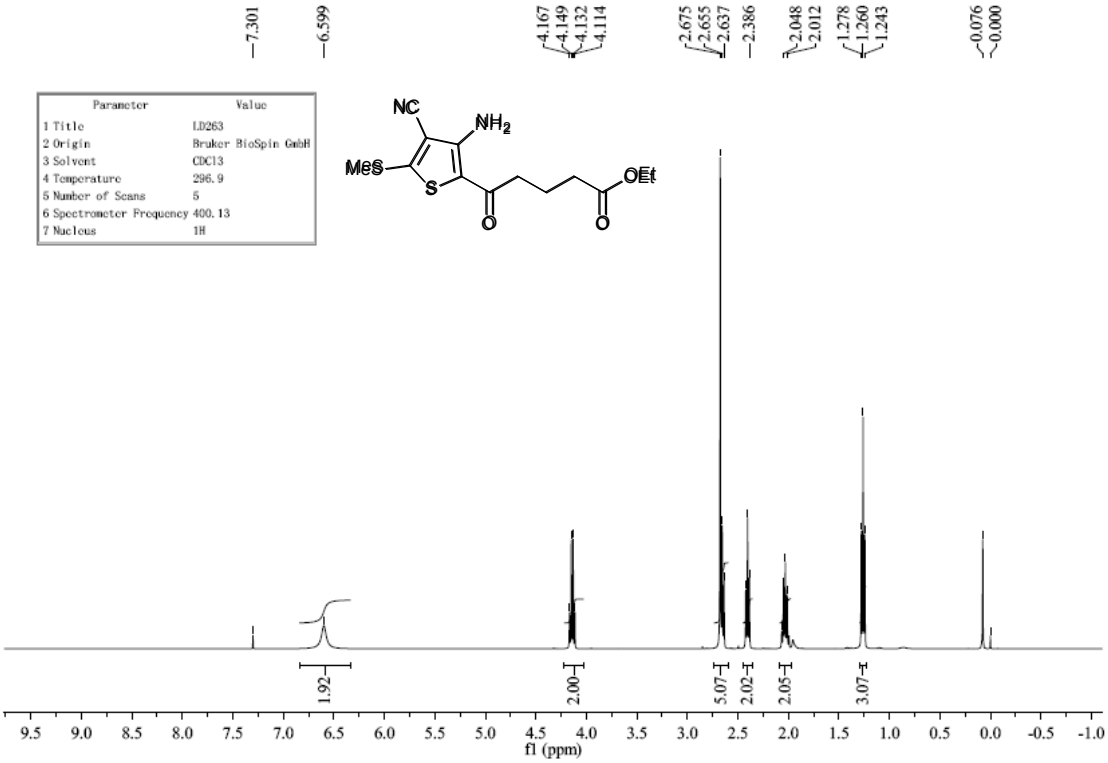
^{1}H NMR (400 MHz, $CDCl_3$) of **10i**



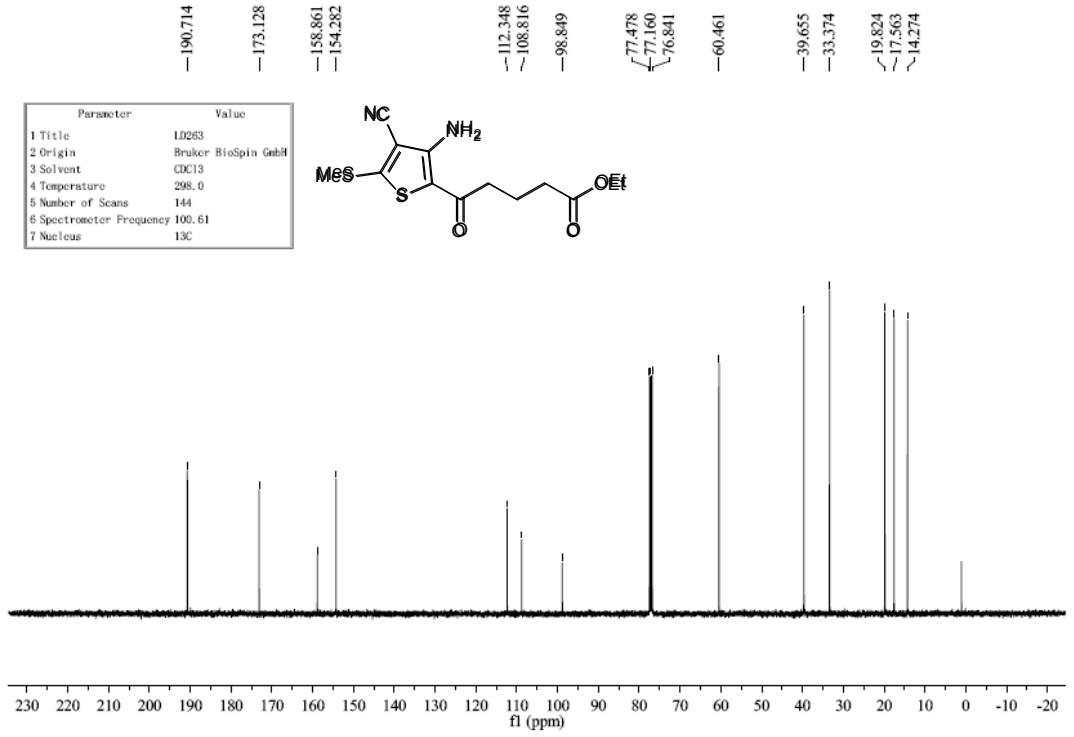
^{13}C NMR (101 MHz, $CDCl_3$) of **10i**



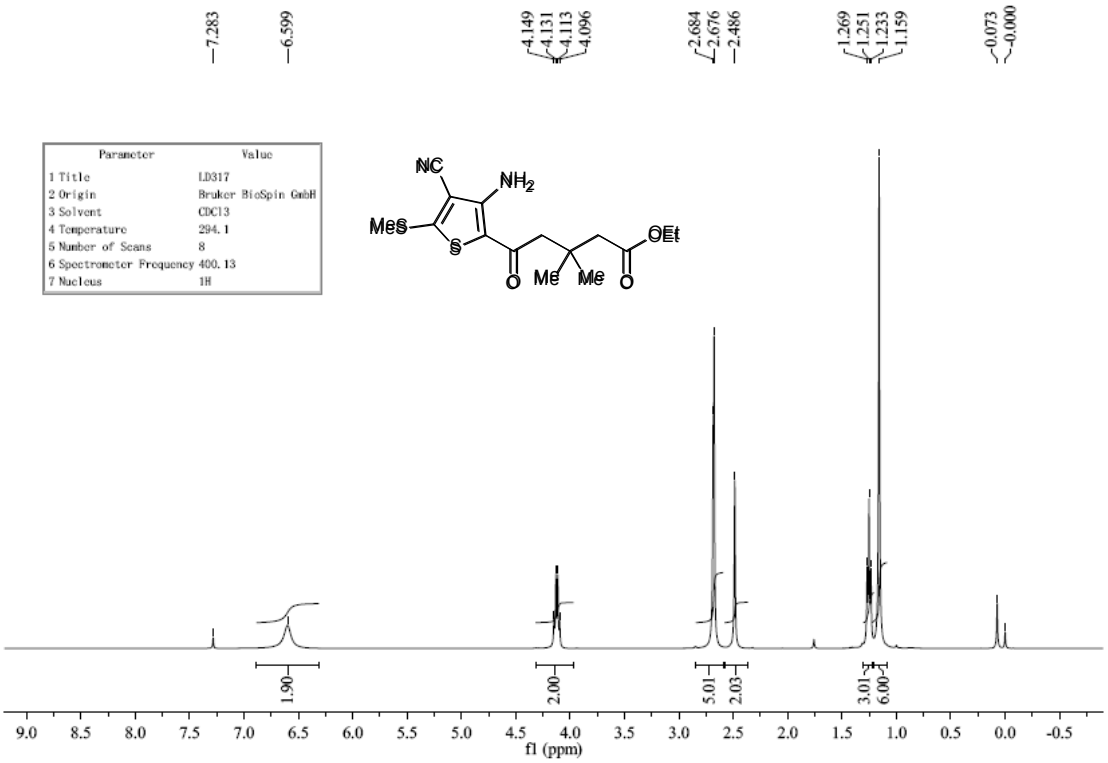
^{1}H NMR (400 MHz, $CDCl_3$) of **10j**



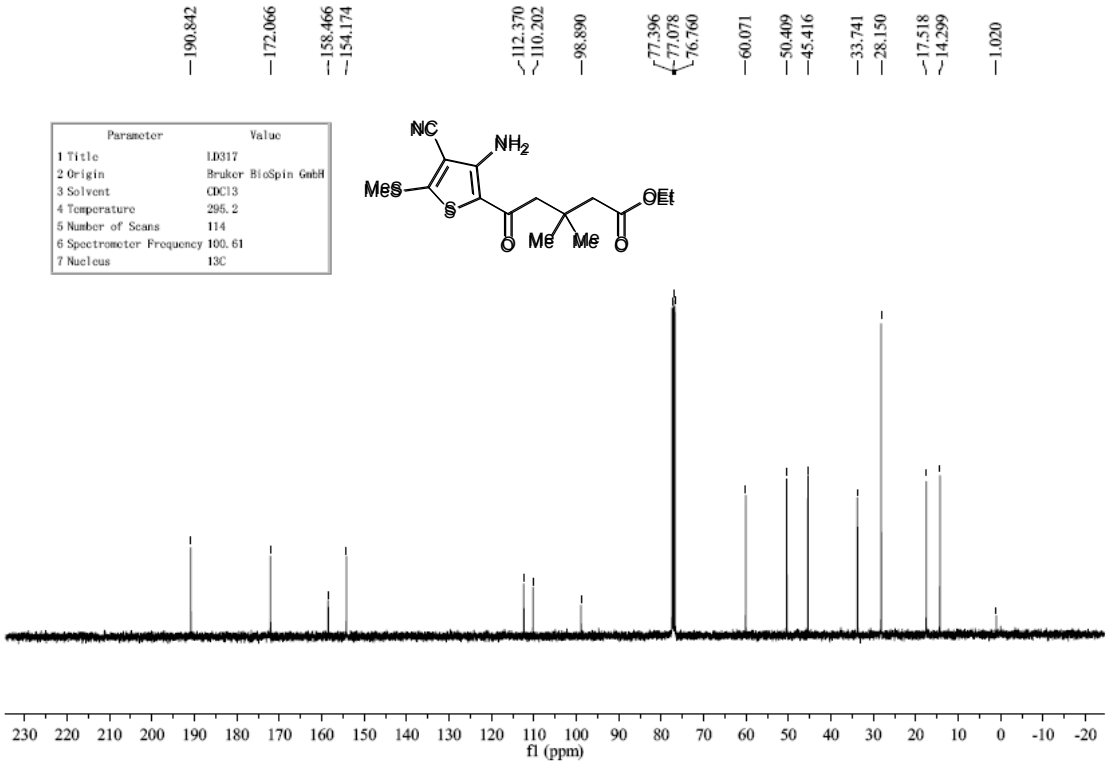
^{13}C NMR (101 MHz, $CDCl_3$) of **10j**



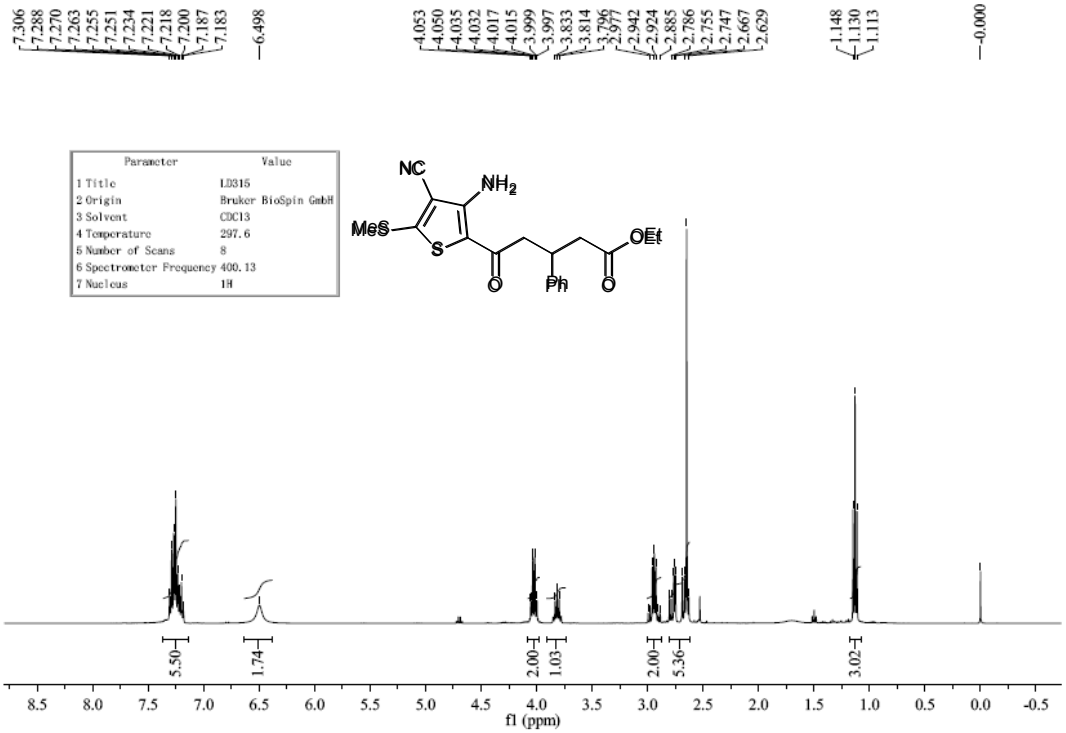
^{1}H NMR (400 MHz, $CDCl_3$) of **10k**



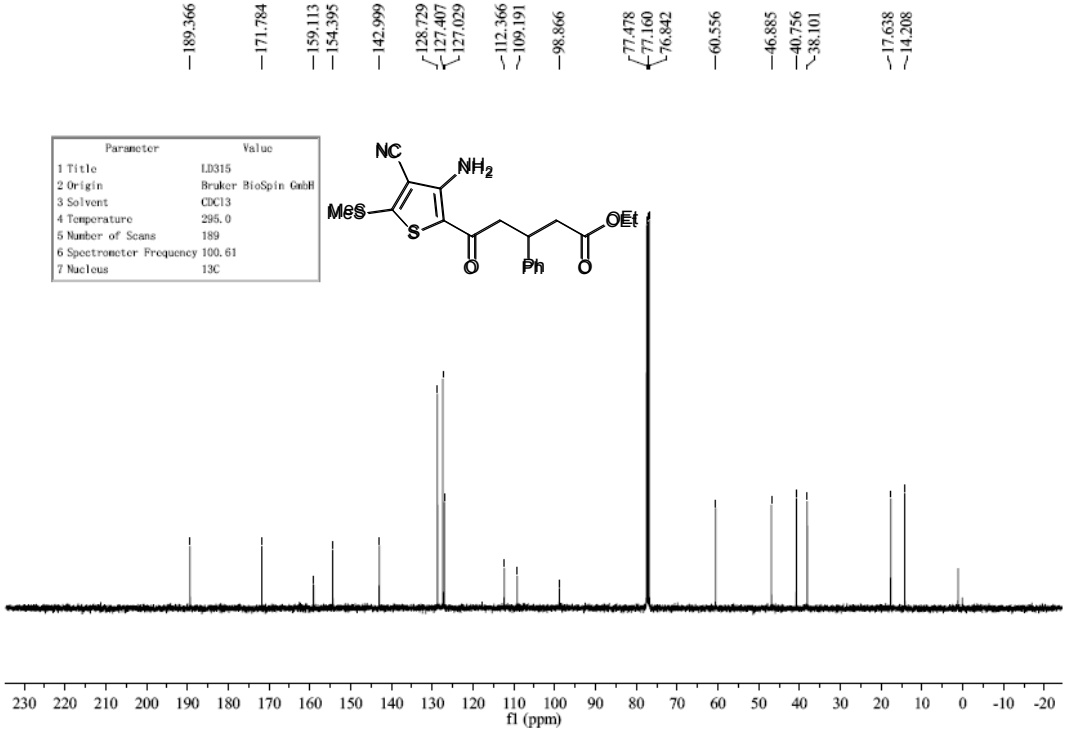
^{13}C NMR (101 MHz, $CDCl_3$) of **10k**



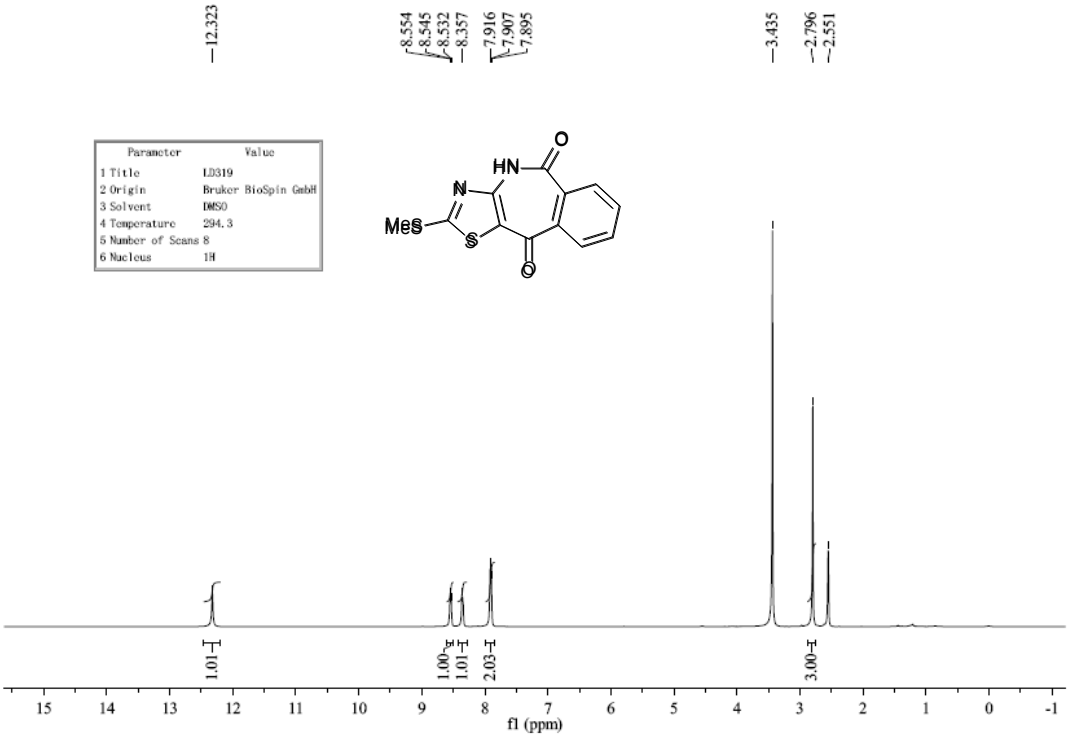
^{1}H NMR (400 MHz, $CDCl_3$) of **10l**



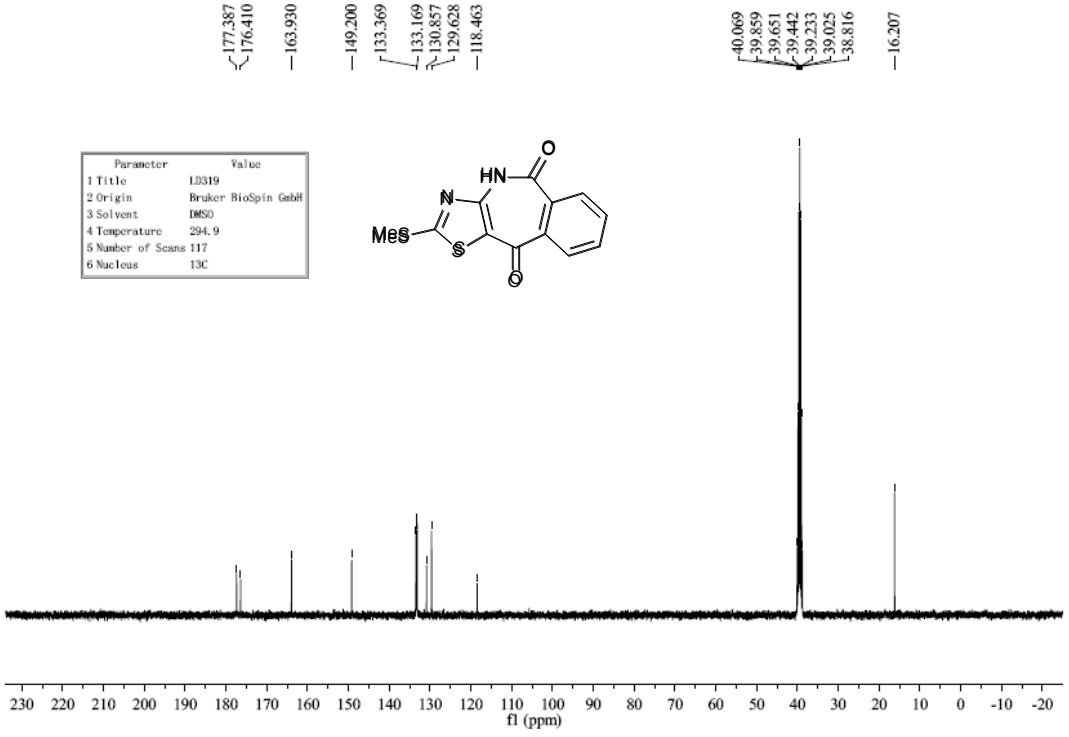
^{13}C NMR (101 MHz, $CDCl_3$) of **10l**



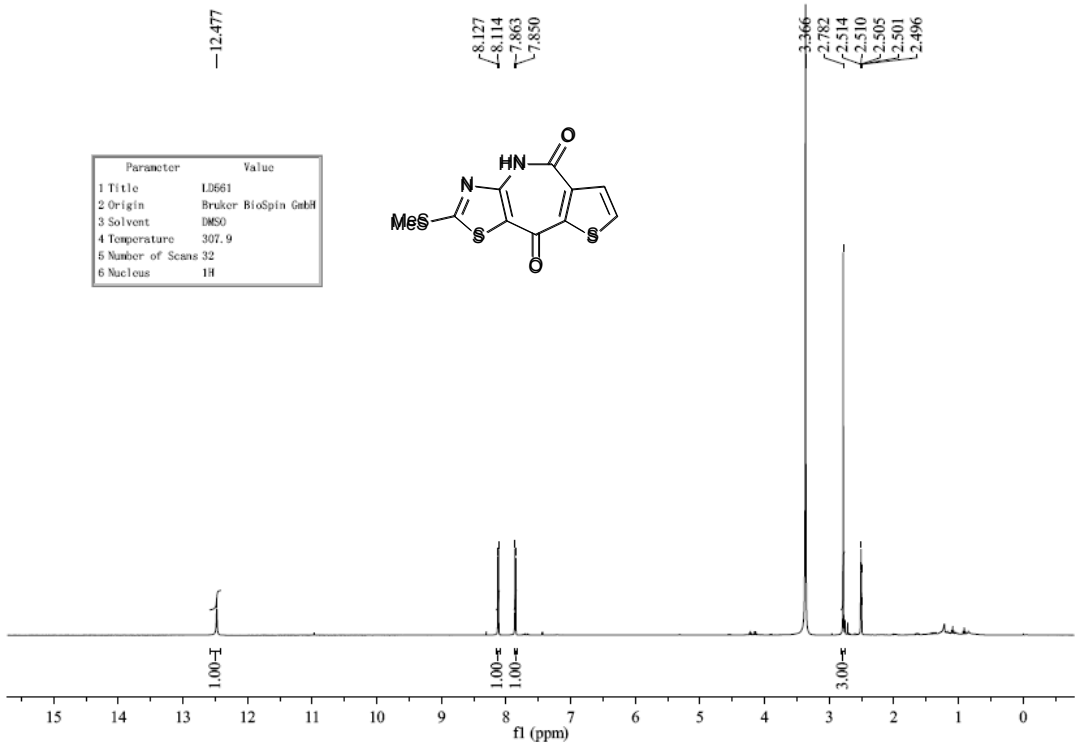
^{1}H NMR (400 MHz, DMSO-d_6) of **11a**



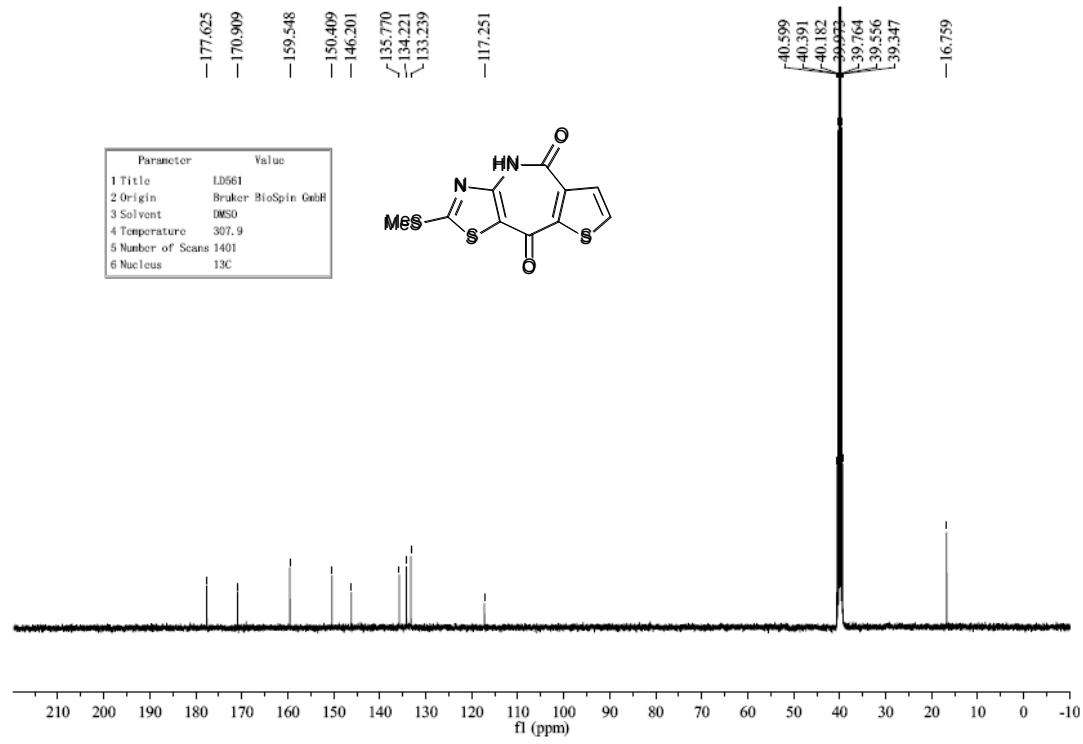
^{13}C NMR (101 MHz, DMSO-d_6) of **11a**



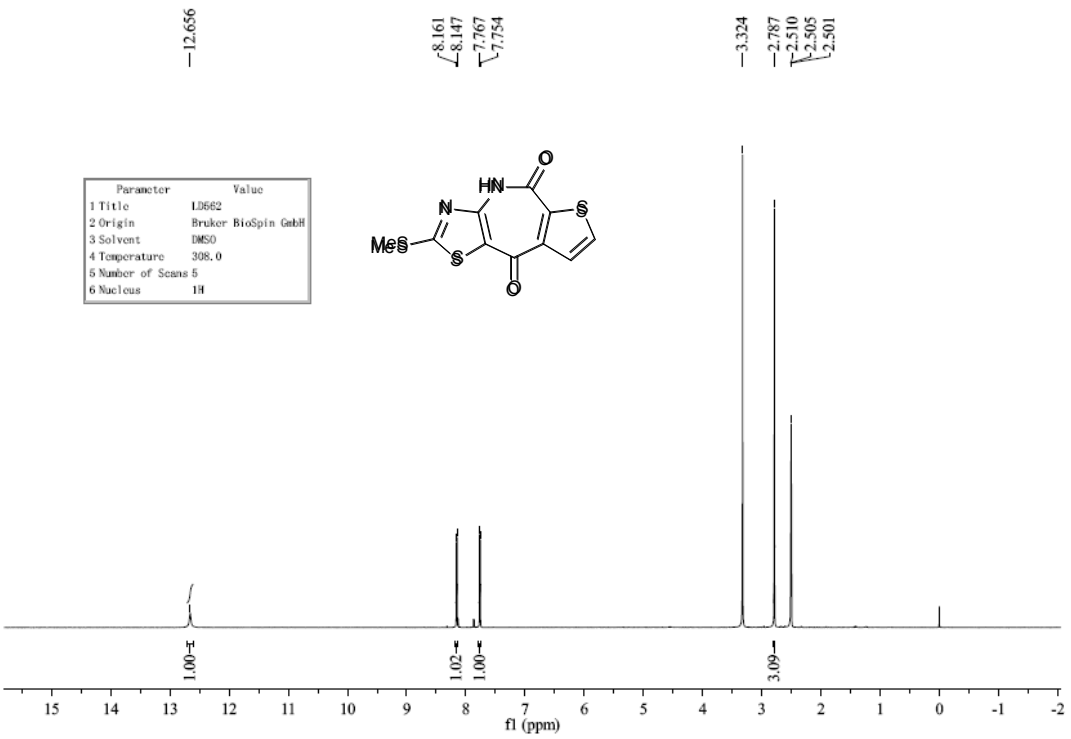
^{1}H NMR (400 MHz, DMSO-d_6) of **11b**



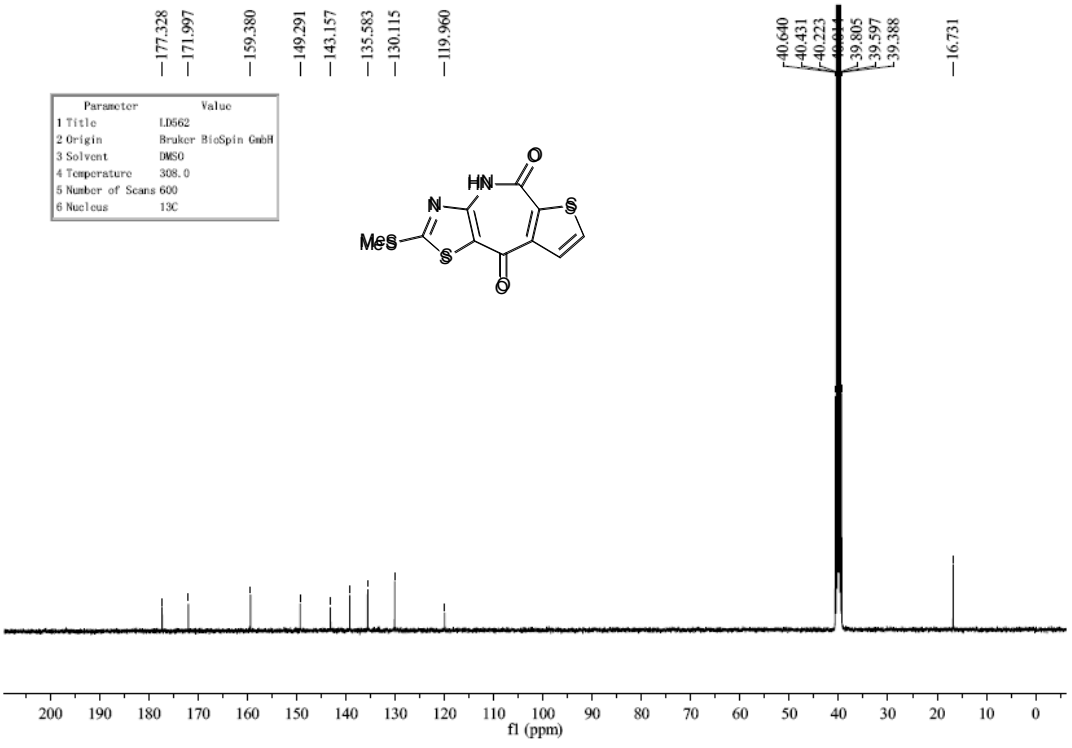
^{13}C NMR (101 MHz, DMSO-d_6) of **11b**



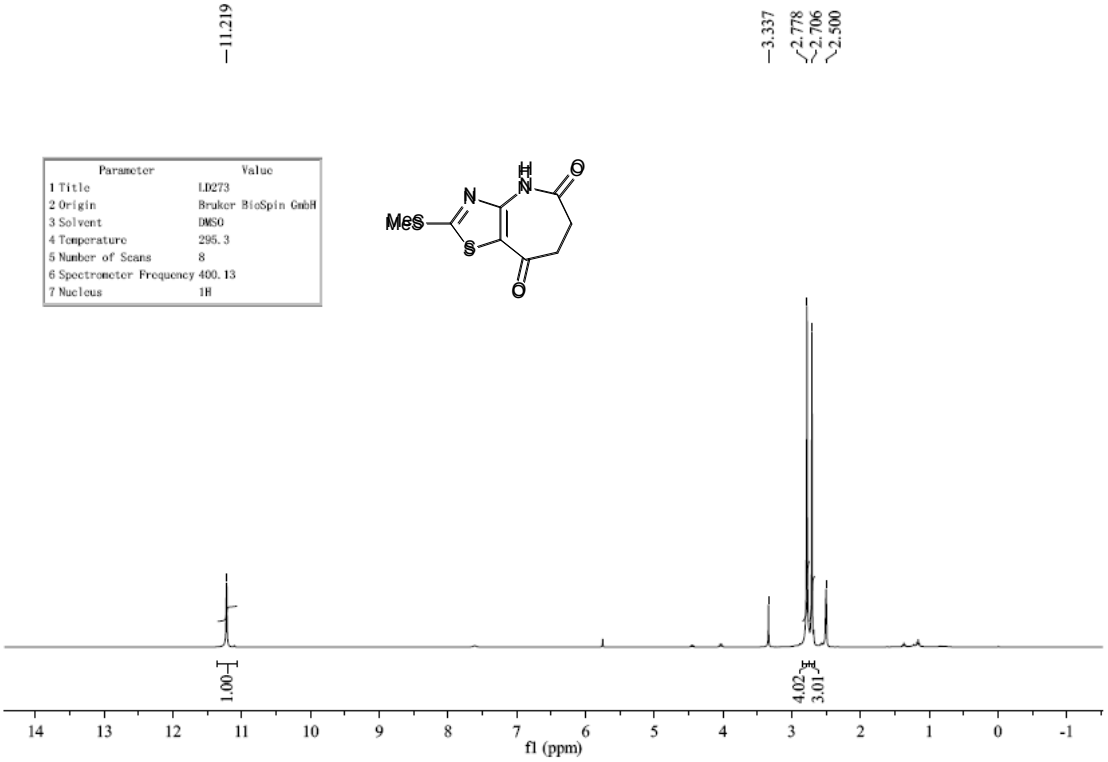
^{1}H NMR (400 MHz, DMSO-d_6) of **11b'**



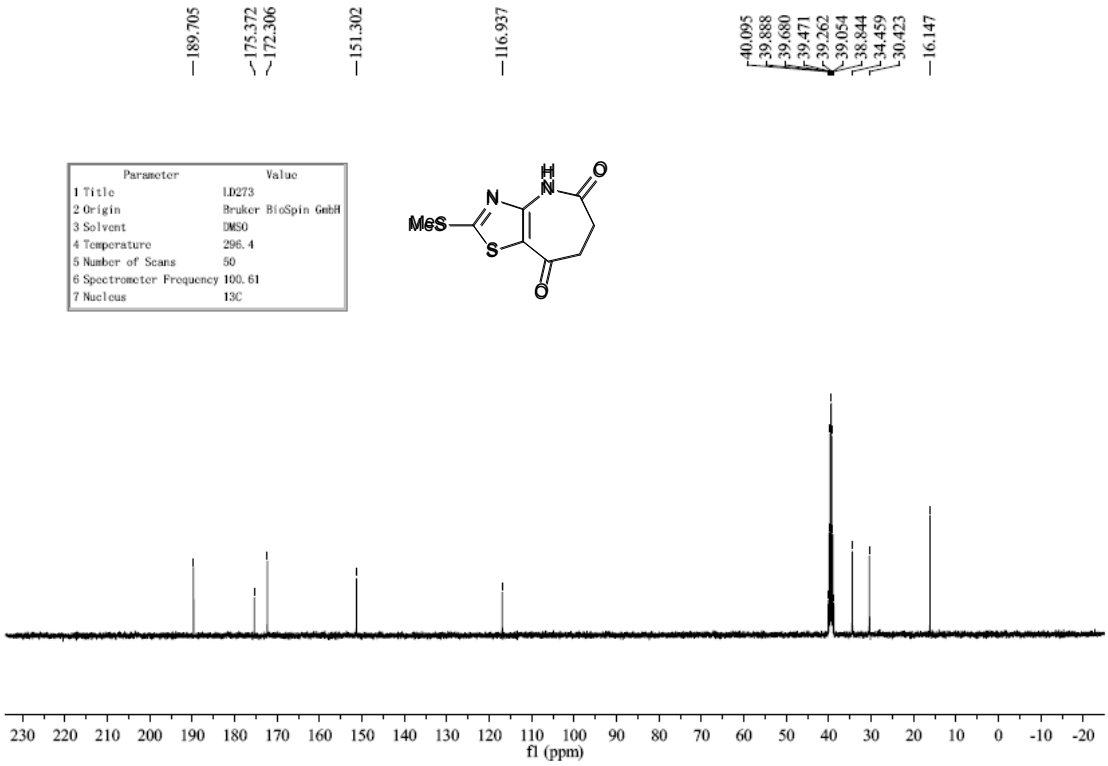
^{13}C NMR (101 MHz, DMSO-d_6) of **11b'**



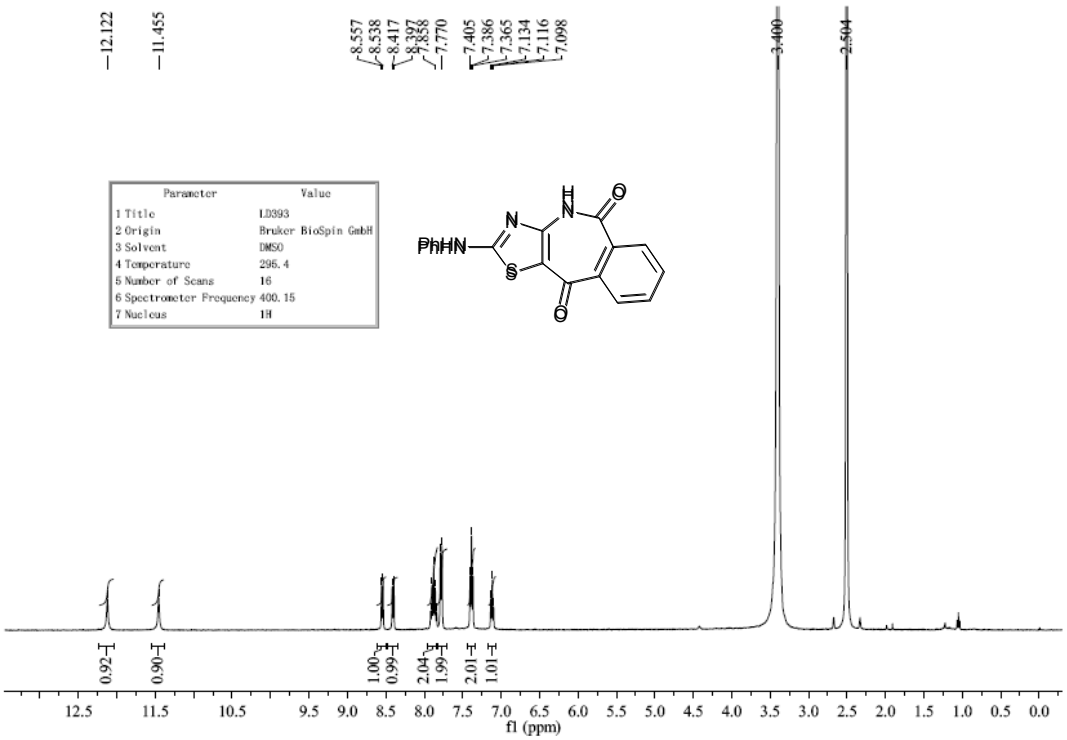
^{1}H NMR (400 MHz, DMSO-d_6) of **11c**



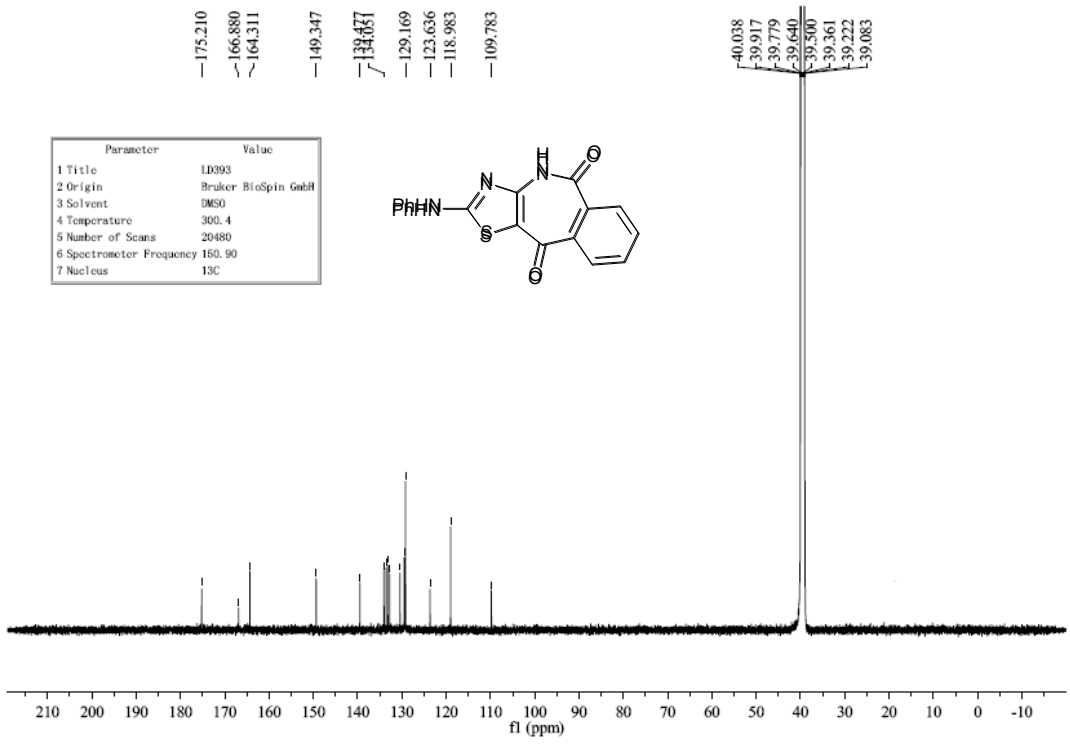
^{13}C NMR (101 MHz, DMSO-d_6) of **11c**



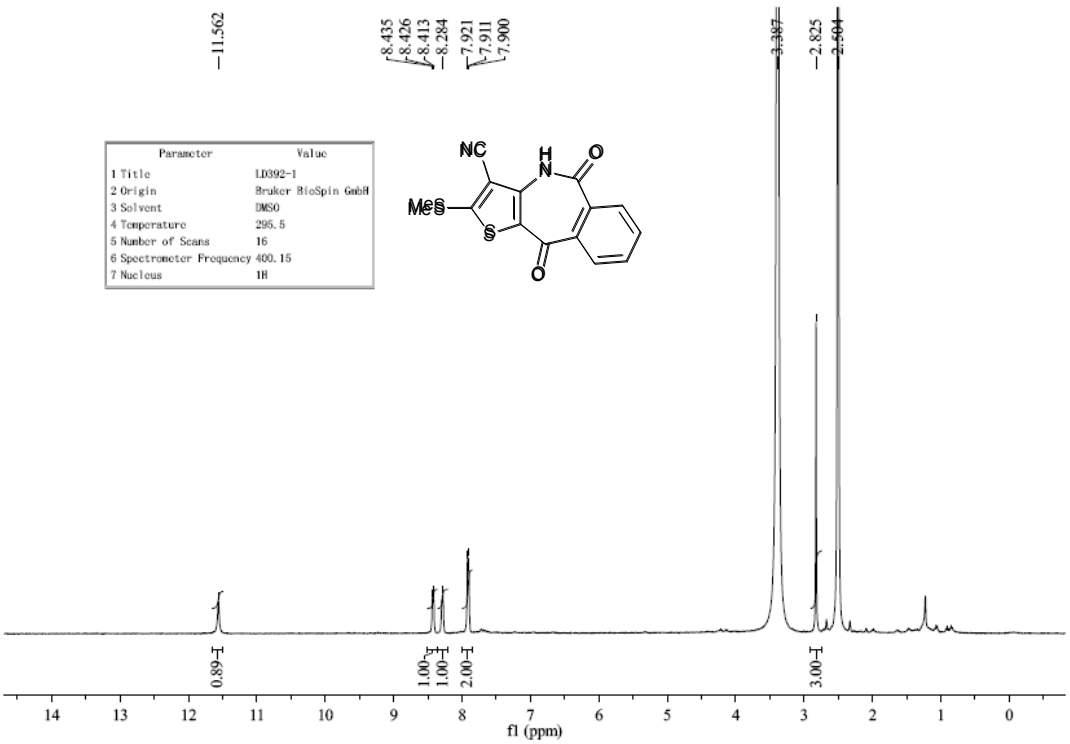
^{1}H NMR (400 MHz, DMSO-d_6) of **11d**



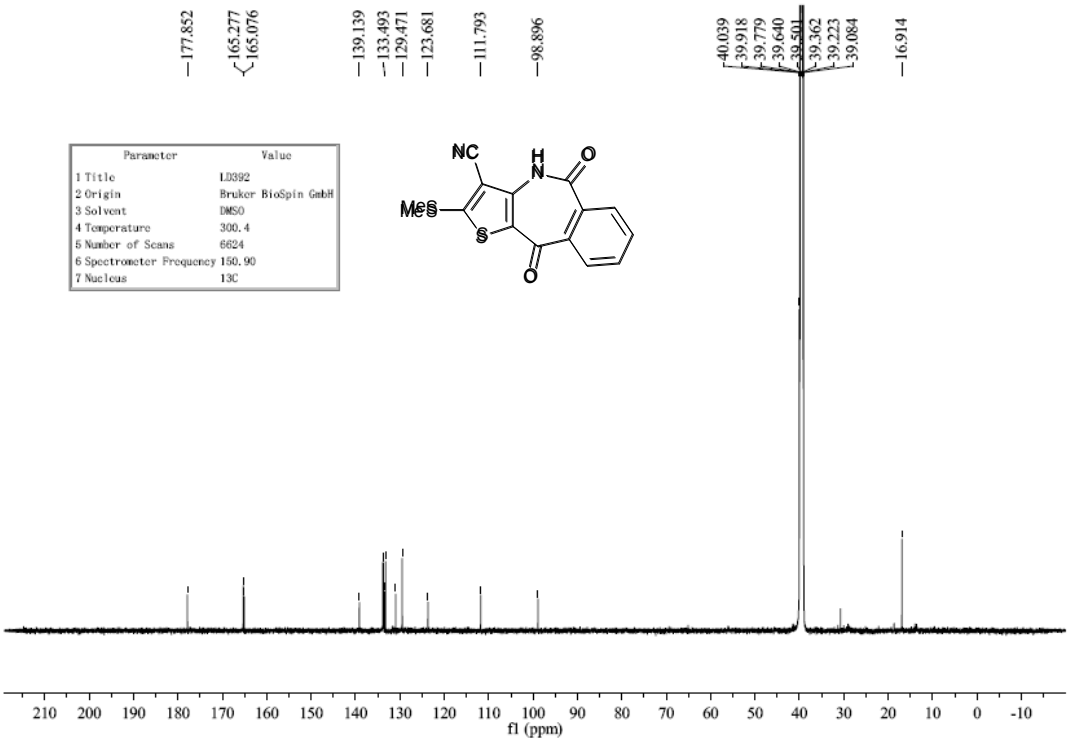
^{13}C NMR (151 MHz, DMSO-d_6) of **11d**



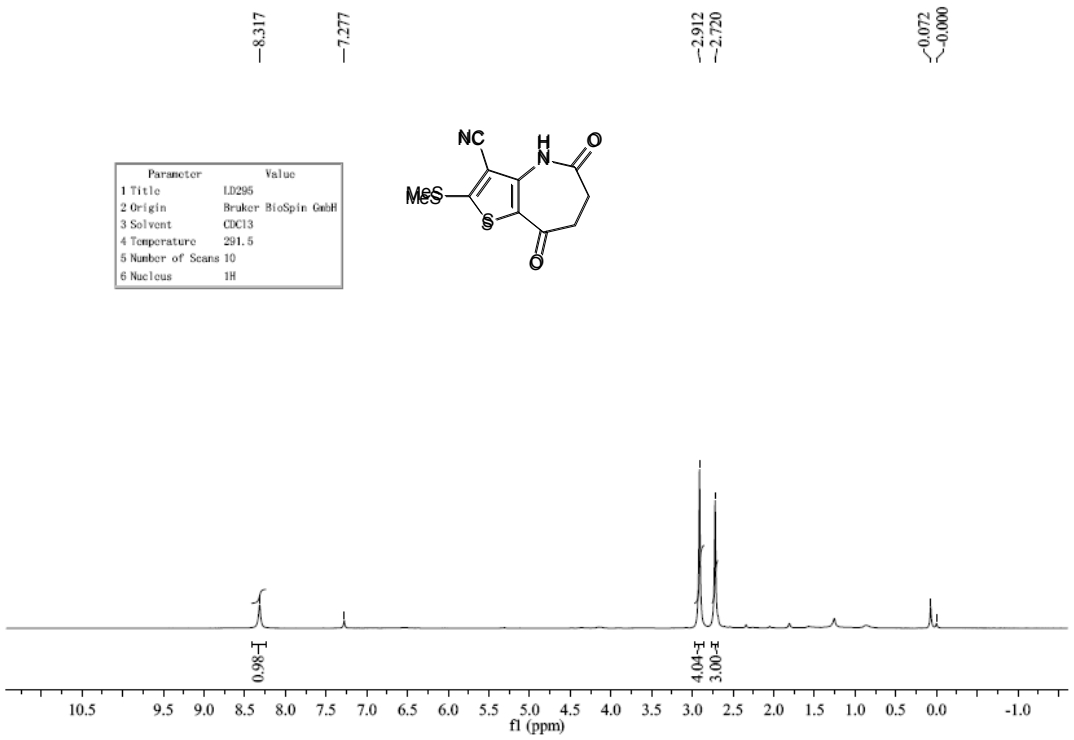
^{1}H NMR (400 MHz, DMSO-d_6) of **11e**



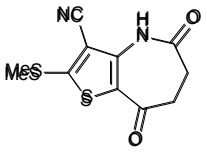
^{13}C NMR (151 MHz, DMSO-d_6) of **11e**

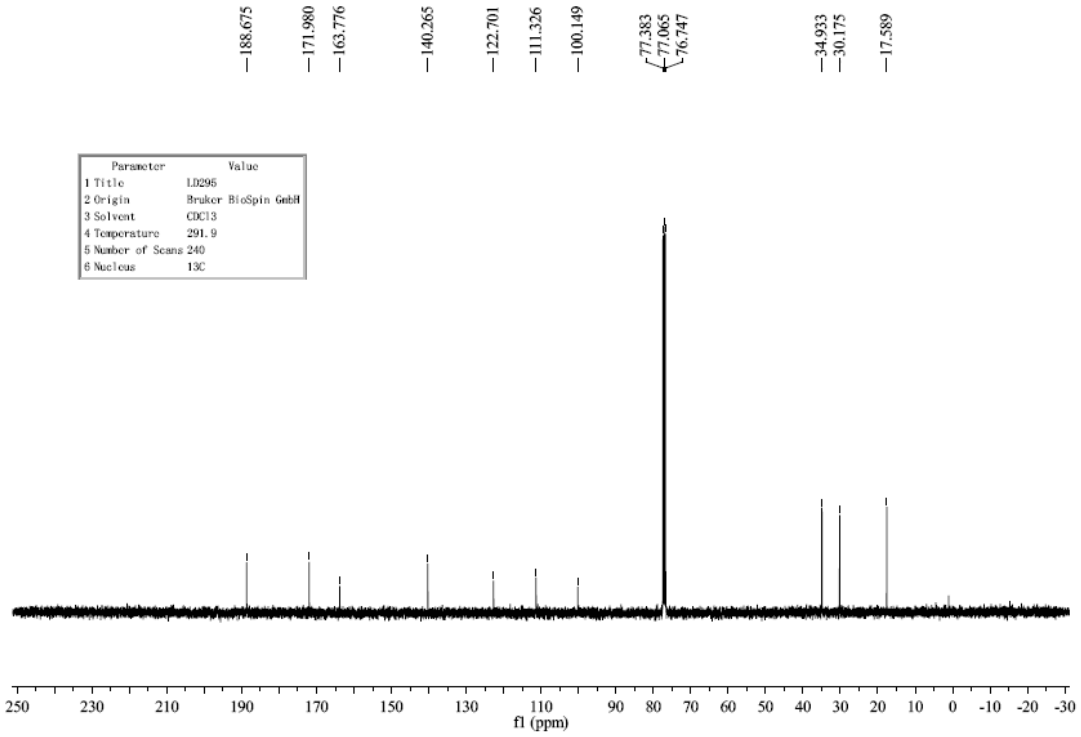


^{1}H NMR (400 MHz, $CDCl_3$) of **11f**

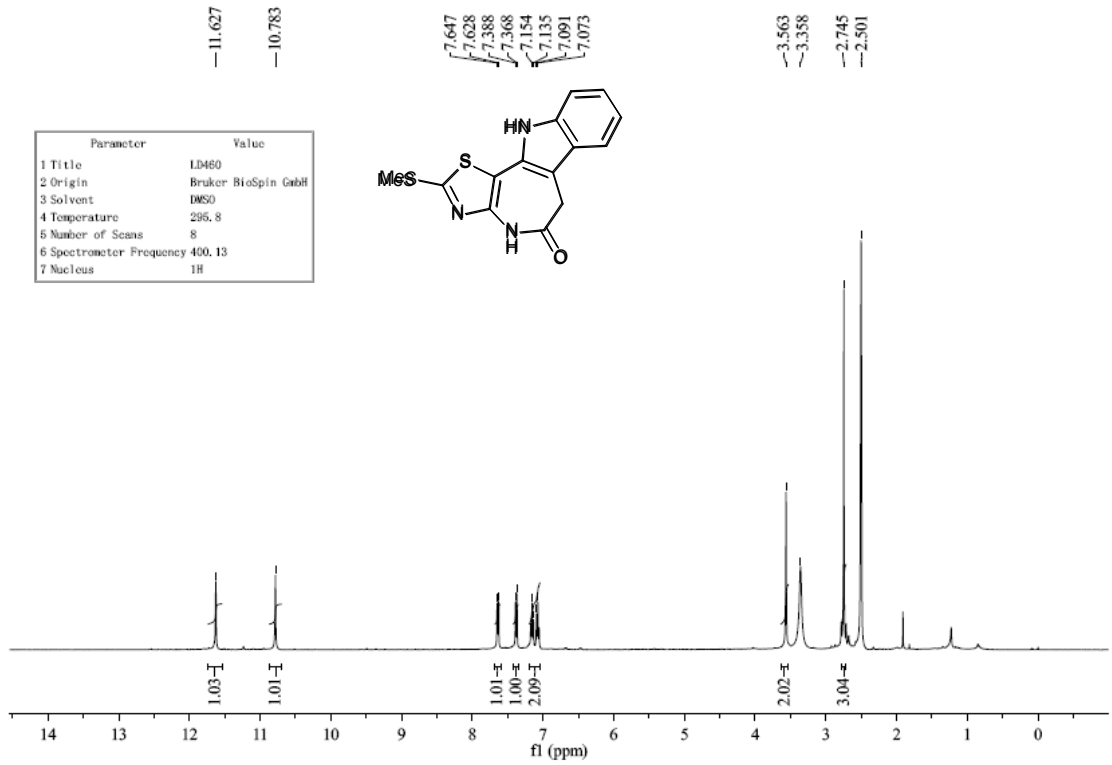


^{13}C NMR (101 MHz, $CDCl_3$) of **11f**





^{1}H NMR (400 MHz, DMSO-d_6) of **13**



^{13}C NMR (101 MHz, DMSO-d_6) of **13**