Electronic Supplementary Information

Aryldiazonium ion initiated C-N bond cleavage for regioselective ring-opening of N-sulfonylazetidines with thiol nucleophiles

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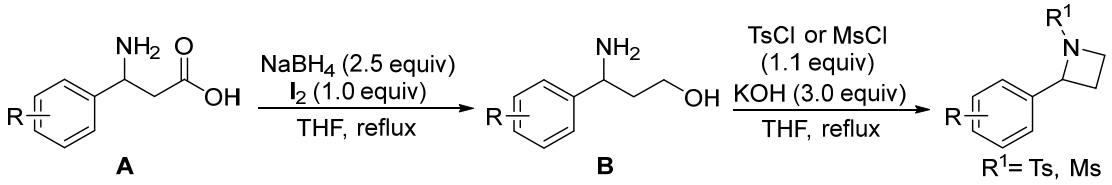
1. General information

All reactions were carried out under argon atmosphere using Schlenk techniques. Thiol nucleophiles and catalyst *p*-NO_2-$C_6H_4N_2BF_4$ were purchased from Adamas-Beta. Chromatographic purification of products was accomplished using forced-flow chromatography on Silicycle SiliaFlash® P60 40-63 mm, 60 Å silica gel. Analytical thin layer chromatography (TLC) was performed on precoated silica gel GF254 plates. Visualization of the developed chromatogram was performed by UV light or staining with iodine (dispersed in silica gel). ^{1}H NMR spectra (500 MHz), ^{13}C NMR (125 MHz) and ^{19}F NMR (470 MHz) spectra data were recorded on Bruker AVANCE-500 spectrometer. ^{1}H NMR chemical shifts are reported in parts per million (ppm) and are referenced to residual protium in the NMR solvent (7.26 for $CHCl_3$, 7.16 for C_6D_5H). ^{13}C NMR chemical shifts are reported in parts per million (ppm) and are referenced to are referenced to the carbon resonances of the solvent residual peak (77.16 for $CDCl_3$, 128.06 for C_6D_6, 39.52 for $(CD_3)_2SO$). ^{19}F NMR data recorded in $CDCl_3$ are listed by using $CFCl_3$ as external reference. Data for ^{1}H NMR are reported as follows: chemical shift (d ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz) and integration. Data for ^{13}C NMR are recorded with broad-band proton decoupling technique and are reported in terms of chemical shift. Mass spectra were obtained on a Bruker Apex IV RTMS. Diffraction of single crystals was performed on a Bruker SMART Bruker Platon II area detector diffractometer using graphite-monochromated Mo *K*α radiation (λ = 0.71073 Å) or Cu *K*α radiation (λ = 1.54178 Å) at 300 K, ϕ and ω scan technique.

2. Experimental procedures and characterization data for substrates.

2.1. General procedure for the synthesis of 1a-1q

Preparation of azetidines 1a-1h, (*S*)-1a:

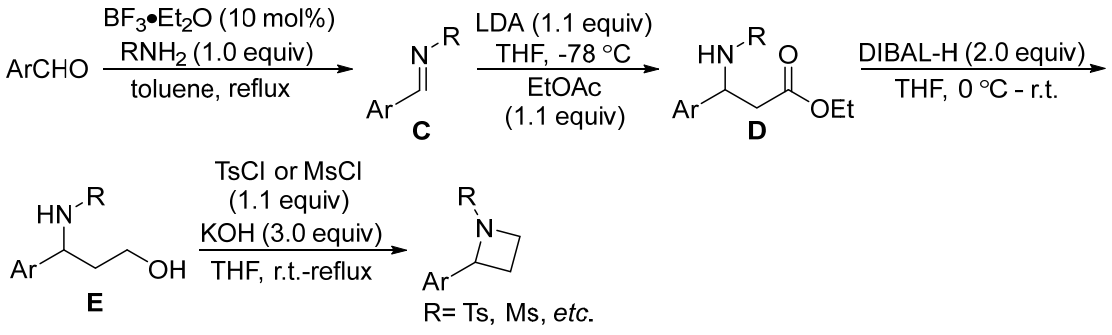


Under anhydrous and oxygen-free argon protection, a freshly distilled THF (8 mL) and sodium borohydride (283.7 mg, 7.5 mmol) were placed in a dried 50 mL three-neck flask. An ice-water bath was applied, and a solution of iodine (761.4 mg, 3.0 mmol) in THF (4 mL) was added dropwise under stirring. After the addition was complete, the mixture was stirred at room temperature for 0.5 hour. Amino acid (3.0 mmol) was then introduced[1], and the reaction was heated under reflux for 18–48 hours. The mixture was extracted with CH_2Cl_2 (3 × 15 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The crude product was further purified by vacuum distillation or recrystallization as appropriate to afford compound **B** as a white solid in 70–90% yield.

To a flame-dried flask equipped with a stir bar was charged KOH (336.6 mg, 6.0 mmol) and THF (3.0 mL). A solution of compound **B** (2.0 mmol) in THF (5 mL) was then added dropwise at room temperature[2]. Subsequently, TsCl or MsCl (2.2 mmol) was added portionwise, and the resulting mixture was heated under reflux for 2.0 h. After the reaction was confirmed complete by TLC analysis, cold water (10 mL) was added. The mixture was extracted with EtOAc, and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by flash column chromatography using a gradient of 10–20% ethyl acetate in petroleum ether as the eluent to afford the desired product in 72-85% yield.

(*S*)-**1a** is synthesized by using the pure enantiomer 3-amino-3-phenylpropanoic acid through the above steps.

Preparation of azetidines 1i-1q:



Follow a procedure described in the literature[3], to the solution of the corresponding aldehyde (5.0 mmol) in toluene (30 mL) was added sulfamide (5.0 mmol) and $BF_3 \cdot Et_2O$ (0.5 mmol). The mixture was refluxed using a Dean-Stark apparatus. After the reaction was complete as monitored by TLC, the solution was cooled to room temperature, concentrated under reduced pressure, and recrystallized from EtOAc/Hexanes. The product was used for the next step without further purification.

To a flame-dried flask was added THF (10 mL), followed by a solution of LDA 1.0 M in THF (5.5 mL) at -78°C. Dried ethyl acetate (5.5 mmol) was then added dropwise. After the reaction was allowed to stir at -78 °C for 1.0 h, a solution of **C** (5.0 mmol) in THF (15 mL) was added dropwise. The reaction was stirred at that temperature until the reaction completion as monitored by TLC. The reaction was quenched with saturated aqueous NH_4Cl solution and allowed to warm to room temperature. The reaction mixture was then extracted with EtOAc, washed with saturated brine, dried over Na_2SO_4, concentrated under reduced pressure, and purified by flash column chromatography with a gradient of 10-25% ethyl acetate in petroleum ether as eluent.

To a flame-dried flask containing **D** of the previous step was added THF (10 mL) under Argon. After the reaction was cooled to 0 °C, a solution of DIBAL-H 1.0 M in toluene (10 mL) was then added dropwise. The reaction was then allowed to stir at room temperature for 5.0 h. After the reaction completion as monitored by TLC, water (10 mL) and then 15% aqueous NaOH solution (5.0 mL) were added at 0 °C. The reaction mixture was stirred for 15 min, extracted with EtOAc, washed with saturated brine, dried over Na_2SO_4, concentrated, and passed through a short silica gel plug (5 cm) to give the crude product **E**. It was used as starting material for the next step without any further purification.

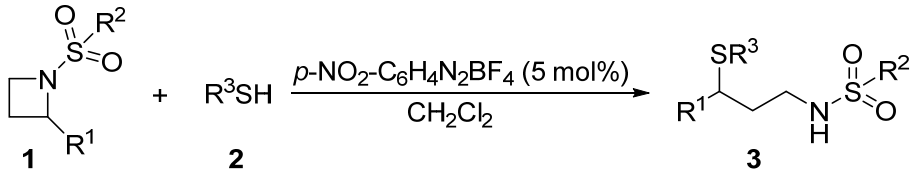
To a flame-dried flask equipped with a stir bar was added KOH (337 mg, 6.0 mmol), followed by THF (4.0 mL). A solution of alcohol **E** (2.0 mmol) in THF (6.0 mL) was then added dropwise at room temperature. After that, TsCl (419 mg, 2.2 mmol) was added portionwise and the reaction mixture was refluxed for 2.0 h. After the reaction was complete as monitored by TLC, cold water (10 mL) was added, extracted with EtOAc, washed with brine, dried over Na_2SO_4, concentrated, and purified via flash column chromatography with a gradient of 10-20% ethyl acetate in petroleum ether as eluent to afford the desired product in 72-85% yield.

The spectroscopic data of all known compounds are in agreement with those previously reported.

2.2. Preparation of aryldiazonium tetrafluoroborates [4]

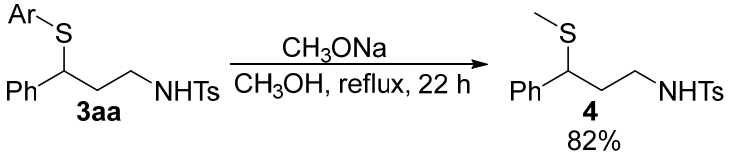
Arylamine (50 mmol) was dissolved in a mixture of hydrofluoroboric acid (40 wt.%, 17 mL) and distilled water (20 mL). After cooling the reaction mixture to 0°C, the solution of sodium nitrite (3.4 g in 7.5 mL distilled water) was added dropwise into the reaction system (a total of 5 minutes are required). The resulting mixture was stirred for 1.0 h and the precipitate was collected by filtration and redissolved in minimum amount of acetone. Diethyl ether was added until precipitation of aryldiazonium tetrafluoroborate, which is filtered, washed several times with diethyl ether and dried under vacuum. The desired product was obtained with an 83% yield.

2.3 General procedure for products 3aa-3qa and 3ab-3am.



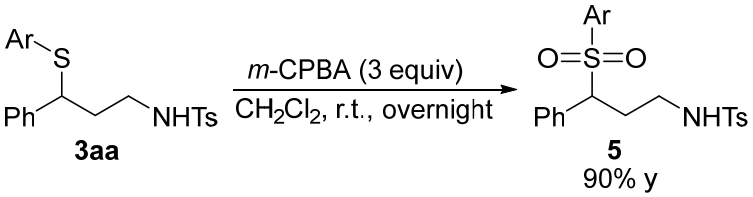
Under anhydrous and oxygen-free argon protection, to an oven-dried Schlenk tube was added azetidines **1** (0.10 mmol), **2** (0.12 mmol), and 1 mL of dichloromethane. The reaction mixture was stirred at 35 or 50 °C until the disappearance of **1** as monitored by TLC (visualized by UV light). Then 4 mL of distilled water and 4 mL of ethyl acetate were added, and the phases were separated. The aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated via rotary evaporation under reduced pressure to provide the crude mixture. Then the crude mixture was purified by column chromatography (eluting with petroleum ether/EtOAc (v/v): 8:1-4:1) to furnish the desired products.

2.4 Synthesis of products 4.



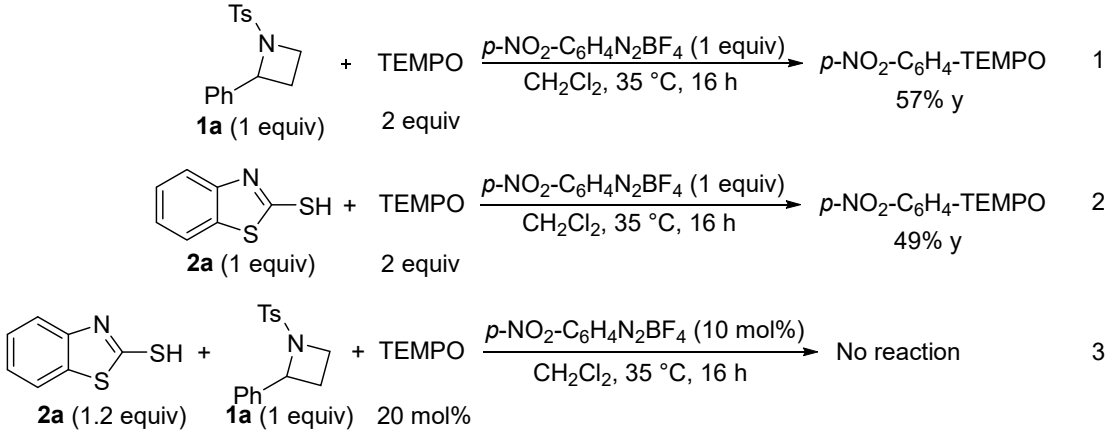
At room temperature, under anhydrous and oxygen-free argon protection, to an oven-dried Schlenk tube was added azetidines **3aa** (0.10 mmol), CH_3ONa (2.0 mmol), and 2.0 mL of CH_3OH. The reaction mixture was stirred at 60 °C in a heating block for 16 h and then quenched with a saturated aqueous solution of NH_4Cl (6.0 mL). The mixture was extracted with ethyl acetate (5 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (eluent: hexanes/ethyl acetate =10:1→2:1) to give the desired product **4** as a colorless oil in 66% yield (22.1 mg).

2.5 Synthesis of the product 5.



Under anhydrous and oxygen-free argon protection, to an oven-dried Schlenk tube, to a stirred solution of benzothiazole moiety γ-amino thioether **3aa** (45.4 mg, 0.10 mmol) in CH_2Cl_2 (2.0 mL) at 0 °C, *m*-CPBA (51.7 mg, 0.30 mmol) was added. After 10 min, the cold bath was removed and the reaction was stirred for 4.0 hours. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction was quenched with saturated aqueous sodium bicarbonate solution (2.0 mL). The aqueous phase was extracted with CH_2Cl_2 (2×5 mL), dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. Purification of the crude mixture by flash silica gel chromatography (petroleum ether/ethyl acetate = 15:1) afforded the **5** (43.9 mg, yield: 90%) as a white solid.

2.6. Supporting experiments for the proposed mechanism.



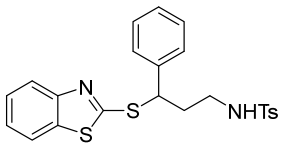
Equation 1: Under anhydrous and oxygen-free argon protection, to an oven-dried Schlenk tube were added azetidine (**1a**, 0.10 mmol), para-nitrophenyldiazonium tetrafluoroborate (0.10 mmol), TEMPO (0.20 mmol) and CH_2Cl_2 (1.0 mL). The tube was sealed and the reaction mixture was allowed to stir at 35°C for 16 h. After being evaporated the solvent, the residue was purified by column chromatography to afford the aryl/TEMPO adduct in 57% yield.

Equation 2: Under anhydrous and oxygen-free argon protection, to an oven-dried Schlenk tube were added para-nitrophenyldiazonium tetrafluoroborate (0.10 mmol), benzo[d]thiazole-2-thiol (**2a**, 0.10 mmol), TEMPO (0.20 mmol) and CH_2Cl_2 (1.0 mL). The tube was sealed and the reaction mixture was allowed to stir at room temperature for 16 h. After being evaporated the solvent, the residue was purified by column chromatography to afford the aryl/TEMPO adduct in 49% yield.

Equation 3: Under anhydrous and oxygen-free argon protection, to an oven-dried Schlenk tube were added azetidine (**1a**, 0.10 mmol), benzo[d]thiazole-2-thiol (**2a**, 0.12 mmol), para-nitrophenyldiazonium tetrafluoroborate (10 mol%), TEMPO (20 mol%) and CH_2Cl_2 (1.0 mL). The tube was sealed and the reaction mixture was allowed to stir at room temperature for 16 h. There is no monitor conduct aryl/TEMPO and desired product **3aa** by TLC.

2.7. Characterization of 3aa-5

N-(3-(benzo[d]thiazol-2-ylthio)-3-phenylpropyl)-4-methylbenzenesulfonamide (3aa)



Compound **3aa**: a yellow solid. M.p. = 123-124 °C. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 42.2 mg, 93% yield.

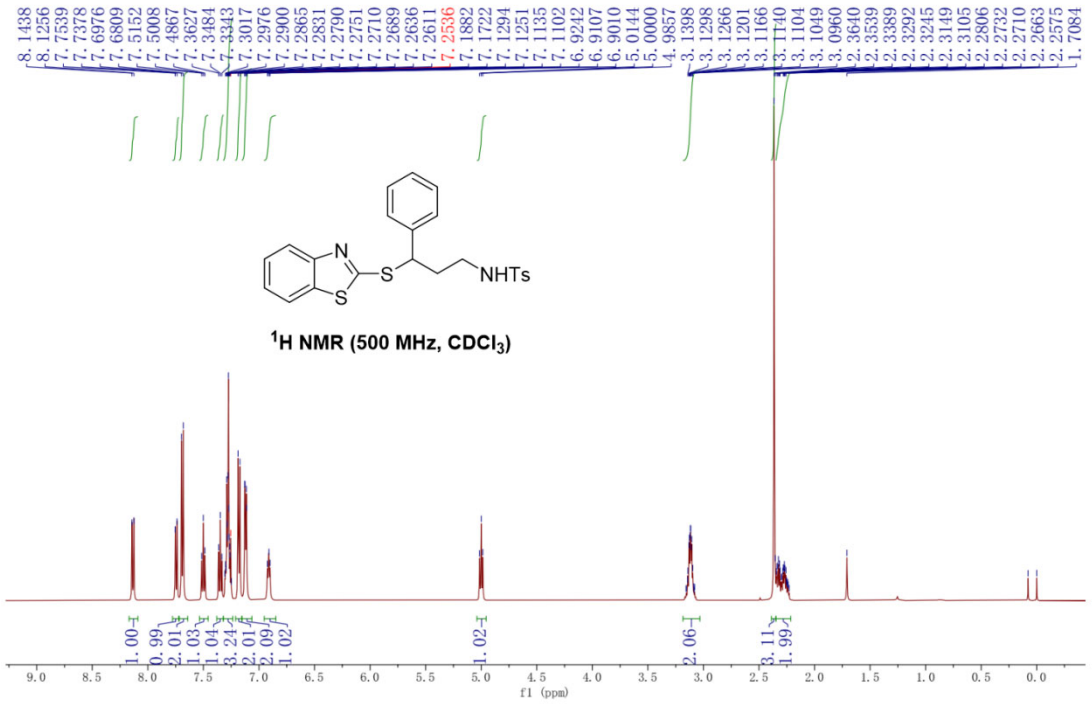
Compound (*S*)-**3aa**: 30% ee, **HPLC**: Daicel CHIRALCEL ID column, 30% IPA in hexanes, 1.0 mL/min, λ＝254 nm, t_R(minor) = 14.5 min, t_R(major) = 13.7 min;

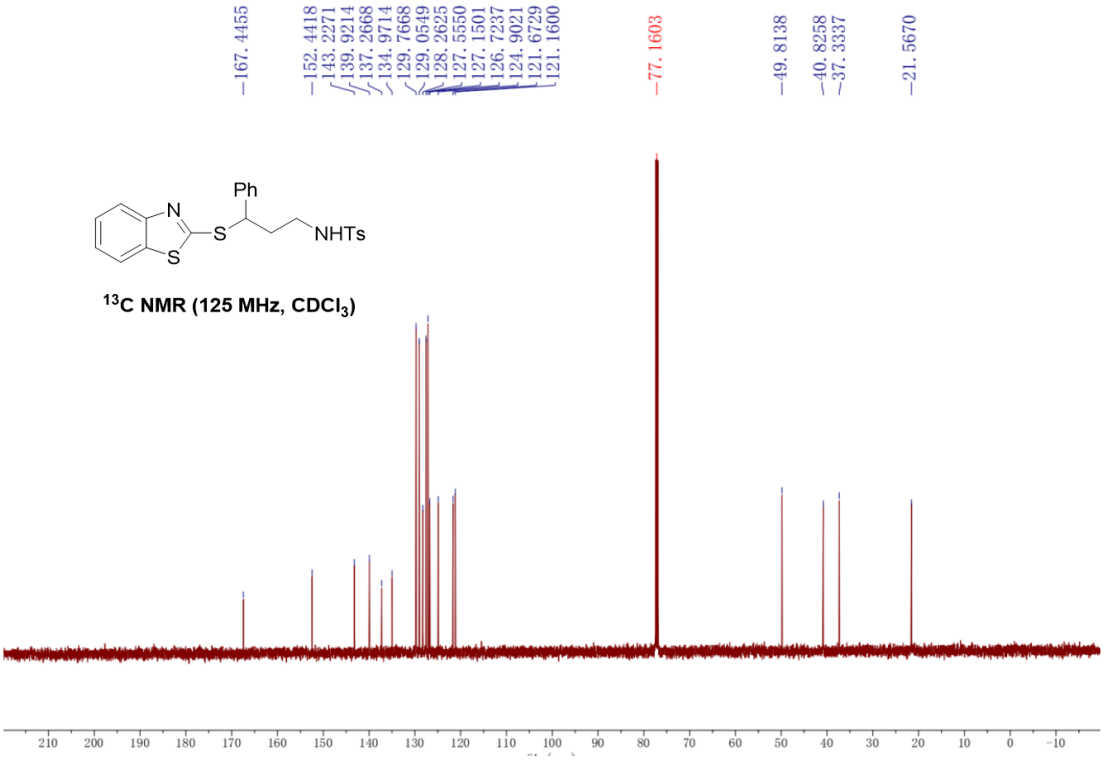
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.13 (d, *J* = 9.1 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.50 (t, *J* = 7.1 Hz, 1H), 7.35 (t, *J* = 7.1 Hz, 1H), 7.32-7.24 (m, 3H), 7.18 (d, *J* = 8.0 Hz,

2H), 7.12 (dd, *J* = 7.7, 1.9 Hz, 2H), 6.91 (t, *J* = 4.8 Hz, 1H), 5.00 (t, *J* = 7.2 Hz, 1H), 3.18-3.03 (m, 2H), 2.36 (s, 3H), 2.35-2.21 (m, 2H).

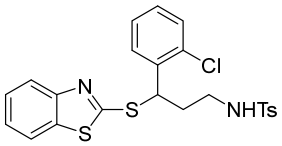
^{13}C NMR (125 MHz, Chloroform-*d*) δ 167.4, 152.4, 143.2, 139.9, 137.3, 135.0, 129.8, 129.1, 128.3, 127.6, 127.2, 126.7, 124.9, 121.7, 121.2, 49.8, 40.8, 37.3, 21.6.

HRMS (ESI) m/z: calcd for $[C_{23}H_{22}N_2O_2S_3+H]^+$ requires: 455.0916, found: 455.0924.





N-(3-(benzo[d]thiazol-2-ylthio)-3-(2-chlorophenyl)propyl)-4-methylbenzenesulfonamide (3ba)

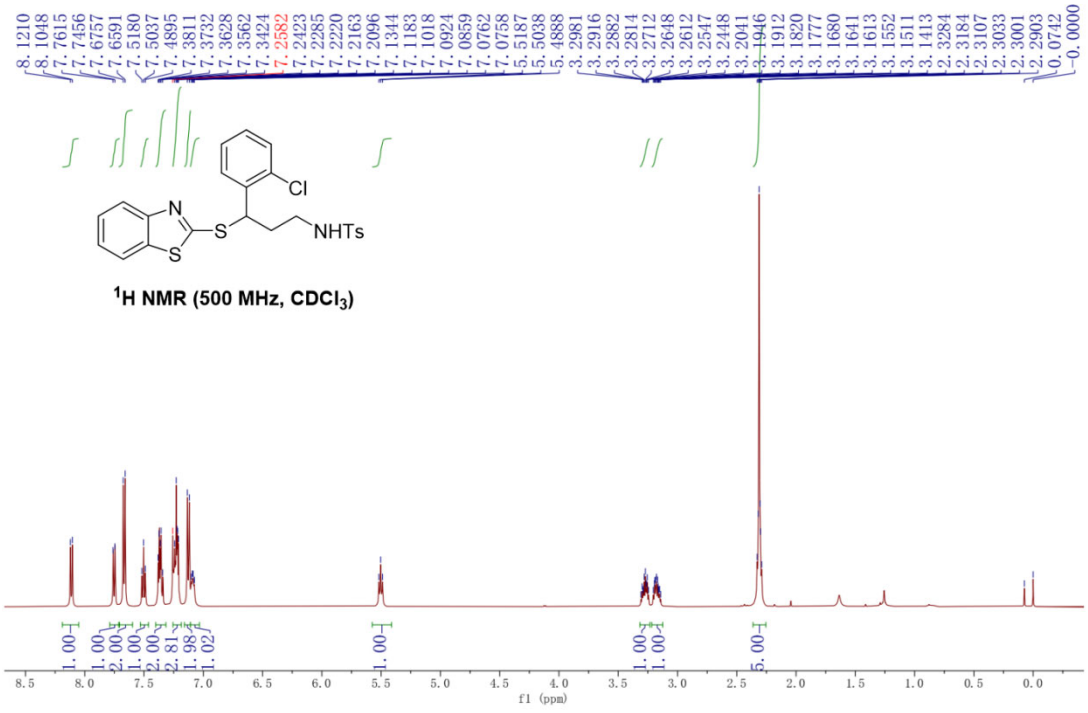


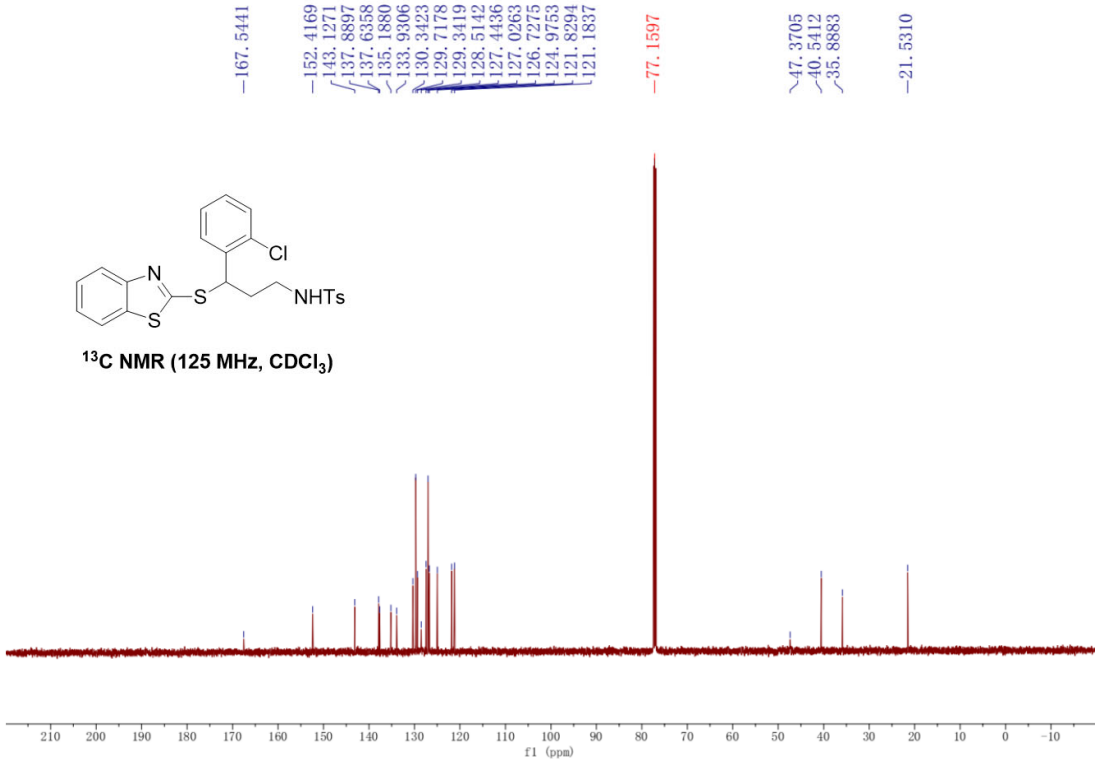
Compound **3ba**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 45.5 mg, 93% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.11 (d, *J* = 8.1 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.3 Hz, 2H), 7.50 (t, *J* = 7.1 Hz, 1H), 7.40-7.32 (m, 2H), 7.26-7.19 (m, 3H), 7.13 (d, *J* = 8.1 Hz, 2H), 7.09 (t, *J* = 4.7 Hz, 1H), 5.50 (t, *J* = 7.5 Hz, 1H), 3.28 (m, 1H), 3.17 (m, 1H), 2.36-2.25 (m, 5H).

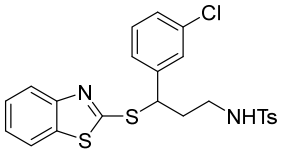
^{13}C NMR (125 MHz, Chloroform-*d*) δ 167.5, 152.4, 143.1, 137.9, 137.6, 135.2, 133.9, 130.3, 129.7, 129.3, 128.5, 127.4, 127.0, 126.7, 125.0, 121.8, 121.2, 47.4, 40.5, 35.9, 21.5.

HRMS (ESI) m/z: calcd for $[C_{23}H_{21}ClN_2O_2S_3+H]^+$ requires: 489.0526, found: 489.0533.





N-(3-(benzo[d]thiazol-2-ylthio)-3-(3-chlorophenyl)propyl)-4-methylbenzenesulfonamide(3ca)

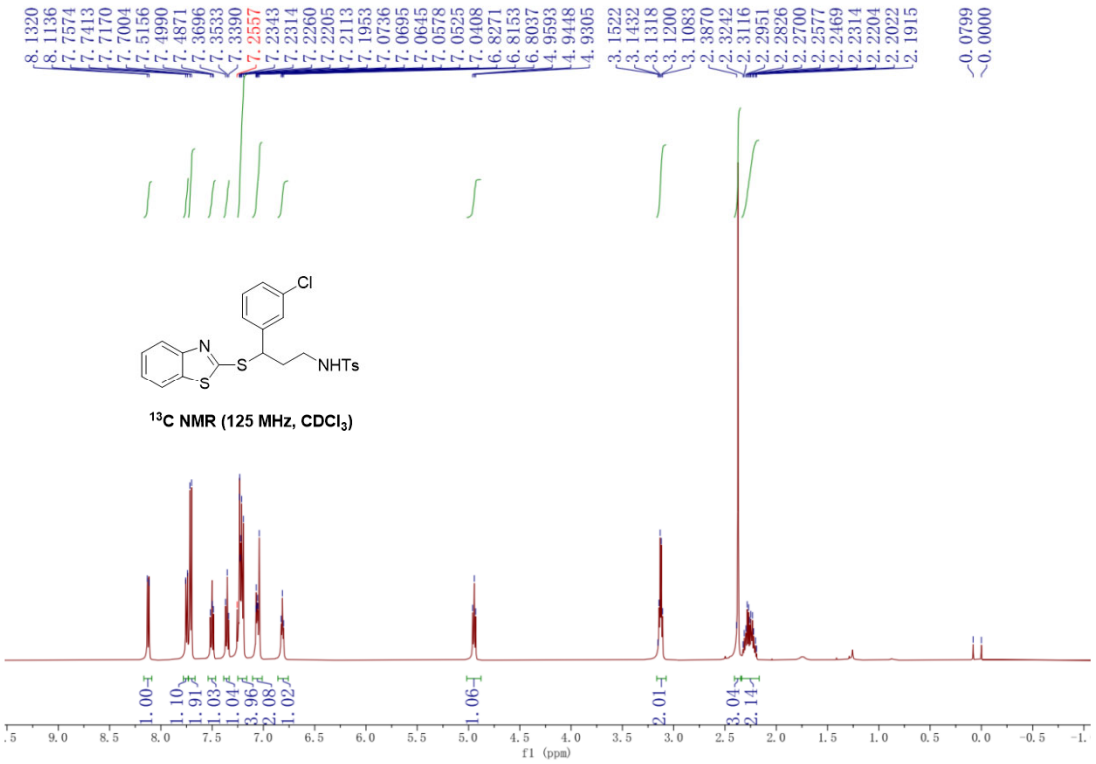


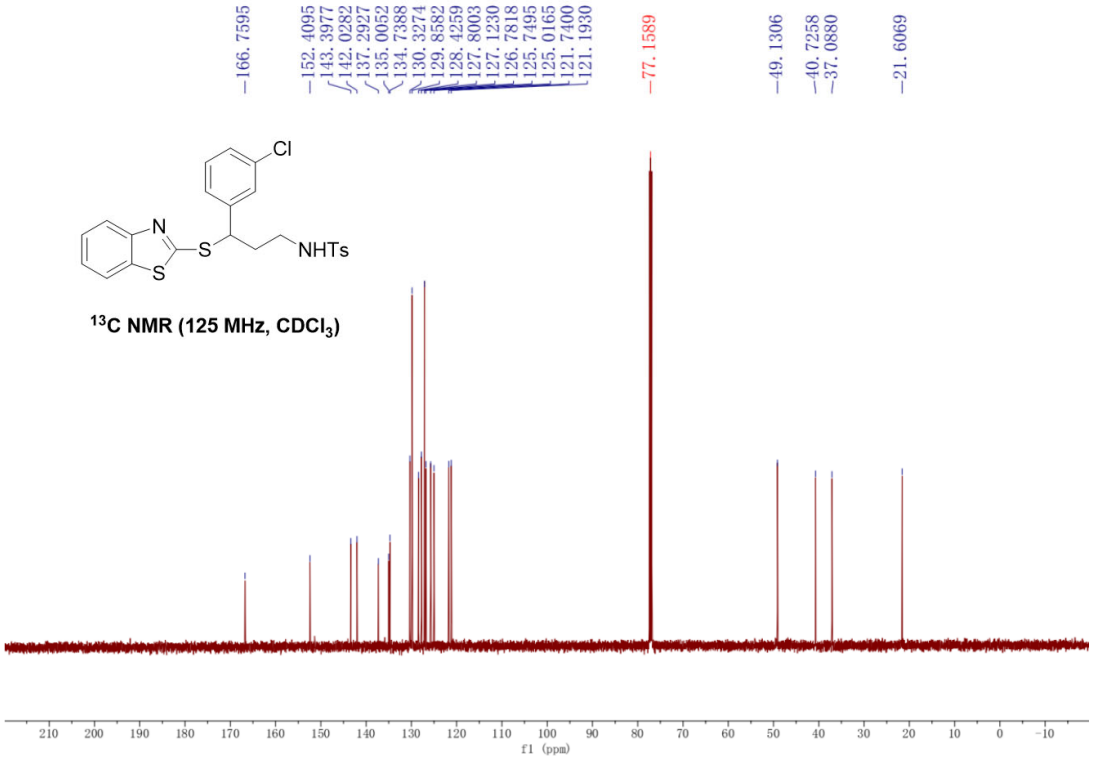
Compound **3ca**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 46.3 mg, 95% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 9.2 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.54-7.47 (t, *J* = 8.3 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.23-7.16 (m, 4H), 7.11-7.01 (m, 2H), 6.82 (t, *J* = 5.9 Hz, 1H), 4.94 (t, *J* = 7.2 Hz, 1H), 3.15-3.10 (m, 2H), 2.39 (s, 3H), 2.32-2.19 (m, 2H).

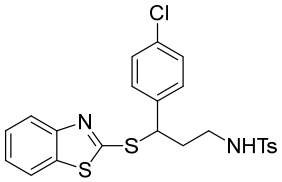
^{13}C NMR (125 MHz, Chloroform-*d*) δ 166.8, 152.4, 143.4, 142.0, 137.3, 135.0, 134.7, 130.3, 129.9, 128.4, 127.8, 127.1, 126.8, 125.7, 125.0, 121.7, 121.2, 49.1, 40.7, 37.1, 21.6.

HRMS (ESI) m/z: calcd for $[C_{23}H_{21}ClN_2O_2S_3+H]^+$ requires: 489.0526, found: 489.0534.


Cl
N
S
S
NHTs
13C NMR (125 MHz, CDCl3)
f1 (ppm)


Cl
N
S
S
NHTs
13C NMR (125 MHz, CDCl3)
f1 (ppm)

N-(3-(benzo[d]thiazol-2-ylthio)-3-(4-chlorophenyl)propyl)-4-methylbenzenesulfonamide (3da)

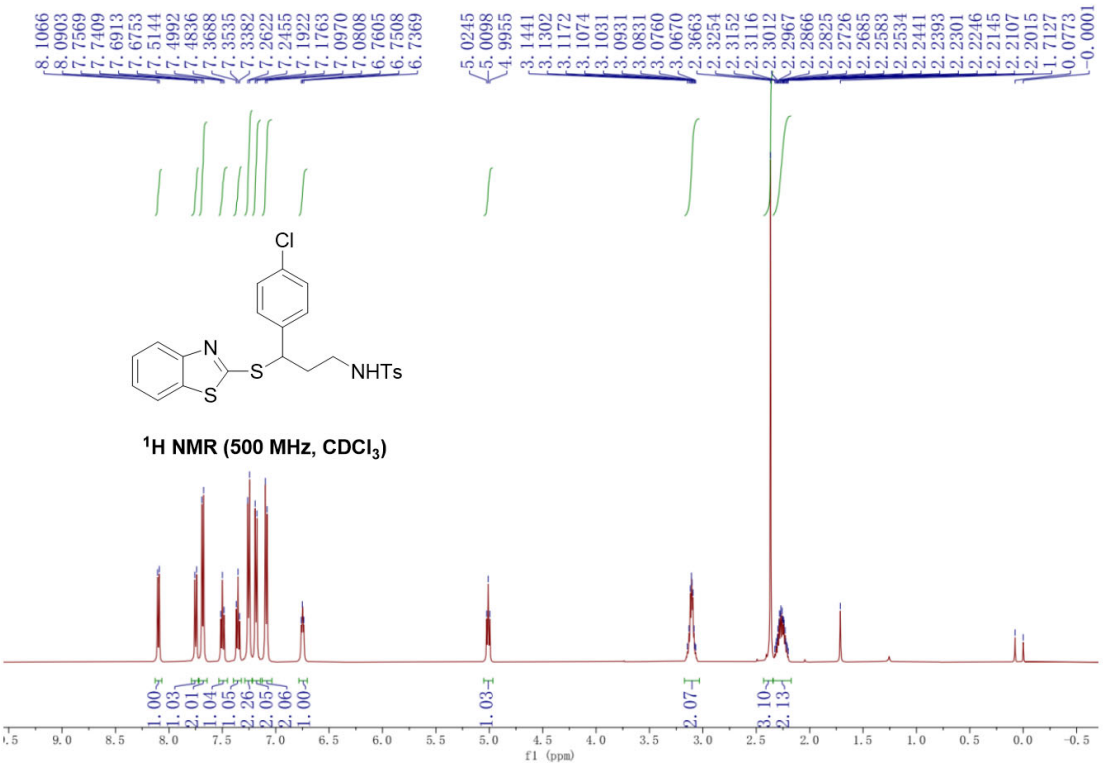


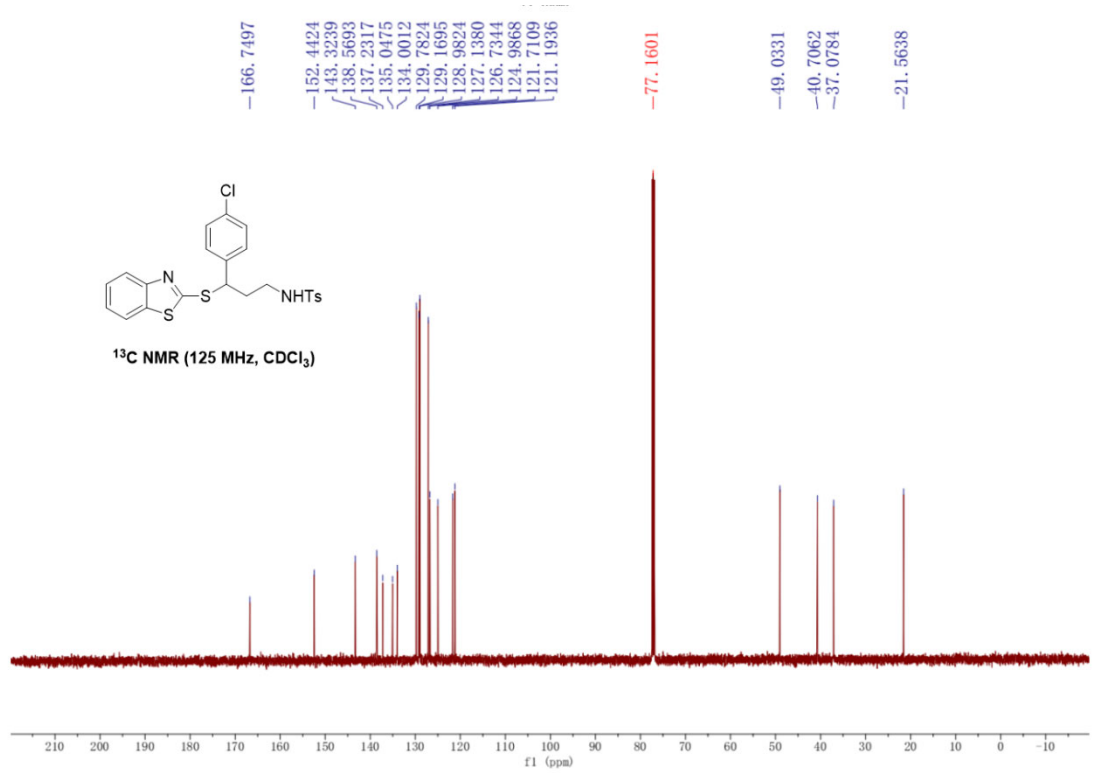
Compound **3da**: a white solid. M.p. = 136-137 °C. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 43.8 mg, 90% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.17-8.09 (d, *J* = 8.1 Hz, 1H), 7.75 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.73-7.67 (m, 2H), 7.50 (ddd, *J* = 8.3, 7.2, 1.3 Hz, 1H), 7.39-7.33 (m, 1H), 7.25-7.16 (m, 4H), 7.11-7.01 (m, 2H), 6.82 (t, *J* = 5.8 Hz, 1H), 4.94 (t, *J* = 7.2 Hz, 1H), 3.17-3.09 (m, 2H), 2.37 (s, 3H), 2.34-2.17 (m, 2H).

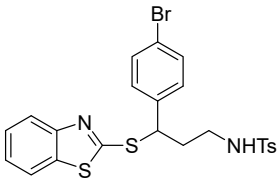
^{13}C NMR (125 MHz, Chloroform-*d*) δ 166.7, 152.4, 143.3, 138.6, 137.2, 135.0, 134.0, 129.8, 129.2, 129.0, 127.1, 126.7, 125.0, 121.7, 121.2, 49.0, 40.7, 37.1, 21.6.

HRMS (ESI) m/z: calcd for $[C_{23}H_{21}ClN_2O_2S_3+H]^+$ requires: 489.0526, found: 489.0534.





N-(3-(benzo[d]thiazol-2-ylthio)-3-(4-bromophenyl)propyl)-4-methylbenzenesulfonamide (3ea)

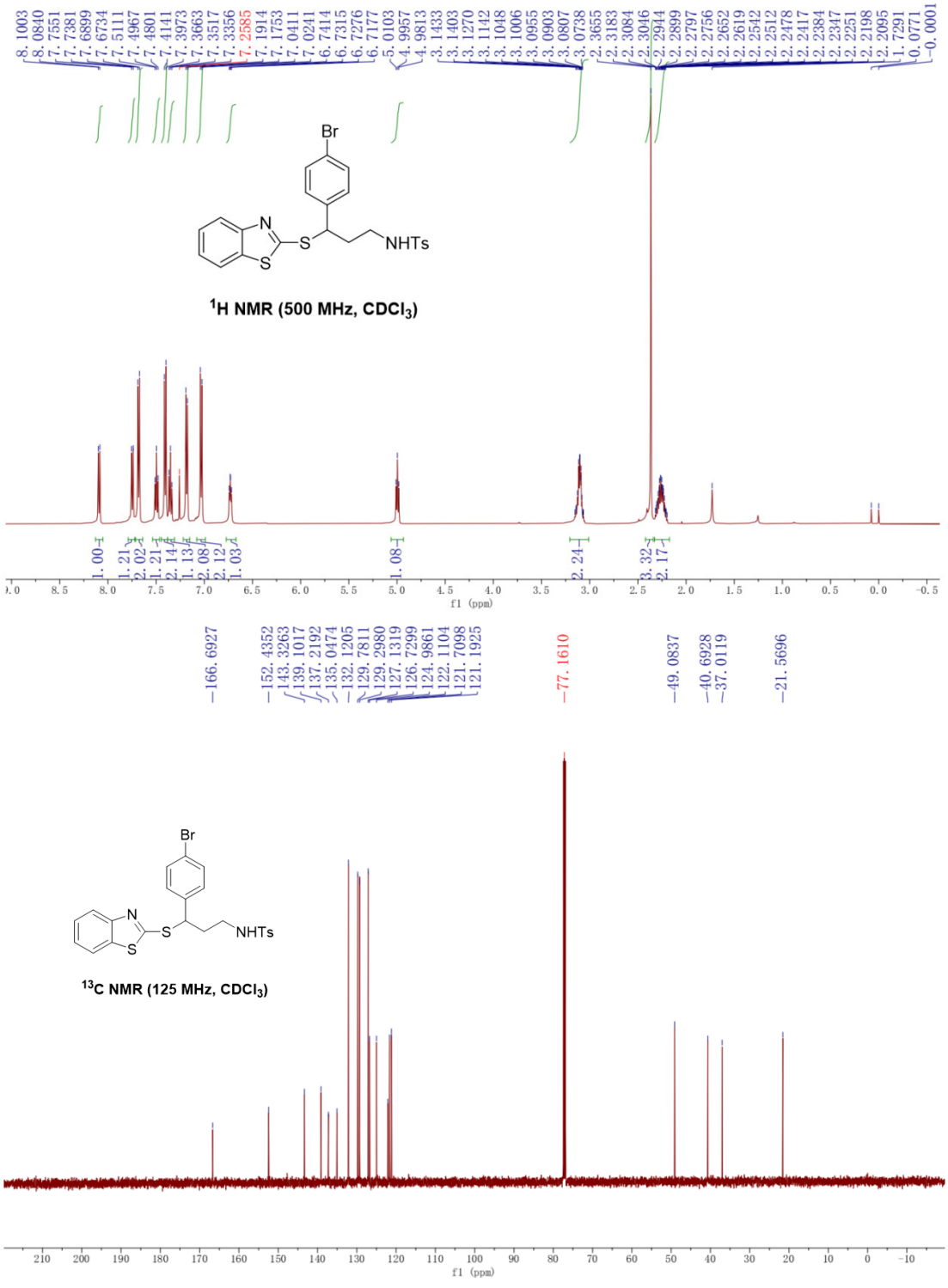


Compound **3ea**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 48.6 mg, 91% yield.

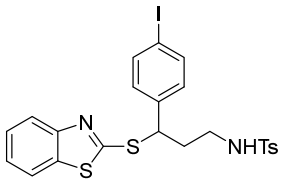
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 8.5 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.50 (t, *J* = 7.7 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 8.5 Hz, 2H), 6.73 (t, *J* = 6.9, 5.0 Hz, 1H), 5.00 (t, *J* = 7.2 Hz, 1H), 3.21-3.01 (m, 2H), 2.37 (s, 3H), 2.32-2.19 (m, 2H).

^{13}C NMR (125 MHz, Chloroform-*d*) δ 166.7, 152.4, 143.3, 139.1, 137.2, 135.0, 132.1, 129.8, 129.3, 127.1, 126.7, 125.0, 122.1, 121.7, 121.2, 49.1, 40.7, 37.0, 21.6.

HRMS (ESI) m/z: calcd for $[C_{23}H_{21}BrN_2O_2S_3+H]^+$ requires: 533.0021, found: 533.0025.



N-(3-(benzo[d]thiazol-2-ylthio)-3-(4-iodophenyl)propyl)-4-methylbenzenesulfonamide (3fa)



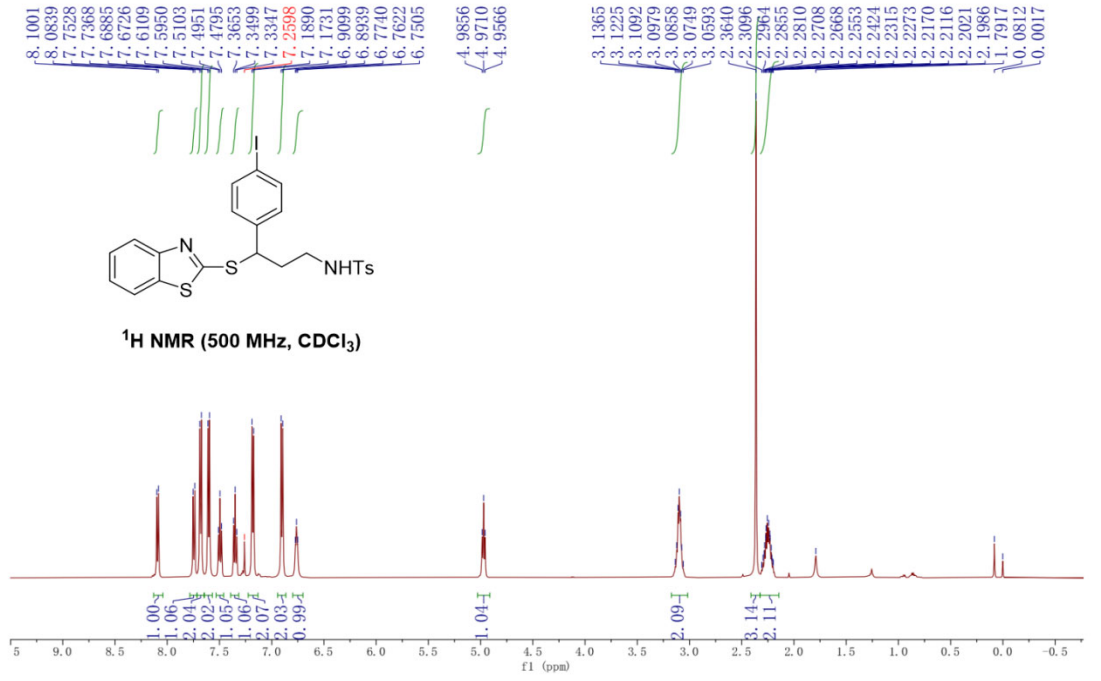
Compound **3fa**: a red oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 48.9

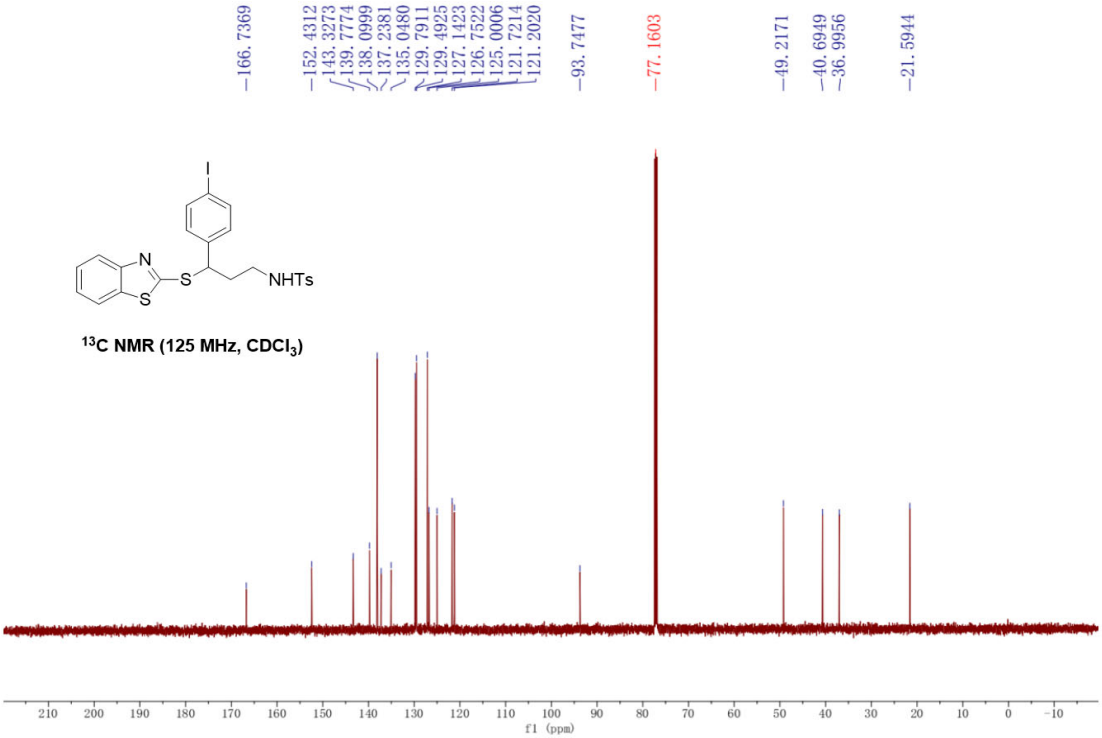
mg, 84% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.1 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.49 (t, *J* = 7.7 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 7.9 Hz, 2H), 6.90 (d, *J* = 8.0 Hz, 2H), 6.76 (t, *J* = 5.9 Hz, 1H), 4.97 (t, *J* = 7.3 Hz, 1H), 3.13-3.06 (m, 2H), 2.36 (s, 3H), 2.32–2.14 (m, 2H).

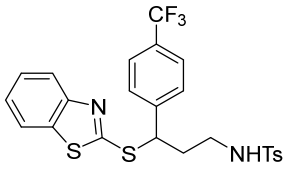
^{13}C NMR (125 MHz, Chloroform-*d*) δ 166.7, 152.4, 143.3, 139.8, 138.1, 137.2, 135.0, 129.8, 129.5, 127.1, 126.8, 125.0, 121.7, 121.2, 93.7, 49.2, 40.7, 37.0, 21.6.

HRMS (ESI) m/z: calcd for $[C_{23}H_{21}IN_2O_2S_3+H]^+$ requires: 580.9883, found: 580.9880.





N-(3-(benzo[d]thiazol-2-ylthio)-3-(4-(trifluoromethyl)phenyl)propyl)-4-methylbenzenesulfonamide (3ga)



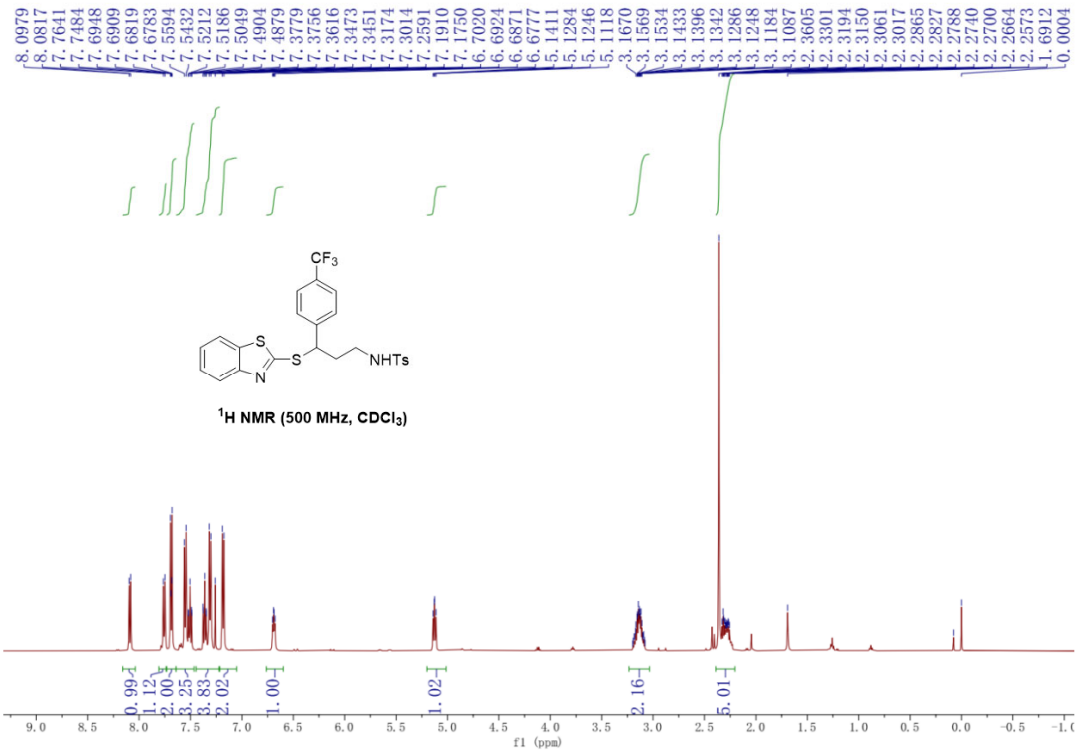
Compound **3ga**: a colorless oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 3/1, 43.4 mg, 83% yield.

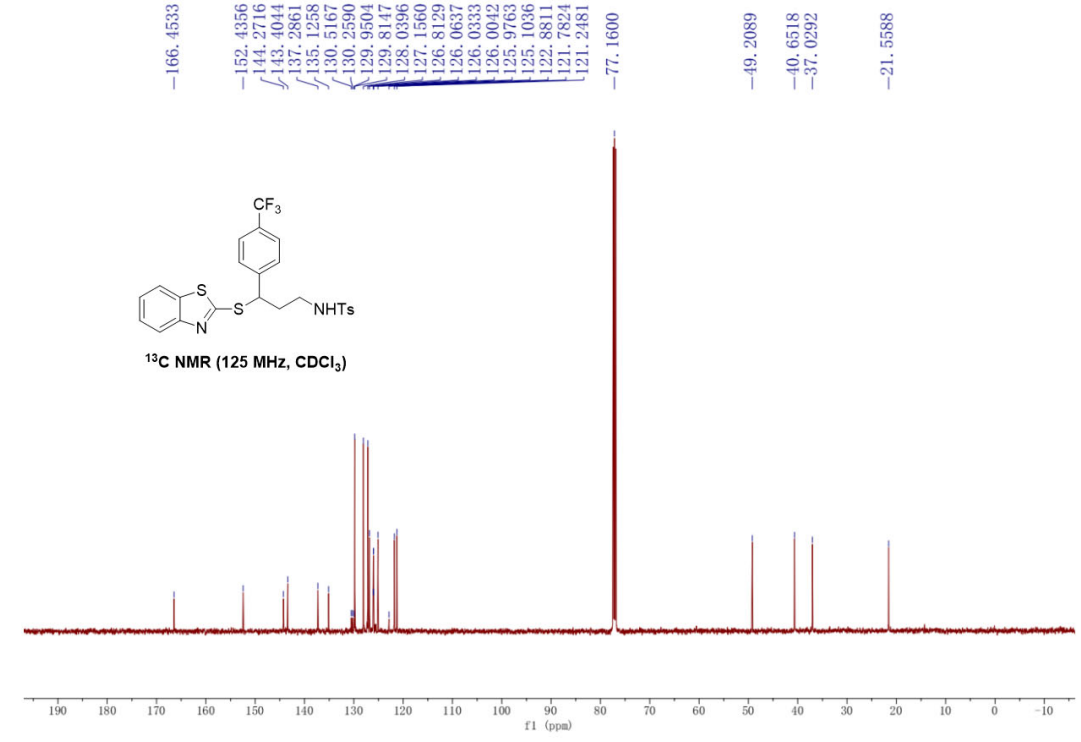
^{1}H NMR (500 MHz, Chloroform-d) δ 8.09 (d, *J* = 8.1 Hz, 1H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.68 (d, *J* = 6.5 Hz, 2H), 7.55 (d, *J* = 8.1 Hz, 3H), 7.50 (t, *J* = 8.2 Hz,1H), 7.37 (t, *J* = 8.2 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.69 (dd, *J* = 7.4, 4.7 Hz, 1H), 5.13 (dd, *J* = 8.3, 6.4 Hz, 1H), 3.21 – 3.05 (m, 2H), 2.36 (s, 3H), 2.35 – 2.22 (m, 2H).

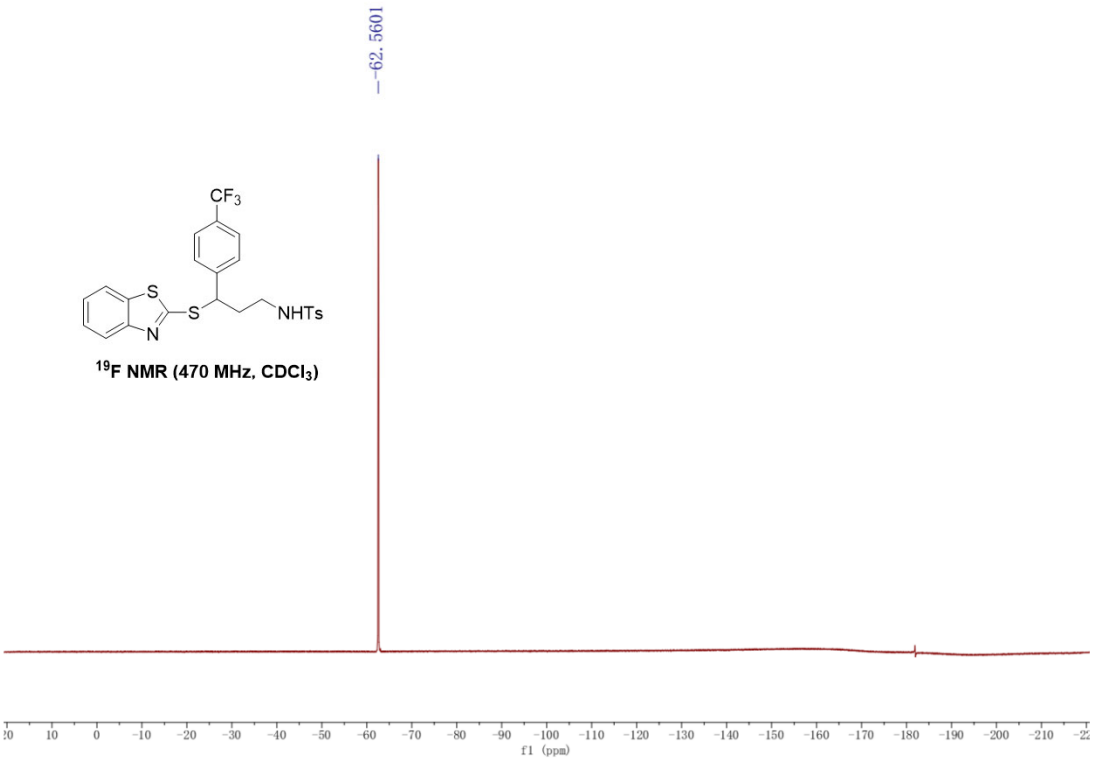
^{13}C NMR (125 MHz, Chloroform-d) δ 166.5, 152.4, 144.3, 143.4, 137.3, 135.1, 130.4 ($^{2}J_{C\text{-}F}$ = 32.2 Hz), 129.8, 128.0, 127.2, 126.8, 126.1 ($^{3}J_{C\text{-}F}$ = 3.6 Hz), 125.1, 124.0 ($^{1}J_{C\text{-}F}$ = 277.8 Hz), 121.8, 121.2, 49.2, 40.7, 37.0, 21.6.

^{19}F NMR (470 MHz, Chloroform-*d*) δ (m) (-62.56)

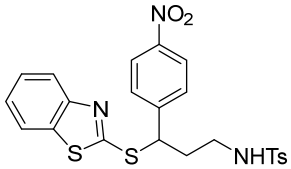
HRMS (ESI) m/z: calcd for $[C_{24}H_{22}F_3N_2O_2S_3+H]^+$ requires: 523.0790, found: 523.0788.







N-(3-(benzo[d]thiazol-2-ylthio)-3-(4-nitrophenyl)propyl)-4-methylbenzenesulfonamide (3ha)

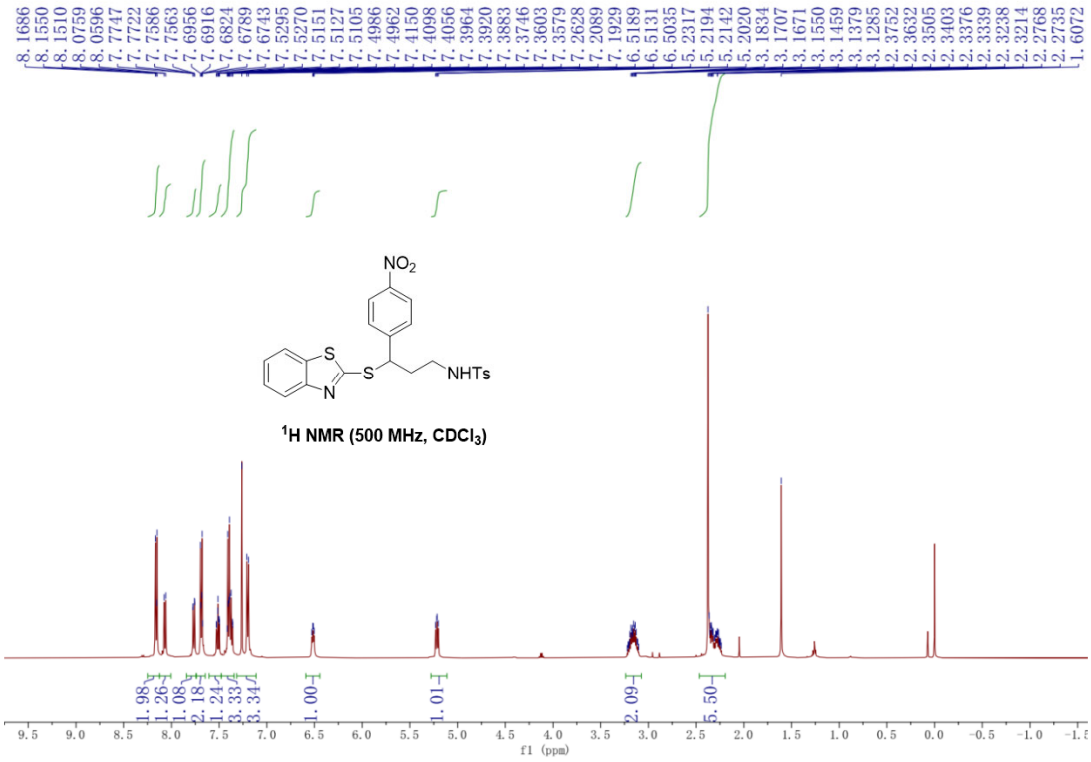


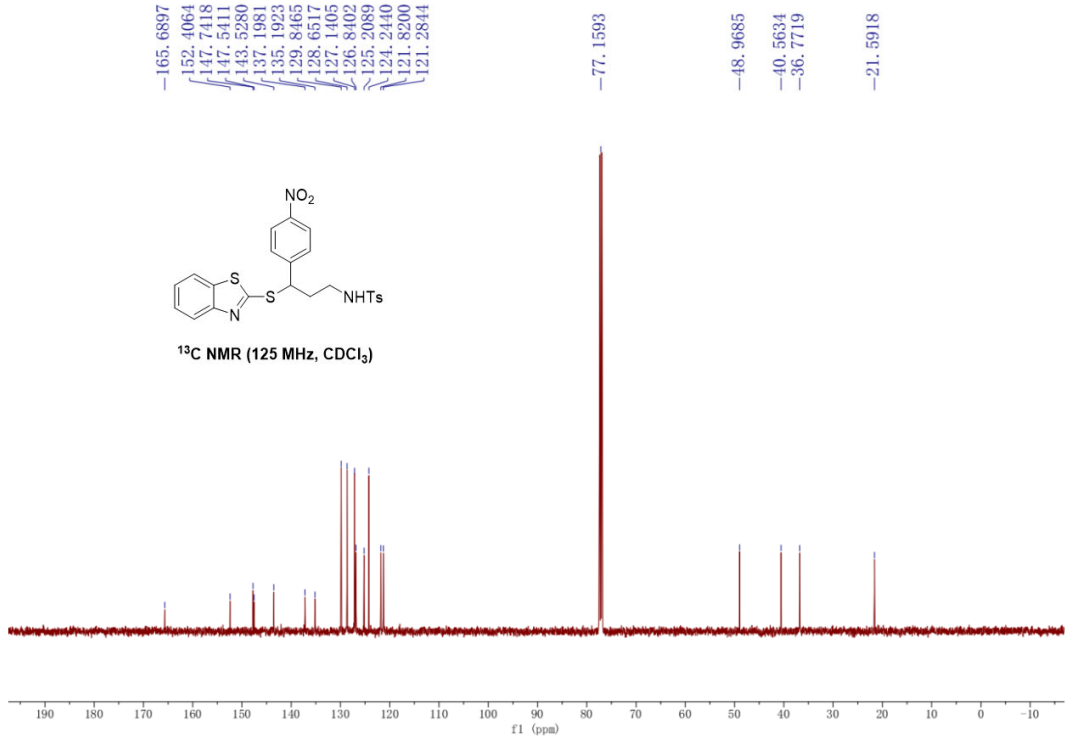
Compound **3ha**: a white solid. M.p. = 134-135 °C. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 40.5 mg, 81% yield.

^{1}H NMR (500 MHz, Chloroform-d) δ 8.16 (d, *J* = 8.8 Hz, 2H), 8.07 (d, *J* = 8.2 Hz, 1H), 7.77 (d, *J* = 8.0, 1.2 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.51 (t, *J* = 8.3, 7.2, 1.2 Hz, 1H), 7.46 – 7.34 (m, 4H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.52 (dd, *J* = 7.7, 4.8 Hz, 1H), 5.22 (dd, *J* = 8.7, 6.1 Hz, 1H), 3.24 – 3.08 (m, 3H), 2.38 (s, 4H), 2.35 – 2.22 (m, 2H).

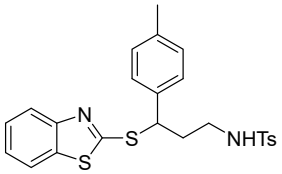
^{13}C NMR (125 MHz, Chloroform-d) δ 165.7, 152.4, 147.7, 147.5, 143.5, 137.2, 135.2, 129.8, 128.7, 127.1, 126.8, 125.2, 124.2, 121.8, 121.3, 49.0, 40.6, 36.8, 21.6.

HRMS (ESI) m/z: calcd for $[C_{23}H_{21}N_3O_4S_3+H]^+$ requires: 500.0767, found: 500.0757.





N-(3-(benzo[d]thiazol-2-ylthio)-3-(p-tolyl)propyl)-4-methylbenzenesulfonamide (3ia)

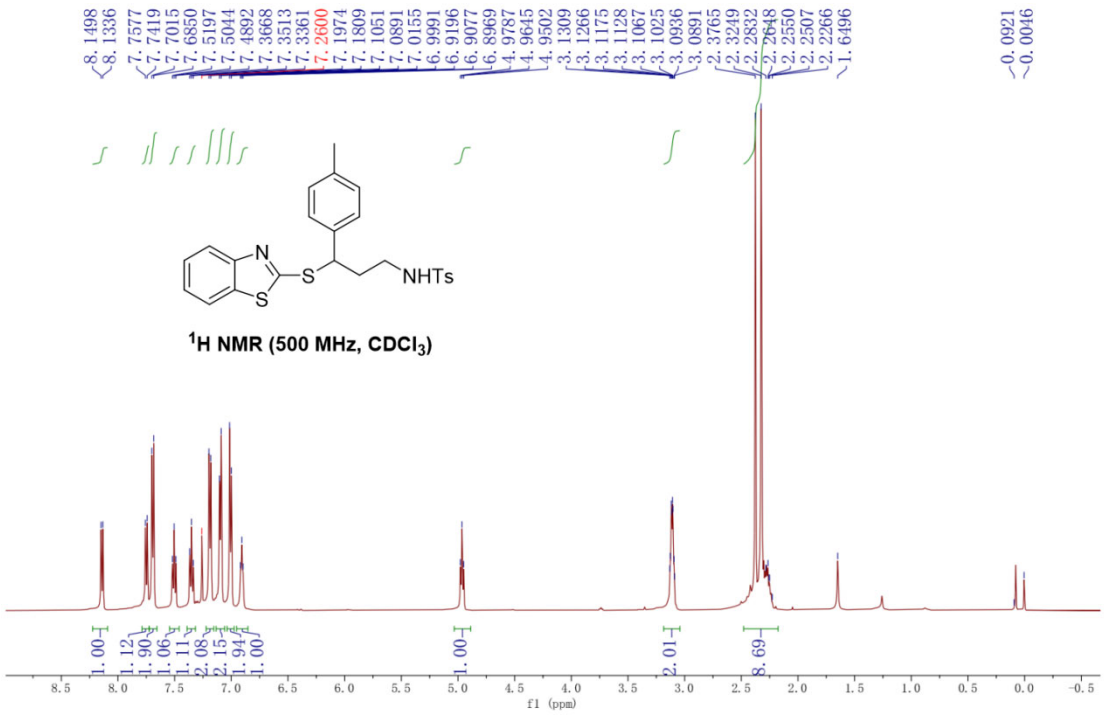


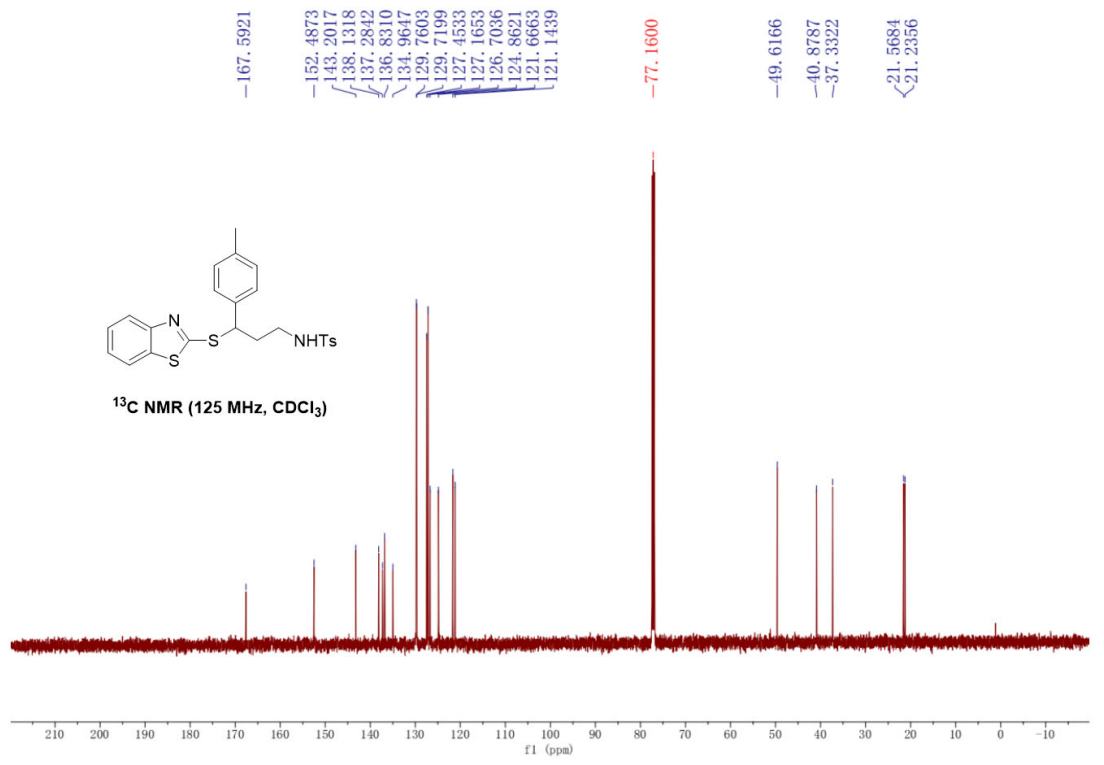
Compound **3ia**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 44.3 mg, 95% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 8.1 Hz, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.19 (d, *J* = 8.2 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.2 Hz, 2H), 6.91 (d, *J* = 6.0 Hz, 1H), 4.96 (t, *J* = 7.1 Hz, 1H), 3.13-3.09 (m, 2H), 2.38 (s, 3H), 2.32(s, 3H), 2.28-2.22(m, 2H).

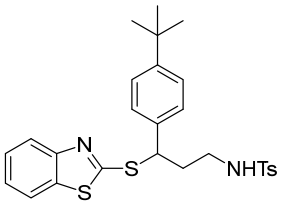
^{13}C NMR (125 MHz, Chloroform-*d*) δ 167.6, 152.5, 143.2, 138.1, 137.3, 136.8, 135.0, 129.8, 129.7, 127.5, 127.2, 126.7, 124.9, 121.7, 121.1, 49.6, 40.9, 37.3, 21.6, 21.2.

HRMS (ESI) m/z: calcd for $[C_{24}H_{24}N_2O_2S_3+H]^+$ requires: 469.1073, found: 469.1079.


8.1498
8.1336
7.7577
7.7419
7.7015
7.6850
7.5197
7.5044
7.4892
7.3668
7.3513
7.3361
7.2600
7.1974
7.1809
7.1051
7.0891
7.0155
6.9991
6.9196
6.9077
6.8969
4.9787
4.9645
4.9502
3.1309
3.1266
3.1175
3.1128
3.1067
3.1025
3.0936
3.0891
2.3765
2.3249
2.2832
2.2648
2.2550
2.2507
2.2266
1.6496
0.0921
0.0046
N
S
S
NHTs
1H NMR (500 MHz, CDCl3)
1.00
1.12
1.90
1.06
1.11
2.08
2.15
1.94
1.00
1.00
2.01
8.69
f1 (ppm)


167.5921
152.4873
143.2017
138.1318
137.2842
136.8310
134.9647
129.7603
129.7199
127.4533
127.1653
126.7036
124.8621
121.6663
121.1439
77.1600
49.6166
40.8787
37.3322
21.5684
21.2356
N
S
S
NHTs
13C NMR (125 MHz, CDCl3)
f1 (ppm)

N-(3-(benzo[d]thiazol-2-ylthio)-3-(4-(tert-butyl)phenyl)propyl)-4-methylbenzenesulfonamide (3ja)

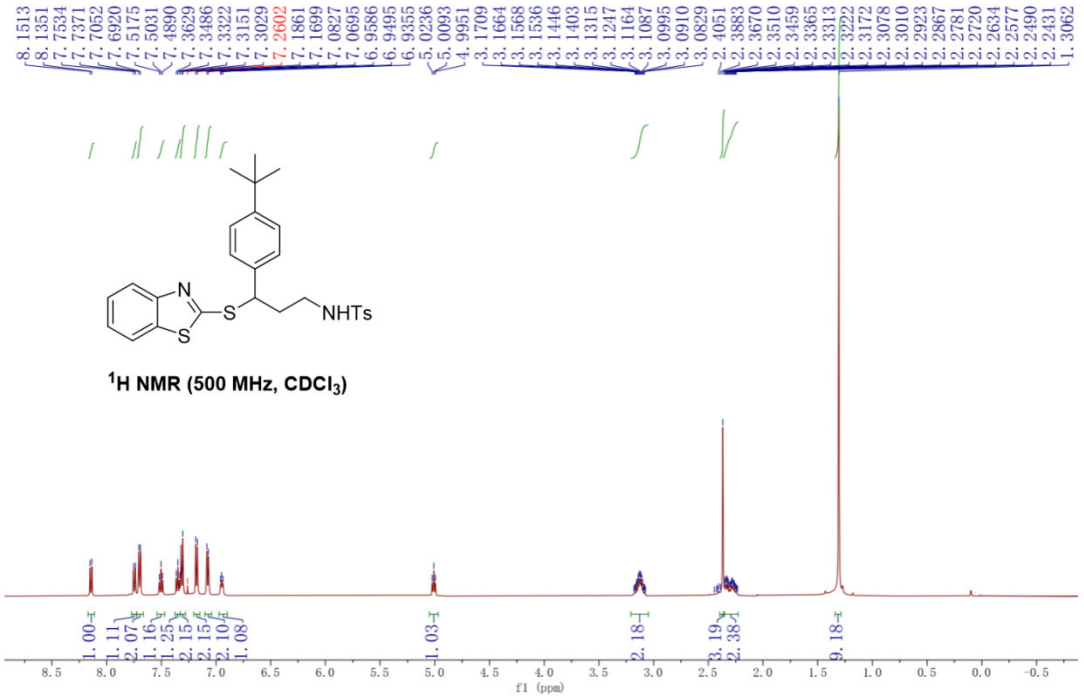


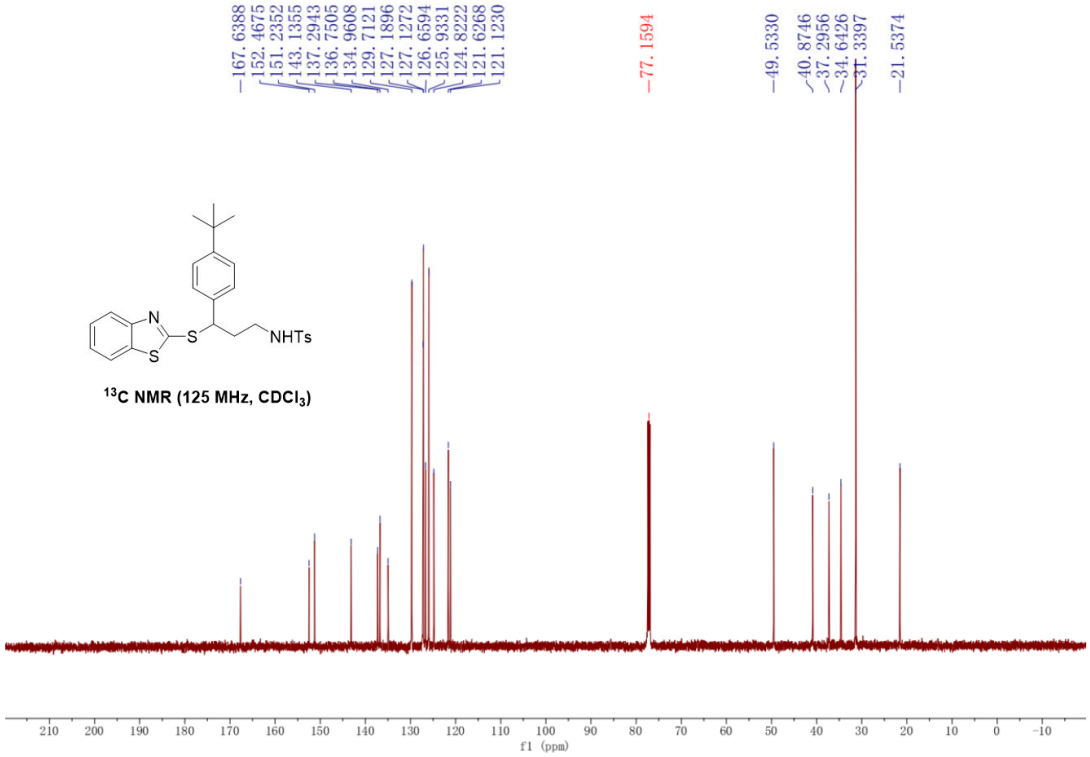
Compound **3ja**: a colorless oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 49.7 mg, 97% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 8.1 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.70 (d, *J* = 6.6 Hz, 2H), 7.50 (t, *J* = 7.1 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.30 (d, *J* = 8.2 Hz，2H), 7.18 (d, *J* = 8.1 Hz, 2H), 7.08 (d, *J* = 6.6 Hz, 2H), 6.95 (t, *J* = 4.6 Hz，1H), 5.01 (t, *J* = 7.1 Hz, 1H), 3.18-3.07 (m, 2H), 2.37 (s, 3H), 2.35-2.23 (m, 2H), 1.31 (s, 9H).

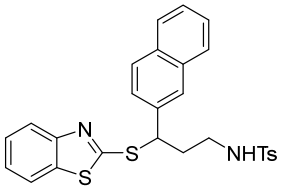
^{13}C NMR (125 MHz, Chloroform-*d*) δ 167.6, 152.5, 151.2, 143.1, 137.3, 136.8, 135.0, 129.7, 127.2, 127.1, 126.7, 125.9, 124.8, 121.6, 121.1, 49.5, 40.9, 37.3, 34.6, 31.3, 21.5.

HRMS (ESI) m/z: calcd for $[C_{27}H_{30}N_2O_2S_3+H]^+$ requires: 511.1542, found: 511.1551.





N-(3-(benzo[d]thiazol-2-ylthio)-3-(naphthalen-2-yl)propyl)-4-methylbenzenesulfonamide (3ka)

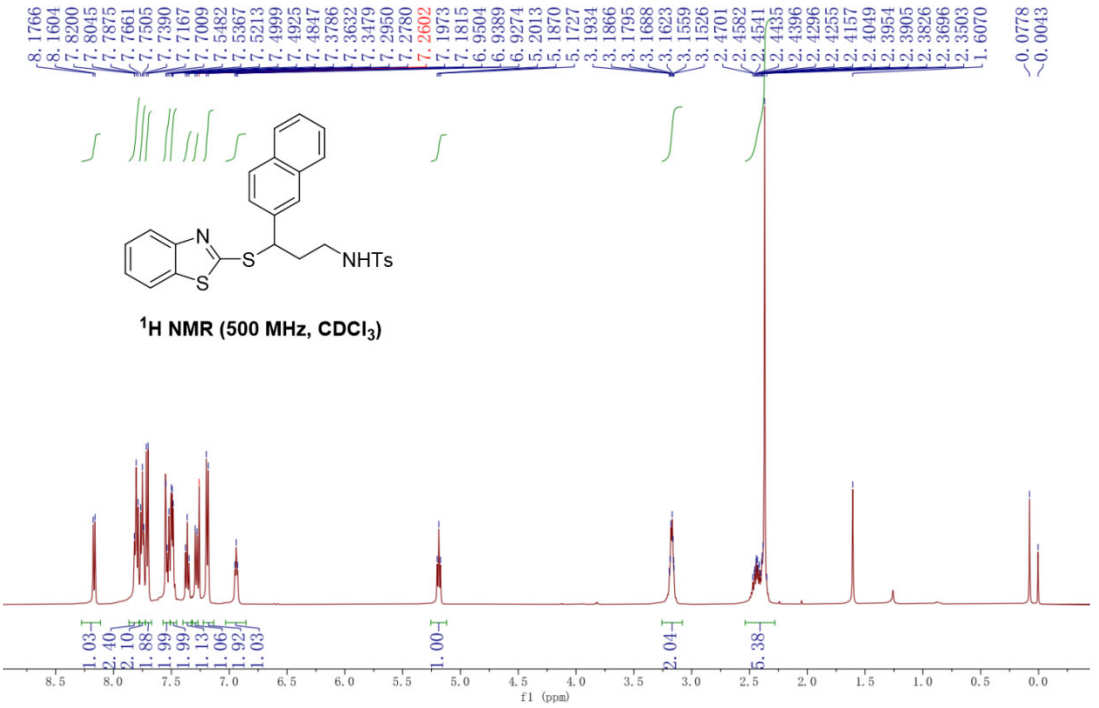


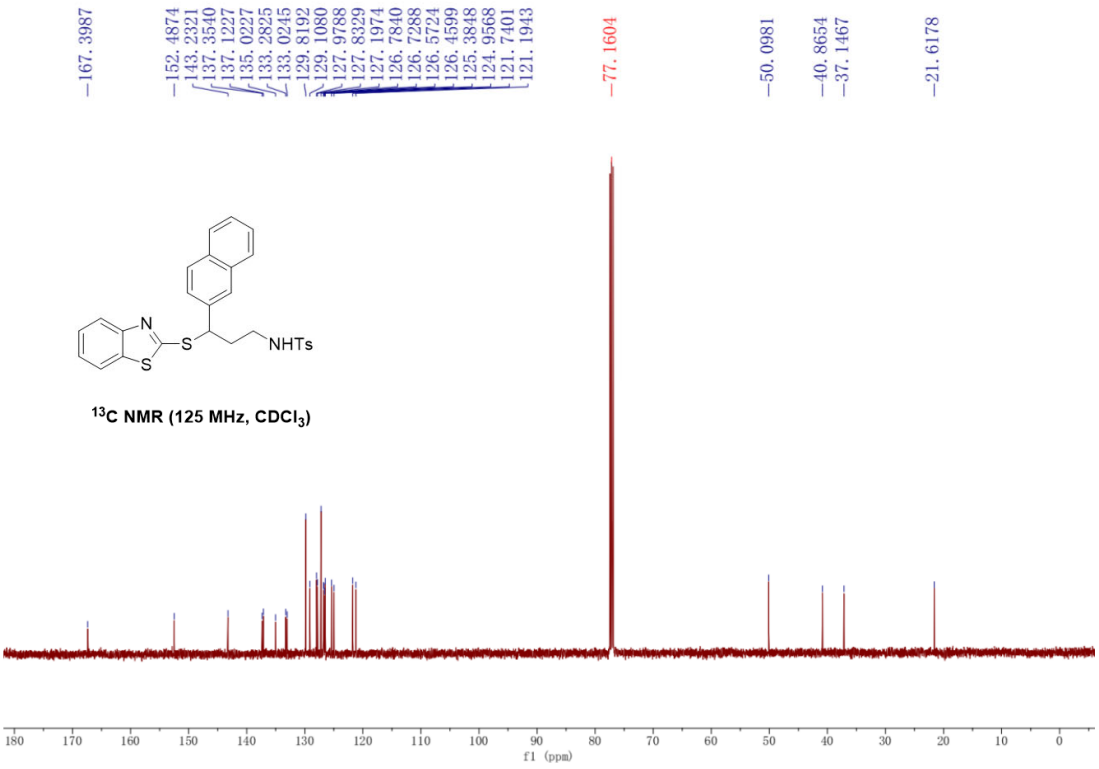
Compound **3ka**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 47.0 mg, 93% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.17 (d, *J* = 8.1 Hz, 1H), 7.80 (t, *J* = 8.1 Hz, 2H), 7.75 (t, *J* = 6.8 Hz, 2H), 7.71 (d, *J* = 7.9 Hz, 2H), 7.58–7.46 (m, 3H), 7.36 (t, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 8.5 Hz, 1H), 7.19 (d, *J* = 7.9 Hz, 2H), 6.94 (t, *J* = 5.8 Hz, 1H), 5.19 (t, *J* = 7.1 Hz, 1H), 3.2–3.14 (m, 2H), 2.52–2.40 (m, 2H), 2.37 (s, 3H).

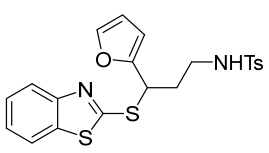
^{13}C NMR (125 MHz, Chloroform-*d*) δ 167.4, 152.5, 143.2, 137.4, 137.1, 135.0, 133.3, 133.0, 129.8, 129.1, 128.0, 127.8, 127.2, 126.8, 126.7, 126.6, 126.5, 125.4, 125.0, 121.7, 121.2, 50.1, 40.9, 37.1, 21.6.

HRMS (ESI) m/z: calcd for $[C_{27}H_{24}N_2O_2S_3+H]^+$ requires: 505.1073, found: 505.1078.





N-(3-(benzo[d]thiazol-2-ylthio)-3-(furan-2-yl)propyl)-4-methylbenzenesulfonamide (3la)



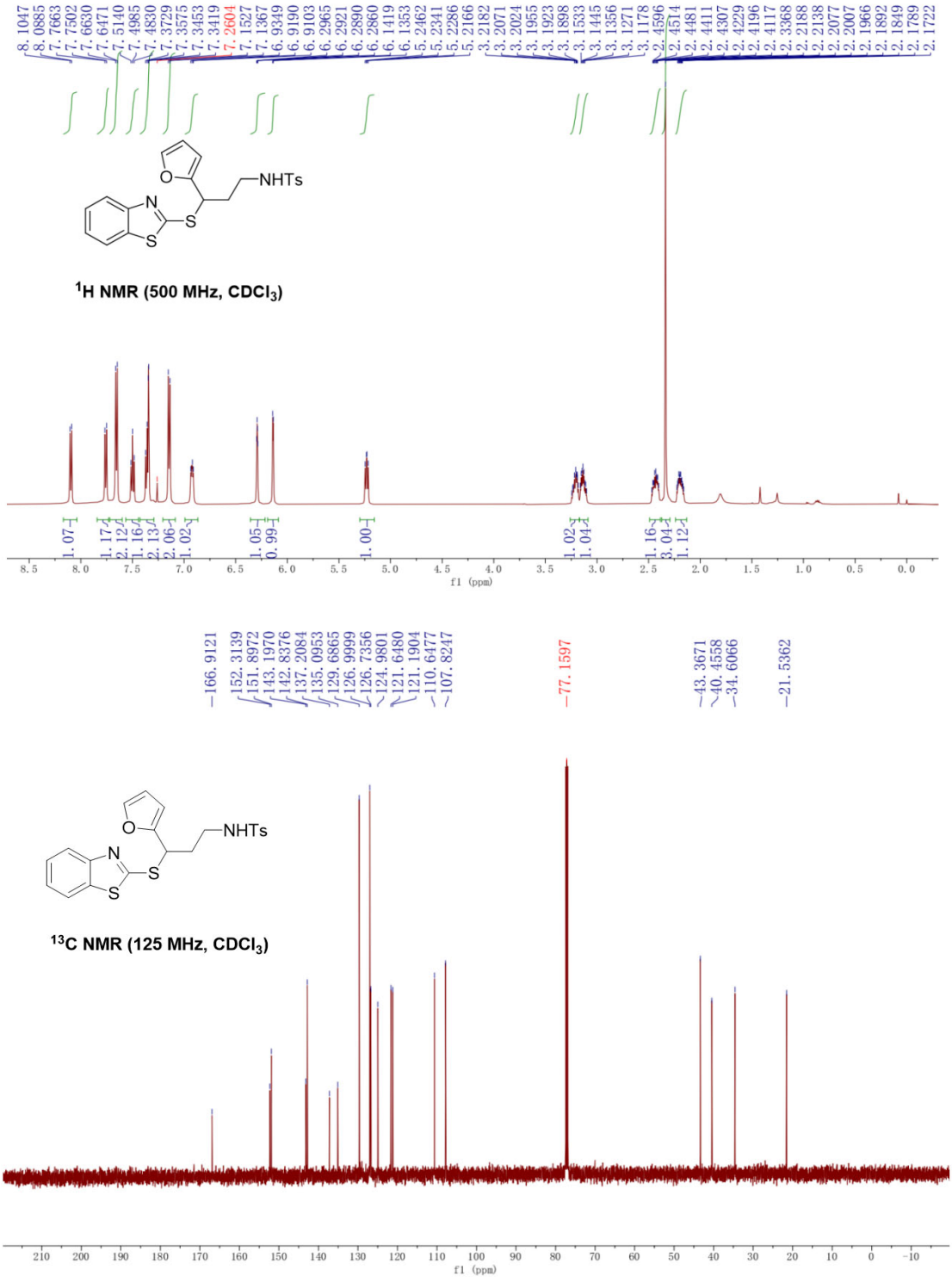
Compound **3la**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1,

29.7 mg, 67% yield.

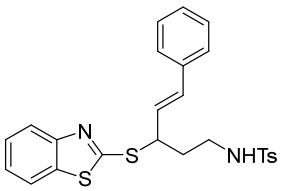
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.1 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.50 (t, *J* = 7.7 Hz, 1H), 7.39–7.28 (m, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.92 (t, *J* = 4.5 Hz, 1H), 6.29 (dd, *J* = 3.4, 1.8 Hz, 1H), 6.14 (d, *J* = 3.3 Hz, 1H), 5.23 (t, *J* = 6.4 Hz,1H), 3.26–3.18 (m, 1H), 3.17–3.08 (m, 1H), 2.49–2.35 (m, 1H), 2.34 (s, 3H), 2.24–2.14 (m, 1H).

^{13}C NMR (125 MHz, Chloroform-*d*) δ 166.9, 152.3, 151.9, 143.2, 142.8, 137.2, 135.1, 129.7, 127.0, 126.7, 125.0, 121.6, 121.2, 110.6, 107.8, 43.4, 40.5, 34.6, 21.5.

HRMS (ESI) m/z: calcd for $[C_{21}H_{20}N_2O_3S_3+Na]^+$ requires: 467.0528, found: 467.0537.



(*E*)-N-(3-(benzo[d]thiazol-2-ylthio)-5-phenylpent-4-en-1-yl)-4-methylbenzenesulfonamide (3ma)

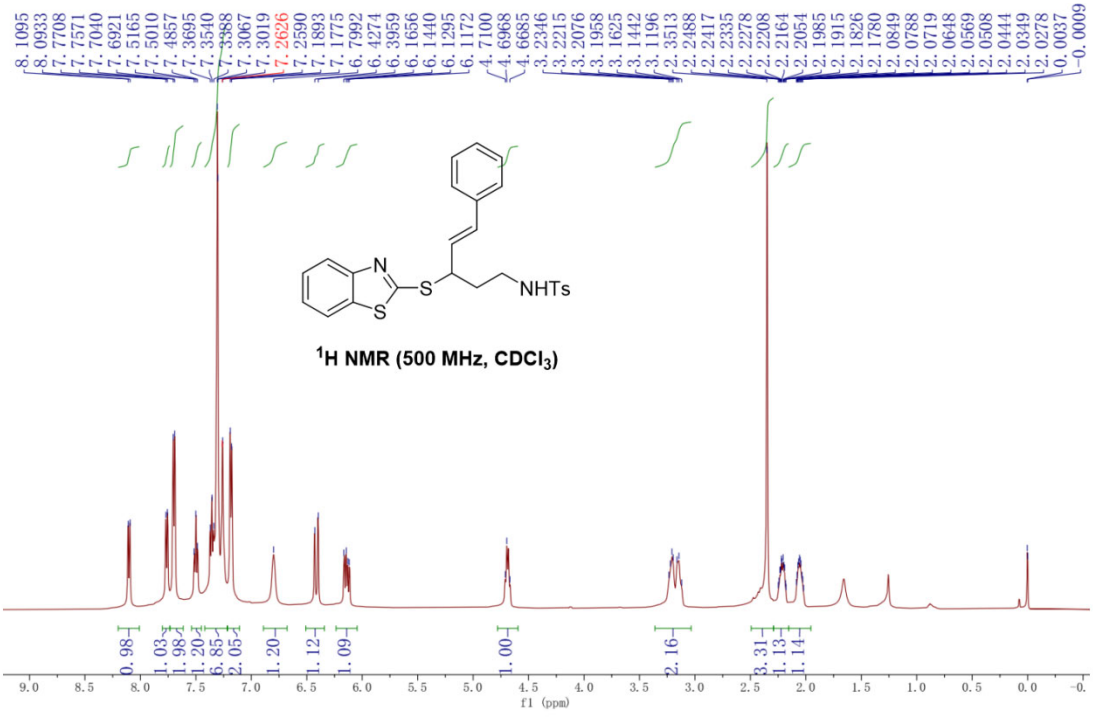


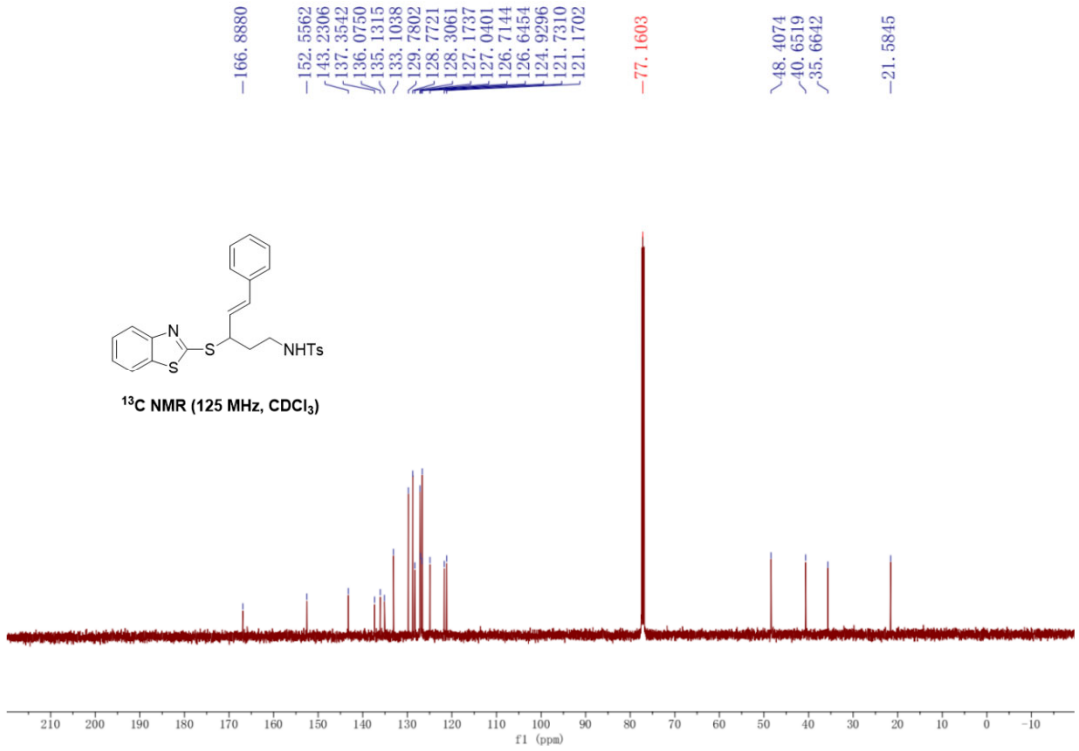
Compound **3ma**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 42.0 mg, 87% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.1 Hz, 1H), 7.76 (d, *J* = 6.9 Hz, 2H), 7.70 (d, *J* = 5.9 Hz, 2H), 7.50 (t, *J* = 7.7 Hz, 1H), 7.37–7.24 (m, 7H), 7.18 (d, *J* = 5.9 Hz, 2H), 6.80 (s, 1H), 6.41 (d, *J* = 15.8 Hz, 1H), 6.14 (dd, J = 18.1, 10.8 Hz, 1H), 4.73–4.65 (m, 1H), 3.27–3.09 (m, 2H), 2.35 (s, 3H), 2.25–2.18 (m, 1H), 2.12–1.98 (m, 1H).

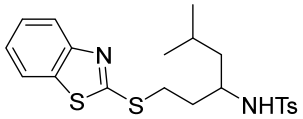
^{13}C NMR (125 MHz, Chloroform-*d*) δ 166.9, 152.6, 143.2, 137.4, 136.1, 135.1, 133.1, 129.8, 128.8, 128.3, 127.2, 127.0, 126.7, 126.6, 124.9, 121.7, 121.2, 48.4, 40.7, 35.7, 21.6.

HRMS (ESI) m/z: calcd for $[C_{25}H_{24}N_2O_2S_3+Na]^+$ requires: 503.0892, found: 503.0899.





N-(3-(benzo[d]thiazol-2-ylthio)-5-methylhexyl)-4-methylbenzenesulfonamide (3na)

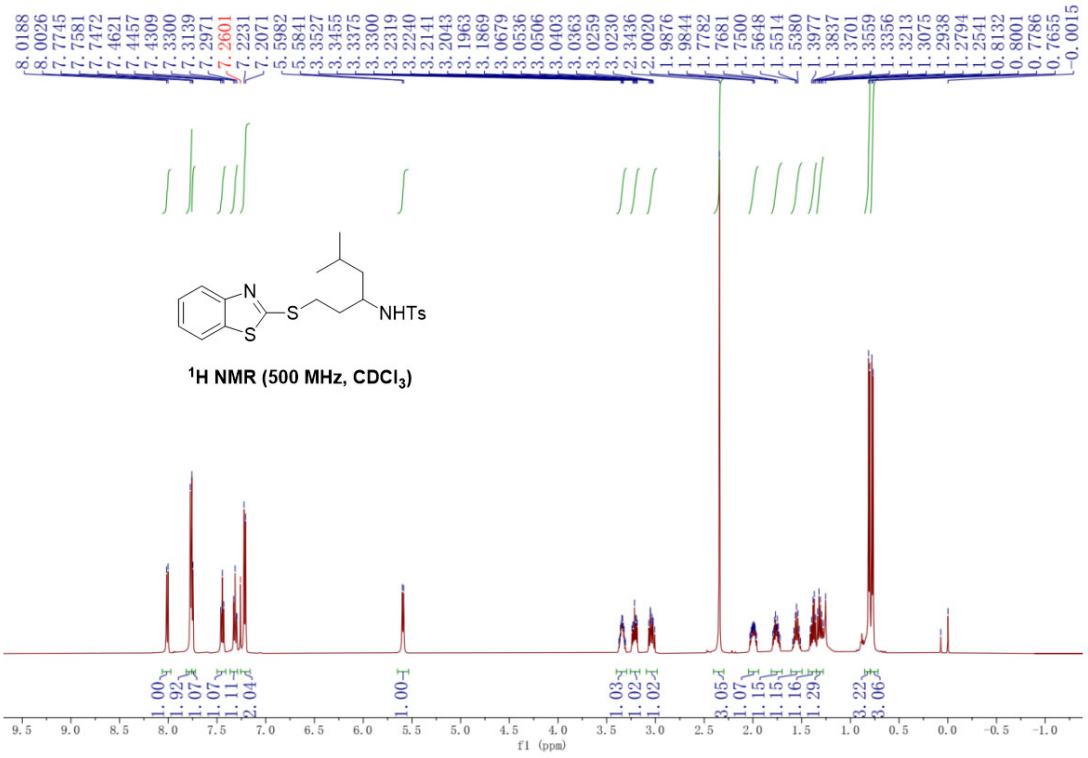


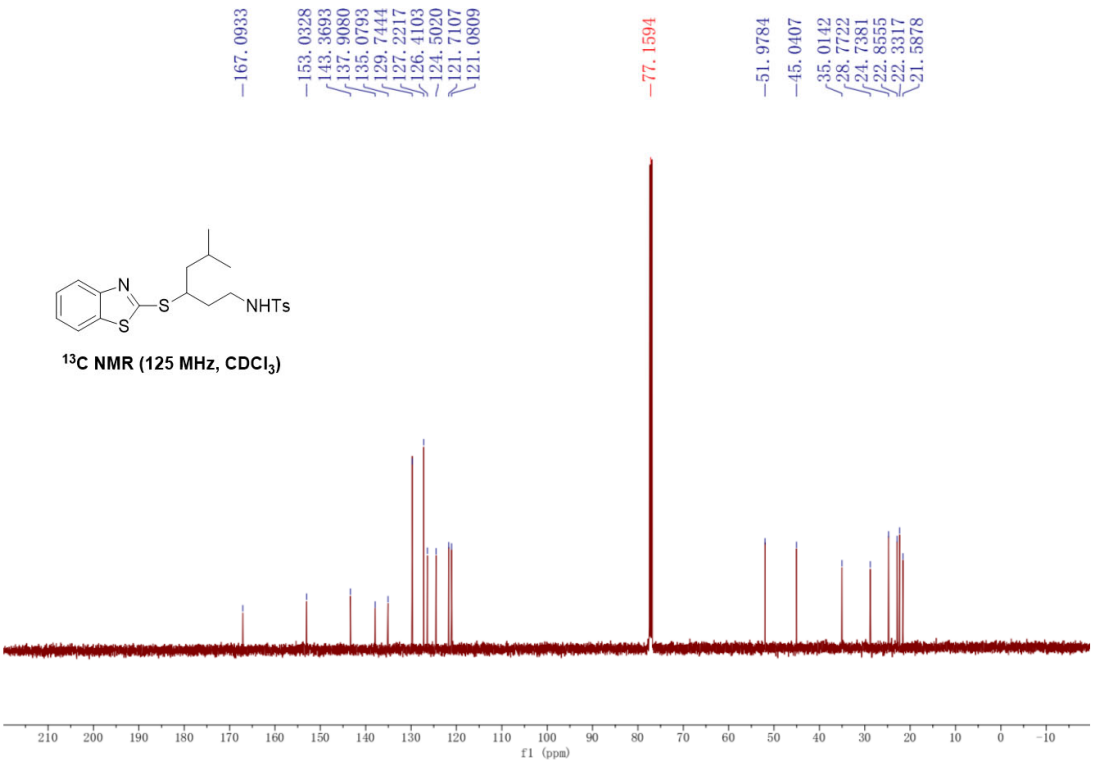
Compound **3na**: a yellow solid. M.p. = 115-116 °C. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 19.7 mg, 45% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.01 (d, *J* = 8.1 Hz, 1H), 7.77 (d, *J* = 8.2 Hz, 2H), 7.75 (d, *J* = 5.5 Hz 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.32 (t, *J* = 8 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 5.59 (d, *J* = 7.1 Hz, 1H), 3.39–3.29 (m, 1H), 3.26–3.17 (m, 1H), 3.09–2.99 (m, 1H), 2.34 (s, 3H), 2.00 (m, 1H), 1.76 (m, 1H), 1.55 (m, 1H), 1.38 (m, 1H), 1.31 (m, 1H), 0.81 (d, *J* = 6.6 Hz, 3H), 0.77 (d, *J* = 6.5 Hz, 3H).

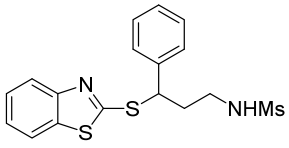
^{13}C NMR (125 MHz, Chloroform-*d*) δ 167.1, 153.0, 143.4, 137.9, 135.1, 129.7, 127.2, 126.4, 124.5, 121.7, 121.1, 52.0, 45.0, 35.0, 28.8, 24.7, 22.9, 22.3, 21.6.

HRMS (ESI) m/z: calcd for $[C_{21}H_{26}N_2O_2S_3+H]^+$ requires: 435.1229, found: 435.1237.





N-(3-(benzo[d]thiazol-2-ylthio)-3-phenylpropyl)methanesulfonamide (3oa)

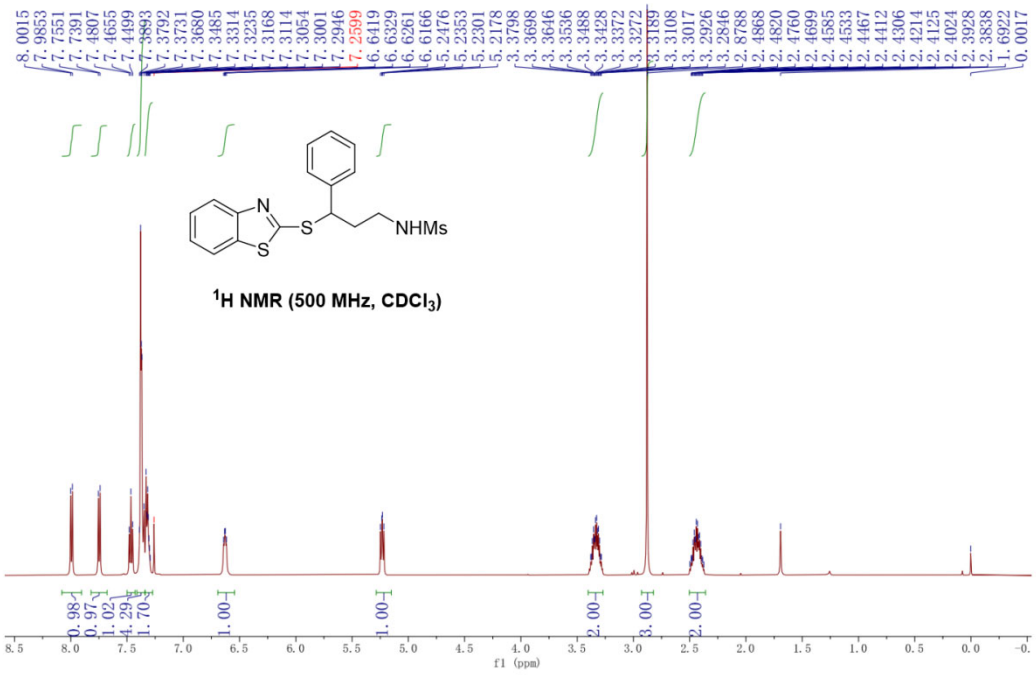


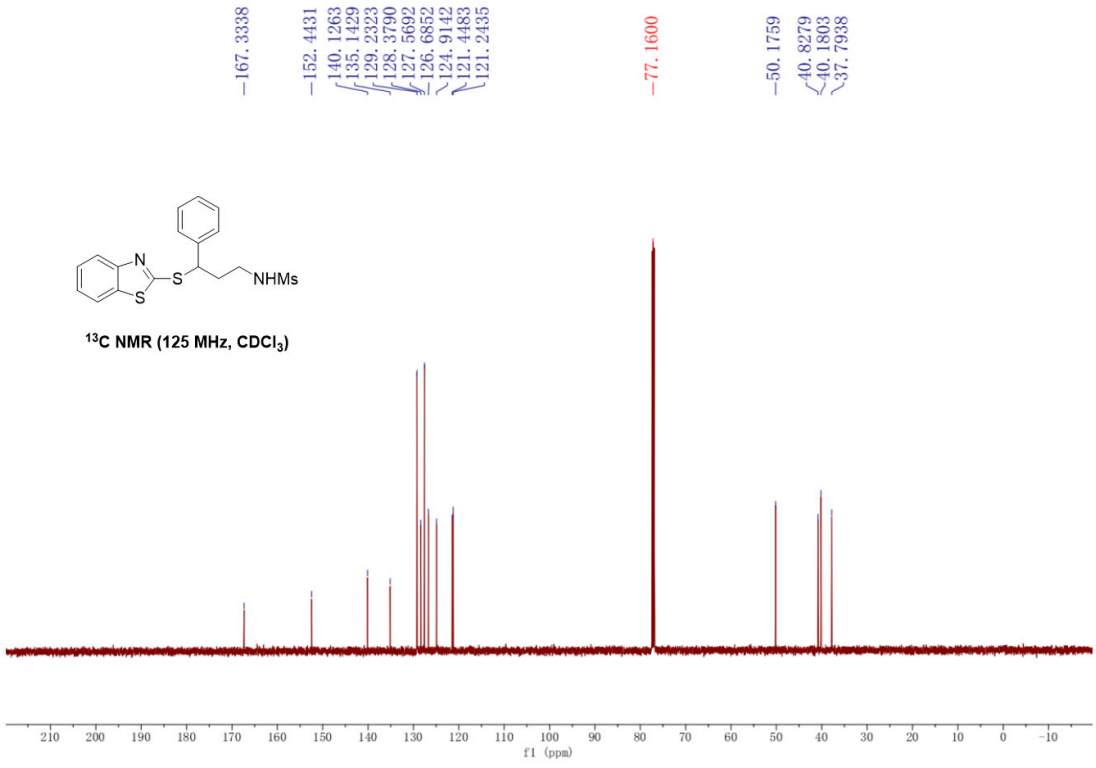
Compound **3oa**: a white solid. M.p. = 116-117 °C. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 34.2 mg, 90% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.99 (d, *J* = 8.1 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.41–7.29 (m, 3H), 6.63 (t, *J* = 7.6 Hz, 1H), 5.23 (dd, *J* = 8.8, 6.2 Hz, 1H), 3.39-3.28 (m, 2H), 2.88 (s, 3H), 2.50-2.37 (m, 2H).

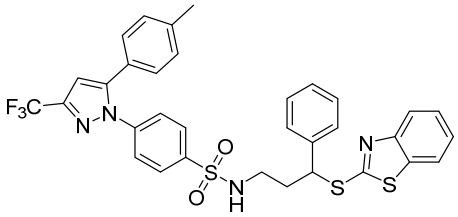
^{13}C NMR (125 MHz, Chloroform-*d*) δ 167.3, 152.4, 140.1, 135.1, 129.2, 128.4, 127.6, 126.7, 124.9, 121.4, 121.2, 50.2, 40.8, 40.2, 37.8.

HRMS (ESI) m/z: calcd for $[C_{17}H_{18}N_2O_2S_3+Na]^+$ requires: 401.0423, found: 401.0429.





N-(3-(benzo[d]thiazol-2-ylthio)-3-phenylpropyl)-4-(5-(p-tolyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide (3qa)



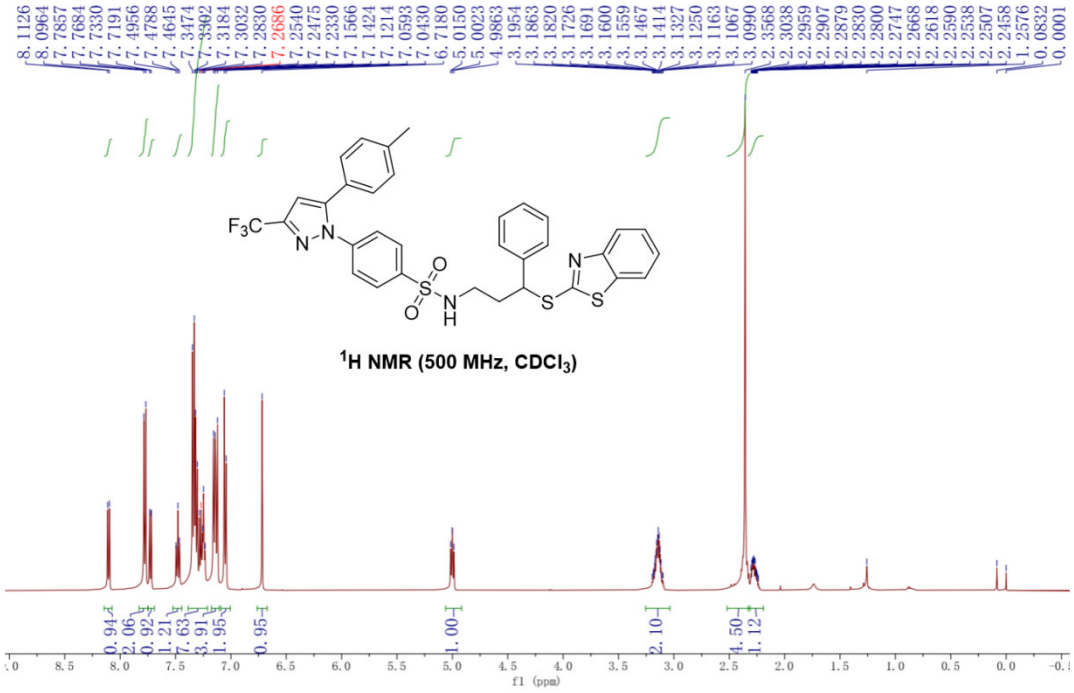
Compound **3qa**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 62.8 mg, 94% yield.

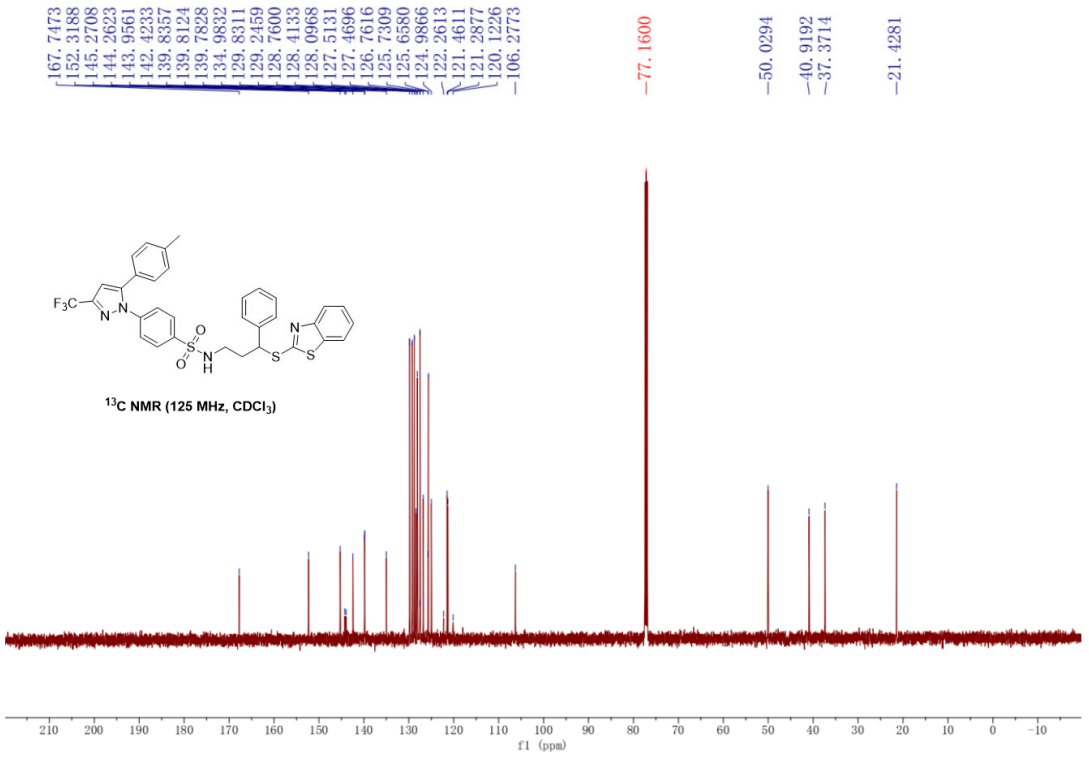
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.1 Hz, 1H), 7.78 (d, *J* = 8.7 Hz, 2H), 7.73 (d, *J* = 6.9 Hz, 1H), 7.47 (t, *J* = 8.4 Hz, 1H), 7.40–7.22 (m, 7H), 7.18–7.11 (m, 4H), 7.05 (d, *J* = 8.2 Hz, 2H), 6.72 (s, 1H), 5.00 (t, 1H), 3.21–3.07 (m, 2H), 2.36 (s, 3H), 2.30–2.22 (m, 1H).

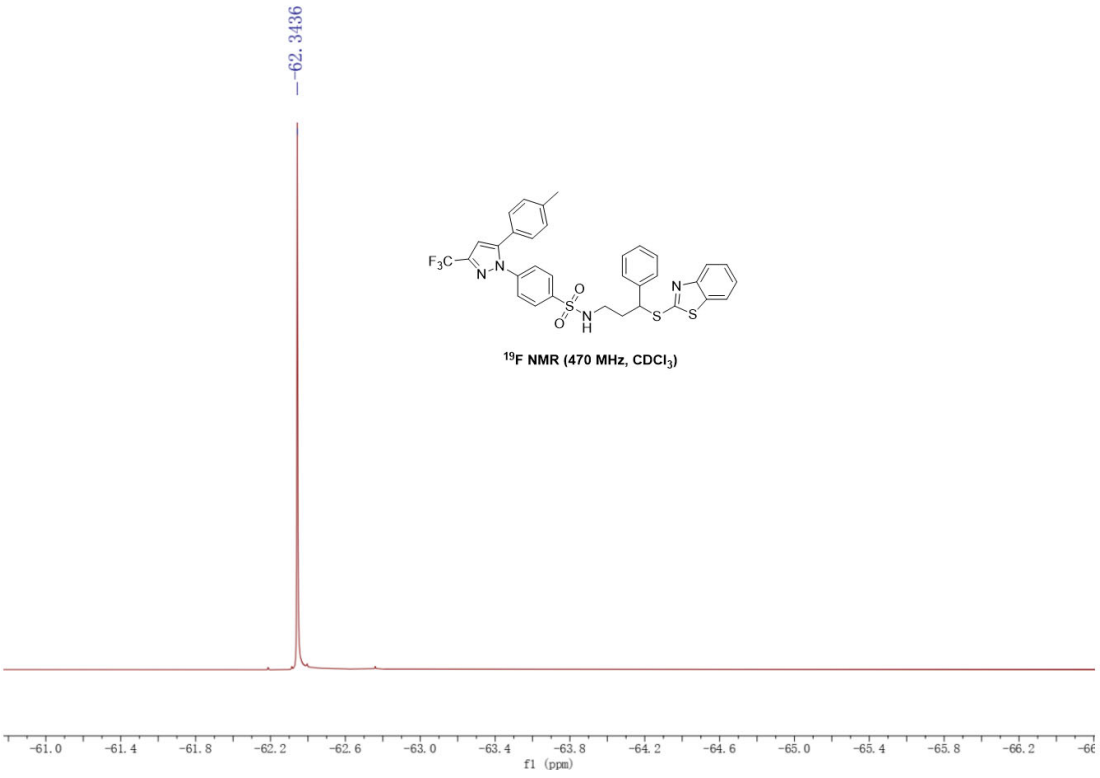
^{13}C NMR (125 MHz, Chloroform-*d*) δ 167.7, 152.3, 145.3, 144.1 (q, $^{2}J_{C\text{-}F}$ = 38.3 Hz), 142.4, 139.8 (q, $^{3}J_{C\text{-}F}$ = 2.9 Hz) 139.8, 135.0, 129.8, 129.2, 128.8, 128.4, 128.1, 127.5, 127.5, 126.8, 125.7, 125.7, 125.0, 121.5, 121.3, 121.2 (q, $^{1}J_{C\text{-}F}$ = 267.3 Hz), 106.3, 50.0, 40.9, 37.4, 21.4.

^{19}F NMR (470 MHz, Chloroform-*d*) δ (s) -62.3

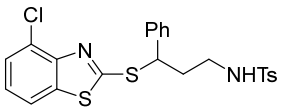
HRMS (ESI) m/z: calcd for $[C_{33}H_{27}F_3N_4O_2S_3+H]^+$ requires: 665.1321, found: 665.1331.




167.7473
152.3188
145.2708
144.2623
143.9561
142.4233
139.8357
139.8124
139.7828
134.9832
129.8311
129.2459
128.7600
128.4133
128.0968
127.5131
127.4696
126.7616
125.7309
125.6580
124.9866
122.2613
121.4611
121.2877
120.1226
106.2773
77.1600
50.0294
40.9192
37.3714
21.4281
F3C
N
O
S
N
H
O
N
S
S
13C NMR (125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


62.3436
F3C
N
O
S
N
H
O
N
S
S
19F NMR (470 MHz, CDCl3)
-61.0 -61.4 -61.8 -62.2 -62.6 -63.0 -63.4 -63.8 -64.2 -64.6 -65.0 -65.4 -65.8 -66.2
f1 (ppm)

N-(3-((4-chlorobenzo[d]thiazol-2-yl)thio)-3-phenylpropyl)-4-methylbenzenesulfonamide (3ab)

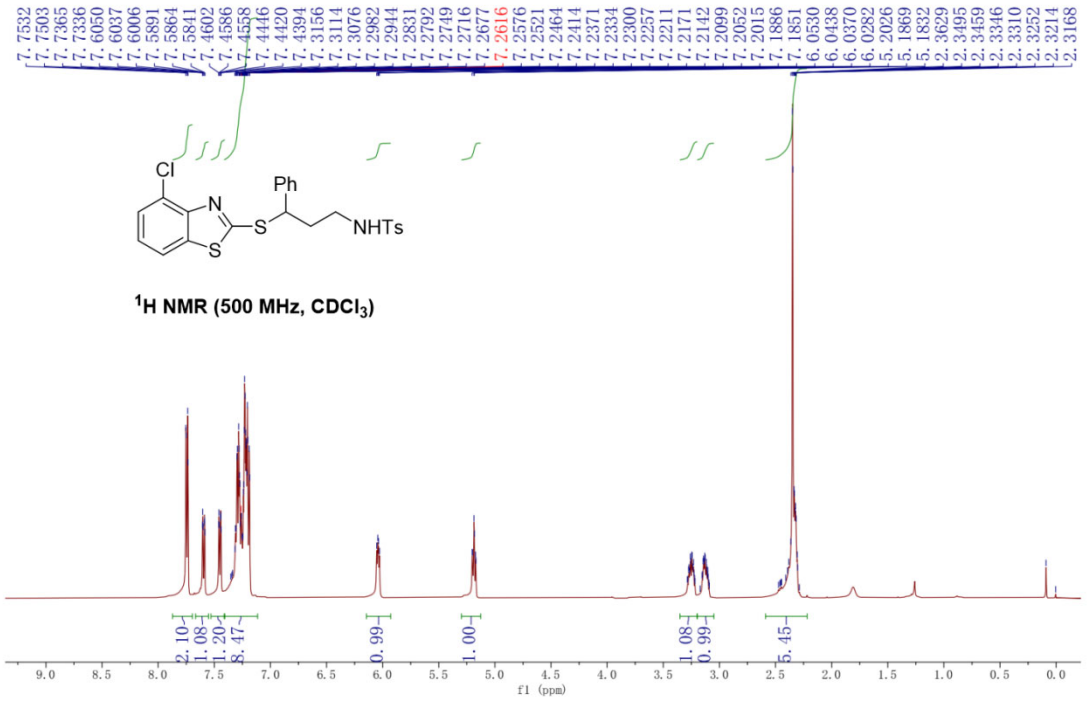


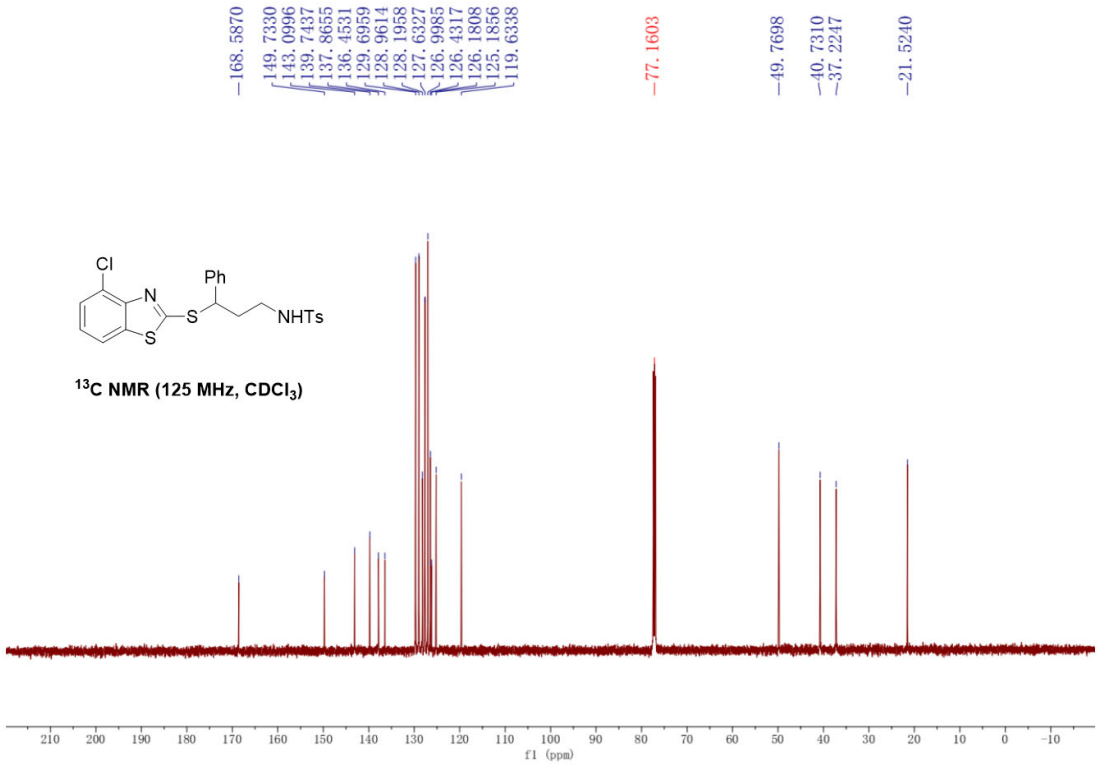
Compound **3ab**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 43.7 mg, 89% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 8.6 Hz, 1H), 7.45 (d, *J* = 6.8 Hz, 1H), 7.41–7.11 (m, 8H), 6.04 (dd, *J* = 7.9, 4.5 Hz, 1H), 5.19 (t, *J* = 6.5 Hz, 1H), 3.35–3.20 (m, 1H), 3.20–3.05 (m, 1H), 2.59–2.22 (m, 5H).

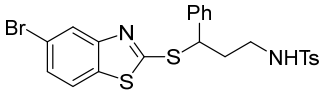
^{13}C NMR (125 MHz, Chloroform-*d*) δ 168.6, 149.7, 143.1, 139.7, 137.9, 136.5, 129.7, 129.0, 128.2, 127.6, 127.0, 126.4, 126.2, 125.2, 119.6, 49.8, 40.7, 37.2, 21.5.

HRMS (ESI) m/z: calcd for $[C_{23}H_{21}ClN_2O_2S_3+H]^+$ requires: 489.0526, found: 489.0520.





N-(3-((5-bromobenzo[d]thiazol-2-yl)thio)-3-phenylpropyl)-4-methylbenzenesulfonamide (3ac)

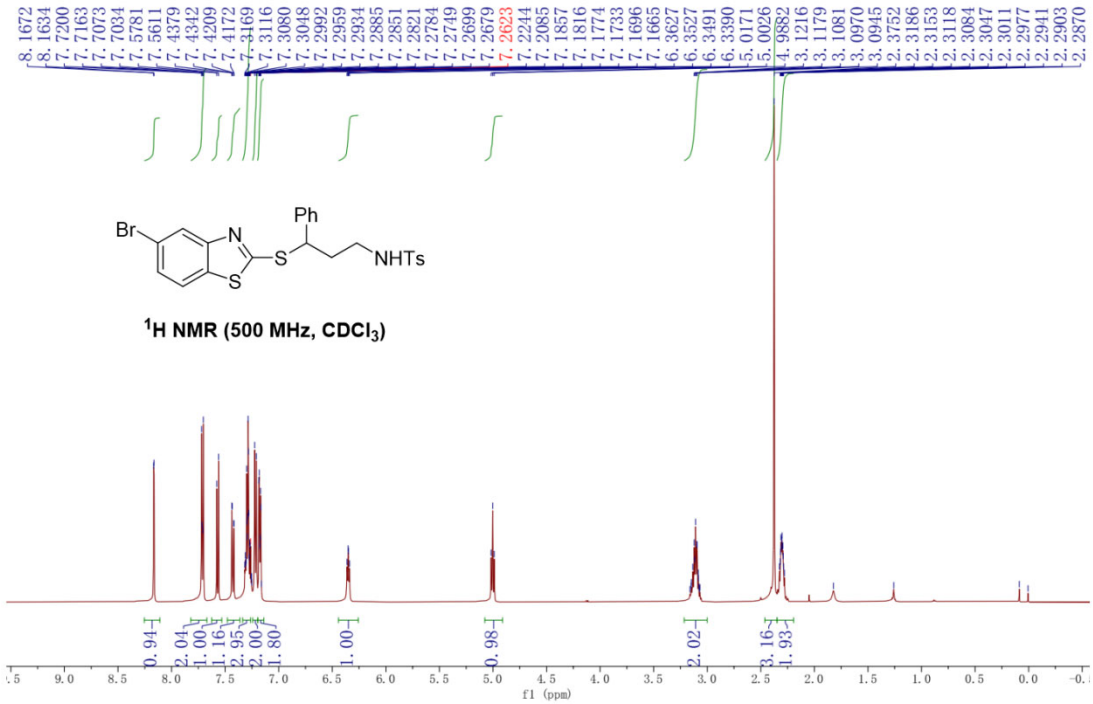


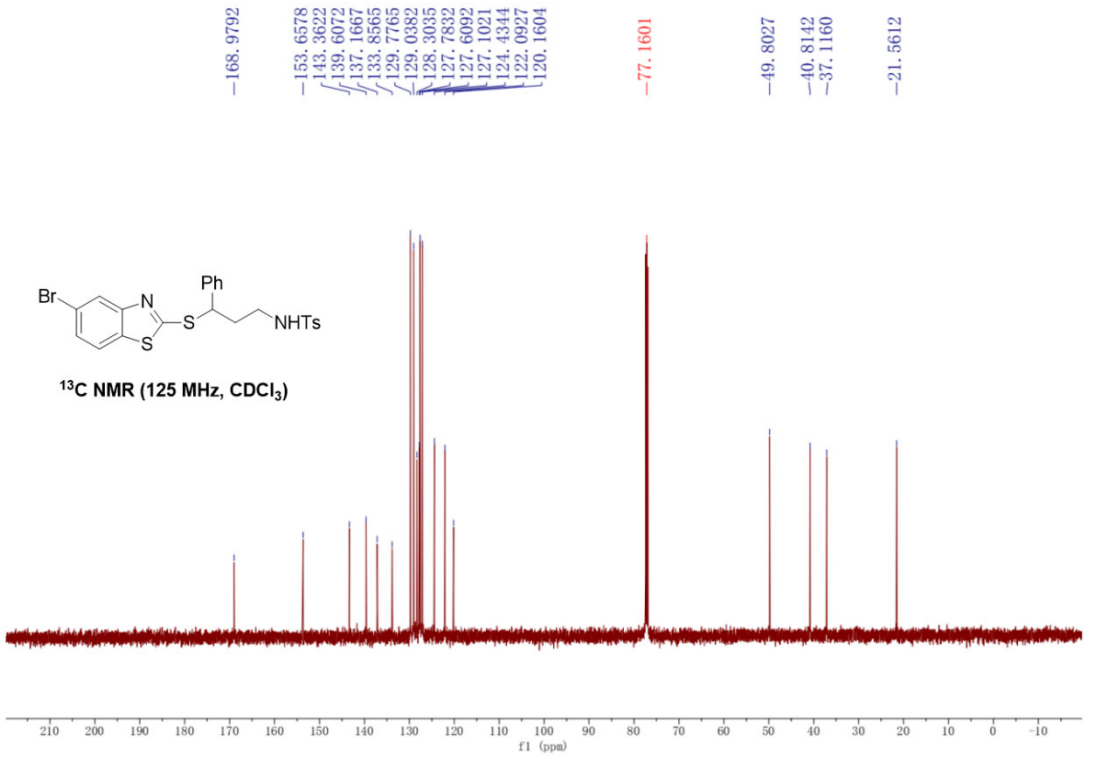
Compound **3ac**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 45.4 mg, 85% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.17 (d, *J* = 1.9 Hz, 1H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.57 (d, *J* = 8.5 Hz, 1H), 7.43 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.34–7.24 (m, 3H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.19–7.14 (m, 2H), 6.35 (dd, *J* = 6.8, 5.0 Hz, 1H), 5.00 (t, *J* = 7.2 Hz, 1H), 3.15–3.05 (m, 2H), 2.38 (s, 3H), 2.36–2.23 (m, 2H).

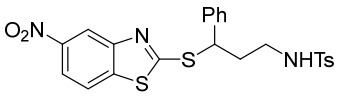
^{13}C NMR (125 MHz, Chloroform-*d*) δ 169.0, 153.7, 143.4, 139.6, 137.2, 133.9, 129.8, 129.0, 128.3, 127.8, 127.6, 127.1, 124.4, 122.1, 120.2, 49.8, 40.8, 37.1, 21.6.

HRMS (ESI) m/z: calcd for $[C_{23}H_{21}BrN_2O_2S_3+H]^+$ requires: 533.0021, found: 533.0029.





4-methyl-N-(3-((5-nitrobenzo[d]thiazol-2-yl)thio)-3-phenylpropyl)benzenesulfonamide (3ad)

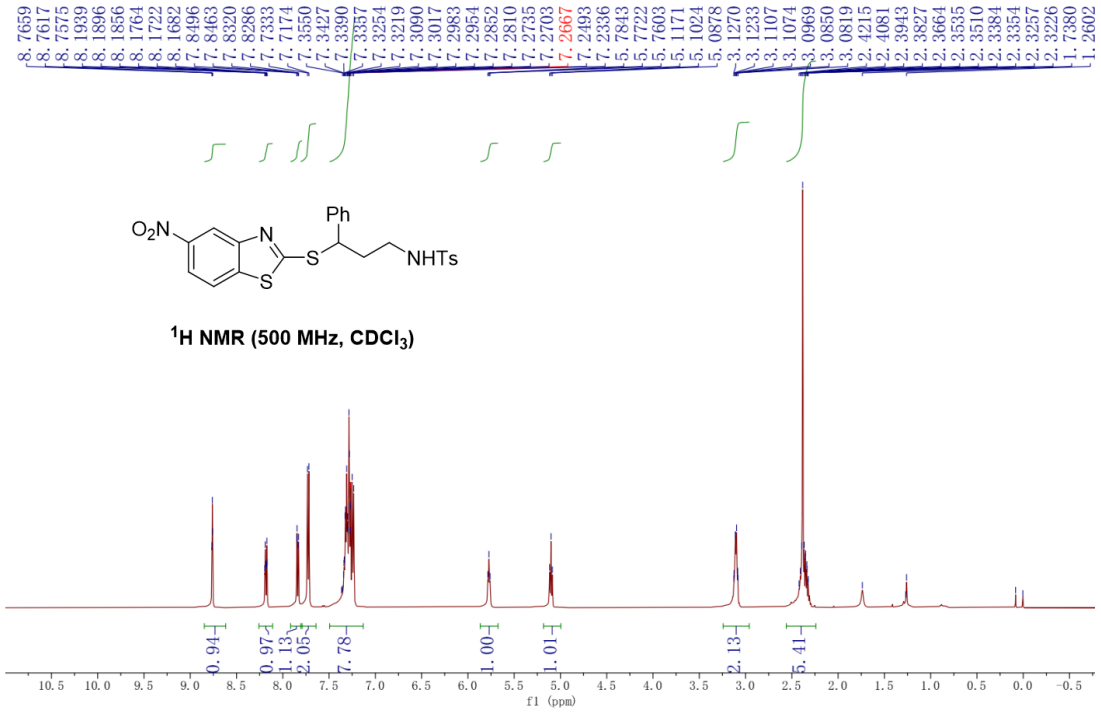


Compound **3ad**: a yellow solid. M.p. = 133-134 °C. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 32.1 mg, 65% yield.

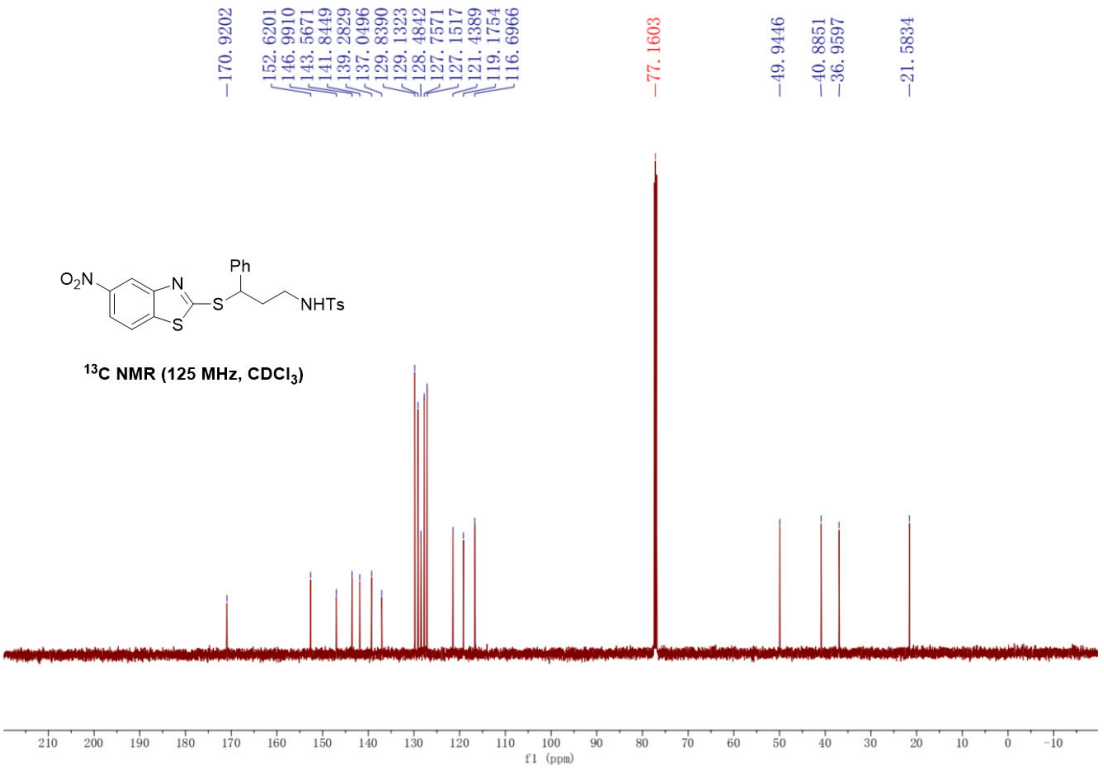
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.76 (s, 1H), 8.18 (d, *J* = 8.7 Hz, 1H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.73 (d, *J* = 7.9 Hz, 2H), 7.49–7.13 (m, 7H), 5.77 (t, *J* = 6.0 Hz, 1H), 5.10 (t, *J* = 7.3 Hz, 1H), 3.24–2.96 (m, 2H), 2.38 (s, 3H), 2.37–2.29 (m, 2H).

^{13}C NMR (125 MHz, Chloroform-*d*) δ 170.9, 152.6, 147.0, 143.6, 141.8, 139.3, 137.0, 129.8, 129.1, 128.5, 127.8, 127.2, 121.4, 119.2, 116.7, 49.9, 40.9, 37.0, 21.6.

HRMS (ESI) m/z: calcd for $[C_{23}H_{21}N_3O_4S_3+H]^+$ requires: 500.0767, found: 500.0768.

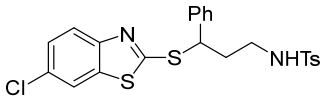


^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (125 MHz, $CDCl_3$)

N-(3-((6-chlorobenzo[d]thiazol-2-yl)thio)-3-phenylpropyl)-4-methylbenzenesulfonamide (3ae)

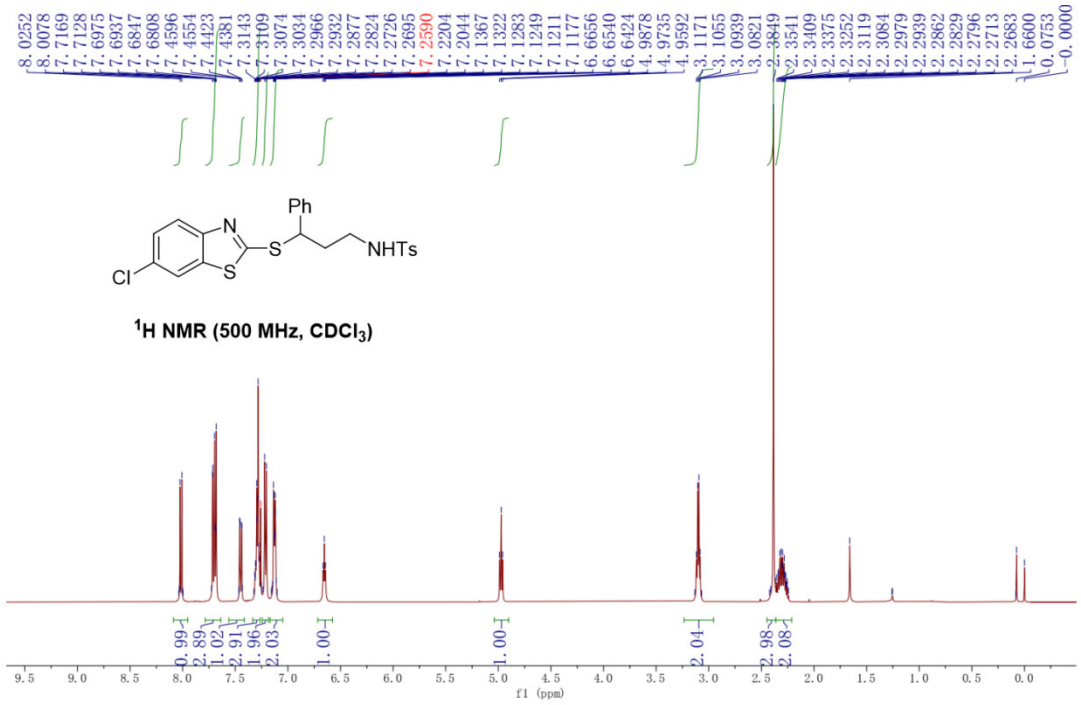


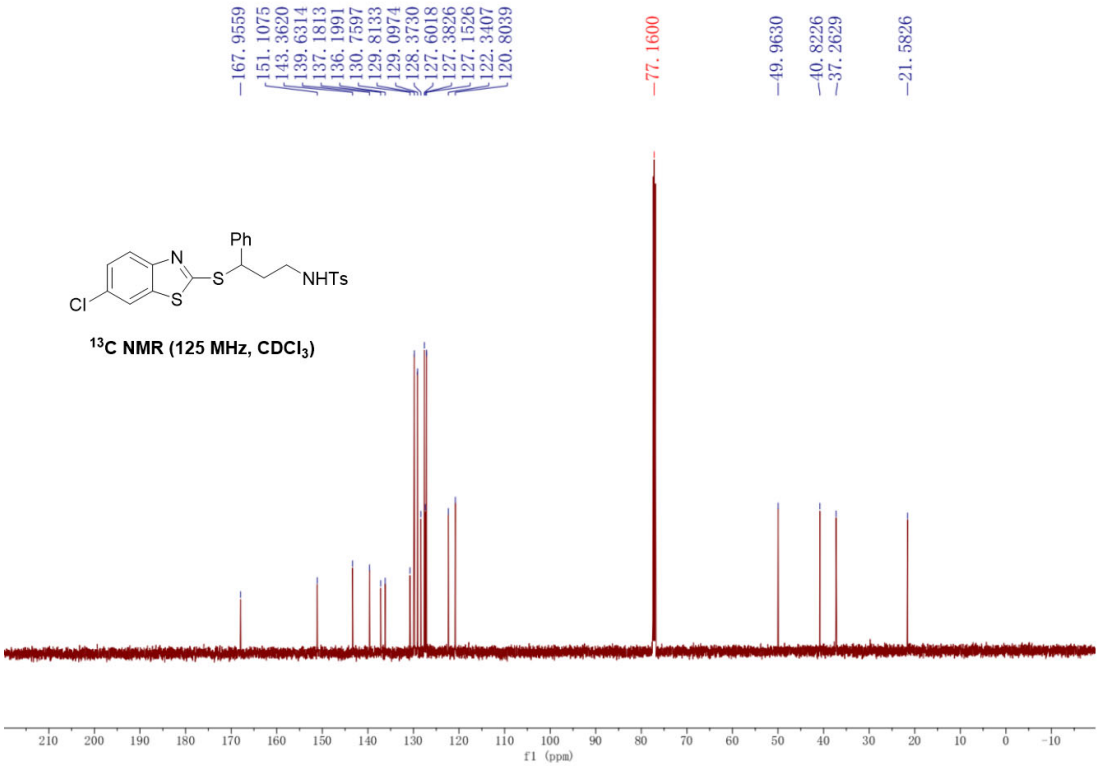
Compound **3ae**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 39.1 mg, 80% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.02 (d, *J* = 8.7 Hz, 1H), 7.71 (d, *J* = 2.1 Hz, 1H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.45 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.33–7.26 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.13 (dd, *J* = 7.5, 2.0 Hz, 2H), 6.65 (t, *J* = 5.8 Hz, 1H), 4.97 (t, *J* = 7.1 Hz, 1H), 3.10 (q, *J* = 5.8 Hz, 2H), 2.38 (s, 3H), 2.36–2.22 (m, 2H).

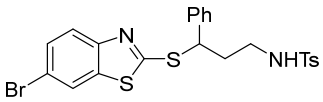
^{13}C NMR (125 MHz, Chloroform-*d*) δ 168.0, 151.1, 143.4, 139.6, 137.2, 136.2, 130.8, 129.8, 129.1, 128.4, 127.6, 127.4, 127.2, 122.3, 120.8, 50.0, 40.8, 37.3, 21.6.

HRMS (ESI) m/z: calcd for $[C_{23}H_{21}ClN_2O_2S_3+H]^+$ requires: 489.0526, found: 489.0523.





N-(3-((6-bromobenzo[d]thiazol-2-yl)thio)-3-phenylpropyl)-4-methylbenzenesulfonamide (3af)

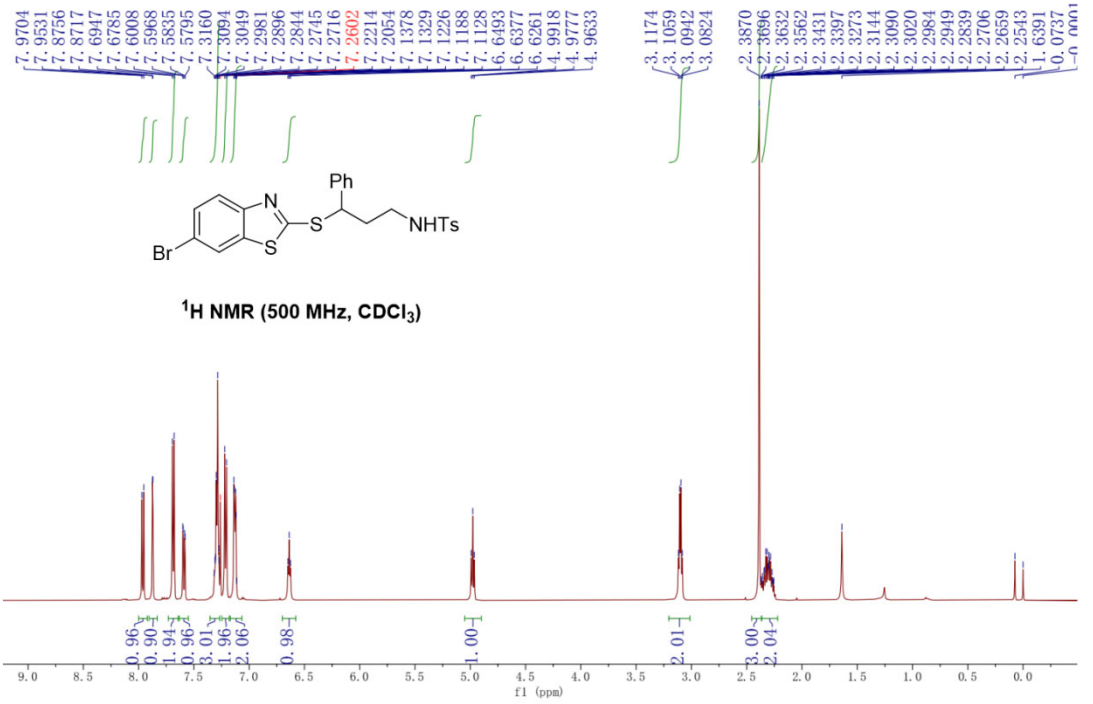


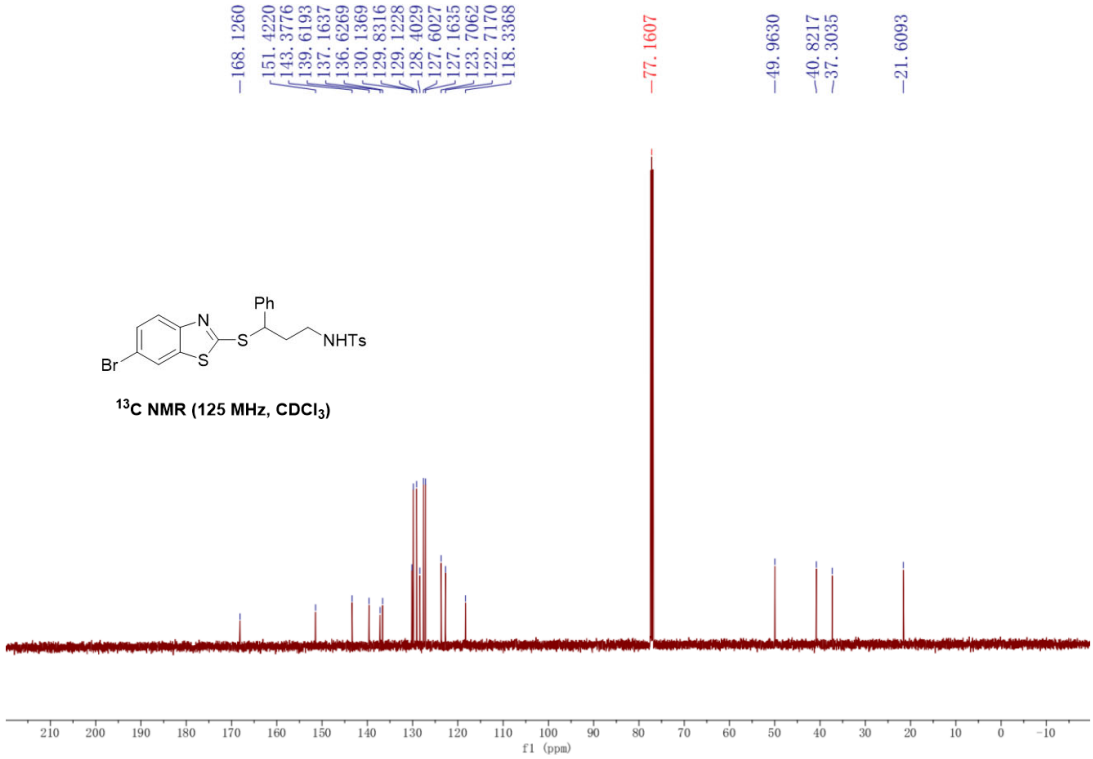
Compound **3af**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 40.4 mg, 75% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 8.7 Hz, 1H), 7.87 (d, *J* = 1.9 Hz, 1H), 7.69 (d, *J* = 8.1 Hz, 2H), 7.59 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.35–7.27 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.13 (dd, *J* = 7.3, 2.2 Hz, 2H), 6.64 (t, *J* = 5.8 Hz, 1H), 4.98 (t, *J* = 7.1 Hz, 1H), 3.10 (q, *J* = 5.8 Hz, 2H), 2.39 (s, 3H), 2.36–2.22 (m, 2H).

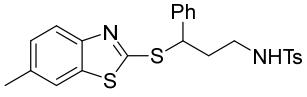
^{13}C NMR (125 MHz, Chloroform-*d*) δ 168.1, 151.4, 143.4, 139.6, 137.2, 136.6, 130.1, 129.8, 129.1, 128.4, 127.6, 127.2, 123.7, 122.7, 118.3, 50.0, 40.8, 37.3, 21.6.

HRMS (ESI) m/z: calcd for $[C_{23}H_{21}BrN_2O_2S_3+H]^+$ requires: 533.0021, found: 533.0021.





4-methyl-N-(3-((6-methylbenzo[d]thiazol-2-yl)thio)-3-phenylpropyl)benzenesulfonamide (3ag)



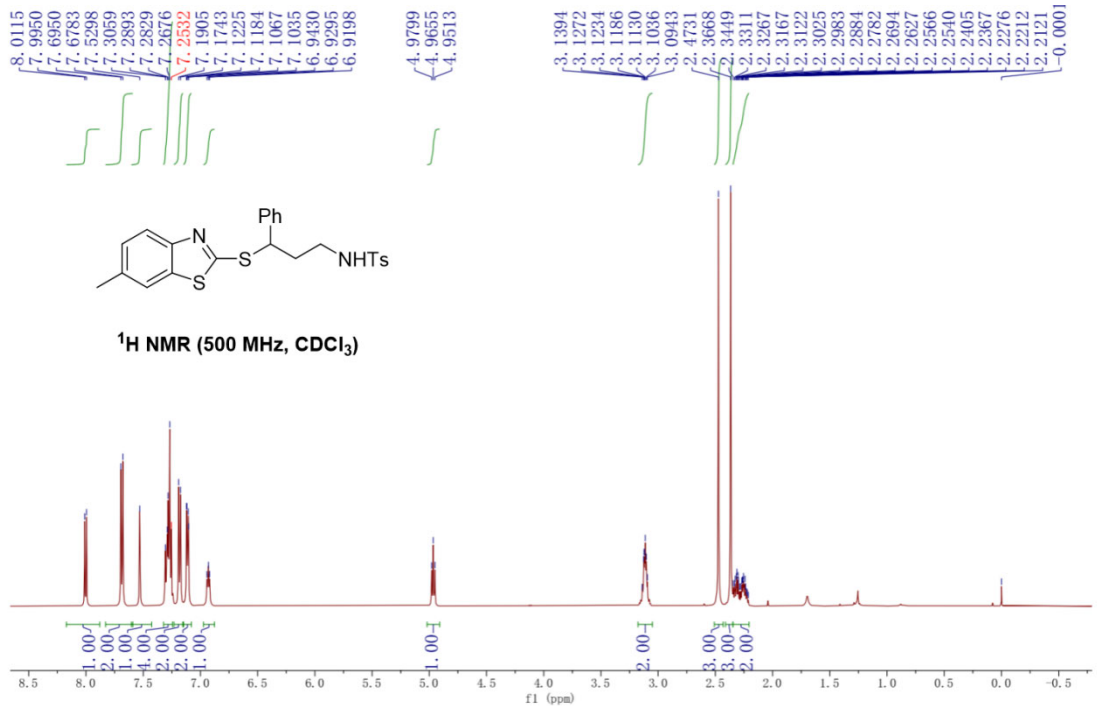
Compound **3ag**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1,

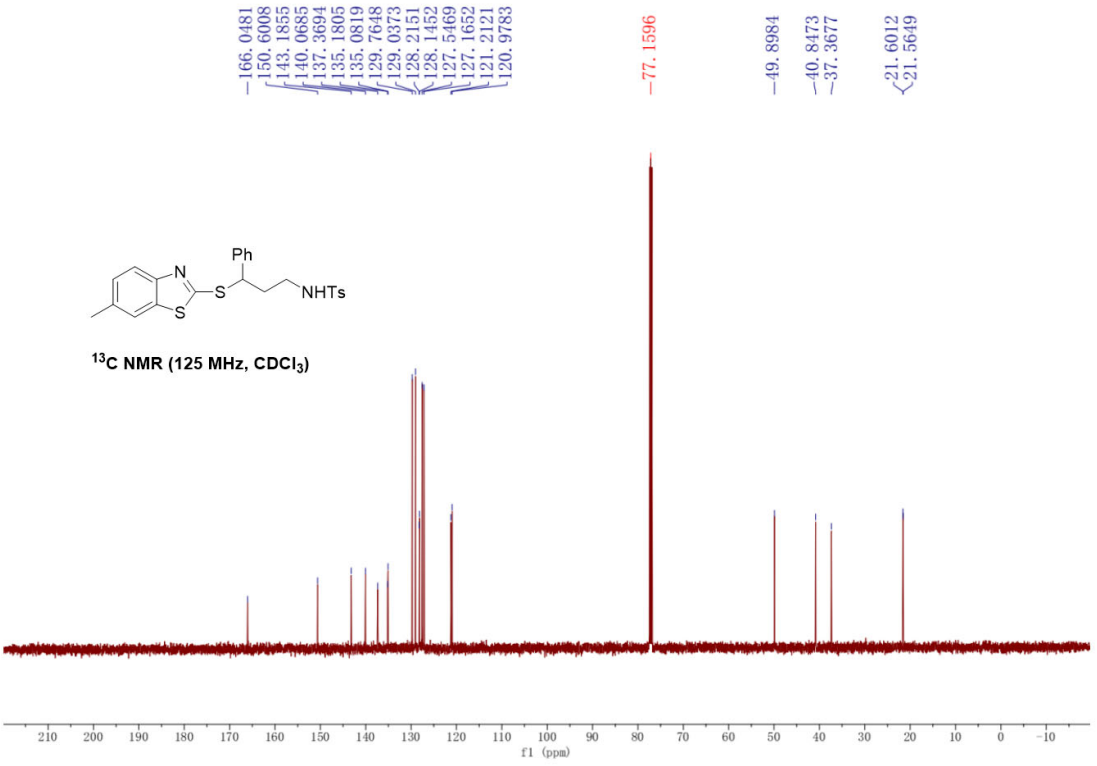
42.0 mg, 90% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.00 (d, *J* = 8.2 Hz, 1H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.53 (s, 1H), 7.34–7.22 (m, 4H), 7.18 (d, *J* = 8.1 Hz, 2H), 7.11 (dd, *J* = 7.7, 1.8 Hz, 2H), 6.93 (t, *J* = 5.0 Hz, 1H), 4.97 (t, *J* = 7.2 Hz, 1H), 3.18–3.05 (m, 1H), 2.47 (s, 3H), 2.37 (s, 3H), 2.35–2.20 (m, 2H).

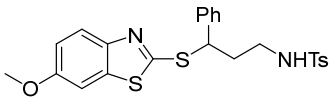
^{13}C NMR (125 MHz, Chloroform-*d*) δ 166.7, 152.3, 143.3, 142.0, 137.2, 134.9, 134.7, 130.3, 129.8, 128.4, 127.7, 127.0, 126.7, 125.7, 124.9, 121.7, 121.1, 49.1, 40.7, 37.0, 21.5.

HRMS (ESI) m/z: calcd for $[C_{24}H_{24}N_2O_2S_3+H]^+$ requires: 469.1073, found: 469.1076.





N-(3-((6-methoxybenzo[d]thiazol-2-yl)thio)butyl)-4-methylbenzenesulfonamide (3ah)

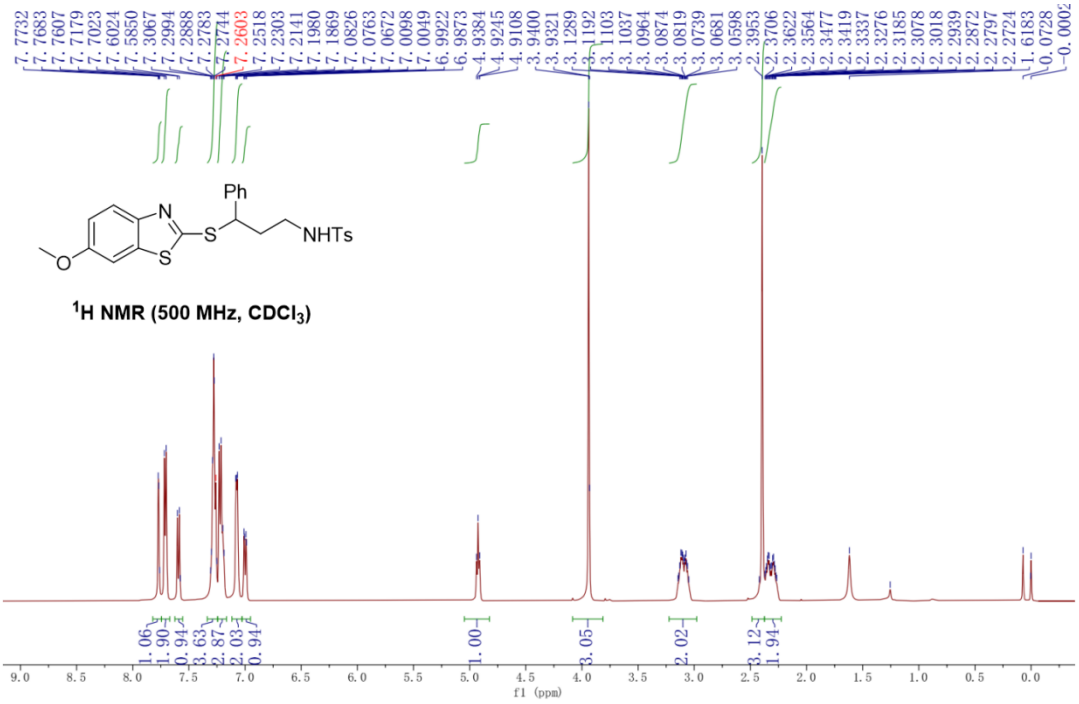


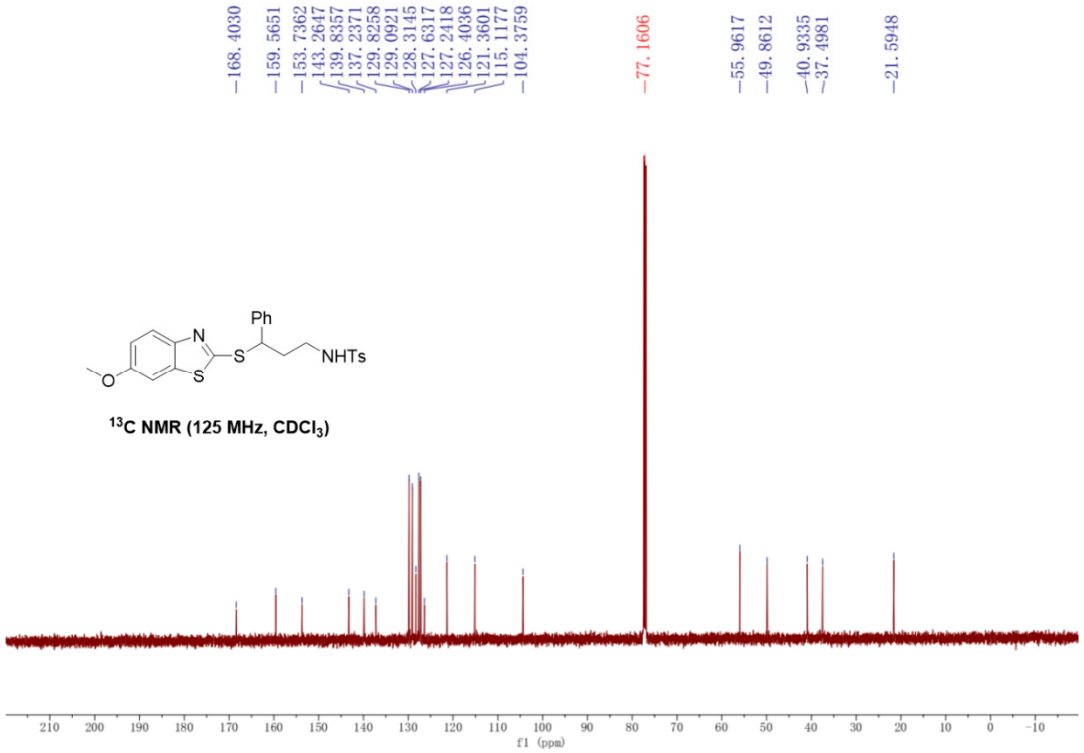
Compound **3ah**: a colorless oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 40.0 mg, 83% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.77 (s, 1H), 7.71 (d, *J* = 7.8 Hz, 2H), 7.59 (d, *J* = 8.7 Hz, 1H), 7.34–7.24 (m, 3H), 7.24-7.17 (m, 3H), 7.10–7.05 (m, 2H), 7.00 (dd, *J* = 8.8, 2.4 Hz, 1H), 4.92 (t, *J* = 6.9 Hz, 1H), 3.94 (s, 3H), 3.18–2.98 (m, 2H), 2.40 (s, 3H), 2.37–2.22 (m, 2H).

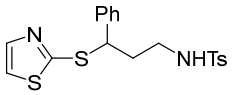
^{13}C NMR (125 MHz, Chloroform-*d*) δ 168.4, 159.6, 153.7, 143.3, 139.8, 137.2, 129.8, 129.1, 128.3, 127.6, 127.2, 126.4, 121.4, 115.1, 104.4, 56.0, 49.9, 40.9, 37.5, 21.6.

HRMS (ESI) m/z: calcd for $[C_{24}H_{24}N_2O_3S_3+H]^+$ requires: 485.1022, found: 485.1026.





4-methyl-N-(3-phenyl-3-(thiazol-2-ylthio)propyl)benzenesulfonamide (3ai)

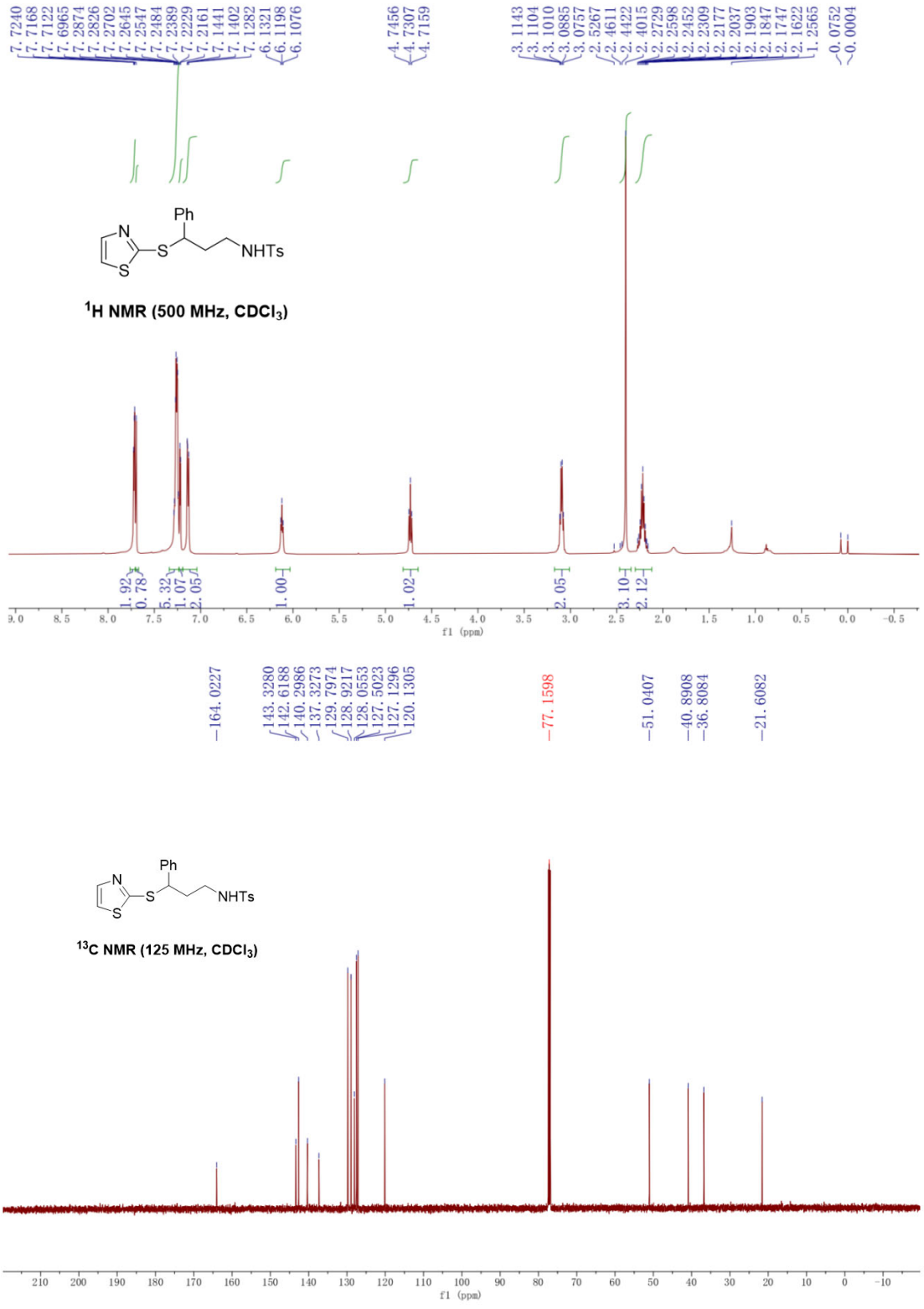


Compound **3ai**: a yellow solid. M.p. = 108-109 °C. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 28.3 mg, 70% yield.

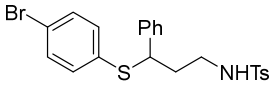
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.74–7.68 (m, 3H), 7.33–7.20 (m, 7H), 7.14 (d, 2H), 6.12 (t, *J* = 6.1 Hz, 1H), 4.73 (t, *J* = 7.4 Hz, 1H), 3.16–3.04 (m, 2H), 2.40 (s, 3H), 2.29–2.14 (m, *J* = 7.8, 7.2 Hz, 2H).

^{13}C NMR (125 MHz, Chloroform-*d*) δ 164.0, 143.3, 142.6, 140.3, 137.3, 129.8, 128.9, 128.1, 127.5, 127.1, 120.1, 51.0, 40.9, 36.8, 21.6.

HRMS (ESI) m/z: calcd for $[C_{19}H_{20}N_2O_2S_3+Na]^+$ requires: 427.0579, found: 427.0587.



N-(3-((4-bromophenyl)thio)-3-phenylpropyl)-4-methylbenzenesulfonamide (3aj)



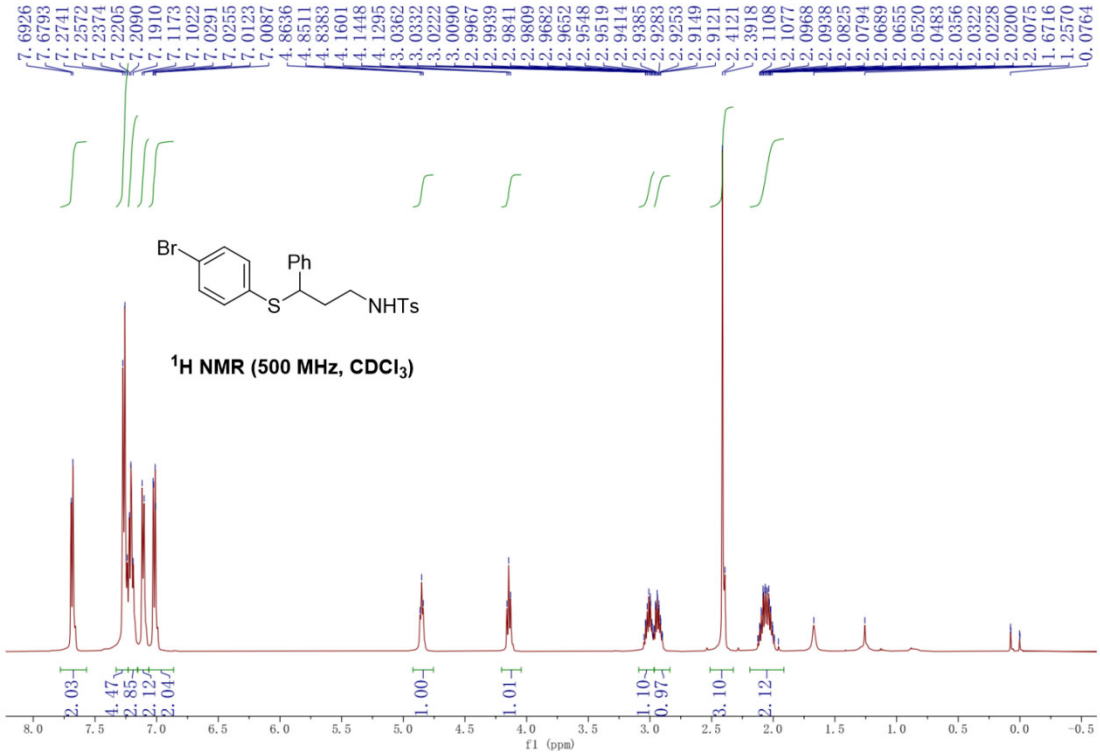
Compound **3aj**: a red oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 37.5

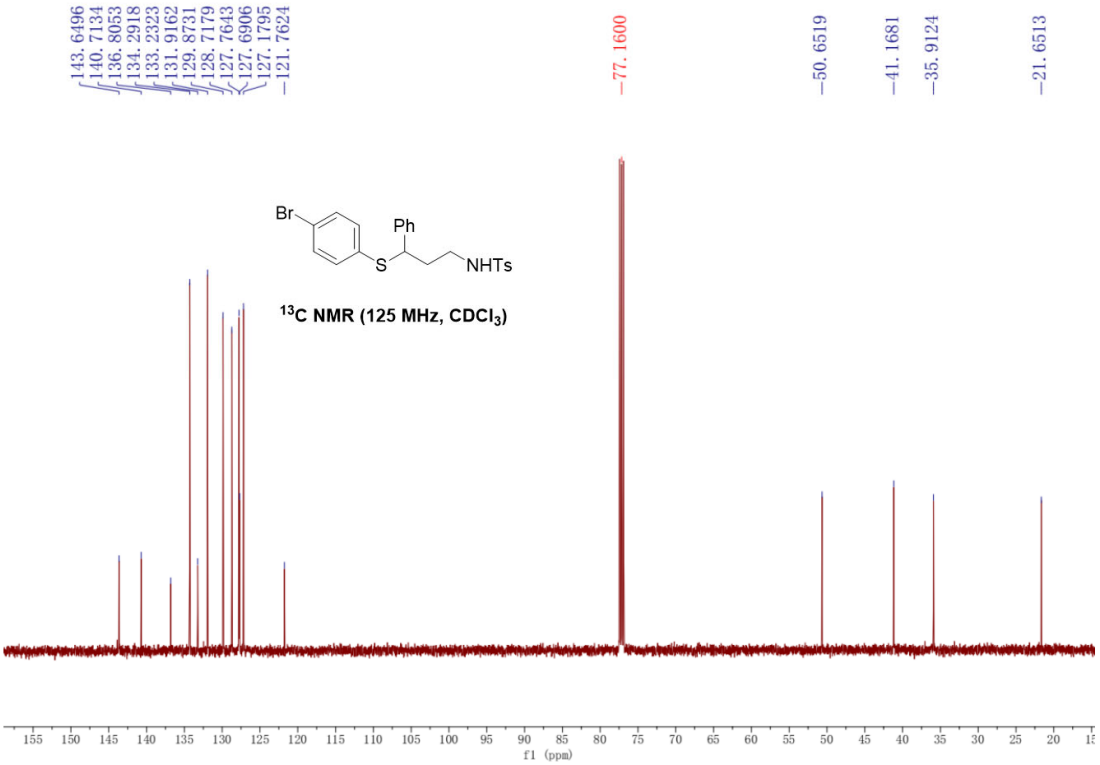
mg, 79% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 6.7 Hz, 2H), 7.34–7.16 (m, 7H), 7.11 (d, *J* = 7.6 Hz, 2H), 7.02 (dd, *J* = 8.4, 1.8 Hz, 2H), 4.85 (t, *J* = 6.3 Hz, 1H), 4.14 (t, *J* = 7.7 Hz, 1H), 3.07–2.88 (m, 2H), 2.40 (s, 3H), 2.13–1.98 (m, 2H).

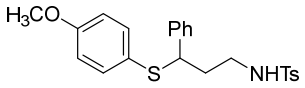
^{13}C NMR (125 MHz, Chloroform-*d*) δ 143.6, 140.7, 136.8, 134.3, 133.2, 131.9, 129.9, 128.7, 127.8, 127.7, 127.2, 121.8, 50.7, 41.2, 35.9, 21.7.

HRMS (ESI) m/z: calcd for $[C_{22}H_{22}BrNO_2S_2+Na]^+$ requires: 498.0168, found: 498.0176.





N-(3-((4-methoxyphenyl)thio)-3-phenylpropyl)-4-methylbenzenesulfonamide (3ak)

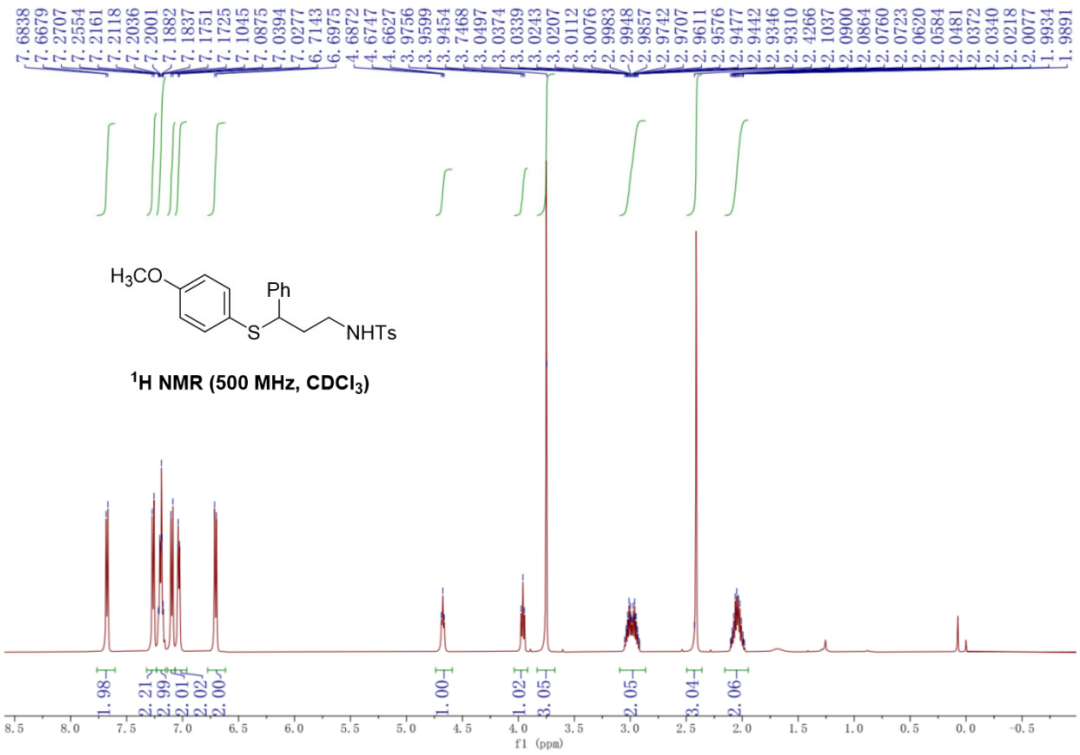


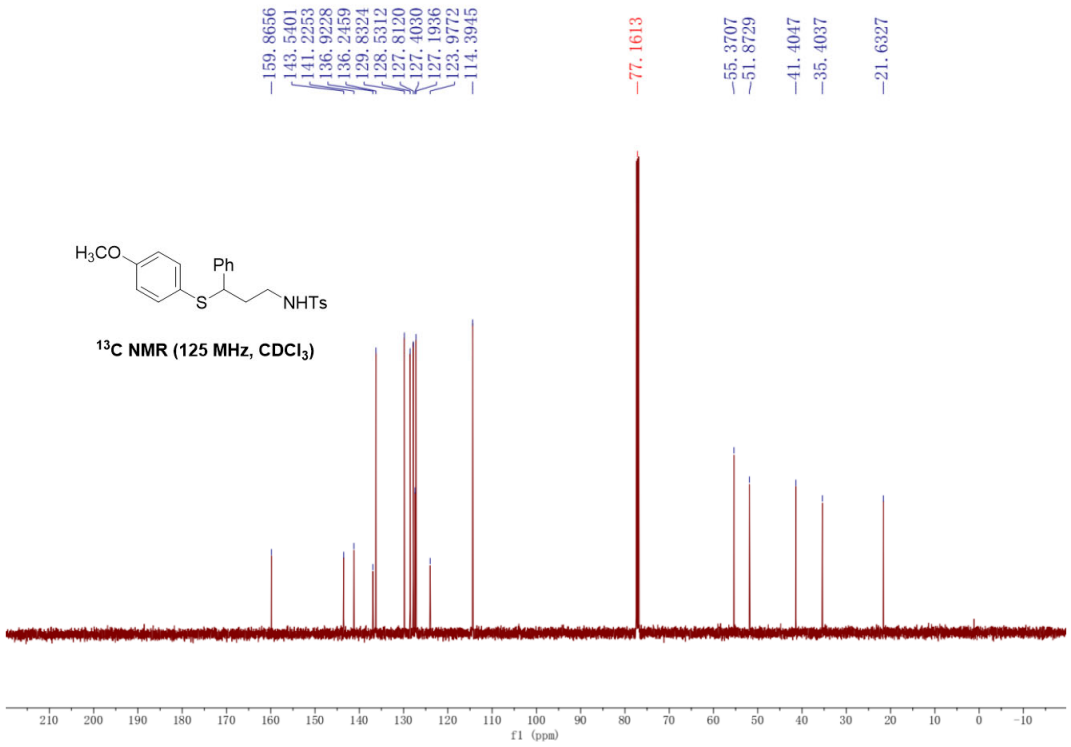
Compound **3ak**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 34.3 mg, 83% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 7.9 Hz, 2H), 7.26 (d, *J* = 7.7 Hz, 2H), 7.23–7.15 (m, 3H), 7.10 (d, *J* = 8.5 Hz, 2H), 7.03 (d, *J* = 5.8 Hz, 2H), 6.71 (d, *J* = 8.4 Hz, 2H), 4.67 (t, *J* = 6.1 Hz, 1H), 3.96 (t, *J* = 7.5 Hz, 1H), 3.75 (s, 3H), 3.07–2.90 (m, 2H), 2.43 (s, 3H), 2.12–1.99 (m, 2H).

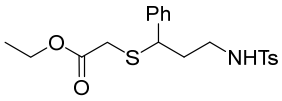
^{13}C NMR (125 MHz, Chloroform-*d*) δ 159.9, 143.5, 141.2, 136.9, 136.2, 129.8, 128.5, 127.8, 127.4, 127.2, 124.0, 114.4, 55.4, 51.9, 41.4, 35.4, 21.6.

HRMS (ESI) m/z: calcd for $[C_{23}H_{25}NO_3S_2+Na]^+$ requires: 450.1168, found: 450.1176.





ethyl 2-((3-((4-methylphenyl)sulfonamido)-1-phenylpropyl)thio)acetate (3am)

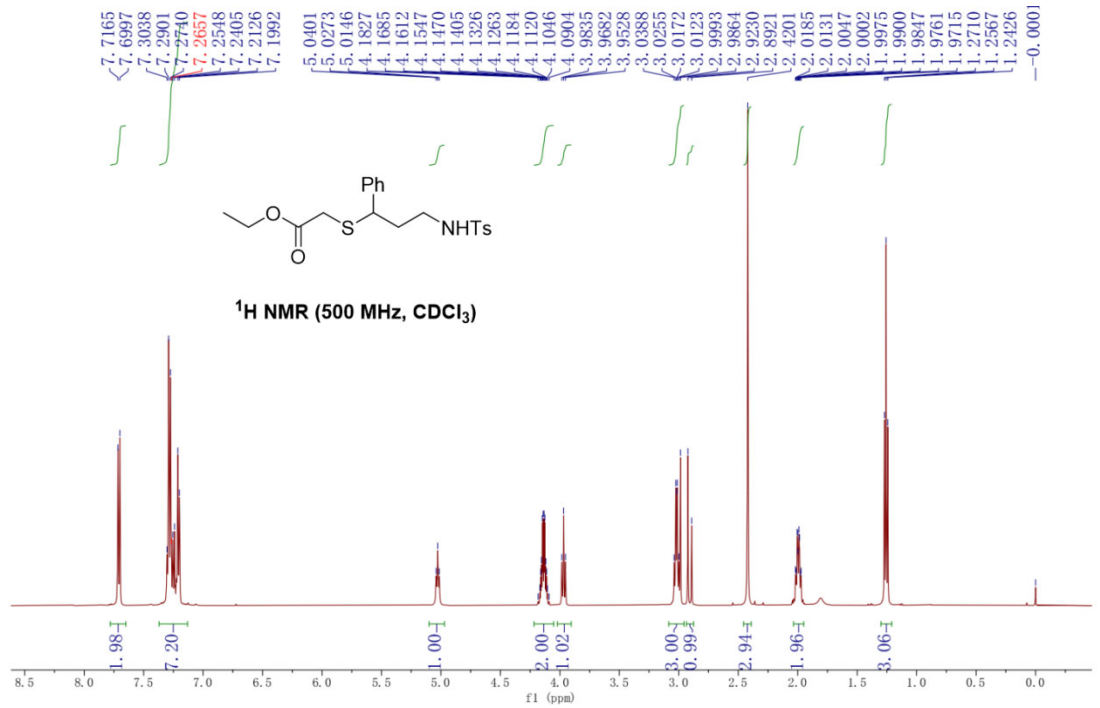


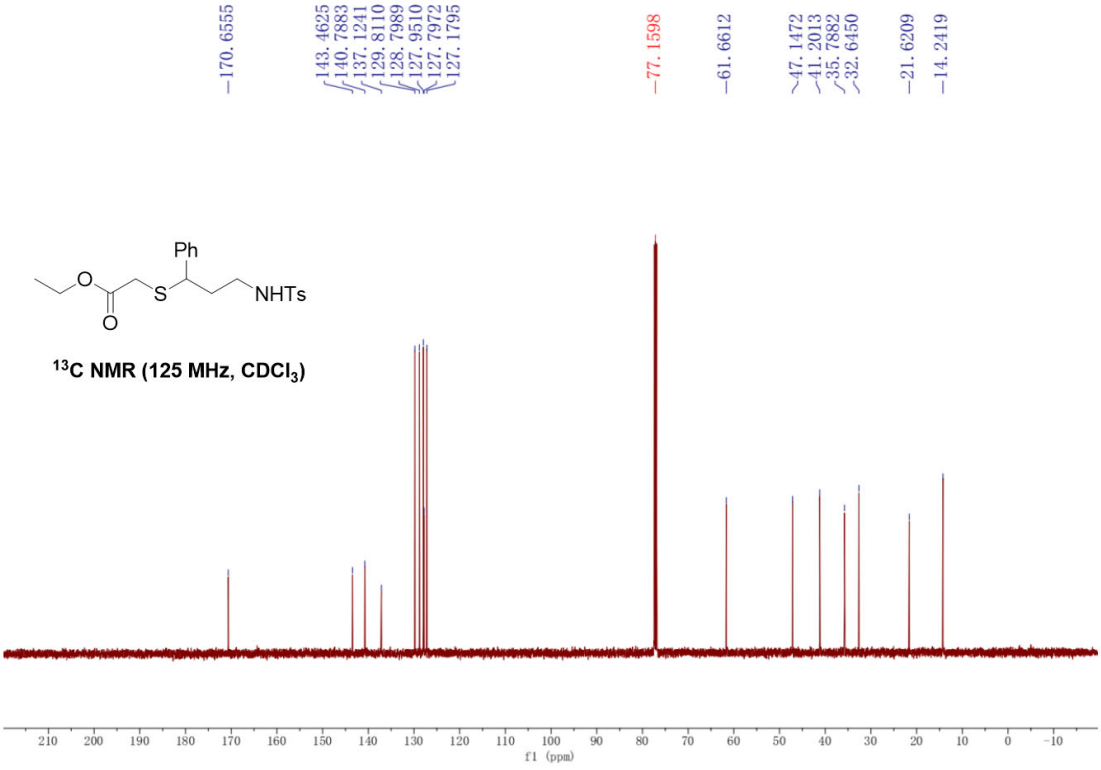
Compound **3am**: a yellow oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 33.3 mg, 82% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 8.4 Hz, 2H), 7.36–7.14 (m, 7H), 5.03 (t, *J* = 6.4 Hz, 1H), 4.20–4.07 (m, 2H), 3.97 (t, *J* = 7.7 Hz, 1H), 3.08–2.97 (m, 3H), 2.91 (d, *J* = 15.5 Hz, 1H), 2.42 (s, 3H), 2.06–1.93 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).

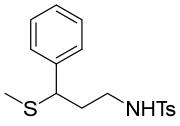
^{13}C NMR (125 MHz, Chloroform-*d*) δ 170.7, 143.5, 140.8, 137.1, 129.8, 128.8, 128.0, 127.8, 127.2, 61.7, 47.1, 41.2, 35.8, 32.6, 21.6, 14.2.

HRMS (ESI) m/z: calcd for $[C_{20}H_{25}NO_4S_2+Na]^+$ requires: 430.1117, found: 430.1124.





4-methyl-N-(3-(methylthio)-3-phenylpropyl)benzenesulfonamide (4)

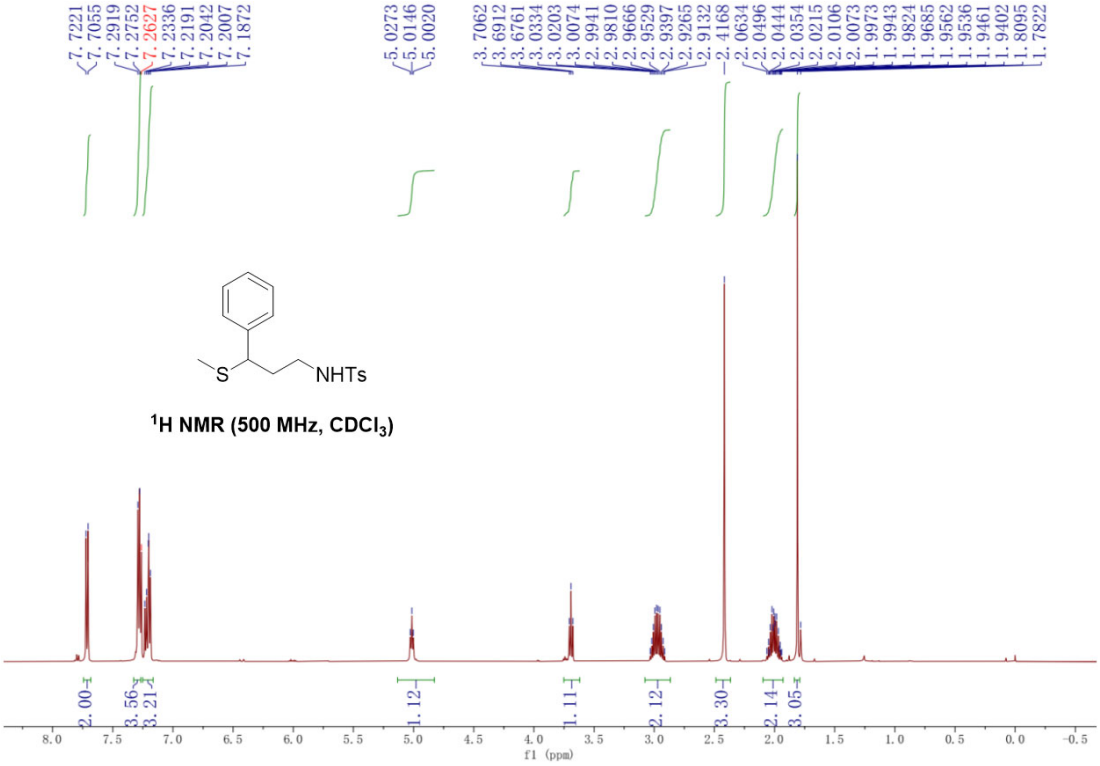


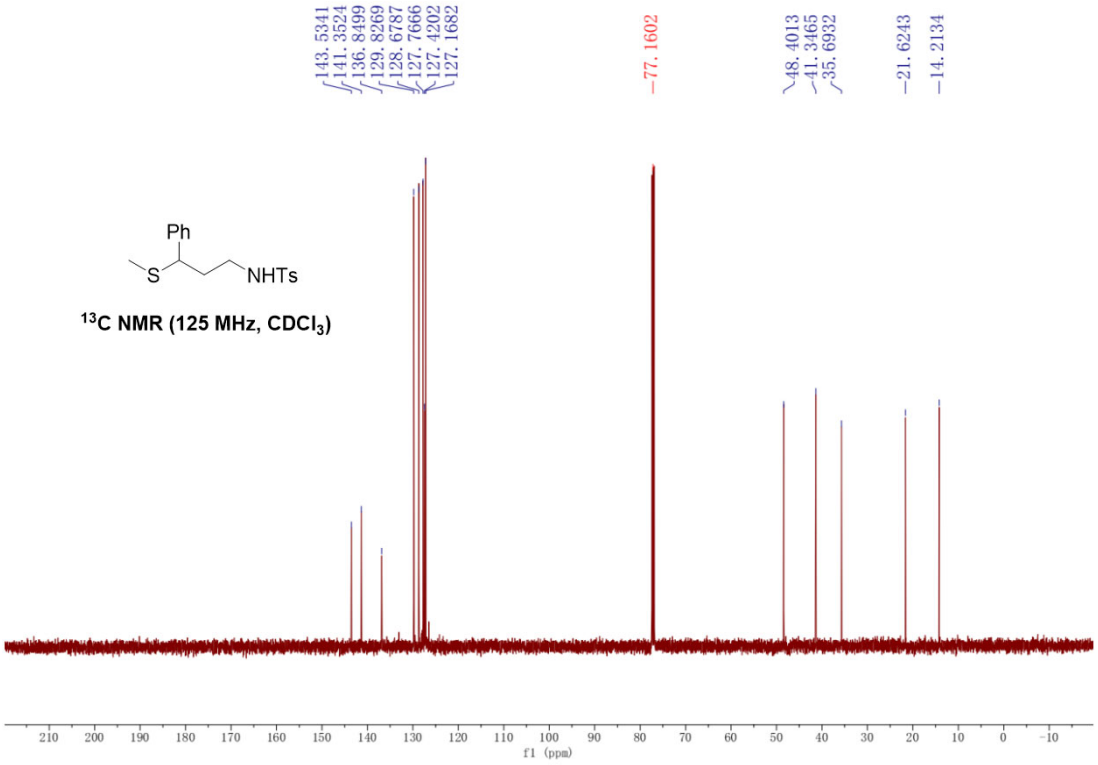
Compound **4**: a colorless oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 4/1, 22.1 mg, 66% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 4H), 7.24–7.16 (m, 3H), 5.01 (t, *J* = 6.3 Hz, 1H), 3.69 (t, *J* = 7.5 Hz, 1H), 3.05–2.90 (m, 2H), 2.42 (s, 3H), 2.09–1.93 (m, 2H), 1.81 (s, 3H).

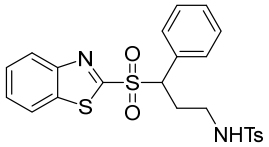
^{13}C NMR (125 MHz, Chloroform-*d*) δ 143.5, 141.4, 136.8, 129.8, 128.7, 127.8, 127.4, 127.2, 48.4, 41.3, 35.7, 21.6, 14.2.

HRMS (ESI) m/z: calcd for $[C_{17}H_{21}NO_2S_2+Na]^+$ requires: 358.0914, found:358.0906.





N-(3-(benzo[d]thiazol-2-ylsulfonyl)-3-phenylpropyl)-4-methylbenzenesulfonamide (5)

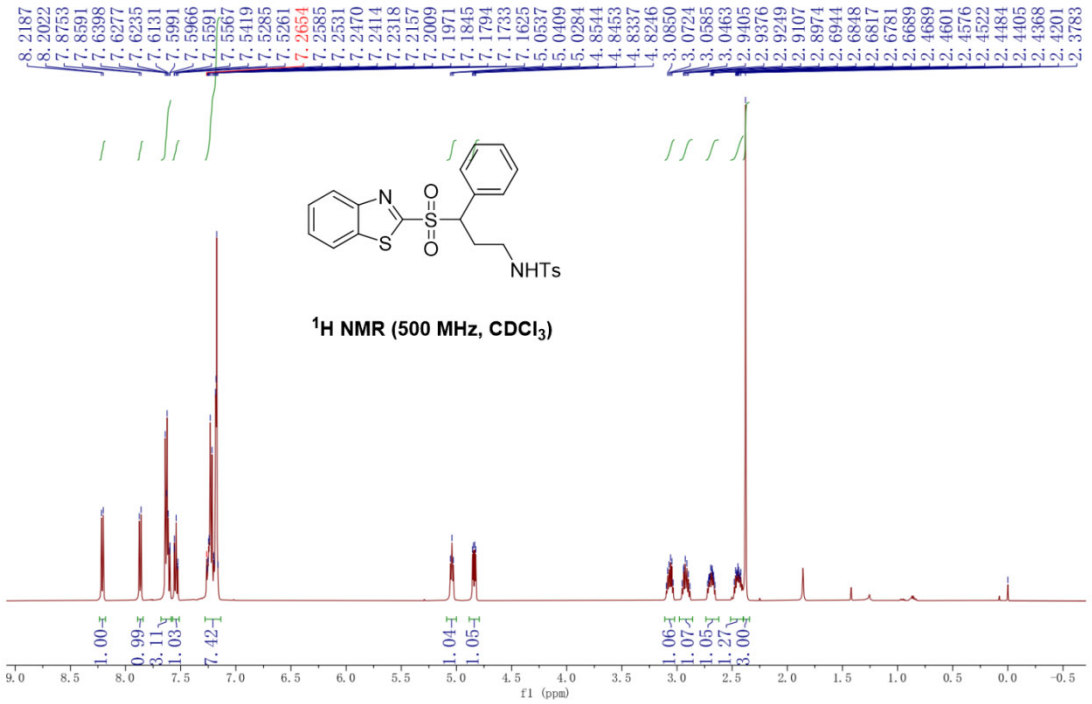


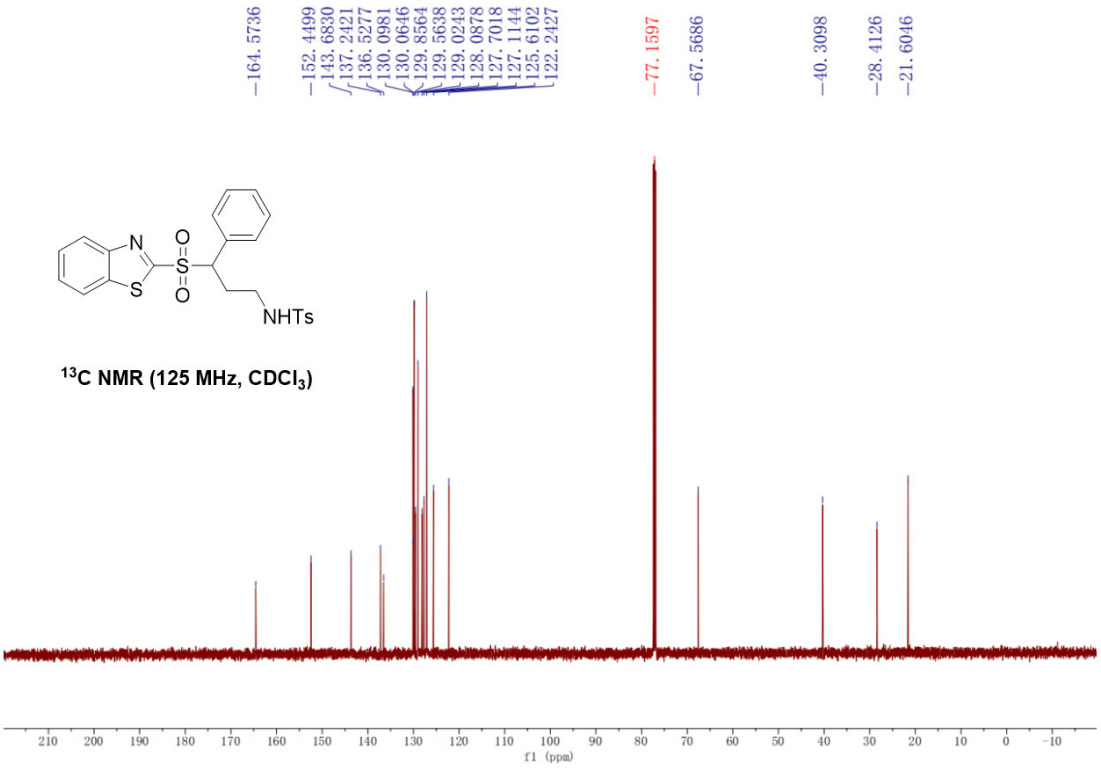
Compound **5**: a yellow solid. M.p. = 132-133 °C. Column chromatography, eluent: petroleum ether/ethyl acetate, 1/1, 43.9 mg, 90% yield.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.21 (d, *J* = 8.3 Hz, 1H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.66–7.58 (m, 3H), 7.58–7.51 (m, 1H), 7.28–7.14 (m, 8H), 5.04 (t, *J* = 6.3 Hz, 1H), 4.84 (dd, *J* = 10.3, 4.6 Hz, 1H), 3.11–3.02 (m, 1H), 2.97–2.87 (m, 1H), 2.74–2.64 (m, 1H), 2.50–2.39 (m, 1H), 2.38 (s, 3H).

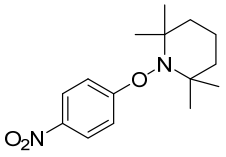
^{13}C NMR (125 MHz, Chloroform-*d*) δ 164.6, 152.4, 143.7, 137.2, 136.5, 130.1, 130.1, 129.9, 129.6, 129.0, 128.1, 127.7, 127.1, 125.6, 122.2, 67.6, 40.3, 28.4, 21.6.

HRMS (ESI) m/z: calcd for $[C_{23}H_{22}N_2O_4S_3+Na]^+$ requires: 509.0634, found: 509.0634.





2,2,6,6-tetramethyl-1-(4-nitrophenoxy)piperidine



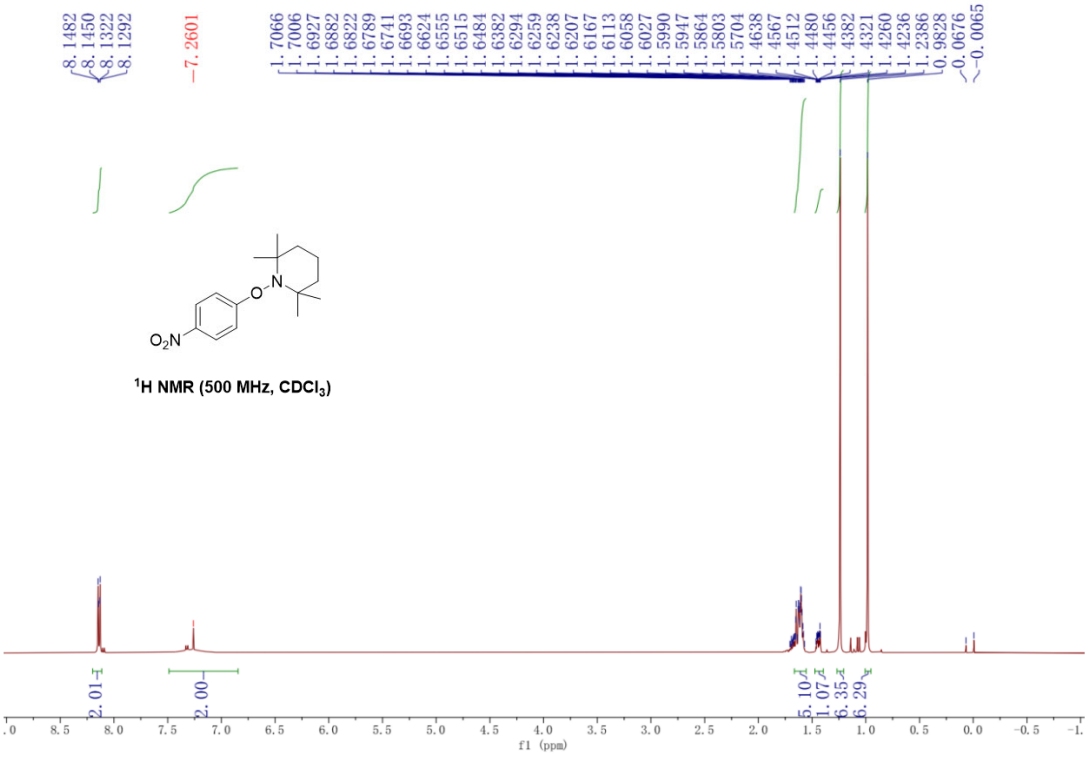
A red oil. Column chromatography, eluent: petroleum ether/ethyl acetate, 30/1.

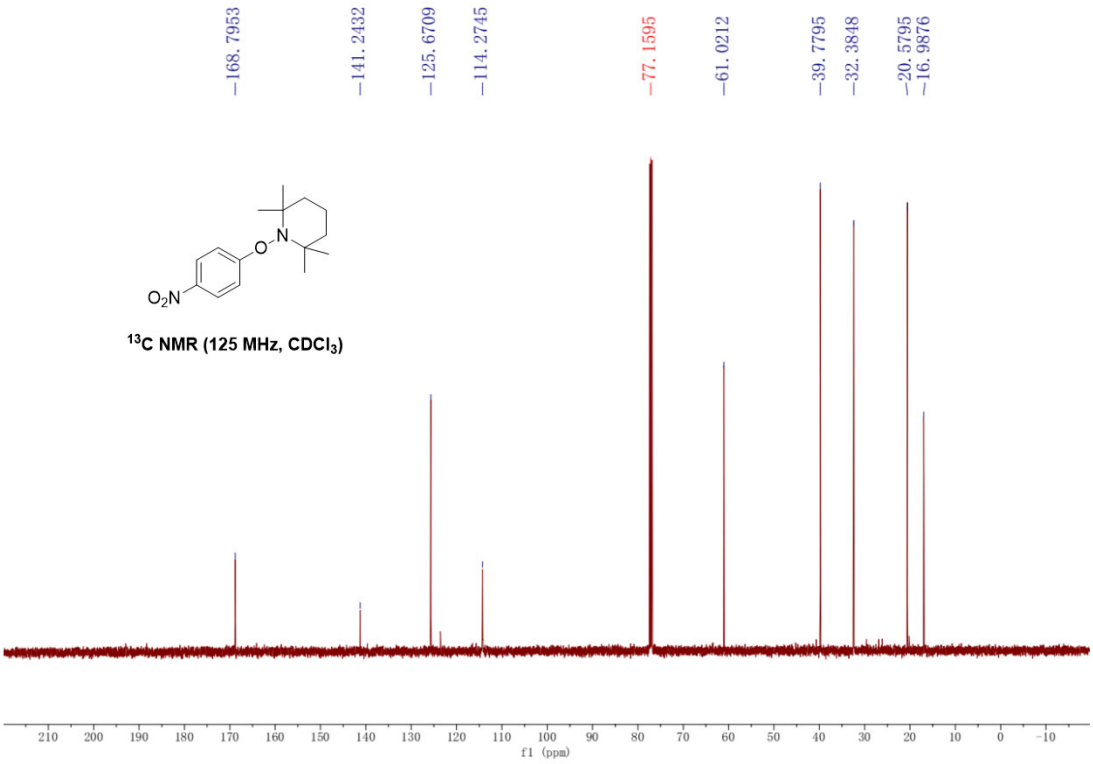
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 8.5 Hz, 2H), 7.26 (bs, 2H), 1.67–1.56 (m, 5H), 1.48–1.41 (m, 1H), 1.24 (s, 6H), 0.98 (s, 6H).

^{13}C NMR (125 MHz, Chloroform-*d*) δ 168.8, 141.2, 125.7, 114.3, 61.0, 39.8, 32.4, 20.6, 17.0.

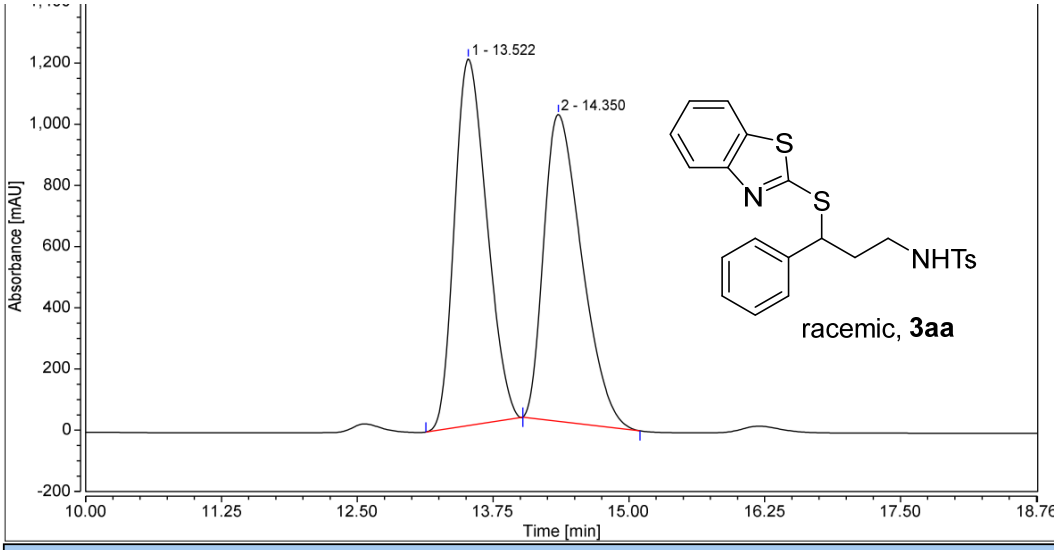
HRMS (ESI) m/z: calcd for $[C_{15}H_{22}N_2O_3+Na]^+$ requires: 301.1523, found: 301.1528.

The spectral data agree with those previously reported.[5]



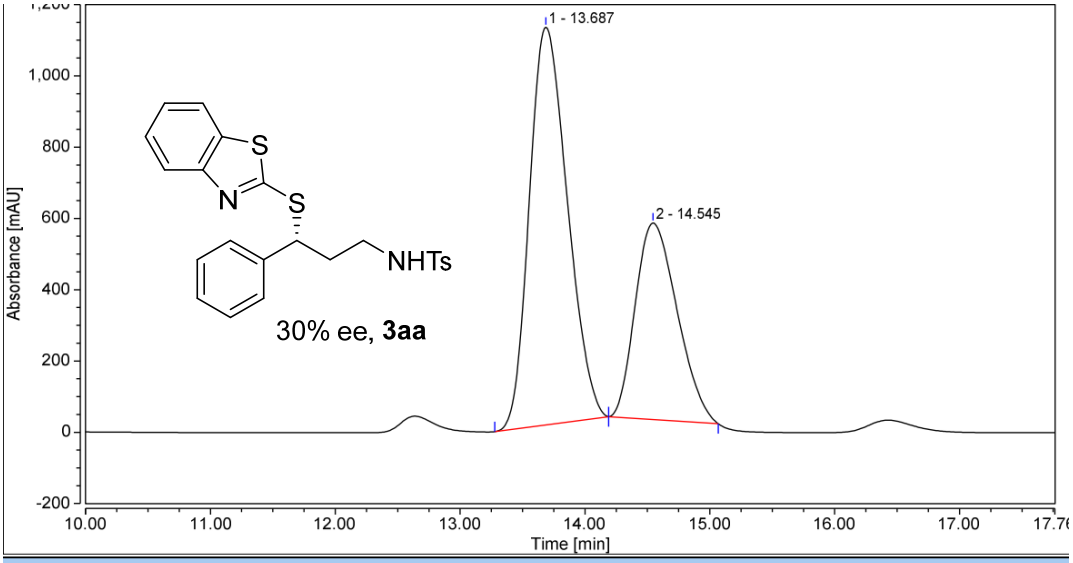


2.8. Copies of HPLC traces



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.522	412.965	1198.086	50.33	54.43	n.a.
2		14.350	407.597	1003.135	49.67	45.57	n.a.



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.687	393.751	1116.177	64.74	66.93	n.a.
2		14.545	214.472	551.477	35.26	33.07	n.a.

2.9. References

[1]. M. J. McKennon, A. I. Meyers, K. Drauz and M. A. Schwarm, *J. Org. Chem*., 1993, **58**, 3569.

[2]. (a) B. A. B. Prasad, A. Bisai and V. K. Singh, *Org. Lett*., 2004, **6**, 4829-4831. (b) T. N. Nguyen and J. A. May, *Org. Lett*., 2018, **20**, 3618.

[3]. (a) J. Zhu, S.-D. Tang, X.-M. Kan, S.-Z. Fan, P.-F. Wang and P.-J. Yang, *Chin. J. Org. Chem.*, 2024, **44**, 2796; (b) M. K. Ghorai, S. Das, K. Das and A. Kumar, *Org. Biomol. Chem*., 2015, **13**, 9042.

[4]. P. Hanson, J. R. Jones, A. B. Taylor, P. H. Walton and A. W. Timmsb, *J. Chem. Soc. Perkin Trans.*, **2**, 2002, 1135.
[5] M. D. Perretti, D. M. Monzón, F. P. Crisóstomo, V. S. Martín and R. Carrillo, *Chem. Commun.,* 2016, *52*, 9036.