

Supporting information for

Copper-Catalyzed Coupling Reactions of Cyclobutanone Oxime Esters with Sulfur Nucleophiles at Room Temperature

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1. Optimization of Reaction Conditions

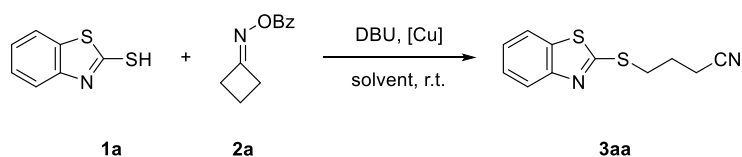
Table S1. Optimization of Reaction Conditions^a

	1a	2a		3aa	4aa	
Entry	1a	2a	DBU	[Cu]/mol %	[S]/mL	Yield ^b (%) 3aa/4aa
1	0.2 mmol	0.2 mmol	0.4 mmol	Cu(OTf) ₂ /15%	1,4-dioxane/2	31/40
2	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /15%	1,4-dioxane/2	36/31
3	0.3 mmol	0.2 mmol	0.6 mmol	Cu(OTf) ₂ /15%	1,4-dioxane/2	19/46
4	0.3 mmol	0.2 mmol	0.6 mmol	Cu(OTf) ₂ /15%	1,4-dioxane/1	trace/62
5	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /15%	1,4-dioxane/1	40/33

^aReaction conditions: To a 10 mL single-necked flask was added **1a**, **2a** and [Cu] (15 mol % of **2a**), to a 4.5 mL sample tube was added DBU (2.0 equiv of **1a**) and solvent, then transfer the solution of the sample to flask and stirred for 30 min at room temperature, ^bIsolated yields.

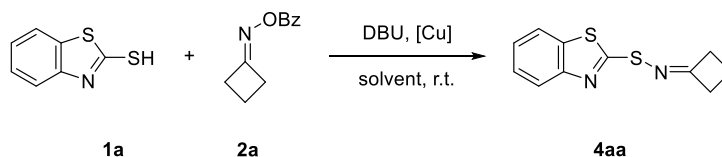
To initiate our study, we selected cyclobutanone *O*-benzoyl oxime **2a** as iminyl radical precursor to trigger C-C single bond cleavage, and 2-mercaptobenzothiazole **1a** as sulfur nucleophiles. When DBU was used as a base and Cu(OTf)₂ as a catalyst, the desired product **3aa** and the unexpected product **4aa** were obtained (Table S1, entry 1). Then we found the molar ratio of **1a** to **2a** and the amount of solvent and its polarity have a decisive role on these processes (Table S1, entry 2-5), so we decided to seek the optimal conditions for **3aa** and **4aa**, separately. In addition, both **3aa** and **4aa** were not observed without DBU or copper salts (or in the presence of CuO and Cu₂O).

Continued from the above works, the optimum conditions for **3aa** was investigated. We kept the molar ratio of **1a/2a** to be 2/3 (0.2 mmol : 0.3 mmol) and used 2 equiv (relative to **1a**) of DBU, then the catalyst and solvent were explored. Ethyl acetate was found better than other solvents (Table S2, entry 1-7), and Cu(OTf)₂ was better than other copper salts (Table S2, entry 7-14). Then, the percentage of Cu(OTf)₂ was changed, the better yield of **3aa** (58%) was obtained when 30 mol% of Cu(OTf)₂ was added (Table S2, entry 15-19). Next, when 1.5 mL of ethyl acetate was added, the better yield (60%) was gotten (Table S2, entry 20-22). Cheerfully, when 3 equiv (relative to **1a**) of DBU was added, **3aa** was obtained in 79% yield. Finally, the best yield (87%) was obtained when 0.4 mmol of **2a** was added and 0.2 mmol of **1a** was added (Table S2, entry 28). In addition, it made no difference when the reaction was performed in the dark or ambient light, and no product was obtained in the absence of copper salt.

Table S2. Optimization of Reaction Conditions for 3aa^a

Entry	1a	2a	DBU	[Cu]/mol %	[S]/mL	Yield ^b (%)
1	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /15%	1,4-dioxane/1	40
2	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /15%	toluene/1	42
3	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /15%	DCE/1	42
4	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /15%	DMSO/1	41
5	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /15%	MeCN/1	44
6	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /15%	DMF/1	39
7	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /15%	EtOAc/1	49
8	0.2 mmol	0.3 mmol	0.4 mmol	CuBr ₂ /15%	EtOAc/1	41
9	0.2 mmol	0.3 mmol	0.4 mmol	CuBr /15%	EtOAc/1	40
10	0.2 mmol	0.3 mmol	0.4 mmol	CuCl ₂ /15%	EtOAc/1	43
11	0.2 mmol	0.3 mmol	0.4 mmol	CuCl /15%	EtOAc/1	39
12	0.2 mmol	0.3 mmol	0.4 mmol	CuI /15%	EtOAc/1	43
13	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OAc) ₂ /15%	EtOAc/1	40
14	0.2 mmol	0.3 mmol	0.4 mmol	CuCN /15%	EtOAc/1	44
15	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /20%	EtOAc/1	51
16	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /25%	EtOAc/1	56
17	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /30%	EtOAc/1	58
18	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /35%	EtOAc/1	58
19	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /40%	EtOAc/1	57
20	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /30%	EtOAc/0.5	50
21	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /30%	EtOAc/1.5	60
22	0.2 mmol	0.3 mmol	0.4 mmol	Cu(OTf) ₂ /30%	EtOAc/2	59
23	0.2 mmol	0.3 mmol	0.2 mmol	Cu(OTf) ₂ /30%	EtOAc/1.5	trace
24	0.2 mmol	0.3 mmol	0.3 mmol	Cu(OTf) ₂ /30%	EtOAc/1.5	trace
25	0.2 mmol	0.3 mmol	0.5 mmol	Cu(OTf) ₂ /30%	EtOAc/1.5	70
26	0.2 mmol	0.3 mmol	0.6 mmol	Cu(OTf) ₂ /30%	EtOAc/1.5	79
27	0.2 mmol	0.3 mmol	0.7 mmol	Cu(OTf) ₂ /30%	EtOAc/1.5	79
28	0.2 mmol	0.4 mmol	0.6 mmol	Cu(OTf) ₂ /30%	EtOAc/1.5	87

^aReaction conditions: To a 10 mL single-necked flask was added **1a**, **2a** and [Cu] (mol % of **2a**), to a 4.5 mL sample tube was added DBU (1-3.5 equiv of **1a**) and solvent, then transfer the solution in the sample to flask and stirred for 30 min at room temperature, ^bIsolated yields.

Table S3. Optimization of Reaction Conditions for 4aa^a

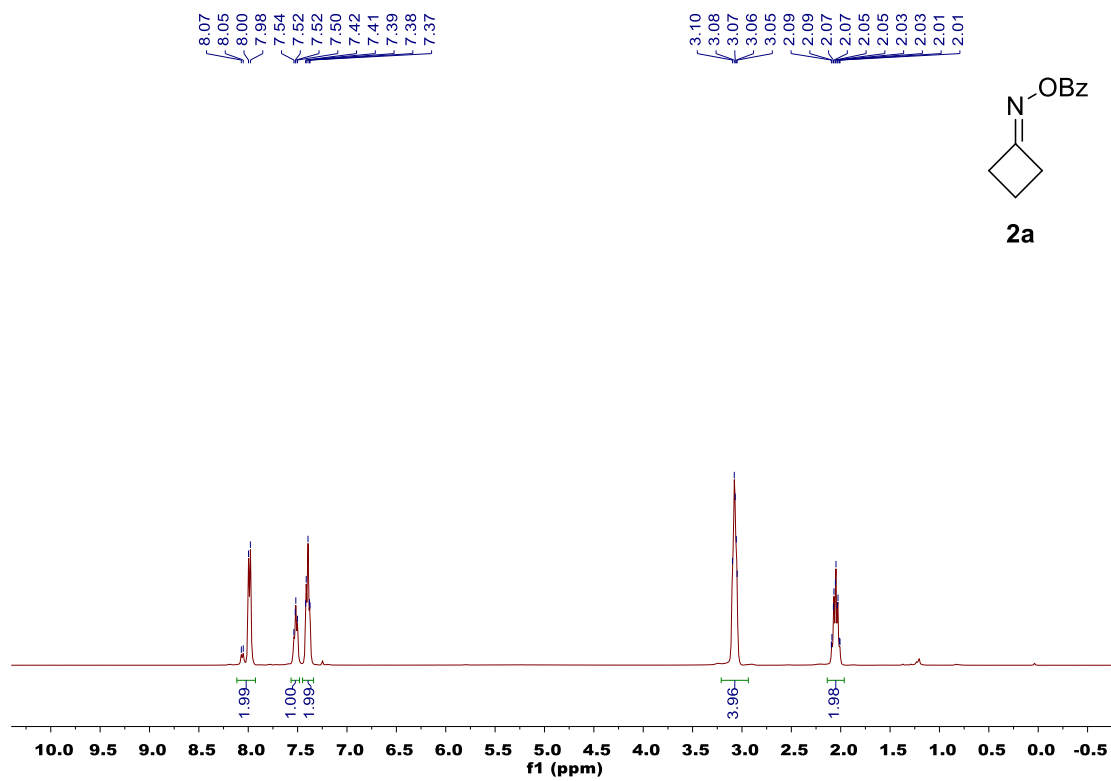
Entry	1a	2a	DBU	[Cu]/mol %	[S]/mL	Yield ^b (%)
1	0.3 mmol	0.2 mmol	0.6 mmol	Cu(OTf) ₂ /15%	THF/1	33
2	0.3 mmol	0.2 mmol	0.6 mmol	Cu(OTf) ₂ /15%	DCE/1	43
3	0.3 mmol	0.2 mmol	0.6 mmol	Cu(OTf) ₂ /15%	DCM/1	55
4	0.3 mmol	0.2 mmol	0.6 mmol	Cu(OTf) ₂ /15%	CHCl ₃ /1	28
5	0.3 mmol	0.2 mmol	0.6 mmol	Cu(OTf) ₂ /15%	toluene/1	65
6	0.3 mmol	0.2 mmol	0.6 mmol	Cu(OTf) ₂ /15%	DMF/1	52
7	0.3 mmol	0.2 mmol	0.6 mmol	Cu(OTf) ₂ /15%	DMSO/1	40
8	0.3 mmol	0.2 mmol	0.6 mmol	Cu(OTf) ₂ /15%	MeCN/1	41
9	0.3 mmol	0.2 mmol	0.6 mmol	Cu(OTf) ₂ /15%	Acetone/1	50
10	0.3 mmol	0.2 mmol	0.6 mmol	CuBr ₂ /15%	toluene/1	76
11	0.3 mmol	0.2 mmol	0.6 mmol	CuBr/15%	toluene/1	66
12	0.3 mmol	0.2 mmol	0.6 mmol	CuCl ₂ /15%	toluene/1	74
13	0.3 mmol	0.2 mmol	0.6 mmol	CuCl/15%	toluene/1	60
14	0.3 mmol	0.2 mmol	0.6 mmol	CuI/15%	toluene/1	70
15	0.3 mmol	0.2 mmol	0.6 mmol	Cu(OAc) ₂ /15%	toluene/1	71
16	0.3 mmol	0.2 mmol	0.6 mmol	CuBr ₂ /15%	toluene/2	73
17	0.3 mmol	0.2 mmol	0.6 mmol	CuBr ₂ /15%	toluene/0.5	63
18	0.3 mmol	0.2 mmol	0.6 mmol	CuBr ₂ /30%	toluene/1	75
19	0.3 mmol	0.2 mmol	0.9 mmol	CuBr ₂ /15%	toluene/1	85

^aReaction conditions: To a 10 mL single-necked flask was added **1a**, **2a** and [Cu] (mol % of **2a**), to a 4.5 mL sample tube was added DBU (2-3 equiv of **1a**) and solvent, then transfer the solution in the sample to flask and stirred for 1 h at room temperature, ^bisolated yields.

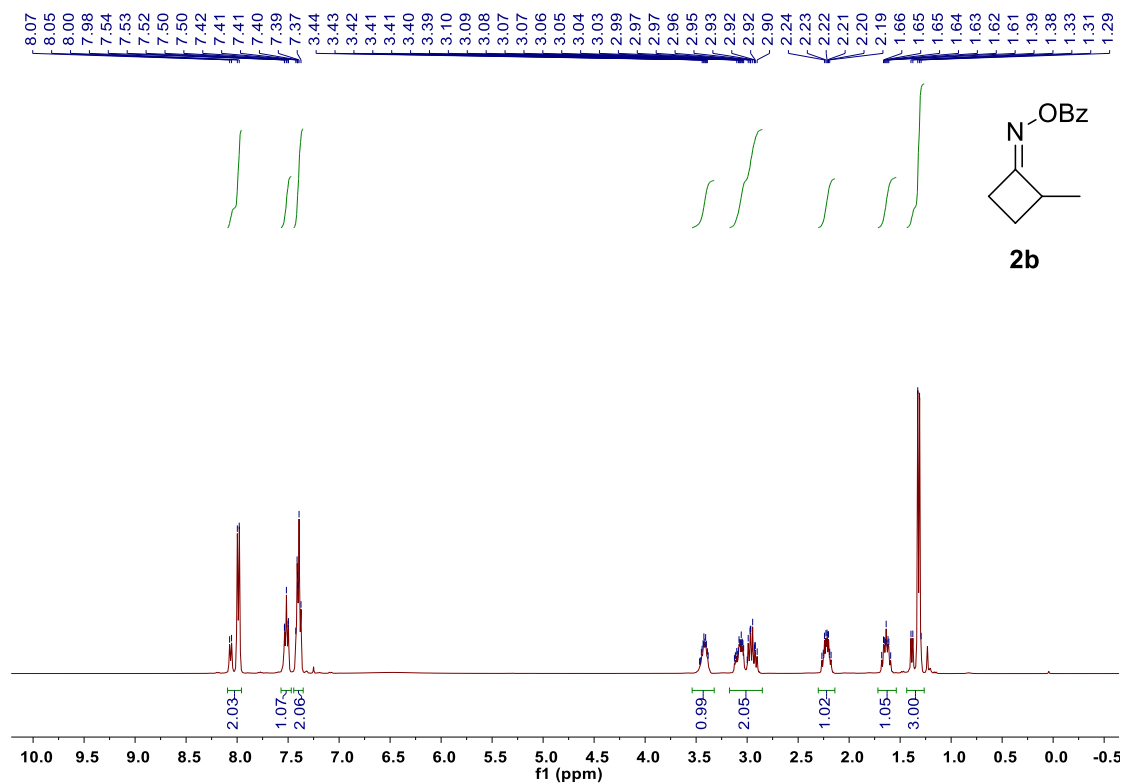
After optimizing the conditions for **3aa**, we kept the molar ratio of **1a** to **2a** to be 3:2 (0.3 mmol : 0.2 mmol), and the solvents were first screened. Toluene was proved to be the best solvent providing **4aa** in 65% yield (Table S3, entry 1-9). Then, several copper salts were investigated, CuBr₂ was chosen as the best catalyst which provided **4aa** in 76% yield (Table S3, entry 10-15). Next, the volume of toluene was changed to 2 mL and 0.5 mL, two decreased yields were obtained (Table S3, entry 16-17). When the percentage of catalyst was increased to 30%, the yield of **4aa** did not change obviously (Table S3, entry 18). Finally, the optimum conditions for **4aa** were found with 85% yield when 3.0 equiv (relative to **1a**) of DBU was added (Table S3, entry 19). Similar to the generation of **3aa**, it made no difference when the reaction was performed in the dark or ambient light, and no product was obtained in the absence of copper salt.

2. Copies of NMR Spectra

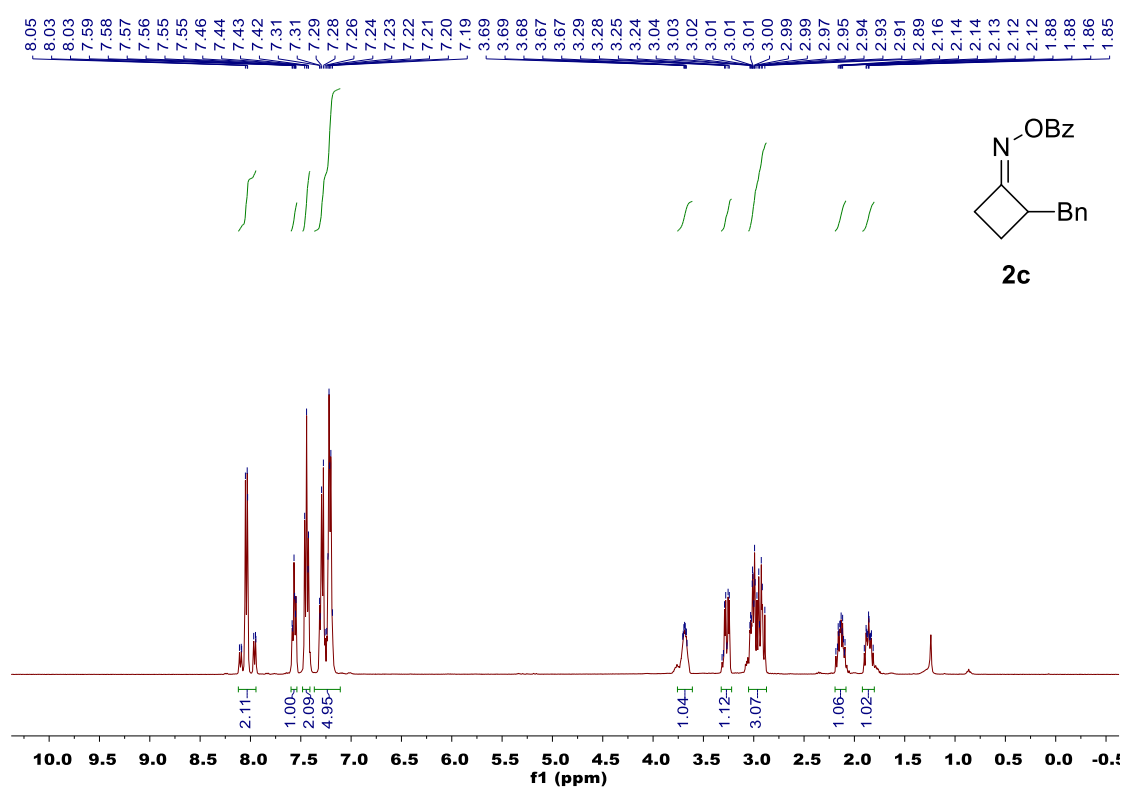
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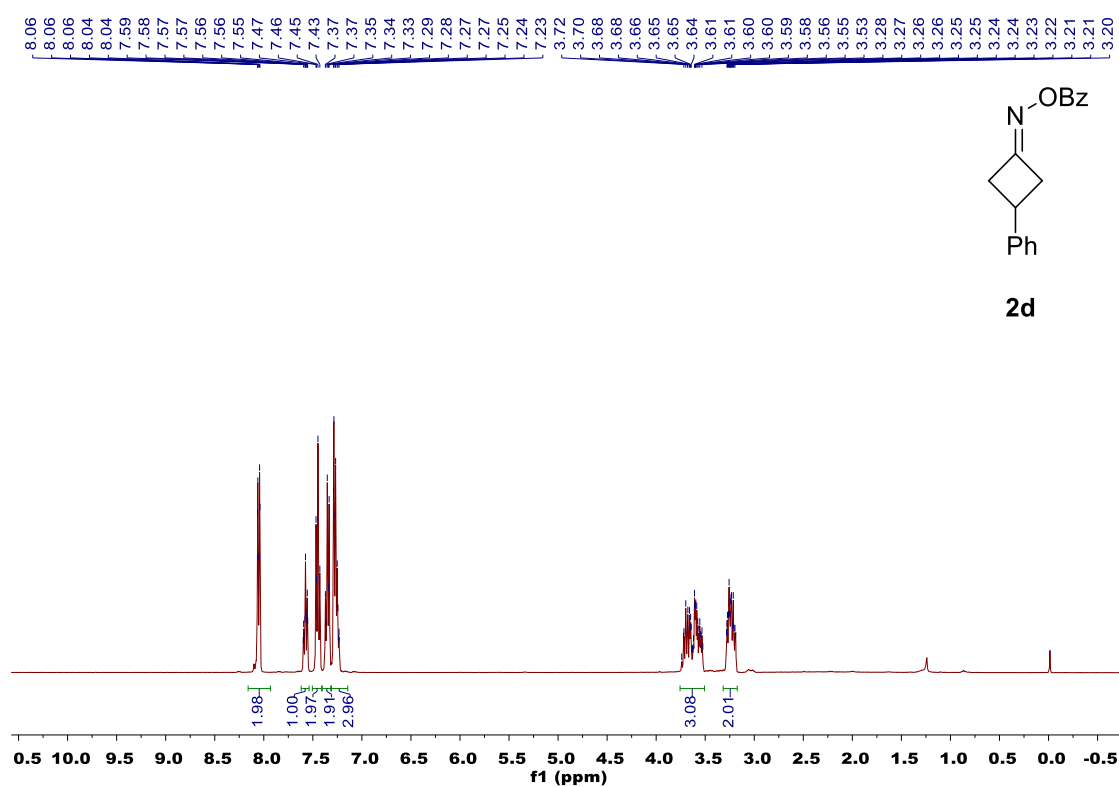
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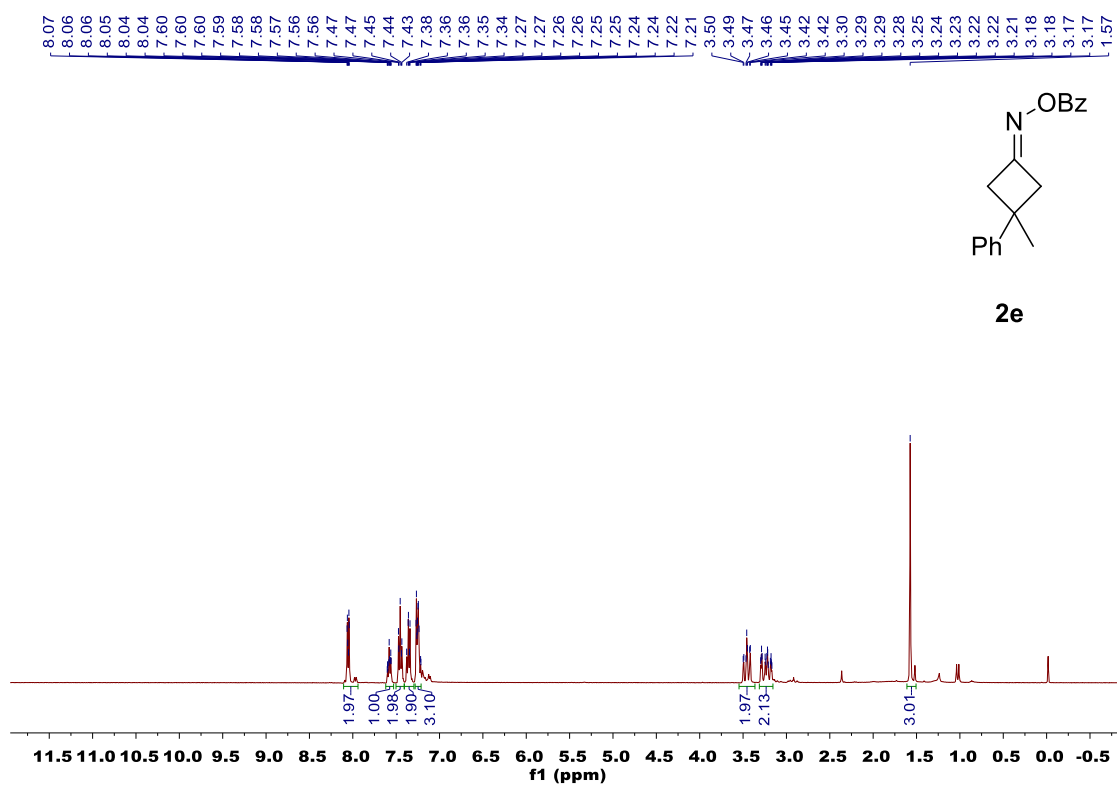
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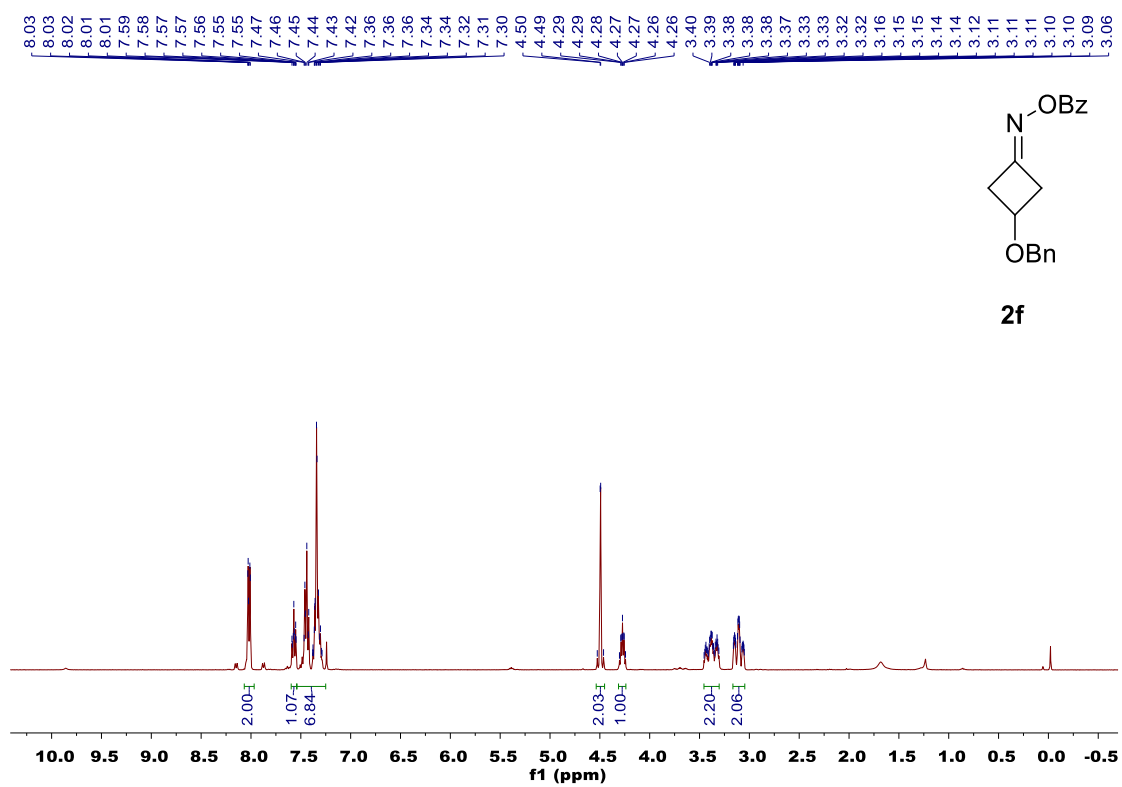
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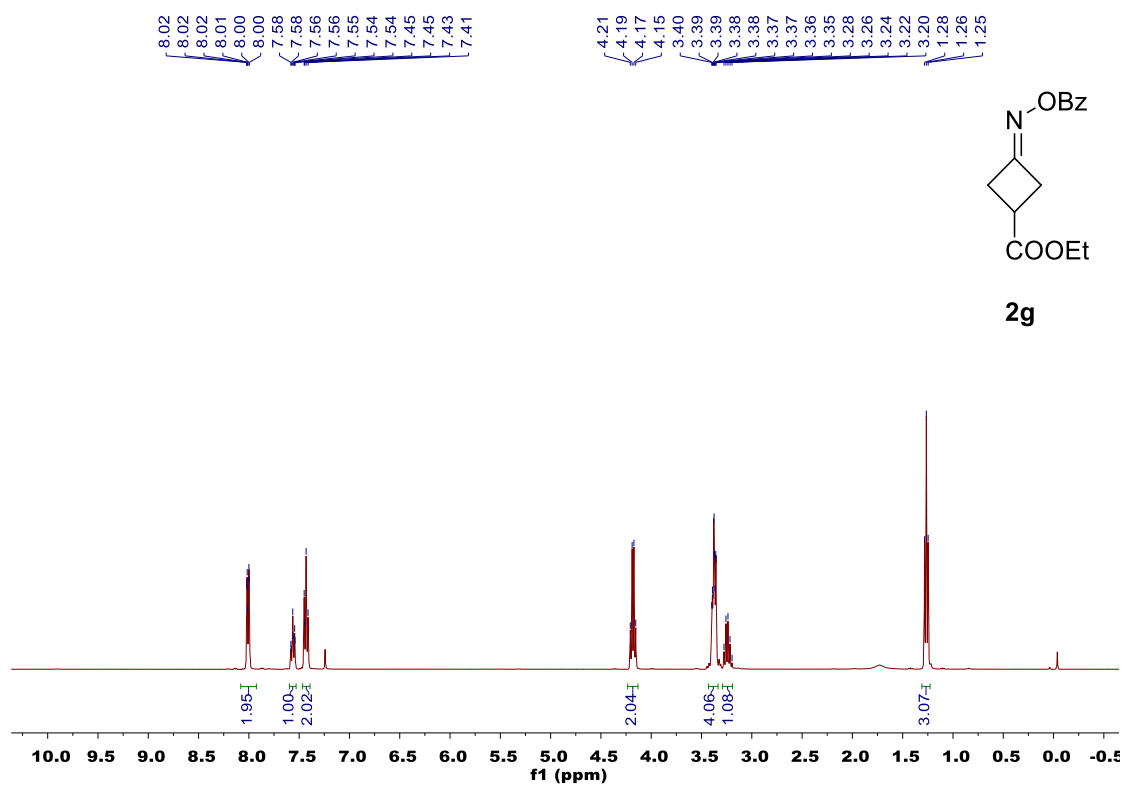
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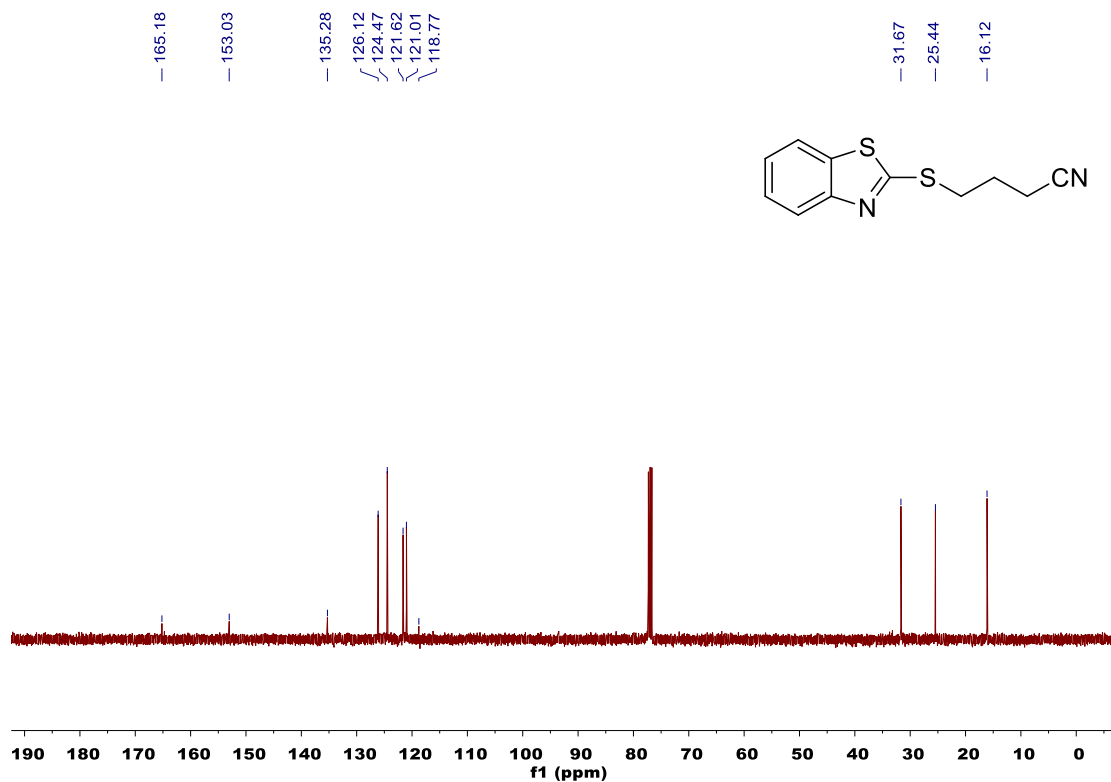
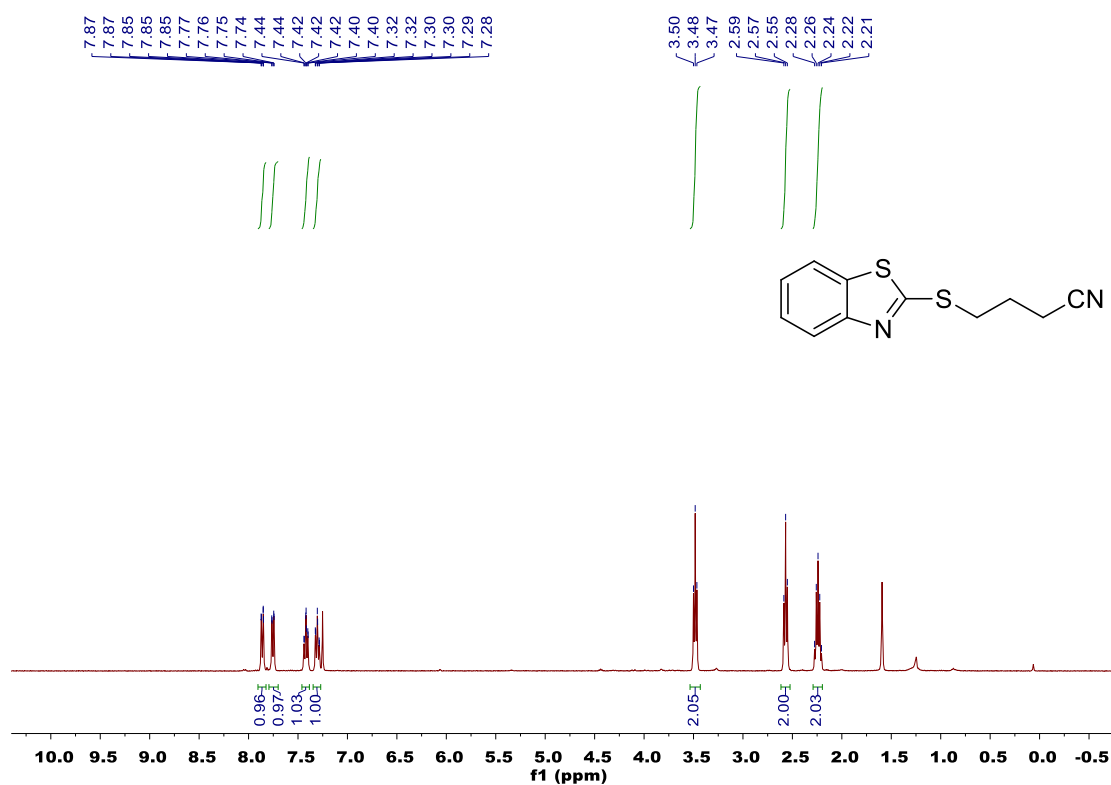
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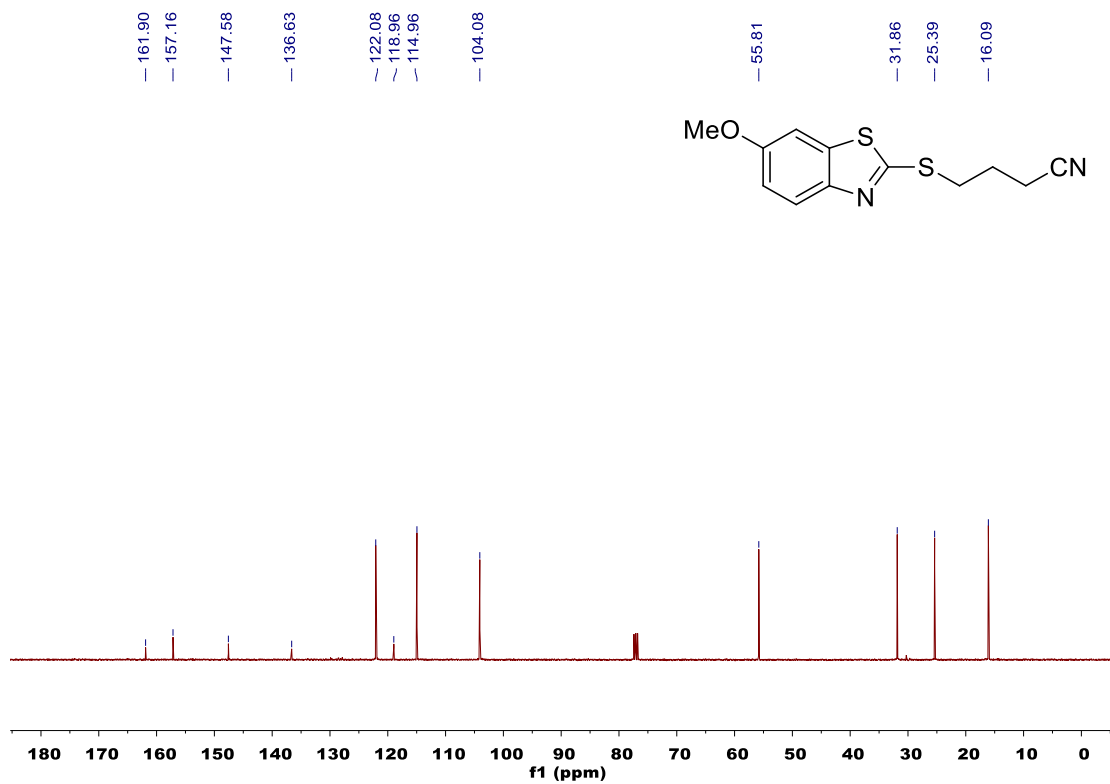
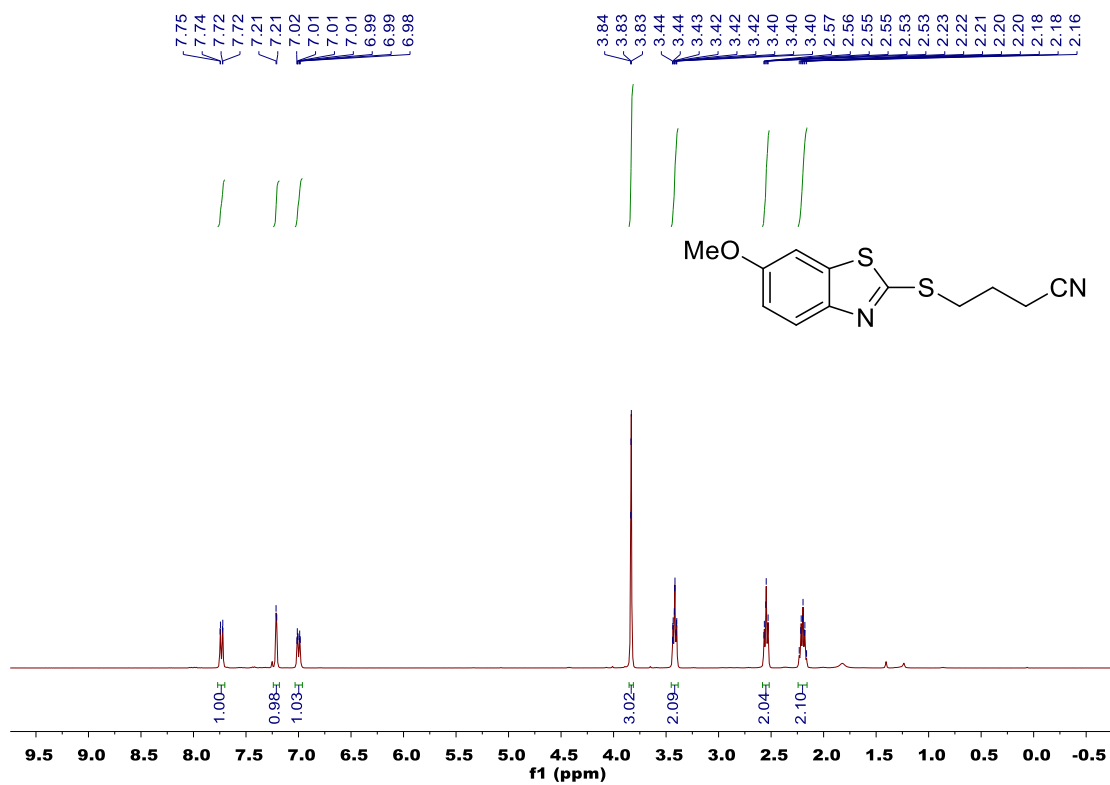
ethyl 3-((benzyloxy)imino)cyclobutanecarboxylate (2g)



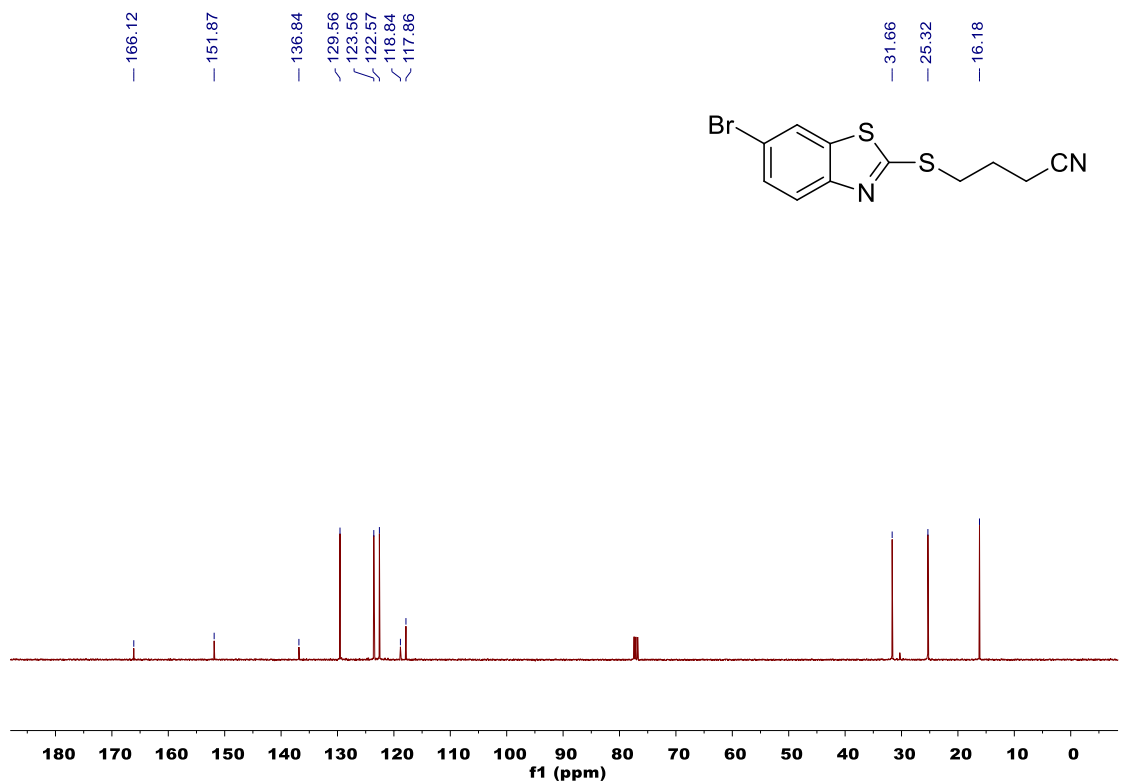
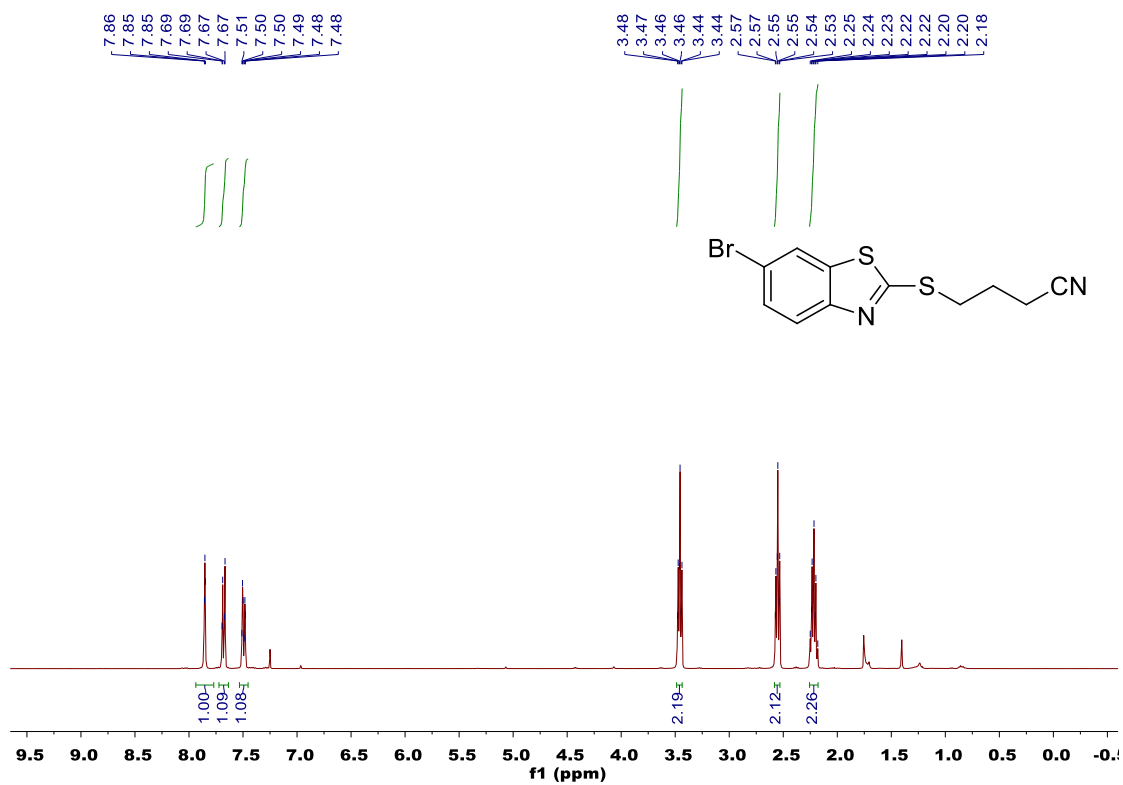
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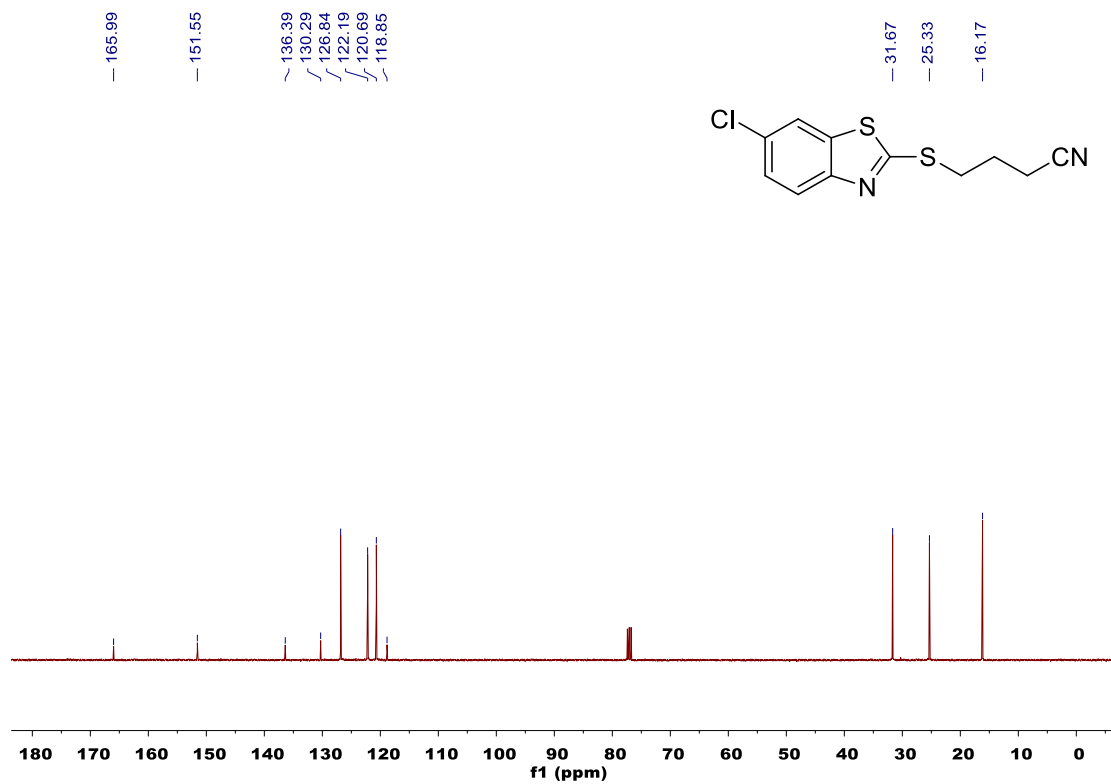
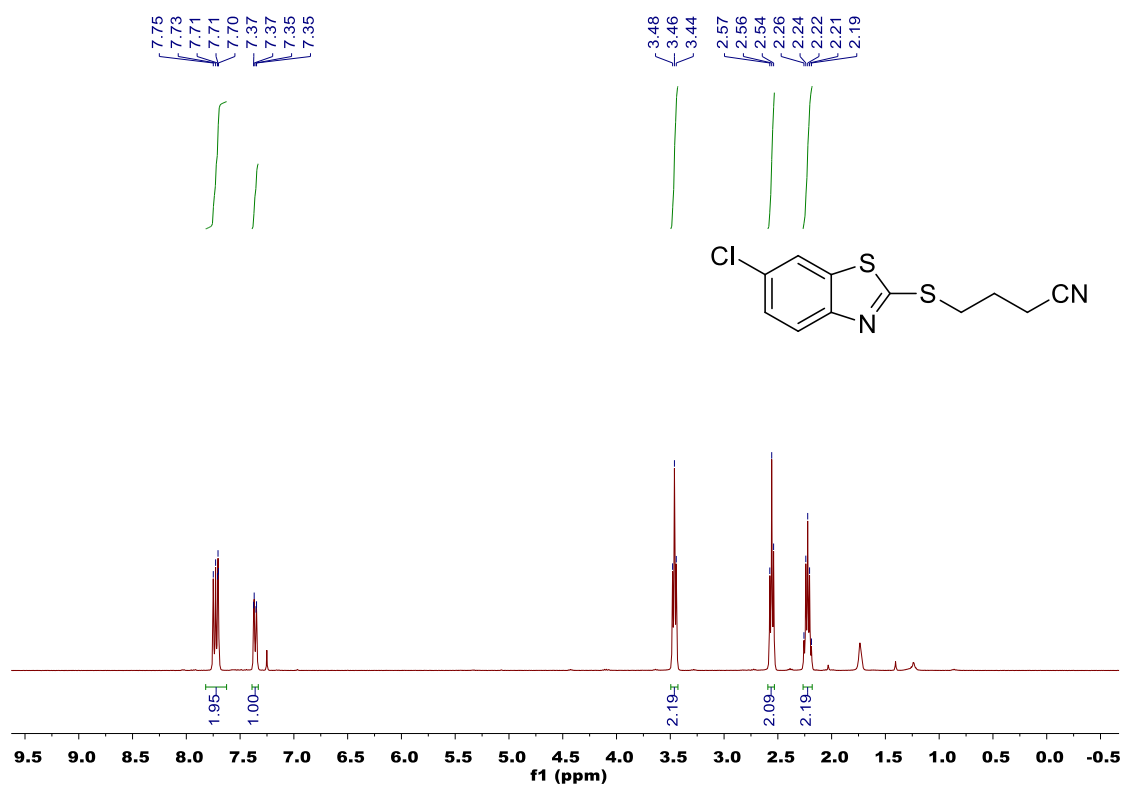
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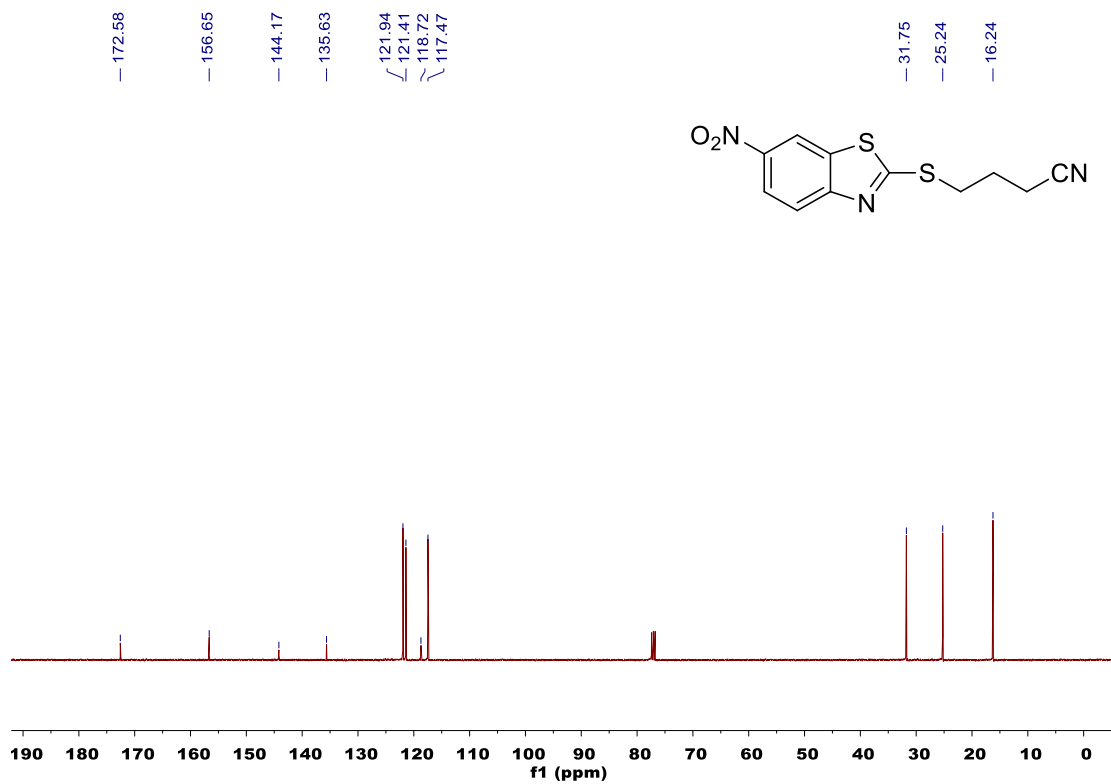
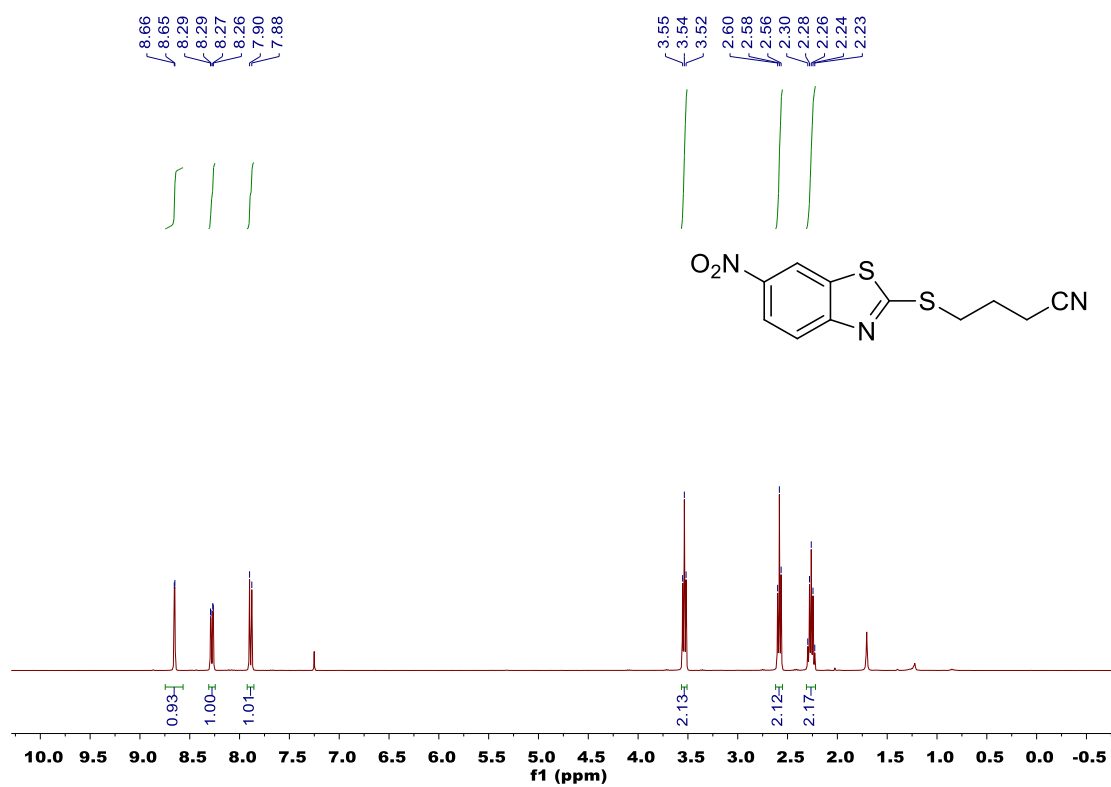
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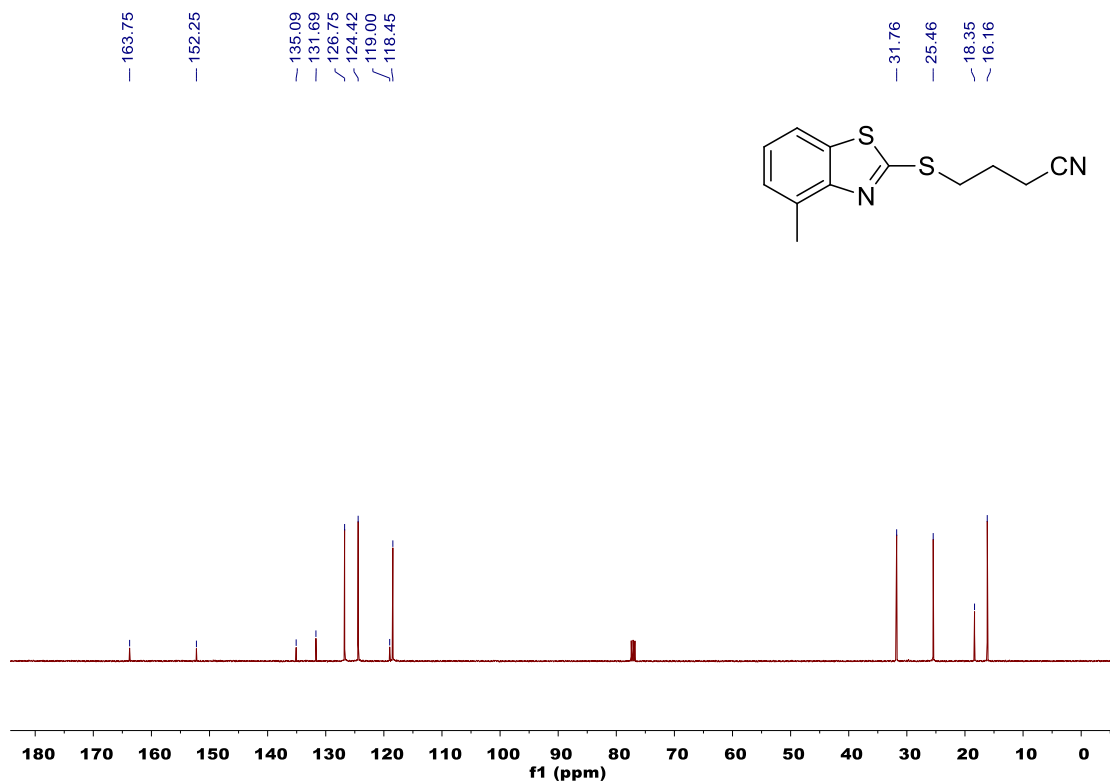
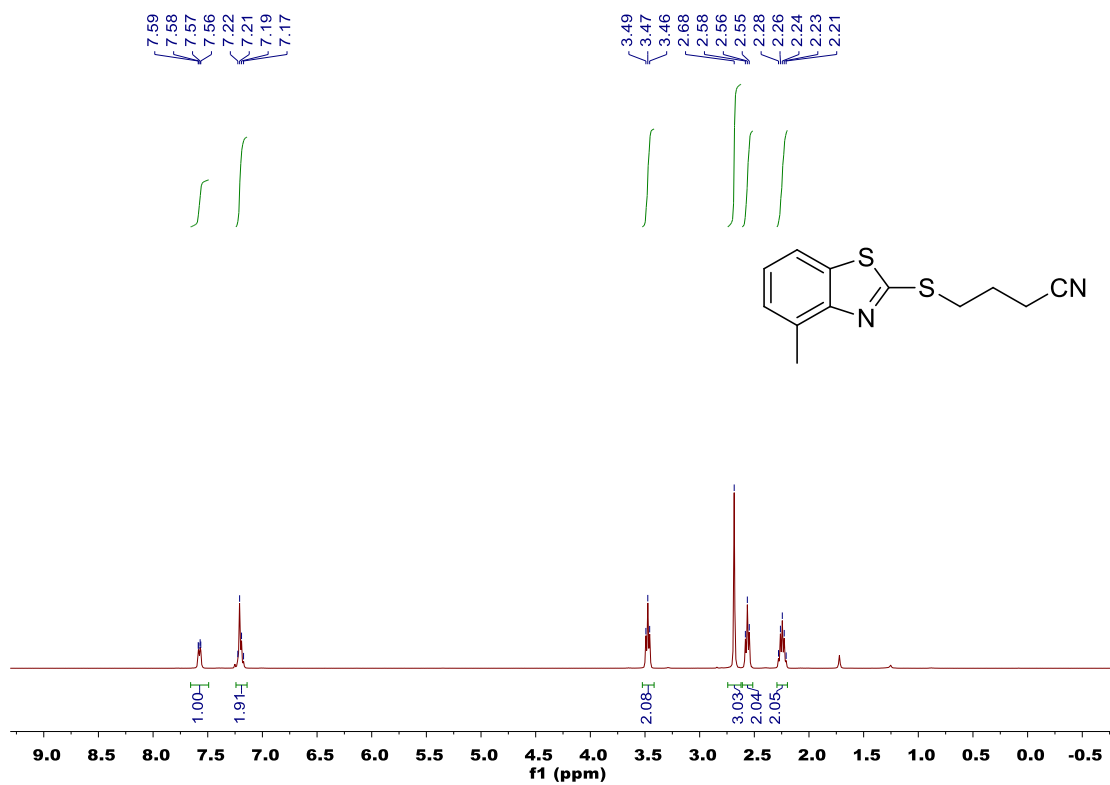
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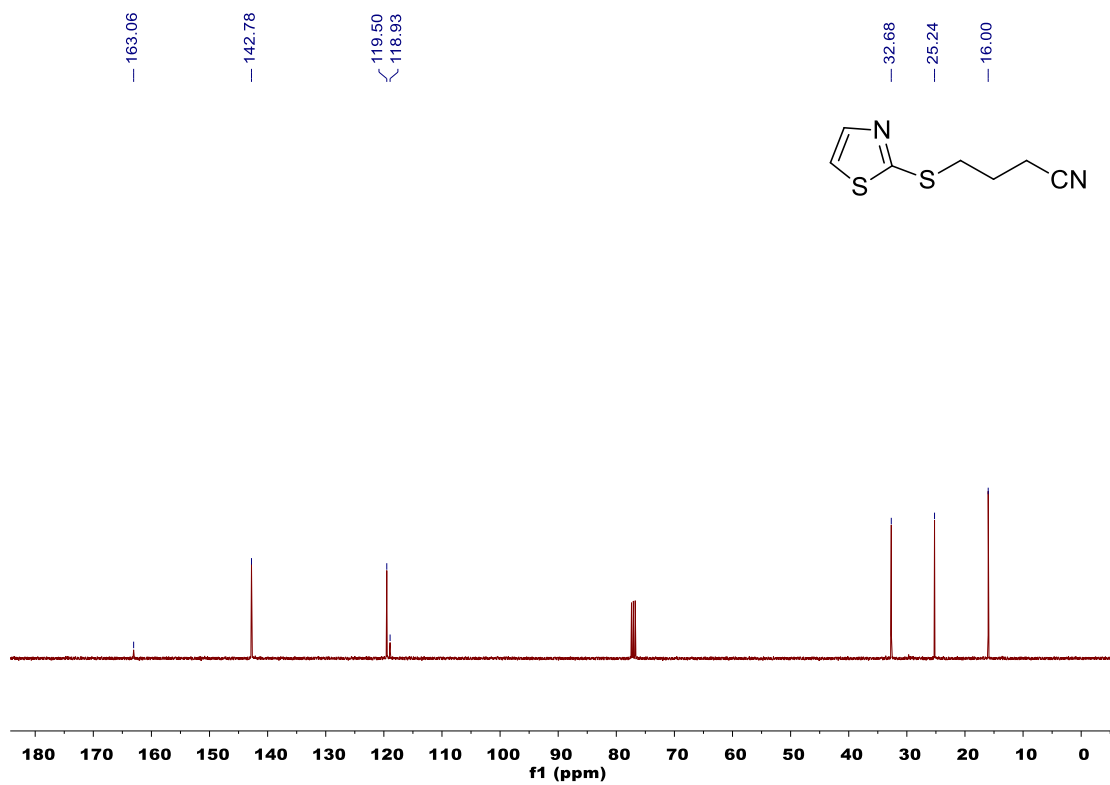
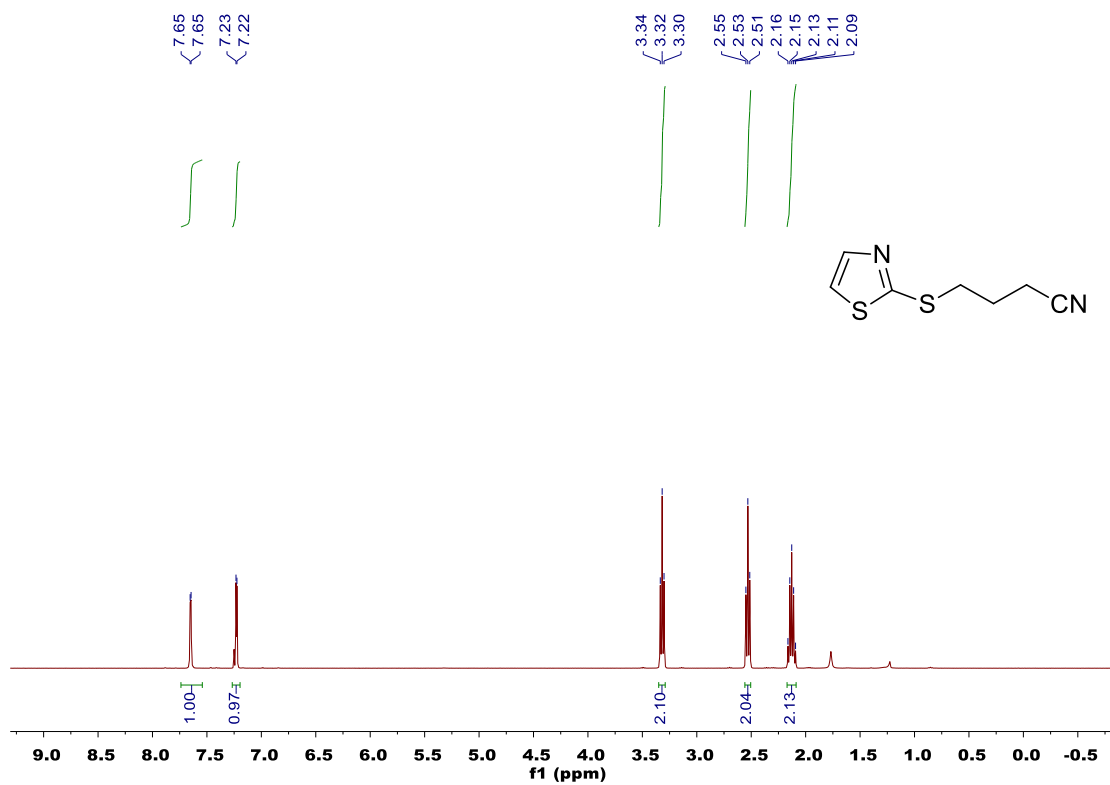
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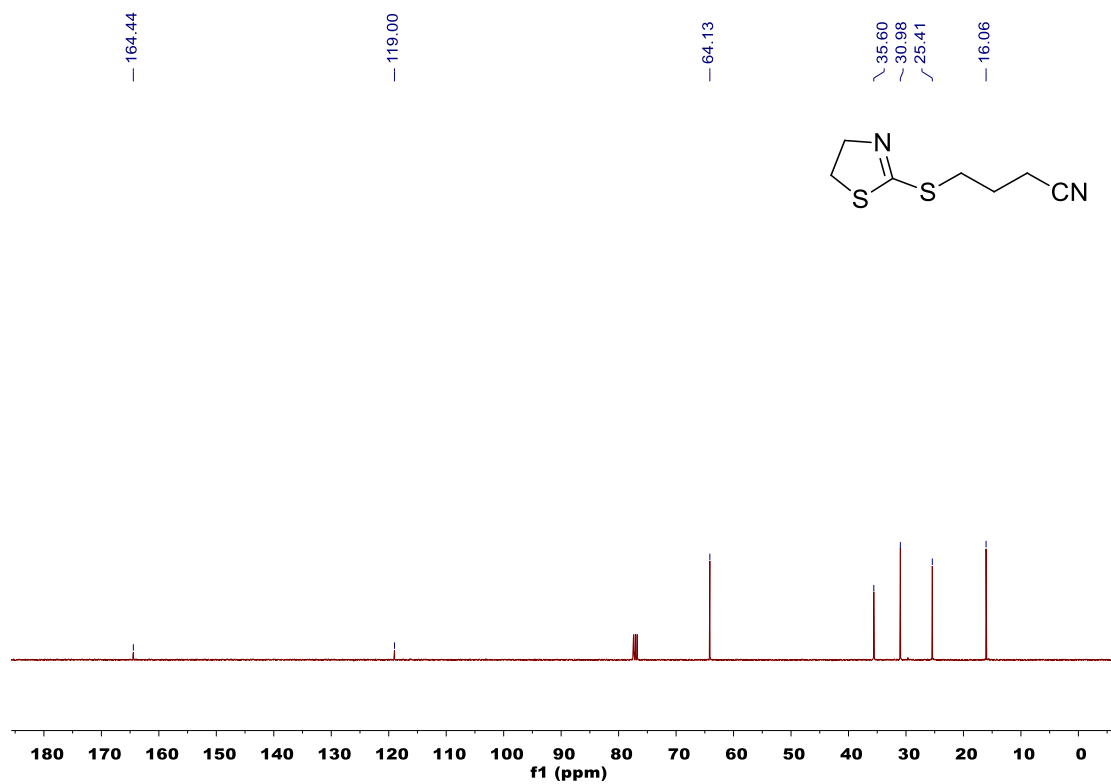
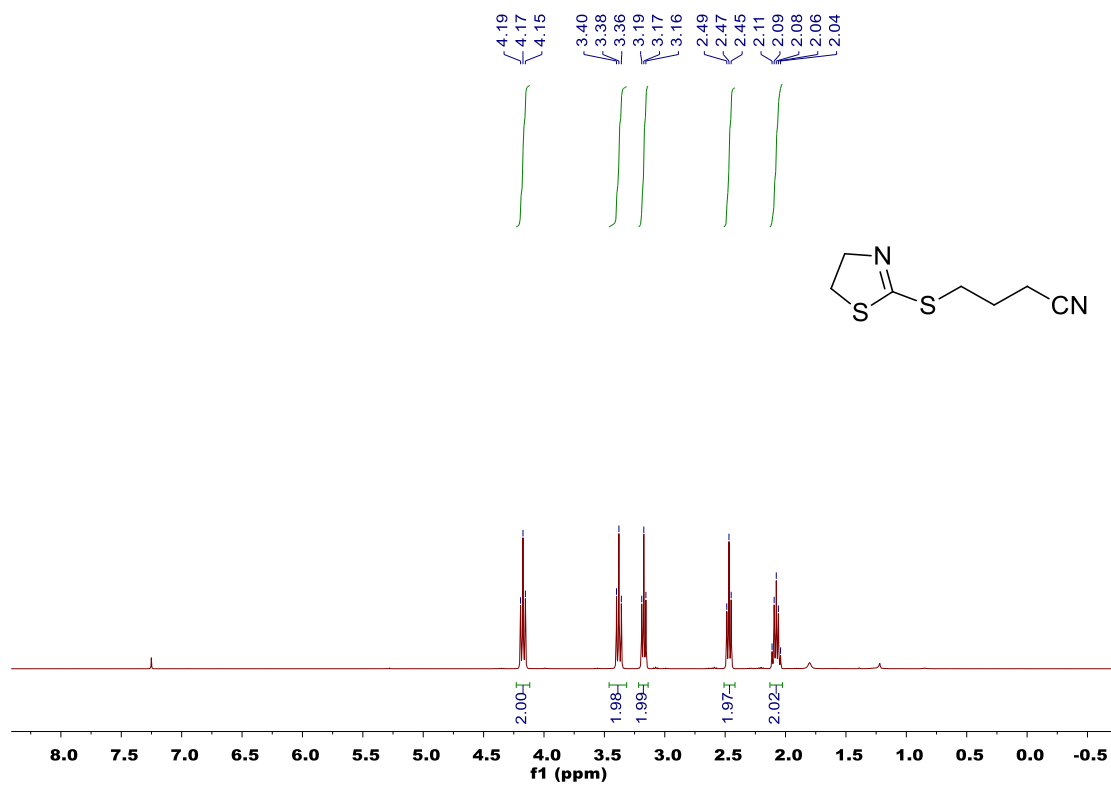
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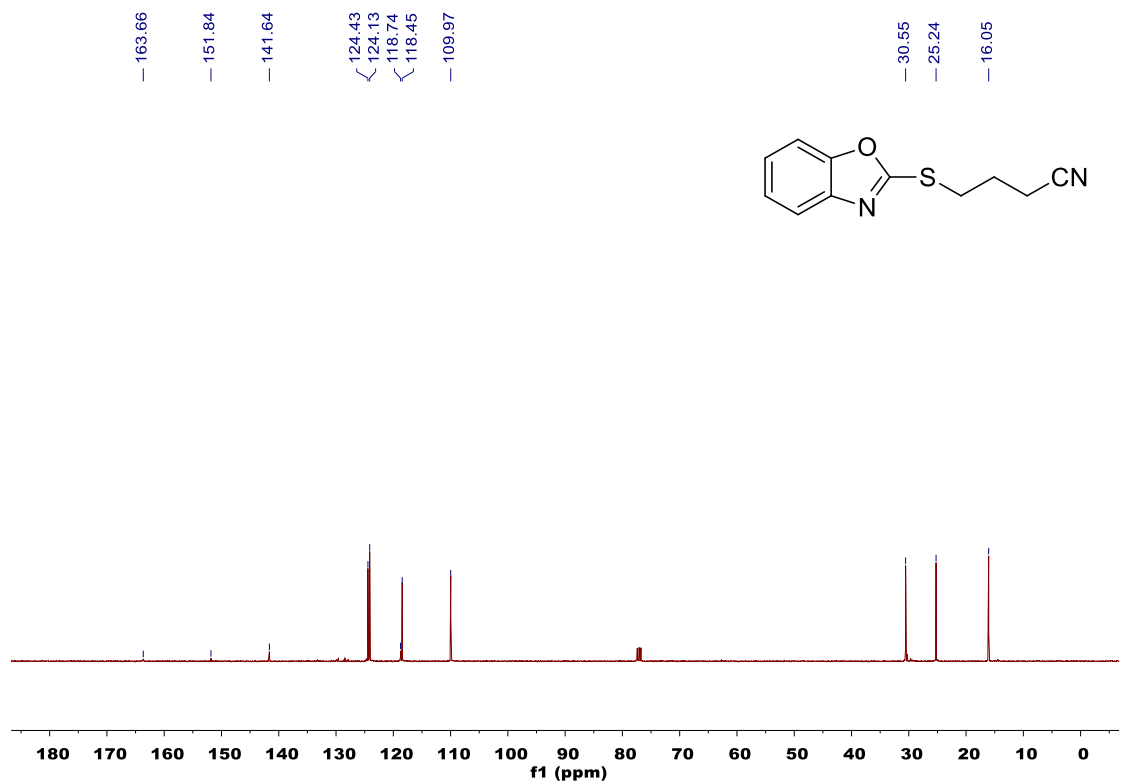
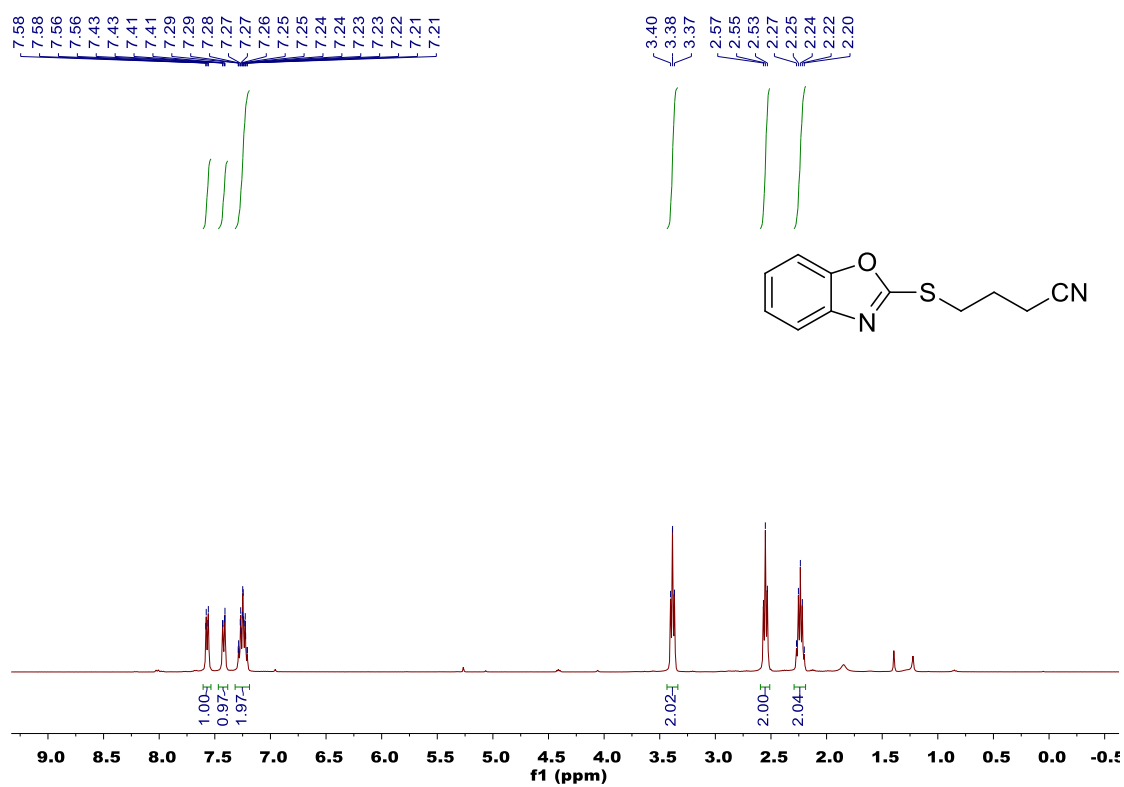
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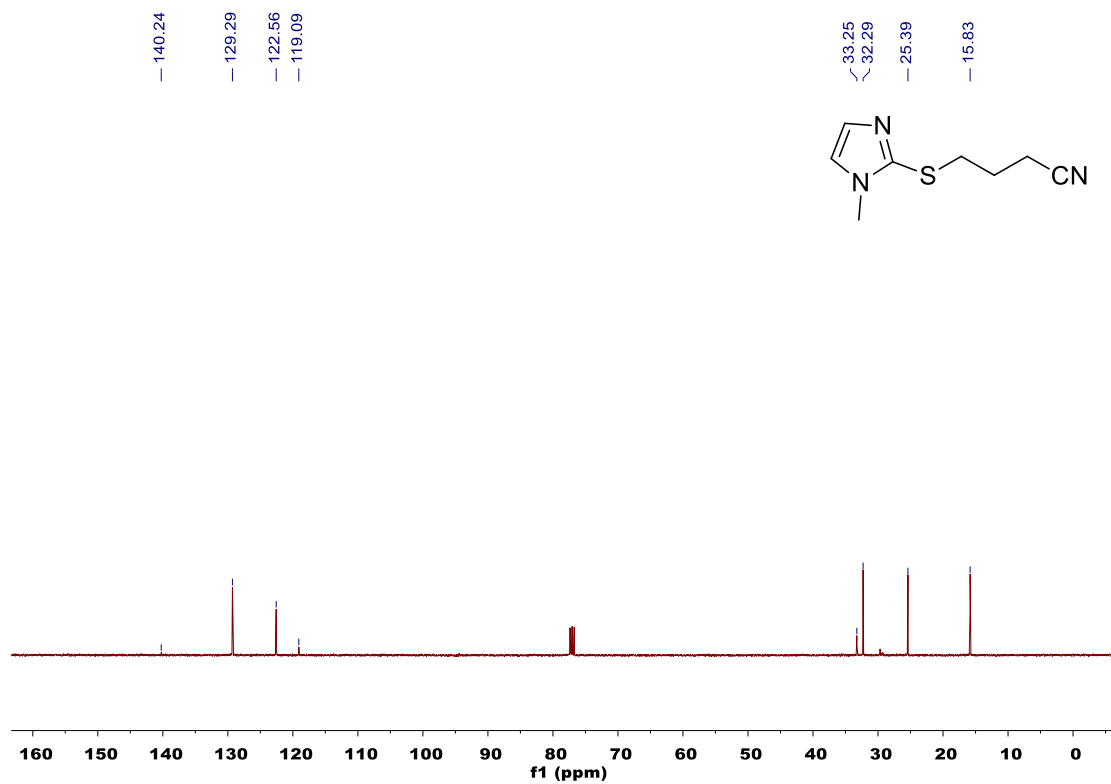
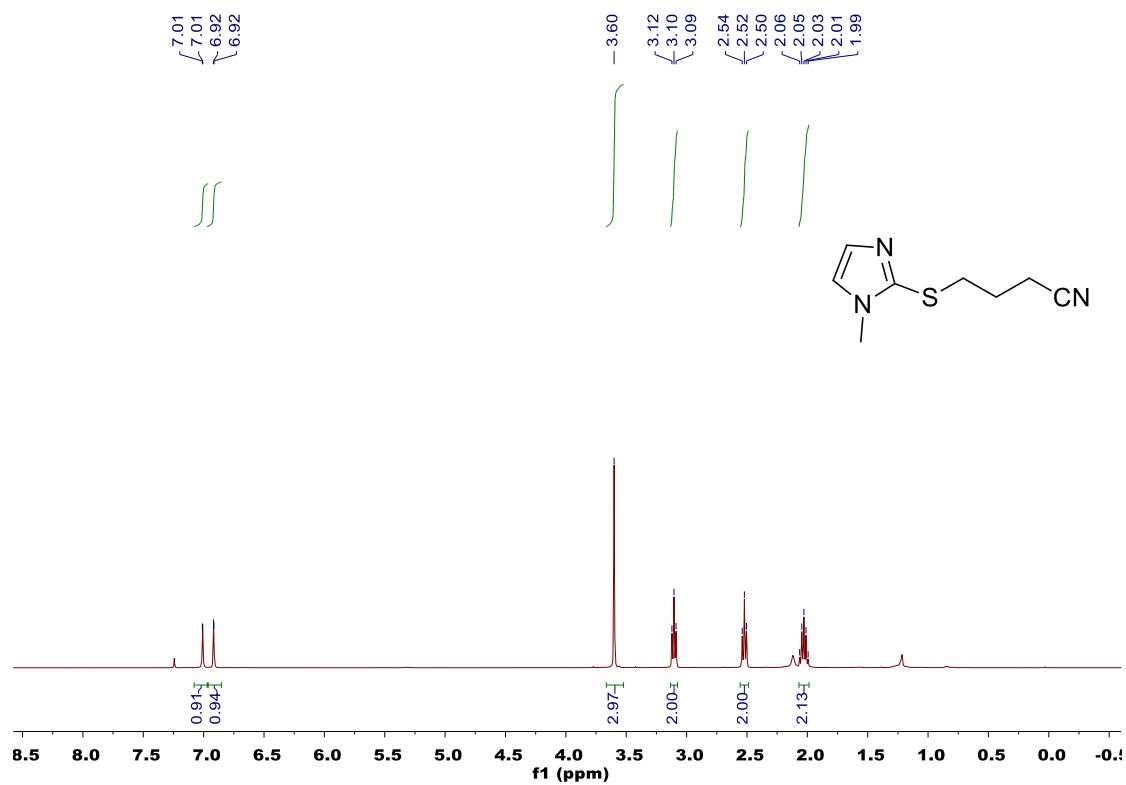
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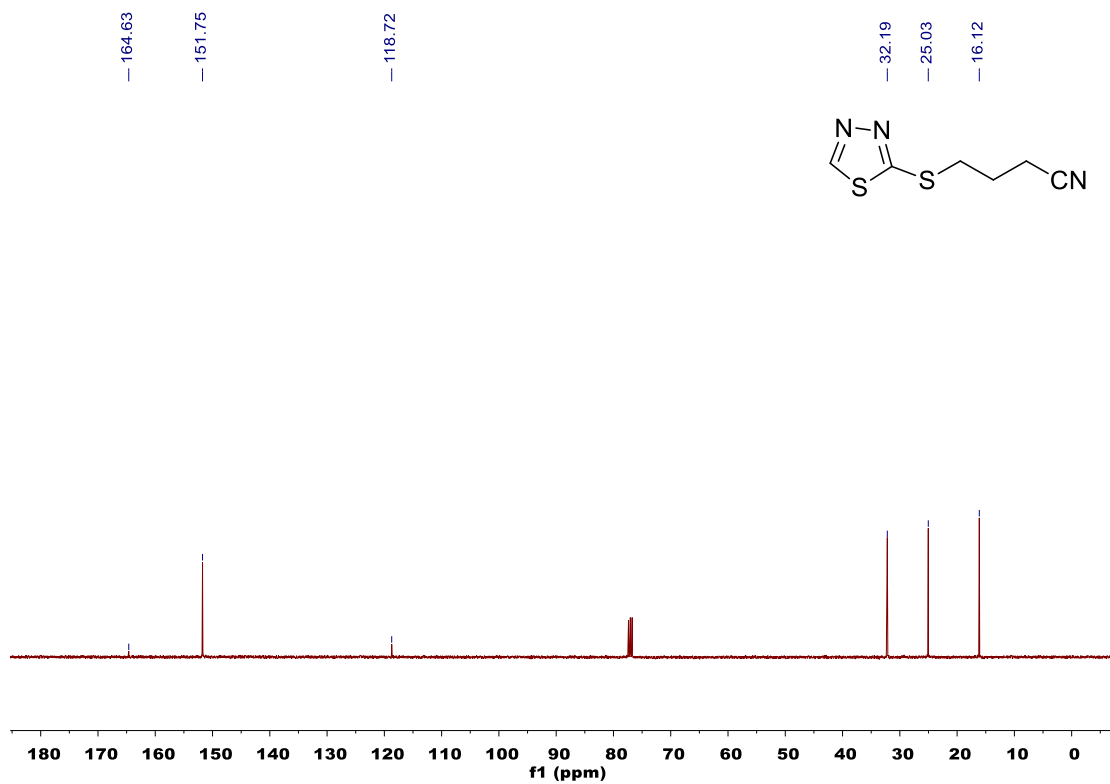
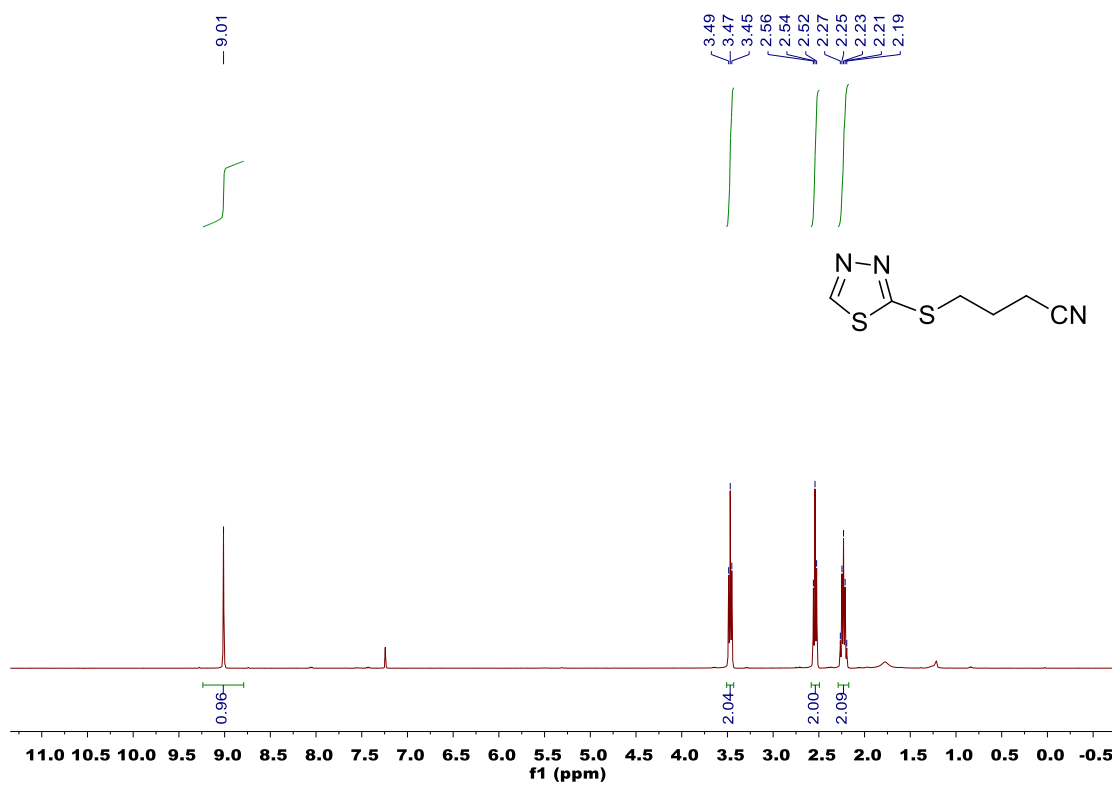
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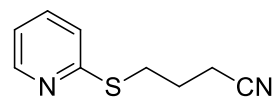
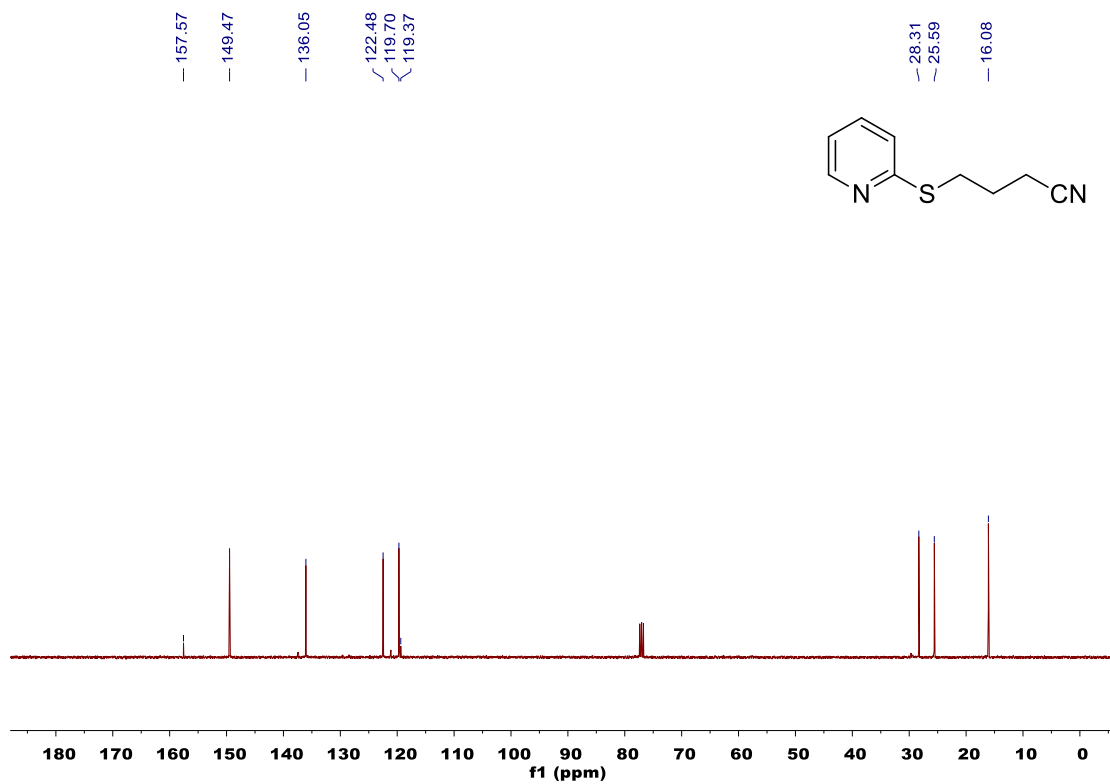
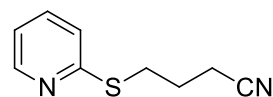
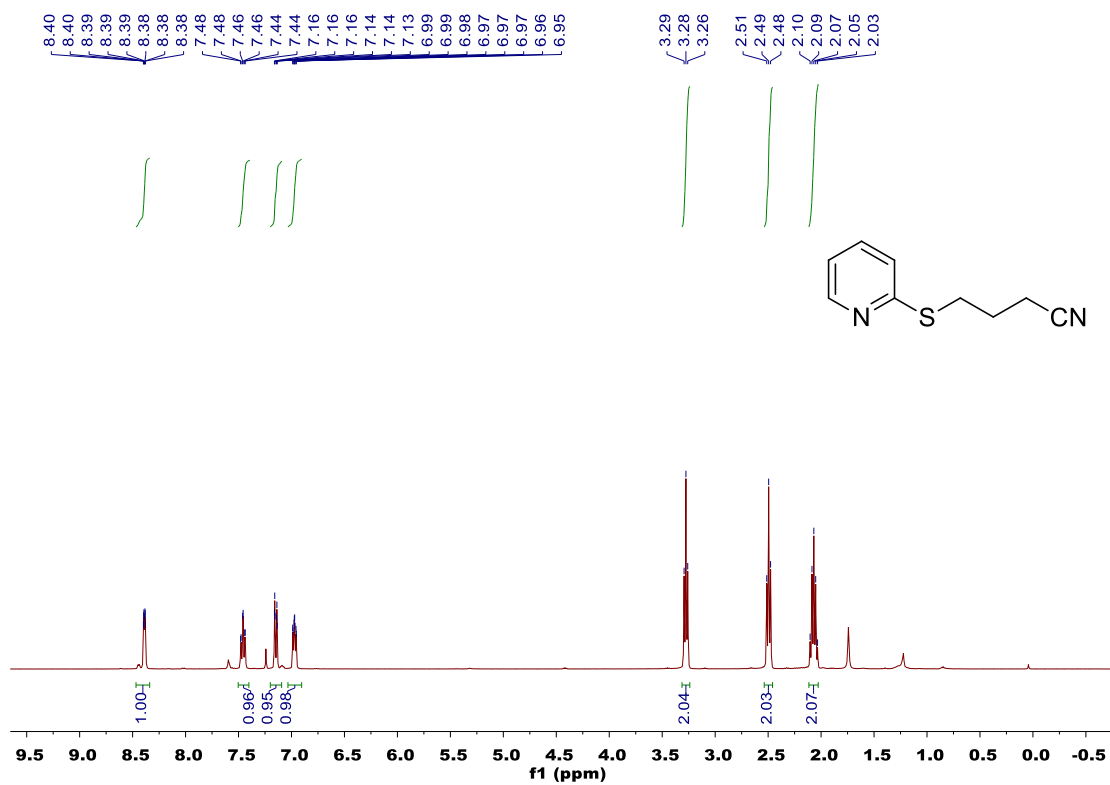
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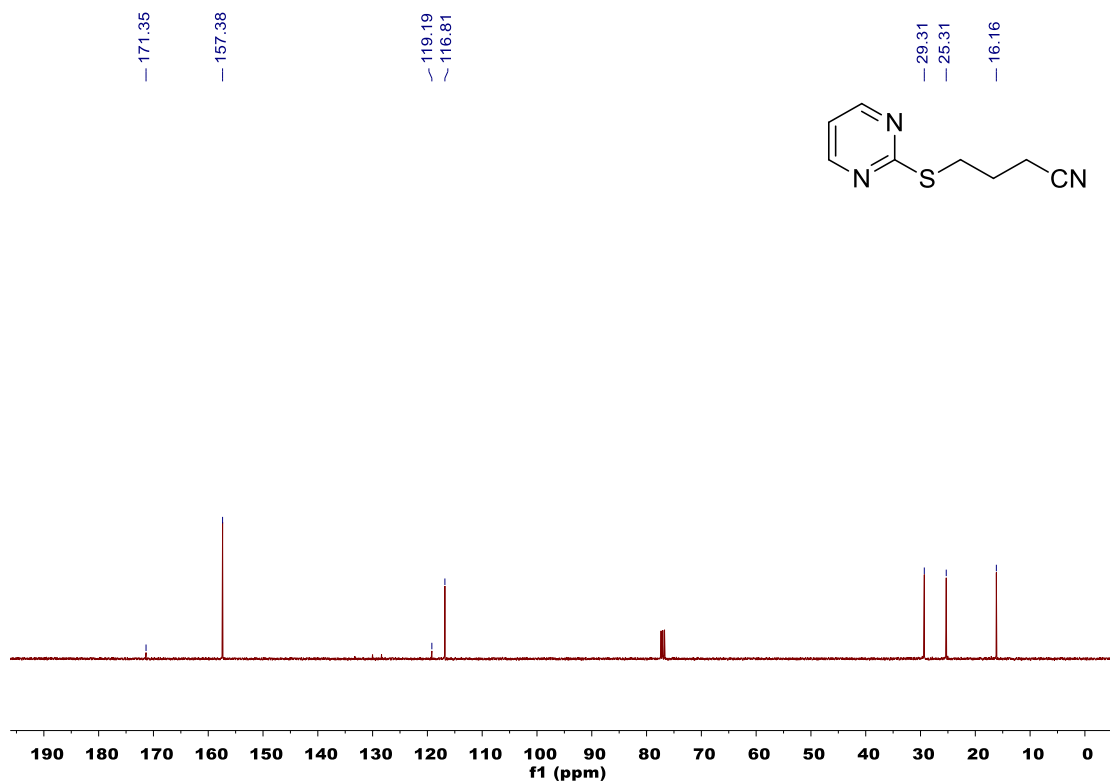
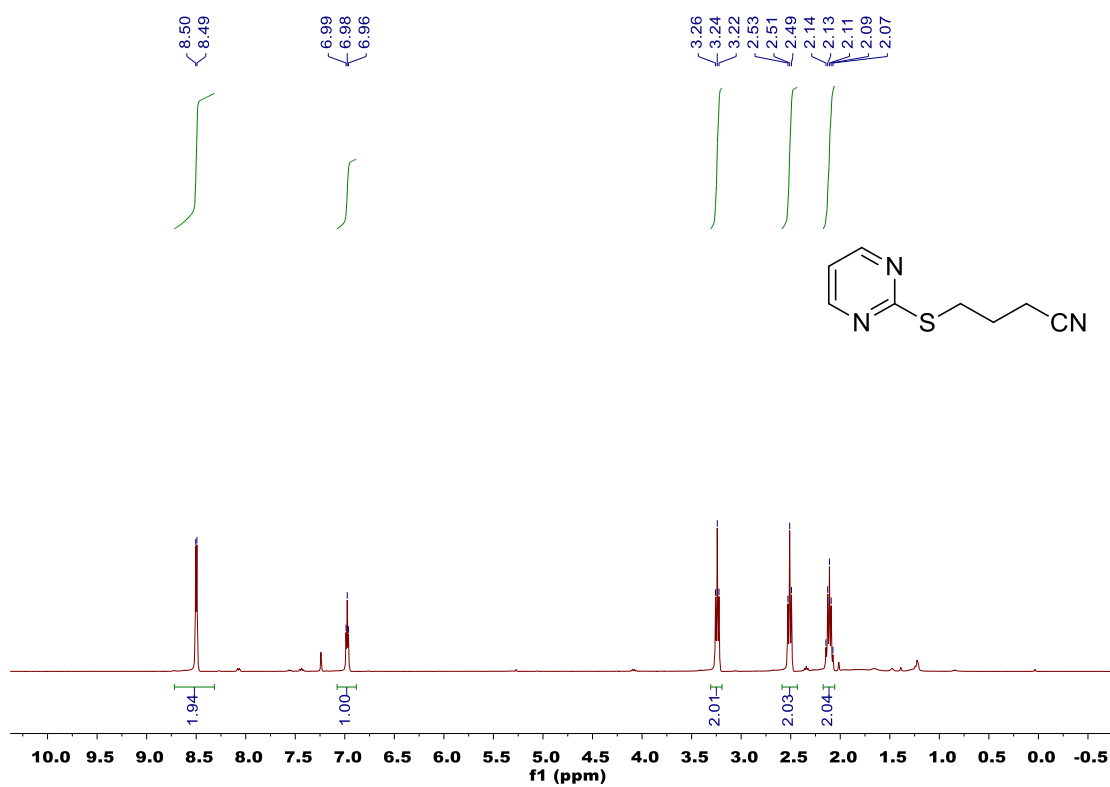
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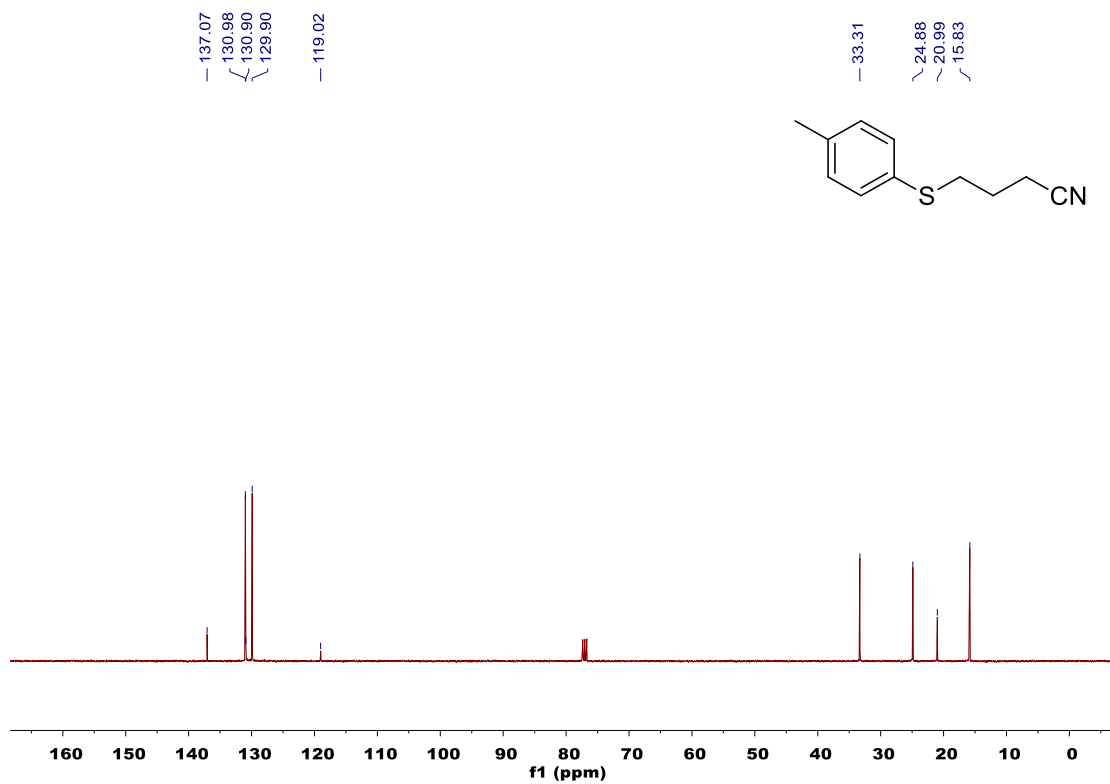
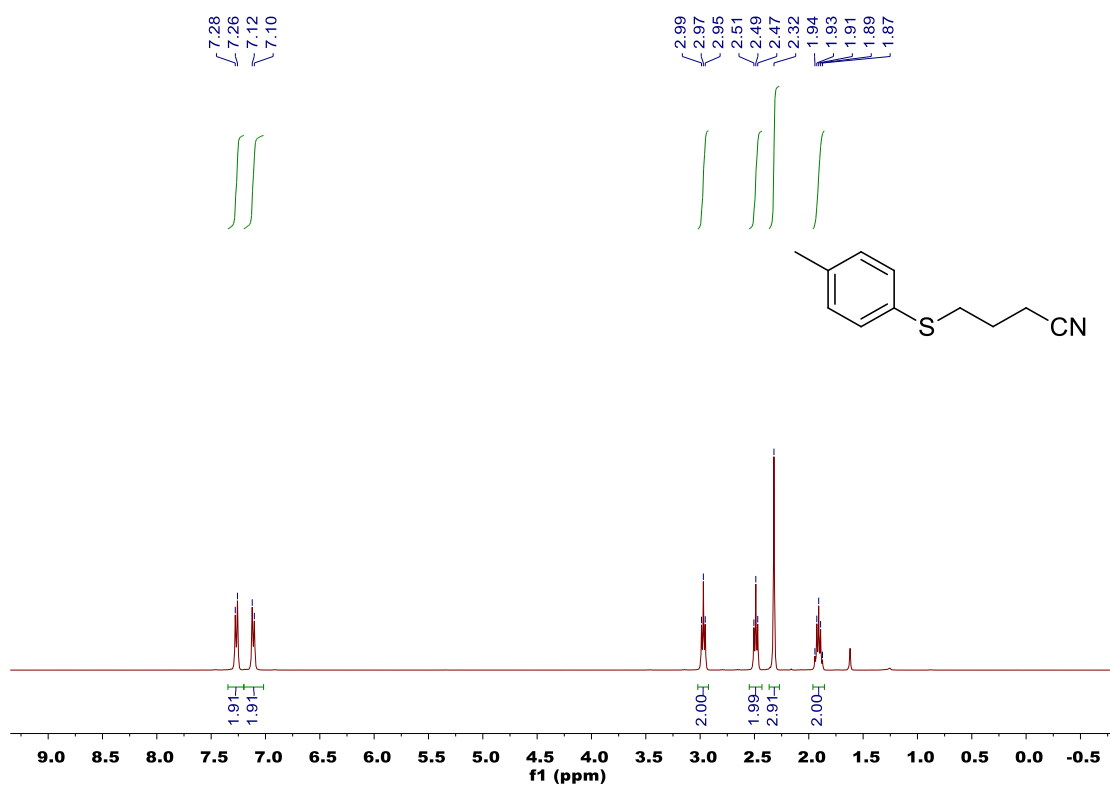
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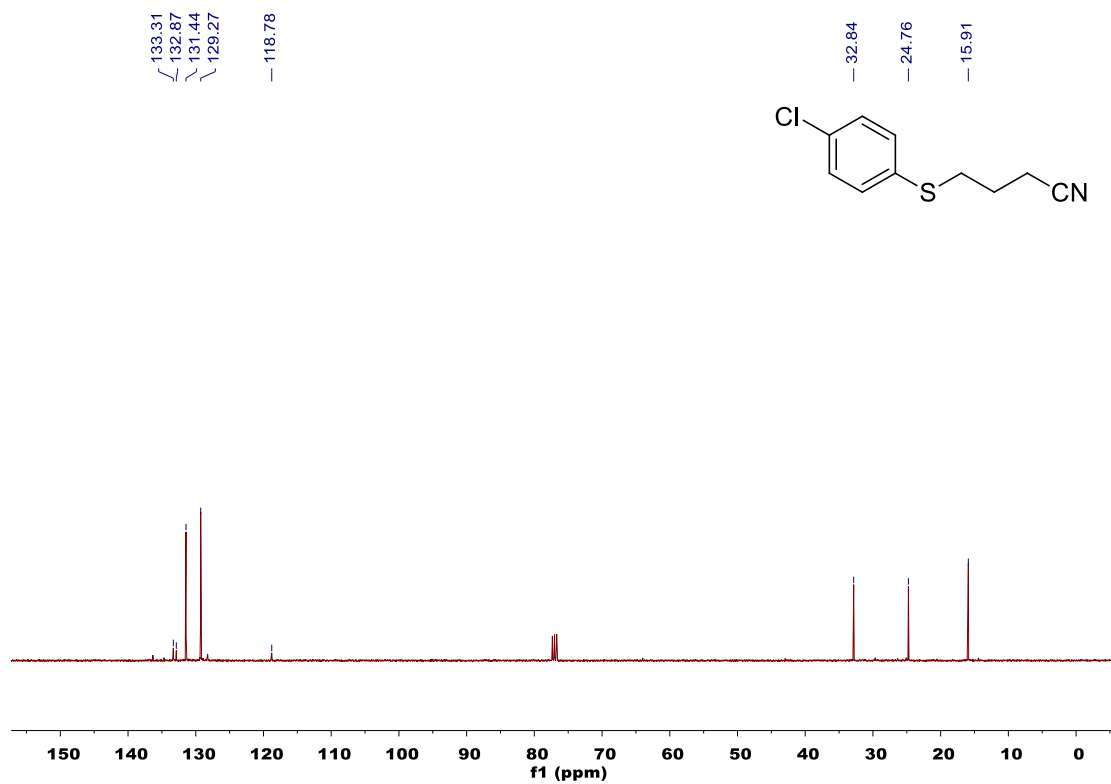
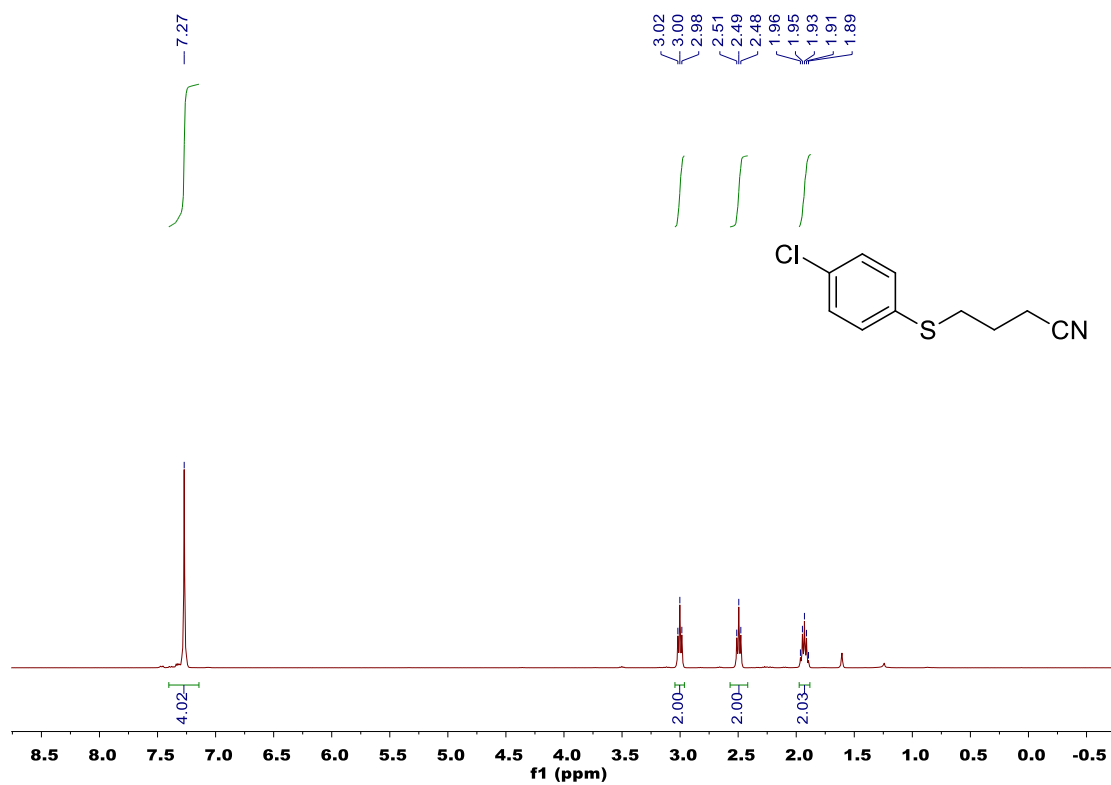
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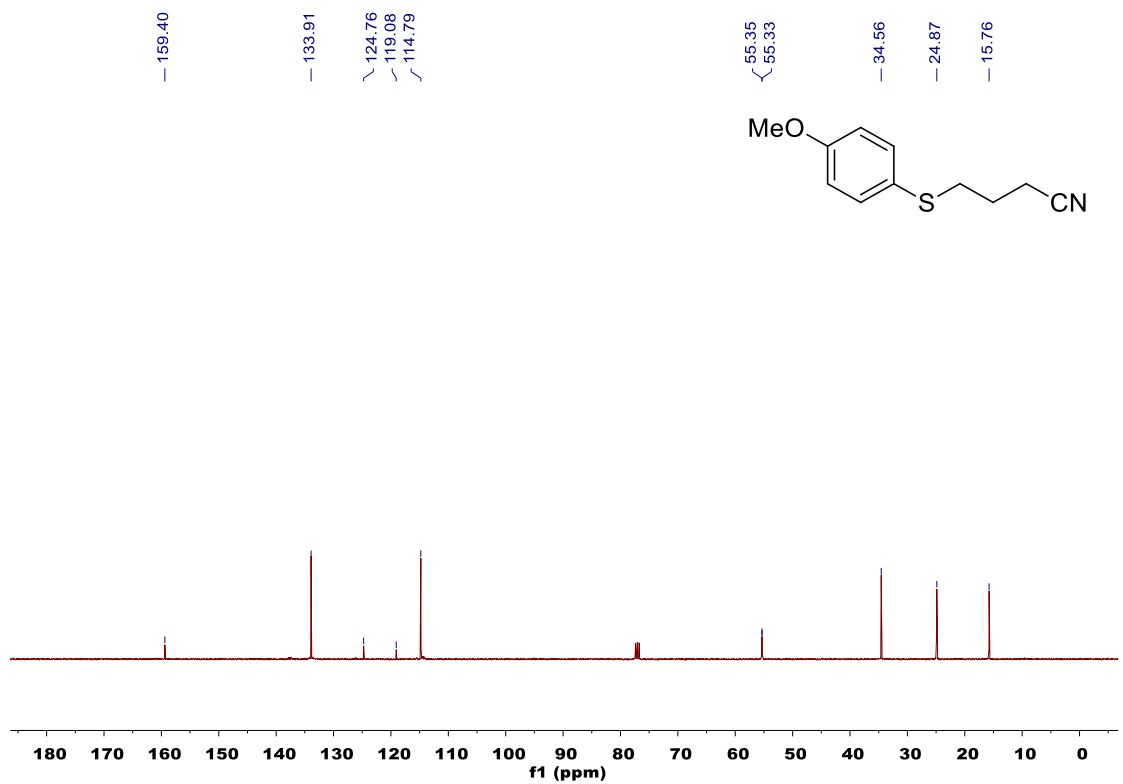
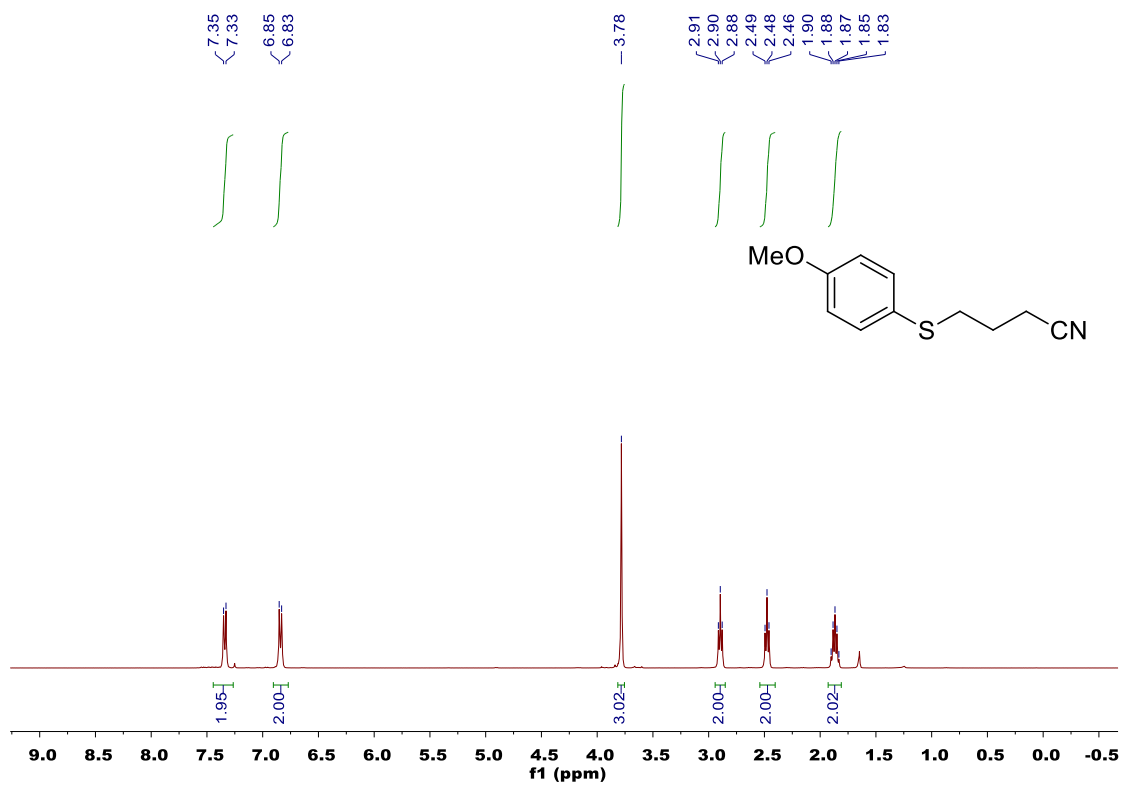
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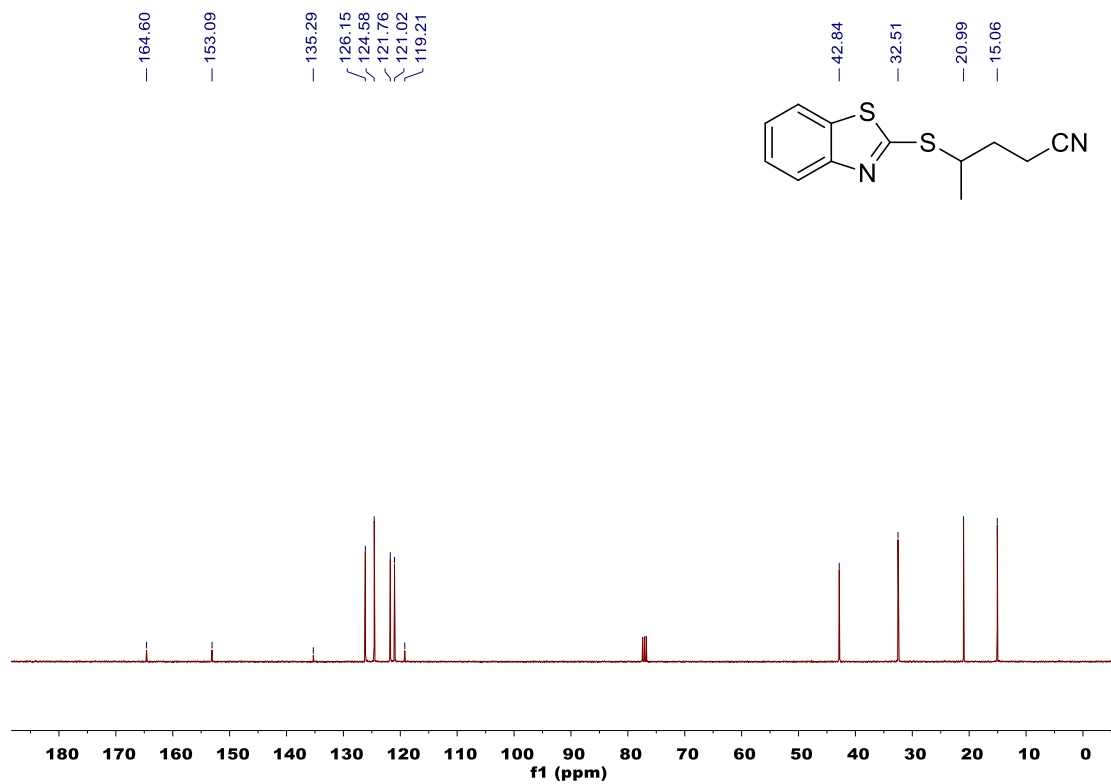
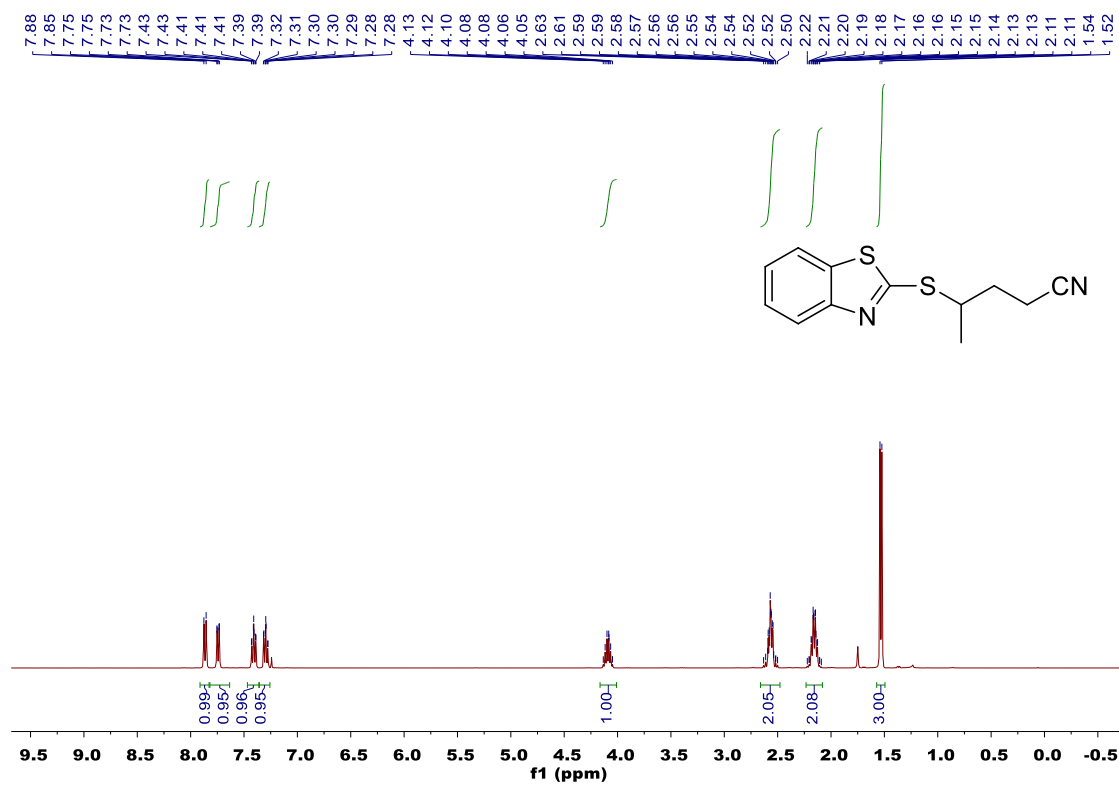
4-((4-chlorophenyl)thio)butanenitrile (3oa)



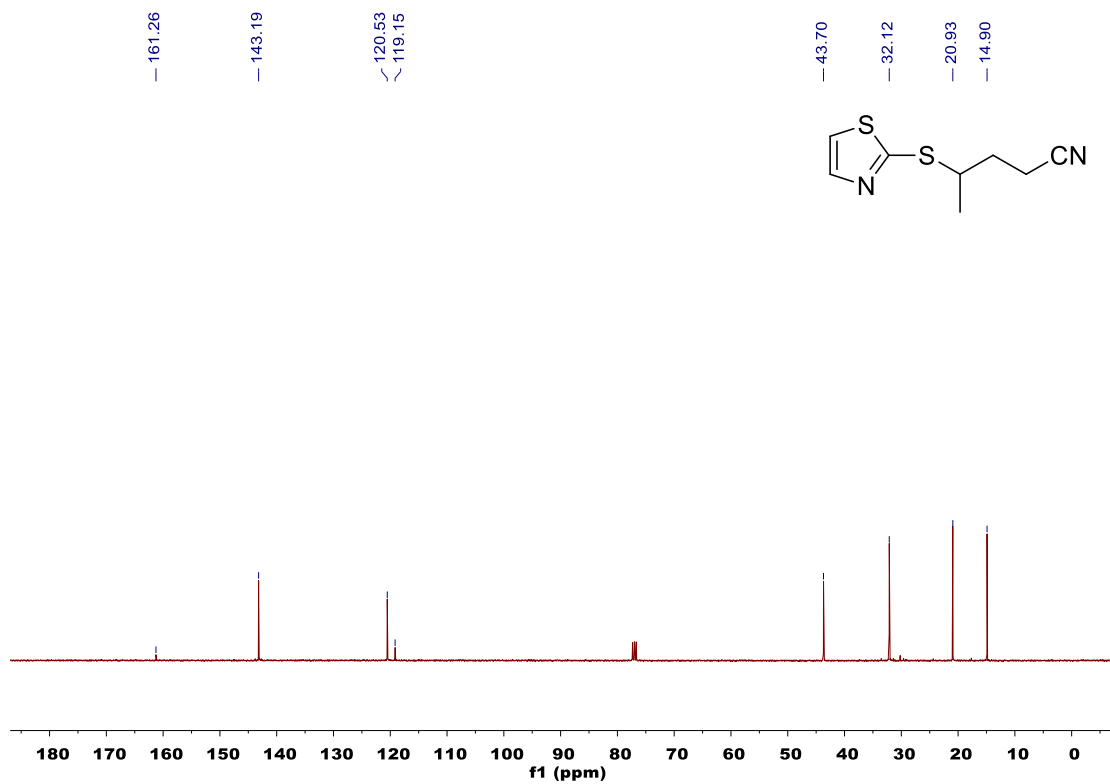
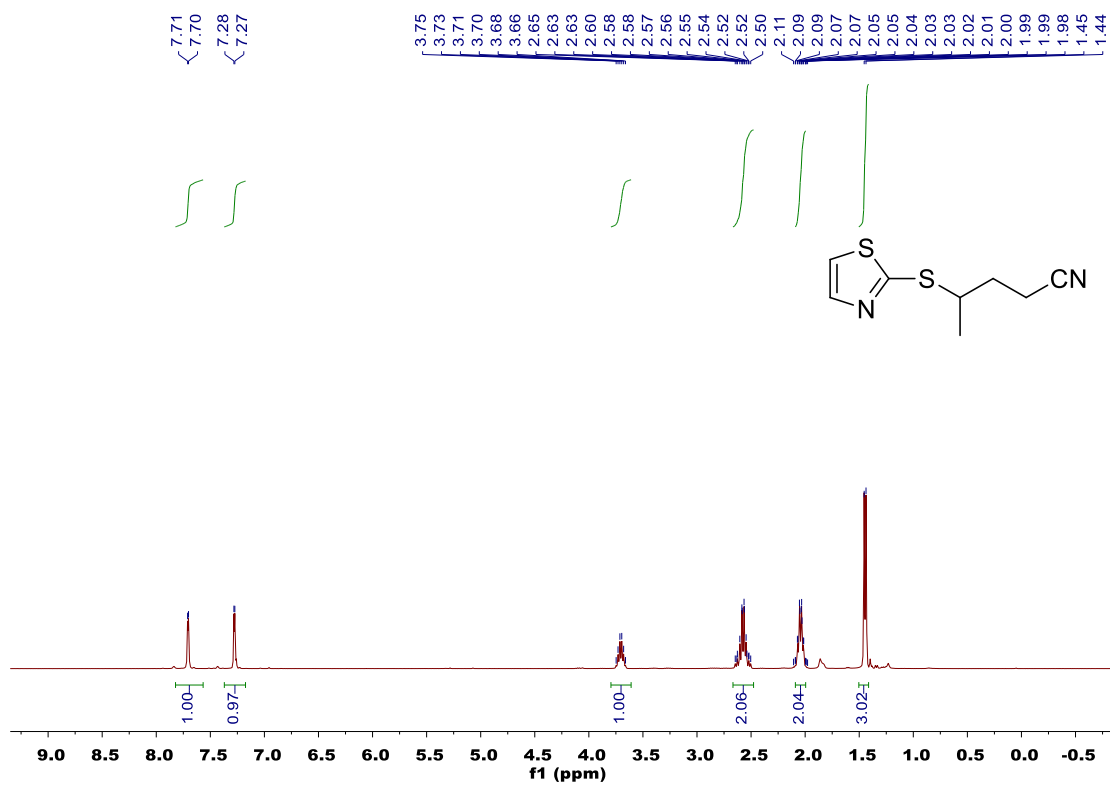
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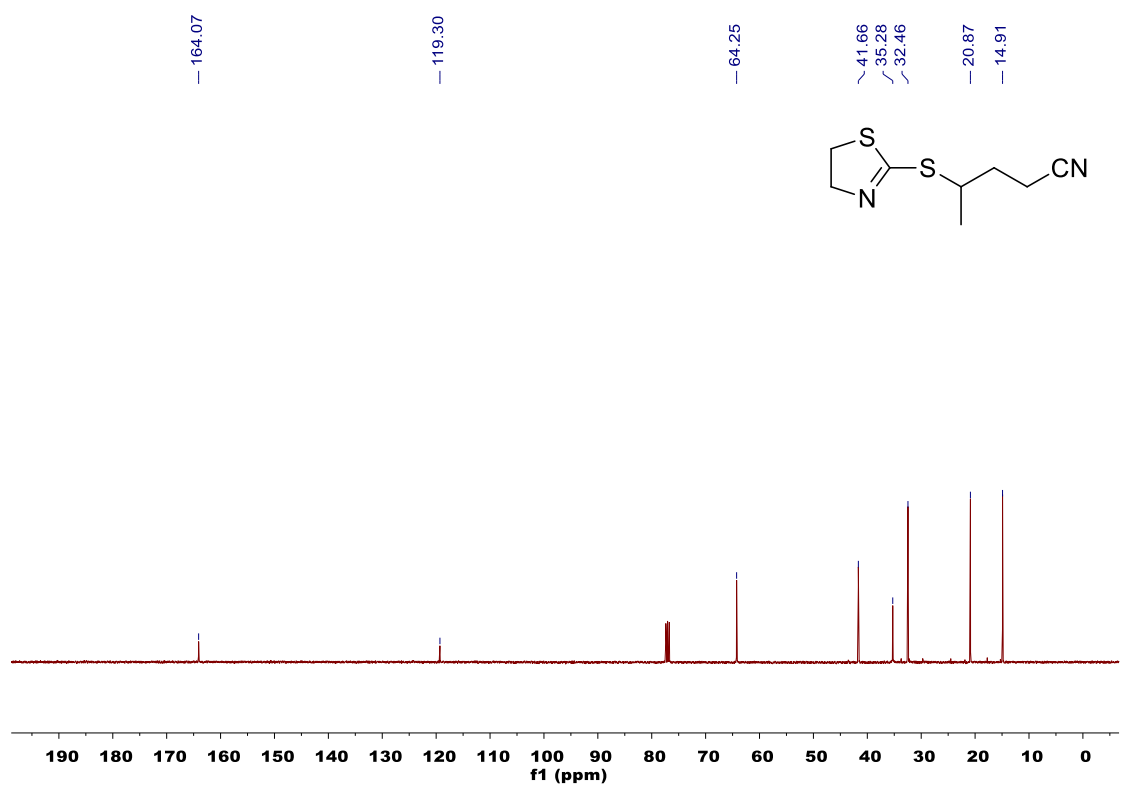
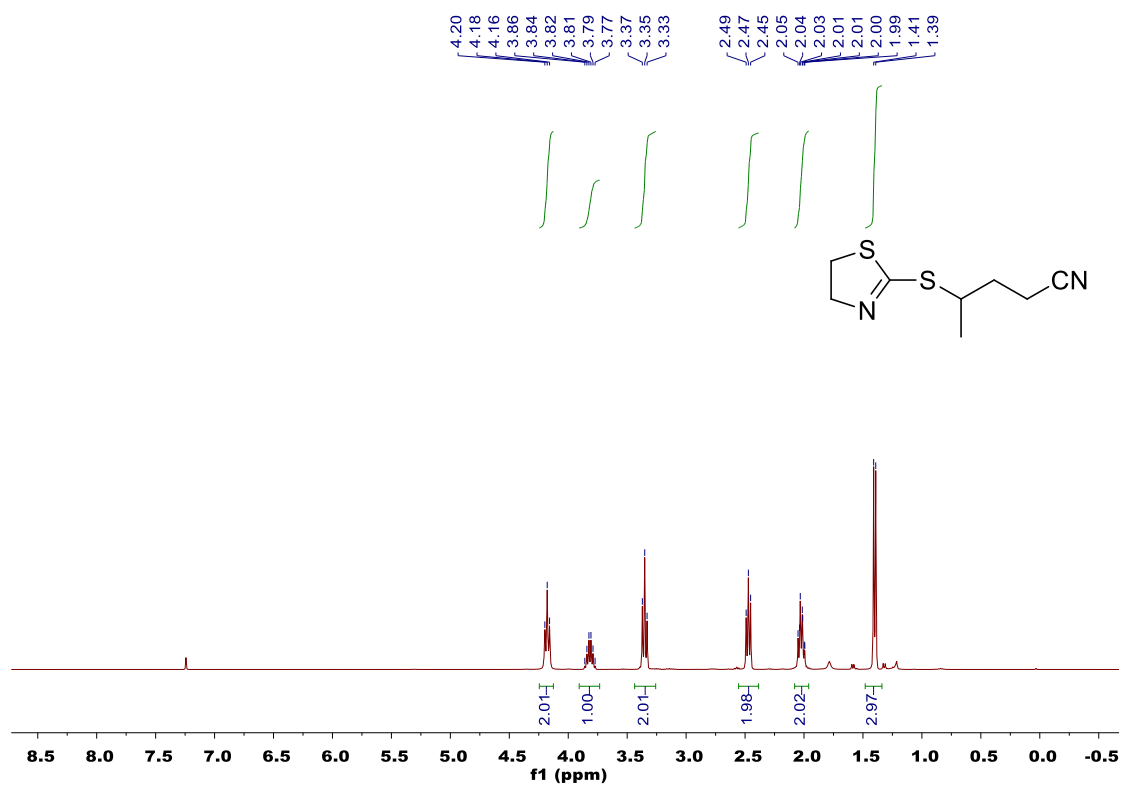
4-(benzo[d]thiazol-2-ylthio)pentanenitrile (3ab)



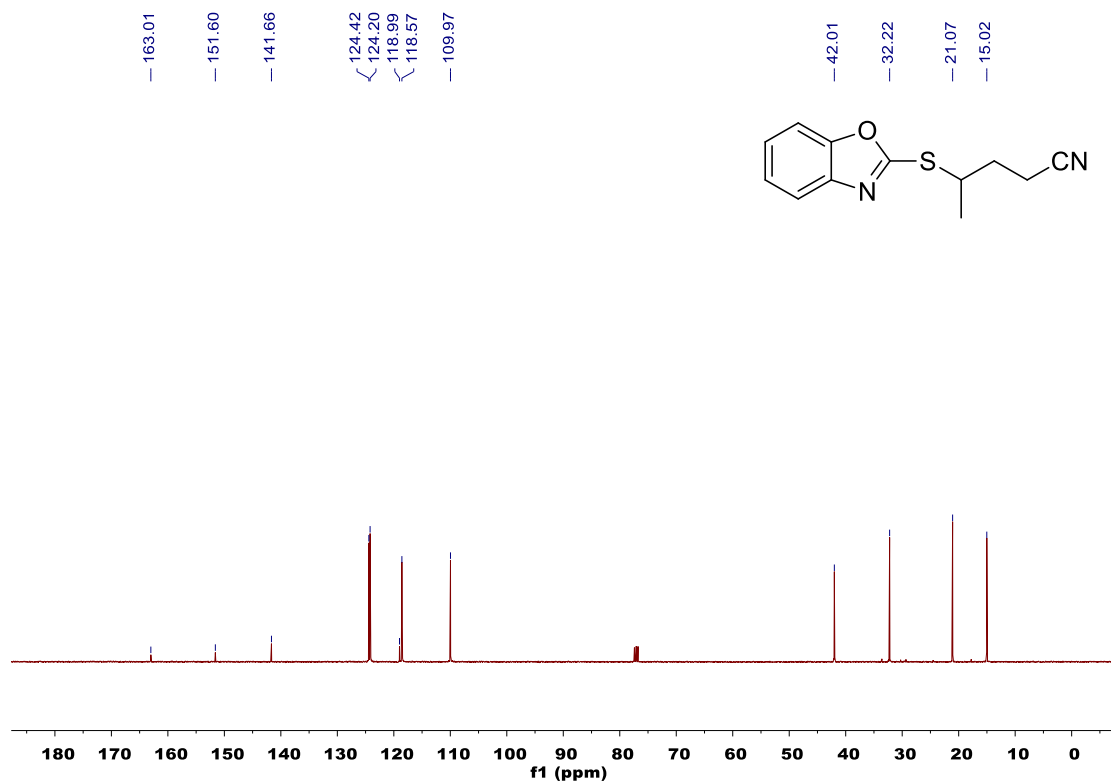
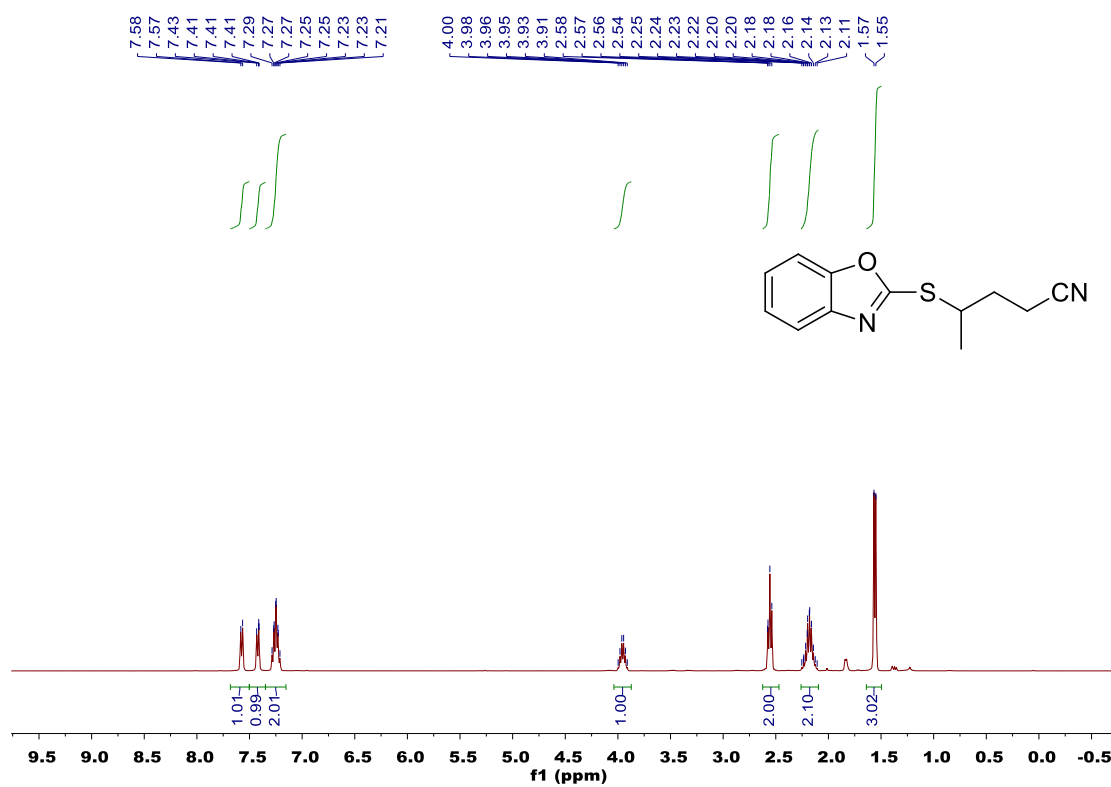
4-(thiazol-2-ylthio)pentanenitrile (3gb)



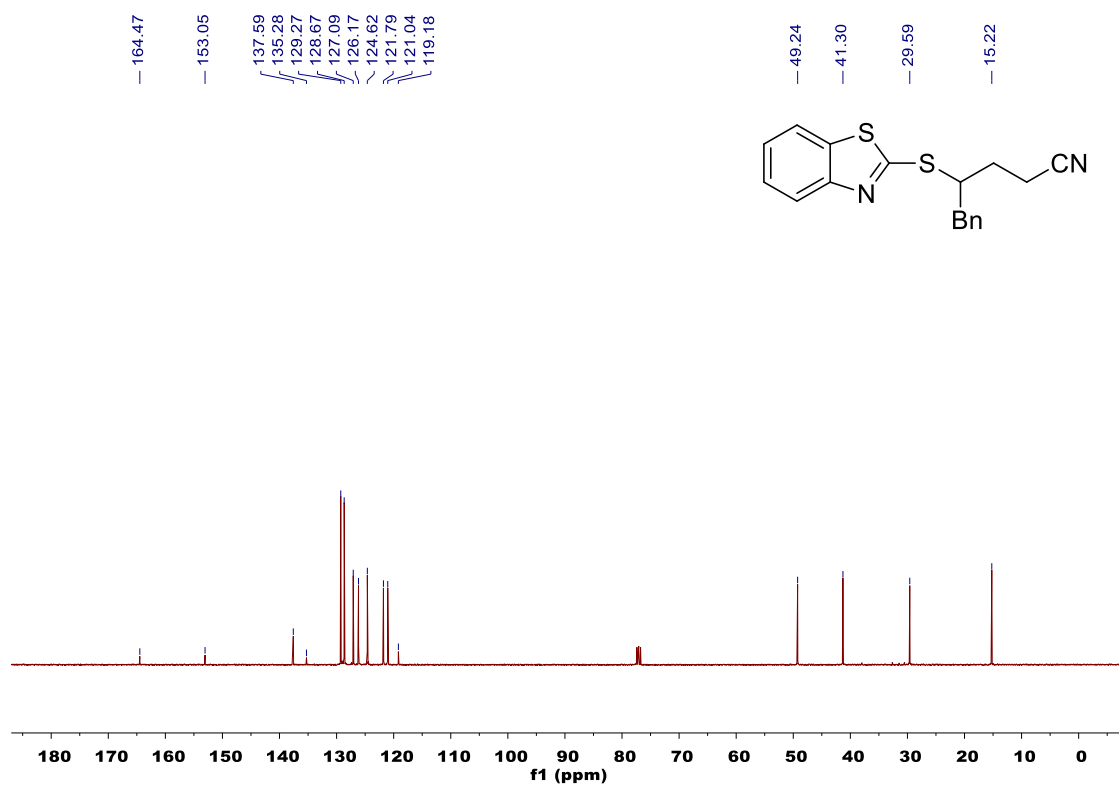
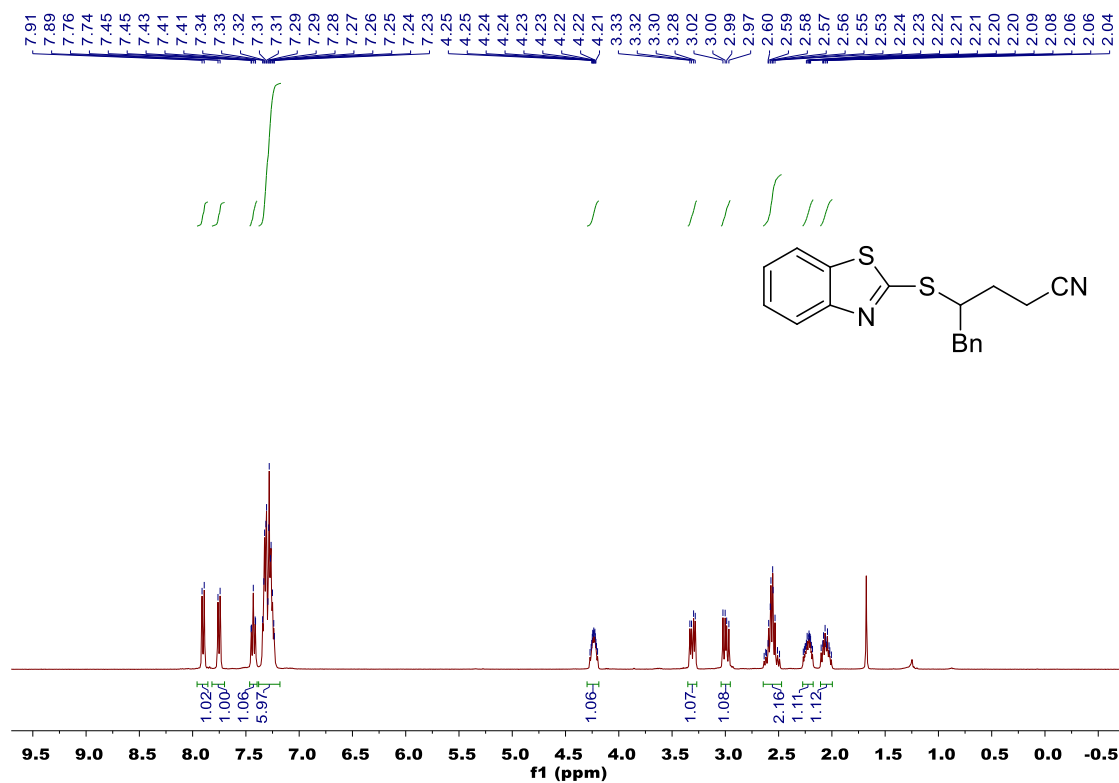
4-((4,5-dihydrothiazol-2-yl)thio)pentanenitrile (3hb)



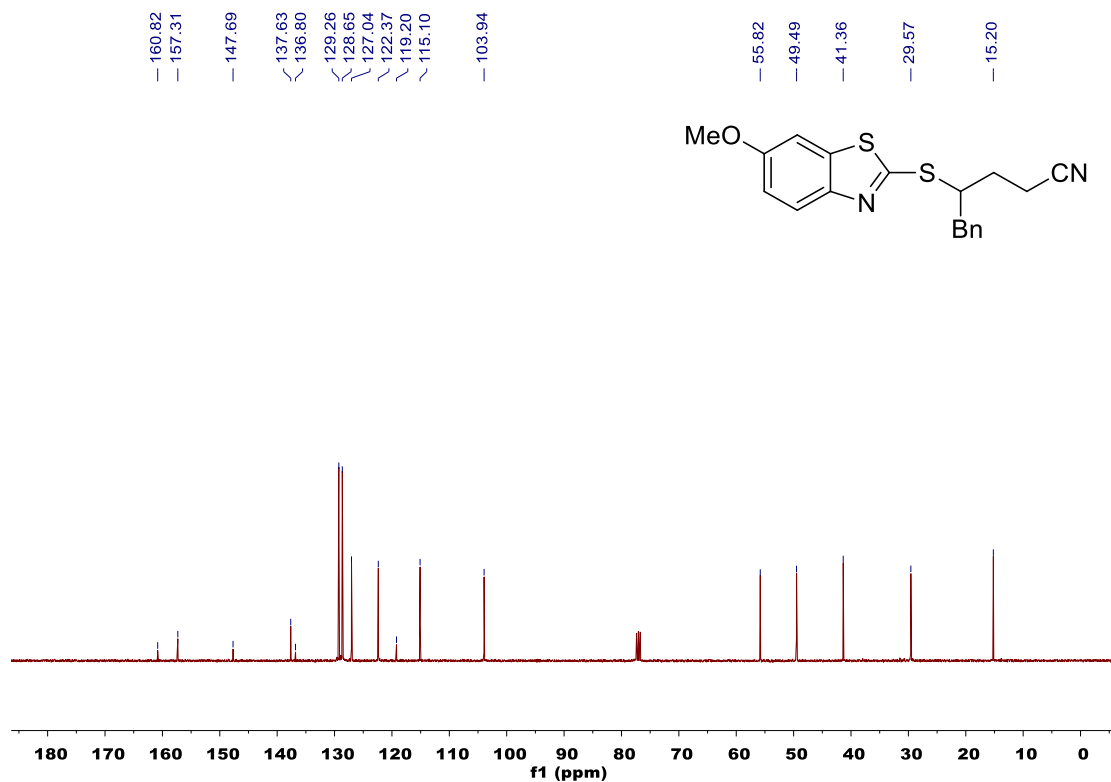
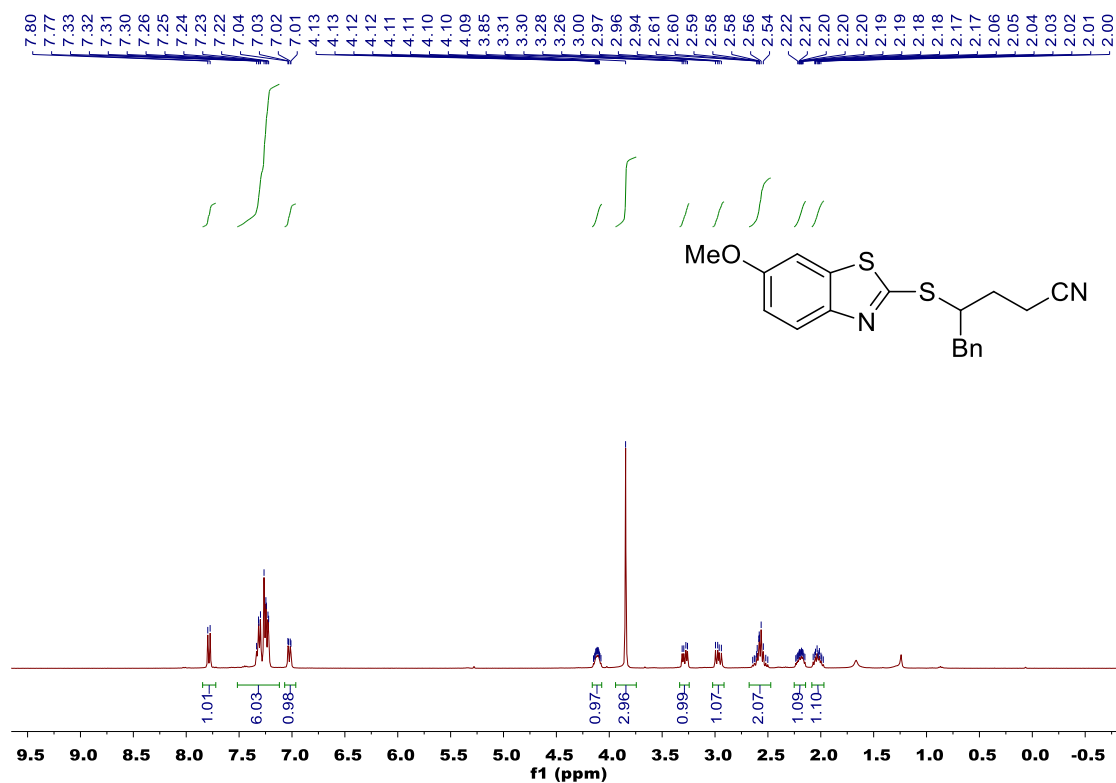
4-(benzo[d]oxazol-2-ylthio)pentanenitrile (3ib)



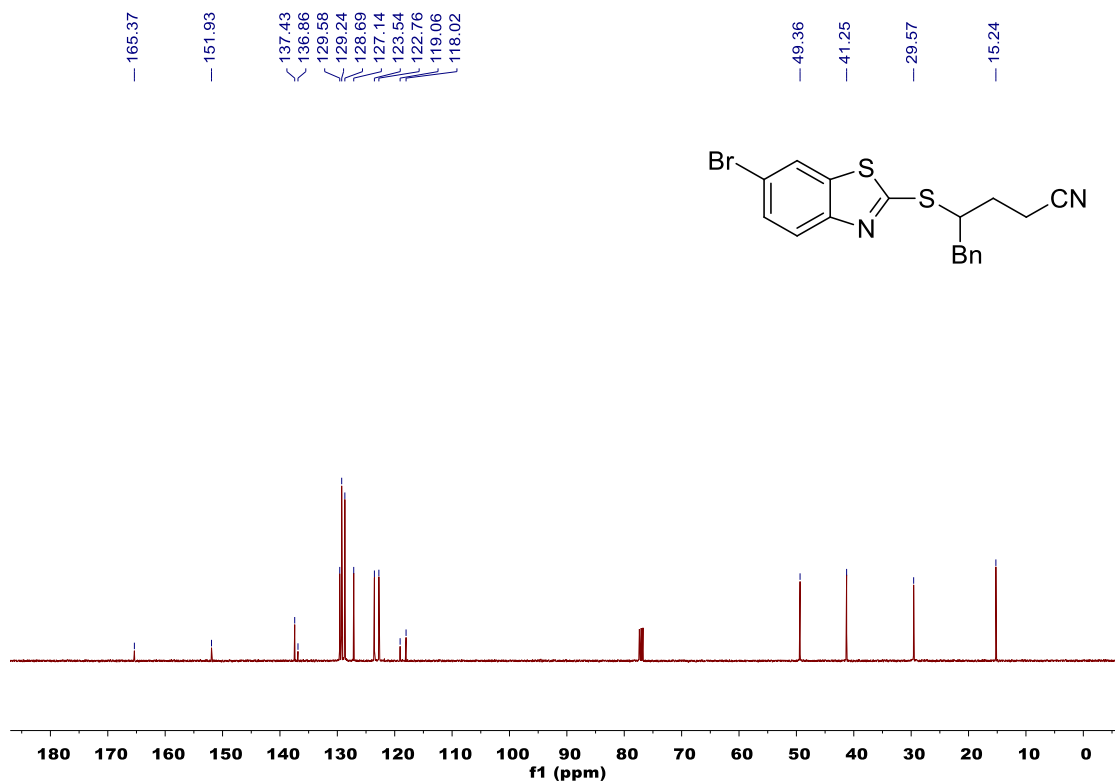
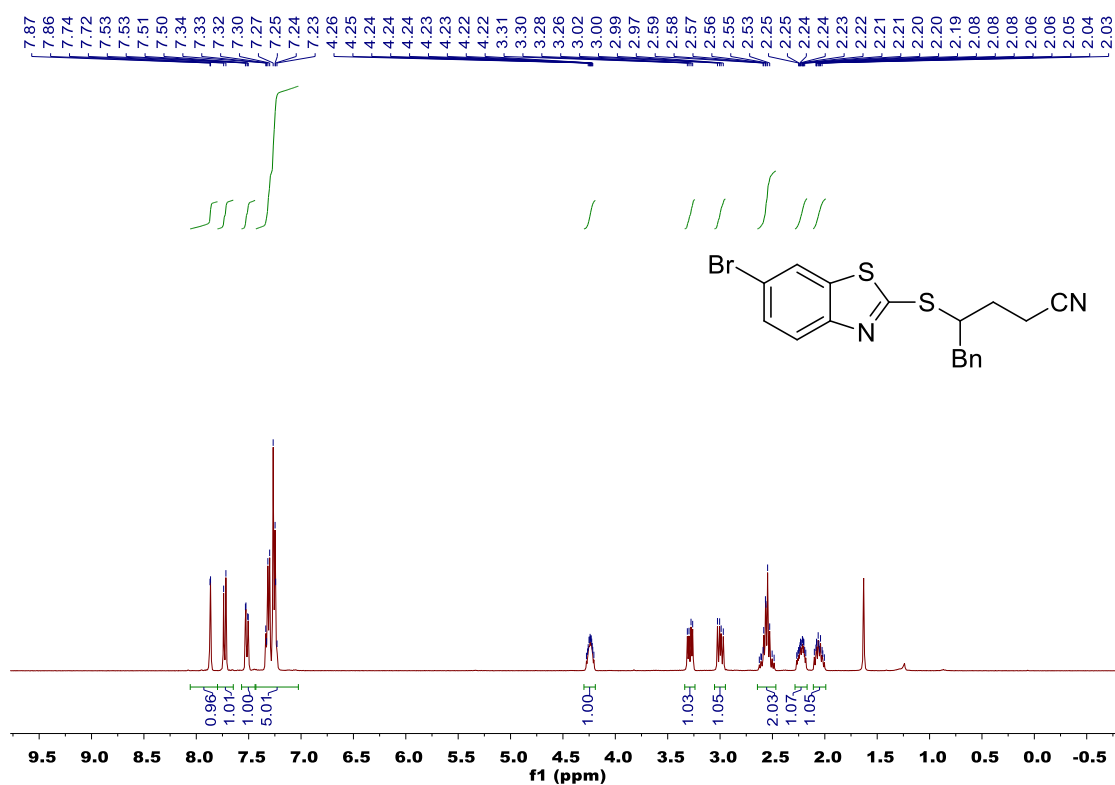
4-(benzo[d]thiazol-2-ylthio)-5-phenylpentanenitrile (3ac)



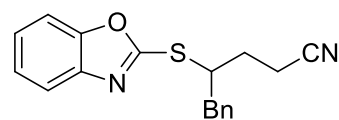
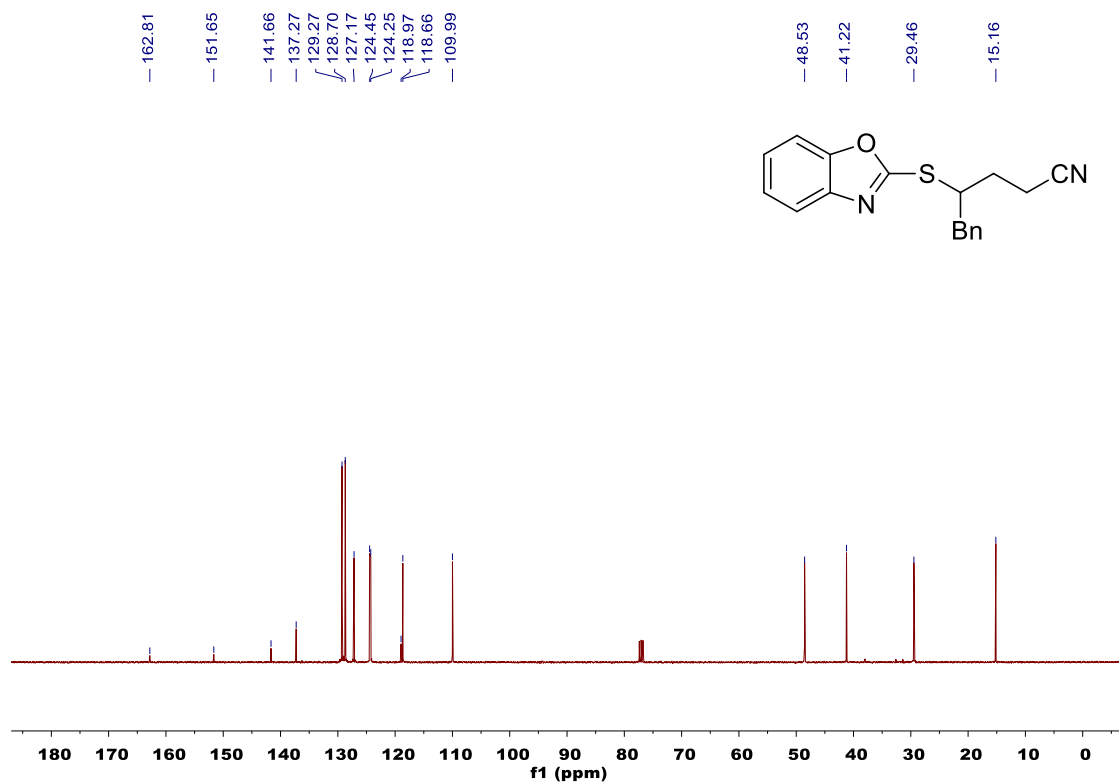
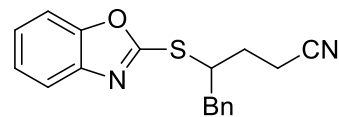
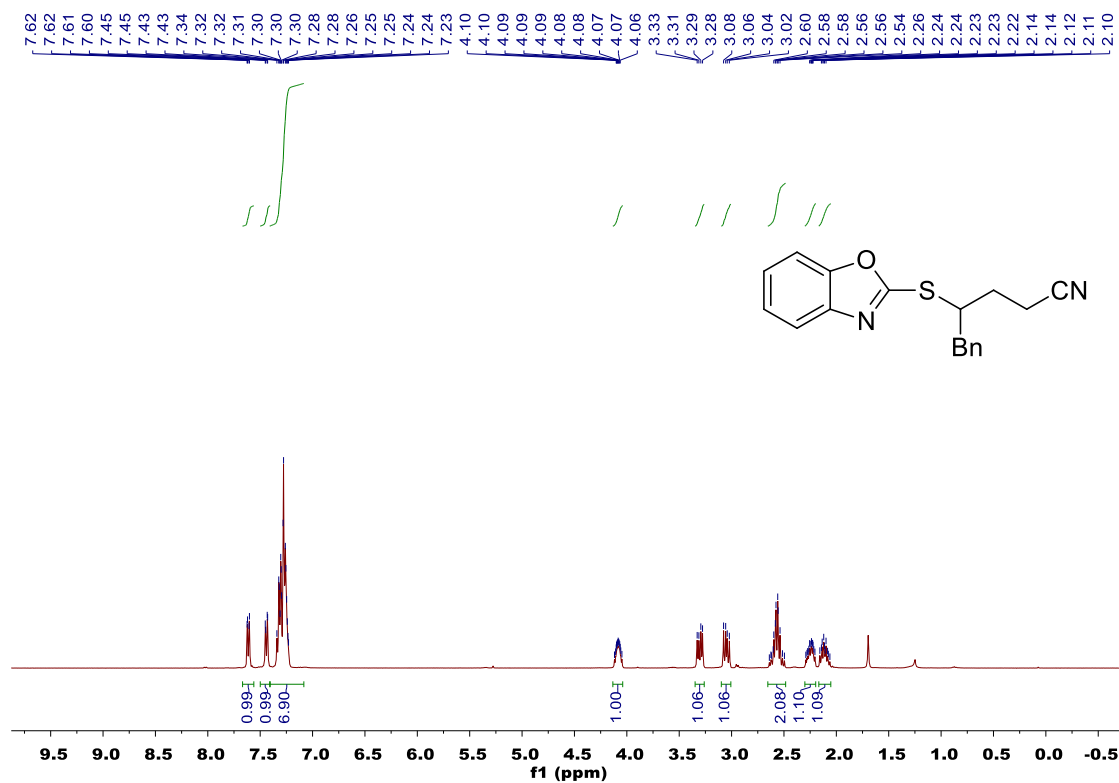
3-benzyl-4-((6-methoxybenzo[d]thiazol-2-yl)thio)butanenitrile (3bc)



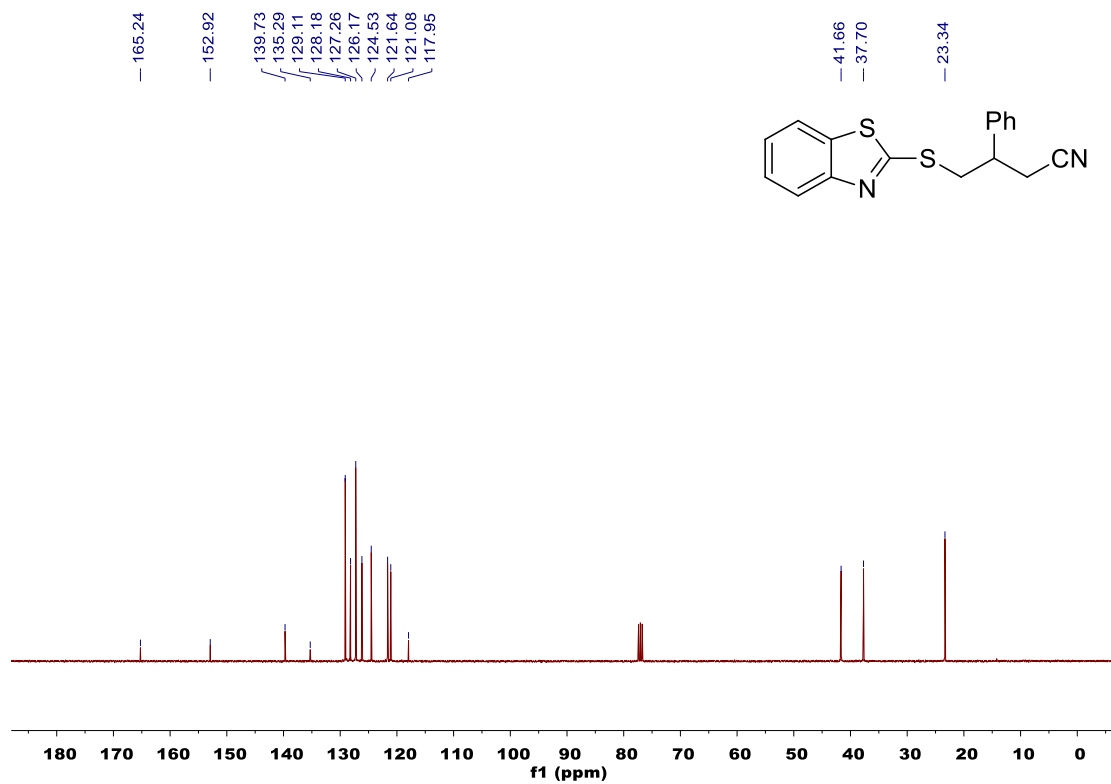
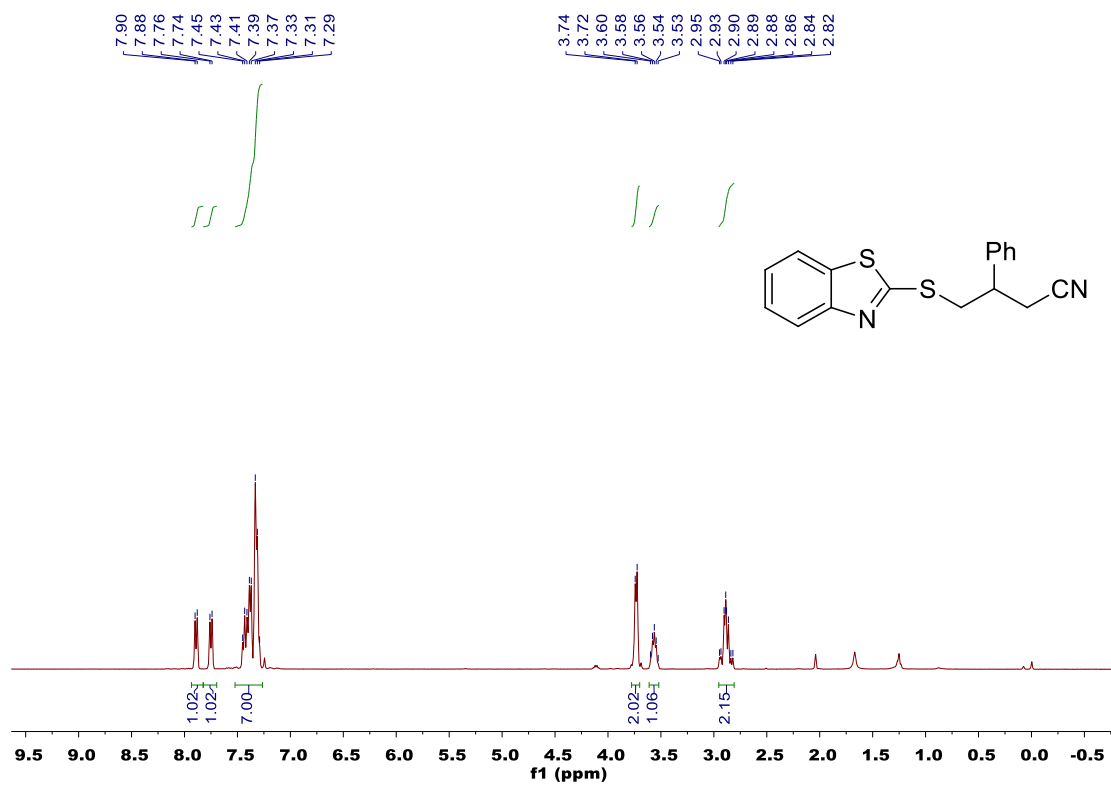
4-((6-bromobenzo[d]thiazol-2-yl)thio)-5-phenylpentanenitrile (3cc)



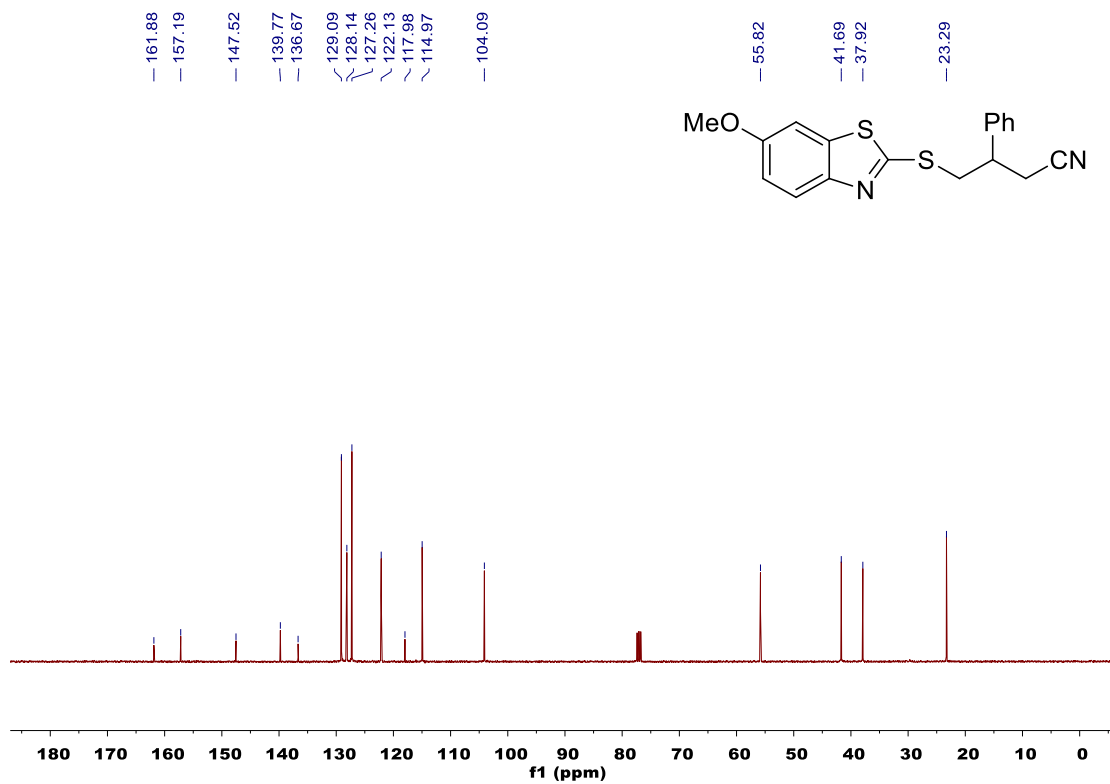
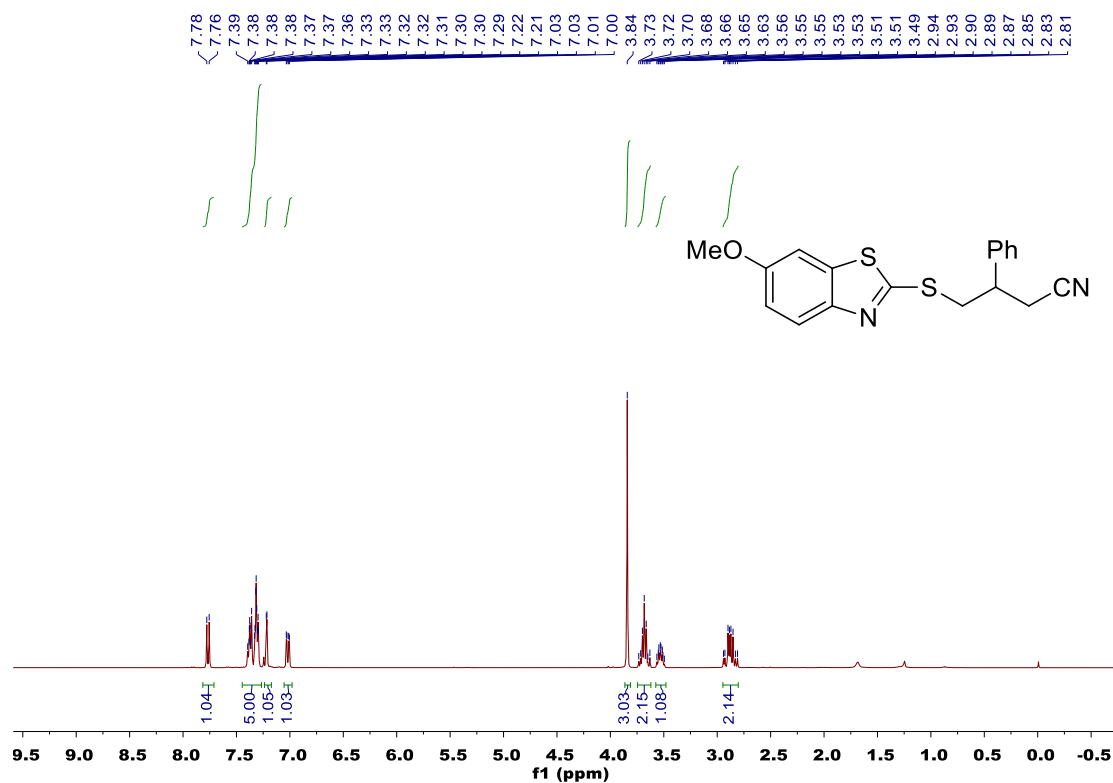
4-(benzo[d]oxazol-2-ylthio)-5-phenylpentanenitrile (3ic)



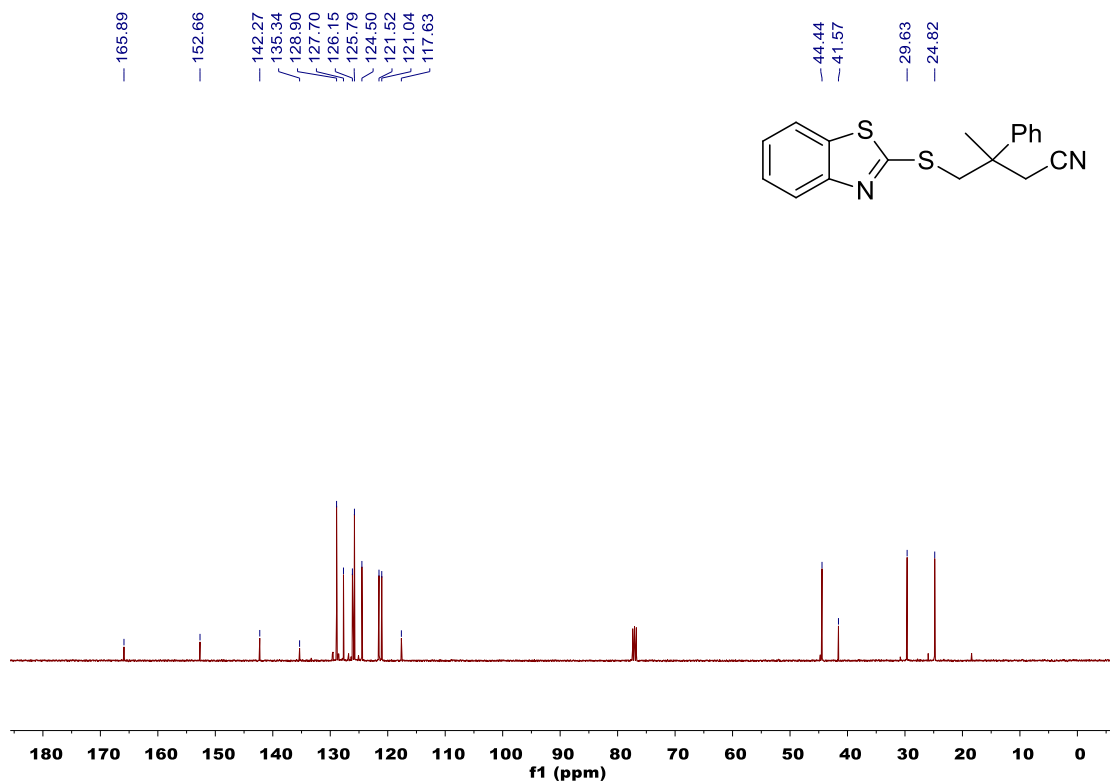
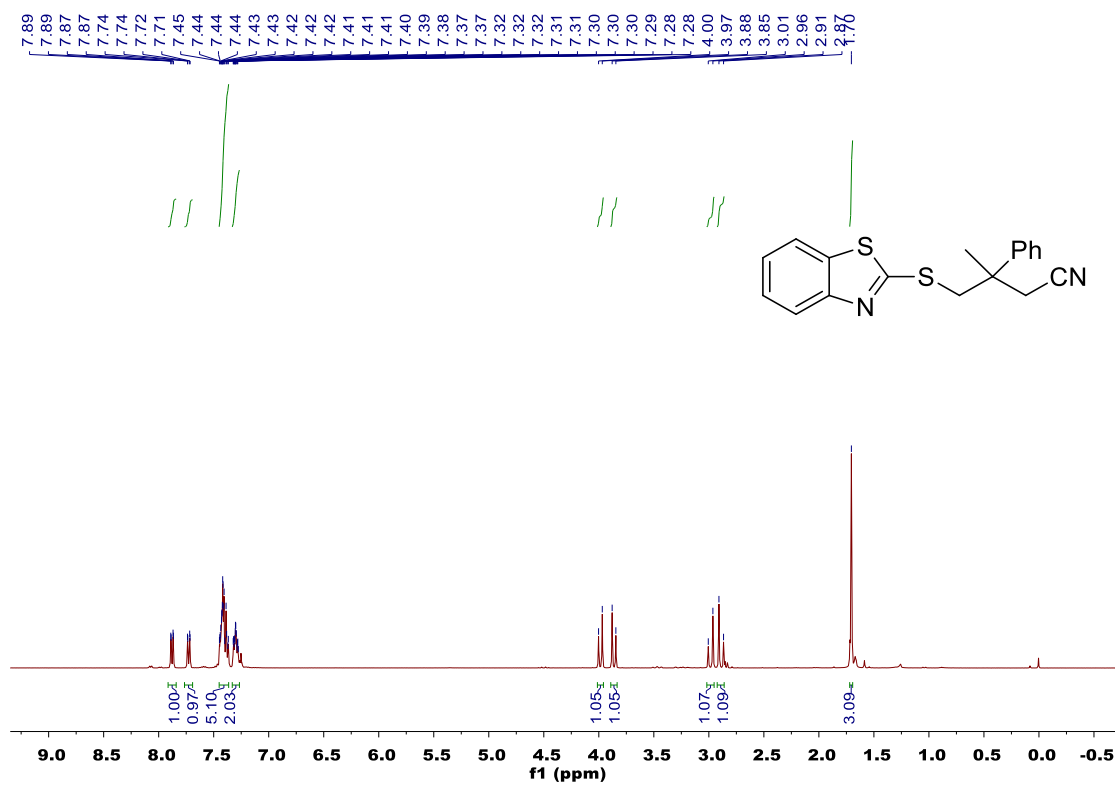
4-(benzo[d]thiazol-2-ylthio)-3-phenylbutanenitrile (3ad)



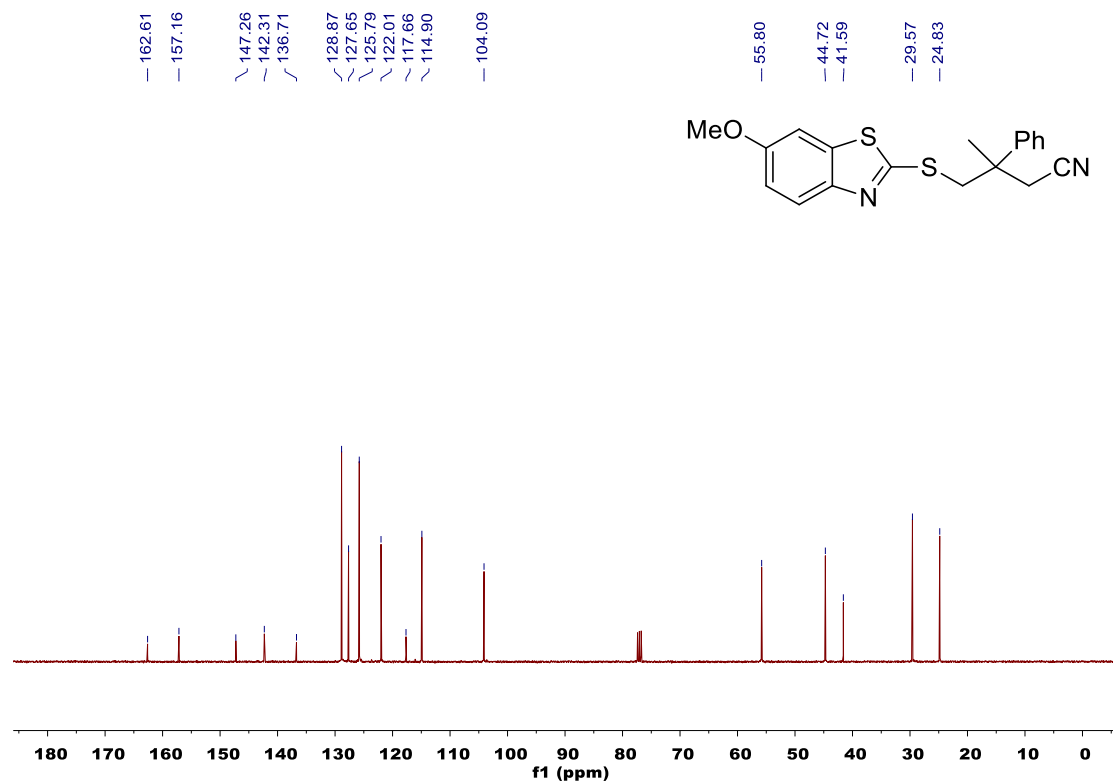
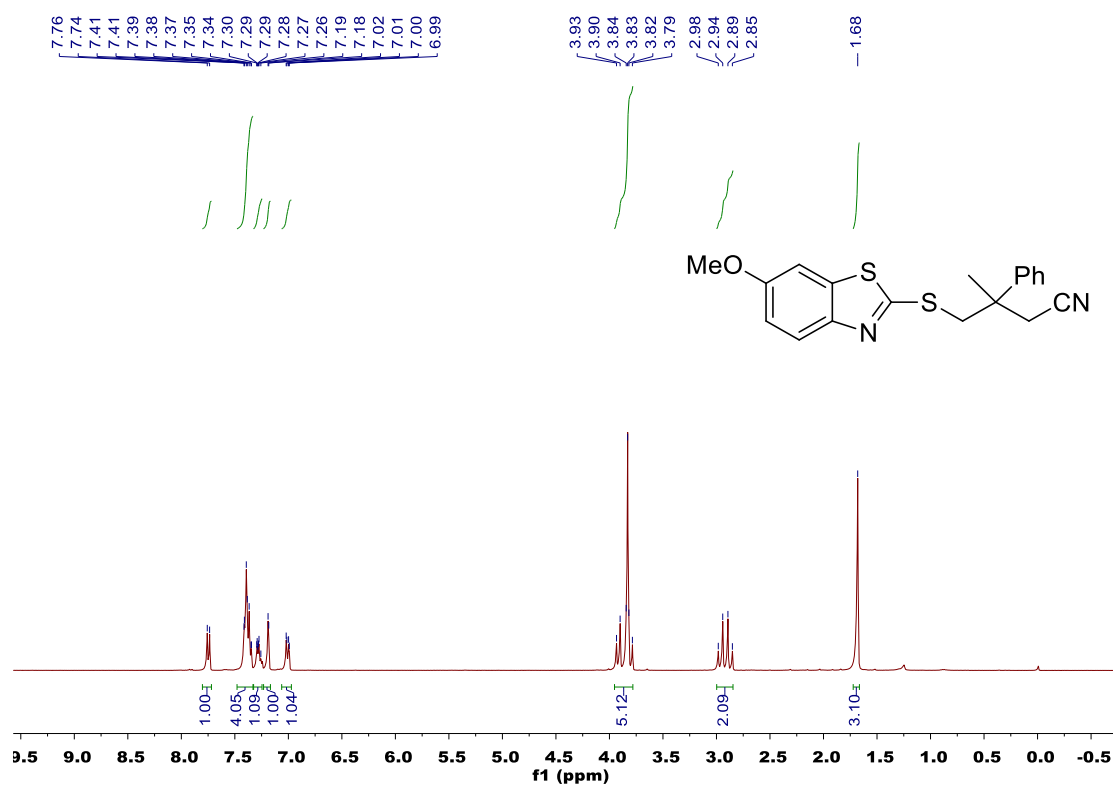
4-((6-methoxybenzo[d]thiazol-2-yl)thio)-3-phenylbutanenitrile (3bd)



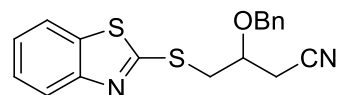
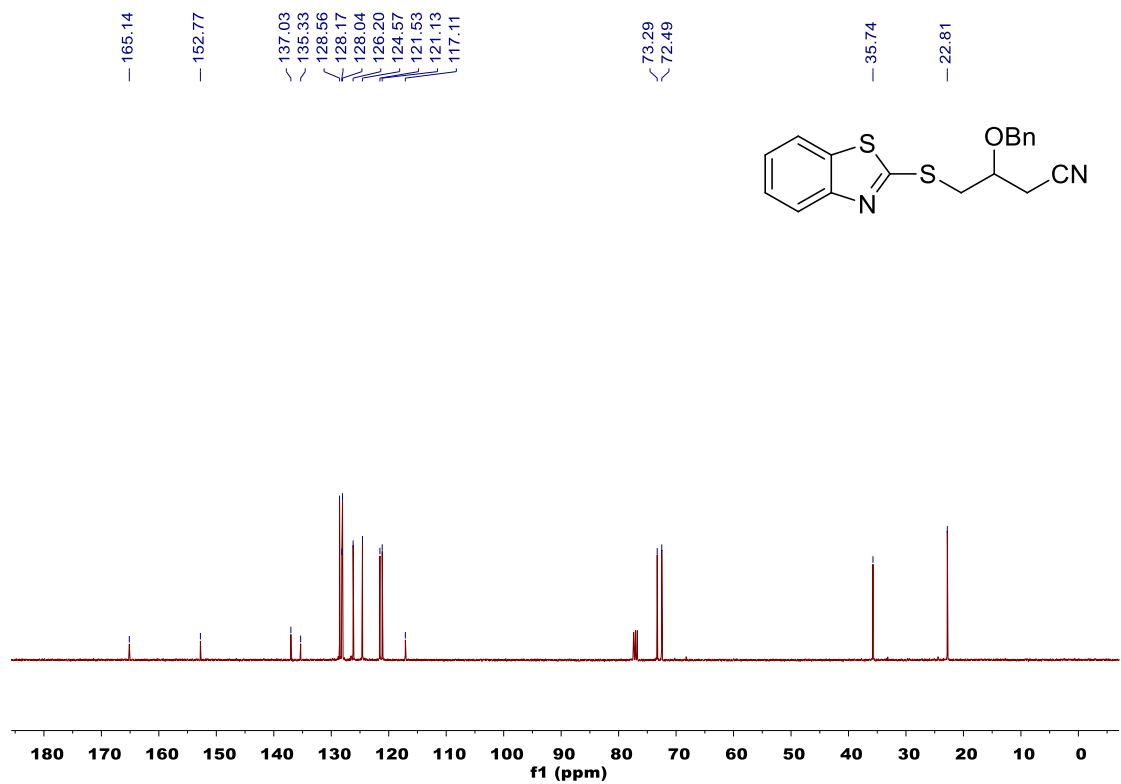
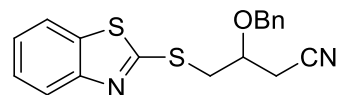
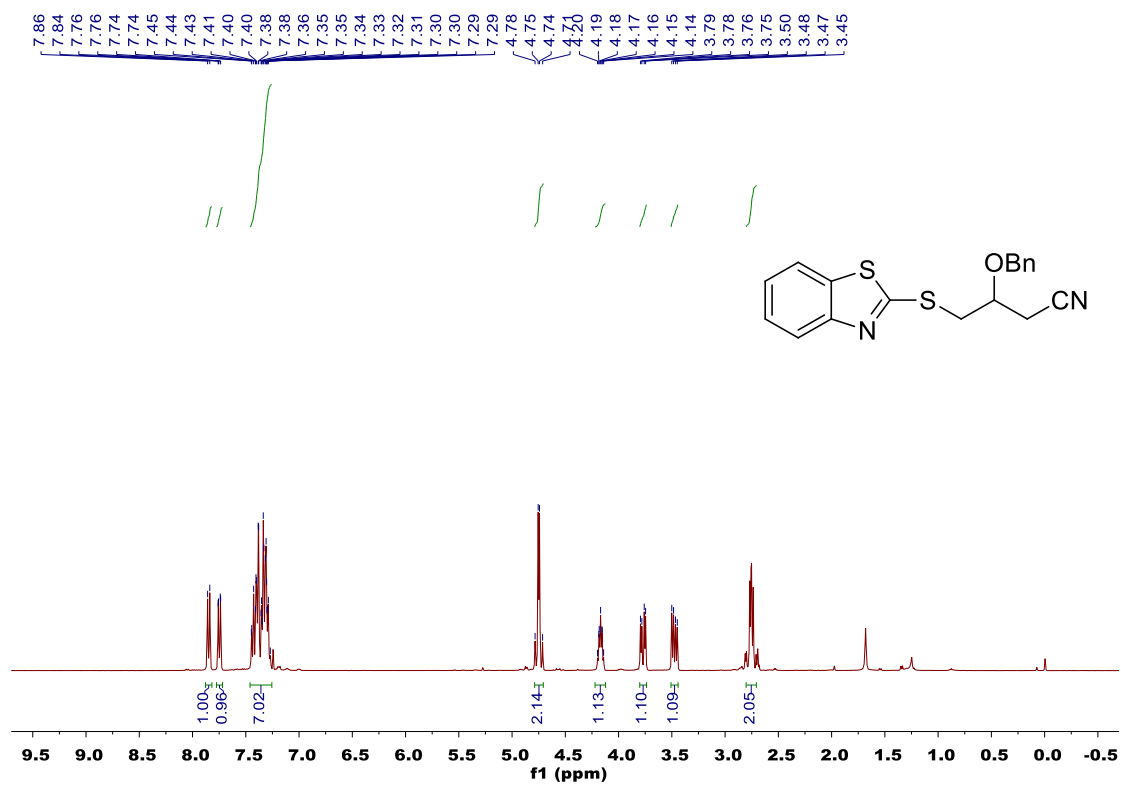
4-(benzo[d]thiazol-2-ylthio)-3-methyl-3-phenylbutanenitrile (3ae)



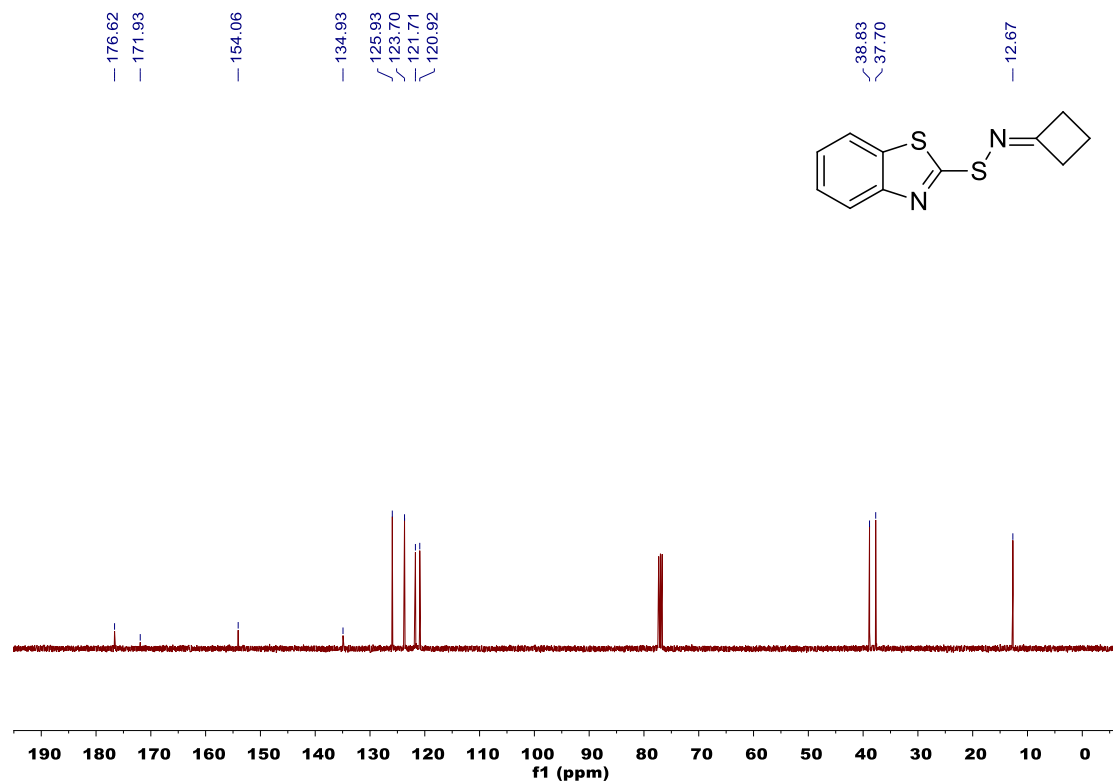
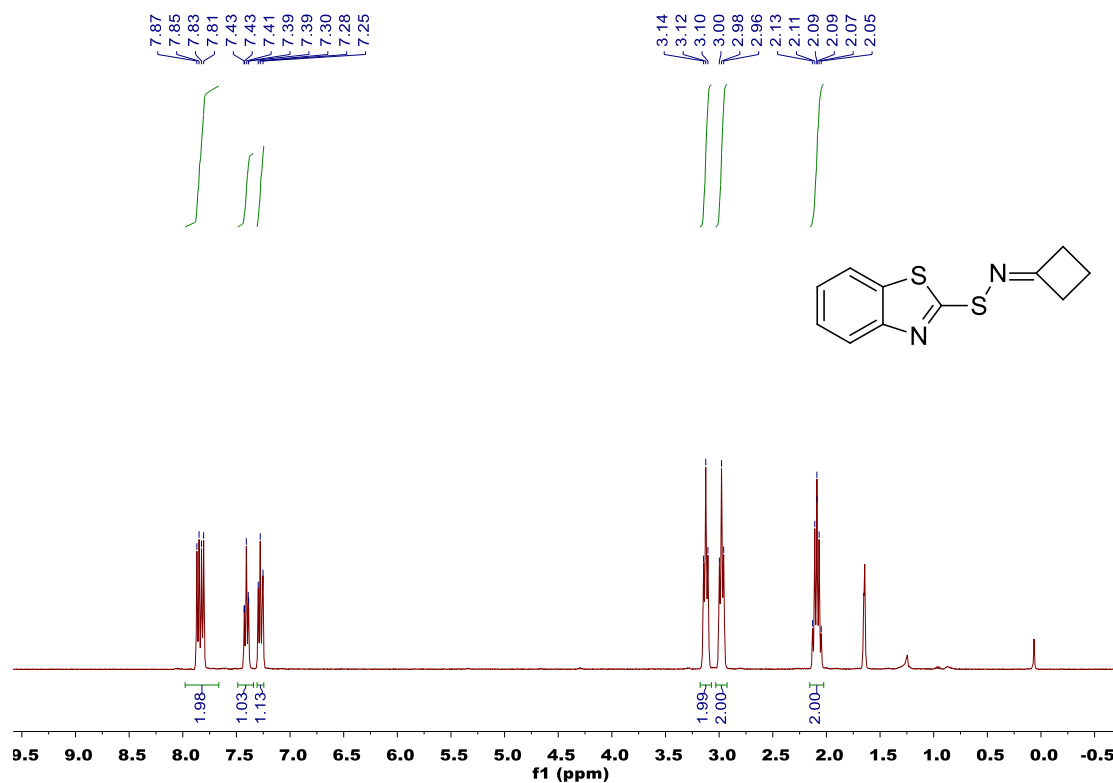
4-((6-methoxybenzo[d]thiazol-2-yl)thio)-3-methyl-3-phenylbutanenitrile (3be)



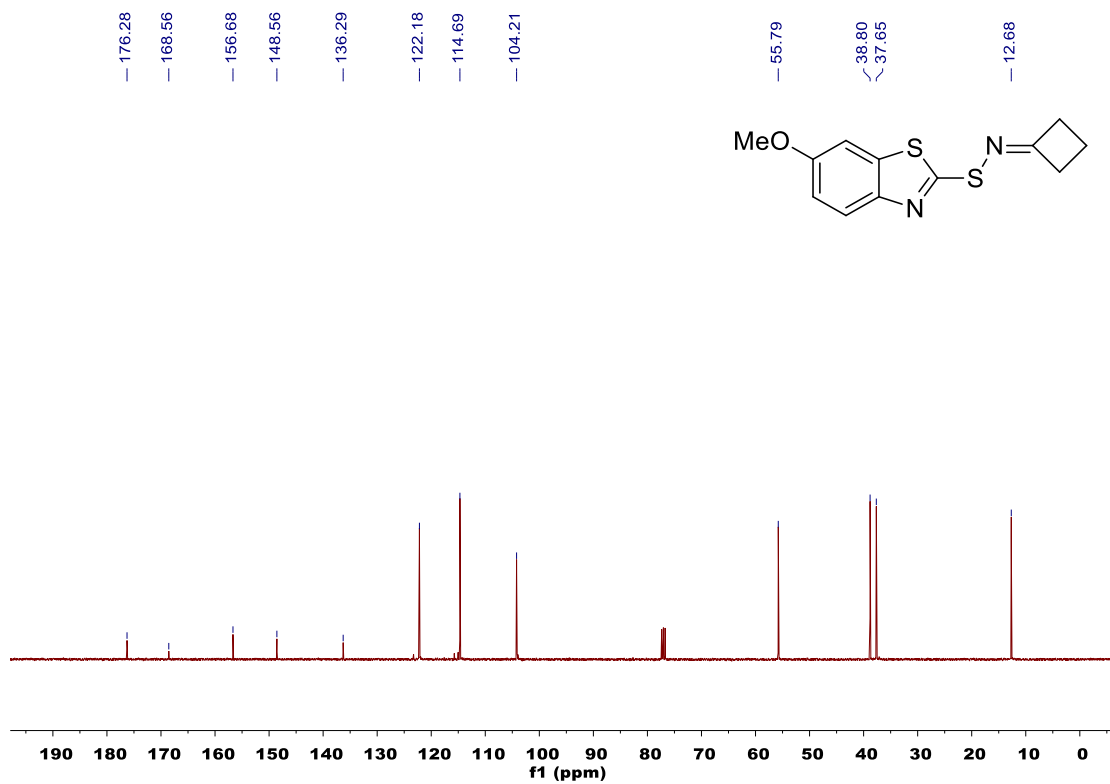
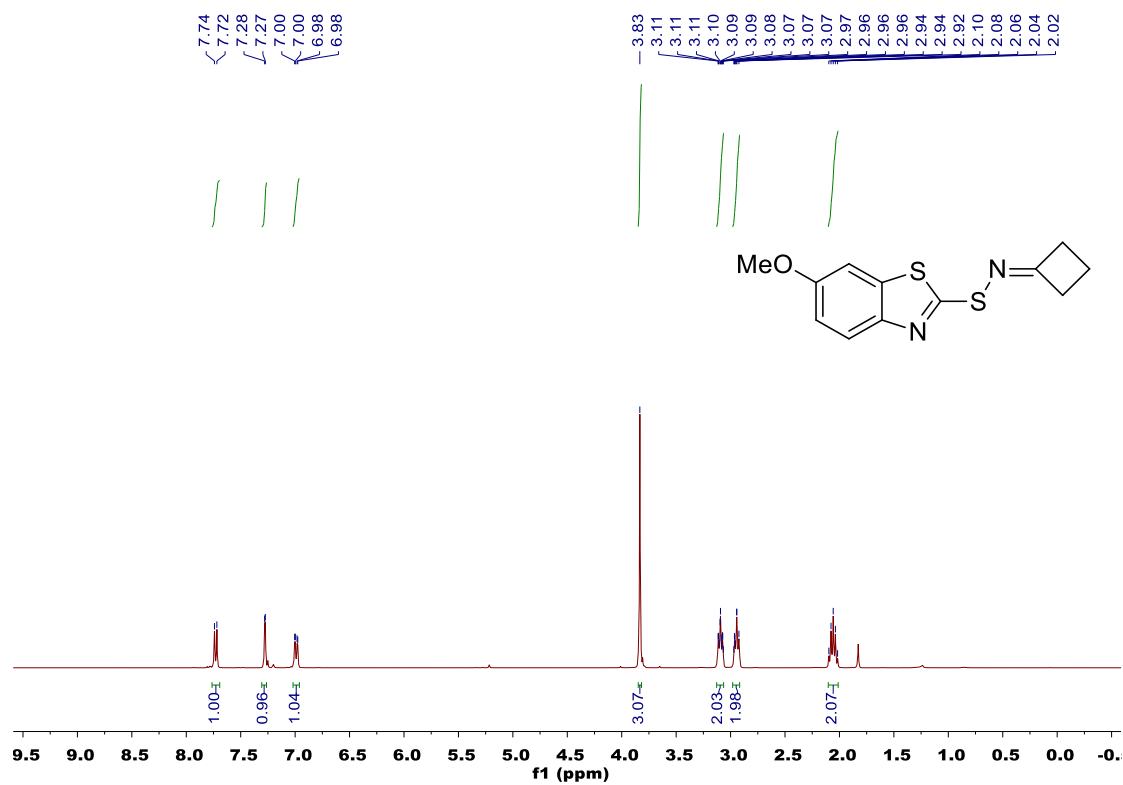
4-(benzo[d]thiazol-2-ylthio)-3-(benzyloxy)butanenitrile (3af)



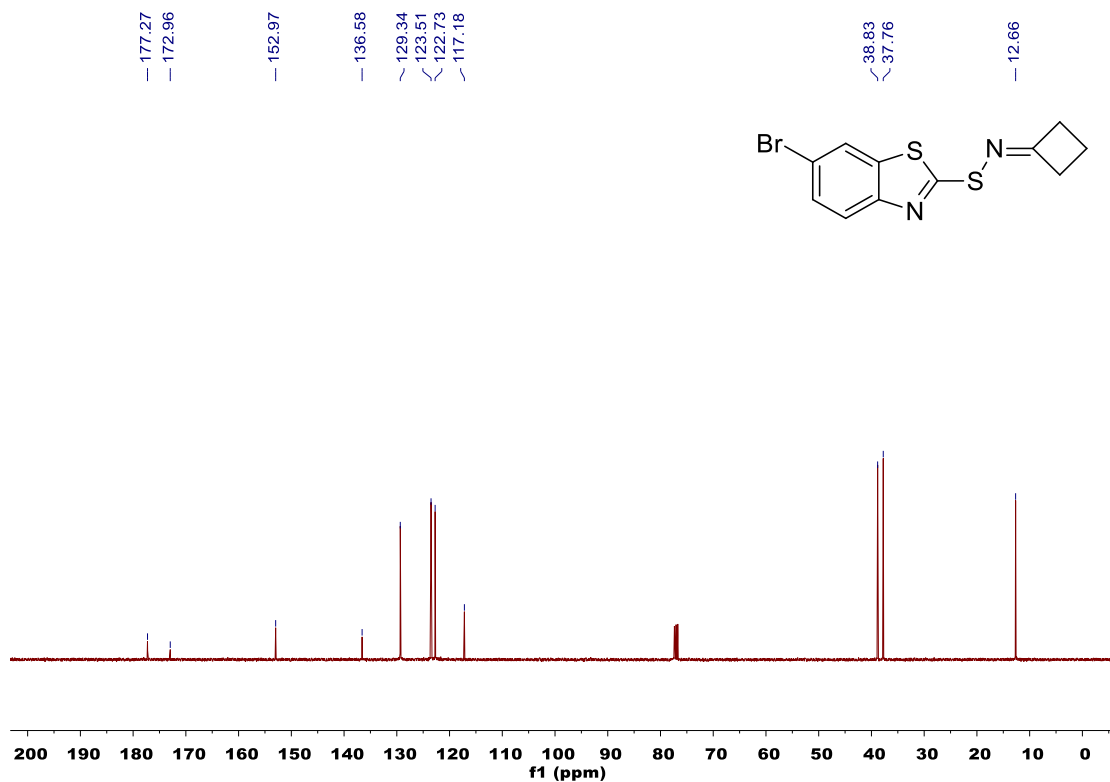
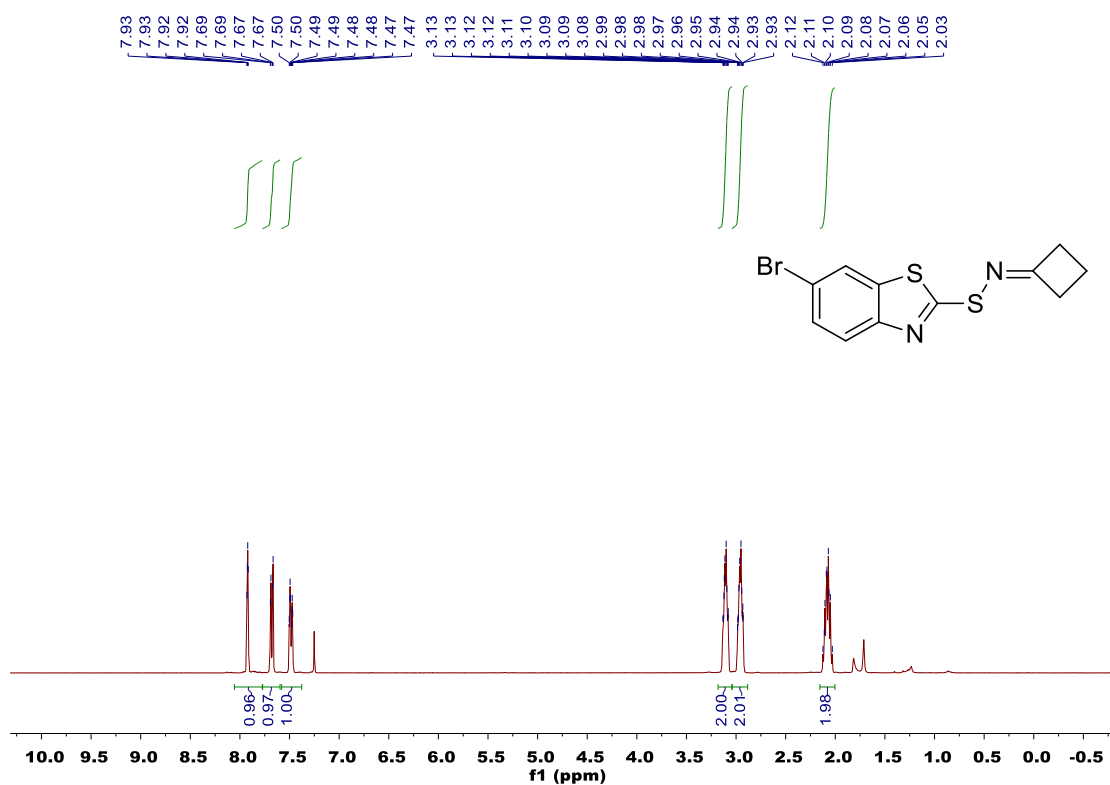
S-(benzo[d]thiazol-2-yl)-N-cyclobutylidenethiohydroxylamine (4aa)



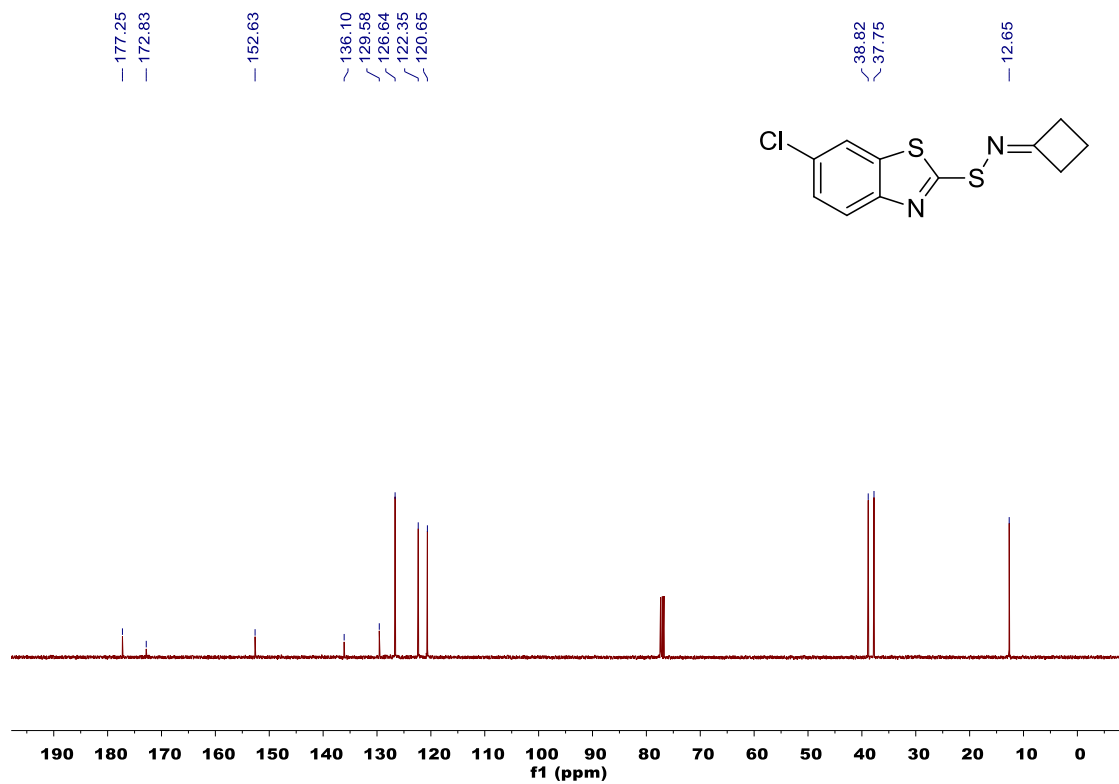
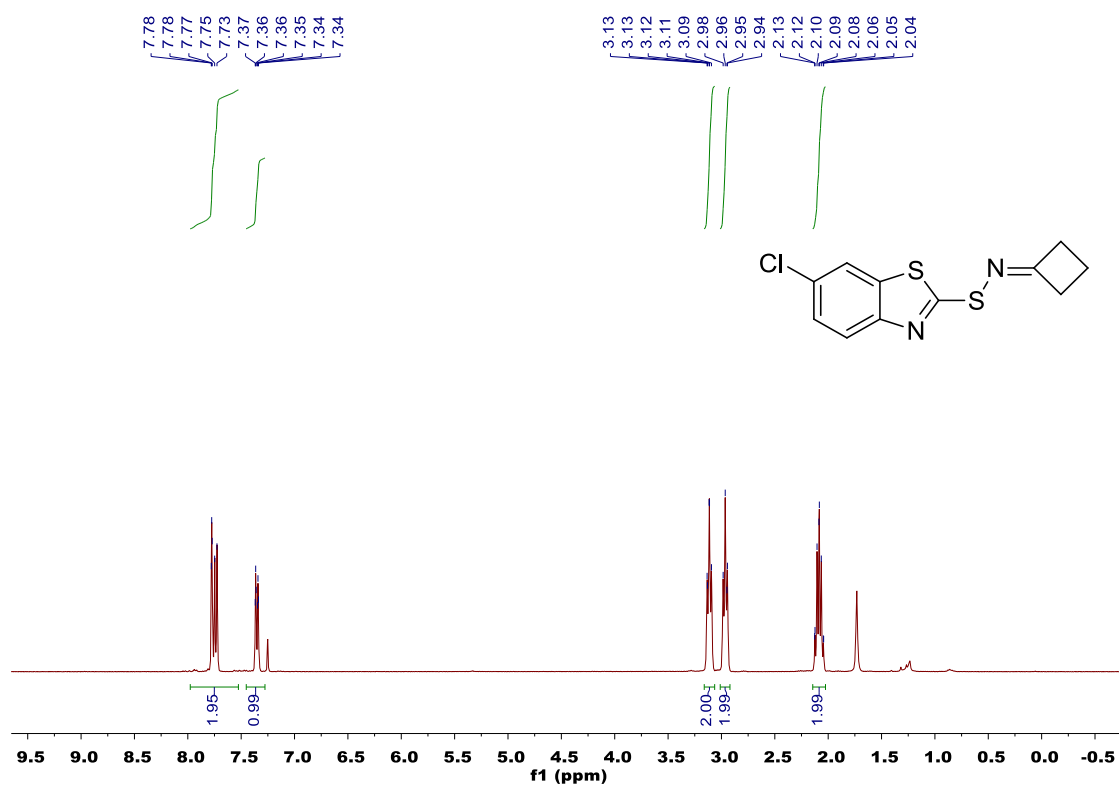
N-cyclobutylidene-S-(6-methoxybenzo[d]thiazol-2-yl)thiohydroxylamine (4ba)



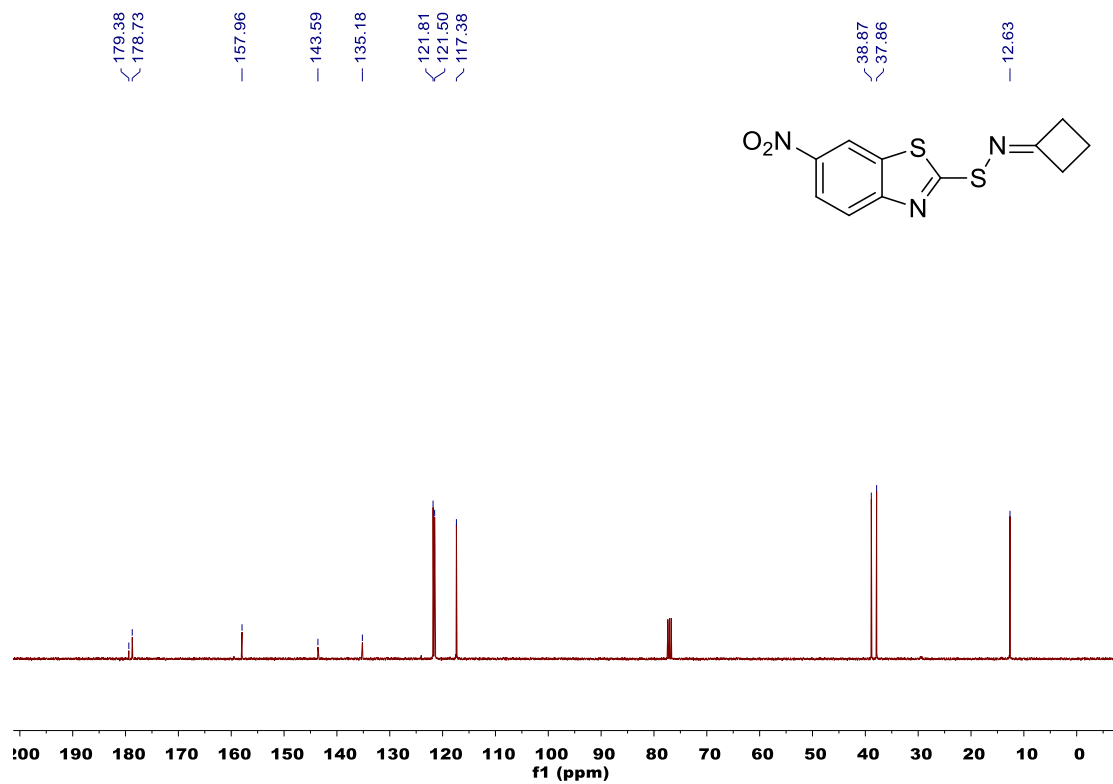
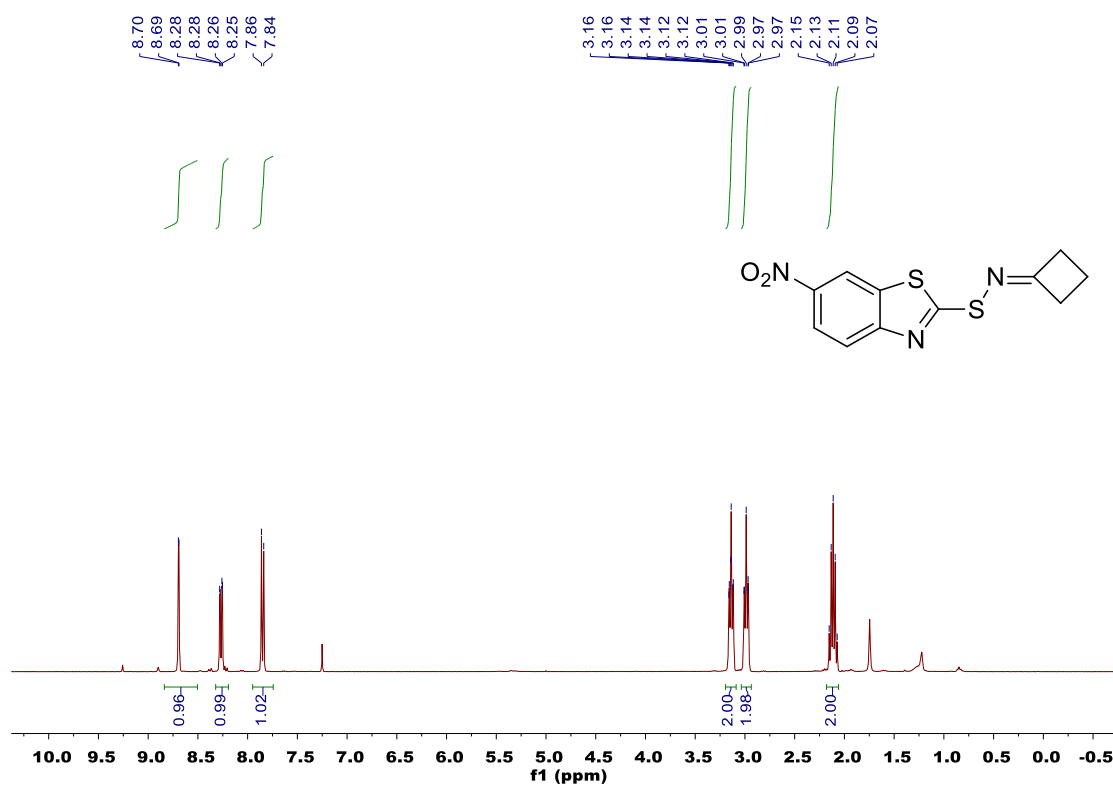
S-(6-bromobenzo[d]thiazol-2-yl)-N-cyclobutylidenethiohydroxylamine (4ca)



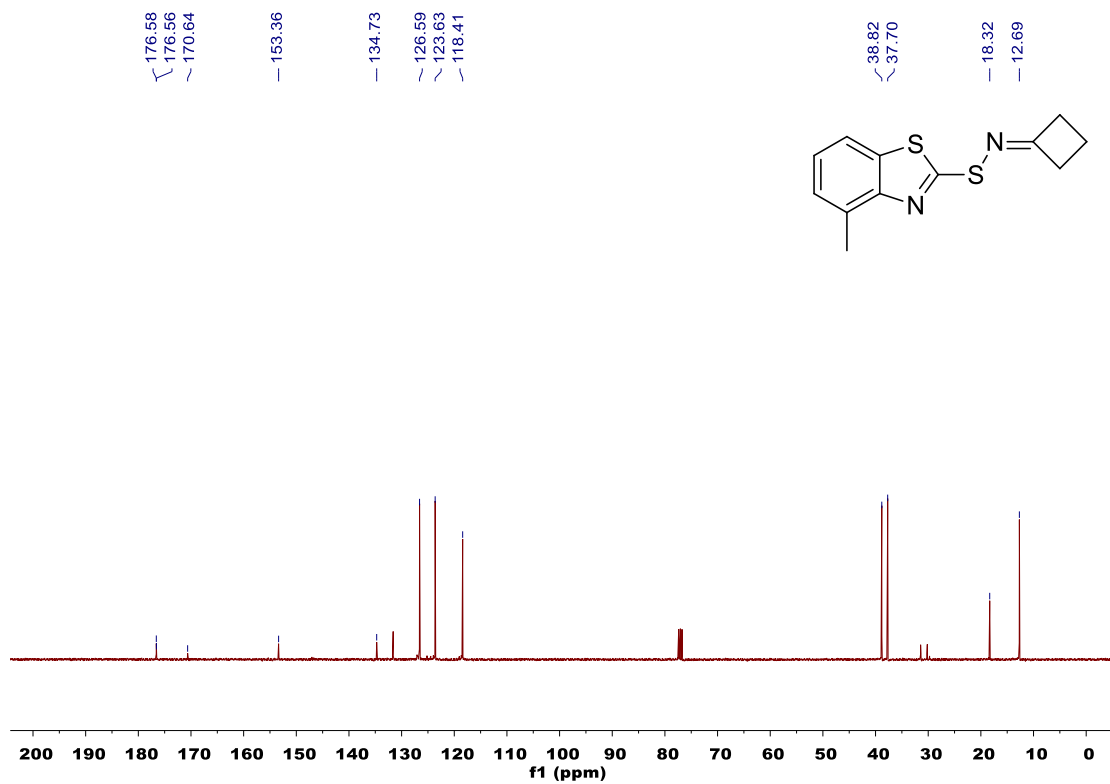
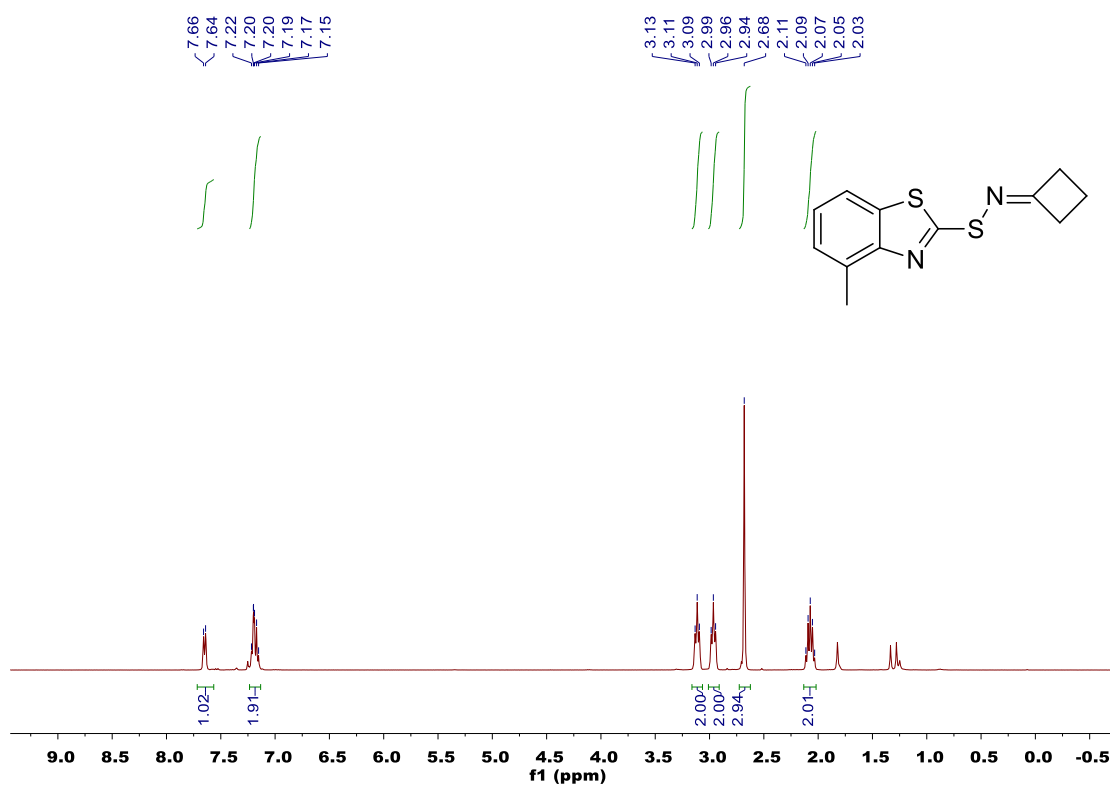
S-(6-chlorobenzo[d]thiazol-2-yl)-N-cyclobutylidenethiohydroxylamine (4da)



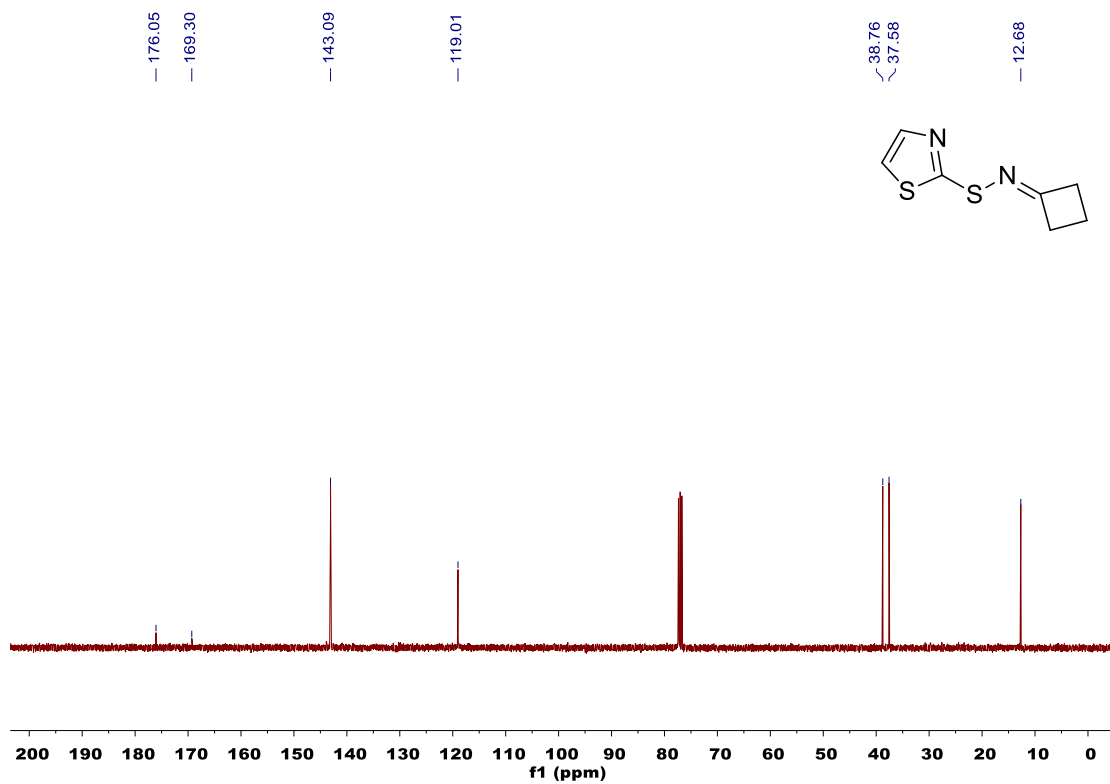
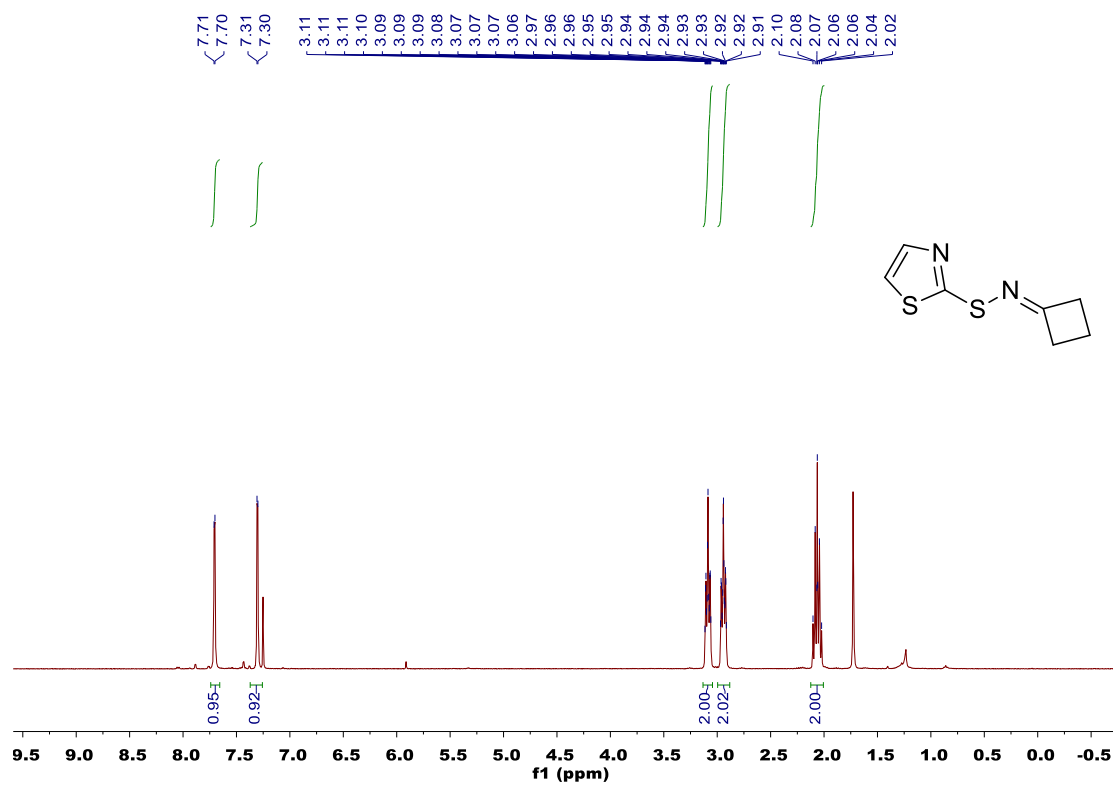
N-cyclobutylidene-S-(6-nitrobenzo[d]thiazol-2-yl)thiohydroxylamine (4ea)



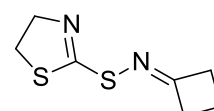
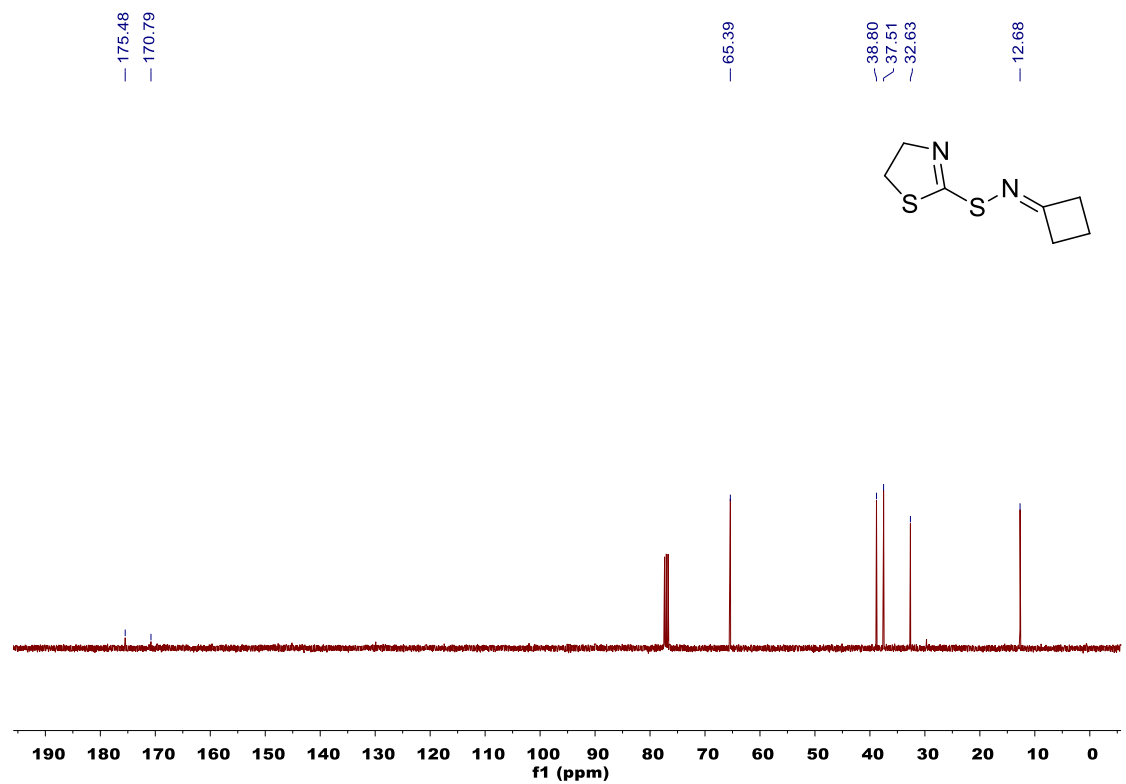
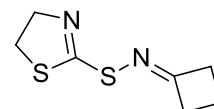
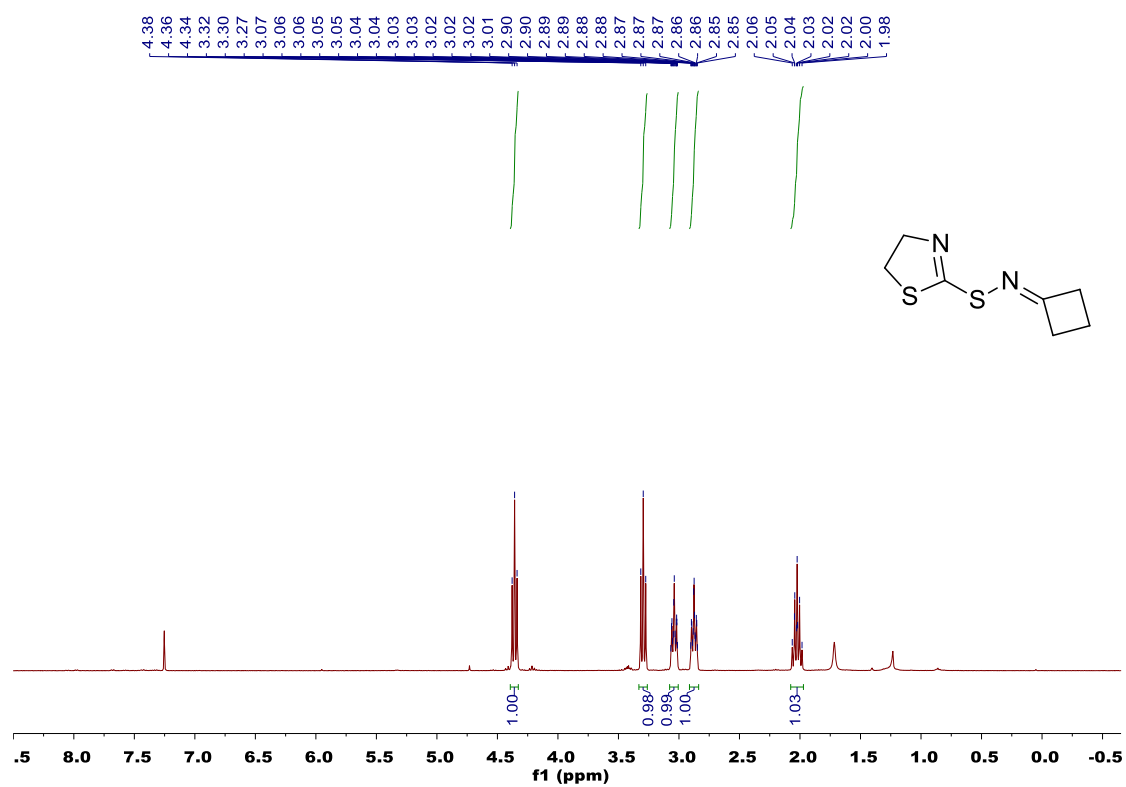
***N*-cyclobutylidene-S-(4-methylbenzo[d]thiazol-2-yl)thiohydroxylamine (4fa)**



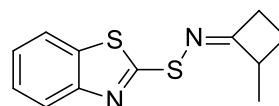
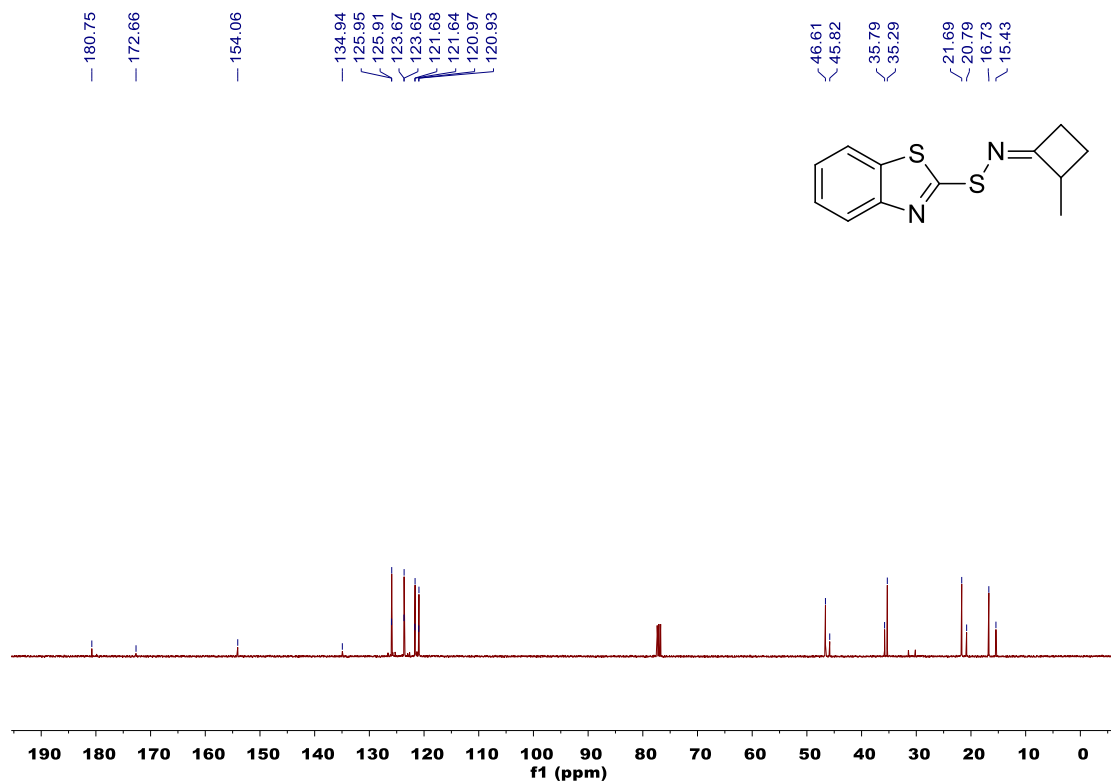
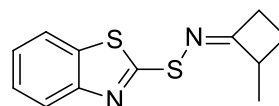
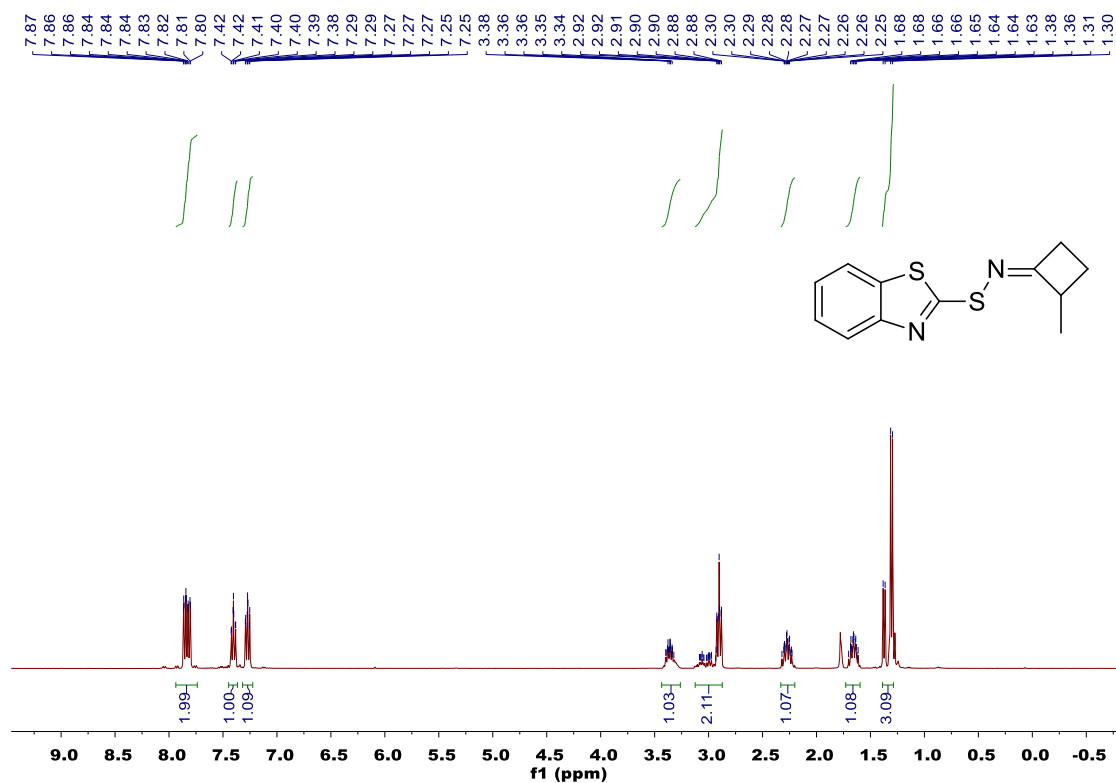
N-cyclobutylidene-S-(thiazol-2-yl)thiohydroxylamine (4ga)



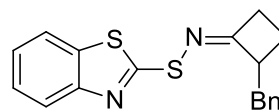
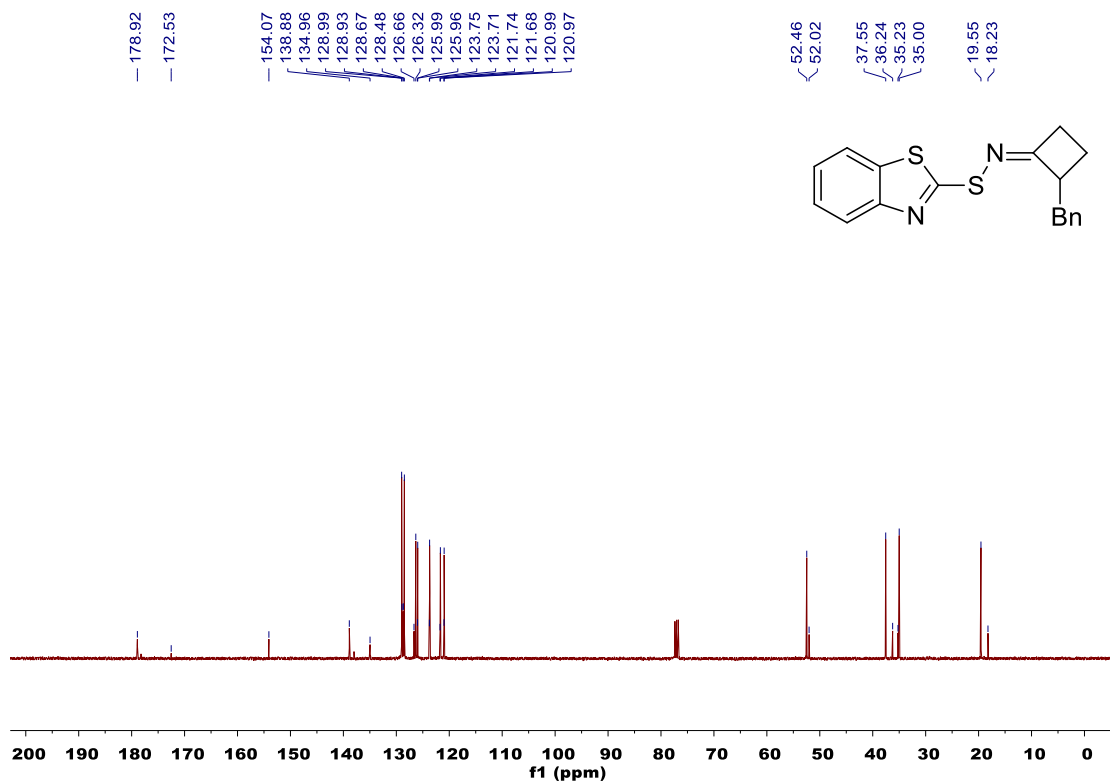
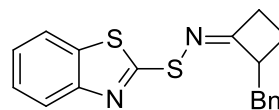
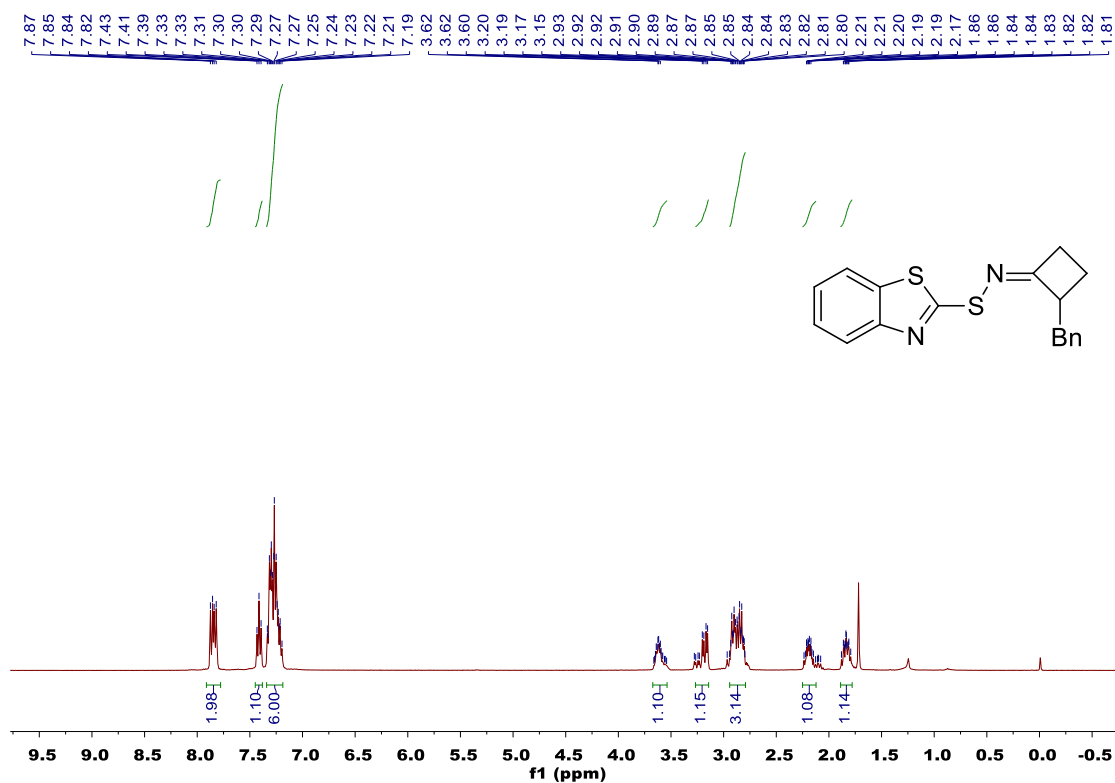
N-cyclobutylidene-S-(4,5-dihydrothiazol-2-yl)thiohydroxylamine (4ha)



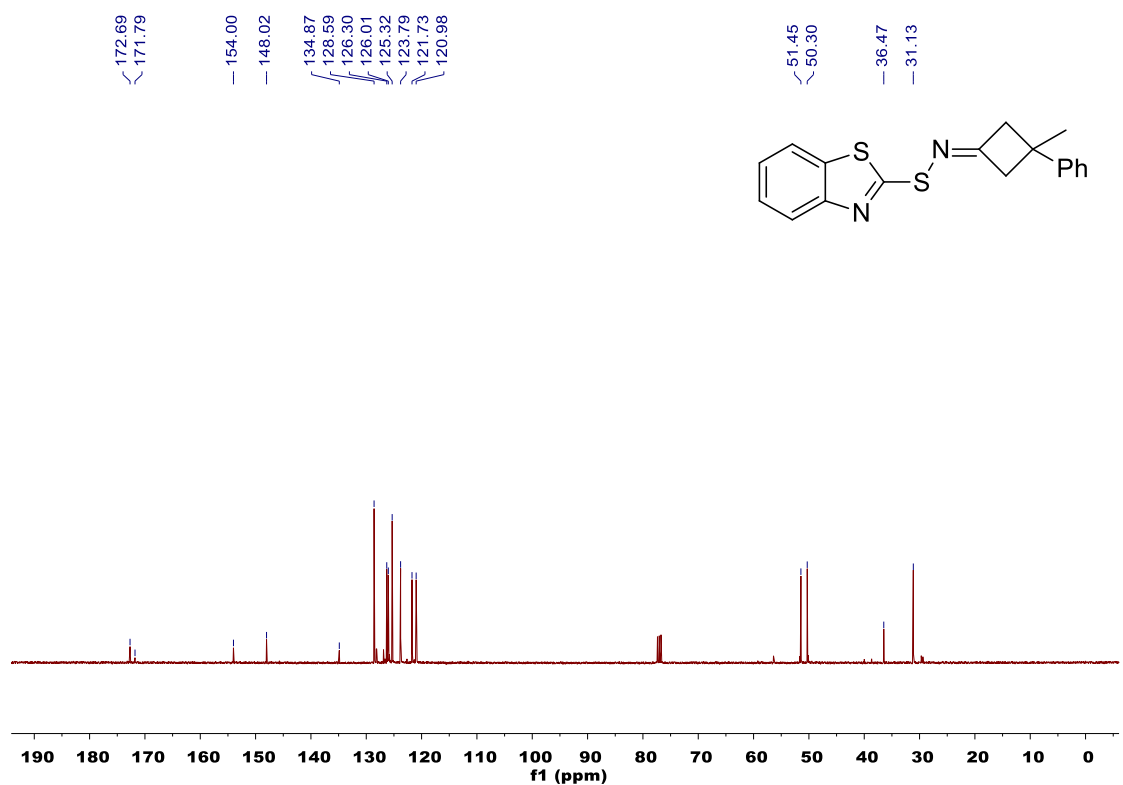
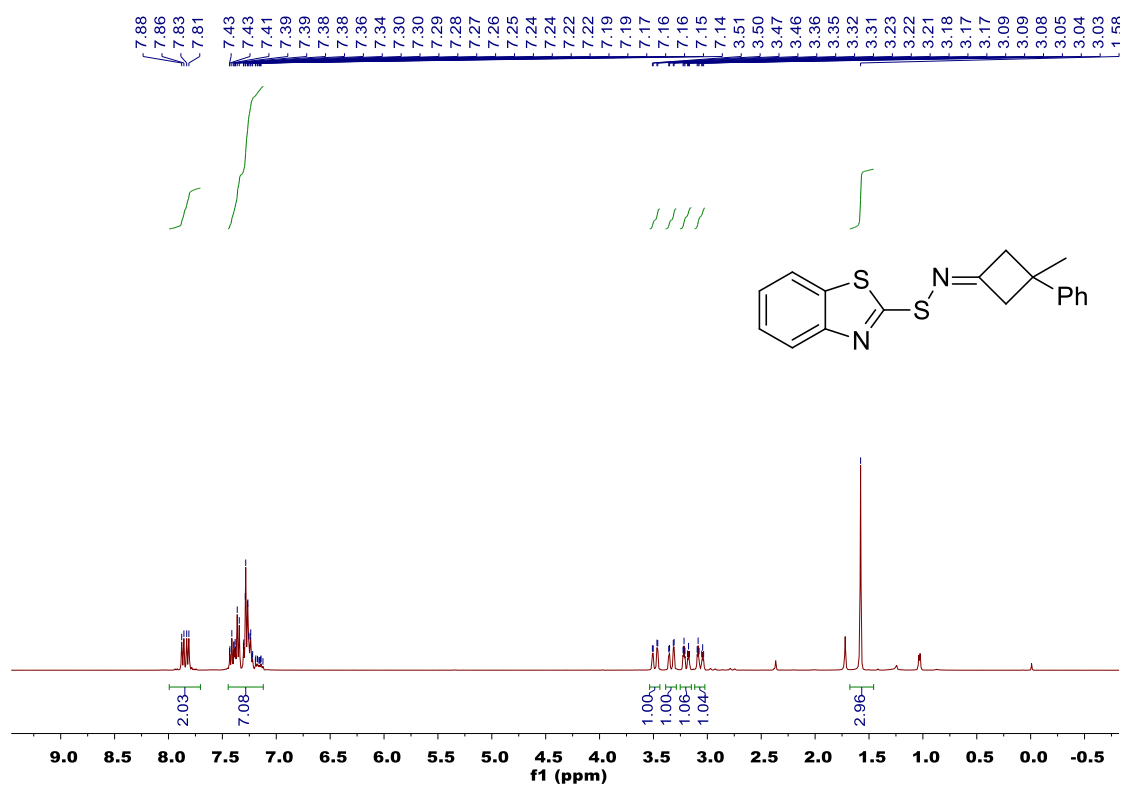
S-(benzo[d]thiazol-2-yl)-N-(2-methylcyclobutylidene)thiohydroxylamine (4ab, E/Z mixture)



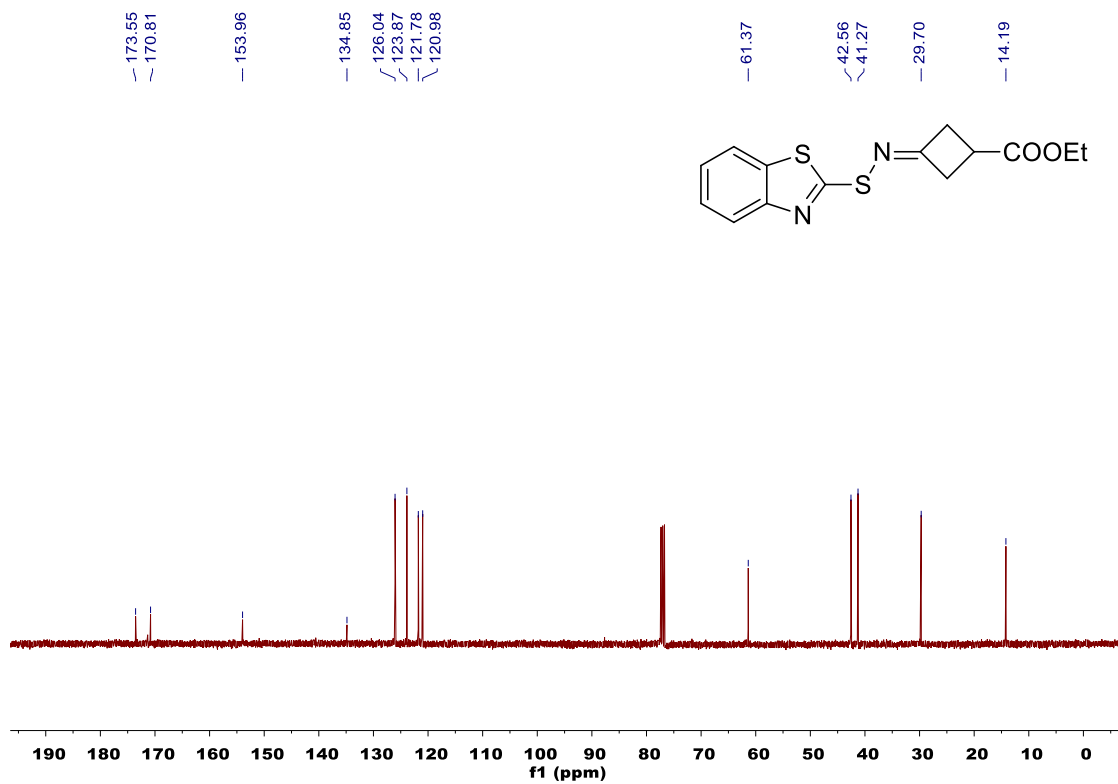
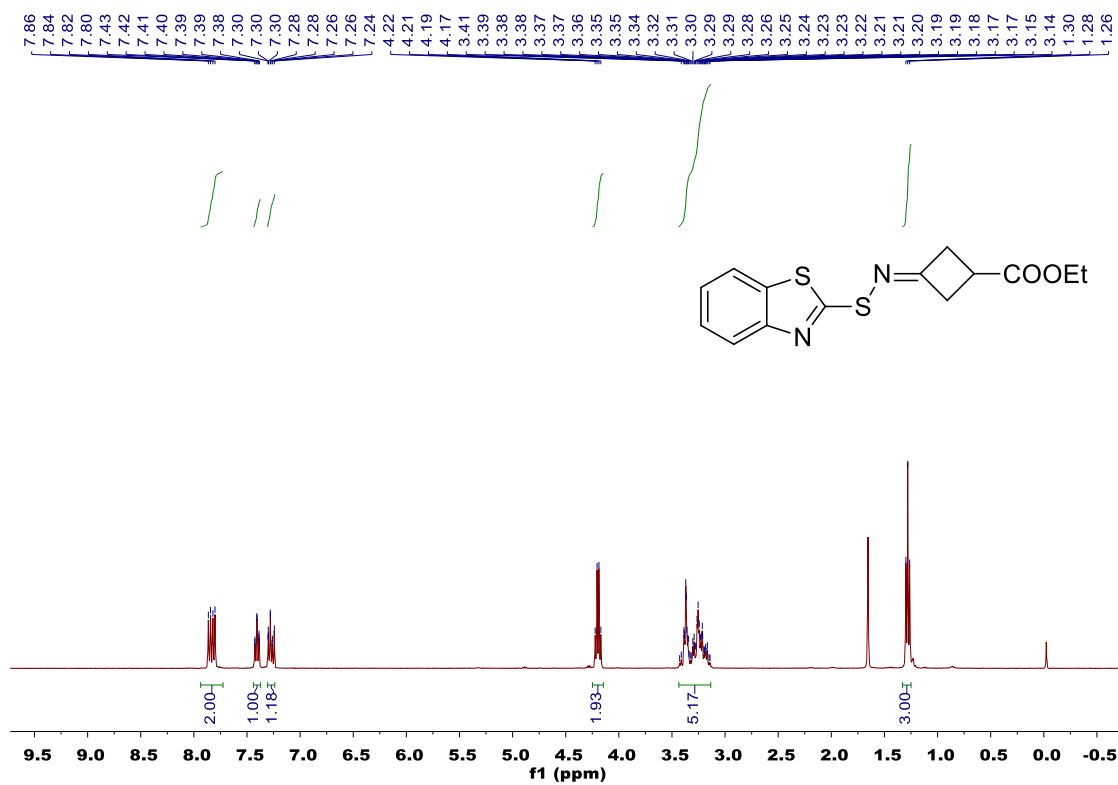
S-(benzo[d]thiazol-2-yl)-N-(2-benzylcyclobutylidene)thiohydroxylamine (4ac, E/Z mixture)



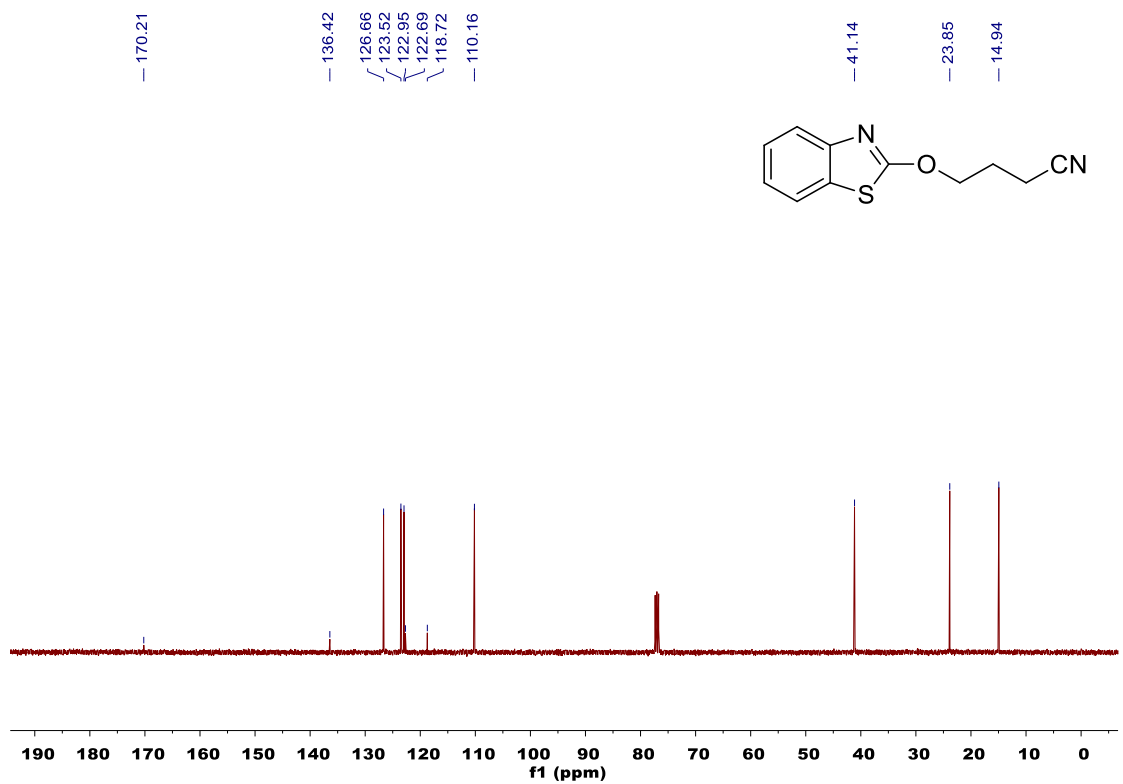
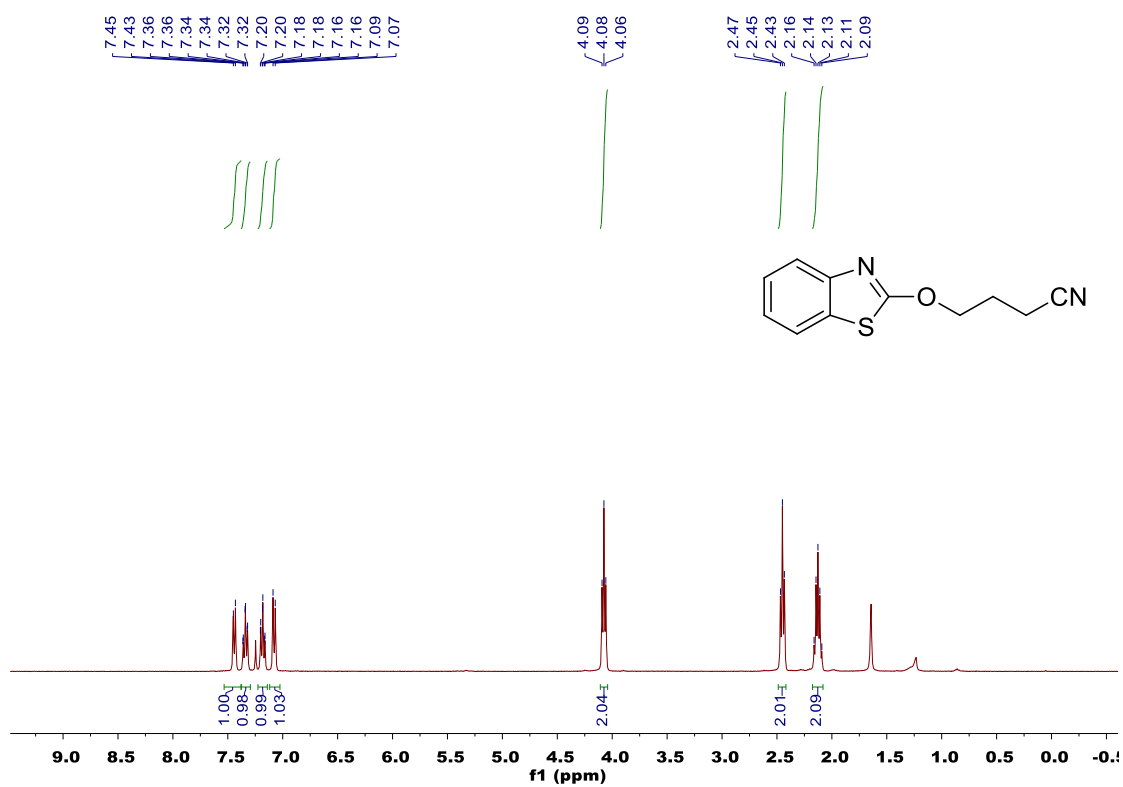
(benzo[d]thiazol-2-yl)-N-(3-methyl-3-phenylcyclobutylidene)thiohydroxamine (4ae)



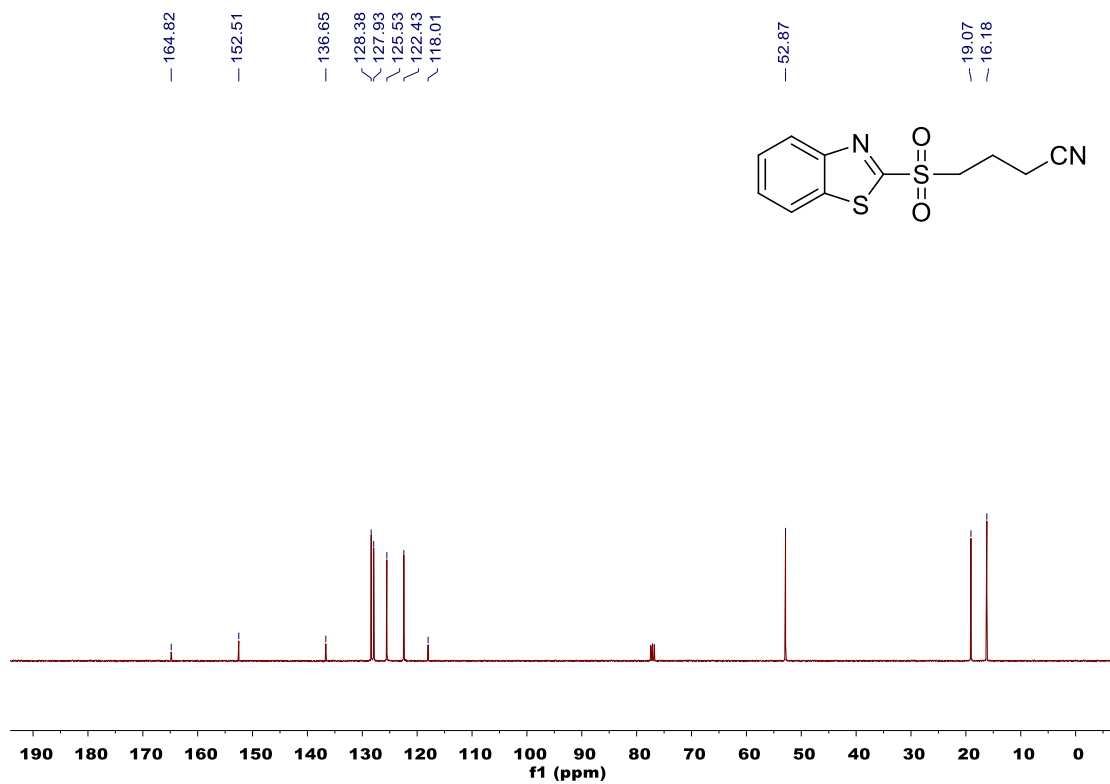
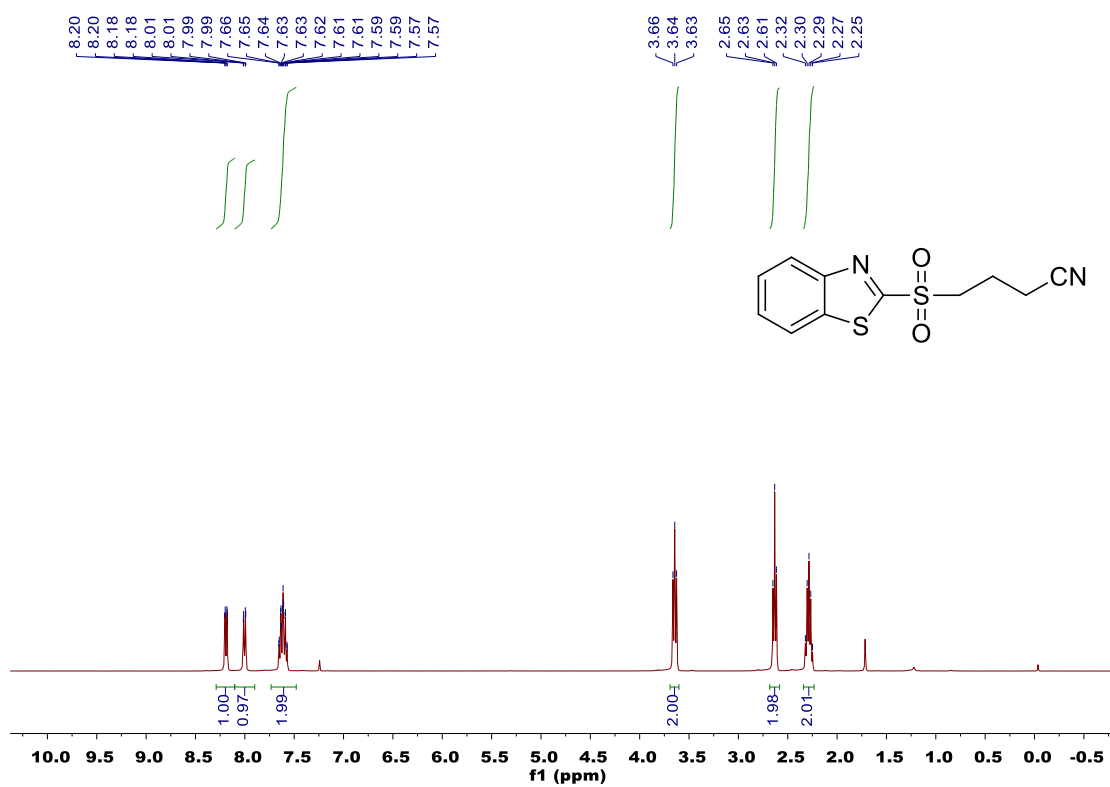
ethyl 3-((benzo[d]thiazol-2-ylthio)imino)cyclobutanecarboxylate (4ag)



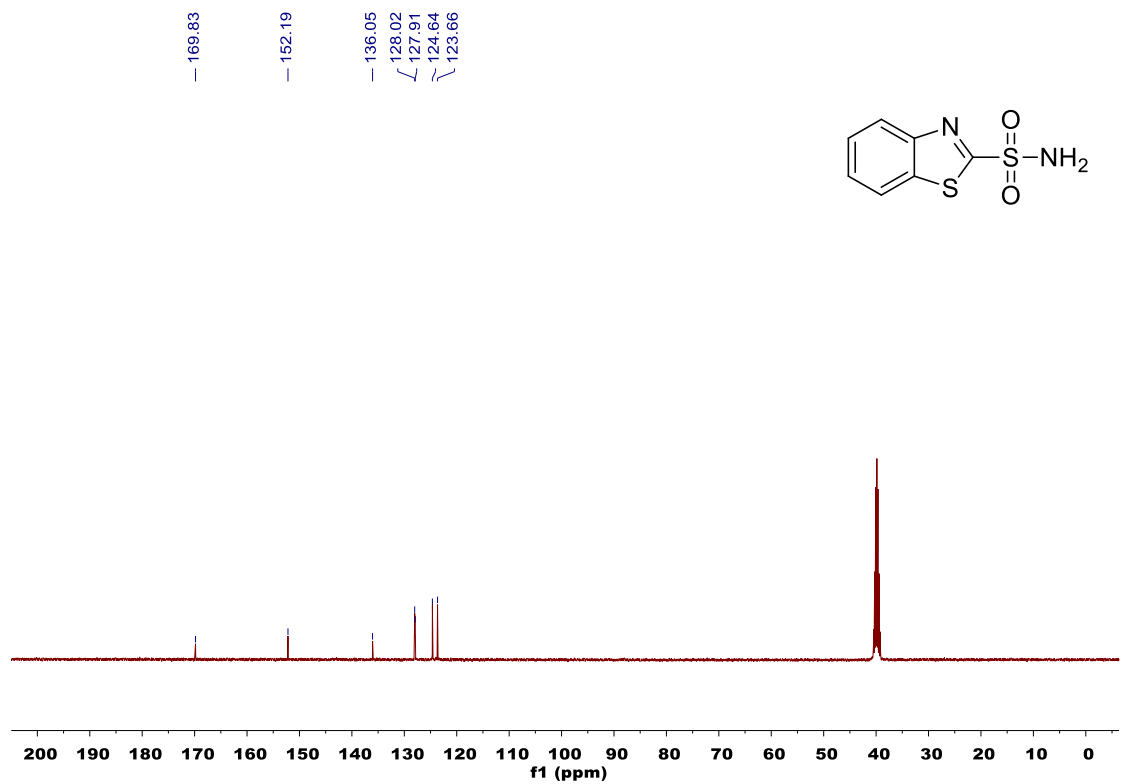
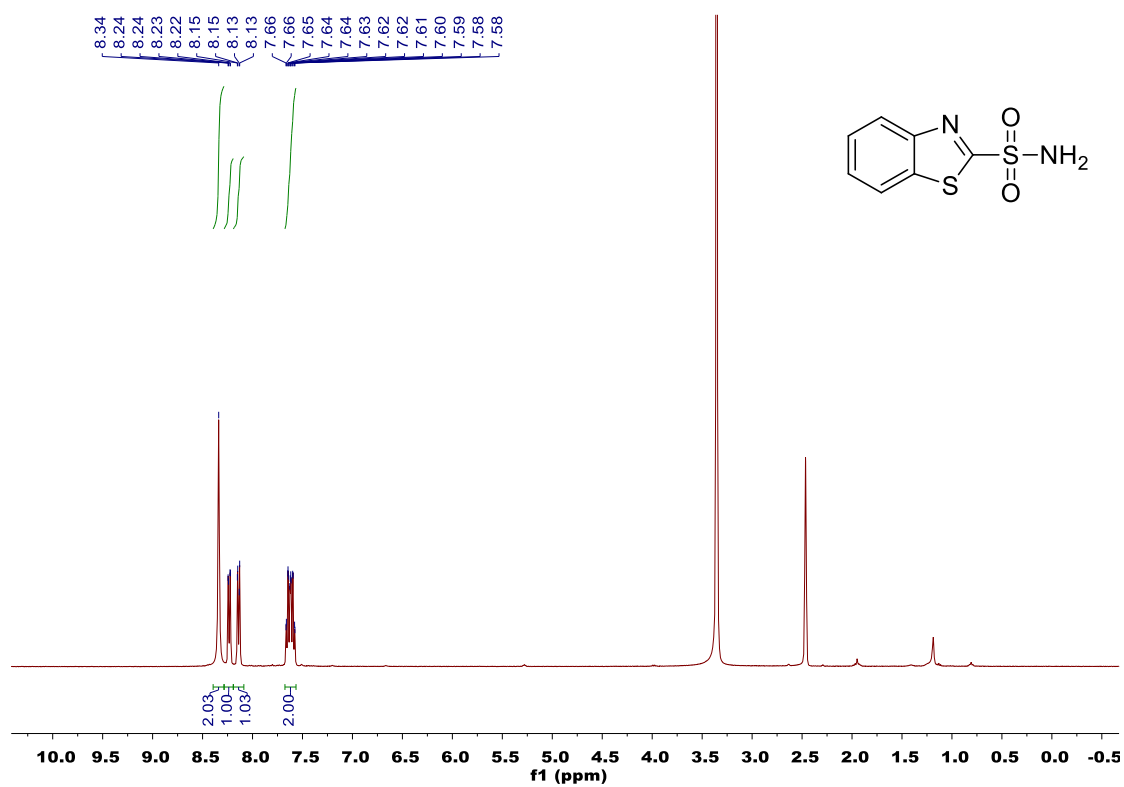
4-(benzo[d]thiazol-2-yloxy)butanenitrile (6)



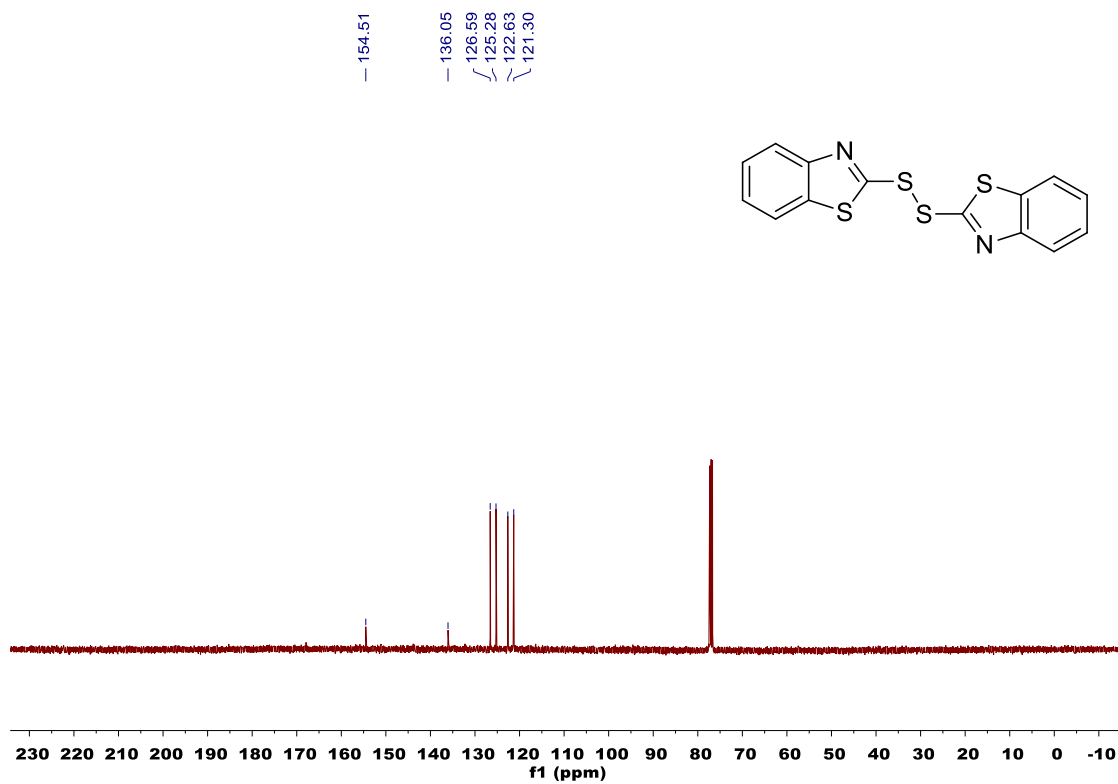
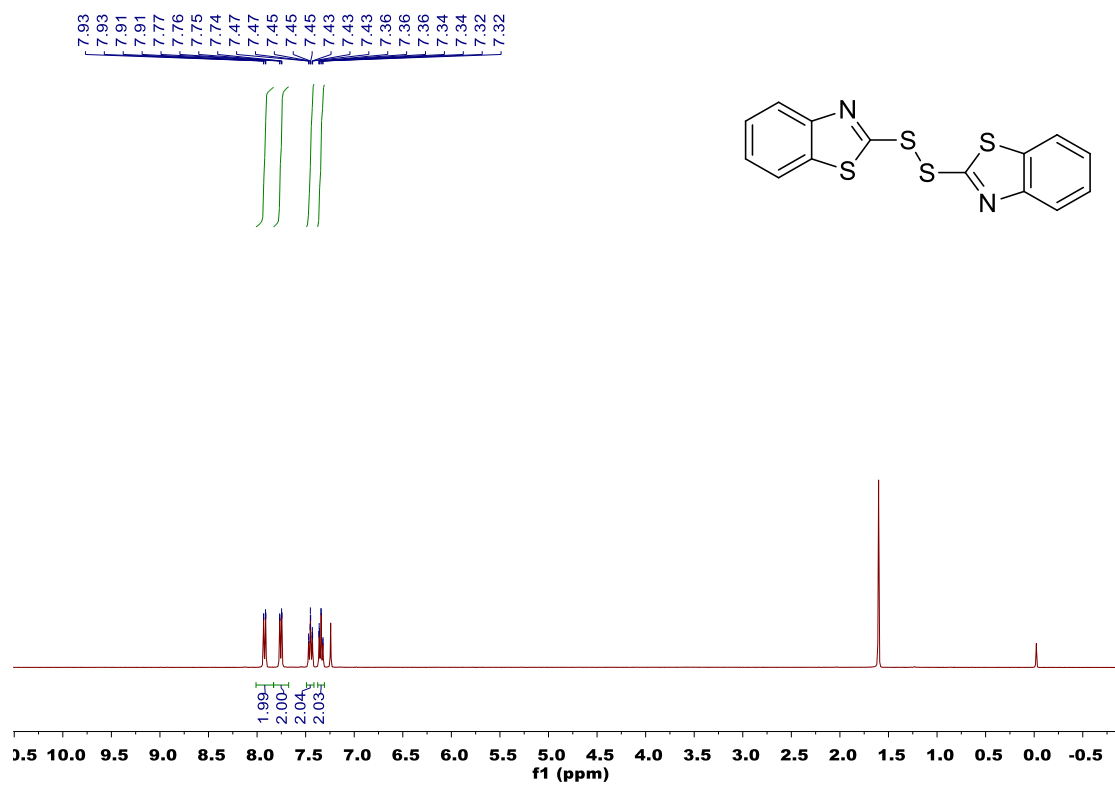
4-(benzo[d]thiazol-2-ylsulfonyl)butanenitrile (7)



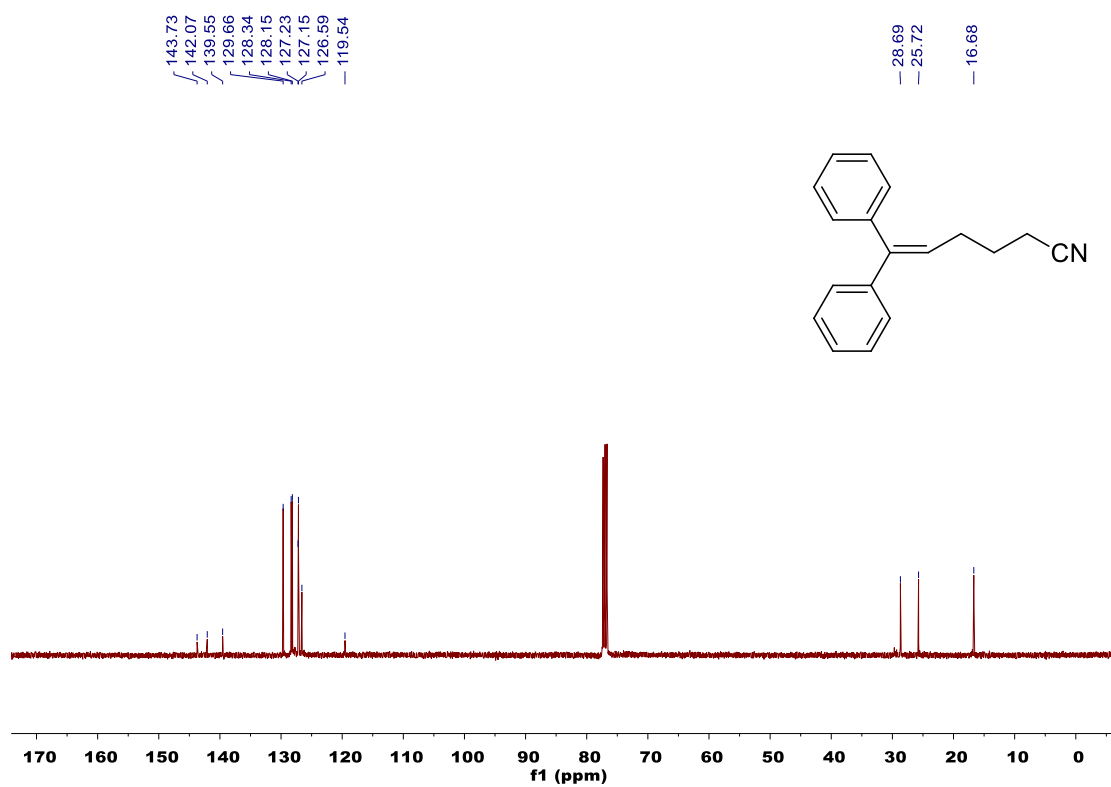
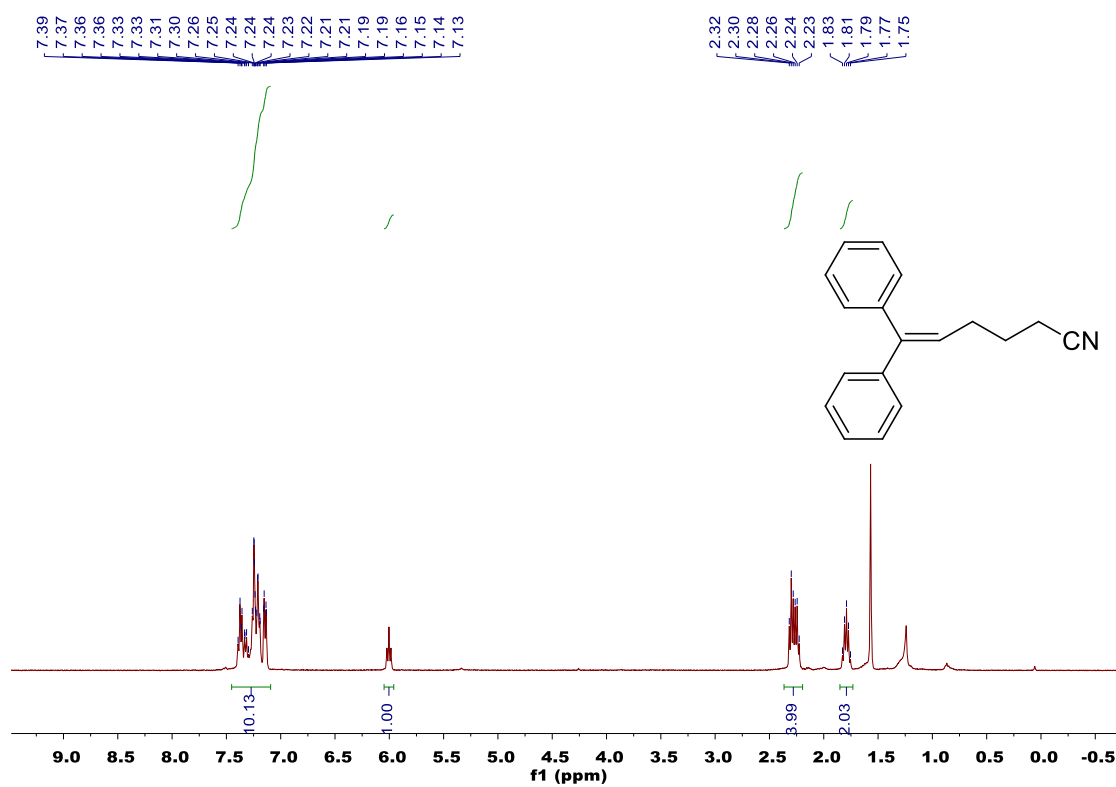
benzo[d]thiazole-2-sulfonamide (8)



1,2-bis(benzo[d]thiazol-2-yl)disulfane (9)



6,6-diphenylhex-5-enitrile (10)



5-phenylpent-4-enenitrile (11)

