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Rhodium-catalyzed *ortho*-selective C-H halogenation of 2-arylbenzo[d]thiazoles using *N*-halosuccinimides as halogen sources

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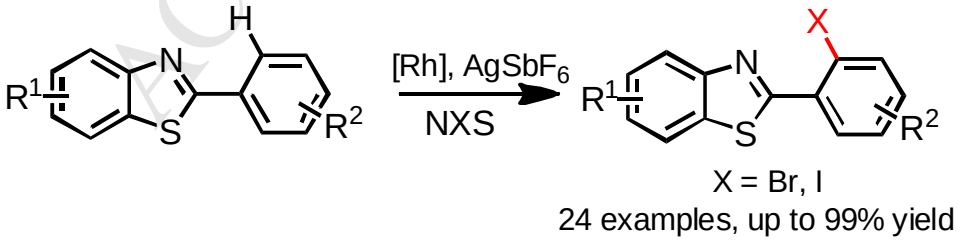
Abstract: A series Rh(III)-catalyzed *ortho*-selective C-H halogenation of 2-arylbenzo[d]thiazoles has been developed using *N*-halosuccinimides (NXS, X = Br and I) as halogen sources. *ortho*-Brominated and iodinated various 2-arylbenzo[d]thiazoles could be accessed in good to excellent yields and high regioselectivity under mild reaction conditions.

Keywords: 2-Arylbenzo[d]thiazoles; Halogenation; *N*-halosuccinimides

Graphical Abstract:



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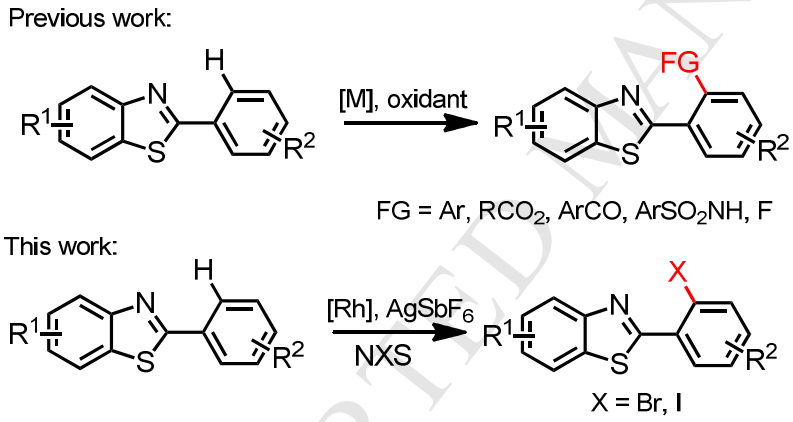
1. Introduction

Aromatic halides serve as important structural motifs extensively used as coupling partners,[1] electrophiles,[2] and promising building blocks[3] in organic synthesis. The traditional methods for the synthesis of aromatic halides mainly involve electrophilic aromatic substitution[4] and directed *ortho* lithiation (DoL)/electrophilic substitution.[5] Low yield or poor regioselectivity of the two prevalent strategies lead to urge to develop a new straightforward protocol for the direct *ortho*-C-H halogenation of arenes. In fact, transition metal-catalyzed C-H functionalization[6]/halogenation has emerged over the past decade as another particularly useful and environmentally friendly method for preparing halogenated aromatic products with high yield and selectivity. Pd[7]-, Cu[8]-, and Au[9]-catalyzed C-H halogenation of arenes are well-documented. For instance, Yu and co-workers reported the Pd-catalyzed *ortho*-halogenation of arenes, using carboxylic acid[7d,g] and amide[7e,m,n] as directing groups. Copper-based catalytic systems also have been well-demonstrated directed by pyridine.[8] In contract, the only one Rh-catalyzed C-H halogenation reaction of benzamides, acetamides, and phenylpyridines was reported by Glorius.[10] Herein, we report Rh-catalyzed C-H halogenation of 2-arylbenzo[d]thiazoles using N-halosuccinimides (NXS, X = Br and I) as halogen sources.

Benzothiazoles as one of numerous bioactive natural products and pharmaceuticals have consequently attracted the continued interest of synthetic chemists for many

years.[11] Based on transition metal-catalyzed direct C-H functionalization protocol, recently we and other groups developed the synthesis of various *ortho*-functionalized 2-arylbenzo[d]thiazoles, including arylation, acylation, acyloxylation, fluorination, and amidation (Scheme 1).[12] Recently, Rh-catalyzed direct C-H bond functionalizations,[13] including oxygenation, amination, arylation, alkenylation of various organic molecules, has become a valuable synthetic method. Herein, we report the Rh-catalyzed direct C-H bond bromination and iodination of 2-arylbenzo[d]thiazoles using *N*-halosuccinimides as halogen sources with excellent regioselectivity and reactivity.

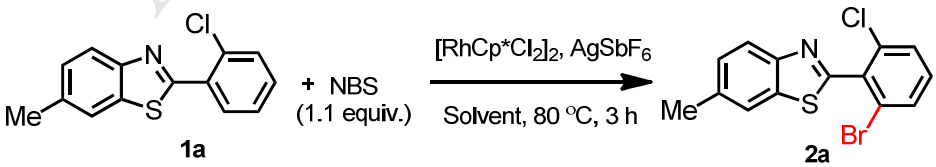


Scheme 1. Direct C-H functionalization of 2-arylbenzo[d]thiazoles.

Our initial investigations focused on the $[RhCp^*Cl_2]_2$-catalyzed bromination of 2-(2-chlorophenyl)-6-methylbenzo[d]thiazole **1a** under various conditions using *N*-bromosuccinimide (NBS) as the bromination reagent. Without additive, the desired brominated product **2a** was obtained only in moderate yield 43% (Table 1, entry 1). In order to improve the conversion, $AgSbF_6$ as a commonly used additive was examined. Delightedly, we found that the addition of $AgSbF_6$ (40 mol %) in the reaction system

dramatically increased the yield 79% of desired product **2a** (Table 1, entry 2). However, only inferior results were displayed when other additives were used, such as Ag_2CO_3, $AgNO_3$, AgOAc, and AgOTf. Gratifyingly, lowering the amount of the Rh-catalyst improved the efficiency of this catalytic system significantly (Table 1, entries 2-4). Product **2a** was obtained in 95% yield upon decreasing the loading of the Rh(III) catalyst to 1 mol% (Table 1, entry 4). Definitely, a control reaction showed that omission of the Rh(III) catalyst resulted in complete inactivity of this catalytic system. Notably, it was found the amount of additive $AgSbF_6$ slightly affects the outcome of the reaction (Table 1, entries 6-9). Decreasing the amount of $AgSbF_6$ led to the decrease of both the reaction activity and efficiency. An excellent conversion was observed in 1 h in the presence of 40 mol% $AgSbF_6$. However, when the reaction was carried out with 4 mol% $AgSbF_6$, only 79% yield of product **2a** and 15% substrate **1a** were obtained in more than 24 h (Table 1, entry 9). Among various solvents examined, DCE provided the best results, whereas 1,4-dioxane gave inferior results, while toluene, CH_3CN, and DMF failed to yield the desired product (Table 1, entries 10-13).

Table 1. Optimization of ortho-bromination reaction conditions[a].



entry	$[RhCp^*Cl_2]_2$	$AgSbF_6$	solvent	yield (%)[b]
1	$[RhCp^*Cl_2]_2$ (4%)	-	DCE	43
2	$[RhCp^*Cl_2]_2$ (4%)	$AgSbF_6$	DCE	79
3	$[RhCp^*Cl_2]_2$ (2.5%)	$AgSbF_6$	DCE	88
4	$[RhCp^*Cl_2]_2$ (1%)	$AgSbF_6$	DCE	95
5	-	$AgSbF_6$	DCE	n.r.
6	$[RhCp^*Cl_2]_2$ (1%)	$AgSbF_6$ (20%)	DCE	86
7	$[RhCp^*Cl_2]_2$ (1%)	$AgSbF_6$ (10%)	DCE	85
8	$[RhCp^*Cl_2]_2$ (1%)	$AgSbF_6$ (8%)	DCE	83
9	$[RhCp^*Cl_2]_2$ (1%)	$AgSbF_6$ (4%)	DCE	79
10	$[RhCp^*Cl_2]_2$ (1%)	$AgSbF_6$	1,4-dioxane	57
11	$[RhCp^*Cl_2]_2$ (1%)	$AgSbF_6$	toluene	n.r.
12	$[RhCp^*Cl_2]_2$ (1%)	$AgSbF_6$	CH_3CN	n.r.
13	$[RhCp^*Cl_2]_2$ (1%)	$AgSbF_6$	DMF	n.r.

[a] Reaction conditions: 2-(2-chlorophenyl)-6-methylbenzo[d]thiazole **1a** (0.2 mmol), NBS (1.1 equiv, 0.22 mmol), $[RhCp^*Cl_2]_2$ (1-4 mol%), $AgSbF_6$ (40 mol%), 80 ^oC, solvent (2 mL). [b] Isolated yield based on **1a**, n.r. = no reaction.

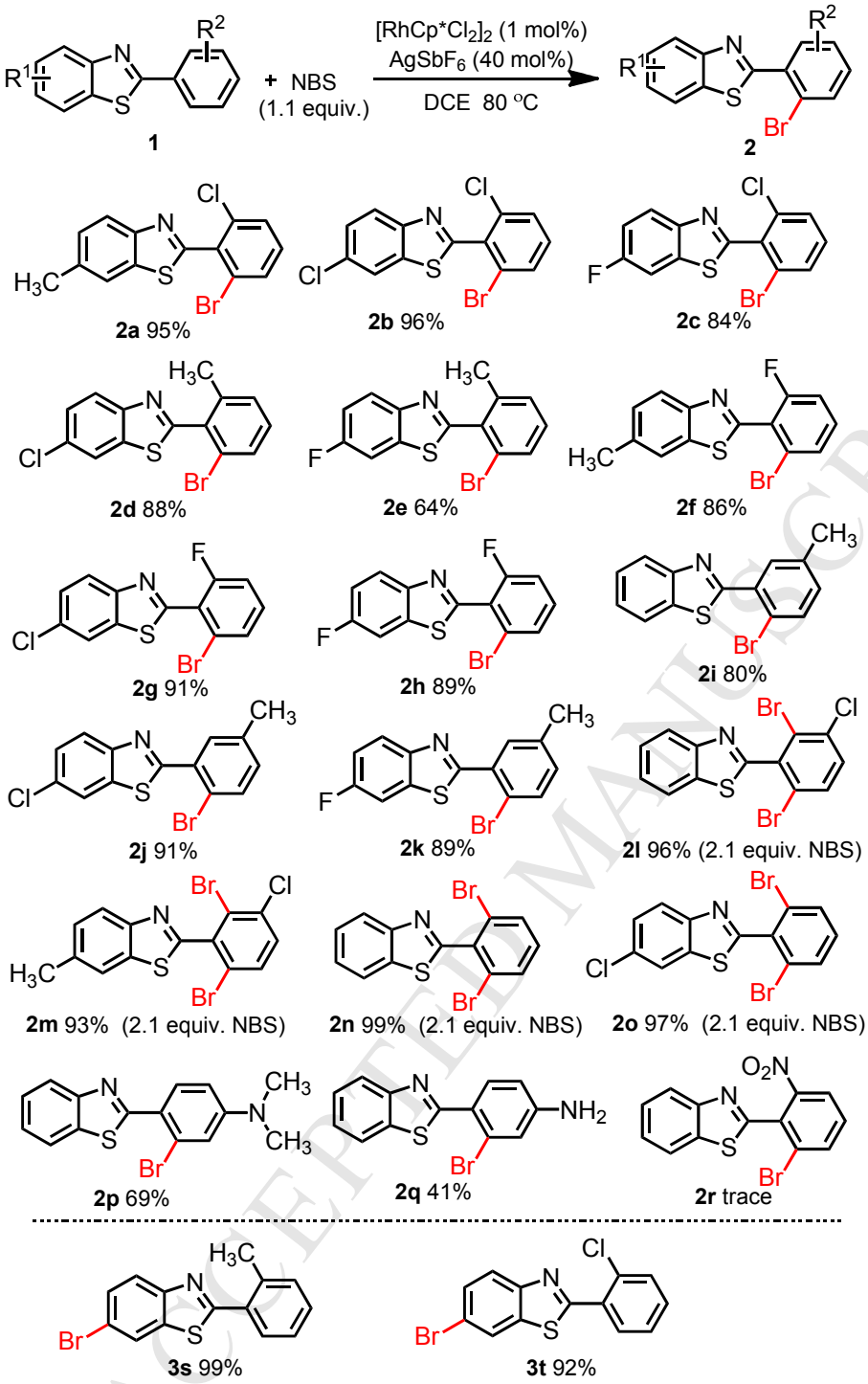
2. Results and Discussion

In order to investigate the reaction scope of the protocol, subsequently we examined the generality of Rh-catalyzed *ortho*-bromination of substituted 2-arylbenzo[d]thiazoles **2** under optimized conditions {$[RhCp^*Cl_2]_2$ (1 mol%), $AgSbF_6$ (40 mol%), DCE, 80 ^oC} (Table 2). A wide range of 2-arylbenzo[d]thiazole derivatives were smoothly transformed into the corresponding *ortho*-brominated products in good to excellent yields. Substrates bearing electron-donating groups (such as methyl, amino, and

N,N-dimethylamino) or electron-withdrawing groups (such as F and Cl) as well as those *ortho*-, *meta*- and *para*-substituted derivatives were well tolerated. For instance, 2-arylbenzo[d]thiazoles **2** containing halogen (F, Cl) and methyl substituents on the *ortho*-position of 2-aryl ring undergo the C-H bond bromination process smoothly under the optimized conditions to give the corresponding products in 64-96% yields (**2a-h**). To those substrates **1i-k** with a methyl group at the *meta*-position of 2-aryl ring undergo the bromination reaction efficiently to give one regioisomeric mono-brominated products **2i-k** at the less sterically hindered position in good yields (80-91%). Replacing methyl by chlorine as a substituent at the *meta*-position led to a mixture of *mono*- and di-brominated compounds under standard conditions, but gave only high yields (96% and 93%) of di-brominated products (**2l** and **2m**) when 2.1 equiv NBS was used. To those substrates without substituents at the 2-phenyl ring also afforded almost quantitative di-bromonated products (**2n** and **2o**) in the presence of 2.1 equiv NBS. For the substrates **1p-q** bearing electron-donating groups (N,N-dimethylamino and amino, respectively), the desired mono-brominated products **2p-q** were isolated in moderate yield. Unfortunately, the functional group R^2 couldn't tolerate the very strong electron-withdrawing group (such as nitro, **1r**). Interesting, for substrates **1s** and **1t**, the bromination reaction was not a ligand-directed *ortho*-C-H activation process under the standard conditions, but compounds **3s** and **3t** were obtained in high yields via electrophilic aromatic substitution at the *para*-position to the nitrogen atom in the benzo ring of benzothiazole moiety. To the substrates **1f** and

1m with a methyl at the *para*-position, the electrophilic substitution reaction could not be carried out under the standard conditions, and only the C-H activated products **2f** and **2m** were observed. Although we could not explain the exact mechanism, we can conclude from the results that C-H activation may be prior to electrophilic substitution when the *ortho*-position of 2-aryl was not be occupied by substitutents (such as **1i**, **1l**, and **1p-q**).

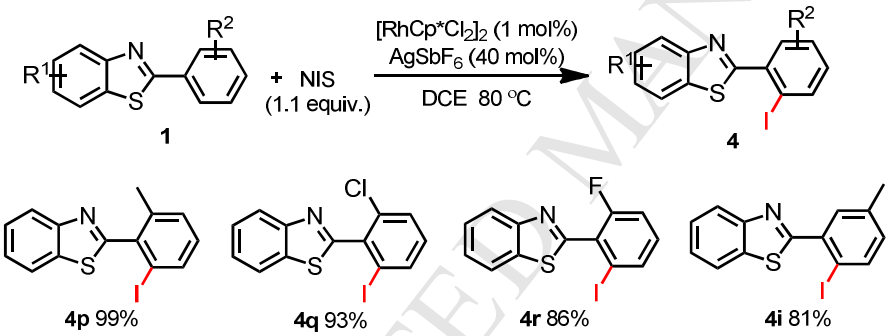
Table 2. *ortho*-Bromination of various 2-arylbenzo[d]thiazoles **1**[a,b]



To further exemplify the synthetic utility of this protocol, the *ortho*-iodination reaction of 2-arylbenzo[d]thiazoles by using NIS as the iodination reagent was evaluated. Several 2-arylbenzo[d]thiazoles were studied as found in Table 3. In general, the iodination reaction occurred smoothly, leading to the desired products

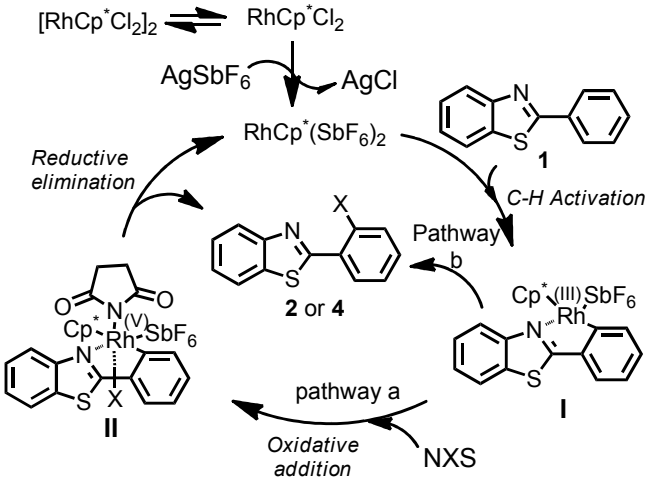
in good to excellent yields. The substrates 2-arylbenzo[d]thiazoles **1p-r** bearing 2-Me, 2-Cl, and 2-F substituents on the aryl ring reacted with NIS to give target products **4p-r** in 99%, 93%, and 86% yields, respectively. Surprisingly, without any electrophilic aromatic substitution product was detected. The detail reason is ambiguous. Interesting, when *meta*-substituted substrate, 2-(*m*-tolyl)benzo[d]thiazole **1i** was used, provided only the mono-iodinated product **4i** at the less sterically hindered position in good yield 81%. In a similar vein, steric hindrance showed non-ignorable influence on *ortho*-iodination activity.

Table 3. *ortho*-Iodination of 2-arylbenzo[d]thiazoles **1**.



Based on previous works,[7-10] the plausible mechanism for the *ortho*-halogenation of **1** with N-halosuccinimides (NXS, X = Br and I) is illustrated in Scheme 1. Firstly, $[RhCp^*Cl_2]_2$ is dissociated into unsaturated monomeric complexes $RhCp^*Cl_2$, then $RhCp^*(SbF_6)_2$ species may be formed in the presence of $AgSbF_6$. Secondly, involves C-H bond activation through coordination at the *ortho*-position of the substrate leading to a five-membered rhodacycle intermediate **I**. Thirdly, rhodacycle **I** was oxidized into Rh(V) intermediate **II** by *N*-halosuccinimides. Finally, involves the formation of C-X (X = Br, I) bond via reductive elimination

leading to the halogenated product along with regeneration of the Rh(III) catalyst (pathway a). Although we can not deny the transformation may undergo a nucleophlic addition type reaction (pathway b).



Scheme 2. Proposed catalytic cycle.

Scheme 2. Proposed catalytic cycle.

Conclusion

In summary, an *ortho*-selective C-H bromination and iodination of 2-arybenzo[d]thiazoles have been developed using only 1% loading of Rh(III) catalyst and commercially available halogenation reagents (NXS). *ortho*-Brominated and iodinated various 2-arylbenzo[d]thiazoles could be accessed in good to excellent yields and high regioselectivity under mild reaction conditions. Further extension the application and mechanism of this protocol is currently underway in our laboratory.

Experimental

General procedure for Rh-catalyzed *ortho*-C-H halogenation of

2-arylbenzo[d]thiazoles: In a sealed tube, $AgSbF_6$ (40 mmol%) was added to a solution of 2-arylbenzo[d]thiazole (0.2 mmol), $[RhCp^*Cl_2]_2$ (1 mmol%) and NBS (0.22 mmol, 1.1 equiv) in 1,2-dichloroethane (DCE) (2 mL). The resulting mixture was stirred at 80 ^oC for 1-3 h (monitored by TLC). After being cooling to room temperature, evaporation of the solvent under reduced pressure followed purification by silica gel chromatography using petroleum ether/ethyl acetate (20:1) as eluent to provide the destination products **2-4**.

2-(2-bromo-6-chlorophenyl)-6-methylbenzo[d]thiazole (**2a**):

Isolated (Rf = 0.27, EtOAc-petroleum ether = 1:20 v/v) as a colorless oil (63 mg, 95% yield); ^1H NMR (400 MHz, $CDCl_3$) δ = 2.53 (s, 3H), 7.29 (t, *J* = 8.2 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.76 (s, 1H), 8.04 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.6, 121.3, 123.4, 124.8, 127.9, 128.7, 131.3, 131.6, 134.2, 135.5, 136.0, 136.5, 151.0, 162.6; IR (KBr) ν/cm^{-1}: 3051, 2924, 2853, 1579, 1554, 1427, 1085, 702, 683; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_9BrClNS$: 337.9328; found: 337.9329.

2-(2-bromo-6-chlorophenyl)-6-chlorobenzo[d]thiazole (**2b**):

Isolated (Rf = 0.32, EtOAc/petroleum ether = 1:20) as a yellow oil (69 mg, 96% yield); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.32 (t, *J* = 8.2 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.8 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.95 (s, 1H), 8.08 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 120.8, 124.1, 124.2, 126.6, 126.7, 128.2,

130.9, 131.4, 133.1, 134.9, 137.0, 150.9, 163.7; IR (KBr) ν/cm^{-1}: 3054, 1592, 1554, 1427, 1081, 695; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{13}H_6BrCl_2NS$: 357.8861; found: 357.8876.

2-(2-bromo-6-chlorophenyl)-6-fluorobenzo[d]thiazole (**2c**):

Isolated (Rf = 0.32, EtOAc-petroleum ether = 1:20 v/v) as a yellow oil (56 mg, 84% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.28 (dd, *J* = 8.8 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 8.11 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 107.7 (d, $^2J_{CF}$ = 27.2 Hz), 115.0 (d, $^2J_{CF}$ = 24.8 Hz), 124.7, 125.0 (d, $^3J_{CF}$ = 9.5 Hz), 128.8, 131.4, 131.9, 133.7, 135.5, 137.3 (d, $^3J_{CF}$ = 11.4 Hz), 149.5, 160.8 (d, $^1J_{CF}$ = 245 Hz); IR (KBr) ν/cm^{-1}: 3068, 1610, 1565, 1456, 1224, 1086, 703, 678; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{13}H_6BrClFNS$: 341.9157; found: 341.9153.

2-(2-bromo-6-methylphenyl)-6-chlorobenzo[d]thiazole (**2d**):

Isolated (Rf = 0.28, EtOAc-petroleum ether = 1:20 v/v) as a brown oil (59 mg, 88% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.22 (s, 3H), 7.25 (d, *J* = 6.4 Hz, 2H), 7.51 (td, *J* = 8.6 Hz, 1H), 7.53 (d, *J* = 6.4 Hz, 1H), 7.93 (s, 1H), 8.04 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 19.5, 120.2, 122.5, 123.4, 125.9, 128.1, 129.3, 130.1, 130.5, 133.1, 136.5, 139.0, 150.6, 165.6; IR (KBr) ν/cm^{-1}: 3060, 2960, 2854, 1683, 1592, 1445, 1083, 700, 681; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{14}H_9BrClNS$: 337.9328; found: 337.9394.

6-fluoro-2-(o-tolyl)benzo[d]thiazole (**2e**):

Isolated (Rf = 0.29, EtOAc-petroleum ether = 1:20 v/v) as a yellow oil (40 mg, 64% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.23 (s, 3H), 7.25-7.35 (m, 3H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 8.08 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 19.6, 106.6 (d, $^{2}J_{CF}$ = 26.6 Hz), 113.7 (d, $^{2}J_{CF}$ = 24.8 Hz), 122.6, 123.6 (d, $^{3}J_{CF}$ = 9.3 Hz), 128.1, 129.3, 130.0, 133.2, 139.0, 148.7, 159.6 (d, $^{1}J_{CF}$ = 245 Hz), 164.8; IR (KBr) ν/cm^{-1}: 3066, 2958, 2854, 1610, 1565, 1455, 1253, 705, 685; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_9BrFNS$: 321.9703; found: 321.9696.

2-(2-bromo-6-fluorophenyl)-6-methylbenzo[d]thiazole (**2f**):

Isolated (Rf = 0.29, EtOAc-petroleum ether = 1:20 v/v) as a brown oil (54 mg, 86% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.53 (s, 3H), 7.18 (t, *J* = 8.6 Hz, 1H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.75 (s, 1H), 8.04 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.5, 115.0 (d, $^{2}J_{CF}$ = 22.0 Hz), 121.1, 123.4, 124.3, 127.8, 128.8, 132.0 (d, $^{3}J_{CF}$ = 9.0 Hz), 135.9, 136.6, 151.2, 158.7, 160.7 (d, $^{1}J_{CF}$ = 253 Hz); IR (KBr) ν/cm^{-1}: 3055, 2953, 2853, 1607, 1567, 1447, 1251, 703, 686; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_9BrFNS$: 321.9703; found: 321.9699.

2-(2-bromo-6-fluorophenyl)-6-chlorobenzo[d]thiazole (**2g**):

Isolated (Rf = 0.32, EtOAc-petroleum ether = 1:20 v/v) as a milky solid (61 mg, 91%

yield), mp: 108-110 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.19 (t, *J* = 8.8 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.51 (d, *J* = 8.8 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.94 (s, 1H), 8.07 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 115.2 (d, $^{2}J_{CF}$ = 21.8 Hz), 121.1, 124.1, 124.7, 127.2, 128.9, 129.0, 131.9, 132.4 (d, $^{3}J_{CF}$ = 8.9 Hz), 137.5, 151.5, 160.7 (d, $^{1}J_{CF}$ = 253 Hz); IR (KBr) ν/cm^{-1}: 3066, 1589, 1567, 1444, 1247, 1104, 695, 545; HRMS (ESI): *m/z* [M + H]$^{+}$ calcd for $C_{13}H_6BrClFNS$: 341.9157; found: 341.9150.

2-(2-bromo-6-fluorophenyl)-6-fluorobenzo[d]thiazole (**2h**):

Isolated (Rf = 0.33, EtOAc-petroleum ether = 1:20 v/v) as a yellow oil (57 mg, 89% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.18 (d, *J* = 8.4 Hz, 1H), 7.20 (d, *J* = 8.8 Hz, 1H), 7.28 (t, *J* = 7.2 Hz, 1H), 7.36 (d, *J* = 6.0 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 8.12 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 106.5 (d, $^{2}J_{CF}$ = 26.7 Hz), 114.2 (d, $^{2}J_{CF}$ = 23.4 Hz), 123.1, 123.9 (d, $^{3}J_{CF}$ = 9.4 Hz), 127.9 (d, $^{3}J_{CF}$ = 3.6 Hz), 131.3 (d, $^{3}J_{CF}$ = 9.1 Hz), 136.3, 148.6, 158.5, 159.7 (d, $^{1}J_{CF}$ = 245 Hz), 159.8 (d, $^{1}J_{CF}$ = 245 Hz); IR (KBr) ν/cm^{-1}: 3073, 1698, 1566, 1489, 1252, 704, 683; HRMS (ESI): *m/z* [M + H]$^{+}$ calcd for $C_{13}H_6BrF_2NS$: 325.9452; found: 325.9454.

2-(2-bromo-5-methylphenyl)benzo[d]thiazole (**2i**): Isolated (Rf = 0.29, EtOAc-petroleum ether = 1:20 v/v) as a yellow oil (48 mg, 80% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.28 (s, 3H), 7.03 (d, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.73 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 1H),

8.04 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.8, 118.7, 121.4, 123.5, 125.4, 126.2, 132.2, 132.6, 133.8, 134.0, 136.1, 137.7, 152.7, 165.8; IR (KBr) ν/cm^{-1}: 3058, 2954, 2850, 1591, 1484, 1459, 708, 693; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{10}BrNS$: 303.9797; found: 303.9790.

2-(2-bromo-5-methylphenyl)-6-chlorobenzo[d]thiazole (**2j**):

Isolated (Rf = 0.28, EtOAc-petroleum ether = 1:20 v/v) as a white flake (61 mg, 91% yield), mp: 124-126 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.27 (s, 3H), 7.03 (s, 1H), 7.37 (s, 1H), 7.49 (s, 1H), 7.78 (s, 2H), 7.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.8, 118.6, 120.9, 124.2, 127.1, 131.3, 132.4, 132.6, 133.5, 133.9, 137.2, 137.7, 151.1, 166.2; IR (KBr) ν/cm^{-1}: 3077, 2956, 2850, 1591, 1483, 1467, 1107, 706, 698; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_9BrClNS$: 337.9328; found: 337.9329.

2-(2-bromo-5-methylphenyl)-6-fluorobenzo[d]thiazole (**2k**):

Isolated (Rf = 0.29, EtOAc-petroleum ether = 1:20 v/v) as a flavescent solid (56 mg, 89% yield), mp: 98-100 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.30 (s, 3H), 7.05 (d, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.74 (s, 1H), 7.99 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.8, 107.4 (d, $^2J_{CF}$ = 26.5 Hz), 115.0 (d, $^2J_{CF}$ = 24.7 Hz), 118.6, 124.3, 132.3, 132.5, 133.7, 133.9, 137.1 (d, $^3J_{CF}$ = 11.1 Hz), 137.7, 149.3, 160.5 (d, $^1J_{CF}$ = 245 Hz), 165.5; IR (KBr) ν/cm^{-1}: 3059, 2955, 2853, 1683, 1598, 1461, 1230, 706, 518. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_9BrClNO$: 321.9703; found: 321.9703.

2-(2,6-dibromo-3-chlorophenyl)benzo[d]thiazole (**2l**):

Isolated (Rf = 0.33, EtOAc-petroleum ether = 1:20 v/v) as a yellow oil (76 mg, 96% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.47 (d, *J* = 8.8 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.62 (d, *J* = 8.8 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 99.9, 118.1, 121.7, 122.2, 124.1, 125.3, 126.0, 126.4, 132.2, 132.3, 135.0, 136.2, 137.8, 152.6; IR (KBr) ν/cm^{-1}: 3056, 1555, 1494, 1417, 1080, 707, 680; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_6Br_2ClNS$: 401.8356; found: 401.8354.

2-(2,6-dibromo-3-chlorophenyl)-6-methylbenzo[d]thiazole (**2m**):

Isolated (Rf = 0.32, EtOAc-petroleum ether = 1:20 v/v) as a white solid (77 mg, 93% yield), mp: 107-109 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.53 (s, 3H), 7.37 (d, *J* = 8.8 Hz, 1H), 7.45 (d, *J* = 8.8 Hz, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.76 (s. 1H), 8.04 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.6, 121.4, 122.4, 123.6, 125.4, 128.0, 132.1, 132.3, 134.9, 136.2, 136.4, 137.9, 150.8, 164.1; IR (KBr) ν/cm^{-1}: 3067, 2956, 2851, 1602, 1590, 1444, 1104, 696, 677; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_8Br_2ClNS$: 415.8513; found: 415.8519.

2-(2,6-dibromophenyl)benzo[d]thiazole (**2n**):

Isolated (Rf = 0.33, EtOAc-petroleum ether = 1:20 v/v) as a brown oil (73 mg, 99% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.22 (t, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.8 Hz,

1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.98 (d, *J* = 7.6 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 121.7, 124.0, 124.5, 125.8, 126.3, 131.9, 132.1, 135.8, 136.3, 152.8, 165.3; IR (KBr) ν/cm^{-1}: 3060, 1592, 1550, 1458, 726, 690; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_7Br_2NS$: 367.8746; found: 367.8750.

6-chloro-2-(2,6-dibromophenyl)benzo[d]thiazole (**2o**):

Isolated (Rf = 0.35, EtOAc-petroleum ether = 1:20 v/v) as a pink solid (67 mg, 97% yield), mp: 126-128 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.45 (d, *J* = 8.4 Hz, 1H), 7.49 (d, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 121.3, 124.4, 124.8, 127.1, 131.9, 132.0, 132.2, 135.4, 137.5, 151.3, 165.8; IR (KBr) ν/cm^{-1}: 3068, 1591, 1508, 1434, 1093, 707, 674; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_6Br_2ClNS$: 401.8276; found: 401.8240.

4-(benzo[d]thiazol-2-yl)-3-bromo-N,N-dimethylaniline (2p):

Isolated (Rf = 0.57, EtOAc–petroleum ether = 1:10) as a colorless oil (45 mg, 69% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.89 (s, 6H), 7.10 (d, *J* = 8.4 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 8.30 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 43.7, 118.2, 120.1, 121.5, 123.0, 125.0, 126.3, 127.3, 128.6, 133.0, 134.9, 154.1, 166.2; IR (KBr) ν/cm^{-1}: 3435, 3056, 2939, 2830, 1597, 1477, 1326, 701, 657; HRMS (ESI): *m/z*

$[M + H]^+$ calcd for $C_{15}H_{13}BrN_2S$ 333.0063; found: 333.0069.

4-(benzo[d]thiazol-2-yl)-3-bromoaniline (2q):

Isolated (Rf = 0.30, EtOAc–petroleum ether = 1:10) as a colorless oil (25 mg, 41% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.43 (s, 2H), 6.80 (d, *J* = 8.4 Hz, 1H), 7.33 (t, *J* = 8.2 Hz, 1H), 7.45 (t, *J* = 8.2 Hz, 1H), 7.80 (dd, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 8.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 109.1, 115.1, 121.4, 122.7, 124.7, 125.0, 126.2, 127.9, 131.7, 134.6, 146.5, 154.1, 166.8; IR (KBr) ν/cm^{-1}: 3437, 3028, 1642, 1594, 1467, 703, 577; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_9BrN_2S$ 304.9750; found: 304.9759.

2-(2-bromo-6-methylphenyl)benzo[d]thiazole (**3s**):

Isolated (Rf = 0.32, EtOAc-petroleum ether = 1:20 v/v) as a brown oil (60 mg, 99% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.23 (s, 3H), 7.24 (d, *J* = 7.2 Hz, 1H), 7.24 (s, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.54 (t, *J* = 8.2 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 8.14 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.6, 121.6, 123.6, 123.7, 125.5, 126.1, 129.1, 130.2, 130.9, 136.3, 140.1, 153.1; IR (KBr) ν/cm^{-1}: 3059, 2954, 2853, 1593, 1561, 1447, 699; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{10}BrNS$: 303.9797; found: 303.9797.

6-bromo-2-(2-chlorophenyl)benzo[d]thiazole (**3t**):

Isolated (Rf = 0.31, EtOAc-petroleum ether = 1:20 v/v) as a colorless oil (59 mg, 92%

yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.32 (t, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 8.8 Hz, 1H), 8.02 (d, *J* = 8.8 Hz, 1H), 8.11 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 118.5, 123.2, 123.6, 124.1, 127.8, 128.8, 130.4, 130.9, 132.6, 134.4, 136.9, 150.7, 163.2; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_7BrClNS$: 323.9251; found: 323.9275.

2-(2-iodo-6-methylphenyl)benzo[d]thiazole (**4p**):

Isolated (Rf = 0.38, EtOAc-petroleum ether = 1:20 v/v) as a white solid (70 mg, 99% yield), mp: 113-115 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.16 (s, 3H), 7.18 (t, *J* = 7.8 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.6, 121.6, 123.6, 123.7, 125.5, 126.1, 129.1, 130.2, 130.9, 136.3, 140.1, 153.1, 166.1; IR (KBr) ν/cm^{-1}: 3053, 2953, 2850, 1685, 1586, 1454, 705, 587; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{10}INS$: 351.9659; found: 351..9646.

2-(2-chloro-6-iodophenyl)benzo[d]thiazole (**4q**):

Isolated (Rf = 0.37, EtOAc-petroleum ether = 1:20 v/v) as a yellow oil (69 mg, 93% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.10 (t, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 99.1, 121.7, 124.0, 125.8, 126.3, 129.5, 132.1, 134.3, 136.3, 137.6, 137.7, 152.7, 166.4; IR (KBr) ν/cm^{-1}: 3059, 1647, 1593, 1423, 1083, 707, 544; HRMS (ESI): *m/z* $[M + H]^+$

calcd for $C_{13}H_7ClINS$: 371.9032; found: 371.9027.

2-(2-fluoro-6-iodophenyl)benzo[d]thiazole (**4r**):

Isolated (Rf = 0.37, EtOAc-petroleum ether = 1:20 v/v) as a yellow solid (58 mg, 86% yield), mp: 102-104 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.18 (t, *J* = 6.4 Hz, 1H), 7.19 (d, *J* = 8.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 6 .4 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 98.6, 115.9 (d, $^2J_{CF}$ = 22. 0Hz), 121.6, 124.0, 125.8, 126.3, 127.5 (d, $^2J_{CF}$ = 16.8 Hz), 132.7 (d, $^3J_{CF}$ = 8.6 Hz), 135.2, 136.4, 152.9, 159.9 (d, $^1J_{CF}$ = 253 Hz), 162.5; IR (KBr) ν/cm^{-1}: 3058, 1689, 1598, 1445, 1248, 708, 543; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{13}H_7FINS$: 355.9408; found: 355.9401.

2-(2-iodo-5-methylphenyl)benzo[d]thiazole (**4i**):

Isolated (Rf = 0.40, EtOAc-petroleum ether = 1:20 v/v) as a yellow oil (56 mg, 81% yield); ^1H NMR (400 MHz, $CDCl_3$) δ = 2.35 (s, 3H), 6.97 (dd, *J* = 8.4 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 8.2 Hz, 1H), 7.54 (s, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 7.2 Hz, 1H), 8.14 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.8, 92.1, 121.5, 123.6, 125.4, 126.2, 132.2, 132.3, 136.1, 138.2, 138.4, 140.4, 153.0, 168.0; IR (KBr) ν/cm^{-1}: 3058, 2953, 2853, 1592, 1498, 1456, 708, 527; HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_9INS$: 351.9659; found: 351.9671.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/

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Jimenez, M. V.; Bartolome, M. I.; Isabel, M.; Perez-Torrente, J. J.; Gomez, D.; Modrego, F. J.; Oro, L. A. *ChemCatChem*, **2013**, *5*, 263; (c) Lewis, J. C.; Berman, A. M.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2008**, *130*, 2493; (d) Shi, J.; Yan, Y.; Li, Q.; Xu, H. E.; Yi, W. *Chem. Comm.* **2014**, *50*, 6483.

Rhodium-Catalyzed *ortho*-selective C-H halogenation of 2-arylbenzo[d]thiazoles using N-halosuccinimides as halogen sources

Qiuping Ding,*[a,b] Xiaoli Zhou, [b] Shouzhi Pu[*a], and Banpeng Cao[a]

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[b] Key Laboratory of Functional Small Organic Molecules, Ministry of Education and College of Chemistry & Chemical Engineering, Jiangxi Normal University, Nanchang, Jiangxi 330022, P. R. China

Supporting Information

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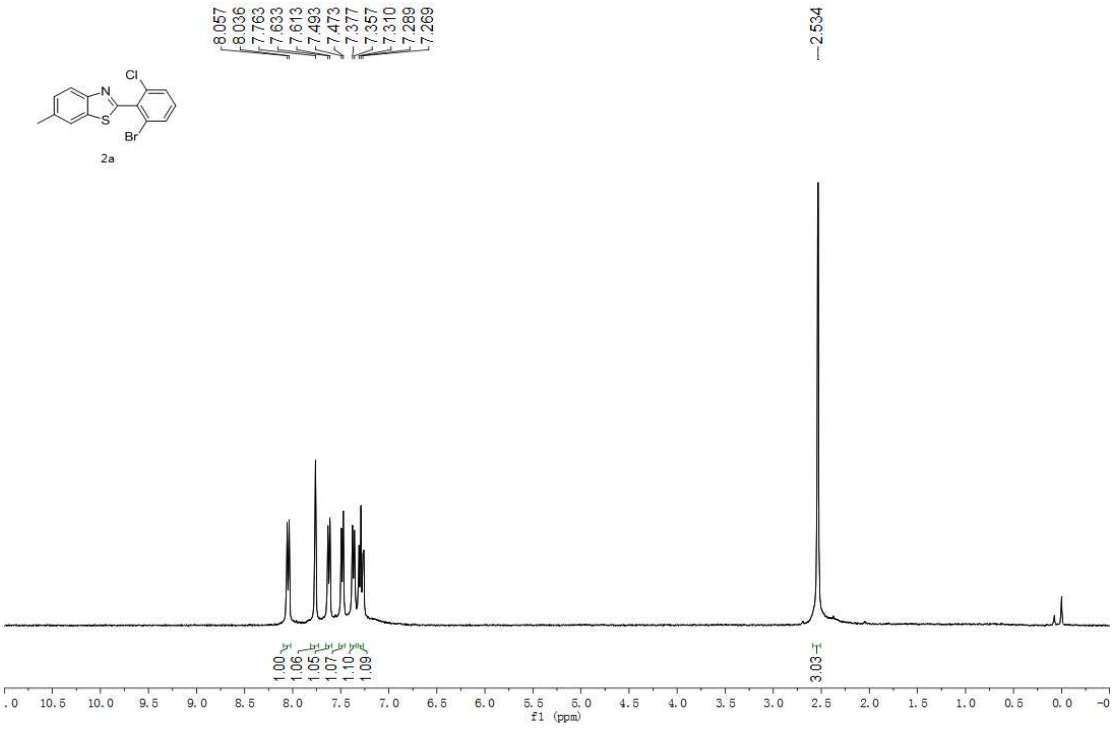
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S
Br
2a
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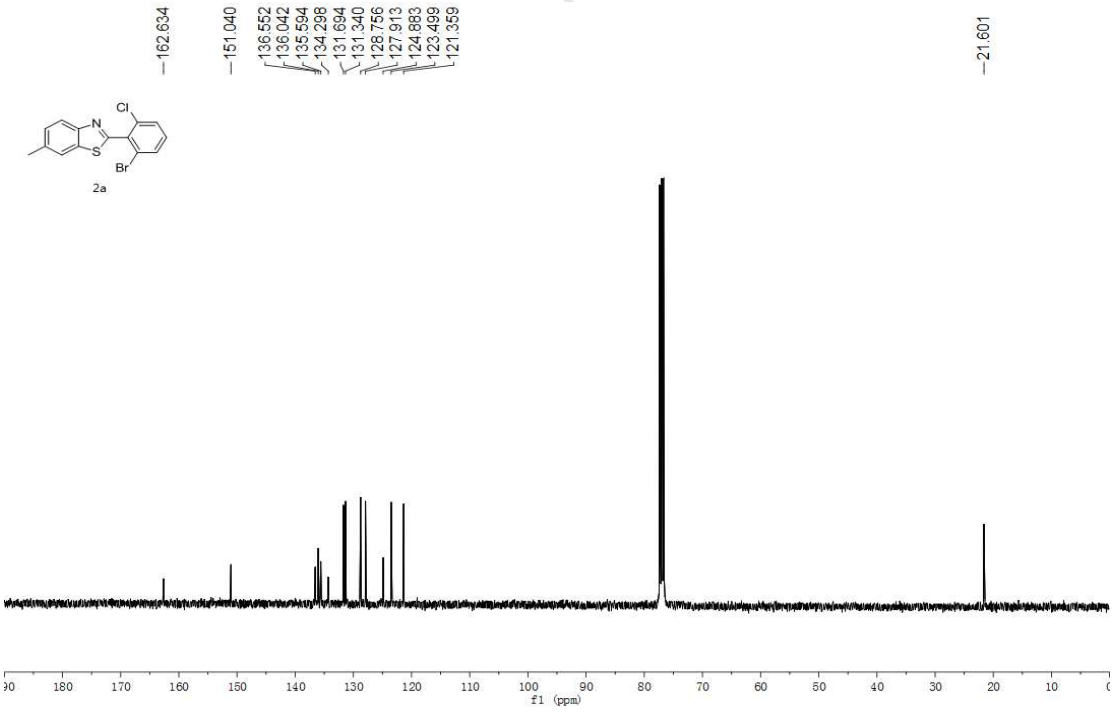
1.05
1.07
1.10
1.09
3.03
f1 (ppm)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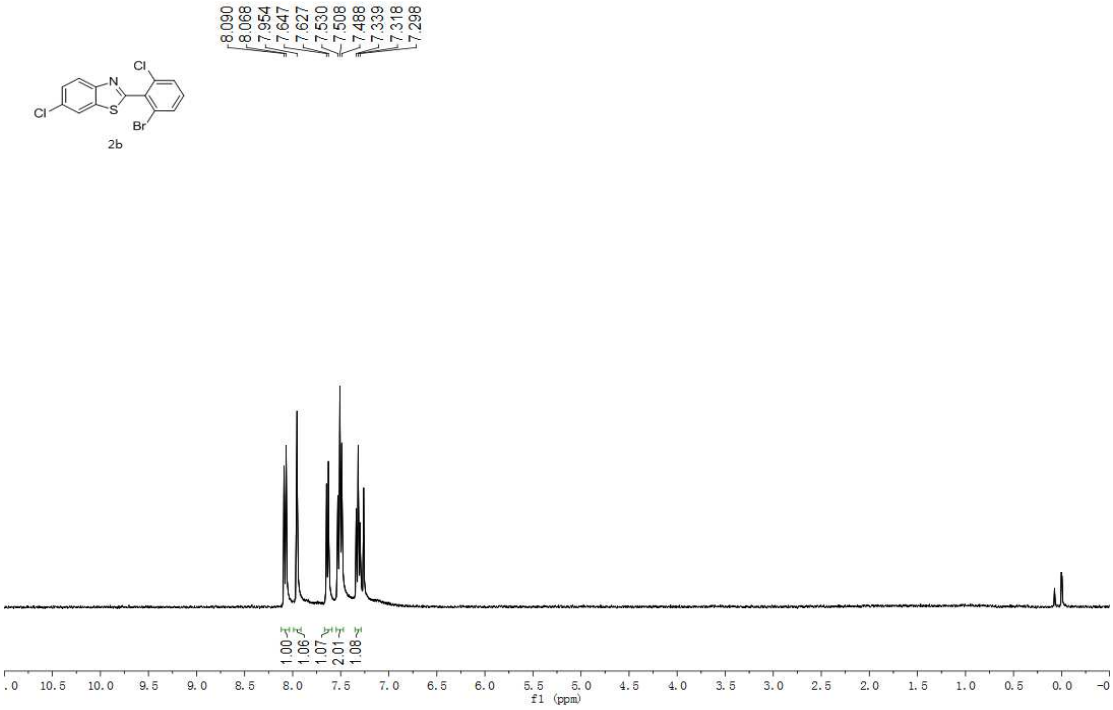
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S
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Br
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1.07
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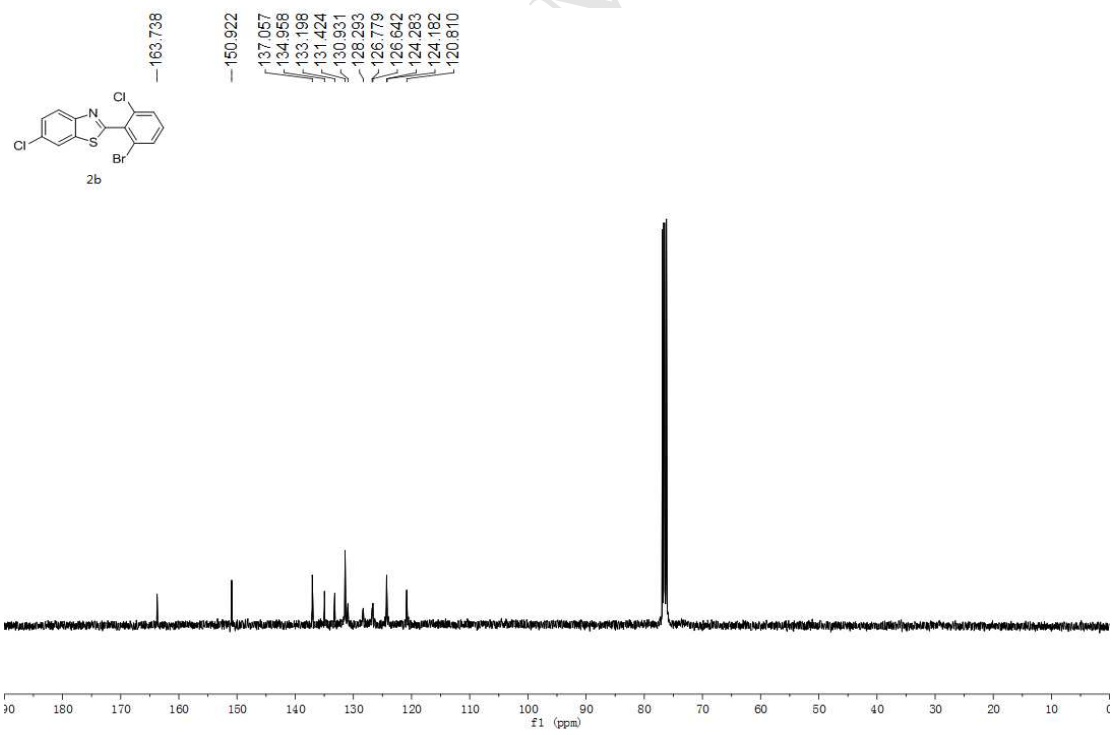
1.08
f1 (ppm)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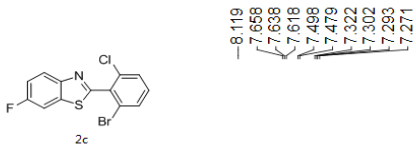
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Br
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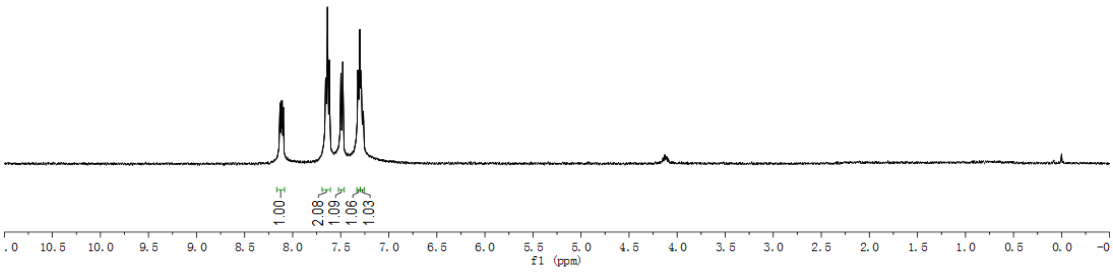
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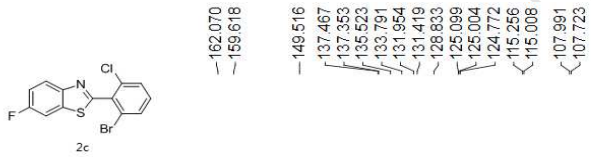
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S
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Br
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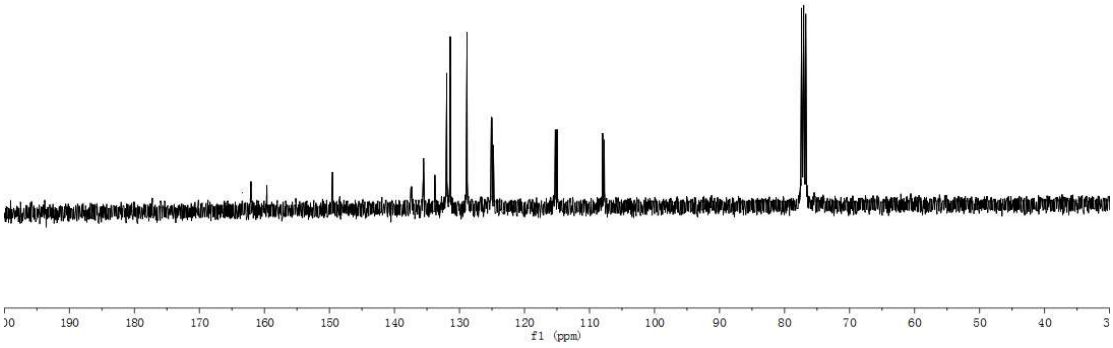
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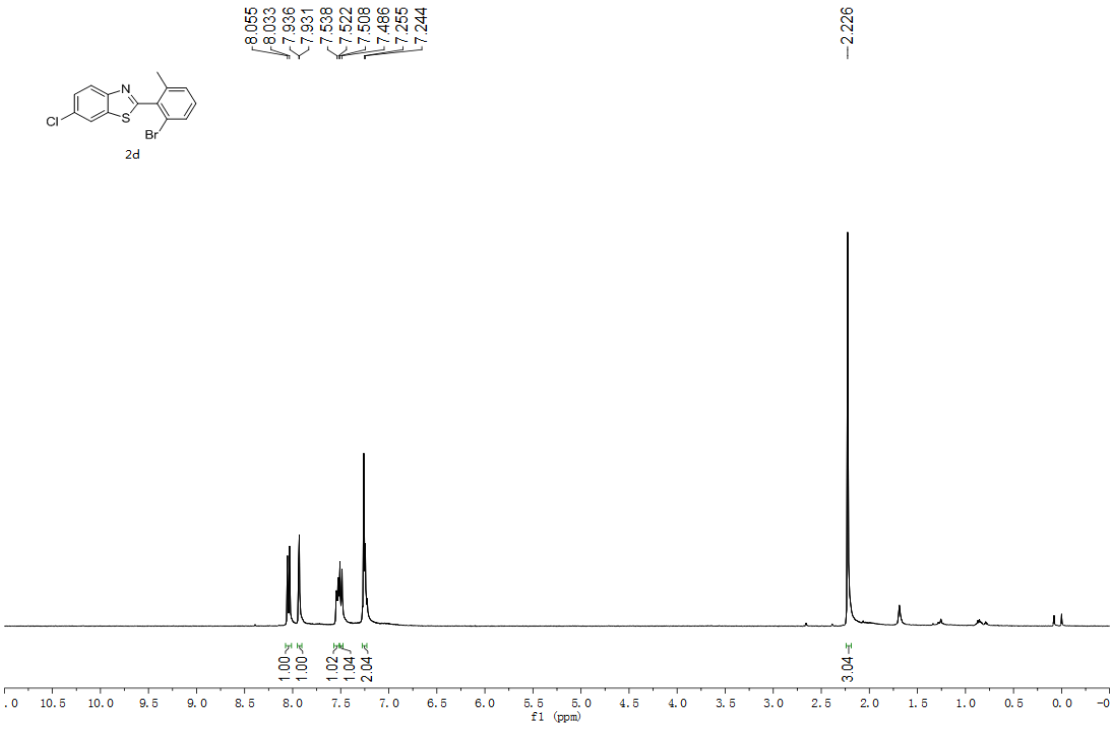
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Br
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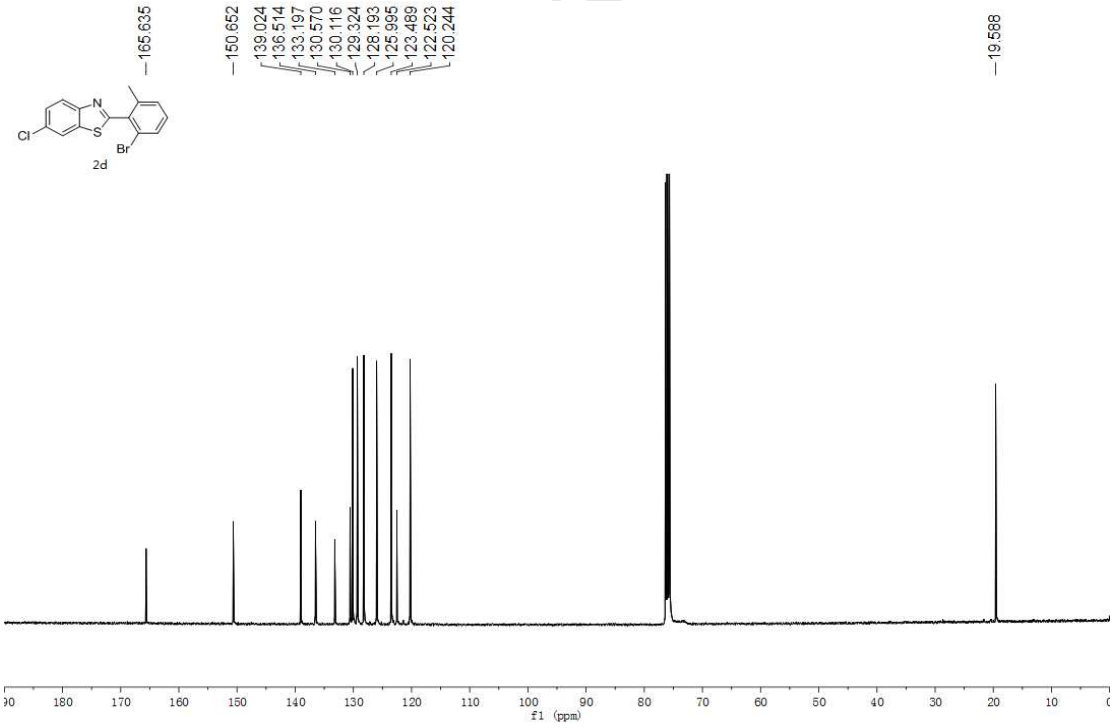
f1 (ppm)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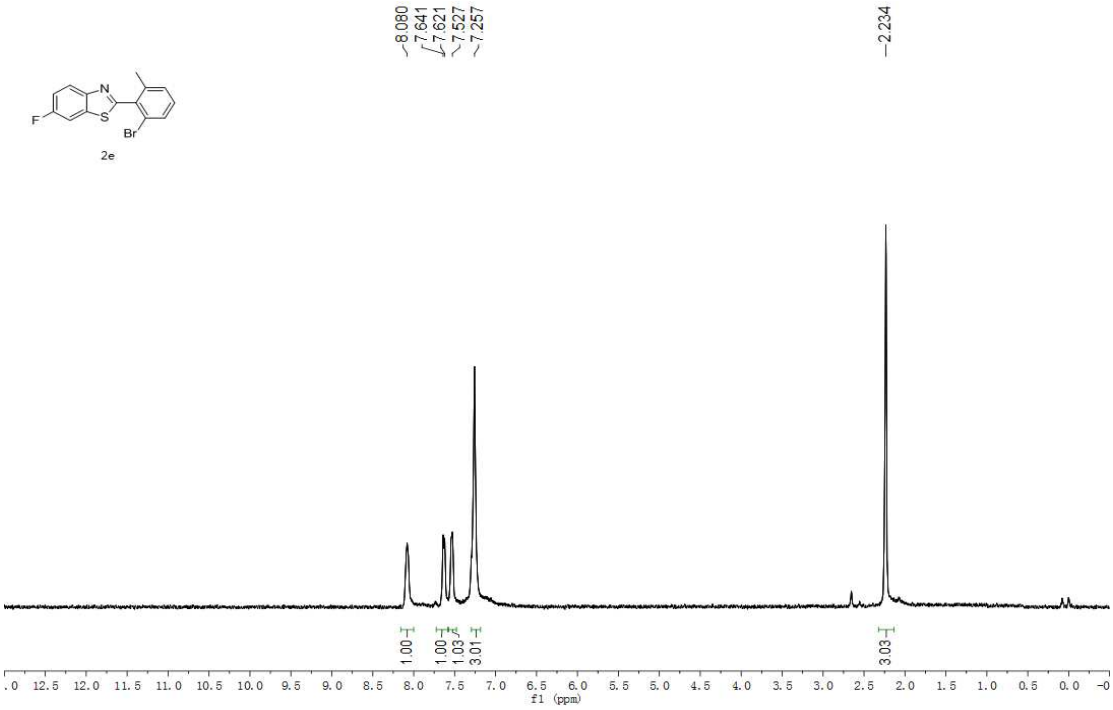
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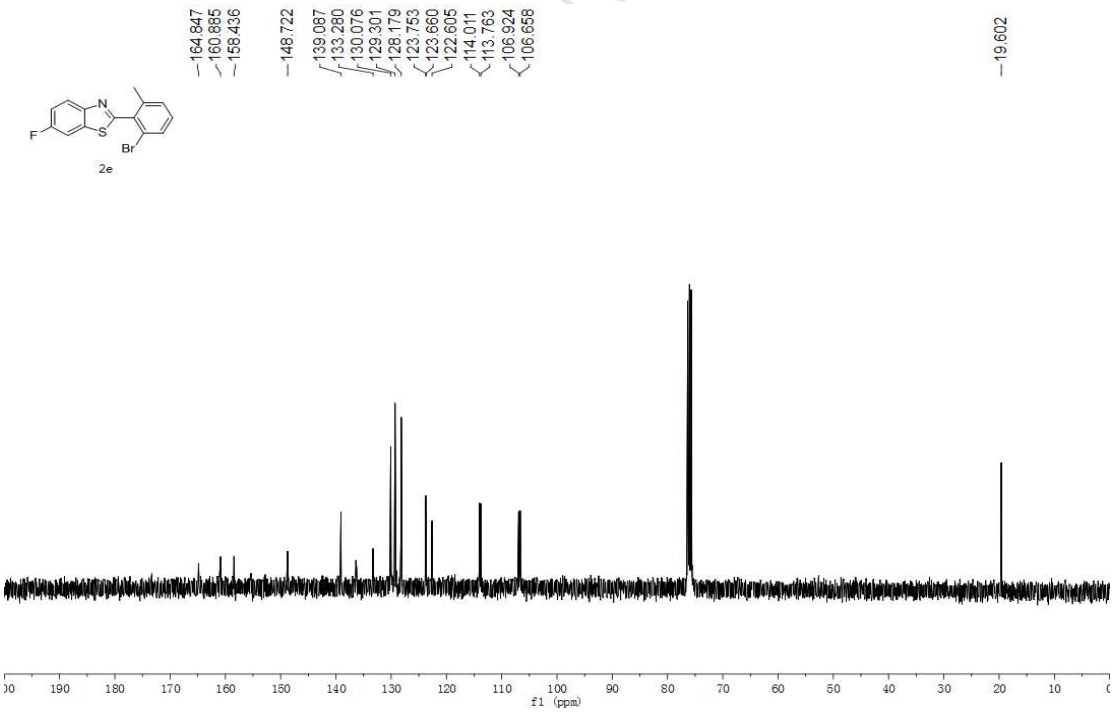
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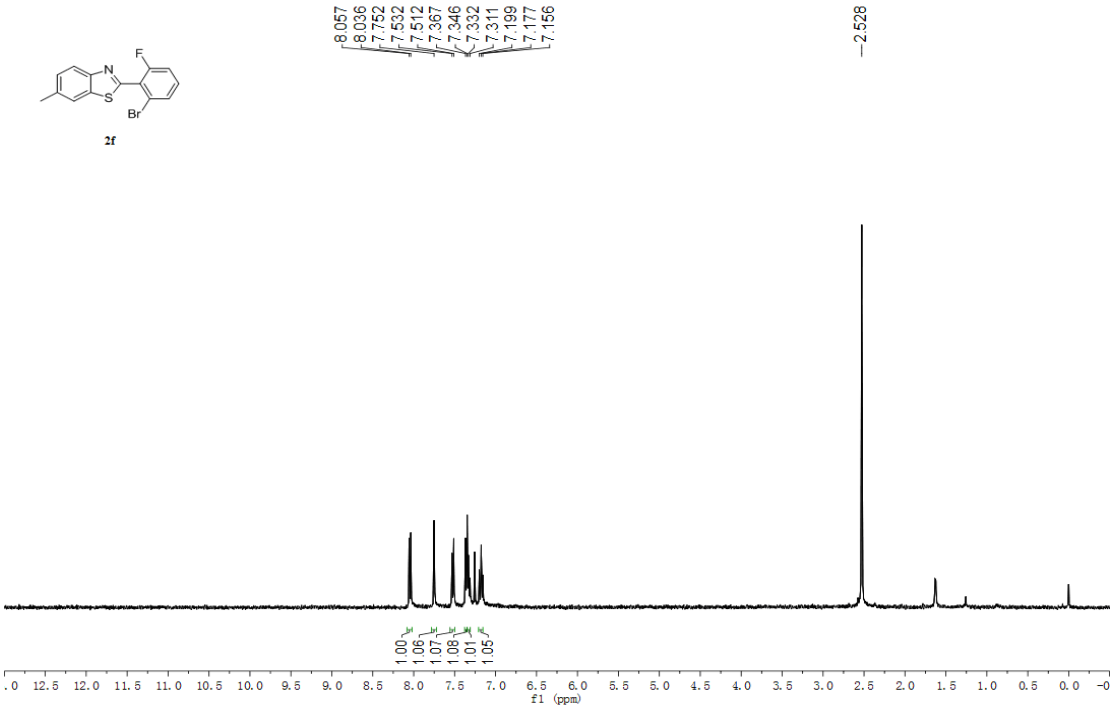
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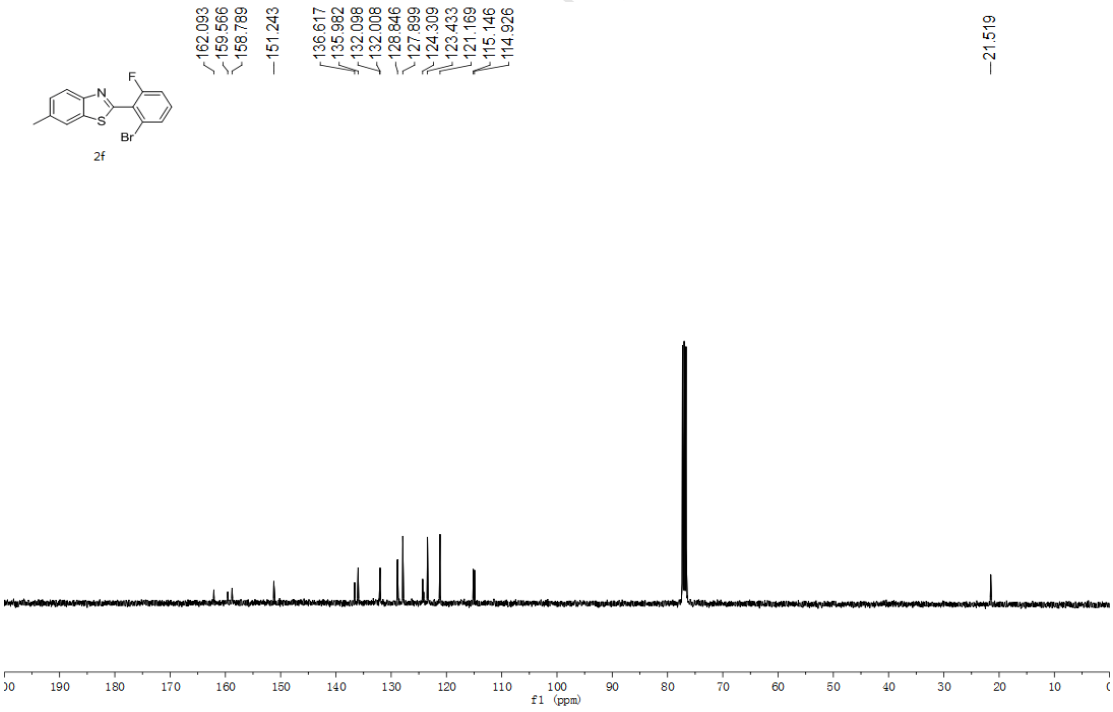
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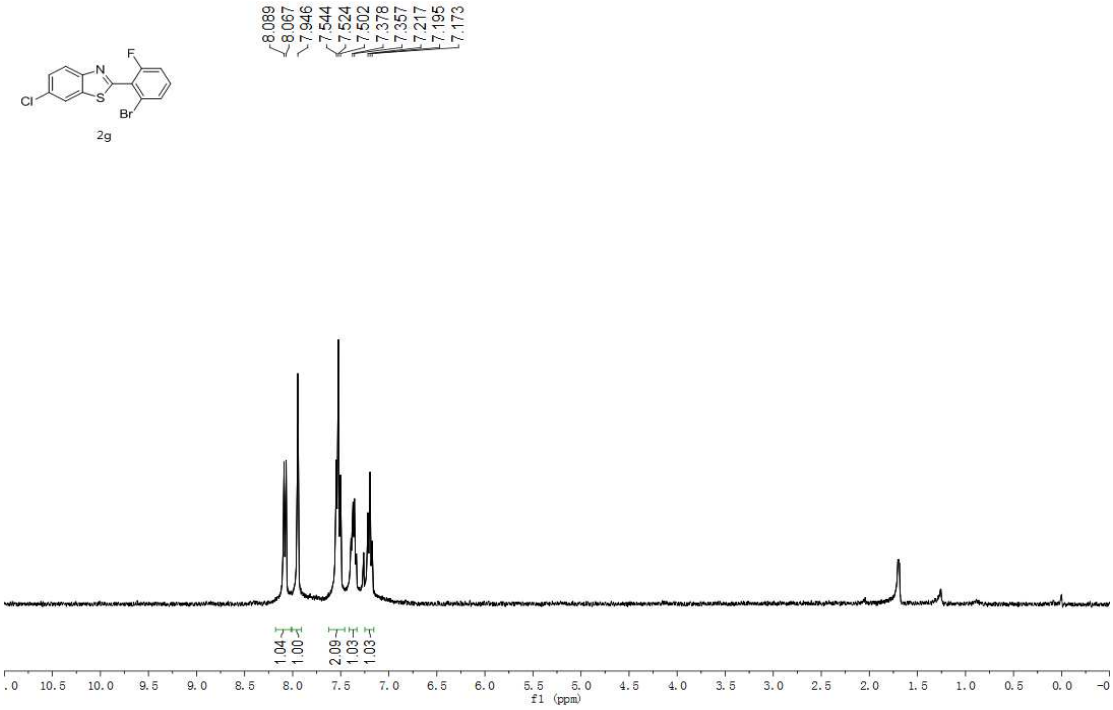
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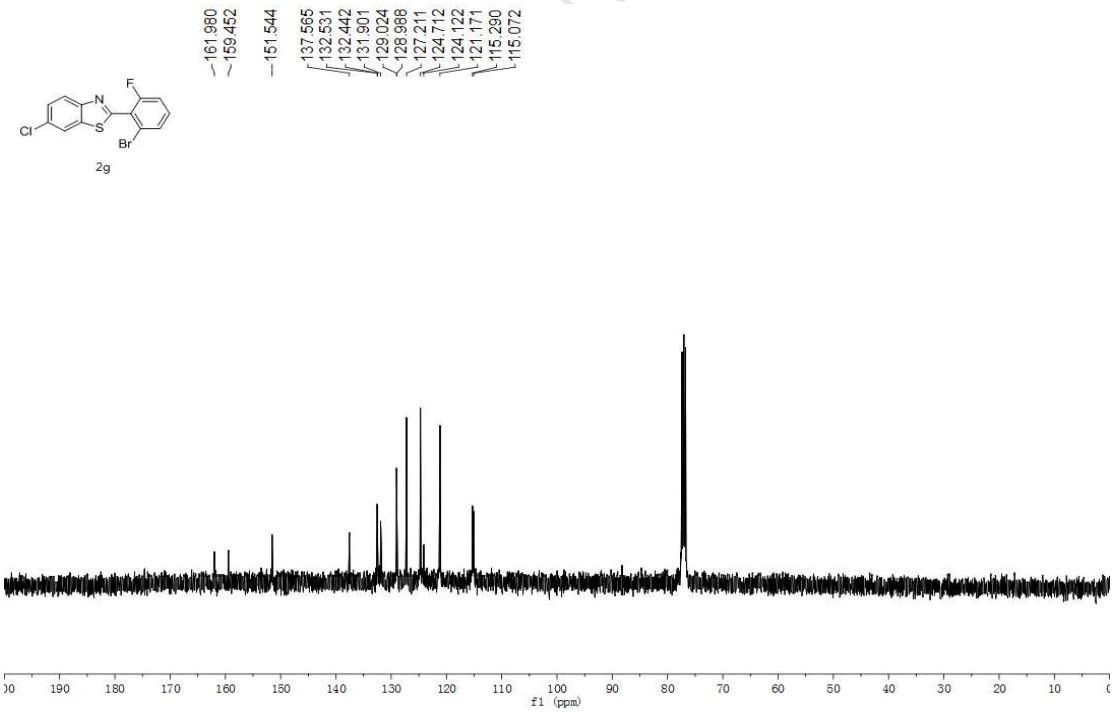
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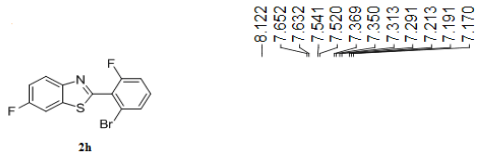
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Br
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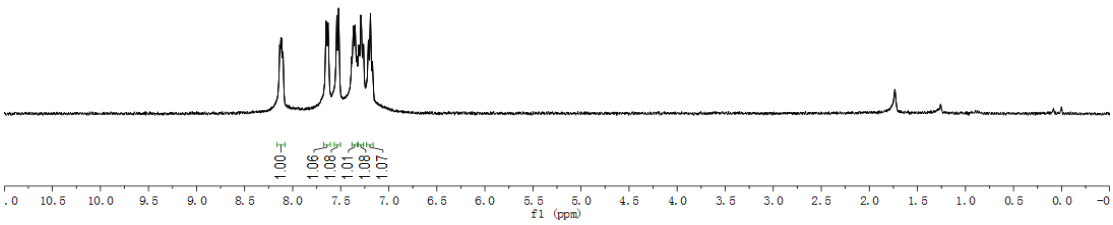
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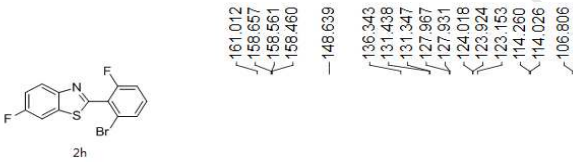
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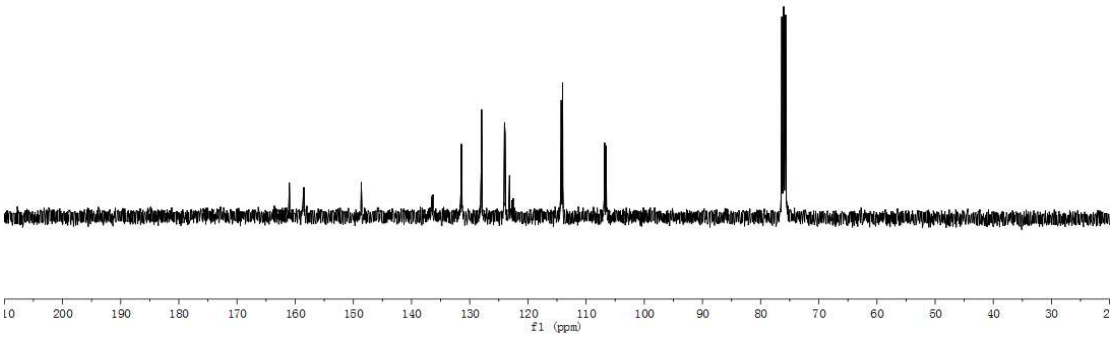
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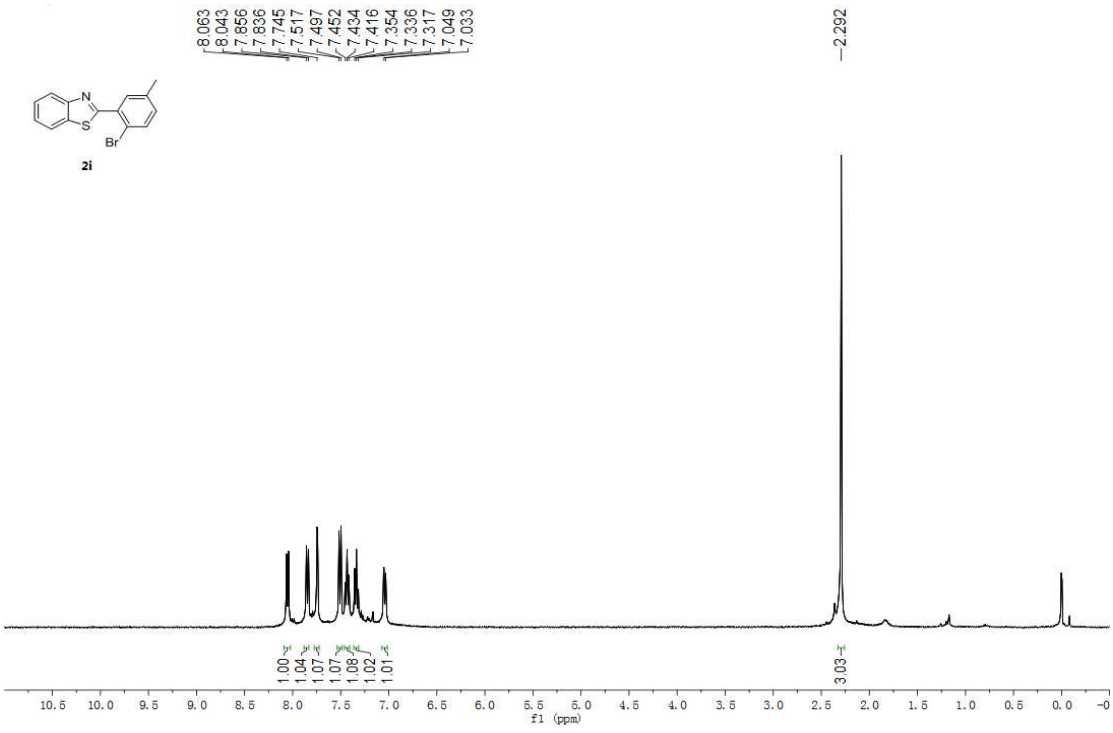
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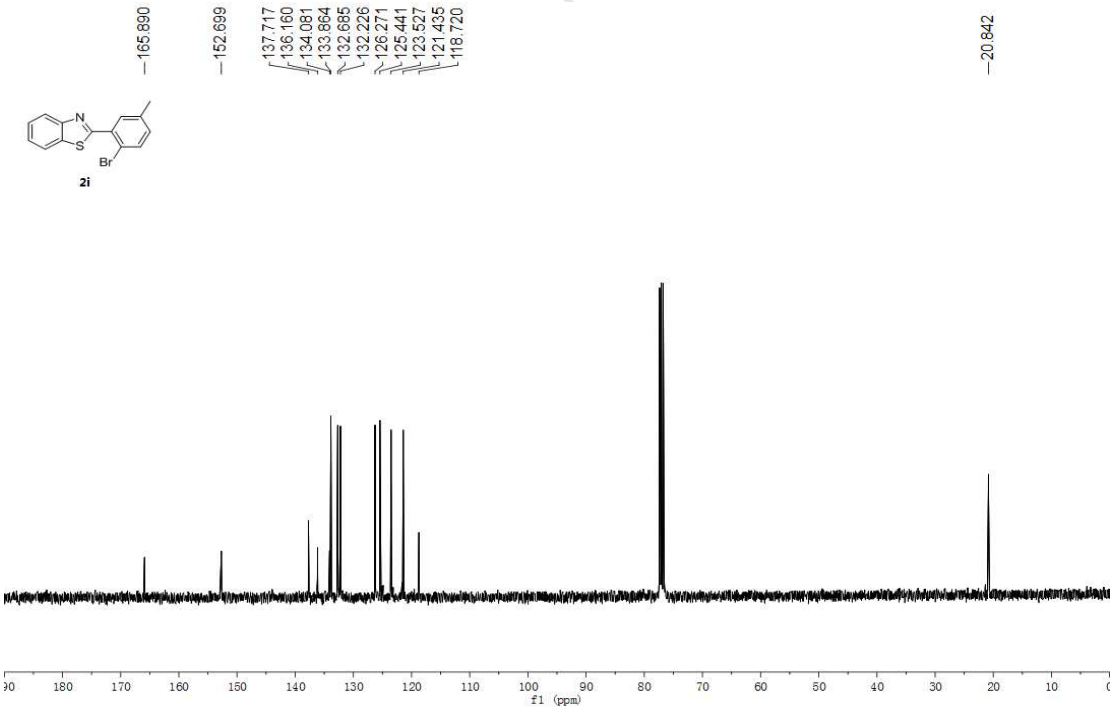
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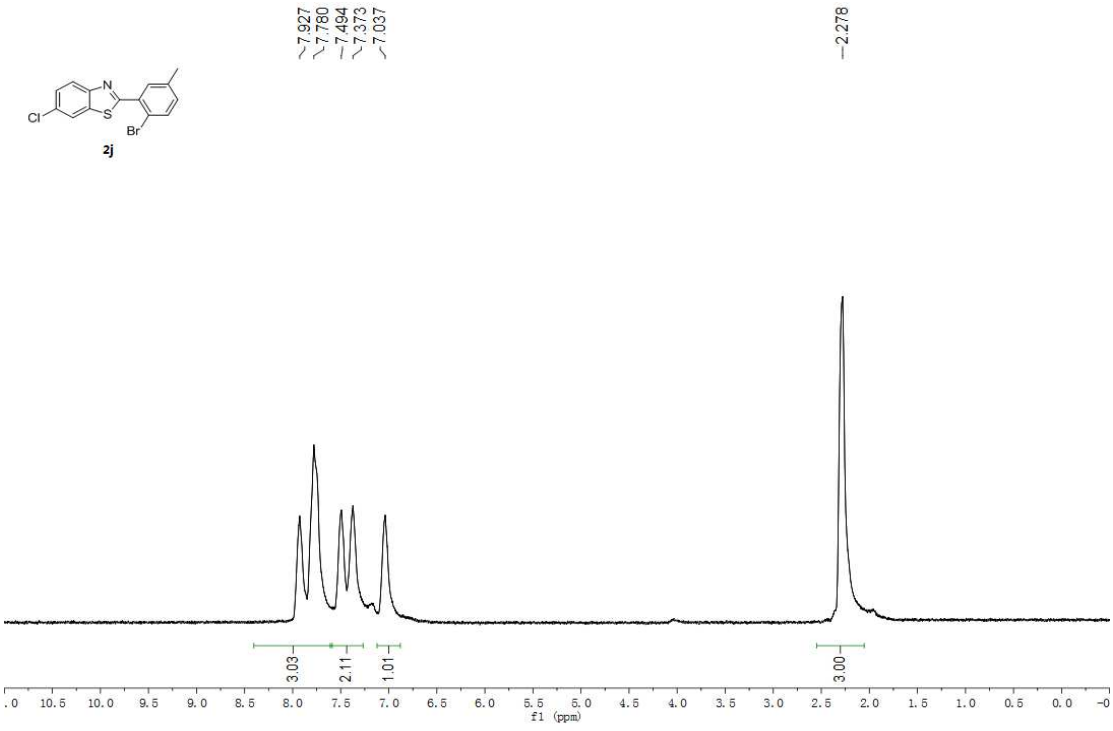
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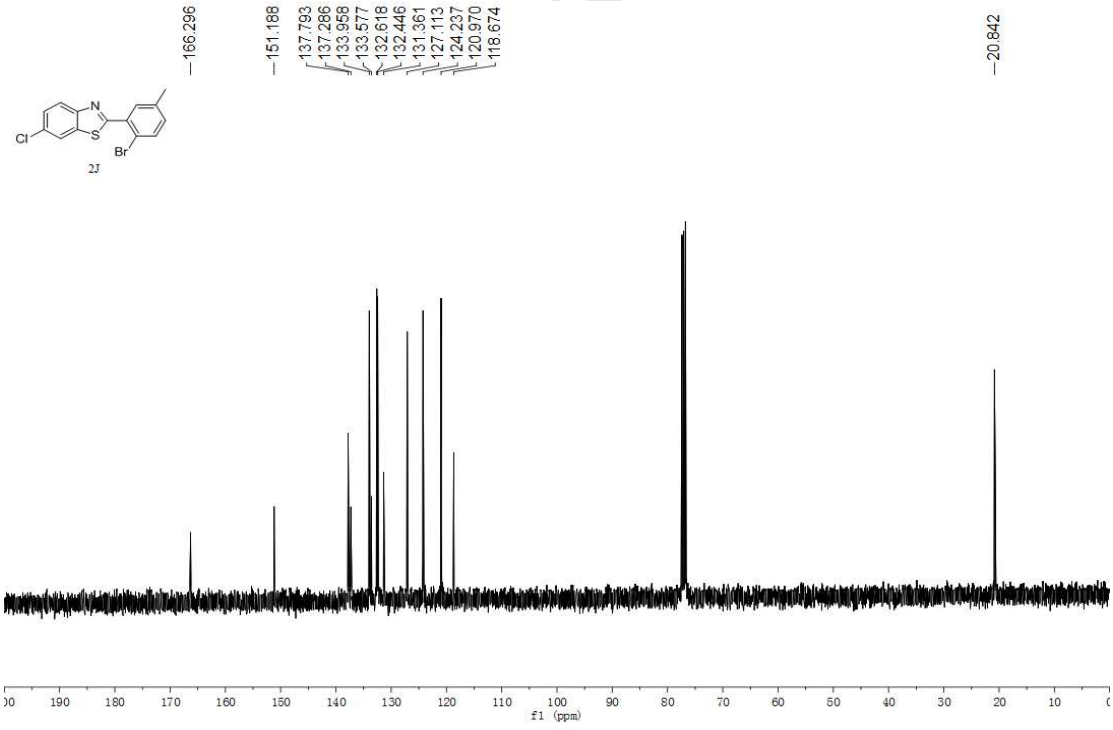
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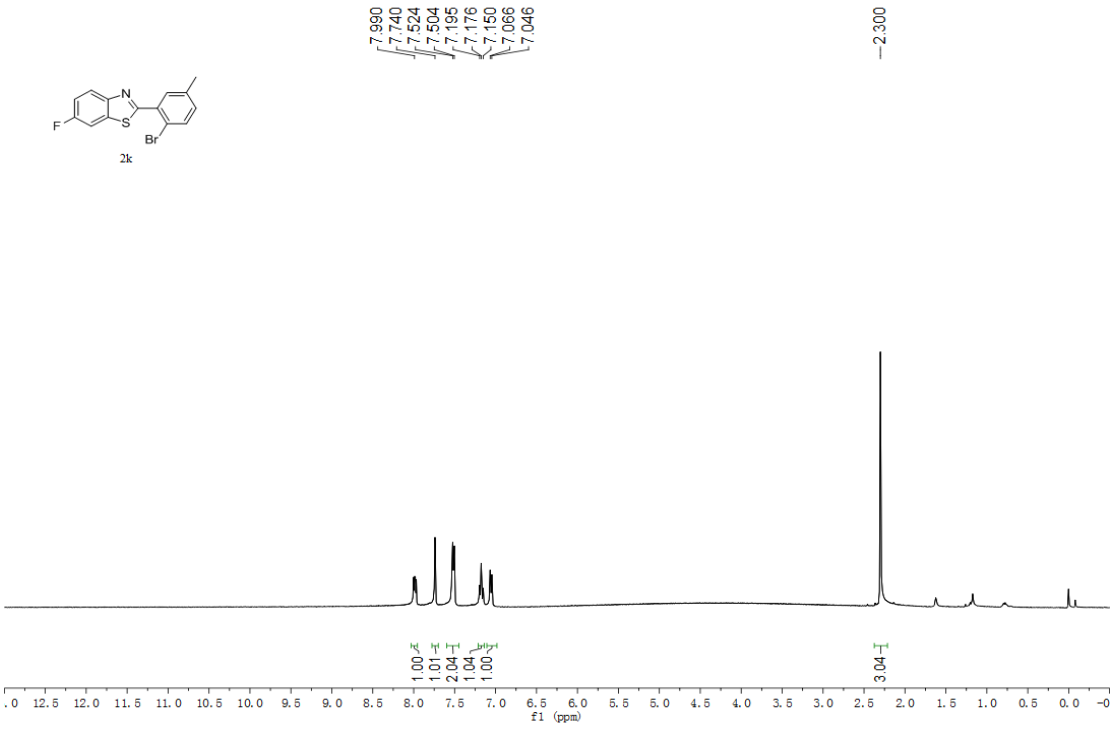
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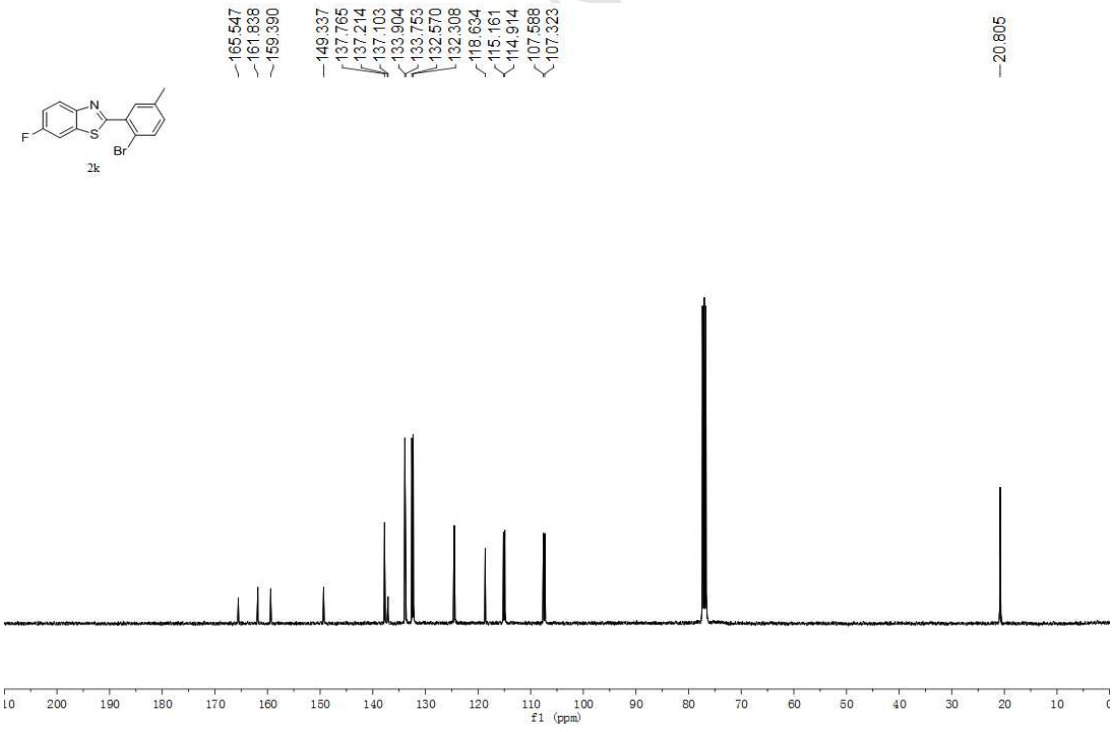
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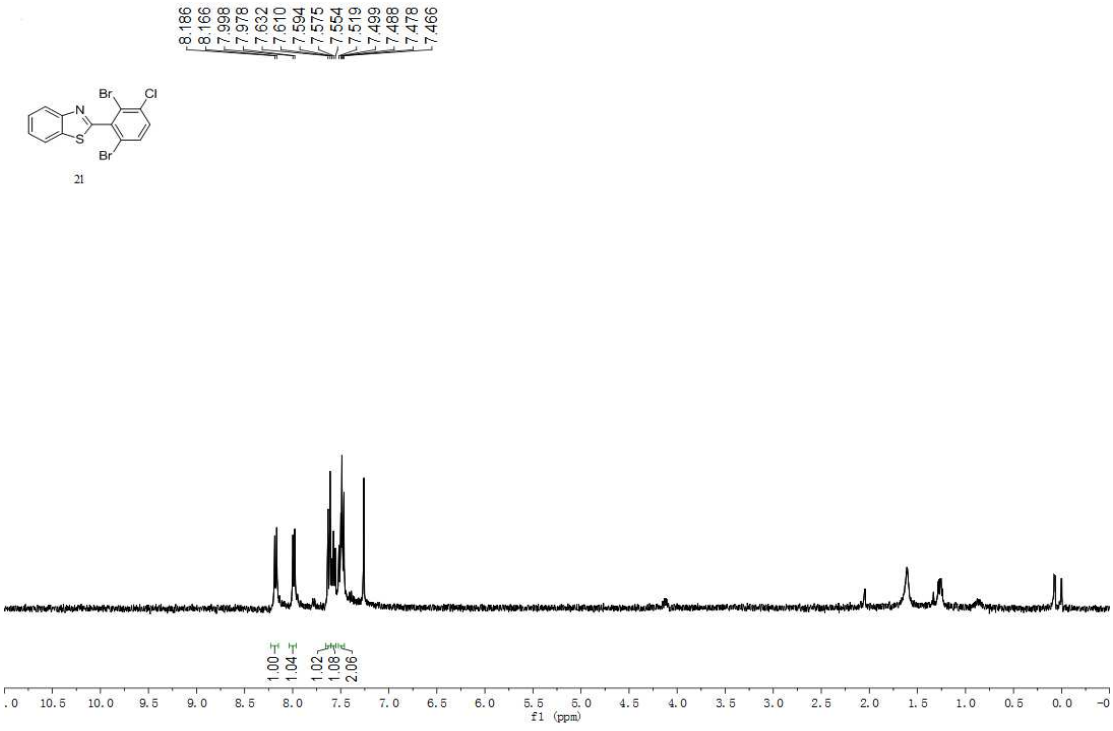
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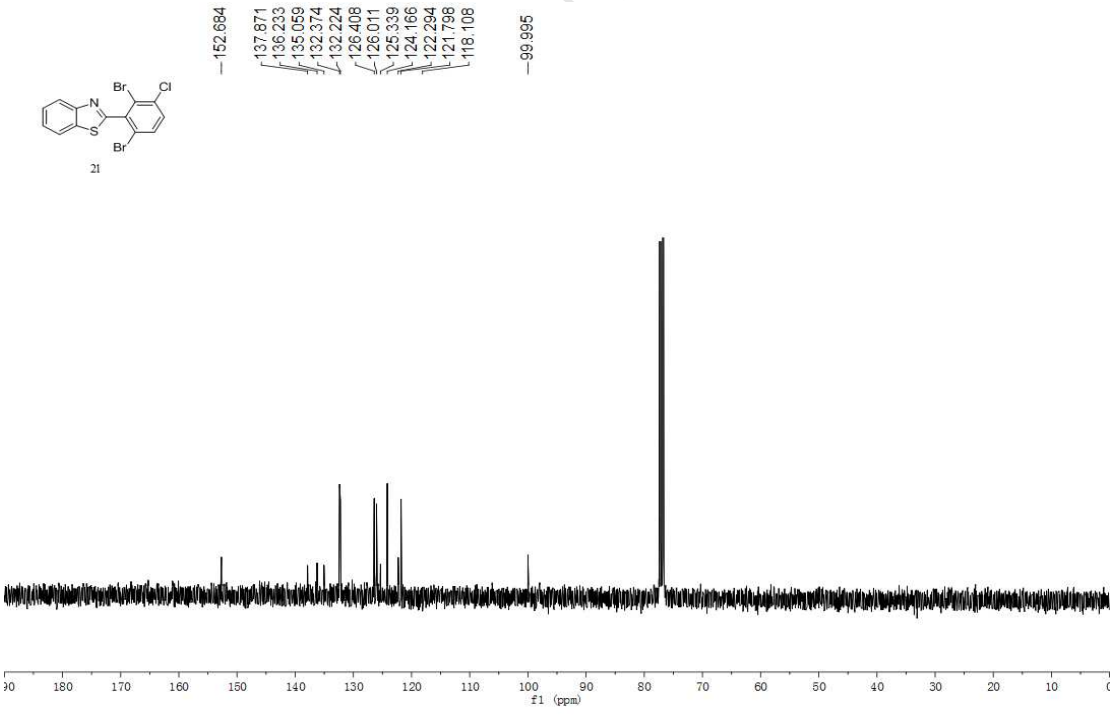
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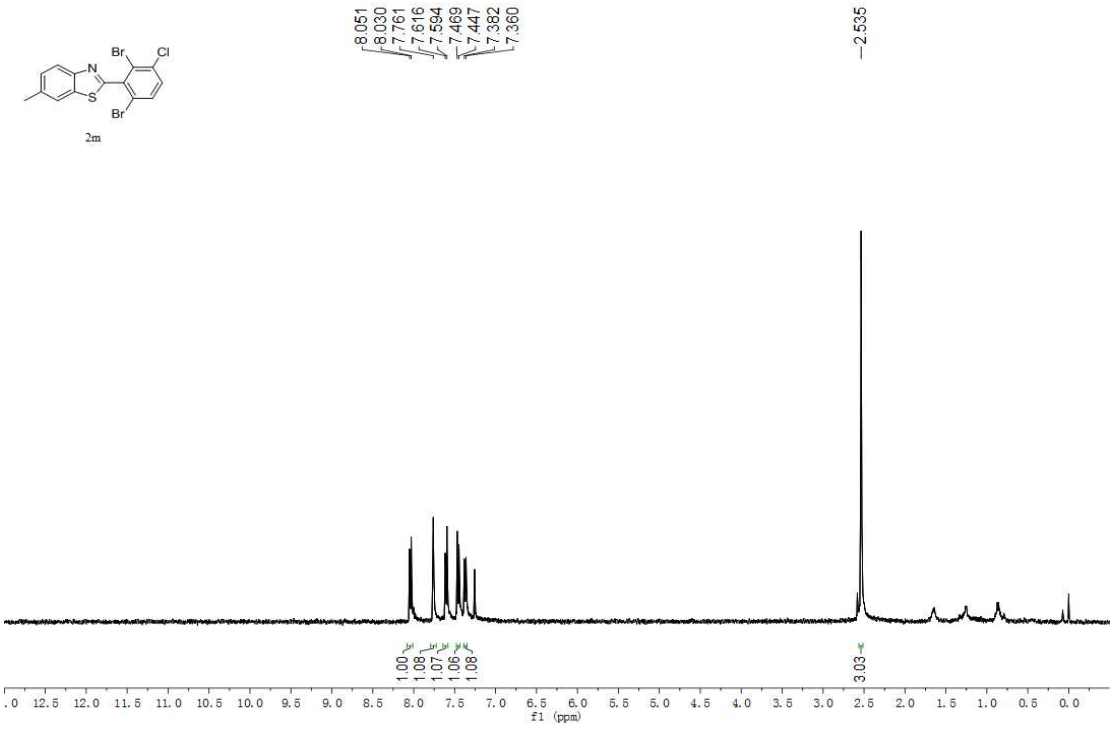
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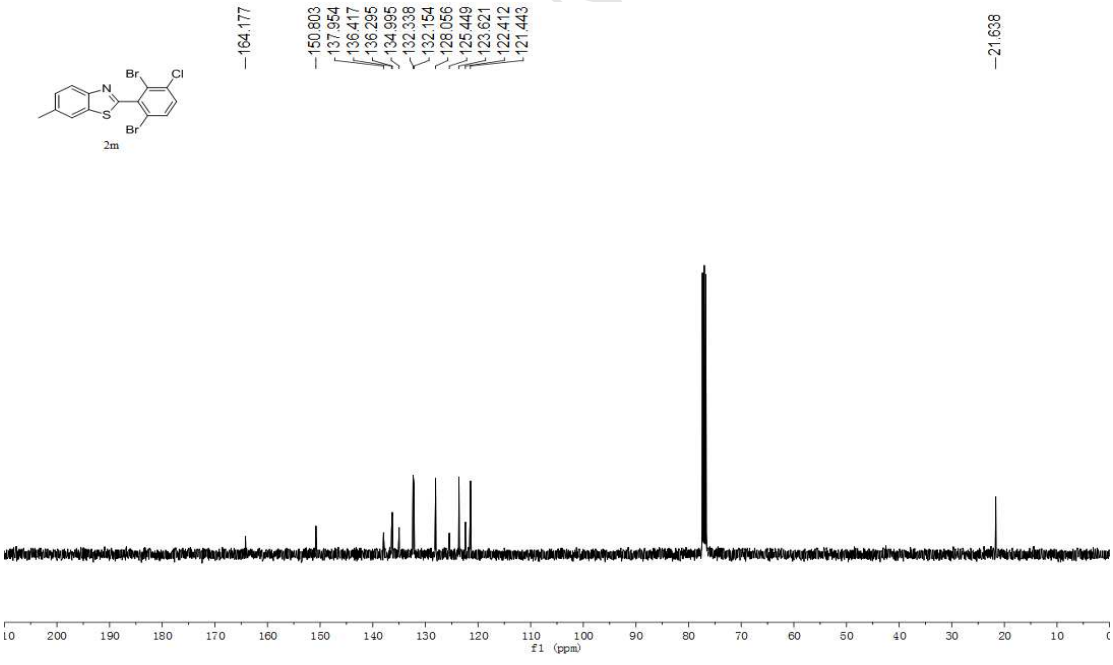
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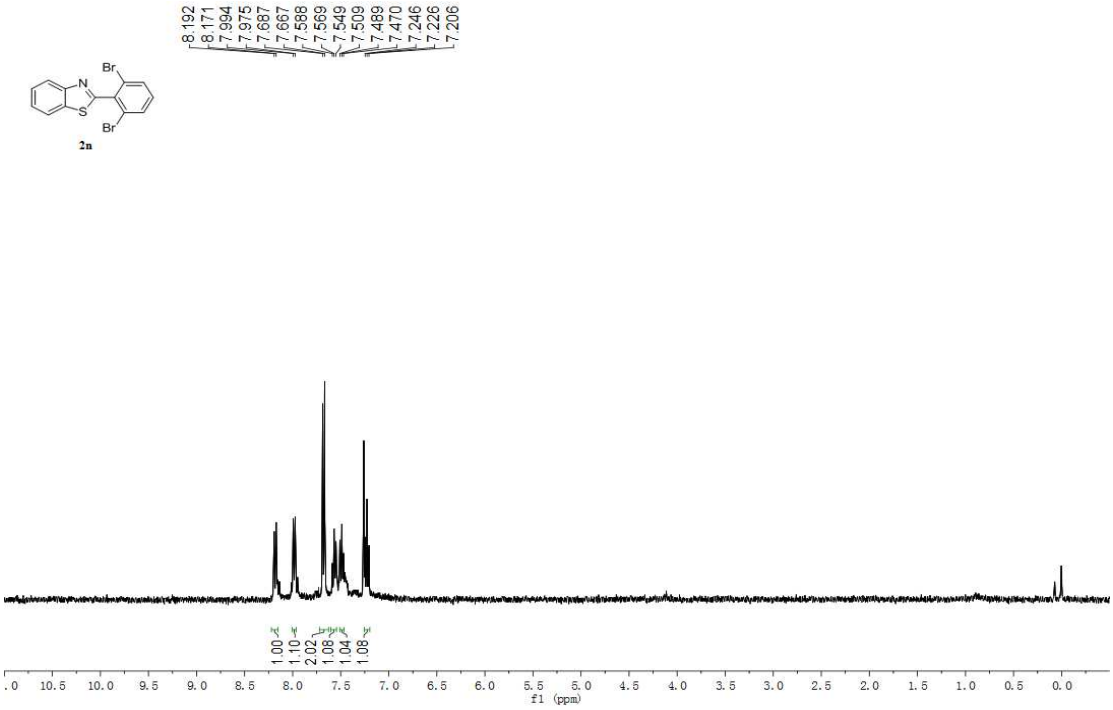
f1 (ppm)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1.04
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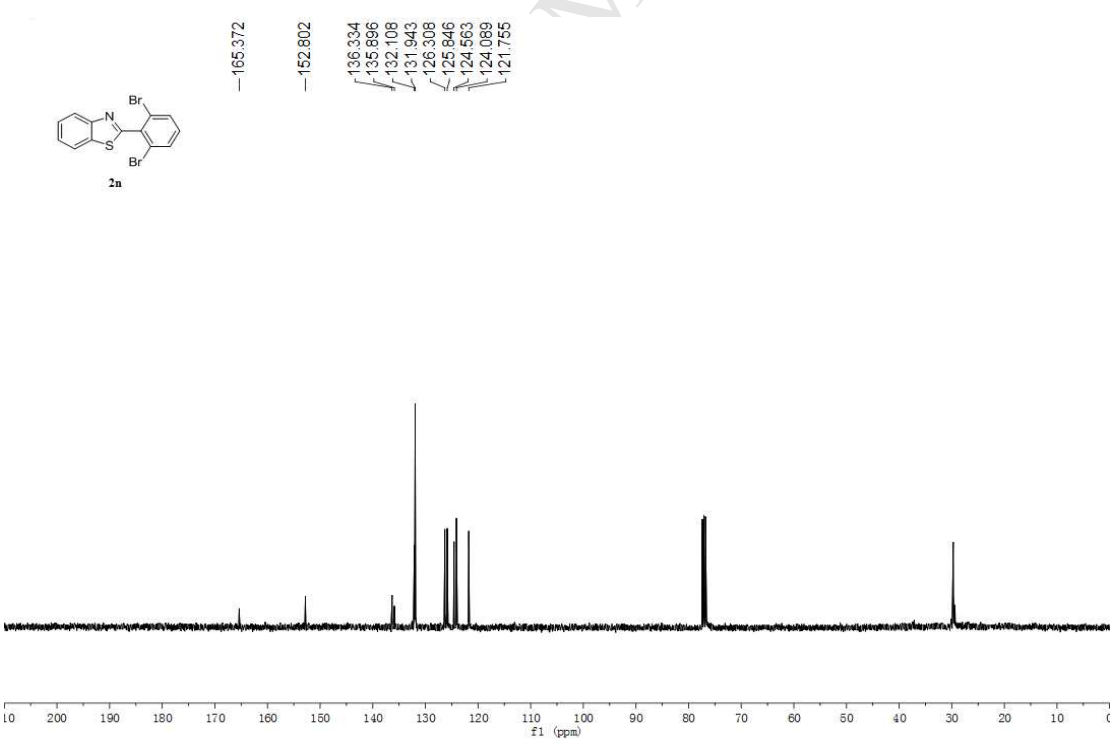
f1 (ppm)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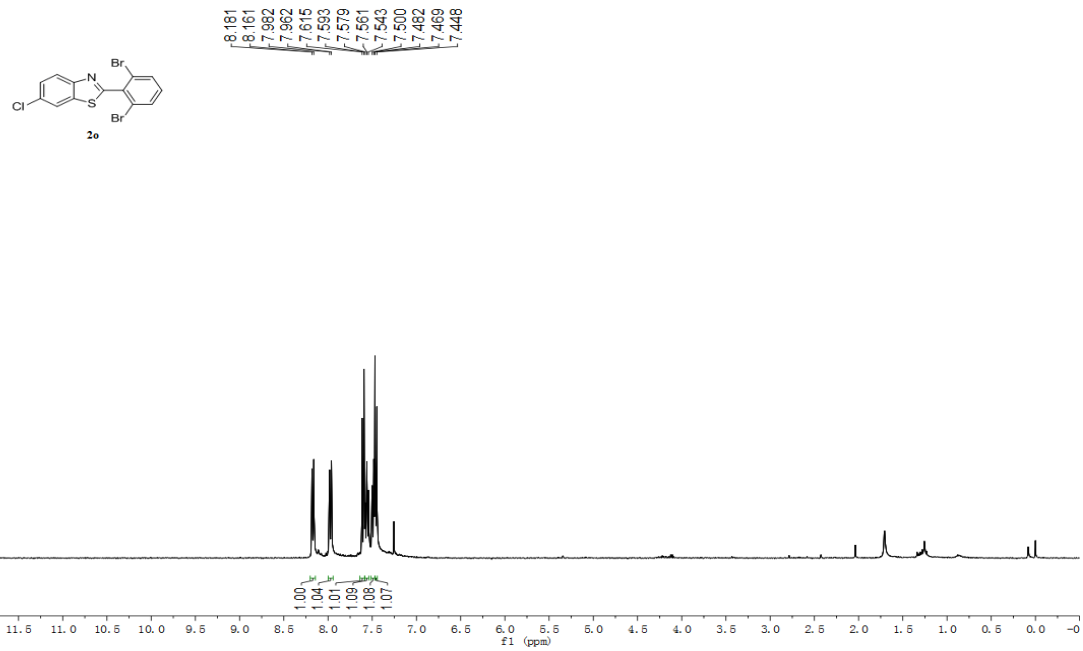
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N
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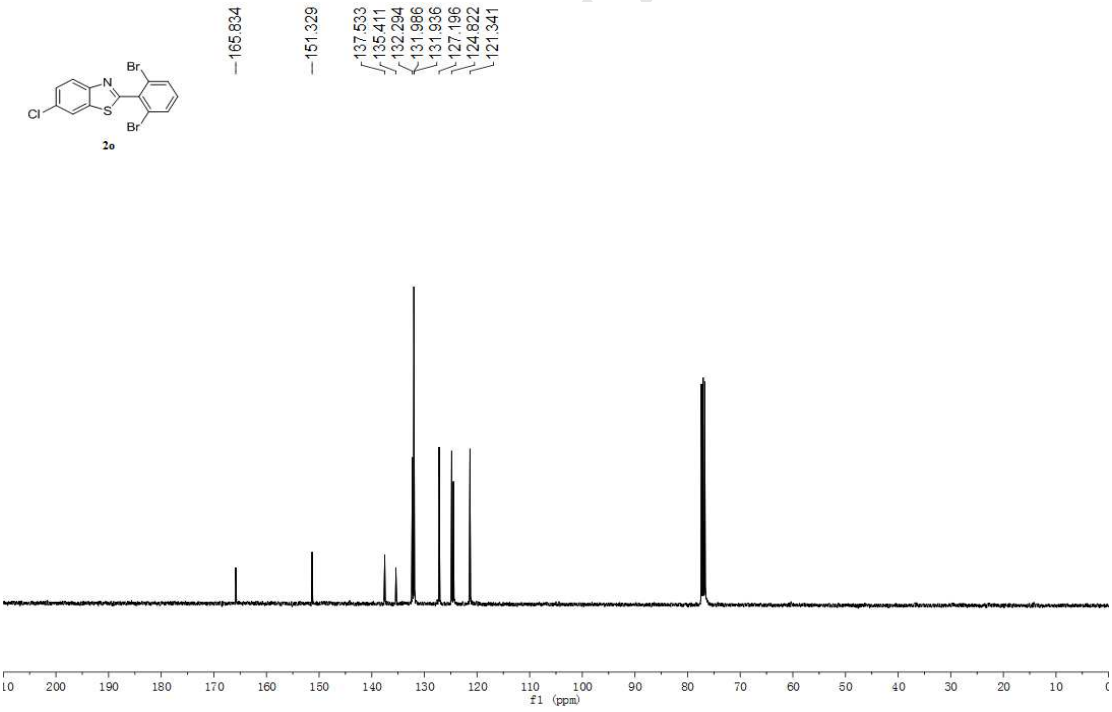
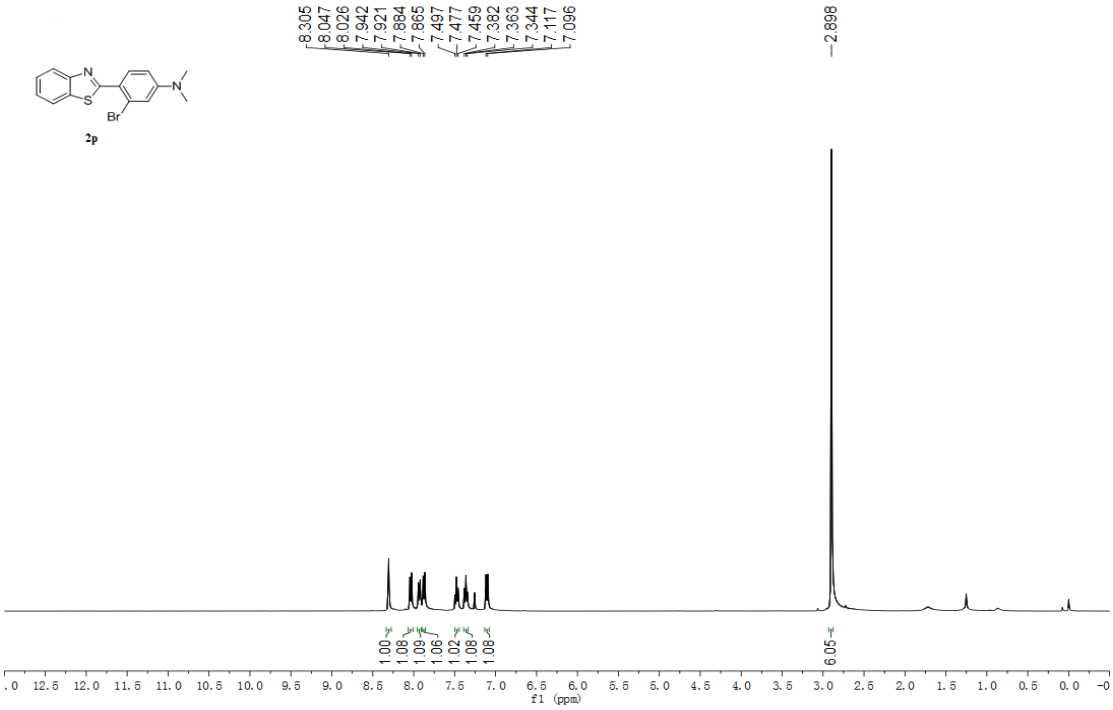
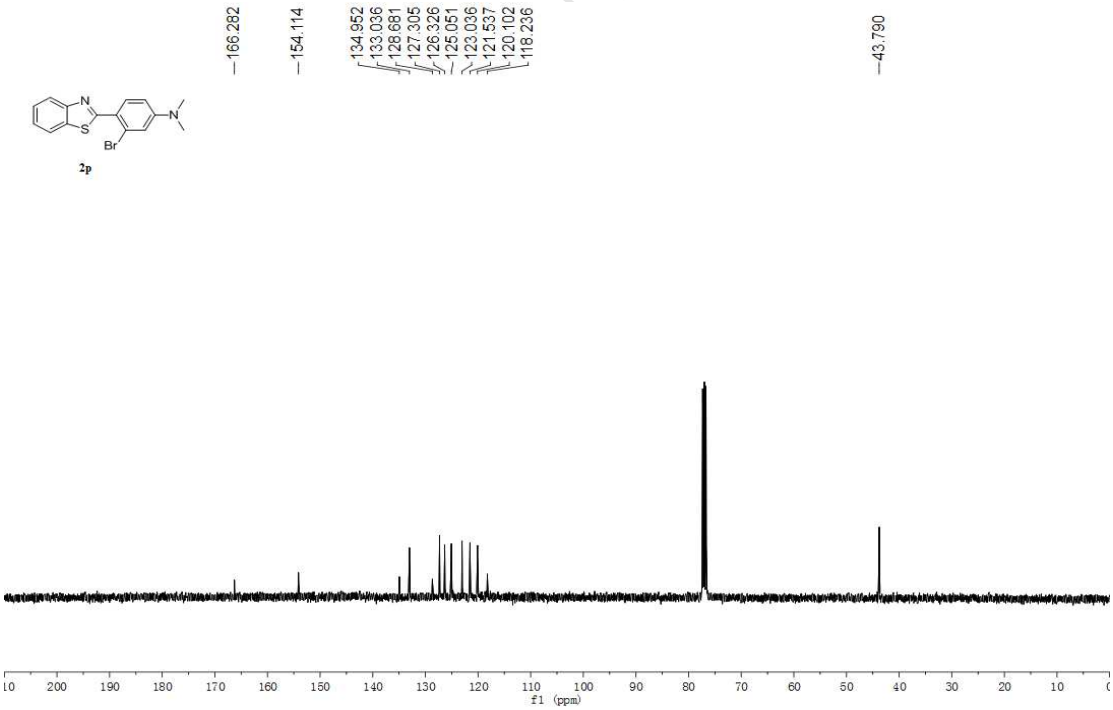
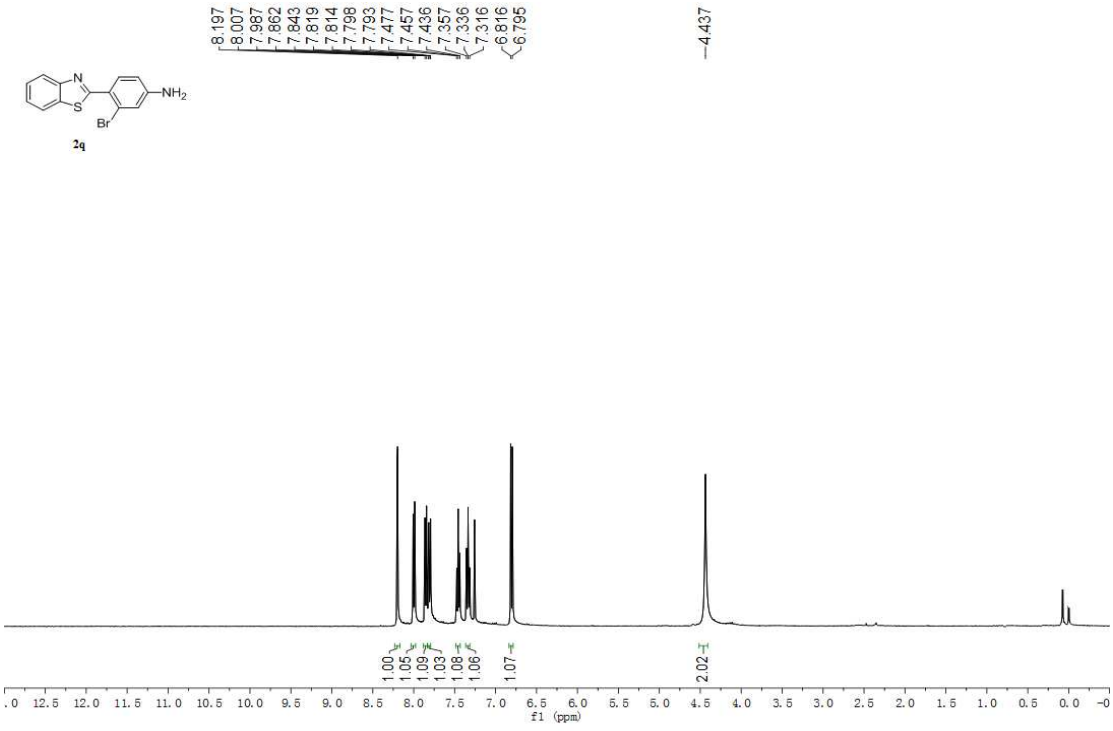
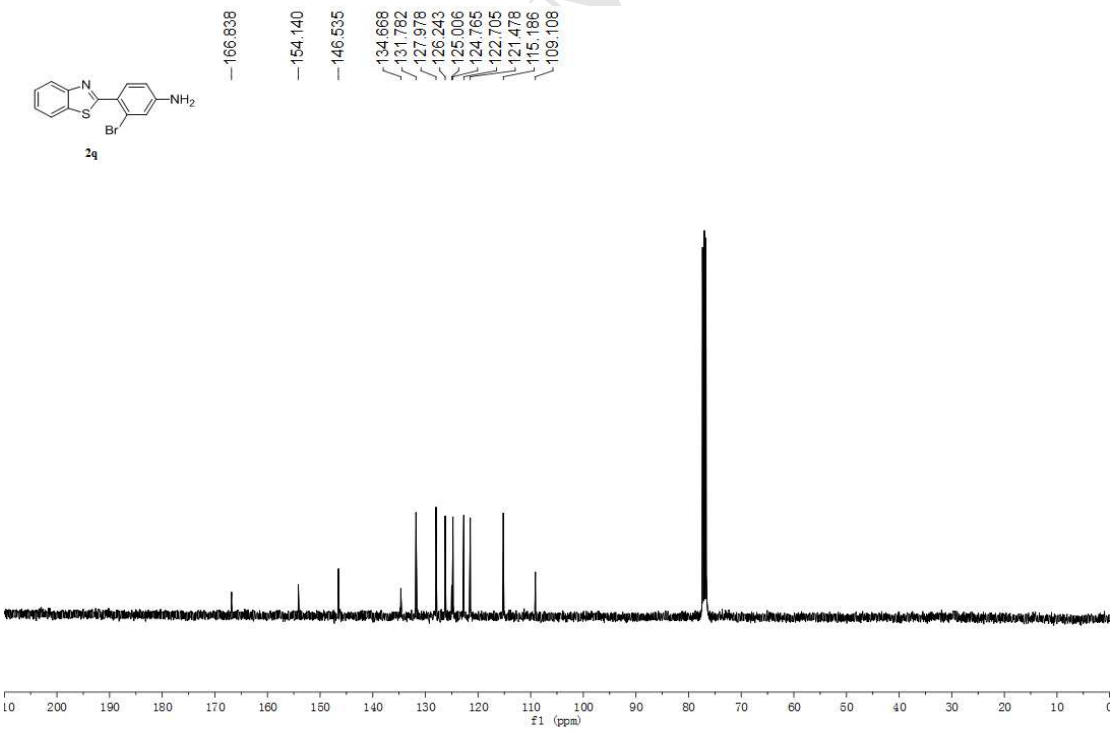
S
Br
2o
1.00
1.04
1.01
1.09
1.08
1.07
f1 (ppm)

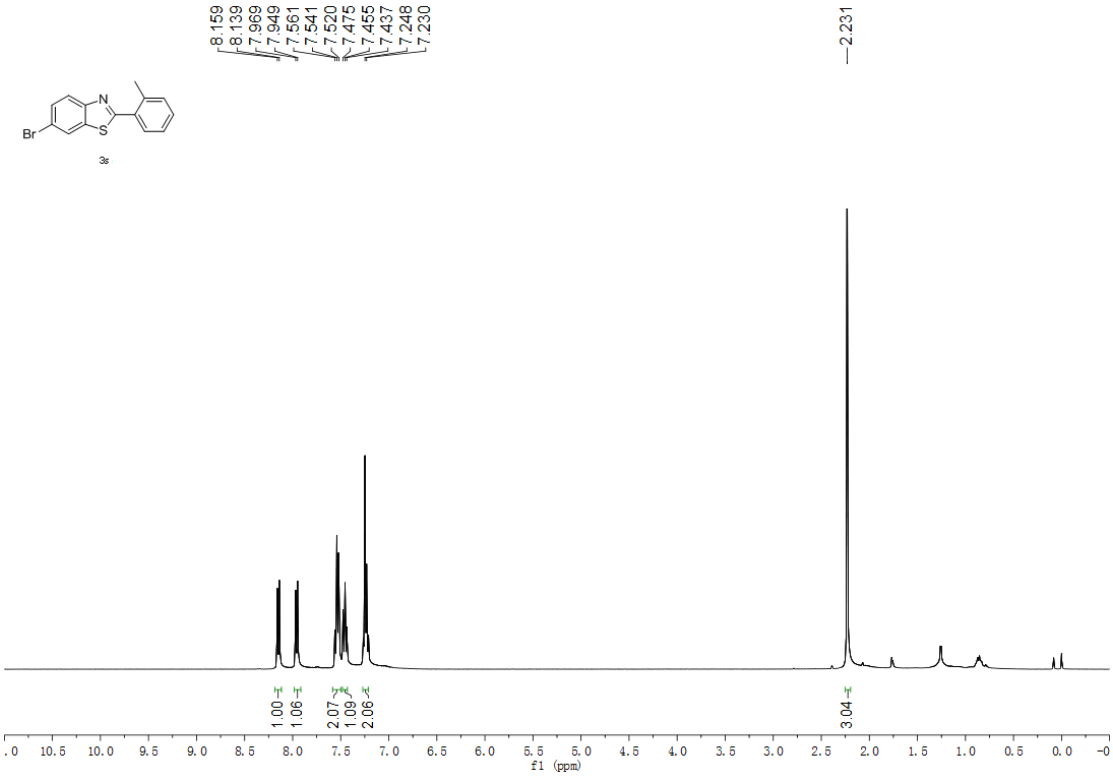

165.834
151.329
137.533
135.411
132.294
131.986
131.936
127.196
124.822
121.341
Br
N
Cl
S
Br
2o
f1 (ppm)

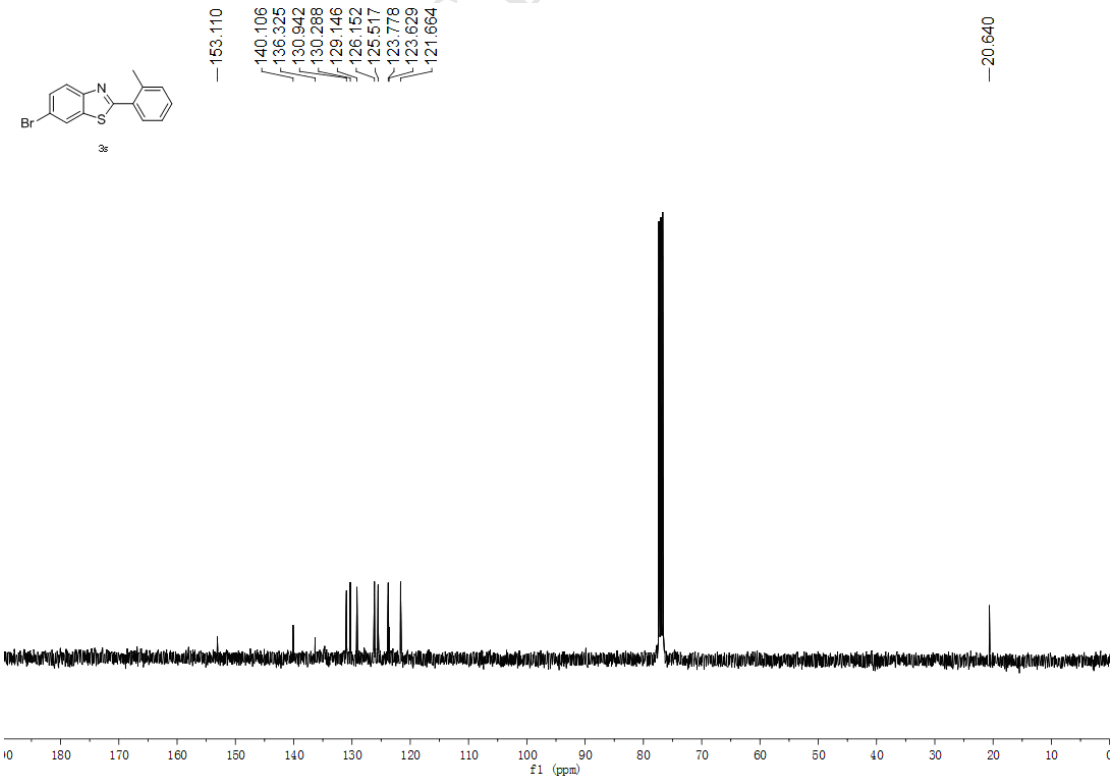

8.305
8.047
8.026
7.942
7.921
7.884
7.865
7.497
7.477
7.459
7.382
7.363
7.344
7.117
7.096
2.898
Br
2p
1.00
1.08
1.09
1.06
1.02
1.08
1.08
6.05
f1 (ppm)

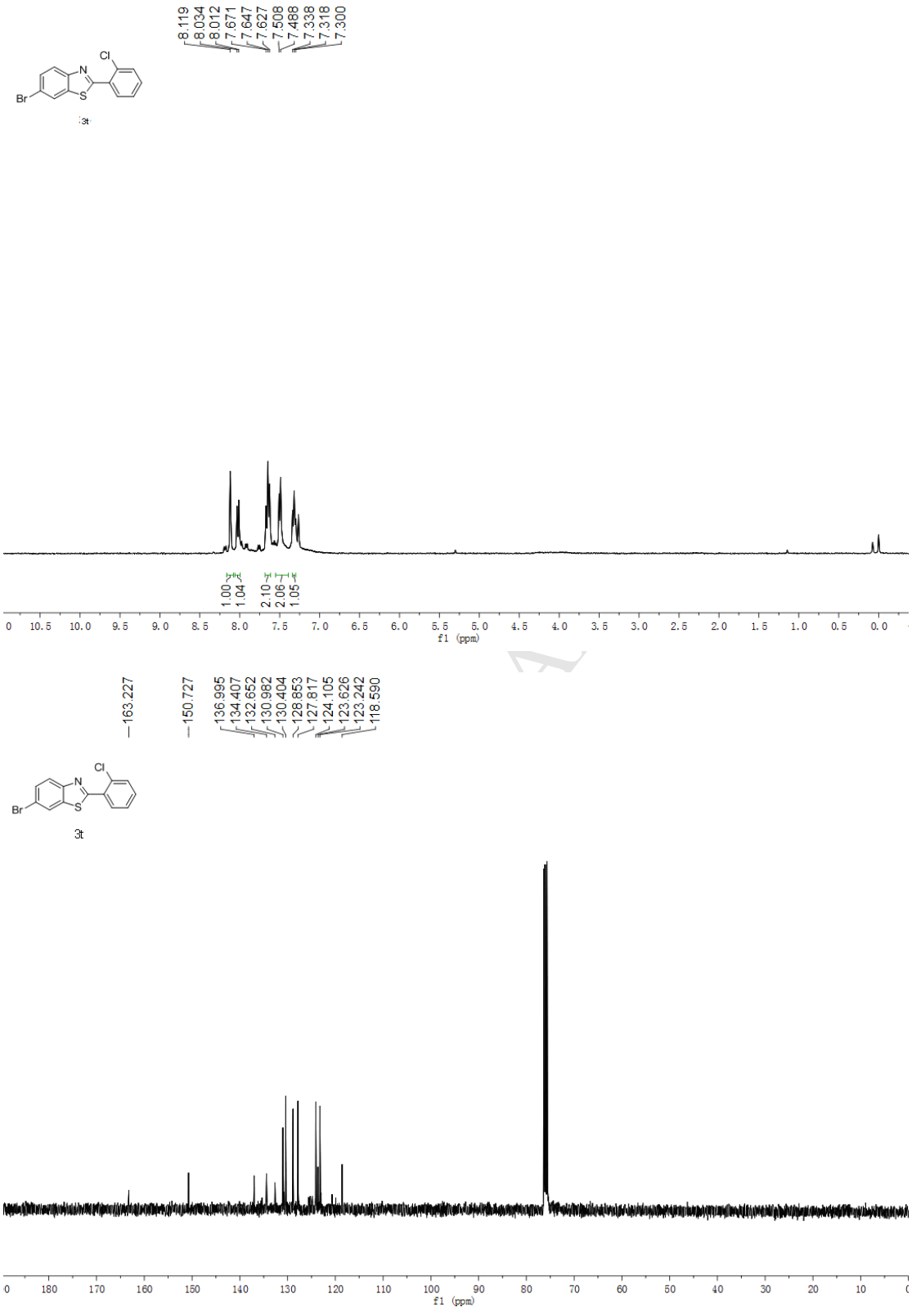

166.282
154.114
134.952
133.036
128.681
127.305
126.326
125.051
123.036
121.537
120.102
118.236
43.790
Br
2p
f1 (ppm)

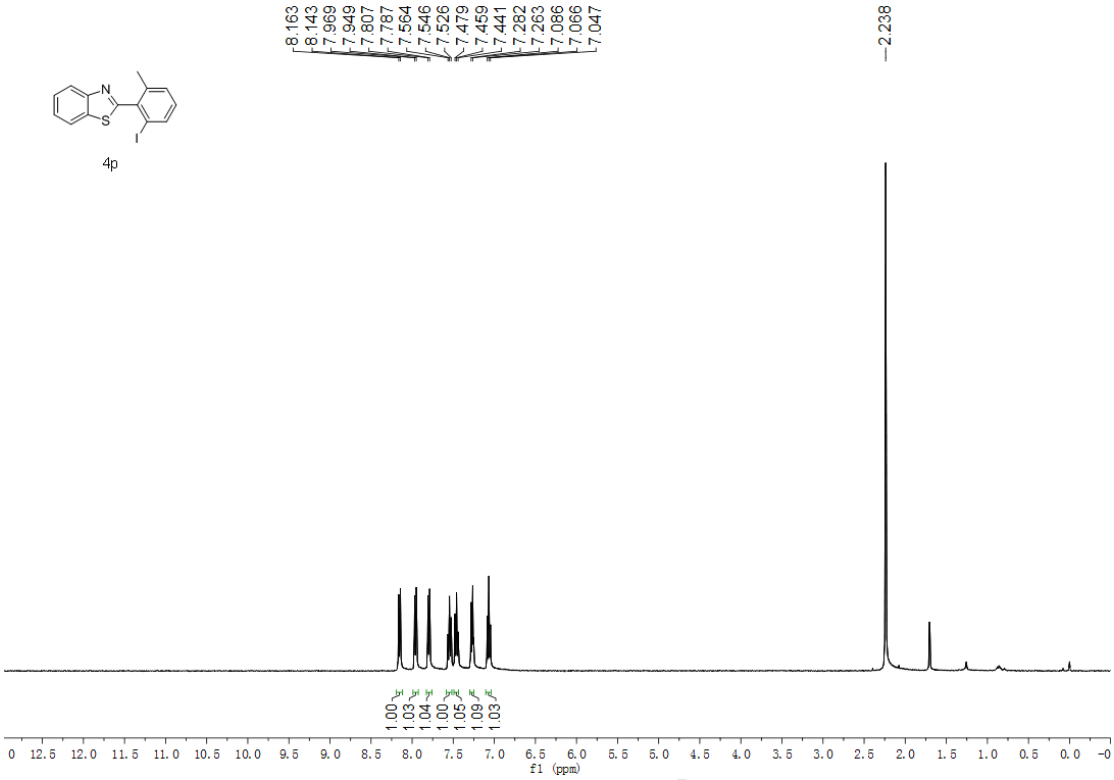

8.197
8.007
7.987
7.862
7.843
7.819
7.814
7.798
7.793
7.477
7.457
7.436
7.357
7.336
7.316
6.816
6.795
4.437
NH2
Br
2q
1.00
1.05
1.09
1.03
1.08
1.06
1.07
2.02
f1 (ppm)

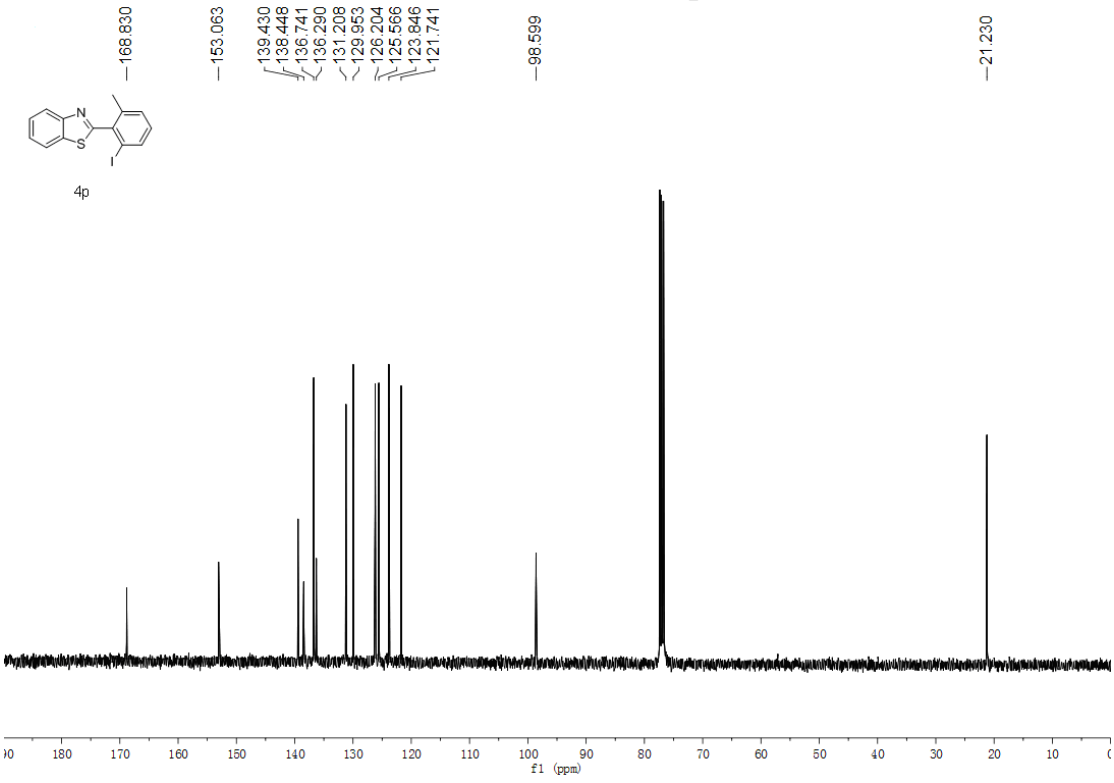

166.838
154.140
146.535
134.668
131.782
127.978
126.243
125.006
124.765
122.705
121.478
115.186
109.108
NH2
Br
2q
f1 (ppm)

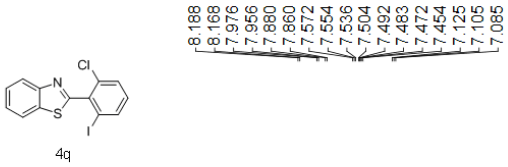

8.159
8.139
7.969
7.949
7.561
7.541
7.520
7.475
7.455
7.437
7.248
7.230
2.231
Br
3s
1.00
1.06
2.07
1.09
2.06
3.04
f1 (ppm)


153.110
140.106
136.325
130.942
130.288
129.146
126.152
125.517
123.778
123.629
121.664
20.640
Br
3s
f1 (ppm)

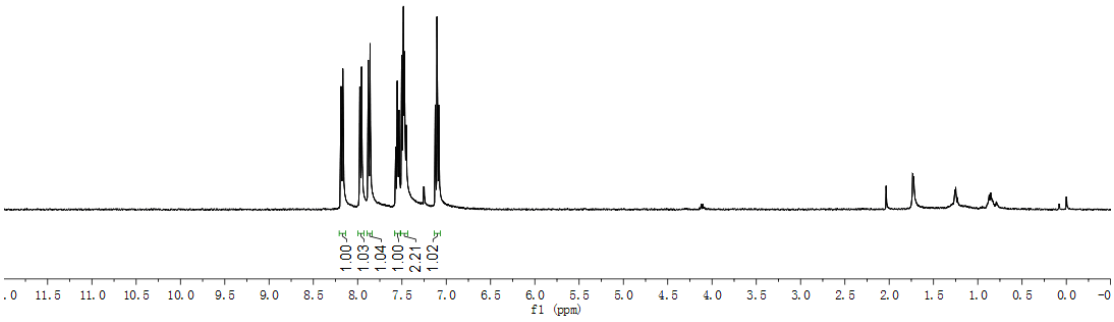

8.119
8.034
8.012
7.671
7.647
7.627
7.508
7.488
7.338
7.318
7.300
Cl
N
S
Br
3t
1.00
1.04
2.10
2.06
1.05
f1 (ppm)
163.227
150.727
136.995
134.407
132.652
130.982
130.404
128.853
127.817
124.105
123.626
123.242
118.590
Cl
N
S
Br
3t
f1 (ppm)

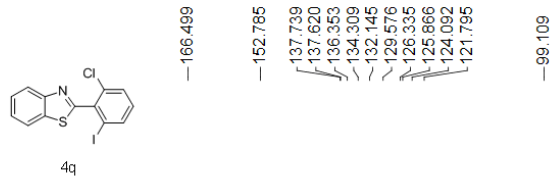

8.163
8.143
7.969
7.949
7.807
7.787
7.564
7.546
7.526
7.479
7.459
7.441
7.282
7.263
7.086
7.066
7.047
2.238
4p
1.00
1.03
1.04
1.00
1.05
1.09
1.03
f1 (ppm)


168.830
153.063
139.430
138.448
136.741
136.290
131.208
129.953
126.204
125.566
123.846
121.741
98.599
21.230
4p
f1 (ppm)

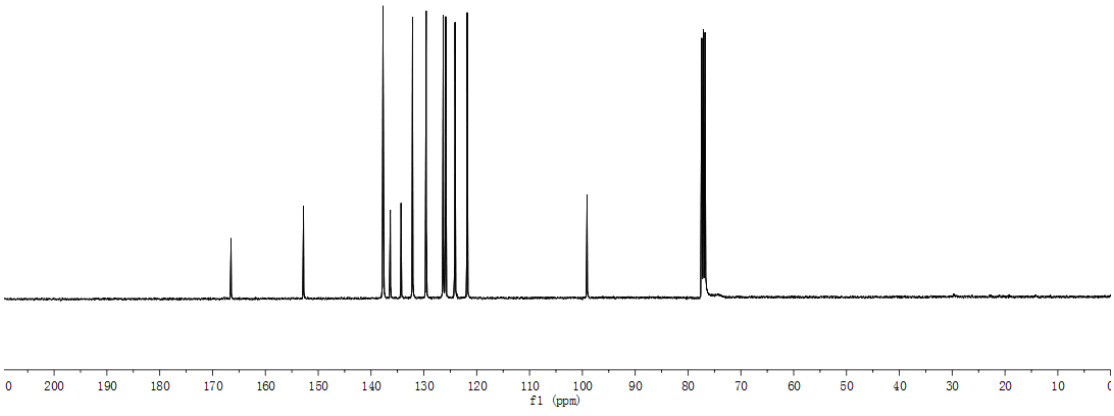

8.188
8.168
7.976
7.956
7.880
7.860
7.572
7.554
7.536
7.504
7.492
7.483
7.472
7.454
7.125
7.105
7.085
Cl
N
S
I

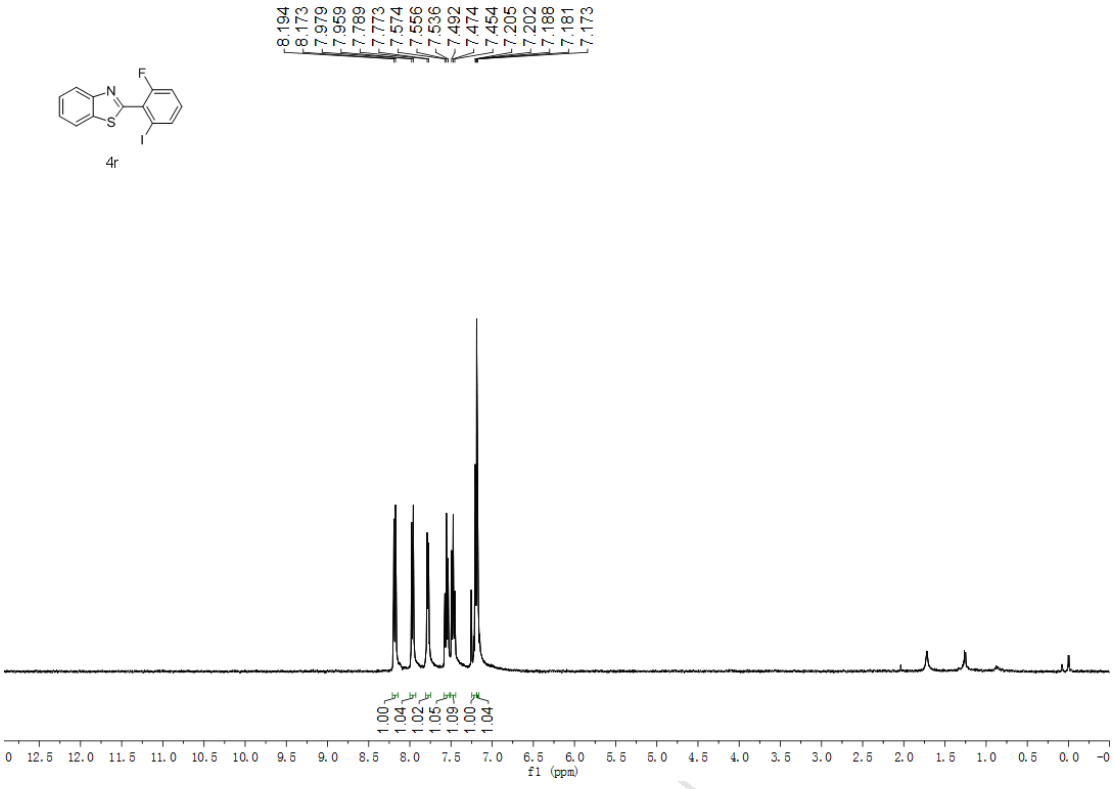
4q

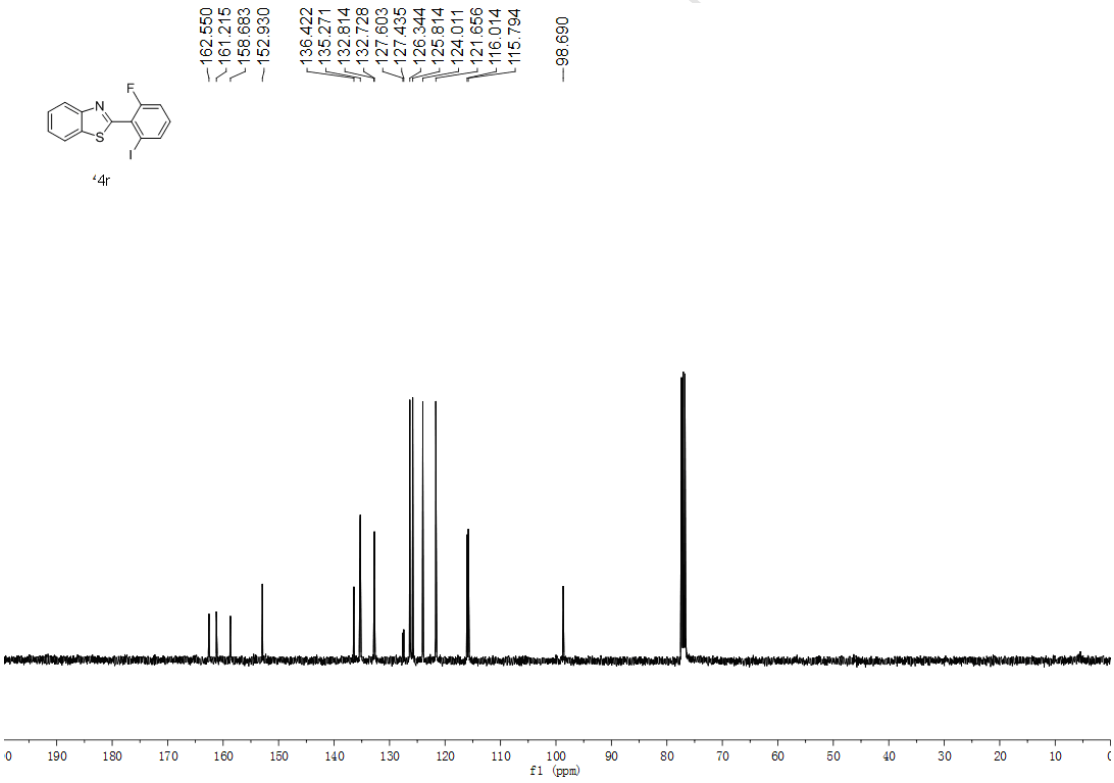

1.00
1.03
1.04
1.00
2.21
1.02
f1 (ppm)

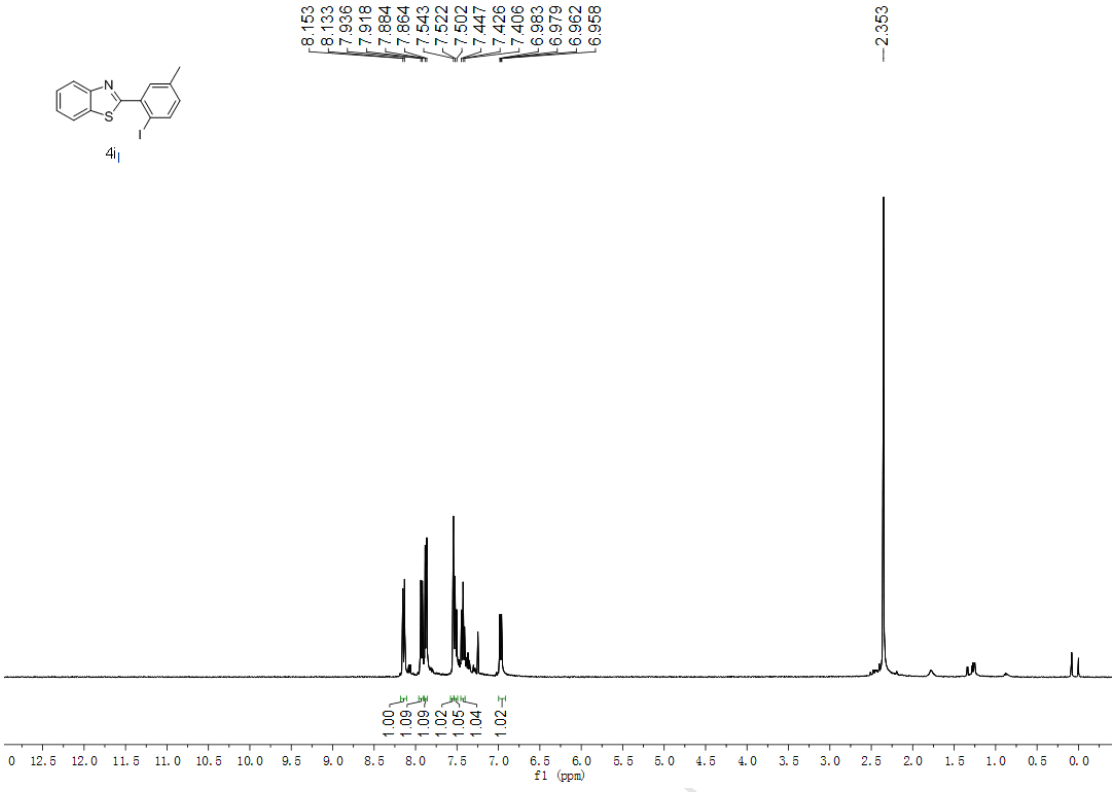

166.499
152.785
137.739
137.620
136.353
134.309
132.145
129.576
126.335
125.866
124.092
121.795
99.109
Cl
N
S
I

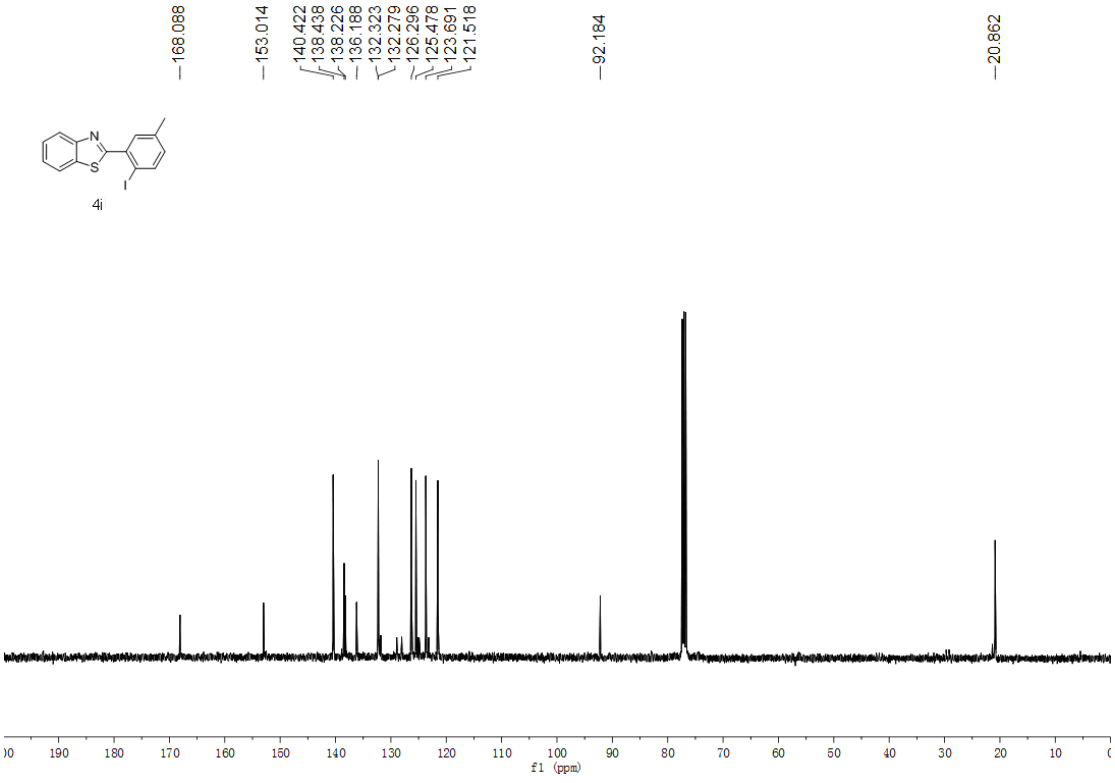
4q


f1 (ppm)


8.194
8.173
7.979
7.959
7.789
7.773
7.574
7.556
7.536
7.492
7.474
7.454
7.205
7.202
7.188
7.181
7.173
F
N
S
I
4r
1.00
1.04
1.02
1.05
1.09
1.00
1.04
f1 (ppm)


162.550
161.215
158.683
152.930
136.422
135.271
132.814
132.728
127.603
127.435
126.344
125.814
124.011
121.656
116.014
115.794
98.690
F
N
S
I
4r
f1 (ppm)


8.153
8.133
7.936
7.918
7.884
7.864
7.543
7.522
7.502
7.447
7.426
7.406
6.983
6.979
6.962
6.958
2.353
4i
1.00
1.09
1.09
1.02
1.05
1.04
1.02
f1 (ppm)


168.088
153.014
140.422
138.438
138.226
136.188
132.323
132.279
126.296
125.478
123.691
121.518
92.184
20.862
4i
f1 (ppm)