Supporting Information

Asymmetric Tandem Reactions of *N*-Sulfonylimines and α,β-Unsaturated Aldehydes: An Alternative Reaction Pathway to That of Using Saturated Aldehydes

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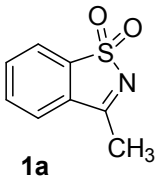
1. General Information

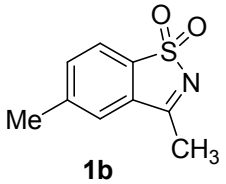
^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Varian MERCURY plus-400 spectrometer with TMS as an internal standard. HRMS was performed at the Analysis Center of Shanghai Jiao Tong University. Enantioselectivity was measured by high performance liquid chromatography (HPLC) using Daicel Chiralcel AS-H, OD-H and IC-3 columns with hexane / *i*-PrOH as a eluent. Column chromatography was performed using 100–200 mesh silica gel. Melting points were measured with SGW X-4 micro melting point apparatus. All commercially available substrates were used as received.

2. Data for Substrates[1-6]



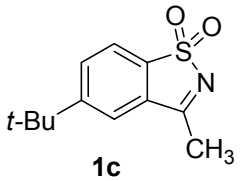
1a

3-Methylbenzo[*d*]isothiazole 1,1-dioxide (1a): White solid (2.6 g, 68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 – 7.91 (m, 1H), 7.76 – 7.74 (m, 2H), 7.70 – 7.68 (m, 1H), 2.67 (s, 3H).



1b

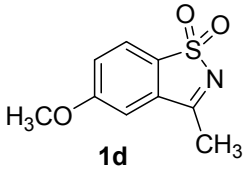
3,5-Dimethylbenzo[*d*]isothiazole 1,1-dioxide (1b): White solid (0.6 g, 65%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.00 (d, J = 7.6 Hz, 1H), 7.85 (s, 1H), 7.68 (d, J = 7.6 Hz, 1H), 2.66 (s, 3H), 2.47 (s, 3H).



1c

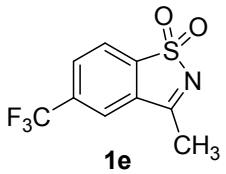
5-(*tert*-Butyl)-3-methylbenzo[*d*]isothiazole 1,1-dioxide (1c): white solid (0.2 g, 60%), m.p. 186 – 187 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 8.0 Hz, 1H), 7.76 (dd, J = 8.0, 1.6 Hz, 1H), 7.63 (d, J = 1.2 Hz, 1H), 2.65 (s, 3H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 158.8, 136.9, 132.2, 130.9, 122.3, 121.1, 35.8, 31.3, 17.6; IR: 2963, 2874, 1557, 1465, 1416, 1372, 1319,

1276, 1184, 1153, 1103, 1020, 892, 837, 797, 736, 625; HRMS (ESI): calcd for $C_{12}H_{16}NO_2S$ $[M+H]^+$: 238.0902, found 238.0903.



1d

5-Methoxy-3-methylbenzo[*d*]isothiazole 1,1-dioxide (1d): white solid (0.4 g, 54%). m.p. 169 – 170 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.03 (d, J = 8.4 Hz, 1H), 7.53 (d, J = 2.4 Hz, 1H), 7.35 (dd, J = 8.4, 2.4 Hz, 1H), 3.91 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 175.1, 164.7, 134.4, 130.5, 124.1, 119.6, 111.6, 57.1, 18.1; IR: 1614, 1556, 1316, 1275, 1239, 1170, 1123, 1069, 836, 801, 730, 607, 554; HRMS (ESI): calcd for $C_9H_{10}NO_3S$ $[M-H]^-$: 211.9993, found 211.9989.



1e

3-Methyl-5-(trifluoromethyl)benzo[*d*]isothiazole 1,1-dioxide (1e): white solid (0.3 g, 54%). m.p. 210 – 212 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 – 8.02 (m, 2H), 7.91 (s, 1H), 2.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 142.8, 132.5, 130.9, 123.2, 121.4, 17.9; IR: 1614, 1556, 1316, 1275, 1239, 1170, 1123, 1069, 836, 801, 730, 607, 554; HRMS (ESI): calcd for $C_9H_7F_3NO_2S$ $[M+H]^+$: 250.0150, found 250.0147.

3. References

[1] J. G. Lombardino, *J. Org. Chem*. 1971, **36**, 1843.

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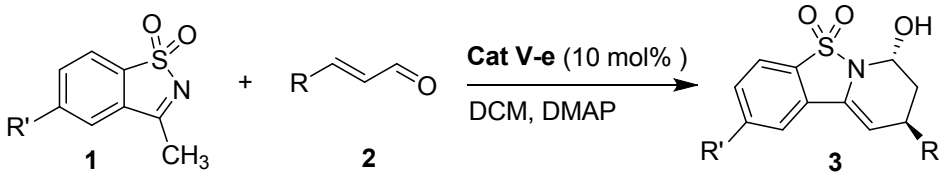
[3] L. Xu, H. Shu, Y. Liu, S. H. Zhang and M. L. Trudell, *Tetrahedron* 2006, **62**, 7902.

[4] Q. Yang, G. Shang, W. Z. Gao, J. G. Deng and X. M. Zhang, *Angew. Chem., Int. Ed*. 2006, **45**, 3832.

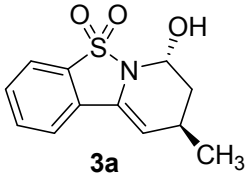
[5] X. F. Xiong, H. Zhang, J. Peng and Y.-C. Chen, *Chem. Eur. J*. 2011, **17**, 2358.

[6] G. Yang and W. Zhang, *Angew. Chem., Int. Ed*. 2013, **52**, 7540.

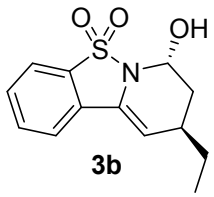
4. General Procedure for the Organocatalytic Tandem Reactions



The **cat** (4.3 mg, 0.01 mmol), DMAP (12.2 mg, 0.10 mmol) and different *α,β*-unsaturated aldehydes (1.2 equiv, 0.12 mmol) were dissolved in DCM (1 mL) at 25 °C. The solution was stirred for 5 min, and then the appropriate cyclic sulfamidate (0.10 mmol) was added. The reaction mixture was stirred at 25 ℃ until the complete consumption of cyclic sulfamidate (monitored by TLC). The solvent was then evaporated and the crude products was purified by flash column silica-gel chromatography (PE / EA = 6 / 1) to give the adduct **3**. Remarkably, the direct organocatalytic tandem reaction can be easily scaled up to a gram-scale. Thus, treating **1a** (1.00 g) with (*E*)-3-(2-chlorophenyl)acrylaldehyde **2f** (0.92 g, 1.2 equiv) under the standard reaction conditions smoothly provided the desired product **3f** (1.33 g, 70%, > 20:1 dr and 98% ee).

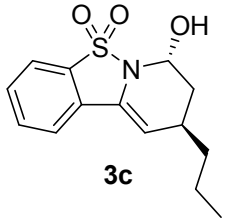


(7*R*,9*R*)-9-Methyl-7-hydroxy-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3a): Colorless oil (22.6 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, J = 7.6 Hz, 1H), 7.67 – 7.60 (m, 2H), 7.55 – 7.51 (m, 1H), 5.86 (t, J = 2.8 Hz, 1H), 5.62 (dd, J = 2.4, 0.8 Hz, 1H), 3.54 (s, 1H), 2.90 – 2.80 (m, 1H), 2.26 – 2.20 (m, 1H), 1.58 – 1.51 (m, 1H), 1.20 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.4, 132.0, 130.0, 128.2, 121.4, 121.2, 108.2, 72.3, 36.0, 23.4, 20.6; HRMS (ESI): calcd for $C_{12}H_{12}NO_3S$ $[M-H]^-$: 250.0538, found 250.0531; IR: 3456, 2960, 2928, 2872, 1732, 1665, 1469, 1384, 1335, 1301, 1252, 1176, 1161, 1029, 980, 950, 872, 760; HPLC (Chiralcel IC-3, Hexane / *i*-PrOH = 90 : 10, UV = 254 nm, flow rate = 1.0 mL / min) t_{R1} = 79.51 min (major) and t_{R2} = 110.88 min (minor); ee = 83%; $[\alpha]^{25}_{D}$ = +38.6 (*c* 0.2, CH_3OH).



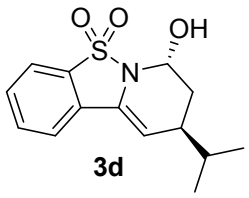
3b

(7*R*,9*R*)-9-Ethyl-7-hydroxy-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3b): Pale yellow solid (24.4 mg, 92%). m.p. 100 – 101 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 7.6 Hz, 1H), 7.70 – 7.68 (m, 1H), 7.65 – 7.61 (m, 1H), 7.56 – 7.52 (m, 1H), 5.88 (t, J = 2.8 Hz, 1H), 5.70 – 5.69 (m, 1H), 3.49 (s, 1H), 2.70 – 2.64 (m, 1H), 2.30 – 2.23 (m, 1H), 1.61 – 1.52 (m, 1H), 1.04 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.3, 132.0, 130.1, 130.0, 128.5, 121.4, 121.2, 106.6, 72.3, 33.7, 29.84, 27.9, 11.4; HRMS (ESI): calcd for $C_{13}H_{14}NO_3S$ [M-H]$^-$: 264.0694, found 264.0690; IR: 3480, 2963, 2924, 2852, 1732, 1716, 1668, 1470, 1338, 1304, 1260, 1177, 1134, 1023, 949, 800, 761, 592, 571, 523; HPLC (Chiralcel IC-3, Hexane / *i*-PrOH = 80 : 20, UV = 254 nm, flow rate = 0.9 mL / min) t_{R1} = 44.87 min (major) and t_{R2} = 58.81 min (minor); ee = 91%; $[\alpha]^{25}_D$ = +9.5 (*c* 0.2, CH_3OH).



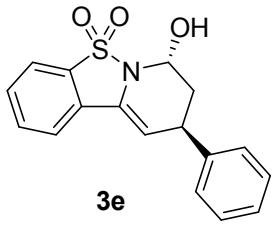
3c

(7*R*,9*R*)-7-Hydroxy-9-propyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3c): Colorless oil (25.9 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.0 Hz, 1H), 7.69 – 7.61 (m, 2H), 7.55 – 7.52 (m, 1H), 5.87 (s, 1H), 5.69 (d, J = 1.2 Hz, 1H), 3.54 (s, 1H), 2.77 – 2.74 (m, 1H), 2.28 – 2.22 (m, 1H), 1.57 – 1.44 (m, 5H), 0.98 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.3, 131.9, 130.1, 129.9, 128.3, 121.3, 121.2, 106.8, 72.2, 37.2, 34.2, 28.0, 20.1, 14.3; HRMS (ESI): calcd for $C_{14}H_{16}NO_3S$ [M-H]$^-$: 278.0851, found 278.0844; IR: 3449, 2958, 2928, 2872, 2026, 1638, 1455, 1384, 1338, 1301, 1176, 1051, 950, 753, 592, 533; HPLC (Chiralcel IC-3, Hexane / *i*-PrOH = 80 : 20, UV = 254 nm, flow rate = 0.9 mL / min) t_{R1} = 44.80 min (major) and t_{R2} = 57.90 min (minor); ee = 93%; $[\alpha]^{25}_D$ = +15.3 (*c* 0.2, CH_3OH).



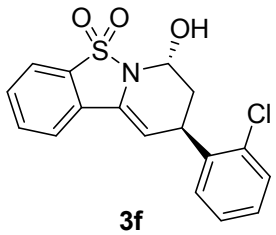
3d

(7*R*,9*R*)-7-Hydroxy-9-*iso*-propyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3d): White solid (22.9 mg, 82%). m.p. 153 – 154 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.0 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.66 – 7.61 (m, 1H), 7.54 (t, J = 7.2 Hz, 1H), 5.91 (t, J = 2.8 Hz, 1H), 5.72 – 5.71 (m, 1H), 3.57 (s, 1H), 2.68 – 2.62 (m, 1H), 2.19 – 2.09 (m, 1H), 1.87 – 1.80 (m, 1H), 1.71 – 1.64 (m, 1H), 1.00 (dd, J = 6.4, 2.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.3, 130.2, 130.1, 130.0, 129.1, 121.4, 121.2, 105.4, 72.5, 34.4, 31.4, 30.6, 19.7, 19.7; HRMS (ESI): calcd for $C_{14}H_{16}NO_3S$ $[M+H]^+$: 280.1007, found 280.1008; IR: 2960, 2926, 2868, 1457, 1471, 1397, 1301, 1223, 1175, 1160, 1130, 1105, 1046, 1029, 1010, 990, 758, 600, 582; HPLC (Chiralcel IC-3, Hexane / *i*-PrOH = 80 : 20, UV = 254 nm, flow rate = 0.9 mL / min) t_{R1} = 44.42 min (major) and t_{R2} = 55.44 min (minor); ee = 98%; $[\alpha]^{25}_D$ = +25.5 (*c* 0.1, CH_3OH).



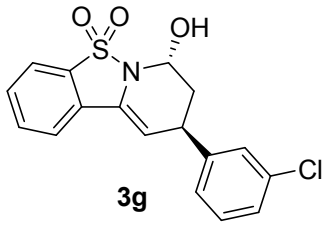
3e

(7*R*,9*R*)-7-Hydroxy-9-phenyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3e): White solid (26.4 mg, 84%). m.p. 131 – 133 °C ; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J = 7.6 Hz, 1H), 7.70 – 7.63 (m, 2H), 7.60 – 7.56 (m, 1H), 7.39 – 7.35 (m, 2H), 7.32 – 7.29 (m, 3H), 5.93 (dd, J = 5.2, 2.8 Hz, 1H), 5.83 (dd, J = 2.4, 1.2 Hz, 1H), 4.03 (ddd, J = 12.4, 6.0, 2.8 Hz, 1H), 3.70 (t, J = 2.4 Hz, 1H), 2.49 – 2.44 (m, 1H), 1.99 – 1.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.4, 133.3, 131.9, 130.1, 129.8, 128.9, 128.9, 127.7, 127.1, 121.3, 121.2, 105.6, 72.1, 36.8, 34.9; HRMS (ESI): calcd for $C_{17}H_{14}NO_3S$ $[M-H]^-$: 312.0694, found 312.0686; IR: 3454, 2927, 2026, 1638, 1470, 1453, 1384, 1304, 1264, 1174, 1159, 1063, 1047, 949, 891, 758, 701, 664, 594, 561, 527; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 80 : 20, UV = 254 nm, flow rate = 0.7 mL / min), t_{R1} = 27.18 min (major) and t_{R2} = 47.40 min (minor); ee = 94%; $[\alpha]^{25}_D$ = 7.4 (*c* 0.2, CH_3OH).



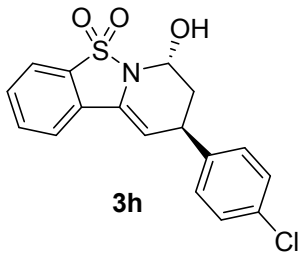
3f

(7*R*,9*R*)-9-(2-Chlorophenyl)-7-hydroxy-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3f): White solid (29.6 mg, 85%). m.p. 165 – 166 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 – 7.82 (m, 1H), 7.73 – 7.64 (m, 2H), 7.60 – 7.56 (m, 1H), 7.42 – 7.39 (m, 1H), 7.31 – 7.18 (m, 3H), 5.92 (t, J = 2.8 Hz, 1H), 5.79 (dd, J = 2.4, 1.2 Hz, 1H), 4.54 (ddd, J = 12.0, 5.6, 2.8 Hz, 1H), 3.78 (s, 1H), 2.59 – 2.53 (m, 1H), 1.88 – 1.81 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 133.9, 133.5, 132.1, 130.4, 130.0, 129.9, 129.8, 129.1, 128.5, 127.6, 121.5, 121.5, 104.7, 72.4, 34.8, 32.1; HRMS (ESI): calcd for $C_{17}H_{13}NO_3SCl$ $[M-H]^-$: 346.0305, found 346.0305; IR: 3470, 2927, 1649, 1471, 1438, 1384, 1305, 1261, 1175, 1159, 1102, 1063, 1051, 1034, 998, 949, 902, 822, 757, 715, 702, 654, 619, 597, 562, 537, 499; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 80 : 20, UV = 254 nm, flow rate = 0.7 mL / min) t_{R1} = 28.38 min (major) and t_{R2} = 44.84 min (minor); ee = 95%; $[\alpha]^{25}_{D}$ = +15.9 (*c* 0.2, CH_3OH).



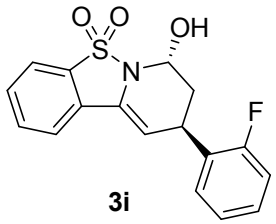
3g

(7*R*,9*R*)-9-(3-Chlorophenyl)-7-hydroxy-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3g): White solid (27.7 mg, 80%). m.p. 73 – 74 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 7.6 Hz, 1H), 7.72 – 7.65 (m, 2H), 7.61 – 7.57 (m, 1H), 7.29 – 7.26 (m, 3H), 7.19 – 7.17 (m, 1H), 5.92 (s, 1H), 5.78 – 5.76 (dd, J = 2.4, 1.2 Hz, 1H), 4.01 (ddd, J = 12.4, 5.6, 2.4 Hz, 1H), 3.72 (s, 1H), 2.47 – 2.41 (m, 1H), 1.92 (t, J = 12.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.7, 134.9, 133.6, 132.2, 130.5, 130.4, 130.1, 129.8, 129.5, 128.1, 127.5, 126.2, 121.5, 104.7, 72.2, 36.9, 35.0; HRMS (ESI): calcd for $C_{17}H_{14}NO_3SCl$ $[M+Na]^+$: 370.0281, found 370.0281; IR: 3453, 2920, 2850, 1640, 1596, 1470, 1430, 1384, 1305, 1259, 1175, 1159, 1095, 1062, 950, 917, 785, 759, 723, 694, 658, 598, 558; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 70 : 30, UV = 254 nm, flow rate = 0.4 mL / min) t_{R1} = 31.97 min (major) and t_{R2} = 59.03 min (minor); ee = 98%; $[\alpha]^{25}_{D}$ = +24.3 (*c* 0.3, CH_3OH).



3h

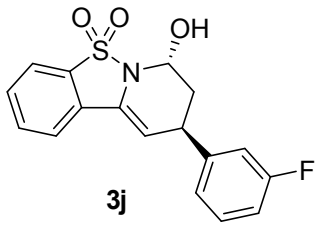
(7*R*,9*R*)-9-(4-Chlorophenyl)-7-hydroxy-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3h): White solid (28.3 mg, 82%). m.p. 143 – 144 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 – 7.82 (m, 1H), 7.71 – 7.64 (m, 2H), 7.61 – 7.57 (m, 1H), 7.34 – 7.31 (m, 2H), 7.24 – 7.22 (m, 2H), 5.92 (t, J = 2.4 Hz, 1H), 5.76 (dd, J = 2.4, 1.2 Hz, 1H), 4.01 (ddd, J = 12.0, 5.6, 2.8 Hz, 1H), 3.69 (s, 1H), 2.46 – 2.40 (m, 1H), 1.94 – 1.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 133.6, 133.0, 132.1, 130.5, 129.8, 129.4, 129.3, 129.2, 121.5, 121.5, 105.0, 72.2, 36.9, 34.6; HRMS (ESI): calcd for $C_{17}H_{13}NO_3SCl$ [M-H]$^-$: 346.0305, found 346.0293; IR: 3463, 1647, 1491, 1470, 1408, 1384, 1304, 1260, 1174, 1159, 1090, 1062, 1048, 1014, 950, 891, 831, 759, 625, 612, 596, 561, 522, 501; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 70 : 30, UV = 254 nm, flow rate = 0.4 mL / min) t_{R1} = 37.06 min (major) and t_{R2} = 63.13 min (minor); ee > 99%; $[\alpha]^{25}_{D}$ = +18.3 (*c* 0.2, CH_3OH).



3i

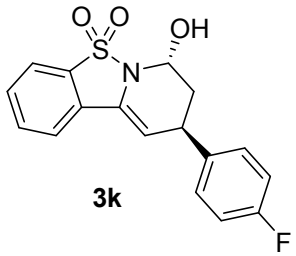
(7*R*,9*R*)-9-(2-Fluorophenyl)-7-hydroxy-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3i): Pale yellow solid (29.8 mg, 90%). m.p. 171 – 172 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 7.6 Hz, 1H), 7.71 – 7.63 (m, 2H), 7.60 – 7.55 (m, 1H), 7.29 – 7.23 (m, 2H), 7.15 – 7.05 (m, 2H), 5.94 (dd, J = 5.2, 2.4 Hz, 1H), 5.78 (d, J = 1.6 Hz, 1H), 4.37 (ddd, J = 12.4, 5.6, 2.4 Hz, 1H), 3.70 (t, J = 2.4 Hz, 1H), 2.52 – 2.46 (m, 1H), 2.01 – 1.94 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2, 159.8, 133.5, 132.1, 130.4, 130.1, 129.9, 129.5, 129.3, 129.3, 128.9, 128.8, 124.7, 124.7, 121.5, 121.4, 116.0, 115.8, 104.6, 72.3, 34.9, 28.6; HRMS (ESI): calcd for $C_{17}H_{13}NO_3SF$ [M-H]$^-$: 330.0600, found 330.0583; IR: 3468, 2925, 1666, 1584, 1491, 1470, 1455, 1384, 1305, 1262, 1226, 1174, 1160, 1109, 1062, 950, 908, 832, 792, 757, 658, 619, 597, 563; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 90 : 10, UV = 254 nm, flow rate = 0.7 mL / min) t_{R1} =

57.11 min (major) and t_{R2} = 89.74 min (minor); ee = 99.7%; $[\alpha]^{25}_{D}$ = +39.9 (*c* 0.2, CH_3OH).



3j

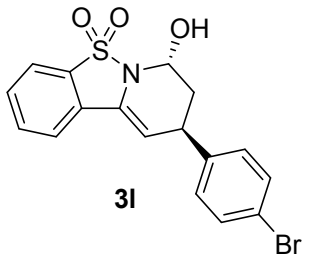
((7*R*,9*R*)-9-(3-Fluorophenyl)-7-hydroxy-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3j): Pale yellow solid (28.1 mg, 85%). m.p. 72 – 73 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 – 7.83 (m, 1H), 7.72 – 7.65 (m, 2H), 7.61 – 7.57 (m, 1H), 7.35 – 7.30 (m, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.02 – 6.96 (m, 2H), 5.93 (dd, *J* = 5.2, 2.4 Hz, 1H), 5.78 (dd, *J* = 2.4, 1.2 Hz, 1H), 4.03 (ddd, *J* = 12.4, 6.0, 2.8 Hz, 1H), 3.68 (t, *J* = 2.4 Hz, 1H), 2.48 – 2.42 (m, 1H), 1.96 – 1.89 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 161.8, 146.0, 146.0, 133.4, 132.0, 130.4, 130.3, 129.6, 129.2, 123.4, 121.3, 114.7, 114.5, 114.1, 113.9, 104.6, 72.0, 36.6, 34.7; HRMS (ESI): calcd for $C_{17}H_{13}NO_3SF$ $[M-H]^-$: 330.0600, found 330.0578; IR: 3459, 2928, 2360, 1638, 1470, 1448, 1384, 1305, 1247, 1175, 1160, 1063, 948, 870, 760, 695, 585, 559; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 70 : 30, UV = 254 nm, flow rate = 0.4 mL / min) t_{R1} = 30.40 min (major) and t_{R2} = 56.80 min (minor); ee = 99.5%; $[\alpha]^{25}_{D}$ = –26.0 (*c* 0.2, CH_3OH).



3k

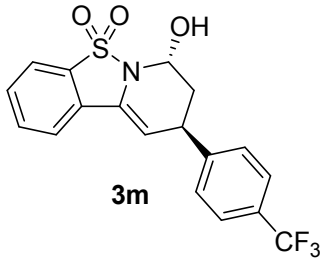
(7*R*,9*R*)-9-(4-Fluorophenyl)-7-hydroxy-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3k): White solid (28.9 mg, 87%). m.p. 161 – 162 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 – 7.82 (m, 1H), 7.71 – 7.64 (m, 2H), 7.61 – 7.57 (m, 1H), 7.27 – 7.23 (m, 2H), 7.07 – 7.00 (m, 2H), 5.92 (dd, *J* = 4.8, 2.4 Hz, 1H), 5.77 (dd, *J* = 2.4, 1.2 Hz, 1H), 4.02 (ddd, *J* = 12.0, 5.6, 2.4 Hz, 1H), 3.68 (t, *J* = 2.4 Hz, 1H), 2.46 – 2.40 (m, 1H), 1.95 – 1.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.3, 160.8, 139.3, 133.5, 132.2, 130.4, 129.9, 129.4, 129.3, 121.5, 121.5, 116.0, 115.8, 105.4, 72.3, 37.1, 34.5; HRMS (ESI): calcd for $C_{17}H_{13}NO_3SF$ $[M-H]^-$: 330.0600, found 330.0594; IR: 3455, 2928, 2342, 1664, 1604, 1509, 1470, 1384, 1304, 1261, 1222, 1174, 1158, 1107, 1063,

1049, 950, 893, 835, 787, 760, 639, 617, 596, 557, 532, 510; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 70 : 30, UV = 254 nm, flow rate = 0.4 mL / min) t_{R1} = 32.65 min (major) and t_{R2} = 61.13 min (minor); ee = 99%; $[\alpha]^{25}_{D}$ = +13.9 (*c* 0.2, CH_3OH).



3l

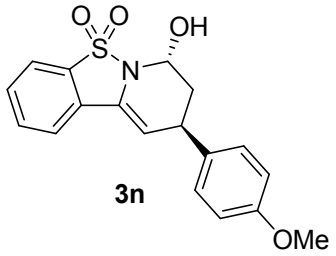
(7*R*,9*R*)-9-(4-Bromophenyl)-7-hydroxy-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3l): Pale yellow solid (30.5 mg, 78%). m.p. 174 – 176 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 – 7.83 (m, 1H), 7.71 – 7.65 (m, 2H), 7.61 – 7.57 (m, 1H), 7.50 – 7.48 (m, 2H), 7.19 – 7.16 (m, 2H), 5.92 (d, *J* = 2.0 Hz, 1H), 5.76 (dd, *J* = 2.4, 1.2 Hz, 1H), 4.00 (ddd, *J* = 12.4, 6.0, 2.8 Hz, 1H), 3.60 (t, *J* = 2.0 Hz, 1H), 2.46 – 2.40 (m, 1H), 1.94 – 1.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.4, 133.4, 132.0, 131.6, 130.3, 129.6, 129.4, 129.3, 104.7, 72.0, 36.6, 34.5; HRMS (ESI): calcd for $C_{17}H_{13}NO_3SBr$ $[M-H]^-$: 389.9800, found 389.9775; IR: 3461, 2926, 2853, 1647, 1487, 1470, 1404, 1384, 1304, 1244, 1174, 1159, 1063, 1049, 1009, 950, 892, 824, 759, 720, 684, 608, 595, 561, 534, 499; HPLC: (Chiralcel AS-H, Hexane / *i*-PrOH = 70 : 30, UV = 254 nm, flow rate = 0.4 mL / min) t_{R1} = 40.48 min (major) and t_{R2} = 68.16 min (minor); ee = 99%; $[\alpha]^{25}_{D}$ = +36.3 (*c* 0.3, CH_3OH).



3m

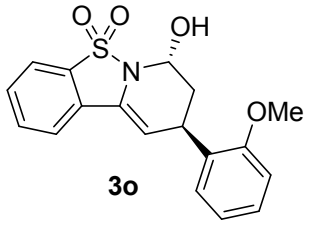
(7*R*,9*R*)-7-Hydroxy-9-(4-(trifluoromethyl)phenyl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3m): Colorless oil (38.1 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 7.6 Hz, 1H), 7.72 – 7.65 (m, 2H), 7.63 – 7.58 (m, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 5.94 (dd, *J* = 4.8, 2.4 Hz, 1H), 5.77 (dd, *J* = 2.4, 1.2 Hz, 1H), 4.10 (ddd, *J* = 12.4, 5.6, 2.4 Hz, 1H), 3.70 (d, *J* = 2.0 Hz, 1H), 2.49 – 2.43 (m, 1H), 1.97 – 1.90 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.5, 133.4, 132.0, 130.4, 129.6, 129.5, 129.5, 129.3, 128.4, 128.1, 125.8, 122.7, 121.4, 121.3, 104.1,

71.9, 36.6, 34.9; HRMS (ESI): calcd for $C_{18}H_{13}NO_3SF_3$ $[M-H]^-$: 380.0568, found 380.0560; IR: 3458, 2929, 2026, 1634, 1470, 1419, 1384, 1325, 1264, 1174, 1160, 1119, 1065, 1017, 949, 894, 759, 610, 560; HPLC: (Chiralcel AS-H, Hexane / *i*-PrOH = 70 : 30, UV = 254 nm, flow rate = 0.4 mL / min) t_{R1} = 26.38 min (major) and t_{R2} = 42.50 min (minor); ee = 96%; $[\alpha]^{25}_D$ = +25.0 (*c* 0.2, CH_3OH).



3n

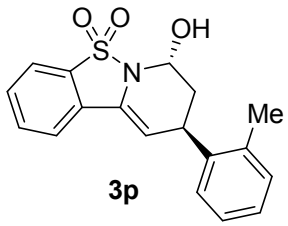
(7*R*,9*R*)-7-Hydroxy-9-(4-methoxyphenyl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3n): Colorless oil (25.1 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.0 Hz, 1H), 7.70 – 7.63 (m, 2H), 7.59 – 7.55 (m, 1H), 7.22 – 7.19 (m, 2H), 6.90 – 6.88 (m, 2H), 5.92 (s, 1H), 5.80 (t, *J* = 1.2 Hz, 1H), 3.98 (ddd, *J* = 12.4, 6.0, 2.4 Hz, 1H), 3.81 (s, 3H), 3.68 (s, 1H), 2.45 – 2.39 (m, 1H), 1.92 (t, *J* = 12.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.8, 135.6, 133.5, 132.1, 130.3, 130.0, 129.0, 128.9, 121.5, 121.4, 114.4, 106.2, 72.4, 55.5, 37.1, 34.3; HRMS (ESI): calcd for $C_{18}H_{16}NO_4S$ $[M-H]^-$: 342.0800, found 342.0797; IR: 3452, 2928, 1637, 1512, 1469, 1384, 1304, 1250, 1174, 1159, 1063, 950, 830, 761, 538; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 80 : 20, UV = 254 nm, flow rate = 0.7 mL / min) t_{R1} = 46.42 min (major); ee > 99%; $[\alpha]^{25}_D$ = +14.7 (*c* 0.3, CH_3OH).



3o

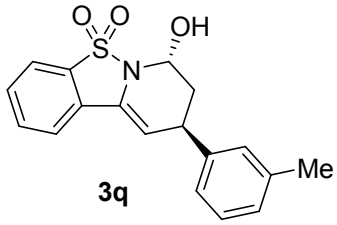
(7*R*,9*R*)-7-Hydroxy-9-(2-methoxyphenyl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3o): White solid (27.4 mg, 80%). m.p. 83 – 85 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 – 7.81 (m, 1H), 7.71 – 7.69 (m, 1H), 7.65 (td, *J* = 7.2, 1.2 Hz, 1H), 7.56 (td, *J* = 8.0, 0.8 Hz, 1H), 7.29 – 7.21 (m, 2H), 7.21 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.97 – 6.90 (m, 2H), 5.92 (dd, *J* = 4.8, 2.4 Hz, 1H), 5.82 (dd, *J* = 2.4, 1.2 Hz, 1H), 4.46 (ddd, *J* = 12.0, 5.6, 2.4 Hz, 1H), 3.86 (s, 3H), 3.60 (t, *J* = 2.4 Hz, 1H), 2.53 – 2.47 (m, 1H), 1.94 – 1.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ

157.0, 133.2, 131.8, 131.3, 130.0, 129.9, 128.9, 128.2, 128.0, 121.2, 121.2, 120.8, 110.5, 106.2, 72.5, 55.4, 34.4, 28.3; HRMS (ESI): calcd for $C_{18}H_{16}NO_4S$ $[M-H]^-$: 342.0800, found 342.0790; IR: 3457, 2928, 2026, 1640, 1492, 1469, 1384, 1303, 1242, 1174, 1159, 1047, 949, 755, 659, 559; HPLC: (Chiralcel AS-H, Hexane / *i*-PrOH = 80 : 20, UV = 254 nm, flow rate = 0.7 mL / min) t_{R1} = 39.86 min (major) and t_{R2} = 52.46 min (minor); ee = 99%; $[\alpha]^{25}_D$ = +11.0 (*c* 0.2, CH_3OH).



3p

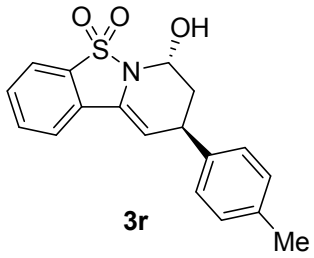
(7*R*,9*R*)-7-Hydroxy-9-(o-tolyl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3p): Pale yellow solid (28.9 mg, 88%). m.p. 72 – 74 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 7.6 Hz, 1H), 7.72 – 7.64 (m, 2H), 7.60 – 7.56 (m, 1H), 7.24 – 7.18 (m, 4H), 5.93 (d, *J* = 1.6 Hz, 1H), 5.82 (d, *J* = 1.2 Hz, 1H), 4.28 (ddd, *J* = 12.0, 5.6, 2.4 Hz, 1H), 3.74 (s, 1H), 2.47 – 2.44 (m, 1H), 2.43 (s, 3H), 1.87 (t, *J* = 12.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.5, 135.7, 133.3, 131.8, 130.6, 130.0, 129.8, 129.1, 127.5, 126.9, 126.7, 121.3, 121.2, 106.0, 72.2, 35.3, 30.9, 19.2; HRMS (ESI): calcd for $C_{18}H_{17}NO_3NaS$ $[M+Na]^+$: 350.0827, found 350.0818; IR: 3471, 2928, 2342, 1662, 1489, 1469, 1384, 1305, 1250, 1217, 1200, 1159, 1175, 1062, 1042, 998, 949, 888, 827, 758, 732, 659, 618, 596, 562, 537, 494; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 75 : 25, UV = 254 nm, flow rate = 0.35 mL / min) t_{R1} = 36.90 min (major) and t_{R2} = 64.02 min (minor); ee = 94%; $[\alpha]^{25}_D$ = +16.3 (*c* 0.2, CH_3OH).



3q

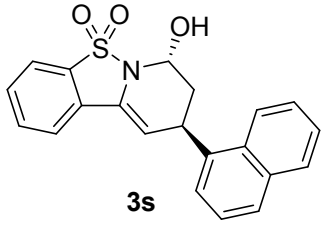
(7*R*,9*R*)-7-Hydroxy-9-(*m*-tolyl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3q): Colorless oil (27.4 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 8.0 Hz, 1H), 7.72 – 7.64 (m, 2H), 7.61 – 7.57 (m, 1H), 7.28 – 7.24 (m, 1H), 7.12 – 7.10 (m, 3H), 5.94 (t, *J* = 2.8 Hz, 1H), 5.85 – 5.82 (m, 1H), 4.02 – 3.97 (m, 1H), 2.49 – 2.43 (m, 1H), 2.37 (s, 3H), 2.00 – 1.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.6, 138.8, 133.5, 132.2, 130.3, 130.1, 129.1, 129.0, 128.7, 128.0, 125.0, 121.5, 106.0, 72.4, 37.0, 35.1, 21.6; HRMS (ESI): calcd for

$C_{18}H_{17}NO_3NaS$ $[M+Na]^+$: 350.0827, found 350.0823; IR: 3457, 2922, 2026, 1640, 1469, 1384, 1306, 1175, 1063, 950, 760; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 75 : 25, UV = 254 nm, flow rate = 0.35 mL / min) t_{R1} = 34.60 min (major) and t_{R2} = 57.23 min (minor); ee = 99%; $[\alpha]^{25}_D$ = +13.7 (*c* 0.2, CH_3OH).



3r

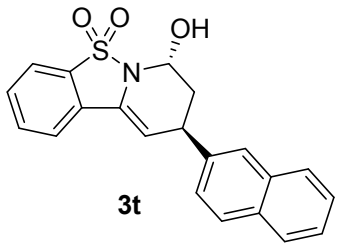
(7*R*,9*R*)-7-Hydroxy-9-(*p*-tolyl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3r): Colorless oil (28.0 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 – 7.81 (m, 1H), 7.70 – 7.63 (m, 2H), 7.59 – 7.56 (m, 1H), 7.18 (s, 4H), 5.92 (dd, *J* = 5.2, 2.4 Hz, 1H), 5.81 (dd, *J* = 2.8, 1.2 Hz, 1H), 3.99 (ddd, *J* = 12.4, 6.0, 2.4 Hz, 1H), 3.67 (t, *J* = 2.4 Hz, 1H), 2.47 – 2.41 (m, 1H), 2.36 (s, 3H), 1.98 – 1.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.6, 136.9, 133.5, 132.1, 130.3, 130.0, 129.7, 129.0, 121.5, 121.4, 106.1, 72.4, 37.0, 34.7, 21.2; HRMS (ESI): calcd for $C_{18}H_{17}NO_3NaS$ $[M+Na]^+$: 350.0827, found 350.0836; IR: 3457, 2924, 1642, 1513, 1470, 1384, 1305, 1243, 1174, 1159, 1062, 950, 814, 759, 639, 616, 559; HPLC: (Chiralcel AS-H, Hexane / *i*-PrOH = 75 : 25, UV = 254 nm, flow rate = 0.35 mL / min) t_{R1} = 38.88 min (major) and t_{R2} = 58.86 min (minor); ee = 97%; $[\alpha]^{25}_D$ = +10.8 (*c* 0.4, CH_3OH).



3s

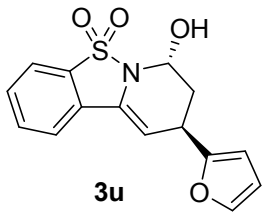
(7*R*,9*R*)-7-Hydroxy-9-(naphthalen-1-yl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3s): White solid (29.1 mg, 80%). m.p. 104 – 106 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, *J* = 8.4 Hz, 1H), 7.92 – 7.90 (m, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.82 – 7.79 (m, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.69 – 7.65 (m, 1H), 7.61 – 7.44 (m, 5H), 6.00 (t, *J* = 2.4 Hz, 2H), 4.86 (s, 1H), 3.74 (s, 1H), 2.69 – 2.63 (m, 1H), 2.08 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.5, 134.3, 133.5, 132.2, 131.5, 130.3, 130.1, 129.5, 129.3, 127.9, 126.7, 126.1, 125.9, 125.2, 123.2, 121.5, 121.5, 106.2, 72.6, 35.9, 29.9; HRMS (ESI): calcd for $C_{21}H_{16}NO_3S$ $[M-H]^-$: 362.0851, found

362.0843; IR: 3061, 2961, 2925, 2854, 1715, 1668, 1470, 1456, 1338, 1305, 1260, 1176, 1158, 1048, 949, 863, 799, 780, 761, 660, 596, 567; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 80 : 20, UV = 254 nm, flow rate = 0.6 mL / min) t_{R1} = 36.72 min (major) and t_{R2} = 57.91 min (minor); ee = 94%; $[\alpha]^{25}_{D}$ = – 47.3 (*c* 0.2, CH_3OH).



3t

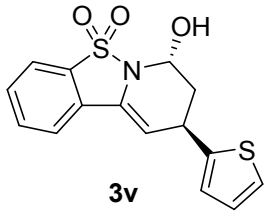
(7*R*,9*R*)-7-Hydroxy-9-(naphthalen-2-yl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3t): Pale yellow solid (31.0 mg, 85%). m.p. 122 – 123 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.09 (d, *J* = 8.0 Hz, 1H), 7.98 (d, *J* = 7.6 Hz, 1H), 7.91 – 7.87 (m, 3H), 7.82 (s, 1H), 7.78 – 7.74 (m, 1H), 7.67 (t, *J* = 8.0 Hz, 1H), 7.49 – 7.44 (m, 3H), 6.86 (d, *J* = 6.4 Hz, 1H), 6.14 (t, *J* = 1.2 Hz, 1H), 5.64 – 5.62 (m, 1H), 4.10 – 4.05 (m, 1H), 2.30 – 2.27 (m, 1H), 1.88 – 1.92 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 142.2, 134.1, 133.9, 132.7, 131.2, 129.8, 129.5, 128.9, 128.2, 128.1, 127.0, 126.8, 126.4, 126.3, 126.0, 122.6, 121.5, 105.3, 71.8, 39.2, 35.0; HRMS (ESI): calcd for HRMS (ESI): calcd for $C_{21}H_{16}NO_3S$ $[M-H]^-$: 362.0851, found 362.0846; IR: 3502, 3086, 2923, 2850, 1667, 1470, 1454, 1306, 1252, 1175, 1160, 1102, 1035, 995, 950, 760, 729, 701, 603, 556; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH =80 : 20, UV = 254 nm, flow rate = 0.7 mL / min) t_{R1} = 32.65 min (major) and t_{R2} = 59.76 min (minor); ee = 96%; $[\alpha]^{25}_{D}$ = +47.6 (*c* 0.1, DMSO).



3u

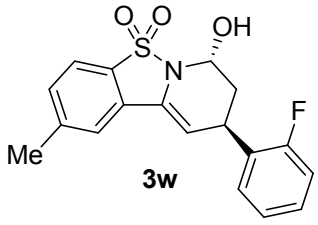
(7*R*,9*R*)-9-(Furan-2-yl)-7-hydroxy-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3u): Colorless oil (21.2 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 – 7.80 (m, 1H), 7.72 – 7.69 (m, 1H), 7.67 – 7.63 (m, 1H), 7.59 – 7.55 (m, 1H), 7.38 (dd, *J* = 1.6, 0.8 Hz, 1H), 6.35 (dd, *J* = 2.8, 1.6 Hz, 1H), 6.15 (dt, *J* = 3.2, 0.8 Hz, 1H), 5.95 (d, *J* = 2.0 Hz, 1H), 5.84 (dd, *J* = 2.4, 1.2 Hz, 1H), 4.15 (ddd, *J* = 12.0, 5.6, 2.4 Hz, 1H), 3.60 (t, *J* = 2.0 Hz, 1H), 2.54 – 2.48 (m, 1H), 2.11 – 2.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.7, 142.0, 133.5, 132.2, 130.4, 129.8,

129.1, 121.5, 121.4, 110.5, 105.3, 102.6, 72.1, 33.2, 28.8; HRMS (ESI): calcd for $C_{15}H_{12}NO_4S$ $[M-H]^-$: 302.0487, found 302.0483; IR: 3455, 2924, 2853, 2026, 1638, 14699, 1384, 1305, 1175, 1063, 741, 617; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 80 : 20, UV = 254 nm, flow rate = 0.7 mL / min) t_{R1} = 33.47 min (major) and t_{R2} = 47.18 min (minor); ee = 94%; $[\alpha]^{25}_D$ = +30.9 (*c* 0.2, CH_3OH).



3v

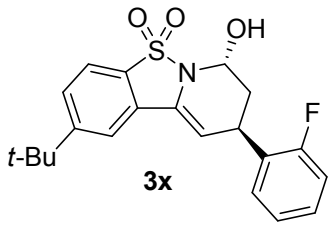
(7*R*,9*R*)-7-Hydroxy-9-(thiophen-2-yl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3v): White solid (25.5 mg, 80%). m.p. 186 – 187 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 7.6 Hz, 1H), 7.72 – 7.64 (m, 2H), 7.60 – 7.56 (m, 1H), 7.22 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.00 – 6.97 (m, 2H), 5.93 (t, *J* = 2.8 Hz, 1H), 5.84 (dd, *J* = 2.4, 1.2 Hz, 1H), 4.37 (ddd, *J* = 12.0, 5.6, 2.4 Hz, 1H), 3.67 (s, 1H), 2.59 – 2.53 (m, 1H), 2.09 – 2.02 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.8, 133.5, 132.2, 130.5, 129.8, 128.8, 127.2, 124.5, 124.2, 121.6, 121.5, 105.2, 72.2, 37.3, 30.5; HRMS (ESI): calcd for $C_{15}H_{12}NO_3S_2$ $[M-H]^-$: 318.0259, found 318.0253; IR:2919, 2850, 1731, 1715, 1680, 1661, 1650, 1632, 1470, 1456, 1306, 1259, 1175, 1160, 1101, 1062, 949, 760, 703; HPLC (Chiralcel IC-3, Hexane / *i*-PrOH = 80 : 20, UV = 254 nm, flow rate = 0.9 mL / min) t_{R1} = 41.91 min (major) and t_{R2} = 50.68 min (minor); ee = 89%; $[\alpha]^{25}_D$ = +40.5 (*c* 0.3, CH_3OH).



3w

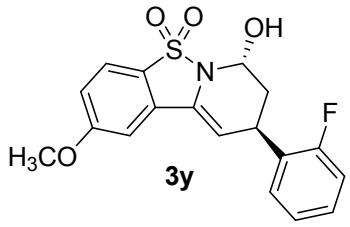
(7*R*,9R)-9-(2-Fluorophenyl)-7-hydroxy-2-methyl-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (3w): White solid (28.3 mg, 82%). m.p. 160 – 162 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.0 Hz, 1H), 7.52 (s, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 732 – 7.27 (m, 2H), 7.18 – 7.08 (m, 2H), 5.95 (dd, *J* = 5.2, 2.8 Hz, 1H), 5.78 (d, *J* = 1.2 Hz, 1H), 4.40 – 4.35 (m, 1H), 3.77 (t, *J* = 2.4 Hz, 1H), 2.53 – 2.47 (m, 4H), 2.03 – 1.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3, 159.8, 144.7, 131.7, 131.5, 130.4, 130.3, 129.9, 129.6, 129.4, 129.4, 128.9, 128.8,

124.8, 124.8, 121.6, 121.3, 116.1, 115.9, 104.3, 72.4, 35.0, 28.7, 22.2; HRMS (ESI): calcd for $C_{18}H_{15}NO_3SF$ $[M-H]^-$: 344.0757, found 344.0756; IR: 2922, 2850, 1716, 1489, 1456, 1300, 1262, 1224, 1169, 1145, 1044, 801, 757, 704, 677, 652, 626, 564, 545, 518; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 65 : 35, UV = 254 nm, flow rate = 0.35 mL / min) t_{R1} = 36.10 min (major) and t_{R2} = 52.81 min (minor); ee = 99.5%; $[\alpha]^{25}_D$ = +4.3 (*c* 0.1, CH_3OH).



3x

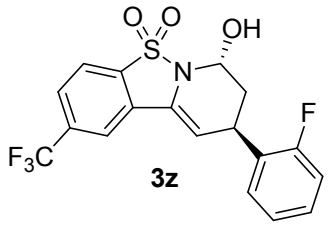
(7R,9R)-2-(tert-butyl)-9-(2-fluorophenyl)-7-hydroxy-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridine 5,5-dioxide (3x): White solid (30.9 mg, 80%). m.p. 235 – 236 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.73 (m, 1H), 7.66 – 7.60 (m, 2H), 7.32 – 7.24 (m, 2H), 7.16 – 7.06 (m, 2H), 5.92 (s, 1H), 5.79 (s, 1H), 4.39 – 4.35 (m, 1H), 3.66 (s, 1H), 2.50 – 2.45 (m, 1H), 1.99 (t, *J* = 12.8 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 130.0, 129.8, 129.4, 129.4, 128.9, 128.8, 128.2, 124.7, 121.1, 117.8, 116.0, 115.8, 104.1, 72.4, 35.7, 34.9, 31.3, 28.6.; HRMS (ESI): calcd for $C_{21}H_{23}NO_3SF$ $[M+H]^+$: 388.1383, found 388.1389; IR: 3501, 2964, 2870, 1669, 1602, 1585, 1560, 1491, 1455, 1431, 1397, 1305, 1265, 1226, 1181, 1153, 1046, 1033, 1005, 964, 824, 759, 628, 661, 595; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 93 : 7, UV = 254 nm, flow rate = 0.55 mL / min), t_{R1} = 38.91 min (major) and t_{R2} = 44.58 min (minor); ee = 95%; $[\alpha]^{25}_D$ = – 4.3 (*c* 0.4, CH_3OH).



3y

(7R,9R)-9-(2-fluorophenyl)-7-hydroxy-2-methoxy-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridine 5,5-dioxide (3y): White solid (30.6 mg, 85%). m.p. 184 – 185 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 10.8, 6.4 Hz, 1H), 7.29 – 7.24 (m, 2H), 7.15 – 7.05 (m, 4H), 5.90 (s, 1H), 5.73 (s, 1H), 4.36 (ddd, *J* =12.0, 5.6, 2.0 Hz, 1H), 3.89 (s, 3H), 2.50 – 2.44 (m, 1H), 1.98 (t, *J* = 13.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 132.4, 129.5, 129.4, 129.3, 128.9, 128.8, 124.7, 124.7, 123.0, 118.0, 116.0, 115.8, 104.7, 104.5, 72.4, 56.1, 34.8, 28.7; HRMS (ESI): calcd

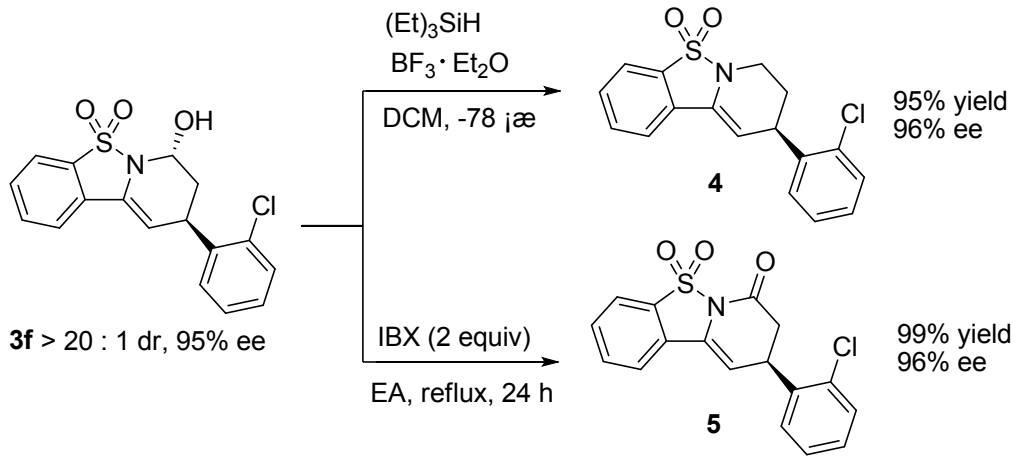
for $C_{18}H_{17}NO_4SF$ $[M+H]^+$: 362.0862, found 362.0859; IR: 2925, 2855, 1599, 1489, 1477, 1454, 1296, 1260, 1225, 1198, 1170, 1134, 1048, 811, 756; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 70 : 30, UV = 254 nm, flow rate = 0.45 mL / min), t_{R1} = 39.46 min (major) and t_{R2} = 56.07 min (minor); ee = 97%; $[\alpha]^{25}_D$ = – 2.0 (*c* 0.4, CH_3OH).



3z

(7R,9R)-9-(2-fluorophenyl)-7-hydroxy-2-(trifluoromethyl)-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridine 5,5-dioxide (3z): White solid (29.9 mg, 75%). m.p. 172 – 173 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.95 (m, 2H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.29 – 7.25 (m, 2H), 7.16 – 7.07 (m, 2H), 5.95 (s, 1H), 5.91 (s, 1H), 4.38 (ddd, *J* = 12.0, 5.6, 2.4 Hz, 1H), 3.64 (s, 1H), 2.51 – 2.47 (m, 1H), 2.01 (t, *J* = 12.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 134.8, 130.7, 129.6, 129.5, 129.3, 129.3, 129.1, 129.0, 128.5, 127.1, 124.8, 122.5, 118.9, 116.1, 115.9, 106.7, 72.5, 34.7, 28.8; HRMS (ESI): calcd for $C_{18}H_{12}NO_2SF_4$ $[M-OH]^+$: 382.0525, found 382.0524; IR: 3501, 2961, 2926, 2855, 1667, 1585, 1491, 1444, 1261, 1228, 1171, 1135, 1047, 1007, 960, 899, 809, 760, 714, 659, 606, 594; HPLC (Chiralcel AS-H, Hexane / *i*-PrOH = 93 : 7, UV = 254 nm, flow rate = 0.5 mL / min), t_{R1} =51.17 min (major) and t_{R2} = 74.11 min (minor); ee = 98%; $[\alpha]^{25}_D$ = 22.8 (*c* 0.3, CH_3OH).

5. Procedure for the Synthesis of 4 and 5

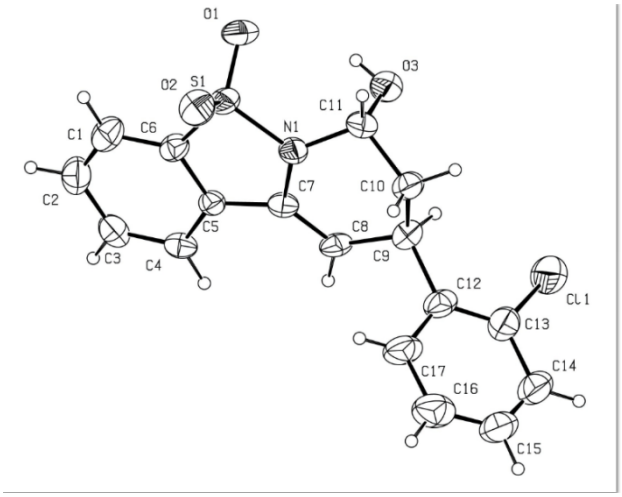


(*R*)-9-(2-Chlorophenyl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridine 5,5-dioxide (**4**): To a solution of **3f** (34.7 mg, 0.1 mmol) was added triethylsilane (0.2 mmol) in anhydrous DCM (2 mL) and $BF_3.Et_2O$ (28 μL, 0.22 mol) at –78 °C and the reaction mixture was stirred under the same temperature for 2 h. The reaction was quenched with aqueous $NaHCO_3$ and extracted with DCM. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel to afford the desired product **4** as a colorless oil (31.5 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J = 7.6 Hz, 1H), 7.72 (d, J = 7.6 Hz, 1H), 7.66 (t, J = 7.2 Hz, 1H), 7.59 (t, J = 7.6 Hz, 1H), 7.45 – 7.39 (m, 1H), 7.29 – 7.19 (m, 3H), 5.67 (d, J = 4.0 Hz, 1H), 4.27 (dd, J = 10.4, 6.0 Hz, 1H), 3.72 – 3.58 (m, 2H), 2.48 – 2.40 (m, 1H), 2.09 – 2.01 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.1, 133.7, 133.2, 132.8, 132.7, 130.3, 130.0, 129.5, 128.5, 127.3, 121.5, 121.2, 102.3, 36.4, 34.8, 28.1; HRMS (ESI): calcd for $C_{17}H_{15}NO_2SCl$ $[M+H]^+$ 332.0512, found 332.0512; IR: 3064, 2927, 2874, 1716, 1732, 1667, 1598, 1569, 1473, 1436, 1377, 1310, 1266, 1254, 1176, 1160, 1063, 1054, 984, 965, 844, 819, 756, 701, 679, 626, 596, 568, 526; HPLC (Chiralcel OD-H, Hexane / *i*-PrOH = 80 : 20, UV = 254 nm, flow rate = 0.8 mL / min) t_{R1} = 18.91 min (minor) and t_{R2} = 24.76 min (major); ee = 96%; $[\alpha]^{25}_D$ = +1.8 (*c* 0.3, CH_3OH).

(*R*)-9-(2-Chlorophenyl)-8,9-dihydro-7*H*-benzo[4,5]isothiazolo[2,3-*a*]pyridin-7-one 5,5-dioxide (**5**): A suspension of **3f** (34.7 mg, 0.1 mmol) and IBX (84.0mg, 0.3mmol) in EtOAc (5 mL) was heated under reflux conditions at 100 °C. After the reaction mixture was stirred for 12 h, the organic layer was filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford the desired product **5** as a white solid (34.3 mg, 99%). m.p. 212 – 213 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 – 7.87 (m, 1H), 7.77 – 7.72 (m, 2H), 7.68 – 7.64 (m, 1H), 7.44 – 7.41 (m, 1H), 7.29 – 7.25 (m, 3H), 6.09 (d, J = 4.4 Hz, 1H), 4.63 – 4.58 (m, 1H), 3.16 (dd, J = 16.4, 7.2 Hz, 1H), 2.88 (dd, J = 16.4, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 138.4, 134.4, 133.4, 132.6, 131.4, 130.7, 130.4, 129.3, 128.2, 128.1, 126.7, 121.9, 121.9, 104.8, 38.1, 35.9; HRMS (ESI): calcd for $C_{17}H_{11}NO_3SCl$ $[M-H]^-$ 344.0148, found 344.0149; IR: 2921, 2850, 1716, 1471, 1346, 1318, 1278, 1182, 1163, 1134, 1051, 1029, 760, 734, 559, 505; HPLC (Chiralcel OD-H, Hexane / *i*-PrOH = 60 : 40, UV = 254 nm, flow rate = 1.0 mL / min) t_{R1} = 18.24 min (minor) and t_{R2} = 29.71 min (major); ee = 96%; $[\alpha]^{25}_D$ = +58.2 (*c* 0.2, DMSO).

6. X-ray Data of Compound 3f

Structure of Compound 3f



Data of crystal 3f

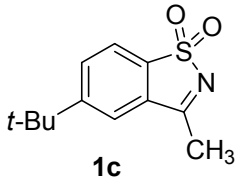
Table 1. Crystal data and structure refinement of 3f

Identification code	**3f**
Empirical formula	$C_{17}H_{14}ClNO_3S$
Formula weight	347.80
Temperature	293 K
Wavelength	0.71073 A
Crystal system, space group	monoclinic , P 1 21 1
Unit cell dimensions	a = 7.7401(4) A alpha = 90 deg. b = 14.0157(10) A beta = 91.699 (5) deg. c = 14.8926(10) gamma = 90 deg.
Volume	1614.88 (18) A^3
Z, Calculated density	4, 1.431 mg / m^3
F(000)	720.0
wR2 Reflections	0.1783 (5063)
F(000')	721.38
H,k,lmax	9, 16, 17
Nref	5063
Tmin,Tmax	0.894, 1.000

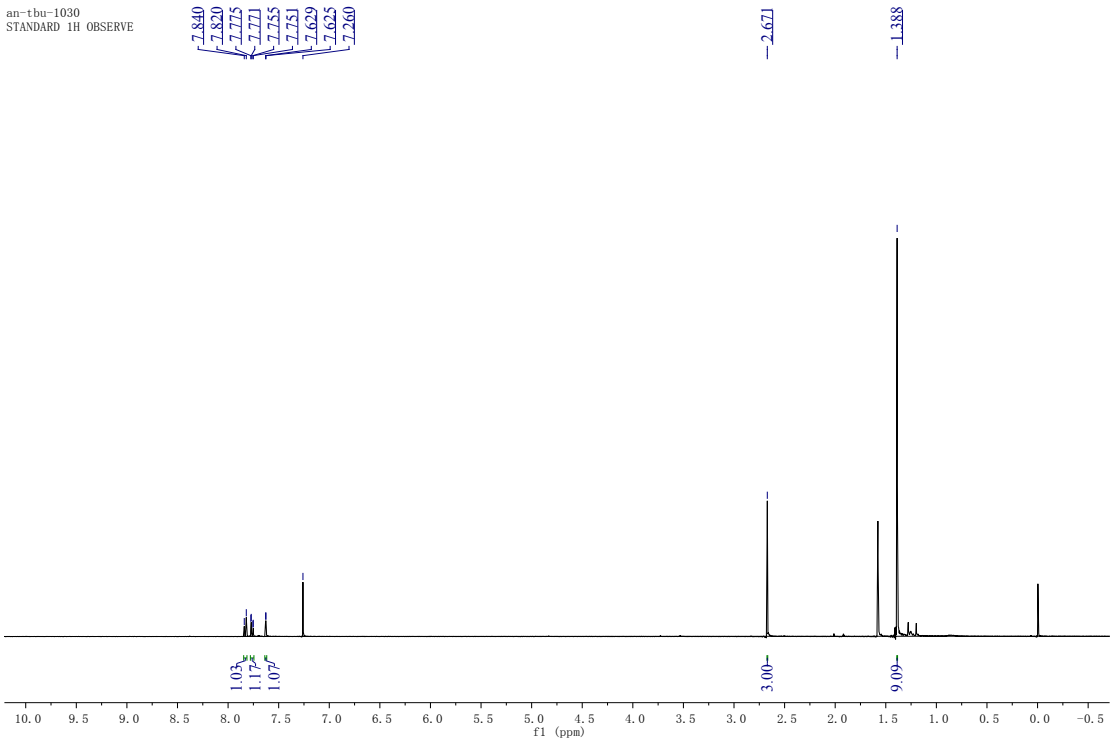
Data completeness	1.64 / 0.85

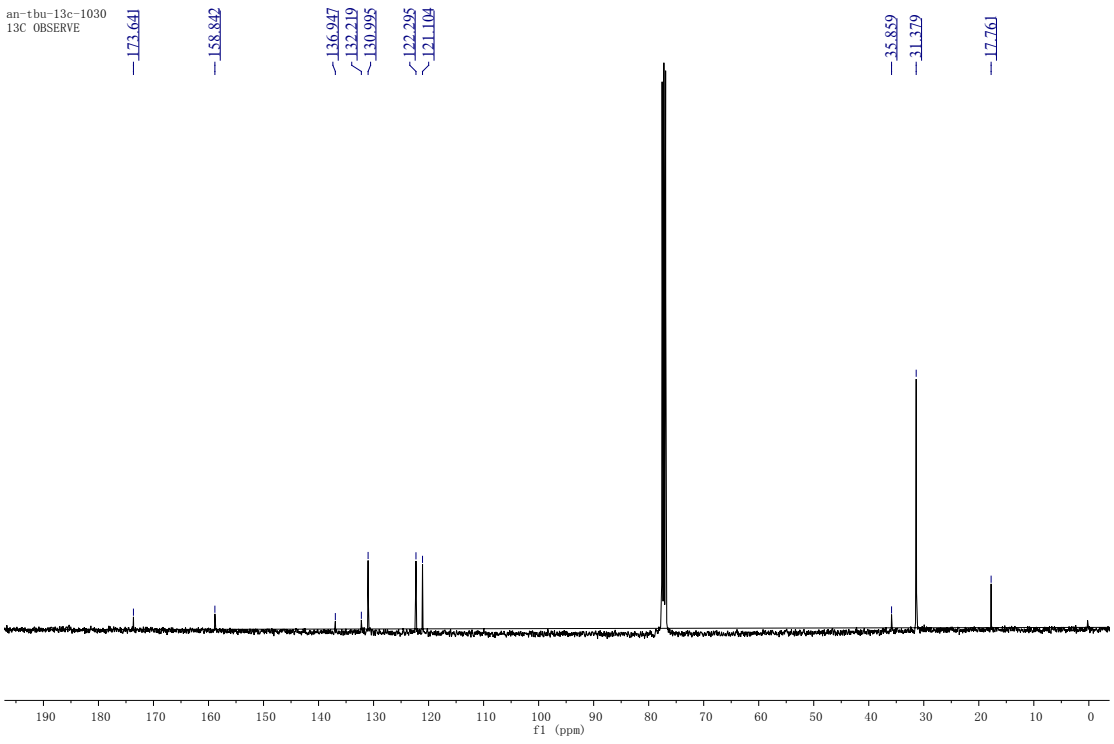
Note: These data (CCDC 1015580) can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac. uk/data_request/cif.

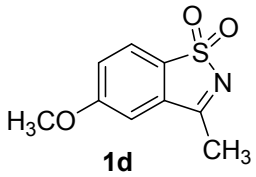
7. NMR Spectra



1c



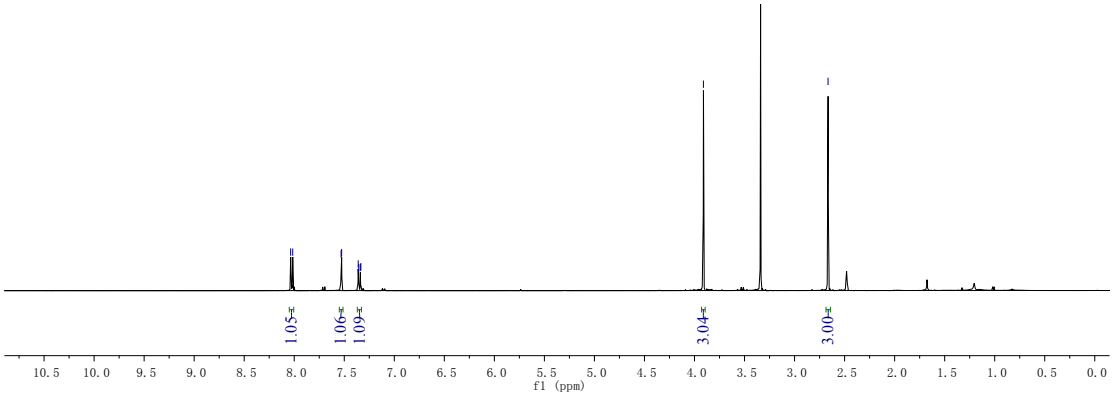




1d

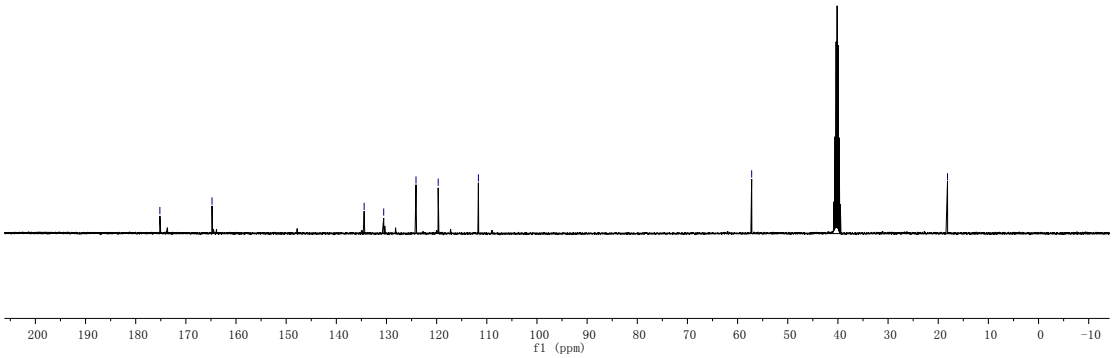
STANDARD 1H OBSERVE

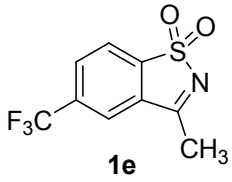
8.026
8.015
7.532
7.526
7.361
7.355
7.340
7.334
3.911
2.665



13C OBSERVE

175.18
164.78
134.45
130.56
124.12
119.69
111.68
57.19
18.15

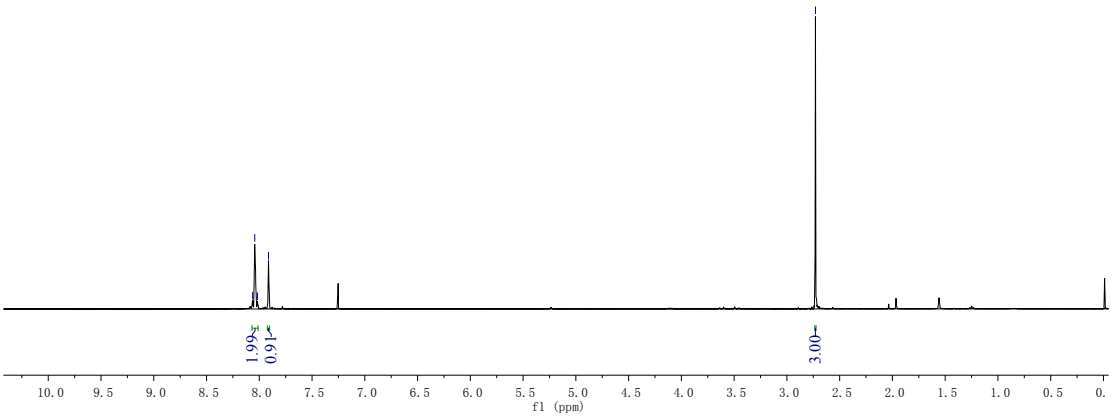




1e

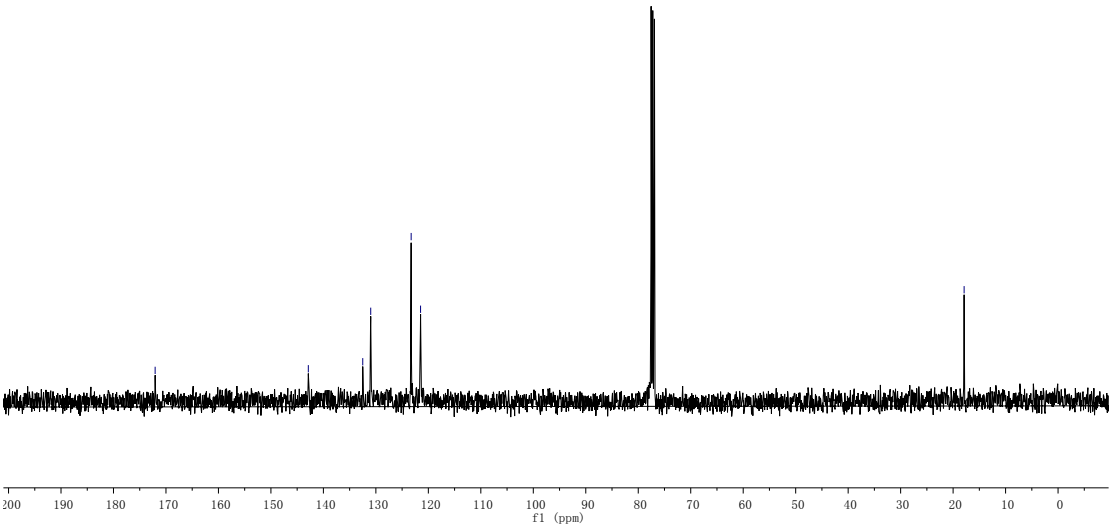
an-cf3-diwu-1027
STANDARD 1H OBSERVE

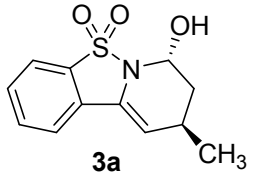
8.063
8.043
8.017
7.913
2.729



an-cf3-13c
13C OBSERVE

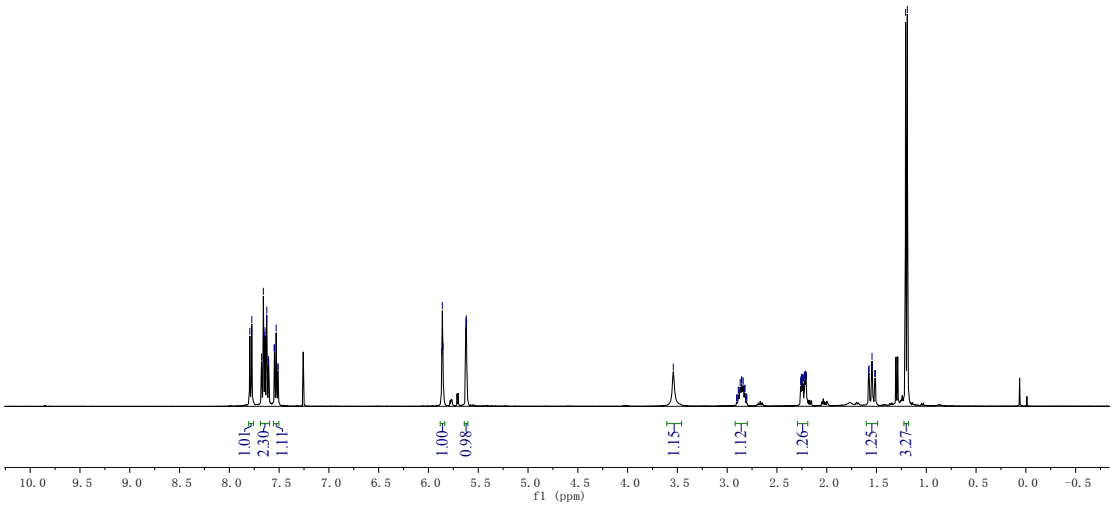
172.06
142.87
132.50
130.98
123.28
121.48
17.90



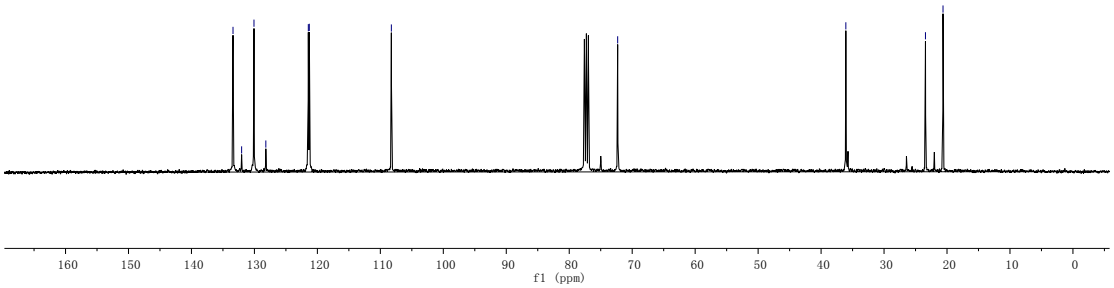

O
O
OH
S
N
CH3

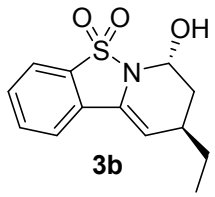
3a


an-v-73-peak1-badouqua
STANDARD 1H OBSERVE
7.778
7.775
7.677
7.658
7.644
7.642
7.626
7.624
7.607
7.604
7.550
7.547
7.530
7.513
7.510
5.867
5.860
5.854
5.626
5.624
5.620
5.618
3.541
2.869
2.857
2.851
2.839
2.826
2.220
2.217
2.214
2.211
1.581
1.574
1.551
1.545
1.541
1.517
1.511
1.208
1.190


1.01
2.30
1.11
1.00
0.98
1.15
1.12
1.26
1.25
3.27
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)


an-v-73-pak1-13C
13C OBSERVE
133.401
132.033
130.070
128.189
121.438
121.283
108.251
72.308
36.068
23.422
20.635

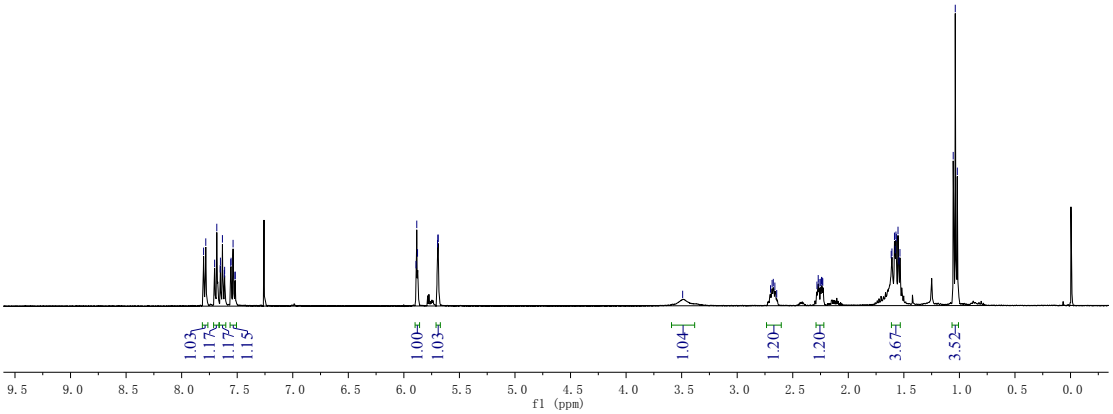

160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



3b

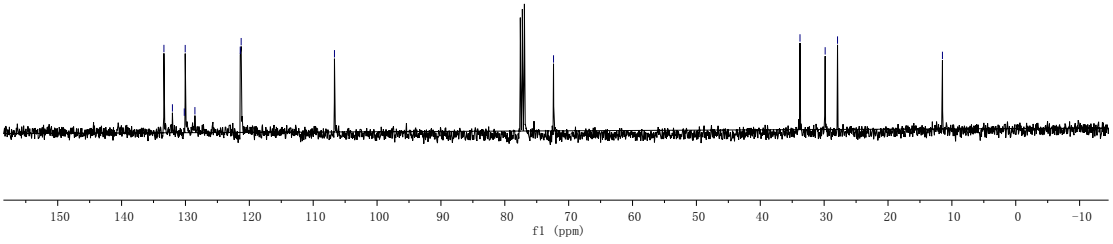
an-91-3b-h-02
STANDARD 1H OBSERVE

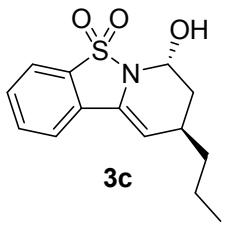
7.803 7.783 7.703 7.684 7.653 7.651 7.633 7.616 7.613 7.558 7.555 7.537 7.520 7.518 5.891 5.884 5.877 5.697 5.694 5.691 3.491 2.700 2.686 2.675 2.661 2.644 2.271 2.241 2.234 1.585 1.571 1.553 1.535 1.037 1.019



an-91-3b-13c
13C OBSERVE

133.37 132.04 130.19 130.04 128.52 121.42 121.28 106.67 72.37 33.78 29.84 27.90 11.48

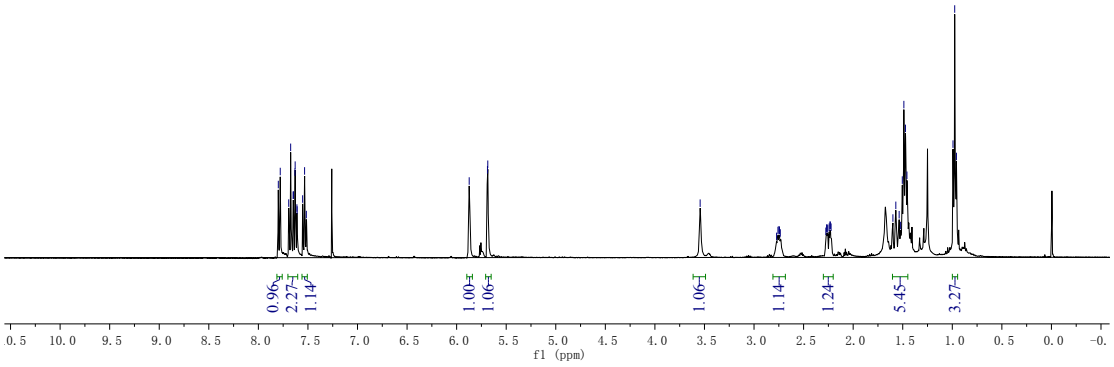




3c

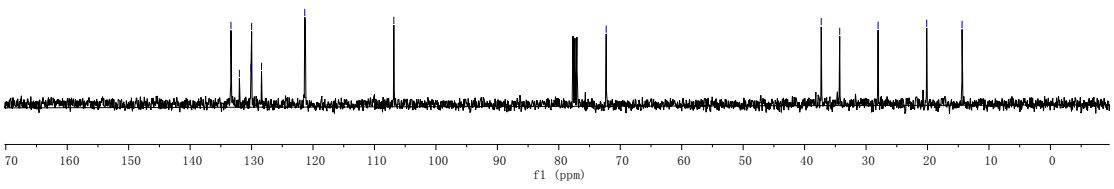
an-qingyequan-h
STANDARD 1H OBSERVE

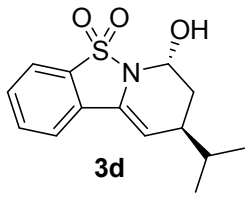
7.799 7.779 7.694 7.674 7.649 7.647 7.631 7.629 7.611 7.609 7.554 7.534 7.516 5.873 5.689 5.686 3.544 2.759 2.749 2.743 2.735 2.242 2.234 2.230 1.489 1.472 1.458 1.455 0.976 0.958



an-185-3-13c
13C OBSERVE

133.35 131.98 130.11 129.99 128.38 121.34 121.25 106.85 72.29 37.29 34.29 28.05 20.13 14.38

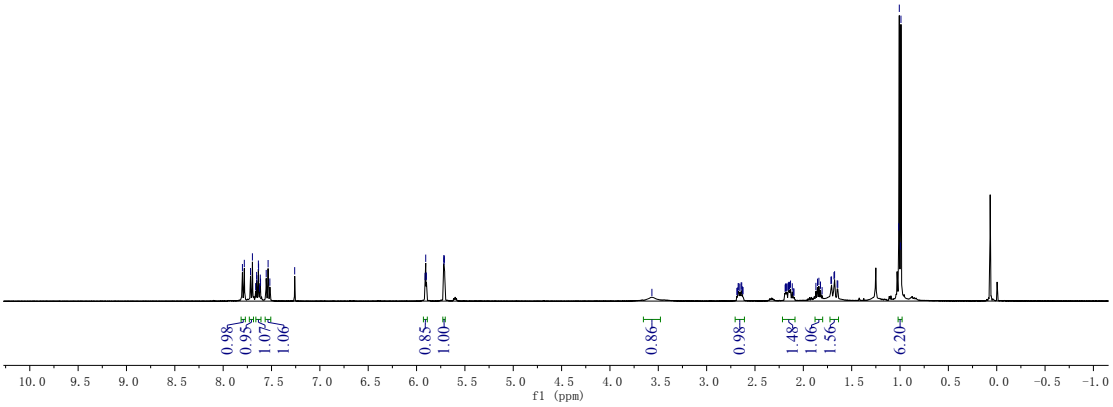




3d

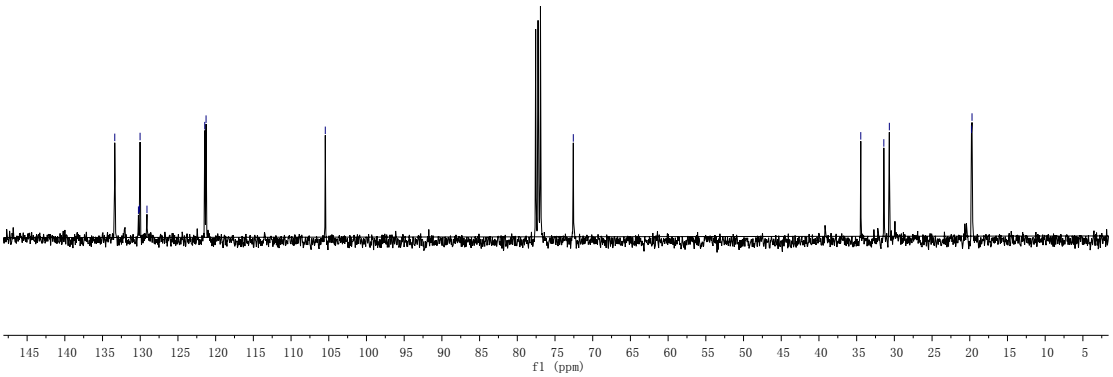
an-143-3-yibingji
STANDARD 1H OBSERVE

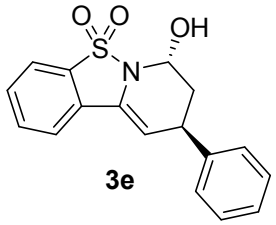
7.801, 7.781, 7.717, 7.697, 7.664, 7.654, 7.652, 7.636, 7.634, 7.623, 7.616, 7.613, 7.555, 7.535, 7.517, 7.260, 5.912, 5.905, 5.898, 5.719, 5.716, 5.712, 3.566, 2.674, 2.668, 2.656, 2.643, 2.637, 2.629, 1.853, 1.839, 1.715, 1.708, 1.683, 1.677, 1.613, 1.007, 0.997, 0.990



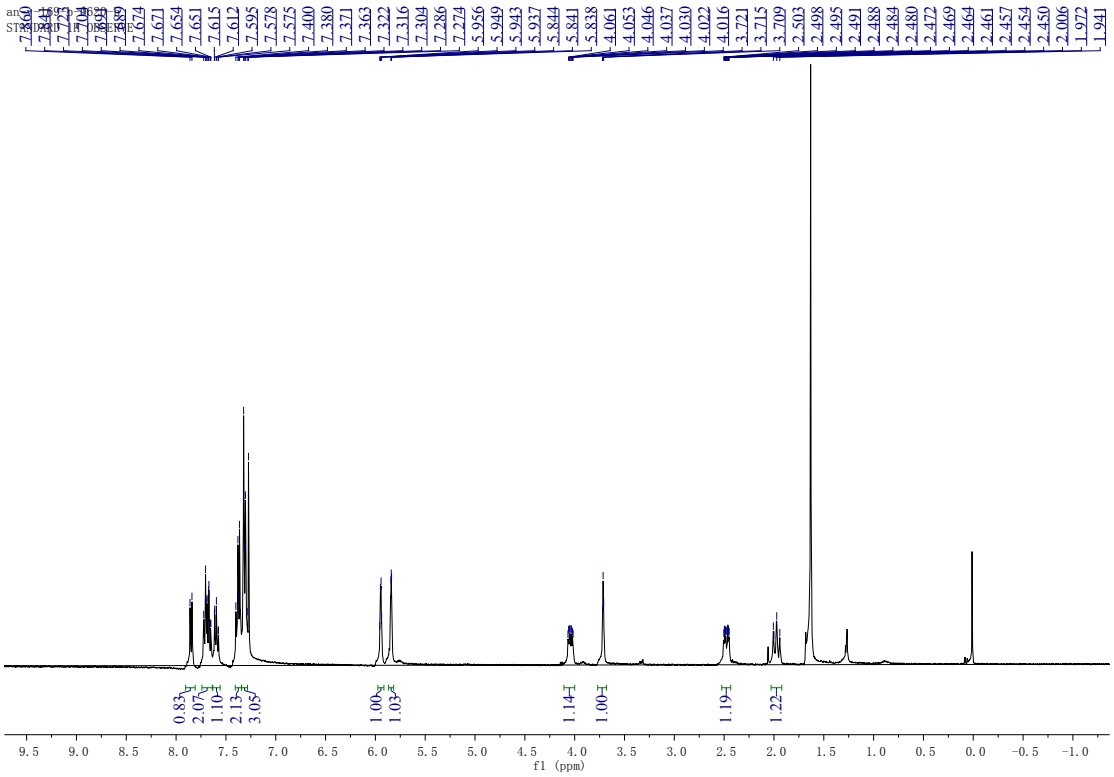
an-13c
13C OBSERVE

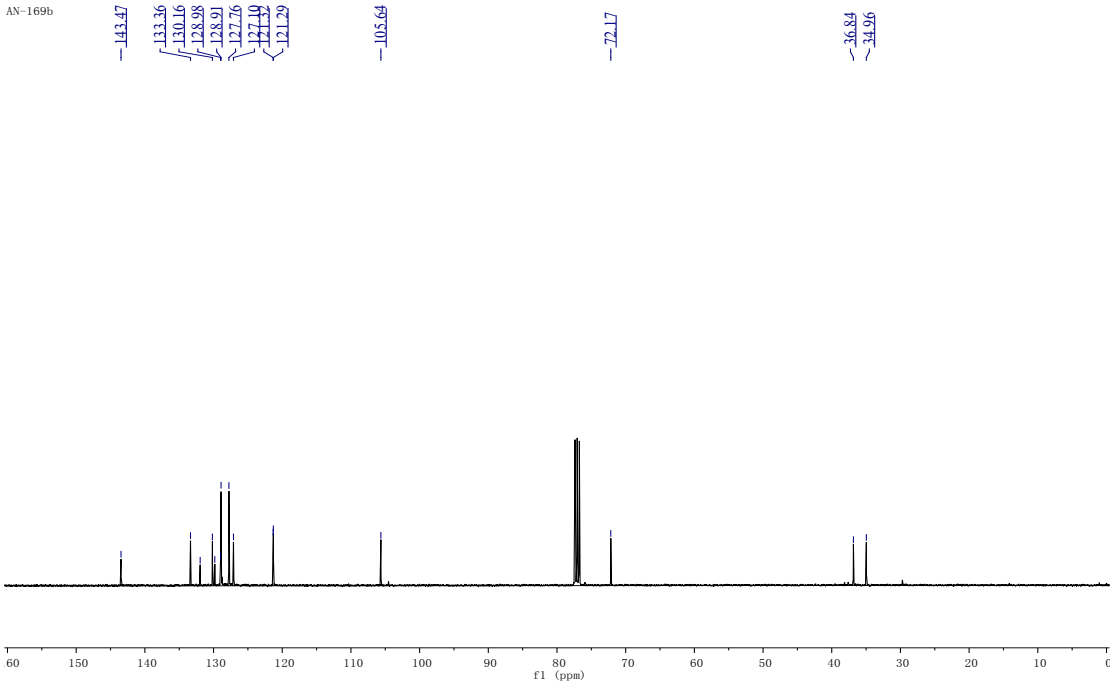
133.377, 130.239, 130.096, 130.021, 129.107, 121.446, 121.271, 105.461, 72.574, 34.454, 31.397, 30.665, 19.779, 19.702

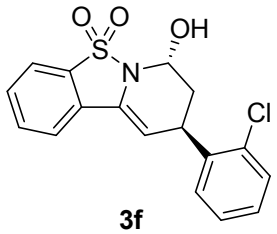



O
O
S
N
OH

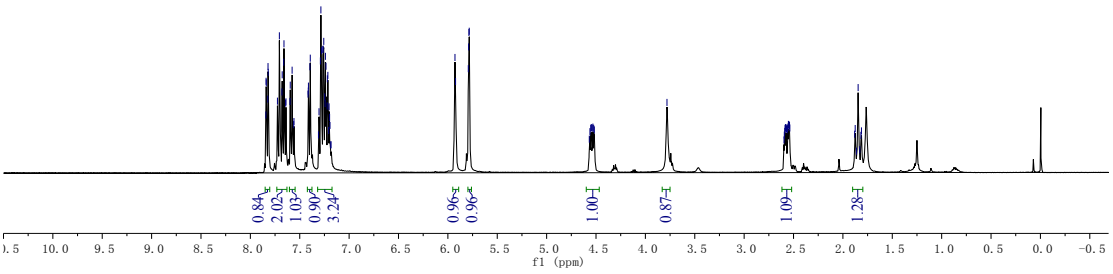
3e


0.83
2.07
1.10
2.13
3.05
1.00
1.03
1.14
1.00
1.19
1.22
f1 (ppm)

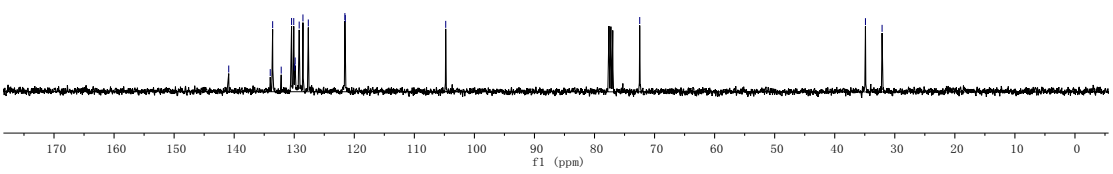

AN-169b
143.47
133.36
130.16
128.98
128.91
127.76
127.10
121.29
105.64
72.17
36.84
34.96
f1 (ppm)

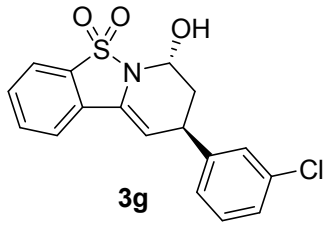


3f

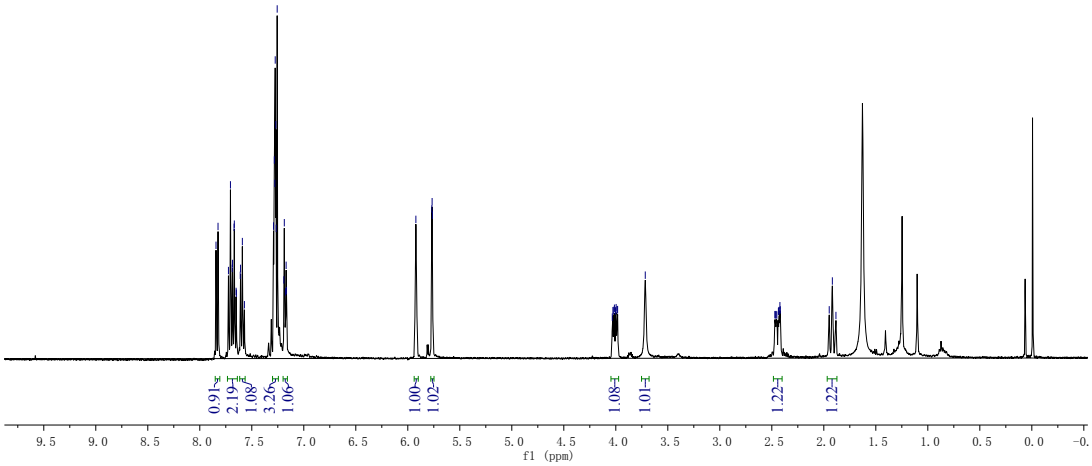


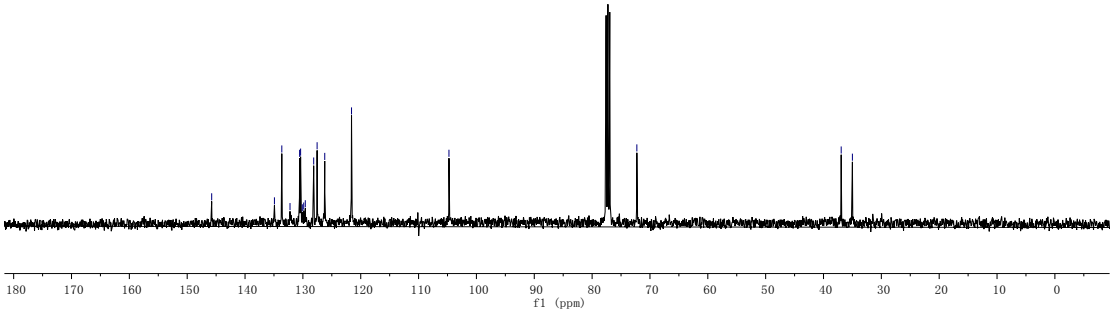
an-o-cl-13c-0623
13C OBSERVE

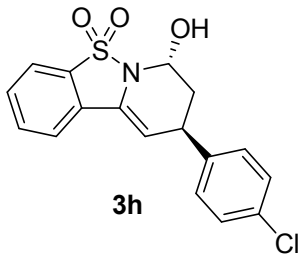



O
O
OH
S
N
Cl

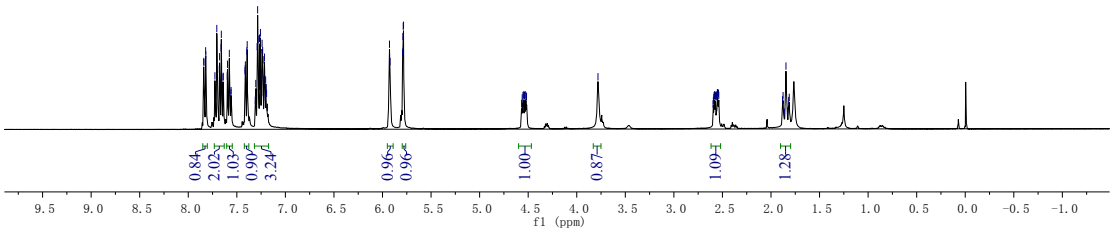
3g

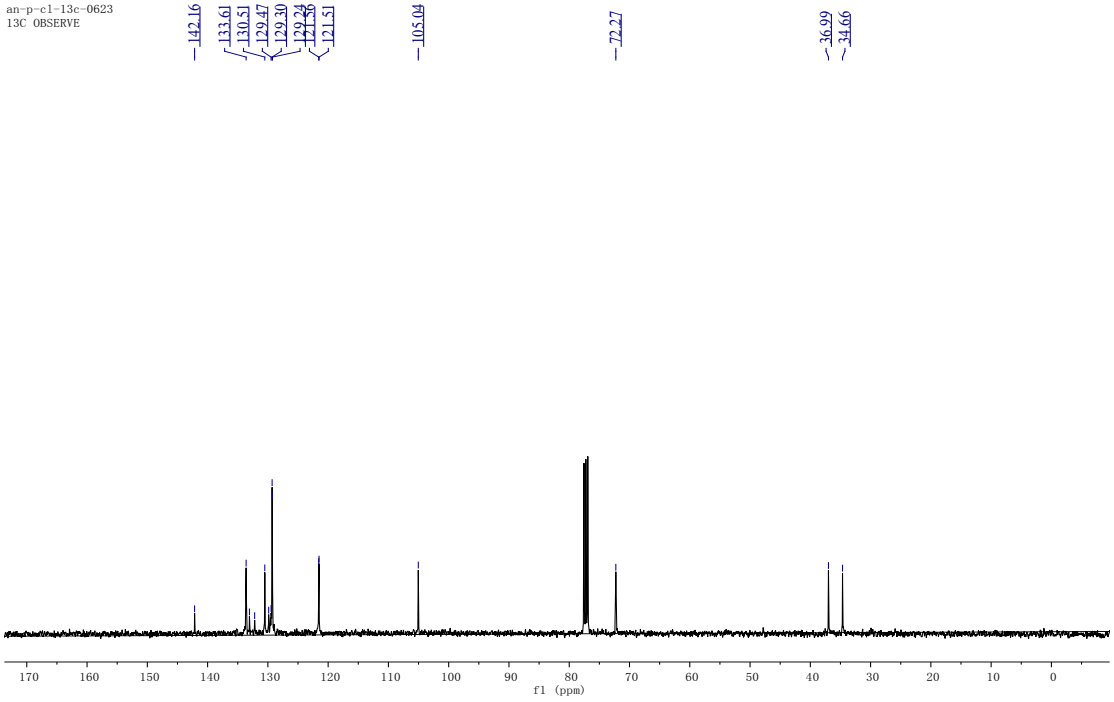

0.91
2.19
1.08
3.26
1.06
1.00
1.02
1.08
1.01
1.22
1.22
f1 (ppm)

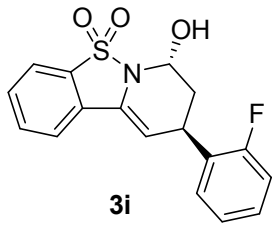

f1 (ppm)


O
O
OH
S
N
Cl

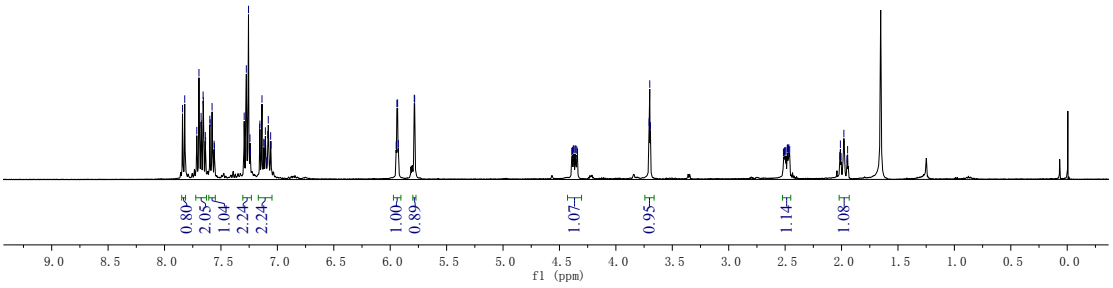
3h

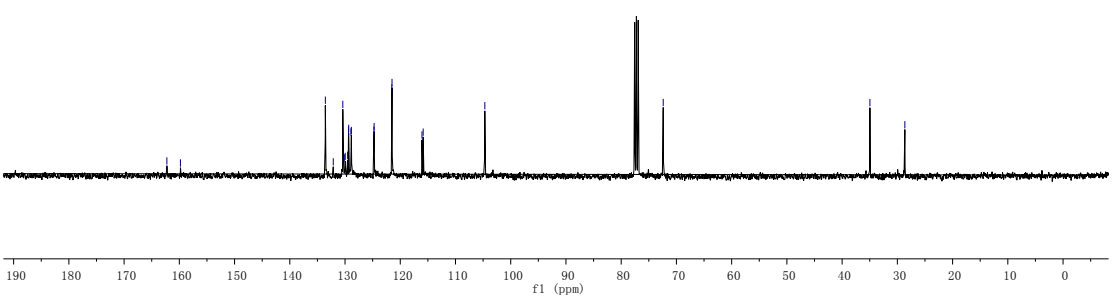

0.84
2.02
1.03
0.90
3.24
0.96
0.96
1.00
0.87
1.09
1.28
f1 (ppm)

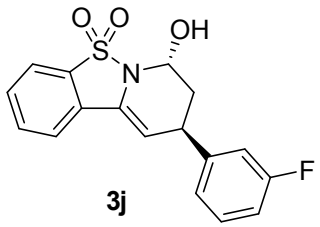

an-p-c1-13c-0623
13C OBSERVE
142.16
133.61
130.51
129.47
129.30
105.04
72.27
36.99
34.66
f1 (ppm)


O
O
S
N
OH
F

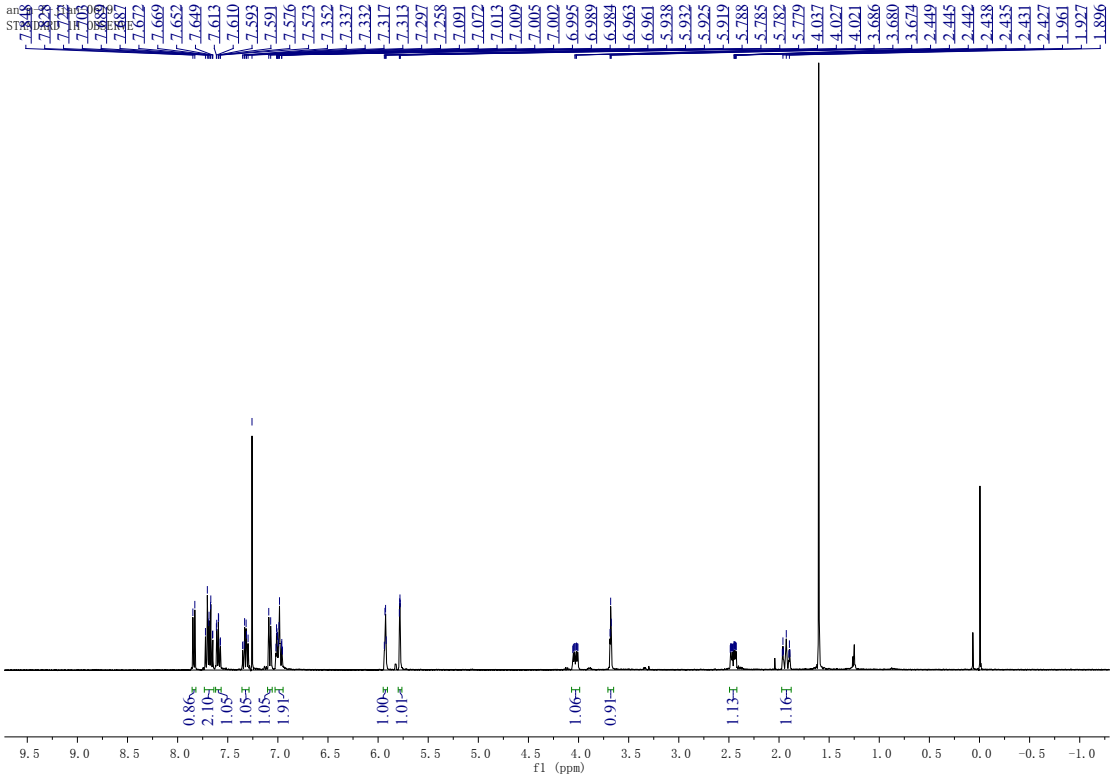
3i

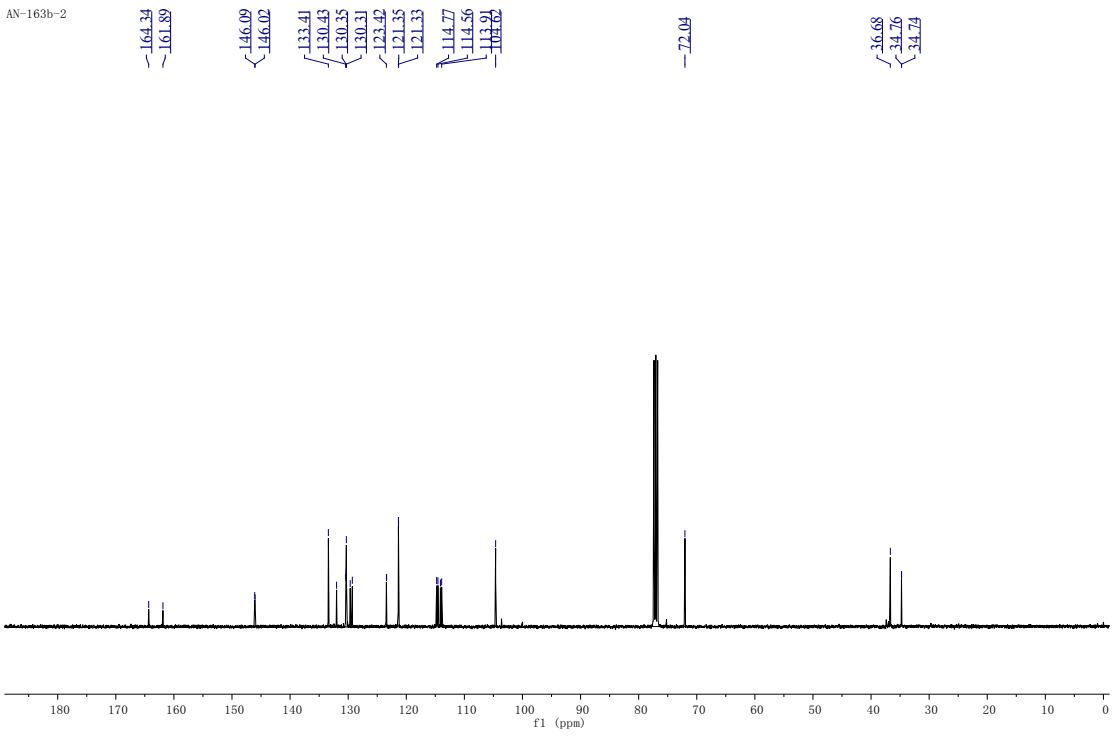

0.80
2.05
1.04
2.24
2.24
1.00
0.89
1.07
0.95
1.14
1.08
f1 (ppm)

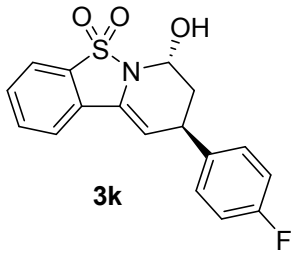

f1 (ppm)



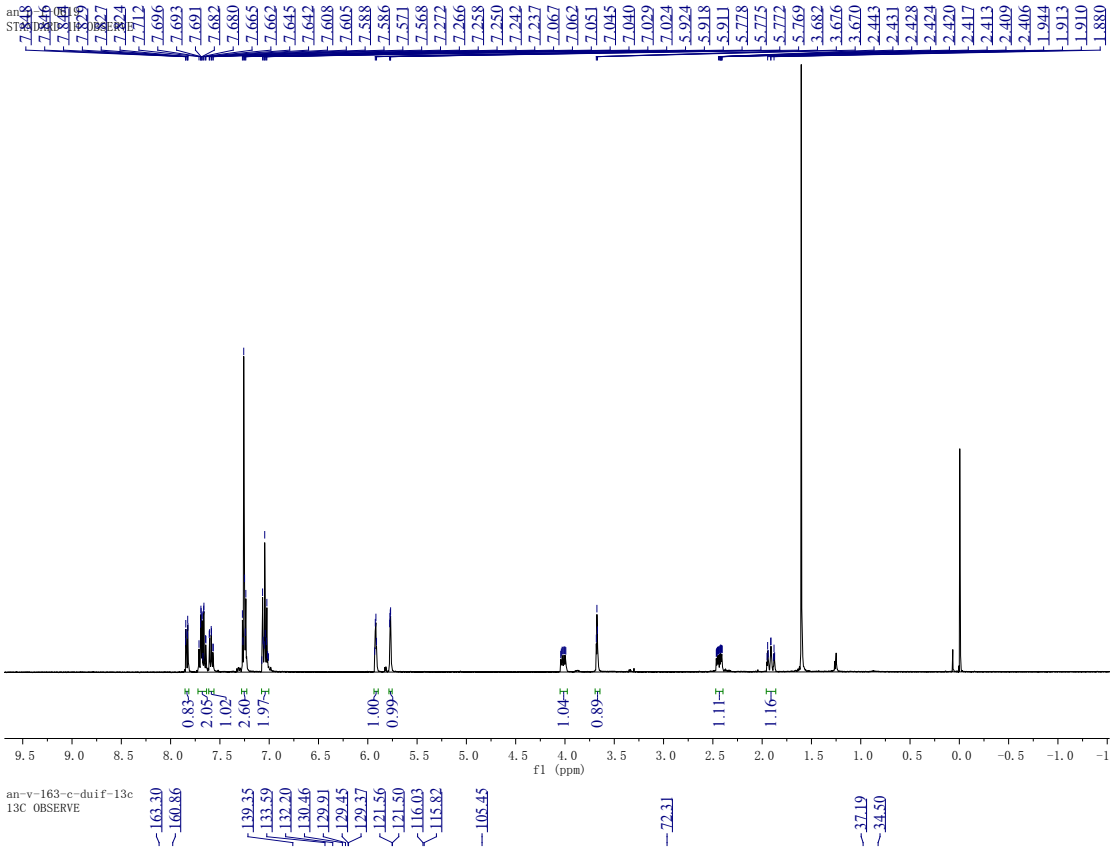
3j

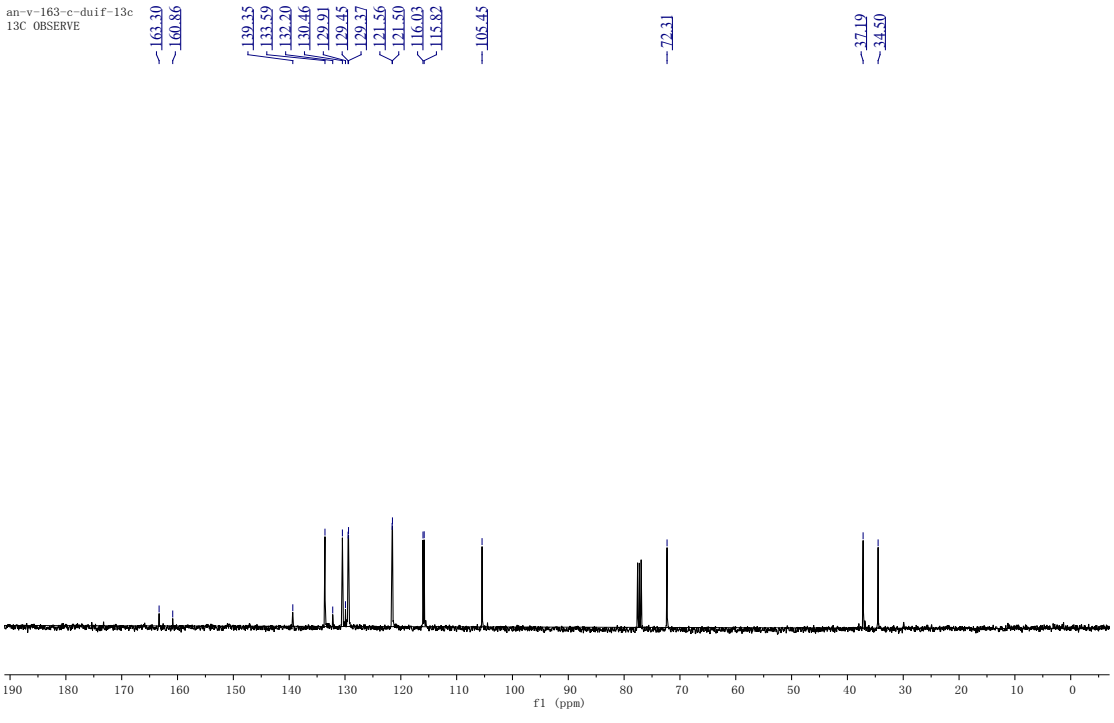


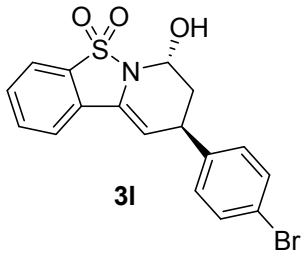



O
O
S
N
OH
F

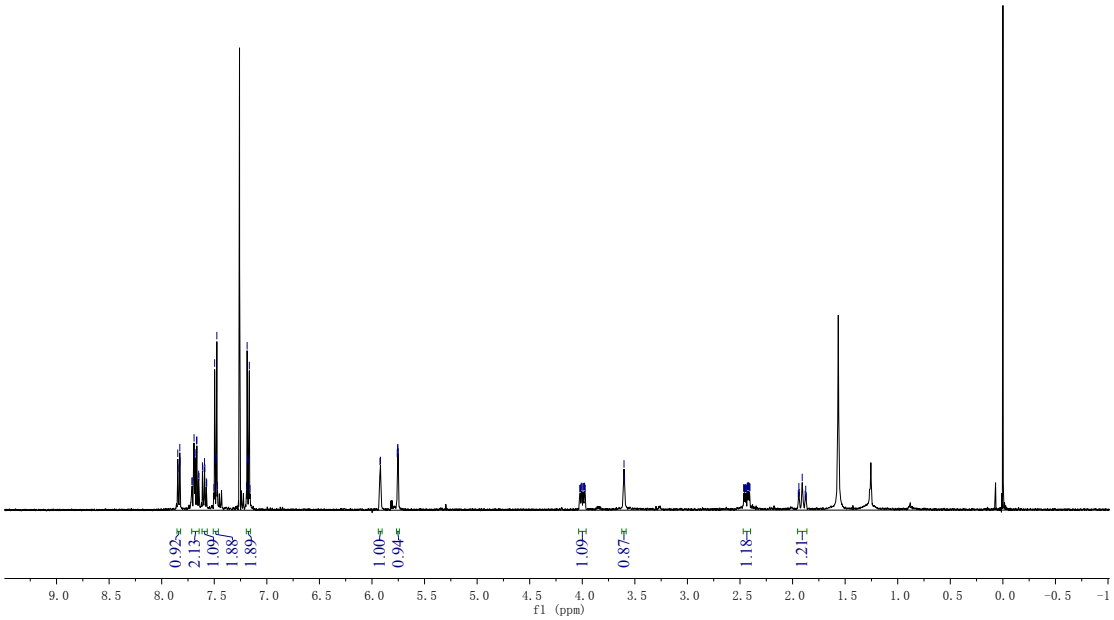
3k


0.83
2.05
1.02
2.60
1.97
1.00
0.99
1.04
0.89
1.11
1.16
f1 (ppm)

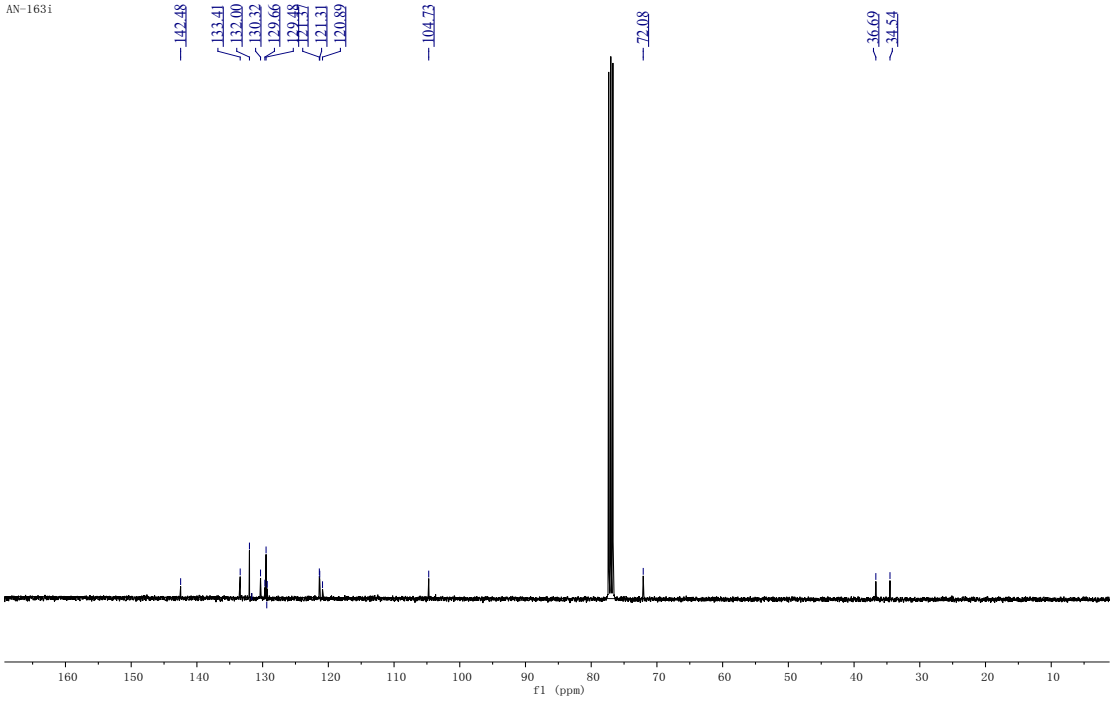

an-v-163-c-duif-13c
13C OBSERVE
163.30
160.86
139.35
133.59
132.20
130.46
129.91
129.45
129.37
121.56
121.50
116.03
115.82
105.45
72.31
37.19
34.50
f1 (ppm)

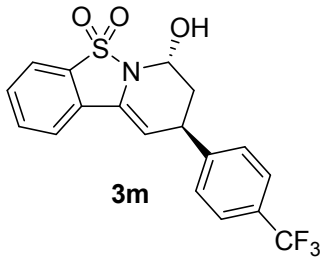

O
O
S
N
OH
Br

3l

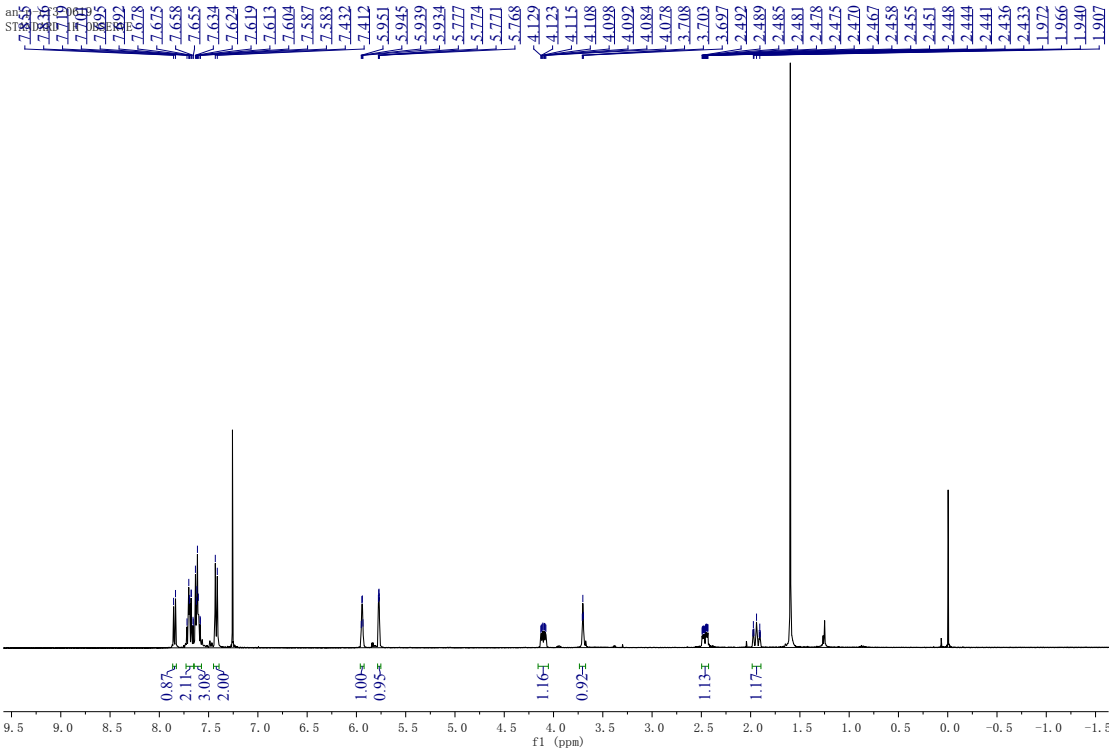

0.92
2.13
1.09
1.88
1.89
1.00
0.94
1.09
0.87
1.18
1.21
f1 (ppm)

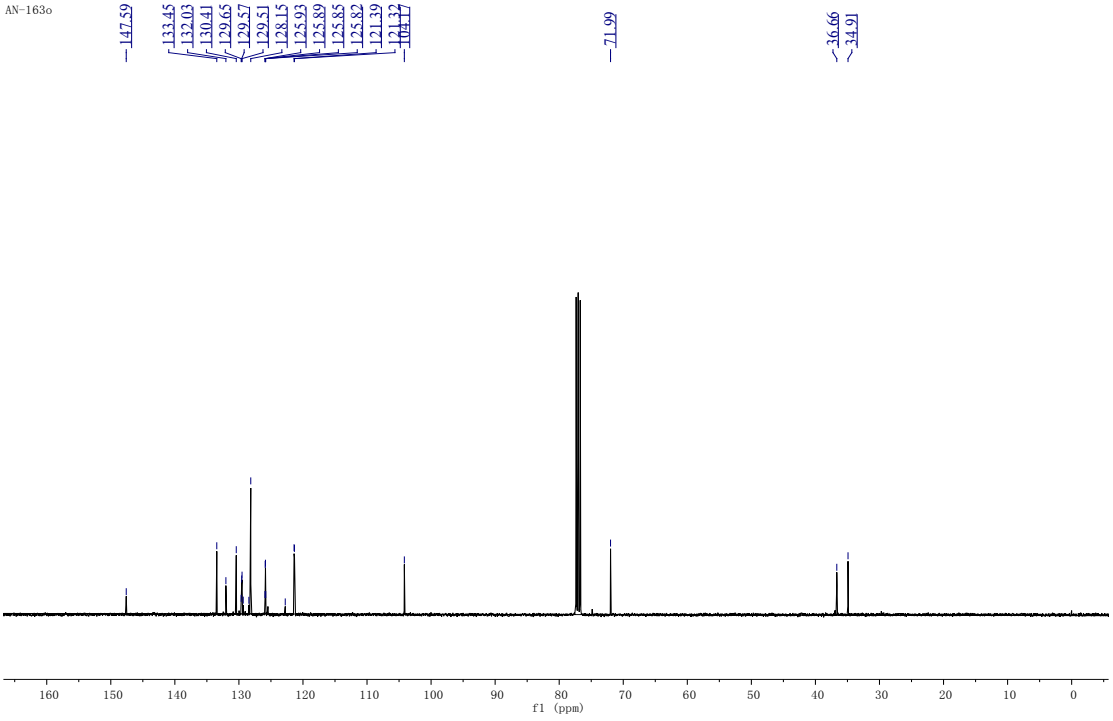
AN-163i

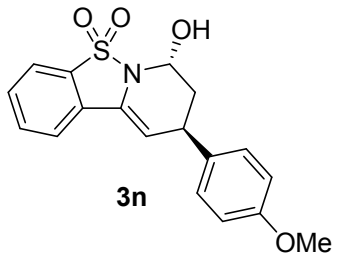

142.48
133.41
132.00
130.32
129.66
129.48
121.31
120.89
104.73
72.08
36.69
34.54
f1 (ppm)


O
O
S
N
OH
CF3

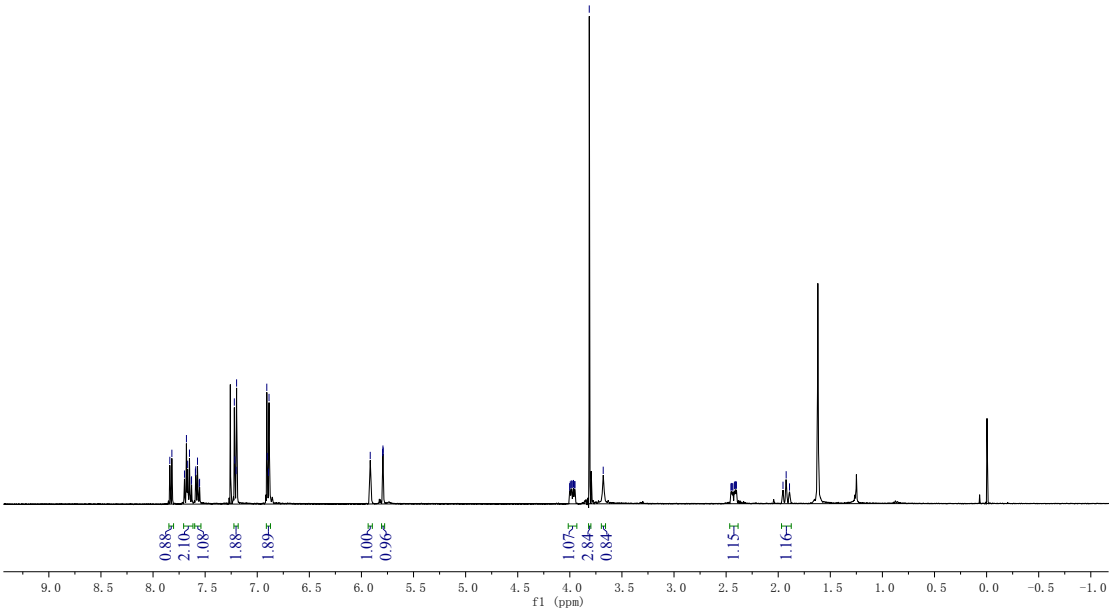
3m

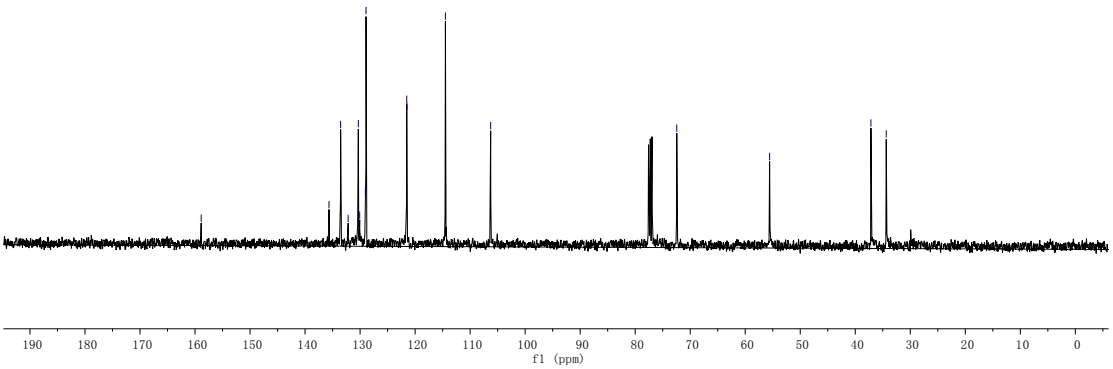

0.87
2.11
3.08
2.00
1.00
0.95
1.16
0.92
1.13
1.17
f1 (ppm)

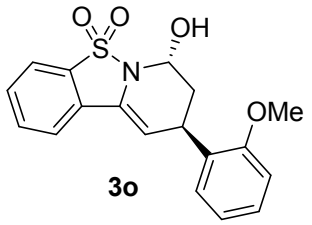

AN-163o
147.59
133.45
132.03
130.41
129.65
129.57
129.51
128.15
125.93
125.89
125.85
125.82
121.39
121.37
104.17
71.99
36.66
34.91
f1 (ppm)


O
O
OH
S
N
OMe

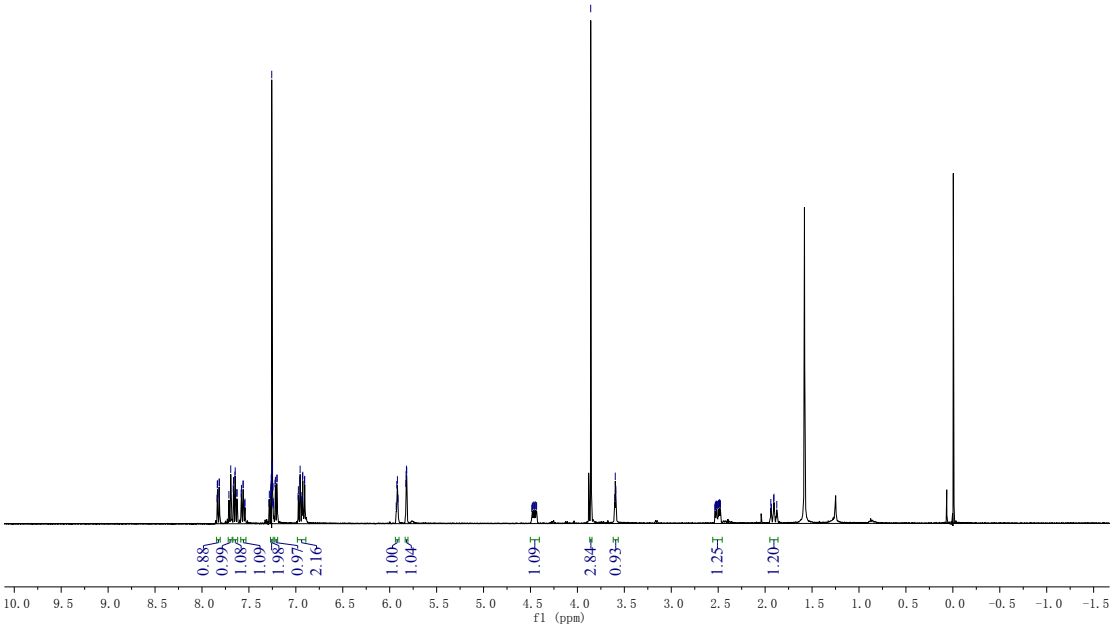
3n

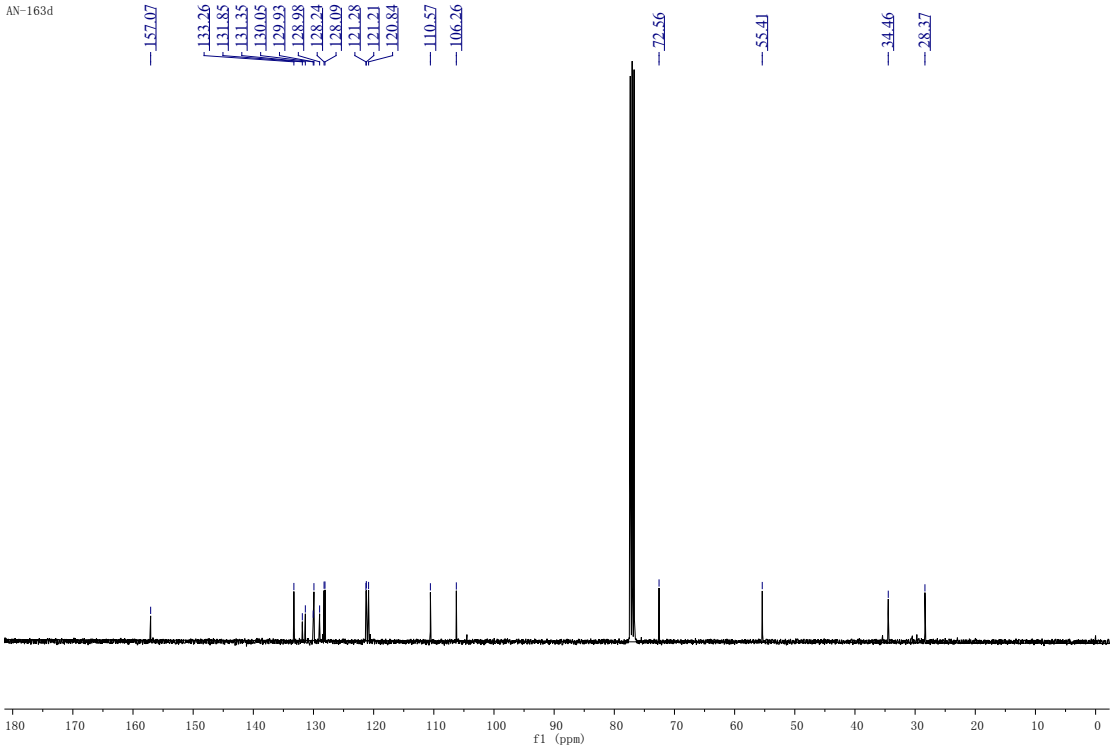

0.88
2.10
1.08
1.88
1.89
1.00
0.96
1.07
2.84
0.84
1.15
1.16
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

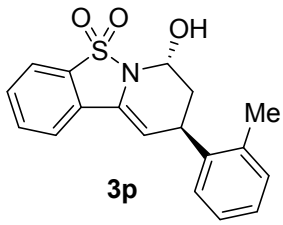

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


O
O
S
N
OH
OMe

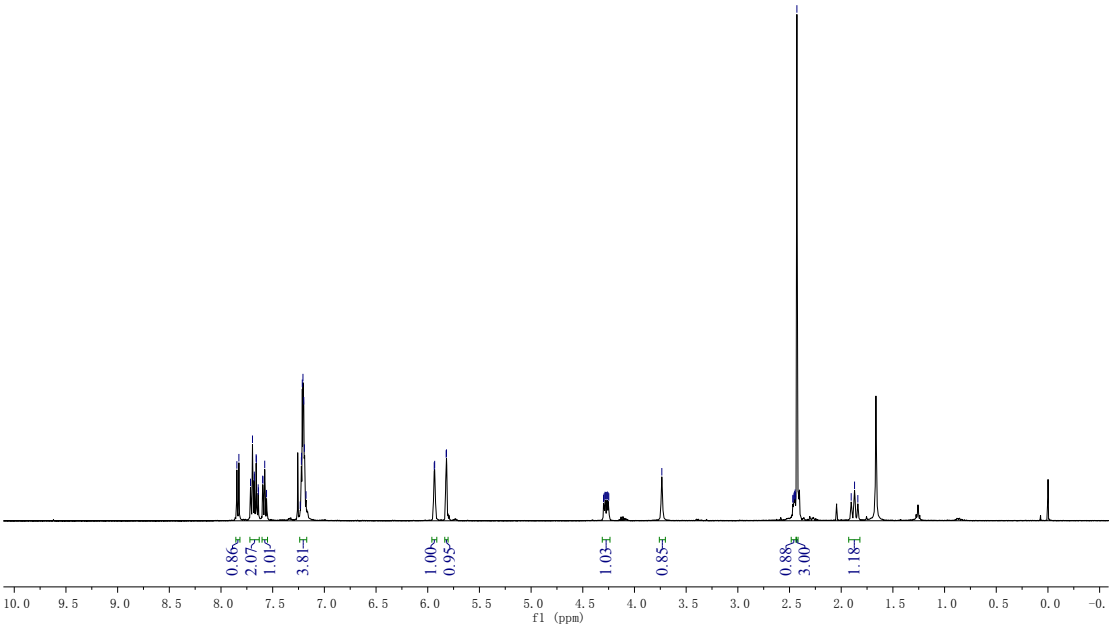
3o

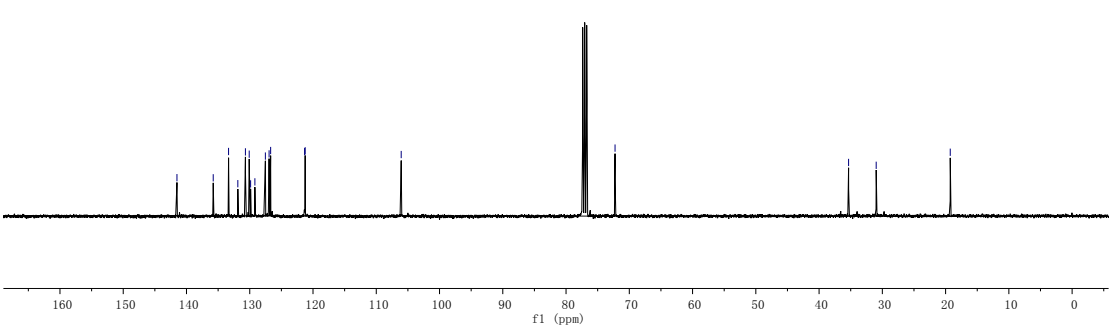

0.88
0.99
1.08
1.09
1.98
0.97
2.16
1.00
1.04
1.09
2.84
0.93
1.25
1.20
f1 (ppm)

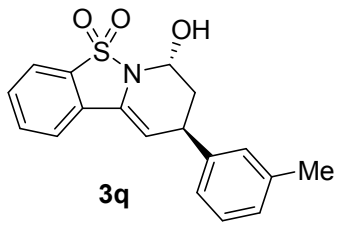

AN-163d
157.07
133.26
131.85
131.35
130.05
129.93
128.98
128.24
128.09
121.28
121.21
120.84
110.57
106.26
72.56
55.41
34.46
28.37
f1 (ppm)



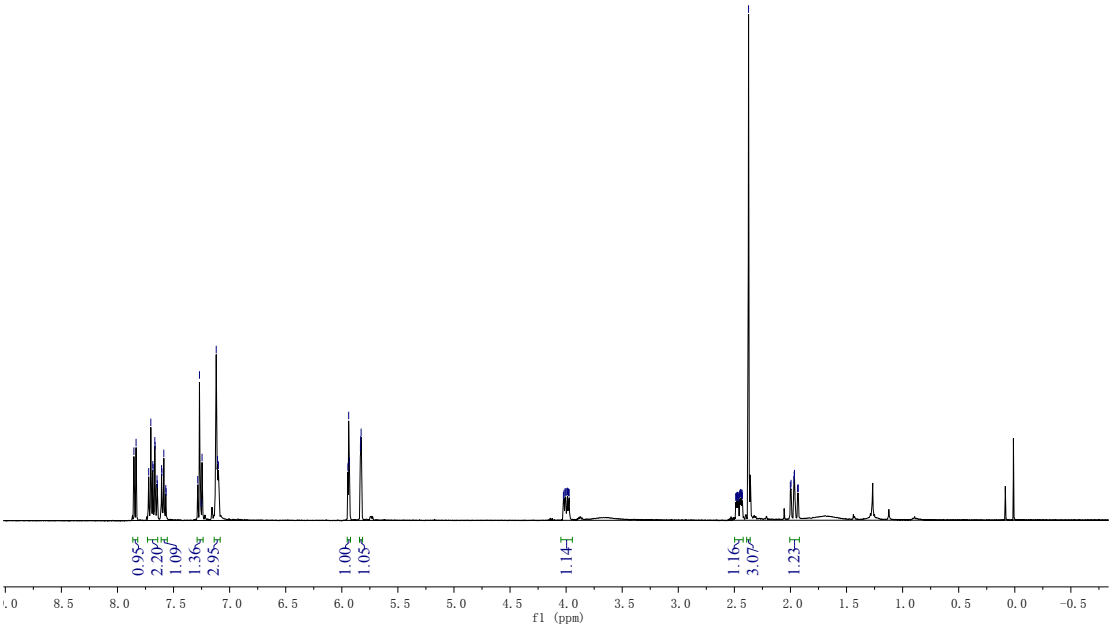
3p



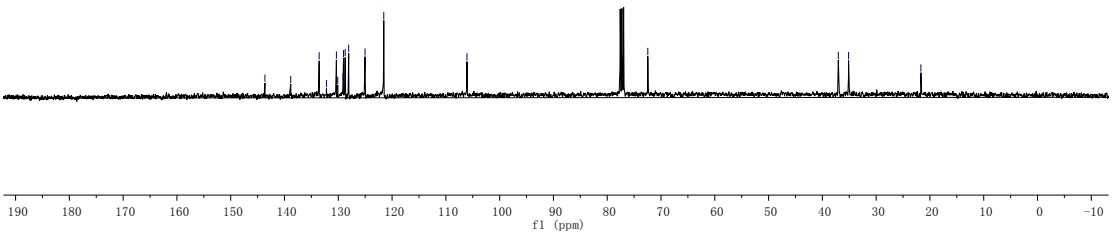


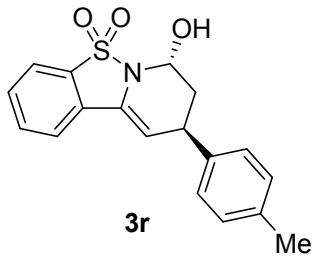

O
O
S
N
OH
Me

3q

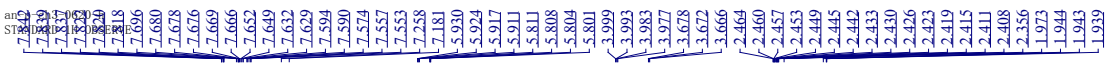

0.95
2.20
1.09
1.36
2.95
1.00
1.05
1.14
1.16
3.07
1.23
f1 (ppm)

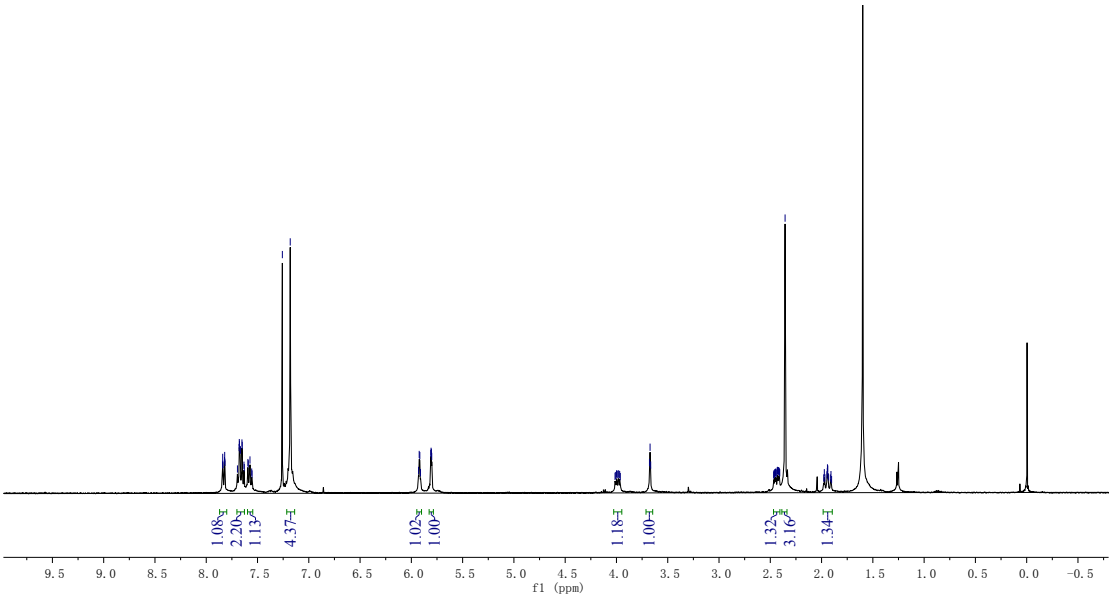

an-m-ch3-13c-0729
13C OBSERVE

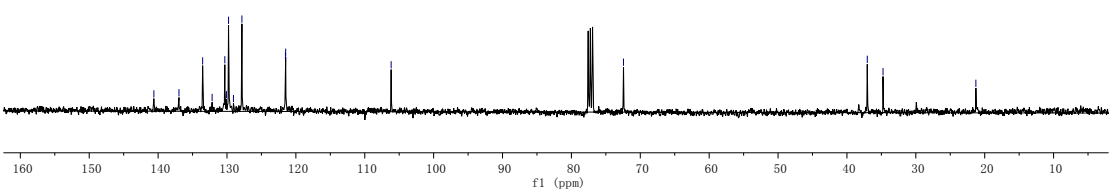

f1 (ppm)

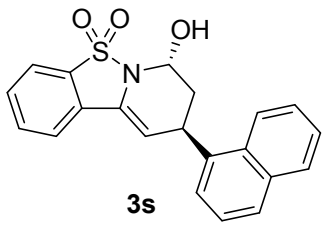

O
O
OH
S
N
Me

3r

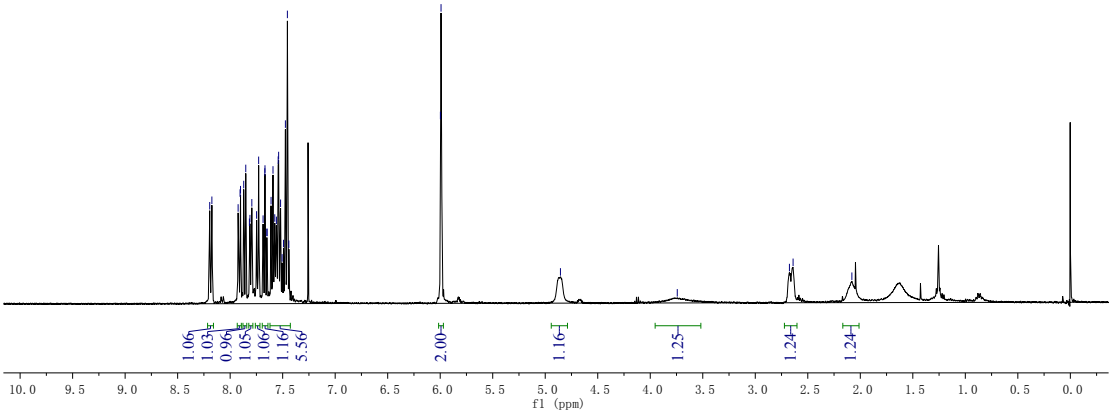


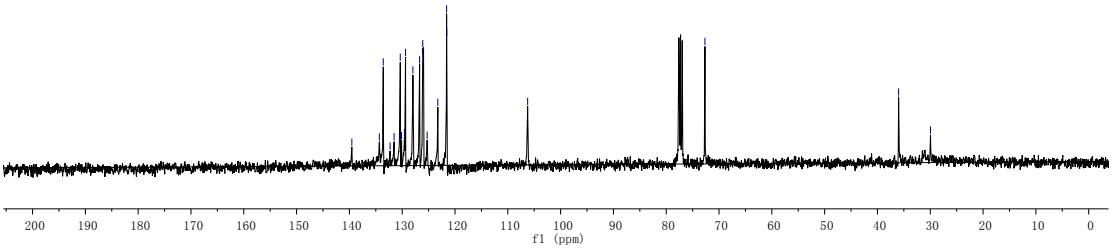

1.08
2.20
1.13
4.37
1.02
1.00
1.18
1.00
1.32
3.16
1.34
f1 (ppm)

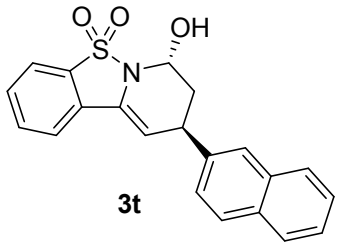

f1 (ppm)



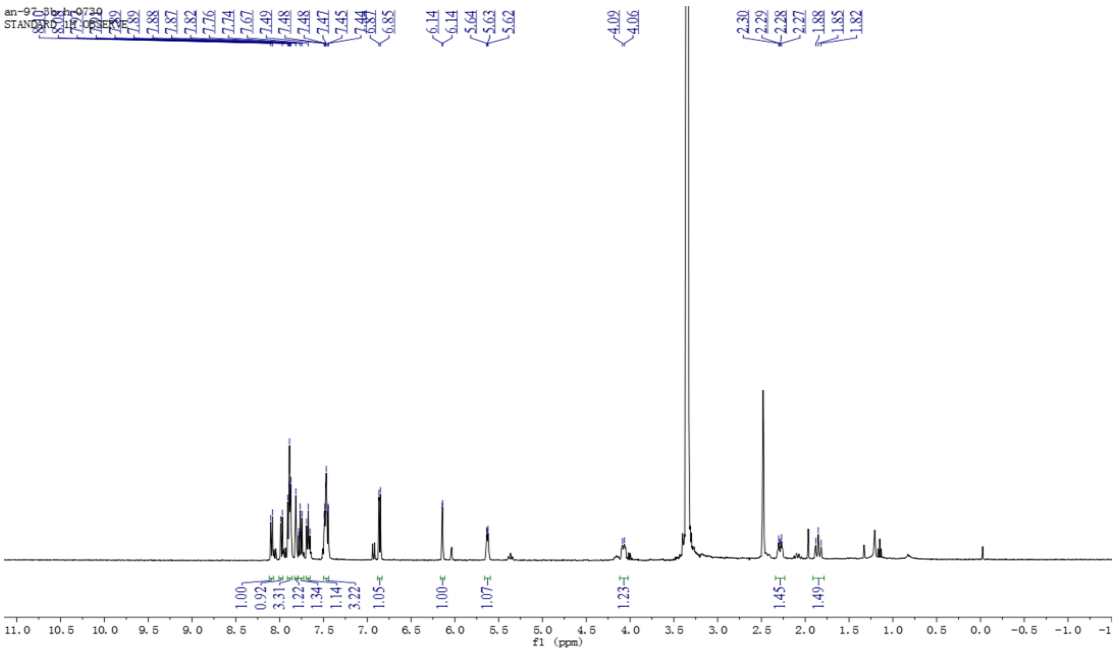
3s



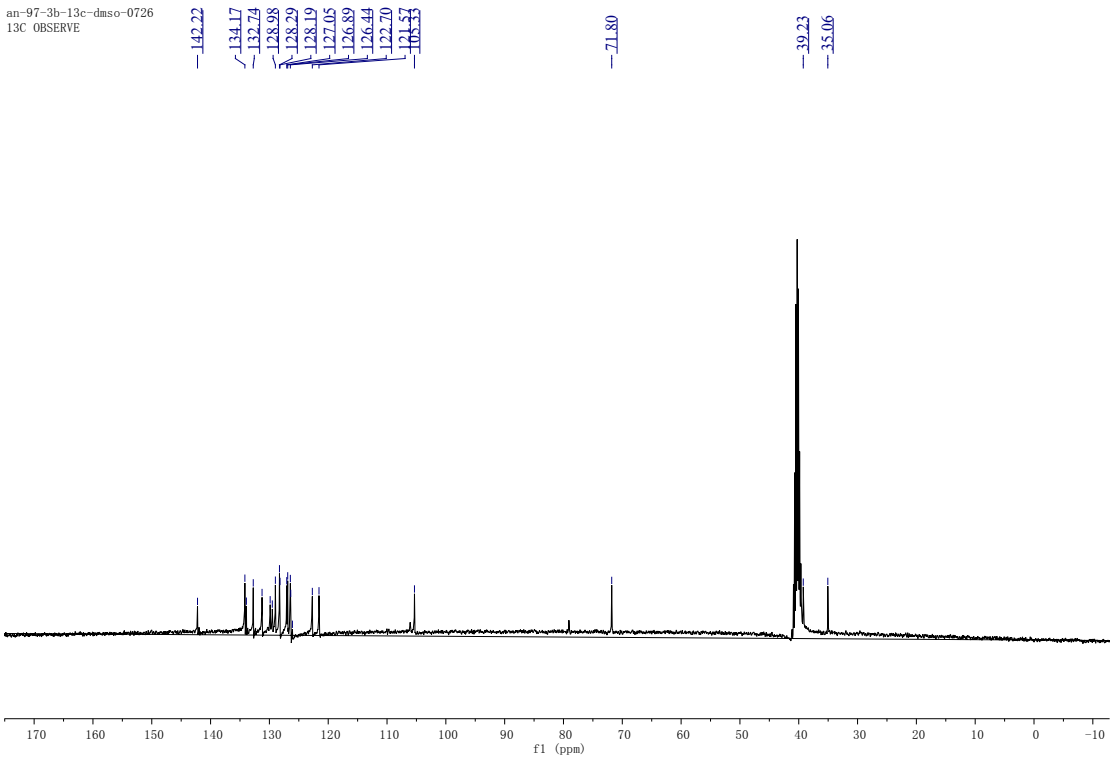


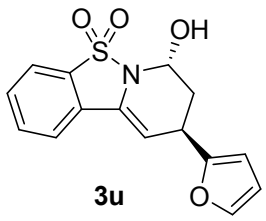


3t

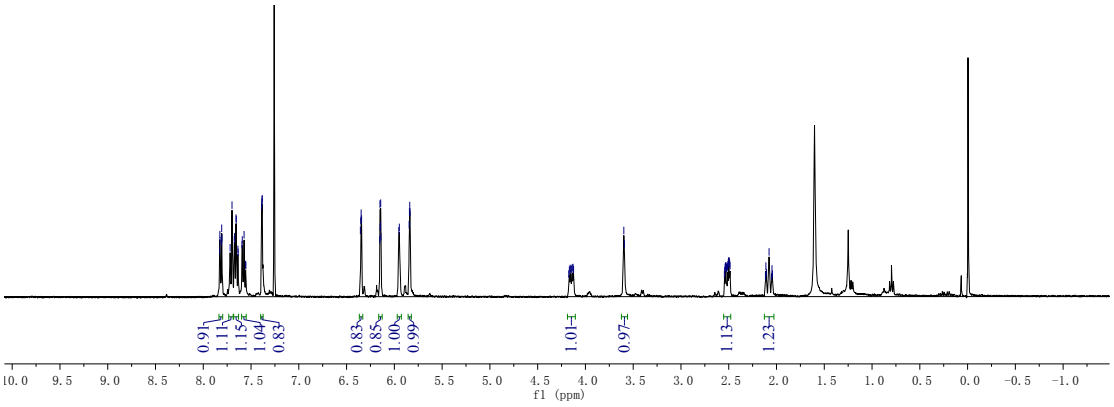


an-97-3b-13c-dmso-0726
13C OBSERVE

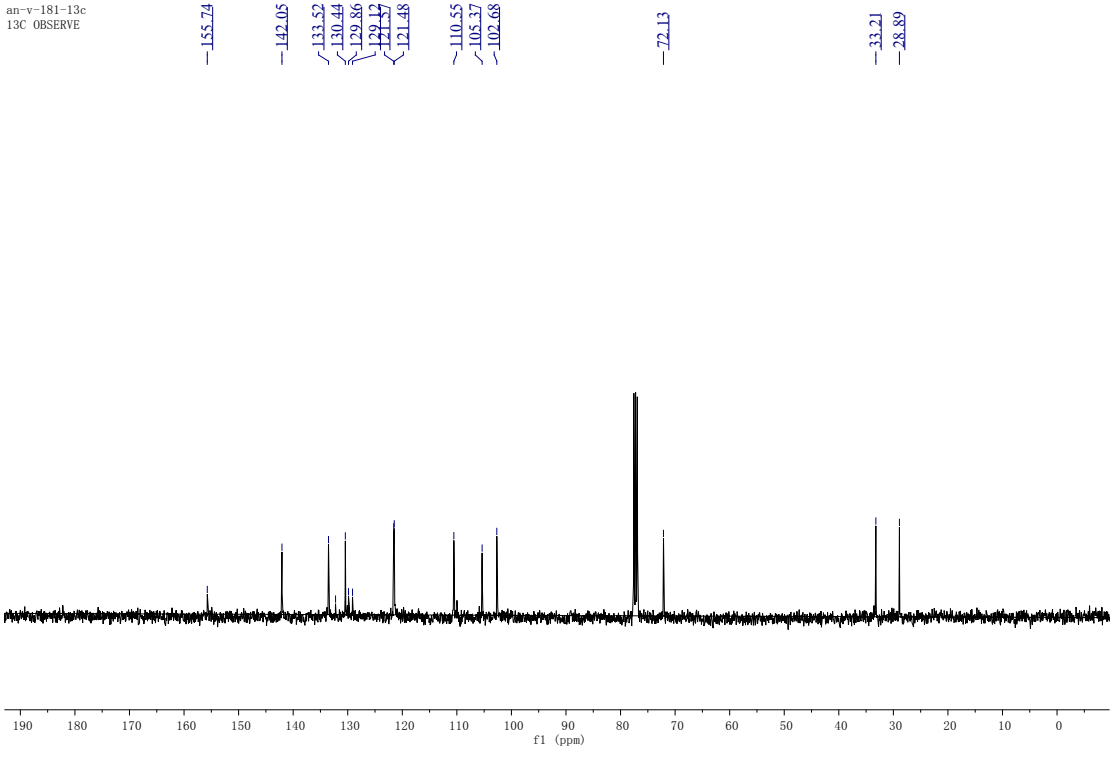


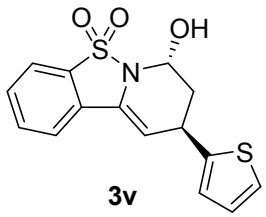


3u

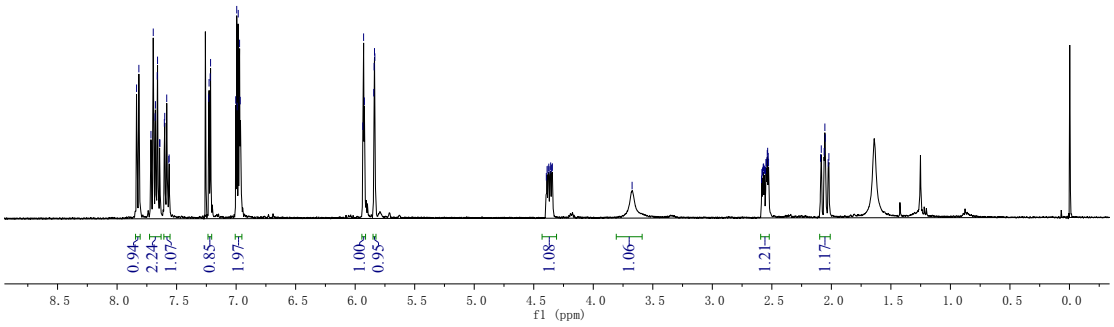


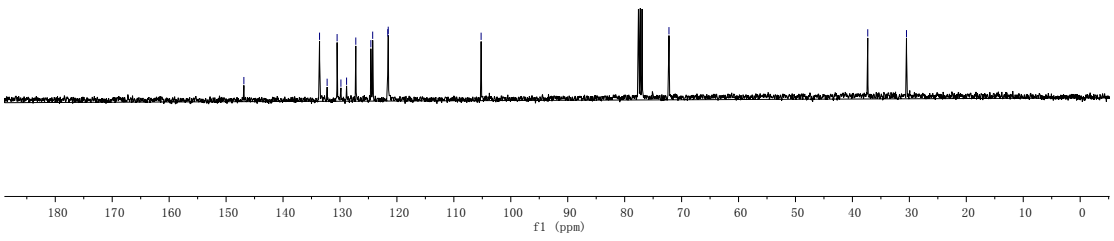
an-v-181-13c
13C OBSERVE

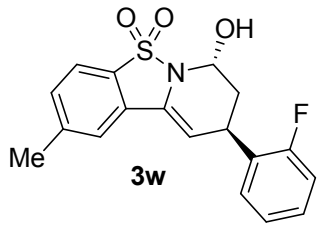




3v

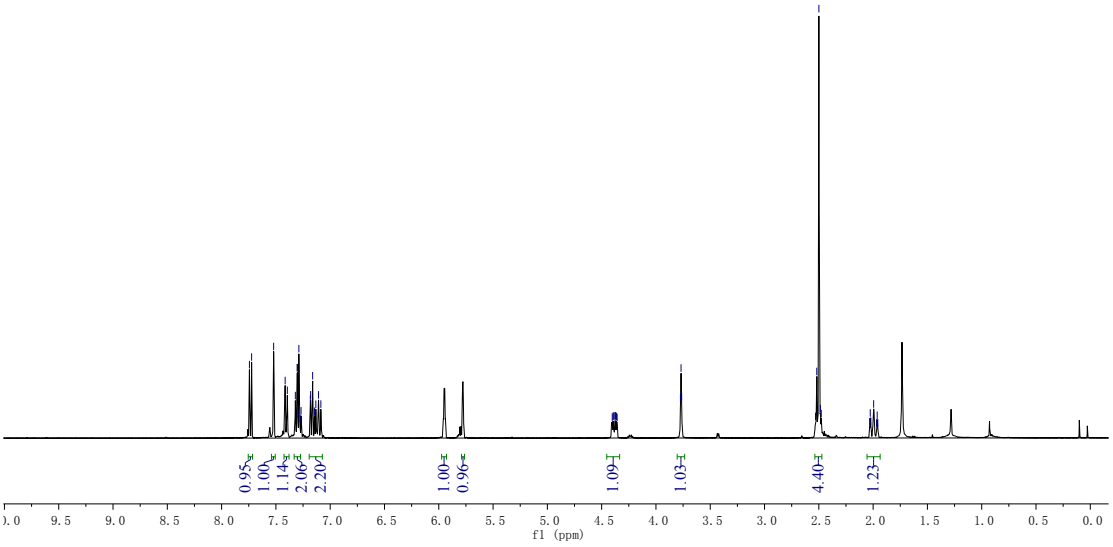




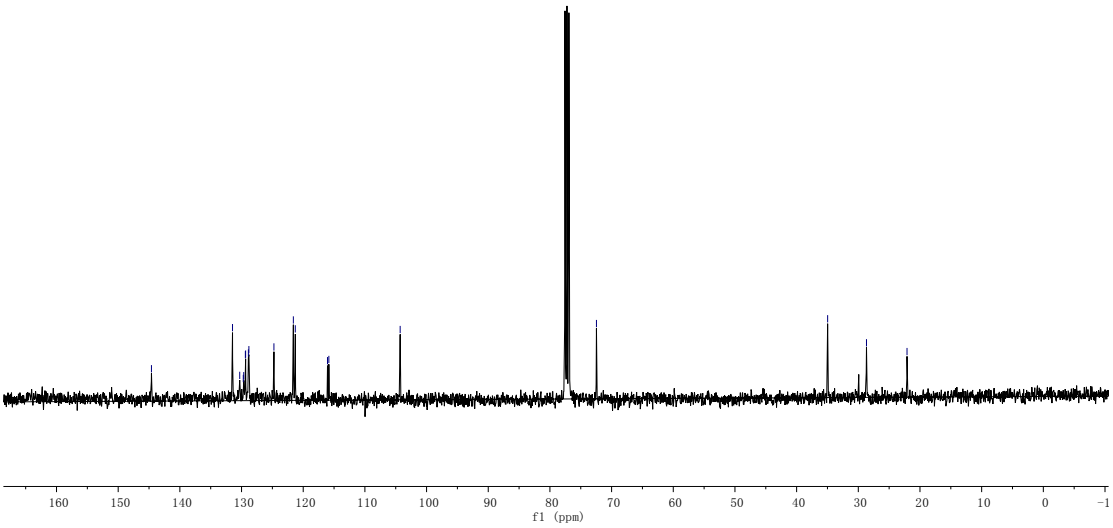

O
O
S
N
OH
F
Me

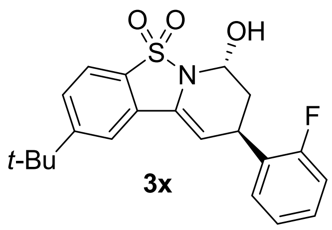
3w


an-99-3-0815
STANDARD 1H
7.824
7.821
7.415
7.395
7.321
7.304
7.302
7.296
7.288
7.283
7.277
7.268
7.264
7.183
7.180
7.162
7.146
7.143
7.132
7.107
7.086
4.402
4.394
4.388
4.379
4.372
4.364
4.358
3.775
3.769
3.763
2.531
2.519
2.511
2.499
2.486
2.478
2.032
2.026
2.021
1.995
1.968
1.963
1.957


0.95
1.00
1.14
2.06
2.20
1.00
0.96
1.09
1.03
4.40
1.23
f1 (ppm)

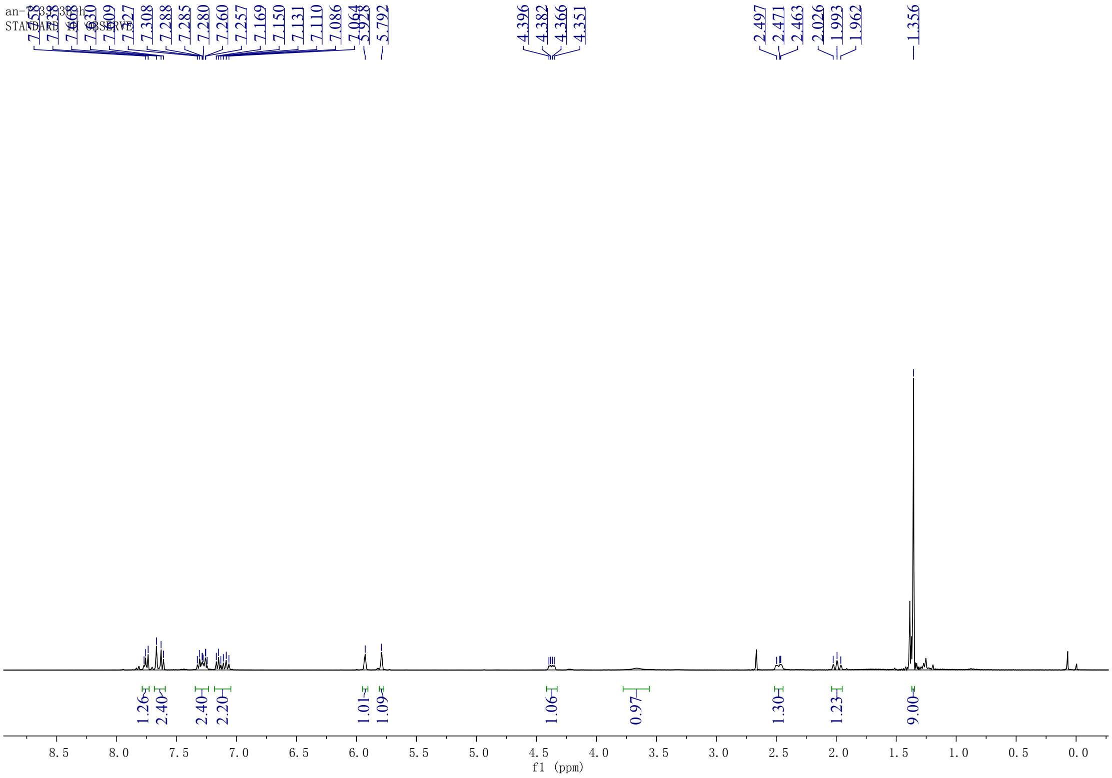

an-99-3b-13c
13C OBSERVE
144.61
131.47
130.30
129.64
129.38
129.34
128.89
128.81
124.75
121.60
121.28
116.06
115.84
104.28
72.45
34.97
28.67
22.10


f1 (ppm)

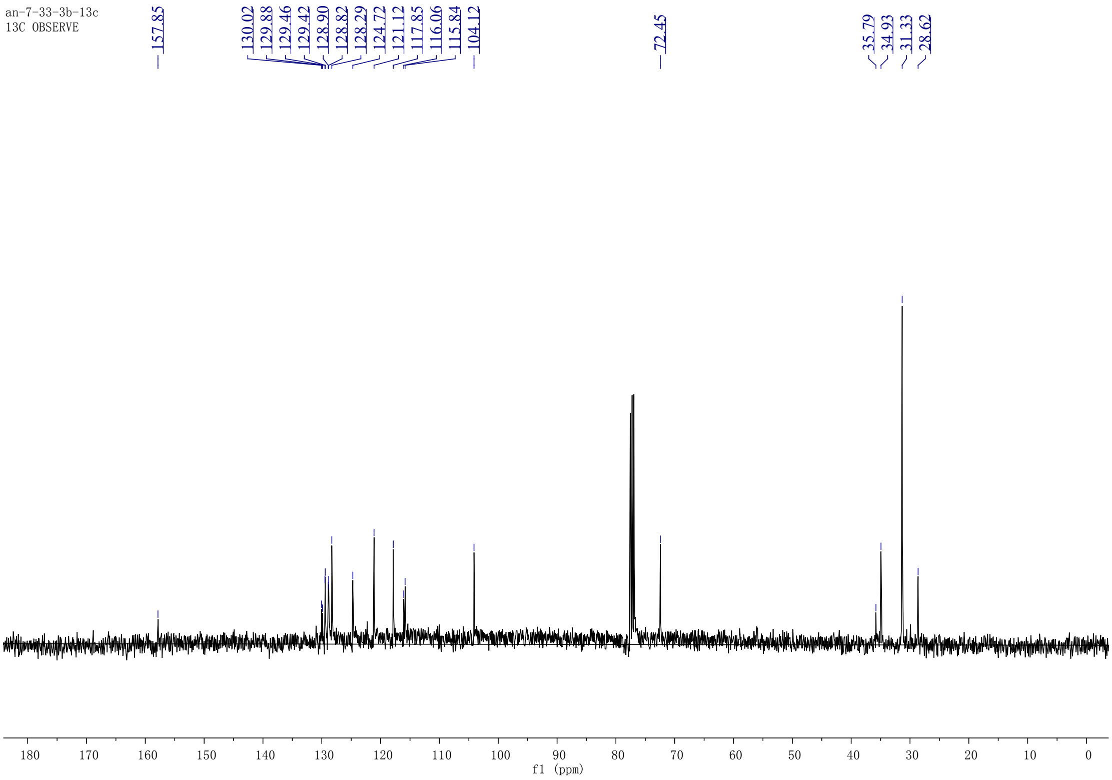


OH
F
t-Bu

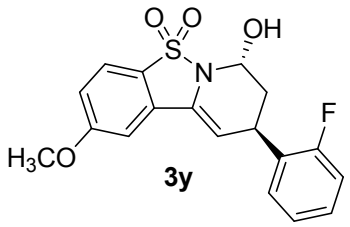
3x



7.308
7.288
7.285
7.280
7.260
7.257
7.169
7.150
7.131
7.110
7.086
5.792
4.396
4.382
4.366
4.351
2.497
2.471
2.463
2.026
1.993
1.962
1.356
1.26
2.40
2.40
2.20
1.01
1.09
1.06
0.97
1.30
1.23
9.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

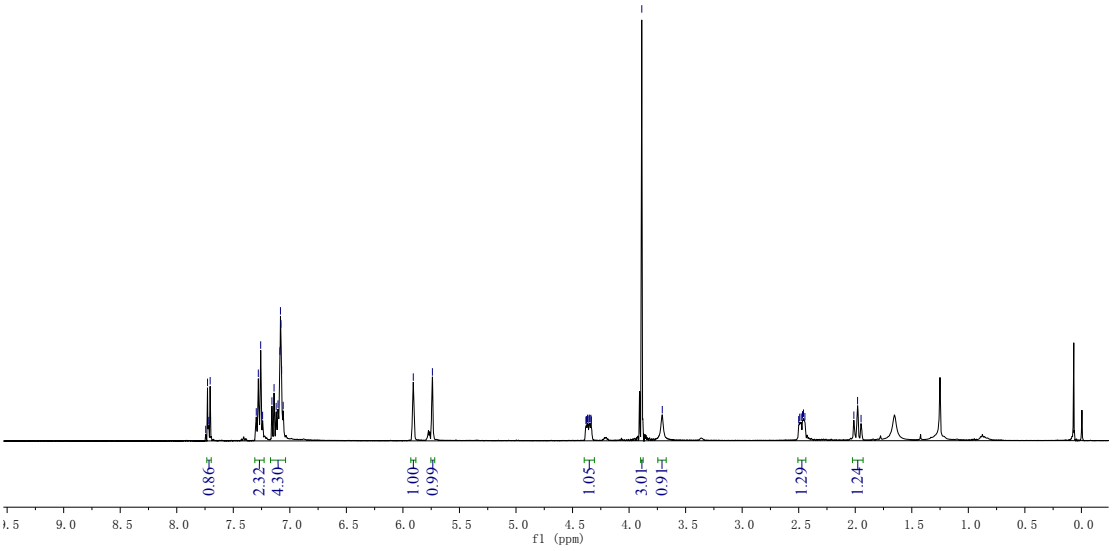


an-7-33-3b-13c
13C OBSERVE
157.85
130.02
129.88
129.46
129.42
128.90
128.82
128.29
124.72
121.12
117.85
116.06
115.84
104.12
72.45
35.79
34.93
31.33
28.62
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



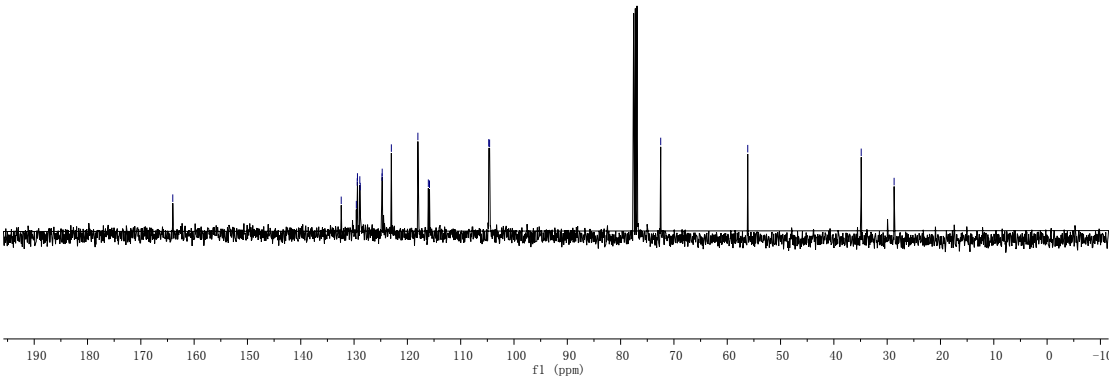
an-7-31-3b
STANDARD 1H OBSERVE

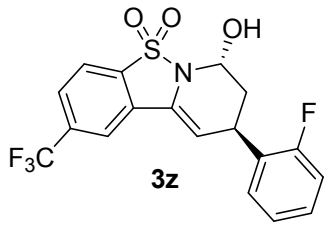
7.744 7.728 7.717 7.705 7.229 7.258 7.158 7.140 7.105 7.088 7.083 7.079 7.072 5.968 5.739 4.382 4.377 4.368 4.363 4.352 4.347 4.338 4.333 3.888 3.706 2.500 2.491 2.478 2.466 2.458 2.445 2.012 1.979 1.949



an-7-31-3b-13c
13C OBSERVE

164.01 132.41 129.58 129.40 129.36 128.92 128.84 124.75 124.72 123.01 118.03 116.07 115.85 104.75 104.58 72.48 56.15 34.87 28.70

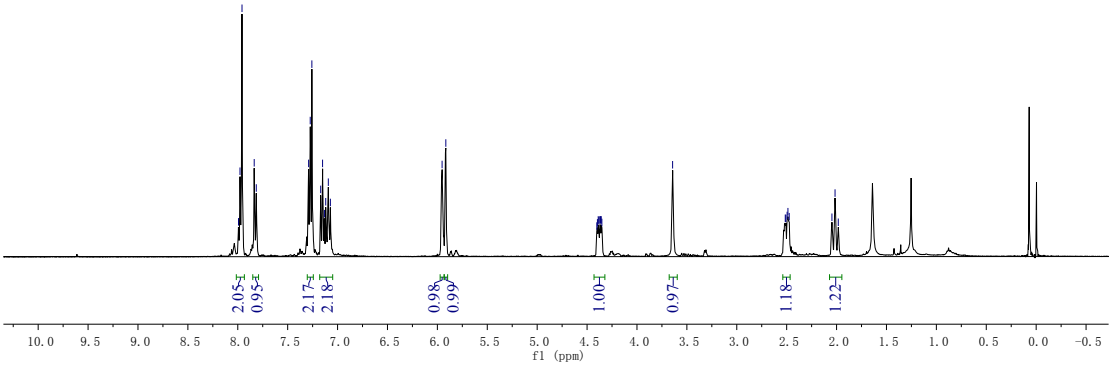




3z

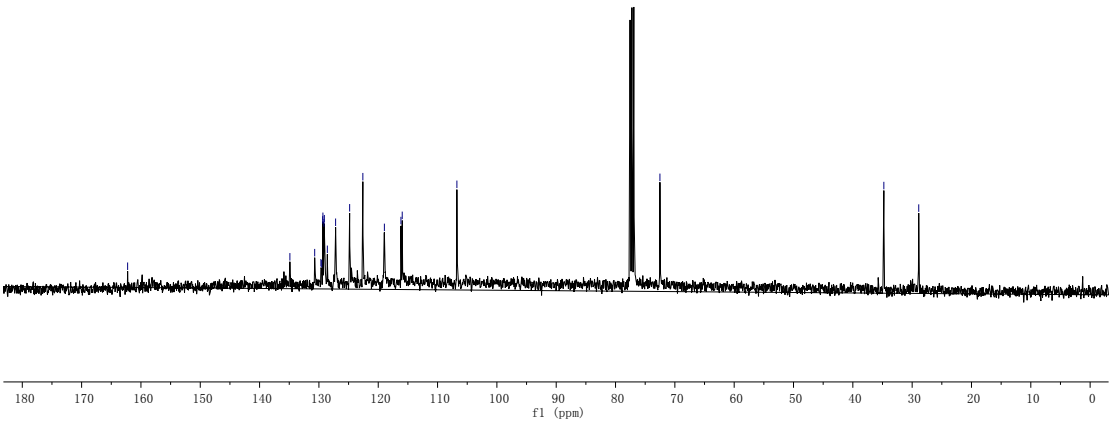
an-7-35-3b-cf3
STANDARD 1H OBSERVE

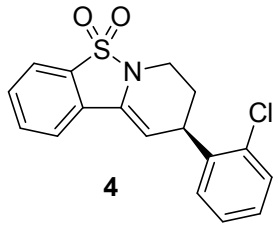
7.993 7.978 7.958 7.835 7.815 7.290 7.274 7.258 7.169 7.150 7.119 5.915 4.402 4.396 4.388 4.382 4.372 4.366 4.358 4.352 3.643 2.514 2.508 2.495 2.487 2.475 2.047 2.015 1.983



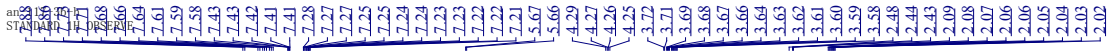
an-7-35-3b-13c-cf3
13C OBSERVE

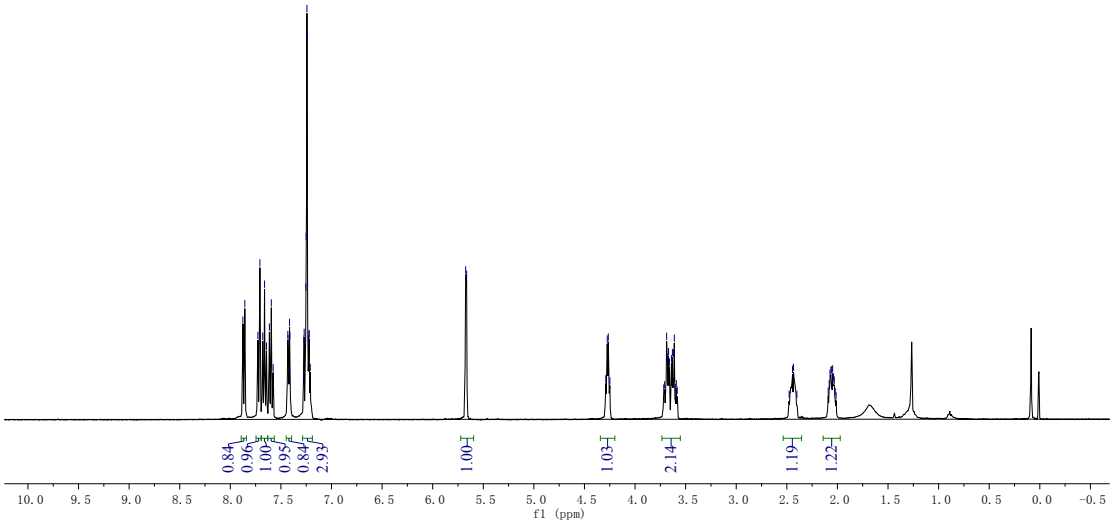
162.23 134.89 130.71 129.67 129.53 129.36 129.33 129.17 129.08 128.58 127.19 124.82 122.59 118.96 116.17 115.96 106.74 72.52 34.77 28.89

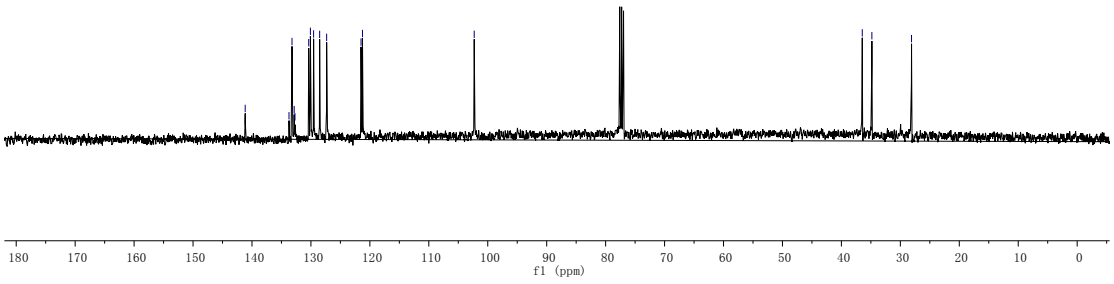


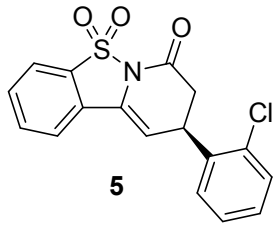


4



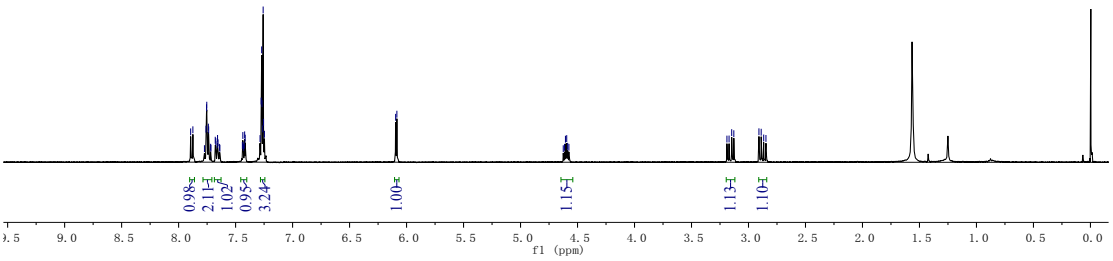




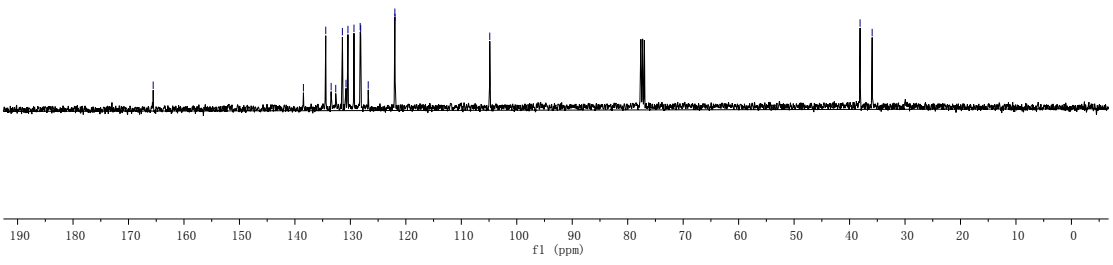

O
O
O
S
N
Cl

5

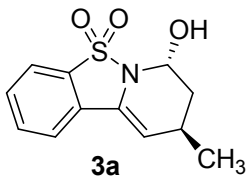

STANDARD 1H OBSERVE
7.74
7.66
7.44
7.42
7.42
7.29
7.28
7.27
7.27
7.26
7.26
7.26
7.25
6.10
6.09
4.63
4.61
4.61
4.59
4.59
4.58
3.19
3.17
3.15
3.13
2.91
2.89
2.87
2.85


0.98
2.11
1.02
0.95
3.24
1.00
1.15
1.13
1.10
f1 (ppm)

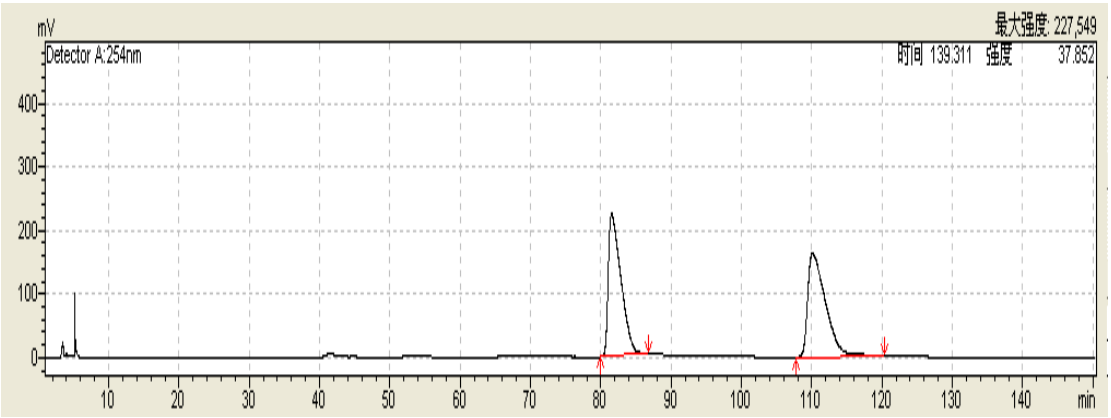

an-115-3b-13c
13C OBSERVE
165.55
138.47
134.44
133.47
132.64
131.44
130.79
130.44
129.35
128.23
128.14
126.78
121.98
121.95
104.87
38.10
35.93


f1 (ppm)

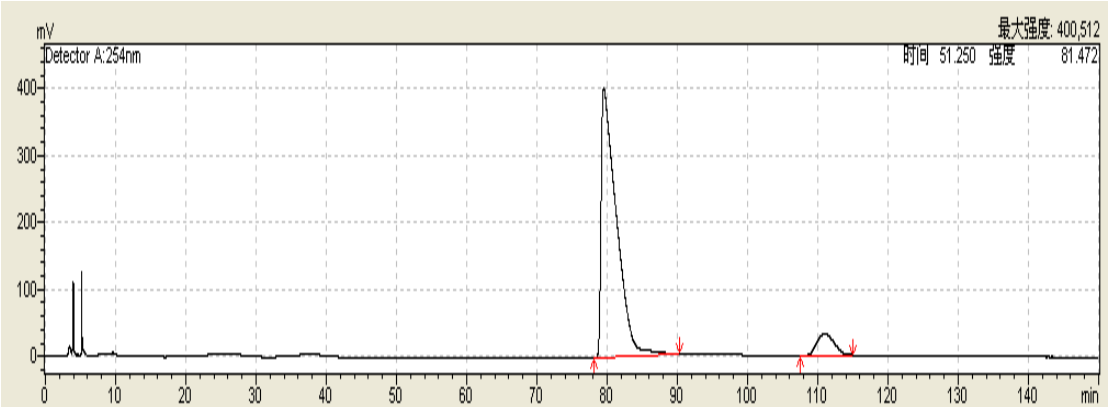
8. HPLC Spectra



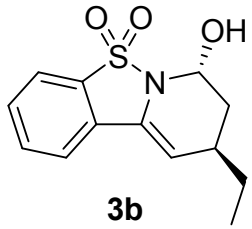
3a



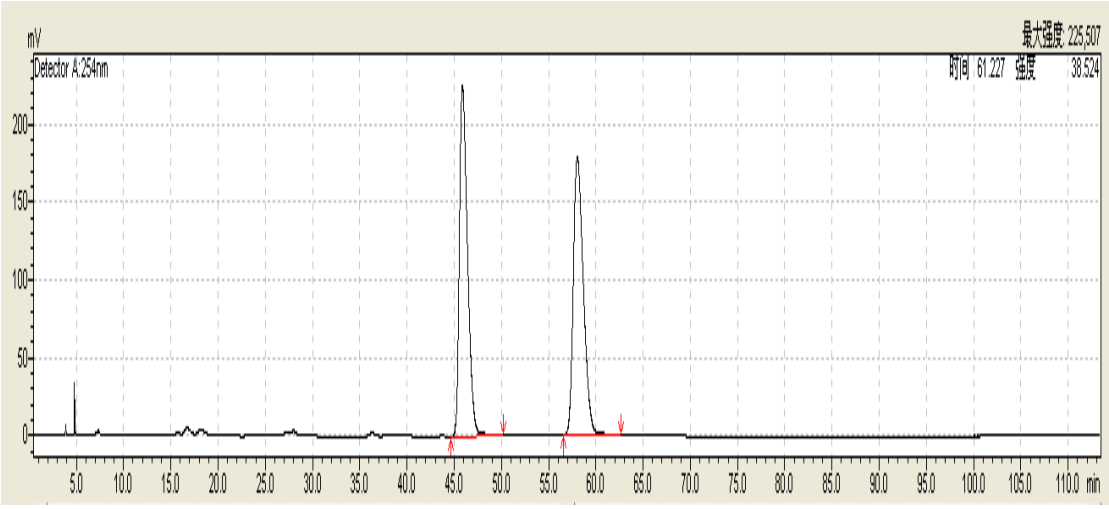
Peak	Retention time	Area (%)
1	81.549	49.456
2	110.133	50.544



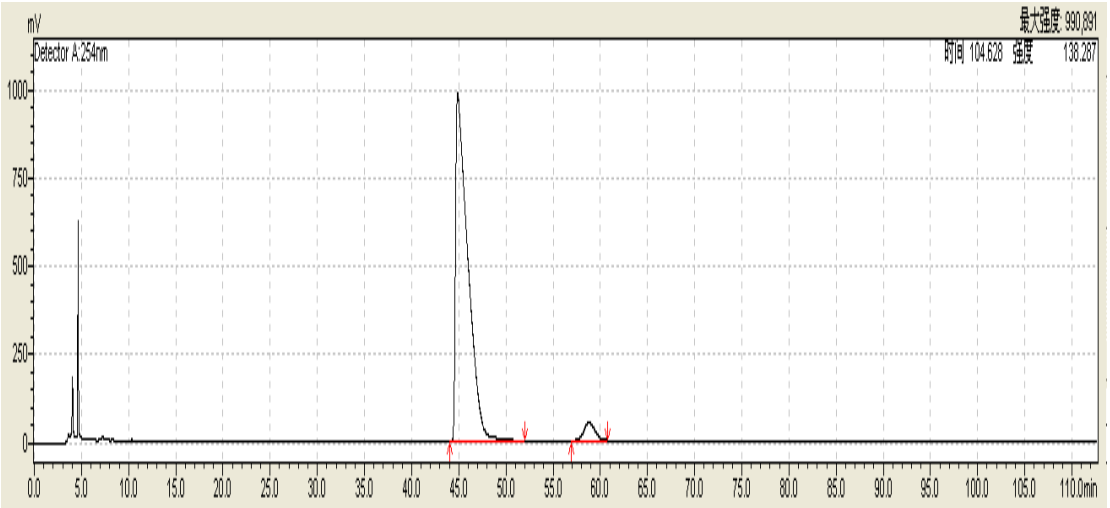
Peak	Retention time	Area (%)
1	79.517	91.758
2	110.887	8.242



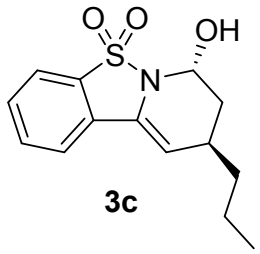
3b



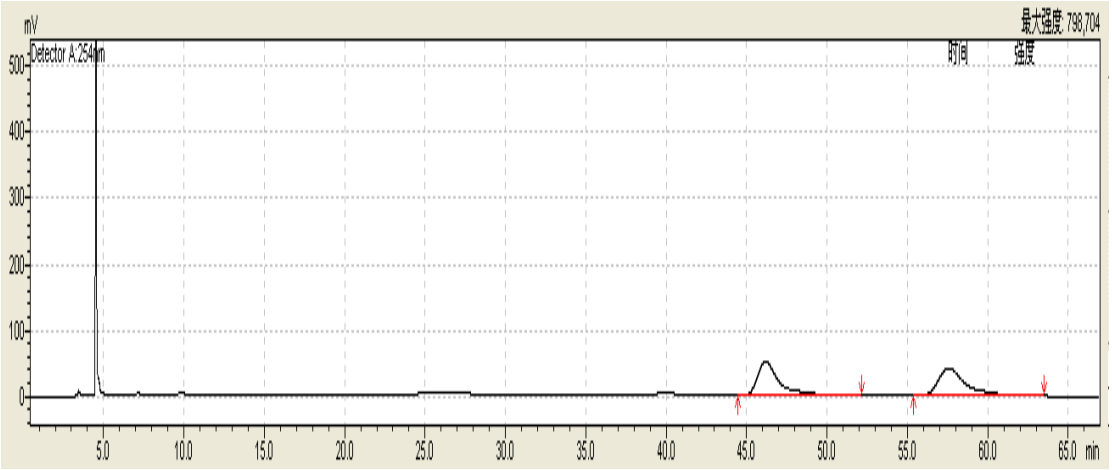
Peak	Retention time	Area (%)
1	45.873	50.306
2	58.032	49.694



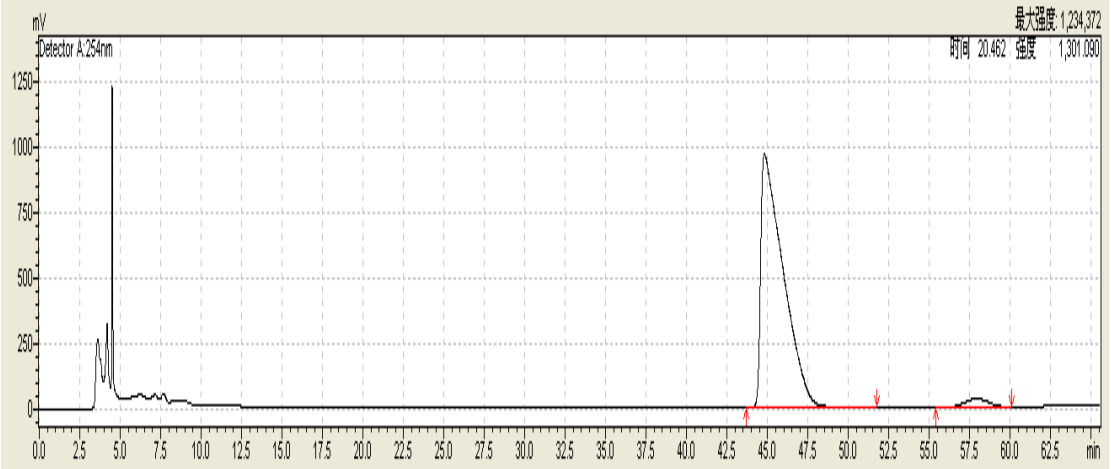
Peak	Retention time	Area (%)
1	44.870	95.656
2	58.815	4.344



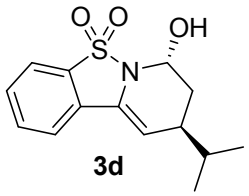
3c



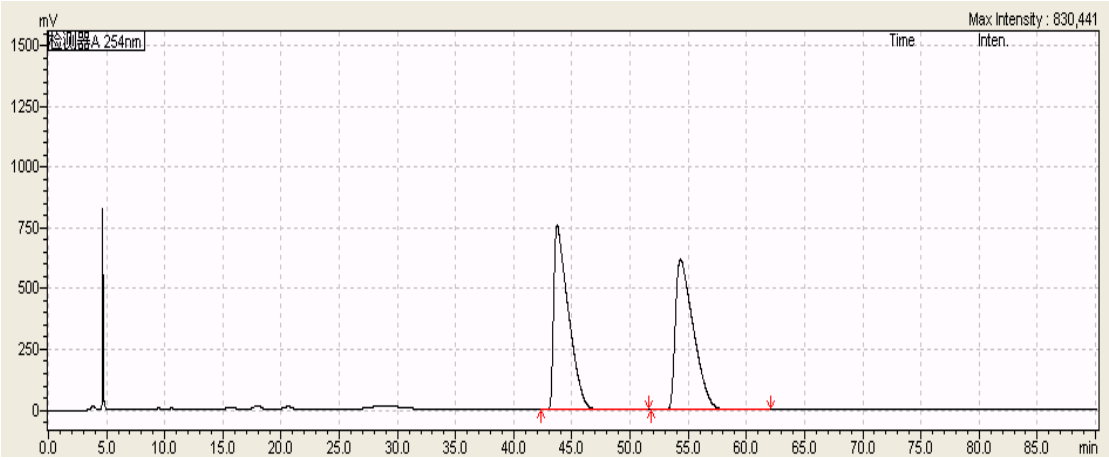
Peak	Retention time	Area (%)
1	46.175	50.026
2	57.578	49.974



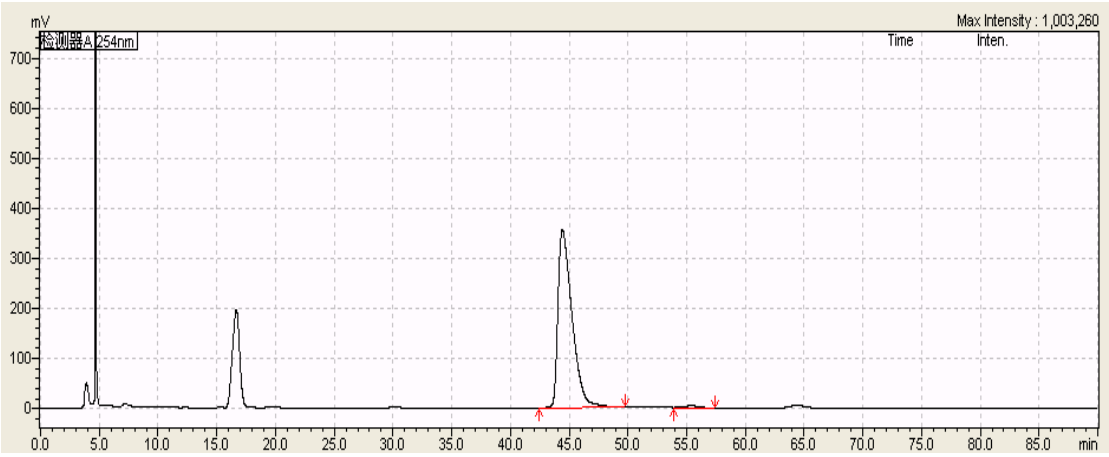
Peak	Retention time	Area (%)
1	44.803	96.762
2	57.902	3.238



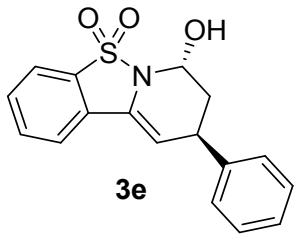
3d



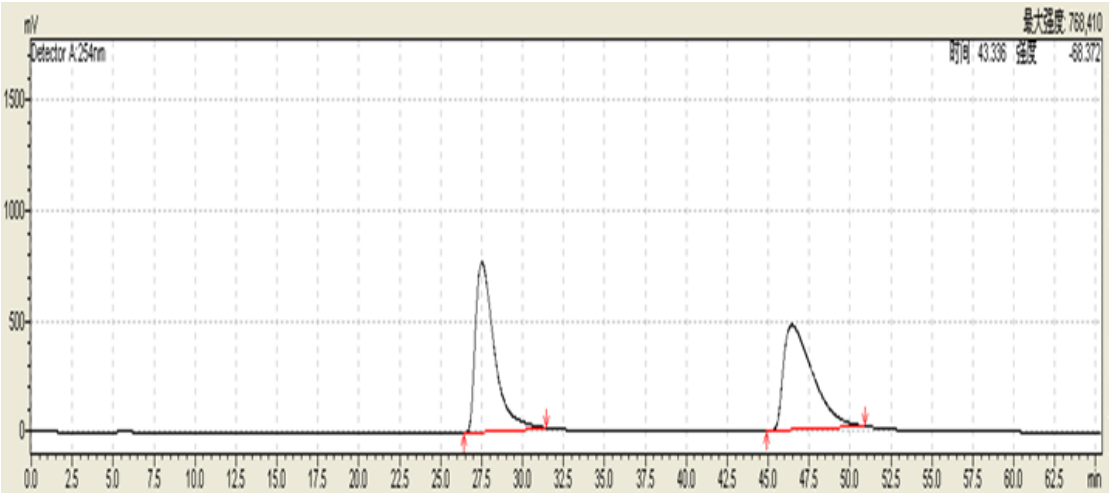
Peak	Retention time	Area (%)
1	43.721	49.958
2	54.325	50.042



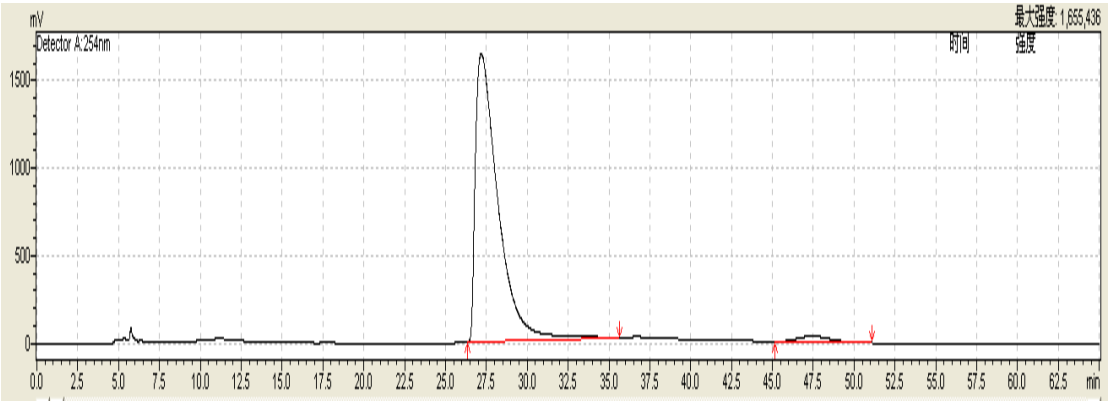
Peak	Retention time	Area (%)
1	44.427	98.967
2	55.447	1.033



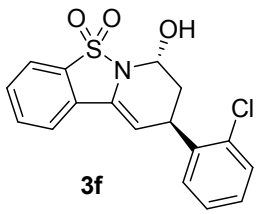
3e



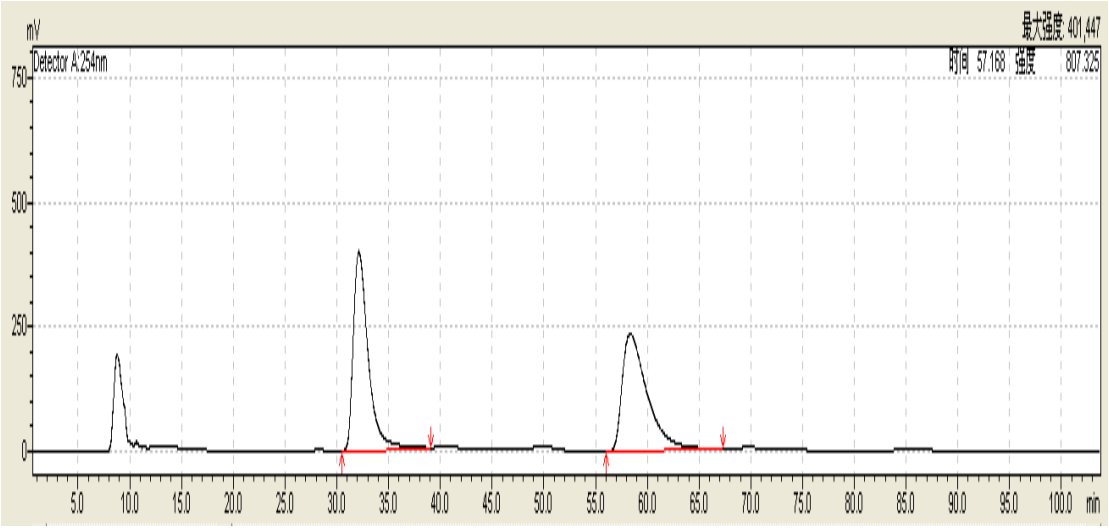
Peak	Retention time	Area (%)
1	27.514	49.829
2	46.448	50.171



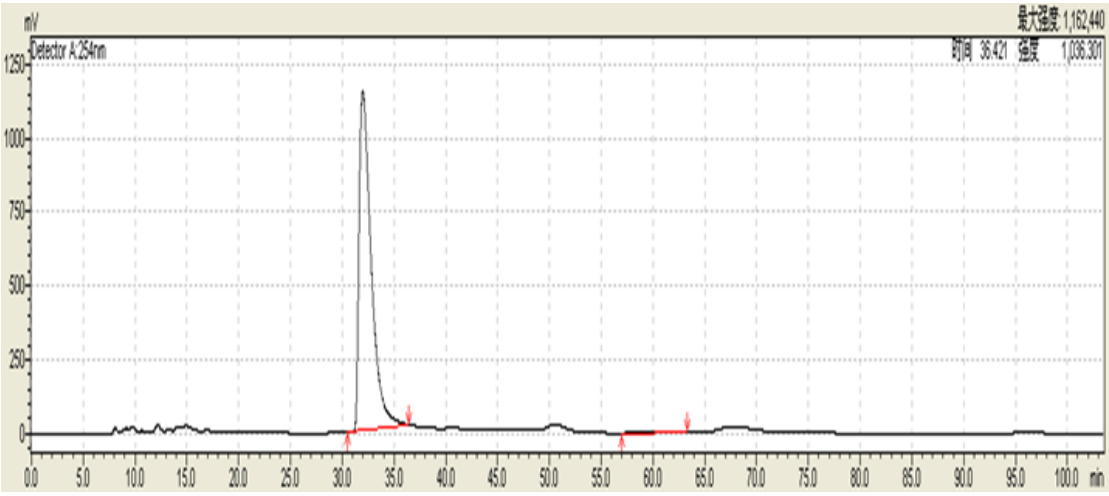
Peak	Retention time	Area (%)
1	27.187	97.232
2	47.409	2.768



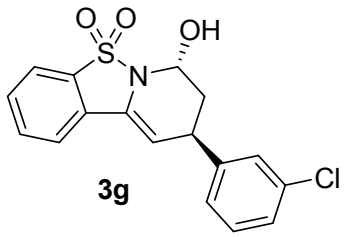
3f



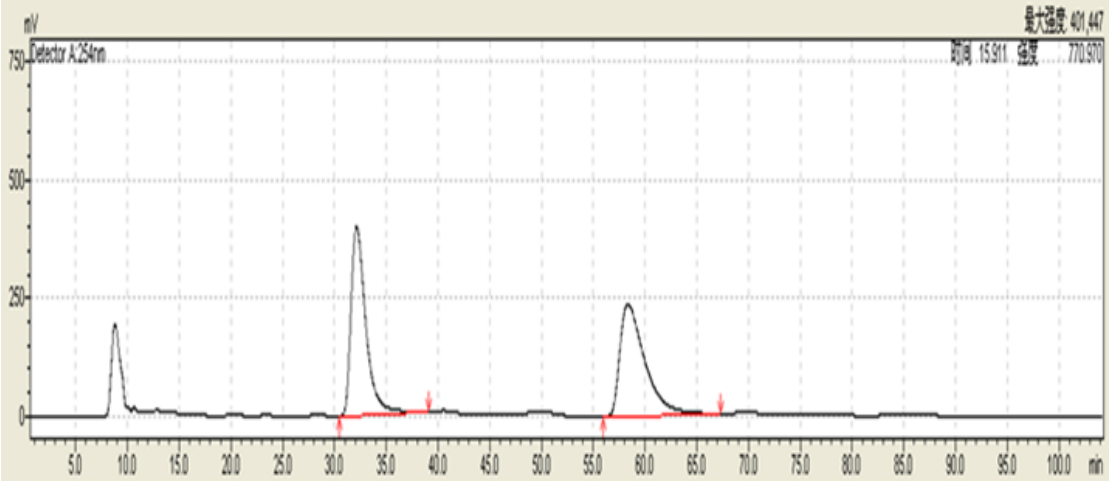
Peak	Retention time	Area (%)
1	32.138	50.372
2	58.344	49.628



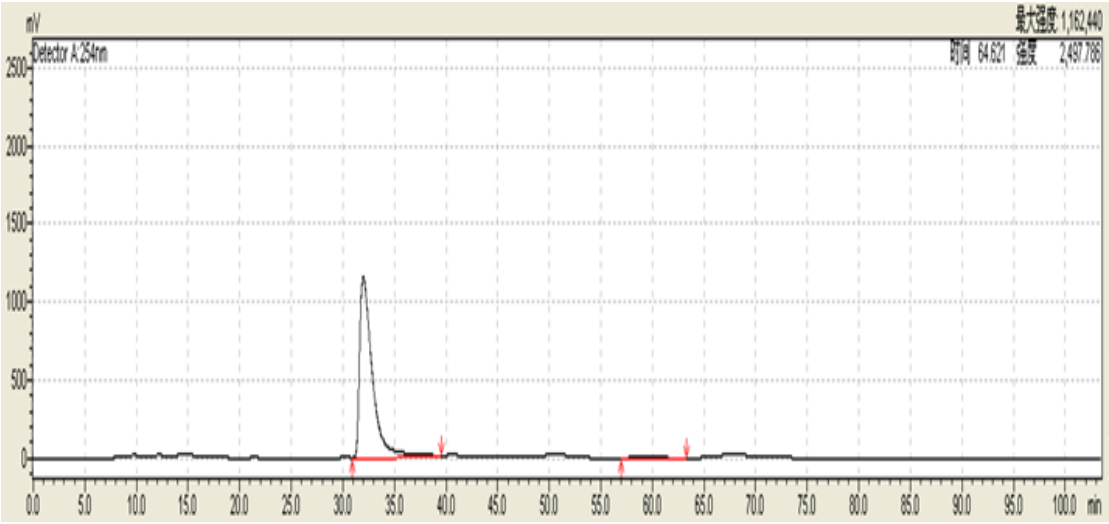
Peak	Retention time	Area (%)
1	31.978	99.034
2	59.035	0.966



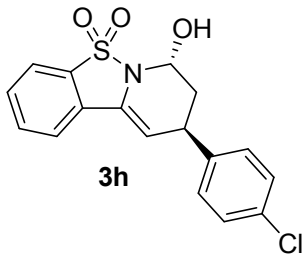
3g



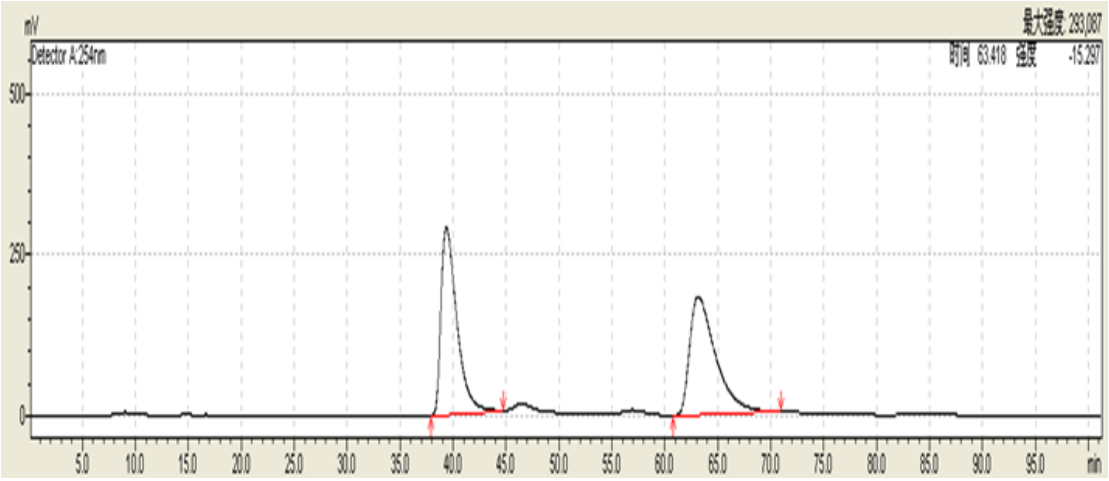
Peak	Retention time	Area (%)
1	32.138	50.372
2	58.344	49.628



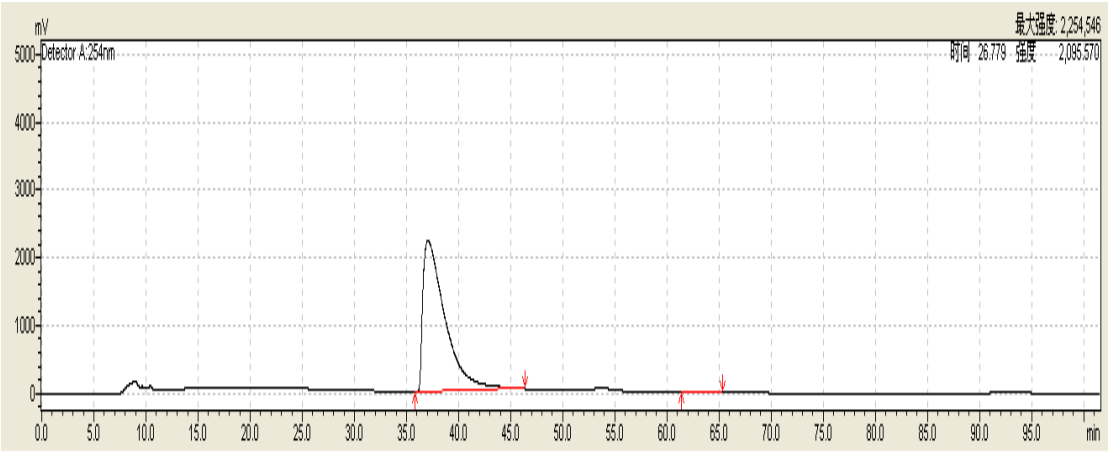
Peak	Retention time	Area (%)
1	31.978	98.993
2	59.035	1.007



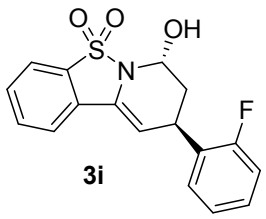
3h



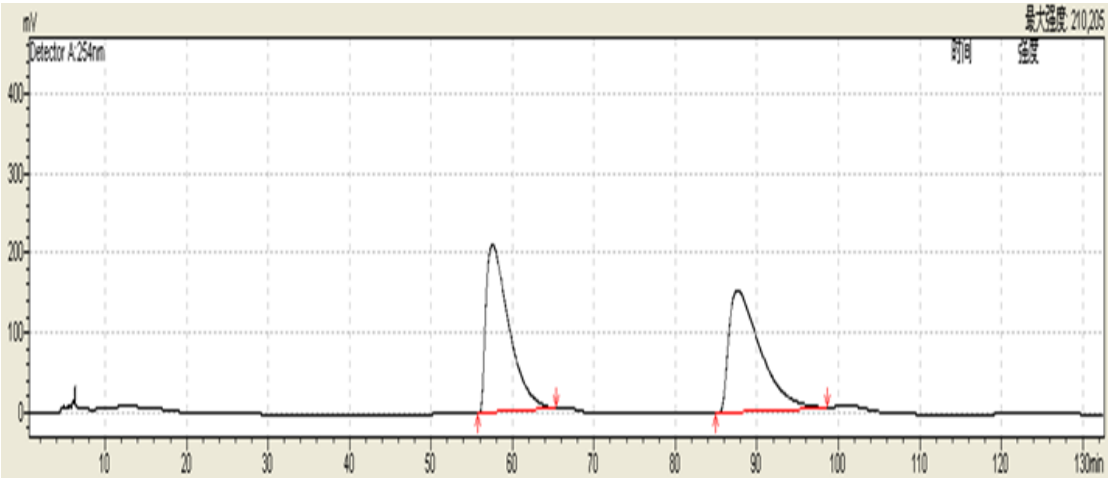
Peak	Retention time	Area (%)
1	39.360	50.003
2	63.153	49.997



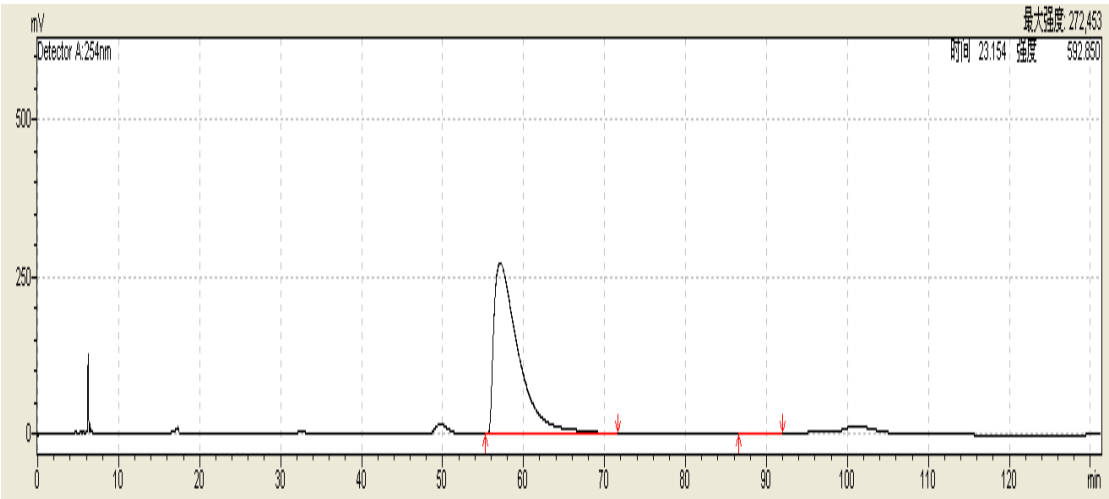
Peak	Retention time	Area (%)
1	37.065	99.910
2	63.130	0.090



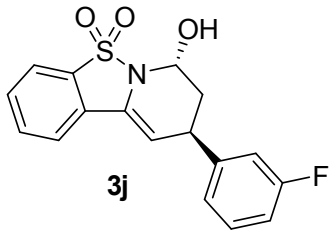
3i



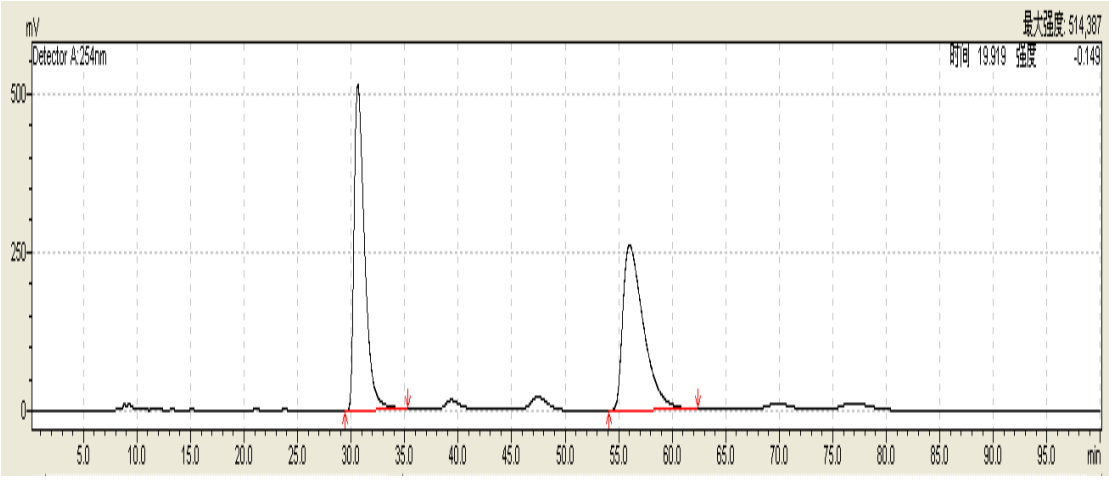
Peak	Retention time	Area (%)
1	57.512	50.107
2	87.641	49.893



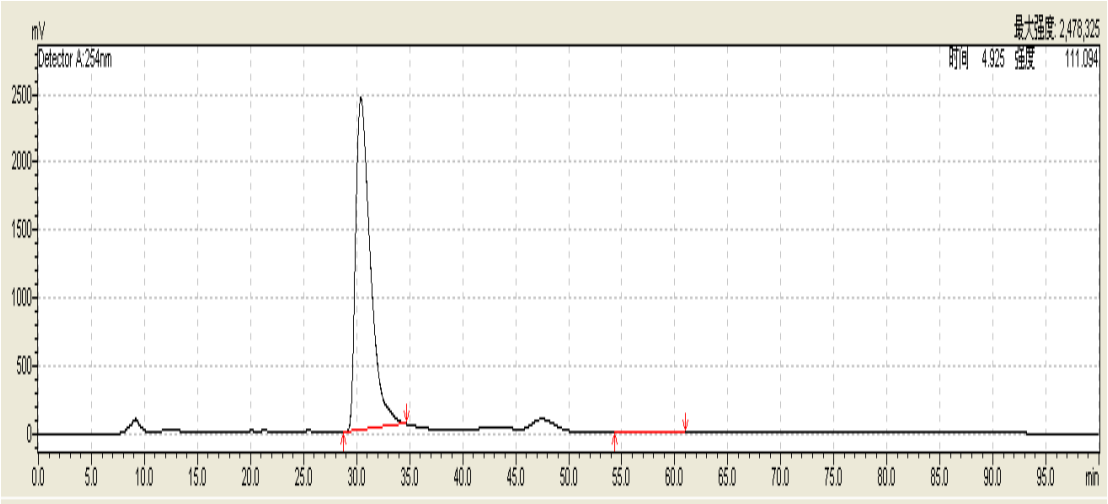
Peak	Retention time	Area (%)
1	57.115	99.818
2	89.747	0.182



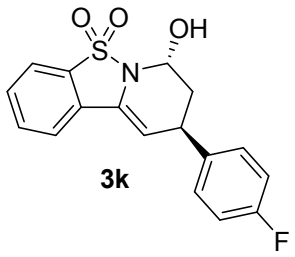
3j



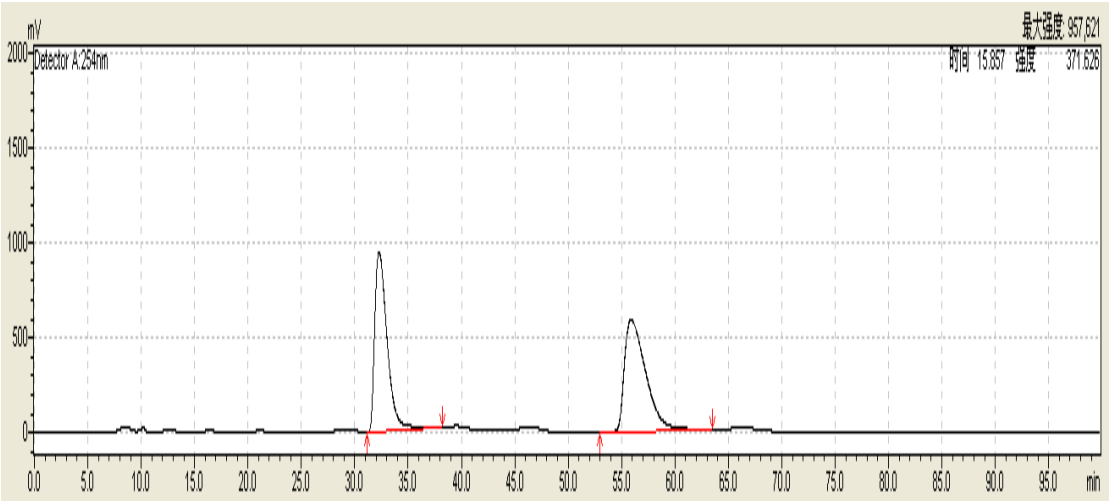
Peak	Retention time	Area (%)
1	30.621	50.053
2	56.012	49.947



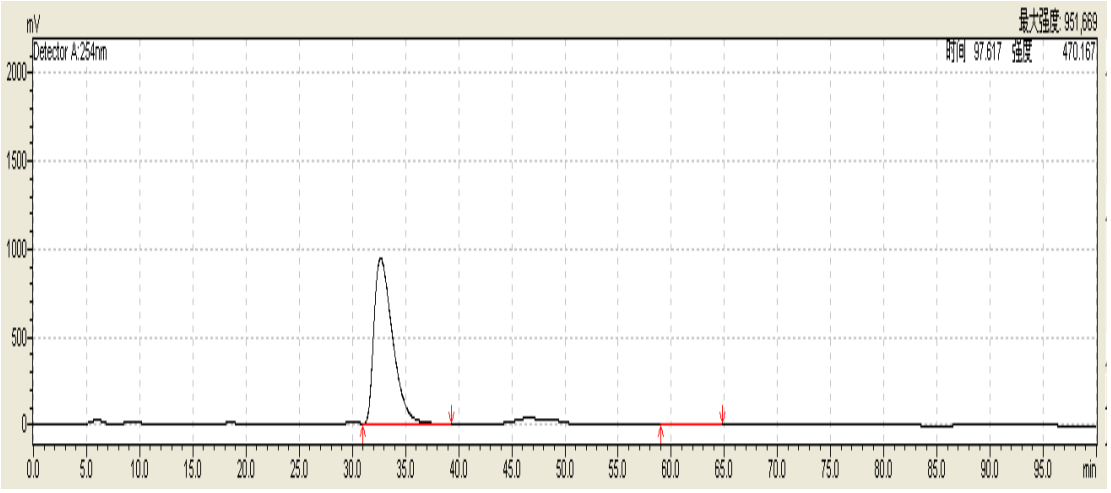
Peak	Retention time	Area (%)
1	30.4000	99.754
2	56.808	0.246



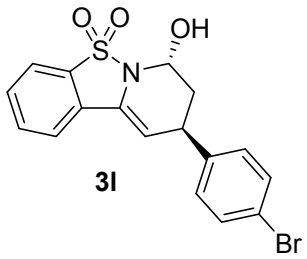
3k



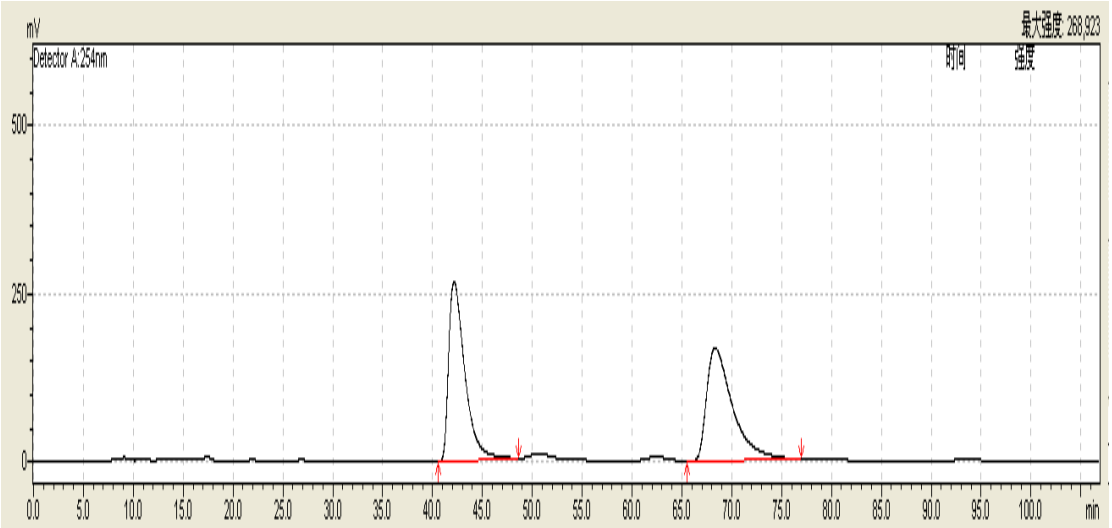
Peak	Retention time	Area (%)
1	32.282	49.644
2	55.903	50.356



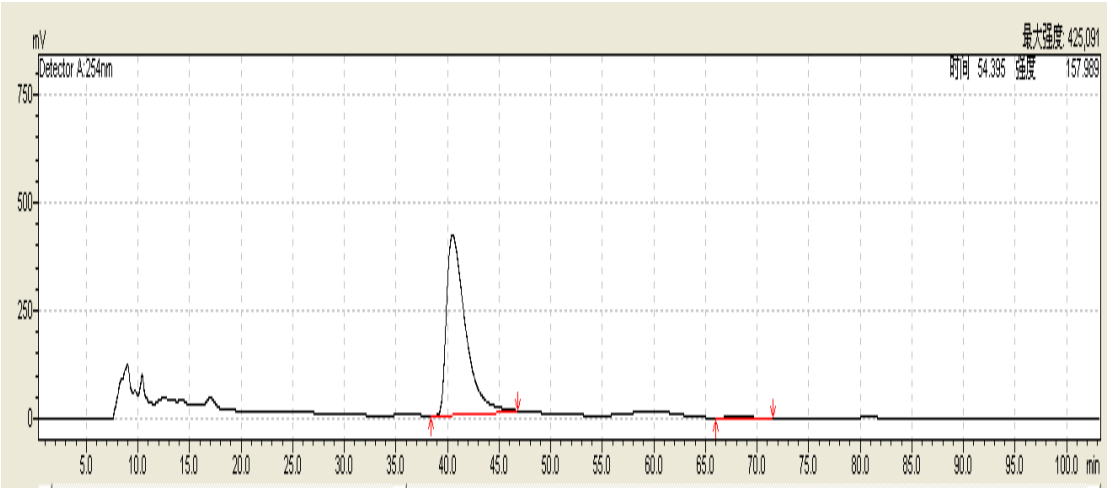
Peak	Retention time	Area (%)
1	32.653	99.295
2	61.131	0.705



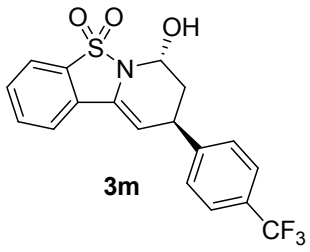
3l



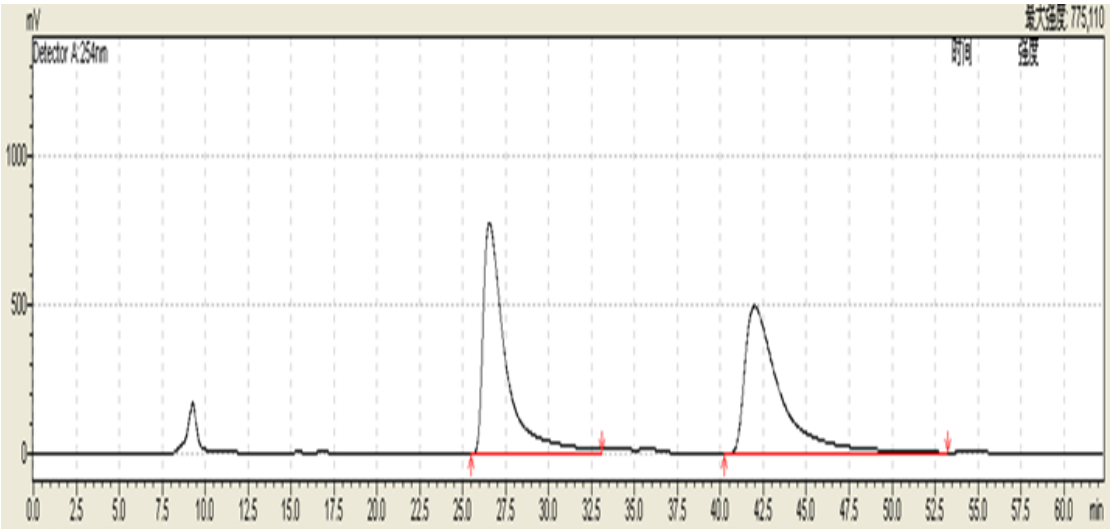
Peak	Retention time	Area (%)
1	42.154	49.634
2	68.335	50.366



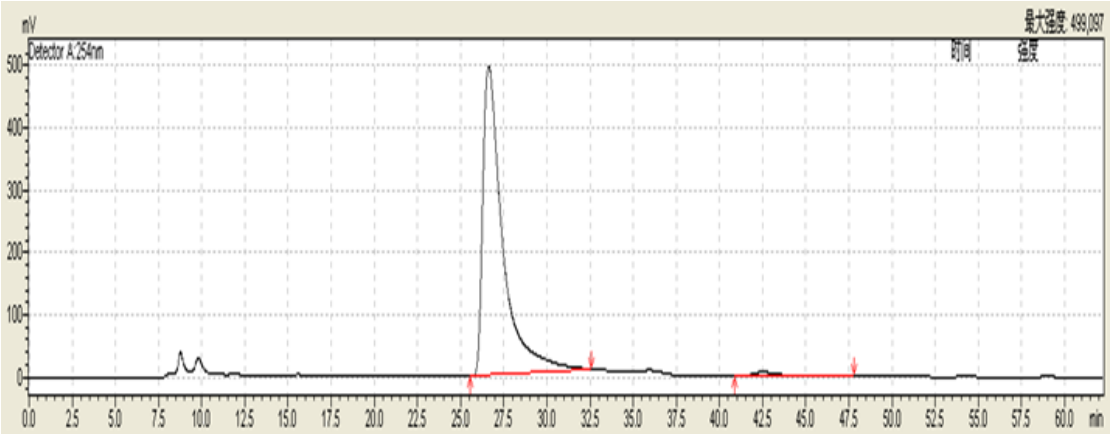
Peak	Retention time	Area (%)
1	40.486	99.356
2	68.166	0.644



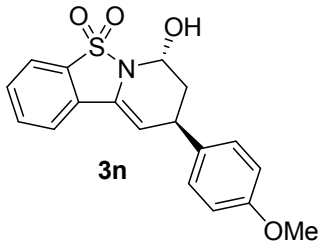
3m



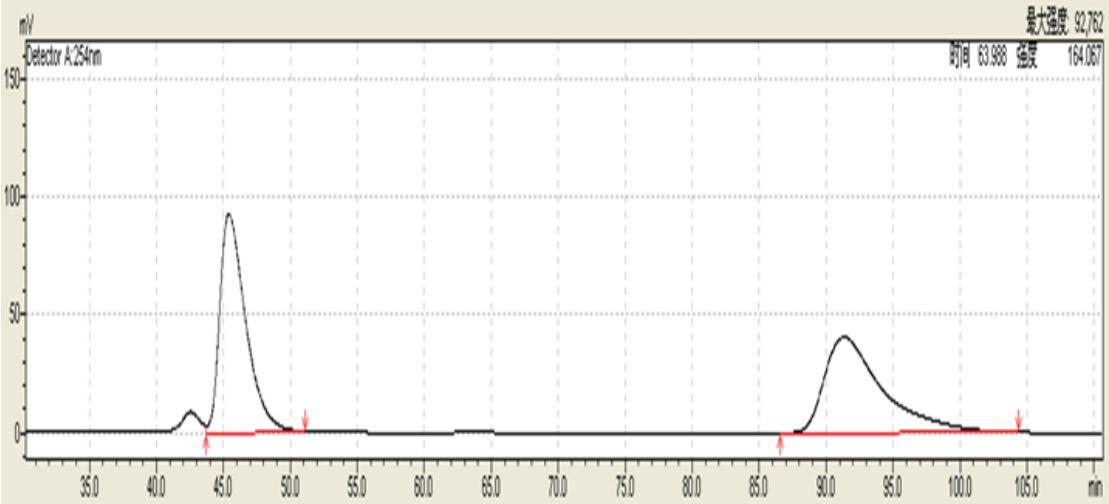
Peak	Retention time	Area (%)
1	26.547	50.373
2	41.984	49.627



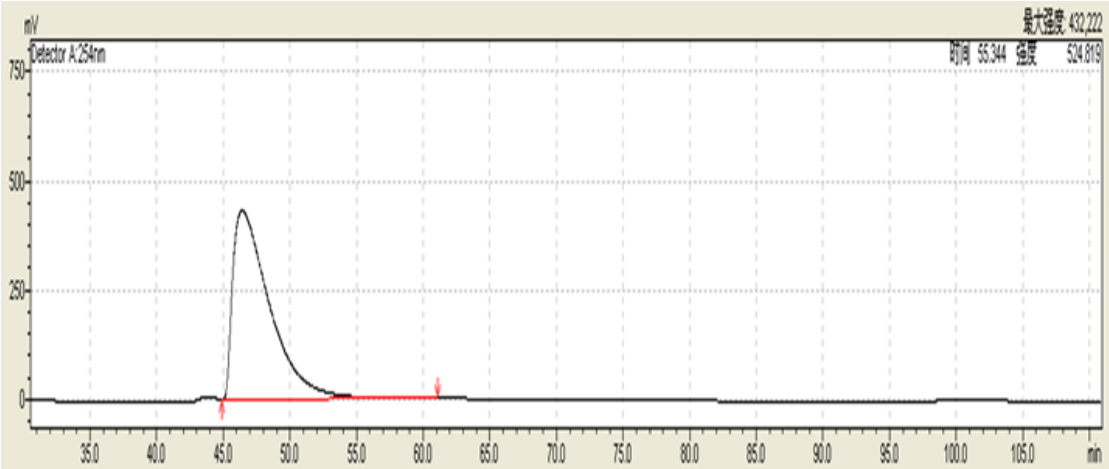
Peak	Retention time	Area (%)
1	26.622	98.050
2	42.520	1.950



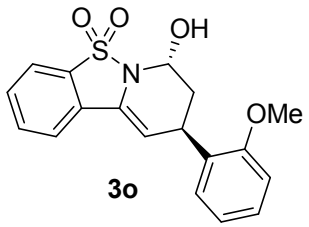
3n



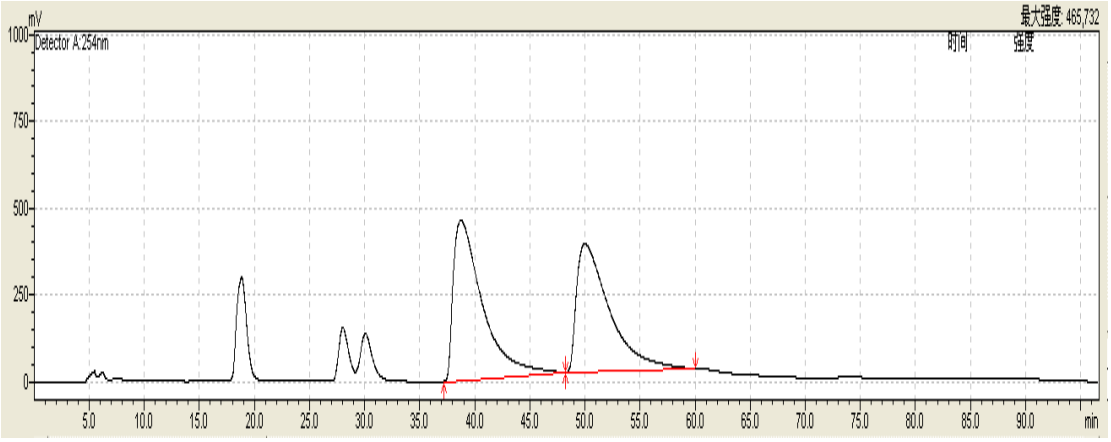
Peak	Retention time	Area (%)
1	45.415	50.284
2	91.343	49.716



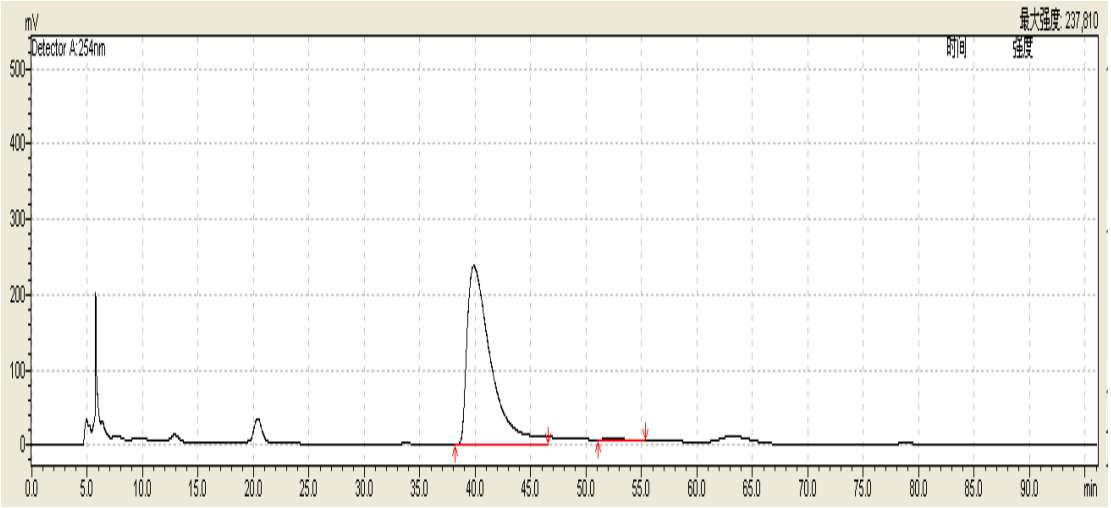
Peak	Retention time	Area (%)
1	46.420	100
2	-	0



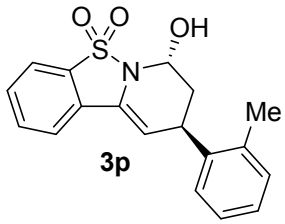
3o



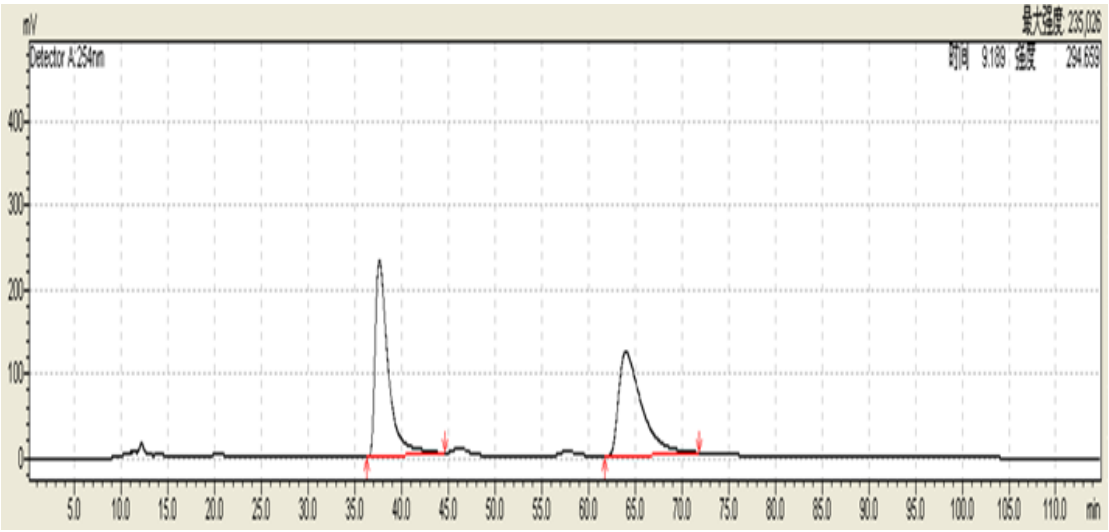
Peak	Retention time	Area (%)
1	38.749	49.564
2	49.998	50.436



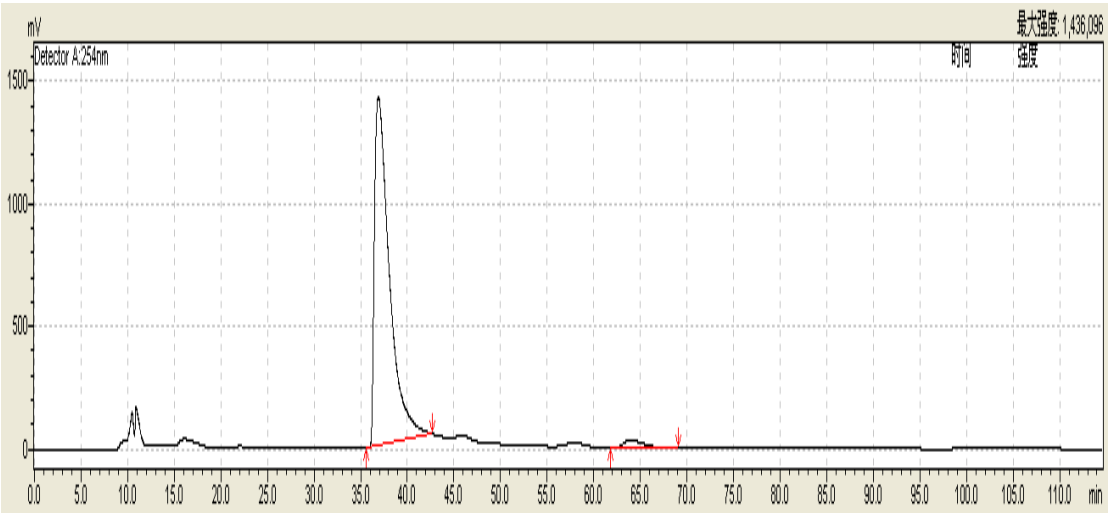
Peak	Retention time	Area (%)
1	39.868	99.399
2	52.461	0.601



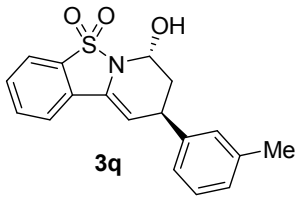
3p



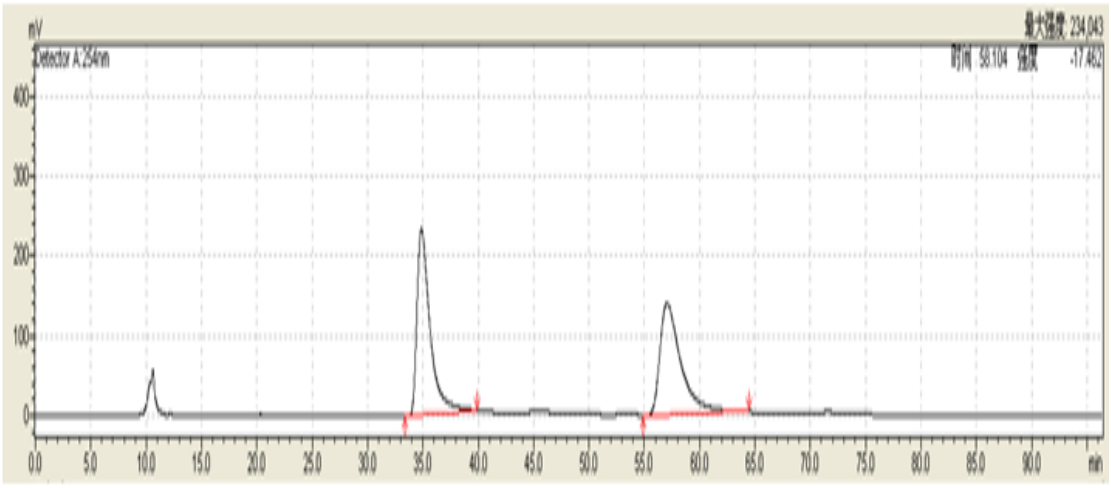
Peak	Retention time	Area (%)
1	37.638	49.748
2	64.021	50.252



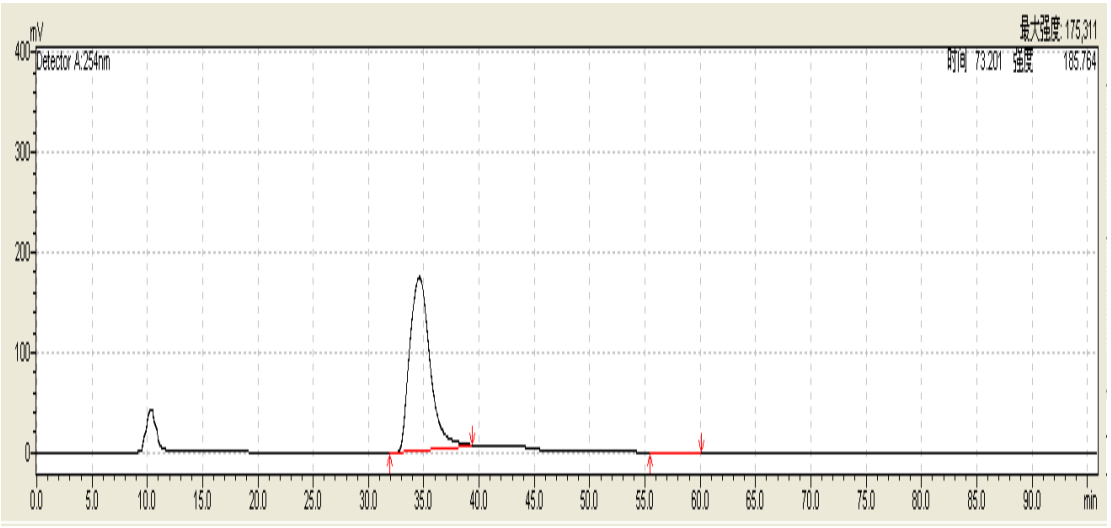
Peak	Retention time	Area (%)
1	36.900	97.159
2	64.023	2.841



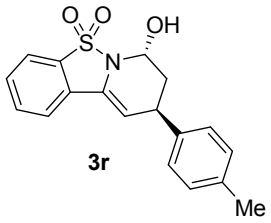
3q



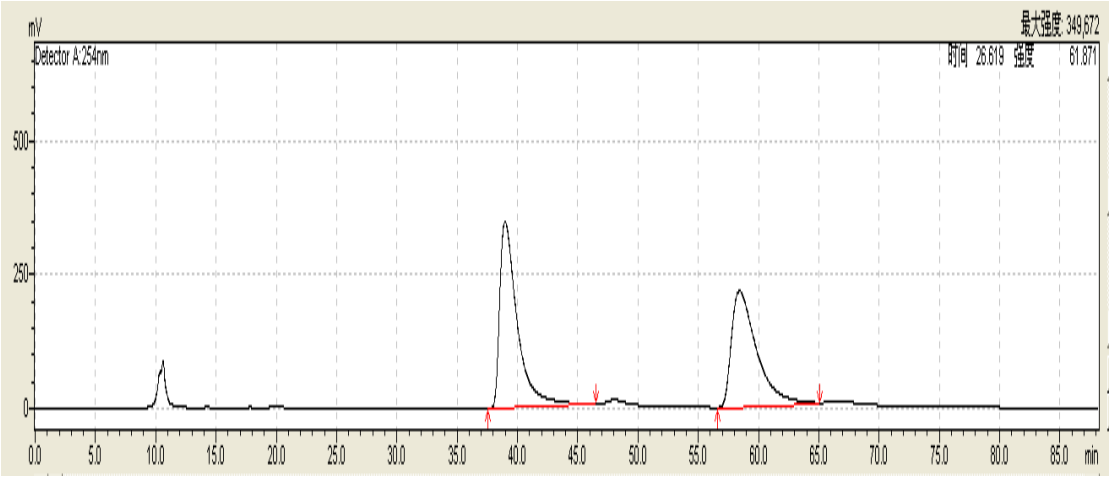
Peak	Retention time	Area (%)
1	34.866	50.002
2	57.053	49.998



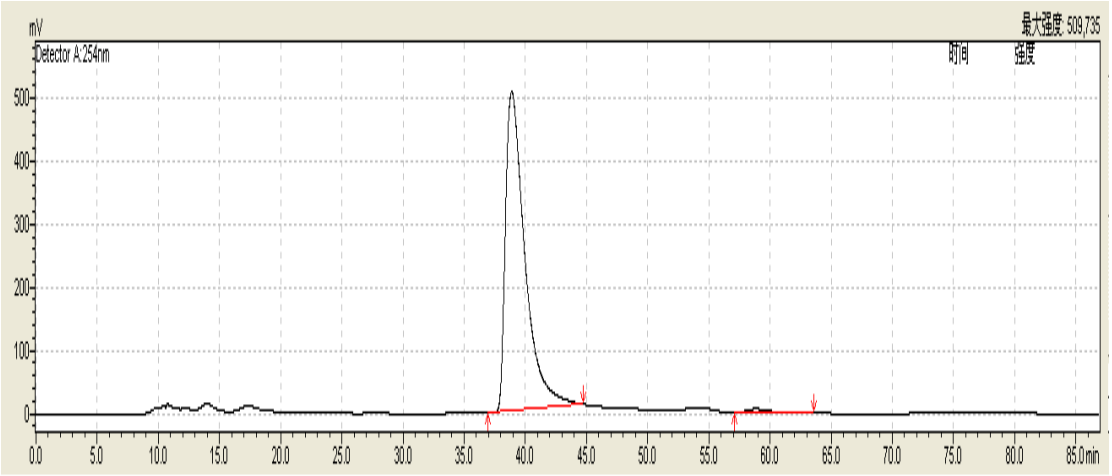
Peak	Retention time	Area (%)
1	34.601	99.448
2	57.237	0.552



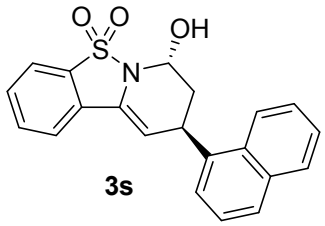
3r



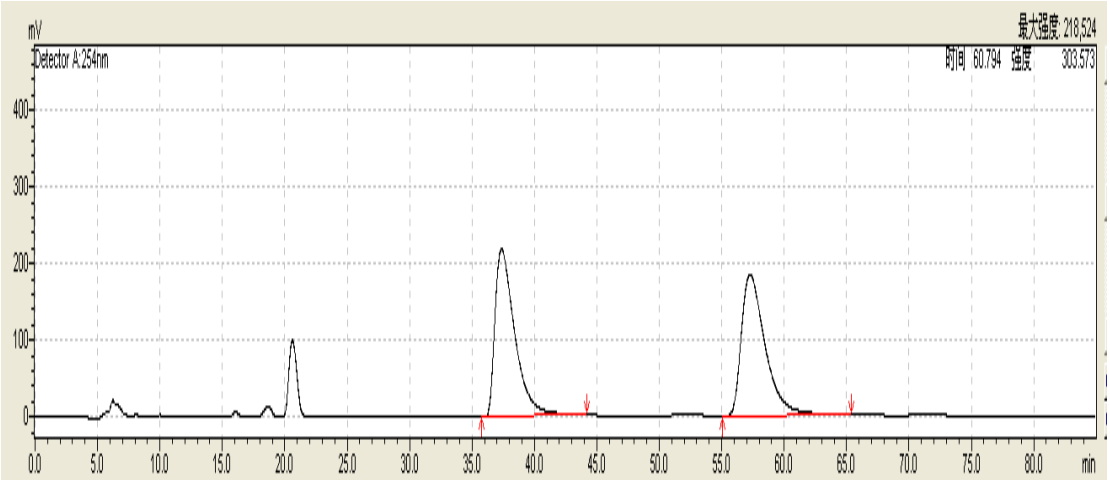
Peak	Retention time	Area (%)
1	38.975	49.992
2	58.422	50.008



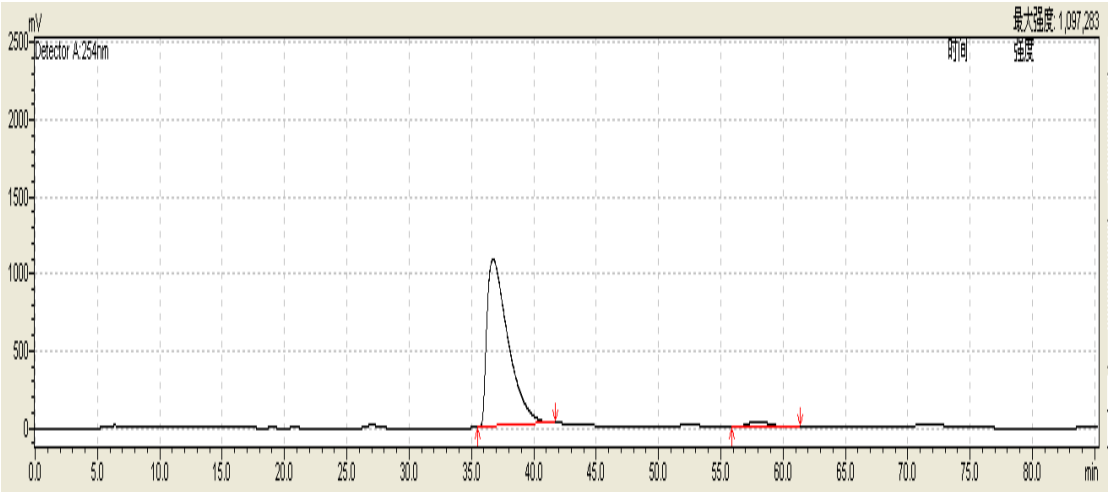
Peak	Retention time	Area (%)
1	38.881	98.677
2	58.867	1.323



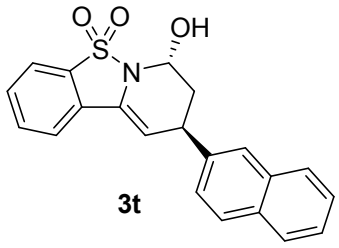
3s



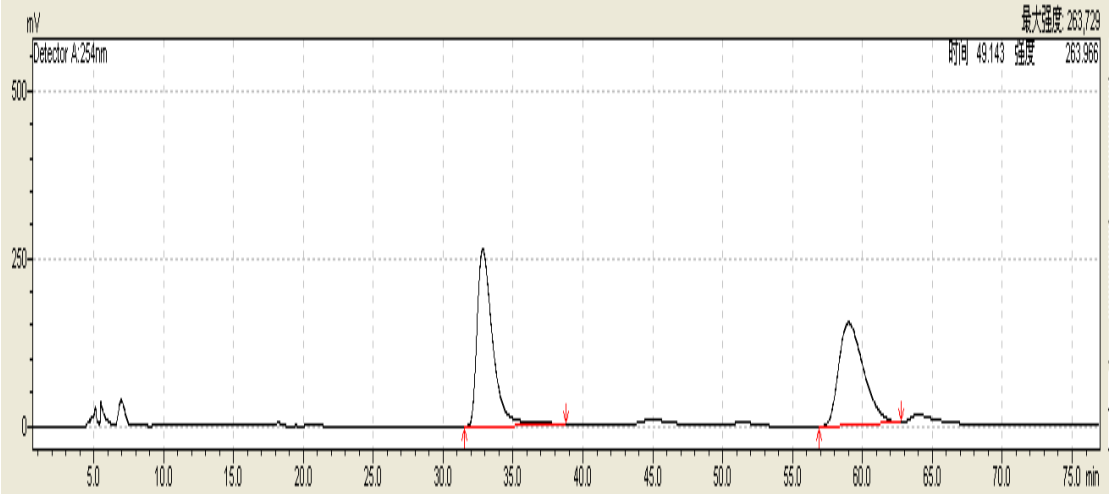
Peak	Retention time	Area (%)
1	37.360	49.712
2	57.259	50.288



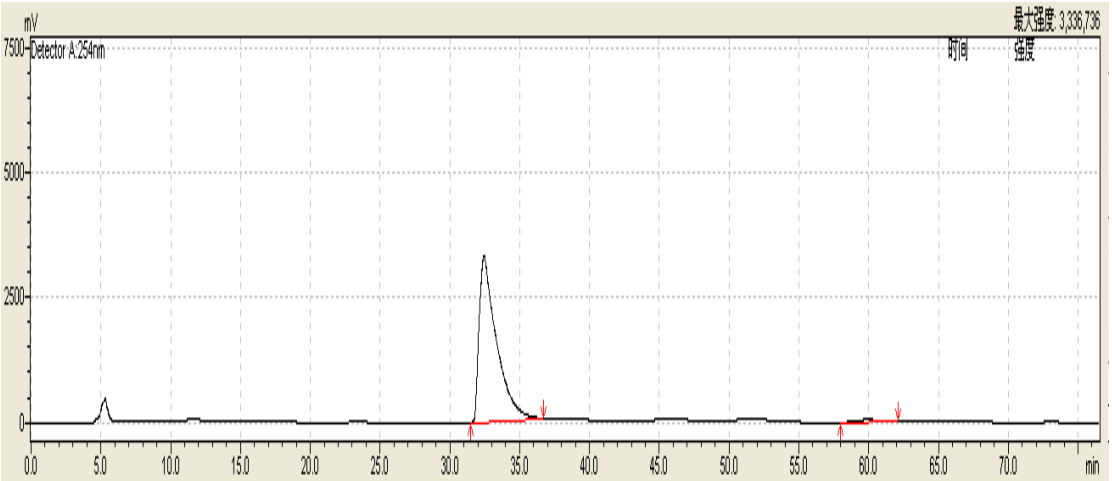
Peak	Retention time	Area (%)
1	36.725	96.917
2	57.911	3.083



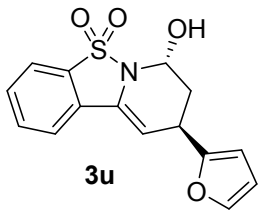
3t



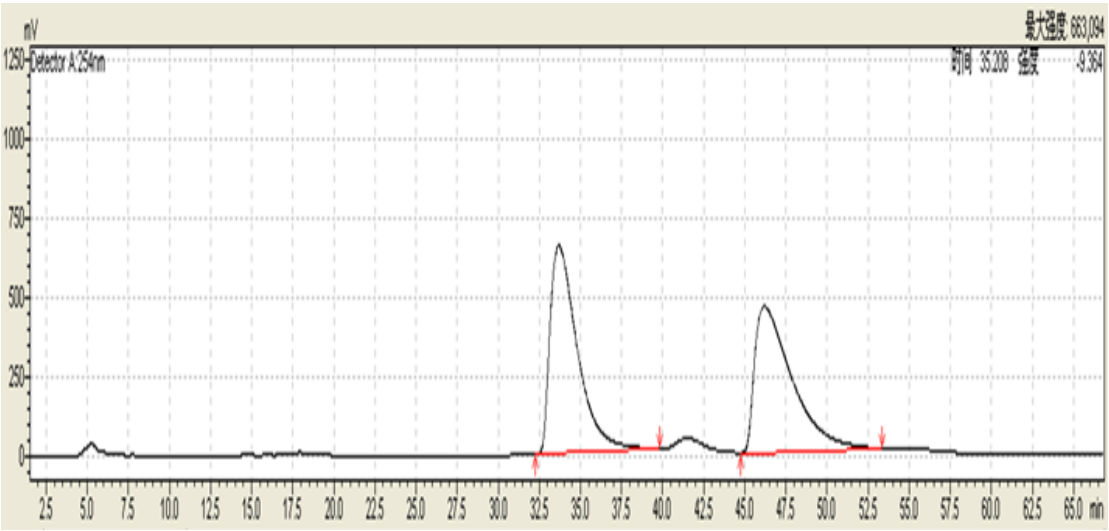
Peak	Retention time	Area (%)
1	32.828	50.258
2	59.003	49.742



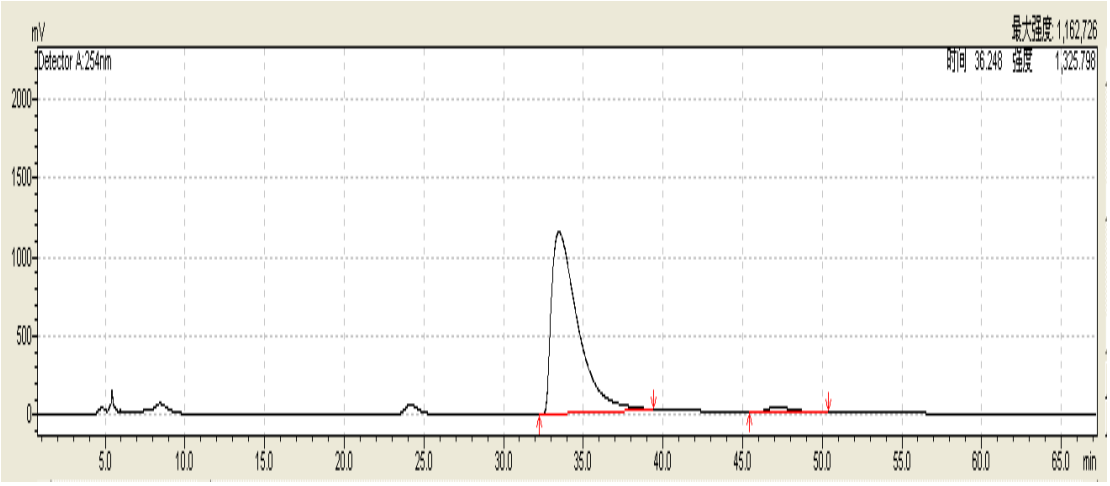
Peak	Retention time	Area (%)
1	32.443	98.350
2	59.936	1.650



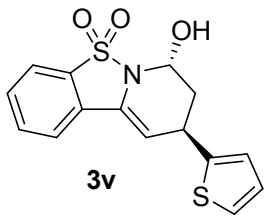
3u



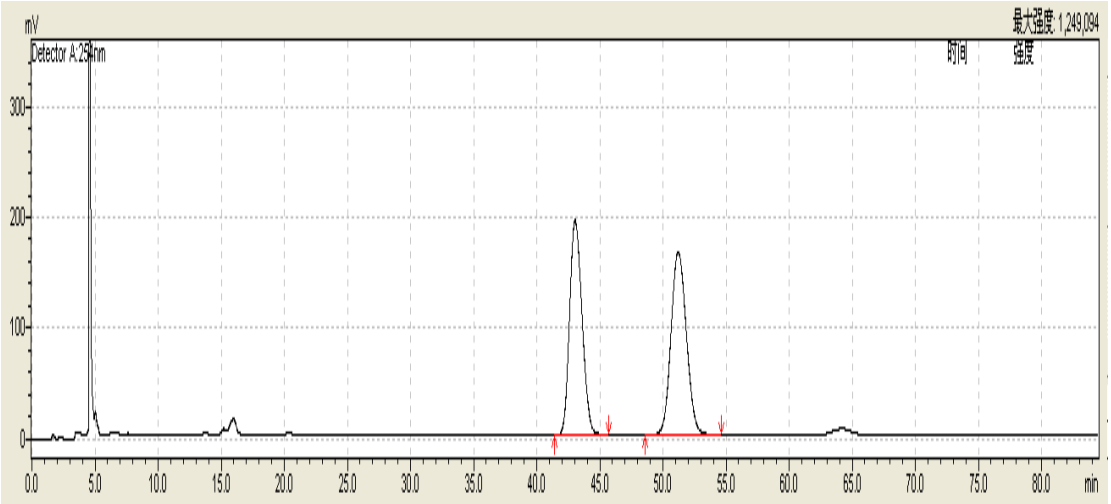
Peak	Retention time	Area (%)
1	33.687	50.000
2	46.190	50.000



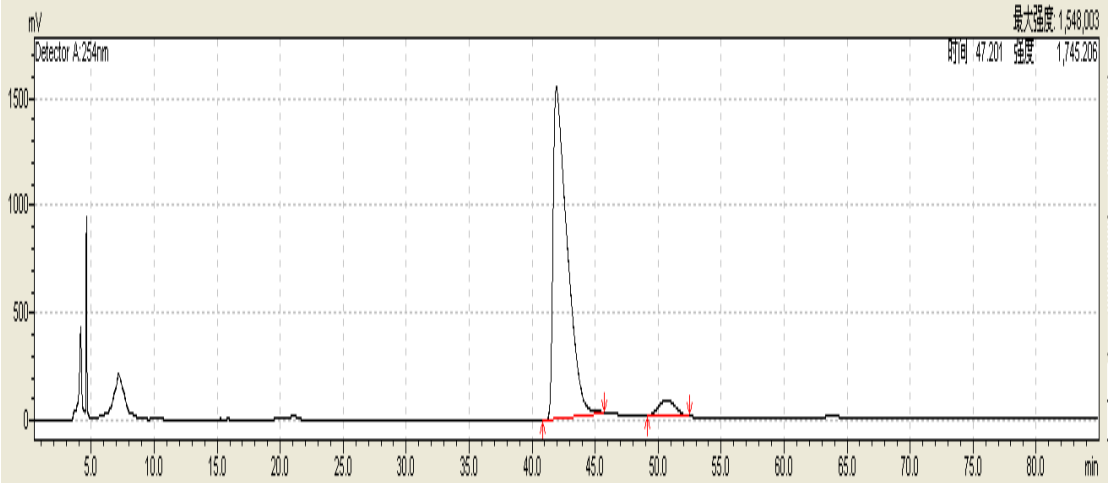
Peak	Retention time	Area (%)
1	33.473	97.399
2	47.182	2.601



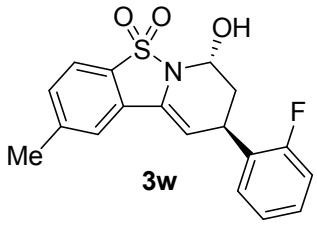
3v



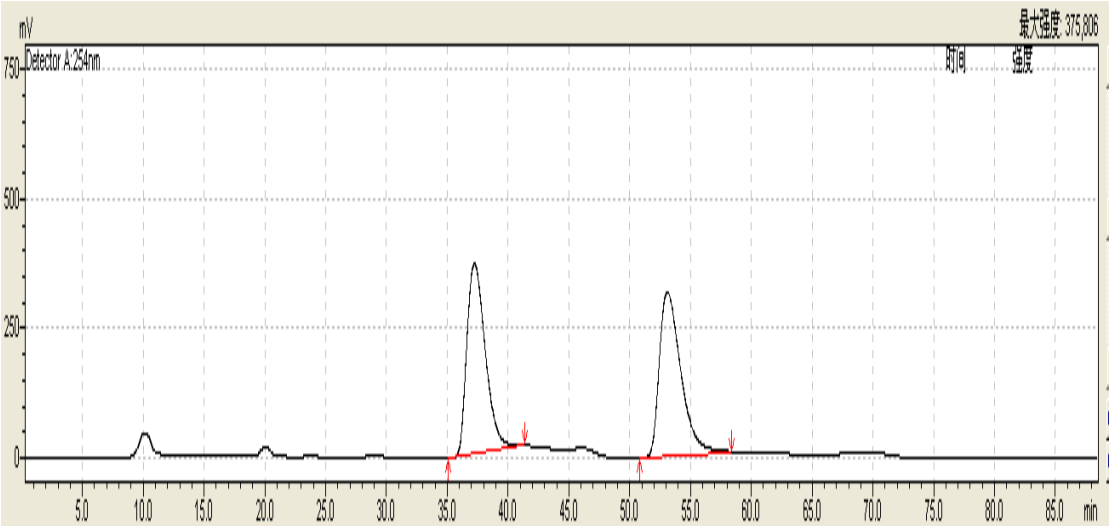
Peak	Retention time	Area (%)
1	43.039	49.360
2	51.209	50.640



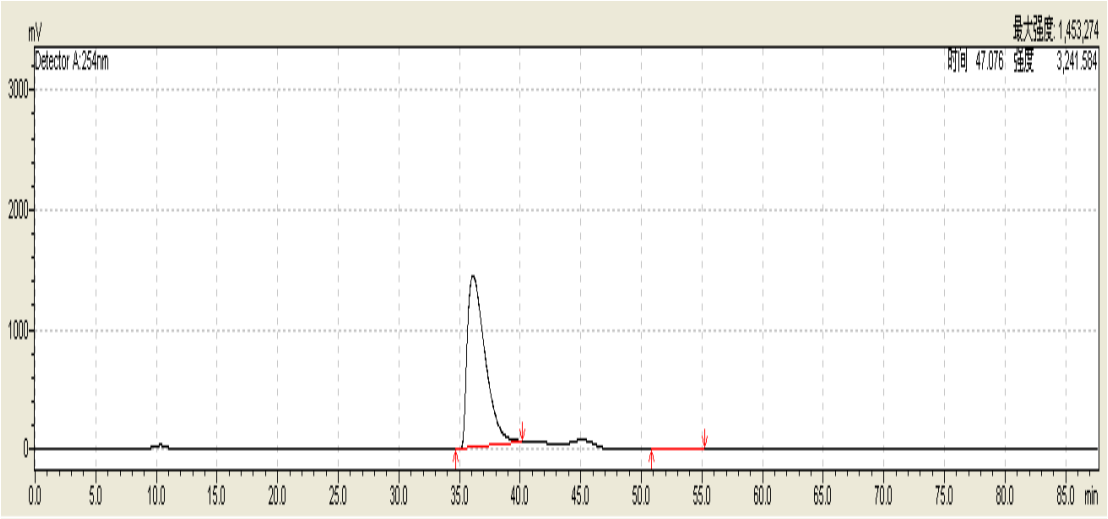
Peak	Retention time	Area (%)
1	41.918	94.845
2	50.686	5.155



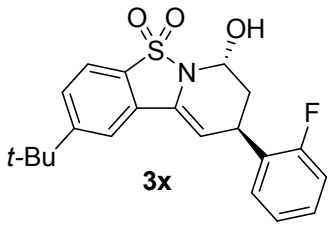
3w



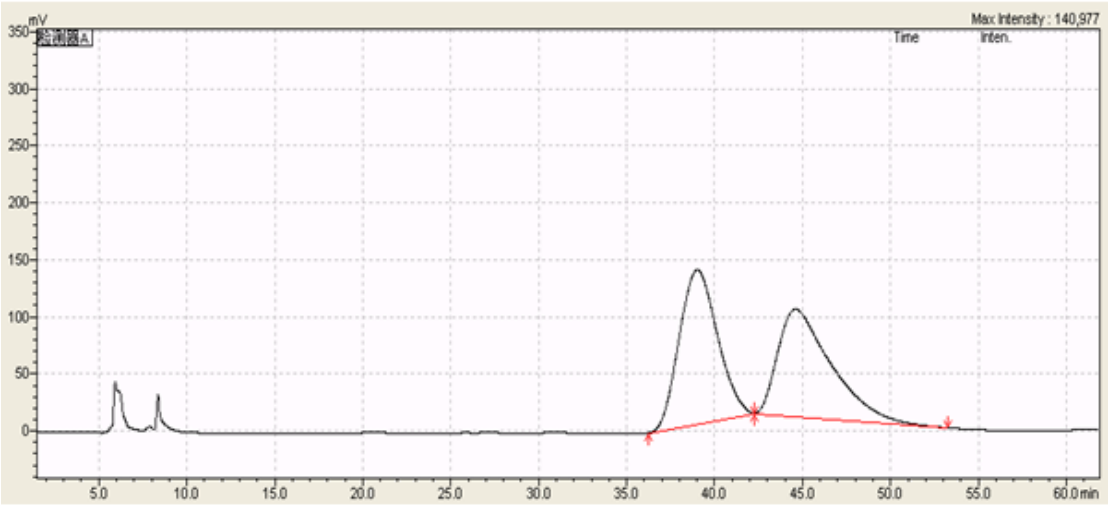
Peak	Retention time	Area (%)
1	37.239	49.797
2	53.095	50.203



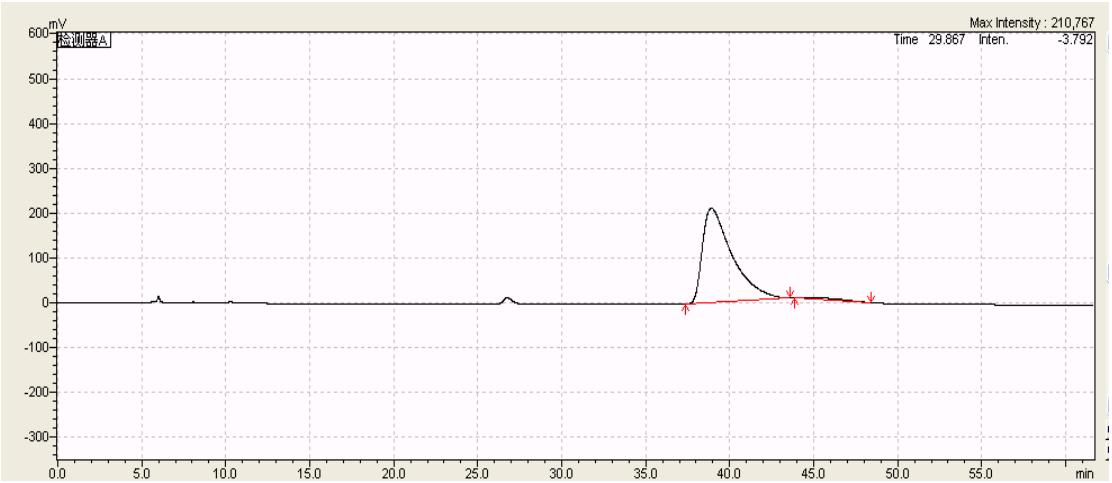
Peak	Retention time	Area (%)
1	36.108	99.700
2	52.810	0.300



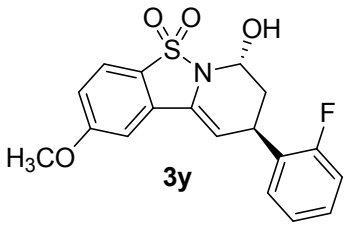
3x



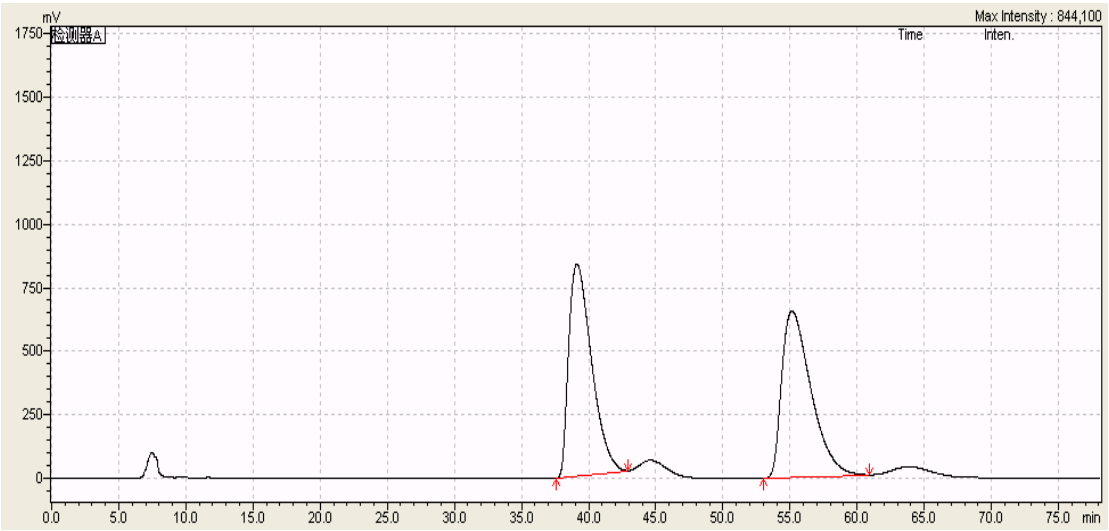
Peak	Retention time	Area (%)
1	39.023	50.684
2	44.604	49.316



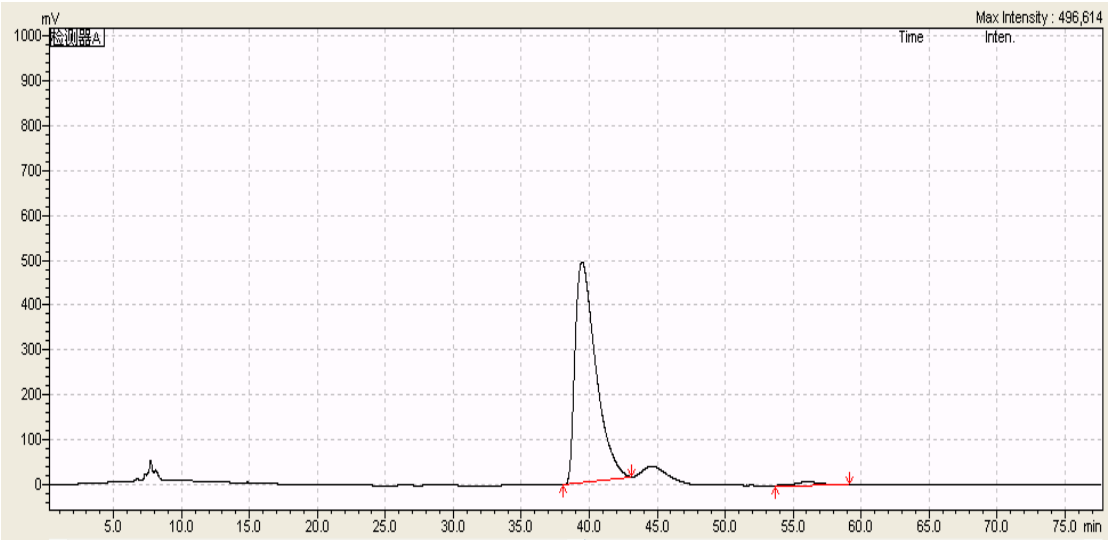
Peak	Retention time	Area (%)
1	38.911	97.729
2	44.583	2.271



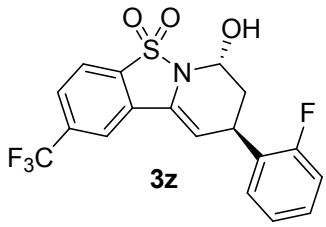
3y



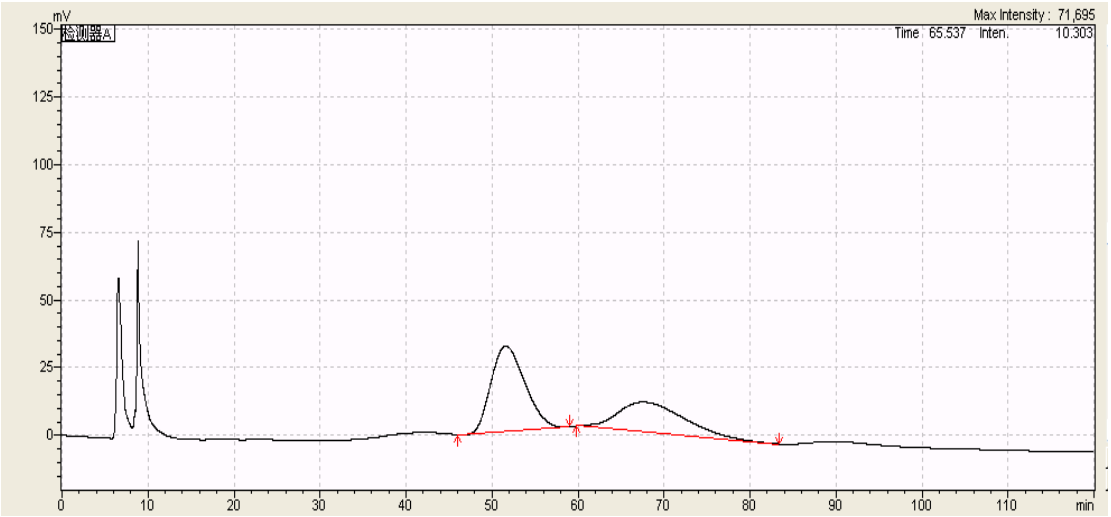
Peak	Retention time	Area (%)
1	39.126	49.862
2	55.144	50.138



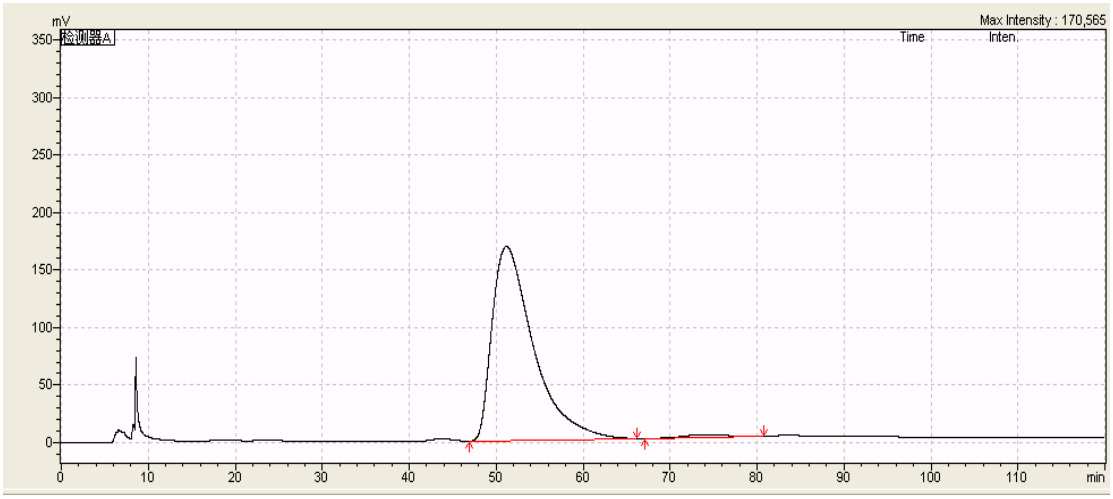
Peak	Retention time	Area (%)
1	39.466	98.310
2	56.076	1.690



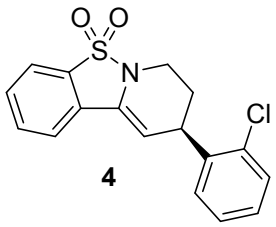
3z



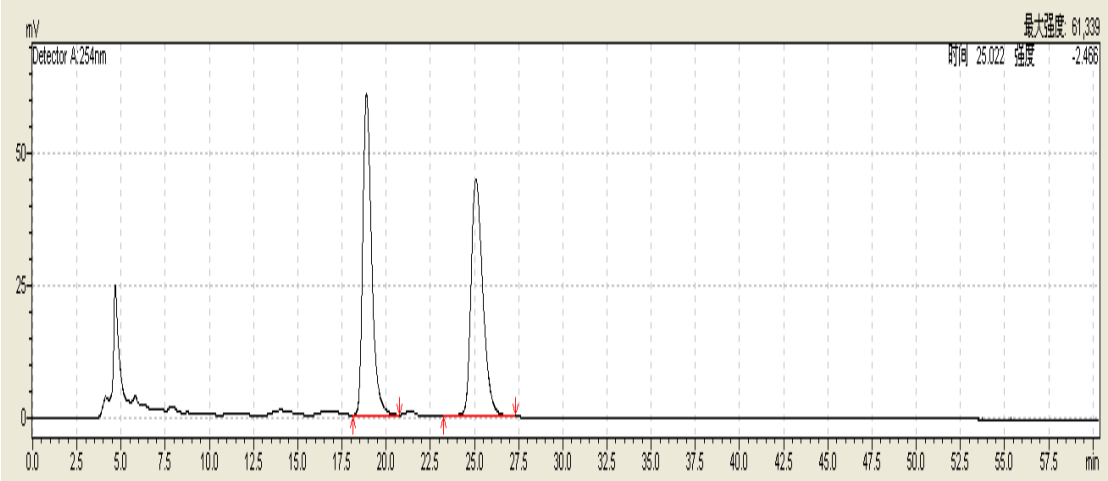
Peak	Retention time	Area (%)
1	51.604	50.905
2	67.565	49.095



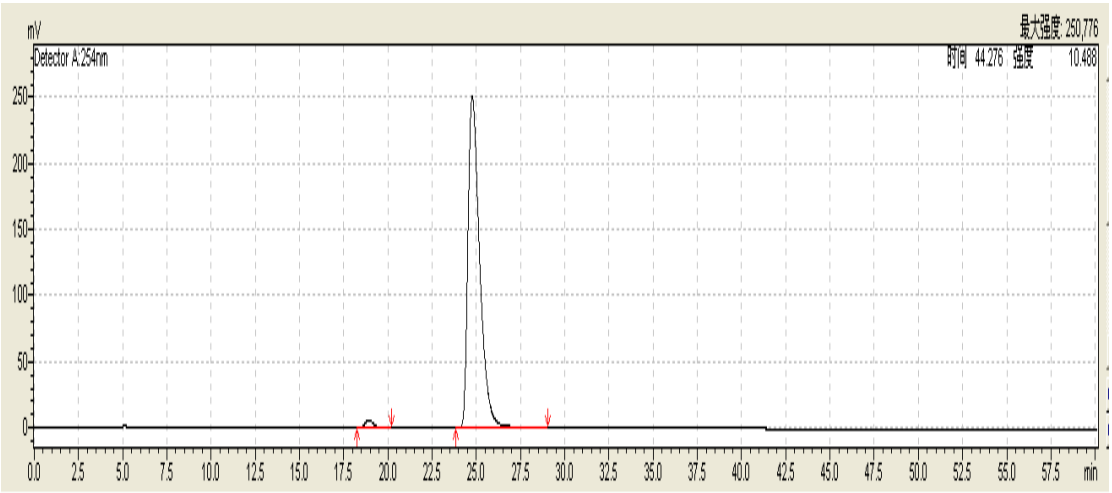
Peak	Retention time	Area (%)
1	51.174	98.804
2	74.112	1.196



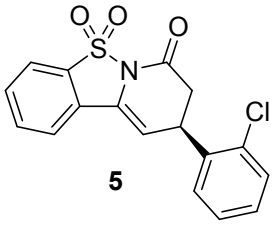
4



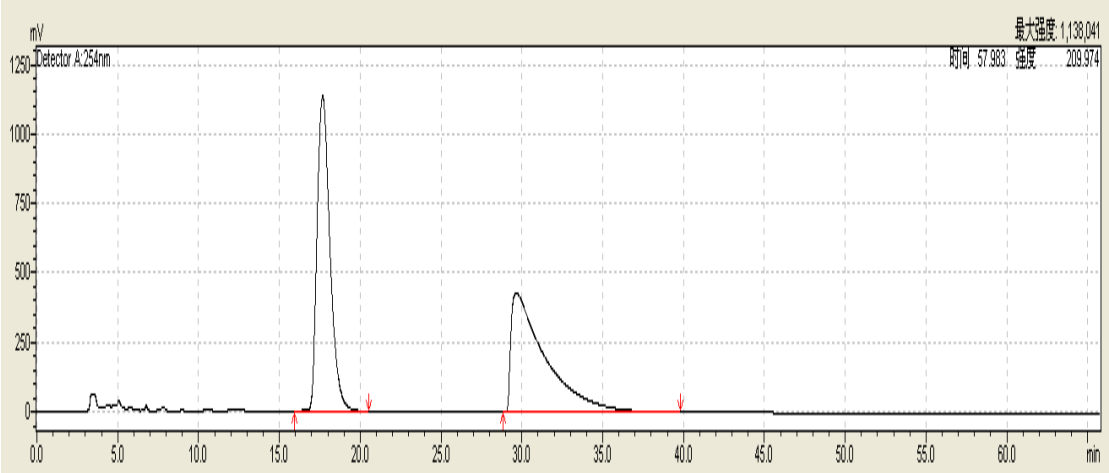
Peak	Retention time	Area (%)
1	18.885	50.208
2	25.081	49.792



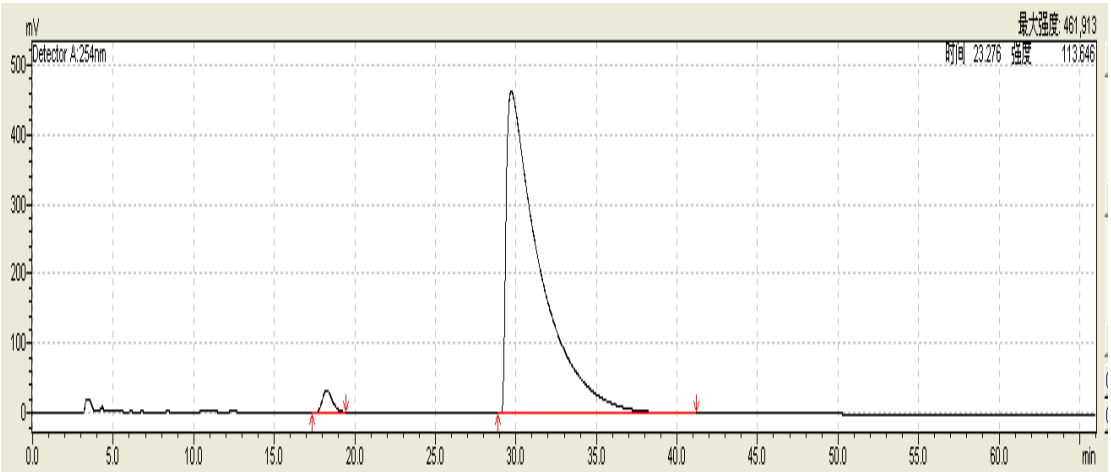
Peak	Retention time	Area (%)
1	18.911	1.731
2	24.766	98.269



5



Peak	Retention time	Area (%)
1	17.675	49.786
2	29.645	50.214



Peak	Retention time	Area (%)
1	18.241	2.088
2	29.712	97.912