Supporting Information

Proteolytic adduct-cyclization facilitates site-centric target deconvolution of isothiocyanates

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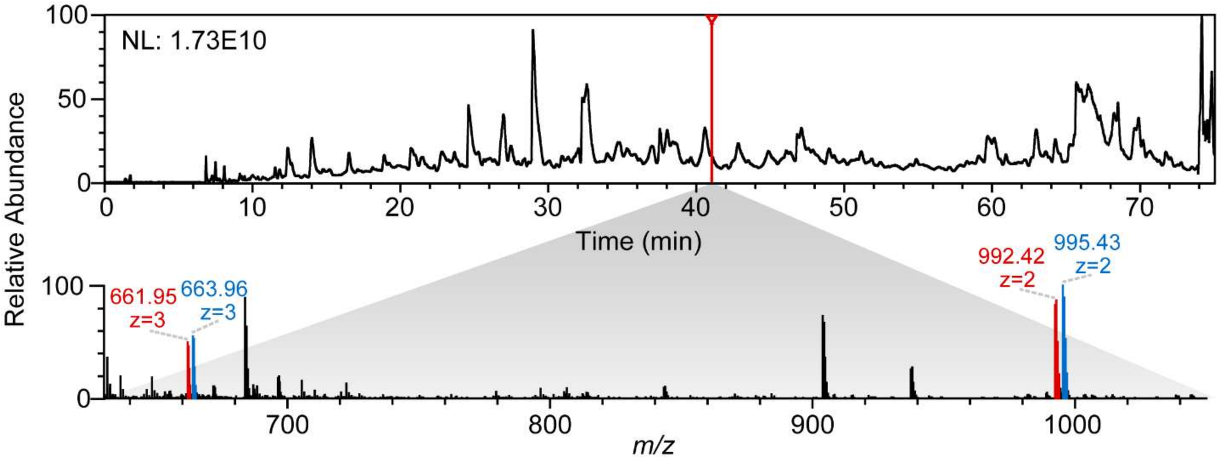
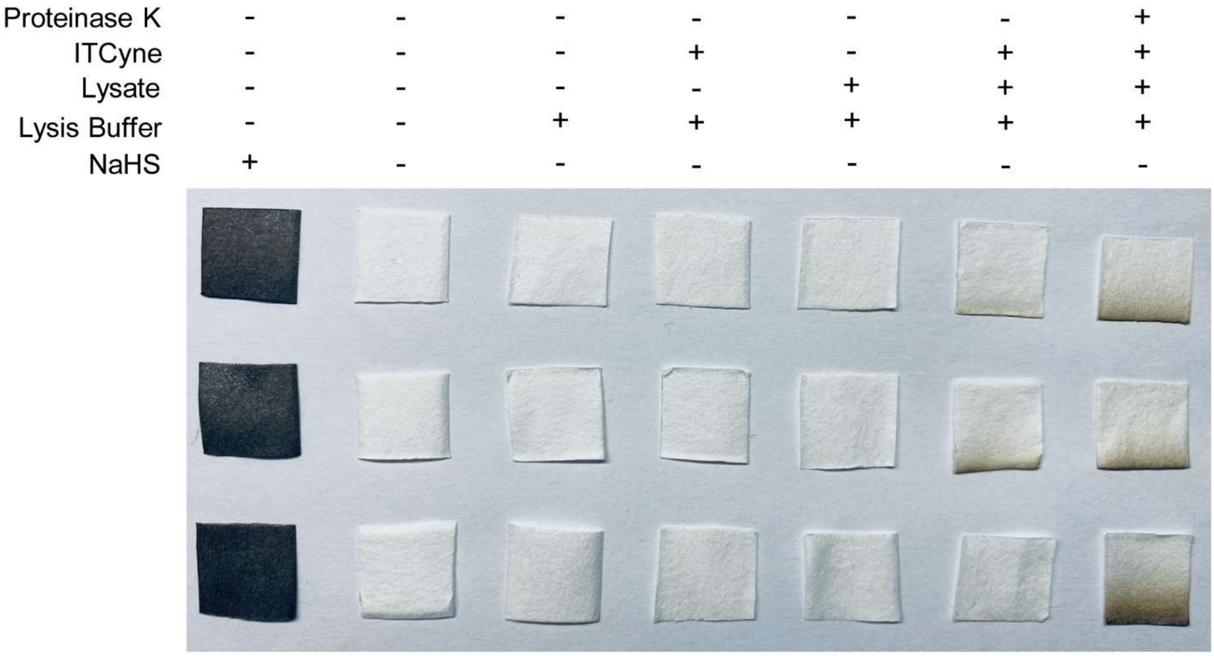
Supplementary Table 1. Reporting summary by pChem search of the data generated from ITCyne-based chemoproteomics. PSM: peptide-spectrum match.

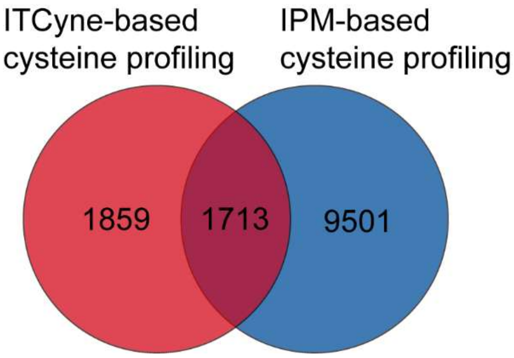
Rank	Accurate Mass	Top1 Site|Probability	Others	#PSM	#PSM L|H
1	220.09571	C|0.952	N-SIDE(0.71);	680	265|415



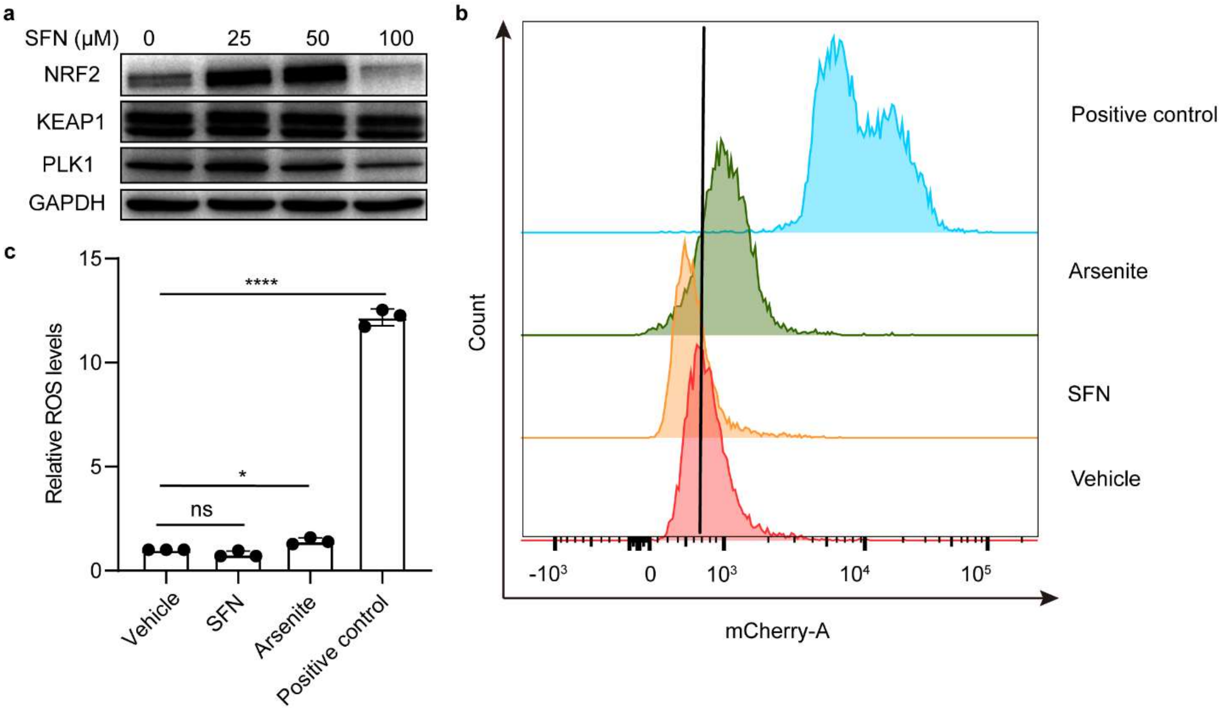
Supplementary Figure 1. Display of LC-MS/MS data from a representative thermo. Raw file. (**a**) The total ion current chromatogram showing that a large number of peaks are evenly distributed across a chromatographic time scale. NL, normalized intensity. (**b**) The full-scan MS spectrum of a randomly selected peak from a (denoted by the line in red color), showing a number of paired L (red) and H (blue) isotopic peaks with a m/z shift of 2 (charge 3+) or 3 (charge 2+). z = charge status.



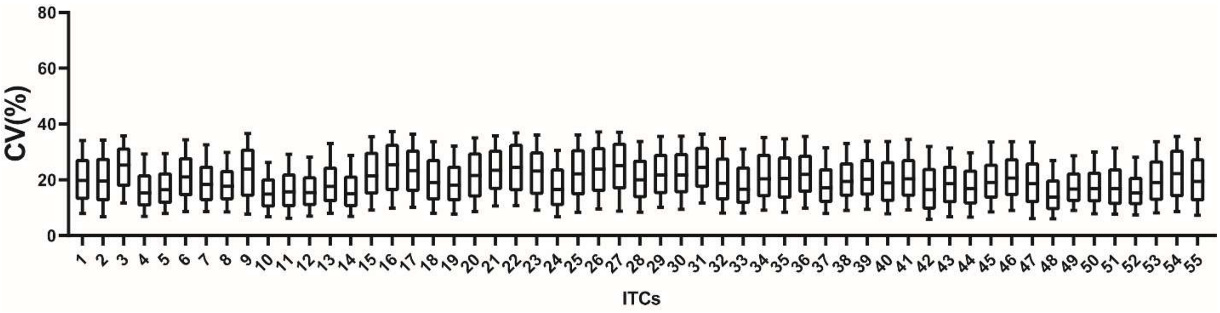
Supplementary Figure 2. H_2S production capacity of an isothiocyanate in cell lysates measured by lead acetate/lead sulfide assay.



Supplementary Figure 3. Venn diagram showing the coverage of sites mapped by using ITCyne- and IPM-based cysteine profiling. The ITCyne-based cysteine profiling was performed as described in the main text. The IPM-based cysteine profiling was performed in parallel as previously described (Fu L, *et al.*, *Nat Protoc*, 2020, 15: 2891-2919). Specifically, the same amount of starting material was incubated with 100 μM IPM for 1h, harvested and lysed. After proteolytic digestion with trypsin, the resulting peptides are reacted with azido biotin with a UV-cleavable linker (Az-UV-biotin). The biotinylated peptides are captured by streptavidin, and photoleased for LC-MS/MS analysis.



Supplementary Figure 4. (**a**) Representative immunoblots showing SFN-mediated biphasic NRF2 regulation. HEK293T cells were titrated with SFN at indicated concentration, while DMSO was used as vehicle control. The immunoblots are representative of three biological replicates. **(b-c)** Representative flow cytometry histogram (**b**) and quantification (**c**) of ROS levels in HEK293 cells treated with chemicals as indicated and vehicle control (See Methods for details).



Supplementary Figure 5. Reproducibility of ITCyne-based QTRP analysis. Boxplots showing the distribution of CV values of the $R_{\text{control/compound}}$ (or $R_{\text{H/L}}$) values determined for each ITC compound. Data was obtained from at least three replicates. Lines in boxes denote median values and whisker lines denote the 25th and 75th percentiles.

General synthetic methods

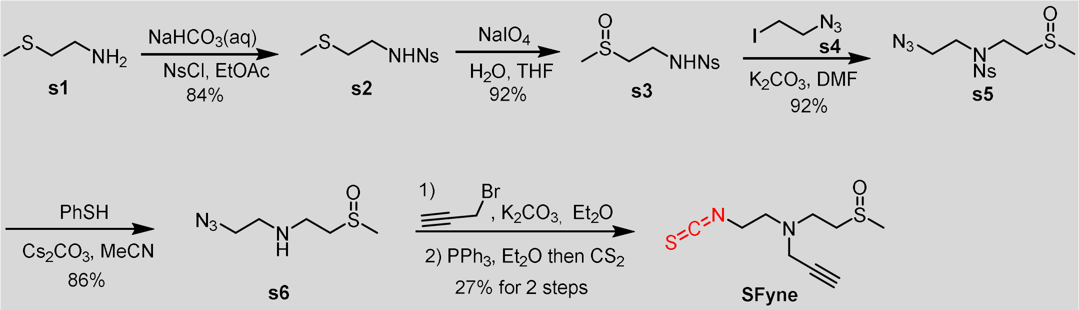
Instrumentation and methods

^{1}H NMR spectra were recorded on a Bruker 400 MHz spectrometer at ambient temperature with $CDCl_3$ as the solvent unless otherwise stated. ^{13}C NMR spectra were recorded on a Bruker 100 MHz spectrometer (with complete proton decoupling) at ambient temperature. Chemical shifts are reported in parts per million related to chloroform (^{1}H, δ 7.26; ^{13}C, δ 77.00). Data for ^{1}H NMR are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants and integration. High-resolution mass spectra were obtained at the Peking University Mass Spectrometry Laboratory using a Bruker Fourier Transform Ion Cyclotron Resonance Mass Spectrometer Solarix XR and using a TripleTOF 6600 Quadrupole Time of Flight Mass Spectrometer at the Shenzhen Bay Laboratory Mass Spectrometry Center. The samples were analyzed by HPLC/MS on a Waters Auto Purification LC/MS system (3100 Mass Detector, 2545 Binary Gradient Module, 2767 Sample Manager, and 2998 Photodiode Array (PDA) Detector). The system was equipped with a Waters C18 5m SunFire separation column (150*4.6 mm), equilibrated with HPLC grade water (solvent A) and HPLC grade acetonitrile (solvent B) with a flow rate of 0.3 mL/min. Analytical thin layer chromatography was performed using 0.25 mm silica gel 60–F plates. Flash chromatography was performed using 200-400 mesh silica gel. Yields refer to chromatographically and spectroscopically pure materials, unless otherwise stated.

Reagents and solvents

All chemical reagents were used as supplied by Sigma–Aldrich, J&K, Alfa Aesar Chemicals, Bidepharm, Aladdin and Energy chemicals. Anhydrous DCM with molecular sieves was purchased from Adamas. All reactions were carried out in oven-dried glassware under an argon atmosphere.

Synthesis of SFyne.



To a stirred solution of Compound **s1** (0.91 g, 10 mmol, 1 eq) in EtOAc (10 mL) and sat. NaHCO3 (10 mL) at RT was added NsCl (3.09 g, 13 mmol, 1.3 eq). After stirring for 3 h, the organic phase was washed with brine (5 mL) and dried over Na2SO4. The crude product was purified by column chromatography (SiO2, eluent: PE/EA=6:1 to 2:1) to afford product **s2** (2.32 g, 8.4 mmol, 84%) as colorless oil. 1H NMR (400 MHz, CDCl3) δ 8.20 – 8.09 (m, 1H), 7.93 – 7.85 (m, 1H), 7.83 – 7.71 (m, 2H), 6.17 (s, 1H), 3.74 – 3.57 (m, 2H), 3.11 – 3.02 (m, 1H), 2.88 (dt, J = 29.0, 11.5 Hz, 1H), 2.65 (s, 3H). 13C NMR (101 MHz, DMSO) δ 147.8, 134.3, 132.8, 132.3, 129.6, 124.6, 52.9, 38.1, 36.7. ESI+-MS: [M+H]+ calculated for C9H13N2O4S2+: 277.0311; found: 277.0314.

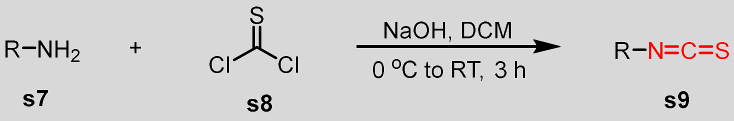
To a stirred solution of Compound **s2** (1.38 g, 5 mmol, 1 eq) in THF (10 mL) and H2O (10 mL) at RT was added NaIO4 (2.14 g, 10 mmol, 2 eq). After stirring for 3 h, the solution was added EtOAc (20 mL) and sat. Na2S2O3(20 mL), the organic phase washed with brine (5 mL) and dried over Na2SO4. The crude product was purified by column chromatography (SiO2, eluent: PE/EA=5:1 to 2:1) to afford product **s3** (1.34 g, 4.6 mmol, 92%) as white solid. 1H NMR (400 MHz, CDCl3) δ 8.18 – 8.09 (m, 1H), 7.93 – 7.85 (m, 1H), 7.79 – 7.70 (m, 2H), 5.79 (s, 1H), 3.32 (q, J = 6.2 Hz, 2H), 2.65 (t, J = 6.5 Hz, 2H), 2.03 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 148.0, 133.7, 133.6, 132.8, 130.9, 125.4, 42.1, 33.7, 14.9. ESI+-MS: [M+H]+ calculated for C9H13N2O5S2+: 293.0260; found: 293.0257.

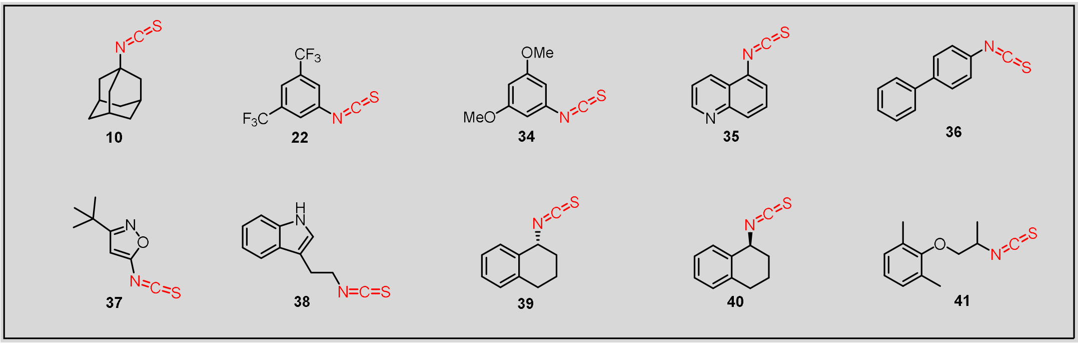
To a stirred solution of Compound **s3** (584 mg, 2 mmol, 1 eq) and Compound **s4** (591 mg, 3 mmol, 1.5 eq) in DMF (6 mL) at RT was added K2CO3 (552 mg, 4 mmol, 2 eq). After stirring for 3 h, the solution was added EtOAc (20 mL) and the organic phase washed with brine (10 mL x 3) and dried over Na2SO4. The crude product was purified by column chromatography (SiO2, eluent: PE/EA=6:1 to 2:1) to afford product **s5** (664 mg, 1.84 mmol, 92%) as colorless oil. 1H NMR (400 MHz, CDCl3) δ 8.06 – 7.98 (m, 1H), 7.78 – 7.68 (m, 2H), 7.68 – 7.61 (m, 1H), 3.82 – 3.71 (m, 2H), 3.56 – 3.47 (m, 4H), 3.09 (dt, J = 15.2, 7.6 Hz, 1H), 2.99 – 2.87 (m, 1H), 2.60 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 148.0, 134.2, 132.0, 131.8, 130.8, 124.3, 53.0, 49.8, 48.0, 42.5, 38.6. ESI+-MS: [M+H]+ calculated for C11H16N5O5S2+: 362.0587; found: 362.0584.

To a stirred solution of Compound **s5** (361 mg, 1 mmol, 1 eq) in ACN (4 mL) at RT was added 3-Bromopropyne (330 mg, 3 mmol, 3 eq) and Cs2CO3 (652 mg, 2 mmol, 2 eq). After stirring for 16 h, the solution was added EtOAc (20 mL) and the organic phase washed with brine (10 mL) and dried over Na2SO4. The crude product was purified by column chromatography (SiO2, eluent: DCM/MeOH=100:1 to 22:1) to afford product **s6** (151 mg, 0.86 mmol, 86%) as colorless oil. 1H NMR (400 MHz, CDCl3) δ 3.48 – 3.33 (m, 2H), 3.21 – 3.03 (m, 2H), 2.88 – 2.72 (m, 4H), 2.59 (s, 3H), 1.69 (s, 1H). 13C NMR (101 MHz, CDCl3) δ 54.7, 51.1, 48.3, 42.9, 38.9. ESI+-MS: [M+H]+ calculated for C5H13N4OS+: 177.0804; found: 177.0801.

To a stirred solution of Compound **s6** (88 mg, 0.5 mmol, 1 eq) in ether (2 mL) at RT was added PhSH(119 mg, 1 mmol, 2 eq) and K2CO3 (138 mg, 1 mmol, 2 eq). After stirring for 3 h, the solution was added EtOAc (20 mL) and the organic phase washed with brine (10 mL) and dried over Na2SO4. To a solution of the crude product in ether (2 mL) was added triphenylphosphine (262 mg, 1 mmol, 2 eq). After the reaction had been refluxed for 3 h, the solvent was removed under vacuum. To this residue was added carbon disulfide (1 mL); after this mixture was refluxed for 1 h, the solvent was removed under vacuum. The crude product was purified by column chromatography (SiO2, eluent: DCM/MeOH=100:1 to 22:1) to afford product **SFyne** (31 mg, 27%) as colorless oil. 1H NMR (400 MHz, CDCl3) δ 3.64 – 3.57 (m, 2H), 3.51 (t, J = 2.4 Hz, 2H), 3.12 – 3.04 (m, 2H), 2.93 – 2.79 (m, 4H), 2.65 (s, 3H), 2.26 (t, J = 2.3 Hz, 1H). 13C NMR (126 MHz, CDCl3) δ 77.4, 74.0, 53.4, 53.1, 46.8, 43.6, 42.3, 39.0. ESI+-MS: [M+H]+ calculated for C9H15N2OS2+: 231.0620; found: 231.0619.

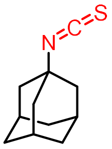
Synthesis of isothiocyanate compounds





A solution of thiophosgene **s8** (3 equiv., 1.5 mmol) in anhydrous DCM (3 ml) was cooled to 0 °C under argon atmosphere. A solution of primary amine **s7** (1 equiv., 0.5 mmol) in anhydrous DCM (1 ml) was added to the above solution. Finely crushed NaOH (3 equiv., 1.5 mmol) was added, and the resulting reaction mixture was allowed to warm to room temperature over 3 h. Remove the resulting solids by filtration through kieselguhr. The solvent was removed in vacuo and the residue was purified by flash chromatography to afford the desired compounds **s9**.

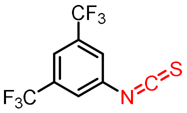
(3s,5s,7s)-1-isothiocyanatoadamantane (10)



10

The residue was purified by flash chromatography (silica gel, 10% EtOAc in petrol ether) to afford the desired compounds **10** as white solid (81 mg, 84%). ^{1}**H NMR** (400 MHz $CDCl_3$): δ 2.11 (s, 3H), 1.98 (d, J = 4 Hz, 6H), 1.66 (d, J = 4 Hz, 6H); ^{13}**C NMR** (100 MHz $CDCl_3$): δ 58.4, 43.7, 35.5, 29.2; **HRMS (ESI)**: [M-NCS]$^{\cdot}$ calculated for $C_{10}H_{15}^{\cdot}$: 135.1174, found: 135.1167.

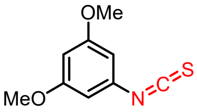
1-isothiocyanato-3,5-bis(trifluoromethyl)benzene (22)



22

The residue was purified by flash chromatography (silica gel, 10% DCM in petrol ether) to afford the desired compounds **22** as colorless liquid (120 mg, 89%). ^{1}**H NMR** (400 MHz $CDCl_3$): δ 7.76 (s, 1H), 7.64 (s, 2H); ^{13}**C NMR** (100 MHz $CDCl_3$): δ 140.9, 134.0, 133.4 (q, J = 30 Hz), 125.8 (m), 122.5 (q, J = 270 Hz), 120.5 (m); **HRMS (ESI)**: $[M+H]^+$ calculated for $C_9H_4F_6NS^+$: 271.9963, found: 271.9971.

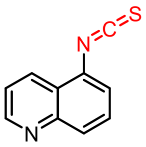
1-isothiocyanato-3,5-dimethoxybenzene (34)



34

The residue was purified by flash chromatography (silica gel, 10% EtOAc in petrol ether) to afford the desired compounds **34** as brown solid (79 mg, 81%). ^{1}**H NMR** (400 MHz $CDCl_3$): δ 6.37 (s, 3H), 3.77 (s, 6H); ^{13}**C NMR** (100 MHz $CDCl_3$): δ 161.1, 135.3, 132.5, 104.0, 100.3, 55.5; **HRMS (ESI)**: $[M+H]^+$ calculated for $C_9H_{10}NO_2S^+$: 196.0427, found: 196.0434.

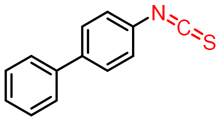
5-isothiocyanatoquinoline (35)



35

The residue was purified by flash chromatography (silica gel, 10% EtOAc in petrol ether) to afford the desired compounds **35** as yellow solid (71 mg, 76%). **^{1}H NMR** (400 MHz $CDCl_3$): δ 8.99 (d, J = 8 Hz, 1H), 8.46 (d, J = 8 Hz, 1H), 8.06 (d, J = 8 Hz, 1H), 7.67 (t, J = 8 Hz, 1H), 7.53 (q, J = 4 Hz, 1H), 7.50 (d, J = 8 Hz, 1H); **^{13}C NMR** (100 MHz $CDCl_3$): δ 151.4, 148.4, 137.5, 131.2, 129.2, 129.0, 127.6, 124.7, 123.9, 122.1; **HRMS (ESI)**: $[M+H]^+$ calculated for $C_{10}H_7N_2S^+$: 187.0324, found: 187.0330.

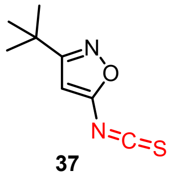
4-isothiocyanato-1,1'-biphenyl (36)



36

The residue was purified by flash chromatography (silica gel, 10% EtOAc in petrol ether) to afford the desired compounds **36** as white solid (68 mg, 65%). **^{1}H NMR** (400 MHz $CDCl_3$): δ 7.56 (m, 4H), 7.45 (t, J = 8 Hz, 2H), 7.37 (t, J = 8 Hz, 1H), 7.30 (d, J = 8 Hz, 2H); **^{13}C NMR** (100 MHz $CDCl_3$): δ 140.3, 139.7, 135.5, 130.2, 128.9, 128.1, 127.8, 127.0, 126.1; **HRMS (ESI)**: $[M+H]^+$ calculated for $C_{13}H_{10}NS^+$: 212.0528, found: 212.0532.

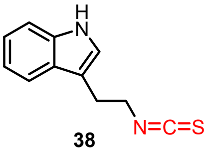
3-(tert-butyl)-5-isothiocyanatoisoxazole (37)



37

The residue was purified by flash chromatography (silica gel, 10% DCM in petrol ether) to afford the desired compounds **37** as brown liquid (70 mg, 77%). **^{1}H NMR** (400 MHz $CDCl_3$): δ 5.87 (s, 1H), 1.31 (s, 9H); **^{13}C NMR** (100 MHz $CDCl_3$): δ 173.8, 152.6, 148.2, 93.9, 32.6, 29.1; **HRMS (ESI)**: $[M+H]^+$ calculated for $C_8H_{11}N_2OS^+$: 183.0587, found: 183.0588.

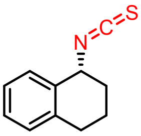
3-(2-isothiocyanatoethyl)-1H-indole (38)



38

The residue was purified by flash chromatography (silica gel, 20% EtOAc in petrol ether) to afford the desired compounds **38** as yellow liquid (30 mg, 30%). **^{1}H NMR** (400 MHz $CDCl_3$): δ 8.09 (s, 1H), 7.56 (d, J = 8 Hz, 1H), 7.40 (d, J = 8 Hz, 1H), 7.23 (t, J = 8 Hz, 1H), 7.15 (t, J = 8 Hz, 1H), 7.13 (s, 1H), 3.78 (t, J = 8 Hz, 2H), 3.18 (t, J = 8 Hz, 2H); **^{13}C NMR** (100 MHz $CDCl_3$): δ 136.2, 126.8, 122.9, 122.3, 119.7, 118.2, 111.4, 111.2, 45.6, 26.5; **HRMS (ESI)**: $[M+H]^+$ calculated for $C_{11}H_{11}N_2S^+$: 203.0637, found: 203.0641.

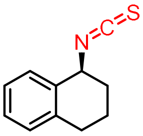
(R)-1-isothiocyanato-1,2,3,4-tetrahydronaphthalene (39)



39

The residue was purified by flash chromatography (silica gel, 10% EtOAc in petrol ether) to afford the desired compounds **39** as brown solid (95 mg, Quant.). **^{1}H NMR** (400 MHz $CDCl_3$): δ 7.35 (m, 1H), 7.23 (t, J = 4 Hz, 2H), 7.13 (m, 1H), 4.94 (t, J = 8 Hz, 2H), 2.86 (m, 1H), 2.75 (m, 1H), 2.12 (m, 2H), 2.00 (m, 1H), 1.86 (m, 1H); **^{13}C NMR** (100 MHz $CDCl_3$): δ 136.4, 133.2, 131.8, 129.4, 128.6, 128.3, 126.5, 55.7, 30.8, 28.5, 19.3; **HRMS (ESI)**: [M-NCS]$^{\cdot}$ calculated for $C_{10}H_{11}^{\cdot}$: 131.0861, found: 131.0853.

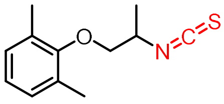
(S)-1-isothiocyanato-1,2,3,4-tetrahydronaphthalene (40)



40

The residue was purified by flash chromatography (silica gel, 10% EtOAc in petrol ether) to afford the desired compounds **40** as brown solid (86 mg, 91%). **^{1}H NMR** (400 MHz $CDCl_3$): δ δ 7.35 (m, 1H), 7.23 (t, J = 4 Hz, 2H), 7.13 (m, 1H), 4.94 (t, J = 8 Hz, 2H), 2.86 (m, 1H), 2.75 (m, 1H), 2.12 (m, 2H), 2.00 (m, 1H), 1.86 (m, 1H); **^{13}C NMR** (100 MHz $CDCl_3$): δ136.4, 133.2, 131.7, 129.4, 128.6, 128.3, 126.5, 55.7, 30.8, 28.5, 19.3; **HRMS (ESI)**: [M-NCS]$^{\cdot}$ calculated for $C_{10}H_{11}^{\cdot}$: 131.0861, found: 131.0852.

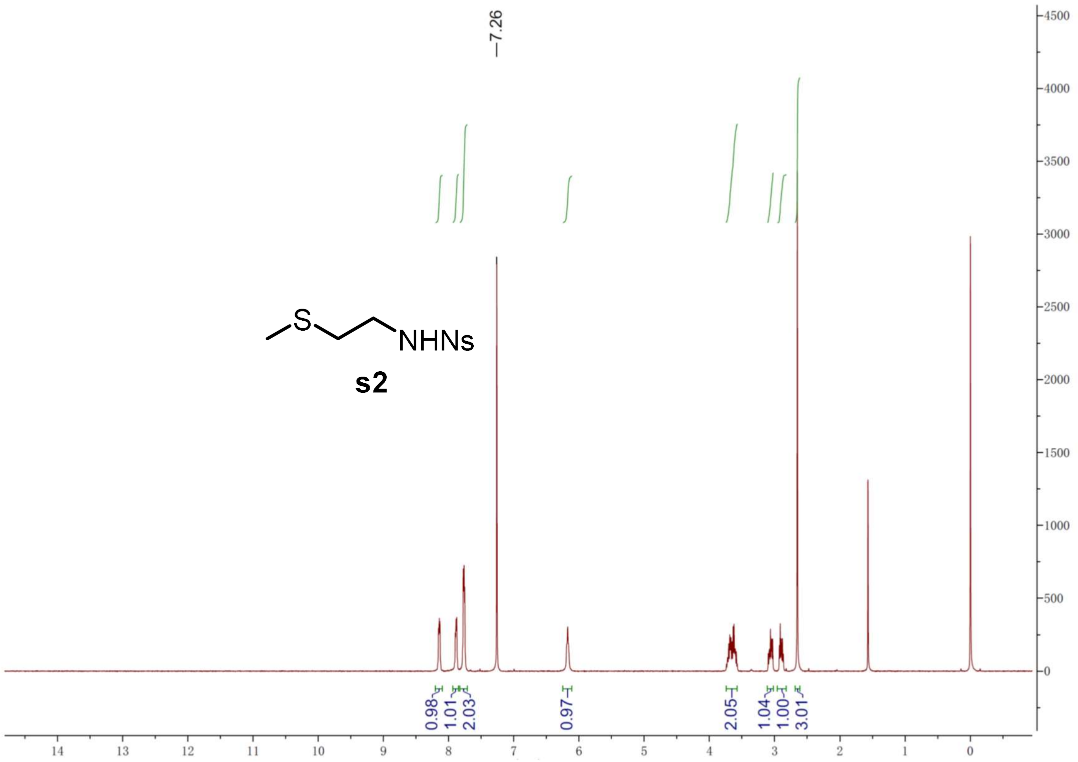
2-(2-isothiocyanatopropoxy)-1,3-dimethylbenzene (41)

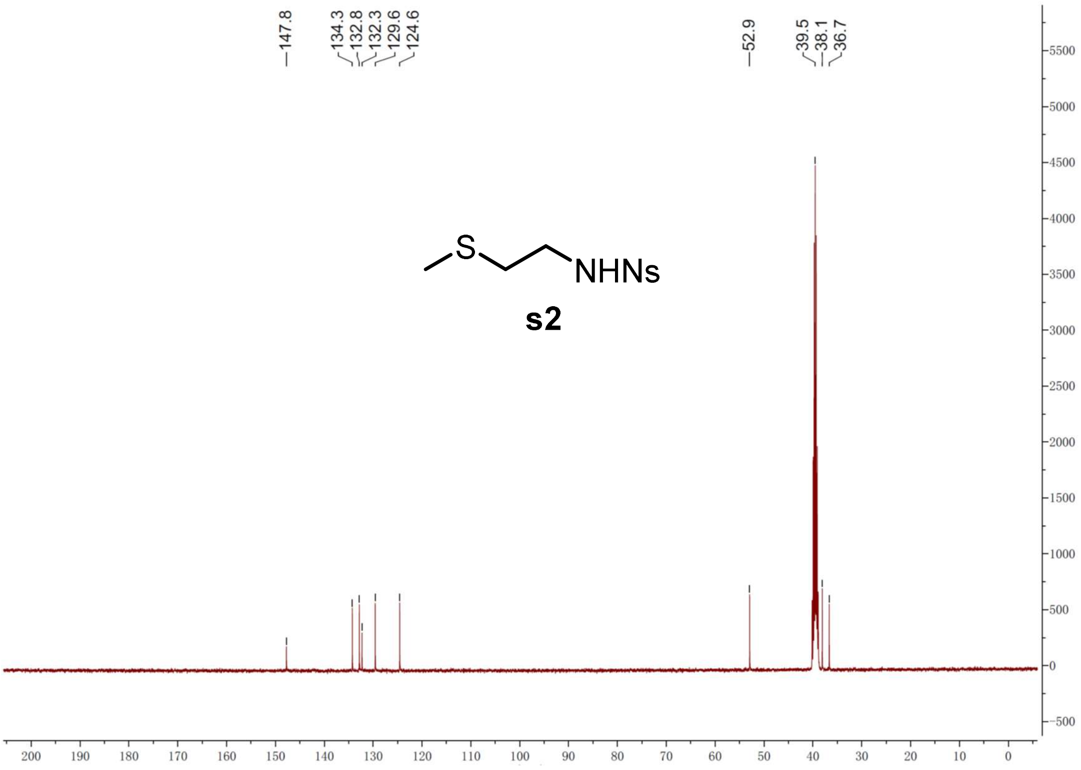


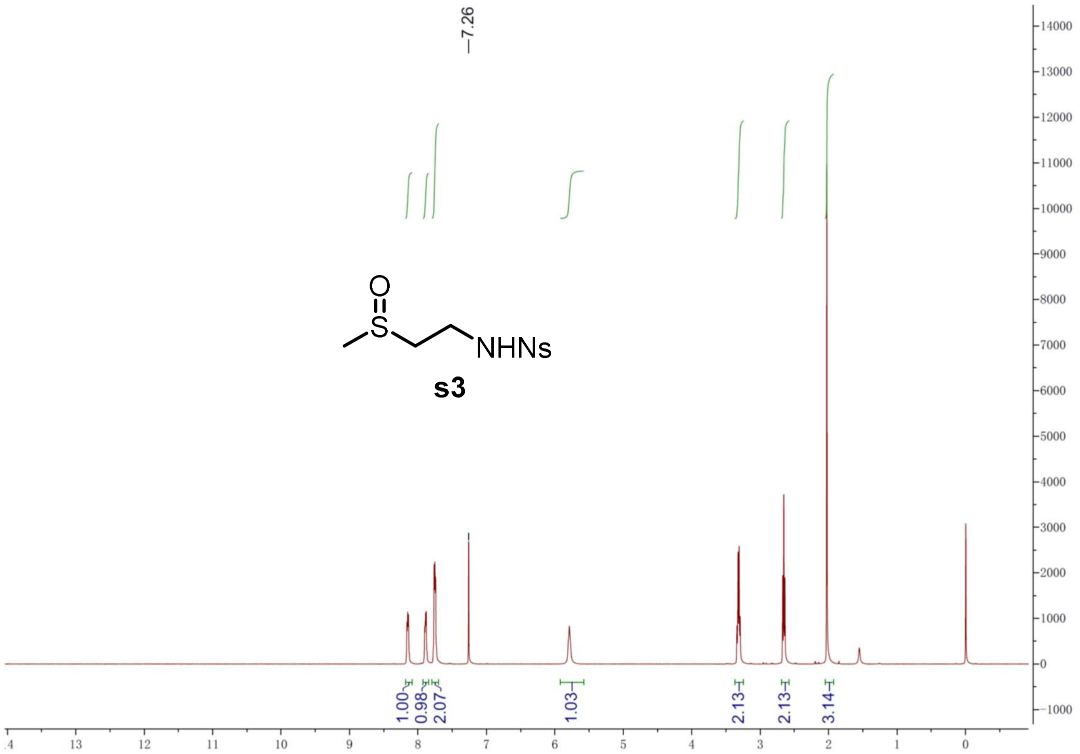
41

The residue was purified by flash chromatography (silica gel, 10% EtOAc in petrol ether) to afford the desired compounds **41** as brown liquid (97 mg, 88%). **^{1}H NMR** (400 MHz $CDCl_3$): δ 6.95 (d, J = 8 Hz, 2H), 6.87 (d, J = 8 Hz, 1H), 4.08 (m, 1H), δ 6.95 (d, J = 4 Hz, 2H), 2.23 (s, 6H), 1.43 (d, J = 4 Hz, 3H); **^{13}C NMR** (100 MHz $CDCl_3$): δ 154.7, 132.8, 130.7, 129.0, 124.3, 74.1, 53.6, 18.3, 16.2; **HRMS (ESI)**: $[M+H]^+$ calculated for $C_{12}H_{16}NOS^+$: 222.0947, found: 222.0947.

^{1}H NMR and ^{13}C NMR Spectra







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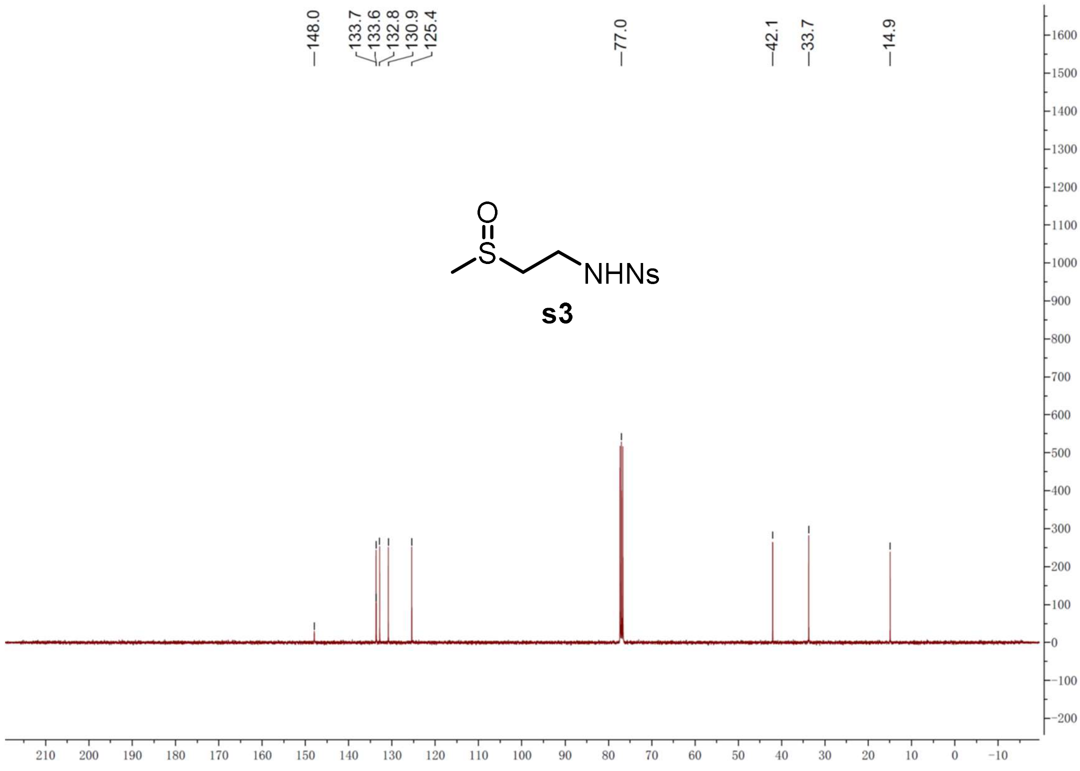

148.0
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NHNs
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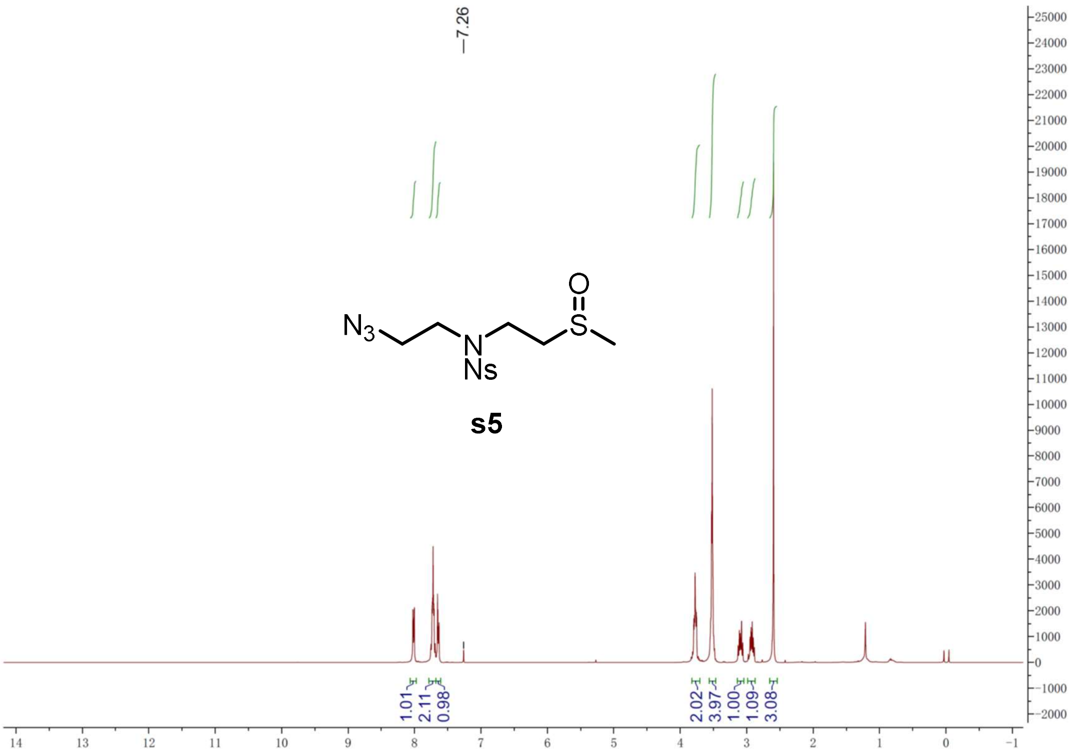
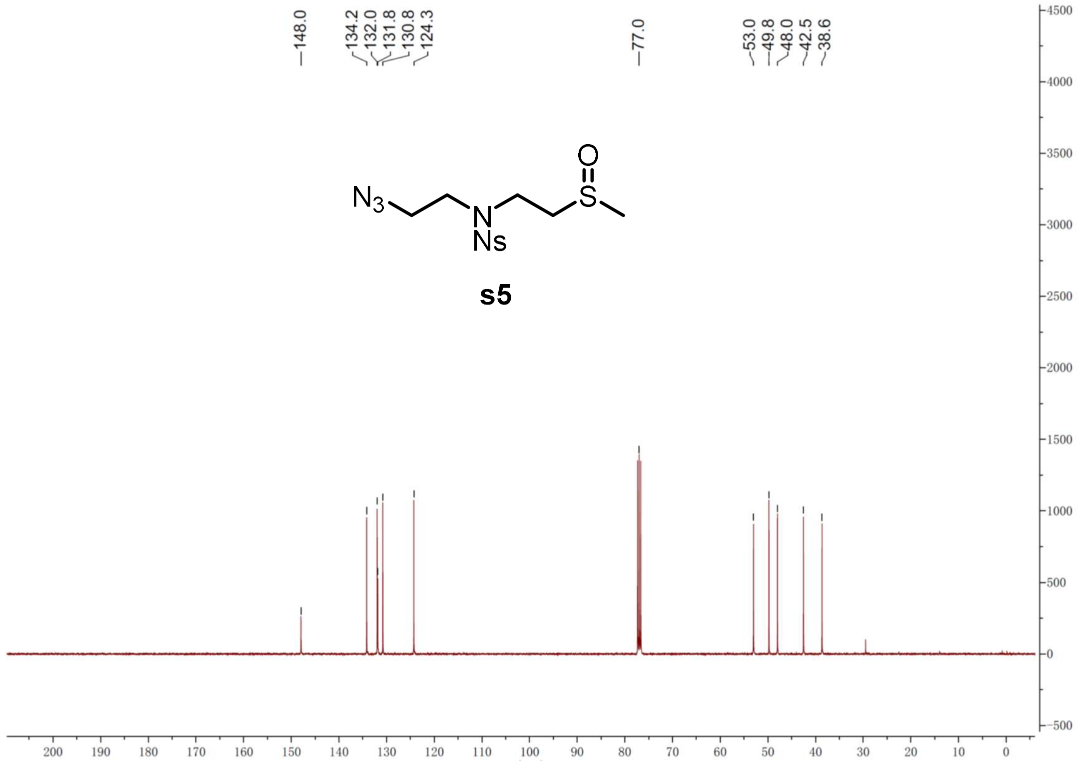
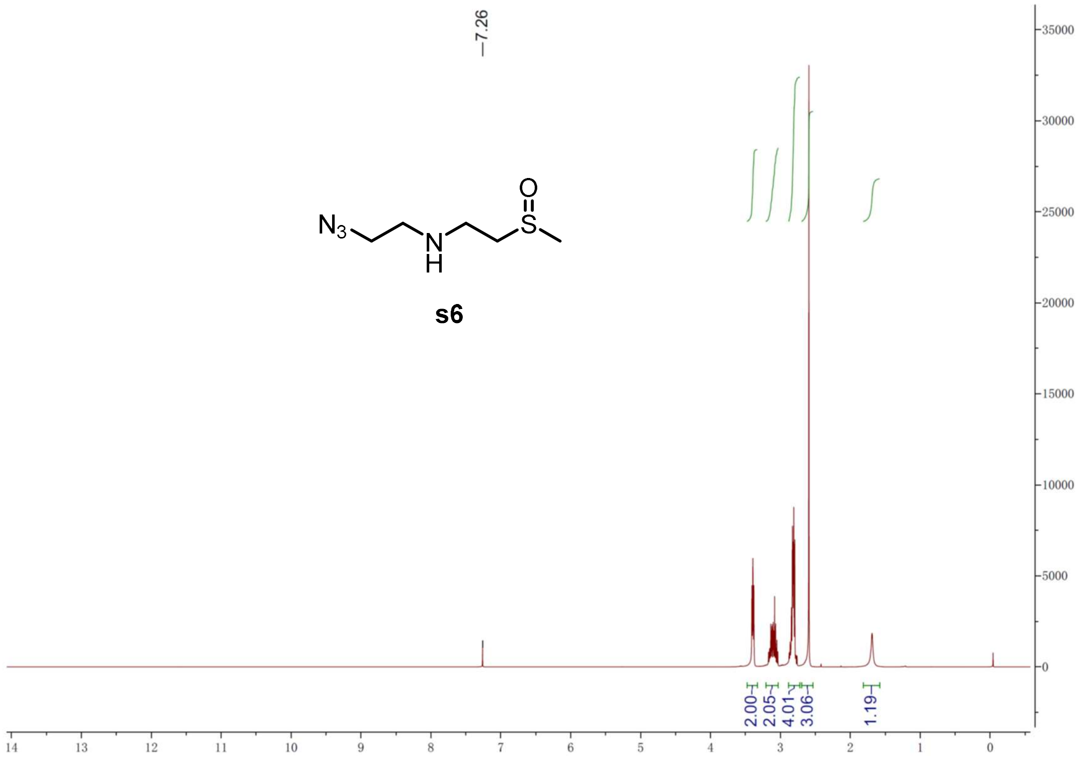
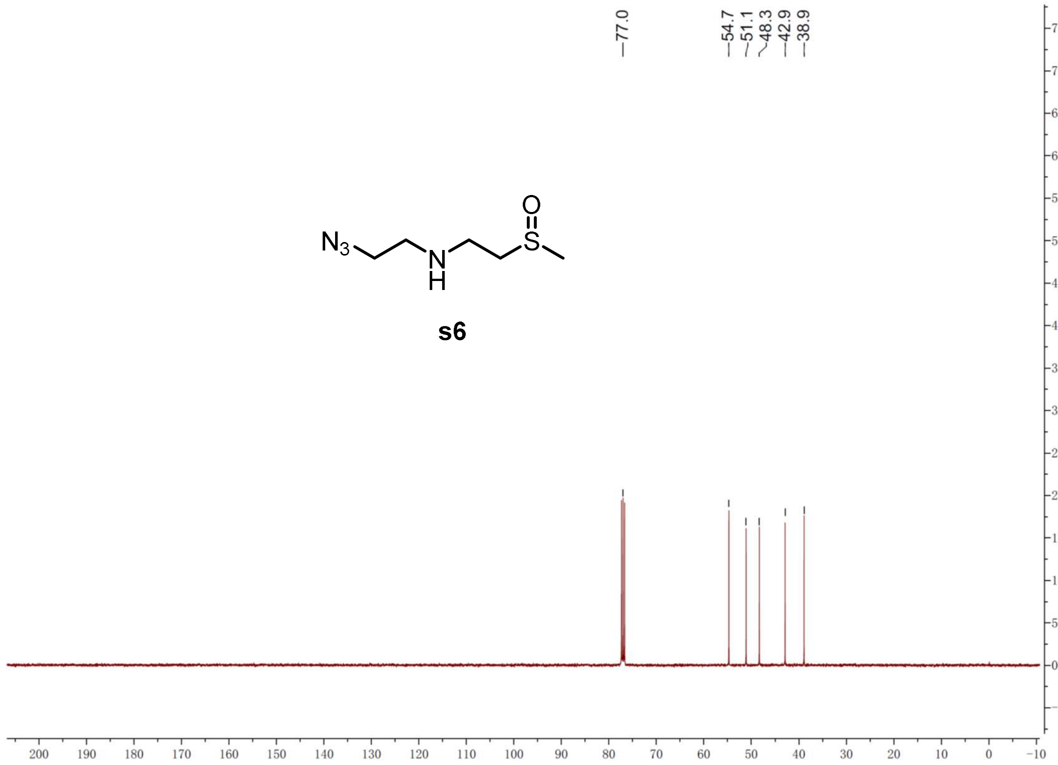
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
−100
−200
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10


7.26
N3
N
Ns
S
O
s5
1.01
2.11
0.98
2.02
3.97
1.00
1.09
3.08
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
25000 24000 23000 22000 21000 20000 19000 18000 17000 16000 15000 14000 13000 12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 -1000 -2000

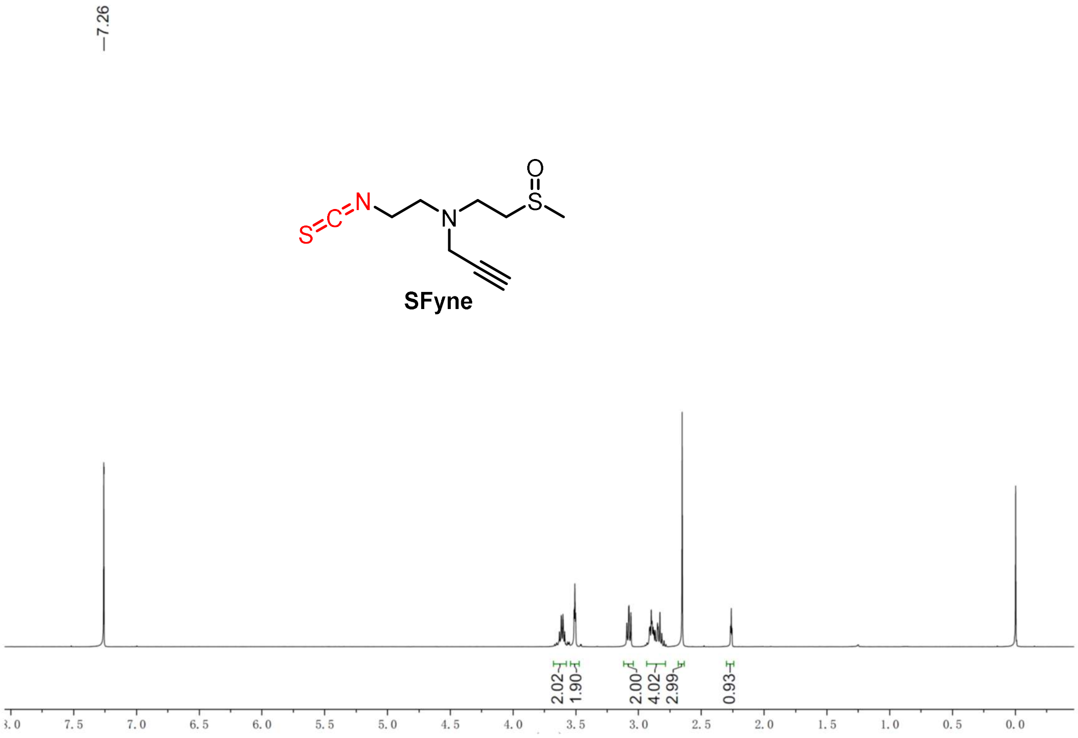

148.0
134.2
132.0
131.8
130.8
124.3
77.0
53.0
49.8
48.0
42.5
38.6
N3
N
Ns
S
O
s5
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
4500 4000 3500 3000 2500 2000 1500 1000 500 0 -500

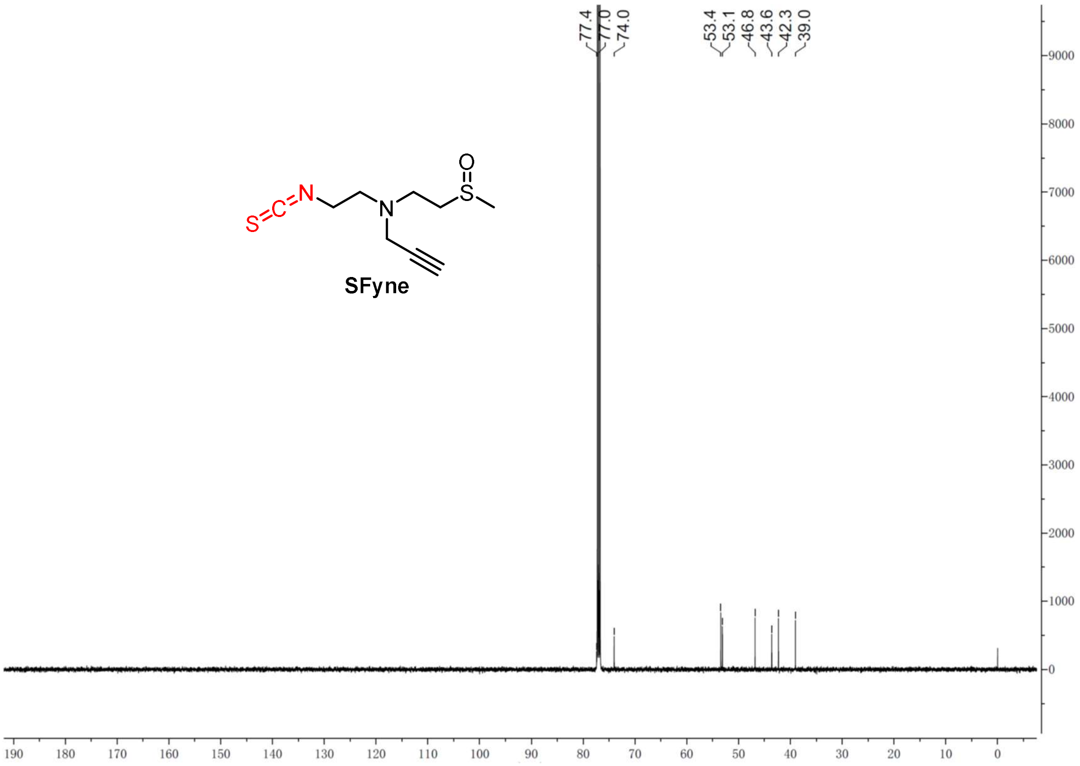

7.26
N3
N
H
O
S
2.00
2.05
4.01
3.06
1.19
35000
30000
25000
20000
15000
10000
5000
0
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0

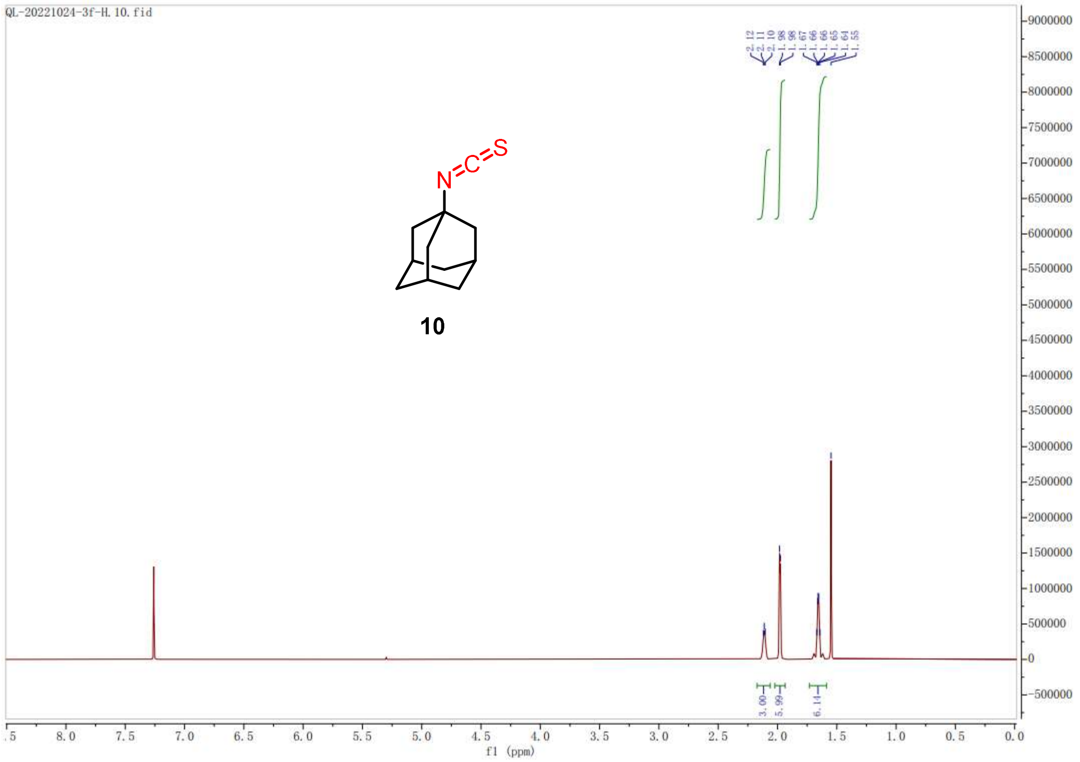
s6

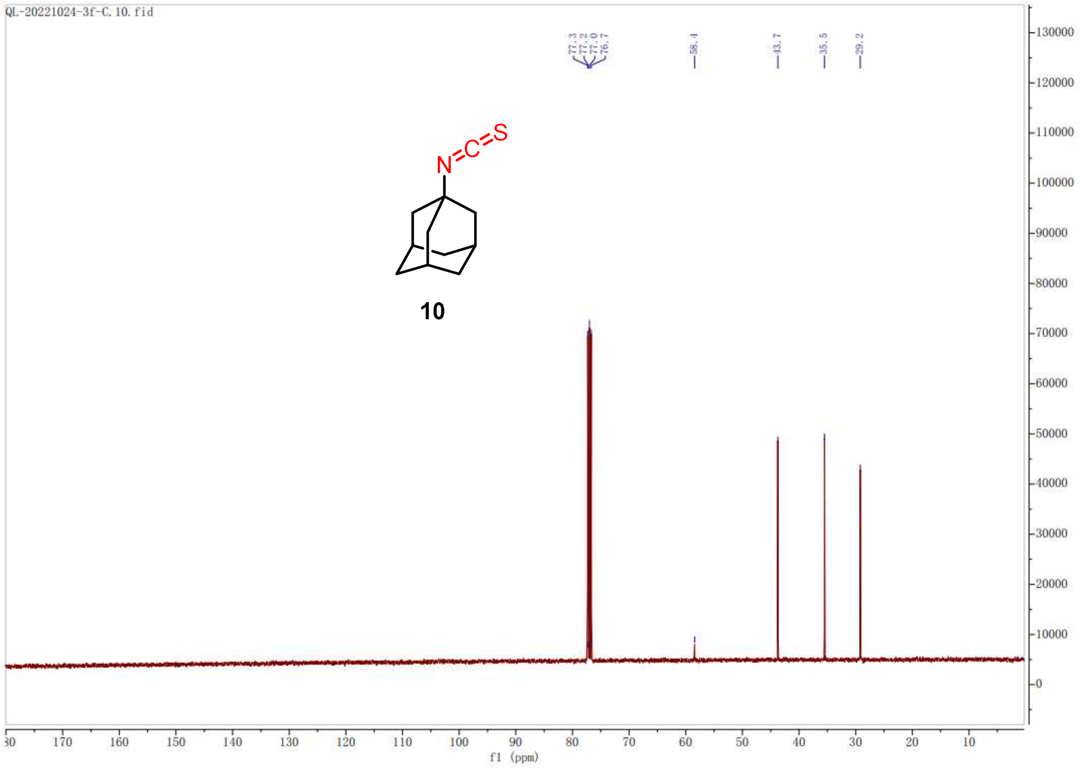

77.0
54.7
51.1
48.3
42.9
38.9
N3
N
H
O
S
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
−500
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10

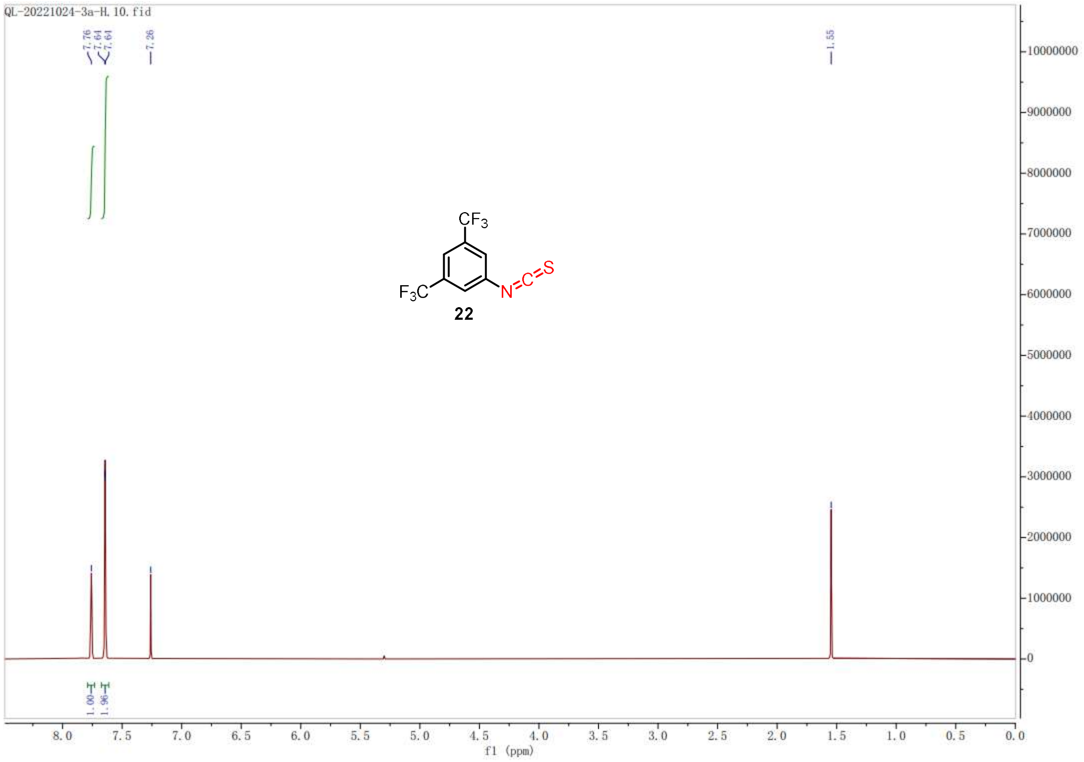
s6

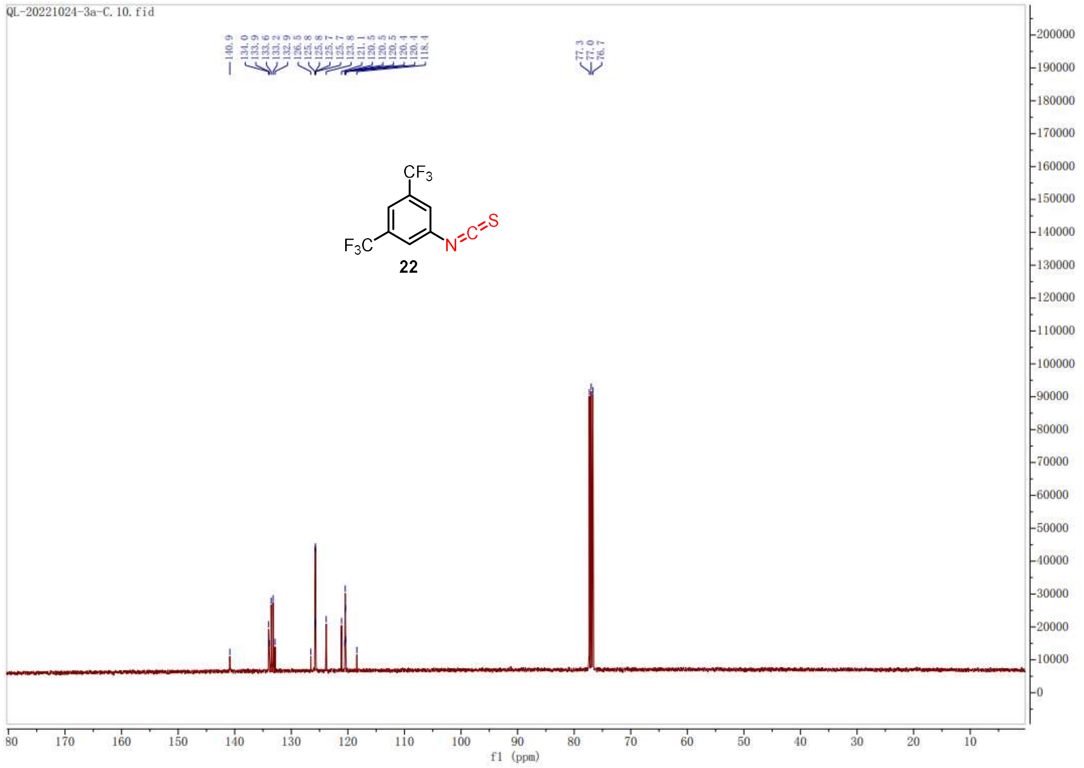

7.26
S=C=N
N
S
O
SFyne
2.02
1.90
2.00
4.02
2.99
0.93
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

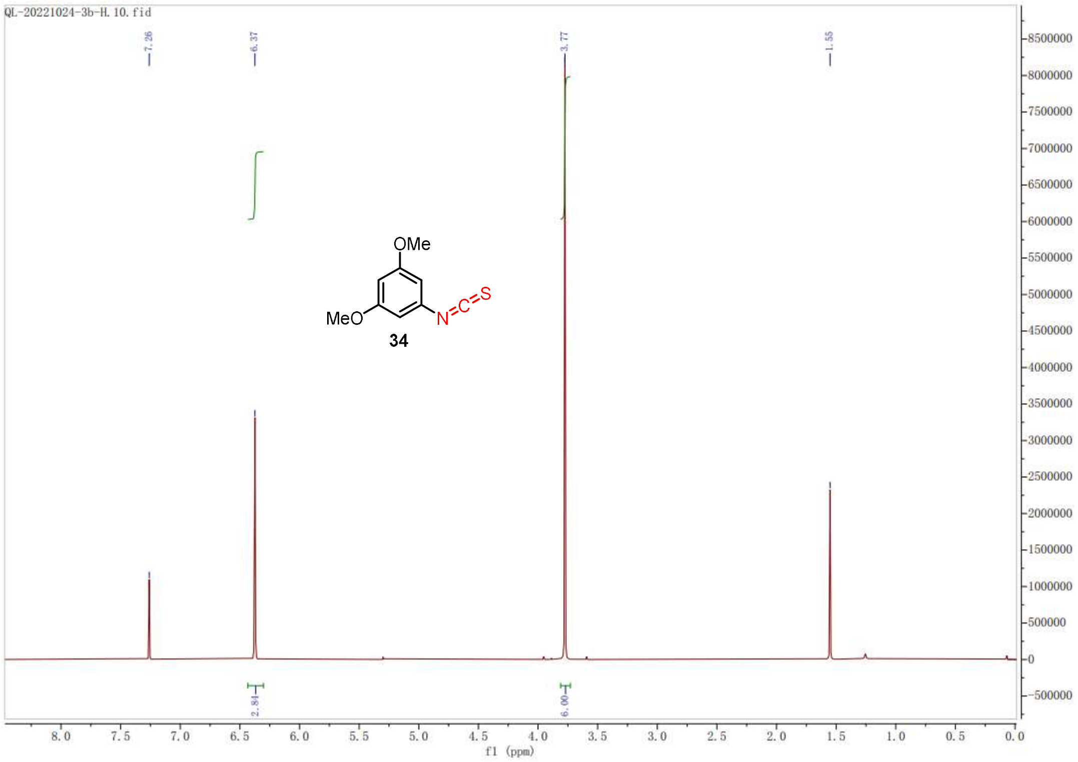

77.4
77.0
74.0
53.4
53.1
46.8
43.6
42.3
39.0
S=C=N
N
S
O
SFyne
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

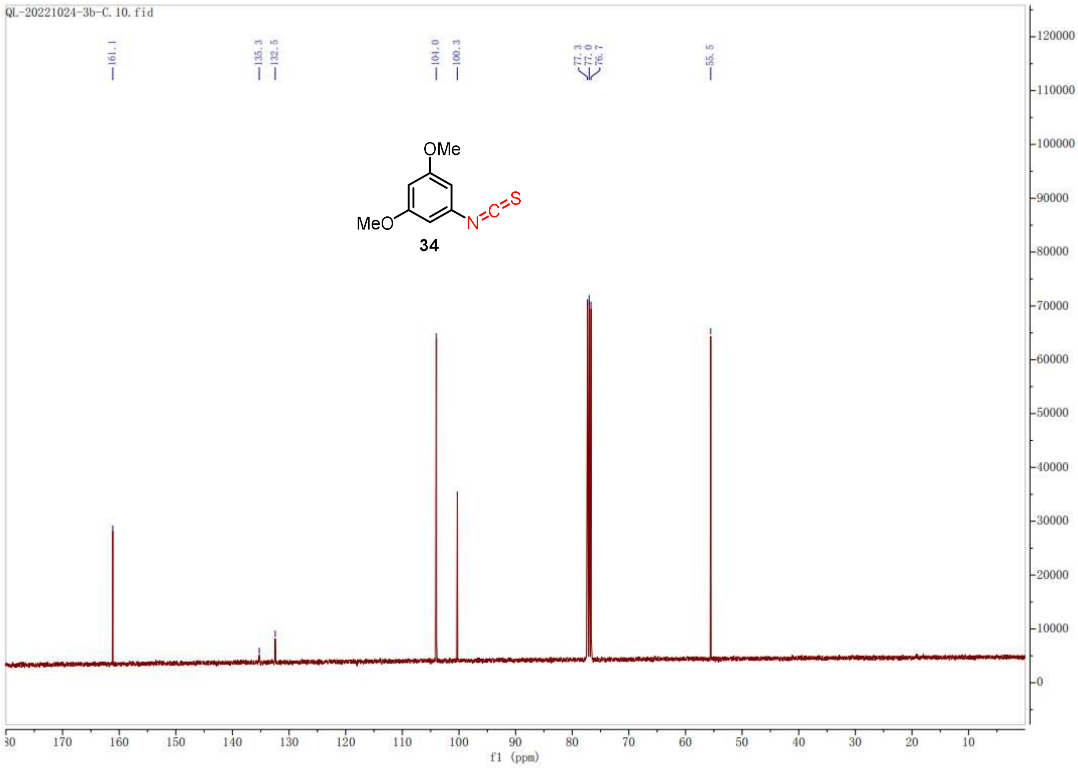

QL-20221024-3f-H.10.fid
2.12
2.11
2.10
1.98
1.98
1.67
1.66
1.66
1.65
1.64
1.55
N=C=S
10
3.00
5.99
6.14
9000000
8500000
8000000
7500000
7000000
6500000
6000000
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

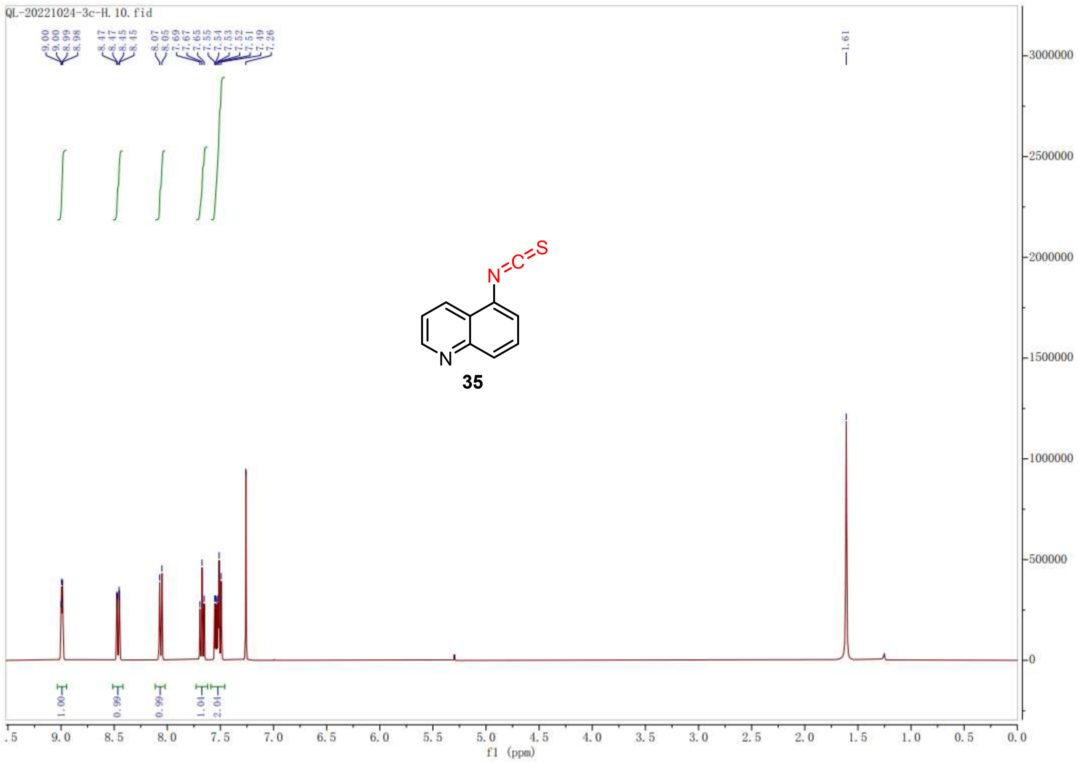

QL-20221024-3f-C.10.fid
77.3
77.2
77.0
76.7
58.4
43.7
35.5
29.2
N=C=S
10
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

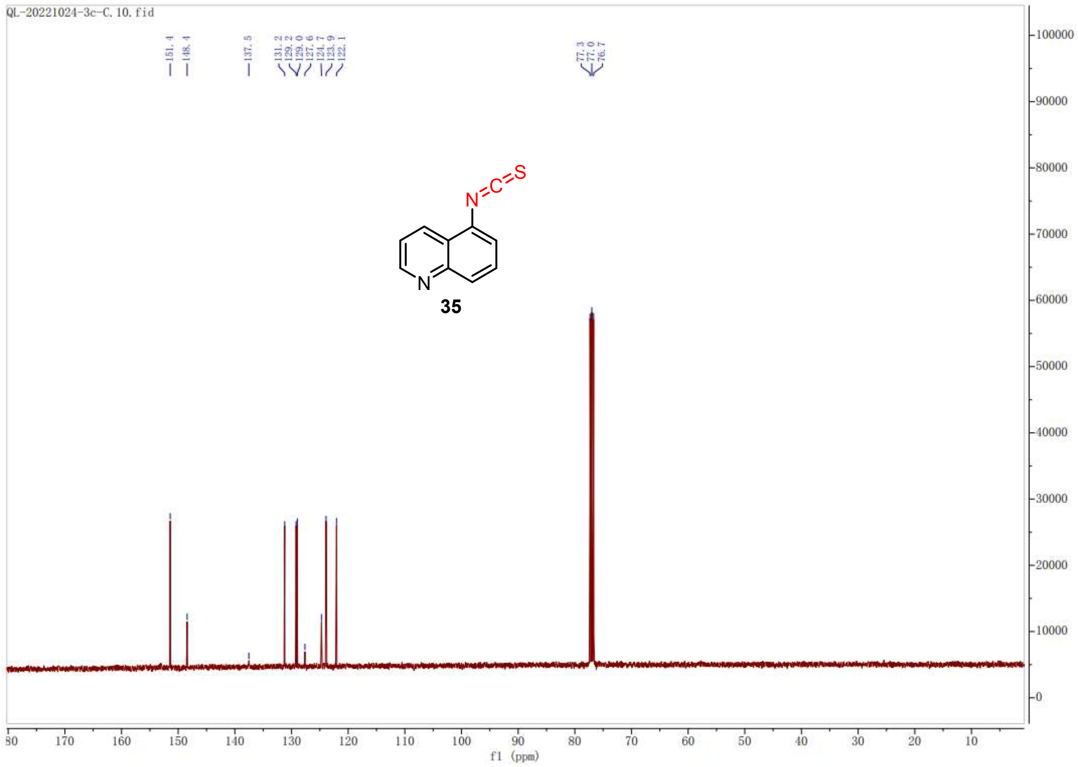

QL-20221024-3a-H. 10. fid
7.76
7.64
7.64
7.26
1.55
CF3
F3C
N=C=S
22
1.00
1.96
10000000
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

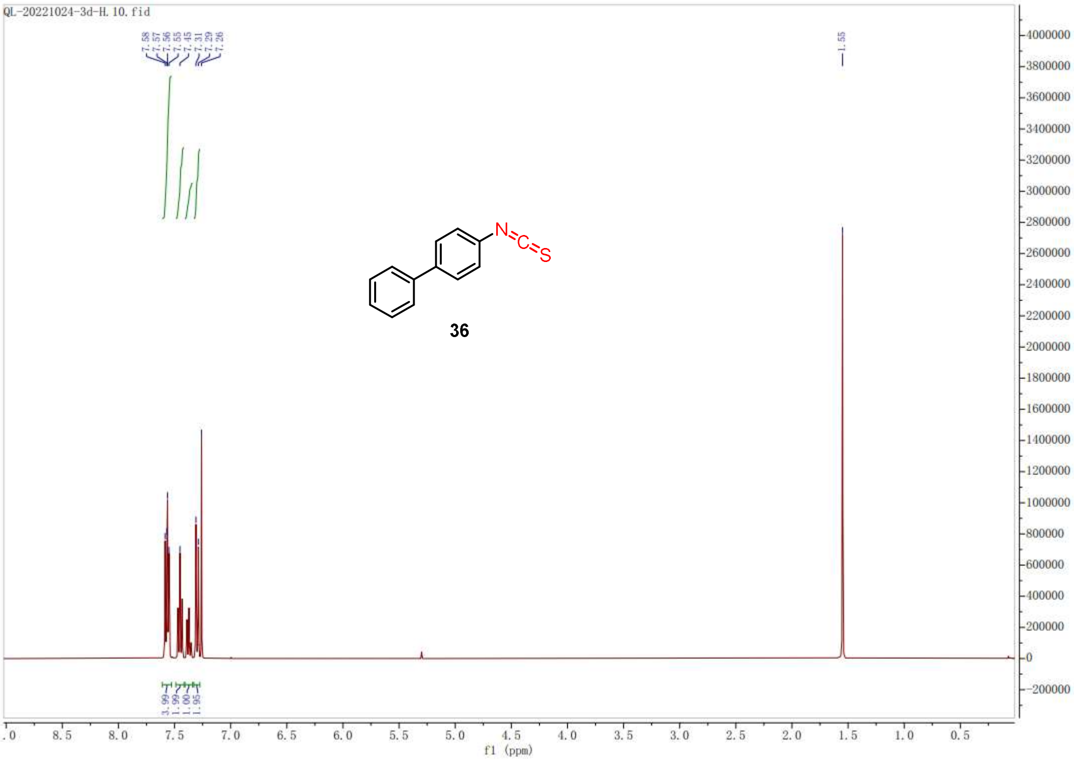

QL-20221024-3a-C. 10. fid
140.9
134.0
133.9
133.6
133.2
132.9
126.5
125.8
125.8
125.7
125.7
123.8
121.1
120.5
120.5
120.5
120.4
120.4
118.4
77.3
77.0
76.7
CF3
F3C
N=C=S
22
200000
190000
180000
170000
160000
150000
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

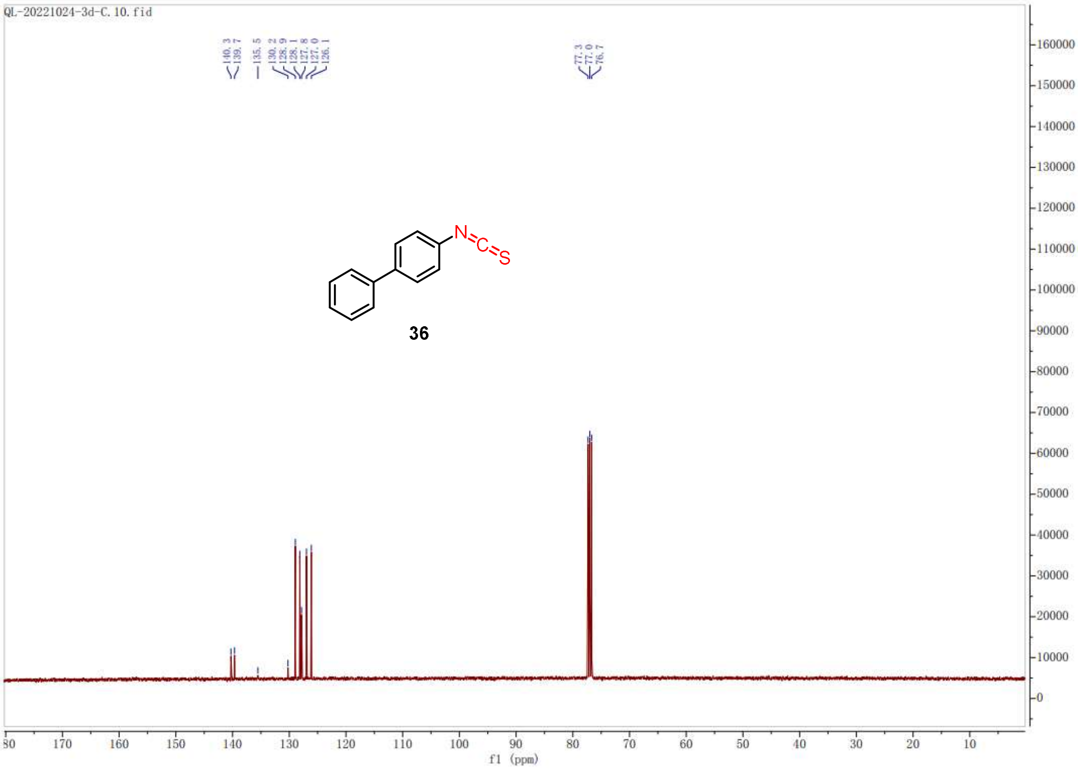

QL-20221024-3b-H.10.fid
7.26
6.37
3.77
1.55
OMe
MeO
N=C=S
34
2.84
6.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
8500000
8000000
7500000
7000000
6500000
6000000
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000

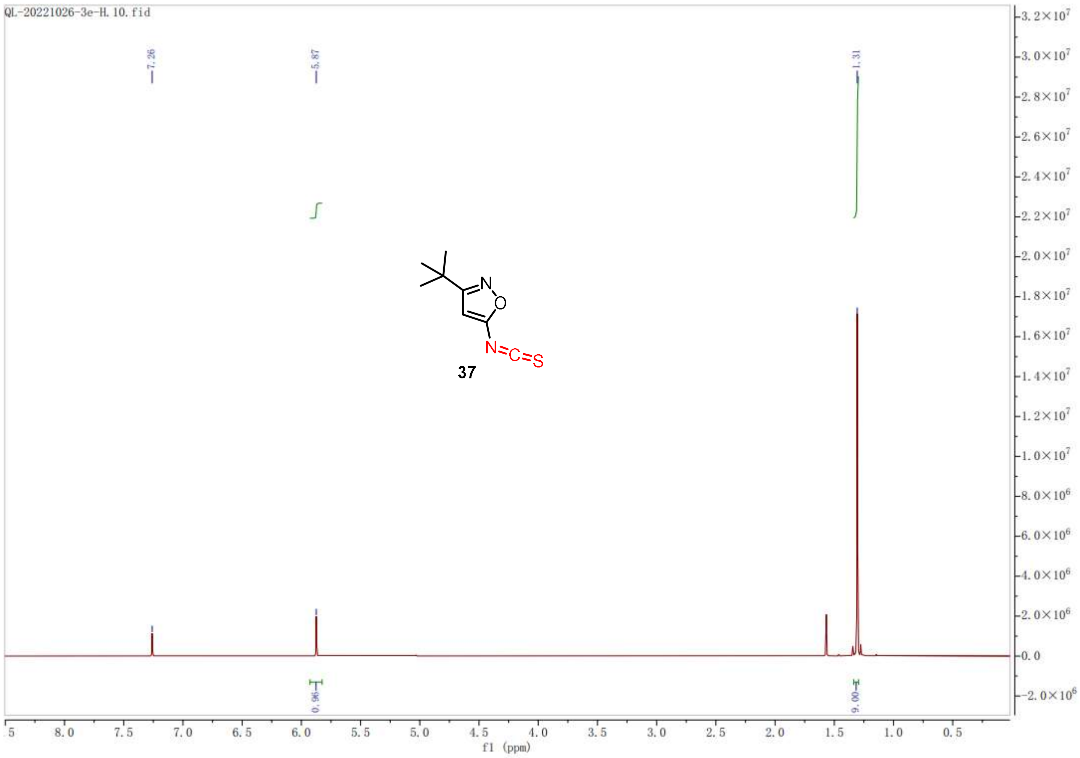

QL-20221024-3b-C.10.fid
161.1
135.3
132.5
104.0
100.3
77.3
77.0
76.7
55.5
OMe
MeO
N=C=S
34
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0

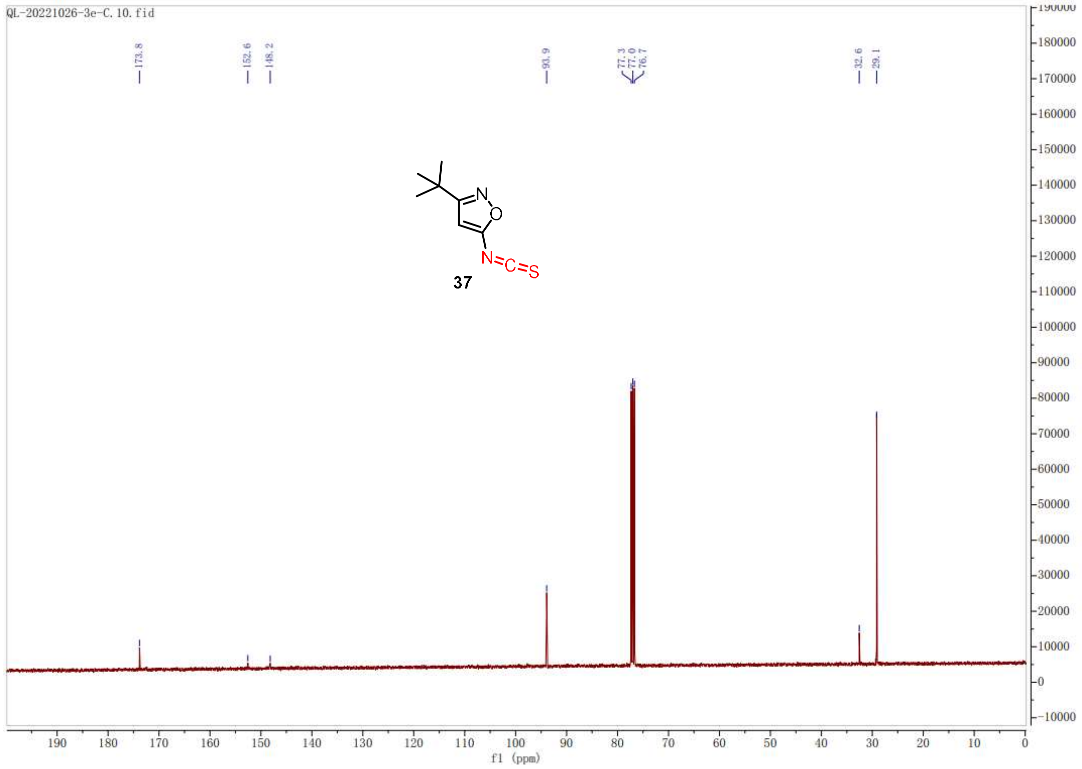

QL-20221024-3c-H.10.fid
9.00
9.00
8.99
8.98
8.47
8.47
8.45
8.45
8.07
8.05
7.69
7.67
7.65
7.55
7.54
7.53
7.52
7.51
7.49
7.26
1.61
N=C=S
N
35
1.00
0.99
0.99
1.01
2.04
f1 (ppm)
3000000
2500000
2000000
1500000
1000000
500000
0

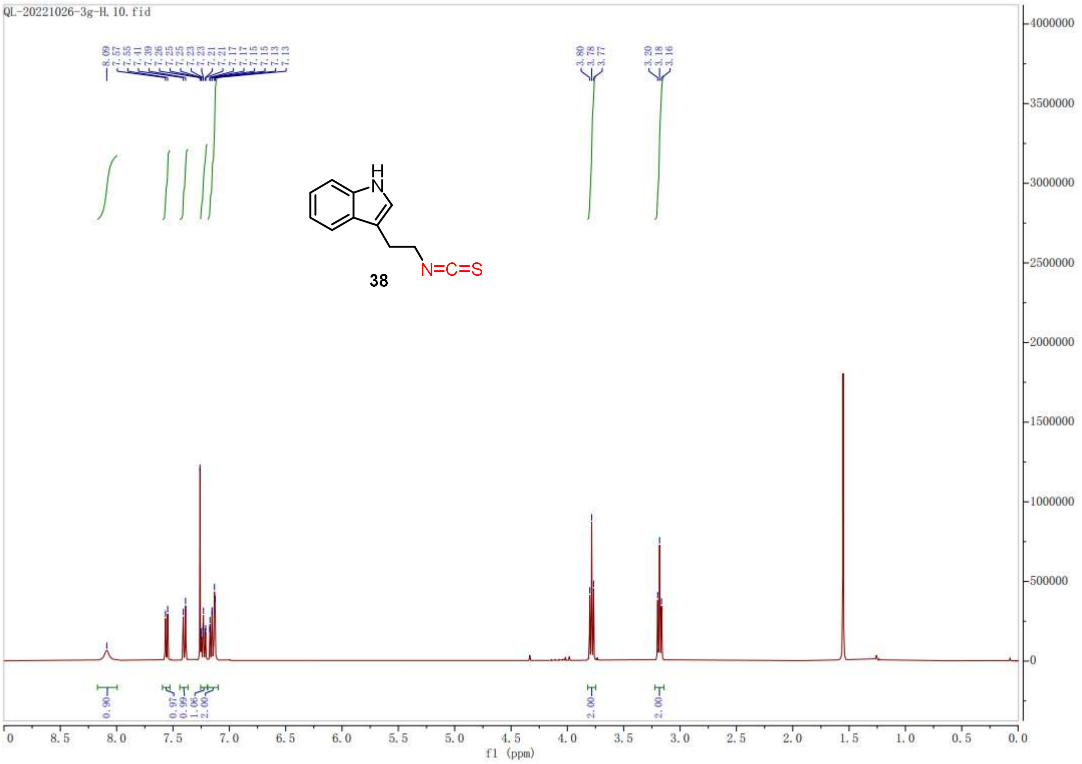

QL-20221024-3c-C.10.fid
151.4
148.4
137.5
131.2
129.2
129.0
127.6
124.7
123.9
122.1
77.3
77.0
76.7
N=C=S
N
35
f1 (ppm)
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0

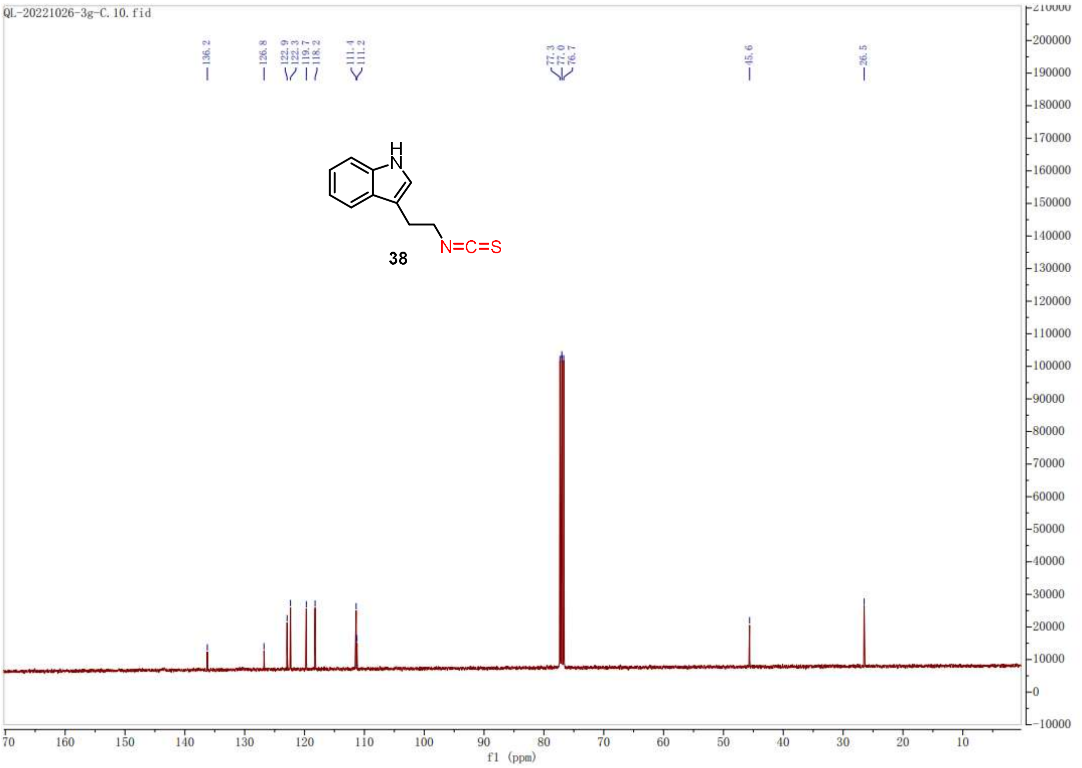

QL-20221024-3d-H.10.fid
7.58
7.57
7.56
7.55
7.45
7.31
7.29
7.26
1.55
N=C=S
36
3.99
1.99
1.00
1.95
4000000
3800000
3600000
3400000
3200000
3000000
2800000
2600000
2400000
2200000
2000000
1800000
1600000
1400000
1200000
1000000
800000
600000
400000
200000
0
-200000
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

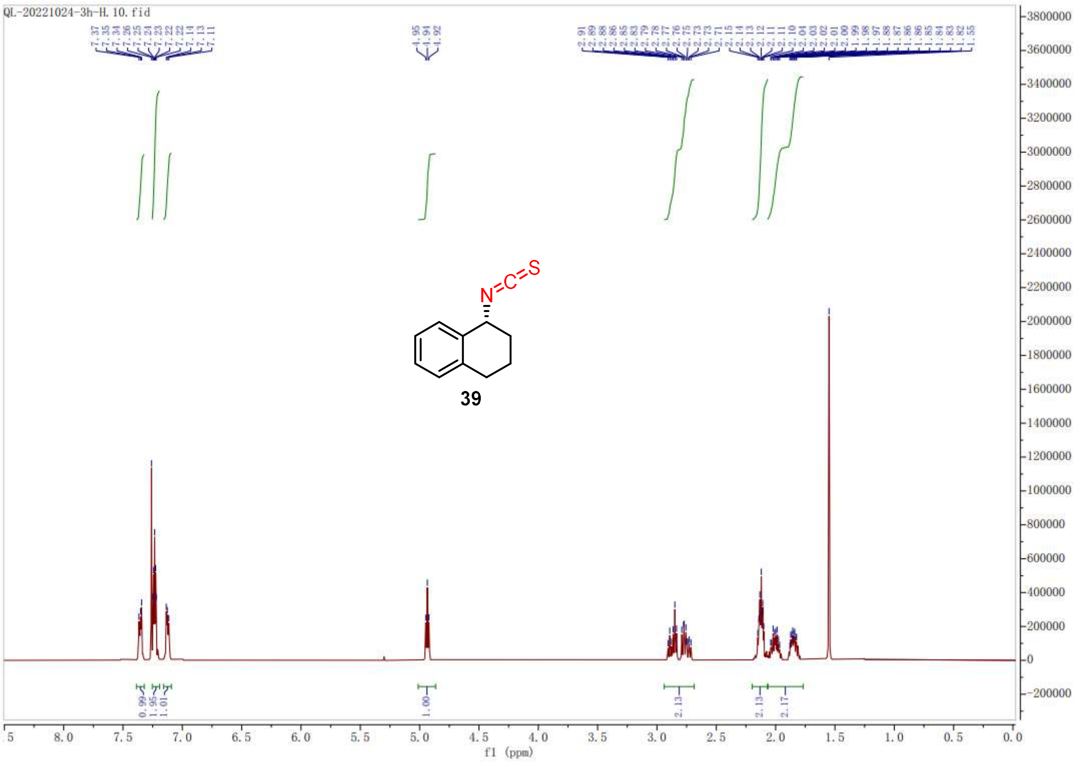

QL-20221024-3d-C.10.fid
140.3
139.7
135.5
130.2
128.9
128.1
127.8
127.0
126.1
77.3
77.0
76.7
N=C=S
36
160000
150000
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

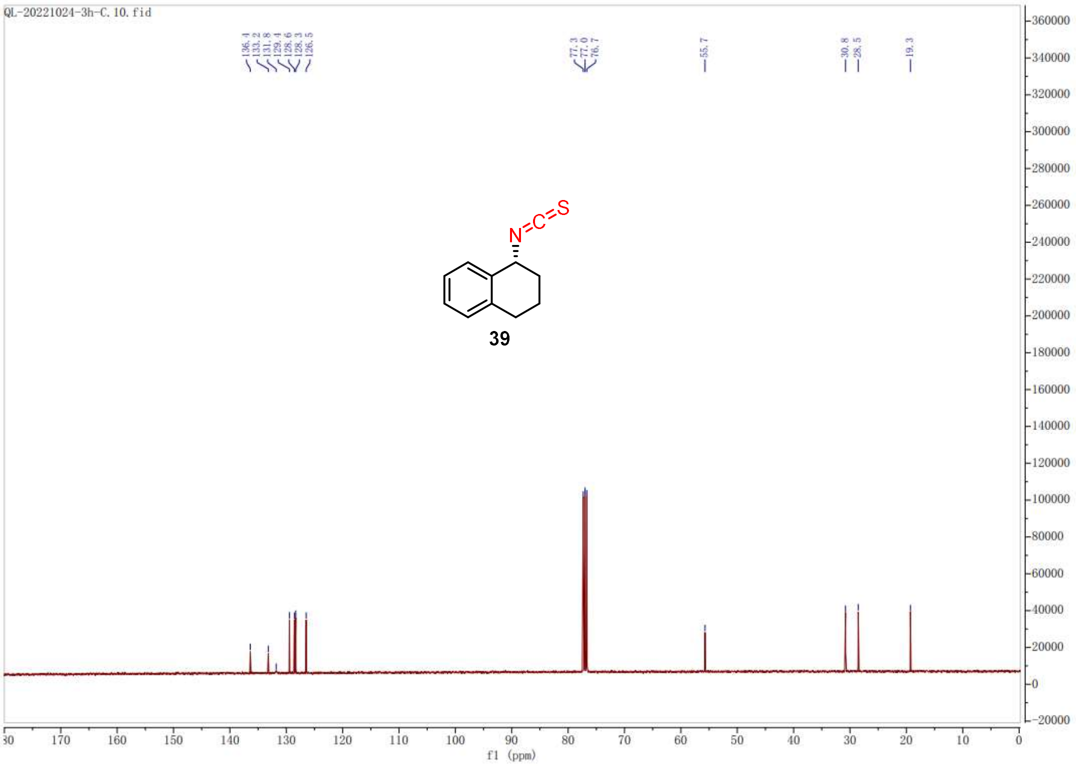

QL-20221026-3e-H.10.fid
7.26
5.87
1.31
0.96
9.00
N
O
N=C=S
37
3.2×10^7
3.0×10^7
2.8×10^7
2.6×10^7
2.4×10^7
2.2×10^7
2.0×10^7
1.8×10^7
1.6×10^7
1.4×10^7
1.2×10^7
1.0×10^7
8.0×10^6
6.0×10^6
4.0×10^6
2.0×10^6
0.0
−2.0×10^6
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

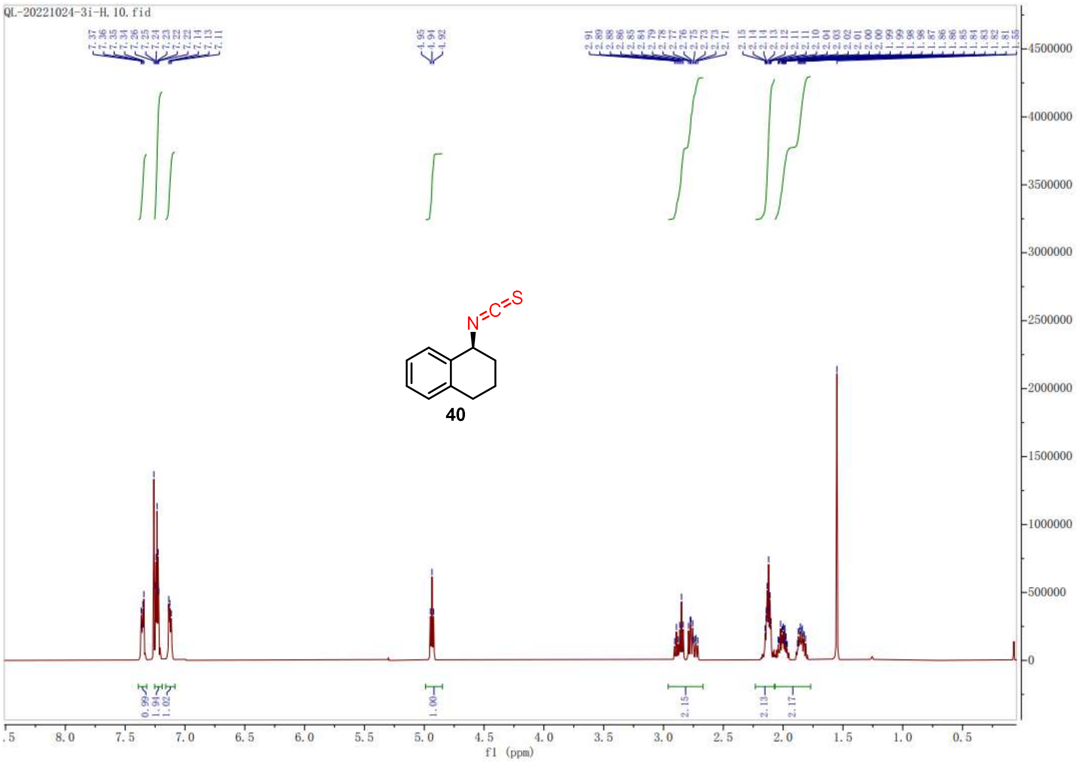

QL-20221026-3e-C.10.fid
173.8
152.6
148.2
93.9
77.3
77.0
76.7
32.6
29.1
N
O
N=C=S
37
190000
180000
170000
160000
150000
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
−10000
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

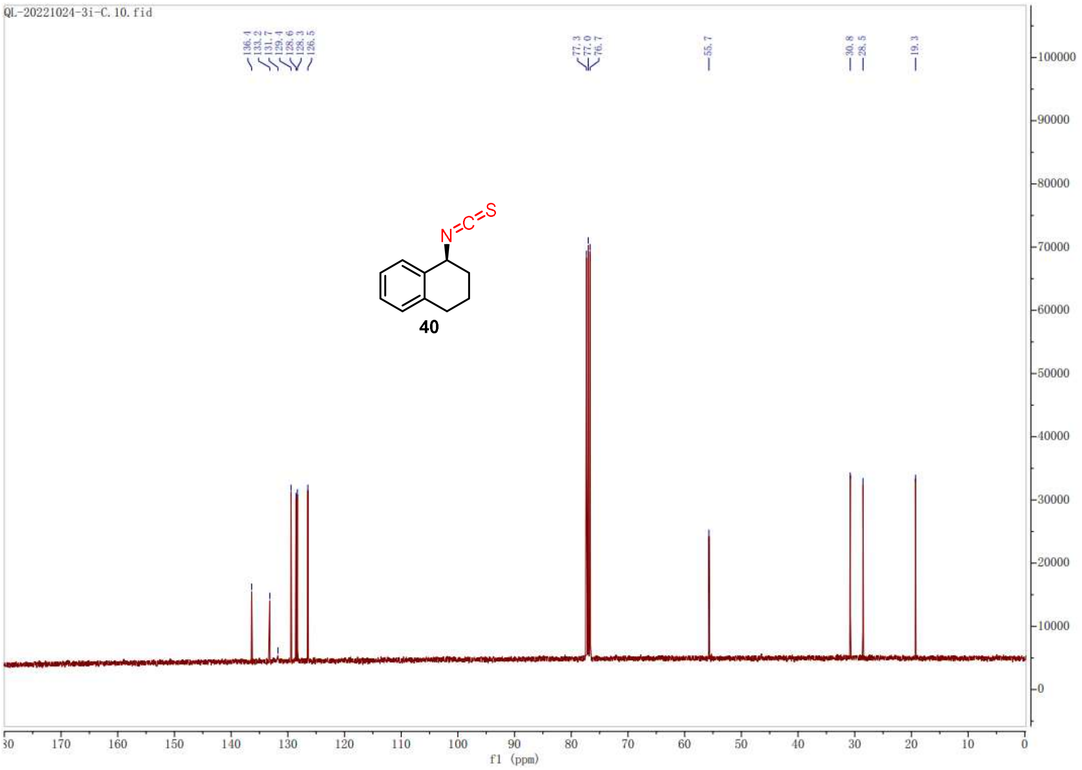

QL-20221026-3g-H.10.fid
8.09
7.57
7.55
7.41
7.39
7.26
7.25
7.25
7.23
7.23
7.21
7.21
7.17
7.17
7.15
7.15
7.13
7.13
3.80
3.78
3.77
3.20
3.18
3.16
H
N
N=C=S
38
0.90
0.97
0.99
1.06
2.00
2.00
2.00
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

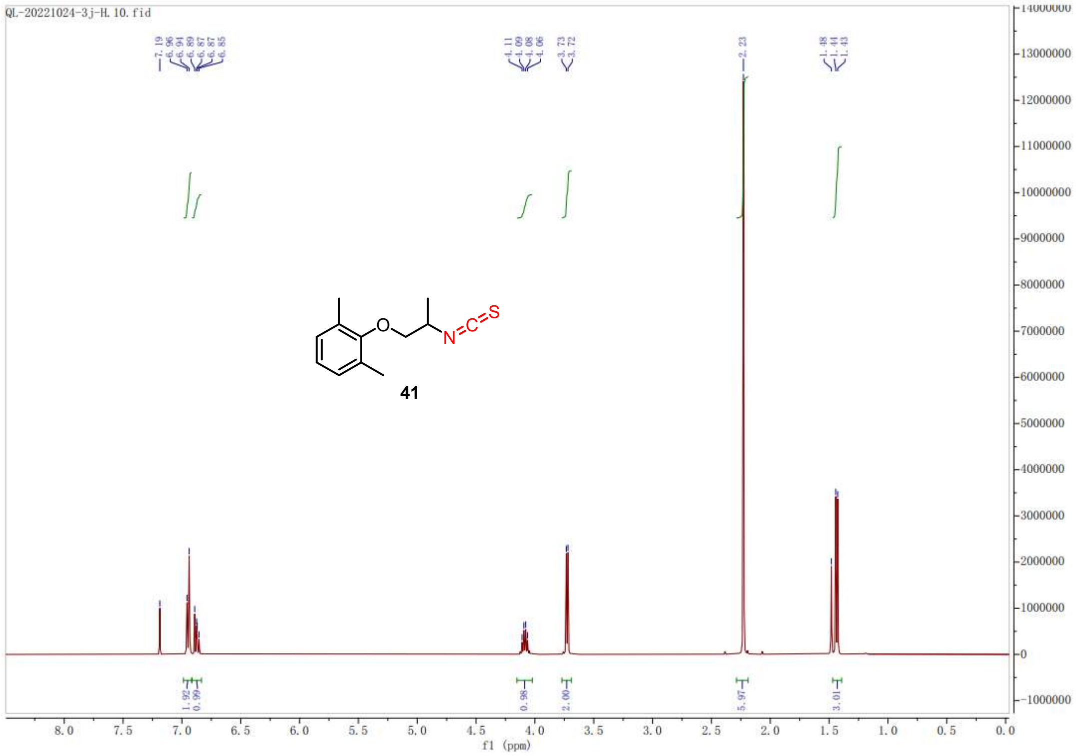

QL-20221026-3g-C.10.fid
136.2
126.8
122.9
122.3
119.7
118.2
111.4
111.2
77.3
77.0
76.7
45.6
26.5
H
N
N=C=S
38
210000
200000
190000
180000
170000
160000
150000
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

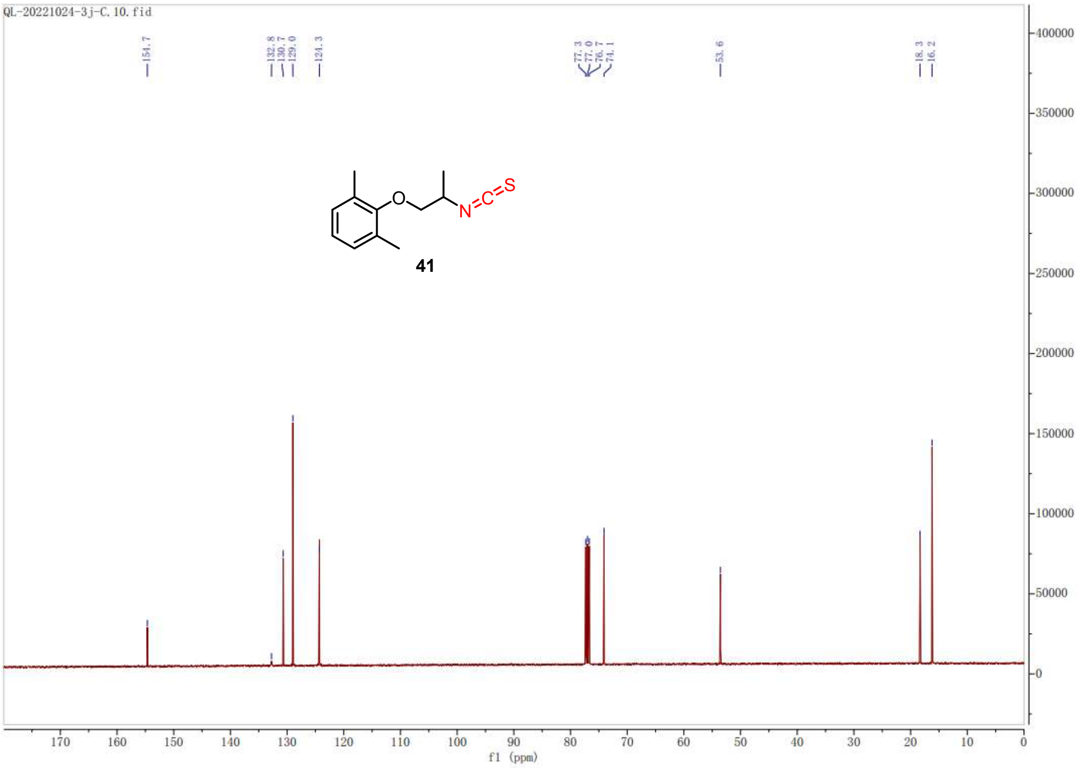

QL-20221024-3h-H.10.fid
7.37 7.35 7.34 7.26 7.25 7.24 7.23 7.22 7.22 7.14 7.13 7.11
4.95 4.94 4.92
2.91 2.89 2.88 2.86 2.85 2.83 2.79 2.78 2.77 2.76 2.75 2.73 2.73 2.71 2.15 2.14 2.13 2.12 2.11 2.11 2.10 2.04 2.03 2.02 2.01 2.00 1.99 1.98 1.97 1.88 1.87 1.86 1.86 1.85 1.84 1.83 1.82 1.55
N=C=S
39
0.99 1.95 1.01
1.00
2.13
2.13 2.17
f1 (ppm)


QL-20221024-3h-C.10.fid
136.4 133.2 131.8 129.4 128.6 128.3 126.5
77.3 77.0 76.7
55.7
30.8 28.5
19.3
N=C=S
39
f1 (ppm)


QL-20221024-3i-H.10.fid
7.37 7.36 7.35 7.34 7.26 7.25 7.24 7.23 7.22 7.22 7.14 7.13 7.11
4.95 4.94 4.92
2.91 2.89 2.88 2.86 2.85 2.84 2.79 2.78 2.77 2.76 2.75 2.73 2.71
2.15 2.14 2.14 2.13 2.12 2.11 2.11 2.10 2.04 2.03 2.02 2.01 2.00 2.00 1.99 1.99 1.98 1.98 1.87 1.86 1.86 1.85 1.84 1.83 1.82 1.81 1.55
N=C=S
40
0.99
1.91
1.02
1.00
2.15
2.13
2.17
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)
4500000 4000000 3500000 3000000 2500000 2000000 1500000 1000000 500000 0


QL-20221024-3i-C.10.fid
136.4 133.2 131.7 129.4 128.6 128.3 126.5
77.3 77.0 76.7
55.7
30.8 28.5
19.3
N=C=S
40
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
100000 90000 80000 70000 60000 50000 40000 30000 20000 10000 0


QL-20221024-3j-H.10.fid
7.19
6.96
6.94
6.89
6.87
6.87
6.85
4.11
4.09
4.08
4.06
3.73
3.72
2.23
1.48
1.44
1.43
O
N
C
S
41
1.92
0.99
0.98
2.00
5.97
3.01
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
14000000
13000000
12000000
11000000
10000000
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
-1000000


QL-20221024-3j-C.10.fid
154.7
132.8
130.7
129.0
124.3
77.3
77.0
76.7
74.1
53.6
18.3
16.2
O
N
C
S
41
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
400000
350000
300000
250000
200000
150000
100000
50000
0