Supporting Information

Pd/P/dba-Promoted Cascade Annulations to Fused Medium-sized Sulfoximine Polyheterocycles

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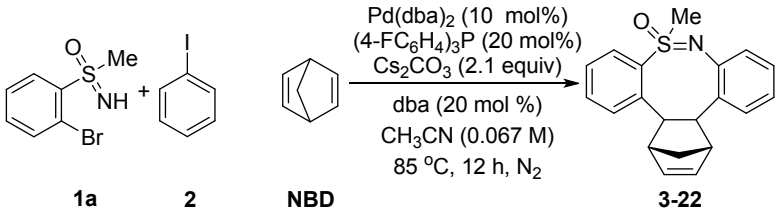
Content

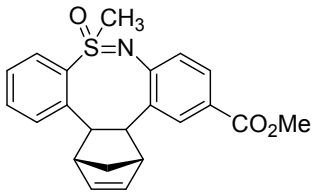
1. General remarks.

Unless otherwise noted, commercial reagents were purchased from commercial suppliers and were used as received. All solvents were dried and distilled according to standard procedures before use. The Flash column chromatography was performed using silica gel (60 Å pore size, 32-63 μm, standard grade). Analytical thin-layer chromatography (TLC) was performed using glass plates pre-coated with 0.25 mm 230-400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Organic solutions were concentrated on rotary evaporators at ~20 Torr (house vacuum) at 25-35 °C. Nuclear magnetic resonance (NMR) spectra were recorded in parts per million (ppm) from internal trimethylsilane (TMS) on the δ scale. High resolution mass spectrometry (HRMS) spectra analysis was performed by electrospray ionization (ESI-micrOTOF).

2. General procedure for the synthesis of bridged heterocycles 3-22.

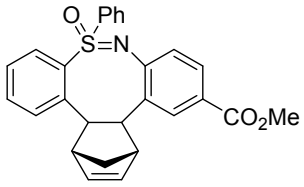


To a screw capped schlenk tube equipped with a stir bar was charged with *ortho*-bromo-*N*H-sulfoximine **1** (0.30 mmol), aryl iodide **2** (0.36 mmol), $Pd(dba)_2$ (10 mol %), (p-$FC_6H_4)_3P$ (20 mol %), Norbornadiene (3.0 equiv.), Cs_2CO_3 (2.1 equiv.), and dry MeCN (4.5 mL). The reaction was purged with N_2, and then heated to 85-105 °C at oil bath for about 12 h. The reaction was monitored by TLC. Upon completion, the reaction was allowed to cool to room temperature, diluted with ethyl acetate (5.0 mL), then filtered through a short pad of silica. The solid residue was washed with ethyl acetate (~10 mL) unless otherwise noted. Concentration of the filtrate under reduced pressure provided the crude product, which was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 10:1 ~ 2:1, *v*/*v*) to afford the desired compounds **3-22**.



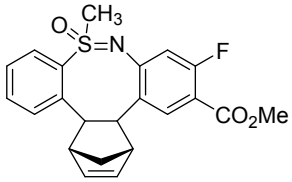
(1*S*,4*R*)-9-Methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**3a**).

Yield: 81%, 92 mg; yellow solid, mp: 198-200 °C. Eluent: ethyl acetate/petroleum ether = 1 : 3. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.51 (d, J = 8.1 Hz, 1H), 7.24-7.20 (m, 3H), 7.05-7.01(m, 1H), 6.71 (d, J = 8.1 Hz, 1H), 6.38 (d, J = 3.9 Hz, 2H), 4.08 (d, J = 9.7 Hz, 1H), 3.73 (s, 3H), 3.44 (s, 3H), 3.29 (d, J = 9.6 Hz, 1H), 3.20 (s, 2H), 2.01 (d, J = 8.5 Hz, 1H), 1.80 (d, J = 8.5 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.2, 151.2, 143.5, 140.1, 139.4, 138.9, 136.5, 132.9, 128.0, 127.8, 127.6, 126.4, 125.3, 124.9, 123.9, 51.9, 46.9, 46.2, 46.1,45.8, 45.0. **HRMS (ESI)** calculated for $C_{22}H_{22}NO_3S$ $[M+H]^+$: 380.1315, found: 380.1319.



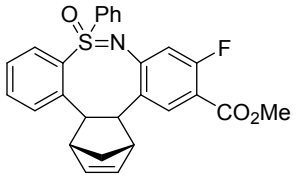
Methyl(1*S*,4*R*)-9-phenyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**3b**).

Yield: 75%, 99 mg; white solid, mp: 227-228 ^{o}C. Eluent: ethyl acetate/petroleum ether = 1 : 3. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 8.24 (s, 2H), 7.86 (s, 1H), 7.78-7.63 (m, 4H), 7.26 (d, *J* = 6.4 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 8.2 Hz, 1H), 6.80 (t, *J* = 7.5 Hz, 1H), 6.50 (d, *J* = 14.1 Hz, 2H), 6.23 (d, *J* = 7.9 Hz, 1H), 4.61 (d, *J* = 9.6 Hz, 1H), 3.82 (s, 3H), 3.47 (d, *J* = 9.6 Hz, 1H), 3.32 (d, *J* = 9.2 Hz, 2H), 2.17 (d, *J* = 8.5 Hz, 1H), 1.91 (d, *J* = 8.3 Hz, 1H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 167.2, 152.0, 143.7, 139.8, 139.7, 139.5, 139.3, 138.6, 137.3, 133.8, 132.2, 128.6, 127.9, 126.5, 126.4, 126.2, 125.9, 125.2, 124.5, 51.8, 47.5, 46.7, 45.9, 45.8, 45.6. **HRMS (ESI)** calculated for $C_{27}H_{24}NO_3S$ $[M+H]^+$: 442.1471, found: 442.1475.



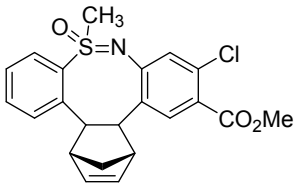
Methyl(1*S*,4*R*)-12-fluoro-9-methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**4a**).

Yield: 60%, 71.5 mg; white solid, mp: 213-214 ^{o}C. Eluent: ethyl acetate/petroleum ether = 1 : 3. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.61 (d, *J* = 6.5 Hz, 1H), 7.33-7.27 (m, 3H), 7.15 (s, 1H), 6.51 6.45 (m, 3H), 4.16 (d, *J* = 8.4 Hz, 1H), 3.83 (s, 3H), 3.51 (s, 3H), 3.27-3.25 (m, 3H), 2.04 (s, 1H), 1.87 (s, 1H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 165.1 (d, *J* = 4.0 Hz), 160.7 (d, ^{1}J = 257 Hz), 152.6, 143.6, 139.9, 139.0, 136.1, 135.2, 133.0, 129.7, 127.5, 126.6, 123.8, 113.6 (d, ^{2}J = 22 Hz), 112.8 (d, ^{2}J = 9.8 Hz), 52.0, 46.5, 46.12, 46.1, 45.8, 45.7, 45.0. **HRMS (ESI)** calculated for $C_{22}H_{21}FNO_3S$ $[M+H]^+$: 398.1221, found: 398.1228.



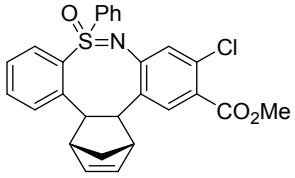
Methyl(1*S*,4*R*)-12-fluoro-9-phenyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**4b**).

Yield: 64%, 88 mg; white solid, mp: 220-221 ^{o}C. Eluent: ethyl acetate/petroleum ether = 1 : 3. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.14-8.19 (m, 2H), 7.78-7.69 (m, 4H), 7.28-7.22 (m, 2H), 6.88-6.78 (m, 2H), 6.54-6.46 (m, *2*H), 6.25 (d, *J* = 7.8 Hz, 1H), 4.58 (d, *J* = 9.6 Hz, 1H), 3.85 (s, 3H), 3.41 (d, *J* = 9.6 Hz, 1H), 3.31 (s, 2H), 2.13 (d, *J* = 8.6 Hz, 1H), 1.90 (d, *J* = 8.6 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.1, 160.6 (d, ^{1}J = 256 Hz), 153.5, 143.8, 139.9, 139.3, 138.9, 137.1, 134.6, 134.0, 132.4, 130.5, 129.1, 126.5, 126.0, 125.2, 114.2 (d, ^{2}J = 22 Hz), 112.5 (d, ^{2}J = 21 Hz), 52.0, 47.7, 46.6, 45.8, 45.6, 45.2. **HRMS (ESI)** calculated for $C_{27}H_{23}FNO_3S$ $[M+H]^+$: 460.1377, found: 460.1367.



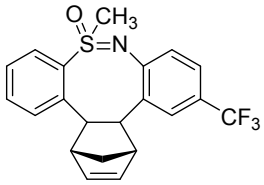
Methyl(1*S*,4*R*)-12-chloro-9-methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**5a**).

Yield: 82%, 102 mg; white solid, mp: 209-210 ^{o}C. Eluent: ethyl acetate/petroleum ether = 1 : 3. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.58 (s, 1H), 7.37-7.31 (m, 3H), 7.17 (d, *J* = 6.7 Hz, 1H), 6.81 (s, 1H), 6.45 (s, 2H), 4.15 (d, *J* = 12.0 Hz, 1H), 3.83 (s, 3H), 3.52 (s, 3H), 3.28-3.22 (m, 3H), 2.02 (d, *J* = 8.1 Hz, 1H), 1.86 (d, *J* = 7.8 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.0, 150.9, 143.3, 139.8, 139.1, 137.9, 136.1, 133.1, 131.8, 129.8, 127.9, 127.5, 126.7, 123.8, 52.1, 46.4, 46.3, 46.1, 45.9, 45.7, 45.0. **HRMS (ESI)** calculated for $C_{22}H_{20}ClNO_3S$ $[M+H]^+$: 414.1025, found: 414.1038.



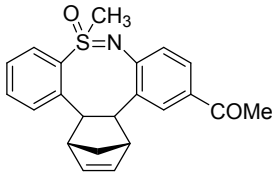
Methyl(1*S*,4*R*)-12-chloro-9-phenyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**5b**).

Yield: 71%, 101 mg; white solid, mp: 233-234 °C. Eluent: ethyl acetate/petroleum ether = 1 : 3. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.21 (s, 2H), 7.78-7.71 (m, 4H), 7.28-7.22 (m, 2H), 7.11 (s, 1H), 6.88-6.84 (m, 1H), 6.53 (m, 1H), 6.48-6.45 (m, 1H), 6.26 (d, *J* = 7.9 Hz, 1H), 4.60 (d, *J* = 9.7 Hz, 1H), 3.85 (s, 3H), 3.40 (d, *J* = 9.7 Hz, 1H), 3.31 (d, *J* = 10.1 Hz, 2H), 2.10 (d, *J* = 8.6 Hz, 1H), 1.90 (d, *J* = 8.6 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.1, 151.7, 143.6, 140.0, 139.2, 138.8, 137.3, 137.1, 134.0, 132.4, 131.8, 130.6, 129.4, 128.5, 126.4, 126.2, 125.2, 123.3, 52.1, 47.5, 46.8, 45.8, 45.6, 45.4. **HRMS(ESI)** calculated for $C_{27}H_{23}ClNO_3S$ $[M+H]^+$: 476.1082, found: 476.1082.



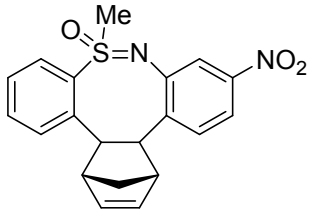
((1*S*,4*R*)-9-Methyl-13-(trifluoromethyl)-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine 9-oxide (**6**).

Yield: 71%, 83 mg; white solid, mp: 209-210 °C. Eluent: ethyl acetate/petroleum ether = 1 : 3. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.35-7.26 (m, 4H), 7.13 (t, *J* = 7.4 Hz, 2H), 6.81 (d, *J* = 8.1 Hz, 1H), 6.45 (s, 2H), 4.18 (d, *J* = 9.6 Hz, 1H), 3.51 (s, 3H), 3.38 (d, *J* = 9.6 Hz, 1H), 3.29 (s, 1H), 3.22 (s, 1H), 2.03 (d, *J* = 8.4 Hz, 1H), 1.87 (d, *J* = 8.4 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 149.4, 143.3, 140.1, 140.0, 139.0, 136.4, 132.9, 127.5, 126.6, 125.5, 125.0, 123.9, 123.4 (q, *J* = 258.0 Hz), 123.3, 123.2, 46.9, 46.1, 46.2, 45.9, 45.6, 45.0. **HRMS (ESI)** calculated for $C_{21}H_{19}F_3NOS$ $[M+H]^+$: 390.1134, found: 390.1142.



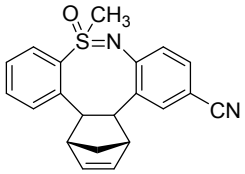
1-((1*S*,4*R*)-9-Methyl-9-oxido-1,4,4a,14b-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2] thiazocin-13-yl)ethan-1-one (**7**).

Yield: 63%, 69 mg; white solid, mp: 230-231 ^{o}C. Eluent: ethyl acetate/petroleum ether = 1 : 3. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.71 (d, *J* = 1.5 Hz, 1H), 7.51-7.49 (m, 1H), 7.33-7.27 (m, 3H), 7.13-7.09 (m, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.46-6.45 (m, 2H), 4.18 (d, *J* = 9.6 Hz, 1H), 3.52 (s, 3H), 3.37 (d, *J* = 9.7 Hz, 1H), 3.28 (s, 2H), 2.45 (s, 3H), 2.08 (d, *J* = 8.6 Hz, 1H), 1.88 (d, *J* = 8.6 Hz, 1H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 197.4, 151.6, 143.5, 140.1, 139.5, 139.0, 136.5, 132.9, 132.4, 127.6, 127.3, 126.5, 126.4, 125.3, 123.8, 46.9, 46.2, 46.1, 45.9, 45.8, 45.1, 26.4. **HRMS (ESI)** calculated for $C_{22}H_{22}NO_2S$ $[M+H]^+$: 364.1366, found: 364.1361.



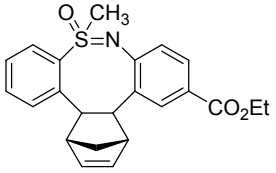
(1*S*,4*R*)-9-Methyl-12-nitro-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine 9-oxide (**8**).

Yield: 67%, 73 mg; yellow solid, mp: 207-210 ^{o}C. Eluent: ethyl acetate/petroleum ether = 1 : 3. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.69-7.66 (m, 1H), 7.56 (d, *J* = 2.4 Hz, 1H), 7.36-7.31 (m, 3H), 7.20-7.14 (m, 2H), 6.47 (s, 2H), 4.23 (d, *J* = 8.0 Hz, 1H), 3.56 (s, 3H), 3.41 (d, *J* = 10.0 Hz, 1H), 3.30 (s, 1H), 3.22 (s, 1H), 2.03 (d, *J* = 8.0 Hz, 1H), 1.88 (d, *J* = 8.0 Hz, 1H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 148.1, 147.3, 146.4, 142.9, 139.8, 139.1, 136.2, 133.0, 127.5, 126.9, 126.7, 124.2, 120.1, 118.3, 47.5, 46.2, 46.1, 46.0, 45.6, 44.9. **HRMS (ESI)** calculated for $C_{20}H_{19}N_2O_3S$ $[M+H]^+$: 367.1111, found: 367.1110.



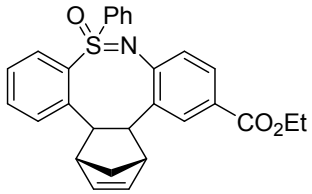
(1*S*,4*R*)-9-Methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thia-zocine-13-carbonitrile 9-oxide (**9**).

Yield: 43%, 45 mg; white solid, mp: 218-219 ^{o}C. Eluent: ethyl acetate/petroleum ether = 1 : 3. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.38 (t, *J* = 7.5 Hz, 1H), 7.31 (t, 3H), 7.18-7.13 (m, 2H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.45 (s, 2H), 4.19 (d, *J* = 9.6 Hz, 1H), 3.52 (s, 3H), 3.34-3.29 (m, 2H), 3.17 (s, 1H), 2.00 (d, *J* = 8.6 Hz, 1H), 1.87 (d, *J* = 8.5 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 151.3, 143.2, 140.8, 139.8, 139.2, 136.2, 133.1, 130.5, 130.4, 127.5, 126.7, 126.2, 123.8, 119.6, 106.4, 46.6, 46.2, 46.1, 45.9, 45.6, 45.1. **HRMS (ESI)** calculated for $C_{21}H_{19}N_2OS$ $[M+H]^+$: 347.1213, found: 347.1232.



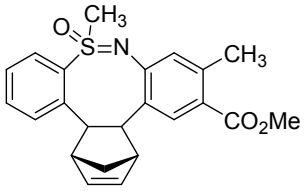
Ethyl(1*S*,4*R*)-9-methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thia-zocine-13-carboxylate 9-oxide (**10a**).

Yield: 63%, 74 mg; white solid, mp: 174-173 ^{o}C. Eluent: ethyl acetate/petroleum ether = 1 : 3. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.68 (s, 1H), 7.51 (m, 1H), 7.25-7.19 (m, 3H), 7.05-7.02 (m, 1H), 6.70 (d, *J* = 8.2 Hz, 1H), 6.39-6.36 (m, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 4.10-4.08 (m, 1H), 3.43 (s, 3H), 3.29 (d, *J* = 9.7 Hz, 1H), 3.20 (s, 2H), 2.02 (d, *J* = 8.6 Hz, 1H), 1.79 (d, *J* = 8.6 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.7, 151.1, 143.5, 140.1, 139.3, 138.9, 136.6, 132.8, 127.9, 127.8, 127.6, 126.3, 125.3, 125.2, 123.9, 60.6, 46.9, 46.2, 46.1, 45.9, 45.7, 45.0, 14.3. **HRMS (ESI)** calculated for $C_{23}H_{24}NO_3S$ $[M+H]^+$: 394.1471, found: 394.1470.



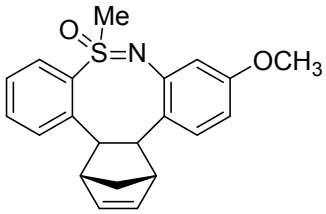
Ethyl(1*S*,4*R*)-9-phenyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**10b**).

Yield: 65%, 89 mg; white solid, mp: 176-177 °C. Eluent: ethyl acetate/petroleum ether =1: 3. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.24 (s, 2H), 7.87 (s, 1H), 7.78-7.63 (m, 4H), 7.27 (d, *J* = 6.3 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 8.2 Hz, 1H), 6.80 (t, *J* = 7.6 Hz, 1H), 6.54-6.47 (m, 2H), 6.23 (d, *J* = 7.9 Hz, 1H), 4.60 (d, *J* = 9.7 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.47 (d, *J* = 9.7 Hz, 1H), 3.34-3.42 (m, 2H), 2.18 (d, *J* = 8.6 Hz, 1H), 1.91 (d, *J* = 8.6 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.7, 151.8, 143.9, 139.8, 139.5, 139.4, 138.5, 137.3, 133.8, 132.2, 130.6, 128.7, 127.8, 126.5, 126.1, 125.8, 125.2, 124.8, 60.6, 47.5, 46.7, 45.8, 45.6, 14.4. **HRMS(ESI)** calculated for $C_{28}H_{26}NO_3S$ $[M+H]^+$: 456.1628, found: 456.1626.



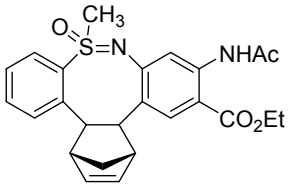
Methyl(1*S*,4*R*)-9,12-dimethyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**11**).

Yield: 72%, 85 mg; white solid, mp: 223-224 °C. Eluent: ethyl acetate/petroleum ether =1: 3. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.64 (s, 1H), 7.36-7.29 (m, 3H), 7.12 (t, *J* = 6.2 Hz, 1H), 6.60 (s, 1H), 6.44 (s, 2H), 4.15 (d, *J* = 8.0 Hz , 1H), 3.79 (s, 3H), 3.51 (s, 3H), 3.31 (d, *J* = 9.7 Hz, 1H), 3.26 (d, *J* = 9.8 Hz, 2H), 2.36 (s, 3H), 2.06 (d, *J* = 8.4 Hz, 1H), 1.85 (d, *J* = 8.2 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.0, 150.1, 143.7, 140.1, 138.9, 138.8, 136.5, 136.1, 132.8, 129.1, 128.6, 127.5, 126.4, 124.0, 123.9, 51.5, 46.4, 46.3, 46.0, 45.9, 45.7, 45.1, 21.4. **HRMS (ESI)** calculated for $C_{23}H_{24}NO_3S$ $[M+H]^+$: 394.1471, found: 394.1462.



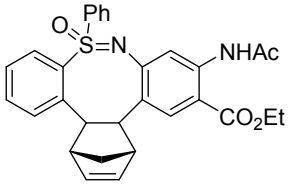
(1*S*,4*R*)-12-Methoxy-9-methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine 9-oxide (**12**).

Yield: 69%, 73 mg; white solid, mp: 186-189 °C. Eluent: ethyl acetate/petroleum ether =1: 4. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.35-7.26 (m, 3H), 7.13-7.09 (m, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.46-6.44 (m, 1H), 6.41-6.35 (m, 3H), 4.09 (d, *J* = 9.5 Hz, 1H), 3.64 (s, 3H), 3.48 (s, 3H), 3.32 (d, *J* = 9.5 Hz, 1H), 3.26 (s, 1H), 3.17 (s, 1H), 2.03 (d, *J* = 8.4 Hz, 1H), 1.79 (d, *J* = 8.4 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 158.0, 147.1, 144.0, 140.3, 138.6, 136.8, 132.5, 131.2, 127.4, 126.4, 126.2, 124.3, 111.3, 108.6, 55.2, 46.3, 46.2, 46.0, 45.7, 45.6, 44.9. **HRMS (ESI)** calculated for $C_{21}H_{22}NO_2S$ $[M+H]^+$: 352.1366, found: 352.1360.



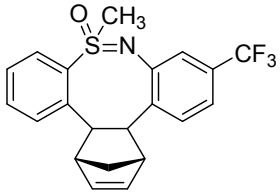
Ethyl(1S,4R)-12-acetamido-9-methyl-1,4,4a,14b-tetrahydro-9λ^4-1,4-methanotribenzo[c,e,g][1,2]thiazocine-13-carboxylate 9-oxide (**13a**).

Yield: 79%, 107 mg; white solid, mp: 283-284 °C. Eluent: ethyl acetate/petroleum ether =1: 3. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.83 (s, 1H), 8.06 (s, 1H), 7.61 (s, 1H), 7.25-7.05 (m, 3H), 7.05-7.03 (m, 1H), 6.39-6.34 (m, 2H), 4.20-4.16 (m, 2H), 4.05 (d, *J* = 9.5 Hz, 1H), 3.45 (s, 3H), 3.26 (d, *J* = 9.6 Hz, 1H), 3.20 (s, 1H), 3.13 (s, 1H), 2.05 (s, 3H), 1.94 (d, *J* = 8.4 Hz, 1H), 1.77 (d, *J* = 8.4 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.7, 168.2, 152.5, 143.3, 140.3, 140.0, 138.8, 136.8, 133.5, 132.7, 128.3, 127.5, 126.5, 124.3, 116.9, 110.1, 61.0, 46.4, 46.2, 46.0, 45.7, 45.5, 44.9, 25.5, 14.2. **HRMS (ESI)** calculated for $C_{25}H_{27}N_2O_4S$ $[M+H]^+$: 451.1686, found: 451.1684.



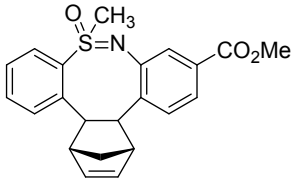
Methyl(1*S*,4*R*)-12-acetamido-9-phenyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**13b**).

Yield: 75%, 115 mg; white solid, mp: 273-274 °C. Eluent: ethyl acetate/petroleum ether =1: 3. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 10.94 (s, 1H), 8.50 (s, 2H), 7.81 (s, 1H), 7.74 (d, *J* = 5.0 Hz, 3H), 7.27-7.23 (m, 2H), 6.83 (t, *J* = 7.5 Hz, 1H), 6.53-6.46 (m, 2H), 6.29 (d, *J* = 7.8 Hz, 1H), 4.57 (d, *J* = 9.6 Hz, 1H), 4.33-4.28 (m, 2H), 3.44 (d, *J* = 9.6 Hz, 1H), 3.30 (d, *J* = 16.4 Hz, 2H), 2.17 (s, 3H), 2.10 (d, *J* = 8.4 Hz, 1H), 1.88 (d, *J* = 8.4 Hz, 1H), 1.70 (s, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 168.9, 168.3, 153.3, 143.7, 140.2, 139.8, 139.3,139.2, 137.5, 133.8, 132.8, 132.1,130.7,129.4, 129.2, 126.3, 126.0, 125.5, 117.6, 109.8, 61.0, 47.4, 46.6, 45.6, 45.5, 45.3, 25.5, 14.2. **HRMS (ESI)** calculated for $C_{30}H_{29}N_2O_4S$ $[M+H]^+$: 513.1843, found: 513.1849.



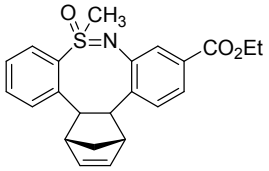
(1*S*,4*R*)-9-Methyl-12-(trifluoromethyl)-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine 9-oxide (**14**).

Yield: 44%, 51 mg; yellow solid, mp: 146-147 °C. Eluent: ethyl acetate/petroleum ether =1: 3. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.29-7.18 (m, 3H), 7.05 (m, 2H), 6.97 (d, *J* = 8.2 Hz, 1H), 6.90 (s, 1H), 6.38-6.36 (m, 2H), 4.11 (d, *J* = 9.7 Hz, 1H), 3.43 (s, 3H), 3.31 (d, *J* = 9.8 Hz, 1H), 3.20 (s, 1H), 3.12 (s, 1H), 1.95 (d, *J* = 8.5 Hz, 1H), 1.77 (d, *J* = 8.5 Hz, 1H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 146.8, 143.5, 143.2, 140.0, 138.9, 136.4, 132.8, 132.7, 127.4, 126.6, 126.5 (q, *J* = 262 Hz), 125.4, 124.1, 122.7, 121.9, 119.9, 47.1, 46.1, 46.1, 45.9, 45.6, 44.9, 29.7. **HRMS (ESI)** calculated for $C_{21}H_{19}F_3NOS$ $[M+H]^+$: 390.1134, found: 390.1137.



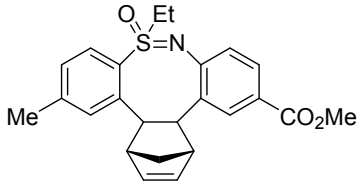
Methyl(1*S*,4*R*)-9-methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-12-carboxylate 9-oxide (**15**).

Yield: 46%, 52 mg; white solid, mp: 190-189 ^{o}C. Eluent: ethyl acetate/petroleum ether =1: 3. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.48 (d, *J* = 8.0 Hz, 1H), 7.40 (s, 1H), 7.31 (d, *J* = 5.9 Hz, 2H), 7.27 (d, *J* = 3.8 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.46-6.44 (m, 2H), 4.18 (d, *J* = 9.7 Hz, 1H), 3.81 (s, 3H), 3.52 (s, 3H), 3.42 (d, *J* = 9.7 Hz, 1H), 3.25 (d, *J* = 22.9 Hz, 2H), 2.04 (d, *J* = 8.4 Hz, 1H), 1.85 (d, *J* = 8.4 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.0, 146.3, 145.4, 143.2, 140.1, 138.8, 136.7, 132.7, 128.2, 127.5, 126.5, 126.2, 126.1, 124.6, 124.3, 51.9, 47.5, 46.2, 45.9, 45.6, 44.9. **HRMS (ESI)** calculated for $C_{22}H_{22}NO_3S$ $[M+H]^+$: 380.1315, found: 380.1308.



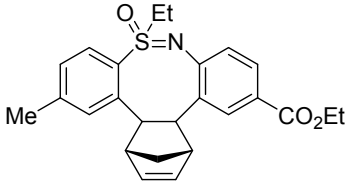
Ethyl(1*S*,4*R*)-9-methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-12-carboxylate 9-oxide (**16**).

Yield 65%, 77 mg; white solid, mp: 169-170 ^{o}C. Eluent: ethyl acetate/petroleum ether =1: 3. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.50-7.48 (m, 1H), 7.40 (d, *J* = 1.7 Hz, 1H), 7.32-7.28 (m, 3H), 7.12-7.09 (m, 2H), 6.47 -6.43 (m, 2H), 4.29-4.25 (m, 2H), 4.18 (d, *J* = 9.7 Hz, 1H), 3.52 (s, 3H), 3.41 (d, *J* = 9.7 Hz, 1H), 3.27 (s, 1H), 3.21 (s, 1H), 2.04 (d, *J* = 8.5 Hz, 1H), 1.85 (d, *J* = 8.5 Hz, 1H), 1.32 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 166.6, 146.3, 145.2, 143.2, 140.1, 138.8, 136.7, 132.6, 128.6, 127.5, 126.5, 126.2, 126.0, 124.5, 124.3, 60.7, 47.4, 46.2, 45.94, 45.92, 45.6, 44.9, 14.3. **HRMS (ESI)** calculated for $C_{23}H_{24}NO_3S$ $[M+H]^+$: 394.1472, found: 394.1470.



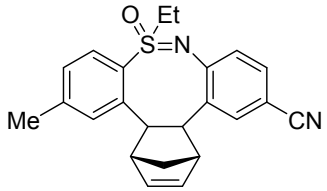
Methyl(1*S*,4*R*)-9-ethyl-6-methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**17**).

Yield: 82%, 100 mg; white solid, mp: 168-169 °C. Eluent: ethyl acetate/petroleum ether =1: 3. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.76 (s, 1H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.10-7.07 (m, 2H), 6.87 (d, *J* = 7.9 Hz, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 6.44 (s, 2H), 4.23 (d, *J* = 9.6 Hz, 1H), 3.81 (s, 3H), 3.75-3.63 (m, 1H), 3.54-3.48 (m, 1H), 3.35 (d, *J* = 9.6 Hz, 1H), 3.26 (s, 2H), 2.25 (s, 3H), 2.08 (d, *J* = 8.5 Hz, 1H), 1.86 (d, *J* = 8.4 Hz, 1H), 1.67 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 167.3, 151.9, 143.9, 143.0, 139.9, 139.2, 139.1, 132.5, 128.2, 128.0, 127.9, 126.8, 125.8, 124.4, 123.5, 51.8, 50.7, 46.6, 46.5, 45.9, 45.8, 21.7, 7.4. **HRMS (ESI)** calculated for $C_{24}H_{25}NO_3S$ $[M+H]^+$: 408.1628, found: 408.1635.



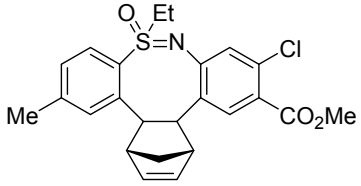
Ethyl(1*S*,4*R*)-9-Ethyl-6-methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**18**).

Yield: 47%, 59.3 mg; white solid, mp: 166-167 °C. Eluent: ethyl acetate/petroleum ether = 1: 3. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.77 (s, 1H), 7.59-7.56 (m, 1H), 7.09 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 7.9 Hz, 1H), 6.72 (d, *J* = 8.2 Hz, 1H), 6.44 (s, 2H), 4.28-4.21 (m, 3H), 3.73-3.66 (m, 1H), 3.54-3.49 (m, 1H), 3.35 (d, *J* = 9.7 Hz, 1H), 3.27 (s, 2H), 2.26 (s, 3H), 2.08 (d, *J* = 8.5 Hz, 1H), 1.86 (d, *J* = 8.4 Hz, 1H), 1.67 (t, *J* = 7.2 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 166.9, 151.8, 143.9, 143.0, 139.9, 139.1, 132.5, 128.2, 128.0, 127.8, 126.7, 125.7, 124.8, 123.5, 60.6, 50.7, 46.6, 46.5, 46.0, 45.8, 45.8, 21.7, 14.3, 7.5. **HRMS (ESI)** calculated for $C_{25}H_{28}NO_3S$ $[M+H]^+$: 422.1784, found: 422.1779.



(1*S*,4*R*)-9-ethyl-6-methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carbonitrile 9-oxide (**19**).

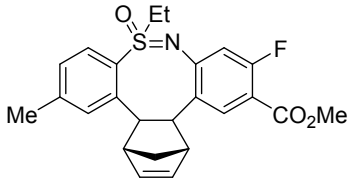
Yield: 60%, 67 mg; white solid, mp: 183-184 °C. Eluent: ethyl acetate/petroleum ether =1: 3. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.33 (s, 1H), 7.17-7.14 (m, 1H), 7.09 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 6.44 (q, *J* = 5.5 Hz, 2H), 4.25 (d, *J* = 9.7 Hz, 1H), 3.75-3.66 (m, 1H), 3.55-3.11 (m, 1H), 3.32-3.28 (m, 2H), 3.16 (s, 1H), 2.30 (s, 3H), 1.99 (d, *J* = 8.6 Hz, 1H), 1.86 (d, *J* = 8.6 Hz, 1H), 1.66 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 152.0, 143.6, 143.4, 140.5, 139.5, 139.4, 132.1, 130.7, 130.3, 128.1, 127.0, 126.7, 123.4, 119.9, 105.8, 50.8, 46.6, 46.3, 46.0, 45.7, 45.6, 21.7, 7.5. **HRMS (ESI)** calculated for $C_{23}H_{23}N_2OS$ $[M+H]^+$: 375.1526, found: 375.1497.



Methyl(1*S*,4*R*)-12-chloro-9-ethyl-6-methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**20**).

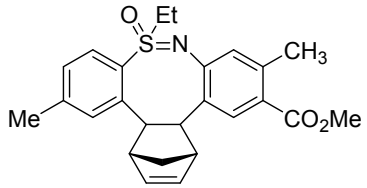
Yield: 65%, 86 mg; white solid, mp: 205-206 °C. Eluent: ethyl acetate/petroleum ether =1: 3. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.59 (s, 1H), 7.12-7.07 (m, 2H), 6.93 (d, *J* = 8.0 Hz, 1H), 6.77 (s, 1H), 6.43 (s, 2H), 4.23 (d, *J* = 9.6 Hz, 1H), 3.84 (s, 3H), 3.74-3.68 (m, 1H), 3.55-3.50 (m, 1H), 3.27 (d, *J* = 8.3 Hz, 2H), 3.22 (s, 1H), 2.29 (s, 3H), 2.01 (d, *J* = 8.5 Hz, 1H), 1.85 (d, *J* = 8.5 Hz, 1H), 1.66 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 166.2, 151.7, 143.7, 143.3, 139.5 139.4, 137.7, 132.1, 131.7, 130.0, 128.2, 128.1, 127.1, 123.4, 123.2, 52.1, 50.8, 46.7, 46.1, 45.9, 45.8, 21.7, 7.5.

HRMS (ESI) calculated for $C_{24}H_{25}ClNO_3S$ $[M+H]^+$: 442.1238, found: 442.1234.



Methyl(1*S*,4*R*)-9-ethyl-12-fluoro-6-methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**21**).

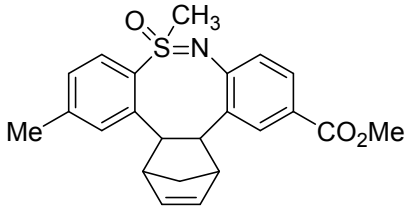
Yield: 85%, 108 mg; white solid, mp: 171-172 °C. Eluent: ethyl acetate/petroleum ether = 1 : 3. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.62 (d, *J* = 8.3 Hz, 1H), 7.12-7.07 (m, 2H), 6.92 (d, *J* = 7.9 Hz, 1H), 6.46 (d, *J* = 12.2 Hz, 3H), 4.22 (d, *J* = 9.6 Hz, 1H), 3.84 (s, 3H), 3.73-3.68 (m, 1H), 3.55-3.50 (m, 1H), 3.26 (t, *J* = 10.2 Hz, 3H), 2.28 (s, 3H), 2.04 (d, *J* = 8.5 Hz, 1H), 1.86 (d, *J* = 8.5 Hz, 1H), 1.65 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.3, 160.7 (d, ^1J = 257 Hz), 153.5, 143.9, 143.3, 139.7, 139.3, 135.0, 132.1, 129.8, 128.2, 126.9, 123.4, 113.9 (d, ^2J = 22 Hz), 112.3 (d, ^2J = 19 Hz), 52.0, 50.8, 46.9, 45.9, 45.8, 45.8, 45.7, 21.7, 7.5. **HRMS (ESI)** calculated for $C_{24}H_{25}FNO_3S$ $[M+H]^+$: 426.1534, found: 426.1510.



Methyl(1*S*,4*R*)-9-ethyl-6,12-dimethyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**22**).

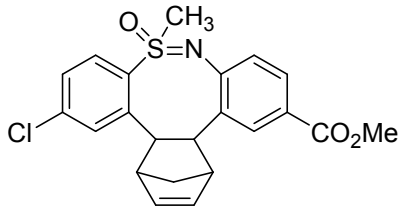
Yield: 71%, 90 mg; white solid, mp: 207-208 °C. Eluent: ethyl acetate/petroleum ether = 1 : 3. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 (s, 1H), 7.11-7.09 (m, 2H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.56 (s, 1H), 6.43 (s, 2H), 4.21 (d, *J* = 9.6 Hz, 1H), 3.80 (s, 3H), 3.73-3.26 (m, 1H), 3.54-3.49 (m, 1H), 3.30-3.24 (m, 3H), 2.36 (s, 3H), 2.27 (s, 3H), 2.05 (d, *J* = 8.4 Hz, 1H), 1.84 (d, *J* = 8.4 Hz, 1H), 1.66 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR**

(100 MHz, $CDCl_3$) δ 168.2, 150.8, 144.1, 142.9, 139.8, 139.1, 138.7, 135.9, 132.5, 129.3, 129.0, 128.1, 126.7, 123.6, 123.5, 51.5, 50.8, 46.8, 46.0, 45.9, 45.8, 45.7, 21.7, 21.3, 7.6. **HRMS (ESI)** calculated for $C_{25}H_{27}NO_3S$ $[M+H]^+$: 422.1785, found: 422.1770.



Methyl-6,9-dimethyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**23**).

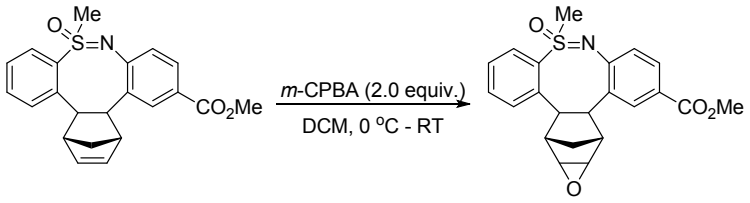
Yield 66%, 78 mg; white solid; mp: 199-200 °C. Eluent: ethyl acetate/petroleum ether =1: 2. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.75 (s, 1H), 7.60-7.58 (m, 1H), 7.16 (d, *J* = 8.2 Hz, 1H), 7.07 (s, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.47-6.41 (m,2H), 4.11 (d, *J* = 9.6 Hz, 1H), 3.81 (s, 3H), 3.48 (s, 3H), 3.35 (d, *J* = 9.6 Hz, 1H), 3.27 (s, 2H), 2.26 (s, 3H), 2.07 (d, *J* = 8.4 Hz, 1H), 1.87 (d, *J* = 8.6 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.3, 151.4, 143.4, 143.3, 140.1, 139.5, 138.7, 133.7, 128.2, 128.0, 127.9, 126.9, 125.3, 124.8, 124.1, 51.8, 46.8, 46.2, 46.1, 45.8, 45.7, 45.1, 21.7. **HRMS (ESI)** calculated for $C_{23}H_{24}NO_3S$ $[M+H]^+$: 394.1471, found: 394.1473.



Methyl-6-chloro-9-methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**24**)

Yield 52%, 65 mg; white solid; mp: 200-201 °C. Eluent: ethyl acetate/petroleum ether =1: 2. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.76 (s, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.27-7.24 (m, 2H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.79 (d, *J* = 8.2 Hz, 1H), 6.48-6.42 (m, 2H), 4.12 (d, *J* = 9.6 Hz, 1H), 3.83 (s, 3H), 3.50 (s, 3H), 3.36 (d, *J* = 9.6 Hz, 1H), 3.26 (d, *J* = 16.0Hz, 2H), 2.04 (d, *J* = 8.8Hz, 1H), 1.89 (d, *J* = 8.6 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 167.0, 150.8, 145.8, 140.3, 139.1, 138.9, 138.7, 135.2, 128.2, 127.9, 127.9, 126.5, 125.3, 125.3, 51.9, 47.0, 46.3, 46.1, 46.0, 45.7, 45.2. **HRMS (ESI)** calculated for $C_{22}H_{21}ClNO_3S$ $[M+H]^+$: 414.0925, found:414.0927.

3. General procedure for the oxidation reaction of bridged heterocycles 3a.

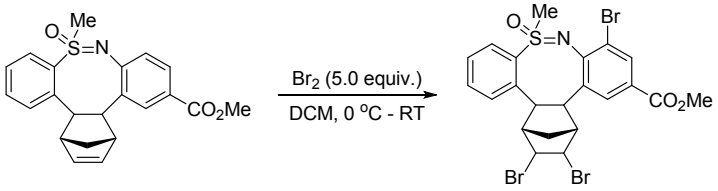


To a stirred solution of **3a** (75.8 mg, 0.20 mmol) in DCM (3.0 mL) at 0 °C was added *m*-chloroperbenzoic acid (98.7 mg, 0.40 mmol), and the resulting light yellow solution was kept stirring for 12 h at room temperature. After diluting with DCM, the reaction was quenched with 1 M aq. KOH solution. The water layer was extracted with DCM and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography (PE/EA = 4:1) to give compound **26** as a yellow solid.

Methyl(2*S*,13*R*)-7-methyl-1*a*,2,2*a*,12*b*,13,13*a*-hexahydro-7λ^4-2,13-methanobenzo[*c*]benzo[*g*]oxireno[2',3':4,5]benzo[1,2-*e*][1,2]thiazocine-11-carboxylate 7-oxide (**26**)

Yield: 71%, 55.8 mg; yellow solid, mp: 186-187 °C. Eluent: ethyl acetate/petroleum ether = 1 : 5. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.01 (d, *J* = 1.2 Hz, 1H), 7.88-7.86 (m, 2H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.22-7.18 (m, 1H), 7.11-7.07 (m, 1H), 6.58 (d, *J* = 7.9 Hz, 1H), 4.12 (d, *J* = 9.2 Hz, 1H), 3.99 (d, *J* = 9.2 Hz, 1H), 3.90 (s, 3H), 3.53-3.52 (m, 1H), 3.41-3.40 (m, 1H), 3.09 (s, 3H), 3.03 (s, 1H), 2.62 (s, 1H), 1.62-1.58 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.1, 152.8, 140.3, 139.5, 136.8, 133.5, 132.6, 130.6, 130.1, 129.4, 128.5, 127.3, 124.9, 52.8, 52.1, 51.7, 46.4, 46.1, 45.4, 44.8, 42.3, 23.9. **HRMS (ESI)** calculated for $C_{22}H_{22}NO_4S$ $[M+H]^+$: 396.1264, found: 396.1241.

4. General procedure for the bromination of bridged heterocycles 3a.



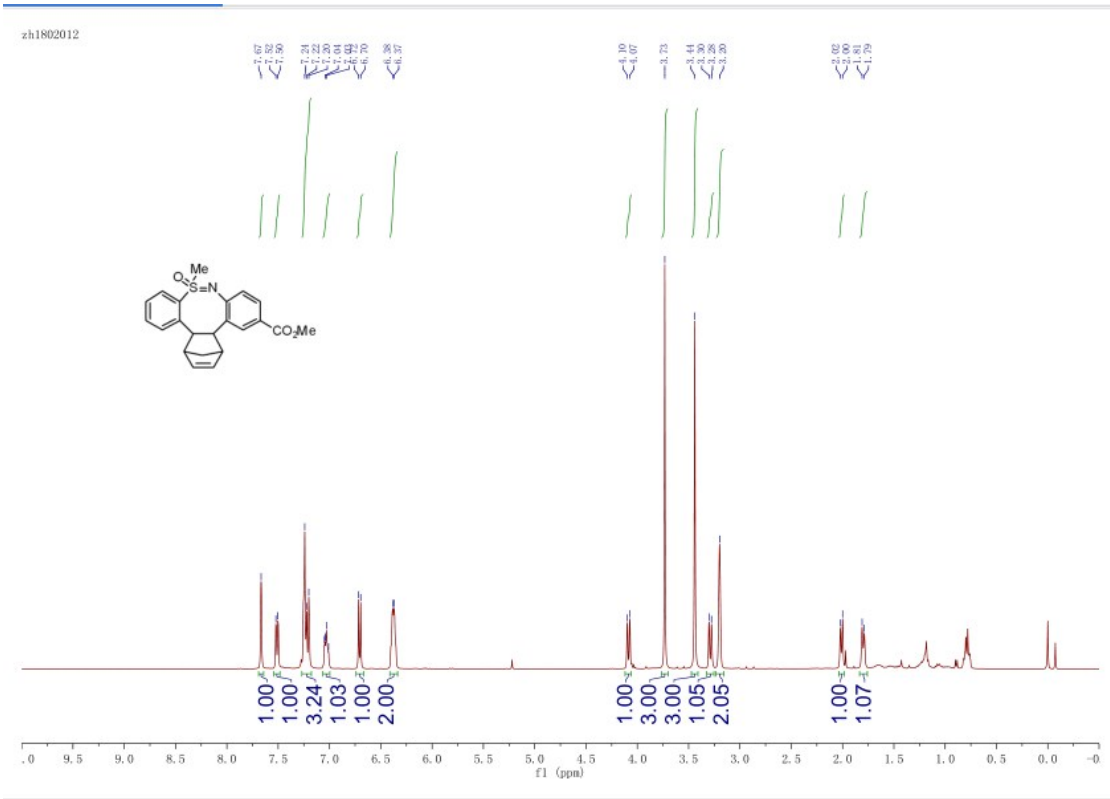
Bromine (119.8 mg, 0.75 mmol) in DCM (3.0 mL) was added to a solution of compound **3a** (57.0 mg, 0.15 mmol) in DCM (3.0 mL) at 0 °C. The reaction was kept stirring for 3 h at room temperature and then quenched with $Na_2S_2O_3$ solution. The reaction was extracted with DCM. The aqueous layer was washed with DCM and brine, dried over anhydrous $MgSO_4$, and solvent was removed under reduced pressure. The obtained residue was purified by column chromatography (PE/EA = 3:1) to give product **24** (50.7 mg, 55% yield) as a white solid.

Methyl(1*S*,4*R*)-8-bromo-9-methyl-1,4,4*a*,14*b*-tetrahydro-9λ^4-1,4-methanotribenzo[*c*,*e*,*g*][1,2]thiazocine-13-carboxylate 9-oxide (**27**)

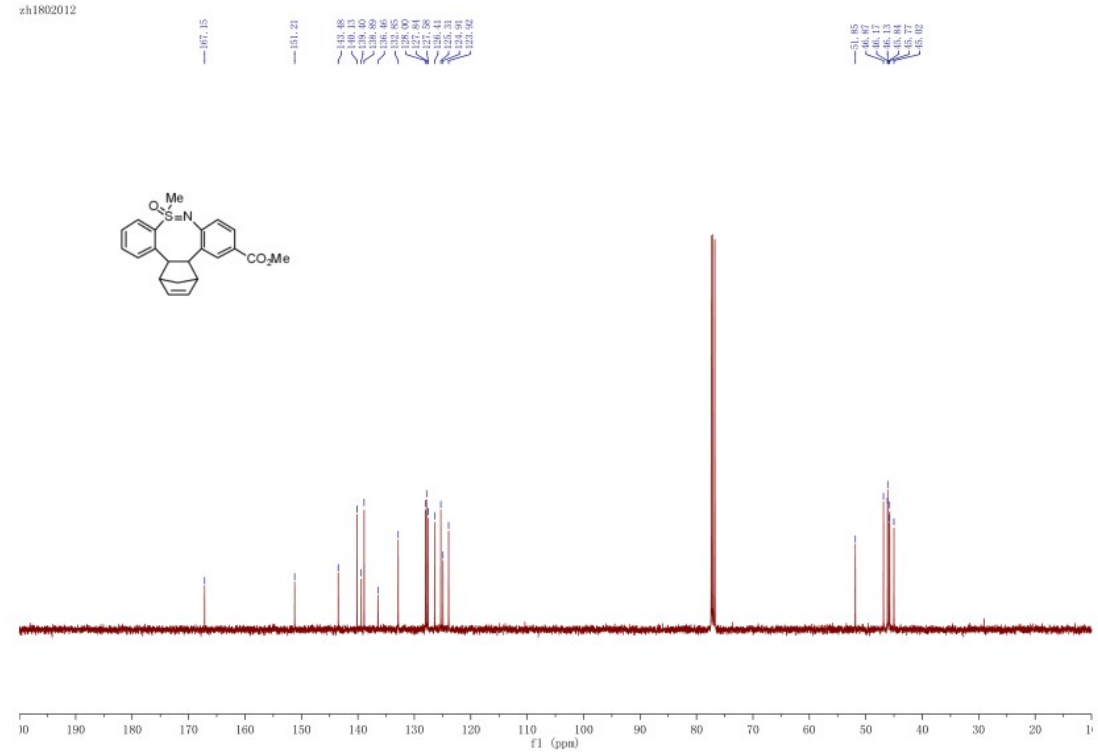
Yield: 54%, 49 mg; white solid, mp: 157-158 °C. Eluent: ethyl acetate/petroleum ether =1: 4. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.90 (d, *J* = 1.7 Hz, 1H), 7.64 (d, *J* = 1.3 Hz, 1H), 7.39-7.33 (m, 2H), 7.19 (t, *J* = 8.5 Hz, 2H), 4.67 (t, *J* = 3.8 Hz, 1H), 4.58 (d, *J* = 9.8 Hz, 1H), 4.29 (s, 1H), 4.19 (d, *J* = 9.9 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.00-2.97 (m, 2H), 2.46 (d, *J* = 11.2 Hz, 1H), 2.31 (d, *J* = 10.9 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.8, 149.7, 140.0, 138.9, 135.4, 133.1, 131.8, 127.4, 126.4, 126.3, 125.3, 123.5, 122.0, 59.7, 59.5, 52.2, 51.2, 49.5, 48.0, 45.4, 34.5. **HRMS (ESI)** calculated for $C_{22}H_{21}Br_3NO_3S$ $[M+H]^+$: 615.8714, found: 615.8720.

5. **^{1}H** and **^{13}C NMR** spectra of all new compounds (**S23-S51**)

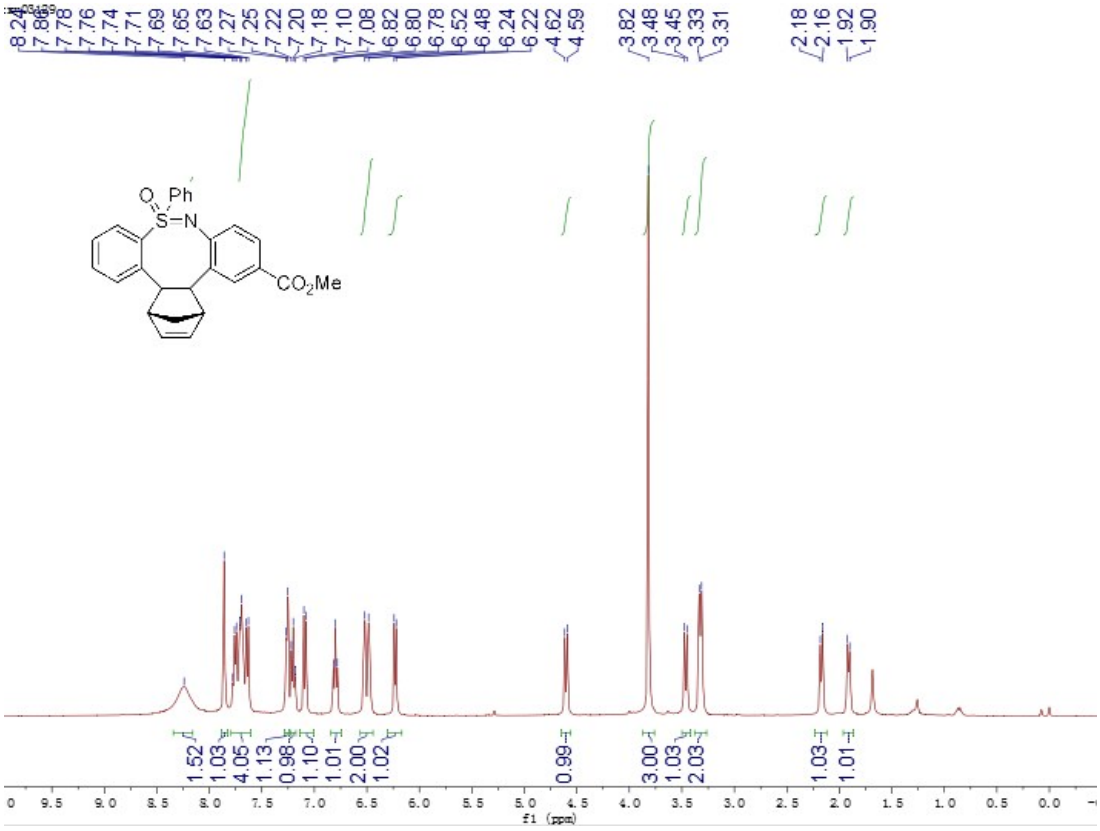
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 3a



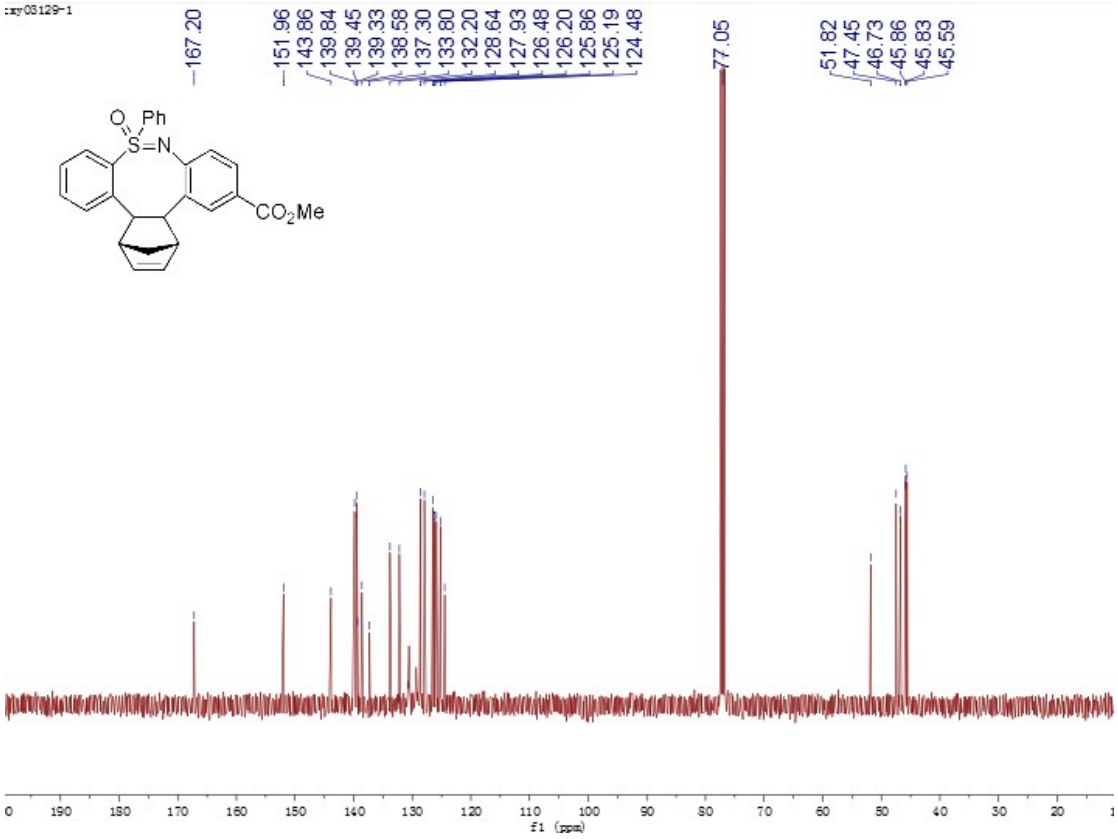
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 3a


zh1802012
167.15
151.21
143.48
140.13
139.40
138.89
136.46
132.85
128.60
127.94
127.58
126.41
125.31
124.91
123.92
51.85
46.87
46.17
46.13
45.84
45.77
45.02
Me
O
S=N
CO2Me
f1 (ppm)

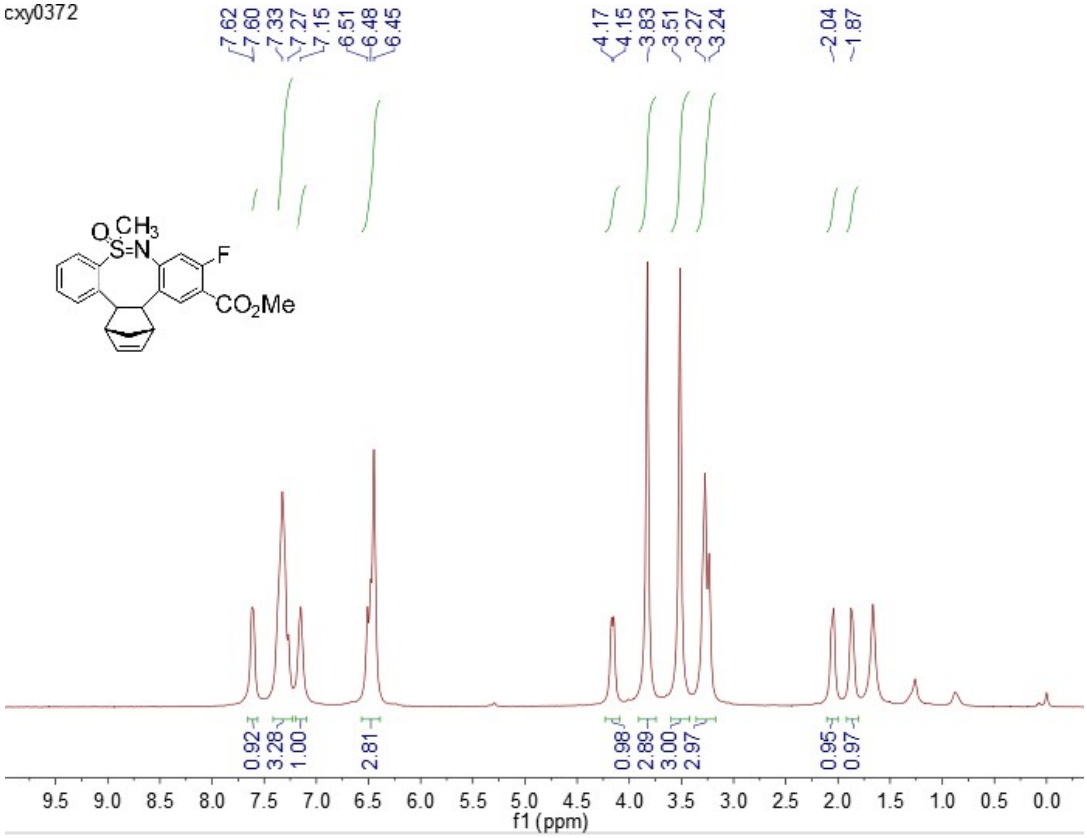
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 3b



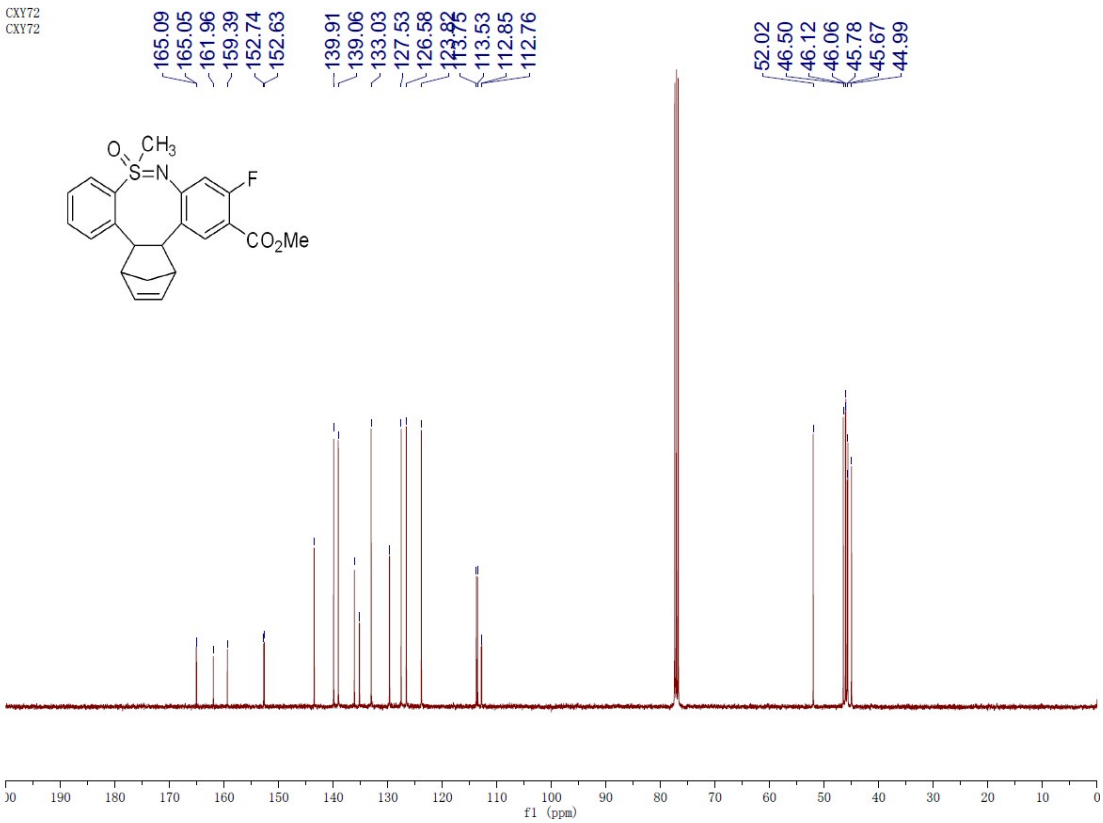
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 3b


:xy03129-1
167.20
151.96
143.86
139.84
139.45
139.33
138.58
137.30
133.80
132.20
128.64
127.93
126.48
126.20
125.86
125.19
124.48
77.05
51.82
47.45
46.73
45.86
45.83
45.59
Ph
O
S=N
CO2Me
f1 (ppm)

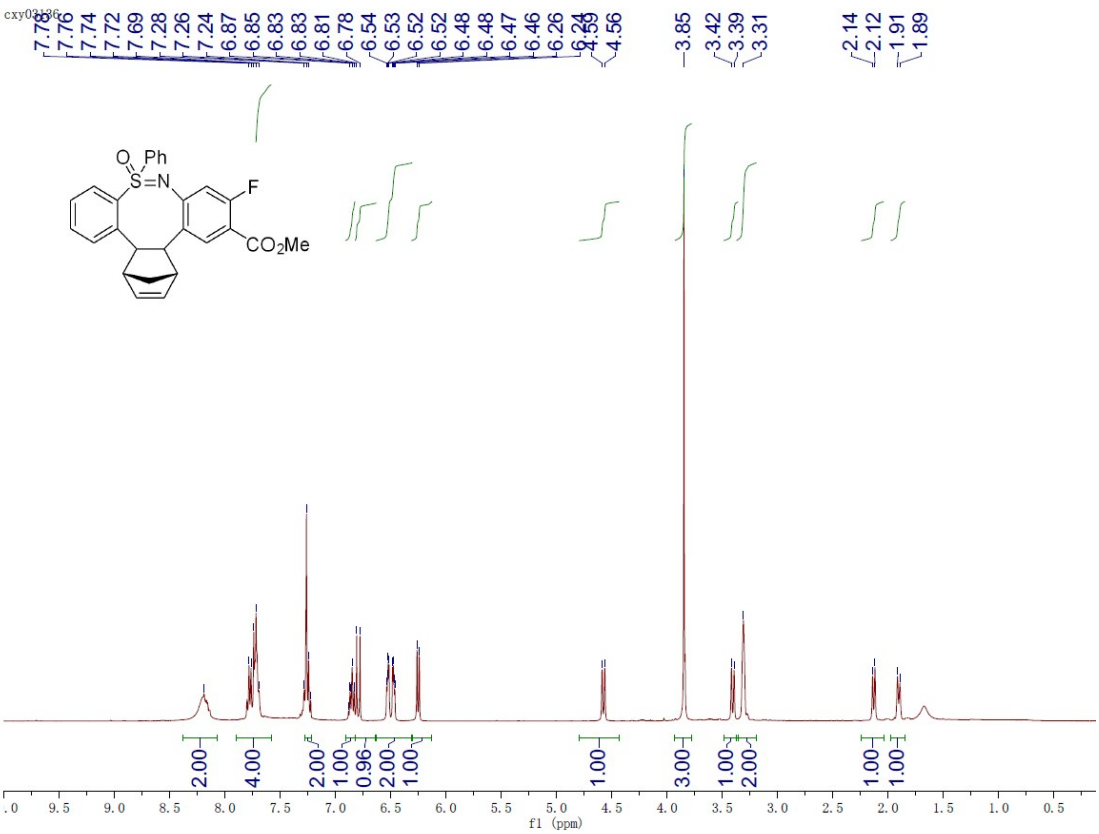
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4a



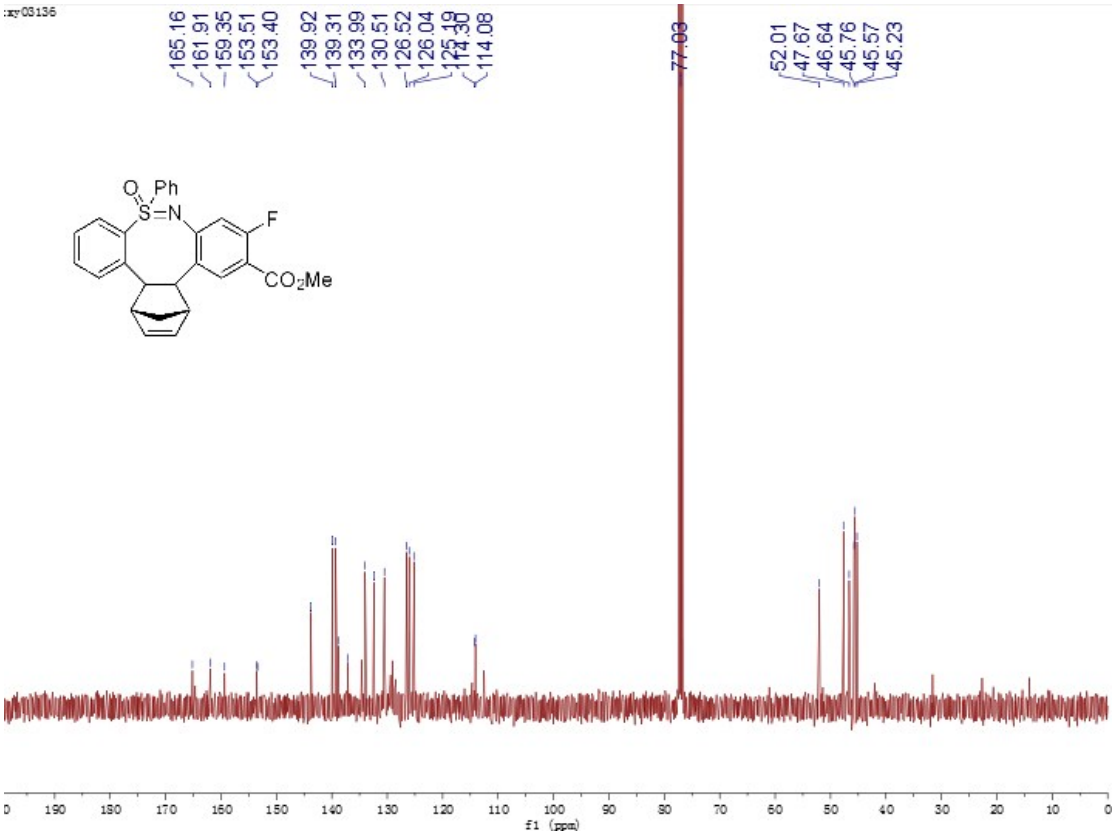
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4a



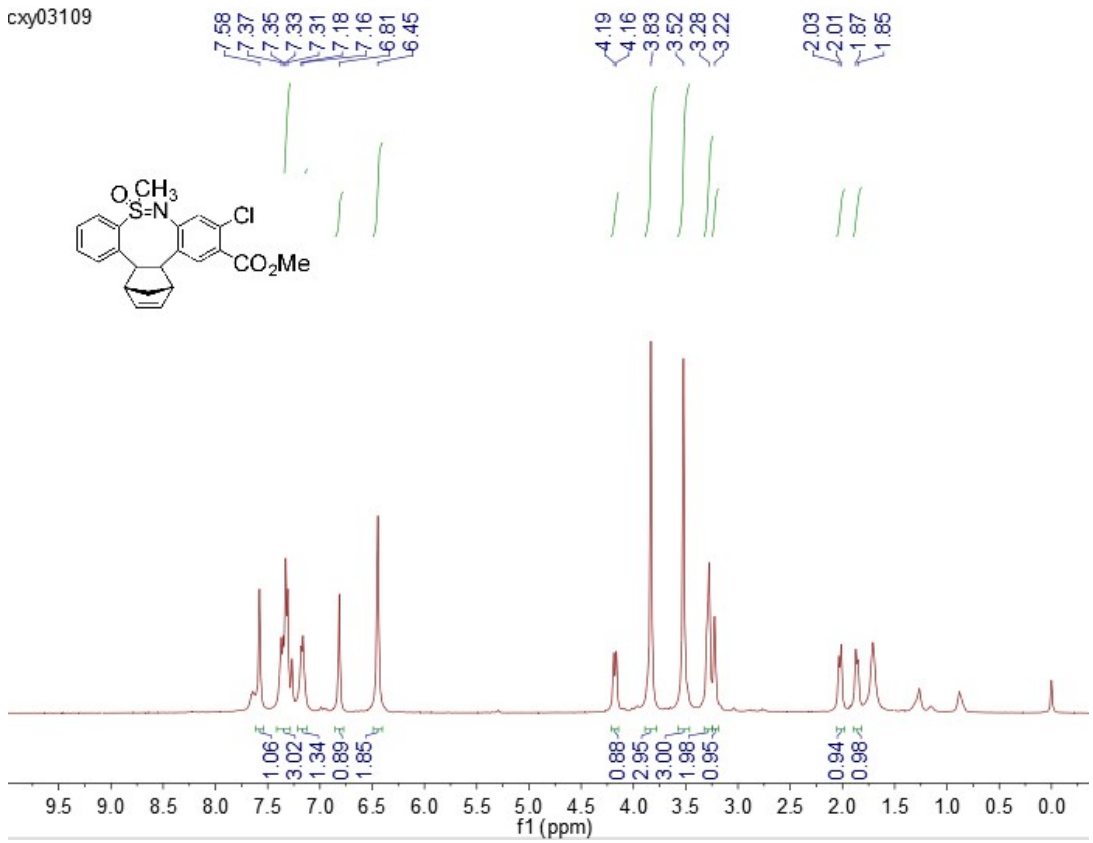
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 4b



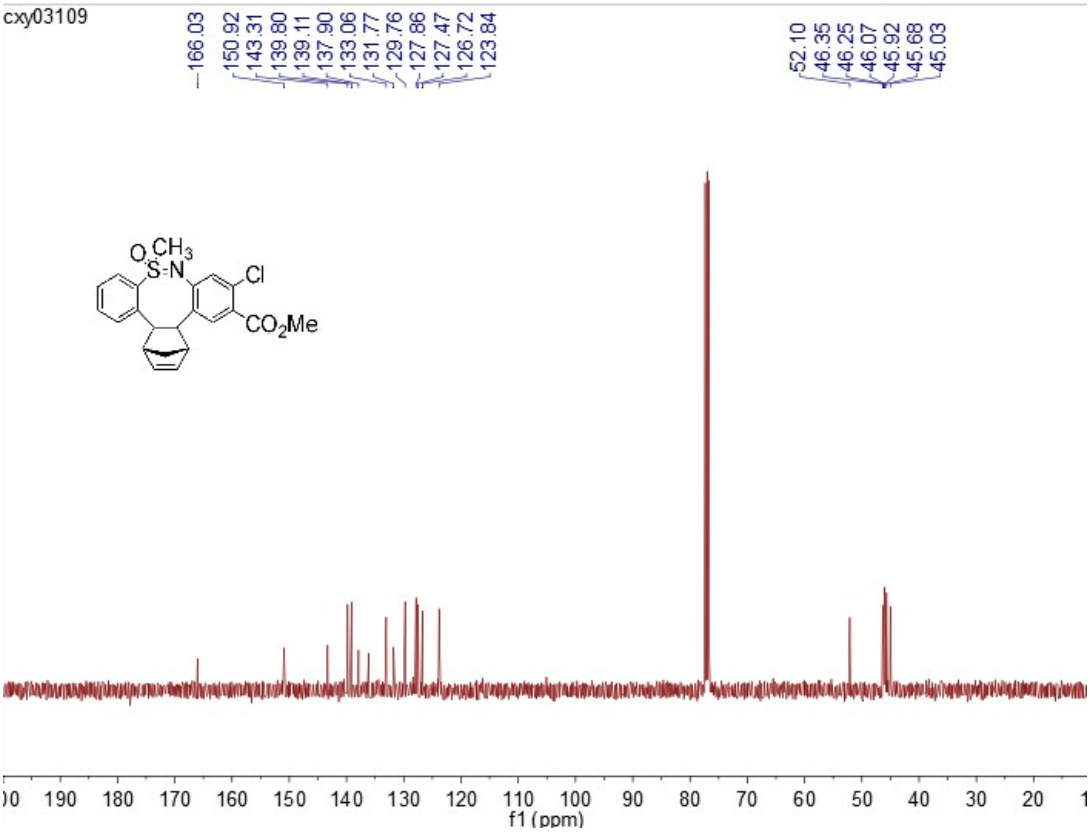
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 4b



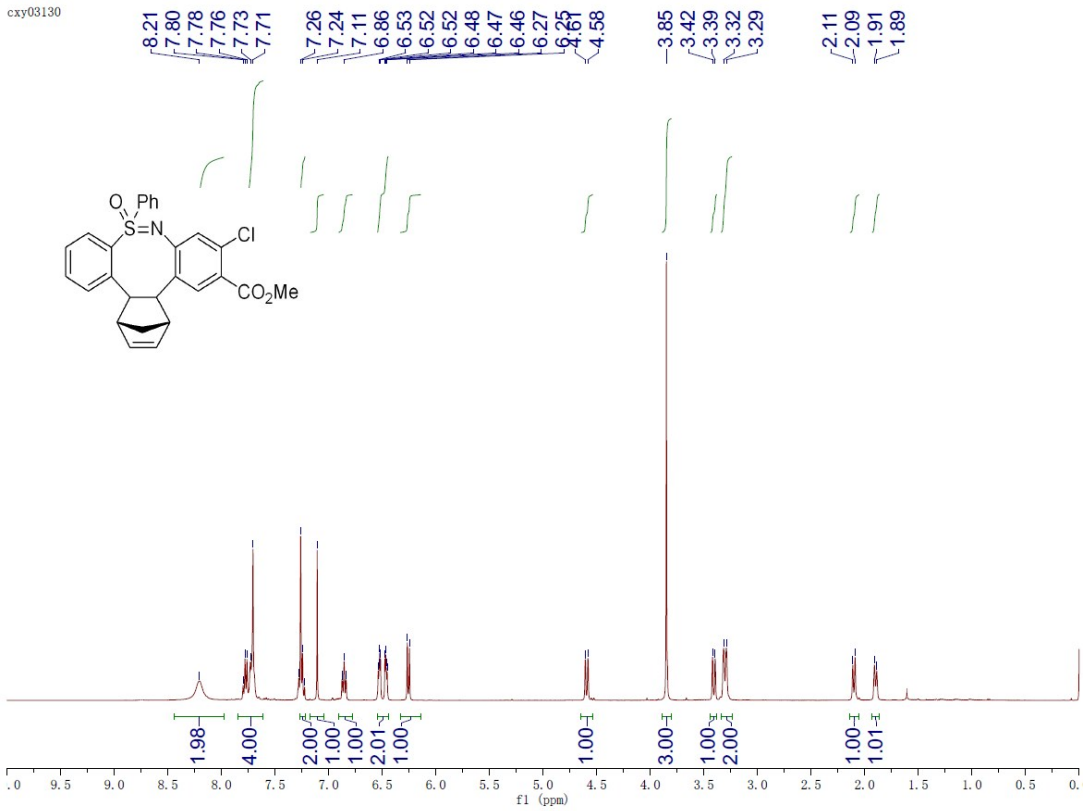
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 5a



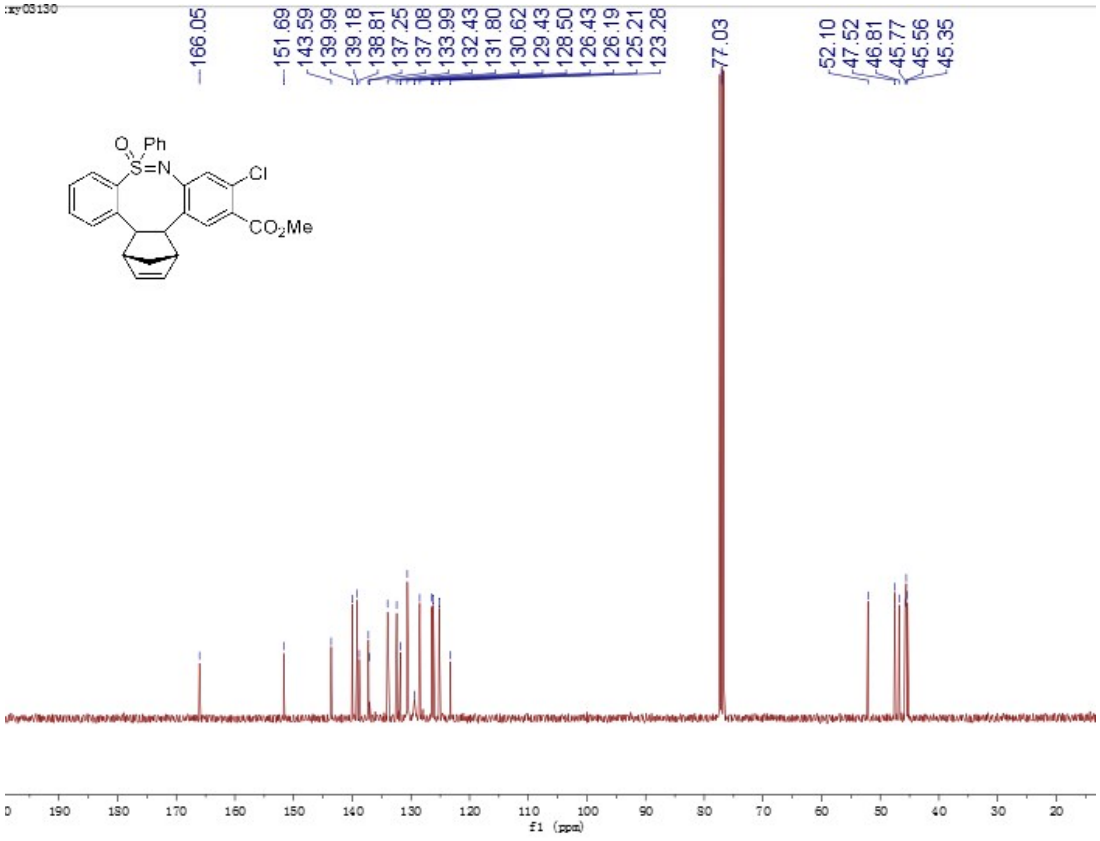
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 5a



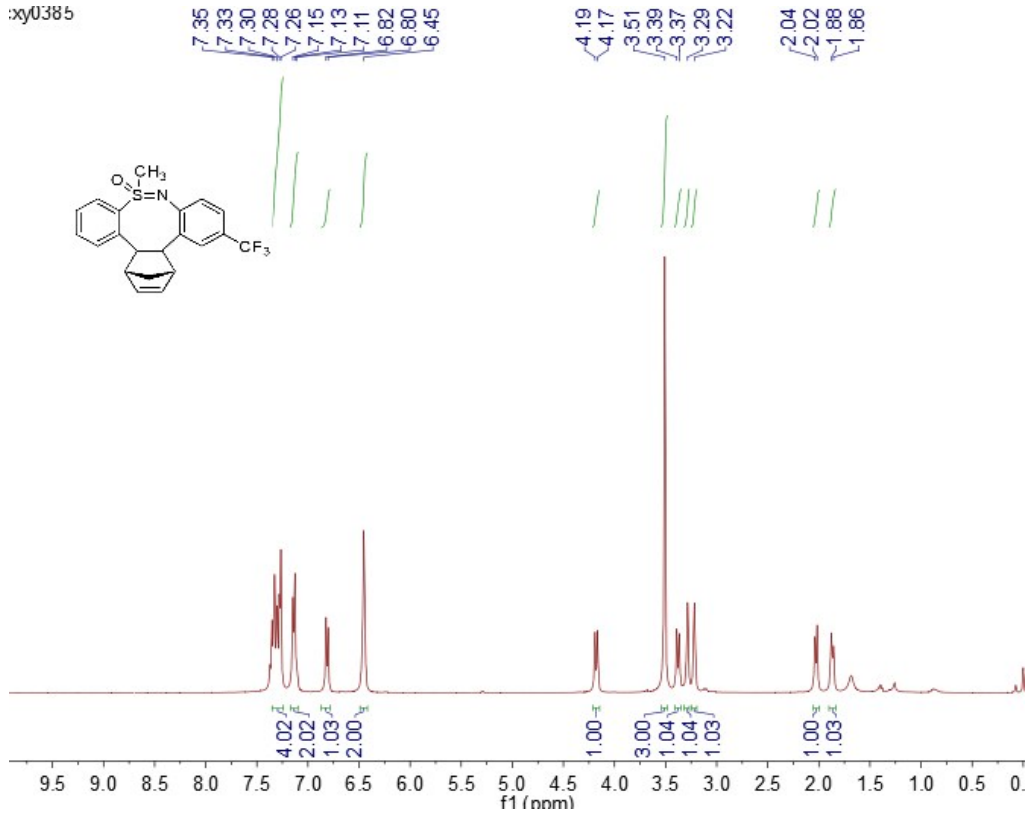
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 5b



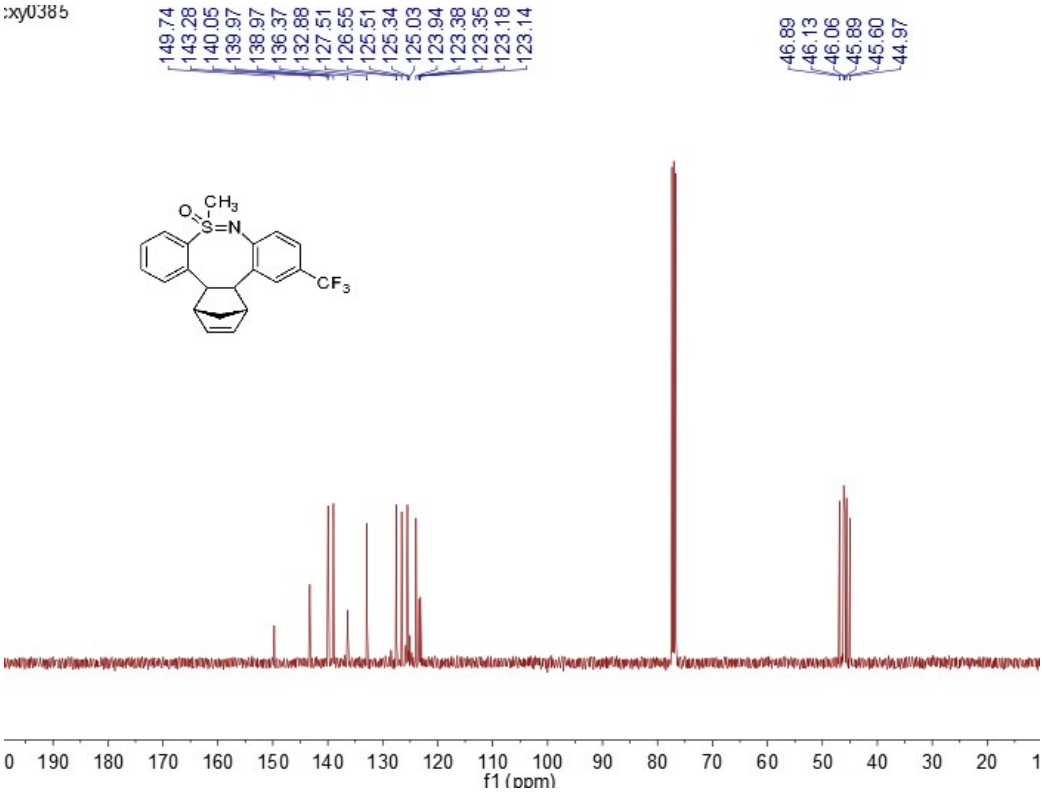
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 5b


xy05130
166.05
151.69
143.59
139.99
139.18
138.81
137.25
137.08
133.99
132.43
131.80
130.62
129.43
128.50
126.43
126.19
125.21
123.28
77.03
52.10
47.52
46.81
45.77
45.56
45.35
O
Ph
S=N
Cl
CO2Me
f1 (ppm)

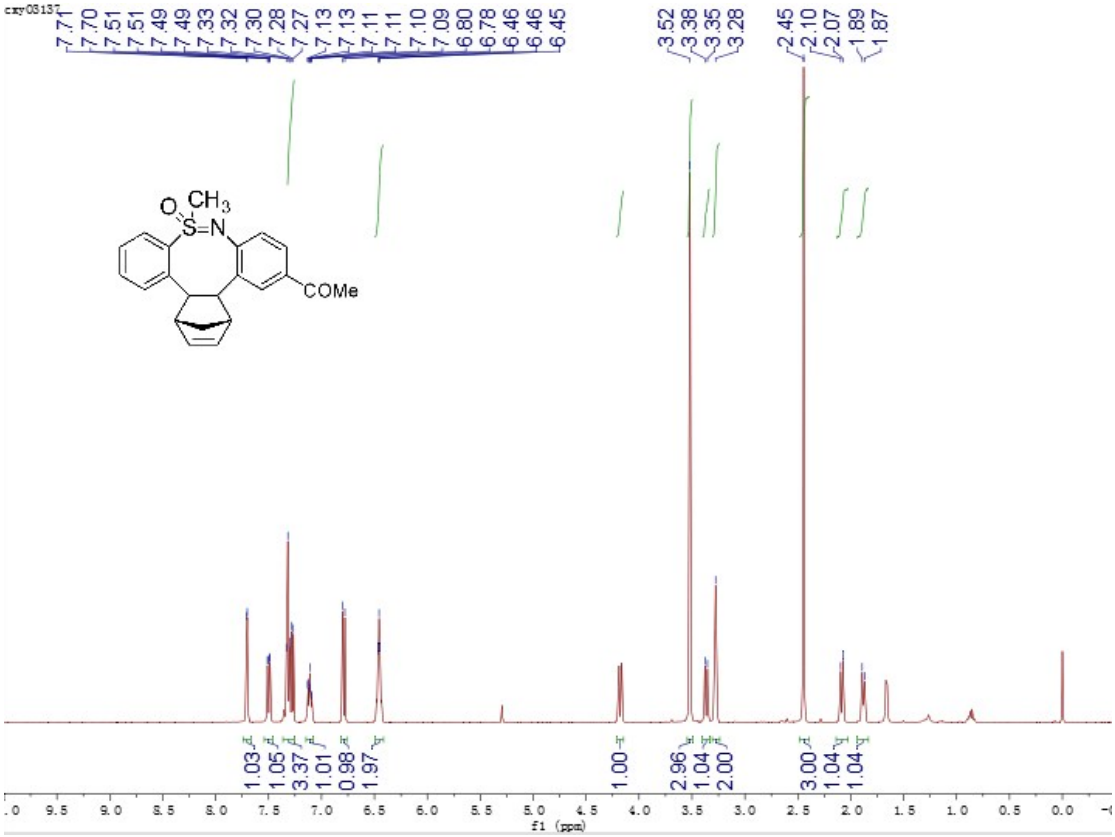
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 6



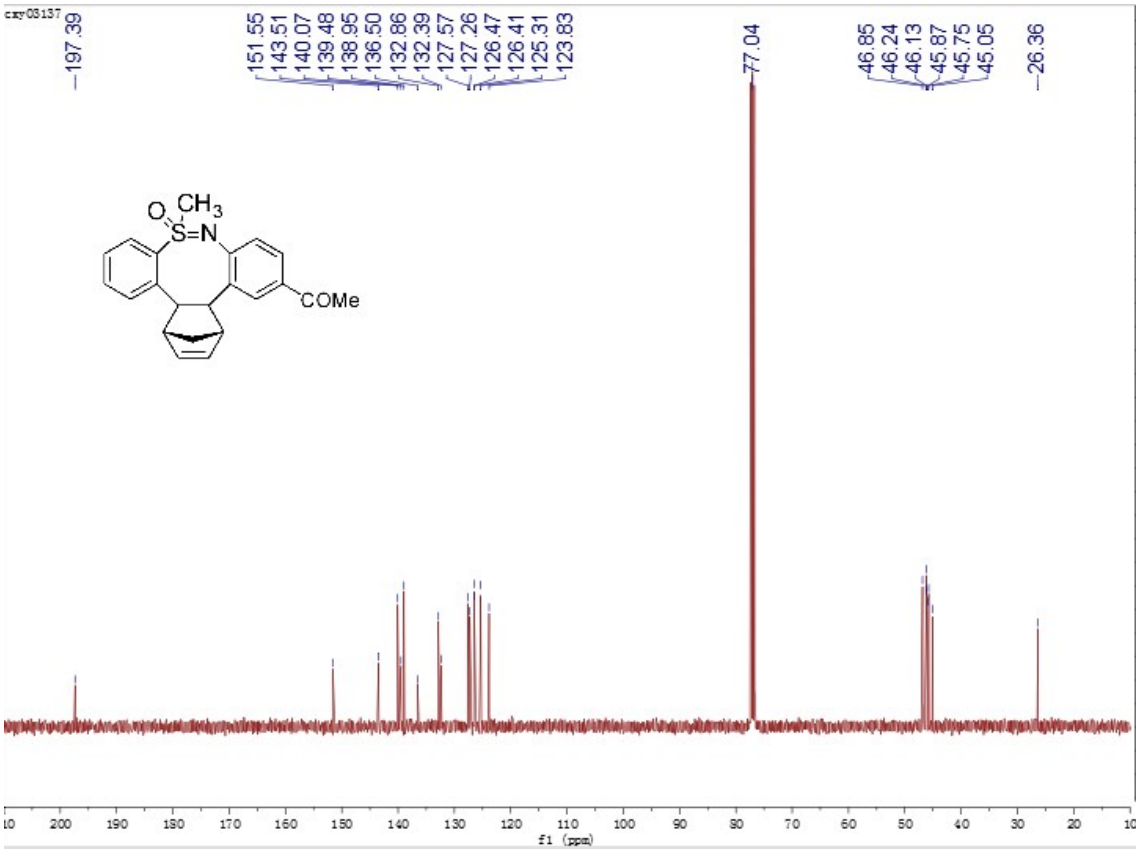
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 6



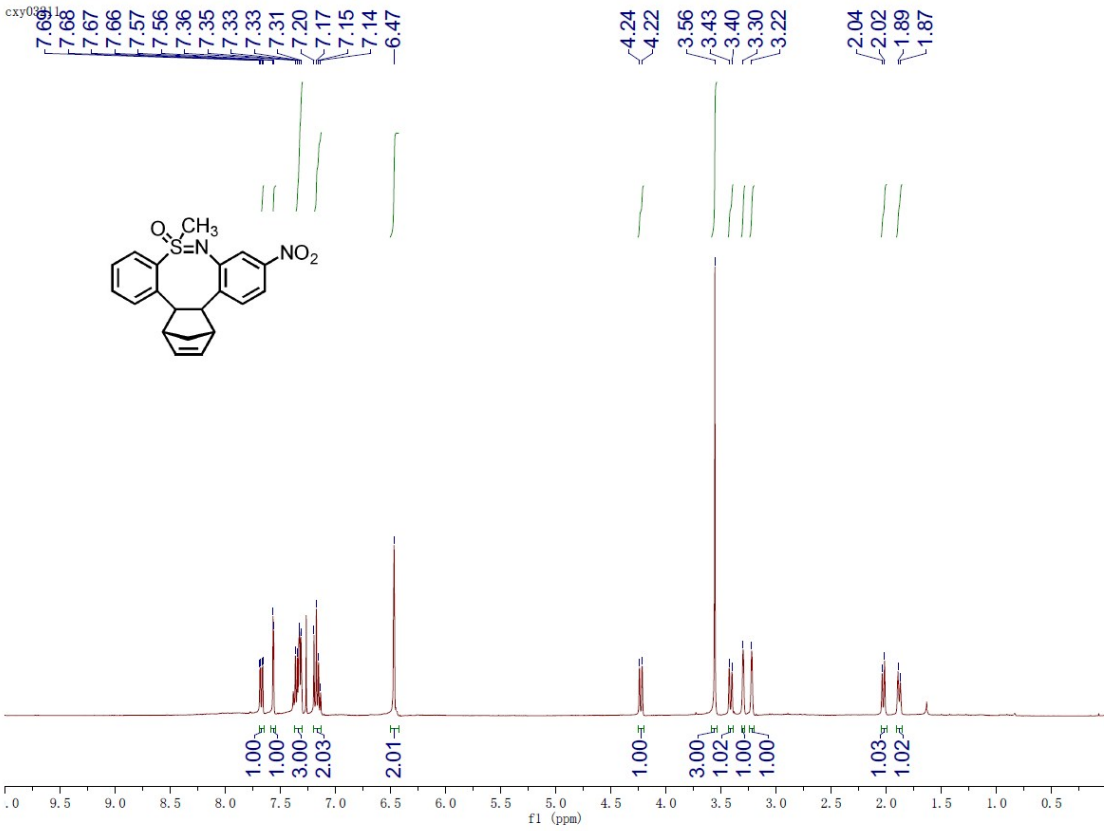
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 7



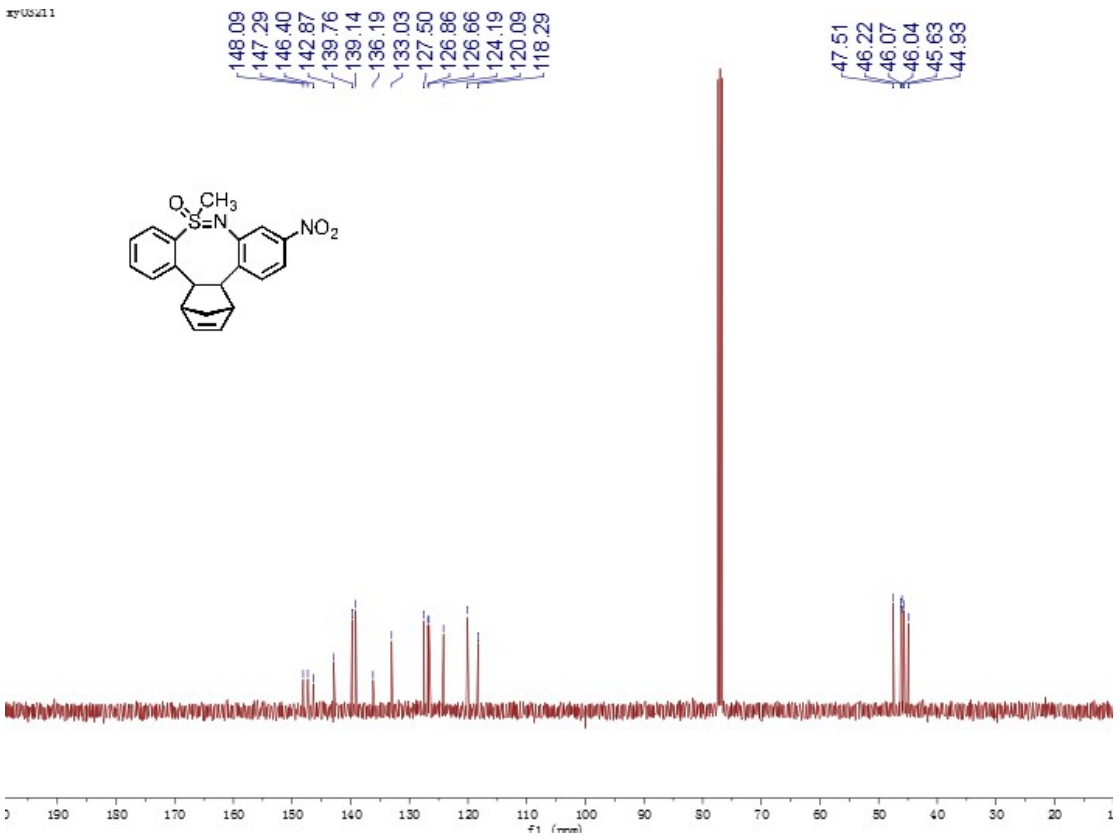
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 7



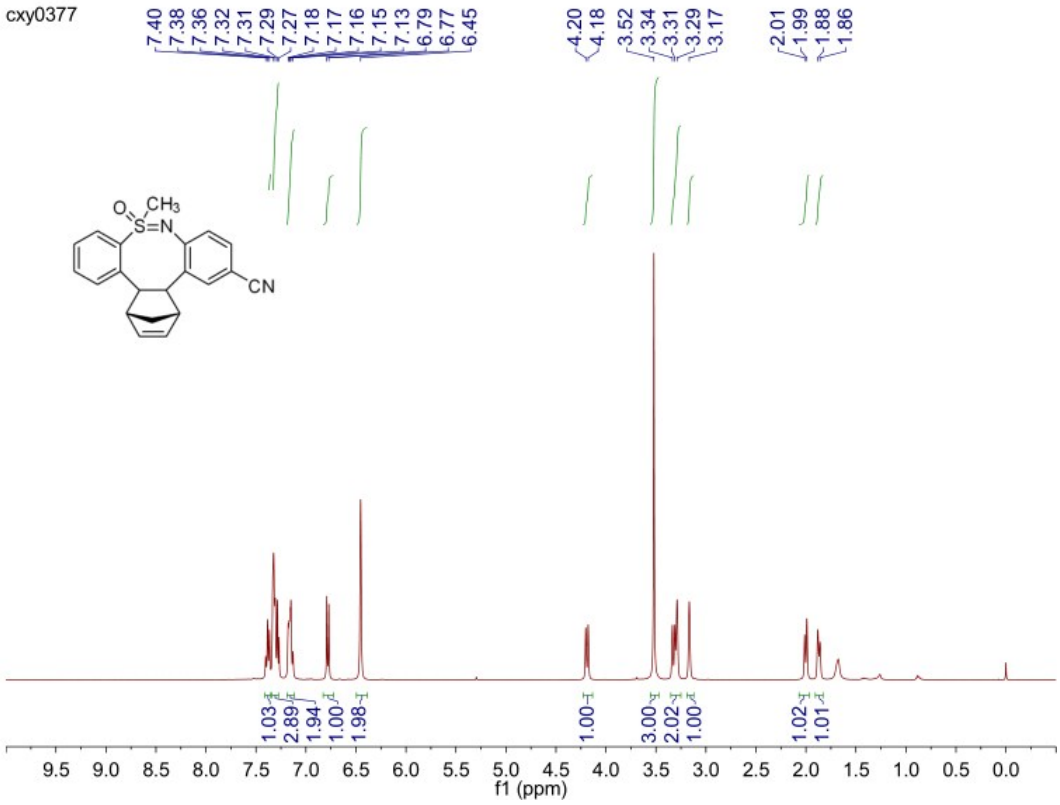
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 8



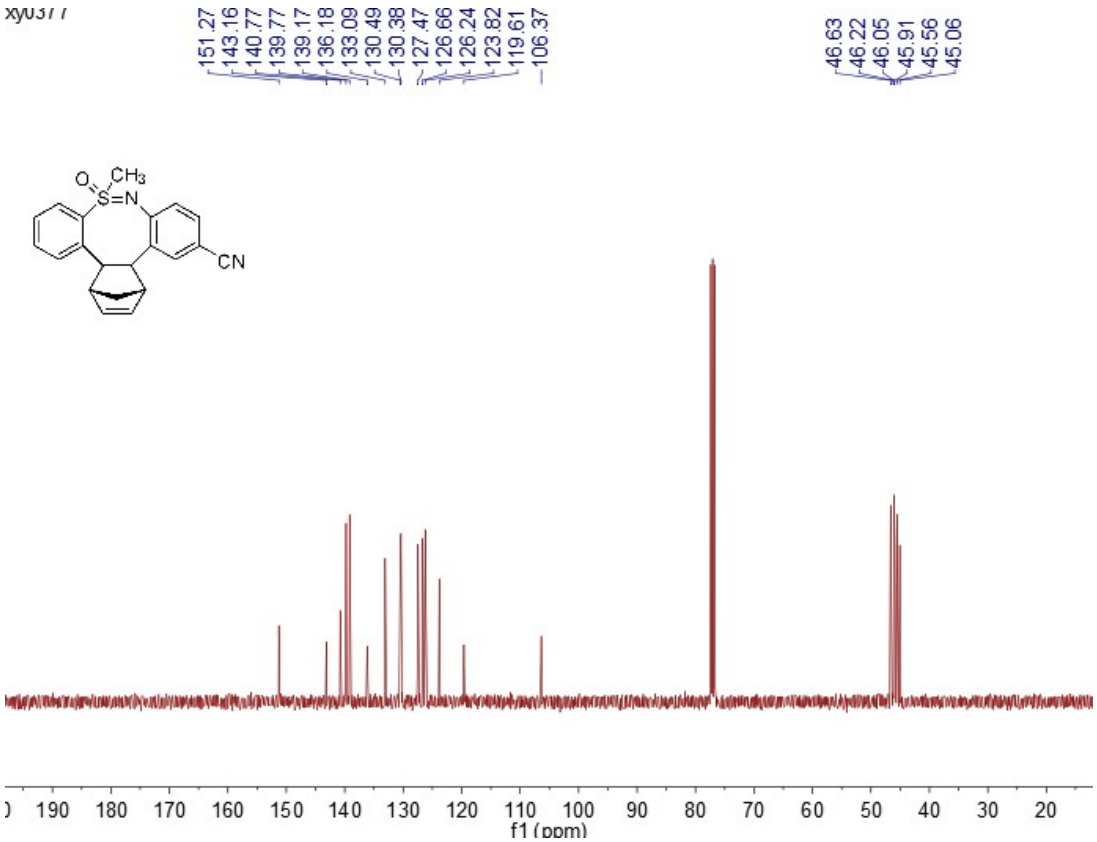
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 8



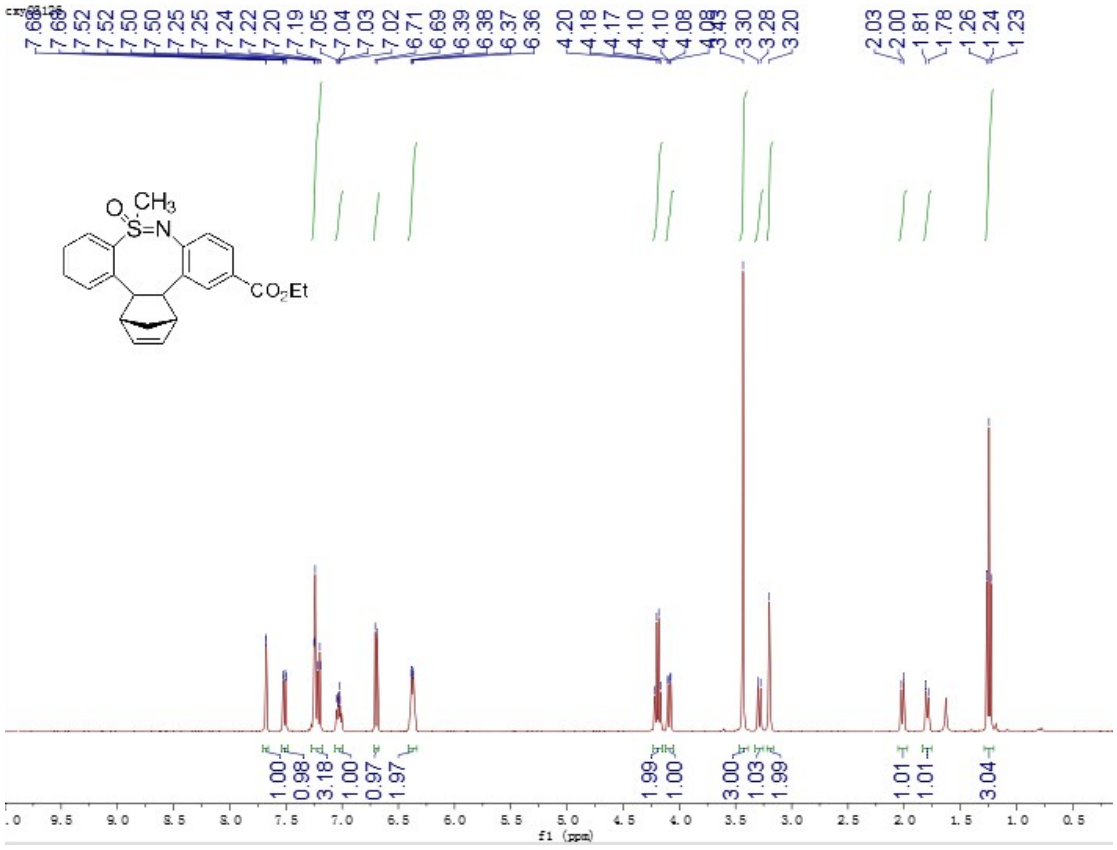
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 9



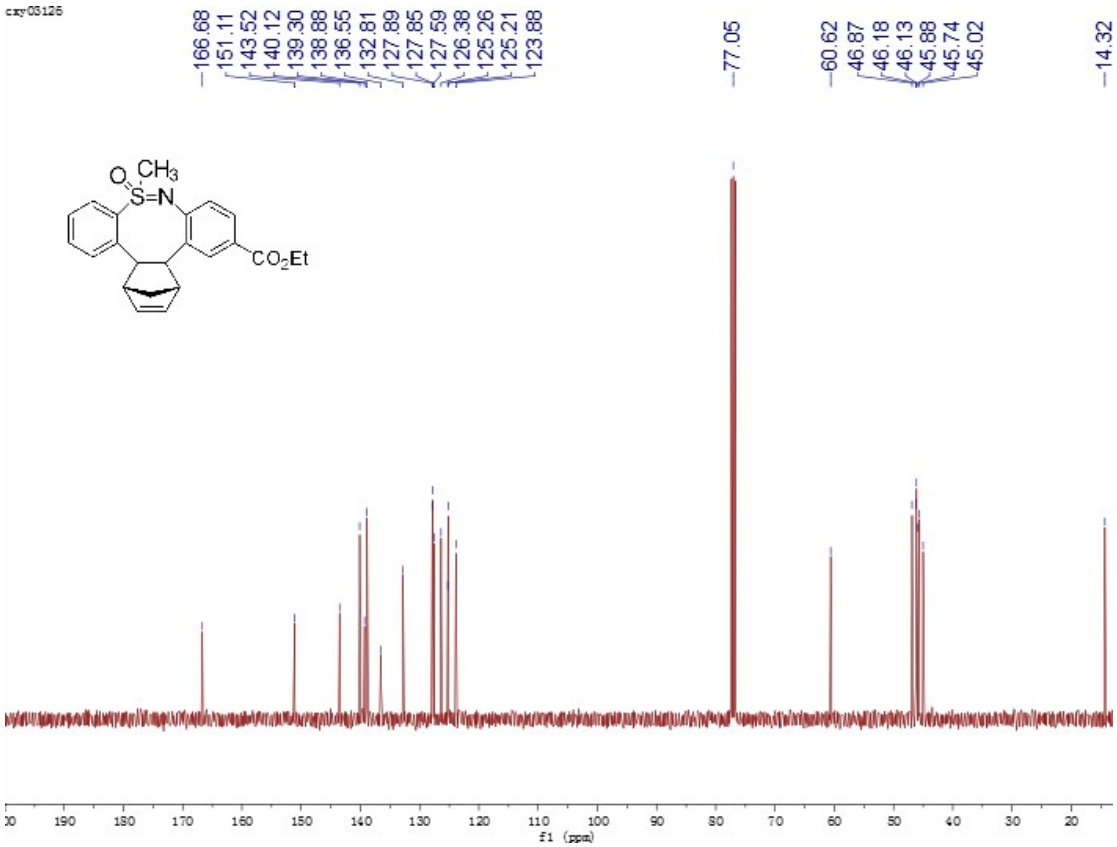
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 9


xyu377
151.27
143.16
140.77
139.77
139.17
136.18
133.09
130.49
130.38
127.47
126.66
126.24
123.82
119.61
106.37
46.63
46.22
46.05
45.91
45.56
45.06
O
CH3
S=N
CN
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

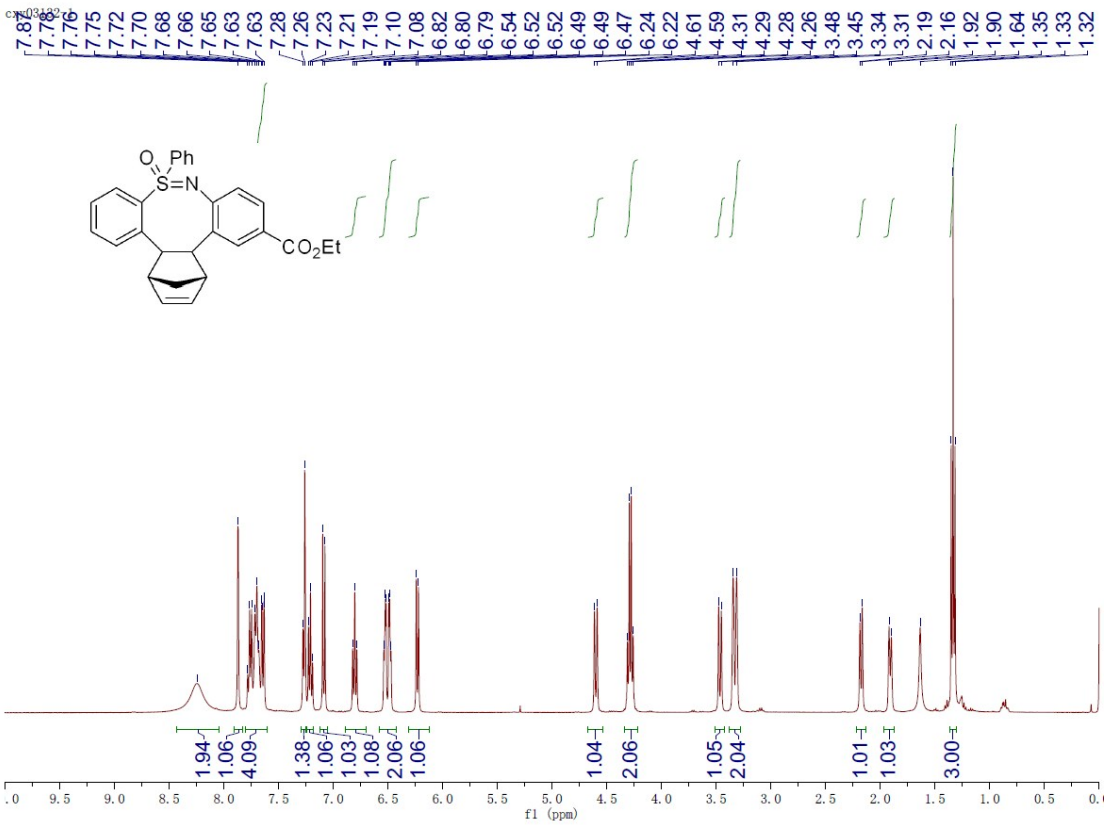
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 10a



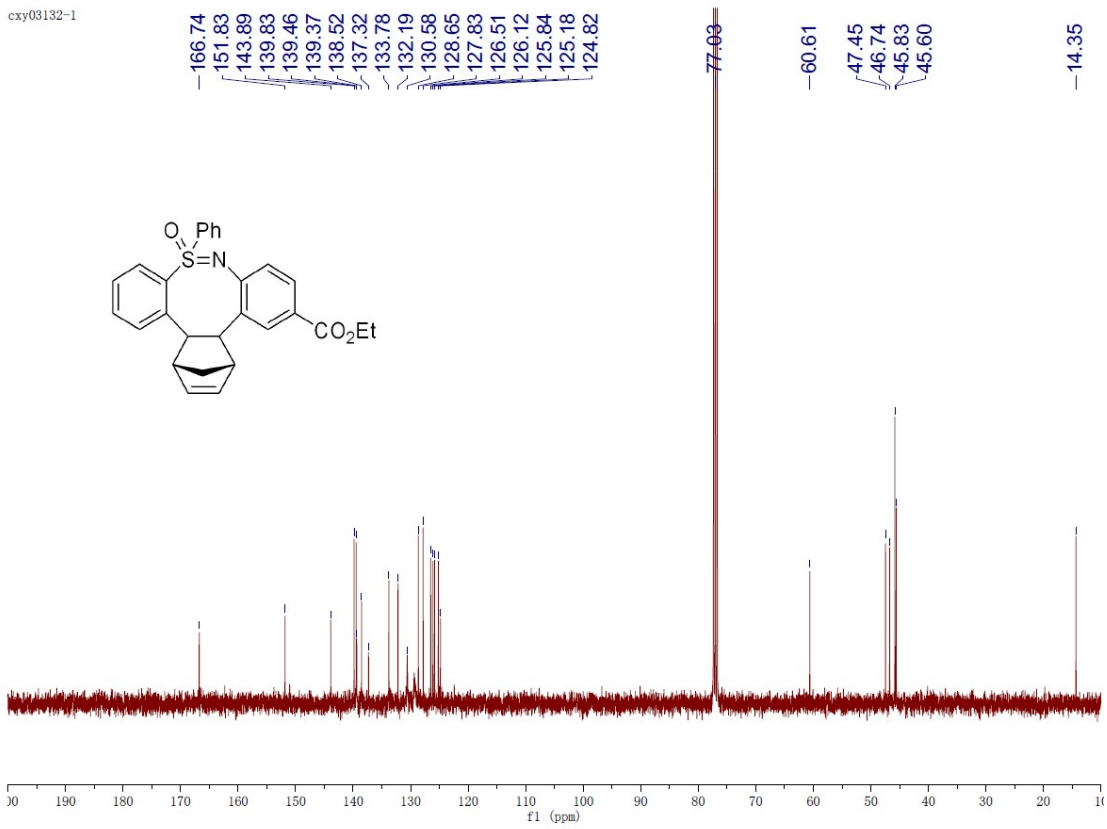
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 10a



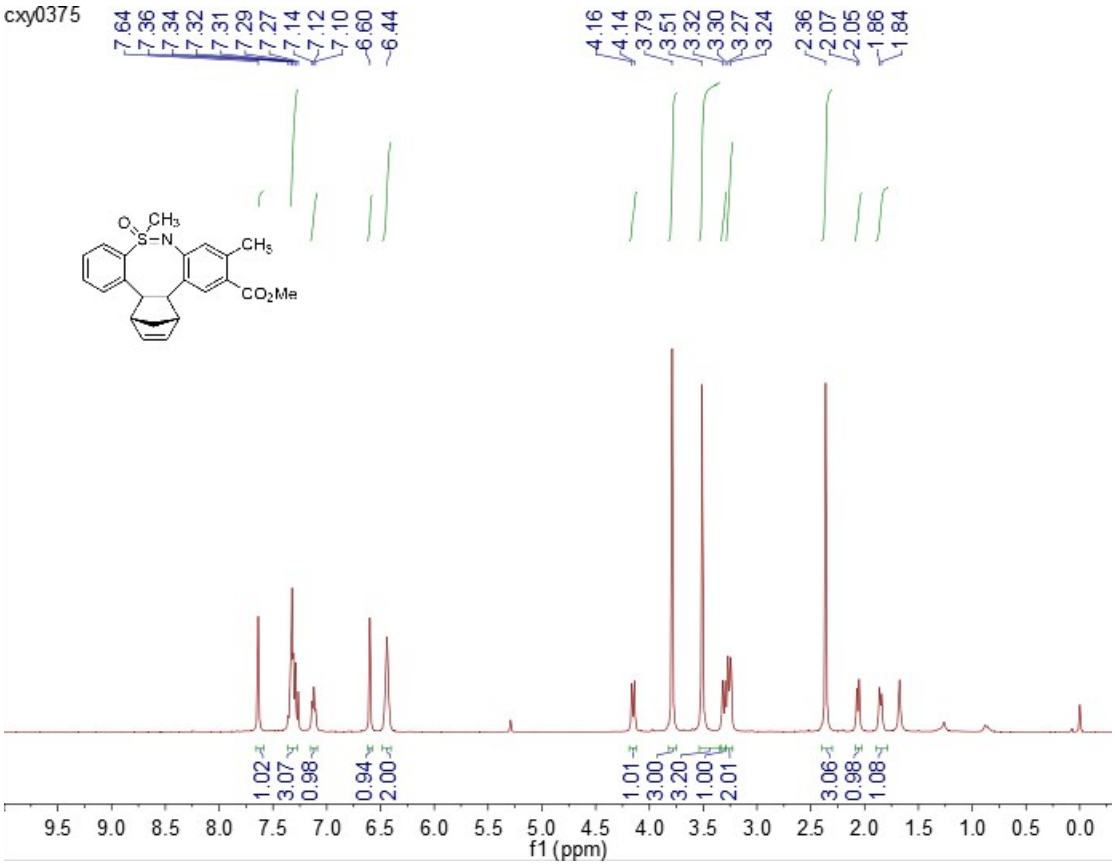
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 10b



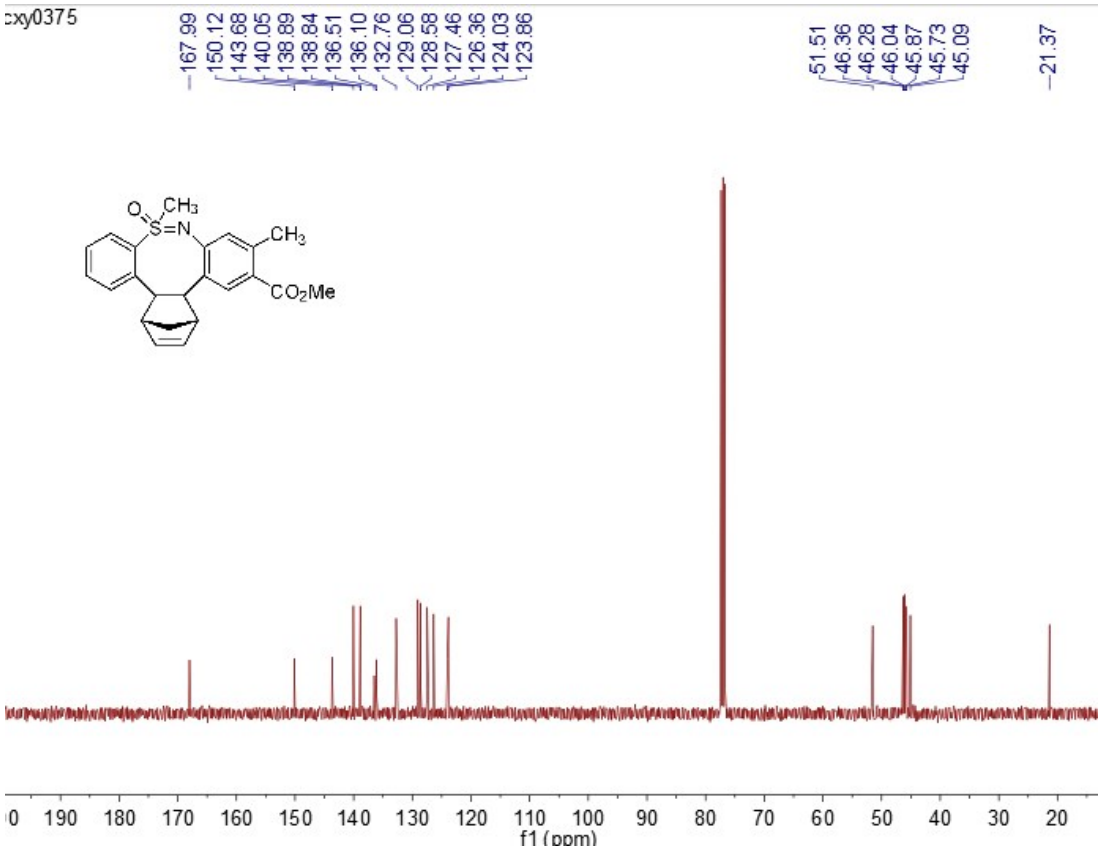
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 10b



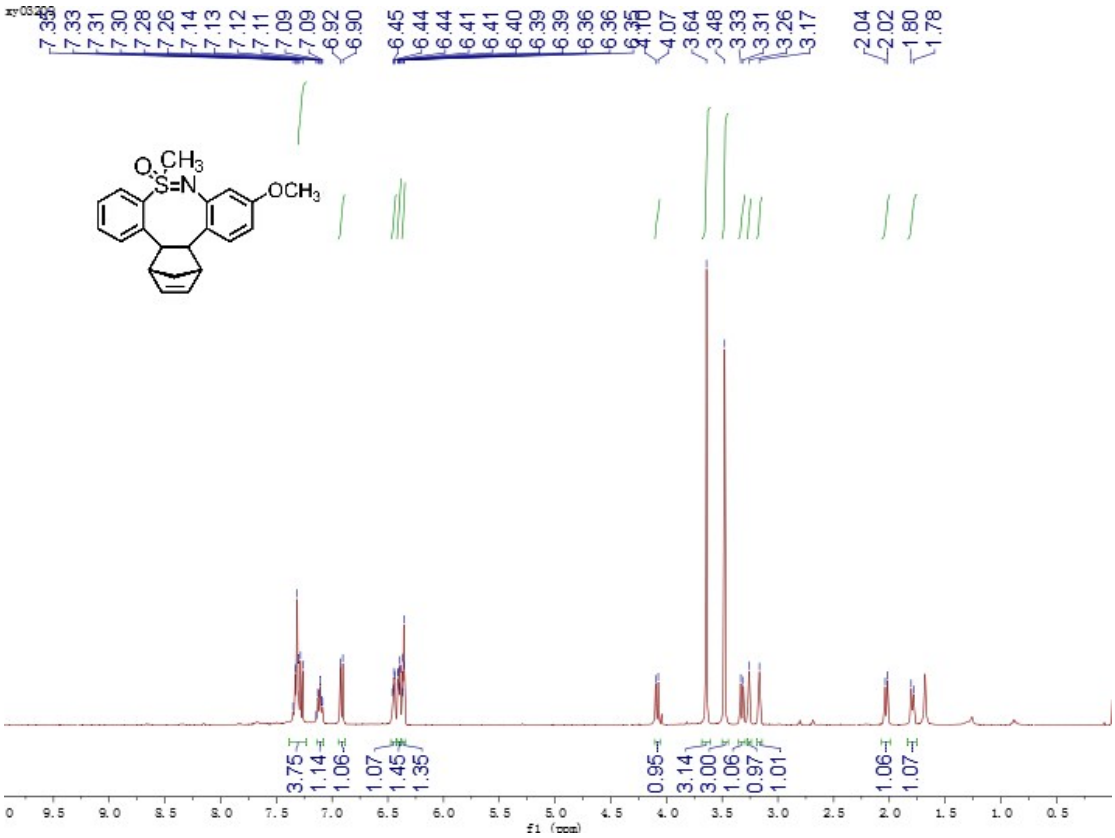
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 11



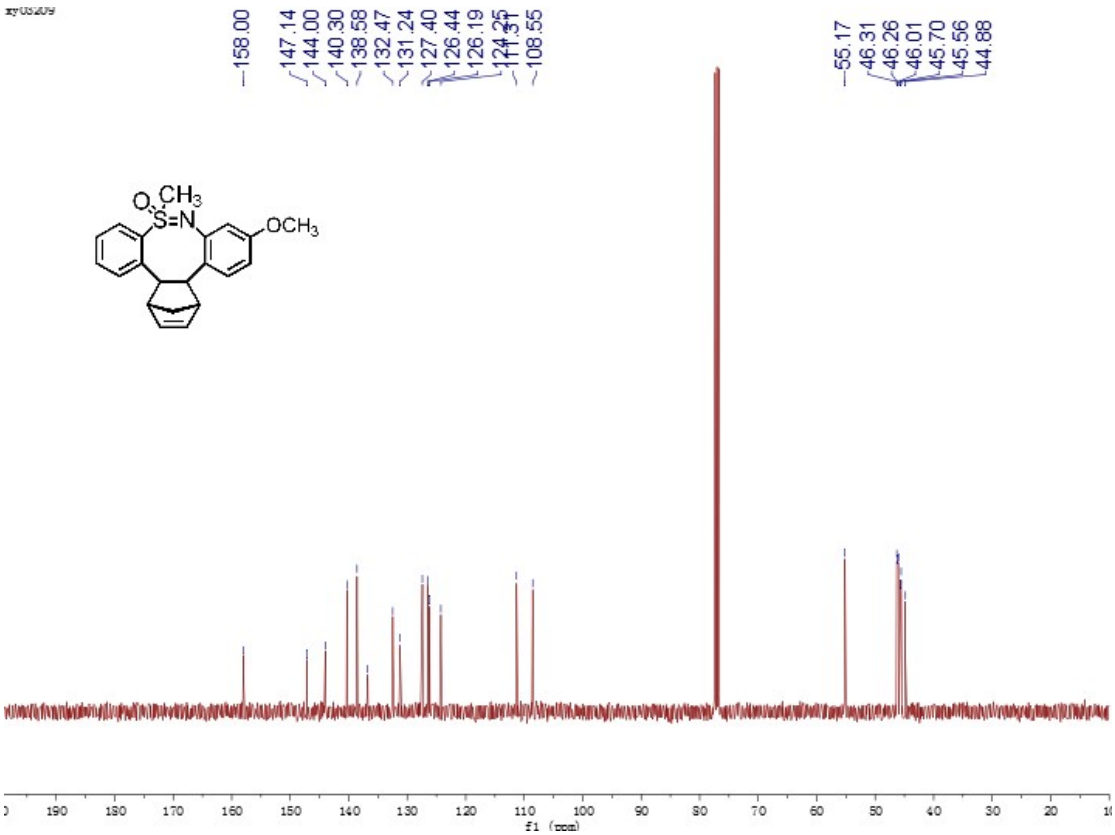
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 11



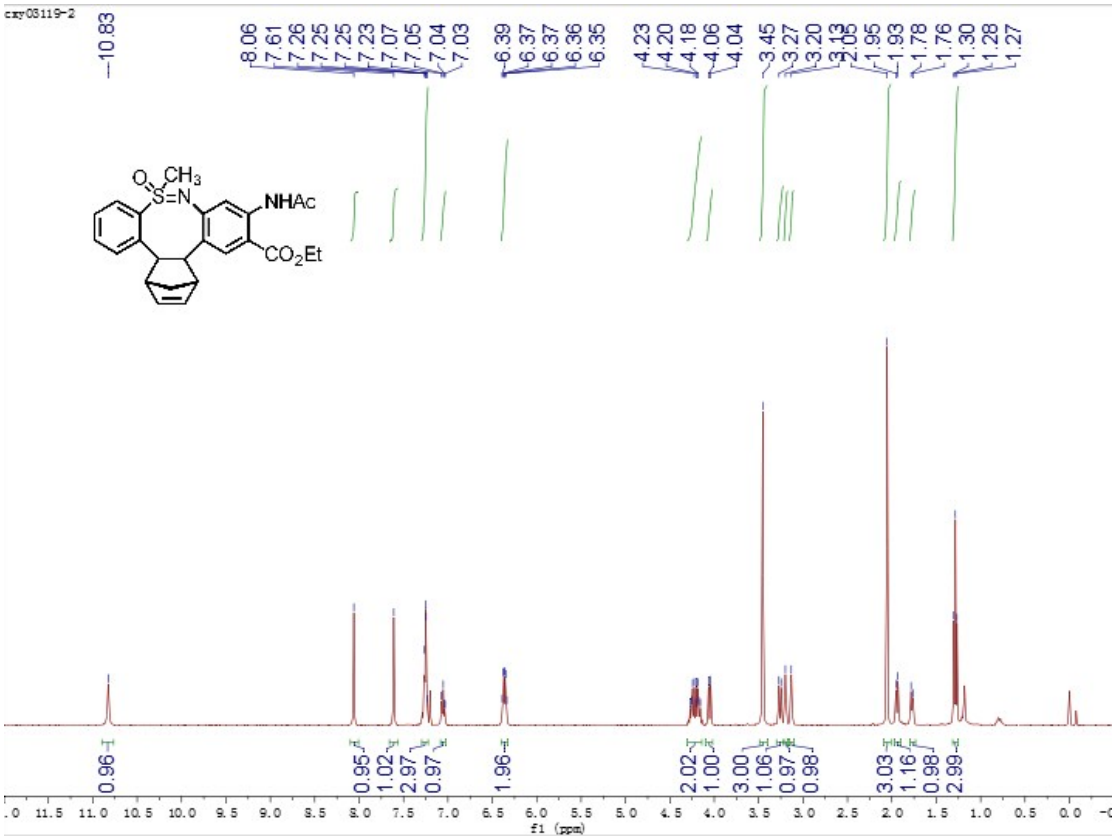
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 12



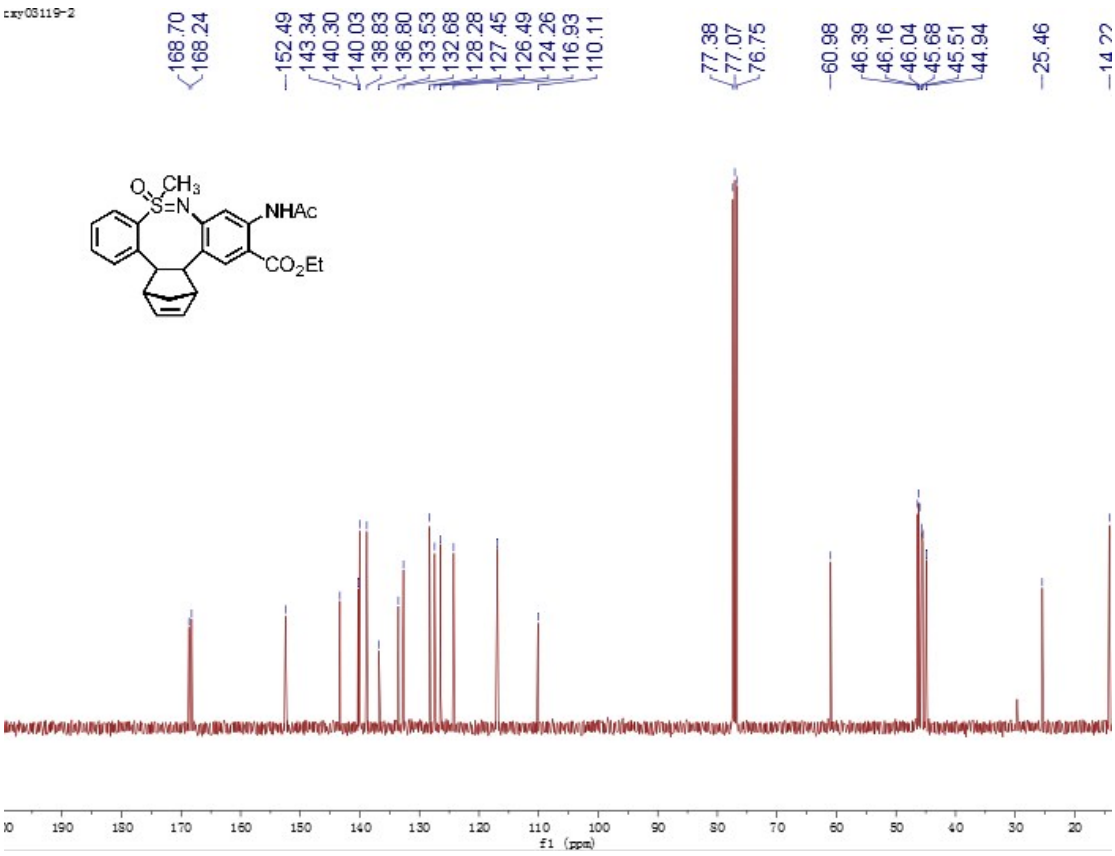
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 12



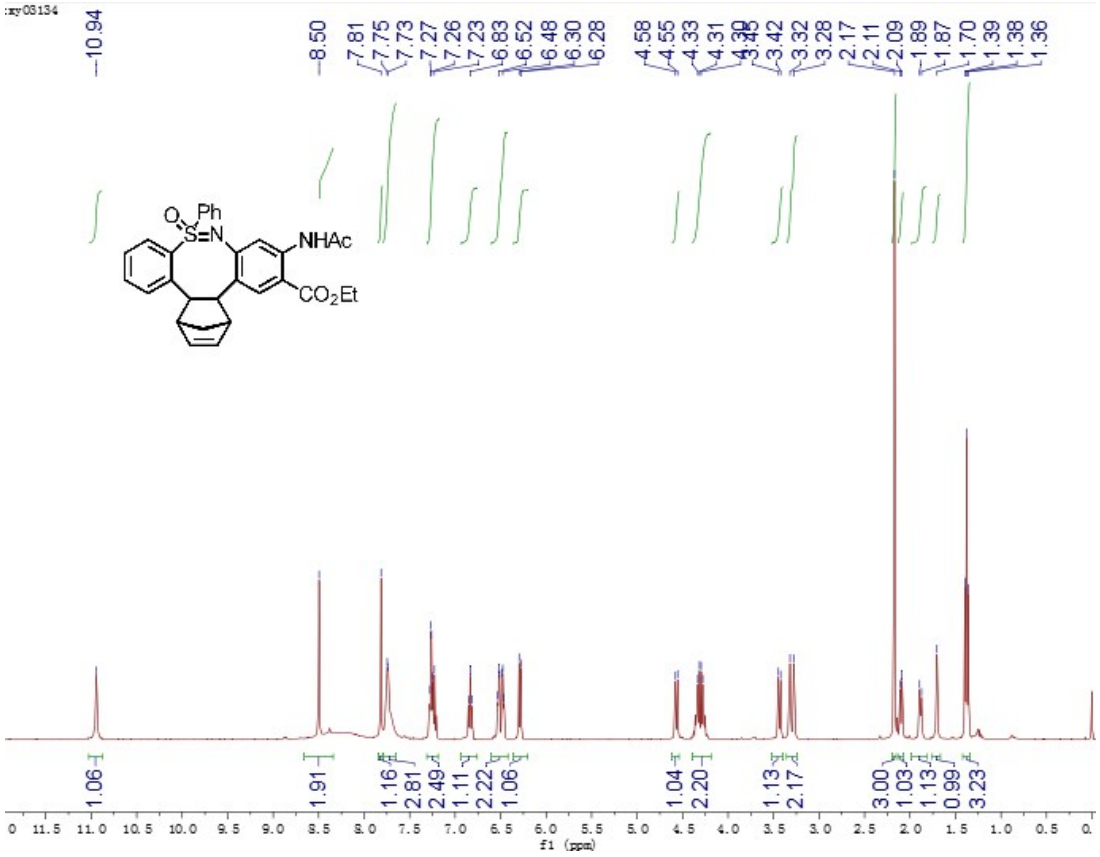
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 13a



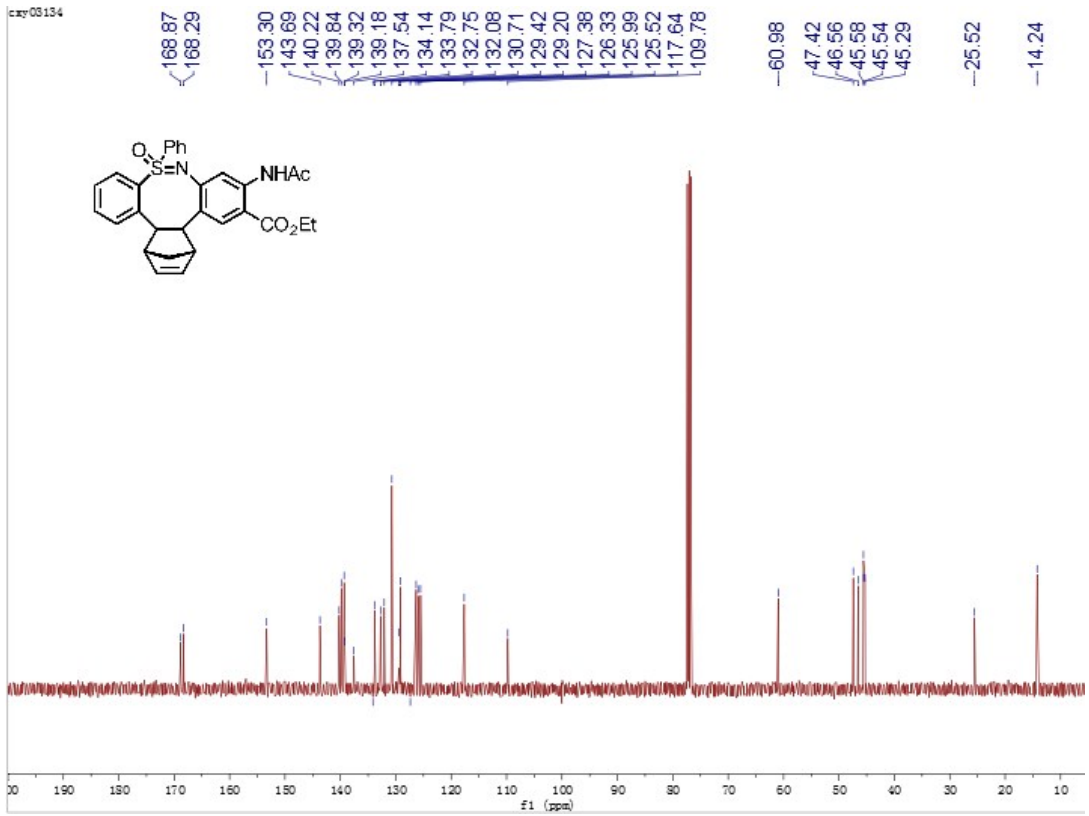
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 13a



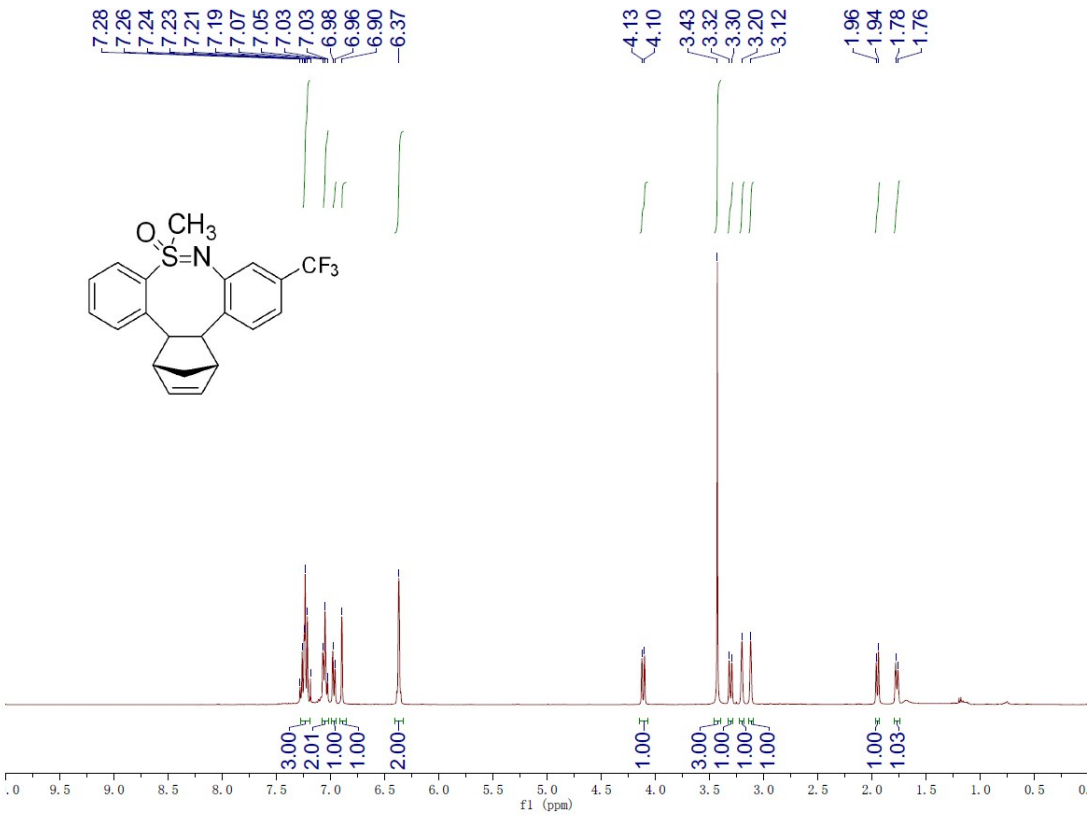
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 13b



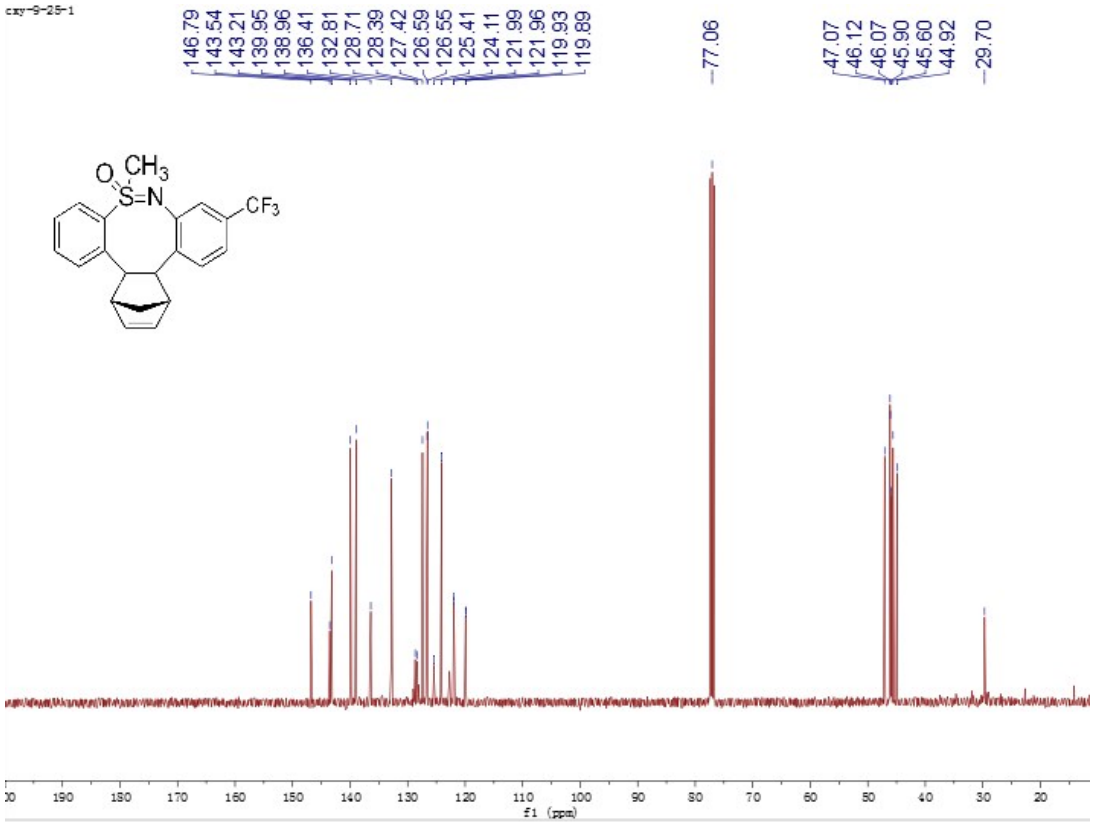
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 13b



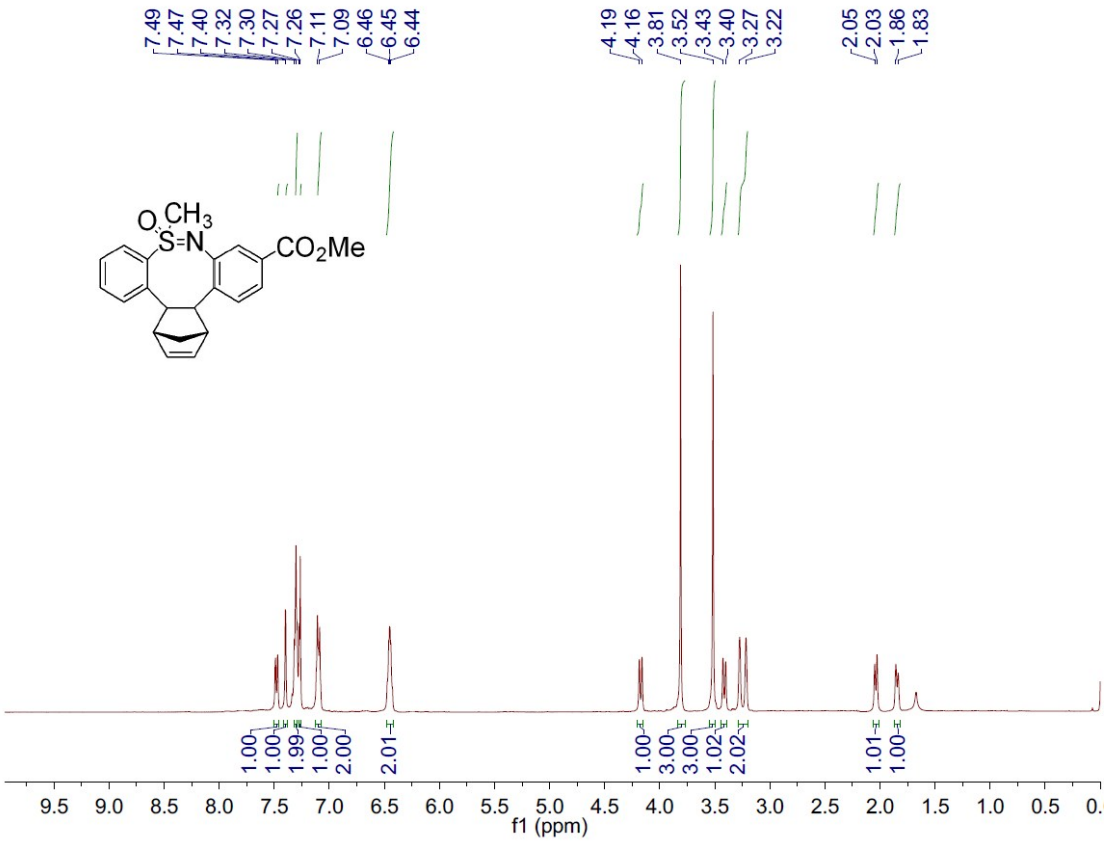
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 14



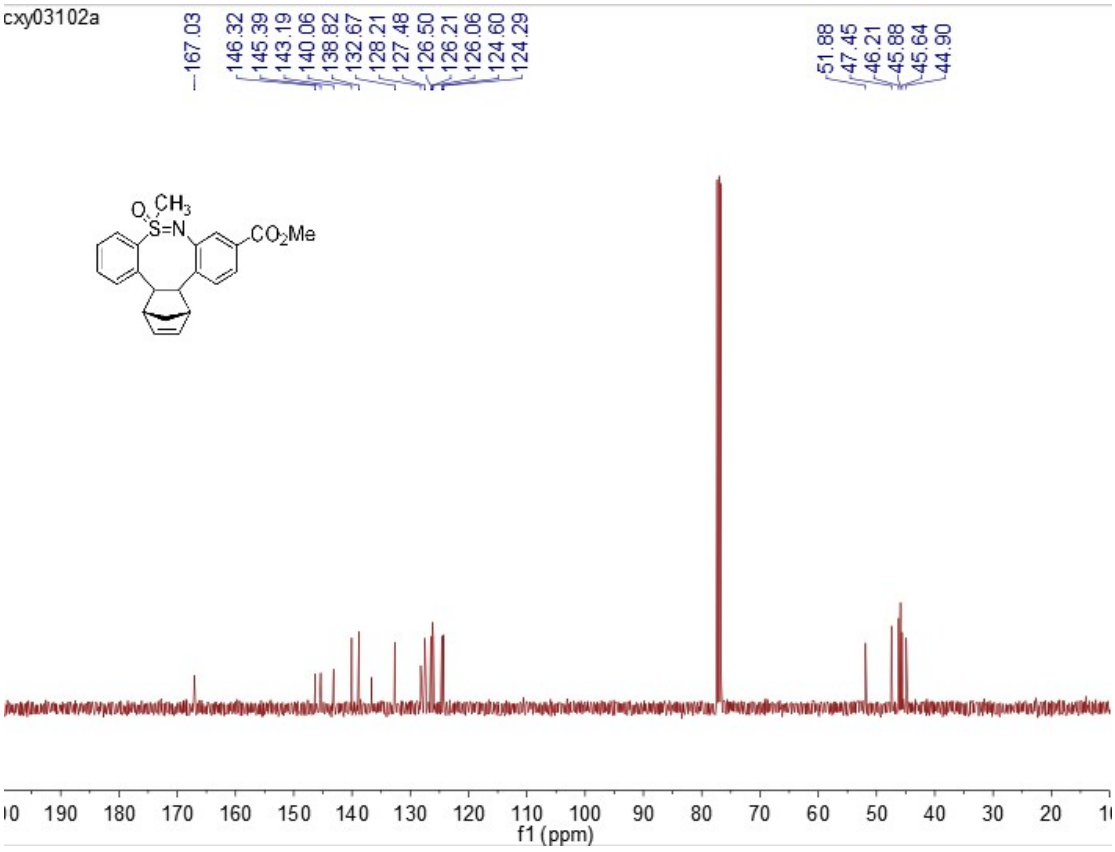
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 14


cxy-9-25-1
146.79
143.54
143.21
139.95
138.96
136.41
132.81
128.71
128.39
127.42
126.59
126.55
125.41
124.11
121.99
121.96
119.93
119.89
77.06
47.07
46.12
46.07
45.90
45.60
44.92
29.70
O
CH3
S=N
CF3
f1 (ppm)

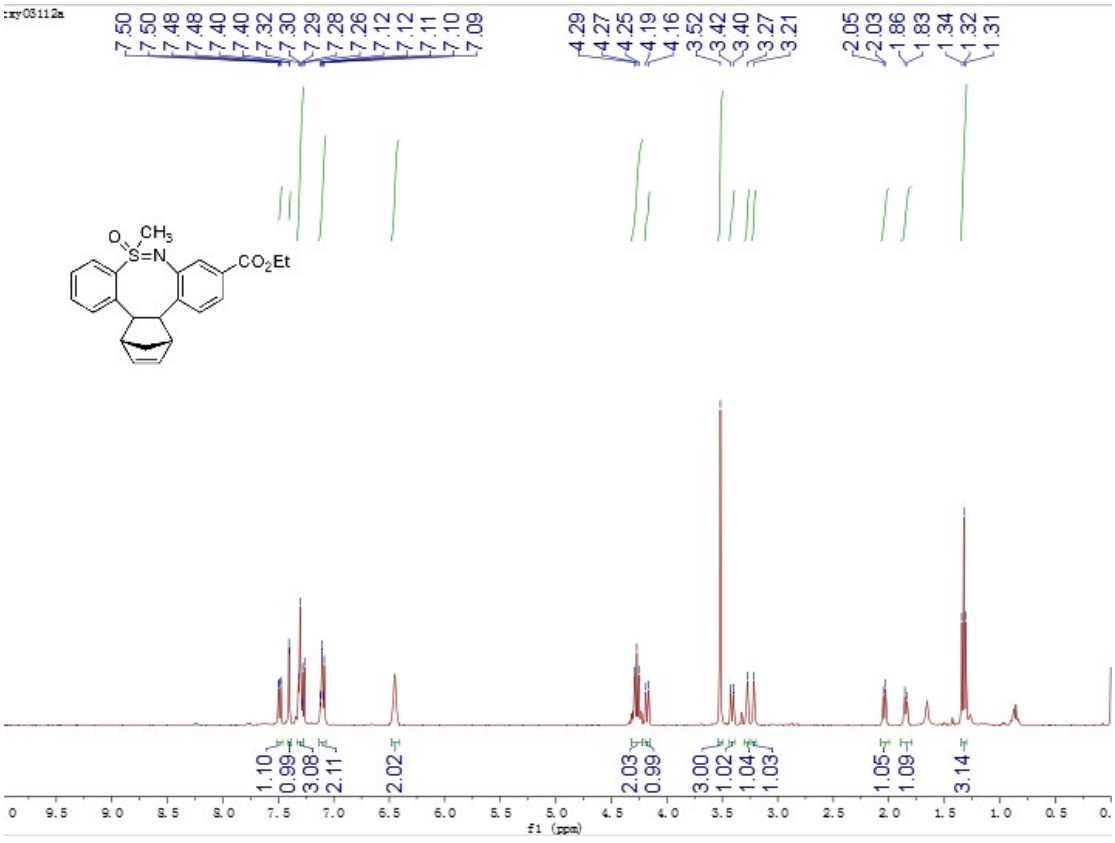
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 15



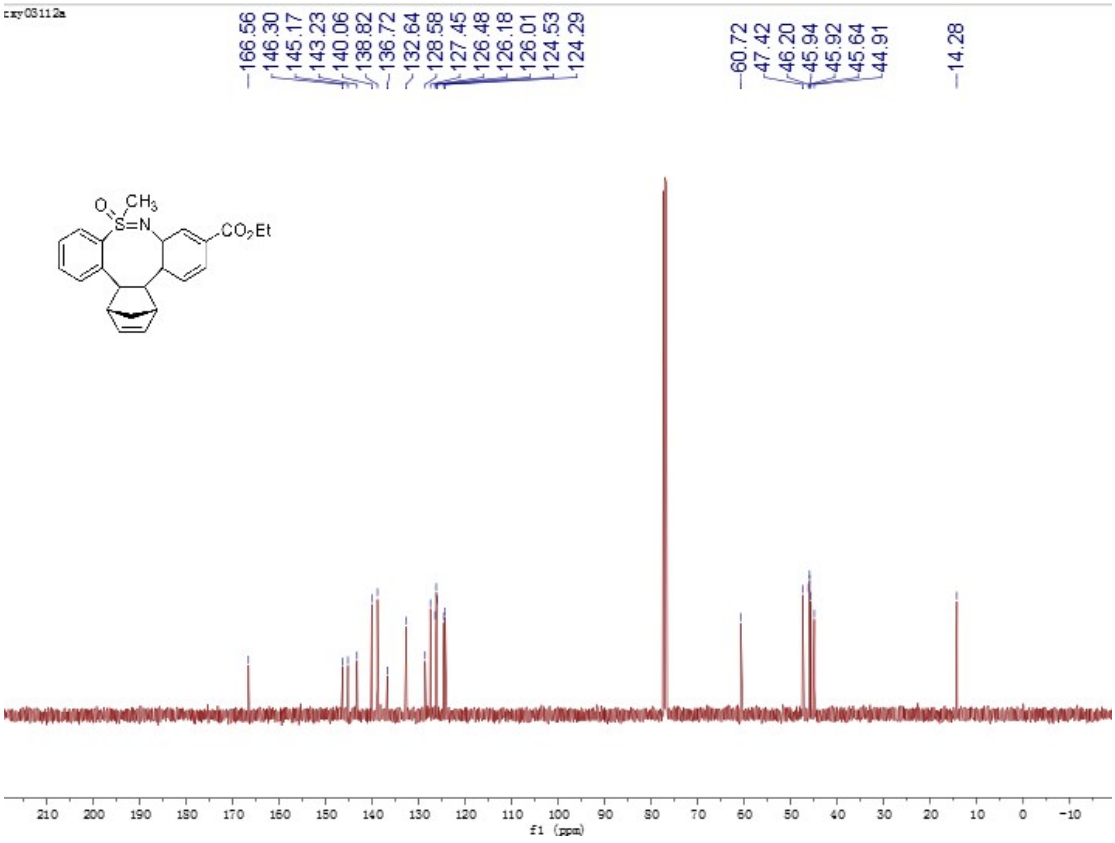
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 15



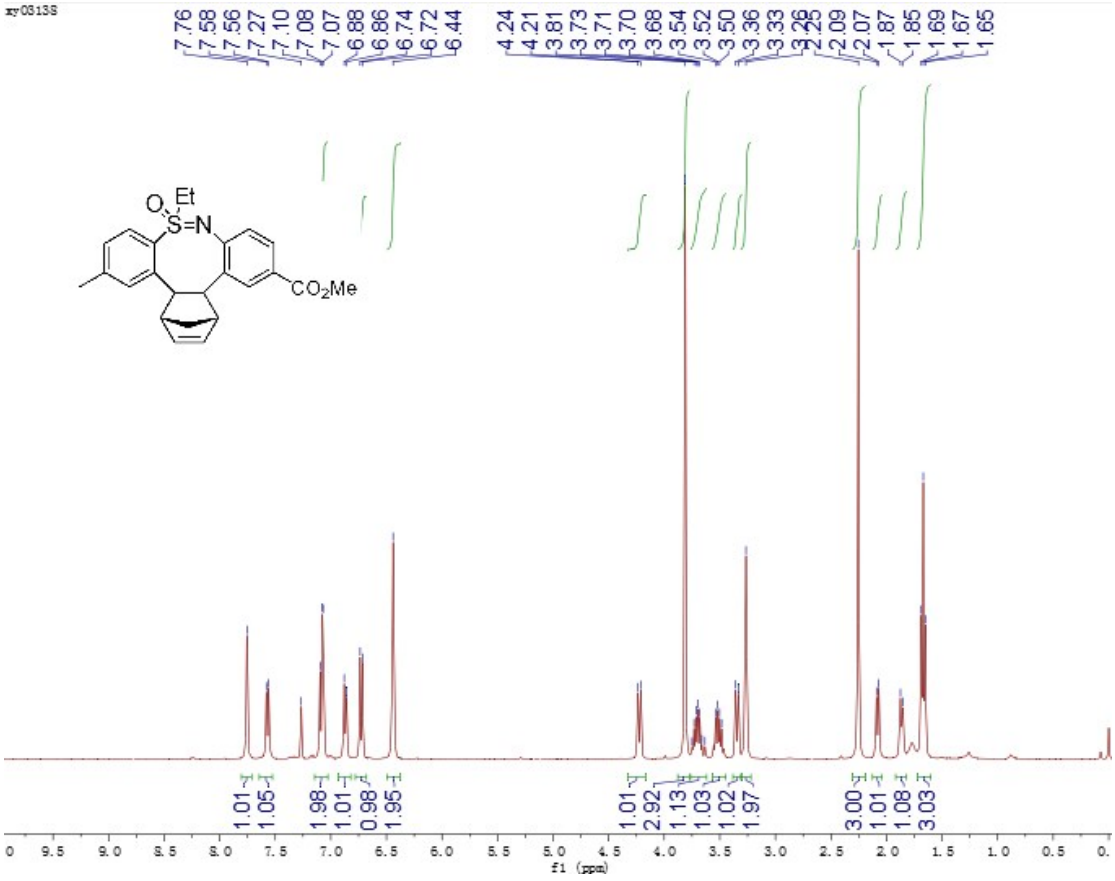
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 16



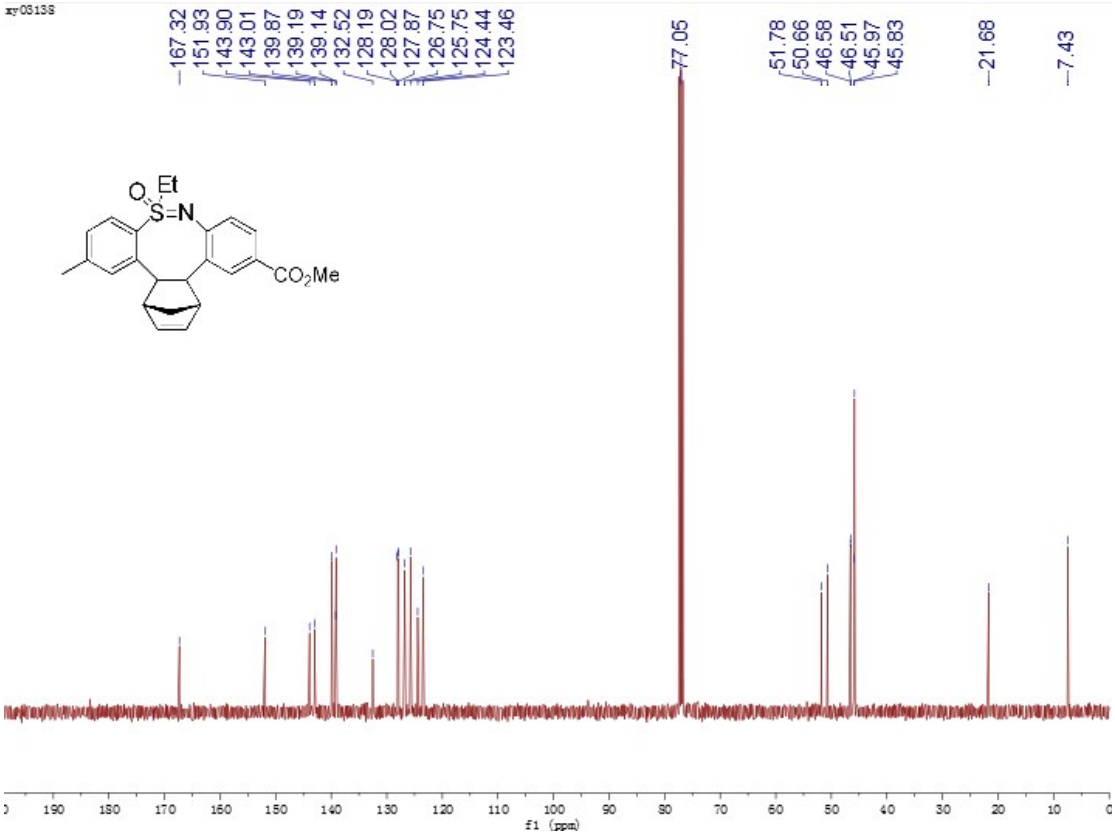
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 16



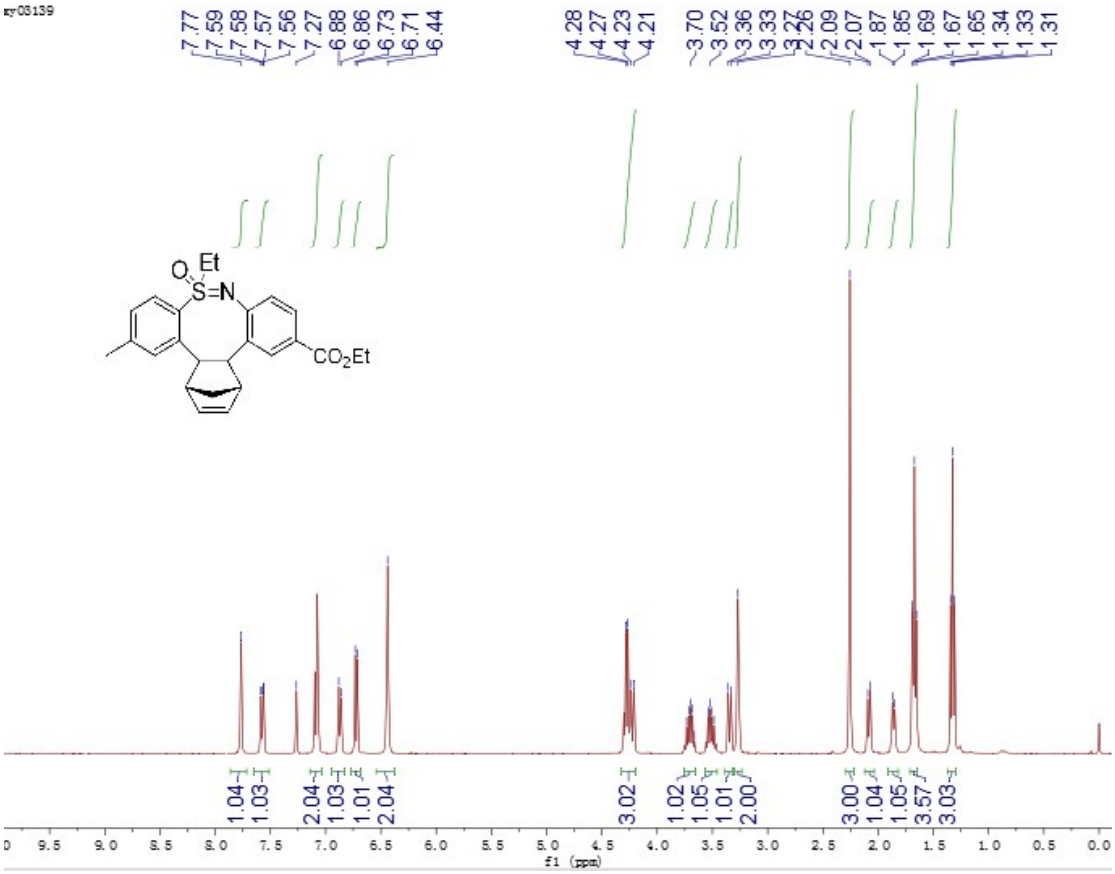
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 17



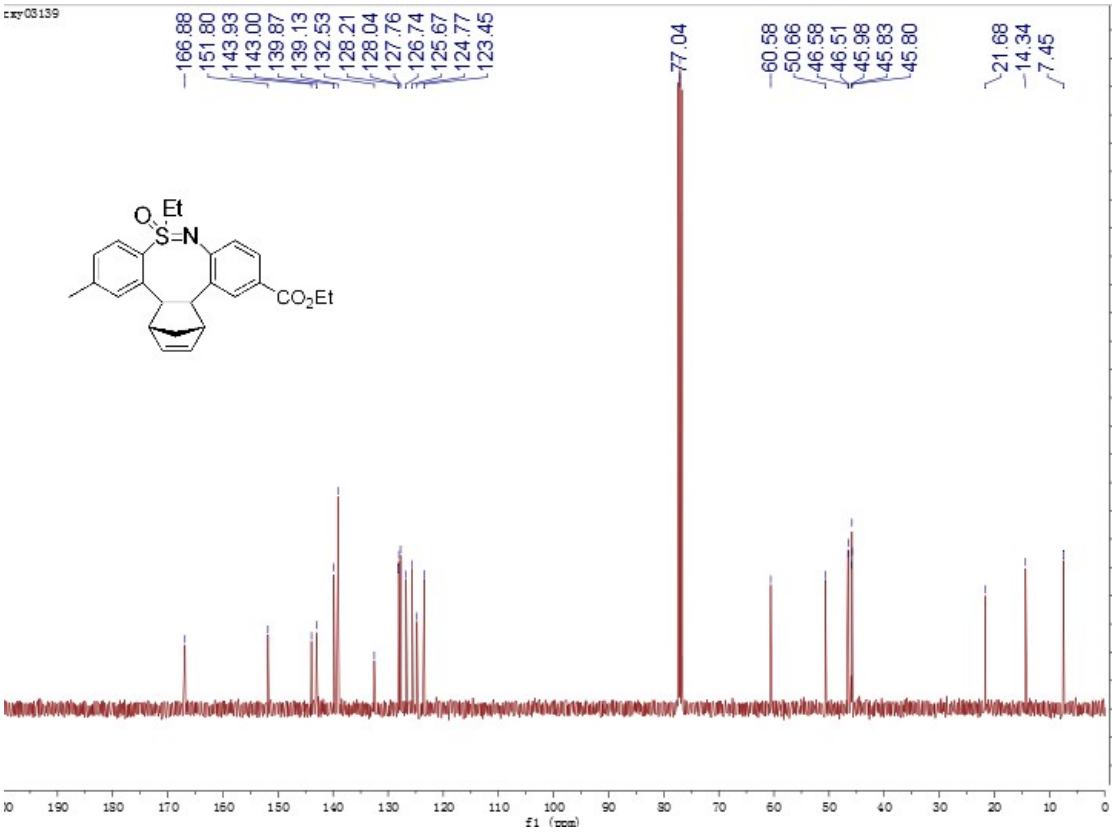
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 17



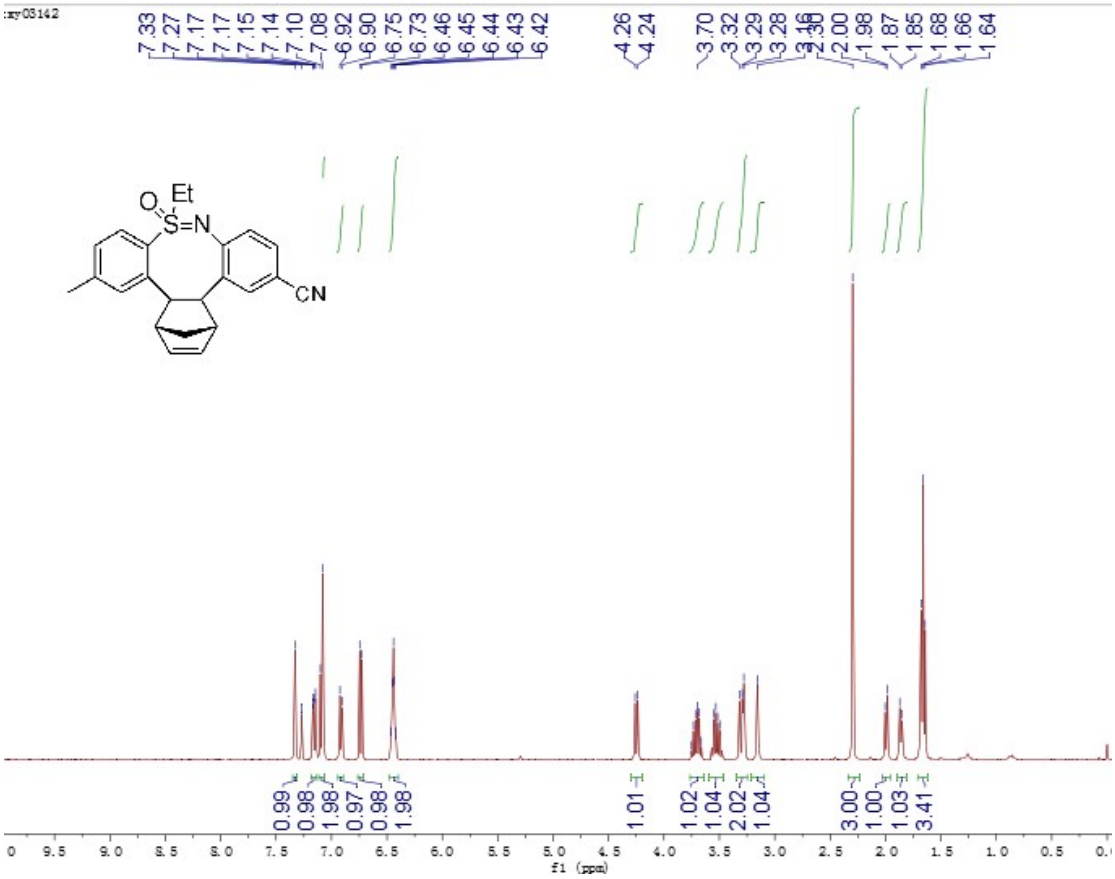
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 18



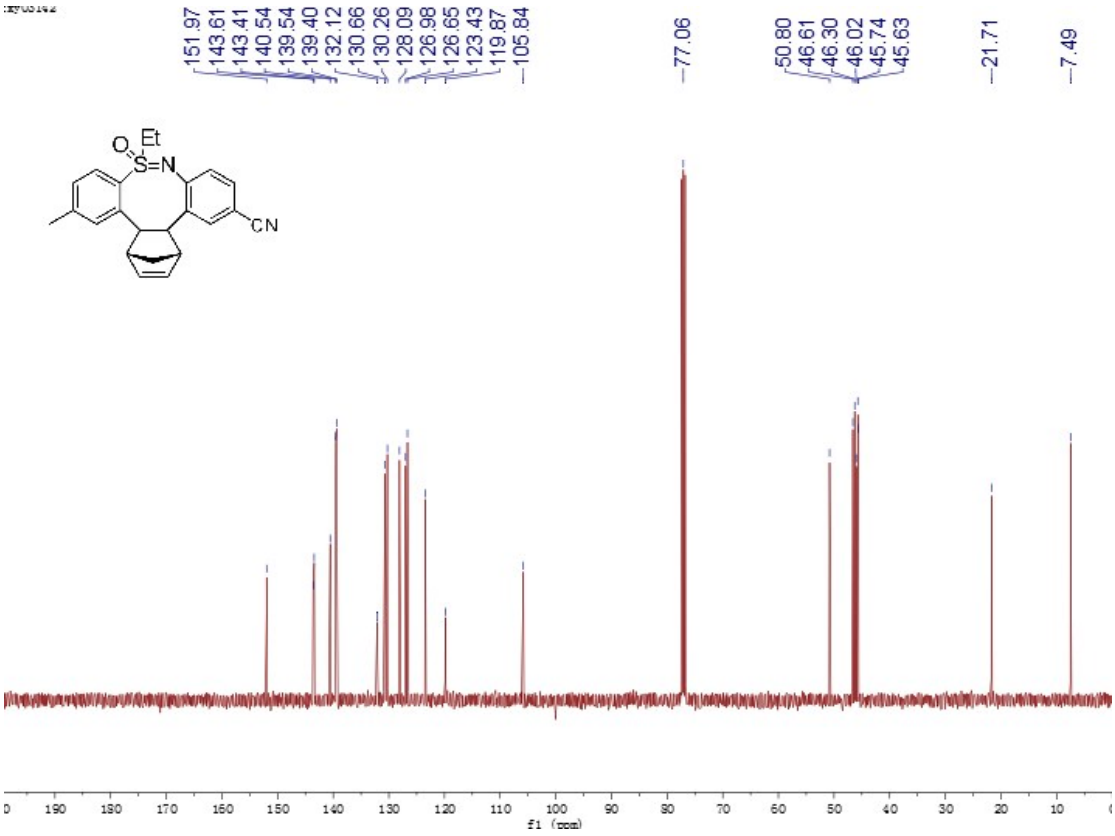
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 18



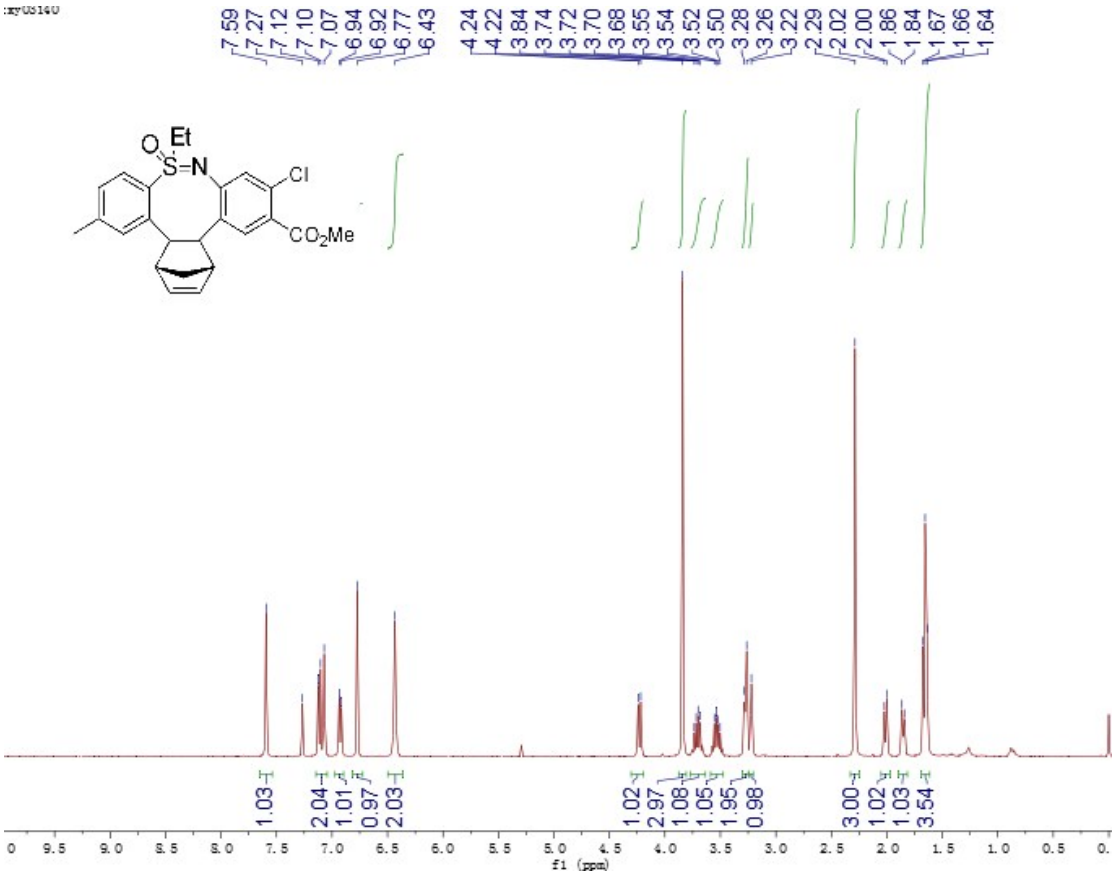
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 19



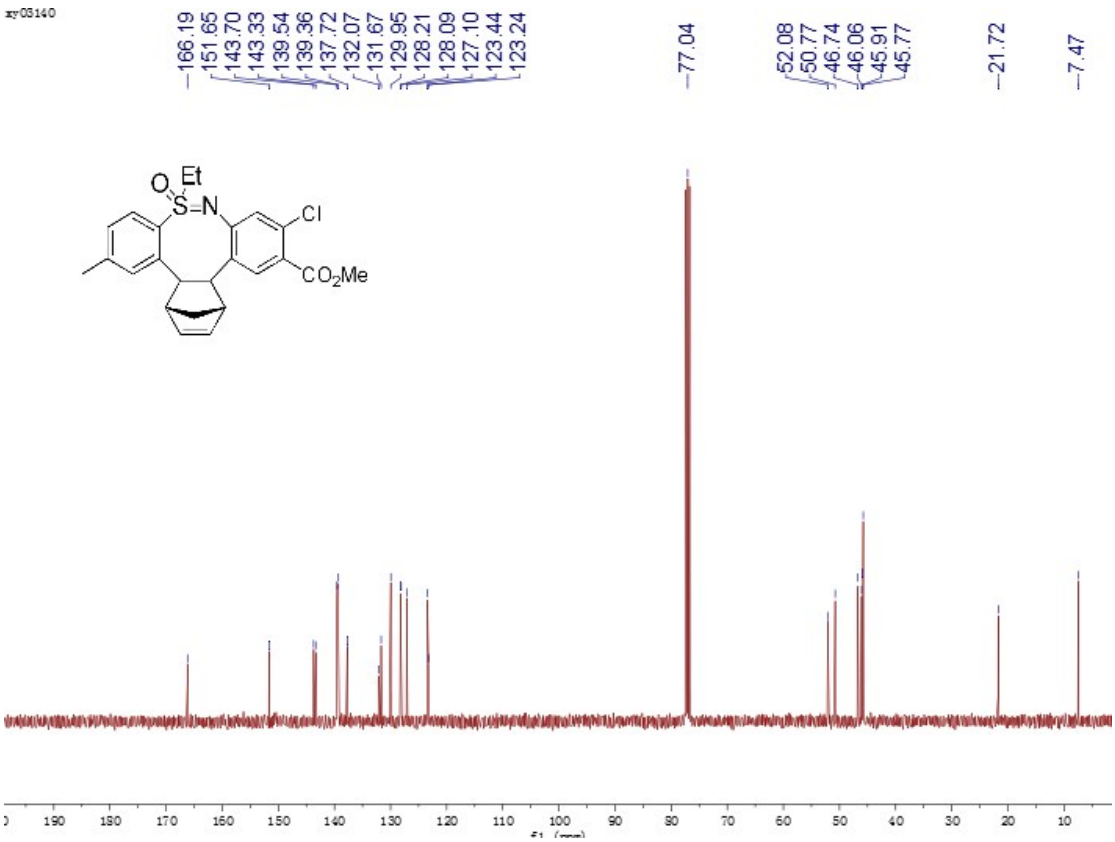
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 19



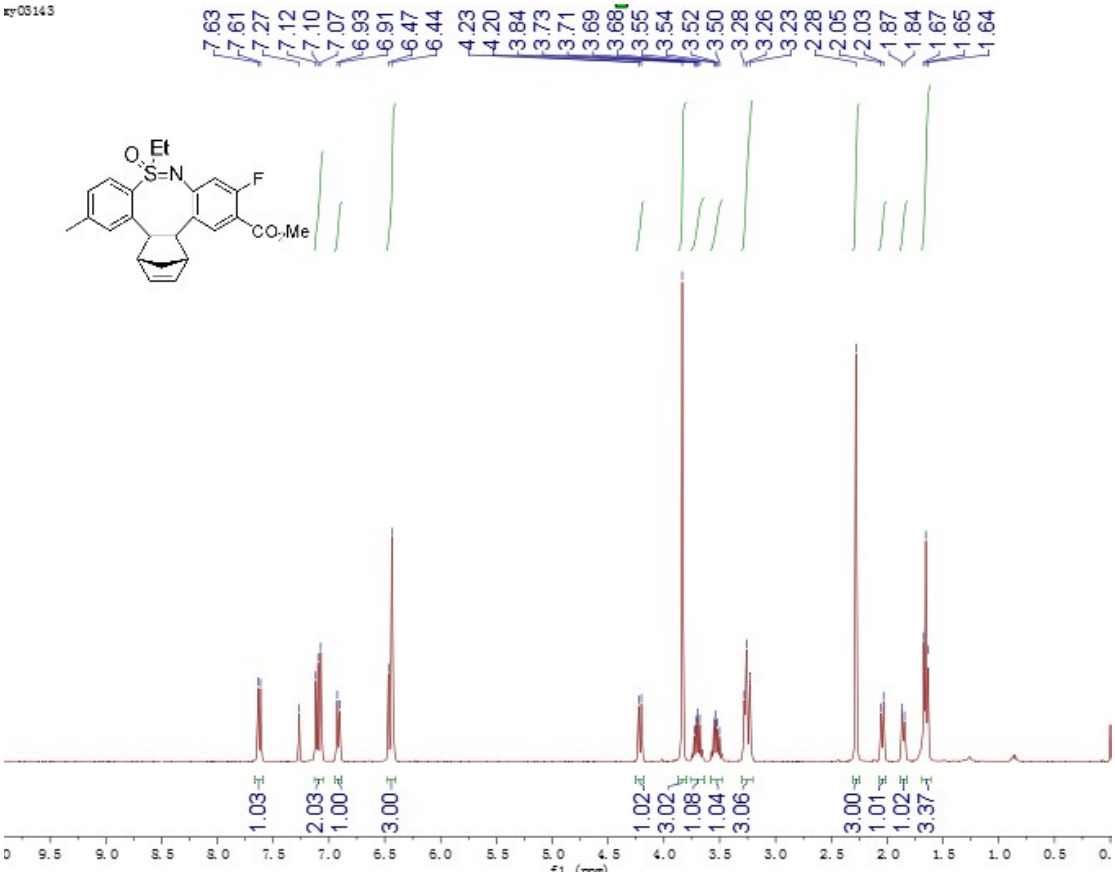
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 20



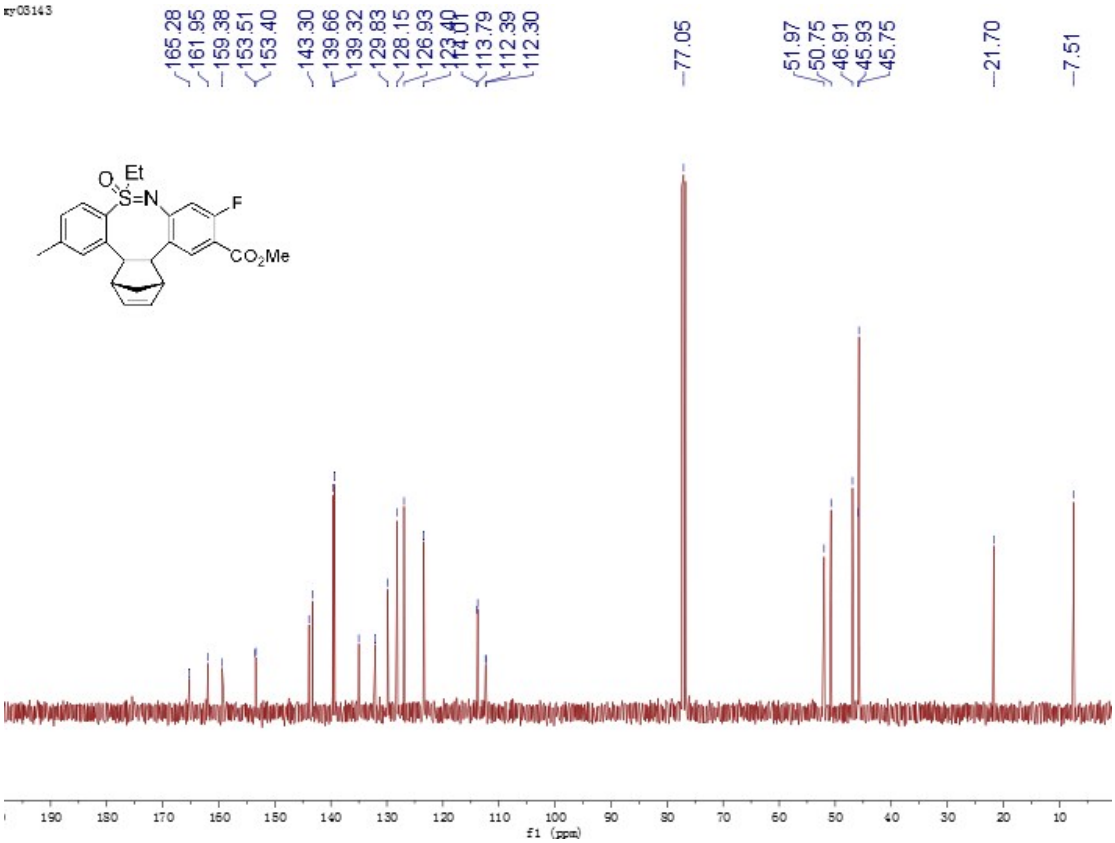
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 20



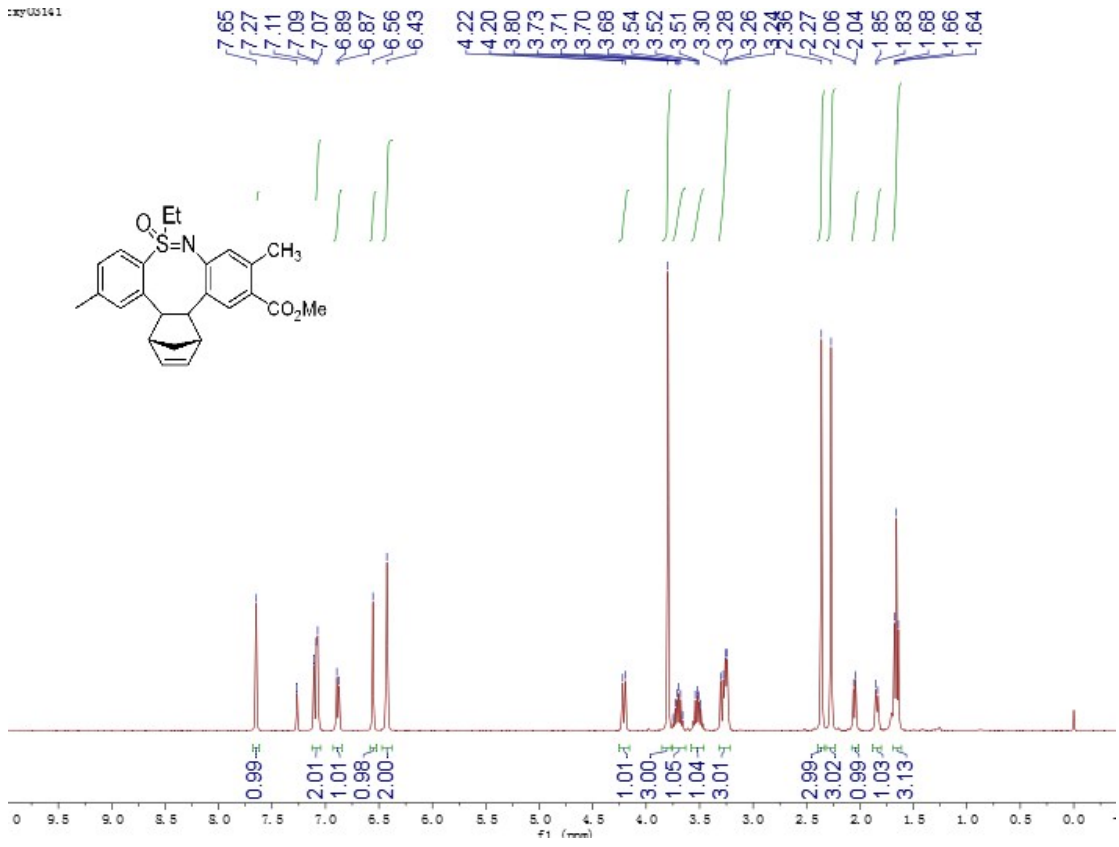
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 21



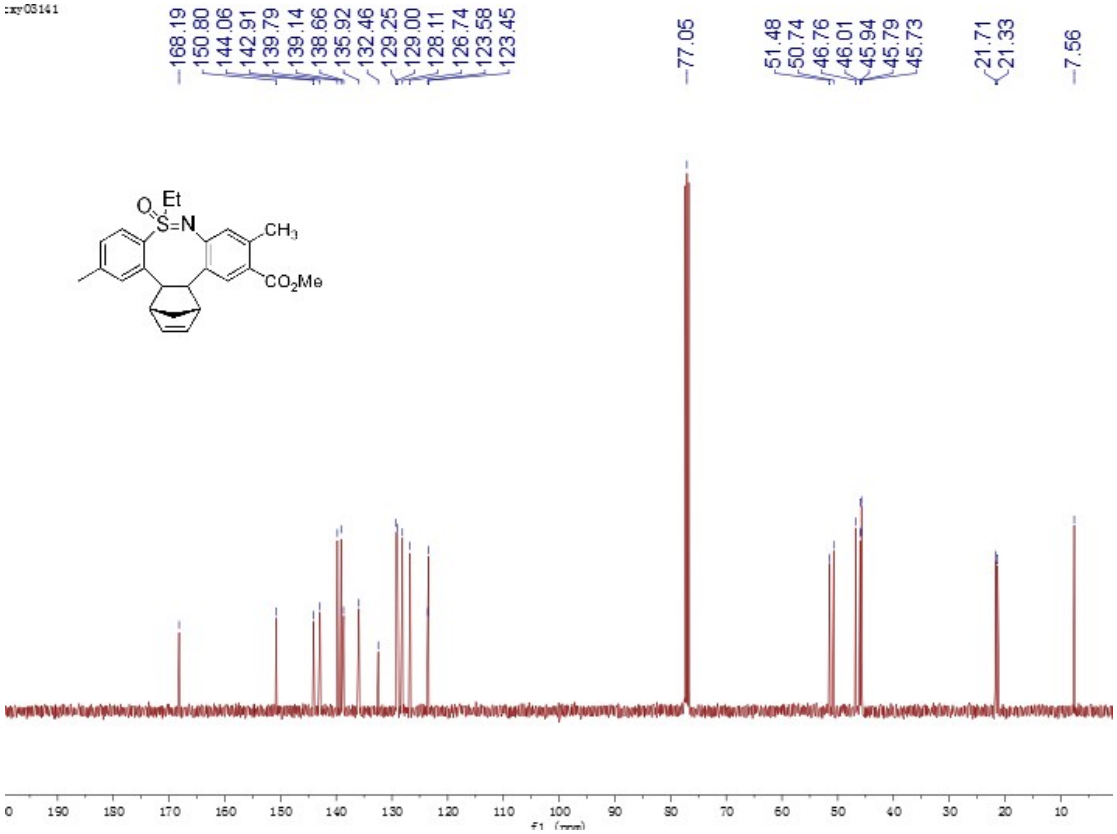
^{13}CNMR spectrum (100 MHz, $CDCl_3$) of 21



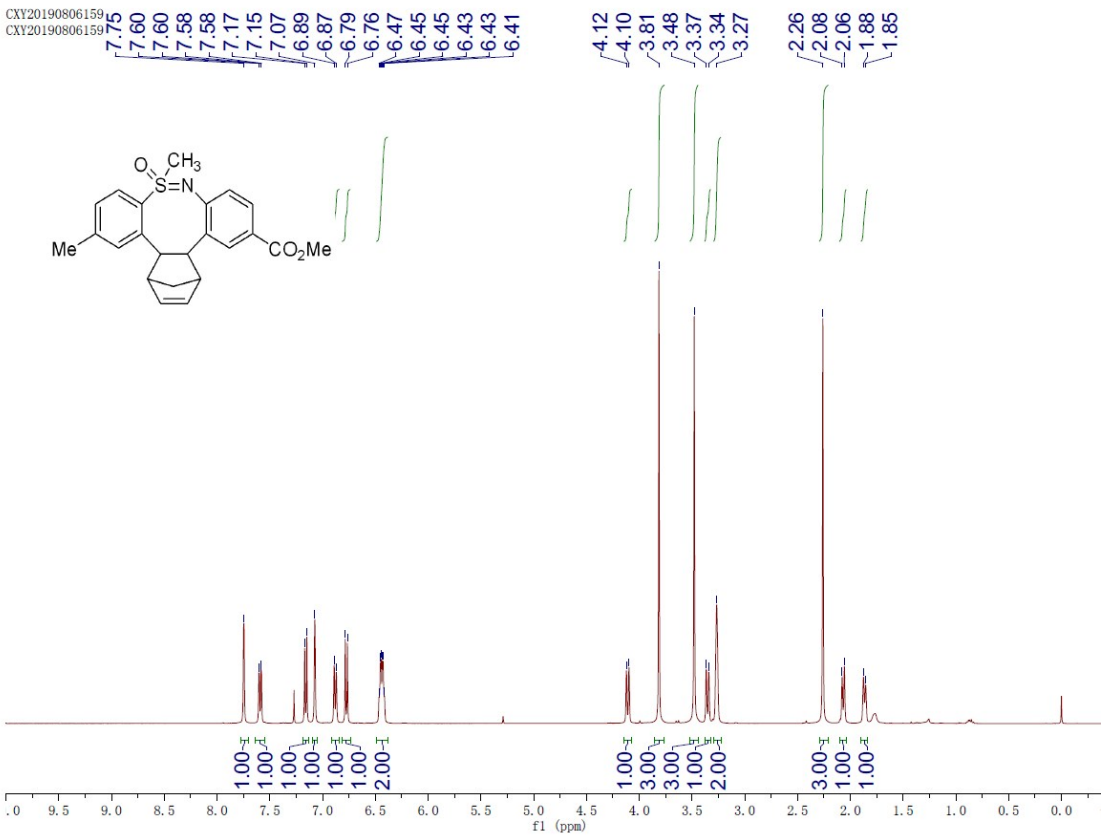
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 22



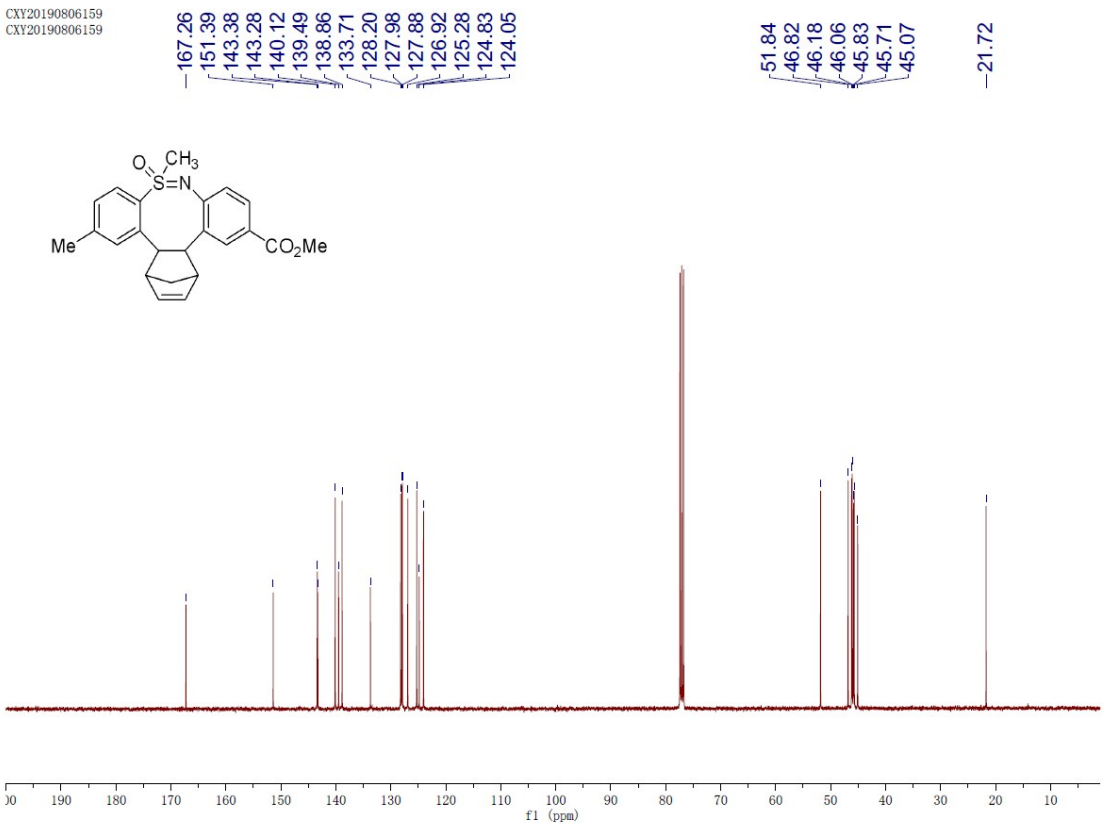
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 22



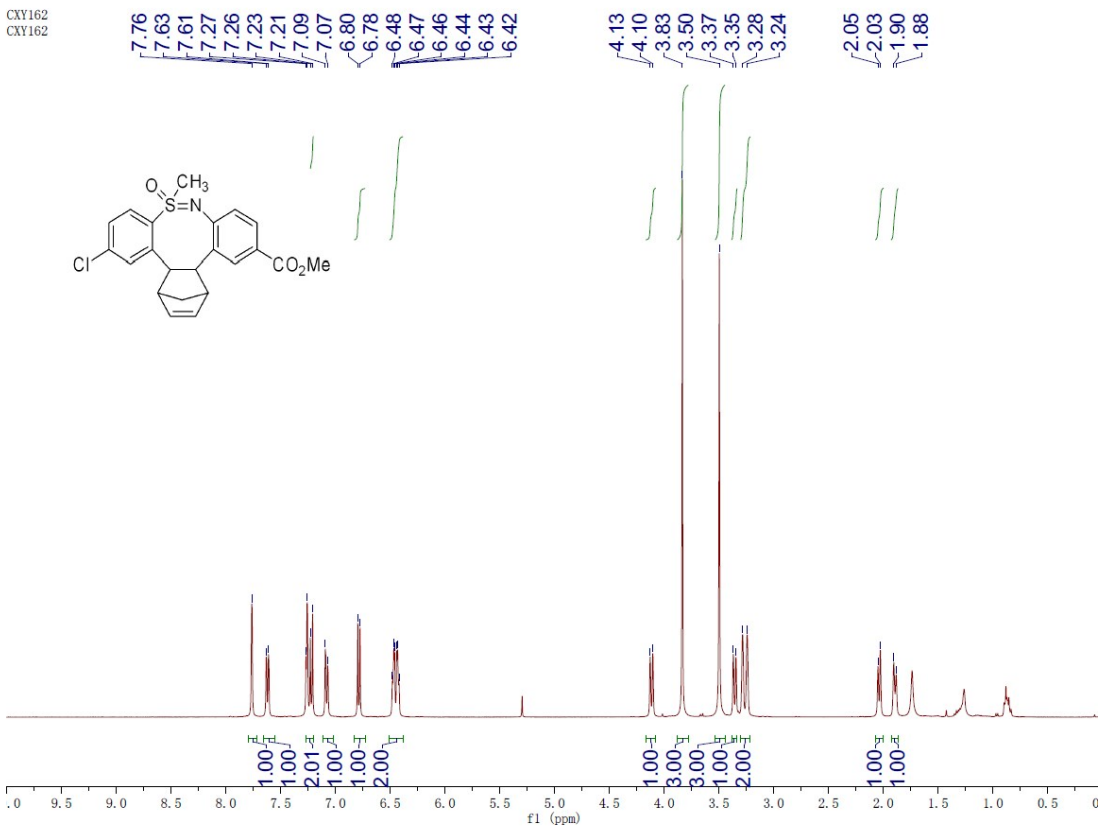
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 23



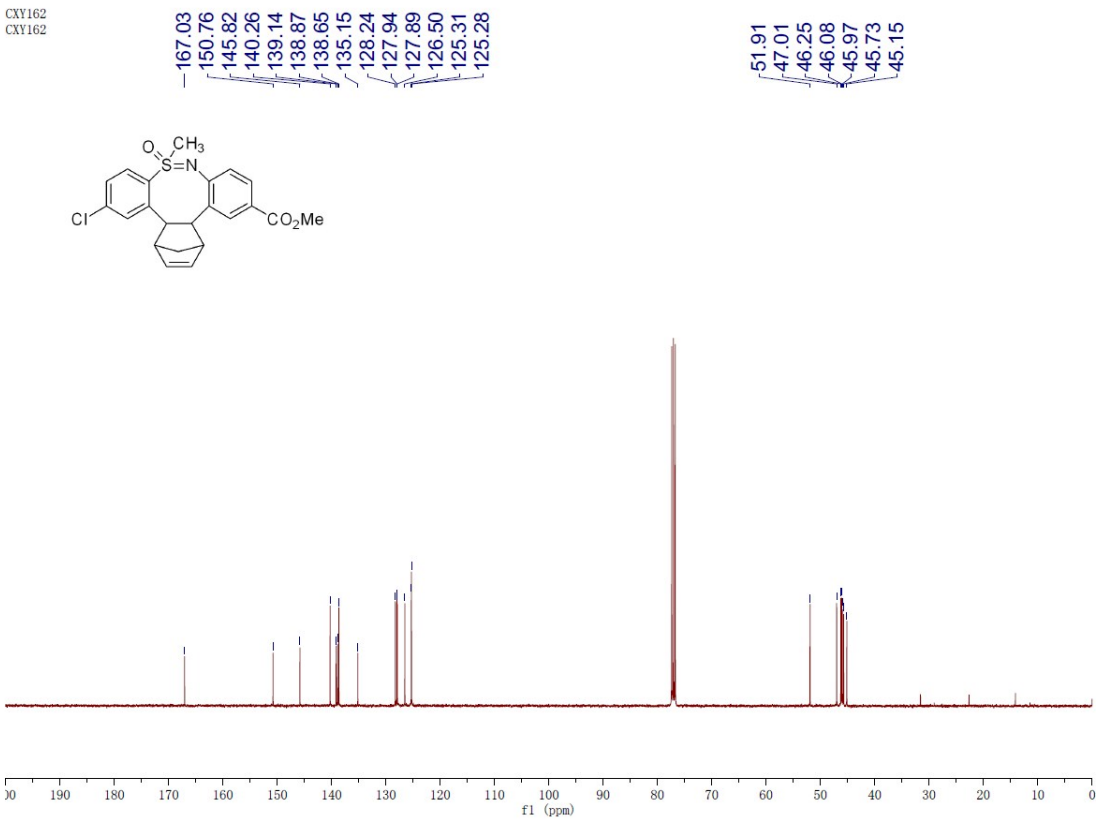
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 23



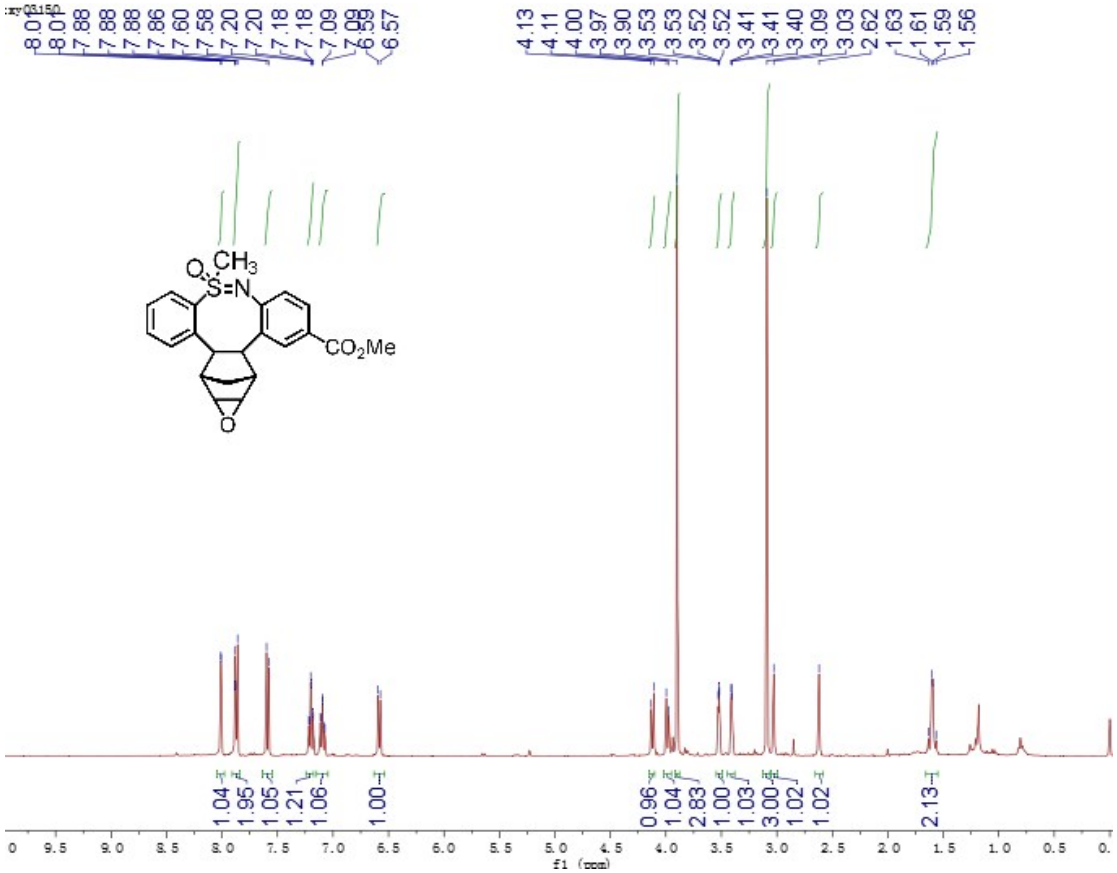
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 24



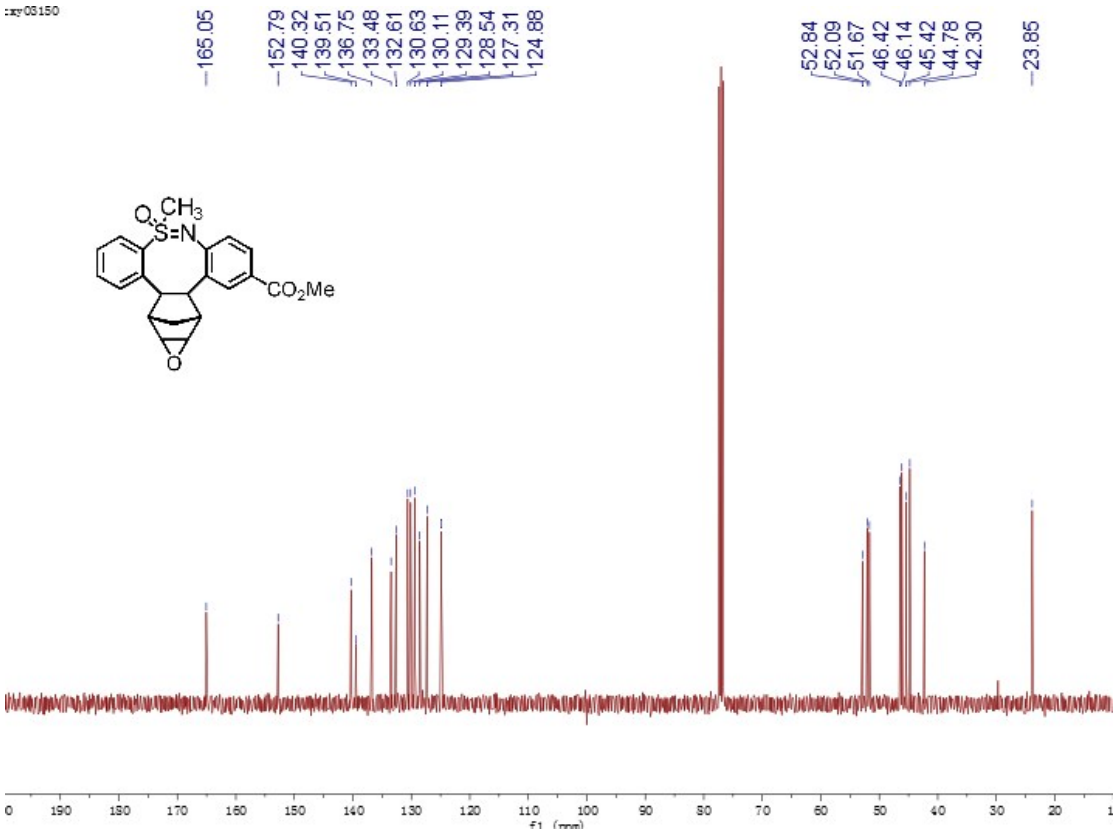
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 24



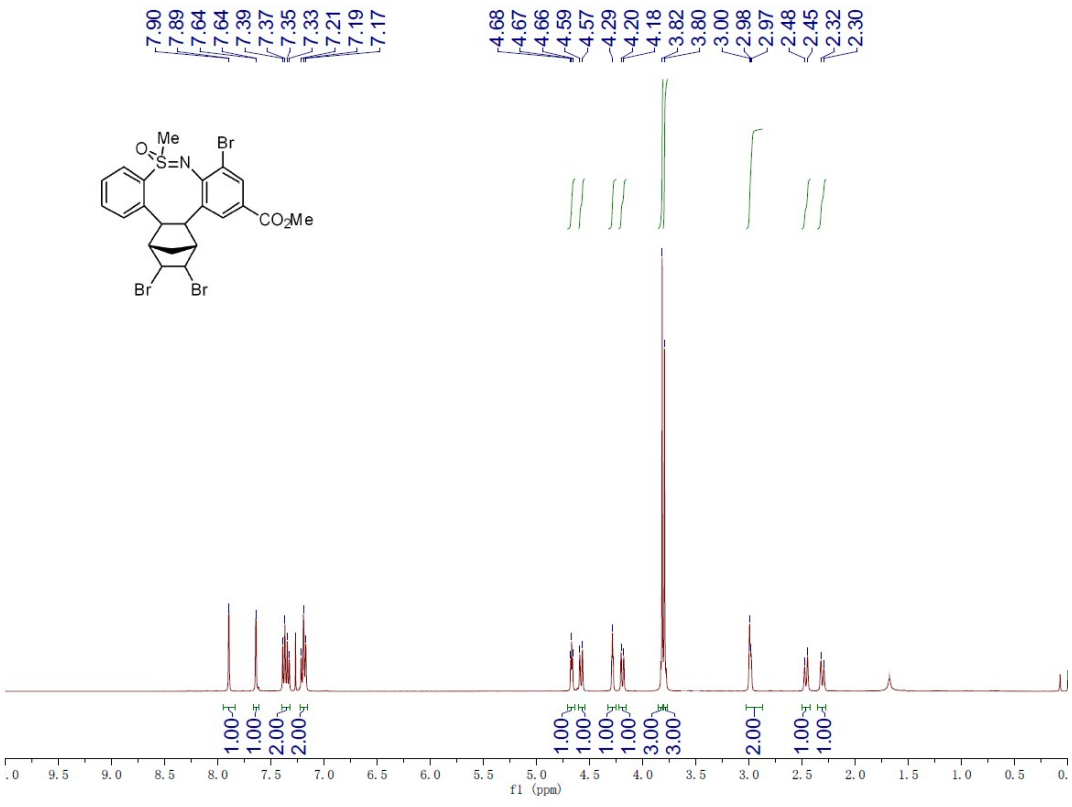
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 26



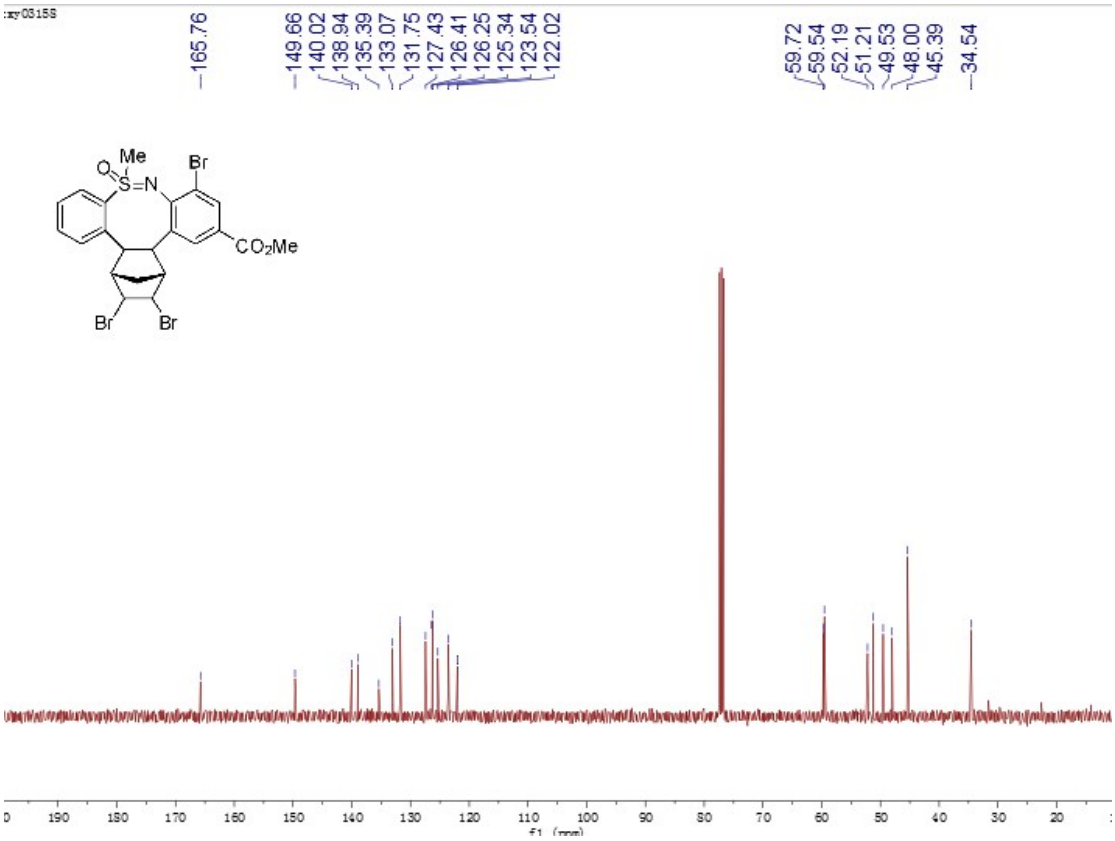
^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 26



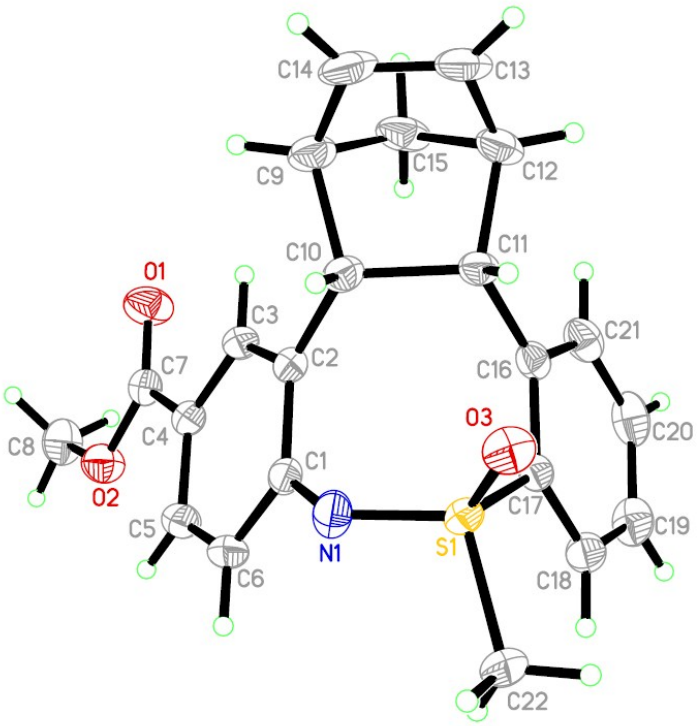
^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 27

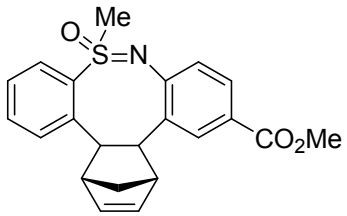


^{13}C NMR spectrum (100 MHz, $CDCl_3$) of 27



6. X-ray ORTEP illustration of compound 3a.





3a

Crystal data and structure refinement for compound **3a**.

```
Bond precision:  C-C = 0.0032 A          Wavelength=0.71073

Cell:           a=19.5977(12)    b=8.1238(4)       c=23.2996(12)
                alpha=90         beta=90.182(5)    gamma=90
Temperature:    293 K

                Calculated                Reported
Volume          3709.5(3)                 3709.5(3)
Space group     C 2/c                     C 2/c
Hall group      -C 2yc                    -C 2yc
Moiety formula  C22 H21 N O3 S            ?
Sum formula     C22 H21 N O3 S            C22 H21 N O3 S
Mr              379.46                    379.46
Dx,g cm-3       1.359                     1.359
Z               8                         8
Mu (mm-1)       0.197                     0.197
F000            1600.0                    1600.0
F000'           1601.67
h,k,lmax        23,9,28                   23,9,28
Nref            3474                      3319
Tmin,Tmax       0.958,0.965               0.765,1.000
Tmin'           0.958

Correction method= # Reported T Limits: Tmin=0.765 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.955          Theta(max)= 25.593

R(reflections)= 0.0412( 2988)     wR2(reflections)= 0.1121( 3319)

S = 1.007                 Npar= 244
```

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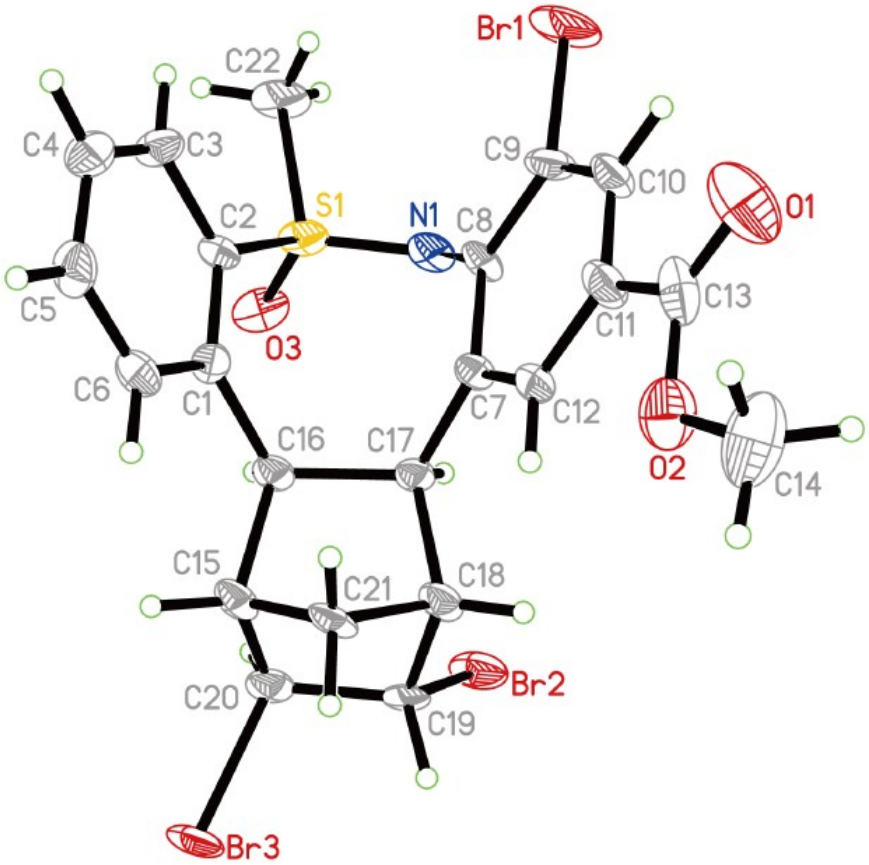
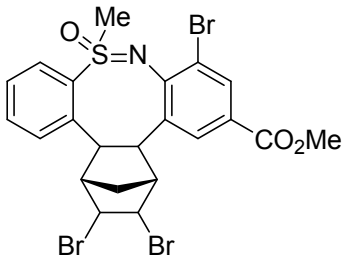
7. X-ray ORTEP illustration of compound **27** (**S46-S47**).





27

Crystal data and structure refinement for compound **24**.

Bond precision: C-C = 0.0213 A Wavelength=0.71073

Cell: a=8.1990(7) b=11.3055(13) c=14.2419(11)
alpha=100.441(8) beta=100.282(7) gamma=91.136(8)
Temperature: 293 K

	Calculated	Reported
Volume	1275.6(2)	1275.6(2)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C22 H20 Br3 N O3 S, C H2 Cl2	?
Sum formula	C23 H22 Br3 Cl2 N O3 S	C23 H22 Br3 Cl2 N O3 S
Mr	703.08	703.10
Dx,g cm-3	1.831	1.831
Z	2	2
Mu (mm-1)	5.062	5.062
F000	692.0	692.0
F000'	691.42	
h,k,lmax	9,13,16	9,13,16
Nref	4541	4471
Tmin,Tmax	0.341,0.402	0.026,1.000
Tmin'	0.316	

Correction method= # Reported T Limits: Tmin=0.026 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.985 Theta(max)= 25.098

R(reflections)= 0.1666(2341) wR2(reflections)= 0.3351(4471)

S = 1.094 Npar= 299
