

# **Co(II)/SpiroBox-catalyzed Enantioselective Mukaiyama-Mannich Reaction for the Synthesis of Quaternary $\alpha$ -Amino Acid Derivatives**

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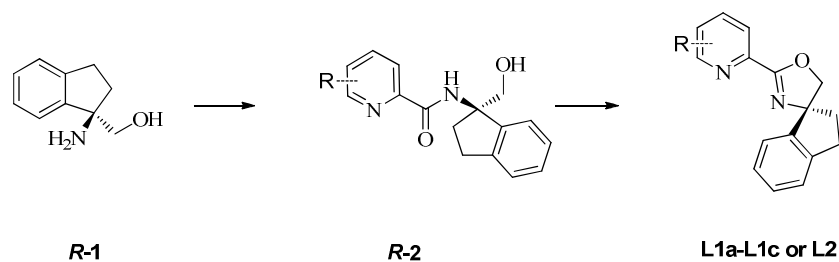
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## 1. Experimental Section

### 1.1. General

All the reagents were purchased from Aldrich, TCI, Energy chemical and other local suppliers, and used without purification. Toluene, methanol, dichloromethane, chloroform, acetonitrile and tetrahydrofuran were used without purification unless otherwise stated. All reactions were monitored by TLC. Chromatography refers to open column chromatography on silica gel (200-300mesh). <sup>1</sup>H NMR spectra were recorded on 500 or 400 MHz, <sup>13</sup>C NMR spectra were recorded on 126 or 101 MHz by using a Bruker Avance spectrometer. Chemical shifts were reported in parts per million (δ) relative to tetramethylsilane (TMS). Mass spectra were performed on an Ultima Global spectrometer with an ESI source. Optical rotations were measured on Rudolph Autopol IV-Tautomatic polarimeter and reported as follows:  $[\alpha]_D^{20}$  (c g/100 mL, solvent). Chiral HPLC analysis was performed using a Shimadzu LC-20AT UFLC. Substrates silyl enol ethers were synthesized according to the already reported literatures<sup>[1]</sup>. Substrates cyclic *N*-sulfonyl ketimino ester were synthesized according to the known procedures<sup>[2]</sup>. The (*R*)-indane-based chiral amino alcohol was synthesized according to reported literature<sup>[3]</sup> and our pioneering studies<sup>[4]</sup>.

## 1.2. General procedure for synthesis of ligands **L1a-L1c** and **L2**



To a solution of substituted 2-pyridine carboxylic acid or 2-Quinoline carboxylic acid (2.62 mmol) in anhydrous DCM (10 mL) was added *N*-hydroxybenzotriazole (HOBT) (2.88 mmol), *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDCI·HCl) (2.88 mol), and triethylamine (4.32 mmol) at 0 °C sequentially. The reaction mixture was stirred at room temperature for 1 hour. Then chiral amino alcohol **R-1** (2.62 mmol) was added and the reaction mixture was allowed warm to room temperature and stirred for 3 hours. The solvent was evaporated to obtain the intermediate **R-2**. The intermediate **R-2** was used directly without further purification. To a solution of triphenylphosphine (3.14 mmol), and 2,3-dichloro-5,6-dicyano-1,4-benzoquinon (DDQ, 3.14 mmol) in DCM (10 mL) was added the intermediate **R-2** slowly at 0 °C. The reaction mixture was warmed to room temperature and monitored by TLC. The reaction mixture was filtrated through celite, washed with 5% sodium hydroxide. The aqueous phase was extracted with DCM. The combined organic layers were dried over anhydrous sodium sulfate, filtrated, and concentrated under reduced pressure. The residue was purified by chromatography with petroleum ether/ethyl acetate 3:1 (v/v) to give **L1a-L1c** or **L2**.

**(R)-2'-(Pyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole] (L1a)** Yellow oil,  $[\alpha]_{\text{D}}^{20} = +70.2$  (c = 0.4, MeOH), 49% yield.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.74 (d,  $J = 4.9$  Hz, 1H), 8.13 (d,  $J = 7.9$  Hz, 1H), 7.78 (t,  $J = 7.8$  Hz, 1H), 7.43-7.40 (m, 1H), 7.27 (d,  $J = 11.5$  Hz, 4H), 4.69 (d,  $J = 8.8$  Hz, 1H), 4.59 (d,  $J = 8.8$  Hz, 1H), 3.23-3.18 (m, 1H), 3.00-2.98 (m, 1H), 2.59-2.55 (m, 1H), 2.30-2.26 (m, 1H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  162.36, 149.96, 147.02, 145.93, 143.61, 136.83, 128.49, 127.39, 125.83, 124.92, 124.39, 123.60, 81.21, 79.12, 40.38, 30.44. HRMS (ESI): calcd for  $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}$   $[\text{M}+\text{Na}]^+$  : 273.1004, found 273.1008.

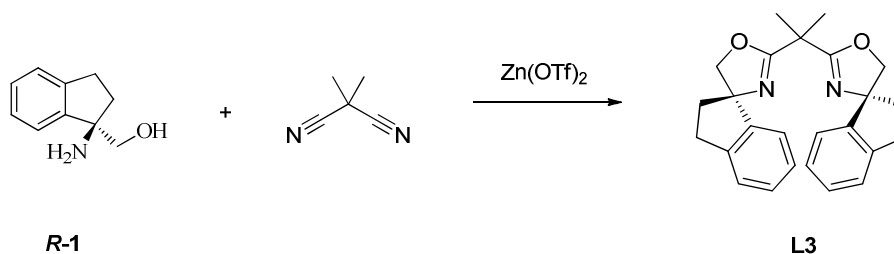
**(R)-2'-(5-(Trifluoromethyl)pyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole] (L1b)** White solid, m.p.: 104.5-105.3 °C,  $[\alpha]_{\text{D}}^{20} = +87.5$  (c = 0.2, MeOH), 55% yield.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.90 (s, 1H), 8.17 (d,  $J = 8.2$  Hz, 1H), 7.95 (dd,  $J = 8.3, 2.3$  Hz, 1H), 7.23-7.12 (m, 4H), 4.64 (d,  $J = 8.8$  Hz, 1H), 4.53 (d,  $J = 8.9$  Hz, 1H), 3.17-3.11 (m, 1H), 2.92-2.89 (m, 1H), 2.53-2.47 (m, 1H), 2.23-2.18 (m, 1H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  161.09, 149.96, 146.62 (q,  $J = 4.1$  Hz), 145.32, 143.46, 133.96 (q,  $J = 3.6$  Hz), 128.49, 128.10 (q,  $J = 33.2$  Hz), 127.27, 124.83, 123.94, 123.31, 123.14 (q,  $J = 273.4$  Hz), 81.24, 79.09, 40.14, 30.25. HRMS (ESI): calcd for  $\text{C}_{17}\text{H}_{13}\text{F}_3\text{N}_2\text{O}$   $[\text{M}+\text{Na}]^+$  : 341.0878, found 341.0883.

**(R)-2'-(5-Methoxypyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole] (L1c)** White solid, m.p.: 107.7-108.5 °C,  $[\alpha]_{\text{D}}^{20} = +46.4$  (c = 0.2, MeOH), 56% yield.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.40 (d,  $J = 2.9$  Hz, 1H), 8.08 (d,  $J = 8.7$  Hz, 1H), 7.28-7.20 (m, 5H), 4.65 (d,  $J = 8.7$  Hz, 1H), 4.56 (d,  $J = 8.4$  Hz, 1H), 3.92 (s, 3H),

3.24-3.18 (m, 1H), 3.01-2.95 (m, 1H), 2.59-2.54 (m, 1H), 2.30-2.25 (m, 1H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  161.96, 157.23, 145.95, 143.37, 139.11, 137.81, 128.20, 127.16, 125.15, 124.69, 123.41, 120.08, 80.91, 78.87, 55.75, 40.20, 30.24. HRMS (ESI): calcd for  $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_2$   $[\text{M}+\text{H}]^+$ : 281.1290, found 281.1288,  $[\text{M}+\text{Na}]^+$ : 303.1109, found 303.1106.

**(R)-2'-(Quinolin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole] (L2)** White solid, m.p.: 132.5-133.2 °C,  $[\alpha]_{\text{D}}^{20} = +89.7$  (c = 0.3, MeOH), 67% yield.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.31 (d,  $J = 8.5$  Hz, 1H), 8.27-8.22 (m, 2H), 7.87 (d,  $J = 8.2$  Hz, 1H), 7.78 (t,  $J = 7.8$  Hz, 1H), 7.62 (t,  $J = 7.5$  Hz, 1H), 7.29-7.26 (m, 4H), 4.76 (d,  $J = 8.8$  Hz, 1H), 4.67 (d,  $J = 8.8$  Hz, 1H), 3.25-3.19 (m, 1H), 3.04-3.00 (m, 1H), 2.64-2.59 (m, 1H), 2.34-2.29 (m, 1H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  162.51, 147.63, 146.95, 145.74, 143.44, 136.72, 130.38, 130.08, 128.83, 128.38, 127.99, 127.57, 127.30, 124.80, 123.49, 121.14, 81.17, 79.27, 40.30, 30.30. HRMS (ESI): calcd for  $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}$   $[\text{M}+\text{Na}]^+$ : 323.1160, found 323.1162.

### 1.3. General procedure for synthesis of ligand L3

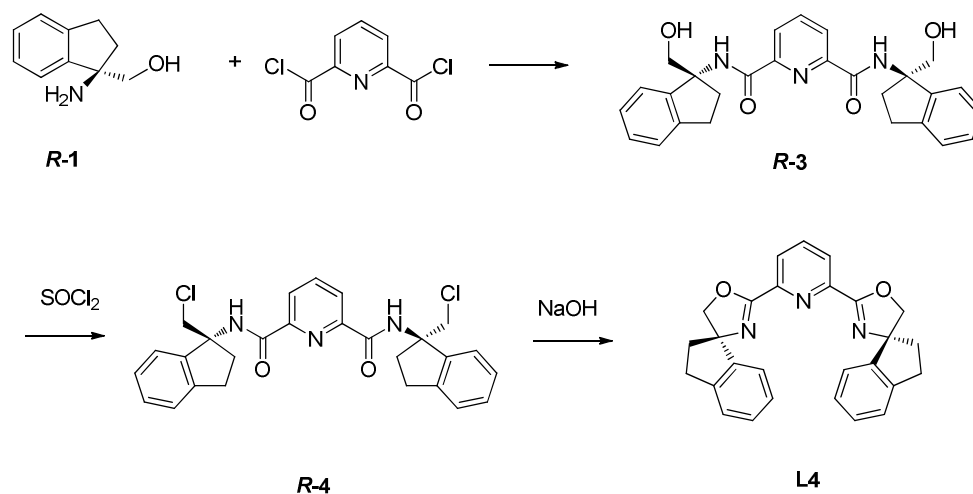


A 100-ml three-necked round-bottomed flask fitted with a reflux condenser was charged with 2, 2-dimethyl malononitrile (1.31 mmol),  $\text{Zn}(\text{OTf})_2$  (1.31 mmol) and

chiral amino alcohol *R*-1 (2.62 mmol). The system was purged with argon and toluene (50 mL) was added. The solution was heated under reflux for 48 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by chromatography with petroleum ether/ethyl acetate 3:1 (v/v) to give **L3**.

**Bis((*R*)-2,3-dihydro-5'*H*-spiro[indene-1,4'-oxazol]-2'-yl)propane (**L3**)** White solid, m.p.: 66.1-67.5 °C,  $[\alpha]_D^{20} = +18.4$  (c= 0.3, MeOH), 69% yield. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.25-7.16 (m, 8H), 4.40 (d, *J* = 8.5 Hz, 2H), 4.34 (d, *J* = 8.5 Hz, 2H), 3.13-3.07 (m, 2H), 2.97-2.90 (m, 2H), 2.53-2.47 (m, 2H), 2.21-2.15 (m, 2H), 1.64 (s, 6H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 169.05, 146.30, 142.98, 128.11, 127.19, 124.60, 123.31, 80.28, 79.48, 39.58, 38.72, 30.21, 24.66. HRMS (ESI): calcd for C<sub>25</sub>H<sub>27</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 387.2073, found 387.2065, [M+Na]<sup>+</sup>: 409.1892, found 409.1881.

#### 1.4. General procedure for synthesis of ligand **L4**



Pyridine-2,6-dicarboxylic acid (5 mmol) was treated with SOCl<sub>2</sub> (10 mL) at 80 °C over night. Excess SOCl<sub>2</sub> was then removed under reduced pressure to give the acid

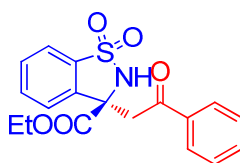
chloride as a white solid (100% yield). A solution of crude 2,6-pyridine carbonyl dichloride in DCM was slowly added to a solution of *R*-1 (10 mmol) and triethylamine (30 mmol) in DCM (20 mL) at 0 °C for 2h. The reaction mixture was warmed to room temperature, SOCl<sub>2</sub> (20 mmol) was added. The mixture was heated to reflux for 2 h and then poured into ice water. The organic layer was washed with brine and Na<sub>2</sub>CO<sub>3</sub> aqueous and then dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After evaporating the solvent, The solid was treated with alcohol (20 mL) and NaOH (40 mmol) at room temperature for 24h. The mixture was extracted with DCM and brine, the organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>. After evaporating the solvent, the crude product was purified by chromatography with ether/ethyl acetate 2:1 (v/v) to give **L4** as white solid.

**2,6-Bis((*R*)-2,3-dihydro-5'*H*-spiro[indene-1,4'-oxazol]-2'-yl)pyridine (L4)**

White solid, m.p.: 177.1-176.4 °C,  $[\alpha]_D^{20} = +16.5$  (c = 0.3, MeOH), 47% yield. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.28 (d, *J* = 7.8 Hz, 2H), 7.86 (t, *J* = 7.8 Hz, 1H), 7.25 (dd, *J* = 14.4, 2.5 Hz, 8H), 4.68 (d, *J* = 8.9 Hz, 2H), 4.61 (d, *J* = 8.8 Hz, 2H), 3.20-3.14 (m, 2H), 3.01-2.95 (m, 2H), 2.55-2.50 (m, 2H), 2.29-2.24 (m, 2H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 161.90, 146.81, 145.60, 143.40, 137.40, 128.39, 127.30, 126.27, 124.81, 123.46, 81.01, 79.19, 40.33, 30.23. HRMS (ESI): calcd for C<sub>27</sub>H<sub>23</sub>N<sub>3</sub>O<sub>2</sub> [M+H]<sup>+</sup> : 422.1869, found 422.1866, [M+Na]<sup>+</sup> : 444.1688, found 444.1679.

## 2. General procedure for asymmetric Mukaiyama-Mannich reaction

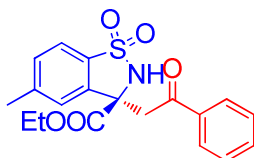
**L3** (2.3 mg, 0.006 mmol) and  $\text{Co}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  (1.8 mg, 0.005 mmol) were dissolved in  $\text{CHCl}_3$  (1.0 mL) in a Schlenk tube under an Ar atmosphere at room temperature for 1h. Then cyclic *N*-sulfonyl ketimino ester (0.1 mmol) was added and the mixture was stirred at 0 °C for 30 min before enol silyl ether (0.2 mmol) was added. The mixture was stirred at 0 °C until the reaction was completed (monitored by TLC). The solvent was removed under vacuum, and the residue was purified by chromatography on silica gel with petroleum ether/ethyl acetate 3:1 (v/v) to give the product.



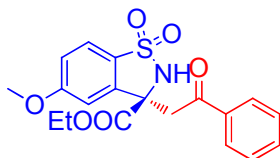
**(*R*)-ethyl 3-(2-oxo-2-phenylethyl)-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (1aa)** White solid, m.p.: 83.5-84.9 °C,  $[\alpha]_{\text{D}}^{20} = +155.7$  ( $c = 0.15$ , DCM), 98% yield and 99% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_{\text{r}} = 15.142$  min for (*S*)-isomer (minor),  $t_{\text{r}} = 19.892$  min for (*R*)-isomer (major).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.95-7.89 (m, 2H), 7.84 (dt,  $J = 7.6, 1.0$  Hz, 1H), 7.71 (d,  $J = 3.7$  Hz, 2H), 7.67-7.57 (m, 2H), 7.47 (t,  $J = 7.8$  Hz, 2H), 6.07 (s, 1H), 4.40-4.25 (m, 2H), 4.09 (d,  $J = 17.7$  Hz, 1H), 3.73 (d,  $J = 17.7$  Hz, 1H), 1.31 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  195.95, 169.61, 136.95, 135.62, 134.02, 133.66, 130.83, 128.81, 128.21, 124.25, 121.91, 65.48, 63.52,



49.16, 13.96. HRMS (ESI): calcd for C<sub>18</sub>H<sub>17</sub>NO<sub>5</sub>S [M+Na]<sup>+</sup> : 382.0725, found 382.0721.

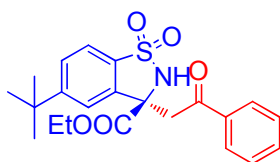


**(R)-ethyl 5-methyl-3-(2-oxo-2-phenylethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1ba)** White solid, m.p.: 90.8-92.2 °C,  $[\alpha]_{\text{D}}^{20} = +134.6$  (c = 0.22, DCM), 98% yield and 99% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_{\text{r}} = 11.937$  min for (*S*)-isomer (minor),  $t_{\text{r}} = 16.372$  min for (*R*)-isomer (major). <sup>1</sup>H NMR (500 MHz, Chloroform-*d*)  $\delta$  7.85 (d,  $J = 7.7$  Hz, 2H), 7.64 (d,  $J = 8.0$  Hz, 1H), 7.53 (t,  $J = 7.4$  Hz, 1H), 7.45-7.33 (m, 4H), 5.96 (s, 1H), 4.32-4.16 (m, 1H), 4.25-4.18 (m, 1H), 4.02 (d,  $J = 17.7$  Hz, 1H), 3.63 (d,  $J = 17.7$  Hz, 1H), 2.43 (s, 3H), 1.25 (t,  $J = 7.1$  Hz, 3H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  196.09, 169.75, 144.88, 137.20, 135.62, 134.00, 132.85, 131.77, 128.79, 128.20, 124.39, 121.63, 65.32, 63.45, 49.31, 21.90, 13.97. HRMS (ESI): calcd for C<sub>19</sub>H<sub>19</sub>NO<sub>5</sub>S [M+Na]<sup>+</sup> :396.0082, found 396.0077.

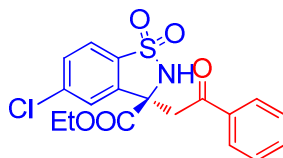


**(R)-ethyl 5-methoxy-3-(2-oxo-2-phenylethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1ca)** White solid, m.p.: 144.1-145.6 °C,  $[\alpha]_{\text{D}}^{20} = +174.4$  (c = 0.35, DCM), 98% yield and 98% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254

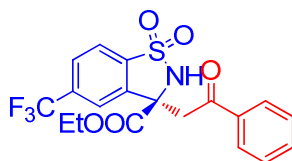
nm), retention times:  $t_r = 15.062$  min for (*S*)-isomer (minor),  $t_r = 19.906$  min for (*R*)-isomer (major).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.91 (d,  $J = 7.0$  Hz, 2H), 7.73 (d,  $J = 8.2$  Hz, 1H), 7.60 (t,  $J = 7.4$  Hz, 1H), 7.47 (t,  $J = 7.7$  Hz, 2H), 7.12 (d,  $J = 8.2$  Hz, 2H), 6.03 (s, 1H), 4.43-4.24 (m, 2H), 4.05 (d,  $J = 17.7$  Hz, 1H), 3.91 (s, 3H), 3.74 (d,  $J = 17.7$  Hz, 1H), 1.32 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  195.97, 169.61, 163.94, 139.54, 135.63, 134.01, 128.81, 128.21, 127.58, 123.31, 117.24, 108.60, 65.17, 63.49, 56.06, 49.33, 14.02. HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{19}\text{NO}_6\text{S}$   $[\text{M}+\text{Na}]^+$ : 412.0831, found 412.0822



**(*R*)-ethyl 5-(*tert*-butyl)-3-(2-oxo-2-phenylethyl)-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (1da)** White solid, m.p.: 136.7-137.9 °C,  $[\alpha]_{\text{D}}^{20} = +136.9$  ( $c = 0.17$ , DCM), 97% yield and 98% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r = 7.487$  min for (*S*)-isomer (minor),  $t_r = 13.062$  min for (*R*)-isomer (major).  $^1\text{H}$  NMR (500 MHz, Chloroform-*d*)  $\delta$  7.86 (d,  $J = 7.7$  Hz, 2H), 7.68 (d,  $J = 8.3$  Hz, 1H), 7.60 (d,  $J = 7.5$  Hz, 2H), 7.53 (t,  $J = 7.4$  Hz, 1H), 7.40 (t,  $J = 7.6$  Hz, 2H), 5.98 (s, 1H), 4.38-4.31 (m, 1H), 4.22-4.15 (m, 1H), 3.99 (d,  $J = 17.7$  Hz, 1H), 3.68 (d,  $J = 17.7$  Hz, 1H), 1.31 (s, 9H), 1.24 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  196.06, 169.75, 158.15, 137.08, 135.66, 133.99, 132.84, 128.79, 128.50, 128.24, 121.42, 120.61, 65.52, 63.33, 49.26, 35.63, 31.21, 14.05. HRMS (ESI): calcd for  $\text{C}_{22}\text{H}_{25}\text{NO}_5\text{S}$   $[\text{M}+\text{Na}]^+$ : 438.1351, found 438.1344.

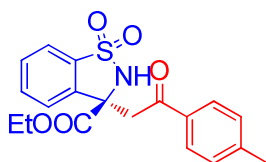


**(R)-ethyl 5-chloro-3-(2-oxo-2-phenylethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1ea)** White solid, m.p.: 87.8-88.6 °C,  $[\alpha]_D^{20} = +139.3$  (c = 0.18, DCM), 99% yield and 99% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r = 15.386$  min for (*S*)-isomer (minor),  $t_r = 21.657$  min for (*R*)-isomer (major).  $^1\text{H}$  NMR (500 MHz, Chloroform-*d*)  $\delta$  7.92 (d,  $J = 6.9$  Hz, 2H), 7.77 (d,  $J = 8.3$  Hz, 1H), 7.68 (d,  $J = 1.7$  Hz, 1H), 7.65-7.57 (m, 2H), 7.48 (t,  $J = 7.8$  Hz, 2H), 6.11 (s, 1H), 4.43-4.27 (m, 2H), 4.05 (d,  $J = 17.5$  Hz, 1H), 3.74 (d,  $J = 17.6$  Hz, 1H), 1.33 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  195.64, 169.11, 140.14, 139.00, 135.45, 134.21, 134.15, 131.33, 128.86, 128.23, 124.59, 123.11, 65.10, 63.83, 49.05, 13.96. HRMS (ESI): calcd for  $\text{C}_{18}\text{H}_{16}\text{ClNO}_5\text{S}$   $[\text{M}+\text{Na}]^+$ : 416.0335, found 416.0326.

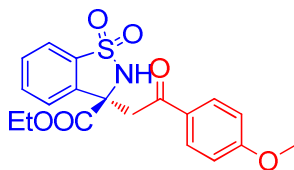


**(R)-ethyl 3-(2-oxo-2-phenylethyl)-5-(trifluoromethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1fa)** White solid, m.p.: 99.3-100.7 °C,  $[\alpha]_D^{20} = +117.7$  (c = 0.32, DCM), 69% yield and 99% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r = 8.895$  min for (*S*)-isomer (minor),  $t_r = 16.202$  min for (*R*)-isomer (major).  $^1\text{H}$  NMR (500 MHz,

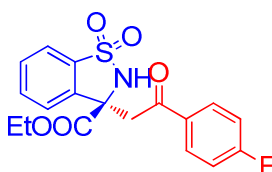
Chloroform-*d*)  $\delta$  7.98 (d,  $J = 7.5$  Hz, 2H), 7.95-7.89 (m, 3H), 7.62 (t,  $J = 7.4$  Hz, 1H), 7.49 (t,  $J = 7.8$  Hz, 2H), 6.20 (s, 1H), 4.45-4.39 (m, 1H), 4.35-4.28 (m, 1H), 4.10 (d,  $J = 17.6$  Hz, 1H), 3.77 (d,  $J = 17.6$  Hz, 1H), 1.33 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  196.08, 169.50, 139.58, 138.62, 136.30 (d,  $J = 33.4$  Hz), 135.92, 134.77, 129.43, 128.80, 128.70 (q,  $J = 3.5$  Hz), 123.39, 122.44 (q,  $J = 274.7$  Hz), 122.29 (q,  $J = 3.8$  Hz), 65.94, 64.47, 49.50, 14.47. HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{16}\text{F}_3\text{NO}_5\text{S}$   $[\text{M}+\text{Na}]^+$  :450.0599, found 450.0591.



**(*R*)-ethyl 3-(2-oxo-2-(4-tolyl)ethyl)-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (1ab)** White solid, m.p.: 76.2-77.7 °C,  $[\alpha]_{\text{D}}^{20} = +47.9$  ( $c = 0.16$ , DCM), 99% yield and 96% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_{\text{r}} = 20.138$  min for (*S*)-isomer (minor),  $t_{\text{r}} = 22.912$  min for (*R*)-isomer (major).  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ )  $\delta$  8.42 (s, 1H), 7.81 (dd,  $J = 15.2, 8.0$  Hz, 3H), 7.75-7.68 (m, 2H), 7.64-7.59 (m, 1H), 7.26 (d,  $J = 8.0$  Hz, 2H), 4.25 (d,  $J = 18.1$  Hz, 1H), 4.09-3.99 (m, 2H), 3.53 (d,  $J = 18.5$  Hz, 1H), 2.30 (s, 3H), 1.05 (t,  $J = 7.0$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  195.59, 169.74, 144.36, 136.16, 135.04, 133.43, 133.03, 130.74, 129.31, 128.27, 124.76, 120.97, 64.91, 61.87, 49.09, 21.16, 13.72. HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{19}\text{NO}_5\text{S}$   $[\text{M}+\text{Na}]^+$  :396.0882, found 396.0877.

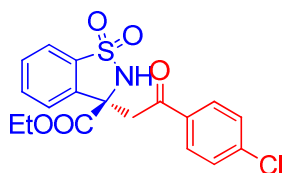


**(R)-ethyl 3-(2-(4-methoxyphenyl)-2-oxoethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1ac)** White solid, m.p.: 66.3-67.6 °C,  $[\alpha]_{\text{D}}^{20} = +79.8$  (c = 0.12, DCM), 96% yield and 99% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_{\text{r}} = 22.639$  min for (*R*)-isomer (major),  $t_{\text{r}} = 29.657$  min for (*S*)-isomer (minor).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.89 (d,  $J = 8.9$  Hz, 2H), 7.84 (d,  $J = 7.4$  Hz, 1H), 7.70 (d,  $J = 2.5$  Hz, 2H), 7.66-7.62 (m, 1H), 6.93 (d,  $J = 8.9$  Hz, 2H), 6.07 (s, 1H), 4.40-4.23 (m, 2H), 4.04 (d,  $J = 17.5$  Hz, 1H), 3.88 (s, 3H), 3.68 (d,  $J = 17.5$  Hz, 1H), 1.31 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  194.36, 169.73, 164.20, 137.01, 135.59, 133.61, 130.76, 130.57, 128.71, 124.28, 121.86, 113.97, 65.60, 63.43, 55.56, 48.83, 13.96. HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{19}\text{NO}_6\text{S}$   $[\text{M}+\text{Na}]^+$ : 412.0831, found 412.0822.

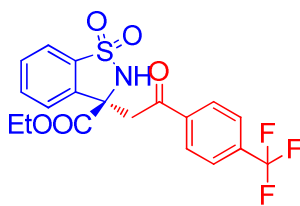


**(R)-ethyl 3-(2-(4-fluorophenyl)-2-oxoethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1ad)** White solid, m.p.: 71.4-72.3 °C,  $[\alpha]_{\text{D}}^{20} = +123.9$  (c = 0.27, DCM), 93% yield and 97% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_{\text{r}} = 13.268$  min for (*R*)-isomer (major),  $t_{\text{r}} = 19.243$  min for

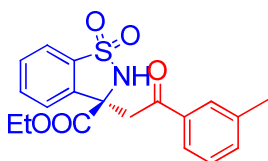
(*S*)-isomer (minor).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.99-7.92 (m, 2H), 7.84 (d,  $J = 7.5$  Hz, 1H), 7.70 (d,  $J = 4.4$  Hz, 2H), 7.68-7.62 (m, 1H), 7.14 (t,  $J = 8.6$  Hz, 2H), 6.05 (s, 1H), 4.41-4.25 (m, 2H), 4.04 (d,  $J = 17.6$  Hz, 1H), 3.70 (d,  $J = 17.6$  Hz, 1H), 1.32 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  194.37, 169.51, 166.25 (d,  $J = 256.5$  Hz), 136.88, 135.65, 133.68, 132.12 (d,  $J = 3.0$  Hz), 130.99, 130.90 (d,  $J = 5.5$  Hz), 124.21, 121.92, 116.02 (d,  $J = 22.0$  Hz), 65.44, 63.58, 49.00, 13.96. HRMS (ESI): calcd for  $\text{C}_{18}\text{H}_{16}\text{FNO}_5\text{S}$   $[\text{M}+\text{Na}]^+$ : 400.0631, found 400.0623.



**(*R*)-ethyl 3-(2-(4-chlorophenyl)-2-oxoethyl)-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (1ae)** White solid, m.p.: 88.1-89.3 °C,  $[\alpha]_{\text{D}}^{20} = +119.1$  ( $c = 0.35$ , DCM), 98% yield and 97% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_{\text{r}} = 15.342$  min for (*R*)-isomer (major),  $t_{\text{r}} = 21.386$  min for (*S*)-isomer (minor).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.89-7.81 (m, 3H), 7.70 (d,  $J = 3.1$  Hz, 2H), 7.67-7.63 (m, 1H), 7.45 (d,  $J = 8.3$  Hz, 2H), 6.05 (s, 1H), 4.41-4.25 (m, 2H), 4.03 (d,  $J = 17.6$  Hz, 1H), 3.69 (d,  $J = 17.4$  Hz, 1H), 1.31 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  194.79, 169.46, 140.59, 136.84, 135.63, 133.95, 133.71, 130.90, 129.62, 129.17, 124.22, 121.92, 65.40, 63.61, 49.03, 13.97. HRMS (ESI): calcd for  $\text{C}_{18}\text{H}_{16}\text{ClNO}_5\text{S}$   $[\text{M}+\text{Na}]^+$ : 416.0335, found 416.0329.

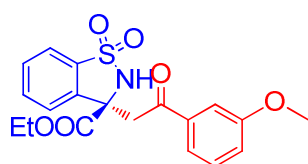


**(R)-ethyl 3-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1af)** White solid, m.p.: 54.4-55.6 °C,  $[\alpha]_D^{20} = +106.3$  ( $c = 0.22$ , DCM), 85% yield and 99% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r = 15.730$  min for (*R*)-isomer (major),  $t_r = 21.503$  min for (*S*)-isomer (minor).  $^1\text{H NMR}$  (500 MHz, Chloroform-*d*)  $\delta$  7.96 (d,  $J = 8.2$  Hz, 2H), 7.78 (d,  $J = 7.7$  Hz, 1H), 7.67 (d,  $J = 8.2$  Hz, 2H), 7.64 (d,  $J = 2.5$  Hz, 2H), 7.61-7.57 (m, 1H), 5.99 (s, 1H), 4.35-4.20 (m, 2H), 3.99 (d,  $J = 17.7$  Hz, 1H), 3.68 (d,  $J = 17.8$  Hz, 1H), 1.25 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  194.65, 168.84, 137.75, 136.29, 135.18, 134.71 (q,  $J = 32.6$  Hz), 133.26, 130.47, 128.10, 125.40 (q,  $J = 3.8$  Hz), 123.69, 122.91 (q,  $J = 273.4$  Hz), 121.45, 64.83, 63.20, 48.73, 13.46. HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{16}\text{F}_3\text{NO}_5\text{S}$   $[\text{M}+\text{Na}]^+$ : 450.0599, found 450.0592.



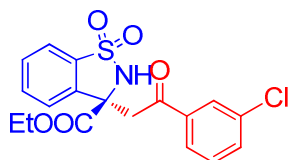
**(R)-ethyl 3-(2-oxo-2-(3-tolyl)ethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1ag)** White solid, m.p.: 77.9-79.3 °C,  $[\alpha]_D^{20} = +122.1$  ( $c = 0.28$ , DCM), 99% yield and 94% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r = 15.028$  min for (*S*)-isomer (minor),  $t_r = 24.494$  min for (*R*)-isomer (major).  $^1\text{H NMR}$  (500 MHz,  $\text{DMSO}-d_6$ )  $\delta$  8.54 (s, 1H), 7.92-7.78 (m,

5H), 7.75-7.69 (m, 1H), 7.51 (d,  $J = 7.5$  Hz, 1H), 7.44 (t,  $J = 7.6$  Hz, 1H), 4.37 (d,  $J = 18.4$  Hz, 1H), 4.20-4.19 (m, 2H), 3.66 (d,  $J = 18.4$  Hz, 1H), 2.38 (s, 3H), 1.15 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  196.65, 170.21, 138.75, 136.66, 135.99, 135.55, 134.92, 133.94, 131.26, 129.19, 129.16, 125.76, 125.27, 121.48, 65.39, 62.39, 49.75, 21.23, 14.23. HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{19}\text{NO}_5\text{S}$   $[\text{M}+\text{Na}]^+$ : 396.0882, found 396.0877.

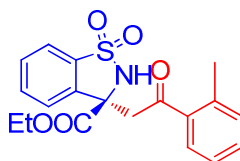


**(*R*)-ethyl 3-(2-(3-methoxyphenyl)-2-oxoethyl)-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (1ah)** White solid, m.p.: 65.1-66.5 °C,  $[\alpha]_{\text{D}}^{20} = +159.5$  ( $c = 0.13$ , DCM), 98% yield and 95% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 70:30 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_{\text{r}} = 13.381$  min for (*S*)-isomer (minor),  $t_{\text{r}} = 40.464$  min for (*R*)-isomer (major).  $^1\text{H}$  NMR (500 MHz,  $\text{DMSO-}d_6$ )  $\delta$  8.53 (s, 1H), 7.89 (d,  $J = 7.7$  Hz, 1H), 7.82 (q,  $J = 8.2$  Hz, 2H), 7.73 (d,  $J = 6.8$  Hz, 1H), 7.61 (d,  $J = 7.7$  Hz, 1H), 7.48 (dd,  $J = 17.1, 9.1$  Hz, 2H), 7.26 (dd,  $J = 8.2, 2.7$  Hz, 1H), 4.39 (d,  $J = 18.5$  Hz, 1H), 4.20-4.09 (m, 2H), 3.83 (s, 3H), 3.69 (d,  $J = 18.6$  Hz, 1H), 1.15 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{DMSO-}d_6$ )  $\delta$  196.47, 170.23, 159.93, 137.35, 136.61, 135.54, 133.94, 131.26, 130.45, 125.29, 121.48, 121.14, 120.58, 112.95, 65.42, 62.40, 55.87, 49.77, 14.22. HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{19}\text{NO}_6\text{S}$   $[\text{M}+\text{Na}]^+$ : 412.0831, found 412.0823.



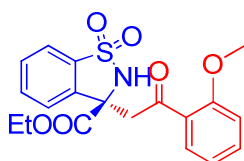


**(R)-ethyl 3-(2-(3-chlorophenyl)-2-oxoethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1ai)** White solid, m.p.: 81.1-82.7 °C,  $[\alpha]_D^{20} = +109.8$  (c = 0.16, DCM), 97% yield and 95% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r = 21.784$  min for (*S*)-isomer (minor),  $t_r = 33.071$  min for (*R*)-isomer (major).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.89 (s, 1H), 7.84 (d,  $J = 7.9$  Hz, 1H), 7.79 (d,  $J = 7.9$  Hz, 1H), 7.70 (d,  $J = 2.9$  Hz, 2H), 7.67-7.63 (m, 1H), 7.58 (d,  $J = 8.0$  Hz, 1H), 7.42 (t,  $J = 7.8$  Hz, 1H), 6.04 (s, 1H), 4.41-4.25 (m, 2H), 4.04 (d,  $J = 17.7$  Hz, 1H), 3.70 (d,  $J = 17.7$  Hz, 1H), 1.32 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  194.77, 169.40, 137.09, 136.80, 135.66, 135.21, 133.93, 133.73, 130.92, 130.18, 128.31, 126.30, 124.22, 121.94, 65.34, 63.64, 49.16, 13.97. HRMS (ESI): calcd for  $\text{C}_{18}\text{H}_{16}\text{ClNO}_5\text{S}$   $[\text{M}+\text{Na}]^+$ : 416.0335, found 416.0326.

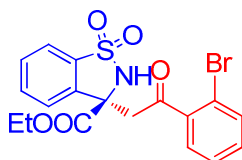


**(R)-ethyl 3-(2-(2-tolylethyl)-2-oxoethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1aj)** White solid, m.p.: 66.7-67.7 °C,  $[\alpha]_D^{20} = +102.9$  (c = 0.37, DCM), 95% yield and 97% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r = 11.334$  min for (*S*)-isomer (minor),  $t_r = 16.863$  min for (*R*)-isomer (major).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.83 (d,  $J = 7.6$  Hz, 1H),

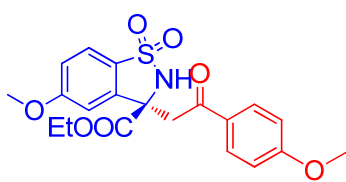
7.72-7.60 (m, 4H), 7.41 (t,  $J = 7.5$  Hz, 1H), 7.31-7.21 (m, 2H), 6.09 (s, 1H), 4.41-4.27 (m, 2H), 4.04 (d,  $J = 17.7$  Hz, 1H), 3.65 (d,  $J = 17.7$  Hz, 1H), 2.53 (s, 3H), 1.33 (t,  $J = 7.2$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.81, 169.33, 138.80, 136.63, 135.35, 135.26, 133.24, 131.97, 131.93, 130.39, 128.67, 125.48, 123.85, 121.51, 65.32, 63.11, 51.03, 21.20, 13.62. HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{19}\text{NO}_5\text{S}$   $[\text{M}+\text{Na}]^+$ : 396.0882, found 396.0877.



**(*R*)-ethyl 3-(2-(2-methoxyphenyl)-2-oxoethyl)-2,3-dihydrobenzo[*d*]isothiazole-1,1-dioxide-3-carboxylate (1ak)** White solid, m.p.: 99.7-100.8 °C,  $[\alpha]_{\text{D}}^{20} = +143.6$  ( $c = 0.23$ , DCM), 98% yield and 95% ee, determined by chiral HPLC analysis (Chiralcel AD-H hexane/isopropanol, 70:30 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_{\text{r}} = 38.396$  min for (*S*)-isomer (minor),  $t_{\text{r}} = 50.468$  min for (*R*)-isomer (major).  $^1\text{H}$  NMR (500 MHz, Chloroform-*d*)  $\delta$  7.86 (dd,  $J = 7.9, 1.9$  Hz, 1H), 7.82 (d,  $J = 7.7$  Hz, 1H), 7.69 (d,  $J = 5.6$  Hz, 2H), 7.64-7.61 (m 1H), 7.54-7.47 (m, 1H), 7.03 (t,  $J = 7.6$  Hz, 1H), 6.96 (d,  $J = 8.3$  Hz, 1H), 6.05 (s, 1H), 4.38-4.24 (m, 2H), 4.12 (d,  $J = 18.4$  Hz, 1H), 3.86 (s, 3H), 3.74 (d,  $J = 18.6$  Hz, 1H), 1.30 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  196.32, 169.48, 158.98, 136.71, 135.03, 134.51, 133.07, 130.41, 130.11, 125.26, 123.88, 121.29, 120.35, 111.19, 65.42, 62.77, 55.07, 54.01, 13.48. HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{19}\text{NO}_6\text{S}$   $[\text{M}+\text{Na}]^+$ : 412.0831, found 412.0822.

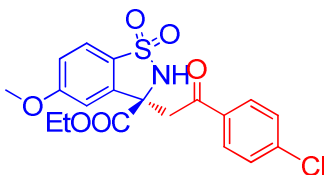


**(R)-ethyl 3-(2-(2-bromophenyl)-2-oxoethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1a)** White solid, m.p.: 75.4-77.1 °C,  $[\alpha]_D^{20} = +110.7$  (c = 0.22, DCM), 93% yield and 96% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r = 18.290$  min for (*S*)-isomer (minor),  $t_r = 36.347$  min for (*R*)-isomer (major).  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  7.82 (d,  $J = 7.5$  Hz, 1H), 7.68 (d,  $J = 4.2$  Hz, 2H), 7.63 (dd,  $J = 8.0, 4.3$  Hz, 2H), 7.52 (dd,  $J = 7.7, 1.8$  Hz, 1H), 7.39 (t,  $J = 7.5$  Hz, 1H), 7.33 (td,  $J = 7.6, 1.8$  Hz, 1H), 6.07 (s, 1H), 4.43-4.32 (m, 2H), 4.09 (d,  $J = 17.9$  Hz, 1H), 3.67 (d,  $J = 18.0$  Hz, 1H), 1.36 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  199.11, 169.28, 139.34, 136.84, 135.65, 134.10, 133.68, 132.56, 130.86, 129.32, 127.63, 124.20, 121.88, 119.12, 65.54, 63.74, 52.29, 14.04. HRMS (ESI): calcd for  $\text{C}_{18}\text{H}_{16}\text{BrNO}_5\text{S}$   $[\text{M}+\text{Na}]^+$ : 459.9830, found 459.9821.

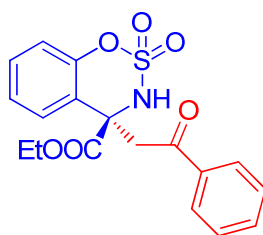


**(R)-ethyl 5-methoxy-3-(2-(4-methoxyphenyl)-2-oxoethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1am)** White solid, m.p.: 131.1-132.3 °C,  $[\alpha]_D^{20} = +147.7$  (c = 0.14, DCM), 97% yield and 97% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r = 18.830$  min for (*R*)-isomer (major),  $t_r = 28.530$  min for (*S*)-isomer (minor).  $^1\text{H}$  NMR (500 MHz,

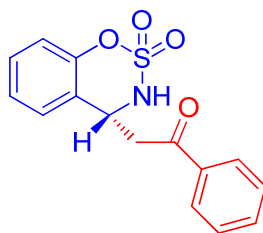
DMSO-*d*<sub>6</sub>)  $\delta$  8.29 (s, 1H), 7.98 (d,  $J$  = 8.4 Hz, 2H), 7.78 (d,  $J$  = 8.5 Hz, 1H), 7.27 (s, 1H), 7.23 (d,  $J$  = 8.7 Hz, 1H), 7.05 (d,  $J$  = 8.4 Hz, 2H), 4.38 (d,  $J$  = 18.3 Hz, 1H), 4.24-4.04 (m, 2H), 3.89 (s, 3H), 3.85 (s, 3H), 3.56 (d,  $J$  = 18.3 Hz, 1H), 1.15 (t,  $J$  = 7.0 Hz, 3H). <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  194.93, 170.25, 164.08, 163.50, 139.34, 131.05, 128.98, 127.66, 122.99, 117.89, 114.44, 109.36, 65.21, 62.31, 56.53, 56.08, 49.49, 14.28. HRMS (ESI): calcd for C<sub>20</sub>H<sub>21</sub>NO<sub>7</sub>S [M+Na]<sup>+</sup> : 442.0936, found 442.0929.



**(*R*)-ethyl 3-(2-(4-chlorophenyl)-2-oxoethyl)-5-methoxy-2,3-dihydrobenzo[*d*]isothiazole-3-carboxylate 1,1-dioxide (1an)** White solid, m.p.: 103.8-104.9 °C,  $[\alpha]_D^{20}$  = +139.2 (c = 0.35, DCM), 98% yield and 99% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r$  = 16.984 min for (*S*)-isomer (minor),  $t_r$  = 20.709 min for (*R*)-isomer (major). <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  8.26 (s, 1H), 7.94 (d,  $J$  = 8.5 Hz, 2H), 7.70 (d,  $J$  = 8.6 Hz, 1H), 7.54 (d,  $J$  = 8.6 Hz, 2H), 7.20 (d,  $J$  = 2.3 Hz, 1H), 7.14 (dd,  $J$  = 8.6, 2.3 Hz, 1H), 4.39 (d,  $J$  = 18.8 Hz, 1H), 4.12-3.95 (m, 2H), 3.80 (s, 3H), 3.54 (d,  $J$  = 18.5 Hz, 1H), 1.05 (t,  $J$  = 7.1 Hz, 3H). <sup>13</sup>C NMR (126 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  195.75, 170.14, 163.53, 139.26, 134.70, 130.60, 129.39, 127.62, 123.01, 117.96, 109.35, 65.09, 62.40, 56.55, 49.65, 14.27. HRMS (ESI): calcd for C<sub>19</sub>H<sub>18</sub>ClNO<sub>6</sub>S [M+Na]<sup>+</sup> : 446.0441, found 446.0433

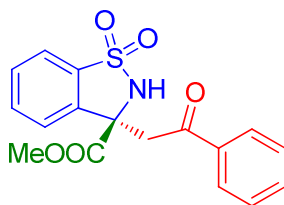


**(R)-ethyl 4-(2-oxo-2-phenylethyl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide (1ga)** White solid, m.p.: 97.7-98.5 °C,  $[\alpha]_D^{20} = -33.1$  (c = 0.35, DCM), 83% yield and 73% ee, determined by chiral HPLC analysis (Chiralcel AD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r = 21.361$  min for (*R*)-isomer (major),  $t_r = 30.033$  min for (*S*)-isomer (minor).  $^1\text{H}$  NMR (500 MHz, Chloroform-*d*)  $\delta$  7.94 (d,  $J = 8.5$  Hz, 2H), 7.65 (d,  $J = 8.1$  Hz, 1H), 7.60 (t,  $J = 7.4$  Hz, 1H), 7.48 (t,  $J = 7.8$  Hz, 2H), 7.44-7.38 (m, 1H), 7.27 (d,  $J = 7.6$  Hz, 2H), 7.09 (d,  $J = 8.2$  Hz, 1H), 6.43 (s, 1H), 4.56 (d,  $J = 17.9$  Hz, 1H), 4.37 (q,  $J = 7.1$  Hz, 2H), 3.83 (d,  $J = 17.9$  Hz, 1H), 1.32 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  195.23, 169.43, 150.74, 135.96, 133.87, 130.89, 128.80, 128.19, 127.31, 125.85, 120.03, 119.45, 99.99, 65.27, 63.94, 47.07, 13.90. HRMS (ESI): calcd for  $\text{C}_{18}\text{H}_{17}\text{NO}_6\text{S}$   $[\text{M}+\text{Na}]^+$ : 398.0674, found 398.066.



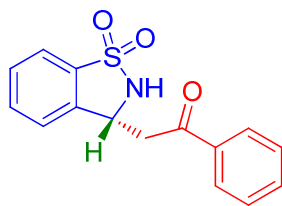
**(R)-2-(2,2-dioxido-3,4-dihydrobenzo[e][1,2,3]oxathiazin-4-yl)-1-phenylethanone (1ha)** White solid, m.p.: 79.2-81.1 °C,  $[\alpha]_D^{20} = -11.2$  (c = 0.35, DCM), 56% yield and 16% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r =$

12.003 min for (*R*)-isomer (major),  $t_r = 14.367$  min for (*S*)-isomer (minor).  $^1\text{H}$  NMR (500 MHz, Chloroform-*d*)  $\delta$  7.98 (d,  $J = 6.9$  Hz, 2H), 7.63 (t,  $J = 7.4$  Hz, 1H), 7.50 (t,  $J = 7.7$  Hz, 2H), 7.34-7.31 (m 1H), 7.15 (d,  $J = 4.4$  Hz, 2H), 7.07 (d,  $J = 8.3$  Hz, 1H), 5.84 (d,  $J = 8.2$  Hz, 1H), 5.42 (td,  $J = 7.6, 3.7$  Hz, 1H), 4.29 (dd,  $J = 18.2, 7.2$  Hz, 1H), 3.43 (dd,  $J = 18.2, 3.8$  Hz, 1H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  197.77, 151.24, 136.14, 134.16, 129.62, 128.92, 128.25, 125.95, 125.47, 121.61, 119.14, 53.67, 41.80. HRMS (ESI): calcd for  $\text{C}_{15}\text{H}_{13}\text{NO}_4\text{S}$   $[\text{M}+\text{Na}]^+$ : 326.0463, found 326.0459.



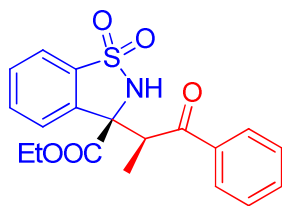
**(*R*)-methyl 3-(2-oxo-2-phenylethyl)-2,3-dihydrobenzo[*d*]isothiazole**

**-3-carboxylate 1,1-dioxide (1ia)** White solid, m.p.: 129.4-130.5 °C,  $[\alpha]_{\text{D}}^{20} = +109.4$  ( $c = 0.53$ , DCM), 98% yield and 98% ee, determined by chiral HPLC analysis (Chiralcel AD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r = 22.754$  min for (*S*)-isomer (minor),  $t_r = 44.140$  min (major) for (*R*)-isomer.  $^1\text{H}$  NMR (500 MHz, Chloroform-*d*)  $\delta$  7.91 (d,  $J = 4.9$  Hz, 2H), 7.84 (dd,  $J = 7.7, 3.4$  Hz, 1H), 7.71 (t,  $J = 3.9$  Hz, 2H), 7.67-7.64 (m, 1H), 7.60 (q,  $J = 4.4$  Hz, 1H), 7.49-7.45 (m, 2H), 6.09 (s, 1H), 4.12 (dd,  $J = 17.8, 3.5$  Hz, 1H), 3.86 (d,  $J = 3.6$  Hz, 3H), 3.73 (dd,  $J = 17.8, 3.5$  Hz, 1H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  196.11, 170.25, 136.64, 135.50, 134.10, 133.74, 130.90, 128.82, 128.24, 126.42, 124.31, 121.91, 65.43, 54.15, 49.28. HRMS (ESI): calcd for  $\text{C}_{17}\text{H}_{15}\text{NO}_5\text{S}$   $[\text{M}+\text{Na}]^+$ : 368.0569, found 368.0568.



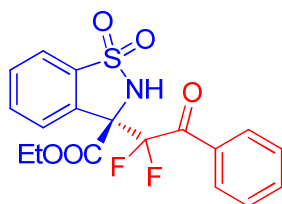
**(R)-2-(1,1-dioxido-2,3-dihydrobenzo[d]isothiazol-3-yl)-1-phenylethanone (1ja)**

White solid, m.p.: 158.5-159.8 °C,  $[\alpha]_D^{20} = +139.2$  ( $c = 0.35$ , DCM), 94% yield and 66% ee, determined by chiral HPLC analysis (Chiralcel AD-H hexane/isopropanol, 80:20 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r = 38.289$  min for (*S*)-isomer (minor),  $t_r = 46.120$  min (major) for (*R*)-isomer.  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  8.00-7.86 (m, 3H), 7.74 (d,  $J = 7.8$  Hz, 1H), 7.67-7.60 (m, 2H), 7.58 (t,  $J = 7.3$  Hz, 1H), 7.53-7.49 (m, 1H), 7.46 (t,  $J = 7.8$  Hz, 2H), 5.11 (dd,  $J = 9.1, 4.3$  Hz, 1H), 3.61 (dd,  $J = 17.7, 3.2$  Hz, 1H), 3.41 (dd,  $J = 17.7, 9.6$  Hz, 1H).  $^{13}\text{C}$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  196.87, 140.55, 136.36, 136.27, 133.51, 132.88, 129.29, 128.89, 128.76, 128.08, 125.53, 125.08, 120.47, 52.75, 44.67. HRMS (ESI): calcd for  $\text{C}_{15}\text{H}_{13}\text{NO}_3\text{S}$   $[\text{M}+\text{Na}]^+$ : 310.0514, found 310.0506.



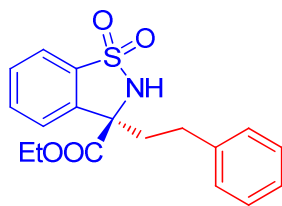
**(R)-ethyl 3-((S)-1-oxo-1-phenylpropan-2-yl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1ap)** White solid, m.p.: 97.6-98.8 °C,  $[\alpha]_D^{20} = +50.3$  ( $c = 0.10$ , DCM), 37% yield and 94% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 90:10 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_r = 16.675$  min for (*S*)-isomer (minor),  $t_r = 22.439$  min for (*R*)-isomer (major).  $^1\text{H}$  NMR (500 MHz, Chloroform- $d$ )  $\delta$  7.93 (d,  $J = 8.4$  Hz, 2H),

7.81 (t,  $J = 7.2$  Hz, 2H), 7.65-7.56 (m, 3H), 7.46 (t,  $J = 7.7$  Hz, 2H), 6.14 (s, 1H), 4.44 (q,  $J = 7.1$  Hz, 2H), 4.27 (q,  $J = 7.4$  Hz, 1H), 1.49 (d,  $J = 7.4$  Hz, 3H), 1.42 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  201.14, 169.13, 137.32, 137.30, 135.74, 133.69, 132.67, 130.57, 128.84, 128.62, 126.41, 121.68, 68.92, 63.53, 50.32, 14.73, 14.07. HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{19}\text{NO}_5\text{S}$   $[\text{M}+\text{Na}]^+$  : 396.0882, found 396.0878.



**(R)-ethyl 3-(1,1-difluoro-2-oxo-2-phenylethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1aq)** White solid, m.p.: 115.3-117.1 °C,  $[\alpha]_{\text{D}}^{20} = +56.7$  ( $c = 0.25$ , DCM), 44% yield and 64% ee, determined by chiral HPLC analysis (Chiralcel AD-H hexane/isopropanol, 70:30 v/v, 1.0 mL/min, UV 254 nm), retention times:  $t_{\text{r}} = 13.623$  min for (*S*)-isomer (minor),  $t_{\text{r}} = 20.114$  min for (*R*)-isomer (major).  $^1\text{H}$  NMR (500 MHz, Chloroform-*d*)  $\delta$  8.09 (d,  $J = 7.8$  Hz, 2H), 7.98-7.93 (m, 1H), 7.87 (d,  $J = 8.5$  Hz, 1H), 7.78-7.72 (m, 2H), 7.67 (t,  $J = 7.4$  Hz, 1H), 7.51 (t,  $J = 7.8$  Hz, 2H), 5.98 (s, 1H), 4.44-4.37 (m, 2H), 1.35 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  187.80 (dd,  $J = 32.1, 28.8$  Hz), 165.61 (dd,  $J = 7.4, 2.2$  Hz), 136.63, 135.26, 133.63, 131.84, 131.18 (t,  $J = 3.2$  Hz), 130.44 (dd,  $J = 4.1, 2.2$  Hz), 130.35 (d,  $J = 1.8$  Hz), 128.87, 127.06 (d,  $J = 5.6$  Hz), 121.98, 115.43 (t,  $J = 269.8$  Hz), 68.55 (dd,  $J = 26.0, 23.8$  Hz), 64.44, 13.88. HRMS (ESI): calcd for  $\text{C}_{18}\text{H}_{15}\text{F}_2\text{NO}_5\text{S}$   $[\text{M}+\text{Na}]^+$  : 418.0537, found 418.0531.



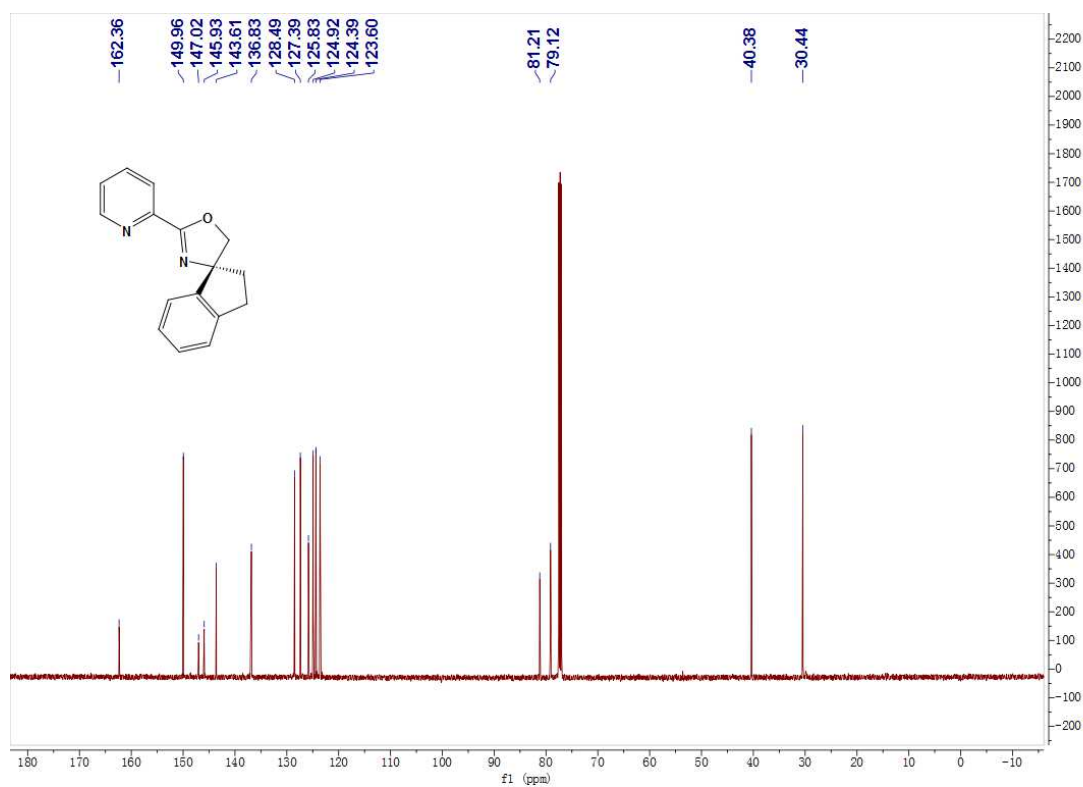
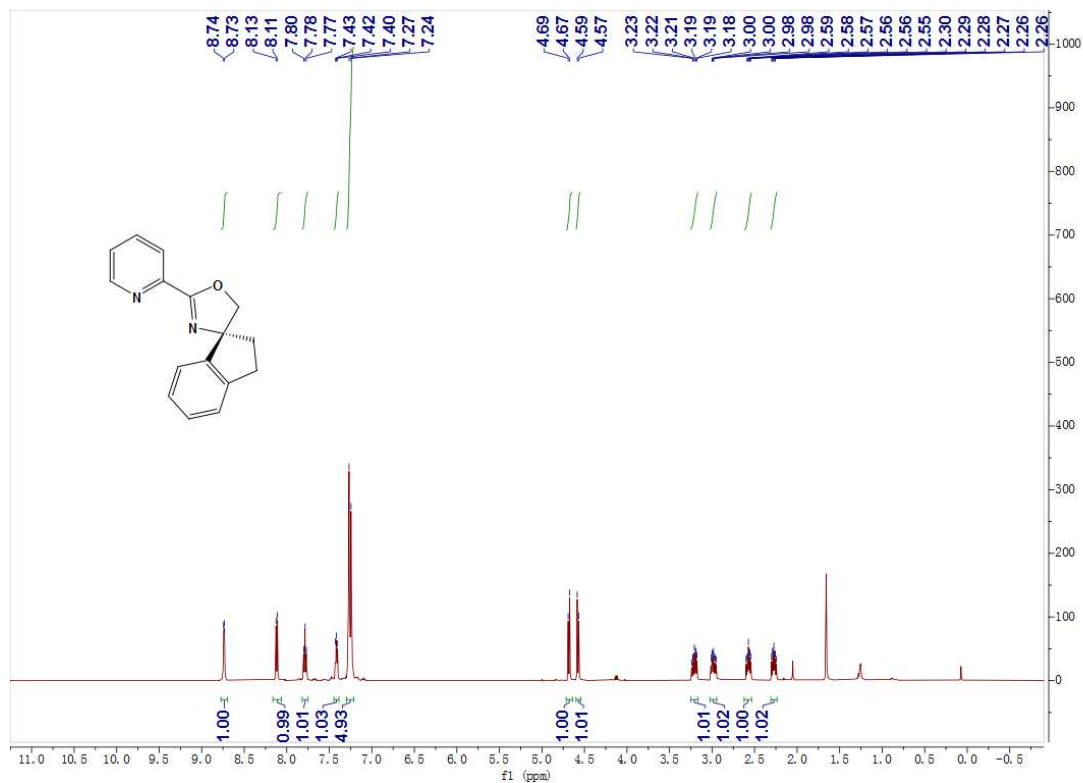


**(R)-ethyl 3-phenethyl-2,3-dihydrobenzo[d]isothiazole-3-carboxylate**

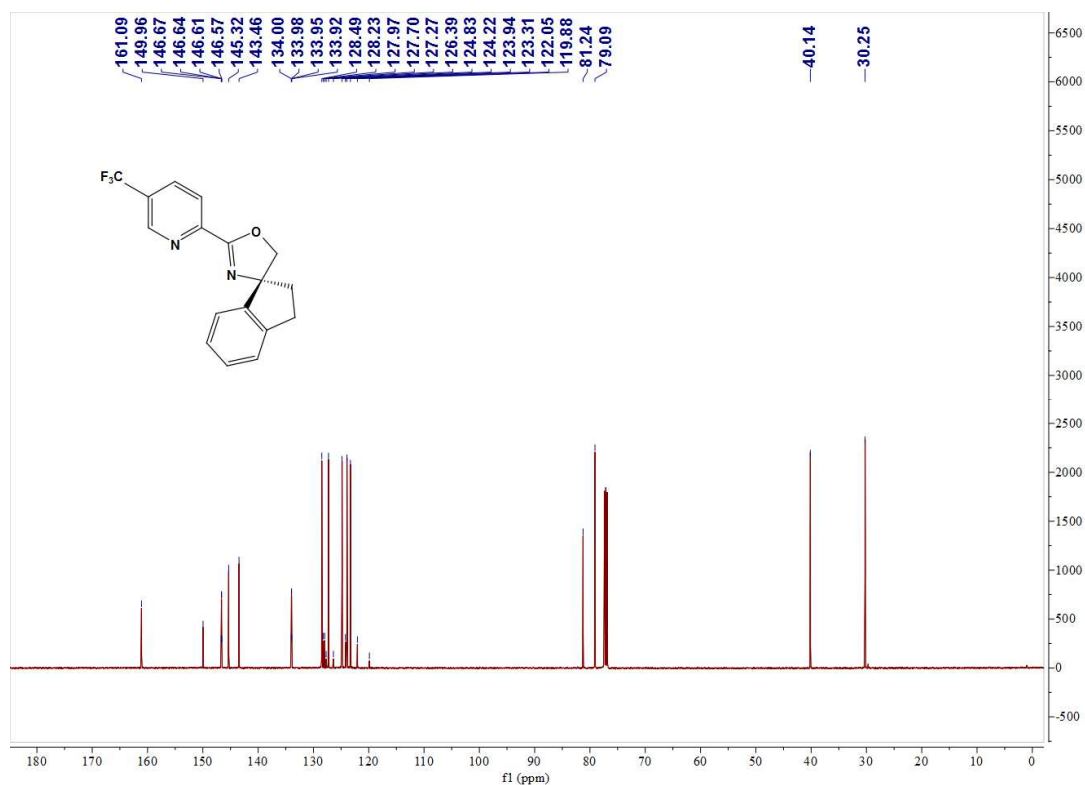
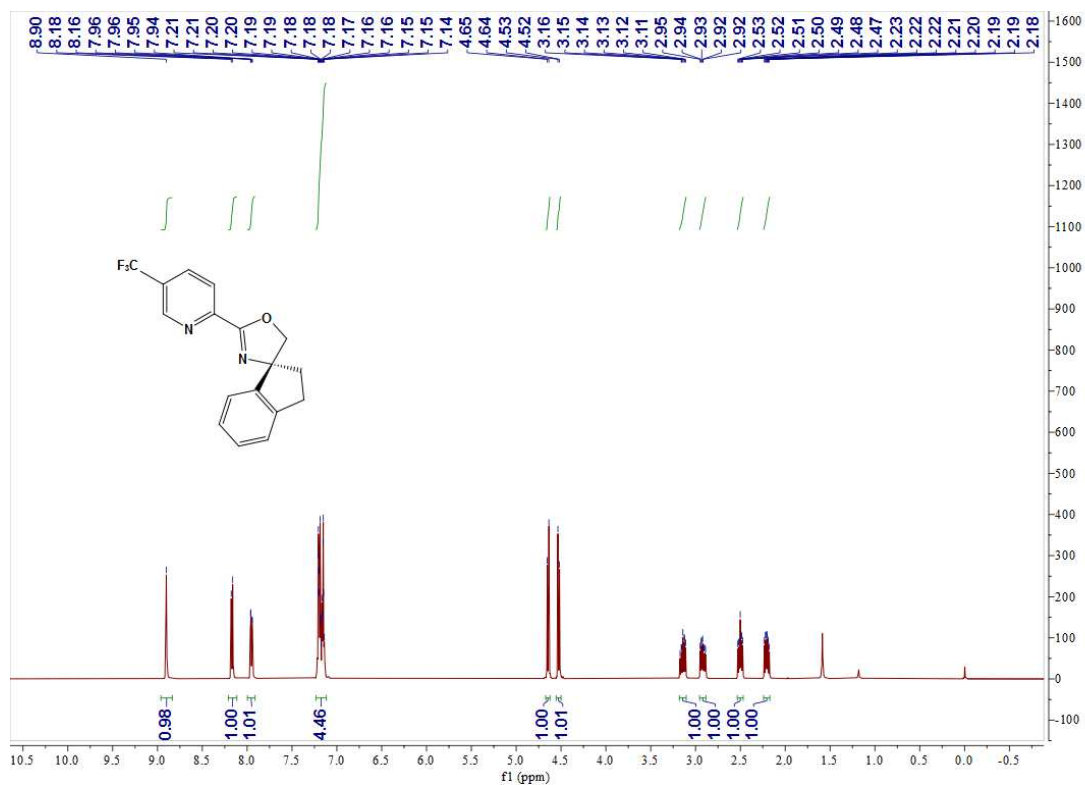
**1,1-dioxide (4)** White solid, m.p.: 74.1-75.5 °C,  $[\alpha]_D^{20} = +46.9$  (c = 0.25, DCM), 72% yield and 97% ee, determined by chiral HPLC analysis (Chiralcel OD-H hexane/isopropanol, 70:30 v/v, 0.8 mL/min, UV 254 nm), retention times:  $t_r = 9.739$  min for (*R*)-isomer (major),  $t_r = 14.089$  min (minor) for (*S*)-isomer.  $^1\text{H}$  NMR (500 MHz, Chloroform-*d*)  $\delta$  7.58 (d,  $J = 7.9$  Hz, 1H), 7.39 (s, 1H), 7.30 (d,  $J = 8.0$  Hz, 1H), 7.21-7.16 (m, 2H), 7.10 (dd,  $J = 15.2, 7.2$  Hz, 3H), 5.74 (s, 1H), 4.27-4.13 (m, 2H), 2.73-2.63 (m, 1H), 2.62-2.54 (m, 1H), 2.49-2.41 (m, 1H), 2.39 (s, 3H), 2.26-2.20 (m, 1H), 1.28 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  169.49, 144.15, 139.74, 137.98, 132.16, 130.95, 127.98, 127.96, 125.75, 124.51, 120.77, 68.30, 63.09, 41.56, 30.47, 21.39, 13.64. HRMS (ESI): calcd for  $\text{C}_{19}\text{H}_{21}\text{NO}_4\text{S}$   $[\text{M}+\text{Na}]^+$ : 382.1089, found 382.1081.

### 3. NMR spectrum and HPLC trace of compounds

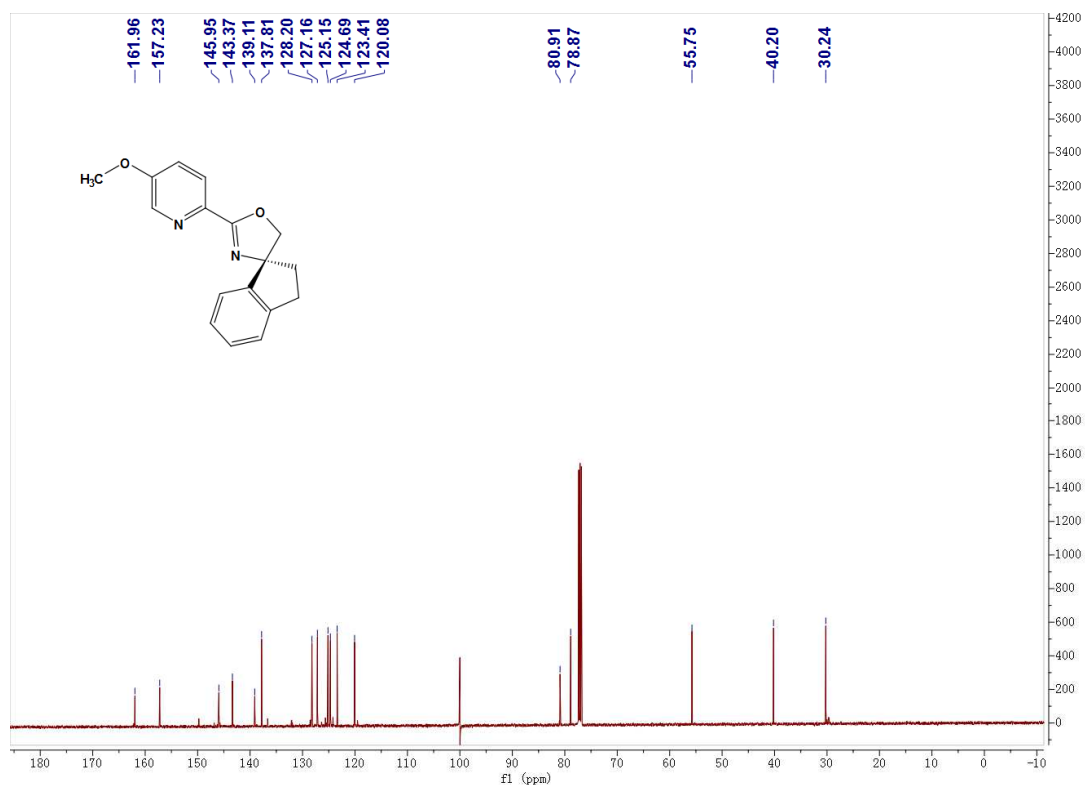
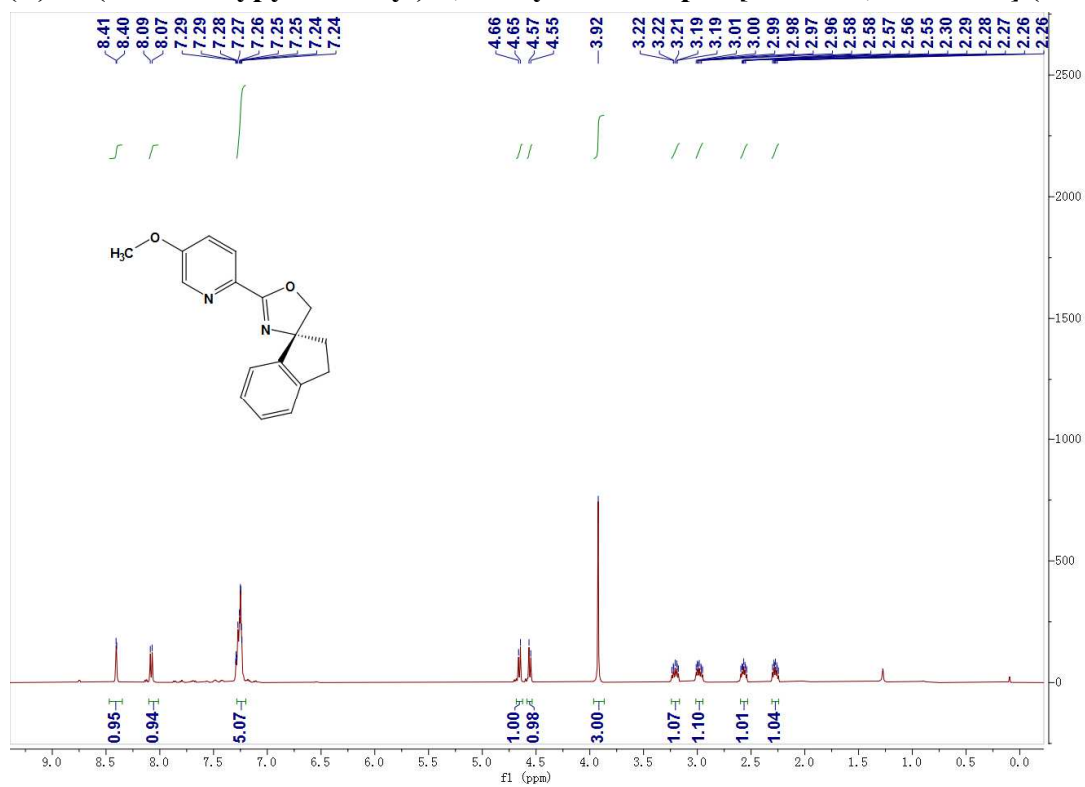
#### (*R*)-2'-(Pyridin-2-yl)-2,3-dihydro-5'*H*-spiro[indene-1,4'-oxazole] (L1a)



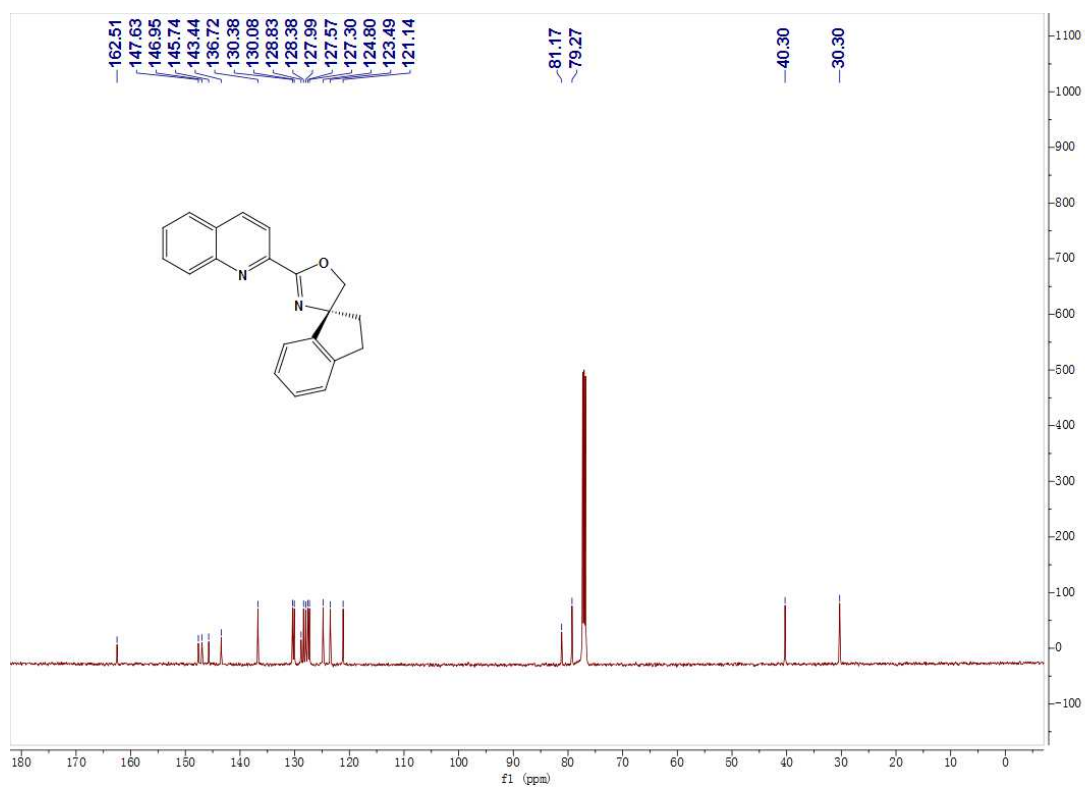
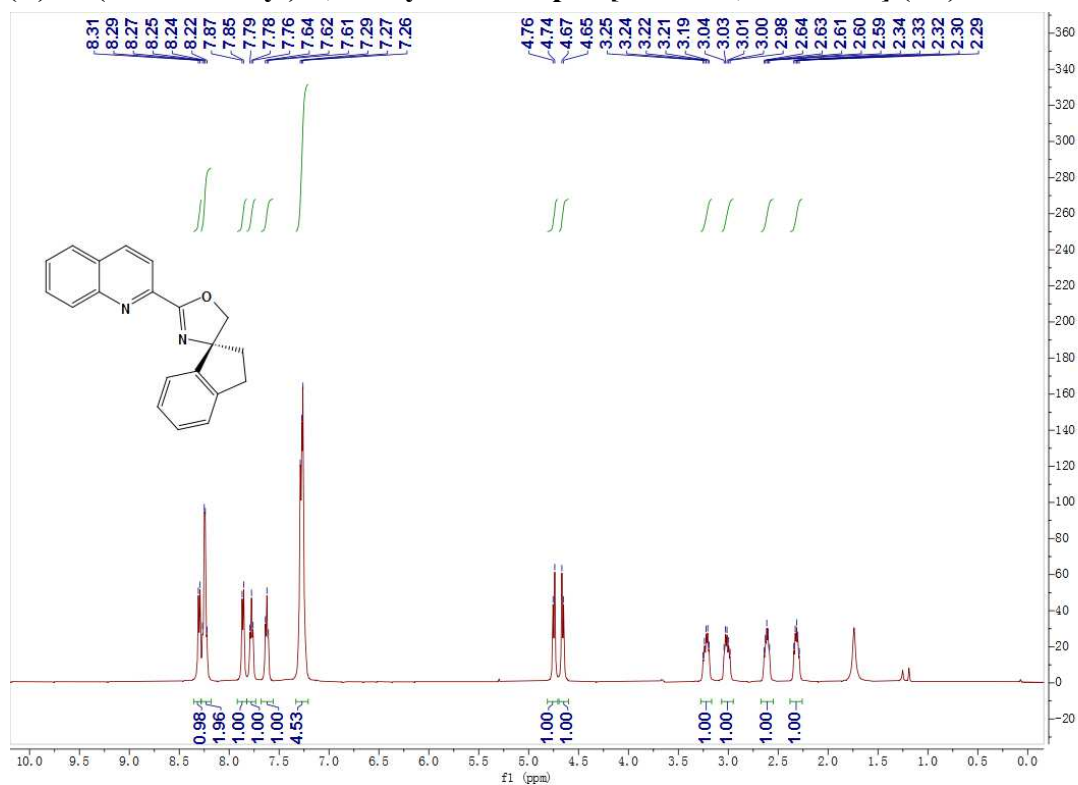
**(R)-2'-(5-(Trifluoromethyl)pyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole] (L1b)**



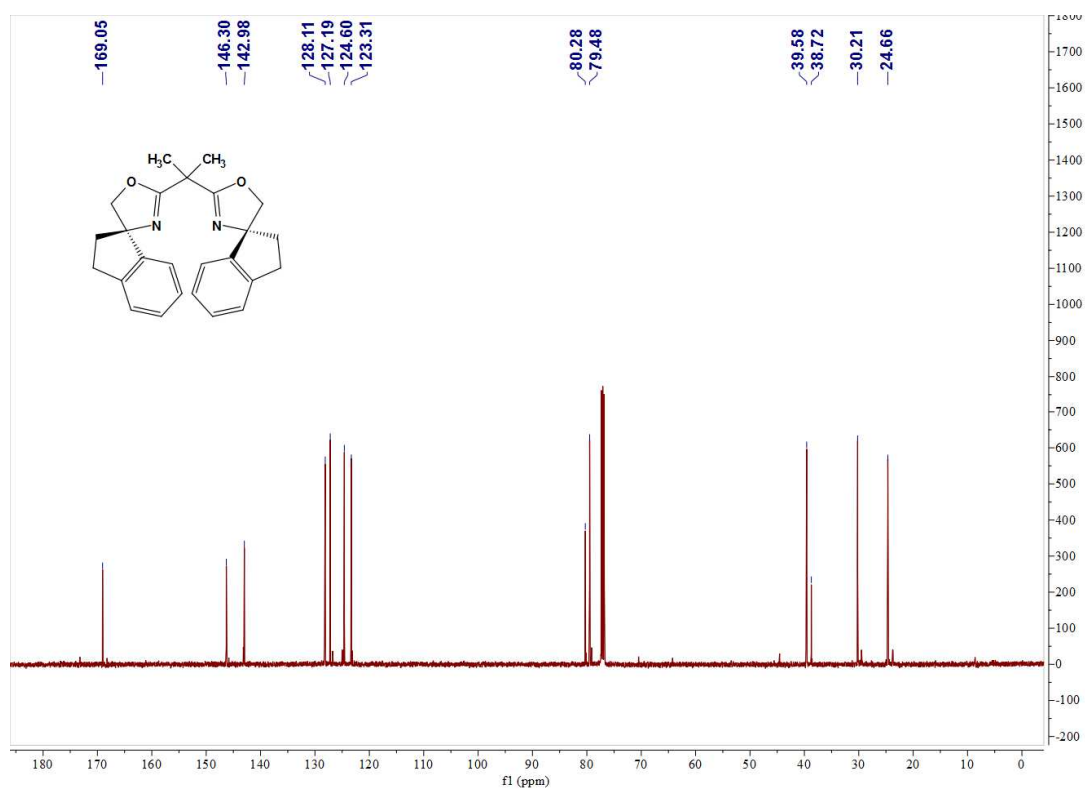
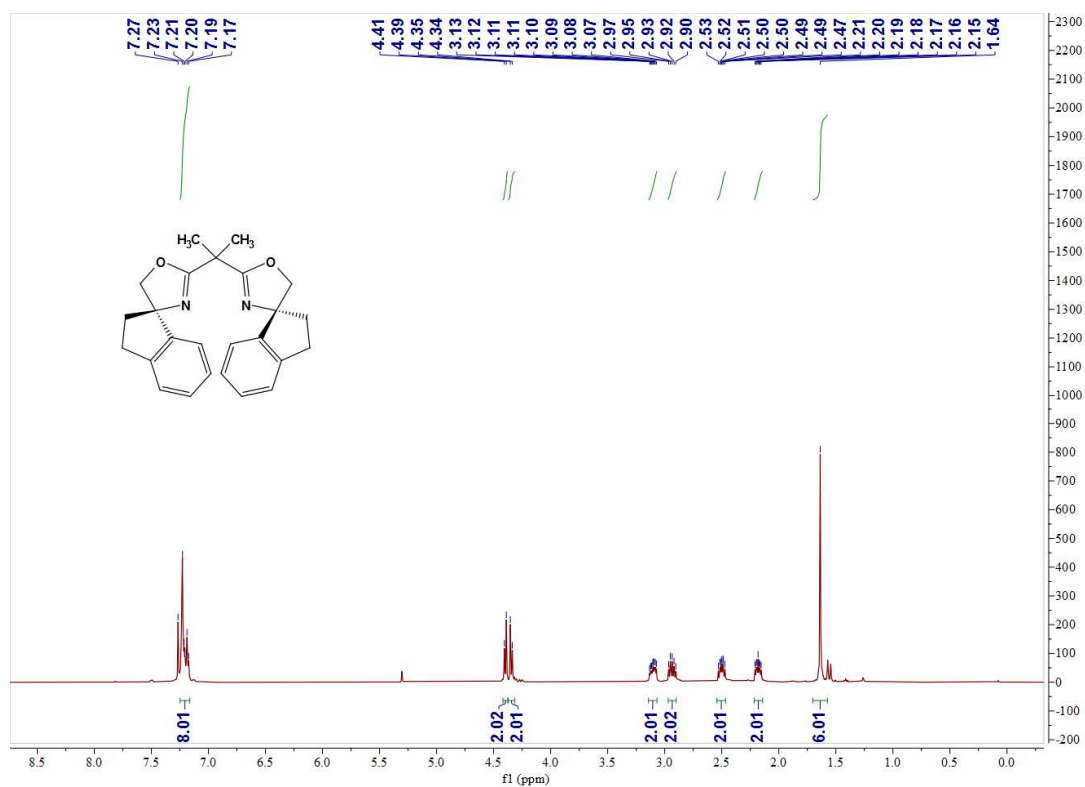
**(R)-2'-(5-Methoxypyridin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole] (L1c)**



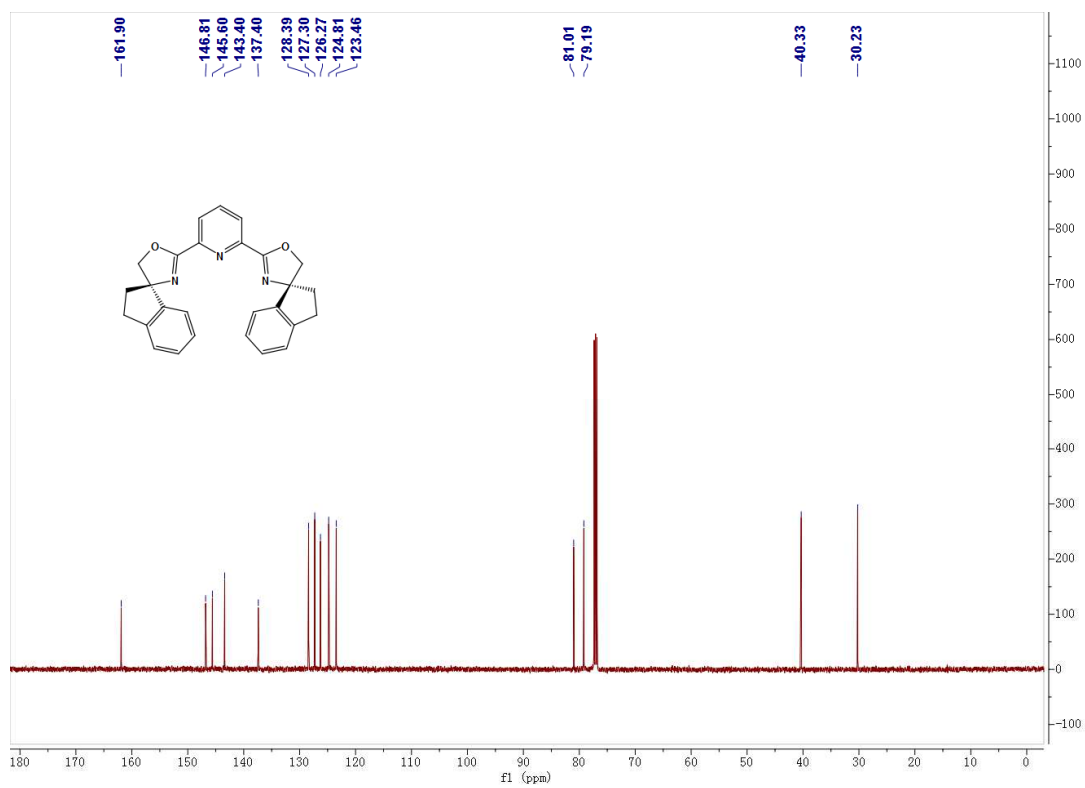
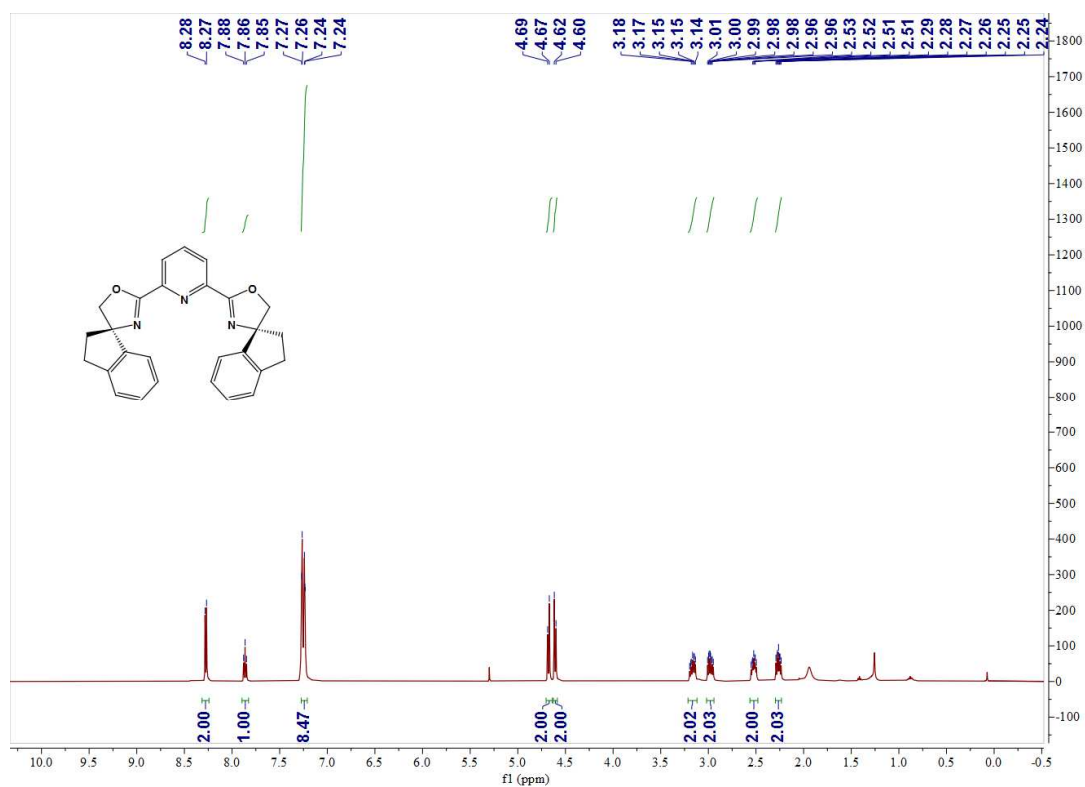
**(R)-2'-(Quinolin-2-yl)-2,3-dihydro-5'H-spiro[indene-1,4'-oxazole] (L2)**



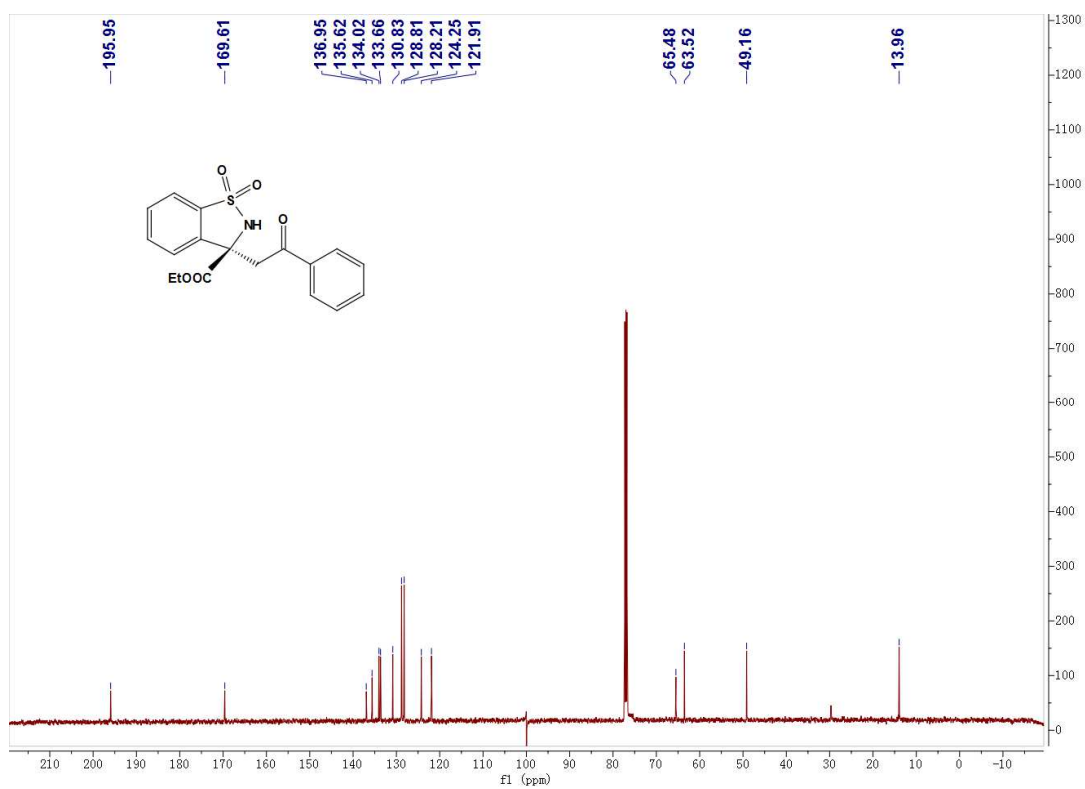
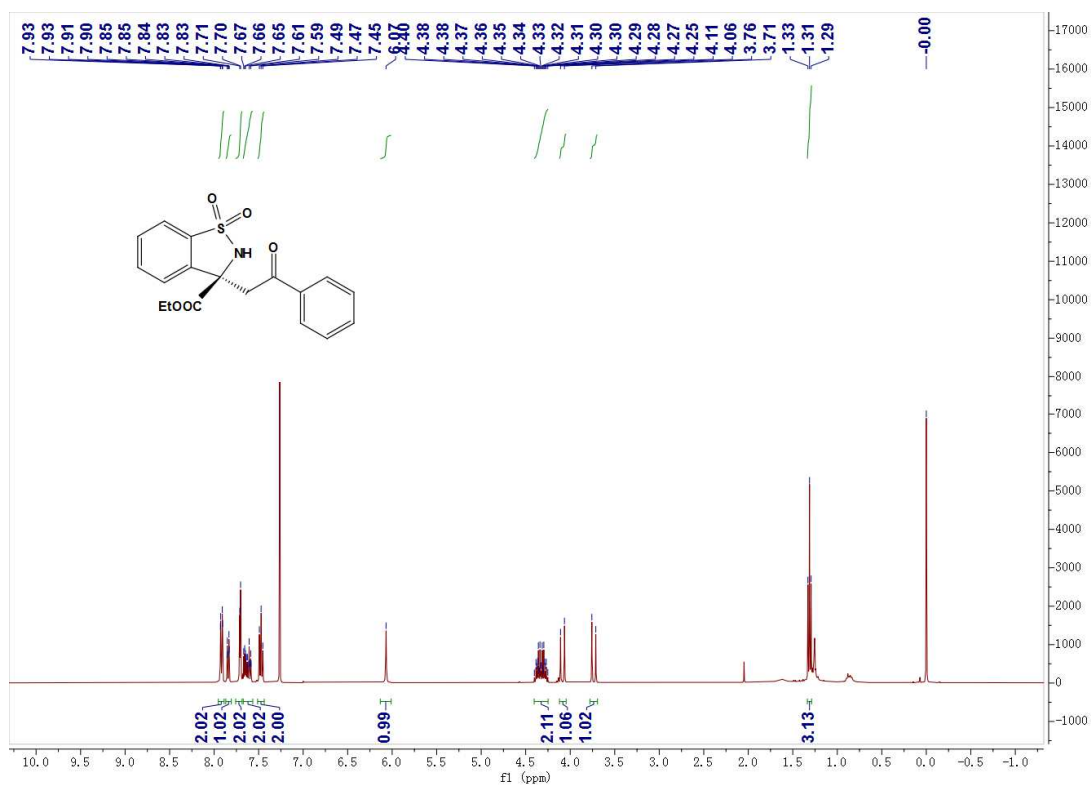
**Bis((*R*)-2,3-dihydro-5'*H*-spiro[indene-1,4'-oxazol]-2'-yl)propane (L3)**



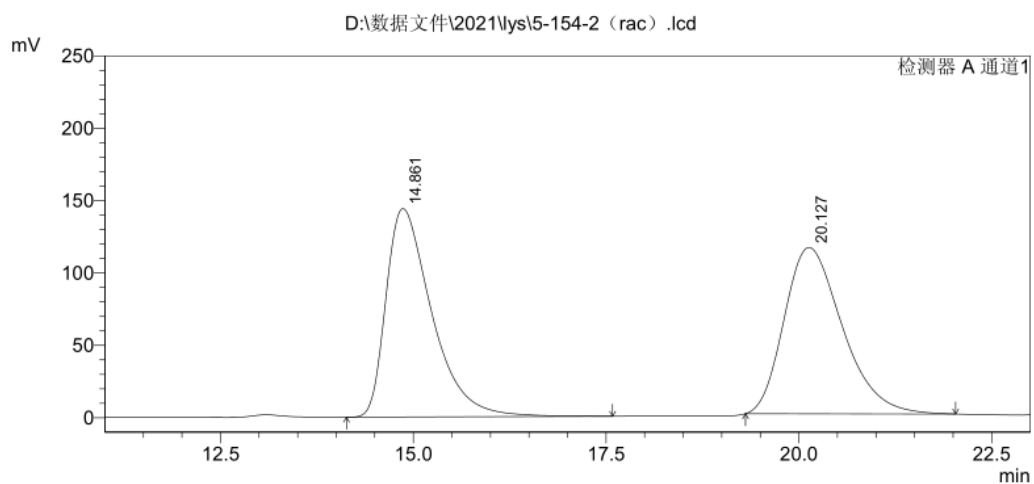
# 2,6-Bis((*R*)-2,3-dihydro-5'*H*-spiro[indene-1,4'-oxazol]-2'-yl)pyridine (L4)



**(R)-ethyl 3-(2-oxo-2-phenylethyl)-2,3-dihydrobenzo[d]isothiazole 1,1-dioxide (1aa)**

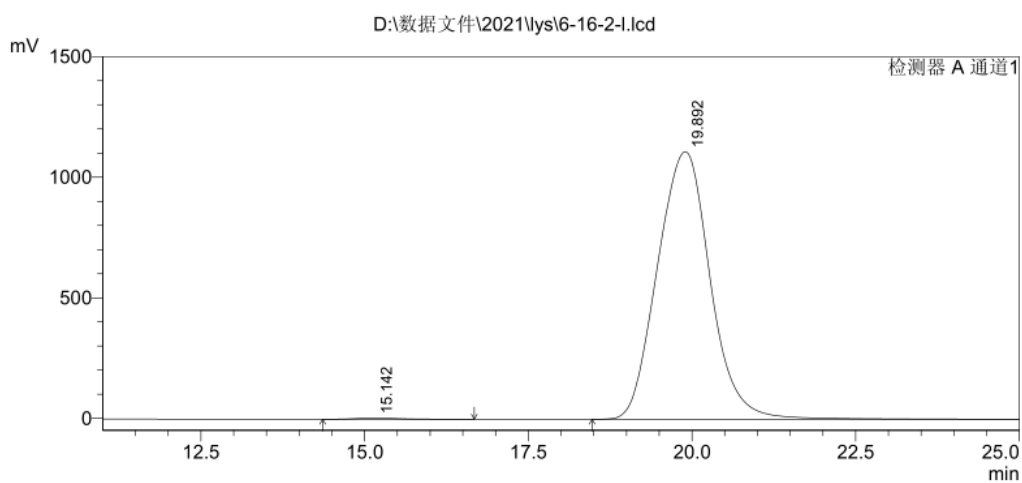






峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	14.861	5947858	144039	49.647	55.618
2	20.127	6032448	114940	50.353	44.382
总计		11980306	258980	100.000	100.000

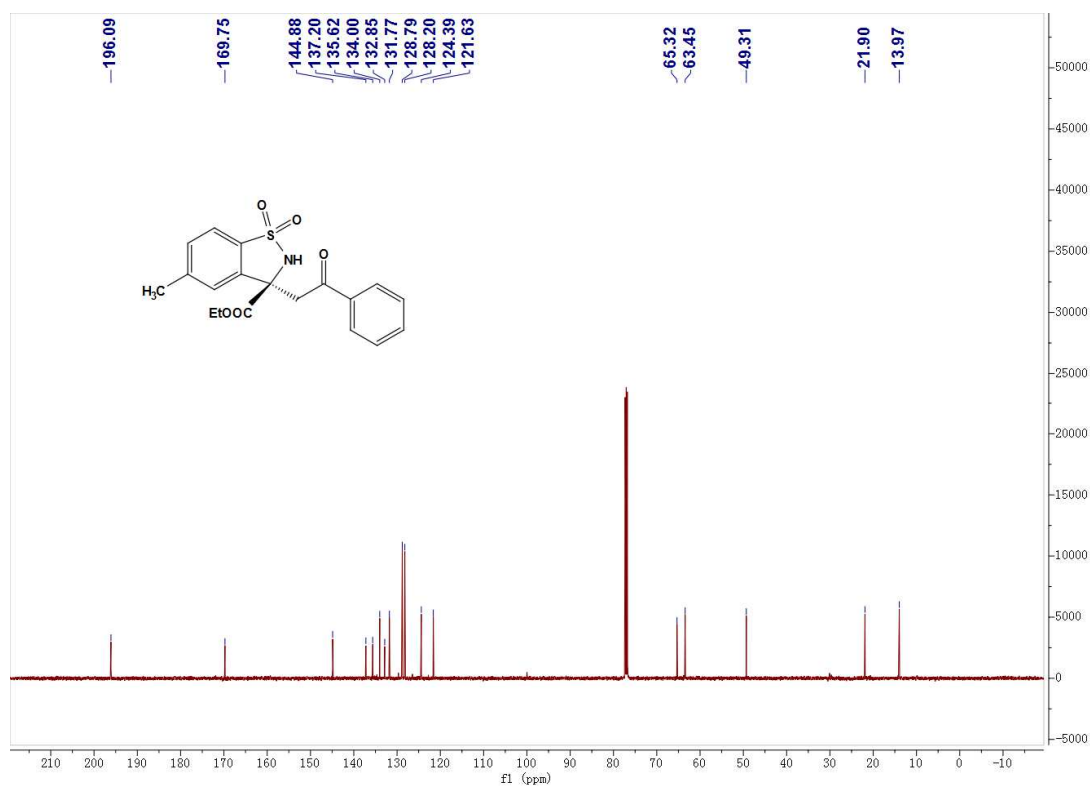
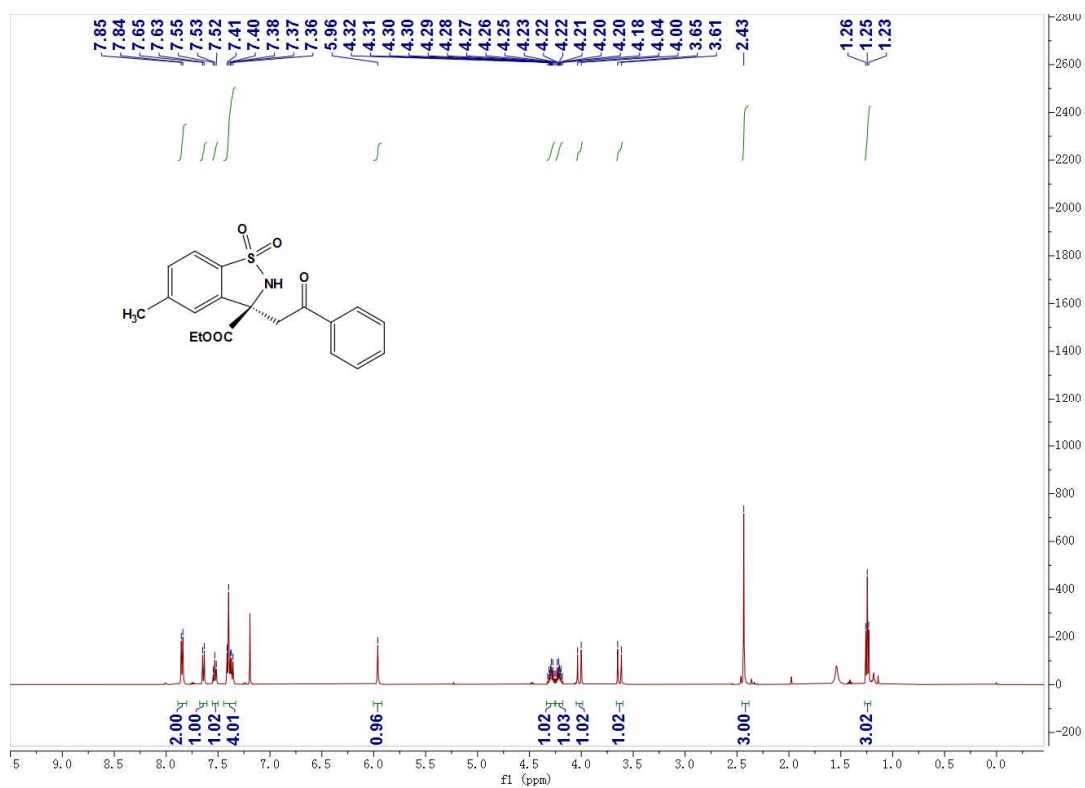


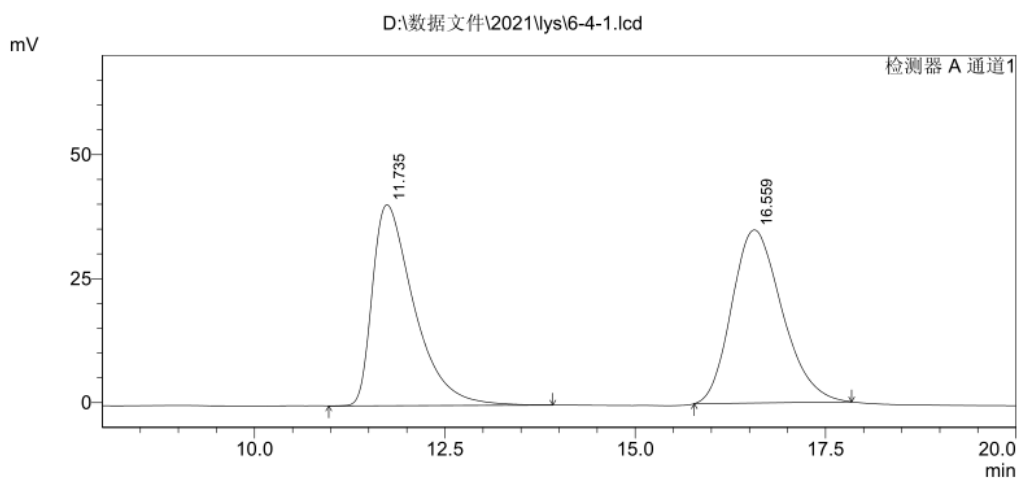
峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	15.142	202655	4826	0.325	0.433
2	19.892	62134110	1109354	99.675	99.567
总计		62336765	1114180	100.000	100.000

**(R)-ethyl 5-methyl-3-(2-oxo-2-phenylethyl)-2,3-dihydrobenzo[d]isothiazole**

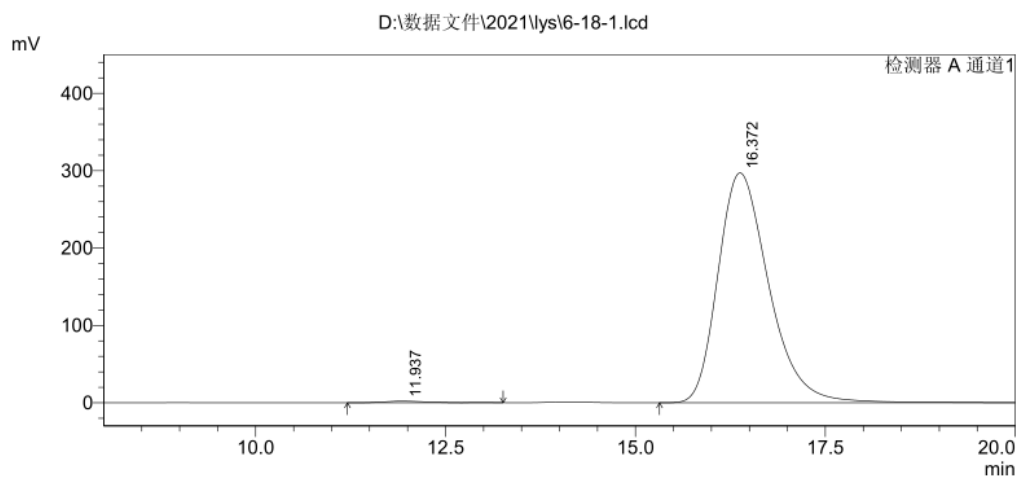
**-3-carboxylate 1,1-dioxide (1ba)**





峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	11.735	1544441	40506	49.029	53.729
2	16.559	1605609	34884	50.971	46.271
总计		3150050	75390	100.000	100.000

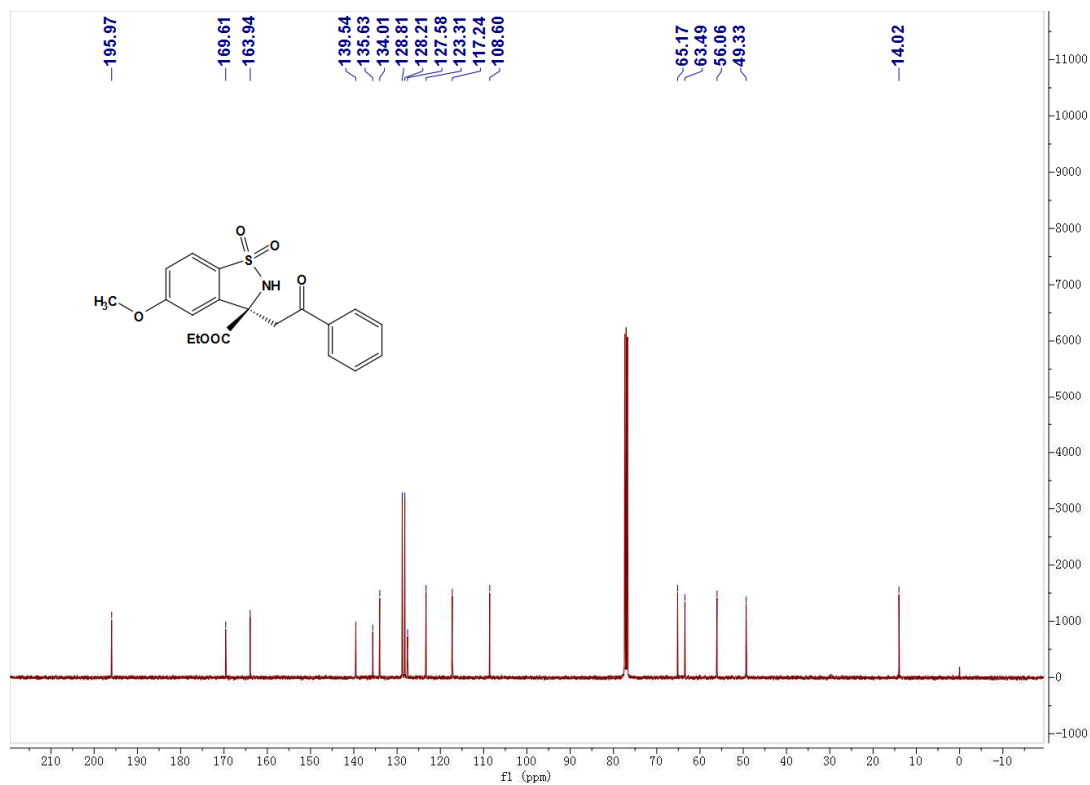
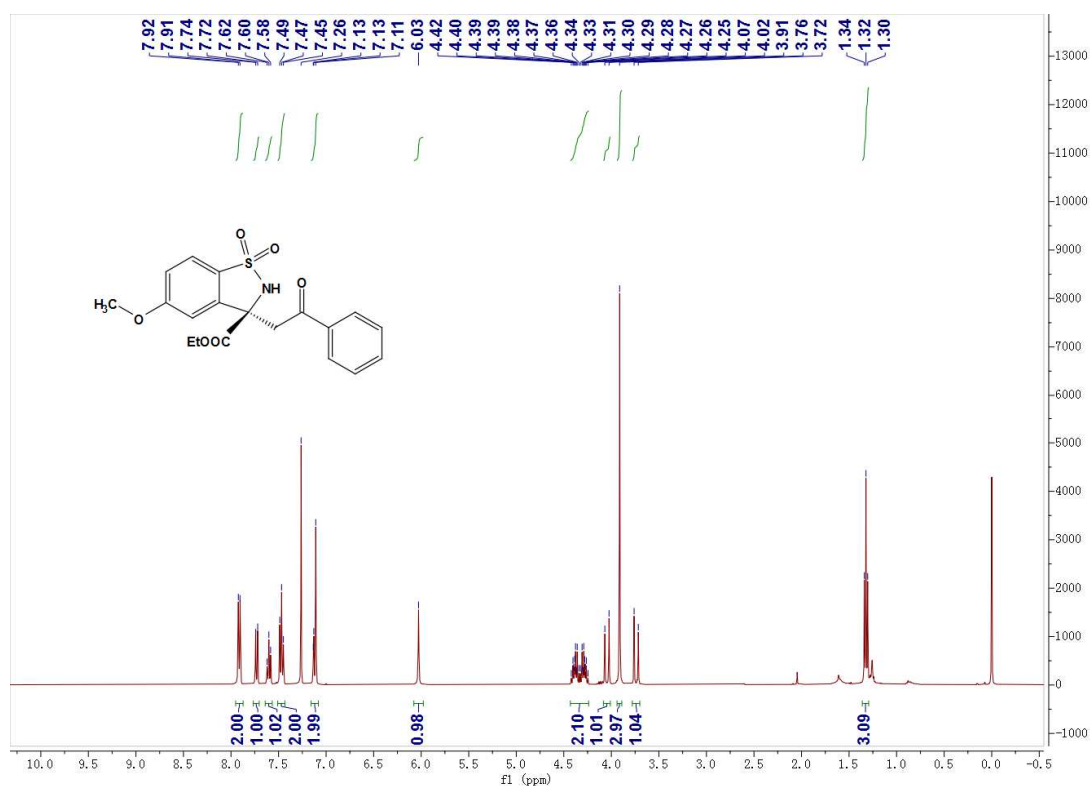


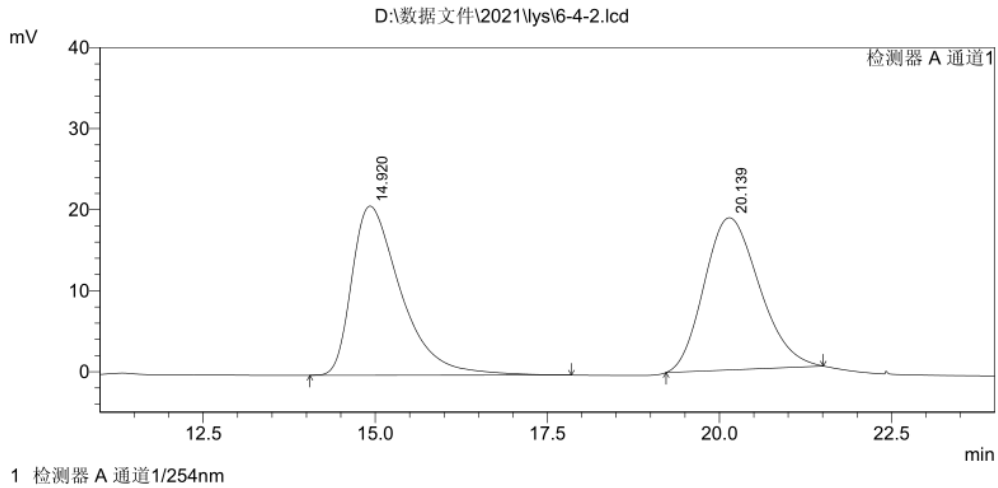
峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	11.937	81057	2095	0.582	0.700
2	16.372	13838300	297195	99.418	99.300
总计		13919358	299290	100.000	100.000

**(R)-ethyl 5-methoxy-3-(2-oxo-2-phenylethyl)-2,3-dihydrobenzo[d]isothiazole**

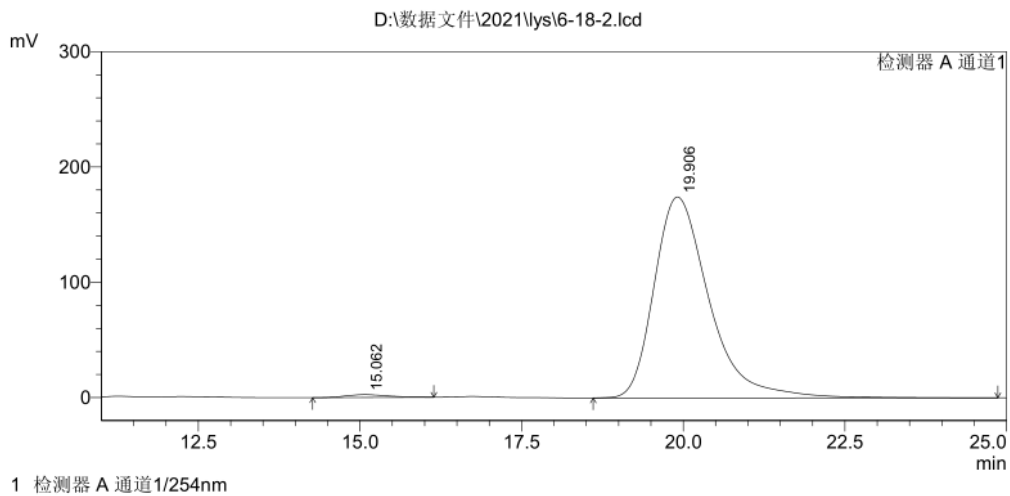
**-3-carboxylate 1,1-dioxide (1ca)**





峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	14.920	1039324	20877	49.834	52.638
2	20.139	1046257	18785	50.166	47.362
总计		2085581	39662	100.000	100.000

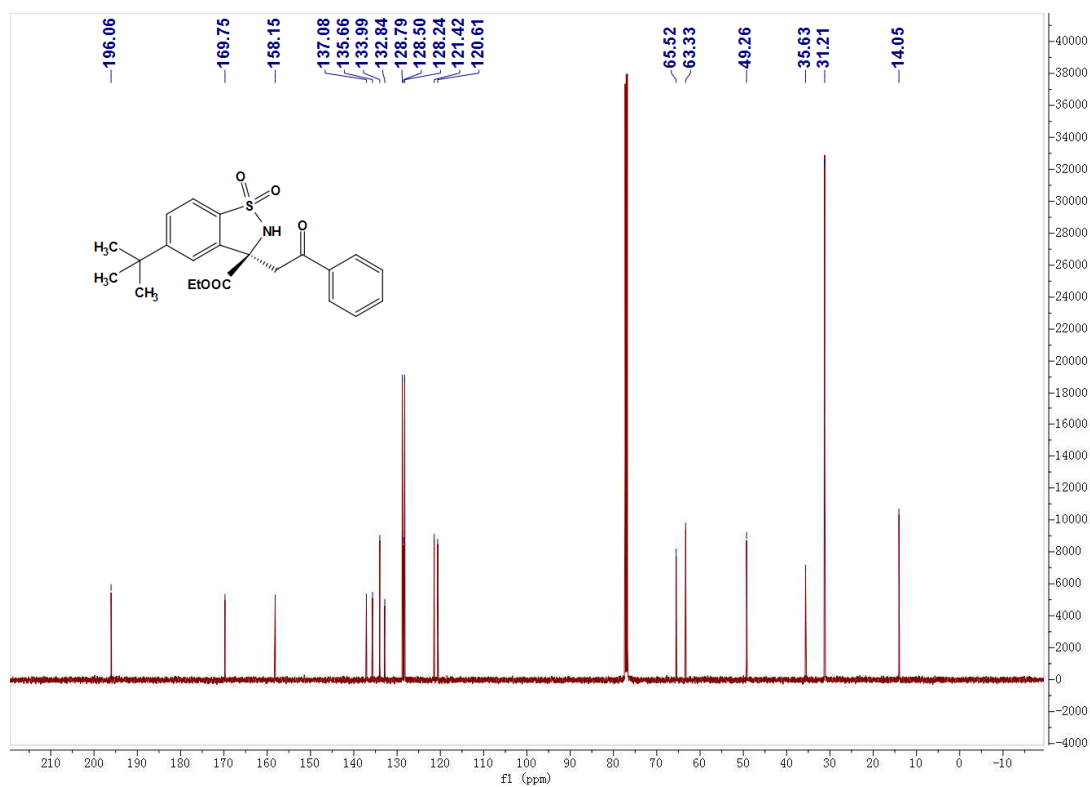
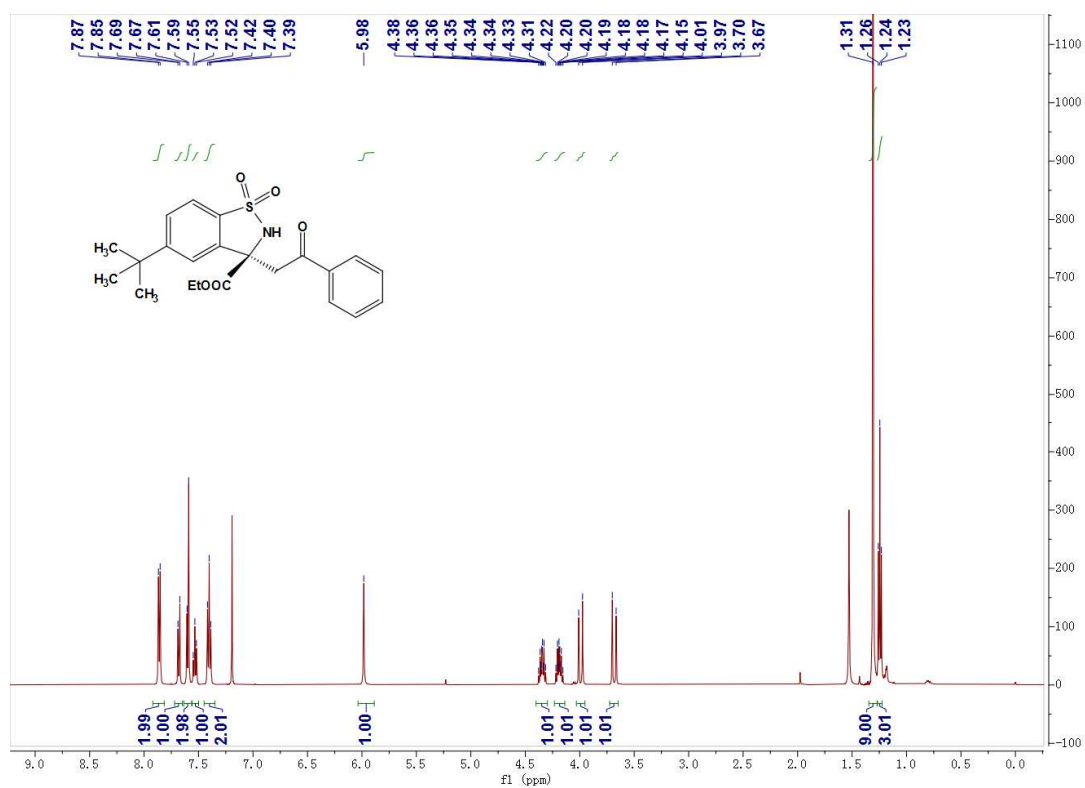


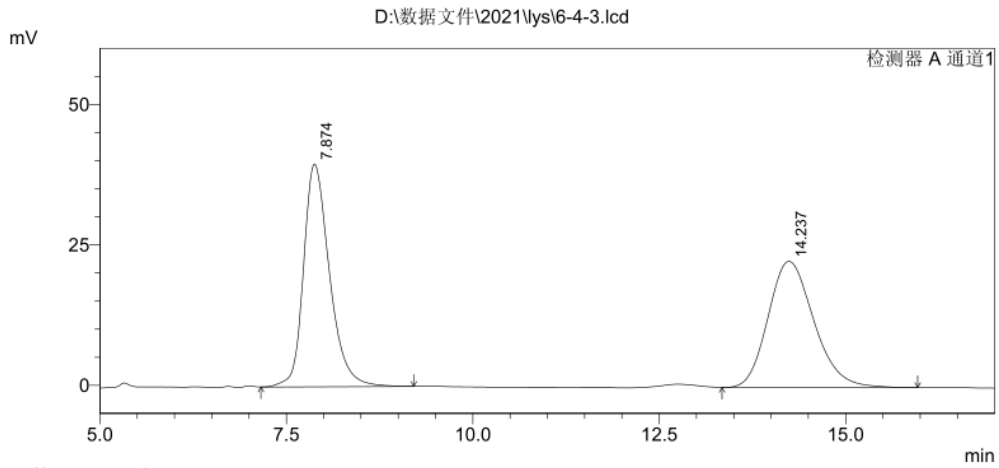
峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	15.062	113477	2476	1.090	1.401
2	19.906	10293229	174255	98.910	98.599
总计		10406706	176731	100.000	100.000

**(R)-ethyl 5-(tert-butyl)-3-(2-oxo-2-phenylethyl)-2,3-dihydrobenzo[d]isothiazole**

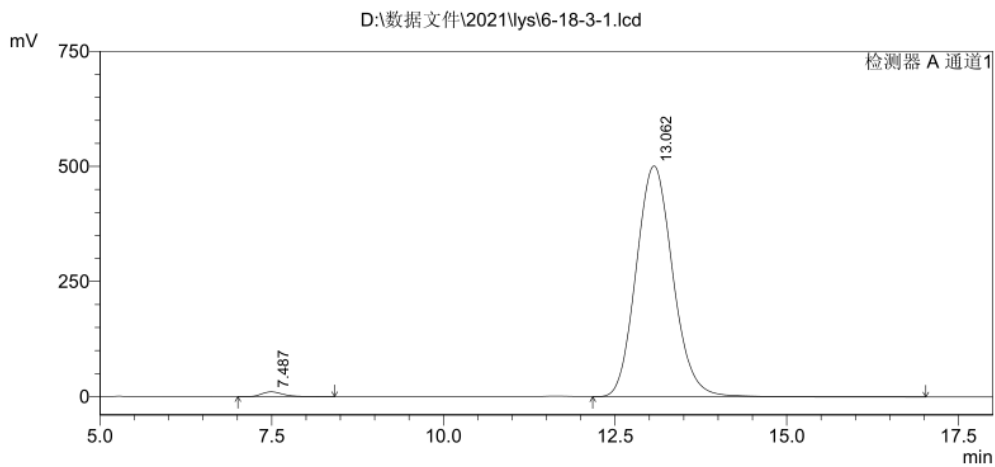
**-3-carboxylate 1,1-dioxide (1da)**





峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	7.874	962873	39663	50.063	63.831
2	14.237	960460	22474	49.937	36.169
总计		1923333	62137	100.000	100.000

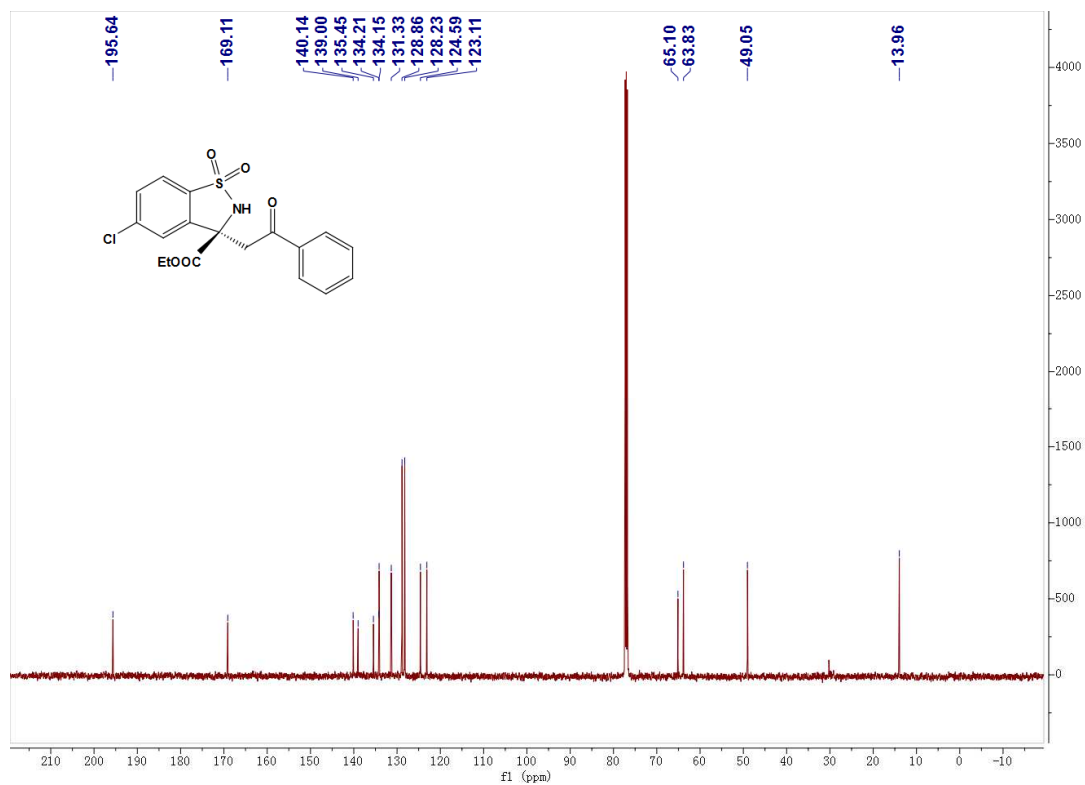
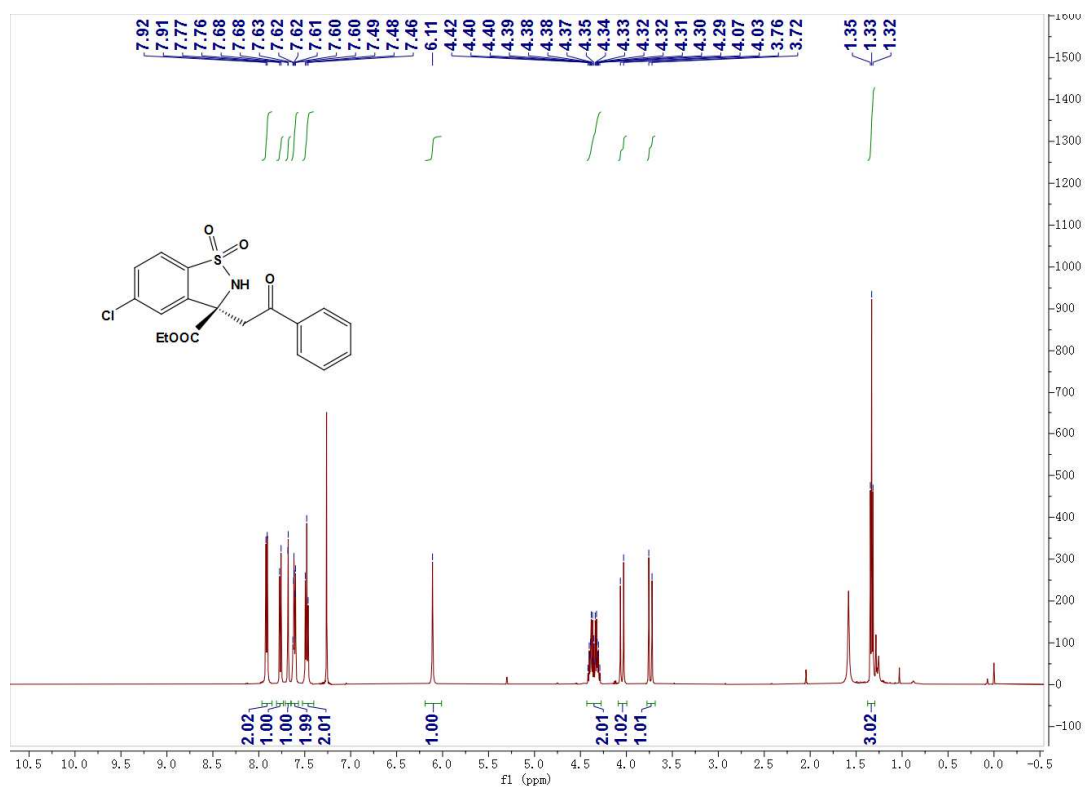


峰表

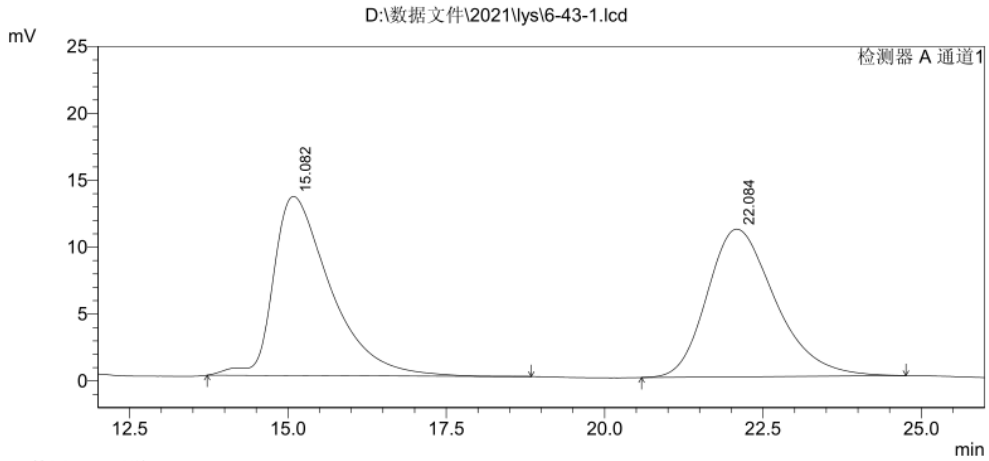
峰#	保留时间	面积	高度	面积 %	高度 %
1	7.487	222412	10310	1.179	2.014
2	13.062	18641668	501745	98.821	97.986
总计		18864080	512055	100.000	100.000

**(R)-ethyl 5-chloro-3-(2-oxo-2-phenylethyl)-2,3-dihydrobenzo[d]isothiazole**

**-3-carboxylate 1,1-dioxide (1ea)**



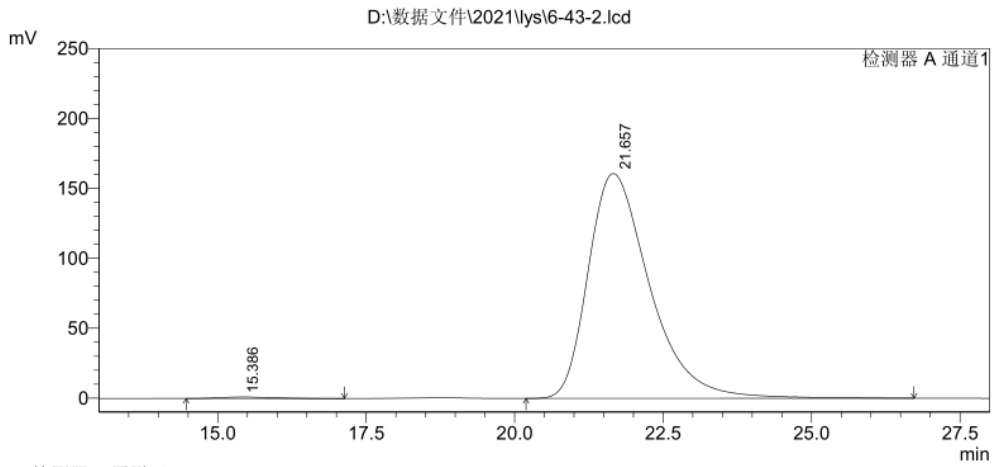




1 检测器 A 通道1/254nm

峰表

检测器 A Ch1 254nm					
峰#	保留时间	面积	高度	面积 %	高度 %
1	15.082	842422	13386	50.445	54.790
2	22.084	827553	11045	49.555	45.210
总计		1669975	24431	100.000	100.000



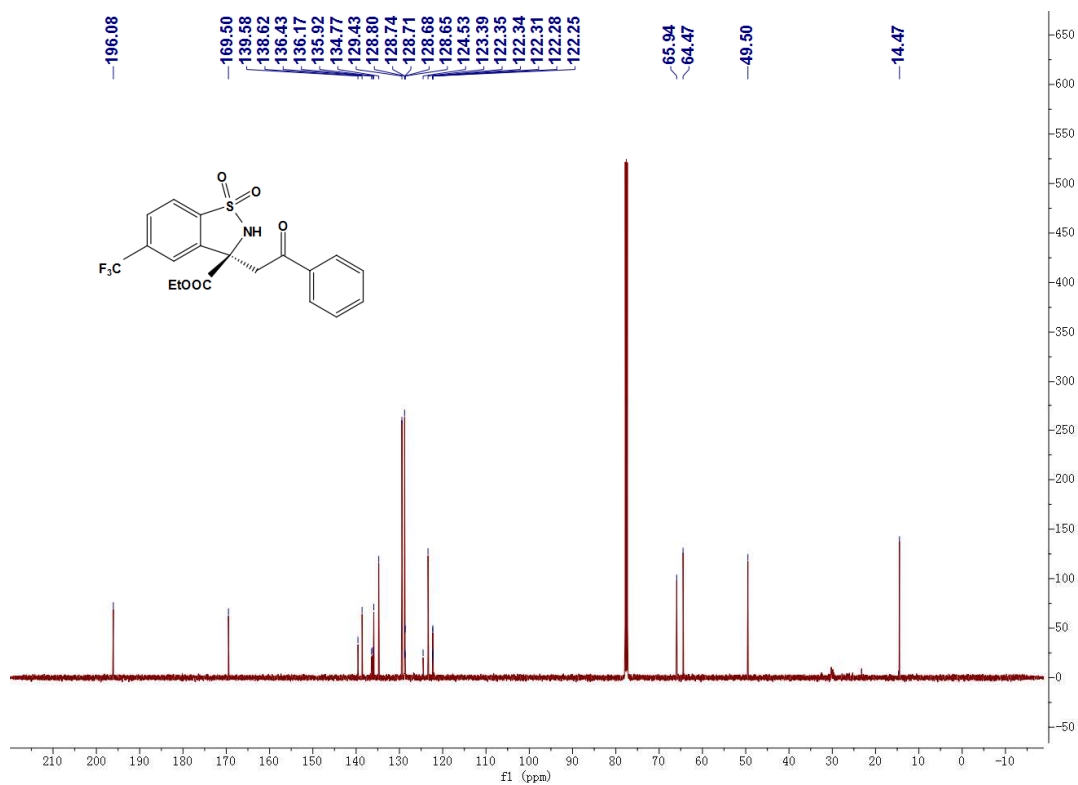
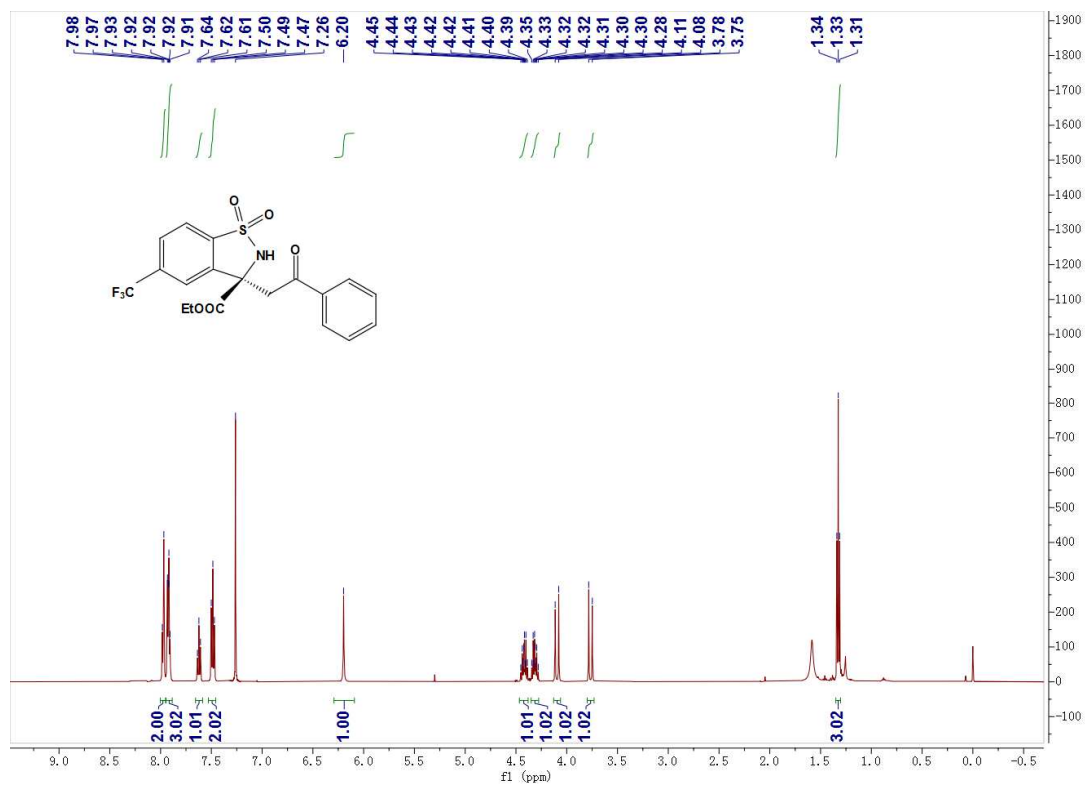
1 检测器 A 通道1/254nm

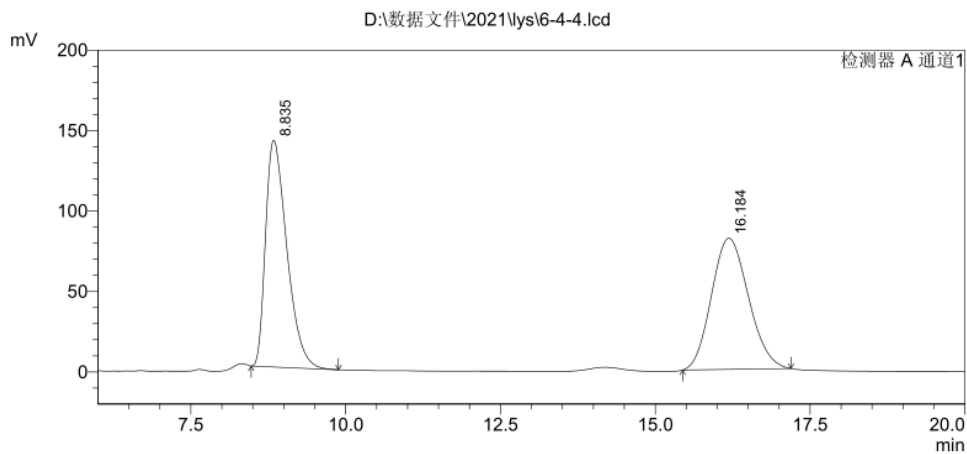
峰表

检测器 A Ch1 254nm					
峰#	保留时间	面积	高度	面积 %	高度 %
1	15.386	60961	1034	0.523	0.639
2	21.657	11586788	160829	99.477	99.361
总计		11647748	161863	100.000	100.000

**(R)-ethyl 3-(2-oxo-2-phenylethyl)-5-(trifluoromethyl)-2,3-dihydrobenzo[d]**

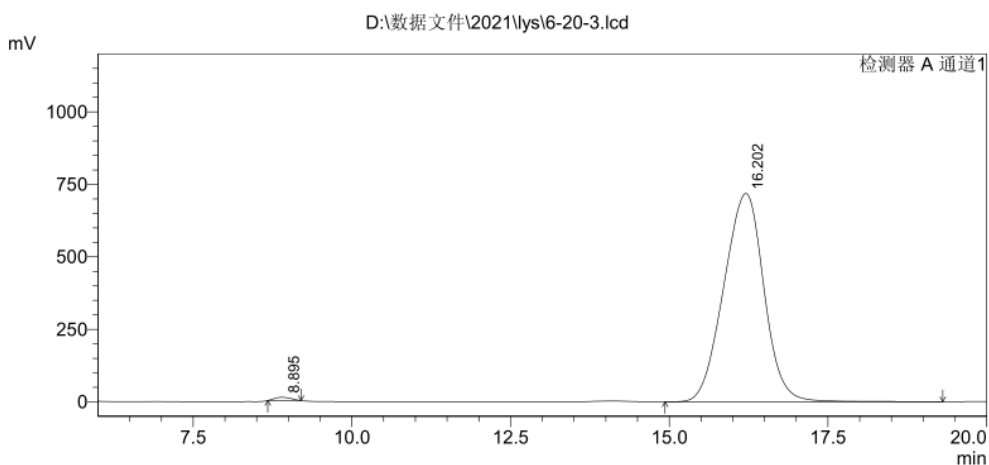
**isothiazole-3-carboxylate 1,1-dioxide (1fa)**





峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	8.835	3371592	140953	49.852	63.347
2	16.184	3391599	81556	50.148	36.653
总计		6763191	222510	100.000	100.000

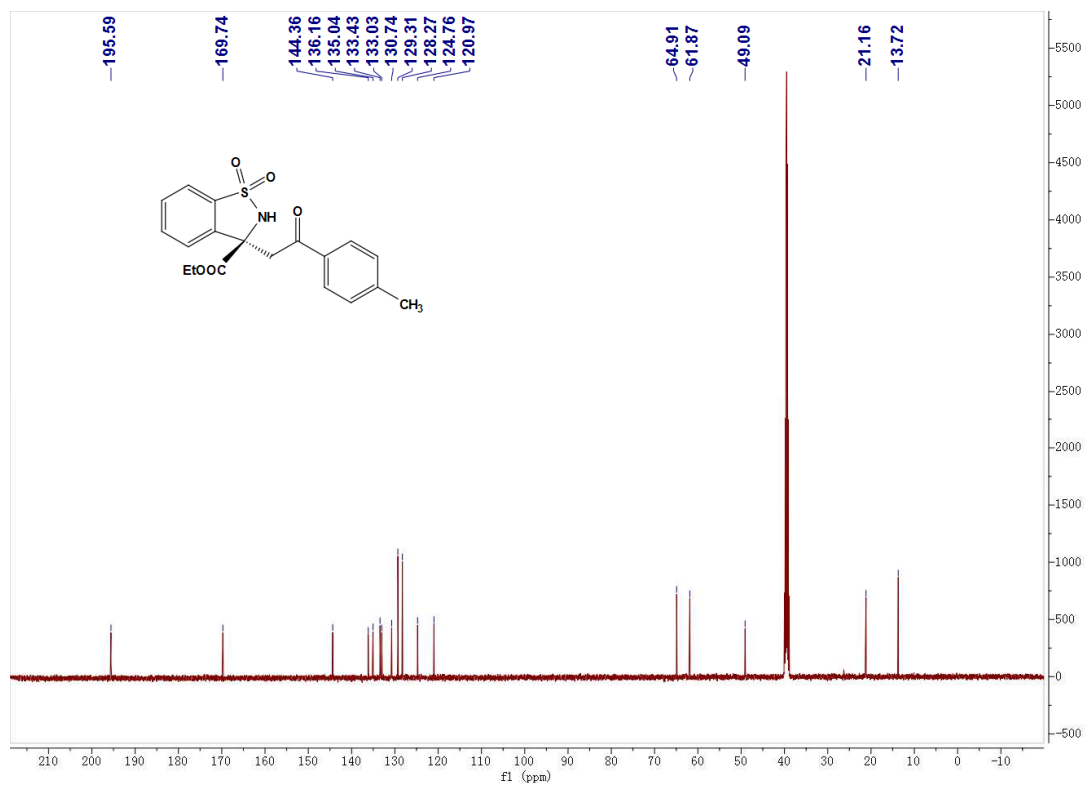
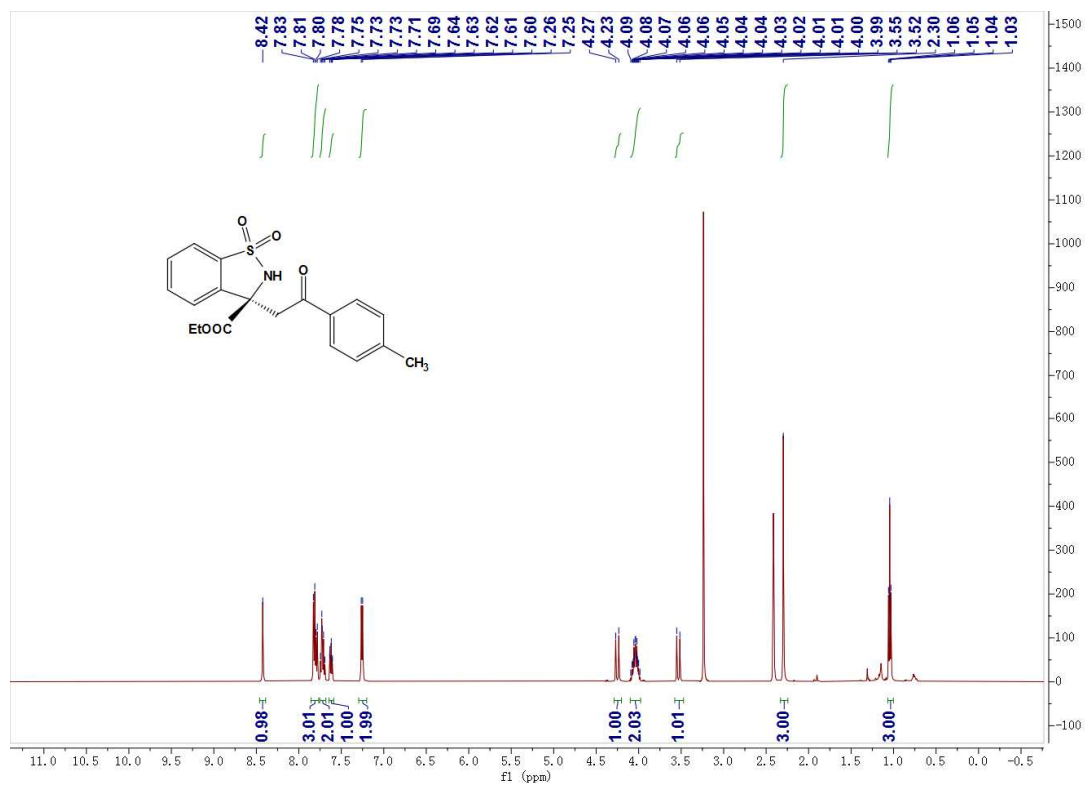


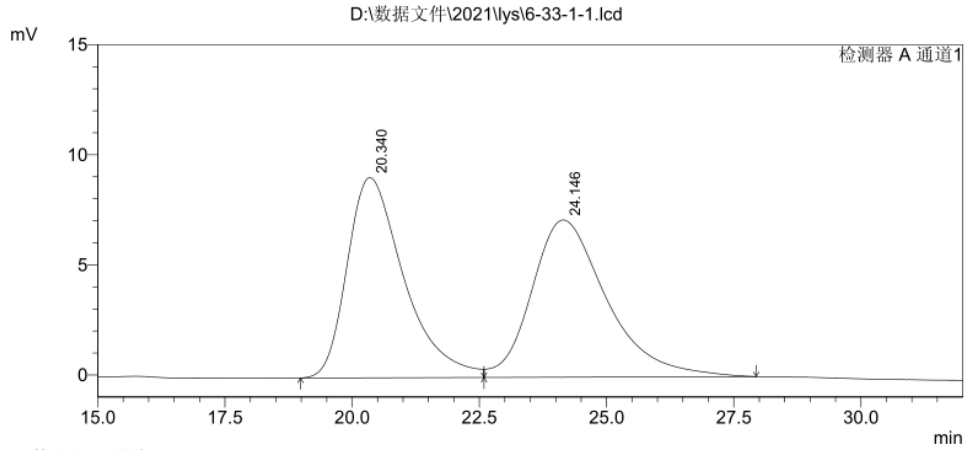
峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	8.895	205011	11600	0.644	1.589
2	16.202	31607235	718418	99.356	98.411
总计		31812246	730017	100.000	100.000

**(R)-ethyl 3-(2-oxo-2-(4-tolyl)ethyl)-2,3-dihydrobenzo[d] isothiazole**

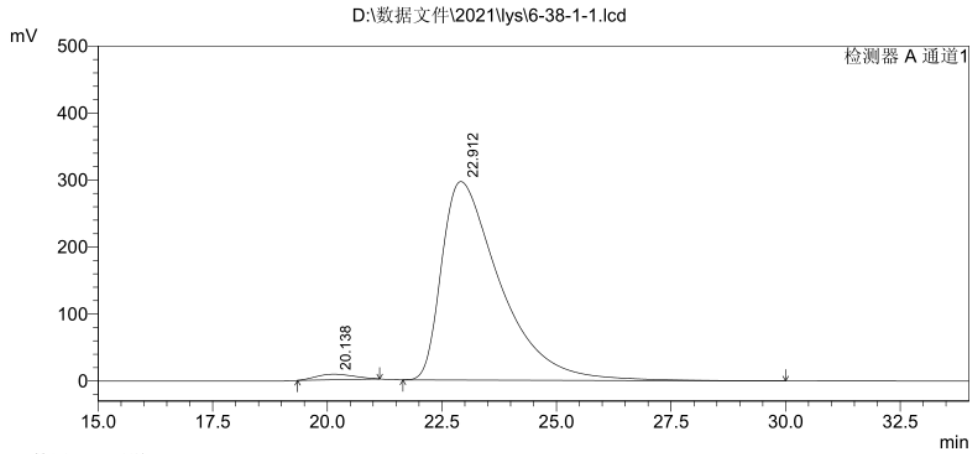
**-3-carboxylate 1,1-dioxide (1a)**





峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	20.340	706770	9088	49.118	56.006
2	24.146	732148	7139	50.882	43.994
总计		1438918	16227	100.000	100.000

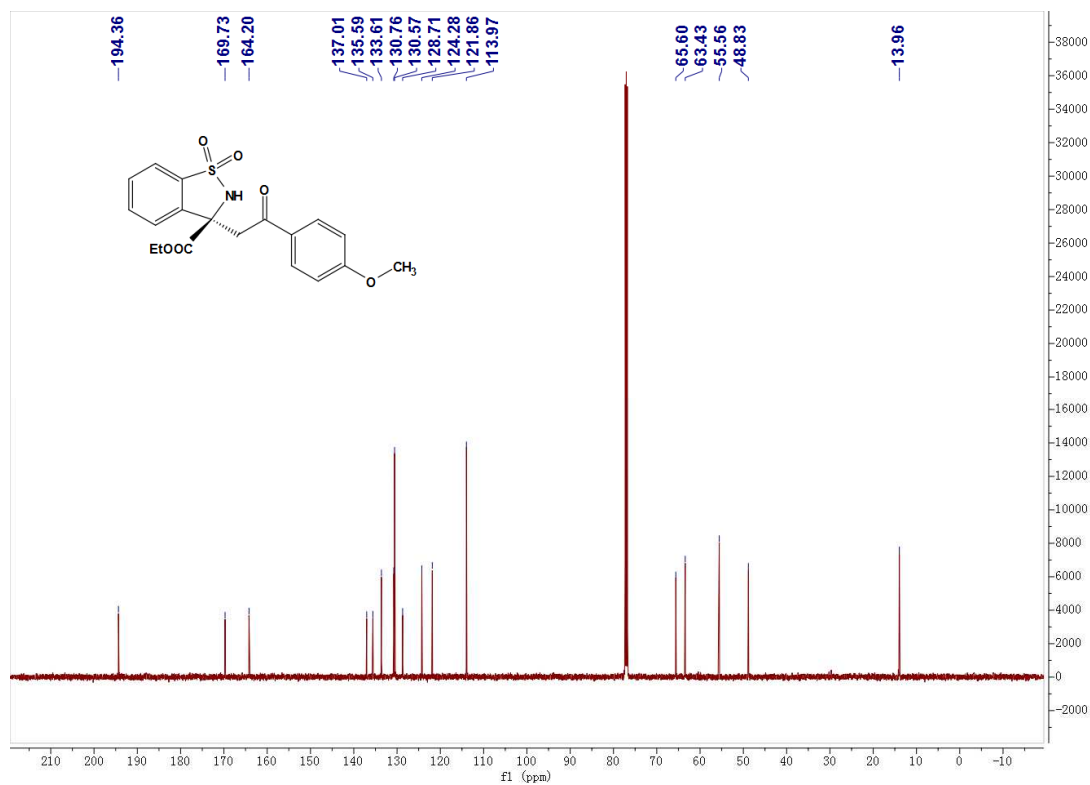
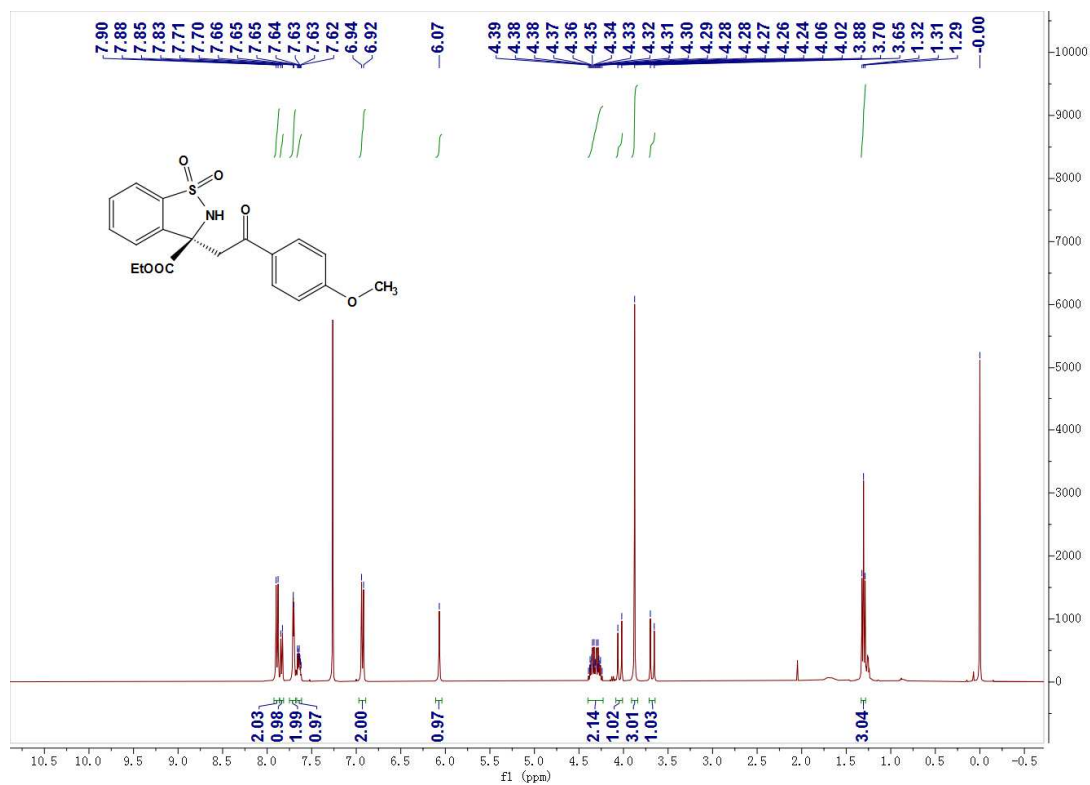


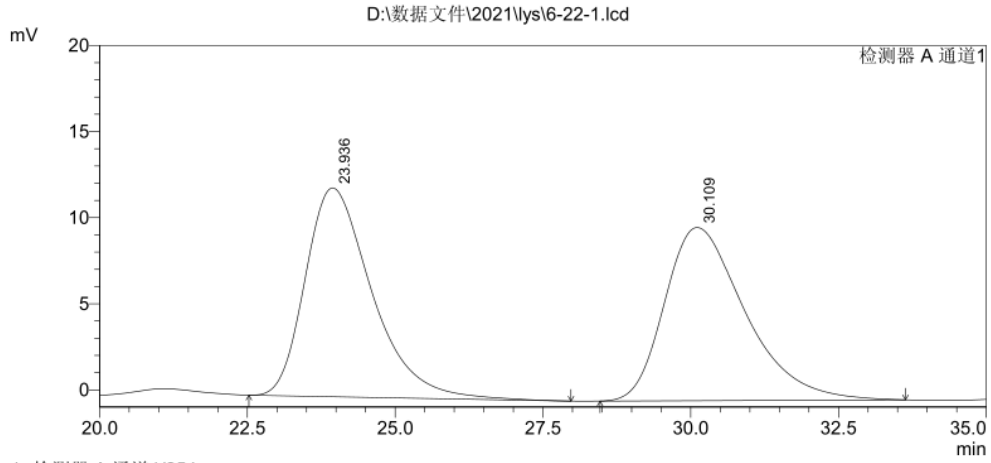
峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	20.138	475846	8290	1.773	2.721
2	22.912	26366274	296338	98.227	97.279
总计		26842120	304629	100.000	100.000

**(R)-ethyl 3-(2-(4-methoxyphenyl)-2-oxoethyl)-2,3-dihydrobenzo[d]isothiazole**

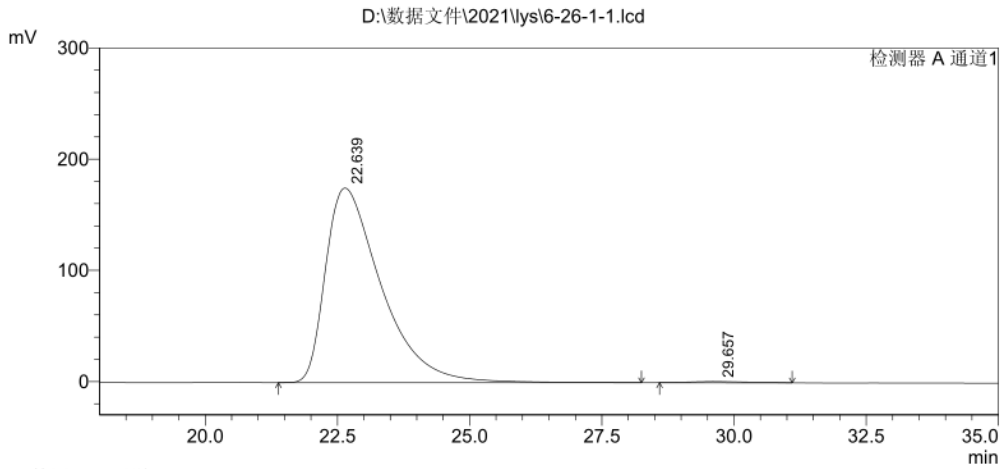
**-3-carboxylate 1,1-dioxide (1ac)**





峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	23.936	953153	12127	49.979	54.663
2	30.109	953941	10058	50.021	45.337
总计		1907094	22185	100.000	100.000

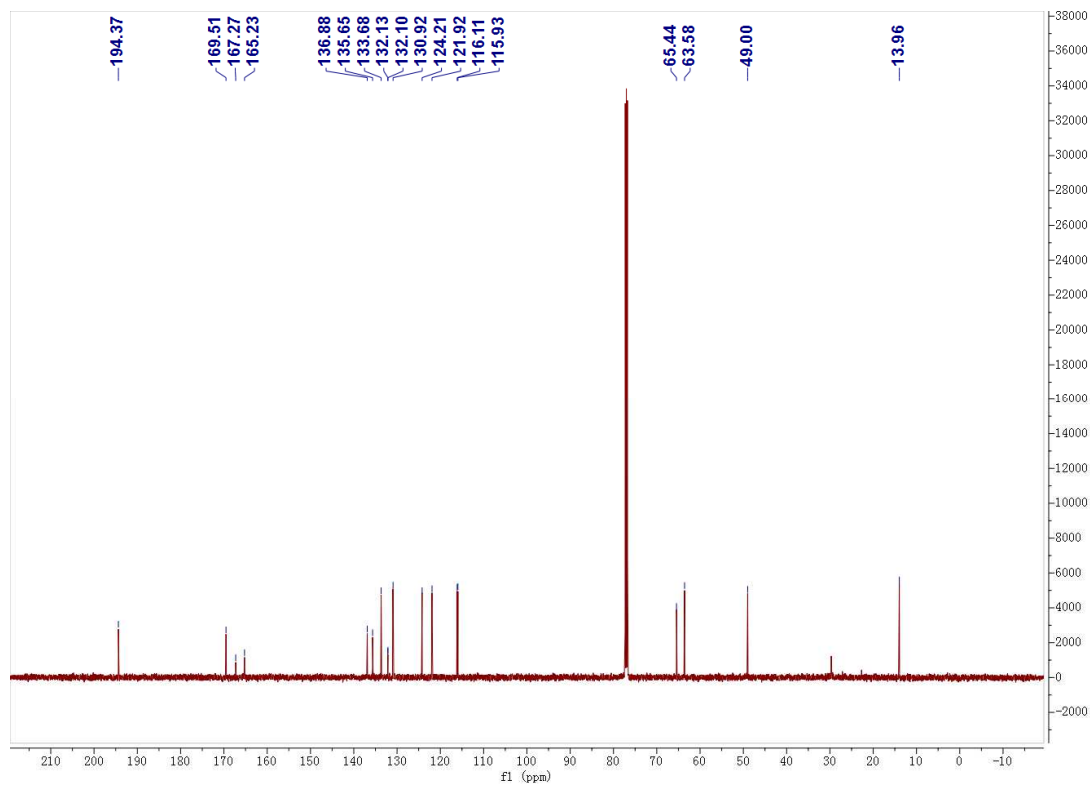
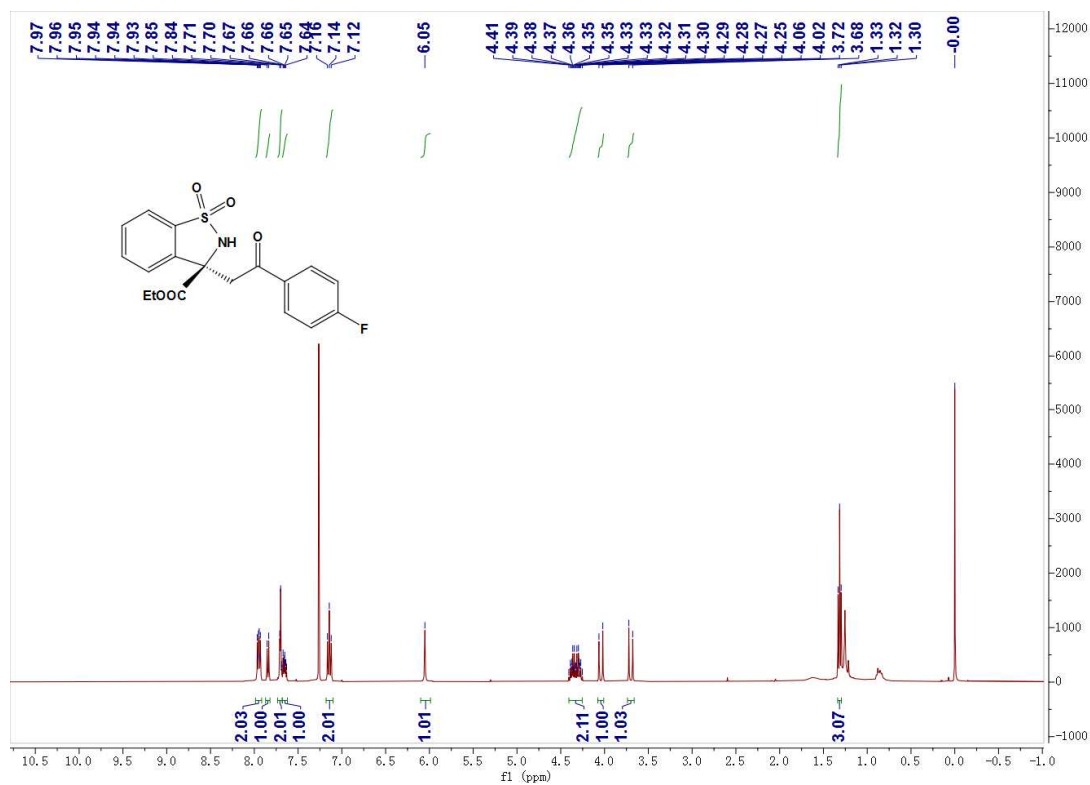


峰表

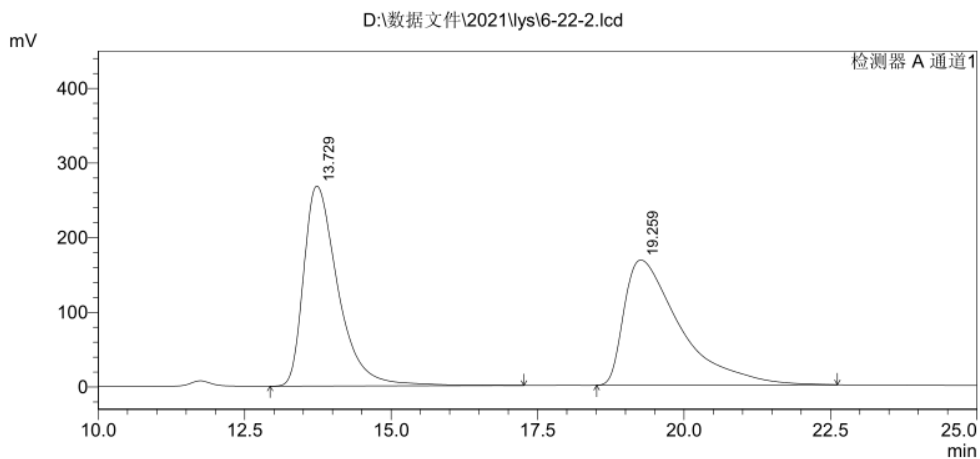
峰#	保留时间	面积	高度	面积 %	高度 %
1	22.639	12886642	175070	99.417	99.444
2	29.657	75573	979	0.583	0.556
总计		12962214	176048	100.000	100.000

**(R)-ethyl 3-(2-(4-fluorophenyl)-2-oxoethyl)-2,3-dihydrobenzo[d]isothiazole**

**-3-carboxylate 1,1-dioxide (1ad)**

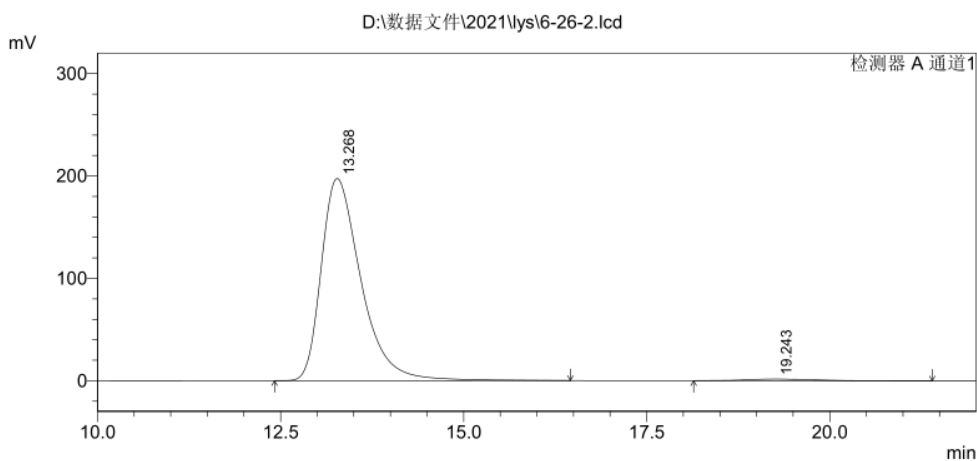






峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	13.729	10951424	268133	49.521	61.507
2	19.259	11163219	167810	50.479	38.493
总计		22114643	435943	100.000	100.000

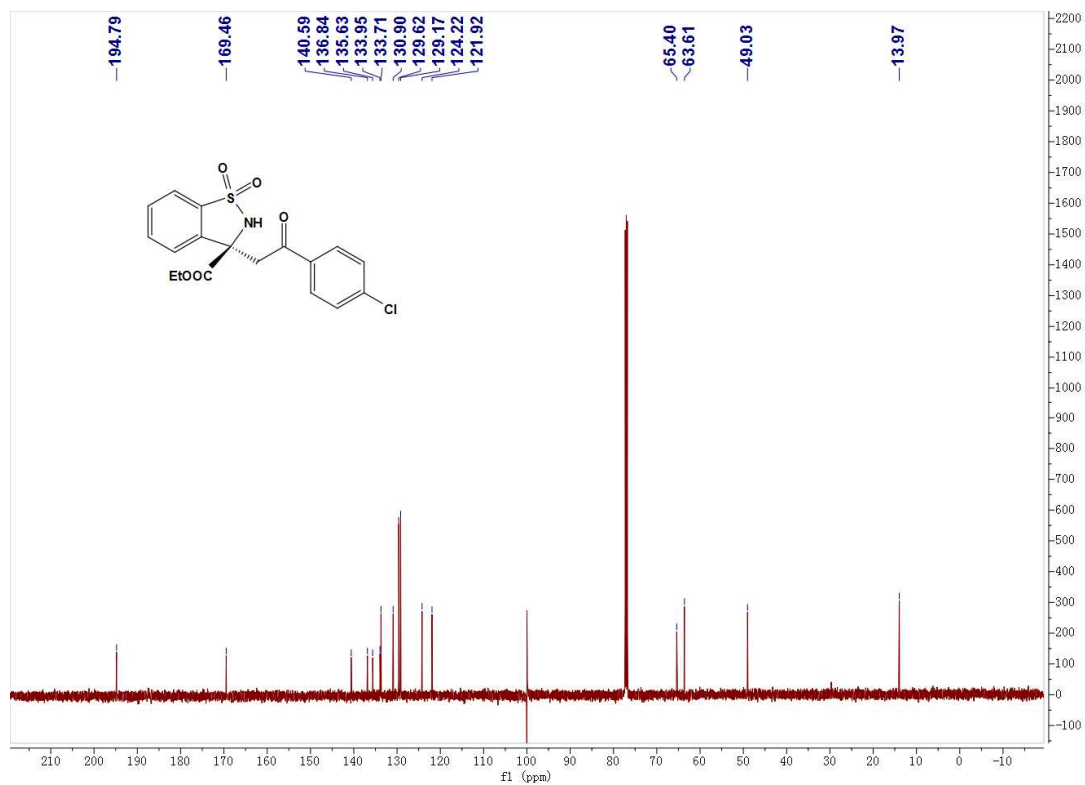
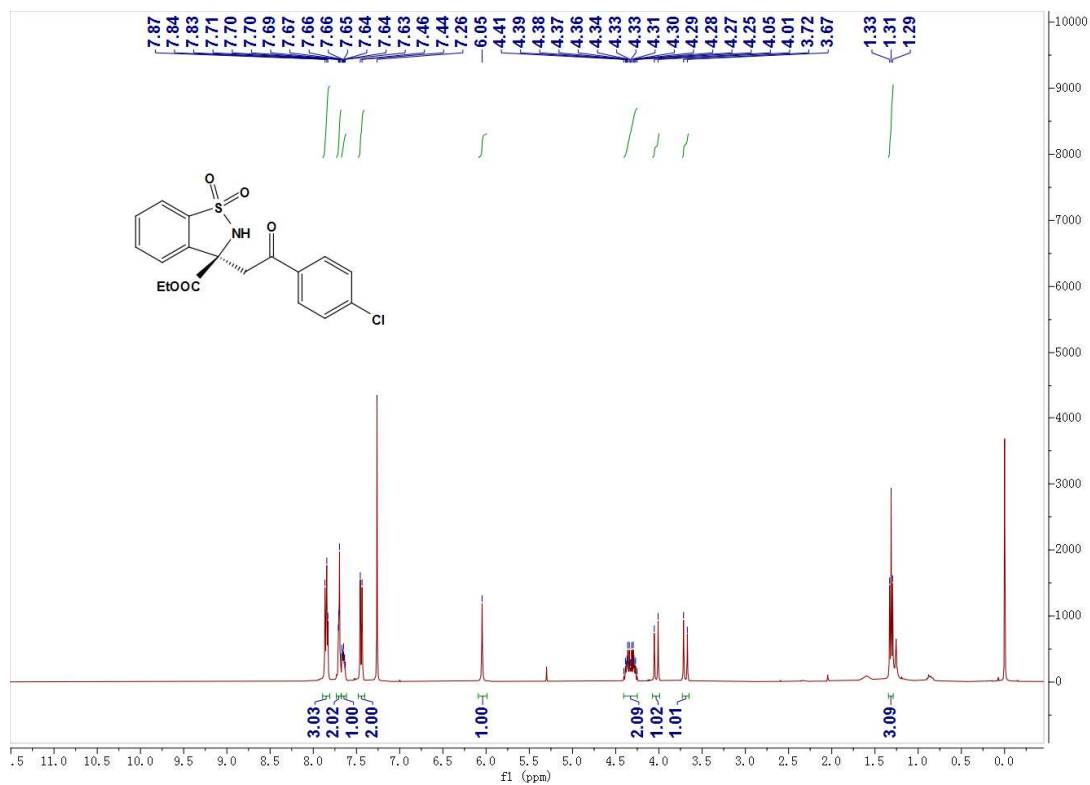


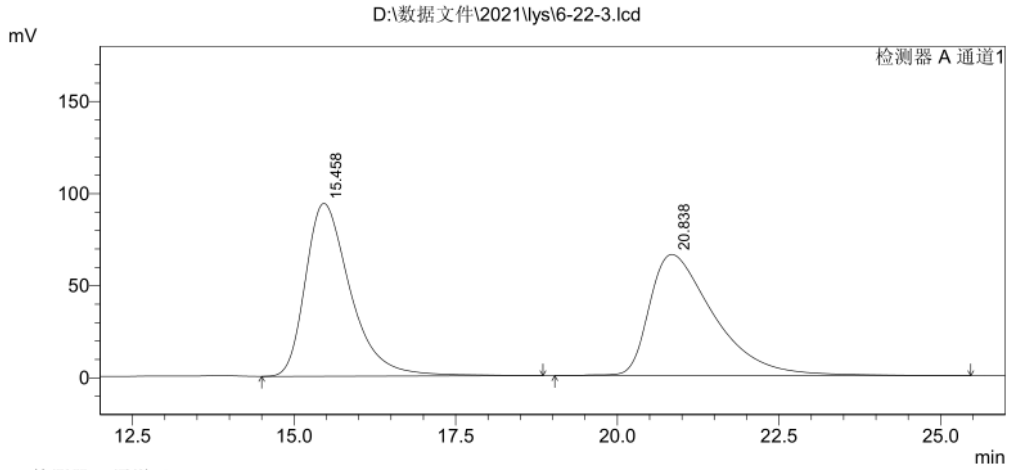
峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	13.268	7451167	197458	98.538	99.173
2	19.243	110524	1647	1.462	0.827
总计		7561692	199104	100.000	100.000

**(R)-ethyl 3-(2-(4-chlorophenyl)-2-oxoethyl)-2,3-dihydrobenzo[d]isothiazole**

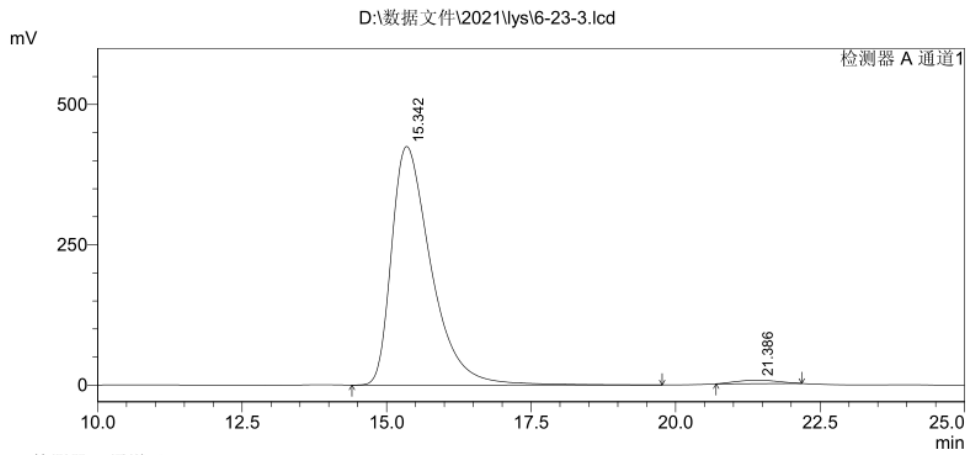
**-3-carboxylate 1,1-dioxide (1ae)**





峰表

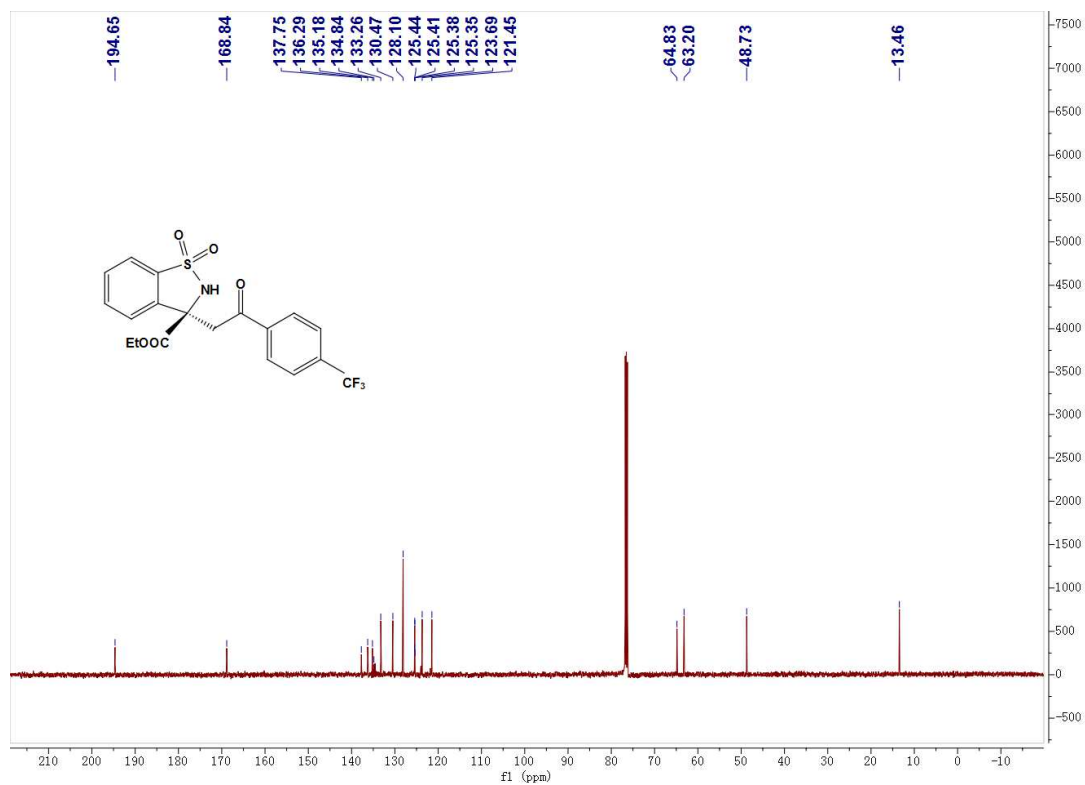
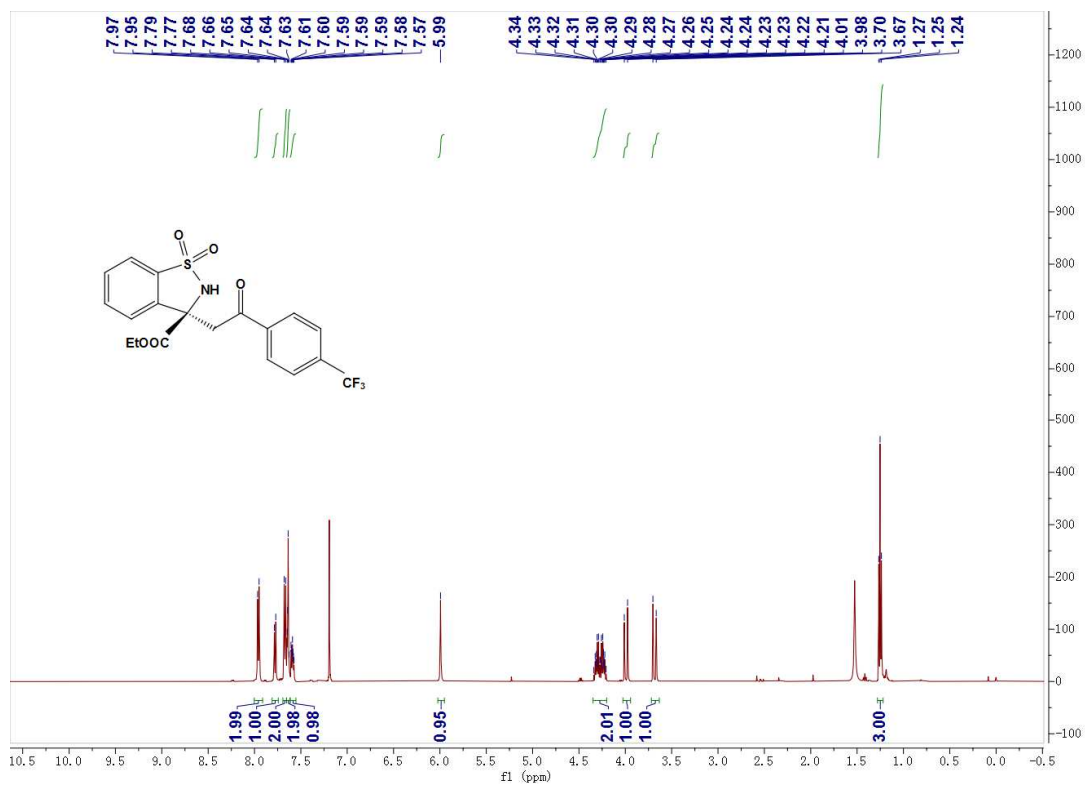
峰#	保留时间	面积	高度	面积 %	高度 %
1	15.458	4547351	93882	49.755	58.783
2	20.838	4592090	65827	50.245	41.217
总计		9139440	159709	100.000	100.000

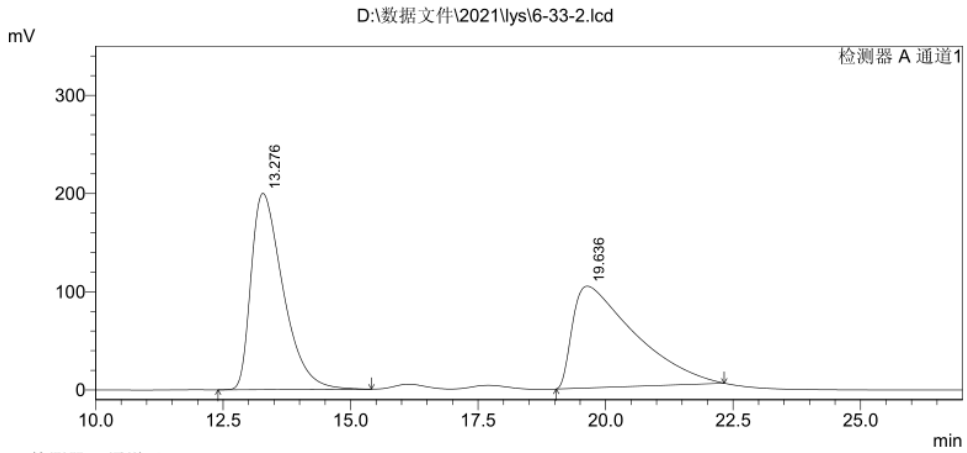


峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	15.342	20239974	425240	98.482	98.551
2	21.386	311910	6251	1.518	1.449
总计		20551885	431490	100.000	100.000

**(R)-ethyl 3-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (1af)**

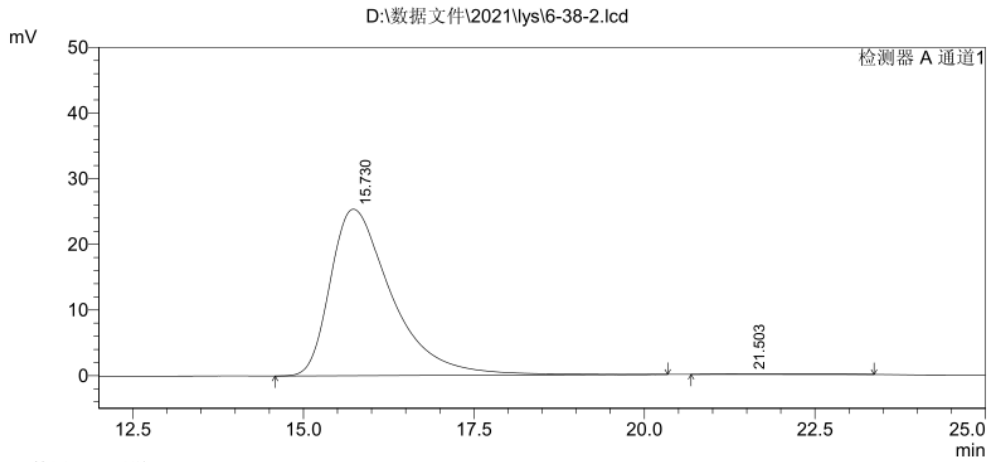




1 检测器 A 通道1/254nm

峰表

检测器 A Ch1 254nm					
峰#	保留时间	面积	高度	面积 %	高度 %
1	13.276	8730102	200051	49.907	65.879
2	19.636	8762581	103615	50.093	34.121
总计		17492683	303666	100.000	100.000



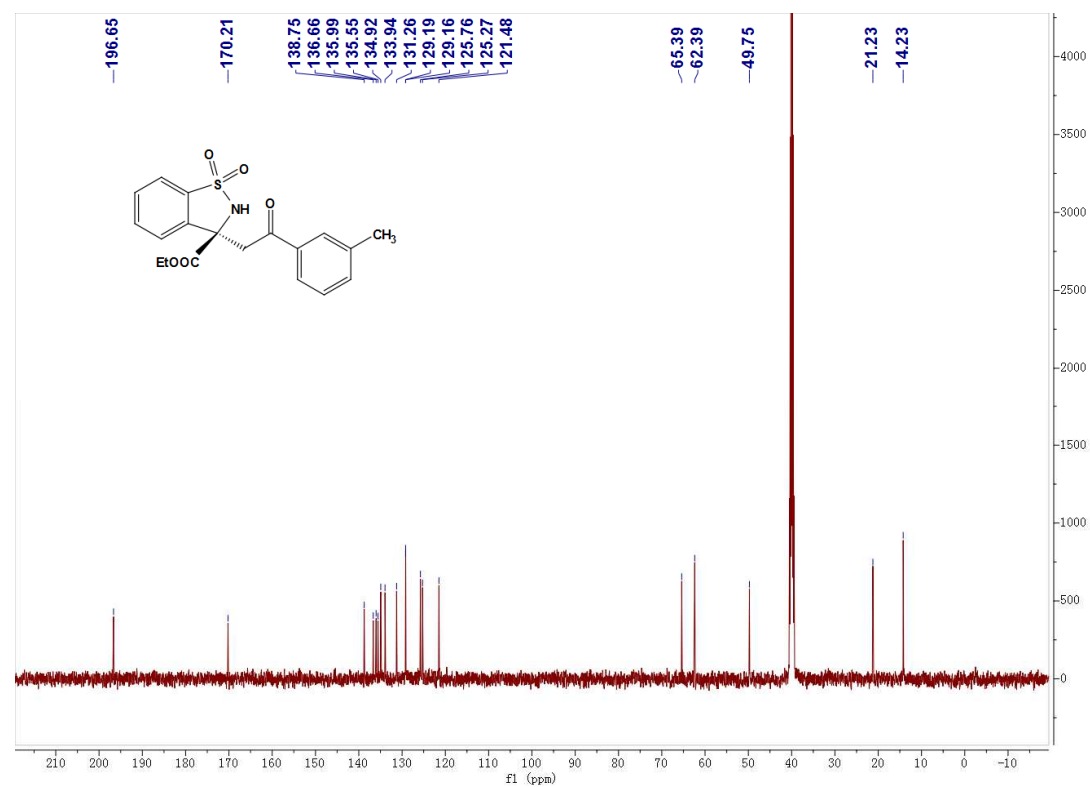
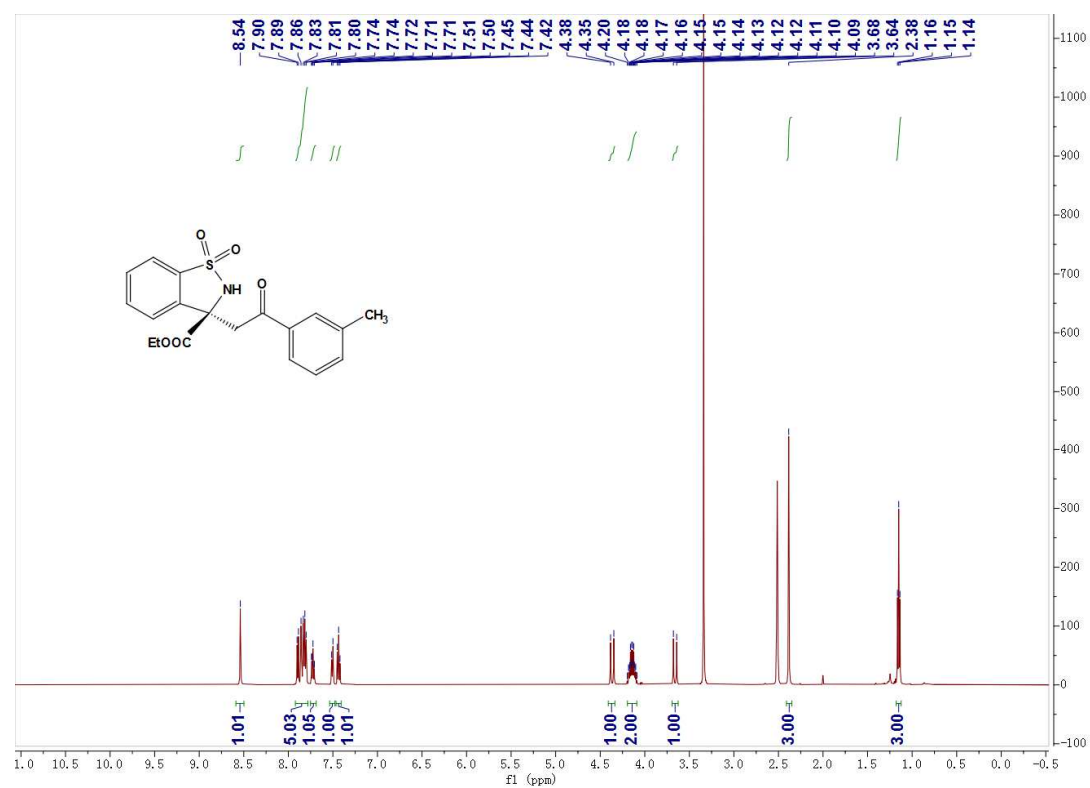
1 检测器 A 通道1/254nm

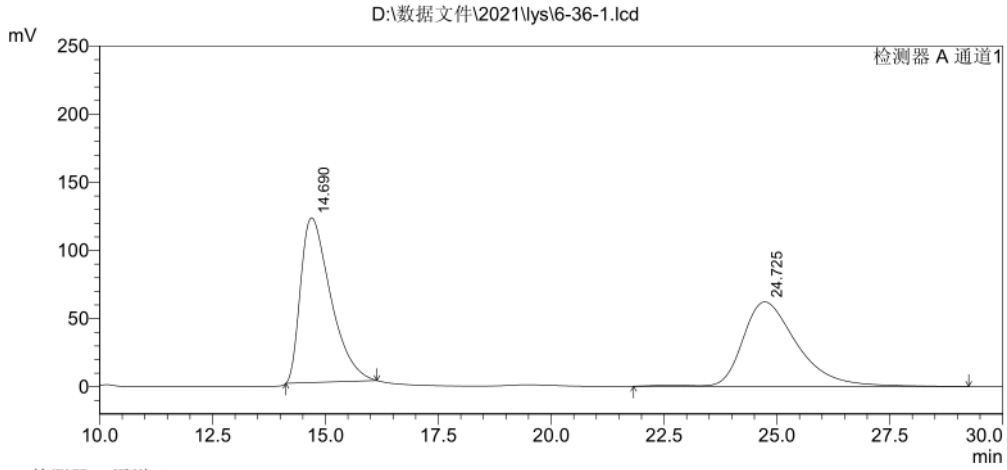
峰表

检测器 A Ch1 254nm					
峰#	保留时间	面积	高度	面积 %	高度 %
1	15.730	1589715	25383	99.363	99.616
2	21.503	10184	98	0.637	0.384
总计		1599899	25481	100.000	100.000

**(R)-ethyl 3-(2-oxo-2-(3-tolyl)ethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate**

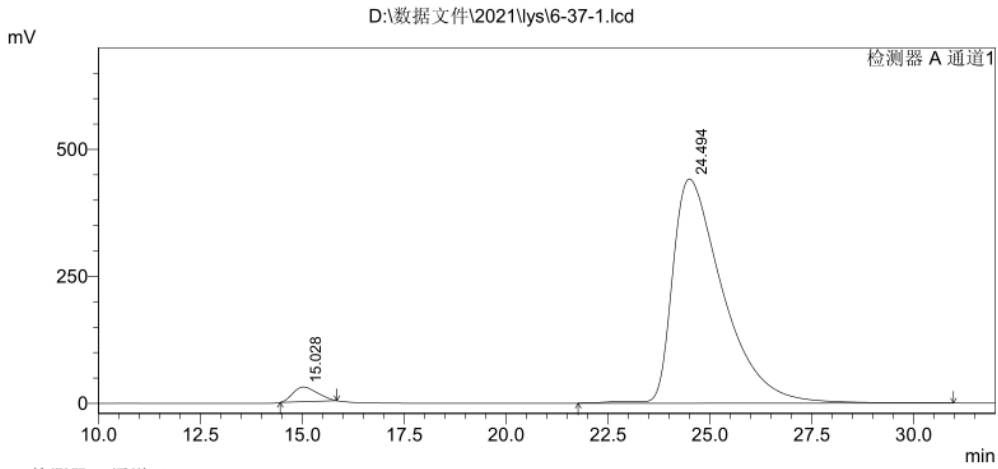
**1,1-dioxide (1ag)**





峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	14.690	5610837	120963	51.964	66.137
2	24.725	5186669	61935	48.036	33.863
总计		10797506	182897	100.000	100.000

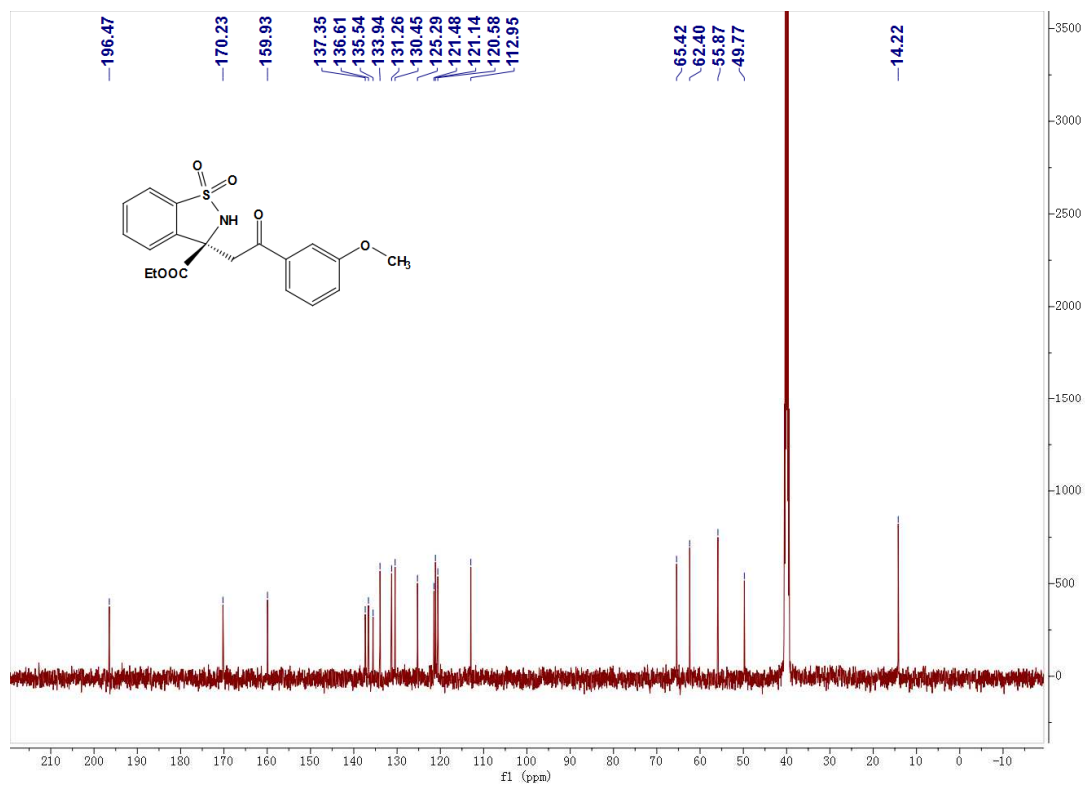
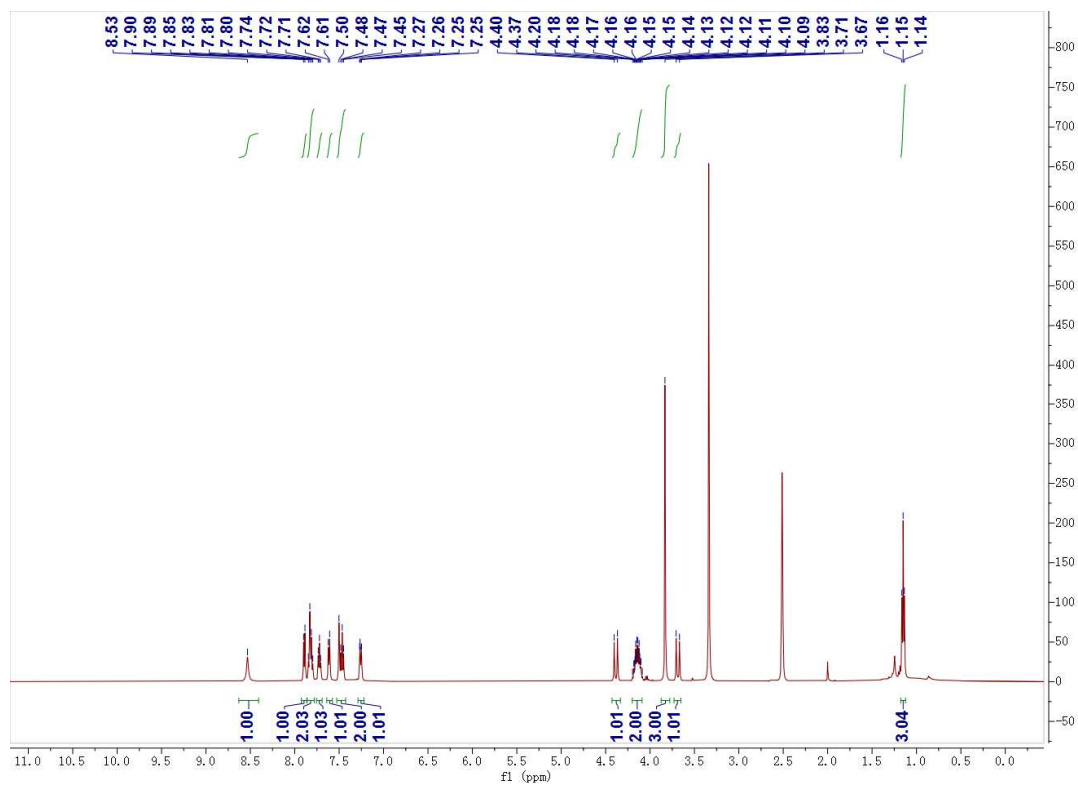


峰表

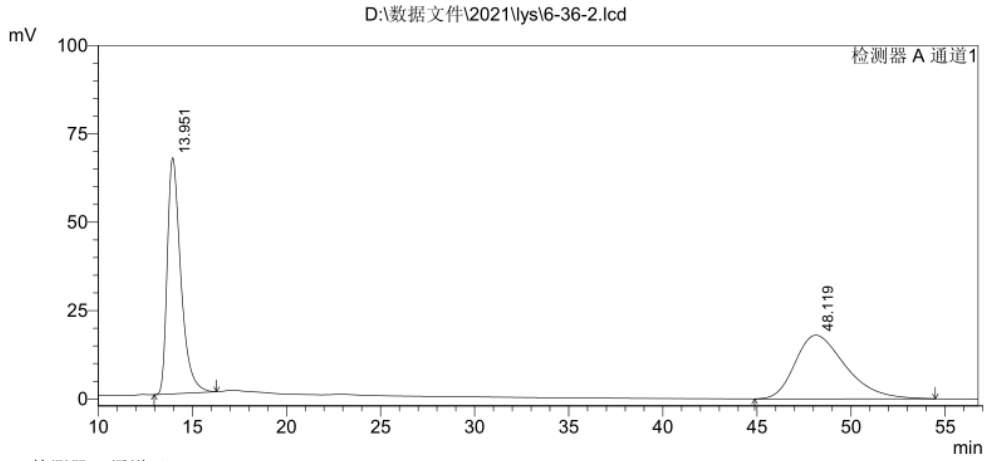
峰#	保留时间	面积	高度	面积 %	高度 %
1	15.028	1207153	28930	3.081	6.150
2	24.494	37967430	441509	96.919	93.850
总计		39174583	470439	100.000	100.000

**(R)-ethyl 3-(2-(3-methoxyphenyl)-2-oxoethyl)-2,3-dihydrobenzo[d]**

**isothiazole-3-carboxylate 1,1-dioxide (1ah)**

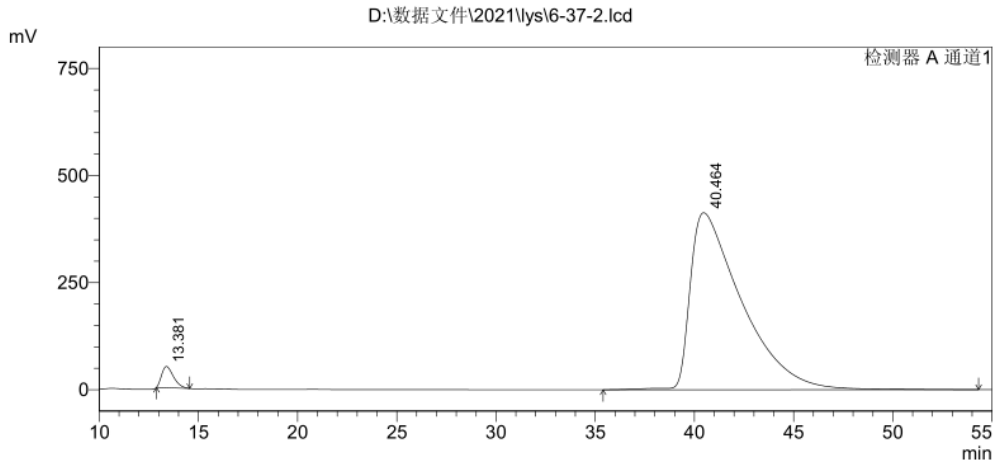






峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	13.951	3344537	66806	49.982	78.771
2	48.119	3346904	18005	50.018	21.229
总计		6691441	84811	100.000	100.000

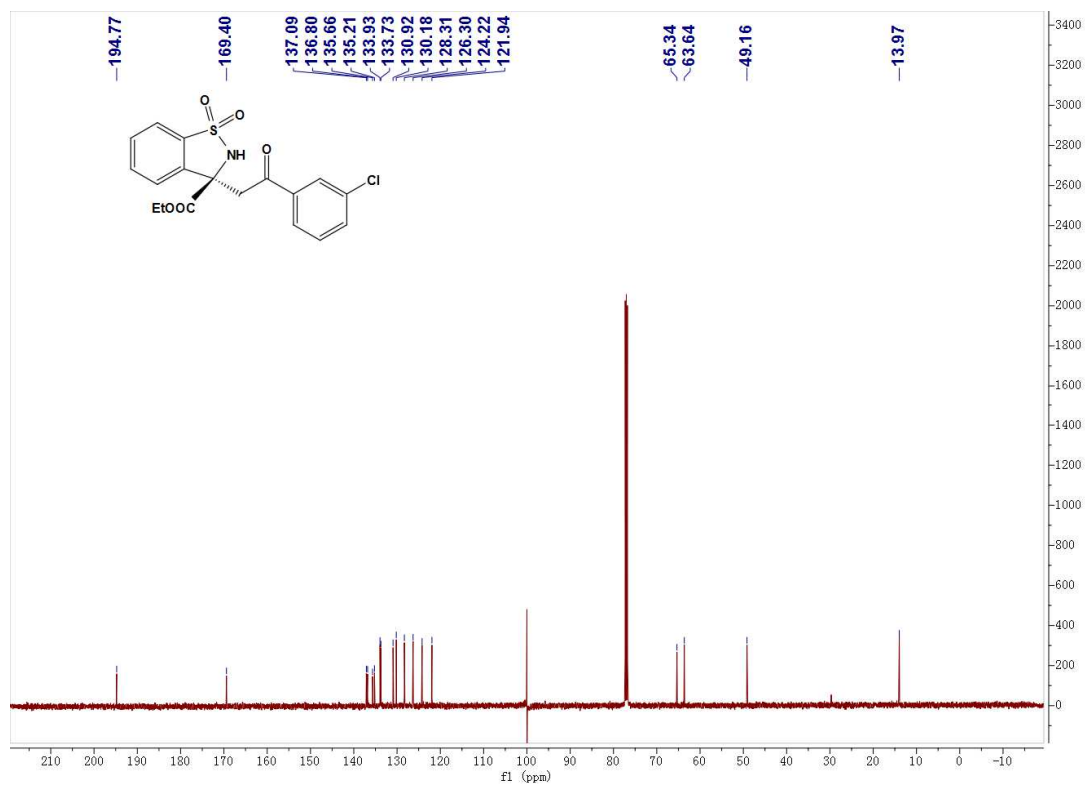
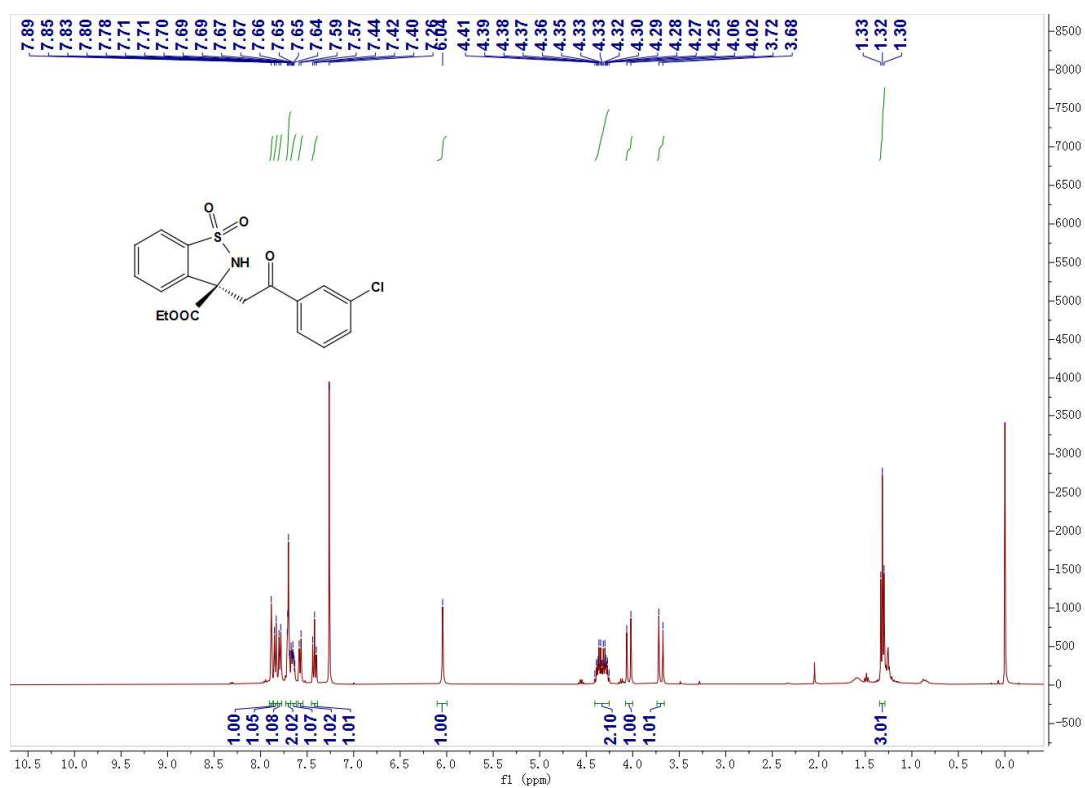


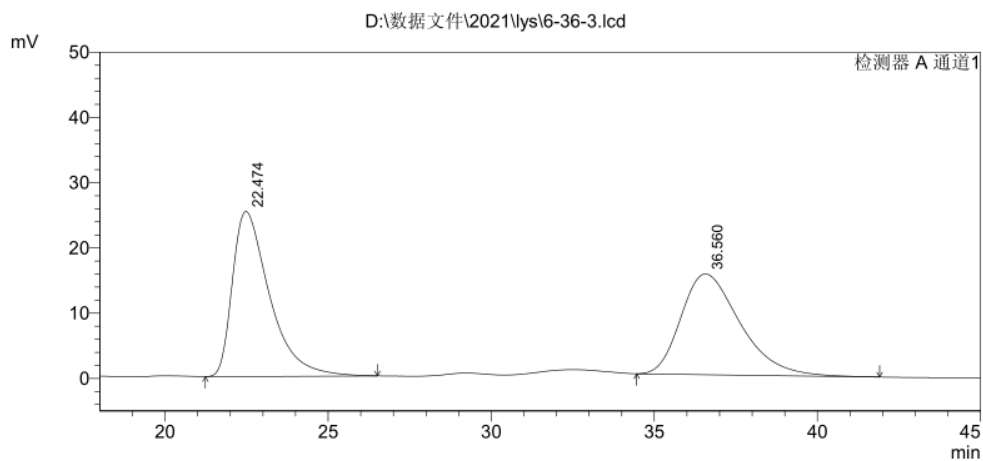
峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	13.381	2055418	49516	2.682	10.702
2	40.464	74580817	413172	97.318	89.298
总计		76636235	462688	100.000	100.000

**(R)-ethyl 3-(2-(3-chlorophenyl)-2-oxoethyl)-2,3-dihydrobenzo[d]isothiazole**

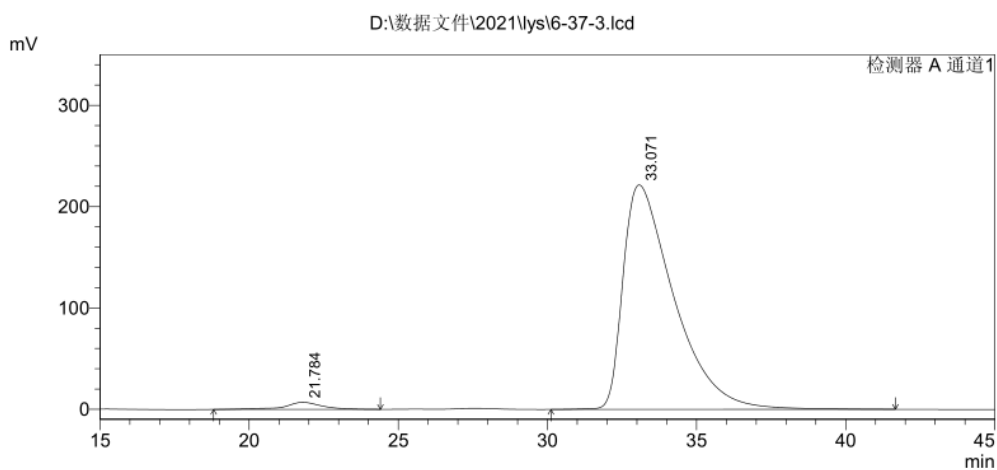
**-3-carboxylate 1,1-dioxide (1ai)**





峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	22.474	2005817	25294	50.729	62.080
2	36.560	1948186	15450	49.271	37.920
总计		3954003	40744	100.000	100.000

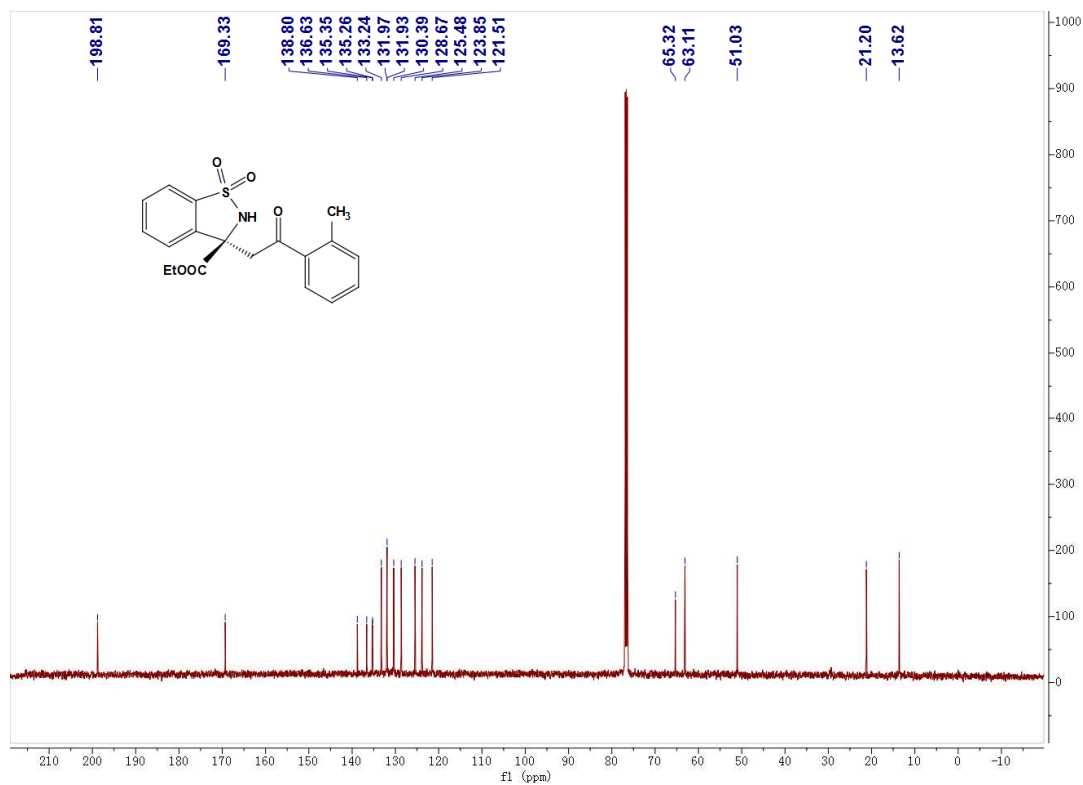
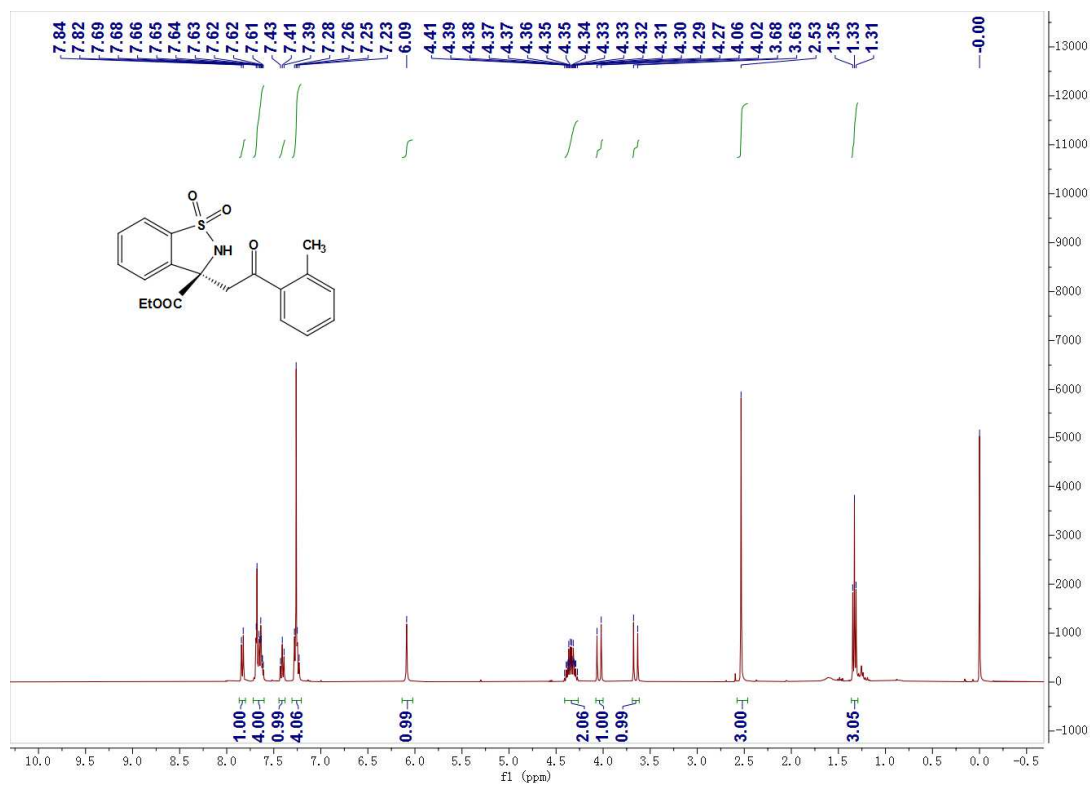


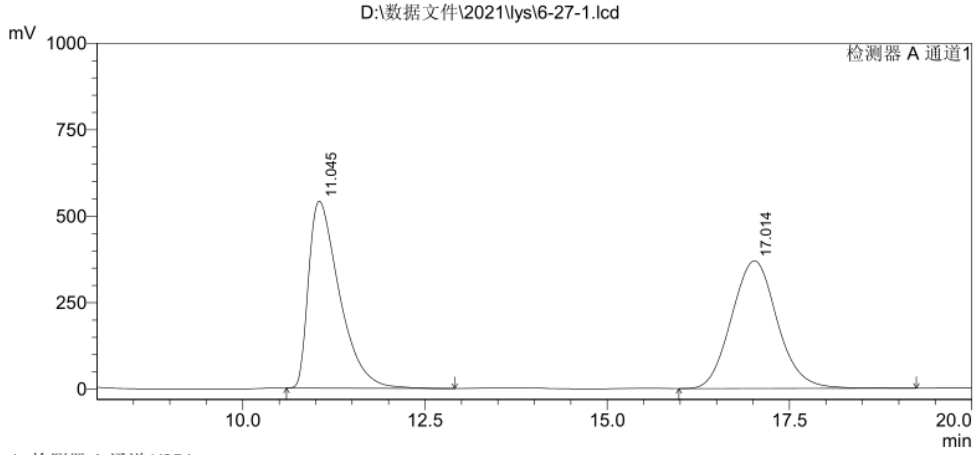
峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	21.784	609510	6998	2.263	3.060
2	33.071	26319093	221646	97.737	96.940
总计		26928603	228644	100.000	100.000

**(R)-ethyl 3-(2-oxo-2-(2-tolyl)ethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate**

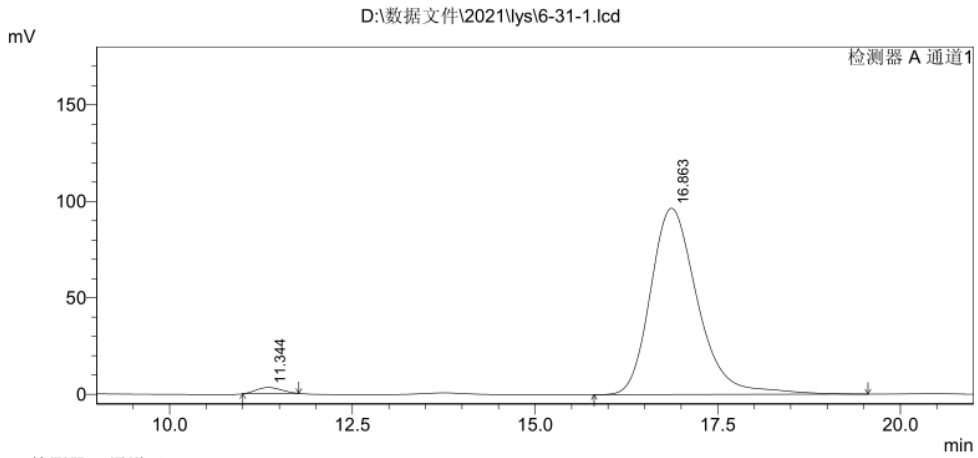
**1,1-dioxide (1aj)**





峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	11.045	15928609	540714	49.701	59.424
2	17.014	16120497	369207	50.299	40.576
总计		32049106	909921	100.000	100.000

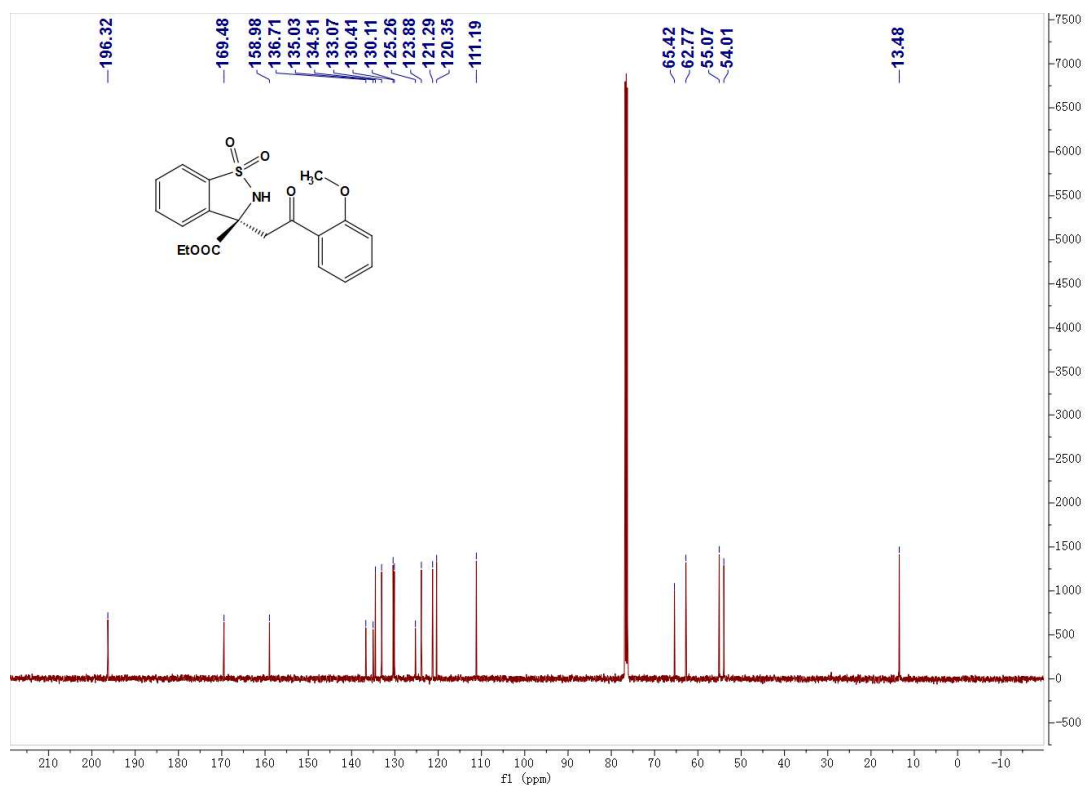
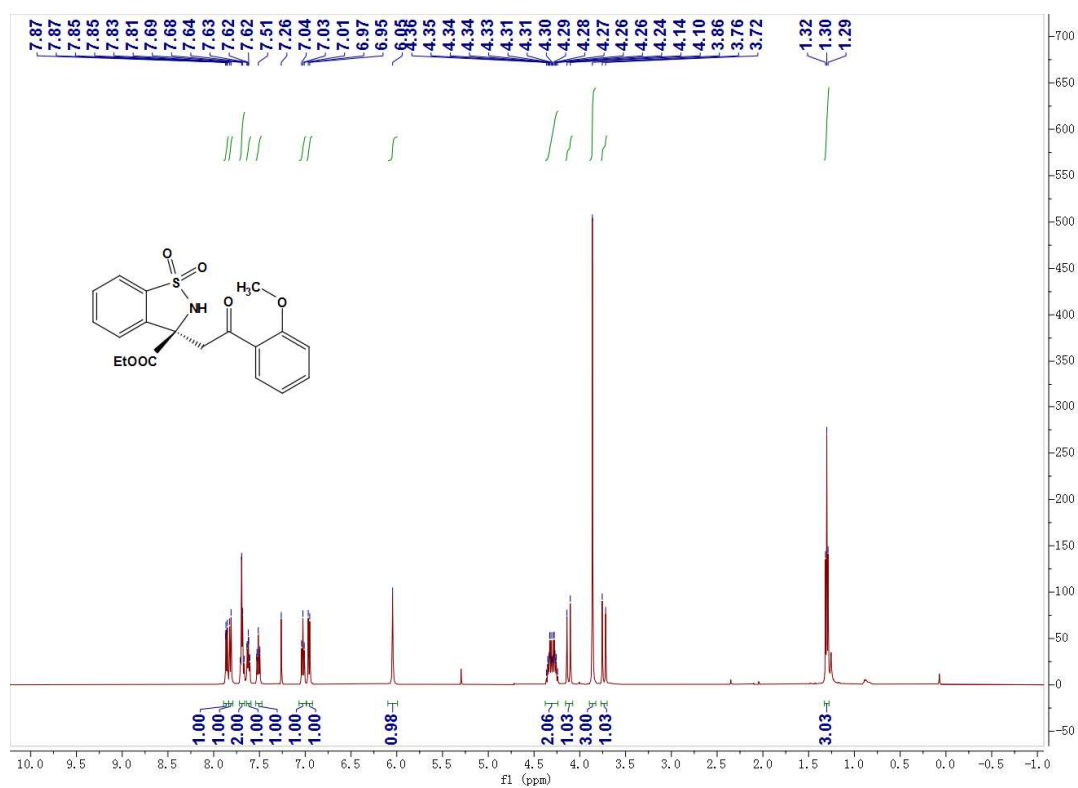


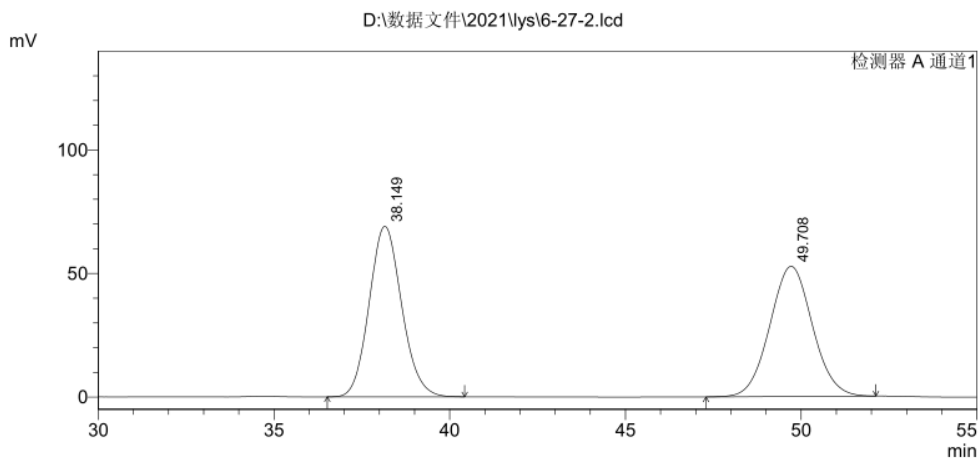
峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	11.344	76173	3175	1.730	3.186
2	16.863	4326219	96468	98.270	96.814
总计		4402392	99643	100.000	100.000

**(R)-ethyl 3-(2-(2-methoxyphenyl)-2-oxoethyl)-2,3-dihydrobenzo[d]isothiazole**

**-3-carboxylate 1,1-dioxide (1ak)**

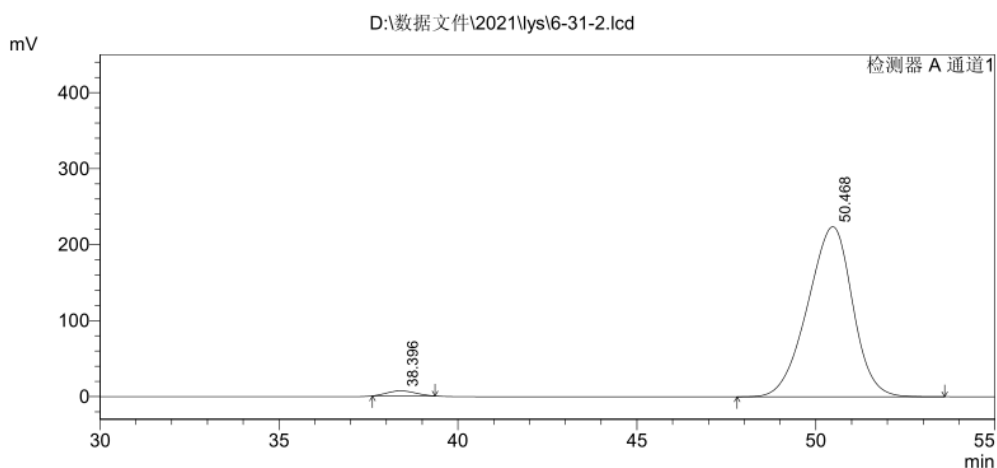




峰表

检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	38.149	4450958	69077	50.008	56.721
2	49.708	4449585	52706	49.992	43.279
总计		8900543	121783	100.000	100.000



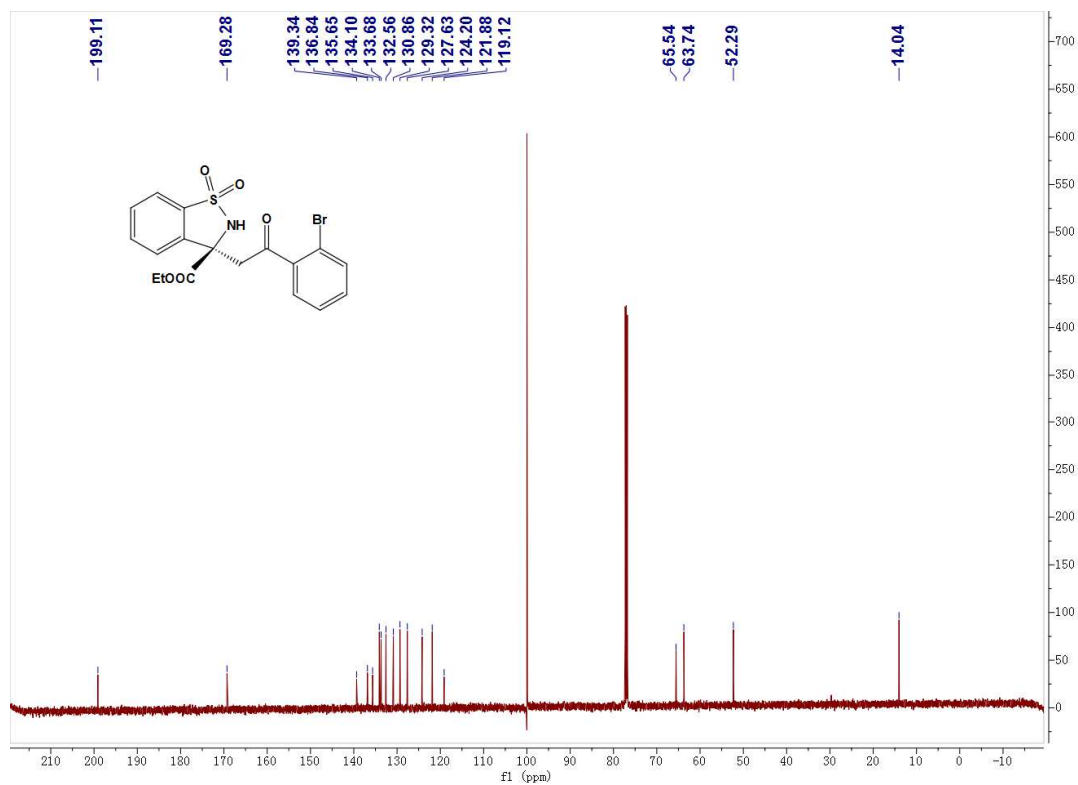
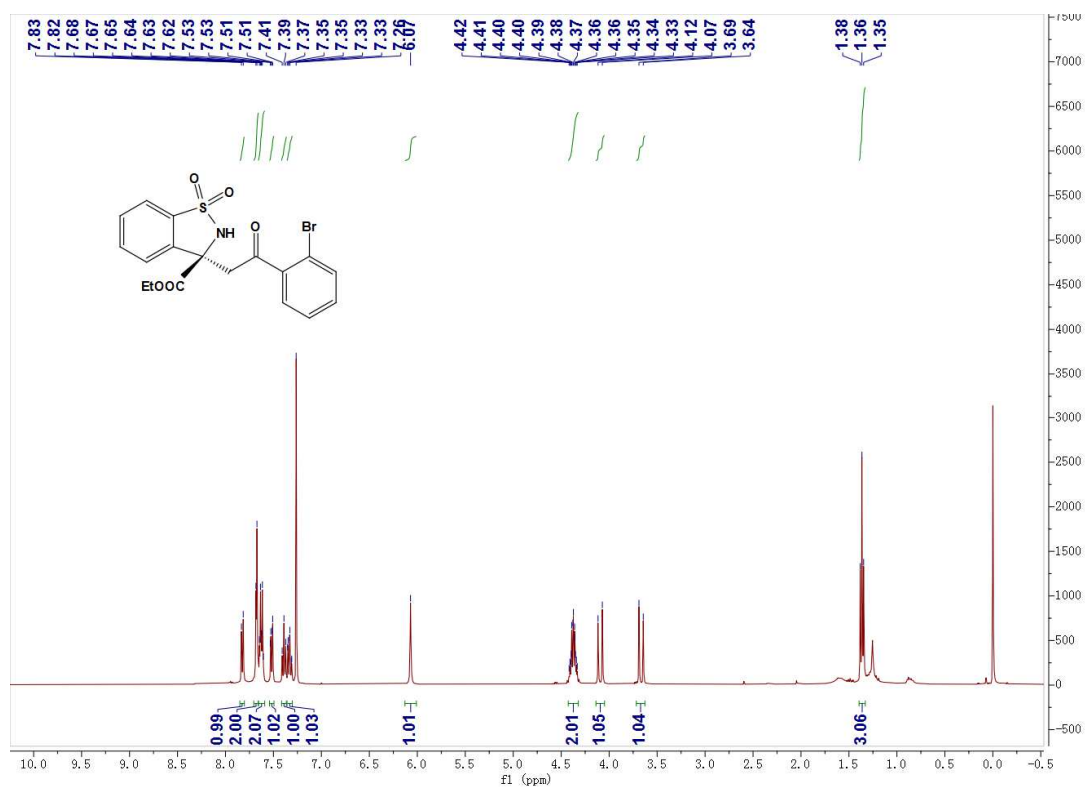
峰表

检测器 A Ch1 254nm

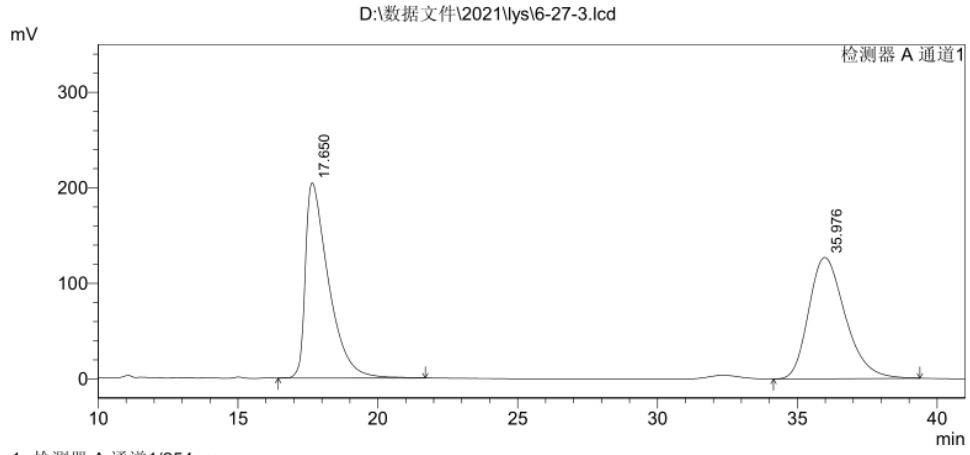
峰#	保留时间	面积	高度	面积 %	高度 %
1	38.396	363561	6648	1.824	2.884
2	50.468	19568794	223864	98.176	97.116
总计		19932355	230512	100.000	100.000

**(R)-ethyl 3-(2-(2-bromophenyl)-2-oxoethyl)-2,3-dihydrobenzo[d]isothiazole**

**-3-carboxylate 1,1-dioxide (1a)**

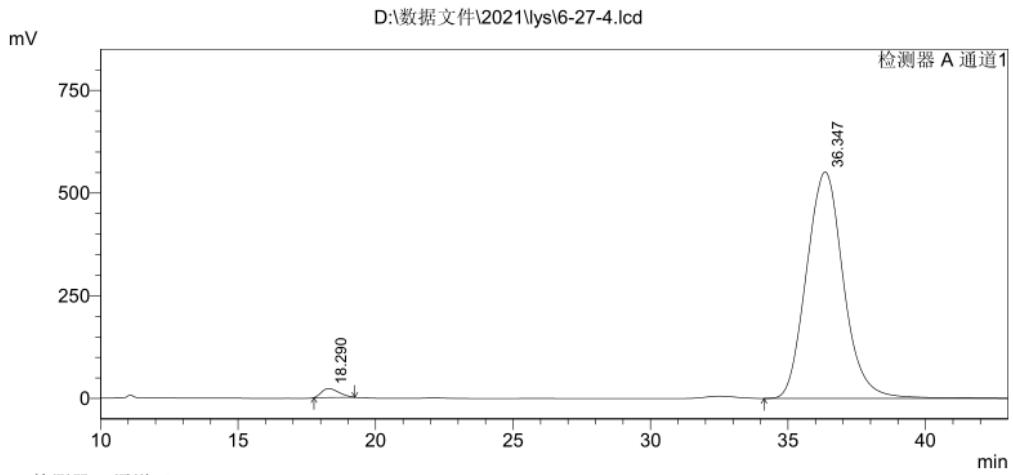






峰表

检测器 A Ch1 254nm					
峰#	保留时间	面积	高度	面积 %	高度 %
1	17.650	11759194	204457	50.458	61.692
2	35.976	11545939	126957	49.542	38.308
总计		23305133	331414	100.000	100.000

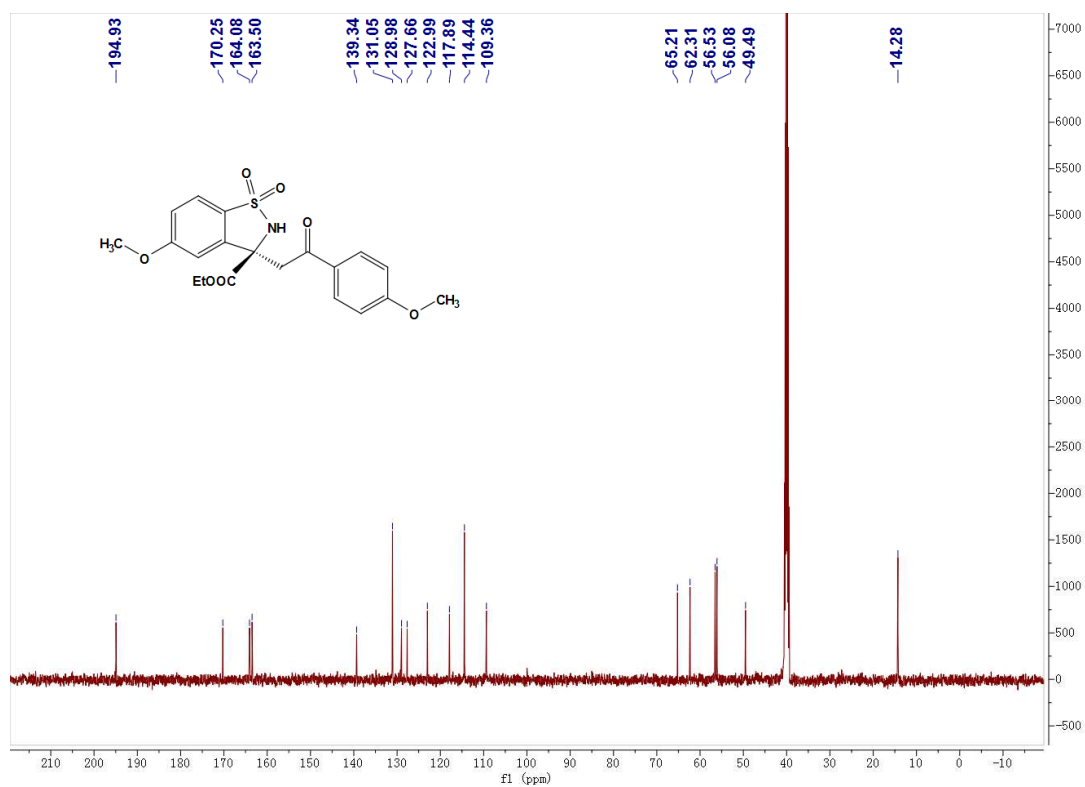
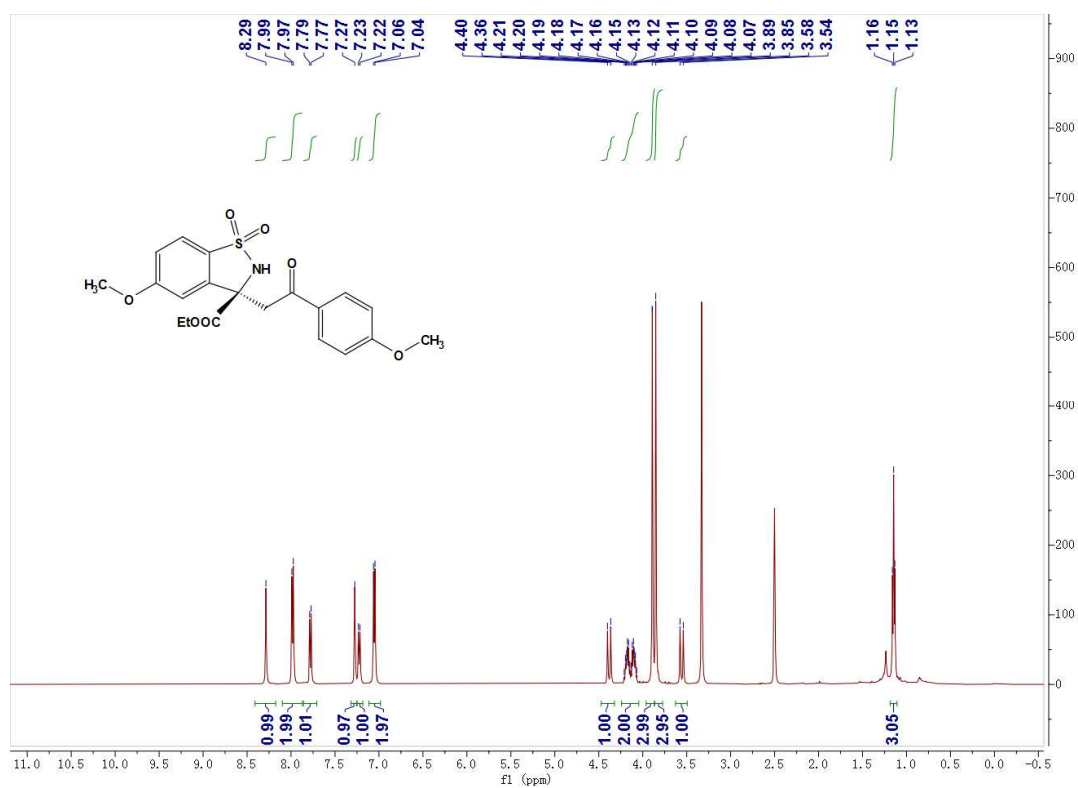


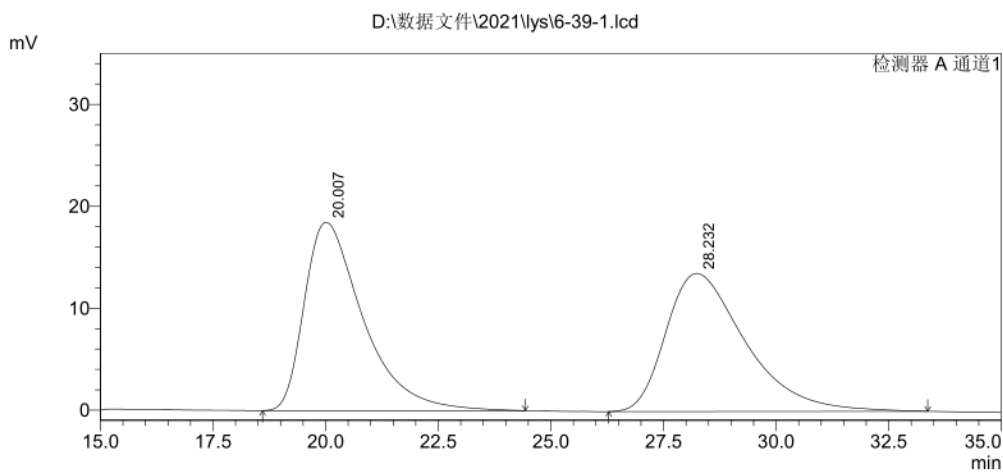
峰表

检测器 A Ch1 254nm					
峰#	保留时间	面积	高度	面积 %	高度 %
1	18.290	944502	21588	1.793	3.767
2	36.347	51745338	551531	98.207	96.233
总计		52689840	573118	100.000	100.000

**(R)-ethyl 5-methoxy-3-(2-(4-methoxyphenyl)-2-oxoethyl)-2,3-dihydrobenzo[d]**

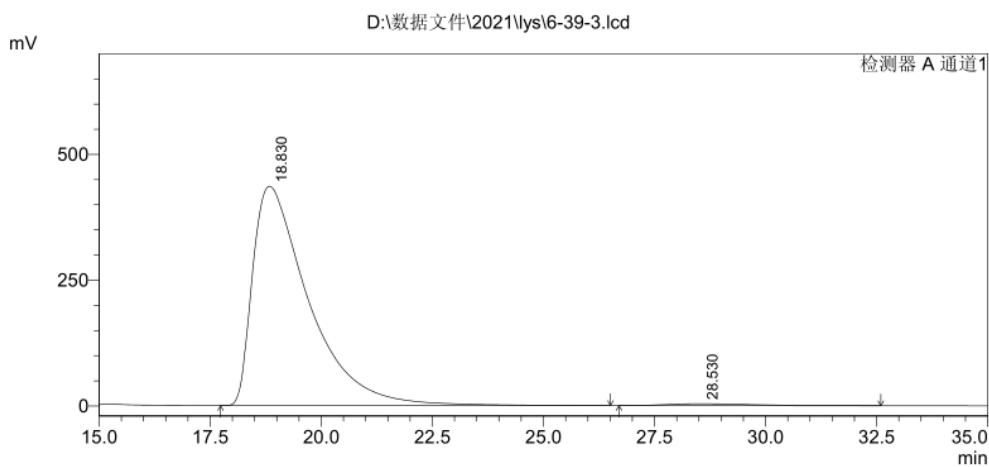
**isothiazole-3-carboxylate 1,1-dioxide (1am)**





峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	20.007	1677070	18480	50.157	57.704
2	28.232	1666542	13545	49.843	42.296
总计		3343611	32025	100.000	100.000

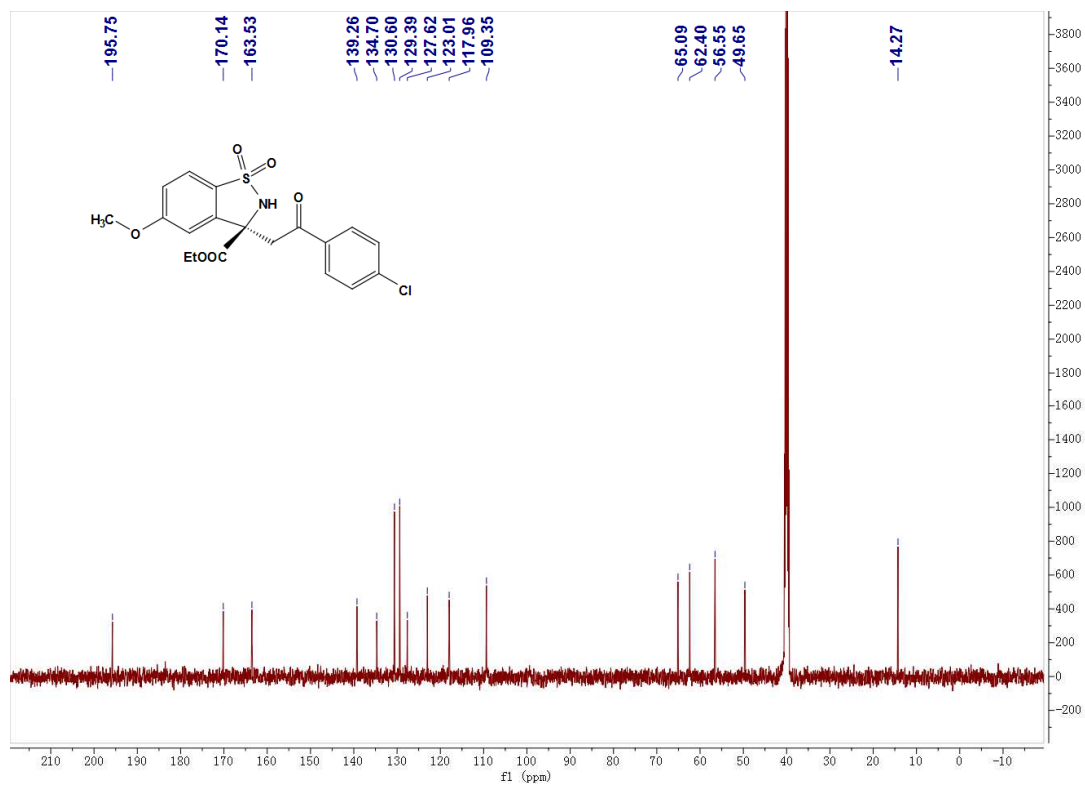
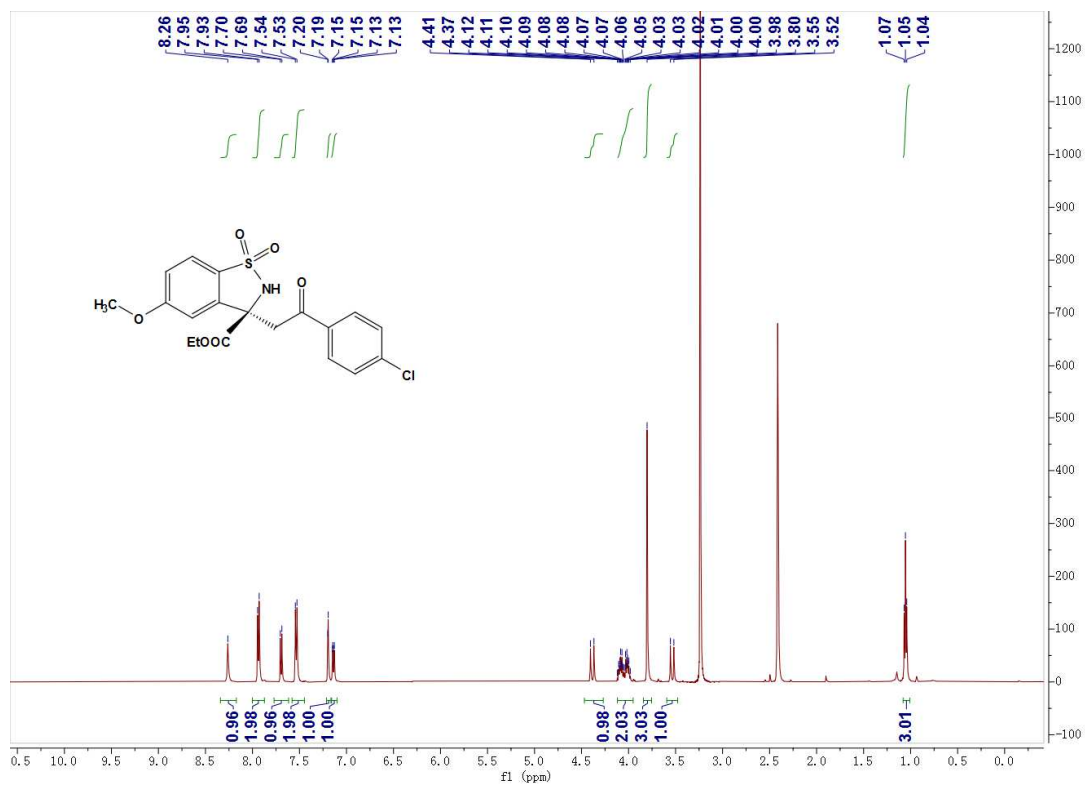


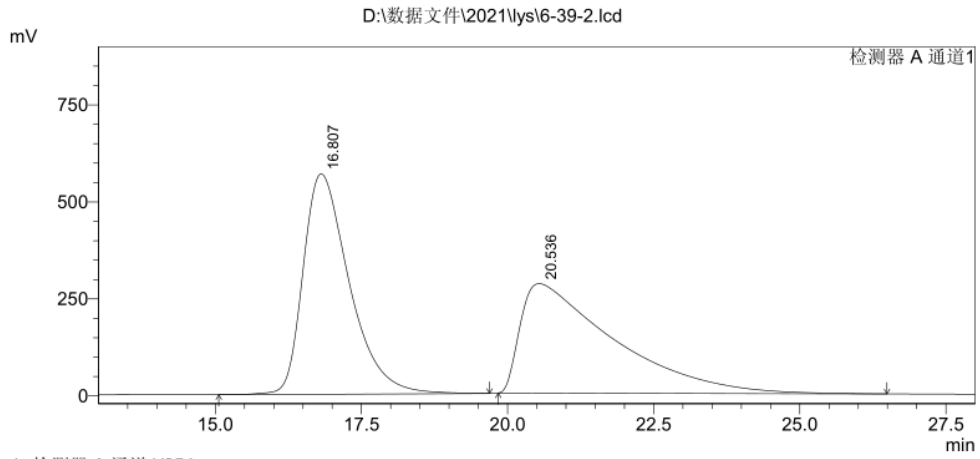
峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	18.830	38359718	435881	98.739	99.160
2	28.530	490085	3694	1.261	0.840
总计		38849803	439575	100.000	100.000

**(R)-ethyl 3-(2-(4-chlorophenyl)-2-oxoethyl)-5-methoxy-2,3-dihydrobenzo[d]**

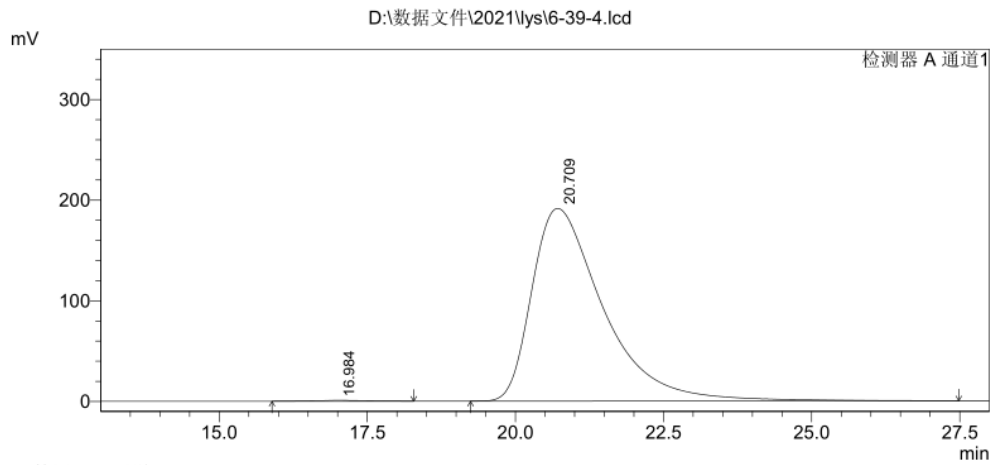
**isothiazole-3-carboxylate 1,1-dioxide (1an)**





峰表

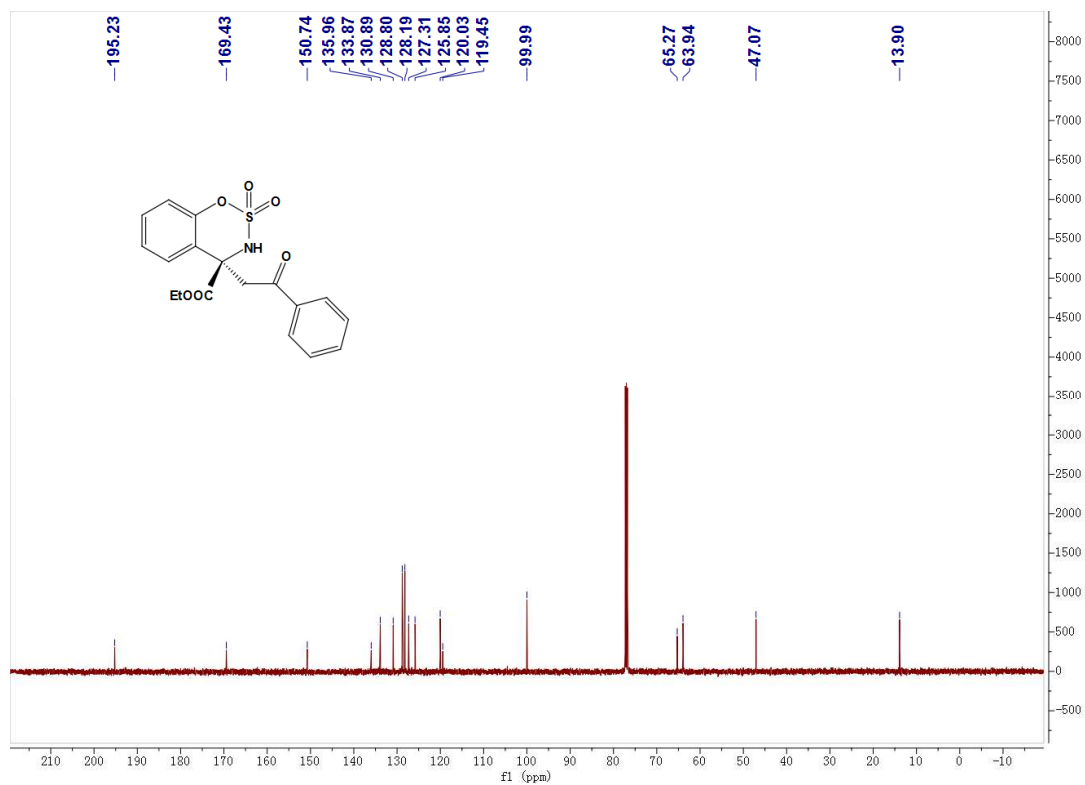
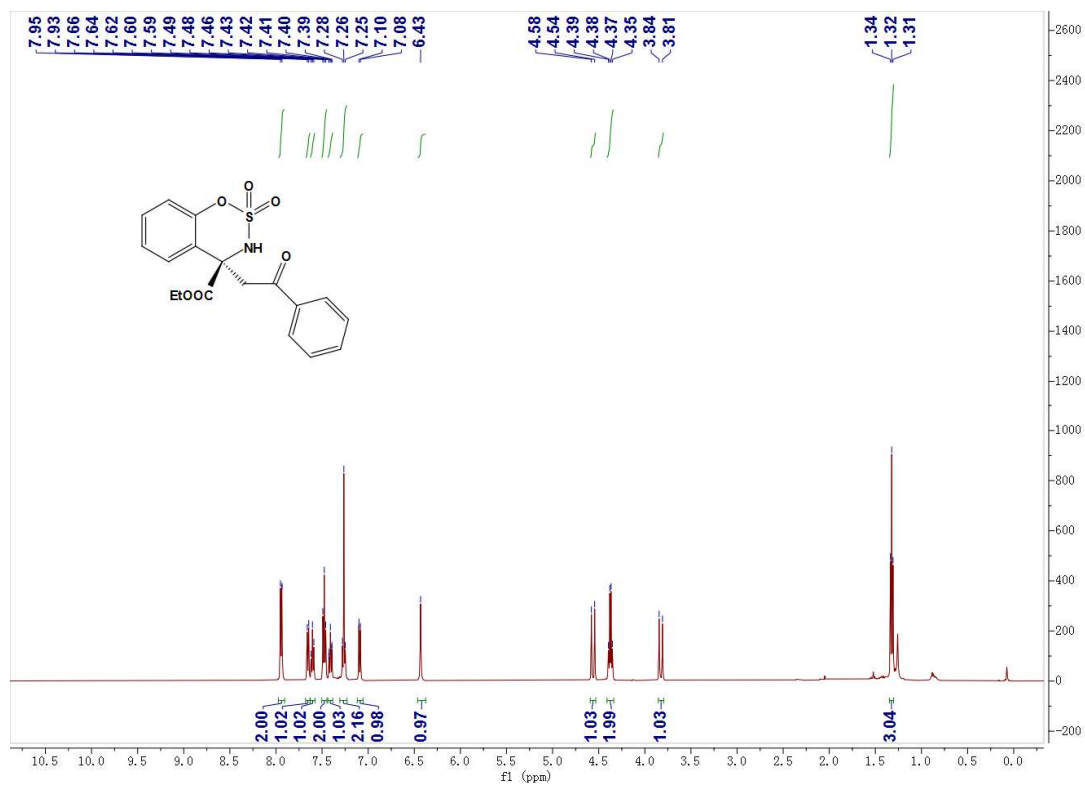
峰#	保留时间	面积	高度	面积 %	高度 %
1	16.807	31194504	567990	49.925	66.815
2	20.536	31288125	282107	50.075	33.185
总计		62482629	850097	100.000	100.000

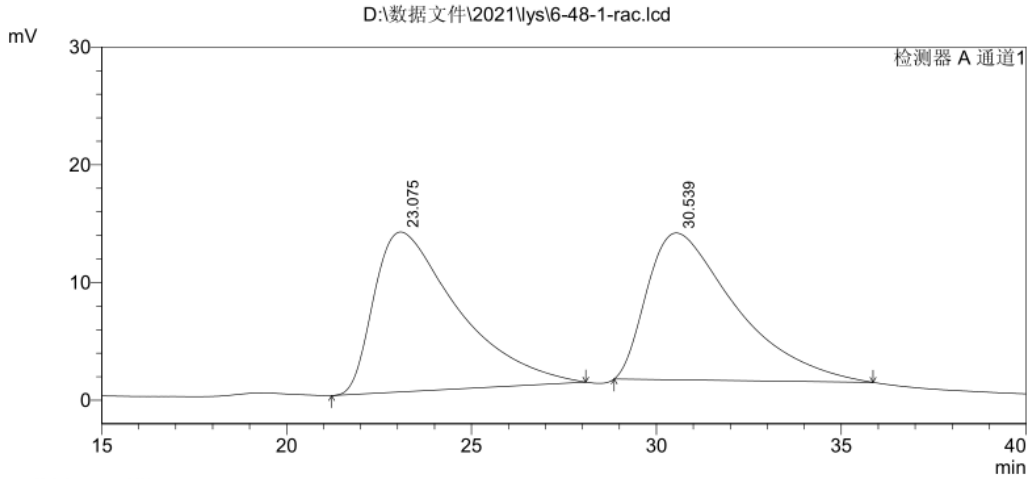


峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	16.984	48401	785	0.300	0.408
2	20.709	16092418	191535	99.700	99.592
总计		16140819	192320	100.000	100.000

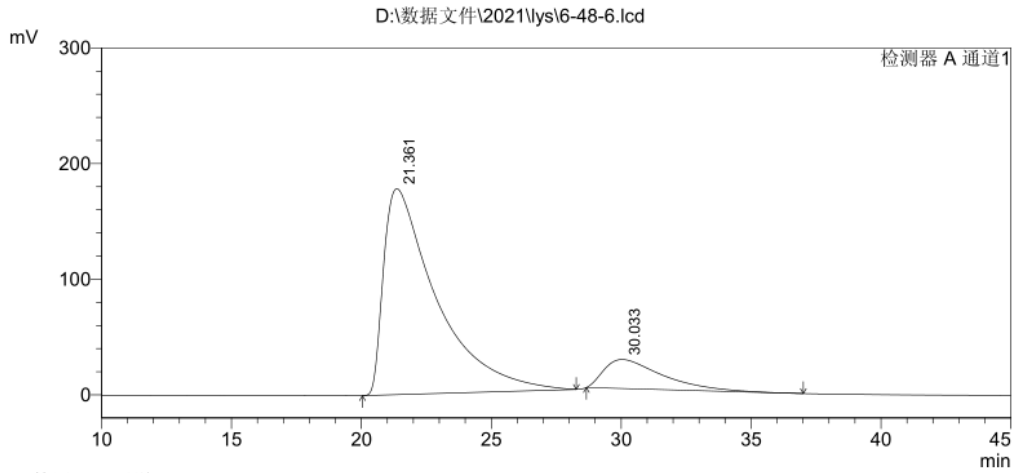
**Ethyl 4-(2-oxo-2-phenylethyl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylate 2,2-dioxide (1ga)**





峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	23.075	2147179	13586	50.728	52.146
2	30.539	2085587	12468	49.272	47.854
总计		4232766	26054	100.000	100.000

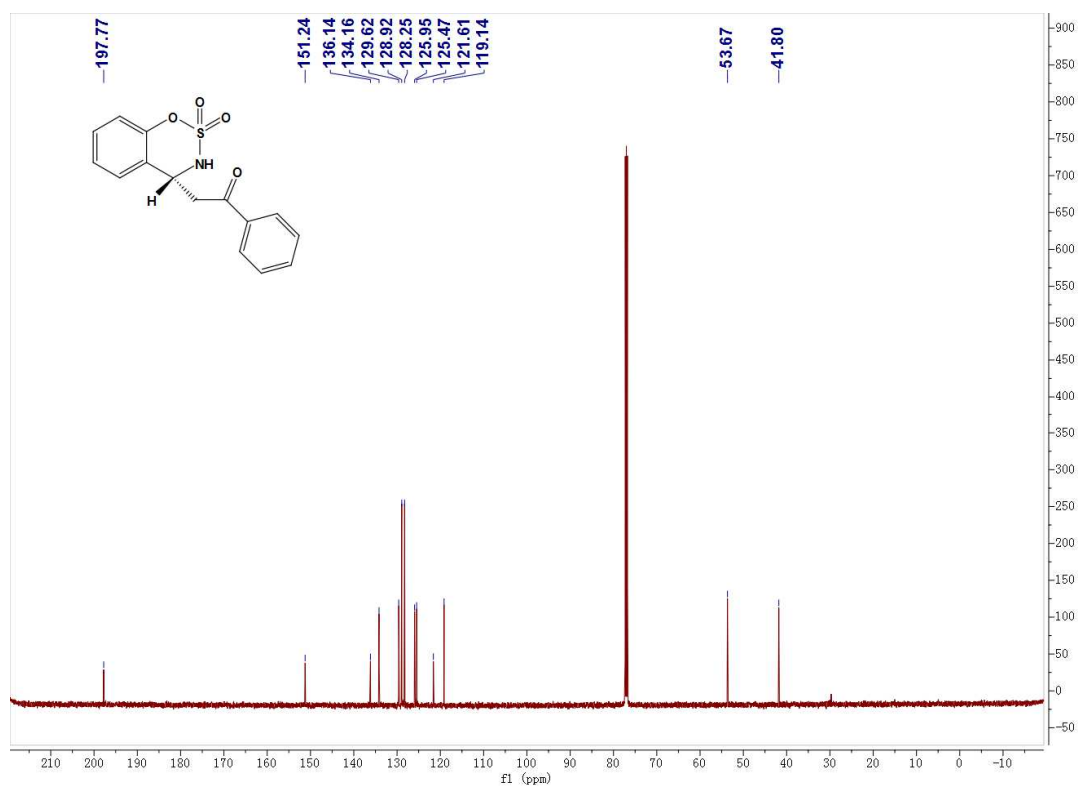
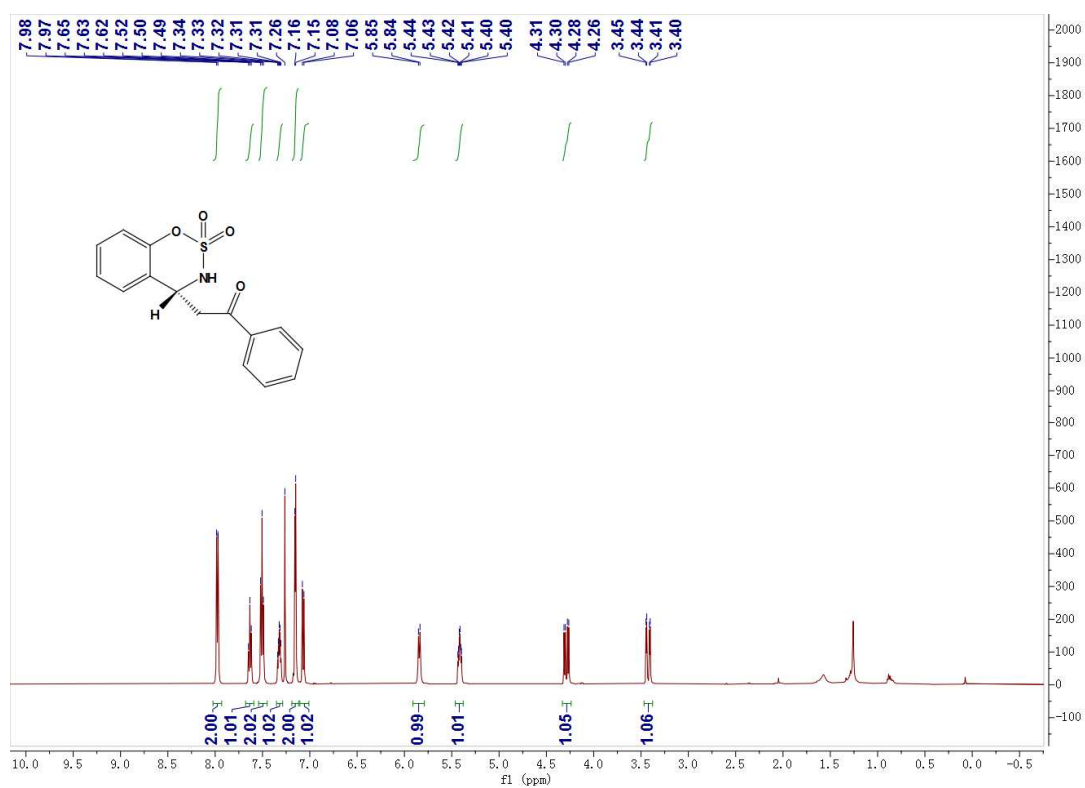


峰表

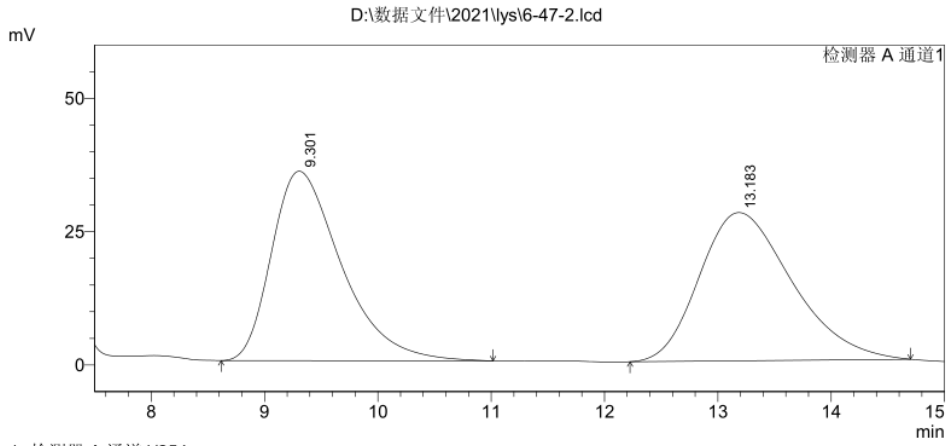
峰#	保留时间	面积	高度	面积 %	高度 %
1	21.361	25222970	178034	86.478	87.646
2	30.033	3943942	25094	13.522	12.354
总计		29166912	203129	100.000	100.000

# 2-(2,2-dioxido-3,4-dihydrobenzo[e][1,2,3]oxathiazin-4-yl)-1-phenylethanone

(1ha)

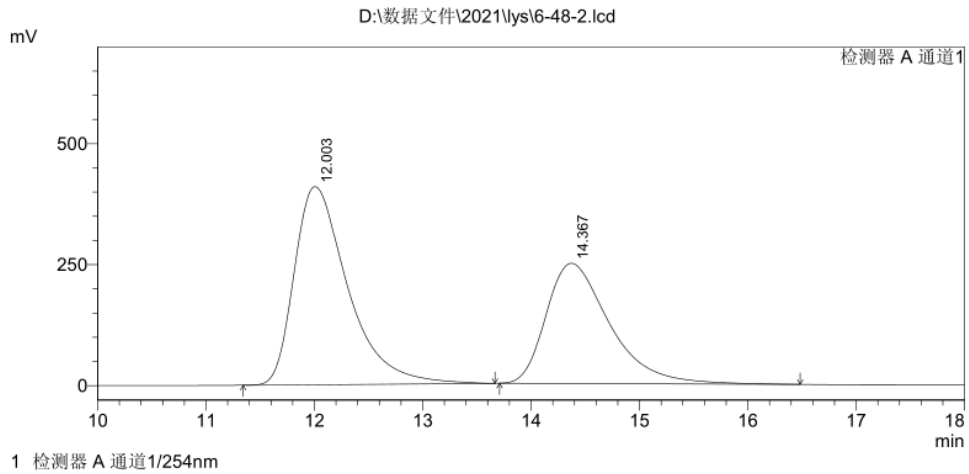






峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	9.301	1522530	35527	49.111	56.109
2	13.183	1577683	27791	50.889	43.891
总计		3100213	63318	100.000	100.000

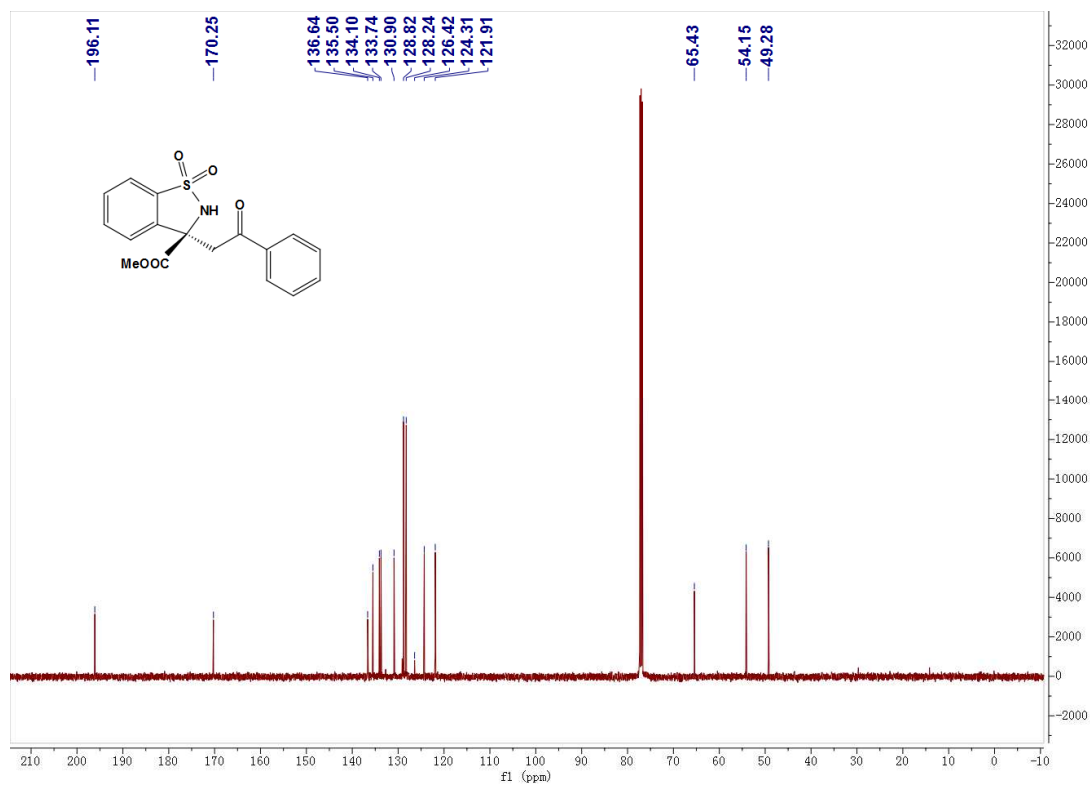
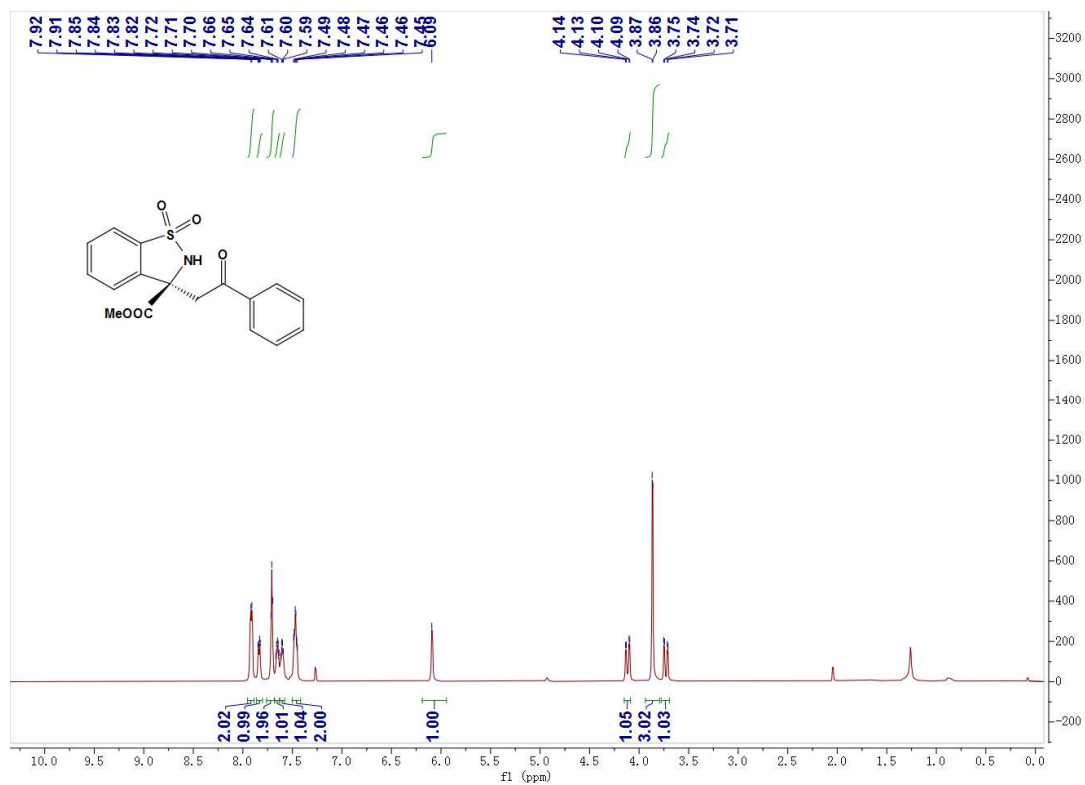


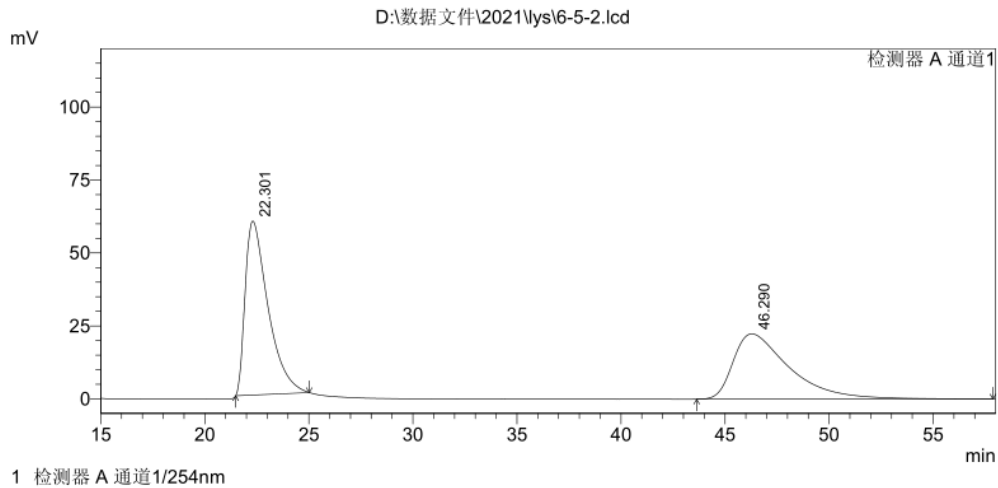
峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	12.003	14096828	409530	58.178	62.248
2	14.367	10133855	248368	41.822	37.752
总计		24230683	657898	100.000	100.000

**(R)-methyl 3-(2-oxo-2-phenylethyl)-2,3-dihydrobenzo[d]isothiazole-3-carboxylate**

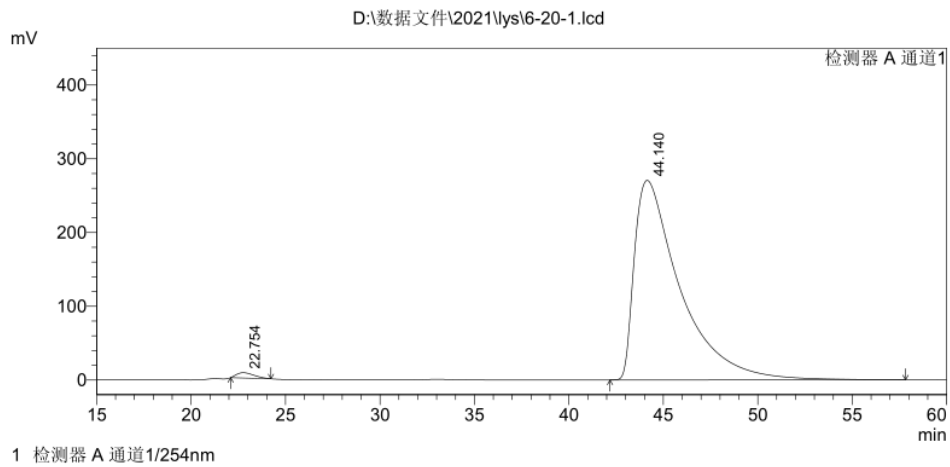
**1,1-dioxide (1ia)**





峰表

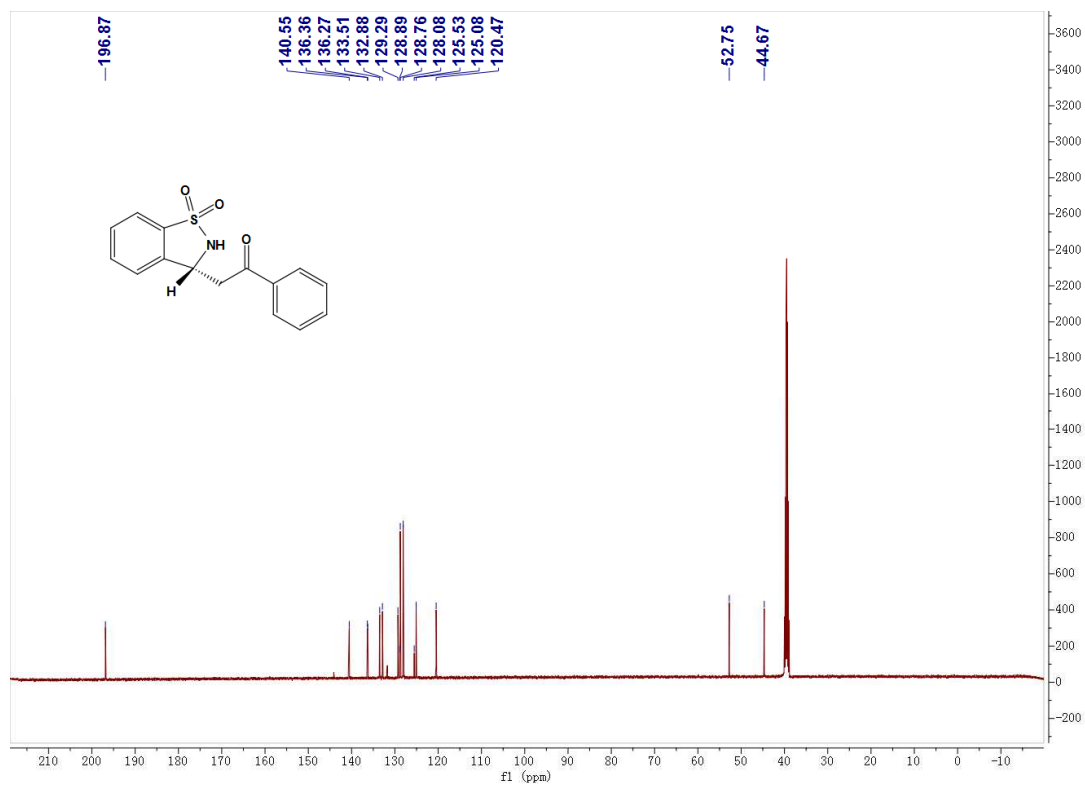
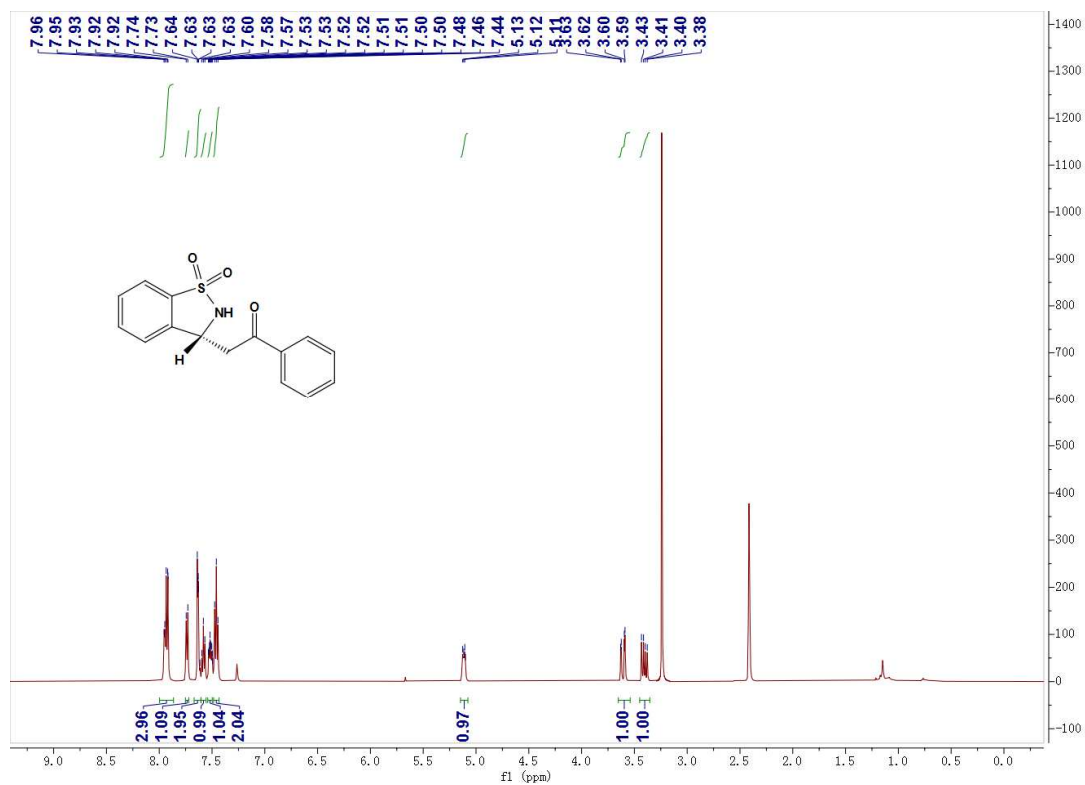
峰#	保留时间	面积	高度	面积 %	高度 %
1	22.301	4555618	59577	51.951	72.678
2	46.290	4213462	22397	48.049	27.322
总计		8769080	81974	100.000	100.000

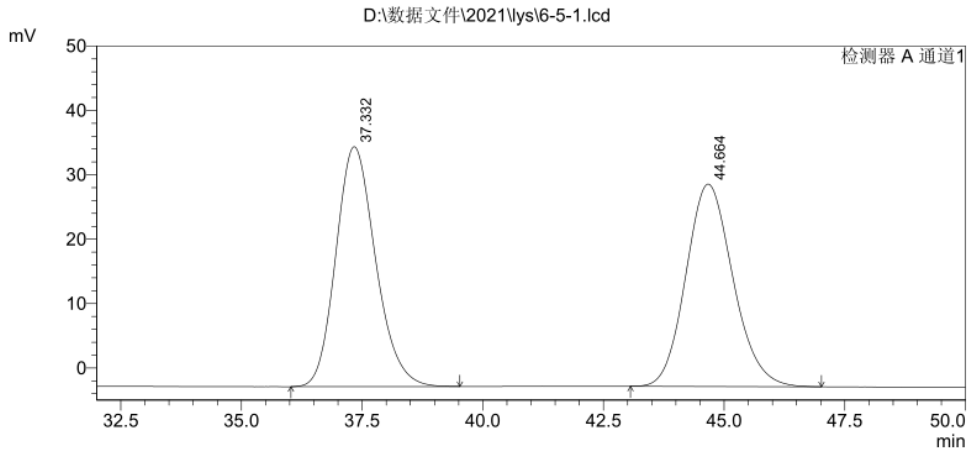


峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	22.754	460760	7140	0.998	2.568
2	44.140	45727487	270852	99.002	97.432
总计		46188246	277992	100.000	100.000

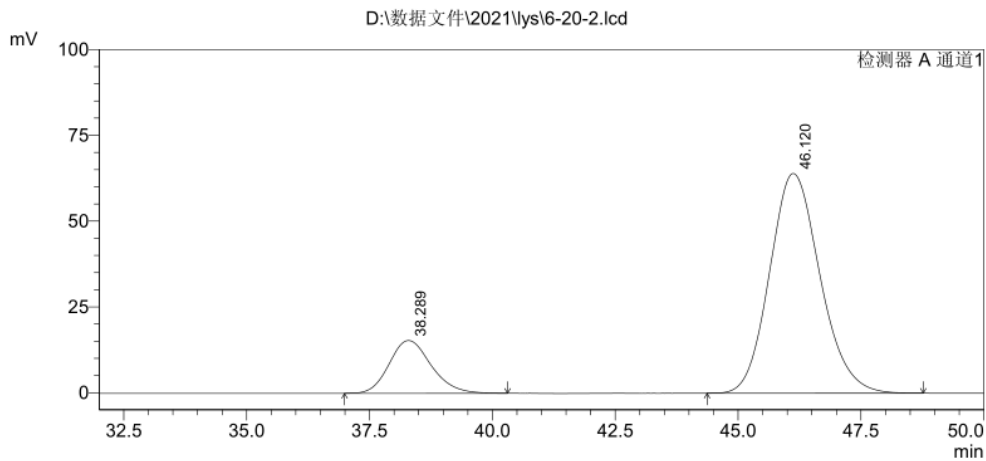
**(R)-2-(1,1-dioxido-2,3-dihydrobenzo[d]isothiazol-3-yl)-1-phenylethanone (1ja)**





峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	37.332	2134060	37251	50.007	54.232
2	44.664	2133421	31437	49.993	45.768
总计		4267482	68688	100.000	100.000

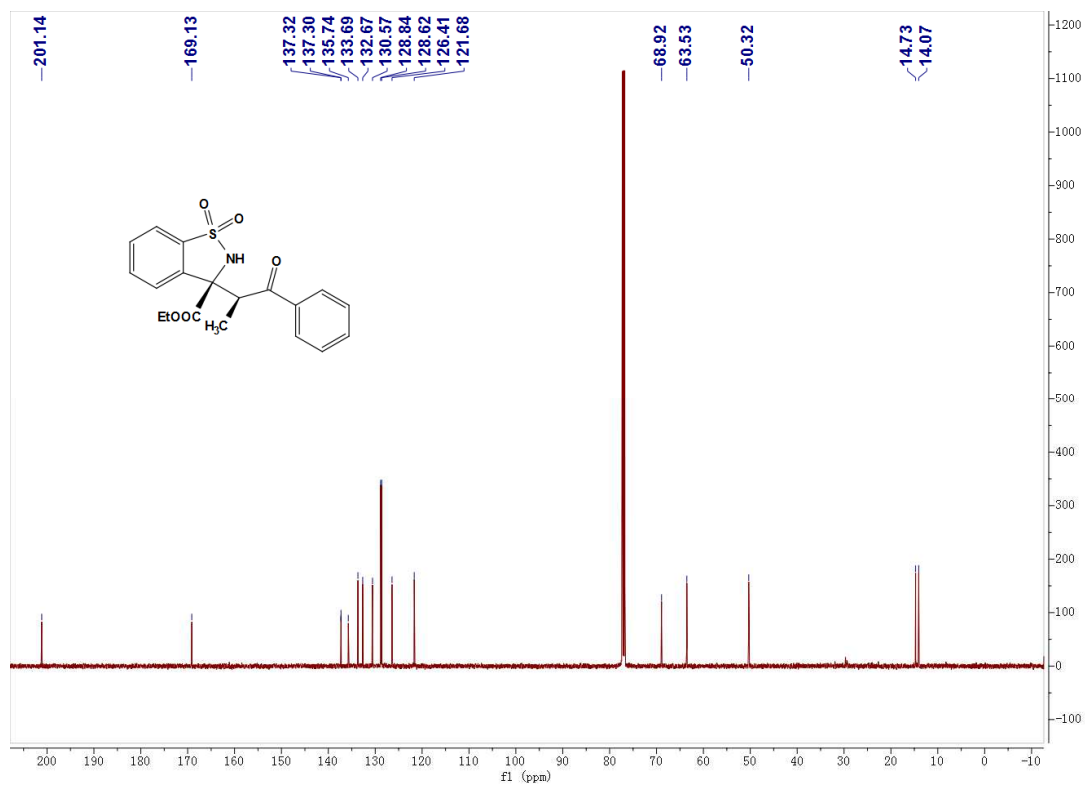
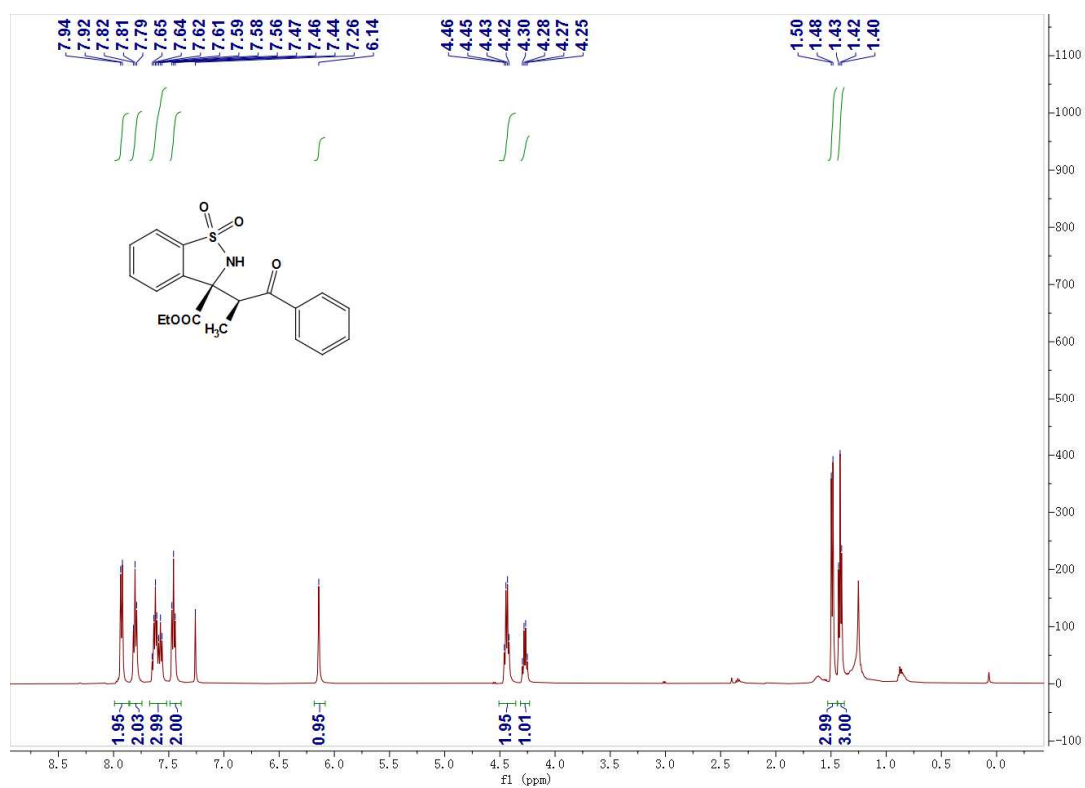


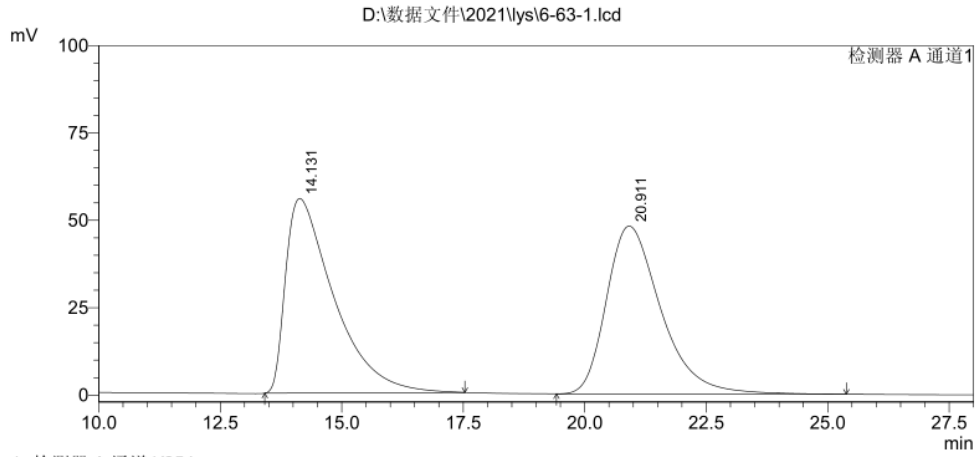
峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	38.289	919771	15445	16.741	19.417
2	46.120	4574356	64100	83.259	80.583
总计		5494127	79545	100.000	100.000

**(R)-ethyl 3-((S)-1-oxo-1-phenylpropan-2-yl)-2,3-dihydrobenzo[d]isothiazole**

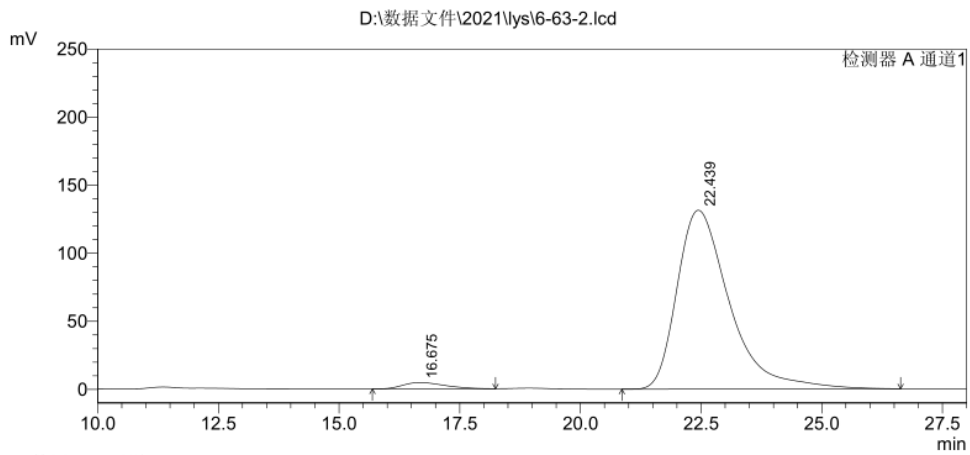
**-3-carboxylate 1,1-dioxide (1ap)**





峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	14.131	3847105	55686	50.626	53.678
2	20.911	3752004	48055	49.374	46.322
总计		7599110	103741	100.000	100.000

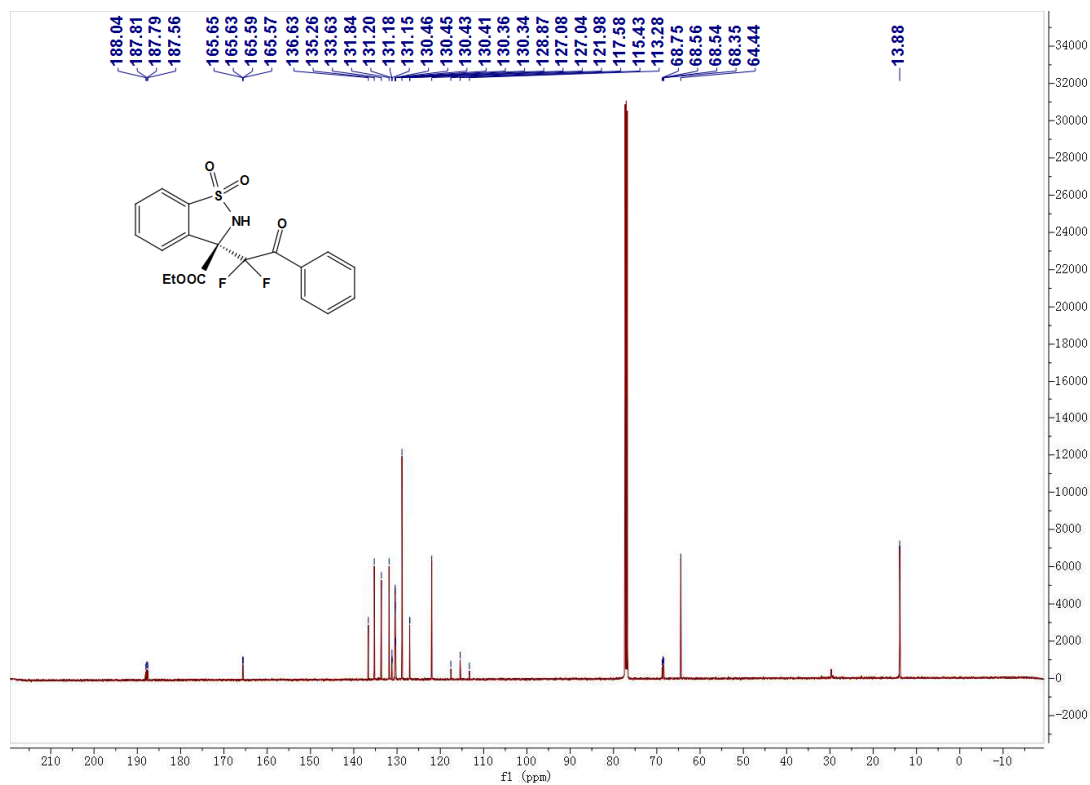
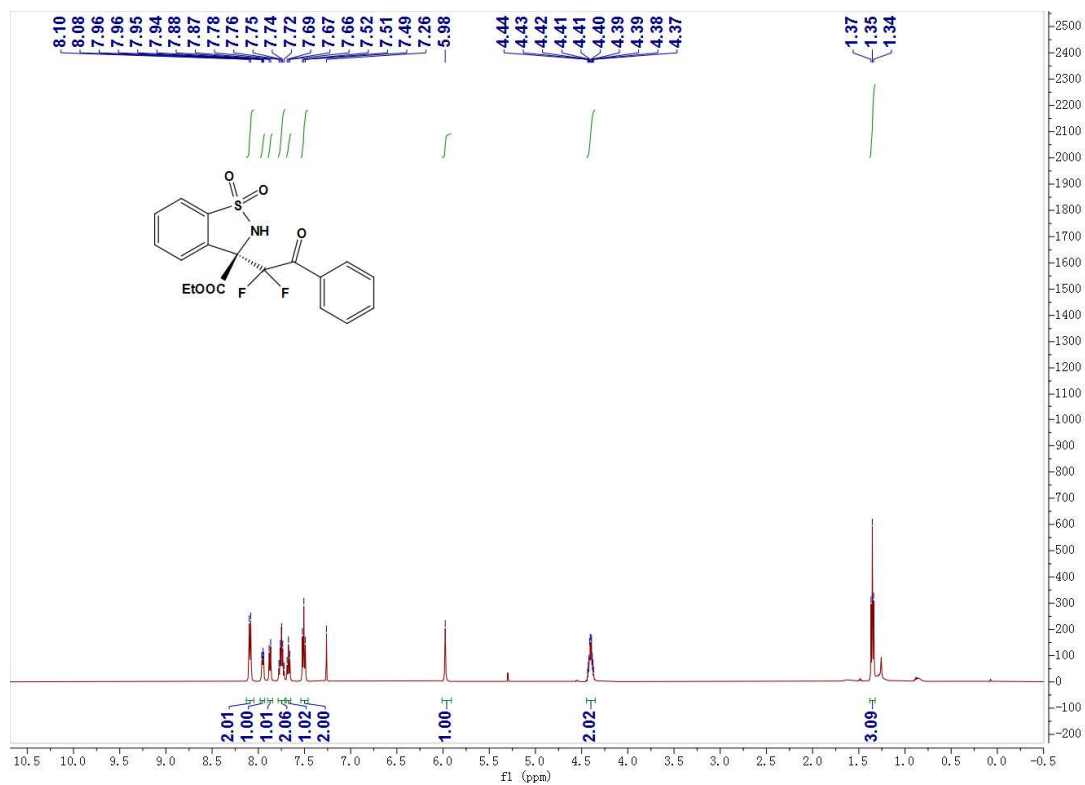


峰表

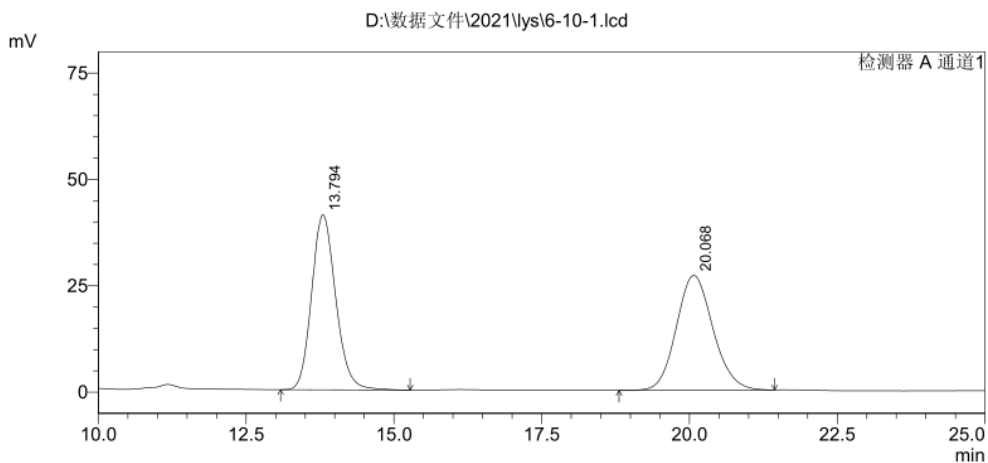
峰#	保留时间	面积	高度	面积 %	高度 %
1	16.675	284806	4696	2.785	3.448
2	22.439	9943051	131483	97.215	96.552
总计		10227857	136179	100.000	100.000

**(R)-ethyl 3-(1,1-difluoro-2-oxo-2-phenylethyl)-2,3-dihydrobenzo[d]isothiazole**

**-3-carboxylate 1,1-dioxide (1aq)**



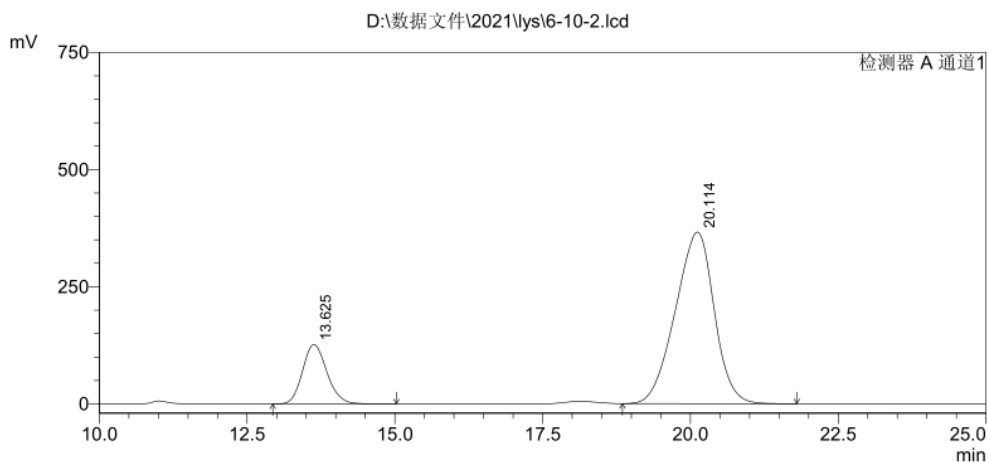




1 检测器 A 通道1/254nm

峰表

检测器 A Ch1 254nm					
峰#	保留时间	面积	高度	面积 %	高度 %
1	13.794	1168037	41162	50.033	60.387
2	20.068	1166512	27002	49.967	39.613
总计		2334549	68164	100.000	100.000



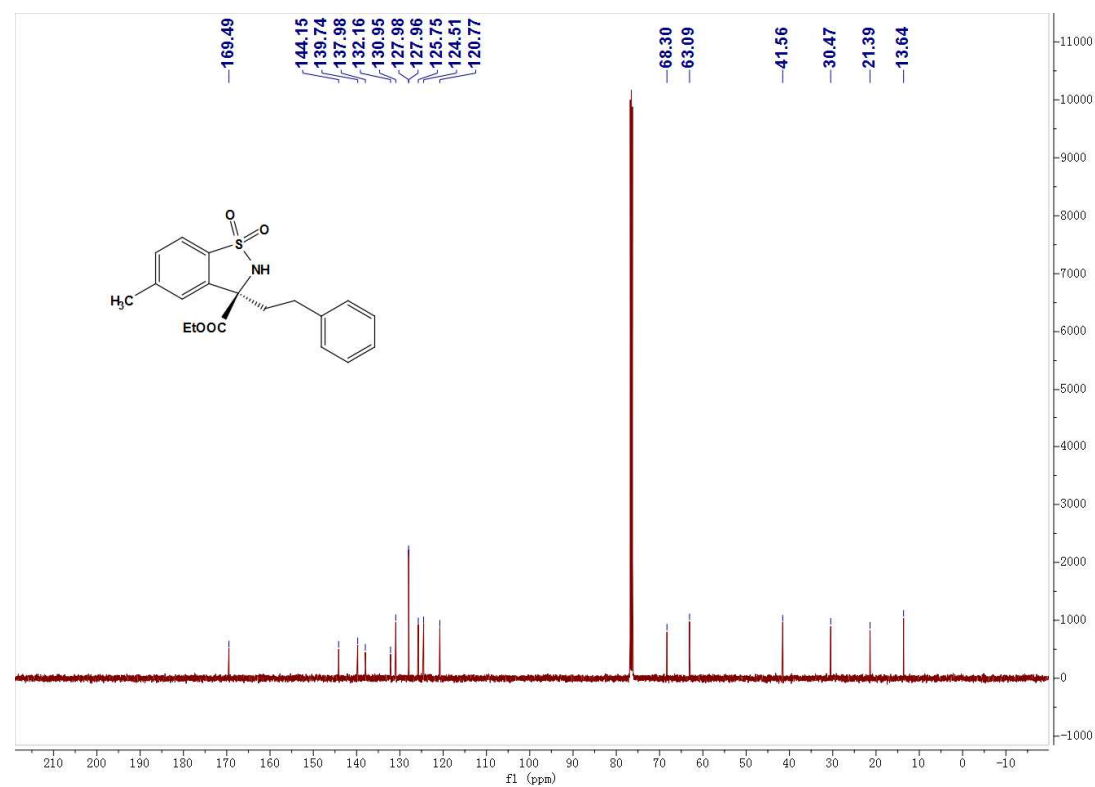
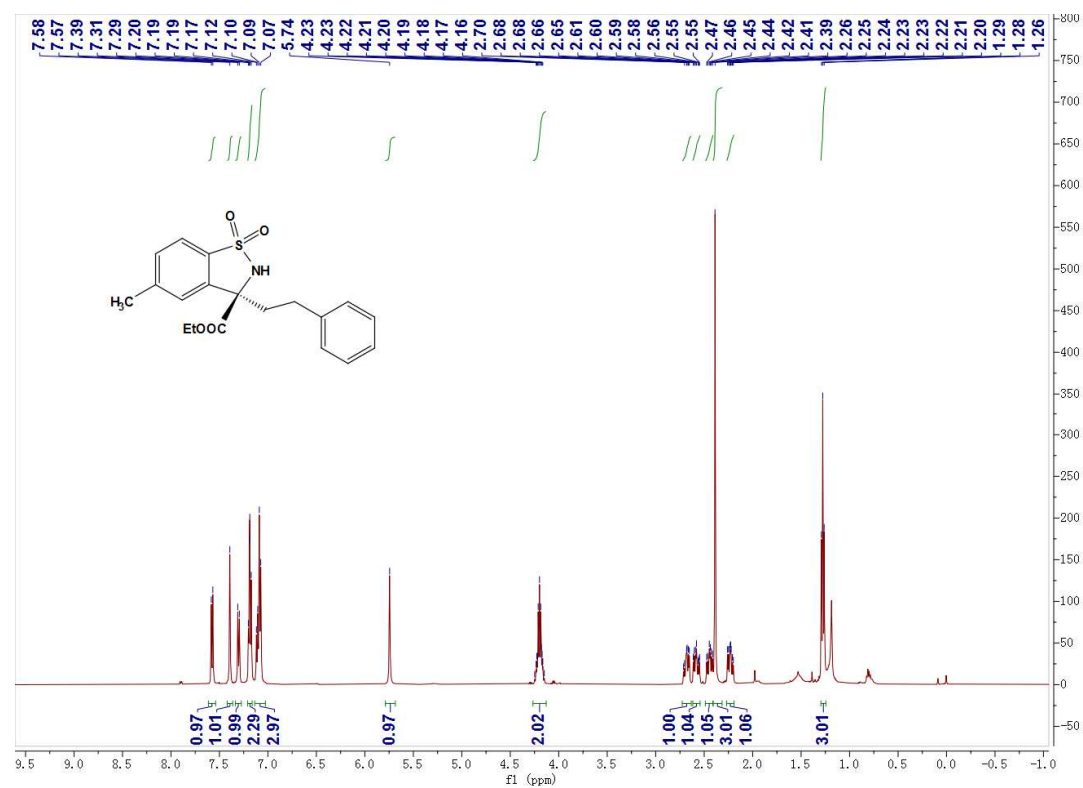
1 检测器 A 通道1/254nm

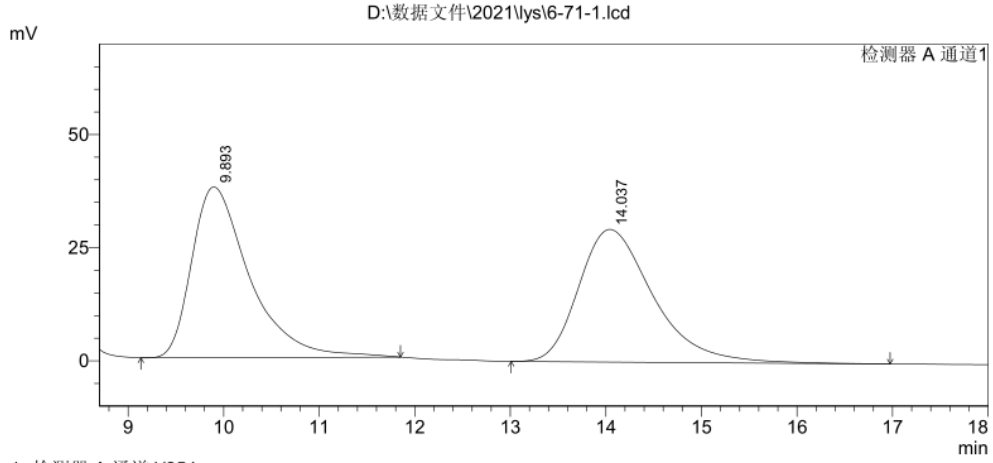
峰表

检测器 A Ch1 254nm					
峰#	保留时间	面积	高度	面积 %	高度 %
1	13.625	3641993	126843	17.869	25.734
2	20.114	16739240	366066	82.131	74.266
总计		20381233	492909	100.000	100.000

**(R)-ethyl 3-phenethyl-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide**

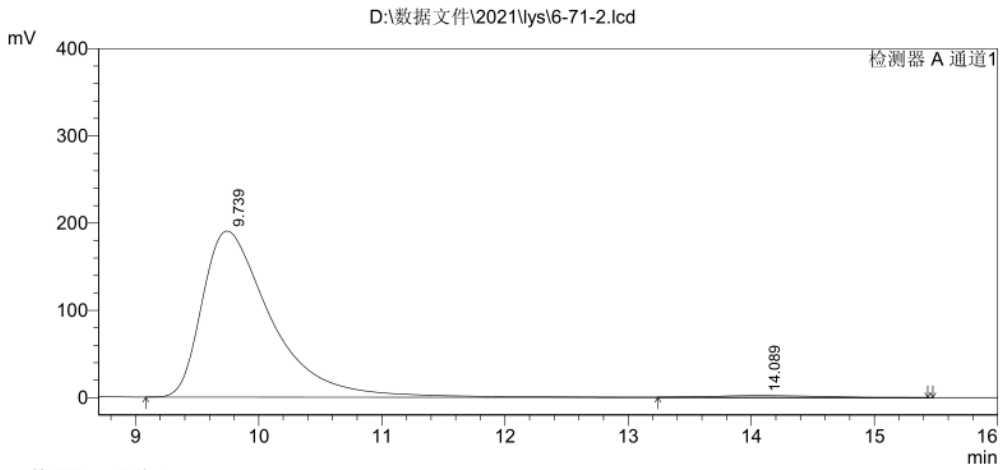
**(4)**





峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	9.893	1585621	37703	49.958	56.274
2	14.037	1588287	29296	50.042	43.726
总计		3173908	67000	100.000	100.000



峰表

峰#	保留时间	面积	高度	面积 %	高度 %
1	9.739	7470785	190500	98.566	98.902
2	14.089	108690	2115	1.434	1.098
总计		7579476	192614	100.000	100.000

## 5. References

- [1] D. Connors, N. Goroff, *Org. Lett.* **2016**, 18, 4262.
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