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Supporting Information for

Environmentally friendly synthesis of unsymmetrical dialkyl disulfides by reacting organic halides with thiourea and sodium thiosulfate in an aqueous medium

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1.Materials and methods

All reactions were conducted in an Easy Max™ 102. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Advance III 300 MHz spectrometer in CD_3OD or CD_3Cl using TMS as internal standard. Chemical shifts are reported in ppm (δ), and coupling contants (J) in Hz. LC-MS analyses were performed on an Agilent 6410 Triple Quad LC/MS instrument. All the products are unknown compounds. All chemicals (AR grade) were commercially available and used without further purification.

2.Typical procedure for the formation of unsymmetrical disulfides

First, $Na_2S_2O_3 \cdot 5H_2O$ (248.2 mg, 1.0 mmol, 1.25 equiv.), alkyl halide (1.0 mmol, 1.25 equiv.), and EtOH/H_2O (0.25 mL/0.5 mL), were added to a pressure resistant tube. The mixture was stirred under reflux (100^{o}C) for 2 h under N_2 atmosphere, and the solvent was then removed under reduced pressure.[1] In the second step, a different alkyl halide R^2X (0.8 mmol, 1.0 equiv.) was added, followed by addition of thiourea (0.96 mmol, 1.2 equiv.), Na_2CO_3 (0.96 mmol, 1.2 equiv.), SDBS (0.1 mmol, 0.125 equiv.) and H_2O (1 mL), the system was then heated to 80^{o}C for 7 h under N_2 atmosphere. After the heating was completed, the mixture was cooled to room temperature. Then the reaction mixture was extracted with EtOAc. The combined organic extract was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure, and the residue was purified by column chromatography (petroleum ether–ethyl acetate) to afford the corresponding unsymmetrical disulfides.

3. A typical scale-up procedure

First, $Na_2S_2O_3 \cdot 5H_2O$ (12.41 g, 50 mmol, 1.25 equiv.), 4-chlorobutanenitrile (5.15 g, 50 mmol, 1.25 equiv.), and EtOH/H_2O (12.5 mL/25 mL), were added to a pressure resistant tube. The mixture was stirred under reflux (100^{o}C) for 2 h under N_2 atmosphere, and the solvent was then removed under reduced pressure.[1] In the second step, 1-bromohexane (8.25 g, 40 mmol, 1.0 equiv.) was added, followed by addition of thiourea (3.65 g, 48 mmol, 1.2 equiv.), Na_2CO_3 (5.04 g, 48 mmol, 1.2 equiv.), SDBS (1.74 g, 5 mmol, 0.125 equiv.) and H_2O (50 mL), the system was then heated to 80^{o}C for 7 h under N_2 atmosphere. After the heating was completed, the mixture

was cooled to room temperature. Then the reaction mixture was extracted with EtOAc. The combined organic extract was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure, and the residue was purified by column chromatography (petroleum ether–ethyl acetate) to afford 4-(hexyldisulfaneyl)butanenitrile in 8.57 g, 79% yield.

4.Characterization data of the compounds

4-(hexyldisulfaneyl)butanenitrile (2a). Colorless oil. 152 mg (0.70 mmol, 88% yield). ^{1}H NMR (300 MHz, CD_3OD) δ 2.75 (t, *J* = 7.1 Hz, 2H), 2.68 (t, *J* = 7.4 Hz, 2H), 2.55 (t, *J* = 7.2 Hz, 2H), 2.07-1.95 (m, 2H), 1.72-1.60 (m, 2H), 1.44-1.24 (m, 6H), 0.92-0.84 (m, 3H).^{13}C NMR (75 MHz, CD_3OD) δ 120.8, 39.8, 37.7, 32.9, 30.5, 29.5, 26.2, 23.9, 16.3, 14.7. LC-MS m/z: calcd for $C_{10}H_{19}NNaS_2$ $[M+Na]^+$240.09, found: 240.01.

4-(heptyldisulfaneyl)butanenitrile (2b). Colorless oil. 140 mg (0.61 mmol, 76% yield). ^{1}H NMR (300 MHz, CD_3OD) δ 2.76 (t, *J* = 7.0 Hz, 2H), 2.69 (t, *J* = 7.3 Hz, 2H), 2.55 (t, *J* = 7.1 Hz, 2H), 2.07-1.95 (m, 2H), 1.73-1.59 (m, 2H), 1.44-1.22 (m, 8H), 0.94-0.83 (m, 3H).^{13}C NMR (75 MHz, CD_3OD) δ 120.5, 39.5, 37.4, 32.9, 30.2, 30.0, 29.5, 25.9, 23.7, 16.1, 14.4. LC-MS m/z: calcd for $C_{11}H_{21}NNaS_2$ $[M+Na]^+$254.10, found: 254.00.

4-(isopentyldisulfaneyl)butanenitrile (2c). Colorless oil. 141 mg (0.70 mmol, 87% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.77 (t, *J* = 6.9 Hz, 2H), 2.69 (t, *J* = 7.8 Hz, 2H), 2.51 (t, *J* = 7.3 Hz, 2H), 2.13-2.02 (m, 2H), 1.72-1.62 (m, 1H), 1.55 (q, *J* = 7.3 Hz, 2H), 0.91 (d, *J* = 6.1 Hz, 6H).^{13}C NMR (75 MHz, $CDCl_3$) δ 118.6, 37.9, 36.6, 36.1, 26.9, 24.2, 22.0, 15.4. LC-MS m/z: calcd for $C_9H_{17}NNaS_2$ $[M+Na]^+$226.07, found: 225.90.

4-(butyldisulfaneyl)butanenitrile (2d). Colorless oil. 113 mg (0.60 mmol, 75% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.76 (t, *J* = 5.9 Hz, 2H), 2.51 (t, *J* = 7.0 Hz, 2H), 2.13-2.02 (m, 2H), 1.76-1.65 (m, 1H), 1.58-1.47 (m, 1H), 1.34-1.23 (m, 4H), 0.98 (t, *J* = 7.4 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 119.2, 48.1, 37.3, 29.0, 24.7, 20.3, 15.9, 11.7. LC-MS m/z: calcd for $C_8H_{15}NNaS_2$ $[M+Na]^+$212.05, found: 212.00.

4-(pentyldisulfaneyl)butanenitrile (2e). Colorless oil. 118 mg (0.58 mmol, 73% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.77 (t, *J* = 6.8 Hz, 2H), 2.68 (t, *J* = 7.4 Hz, 2H), 2.51 (t, *J* = 7.0 Hz, 2H), 2.14-2.02 (m, 2H), 1.73-1.58 (m, 2H), 1.42-1.28 (m, 4H), 0.94-0.86 (m, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 119.2, 39.0, 36.7, 30.8, 29.0, 24.7, 22.4, 15.9, 14.1. LC-MS m/z: calcd for $C_9H_{17}NNaS_2$ $[M+Na]^+$226.07, found: 226.00.

4-(*iso*-butyldisulfaneyl)butanenitrile (2f). Colorless oil. 17 mg (0.09 mmol, 11% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.77 (t, *J* = 6.5 Hz, 2H), 2.60 (d, *J* = 5.9 Hz, 2H), 2.52 (t, *J* = 6.8 Hz, 2H), 2.14-2.03 (m, 2H), 1.99-1.87 (m, 1H), 1.00 (d, *J* = 6.1 Hz, 6H).^{13}C NMR (75 MHz, $CDCl_3$) δ 119.2, 48.6, 36.4, 28.4, 24.7, 21.9, 15.9. LC-MS m/z: calcd for $C_8H_{15}NNaS_2$ $[M+Na]^+$212.05, found: 211.80.

4-(*sec*-butyldisulfaneyl)butanenitrile (2h). Colorless oil. 30 mg (0.16 mmol, 20% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.81-2.70 (m, 3H), 2.51 (t, *J* = 7.1 Hz, 2H),

2.14-2.01 (m, 2H), 1.77-1.65 (m, 1H), 1.61-1.47 (m, 1H), 1.31 (d, J = 6.7 Hz, 3H), 0.98 (t, J = 8.3 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 119.2, 48.1, 37.3, 29.0, 24.7, 20.3, 15.9, 11.7. LC-MS m/z: calcd for $C_8H_{15}NNaS_2$ $[M+Na]^+$212.05, found: 212.00.

4-(cyclohexyldisulfaneyl)butanenitrile (2i). Colorless oil. 20 mg (0.10 mmol, 12% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.76 (t, J = 6.9 Hz, 2H), 2.51 (t, J = 6.9 Hz, 2H), 2.13-1.97 (m, 3H), 1.84-1.57 (m, 4H), 1.45-1.22 (m, 5H), 0.96 (t, J = 7.2 Hz, 1H).^{13}C NMR (75 MHz, $CDCl_3$) δ 119.2, 49.6, 37.6, 33.0, 26.2, 25.7, 24.7, 15.9. LC-MS m/z: calcd for $C_{10}H_{17}NNaS_2$ $[M+Na]^+$238.07, found: 238.00.

4-(cyclopentyldisulfaneyl)butanenitrile (2j). Colorless oil. 66 mg (0.32 mmol, 41% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.32-3.22 (m, 1H), 2.79 (t, J = 6.9 Hz, 2H), 2.51 (t, J = 7.1 Hz, 2H), 2.14-2.03 (m, 2H), 2.03-1.90 (m, 2H), 1.79-1.53 (m, 6H).^{13}C NMR (75 MHz, $CDCl_3$) δ 119.2, 50.2, 36.9, 33.2, 24.8, 15.9. LC-MS m/z: calcd for $C_9H_{15}NNaS_2$ $[M+Na]^+$224.05, found: 223.80.

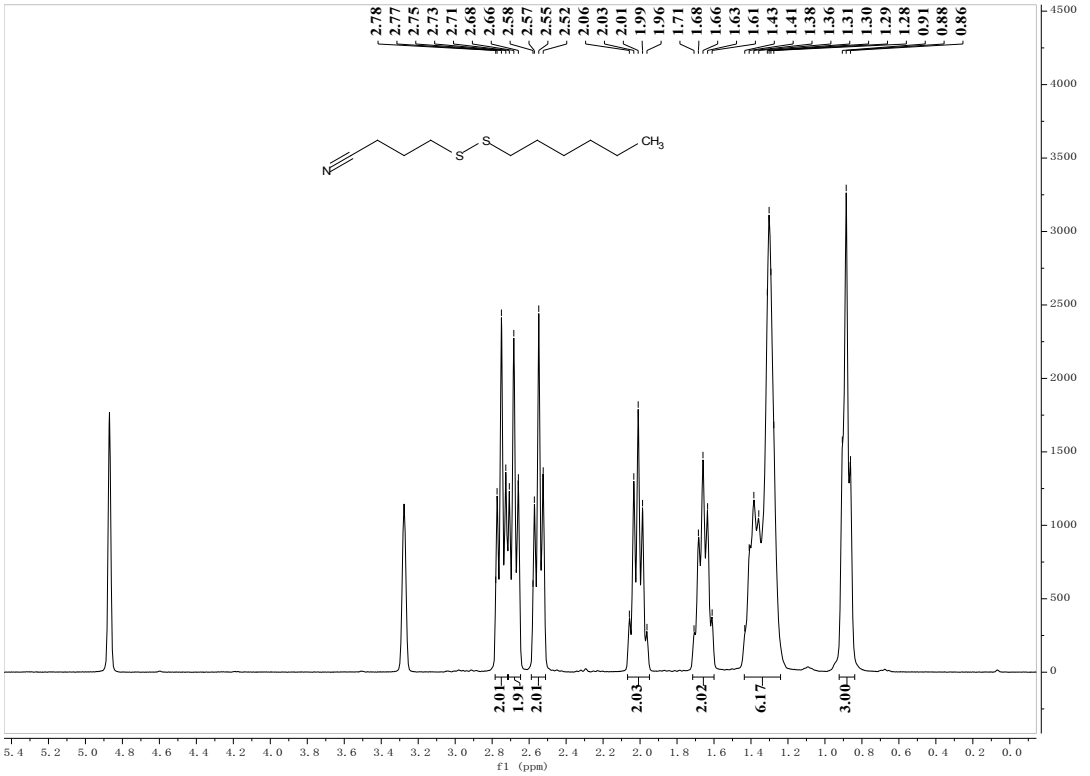
6-(isopentyldisulfaneyl)hexanenitrile (2k). Colorless oil. 170 mg (0.74 mmol, 92% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.73-2.63 (m, 4H), 2.36 (t, J = 7.1 Hz, 2H), 1.79-1.63 (m, 5H), 1.61-1.49 (m, 4H), 0.90 (d, J = 6.6 Hz, 6H).^{13}C NMR (75 MHz, $CDCl_3$) δ 119.3, 38.0, 38.0, 36.9, 36.8, 28.0, 27.2, 26.9, 26.9, 24.8, 24.7, 22.0, 16.8. LC-MS m/z: calcd for $C_{11}H_{21}NNaS_2$ $[M+Na]^+$254.10, found: 254.00.

6-(pentyldisulfaneyl)hexanenitrile (2l). Colorless oil. 166 mg (0.72 mmol, 90% yield).^{1}H NMR (300 MHz, $CDCl_3$) δ 2.67 (t, J = 7.4 Hz, 4H), 2.36 (t, J = 7.1 Hz, 2H), 1.80-1.62 (m, 6H), 1.61-1.50 (m, 2H), 1.41-1.24 (m, 4H), 0.94-0.84 (m, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 119.7, 39.3, 39.2, 38.4, 38.4, 30.8, 29.0, 28.4, 27.6, 25.2, 25.2, 22.4, 17.2, 14.1. LC-MS m/z: calcd for $C_{11}H_{21}NNaS_2$ $[M+Na]^+$254.10, found: 254.00.

6-(hexyldisulfaneyl)hexanenitrile (2m). Colorless oil. 166 mg (0.68 mmol, 85% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.67 (t, J = 7.4 Hz, 4H), 2.36 (t, J = 7.1 Hz, 2H), 1.78-1.63 (m, 6H), 1.61-1.52 (m, 2H), 1.44-1.23 (m, 6H), 0.92-0.84 (m, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 119.7, 39.3, 39.2, 38.4, 38.4, 31.5, 29.3, 28.4, 28.3, 27.6, 25.2, 25.2, 22.7, 17.2, 14.2. LC-MS m/z: calcd for $C_{12}H_{23}NNaS_2$ $[M+Na]^+$268.12, found: 268.00.

4-(benzyldisulfaneyl)butanenitrile (2n). Light yellow oil. 123 mg (0.55 mmol, 75%yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, 5H), 3.89 (s, 2H), 2.36 (t, J = 6.7 Hz, 4H), 1.87 (p, J = 6.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.3, 129.3, 128.6, 127.7, 119.0, 43.4, 36.0, 24.4, 15.7. LC-MS m/z: calcd for $C_{11}H_{13}NNaS_2$ $[M+Na]^+$246.34, found: 245.90.

5.Copies of ^{1}H, ^{13}C NMR Spectra and LC-MS of the Products



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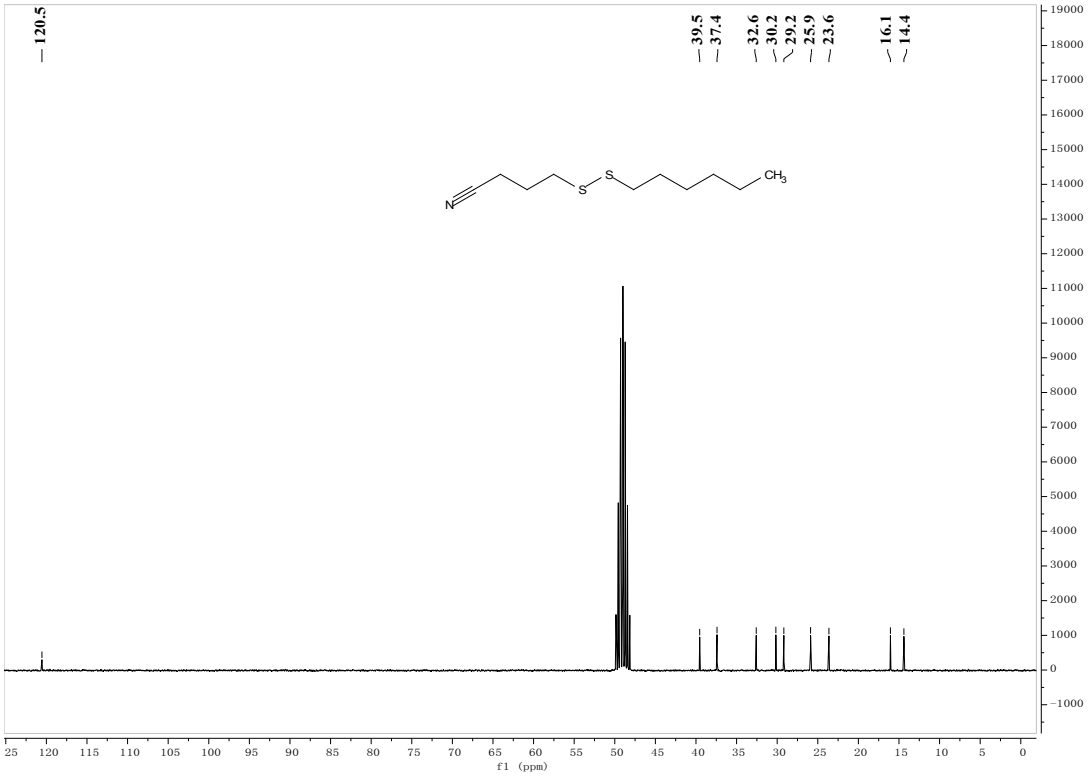

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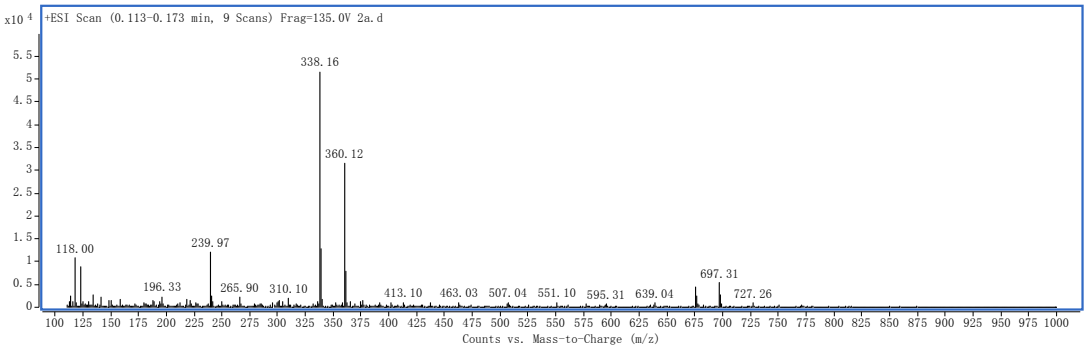

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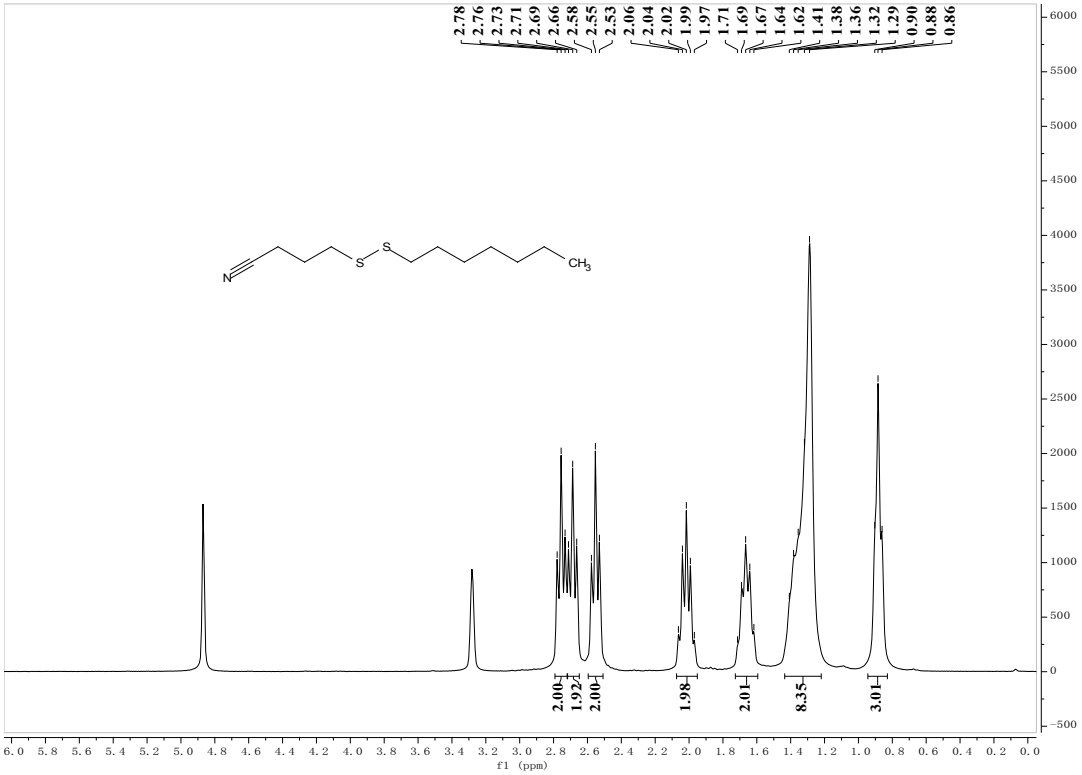

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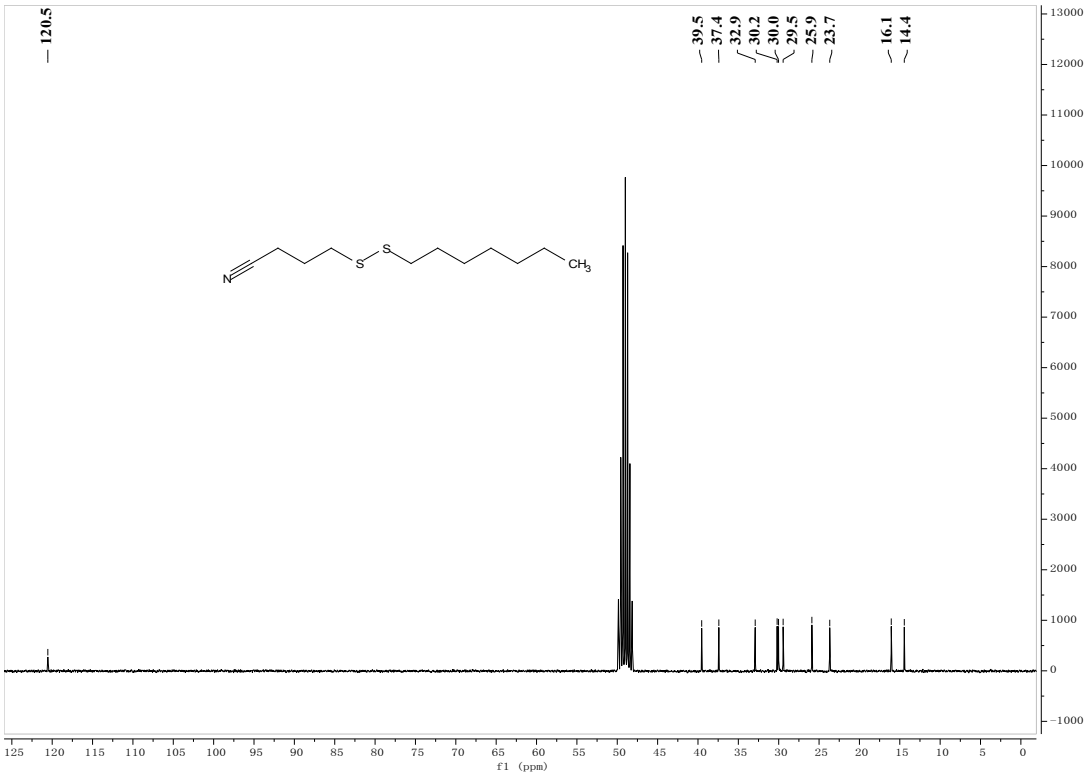

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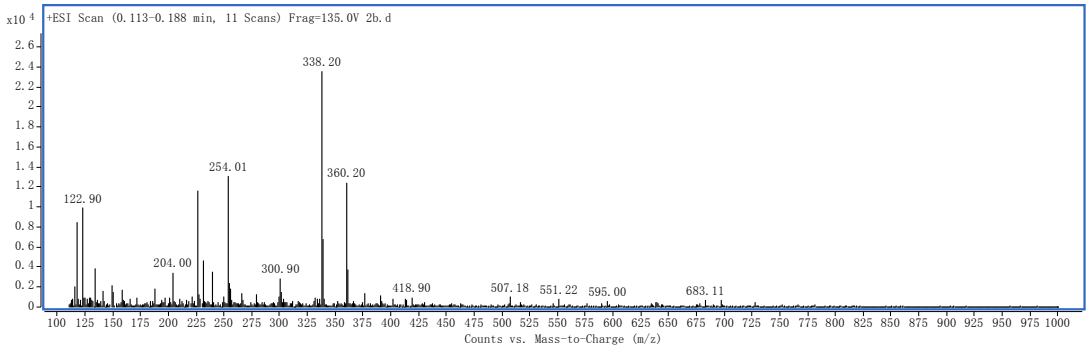

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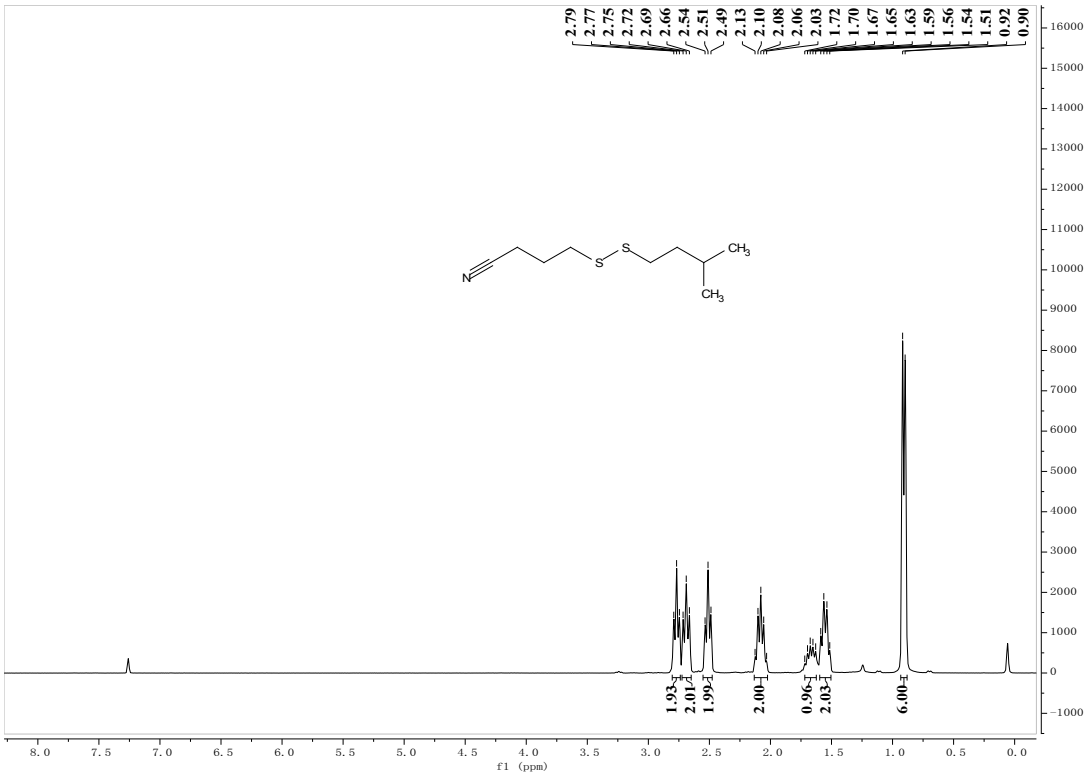
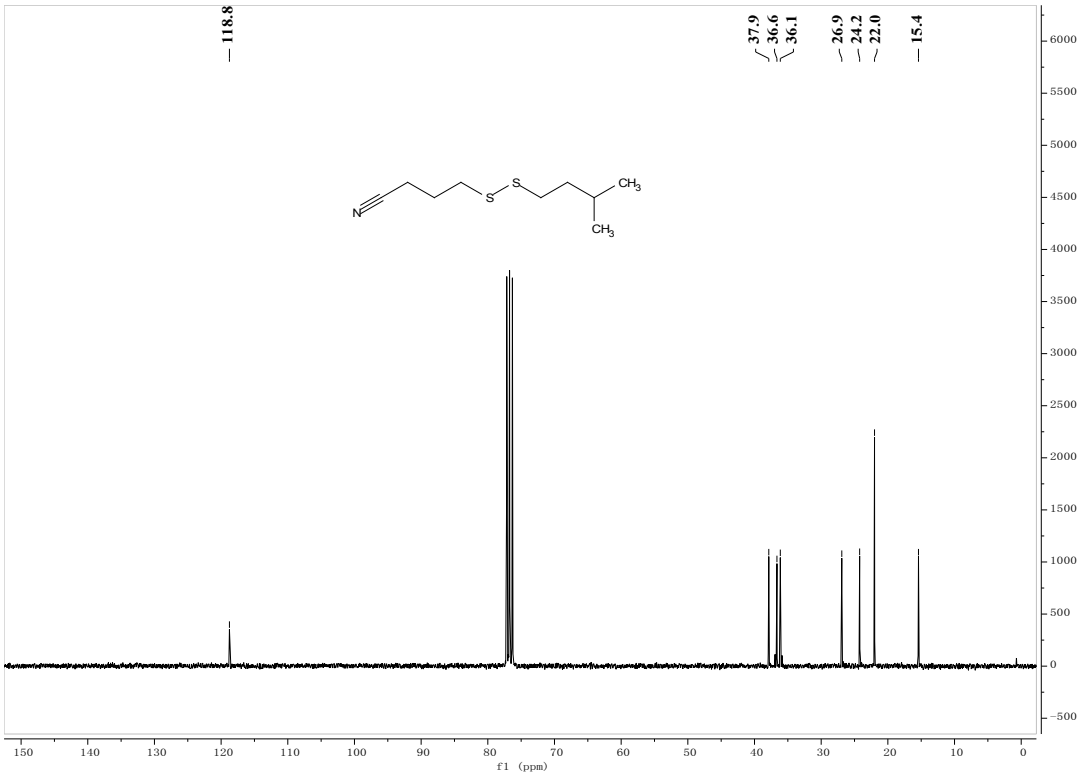


^{1}H-NMR (300 MHz, $CDCl_3$) of 4-(isopentyldisulfaneyl)butanenitrile (2c)



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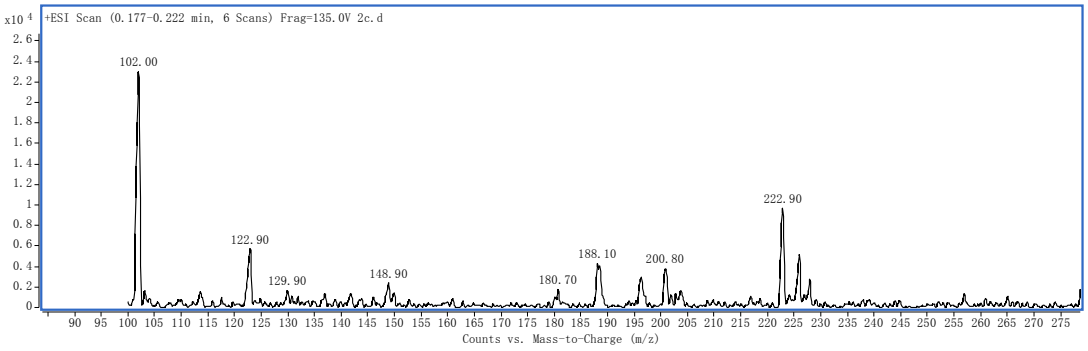

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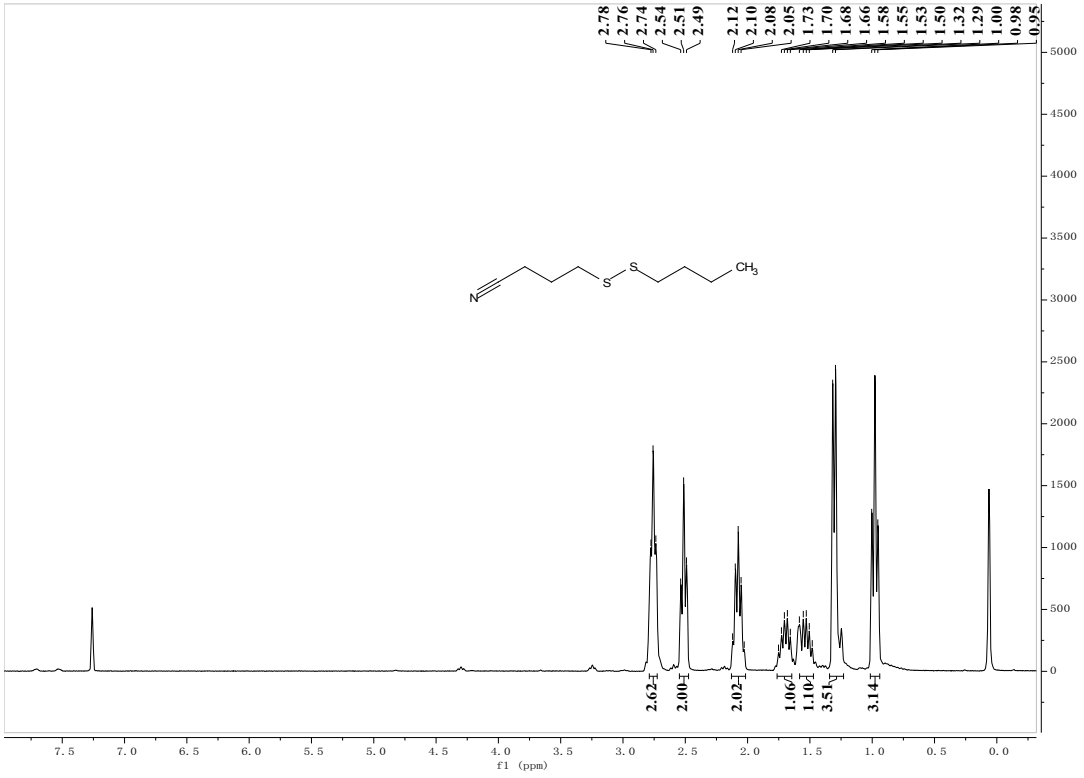

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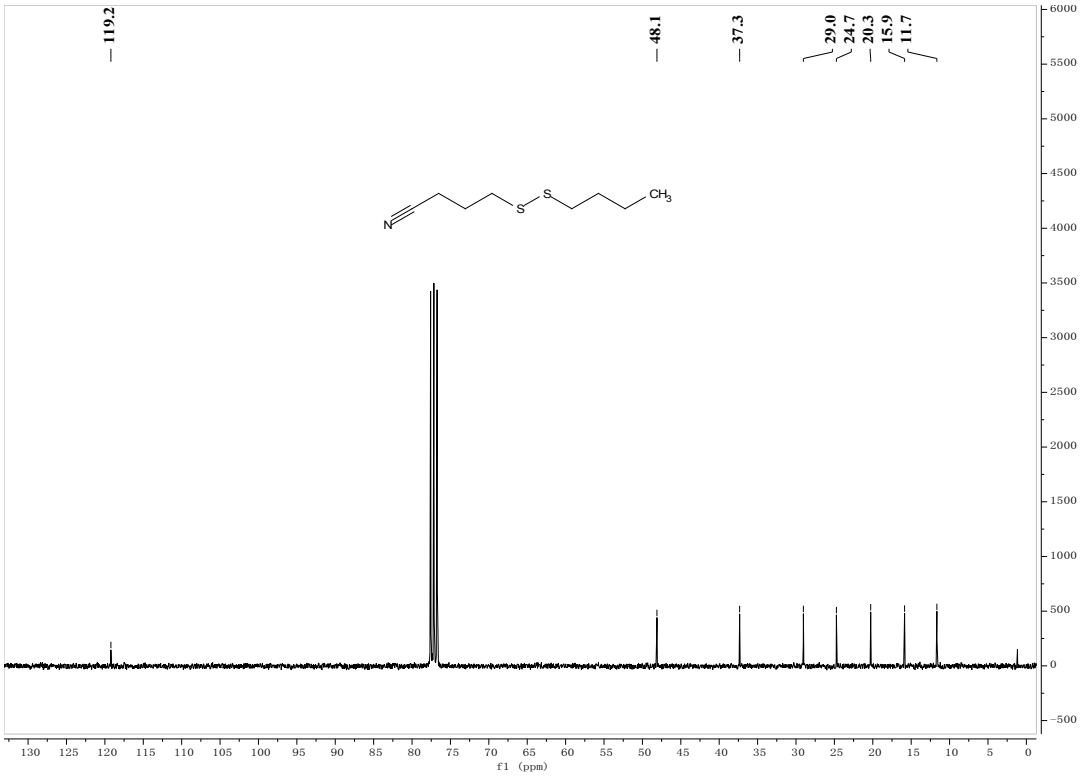

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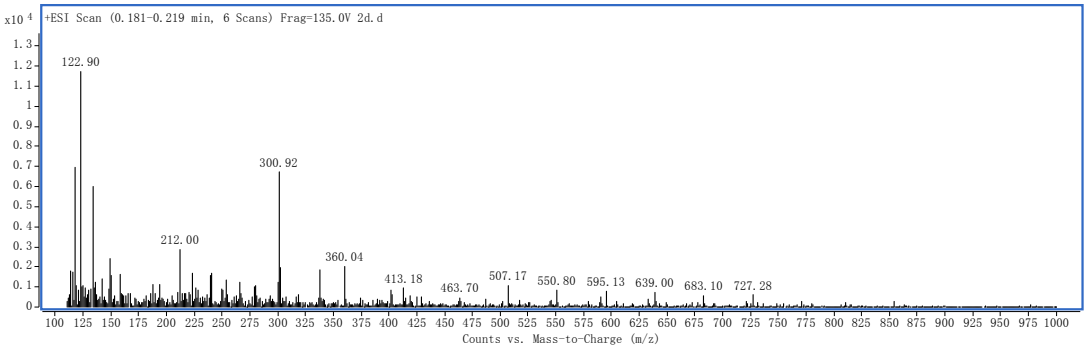

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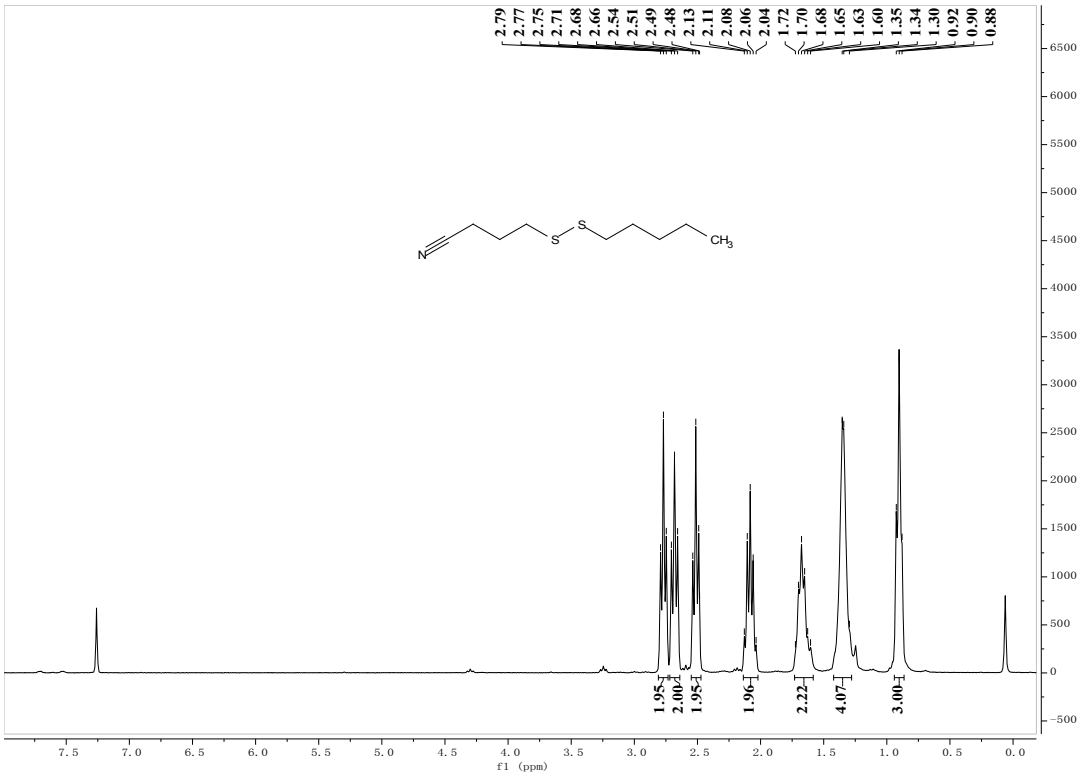

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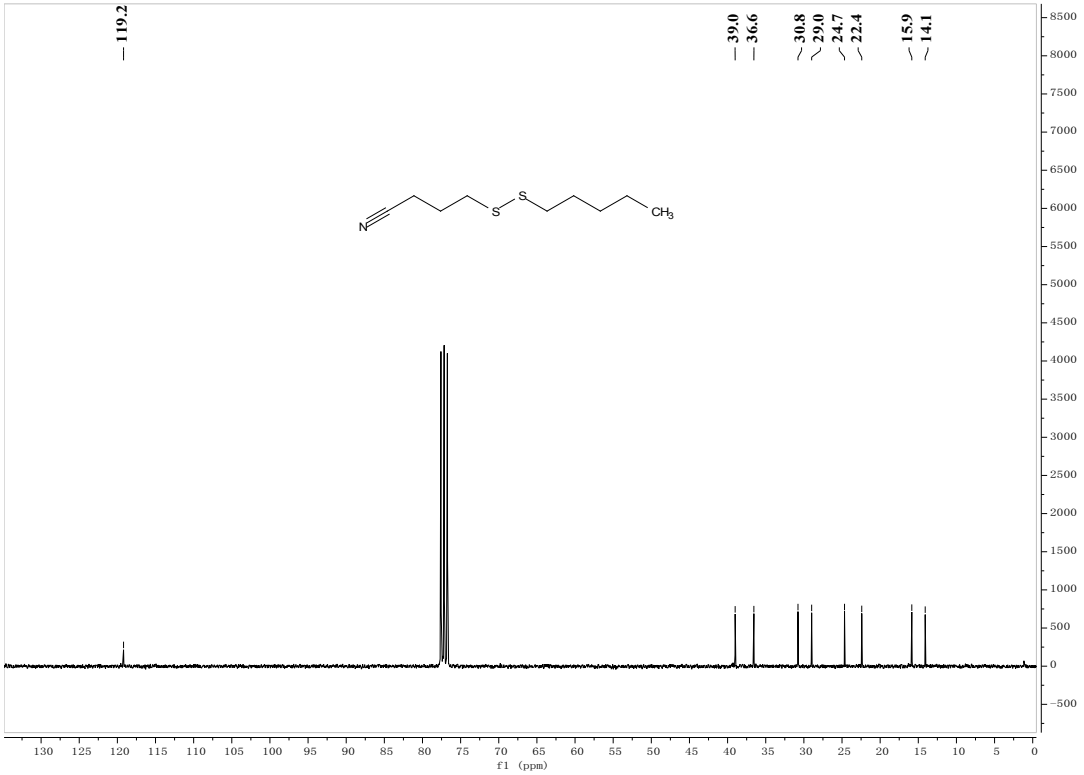

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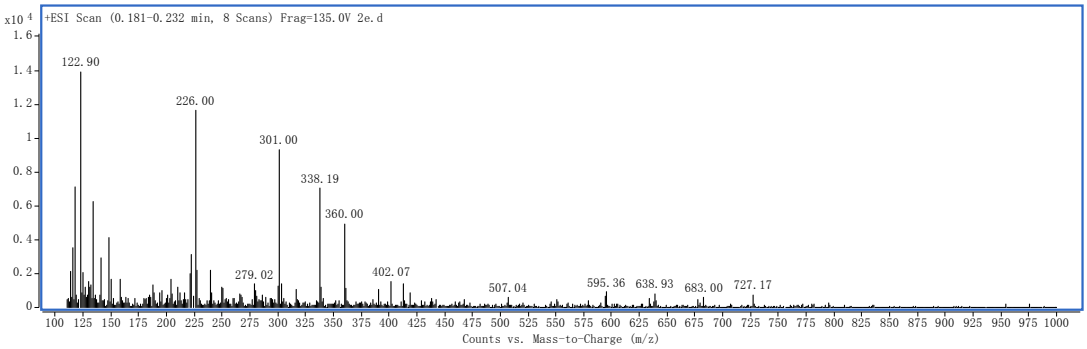

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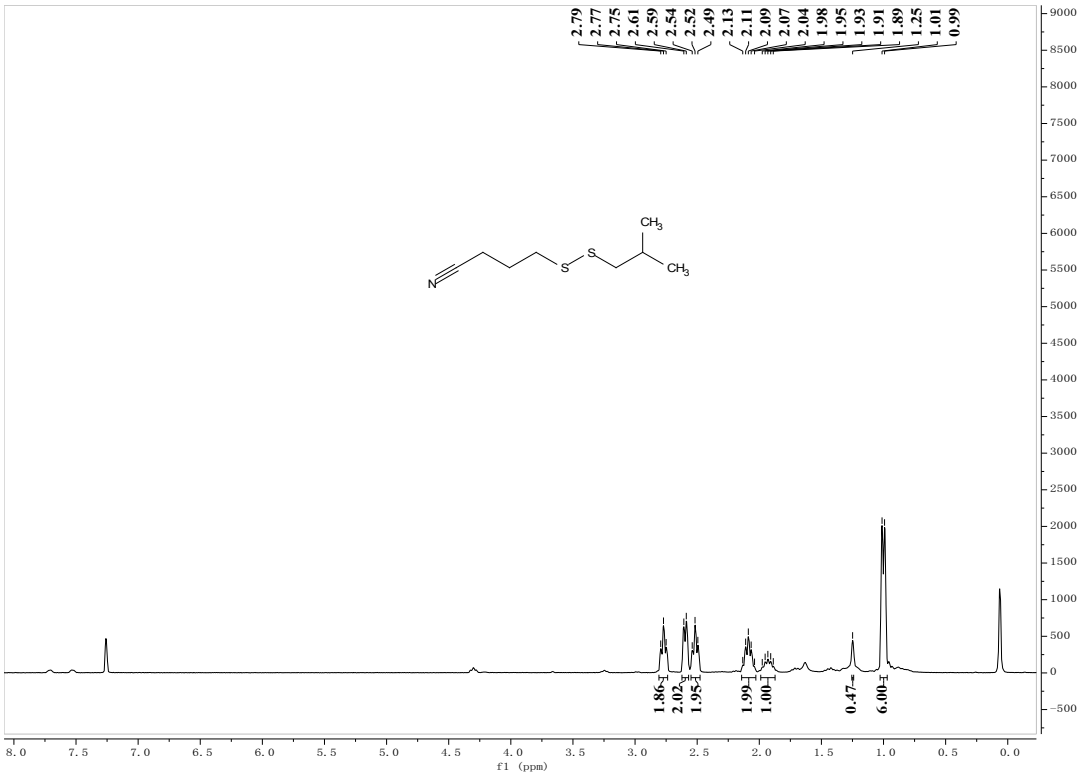

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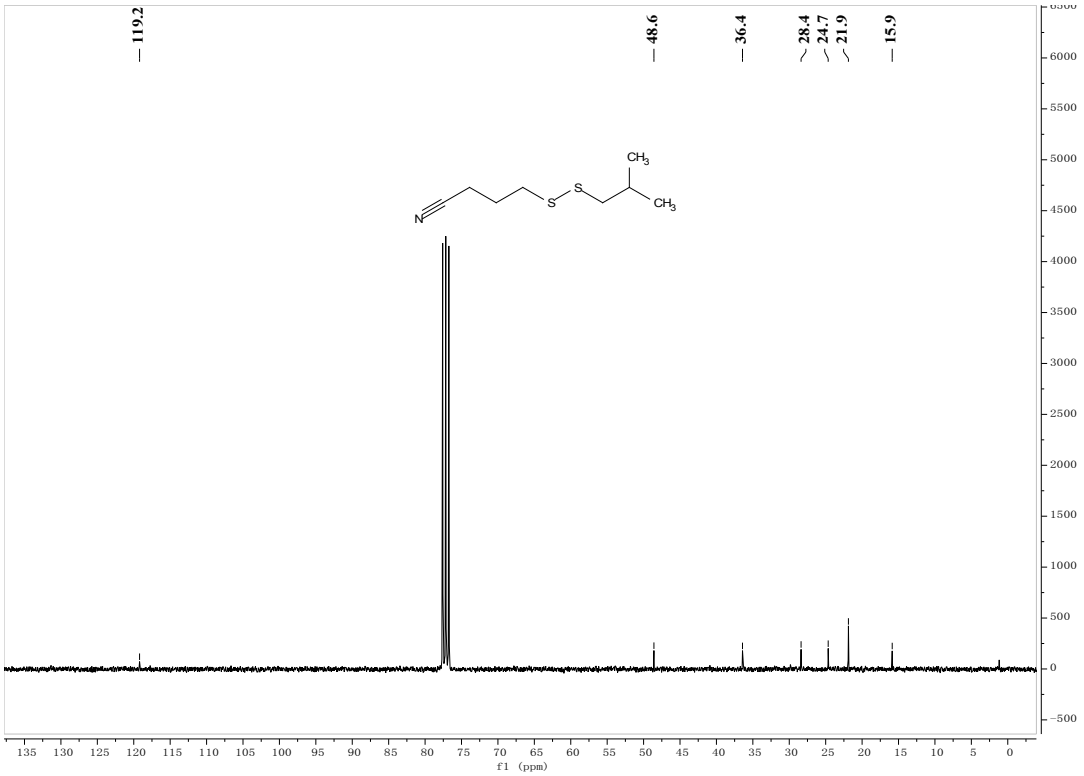

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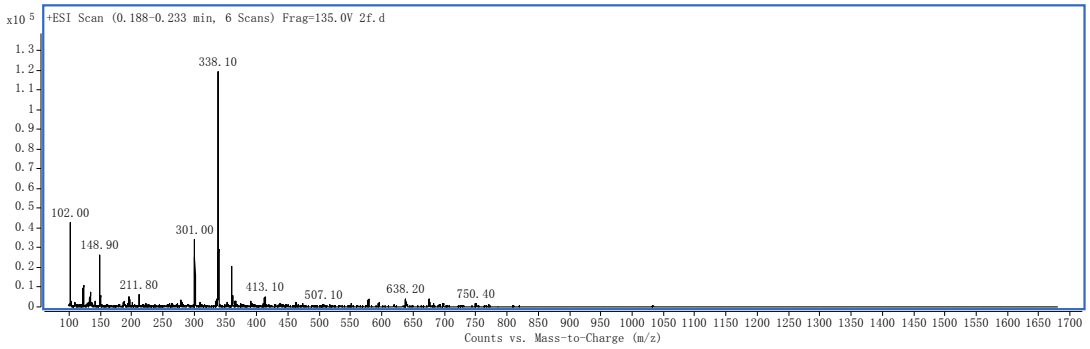

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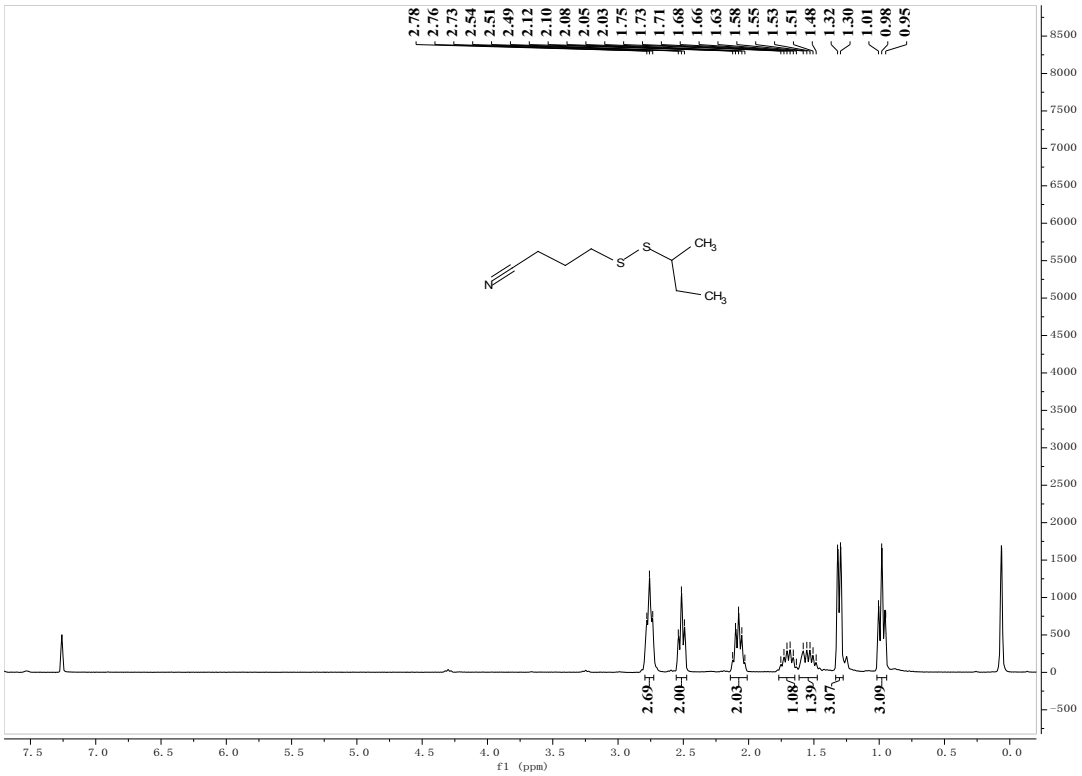

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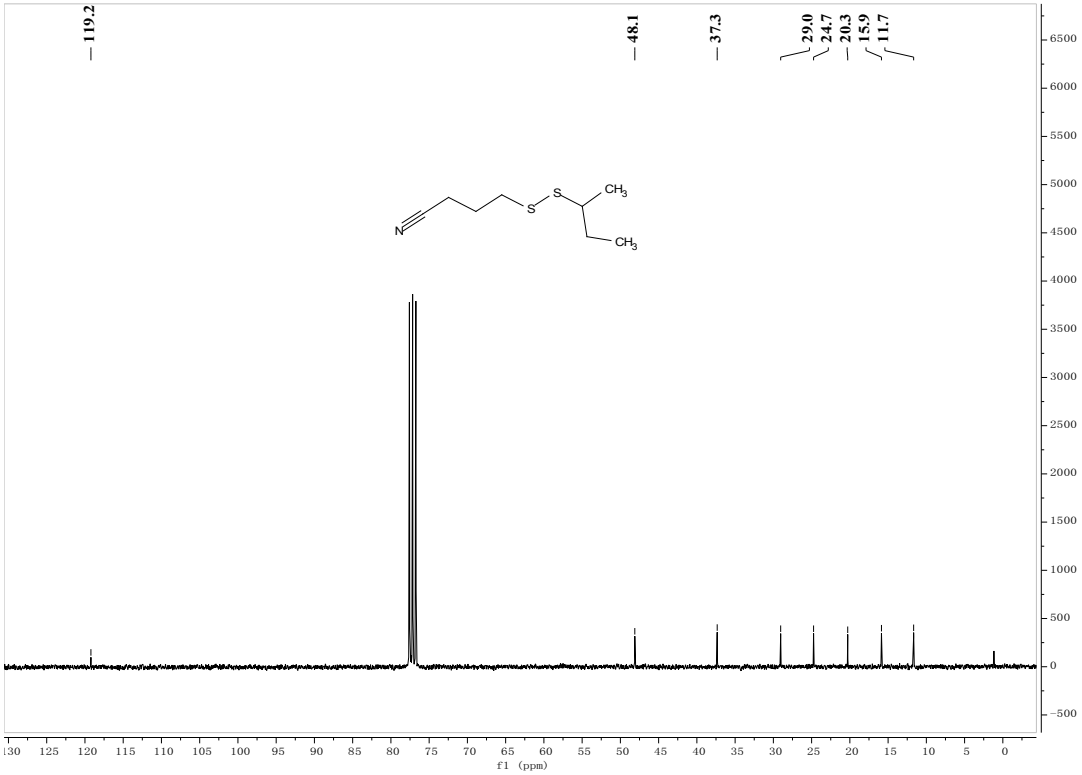

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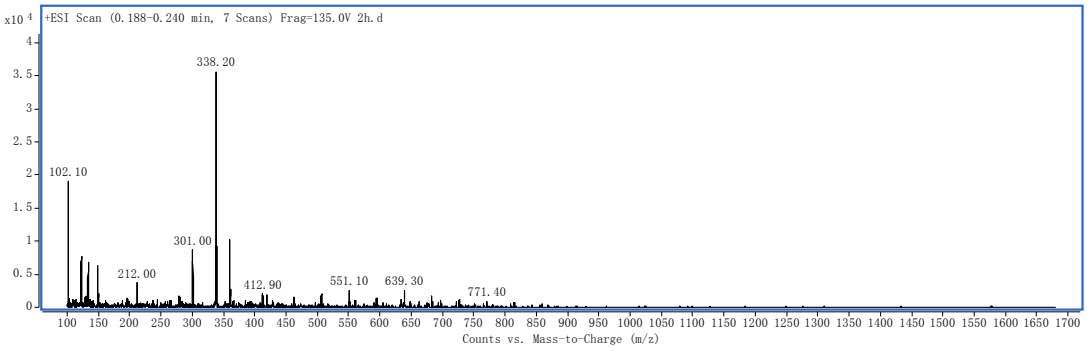
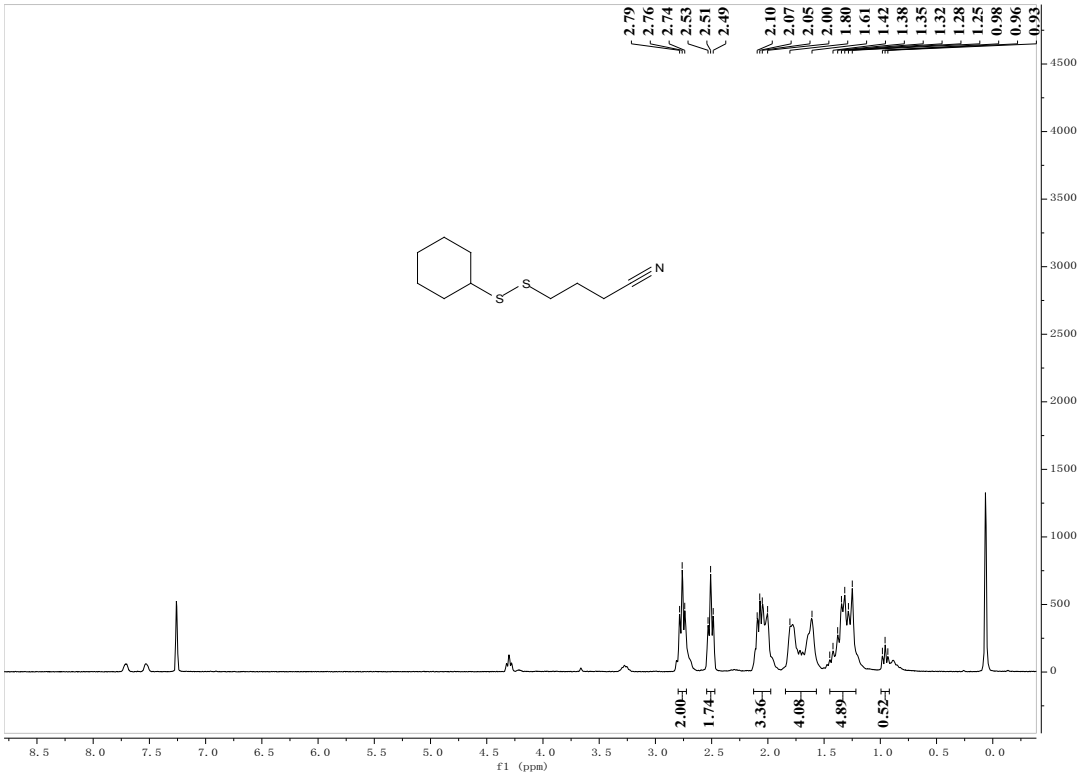


LC-MS of 4-(sec-butyldisulfaneyl)butanenitrile (2h)



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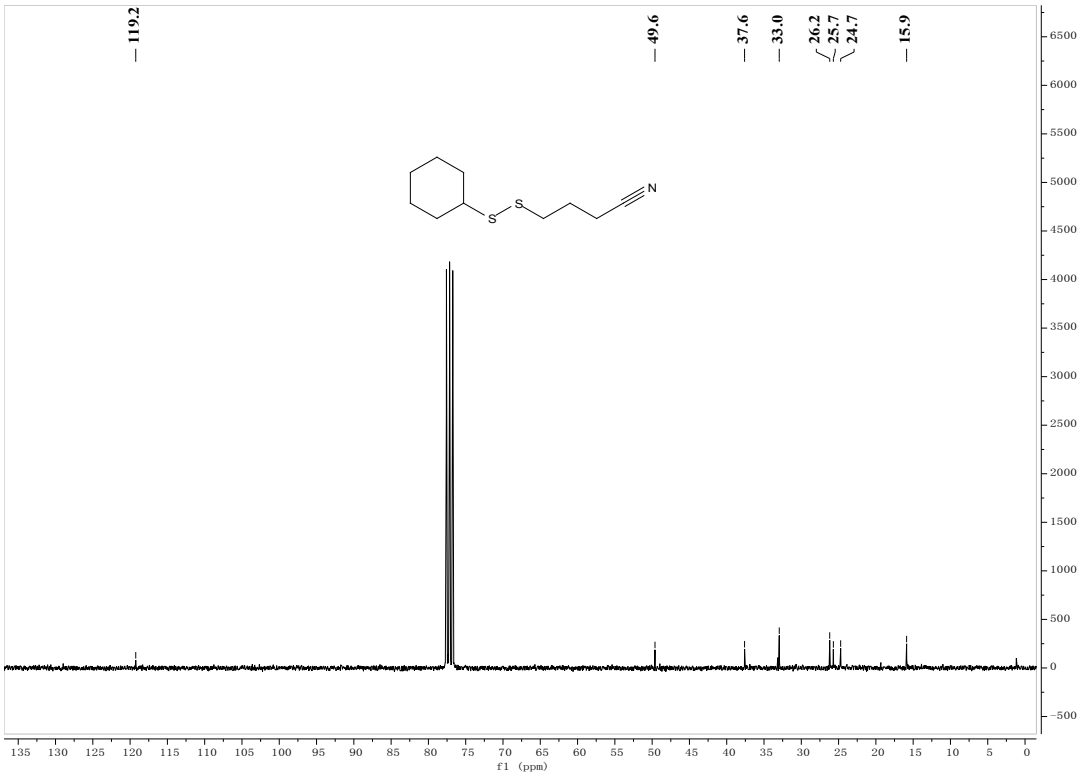

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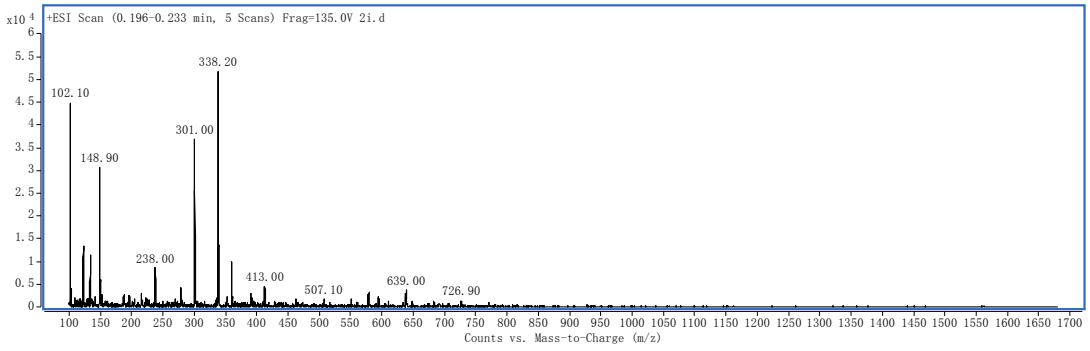

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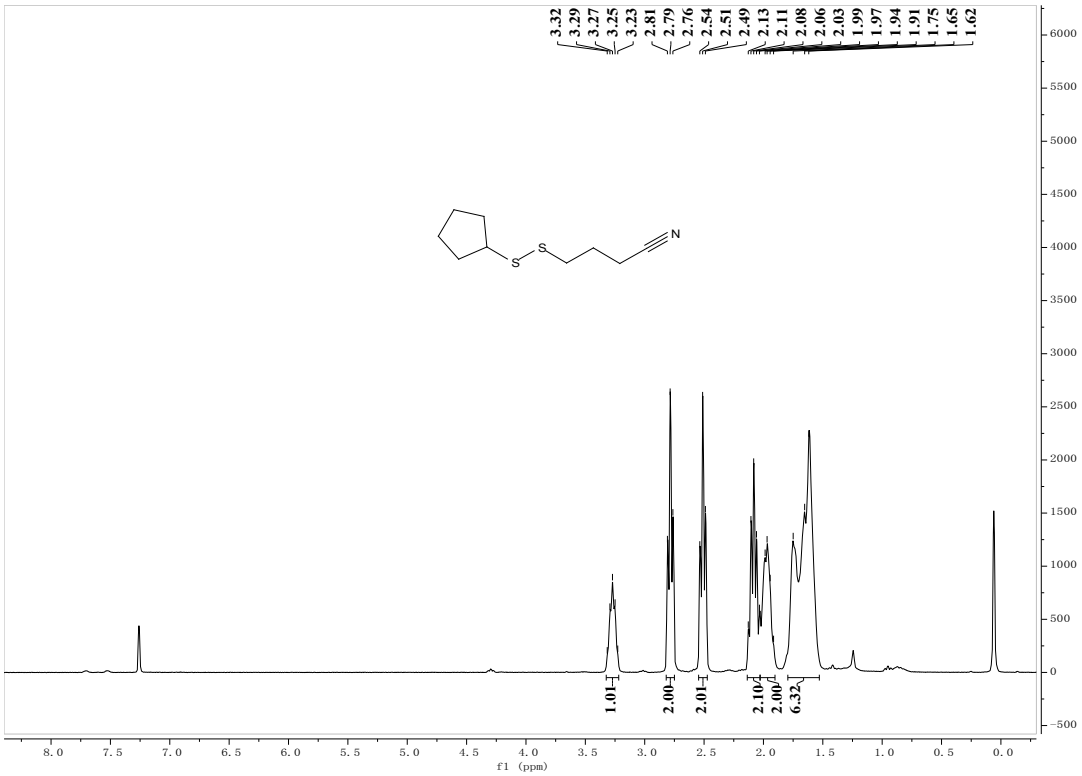
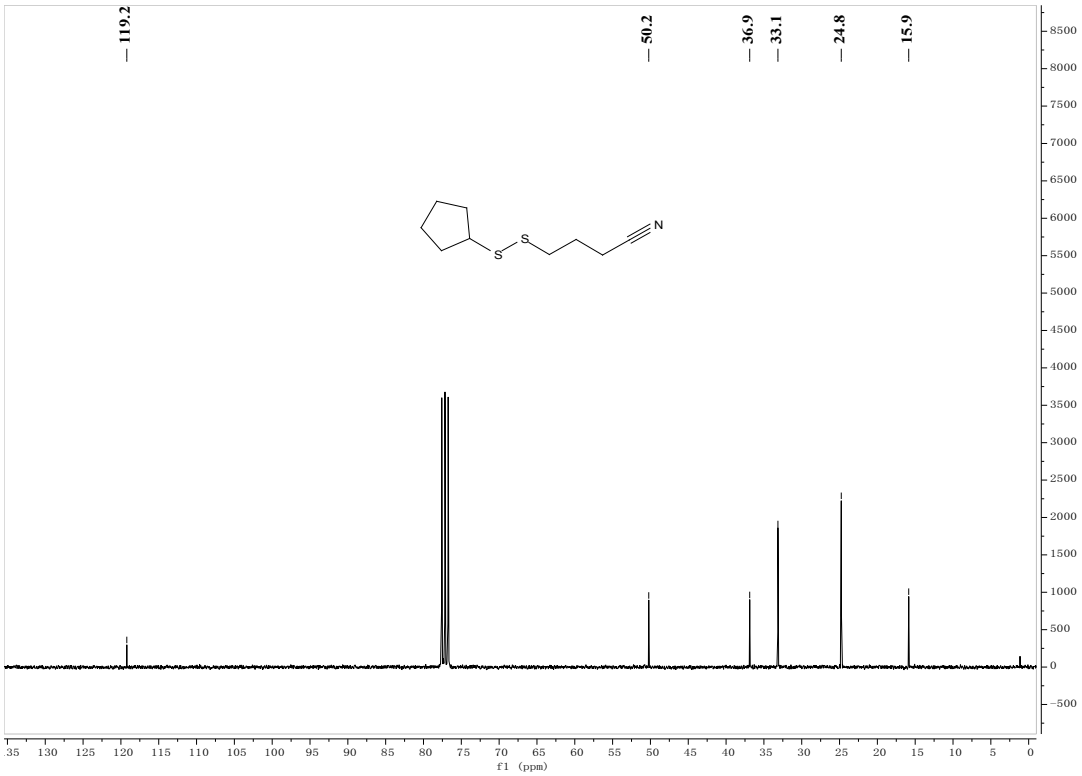
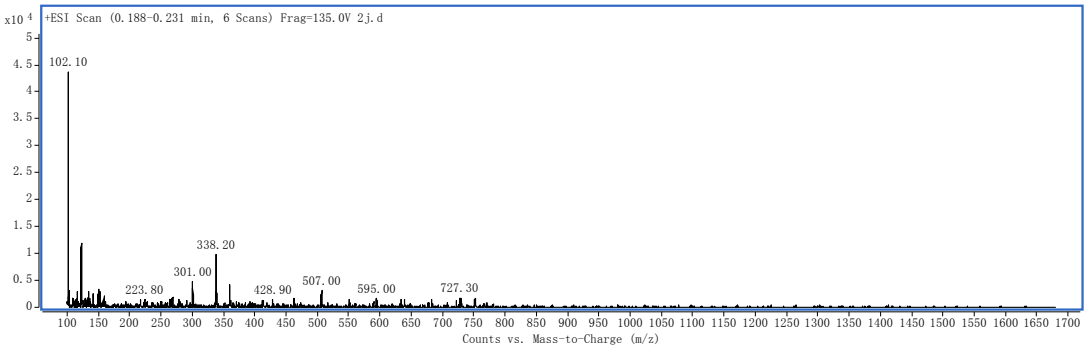


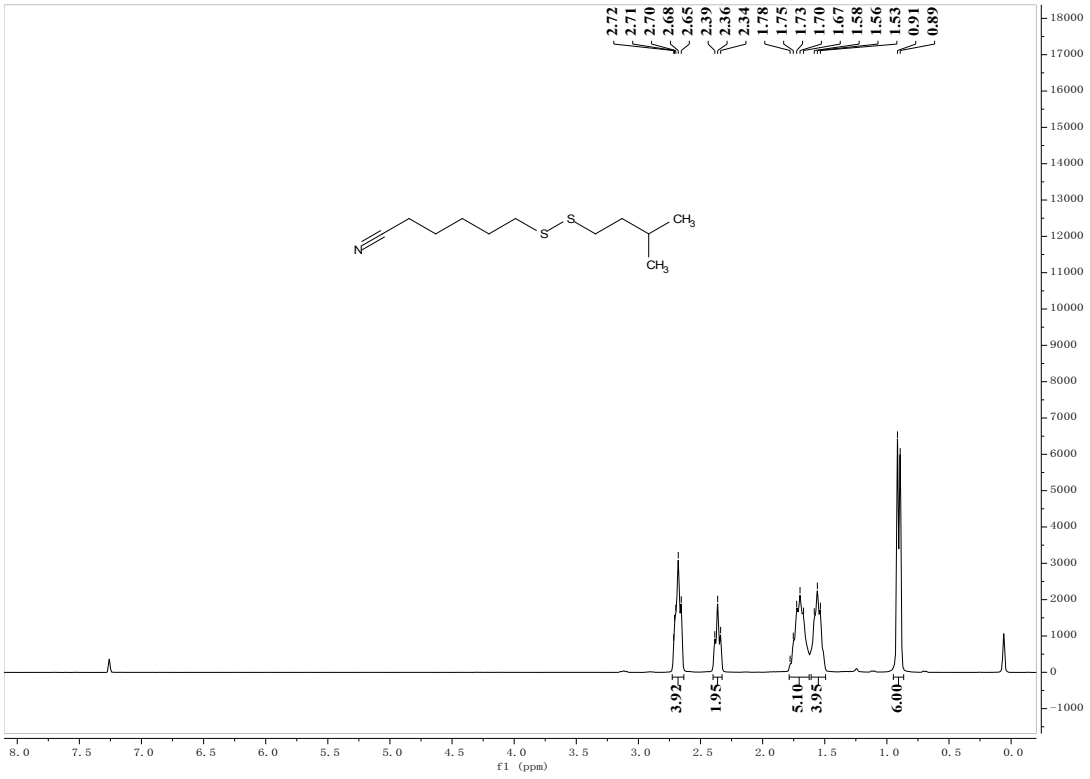
^{1}H-NMR (300 MHz, $CDCl_3$) of 4-(cyclopentyldisulfaneyl)butanenitrile (2j)



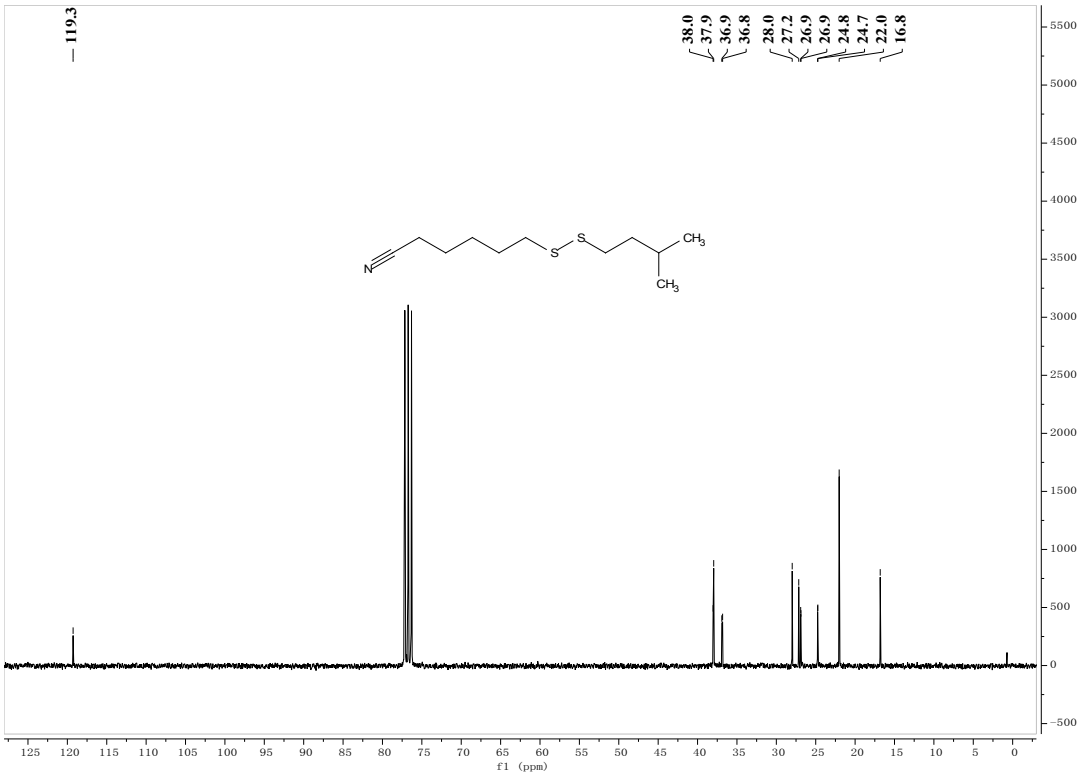
^{13}C-NMR (75 MHz, $CDCl_3$) of 4-(cyclopentyldisulfaneyl)butanenitrile (2j)



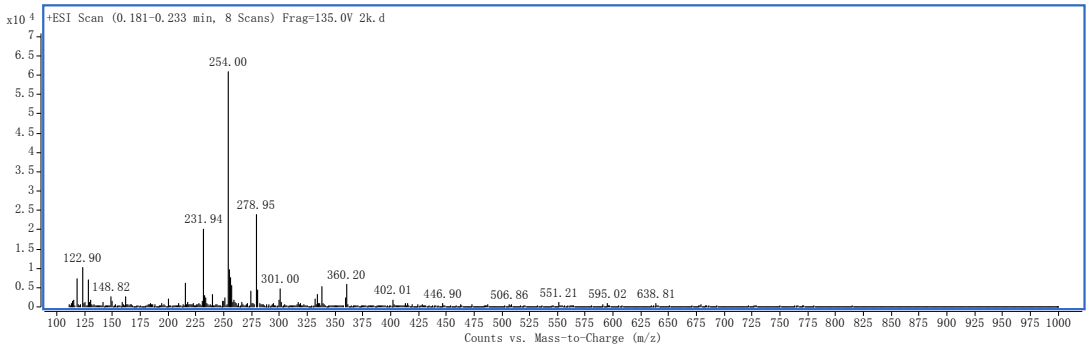
LC-MS of 4-(cyclopentyldisulfaneyl)butanenitrile (2j)



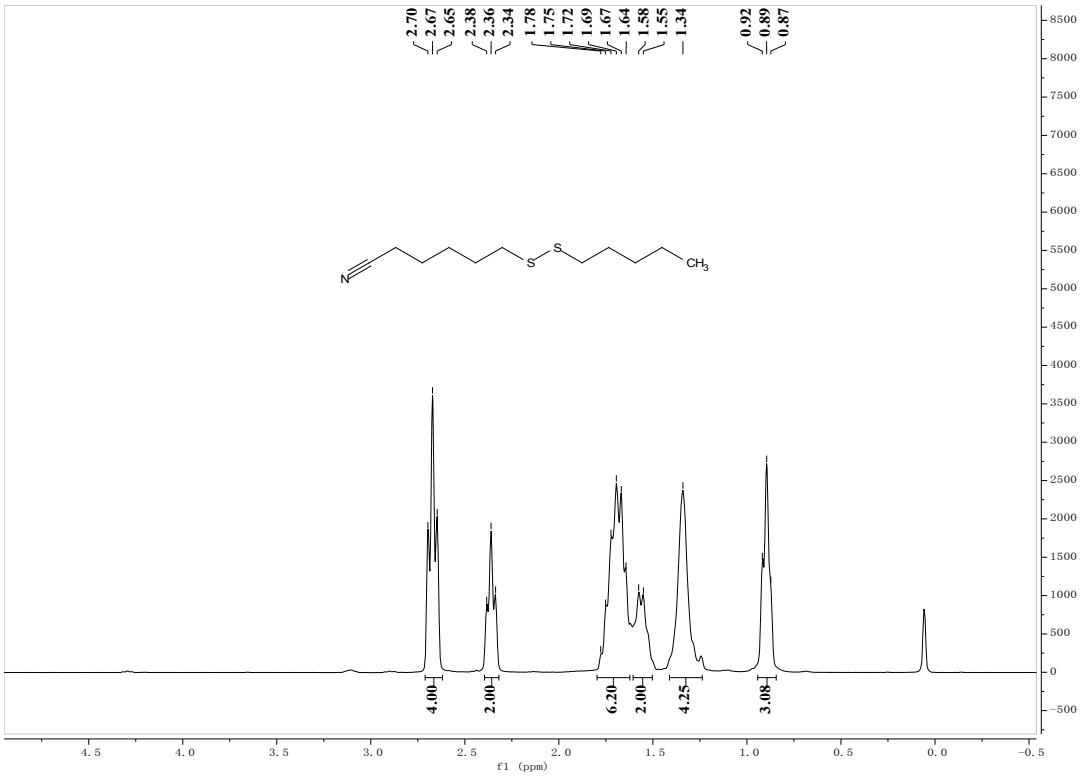
^{1}H-NMR (300 MHz, $CDCl_3$) of 6-(isopentyldisulfaneyl)hexanenitrile (2k)



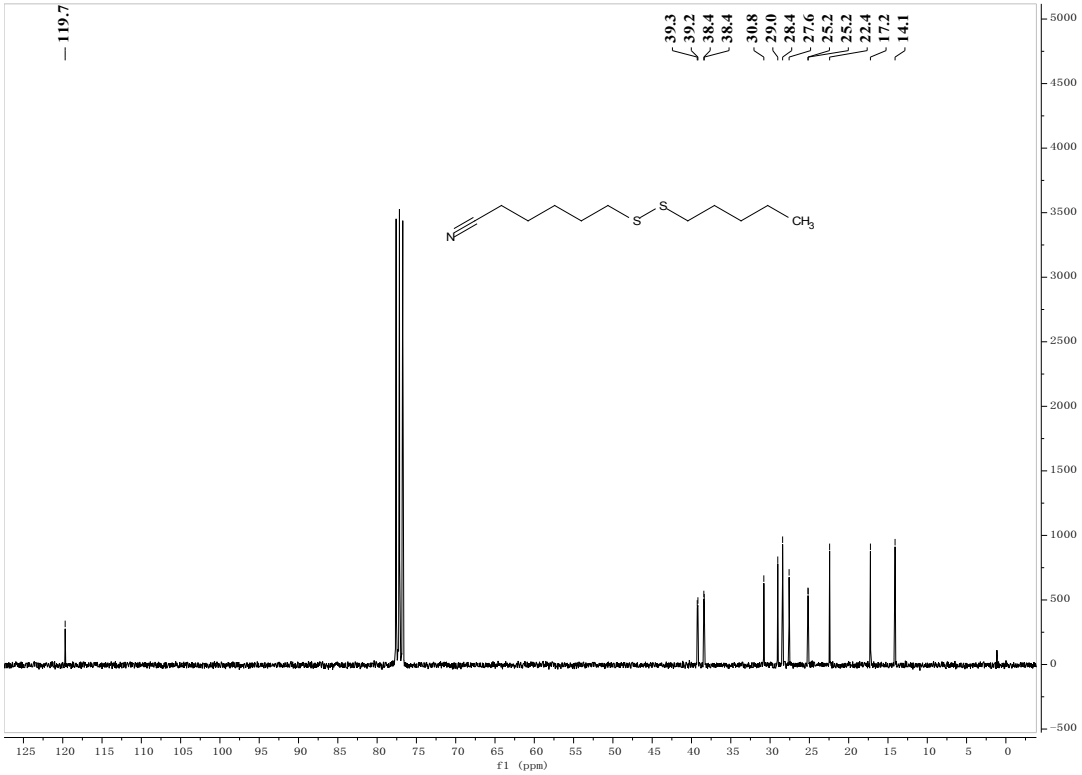
^{13}C-NMR (75 MHz, $CDCl_3$) of 6-(isopentyldisulfaneyl)hexanenitrile (2k)



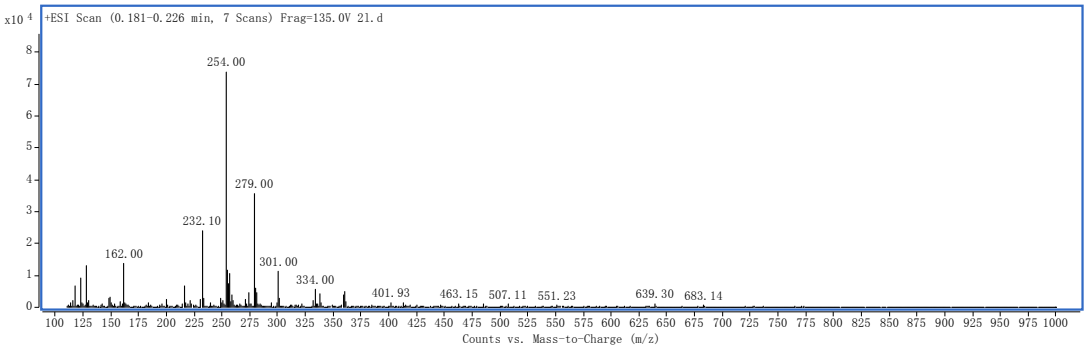
LC-MS of 6-(isopentyldisulfaneyl)hexanenitrile (2k)



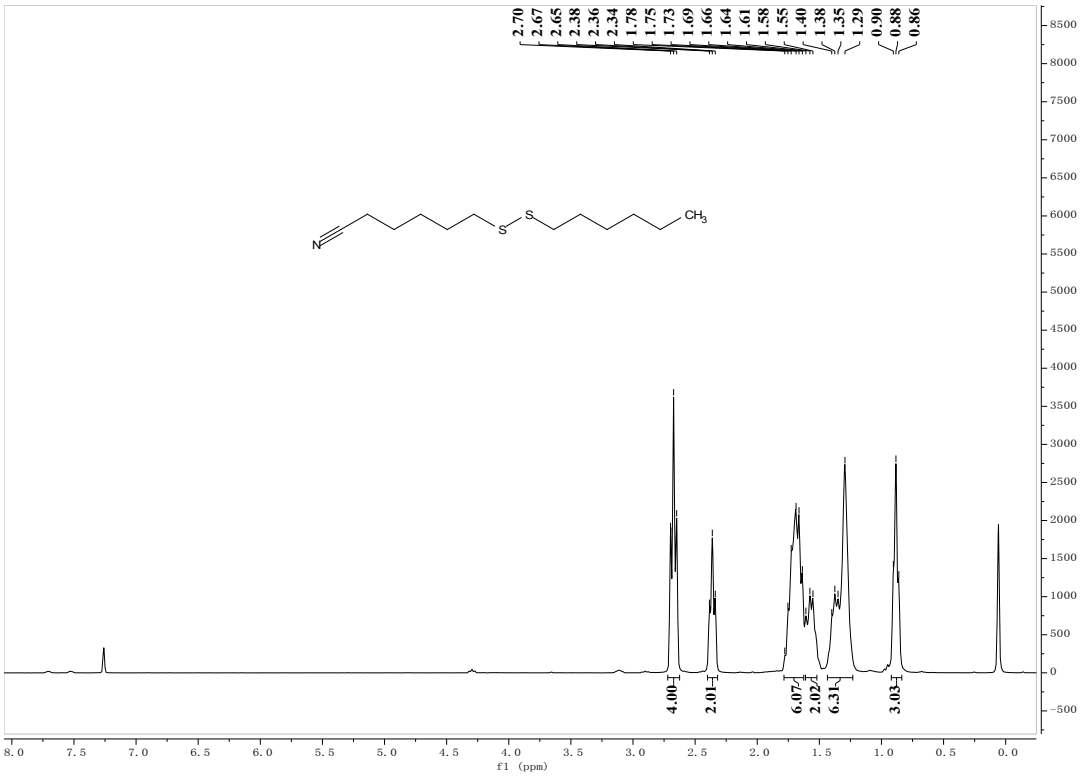
^{1}H-NMR (300 MHz, $CDCl_3$) of 6-(pentyldisulfaneyl)hexanenitrile (2l)



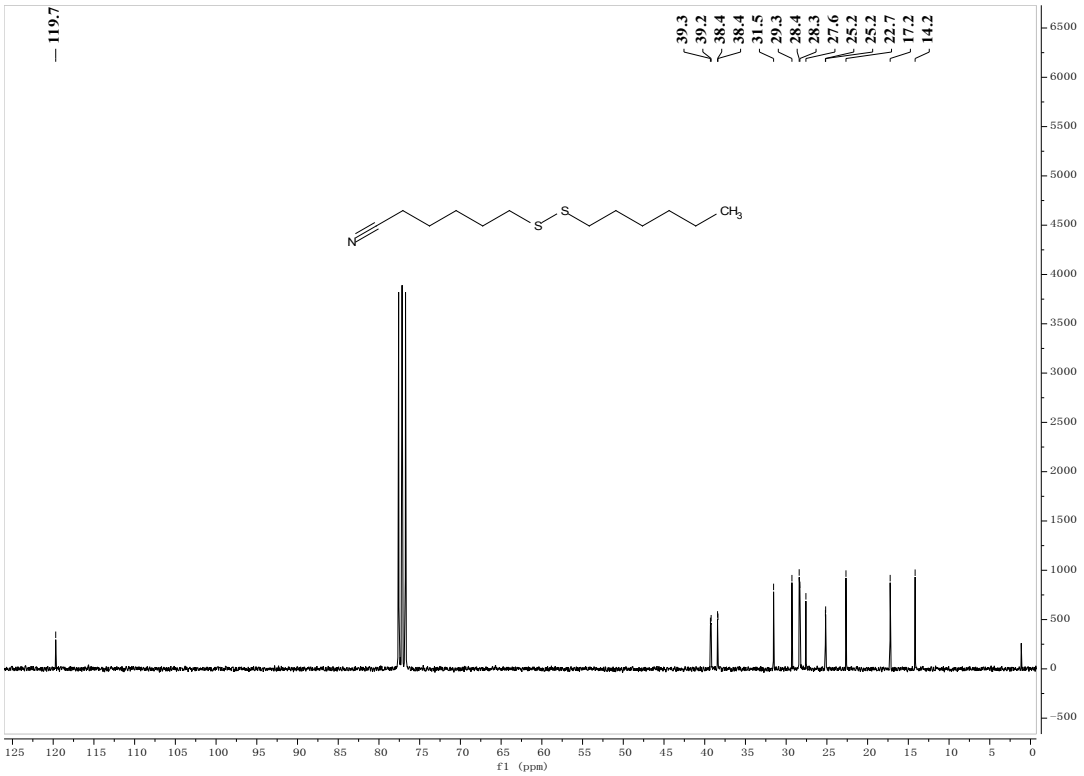
^{13}C-NMR (75 MHz, $CDCl_3$) of 6-(pentyldisulfaneyl)hexanenitrile (2l)



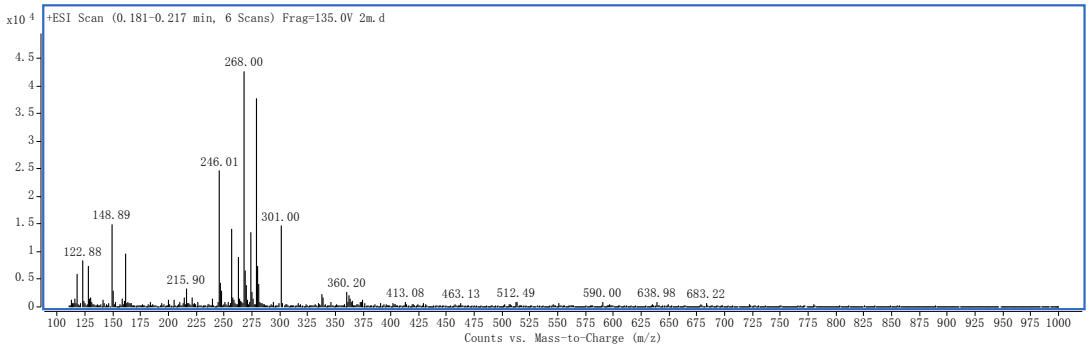
LC-MS of 6-(pentyldisulfaneyl)hexanenitrile (2l)



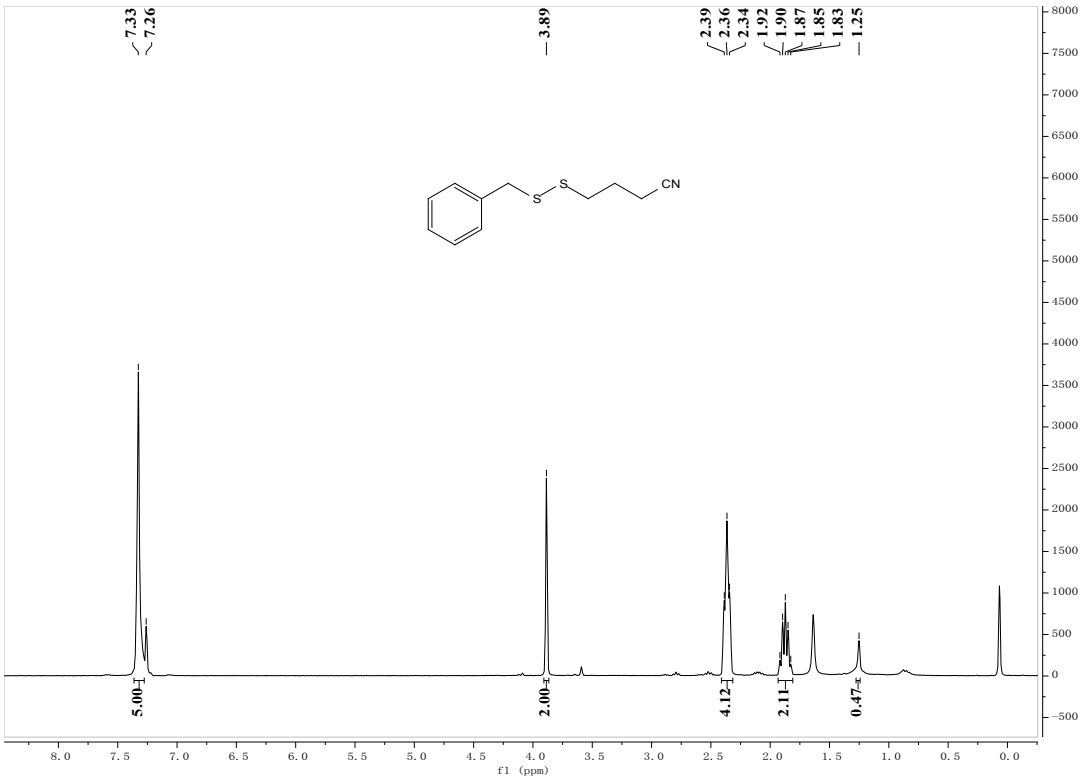
^{1}H-NMR (300 MHz, $CDCl_3$) of 6-(hexyldisulfaneyl)hexanenitrile (2m)



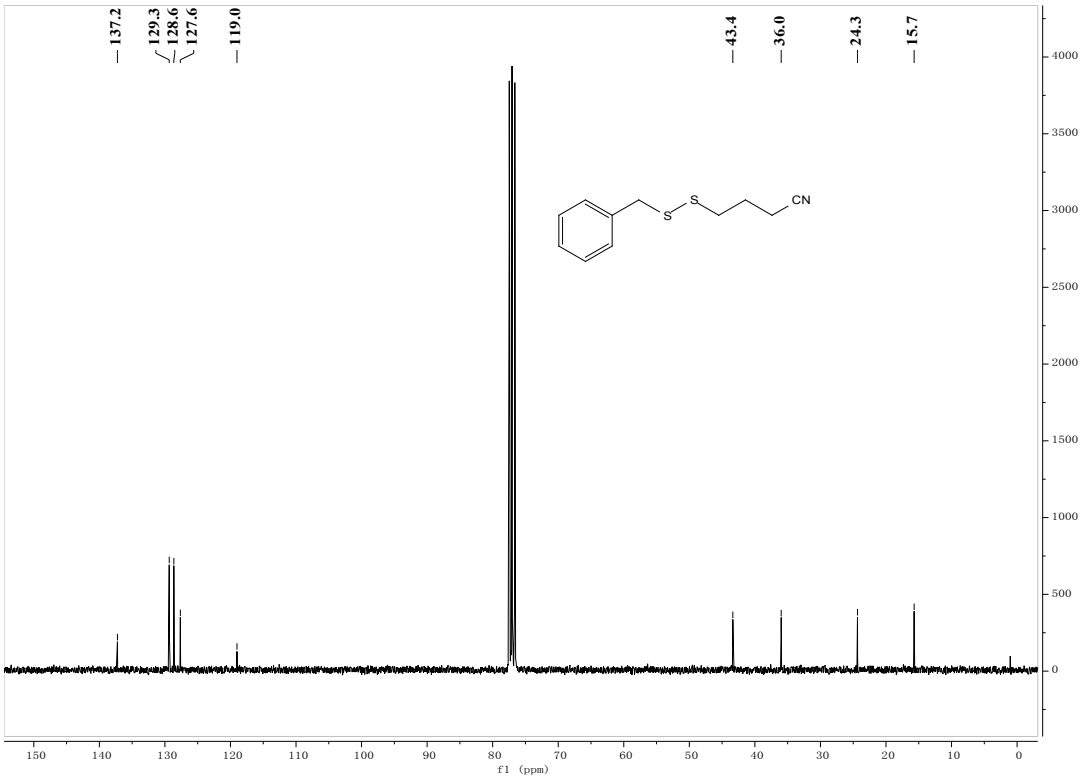
^{13}C-NMR (75 MHz, $CDCl_3$) of 6-(hexyldisulfaneyl)hexanenitrile (2m)



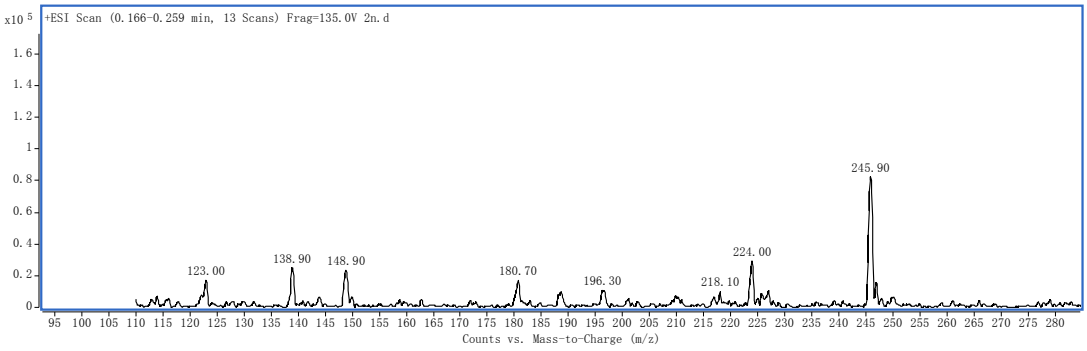
LC-MS of 6-(hexyldisulfaneyl)hexanenitrile (2m)



^{1}H-NMR (300 MHz, $CDCl_3$) of 4-(benzyldisulfaneyl)butanenitrile (2n)



^{13}C-NMR (75 MHz, $CDCl_3$) of 4-(benzyldisulfaneyl)butanenitrile (2n)



LC-MS of 4-(benzyldisulfaneyl)butanenitrile (2n)

6.Notes and references

1 X. Xiao, M. Feng and X. Jiang, *Chem. Commun.*, 2015, **51**, 4208-4211.