N-Cyano Sulfoximine-Mediated Thiazole Ligation with *N*-Terminal Cysteine under Mild Aqueous Conditions

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Supporting information

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General methods

Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F_{254} glass plates precoated with a 0.2 mm thickness of silica gel. The TLC plates were visualized by shortwave (254 nm). Flash chromatography was carried out with Kieselgel 60 (230–400 mesh) silica gel. Melting points: Barnstead / Elecrothermal 9300, measurements were performed in open glass capillaries without corrections. NMR spectra: Bruker AV 300 MHz (^{1}H–NMR: 300 MHz), AV 400 MHz (^{1}H–NMR: 400 MHz, ^{13}C–NMR: 100 MHz), the spectra were recorded in $CDCl_3$, MeOD using TMS as internal standard. Since TMS cannot be used in D_2O, we used the residual D_2O peak (δ 4.79 ppm) as the internal standard. The spectra are reported in ppm. ^{1}H NMR data are reported as: (s = singlet, d = doublet, dd = doublet of doublet, ddd = doublet of doublet of doublet, dt = doublet of triplet, t = triplet, q = quartet, br = broad singlet, quin = quintet, m = multiplet; coupling constant(s) in Hz; integration, proton assignment). IR spectra were recorded using a BRUKER ALPHA Ⅱ ATR spectrometer. UV-vis spectra were recorded using a Thermoscientific GENESYS 150 spectrophotometer. LC/MS analysis were performed using an Agilent 1260 Infinity II LC system equipped with a single quadrupole mass spectrometer with electrospray ionization (ESI). High resolution mass spectra (HRMS) was performed at JEOL JMS-700 (FAB), Sciex 1290 infinity II/ TripleTOF 5600 plus(ESI), Waters Xevo G2-XS QTof(ESI). HPLC was performed at the Shimadzu Nexera seriese. HPLC analyses were conducted on a Shimadzu Nexera series system. Separation was performed using a C_{18} reverse phase column (250 × 4.6 mm, 5 μm particle size) with a 20 min gradient of 95:5 (v/v) water:acetonitrile, both containing 0.1% formic acid as an additive. All solvents were purified using column filter solvent purification system before use unless otherwise indicated. Reagents were purchased and used without further purification.

Solubility Measurement (μSOL-Based Semi-Equilibrium Method), lit.[1]

Preparation of Standard (STD) Solutions

A 50 mM stock solution of the reference compound was prepared in methanol (MeOH).

Serial dilutions were performed in 1.5 mL microtubes to obtain standard concentrations ranging from 1 to 500 μM in MeOH.

Preparation of Sample Solutions

Sample solutions were prepared at a final concentration of 250 μM in 1× phosphate-buffered saline (PBS, pH 7.4).

The suspensions were shaken at 1500 rpm for 24 h to reach semi-equilibrium.

Prior to measurement, samples were centrifuged to sediment undissolved solids, and the supernatant was carefully collected for UV–Vis analysis.

UV–Vis Spectrophotometric Measurement

Standard Curve Preparation:

The absorbance of each standard solution (1–500 μM) was measured using a Hellma 108F-QS cuvette at the appropriate λ_{max}, with MeOH as the blank reference.

A standard calibration curve was constructed by linear regression of absorbance versus concentration.

Sample Measurement:

An aliquot (200 μL) of each equilibrated sample solution (250 μM in PBS, pH 7.4) was transferred to a Hellma 108F-QS cuvette.

Absorbance was measured under the same conditions as for the standard curve, using PBS (1×, pH 7.4) as the blank reference.

Sample concentrations were determined by interpolation from the standard curve.

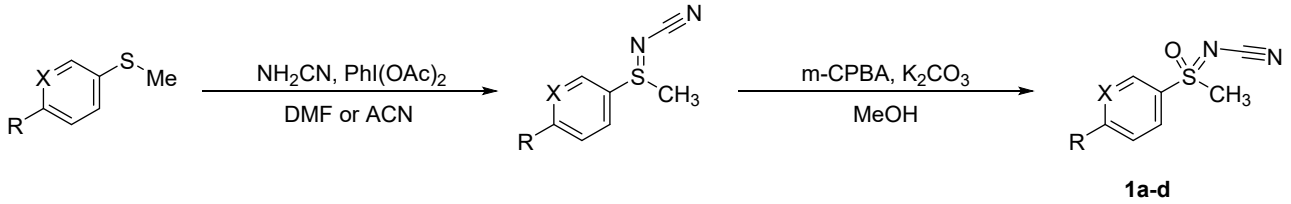
Data Analysis

All absorbance data were processed using ORIGIN software.

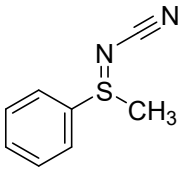
The measured solubility values represent the semi-equilibrium solubility under near-physiological pH conditions.

Experimental sections

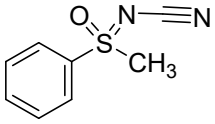
- Synthesis of *N*-Cyano Sulfoximines **1a-d**



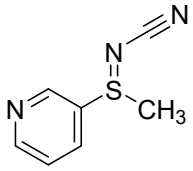
***(E)*-*N*-(methyl(pyridin-3-yl)-λ⁴-sulfaneylidene)cyanamide** : 89% yield, lit.[2]



***N*-(methyl(oxo)(pyridin-3-yl)-λ⁶-sulfaneylidene)cyanamide [1a]** : 59% yield, lit.[2]

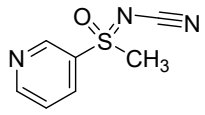


***(E)*-*N*-(methyl(pyridin-3-yl)-λ⁴-sulfaneylidene)cyanamide**



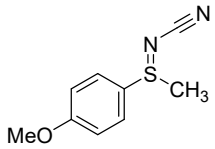
To a solution of 3-(methylthio)pyridine (200 mg, 2.0 mmol) and phenyliodine(III) diacetate (964 mg, 3.0 mol) in DMF (20 mL) was added cyanamide (252 mg, 6.0 mmol) at 0 ℃. The reaction mixture was stirred at 0 ℃ for 2 h and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on a silica gel (DCM:MeOH=20:1) to give the desired compound as a white oil (199.6 mg, 60% yield). ^{1}H NMR (400 MHz, MeOD) : δ 9.01 (d, J = 2.8 Hz, 1H), 8.85 (dd, J = 4.9, 1.6 Hz, 1H), 8.38 (ddd, J = 8.2, 2.4, 1.5 Hz, 1H), 7.72 (dd, J = 8.3, 4.8 Hz, 1H), 3.21 (s, 3H)., ^{13}C NMR (100 MHz, MeOD) : δ 154.51, 148.39, 135.91, 135.30, 126.43, 121.88, 36.26 HRMS (FAB+): Calcd for $C_7H_8N_3S$ $[M+H]^+$, 166.0433; found, 166.0432

***N*-(methyl(oxo)(pyridin-3-yl)-λ⁶-sulfaneylidene)cyanamide** [**1b**]

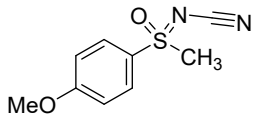


To a solution of *(E)-N*-(methyl(pyridin-3-yl)-λ⁴-sulfaneylidene)cyanamide (199 mg, 1.2 mmol) and potassium carbonate (182 mg, 1.32 mmol) in MeOH (24.0 mL) was added 75% meta-chloroperoxybenzoic acid (326 mg, 1.32 mmol) at 0 ℃. The reaction mixture was stirred at rt for 4 h and quenched with water. The reaction mixture was extracted with EtOAc and washed with brine. The organic layer was dried over MgSO4, filtered, and evaporated. The residue was purified by column chromatography on a silica gel (EtOAc/hexane = 2:1) to give the desired compound as a white solid (132 mg, 60% yield). m.p = 69 -70 ^{1}H NMR (400 MHz, $CDCl_3$) : δ 9.21 (d, J = 2.2 Hz, 1H), 9.01 (dd, J = 4.8, 1.3 Hz, 1H), 8.30 (ddd, J = 8.2, 2.2, 1.6 Hz, 1H), 7.65 (dd, J = 8.2, 4.8 1H), 3.42 (s, 3H)., ^{13}C NMR (100 MHz, $CDCl_3$) : δ 155.98, 148.95, 135.97, 133.32, 124.67, 111.08, 45.20. HRMS (FAB+): Calcd for $C_7H_8N_3OS$ $[M+H]^+$, 182.0383; found, 182.0389

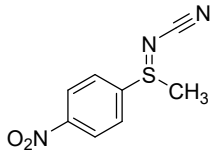
***(E)-N*-((4-methoxyphenyl)(methyl)-λ⁴-sulfaneylidene)cyanamide** : 86% yield, lit.[2]



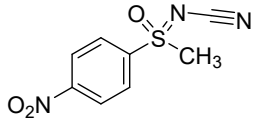
***N*-((4-methoxyphenyl)(methyl)(oxo)-λ⁶-sulfaneylidene)cyanamide [1c]** : 68% yield, lit.[2]



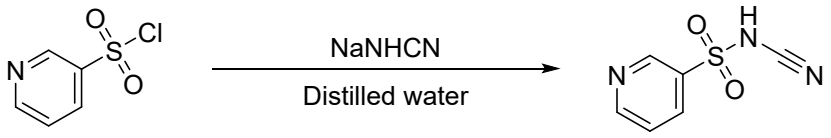
***(E)-N*-(methyl(4-nitrophenyl)-λ⁴-sulfaneylidene)cyanamide** : 68% yield, lit.[24]



***N*-(methyl(4-nitrophenyl)(oxo)-λ⁶-sulfaneylidene)cyanamide [1d]** : 88% yield, lit.[24]

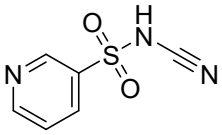


- Synthesis of *N*-Cyano Sulfonamide **1ba**



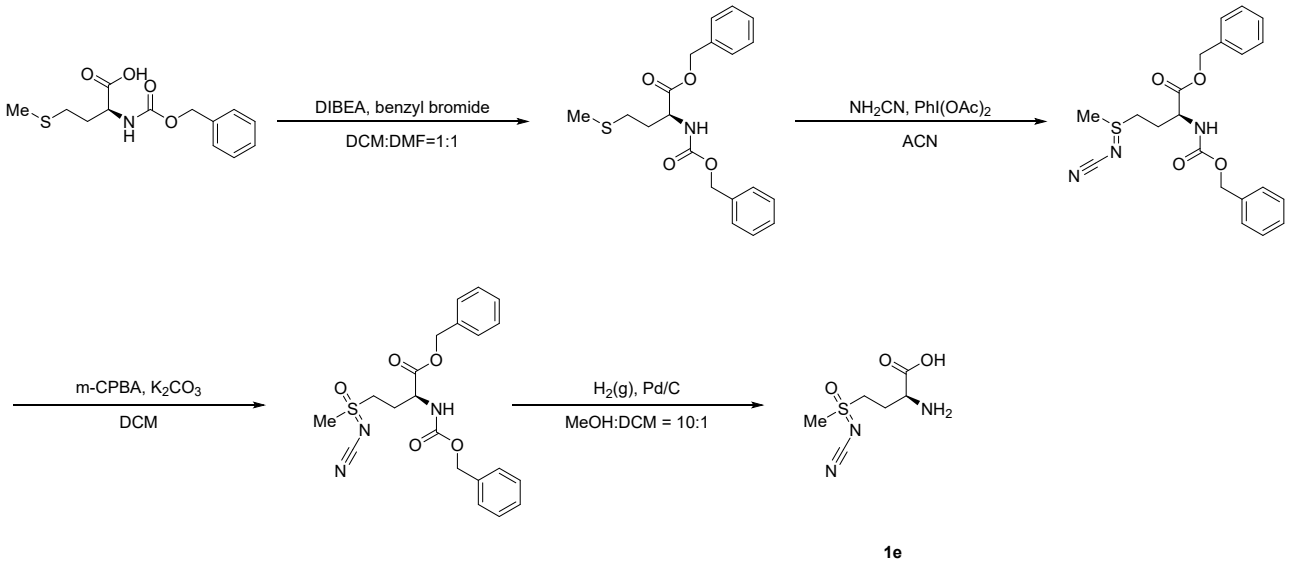
1ba

***N*-Cyanopyridine-3-sulfonamide** [**1ba**] lit[3]

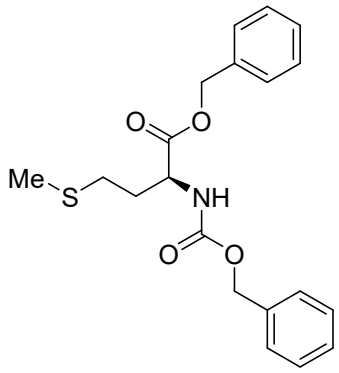


To a solution of Pyridine-3-sulfonyl chloride (200 mg, 1.1 mmol) in Distilled water (24.0 mL) was added Sodium hydrogencyanamide (82.6 mg, 1.3 mmol) at 0 ℃. The reaction mixture was stirred at 0 ℃ for 5 h. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography on a silica gel (DCM/MeOH = 7:1) to give the desired compound as a white solid (49 mg, 24% yield). m.p = 69-71; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 9.02 (d, J = 2.4 Hz, 1H), 8.73 (dd, J = 4.9, 1.6 Hz, 1H), 8.31 (dt, J = 8.1, 2.0 Hz, 1H), 7.64 (dd, J = 8.2, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 152.71, 147.60, 142.03, 135.81, 129.62, 125.37; IR (neat) 3344, 3234, 3091, 2251, 2176, 1631, 1550, 1462, 1294, 1210, 1148, 1105, 1043, 1021, 813, 741, 700.78, 675, 631, 611, 584, 521cm^{-1}; LC/MS (ESI+) : Calcd for $C_6H_6N_3O_2S$ $[M+H]^+$, 184.02; found, 183.90

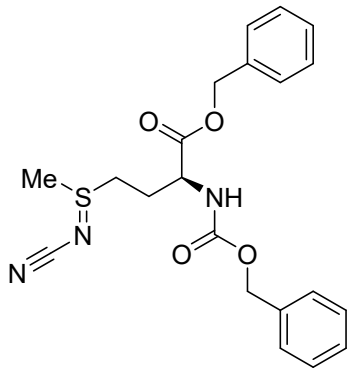
- Synthesis of *N*-Cyano Sulfoximines **1e**



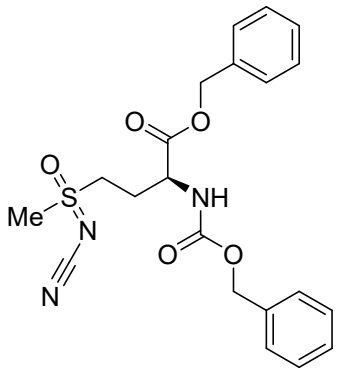
Benzyl ((benzyloxy)carbonyl)-L-methioninate : 76% yield, lit[4]



Benzyl (5*S*,*E*)-1-cyano-2-methyl-7-oxo-9-phenyl-8-oxa-2λ⁴-thia-1,6-diazanon-1-ene-5-carboxylate : 86% yield, lit[4]

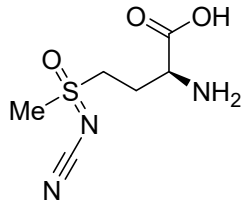


Benzyl (2*S*)-2-(((benzyloxy)carbonyl)amino)-4-(*N*-cyano-S-methylsulfonimidoyl)butanoate. lit.[4]



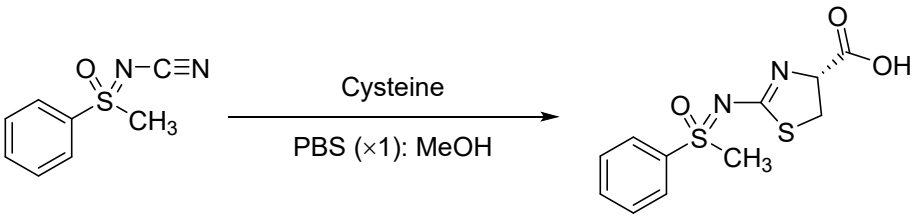
To a solution of Benzyl (5*S*,*E*)-1-cyano-2-methyl-7-oxo-9-phenyl-8-oxa-2λ⁴-thia-1,6-diazanon-1-ene-5-carboxylate (434.5 mg, 1.0 mmol) in DCM (21 mL), were added potassium carbonate (622 mg, 3.1 mmol) and meta-chloroperoxybenzoic acid (388.6 mg, 1.6 mmol) at 0 °C. The reaction mixture was stirred at rt for 4 h and quenched with water. The reaction mixture was extracted with EtOAc and washed with brine. The organic layer was dried over Na_2SO_4, filtered, and evaporated. The residue was purified by column chromatography on a silica gel (DCM/MeOH = 20:1) to give the desired compound as a white oil (357 mg, 79% yield). ^{1}H NMR (400 MHz, MeOD) : δ 7.41-7.25 (m, 10H), 5.20 (s, 2H), 5.10 (s, 2H), 4.44 (dd, J = 8.8, 5.0 Hz, 1H), 3.74-3.50 (m, 2H), 3.37 (s, 3H), 2.56-2.41 (m, 1H), 2.36-2.20 (m, 1H)., ^{13}C NMR (100 MHz, MeOD) : δ 172.11, 158.58, 138.00, 137.02, 129.64, 129.51, 129.43, 129.33, 129.09, 128.88, 113.84, 68.39, 67.92, 53.78, 52.51, 40.50, 40.44, 25.28.

(2*S*)-2-Amino-4-(*N*-cyano-S-methylsulfonimidoyl)butanoic acid [**1e**].

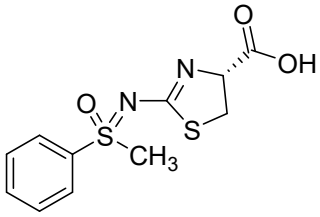


To a solution of Benzyl (2*S*)-2-(((benzyloxy)carbonyl)amino)-4-(*N*-cyano-S-methylsulfonimidoyl)butanoate (200 mg, 0.5 mmol) in MeOH : DCM = 10 : 1 (30 mL) was added 10% Pd/C (20 mg) at rt. The reaction was carried out in a Parr reactor under 50-60 psi of H_2 gas overnight and The Pd/C catalyst was removed by filtration through a Celite pad. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography on a C18 (H_2O:ACN=19:1) to give the desired compound as a white solid (1.03 g, 93% yield). ^{1}H NMR (400 MHz, D_2O) : δ 7.37 (s, 1H), 3.88-3.79 (m, 2H), 3.77-3.71 (m, 1H), 3.48 (s, 3H), 3.44 – 3.26 (m, 2H), 3.08 (s, 2H), 2.42-35 (m, 2H), 2.35 – 2.26 (m, 1H). ; IR (neat) 2999, 2919, 2192, 1578, 1519, 1450, 1400, 1324, 1237, 1192, 1144, 1072, 1022, 966, 928, 822, 773, 539cm^{-1}; HRMS (ESI+): Calcd for $C_6H_{11}N_3O_3S$ [M+Na$^+$], 228.0413; found,, 228.0421

- Synthesis of thiazole **2a**



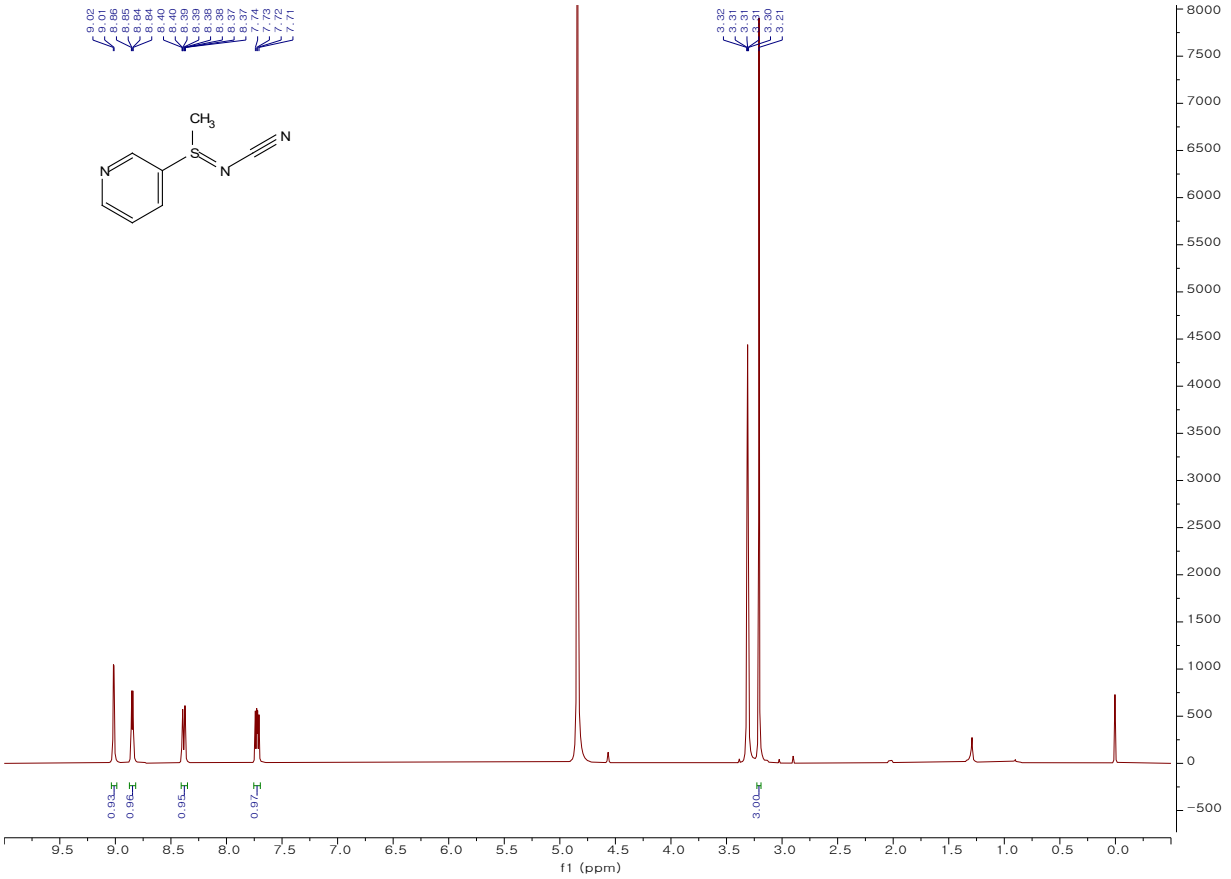
(4*R*)-2-((methyl(oxo)(phenyl)-λ⁶-sulfaneylidene)amino)-4,5-dihydrothiazole-4-carboxylic acid



To a solution of *N*-(methyl(oxo)(pyridin-3-yl)-λ⁶-sulfaneylidene)-cyanamide (50 mg, 0.3 mmol) in PBS(x1) pH 7.4 : MeOH = 8 : 1 (3 mL), were added Cysteine (67 mg, 0.6 mmol) at rt. The reaction mixture was stirred at 40°C for 48 h. The solvent was evaporated under reduced pressure. The residue was purified by reverse column chromatography on a C18 (H_2O : ACN = 9 : 1) to give the desired compound as a white solid (12 mg, 15% yield). m.p = 99.8 – 101.3, ^{1}H NMR (400 MHz, D_2O) : δ 8.10 – 8.00 (m, 2H), 7.92 – 7.83 (m, 1H), 7.78 – 7.72 (m, 2H), 4.74 – 4.62 (m, 1H), 3.91 – 3.49 (m, 5H)., ^{13}C NMR (100 MHz, D_2O) : δ 175.52, 175.35, 174.92, 174.16, 135.86, 135.83, 134.25, 134.22, 130.20, 130.16, 127.76, 127.73, 64.86, 63.11, 44.36, 44.30, 36.17, 36.12., HRMS (ESI+): Calcd for $C_{11}H_{12}N_2O_3S_2$ $[M+Na]^+$, 307.0182; found, 307.0181. HPLC: 98.63%, R_f = 9.91 min, 10.10 min

Figure S1 – S2. Experimental analysis of **1b**

Figure S1. ^{1}H and ^{13}C NMR spectroscopy



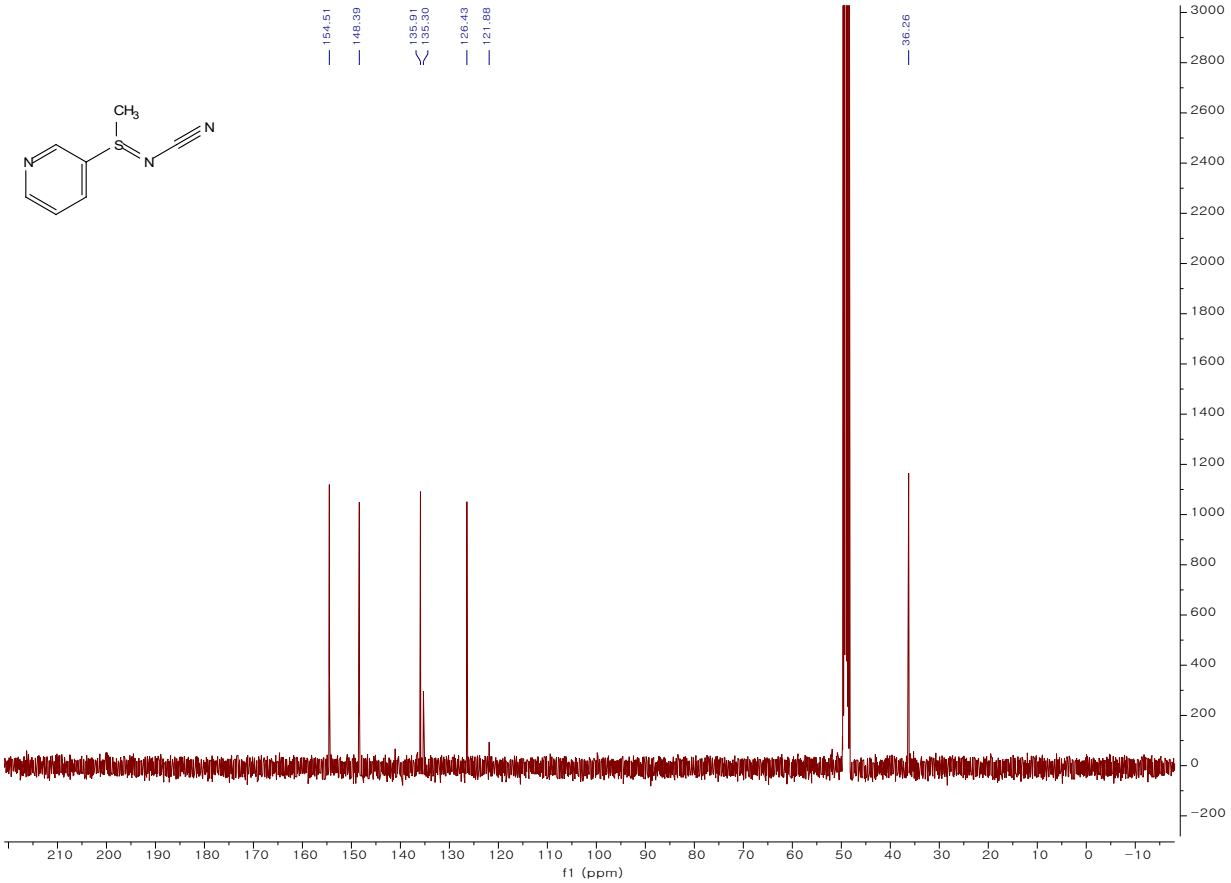
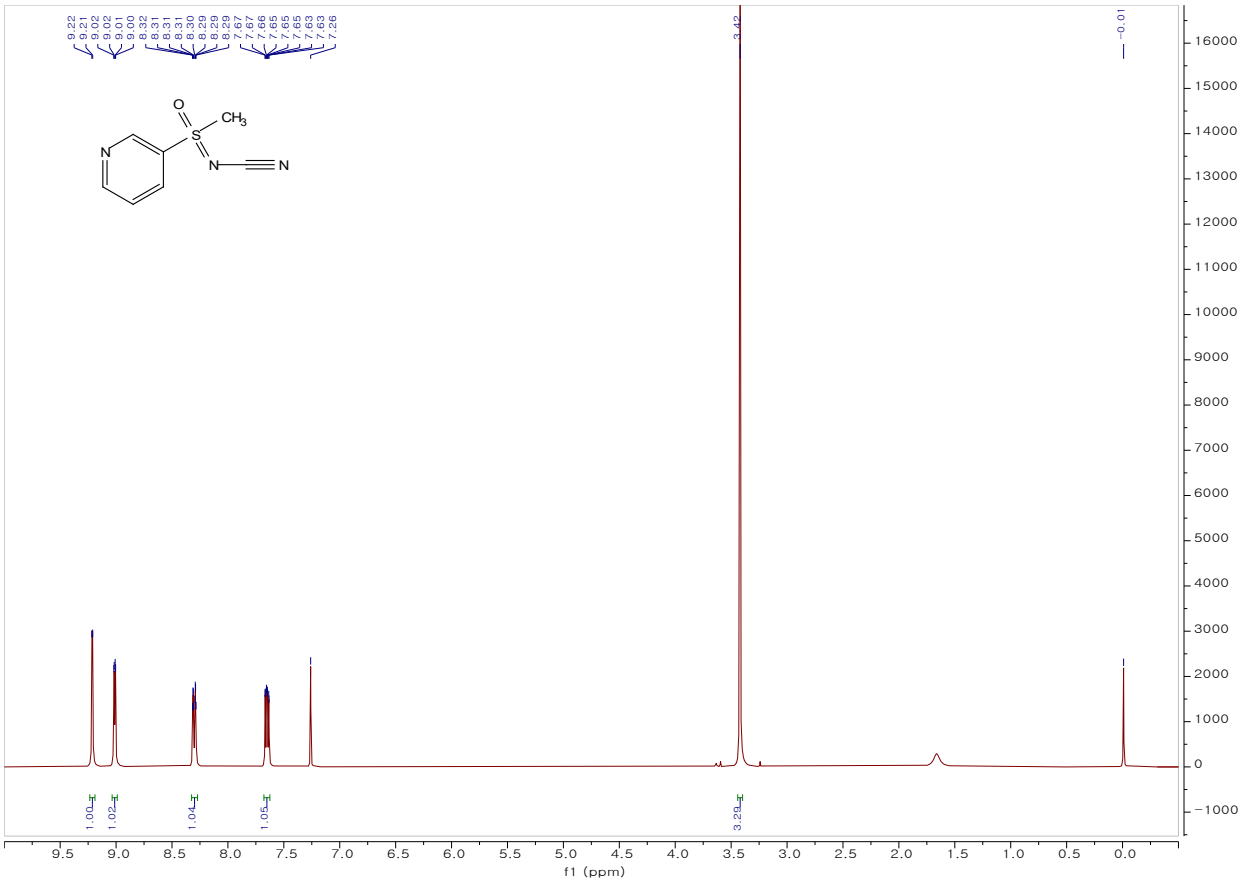


Figure S2. ^{1}H and ^{13}C NMR spectroscopy of **1b**



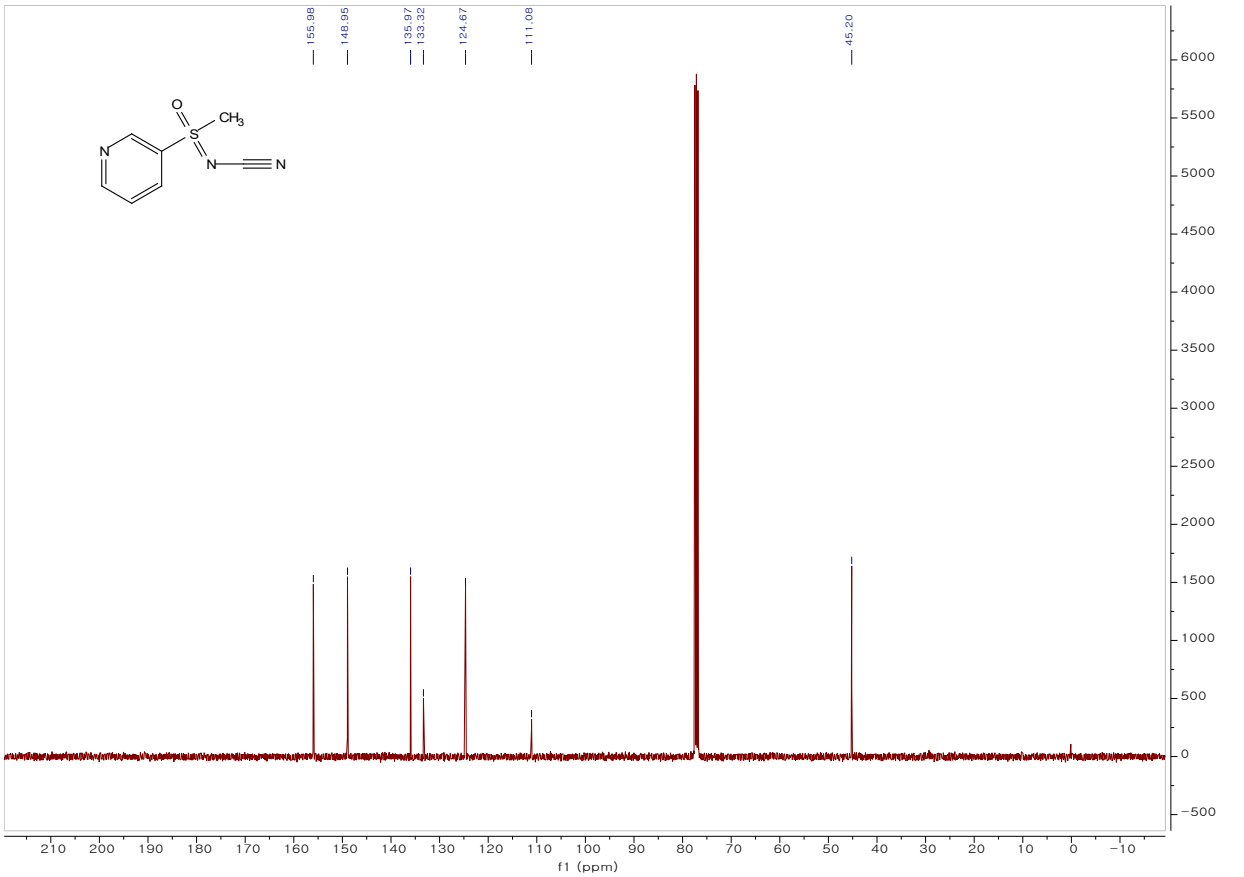
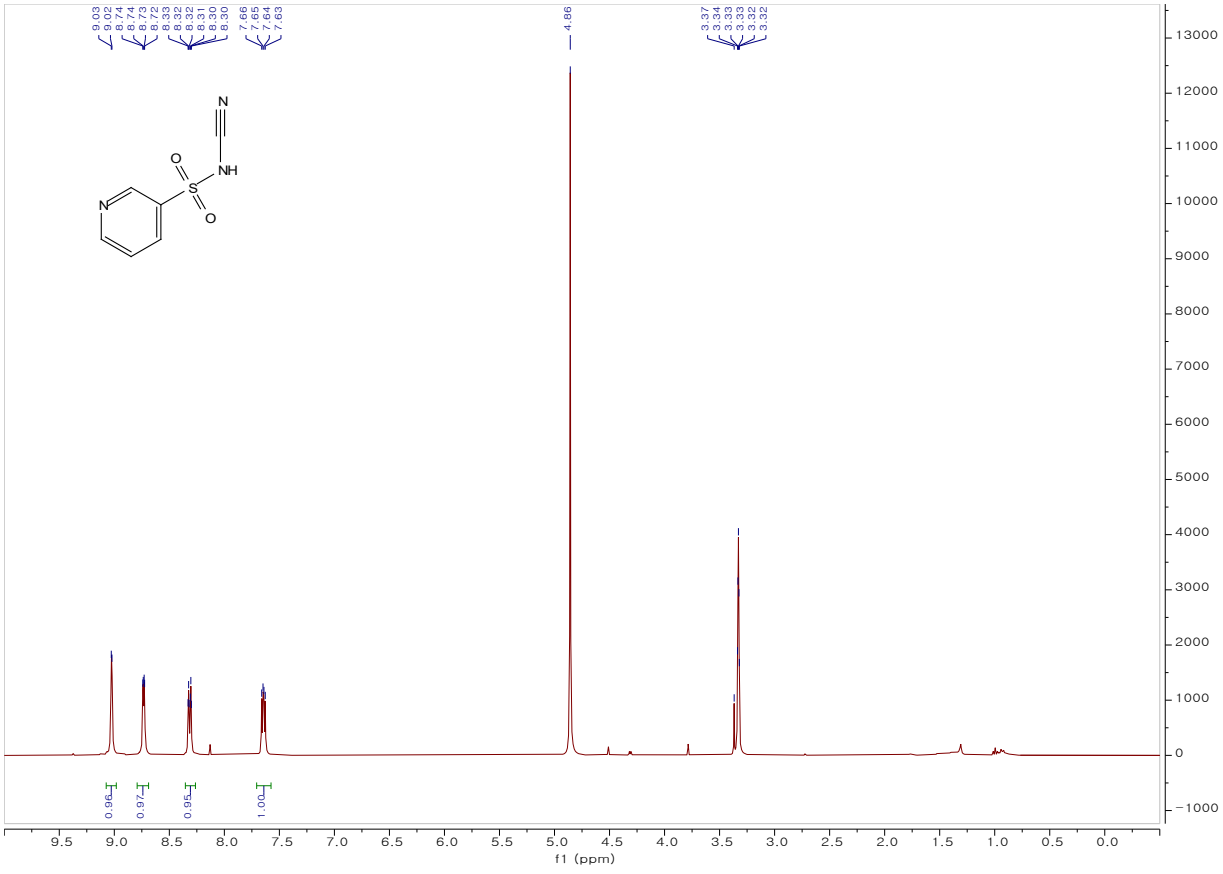


Figure S3. Experimental analysis of **1ba**

Figure S3-1. ^{1}H and ^{13}C NMR spectroscopy of **1ba**



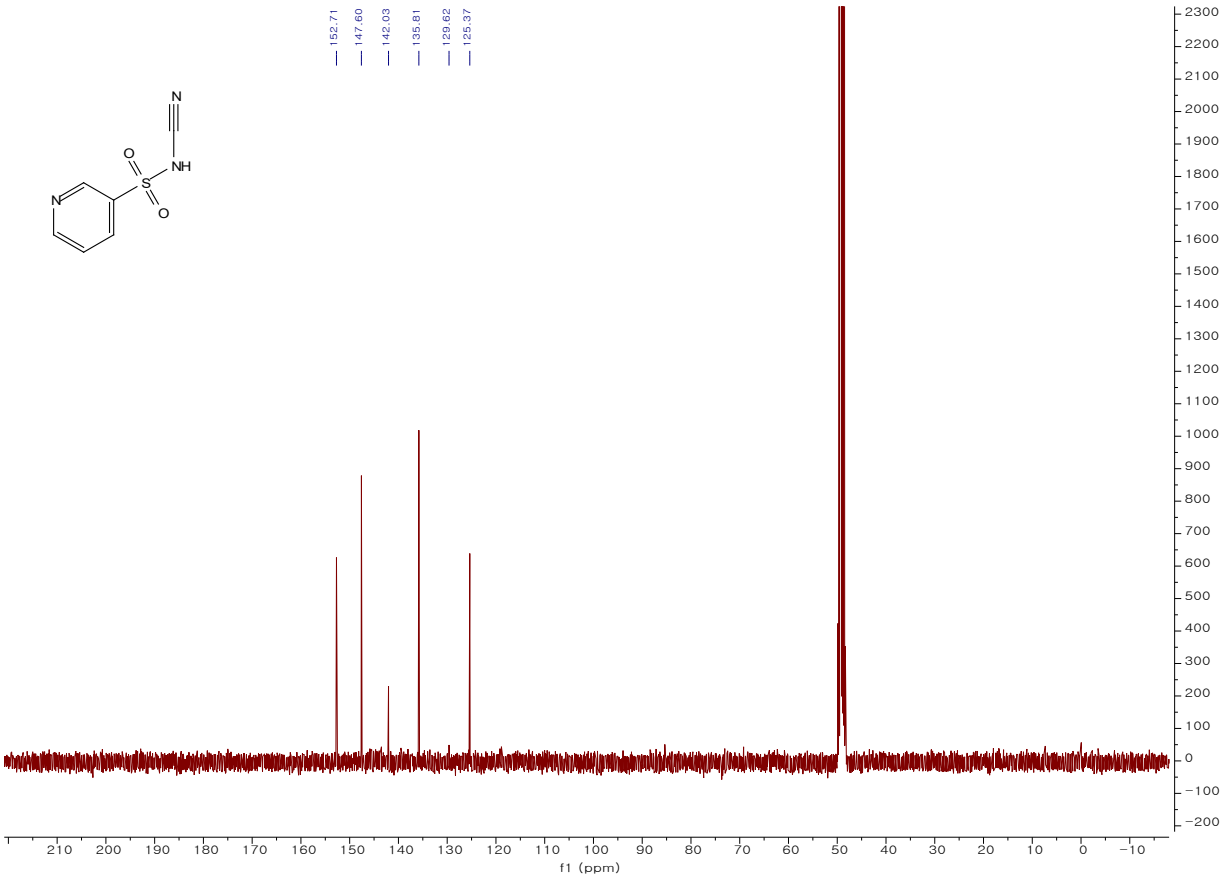


Figure S3-2. IR analysis data of **1ba**

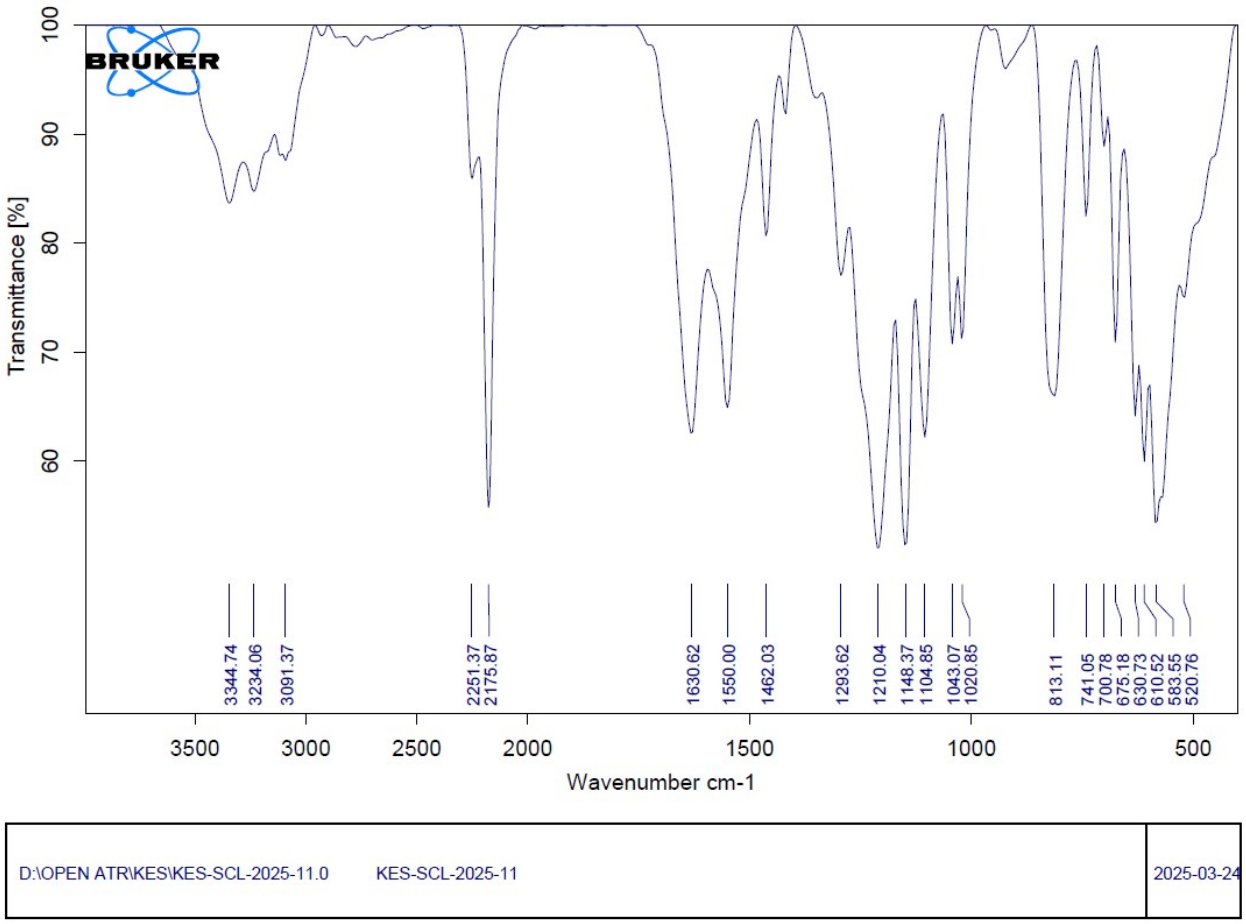


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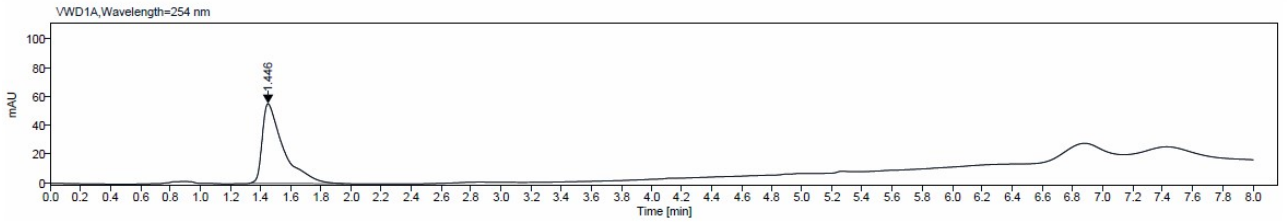
Figure S3-3. LC/MS analysis data of **1ba**

- UV data of **1ba**



- MS data of **1ba**

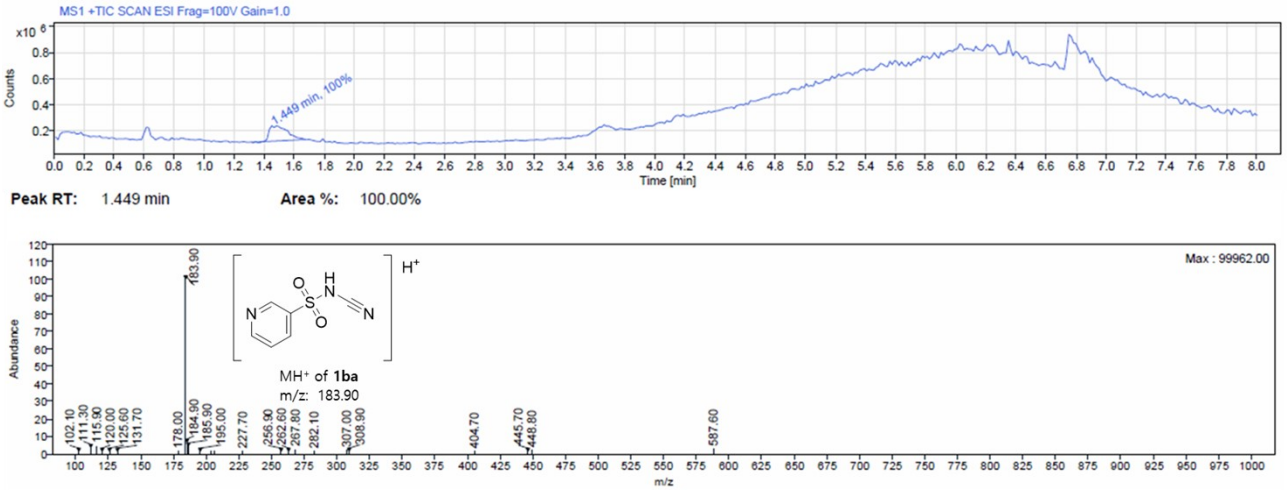
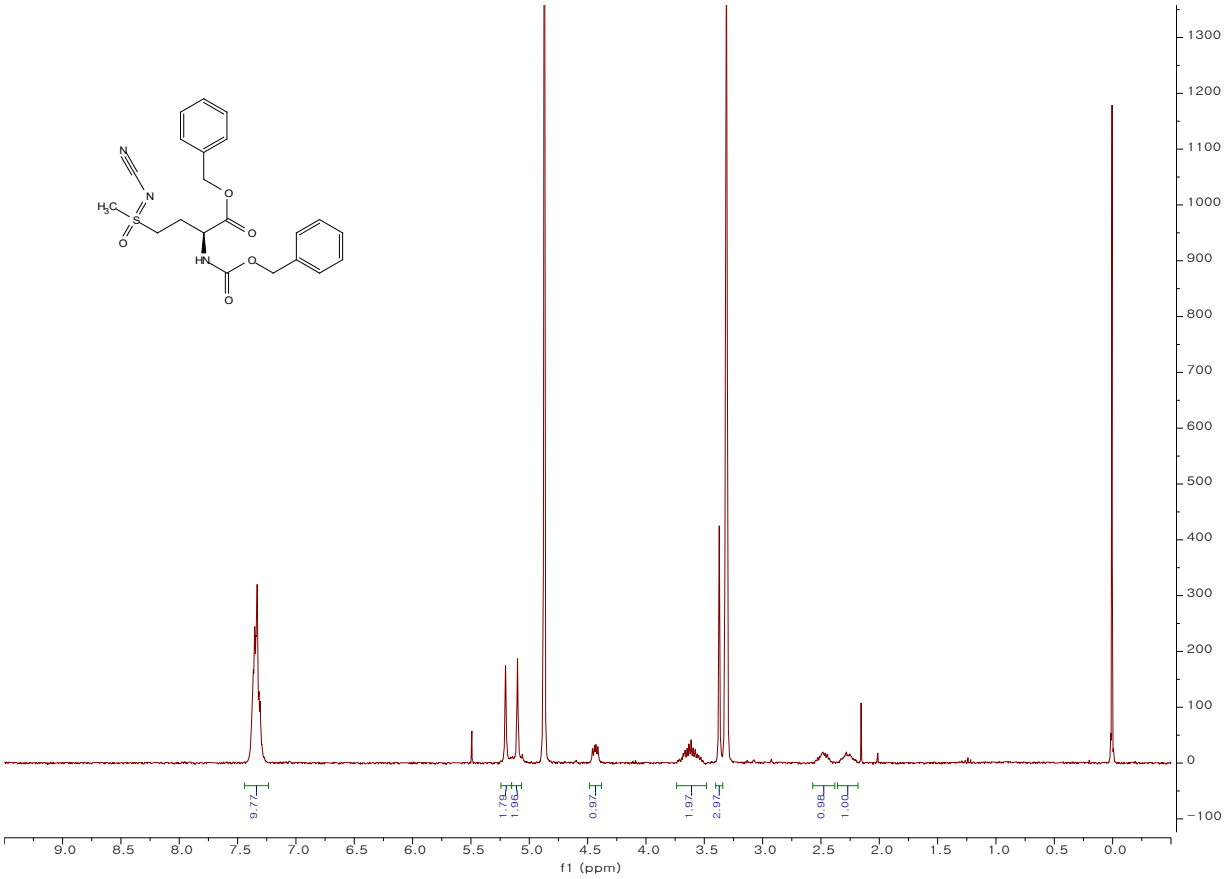


Figure S4 - S5. Experimental analysis of **1e**

Figure S4. ^{1}H and ^{13}C NMR spectroscopy of **1e** starting material



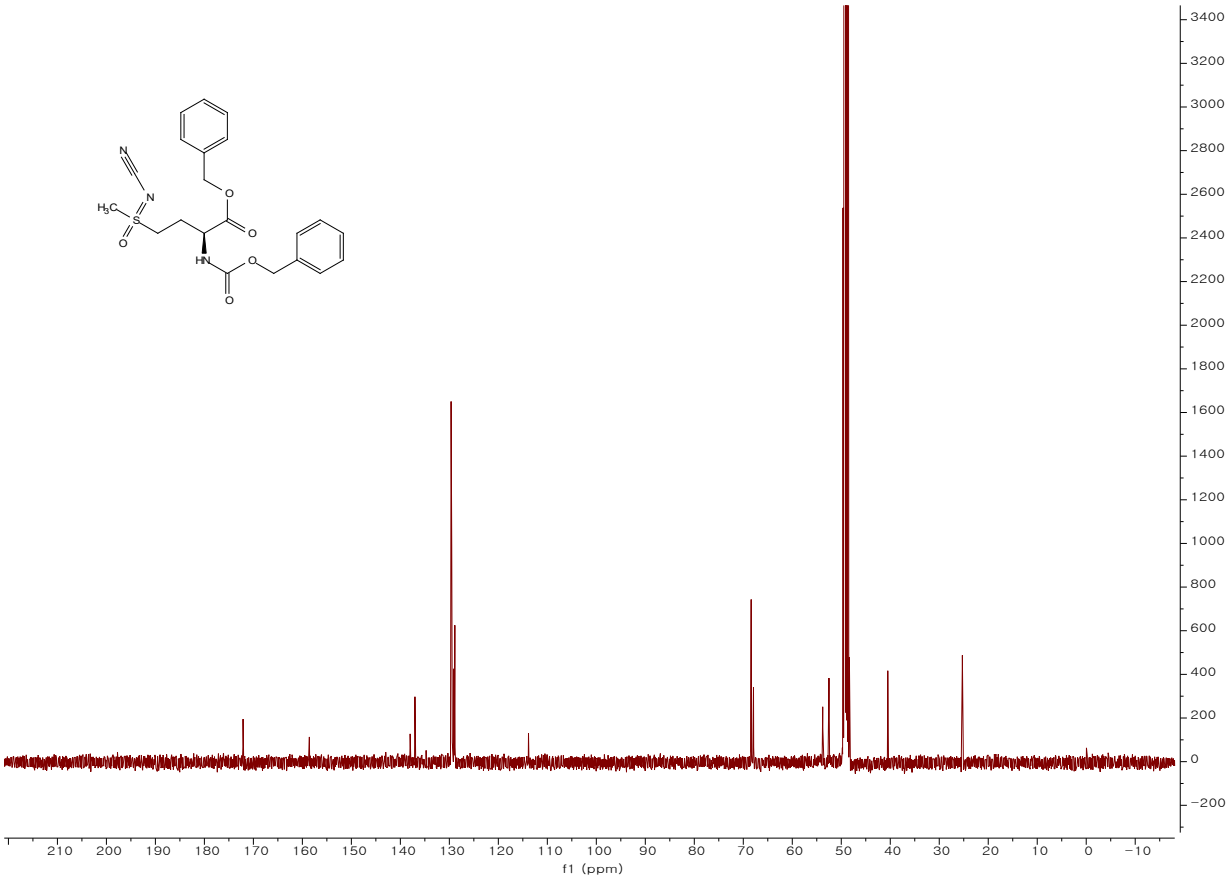


Figure S5-1. ^{1}H NMR spectroscopy of **1e**.

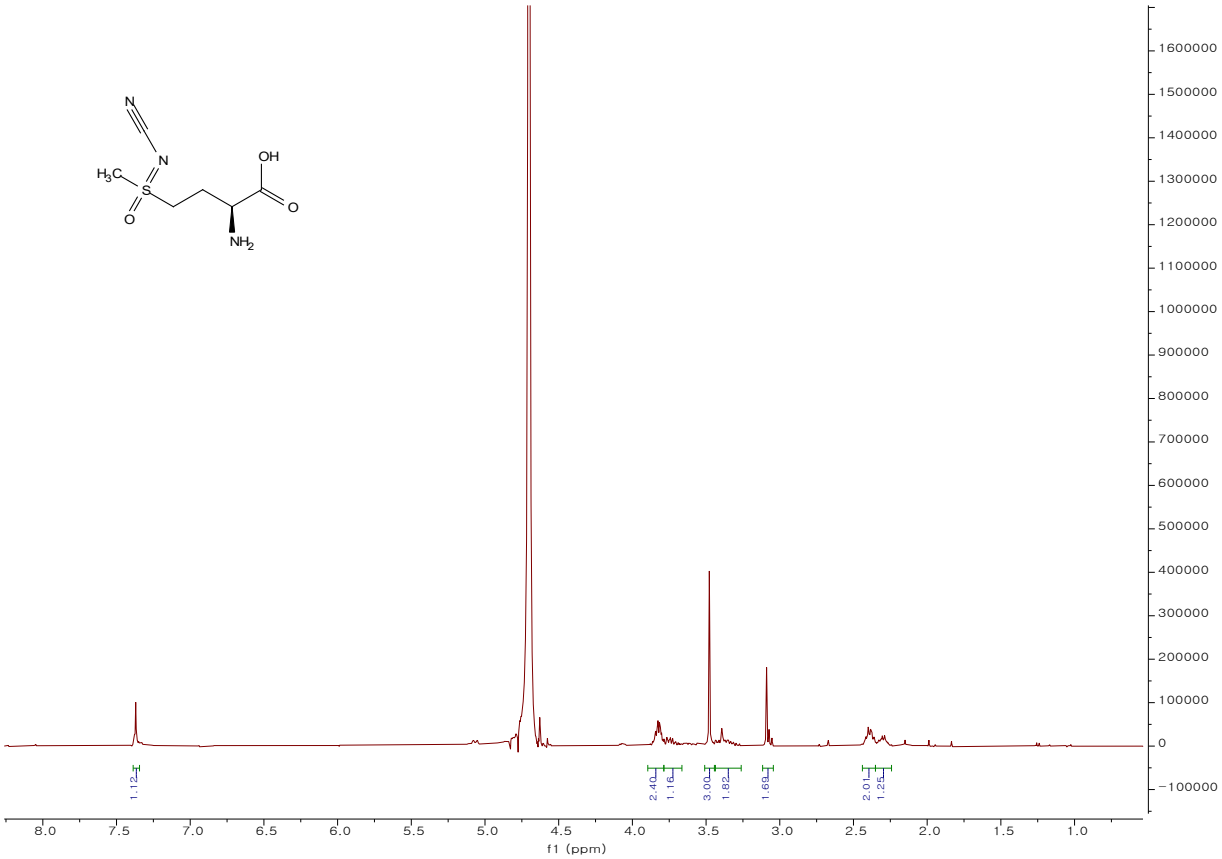
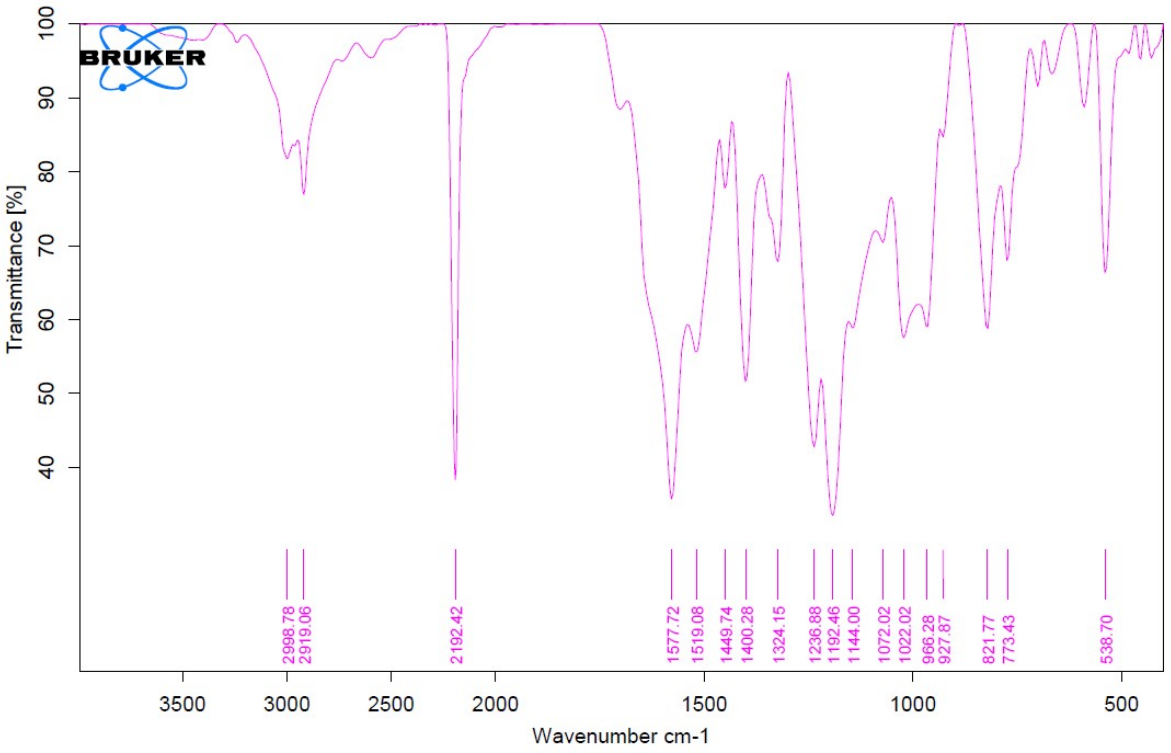


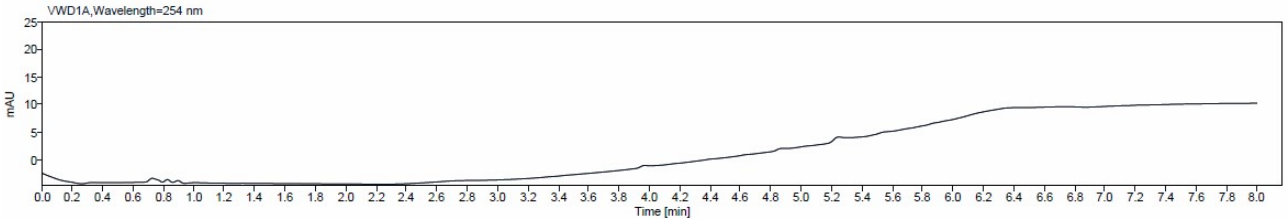
Figure S5-2. IR analysis data of **1e**



D:\분석 결과\OPEN ATR\SJP\KES-SCL-2025-34.0 KES-SCL-2025-34	2025-08-07

Figure S5-3. LC/MS analysis data of **1e**

- UV data of **1e**



- MS data of **1e**

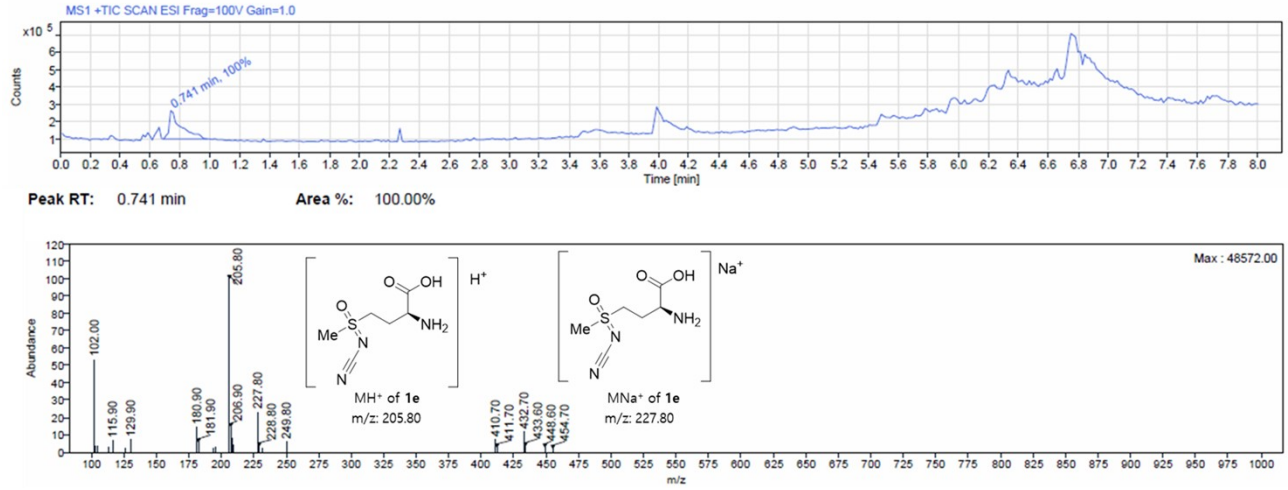
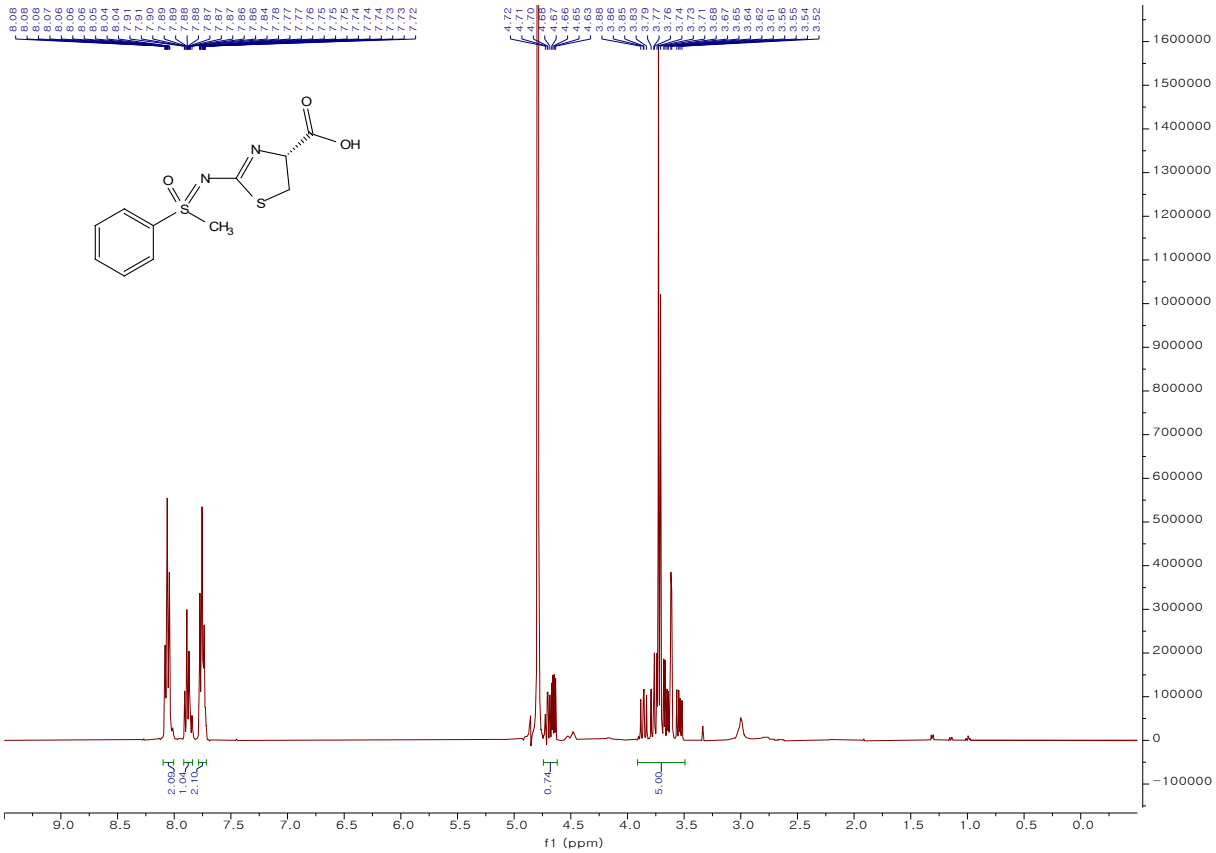


Figure S6. Experimental analysis of **2a**

Figure S6-1. ^{1}H and ^{13}C NMR spectroscopy of **2a**



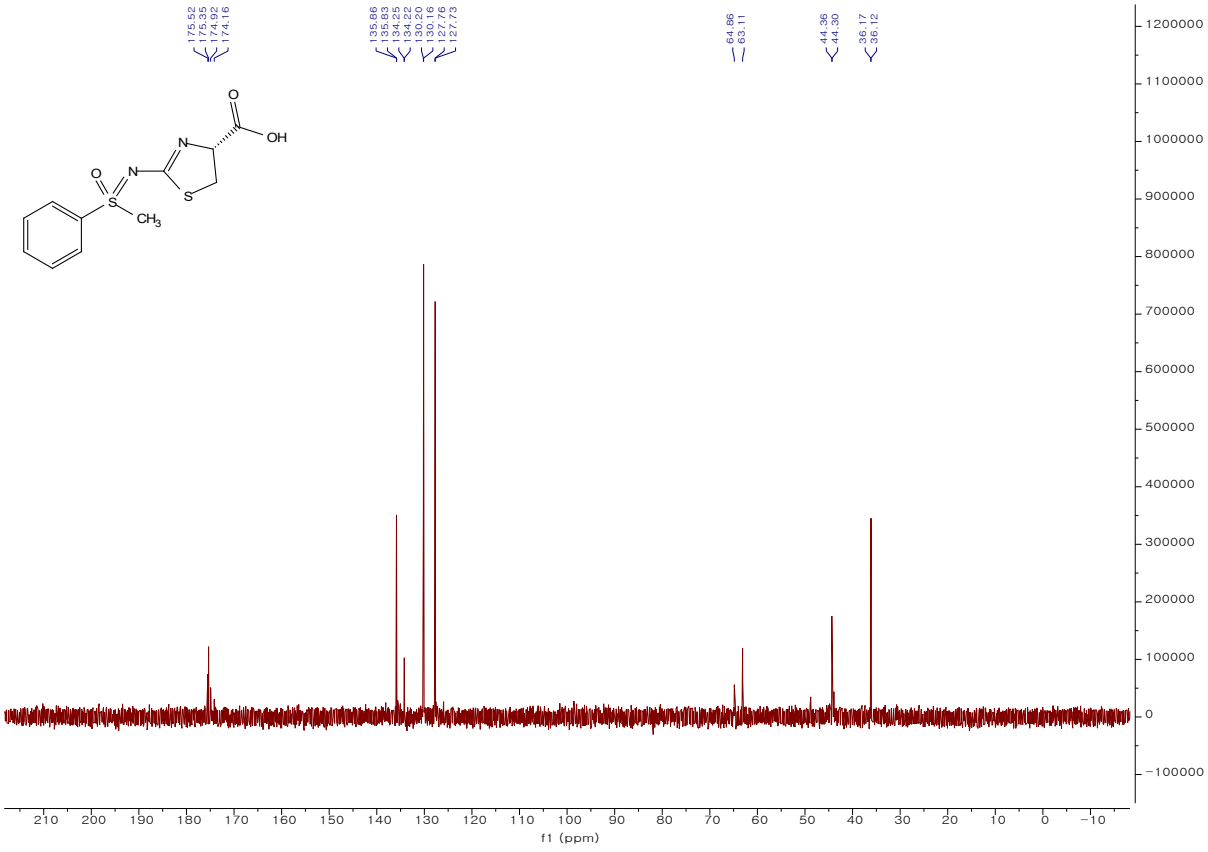
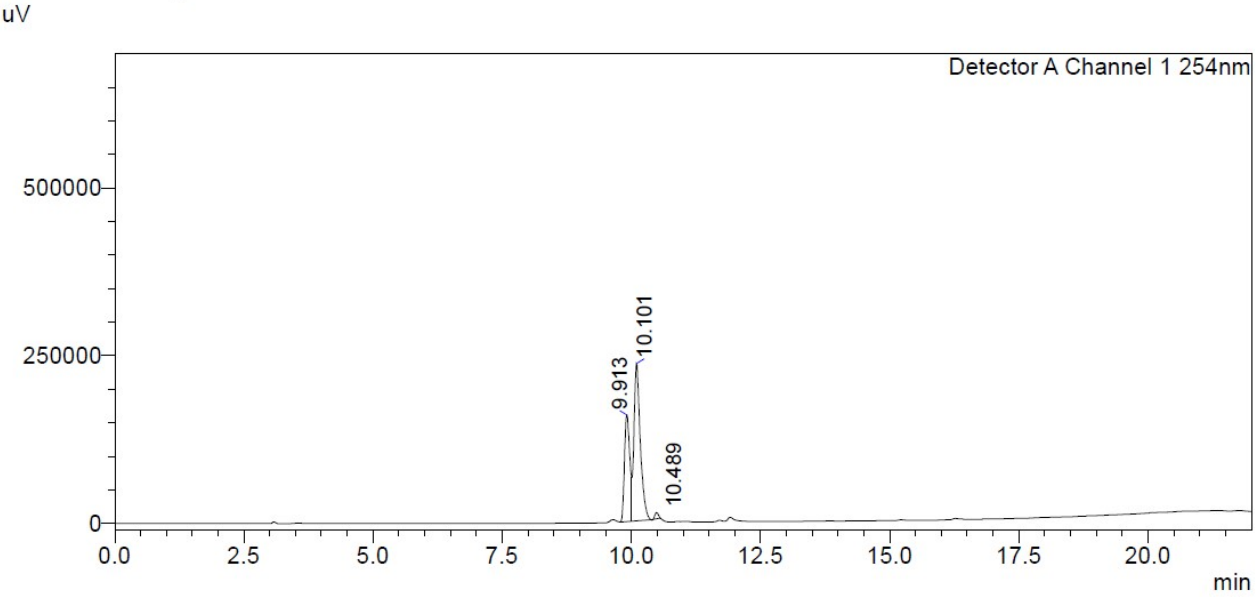


Figure S6-2. HPLC analysis data of **2a**

<Chromatogram>



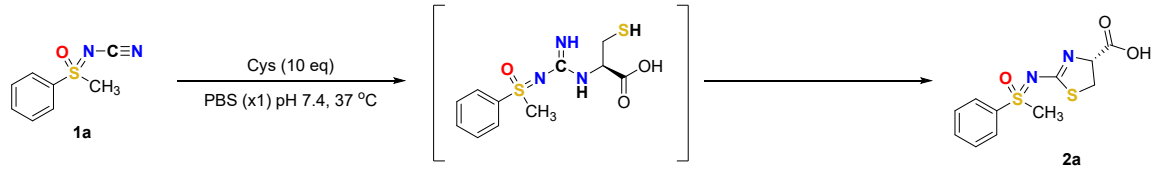
<Peak Table>

Detector A Channel 1 254nm

Peak#	Ret. Time	Area%	Area	Height	Name
1	9.913	36.054	1151402	158607	
2	10.101	62.578	1998467	234557	
3	10.489	1.367	43669	9015	
Total		100.000	3193538	402179	

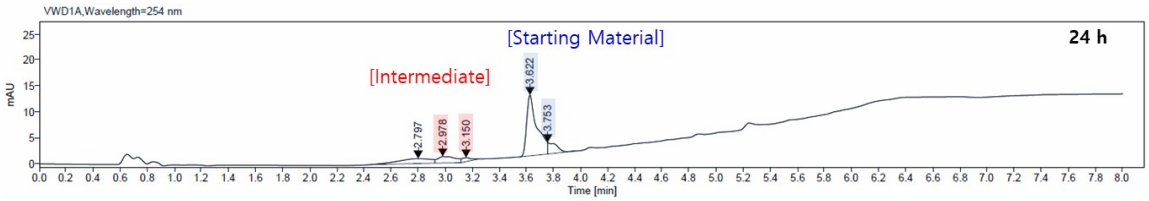
Figure S7. LC/MS analysis data of **Table 1.**

Figure S7. LC/MS data of **Entry 1**.



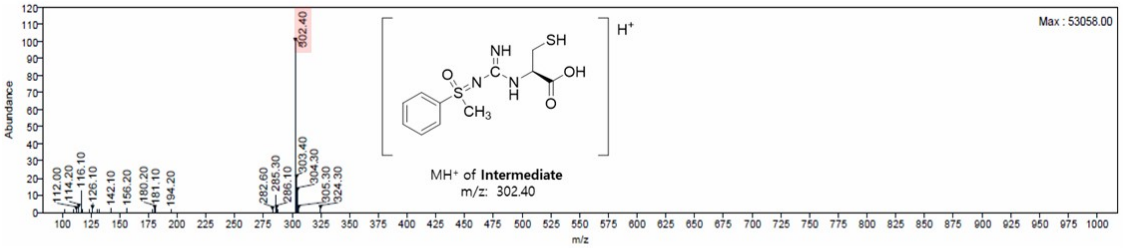
Exact Mass: 180.04 Exact Mass: 301.06 Exact Mass: 284.03

- LC/MS data of **24 h**

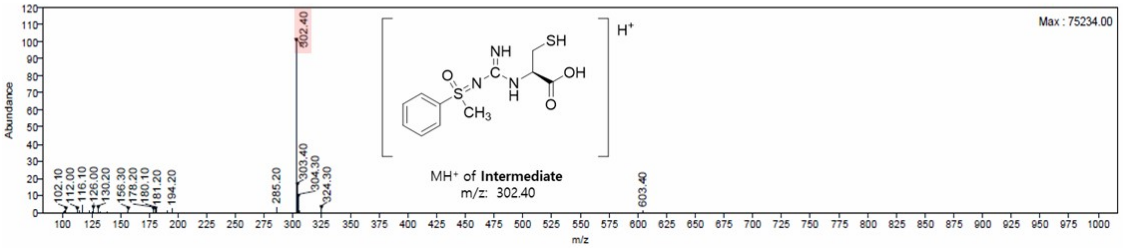


[Intermediate]

Peak RT: 2.998 min **Area %:** 4.26%

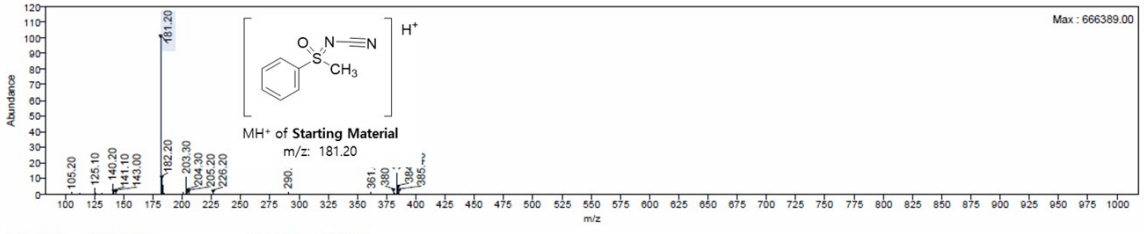


Peak RT: 3.178 min **Area %:** 3.93%

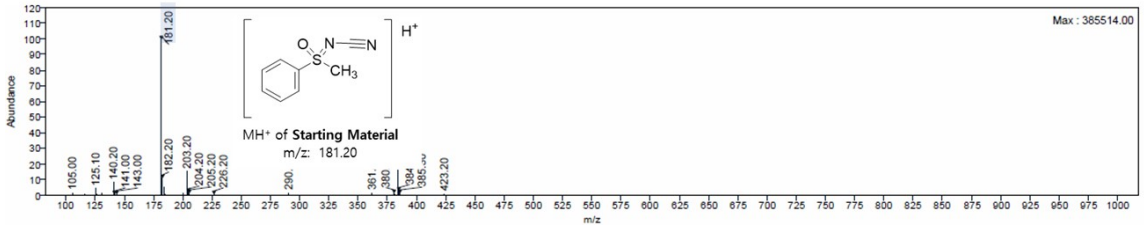


[Starting Material]

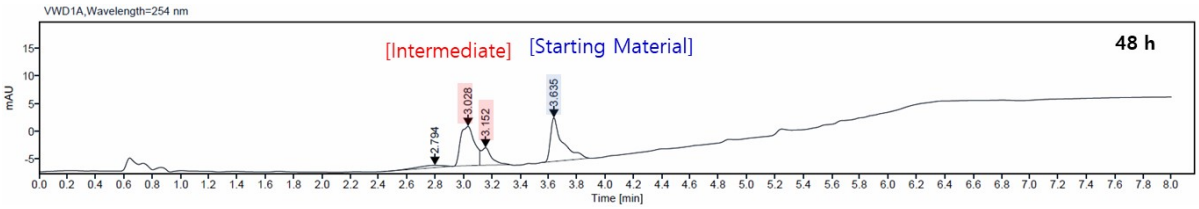
Peak RT: 3.65 min **Area %:** 37.98%



Peak RT: 3.688 min **Area %:** 33.52%

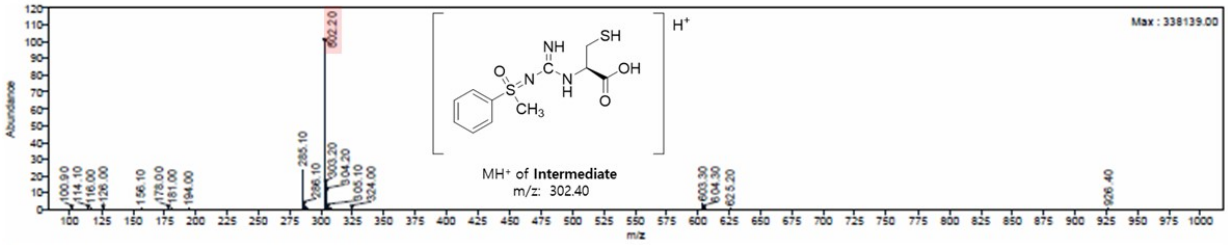


- LC/MS data of **48 h**

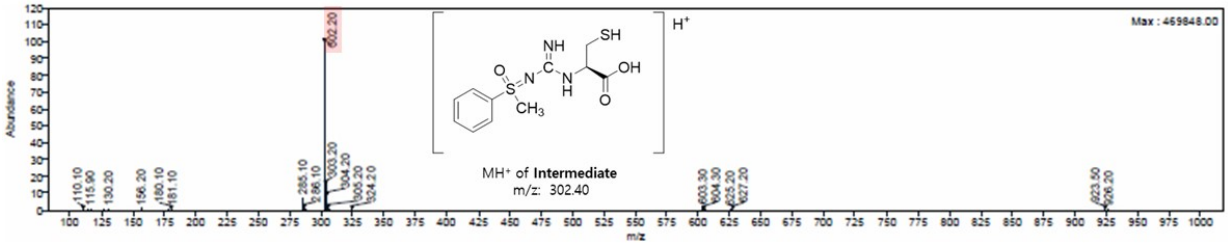


[Intermediate]

Peak RT: 3.014 min **Area %:** 23.84%

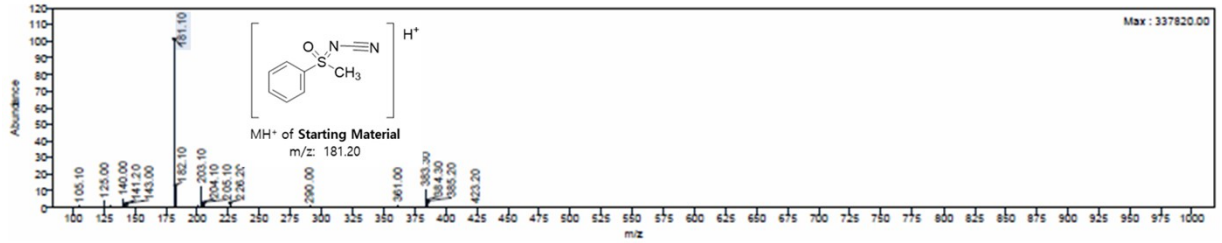


Peak RT: 3.184 min **Area %:** 24.30%

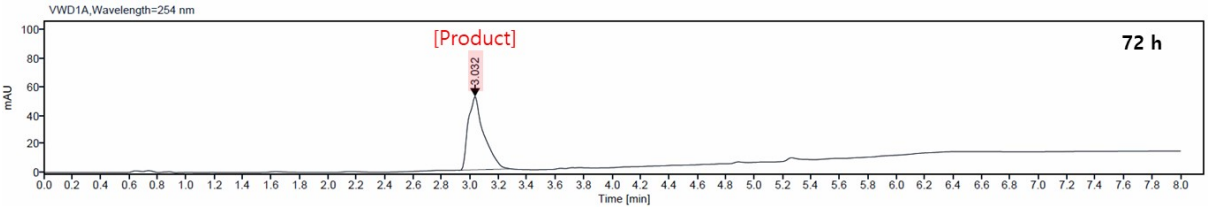


[Starting Material]

Peak RT: 3.719 min **Area %:** 17.94%



- LC/MS data of **72 h**



[Product]

Peak RT: 3.056 min **Area %:** 100.00%

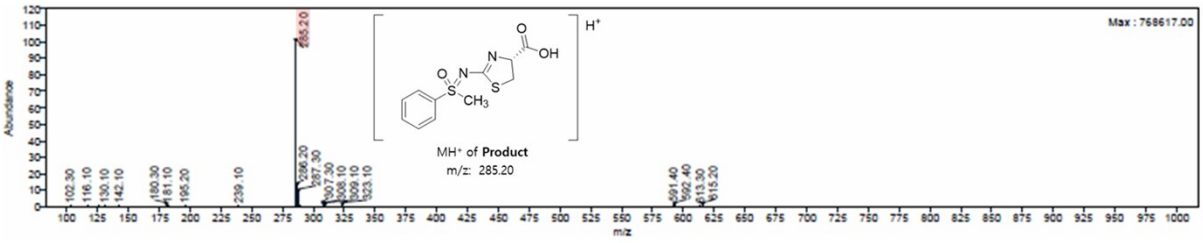
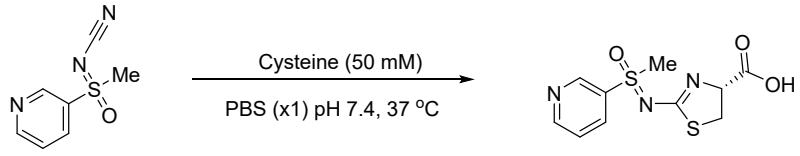


Figure S8 – S10. LC/MS analysis data of **Table 2.**

Figure S8. LC/MS data of **Entry 2.**



(5 mM)

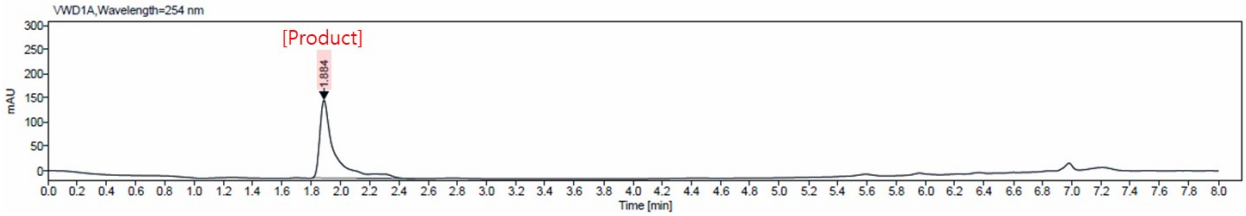
1b

Exact Mass: 181.03

2b

Exact Mass: 285.02

- LC/MS UV data of **25 h**



- LC/MS MS data of **25 h**

[Product]

Peak RT: 1.966 min **Area %:** 22.78%

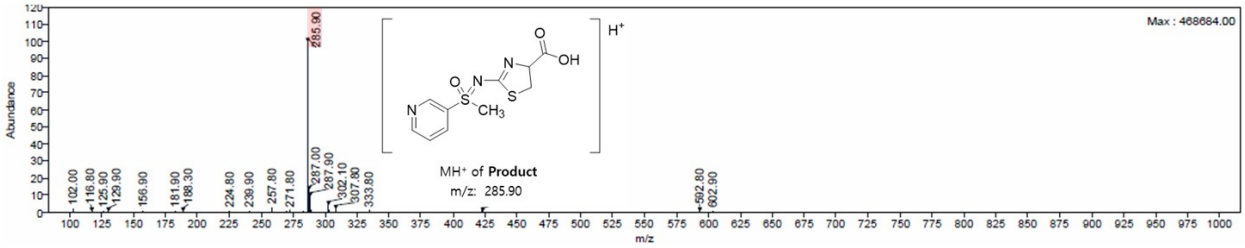
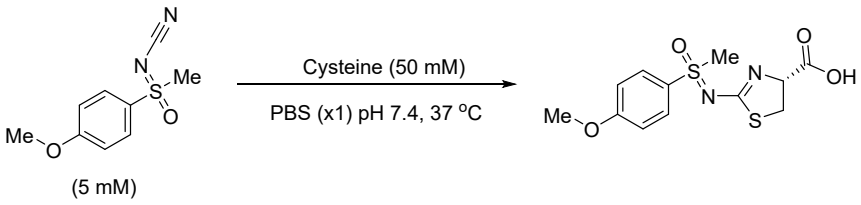


Figure S9. LC/MS data of **Entry 3**



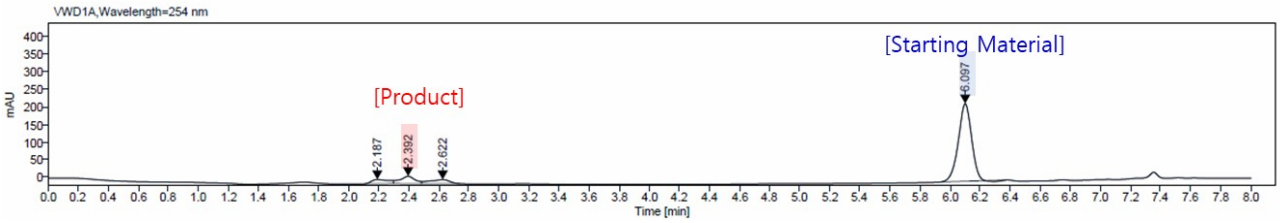
1c

Exact Mass: 210.05

2c

Exact Mass: 314.04

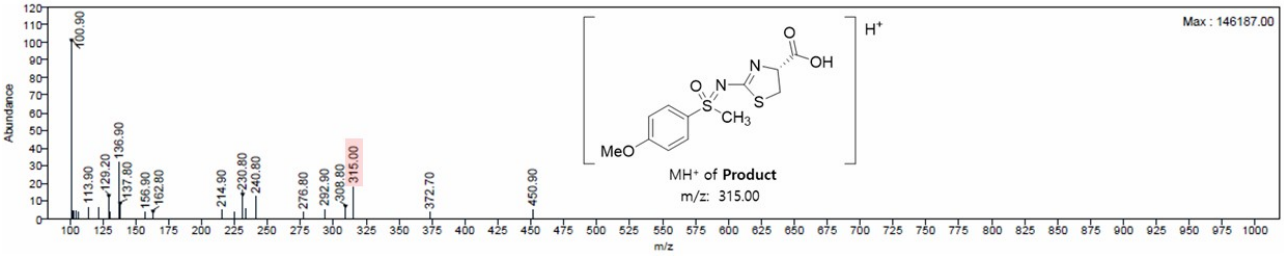
- LC/MS UV data of **49 h**



- LC/MS MS data of **49 h**

[Product]

Peak RT: 2.397 min **Area %:** 2.41%



[Starting Material]

Peak RT: 6.16 min **Area %:** 27.14%

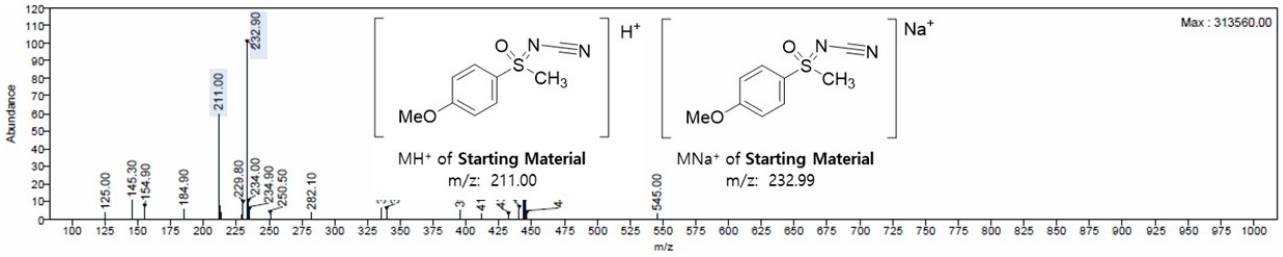
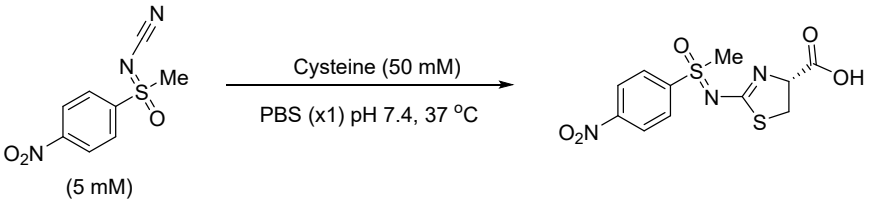


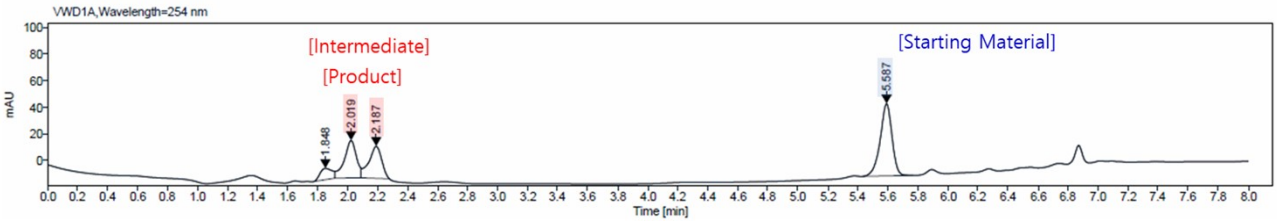
Figure S10. LC/MS data of **Entry 4.**



1d
Exact Mass: 225.02

2d
Exact Mass: 329.01

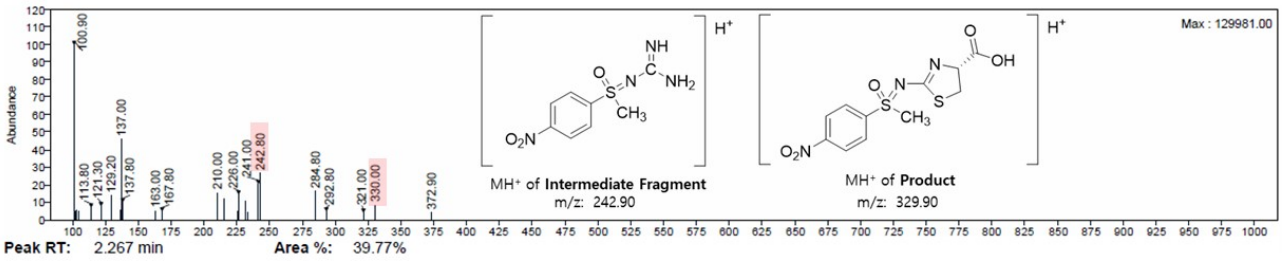
- LC/MS UV data of **49 h**



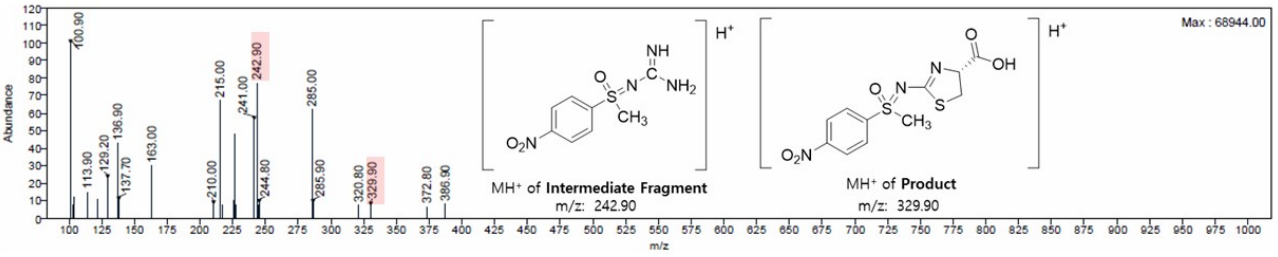
- LC/MS MS data of **49 h**

[Intermediate & Product]

Peak RT: 2.095 min **Area %:** 18.73%



Peak RT: 2.267 min **Area %:** 39.77%



[Starting Material]

Peak RT: 5.639 min **Area %:** 10.27%

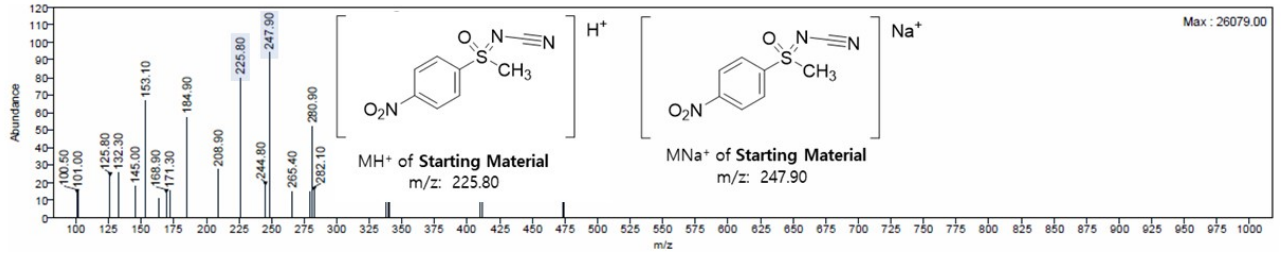
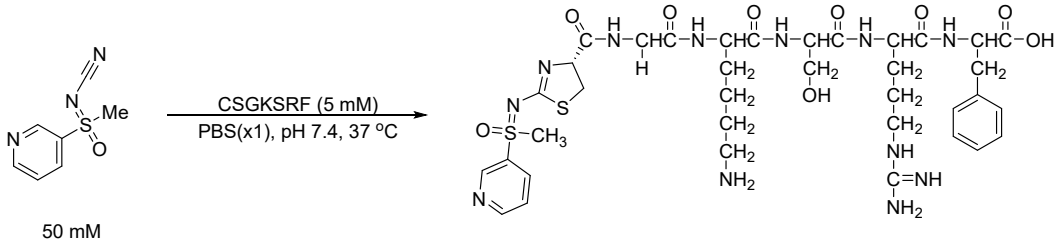
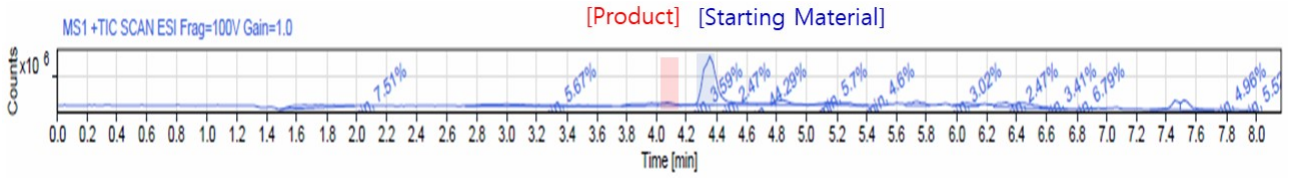


Figure S11 – S13 LC/MS analysis of **peptide-1b** click adduct**.**

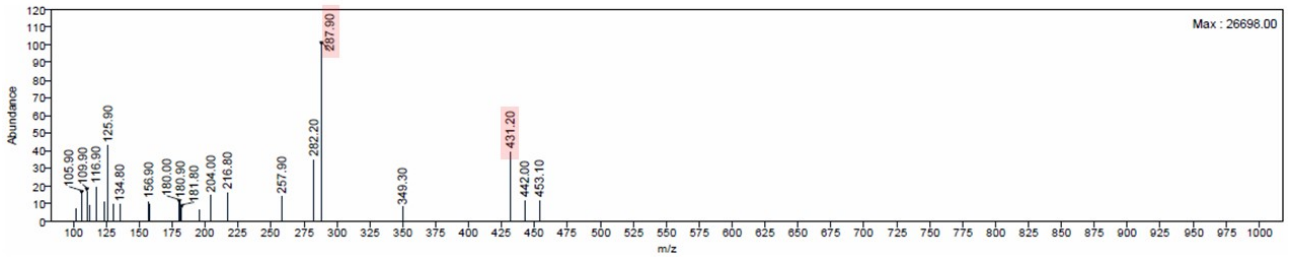
Figure S11. LC/MS data of **Peptide1-1b** click adduct**.**

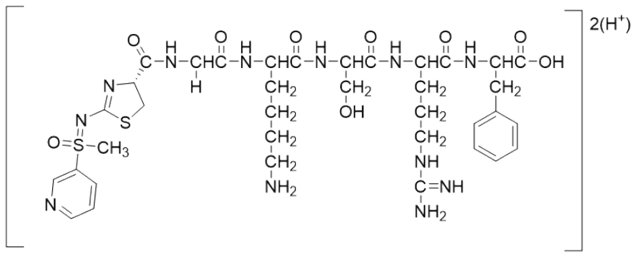


- LC/MS MS data of **28 h**

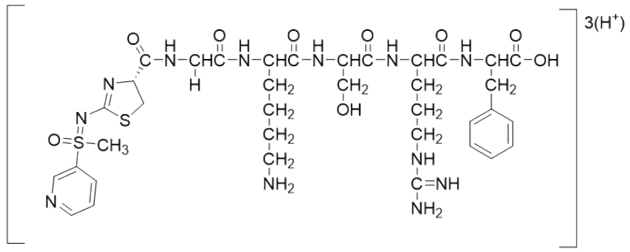


Peak RT: 4.066 min **Area %:** 2.47%



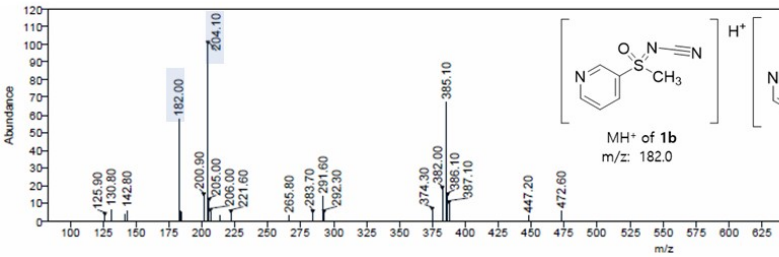


M2(H⁺) of **Product**
m/z : 431.0



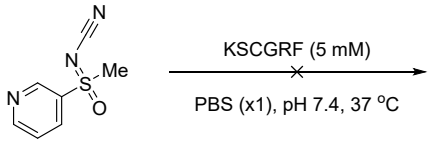
M3(H⁺) of **Product**
m/z : 287.7

Peak RT: 4.351 min **Area %:** 44.29%



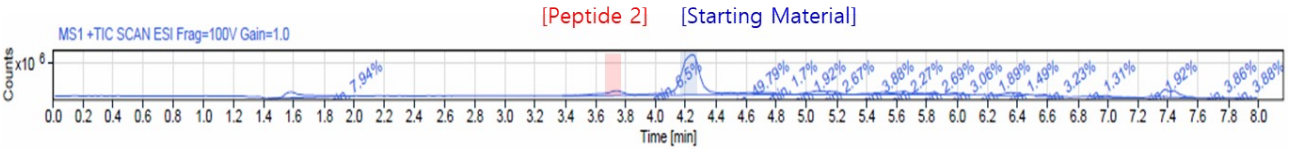
MH⁺ of **1b**
m/z: 182.0

Figure 12. LC/MS data of **Peptide2-1b** click adduct.

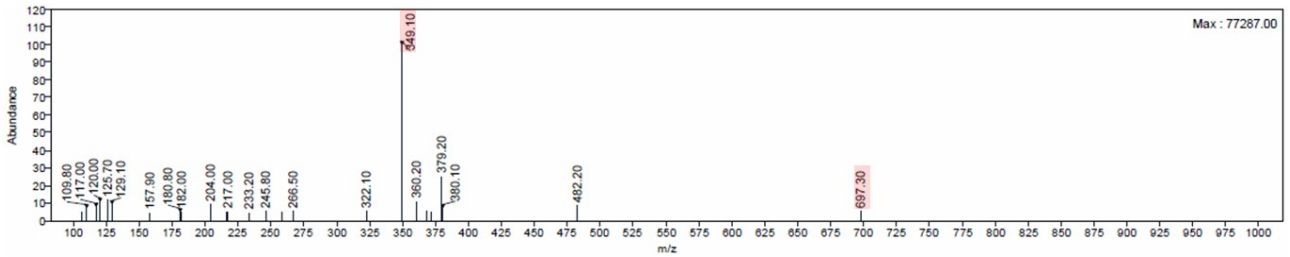


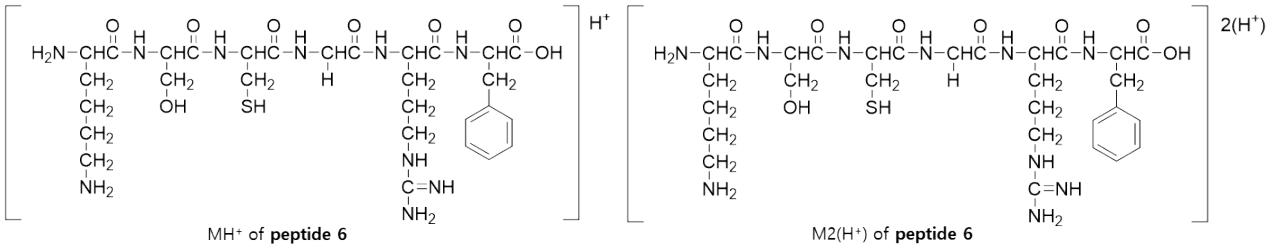
50 mM

- LC/MS MS data of **28 h**



Peak RT: 3.736 min **Area %:** 6.50%

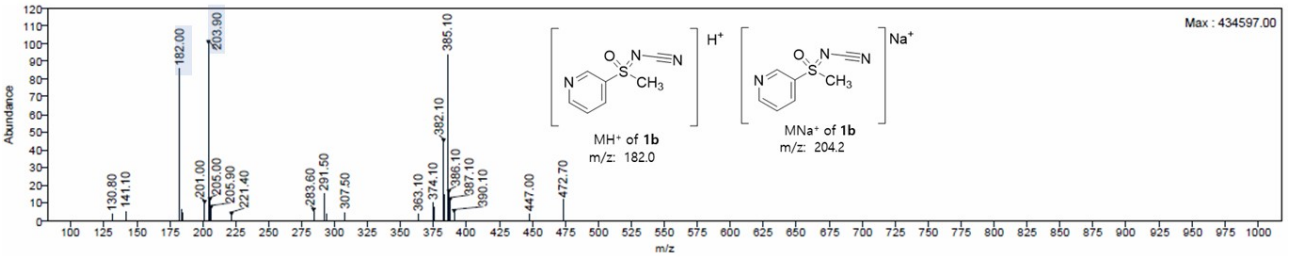




MH⁺ of **peptide 6**
m/z: 697.8

M2(H⁺) of **peptide 6**
m/z: 349.4

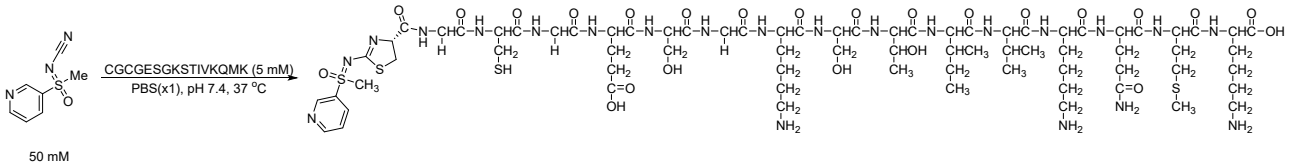
Peak RT: 4.239 min **Area %:** 49.79%



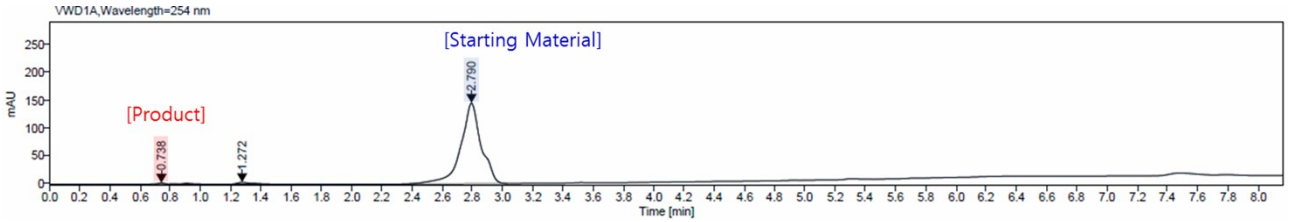
MH⁺ of **1b**
m/z: 182.0

MNa⁺ of **1b**
m/z: 204.2

Figure 13. LC/MS data of **Peptide3-1b** click adduct.

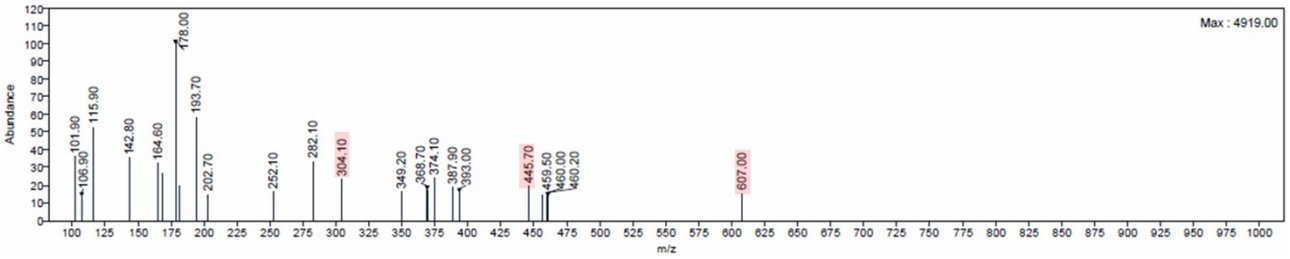


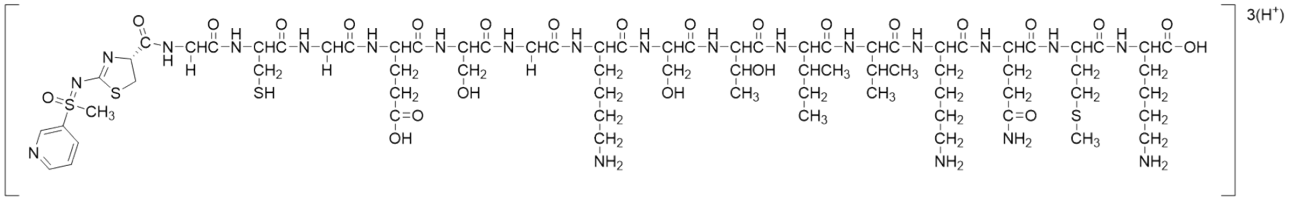
- LC/MS UV data of **3 h**



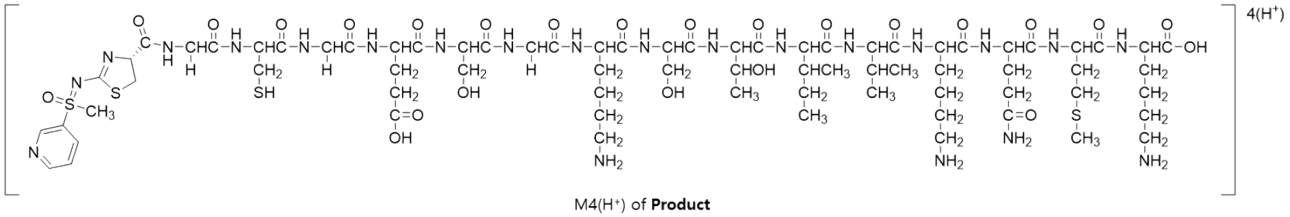
- LC/MS MS data of **3 h**

Peak RT: 0.767 min **Area %:** 1.55%

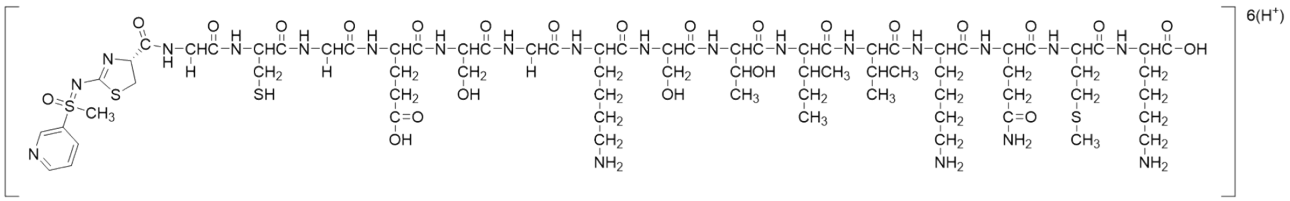




M3(H⁺) of **Product**
m/z : 607.3



M4(H⁺) of **Product**
m/z : 455.7



M6(H⁺) of **Product**
m/z : 304.1

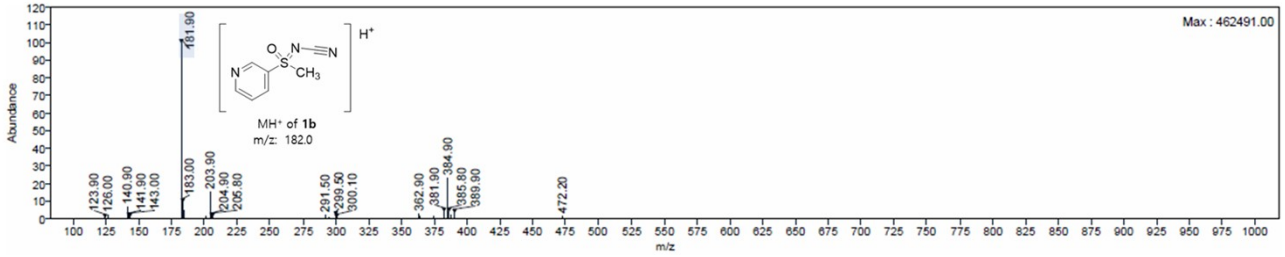
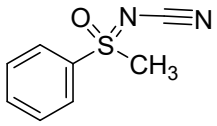
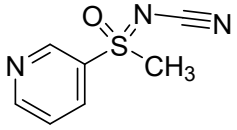
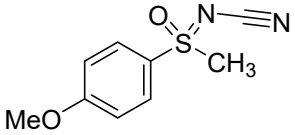
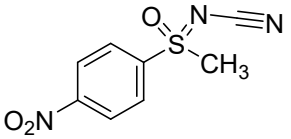
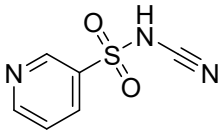
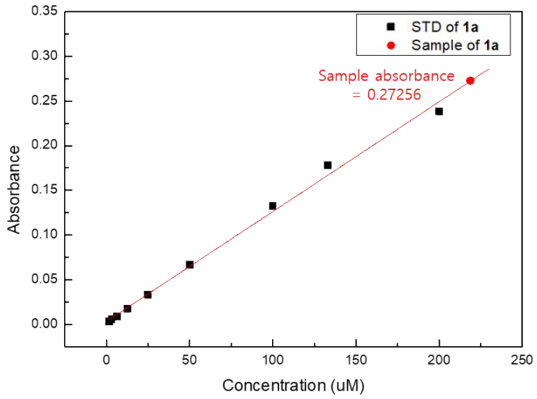

Max : 462491.00
Abundance
m/z
MH+ of 1b
m/z: 182.0
H+
181.90
123.90
126.00
140.90
141.90
143.00
183.00
203.90
204.90
205.80
291.50
299.50
300.10
362.90
381.90
384.90
385.80
389.90
472.20

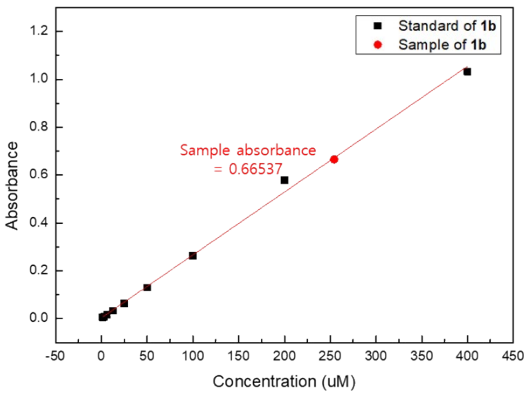
Table S1. μSOL analysis data of **Figure 3**

Entry	Sample	Wave length (nm)	Initial amount (μg)	Measured amount (μg)	Solubility (%)
1	 **1a**	266	45.1	39.4	88
2	 **1b**	258	45.3	46.1	102
3	 **1c**	246	52.6	12.7	24
4	 **1d**	246	56.3	6.6	12
5	 **1ba**	236	45.8	27.5	60

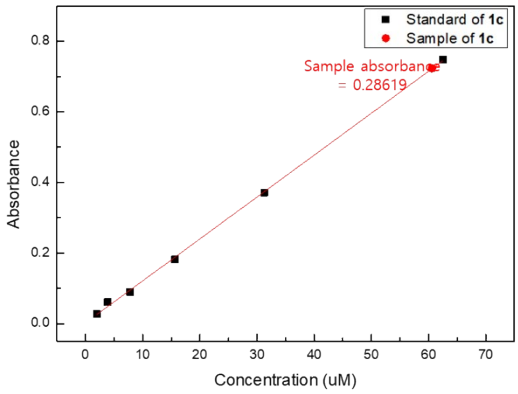
- UV data of *N*-Cyano sulfoximine **1a-d**



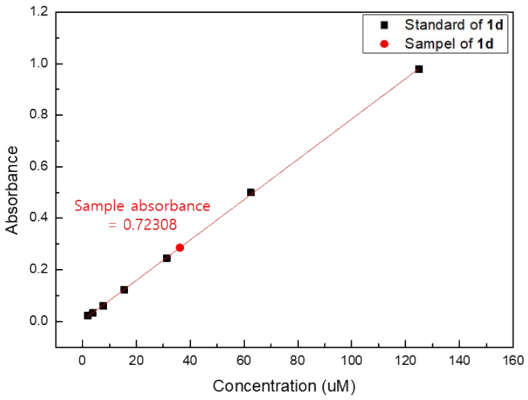
Equation	Y = a + bx		
Adj. R^2	0.99438		
		Value	Standard Error
C	Intercept	0.00342	0.0029
	Slope	0.00123	3.26×10^{-5}



Equation	Y = a + bx		
Adj. R^2	0.99634		
		Value	Standard Error
C	Intercept	0.00389	0.00866
	Slope	0.00263	5.63×10^{-5}

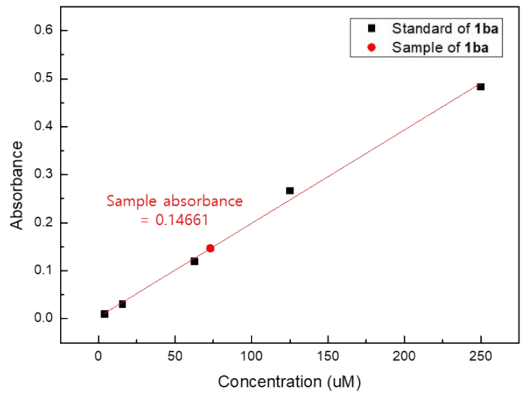


Equation	Y = a + bx		
Adj. R^2	0.99929		
		Value	Standard Error
C	Intercept	0.00274	0.00418
	Slope	0.01188	1.42×10^{-4}



Equation	Y = a + bx		
Adj. R^2	0.99984		
		Value	Standard Error
C	Intercept	0.00306	0.0022
	Slope	0.00783	4.03×10^{-5}

- UV data of *N*-Cyano sulfonamide **1ba**



Equation	Y = a + bx		
Adj. R^2	0.99584		
		Value	Standard Error
C	Intercept	0.00415	0.00807
	Slope	0.00195	6.29×10^{-5}

Figure S14 – S16. NMR spectroscopies of **Table 3.**

Figure S14. ^{1}H spectroscopy of **Entry 1.**

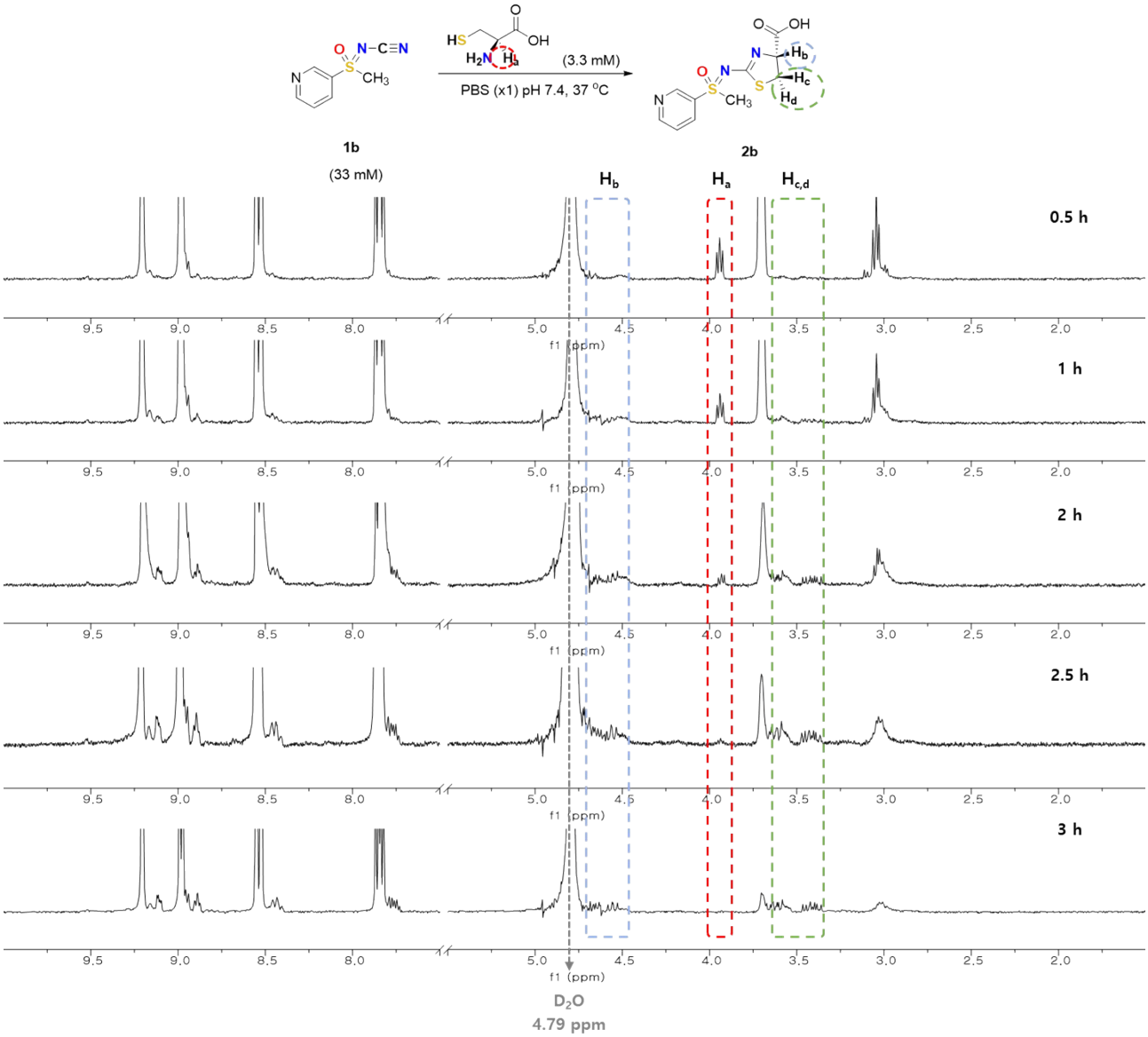


Figure S15. ^{1}H spectroscopy of **Entry 2.**

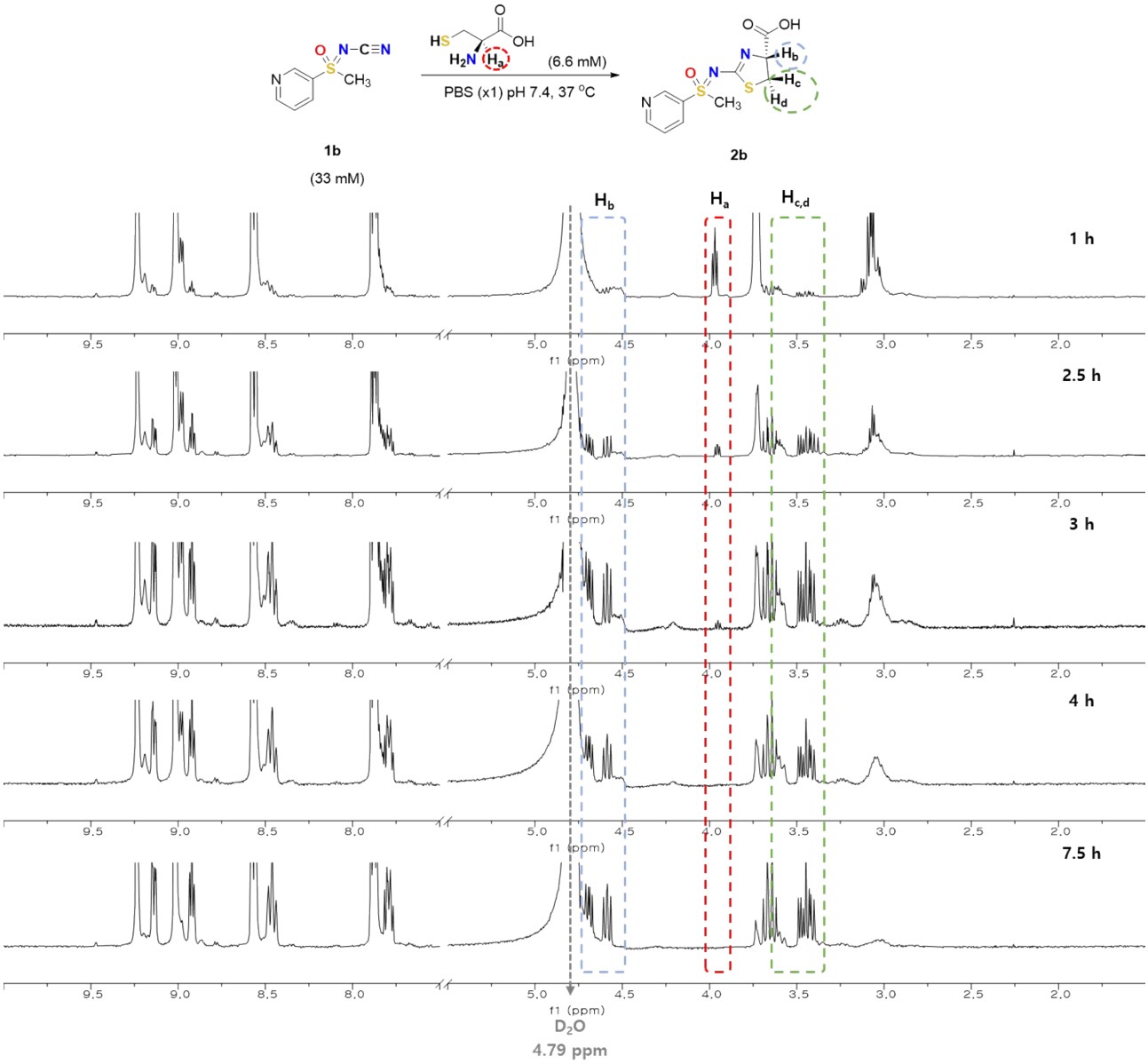


Figure S16. ^{1}H spectroscopy of **Entry 3.**

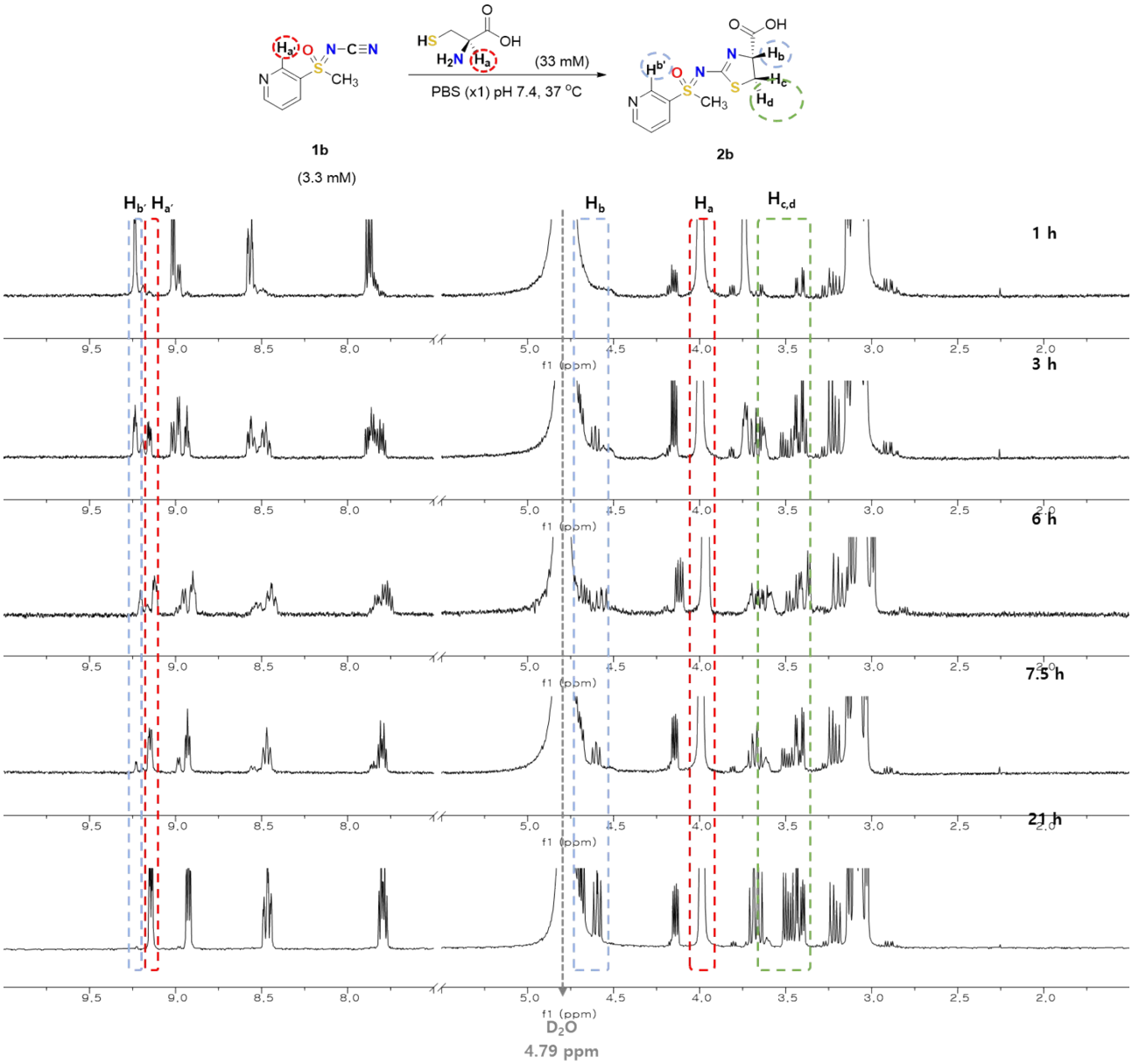
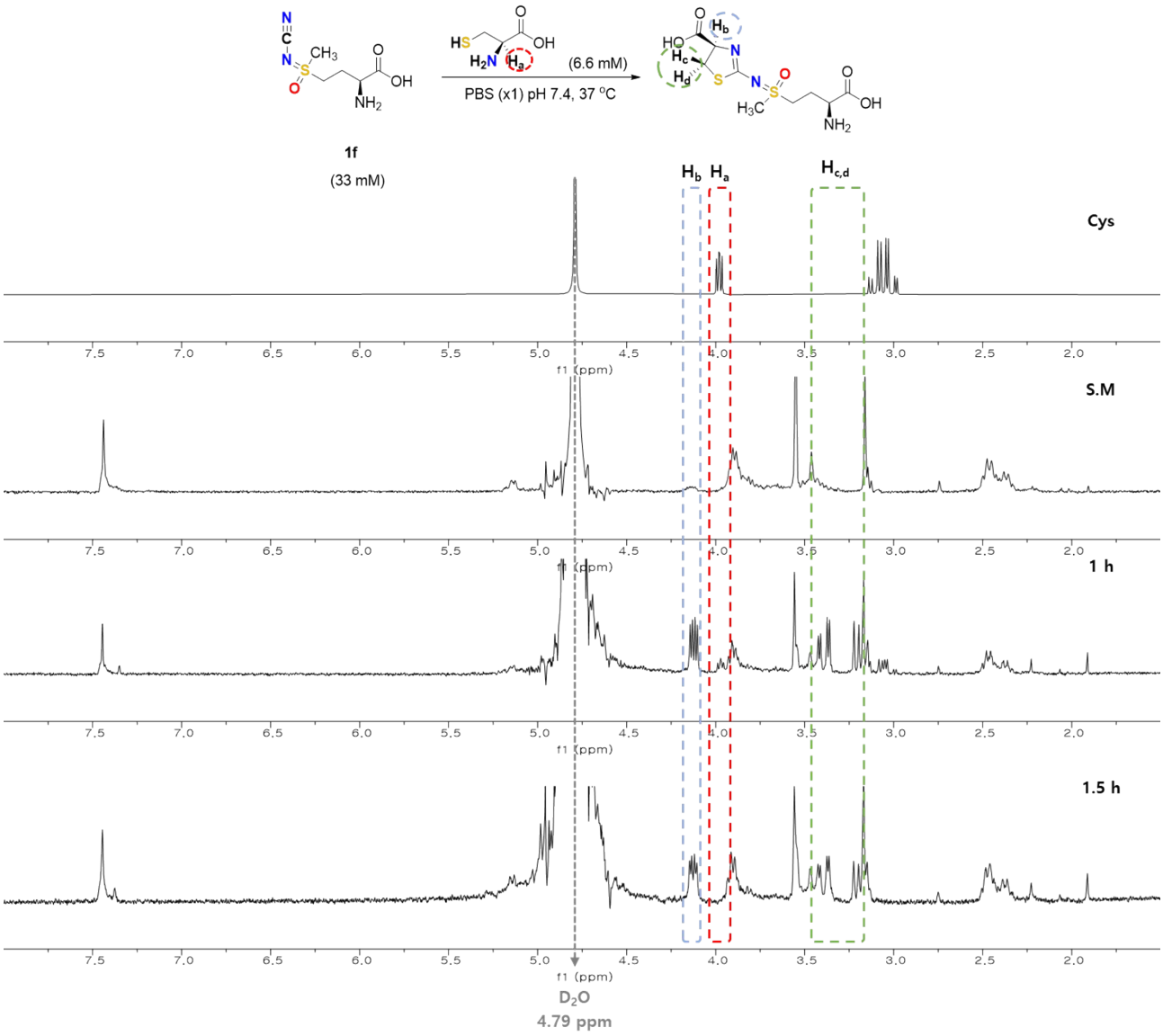


Figure S17. NMR spectroscopies of **Figure 6.**

Figure S17. NMR spectroscopies of **Figure 6.**



X-ray data of **1ba**

3. X-ray Crystallographic Results

3.1 X-ray Crystallographic Data

Table S2. Crystal data and structure refinement for KES_SCL_2025_13_a.

Identification code	KES_SCL_2025_13_a	
Empirical formula	C6 H6 Cl N3 O2 S	
Formula weight	219.65	
Temperature	223(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 5.7714(17) Å	α= 97.665(11)°.
	b = 7.345(2) Å	β= 106.034(9)°.
	c = 9.348(3) Å	γ = 92.663(9)°.
Volume	376.0(2) $Å^3$	
Z	2	
Density (calculated)	1.940 Mg/m^3	
Absorption coefficient	0.748 mm^{-1}	
F(000)	224	
Crystal size	0.160 x 0.135 x 0.121 mm^3	
Theta range for data collection	2.294 to 26.175°.	
Index ranges	-7<=h<=7, -9<=k<=9, -11<=l<=11	
Reflections collected	10750	
Independent reflections	1477 [R(int) = 0.0380]	
Completeness to theta = 25.242°	98.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7453 and 0.6957	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1477 / 0 / 118	
Goodness-of-fit on F^2	1.076	
Final R indices [I>2sigma(I)]	R1 = 0.0546, wR2 = 0.1835	
R indices (all data)	R1 = 0.0572, wR2 = 0.1891	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.730 and -1.049 $e.Å^{-3}$	

Table S3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for KES_SCL_2025_13_a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	7018(1)	5940(1)	1990(1)	12(1)
O(1)	8645(4)	4991(3)	1289(3)	22(1)
O(2)	4953(4)	4893(3)	2155(3)	20(1)
N(1)	8963(5)	7575(4)	6457(3)	19(1)
N(2)	6321(5)	7635(3)	1099(3)	15(1)
N(3)	2578(5)	9175(4)	978(3)	24(1)
C(1)	7757(5)	6851(4)	5046(3)	15(1)
C(2)	8751(5)	6898(4)	3845(3)	12(1)
C(3)	11096(6)	7686(4)	4114(4)	18(1)
C(4)	12349(6)	8417(4)	5582(4)	19(1)
C(5)	11209(6)	8336(4)	6707(4)	19(1)
C(6)	4316(6)	8393(4)	1078(3)	15(1)
Cl(1)	8542(2)	7325(2)	-918(1)	47(1)

Table S4. Bond lengths [Å] and angles [°] for KES_SCL_2025_13_a.

S(1)-O(1)	1.441(2)
S(1)-O(2)	1.444(2)
S(1)-N(2)	1.594(3)
S(1)-C(2)	1.776(3)
N(1)-C(5)	1.333(4)
N(1)-C(1)	1.334(4)
N(1)-H(1N)	0.8700
N(2)-C(6)	1.304(4)
N(2)-H(2)	0.8700
N(3)-C(6)	1.167(4)
C(1)-C(2)	1.398(4)
C(1)-H(1)	0.9400
C(2)-C(3)	1.389(4)
C(3)-C(4)	1.383(5)
C(3)-H(3)	0.9400
C(4)-C(5)	1.391(5)
C(4)-H(4)	0.9400
C(5)-H(5)	0.9400

O(1)-S(1)-O(2)	118.66(14)
O(1)-S(1)-N(2)	104.98(14)
O(2)-S(1)-N(2)	113.56(13)
O(1)-S(1)-C(2)	106.62(14)
O(2)-S(1)-C(2)	105.79(14)
N(2)-S(1)-C(2)	106.46(13)
C(5)-N(1)-C(1)	117.6(3)
C(5)-N(1)-H(1N)	121.2
C(1)-N(1)-H(1N)	121.2
C(6)-N(2)-S(1)	120.3(2)
C(6)-N(2)-H(2)	119.8
S(1)-N(2)-H(2)	119.8
N(1)-C(1)-C(2)	122.4(3)
N(1)-C(1)-H(1)	118.8
C(2)-C(1)-H(1)	118.8
C(3)-C(2)-C(1)	119.7(3)
C(3)-C(2)-S(1)	120.4(2)
C(1)-C(2)-S(1)	119.9(2)
C(4)-C(3)-C(2)	117.7(3)

C(4)-C(3)-H(3)	121.1
C(2)-C(3)-H(3)	121.1
C(3)-C(4)-C(5)	118.8(3)
C(3)-C(4)-H(4)	120.6
C(5)-C(4)-H(4)	120.6
N(1)-C(5)-C(4)	123.7(3)
N(1)-C(5)-H(5)	118.1
C(4)-C(5)-H(5)	118.1
N(3)-C(6)-N(2)	173.9(3)

Symmetry transformations used to generate equivalent atoms:

Table S5. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for KES_SCL_2025_13_a. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	12(1)	13(1)	10(1)	1(1)	1(1)	1(1)
O(1)	22(1)	27(1)	16(1)	-2(1)	5(1)	10(1)
O(2)	19(1)	20(1)	19(1)	4(1)	1(1)	-6(1)
N(1)	25(2)	18(1)	13(1)	1(1)	9(1)	-1(1)
N(2)	14(1)	19(1)	13(1)	6(1)	4(1)	1(1)
N(3)	24(2)	26(2)	26(2)	7(1)	8(1)	9(1)
C(1)	15(2)	14(1)	16(2)	2(1)	5(1)	0(1)
C(2)	12(1)	12(1)	11(1)	2(1)	2(1)	3(1)
C(3)	16(2)	21(2)	17(2)	1(1)	7(1)	0(1)
C(4)	13(2)	20(2)	21(2)	2(1)	1(1)	-2(1)
C(5)	26(2)	14(1)	13(1)	1(1)	0(1)	-1(1)
C(6)	19(2)	14(1)	10(1)	1(1)	3(1)	-1(1)
Cl(1)	46(1)	53(1)	45(1)	6(1)	16(1)	3(1)

Table S6. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for KES_SCL_2025_13_a.

	x	y	z	U(eq)
H(1N)	8308	7551	7189	22
H(2)	7283	8056	625	18
H(1)	6182	6289	4852	18
H(3)	11806	7722	3326	21
H(4)	13943	8958	5816	22
H(5)	12072	8847	7699	23

X-ray data of **1b**

3.2 X-ray Crystallographic Structure.

3.2.1 Crystal structure.

Table S7. Crystal data and structure refinement for KES_SCL_2025_16_a.

Identification code	KES_SCL_2025_16_a	
Empirical formula	C7 H7 N3 O S	
Formula weight	181.22	
Temperature	223(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 9.0926(13) Å	α= 90°.
	b = 7.0943(9) Å	β= 93.758(5)°.
	c = 12.7455(18) Å	γ = 90°.
Volume	820.4(2) $Å^3$	
Z	4	
Density (calculated)	1.467 Mg/m^3	
Absorption coefficient	0.345 mm^{-1}	
F(000)	376	
Crystal size	0.170 x 0.138 x 0.103 mm^3	
Theta range for data collection	2.671 to 28.345°.	
Index ranges	-12<=h<=12, -9<=k<=9, -17<=l<=16	
Reflections collected	14117	
Independent reflections	2045 [R(int) = 0.0458]	
Completeness to theta = 25.242°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7457 and 0.6832	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2045 / 0 / 109	
Goodness-of-fit on F^2	1.046	
Final R indices [I>2sigma(I)]	R1 = 0.0321, wR2 = 0.0809	
R indices (all data)	R1 = 0.0395, wR2 = 0.0854	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.279 and -0.315 $e.Å^{-3}$	

Table S7. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for KES_SCL_2025_16_a. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	7263(1)	6807(1)	4044(1)	27(1)
O(1)	5886(1)	6353(2)	3480(1)	41(1)
N(1)	5055(2)	8454(2)	6482(1)	38(1)
N(2)	8503(1)	5276(2)	4125(1)	32(1)
N(3)	8230(2)	2349(2)	5151(1)	45(1)
C(1)	5437(2)	7887(2)	5536(1)	31(1)
C(2)	6882(2)	7562(2)	5318(1)	24(1)
C(3)	8006(2)	7830(2)	6091(1)	33(1)
C(4)	7618(2)	8409(3)	7070(1)	38(1)
C(5)	6147(2)	8690(3)	7222(1)	37(1)
C(6)	8291(2)	3732(2)	4683(1)	30(1)
C(7)	8138(2)	8683(2)	3455(1)	38(1)

Table S8. Bond lengths [Å] and angles [°] for KES_SCL_2025_16_a.

S(1)-O(1)	1.4390(12)
S(1)-N(2)	1.5634(13)
S(1)-C(7)	1.7448(17)
S(1)-C(2)	1.7661(14)
N(1)-C(5)	1.334(2)
N(1)-C(1)	1.338(2)
N(2)-C(6)	1.327(2)
N(3)-C(6)	1.151(2)
C(1)-C(2)	1.381(2)
C(1)-H(1)	0.9400
C(2)-C(3)	1.385(2)
C(3)-C(4)	1.382(2)
C(3)-H(3)	0.9400
C(4)-C(5)	1.379(2)
C(4)-H(4)	0.9400
C(5)-H(5)	0.9400
C(7)-H(7A)	0.9700
C(7)-H(7B)	0.9700
C(7)-H(7C)	0.9700
O(1)-S(1)-N(2)	118.52(8)
O(1)-S(1)-C(7)	111.25(9)
N(2)-S(1)-C(7)	102.20(8)
O(1)-S(1)-C(2)	108.08(7)
N(2)-S(1)-C(2)	109.51(7)
C(7)-S(1)-C(2)	106.64(8)
C(5)-N(1)-C(1)	116.69(14)
C(6)-N(2)-S(1)	118.65(11)
N(1)-C(1)-C(2)	122.56(14)
N(1)-C(1)-H(1)	118.7
C(2)-C(1)-H(1)	118.7
C(1)-C(2)-C(3)	120.12(13)
C(1)-C(2)-S(1)	118.85(11)
C(3)-C(2)-S(1)	121.03(11)
C(4)-C(3)-C(2)	117.59(14)
C(4)-C(3)-H(3)	121.2
C(2)-C(3)-H(3)	121.2
C(5)-C(4)-C(3)	118.46(15)

C(5)-C(4)-H(4)	120.8
C(3)-C(4)-H(4)	120.8
N(1)-C(5)-C(4)	124.57(15)
N(1)-C(5)-H(5)	117.7
C(4)-C(5)-H(5)	117.7
N(3)-C(6)-N(2)	174.07(17)
S(1)-C(7)-H(7A)	109.5
S(1)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
S(1)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table S9. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for KES_SCL_2025_16_a. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	25(1)	31(1)	24(1)	-3(1)	4(1)	3(1)
O(1)	32(1)	55(1)	35(1)	-13(1)	-4(1)	3(1)
N(1)	31(1)	50(1)	34(1)	-6(1)	11(1)	2(1)
N(2)	29(1)	32(1)	36(1)	0(1)	10(1)	4(1)
N(3)	43(1)	38(1)	55(1)	5(1)	-2(1)	-2(1)
C(1)	24(1)	38(1)	31(1)	-2(1)	4(1)	0(1)
C(2)	25(1)	25(1)	23(1)	-1(1)	5(1)	0(1)
C(3)	25(1)	42(1)	32(1)	-2(1)	2(1)	2(1)
C(4)	37(1)	50(1)	28(1)	-4(1)	-2(1)	0(1)
C(5)	42(1)	43(1)	27(1)	-4(1)	9(1)	-1(1)
C(6)	24(1)	32(1)	34(1)	-6(1)	1(1)	1(1)
C(7)	46(1)	36(1)	32(1)	8(1)	14(1)	6(1)

Table S10. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for KES_SCL_2025_16_a.

	x	y	z	U(eq)
H(1)	4692	7703	4999	37
H(3)	8997	7625	5954	40
H(4)	8341	8607	7621	46
H(5)	5895	9074	7893	45
H(7A)	9062	8957	3851	57
H(7B)	8332	8348	2740	57
H(7C)	7508	9786	3449	57

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